Development of Amino Acid-Derived Ligands for Enantioselective Synthesis of Amines and Alcohols

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DEVELOPMENT OF AMINO ACID-DERIVED LIGANDS FOR ENANTIOSELECTIVE SYNTHESIS OF AMINES AND ALCOHOLS

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Abstract

■ Chapter One

Development of Simple Organic Molecules as Catalysts for Enantioselective Allyl Additions to N-Phosphinoylaldimines and Isatins

A new catalytic protocol for the enantioselective addition of organoborates to imines and carbonyls is described. This novel method, which does not require transition metals utilizes a modular and easily accessed aminophenol to dictate the stereochemistry of the products. Allyl-additions to *N*-phosphinoylaldimines and isatins, as well as allenyl-additions to isatins are studied and literature relevant to these transformations is discussed. Additionally, two separate methods for obtaining "crotyl-type" addition products to aldimines; one requiring α-chiral allylboronates and the other requiring a zinc-alkoxide, are discussed. Studies to elucidate the mechanism of this catalytic protocol are also contained in this chapter.

■ Chapter Two

Enantioselective Additions to Fluorinated Ketones: A Platform for Studying the Interaction Between Organofluorine and a Small Molecule

Utilizing the new protocol discussed in Chapter One, allyl- and allenyl-groups are added enantioselectively to ketones containing a fluorinated substituent. Myriad tertiary alcohols are synthesized, demonstrating the value of this method. This study also allows for examining how organofluorine containing compounds bind to other organic molecules, which is a current topic of intense interest in the field of medicinal chemistry. Mechanistic studies support the idea that, in many cases, the fluorine of the substrate is electrostatically attracted to the ammonium-ion in the catalyst.

■ Chapter Three

Enantioselective Additions of Organoboronates to Ketones and Alphaketoesters Promoted by an Aminophenol Containing Catalyst

Modification of the aminophenol disclosed in Chapter One allows for increased enantioselectivity for the allyl-addition to both simple ketones (such as acetophenone) and alphaketoesters. For simple ketones, a critical component of the optimal catalyst is replacing the *tert*-butyl group *ortho* to the phenol with the sterically large triphenylsilyl group. For alphaketoesters, this *tert*-butyl group was replaced with the sterically smaller metyl group. Rationale for why these contradictory changes in the catalyst structure lead to higher enantioselectivity for reactions with these two classes of ketones is discussed.

■ Chapter Four

Ag-Catalyzed Enantioselective Vinylogous Mannich Reactions of γ-Substituted Siloxyfurans with Aldimines

A previously disclosed Ag-catalyzed enantioselective vinylogous Mannich reaction (EVM) with α-, β-, and unsubstituted siloxyfurans is extended to include γ-substituted siloxyfurans. This method, which generates a tertiary stereogenic center concurrent with an adjacent to a quaternary stereogenic center, requires a rarely used 2-thiomethylaniline *N*-protecting group for the aldimines.

Acknowledgements

I'll be forever grateful for the education I received while at Boston College. First and foremost I need to thank Professor Amir Hoveyda for all his influence in making me a better scientist as well as a better leader. Observing the way he carries himself on a day-to-day basis taught me a lot, but there was also a substantial amount of lessons he went out of his way to teach me.

Without the input of Tanya Pilyugina, I would not have made it this far. I was in an unfortunate situation where I had not really been mentored entering the second half of my third year, and she spent a lot of her valuable time teaching me skills, such as how to design and experiment and how to determine what order to do experiments in, that I just did not have at that time. It is no coincidence that my productivity went up substantially after working with her on the project detailed in Chapter 1. It was a great privilege to work on such an interesting project; especially considering it would not have existed without her. I'm also quite lucky to count her as a friend.

Sebastian Torker has been a tremendous co-worker and friend to me in the four years we have overlapped. Although he left the aminophenol project to work on ruthenium metathesis, he had a large amount of experimental and intellectual contributions. I've never met anyone else who can think and talk about one focused issue as long as he can. Chapters one and two would not be the same without him.

Erika Vieira developed not only the allenyl-addition to isatins, but she also was critical to discovering protecting groups for isatins that can be easily removed following addition of an allyl- or allenyl-group. I miss her logical way of looking at any problem, whether it's a mechanistic question, or how to best survive the rigors of graduate school.

Her unparalleled proofreading skills would have undoubtedly made this document better, but I was not about to make her read all this after she graduated.

I greatly appreciate all others I've directly collaborated with. Hiroshi Miyamoto, for taking the zinc-catalyzed crotyl-addition in Chapter One from an interesting observation to a synthetically useful transformation. Dan Robbins, for all the incredible work on the ketone allyl-additions in Chapter Three. KyungA Lee, for helping with the work described in Chapter Two and thanks in advance for finishing off the work started in Chapter Two and Three. Fredrik Haeffner, for all the computational help as well as numerous stimulating arguments over the years. Hiroki Mandai for helping whenever you could my early years.

I acknowledge Nick Mszar, Farid van der Mei, KyungA Lee, and Hwanjong Jang for proofreading various Chapters of this document and making it far better than it was originally. The same is true for Professors Amir Hoveyda, James Morken, and Jeffry Byers.

I also need to thank Erika, Sebastian and Tanya, in addition to Liz Kiesewetter, Nick Mszar, Tyler Mann, Jenn Dabrowski, Kashif Khan, Dan Robbins, Jamie Garcia, Bobby O'Brien, Deb Lynch, Andrew Levine, Hilan Kaplan, Julie Martell, and Carolyn Heusser for providing moral support/friendship/someone to bounce ideas off of whenever I needed.

Deb Lynch, Tricia May, Jenn Dabrowski, Erika Vieira, Pam Lombardi, Tyler Mann and Kevin McGrath: I noticed and appreciated how much time you spent making sure making sure the lab is running smoothly. I know it sometimes seems like no one does, but trust me, we do.

My family, especially my parents and brother: I'm lucky to have such an indefatigably (like that John?) loving group to fall back on when things get rough.

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Chapter One

Development of Simple Organic Molecules as Catalysts for Enantioselective Allyl Additions to *N*-Phosphinoylaldimines and Isatins

1.1 Introduction

Enantiomerically pure compounds are prevalent throughout biology, from simple amino acids and sugars, to more complex proteins and nucleic acids. It should, therefore, not come as a surprise that the presence of stereogenic centers are an extremely important structural aspect of biologically active molecules. Examination of a large database of biologically tested molecules made in the pharmaceutical industry reveals that as a drug candidate progresses from the discovery phase to a finished drug, the likelihood of it

Table 1.1. Presence of Stereochemistry in Pharmaceuticals Versus their Development Stage (1980–2008)

Percentage of molecules containing at least one stereogenic center (Number of molecules)	46% (1.3 Million)	49% (249)	52% (369)	62% (120)	61% (1089)
Stage of Development	Discovery	Phase I	Phase II	Phase III	Market

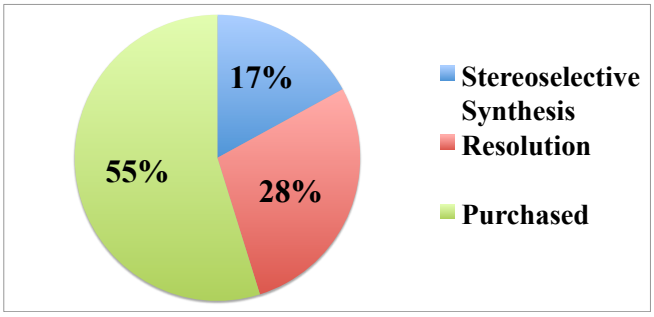
containing a stereogenic center increases from a 46% chance to a 61% chance (Table 1.1).[1] While the increase between each stage is generally not statistically significant, (except between Phase II and Phase III) the overall change from 46% to 61% represents a

(1) Lovering, F.; Bikker, J.; Humblet, C. *J. Med. Chem.* **2009**, *52*, 6752–6756.

significant 32% increase.[2] Importantly this is not simply a matter of more complex compounds are more drug-like. The same study showed that another measure of molecular complexity, average molecular weight, decreased from 449 amu to 360 amu as a candidate moved from discovery to market.[1] The fact that a drug on the market is more likely to be chiral than a molecule made in discovery raises two major questions: 1) Why don't medicinal chemists start with a larger percentage of chiral compounds in discovery considering these compounds are more likely to resemble the finished product? and 2) What is the reason that stereogenic centers are important in pharmaceuticals?

Regarding the first question, the likely answer is that it is still non-trivial to stereoselectively synthesize a desired compound in a reliable, simple, and cost-effective manner.[1, 3] Supporting this statement are two separate analyses of the way a stereogenic center is incorporated into enantiopure molecules in the medicinal programs of GlaxoSmithKline, AstraZeneca, and Pfizer (Chart 1.1 and 1.2).[3a,3b] Analysis by Carey *et al.* in 2006[3a] of a selection of biologically-active compounds in the early stages of

Chart 1.1. Source of Stereochemistry of Molecules Synthesized in Medicinal Chemistry (Carey, *et al.*, 2006)



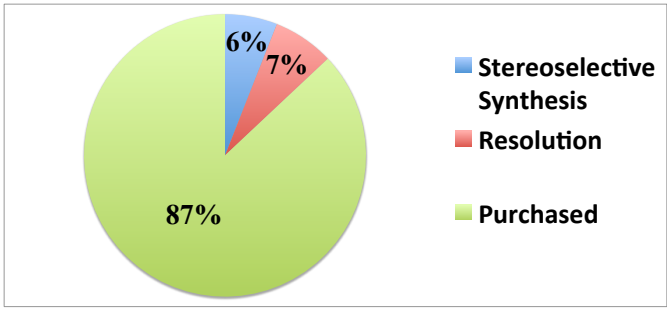
(2) It should be noted that the authors find a similar trend pertaining to the fraction of sp^3 atoms in a molecule and clinical success. That is, the fraction of sp^3 carbons in a molecule (Fsp^3) increases as it progresses from discovery to market. Based on data analysis, it seems these trends are independent of each other and are individually significant.

(3) (a) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337–2347. (b) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451–3479. (c) Cooper, T. W. J.; Campbell, I. B.; Macdonald, S. J. F. *Angew. Chem. Int. Ed.* **2010**, *49*, 8082–8091.

development shows that 55% of all stereogenic centers come from purchased enantiomerically pure compounds. The second major source of stereogenic centers, 28%, are obtained through resolution (by a chiral salt complex, chromatographic separation of diastereomers, kinetic resolution, chromatography through a chiral stationary phase, etc.), and the last 17% of stereogenic centers are obtained by stereoselective synthesis, with enantioselective catalysis being favored over diastereoselective induction in a 3:2 ratio.

Five years later, using a much larger data set of molecules, Roughley and Jordan[3b] reported that 87% of all stereogenic centers in molecules made by medicinal chemists, where it is known how they were installed into a molecule, originated from a purchased

Chart 1.2. Source of Stereochemistry of Molecules Synthesized in Medicinal Chemistry (Roughly, *et al.*, 2011)



enantiomerically pure starting material (Chart 1.2). That leaves only 13% of the stereogenic centers being formed through either a resolution or a stereoselective (either enantio- or diastereoselective) transformation. Regardless of the differences between the two reviews, it is obvious that the introduction of a stereogenic center is still not regarded as an easy task by medicinal chemists, as they overwhelmingly prefer to either purchase the source of chirality or set it through resolution instead of carrying out a stereoselective process. Therefore, development of reliable and practical methods for the stereoselective synthesis of molecules is still a critical goal in organic chemistry, even though there have

been major advances made in the last four decades.[4] Driving home the point that chiral molecules are still challenging compounds to work with in medicinal chemistry (from a manuscript published recently in 2010), Tony W. J. Cooper, Ian B. Campbell, and Simon J. F. Macdonald (all experienced medicinal chemists from GlaxoSmithKline) state[3c] "... the introduction of a stereogenic center (or a further stereogenic center) in a lead series is rarely undertaken lightly, particularly when the stereogenic center is not embedded in a commercially available molecule or cannot be introduced with good stereoselectivity […] In our experience, considerable nerve is required from the medicinal chemist to justify the 'time delays' that might result" (pg. 8090).

Concerning why the presence of stereochemistry is important in the success of a drug, Frank Lovering of Pfizer has compellingly hypothesized that as the number of stereogenic centers increases, a drug is less likely to have unacceptable levels of toxicity.[5] This reduction in toxicity is in large part due to a reduction in the "promiscuity"[6] of a molecule i.e. increasing the amount of stereogenic centers reduces the amount of targets (and therefore off-target effects) of a molecule. The importance of toxicity cannot be overstated, as it is currently the most likely reason for a drug to fail in clinical trials.[7,8] Decreasing promiscuity is especially important for amine (i.e. ionizable amines) containing compounds, which are about four times as promiscuous as molecules that do

(4) *Principles of Asymmetric Synthesis: 2nd Edition*; Gawley, R. E., Aubé, J., Eds.; Elsevier: Oxford, United Kingdom, **2012**.
(5) Lovering, F. *Med. Chem. Commun.* **2013**, *4*, 515–519.
(6) Lovering defines promiscuity as "the number of targets inhibited at greater than 50 percent at 10 μM divided by the number of targets tested" (page 515). A possible flaw in this measurement is that a molecule with no biological activity would have a promiscuity of 0. One assumes such molecules have been excluded from the study, but the fact that Lovering does not comment on this possible flaw is a bit worrisome.
(7) Leeson, P. D.; Springthorpe, B. *Nat. Rev. Drug Discovery* **2007**, *6*, 881–890.
(8) Specifically failure in phase I-II (where a drug is most likely to fail). The cause of failure in phase III is not dominated by toxicity.

not contain an amine (average promiscuity of 0.25 vs. 0.06).[5] As the number of stereogenic centers increase, the promiscuity of the molecule is reduced. For molecules containing an amine, there is a 58% decrease in promiscuity (from 0.31 to 0.13, Table

Table 1.2. Average Promiscuity of an Amine-Containing Molecule Versus the Number of Stereogenic Centers

Average promiscuity	0.31	0.26	0.21	0.13
Number of Stereogenic Centers	0	1	2	>2

1.2) when moving from no stereogenic centers to >2 stereogenic centers.[5,9] Bearing in mind that most targets of small molecules are enantiopure proteins, it is expected that chirality leads to a more discriminating pharmaceutical agent. Considering that toxicity is the leading cause of failure in Phase I and II (but not phase III)[7,8] clinical trials, and that increasing the number of stereogenic centers in a molecule decreases its promiscuity (and likely its toxicity as well),[5] one can draw a correlation with the data in Table 1.1, which shows a significant increase in the presence of stereochemistry when comparing compounds in Phase I and II versus those in Phase III and the market.

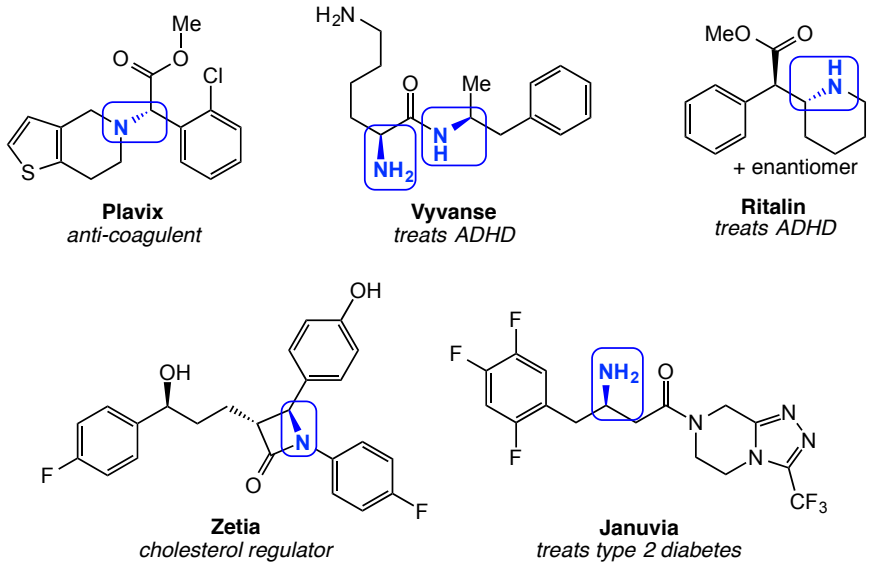
If low promiscuity is so important, and amine-containing compounds are so much more promiscuous than those without amines, why do chemists put amines in potential drugs? The answer is that ionizable-amines readily act as hydrogen-bond acceptors and/or donors, making up a large amount of the interactions that are so critically important for molecular recognition.[10] Another major reason for their presence is that ionizable-amines decrease the lipophilicity of the molecule of interest.[3b] Accordingly, nitrogen is contained in approximately 90% of potential active pharmaceutical

(9) Analogous to the statement in footnote 2, a similar trend, that increasing Fsp^3 of a molecule decreases its promiscuity, is observed.
(10) Bissantz, C.; Kuhn, B.; Stahl, M. *J. Med. Chem.* **2010**, *53*, 5061–5084.

ingredients;[3a] with aliphatic amines occurring in 43% of the molecules surveyed and amines bearing at least one aryl substituent existing in approximately 33% of all molecules surveyed.[3b] Amides are present in 54% the molecules surveyed.[3b]

Since nitrogen is nearly ubiquitous in compounds of interest to medicinal chemists, and chirality is an important property of successful drugs, stereogenic centers where one of the substituents is nitrogen are a common functional group in many active pharmaceutical ingredients. Out of the top 25 small-molecule drugs in terms of revenue from 2012, 10 of them (40%) contain a nitrogen-bonded stereocenter.[11] Scheme 1.1

Scheme 1.1. Representative Best-selling Drugs Containing a Nitrogen-Bonded Stereocenter



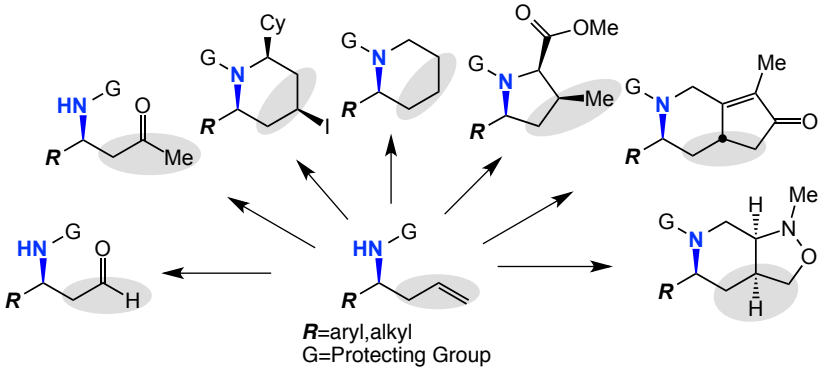
shows the structure of five of these compounds. All of these drugs besides Ritalin (Scheme 1.1) are sold as a single enantiomer. Notably, the enantiopure version of Ritalin (enantiomer depicted in Scheme 1.1, marketed as Focalin) has been shown to be more effective at treating ADHD than Ritalin and is also in the top 200 of revenue-producing drugs.[11]

(11) Vitaku, E.; Ilardi, E. A.; Njardarson, J. T. "Top 200 Pharmaceutical Products by US Retail Sales in 2012" Njardarson Group 25 Jun. 2014 <http://cbc.arizona.edu/njardarson/group/top-pharmaceuticals-poster>

Discovery of such blockbuster drugs requires medicinal chemists to have made a lead compound containing important structural features present in the finished product.[1,3,5] Since stereogenic carbons bound to nitrogen are important moieties in active pharmaceutical agents, the development of reliable and practical methods to install such functionality in a diverse array of molecules is a critical goal for the advancement of medicine.[12]

A desirable sub-class of enantiomerically enriched amines is homoallylamines.[13] Chiral homoallylamines are valuable synthetic intermediates in the synthesis of

Scheme 1.2 Utility of Chiral Homoallylamines in Organic Synthesis

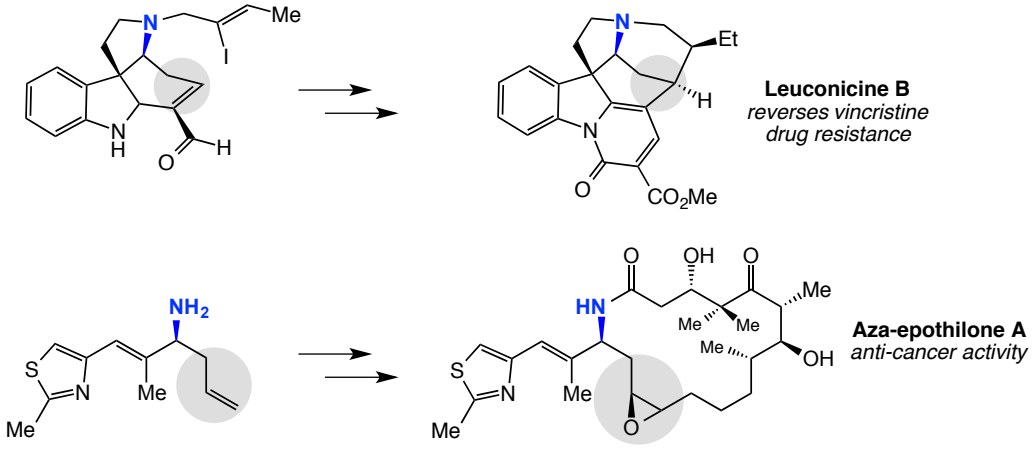


heterocycles, bicycles, amino aldehydes, and many other nitrogen containing functional groups (Scheme 1.2).[14] Such versatility has lead to their employment in various syntheses of biologically active compounds, such as the anti- cancer agent aza-epothilone[15]

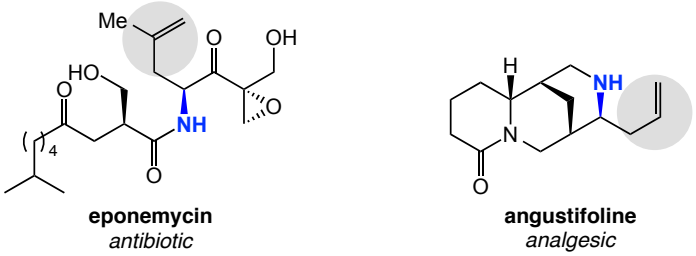
(12) *Chiral Amine Synthesis*; Nugent, T. C., Ed.; Wiley-VCH: Weinheim, Germany, **2010**.
(13) For reviews regarding homoallylamines, see: (a) Puentes, C. O.; Kouznetsov, V. *J. Heterocyclic Chem*., **2002**, *39*, 595–614. (b) Ding, H.; Friestad, G. K. *Synthesis,* **2005**, *17*, 2815–2829.
(14) For representative functionalizations of homoallylamines, see: (a) Friestad, G. K.; Korapala, C. S.; Ding, H. *J. Org. Chem*. **2006**, *71*, 281–289. (b) Yadav, J. S.; Reddy, B. V. S.; Chaya, D. N.; Kumar, G. G. K. S. N.; Aravind, S.; Kunwar, A. C.; Madavi, C. *Tetrahedron Letters* **2008**, *49*, 3330–3334. (c) Spangenberg, T.; Breit, B.; Mann, A. *Org. Lett*. **2009**, *11*, 261-264. (d) Lorthiois, E.; Marek, I.; Normant, J. F. *J. Org. Chem*. **1998**, *63,* 2442–2450. (e) Ferry, A.; Billard, T.; Langlois, B. R. *Synlett* **2005**, *6*, 1027-1029. (f) Sunderhaus, J. D.; Dockendorff, C.; Martin, S. F. *Tetrahedron* **2009**, *65*, 6454–6469.
(15) (a) Borzilleri, R. M. *et al. J. Am. Chem. Soc.*, **2000**, *122*, 8890–8897. It should be noted that the synthetic route involving a chiral homoallylamine was inefficient due to a ring-closing metathesis that was both afforded a 1:5 mixture of olefin isomers, with the undesired *E* isomer dominating. Recent advances in olefin metathesis may make it possible to address such shortcomings, see: (b) Yu, M.; Wang, C.; Kyle, A. F.; Jakubec, P.; Dixon, D. J.; Schrock, R. R.; Hoveyda, A. H. *Nature*, **2011**, *479*, 88–93. (c) Wang, C.; Yu,

(Scheme 1.3), leuconicine A and B, both of which negate multidrug resistance in cancer cell lines,[16] and the immunosuppressant FR235222.[17] In addition to being a valuable building block, the homoallylamine moiety itself appears as a structural unit in a number of alkaloids, such as the antibiotic eponemycin[18] and the analgesic augustifoline[19] (Scheme 1.4).

Scheme 1.3 Chiral Homoallylamines in the Synthesis of Biologically Active Targets



Scheme 1.4 Natural Products Bearing the Homoallylamine Motif



1.2 Background

The substantial utility of enantiomerically enriched homoallylamines has led to the development of a number of methodologies for the stereoselective addition of an allyl

M.; Kyle, A. F.; Jakubec, P.; Dixon, D. J.; Schrock, R. R.; Hoveyda, A. H. *Chem. Eur. J.* **2013**, *19*, 2726–2740.
(16) Sirasani, G.; Andrade, R. B. *Org. Lett.* **2011**, *13*, 4736–4737.
(17) Xie, W.; Zou, B.; Pei, D.; Ma, D. *Org. Lett.* **2005**, *7*, 2775–2777.
(18) Schmidt, U.; Schmidt, J. *Synthesis* **1994**, 300–305.
(19) Hassall, C. H.; Wilson, E. M.; *J. Chem. Soc.* **1964**, 2657–2663.

unit to imines. These methods can be divided into two major classifications: stoichiometric methods,[20] where stereoselectivity is controlled by at least one equivalent of an enantiomerically enriched reaction component and catalytic methods,[21] where a catalytic enantioselective transformation dictates the stereochemistry of the desired product. Both will be discussed below.

1.2.1 Background-Stoichiometric Methods

For stoichiometric methods to access enantiomerically enriched homoallylamines (Scheme 1.5), the component that determines the stereochemical outcome of the transformation is almost invariably either a chiral allyl-containing reagent or an imine substrate containing a chiral auxiliary. A variety of allyl reagents, such as an allylboron,[22] allylsilane,[23,24] or allylzinc[25] have been reported. Chiral alcohols can also be used as the source of the allyl-group in Ti-mediated Kulinkovich-type reactions.[26]

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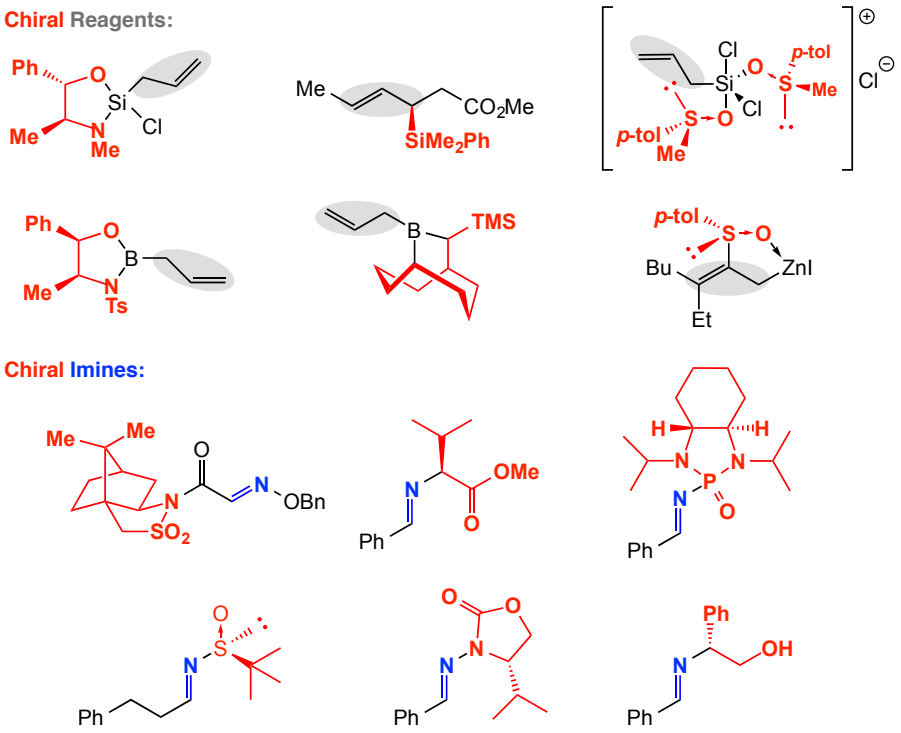
(20) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2013**, *113*, 5595–5698.
(21) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774–7854.
(22) For reviews addressing the use of a chiral allylboron, see: (a) Ramachandran, P. V.; Burghardt, T. E. *Pure Appl. Chem.* **2006**, *78*, 1397–1406. (b) Ramadhar, T. R., Batey, R. A. *Synthesis* **2011**, *9*, 1321–1346. For representative examples, see: (c) Itsuno, S.; Watanabe, K.; Ito, K.; El-Shehawy, A. A.; Sarhan, A. A. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 109–110. (d) Chataigner, I.; Zammattio, F.; Lebreton, J.; Villiéras, J. *Synlett* **1998**, *3*, 275–276. (e) Sugiura, M.; Hirano, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 7182–7183. (f) Ramachandran, P. V.; Burghardt, T. E. *Chem. Eur. J.* **2005**, *11*, 4387–4395. (g) Hernandez, E.; Canales, E.; Gonzalez, E.; Soderquist, J. A. *Pure Appl. Chem.* **2006**, *78*, 1389–1396. (h) Ramachandran, P. V.; Biswas, D. *Org. Lett.* **2007**, *7*, 3025–3027. (i) Wu, T. R.; Chong, J. M. *J. Am. Chem. Soc.* **2006**, *128*, 9646–9647.
(23) For methods employing an isolated chiral allylsilane, see: (a) Panek, J. S.; Jain, N. F. *J Org. Chem.* **1994**, *59*, 2674–2675. (b) Schaus, J. V.; Jain, N.; Panek, J. S. *Tetrahedron* **2000**, *56*, 10263–10274. (c) Berger, R.; Rabbat, P. M. A.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 9596–9597. (d) Rabbat, P. M. A.; Valdez, S. C.; Leighton, J. L. *Org. Lett.* **2006**, *8*, 6119–6121. (e) Perl, N. R.; Leighton, J. L. *Org. Lett.* **2007**, *9*, 3699–3701. (f) Huber, J. D.; Perl, N. R.; Leighton, J. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 3037–3039. (g) Feske, M. I.; Santanilla, A. B.; Leighton, J. L. *Org. Lett.* **2010**, *12*, 688–691.
(24) For representative examples of chiral allylsilanes generated *in-situ* from allyltrichlorosilanes and a stoichiometric amount of an enantiomerically-pure Lewis base, see: (a) Kobayashi, S.; Ogawa, C.; Konishi, H.; Sugiura, M. *J. Am. Chem. Soc.* **2003**, *125*, 6610–6611. (b) García-Flores, F.; Flores-Michel, L. S.; Juaristi, E. *Tetrahedron Letters* **2006**, *47*, 8235–8238. (c) Fernández, I. Valdivia, V.; Leal, M. P.; Khiar, N. *Org. Lett.* **2007**, *9*, 2215–2218.
(25) Sklute, G.; Marek, I. *J. Am. Chem. Soc.* **2006**, *128*, 4642–4649.
(26) (a) Takahashi, M. McLaughlin, M.; Micalizio, G. C. *Angew. Chem. Int. Ed.* **2009**, *48*, 3648–3652. (b) Lysenko, I. L.; Lee, H. G.; Cha, J. K. *Org. Lett.* **2009**, *11*, 3132–3134. (c) Chen, M. Z. *et al. J. Org. Chem.* **2010**, *75*, 8048–8059. (d) Yang, D.; Micalizio, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 9216–9219.

Scheme 1.5 Representative Chiral Reagents and Imines in Stoichiometric Methods



Chiral auxiliaries for imines and hydrazones that have been shown to affect diastereoselective allyl-addition range from nitrogen-protecting groups derived from amino acids and amino alcohols,[27] *tert*-butylsulfinamides (Ellman's Auxiliary),[28] and other moieties[29], to auxiliaries that are present elsewhere in the imine[30]. When compared

(27) For recent representative examples, see: (a) Yanada, R.; Kaieda, A.; Takemoto, Y. *J. Org. Chem.* **2001**, *66*, 7516–7518. (b) Sugimoto, Y.; Imamura, H.; Sakoh, H.; Yamada, K.; Morishima, H. *Synlett* **2001**, *11*, 1747–1750. c) Cook, G. R.; Maity, B. C.; Kargbo, R. *Org. Lett.* **2004**, *6*, 1741–1743. (d) Dalmolen, J. *et al. Eur. J. Org. Chem.* **2004**, 1544–1557. (e) Vilaivan, T.; Winotapan, C.; Banphavichit, V.; Shinada, T.; Ohfune, Y. *J. Org. Chem.* **2005**, *70*, 3464–3471. (f) Friestad, G. K.; Korapala, C. S.; Ding, H. *J. Org. Chem.* **2006**, *71*, 281–289.

(28) For a review of indium-promoted diastereoselective allyl-additions to *tert*-butyl *N*-sulfinyl imines, see: (a) Foubelo, F.; Yus, M. *Eur. J. Org. Chem.* **2014**, 485–491. For representative examples of diasteroselective allyl-additions to *tert*-butyl *N*-sulfinyl imines, see: (b) Cogan, D. A.; Liu, G.; Ellman, J. *Tetrahedron* **1999**, *55*, 8883–8904. (c) Foubelo, F.; Yus, M. *Tetrahedron: Asymmetry* **2004**, *15*, 3823–3825. (d) Grigg, R.; McCaffrey, S.; Sridharan, V.; Fishwick, C. W. G.; Kilner, C.; Korn, S.; Bailey, K.; Blacker, J. *Tetrahedron* **2006**, *62*, 12159–12171. (e) Sun, X.-W.; Xu, M.-H; Lin, G.-Q. *Org. Lett.* **2006**, *8*, 4979–4982. (f) Sun, X.-W.; Liu, M.; Xu, M.-H; Lin, G.-Q. *Org. Lett.* **2008**, *10*, 1259–1262. (g) González-Gómez, J. C.; Medjahdi, M.; Foubelo, F.; Yus, M. *J. Org. Chem.* **2010**, *75*, 6308–6311. (h) Liu, M.; Shen, A.; Sun, X.-W.; Deng, F.; Xu, M.-H.; Lin, G.-Q. *Chem. Commun.* **2010**, *46*, 8460–8462. (i) Guo, T.; Song, R.; Yuan, B.-H., Chen, X.-Y., Sun, X.-W., Lin, G.-Q. *Chem. Commun.* **2013**, *49*, 5402–5404.

(29) For additions to an imine derived from an aminosugar, see: (a) Laschat, S.; Kunz, H. *J. Org. Chem.* **1991**, *56*, 5883–5889. For additions to an imine with a chiral *N*-phosphinoyl group, see: (c) Kattuboina, A.;

to methods where the enantioselectivity of the product is determined by a catalytic amount of an enantiomerically pure molecule (or molecules), all of the methods mentioned previously have fundamental disadvantages to them resulting from their use of a stoichiometric amount of a chiral molecule.[31] Enantiomerically pure molecules capable of such control are precious, and even when considering a chiral catalyst that operates at a high 10 mol % catalyst loading, this catalytic transformation uses one-tenth of the amount of chiral molecules that a stoichiometric method does to access the same amount of desired product. A catalyst that is even more efficient further magnifies the economic advantage of enantioselective catalysis. Even if an auxiliary can be recycled in high yield (and many cannot), there is always cost associated with this process, and if the auxiliary is never going to be used again, recycling becomes pointless. Additionally, the purification of catalytic reactions is generally easier due to only needing to separate the product from a catalytic amount of the chiral molecule, rather than one (or more) equivalents.

A point worth mentioning is that the *tert*-butylsulfinamide chiral auxiliary (Ellman's auxiliary) is used often to promote diastereoselective additions to imines.[32] This protecting group has the desirable traits of being relatively inexpensive (though still more expensive than most achiral protecting groups) as either enantiomer, being easy to remove, and being simple to install. Still, as it is a chiral auxiliary, one is limited to it as the protecting group on the resultant amine formed, rather than whatever protecting group

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Kaur, P.; Nguyen, T.; Li, G. *Tetrahedron Lett.* **2008**, *49*, 3722–3724. For additions to iminium ions derived from an enantiopure 1-(1-naphthyl)ethylamine, see: (d) Suh, Y-g. *et al. Org. Lett.* **2011**, *13*, 5920–5923.
(30) Kulkarni, N. A.; Yao, C-f.; Chen, K. *Tetrahedron* **2007**, *63*, 7816–7822.
(31) Mulzer, J. "Chapter 3: Basic Principles of Asymmetric Synthesis" in *Comprehensive Asymmetric Catalysis, Volume I*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Heidelberg, Germany, **1999**.
(32) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600–3740.

is ideally desired. Also, in catalytic reactions, in order to obtain an efficient and enantioselective transformation with a desired substrate, multiple catalyst structures are often examined. Modifying the chiral-auxiliary structure while maintaining its desirable traits of being inexpensive, easy to install and remove, is far more difficult than modifying the catalyst structure/system. As a catalyst is used sub-stoichiometrically, the bar for it being easy to access is much lower than that of a chiral-auxiliary. A catalyst is also not intimately tied to the ease of imine formation and nitrogen protecting-group removal in the way an auxiliary is. One advantage that a chiral-auxiliary based approach has is that it is often possible to separate the diastereomers of the product, allowing for, after removal of the auxiliary, isolation of enantiopure material. Additionally, catalytic methods can have the drawbacks of both catalyst poisoning and having to compete with a background reaction.

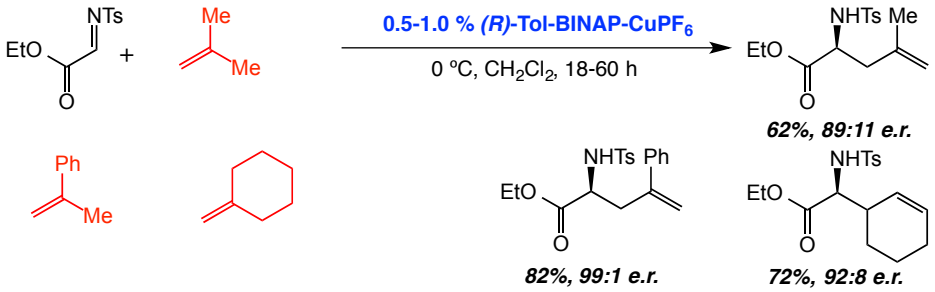
1.2.2 Background-Catalytic Methods

Due to the benefits discussed above, catalytic enantioselective protocols are an attractive strategy for the stereoselective synthesis of homoallylamines.[21] Two pioneering reports in this field were published in 1998. K. A. Jørgenson reported a Cu-catalyzed ene reaction to tosyl-protected α-imino esters (Scheme 1.6)[33] and Y. Yamamoto reported the addition of tri-butyl allylstannane to a range of aldimines catalyzed by a bis-Pd-π-allyl complex.[34] While undeniably important to the development of the field, these two initial methods have major drawbacks. The method from the Jørgenson group is extremely limited, since it only works for highly activated α-imino esters and not with imines derived from aromatic and aliphatic imines. It is additionally restricted to 2-substituted

(33) Yao, S.; Fang, X.; Jørgensen, K. A. *Chem. Commun.* **1998**, 2547–2548.
(34) Nakamura, H.; Nakamura, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4242–4243.

allyl groups; even reducing the size of this group to a methyl group results in a decrease in enantioselectivity (Scheme 1.6). The method by Yamamoto, while applicable to imines that are not α-imino esters, employs tri-butyl allylstannane as the allyl source. The toxicity of allylstannanes[35] makes them fundamentally unattractive.

Scheme 1.6 Cu-Catalyzed Ene Reaction Reported by Jørgenson



In order to increase synthetic utility, Yamamoto developed a method using a similar catalytic system that employs an allylsilane[36] as the nucleophile (Scheme 1.7).[37] All products are obtained in a synthetically useful yield of ≥76%, but a noticeable drop in the e.r. of the product is observed with non aryl-substituted imines, especially those with aliphatic substitution (Scheme 1.7). An additional drawback is that dimer **1.1** is difficult to access, being obtained in only 6% overall yield from the expensive ($17/mmol)[36] $Pd(CF_3COO)_2$. This would be less of a problem if the catalytic system was more efficient, but 5 mol % catalyst loading of dimer **1.1** (10 mol % loading of catalyst) is

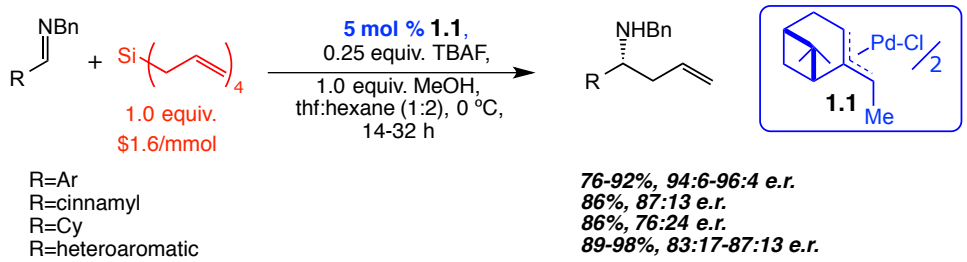
(35) For an improvement of Yamamoto's original method that still uses allylstannane, see: (a) Fernandes, R. A.; Stimac, A.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 14133–14139. For other methods employing allylstannane, see: (b) Fang, X.; Johannsen, M.; Yao, S.; Gathergood, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **1999**, *64*, 4844–4849. (c) Gastner, T.; Ishitani, H.; Akiyama, R.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 1896–1898. (d) Aydin, J.; Kumar, K. S.; Sayah, M. J.; Wallner, O. A.; Szabó, K. J. *J. Org. Chem.* **2007**, *72*, 4689–4697. (e) Colombo, F.; Annunziata, R.; Benaglia, M. *Tetrahedron Lett.* **2007**, *48*, 2687–2690. (f) Li, X.; Liu, X.; Fu, Y.; Wang, L.; Zhou, L.; Feng, X. *Chem. Eur. J.* **2008**, *14*, 4796–4798. (g) Fernandes, R. A.; Chaudhari, D. A. *Eur. J. Org. Chem.* **2012**, 1945–1952.

(36) Prices for all metals, metal salts and ligands are from the Strem catalog unless otherwise noted. Prices for all allylsilanes are from the Gelest catalog. Prices for all other chemicals are from the Aldrich catalog unless otherwise noted.

(37) Fernandes, R. A.; Yamamoto, Y. *J. Org. Chem.* **2004**, *69*, 735–738.

required to obtain full conversion in 14–32 hours, corresponding to a turnover frequency of 0.64 to 0.28/h.

Scheme 1.7 Pd-Catalyzed Allyl-Addition of Imines Using Tetraallylsilane



Although allylsilanes are inexpensive and essentially harmless, catalytic enantioselective additions to imines that employ allylsilanes tend to suffer from such low reactivity. Because of this, many of these methods are generally limited to the highly activated α-imino esters discussed previously.[38] Those that are not limited in this way require high-catalyst loadings and long reaction times.[39]

An interesting strategy for the enantioselective allyl-addition to imines is to use an achiral homoallylamine as the imine protecting group and to use a chiral catalyst to affect an enantioselective aza-Cope rearrangement.[40] The Wulff group described an impressive application of this strategy in 2011 (Scheme 1.8).[40b,c] Following hydrolysis of the ketimine that is formed after the aza-Cope rearrangement, the homoallylamines are

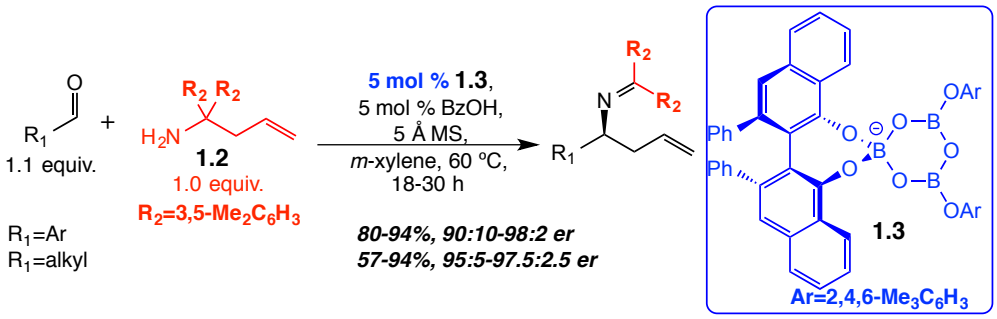
(38) (a) Lectka, T. *et al. J. Am. Chem. Soc.* **2001**, *124*, 67–77. (b) Hamada, T.; Manabe, K.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3927–3930. (c) Kiyohara, H.; Nakamura, Y.; Matsubara, R.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2006**, *45*, 1615–1617. For a similar example to (c) using an allylboronate, see: (d) Fujita, M.; Nagano, T.; Schneider, U.; Hamada, T.; Ogawa, C.; Kobayashi, S. *J. Am. Chem. Soc.* **2008**, 130, 2914–2915. For an example with highly-activated ketimines derived from isatins, see: (e) Nakamura, S.; Hyodo, K.; Nakamura, M.; Nakane, D.; Masuda, H. *Chem. Eur. J.* **2013**, *19*, 7304–7309. For a method that is limited in scope to imines derived from benzaldehyde which contain a difficult to remove protecting group, see: (f) Naodovic, M.; Wadamoto, M.; Yamamoto, H. *Eur. J. Org. Chem.* **2009,** 5129–5131. For a catalytic enantioselective allyl-addition to cyclic imines, see: Itoh, T. *et al. J. Org. Chem.* **2011**, *76*, 534–542.

(39) (a) Momiyama, N.; Nishimoto, H.; Terada, M. *Org. Lett.* **2011**, *13*, 2126–2129. (b) Gandhi, S.; List, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 2573–2576.

(40) (a) Rueping, M.; Antonchick, A. P. *Angew. Chem. Int. Ed.* **2008**, 47, 10090–10093. (b) Ren, H.; Wulff, W. D. *J. Am. Chem. Soc.* **2011**, *133*, 5656–5659. (c) Desai, A. A.; Ren. H.; Mukherjee, M.; Wulff, W. D. *Org. Process. Res. Dev.* **2011**, *15*, 1108–1115.

formed analytically pure without the need for column chromatography in the yields and enantioselectivities shown in Scheme 1.8. Importantly, alkyl-substituted homoallylamines are formed in >95:5 e.r., which contrasts with most other methods where such products are formed in low selectivities, if at all. An additional advantage of this method is that it starts with the aldehyde, therefore eliminating an additional step normally required for imine addition. The drawbacks of this technique are that it needs the achiral homoallylamine **1.2** (a four-step synthesis); requires relatively long reactions times, and uses the sensitive boronate complex **1.3**, which must be generated before each reaction from BH_3•SMe_2, mesityl alcohol, and expensive VANOL ($260/mmol from Sigma-Aldrich). Even with these flaws, this is one of the most impressive methods to date for the enantioselective synthesis of homoallylamines.

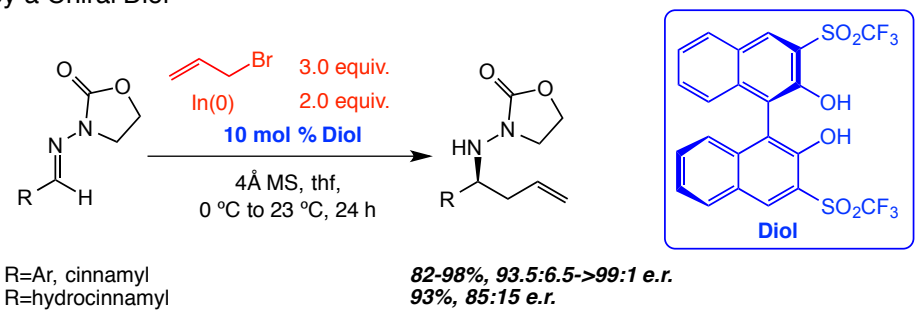
Scheme 1.8 Catalytic Enantioselective Aza-Cope Rearrangement



Allylindiums, generally generated *in situ* from a Barbier-type reaction between a super-stoichiometric (based on the imine) amount of indium metal and an allylhalide, have a low level of toxicity, favorable levels of reactivity as well as high chemoselectivity. Unfortunately, indium is a rare metal whose value is likely to keep increasing due to the rising demand for the light-emitting diodes and high-definition

displays it is used in.[41] Regarding the catalytic synthesis of chiral homoallylamines, methods employing allylindium[42] generally proceed with high levels of enantioselectivity for aryl hydrazone substrates, but proceed in lower levels of enantioselectivity for the corresponding alkyl substrates. An illustrative report by Cook and Lloyd-Jones shows selectivities that range from 93.5:6.5 e.r. to >99:1 e.r. for aryl hydrazones to 85:15 e.r. for an alkyl-hydrazone (Scheme 1.9).[42a] This lower level of enantioselectivity is proposed to be from a more efficient uncatalyzed addition of allylindium to alkyl-substituted hydrazones vs. aryl-substituted ones[42a] Additionally, removal of the hydrazone protecting group from the product without reducing the homoallylamine olefin requires super-stoichiometric amounts of rare and expensive SmI_2.[24a]

Scheme 1.9 Enantioselective Addition of Allylindium to Hydrazones Catalyzed by a Chiral Diol

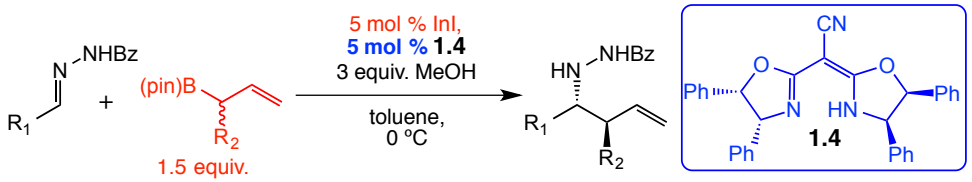


In order to decrease the amount of precious indium used, a method for enantioselective allyl-additions to homoallylamines whereby the nucleophilic allylindium species is generated from a catalytic amount of indium was developed by the Kobayashi group (Scheme 1.10).[43] Setting it apart from most other catalytic protocols, this method

(41) Nakamura, E.; Sato, K. *Nature Mater.* **2011**, *10*, 158–161.
(42) (a) Kargbo, R.; Taakahashi, Y.; Bhor, S.; Cook, G. R.; Lloyd-Jones, G. C.; Shepperson, I. R. *J. Am. Chem. Soc.* **2007**, *129*, 3846–3847. (b) Tan, K. L.; Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2007**, *46*, 1315–1317. (c) Kim, S. J.; Jang, D. O. *J. Am. Chem. Soc.* **2010**, *132*, 12168–12169.
(43) Chakrabarti, A.; Konishi, H.; Yamamguchi, M.; Schneider, U.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 1838–1841.

can be used to generate products that contain an additional stereogenic center on the allylic carbon (crotyl–addition type products) in synthetically useful enantio- and

Scheme 1.10 Enantioselective Addition of Catalytically Generated Allylindium to Hydrazones



R_1=Ar, R_2=H
R_1=Cy,R_2=H
R_1=Ar, R_2=Me
R_1=Ar,R_2=Cl

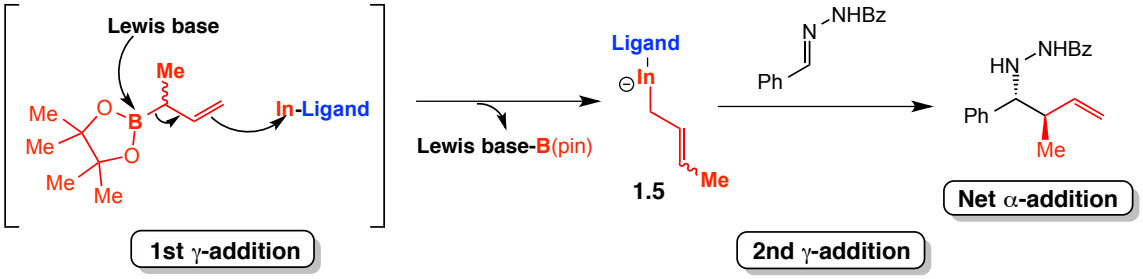
88-98%, 90:10-98:2 e.r., 12-48 h
87%, 65:35 e.r., 38 h
83-98%, 90:10-98:2 e.r., 7:1-19:1 d.r., 6-45 h
71-89%, 91:9-93:7 e.r., 33:1-99:1 d.r., 48-96 h

diastereoselectivities (Scheme 1.10). Interestingly, this transformation is one of the rare examples in allyl-addition literature where the carbon α to the boron in the nucleophile ends up directly bound to the electrophile (α-addition) instead of the carbon γ to the boron in the nucleophile (γ-addition).[44] In all examples shown in the manuscript, the ratio of α-addition to γ-addition is at least 49:1. The authors propose this intriguing regioselectivity results from an initial γ-addition of the allylboronate (promoted by a Lewis base; the authors suggest the identity of the Lewis base is likely the hydrazone substrate) to the indium-ligand complex (Scheme 1.11) to form complex **1.5**. This allylmetal species then adds to the hydrazone substrate in a γ-selective fashion *via* a six-membered transition state to afford the net α-addition product. Overall, two γ-additions afford the product of a net α-addition. Unfortunately, even though the allylindium is

(44) For examples that afford the α-addition product and are proposed to occur through a γ-addition of the starting allyl nucleophile to a catalyst to generate an allylmetal, followed by a second γ-addition of this allylmetal to the substrate (two γ-additions result in the product of net α-addition), see: Ref. 38d, (a) Kobayashi, S.; Konishi, H.; Schneider, U. *Chem. Commun.* **2008**, 2313–2315. (b) Kobayashi, S.; Endo, T.; Schneider, U.; Ueno, M. *Chem. Commun.* **2010**, *46*, 1260–1262. (c) Fandrick, K. R. *et al. Org. Lett.* **2010**, *12*, 3748–3751. (d) Kobayashi, S.; Endo, T.; Ueno, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 12262–12265. (e) Cui, Y.; Yamashita, Y.; Kobayashi, S. *Chem. Commun.* **2012**, *48*, 10319–10321. (f) Kobayshi, S.; Endo, T.; Yoshino, T.; Schneider, U.; Ueno, M. *Chem. Asian J.* **2013**, *8*, 2033–2045. For reports where the author explains the α-addition product by a γ-addition to the substrate followed by a Lewis acid catalyzed sigmatropic-rearrangement, see: (g) Ramachandran, P. V.; Pratihar, D.; Biswas, D. *Chem. Commun.* **2005**, 1988–1989. (h) Selander, N.; Szabó, K. J. *J. Org. Chem.* **2009**, *74*, 5695–5698.

generated catalytically, which should diminish advantageous background reactions; additions to alkyl-substituted hydrazones are much less selective than aryl-substituted

Scheme 1.11 Proposed Mechanism for the Formation of α-Addition Products



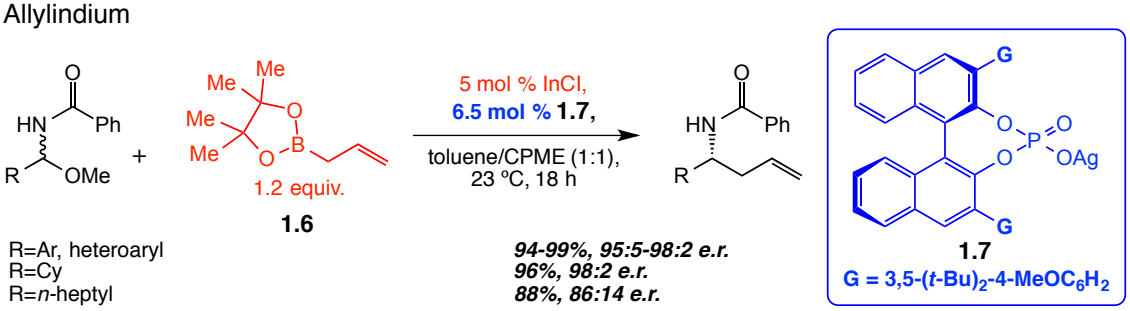
ones (Scheme 1.10). This issue is partially addressed in a subsequent report, where the cyclohexyl-substituted homoallylamine is obtained in 98:2 e.r., but aliphatic homoallylamines not containing alpha-branching are obtained in 86:14 e.r (Scheme 1.12).[45] The newer method also suffers from the use of the Ag-salt of an expensive chiral phosphoric acid (**1.7**) as well as a nitrogen-protecting group that requires a two-step procedure of DIBAL-H followed by HCl in MeOH for removal.[46,47]

Importantly, even though the active allyl nucleophile in these two methods is a catalytically generated allylindium species, the stoichiometric sources of the allyl functionality are allylborons. Allylborons are essentially non-toxic and the reactivity and stability of this class of reagents can be greatly varied by modifying the substituents of the boron.[22a,b] A particularly noteworthy allylboron is the allylboronate[48] allylboronic[49]

(45) Huang, Y.-Y.; Chakrabarti, A.; Morita, N.; Schneider, U.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 11121–11124.
(46) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2007**, *129*, 15398–15404.
(47) For an alternative method for removal of acyl-protecting groups from imines, see: Spaggiari, A.; Blaszczak, L. C.; Prati, F. *Org. Lett.* **2004**, *6*, 3885–3888. It should be noted that there are no examples of this method being applied to molecules containing an alkene.
(48) For a review on the use of allylboronates as nucleophiles in catalytic, enantioselective additions to imines and carbonyls, see: Huo, H.-X.; Duvall, J. R.; Huang, M.-Y.; Hong, R. *Org. Chem. Front.* **2014**, *1*, 303–320.

acid pinacol ester (**1.6**, Scheme 1.12), which has an optimal balance of being reactive enough to participate in a wide variety of transformations while still being stable enough to air and moisture to be convenient to use.

Scheme 1.12 Improved Method for Homoallylamine Synthesis *via* Catalytically Generated Allylindium



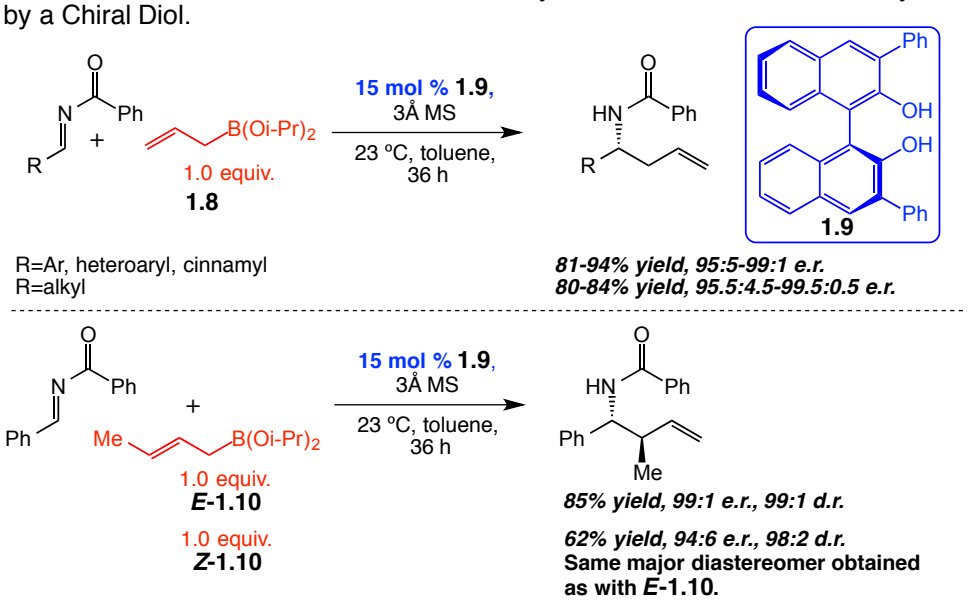
Replacing the pinacol group of **1.6** with two isopropoxy groups results in the more reactive allyldiisopropoxyborane **1.8** (Scheme 1.13). This increased reactivity is required by the Schaus group to obtain noticeable reactivity (<2% conversion under all conditions when employing **1.6**), but the cost of this reactivity is that boronate **1.8** is far less stable than **1.6** and requires the reaction to be rigorously anhydrous (Scheme 1.13).[46] Even though Schaus' method requires this reactive allylboronate, long reactions times, high catalyst loading (a turnover frequency of 0.16/h),[50] and a difficult to remove protecting group,[47] it is still a noteworthy method for several reasons. First, because of the uniformly high levels of enantioselectivity and yields obtained for aryl-,heteroaryl-, cinnamyl- as well as the traditional troublesome alkyl-substituted aldimines. Secondly, it is the only catalytic method to enantioselectively add allylboronates to imines without

(49) For a book on the subject of boronic acids and their derivatives, see: *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials, 2nd Edition*; Hall, D. G. Ed.; Wiley-VCH: Weinheim, Germany, **2011**.

(50) Using a very similar system, the catalyst efficiency and selectivity for the enantioselective allylation of ketones was enhanced by performing the reactions in *tert*-butanol. A more stable allyldioxaborolane was used as the allylating agent. The authors propose that product release is the turnover limiting step and the facility of this step can be increased in the presence of excess alcohol. This has not been applied to reactions with imines. See Barnett, D. S.; Moquist, P. N.; Schaus, S. E. *Angew. Chem. Int. Ed.* **2009**, *48*, 8679–8682.

going through the intermediacy of an allylmetal. Lastly, high levels of enantio- and diastereoselectivities obtained when crotylboronate ***E*-1.10** is employed (Scheme 1.13). Interestingly, when ***Z*-1.10** is used, the yield and selectivities obtained are lower; however the *same major enantiomer* is obtained as with ***E*-1.10** (Scheme 1.13), rendering the *syn*-croyl product unattainable. The authors suggest this is due to a more favorable boat-like transition state occurring when ***Z*-1.10** is used.[46]

Scheme 1.13 Enantioselective Addition of Allylboronates to Aldimines Catalyzed by a Chiral Diol.

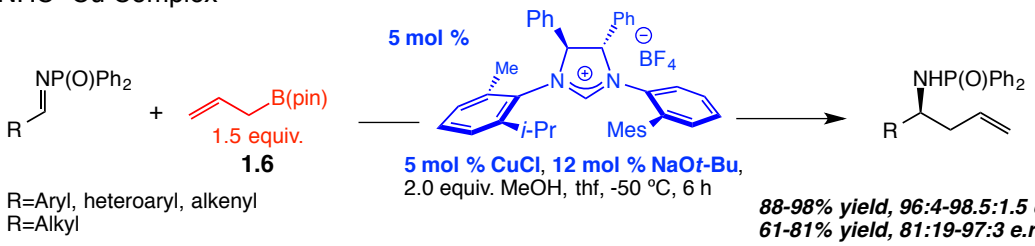


All other protocols that use allylborons[51] for the catalytic enantioselective allyl-addition to imines proceed through an allylmetal[52] intermediate. One example forms allylrhodiums from potassium allyltrifluoroborates (synthesized from the corresponding

(51) An interesting strategy for the catalytic enantioselective synthesis of homoallylamines is to form a stoichiometric amount of an enantiomerically enriched allylboron through a catalytic enantioselective process and then add this allylboron to an imine. See Sieber, J. D.; Morken, J. P *J. Am. Chem. Soc.* **2006**, *128*, 74–75.

(52) For a method proposed to go through an allyl-Pd species and uses allyl alcohol as the allyl source, see: Qiao, X.-C.; Zhu, S.-F.; Chen, W.-Q.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2010**, *21*, 1216–1220.

Scheme 1.14 Enantioselective Addition of Allylboronates to Aldimines Catalyzed by an NHC–Cu Complex

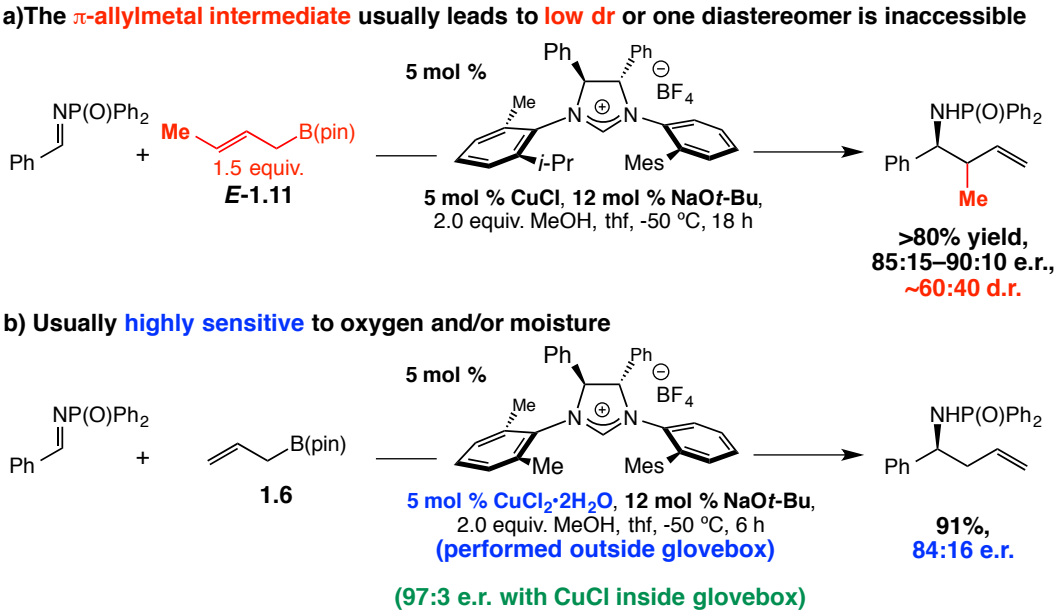


allylboronic acid pinacol esters) and adds these nucleophiles to a limited class of cyclic imines.[53] More attractive strategies utilize either a bis-phosphine–Cu[54] or *N*-heterocyclic carbene–Cu [55] catalyst to achieve enantioselective allyl-additions to ketimines or aldimines respectively. Both methods are proposed to operate through a nucleophilic allylcopper species, which is generated through transmetalation of a copper-alkoxide complex with allylboronate **1.6**. These protocols are among the most efficient catalytic methods for imine allylation, with turnover frequencies as high as 18/h.[56] The second method (Scheme 1.14), developed in the Hoveyda laboratory, also has the advantage of being applicable to the enantioselective synthesis of alkyl-substituted homoallylamines. Two major shortcomings of this method (Scheme 1.15) are: a) use of crotylboronate ***E*-1.11** (***Z*-1.11** behaves similarly) affords products in ~3:2 diastereomeric ratio (Scheme 1.15a) and b) notable sensitivity to oxygen and/or moisture.[57] Performing the reaction outside of a glovebox with $CuCl_2$•$2H_2O$ (Scheme 1.15b)[58] led to slightly diminished

(53) (a) Luo, Y.; Hepburn, H. B.; Chotsaeng, N.; Lam, H. W. *Angew. Chem. Int. Ed.* **2012**, *51*, 8309–8313. (b) Hepburn, H. B.; Chotsaeng, N.; Luo, Y.; Lam, H. W. *Synthesis* **2013**, *45*, 2649–2661.
(54) Wada, R.; Shibuguchi, T.; Makino, S.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 7687–7691.
(55) Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 3332–3335.
(56) Efficiencies are especially impressive when excluding methods that require a highly activated α-imino ester, such as the one in reference 38c.
(57) Vieira, E. M.; Haeffner, F.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2012**, *51*, 6618–6621.
(58) Use of $CuCl_2$•$2H_2O$ worked well for the protocol developed for enantioselective propargyl-addition to imines (Ref. 57). As that protocol is proposed to proceed with a very similar mechanism to the allyl-addition protocol, the lower enantioselectivity is not believed to be due to a copper (II) salt, but rather

efficiency (92% vs. >98% conv.) as well as much lower enantioselectivity (84:16 e.r. vs. 97:3 e.r.).

Scheme 1.15 Some Disadvantages of an Allylmetal Pathway



Collectively, these reports represent substantial progress in the development catalytic enantioselective methods for the enantioselective allyl-addition to imines. Nevertheless, they all have notable shortcomings. It is rare to find the following desired attributes, and no method has all of them: the protecting group of the homoallylamine is easily removed (e.g. in one step and ≥ 85% yield of the free homoallylamine without resorting to exotic conditions such as super-stoichiometric samarium iodide),[35e,38g,39b,40,51,55] short reaction times (e.g. less than eight hours),[38e,38g,54,55] the ability to afford alkyl-substituted as well as aryl-substituted homoallylamines in high enantioselectivities (e.g. ≥ 90:10 e.r.),[39b,40b–c,42c,45,46,51,55] and the ability to promote diastereoselective crotyl-type additions (e.g. ≥ 90:10 e.r and d.r.).[35c,38a,38c,39a,43,46,53] Beyond these attributes, these methods all have notable flaws, such as: narrow

sensitivity to moisture and/or oxygen. It is interesting to note that the propargylation protocol is far more robust than the allylation protocol, perhaps due to increased stability of the allenyl–Cu species.

substrate/nucleophile scope[38f–g,40a,51] (e.g. restricted to highly activated substrates like α-imino esters[33,35b,35e,38a–e] or cyclic dioxobenzathiazenes[53]), high catalyst loading (e.g. ≥10 mol %),[33,34,35a,35c,35f,35g,37,38b–c,38e,39,40a,42,43,46,54] cryogenic temperatures (e.g. -50º C or less),[38a,38f,55] use of precious metals (either catalytically[34,35a,35d–g,37,38f,43,45,51–53] or stoichiometrically[38d,42]) use of difficult-to-access or expensive ligands/catalysts (e.g. >$100/mmol),[34,35a,35d,37,38f,39,40,45,52-55] or employing an undesirable allyl source (e.g. those that are toxic,[34,35,] sensitive,[46] or difficult-to-access[40b–c]).

Considering the state-of-the-art, development of an efficient and selective catalytic method that utilizes components that are readily accessible and handled easily represents a significant advance in enantioselective catalysis. The previous method developed in the Hoveyda laboratory[55] (Scheme 1.14) suggested that relying on the intermediacy of an allylmetal lead to the shortcomings discussed previously (Scheme 1.15). We therefore investigated whether it was possible to develop a transition metal-free catalytic protocol that was not overly moisture/oxygen sensitive (can be performed outside of a glovebox) and could stereoselectively access crotyl-addition products (and ideally other substitutions besides methyl as well) without sacrificing the efficiency and enantioselectivity of the copper-based protocol.

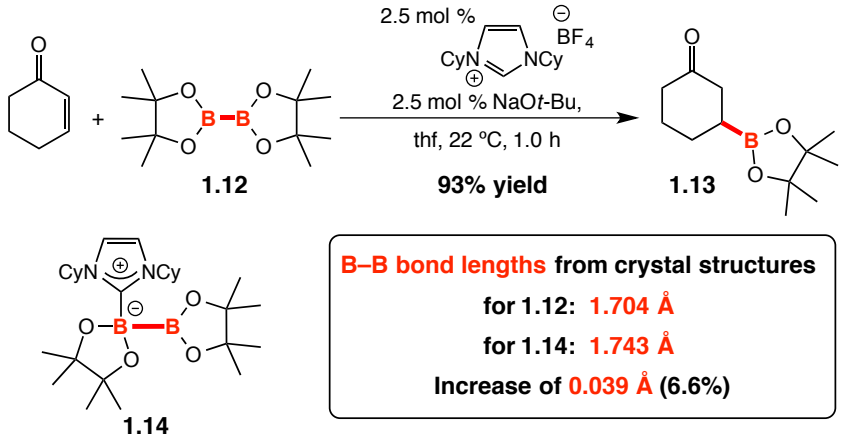
1.3 Discovery of New Catalysts by Dr. Tatiana Pilyugina

The initial proposal for a new catalytic manifold was to harness the nucleophilicity of *N*-heterocyclic carbenes (NHCs)[59] by using these molecules to activate

(59) For reviews of NHCs as catalysts for various transformations in organic chemistry, see: (a) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655. (b) Marion, N.; Díez-González, S.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2007**, *46*, 2988–3000.

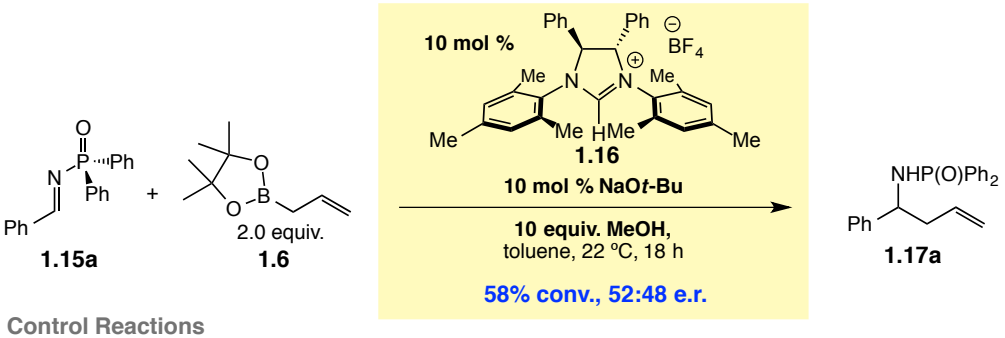
allylboronates[60] for addition to imines; this process could be rendered enantioselective through the use of a chiral NHC. Our group has utilized this mode of catalysis to promote additions of $B_2(pin)_2$ **1.12** (Scheme 1.16) to enones in both racemic[61] and enantioselective[62] fashions. Mechanistic studies[61,63] suggest that the catalyst operates by coordinating to the empty p-orbital of boron resulting in a weakening of the B-B bond (Scheme 1.16), which in turn raises the nucleophilicity of the sp^2-hydridized boron in **1.14**.[64] We were excited to see if this emerging catalytic manifold[65] could be used to activate a C-B bond, namely the one in allylB(pin) **1.6**, enough to promote its addition to an imine.

Scheme 1.16 Conjugate Addition of Boron to Enones through Activation of $B_2(pin)_2$ with an NHC Catalyst

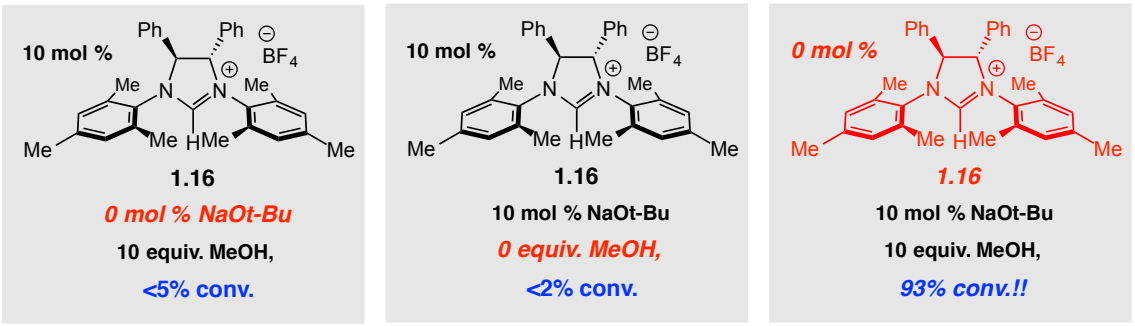


(60) For relevant reviews, see: (a) Curran, D. P.; Solovyev, A.; Brahmi, M. M.; Fensterbank, L.; Malacria, M.; Lacôte, E. *Angew. Chem. Int. Ed.* **2011**, *50*, 10294–10317. (b) Cid, J.; Gulyás, H.; Carbó, J. J.; Fernández, E. *Chem. Soc. Rev.* **2012**, *41*, 3558–3570.
(61) Lee, K.-s.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7253–7255.
(62) (a)Wu, H.; Radomkit, S.; O'Brien, J. M.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 8277–8285. (b) Radomkit, S.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2014**, *53*, 3387–3391.
(63) Kleeberg, C. *et al. J. Org. Chem.* **2012**, *77*, 785–789.
(64) Denmark, S. E.; Beutner, G. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 1560–1638.
(65) For other representative examples, none of which activate a C-B bond, see: (a) O'Brien, J. M.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7712–7715. (b) Kleeberg, C.; Borner, C. *Eur. J. Inorg. Chem.* **2013**, 2799–2806. (c) Wen, K.; Chen, J.; Gao, F.; Bhadury, P. S.; Fan, E.; Sun, Z. *Org. Biomol. Chem.* **2013**, *11*, 6350–6356.

Scheme 1.17 NHC-Catalyzed Allyl-Additions to Phosphinoylimines and Important Control Reactions



Control Reactions



Initial investigations by graduate student Erika Vieira were followed up by post-doctoral researcher Dr. Tatiana Pilyugina. Phosphinoylimines,[66] such as **1.15a** (Scheme 1.17) were chosen as substrates for a variety of reasons. The phosphinoyl protecting group is easily removed under acidic or reducing conditions[67] to afford the free amine in high yield. Moreover, even though this protecting group has a large molecular weight, it significantly eases purifications by increasing the tendency of both the starting imine and the homoallylamide (e.g. **1.17a**) products to be crystalline. In many cases expensive and tedious column chromatography can be altogether avoided, which more than makes up for its otherwise low atom economy. As an example, our group has shown that when the NHC–Cu-catalyzed allyl-addition is performed on a gram-scale, analytically pure product can be isolated in 75% following a simple filtration (no chromatography necessary).[55]

(66) For a review of these compounds, see: Weinreb, S. M.; Orr, R. K. *Synthesis*, **2005**, *8*, 1205–1227.
(67) Burgos, P. O.; Fernández, I.; Iglesias, M. J.; García-Granda, S.; Ortiz, F. L. *Org. Lett.* **2008**, *10*, 537–540.

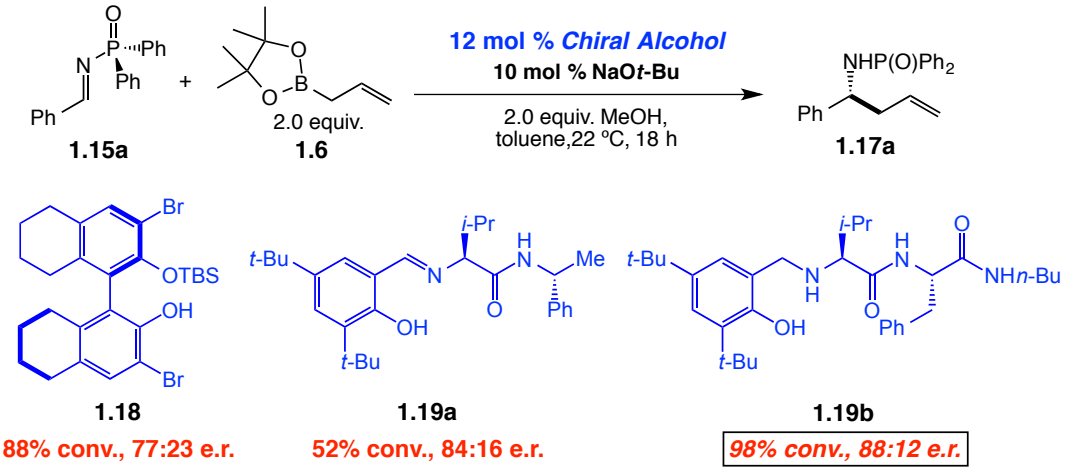
Phosphinoylimines also are suitably activated, having electrophilicities comparable to that of *N*-Boc aldimines.[68] Allylboron **1.6** was chosen due to its aforementioned favorable balance of reactivity and stability, and methanol was determined to be critical for reactivity early on in the study, which was believed to be because it facilitates catalyst turnover.

The equation in the top of Scheme 1.17 is representative of optimized conditions. With 10 mol % catalyst loading of chiral imidazolinium salt **1.16** as the NHC precursor, the reaction proceeds in 58% conversion and affords desired product in nearly racemic (52:48 e.r.) form. Other than the lack of enantioselectivity, reproducibility issues also mar this transformation, with conversions varying as much as +/- 30% from reaction to reaction. Hoping to better understand the system, Dr. Pilyugina carried out a series of critically important control reactions (Scheme 1.17). Fitting in with the hypothesis of an NHC-catalyzed transformation, when the reaction is performed in the absence of NaO*t*-Bu, <5% conversion to **1.17a** is observed. Omitting methanol also leads to <2% conversion. Surprisingly, leaving out imidazolinium salt **1.16** results in a much more efficient transformation, implying that an alkoxide (presumably NaOMe due to the presence of MeOH) is a better catalyst for this transformation than an NHC. Additionally, this base-catalyzed protocol proved to be far more reliable than the NHC-catalyzed one in terms of consistent conversions. It is, however, only capable of producing racemic homoallylamides.

(68) Appel, R.; Mayr, H. *J. Am. Chem. Soc.* **2011**, *133*, 8240–8251.

Dr. Pilyugina then decided to screen catalytic amounts of chiral alcohols[69] to determine if these molecules are capable of engendering an enantioselective transformation. After screening various alcohols as promoters for the enantioselective allylation of aldimine **1.15a**, what gave rise to the highest selectivity was chiral phenol **1.18** (Scheme 1.18).[70] Structural modifications of **1.18**, such as changing the alcohol-protecting group, the nature of the halide substituent, or the backbone (e.g. hydrogenated vs. non-hydrogenated) did not give rise to a more selective catalyst. In order to obtain a more active and selective catalytic reaction, more substantial changes in the structure of **1.18** were investigated. Wanting to keep the phenol moiety intact, amino acid based **1.19a**, based on ligands previously developed in our group, was synthesized.[71] Such

Scheme 1.18 Enantioselective Allyl-Additions Promoted by Chiral Phenols



amino acid based phenols not only afford higher enantioselectivity for the allyl-addition product **1.17a**, they also allow for more rapid structure modification due to their facile

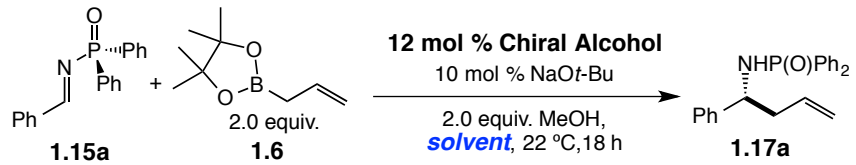
(69) We initially felt that the identity of the active catalyst was a chiral phenoxide that operated in the same way the NHC in Scheme 1.16 is proposed to operate. Mechanistic studies (to be discussed in a later section) suggest that this is not the case.
(70) The choice of this phenol was inspired by other work in our group. See: Malcolmson, S. J.; Meek, S. J.; Sattely, E. S.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2008**, *456*, 933–937.
(71) Cole, B. M.; Shimizu, K. D.; Kruger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **1997**, *35*, 1668–1671.

modularity and ease of synthesis.[71] Changing aminophenol **1.19a** eventually led to a **1.19b**, which was both more efficient and more enantioselective than either **1.18** or **1.19a**. It was at this point that I joined the project. With a promising reaction in hand, we turned our attention to optimization of the reaction through alterations to the structure of **1.19b** and reaction conditions.

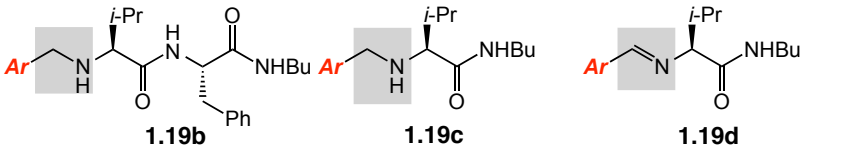
1.4 Development of Enantioselective Allyl-Additions to N-Phosphinoylaldimines Promoted by a Chiral Aminophenol

We initially chose to examine the reaction solvent along with whether the linker between the aryl ring of the phenol and the nitrogen from the amino acid is an amide,

Table 1.3 Screen of Solvent and General Phenol Structure



Catalyst Structures: *Ar*=2-OH-3,5-(*t*Bu)C_6H_2



entry	ligand	*solvent*	conv (%)[a]	e.r.[b]
1	***1.19b***	***toluene***	***98***	***89:11***
2	***1.19c***	***toluene***	***>98***	***88:12***
3	1.19d	toluene	30	74:26
4	1.19e	toluene	94	62:38
5	1.19f	toluene	82	62:38
6	1.19g	toluene	55	racemic
7	1.19b	thf	17	62:38
8	1.19b	CH_2Cl_2	11	66:34
9	1.19e	thf	73	58:42
10	1.19e	CH_2Cl_2	86	racemic
11	1.19f	thf	85	racemic
12	1.19f	CH_2Cl_2	95	racemic

[a] Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture. [b]Determined by HPLC analysis.

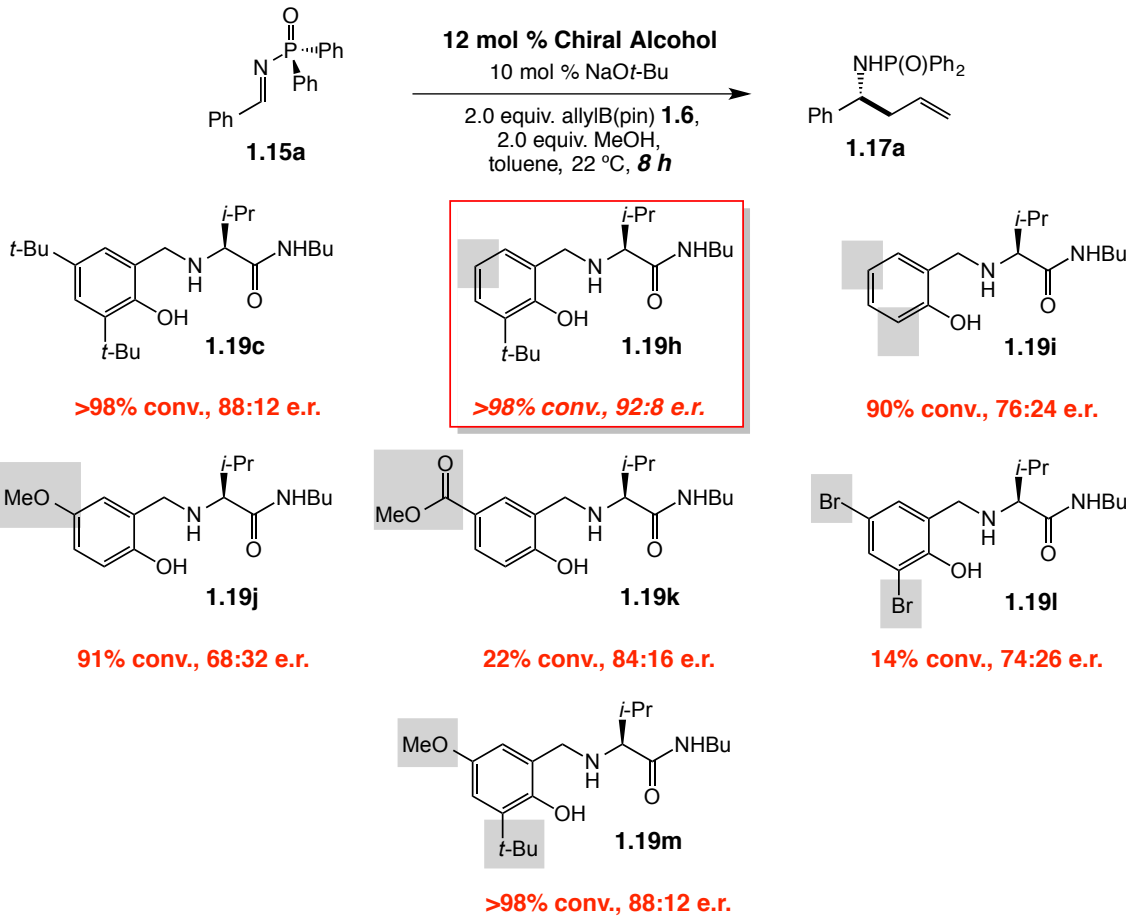
imine, or amine (Table 1.3). Toluene remained the optimal solvent, with reactions performed in more polar solvents furnishing products of low to negligible enantiopurity.

Notably, mono-amino acid containing **1.19c** behaves the same as the previously optimal **1.19b** (compare entries 1 and 2, Table 1.3). Due to the greater facility with which aminophenols bearing a single amino acid can be synthesized, **1.19c** has an inherent advantage over **1.19b**. Imine containing chiral phenol **1.19d** produced homoallylamines with 74:26 er, but was less active than amine containing **1.19b** and **1.19c** (Table 1.3, entries 1-3). Chiral phenols **1.19e** and **1.19f**, which are analogous to **1.19b** and **1.19c** only with an amide instead of amine functionality, show reasonable activity, but promote less enantioselective reactions (entries 1-2 vs. entries 4-5, Table 1). Changing the linker in these molecules results in multiple differences between the resultant compounds, making it difficult to extrapolate as to precisely why **1.19c** promotes a more efficient and enantioselective transformation than **1.19d** or **1.19f**. Imine containing **1.19d** and amide containing **1.19f** have significantly more acidic phenol protons than **1.19c**, which has an amine linker. The linkers in **1.19d** and **1.19f** are also more rigid than the amine linker in **1.19c**. Additionally, the Lewis basicity of the nitrogen is different between these functional groups as is the presence and acidity of any hydrogen on them.

From these preliminary investigations, we decided to carry out modifications to the structure of the chiral phenol, using **1.19c** as a starting point and decreasing the reaction time for the screening reactions from 18 h to 8h. The first site selected for modification was the *N*-terminus (Scheme 1.19). Removal of the *tert*-butyl group *para* to the phenol (**1.19h**) affords higher selectivities. Comparing **1.19h** with **1.19i** or **1.19j** with

1.19m, it becomes clear that the *tert*-butyl group *ortho* to the phenol is important for both reactivity and enantioselectivity. The electron poor phenols **1.19k** and **1.19l** are less active than the more electron rich compounds **1.19j** and **1.19m**, although comparing the series of **1.19i-k** suggests electron poor aminophenols are more enantioselective. With the further optimized structure represented by **1.19h** in Scheme 1.19, we turned our attention to determining the ideal amino acid to incorporate into this aminophenol.

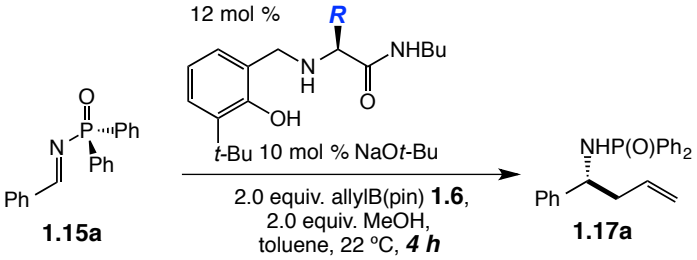
Scheme 1.19 Modifications to Aminophenol *N*-Terminus



Reducing the reaction time further (from 8 h in Scheme 1.19, to 4 h in Table 1.4), we were pleased to see that the reaction featuring aminophenol **1.19h** still proceeds to full conversion (entry 1, Table 1.4). Altering the amino acid moiety of the aminophenol shows that incorporation of amino acids lacking α-branching give rise to catalytic

reactions that are less efficient than when incorporating amino acids bearing α-branching (compare entries 1, 2, 4, and 9 with 3, 5, 6, and 8, Table 1.4). The amino acids valine or *tert*-leucine emerged as the top two candidates, and we decided to continue using valine in synthesis of new aminophenols due to its substantially lower price when compared to *tert*-leucine (entries 1 and 4, Table 1.3). Next, we focused on modification of the *C*-terminus of the chiral phenoxide precursors in the hopes of generating a more selective and efficient catalytic reaction.

Table 1.4 Modifications to Amino Acid Substituent

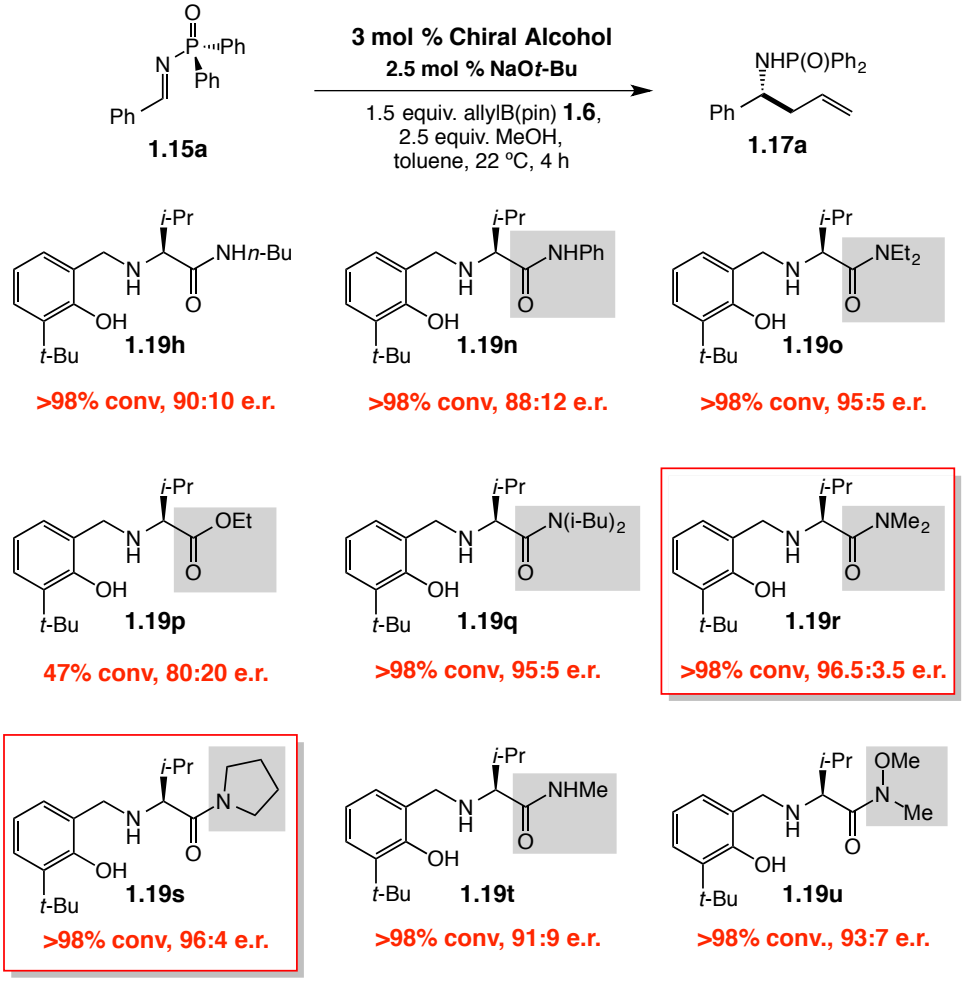


entry	*R*	conv (%)[a]	e.r.[b]
1	**Val (1.19h)**	>98	92:8
2	**Ile**	>98	89:11
3	**Leu**	83	81:19
4	**Tle**	>98	95:5
5	**Phe**	22	79:21
6	**Cys(Bn)**	28	73:27
7	**Thr(O*t*-Bu**	>98	61:39
8	**Ser(O*t*-Bu)**	42	72:28
9	**Phg**	93	58:42

[a] Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture. [b]Determined by HPLC analysis.

We were curious to learn whether the proton located on the amide nitrogen of the aminophenol is critical to the catalysts' reactivity or selectivity (Scheme 1.20). Intriguingly, not only is this proton non-essential for reactivity or selectivity, reactions with tertiary amide containing **1.19o** are more enantioselective than those from secondary amide containing **1.19h** and **1.19n** (Scheme 1.20). When the amide is changed to an ester, the efficiency and enantioselectivity of the catalytic reaction is greatly diminished (**1.19p**). Such a decrease likely indicates the importance of the Lewis basicity of the

Scheme 1.20 Modifications to Aminophenol *C*-Terminus



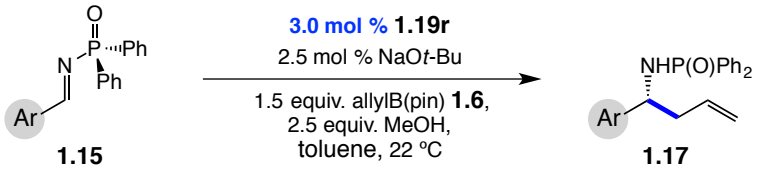
carbonyl group on the catalyst. To determine if the increase in selectivity between **1.19h** and **1.19o** could be simply from an increase in sterics (rather than an increase in Lewis basicity), the size of the amide group was further increased to diisobutylamide containing **1.19q**. As **1.19q** promotes a reaction that is essentially identical to that with smaller diethylamide containing **1.19o**, it suggests that increasing the sterics of the amide does not increase the enantioselectivity of the transformation. Changing the amide to a dimethylamide (**1.19r**) or a pyrrolidinyl amide (**1.19s**) should increase the Lewis basicity of the carbonyl due to an increased overlap of the nitrogen lone pair with the π-orbitals of

the carbonyl.[72] Further supporting the idea that a stronger Lewis basic carbonyl results in a more selective catalyst, these two aminophenols afford products in the highest enantiomeric ratios observed thus far for this class of catalysts (Scheme 1.20). Again examining size, to confirm that this increase in enantioselectivity was not due to decreasing the size of the substituents on the nitrogen of the amide, sterically smaller **1.19t**, derived from methylamine, was synthesized and employed in the transformation being studied. It behaves the same to **1.19h**, suggesting optimal aminophenols **1.19r** and **1.19s** are not more selective than **1.19h** simply because they are smaller in size. Spectroscopically, the carbonyl's Lewis basicity can be observed, since the IR stretching frequency correlates with bond strength. Weakening of the carbonyl bond leads to more single bond character (and a lower IR frequency), which leads to more anionic-like properties of the oxygen, and thus a stronger Lewis base. The carbonyl expected to have the highest Lewis basicity is that of pyrrolidine derived **1.19s**,[72] and the amide carbonyl in this compound has a stretching frequency of 1632 cm^{-1}. Moving through a representative list, dimethylamine derived **1.19r** has a stretching frequency of 1638 cm^{-1}, *n*-butylamine derived **1.19h** has a stretching frequency of 1644 cm^{-1}, aniline derived **1.19n** has a stretching frequency of 1655 cm^{-1}, and ethyl ester containing **1.19p** has a stretching frequency of 1728 cm^{-1}.

Having developed a suitable aminophenol for use in the catalytic enantioselective synthesis of homoallylamide **1.17a**, we subsequently focused on modifying the aldimine substrate to probe what structural features are tolerated by our newly established protocol. Examining different aryl-substituted aldimines (Table 1.5) shows that the

(72) (a) Hickmott, P. W. *Tetrahedron* **1982,** *38*, 1975–2050. (b) Spivey, A. C.; Arseniyadis, S. *Angew. Chem. Int. Ed.* **2004**, *43*, 5436–5441.

Table 1.5 Allyl-Additions to Aryl-Substituted Imines



1.15 **1.17**

entry	Ar	time (h)	conv. (%)[a]	yield (%)[b]	e.r.[c]
1	Ph; **1.15a**	4.0	>98	95	96.5:3.5
2	*o*-FC_6H_4; **1.15b**	4.0	>98	91	98:2
3	*o*-BrC_6H_4; **1.15c**	4.0	>98	86	97.5:2.5
4	*o*-MeC_6H_4; **1.15d**	6.0	>98	91	93.5:6.5
5	*m*-BrC_6H_4; **1.15e**	4.0	>98	95	98:2
6	*p*-BrC_6H_4; **1.15f**	6.0	>98	91	97:3
7	*p*-$CF_3C_6H_4$; **1.15g**	4.0	>98	93	98:2
8	*p*-$MeO_2CC_6H_4$; **1.15h**	4.0	>98	98	98:2
9	*p*-$MeOC_6H_4$; **1.15i**	4.0	>98	98	96.5:3.5
10	*p*-MeC_6H_4; **1.15j**	4.0	>98	98	96.5:3.5
11	*p*-(*n*-Bu)$_2C_6H_4$; **1.15k**	4.0	95	93	92:8
12	2-furyl; **1.15l**	6.0	>98	93	98:2
13	3-pyridyl; **1.15m**	4.0	90	75	98:2
14	4-pyridyl; **1.15n**	6.0	98	74	98:2

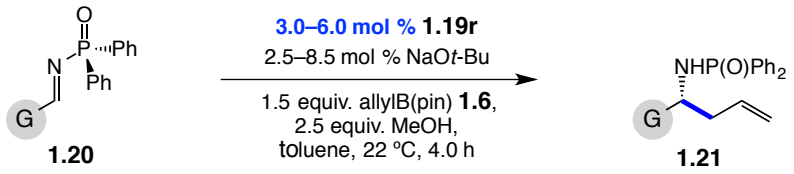
All data are the average of at least two trials. [a]Conversion to the desired product as measured by analysis the 400 MHz ^{1}H NMR specta of the unpurified reaction mixture versus an internal standard of 9-methylanthracene. [b]Yield of isolated product. [c]Determined by HPLC analysis. See experimental section for details.

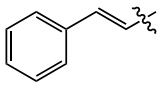
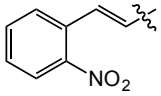
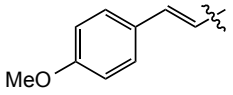
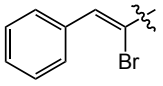
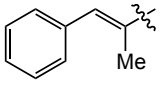
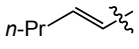
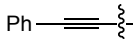
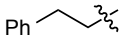
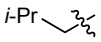
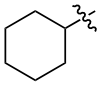
method tolerates a wide range of aryl-groups, including those that are *ortho*-substituted as in entries 1 to 4 (although increasing the size of this group to a methyl group results in a small reduction in enantioselectivity and reactivity, see entry 4), *meta*-substituted (entry 5), electron poor (entries 6 to 8), electron rich (entries 9 to 11), as well as heterocycles containing oxygen (entry 12) and nitrogen (entries 13 and 14). A general trend is that reactions with substrates that contain electron poor groups are more efficient and enantioselective than those with electron rich structures.

Alkenyl-substituted aldimines (Table 1.6) undergo allyl-addition to form nearly a single enantiomer in most cases (entries 1 to 3), although increasing the sterics of the olefin moiety does lead to lower enantioselectivities, and in some cases, reactivities, as exemplified by comparing aldimines **1.20a** to **1.20c** with **1.20d** and then **1.20e** (Table 1.6). Even the homoallylamide derived from the aldimine containing a sterically small

alkynylaldimine **1.20g** is afforded in a synthetically useful enantiomeric ratio of 88:12 (entry 7, Table 1.6). Catalytic enantioselective allylation of aliphatic aldimines afforded

Table 1.6 Allyl-Additions to Alkenyl-, Alkynyl-, and Alkyl-Substituted Imines



entry	G		**1.19r** (mol %); NaO*t*-Bu (mol %)	conv. (%)[a]	yield (%)[b]	e.r.[c]
1		**1.20a**	3.0; 2.5	>98	84	>99:1
2		**1.20b**	3.0; 2.5	>98	95	>99:1
3		**1.20c**	3.0; 2.5	>98	98	>99:1
4		**1.20d**	3.0; 2.5	>98	96	98:2
5[d]		**1.20e**	3.0; 2.5	85	76	93:7
6		**1.20f**	3.0; 2.5	>98	95	98:2
7		**1.20g**	3.0; 2.5	>98	95	88:12
8		**1.20h**	6.0; 5.0	66	50	>99:1
9		**1.20i**	6.0; 5.0	70	51	>99:1
10		**1.20j**	6.0; 8.5	90	71	97.5:2.5

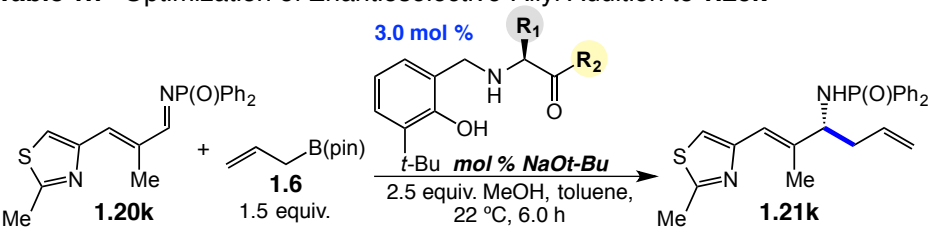
All data are the average of at least two trials. [a]Conversion to the desired product as measured by analysis the 400 MHz ^{1}H NMR specta of the unpurified reaction mixture versus an internal standard of 9-methylanthracene. [b]Yield of isolated product. [c]Determined by HPLC analysis. [d]Reaction time = 8.0 h. See experimental section for details.

highly enantiomerically enriched homoallylamides (>97:3 e.r.) but only in 50-71% isolated yield (Table 1.6). Examining the ^{1}H NMR spectra of the unpurified reaction mixture in entry 8 or 9 reveals no starting material present but approximately 20% of a

hemiaminal ether derived from addition of methanol to the starting imines.[73] This suggests that the lower yields observed stem from decomposition of alkyl aldimines during the reaction. Extensive modifications to reaction conditions, such as increased reaction time and catalyst loading, decreased reaction temperature, other protic additives, slow addition of methanol or substrate, or increasing the amount of allylboronate **1.6** do not result in higher yields. For α-branched imine **1.20j**, a slight excess of NaO*t*-Bu led to a cleaner reaction, possibly by favoring collapse of the hemiaminal to the imine (entry 10, Table 1.6). Applying this modification to γ- or β- branched aliphatic aldimines (entries 8 and 9, Table 1.6) led to no improvement in yield, likely due to their decreased sterics not favoring the collapse of the hemiaminal ether intermediates to the starting imine.

In order to further challenge the method as well as demonstrate the synthesis of compounds that can serve as intermediates in the synthesis of biologically active compounds, we targeted the aldimine **1.20k** as a substrate (Table 1.7). The resultant

Table 1.7 Optimization of Enantioselective Allyl Addition to **1.20k**



entry	*NaOt-Bu* (mol%)	R_1 ; R_2	conv. (%)[a]	yield (%)[b]	e.r.[c]
1	2.5	*i*-Pr; NMe_2; **1.19r**	91	75	92:8
2	5.0	*i*-Pr; NMe_2; **1.19r**	>98	76	93.5:6.5
3	10	*i*-Pr; NMe_2; **1.19r**	>98	77	93.5:6.5
4	20	*i*-Pr; NMe_2; **1.19r**	>98	89	93.5:6.5
5[d]	20	*i*-Pr; pyrrolidine; **1.19s**	>98	86	95.5:4.5
6	20	*t*-Bu; NMe_2; **1.19v**	>98	83	96:4

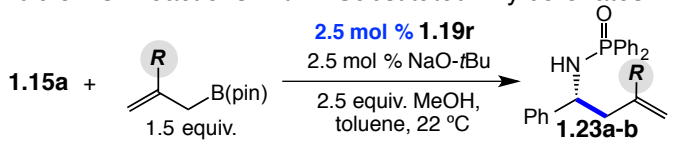
[a]Conversion to the desired product as measured by analysis the 400 MHz ^{1}H NMR specta of the unpurified reaction mixture versus an internal standard of 9-methylanthracene. [b]Yield of isolated product. [c]Determined by HPLC analysis. [d]Data are the average of two trials. See experimental section for details.

(73) The ^{1}H NMR spectrum of the unpurified reaction mixture in entry 8 does not show this hemiaminal.

homoallylamine can be used to synthesize the anti-cancer agent aza-epothilone A (Scheme 1.3). Performing this transformation under the conditions used for previous enantioselective allyl-additions to aldimines led to less than complete conversion as well as a less-than-ideal enantioselectivity (entry 1, Table 1.7). This is likely due to the sterics of the alkenyl substituent, rather than the presence of the thiazole, since the aldimine **1.20e** (Table 1.6), which has a comparably sized aldimine substituent, behaves similarly. To improve the transformation, we first increased the amount of NaO*t*-Bu, which we had occasionally observed to improve the enantioselectivity and reactivity of the aminophenol-promoted enantioselective allyl addition. By making this change, the yield of **1.21k** was increased along with its enantiopurity (Table 1.7, entries 1 to 4). Modifications to the aminophenol utilized led to an increase in the enantioselectivity of the transformation. The pyrrolidine containing aminophenol **1.19s** was chosen as optimal because although it promotes reactions with similar efficiency and enantioselectivity as aminophenol **1.19v**, pyrrolidine is cheap and readily available while *tert*-Leucine, needed for the synthesis of **1.19v**, is not.

In the interest of further displaying reaction generality, the scope of the reaction was expanded to include 2-substituted allylboronates in addition to the previously studied

Table 1.8 Reactions with 2-Substituted Allylboronates



entry	R	time (h)	conv. (%)[a]	yield (%)[b]	e.r.[c]
1	Me; **1.22a**	4.0	>98	96	97.5:2.5
2	Ph; **1.22b**	6.0	>98	98	97.5:2.5

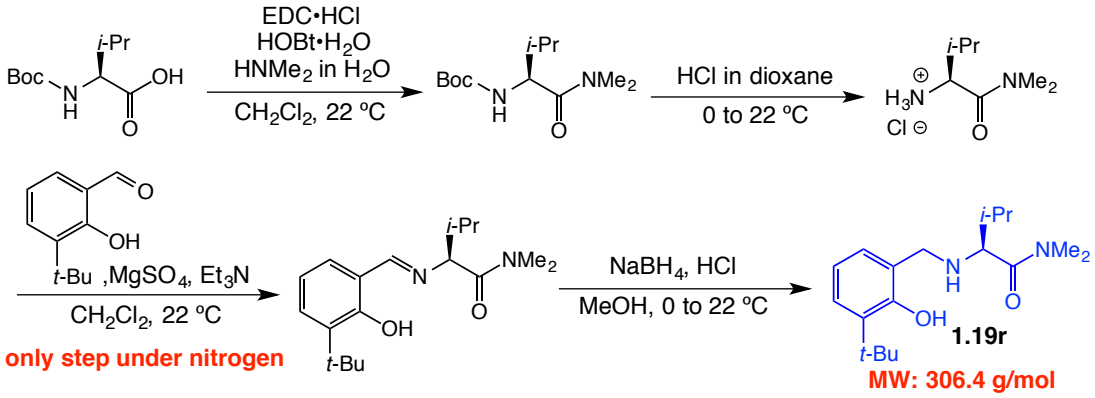
All data are the average of at least two trials. [a]Conversion to the desired product as measured by analysis the 400 MHz ^{1}H NMR specta of the unpurified reaction mixture versus an internal standard of 9-methylanthracene. [b]Yield of isolated product. [c]Determined by HPLC analysis. See experimental section for details.

unsubstituted **1.6** (Table 1.8). These reactions proceed efficiently to afford the desired products in both high yield and enantioselectivity (Table 1.8).

Favorable aspects regarding the practicality of the enantioselective allyl-addition to aldimines promoted by aminophenol **1.19r** deserve special mention. The aminophenol

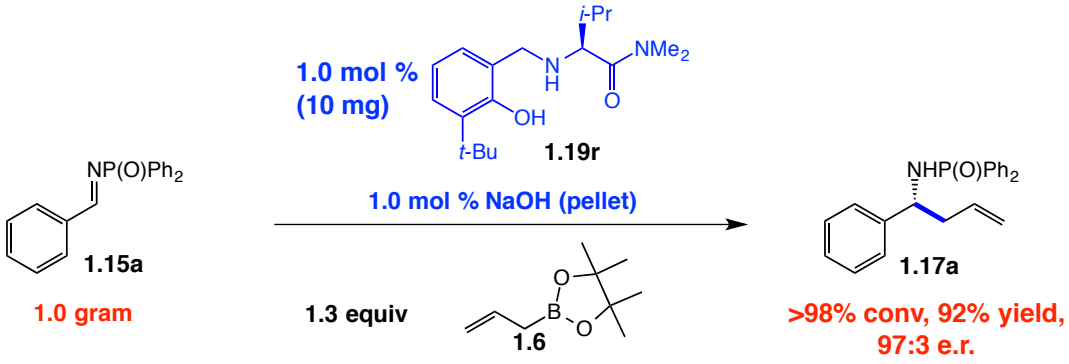
Scheme 1.21 Practicality of Method

a) Ease of Aminophenol Synthesis:



- **73% yield over four steps (~5 g scale).**
- **No silica gel chromatography required.**
- **Crystalline solid; Indefinitely stable at 22 °C.**
- **All reagents commercially available for <$5/mmol**

b) Ease of Catalytic Reaction:



1.5 equiv. MeOH, toluene, **22 °C, 2.0 h**

- **Performed in a common fume hood.**
- **Reaction vessel not flame dried.**
- **Commercial (as received) allyB(pin), NaOH, MeOH used.**
- **Workup: only solvent evaporation.**
- **Product purification: trituration (silica gel chromatography not needed).**

takes only four simple steps to synthesize and can be performed on approximately a 5g scale to afford **1.19r** in 73% yield *without the use of silica gel chromatography*. Just one step is performed under a nitrogen atmosphere (all others can be performed in an open reaction vessel, Scheme 1.21a) with reagents that are all commercially available for less than $5/mmol. The most expensive component is the 3-*tert*-butyl-salicylaldehyde ($4.5/mmol from Aldrich); all other components are less than $0.20/mmol. Importantly, the other enantiomer of **1.19r** is easily accessible, as Boc-D-Valine is only $0.50/mmol (from Advanced Chemtech, where we purchase most of our amino acids; for comparison, Boc-L-Valine is $0.19/mmol).

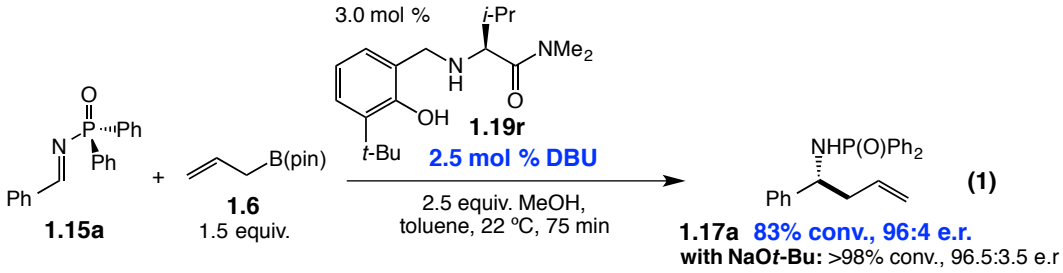
Additionally, the allyl-addition can be performed on a gram scale outside of a glovebox with reagents that were used as received.[74] Using only 1.0 mol% of the aminophenol and less reactive NaOH (instead of NaO*t*-Bu), the transformation proceeds to full conversion in two hours, affording homoallylamide **1.17a** in 92% yield and 97:3 e.r. The product is purified after the reaction by trituration (again, *no silica gel chromatography is necessary*), and **1.17a** obtained in this manner passes elemental analysis after being put under vacuum (~1 Torr) overnight to remove solvent.

1.5 Investigation of Reaction Mechanism

Following these studies to illustrate the efficiency, enantioselectivity, and utility of this new catalytic transformation, we turned our attention to elucidating a plausible reaction mechanism. We began by ruling out the possibility that a small impurity of a transition metal in the NaO*t*-Bu used in the reaction was actually the active catalyst in

(74) The methanol purchased does need to be of the anhydrous variety. The toluene used was dispersed from a solvent purification system. See the experimental section for details. The reaction must be performed under a nitrogen atmosphere.

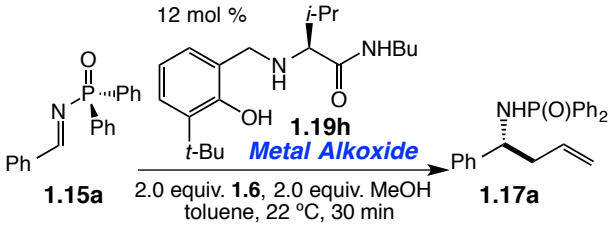
this transformation.[75] As shown in Eq. 1, freshly distilled amide base 1,8-diazabicycloundec-7-ene (DBU) promotes a comparably efficient and enantioselective transformation to NaO*t*-Bu, suggesting that a transition metal impurity does not play a critical role in the catalytic cycle. The drop in efficiency (Eq. 1) likely stems from the difference in pKa between NaO*t*-Bu and DBU. This experiment also confirms that the



(1)

structure of the base does not play a significant role in determining enantioselectivity, since the disparate structures of DBU and NaO*t*-Bu lead to essentially the same enantioselectivity. Following this trend, the countercation of the metal alkoxide (Table 1.9) also does not greatly affect the transformation (although Zn(O*t*-Bu)$_2$ does lead to a slightly more efficient transformation), which we discovered during initial optimization

Table 1.9 Initial Optimization of Metal Alkoxide



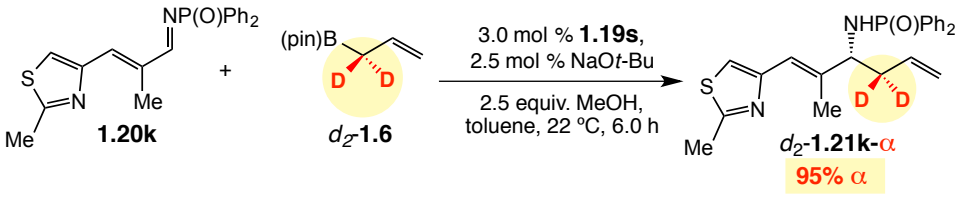
entry	MO*t*-Bu	conv (%)[a]	e.r.[b]
1	NaO*t*-Bu; 10 mol %	88	93:7
2	LiO*t*-Bu; 10 mol %	79	93:7
3	Zn(O*t*-Bu)$_2$; 5.0 mol %	>98	92:8

[a] Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture. [b]Determined by HPLC analysis.

(75) For a representative example, see: Arvela, R. K.; Leadbeater, N. E.; Sangi, M. S.; Williams, V. A; Granados, P.; Singer, R. D. *J. Org. Chem.* **2005**, *70*, 161–168.

of the reaction (note the aminophenol in Table 1.9 is not the optimal aminophenol, but the one from preliminary studies).

A crucial observation for understanding the reaction mechanism, shown in Eq. 2, is that the enantioselective allyl-addition greatly favors the formation of α-addition products (that is, the carbon of the allyl group directly attached to the boron of the nucleophile becomes the carbon of the allyl group directly attached to the newly formed stereogenic carbon in the homoallylamide) versus the γ-addition product, which is far

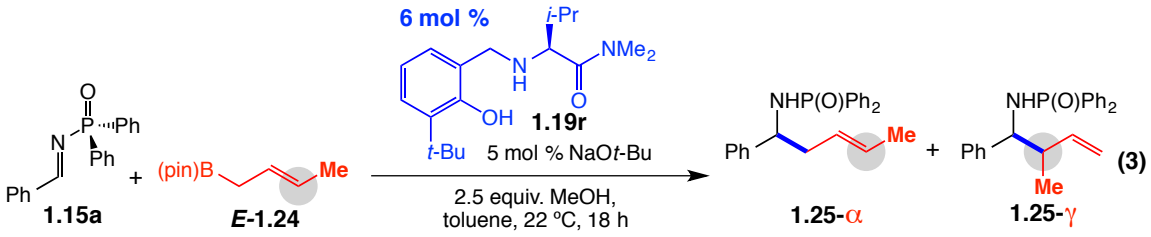


(2)

more common for transformations involving an allylboronate (see Scheme 1.11 and its discussion).[44] This result is surprising because all other reported α-selective additions to carbonyls or imines involving allylborons as the nucleophile are proposed to obtain their selectivity through an allylmetal[76] intermediate or a metal-catalyzed rearrangement.[43-45,53] The α-selectivity of the more commonly encountered/proposed allylmetal intermediates is therefore strongly dependent on the substitution of the allylboron, with nucleophiles bearing only deuterium substitution (such as d_2-**1.6** in Eq. 2) affording a 1:1 mixture of α- and γ-addition products due to the propensity of such allylmetals to readily isomerize.[53,77,78]

(76) For a review on the reactivity and selectivity of allylmetals, see: Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
(77) Schneider, U.; Dao, H. T.; Kobayashi, S. *Org. Lett.* **2010**, *12*, 2488–2491.
(78) For an example of an α-selective conjugate addition of d_2-**1.6** that is proposed to go through an allylpalladium species, see: Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 4978–4983.

Knowing that our newly developed reaction afforded products with α-selectivity, we sought to determine whether this selectivity arose from two γ-selective additions[43-45,53] leading to a *net α-addition* (such as the process shown in Scheme 1.11), *or a single α-addition*.[79] If the catalyst operates through a *single α-addition*, then the terminal methyl group of *trans*-crotylboronate ***E*-1.24** (Eq. 3) should not affect the transformation. As seen in Equation 3, use of ***E*-1.24** leads to a far less efficient transformation (though notably still an α-selective one),[80] suggesting that the catalyst operates through two γ-selective additions (*net α-addition*).[44c]



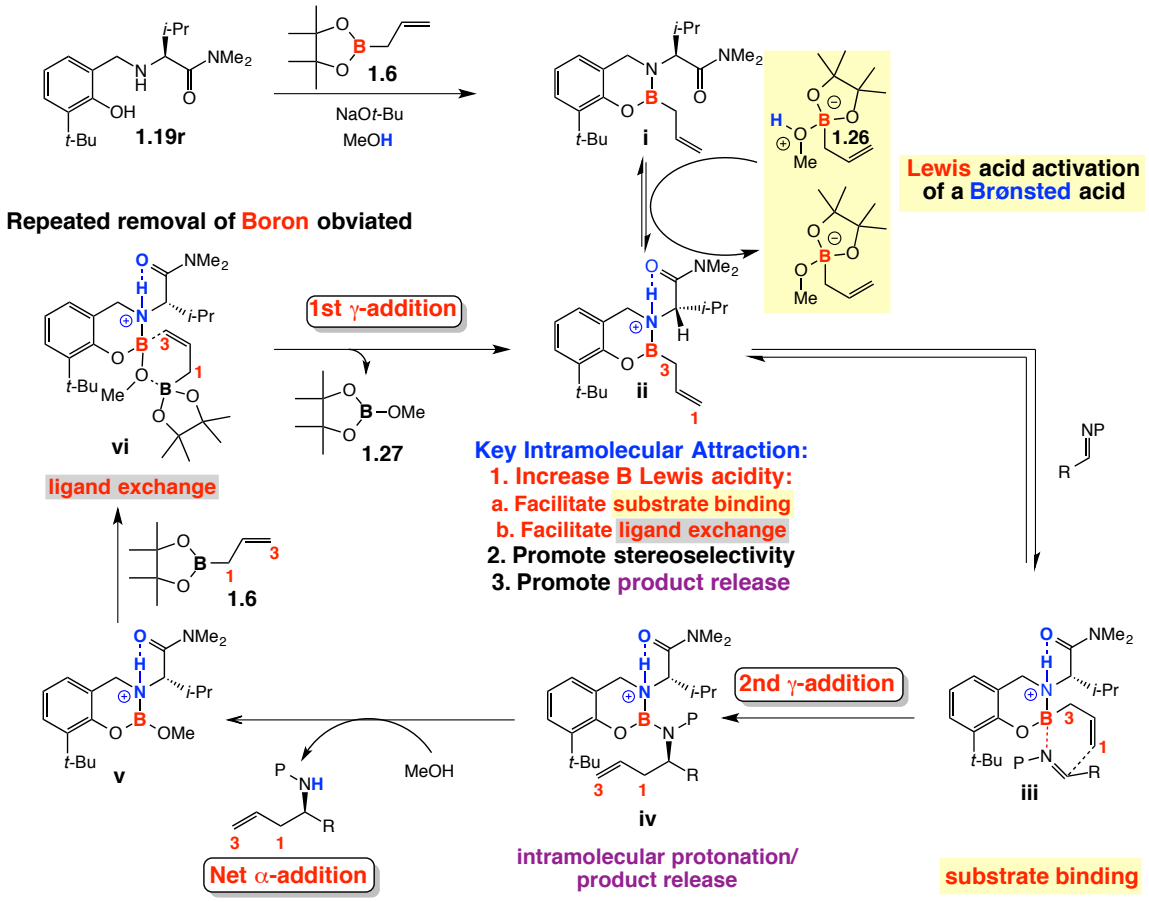
If catalyst operates through a ***single*** α–addition, then this distant **Me** should not affect reactivity

These and other mechanistic and computational experiments (to be discussed in further detail below) led us to propose the catalytic cycle illustrated in Scheme 1.22. Reaction of aminophenol **1.19r** with allylboronic acid pinacol ester **1.6** in the presence of NaO*t*-Bu and MeOH forms chiral allylboron **i**, which we propose is protonated by **1.26** (a Lewis acid activated by a Brønstead acid) to form **ii**.[81] Although the presence of NaO*t*-Bu in solution makes it tempting to refer to the reaction conditions as overall basic, the

(79) For a related transformation where aryl-, alkenyl-, and alknylboronates are added to imines through a single α-addition, see: Bishop, J. A.; Lou, S.; Schaus, S. E. *Angew. Chem. Int. Ed.* **2009**, *48*, 4337–4340.
(80) Increasing reaction time did not significantly increase conversion (~40% conv. after 48h).
(81) For relevant reviews, see: (a) Yamamoto, H.; Futatsugi, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 1924–1942. (b) Yamamoto, H.; Futatsugi, K. "Chapter 1: Recent Advance of 'Combined Acid' Strategy for Asymmetric Catalysis" in *Acid Catalysis in Modern Organic Synthesis*; Yamamoto, H.; Ishihara, K. Eds.; Wiley-VCH: Weinheim, Germany, **2008**.

stoichiometric amount of MeOH and allylboronate **1.6** makes it more accurate to describe the reaction mixture as a buffered acidic solution. This proton in **ii**[82] we propose is key for a variety of reasons, including: 1) The Lewis acidity of **ii** is greatly increased, which

Scheme 1.22 Catalytic Cycle Explaining α-Addition and Highlighting a Key Protonation



promotes substrate binding (**ii→iii**), allyl-addition to the imine (**iii→iv**), and exchange of the allyl ligand from **1.6** onto the catalyst (**v→vi→ii**). 2) The intramolecular attraction[83] of the amide carbonyl to the proton locks the arm containing the stereogenic center into place, increasing structural rigidity, which allows for better discrimination of the

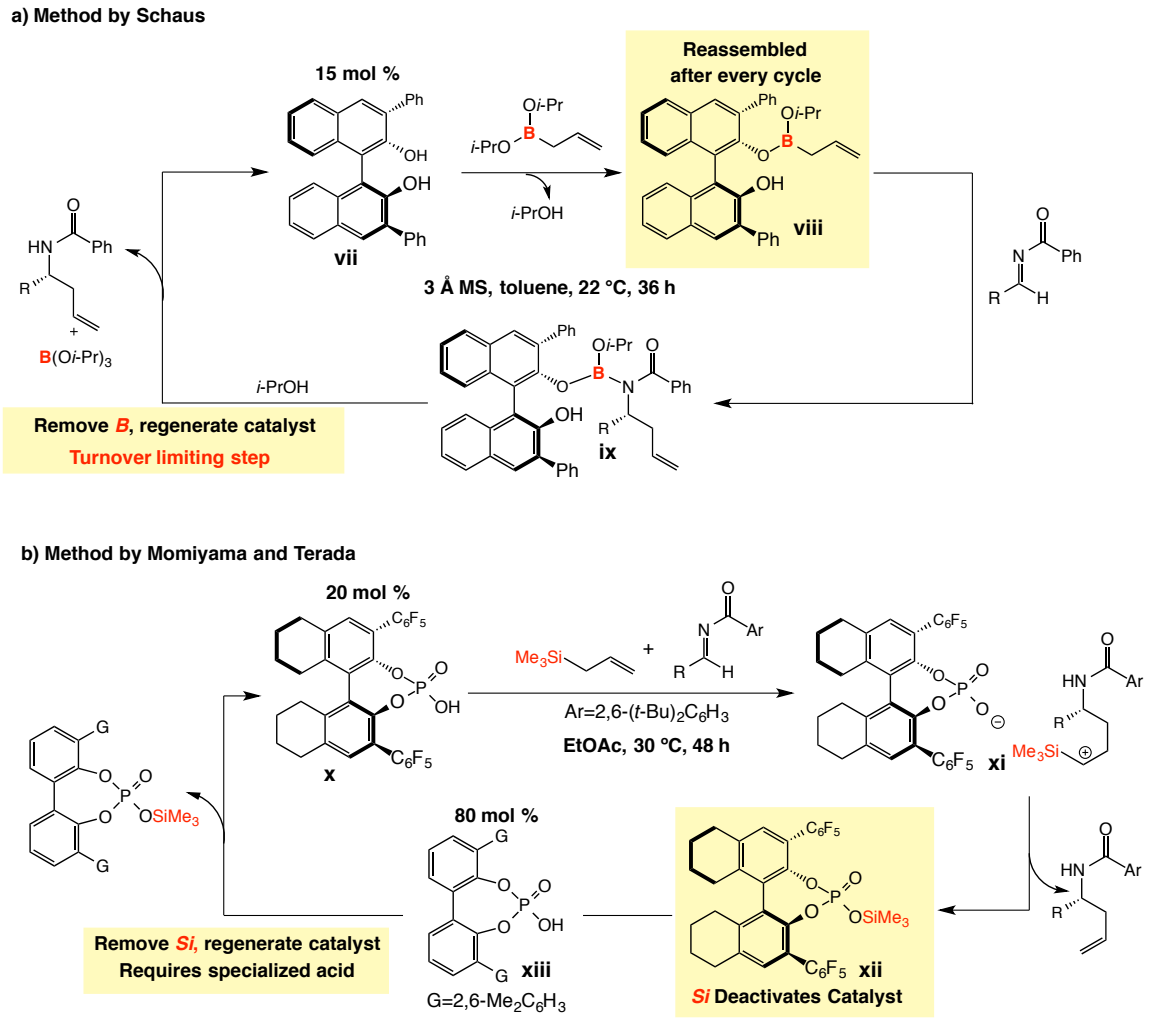
(82) For a review of the such compounds, see: De Vries, T. S.; Prokofjevs, A.; Vedejs, E. *Chem. Rev.* **2012**, *112*, 4246–4282.

(83) We use the term 'intramolecular attraction' instead of hydrogen bond due to the relative rarity of five-membered intramolecular hydrogen bonds. See: Kuhn, B.; Mohr, P.; Stahl, M. *J. Med. Chem.* **2010**, *53*, 2601–2611.

enantiotopic faces of the substrate. 3) The presence of the proton in **iv** allows for intramolecular protonation of the catalyst-homoallylamide N-B bond, facilitating product release and catalyst turnover (Scheme 1.22).

Another factor that facilitates catalyst turnover is that it is the same boron molecule bound to the aminophenol throughout catalytic turnover (from **ii** all the way back to **ii**), obviating removal of the aminophenol from boron after each catalytic cycle (as well as reformation of the active catalyst) and likely increasing catalytic efficiency. It is this catalyst release step that plagues other metal-free allyl-additions to aldimines

Scheme 1.23 Problematic Catalyst Release Steps in Previous Metal-Free Catalytic Methods for Imine Allylation



(Scheme 1.23). In a method by Schaus,[46] the B-O bond in **ix** must be cleaved to afford free catalyst **vii**; this catalyst must then exchange onto the allylboronate to afford chiral allylboronate **viii** (Scheme 1.23a).[84] Mechanistic studies support this catalyst regeneration (**ix** to **vii**) is the turnover-limiting step.[50] Avoiding this step (as well as the reformation step of **vii** to **viii**) is likely an important reason as to why our methodology is so much more efficient.

Catalyst turnover is also problematic in a method developed in the laboratories of Momiyama and Terada (Scheme 1.23b).[39] Silylated catalyst **xii** is not effective at promoting the reaction and removal of this silyl group (**xii→x**) requires an equivalent of specially synthesized acid **xiii**, which is about as difficult to access as **x** itself. All other acids examined by the authors lead to much lower levels of enantioselectivity. Not having to release the catalyst from the residual heteroatom of the allyl group (in our case, boron; in Momiyama and Terada's case, silicon) precludes such a complication.

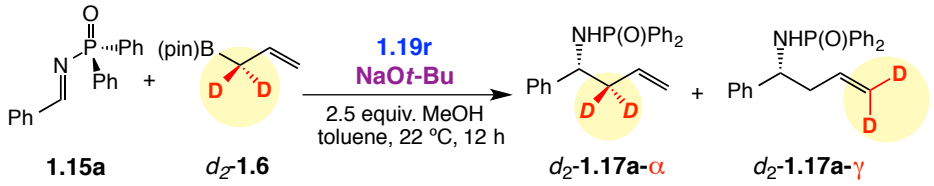
Scheme 1.22 also accounts for the observed α-selectivity. Starting from **v**, allyl transfer from **1.6** occurs through a γ-selective S_E2' addition (**vi**) to form **ii**. Note the reversal of the 1 and 3 carbons of the allyl group, labeled in red, from **1.6**. to **ii**. A second γ-selective allylation (**ii→iv**; again, note the labeled 1 and 3 carbons) results in a homoallylamide that is the product of net α-addition (Scheme 1.22).

If initial chiral allylboron **i** (Scheme 1.22) is formed through simple exchange of aminophenol **1.19r** with the pinacol of **1.6**, the initial homoallylamides formed should be γ-selective since there would only be a single γ-selective allylation (**ii→iv**); subsequent

(84) A later theoretical study strongly suggests that the identity of active catalyst is actually when both phenols of the catalyst exchange onto the allylboronate to form two covalent O-B bonds, rather than just one as shown in **viii** (Scheme 1.23). Paton, R. S.; Goodman, J. M.; Pellegrinet, S. C. *Org. Lett.* **2009**, *11*, 37–40.

catalyst turnovers would be α-selective. It therefore stands to reason that increasing the catalyst loading would result in lower α-selectivity; however, as seen in entries 1 to 3 in Table 1.10, this is not the case. No change in the α to γ selectivity suggests three

Table 1.10 Regioselectivity as a Function of Catalyst Loading



1.15a d_2-**1.6** d_2-**1.17a-α** d_2-**1.17a-γ**

entry	**1.19r** (mol %)	**NaO*t*-Bu** (mol %)	d_2-**1.6** α:γ[a]	d_2-**1.17a** α:γ[a]
1	**3.0 mol %**	**2.5 mol %**	92:8	91:9
2	**12 mol %**	**10 mol %**	92:8	92:8
3[b]	**30 mol %**	**25 mol %**	92:8	92:8
4	**0 mol %**	**2.5 mol %**	97:3	88:12

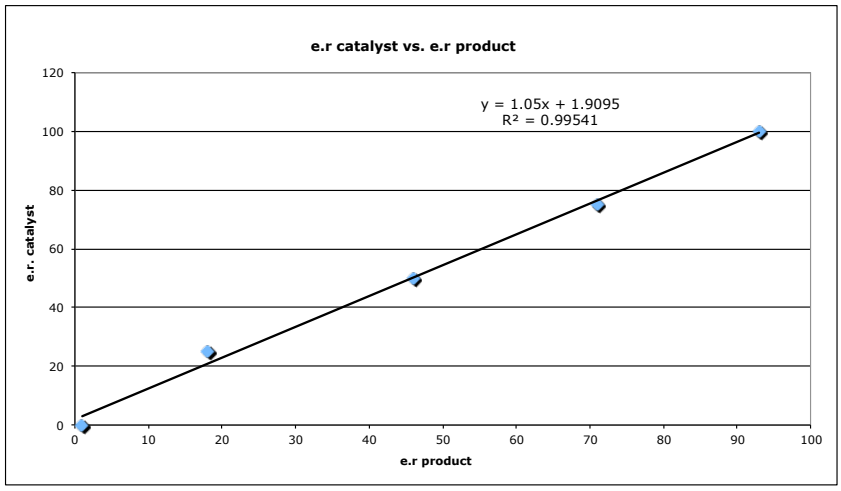
[a] Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction of purified compound. These ratios are ≤2% different from those obtained through 76 MHz ^{2}H NMR. [b] Average of two trials.

possibilities: 1) Formation of **i** from **1.6** does not proceed through a simple ligand exchange. 2) The initial catalyst formed is **v**, which goes on to form **ii**. 3) Under catalytic conditions, only a small fraction of aminophenol **1.19r** is initiated to form **i**, meaning most of the aminophenol added does not enter the catalytic cycle. We do not yet have definitive proof as to which of these scenarios is operative. An extremely surprising result in Table 1.10 is that even without the aminophenol, the reaction is still noticeably α-selective (entry 4), indicating that the alkoxide catalyzed allyl-addition is more mechanistically interesting than originally proposed in Scheme 1.16 (Lewis base activation of allylboron.[85] To better understand factors contributing to the enantioselectivity of the catalytic protocol, we first investigated if there is an observable

(85) Studying the reaction mechanism of such a transformation is a worthwhile endeavor; unfortunately, such studies are yet to be carried out.

non-linear effect.[86] Plotting the ee of the aminophenol **1.19r** vs. the ee of the product **1.17a** (conditions from entry 1 of Table 1.5) affords a straight line (Graph 1.1), which does not suggest that more than one molecule of aminophenol is present in the enantio-determining step (although it does not rule it out). Kinetic studies by Dr. Sebastian Torker indicate a buildup of negative charge on the aldimine in the turnover-limiting step (ρ value of +1.3, see experimental section for details), likely meaning this step is the allyl-addition to the aldimine.

Graph 1.1 Investigation of Nonlinear Effects



1.5.1 Investigation of Reaction Mechanism-Computational and Spectroscopic Studies

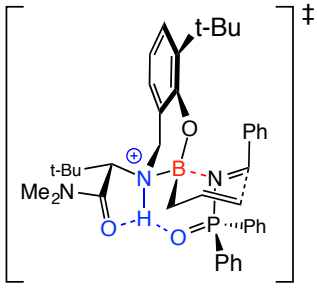
Computational studies (see experimental section for details) by Dr. Fredrik Haeffner to elucidate the stereochemical model were critical to this study, as it was these studies that led him to initially propose protonation of the aminophenol-allylboron complex (**i→ii**; Scheme 1.22). The aminophenol derived from L-*tert*-leucine **1.19v** (Table 1.7) was modeled instead of **1.19r** due to fewer possible conformers present in **1.19v** (Scheme 1.24). The transition state leading to the major (*R*) enantiomer observed

(86) Kagan, H. T.; Luukas, T. O. "Chapter 4: Non-Linear Effects and Autocatalysis" in *Comprehensive Asymmetric Catalysis, Volume I*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: Heidelberg, Germany, **1999**.

is shown in Scheme 1.24a. We propose the protonated amine of the catalyst plays yet another influential role by forming a six-membered hydrogen bond with the phosphinoyl

Scheme 1.24 Stereochemical Model Based on Calculations

a) Calculated Transition State Complex Which Leads to the *R* (Major) Enantiomer

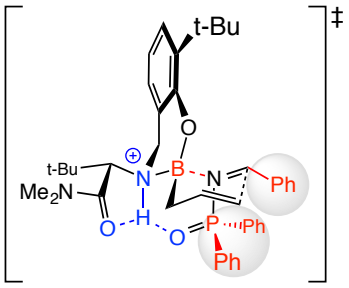


***R*-TS1.1**

0.0 kcal/mol

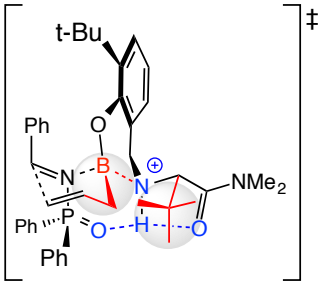
Please Note: The energy of complex ***R*-TS1.1** is used as a zero point reference.

b) Calculated Transition State Complexes Which Lead to the *S* (Minor) Enantiomer and their Energies Relative to *R*-TS-1.1



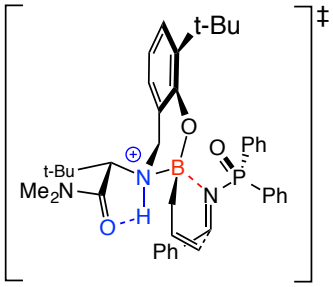
***S*-TS1.1**

+2.4 kcal/mol



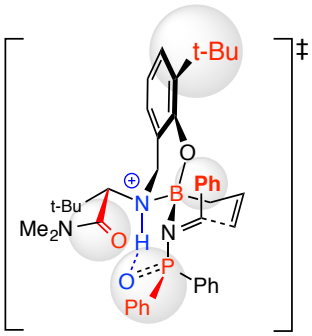
***S*-TS1.2**

+5.9 kcal/mol



***S*-TS1.3**

+7.5 kcal/mol

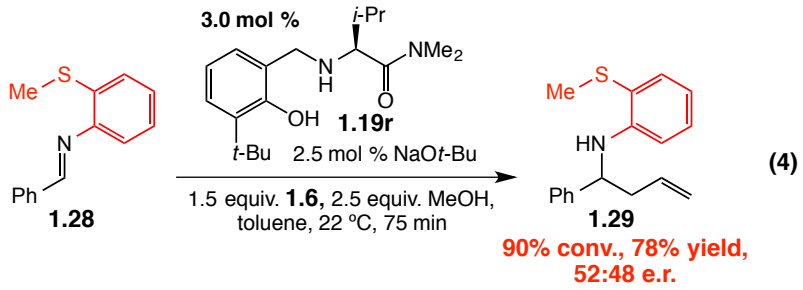


***S*-TS1.4**

+10.8 kcal/mol

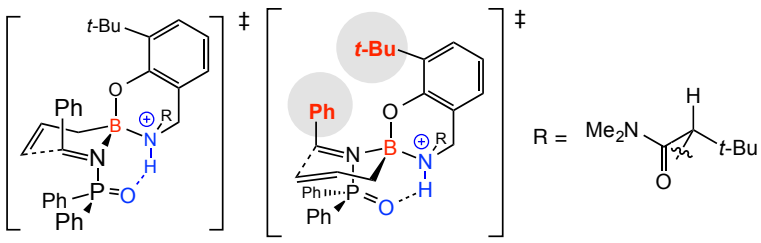
Please Note: (a) The energy of complex ***R*-TS1.1** is used as a zero point reference. (b) The aminophenol derived from L-*tert*-leucine **1.19v** (Table 1.7) was modeled instead of **1.19r** due to fewer possible conformers present in **1.19v**.

oxygen of the aldimine substrate (***R*-TS1.1**, Scheme 1.24a). Supporting this hypothesis, allyl addition to *N*-aryl aldimine **1.28**, which does not containing a second point forhydrogen bonding, proceeds with nearly no enantioselectivity (Eq. 4). This proton also forms a five-membered intermolecular attraction[83] with the dimethylamide, further rigidifying the catalyst structure. The increased energy of ***S*-TS1.1** is from the higher energy of the *cis*-configureation of the phosphinoyl aldimine vs. its *trans*-configuration (as in ***R*-TS1.1**). Attributes of the catalyst we propose to discriminate against formation of the minor enantiomer (Scheme 1.24b) include the *tert*-butyl group of the amino acid moiety clashing with the allyl group in ***S*-TS1.2**, lack of the favorable hydrogen bond



between the substrate and the catalyst in ***S*-TS1.3** (again, see Eq. 4), and, in ***S*-TS1.4**, unfavorable steric interactions between the aldimine protecting group and the amide functionality of the catalyst, as well as between the aldimine and the *tert*-butyl group on the phenol ring. This second interaction is difficult to see from the perspective the transition states are drawn in Scheme 1.24, but is much easier to see Scheme 1.25.

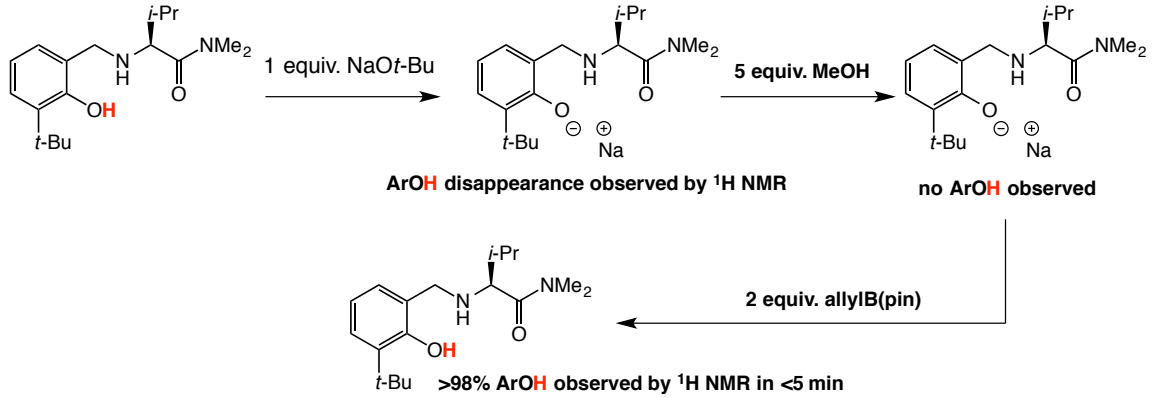
Scheme 1.25 Alternate View of Relevant Transition States Which Illustrate the Clash Between the Substrate and the *tert*-Butyl Group on the Catalyst's Aryl Ring



***R*-TS1.1** ***S*-TS1.4**

The idea of a protonated catalyst is further supported by NMR observations (Scheme 1.26). Addition of five equivalents of methanol to a solution of deprotonated aminophenol **1.19r** (formed by mixing the aminophenol with one equivalent of NaO*t*-Bu

Scheme 1.26 NMR Study Showing an Overall Acidic Solution

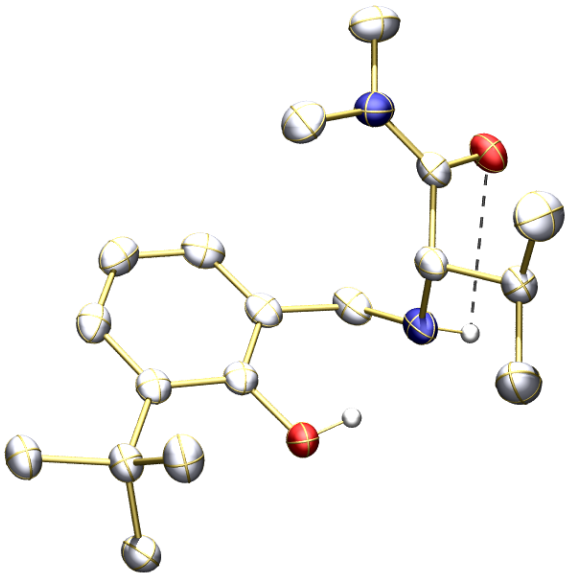


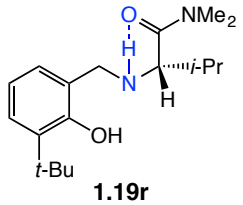
in toluene) leads to essentially no change in the ^{1}H NMR spectrum.[87] However, when two equivalents of allylB(pin) are added, complete protonation of the phenonoxide is observed in <5 minutes, supporting the proposal of the catalytic solution being overall acidic, but also that the acidity comes from Lewis acid (in our case, **1.6**) activation of Brønsted acidic methanol.

Lending credence to the proton-amide interaction hypothesized in Scheme 1.24, the X-Ray crystal structures of **1.19r** (Figure 1.1) and the HCl salt of **1.19r** (Figure 1.2) both show this interaction. The bond length and bond angle from calculated transition state ***R*-TS1.1** (Scheme 1.24) are 2.42 Å and 100º respectively,[88] and fall almost exactly between the values for **1.19r** and **1.19•HCl**.

(87) Addition of two equivalents of allylB(pin) to deprotonated **1.19r** (without MeOH present) also leads to no protonation of the phenol moiety.
(88) The upper distance for an intermolecular hydrogen bond is ~2.35 Å and the angle is from ~100º to ~180º. See reference 83.

Figure 1.1 Insight about Proton-Amide Interaction through X-Ray Crystal Structure of **1.19r**



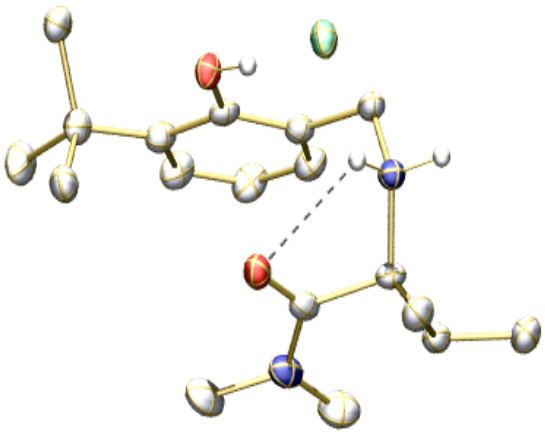


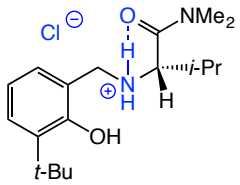
1.19r

H-O Bond Length: 2.82 Å

N-H-O Bond Angle: 86°

Figure 1.2 Insight about Proton-Amide Interaction through X-Ray Crystal Structure of **1.19r•HCl**





1.19r•HCl

H-O Bond Length: 2.13 Å

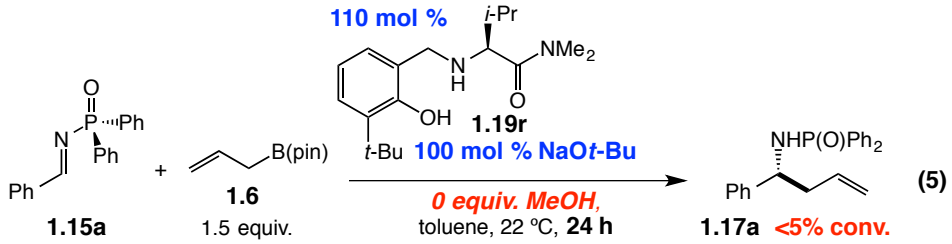
N-H-O Bond Angle: 111°

1.5.2 Investigation of Reaction Mechanism-Importance of Methanol

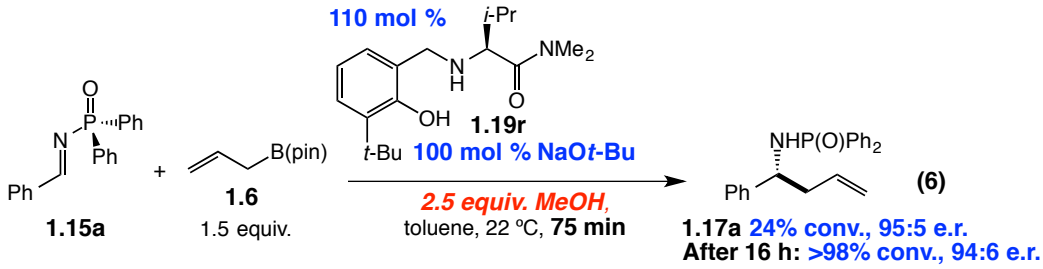
Congruent to methanol being important for more than just turnover,[89] <5% conversion to product is observed even with stoichiometric amounts of NaO*t*-Bu and

(89) Other than protonation of **i** (Scheme 1.22), methanol likely also assists in removing pinacol from allylboronic acid pinacol ester **1.6** to form a more sterically accessible dimethoxy- or monomethoxy, monopinacol boronate. See Reference 62 for an example.

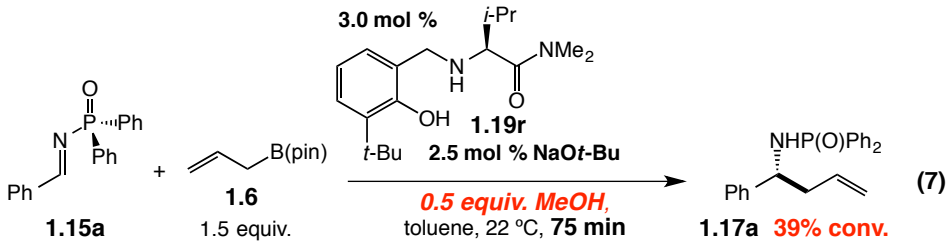
aminophenol (Eq. 5). Related observations to this are: 1) Reactions with stoichiometric amounts of aminophenol and NaO*t*-Bu as well as 2.5 equivalents of methanol (Eq. 6) do



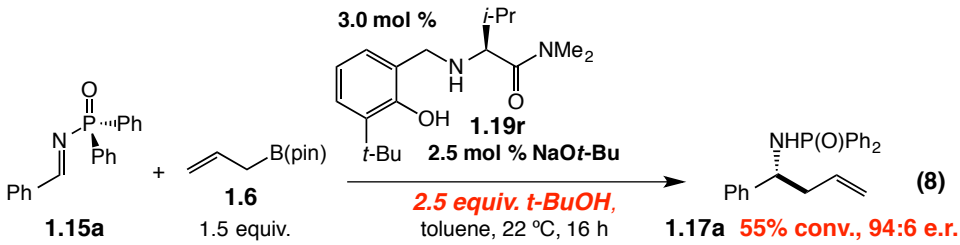
afford enantiomerically enriched homoallylamides, although they are slower than those that use catalytic amounts, indicating that it is the absence of MeOH that accounts for the



lack of reactivity in equation 5. 2) In a catalytic reaction, use of only 0.5 equivalents of methanol leads to 39% conversion to the desired product (Eq. 7), showing that methanol



is indeed needed for catalytic turnover. 3) As mixing **1.19r** and NaO*t*-Bu in Equation 5 affords an equivalent of *tert*-butanol, it stands to reason that *tert*-butanol is far less efficient at promoting this transformation than methanol. Indeed, replacing methanol with *tert*-butanol (Eq. 8) results in a far more sluggish transformation than that with

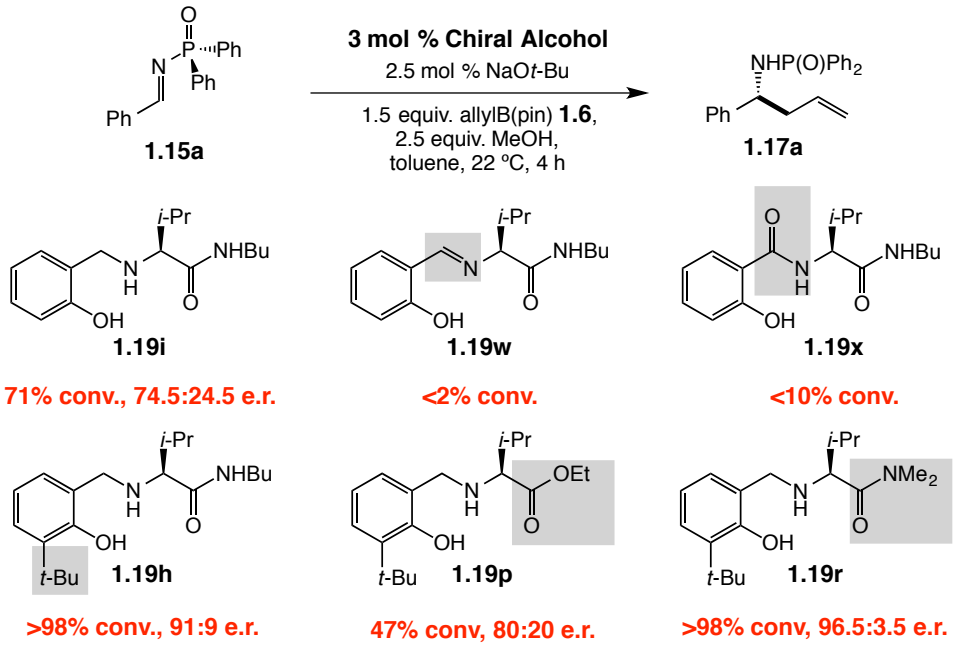


methanol (>98% conv. in 75 minutes under otherwise the same conditions as in Equation 8). 4) MeOD behaves identically to MeOH as a protic additive, consistent with proton transfer not being kinetically significant (no kinetic isotope effect).[90]

1.5.3 Investigation of Reaction Mechanism-Structural Modifications of Aminophenol

To further gain insight into the reaction mechanism, we next undertook an investigation of modified amino alcohols to see how they behave in the reaction. First we

Scheme 1.27 Revisitation of Key Data from Screening



All data are the average of at least two trials. Conversion is to the desired product as measured by analysis the 400 MHz ^{1}H NMR specta of the unpurified reaction mixture versus an internal standard of 9-methylanthracene. Enantiomeric ratios are determined by HPLC analysis. See experimental section for details.

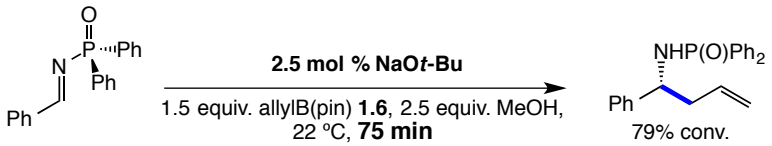
(90) The strength of hydrogen bonding interactions are nearly the same to deuterium bonding interactions. Scheiner, S.; Cuma, M. *J. Am. Chem. Soc.* **1996**, *118*, 1511–1521.

revisited selected chiral alcohols from screening in order to compare them under the same conditions and to confirm key observations we learned from screening to be true (Scheme 1.27). The results in Scheme 1.27 are fully consistent with previous observations made about the importance of the amine linker versus an imine or amide linker (**1.19i** versus **1.19w** and **1.19x** in Scheme 1.27 compared data in Table 1.3), the importance of the *tert*-butyl group (**1.19h** vs. **1.19i**; see Scheme 1.25 and Scheme 1.19), and the importance of a Lewis basic carbonyl (**1.19r** versus **1.19p** and **1.19h**; see Scheme 1.20 and the discussion surrounding it).

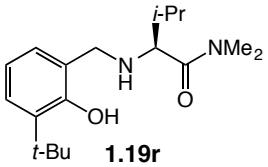
More systematic changes to the structure of aminophenol **1.19r** are shown in Scheme 1.28, and these compounds are employed in the catalytic allyl-addition to phosphinoyl aldimine **1.15a**. To better compare efficiencies, the reaction time for these studies is 75-minutes.[91] Removal of the *tert*-butyl group from **1.19r** to afford **1.30a** leads to a less selective and less active catalyst. Interestingly, the drop in enantioselectivity is nearly the same when comparing **1.19i** with **1.19h** (Scheme 1.27); with $\Delta\Delta G^{\ddagger}$=0.67 kcal/mol for **1.19r** versus **1.30a** and 0.72 kcal/mol for **1.19i** versus **1.19h**. This suggests that the presence of the *tert*-butyl group and the amide in **1.19r** do not have the same role in determining stereoselectivity. The hypothesis for how a substituent *ortho* to the phenol influences enantioselectivity is, as previously shown in Scheme 1.25, by hampering ***S*-TS1.4** in Scheme 1.24. The result with **1.30b** (Scheme 1.28) is consistent with this idea. The reason for the increase in efficiency between **1.30a** and **1.19r** (as well as **1.30b**) may be due to sterically preventing inactive forms of the aminophenol, such as dimers or adducts with the aldimine substrate.

(91) Subsequent kinetics studies show that under ideal conditions, the allyl-addition to **1.15a** promoted by aminophenol **1.19r** is complete in as little as 20-minutes. Still, 75-minutes affords useful data, as many of the compounds in Scheme 1.28 do not reach full conversion.

Scheme 1.28 Structure-Activity Relationships for Aminophenol **1.19r**

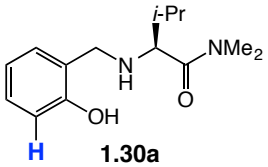


As above plus 3.0 mol % of the molecule shown



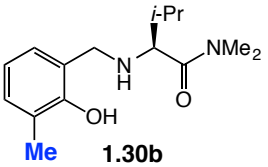
1.19r

>98% conv., 96.5:3.5 e.r.



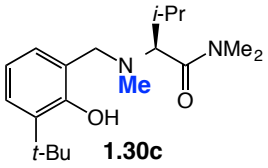
1.30a

82% conv., 88.5:11.5 e.r.



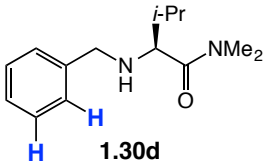
1.30b

>98% conv., 89:11 e.r.



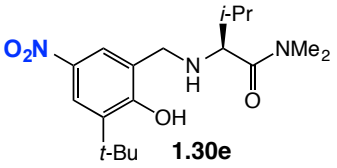
1.30c

29% conv., 72:28 e.r.



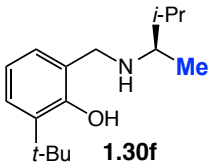
1.30d

76% conv., racemic



1.30e

6% conv., 95:5 e.r.



1.30f

70% conv., 61:39 e.r.

All data are the average of at least two trials. Conversion is to the desired product as measured by analysis the 400 MHz ^{1}H NMR specta of the unpurified reaction mixture versus an internal standard of 9-methylanthracene. Enantiomeric rations are determined by HPLC analysis. See experimental section for details.

Replacing the hydrogen on the amine linker with a methyl group gives **1.30c**, which causes a far less enantioselective and efficient transformation than **1.19r**. This result fits nicely with what we propose in Scheme 1.22, since **1.30c** cannot form oxazaborolidine ***i*** and therefore should not be very active or selective. That **1.30c** does engender some enantioselectivity and reaction is not very surprising since the initial compounds examined by Dr. Pilyugina (**1.18** in Scheme 1.18) did not have the ability to form anything resembling ***i*** either. We propose those compounds (and probably **1.30c**) act by exchanging with allylboronic acid pinacol ester to give a mono-phenoxy, mono-

alkoxy allylboronate, which is sufficiently Lewis acidic enough to react with the substrate.[92]

Demonstrating the crucial nature of the phenol moiety of **1.19r**, employing of des-hydroxy **1.30** leads to a transformation that is not significantly different than when no chiral compound is added (that is to say, with just NaO*t*-Bu as a catalyst, top equation in Scheme 1.28). Again, this is completely in line with what we have proposed for the reaction mechanism, although it does suggest that the phenol moiety is more important than the amine moiety.

An interesting point related to the result with **1.30d** (Scheme 1.28) is if the NaO*t*-Bu completely swamps any affect of **1.30d**, why does NaO*t*-Bu not cause lower enantioselectivity with other aminophenols? Based on the relative rates of the NaO*t*-Bu catalyzed reaction versus the transformation containing **1.19r**, the aminophenol-based catalyst is not simply out competing NaO*t*-Bu. In the presence of *para*-nitro containing **1.30e**, desired product is obtained in high 95:5 e.r., but the reaction only goes to 6% conversion, much less than the 79% conversion when just using NaO*t*-Bu.[93] The mix of high enantioselectivity and low conversion suggest that the NaO*t*-Bu pathway is non-operative[94] when an aminophenol is present, especially combined with the multitude of examples where transformations in the presence of an aminophenol are slower than with just NaO*t*-Bu (**1.30c** in Scheme 1.28 and **1.19p** are just two examples). This fascinating observation is still not fully understood, and requires a better comprehension of the

(92) This is reminiscent of the mechanism proposed by Professor S. E. Schaus. See ref. 46 and Scheme 1.13.
(93) About 61% yield of aminophenol **1.30e** is obtained from the reaction, indicating that **1.30e** does not simply decompose under the reaction conditions.
(94) For a recent mechanistic study on a transformation where the "background" reaction is not operative in the presence of the catalyst, see: Denmark, S. E.; Chi, H. M. *J. Am. Chem. Soc.* **2014**, *136*, 3655–3663.

mechanism of the NaO*t*-Bu catalyzed transformation in order to propose a reasonable hypothesis.

Why **1.30e** affords lower selectivity may be due to a) The phenol oxygen is rendered much less nucleophilic by the electron-withdrawing nitro group and therefore has difficulties exchanging onto a molecule of boron to make **i** (Scheme 1.22) b) The pH of the reaction is changed so much by the much more acidic phenol proton that the reaction is inhibited.[95]

The importance of a Lewis basic carbonyl has been previously observed (Scheme 1.20 and surrounding discussion) and is fully consistent to the mechanism proposed in Scheme 1.22. The stronger the Lewis base the stronger the intramolecular interaction between that carbonyl and the key proton becomes. This both rigidifies the catalyst as well as stabilizes protonated catalyst **ii** versus the unprotonated **i** (Scheme 1.22). Coinciding with these statements, the catalytic reaction using amide-lacking aminophenol **1.30f** is less efficient and almost completely racemic (Scheme 1.28). Why this transformation is faster than when ester-containing **1.19p** is used (Scheme 1.27) may be because **1.30f** is smaller in size than **1.19p**, leading to more efficient transformations through a non-protonated intermediate similar to **i (**Scheme 1.22).

1.5.4 Investigation of Reaction Mechanism-Additional Kinetic Data

Additional kinetic experiments were carried out by Dr. Sebastian Torker, but these studies had issues with reproducibility, so the reader is cautioned about inferring too much from them.[96] The data were obtained with *para*-dibutylamino aldimine **1.15k** as the substrate in order to obtain slow enough reactivity to accurately measure. Some

(95) Additives that are too acidic completely shut down the reaction. Addition of 3.0 mol % of acetic acid leads to <2% conversion regardless of the aminophenol (conditions otherwise as in Scheme 1.28).
(96) Data are included here to compile some interesting observations that would otherwise go unreported.

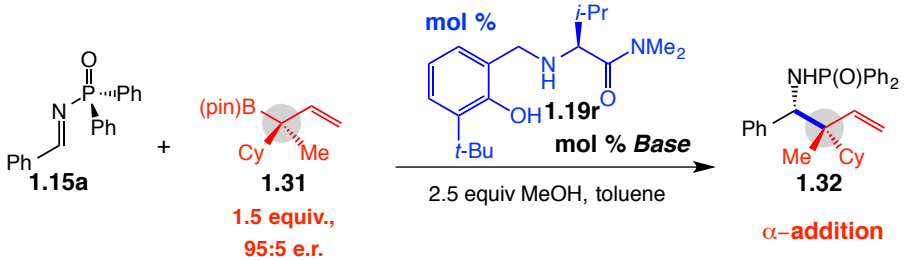
interesting trends are a) An Eyring plot showed activation parameters of $\Delta S^{\ddagger}$= -50.8 cal/mol•k and $\Delta H^{\ddagger}$= +6.4 kcal/mol. The large value for $\Delta S^{\ddagger}$, if true, is consistent with a highly ordered turnover-limiting step, likely due to non-polar toluene molecules from the solvent adopting conformations to better stabilize a charged transition state. Related to this, the selectivity does not increase upon cooling (or heating) the reaction, indicating the enantioselectivity is largely derived from entropic considerations. Thus the models in Scheme 1.24 should be considered working rather than actual models. b) Overall reaction order is ~0.6 when using aminophenol **1.19r** c) Reaction order in aldimine is ~0. d) Reaction order in allylB(pin) is 0. e) Methanol slows down the reaction rate once its concentration exceeds that of the aldimine; the reaction is ~0 order in methanol when it is at a lower concentration than the aldimine. f) While there is a Hammett correlation when using aminophenol **1.19r**, there is no such correlation when aminophenol **1.30f** is used (Scheme 1.28), indicating a change in the turnover-limiting step. g) When aminophenol **1.30f** is used, the overall order increases to ~1.6, further confirming the change of the turnover-limiting step. h) Generation of (pin)B-OMe **1.27** (Scheme 1.22) occurs at a rate identical to the rate of the reaction.

1.6 Investigation of Mechanism of Allyl-Transfer as well as Obtaining Synthetically Useful "Crotyl-type" Addition Products by Studying the Reactivity and Selectivity of α-Chiral Allylboronates.

Having obtained a much greater understanding of the reaction mechanism, we next wished to extend our method to the synthesis of homoallylamides with tertiary or quaternary stereogenic centers between the stereogenic center attached to nitrogen and the olefin of the allyl group as in **1.32** (Table 1.11). As shown already in Equation 3,

crotylboronate ***1.11*** does not efficiently or selectively add to aldimines under the catalytic manifold, which we hypothesized to be due to an unfavorable first γ-addition in the catalytic cycle (see **vi** to **ii** in Scheme 1.22). Keeping this in mind, we next attempted to utilize the unique α-selectivity of our system to catalyze the addition of enantiomerically enriched allylboronate[97] **1.31** to imine **1.15a** (Table 1.11). Not only would this demonstrate the utility of this class of catalyst's selective α–addition, but it would allow access to products that otherwise can be difficult to synthesize.[98] Under typical conditions for enantioselective allyl addition to **1.15a** we were pleased to find that the

Table 1.11 Optimization of Reaction Conditions for Addition of Enantiomerically Enriched Allylboronate **1.31** to Imine **1.15a**.[a]



entry	**1.19r** (mol %)	***Base*** (mol %)	temp (°C)	time (h)	conv. (%)[b]	d.r.[b]	yield (%)[c]	e.r.[d]
1	6	NaO*t*-Bu (5.0)	22	18	24	81:19	nd	95.5:4.5
2*	6	NaO*t*-Bu (5.0)	50	18	47	85:15	nd	94:6
3*	6	NaO*t*-Bu (5.0)	50	48	58	91:9	nd	94.5:5.5
4	12	NaO*t*-Bu (10.0)	50	18	42	91:9	nd	94:6
5	3	NaO*t*-Bu (2.5)	50	18	48	88:12	nd	93:7
6	6	LiO*t*-Bu (5.0)	50	18	64	88:12	nd	95:5
7	6	$Zn(Ot\text{-}Bu)_2$ (2.5)	50	18	>98	89:11	74	94:6
8*	***6***	***$Zn(Ot\text{-}Bu)_2$ (2.5)***	***22***	***18***	***>98***	***89:11***	***74***	***95:5***
9	6	$Zn(Ot\text{-}Bu)_2$ (2.5)	22	4	24	89:11	nd	nd

[a] >98:<2 α:γ ratio in all cases. [b]Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture. [c]Yield of isolated major diastereomer. [d] For major diastereomer. Determined by HPLC analysis. *Average of two experiments.

desired product was afforded as a single regioisomer (no γ-addition was detected) as well as in >90% ee and >4:1 d.r. (entry 1). The only problem left to overcome was the low level of reactivity (24% conversion after 18 hours). Increasing the temperature initially

(97) Guzman-Martinez, A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10634–10637.
(98) (a) Yin, L.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 9610–9611. (b) Kolodney, G.; Sklute, G.; Perrone, S.; Knochel, P.; Marek, I. *Angew. Chem. Int. Ed.* **2007**, *46*, 9291–9294.

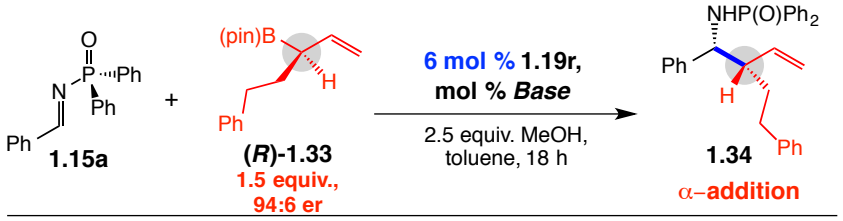
doubled the conversion while barely decreasing the enantioselectivity; however the reaction seemed to die off as increasing the reaction time did not greatly increase conversion (entries 2 and 3). Increasing or decreasing the catalyst loading showed little change in reactivity as well (entries 4 and 5). Since this transformation involves both an enantiomerically enriched catalyst and reagent, we worried there may be a matched mismatched interaction, but the antipode of aminophenol **1.19r** under conditions in entry 2 gave similar results although the opposite major diastereomer (40% conv., 21:79 dr).

Allylboronate **1.31** contains a quaternary stereogenic center directly next to the boron, so we hypothesized that the activation of boron may be what is slowing down the catalytic reaction. To address this we first tried a sterically less hindered aminophenol (Me group containing **1.30b** [Scheme 1.28] instead of *t*-Bu group containing in **1.19r**), but we observed <2% conversion to desired product. Another attempt to increase conversion was increasing the equivalents of methanol to 12.5 in hopes it would exchange with the pinacol group on **1.31** to make the boron less hindered, but this lead to no increase in conversion versus entry 2 of Table 1.11. Taking into consideration past results suggesting $Zn(O\textit{t}\text{-Bu})_2$ to be superior to $NaO\textit{t}$-Bu in terms of reactivity for this class of catalysts (Table 1.9), we examined it and $LiO\textit{t}$-Bu as bases (entries 6-9, Table 1.11). By using $Zn(O\textit{t}\text{-Bu})_2$, the reaction went to full conversion in 18 hours at room temperature affording isolated major diastereomer in 74% yield and 95:5 e.r. (entry 8). It is still unclear exactly what role the Zn salt plays, but one possibility is that since zinc posseses a +2 charge, it is better at sequestering free pinacol than +1 sodium. This helps form a more sterically accessible dimethylborate which may help in catalyst initiation. We do not believe that a meaningful role of the $Zn(O\textit{t}\text{-Bu})_2$ is to cause the formation of

an allylzinc[38d,44b–f] species, since the enantioselectivity are the same when using Zn(O*t*-Bu)$_2$ versus NaO*t*-Bu (cf. entry 1 and 8) that does not form an allylmetal species with allylboronate **1.6**.

Investigations were then carried out into using an enantiomerically enriched allylboronate with a tertiary stereogenic center ((**R**)-**1.33)** as a nucleophile (Table 1.12).

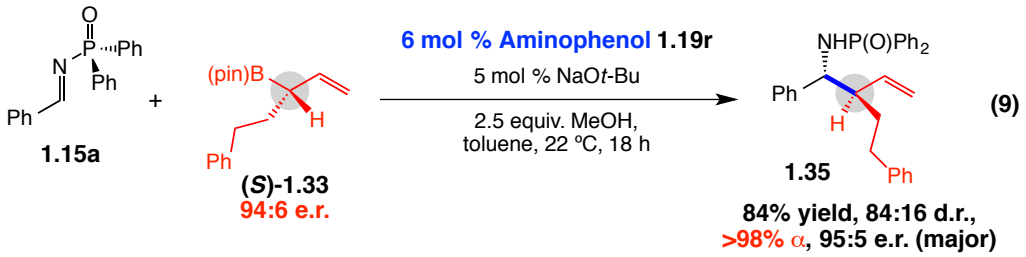
Table 1.12 Optimization of Reaction Conditions for Addition of Enantiomerically Enriched Allylboronate **(*R*)-1.33** to Imine **1.15a**.[a]



entry	***Base*** (mol %)	temp. (°C)	conv. (%)[b]	d.r.[b]	yield (%)[c]	e.r.[d]
1*	***NaOt-Bu (5.0)***	***22***	***>98***	***83:17***	***93***	***96:4***
2	NaO*t*-Bu (5.0)	50	>98	83:17	88	96:4
3	ZnO*t*-Bu (2.5)	22	>98	75:25	94	93:7

[a] >98:<2 α:γ ratio in all cases. [b]Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture. [c]Yield of isolated mixture of diastereomers. [d] Enantiomeric ratio of major diastereomer. Determined by HPLC analysis. *Average of two experiments.

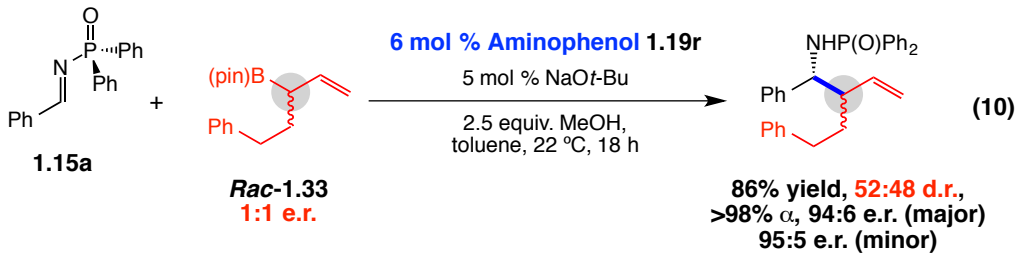
A brief optimization shows that NaO*t*-Bu as a base at room temperature leads to an optimal reaction in terms a d.r. and conversion (Table 1.12). Containing a tertiary stereogenic center rather than a quaternary one likely makes **1.33** far more reactive than **1.31**. Employing **(*S*)-1.33**, the opposite enantiomer of the allylboronate shown in Table



(9)

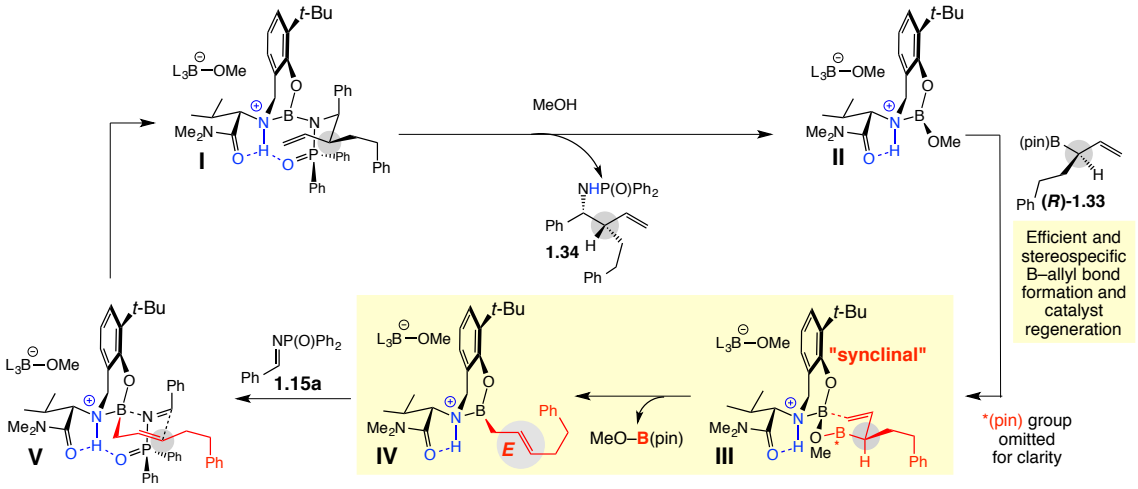
1.12, results in a very similar reaction to entry 1 of Table 1.12 in terms of yield, e.r., and d.r., but the opposite major diastereomer is afforded (Equation 9). Therefore, by combining the correct enantiomer of the allylboronate coupled with the correct

enantiomer of the catalyst, all four possible stereoisomers of the product can be obtained selectively, making our method only the second example where this is possible in the literature of catalytic, enantioselective allyl-additions to imines.[53] Notably, enantiomerically enriched allylboronates are required to obtain diastereoselectivity, as using ***Rac*-1.33** affords the product in 1:1 d.r., though undiminished enantioselectivity (Equation 10).

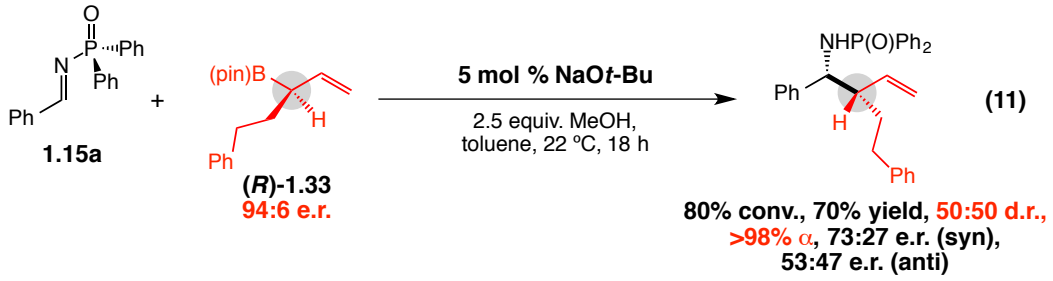


In addition to affording synthetically useful products, these reactions with enantiomerically enriched borolanes give valuable insight into the reaction mechanism. Using X-ray crystallography, the absolute stereochemistry of each product was established to be what is shown in Table 1.11, Table 1.12, and Equation 9. Importantly, this outcome requires the stereogenicity of the allylboronate to invert during the catalytic

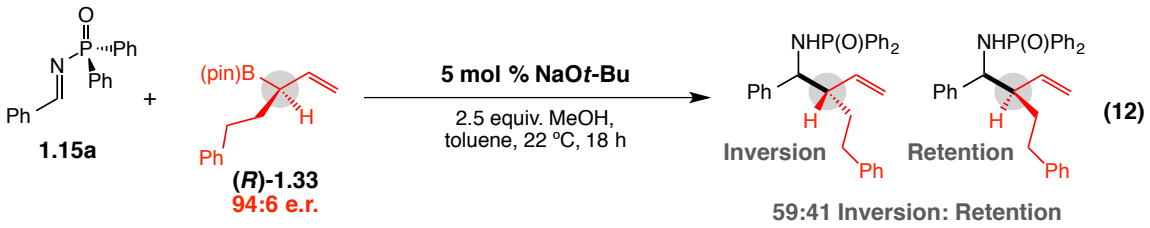
Scheme 1.29 Models and Mechanism of Allyl Transfer



cycle. A plausible reason for the formation of **1.34** is shown in Scheme 1.29. Following release of product **1.34** leading to the start of a new catalytic cycle (**I→II**, Scheme 1.29), boronate **II** is formed. The hydrogen bonding between the amide oxygen and the N-H proton in **II** is critical for selective allyl transfer of **1.33** to the catalyst as this amide blocks **1.33** from approaching the boron from left side of **II** (Scheme 1.29). If the allyl group reacted from the front of **II**, the opposite diastereomer of product would be obtained. We propose that the methoxy group on the catalyst in **II** assists in the allyl transfer which goes through synclinal-like transition state **III** and forms **IV** with high levels of selectivity for a single olefin isomer. Allyl-addition through a six-membered transition state affords **V**, which constitutes a net inversion of stereochemistry from **(*R*)-1.33** to **1.34**.

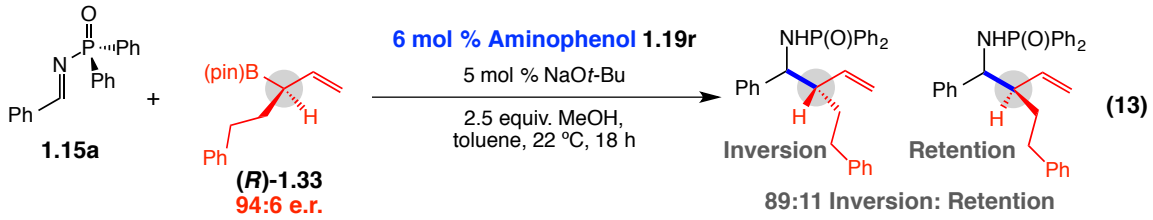


Also supporting the importance of the aminophenol in selective allyl transfer, reaction in the absence of the aminophenol affords no diastereoselectivity and low-enantioselectivity, although still high levels of α-selectivity.[99] Looking at this another



(99) The α-selectivity as well as the small amount of enantioselectivity again suggests that studying the mechanism of the NaO*t*-Bu catalyzed reaction to be a worthwhile endeavor. See footnote 85.

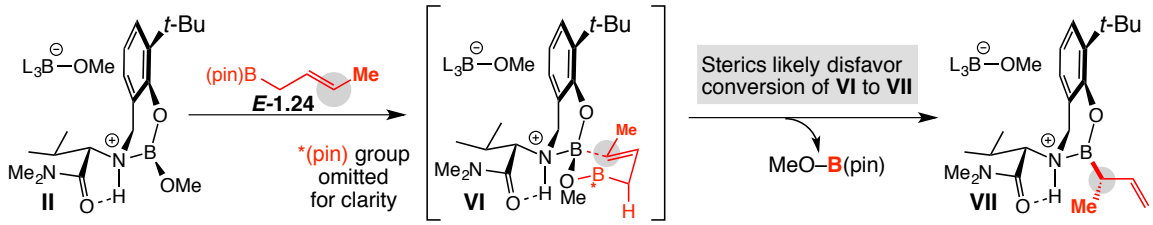
way (equation 12), the stereochemistry of the products show a ratio of those where allylboron **1.33** inverts to those where it does not of 59:41. Compare this to when aminophenol is present in Equation 13, where the ratio is 89:11. With the establishment of α-substituted allylboronates as competent nucleophiles under the aminophenol promoted manifold, we next revisited looking at γ-substituted crotylboronic acid ***E*-1.24** (see Equation 3).



(13)

Based on our mechanistic understanding, the low reactivity we see with *trans*-crotylboronic acid pinacol ester ***E*-1.24** is likely due to increased sterics of the γ-addition to the catalyst, shown as **II** to **VII** in Scheme 1.30. However, preceding data show that γ-

Scheme 1.30 Proposal for Poor Reactivity of ***E*-1.24**



addition of a similar allyl group to the substrate occurs readily (**V→I**, Scheme 1.29). This inspired us to introduce a third γ-addition to the catalytic cycle, allowing for *net* γ-*addition* of crotylboronates to aldimines (Scheme 1.31). Studies by Kobayashi and Fandrick suggest the use of a zinc-alkoxide may accomplish this goal by transmetalating

with allylboronate[100] in a γ-selective fashion to give **VIII** (Scheme 1.31).[38d,44b–f] Changing the base from NaO*t*-Bu to Zn(O*t*-Bu)$_2$ results in much more efficient transformation as well as switching the reaction to be γ-selective (Table 1.13, cf. entry 1 and 2). Lowering the reaction temperature decreases the reactivity without greatly affecting regio- or stereoselectivity (entry 3 and 4).

Scheme 1.31 A 3rd γ-Addition in Order to Affect an Efficient and Net γ-Selective Transformation

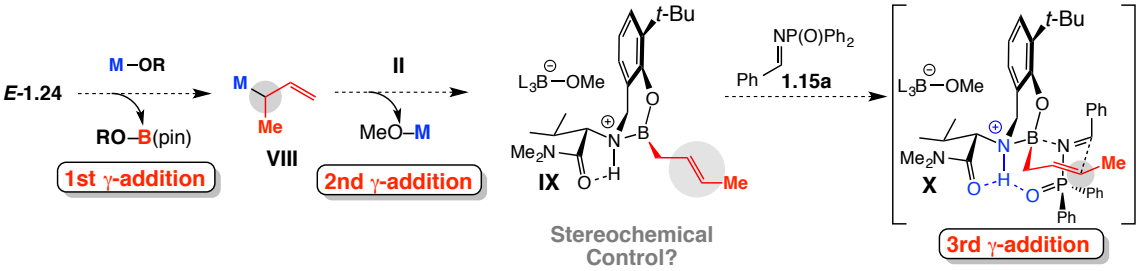
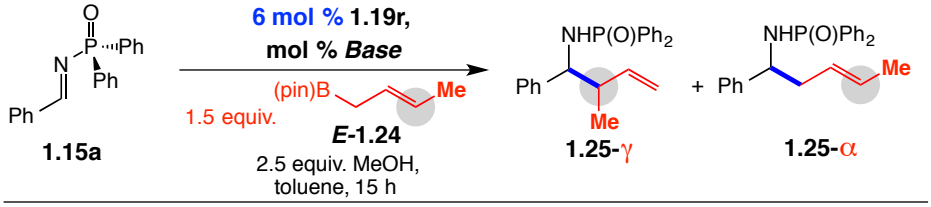


Table 1.13 Optimization of Addition of *E*-Crotylboronate to Aldimine **1.15a.**



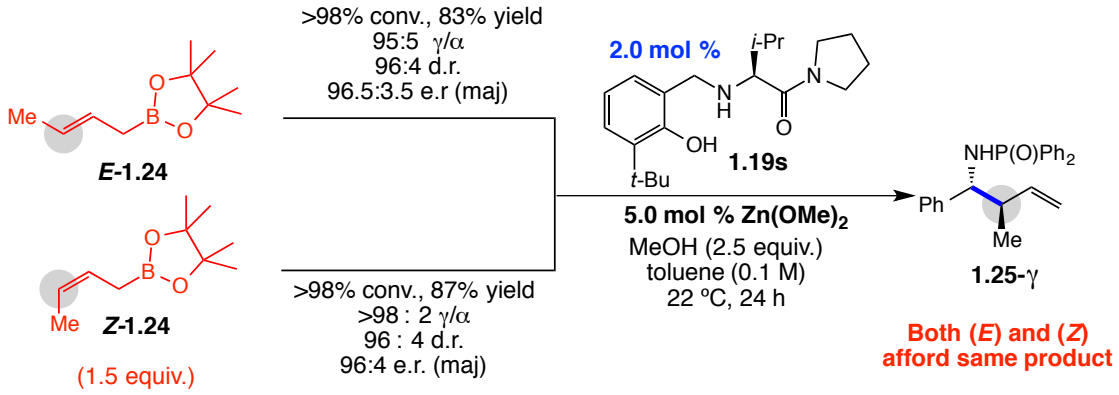
entry	***Base* (mol %)**	***temp*** (°C)	conv. (%)[a]	γ:α **ratio**[b]	d.r. (γ)[c]	yield (%)	e.r.(γ) (maj./min.)[d]
1	NaO*t*-Bu (5.0)	22	35	25:75	88:12	n.d.	n.d.
2*	**Zn(O*t*-Bu)$_2$ (2.5)**	**22**	**>98**	**74:26**	**87:13**	**83%**	**95:5/88:12**
3	Zn(O*t*-Bu)$_2$ (2.5)	4	59	70:30	88:12	n.d.	96:4/88:12
4	Zn(O*t*-Bu)$_2$ (2.5)	-15	<5	-	-	n.d.	-

n.d.=not determined [a] Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture. [b] Determined by 400 MHz ^{1}H NMR analysis of isolated product. [c] Yield of isolated product. [d] Determined by HPLC analysis. *Average of two experiments.

With my input, visiting scholar Dr. Hiroshi Miyamoto carried out further reaction optimization. Use of the sterically smaller Zn(OMe)$_2$ is crucial for high γ:α selectivity (Scheme 1.32), perhaps due to it being better able to promote the first transmetalation.

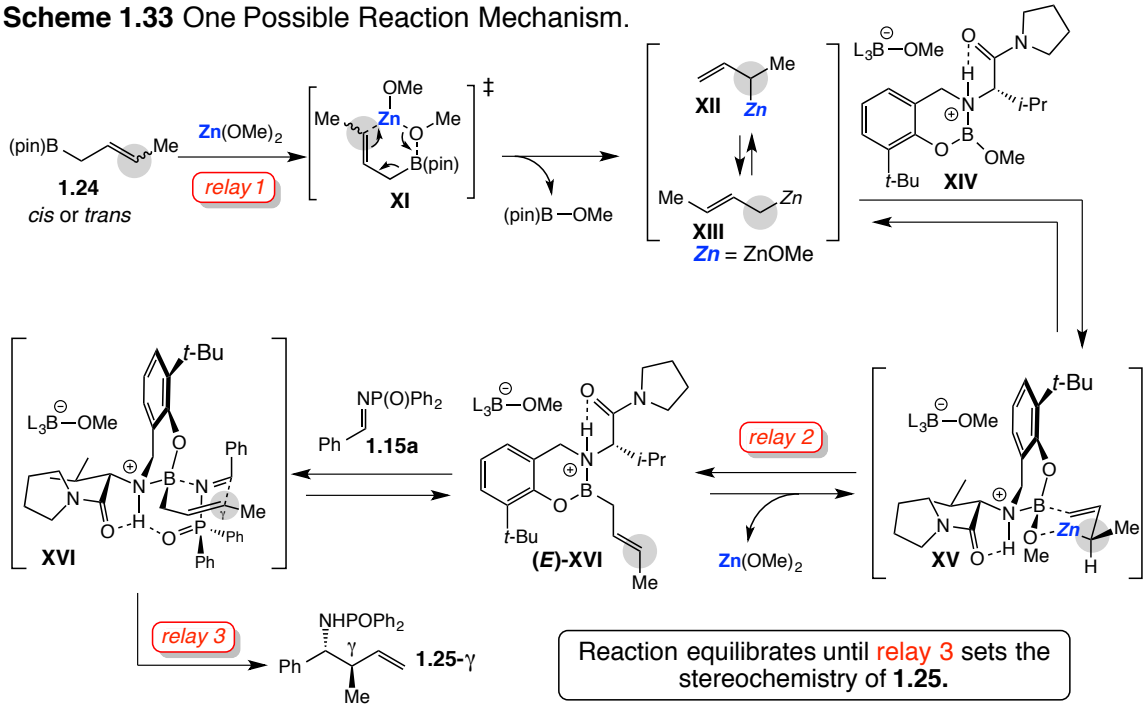
(100) The study by Fandrick (ref 44c) shows that crotylboronate **1.24** is not compatible with their conditions (it gives <2% conversion), which brings of the interesting point of why exactly the **1.24** seems to transmetallate with zinc methoxide in our case. Perhaps the aminophenol promotes transmetallation, or it could be something as subtle as a solvent effect (the Fandrick group uses THF while our chemistry uses toluene).

Scheme 1.32 Optimized Conditions Comparing *E*- and *Z*- Crotylboronates.



The observation that both ***E***- and ***Z***-crotylboronates **1.24** afford the same major stereoisomer of product is consistent with a rapidly equilibrating allylzinc intermediate (**XII**→**XIII**, Scheme 1.33).[101]

Scheme 1.33 One Possible Reaction Mechanism.



A possible reaction mechanism is shown in Scheme 1.33. Relay 1 proceeds through transition state **XI** to afford **XII**, which is in rapid equilibrium with **XIII**. As

(101) As this point we can not rule out the possibility that both **(*E*)-** and **(*Z*)-XVI** (Scheme 1.33) react with the aldimine to give the same stereochemical outcome due to **(*Z*)-XVI** reacting through a chair transition state and **(*E*)-XVI** reacting through a boat transition state. For a related example, see ref 46.

shown in Scheme 1.30, **XII** should be greatly preferred over **XIII** to react with oxazaborolidine **XIV**. Reaction of **XII** through transition state **XV** is the second relay (γ-addition) and produces **(*E*)-XVI** as well as regenerating $Zn(OMe)_2$. Aldimine binds to the allylboron and reacts to afford **1.25**-γ through the third relay. To explain the stereoconvergence with ***E***- and ***Z***-crotylboronates, we propose the reaction is in equilibrium until the final step (Scheme 1.33). There are still many experiments to run to elucidate this mechanism.

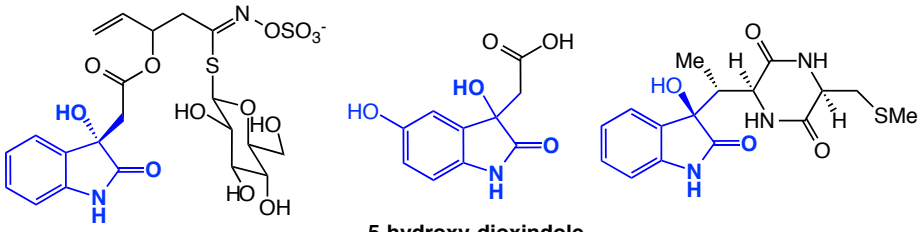
1.7 Additions to Isatins

In order to enhance the utility of this new catalytic method, we wished to extend the electrophile scope to include carbonyls as well as imines. When deciding what type of carbonyl, we chose to focus on isatins for three main reasons: 1) The products of allyl-addition to isatins are highly-useful. 2) Catalytic enantioselective methods to obtain these products are less than ideal. 3) Isatins, much like *N*-phosphinoylimines, posses the potential to have a second point of binding with the catalyst.

Much like homoallylamines discussed earlier, 3-allyl-3-hydroxy oxindoles (AHOs) are flexible chiral intermediates useful in the synthesis of molecules of biological significance. Arising biosynthetically from the oxidation of indoles, the 3-hydroxy oxindole pattern is found in a myriad of natural products capable of inducing a wide variety of effects in various organisms (Scheme 1.34).[102] Examples include the urease

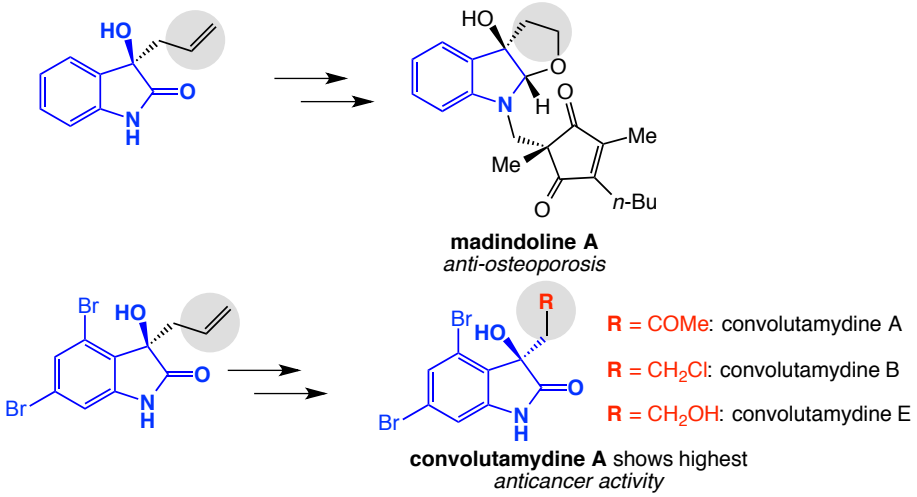
(102) For reviews encompassing the synthesis and bioactivity of 3-hydroxy oxindoles, see: (a) Ruiz-Sanchis, P.; Savina, S. A. S.; Albericio, F.; Álvarez, M. *Chem. Eur. J.* **2011**, *17*, 1388–1408. (b) Ishikura, M.; Yamada, K. *Nat. Prod. Rep.* **2009**, *26*, 803–852. (c) Peddibhotla, S. *Curr. Bioact. Compd.* **2009**, *5*, 20–38. (d) Kumar, A.; Chimni, S. S. *RSC Advances*, **2012**, *2*, 9748–9762.

Scheme 1.34 3-Hydroxy Oxindole Containing Biologically Active Compounds



inhibitor[103] 3'-hydroxyglucoisatisin, rice growth regulator 5-hydroxy-dioxindole-3-acetic acid[104], anti-leukemia maremycin B,[105] neuron cell protector neuroprotectin B,[106] and TMC-95 A-D,[107] which are reversible inhibitors of the 20S proteasome, and have many applications in biology research.[108] Utilizing the myriad transformations of the olefin present in AHOs, many alkaloids can be synthesized. Such examples where AHOs can

Scheme 1.35 Chiral 3-Allyl-3-Hydroxy Oxindoles in Natural Product Synthesis

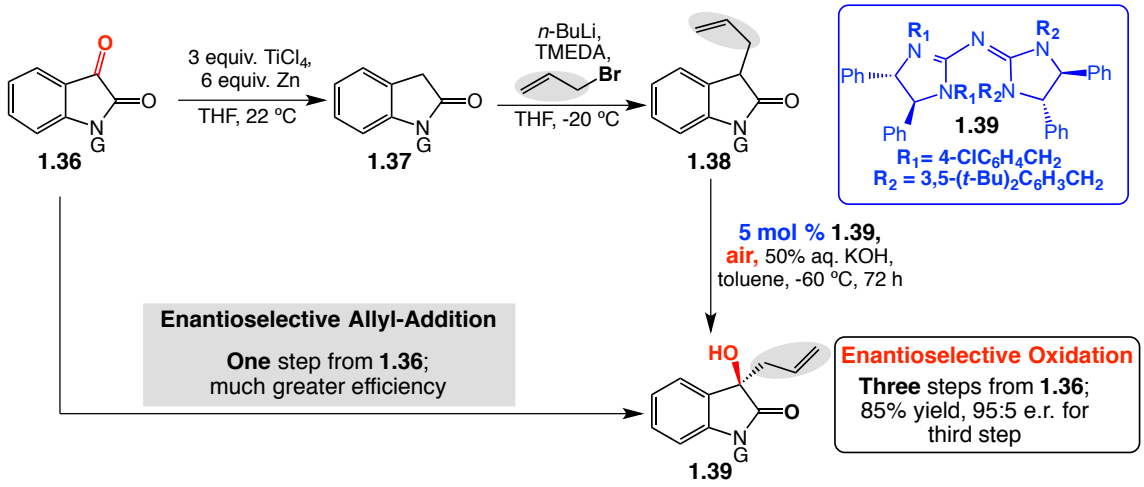


(103) Ahmad, I.; Fatima, I.; Afza, N.; Malik.; Lodhi, M.; Arid.; Iqbal, M. *J. Enzyme Inhib. Med. Chem.* **2008**, *33*, 918–921.
(104) Suzuki, Y.; Kinashi, H.; Takeuchi, S.; Kawarada, A. *Phytochemistry* **1977**, *16*, 635–637.
(105) Tang, Y.-Q.; Sattler, I.; Thiericke, R.; Grabley, S.; Feng, X.-Z. *Eur. J. Org. Chem.* **2001**, 261–267.
(106) Kobayashi, H.; Shin-ya, K.; Furihata, K.; Nagai, K.; Suzuki, K.-I.; Hayakawa, Y.; Seto, H. *J. Antibiot.* **2001**, *54*, 1019–1024.
(107) Kohno, J.; Koguchi, Y.; Nishio, M.; Nakao, K.; Kuroda, M.; Shimizu, R.; Ohnuki, T.; Komatsubara, S. *J. Org. Chem.* **2000**, *65*, 990–995.
(108) (a) Groll, M.; Götz, M.; Kaiser, M.; Weyher, E.; Moroder, L. *Chem. Biol.* **2006**, *13*, 607–614. (b) Coste, A.; Couty, F.; Evano, G. *C. R. Chemie* **2008**, *11*, 1544–1573.

be employed as key intermediates are madindoline A and B,[109] whose anti-osteoporosis activity is strongly dependent of the correct stereochemistry of the 3-hydroxy oxindole;[110] convolutamydine A,[111] B, and E,[112] of which A has the highest anticancer activity;[113] and alkaloids CPC-1[114] and alline.[115]

Catalytic, enantioselective methods that access 3-allyl-3-hydroxy oxindoles fall into two main categories; enantioselective oxidations and enantioselective allyl-additions.

Scheme 1.36 Allyl-Addition is a More Efficient Strategy than Oxidation to Access AHOs



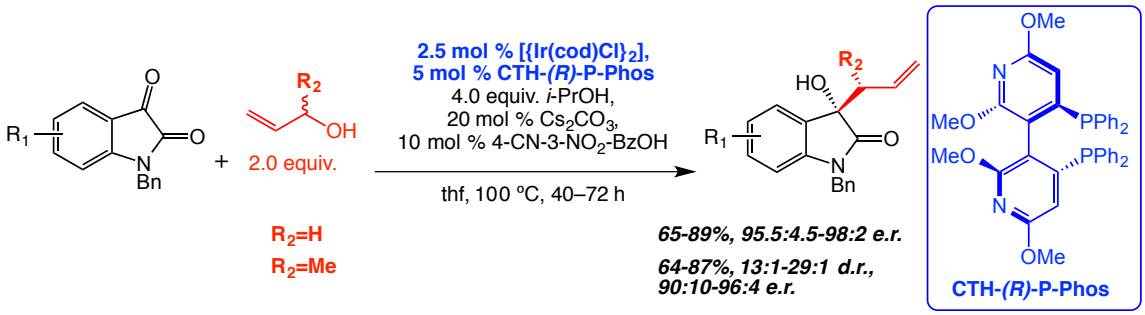
Strategically, the allyl-addition methods have an advantage versus oxidations since the allyl-addition can be performed directly on an isatin to afford the desired AHO (**1.36→1.39**, Scheme 1.36), whereas the oxidation must be performed on alpha-allyl-oxindole **1.38**, which requires two steps from isatin **1.36** to synthesize (Scheme 1.36). As

(109) Itoh, T.; Ishikawa, H.; Hayashi, Y. *Org. Lett.* **2009**, *11*, 3854–3857.
(110) Yamamoto, D. *et al. Bioorg. Med. Chem. Lett.* **2006**, *16*, 2807–2811.
(111) Cravotto, G. *et al. Tetrahedron Asymmetry* **2006**, *17*, 3070–3074.
(112) Nakamura, T.; Shirokawa, S.-i.; Hosokawa, S.; Nakazaki, A.; Kobayashi, S. *Org. Lett.* **2006**, *8*, 677–679.
(113) Zhang, H.-P. *et al. Tetrahedron* **1995**, *51*, 5523–5528.
(114) Kitajima, M.; Mori, I.; Arai, K.; Kogure, N.; Takayama, H. *Tetrahedron Letters* **2006**, *47*, 3199–3202.
(115) Kawasaki, T.; Takamiya, W.; Okamoto, N.; Nagaoka, M.; Hirayama, T. *Tetrahedron Letters* **2006**, *47*, 5379–5382.

the representative example in Scheme 1.36 illustrates,[116] low catalytic efficiencies are a general problem with this method.[117]

Out of all extant methods for catalytic enantioselective allyl-additions to isatins, the only one that can afford a wide range of products in greater than 95:5 enantiomeric ratio requires 5 mol % of precious iridium (2.5 mol % of $[Ir(cod)Cl]_2$ which is $56/mmol

Scheme 1.37 Iridium-Catalyzed Enantioselective Allyl-Addition to Isatins Reported by Krische

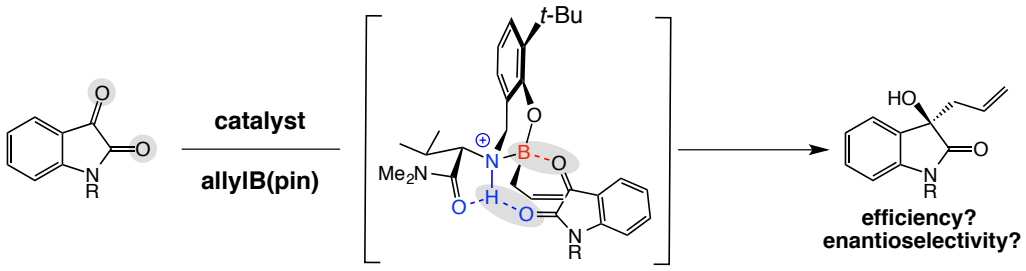


from Strem) and an expensive phosphine ligand ($308/mmol from Strem) as well as 40 hours at 100 ºC in a pressure vessel (Scheme 1.37).[118] In addition to having less-than-ideal enantioselectivities, the other protocols require use of toxic allylstannanes[114,119] or mercury salts[120] and/or precious metals and difficult-to-access ligands.[121] We were hopeful our catalytic protocol would be as amenable to isatins as it is to *N*-phosphinoylaldimines.

Based on the our proposed stereochemical model for the major enantiomer of the aldimine allyl-addition (***R*-TS1.1**, Scheme 1.24), the amide carbonyl of an isatin may be

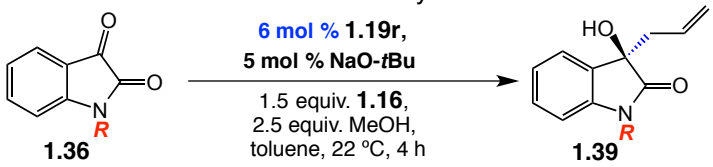
(116) Yang, Y.; Moinodeen, F.; Chin, W.; Ma, T.; Jiang, Z.; Tan, C.-H. *Org. Lett.* **2012**, *14*, 4762–4765.
(117) Low enantioselectivities are also common. For representative examples, see: (a) Sano, D.; Nagata, K.; Itoh, T. *Org. Lett.* **2008**, *10*, 1593–1595. (b) Bui, T.; Candeias, N. R.; Barbas, C. F. *J. Am. Chem. Soc.* **2010**, *132*, 5574–5575.
(118) Itoh, J.; Han, S. B.; Krische, M. J. *Angew. Chem. Int. Ed.* **2009**, *48*, 6313–6316.
(119) (a)Hanhan, N. V.; Sahin, A. H.; Chang, T. W.; Fettinger, J. C.; Franz, A. K. *Angew. Chem. Int. Ed.* **2010**, *49*, 744–747. (b) Wang, T.; Hao, X.-Q.; Huang, J.-J. Wang, K.; Gong, J.-F.; Song, M.-P. *Organometallics* **2014**, *33*, 194–205.
(120) Cao, Z.-Y.; Zhang, Y.; Ji, C.-B.; Zhou, J. *Org. Lett.* **2011**, *13*, 6398–6401.
(121) (a) Qiao, X.-C.; Zhu, S.-F.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2009**, *20*, 1254–1261. (b) Hanhan, N. V.; Tang, Y. C.; Tran, N. T.; Franz, A. K. *Org. Lett.* **2012**, *14*, 2218–2221.

Scheme 1.38 Proposed Two-Point Binding of Isatins with Catalyst Should Lead to High Enantioselectivity



able to serve as the second point of binding to the catalyst that we propose to be critical to obtaining high enantioselectivity (Scheme 1.38).[122] Under the same conditions used for the catalytic enantioselective allylation of imines, isatins with various *N*-substitutions were examined (Table 1.14). While unprotected isatin **1.36a** and *N*-Me isatin **1.36b** are

Table 1.14 Initial Examination of Allyl-Additions to Isatins



entry	*R*	conv. (%)[a]	yield (%)[b]	e.r.[c]
1	H; **1.36a**	5	-	-
2	Me; **1.36b**	30	n.d.	n.d.
3	Bn; **1.36c**	>98	88	98:2

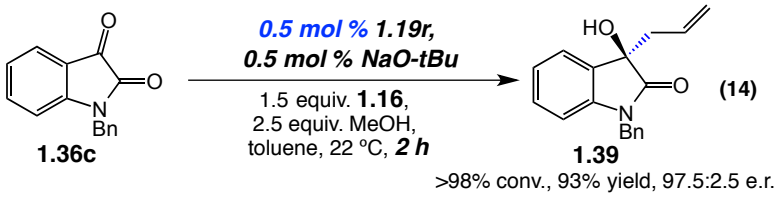
n.d. = not determined [a] Conversion to desired as determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture versus an internal standard of 9-methylanthracene. [b] Yield of isolated product. [c]Determined by HPLC analysis.

not efficient substrates under these conditions, reactions with *N*-Bn isatin **1.36c** expediently give a high yield of AHO with 98:2 enantioselectivity (Table 1.14). The lack of conversion in entry 1 probably results from the acidity of the free proton in isatin **1.36a**. Consistent with this, addition of 10 mol % of **1.36a** to the reaction with **1.36c** in entry 3 completely shuts down the reaction (<2% conv.) It is worth noting that the low reactivity in entry 2 is likely the result of **1.36b** being insoluble under the reaction

(122) This second point of binding forms a seven-membered-ring as opposed to the six-membered-ring proposed for the phosphinoylaldimines.

conditions (Table 1.14). It may therefore be possible to modify the solvent in order to obtain higher conversion to product.

With the excellent lead result from entry 3 of Table 1.14 in hand, we investigated how far the catalyst loading and reaction time can be reduced for the enantioselective allyl addition to **1.36c**. Only 0.5 mol % of aminophenol and NaO*t*-Bu is needed for an efficient and selective reaction to proceed in two hours (Equation 14). This high

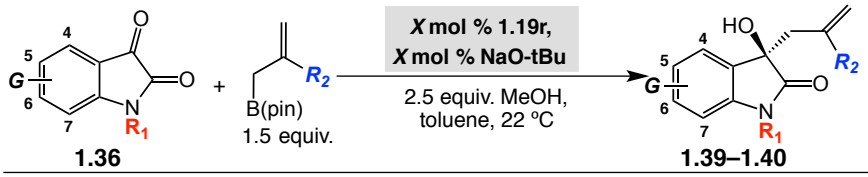


(14)

selectivity is especially impressive considering when **1.19r** and NaO*t*-Bu are omitted from the system, the background reaction is extremely efficient (66% conversion in 1 h) under otherwise identical conditions as in Equation 14. Based on the rate of this background reaction versus the rate of the catalytic reaction, again it seems the background reaction is somehow suppressed under catalytic conditions (See. **1.30d** in Scheme 1.28 and related discussion).

Following this optimization, we examined how substituted isatins behaved as substrates (Table 1.15). Electron rich substrates afford products in high yield and enantioselectivity (entries 2 and 3), but when the isatins are electron poor, the enantiomeric ratio drops to 91.5:8.5 (entries 4 and 10). Attempts to raise these selectivities through lowering the reaction temperature, catalyst modification, or increasing catalyst loadings were unsuccessful. As a further demonstration of reaction generality, changing the allyl source to methallylboronic acid pinacol ester **1.22a** results in a selective and efficient reaction when **1.16** is used as the electrophile (entry 5). In

Table 1.15 Scope of Catalytic Enantioselective Allyl Additions to Isatins

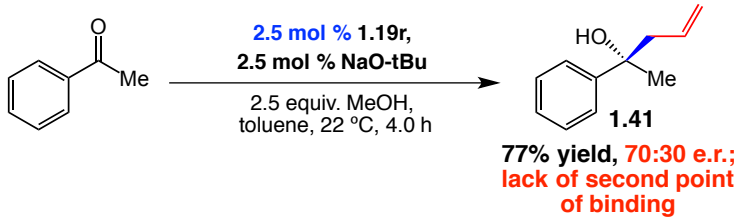


1.36 1.39–1.40

entry	*G*	*R*$_1$	*R*$_2$	*X* (mol %)	time (h)	yield (%)[a]	e.r.[b]
1	H	Bn; **1.36c**	H	0.5	2.0	93; **1.39c**	97.5:2.5
2	5-Me	Bn; **1.36d**	H	0.5	2.0	91; **1.39d**	98.5:1.5
3	5-OMe	Bn; **1.36e**	H	0.5	4.0	92; **1.39e**	97:3
4	4,7-Cl_2	Bn; **1.36f**	H	2.0	4.0	93; **1.39f**	91.5:8.5
5	H	Bn; **1.36c**	Me	0.5	1.0	97; **1.40**	95:5
6	H	PMB; **1.36g**	H	0.5	1.0	98; **1.39g**	99:1
7	4,6-Br_2	PMB; **1.36h**	H	2.0	0.25	86; **1.39h**	93:7
8	H	TBS; **1.36i**	H	0.5	1.5	96; **1.39i**	98.5:1.5
9	5-OMe	TBS; **1.36j**	H	0.5	3.0	95; **1.39j**	98:2
10	4,6-Br_2	SEM; **1.36k**	H	2.0	2.0	95; **1.39k**	91.5:8.5

All data are the average of at least two experiments. All conversions are >98% as determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixtures [a] Yield of isolated product. [b]Determined by HPLC analysis.

support of the hypothesis that two points of binding between the substrate and the catalyst is needed to obtain products in high levels of enantioselectivity, allyl-addition to acetophenone affords the homoallyl alcohol in only 70:30 e.r (Equation 15).



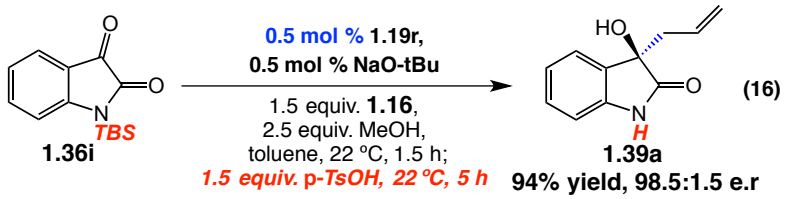
1.41

77% yield, 70:30 e.r.; lack of second point of binding

(15)

We then focused on the synthesis of enantiomerically enriched AHOs that can be used for the synthesis of medicinally relevant compounds madindoline A and convulutamydine A (Scheme 1.35). Accessing these compounds entails not only enantioselective allyl addition to the requisite *N*-protected isatins, but also practical and efficient removal of the protecting groups to produce the secondary amide-containing oxindole desired product. Isatins with a PMB-protected nitrogen undergo aminophenol promoted allylation efficiently (≤1 h, ≤2 mol% catalyst loading) and with high levels of enantioselectivity (entries 6 and 7, Table 1.35), but this protecting group could not be

removed under various conditions.[123] Examining TBS as a protecting group, which is rarely used for isatins,[124] also leads to efficient and enantioselective transformations (entries 8 and 9, Table 1.15), but in this case, the silyl group of the AHO can be easily removed with *p*-TsOH in MeOH affording the desired compound in 94% yield over two steps (Equation 16). Unfortunately, efforts toward enantioselective allyl addition to the

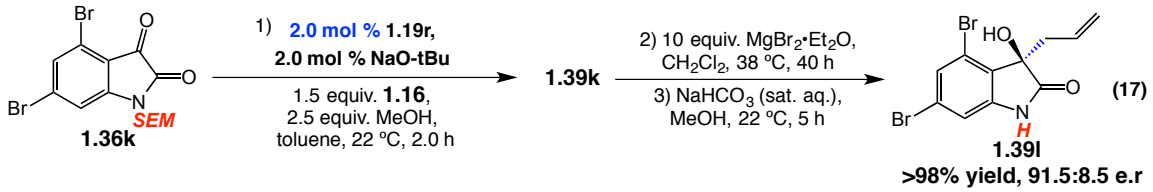


TBS-protected 4,6-dibromoisatin, requisite for the synthesis of convulutamydine A, were unsuccessful. Likely due to the strong electron withdrawing nature of 4,6-dibromoisatin, the silyl group *N*-silyl 4,6-dibromoisatin is extremely labile and is cleaved under the reaction conditions. We investigated obtaining enantioselective allyl addition in the presence of an unprotected isatin *N*-H, but no changes that we pursued, such as using stoichiometric amounts of base, revealed any promising leads.

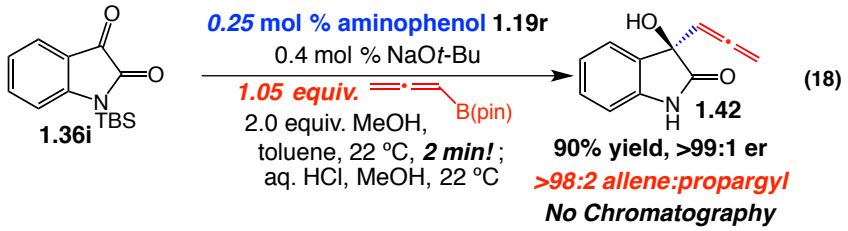
Following the difficulty with the silyl-protecting group on the isatin needed for convulutamydine A, we next examined SEM as the protecting group of 4,6-dibromoisatin. This substrate behaves similarly to the PMB protected isatin (cf. entries 10 and 7) under the reaction conditions. Pleasingly, the SEM group can be removed after addition of the allyl group (Equation 17). By stirring the SEM protected 4,6-dibromo AHO with $MgBr_2 \bullet Et_2O$ in dichloromethane at 22 ºC followed by stirring in

(123) Dr. Erika Vieira studied the PMB protecting group removal. She also was the main contributor ininvestigating the TBS protecting group and made key contributions to the SEM protecting group studies.
(124) As far as we know, the only example is in the supporting information of a report by the Wood group, see: Reisman, S. E.; Ready, J. M.; Hasuoka, A.; Smith, C. J.; Wood, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 1448–1449.

aqueous saturated sodium bicarbonate (to collapse the resultant hemiaminal), the deprotected AHO was obtained in >98% yield.

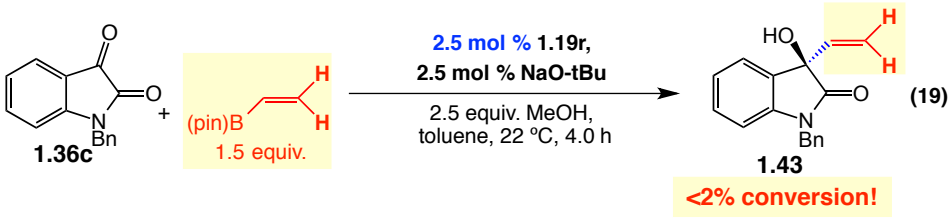


These investigations of allyl-additions to aldimines led us probe whether it was possible to take advantage of the net α-addition of our catalytic protocol and perform additions of allenylboronic acid pinacol ester to obtain homoallenylalcohols. These studies were carried out by Dr. Erika Vieira, but should be at least mentioned here (Equation 18). With 0.25 mol % of aminophenol, a gram-scale reaction proceeds in only two minutes (corresponding to a TOF of >10,000/h); following deprotection of the amide nitrogen and trituration of the resultant product (no chromatography is needed), the homoallenyl alcohol is obtained in 90% yield, >98:2 α:γ selectivity, and >99:1 e.r. The



high regioselectivity of the allenyl-addition product supports our proposed mechanism of net α-addition. Fully consistent with our hypothesis of two γ-additions leading to a net α- addition, vinylB(pin), which is electronically similar to allenylB(pin) and lacks a γ-substituent, is not added to isatins under the reaction conditions (Equation 19).[125] If the

(125) Under the conditions in Equation 18, allenylB(pin) is added to **1.36c** efficiently (>98% conversion) and with 98:2 e.r. and complete regioselectivity (>98:2 α:γ)



reaction proceeds through a single α-addition, vinylB(pin) should add to **1.36c** with efficiencies similar to allenylB(pin).[126]

1.8 Conclusion

We have developed a new class of catalysts for enantioselective allyl- and allenyl-additions to unsaturated electrophiles. A wide range of substrates are tolerated, such as alkyl-, aryl-, heteroaryl-,alkenyl, and alkynyl-substituted aldimines, as well as a variety of isatins. Additionally, the method is amenable to scale-up, does not require rigorously anhydrous reaction conditions, and proceeds efficiently at ambient conditions with low catalyst loadings of a simple-to-access aminophenol. These traits, of which no other catalytic method for the enantioselective allyl-addition to imines or isatins posseses, make this new methodology significantly impactful.

Perhaps even more notably, these catalysts operate in a mechanistically distinct fashion from any other reported catalyst for imine or ketone allylation, with α-addition products being obtained with a metal-free[127] catalyst. Even with the understanding of the mechanism we have obtained, there are still many questions to be answered, chief among them how does the catalyst initiate and how does the reaction promoted by NaO*t*-Bu occur (that is, without aminophenol)? One possibility is that a Lewis acidic boron species (maybe a trimethylborate-like species) is generated *in situ* which is then allylated by the

(126) Similarly, BnB(pin) does not add to aldimines under the conditions in Table 1.5.
(127) While there is sodium present in the reaction, it does not play a key role in catalysis as evidenced by DBU capably serving as a base for the aminophenol promoted enantioselective allyl-addition to imines. See Equation 1.

stoichiometric allylB(pin) to make dimethoxyallylboron. This reagent may be active enough to add to the aldimine. To test this hypothesis, one could synthesize dimethoxyallylboron and determine if it adds to the imine uncatalyzed. If it still requires NaO*t*-Bu, then synthesis of α-deuterated dimethoxyallylboronate would be interesting to see if it adds with γ-selectivity (as it would not require allyl-transfer before addition based on our hypothesis). Answering these questions will likely lead to insight into how the catalyst loading can be lowered even further by modifying the reaction conditions to more greatly favor complete initiation of the aminophenol added to the reaction.

With regard to the crotyl-addition catalyzed by zinc-alkoxide, one interesting question is whether the reaction truely goes through three γ-additions (as shown in Scheme 1.33) or whether an aminophenol-bound zinc-alkoxide transmetallates with the allylboron, isomerizes, and then adds to the imine. This latter scenario may be disfavored by the steric interactions proposed in Scheme 1.30, but we do not have definitive evidence disproving this mechanistic pathway.

1.9 General Experimental Section

■ **General.** Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, λ_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm, CD_3OD: δ 3.34 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian

Unity INOVA 400 (100 MHz) or a Varian Unity INOVA 500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). Data are reported as follows: chemical shift, multiplicity (singlet unless otherwise noted), and coupling constants (Hz). ^2H NMR spectra were recorded on a Varian Unity INOVA 500 (76 MHz) tuned to the lock channel. High-resolution mass spectrometry was performed on a JEOL AccuTOF-DART (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios (er) values were determined by HPLC analysis using either a Shimadzu LC-2010AHT or SCL-10AVP chromatograph (Chiral Technologies Chiralcel OD (4.6 x 250 mm), Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), Chiral Technologies Chiralcel OJ-H (4.6 x 250 mm), Chiral Technologies Chiralpak AD-H (4.6 x 250 mm), Chiral Technologies Chiralcel AZ-H (4.6 x 250 mm) columns), or GLPC (gas-liquid partition chromatography) with an Agilent chromatograph (Alltech Associated Chiraldex CD-BDM column (30 m x 0.25 mm) or a Hewlett Packard 5890 Series II chromatograph (Alltech Associated Betadex 120 column (30 m x 0.25 m). Specific rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter. Melting points were determined using a Thomas Hoover Uni-melt capillary melting point apparatus. Selected single crystals suitable for X-ray crystallographic analysis were used for structural determination. The X-ray intensity data were measured at 100(2) K (Oxford Cryostream 700) on a Bruker Kappa APEX Duo diffractometer system equipped with a sealed Mo-target X-ray tube (λ = 0.71073 Å) and a high brightness IμS copper source (λ = 1.54178 Å). The crystals were mounted on agoniometer head with paratone oil. The detector was placed at a distance of 5.000 or

6.000 cm from the crystal. For each experiment, data collection strategy was determined by APEX software package and all frames were collected with a scan width of 0.5° in ω and φ with an exposure time of 10 or 20s/frame. The frames were integrated with the Bruker SAINT Software package using a narrow-frame integration algorithm to a maximum 2θ angle of 56.54° (0.75 Å resolution) for Mo data and of 134° (0.84 Å resolution) for Cu data. The final cell constants are based upon the refinement of the XYZcentroids of several thousand reflections above 20 σ(I). Analysis of the data showed negligible decay during data collection. Data were corrected for absorption effects using the empirical method (SADABS). The structures were solved and refined by full-matrix least squares procedures on ||F2|| using the Bruker SHELXTL (version 6.12) software package. All hydrogen atoms were included in idealized positions for structure factor calculations except for those forming hydrogen bonds or on a chiral center. Anisotropic displacement parameters were assigned to all non-hydrogen atoms, except those disordered.

■ **Solvents:** Unless otherwise noted, solvents were purged with Ar and purified under a positive pressure of dry Ar by a modified Innovative Technologies purification system. Toluene (Fisher, ACS Grade) was passed successively through activated copper and alumina columns. Dichloromethane (Fisher, ACS Grade) and diethyl ether (Aldrich, Chromasolv®) were passed successively through two activated alumina columns. Tetrahydrofuran was purified by distillation from sodium benzophenone ketyl immediately prior to use. Dimethyl Sulfoxide (anhydrous, 99.9+%) was purchased from Alfa Aesar and used as received. $CDCl_3$ was purchased from Cambridge Isotope Laboratories and stored over activated 4Å molecular sieves prior to use. CD_3OD was

purchased from Cambridge Isotope Laboratories and used as received. $CD_3C_6D_5$ (d_8–toluene) was purchased from Cambridge Isotope Laboratories and distilled from sodium metal onto activated 4Å molecular sieves prior to use. All work-up and purification procedures were carried out in air with reagent grade solvents (purchased from Fisher).

■ **Reagents:**

Allenylboronic Acid Pinacol Ester (19) was obtained from Frontier Scientific and used as received.

Allylboronates: Allylboronic acid pinacol ester (**1a**) was purchased from Aldrich or obtained as a gift from Frontier Scientific, Inc and distilled prior to use. 1,1-Di-deuterioallylboronic acid pinacol ester (***d*$_2$-1a**) was synthesized and purified in accordance with a procedure in the literature.[128] (2-Methylallyl)boronic acid pinacol ester (**1b**) was synthesized and purified in accordance with a procedure in the literature.[129] (2-Phenylallyl)boronic acid pinacol ester (**1c)** was synthesized and purified in accordance with a procedure in the literature.[130] Enantiomerically enriched α-substituted allylboronates ***S*-9**, ***R*-9**, and **12** were synthesized and purified in accordance with a procedure in with the literature.[131]

Benzyl Chloride was purchased from Aldrich and distilled from $CaCl_2$ prior to use.

Boc-Val-OH was purchased from Advanced ChemTech and used as received.

***tert*-Butanol** was purchased from Aldrich and distilled from sodium metal before use.

***n*-Butylamine** was purchased from Aldrich and used as received.

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(128) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 4978–4983.
(129) Zhang, P.; Roundtree, I. A.; Morken, J. P. *Org. Lett.* **2012**, *14*, 1416–1419.
(130) Corberan, R.; Mszar, N. W.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 7079–7082.
(131) Guzman-Martinez, A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10634–10637.

***tert*-Butyldimethylsilyl Chloride** was purchased from Strem and used as received.

3-*tert*-Butyl-2-hydroxybenzaldehyde was purchased from Aldrich and used as received.

1,8-Diazabicycloundec-7-ene (DBU) was purchased from Aldrich and distilled from CaH_2 prior to use.

Diethylzinc was purchased from Aldrich and used as received.

Dimethylamine (40 wt % in H_2O) was purchased from Aldrich and used as received.

1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide Hydrochloride (EDC•HCl) was purchased from Advanced ChemTech and used as received.

Hydrochloric Acid (4.0 M in 1,4-dioxane) was purchased from Aldrich and used as received.

Hydrochloric Acid (12 M, 36.5-38.0 wt %) was purchased from Alfa Aesar and used as received.

1-Hydroxy-benzotriazole Hydrate (HOBt•H_2O) was purchased from Advanced ChemTech and used as received.

Isatins. Isatin and 5-methylisatin were purchased from Aldrich and used as received. 5-methoxyisatin was purchased from Oakwood and used as received. 4,6-Dibromoisatin was purchased from D-L Chiral Chemicals and was dissolved in methanol and copious purple solid impurities were removed by filtration.

L-*tert*-Leucine was purchased from Chem-Impex and Boc protected prior to use.

Magnesium Sulfate was purchased from Fisher and flame-dried under vacuum prior to use.

Magnesium Bromide Diethyl Etherate ($MgBr_2$•Et_2O) was purchased from Aldrich

and used as received.

Methanol was purchased from Acros (99.8% anhydrous) and distilled at 1 atm from sodium metal prior to use or used as received.

Potassium Carbonate was purchased from Fisher and dried at 80 ºC under vacuum for 12 h prior to use.

Pyrrolidine was purchased from Aldrich and used as received.

Sodium Borohydride was purchased from Aldrich and used as received.

Sodium *tert*-Butoxide was purchased from Strem and used as received.

Sodium Hydride (60 wt% in oil) was purchased from Strem and used as received.

Sodium Periodate was purchased from Acros and used as received.

Titanium Tetrachloride ($TiCl_4$) was purchased from Aldrich and used as received.

Triethylamine was purchased from Aldrich and distilled from CaH_2 prior to use.

2-(Trimethylsilyl)ethoxymethyl Chloride, technical grade (SEM-Cl) was purchased from Aldrich and used as received.

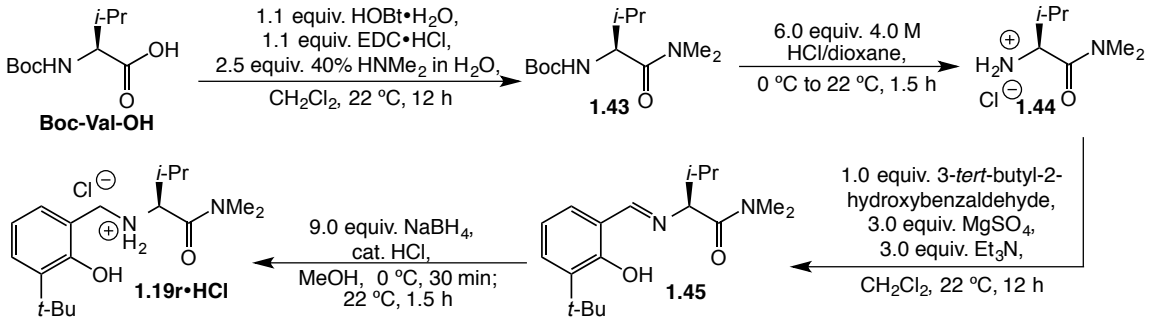
***p*-Toluenesulfonic Acid Monohydrate** was purchased from Aldrich and used as received.

L-Valine Ethyl Ester Hydrochloride was purchased from Aldrich and used as received.

Zinc *tert*-Butoxide was prepared by reaction of *tert*-butanol with diethylzinc. A flame-dried round bottom flask is purged with nitrogen, sealed with a septum and electrical tape, and charged with toluene (100 mL) and *tert*-butanol (1.8 mL, 19 mmol) by syringe. The solution is cooled to –78 ºC and diethylzinc (**Caution Pyrophoric!** 1.5 mL, 15 mmol) is added dropwise by syringe over 10 minutes. The reaction is allowed to warm to

22 ºC and to stir for 18 h. The toluene is removed by distillation under nitrogen at 1 atm. and the resulting solid is dried under vacuum for 12 h. The solid is removed from the flask in a nitrogen-filled glovebox to afford 1.5 g (7.1 mmol, 46% yield) of a white powder.

Scheme 1.39. Representative Experimental Procedure for Synthesis of Aminophenol **1.19r**



EDC•HCl (4.22 g, 22.0 mmol), reagent grade CH_2Cl_2 (80 mL), HOBt•H_2O (3.36 g, 22.0 mmol), and Boc-Val-OH (4.34 g, 20.0 mmol) are added successively at 22 °C under air to a 250 mL round bottom flask equipped with a stir bar. The light yellow solution is allowed to stir for five minutes and dimethylamine (40 wt % in H_2O, 5.3 mL, 50 mmol) is added drop-wise over one minute. The flask with the resulting light yellow solution is sealed with a rubber septum and allowed to stir for 12 h at 22 °C. An aqueous solution of citric acid (10 wt %, 80 mL) is then added and the mixture is allowed to stir for 0.5 h during which time a white precipitate is formed. The precipitate is removed by filtration and the resulting two layers are separated. The organic layer is washed sequentially with an aqueous solution of citric acid (10 wt %, 80 mL), a saturated aqueous solution of $NaHCO_3$ (80 mL), and brine (80 mL) and is dried over Na_2SO_4 to give (*S*)-*tert*-butyl (1-(dimethylamino)-3-methyl-1-oxobutan-2-yl)carbamate (**S2**) as pale yellow oil, which is employed without purification in the subsequent deprotection.

In a 100 mL round bottom flask, (*S*)-*tert*-butyl (1-(dimethylamino)-3-methyl-1-oxobutan-

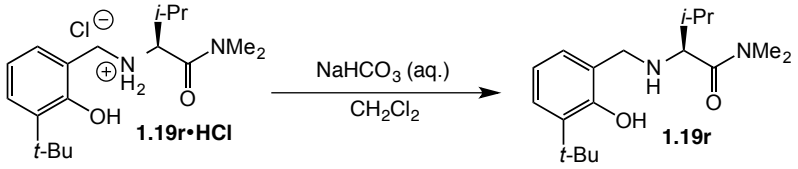
2-yl)carbamate **1.43** (4.65 g, 19.3 mmol, 1.00 equiv.) is allowed to stir with a 4.0 M solution of hydrochloric acid in dioxane (28.9 mL, 116 mmol, 6.00 equiv.) for 1.5 h at 22 °C under air, after which the solution is purged with nitrogen for 30 min (removal of HCl gas) and the solvent is removed under reduced pressure to yield (*S*)-2-amino-*N*,*N*,3-trimethylbutanamide as HCl salt **1.44**, which is used without purification in the subsequent condensation.

To the same flask (purged with nitrogen) is added 3-(*tert*-butyl)-2-hydroxybenzaldehyde (3.43 g, 19.3 mmol, 1.00 equiv.) and $MgSO_4$ (6.93 g, 57.8 mmol, 3.00 equiv.), followed by the addition of dichloromethane (70 mL) and triethylamine (8.11 mL, 57.8 mmol, 3.00 equiv.) through a syringe. The mixture is allowed to stir overnight at 22 °C under nitrogen during which time the solution becomes bright yellow. The mixture is filtered through a small plug of silica gel to remove both $MgSO_4$ and triethylamine hydrochloride (which inhibits the following reduction) and silica plug is eluted with hexanes:ethyl acetate (2:1) until the solution becomes colorless. After evaporation of the volatiles, the remaining yellow oil is washed several times with hexanes (to remove residual triethylamine hydrochloride salt) and the combined filtrates are concentrated to afford (*S*,*E*)-2-((3-(*tert*-butyl)-2-hydroxybenzylidene)amino)-*N*,*N*,3-trimethyl-butanamide (**1.44**) as yellow oil, which is utilized without purification in the follow-up reduction procedure.

To a 500 mL round bottom flask containing a solution of imine **1.44** in 50 mL MeOH cooled to 0 ºC, $NaBH_4$ is added (5.83 g, 154 mmol, 8.00 equiv.) followed by a drop of 12 M aqueous hydrochloric acid. There is vigorous gas evolution upon addition of the acid and the yellow color of the solution disappears immediately. After the solution is allowed to stir for 30 min, the excess reducing agent is quenched through slow addition of a 2.0 M

solution of aqueous HCl until the pH is less than one. The aqueous phase is then washed with dichloromethane (4 x 50 mL) and the combined organic layers are dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The white solid is purified by trituration from 10 mL dichloromethane and 80 mL hexanes to afford (*S*)-*N*-(3-(*tert*-butyl)-2-hydroxybenzyl)-1-(dimethylamino)-3-methyl-1-oxobutan-2-aminium chloride **1.19r•HCl** as a white solid (5.30 g, 15.5 mmol, 77.5% yield based on Boc-Val-OH). Crystals suitable for X-ray crystallography were grown by vapor diffusion from a dichloromethane/toluene solvent system.

(*S*)-*N*-(3-(*tert*-Butyl)-2-hydroxybenzyl)-1-(dimethylamino)-3-methyl-1-oxobutan-2-aminium (1.19r•HCl; see above): M.p. = 182–183 °C. IR (neat): 2952 (br, s), 2821 (m), 2733 (m), 1664 (s), 1649 (s), 1548 (m), 1438 (s), 1396 (s), 1373 (m), 1360 (m), 1323 (m), 1285 (m), 1209 (s), 1176 (s), 1139 (m), 1097 (m), 874 (m), 792 (m), 756 (s), 484 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.62 (1H, br s), 8.24 (1H, br s), 7.61 (1H, br s), 7.30 (1H, dd, *J* = 7.6, 1.6 Hz), 7.04 (1H, dd, *J* = 7.6, 1.6 Hz), 6.85 (1H, t, *J* = 7.6 Hz), 4.44–4.38 (1H, m), 4.29–4.21 (2H, m), 2.95 (3H, s), 2.86 (3H, s), 2.50–2.44 (1H, m), 1.40 (9H, s), 1.13 (6H, app d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 155.3, 141.3, 130.1, 129.1, 121.0, 119.9, 61.0, 47.9, 37.6, 36.2, 35.2, 30.3, 30.0, 18.7, 18.5.



(*S*)-2-((3-(*tert*-Butyl)-2-hydroxybenzyl)amino)-*N*,*N*,3-trimethylbutanamide (1.19r, Scheme 1.27): The salt **1.19r•HCl** (5.30 g, 15.5 mmol) is dissolved in 100 mL dichloromethane and deprotonated with 200 mL of a saturated aqueous solution of

$NaHCO_3$. The layers are separated and the aqueous phase is washed twice with 50 mL dichloromethane. The combined organic phases are dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to afford **1.19r** as white solid (4.45 g, 14.5 mmol, 73% yield based on Boc-Val-NMe_2 **S1**). Crystals suitable for X-ray crystallography were grown by slow evaporation of ethyl acetate. See Part D of the Supplementary Information for the X-ray crystal structure. M.p. = 97–99 ºC. IR (neat): 3310 (w), 2943 (w, br), 2872 (w, br), 1638 (s), 1589 (w), 1485 (m), 1459 (m), 1241 (m), 1183 (m), 929 (m), 870 (w), 855 (w), 841(w), 753 (s), 648 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 11.03 (1H, br s), 7.19 (1H, dd, J = 7.0, 1.2 Hz), 6.80–6.75 (1H, m), 6.70 (1H, t, J = 7.6 Hz), 4.10 and 3.46 (2H, ABq, J_{AB} = 13.6 Hz), 3.28 (1H, br s), 3.04 (3H, s), 2.89 (3H, s), 2.65 (1H, br s), 1.90–1.84 (1H, m), 1.42 (9H, s), 0.97 (3H, d, J = 6.8 Hz), 0.94 (3H, d, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 157.1, 137.1, 126.9, 126.2, 122.9, 118.5, 61.2, 51.5, 37.1, 35.8, 34.8, 31.3, 29.6, 20.1, 18.0; HRMS Calcd for $C_{18}H_{31}N_2O_2$ $[M + H]^+$: 307.23855; Found: 307.23736. $[\alpha]^{20}_D$ = –37 (c = 0.68, $CHCl_3$).

(*S*)-*N*-Butyl-2-((2-hydroxybenzyl)amino)-3-methylbutanamide (1.19i, Scheme 1.27): The title compound is prepared according to the representative synthesis of aminophenol **1.19r** except for the following changes: 1) For the amide formation (step 1), 2.5 equiv. of neat *n*-butylamine is used instead of dimethylamine. 2) For the imine formation (step 3) salicylaldehyde is utilized. 3) The product from the reduction is quenched with a saturated solution of aqueous $NaHCO_3$ (formation of the HCl salt is omitted) and the aminophenol is then purified by silica gel chromatography (100% dichloromethane to 98:2 dichloromethane:methanol) to afford **1.19i** as an off-white solid. M.p. = 50–52 ºC. IR (neat): 3318 (w), 3294 (w, br), 3255 (w), 2958 (w), 2930 (w, br), 2872 (w), 1628 (s),

1560 (m), 1469 (m), 1387 (w), 1253 (s), 1101 (w), 970 (w), 750 (s), 682 (w, br) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.58 (1H, br s), 7.18 (1H, dt, *J* = 7.9, 1.4 Hz), 6.93 (1H, d, *J* = 7.6 Hz), 6.85 (1H, d, *J* = 8.1 Hz), 6.77 (1H, t, *J* = 7.1 Hz), 5.46 (1H, br s), 4.10 and 3.64 (2H, ABq, J_{AB} = 13.9 Hz), 3.34 (2H, app. dd, *J* = 13.0, 7.1 Hz), 2.66 (1H, d, *J* = 7.0 Hz), 2.41 (1H, br s), 1.94–1.85 (1H, m), 1.56–1.49 (2H, m), 1.42–1.33 (2H, m), 1.01 (3H, d, *J* = 6.8 Hz), 0.97–0.93 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 158.1, 129.1, 128.8, 122.4, 119.3, 116.5, 67.5, 51.0, 39.4, 31.9, 31.7, 20.2, 19.8, 19.2, 13.9; HRMS Calcd for $C_{16}H_{27}N_2O_2$ $[M + H]^+$: 279.20725; Found: 279.20754. $[\alpha]^{20}_D$ = –33 (*c* = 0.55, $CHCl_3$).

(*S*,*E*)-*N*-Butyl-2-((2-hydroxybenzylidene)amino)-3-methylbutanamide (1.19w, Scheme 1.27):

This material is synthesized in a manner analogous to aminophenol **2a** except the final reduction step is not performed. The analytical data are fully consistent with those reported previously.[132]

(*S*)-*N*-(1-(Butylamino)-3-methyl-1-oxobutan-2-yl)-2-hydroxybenzamide (1.19x, Scheme 1.27):

The title compound is prepared according to the representative synthesis of aminophenol **1.19i** except after the second step; H_2N-Val-NH*n*-Bu is treated with salicylic acid under the standard amide formation conditions outlined in the first step. The resulting off-white solid is purified by silica gel chromatography (5:1 hexanes:ethyl acetate) to afford **2c** as a white solid. M.p. = 123–125 ºC. IR (neat): 3279 (w), 3090 (w, br), 2930 (m), 1620 (s), 1605 (s), 1547 (s), 1530 (s), 1454 (s), 1371 (m, br), 1229 (m), 756 (s), 643 (m) cm^{-1}; ^1H

(132) Wen, J.; Zhao, J.; Wang, X.; Dong, J.; You, T. *J. Mol. Cat. A: Chem*, **2006**, *245*, 242–247.

NMR (400 MHz, $CDCl_3$): δ 12.07 (1H, s), 7.51 (1H, d, J = 8.0 Hz), 7.40–7.36 (1H, m), 7.29 (1H, br s), 6.97 (1H, dd, J = 8.4, 0.9 Hz), 6.85–6.81 (1H, m), 6.00 (1H, br s), 4.36 (1H, t, J = 7.7 Hz), 3.39–3.30 (1H, m), 3.27–3.19 (1H, m), 2.25–2.17 (1H, m), 1.54–1.47 (2H, m), 1.39–1.30 (2H, m), 1.03 (3H, d, J = 3.3 Hz), 1.01 (3H, d, J = 3.2 Hz), 0.91 (3H, t, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 169.8, 161.4, 134.5, 126.3, 119.0, 118.5, 114.4, 58.9, 39.6, 31.7, 31.6, 20.2, 19.3, 18.7, 13.8; HRMS Calcd for $C_{16}H_{25}N_2O_3$ $[M + H]^+$: 293.18652; Found: 293.18532. $[\alpha]^{20}_D$ = –34 (c = 0.63, $CHCl_3$).

(*S*)-*N*-Butyl-2-((3-(*tert*-butyl)-2-hydroxybenzyl)amino)-3-methylbutanamide (1.19h, Scheme 1.27): The title compound is prepared according to the representative synthesis of aminophenol **1.19r** except for the following changes: 1) For the first amide formation, 2.5 equiv. of neat *n*-butylamine is used instead of dimethylamine. 2) The reduction is quenched with a saturated solution of aqueous $NaHCO_3$ (formation of the HCl salt is omitted) and the desired product is purified by silica gel chromatography (100% dichloromethane to 98:2 dichloromethane:methanol) to afford **1.19h** as a white solid. M.p. = 97–99 ºC. IR (neat): 3268 (w, br), 3084 (w, br), 2957 (m), 2871 (w), 1644 (s), 1561 (m), 1435 (s), 1259 (s), 835 (m), 784 (m), 750 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.83 (1H, br s), 7.21 (1H, dd, J = 7.8, 1.6 Hz), 6.80 (1H, dd, J = 7.3, 1.6 Hz), 6.71 (1H, t, J = 7.6 Hz), 5.52 (1H, br s), 4.13 and 3.59 (2H, ABq, J_{AB} = 13.8 Hz), 3.37–3.29 (2H, m), 2.59 (1H, d, J = 7.3 Hz), 1.90–1.81 (1H, m), 1.58–1.46 (2H, m), 1.43-1.33 (11H, m), 1.00 (3H, d, J = 6.8 Hz), 0.95 (3H, t, J = 7.3 Hz), 0.91 (3H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 157.1, 137.1, 127.0, 126.3, 122.6, 118.5, 67.0, 51.2, 39.3, 34.8, 31.9, 31.7, 29.6, 20.2, 20.0, 19.1, 13.8; HRMS Calcd for $C_{20}H_{35}N_2O_2$ $[M + H]^+$: 335.26985; Found: 335.27112. $[\alpha]^{20}_D$ = –68 (c = 0.63, $CHCl_3$).

(*S*)-Ethyl 2-((3-(*tert*-butyl)-2-hydroxybenzyl)amino)-3-methylbutanoate (1.19p, Scheme 1.27): The title compound is prepared according to the representative synthesis of aminophenol **1.19r** except for the following changes: 1) Initial amide formation carried out with L-Valine methyl ester hydrochloride instead of Boc-Val-OH. 2) The reduction is quenched with a saturated solution of aqueous $NaHCO_3$ (formation of the HCl salt is omitted) and the desired product is purified by silica gel chromatography (100% hexanes to 30:1 hexanes:diethyl ether) to afford **1.19p** as a yellow oil. IR (neat): 2960 (m, br), 1728 (s), 1459 (s), 1237 (m), 1186 (s), 1140 (s), 1023 (m), 747 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.57 (1H, br s), 7.21 (1H, dd, J = 7.8, 1.7 Hz), 6.84–6.82 (1H, m), 6.72 (1H, t, J = 7.6 Hz), 4.28–4.21 (2H, m), 4.08 and 3.66 (2H, ABq, J_{AB} = 13.3 Hz), 3.08 (1H, d, J = 4.9 Hz), 2.27 (1H, br s), 2.04–1.96 (1H, m), 1.41 (9H, s), 1.31 (3H, t, J = 7.1 Hz), 0.99 (6H, app dd, J = 10.5, 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 156.9, 137.1, 127.1, 126.4, 122.8, 118.6, 65.6, 61.0, 51.9, 34.8, 31.5, 29.7, 19.7, 18.3, 14.5; HRMS Calcd for $C_{18}H_{30}NO_3$ $[M + H]^+$: 308.22257; Found: 308.22291. $[\alpha]^{20}_D$ = –42 (c = 0.73, $CHCl_3$).

(*S*)-2-((3-(*tert*-Butyl)-2-hydroxybenzyl)amino)-3-methyl-1-(pyrrolidin-1-yl)butan-1-one (1.19s, Scheme 1.20): The title compound is prepared according to the representative synthesis of aminophenol **1.19r** except for the following changes: 1) For the first step, 2.5 equiv. of neat pyrrolidine is used instead of dimethylamine. 2) For the reduction of the imine in the last step of the synthesis, 20.0 equiv. $NaBH_4$ is used. 3) The reduction is quenched with a saturated solution of aqueous $NaHCO_3$ (formation of the HCl salt is omitted) and the desired product is purified by silica gel chromatography (hexanes to 5:1 hexanes:ethyl acetate to 3:1 hexanes:ethyl acetate) to afford **1.19s** as a clear, colorless oil.

IR (neat): 3279 (w, br), 2956 (w, br), 2873 (w), 1632 (s), 1424 (s), 1356 (w), 1239 (m), 1184 (w), 1141 (w), 1085 (w), 880 (m), 748 (s), 529 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.06 (1H, br s), 7.19 (1H, dd, *J* = 7.0, 1.2 Hz), 6.77 (1H, dd, *J* = 7.3, 1.5 Hz), 6.69 (1H, t, *J* = 7.5 Hz), 4.13 (1H, app d, *J* = 13.6 Hz), 3.66–3.60 (1H, m), 3.53–3.45 (2H, m), 3.28–3.14 (2H, m), 3.05 (1H, d, *J* = 6.7 Hz), 2.60 (1H, br s), 1.91–1.81 (5H, m), 1.42 (9H, s), 1.00 (3H, d, *J* = 6.7 Hz), 0.93 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 157.2, 137.1, 126.8, 126.2, 122.9, 118.4, 63.4, 51.3, 46.5, 45.8, 34.8, 31.4, 29.6, 26.2, 24.3, 20.1, 18.5; HRMS Calcd for $C_{20}H_{33}N_2O_2$ $[M + H]^+$: 333.25420; Found: 333.25561. $[\alpha]^{20}_D = -58$ (*c* = 0.58, $CHCl_3$).

(*S*)-2-((3-(*tert*-Butyl)-2-hydroxybenzyl)amino)-*N*,*N*,3,3-tetramethylbutanamide (1.19v, Table 1.7): The title compound is prepared according to the representative synthesis of aminophenol **1.19r** except for the following changes: 1) Initial amide formation carried out with Boc-Tle-OH instead of Boc-Val-OH. 2) The product from the reduction process is quenched with a saturated solution of aqueous $NaHCO_3$ (formation of the HCl salt is omitted) and the desired product is purified by silica gel chromatography (9:1 hexanes:ethyl acetate to 6:1 hexanes:ethyl acetate to 4:1 hexanes:ethyl acetate) to afford **1.19v** as a white solid. M.p. = 96–98 ºC. IR (neat): 2948 (w, br), 1639 (s), 1460 (m), 1433 (m), 1352 (m), 1240 (m), 1135 (m), 878 (m), 782 (m), 751 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.87 (1H, br s), 7.19 (1H, d, *J* = 7.3 Hz), 6.77 (1H, d, *J* = 7.3 Hz), 6.70 (1H, t, *J* = 7.5), 4.09 and 3.40 (2H, ABq, J_{AB} = 13.6 Hz), 3.31 (1H, d, *J* = 11.3 Hz), 3.03 (3H, s), 2.89 (3H, s), 2.71 (1H, br s), 1.40 (9H, s), 0.96 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 157.0, 137.2, 126.9, 126.3, 122.9, 118.5, 62.4, 51.3, 38.0, 35.8, 34.8, 34.7, 29.6, 27.0; HRMS Calcd for $C_{19}H_{33}N_2O_2$ $[M + H]^+$:

321.25420; Found: 321.25442. $[\alpha]^{20}_{D} = -33$ (*c* = 0.93, $CHCl_3$).

(*S*)-2-((3-(*tert*-butyl)-2-hydroxybenzyl)amino)-3-methyl-*N*-phenylbutanamide (1.19n, Scheme 1.20): M.p. = 125–127 ºC. IR (neat): 3280 (w), 2958 (w, br), 2874 (w, br), 1655 (m), 1637 (m), 1597 (m), 1437 (m), 1237 (m), 741 (s), 693 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.65 (1H, br s), 7.55–7.53 (2H, m), 7.38–7.34 (2H, m), 7.26–7.22 (1H, m), 7.18–7.14 (2H, m), 6.83 (1H, dd, *J* = 7.3, 1.3 Hz), 6.74 (1H, t, *J* = 7.6 Hz), 4.21 (1H, d, *J* = 13.8 Hz), 3.69 (1H, d, *J* = 13.8 Hz), 2.81 (1H, d, *J* = 6.9 Hz), 2.55 (1H, br s), 1.85 (1H, dq, *J* = 13.6, 6.8 Hz), 1.43 (9H, s), 1.06 (3H, d, *J* = 6.8 Hz), 1.00 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 157.0, 137.2, 137.2, 129.3, 127.2, 126.5, 125.0, 122.5, 120.1, 118.7, 67.5, 51.2, 34.9, 31.9, 29.6, 20.0, 18.9; HRMS Calcd for $C_{22}H_{31}N_2O_2$ $[M + H]^+$: 355.23855; Found: 355.23950. $[\alpha]^{20}_{D} = -142$ (*c* = 0.767, $CHCl_3$).

(*S*)-2-((2-Hydroxybenzyl)amino)-*N*,*N*,3-trimethylbutanamide (1.30a, Scheme 1.28): The title compound is synthesized analogously to **1.19r** and purified by silica gel chromatography (slurry packed in 95:5 hexanes:triethylamine and eluted with 5:1 to 1:1 hexanes:ethyl acetate) to afford **1.19i** as an off-white solid. M.p. = 70–72 ºC. IR (neat): 2964 (w), 2928 (w), 2983 (w), 1637 (s), 1589 (m), 1467 (m), 1399 (m), 1353 (w), 1256 (s), 1125 (m), 1105 (w), 1075 (m), 892 (m), 848 (m), 752 (s), 628 (m), 464 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.81 (1H, br s), 7.17 (1H, dt, *J* = 7.7, 1.7 Hz), 6.92 (1H, dd, *J* = 7.4, 1.7 Hz), 6.85 (1H, dd, *J* = 8.1, 1.2 Hz), 6.78–6.74 (1H, m), 4.05 and 3.53 (2H, ABq, J_{AB} = 13.8 Hz), 3.34 (1H, d, *J* = 6.0 Hz), 3.04 (3H, s), 2.91 (3H, s), 1.94–1.81 (1H, m), 0.98 (6H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 158.2, 129.0, 128.7, 122.6, 119.3, 116.5, 61.7, 51.4, 37.1, 35.9, 31.4, 20.1, 18.0; HRMS Calcd for $C_{14}H_{23}N_2O_2$ $[M + H]^+$: 251.17595; Found: 251.17545. $[\alpha]^{25.1}_{D} = -23$ (*c* = 0.44, $CHCl_3$).

(*S*)-2-((2-Hydroxy-3-methylbenzyl)amino)-*N*,*N*,3-trimethylbutanamide (1.30b): The title compound is synthesized analogously to **1.19r** and purified by silica gel chromatography (5:1 to 2:1 hexanes:ethyl acetate) to afford **1.30b** as a pale yellow oil. IR (neat): 3291 (w, br), 2960 (w, br), 2037 (w), 1637 (s), 1596 (w), 1467 (s), 1397 (s), 1262 (m), 1230 (m), 1125 (m), 1078 (m), 831 (m), 764 (s), 739 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.89 (1H, s), 7.04 (1H, d, J = 7.5 Hz), 6.81–6.73 (1H, m), 6.67 (1H, t, J = 7.4 Hz), 4.01 and 3.51 (2H, ABq, J_{AB} = 13.6 Hz), 3.33 (1H, d, J = 6.0 Hz), 3.04 (3H, s), 2.93 (3H, s), 2.24 (3H, s), 1.91–1.83 (1H, m), 0.98 (6H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 156.3, 130.2, 126.3, 125.4, 121.9, 118.8, 61.8, 51.5, 37.2, 35.9, 31.4, 20.1, 18.1, 15.9; HRMS Calcd for $C_{15}H_{25}N_2O_2$ $[M + H]^+$: 265.19160; Found: 265.19277. $[\alpha]^{25.1}{}_D = -13$ (c = 0.77, $CHCl_3$).

(*S*)-2-(Benzylamino)-*N*,*N*,3-trimethylbutanamide (1.30d, Scheme 1.28): The title compound is synthesized analogously to **1.19r**. The analytical data are fully consistent with those reported previously for the racemic compound.[133] $[\alpha]^{24.8}{}_D = -31$ (c = 0.64, $CHCl_3$).

(*S*)-2-((3-(*tert*-Butyl)-2-hydroxy-5-nitrobenzyl)amino)-*N*,*N*,3-trimethylbutanamide (1.30e, Scheme 1.28): The title compound is synthesized analogously to **1.19r** and purified by silica gel chromatography (6:1 to 3:1 hexanes:ethyl acetate) to afford **1.30e** as a yellow-orange solid. M.p. = 110–112 ºC. IR (neat): 3314 (w, br), 2959 (w, br), 2915 (w, br), 2873 (w, br), 1643 (s), 1588 (w), 1433 (m), 1410 (m), 1395 (m), 1334 (s), 1243 (s), 1204 (m), 1171 (m), 1102 (m), 1066 (m), 932 (m), 901 (m), 711 (m), 668 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.60 (1H, s), 8.14 (1H, d, J = 2.7 Hz), 7.77–7.76 (1H, m),

(133) Chen, J.; Cunico, R. F. *Tetrahedron Lett.* **2003**, *44*, 8025–8027.

4.16 and 3.53 (2H, ABq, J_{AB} = 14.3 Hz), 3.27 (1H, d, J = 5.3 Hz), 3.05 (3H, s), 2.93 (3H, s), 1.92–1.84 (1H, m), 1.43 (9H, s), 0.98–0.94 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 164.0, 139.6, 138.1, 122.9, 122.8, 122.6, 61.6, 51.3, 37.1, 36.0, 35.1, 31.1, 29.2, 20.2, 17.7; HRMS Calcd for $C_{18}H_{30}N_3O_4$ $[M + H]^+$: 352.22363; Found: 352.22264. $[\alpha]^{25.1}_D$ = –12 (*c* = 0.86, $CHCl_3$).

(*R*)-2-(*tert*-Butyl)-6-(((3-methylbutan-2-yl)amino)methyl)phenol (1.30f): The title compound is synthesized from 3-*tert*-butyl-2-hydroxybenzaldehyde and (*R*)-(-)-2-amino-3-methylbutane (≥97% ee, Aldrich) analogously to the last two steps to make **1.19r** and purified by silica gel chromatography (slurry packed in 95:5 hexanes:triethylamine and eluted with hexanes to 30:1 hexanes:diethyl ether) to afford **1.30f** as a clear colorless oil. IR (neat): 2958 (m), 22873 (m, br), 1591 (w), 1435 (s), 1388 (m), 1239 (s), 1184 (w), 1140 (w), 1074 (w), 784 (m), 747 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (phenol proton likely too broad to observe) 7.19 (1H, dd, J = 7.9, 1.7 Hz, 1H), 6.90–6.85 (1H, m), 6.73–6.69 (1H, m), 4.03 and 3.88 (2H, ABq, J_{AB} = 13.3 Hz), 2.58 (1H, dq, J = 6.5, 4.7 Hz), 1.82–1.74 (1H, m), 1.42 (9H, s), 1.07 (3H, d, J = 6.5 Hz), 0.92 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 137.0, 126.5, 126.0, 123.7, 118.2, 57.5, 50.9, 34.8, 32.4, 29.6, 19.0, 17.7, 15.7; HRMS Calcd for $C_{16}H_{28}NO$ $[M + H]^+$: 250.21709; Found: 250.21729. $[\alpha]^{25.0}_D$ = –17.2 (*c* = 1.16, $CHCl_3$).

■ **Preparation, Purification, and Analytical Data for Aldimine Substrates**: Aryl-, heteroaryl-, alkenyl-, and alkynyl-substituted *N*-diphenylphosphinoyl imines were synthesized through a $TiCl_4$-promoted reaction between *P*,*P*-diphenylphosphinic amide[134]

(134) *P*,*P*-Diphenylphosphinic amide was routinely synthesized on deca-gram scale according to a previously reported procedure. See: Desrosiers, J-N.; Côté, A.; Boezio, A. A.; Charette, A. B. *Org. Syn.* **2006**, *83*, 8–9.

and the corresponding aldehyde.[135] Alkyl-substituted aldimines as well as aldimines **1.15e**, **1.15g**, **1.15h** and **1.20f** were synthesized through the intermediacy of the corresponding sulfinyl adducts according to previously disclosed methods.[135b, 136] Occasionally, for optimal results, aryl-, heteroaryl-, alkenyl-, and alkynyl-substituted aldimines should be purified by silica gel chromatography (5% triethylamine in the slurry packed bed of silica) shortly before to their use.

General Procedure for Preparation of Aryl-, Heteroaryl-, Alkenyl-, and Alkynyl Aldimines (1.15, Table 1.5): Aldimine **1.15k** was prepared following a modified reported procedure.[135a] A flame-dried 100 mL round-bottom flask, purged with nitrogen, is charged with 4-(dibutylamino) benzaldehyde[137] (5.51 g, 23.6 mmol, 1.25 equiv.), *P*,*P*-diphenylphosphinic amide (4.10 g, 18.9 mmol, 1.00 equiv.), triethylamine (10.6 mL, 75.6 mmol, 4.00 equiv.), and dichloromethane (60 mL). The resulting mixture is allowed to cool to −78 °C, followed by the drop-wise addition of neat $TiCl_4$ (1.14 mL, 10.4 mmol, 0.55 equiv.). The solution is allowed to stir for 12 h at 22 °C and is then filtered through a plug of Celite. The resulting yellow solid is purified by silica gel column chromatography (ethyl acetate:hexanes 2:1 followed by 100% ethyl acetate as eluent) and recrystallized from dichloromethane/hexanes to afford **1.15k** as pale yellow solid (6.40 g, 14.8 mmol, 78% yield).

***(E)*-*N*-(4-(dibutylamino)benzylidene)-*P*,*P*-diphenylphosphinic amide (1.15k, Table 1.5):** M.p. = 113–115 °C. IR (neat): 2951 (w), 2928 (w), 2869 (w), 1579 (m), 1525 (m),

(135) (a) Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561–5568. (b) Yamada, K-i.; Harwood, S. J.; Gröger, H.; Shibasaki, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 3504–3506.
(136) (a) Côté, A.; Boezio, A. A.; Charette, A. B. *Proc. Natl. Acad. Sci.* **2004**, *101*, 5405–5410. (b) Yamaguchi, A.; Matsunaga, S.; Shibasaki, M. *Tetrahedron Lett.* **2006**, *47*, 3985–3989.
(137) Tian, L.; Hu, Z.; Shi, P.; Zhou, H.; Wu, J.; Tian, Y.; Zhou, Y.; Tao, X.; Jiang, M. *J. Lumin.* **2007**, *127*, 423–430

1435 (m), 1364 (m), 1203 (m), 1173 (m), 1104 (m), 831 (s), 807 (m), 725 (m), 695 (s), 580 (m), 545 (s), 522 (s), 510 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.08 (1H, d, *J* = 32.0 Hz), 7.95–7.89 (4H, m), 7.85 (2H, d, *J* = 8.8 Hz), 7.48–7.38 (6H, m), 6.65 (2H, d, *J* = 9.2 Hz), 3.34 (4H, dd, *J* = 7.6, 7.2 Hz), 1.63–1.56 (4H, m), 1.37 (4H, app sextet, *J* = 7.6 Hz), 0.97 (6H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1 (d, *J* = 6.9 Hz), 152.3, 134.4 (d, *J* = 126.0 Hz), 132.7 (br peak as the result of hindered rotation around the (Ar)–(C=NR) bond), 131.7 (d, *J* = 9.1 Hz), 131.4 (d, *J* = 2.7 Hz), 128.4 (d, *J* = 12.3 Hz), 123.5 (d, *J* = 26.2 Hz), 111.0, 51.0, 29.4, 20.4, 14.1; HRMS Calcd for $C_{27}H_{34}N_2OP$ $[M + H]^+$: 433.24087; Found: 433.23945.

(*E*)-*P*,*P*-Diphenyl-*N*-(pyridin-4-ylmethylene)phosphinic amide (1.15n, Table 1.5): The title compound is purified by trituration with pentanes and washing of the resultant solid with diethyl ether to afford a light orange solid. M.p. = 97–99 ºC. IR (neat): 3055 (br, w), 1621 (m), 1593 (w), 1557 (m), 1437 (m), 1411 (w), 1320 (w), 1197 (m), 1123 (m), 1107 (m), 822 (s), 724 (s), 692 (s), 551 (s), 520 (s), 500 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.32 (1H, d, *J* = 31.2 Hz), 8.84–8.82 (2H, m), 7.97–7.90 (4H, m), 7.83–7.82 (2H, m), 7.55–7.42 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): 172.2 (d, *J* = 7.7 Hz), 151.1, 142.0 (d, *J* = 25.2 Hz), 132.3 (d, *J* = 2.8 Hz), 132.1 (d, *J* = 127.3 Hz), 131.7 (d, *J* = 9.4 Hz), 128.8 (d, *J* = 12.6 Hz), 123.0; HRMS Calcd for $C_{18}H_{16}N_2O_1P_1$ $[M + H]^+$: 307.10002; Found: 307.09978.

(*E*)-*N*-((*E*)-3-(2-Nitrophenyl)allylidene)-*P*,*P*-diphenylphosphinic amide (1.20b, Table 1.6): White solid. M.p. = 148–149 °C. IR (neat): 3076 (w), 3041 (w), 2856 (w), 1625 (m), 1608 (m), 1591 (m), 1520 (m), 1437 (w), 1344 (m), 1205 (s), 1157 (w), 1124 (m), 1108 (m), 966 (w), 874 (m), 845 (m), 798 (s), 784 (m), 752 (w), 741 (w), 725 (s), 693 (s),

676 (m), 577 (w), 547 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.09 (1H, dd, *J* = 31.6, 8.8 Hz), 8.06 (1H, d, *J* = 8.4 Hz), 7.94–7.86 (5H, m), 7.70 (1H, t, *J* = 8.0 Hz), 7.67 (1H, t, *J* = 7.6 Hz), 7.58–7.42 (7H, m), 7.02 (1H, ddd, *J* = 15.6, 8.8, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1 (d, *J* = 7.9 Hz), 148.1, 145.0, 133.8, 133.0 (d, *J* = 28.6 Hz), 132.5 (d, *J* = 126.0 Hz), 132.1 (d, *J* = 2.8 Hz), 131.7 (d, *J* = 9.3 Hz), 130.8, 130.7 (d, *J* = 1.4 Hz), 129.0, 128.7 (d, *J* = 12.6 Hz), 125.3; HRMS Calcd for $C_{21}H_{18}N_2O_3P$ $[M + H]^+$: 377.10550; Found: 377.10545.

(*E*)-*N*-((*E*)-3-(4-Methoxyphenyl)allylidene)-*P*,*P*-diphenylphosphinic amide (1.20c, 1.6): Pale yellow solid. M.p. = 150–151 °C. IR (neat): 3064 (w), 3053 (w), 3014 (w), 2939 (w), 2844 (w), 1619 (m), 1586 (s), 1568 (s), 1513 (m), 1436 (m), 1311 (m), 1258 (s), 1203 (s), 1180 (m), 1160 (m), 1123 (m), 1106 (m), 1023 (m), 875 (m), 818 (s), 753 (m), 723 (m), 696 (s), 595 (m), 546 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.01 (1H, dd, *J* = 31.6, 8.8 Hz), 7.91–7.86 (4H, m), 7.53–7.42 (8H, m), 7.33 (1H, d, *J* = 15.6 Hz), 7.00 (1H, ddd, *J* = 15.6, 9.2, 2.0 Hz), 6.93 (2H, d, *J* = 8.4 Hz), 3.85 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1 (d, *J* = 7.7 Hz), 162.0, 150.7, 133.3 (d, *J* = 126.0 Hz), 131.8 (d, *J* = 2.8 Hz), 131.7 (d, *J* = 9.1 Hz), 130.2, 128.6 (d, *J* = 12.5 Hz), 127.6 (d, *J* = 1.2 Hz), 126.7 (d, *J* = 28.5 Hz), 114.6, 55.6; HRMS Calcd for $C_{22}H_{21}NO_2P$ $[M + H]^+$: 362.13099; Found: 362.12964.

(*E*)-*N*-((*Z*)-2-Bromo-3-phenylallylidene)-*P*,*P*-diphenylphosphinic amide (1.20d, Table 1.6): White solid. M.p. = 144–145 °C. IR (neat): 3074 (w), 3061 (w), 3025 (w), 3012 (w), 2958 (w), 1620 (m), 1593 (s), 1569 (m), 1438 (m), 1199 (s), 1160 (w), 1134 (m), 1122 (s), 1106 (m), 1070 (w), 877 (s), 808 (m), 752 (m), 726 (s), 702 (s), 684 (s), 659 (m), 587 (m), 550 (s), 517 (m), 501 (s), 468 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ

8.86 (1H, d, J = 29.2 Hz), 7.99–7.93 (6H, m), 7.78 (1H, s), 7.53–7.43 (9H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3 (d, J = 5.2 Hz), 148.2, 133.8, 132.9 (d, J = 127.0 Hz), 132.0 (d, J = 2.8 Hz), 131.7 (d, J = 9.3 Hz), 131.1, 130.9, 128.7, 128.7 (d, J = 11.5 Hz), 124.1 (d, J = 31.6 Hz); HRMS Calcd for $C_{21}H_{18}BrNOP$ $[M + H]^+$: 410.03094; Found: 410.02999.

(*E*)-*P*,*P*-Diphenyl-*N*-(1-tosylhex-2-en-1-yl)phosphinic amide (not shown in dissertation; precursor to 1.20f, Table 1.6): The title compound is synthesized following a previously reported procedure[135] from *P*,*P*-diphenylphosphinic amide (2.17 g, 10.0 mmol, 1.00 equiv.), (*E*)-hex-2-enal (2.31 mL, 20.0 mmol, 2.00 equiv.), and *p*-toluenesulfinic acid[138] (2.34 g, 15.0 mmol, 1.50 equiv.) to obtain the tile compound as white solid (3.22 g, 7.10 mmol, 71% yield). M.p. = 138–139 °C. IR (neat): 3177 (w, br), 2959 (w), 2933 (w), 2870 (w), 1661 (m), 1596 (w), 1437 (m), 1300 (m), 1281 (m), 1214 (m), 1185 (s), 1170 (m), 1138 (m), 1125 (s), 1106 (m), 1083 (m), 955 (m), 894 (m), 752 (m), 726 (s), 693 (s), 662 (m), 583 (s), 568 (m), 536 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79–7.71 (4H, m), 7.59 (2H, d, J = 8.4 Hz), 7.59–7.54 (2H, m), 7.50–7.43 (4H, m), 7.23 (2H, d, J = 8.0 Hz), 5.90 (1H, ddd, J = 13.6, 11.6, 9.6 Hz), 5.31 (1H, t, J = 10.0 Hz), 4.73 (1H, dd, J = 14.0, 10.4 Hz), 3.28 (1H, app td, J = 10.8, 3.6 Hz), 2.42 (3H, s), 1.97–1.88 (1H, m), 1.52–1.32 (2H, m), 1.20–1.10 (1H, m), 0.82 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 134.7, 132.8, 132.6 (d, J = 2.9 Hz), 132.5 (d, J = 2.9 Hz), 132.2 (d, J = 10.1 Hz), 131.9 (d, J = 10.1 Hz), 131.4 (d, J = 128.0 Hz), 131.1 (d, J = 128.0 Hz), 129.6, 129.2, 128.9 (d, J = 12.9 Hz), 128.9 (d, J = 13.0 Hz), 101.9 (d, J = 9.9 Hz), 67.6, 29.7, 21.8, 20.0, 13.7.

(138) Sisko, J.; Mellinger, M.; Sheldrake, P. W.; Baine, N. H. *Org. Syn.* **2000**, *77*, 198–205.

(*E*)-*N*-((*E*)-Hex-2-en-1-ylidene)-*P*,*P*-diphenylphosphinic amide (1.20f, Table 1.6): Following a modification to a previously reported procedure,[7b] **6** is synthesized through vigorous stirring of a suspension of the requisite sulfinic adduct (see above, 150 mg, 0.330 mmol) in 5 mL of diethyl ether and 5 mL of an aqueous saturated solution of Na_2CO_3 until the white solid dissolves completely (~8 h). The layers are separated and the aqueous phase is washed with diethyl ether. The combined organic phases are dried with anhydrous sodium sulfate and the filtrate is concentrated to dryness. The residue is dissolved again in dichloromethane, filtered, and the solvent is evaporated to afford **6** as colorless viscous oil (97.7 mg, 0.328 mmol, 99% yield). IR (neat): 3056 (w), 2959 (w), 2930 (w), 2871 (w), 1637 (m), 1596 (s), 1203 (s), 1122 (m), 1106 (m), 826 (s), 724 (s), 693 (s), 571 (m), 544 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.86 (1H, dd, J = 32.4, 8.8 Hz), 7.89–7.83 (4H, m), 7.50–7.41 (6H, m), 6.73 (1H, dt, J = 15.6, 6.8 Hz), 6.50–6.42 (1H, m), 2.30 (2H, app quartet, J = 7.2 Hz), 1.53 (2H, app sextet, J = 7.2 Hz), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.5 (d, J = 8.0 Hz), 156.7, 133.1 (d, J = 126.0 Hz), 132.3 (d, J = 26.8 Hz), 131.8 (d, J = 2.8 Hz), 131.6 (d, J = 9.1 Hz), 128.5 (d, J = 12.4 Hz), 35.2, 21.4, 13.8; HRMS Calcd for $C_{18}H_{21}NOP$ $[M + H]^+$: 298.13608; Found: 298.13599.

■ Preparation, Purification, and Analytical Data for Isatin Substrates

General Procedure for Preparation of N-tert-Butyldimethylsilyl Isatins: In a 250 mL flame dried round bottom flask equipped with a stir bar, *tert*-butyldimethylsilyl chloride (4.5 g, 30 mmol) is dissolved in 150 mL dichloromethane. To this solution, in a single portion, isatin (2.2 g, 15 mmol) and 4-dimethylaminopyridine (0.18 g, 1.5 mmol) are added. The flask is sealed with a rubber septum and purged with nitrogen.

Triethylamine (6.3 mL, 45 mmol) is added in one portion through a syringe and mixture is allowed to stir for 24 h at 22 ºC. The volatiles are removed *in vacuo* and the resultant dark orange solid is purified by silica gel chromatography (hexanes to 1:1 hexanes:dichloromethane to dichloromethane) to afford an orange solid, which is recrystallized from hot EtOH (details below) to afford **1.36i** (2.6 g, 9.9 mmol, 67% yield) as an orange crystalline solid. Please note that for long-term storage, *N-tert*-butyldimethylsilyl protected isatins should be kept under an inert atmosphere at –15 ºC.

1-(*tert*-Butyldimethylsilyl)indoline-2,3-dione (**1.36i, Table 1.15**): M.p. = 123–124 °C. IR (neat): 2929 (w), 2853 (w), 1731 (s), 1603 (m), 1589 (m), 1463 (m), 1325 (m), 1252 (m), 1170 (m), 1139 (m), 927 (m), 835 (s), 796 (m), 752 (s), 686 (m), 466 (m), 424 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.61 (1H, m), 7.53–7.49 (1H, m), 7.10–7.03 (2H, m), 1.02 (9H, s), 0.56 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.2, 164.9, 155.4, 138.3, 125.6, 123.4, 120.0, 115.1, 26.4, 19.7, –3.3; HRMS Calcd for $C_{14}H_{20}NO_2Si$ $[M + H]^+$: 262.12633; Found: 262.12608.

1-(*tert*-Butyldimethylsilyl)-5-methoxyindoline-2,3-dione (**1.36j, Table 1.15**): Crimson crystalline solid. M.p. = 169–171 °C. IR (neat): 2929 (w, br), 2859 (w), 1731 (s), 1625 (w), 1589 (w), 1492 (m), 1310 (m), 1270 (m), 1142 (m), 942 (w), 847 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12–7.07 (2H, m), 6.96 (1H, d, J = 9.0 Hz), 3.79 (3H, s), 1.01 (9H, s), 0.54 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.7, 165.3, 156.0, 149.5, 125.6, 120.4, 116.0, 108.8, 56.0, 26.5, 19.8, –3.3; HRMS Calcd for $C_{15}H_{22}NO_3Si$ $[M + H]^+$: 292.13689; Found: 292.13766.

4,6-Dibromo-1-((2-(trimethylsilyl)ethoxy)methyl)indoline-2,3-dione (**1.36k, Table**

1.15): Amide protection performed in accordance to a previously disclosed procedure.[139] Yellow crystalline solid, M.p. = 142–143 °C. IR (neat): 3077 (w), 2896 (w), 1742 (m), 1595 (s), 1562 (m), 1419 (w), 1244 (m), 1073 (s), 1024 (m), 839 (s), 733 (m), 456 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (1H, d, *J* = 1.6 Hz), 7.28 (1H, d, *J* = 1.2 Hz), 5.16 (2H, s), 3.85 (2H, m), 0.94 (2H, m), –0.01 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.5, 157.2, 152.2, 133.5, 131.5, 122.1, 115.3, 114.3, 70.0, 67.1, 17.9, –1.3; HRMS Calcd for $C_{14}H_{21}Br_2N_2O_3Si$ $[M + NH_4]^+$: 450.96882; Found: 450.96873.

Synthesis of N-Bn Isatins: Synthesized in accordance to a published procedure[140] with the following modification: After isolation of the unpurified *N*-protected isatin, a small portion (~10 mg) of the solid is passed through a small plug of silica gel using dichloromethane as the elutant. If a dark (usually maroon) residue remains on the silica gel after the *N*-protected isatin is eluted, then the entire unpurified *N*-Bn isatin is dissolved in dichloromethane and passed through a short plug of silica gel using dichloromethane as an elutant. After concentration *in vacuo*, the isatin is purified as described below.

Purification of N-Bn, N-SEM, and N-TBS isatins: With hot EtOH as the solvent, ~95 % of the resulting solid is dissolved and filtered while hot through a fritted glass funnel (this initial filtration is critical to obtain *N*-protected isatins of sufficient purity). The filtered solids are discarded. The filtrate is allowed to cool to room temperature during which time the desired product crystallizes from solution. The desired product is collected by

(139) Trost, B. M.; Frederiksen, M. U. *Angew. Chem., Int. Ed.* **2005**, *44*, 308–310.
(140) Karimi, A. R.; Sedaghatpour, F. *Synthesis* **2010**, *10*, 1731–1735.

filtration through a fritted glass funnel. Concentrating the mother liquor in vacuo and recrystallization of the resultant solids from hot EtOH yields additional product. The products are then dried azeotropically with anhydrous benzene prior to use.

1-Benzyl-4,7-dichloroindoline-2,3-dione (1.36f, Table 1.15): Orange solid. M.p. = 204–206 °C. IR (neat): 2934 (w), 2857 (w), 1667 (w), 1449 (w), 1424 (w), 1367 (w), 1265 (w), 1061 (m), 1024 (m), 925 (w), 733 (s), 703 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.25 (6H, m), 7.03 (1H, d, J = 8.7 Hz), 5.40 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.4, 158.2, 147.3, 140.8, 135.9, 133.2, 129.0, 128.0, 126.7, 126.7, 117.2, 115.8, 45.3; HRMS Calcd for $C_{15}H_{10}Cl_2N_1O_2$ $[M + H]^+$: 306.00886; Found: 306.00974.

■ **Procedure for *Gram-Scale* Catalytic Enantioselective Allyl Addition to Aldimine 1.15a to Afford Homoallylamide 1.17a (Scheme 1.21)**:

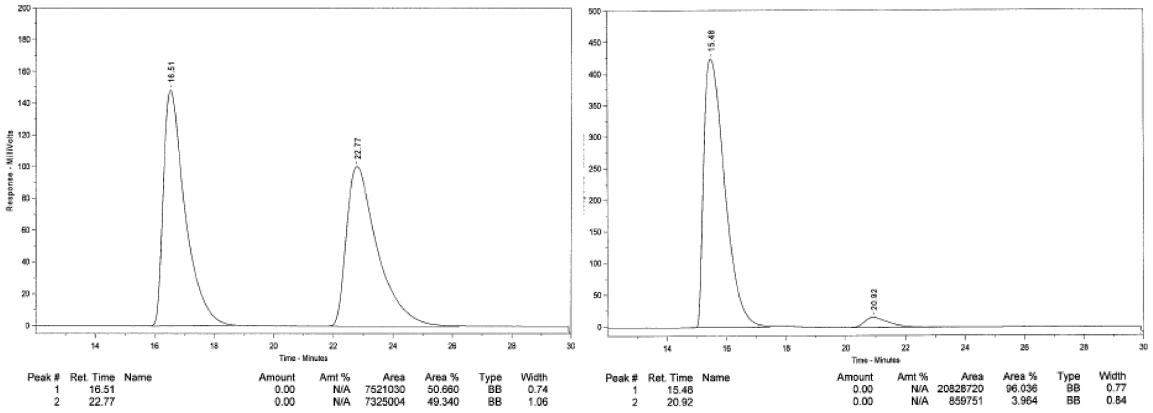
Preparation of the catalyst suspension: Aminophenol **1.19r** (15.0 mg, 0.0490 mmol) is weighed out in air into a 4 mL vial to which is added 263 μL of a solution of sodium hydroxide (1.95 mg, 0.0490 mmol) in reagent-grade methanol [111 mg NaOH pellet (Fisher) is dissolved in 15 ml methanol]). After removal of the solvent *in vacuo*, the resultant white oil is azeotropically dried with reagent grade toluene. The obtained white solid is allowed to dry at 0.5 Torr for 30 min and the vial is sealed with a cap containing a teflon septum. Toluene (1.0 mL) is added to yield a suspension after sonication (2 min).

A round bottom flask (50 mL, equipped with a magnetic stirring bar) is charged with imine **1.15a** (1.00 g, 3.28 mmol) and dried at 0.5 Torr for 30 min, purged with nitrogen and sealed with a rubber septum. Toluene (30 mL) is added, followed by allylboronic acid pinacol ester **1.6** (800 μl, 4.26 mmol) from a septum-sealed bottle (Frontier

Scientific, Inc., as received) and methanol (200 μL, 4.92 mmol) from a septum-sealed bottle (Acros, grade: 99.9% ExtraDry, as received). A suspension of the catalyst containing aminophenol **1.19r** (10.1 mg, 33 μmol, 0.0100 equiv.) and sodium hydroxide (1.31 mg, 33 μmol, 0.0100 equiv.) in 0.67 mL toluene is added with a syringe to the mixture (see below). After two h, the solvent is evaporated and the residue is taken up in 30 mL hexanes. The suspension is allowed to sonicate for two min, filtered and washed with hexanes (4 x 3 mL). The desired product, dried under vacuum, is obtained in 97.5:2.5 er (1.04 g, 3.01 mmol, 92% yield). Elemental analysis for $C_{22}H_{22}NOP$: Calcd: C, 76.06; H, 6.38; N, 4.03. Found: C, 75.77; H, 6.43; N 3.98.

(*R*)-P,P-Diphenyl-*N*-(1-phenylbut-3-en-1-yl)phosphinic amide (1.17a, Table 1.5): The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89–7.84 (2H, m), 7.79–7.74 (2H, m), 7.51–7.47 (1H, m), 7.45–7.41 (3H, m), 7.34–7.18 (7H, m), 5.61 (1H, dddd, J = 17.2, 10.0, 7.2, 7.2 Hz), 5.11–5.03 (2H, m), 4.47 (1H, dddd, J = 10.4, 10.4, 6.4, 6.4 Hz), 3.35 (1H, br dd, J = 9.6, 6.0 Hz), 2.74–2.60 (2H, m); HRMS Calcd for $C_{22}H_{23}NOP$ $[M + H]^+$: 348.15173; Found: 348.15251; $[\alpha]^{20}_D$ = +52 (c = 0.40, $CHCl_3$) for a 96:4 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R of **4a**: 16 min (major) and 21 min (minor).

(141) Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 3332–3335.

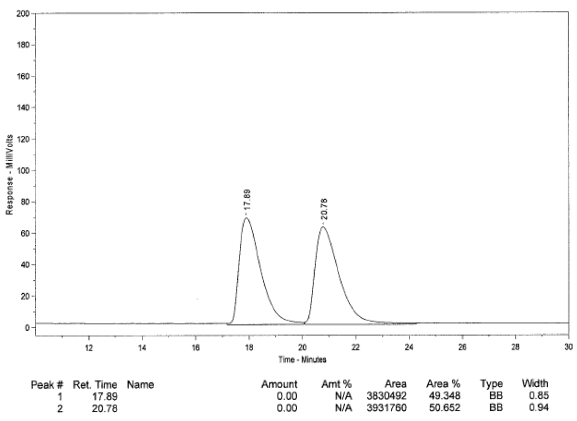


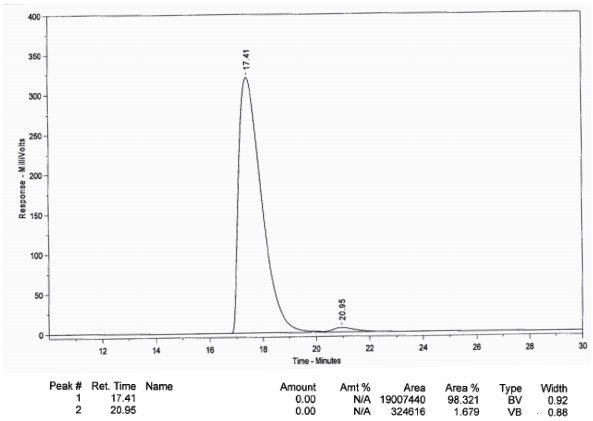
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.5 min	50.660	1	15.5 min	96.036
2	22.8 min	49.340	2	20.9 min	3.964

■ **Representative Procedure for *Small Scale* Catalytic Enantioselective Allyl Additions to Aryl-, Heteroaryl-, Alkenyl-, and Alkynyl *N*-Diphenylphosphinoyl Imines (Table 1.5)**: In a nitrogen-filled glovebox (not needed for gram scale; only used when reactions are performed at mg scale to achieve highly reproducible data), aminophenol **1.19r** (6.9 mg, 0.023 mmol) is added to an oven-dried two dram vial equipped with a stir bar followed by 1.5 mL of a stock solution of NaO*t*-Bu in toluene (9.6 mg, 0.10 mmol/8.0 mL) and the solution is allowed to stir at 22 ºC for ~10 minutes. A separate vial equipped with a stir bar is charged sequentially with aldimine **1.15b** (32.3 mg, 0.100 mmol), 800. μL of toluene, MeOH (10. μL, 0.25 mmol), and allylboronic acid pinacol ester **1.6** (28 μL, 0.15 mmol) under nitrogen. To this mixture is added 200. μL of the **1.19r**/NaO*t*-Bu solution and a cap is attached to the vial and sealed (electrical tape). The clear and colorless solution is allowed to stir at 22 ºC for four hours during which time the solution becomes cloudy and white. The cap is removed and 3 mL of a solution of saturated aqueous $NaIO_4$ is added and the biphasic mixture is allowed to stir for 20

minutes. The aqueous layer is washed with ethyl acetate (4 x 4 mL), dried over Na_2SO_4, and concentrated *in vacuo* to yield a pale yellow solid. The homoallylamide product is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in 95:5 hexanes:triethylamine and eluted with 10 mL hexanes, 10 mL 3:1 hexanes:ethyl acetate, 10 mL 1:1 hexanes:ethyl acetate, 10 mL 1:3 hexanes:ethyl acetate, and 15 mL ethyl acetate) to afford **1.17b** (35.2 mg, 0.0960 mmol, 96% yield) as a white solid.

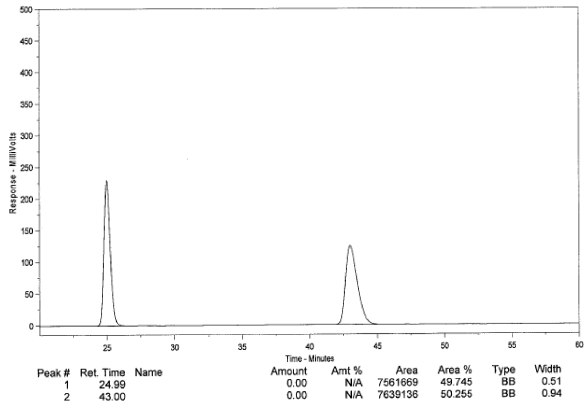
(*R*)-*N*-(1-(2-Fluorophenyl)but-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (1.17b, Table 1.15): The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.82 (2H, m), 7.78–7.72 (2H, m), 7.51–7.47 (1H, m), 7.44–7.39 (3H, m), 7.34–7.29 (2H, m), 7.23–7.18 (1H, m), 7.15 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.05 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 6.97 (1H, ddd, *J* = 10.8, 8.0, 0.8 Hz), 5.61 (1H, dddd, *J* = 17.2, 10.0, 7.2, 7.2 Hz), 5.09–5.01 (2H, m), 4.47 (1H, dddd, *J* = 10.4, 10.4, 6.4, 6.4 Hz), 3.56 (1H, br dd, *J* =10.4, 6.8 Hz), 2.78–2.60 (2H, m); HRMS Calcd for $C_{22}H_{21}FNOP$ $[M + H]^+$: 366.14230; Found: 366.14250. $[\alpha]^{20}_D$ = +34 (*c* =0.39, $CHCl_3$) for a 98.5:1.5 er sample. The enantiomeric purity was determined by HPLC analysis in comparison to authentic racemic material (Chiracel OD, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm) t_R: 17 min (major) and 21 min (minor).

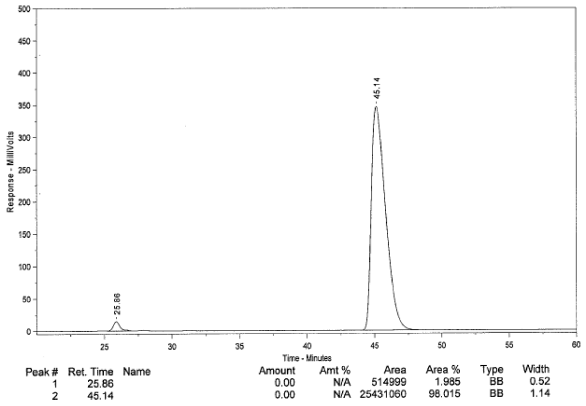




Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	17.9	49.348	1	17.4	98.321
2	20.8	50.652	2	21.0	1.679

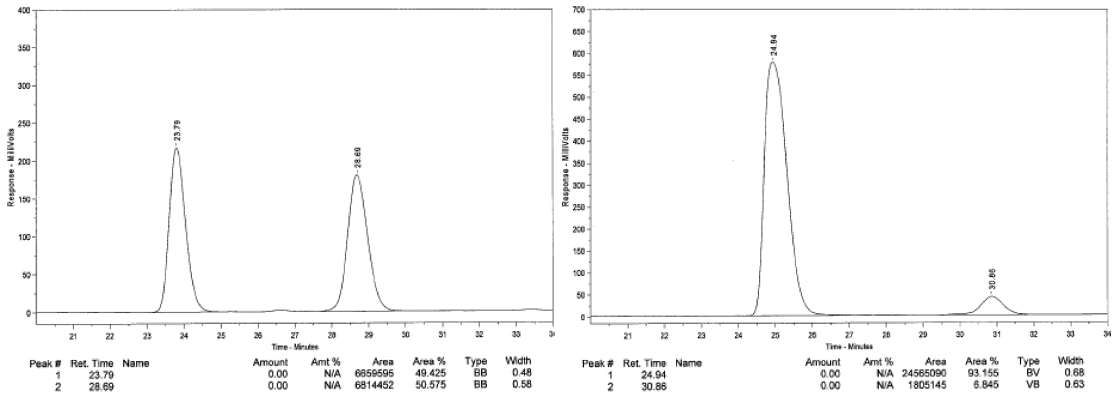
(*R*)-*N*-(1-(2-Bromophenyl)but-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (**1.17c, Table 1.5**): The title compound is purified in a manner identical to **1.17b** affording **1.17c** (38.0 mg, 0.0891 mmol, 89% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.82 (2H, m), 7.75–7.70 (2H, m), 7.51–7.47 (1H, m), 7.44–7.39 (4H, m), 7.35–7.27 (4H, m), 7.07 (1H, ddd, J = 8.8, 8.0, 2.0 Hz), 5.64 (1H, dddd, J = 17.4, 10.4, 7.2, 7.2 Hz), 5.14–5.10 (2H, m), 4.71 (1H, dddd, J = 10.4, 10.4, 6.0, 6.0 Hz), 3.56 (1H, br dd, J = 9.6, 6.0 Hz), 2.64 (2H, app t, J = 6.4 Hz); HRMS Calcd for $C_{22}H_{22}BrNOP$ $[M + H]^+$: 426.06224; Found: 426.06229. $[\alpha]^{20}_D$ = +2.30 (c =1.00, $CHCl_3$) for a 98.0:2.0 er sample. The enantiomeric purity was determined by HPLC analysis in comparison to authentic racemic material (Chiracel AD-H, 87:13 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm) t_R**:** 26 min (minor) and 45 min (major).





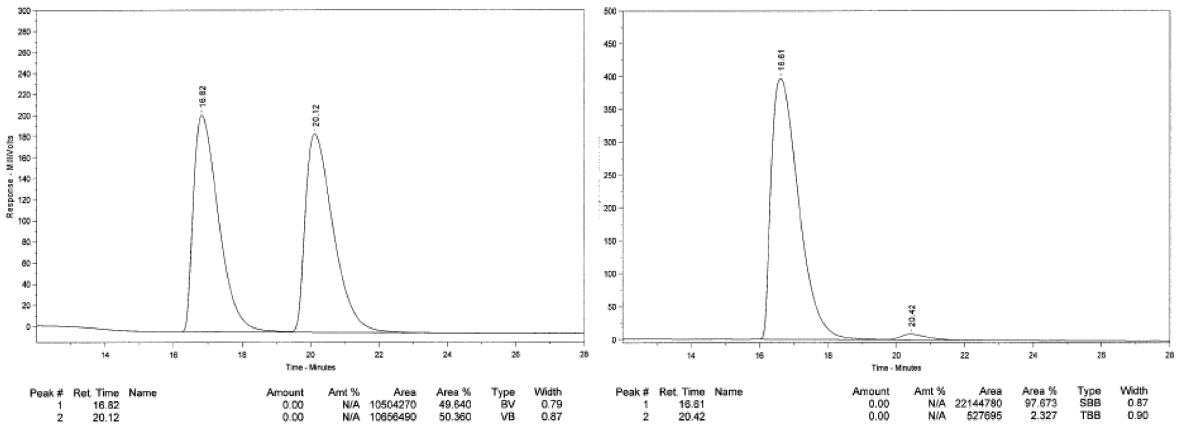
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	25.0	49.745	1	25.9	1.985
2	43.0	50.255	2	45.1	98.015

(*R*)-*P*,*P*-Diphenyl-*N*-(1-(*o*-tolyl)but-3-en-1-yl)phosphinic amide (1.17d, Table 1.5): The title compound is synthesized and purified analogously to **1.17b** (six h reaction time) affording **1.17d** (34.3 mg, 0.0949 mmol, 95% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.83 (2H, m), 7.72–7.67 (2H, m), 7.50–7.46 (1H, m), 7.44–7.38 (3H, m), 7.33 (1H, d, *J* = 7.7 Hz), 7.29–7.21 (3H, m), 7.12 (1H, ddd, *J* = 8.4, 7.6, 1.6 Hz), 7.00 (1H, d, *J* = 7.5 Hz), 5.61 (1H, dddd, *J* = 17.2, 10.0, 7.2, 7.2 Hz), 5.11–5.03 (2H, m), 4.54 (1H, dddd, *J* = 10.0, 10.0, 6.4, 6.4 Hz), 3.43 (1H, br dd, *J* = 9.6, 6.4 Hz), 2.65–2.52 (2H, m), 1.91 (3H, s); HRMS Calcd for $C_{23}H_{25}NOP$ $[M + H]^+$: 362.16738; Found: 362.16744. $[\alpha]^{20}_D$ = +7.20 (*c* =1.00, $CHCl_3$) for a 94:6 er sample. The enantiomeric purity was determined by HPLC analysis in comparison to authentic racemic material (Chiracel AD-H, 87:13 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm) t_R: 25 min (major) and 31 min (minor).



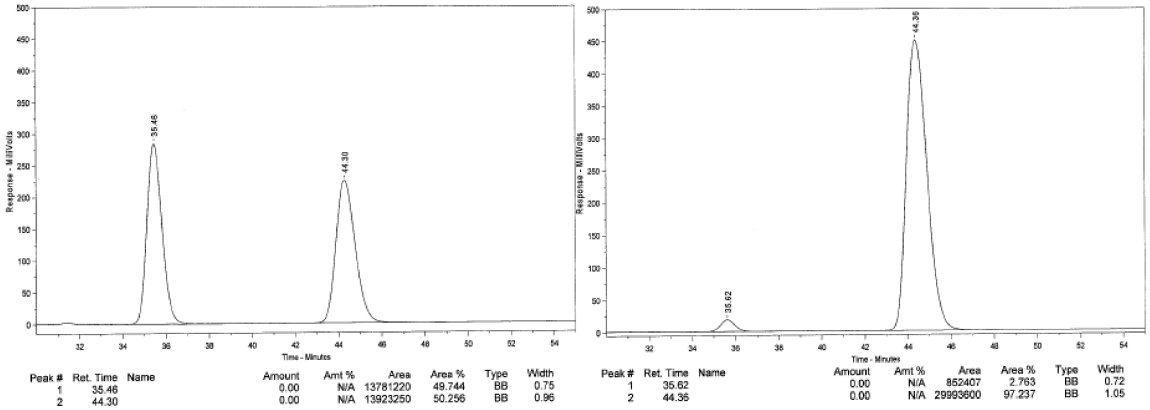
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	23.8	49.425	1	24.9	93.155
2	28.7	50.575	2	30.9	6.845

(*R*)-*N*-(1-(3-Bromophenyl)but-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (**1.17e, Table 1.5**): The title compound is purified identically to **1.17b** affording **1.17e** (39.5 mg, 0.0927 mmol, 93% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.82 (2H, m), 7.77–7.71 (2H, m), 7.53–7.47 (1H, m), 7.45–7.40 (3H, m), 7.35–7.30 (4H, m), 7.13–7.11 (2H, m), 5.58 (1H, dddd, *J* = 17.2, 10.0, 7.2, 7.2 Hz), 5.13–5.07 (2H, m), 4.31 (1H, dddd, *J* = 10.0, 10.0, 6.4, 6.4 Hz), 3.42 (1H, br dd, *J* = 9.4, 6.0 Hz), 2.67–2.58 (2H, m); HRMS Calcd for $C_{22}H_{22}BrNOP$ $[M + H]^+$: 426.06224; Found: 426.06326. $[\alpha]^{20}_D$ = +59 (*c* = 0.57, $CHCl_3$) for a 97.5:2.5 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 17 min (major) and 20 min (minor).



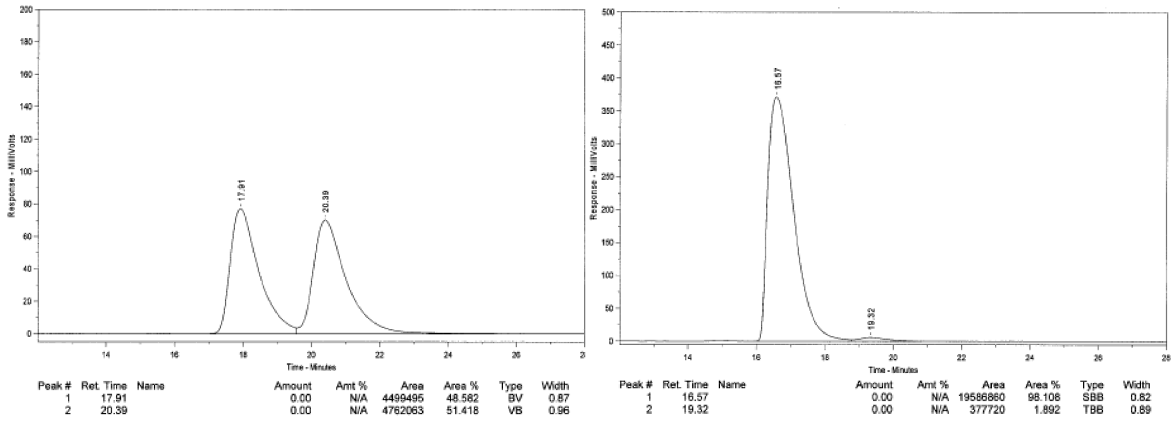
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.8	49.640	1	16.6	97.673
2	20.1	50.360	2	20.4	2.327

(*R*)-*N*-(1-(4-Bromophenyl)but-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (**1.17f, Table 1.5**): The title compound is purified identically to **1.17b** affording **1.17f** (39.2 mg, 0.0920 mmol, 92% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.82 (2H, m) 7.78–7.72 (2H, m), 7.51–7.47 (1H, m), 7.45–7.37 (5H, m), 7.35–7.30 (2H, m), 7.08–7.05 (2H, m), 5.57 (1H, dddd, J = 16.8, 10.0, 7.2, 7.2 Hz), 5.13–5.06 (2H, m), 4.31 (1H, dddd, J = 10.0, 10.0, 6.4, 6.4 Hz), 3.30 (1H, br dd, J = 9.6, 5.6 Hz), 2.69–2.55 (2H, m); HRMS Calcd for $C_{22}H_{22}BrNOP$ $[M + H]^+$: 426.0622; HRMS Calcd for $C_{22}H_{22}BrNOP$ $[M + H]^+$: 426.06224; Found: 426.06197. $[\alpha]^{20}_D$ = +73 (c = 1.0, $CHCl_3$) for a 97:3 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 97:3 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 36 min (minor) and 44 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	35.5	49.744	1	35.6	2.763
2	44.3	50.256	2	44.4	97.237

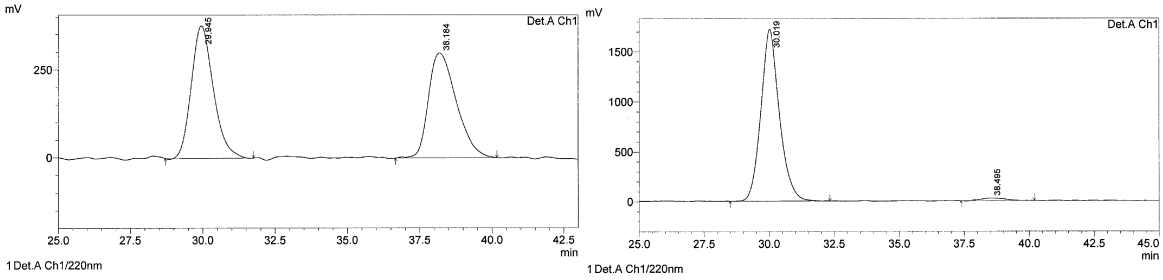
(*R*)-*P*,*P*-Diphenyl-*N*-(1-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)phosphinic amide (**1.17g, Table 1.5**): The title compound is purified identically to **1.17b** affording **1.17g** (38.8 mg, 0.0934 mmol, 93% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.83 (2H, m) 7.75–7.70 (2H, m), 7.52–7.48 (3H, m), 7.45–7.40 (3H, m), 7.32–7.28 (4H, m), 5.58 (1H, dddd, J = 17.2, 10.0, 7.2, 7.2 Hz), 5.14–5.08 (2H, m), 4.41 (1H, dddd, J = 9.6, 9.6, 6.4, 6.4 Hz), 3.49 (1H, br dd, J = 8.8, 6.2 Hz), 2.71–2.58 (2H, m); HRMS Calcd for $C_{23}H_{22}F_3NOP$ $[M + H]^+$: 416.13911; Found: 416.13996. $[\alpha]^{20}_D$ = +57 (c = 0.45, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 17 min (major) and 19 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	17.9	48.582	1	16.6	98.108
2	20.4	51.418	2	19.3	1.892

(*R*)-Methyl-4-(1-((diphenylphosphoryl)amino)but-3-en-1-yl)benzoate (1.17h, Table 1.5): The title compound is synthesized and purified analogously to **4b** except for the following changes: 1) 2.5 mol % aminophenol **1.19r** (instead of 3 mol % **1.19r**) 2) 1.5 equiv. MeOH (instead of 2.5 equiv.). Homoallylamide **1.17h** (74.4 mg, 0.183 mmol, 92% yield) is obtained as a white solid. M.p. = 128 °C. IR (neat): 3144 (w, br), 3055 (w), 3006 (w), 2948 (w), 2872 (w), 1720 (s), 1610 (w), 1435 (m), 1277 (s), 1193 (s), 1181 (s), 1106 (s), 1067 (m), 926 (m), 907 (m), 721 (s), 694 (s), 561 (m), 527 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (2H, d, *J* = 8.4 Hz), 7.86–7.80 (2H, m), 7.74–7.68 (2H, m), 7.47–7.37 (4H, m), 7.30–7.25 (2H, m), 7.25 (2H, d, *J* = 8.0 Hz), 5.55 (1H, dddd, *J* = 17.2, 10.0, 7.6, 6.8 Hz), 5.09–5.03 (2H, m), 4.38 (1H, app tt, *J* = 10.1, 6.2 Hz), 3.88 (3H, s), 3.52 (1H, br dd, *J* = 9.9, 5.9 Hz), 2.70–2.56 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 148.4 (d, *J* = 5.0 Hz), 133.2, 132.9 (d, *J* = 127.0 Hz), 132.5 (d, *J* = 9.7 Hz), 132.0 (d, *J* = 2.7 Hz), 131.9 (d, *J* = 130.0 Hz), 131.9 (d, *J* = 3.9 Hz, one peak is overlapping with the other d at 131.9), 131.9 (d, *J* = 9.5 Hz), 129.8, 129.0, 128.6 (d, *J* = 12.5 Hz),

128.4 (d, J = 12.6 Hz), 126.6, 119.4, 54.3, 52.2, 43.6 (d, J = 4.2 Hz); HRMS Calcd for $C_{24}H_{25}NO_3P$ $[M + H]^+$: 406.15720; Found: 406.15720. $[\alpha]^{20}_D$ = +75.5 (c = 2.40, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD–H, 80:20 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 30 min (major) and 38 min (minor).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.945	20067493	376847	50.019	55.792
2	38.184	20052576	298603	49.981	44.208
Total		40120069	675450	100.000	100.000

PeakTable

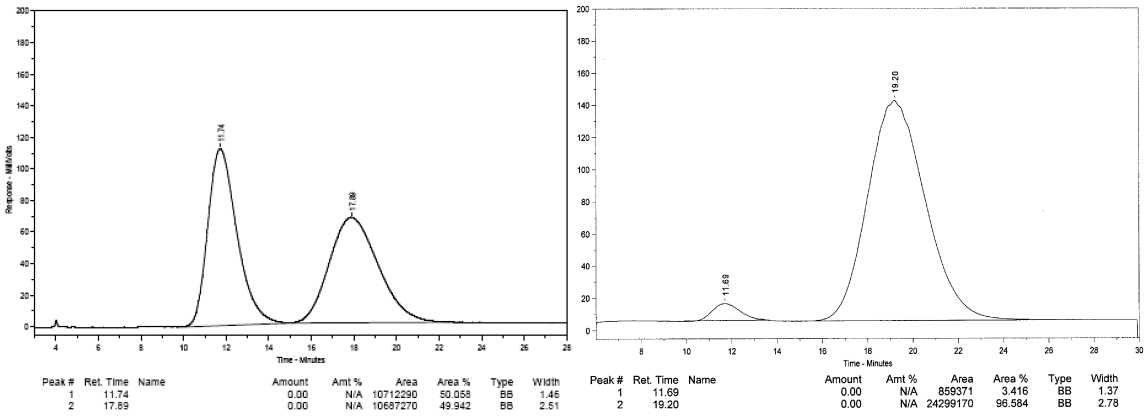
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.019	84765285	1719371	98.190	98.562
2	38.495	1562574	25084	1.810	1.438
Total		86327859	1744455	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	29.9	50.019	1	30.0	98.190
2	38.2	49.981	2	38.5	1.810

(*R*)-*N*-(1-(4-Methoxyphenyl)but-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (**1.17i, Table 1.5**): The title compound is synthesized and purified analogously to **1.17b** except for the following changes: 1) 2.5 mol % aminophenol **1.19r** (instead of 3 mol % **1.19r**) 2) 1.5 equiv. MeOH (instead of 2.5 equiv.). Homoallylamide **1.17i** (74.1 mg, 0.196 mmol, 98% yield) is afforded as a white solid. The analytical data are fully consistent with those reported previously.[141] M.p. = 116–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.83 (2H, m), 7.80–7.75 (2H, m), 7.49–7.38 (3H, m), 7.35–7.30 (2H, m), 7.14–7.10 (2H, m), 6.83–6.79 (2H, m), 5.56 (1H, dddd, J = 17.2, 10.4, 6.8, 6.8 Hz), 5.10–5.02 (2H, m), 4.30 (1H, dddd, J = 9.6, 9.6, 6.4, 6.4 Hz), 3.79 (3H, s), 3.28 (1H, br dd, J = 9.6, 6.0

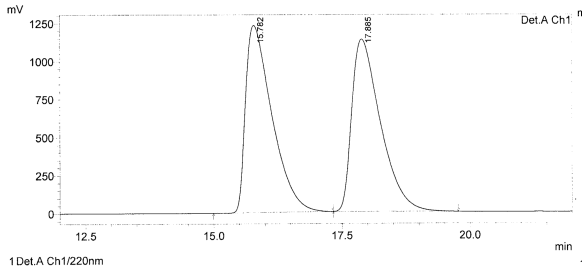
Hz), 2.72–2.57 (2H, m); HRMS Calcd for $C_{23}H_{25}NO_2P$ $[M + H]^+$: 378.16229; Found: 378.16236. $[\alpha]^{20}_D$ = +54.7 (*c* = 1.99, $CHCl_3$) for a 96.5:3.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ–H, 92:8 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 12 min (minor) and 19 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.7	50.058	1	11.7	3.416
2	17.9	49.942	2	19.2	96.584

(*R*)-*P*,*P*-Diphenyl-*N*-(1-(p-4-methylphenyl)but-3-en-1-yl)phosphinic amide (1.17j, Table 1.5): This compound is not listed in Table 2 of the publication, but has been used for determination of the absolute stereochemistry through X-ray analysis. It was synthesized and purified analogously to **1.15b** except for the following changes: 1) 2.5 mol % aminophenol **1.19r** (instead of 3 mol % **1.19r**) 2) 1.5 equiv. MeOH (instead of 2.5 equiv.). Homoallylamide **1.17j** (70.8 mg, 0.196 mmol, 98% yield) is obtained as a white solid. Crystals suitable for X-ray crystallography were obtained by slow evaporation of dichloromethane M.p. = 130–131 °C. IR (neat): 3178 (w, br), 3076 (w), 3052 (w), 3007 (w), 2977 (w), 2919 (w), 2882 (w), 1454 (m), 1435 (m), 1181 (s), 1123 (m), 1108 (m),

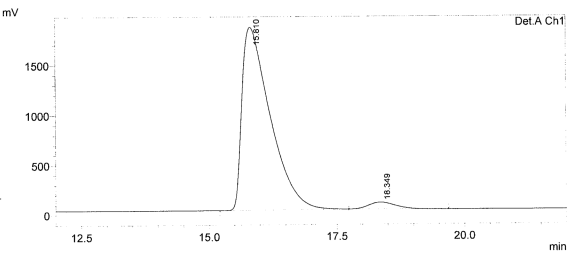
1078 (s), 917 (m), 899 (m), 748 (m), 723 (s), 694 (s), 561 (m), 535 (s), 497 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.88–7.75 (4H, m), 7.49–7.29 (6H, m), 7.09 (4H, app s), 5.58 (1H, app ddt, *J* = 17.2 10.0, 7.2 Hz), 5.10–5.00 (2H, m), 4.33–4.26 (1H, m), 3.40 (1H, br dd, *J* = 10.0, 6.4 Hz), 2.74–2.58 (2H, m), 2.31 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1 (d, *J* = 5.7 Hz), 136.6, 133.9, 133.3 (d, *J* = 127.0 Hz, 1 peak hidden under 133.9), 132.6 (d, *J* = 9.6 Hz), 132.2 (d, *J* = 130.0 Hz), 131.9 (d, *J* = 9.6 Hz), 131.8 (d, *J* = 3 Hz, 1 peak hidden under 131.9), 131.7 (d, *J* = 2.7 Hz), 129.1, 128.5 (d, *J* = 12.5 Hz), 128.3 (d, *J* = 12.6 Hz), 126.4, 118.6, 54.5, 43.7 (d, *J* = 3.8 Hz), 21.1; HRMS Calcd for $C_{23}H_{25}NOP$ $[M + H]^+$: 362.16738; Found: 362.16709. $[\alpha]^{20}_D$ = +50.8 (*c* = 2.11, $CHCl_3$) for a 96.5:3.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD–H, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 16 min (major) and 18 min (minor).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.782	44246577	1233134	49.997	52.052
2	17.885	44252025	1135919	50.003	47.948
Total		88498602	2369052	100.000	100.000



PeakTable

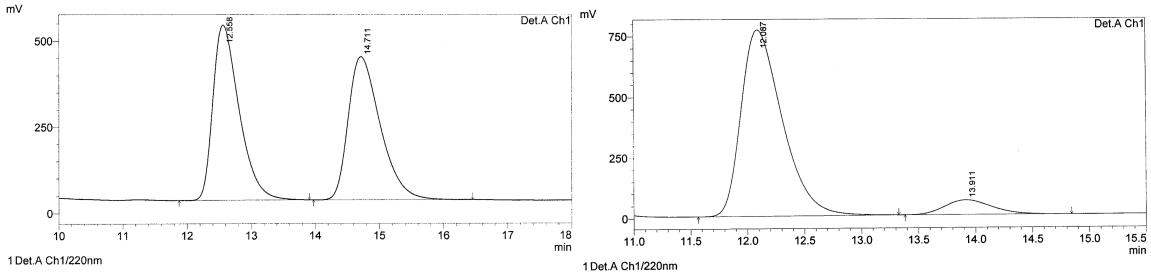
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.810	70757069	1835297	96.568	96.362
2	18.349	2514862	69280	3.432	3.638
Total		73271931	1904578	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	15.8	49.997	1	15.8	96.568
2	17.9	50.003	2	18.3	3.432

(*R*)-*N*-(1-(4-(Dibutylamino)phenyl)but-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (1.17k, Table 1.5): The title compound is synthesized analogously to **1.17b** except for the following changes: 1) 2.5 mol % aminophenol **1.19r** (instead of 3 mol % **1.19r**) 2) 1.5 equiv. MeOH (instead of 2.5 equiv.). 3) Reaction time is six h. 4) After $NaIO_4$ workup (see representative procedure above), the unpurified mixture is treated for 12 h while allowing it to stir with ~ 1 g basic aluminum oxide in 4 mL dichloromethane:diethyl ether (1:1) to hydrolyze unreacted **1.15k**, after which the aluminum oxide is filtered off and washed with dichloromethane and ethyl acetate (20 mL). The product is purified as described for **1.15b**, affording **1.15k** (44.2 mg, 0.0931 mmol, 93% yield) as a white solid. M.p. = 83–84 °C. IR (neat): 3154 (w, br), 3071 (w), 2955 (m), 2930 (m), 2870 (m), 1614 (m), 1519 (m), 1455 (m), 1436 (m), 1368 (w), 1283 (w), 1181 (s), 1107 (s), 1066 (m), 925 (m), 900 (m), 752 (w), 722 (s), 693 (s), 553 (s), 521 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89–7.79 (4H, m), 7.49–7.32 (6H, m), 7.03 (2H, d, J = 8.8 Hz), 6.54 (2H, d, J = 8.8 Hz), 5.63 (1H, app ddt, J = 17.2, 10.0, 7.2 Hz), 5.10–4.99 (2H, m), 4.26–4.19 (1H, m), 3.23 (4H, app dd, J = 7.8, 7.2 Hz), 3.26–3.21 (1H, m, overlapping with the dd at 3.23), 2.75–2.58 (2H, m), 1.59–1.52 (4H, m), 1.40–1.30 (4H, app sextet, J = 7.6 Hz), 0.96 (6H, t, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.3, 134.6, 133.6 (d, J = 127.0 Hz), 132.6 (d, J = 9.5 Hz), 132.4 (d, J = 130.0 Hz), 131.9 (d, J = 9.3 Hz), 131.7 (d, J = 2.7 Hz), 131.6 (d, J = 2.7 Hz), 129.2 (d, J = 6.3 Hz), 128.4 (d, J = 12.3 Hz), 128.3 (d, J = 12.4 Hz), 127.6, 118.1, 111.5, 54.3, 50.9, 43.5 (d, J = 3.7 Hz), 29.5, 20.4, 14.1; HRMS Calcd for $C_{30}H_{40}N_2OP$ $[M + H]^+$: 475.28782; Found: 475.28783. $[\alpha]^{20}_D$ = +61.6 (c = 1.33, $CHCl_3$) for a 92:8 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic

racemic material (Chiracel OD–H, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 12 min (major) and 14 min (minor).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.558	14499159	507916	50.161	54.997
2	14.711	14406117	415611	49.839	45.003
Total		28905276	923527	100.000	100.000

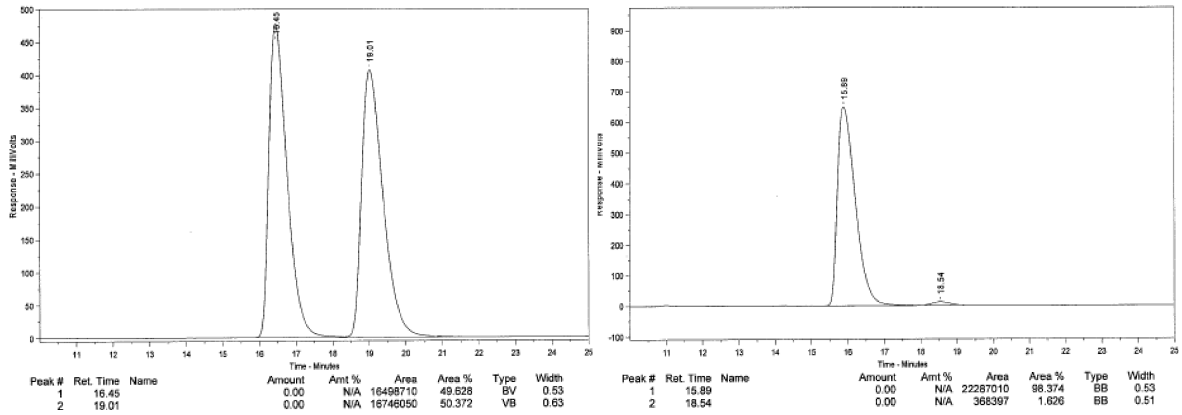
PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.087	19265334	767060	91.817	92.781
2	13.911	1716879	59680	8.183	7.219
Total		20982212	826740	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	12.6	50.161	1	12.1	91.817
2	14.7	49.839	2	13.9	8.183

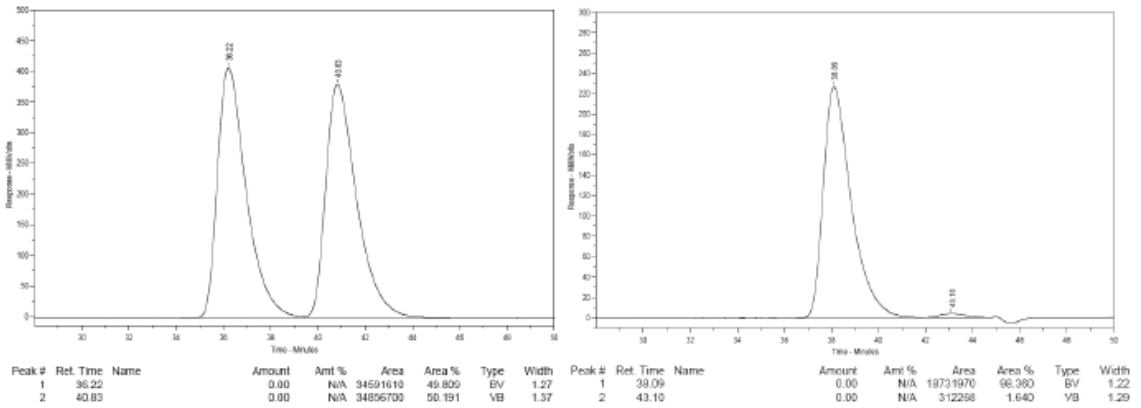
(*R*)-*N*-(1-(Furan-2-yl)but-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (1.17l, Table 1.5): The title compound is synthesized and purified analogously to **1.15b** (only with a six h reaction time) affording **1.17l** (32.2 mg, 0.0955 mmol, 96% yield) as a light tan solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89–7.82 (4H, m), 7.50–7.37 (6H, m), 7.32–7.31 (1H, m), 6.25–6.24 (1H, m), 6.12–6.11 (1H, m), 5.63 (1H, dddd, J = 17.6, 10.0, 7.6, 7.6 Hz), 5.14–5.05 (2H, m), 4.37 (1H, dddd, J = 10.0, 10.0, 6.4, 6.4 Hz), 3.34 (1H, br dd, J = 10.4, 7.2 Hz), 2.79–2.61 (2H, m); HRMS Calcd for $C_{20}H_{21}NO_2P$ $[M + H]^+$: 338.13099; Found: 338.13157. $[\alpha]^{20}_D$ = +53.3 (c = 1.00, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 16 min (major) and 19 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.5	49.828	1	15.9	98.374
2	19.0	50.372	2	18.5	1.626

(*R*)-*P*,*P*-Diphenyl-*N*-(1-(pyridin-3-yl)but-3-en-1-yl)phosphinic amide (**1.17m, Table 1.5**): The title compound is synthesized analogously to **4b** and purified analogously to **4o** (see below). M.p. = 133-134 °C. IR (neat): 3169 (w, br), 1438 (m), 1184 (s), 1123 (m), 1109 (m), 1071 (m), 921 (w), 754 (w), 725 (m), 698 (m), 533 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (2H, br dd, *J* = 4.8, 1.6 Hz), 8.36 (1H, br d, *J* = 2.4 Hz), 7.82–7.77 (2H, m), 7.70–7.65 (2H, m), 7.419–7.42 (2H, m), 7.40–7.34 (3H, m), 7.28–7.23 (2H, m), 7.15–7.11 (1H, m), 5.53 (1H, dddd, *J* = 16.8, 10.4, 7.2, 7.2 Hz), 5.08–5.03 (2H, m), 4.35 (1H, dddd, *J* = 9.6, 9.6, 6.4, 6.4 Hz), 3.33 (1H, br dd, *J* = 8.0, 5.6 Hz), 2.65–2.55 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.6 (d, *J* = 15.6 Hz), 138.5 (d, *J* = 4.5 Hz), 134.4, 132.9, 132.7 (d, *J* = 127 Hz, peak overlaps with doublet at 132.06), 132.5 (d, *J* = 9.7 Hz), 132.2 (d, *J* = 2.2 Hz), 132.1 (d, *J* = 2.9 Hz), 131.9 (d, *J* = 8.9 Hz), 131.8 (d, *J* = 127 Hz, peak overlaps with doublet at 132.5), 128.7 (d, *J* = 12.6 Hz), 128.5 (d, *J* = 12.7 Hz), 123.4, 119.9, 52.5, 43.4 (d, *J* = 4.5 Hz); HRMS Calcd for $C_{21}H_{22}N_2OP$ $[M + H]^+$: 349.14697; Found: 349.14651. $[\alpha]^{25}_D$ = +45.2 (*c* = 1.00, $CHCl_3$) for a 98:2 er sample.

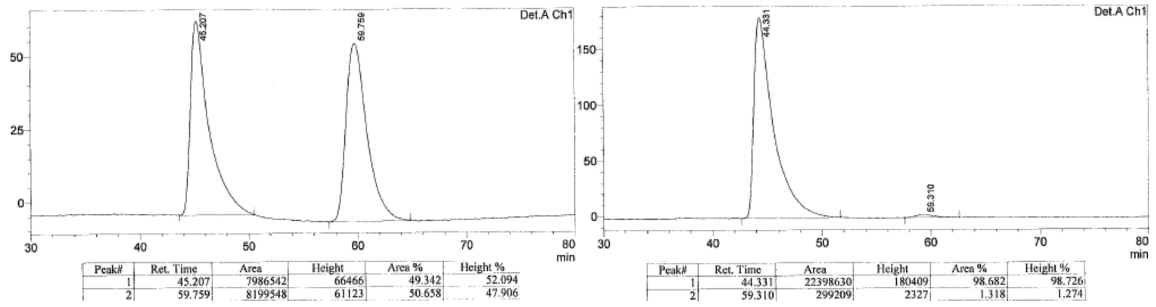
The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H, 86:14 hexanes:*i*-PrOH, 0.6 mL/min, 220 nm): t_R of **4l**: 38 min (major) and 43 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	36.2 min	49.809	1	39.1 min	98.360
2	40.8 min	50.191	2	43.1 min	1.640

(*R*)-*P*,*P*-Diphenyl-*N*-(1-(pyridin-4-yl)but-3-en-1-yl)phosphinic amide (1.17n, Table 1.5): The title compound is synthesized analagously to **1.15b** and purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in 95:5 hexanes:triethylamine and eluted with 50 1:1 mL hexanes:diethyl ether, 20 mL diethyl ether, 5 mL dichloromethane, 20 mL 98:2 dichloromethane:triethylamine, and 40 mL 96:4 dichloromethane:triethylamine) to afford **1.17n** (26.1 mg, 0.0749 mmol, 75% yield) as a white solid. M.p. = 84 ºC (decomp). IR(neat): 3142 (w, br), 3073 (w, br), 3056 (w, br), 2919 (w, br), 1596 (w), 1458 (w), 1438 (m), 1412 (w), 1180 (m), 1121 (m), 1107 (m), 1068 (m), 993 (m), 905 (m), 817 (m), 751 (m), 723 (s), 693 (s), 601 (m), 545 (s), 521 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.53 (2H, br s), 7.90–7.84 (2H, m), 7.79–7.73 (2H, m), 7.55–7.50 (1H, m), 7.48–7.42 (3H, m); 7.36–7.31 (2H, m), 7.17–7.15 (2H,

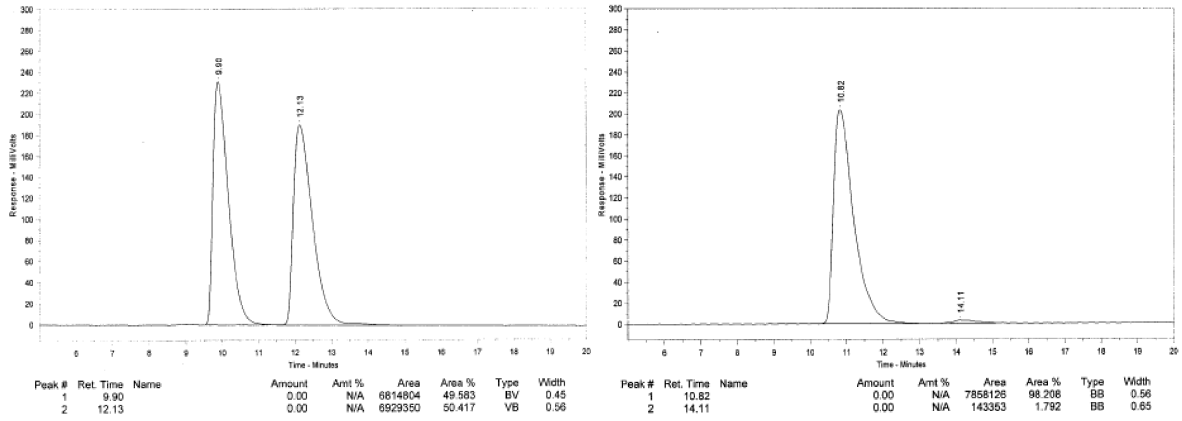
m); 5.61–5.51 (1H, m), 5.17–5.11 (2H, m), 4.36 (1H, m), 3.42 (1H, br dd, J = 9.9, 5.7 Hz), 2.70–2.59 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1 (d, J = 4.7 Hz), 149.9, 132.6 (d, J ~ 128 Hz, more upfield peak is overlapping with the peak at 131.9), 132.5 (d, J = 8.6 Hz), 132.4, 132.3 (d, J = 2.8 Hz), 132.2 (d, J = 2.9 Hz), 131.97 (d, J = 9.5 Hz), 131.9 (d, J = 130.5 Hz), 128.8 (d, J = 12.5 Hz), 128.6 (d, J = 12.7 Hz), 121.9, 120.2, 53.5, 43.1 (d, J = 4.5 Hz); HRMS Calcd for $C_{21}H_{22}N_2OP$ $[M + H]^+$: 349.14697; Found: 349.14696. $[\alpha]^{25}_D$ = + 43 (c = 0.47, $CHCl_3$) for a 98.5:1.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 9:1 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 44.3 min (major) and 59.3 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	45.2	49.342	1	44.3	98.682
2	59.8	50.658	2	59.3	1.318

(*R*)-*N*-(3-Methyl-1-phenylbut-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (1.23a, Table 1.8): The title compound is synthesized and purified analogously to **1.15b** [except allylboronic acid pinacol ester **1.22a** (32 μL, 0.15 mmol) is used as the nucleophile instead of **1.6**], affording **1.23a** (34.4 mg, 0.0952 mmol, 95% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86–7.80 (2H, m), 7.76–7.70 (2H, m), 7.50–7.46 (1H, m), 7.44–7.38 (3H, m),

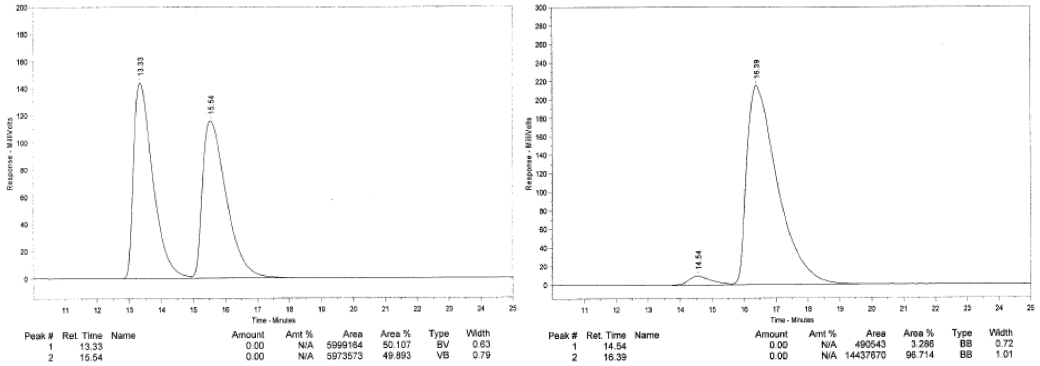
7.29–7.17 (7H, m), 4.78 (1H, s), 4.69 (1H, s), 4.40 (1H, dddd, J = 16.4, 16.4, 8.4, 8.4 Hz), 3.32 (1H, br dd, J = 8.0, 6.0 Hz), 2.62 (1H, dd, J = 13.6, 7.2 Hz), 2.53 (1H, dd, J = 14.0, 7.2 Hz), 1.58 (3H, s); HRMS Calcd for $C_{23}H_{25}NOP$ $[M + H]^+$: 362.16738; Found: 362.16649. $[\alpha]^{20}_D$ = +39 (c = 1.2, $CHCl_3$) for a 97.5:2.5 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 92:8 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 11 min (major) and 14 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	9.90	49.583	1	10.8	98.206
2	12.1	50.417	2	14.1	1.792

(*R*)-*N*-(1,3-Diphenylbut-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (**1.23b, Table 1.8**): The title compound is synthesized and purified analogously to **1.15b** [except allylboronic acid pinacol ester **1.22b** (37 μL, 0.15 mmol) is used as the nucleophile instead of **1.6** and the reaction time is 6 h] affording **4n** (42.1 mg, 0.0994 mmol, >98% yield) as a white foam. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76–7.70 (4H, m), 7.47–7.40 (2H, m), 7.37–7.30 (4H, m), 7.27–7.16 (8H, m), 7.07–7.00 (2H, m), 5.21 (1H, d, J = 1.2 Hz), 4.87 (1H, d, J = 1.2 Hz), 4.27

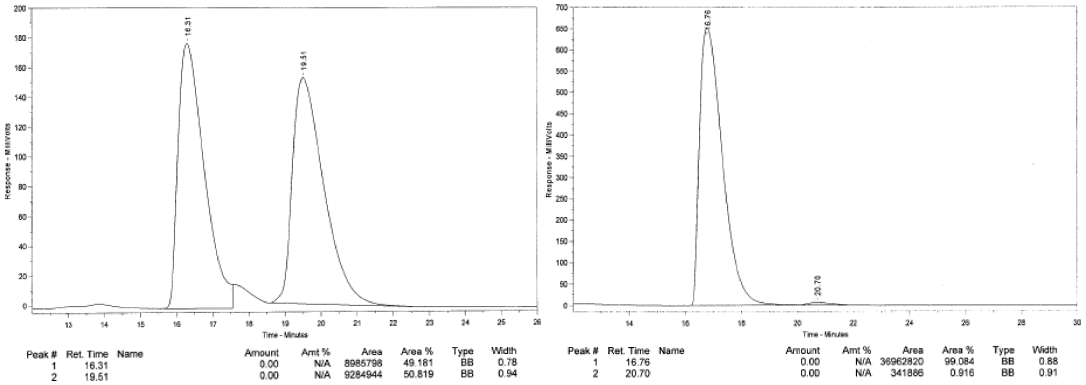
(1H, dddd, J = 8.4, 8.4, 6.4, 6.4 Hz), 3.29 (1H, br dd, J = 8.8, 5.6 Hz), 3.25 (1H, dd, J = 14.0, 6.0 Hz), 2.99 (1H, dd, J = 14.0, 8.0 Hz); HRMS Calcd for $C_{28}H_{27}NOP$ $[M + H]^+$: 424.18303; Found: 424.18255. $[\alpha]^{20}_D$ = +26 (c = 1.7, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 92:8 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 15 min (minor) and 16 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.3	50.107	1	14.5	3.286
2	15.5	49.893	2	16.4	96.714

(*R*,*E*)-*P*,*P*-Diphenyl-*N*-(1-phenylhexa-1,5-dien-3-yl)phosphinic amide (1.21a, Table 1.6): The title compound is synthesized and purified analogously to **1.15b** afford **1.21a** (31.3 mg, 0.0838 mmol, 84% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96–7.87 (4H, m), 7.51–7.39 (6H, m), 7.31–7.26 (4H, m), 7.24–7.21 (1H, m), 6.46–6.42 (1H, m), 6.15 (1H, ddd, J = 15.9, 6.3, 2.4 Hz), 5.78 (1H, dddd, J = 14.4, 7.6, 6.8, 6.8 Hz), 5.20–5.12 (2H, m), 4.01–3.92 (1H, m), 3.09 (1H, br dd, J = 9.6, 6.0 Hz), 2.59–2.45 (2H, m); HRMS Calcd for $C_{24}H_{25}NOP$ $[M + H]^+$: 374.16738; Found: 374.16756. $[\alpha]^{20}_D$ = +89 (c =

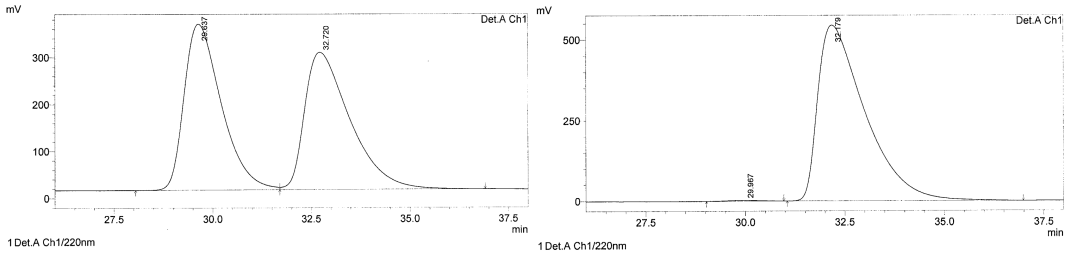
0.65, $CHCl_3$) for a 99:1 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 92:8 hexanes:*i*-PrOH, 0.6 mL/min, 220 nm): t_R: 17 min (major) and 21 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.3	49.181	1	16.8	99.084
2	19.5	50.819	2	20.7	0.916

(*R*,*E*)-*N*-(1-(2-Nitrophenyl)hexa-1,5-dien-3-yl)-*P*,*P*-diphenylphosphinic amide (**1.21b, Table 1.6**): The title compound is purified identically to **1.15b** affording **1.21b** (39.6 mg, 0.095 mmol, 95% yield) as a white solid. M.p. = 135 °C. IR (neat): 3149 (m, br), 3067 (w), 2857 (w), 1641 (w), 1605 (w), 1571 (w), 1520 (s), 1436 (m), 1350 (m), 1178 (s), 1123 (m), 1106 (m), 1067 (m), 952 (m), 918 (m), 745 (m), 724 (s), 691 (s), 541 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00–7.88 (5H, m), 7.55–7.35 (9H, m), 7.01 (1H, dd, J = 16.0, 1.6 Hz), 6.17 (1H, dd, J = 15.6, 5.6 Hz), 5.80 (1H, dddd, J = 16.8, 10.0, 7.6, 6.4 Hz), 5.22–5.14 (2H, m), 4.02–3.96 (1H, m), 3.16 (1H, br dd, J = 9.6, 5.6 Hz), 2.62–2.49 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 137.0 (d, J = 6.0 Hz), 133.3, 133.3, 132.9, 132.9 (d, J = 128.0 Hz), 132.5 (d, J = 9.4 Hz), 132.4 (d, J = 130.0 Hz), 132.0 (2 d peaks exactly overlapping, J = 3 Hz), 132.0 (d, J = 9.3 Hz), 129.2, 128.7 (2 d

peaks exactly overlapping, J = 12.6 Hz), 128.2, 125.9, 124.6, 119.5, 52.5, 42.0 (d, J = 4.2 Hz); HRMS Calcd for $C_{24}H_{24}N_2O_3P$ $[M + H]^+$: 419.15245; Found: 419.15207. $[\alpha]^{20}_D$ = +94.4 (c = 1.00, $CHCl_3$) for a 99.5:0.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD–H, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R :30 min (minor) and 32 min (major).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.637	23154936	353487	49.698	54.717
2	32.720	23436642	292542	50.302	45.283
Total		46591578	646029	100.000	100.000

PeakTable

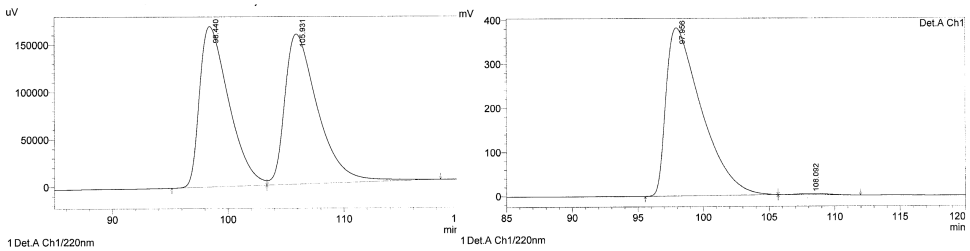
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.967	145427	2568	0.321	0.469
2	32.179	45126070	545396	99.679	99.531
Total		45271497	547963	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	29.6	49.698	1	30.0	0.321
2	32.7	50.302	2	32.2	99.679

(*R*,*E*)-*N*-(1-(4-Methoxyphenyl)hexa-1,5-dien-3-yl)-*P*,*P*-diphenylphosphinic amide (**1.21c, Table 1.6**): The title compound is purified identically to **1.15b** affording **1.21c** (39.4 mg, 0.098 mmol, 98% yield) as a white solid. M.p. = 134 °C. IR (neat): 3180 (w, br), 3059 (w), 2929 (w), 2837 (w), 1607 (w), 1509 (m), 1433 (m), 1248 (m), 1185 (s), 1124 (m), 1108 (m), 1069 (m), 1031 (m), 976 (m), 912 (w), 811 (m), 745 (m), 725 (s), 693 (s), 541 (s), 516 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.96–7.86 (4H, m), 7.51–7.37 (6H, m), 7.22 (2H, d, J = 8.8 Hz), 6.82 (2H, d, J = 8.4 Hz), 6.37 (1H, d, J = 15.6 Hz), 6.01 (1H, dd, J = 16.0, 6.4 Hz), 5.79 (1H, dddd, J = 17.2, 10.4, 7.6, 7.2 Hz), 5.19–5.10 (2H, m), 3.94 (1H, m), 3.80 (3H, s), 3.08 (1H, br dd, J = 9.6, 6.0 Hz),

2.58–2.43 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 133.9, 133.3 (d, J = 127.0 Hz), 132.7 (d, J = 130.0 Hz), 132.6 (d, J = 9.4 Hz), 132.0 (d, J = 9.5 Hz), 131.9 (d, J = 2.8 Hz), 131.8 (d, J = 2.8 Hz), 129.9, 129.6, 129.3 (d, J = 5.7 Hz), 128.6 (d, J = 12.4 Hz), 128.5 (d, J = 12.6 Hz), 127.7, 119.0, 114.0, 55.4, 52.9, 42.4 (d, J = 4.5 Hz); HRMS Calcd for $C_{25}H_{27}NO_2P$ $[M + H]^+$: 404.17794; Found: 404.17730. $[\alpha]^{20}_D$ = +128.2 (c = 1.00, $CHCl_3$) for a 99:1 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD–H, 95:5 hexanes:*i*-PrOH, 0.2 mL/min, 220 nm): t_R: 98 min (major) and 108 min (minor).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	98.440	29803902	169432	48.621	51.643
2	105.931	31494841	158651	51.379	48.357
Total		61298742	328083	100.000	100.000

PeakTable

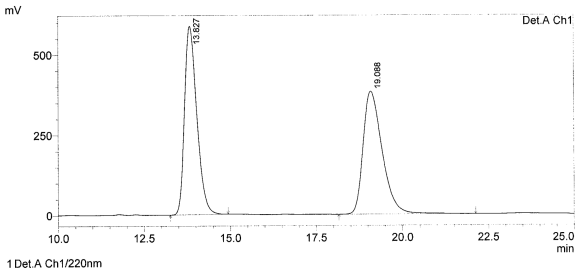
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	97.956	71854288	382013	99.431	99.315
2	108.092	411019	2636	0.569	0.685
Total		72265307	384649	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	98.4	48.621	1	98.0	99.431
2	105.9	51.379	2	108.1	0.569

(*R*,*Z*)-*N*-(2-Bromo-1-phenylhexa-1,5-dien-3-yl)-*P*,*P*-diphenylphosphinic amide (**1.21d, Table 1.6**): The title compound is purified identically to **1.15b** affording **1.21d** (43.4 mg, 0.096 mmol, 96% yield) as a white solid. M.p. = 123 °C. IR (neat): 3133 (m, br), 3077 (w), 3056 (w), 2910 (w), 2861 (w), 1643 (w), 1591 (w), 1458 (w), 1434 (m), 1182 (s), 1123 (m), 1105 (m), 1088 (m), 984 (m), 952 (m), 916 (m), 865 (m), 746 (m), 723 (s), 691 (s), 594 (m), 568 (m), 536 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ

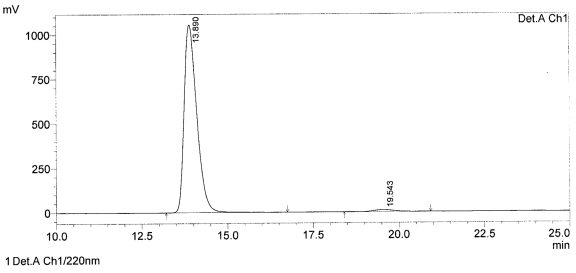
7.95–7.85 (4H, m), 7.54–7.28 (11H, m), 6.56 (1H, s), 5.74 (1H, ddt, *J* = 17.2, 10.0, 7.2 Hz), 5.19–5.08 (2H, m), 4.04–3.95 (1H, m), 3.40 (1H, br dd, *J* = 9.6, 8.4 Hz), 2.68–2.51 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.1, 133.3, 133.0 (d, *J* = 127.0 Hz), 132.8 (d, *J* = 9.8 Hz), 132.2 (d, *J* = 2.7 Hz), 132.1 (d, *J* = 2.9 Hz), 131.9 (d, *J* = 130.0 Hz), 131.8 (d, *J* = 9.6 Hz), 129.7 (d, *J* = 5.4 Hz), 129.4, 129.1, 128.7 (d, *J* = 12.5 Hz), 128.5 (d, *J* = 12.8 Hz), 128.2, 128.1, 118.6, 58.8, 41.3 (d, *J* = 4.3 Hz); HRMS Calcd for $C_{24}H_{24}BrNOP$ $[M + H]^+$: 452.07789; Found: 452.07908. $[\alpha]^{20}_D$ = +7.5 (*c* = 1.00, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD–H, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 14 min (major) and 19 min (minor).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.827	14545482	587197	49.618	60.510
2	19.088	14769733	383220	50.382	39.490
Total		29315216	970417	100.000	100.000



PeakTable

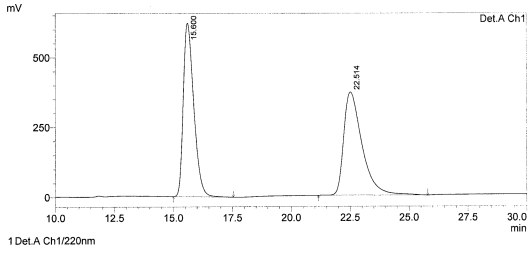
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.890	27103659	1055854	98.297	98.951
2	19.543	469584	11196	1.703	1.049
Total		27573242	1067049	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.8	49.618	1	13.9	98.297
2	19.1	50.382	2	19.5	1.703

(*R*,*E*)-*N*-(2-Methyl-1-phenylhexa-1,5-dien-3-yl)-*P*,*P*-diphenylphosphinic amide (1.21e): Following the $NaIO_4$ workup (see general procedure above), the crude product is treated overnight under stirring with ~ 1 g basic aluminum oxide in 4 ml dichloromethane:ether (1:1) to hydrolyze unreacted **1.20e**, after which the aluminum

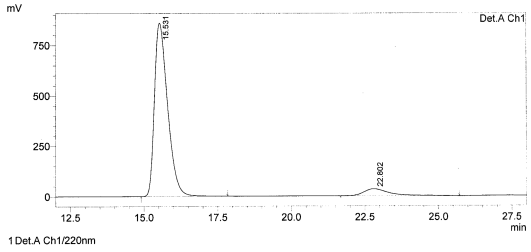
oxide id filtered off and washed with dichloromethane and 20 ml ethyl acetate. After removal of the solvent *in vacuo*, the title compound is purified identically to **1.15b,** affording **1.21e** (30.2 mg, 0.0779 mmol, 78% yield) as a white solid. M.p. = 116–117 ºC. IR (neat): 3172 (m, br), 3055 (w), 2925 (w), 2907 (w), 2882 (w), 2856 (w), 1457 (w), 1447 (w), 1434 (m), 1181 (s), 1122 (m), 1106 (s), 1085 (m), 988 (m), 918 (m), 747 (m), 722 (s), 694 (s), 635 (m), 566 (m), 540 (s), 522 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95–7.86 (4H, m), 7.52–7.38 (6H, m), 7.31 (2H, m), 7.20 (1H, m), 7.13 (2H, m), 6.22 (1H, s), 5.75 (1H, dddd, *J* = 17.2, 10.4, 7.6, 7.6 Hz), 5.17–5.09 (2H, m), 3.85 (1H, m), 3.14 (1H, br dd, *J* = 9.2, 5.6 Hz), 2.61–2.42 (2H, m), 1.80 (3H, d, *J* = 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1 (d, *J* = 4.4 Hz), 137.7, 134.1, 133.3 (d, *J* ~ 126 Hz, 2 peaks overlapping), 132.7 (d, *J* = 9.6 Hz), 132.5 (d, *J* ~ 130 Hz, 2 peaks overlapping), 132.0 (d, *J* ~ 2.7 Hz, two peaks overlapping), 131.9 (d, *J* = 9.3 Hz), 131.9 (d, *J* ~ 3.2 Hz, two peaks overlapping), 129.0, 128.6 (d, *J* = 12.5 Hz), 128.45 (d, *J* = 12.6 Hz), 128.12, 127.09, 126.49, 118.36, 58.10, 40.51 (d, *J* = 4.8 Hz), 14.22; HRMS Calcd for $C_{25}H_{27}NOP$ $[M + H]^+$: 388.18303; Found: 388.18165. $[\alpha]^{25}_{D}$ = + 31.5 (*c* = 1.00, $CHCl_3$) for a 92.5:7.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 15.5 min (major) and 22.8 min (minor).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.600	19256841	620872	49.087	62.656
2	22.514	19973555	370057	50.913	37.344
Total		39230396	990928	100.000	100.000



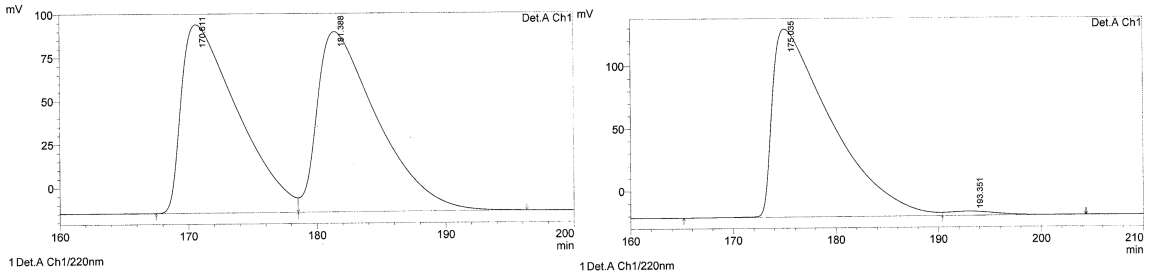
PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.531	26614031	858903	92.524	96.144
2	22.802	2150367	34449	7.476	3.856
Total		28764397	893352	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	15.6	49.087	1	15.5	92.524
2	22.5	50.913	2	22.8	7.476

(*R*,*E*)-*N*-(Nona-1,5-dien-4-yl)-*P*,*P*-diphenylphosphinic amide (**1.21f, Table 1.6**): The title compound is purified identically to **1.15b** affording **1.21f** from freshly prepared **1.20f** (except 2.5 mol % aminophenol **1.19r** used in the reaction instead of 3.0 mol %) affording **1.21f** (32.7 mg, 0.096 mmol, 96% yield) as a white solid. Crystals suitable for x-ray crystallography were obtained by vapor diffusion from a dichloromethane/hexane solvent system at 22 ºC. M.p. = 87 °C. IR (neat): 3121 (m, br), 3057 (w), 2953 (w), 2928 (w), 2868 (w), 1639 (w), 1590 (w), 1458 (m), 1436 (m), 1198 (m), 1182 (m), 1107 (m), 1065 (m), 966 (m), 909 (m), 753 (w), 719 (s), 691 (s), 565 (m), 524 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–7.83 (4H, m), 7.50–7.38 (6H, m), 5.74 (1H, dddd, *J* = 17.2, 10.4, 8.0, 6.8 Hz), 5.50 (1H, dtd, *J* = 15.2, 6.4, 0.8 Hz), 5.39 (1H, ddt, *J* = 15.6, 6.0, 1.0 Hz), 5.15–5.07 (2H, m), 3.78–3.68 (1H, m), 2.93 (1H, br dd, *J* = 9.6, 6.0 Hz), 2.47–2.31 (2H, m), 1.94 (2H, quartet, *J* = 6.8 Hz), 1.33 (2H, app sextet, *J* = 7.2 Hz), 0.86 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.1, 133.4 (d, *J* = 127.0 Hz), 132.9 (d, *J* = 130.0 Hz), 132.6 (d, *J* = 9.4 Hz), 132.0 (d, *J* = 9.5 Hz), 131.8 (2 d exactly overlapping, *J* = 2.5 Hz), 131.7 (d, *J* = 5.7 Hz), 131.5, 128.5 (d, *J* = 12.5 Hz), 128.5 (d, *J* = 12.5 Hz), 118.4, 52.6, 42.7 (d, *J* = 4.5 Hz), 34.4, 22.4, 13.8; HRMS Calcd for $C_{21}H_{27}NOP$ $[M + H]^+$: 340.18303; Found: 340.18359. $[\alpha]^{20}_D$ = +7.40 (*c* = 1.00, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD–H, 98.5:1.5 hexanes:*i*-PrOH, 0.15 mL/min, 220 nm): t_R: 175 min (major) and 193 min (minor).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	170.611	33080046	108668	49.503	51.091
2	181.388	33744364	104028	50.497	48.909
Total		66824410	212697	100.000	100.000

PeakTable

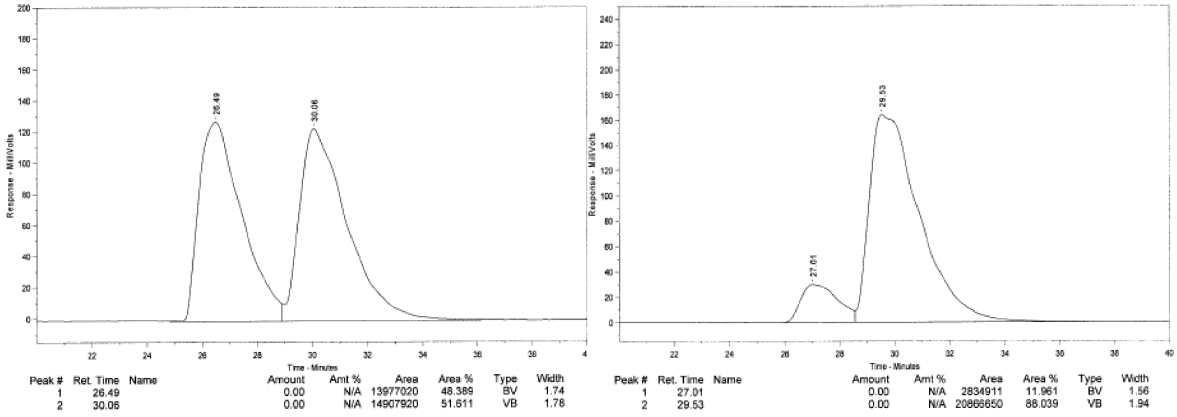
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	175.035	60112701	150311	98.210	97.855
2	193.351	1095862	3295	1.790	2.145
Total		61208563	153606	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	170.6	49.503	1	175.0	98.210
2	181.4	50.497	2	193.4	1.790

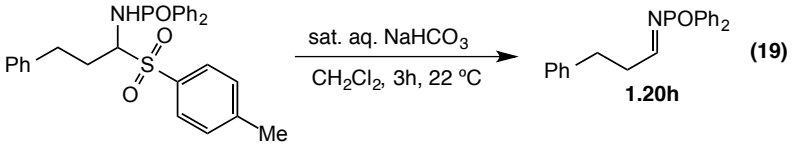
(*R*)-*P*,*P*-Diphenyl-*N*-(1-phenylhex-5-en-1-yn-3-yl)phosphinic amide (**1.21g, Table 1.6**): The title compound is purified identically to **1.15b** affording **1.21g** (33.9 mg, 0.0913 mmol, 91% yield) as a yellow solid. M.p. = 105–107 ºC. IR (neat): 3132 (m, br), 3076 (w), 3055 (w), 2913 (w), 2857 (w), 1641 (w), 1591 (w), 1488 (m), 1312 (m), 1181 (s), 1125 (s), 1107 (s), 1070 (m), 945 (m), 747 (s), 725 (s), 690 (s), 530 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04–7.99 (2H, m), 7.89–7.84 (2H, m), 7.52–7.40 (6H, m), 7.35–7.32 (2H, m), 7.32–7.24 (3H, m) 5.97 (1H, dddd, *J* = 17.0, 10.0, 7.6, 6.9 Hz), 5.29–5.19 (2H, m), 4.31–4.23 (1H, m), 3.37 (1H, dd, *J* = 10.1, 8.3 Hz), 2.70–2.53 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2, 133.0 (d, *J* = 127.6 Hz), 132.9 (d, *J* = 9.8 Hz), 132.1 (d, *J* = 2.7 Hz), 132.0 (d, *J* = 130.4 Hz), 131.8 (d, *J* = 9.8 Hz, only the peak at 131.9 is visible, the other is overlapping), 131.8, 128.8 (d, *J* = 12.6 Hz), 128.8 (d, *J* = 12.9 Hz), 128.4 (d, *J* = 5.5 Hz, only the peak at 128.4 is visible, the other is overlapping), 122.9, 119.7, 89.7 (d, *J* = 8.0 Hz), 84.1, 43.4, 42.9 (d, *J* = 3.5 Hz); HRMS Calcd for $C_{24}H_{23}NOP$ $[M + H]^+$: 372.15173; Found: 372.15177. $[\alpha]^{20}_D$ = -100 (*c* = 0.85, $CHCl_3$) for a 88:12 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with

authentic racemic material (Chiracel OD, 97:3 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 27 min (minor) and 30 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	26.5	48.389	1	27.0	11.961
2	30.1	51.611	2	29.5	88.039

Representative Procedure for Enantioselective Allyl Additions to Alkyl-Substituted *N*-Diphenylphosphinoyl Imines: [136]



Preparation of the alkyl-substituted aldimine: A six-dram vial equipped with an 11 x 4 mm stir bar is charged with sulfinyl adduct (eq. 1, 0.4 mmol) to which is added CH_2Cl_2 (8.0 mL) and a saturated aqueous solution of $NaHCO_3$ (8.0 mL) consecutively. The biphasic mixture is allowed to stir vigorously enough for the solution to be homogeneous for 3 h at 22 °C. The organic layer is separated and the aqueous phase is washed with CH_2Cl_2 (3 x 5 mL). The combined organic layers are dried over $MgSO_4$. The volatiles

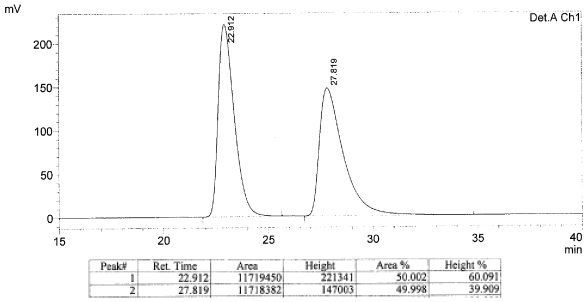
are removed under reduced pressure and the unpurified imine is azeotropically dried under vacuum with anhydrous benzene to afford aldimine **1.20h** as light yellow oil (>98% conversion and yield are assumed). The vessel containing **1.20h** is sealed with a rubber septum and anhydrous toluene (2 mL) is added to prepare a stock solution of 0.1 mmol **1.20h**/500. μL toluene.

Preparation of catalyst solution (small scale): In a nitrogen-filled glovebox (not needed for gram scale; only used when reactions are performed at mg scale to achieve highly reproducible data), aminophenol **1.19r** (6.9 mg, 0.023 mmol) is added to an oven-dried two-dram vial equipped with a stir bar followed by 1.5 mL of a stock solution of NaO*t*-Bu in toluene (9.6 mg, 0.10 mmol/8.0 mL). The vial is sealed with a cap (phenolic open top cap with a red PFTE/white silicone septa) and electrical tape and allowed to stir under nitrogen at 22 ºC for ~10 minutes.

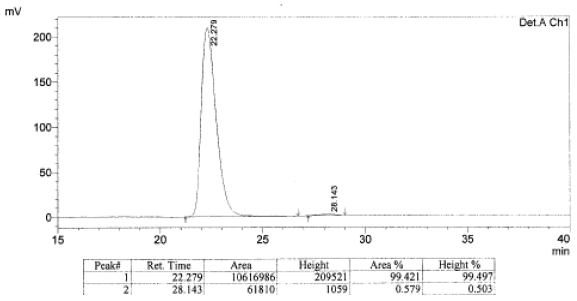
An oven-dried two-dram vial equipped with a stir bar and sealed with a cap (phenolic open top cap with a red PFTE/white silicone septa) and electrical tape is charged with toluene (100. μL), methanol (10. μL, 0.25 mmol), and allylboronic acid pinacol ester (28 μL, 0.15 mmol). To this mixture is added 500. μL of the stock solution of aldimine **1.20h** (described above), followed by 400. μL of the catalyst solution (described above) of [**1.19r** (1.82 mg, 6.00 μmol) and NaO*t*-Bu (0.48 mg, 5.0 μmol)]. The clear and colorless solution is allowed to stir at 22 ºC for four h during which time no visible

change occurs. The cap is removed and 3 mL of saturated aqueous $NaIO_4$ is added and the biphasic mixture is allowed to stir for 20 minutes. The aqueous layer is washed with ethyl acetate (4 x 4 mL), and the combined organic layers are dried over Na_2SO_4 and concentrated *in vacuo*. The resulting yellow oil was purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in 95:5 hexanes:triethylamine and eluted with 10 mL hexanes, 10 mL 3:1 hexanes:ethyl acetate, 10 mL 2:1 hexanes:ethyl acetate, 10 mL 1:1 hexanes:ethyl acetate, and 10 mL ethyl acetate) to afford **1.21h** (19.2 mg, 0.0511 mmol, 51% yield) as a white solid.

(*S*)-*P*,*P*-Diphenyl-*N*-(1-phenylhex-5-en-3-yl)phosphinic amide (**1.21h, Table 1.6**): The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.84 (4H, m), 7.49–7.39 (6H, m), 7.24–7.19 (2H, m), 7.15–7.10 (3H, m), 5.78 (1H, dddd, *J* = 17.2, 10.4, 7.6, 7.6 Hz), 5.14–5.09 (2H, m), 3.25–3.16 (1H, m), 2.82 (1H, br dd, *J* = 10.8, 6.4 Hz), 2.73–2.57 (2H, m), 2.39–2.35 (2H, m), 1.86–1.80 (2H, m); HRMS Calcd for $C_{24}H_{27}NOP$ $[M + H]^+$: 376.18303; Found: 376.18135. $[\alpha]^{20}_D$ = –2.6 (*c* = 0.43, $CHCl_3$) for a >99:1 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 95:5 hexanes:*i*-PrOH, 0.6 mL/min, 220 nm): t_R: 22 min (major) and 28 min (minor).



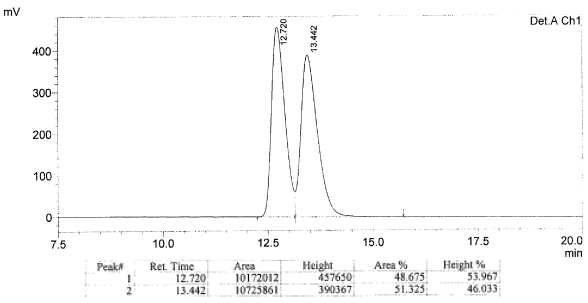
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.912	11719450	221341	50.002	60.091
2	27.819	11718382	147003	49.998	39.909



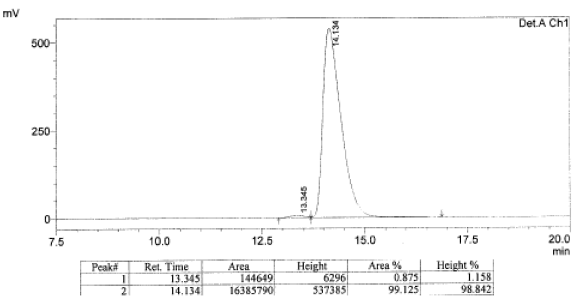
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.279	10616986	209521	99.421	99.497
2	28.143	61810	1059	0.579	0.503

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	22.9	50.002	1	22.3	99.421
2	27.8	49.998	2	28.1	0.579

(*S*)-*N*-(6-Methylhept-1-en-4-yl)-*P*,*P*-diphenylphosphinic amide (**1.21i, Table 1.6**): The title compound is purified identically to **1.21h** affording **1.21i** (17.7 mg, 0.0540 mmol, 54% yield) as a white solid. The analytical data are fully consistent with those reported previously.[141] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93–7.87 (4H, m), 7.51–7.41 (6H, m), 5.79 (1H, dddd, *J* = 17.6, 10.4, 7.6, 7.6 Hz), 5.14–5.10 (2H, m), 3.25–3.14 (1H, m), 2.75 (1H, br dd, *J* = 10.8, 6.0 Hz), 2.39–2.28 (2H, m), 1.84–1.70 (1H, m), 1.42–1.29 (2H, m), 0.80 (3H, d, *J* = 6.6 Hz), 0.76 (3H, d, *J* = 6.5 Hz); HRMS Calcd for $C_{20}H_{27}NOP$ $[M + H]^+$: 328.18303; Found: 328.18398. $[\alpha]^{20}_D$ = –38 (*c* = 0.73, $CHCl_3$) for a 98.5:1.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 95:5 hexanes:*i*-PrOH, 0.6 mL/min, 220 nm): t_R of **S15**: 13 min (minor) and 14 min (major).



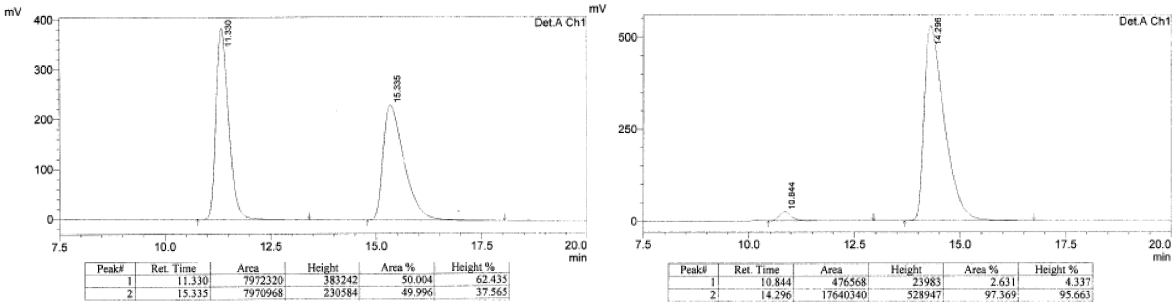
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.720	10172012	457650	48.675	53.967
2	13.442	10725861	390367	51.325	46.033



Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.345	144649	6296	0.875	1.158
2	14.134	16385790	537385	99.125	98.842

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	12.7	48.675	1	13.3	0.875
2	13.4	51.325	2	14.1	99.125

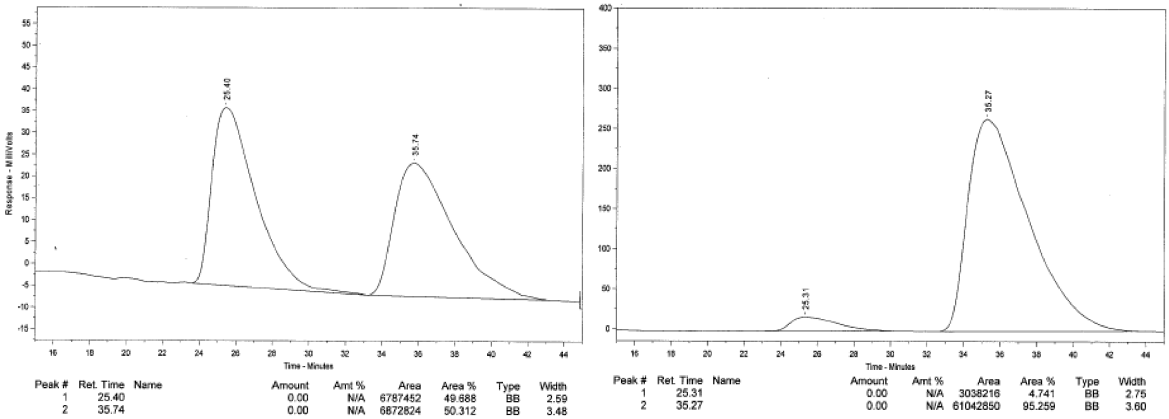
(*R*)-*N*-(1-Cyclohexylbut-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (1.21j, Table 1.6): The title compound is synthesized and purified identically to **1.21g** (except 8.5 mol % of NaO*t*-Bu is used in the reaction instead of 5 mol %) affording **1.21j** (27.2 mg, 0.0769 mmol, 77% yield) as a white solid. M.p. = 120–122 °C. IR (neat): 3207 (w, br), 3075 (w), 3057 (w), 2921 (m), 2850 (m), 1639 (w), 1436 (s), 1187 (s), 1123 (s), 1108 (s), 1067 (m), 994 (w), 909 (m), 722 (s), 694 (s), 533 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93–7.87 (4H, m), 7.50–7.42 (6H, m), 5.77 (1H, dddd, *J* = 17.3, 10.1, 7.3, 7.3 Hz), 5.12–5.06 (2H, m), 3.02–2.87 (1H, m), 2.77 (1H, br dd, *J* = 10.7, 6.1 Hz), 2.09 (2H, app t, *J* = 6.5 Hz), 1.82–1.61 (5H, m), 1.46–1.41 (1H, m), 1.24–1.15 (4H, m), 0.98-0.92 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.1, 133.3 (d, *J* = 128.7 Hz), 133.2 (d, *J* = 129.8 Hz, only peak at 132.8 is visible, the other is overlapping), 132.5 (d, *J* = 9.3 Hz), 132.3 (d, *J* = 9.3 Hz), 131.80 (d, *J* = 1.4 Hz), 131.78 (d, *J* = 1.4 Hz), 127.50 (d, *J* = 12.5 Hz), 127.48 (d, *J* = 12.5 Hz), 117.8, 55.9 (d, *J* = 2.2 Hz), 42.1 (d, *J* = 5.1 Hz), 38.5 (d, *J* = 4.2 Hz), 29.5, 28.8, 26.6, 26.5, 26.4; HRMS Calcd for $C_{22}H_{29}NOP$ $[M + H]^+$: 354.19868; Found: 354.19835. $[\alpha]^{20}_D$ = –21 (*c* = 0.78, $CHCl_3$) for a 97.5:2.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 95:5 hexanes:*i*-PrOH, 0.6 mL/min, 220 nm): t_R of **S16**: 11 min (minor) and 14 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.3	50.004	1	10.8	2.631
2	15.5	49.996	2	14.3	97.369

(*R*,*E*)-*N*-(2-Methyl-1-(2-methylthiazol-4-yl)hexa-1,5-dien-3-yl)-*P*,*P*-diphenylphosphinic amide (1.21k, Table 1.7): The title compound is synthesized analogously to **1.21k** except for the following changes: 1) The aminophenol catalyst **1.19s** is employed as a catalyst instead of **1.19r**. 2) 20 mol % of NaO*t*-Bu is used in the reaction instead of 3 mol %. 3) Reaction time is six h. The product is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in 95:5 hexanes:triethylamine and eluted with 10 mL hexanes, 10 mL 1:1 hexanes:ethyl acetate, 15 mL diethyl ether, 6 mL ethyl acetate and 16 mL 5:1 ethyl acetate:MeOH) to afford **1.21k** (37.7 mg, 0.0923 mmol, 92% yield) as a pale yellow oil. IR (neat): 3357 (w, br), 3193 (w, br), 3076 (w), 3058 (w), 2966 (w), 2926 (w), 2871 (w), 1574 (w), 1437 (m), 1184 (s), 1121(m), 1108 (m), 952 (m), 910 (m), 723 (s), 694 (s), 525 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92–7.84 (4H, m), 7.40–7.37 (6H, m), 6.83 (1H, s), 6.30 (1H, s), 5.70 (1H, dddd, *J* = 17.1, 9.9, 7.2, 7.2 Hz), 5.14–5.06 (2H, m), 3.81 (1H, dddd, *J* = 9.4, 9.4, 6.6, 6.6 Hz), 3.16 (1H, dd, *J* = 9.5, 5.6 Hz), 2.69 (3H, s), 2.60–2.53 (1H, m), 2.50–2.43 (1H, m), 2.00 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 152.9, 139.9 (d, *J* = 5.0 Hz), 133.9, 133.1 (d, *J* = 127.6 Hz), 132.6 (d, *J* = 9.5 Hz), 132.4 (d, *J* = 131.1 Hz),

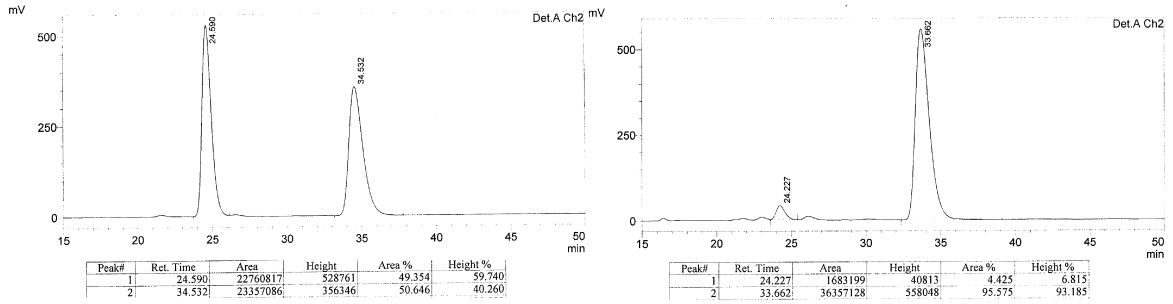
131.9 (d, J = 9.5 Hz), 131.9 (d, J = 2.8 Hz), 131.8 (d, J = 2.8 Hz), 128.6 (d, J = 12.6 Hz), 128.5 (d, J = 12.7 Hz), 120.2, 118.6, 115.7, 58.0, 40.4 (d, J = 4.3 Hz), 19.3, 15.5; HRMS Calcd for $C_{24}H_{26}N_2OPS_1$ $[M + H]^+$: 409.15034; Found: 409.15018. $[\alpha]^{20}_D$ = +94 (c = 0.45, $CHCl_3$) for a 95:5 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD, 86:14 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 25 min (minor) and 35 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	25.4	49.688	1	25.3	4.741
2	35.7	50.312	2	35.3	95.259

(*R*,*E*)-*N*-(4,4-Dideuterio-2-methyl-1-(2-methylthiazol-4-yl)hexa-1,5-dien-3-yl)-*P*,*P*-diphenylphosphinic amide (*d_2*–1.21k, Equation 2): The title compound is synthesized and purified analogously to **4o,** except 1,1-dideuterioallylboronic acid pinacol ester (***d_2*-1a**) is used as the nucleophile (contaminated with ~50% vinylboronic acid pinacol ester). The reaction proceeded to 85% conversion (based on 400 MHz ^{1}H NMR analysis and affords ***d_2*-4o** (24.5 mg, 0.0597 mmol, 60% yield) in 95:5 α:γ addition products (see above; determined by ^{2}H NMR) as yellow oil. The following analytical data is for α addition product α–***d_2*-4o**, unless otherwise noted. IR (neat): 3357 (w, br), 3193 (w, br),

3076 (w), 3058 (w), 2966 (w), 2926 (w), 2871 (w), 1574 (w), 1437 (m), 1184 (s), 1121(m) 1108 (m), 910 (m), 723 (s), 694 (s), 525 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.95–7.85 (4H, m), 7.51–7.36 (6H, m), 6.84 (1H, s), 6.31 (1H, s), 5.70 (1H, dd, *J* = 17.1, 10.1 Hz), 5.15–5.07 (2H, m), 3.79 (1H, app t, *J* = 9.6 Hz), 3.16 (1H, dd, *J* = 9.8, 5.6 Hz), 2.70 (3H, s), 2.60–2.53 (1H, m), 2.50–2.43 (γ-addition product; 0.17 H, m), 2.00 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 152.9, 139.9 (d, *J* = 5.1 Hz), 133.8, 133.0 (d, *J* = 127.7 Hz), 132.6 (d, *J* = 9.5 Hz), 132.4 (d, *J* = 131.1 Hz), 132.0 (d, *J* = 9.5 Hz), 132.0 (d, *J* = 2.9 Hz), 131.9 (d, *J* = 2.6 Hz), 128.6 (d, *J* = 12.6 Hz), 128.5 (d, *J* = 12.7 Hz), 120.2, 118.7, 115.7, 57.9, 40.4–39.2 (m), 19.4, 15.5; ^2H NMR (76 MHz, 9:1 $CHCl_3$:$CDCl_3$): δ 5.22–5.08 (γ-addition product; 0.09H, m), 2.51 (α-addition product; 2H, d, *J* = 6.1 Hz); HRMS Calcd for $C_{24}H_{24}D_2N_2OPS$ $[M + H]^+$: 411.16290; Found: 411.16232. $[\alpha]^{20}_D$ = +47 (*c* = 0.73, $CHCl_3$) for a 95:5 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 86:14 hexanes:*i*-PrOH, 0.5 mL/min, 254 nm): t_R: 25 min (minor) and 35 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	24.6	49.354	1	24.2	4.425
2	34.5	50.646	2	33.7	95.575

■ **Representative Procedure for Enantioselective Allyl Additions with**

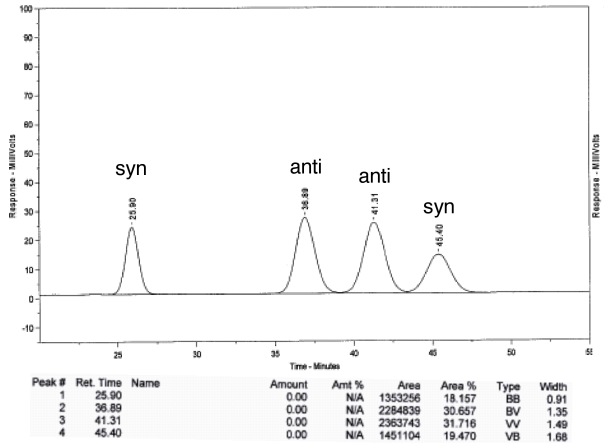
Enantiomerically Enriched Allylboronates (Table 1.11, Table 1.12): *Preparation of catalyst solution and allylboronate solution*: Under an atmosphere of nitrogen, aminophenol **1.19r** (6.1 mg, 0.02 mmol) is added to an oven-dried two-dram vial equipped with a stir bar followed by 1.0 mL of a stock solution of NaO*t*-Bu in toluene (9.6 mg, 0.010 mmol/6.0 mL) and the solution is allowed to stir at 22 ºC for ~10 minutes. In a separate oven-dried two-dram vial, allylboronate ***S*-1.33** (70.8 mg, 0.260. mmol) and MeOH (17.5 μL, 0.690. mmol) are dissolved in 700. μL of toluene to make a stock solution of ***S*-1.33** and MeOH.

An oven-dried one-dram vial equipped with a stir bar is charged with phenyl-substituted aldimine **1.15a** (15.3 mg, 50.0 μmol), 150. μL of toluene, and 200. μL of the prenominate stock solution of ***S*-1.33** (20 mg, 74 μmol) and MeOH (4.0 mg, 13 μmol). To this mixture is added 150. μL of the catalyst solution (described above) of **1.19r** (0.92 mg, 3.0 μmol) and NaO*t*-Bu (0.24 mg, 2.5 μmol) and a cap is attached to the vial and sealed with electrical tape. The clear and colorless solution is allowed to stir at 22 ºC for 18 hours during which time it becomes cloudy and white. The cap is removed and 3 mL of a saturated aqueous solution of $NaIO_4$ is added and the biphasic mixture is allowed to stir for 20 minutes. The aqueous layer is washed with ethyl acetate (4 x 4 mL), dried over Na_2SO_4, and concentrated *in vacuo* to provide a yellow solid. The homoallylamide product was purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in 95:5 hexanes:triethylamine and eluted with 10 mL hexanes, 10 mL 1:1 hexanes:diethyl ether, 30 mL 1:3 hexanes:diethyl ether, 35 mL diethyl ether, 30 mL 4:1 diethyl ether:ethyl acetate) to afford **1.35** (19.3 mg, 0.0427 mmol, 85% yield of a 85:15 ratio of diastereomers) as an off white solid, which is re-

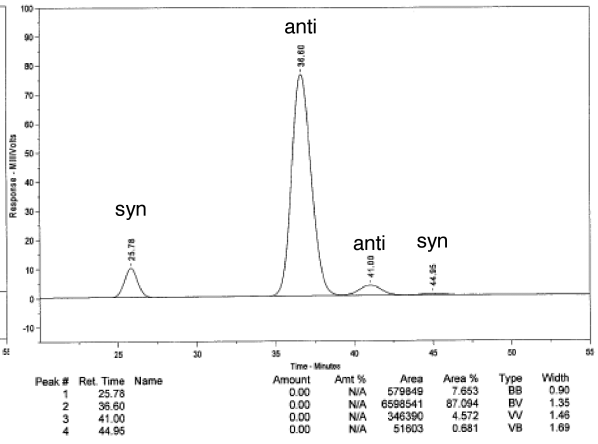
crystallized from CH_2Cl_2/hexanes (vapor diffusion, 22 ºC) to give 6.4 mg (0.014 mmol, 28% yield) of **1.35** as clear, colorless, needles suitable for X-ray crystallography in >20:1 dr and >99:1 e.r. This diastereo- and enantiomerically enriched product was used to obtain the data given below (excluding the HPLC chromatographs). The HPLC chromatograph of the authentic racemic material was obtained from a 60:40 ratio of anti:syn diastereomers (enriched by silica gel chromatography). The excess of the anti diastereomer allowed assignment of which peak corresponds to which diastereomer. The identity and absolute stereochemistry of the major enantiomer of the major diastereomer is determined by X-Ray crystallography.

***N*-((1*R*,2*R*)-2-Phenethyl-1-phenylbut-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (1.35, Equation 9)**: M.p. = 156–158 °C. IR (neat): 3228 (w, br), 3059 (w), 3027 (w), 2916 (w), 2857 (w), 1437 (w), 1187 (m), 1125 (m), 1109 (m), 1069 (m), 917 (m), 745 (m), 723 (m), 692 (s), 534 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.82–7.77 (2H, m), 7.64–7.59 (2H, m), 7.50–7.46 (1H, m), 7.40–7.33 (3H, m), 7.21–7.12 (8H, m), 7.04–7.02 (4H, m), 5.73 (1H, ddd, *J* = 17.5, 10.1, 9.1 Hz), 5.28 (1H, d, *J* = 10.3 Hz), 5.11 (1H, d, *J* = 17.1 Hz), 4.17 (1H, dd, *J* = 18.2, 8.0 Hz), 3.37 (1H, app t, *J* = 7.1 Hz), 2.62 (1H, ddd, *J* = 14.2, 9.4, 5.3 Hz), 2.50–2.43 (1H, m), 2.40–2.33 (1H, m), 1.76-1.68 (1H, m), 1.63–1.53 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6 (d, *J* = 3.1 Hz), 142.0, 138.8, 133.5 (d, *J* = 127.2 Hz), 132.7 (d, *J* = 9.7 Hz, only peak at 132.6 is visible, the other is overlapping), 132.1 (d, *J* = 130.7 Hz, only peak at 131.4 is visible, the other is overlapping), 131.9 (d, *J* = 2.6 Hz), 131.8 (d, *J* = 9.6 Hz), 131.6 (d, *J* = 2.8 Hz), 128.6 (d, *J* = 12.5 Hz), 128.6, 128.4, 128.2, 128.1 (d, *J* = 12.8 Hz), 127.4, 127.1, 125.8, 118.8, 58.1, 51.1 (d, *J* = 5.5 Hz), 33.3, 32.1; HRMS Calcd for $C_{30}H_{31}NOP$ $[M + H]^+$: 452.21433;

Found: 452.21249. $[\alpha]^{20}_{D}$ = +12 (c = 0.43, $CHCl_3$) for a >20:1 dr, >99:1 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AZ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R of **1.35** (anti diastereomer): 37 min (major) and 41 min (minor); t_R of **1.35** (syn diastereomer): 26 min (major) and 45 min (minor).

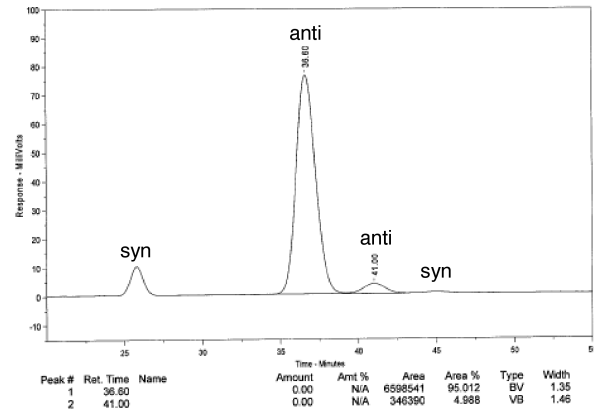


Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	25.90		0.00	N/A	1353256	18.157	BB	0.91
2	36.89		0.00	N/A	2284839	30.657	BV	1.35
3	41.31		0.00	N/A	2363743	31.716	VV	1.49
4	45.40		0.00	N/A	1451104	19.470	VB	1.68

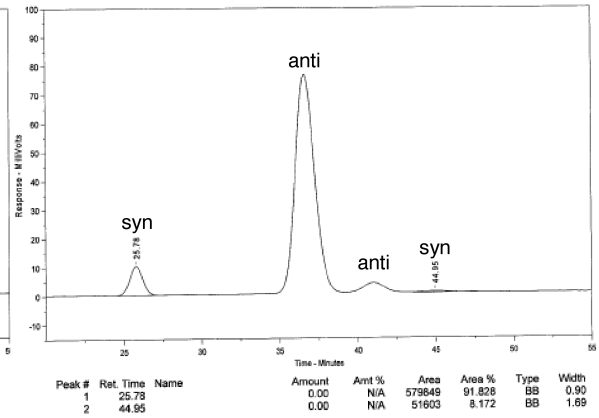


Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	25.78		0.00	N/A	579849	7.653	BB	0.90
2	36.60		0.00	N/A	6598541	87.094	BV	1.35
3	41.00		0.00	N/A	346390	4.572	VV	1.46
4	44.95		0.00	N/A	51603	0.681	VB	1.69

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1 (syn)	25.9	18.157	1 (syn)	25.8	7.653
2 (anti)	36.9	30.657	2 (anti)	36.6	87.094
3 (anti)	41.3	31.716	3 (anti)	41.0	4.572
4 (syn)	45.4	19.470	4 (syn)	45.0	0.681



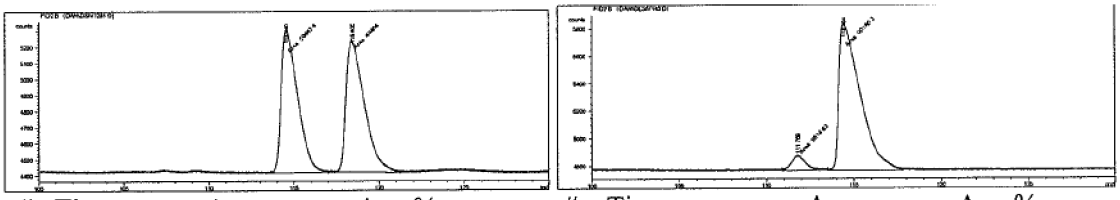
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	36.60		0.00	N/A	6598541	95.012	BV	1.35
2	41.00		0.00	N/A	346390	4.988	VB	1.46



Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	25.78		0.00	N/A	579849	91.828	BB	0.90
2	44.95		0.00	N/A	51603	8.172	BB	1.69

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1 (anti)	36.6	95.012	1 (syn)	25.8	91.828
2 (anti)	41.0	4.988	2 (syn)	45.0	8.172

To measure the enantiomeric purity of ***S*-1.33**, allylboronate ***S*-1.33** was oxidized by hydrogen peroxide to the corresponding alcohol. The enantiomeric purity of allylboronate ***S*-1.33** was determined by GLPC analysis in comparison with authentic racemic material (Betadex 120 column, 110 ºC, 15 psi).

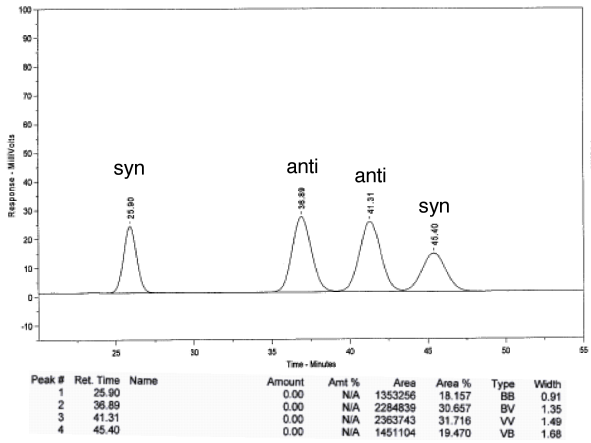


#	Time	Area	Area%
1	114.54	59663	49.690
2	118.40	66041	50.310

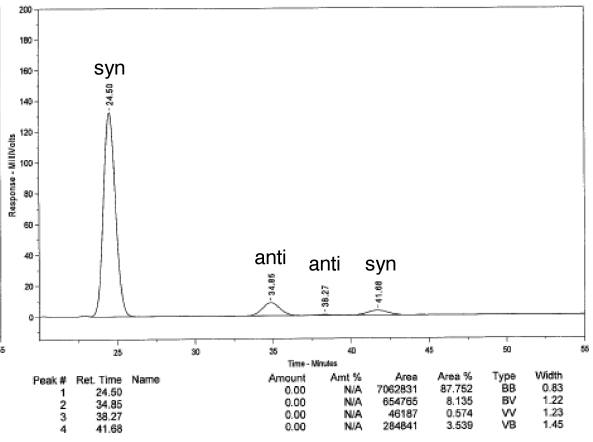
#	Time	Area	Area%
1	111.769	5814.6	6.057
2	114.434	90180.3	93.943

***N*-((1*R*,2*S*)-2-Phenethyl-1-phenylbut-3-en-1-yl)-*P*,*P*-diphenylphosphinic amide (1.34, Table 1.12)**: The title compound is purified analogously to **1.35** affording **1.34** (22.5 mg, 0.0498 mmol, >98 % yield of a 85:15 ratio of diastereomers) as a white solid. Th e resulting solid was recrystallized from CH_2Cl_2/hexanes (vapor diffusion, 22 ºC) to give 7.4 mg (0.016 mmol, 32% yield) of **1.34** as clear, colorless needles suitable for x-ray crystallography in >20:1 dr and >99:1 er. This diastereo- and enantiomerically enriched product was used to obtain the data given below (excluding the HPLC chromatographs). The identity (and absolute stereochemistry of the major enantiomer) of the major diastereomer is determined by X-Ray crystallography (see Part D of the Supplementary Information). M.p. = 161–163 °C. IR (neat): 3215 (w, br), 3056 (w), 3027 (w), 2912 (w), 2855 (w), 1494 (m), 1184 (m), 1122 (m), 1106 (m), 1083 (m), 912 (m), 749 (m), 691 (s),

531 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.84–7.79 (2H, m), 7.67–7.62 (2H, m), 7.51–7.47 (1H, m), 7.42–7.36 (3H, m), 7.26–7.20 (7H, m), 7.15–7.12 (1H, m), 7.07–7.00 (4H, m), 5.49 (1H, ddd, *J* = 17.3, 10.0, 10.0 Hz), 5.30–5.26 (2H, m), 4.22 (1H, ddd, *J* = 11.1, 11.1, 4.7 Hz), 3.67 (1H, dd, *J* = 10.7, 6.4 Hz), 2.68–2.61 (1H, m), 2.58–2.42 (2H, m), 1.76 (1H, dddd, *J* = 13.5, 9.9, 6.3, 3.6 Hz), 1.29–1.19 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3, 140.9 (d, *J* = 5.4 Hz), 137.6, 133.5 (d, *J* = 127.5 Hz, only peak at 134.1 is visible, the other is overlapping), 132.8 (d, *J* = 9.8 Hz, only peak at 132.7 is visible, the other is overlapping), 132.0 (d, *J* = 2.7 Hz), 131.9 (d, *J* = 131.7 Hz), 131.77 (d, *J* = 9.6 Hz), 131.78 (d, *J* = 2.8 Hz), 128.6 (d, *J* = 12.5 Hz), 128.5, 128.4, 128.3 (d, *J* = 12.8 Hz), 128.0, 127.8, 127.2, 125.9, 120.0, 58.0, 52.1 (d, *J* = 3.1 Hz), 34.2, 33.9; HRMS Calcd for $C_{30}H_{31}NOP$ $[M + H]^+$: 452.21433; Found: 452.21376. $[\alpha]^{20}_D$ = –16 (c = 0.20) for a >20:1 dr and >99:1 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material; see explanation of peak assignment in the analytical data for compound **1.35** (Chiracel AZ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R of **1.34** (major diastereomer): 25 min (major) and 42 min (minor); t_R of **1.34** (minor diastereomer): 35 min (major) and 38 min (minor).

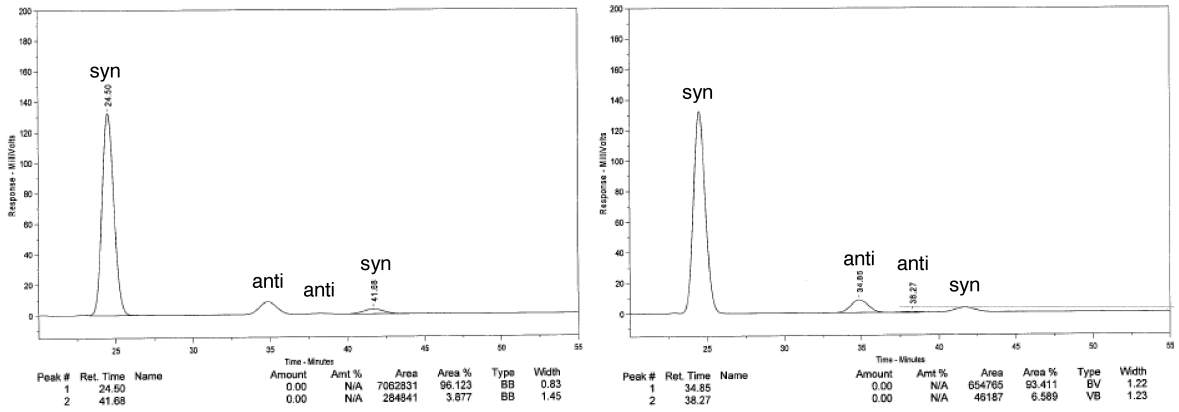


Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	25.90		0.00	N/A	1353256	18.157	BB	0.91
2	36.89		0.00	N/A	2284839	30.657	BV	1.35
3	41.31		0.00	N/A	2363743	31.716	VV	1.49
4	45.40		0.00	N/A	1451104	19.470	VB	1.68



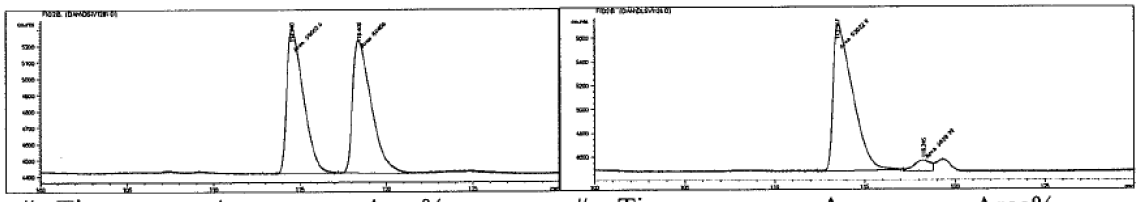
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	24.50		0.00	N/A	7062831	87.752	BB	0.83
2	34.85		0.00	N/A	654785	8.135	BV	1.22
3	38.27		0.00	N/A	46187	0.574	VV	1.23
4	41.68		0.00	N/A	284841	3.539	VB	1.45

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1 (syn)	25.9	18.157	1 (syn)	24.5	87.752
2 (anti)	36.9	30.657	2 (anti)	34.9	8.135
3 (anti)	41.3	31.716	3 (anti)	38.3	0.574
4 (syn)	45.4	19.470	4 (syn)	41.7	3.539



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1 (syn)	24.5	96.123	1 (anti)	34.9	93.411
2 (syn)	41.7	3.877	2 (anti)	38.3	6.589

To measure the enantiomeric purity of ***R*-1.33**, allylboronate ***R*-1.33** was oxidized by hydrogen peroxide to the corresponding alcohol. The enantiomeric purity of allylboronate ***R*-1.33** was determined by GLPC analysis in comparison with authentic racemic material (Betadex 120 column, 110 ºC, 15 psi).



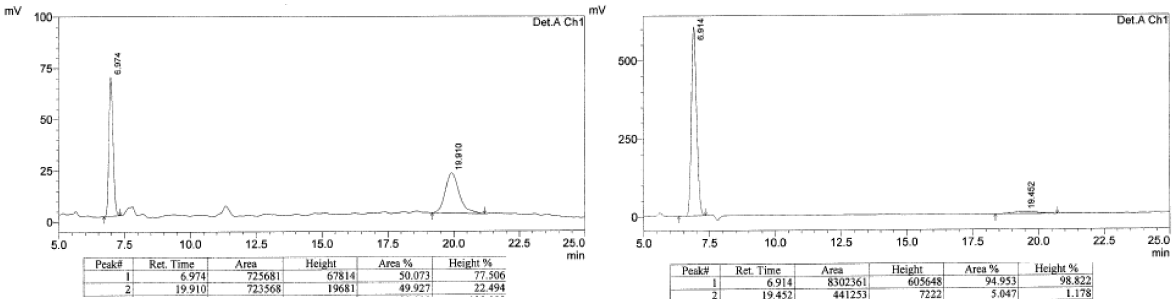
#	Time	Area	Area%
1	114.54	59663	49.690
2	118.40	66041	50.310

#	Time	Area	Area%
1	113.517	93000	95.398
2	118.245	4486.1	4.60

***N*-((1*S*,2*R*)-2-Cyclohexyl-2-methyl-1-phenylbut-3-en-1-yl)-*P*,*P*-diphenylphosphinic**

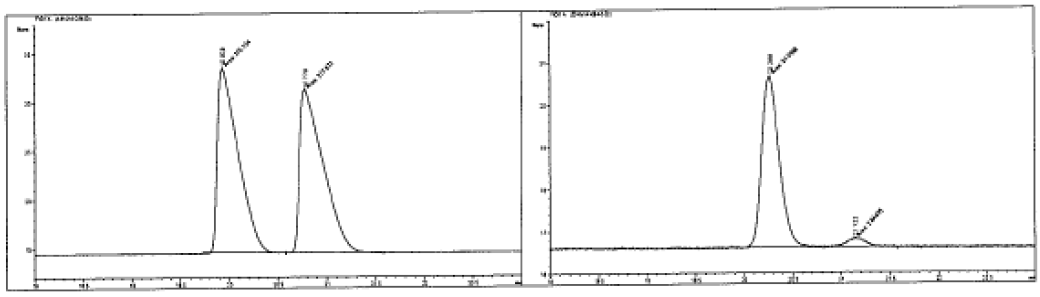
amide (1.32, Table 1.11): The title compound is synthesized in the manner identical to that used for the preparation of **1.35** (except utilizing $Zn(O\textit{t}\text{-Bu})_2$ instead of $NaO\textit{t}\text{-Bu}$). The homoallylamide **1.32** is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in 95:5 hexanes:triethylamine and eluted with 10 mL hexanes, 10 mL 1:1 hexanes:diethyl ether, 30 mL 1:3 hexanes:diethyl ether, 60 mL diethyl ether) to afford **1.32** (17.0 mg, 0.038 mmol, 76 % yield of isolated major diastereomer) as a white solid. Crystals suitable for X-ray crystallography were obtained by vapor diffusion from a diethyl ether/hexane solvent system at 22 ºC. The identity (and absolute stereochemistry of the major enantiomer) of the major diastereomer is determined by X-ray crystallography. M.p. = 137–139 °C. IR (neat): 3221 (w, br), 3058 (w), 2924 (s), 2851 (m), 1452 (m), 1184 (s), 1123 (s), 1108 (s), 1064 (m), 912 (m), 723 (s), 698 (s), 530 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79–7.74 (2H, m), 7.51–7.45 (3H, m), 7.41–7.38 (2H, m), 7.34–7.30 (1H, m), 7.23–7.20 (3H, m), 7.15 (2H, ddd, *J* = 7.7, 7.7, 3.2 Hz), 7.00–6.98 (2H, m), 5.70 (1H, dd, *J* = 17.7, 11.0 Hz), 5.27 (1H, dd, *J* = 10.9, 1.4 Hz), 5.13 (1H, dd, *J* = 17.7, 1.4 Hz), 4.17 (1H, app t, *J* = 11.2 Hz), 3.56 (1H, app t, *J* = 9.8 Hz), 1.81 (1H, d, *J* = 12.9 Hz), 1.67 (1H, d, *J* = 10.8 Hz), 1.60–1.53 (2H, m), 1.36 (1H, d, *J* = 6.9 Hz), 1.22 (3H, s), 1.10–0.67 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 141.9 (d, *J* = 3.3 Hz) 133.7 (d, *J* = 128.3 Hz), 132.8 (d, *J* = 9.9 Hz), 132.0 (d, *J* = 131.8 Hz), 131.83 (d, *J* = 3.1 Hz, only peak at 131.81 is visible, the other is overlapping), 131.79 (d, *J* = 9.4 Hz, only peak at 131.74 is visible, the other is overlapping), 131.5 (d, *J* = 2.8 Hz), 128.6 (d, *J* = 12.4 Hz), 128.4, 128.0 (d, *J* = 12.8 Hz), 127.7, 126.9, 115.9, 59.4, 48.5 (d, *J* = 3.8 Hz), 42.8, 29.1, 27.9, 27.1, 26.9, 26.6, 15.8; HRMS Calcd for $C_{29}H_{35}NOP$ $[M + H]^+$: 444.24563; Found: 444.24499. $[\alpha]^{20}_D$ = +8.9 (*c*

= 0.87, $CHCl_3$) for a 95:5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 90:10 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R of **1.32**: 7.0 min (major) and 20 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	7.0	50.073	1	6.9	94.953
2	19.9	49.927	2	19.5	5.047

To measure the enantiomeric purity of **1.31**, allylboronate **1.31** was oxidized by hydrogen peroxide to the corresponding alcohol. The enantiomeric purity of allylboronate **1.32** was determined by GLPC analysis in comparison with authentic racemic material (Chiral dex CD-BDM column, 140 ºC, 15 psi).



#	Time	Area	Area%	#	Time	Area	Area%
1	19.929	276.1	49.861	1	20.266	51.1	94.727
2	20.779	277.7	50.139	2	21.133	2.8	5.273

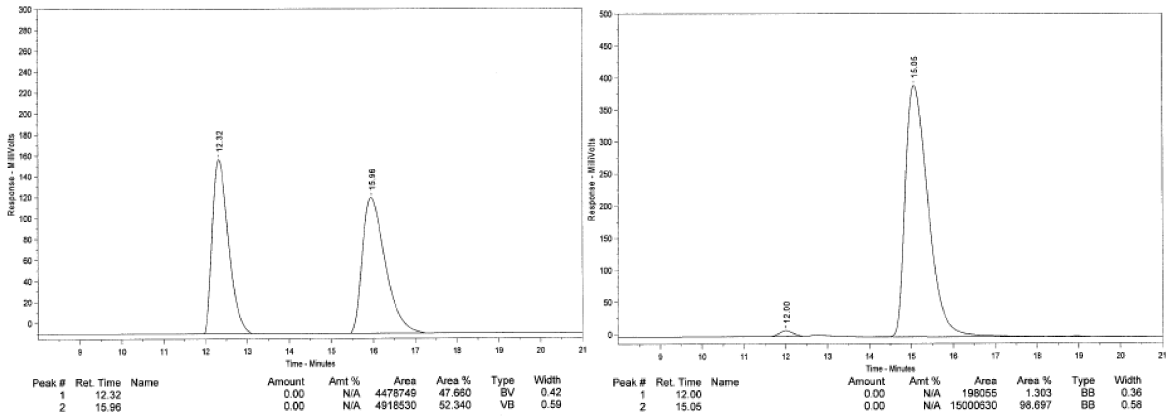
■ **Representative Procedure for *Small Scale* Catalytic Enantioselective Allyl Additions to Isatins (Figure 5a)**: Under an atmosphere of N_2, aminophenol **1.19r** (6.1 mg, 0.020 mmol) is added to an oven-dried two dram vial equipped with a stir bar followed by 2.0 mL of a stock solution of NaO*t*-Bu in toluene (7.7 mg, 0.080 mmol/8.0 mL). The vial is sealed with a cap (phenolic open top cap with a red PFTE/white silicone septa) and electrical tape, removed from the glovebox and allowed to stir under nitrogen at 22 ºC for ~10 minutes.

A separate vial equipped with a stir bar is charged with *N*-TBS-isatin **1.36i** (26.2 mg, 0.100 mmol)**,** sealed with a cap (phenolic open top cap with a red PFTE/white silicone septa) and electrical tape and purged with N_2. To this sealed vial under nitrogen is added toluene (0.95 mL), 50. uL of a catalyst solution [described above; **1.19r** (0.16 mg, 0.50 mmol) and NaO*t*-Bu (0.048 mg, 0.50 mmol)], MeOH (10 μL, 0.25 mmol) and allylboronic acid pinacol ester **1.6** (28 μL, 0.15 mmol) by syringe in the stated order. The clear yellow solution is allowed to stir at 22 ºC for 1.5 h during which time it becomes colorless, which signifies complete consumption of the highly pigmented starting material **1.36i**.

Removal of the TBS group: The cap is removed and the mixture is concentrated *in vacuo*. The resultant pale yellow oil is then dissolved in a solution of *p*-toluenesulfonic acid monohydrate (22.8 mg, 0.120 mmol) in methanol (0.5 mL, Fisher ACS grade). The mixture is allowed to stir at 22 ºC for 3 h after which time 1 mL of a saturated solution of aqueous $NaHCO_3$ is added drop-wise over one minute. Ethyl acetate (1 mL) is subsequently added, the organic and the aqueous layers are separated, which are then washed with ethyl acetate (3 x 1 mL). The combined organic layers are dried over

Na_2SO_4 and concentrated *in vacuo* to provide a white solid that is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in hexanes. The off-white solid residue is dry loaded on silica gel and eluted with 10 mL 4:1 hexanes:ethyl acetate, 20 mL 2:1 hexanes:ethyl acetate, 20 mL 1:1 hexanes:ethyl acetate) to afford **1.39a** (17.5 mg, 0.0925 mmol, 98% yield) as a white solid. Crystals suitable for X-ray crystallography were grown by slow evaporation from methanol at 22 ºC.

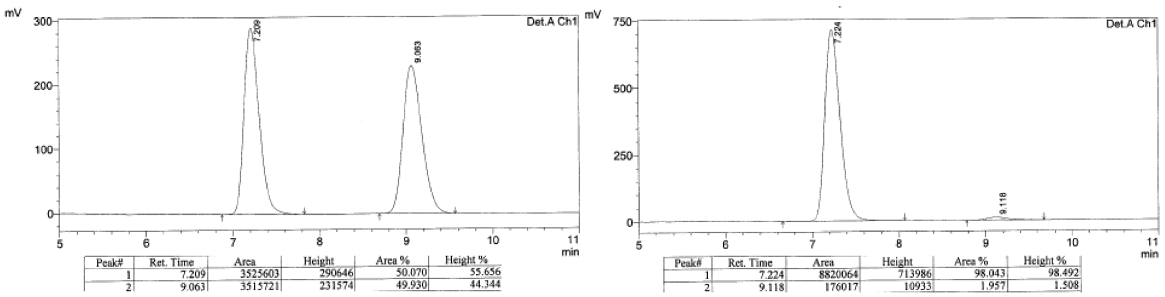
(*R*)-3-Allyl-3-hydroxyindolin-2-one (**1.39a, Equation 15**): The analytical data are fully consistent with those reported previously.[142] ^{1}H NMR (400 MHz, CD_3OD): δ 7.36 (1H, d, J = 7.2 Hz), 7.26 (1H, t, J = 8.5 Hz), 7.07 (1H, t, J = 7.4 Hz), 6.89 (1H, d, J = 7.7 Hz) 5.54 (1H, app dq, J = 16.7, 8.1 Hz), 5.05–4.98 (2H, m), 2.76–2.59 (2H, m); HRMS Calcd for $C_{11}H_{12}N_1O_2$ $[M + H]^+$: 190.08680; Found: 190.08650. $[\alpha]^{20}_D$ = +11 (c = 1.3, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 12 min (minor) and 15 min (major).



(142) Sano, D.; Nagata, K.; Itoh, T. *Org. Lett.* **2008**, *10*, 1593–1595.

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	12.3	47.660	1	12.0	1.303
2	16.0	52.340	2	15.1	98.697

(*R*)-3-Allyl-1-(*tert*-butyldimethylsilyl)-3-hydroxyindolin-2-one (1.36i, Table 1.15): To obtain the *N*-TBS protected hydroxyl-oxindole, after concentration *in vacuo*, the resultant pale yellow oil can be purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted with 10 mL dichloromethane followed by 30 mL 20:1 dichloromethane:diethyl ether) to afford **1.39i** (30.4 mg, 0.100 mmol, >98% yield) as pale yellow oil. IR (neat): 3401 (w, br), 2953 (w), 2929 (w), 2858 (w), 1701 (s), 1613 (m), 1465 (s), 1255 (s), 1171 (s), 1105 (m), 945 (m), 824 (s), 732 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (1H, dd, *J* = 7.4, 1.4 Hz), 7.22 (1H, td, *J* = 7.8, 1.5 Hz), 7.05 (1H, td, *J* = 7.5, 0.8 Hz), 6.99 (1H, d, *J* = 8.0 Hz), 5.54 (1H, dddd, *J* = 16.9, 10.1, 8.5, 6.2 Hz), 5.10–5.04 (2H, m), 2.96 (1H, s), 2.72–2.57 (2H, m), 0.99 (9H, s), 0.51 (3H, s), 0.50 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 145.8, 131.6, 130.9, 129.4, 124.4, 122.7, 120.3, 113.2, 76.3, 43.9, 26.6, 19.8, –3.1, –3.3; HRMS Calcd for $C_{17}H_{26}NO_2Si$ $[M + H]^+$: 304.17328; Found: 304.17280. $[\alpha]^{20}_D$ = +24.2 (*c* = 1.5, $CHCl_3$) for a 94:6 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 7 min (major) and 9 min (minor).

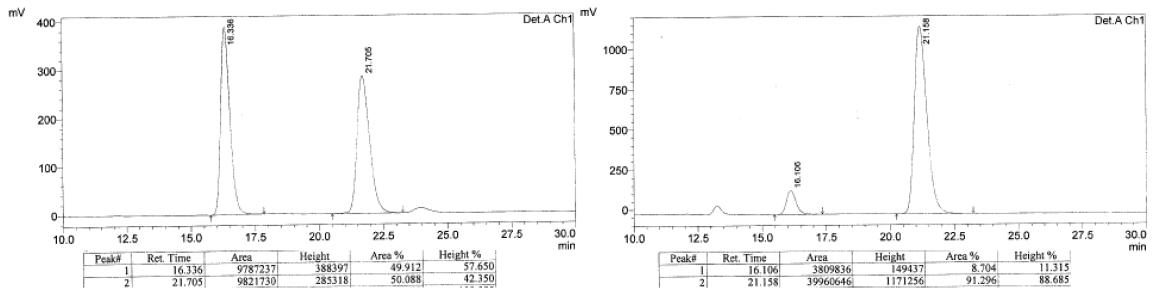


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	7.2	50.070	1	7.2	98.043
2	9.1	49.930	2	9.1	1.957

(*R*)-3-Allyl-4,6-dibromo-3-hydroxyindolin-2-one (**1.39l, Equation 16**): The enantioselective allyl addition to SEM-isatin **1.36k** is carried out following the representative procedure for aminophenol catalyzed enantioselective allyl additions to isatins. The procedure for removal of SEM group is as follows. After 2.0 h, the mixture of the enantioselective allyl addition turns from yellow to colorless (signifying complete consumption of highly pigmented **1.36k**), the cap is removed and the reaction mixture is concentrated *in vacuo*. The resultant pale yellow oil is transferred to a two-dram vial, sealed with a septum and purged with nitrogen. A separate oven dried one-dram vial equipped with a stir bar is charged with $MgBr_2 \bullet Et_2O$ (96.8 mg, 0.375 mmol), sealed with a cap (phenolic open top cap with a red PFTE/white silicone septa) and electrical tape, and removed from the glovebox. The unpurified 3-allyl-3-hydroxy oxindole **1.39l** is transferred through a syringe to the vial containing $MgBr_2 \bullet Et_2O$ using 3 x 300 uL of dichloromethane. The mixture is allowed to stir under nitrogen at 22 ºC for 60 h during which time it becomes a tan slurry. The cap is removed and the tan slurry is dissolved in methanol and passed through a short plug of Celite®; the plug is washed with methanol (15 mL) and the combined solution is concentrated *in vacuo* to afford a tan solid. The

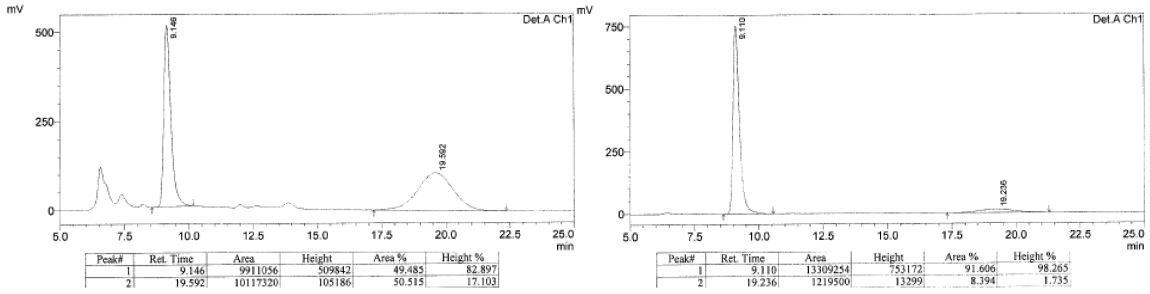
resulting solid is dissolved in 1 mL of methanol and 2 mL of a solution of saturated aqueous $NaHCO_3$, and the cloudy light pink solution is allowed to stir open to the air at 22 ºC for five h. Ethyl acetate (2 mL) is added and the layers separate. The aqueous layer is extracted with 3 x 2 mL of ethyl acetate and the combined organic layers are dried over Na_2SO_4 and concentrated *in vacuo* to afford a light tan solid. The hydroxyoxindole product is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted with 15 mL dichloromethane followed by 10 mL 9:1 dichloromethane:diethyl ether, 10 mL 8:1 dichloromethane:diethyl ether, and 30 mL 4:1 dichloromethane:diethyl ether), affording **1.39l** (14.9 mg, 0.0429 mmol, 86% yield) as a white solid. The analytical data are fully consistent with those reported previously.[143] IR (neat): 3368 (m, br), 3169 (w, br), 2923 (w, br), 1703 (s), 1605 (s), 1572 (s), 1429 (m), 1364 (m), 1334 (m), 1300 (m), 1175 (m), 1086 (m), 1074 (m), 944 (m), 928 (m), 840 (s), 785 (m), 738 (m), 673 (s) cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 7.38 (1H, s), 7.02 (1H, s), 5.39–5.28 (1H, m), 5.09–5.05 (1H, m), 4.97–4.94 (1H, m), 3.26–3.21 (1H, m), 2.72–2.67 (1H, m), 3.24–3.19 (1H, m), 2.92 (1H, br s), 2.84–2.79 (1H, m), 0.91 (2H, t, J = 8.0 Hz), –0.02 (9H, s); HRMS Calcd for $C_{11}H_{10}NO_2Br_2$ $[M + H]^+$: 347.90578; Found: 347.90587. $[\alpha]^{20}_D = -10$ (c = 0.64, CH_3OH) for a 91.5:8.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 86:14 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 16 min (minor) and 21 min (major).

(143) Cao, Z.-Y.; Zhang, Y.; Ji, C.-B.; Zhou, J. *Org. Lett.* **2011**, *13*, 6398–6401.



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.3	49.912	1	16.1	8.704
2	21.7	50.088	2	21.2	91.296

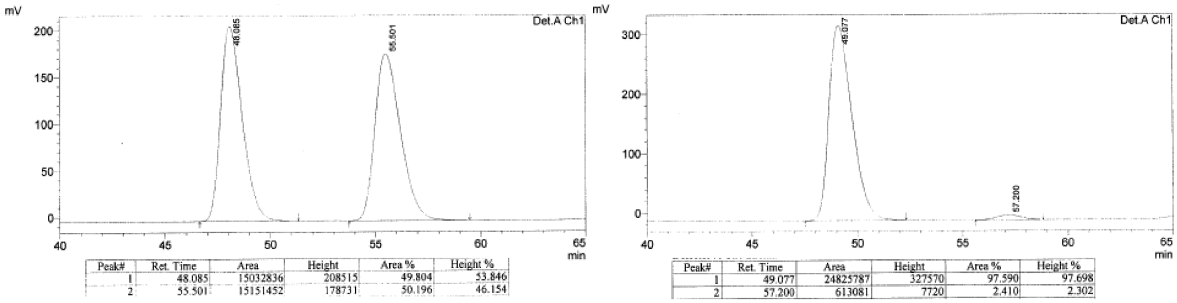
(*R*)-3-Allyl-4,6-dibromo-3-hydroxy-1-((2-(trimethylsilyl)ethoxy)methyl)indolin-2-one (1.39k, able 1.15): If one wishes to obtain the *N*-SEM-protected hydroxyl-oxindole, then after concentration *in vacuo*, purify the resultant yellow oil by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted with 40 mL dichloromethane) to afford **1.39k** (23.0 mg, 0.0481 mmol, 96% yield) as a clear, colorless oil. IR (neat): 3400 (w, br), 3082 (w), 2953 (w), 2923 (w), 2895 (w), 1723 (m), 1597 (s), 1571 (m), 1249 (m), 1077 (s, br), 1010 (m), 922 (m), 857 (m), 831 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (1H, s), 7.16 (1H, s), 5.34 (1H, dddd, J = 17.0, 17.0, 8.4, 8.4 Hz), 5.16–5.10 (2H, m), 5.00–4.97 (2H, m), 3.56–3.46 (2H, m), 3.24–3.19 (1H, m), 2.92 (1H, br s), 2.84–2.79 (1H, m), 0.91 (2H, t, J = 8.0 Hz), –0.02 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 145.0, 129.9, 129.6, 126.2, 124.2, 121.0, 120.0, 112.9, 78.1, 70.0, 66.6, 40.1, 17.9, –1.3; HRMS Calcd for $C_{18}H_{24}NO_3NaSiBr_2$ $[M + Na]^+$: 497.97062; Found: 497.97090. $[\alpha]^{20}_D$ = +5.6 (c = 1.1, $CHCl_3$) for a 91.5:8.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 95:5 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 9 min (major) and 20 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	9.1	49.485	1	9.1	91.606
2	19.6	50.515	2	19.2	8.394

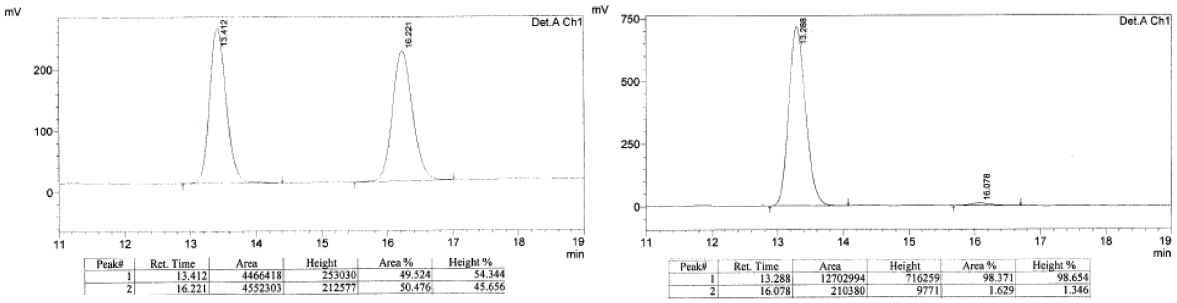
(*R*)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one (1.39c, Table 1.15): 1.39c is purified by silica gel chromatography (10 mm diamter column slurry packed with 2.5 g of silica gel in hexanes and eluted successively with 10 mL hexanes, 10 mL 6:1 hexanes:ethyl acetate, and 20 mL 4:1 hexanes:ethyl acetate) to afford **1.39c** (25.1 mg, 0.090 mmol, 90% yield) as a white solid. The analytical data are fully consistent with those reported previously.[144] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (1H, d, J = 7.3 Hz), 7.30–7.21 (5H, m), 7.19–7.15 (1H, m), 7.03 (1H, app t, J = 7.5 Hz), 5.60 (1H, dddd, J = 16.5, 10.1, 8.5, 6.3 Hz), 5.14–5.06 (2H, m), 4.98 (1H, d, J = 15.7 Hz), 4.69 (1H, d, J = 15.7 Hz), 3.27 (1H, br s), 2.82–2.77 (1H, m), 2.71–2.66 (1H, m); HRMS Calcd for $C_{18}H_{18}NO_2$ $[M + H]^+$: 280.13375; Found: 280.13317. $[\alpha]^{20}_D$ = +15.0 (c = 1.26, $CHCl_3$) for a 97.5:2.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 97.5:2.5 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 49 min (major) and 57 min (minor).

(144) Itoh, J.; Han, S. B.; Krische, M. J. *Angew. Chem. Int. Ed.* **2009**, *48*, 6313–6316.



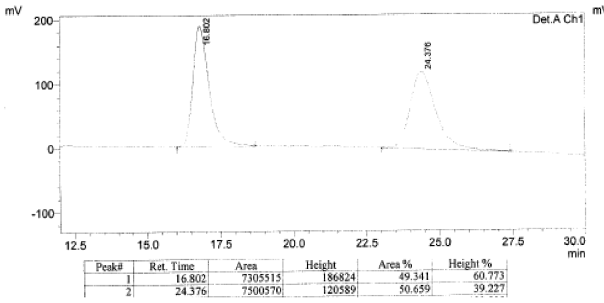
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	48.1	49.804	1	49.1	97.590
2	55.5	50.196	2	57.2	2.410

(*R*)-3-Allyl-1-benzyl-3-hydroxy-5-methylindolin-2-one (1.39d, Table 1.15): 1.39d is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in hexanes and eluted successively with 10 mL hexanes, 10 mL 6:1 hexanes:ethyl acetate, and 20 mL 4:1 hexanes:ethyl acetate) to afford **1.39d** (24.5 mg, 0.084 mmol, 84% yield) as an off-white solid. The analytical data are fully consistent with those reported previously.[144] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.22 (6H, m), 6.99 (1H, d, J = 7.9 Hz), 6.57 (1H, d, J = 8.0 Hz), 5.69–5.58 (1H, m), 5.18–5.09 (2H, m), 4.99 (1H, d, J = 15.7 Hz), 4.70 (1H, d, J = 15.7 Hz), 3.18 (1H, br s), 2.83–2.78 (1H, m), 2.73–2.68 (1H, m), 2.31 (3H, s); HRMS Calcd for $C_{19}H_{20}NO_2$ $[M + H]^+$: 294.14940; Found: 294.14905. $[\alpha]^{20}_D$ = +5.1 (c = 0.95, $CHCl_3$) for a 98.5:1.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 13 min (major) and 16 min (minor).

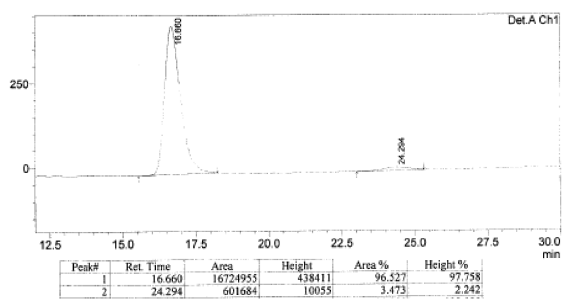


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.4	49.524	1	13.3	98.654
2	16.2	50.476	2	16.1	1.346

(*R*)-3-Allyl-1-benzyl-3-hydroxy-5-methoxyindolin-2-one (1.39e, Table 1.15): 1.39e is purified by silica gel chromatography (10 mm diamter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted successively with 10 mL dichloromethane followed by 30 mL 4:1 dichloromethane:ethyl acetate) to afford **1.39e** (29.5 mg, 0.095 mmol, 95% yield) as an clear, yellow oil. The analytical data are fully consistent with those reported previously.[144] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.22 (5H, m), 7.01 (1H, d, J = 2.5 Hz), 6.71 (1H, dd, J = 8.5, 2.6 Hz), 6.57 (1H, d, J = 8.5 Hz), 5.62 (1H, dddd, J = 16.8, 9.9, 8.5, 6.3 Hz), 5.17–5.08 (2H, m), 4.97 (1H, d, J = 15.7), 4.68 (1H, d, J = 15.7), 3.75 (3H, s), 3.39 (1H, br s), 2.83–2.78 (1H, m), 2.73–2.67 (1H, m); HRMS Calcd for $C_{19}H_{20}NO_3$ $[M + H]^+$: 310.14432; Found: 310.14467. $[\alpha]^{20}_D$ = +5.87 (c = 1.17, $CHCl_3$) for a 97:3 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 16 min (major) and 24 min (minor).



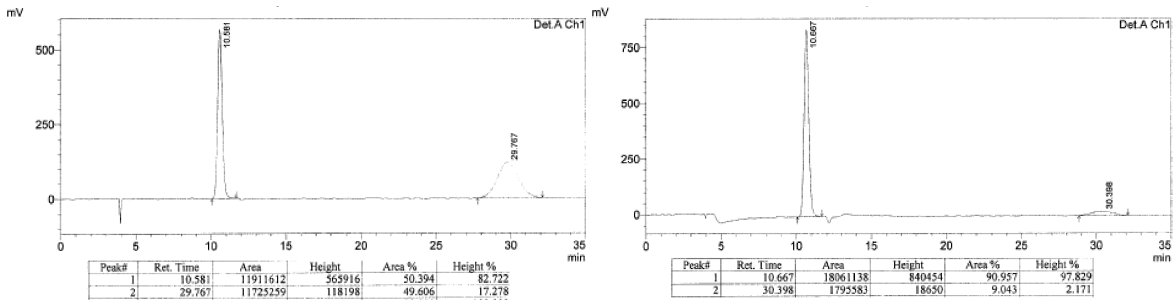
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.802	7305515	186824	49.341	60.773
2	24.376	7500570	120589	50.659	39.227



Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.660	16724955	438411	96.527	97.758
2	24.294	601684	10055	3.473	2.242

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.8	49.341	1	16.7	96.527
2	24.4	50.659	2	24.3	3.473

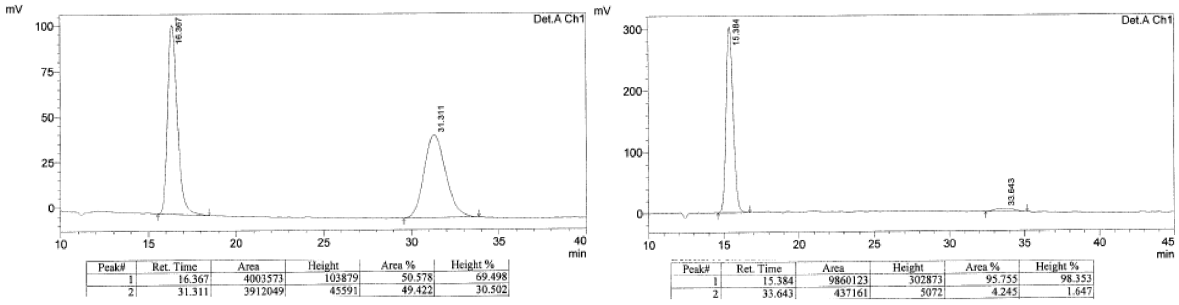
(*R*)-3-Allyl-1-benzyl-4,7-dichloro-3-hydroxyindolin-2-one (1.39f, Table 1.15): 1.39f is purified by silica gel chromatography (10 mm diamter column slurry packed with 2.5 g of silica gel in hexanes and eluted successively with 10 mL hexanes, 20 mL 9:1 hexanes:ethyl acetate, and 15 mL 5:1 hexanes:ethyl acetate) to afford **1.39f** (31.3 mg, 0.090 mmol, 90% yield) as a white solid. mp = 107-109 ºC. IR (neat): 3068(w, br), 2949 (m, br), 2866 (w), 1615 (w), 1451 (w), 1247 (w), 1247 (m), 1112 (m), 990 (w), 816 (s), 780 (m), 727 (s), 697 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.13 (5H, m), 7.13 (1H, d, J = 8.8 Hz), 6.96 (1H, d, J = 8.8 Hz), 5.45–5.29 (1H, m), 5.29–5.11 (3H, m), 5.02 (1H, d, J = 10.1 Hz), 3.27–3.22 (3H, m), 2.96–2.91 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 140.5, 136.8, 133.3, 130.5, 129.7, 128.7, 128.4, 127.4, 126.6, 125.2, 121.1, 114.5, 76.8 (overlaps with $CDCl_3$), 45.1, 40.4; HRMS Calcd for $C_{18}H_{16}Cl_2N_1O_2$ $[M + H]^+$: 348.05581; Found: 348.05632. $[\alpha]^{20}_D$ = +13 (c = 0.76, $CHCl_3$) for a 91:9 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 11 min (major) and 30 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	10.6	50.394	1	10.7	90.957
2	29.8	49.606	2	30.4	9.043

(*R*)-1-Benzyl-3-hydroxy-3-(2-methylallyl)indolin-2-one (1.40, Table 1.15): The title compound is synthesized in the same manner as described for **1.39c** except for the following changes: 1) Reaction time is one h. 2) Allylboronate **1.22a** is employed as the nucleophile instead of allylboronate **1.6** 3) The catalytic enantioselective allyl addition process is quenched with 3 mL of a solution of saturated aqueous $NaIO_4$ (to remove excess pinacol) and allowed to stir for 14 h at 22 ºC. The aqueous layer is washed with ethyl acetate (4 x 4 mL), dried over Na_2SO_4, and concentrated *in vacuo* to provide yellow oil. The product is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted with 34 mL dichloromethane followed by 26 mL 9:1 dichloromethane:ethyl acetate), affording **1.40** (28.7 mg, 0.0976 mmol, 98% yield) as a white solid. M.p. = 52–54 ºC. IR (neat): 3399 (w, br), 3366 (w, br), 1692 (s), 1614 (m), 1466 (m), 1350 (m), 1196 (m), 991 (m), 756 (s), 727 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (1H, d, J = 7.3 Hz), 7.31–7.22 (5H, m), 7.20 (1H, t, J = 7.7 Hz), 7.06 (1H, t, J = 7.5 Hz), 6.69 (1H, d, J = 7.7 Hz), 5.02 and

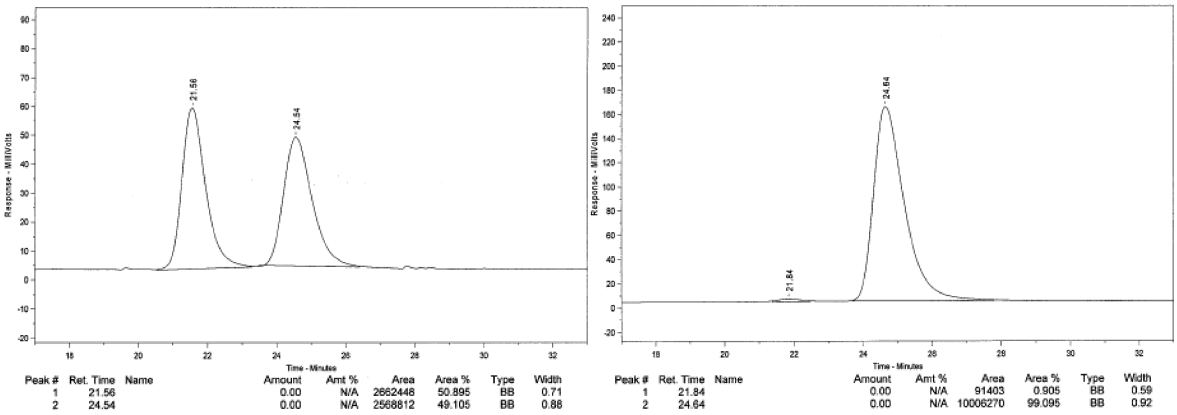
4.72 (2H, ABq, J_{AB} = 15.7 Hz), 4.79 (1H, s), 4.68 (1H, s), 2.93 (1H, s), 2.77 (2H, s), 1.50 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.0, 142.9, 139.1, 135.5, 129.9, 129.8, 128.9, 127.8, 127.4, 124.6, 123.1, 116.5, 109.6, 76.5, 46.3, 44.0, 24.1; HRMS Calcd for $C_{19}H_{20}NO_2$ $[M + H]^+$: 294.14940; Found: 294.14930. $[\alpha]^{20}_D$ = +22 (c = 1.3, $CHCl_3$) for a 96:4 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 15 min (major) and 34 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.4	50.578	1	15.4	95.755
2	31.3	49.422	2	33.6	4.245

(*R*)-3-Allyl-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one (1.39g, Table 1.15): The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted successively with 15 mL dichloromethane, 10 mL 8:1 dichloromethane:diethyl ether, and 10 mL 6:1 dichloromethane:diethyl ether) to afford **1.39g** (30.7 mg, 0.099 mmol, >98% yield) as a clear, colorless oil. The spectroscopic data match those reported previously.[144] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (1H, d, J = 7.3 Hz), 7.22–7.18 (3H, m), 7.05 (1H, t, J = 7.5 Hz), 6.82 (2H, d, J = 8.5 Hz), 6.72 (1H, d, J = 7.8 Hz), 5.67–5.57 (1H, m), 5.16–5.07

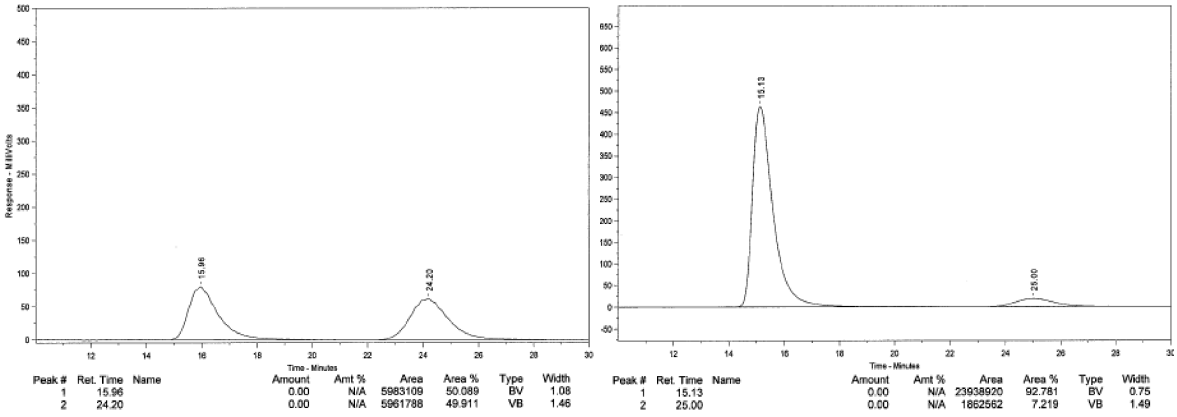
(2H, m), 4.93 (1H, d, J = 15.5 Hz), 4.66 (1H, d, J = 15.5 Hz), 3.76 (3H, s), 3.21 (br, s), 2.83–2.78 (1H, m), 2.72–2.67 (1H, m); HRMS Calcd for $C_{19}H_{20}N_1O_3$ $[M + H]^+$: 310.14432; Found: 310.14458. $[\alpha]^{20}_D$ = +15.5 (c = 1.46, $CHCl_3$) for a 99:1 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 22 min (minor) and 25 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	21.6	50.895	1	21.8	0.905
2	24.5	49.105	2	24.6	99.095

(*R*)-3-Allyl-4,6-dibromo-3-hydroxy-1-(4-methoxybenzyl)indolin-2-one (1.39h, Table 1.15): The titular compound is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted successively with 15 mL dichloromethane, 10 mL 3:1 hexanes:diethyl ether, and 30 mL 2:1 hexanes:diethyl ether) to afford **1.39h** (20.1 mg, 0.043 mmol, 86% yield) as a white solid. mp = 102–104 ºC. IR (neat): 3349 (w, br), 2919 (w), 1707 (s), 1600 (m), 1574 (w), 1511 (m), 1440 (m), 1418 (m), 1352 (m), 1282 (m), 1175 (m), 1087 (m), 1044 (m), 991 (m), 832 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34 (1H, s), 7.17 (2H, d, J = 8.5 Hz), 6.85

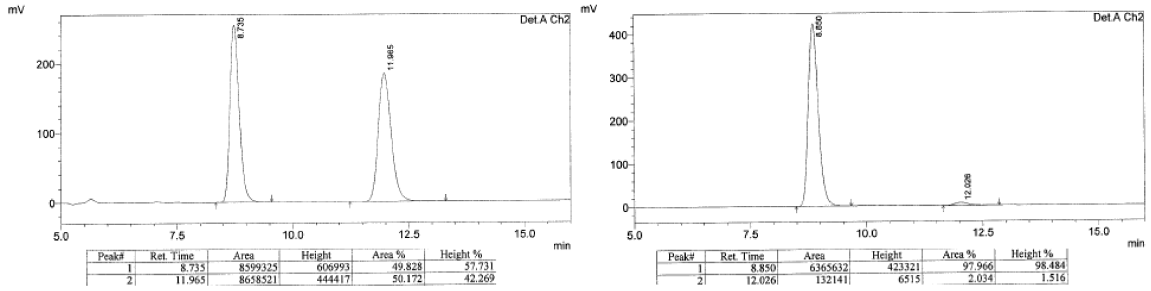
(2H, d, J = 8.6 Hz), 6.78 (1H, s), 5.41–5.30 (1H, m), 5.14 (1H, d, J = 16.9 Hz), 4.99 (1H, d, J = 10.0 Hz), 4.90 (1H, d, J = 15.5 Hz), 4.61 (1H, d, J = 15.5 Hz) 3.79 (3H, s), 3.23 (1H, dd, J = 12.0, 6.6 Hz), 2.91–2.84 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 159.5, 145.8, 129.7, 129.4, 128.8, 126.6, 126.5, 123.9, 121.1, 120.0, 114.5, 112.1, 77.6, 55.4, 43.7, 40.3; HRMS Calcd for $C_{19}H_{18}Br_2N_1O_3$ $[M + H]^+$: 465.96534; Found: 465.96445. $[\alpha]^{20}_D$ = -11 (c = 0.67, $CHCl_3$) for a 93:7 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 15.1 min (major) and 25.0 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.0	50.089	1	15.1	92.781
2	24.2	49.911	2	25.0	7.219

(*R*)-3-Allyl-1-(*tert*-butyldimethylsilyl)-3-hydroxy-5-methoxyindolin-2-one (1.39j, Table 1.15): The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in dichloromethane and eluted with 10 mL dichloromethane, 15 mL 30:1 dichloromethane:diethyl ether, 30 mL 20:1

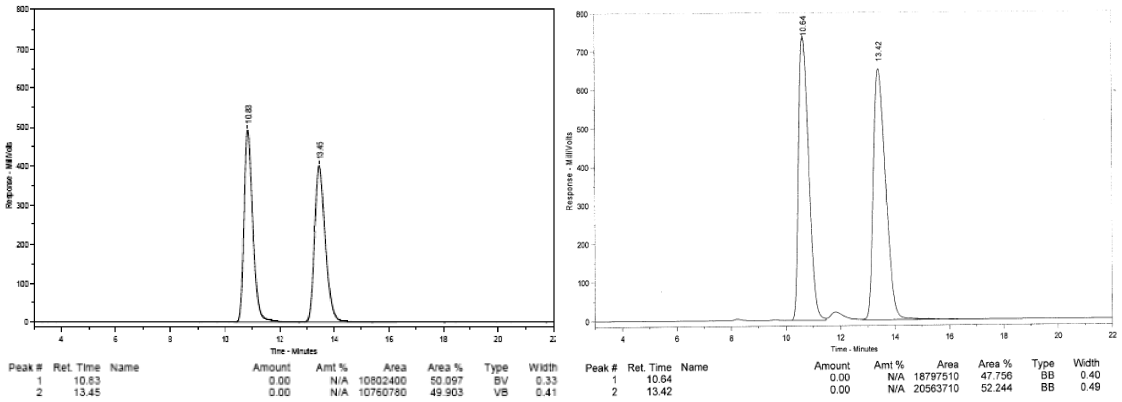
dichloromethane:diethyl ether), affording **1.39j** (31.2 mg, 0.0932 mmol, 93% yield) as a pale orange oil. IR (neat): 3400 (w, br), 2953 (w), 2930 (w), 2858 (w), 1699 (s), 1594 (m), 1482 (s), 1255 (s), 1197 (s), 1120 (w), 1081 (m), 911 (m), 840 (s), 790 (m), 730 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.96 (1H, d, *J* = 2.8 Hz), 6.89 (1H, d, *J* = 8.7 Hz), 6.75 (1H, dd, *J* = 8.7, 2.7 Hz), 5.54 (1H, dddd, *J* = 16.9, 10.1, 9.0, 6.1 Hz), 5.11–5.07 (2H, m), 3.79 (3H, s), 2.99 (1H, s), 2.70–2.56 (2H, m), 0.98 (9H, s), 0.50 (3H, s), 0.48 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.2, 155.8, 138.9, 132.8, 130.8, 120.3, 114.5, 113.7, 110.7, 76.7, 55.9, 44.0, 26.6, 19.8, –3.2, –3.4; HRMS Calcd for $C_{18}H_{28}NO_3Si$ $[M + H]^+$: 334.18384; Found: 334.18318. $[\alpha]^{20}_D$ = +11 (*c* = 1.3, $CHCl_3$) for a 98:2 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 254 nm): t_R: 9 min (major) and 12 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	8.7	49.828	1	8.9	97.966
2	12.0	50.172	2	12.0	2.034

■ **Aminophenol-Catalyzed Enantioselective Allyl Additions to *o*-Thiomethylaniline-derived Aldimines: 2-(methylthio)-*N*-(1-phenylbut-3-en-1-yl)aniline (1.29)** is synthesized analogously to **1.15b** and purified by column chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in 95:5 hexanes:triethylamine and

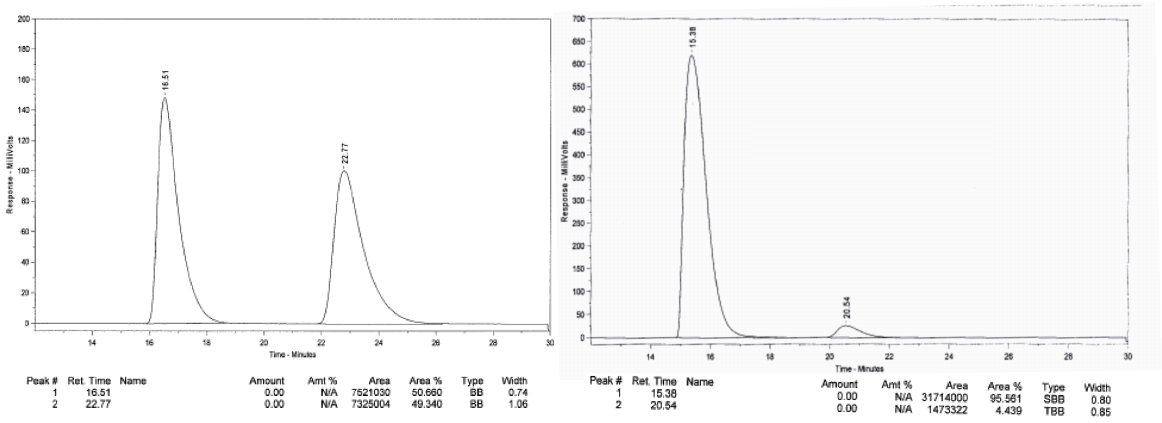
eluted with 50 mL hexanes and 20 mL 50:1 hexanes:diethyl ether) to afford 21 mg (0.078 mmol, 78% yield) of **1.29** as a yellow oil. The analytical data are fully consistent with those reported previously.[141] The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): 11 min (minor) and 13 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	10.8 min	50.097	1	10.6 min	47.756
2	13.5 min	49.903	2	13.4 min	52.244

■ **Representative Example of Utilization of DBU as the Base Instead of NaO*t*-Bu for the Enantioselective Allyl Addition to Aldimine *1.15a***: The reaction is performed following the representative procedure for *small scale* catalytic enantioselective allyl additions to aryl-, heteroaryl-, alkenyl-, and alkynyl *N*-diphenylphosphinoyl imines except for the following changes: 1) 2.5 mol % DBU is used (instead of 2.5 mol % NaO*t*-Bu) 2) Reaction time is 75 min. The conversion to desired product is 83% (judged by 400 MHz ^{1}H NMR spectra of unpurified reaction mixture vs. an internal standard of 9-methylanthracene) which is lower than the >98% conversion obtained when using the same amount of NaO*t*-Bu. The enantiomeric purity was determined by HPLC analysis in

comparison with authentic racemic material (Chiracel OD, 92:8 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R of **1.17a**: 15 min (major) and 21 min (minor).



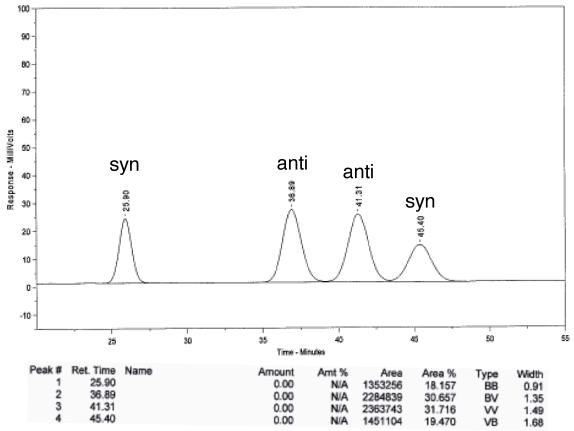
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.5 min	50.660	1	15.4 min	95.561
2	22.8 min	49.340	2	20.5 min	4.439

■■ PROOF of ABSOLUTE STEREOCHEMISTRY of PRODUCTS

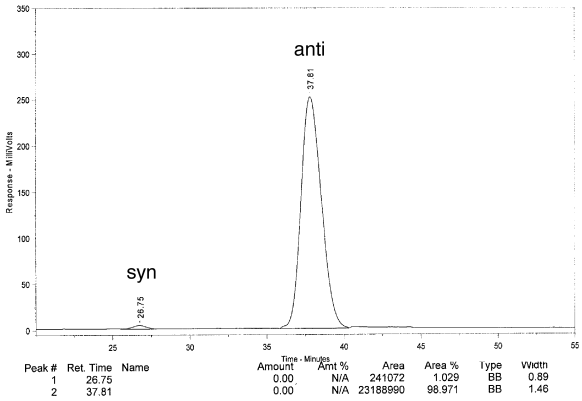
Absolute configuration of homoallylamide 1.17j: Please see X-ray crystallographic data.

Absolute configuration of homoallylamide 1.20f: Please see Part D X-ray crystallographic data. For the catalytic enantioselective allyl additions to aldimines, it should be noted that the absolute stereochemical identities of the major product enantiomers are inferred from the obtained X-ray crystal structures of homoallylic amides **1.17j** and **1.20f**.

Absolute configuration of homoallylamide 1.35: Please see X-ray crystallographic data. The absolute stereochemistry of the obtained crystal was further verified by HPLC analysis in comparison with authentic racemic material



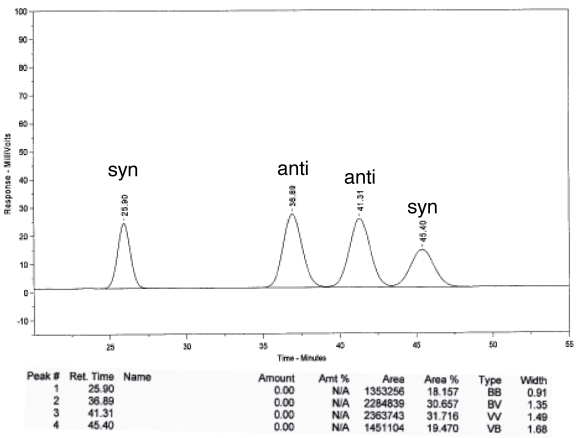
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	25.90		0.00	N/A	1353256	18.157	BB	0.91
2	36.89		0.00	N/A	2284839	30.657	BV	1.35
3	41.31		0.00	N/A	2363743	31.716	VV	1.49
4	45.40		0.00	N/A	1451104	19.470	VB	1.68



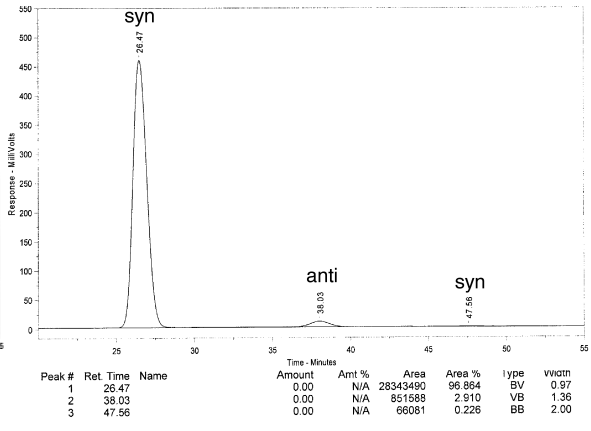
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	26.75		0.00	N/A	241072	1.029	BB	0.89
2	37.81		0.00	N/A	23188990	98.971	BB	1.46

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1 (syn)	25.9	18.157	1 (syn)	26.8	1.029
2 (anti)	36.9	30.657	2 (anti)	37.8	98.971
3 (anti)	41.3	31.716	3 (anti)	-	-
4 (syn)	45.4	19.470	4 (syn)	-	-

Absolute configuration of homoallylamide 1.34: Please see X-ray crystallographic data. The absolute stereochemistry of the obtained crystal was further verified by HPLC analysis in comparison with authentic racemic material.

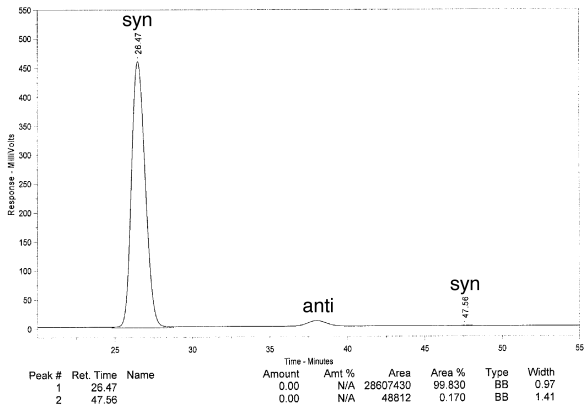


Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	25.90		0.00	N/A	1353256	18.157	BB	0.91
2	36.89		0.00	N/A	2284839	30.657	BV	1.35
3	41.31		0.00	N/A	2363743	31.716	VV	1.49
4	45.40		0.00	N/A	1451104	19.470	VB	1.68

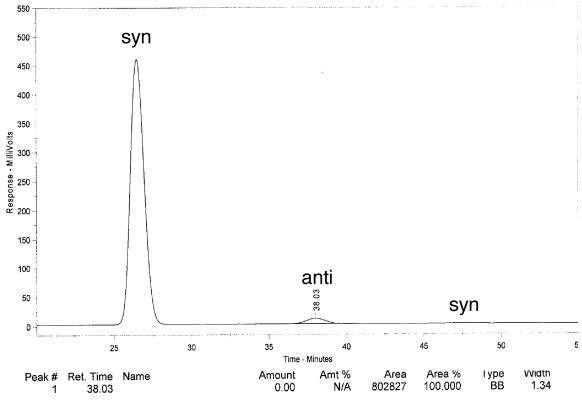


Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	26.47		0.00	N/A	28343490	96.864	BV	0.97
2	38.03		0.00	N/A	851588	2.910	VB	1.36
3	47.56		0.00	N/A	66081	0.226	BB	2.00

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1 (syn)	25.9	18.157	1 (syn)	26.5	96.864
2 (anti)	36.9	30.657	2 (anti)	38.0	2.910
3 (anti)	41.3	31.716	3 (anti)	-	-
4 (syn)	45.4	19.470	4 (syn)	47.6	0.226



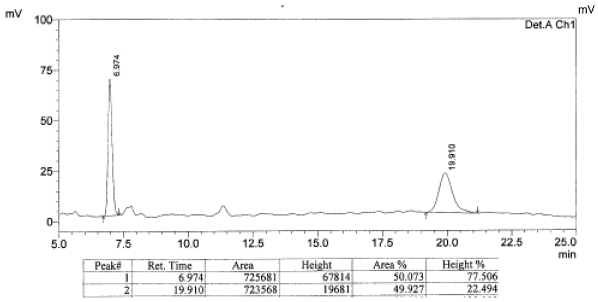
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	26.47		0.00	N/A	28607430	99.830	BB	0.97
2	47.56		0.00	N/A	48812	0.170	BB	1.41



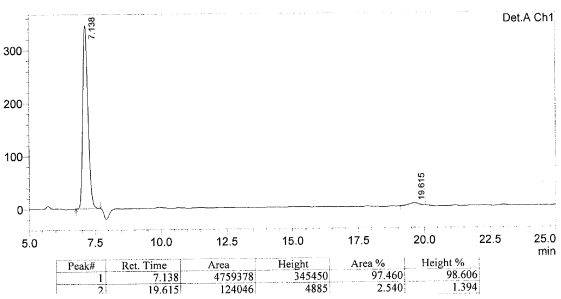
Peak #	Ret. Time	Name	Amount	Amt %	Area	Area %	Type	Width
1	38.03		0.00	N/A	802827	100.000	BB	1.34

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1 (syn)	26.5	99.830	1 (anti)	38.0	100.000
2 (syn)	41.7	0.170	2 (anti)	-	-

Absolute configuration of homoallylamide 1.32: Please see X-ray crystallographic data. The absolute stereochemistry the obtained crystal was further verified by HPLC analysis in comparison with authentic racemic material.



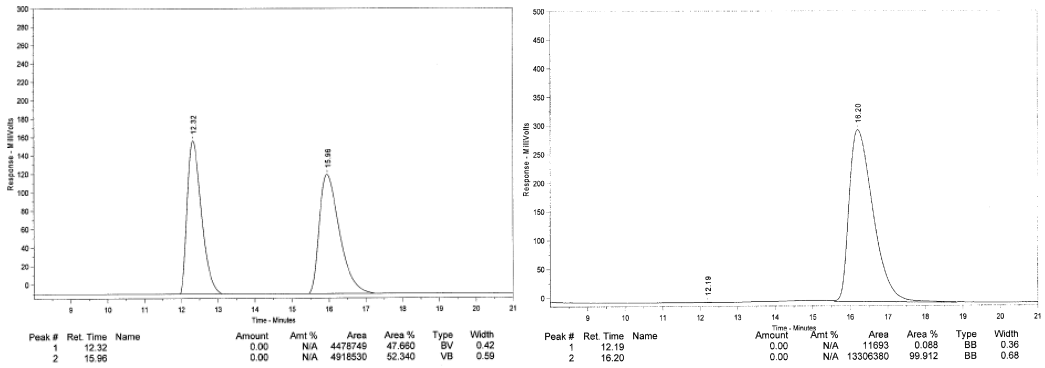
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.974	725681	67814	50.073	77.506
2	19.910	723568	19681	49.927	22.494



Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.138	4759378	345450	97.460	98.606
2	19.615	124046	4885	2.540	1.394

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	7.0	50.073	1	7.1	97.460
2	19.9	49.927	2	19.6	2.540

Absolute configuration of homoallylic alcohol 1.39a: For the aminophenol catalyzed enantioselective allyl additions to isatin, please note that the absolute stereochemistries of the major product enantiomers are inferred from the obtained X-ray crystal structure of homoallylic alcohol **1.39a.** The absolute stereochemistry of the obtained crystal was also verified by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 90:10 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R of: 12 min (minor) and 16 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	12.3	47.660	1	12.2	0.088
2	16.0	52.340	2	16.2	99.912

■ Investigation of the Level of Brønsted Acidity of the Complex Derived from Allylboron Reagent (1.6) and MeOH

General Information Specific to the Following Study (for further information; see above). All vials, stir bars, and NMR tubes were oven-dried (135 ºC) overnight prior to use. The ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (d_8-toluene: δ 7.09 ppm).

Preparation of samples for NMR spectroscopy: In a nitrogen-filled glovebox, aminophenol **1.19r** (7.7 mg, 25 μmol) is weighed into a one-dram vial and dissolved in 700. μL of d_8-toluene. The solution is transferred to an NMR tube and sealed with a cap and Teflon tape; it is then used to obtain **Spectrum 1**.

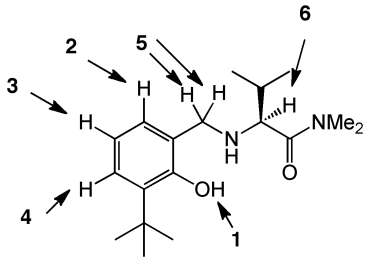
A separate one-dram vial equipped with a stir bar is charged with **1.19r** (30.8 mg, 0.101 mmol) and 2.8 mL of a stock solution of NaO*t*-Bu in d_8-toluene (9.6 mg, 0.10 mmol NaO*t*-Bu/2.8 mL d_8-toluene) to afford a translucent solution. A 700. μL aliquot of this solution (containing NaO*t*-Bu [2.4 mg, 25 μmol] and aminophenol [7.7 mg, 25 μmol]) is added to an NMR tube and sealed with a cap and Teflon tape; it is then used to obtain **Spectrum 2**.

A second 700. μL aliquot is transferred to a one-dram vial containing allylboronic acid pinacol ester (10. μL, 53 μmol) and this mixture is then used to obtain **Spectrum 3**.

Methanol (10. μL, 250 μmol) is added to the remaining 1.4 mL of NaO*t*-Bu and **1.19r** mixture and a 700. μL aliquot (containing NaO*t*-Bu [2.4 mg, 25 μmol], aminophenol **1.19r** [7.7 mg, 25 μmol], and methanol [5.0 μL, 130 μmol)] of the resultant solution is added to an NMR tube and sealed with a cap and Teflon tape; it is then used to obtain **Spectrum 4**.

Allylboronic acid pinacol ester (10. μL, 53 μmol) is added to the remaining solution (containing NaO*t*-Bu [2.4 mg, 25 μmol], aminophenol **1.19r** [7.7 mg, 25 μmol], and methanol [5.0 μL, 130 μmol]), which results in formation of a white precipitate, causing the toluene solution to become cloudy. The latter solution is added to an NMR tube and sealed with a cap and Teflon tape; it is then used to obtain **Spectrum 5**.

Spectrum 1 (^{1}H NMR, 400 MHz, d_8-toluene): Aminophenol **2g**



1: 11.11 ppm (1H, br s)

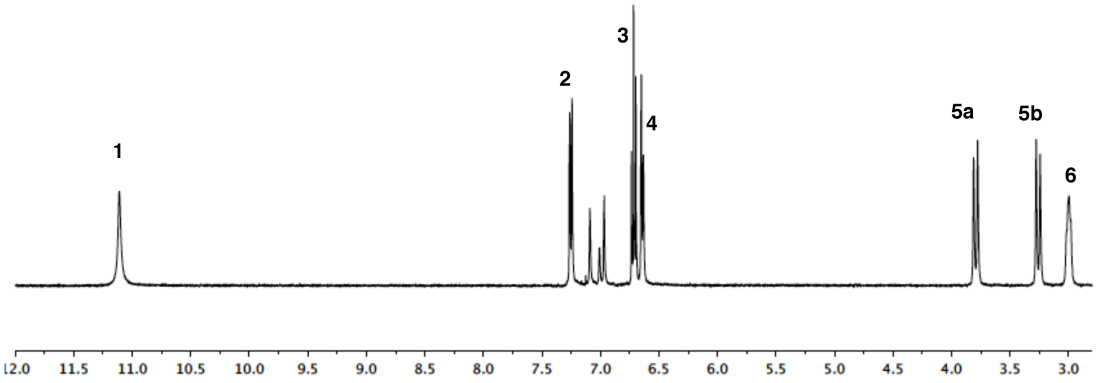
2: 7.27–7.24 ppm (1H, m)

3: 6.72 ppm (1H, t, J = 7.6 Hz)

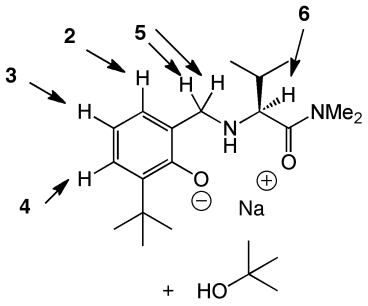
4: 6.65–6.63 ppm (1H, m)

5a, 5b: 3.79, 3.26 ppm (2H, ABq, J_{AB} = 13.5 Hz)

6: 3.02–2.98 ppm (1H, br m)



Spectrum 2 (^{1}H NMR, 400 MHz, d_8-toluene): Aminophenol **2g** (25 μmol, 1 equiv.) and NaO*t*-Bu (25 μmol, 1 equiv.)



2: 7.35–7.33 ppm (1H, m)

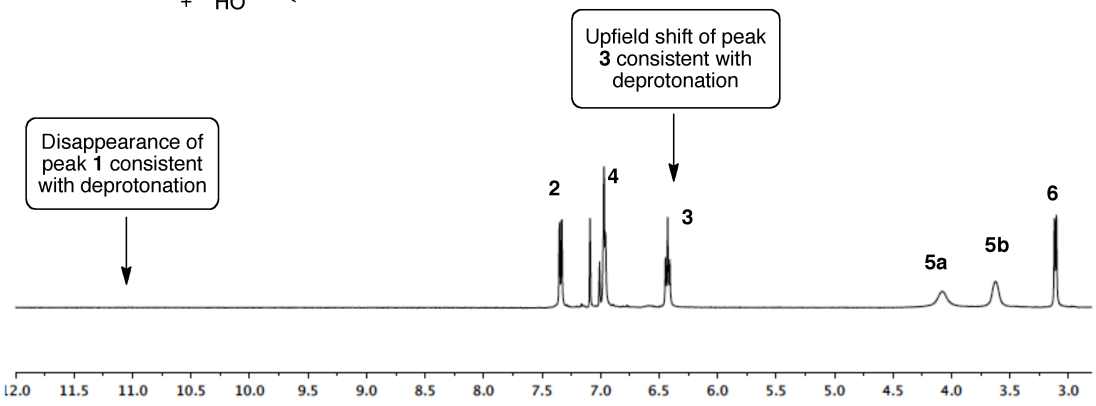
3: 6.43 ppm (1H, t, J = 7.3 Hz)

4: 6.98–6.96 ppm (1H, m)

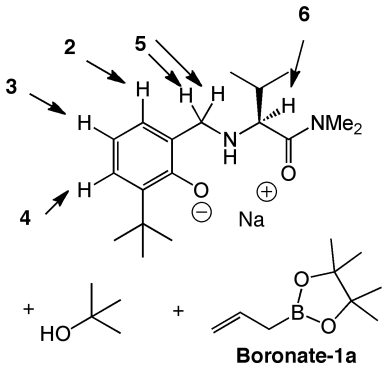
5a: 4.09 ppm (1H, br s)

5b: 3.63 ppm (1H, br s)

6: 3.11 ppm (1H, d, J = 6.4 Hz)



Spectrum 3 (^{1}H NMR, 400 MHz, d_8-toluene): Aminophenol **2g** (25 μmol, 1 equiv.), NaO*t*-Bu (25 μmol, 1 equiv.), and Allylboronate **1a** (53 μmol, 2 equiv.)



2: 7.32 ppm (1H, d, J = 7.4 Hz)

3: 6.42–6.38 ppm (1H, br m)

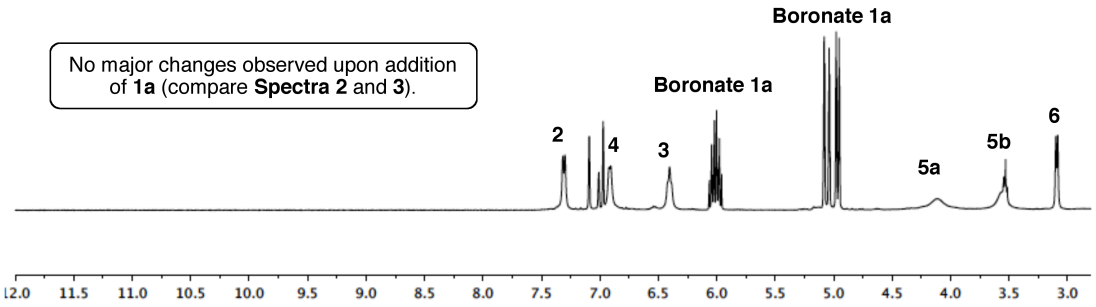
4: 6.92 ppm (1H, br s)

5a: 4.12 ppm (1H, br s)

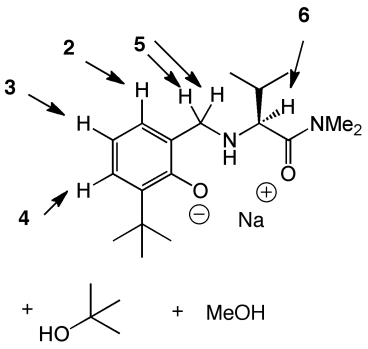
5b: 3.80–3.66 ppm (1H, br m [overlaps with new unknown peak].

6: 3.09 ppm (1H, d, J = 6.3 Hz)

No major changes observed upon addition of **1a** (compare **Spectra 2** and **3**).



Spectrum 4 (^{1}H NMR, 400 MHz, d_8-toluene): Aminophenol **2g** (25 μmol, 1 equiv.), NaO*t*-Bu (25 μmol, 1 equiv.), and MeOH (130 μmol, 5 equiv.)



2: 7.40–7.35 ppm (1H, m)

3: 6.52 ppm (1H, t, J = 7.4 Hz)

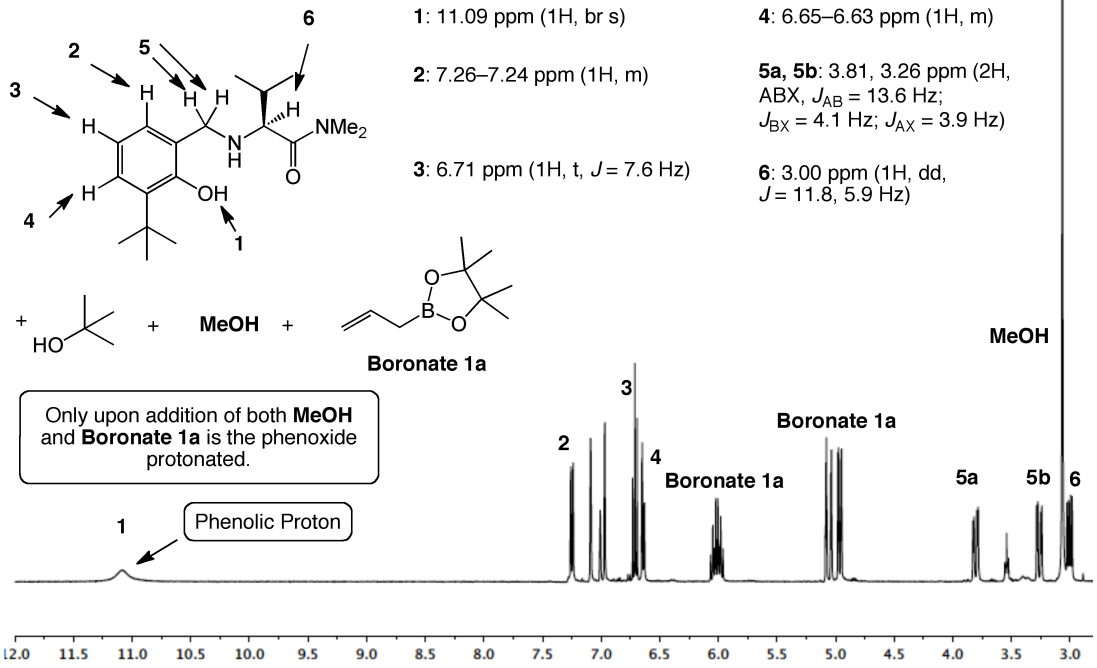
4: 6.97–6.95 ppm (1H, m)

5a, 5b: 3.80, 3.66 ppm (2H, ABq, J_{AB} = 10.9 Hz)

6: 3.14 ppm (1H, d, J = 6.5 Hz)

Absence of peak **1** and chemical shifts of peaks **2-4** indicate addition of MeOH does not protonate the phenoxide of **2g**.

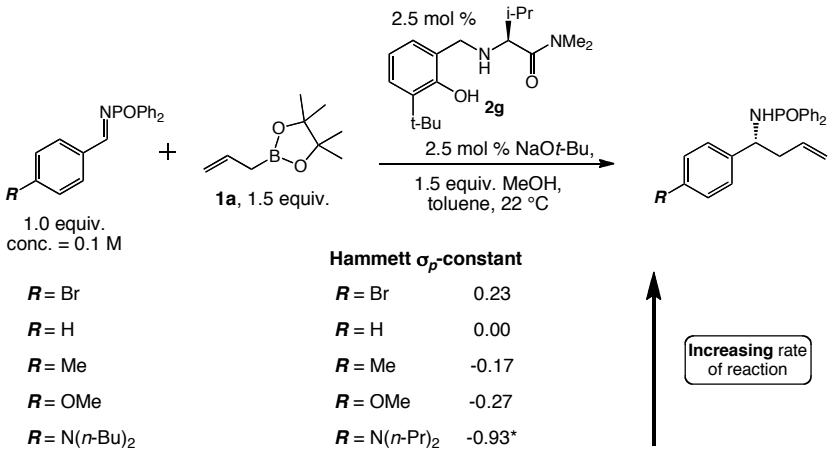
Spectrum 5 (^{1}H NMR, 400 MHz, d_8-toluene): Aminophenol **2g** (25 μmol, 1 equiv.), NaO*t*-Bu (25 μmol, 1 equiv.), Allylboronate **1a** (53 μmol, 2 equiv.), and MeOH (130 μmol, 5 equiv.)



■ Generation of a Hammett Plot for the Aminophenol Catalyzed Enantioselective Allyl Addition to a Series of Aryl-Substituted Aldimines

The electronic effect of the aryl substituent on the reaction rate of the aminophenol catalyzed enantioselective allyl addition to aryl-substituted aldimines was determined by React-IR measurements of conversion of imine [%] as a function of time [min] (Scheme S1).

Scheme S1: Reaction Conditions for the Enantioselective Allylation of Imines Applied in React-IR Measurements to Generate the Hammett Plot



*The σ_p-constant for -N(*n*-Pr)$_2$ has been used for -N(*n*-Bu)$_2$.

General Procedure (for further information; see above): The preparation of stock solutions of reagents (allylboronate **1.6**, MeOH, aminophenol **1.19r**, and NaO*t*-Bu) and weighing of imines were performed in a nitrogen-filled glovebox. All vials and stir bars were oven-dried (135 ºC) overnight prior to use. Rubber septa and caps were oven-dried (60 ºC) overnight prior to use. An 8 mL vial equipped with a stir bar is charged with the desired aldimine (0.200 mmol) and the vial is sealed with a cap. To prepare the stock solution of allylboronate **1.6**, a 4 mL vial is charged with **1.6** (0.450 mL, 2.40 mmol) and toluene (3.55 mL) and sealed with a cap containing a teflon septum. To prepare the stock solution of MeOH, a 4 mL vial is charged with MeOH (0.120 mL, 3.00 mmol) and toluene (3.88 mL) and sealed with a cap containing a teflon septum. To prepare the stock solution of aminophenol **1.19r**, 4 mL vial is charged with aminophenol **1.19r** (15.3 mg, 0.0499 mmol) and toluene (4.00 mL) and sealed with a cap containing a Teflon septum. To prepare the stock solution of NaO*t*-Bu, a 4 mL vial is charged with NaO*t*-Bu (19.2 mg, 0.200 mmol) and toluene (4.00 mL). The NaO*t*-Bu solution is diluted further by charging a 4 mL vial with toluene (3.00 mL) and 1.00 mL of the original stock solution.

The vial was sealed with a cap containing a teflon septum. The prepared solutions and vials containing the imines were taken out of the glovebox and stored in a desiccator for the duration of React-IR measurements.

React-IR measurements: Measurements were performed on a ReactIR iC10 instrument equipped with a 6.3 mm AgX DiComp Fiber probe. Spectra were recorded from 2000 cm^{-1} to 650 cm^{-1} at standard resolution (8 cm^{-1}) in 15 s intervals. The vial containing imine is equipped with a 14/20 rubber septum with a 4 mm diameter hole and attached to the probe, which had been dried with a heat gun (T_{max} = 200 °C). The rubber septum is further sealed with electrical tape. Toluene (0.3 mL) is added with a syringe, followed by the addition of the stock solutions of allylboronate **1.6** (0.50 mL) and MeOH (0.40 mL). After 3 min, the reaction is started by the simultaneous addition of the solutions of aminophenol **1.19r** (0.4 mL) and NaO*t*-Bu (0.4 mL).

Data processing: The decrease in concentration of imine was monitored as a function of time [min] (Figures 1a and 1b). The following IR absorption frequencies characteristic of the imines in this study were used: 834–822 cm^{-1} for R = Br, 836–824 cm^{-1} for R = H, 842–830 cm^{-1} for R = Me, 835–823 cm^{-1} for R = OMe, and 1592–1580 cm^{-1} for R = N(*n*-Bu)$_2$. The intensities were calibrated as following: the difference between the intensities at the start of the reaction and the intensities at the end of the reaction (i.e. when no further change was observed in the concentration of imine) was set to the conversion [%] determined by 400 MHz ^{1}H NMR (100% except for 95% in the case of R = N(*n*-Bu)$_2$).

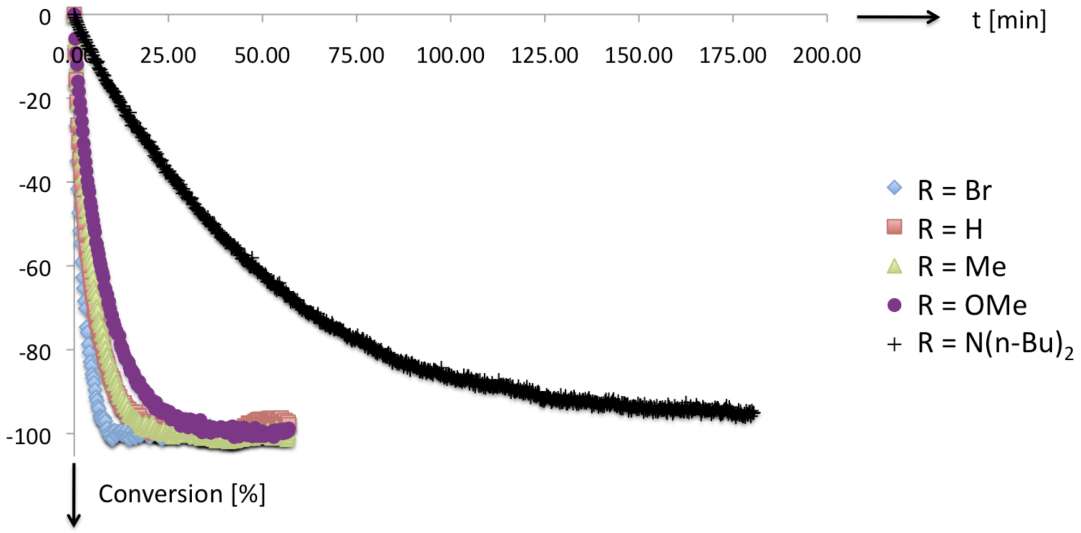


Figure S1a: Conversion of Imine [%] vs Time [min]

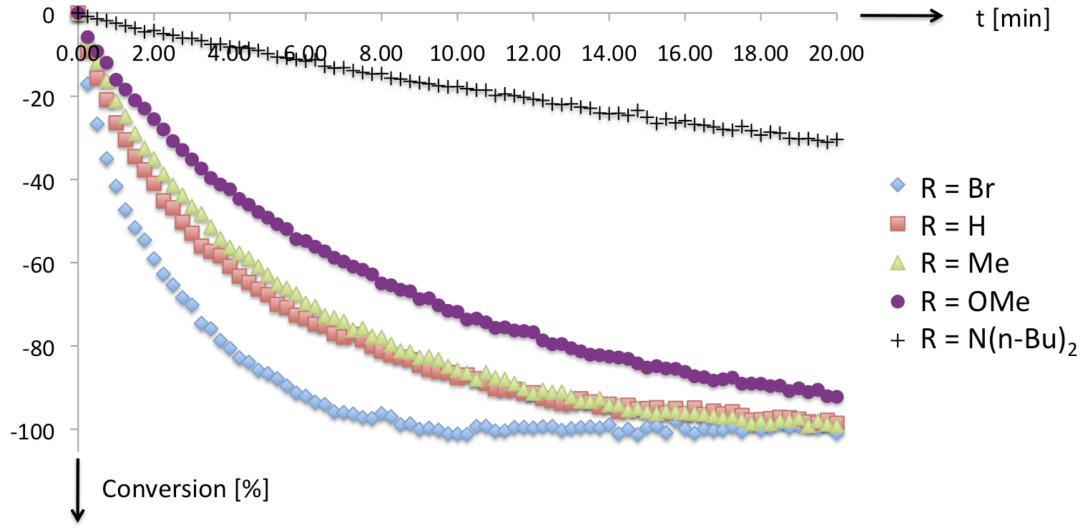
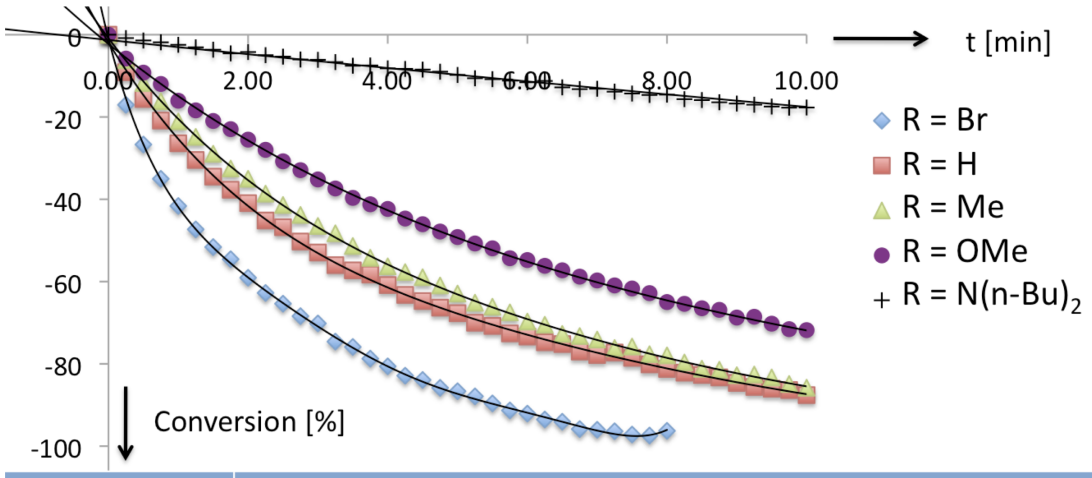


Figure S1b: Conversion of Imine [%] vs Time [min] (Zoomed in Region).

The curves in Figures S1a and S1b were fitted with a 6th-order polynomial function through the use of Microsoft Excel (Figure S1c). In order to obtain a reasonable fit, the curves were truncated after a maximum time (8 min for R = Br, 20 min for R = H, 20 min for R = Me, 40 min for R = OMe, and 180 min for R = N(*n*-Bu)$_2$). The relative rates k_X (for time → 0 min) can be read directly from the equations of the polynomials (values in red), which are used for the generation of the Hammett plot in Graph S1 (plot of

log(k_X/k_H) vs σ_p-constant). Linear regression results in a ρ-value of 1.3 (slope), indicating a faster reaction with more electron deficient aryl substituted aldimines.

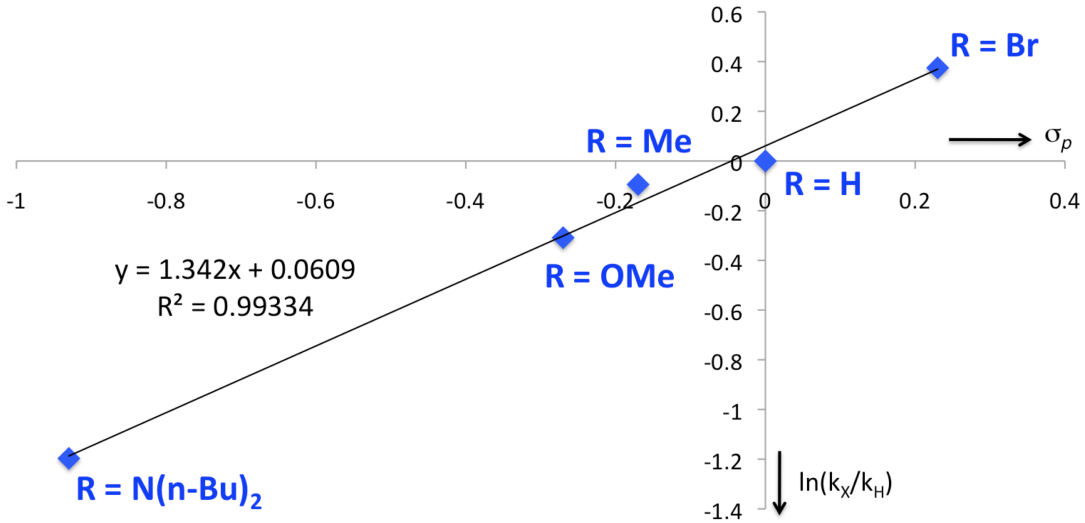


R = Br	y = 0.0088x^6 - 0.23x^5 + 2.3827x^4 - 12.444x^3 + 35.757x^2 - **66.425**x - 0.9584
R = H	y = 2E-05x^6 - 0.0013x^5 + 0.0396x^4 - 0.5957x^3 + 5.1132x^2 -**28.015**x -1.8831
R = Me	y = 9E-06x^6 - 0.0007x^5 + 0.0204x^4 - 0.3258x^3 + 3.216x^2 - **22.544**x - 0.8435
R = OMe	y = 3E-07x^6 - 4E-05x^5 + 0.0022x^4 - 0.0642x^3 + 1.1379x^2 - **13.766**x - 2.2367
R = N(n-Bu)$_2$	y = 6E-12x^6 - 3E-09x^5 + 6E-07x^4 - 8E-05x^3 + 0.0138x^2 - **1.7579**x - 1.2783

Figure S1c: Plot of Conversion of Imine [%] vs Time [min] Including 6th-Order Polynomial Fits

Please Note: The relative rates at t = 0 can be read directly from the polynomial functions (values in **red**).

Graph S1: Hammett Plot [log(k_X/k_H) vs σ_p-constant] Indicating the Electronic Substituent Dependence for the Enantioselective Allylation Under the Conditions Shown in Scheme S1.



■ **DFT Calculations**: All geometry and frequency calculations of the transition states shown in Scheme S2 were carried out employing the hybrid functional B3LYP[145] and the split-valence 6-31G** basis set. The calculations were carried out in toluene, which was simulated by the polarizable dielectric continuum solvation model PCM.[146] Frequency calculations were carried out on the fully optimized geometries. All computed frequencies are real except for the transition state structures, which have one imaginary frequency. Free energies were computed at 298.15 K and 1.0 atm. with harmonic, unscaled frequencies. All quantum chemical calculations were carried out with the Gaussian 09 computer program.[147]

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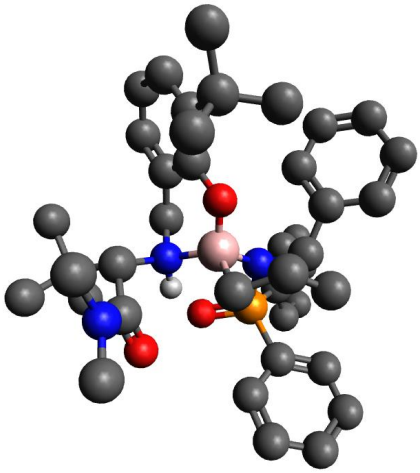
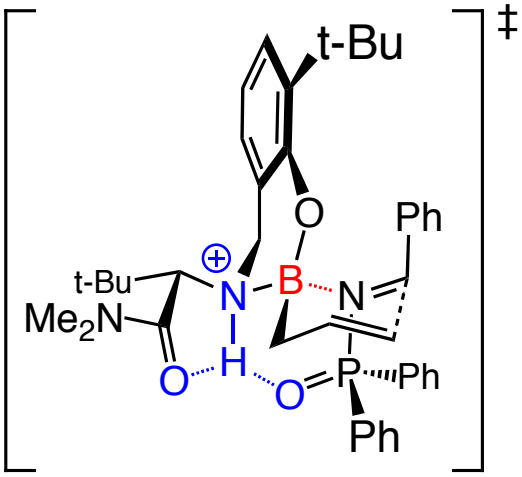
(145) (a) Becke, A. D. *J. Chem. Phys*. **1993**, *98*, 5648-5652; Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B*. **1988**, *37*, 785–789. (b) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys*. **1980**, *58*, 1200–1211. (c) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem*. **1994**, 98, 11623–11627.

(146) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev*. **2005,** *105*, 2999−3093.

(147) Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li,

Transition State Energy for Complex *R*-TS1.1 (Scheme 1.24)





Cartesian coordinates (Angstroms):

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H	2.845	3.498	-3.033
C	-1.530	4.983	-1.725
H	-2.465	3.254	-2.572
H	5.208	3.571	-2.438
H	-0.497	6.545	-0.652
H	-1.613	1.457	-3.522
C	-1.786	3.619	-1.808
C	-0.689	5.479	-0.724
C	2.573	3.276	-1.995
H	2.401	4.227	-1.484
H	4.283	1.440	-3.143

H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

C 4.982 3.358 -1.389
H 1.634 2.723 -1.994
H 4.852 4.319 -0.882
H 0.707 0.874 -3.068
C -1.391 0.596 -2.902
H -5.918 -1.106 -2.868
C 3.713 2.484 -1.315
C 4.005 1.190 -2.114
C -0.079 0.199 -2.737
H 5.856 2.856 -0.960
C -1.189 2.716 -0.908
H -2.184 -0.140 -2.815
C -0.116 4.598 0.192
H -5.159 -3.355 -3.599
H 3.135 0.532 -2.147
C -5.062 -1.574 -2.391
H 4.839 0.639 -1.667
C -4.636 -2.840 -2.799
C -1.614 1.287 -0.936
C -0.361 3.228 0.101
H 0.524 4.972 0.985
H -4.759 0.058 -1.029
H -2.692 1.219 -1.082
C -4.398 -0.911 -1.359
C 3.350 2.117 0.142
C 0.298 -0.915 -1.906
H -2.085 2.015 1.781
H 4.935 3.270 1.022
O 1.420 0.816 -0.501
H 1.301 -1.278 -2.131
C -3.548 -3.449 -2.171
H -0.423 -1.730 -1.893
H -3.599 3.312 3.221
C 4.114 2.594 1.219
H 0.076 2.562 0.832
H -3.226 -4.439 -2.477
C 2.276 1.256 0.479

N	-1.101	0.313	-0.104
C	-3.293	-1.514	-0.733
B	0.412	-0.198	-0.346
C	-3.060	1.611	2.023
C	-2.876	-2.795	-1.139
C	-3.918	2.348	2.839
P	-2.343	-0.731	0.604
H	-2.035	-3.269	-0.642
C	3.872	2.228	2.544
C	-3.464	0.367	1.515
C	2.067	0.822	1.796
H	2.858	-1.505	0.475
H	4.490	2.633	3.339
N	0.828	-1.158	0.907
C	-5.179	1.847	3.164
H	0.004	0.282	2.178
C	2.862	1.319	2.831
C	0.982	-0.187	2.060
H	-5.845	2.422	3.800
H	-0.019	-1.726	1.131
O	-1.674	-1.763	1.479
C	1.999	-2.122	0.728
H	4.078	-2.097	-0.846
O	0.453	-3.555	-0.377
C	-4.733	-0.137	1.856
C	1.592	-3.076	-0.411
H	2.128	-3.964	-3.385
H	4.232	-1.923	2.414
C	-5.584	0.603	2.674
H	2.686	0.991	3.852
N	2.486	-3.397	-1.388
H	1.101	-4.757	-2.160
H	2.911	-1.394	3.453
H	1.172	-0.740	2.975
C	2.104	-4.401	-2.382
C	3.849	-2.897	-1.544
H	-5.056	-1.105	1.487

C 3.340 -2.260 2.952
H 4.042 -4.031 0.993
H 3.980 -2.510 -2.560
C 2.366 -3.004 2.009
H -6.562 0.207 2.930
H 4.571 -3.708 -1.392
C 3.130 -4.273 1.547
H 3.671 -2.949 3.736
H 2.808 -5.240 -2.352
H 2.511 -4.935 0.939
H 0.546 -2.673 3.237
C 1.109 -3.481 2.765
H 3.433 -4.834 2.435
H 0.429 -4.015 2.098
H 1.413 -4.166 3.563

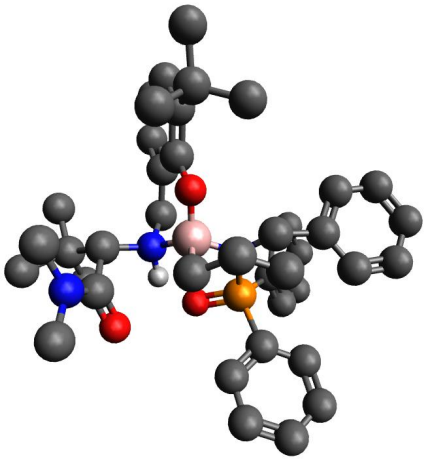
SCF Done: E(RB3LYP) = -2349.81121449 A.U. after 1 cycles

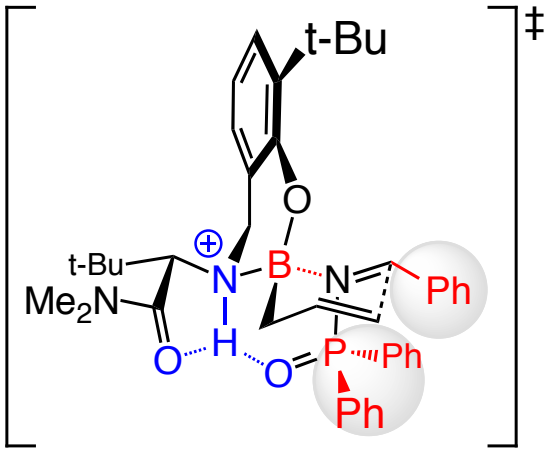
	1	2	3
	A	A	A
Frequencies --	-309.7171	15.8257	27.8170
Red. masses --	8.1218	5.5670	3.9897

Zero-point correction=	0.861950 (Hartree/Particle)
Thermal correction to Energy=	0.909242
Thermal correction to Enthalpy=	0.910186
Thermal correction to Gibbs Free Energy=	0.782800
Sum of electronic and zero-point Energies=	-2348.949264
Sum of electronic and thermal Energies=	-2348.901973
Sum of electronic and thermal Enthalpies=	-2348.901028
Sum of electronic and thermal Free Energies=	-2349.028414

Item	Value	Threshold	Converged?
Maximum Force	0.000000	0.000450	YES
RMS Force	0.000000	0.000300	YES

Transition State Energy for Complex *S*-TS1.1 (Scheme 1.24)





Cartesian coordinates (Angstroms):

H	3.751	2.814	-3.386
H	1.600	4.186	-3.258
H	3.742	5.158	-2.730
C	3.627	2.506	-2.342
H	4.626	2.381	-1.911
C	1.458	3.814	-2.238
H	3.123	1.538	-2.327
C	3.618	4.902	-1.674
H	0.874	2.895	-2.297
H	0.874	4.561	-1.689
H	4.618	4.824	-1.236
C	2.830	3.581	-1.563
H	3.096	5.737	-1.195
H	2.587	-4.468	-1.957
O	1.682	-3.320	-0.246
H	3.273	-3.522	-3.306
C	3.431	-3.861	-2.276
H	4.349	-4.459	-2.244
O	1.449	1.133	-0.699
C	2.650	3.137	-0.094
H	3.638	4.856	0.738
H	1.839	-1.100	-2.200

C 2.645 -2.557 -0.383
C 2.006 1.929 0.274
H -1.628 0.879 -3.621
B 0.744 -0.105 -0.450
C -1.216 0.149 -2.933
N 3.558 -2.710 -1.382
C 3.149 3.916 0.961
H 3.444 -0.616 0.298
C 0.790 -0.944 -1.951
C 2.813 -1.429 0.653
H 1.687 -2.174 3.275
C 0.155 -0.027 -2.868
H 3.597 -0.206 3.217
N 1.422 -0.830 0.837
H 0.273 -1.895 -1.838
C 1.949 1.506 1.609
H 4.733 -0.973 -1.039
C 4.706 -1.856 -1.672
C 3.055 3.531 2.299
H 4.661 -1.527 -2.715
C 2.456 -2.812 2.833
H 0.784 0.715 -3.355
C 4.233 -0.973 2.778
H 1.952 -3.587 2.253
C 3.480 -2.051 1.964
H 3.456 4.172 3.077
H 4.978 -0.464 2.158
C 1.301 0.191 1.946
C 2.470 2.314 2.622
H 5.639 -2.412 -1.531
H 2.983 -3.295 3.662
H 0.231 0.304 2.121
H 4.767 -1.457 3.602
H 1.712 -0.222 2.862
H 2.412 1.985 3.656
C 4.563 -3.080 1.545
H 5.336 -2.637 0.910

H 4.140 -3.947 1.034
H 5.060 -3.444 2.448
H -1.867 -0.684 -2.686
H 0.768 -1.597 1.104
H -3.176 2.810 3.452
H -5.140 1.636 4.419
C -3.423 1.804 3.128
C -4.525 1.143 3.672
C -2.633 1.174 2.168
H -1.775 1.696 1.758
C -4.831 -0.156 3.263
H -5.679 -0.679 3.693
H -1.790 3.507 -0.374
C -2.945 -0.124 1.736
C -4.043 -0.792 2.306
H -0.558 1.797 -1.282
H -3.908 4.769 -0.355
C -2.705 3.024 -0.706
C -1.313 1.041 -1.102
O -0.852 -1.903 1.512
H -4.278 -1.811 2.017
C -3.901 3.739 -0.697
P -1.806 -1.069 0.689
C -2.671 1.683 -1.129
N -0.830 0.110 -0.202
C -5.078 3.138 -1.145
H -0.955 -3.432 -0.608
C -2.716 -2.183 -0.429
C -3.852 1.102 -1.607
H -6.008 3.696 -1.151
C -1.990 -3.291 -0.906
C -5.046 1.823 -1.609
H -3.843 0.099 -2.011
H -4.663 -1.241 -0.357
C -4.077 -2.064 -0.749
C -2.610 -4.233 -1.726
H -2.042 -5.083 -2.090

H -5.950 1.357 -1.989

C -4.694 -3.018 -1.559

C -3.960 -4.096 -2.056

H -5.750 -2.923 -1.793

H -4.443 -4.836 -2.687

SCF Done: E(RB3LYP) = -2349.80692498 A.U. after 1 cycles

	1	2	3
	A	A	A
Frequencies --	-344.5655	12.7728	18.2767
Red. masses --	9.0648	5.1910	4.1843

Zero-point correction= 0.862291 (Hartree/Particle)

Thermal correction to Energy= 0.909628

Thermal correction to Enthalpy= 0.910572

Thermal correction to Gibbs Free Energy= 0.782402

Sum of electronic and zero-point Energies= -2348.944634

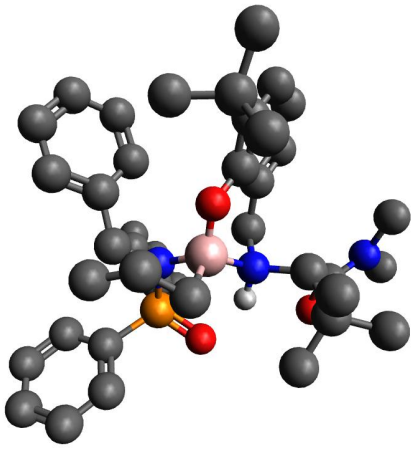
Sum of electronic and thermal Energies= -2348.897297

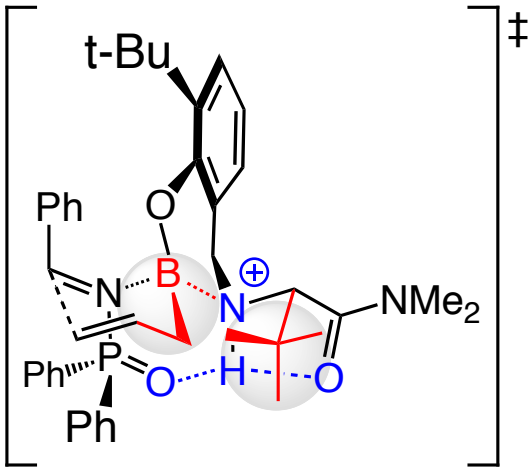
Sum of electronic and thermal Enthalpies= -2348.896353

Sum of electronic and thermal Free Energies= -2349.024523

Item	Value	Threshold	Converged?
Maximum Force	0.000001	0.000450	YES
RMS Force	0.000000	0.000300	YES

Transition State Energy for Complex (*S*)-TS1.2 (Scheme 1.24)





Cartesian coordinates (Angstroms):

H -0.181 3.850 2.912
H -3.556 3.322 -2.949
C 0.467 3.883 2.042
H 0.240 1.790 1.642
H -4.343 5.027 -1.425
H 0.893 5.988 2.223
H 2.342 2.756 -2.636
C 0.693 2.714 1.313
C 1.070 5.079 1.658
C -3.425 2.604 -2.133
H -4.351 2.024 -2.048
H -1.941 4.884 -1.814
C -4.278 4.343 -0.574
H -2.618 1.923 -2.406
H -5.244 3.835 -0.485
H -0.031 2.235 -2.882
C 2.005 1.735 -2.495
H 3.305 0.613 4.518
C -3.119 3.353 -0.814
C -1.829 4.189 -0.974
C 0.680 1.422 -2.758
H -4.123 4.951 0.323
C 1.527 2.721 0.186
H 2.761 0.974 -2.660

C 1.920 5.096 0.548
H 3.407 -1.655 5.523
H -0.957 3.562 -1.159
C 3.125 -0.263 3.903
H -1.631 4.779 -0.074
C 3.180 -1.540 4.468
C 1.920 1.442 -0.488
C 2.154 3.928 -0.172
H 2.409 6.017 0.249
H 2.775 0.891 2.132
H 3.004 1.335 -0.489
C 2.833 -0.109 2.548
C -2.979 2.336 0.343
C 0.161 0.095 -2.581
H 4.917 0.061 0.693
H -4.553 3.194 1.527
O -1.128 1.179 -0.692
H -0.764 -0.070 -3.127
C 2.938 -2.666 3.679
H 0.886 -0.692 -2.785
H 7.024 0.246 -0.574
C -3.823 2.397 1.463
H 2.841 3.960 -1.011
H 2.971 -3.658 4.119
C -2.034 1.281 0.337
N 1.252 0.249 -0.277
C 2.598 -1.240 1.749
B -0.233 0.078 -0.895
C 4.968 -0.328 -0.318
C 2.648 -2.521 2.323
C 6.164 -0.234 -1.030
P 2.265 -1.174 -0.035
H 2.444 -3.391 1.708
C -3.778 1.469 2.503
C 3.851 -0.950 -0.900
C -2.010 0.311 1.353
H -2.997 -1.148 -0.495

H -4.455 1.566 3.346
N -0.910 -1.264 -0.227
C 6.257 -0.768 -2.316
H -1.379 -1.695 1.823
C -2.885 0.407 2.436
C -1.049 -0.843 1.233
H 7.192 -0.699 -2.865
H -0.193 -2.019 -0.260
O 1.538 -2.398 -0.532
C -2.246 -1.920 -0.643
H -4.649 -1.587 0.296
O -1.433 -3.843 0.502
C 3.959 -1.508 -2.187
C -2.404 -3.096 0.352
H -4.024 -4.150 2.877
H -4.040 -1.215 -2.801
C 5.158 -1.411 -2.891
H -2.859 -0.351 3.216
N -3.579 -3.276 1.015
H -2.764 -4.975 1.917
H -2.500 -0.394 -2.892
H -0.051 -0.588 1.588
C -3.718 -4.456 1.871
C -4.794 -2.474 0.905
H 3.116 -2.041 -2.614
C -2.978 -1.364 -3.022
H -4.409 -3.312 -1.719
H -5.111 -2.152 1.902
C -2.397 -2.474 -2.116
H 5.238 -1.847 -3.881
H -5.602 -3.070 0.466
C -3.446 -3.617 -2.139
H -2.897 -1.648 -4.076
H -4.483 -5.128 1.465
H -3.097 -4.510 -1.614
H -0.275 -2.366 -2.746
C -1.088 -3.083 -2.653

H -3.624 -3.897 -3.182

H -0.743 -3.884 -1.994

H -1.270 -3.509 -3.644

SCF Done: E(RB3LYP) = -2349.80034463 A.U. after 1 cycles

	1	2	3
	A	A	A
Frequencies --	-335.3640	16.4052	22.4182
Red. masses --	8.2371	5.2097	4.3949

Zero-point correction= 0.861454 (Hartree/Particle)

Thermal correction to Energy= 0.908946

Thermal correction to Enthalpy= 0.909890

Thermal correction to Gibbs Free Energy= 0.781405

Sum of electronic and zero-point Energies= -2348.938890

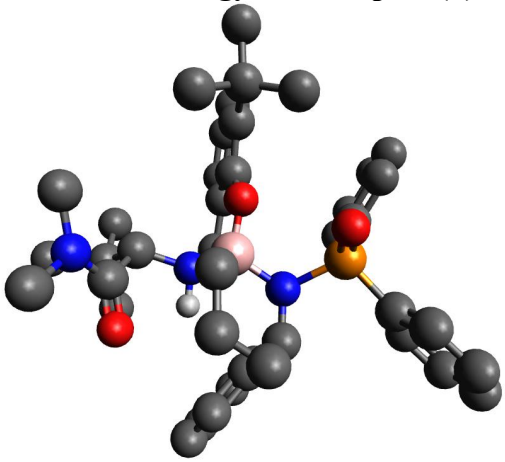
Sum of electronic and thermal Energies= -2348.891398

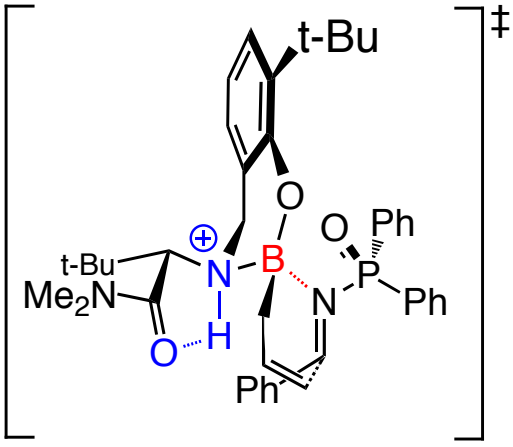
Sum of electronic and thermal Enthalpies= -2348.890454

Sum of electronic and thermal Free Energies= -2349.018940

Item	Value	Threshold	Converged?
Maximum Force	0.000000	0.000450	YES
RMS Force	0.000000	0.000300	YES

Transition State Energy for Complex (*S*)-TS1.3 (Scheme 1.24)





Cartesian coordinates (Angstroms):

C	-0.273	-3.861	2.824
C	-0.769	-2.924	1.919
C	0.422	-4.980	2.362
C	-0.573	-3.082	0.532
C	0.608	-5.154	0.991
C	0.110	-4.219	0.083
C	4.390	-1.903	-3.060
O	2.822	-2.546	-0.908
N	3.992	-0.944	-2.028
C	3.245	-1.383	-0.983
C	5.356	-1.119	0.771
C	4.166	0.318	2.380
C	4.497	0.410	-2.243
C	3.958	-0.849	1.388
C	2.946	-0.462	0.210
C	3.532	-2.133	2.129
B	0.358	-0.146	-0.643
N	1.453	-0.646	0.514
C	0.985	0.068	1.766
O	0.409	1.279	-0.682
C	1.056	1.562	1.598
C	0.807	2.111	0.332
C	1.369	2.396	2.673
C	-0.523	3.952	-1.935
C	0.982	3.494	0.076
C	0.897	4.102	-1.343
C	1.457	3.767	2.474
C	1.924	3.404	-2.267
C	1.288	4.289	1.190
C	1.239	5.607	-1.339
C	-2.803	2.146	2.914
C	-3.265	3.407	2.533
C	-2.513	1.186	1.945
C	-3.439	3.708	1.181
C	-2.678	1.485	0.585

C -3.149 2.752 0.208
O -2.312 0.865 -2.119
P -2.483 0.276 -0.751
C -3.964 -0.797 -0.691
C -4.577 -1.076 -1.923
C -4.554 -1.265 0.496
C -5.749 -1.832 -1.968
C -5.724 -2.021 0.444
C -6.320 -2.308 -0.788
N -1.092 -0.756 -0.265
C 0.562 -0.676 -2.232
C 0.267 -2.092 -2.396
C -1.302 -2.094 -0.341
C -1.008 -2.590 -2.474
H -0.440 -3.719 3.887
H -1.342 -2.079 2.287
H 0.809 -5.711 3.064
H 1.145 -6.021 0.620
H 0.269 -4.381 -0.974
H 3.913 -1.653 -4.014
H 4.091 -2.903 -2.755
H 5.476 -1.867 -3.193
H 6.062 -1.308 1.584
H 5.733 -0.258 0.210
H 5.366 -1.996 0.121
H 3.302 0.536 3.004
H 4.439 1.241 1.859
H 4.989 0.064 3.054
H 4.271 0.715 -3.270
H 5.584 0.443 -2.107
H 4.036 1.132 -1.575
H 3.069 0.594 -0.018
H 2.600 -2.025 2.690
H 4.306 -2.397 2.856
H 3.417 -2.970 1.437
H -0.037 -0.273 1.926
H 1.571 -0.263 2.618

H 1.541 1.968 3.657
H -1.252 4.482 -1.315
H -0.833 2.910 -2.017
H -0.551 4.398 -2.935
H 1.686 4.429 3.302
H 2.943 3.534 -1.885
H 1.885 3.847 -3.268
H 1.717 2.337 -2.362
H 1.409 5.356 1.057
H 2.247 5.804 -0.960
H 0.527 6.191 -0.747
H 1.194 5.984 -2.366
H -2.668 1.910 3.965
H -3.491 4.152 3.289
H -2.163 0.208 2.257
H -3.801 4.687 0.883
H -3.280 2.981 -0.844
H -4.141 -0.678 -2.833
H -4.119 -1.030 1.462
H -6.220 -2.039 -2.924
H -6.175 -2.379 1.364
H -7.234 -2.892 -0.823
H 1.573 -0.421 -2.549
H -0.156 -0.035 -2.749
H 1.094 -2.787 -2.284
H -2.332 -2.394 -0.516
H -1.832 -1.944 -2.757
H -1.186 -3.657 -2.565
H 1.332 -1.656 0.648

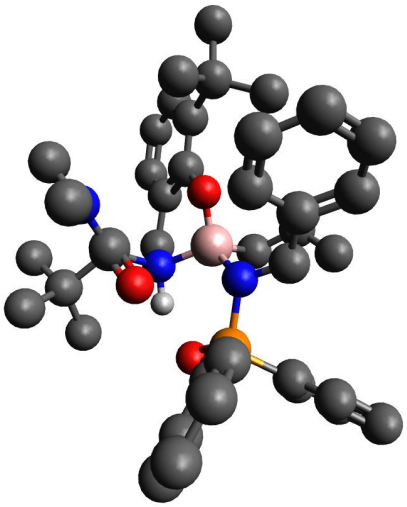
SCF Done: E(RB3LYP) = -2349.80118264 A.U. after 1 cycles

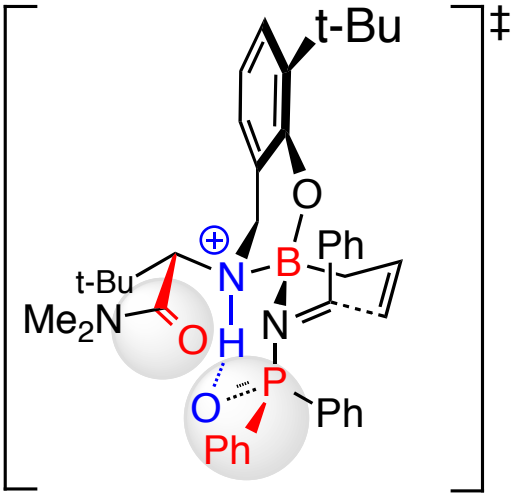
	1	2	3
	A	A	A
Frequencies --	-220.1960	21.2213	23.3750
Red. masses --	6.5227	5.3294	4.2832

Zero-point correction= 0.862703 (Hartree/Particle)
Thermal correction to Energy= 0.909800
Thermal correction to Enthalpy= 0.910744
Thermal correction to Gibbs Free Energy= 0.784683
Sum of electronic and zero-point Energies= -2348.938480
Sum of electronic and thermal Energies= -2348.891383
Sum of electronic and thermal Enthalpies= -2348.890439
Sum of electronic and thermal Free Energies= -2349.016500

Item	Value	Threshold	Converged?
Maximum Force	0.000001	0.000450	YES
RMS Force	0.000000	0.000300	YES

Transition State Energy for Complex (*S*)-TS1.4 (Scheme 1.24)





Cartesian coordinates (Angstroms):

H	1.303	-1.944	3.939
H	3.208	-3.984	0.832
C	0.753	-2.507	3.192
H	0.359	-0.776	1.967
H	5.522	-3.454	1.165
H	0.956	-4.387	4.226
H	-1.023	-3.966	-1.454

C 0.240 -1.846 2.074
C 0.555 -3.877 3.356
C 3.104 -3.231 0.044
H 3.304 -3.723 -0.915
H 3.873 -2.143 2.448
C 5.511 -2.720 0.353
H 2.075 -2.879 0.054
H 5.774 -3.248 -0.569
H 1.063 -2.851 -2.012
C -1.043 -2.925 -1.754
H -5.318 3.294 2.053
C 4.108 -2.080 0.280
C 3.848 -1.399 1.644
C 0.126 -2.325 -2.182
H 6.294 -1.986 0.568
C -0.484 -2.553 1.103
H -1.993 -2.568 -2.138
C -0.181 -4.587 2.402
H -5.146 1.938 4.129
H 2.878 -0.903 1.670
C -4.688 2.410 2.077
H 4.627 -0.656 1.850
C -4.589 1.649 3.242
C -1.197 -1.825 0.014
C -0.705 -3.930 1.294
H -0.356 -5.650 2.529
H -4.049 2.635 0.033
H -2.257 -2.072 0.014
C -3.976 2.039 0.937
C 4.007 -1.021 -0.840
C 0.207 -0.946 -2.562
H -4.543 -1.429 0.263
H 6.052 -1.254 -1.447
O 1.656 -0.573 -0.415
H 1.106 -0.749 -3.142
C -3.769 0.520 3.271
H -0.684 -0.548 -3.048

H -6.177 -2.752 -1.026
C 5.131 -0.714 -1.619
H -1.300 -4.492 0.582
H -3.682 -0.068 4.179
C 2.818 -0.293 -1.120
N -0.935 -0.514 -0.311
C -3.153 0.903 0.962
B 0.418 -0.114 -0.986
C -4.531 -1.384 -0.822
C -3.049 0.146 2.136
C -5.465 -2.122 -1.549
P -2.376 0.473 -0.618
H -2.392 -0.715 2.187
C 5.126 0.264 -2.614
C -3.603 -0.566 -1.489
C 2.814 0.726 -2.102
H 2.303 2.214 -0.211
H 6.025 0.459 -3.190
N 0.634 1.499 -1.224
C -5.496 -2.035 -2.943
H 1.057 1.282 -3.283
C 3.971 0.994 -2.841
C 1.590 1.578 -2.378
H -6.229 -2.604 -3.505
H -0.300 1.870 -1.484
O -2.021 1.655 -1.488
C 1.235 2.374 -0.108
H 3.510 2.089 1.232
O -0.408 1.611 1.439
C -3.658 -0.464 -2.890
C 0.777 1.910 1.271
H 1.719 0.880 4.138
H 3.067 4.476 0.090
C -4.598 -1.199 -3.611
H 3.952 1.781 -3.590
N 1.679 1.900 2.295
H 0.118 1.481 3.621

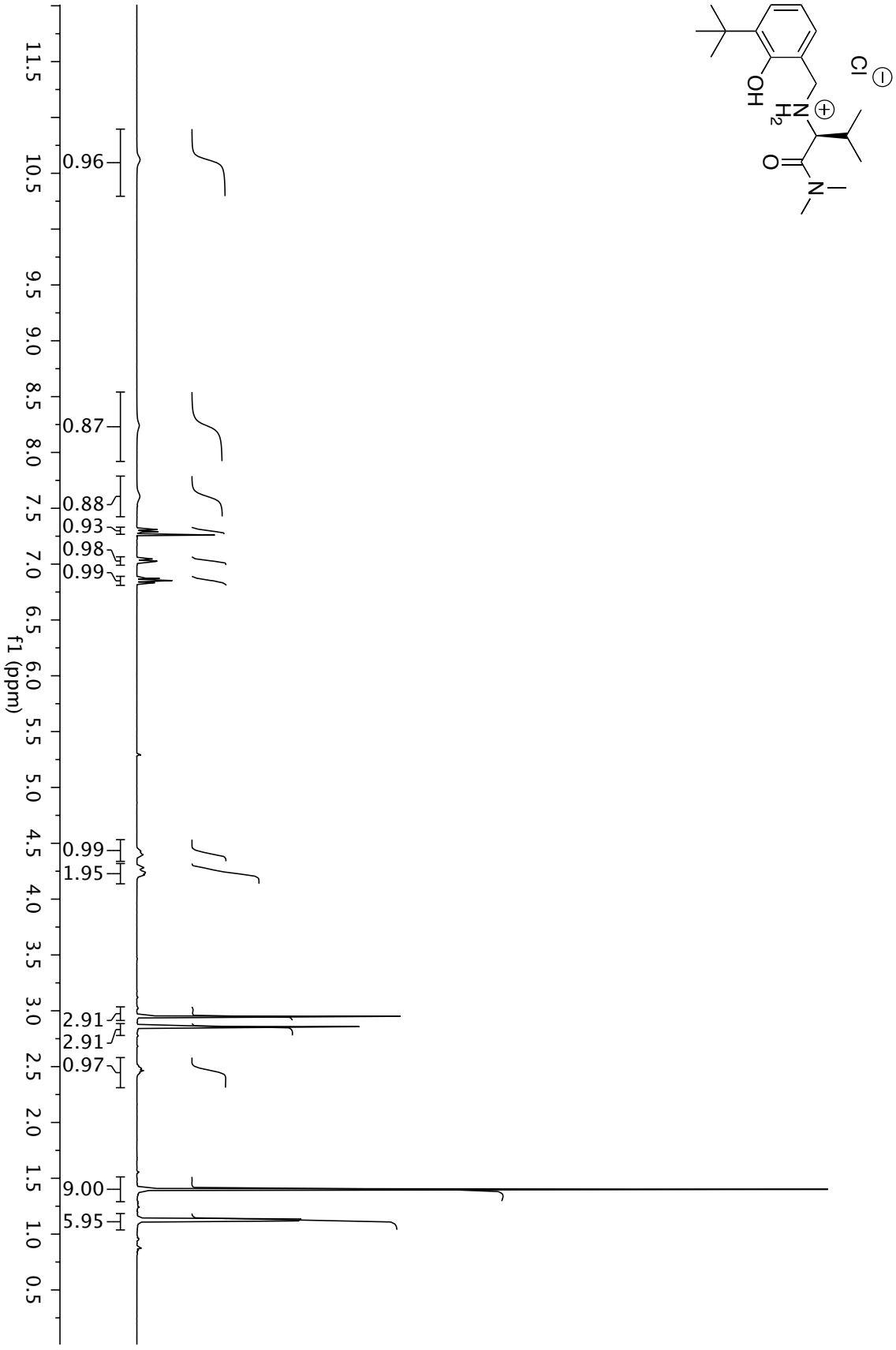
H 2.723 4.259 -1.629
H 1.889 2.614 -2.522
C 1.181 1.705 3.659
C 3.092 2.266 2.221
H -2.984 0.213 -3.404
C 2.310 4.629 -0.685
H 1.186 4.522 1.813
H 3.648 1.642 2.925
C 0.970 3.954 -0.311
H -4.637 -1.111 -4.692
H 3.251 3.315 2.497
C 0.465 4.612 0.996
H 2.166 5.708 -0.794
H 1.342 2.613 4.251
H -0.485 4.184 1.323
H 0.213 3.937 -2.398
C -0.081 4.267 -1.397
H 0.314 5.680 0.816
H -1.056 3.832 -1.163
H -0.205 5.352 -1.452

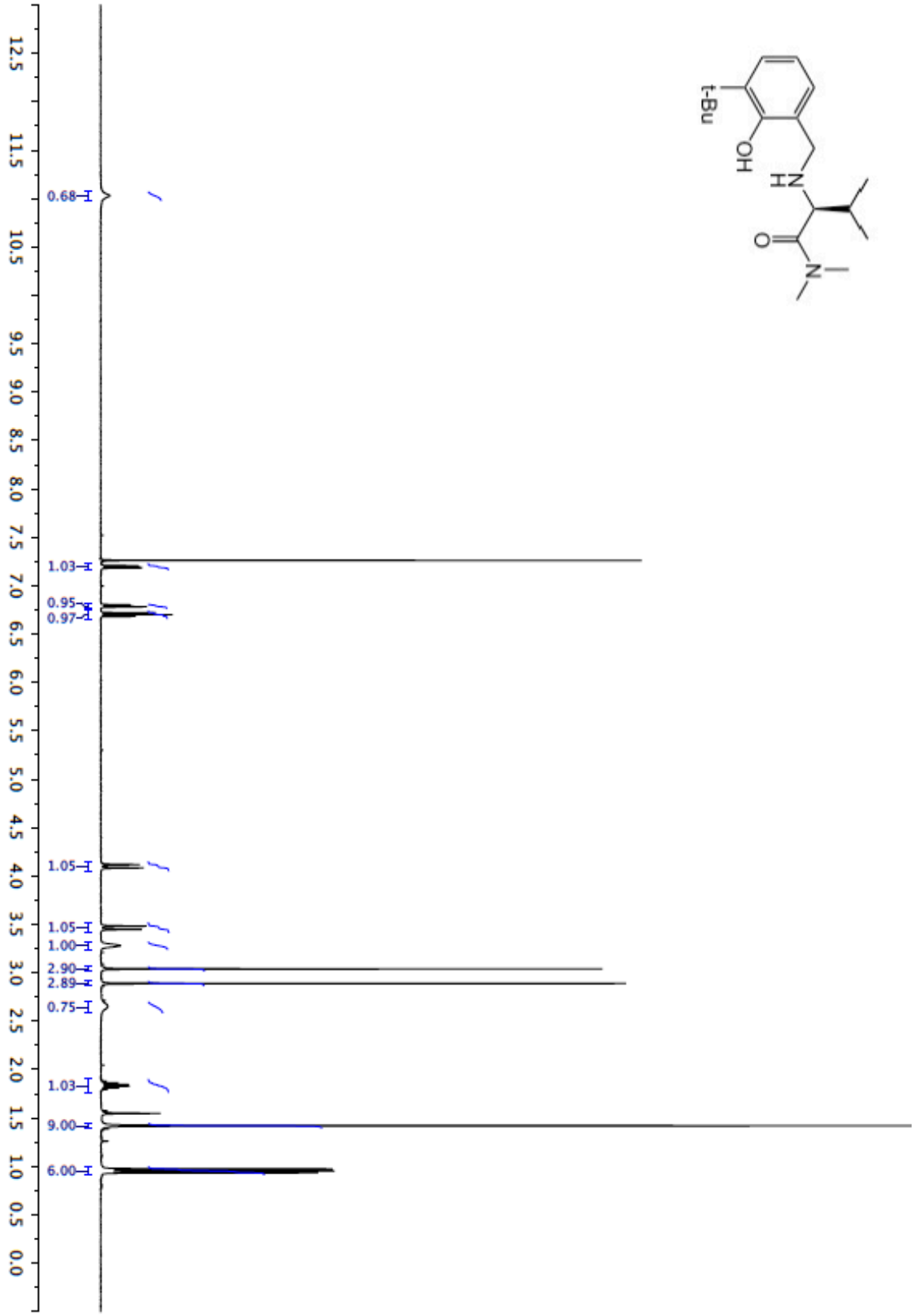
SCF Done: E(RB3LYP) = -2349.79523369 A.U. after 1 cycles

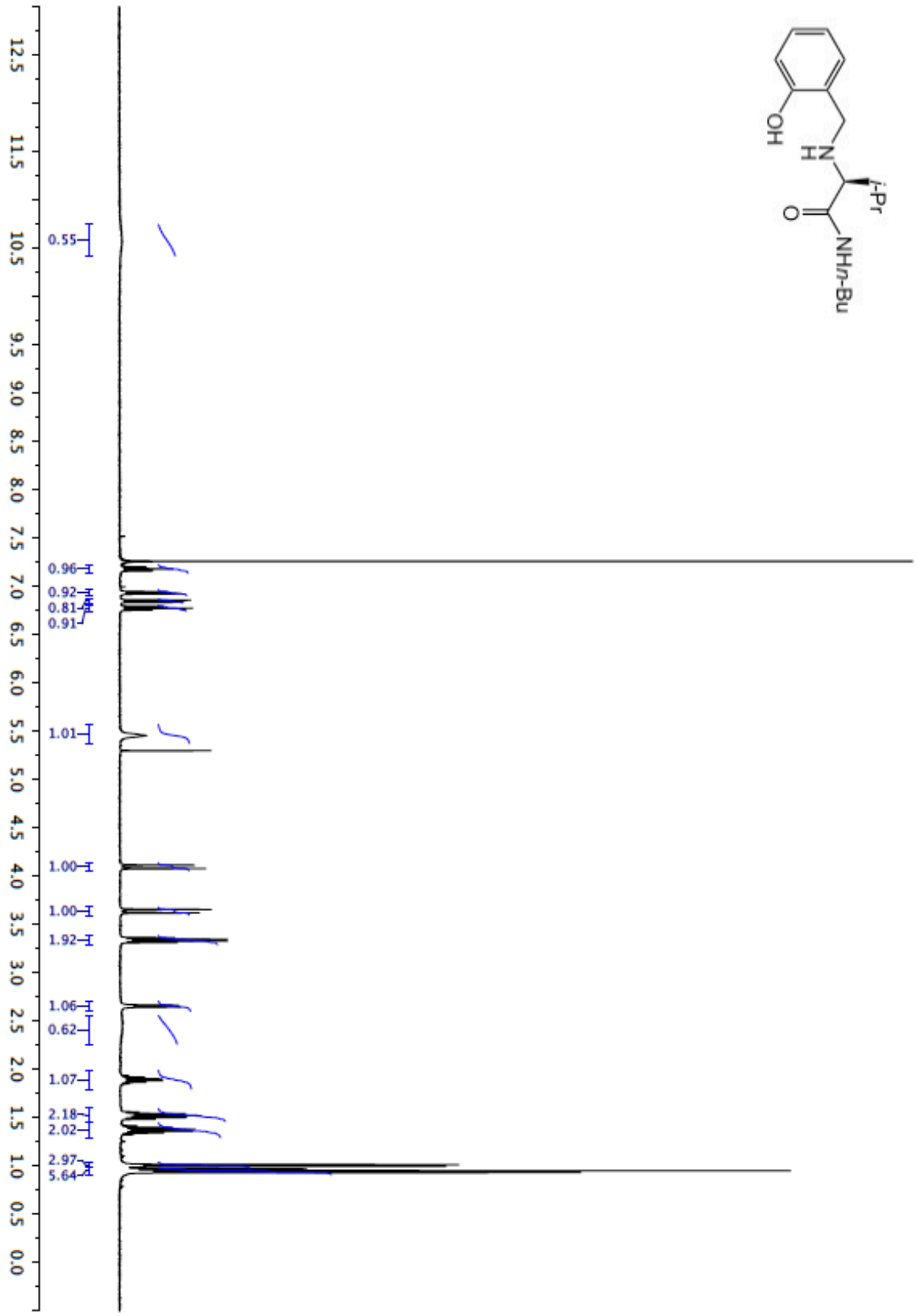
	1	2	3
	A	A	A
Frequencies --	-335.9124	12.6240	29.5812
Red. masses --	8.2872	3.9844	5.0315

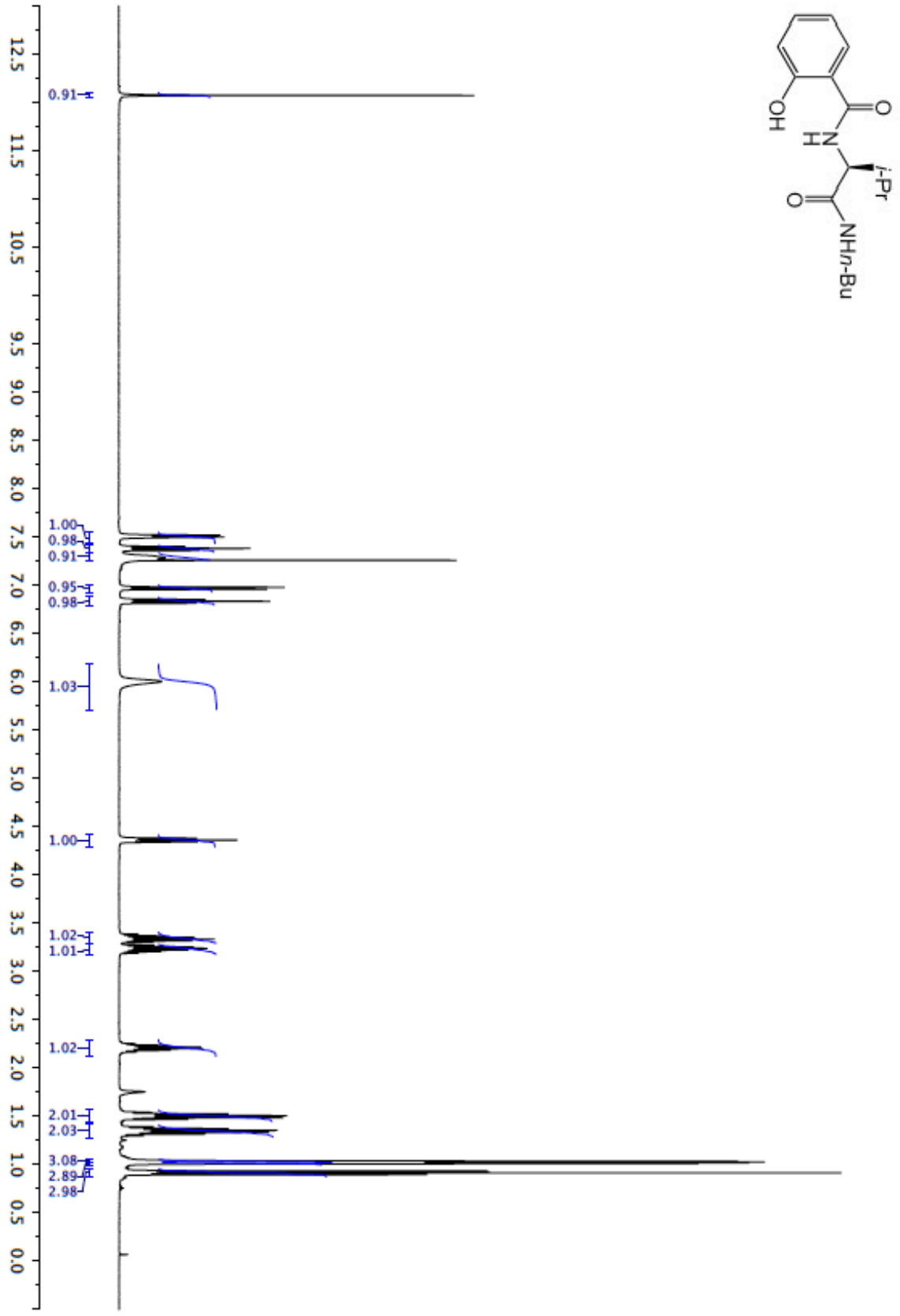
Zero-point correction= 0.862399 (Hartree/Particle)
Thermal correction to Energy= 0.909414
Thermal correction to Enthalpy= 0.910359
Thermal correction to Gibbs Free Energy= 0.783996
Sum of electronic and zero-point Energies= -2348.932835
Sum of electronic and thermal Energies= -2348.885819
Sum of electronic and thermal Enthalpies= -2348.884875
Sum of electronic and thermal Free Energies= -2349.011238

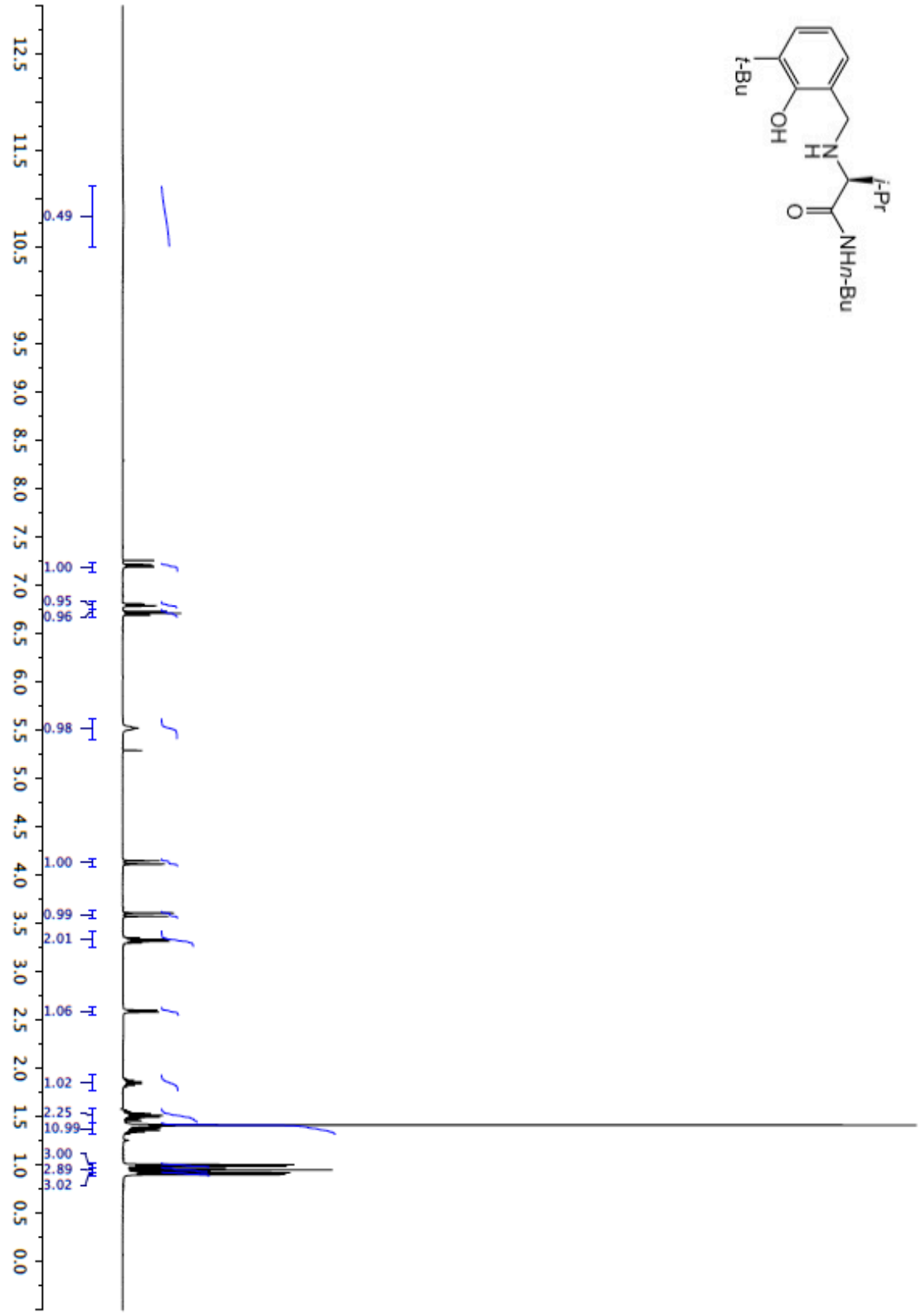
Item	Value	Threshold	Converged?
Maximum Force	0.000011	0.000450	YES
RMS Force	0.000002	0.000300	YES

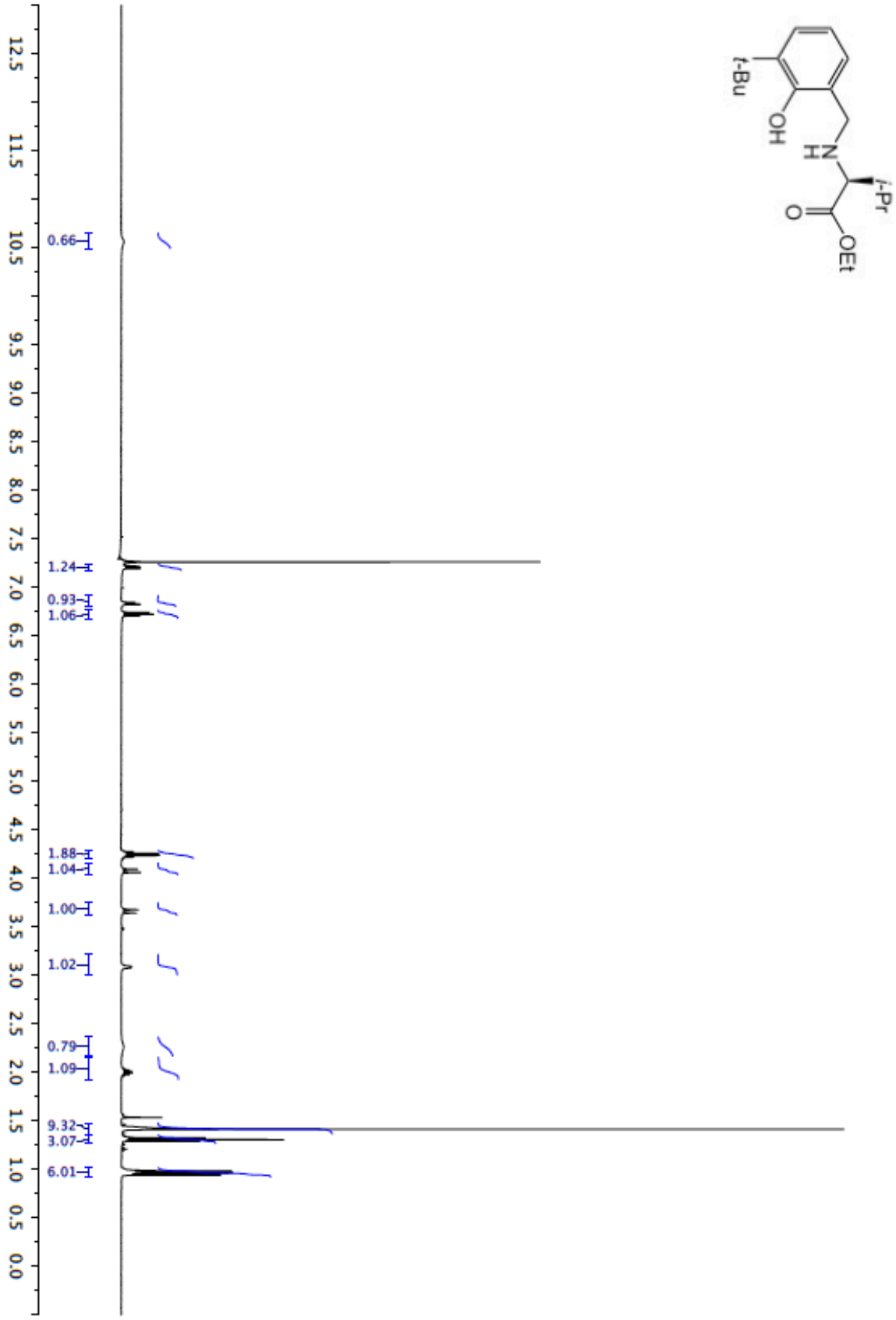

f1 (ppm)
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.96
0.87
0.88
0.93
0.98
0.99
0.99
1.95
2.91
2.91
0.97
9.00
5.95
OH
H2
N
O
N
Cl

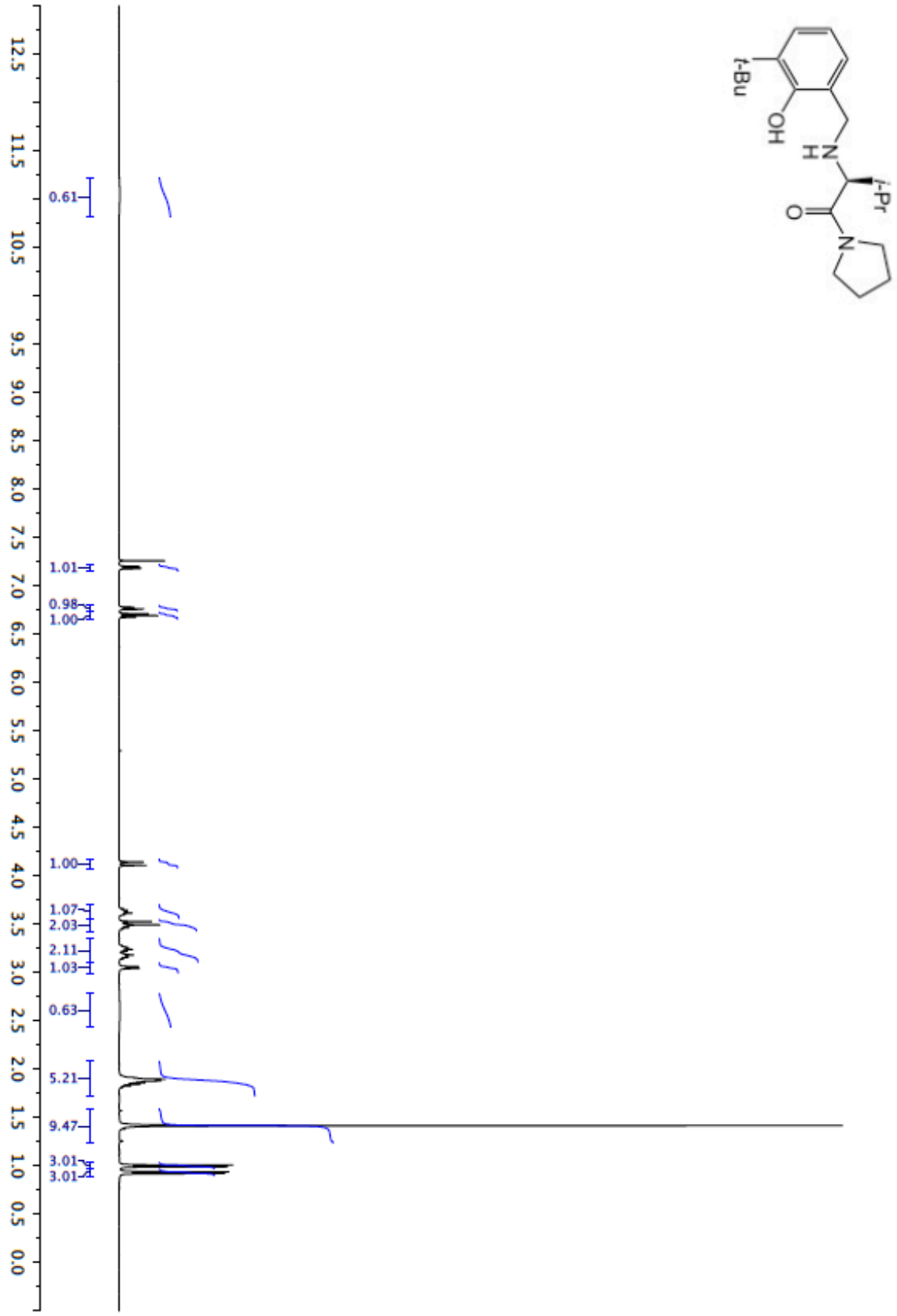

12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.68
1.03
0.95
0.97
1.05
1.05
1.00
2.90
2.89
0.75
1.03
9.00
6.00
t-Bu
HO
HN
O
N

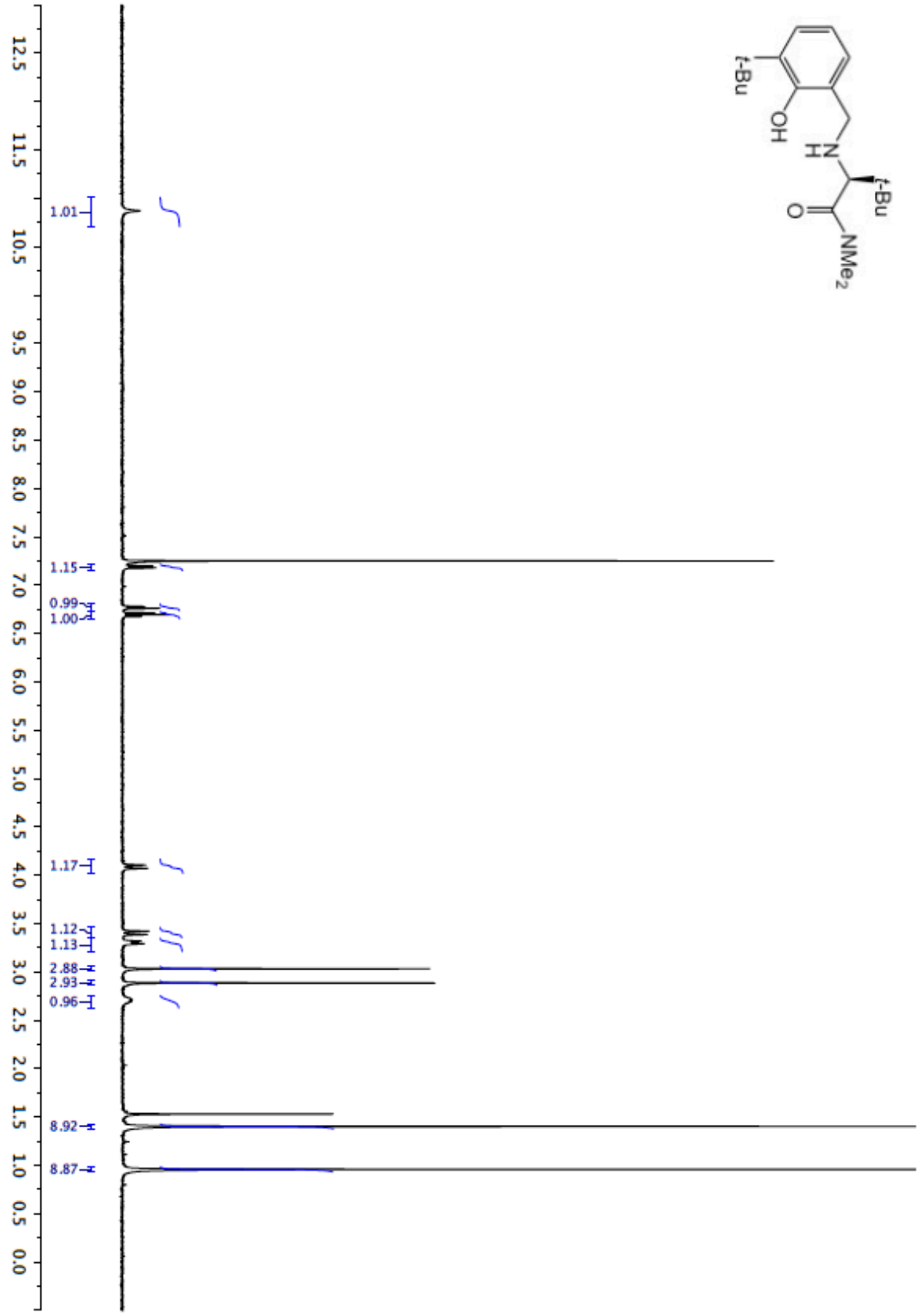

OH
N
H
i-Pr
O
NHn-Bu
0.55
0.96
0.92
0.81
0.91
1.01
1.00
1.00
1.92
1.06
0.62
1.07
2.18
2.02
2.97
5.64

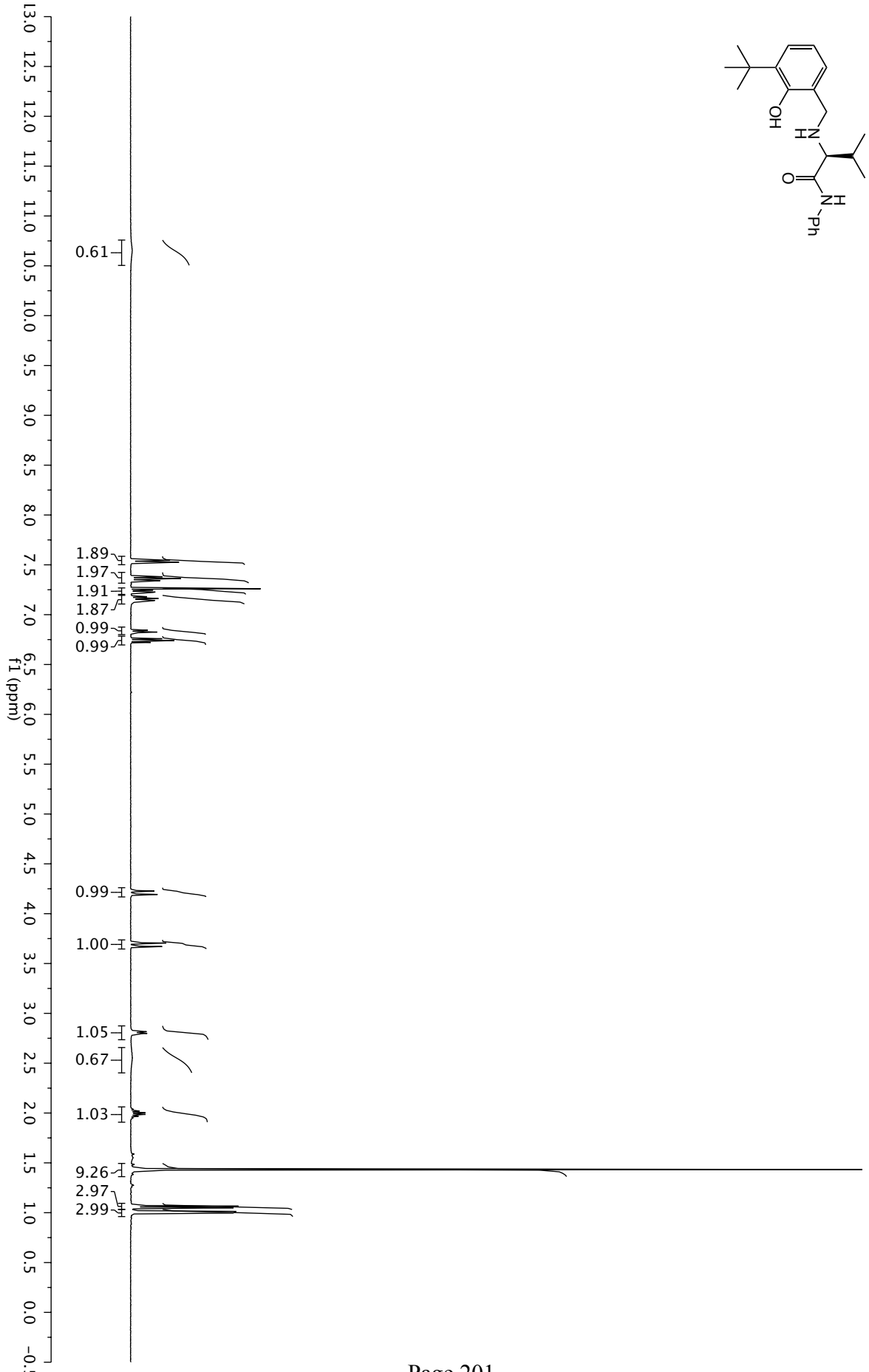

12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.91
1.00
0.98
0.91
0.95
0.98
1.03
1.00
1.02
1.01
1.02
2.01
2.03
3.08
2.89
2.98
OH
O
N
H
O
i-Pr
NHn-Bu

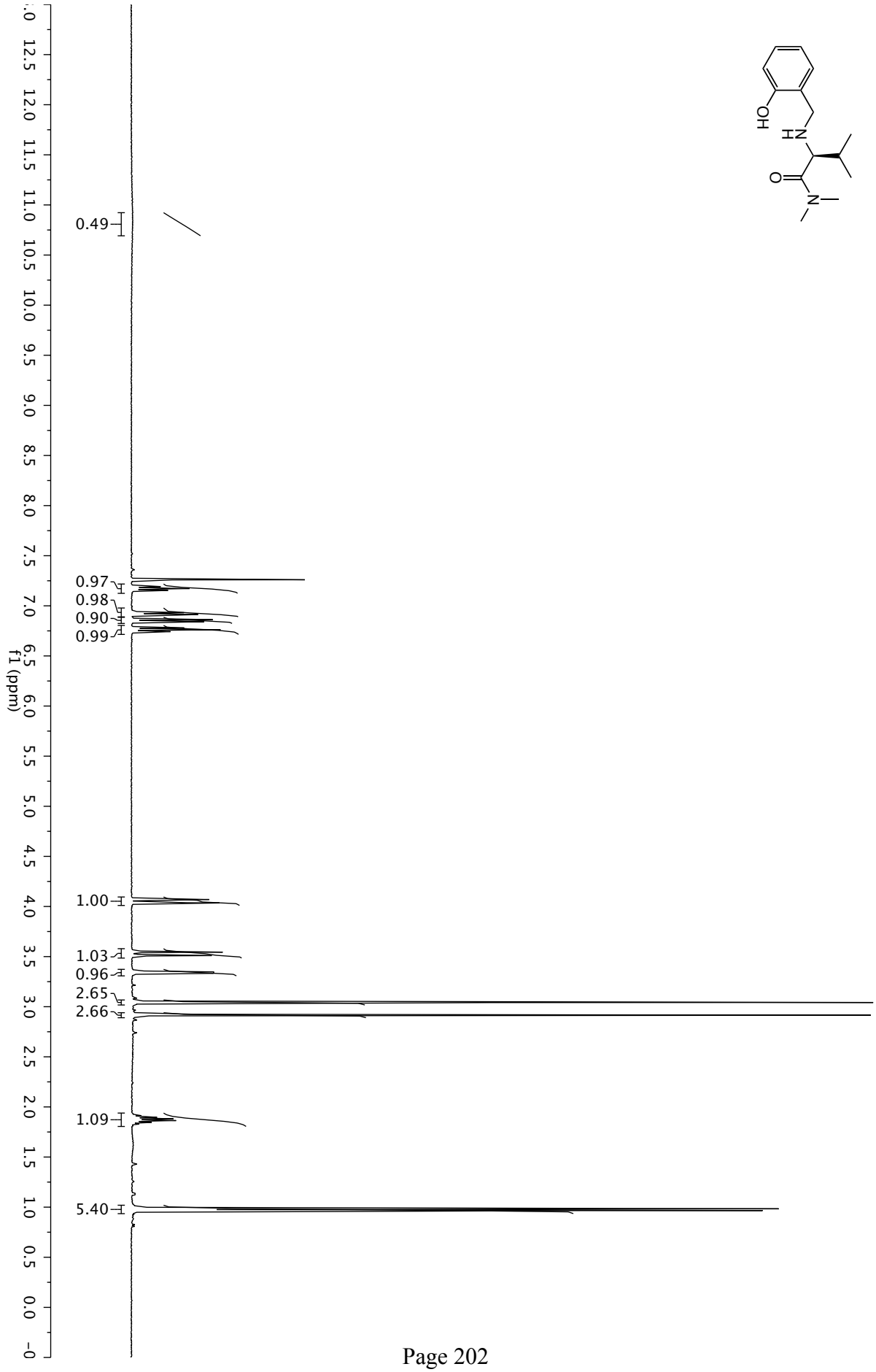

t-Bu
OH
H
N
i-Pr
O
NHn-Bu
0.49
1.00
0.95
0.96
0.98
1.00
0.99
2.01
1.06
1.02
2.25
10.99
3.00
2.89
3.02

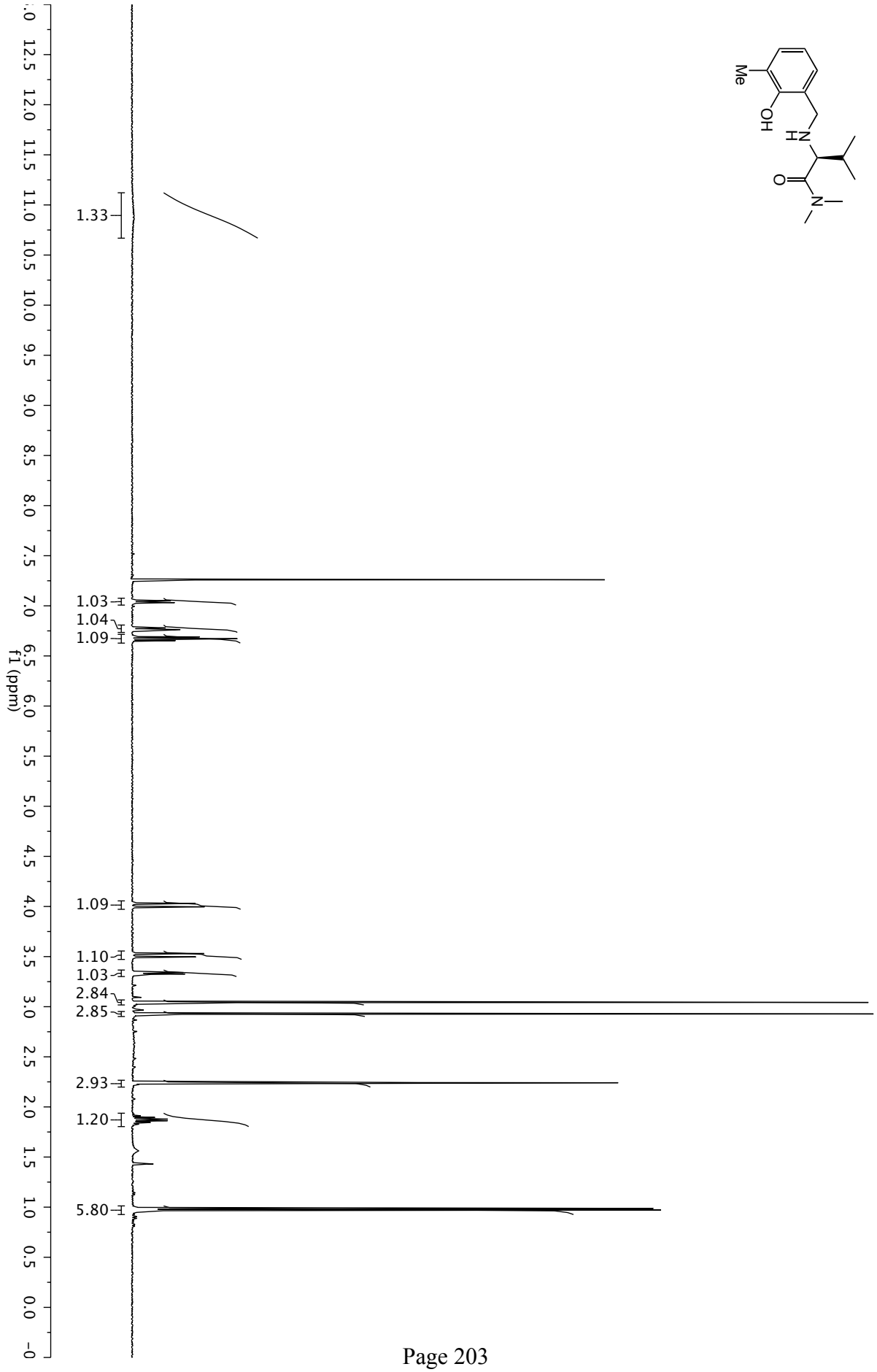

t-Bu
OH
N
H
i-Pr
O
OEt
0.66
1.24
0.93
1.06
1.88
1.04
1.00
1.02
0.79
1.09
9.32
3.07
6.01
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

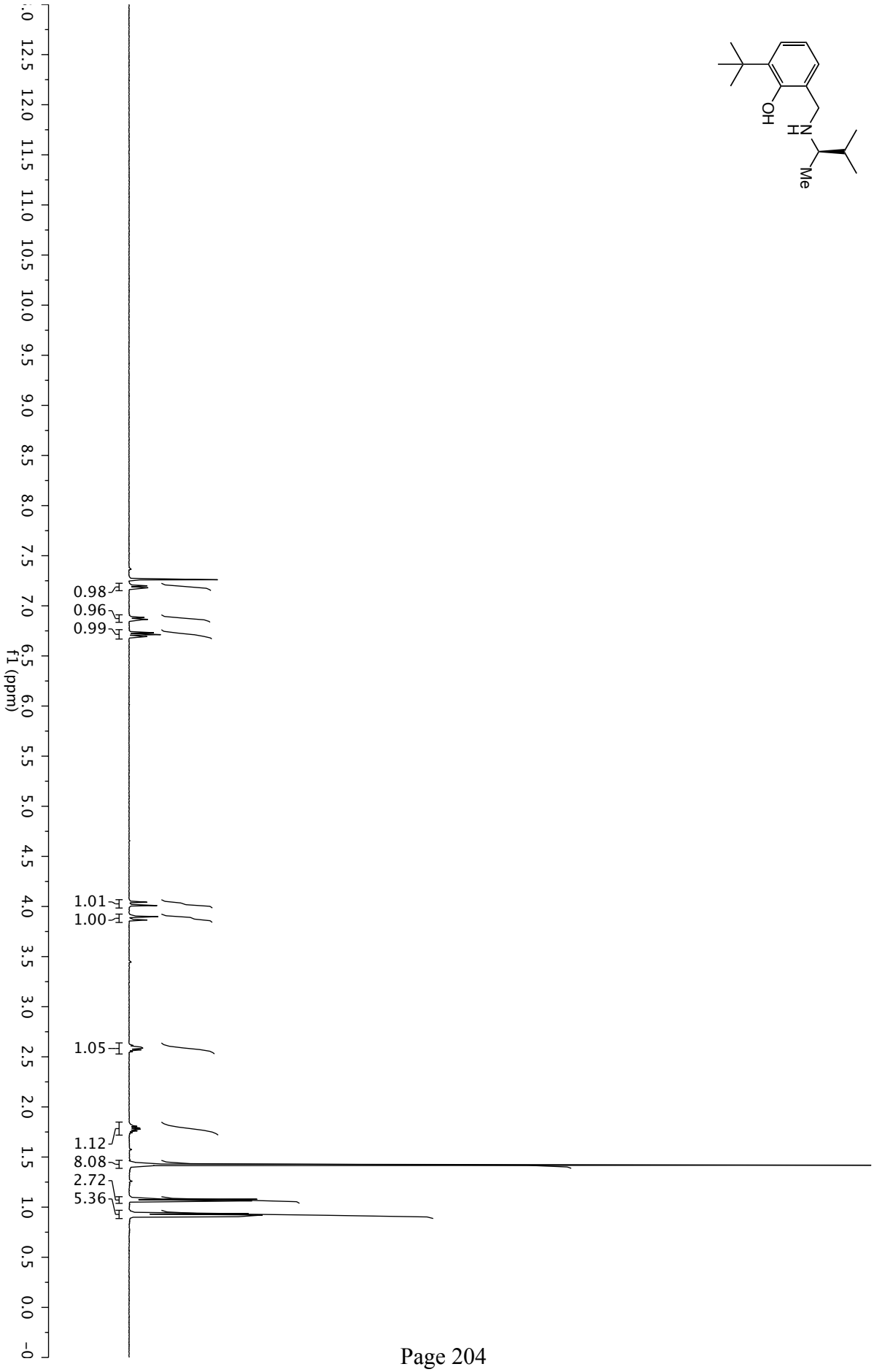

t-Bu
OH
N
H
i-Pr
O
N
0.61
1.01
0.98
1.00
1.00
1.07
2.03
2.11
1.03
0.63
5.21
9.47
3.01
3.01

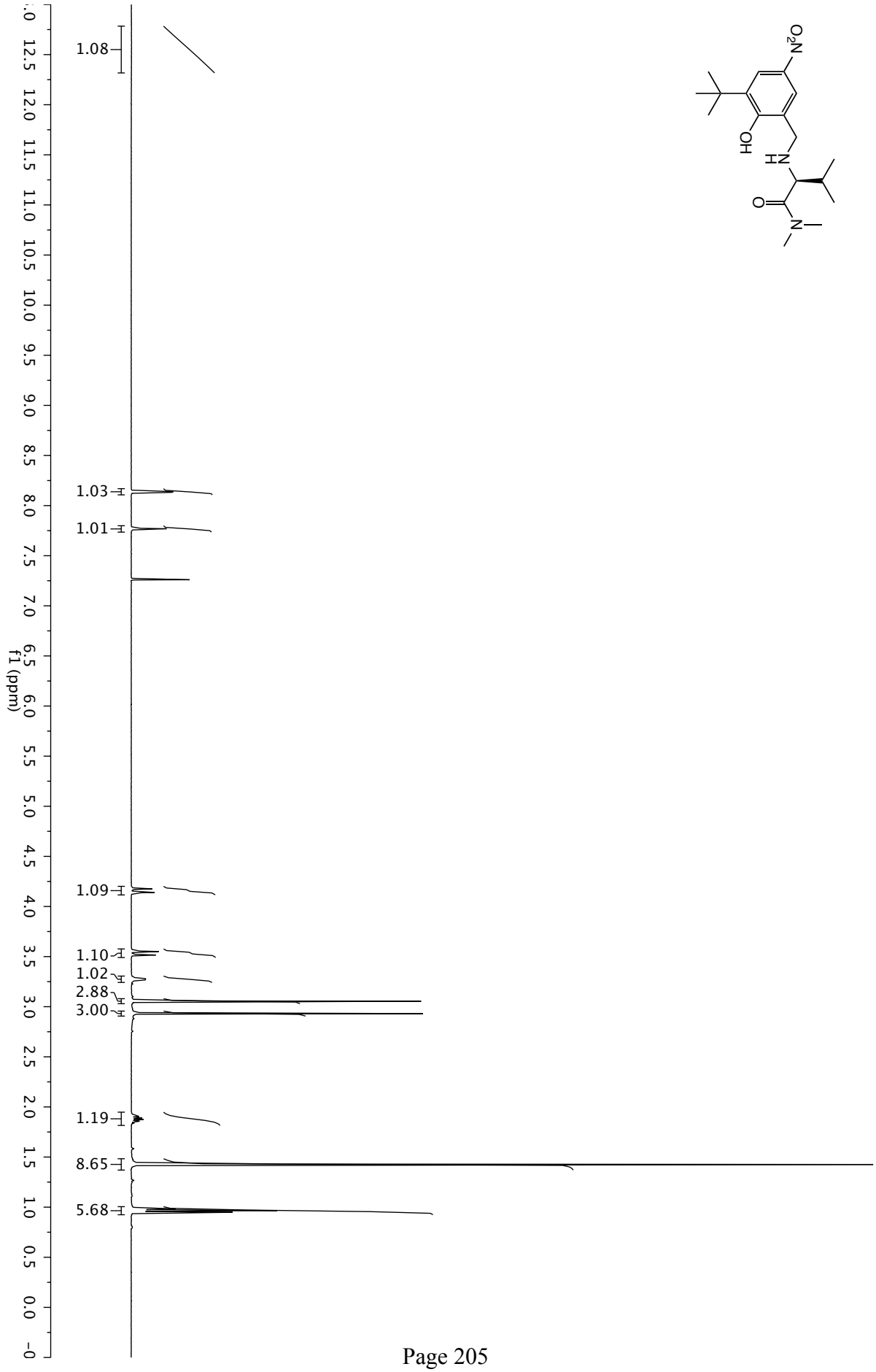

t-Bu
OH
N
H
t-Bu
O
NMe2
1.01
1.15
0.99
1.00
1.17
1.12
1.13
2.88
2.93
0.96
8.92
8.87

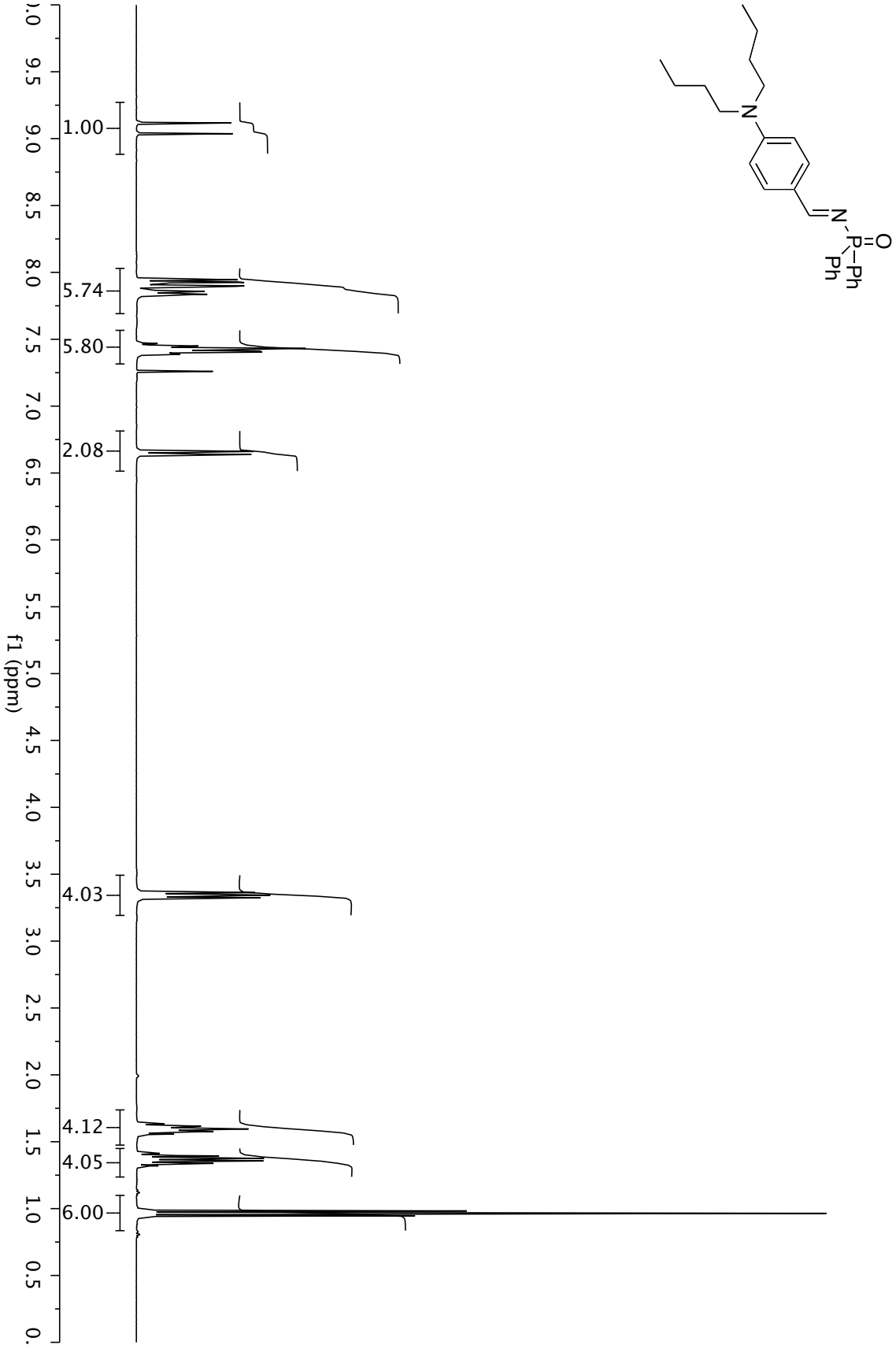

f1 (ppm)
0.61
1.89
1.97
1.91
1.87
0.99
0.99
0.99
1.00
1.05
0.67
1.03
9.26
2.97
2.99
OH
N
H
O
N
H
Ph

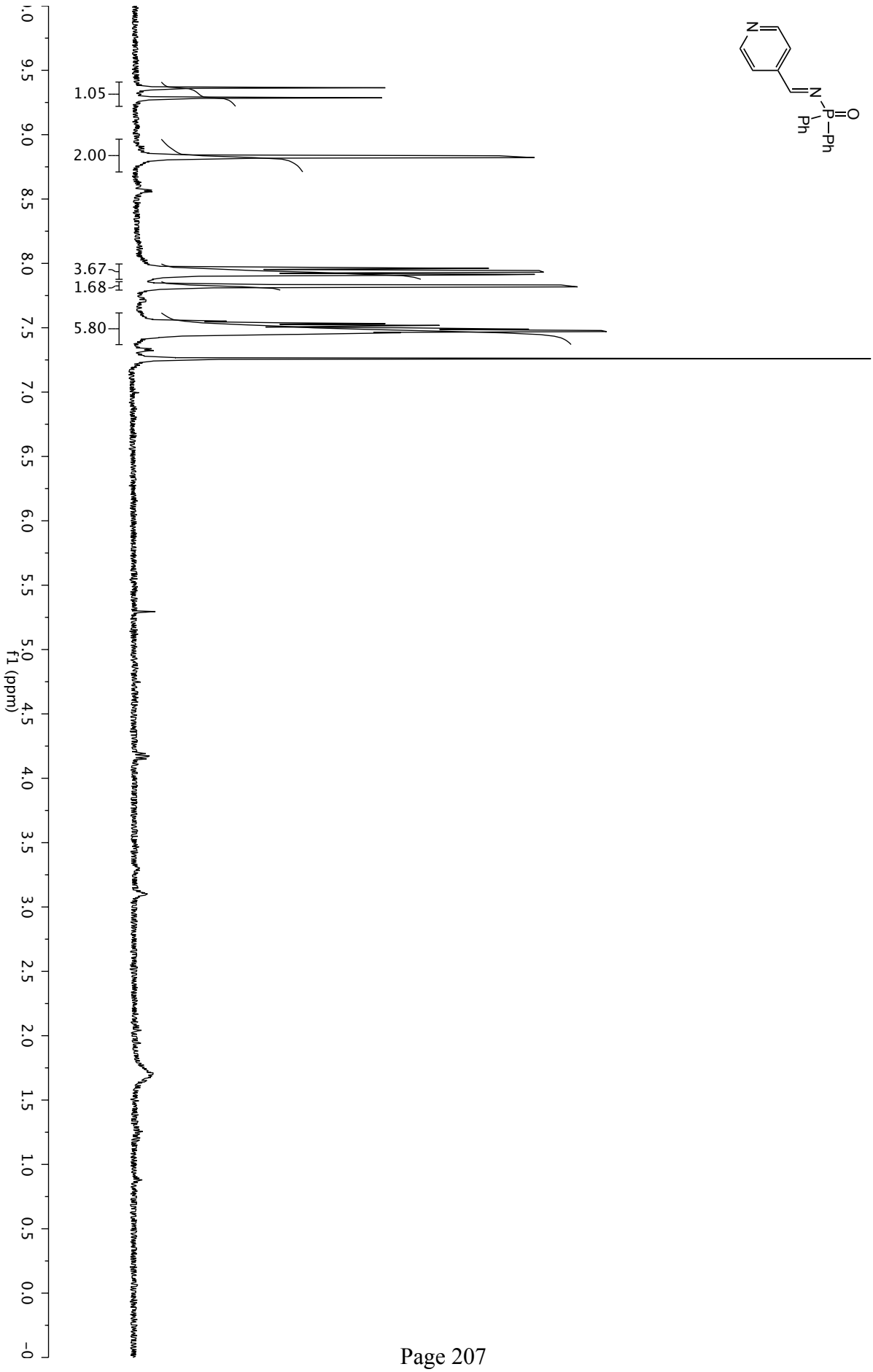

0.49
0.97
0.98
0.90
0.99
1.00
1.03
0.96
2.65
2.66
1.09
5.40
f1 (ppm)
OH
HN
O
N

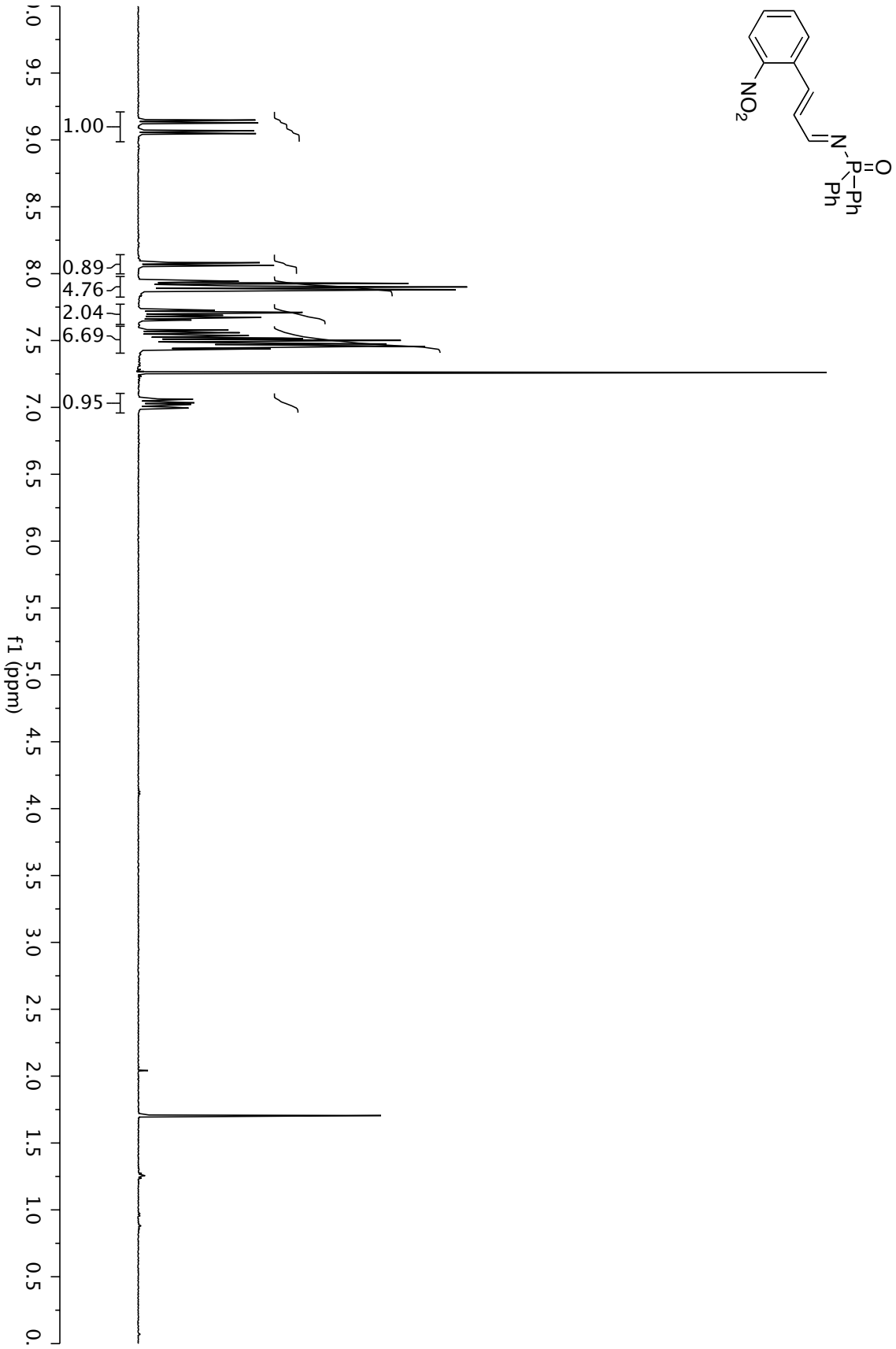

Me
OH
N
H
O
N
1.33
1.03
1.04
1.09
1.09
1.10
1.03
2.84
2.85
2.93
1.20
5.80
f1 (ppm)

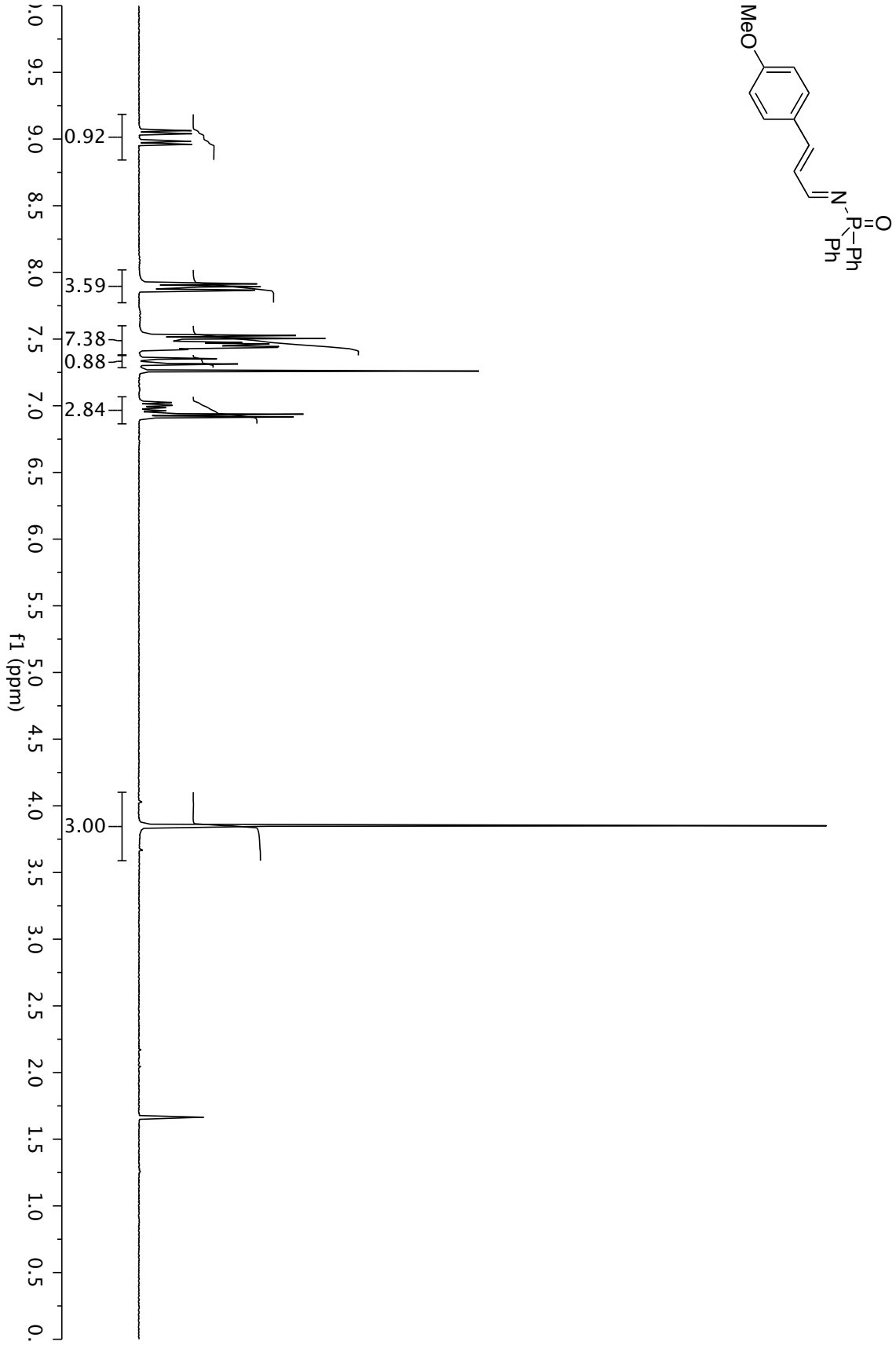

OH
N
H
Me
0.98
0.96
0.99
1.01
1.00
1.05
1.12
8.08
2.72
5.36
f1 (ppm)

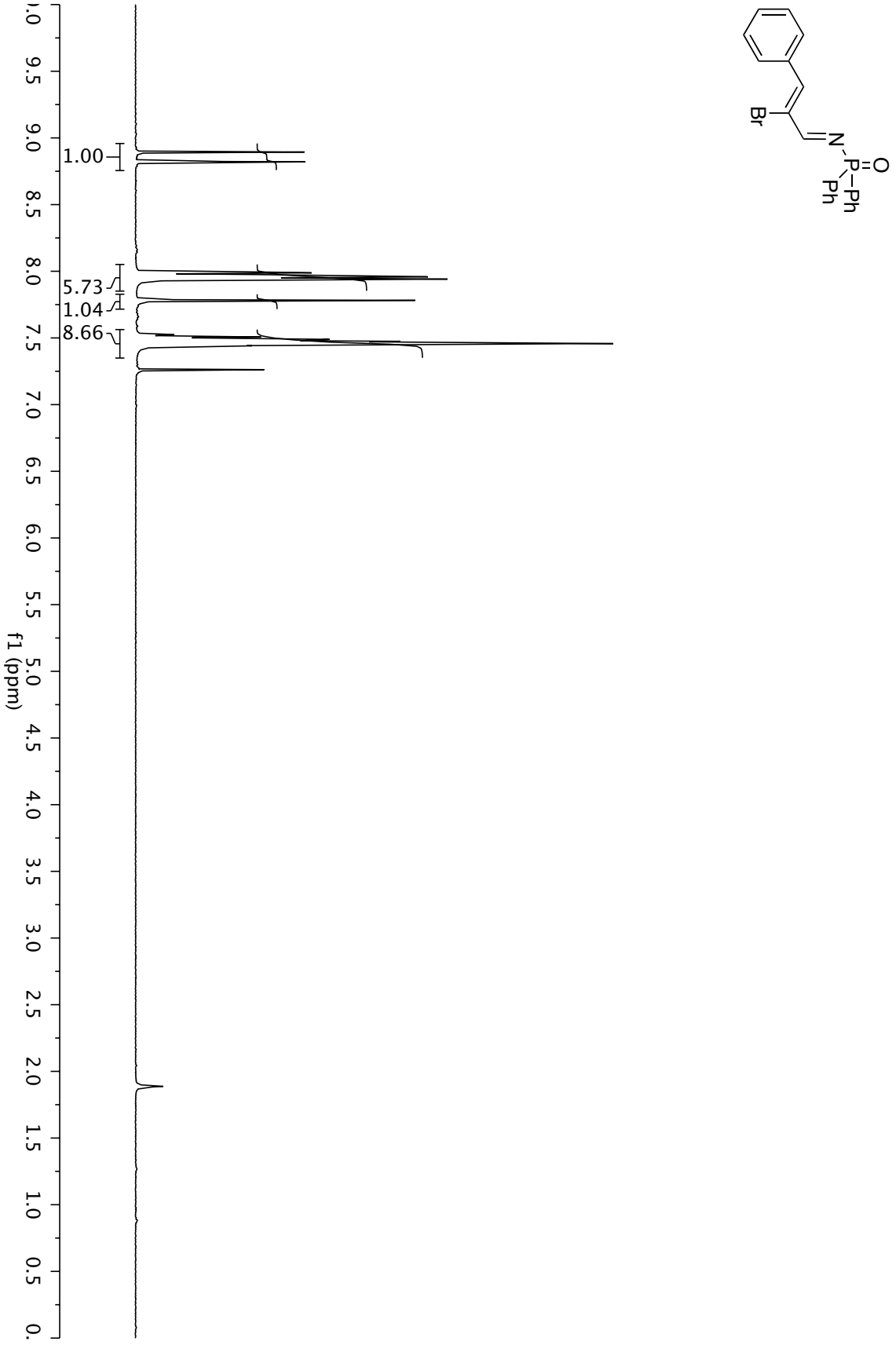

1.08
1.03
1.01
1.09
1.10
1.02
2.88
3.00
1.19
8.65
5.68
f1 (ppm)
O2N
OH
HN
O
N

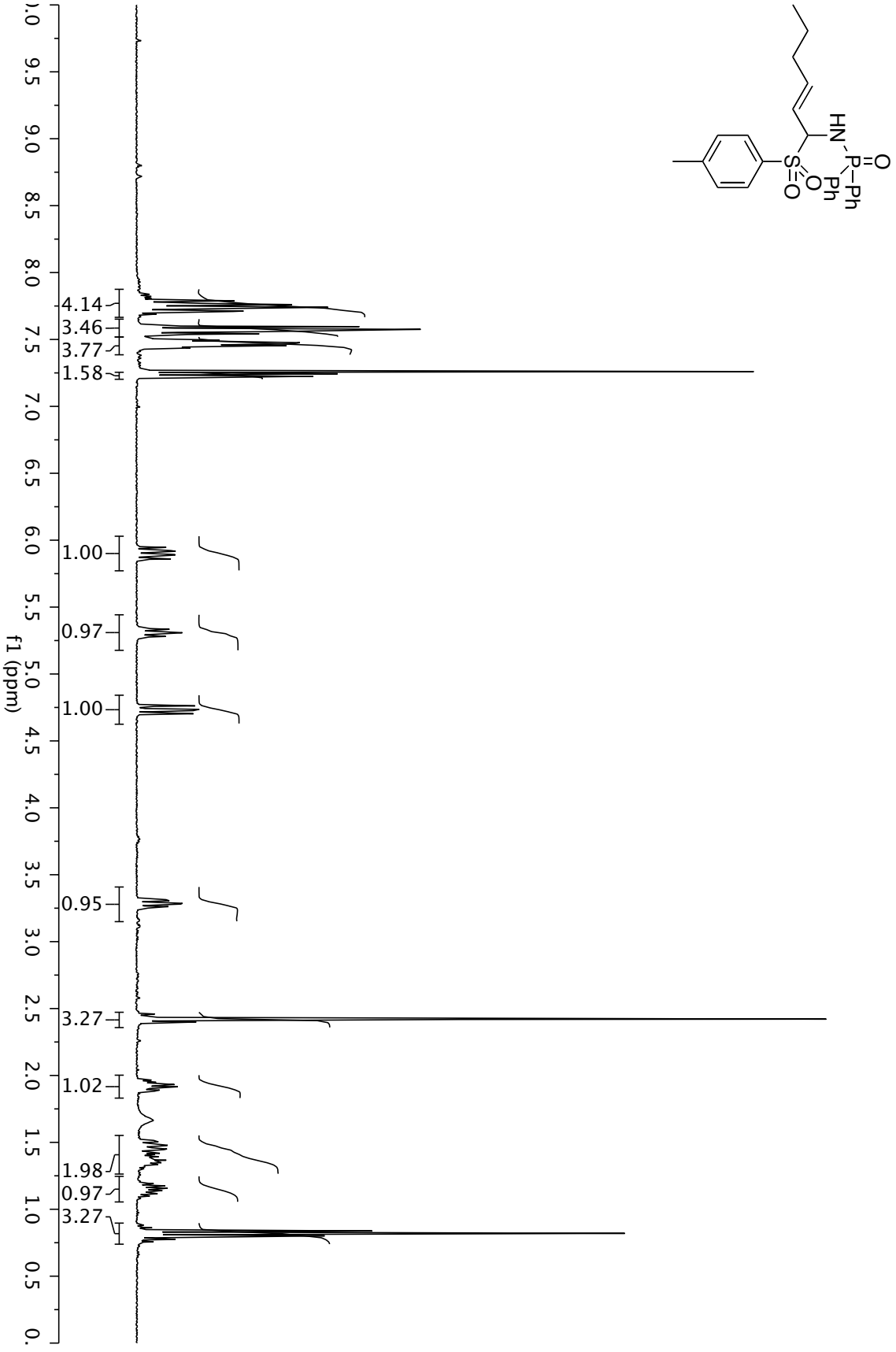

1.00
5.74
5.80
2.08
4.03
4.12
4.05
6.00
f1 (ppm)
N
N
O
P
Ph
Ph

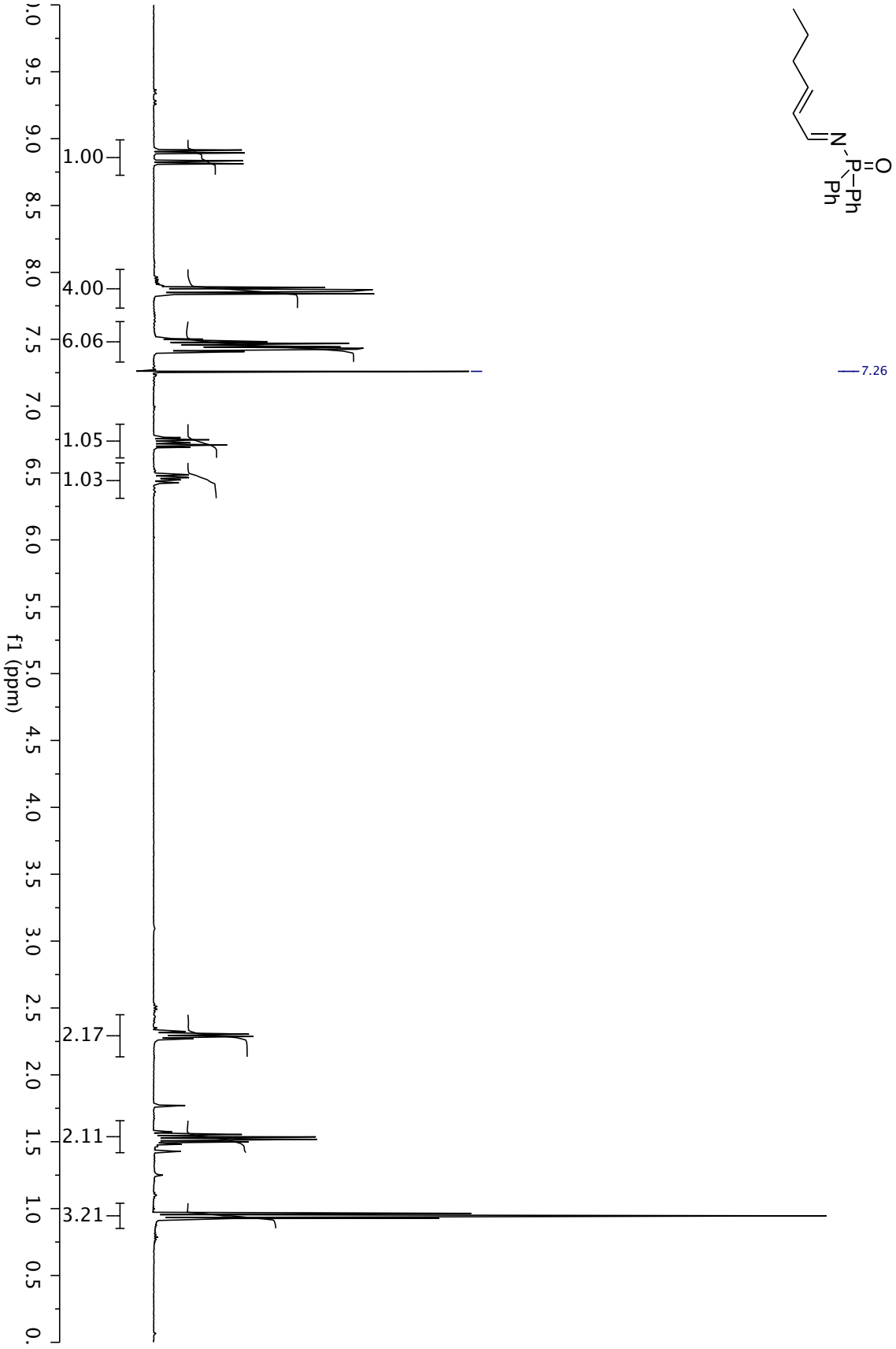

1.05
2.00
3.67
1.68
5.80
f1 (ppm)

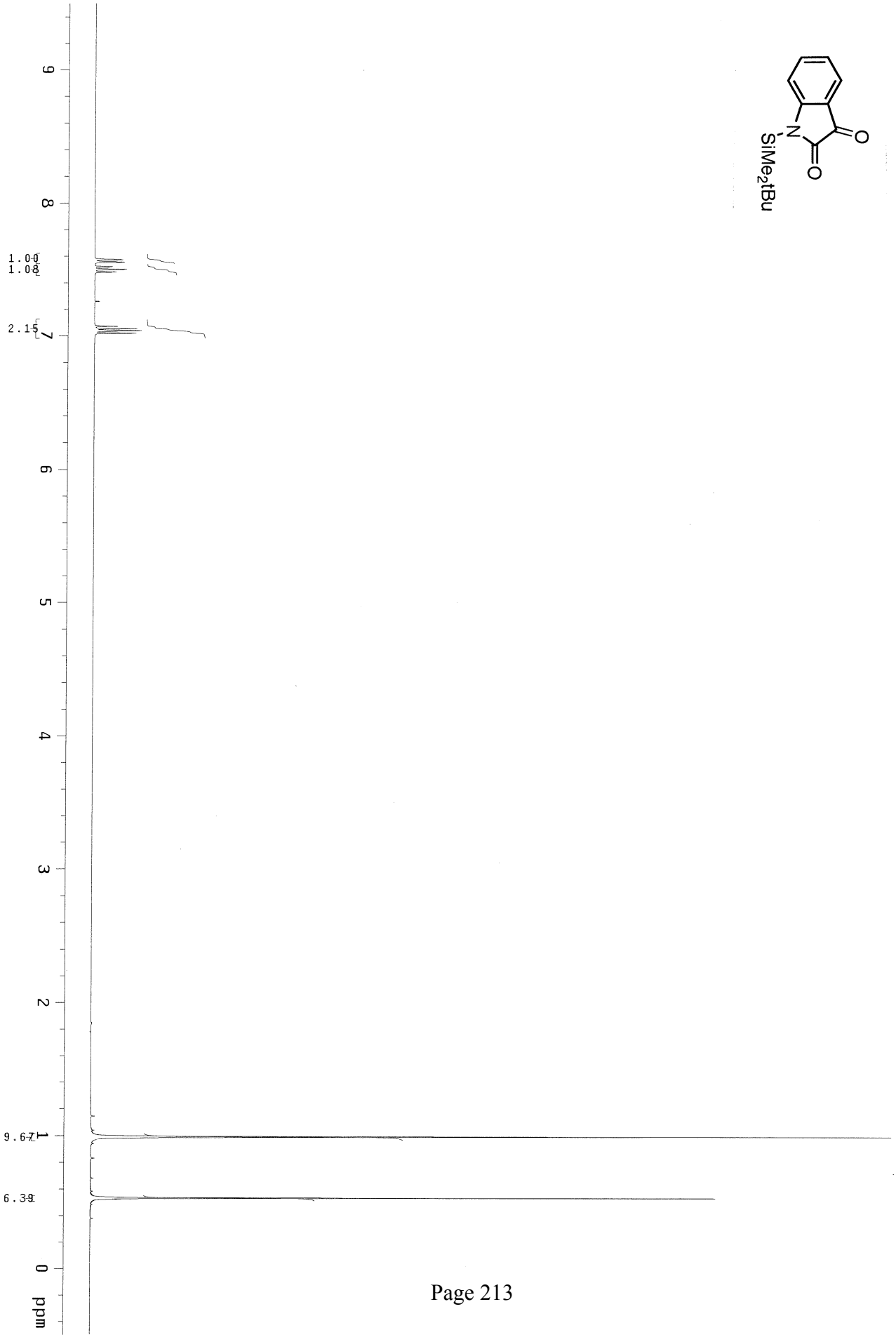

1.00
0.89
4.76
2.04
6.69
0.95
f1 (ppm)
NO2
N
O
P
Ph
Ph

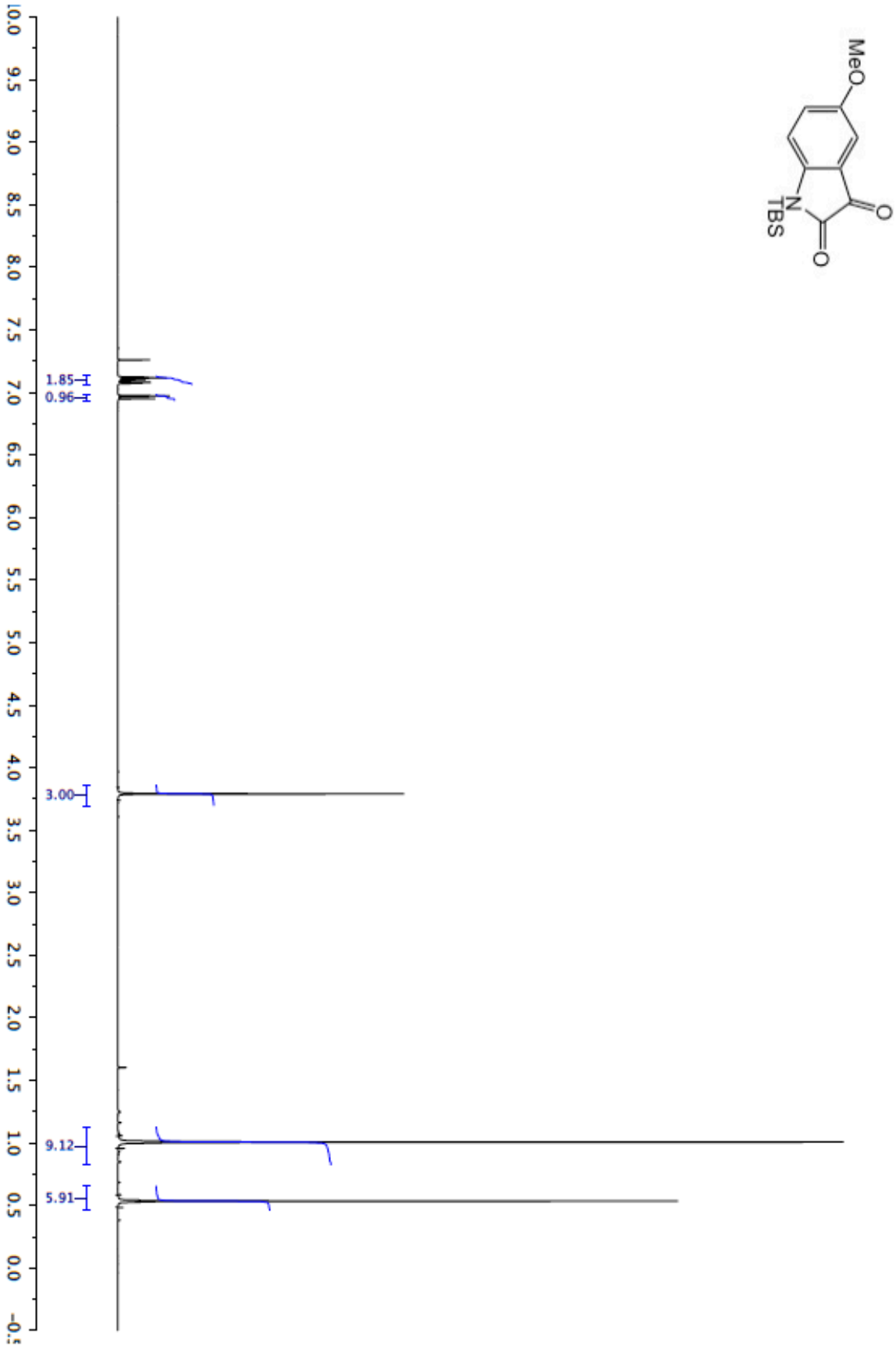

MeO
N
P
O
Ph
Ph
0.92
3.59
7.38
0.88
2.84
3.00
f1 (ppm)

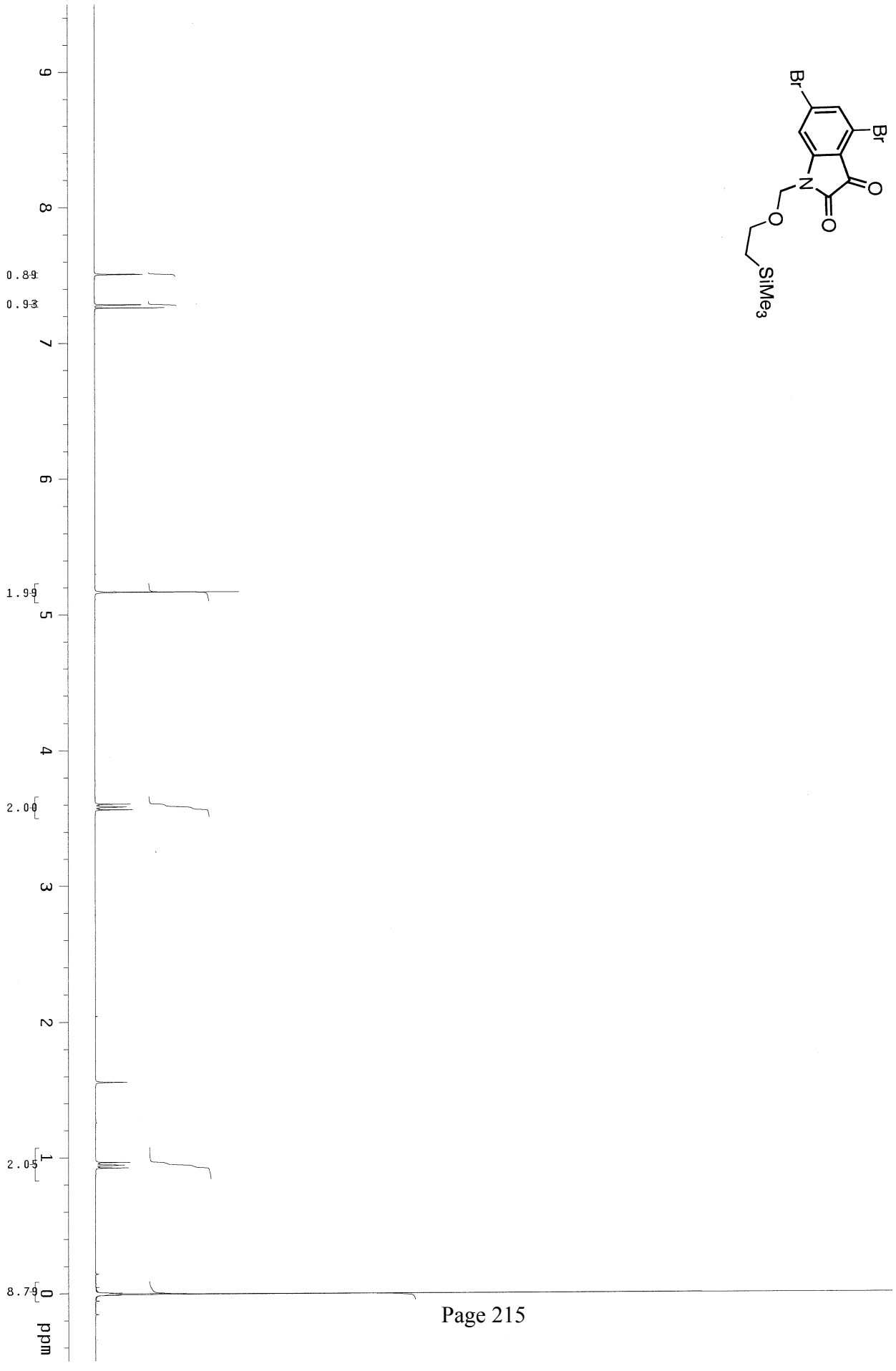

1.00
5.73
1.04
8.66
f1 (ppm)
Br
N
P
O
Ph
Ph

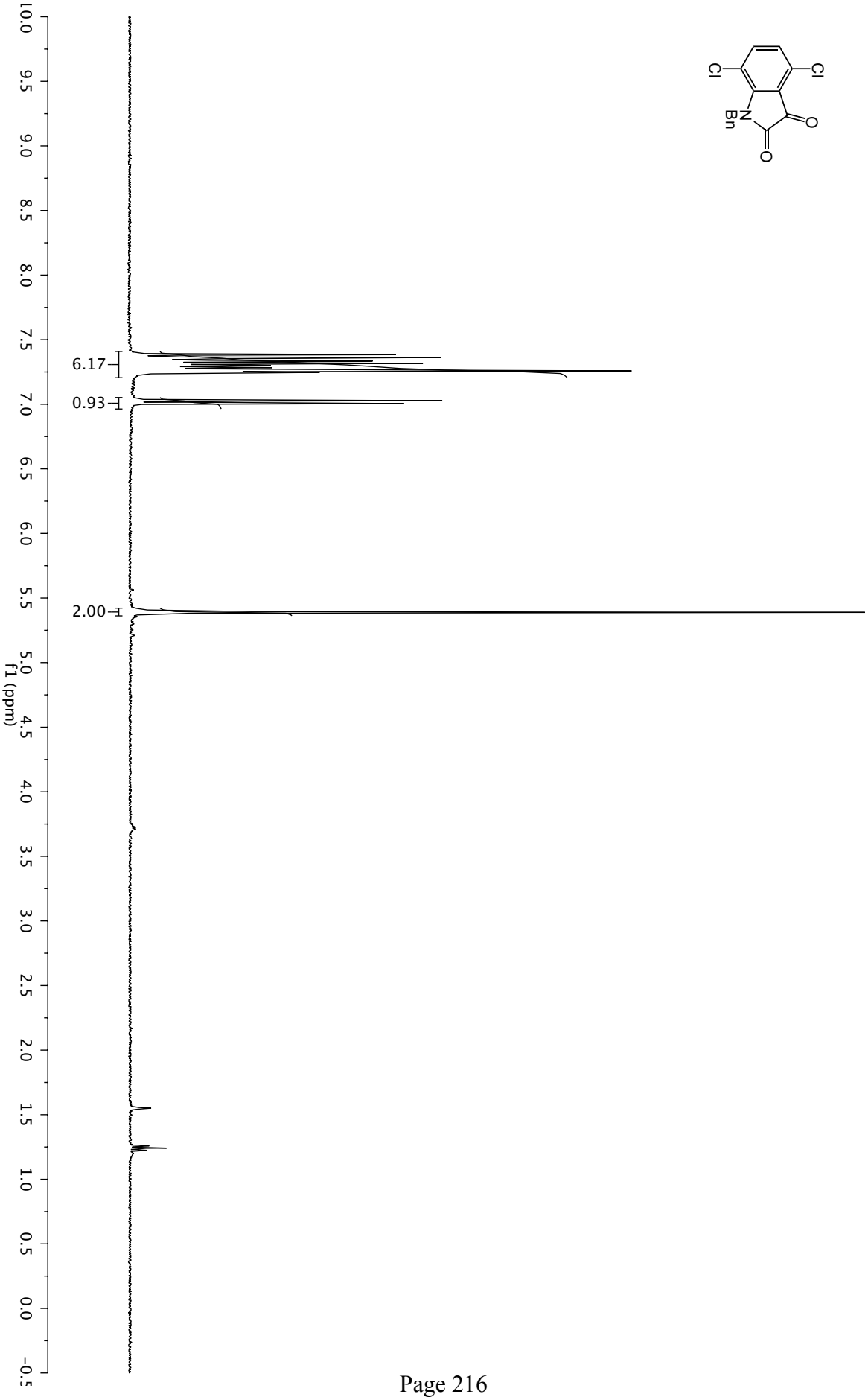

4.14
3.46
3.77
1.58
1.00
0.97
1.00
0.95
3.27
1.02
1.98
0.97
3.27
f1 (ppm)
HN
P
Ph
Ph
O
S
O
O

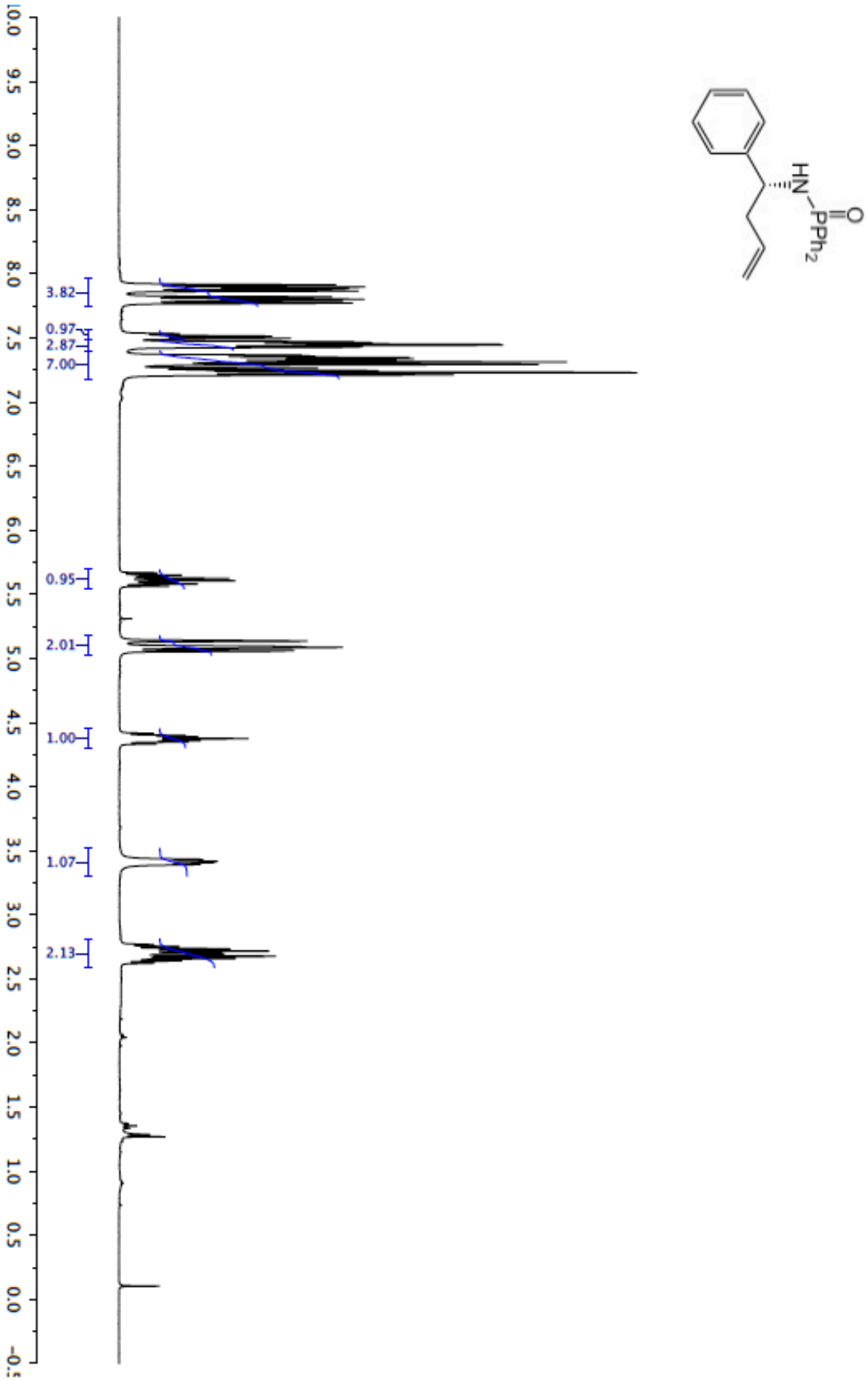

1.00
4.00
6.06
1.05
1.03
2.17
2.11
3.21
7.26
f1 (ppm)

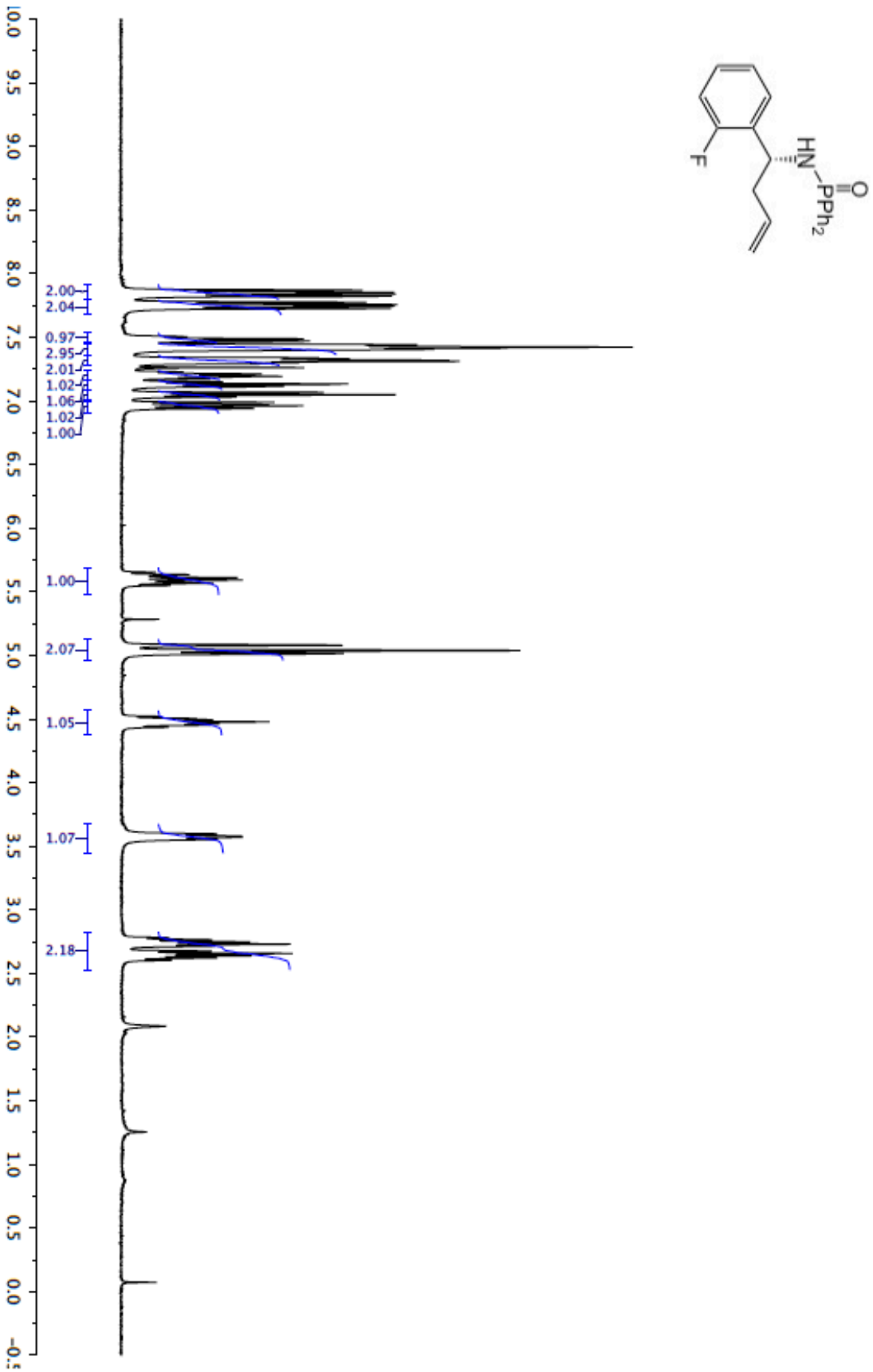

1.00
1.08
2.15
9.67
6.39
9
8
7
6
5
4
3
2
1
0
ppm
N
SiMe2tBu
O
O

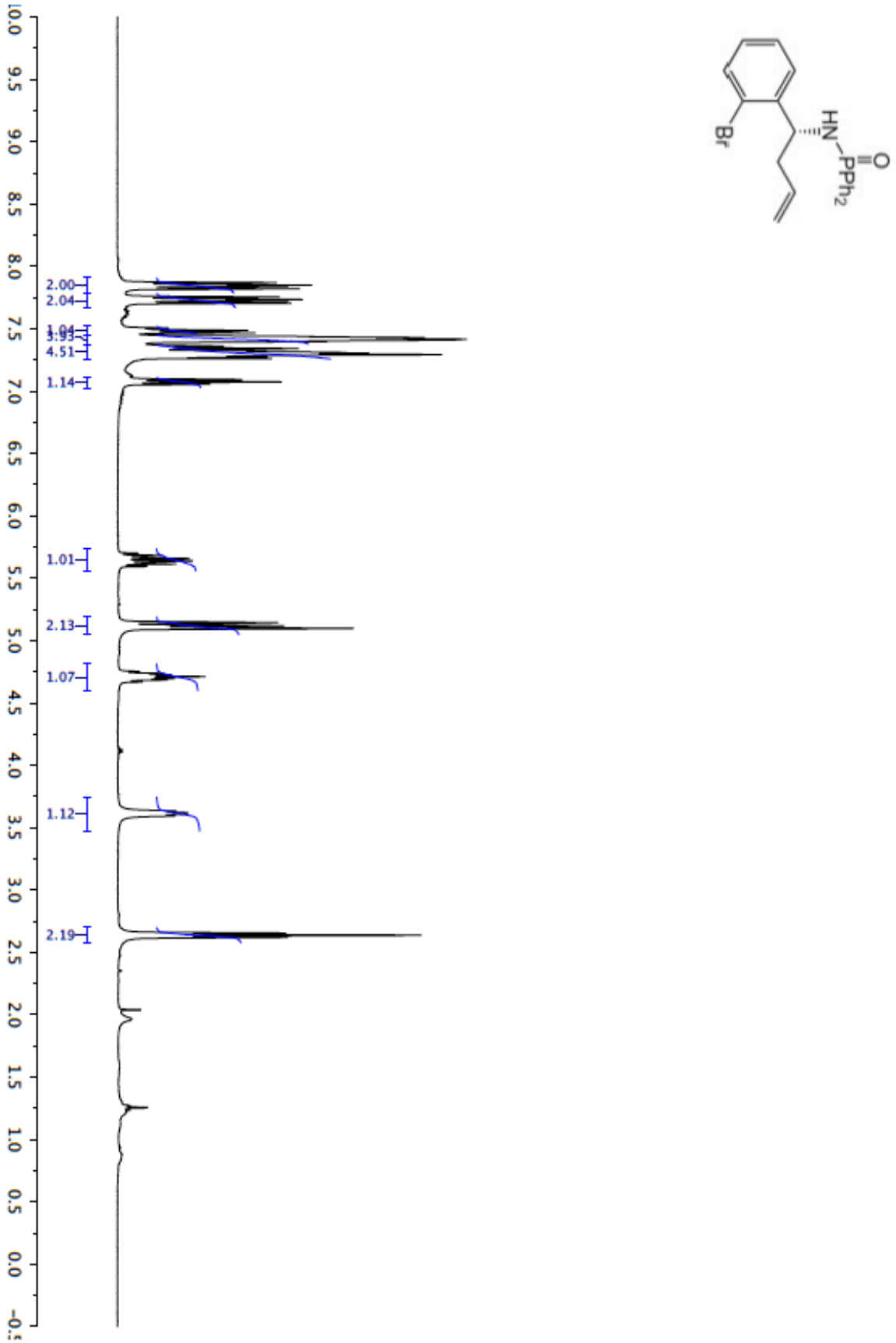

MeO
N
TBS
O
O
1.85
0.96
3.00
9.12
5.91

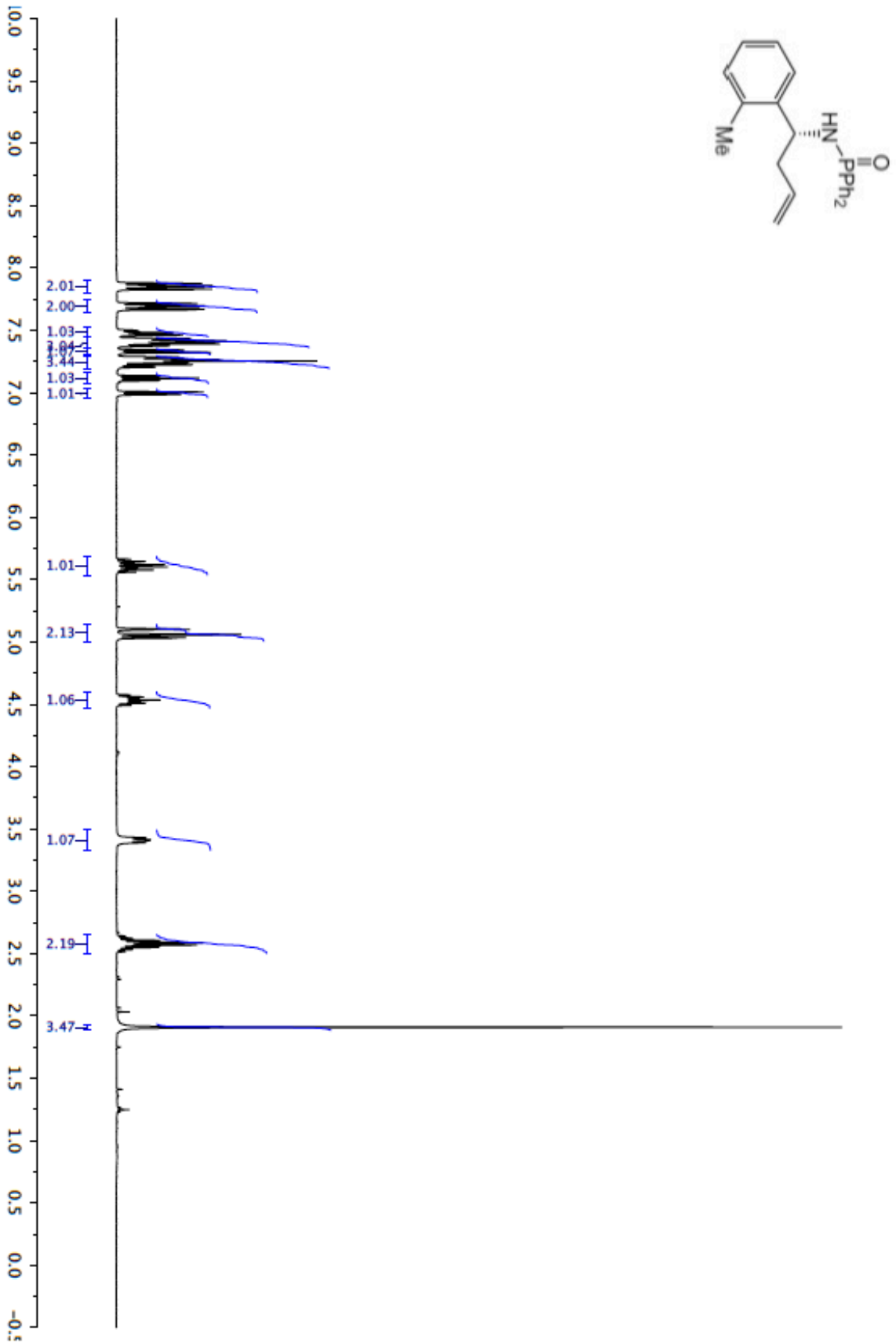

Br
Br
O
N
O
O
SiMe3
0.89
0.93
1.99
2.00
2.05
8.79
9
8
7
6
5
4
3
2
1
0
ppm

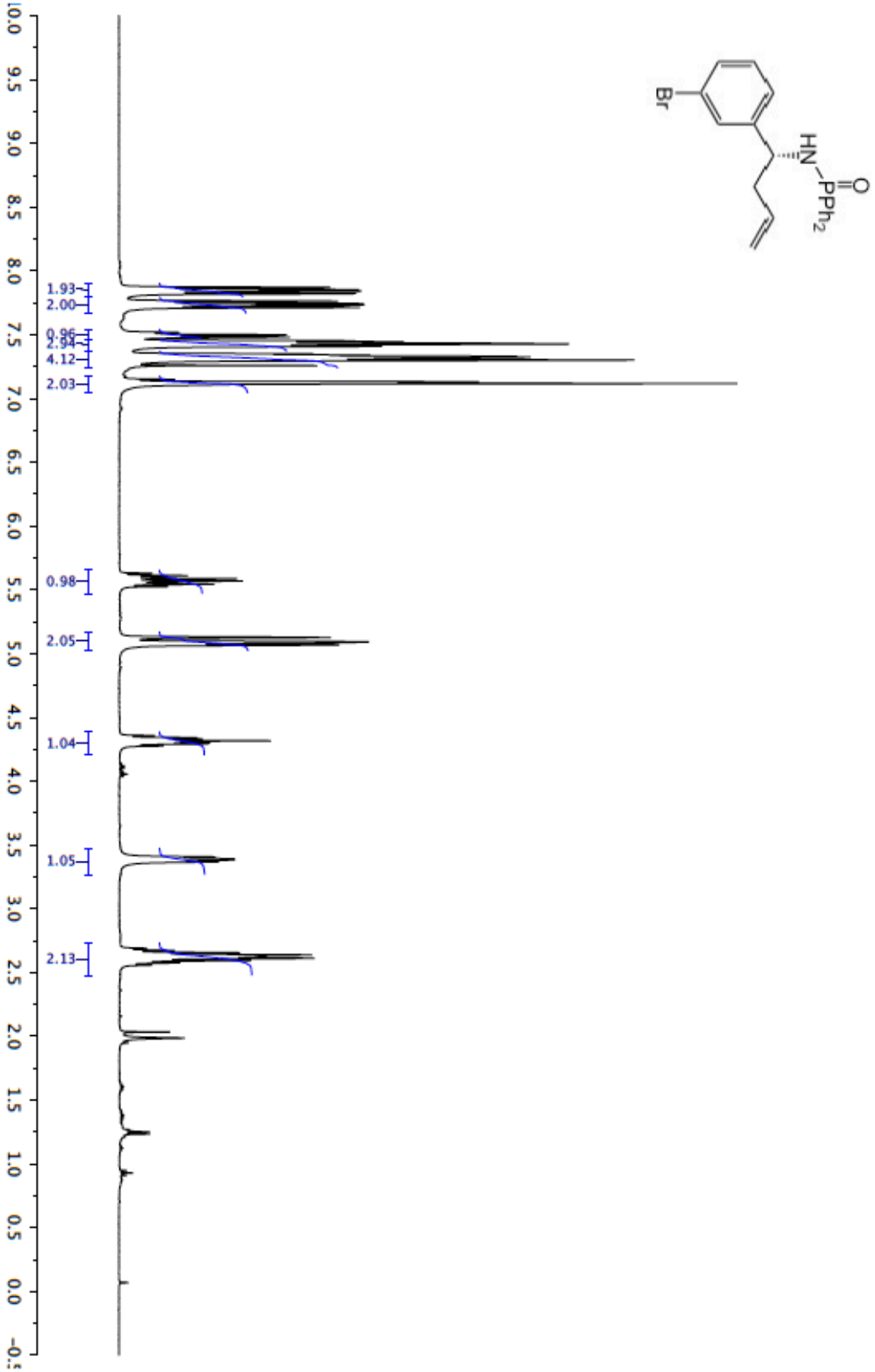

Cl
Cl
N
Bn
O
O
6.17
0.93
2.00
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

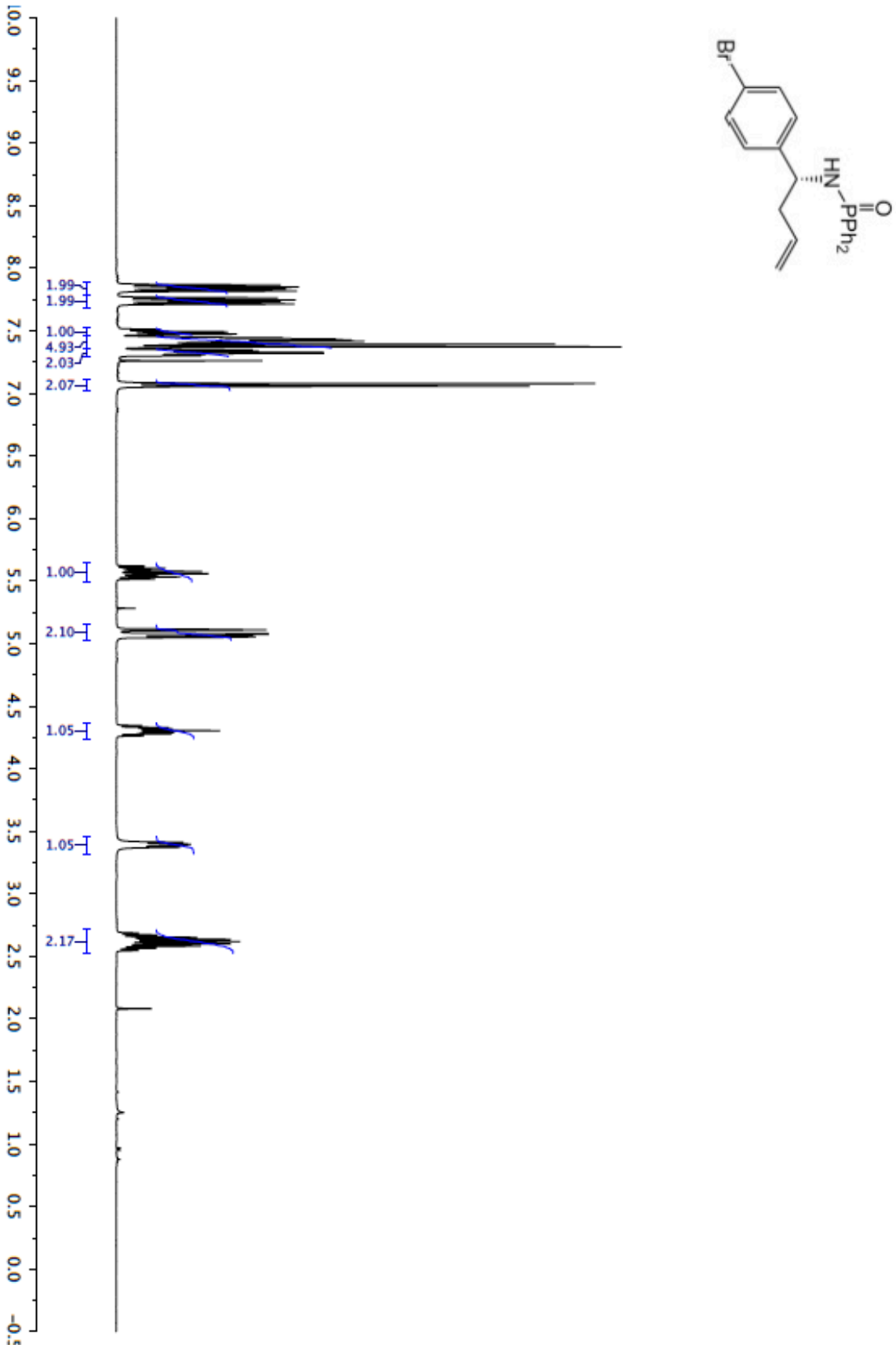

3.82
0.97
2.87
7.00
0.95
2.01
1.00
1.07
2.13
HN
O
PPh2

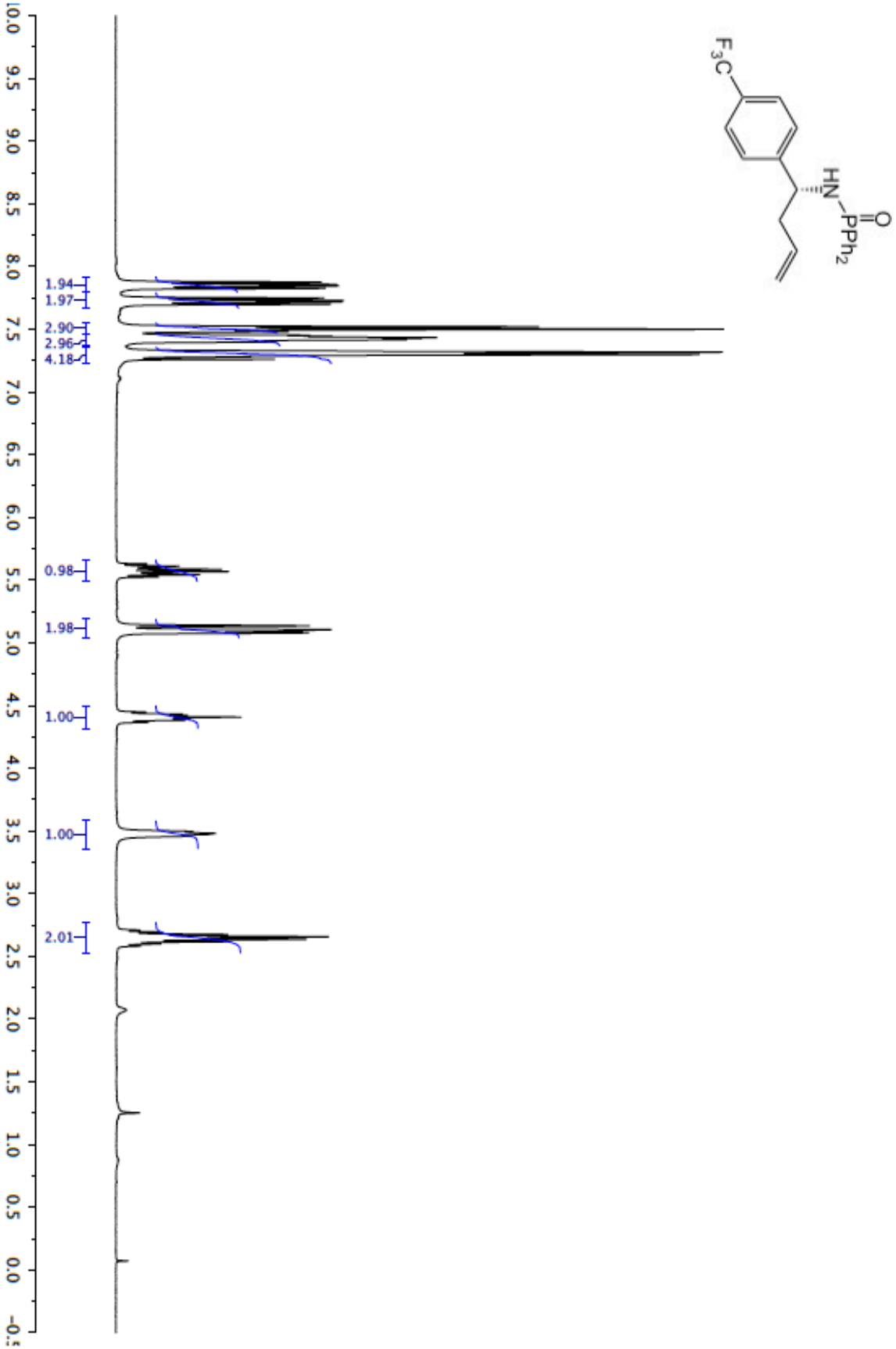

F
HN
O
PPh2
2.00
2.04
0.97
2.95
2.01
1.02
1.06
1.02
1.00
1.00
2.07
1.05
1.07
2.18

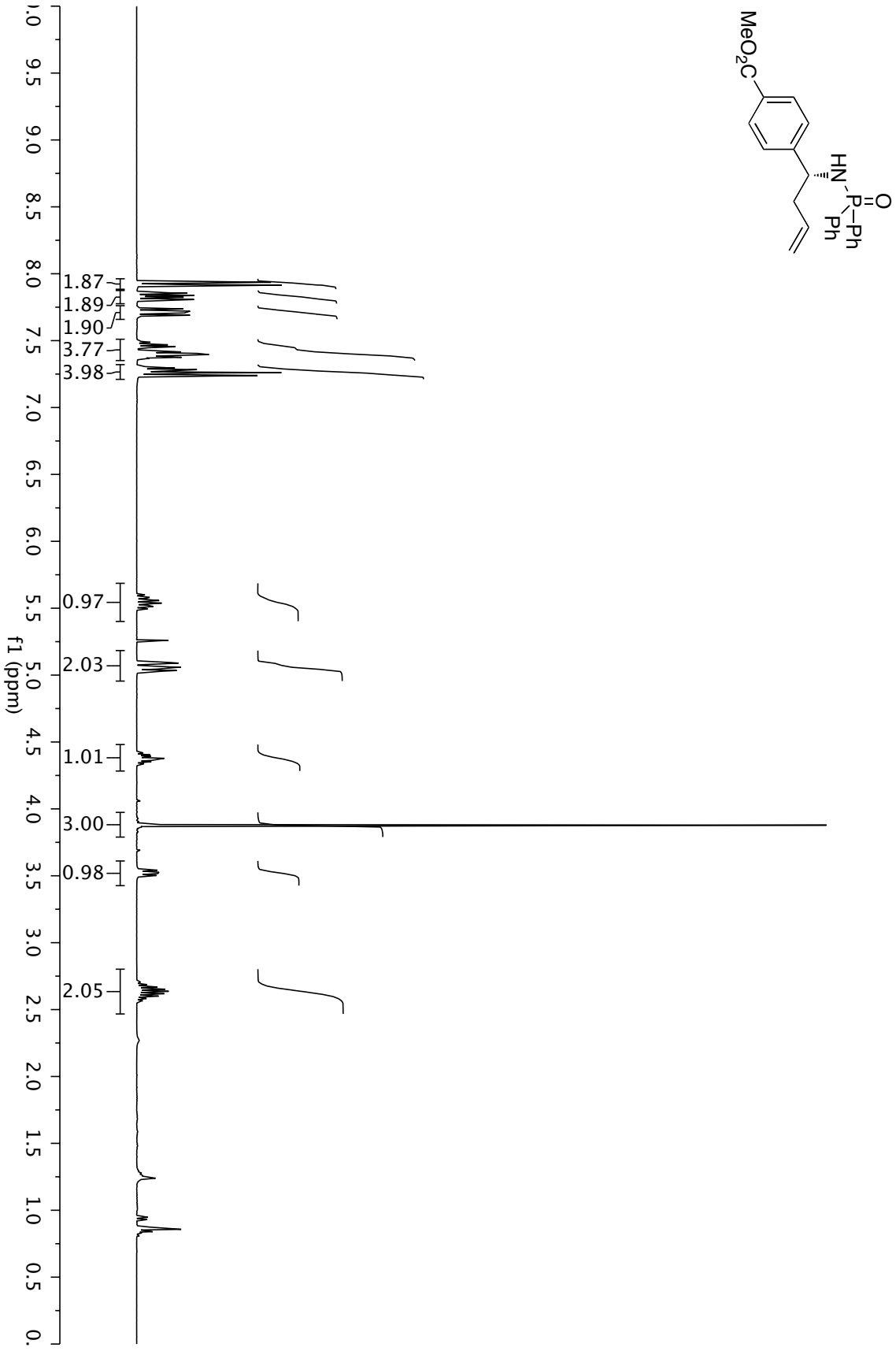

Br
HN
O
PPh2
2.00
2.04
1.04
3.93
4.51
1.14
1.01
2.13
1.07
1.12
2.19

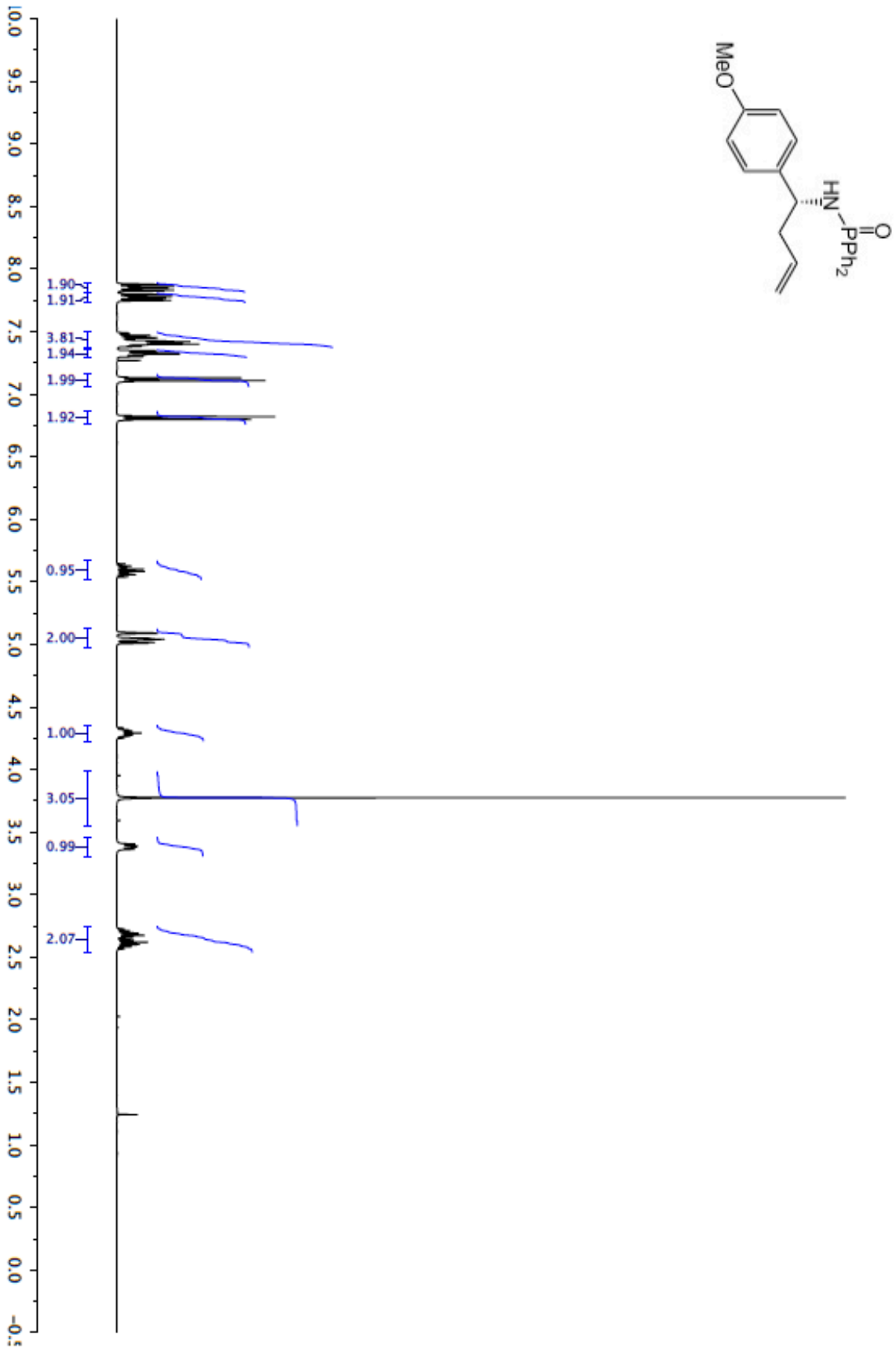

Me
HN
O
PPh2
2.01
2.00
1.03
3.44
1.03
1.01
1.01
2.13
1.06
1.07
2.19
3.47

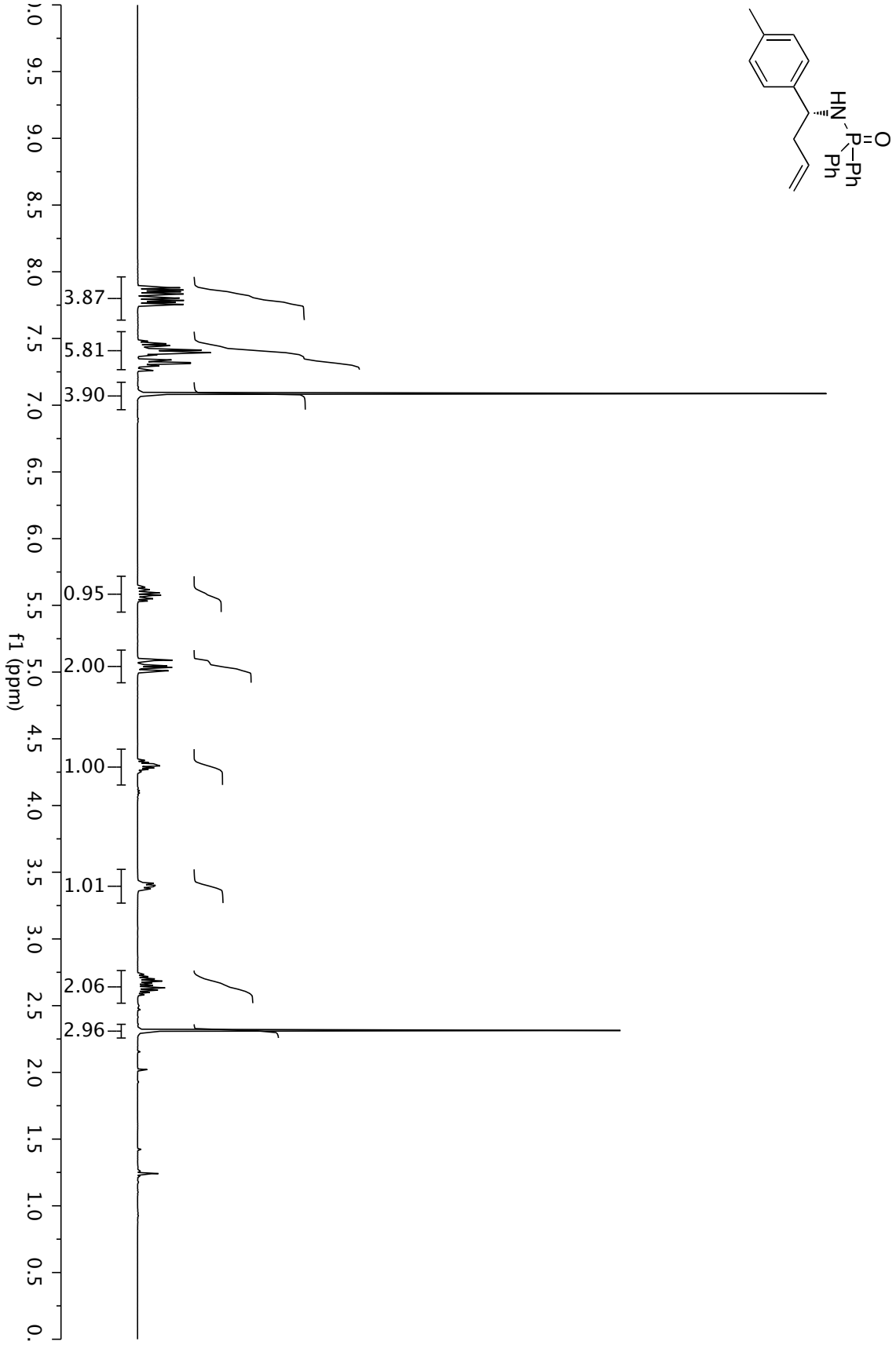

Br
HN
O
PPh2
1.93
2.00
0.96
2.04
4.12
2.03
0.98
2.05
1.04
1.05
2.13

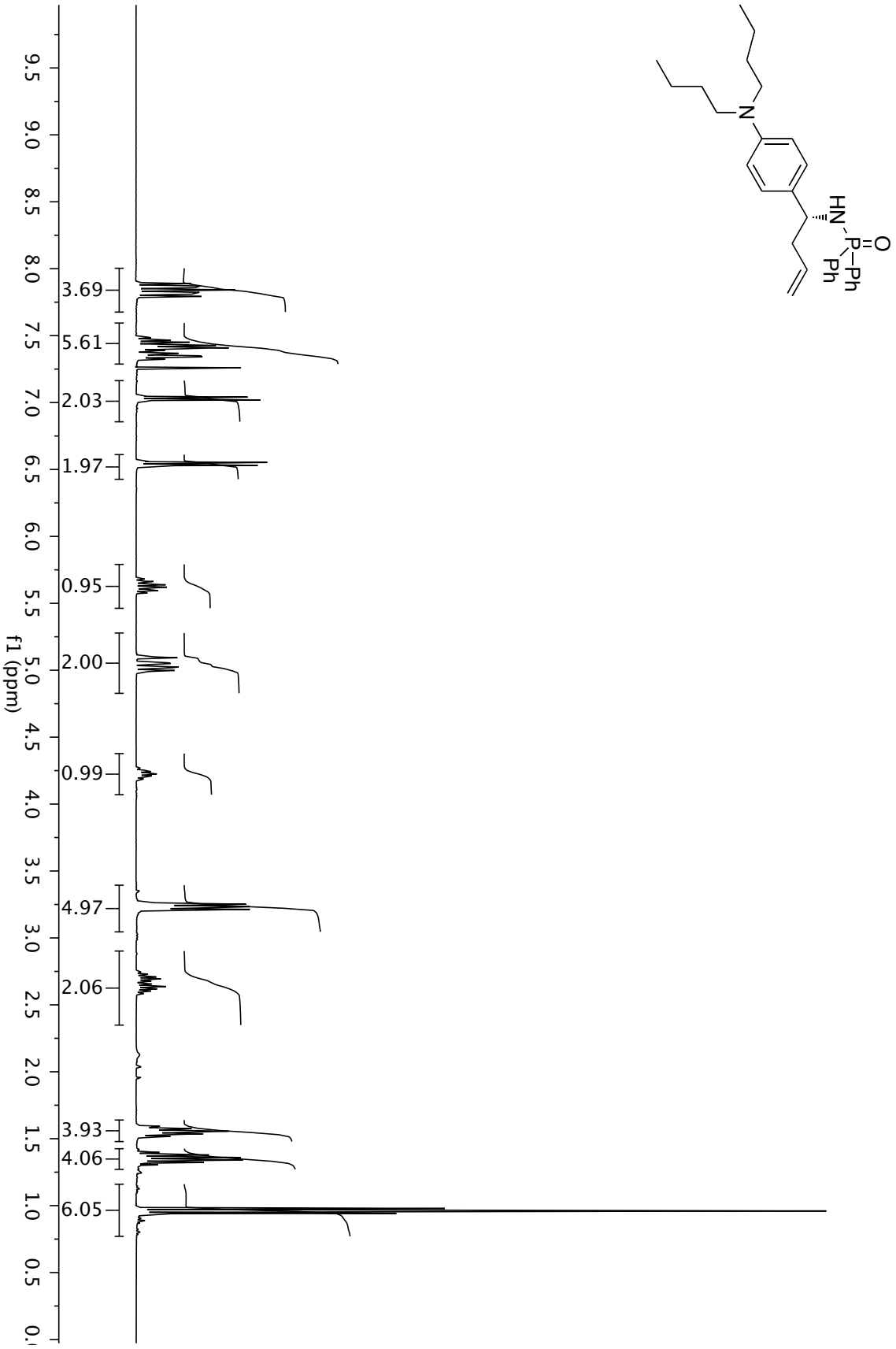

Br
HN
O
PPh2
1.99
1.99
1.00
4.93
2.03
2.07
1.00
2.10
1.05
1.05
2.17

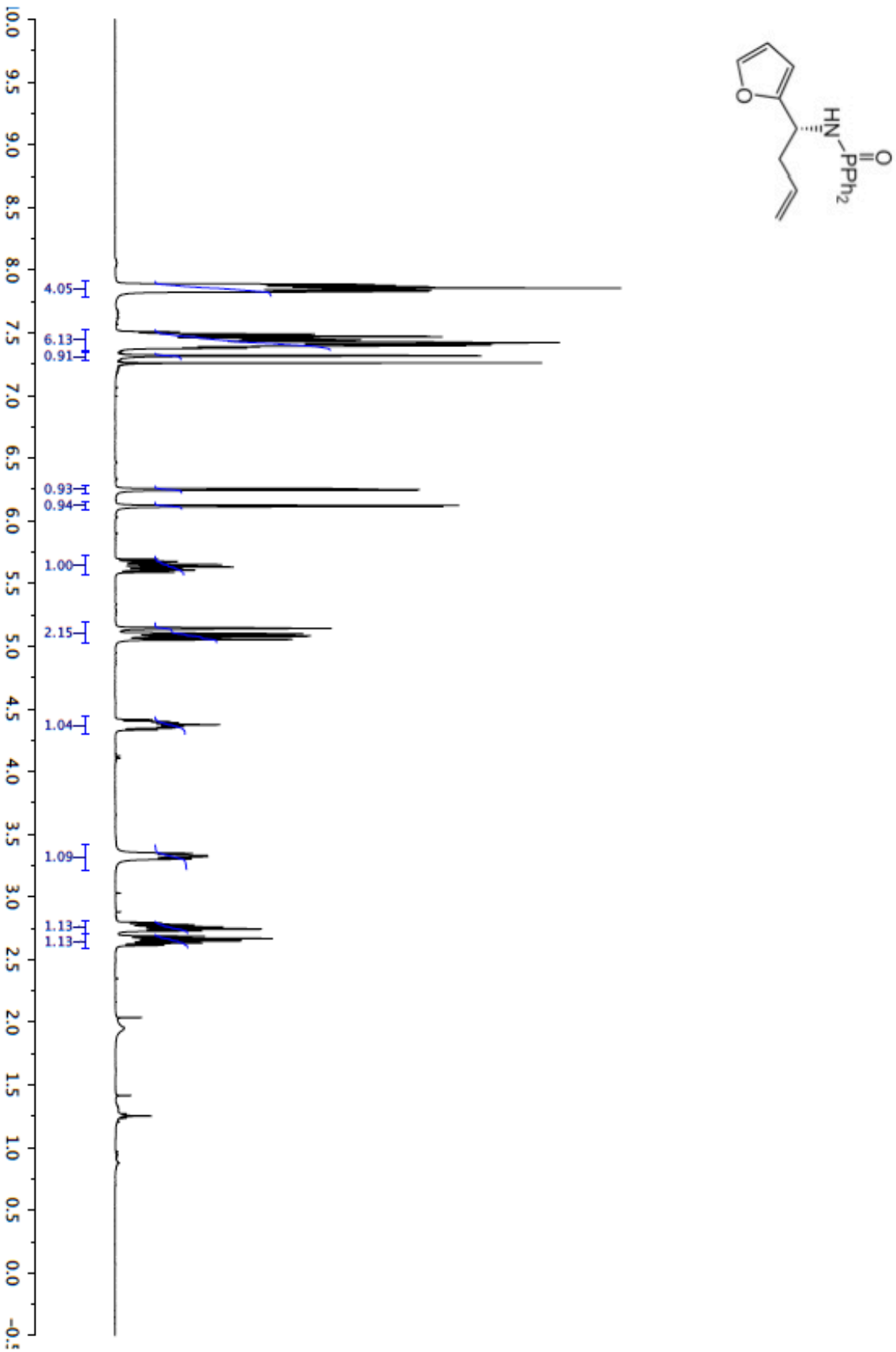

F3C
HN
O
PPh2
1.94
1.97
2.90
2.96
4.18
0.98
1.98
1.00
1.00
2.01

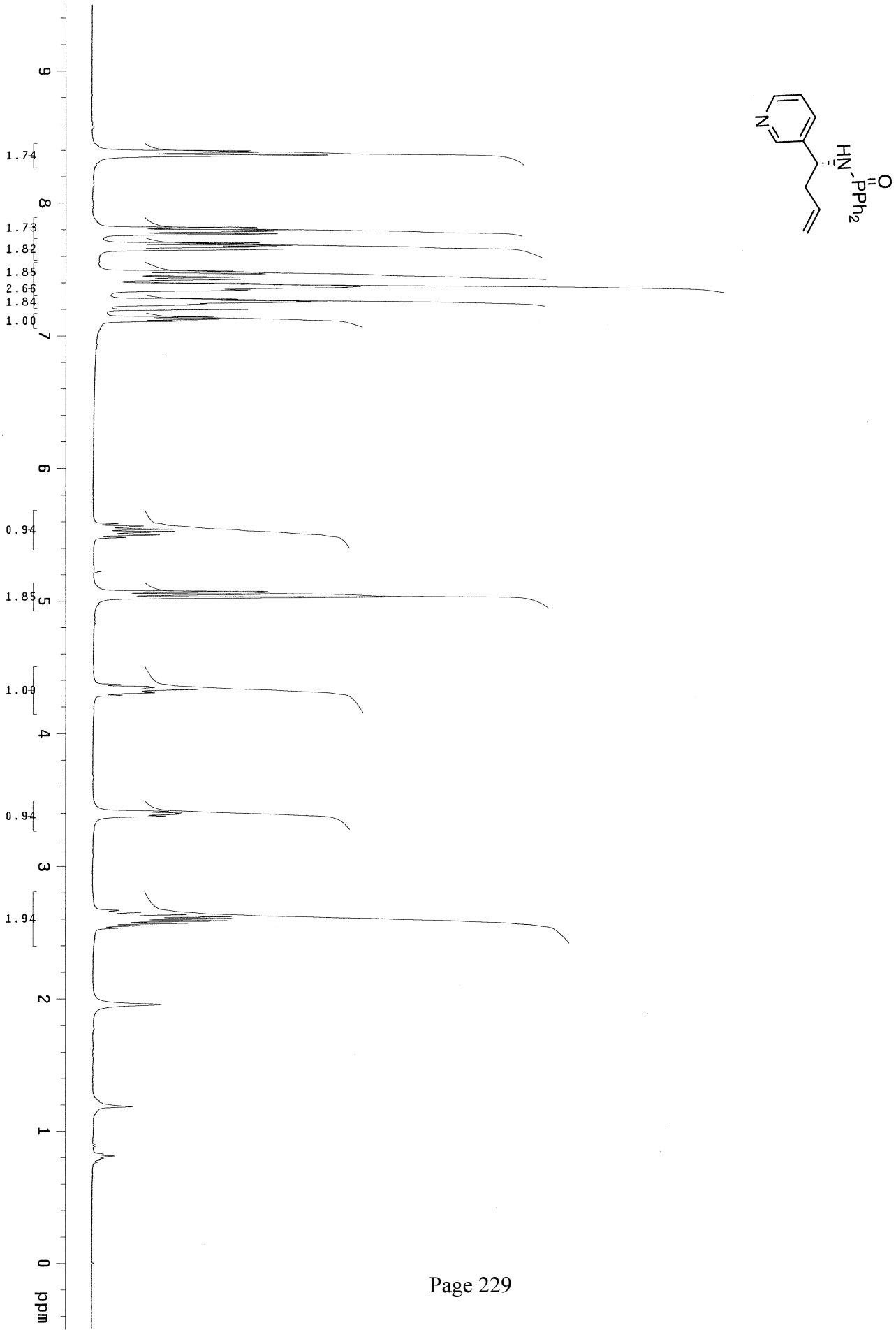

MeO2C
HN
O
P
Ph
Ph
1.87
1.89
1.90
3.77
3.98
0.97
2.03
1.01
3.00
0.98
2.05
f1 (ppm)

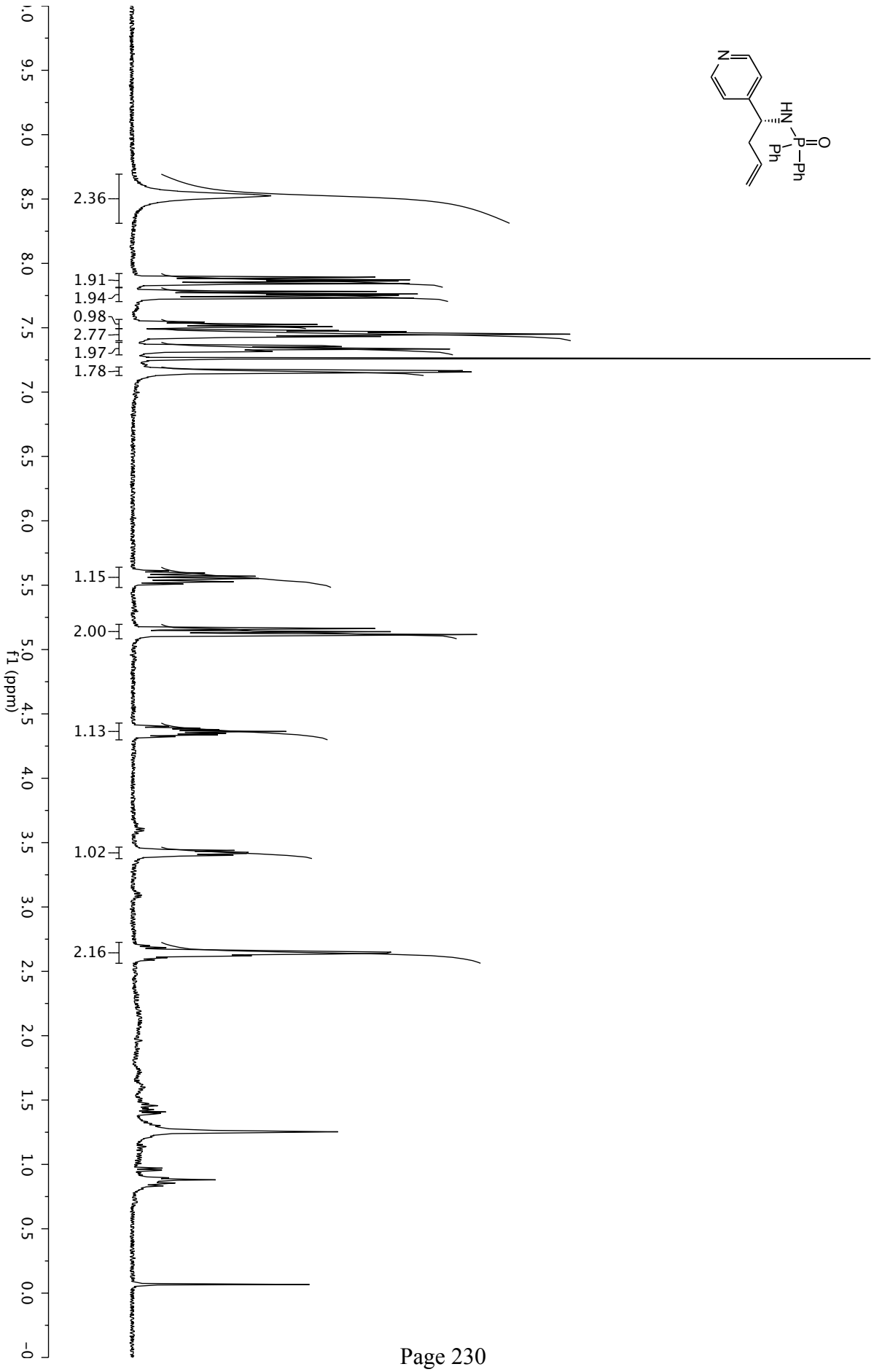

MeO
HN
O
PPh2
1.90
1.91
3.81
1.94
1.99
1.92
0.95
2.00
1.00
3.05
0.99
2.07

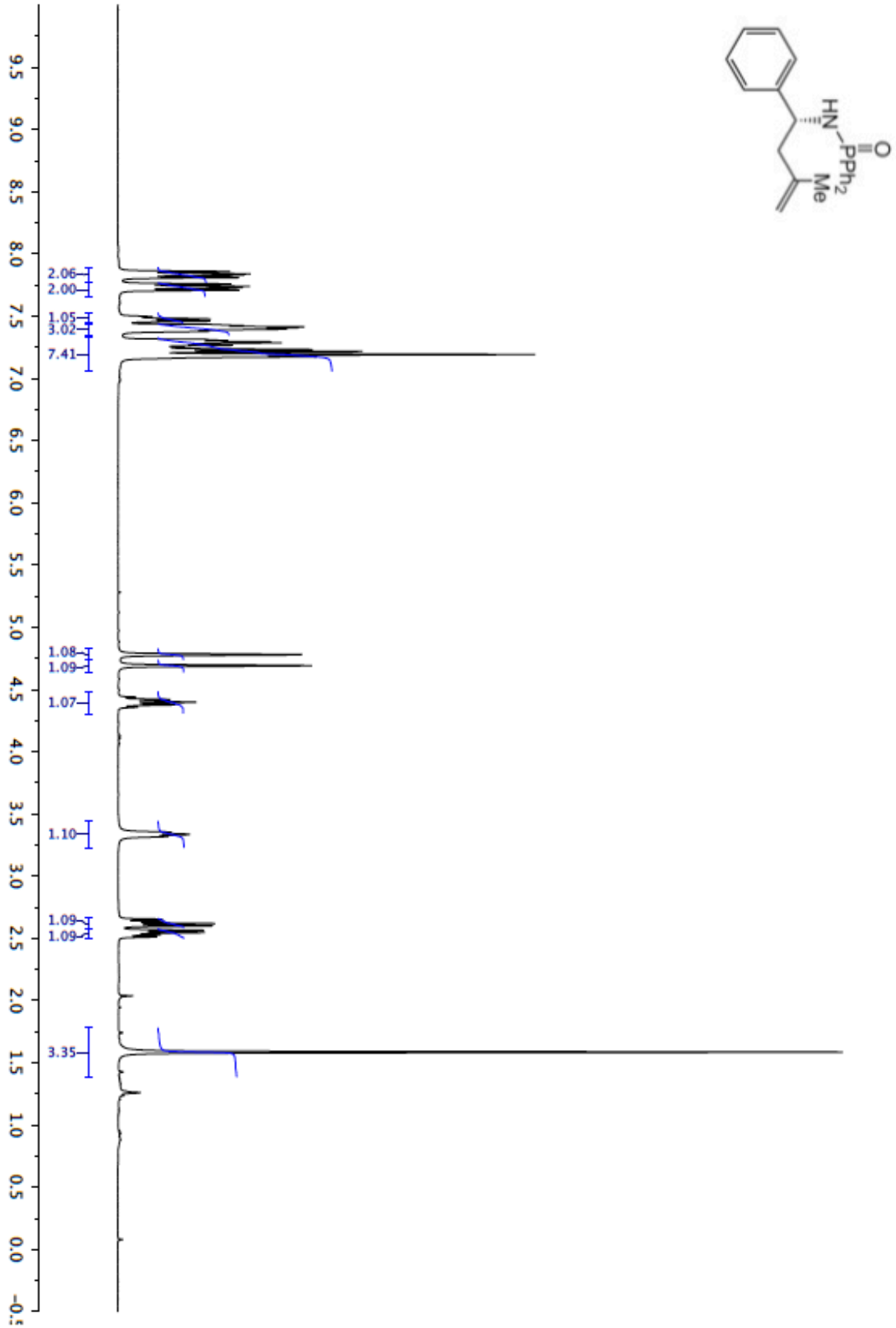

3.87
5.81
3.90
0.95
2.00
1.00
1.01
2.06
2.96
f1 (ppm)
HN
O
P
Ph
Ph

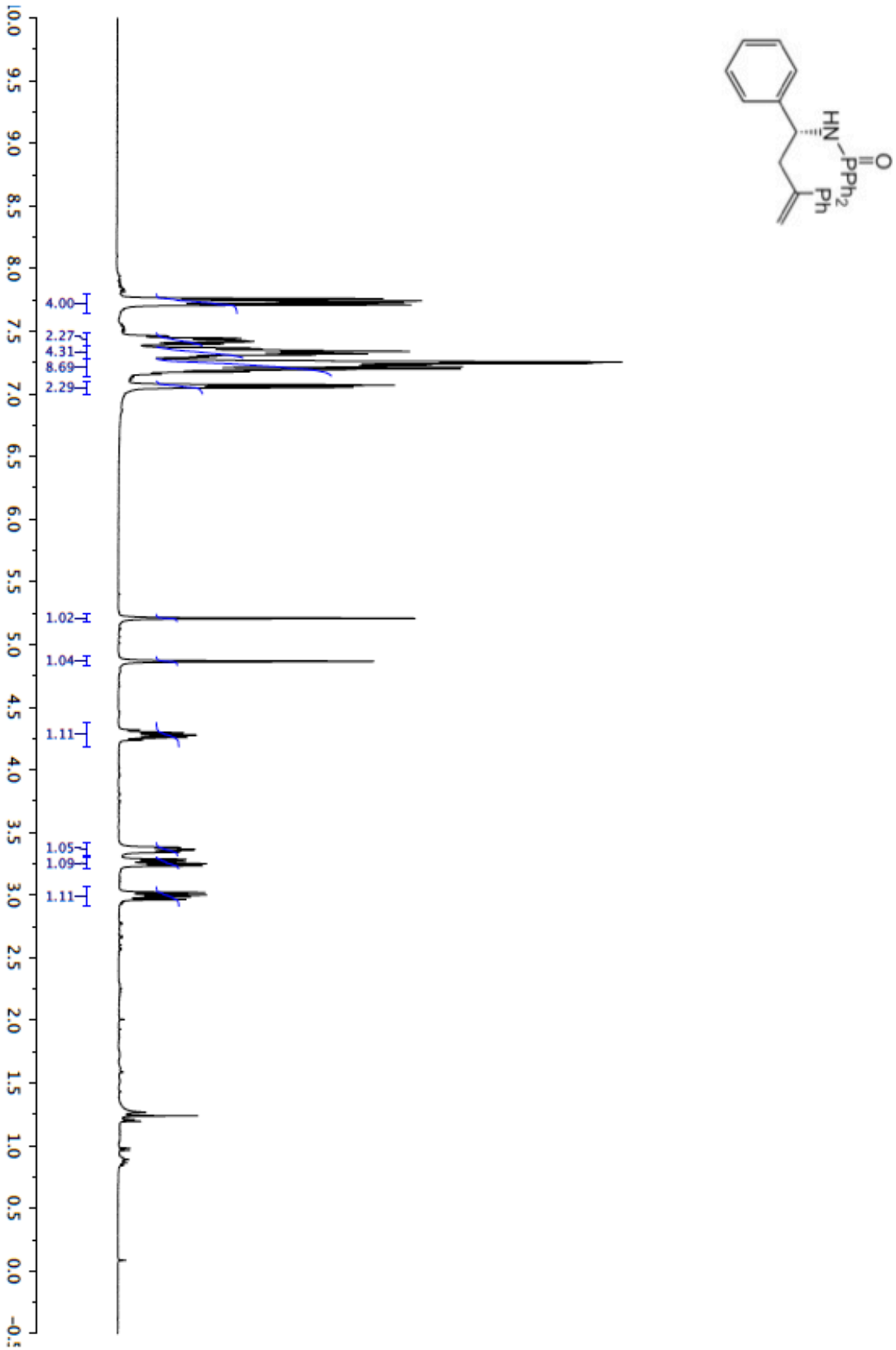

f1 (ppm)
3.69
5.61
2.03
1.97
0.95
2.00
0.99
4.97
2.06
3.93
4.06
6.05
HN
P
O
Ph
Ph
N

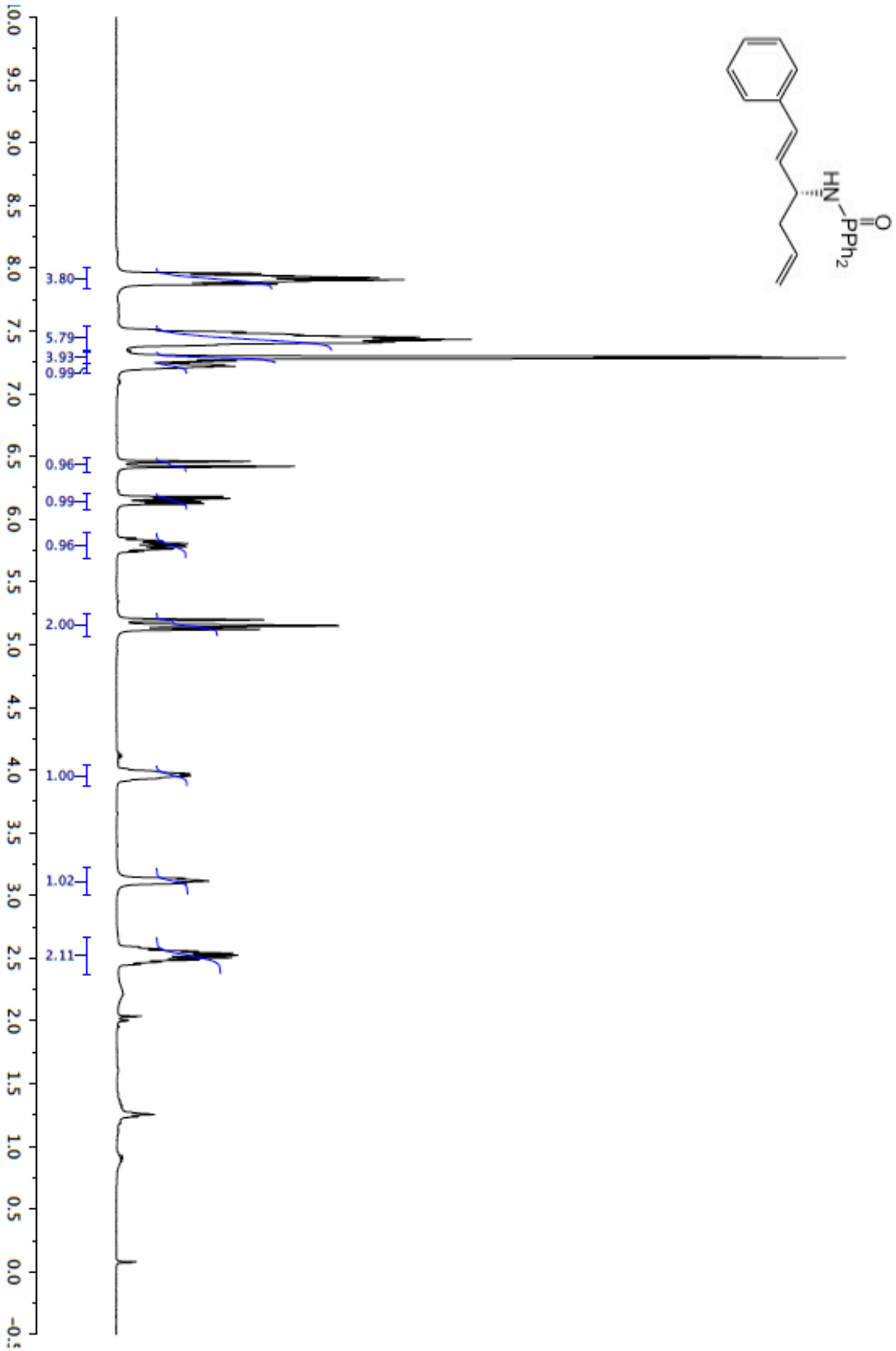

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
4.05
6.13
0.91
0.93
0.94
1.00
2.15
1.04
1.09
1.13
1.13
HN
O
PPh2

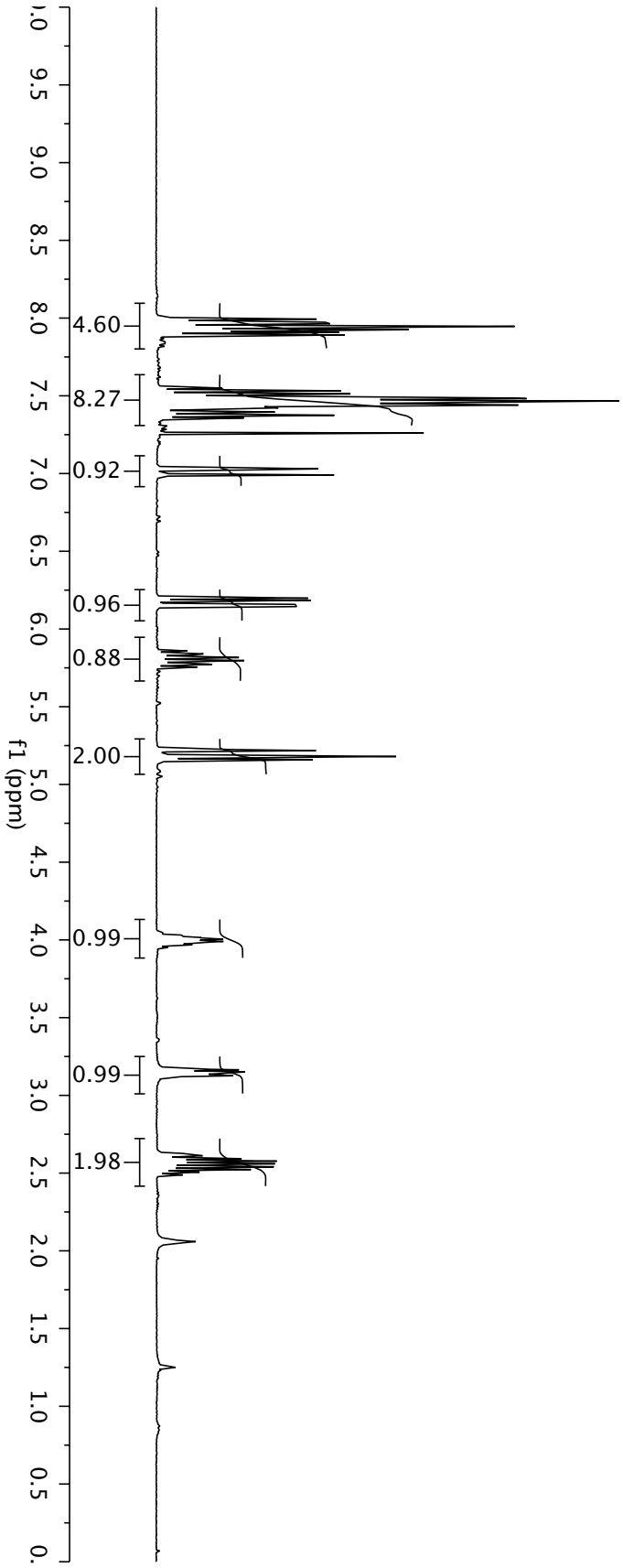

1.74
1.73
1.82
1.85
2.66
1.84
1.00
0.94
1.85
1.00
0.94
1.94
9
8
7
6
5
4
3
2
1
0
ppm
N
HN
O
PPh2

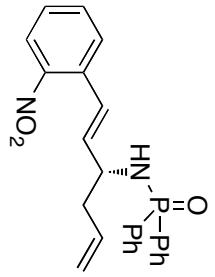

2.36
1.91
1.94
0.98
2.77
1.97
1.78
1.15
2.00
1.13
1.02
2.16
f1 (ppm)
HN
P
O
Ph
Ph
N

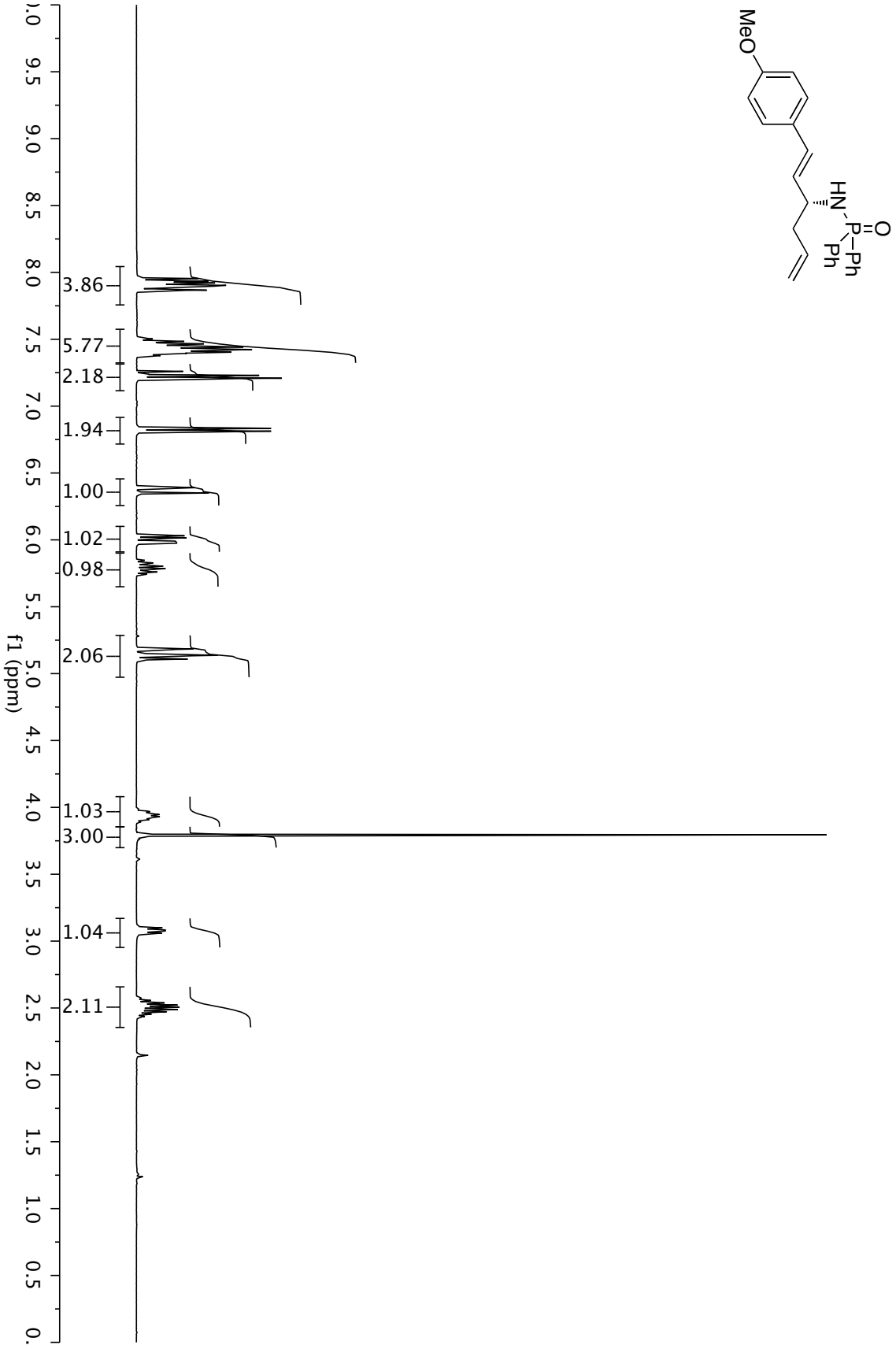

2.06
2.00
1.05
3.02
7.41
1.08
1.09
1.07
1.10
1.09
1.09
3.35
HN
O
PPh2
Me

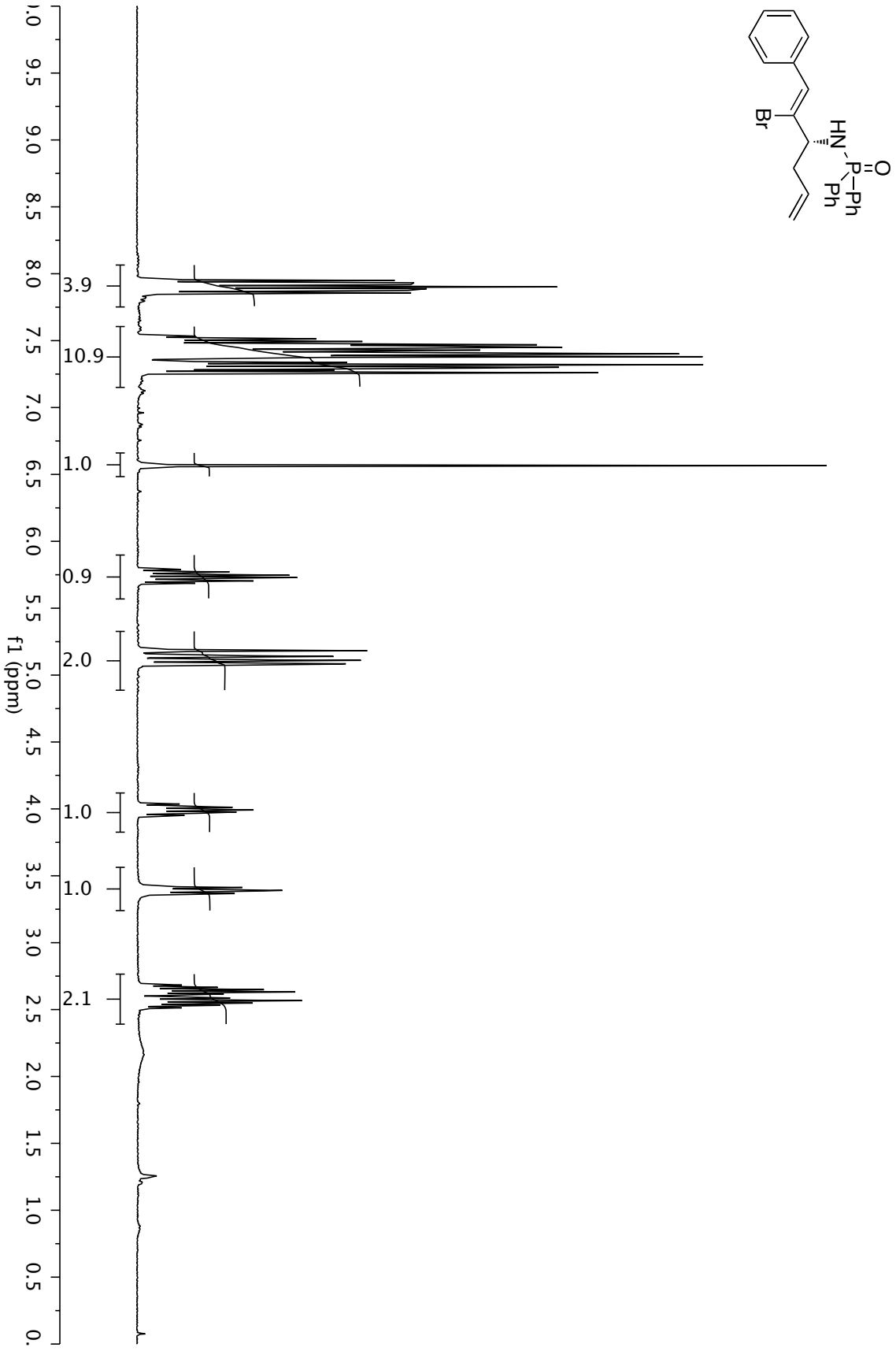

4.00
2.27
4.31
8.69
2.29
1.02
1.04
1.11
1.05
1.09
1.11
HN
O
PPh2
Ph

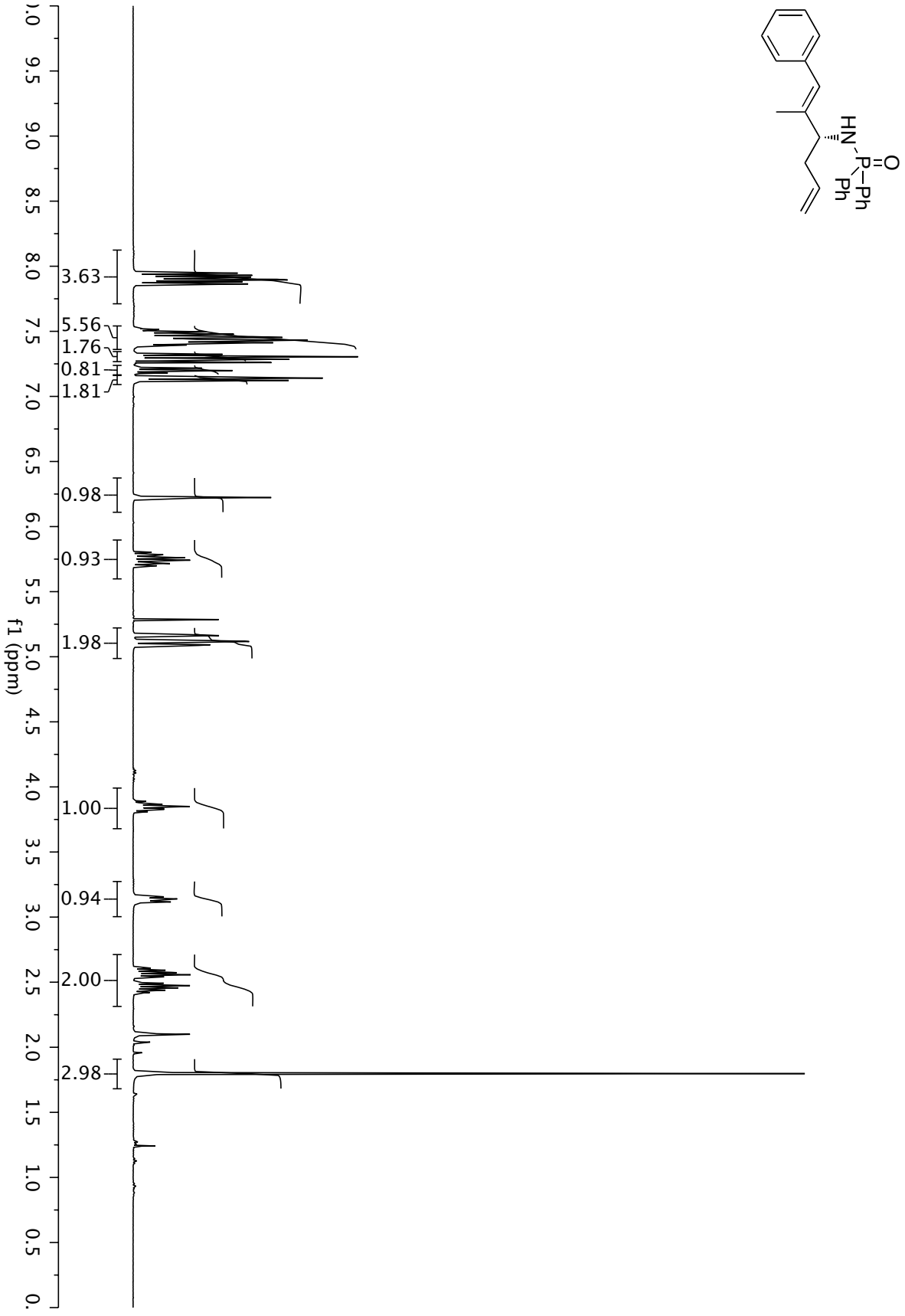

HN
O
PPh2
3.80
5.79
3.93
0.99
0.96
0.99
0.96
2.00
1.00
1.02
2.11

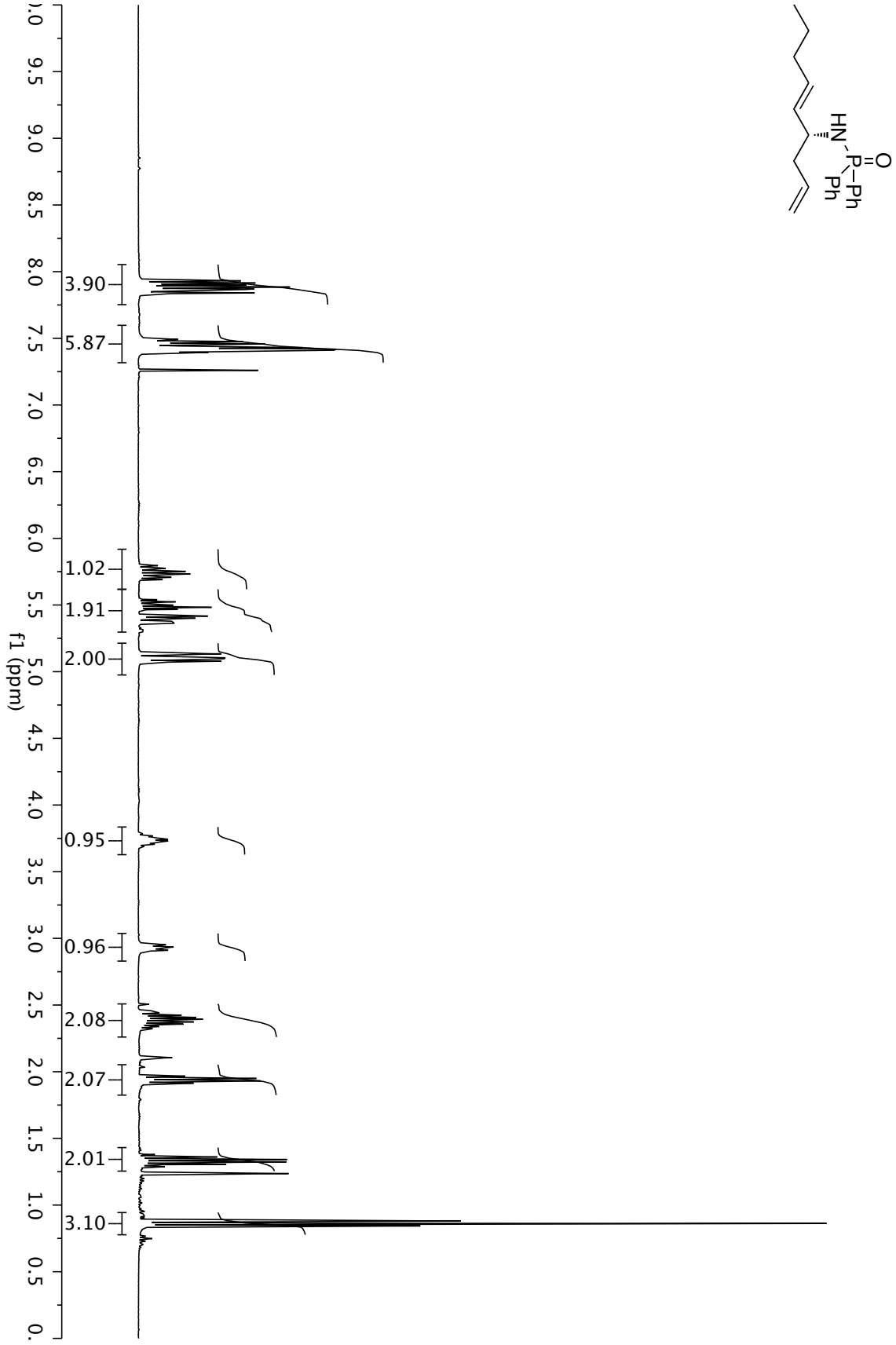

4.60
8.27
0.92
0.96
0.88
2.00
0.99
0.99
1.98
f1 (ppm)

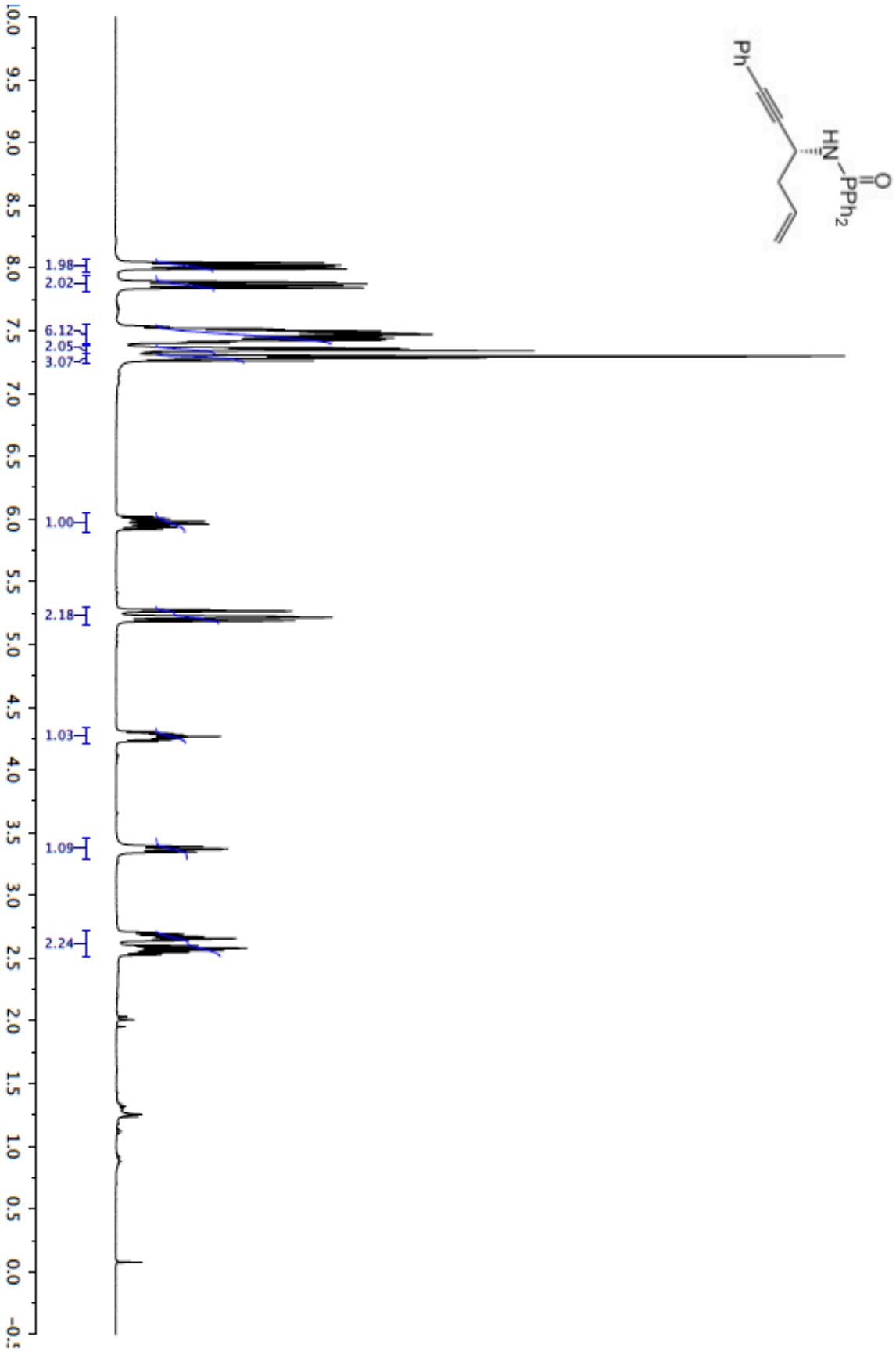

NO2
HN
O
P
Ph
Ph

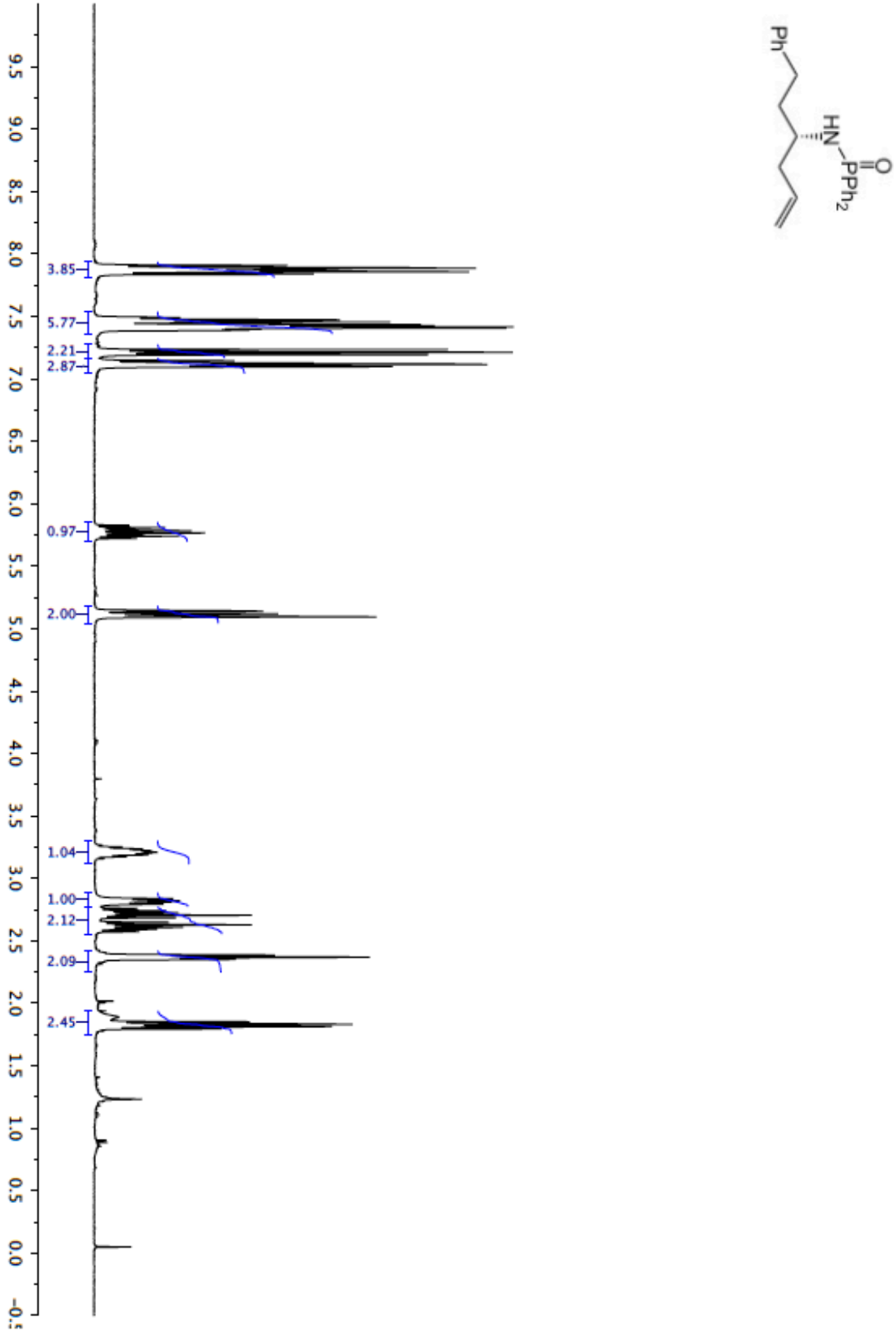

MeO
HN
O
P
Ph
Ph
3.86
5.77
2.18
1.94
1.00
1.02
0.98
2.06
1.03
3.00
1.04
2.11
f1 (ppm)

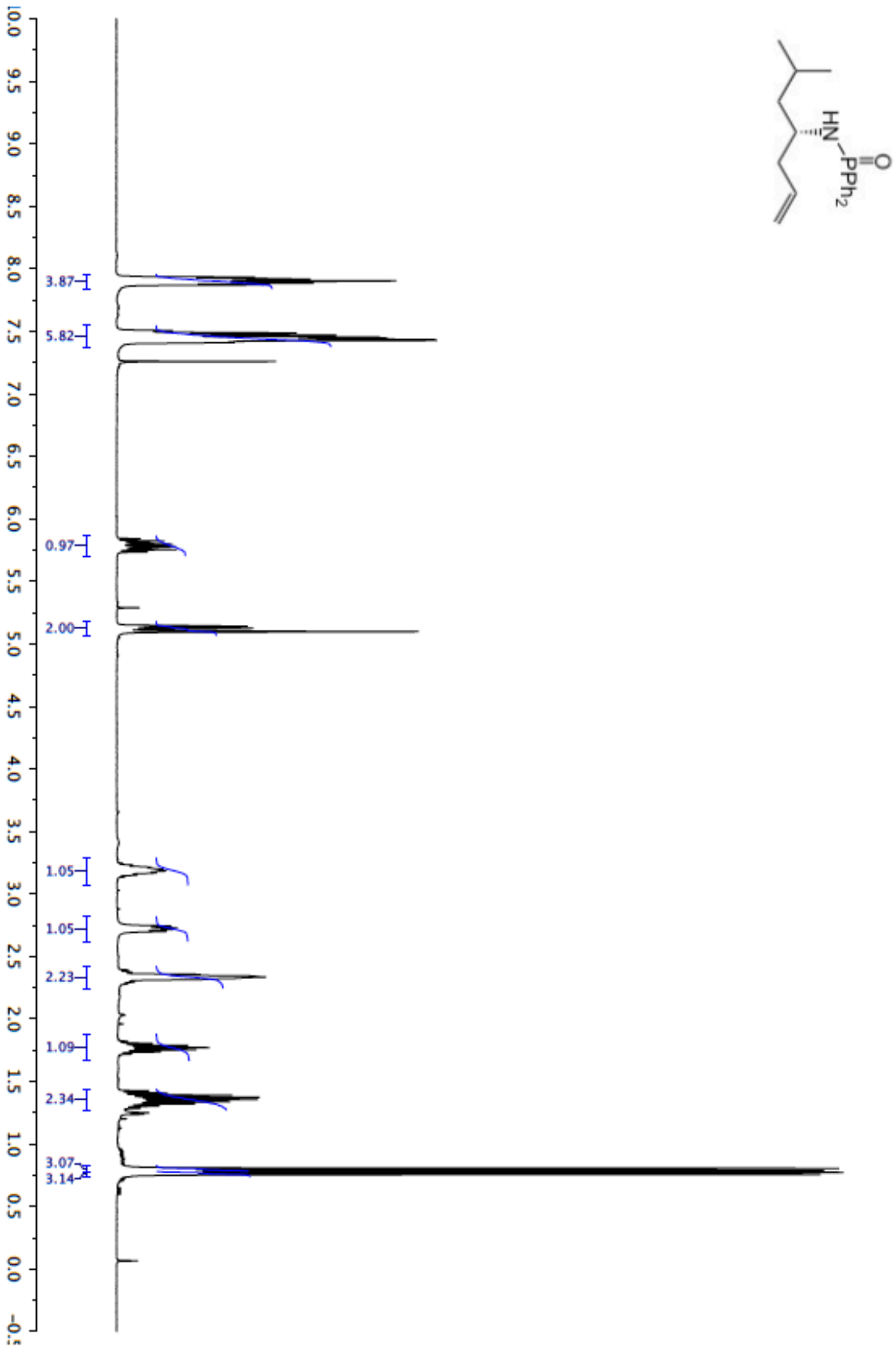

f1 (ppm)
3.9
10.9
1.0
0.9
2.0
1.0
1.0
2.1
Br
HN
O
P
Ph
Ph

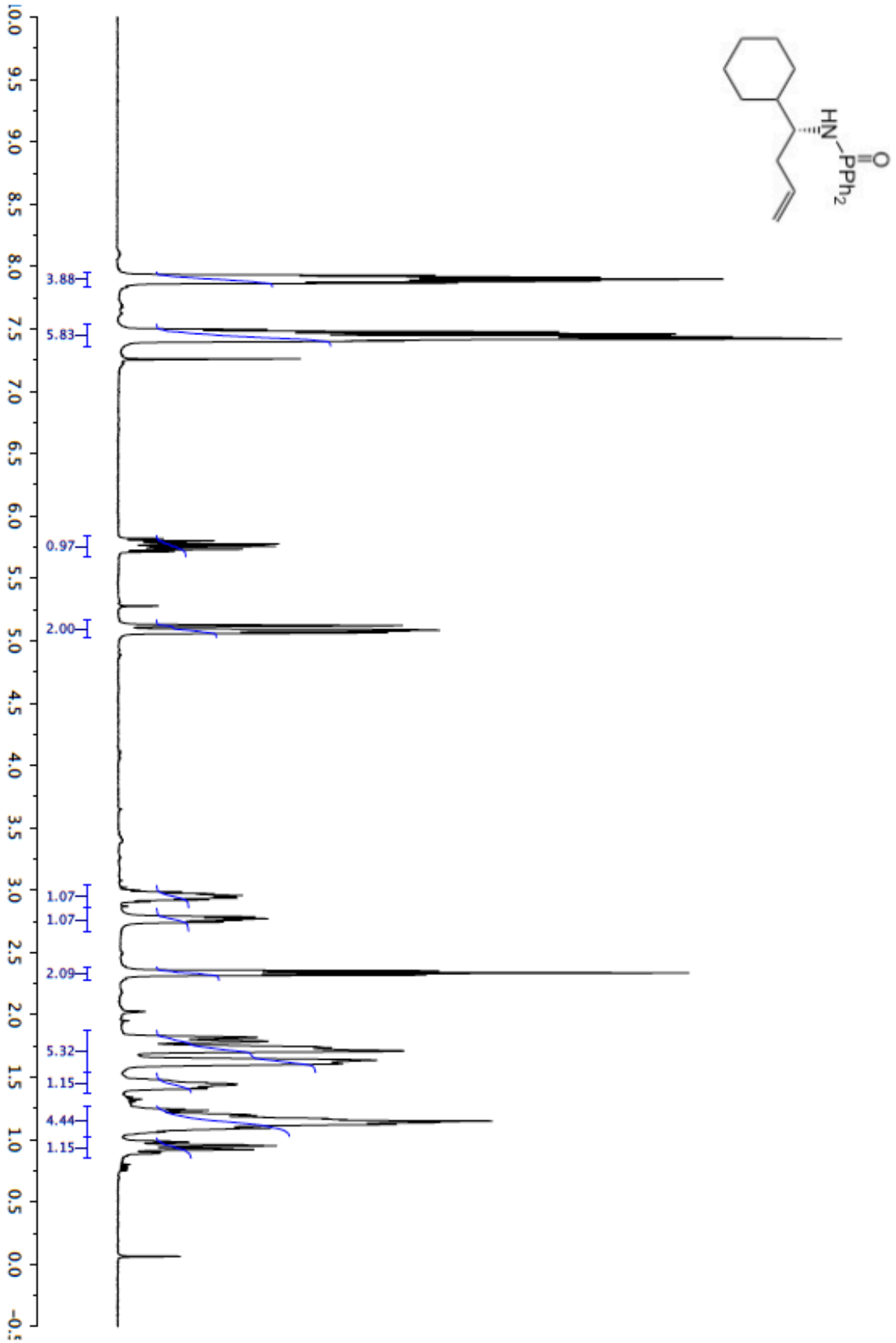

3.63
5.56
1.76
0.81
1.81
0.98
0.93
1.98
1.00
0.94
2.00
2.98
f1 (ppm)
HN
P
O
Ph
Ph

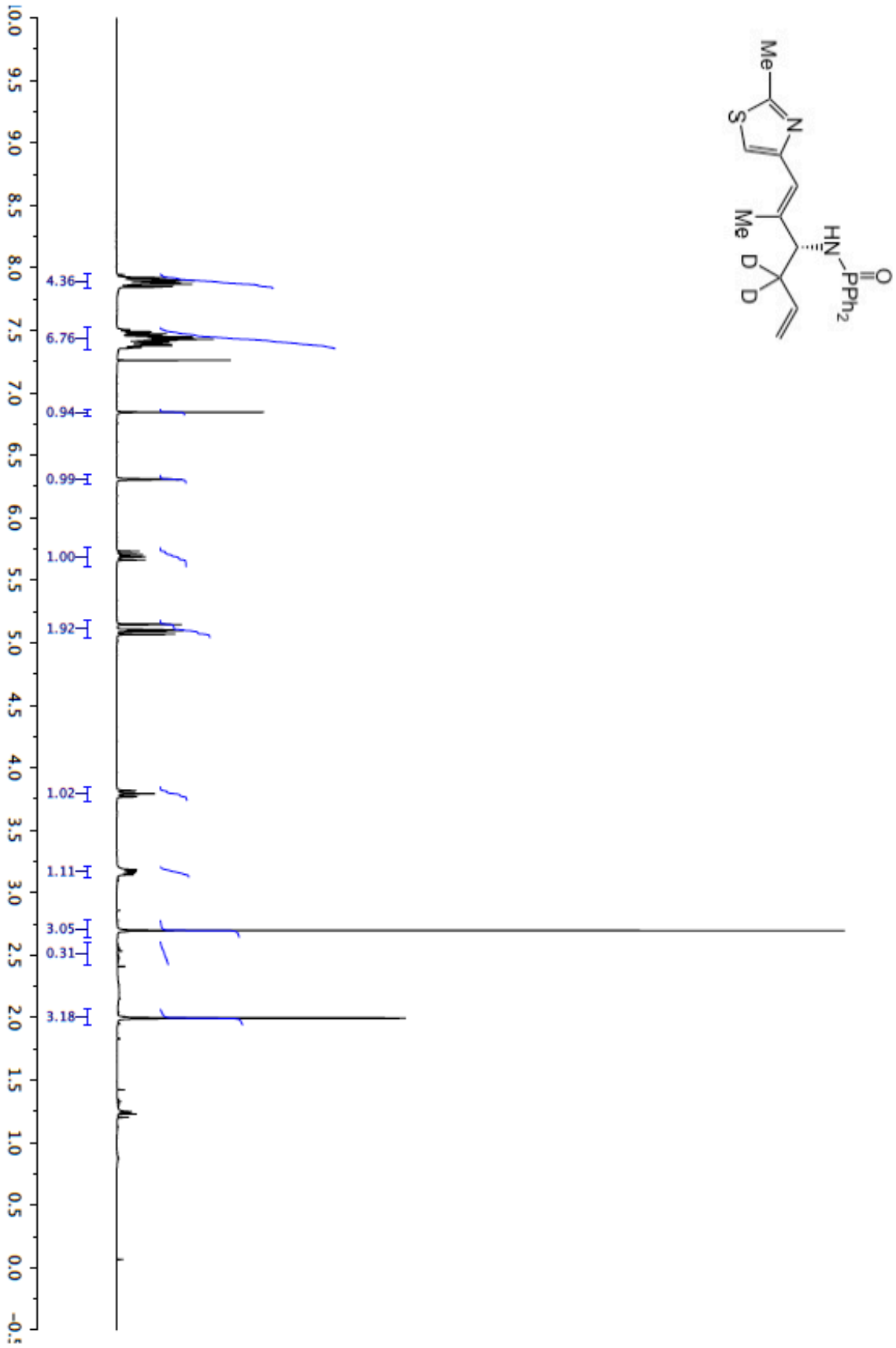

f1 (ppm)
3.90
5.87
1.02
1.91
2.00
0.95
0.96
2.08
2.07
2.01
3.10
HN
O
P
Ph
Ph

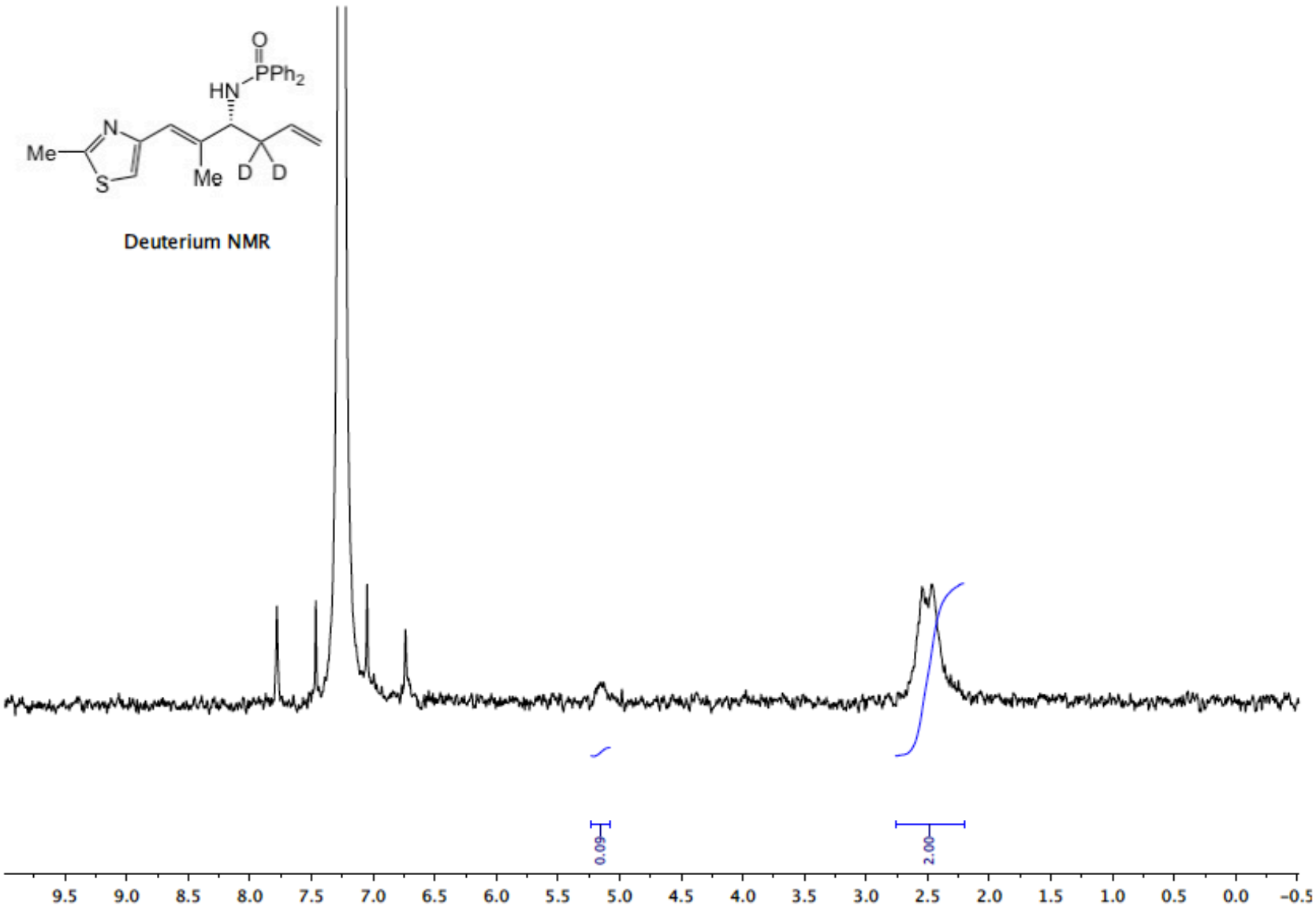

Ph
HN
O
PPh2
1.98
2.02
6.12
2.05
3.07
1.00
2.18
1.03
1.09
2.24

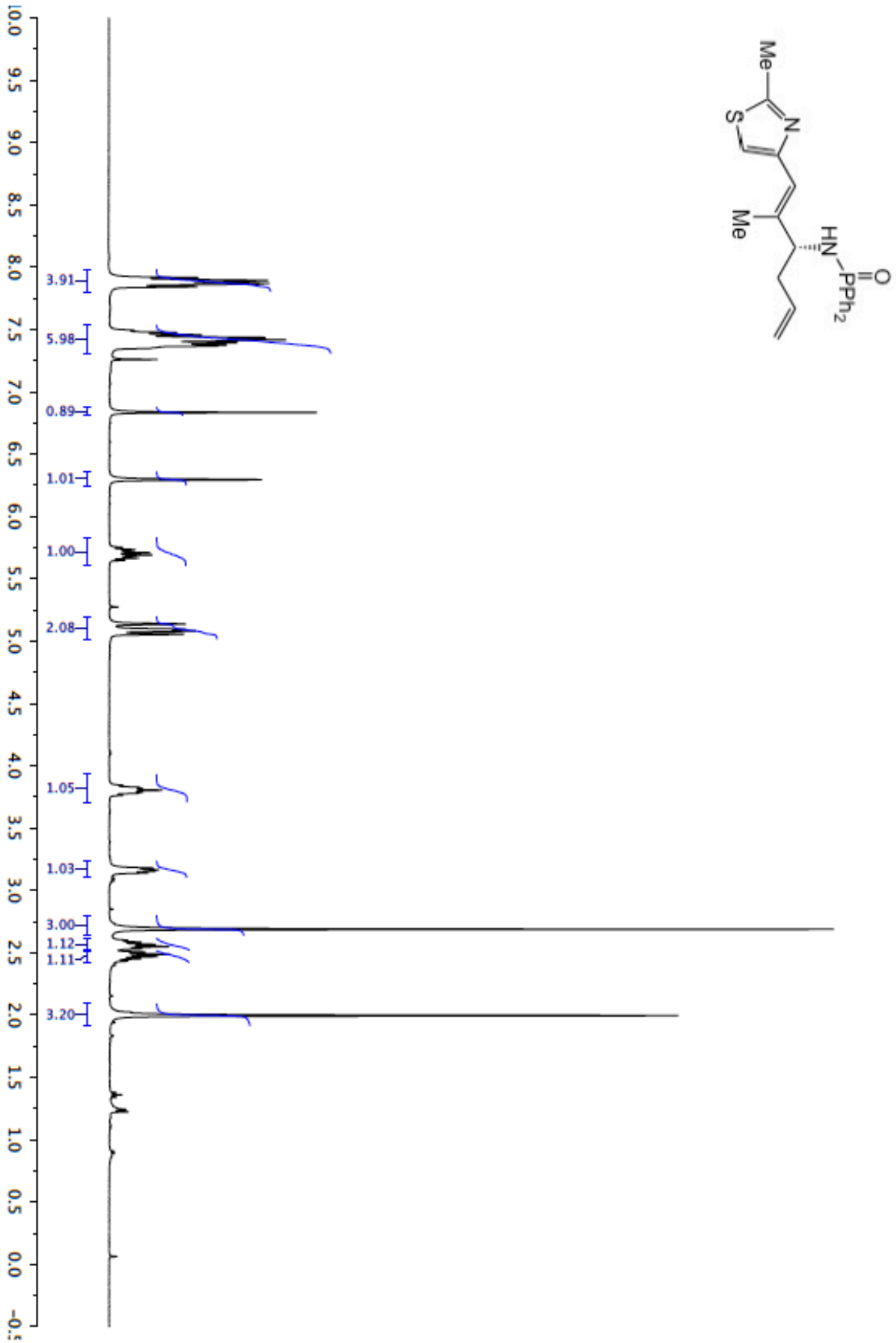

Ph
HN
O
PPh2
3.85
5.77
2.21
2.87
0.97
2.00
1.04
1.00
2.12
2.09
2.45
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

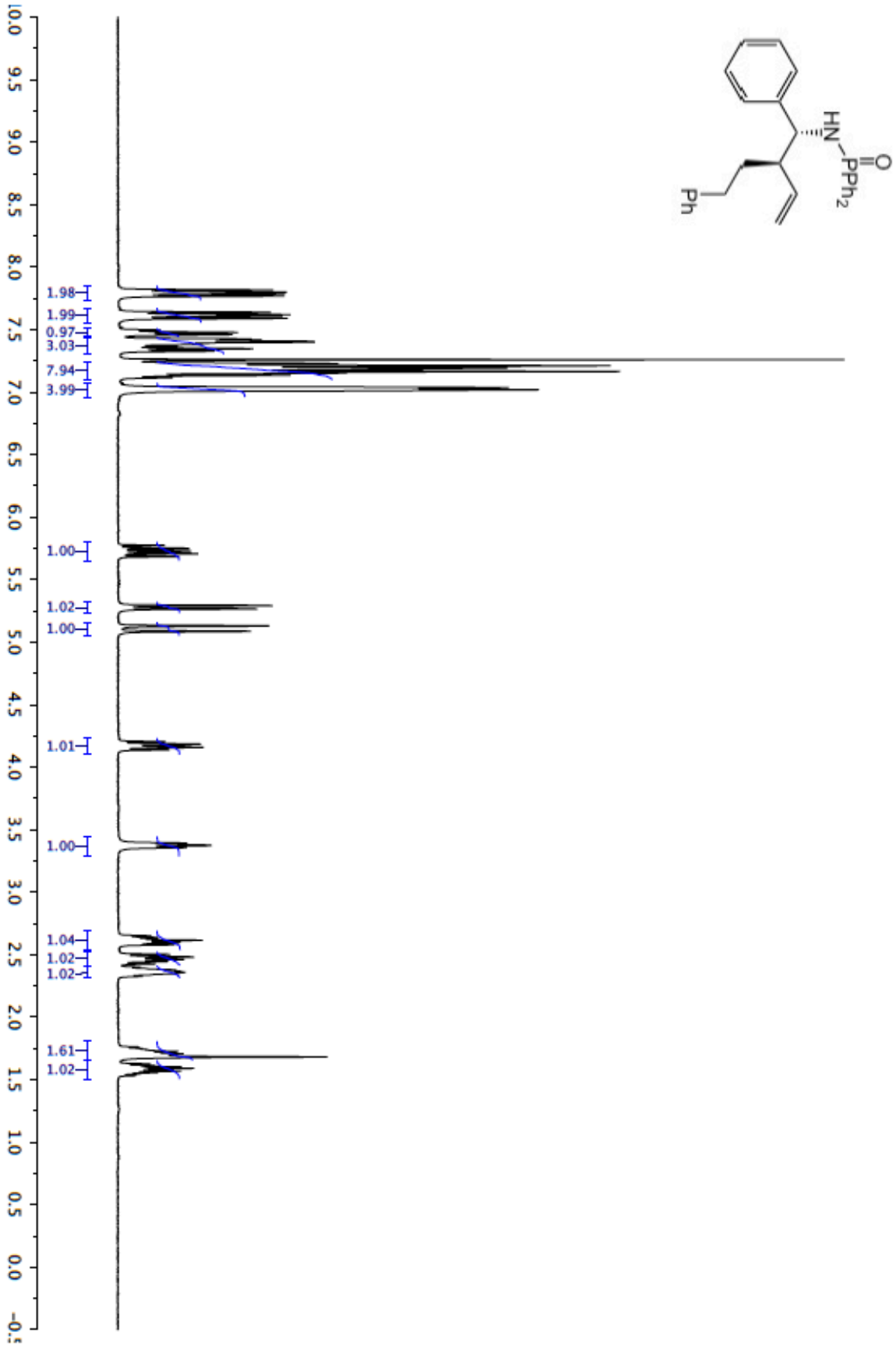

HN
O
PPh2
3.87
5.82
0.97
2.00
1.05
1.05
2.23
1.09
2.34
3.07
3.14

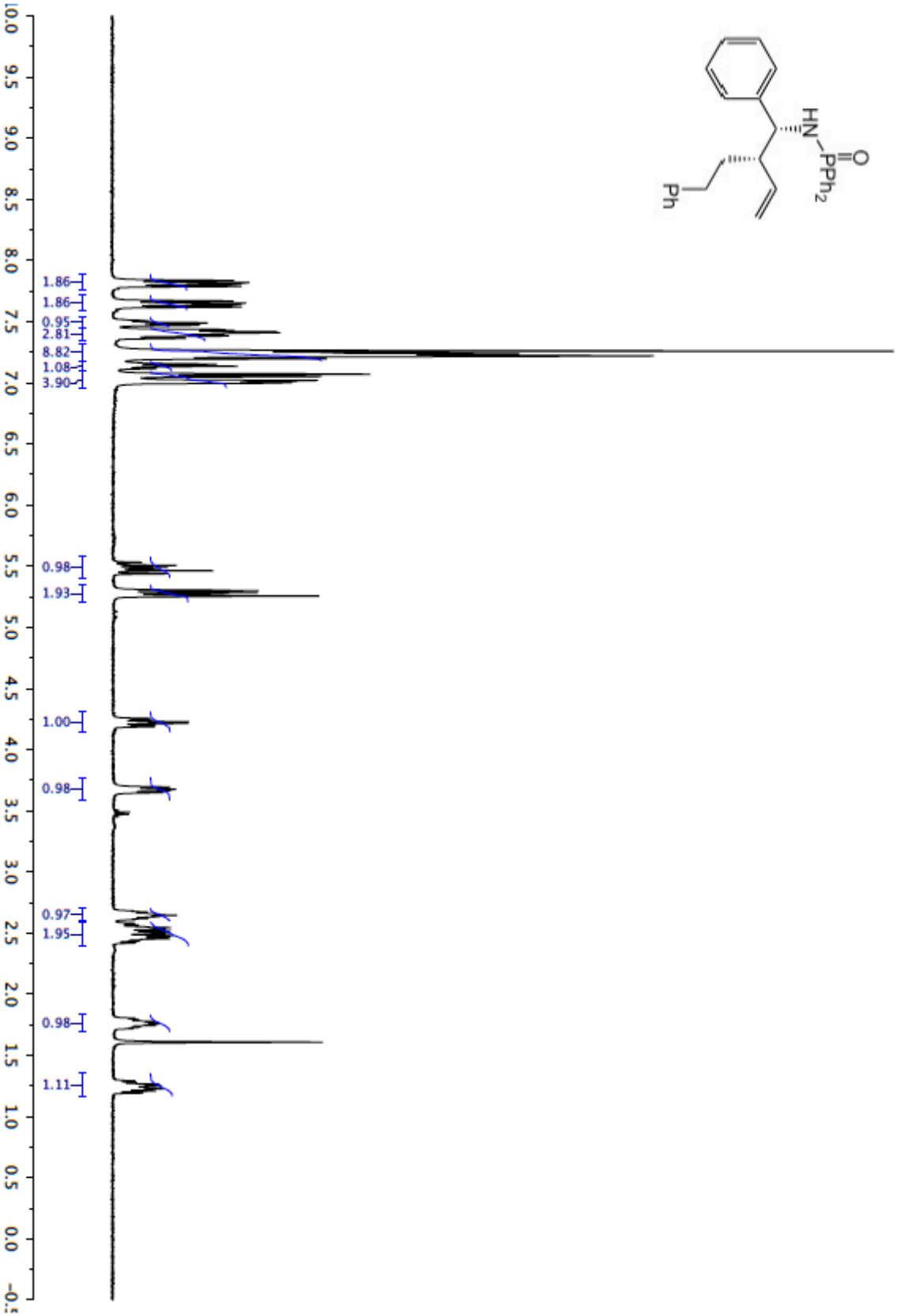

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
3.88
5.83
0.97
2.00
1.07
1.07
2.09
5.32
1.15
4.44
1.15
HN
O
PPh2

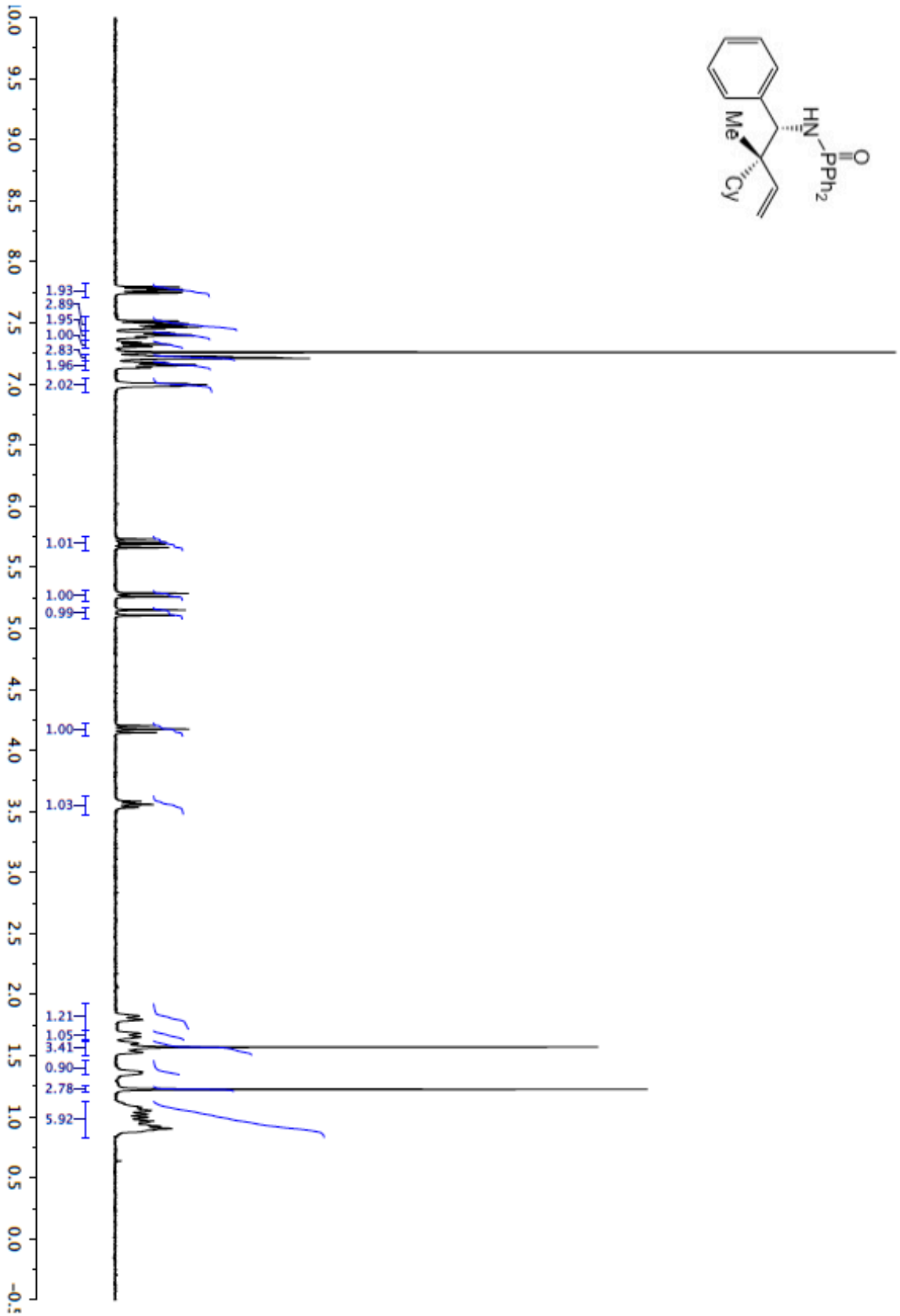

Me
S
N
Me
D
D
HN
O
PPh2
4.36
6.76
0.94
0.99
1.00
1.92
1.02
1.11
3.05
0.31
3.18

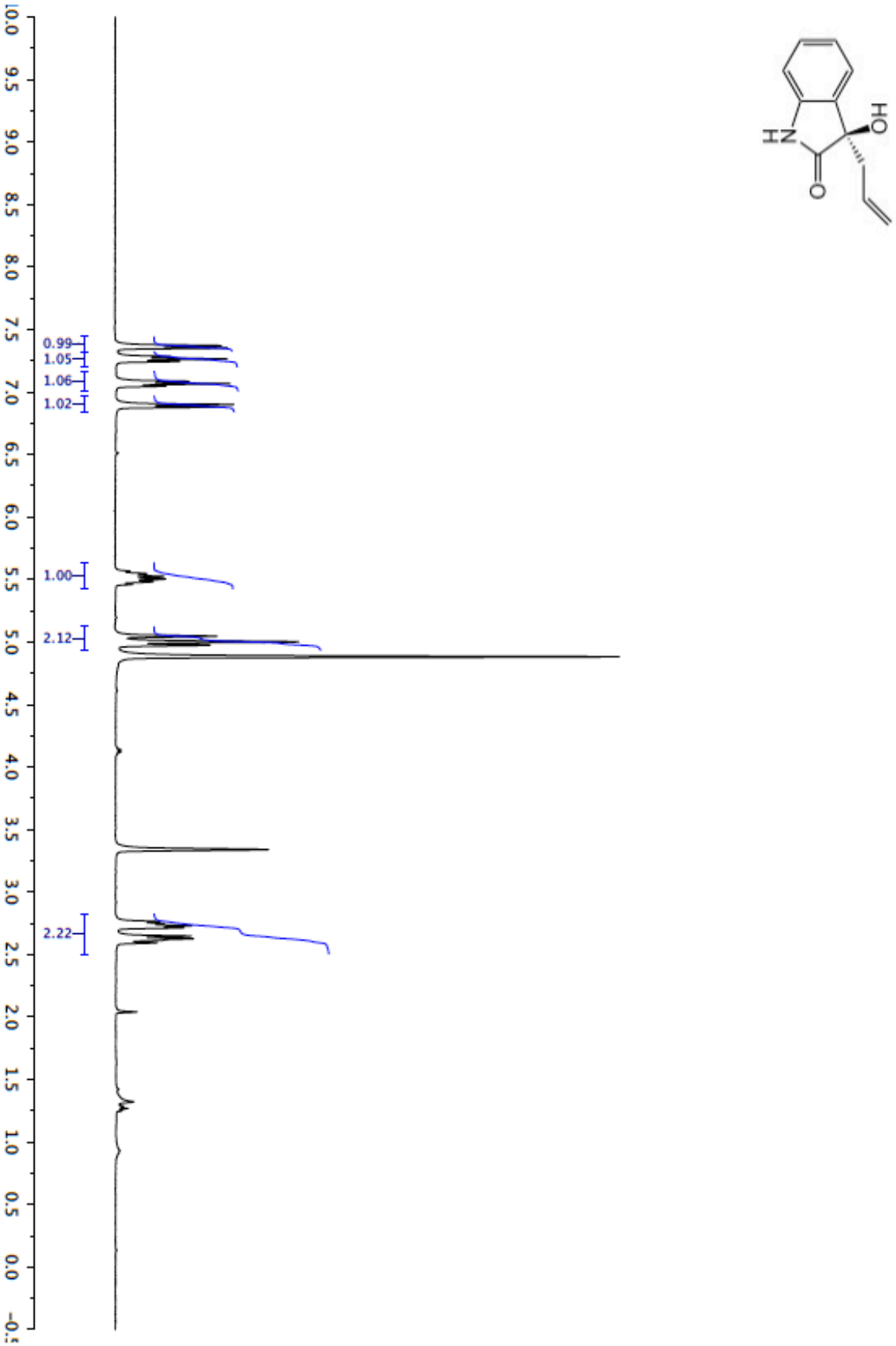

Me
N
S
Me
HN
O
PPh2
D
D
Deuterium NMR
0.69
2.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

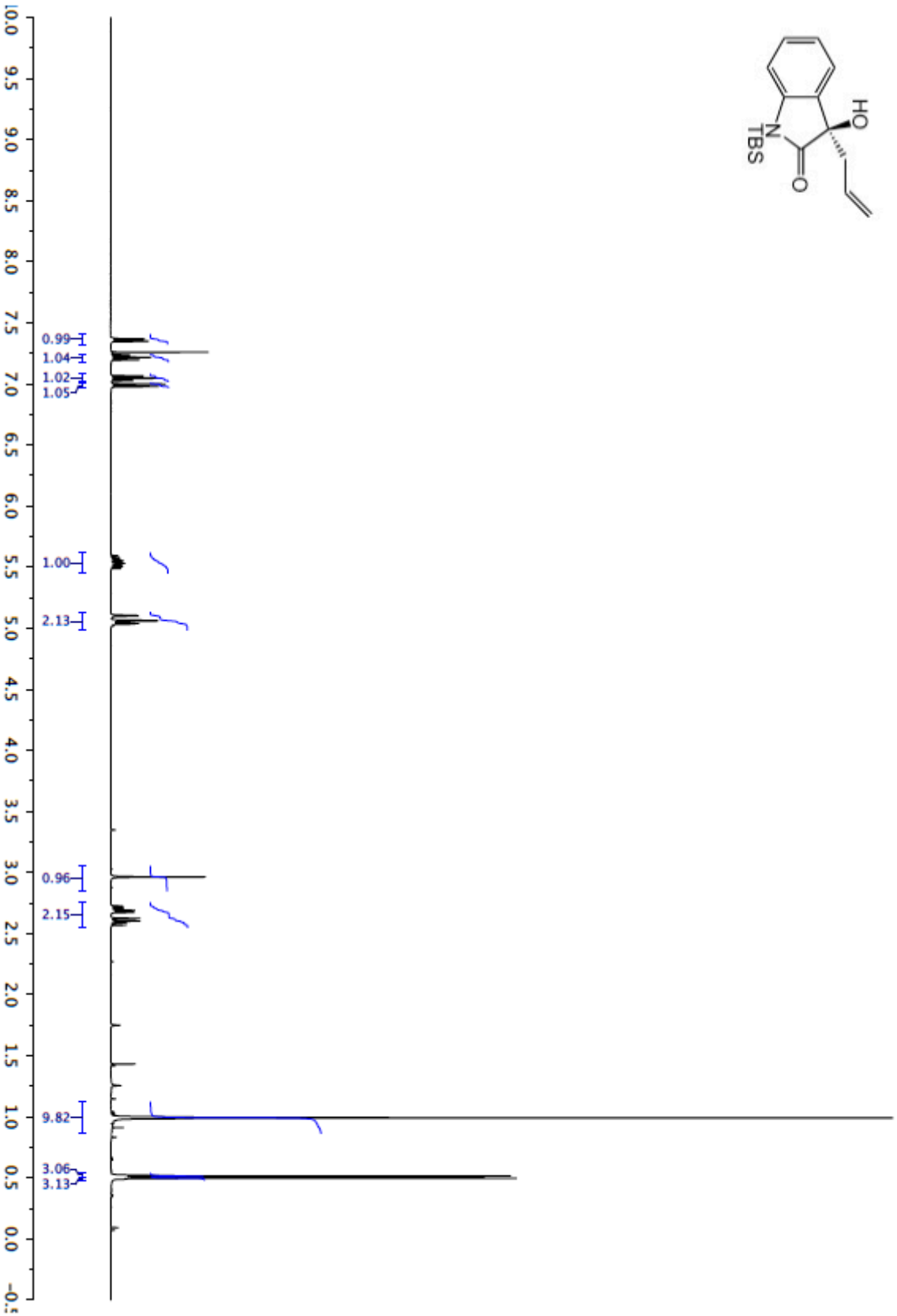

Me
S
N
Me
HN
O
PPh2
3.91
5.98
0.89
1.01
1.00
2.08
1.05
1.03
3.00
1.12
1.11
3.20

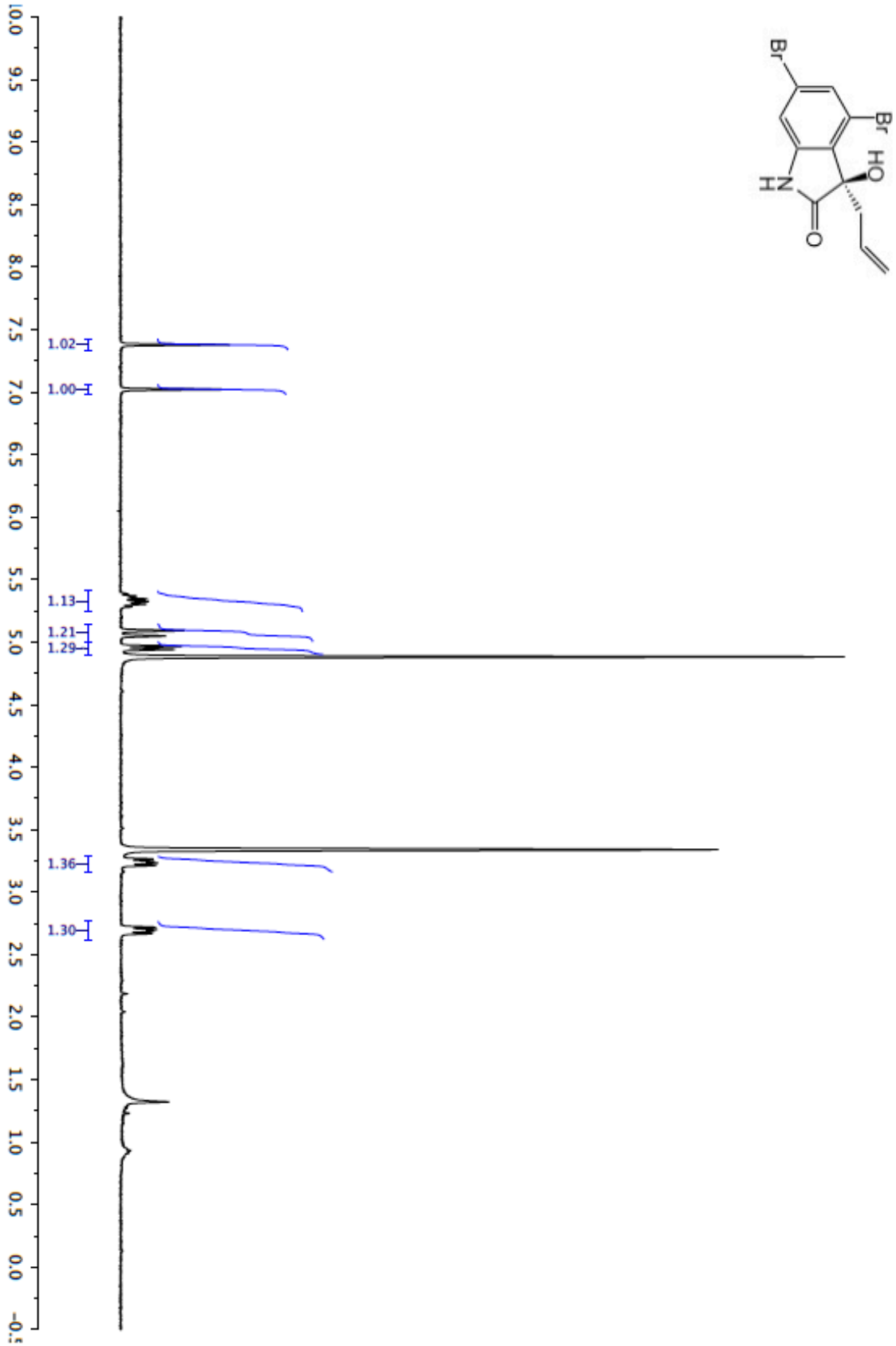

HN
O
PPh2
Ph
1.98
1.99
0.97
3.03
7.94
3.99
1.00
1.02
1.00
1.01
1.00
1.04
1.02
1.02
1.61
1.02

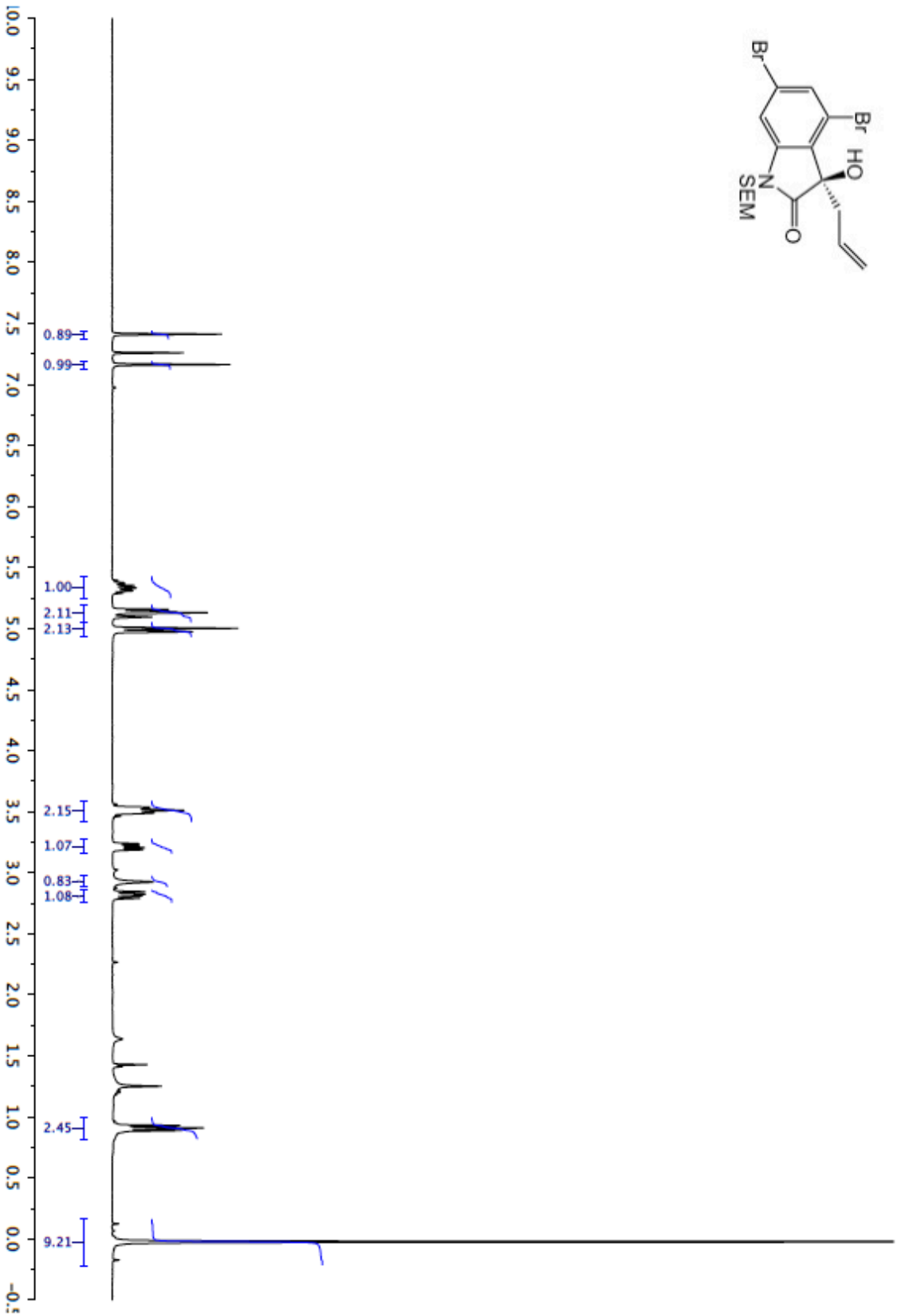

HN
O
PPh2
Ph
1.86
1.86
0.95
2.81
8.82
1.08
3.90
0.98
1.93
1.00
0.98
0.97
1.95
0.98
1.11

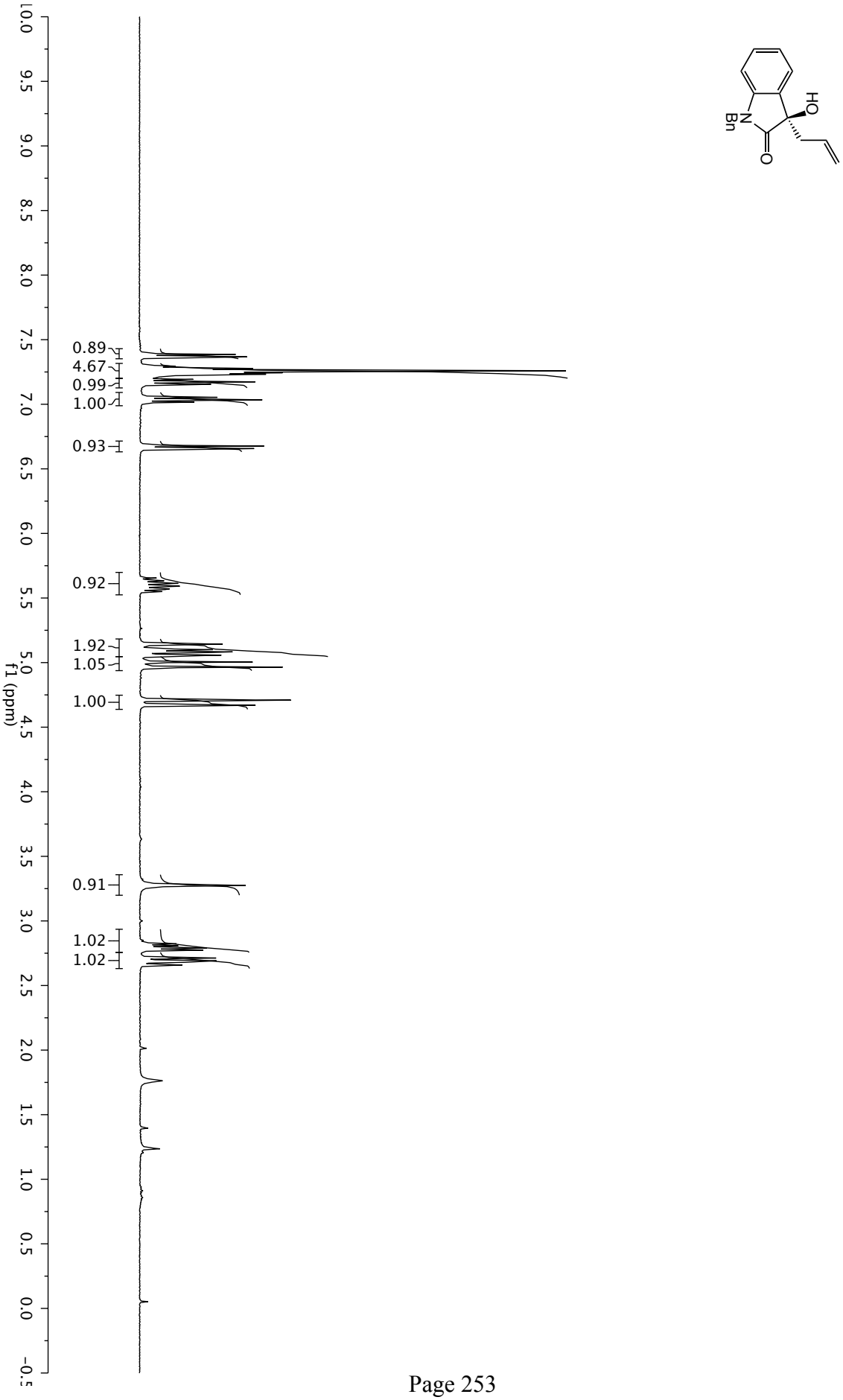

Me
Cy
HN
O
PPh2
1.93
2.89
1.95
1.00
2.83
1.96
2.02
1.01
1.00
0.99
1.00
1.03
1.21
1.05
3.41
0.90
2.78
5.92

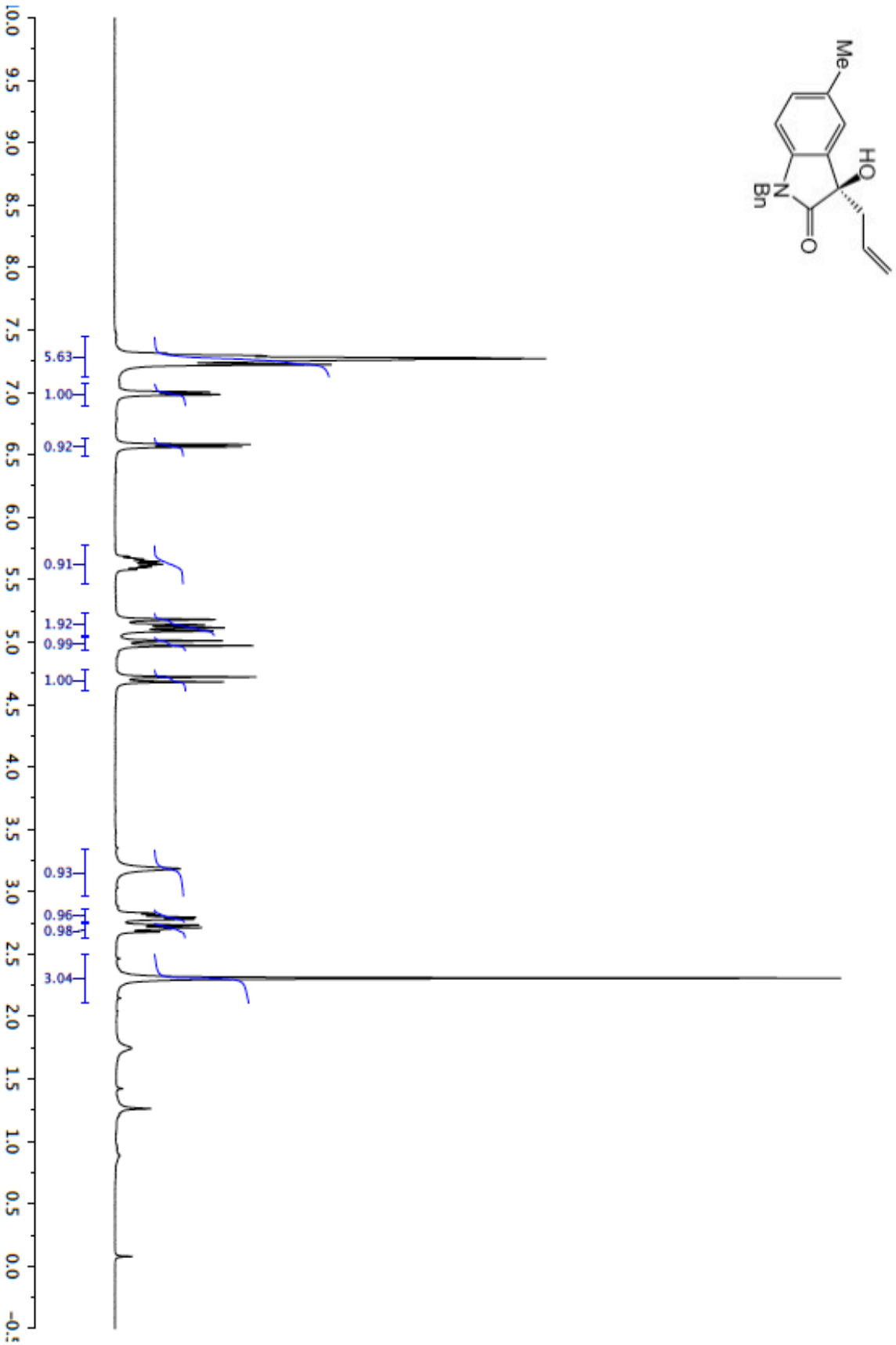

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.99
1.05
1.06
1.02
1.00
2.12
2.22
HO
HN
O

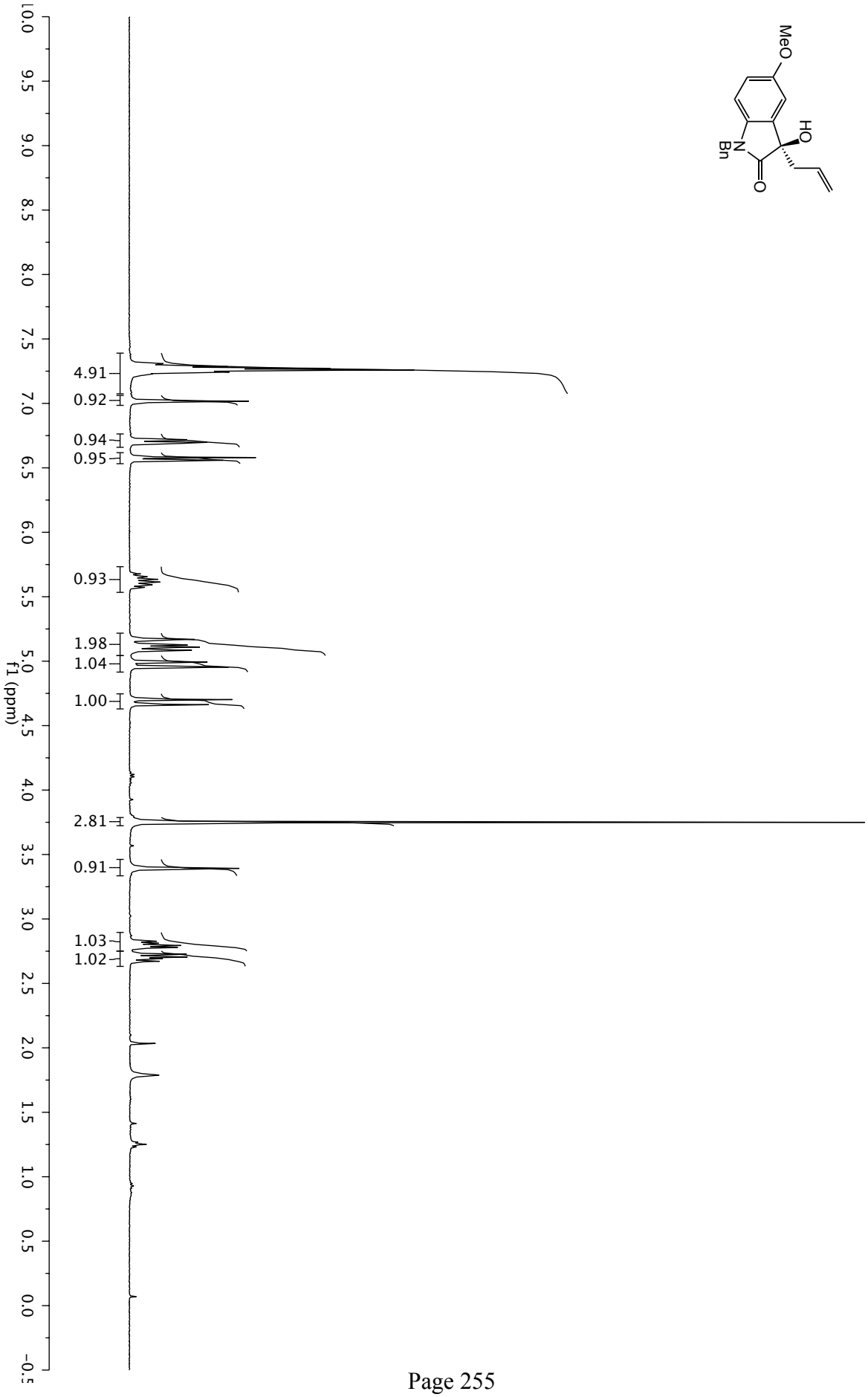

HO
N
TBS
O
0.99
1.04
1.02
1.05
1.00
2.13
0.96
2.15
9.82
3.06
3.13

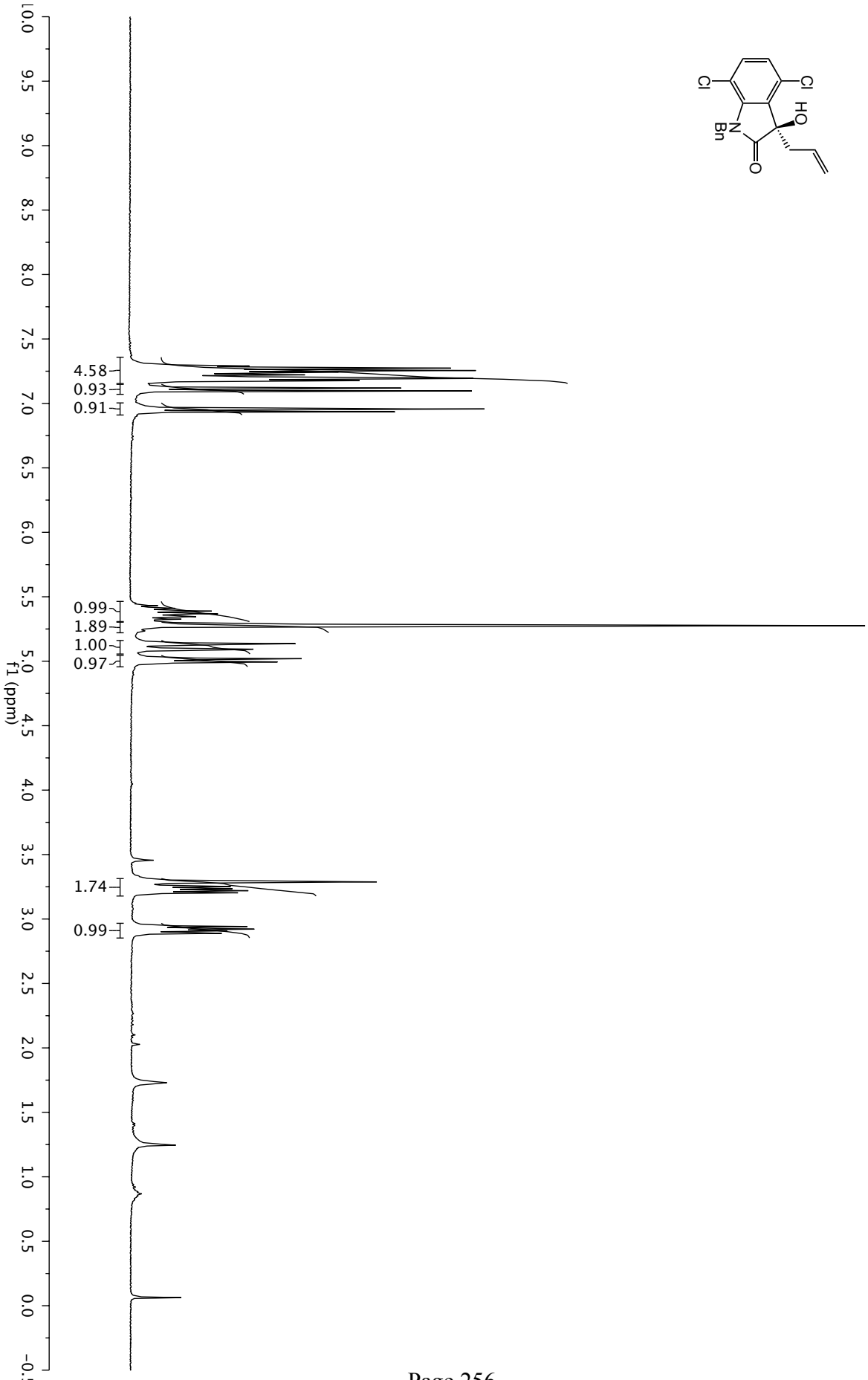

Br
Br
HO
N
H
O
1.02
1.00
1.13
1.21
1.29
1.36
1.30
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

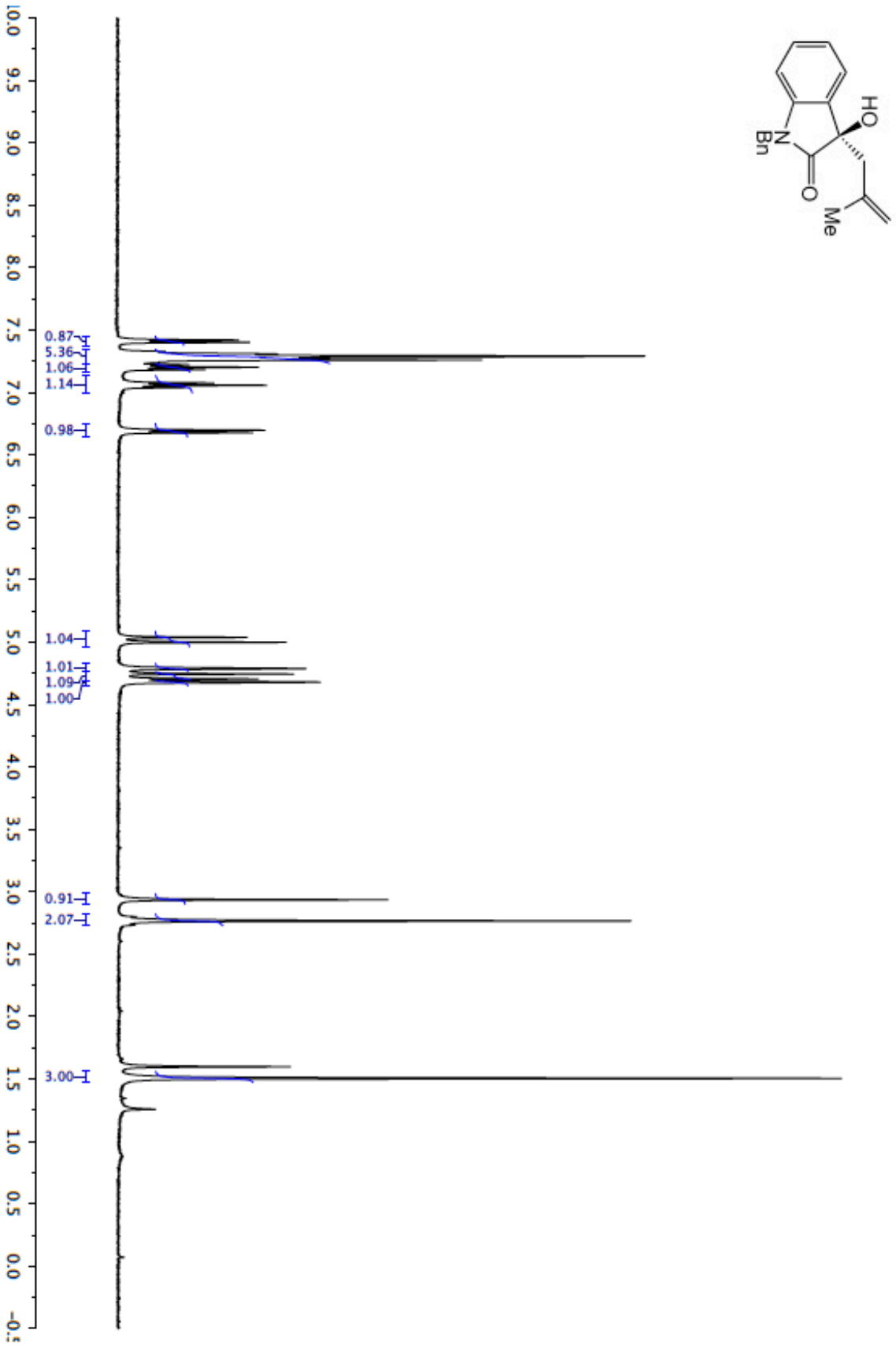

Br
Br
HO
N
SEM
O
0.89
0.99
1.00
2.11
2.13
2.15
1.07
0.83
1.08
2.45
9.21


10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
0.89
4.67
0.99
1.00
0.93
0.92
1.92
1.05
1.00
0.91
1.02
1.02
HO
N
Bn
O


Me
HO
N
Bn
O
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5.63
1.00
0.92
0.91
1.92
0.99
1.00
0.93
0.96
0.98
3.04


MeO
HO
N
Bn
O
4.91
0.92
0.94
0.95
0.93
1.98
1.04
1.00
2.81
0.91
1.03
1.02
f1 (ppm)


4.58
0.93
0.91
0.99
1.89
1.00
0.97
1.74
0.99
f1 (ppm)
Cl
Cl
HO
N
Bn
O


10.0
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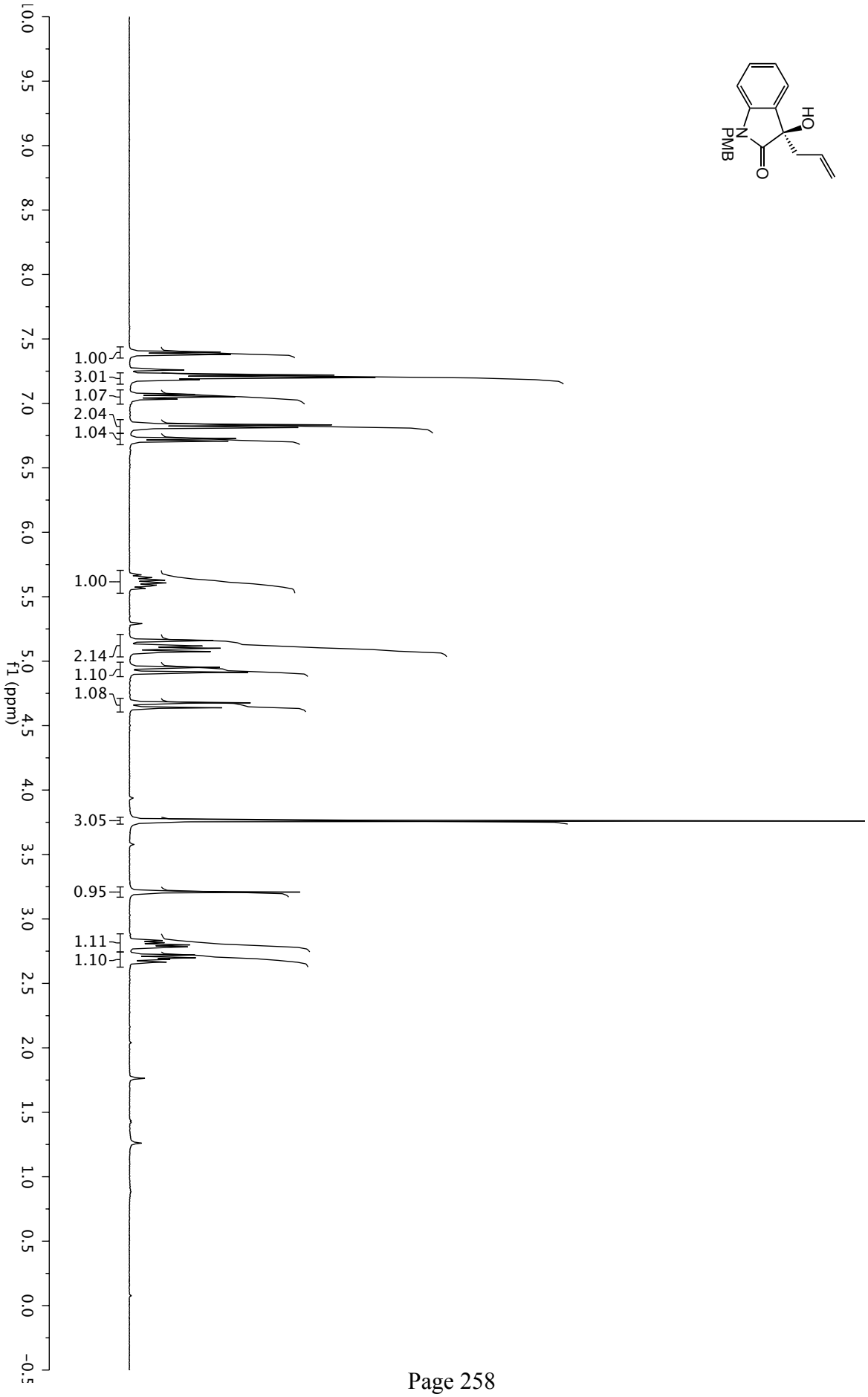
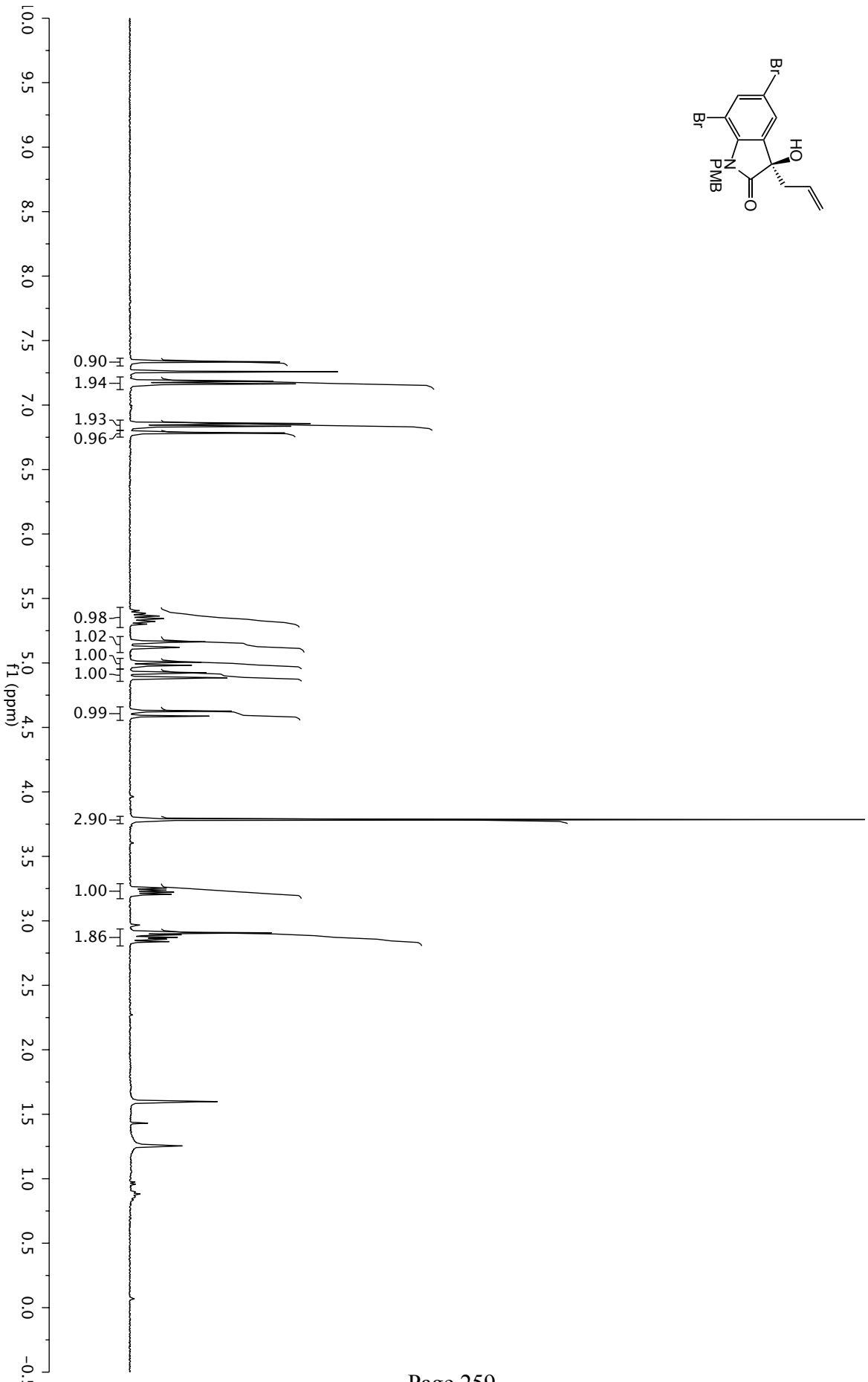
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.87
5.36
1.06
1.14
0.98
1.04
1.01
1.09
1.00
0.91
2.07
3.00
HO
N
Bn
O
Me


HO
N
PMB
O
1.00
3.01
1.07
2.04
1.04
1.00
2.14
1.10
1.08
3.05
0.95
1.11
1.10
f1 (ppm)


Br
Br
HO
N
PMB
O
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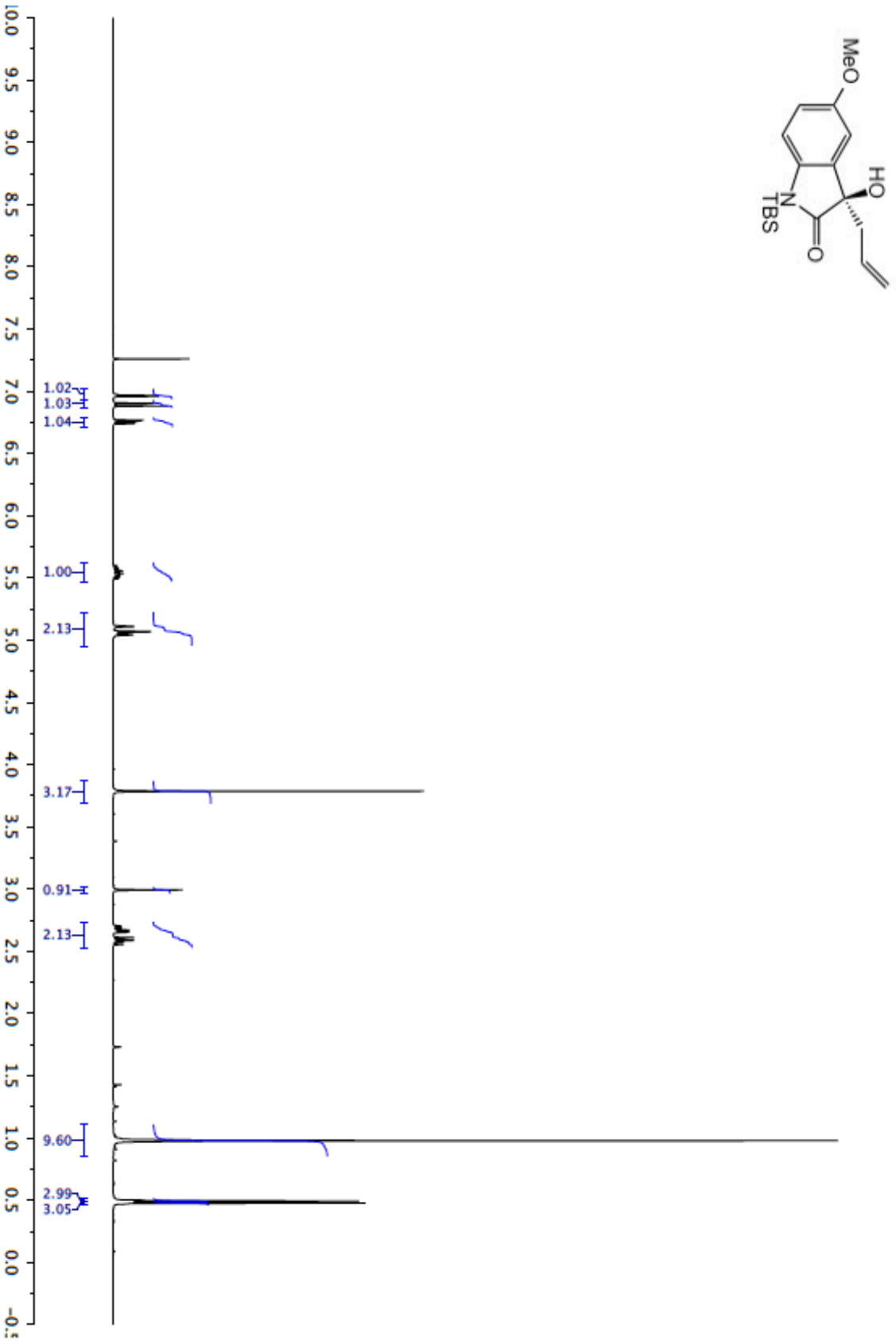
1.94
1.93
0.96
0.98
1.02
1.00
1.00
0.99
2.90
1.00
1.86
f1 (ppm)


MeO
HO
N
TBS
O
1.02
1.03
1.04
1.00
2.13
3.17
0.91
2.13
9.60
2.99
3.05

X-ray Crystal Structure of 1.19•HCl

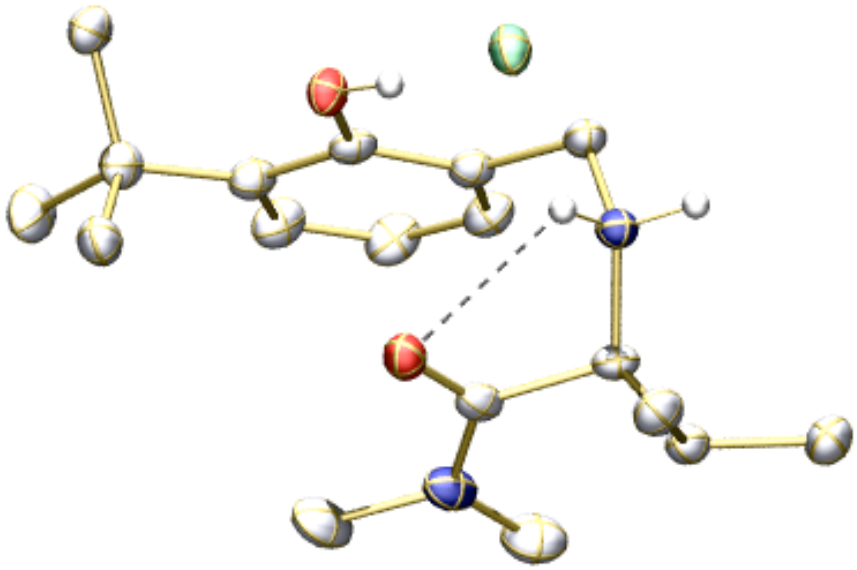


Table 1. Crystal data and structure refinement for $C_{18}H_{31}N_2O_2Cl$ (2g•HCl)

Identification code	$C_{18}H_{31}N_2O_2Cl$	
Empirical formula	$C_{18}H_{31}N_2O_2Cl$	
Formula weight	342.90	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 8.1015(4) Å	α= 90°
	b = 21.8686(12) Å	β= 91.738(3)°
	c = 16.8521(9) Å	γ = 90°
Volume	2984.3(3) $Å^3$	
Z	6	
Density (calculated)	1.145 Mg/m^3	
Absorption coefficient	1.776 mm^{-1}	
F(000)	1116	
Crystal size	0.15 x 0.09 x 0.03 mm^3	
Theta range for data collection	2.62 to 67.29°	
Index ranges	-6<=h<=9, -25<=k<=26, -20<=l<=20	
Reflections collected	25872	
Independent reflections	9770 [R(int) = 0.0418]	

Completeness to theta = 67.29°	98.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9487 and 0.7765
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9770 / 10 / 655
Goodness-of-fit on F^2	1.024
Final R indices [I>2sigma(I)]	R1 = 0.0379, wR2 = 0.0921
R indices (all data)	R1 = 0.0440, wR2 = 0.0956
Absolute structure parameter	0.012(9)
Extinction coefficient	na
Largest diff. peak and hole	0.280 and -0.175 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for $C_{18}H_{31}N_2O_2Cl$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	5873(1)	4279(1)	5833(1)	26(1)
O(1)	4388(2)	5077(1)	7714(1)	26(1)
O(2)	7895(2)	4751(1)	7289(1)	24(1)
N(1)	3799(3)	5997(1)	8272(1)	31(1)
N(2)	4854(3)	5570(1)	6282(1)	22(1)
C(1)	4023(3)	5617(1)	7649(1)	24(1)
C(2)	3712(3)	5890(1)	6820(1)	22(1)
C(3)	6638(3)	5780(1)	6310(1)	23(1)
C(4)	7424(3)	5837(1)	7132(1)	23(1)
C(5)	7982(3)	5329(1)	7574(2)	23(1)
C(6)	8680(3)	5404(1)	8351(2)	26(1)
C(7)	8891(3)	6001(1)	8622(2)	32(1)
C(8)	8415(3)	6508(1)	8179(2)	33(1)
C(9)	7665(3)	6425(1)	7438(2)	29(1)
C(10)	4175(4)	5763(2)	9066(2)	43(1)
C(11)	3392(4)	6643(1)	8206(2)	41(1)
C(12)	1882(3)	5784(1)	6565(1)	25(1)
C(13)	1519(3)	5118(1)	6347(2)	29(1)

C(14)	1342(3)	6214(1)	5893(2)	31(1)
C(15)	9156(3)	4852(1)	8865(1)	27(1)
C(16)	10572(3)	4495(1)	8491(2)	29(1)
C(17)	9771(4)	5044(1)	9704(2)	38(1)
C(18)	7638(3)	4443(1)	8984(2)	30(1)
Cl(2)	5017(1)	2369(1)	3817(1)	29(1)
O(3)	3822(2)	1891(1)	6973(1)	30(1)
O(4)	7517(2)	1357(1)	7073(1)	28(1)
N(3)	3668(3)	2844(1)	7484(1)	29(1)
N(4)	5179(3)	2204(1)	5653(1)	23(1)
C(19)	3894(3)	2444(1)	6886(2)	26(1)
C(20)	4168(3)	2690(1)	6045(1)	23(1)
C(21)	7028(3)	2253(1)	5787(1)	24(1)
C(22)	7548(3)	2410(1)	6627(1)	23(1)
C(23)	7721(3)	1966(1)	7228(2)	24(1)
C(24)	8175(3)	2141(1)	8009(2)	28(1)
C(25)	8439(4)	2760(1)	8151(2)	33(1)
C(26)	8292(4)	3195(1)	7560(2)	34(1)
C(27)	7851(3)	3019(1)	6800(2)	28(1)
C(28)	3285(4)	2597(1)	8261(2)	40(1)
C(29)	3913(4)	3504(1)	7467(2)	33(1)
C(30)	2535(3)	2771(1)	5562(2)	30(1)
C(31)	1605(4)	3334(1)	5836(2)	37(1)
C(32)	1460(4)	2199(2)	5555(2)	40(1)
C(33)	8339(4)	1666(1)	8684(2)	34(1)
C(34)	6708(4)	1328(1)	8784(2)	39(1)
C(35)	8804(5)	1966(2)	9481(2)	50(1)
C(36)	9749(4)	1218(1)	8496(2)	34(1)
Cl(3)	4499(1)	5738(1)	4422(1)	26(1)
O(5)	8331(3)	3526(1)	4414(1)	41(1)
O(6)	5415(2)	3236(1)	2436(1)	30(1)
N(5)	9467(3)	3444(1)	3206(2)	38(1)
N(6)	6261(3)	4407(1)	4024(1)	26(1)
C(37)	8504(4)	3720(1)	3741(2)	32(1)
C(38)	7667(3)	4322(1)	3490(2)	29(1)
C(39)	4789(3)	4001(1)	3827(1)	23(1)
C(40)	4129(3)	4130(1)	2995(1)	24(1)

C(41)	4489(3)	3754(1)	2345(2)	24(1)
C(42)	3970(3)	3922(1)	1566(1)	25(1)
C(43)	3100(3)	4465(1)	1478(2)	30(1)
C(44)	2711(4)	4832(1)	2115(2)	34(1)
C(45)	3234(3)	4661(1)	2870(2)	28(1)
C(46)	10336(5)	2882(2)	3432(2)	53(1)
C(47)	9623(4)	3616(2)	2381(2)	39(1)
C(48)	8878(4)	4867(1)	3540(2)	39(1)
C(49)	9494(5)	4992(2)	4386(2)	61(1)
C(50)	8131(5)	5432(2)	3151(2)	57(1)
C(51)	4327(4)	3517(1)	846(2)	30(1)
C(52)	6180(4)	3407(2)	764(2)	41(1)
C(53)	3426(4)	2900(1)	933(2)	40(1)
C(54)	3689(4)	3812(2)	66(2)	42(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{18}H_{31}N_2O_2Cl$

O(1)-C(1)	1.221(3)
O(2)-C(5)	1.354(3)
O(2)-H(2O)	0.857(18)
N(1)-C(1)	1.354(3)
N(1)-C(11)	1.454(4)
N(1)-C(10)	1.456(4)
N(2)-C(2)	1.491(3)
N(2)-C(3)	1.517(3)
N(2)-H(1N)	0.937(17)
N(2)-H(2N)	0.915(17)
C(1)-C(2)	1.533(3)
C(2)-C(12)	1.548(3)
C(2)-H(2B)	1.0000
C(3)-C(4)	1.512(3)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(9)	1.398(4)
C(4)-C(5)	1.405(3)
C(5)-C(6)	1.420(3)

C(6)-C(7)	1.390(4)
C(6)-C(15)	1.528(3)
C(7)-C(8)	1.386(4)
C(7)-H(7A)	0.9500
C(8)-C(9)	1.383(4)
C(8)-H(8A)	0.9500
C(9)-H(9A)	0.9500
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-C(14)	1.526(3)
C(12)-C(13)	1.528(3)
C(12)-H(12A)	1.0000
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-C(16)	1.539(4)
C(15)-C(18)	1.540(4)
C(15)-C(17)	1.542(3)
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
O(3)-C(19)	1.222(3)
O(4)-C(23)	1.367(3)
O(4)-H(4O)	0.855(18)

N(3)-C(19)	1.350(3)
N(3)-C(29)	1.457(3)
N(3)-C(28)	1.458(3)
N(4)-C(20)	1.507(3)
N(4)-C(21)	1.512(3)
N(4)-H(3N)	0.914(17)
N(4)-H(4N)	0.914(17)
C(19)-C(20)	1.538(3)
C(20)-C(30)	1.542(3)
C(20)-H(20A)	1.0000
C(21)-C(22)	1.505(3)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-C(27)	1.383(4)
C(22)-C(23)	1.407(3)
C(23)-C(24)	1.409(4)
C(24)-C(25)	1.389(4)
C(24)-C(33)	1.543(4)
C(25)-C(26)	1.379(4)
C(25)-H(25A)	0.9500
C(26)-C(27)	1.375(4)
C(26)-H(26A)	0.9500
C(27)-H(27A)	0.9500
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-H(29A)	0.9800
C(29)-H(29B)	0.9800
C(29)-H(29C)	0.9800
C(30)-C(31)	1.524(4)
C(30)-C(32)	1.524(4)
C(30)-H(30A)	1.0000
C(31)-H(31A)	0.9800
C(31)-H(31B)	0.9800
C(31)-H(31C)	0.9800
C(32)-H(32A)	0.9800
C(32)-H(32B)	0.9800

C(32)-H(32C)	0.9800
C(33)-C(34)	1.528(4)
C(33)-C(35)	1.531(4)
C(33)-C(36)	1.545(4)
C(34)-H(34A)	0.9800
C(34)-H(34B)	0.9800
C(34)-H(34C)	0.9800
C(35)-H(35A)	0.9800
C(35)-H(35B)	0.9800
C(35)-H(35C)	0.9800
C(36)-H(36A)	0.9800
C(36)-H(36B)	0.9800
C(36)-H(36C)	0.9800
O(5)-C(37)	1.223(4)
O(6)-C(41)	1.363(3)
O(6)-H(6O)	0.851(18)
N(5)-C(37)	1.353(4)
N(5)-C(47)	1.449(4)
N(5)-C(46)	1.460(4)
N(6)-C(38)	1.485(4)
N(6)-C(39)	1.516(3)
N(6)-H(5N)	0.909(17)
N(6)-H(6N)	0.925(17)
C(37)-C(38)	1.533(4)
C(38)-C(48)	1.544(4)
C(38)-H(38A)	1.0000
C(39)-C(40)	1.512(3)
C(39)-H(39A)	0.9900
C(39)-H(39B)	0.9900
C(40)-C(45)	1.380(3)
C(40)-C(41)	1.408(4)
C(41)-C(42)	1.416(3)
C(42)-C(43)	1.386(4)
C(42)-C(51)	1.536(3)
C(43)-C(44)	1.384(4)
C(43)-H(43A)	0.9500
C(44)-C(45)	1.381(4)

C(44)-H(44A)	0.9500
C(45)-H(45A)	0.9500
C(46)-H(46A)	0.9800
C(46)-H(46B)	0.9800
C(46)-H(46C)	0.9800
C(47)-H(47A)	0.9800
C(47)-H(47B)	0.9800
C(47)-H(47C)	0.9800
C(48)-C(50)	1.518(5)
C(48)-C(49)	1.521(4)
C(48)-H(48A)	1.0000
C(49)-H(49A)	0.9800
C(49)-H(49B)	0.9800
C(49)-H(49C)	0.9800
C(50)-H(50A)	0.9800
C(50)-H(50B)	0.9800
C(50)-H(50C)	0.9800
C(51)-C(52)	1.530(4)
C(51)-C(54)	1.538(4)
C(51)-C(53)	1.545(4)
C(52)-H(52A)	0.9800
C(52)-H(52B)	0.9800
C(52)-H(52C)	0.9800
C(53)-H(53A)	0.9800
C(53)-H(53B)	0.9800
C(53)-H(53C)	0.9800
C(54)-H(54A)	0.9800
C(54)-H(54B)	0.9800
C(54)-H(54C)	0.9800

C(5)-O(2)-H(2O)	116(2)
C(1)-N(1)-C(11)	124.9(2)
C(1)-N(1)-C(10)	117.9(2)
C(11)-N(1)-C(10)	116.9(2)
C(2)-N(2)-C(3)	116.52(19)
C(2)-N(2)-H(1N)	111.0(18)
C(3)-N(2)-H(1N)	106.0(18)

C(2)-N(2)-H(2N)	113.3(18)
C(3)-N(2)-H(2N)	104.4(19)
H(1N)-N(2)-H(2N)	105(2)
O(1)-C(1)-N(1)	124.1(2)
O(1)-C(1)-C(2)	119.4(2)
N(1)-C(1)-C(2)	116.4(2)
N(2)-C(2)-C(1)	106.47(19)
N(2)-C(2)-C(12)	111.52(19)
C(1)-C(2)-C(12)	108.9(2)
N(2)-C(2)-H(2B)	110.0
C(1)-C(2)-H(2B)	110.0
C(12)-C(2)-H(2B)	110.0
C(4)-C(3)-N(2)	115.37(19)
C(4)-C(3)-H(3A)	108.4
N(2)-C(3)-H(3A)	108.4
C(4)-C(3)-H(3B)	108.4
N(2)-C(3)-H(3B)	108.4
H(3A)-C(3)-H(3B)	107.5
C(9)-C(4)-C(5)	119.5(2)
C(9)-C(4)-C(3)	117.6(2)
C(5)-C(4)-C(3)	122.7(2)
O(2)-C(5)-C(4)	122.5(2)
O(2)-C(5)-C(6)	116.8(2)
C(4)-C(5)-C(6)	120.6(2)
C(7)-C(6)-C(5)	117.0(2)
C(7)-C(6)-C(15)	121.9(2)
C(5)-C(6)-C(15)	121.1(2)
C(8)-C(7)-C(6)	123.0(2)
C(8)-C(7)-H(7A)	118.5
C(6)-C(7)-H(7A)	118.5
C(9)-C(8)-C(7)	119.2(2)
C(9)-C(8)-H(8A)	120.4
C(7)-C(8)-H(8A)	120.4
C(8)-C(9)-C(4)	120.5(2)
C(8)-C(9)-H(9A)	119.8
C(4)-C(9)-H(9A)	119.8
N(1)-C(10)-H(10A)	109.5

N(1)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
N(1)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
N(1)-C(11)-H(11A)	109.5
N(1)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
N(1)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(14)-C(12)-C(13)	111.1(2)
C(14)-C(12)-C(2)	111.4(2)
C(13)-C(12)-C(2)	112.7(2)
C(14)-C(12)-H(12A)	107.1
C(13)-C(12)-H(12A)	107.1
C(2)-C(12)-H(12A)	107.1
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(12)-C(14)-H(14A)	109.5
C(12)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(12)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(6)-C(15)-C(16)	110.3(2)
C(6)-C(15)-C(18)	110.2(2)
C(16)-C(15)-C(18)	111.4(2)
C(6)-C(15)-C(17)	111.9(2)
C(16)-C(15)-C(17)	106.8(2)
C(18)-C(15)-C(17)	106.1(2)
C(15)-C(16)-H(16A)	109.5
C(15)-C(16)-H(16B)	109.5

H(16A)-C(16)-H(16B)	109.5
C(15)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
C(15)-C(17)-H(17A)	109.5
C(15)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(15)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(15)-C(18)-H(18A)	109.5
C(15)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(15)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(23)-O(4)-H(4O)	113(2)
C(19)-N(3)-C(29)	127.2(2)
C(19)-N(3)-C(28)	117.9(2)
C(29)-N(3)-C(28)	114.7(2)
C(20)-N(4)-C(21)	115.74(18)
C(20)-N(4)-H(3N)	107.2(18)
C(21)-N(4)-H(3N)	111.7(19)
C(20)-N(4)-H(4N)	112.2(18)
C(21)-N(4)-H(4N)	102.1(19)
H(3N)-N(4)-H(4N)	108(2)
O(3)-C(19)-N(3)	122.9(2)
O(3)-C(19)-C(20)	117.8(2)
N(3)-C(19)-C(20)	119.3(2)
N(4)-C(20)-C(19)	104.64(19)
N(4)-C(20)-C(30)	108.55(19)
C(19)-C(20)-C(30)	112.4(2)
N(4)-C(20)-H(20A)	110.4
C(19)-C(20)-H(20A)	110.4
C(30)-C(20)-H(20A)	110.4
C(22)-C(21)-N(4)	113.9(2)
C(22)-C(21)-H(21A)	108.8

N(4)-C(21)-H(21A)	108.8
C(22)-C(21)-H(21B)	108.8
N(4)-C(21)-H(21B)	108.8
H(21A)-C(21)-H(21B)	107.7
C(27)-C(22)-C(23)	119.9(2)
C(27)-C(22)-C(21)	117.5(2)
C(23)-C(22)-C(21)	122.6(2)
O(4)-C(23)-C(22)	121.7(2)
O(4)-C(23)-C(24)	118.0(2)
C(22)-C(23)-C(24)	120.2(2)
C(25)-C(24)-C(23)	117.3(2)
C(25)-C(24)-C(33)	121.3(2)
C(23)-C(24)-C(33)	121.3(2)
C(26)-C(25)-C(24)	122.6(2)
C(26)-C(25)-H(25A)	118.7
C(24)-C(25)-H(25A)	118.7
C(27)-C(26)-C(25)	119.6(3)
C(27)-C(26)-H(26A)	120.2
C(25)-C(26)-H(26A)	120.2
C(26)-C(27)-C(22)	120.3(2)
C(26)-C(27)-H(27A)	119.8
C(22)-C(27)-H(27A)	119.8
N(3)-C(28)-H(28A)	109.5
N(3)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
N(3)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
N(3)-C(29)-H(29A)	109.5
N(3)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29B)	109.5
N(3)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5
C(31)-C(30)-C(32)	112.2(2)
C(31)-C(30)-C(20)	110.9(2)
C(32)-C(30)-C(20)	113.0(2)

C(31)-C(30)-H(30A)	106.8
C(32)-C(30)-H(30A)	106.8
C(20)-C(30)-H(30A)	106.8
C(30)-C(31)-H(31A)	109.5
C(30)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31B)	109.5
C(30)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
C(30)-C(32)-H(32A)	109.5
C(30)-C(32)-H(32B)	109.5
H(32A)-C(32)-H(32B)	109.5
C(30)-C(32)-H(32C)	109.5
H(32A)-C(32)-H(32C)	109.5
H(32B)-C(32)-H(32C)	109.5
C(34)-C(33)-C(35)	107.6(3)
C(34)-C(33)-C(24)	110.6(2)
C(35)-C(33)-C(24)	111.8(2)
C(34)-C(33)-C(36)	111.2(2)
C(35)-C(33)-C(36)	106.7(2)
C(24)-C(33)-C(36)	108.9(2)
C(33)-C(34)-H(34A)	109.5
C(33)-C(34)-H(34B)	109.5
H(34A)-C(34)-H(34B)	109.5
C(33)-C(34)-H(34C)	109.5
H(34A)-C(34)-H(34C)	109.5
H(34B)-C(34)-H(34C)	109.5
C(33)-C(35)-H(35A)	109.5
C(33)-C(35)-H(35B)	109.5
H(35A)-C(35)-H(35B)	109.5
C(33)-C(35)-H(35C)	109.5
H(35A)-C(35)-H(35C)	109.5
H(35B)-C(35)-H(35C)	109.5
C(33)-C(36)-H(36A)	109.5
C(33)-C(36)-H(36B)	109.5
H(36A)-C(36)-H(36B)	109.5
C(33)-C(36)-H(36C)	109.5

H(36A)-C(36)-H(36C)	109.5
H(36B)-C(36)-H(36C)	109.5
C(41)-O(6)-H(6O)	110(2)
C(37)-N(5)-C(47)	126.3(2)
C(37)-N(5)-C(46)	119.0(3)
C(47)-N(5)-C(46)	114.5(3)
C(38)-N(6)-C(39)	113.96(19)
C(38)-N(6)-H(5N)	112.0(19)
C(39)-N(6)-H(5N)	102.8(19)
C(38)-N(6)-H(6N)	110.3(19)
C(39)-N(6)-H(6N)	104.8(19)
H(5N)-N(6)-H(6N)	113(3)
O(5)-C(37)-N(5)	123.2(3)
O(5)-C(37)-C(38)	119.4(3)
N(5)-C(37)-C(38)	117.3(2)
N(6)-C(38)-C(37)	106.3(2)
N(6)-C(38)-C(48)	111.6(2)
C(37)-C(38)-C(48)	111.8(2)
N(6)-C(38)-H(38A)	109.0
C(37)-C(38)-H(38A)	109.0
C(48)-C(38)-H(38A)	109.0
C(40)-C(39)-N(6)	110.31(19)
C(40)-C(39)-H(39A)	109.6
N(6)-C(39)-H(39A)	109.6
C(40)-C(39)-H(39B)	109.6
N(6)-C(39)-H(39B)	109.6
H(39A)-C(39)-H(39B)	108.1
C(45)-C(40)-C(41)	119.6(2)
C(45)-C(40)-C(39)	117.9(2)
C(41)-C(40)-C(39)	122.3(2)
O(6)-C(41)-C(40)	121.7(2)
O(6)-C(41)-C(42)	117.8(2)
C(40)-C(41)-C(42)	120.4(2)
C(43)-C(42)-C(41)	117.2(2)
C(43)-C(42)-C(51)	121.1(2)
C(41)-C(42)-C(51)	121.7(2)
C(44)-C(43)-C(42)	122.8(2)

C(44)-C(43)-H(43A)	118.6
C(42)-C(43)-H(43A)	118.6
C(45)-C(44)-C(43)	119.1(2)
C(45)-C(44)-H(44A)	120.4
C(43)-C(44)-H(44A)	120.4
C(40)-C(45)-C(44)	120.9(2)
C(40)-C(45)-H(45A)	119.6
C(44)-C(45)-H(45A)	119.6
N(5)-C(46)-H(46A)	109.5
N(5)-C(46)-H(46B)	109.5
H(46A)-C(46)-H(46B)	109.5
N(5)-C(46)-H(46C)	109.5
H(46A)-C(46)-H(46C)	109.5
H(46B)-C(46)-H(46C)	109.5
N(5)-C(47)-H(47A)	109.5
N(5)-C(47)-H(47B)	109.5
H(47A)-C(47)-H(47B)	109.5
N(5)-C(47)-H(47C)	109.5
H(47A)-C(47)-H(47C)	109.5
H(47B)-C(47)-H(47C)	109.5
C(50)-C(48)-C(49)	111.8(3)
C(50)-C(48)-C(38)	111.2(3)
C(49)-C(48)-C(38)	112.3(3)
C(50)-C(48)-H(48A)	107.0
C(49)-C(48)-H(48A)	107.0
C(38)-C(48)-H(48A)	107.0
C(48)-C(49)-H(49A)	109.5
C(48)-C(49)-H(49B)	109.5
H(49A)-C(49)-H(49B)	109.5
C(48)-C(49)-H(49C)	109.5
H(49A)-C(49)-H(49C)	109.5
H(49B)-C(49)-H(49C)	109.5
C(48)-C(50)-H(50A)	109.5
C(48)-C(50)-H(50B)	109.5
H(50A)-C(50)-H(50B)	109.5
C(48)-C(50)-H(50C)	109.5
H(50A)-C(50)-H(50C)	109.5

H(50B)-C(50)-H(50C)	109.5
C(52)-C(51)-C(42)	111.8(2)
C(52)-C(51)-C(54)	107.1(2)
C(42)-C(51)-C(54)	111.5(2)
C(52)-C(51)-C(53)	109.8(2)
C(42)-C(51)-C(53)	109.1(2)
C(54)-C(51)-C(53)	107.5(2)
C(51)-C(52)-H(52A)	109.5
C(51)-C(52)-H(52B)	109.5
H(52A)-C(52)-H(52B)	109.5
C(51)-C(52)-H(52C)	109.5
H(52A)-C(52)-H(52C)	109.5
H(52B)-C(52)-H(52C)	109.5
C(51)-C(53)-H(53A)	109.5
C(51)-C(53)-H(53B)	109.5
H(53A)-C(53)-H(53B)	109.5
C(51)-C(53)-H(53C)	109.5
H(53A)-C(53)-H(53C)	109.5
H(53B)-C(53)-H(53C)	109.5
C(51)-C(54)-H(54A)	109.5
C(51)-C(54)-H(54B)	109.5
H(54A)-C(54)-H(54B)	109.5
C(51)-C(54)-H(54C)	109.5
H(54A)-C(54)-H(54C)	109.5
H(54B)-C(54)-H(54C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for $C_{18}H_{31}N_2O_2Cl$ The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	34(1)	25(1)	21(1)	0(1)	-3(1)	2(1)
O(1)	23(1)	31(1)	24(1)	4(1)	-1(1)	-1(1)

O(2)	26(1)	24(1)	21(1)	-2(1)	-5(1)	0(1)
N(1)	25(1)	44(1)	25(1)	-8(1)	1(1)	-3(1)
N(2)	20(1)	23(1)	22(1)	-1(1)	1(1)	0(1)
C(1)	13(1)	36(1)	23(1)	-2(1)	0(1)	-5(1)
C(2)	17(1)	24(1)	25(1)	-4(1)	4(1)	1(1)
C(3)	16(1)	28(1)	26(1)	4(1)	3(1)	0(1)
C(4)	15(1)	28(1)	27(1)	-1(1)	2(1)	-3(1)
C(5)	13(1)	28(1)	28(1)	-3(1)	2(1)	-1(1)
C(6)	18(1)	30(1)	29(1)	-3(1)	-1(1)	-1(1)
C(7)	24(2)	36(1)	37(2)	-8(1)	-6(1)	-3(1)
C(8)	29(2)	27(1)	42(2)	-9(1)	-5(1)	-2(1)
C(9)	21(1)	27(1)	38(1)	-2(1)	0(1)	-3(1)
C(10)	35(2)	72(2)	22(1)	-9(1)	0(1)	-5(2)
C(11)	39(2)	45(2)	40(2)	-14(1)	6(1)	-4(1)
C(12)	18(1)	34(1)	22(1)	-1(1)	2(1)	1(1)
C(13)	18(1)	38(2)	31(1)	1(1)	-2(1)	-2(1)
C(14)	23(2)	38(1)	32(1)	3(1)	-3(1)	3(1)
C(15)	25(2)	34(1)	22(1)	-3(1)	-5(1)	-1(1)
C(16)	22(1)	36(1)	28(1)	0(1)	-5(1)	1(1)
C(17)	40(2)	46(2)	27(2)	-6(1)	-12(1)	3(1)
C(18)	28(2)	37(2)	26(1)	4(1)	-1(1)	-1(1)
Cl(2)	40(1)	24(1)	24(1)	0(1)	-2(1)	2(1)
O(3)	32(1)	31(1)	29(1)	1(1)	2(1)	-4(1)
O(4)	32(1)	25(1)	26(1)	-1(1)	-6(1)	-1(1)
N(3)	27(1)	33(1)	27(1)	-2(1)	2(1)	-2(1)
N(4)	20(1)	25(1)	24(1)	0(1)	-1(1)	0(1)
C(19)	16(1)	33(1)	29(1)	0(1)	-2(1)	-3(1)
C(20)	20(1)	25(1)	25(1)	-3(1)	0(1)	2(1)
C(21)	19(1)	27(1)	26(1)	1(1)	0(1)	2(1)
C(22)	17(1)	28(1)	24(1)	2(1)	-1(1)	2(1)
C(23)	19(1)	25(1)	30(1)	-1(1)	1(1)	1(1)
C(24)	24(2)	31(1)	29(1)	-1(1)	-4(1)	4(1)
C(25)	33(2)	34(1)	31(1)	-7(1)	-10(1)	4(1)
C(26)	34(2)	25(1)	42(2)	-5(1)	-8(1)	-2(1)
C(27)	23(2)	27(1)	34(1)	4(1)	-3(1)	1(1)
C(28)	48(2)	43(2)	28(2)	-2(1)	10(1)	-1(1)
C(29)	33(2)	34(1)	31(1)	-4(1)	4(1)	4(1)

C(30)	21(2)	42(2)	27(1)	-2(1)	-2(1)	1(1)
C(31)	26(2)	48(2)	37(1)	2(1)	-4(1)	9(1)
C(32)	25(2)	52(2)	41(2)	-7(1)	-6(1)	-2(1)
C(33)	38(2)	34(1)	29(1)	-2(1)	-7(1)	6(1)
C(34)	46(2)	41(2)	30(1)	7(1)	6(1)	7(1)
C(35)	77(3)	42(2)	31(2)	-3(1)	-17(2)	14(2)
C(36)	39(2)	31(1)	32(1)	4(1)	-10(1)	3(1)
Cl(3)	32(1)	25(1)	21(1)	0(1)	-1(1)	1(1)
O(5)	39(1)	48(1)	36(1)	3(1)	-6(1)	10(1)
O(6)	37(1)	32(1)	22(1)	3(1)	2(1)	11(1)
N(5)	29(1)	43(1)	43(1)	-9(1)	-4(1)	9(1)
N(6)	26(1)	32(1)	21(1)	-3(1)	0(1)	0(1)
C(37)	27(2)	39(2)	31(2)	-5(1)	-7(1)	1(1)
C(38)	25(2)	37(1)	25(1)	-1(1)	-1(1)	2(1)
C(39)	23(1)	24(1)	23(1)	-2(1)	2(1)	-2(1)
C(40)	18(1)	28(1)	26(1)	-2(1)	-1(1)	-4(1)
C(41)	18(1)	25(1)	28(1)	1(1)	0(1)	0(1)
C(42)	22(2)	29(1)	26(1)	-1(1)	0(1)	-5(1)
C(43)	27(2)	32(1)	30(1)	6(1)	-8(1)	-1(1)
C(44)	34(2)	28(1)	38(2)	1(1)	-8(1)	6(1)
C(45)	24(2)	24(1)	35(1)	-6(1)	-3(1)	0(1)
C(46)	54(2)	50(2)	56(2)	0(2)	2(2)	20(2)
C(47)	31(2)	49(2)	38(2)	-11(1)	2(1)	1(1)
C(48)	34(2)	42(2)	41(2)	-9(1)	12(1)	-4(1)
C(49)	64(3)	71(2)	48(2)	-23(2)	3(2)	-30(2)
C(50)	60(3)	39(2)	75(3)	6(2)	32(2)	-2(2)
C(51)	35(2)	33(1)	23(1)	0(1)	-3(1)	0(1)
C(52)	44(2)	55(2)	25(1)	0(1)	5(1)	4(2)
C(53)	47(2)	34(2)	36(2)	-7(1)	-8(1)	-1(1)
C(54)	56(2)	46(2)	25(1)	-1(1)	-4(1)	7(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for $C_{18}H_{31}N_2O_2Cl$

	x	y	z	U(eq)

H(2O)	7320(30)	4705(14)	6859(13)	36
H(1N)	4490(30)	5606(12)	5751(11)	26
H(2N)	4910(40)	5157(8)	6370(16)	26
H(2B)	3960	6338	6829	26
H(3A)	7297	5488	6001	28
H(3B)	6699	6183	6044	28
H(7A)	9384	6063	9134	39
H(8A)	8602	6909	8381	39
H(9A)	7312	6770	7136	34
H(10A)	4262	5317	9047	65
H(10B)	3292	5880	9421	65
H(10C)	5224	5936	9264	65
H(11A)	4405	6880	8139	62
H(11B)	2851	6777	8688	62
H(11C)	2645	6707	7745	62
H(12A)	1201	5886	7032	30
H(13A)	348	5075	6194	43
H(13B)	1777	4856	6805	43
H(13C)	2197	4997	5902	43
H(14A)	180	6139	5748	47
H(14B)	2023	6141	5432	47
H(14C)	1477	6639	6069	47
H(16A)	11517	4767	8423	43
H(16B)	10200	4335	7973	43
H(16C)	10900	4154	8840	43
H(17A)	10743	5308	9662	57
H(17B)	10068	4679	10013	57
H(17C)	8895	5268	9968	57
H(18A)	7195	4307	8466	45
H(18B)	6791	4675	9257	45
H(18C)	7962	4086	9304	45
H(4O)	6910(40)	1290(15)	6658(14)	42
H(3N)	4790(40)	1834(9)	5814(16)	28
H(4N)	5070(40)	2218(13)	5112(10)	28
H(20A)	4790	3085	6071	28
H(21A)	7539	1858	5643	29

H(21B)	7456	2569	5427	29
H(25A)	8732	2888	8675	39
H(26A)	8494	3613	7678	40
H(27A)	7753	3317	6391	34
H(28A)	3041	2159	8211	59
H(28B)	2323	2810	8465	59
H(28C)	4234	2655	8627	59
H(29A)	4293	3625	6944	49
H(29B)	4743	3620	7875	49
H(29C)	2868	3710	7571	49
H(30A)	2838	2848	4999	36
H(31A)	570	3375	5523	55
H(31B)	2286	3699	5761	55
H(31C)	1359	3292	6399	55
H(32A)	440	2277	5244	60
H(32B)	1188	2092	6100	60
H(32C)	2061	1859	5316	60
H(34A)	5839	1622	8905	58
H(34B)	6830	1033	9219	58
H(34C)	6409	1111	8291	58
H(35A)	7940	2256	9623	76
H(35B)	9855	2184	9438	76
H(35C)	8915	1651	9892	76
H(36A)	9865	915	8923	51
H(36B)	10785	1445	8454	51
H(36C)	9490	1009	7993	51
H(6O)	5220(40)	3068(14)	2878(13)	45
H(5N)	6530(40)	4301(14)	4533(11)	32
H(6N)	5860(40)	4802(9)	3982(17)	32
H(38A)	7230	4281	2931	35
H(39A)	5124	3566	3869	28
H(39B)	3912	4075	4212	28
H(43A)	2757	4591	959	36
H(44A)	2093	5197	2033	41
H(45A)	2974	4911	3310	33
H(46A)	10179	2800	3997	80
H(46B)	11516	2930	3338	80

H(46C)	9894	2541	3115	80
H(47A)	8932	3975	2265	59
H(47B)	9264	3276	2039	59
H(47C)	10778	3714	2281	59
H(48A)	9863	4752	3229	47
H(49A)	10255	5341	4388	91
H(49B)	10070	4630	4597	91
H(49C)	8553	5087	4717	91
H(50A)	8924	5770	3191	86
H(50B)	7121	5546	3422	86
H(50C)	7865	5347	2591	86
H(52A)	6360	3147	301	61
H(52B)	6624	3204	1243	61
H(52C)	6742	3800	695	61
H(53A)	3646	2640	474	59
H(53B)	2236	2971	962	59
H(53C)	3826	2695	1420	59
H(54A)	3927	3542	-380	63
H(54B)	4239	4206	-6	63
H(54C)	2494	3876	89	63

Table 6. Torsion angles [°] for $C_{18}H_{31}N_2O_2Cl$

C(11)-N(1)-C(1)-O(1)	178.9(3)
C(10)-N(1)-C(1)-O(1)	6.3(4)
C(11)-N(1)-C(1)-C(2)	-3.9(4)
C(10)-N(1)-C(1)-C(2)	-176.6(2)
C(3)-N(2)-C(2)-C(1)	-78.7(2)
C(3)-N(2)-C(2)-C(12)	162.57(19)
O(1)-C(1)-C(2)-N(2)	-34.0(3)
N(1)-C(1)-C(2)-N(2)	148.7(2)
O(1)-C(1)-C(2)-C(12)	86.4(3)
N(1)-C(1)-C(2)-C(12)	-90.9(3)
C(2)-N(2)-C(3)-C(4)	48.5(3)
N(2)-C(3)-C(4)-C(9)	-105.6(3)
N(2)-C(3)-C(4)-C(5)	77.6(3)

C(9)-C(4)-C(5)-O(2)	-175.1(2)
C(3)-C(4)-C(5)-O(2)	1.7(4)
C(9)-C(4)-C(5)-C(6)	4.5(4)
C(3)-C(4)-C(5)-C(6)	-178.7(2)
O(2)-C(5)-C(6)-C(7)	175.1(2)
C(4)-C(5)-C(6)-C(7)	-4.6(4)
O(2)-C(5)-C(6)-C(15)	-5.6(4)
C(4)-C(5)-C(6)-C(15)	174.7(2)
C(5)-C(6)-C(7)-C(8)	1.7(4)
C(15)-C(6)-C(7)-C(8)	-177.6(3)
C(6)-C(7)-C(8)-C(9)	1.3(5)
C(7)-C(8)-C(9)-C(4)	-1.5(4)
C(5)-C(4)-C(9)-C(8)	-1.4(4)
C(3)-C(4)-C(9)-C(8)	-178.4(2)
N(2)-C(2)-C(12)-C(14)	-81.6(3)
C(1)-C(2)-C(12)-C(14)	161.2(2)
N(2)-C(2)-C(12)-C(13)	44.0(3)
C(1)-C(2)-C(12)-C(13)	-73.2(2)
C(7)-C(6)-C(15)-C(16)	-115.4(3)
C(5)-C(6)-C(15)-C(16)	65.3(3)
C(7)-C(6)-C(15)-C(18)	121.1(3)
C(5)-C(6)-C(15)-C(18)	-58.2(3)
C(7)-C(6)-C(15)-C(17)	3.4(4)
C(5)-C(6)-C(15)-C(17)	-175.9(3)
C(29)-N(3)-C(19)-O(3)	172.3(3)
C(28)-N(3)-C(19)-O(3)	-1.5(4)
C(29)-N(3)-C(19)-C(20)	-10.9(4)
C(28)-N(3)-C(19)-C(20)	175.4(2)
C(21)-N(4)-C(20)-C(19)	-86.5(2)
C(21)-N(4)-C(20)-C(30)	153.2(2)
O(3)-C(19)-C(20)-N(4)	-30.7(3)
N(3)-C(19)-C(20)-N(4)	152.3(2)
O(3)-C(19)-C(20)-C(30)	86.9(3)
N(3)-C(19)-C(20)-C(30)	-90.1(3)
C(20)-N(4)-C(21)-C(22)	42.3(3)
N(4)-C(21)-C(22)-C(27)	-95.7(3)
N(4)-C(21)-C(22)-C(23)	83.8(3)

C(27)-C(22)-C(23)-O(4)	-176.5(2)
C(21)-C(22)-C(23)-O(4)	3.9(4)
C(27)-C(22)-C(23)-C(24)	1.0(4)
C(21)-C(22)-C(23)-C(24)	-178.5(2)
O(4)-C(23)-C(24)-C(25)	177.6(3)
C(22)-C(23)-C(24)-C(25)	-0.1(4)
O(4)-C(23)-C(24)-C(33)	-3.6(4)
C(22)-C(23)-C(24)-C(33)	178.7(3)
C(23)-C(24)-C(25)-C(26)	-0.8(5)
C(33)-C(24)-C(25)-C(26)	-179.6(3)
C(24)-C(25)-C(26)-C(27)	0.7(5)
C(25)-C(26)-C(27)-C(22)	0.3(4)
C(23)-C(22)-C(27)-C(26)	-1.2(4)
C(21)-C(22)-C(27)-C(26)	178.4(3)
N(4)-C(20)-C(30)-C(31)	-169.4(2)
C(19)-C(20)-C(30)-C(31)	75.3(3)
N(4)-C(20)-C(30)-C(32)	63.5(3)
C(19)-C(20)-C(30)-C(32)	-51.7(3)
C(25)-C(24)-C(33)-C(34)	120.0(3)
C(23)-C(24)-C(33)-C(34)	-58.8(4)
C(25)-C(24)-C(33)-C(35)	0.1(4)
C(23)-C(24)-C(33)-C(35)	-178.6(3)
C(25)-C(24)-C(33)-C(36)	-117.6(3)
C(23)-C(24)-C(33)-C(36)	63.7(3)
C(47)-N(5)-C(37)-O(5)	174.4(3)
C(46)-N(5)-C(37)-O(5)	0.6(4)
C(47)-N(5)-C(37)-C(38)	-8.5(4)
C(46)-N(5)-C(37)-C(38)	177.7(3)
C(39)-N(6)-C(38)-C(37)	-75.6(2)
C(39)-N(6)-C(38)-C(48)	162.2(2)
O(5)-C(37)-C(38)-N(6)	-23.1(3)
N(5)-C(37)-C(38)-N(6)	159.7(2)
O(5)-C(37)-C(38)-C(48)	98.9(3)
N(5)-C(37)-C(38)-C(48)	-78.3(3)
C(38)-N(6)-C(39)-C(40)	-60.4(3)
N(6)-C(39)-C(40)-C(45)	-74.9(3)
N(6)-C(39)-C(40)-C(41)	100.7(3)

C(45)-C(40)-C(41)-O(6)	177.8(2)
C(39)-C(40)-C(41)-O(6)	2.2(4)
C(45)-C(40)-C(41)-C(42)	1.3(4)
C(39)-C(40)-C(41)-C(42)	-174.3(2)
O(6)-C(41)-C(42)-C(43)	-176.9(2)
C(40)-C(41)-C(42)-C(43)	-0.2(4)
O(6)-C(41)-C(42)-C(51)	4.1(4)
C(40)-C(41)-C(42)-C(51)	-179.3(2)
C(41)-C(42)-C(43)-C(44)	-1.1(4)
C(51)-C(42)-C(43)-C(44)	178.0(3)
C(42)-C(43)-C(44)-C(45)	1.3(4)
C(41)-C(40)-C(45)-C(44)	-1.1(4)
C(39)-C(40)-C(45)-C(44)	174.6(2)
C(43)-C(44)-C(45)-C(40)	-0.2(4)
N(6)-C(38)-C(48)-C(50)	-71.3(3)
C(37)-C(38)-C(48)-C(50)	169.7(2)
N(6)-C(38)-C(48)-C(49)	54.9(3)
C(37)-C(38)-C(48)-C(49)	-64.1(3)
C(43)-C(42)-C(51)-C(52)	122.7(3)
C(41)-C(42)-C(51)-C(52)	-58.2(3)
C(43)-C(42)-C(51)-C(54)	2.9(4)
C(41)-C(42)-C(51)-C(54)	-178.0(3)
C(43)-C(42)-C(51)-C(53)	-115.6(3)
C(41)-C(42)-C(51)-C(53)	63.4(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{18}H_{31}N_2O_2Cl$ [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2O)...Cl(1)	0.857(18)	2.26(2)	3.0861(17)	162(3)
N(2)-H(2N)...Cl(1)	0.915(17)	2.27(2)	3.042(2)	142(2)
N(2)-H(1N)...Cl(3)	0.937(17)	2.259(19)	3.161(2)	161(2)
O(4)-H(4O)...Cl(3)#1	0.855(18)	2.44(2)	3.2538(18)	160(3)

N(4)-H(3N)...O(3)	0.914(17)	2.13(3)	2.603(3)	111(2)
N(4)-H(3N)...Cl(3)#1	0.914(17)	2.50(2)	3.218(2)	136(2)
N(4)-H(4N)...Cl(2)	0.914(17)	2.205(18)	3.113(2)	172(3)
O(6)-H(6O)...Cl(2)	0.851(18)	2.21(2)	3.0290(19)	161(3)
N(6)-H(5N)...Cl(1)	0.909(17)	2.27(2)	3.087(2)	149(3)
N(6)-H(6N)...Cl(3)	0.925(17)	2.45(2)	3.320(2)	157(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+1

X-ray Crystal Structure of 1.19r

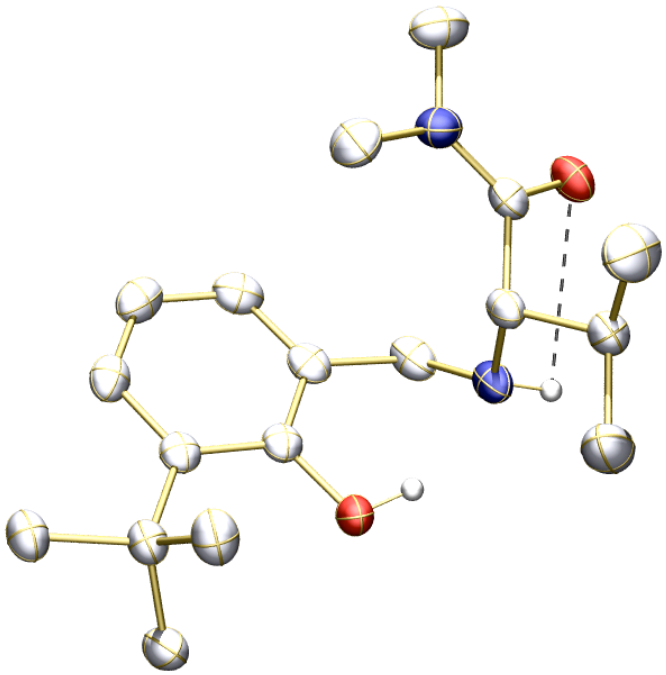


Table 1. Crystal data and structure refinement for $C_{18}H_{30}N_2O_2$

Identification code	$C_{18}H_{30}N_2O_2$	
Empirical formula	$C_{18}H_{30}N_2O_2$	
Formula weight	306.44	
Temperature	143(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.4590(6) Å	α= 90°
	b = 14.9795(12) Å	β= 90°

	c = 16.2770(13) Å γ = 90°
Volume	1818.7(3) $Å^3$
Z	4
Density (calculated)	1.119 Mg/m^3
Absorption coefficient	0.570 mm^{-1}
F(000)	672
Crystal size	0.17 x 0.10 x 0.05 mm^3
Theta range for data collection	4.01 to 67.94°
Index ranges	-8<=h<=3, -18<=k<=17, -19<=l<=19
Reflections collected	13923
Independent reflections	3190 [R(int) = 0.0179]
Completeness to theta = 67.94°	99.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9721 and 0.9093
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3190 / 3 / 210
Goodness-of-fit on F^2	1.064
Final R indices [I>2sigma(I)]	R1 = 0.0292, wR2 = 0.0780
R indices (all data)	R1 = 0.0293, wR2 = 0.0781
Absolute structure parameter	0.09(19)
Extinction coefficient	na
Largest diff. peak and hole	0.144 and -0.103 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for $C_{18}H_{30}N_2O_2$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-318(1)	6477(1)	2399(1)	34(1)
O(2)	4304(1)	8137(1)	390(1)	39(1)
N(1)	1412(2)	7118(1)	1121(1)	33(1)
N(2)	5199(2)	8362(1)	1699(1)	36(1)
C(1)	-51(2)	7283(1)	2771(1)	28(1)
C(2)	-223(2)	7349(1)	3633(1)	28(1)
C(3)	18(2)	8194(1)	3976(1)	33(1)

C(4)	456(2)	8934(1)	3510(1)	37(1)
C(5)	650(2)	8851(1)	2667(1)	36(1)
C(6)	380(2)	8032(1)	2291(1)	31(1)
C(7)	503(2)	7944(1)	1367(1)	36(1)
C(8)	3309(2)	7046(1)	1351(1)	29(1)
C(9)	4330(2)	7894(1)	1115(1)	31(1)
C(10)	5325(2)	8115(1)	2566(1)	44(1)
C(11)	6055(2)	9200(1)	1471(1)	48(1)
C(12)	-610(2)	6519(1)	4160(1)	31(1)
C(13)	882(2)	5825(1)	4040(1)	40(1)
C(14)	-2426(2)	6110(1)	3925(1)	40(1)
C(15)	-673(2)	6747(1)	5081(1)	38(1)
C(16)	4143(2)	6228(1)	933(1)	35(1)
C(17)	6119(2)	6137(1)	1134(1)	54(1)
C(18)	3107(3)	5387(1)	1155(1)	56(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{18}H_{30}N_2O_2$

O(1)-C(1)	1.3656(15)
O(1)-H(1O)	0.839(13)
O(2)-C(9)	1.2351(15)
N(1)-C(7)	1.4659(19)
N(1)-C(8)	1.4678(17)
N(1)-H(1N)	0.898(13)
N(2)-C(9)	1.3472(17)
N(2)-C(11)	1.4563(18)
N(2)-C(10)	1.4629(18)
C(1)-C(6)	1.4043(17)
C(1)-C(2)	1.4111(17)
C(2)-C(3)	1.3956(18)
C(2)-C(12)	1.5382(17)
C(3)-C(4)	1.382(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.385(2)
C(4)-H(4)	0.9500
C(5)-C(6)	1.3858(19)

C(5)-H(5)	0.9500
C(6)-C(7)	1.5127(17)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.5297(17)
C(8)-C(16)	1.5332(19)
C(8)-H(8)	0.991(12)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-C(14)	1.535(2)
C(12)-C(13)	1.5355(19)
C(12)-C(15)	1.5385(17)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(17)	1.516(2)
C(16)-C(18)	1.522(2)
C(16)-H(16)	1.0000
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(1)-O(1)-H(1O)	106.8(11)
C(7)-N(1)-C(8)	115.97(11)
C(7)-N(1)-H(1N)	109.7(10)

C(8)-N(1)-H(1N)	110.8(11)
C(9)-N(2)-C(11)	118.70(12)
C(9)-N(2)-C(10)	125.46(11)
C(11)-N(2)-C(10)	115.81(12)
O(1)-C(1)-C(6)	119.55(11)
O(1)-C(1)-C(2)	119.25(11)
C(6)-C(1)-C(2)	121.20(11)
C(3)-C(2)-C(1)	116.73(11)
C(3)-C(2)-C(12)	122.22(11)
C(1)-C(2)-C(12)	121.03(11)
C(4)-C(3)-C(2)	122.53(12)
C(4)-C(3)-H(3)	118.7
C(2)-C(3)-H(3)	118.7
C(3)-C(4)-C(5)	119.78(12)
C(3)-C(4)-H(4)	120.1
C(5)-C(4)-H(4)	120.1
C(4)-C(5)-C(6)	120.08(12)
C(4)-C(5)-H(5)	120.0
C(6)-C(5)-H(5)	120.0
C(5)-C(6)-C(1)	119.65(12)
C(5)-C(6)-C(7)	120.53(12)
C(1)-C(6)-C(7)	119.80(12)
N(1)-C(7)-C(6)	111.95(10)
N(1)-C(7)-H(7A)	109.2
C(6)-C(7)-H(7A)	109.2
N(1)-C(7)-H(7B)	109.2
C(6)-C(7)-H(7B)	109.2
H(7A)-C(7)-H(7B)	107.9
N(1)-C(8)-C(9)	110.81(10)
N(1)-C(8)-C(16)	109.65(11)
C(9)-C(8)-C(16)	110.53(10)
N(1)-C(8)-H(8)	107.6(9)
C(9)-C(8)-H(8)	110.4(9)
C(16)-C(8)-H(8)	107.7(9)
O(2)-C(9)-N(2)	121.89(12)
O(2)-C(9)-C(8)	118.46(11)
N(2)-C(9)-C(8)	119.64(11)

N(2)-C(10)-H(10A)	109.5
N(2)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
N(2)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
N(2)-C(11)-H(11A)	109.5
N(2)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
N(2)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(14)-C(12)-C(13)	109.77(11)
C(14)-C(12)-C(2)	110.44(11)
C(13)-C(12)-C(2)	109.86(11)
C(14)-C(12)-C(15)	107.73(11)
C(13)-C(12)-C(15)	107.23(11)
C(2)-C(12)-C(15)	111.73(11)
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(12)-C(14)-H(14A)	109.5
C(12)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(12)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(12)-C(15)-H(15A)	109.5
C(12)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(12)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(17)-C(16)-C(18)	111.58(14)

C(17)-C(16)-C(8)	111.74(12)
C(18)-C(16)-C(8)	110.55(11)
C(17)-C(16)-H(16)	107.6
C(18)-C(16)-H(16)	107.6
C(8)-C(16)-H(16)	107.6
C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for $C_{18}H_{30}N_2O_2$. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	36(1)	38(1)	26(1)	-3(1)	4(1)	-7(1)
O(2)	41(1)	46(1)	31(1)	8(1)	8(1)	-2(1)
N(1)	28(1)	46(1)	23(1)	2(1)	-2(1)	-3(1)
N(2)	32(1)	36(1)	40(1)	0(1)	0(1)	-4(1)
C(1)	20(1)	33(1)	30(1)	-1(1)	-1(1)	1(1)
C(2)	20(1)	34(1)	31(1)	0(1)	-1(1)	4(1)
C(3)	27(1)	38(1)	34(1)	-6(1)	-2(1)	8(1)
C(4)	33(1)	31(1)	48(1)	-6(1)	-4(1)	6(1)
C(5)	27(1)	33(1)	48(1)	8(1)	-1(1)	4(1)
C(6)	19(1)	38(1)	34(1)	5(1)	0(1)	4(1)
C(7)	28(1)	47(1)	32(1)	11(1)	-1(1)	1(1)

C(8)	27(1)	38(1)	22(1)	2(1)	0(1)	-3(1)
C(9)	25(1)	35(1)	31(1)	2(1)	5(1)	2(1)
C(10)	39(1)	54(1)	40(1)	-3(1)	-11(1)	-4(1)
C(11)	41(1)	36(1)	68(1)	1(1)	-3(1)	-6(1)
C(12)	31(1)	35(1)	28(1)	1(1)	3(1)	2(1)
C(13)	47(1)	38(1)	36(1)	4(1)	4(1)	10(1)
C(14)	39(1)	46(1)	35(1)	2(1)	4(1)	-9(1)
C(15)	39(1)	46(1)	29(1)	1(1)	3(1)	3(1)
C(16)	35(1)	38(1)	32(1)	-1(1)	4(1)	-3(1)
C(17)	41(1)	48(1)	73(1)	-7(1)	0(1)	10(1)
C(18)	64(1)	38(1)	65(1)	-4(1)	22(1)	-8(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for $C_{18}H_{30}N_2O_2$

	x	y	z	U(eq)
H(1O)	120(20)	6516(10)	1925(9)	40
H(1N)	1270(20)	7029(10)	580(8)	39
H(3)	-124	8263	4553	40
H(4)	624	9497	3768	45
H(5)	968	9357	2347	43
H(7A)	-720	7951	1131	43
H(7B)	1166	8461	1142	43
H(8)	3360(20)	6950(10)	1952(8)	35
H(10A)	4172	8227	2836	67
H(10B)	6260	8473	2832	67
H(10C)	5627	7481	2612	67
H(11A)	6098	9250	871	72
H(11B)	7277	9215	1692	72
H(11C)	5365	9700	1697	72
H(13A)	2038	6088	4194	60
H(13B)	919	5640	3463	60
H(13C)	642	5304	4388	60
H(14A)	-2422	5956	3340	60

H(14B)	-3382	6543	4034	60
H(14C)	-2634	5570	4252	60
H(15A)	476	7006	5249	57
H(15B)	-899	6202	5398	57
H(15C)	-1637	7178	5183	57
H(16)	4036	6315	326	42
H(17A)	6744	6690	987	81
H(17B)	6628	5639	821	81
H(17C)	6263	6024	1723	81
H(18A)	1839	5468	1017	84
H(18B)	3226	5271	1745	84
H(18C)	3590	4880	845	84

Table 6. Torsion angles [°] for $C_{18}H_{30}N_2O_2$

O(1)-C(1)-C(2)-C(3)	-178.35(11)
C(6)-C(1)-C(2)-C(3)	1.33(17)
O(1)-C(1)-C(2)-C(12)	3.12(18)
C(6)-C(1)-C(2)-C(12)	-177.20(11)
C(1)-C(2)-C(3)-C(4)	-1.86(19)
C(12)-C(2)-C(3)-C(4)	176.65(12)
C(2)-C(3)-C(4)-C(5)	0.8(2)
C(3)-C(4)-C(5)-C(6)	0.9(2)
C(4)-C(5)-C(6)-C(1)	-1.42(19)
C(4)-C(5)-C(6)-C(7)	177.15(12)
O(1)-C(1)-C(6)-C(5)	179.94(11)
C(2)-C(1)-C(6)-C(5)	0.27(18)
O(1)-C(1)-C(6)-C(7)	1.36(17)
C(2)-C(1)-C(6)-C(7)	-178.31(12)
C(8)-N(1)-C(7)-C(6)	-65.06(14)
C(5)-C(6)-C(7)-N(1)	139.83(12)
C(1)-C(6)-C(7)-N(1)	-41.61(16)
C(7)-N(1)-C(8)-C(9)	-48.44(13)
C(7)-N(1)-C(8)-C(16)	-170.73(10)
C(11)-N(2)-C(9)-O(2)	3.13(19)
C(10)-N(2)-C(9)-O(2)	-178.84(13)

C(11)-N(2)-C(9)-C(8)	-175.71(12)
C(10)-N(2)-C(9)-C(8)	2.32(19)
N(1)-C(8)-C(9)-O(2)	-56.90(15)
C(16)-C(8)-C(9)-O(2)	64.87(15)
N(1)-C(8)-C(9)-N(2)	121.98(12)
C(16)-C(8)-C(9)-N(2)	-116.25(13)
C(3)-C(2)-C(12)-C(14)	119.40(13)
C(1)-C(2)-C(12)-C(14)	-62.15(15)
C(3)-C(2)-C(12)-C(13)	-119.37(13)
C(1)-C(2)-C(12)-C(13)	59.08(16)
C(3)-C(2)-C(12)-C(15)	-0.49(17)
C(1)-C(2)-C(12)-C(15)	177.96(12)
N(1)-C(8)-C(16)-C(17)	178.59(12)
C(9)-C(8)-C(16)-C(17)	56.14(15)
N(1)-C(8)-C(16)-C(18)	-56.50(15)
C(9)-C(8)-C(16)-C(18)	-178.95(13)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{18}H_{30}N_2O_2$ [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...N(1)	0.839(13)	1.860(14)	2.6297(14)	151.9(15)
N(1)-H(1N)...O(2)#1	0.898(13)	2.167(14)	2.9439(14)	144.4(14)

Symmetry transformations used to generate equivalent atoms:

#1 x-1/2,-y+3/2,-z

X-ray Crystal Structure of 1.17j

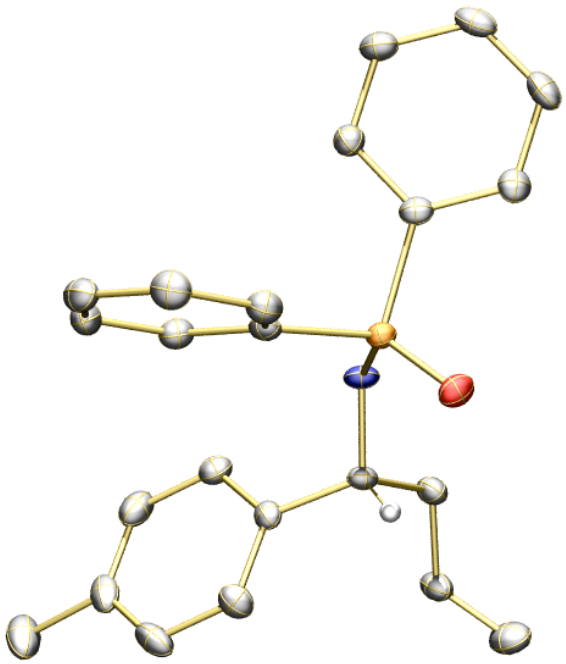


Table 1. Crystal data and structure refinement for $C_{23}H_{24}NOP$

Identification code	$C_{23}H_{24}NOP$	
Empirical formula	$C_{23}H_{24}NOP$	
Formula weight	361.40	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2(1)	
Unit cell dimensions	a = 9.9115(7) Å	α= 90°
	b = 19.7080(12) Å	β= 101.997(4)°
	c = 10.2367(7) Å	γ = 90°
Volume	1955.9(2) $Å^3$	
Z	4	
Density (calculated)	1.227 Mg/m^3	
Absorption coefficient	0.152 mm^{-1}	
F(000)	768	
Crystal size	0.14 x 0.08 x 0.05 mm^3	
Theta range for data collection	2.03 to 28.43°	
Index ranges	-12<=h<=13, -26<=k<=26, -13<=l<=13	
Reflections collected	42680	

Independent reflections	9807 [R(int) = 0.0707]
Completeness to theta = 28.43°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9925 and 0.9791
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9807 / 5 / 483
Goodness-of-fit on F^2	1.019
Final R indices [I>2sigma(I)]	R1 = 0.0419, wR2 = 0.0796
R indices (all data)	R1 = 0.0613, wR2 = 0.0867
Absolute structure parameter	0.04(6)
Extinction coefficient	na
Largest diff. peak and hole	0.360 and -0.247 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	9053(1)	7653(1)	1992(1)	17(1)
O(1)	8854(2)	7958(1)	634(1)	23(1)
N(1)	8318(2)	8098(1)	2991(2)	20(1)
C(1)	9941(3)	10334(1)	4205(3)	45(1)
C(2)	8899(3)	9939(1)	4126(2)	32(1)
C(3)	8960(2)	9179(1)	4177(2)	25(1)
C(4)	8168(2)	8840(1)	2881(2)	19(1)
C(5)	6664(2)	9044(1)	2560(2)	20(1)
C(6)	5698(2)	8734(1)	3176(2)	23(1)
C(7)	4332(2)	8937(1)	2895(2)	26(1)
C(8)	3876(2)	9459(1)	1984(2)	29(1)
C(9)	4839(3)	9758(1)	1368(2)	30(1)
C(10)	6201(2)	9557(1)	1641(2)	25(1)
C(11)	2404(3)	9694(1)	1729(3)	45(1)
C(12)	10858(2)	7526(1)	2686(2)	19(1)
C(13)	11354(2)	7499(1)	4063(2)	24(1)
C(14)	12722(2)	7348(1)	4577(2)	28(1)
C(15)	13616(2)	7227(1)	3721(2)	27(1)

C(16)	13136(2)	7261(1)	2359(2)	26(1)
C(17)	11762(2)	7410(1)	1837(2)	22(1)
C(18)	8271(2)	6825(1)	2005(2)	18(1)
C(19)	9019(2)	6240(1)	2433(2)	23(1)
C(20)	8367(2)	5614(1)	2356(2)	26(1)
C(21)	6966(2)	5564(1)	1842(2)	27(1)
C(22)	6217(2)	6140(1)	1423(2)	31(1)
C(23)	6856(2)	6769(1)	1504(2)	26(1)
P(2)	1823(1)	2359(1)	3130(1)	15(1)
O(2)	1432(1)	2673(1)	4319(1)	22(1)
N(2)	2302(2)	2892(1)	2097(2)	18(1)
C(24)	2526(3)	5298(1)	2712(2)	34(1)
C(25)	3013(2)	4794(1)	2109(2)	24(1)
C(26)	2293(2)	4125(1)	1794(2)	22(1)
C(27)	3094(2)	3516(1)	2530(2)	16(1)
C(28)	4549(2)	3499(1)	2299(2)	17(1)
C(29)	4824(2)	3329(1)	1062(2)	22(1)
C(30)	6148(2)	3380(1)	828(2)	28(1)
C(31)	7240(2)	3607(1)	1811(2)	27(1)
C(32)	6966(2)	3764(1)	3047(2)	28(1)
C(33)	5642(2)	3713(1)	3291(2)	24(1)
C(34)	8661(3)	3702(1)	1536(3)	40(1)
C(35)	409(2)	1896(1)	2116(2)	18(1)
C(36)	-925(2)	2044(1)	2252(2)	21(1)
C(37)	-2044(2)	1693(1)	1503(2)	25(1)
C(38)	-1821(2)	1187(1)	644(2)	25(1)
C(39)	-496(2)	1032(1)	503(2)	24(1)
C(40)	622(2)	1388(1)	1234(2)	21(1)
C(41)	3159(2)	1734(1)	3632(2)	18(1)
C(42)	3063(2)	1295(1)	4685(2)	21(1)
C(43)	3994(2)	766(1)	5009(2)	24(1)
C(44)	5029(2)	671(1)	4313(2)	24(1)
C(45)	5157(2)	1112(1)	3295(2)	24(1)
C(46)	4218(2)	1640(1)	2943(2)	20(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{23}H_{24}NOP$

P(1)-O(1)	1.4889(14)
P(1)-N(1)	1.6299(18)
P(1)-C(12)	1.800(2)
P(1)-C(18)	1.806(2)
N(1)-C(4)	1.472(2)
N(1)-H(1N)	0.855(15)
C(1)-C(2)	1.283(3)
C(1)-H(1A)	0.9500
C(1)-H(1B)	0.9500
C(2)-C(3)	1.499(3)
C(2)-H(2)	0.9500
C(3)-C(4)	1.546(3)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.512(3)
C(4)-H(4)	0.987(16)
C(5)-C(6)	1.393(3)
C(5)-C(10)	1.393(3)
C(6)-C(7)	1.384(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.398(3)
C(7)-H(7)	0.9500
C(8)-C(9)	1.381(4)
C(8)-C(11)	1.501(3)
C(9)-C(10)	1.378(3)
C(9)-H(9)	0.9500
C(10)-H(10)	0.9500
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-C(17)	1.391(3)
C(12)-C(13)	1.393(3)
C(13)-C(14)	1.382(3)
C(13)-H(13)	0.9500
C(14)-C(15)	1.390(3)
C(14)-H(14)	0.9500

C(15)-C(16)	1.378(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.386(3)
C(16)-H(16)	0.9500
C(17)-H(17)	0.9500
C(18)-C(19)	1.393(3)
C(18)-C(23)	1.393(3)
C(19)-C(20)	1.386(3)
C(19)-H(19)	0.9500
C(20)-C(21)	1.383(3)
C(20)-H(20)	0.9500
C(21)-C(22)	1.377(3)
C(21)-H(21)	0.9500
C(22)-C(23)	1.387(3)
C(22)-H(22)	0.9500
C(23)-H(23)	0.9500
P(2)-O(2)	1.4868(14)
P(2)-N(2)	1.6297(18)
P(2)-C(41)	1.803(2)
P(2)-C(35)	1.807(2)
N(2)-C(27)	1.476(2)
N(2)-H(2N)	0.841(15)
C(24)-C(25)	1.313(3)
C(24)-H(24A)	0.9500
C(24)-H(24B)	0.9500
C(25)-C(26)	1.501(3)
C(25)-H(25)	0.9500
C(26)-C(27)	1.546(3)
C(26)-H(26A)	0.9900
C(26)-H(26B)	0.9900
C(27)-C(28)	1.509(3)
C(27)-H(27)	1.005(15)
C(28)-C(33)	1.388(3)
C(28)-C(29)	1.390(3)
C(29)-C(30)	1.385(3)
C(29)-H(29)	0.9500
C(30)-C(31)	1.390(3)

C(30)-H(30)	0.9500
C(31)-C(32)	1.383(3)
C(31)-C(34)	1.503(3)
C(32)-C(33)	1.390(3)
C(32)-H(32)	0.9500
C(33)-H(33)	0.9500
C(34)-H(34A)	0.9800
C(34)-H(34B)	0.9800
C(34)-H(34C)	0.9800
C(35)-C(36)	1.389(3)
C(35)-C(40)	1.393(3)
C(36)-C(37)	1.394(3)
C(36)-H(36)	0.9500
C(37)-C(38)	1.378(3)
C(37)-H(37)	0.9500
C(38)-C(39)	1.385(3)
C(38)-H(38)	0.9500
C(39)-C(40)	1.390(3)
C(39)-H(39)	0.9500
C(40)-H(40)	0.9500
C(41)-C(46)	1.393(3)
C(41)-C(42)	1.401(3)
C(42)-C(43)	1.387(3)
C(42)-H(42)	0.9500
C(43)-C(44)	1.378(3)
C(43)-H(43)	0.9500
C(44)-C(45)	1.381(3)
C(44)-H(44)	0.9500
C(45)-C(46)	1.393(3)
C(45)-H(45)	0.9500
C(46)-H(46)	0.9500
O(1)-P(1)-N(1)	112.21(9)
O(1)-P(1)-C(12)	110.65(9)
N(1)-P(1)-C(12)	111.32(9)
O(1)-P(1)-C(18)	113.47(9)
N(1)-P(1)-C(18)	103.48(9)
C(12)-P(1)-C(18)	105.33(9)

C(4)-N(1)-P(1)	122.62(15)
C(4)-N(1)-H(1N)	116.6(15)
P(1)-N(1)-H(1N)	116.4(15)
C(2)-C(1)-H(1A)	120.0
C(2)-C(1)-H(1B)	120.0
H(1A)-C(1)-H(1B)	120.0
C(1)-C(2)-C(3)	125.4(2)
C(1)-C(2)-H(2)	117.3
C(3)-C(2)-H(2)	117.3
C(2)-C(3)-C(4)	113.09(17)
C(2)-C(3)-H(3A)	109.0
C(4)-C(3)-H(3A)	109.0
C(2)-C(3)-H(3B)	109.0
C(4)-C(3)-H(3B)	109.0
H(3A)-C(3)-H(3B)	107.8
N(1)-C(4)-C(5)	111.13(17)
N(1)-C(4)-C(3)	109.79(16)
C(5)-C(4)-C(3)	111.93(17)
N(1)-C(4)-H(4)	107.0(13)
C(5)-C(4)-H(4)	110.2(13)
C(3)-C(4)-H(4)	106.6(13)
C(6)-C(5)-C(10)	117.6(2)
C(6)-C(5)-C(4)	121.63(18)
C(10)-C(5)-C(4)	120.8(2)
C(7)-C(6)-C(5)	121.0(2)
C(7)-C(6)-H(6)	119.5
C(5)-C(6)-H(6)	119.5
C(6)-C(7)-C(8)	121.2(2)
C(6)-C(7)-H(7)	119.4
C(8)-C(7)-H(7)	119.4
C(9)-C(8)-C(7)	117.5(2)
C(9)-C(8)-C(11)	121.8(2)
C(7)-C(8)-C(11)	120.7(2)
C(10)-C(9)-C(8)	121.6(2)
C(10)-C(9)-H(9)	119.2
C(8)-C(9)-H(9)	119.2
C(9)-C(10)-C(5)	121.2(2)

C(9)-C(10)-H(10)	119.4
C(5)-C(10)-H(10)	119.4
C(8)-C(11)-H(11A)	109.5
C(8)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(8)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(17)-C(12)-C(13)	119.24(18)
C(17)-C(12)-P(1)	119.50(15)
C(13)-C(12)-P(1)	121.14(16)
C(14)-C(13)-C(12)	120.3(2)
C(14)-C(13)-H(13)	119.8
C(12)-C(13)-H(13)	119.8
C(13)-C(14)-C(15)	120.0(2)
C(13)-C(14)-H(14)	120.0
C(15)-C(14)-H(14)	120.0
C(16)-C(15)-C(14)	119.9(2)
C(16)-C(15)-H(15)	120.0
C(14)-C(15)-H(15)	120.0
C(15)-C(16)-C(17)	120.3(2)
C(15)-C(16)-H(16)	119.8
C(17)-C(16)-H(16)	119.8
C(16)-C(17)-C(12)	120.15(19)
C(16)-C(17)-H(17)	119.9
C(12)-C(17)-H(17)	119.9
C(19)-C(18)-C(23)	118.62(19)
C(19)-C(18)-P(1)	123.33(16)
C(23)-C(18)-P(1)	117.98(15)
C(20)-C(19)-C(18)	120.6(2)
C(20)-C(19)-H(19)	119.7
C(18)-C(19)-H(19)	119.7
C(21)-C(20)-C(19)	120.3(2)
C(21)-C(20)-H(20)	119.8
C(19)-C(20)-H(20)	119.8
C(22)-C(21)-C(20)	119.6(2)
C(22)-C(21)-H(21)	120.2

C(20)-C(21)-H(21)	120.2
C(21)-C(22)-C(23)	120.6(2)
C(21)-C(22)-H(22)	119.7
C(23)-C(22)-H(22)	119.7
C(22)-C(23)-C(18)	120.3(2)
C(22)-C(23)-H(23)	119.8
C(18)-C(23)-H(23)	119.8
O(2)-P(2)-N(2)	115.09(9)
O(2)-P(2)-C(41)	110.59(9)
N(2)-P(2)-C(41)	109.20(10)
O(2)-P(2)-C(35)	112.16(9)
N(2)-P(2)-C(35)	104.38(9)
C(41)-P(2)-C(35)	104.77(9)
C(27)-N(2)-P(2)	123.38(13)
C(27)-N(2)-H(2N)	117.9(15)
P(2)-N(2)-H(2N)	117.0(15)
C(25)-C(24)-H(24A)	120.0
C(25)-C(24)-H(24B)	120.0
H(24A)-C(24)-H(24B)	120.0
C(24)-C(25)-C(26)	124.1(2)
C(24)-C(25)-H(25)	117.9
C(26)-C(25)-H(25)	117.9
C(25)-C(26)-C(27)	113.86(16)
C(25)-C(26)-H(26A)	108.8
C(27)-C(26)-H(26A)	108.8
C(25)-C(26)-H(26B)	108.8
C(27)-C(26)-H(26B)	108.8
H(26A)-C(26)-H(26B)	107.7
N(2)-C(27)-C(28)	113.55(16)
N(2)-C(27)-C(26)	108.28(15)
C(28)-C(27)-C(26)	110.55(16)
N(2)-C(27)-H(27)	104.8(12)
C(28)-C(27)-H(27)	112.6(12)
C(26)-C(27)-H(27)	106.6(12)
C(33)-C(28)-C(29)	117.90(19)
C(33)-C(28)-C(27)	120.33(18)
C(29)-C(28)-C(27)	121.52(18)

C(30)-C(29)-C(28)	120.8(2)
C(30)-C(29)-H(29)	119.6
C(28)-C(29)-H(29)	119.6
C(29)-C(30)-C(31)	121.5(2)
C(29)-C(30)-H(30)	119.3
C(31)-C(30)-H(30)	119.3
C(32)-C(31)-C(30)	117.5(2)
C(32)-C(31)-C(34)	120.9(2)
C(30)-C(31)-C(34)	121.6(2)
C(31)-C(32)-C(33)	121.4(2)
C(31)-C(32)-H(32)	119.3
C(33)-C(32)-H(32)	119.3
C(28)-C(33)-C(32)	120.9(2)
C(28)-C(33)-H(33)	119.5
C(32)-C(33)-H(33)	119.5
C(31)-C(34)-H(34A)	109.5
C(31)-C(34)-H(34B)	109.5
H(34A)-C(34)-H(34B)	109.5
C(31)-C(34)-H(34C)	109.5
H(34A)-C(34)-H(34C)	109.5
H(34B)-C(34)-H(34C)	109.5
C(36)-C(35)-C(40)	119.42(19)
C(36)-C(35)-P(2)	118.47(15)
C(40)-C(35)-P(2)	122.09(16)
C(35)-C(36)-C(37)	120.3(2)
C(35)-C(36)-H(36)	119.8
C(37)-C(36)-H(36)	119.8
C(38)-C(37)-C(36)	119.7(2)
C(38)-C(37)-H(37)	120.1
C(36)-C(37)-H(37)	120.1
C(37)-C(38)-C(39)	120.5(2)
C(37)-C(38)-H(38)	119.8
C(39)-C(38)-H(38)	119.8
C(38)-C(39)-C(40)	120.0(2)
C(38)-C(39)-H(39)	120.0
C(40)-C(39)-H(39)	120.0
C(39)-C(40)-C(35)	120.0(2)

C(39)-C(40)-H(40)	120.0
C(35)-C(40)-H(40)	120.0
C(46)-C(41)-C(42)	119.07(19)
C(46)-C(41)-P(2)	122.18(15)
C(42)-C(41)-P(2)	118.55(16)
C(43)-C(42)-C(41)	120.0(2)
C(43)-C(42)-H(42)	120.0
C(41)-C(42)-H(42)	120.0
C(44)-C(43)-C(42)	120.5(2)
C(44)-C(43)-H(43)	119.8
C(42)-C(43)-H(43)	119.8
C(43)-C(44)-C(45)	120.0(2)
C(43)-C(44)-H(44)	120.0
C(45)-C(44)-H(44)	120.0
C(44)-C(45)-C(46)	120.3(2)
C(44)-C(45)-H(45)	119.9
C(46)-C(45)-H(45)	119.9
C(41)-C(46)-C(45)	120.1(2)
C(41)-C(46)-H(46)	120.0
C(45)-C(46)-H(46)	120.0

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for $C_{23}H_{24}NOP$. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	19(1)	17(1)	12(1)	1(1)	1(1)	4(1)
O(1)	28(1)	26(1)	14(1)	2(1)	2(1)	3(1)
N(1)	28(1)	16(1)	15(1)	4(1)	5(1)	5(1)
C(1)	51(2)	38(1)	42(2)	5(1)	4(1)	-8(1)
C(2)	35(1)	25(1)	32(1)	-2(1)	-5(1)	1(1)
C(3)	28(1)	20(1)	23(1)	1(1)	0(1)	2(1)
C(4)	27(1)	15(1)	16(1)	2(1)	5(1)	3(1)
C(5)	29(1)	15(1)	13(1)	-4(1)	0(1)	2(1)
C(6)	30(1)	18(1)	20(1)	2(1)	2(1)	3(1)
C(7)	29(1)	24(1)	26(1)	-5(1)	4(1)	0(1)
C(8)	30(1)	27(1)	26(1)	-4(1)	-3(1)	9(1)
C(9)	41(1)	22(1)	24(1)	1(1)	-1(1)	11(1)
C(10)	36(1)	19(1)	18(1)	0(1)	3(1)	4(1)
C(11)	32(2)	49(2)	49(2)	-3(1)	-2(1)	18(1)
C(12)	22(1)	14(1)	20(1)	-1(1)	2(1)	1(1)
C(13)	25(1)	24(1)	22(1)	0(1)	1(1)	3(1)
C(14)	28(1)	25(1)	26(1)	3(1)	-4(1)	3(1)
C(15)	17(1)	19(1)	42(1)	1(1)	-2(1)	2(1)
C(16)	23(1)	22(1)	36(1)	0(1)	11(1)	0(1)
C(17)	26(1)	18(1)	21(1)	-1(1)	3(1)	-1(1)
C(18)	24(1)	18(1)	13(1)	-2(1)	5(1)	3(1)
C(19)	23(1)	22(1)	23(1)	0(1)	3(1)	3(1)
C(20)	30(1)	20(1)	26(1)	0(1)	4(1)	4(1)
C(21)	34(1)	21(1)	25(1)	-5(1)	6(1)	-7(1)
C(22)	22(1)	30(1)	37(1)	-1(1)	-2(1)	-4(1)
C(23)	24(1)	21(1)	30(1)	1(1)	-1(1)	4(1)
P(2)	18(1)	15(1)	13(1)	0(1)	2(1)	-1(1)
O(2)	28(1)	22(1)	16(1)	-2(1)	7(1)	0(1)
N(2)	23(1)	16(1)	13(1)	-1(1)	0(1)	-5(1)
C(24)	39(1)	21(1)	38(1)	-3(1)	-2(1)	1(1)
C(25)	20(1)	20(1)	31(1)	1(1)	0(1)	-2(1)
C(26)	18(1)	21(1)	26(1)	-1(1)	-1(1)	-1(1)

C(27)	18(1)	17(1)	14(1)	-2(1)	2(1)	-4(1)
C(28)	18(1)	14(1)	20(1)	3(1)	3(1)	1(1)
C(29)	27(1)	17(1)	23(1)	-1(1)	5(1)	-1(1)
C(30)	36(1)	22(1)	31(1)	-1(1)	17(1)	0(1)
C(31)	23(1)	16(1)	44(1)	8(1)	12(1)	3(1)
C(32)	20(1)	28(1)	34(1)	8(1)	-4(1)	-4(1)
C(33)	23(1)	27(1)	20(1)	4(1)	1(1)	0(1)
C(34)	29(1)	26(1)	68(2)	7(1)	21(1)	-1(1)
C(35)	23(1)	15(1)	16(1)	3(1)	3(1)	-2(1)
C(36)	23(1)	19(1)	21(1)	5(1)	8(1)	0(1)
C(37)	16(1)	29(1)	30(1)	9(1)	4(1)	-2(1)
C(38)	23(1)	24(1)	26(1)	7(1)	-3(1)	-9(1)
C(39)	28(1)	20(1)	22(1)	-1(1)	0(1)	-3(1)
C(40)	20(1)	20(1)	22(1)	1(1)	4(1)	0(1)
C(41)	17(1)	18(1)	15(1)	-2(1)	-2(1)	-2(1)
C(42)	22(1)	23(1)	19(1)	1(1)	4(1)	-1(1)
C(43)	29(1)	24(1)	19(1)	6(1)	3(1)	0(1)
C(44)	24(1)	18(1)	27(1)	0(1)	0(1)	2(1)
C(45)	19(1)	23(1)	31(1)	-4(1)	7(1)	0(1)
C(46)	24(1)	20(1)	18(1)	0(1)	5(1)	-3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for $C_{23}H_{24}NOP$

	x	y	z	U(eq)
H(1N)	8320(20)	7925(11)	3756(17)	24
H(1A)	10842	10150	4305	54
H(1B)	9812	10812	4164	54
H(2)	8017	10144	4027	39
H(3A)	8569	9020	4937	30
H(3B)	9937	9034	4341	30
H(4)	8630(20)	8986(11)	2160(19)	23
H(6)	5981	8378	3798	28
H(7)	3691	8718	3329	32

H(9)	4556	10112	740	36
H(10)	6834	9772	1194	30
H(11A)	2303	10045	2381	67
H(11B)	1802	9310	1815	67
H(11C)	2147	9882	825	67
H(13)	10747	7586	4651	29
H(14)	13053	7327	5516	33
H(15)	14556	7122	4074	33
H(16)	13749	7181	1775	32
H(17)	11438	7433	897	26
H(19)	9983	6269	2780	28
H(20)	8886	5218	2659	31
H(21)	6524	5134	1779	32
H(22)	5253	6107	1074	37
H(23)	6327	7164	1216	31
H(2N)	1920(20)	2858(11)	1287(16)	22
H(24A)	1668	5252	2977	41
H(24B)	3033	5709	2882	41
H(25)	3874	4856	1857	29
H(26A)	2142	4045	820	27
H(26B)	1377	4150	2035	27
H(27)	3060(20)	3566(10)	3500(16)	20
H(29)	4096	3176	369	27
H(30)	6312	3256	-22	34
H(32)	7698	3910	3743	34
H(33)	5484	3825	4148	29
H(34A)	8775	4174	1278	60
H(34B)	8781	3399	808	60
H(34C)	9352	3593	2342	60
H(36)	-1076	2387	2858	25
H(37)	-2956	1802	1584	30
H(38)	-2582	942	146	30
H(39)	-350	683	-92	29
H(40)	1530	1285	1131	25
H(42)	2358	1359	5176	26
H(43)	3918	466	5717	29
H(44)	5655	304	4532	29

H(45)	5887	1053	2834	29
H(46)	4301	1937	2233	25

Table 6. Torsion angles [°] for $C_{23}H_{24}NOP$

O(1)-P(1)-N(1)-C(4)	-31.06(19)
C(12)-P(1)-N(1)-C(4)	93.57(17)
C(18)-P(1)-N(1)-C(4)	-153.76(16)
C(1)-C(2)-C(3)-C(4)	-117.7(3)
P(1)-N(1)-C(4)-C(5)	117.35(18)
P(1)-N(1)-C(4)-C(3)	-118.27(18)
C(2)-C(3)-C(4)-N(1)	177.94(19)
C(2)-C(3)-C(4)-C(5)	-58.2(3)
N(1)-C(4)-C(5)-C(6)	41.9(3)
C(3)-C(4)-C(5)-C(6)	-81.2(2)
N(1)-C(4)-C(5)-C(10)	-138.74(19)
C(3)-C(4)-C(5)-C(10)	98.1(2)
C(10)-C(5)-C(6)-C(7)	-0.9(3)
C(4)-C(5)-C(6)-C(7)	178.47(19)
C(5)-C(6)-C(7)-C(8)	0.1(3)
C(6)-C(7)-C(8)-C(9)	0.6(3)
C(6)-C(7)-C(8)-C(11)	-177.5(2)
C(7)-C(8)-C(9)-C(10)	-0.4(3)
C(11)-C(8)-C(9)-C(10)	177.6(2)
C(8)-C(9)-C(10)-C(5)	-0.4(3)
C(6)-C(5)-C(10)-C(9)	1.1(3)
C(4)-C(5)-C(10)-C(9)	-178.31(19)
O(1)-P(1)-C(12)-C(17)	-28.89(18)
N(1)-P(1)-C(12)-C(17)	-154.39(15)
C(18)-P(1)-C(12)-C(17)	94.11(17)
O(1)-P(1)-C(12)-C(13)	155.11(15)
N(1)-P(1)-C(12)-C(13)	29.61(19)
C(18)-P(1)-C(12)-C(13)	-81.89(17)
C(17)-C(12)-C(13)-C(14)	-1.1(3)
P(1)-C(12)-C(13)-C(14)	174.89(16)
C(12)-C(13)-C(14)-C(15)	0.5(3)

C(13)-C(14)-C(15)-C(16)	0.2(3)
C(14)-C(15)-C(16)-C(17)	-0.4(3)
C(15)-C(16)-C(17)-C(12)	-0.2(3)
C(13)-C(12)-C(17)-C(16)	0.9(3)
P(1)-C(12)-C(17)-C(16)	-175.13(15)
O(1)-P(1)-C(18)-C(19)	118.70(18)
N(1)-P(1)-C(18)-C(19)	-119.45(18)
C(12)-P(1)-C(18)-C(19)	-2.5(2)
O(1)-P(1)-C(18)-C(23)	-58.24(19)
N(1)-P(1)-C(18)-C(23)	63.61(18)
C(12)-P(1)-C(18)-C(23)	-179.42(16)
C(23)-C(18)-C(19)-C(20)	0.2(3)
P(1)-C(18)-C(19)-C(20)	-176.75(17)
C(18)-C(19)-C(20)-C(21)	0.6(3)
C(19)-C(20)-C(21)-C(22)	-0.9(3)
C(20)-C(21)-C(22)-C(23)	0.4(4)
C(21)-C(22)-C(23)-C(18)	0.4(4)
C(19)-C(18)-C(23)-C(22)	-0.7(3)
P(1)-C(18)-C(23)-C(22)	176.43(18)
O(2)-P(2)-N(2)-C(27)	35.84(19)
C(41)-P(2)-N(2)-C(27)	-89.21(17)
C(35)-P(2)-N(2)-C(27)	159.20(16)
C(24)-C(25)-C(26)-C(27)	-116.1(2)
P(2)-N(2)-C(27)-C(28)	111.83(18)
P(2)-N(2)-C(27)-C(26)	-124.99(17)
C(25)-C(26)-C(27)-N(2)	-177.98(18)
C(25)-C(26)-C(27)-C(28)	-53.0(2)
N(2)-C(27)-C(28)-C(33)	-134.69(19)
C(26)-C(27)-C(28)-C(33)	103.4(2)
N(2)-C(27)-C(28)-C(29)	51.1(2)
C(26)-C(27)-C(28)-C(29)	-70.9(2)
C(33)-C(28)-C(29)-C(30)	-0.7(3)
C(27)-C(28)-C(29)-C(30)	173.62(19)
C(28)-C(29)-C(30)-C(31)	-0.6(3)
C(29)-C(30)-C(31)-C(32)	1.7(3)
C(29)-C(30)-C(31)-C(34)	-176.4(2)
C(30)-C(31)-C(32)-C(33)	-1.6(3)

C(34)-C(31)-C(32)-C(33)	176.6(2)
C(29)-C(28)-C(33)-C(32)	0.9(3)
C(27)-C(28)-C(33)-C(32)	-173.51(19)
C(31)-C(32)-C(33)-C(28)	0.2(3)
O(2)-P(2)-C(35)-C(36)	20.04(18)
N(2)-P(2)-C(35)-C(36)	-105.21(16)
C(41)-P(2)-C(35)-C(36)	140.04(16)
O(2)-P(2)-C(35)-C(40)	-158.36(15)
N(2)-P(2)-C(35)-C(40)	76.39(18)
C(41)-P(2)-C(35)-C(40)	-38.36(19)
C(40)-C(35)-C(36)-C(37)	-0.7(3)
P(2)-C(35)-C(36)-C(37)	-179.10(15)
C(35)-C(36)-C(37)-C(38)	1.4(3)
C(36)-C(37)-C(38)-C(39)	-1.1(3)
C(37)-C(38)-C(39)-C(40)	0.2(3)
C(38)-C(39)-C(40)-C(35)	0.5(3)
C(36)-C(35)-C(40)-C(39)	-0.3(3)
P(2)-C(35)-C(40)-C(39)	178.10(16)
O(2)-P(2)-C(41)-C(46)	-143.20(16)
N(2)-P(2)-C(41)-C(46)	-15.57(19)
C(35)-P(2)-C(41)-C(46)	95.76(18)
O(2)-P(2)-C(41)-C(42)	41.95(18)
N(2)-P(2)-C(41)-C(42)	169.58(15)
C(35)-P(2)-C(41)-C(42)	-79.09(17)
C(46)-C(41)-C(42)-C(43)	-1.5(3)
P(2)-C(41)-C(42)-C(43)	173.55(16)
C(41)-C(42)-C(43)-C(44)	0.7(3)
C(42)-C(43)-C(44)-C(45)	0.9(3)
C(43)-C(44)-C(45)-C(46)	-1.8(3)
C(42)-C(41)-C(46)-C(45)	0.6(3)
P(2)-C(41)-C(46)-C(45)	-174.26(15)
C(44)-C(45)-C(46)-C(41)	1.1(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{23}H_{24}NOP$ [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(2)#1	0.855(15)	1.998(16)	2.840(2)	169(2)
N(2)-H(2N)...O(1)#2	0.841(15)	1.966(16)	2.796(2)	169(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+1 #2 -x+1,y-1/2,-z

X-ray Crystal Structure of 1.21f

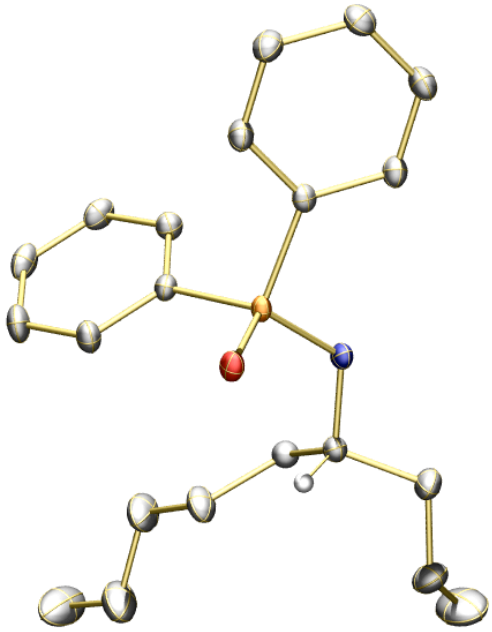


Table 1. Crystal data and structure refinement for $C_{21}H_{26}NOP$

Identification code	$C_{21}H_{26}NOP$	
Empirical formula	$C_{21}H_{26}NOP$	
Formula weight	339.40	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2(1)	
Unit cell dimensions	a = 5.3475(3) Å	α= 90°
	b = 8.4812(4) Å	β= 91.983(2)°

	c = 21.2781(10) Å γ = 90°
Volume	964.45(8) $Å^3$
Z	2
Density (calculated)	1.169 Mg/m^3
Absorption coefficient	0.149 mm^{-1}
F(000)	364
Crystal size	0.30 x 0.24 x 0.08 mm^3
Theta range for data collection	1.92 to 28.48°
Index ranges	-7<=h<=7, -11<=k<=11, -28<=l<=28
Reflections collected	39105
Independent reflections	4895 [R(int) = 0.0215]
Completeness to theta = 28.48°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9882 and 0.9566
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4895 / 77 / 253
Goodness-of-fit on F^2	1.069
Final R indices [I>2sigma(I)]	R1 = 0.0273, wR2 = 0.0718
R indices (all data)	R1 = 0.0278, wR2 = 0.0722
Absolute structure parameter	0.00(5)
Extinction coefficient	na
Largest diff. peak and hole	0.404 and -0.262 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for $C_{21}H_{26}NOP$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	520(1)	-860(1)	8324(1)	13(1)
O(1)	-1929(1)	-1644(1)	8175(1)	17(1)
N(1)	2774(2)	-1603(1)	7910(1)	16(1)
C(1)	5612(4)	-3552(4)	5942(1)	62(1)
C(2)	3843(3)	-3594(2)	6350(1)	36(1)
C(3)	4157(2)	-3166(2)	7029(1)	25(1)
C(4)	2418(2)	-1834(1)	7224(1)	17(1)

C(5)	2527(10)	-366(5)	6853(2)	25(1)
C(6)	698(7)	310(4)	6539(1)	29(1)
C(7)	855(8)	1837(4)	6190(2)	40(1)
C(8)	-89(8)	1743(5)	5514(2)	46(1)
C(9)	17(11)	3306(5)	5178(2)	63(1)
C(5X)	3096(9)	-323(6)	6874(3)	20(1)
C(6X)	1493(8)	673(5)	6602(2)	36(1)
C(7X)	2153(8)	2236(5)	6320(2)	46(1)
C(8X)	1431(9)	2386(6)	5634(2)	60(1)
C(9X)	-1310(11)	2407(8)	5500(3)	80(2)
C(10)	1615(2)	-1035(1)	9129(1)	15(1)
C(11)	3681(2)	-1934(1)	9332(1)	19(1)
C(12)	4308(2)	-2036(2)	9972(1)	22(1)
C(13)	2892(2)	-1251(1)	10408(1)	22(1)
C(14)	841(2)	-353(2)	10210(1)	23(1)
C(15)	211(2)	-247(2)	9573(1)	20(1)
C(16)	159(2)	1236(1)	8196(1)	15(1)
C(17)	1976(2)	2315(1)	8408(1)	19(1)
C(18)	1664(2)	3917(1)	8290(1)	23(1)
C(19)	-454(3)	4460(1)	7960(1)	25(1)
C(20)	-2246(2)	3391(2)	7741(1)	26(1)
C(21)	-1952(2)	1790(2)	7864(1)	21(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{21}H_{26}NOP$

P(1)-O(1)	1.4931(8)
P(1)-N(1)	1.6428(9)
P(1)-C(10)	1.7978(11)
P(1)-C(16)	1.8083(12)
N(1)-C(4)	1.4767(14)
N(1)-H(1N)	0.885(13)
C(1)-C(2)	1.307(3)
C(1)-H(1A)	0.993(17)
C(1)-H(1B)	0.986(16)
C(2)-C(3)	1.4923(19)

C(2)-H(2)	0.980(15)
C(3)-C(4)	1.5302(16)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.477(5)
C(4)-H(4)	0.989(12)
C(5)-C(6)	1.298(5)
C(5)-H(5)	0.9500
C(6)-C(7)	1.497(5)
C(6)-H(6)	0.9500
C(7)-C(8)	1.509(5)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.509(5)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-C(15)	1.3976(15)
C(10)-C(11)	1.3991(15)
C(11)-C(12)	1.3924(17)
C(11)-H(11)	0.9500
C(12)-C(13)	1.3886(17)
C(12)-H(12)	0.9500
C(13)-C(14)	1.3889(17)
C(13)-H(13)	0.9500
C(14)-C(15)	1.3867(17)
C(14)-H(14)	0.9500
C(15)-H(15)	0.9500
C(16)-C(21)	1.3922(15)
C(16)-C(17)	1.3979(16)
C(17)-C(18)	1.3900(17)
C(17)-H(17)	0.9500
C(18)-C(19)	1.3914(18)
C(18)-H(18)	0.9500
C(19)-C(20)	1.388(2)

C(19)-H(19)	0.9500
C(20)-C(21)	1.3902(18)
C(20)-H(20)	0.9500
C(21)-H(21)	0.9500

O(1)-P(1)-N(1)	111.71(5)
O(1)-P(1)-C(10)	114.84(5)
N(1)-P(1)-C(10)	105.01(5)
O(1)-P(1)-C(16)	108.53(5)
N(1)-P(1)-C(16)	111.89(5)
C(10)-P(1)-C(16)	104.70(5)
C(4)-N(1)-P(1)	120.56(7)
C(4)-N(1)-H(1N)	115.7(10)
P(1)-N(1)-H(1N)	118.5(10)
C(2)-C(1)-H(1A)	119.6(17)
C(2)-C(1)-H(1B)	122.8(16)
H(1A)-C(1)-H(1B)	118(2)
C(1)-C(2)-C(3)	125.23(16)
C(1)-C(2)-H(2)	117.9(12)
C(3)-C(2)-H(2)	116.9(12)
C(2)-C(3)-C(4)	113.21(11)
C(2)-C(3)-H(3A)	108.9
C(4)-C(3)-H(3A)	108.9
C(2)-C(3)-H(3B)	108.9
C(4)-C(3)-H(3B)	108.9
H(3A)-C(3)-H(3B)	107.7
C(5)-C(4)-N(1)	114.2(2)
C(5)-C(4)-C(3)	116.2(2)
N(1)-C(4)-C(3)	107.93(9)
C(5)-C(4)-H(4)	99.3(10)
N(1)-C(4)-H(4)	107.5(9)
C(3)-C(4)-H(4)	111.2(10)
C(6)-C(5)-C(4)	127.2(4)
C(6)-C(5)-H(5)	116.4
C(4)-C(5)-H(5)	116.4
C(5)-C(6)-C(7)	125.7(4)
C(5)-C(6)-H(6)	117.2

C(7)-C(6)-H(6)	117.2
C(6)-C(7)-C(8)	113.9(3)
C(6)-C(7)-H(7A)	108.8
C(8)-C(7)-H(7A)	108.8
C(6)-C(7)-H(7B)	108.8
C(8)-C(7)-H(7B)	108.8
H(7A)-C(7)-H(7B)	107.7
C(7)-C(8)-C(9)	112.9(3)
C(7)-C(8)-H(8A)	109.0
C(9)-C(8)-H(8A)	109.0
C(7)-C(8)-H(8B)	109.0
C(9)-C(8)-H(8B)	109.0
H(8A)-C(8)-H(8B)	107.8
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(15)-C(10)-C(11)	119.24(10)
C(15)-C(10)-P(1)	116.15(8)
C(11)-C(10)-P(1)	124.57(8)
C(12)-C(11)-C(10)	119.79(11)
C(12)-C(11)-H(11)	120.1
C(10)-C(11)-H(11)	120.1
C(13)-C(12)-C(11)	120.37(11)
C(13)-C(12)-H(12)	119.8
C(11)-C(12)-H(12)	119.8
C(12)-C(13)-C(14)	120.16(11)
C(12)-C(13)-H(13)	119.9
C(14)-C(13)-H(13)	119.9
C(15)-C(14)-C(13)	119.70(11)
C(15)-C(14)-H(14)	120.2
C(13)-C(14)-H(14)	120.2
C(14)-C(15)-C(10)	120.75(11)
C(14)-C(15)-H(15)	119.6
C(10)-C(15)-H(15)	119.6

C(21)-C(16)-C(17)	119.01(11)
C(21)-C(16)-P(1)	119.24(9)
C(17)-C(16)-P(1)	121.73(9)
C(18)-C(17)-C(16)	120.27(11)
C(18)-C(17)-H(17)	119.9
C(16)-C(17)-H(17)	119.9
C(17)-C(18)-C(19)	120.32(11)
C(17)-C(18)-H(18)	119.8
C(19)-C(18)-H(18)	119.8
C(20)-C(19)-C(18)	119.57(11)
C(20)-C(19)-H(19)	120.2
C(18)-C(19)-H(19)	120.2
C(19)-C(20)-C(21)	120.21(12)
C(19)-C(20)-H(20)	119.9
C(21)-C(20)-H(20)	119.9
C(20)-C(21)-C(16)	120.60(12)
C(20)-C(21)-H(21)	119.7
C(16)-C(21)-H(21)	119.7

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for $C_{21}H_{26}NOP$. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	9(1)	12(1)	18(1)	0(1)	0(1)	0(1)
O(1)	10(1)	16(1)	26(1)	-3(1)	-1(1)	-1(1)
N(1)	11(1)	18(1)	18(1)	-2(1)	0(1)	2(1)
C(1)	57(1)	95(2)	33(1)	-19(1)	9(1)	12(1)
C(2)	36(1)	40(1)	31(1)	-15(1)	0(1)	8(1)
C(3)	26(1)	26(1)	24(1)	-2(1)	3(1)	9(1)
C(4)	14(1)	18(1)	18(1)	-1(1)	0(1)	2(1)
C(5)	24(2)	27(2)	26(2)	3(1)	2(2)	-1(2)
C(6)	30(2)	31(2)	24(1)	10(1)	2(1)	8(2)
C(7)	55(2)	34(2)	30(1)	9(1)	-1(1)	15(2)

C(8)	54(2)	53(2)	32(2)	9(2)	2(1)	20(2)
C(9)	116(4)	41(2)	31(2)	9(2)	-6(2)	15(2)
C(10)	13(1)	12(1)	18(1)	2(1)	1(1)	-1(1)
C(11)	15(1)	19(1)	22(1)	1(1)	2(1)	3(1)
C(12)	18(1)	26(1)	24(1)	5(1)	-1(1)	3(1)
C(13)	23(1)	24(1)	19(1)	5(1)	0(1)	-1(1)
C(14)	25(1)	23(1)	20(1)	1(1)	6(1)	4(1)
C(15)	18(1)	20(1)	22(1)	2(1)	3(1)	4(1)
C(16)	15(1)	13(1)	17(1)	1(1)	2(1)	2(1)
C(17)	18(1)	17(1)	21(1)	1(1)	0(1)	-1(1)
C(18)	28(1)	14(1)	26(1)	0(1)	4(1)	-3(1)
C(19)	30(1)	15(1)	30(1)	4(1)	9(1)	4(1)
C(20)	22(1)	22(1)	33(1)	7(1)	1(1)	7(1)
C(21)	16(1)	20(1)	28(1)	1(1)	-2(1)	2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for $C_{21}H_{26}NOP$

	x	y	z	U(eq)
H(1N)	4340(20)	-1474(19)	8048(7)	19
H(1A)	7340(40)	-3260(30)	6082(13)	74
H(1B)	5330(50)	-3860(30)	5497(8)	74
H(2)	2180(30)	-3950(20)	6204(10)	43
H(3A)	5913	-2841	7116	30
H(3B)	3830	-4109	7287	30
H(4)	640(20)	-2114(19)	7140(7)	20
H(5)	4110	140	6843	31
H(6)	-877	-210	6531	34
H(7A)	2620	2190	6199	48
H(7B)	-128	2642	6410	48
H(8A)	-1840	1362	5503	56
H(8B)	928	965	5289	56

H(9A)	-656	3184	4746	94
H(9B)	1757	3666	5169	94
H(9C)	-983	4084	5399	94
H(5X)	4825	-80	6850	24
H(6X)	-220	375	6584	43
H(7XA)	1313	3082	6554	55
H(7XB)	3981	2399	6374	55
H(8XA)	2162	3370	5471	72
H(8XB)	2167	1493	5404	72
H(9XA)	-1640	2485	5045	120
H(9XB)	-2048	3317	5709	120
H(9XC)	-2053	1434	5658	120
H(11)	4654	-2474	9035	23
H(12)	5711	-2647	10110	27
H(13)	3327	-1328	10844	27
H(14)	-125	186	10508	27
H(15)	-1191	368	9438	24
H(17)	3429	1952	8633	23
H(18)	2904	4644	8437	27
H(19)	-672	5556	7883	30
H(20)	-3677	3753	7507	31
H(21)	-3204	1068	7721	26

Table 6. Torsion angles [°] for $C_{21}H_{26}NOP$

O(1)-P(1)-N(1)-C(4)	47.67(10)
C(10)-P(1)-N(1)-C(4)	172.76(9)
C(16)-P(1)-N(1)-C(4)	-74.24(10)
C(1)-C(2)-C(3)-C(4)	121.7(2)
P(1)-N(1)-C(4)-C(5)	75.1(2)
P(1)-N(1)-C(4)-C(3)	-154.04(9)
C(2)-C(3)-C(4)-C(5)	-54.4(3)
C(2)-C(3)-C(4)-N(1)	175.89(12)
N(1)-C(4)-C(5)-C(6)	-111.9(5)
C(3)-C(4)-C(5)-C(6)	121.5(5)
C(4)-C(5)-C(6)-C(7)	177.3(4)

C(5)-C(6)-C(7)-C(8)	127.5(5)
C(6)-C(7)-C(8)-C(9)	178.3(4)
O(1)-P(1)-C(10)-C(15)	-67.14(10)
N(1)-P(1)-C(10)-C(15)	169.76(9)
C(16)-P(1)-C(10)-C(15)	51.77(10)
O(1)-P(1)-C(10)-C(11)	110.54(10)
N(1)-P(1)-C(10)-C(11)	-12.56(11)
C(16)-P(1)-C(10)-C(11)	-130.55(10)
C(15)-C(10)-C(11)-C(12)	0.16(17)
P(1)-C(10)-C(11)-C(12)	-177.45(9)
C(10)-C(11)-C(12)-C(13)	0.03(18)
C(11)-C(12)-C(13)-C(14)	-0.18(19)
C(12)-C(13)-C(14)-C(15)	0.13(19)
C(13)-C(14)-C(15)-C(10)	0.06(19)
C(11)-C(10)-C(15)-C(14)	-0.20(18)
P(1)-C(10)-C(15)-C(14)	177.61(10)
O(1)-P(1)-C(16)-C(21)	-14.04(11)
N(1)-P(1)-C(16)-C(21)	109.67(10)
C(10)-P(1)-C(16)-C(21)	-137.13(9)
O(1)-P(1)-C(16)-C(17)	167.59(9)
N(1)-P(1)-C(16)-C(17)	-68.70(10)
C(10)-P(1)-C(16)-C(17)	44.50(10)
C(21)-C(16)-C(17)-C(18)	0.30(18)
P(1)-C(16)-C(17)-C(18)	178.68(9)
C(16)-C(17)-C(18)-C(19)	-0.20(19)
C(17)-C(18)-C(19)-C(20)	-0.64(19)
C(18)-C(19)-C(20)-C(21)	1.37(19)
C(19)-C(20)-C(21)-C(16)	-1.3(2)
C(17)-C(16)-C(21)-C(20)	0.43(18)
P(1)-C(16)-C(21)-C(20)	-177.98(10)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{21}H_{26}NOP$ [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)

N(1)-H(1N)...O(1)#1	0.885(13)	2.009(13)	2.8692(12)	163.7(14)

Symmetry transformations used to generate equivalent atoms:

#1 x+1,y,z

X-ray Crystal Structure of 1.35

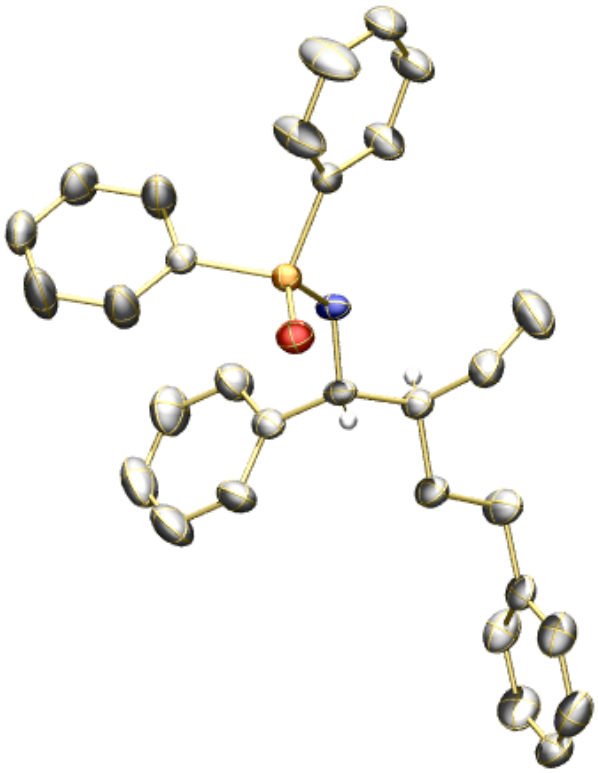


Table 1. Crystal data and structure refinement for $C_{30}H_{30}NOP$ 1.35

Identification code	$C_{30}H_{30}NOP$

Empirical formula	$C_{30}H_{30}NOP$	
Formula weight	451.52	
Temperature	213(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.4229(2) Å	α= 90°
	b = 16.7050(6) Å	β= 90°
	c = 27.7408(11) Å	γ = 90°
Volume	2513.03(16) $Å^3$	
Z	4	
Density (calculated)	1.193 Mg/m^3	
Absorption coefficient	0.131 mm^{-1}	
F(000)	960	
Crystal size	0.20 x 0.08 x 0.04 mm^3	
Theta range for data collection	1.42 to 28.37°	
Index ranges	-6<=h<=7, -22<=k<=22, -37<=l<=37	
Reflections collected	65893	
Independent reflections	6293 [R(int) = 0.0763]	
Completeness to theta = 28.37°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9948 and 0.9742	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6293 / 0 / 313	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0422, wR2 = 0.0906	
R indices (all data)	R1 = 0.0607, wR2 = 0.0990	
Absolute structure parameter	0.01(8)	
Extinction coefficient	na	
Largest diff. peak and hole	0.227 and -0.202 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for $C_{30}H_{30}NOP$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	10237(1)	1920(1)	1447(1)	25(1)
O(1)	12782(2)	1714(1)	1299(1)	34(1)
N(1)	8159(3)	1429(1)	1140(1)	28(1)
C(1)	9453(3)	2960(1)	1370(1)	29(1)
C(2)	7484(4)	3226(1)	1103(1)	47(1)
C(3)	7029(5)	4042(1)	1060(1)	54(1)
C(4)	8565(5)	4584(1)	1272(1)	51(1)
C(5)	10554(6)	4327(1)	1528(1)	81(1)
C(6)	10993(5)	3517(1)	1580(1)	64(1)
C(7)	9832(3)	1752(1)	2088(1)	28(1)
C(8)	7816(4)	2046(2)	2329(1)	56(1)
C(9)	7515(5)	1903(2)	2818(1)	55(1)
C(10)	9196(5)	1470(1)	3065(1)	48(1)
C(11)	11243(6)	1201(2)	2836(1)	75(1)
C(12)	11557(5)	1340(2)	2344(1)	58(1)
C(13)	8636(4)	611(1)	964(1)	29(1)
C(14)	8128(4)	-26(1)	1339(1)	34(1)
C(15)	6030(5)	-6(1)	1619(1)	49(1)
C(16)	5611(6)	-590(2)	1964(1)	64(1)
C(17)	7274(7)	-1203(2)	2026(1)	69(1)
C(18)	9355(6)	-1231(2)	1748(1)	67(1)
C(19)	9771(5)	-646(1)	1408(1)	50(1)
C(20)	7174(4)	486(1)	490(1)	33(1)
C(21)	7710(5)	1155(1)	147(1)	49(1)
C(22)	6103(8)	1636(2)	-48(1)	79(1)
C(23)	7847(4)	-325(1)	262(1)	38(1)
C(24)	6369(5)	-520(1)	-191(1)	51(1)
C(25)	7255(4)	-1271(1)	-441(1)	37(1)
C(26)	5986(4)	-1981(1)	-406(1)	48(1)
C(27)	6824(5)	-2660(1)	-638(1)	58(1)
C(28)	8930(5)	-2649(1)	-903(1)	53(1)
C(29)	10220(4)	-1956(2)	-938(1)	54(1)
C(30)	9382(4)	-1268(1)	-711(1)	49(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{30}H_{30}NOP$

P(1)-O(1)	1.4815(13)
P(1)-N(1)	1.6343(16)
P(1)-C(1)	1.8003(17)
P(1)-C(7)	1.8131(17)
N(1)-C(13)	1.473(2)
N(1)-H(1N)	0.78(2)
C(1)-C(2)	1.373(3)
C(1)-C(6)	1.380(3)
C(2)-C(3)	1.391(3)
C(2)-H(2)	0.9400
C(3)-C(4)	1.363(3)
C(3)-H(3)	0.9400
C(4)-C(5)	1.361(4)
C(4)-H(4)	0.9400
C(5)-C(6)	1.381(3)
C(5)-H(5)	0.9400
C(6)-H(6)	0.9400
C(7)-C(12)	1.361(3)
C(7)-C(8)	1.371(3)
C(8)-C(9)	1.388(3)
C(8)-H(8)	0.9400
C(9)-C(10)	1.349(3)
C(9)-H(9)	0.9400
C(10)-C(11)	1.355(3)
C(10)-H(10)	0.9400
C(11)-C(12)	1.396(3)
C(11)-H(11)	0.9400
C(12)-H(12)	0.9400
C(13)-C(14)	1.514(3)
C(13)-C(20)	1.549(3)
C(13)-H(13)	0.97(2)
C(14)-C(15)	1.378(3)
C(14)-C(19)	1.380(3)
C(15)-C(16)	1.384(3)
C(15)-H(15)	0.9400

C(16)-C(17)	1.377(4)
C(16)-H(16)	0.9400
C(17)-C(18)	1.368(4)
C(17)-H(17)	0.9400
C(18)-C(19)	1.377(3)
C(18)-H(18)	0.9400
C(19)-H(19)	0.9400
C(20)-C(21)	1.498(3)
C(20)-C(23)	1.539(3)
C(20)-H(20)	0.98(2)
C(21)-C(22)	1.301(4)
C(21)-H(21)	0.9400
C(22)-H(22A)	1.01(3)
C(22)-H(22B)	0.93(3)
C(23)-C(24)	1.527(3)
C(23)-H(23)	0.9800
C(23)-H(7B)	0.9800
C(24)-C(25)	1.512(3)
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(25)-C(30)	1.374(3)
C(25)-C(26)	1.375(3)
C(26)-C(27)	1.381(3)
C(26)-H(26)	0.9400
C(27)-C(28)	1.359(4)
C(27)-H(27)	0.9400
C(28)-C(29)	1.357(3)
C(28)-H(28)	0.9400
C(29)-C(30)	1.387(3)
C(29)-H(29)	0.9400
C(30)-H(30)	0.9400
O(1)-P(1)-N(1)	112.31(8)
O(1)-P(1)-C(1)	114.32(8)
N(1)-P(1)-C(1)	105.06(8)
O(1)-P(1)-C(7)	110.45(8)
N(1)-P(1)-C(7)	110.49(8)
C(1)-P(1)-C(7)	103.78(7)

C(13)-N(1)-P(1)	121.21(13)
C(13)-N(1)-H(1N)	115.8(16)
P(1)-N(1)-H(1N)	117.8(16)
C(2)-C(1)-C(6)	118.66(18)
C(2)-C(1)-P(1)	124.10(14)
C(6)-C(1)-P(1)	117.20(15)
C(1)-C(2)-C(3)	120.1(2)
C(1)-C(2)-H(2)	119.9
C(3)-C(2)-H(2)	119.9
C(4)-C(3)-C(2)	120.3(2)
C(4)-C(3)-H(3)	119.8
C(2)-C(3)-H(3)	119.8
C(5)-C(4)-C(3)	120.0(2)
C(5)-C(4)-H(4)	120.0
C(3)-C(4)-H(4)	120.0
C(4)-C(5)-C(6)	120.0(2)
C(4)-C(5)-H(5)	120.0
C(6)-C(5)-H(5)	120.0
C(1)-C(6)-C(5)	120.8(2)
C(1)-C(6)-H(6)	119.6
C(5)-C(6)-H(6)	119.6
C(12)-C(7)-C(8)	118.34(18)
C(12)-C(7)-P(1)	120.43(15)
C(8)-C(7)-P(1)	121.22(14)
C(7)-C(8)-C(9)	120.6(2)
C(7)-C(8)-H(8)	119.7
C(9)-C(8)-H(8)	119.7
C(10)-C(9)-C(8)	120.6(2)
C(10)-C(9)-H(9)	119.7
C(8)-C(9)-H(9)	119.7
C(9)-C(10)-C(11)	119.6(2)
C(9)-C(10)-H(10)	120.2
C(11)-C(10)-H(10)	120.2
C(10)-C(11)-C(12)	120.1(2)
C(10)-C(11)-H(11)	119.9
C(12)-C(11)-H(11)	119.9
C(7)-C(12)-C(11)	120.7(2)

C(7)-C(12)-H(12)	119.6
C(11)-C(12)-H(12)	119.6
N(1)-C(13)-C(14)	113.10(15)
N(1)-C(13)-C(20)	108.47(15)
C(14)-C(13)-C(20)	113.26(15)
N(1)-C(13)-H(13)	105.7(12)
C(14)-C(13)-H(13)	110.4(12)
C(20)-C(13)-H(13)	105.4(11)
C(15)-C(14)-C(19)	118.22(19)
C(15)-C(14)-C(13)	121.40(17)
C(19)-C(14)-C(13)	120.37(19)
C(14)-C(15)-C(16)	120.6(2)
C(14)-C(15)-H(15)	119.7
C(16)-C(15)-H(15)	119.7
C(17)-C(16)-C(15)	120.2(3)
C(17)-C(16)-H(16)	119.9
C(15)-C(16)-H(16)	119.9
C(18)-C(17)-C(16)	119.7(2)
C(18)-C(17)-H(17)	120.2
C(16)-C(17)-H(17)	120.2
C(17)-C(18)-C(19)	119.8(2)
C(17)-C(18)-H(18)	120.1
C(19)-C(18)-H(18)	120.1
C(18)-C(19)-C(14)	121.5(2)
C(18)-C(19)-H(19)	119.3
C(14)-C(19)-H(19)	119.3
C(21)-C(20)-C(23)	110.45(16)
C(21)-C(20)-C(13)	109.87(16)
C(23)-C(20)-C(13)	110.28(15)
C(21)-C(20)-H(20)	107.7(12)
C(23)-C(20)-H(20)	109.2(12)
C(13)-C(20)-H(20)	109.3(12)
C(22)-C(21)-C(20)	126.4(3)
C(22)-C(21)-H(21)	116.8
C(20)-C(21)-H(21)	116.8
C(21)-C(22)-H(22A)	115.1(19)
C(21)-C(22)-H(22B)	118(2)

H(22A)-C(22)-H(22B)	126(3)
C(24)-C(23)-C(20)	113.68(17)
C(24)-C(23)-H(23)	108.8
C(20)-C(23)-H(23)	108.8
C(24)-C(23)-H(7B)	108.8
C(20)-C(23)-H(7B)	108.8
H(23)-C(23)-H(7B)	107.7
C(25)-C(24)-C(23)	112.82(18)
C(25)-C(24)-H(24A)	109.0
C(23)-C(24)-H(24A)	109.0
C(25)-C(24)-H(24B)	109.0
C(23)-C(24)-H(24B)	109.0
H(24A)-C(24)-H(24B)	107.8
C(30)-C(25)-C(26)	117.51(19)
C(30)-C(25)-C(24)	120.9(2)
C(26)-C(25)-C(24)	121.6(2)
C(25)-C(26)-C(27)	120.7(2)
C(25)-C(26)-H(26)	119.6
C(27)-C(26)-H(26)	119.6
C(28)-C(27)-C(26)	121.2(2)
C(28)-C(27)-H(27)	119.4
C(26)-C(27)-H(27)	119.4
C(29)-C(28)-C(27)	118.9(2)
C(29)-C(28)-H(28)	120.5
C(27)-C(28)-H(28)	120.5
C(28)-C(29)-C(30)	120.4(2)
C(28)-C(29)-H(29)	119.8
C(30)-C(29)-H(29)	119.8
C(25)-C(30)-C(29)	121.3(2)
C(25)-C(30)-H(30)	119.3
C(29)-C(30)-H(30)	119.3

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for $C_{30}H_{30}NOP$. The anisotropic

displacement factor exponent takes the form: $-2p^2[\, h^2\, a^{*2}U^{11} + \ldots + 2\, h\, k\, a^*\, b^*\, U^{12}\,]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	23(1)	25(1)	27(1)	-1(1)	-1(1)	2(1)
O(1)	26(1)	38(1)	40(1)	-2(1)	2(1)	3(1)
N(1)	23(1)	26(1)	36(1)	-8(1)	-4(1)	5(1)
C(1)	33(1)	28(1)	27(1)	0(1)	1(1)	2(1)
C(2)	53(1)	33(1)	56(1)	1(1)	-21(1)	2(1)
C(3)	66(2)	34(1)	63(2)	3(1)	-21(1)	11(1)
C(4)	73(2)	28(1)	53(1)	1(1)	-9(1)	6(1)
C(5)	99(2)	30(1)	114(2)	-7(1)	-49(2)	-5(1)
C(6)	64(2)	36(1)	90(2)	-1(1)	-40(1)	1(1)
C(7)	30(1)	26(1)	29(1)	-2(1)	-3(1)	-1(1)
C(8)	49(1)	80(2)	37(1)	11(1)	6(1)	27(1)
C(9)	55(1)	70(2)	39(1)	4(1)	16(1)	16(1)
C(10)	63(2)	54(1)	29(1)	8(1)	2(1)	-2(1)
C(11)	76(2)	107(2)	43(1)	29(2)	6(1)	44(2)
C(12)	54(2)	80(2)	41(1)	15(1)	9(1)	31(1)
C(13)	27(1)	27(1)	32(1)	-8(1)	-3(1)	6(1)
C(14)	38(1)	28(1)	35(1)	-7(1)	-10(1)	1(1)
C(15)	54(1)	43(1)	52(1)	8(1)	2(1)	3(1)
C(16)	73(2)	64(2)	54(1)	14(1)	6(1)	-12(2)
C(17)	102(3)	47(1)	58(2)	19(1)	-23(2)	-14(2)
C(18)	85(2)	44(1)	72(2)	15(1)	-16(2)	14(1)
C(19)	57(1)	38(1)	53(1)	-1(1)	-9(1)	17(1)
C(20)	35(1)	32(1)	32(1)	-6(1)	-7(1)	4(1)
C(21)	68(2)	42(1)	36(1)	-5(1)	-6(1)	0(1)
C(22)	118(3)	52(2)	68(2)	13(1)	-35(2)	2(2)
C(23)	42(1)	36(1)	35(1)	-9(1)	-7(1)	5(1)
C(24)	56(1)	51(1)	47(1)	-17(1)	-19(1)	10(1)
C(25)	43(1)	39(1)	28(1)	-6(1)	-10(1)	-2(1)
C(26)	47(1)	57(1)	41(1)	-9(1)	1(1)	-16(1)
C(27)	83(2)	39(1)	54(1)	-9(1)	-4(1)	-22(1)
C(28)	66(2)	51(1)	41(1)	-14(1)	-9(1)	12(1)
C(29)	44(1)	78(2)	39(1)	-10(1)	4(1)	-2(2)
C(30)	53(2)	51(1)	44(1)	-3(1)	0(1)	-18(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for $C_{30}H_{30}NOP$

	x	y	z	U(eq)
H(1N)	6780(40)	1537(12)	1182(8)	34
H(2)	6441	2856	950	57
H(3)	5656	4222	884	65
H(4)	8251	5135	1241	62
H(5)	11628	4701	1670	97
H(6)	12359	3344	1761	76
H(8)	6629	2346	2161	67
H(9)	6128	2109	2979	66
H(10)	8949	1357	3393	58
H(11)	12454	919	3010	90
H(12)	12976	1148	2187	70
H(13)	10360(40)	603(11)	871(7)	35
H(15)	4874	406	1576	59
H(16)	4185	-566	2157	77
H(17)	6983	-1601	2259	83
H(18)	10498	-1649	1788	80
H(19)	11207	-669	1219	60
H(20)	5410(40)	495(12)	561(7)	39
H(21)	9371	1236	63	58
H(22A)	4370(70)	1590(20)	86(12)	95
H(22B)	6680(60)	2030(20)	-255(12)	95
H(23)	9606	-324	182	45
H(7B)	7572	-749	501	45
H(24A)	4629	-585	-104	62
H(24B)	6488	-69	-416	62
H(26)	4532	-2005	-222	58
H(27)	5922	-3139	-611	70
H(28)	9484	-3114	-1060	63
H(29)	11689	-1941	-1118	64

H(30)	10287	-791	-741	59

Table 6. Torsion angles [°] for $C_{30}H_{30}NOP$

O(1)-P(1)-N(1)-C(13)	32.32(17)
C(1)-P(1)-N(1)-C(13)	157.18(14)
C(7)-P(1)-N(1)-C(13)	-91.49(16)
O(1)-P(1)-C(1)-C(2)	123.78(17)
N(1)-P(1)-C(1)-C(2)	0.20(19)
C(7)-P(1)-C(1)-C(2)	-115.85(18)
O(1)-P(1)-C(1)-C(6)	-53.9(2)
N(1)-P(1)-C(1)-C(6)	-177.49(19)
C(7)-P(1)-C(1)-C(6)	66.5(2)
C(6)-C(1)-C(2)-C(3)	-1.8(3)
P(1)-C(1)-C(2)-C(3)	-179.48(19)
C(1)-C(2)-C(3)-C(4)	1.6(4)
C(2)-C(3)-C(4)-C(5)	-0.1(4)
C(3)-C(4)-C(5)-C(6)	-1.1(5)
C(2)-C(1)-C(6)-C(5)	0.7(4)
P(1)-C(1)-C(6)-C(5)	178.5(3)
C(4)-C(5)-C(6)-C(1)	0.8(5)
O(1)-P(1)-C(7)-C(12)	-12.0(2)
N(1)-P(1)-C(7)-C(12)	112.92(19)
C(1)-P(1)-C(7)-C(12)	-134.92(18)
O(1)-P(1)-C(7)-C(8)	166.88(17)
N(1)-P(1)-C(7)-C(8)	-68.24(19)
C(1)-P(1)-C(7)-C(8)	43.91(19)
C(12)-C(7)-C(8)-C(9)	-2.0(4)
P(1)-C(7)-C(8)-C(9)	179.1(2)
C(7)-C(8)-C(9)-C(10)	-0.2(4)
C(8)-C(9)-C(10)-C(11)	2.6(4)
C(9)-C(10)-C(11)-C(12)	-2.7(5)
C(8)-C(7)-C(12)-C(11)	1.9(4)
P(1)-C(7)-C(12)-C(11)	-179.3(2)
C(10)-C(11)-C(12)-C(7)	0.5(5)
P(1)-N(1)-C(13)-C(14)	84.0(2)

P(1)-N(1)-C(13)-C(20)	-149.53(14)
N(1)-C(13)-C(14)-C(15)	44.7(2)
C(20)-C(13)-C(14)-C(15)	-79.2(2)
N(1)-C(13)-C(14)-C(19)	-135.40(18)
C(20)-C(13)-C(14)-C(19)	100.7(2)
C(19)-C(14)-C(15)-C(16)	0.8(3)
C(13)-C(14)-C(15)-C(16)	-179.3(2)
C(14)-C(15)-C(16)-C(17)	-0.9(4)
C(15)-C(16)-C(17)-C(18)	0.5(4)
C(16)-C(17)-C(18)-C(19)	0.0(4)
C(17)-C(18)-C(19)-C(14)	-0.1(4)
C(15)-C(14)-C(19)-C(18)	-0.3(3)
C(13)-C(14)-C(19)-C(18)	179.8(2)
N(1)-C(13)-C(20)-C(21)	51.5(2)
C(14)-C(13)-C(20)-C(21)	177.98(17)
N(1)-C(13)-C(20)-C(23)	173.53(17)
C(14)-C(13)-C(20)-C(23)	-60.0(2)
C(23)-C(20)-C(21)-C(22)	115.4(3)
C(13)-C(20)-C(21)-C(22)	-122.7(3)
C(21)-C(20)-C(23)-C(24)	-61.9(3)
C(13)-C(20)-C(23)-C(24)	176.50(19)
C(20)-C(23)-C(24)-C(25)	173.42(19)
C(23)-C(24)-C(25)-C(30)	-75.9(3)
C(23)-C(24)-C(25)-C(26)	103.5(2)
C(30)-C(25)-C(26)-C(27)	-0.6(3)
C(24)-C(25)-C(26)-C(27)	179.9(2)
C(25)-C(26)-C(27)-C(28)	0.6(4)
C(26)-C(27)-C(28)-C(29)	0.1(4)
C(27)-C(28)-C(29)-C(30)	-0.7(3)
C(26)-C(25)-C(30)-C(29)	0.0(3)
C(24)-C(25)-C(30)-C(29)	179.5(2)
C(28)-C(29)-C(30)-C(25)	0.7(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{30}H_{30}NOP$ [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(1)#1	0.78(2)	2.21(2)	2.987(2)	174(2)

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z

X-ray Crystal Structure of 1.34

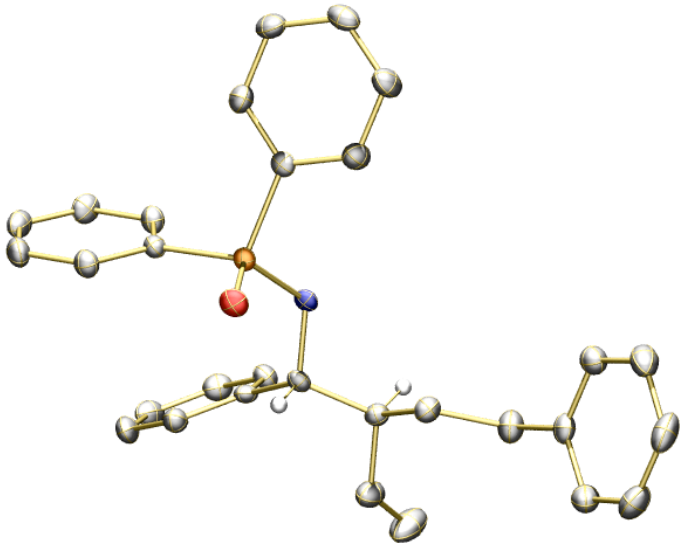


Table 1. Crystal data and structure refinement for $C_{30}H_{30}NOP$

Identification code	$C_{30}H_{30}NOP$	
Empirical formula	$C_{30}H_{30}NOP$	
Formula weight	451.52	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.7855(5) Å	α= 90°
	b = 10.0513(5) Å	β= 93.331(3)°
	c = 11.6042(6) Å	γ = 90°
Volume	1255.87(11) $Å^3$	
Z	2	
Density (calculated)	1.194 Mg/m^3	

Absorption coefficient	0.132 mm^{-1}
F(000)	480
Crystal size	0.25 x 0.08 x 0.05 mm^3
Theta range for data collection	1.76 to 28.33°
Index ranges	-14<=h<=14, -12<=k<=13, -15<=l<=15
Reflections collected	20929
Independent reflections	6086 [R(int) = 0.0557]
Completeness to theta = 28.33°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9935 and 0.9679
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6086 / 6 / 313
Goodness-of-fit on F^2	1.028
Final R indices [I>2sigma(I)]	R1 = 0.0402, wR2 = 0.0759
R indices (all data)	R1 = 0.0599, wR2 = 0.0827
Absolute structure parameter	-0.09(7)
Extinction coefficient	na
Largest diff. peak and hole	0.289 and -0.247 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for $C_{30}H_{30}NOP$ (11). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	-133(1)	612(1)	4531(1)	16(1)
O(1)	102(1)	2053(1)	4761(1)	22(1)
N(1)	-146(1)	-242(2)	5733(1)	16(1)
C(1)	1070(2)	-166(2)	3747(2)	18(1)
C(2)	2273(2)	-174(2)	4250(2)	25(1)
C(3)	3254(2)	-654(2)	3642(2)	28(1)
C(4)	3037(2)	-1123(2)	2532(2)	26(1)
C(5)	1845(2)	-1124(2)	2025(2)	27(1)
C(6)	869(2)	-636(2)	2627(2)	24(1)
C(7)	-1556(2)	397(2)	3651(2)	18(1)

C(8)	-2129(2)	1510(2)	3138(2)	23(1)
C(9)	-3203(2)	1356(2)	2431(2)	27(1)
C(10)	-3700(2)	100(2)	2233(2)	26(1)
C(11)	-3145(2)	-1009(2)	2750(2)	26(1)
C(12)	-2074(2)	-865(2)	3464(2)	22(1)
C(13)	-906(2)	226(2)	6671(2)	17(1)
C(14)	-2240(2)	-265(2)	6510(2)	18(1)
C(15)	-3162(2)	610(2)	6114(2)	23(1)
C(16)	-4386(2)	180(2)	5924(2)	29(1)
C(17)	-4689(2)	-1129(2)	6137(2)	30(1)
C(18)	-3771(2)	-2013(2)	6529(2)	27(1)
C(19)	-2556(2)	-1583(2)	6709(2)	23(1)
C(20)	-265(2)	-147(2)	7849(2)	19(1)
C(21)	-1071(2)	234(2)	8814(2)	30(1)
C(22)	-1255(2)	-473(3)	9747(2)	46(1)
C(23)	1008(2)	542(2)	8016(2)	21(1)
C(24)	1794(2)	-29(2)	9043(2)	28(1)
C(25)	3003(2)	696(2)	9289(2)	22(1)
C(26)	4026(2)	438(2)	8655(2)	26(1)
C(27)	5127(2)	1131(2)	8865(2)	31(1)
C(28)	5209(2)	2115(2)	9700(2)	32(1)
C(29)	4202(2)	2380(2)	10329(2)	33(1)
C(30)	3110(2)	1666(2)	10136(2)	28(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{30}H_{30}NOP$

P(1)-O(1)	1.4922(13)
P(1)-N(1)	1.6385(16)
P(1)-C(1)	1.8060(19)
P(1)-C(7)	1.8061(17)
N(1)-C(13)	1.477(2)
N(1)-H(1N)	0.854(15)
C(1)-C(6)	1.388(3)
C(1)-C(2)	1.391(3)
C(2)-C(3)	1.391(3)
C(2)-H(2)	0.9500

C(3)-C(4)	1.378(3)
C(3)-H(3)	0.9500
C(4)-C(5)	1.383(3)
C(4)-H(4)	0.9500
C(5)-C(6)	1.386(3)
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(7)-C(8)	1.395(3)
C(7)-C(12)	1.398(3)
C(8)-C(9)	1.389(3)
C(8)-H(8)	0.9500
C(9)-C(10)	1.385(3)
C(9)-H(9)	0.9500
C(10)-C(11)	1.386(3)
C(10)-H(10)	0.9500
C(11)-C(12)	1.389(3)
C(11)-H(11)	0.9500
C(12)-H(12)	0.9500
C(13)-C(14)	1.522(2)
C(13)-C(20)	1.541(3)
C(13)-H(13)	0.976(15)
C(14)-C(15)	1.387(3)
C(14)-C(19)	1.390(3)
C(15)-C(16)	1.394(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.382(3)
C(16)-H(16)	0.9500
C(17)-C(18)	1.387(3)
C(17)-H(17)	0.9500
C(18)-C(19)	1.385(3)
C(18)-H(18)	0.9500
C(19)-H(19)	0.9500
C(20)-C(21)	1.507(3)
C(20)-C(23)	1.541(2)
C(20)-H(20)	1.029(15)
C(21)-C(22)	1.318(3)
C(21)-H(21)	0.9500

C(22)-H(22A)	1.036(17)
C(22)-H(22B)	0.995(16)
C(23)-C(24)	1.534(3)
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
C(24)-C(25)	1.506(3)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-C(30)	1.385(3)
C(25)-C(26)	1.386(3)
C(26)-C(27)	1.385(3)
C(26)-H(26)	0.9500
C(27)-C(28)	1.385(3)
C(27)-H(27)	0.9500
C(28)-C(29)	1.370(3)
C(28)-H(28)	0.9500
C(29)-C(30)	1.386(3)
C(29)-H(29)	0.9500
C(30)-H(30)	0.9500
O(1)-P(1)-N(1)	111.48(8)
O(1)-P(1)-C(1)	113.01(8)
N(1)-P(1)-C(1)	104.15(8)
O(1)-P(1)-C(7)	110.32(8)
N(1)-P(1)-C(7)	111.69(8)
C(1)-P(1)-C(7)	105.95(8)
C(13)-N(1)-P(1)	119.56(12)
C(13)-N(1)-H(1N)	113.2(13)
P(1)-N(1)-H(1N)	115.6(14)
C(6)-C(1)-C(2)	118.85(17)
C(6)-C(1)-P(1)	122.79(14)
C(2)-C(1)-P(1)	118.06(14)
C(3)-C(2)-C(1)	120.43(18)
C(3)-C(2)-H(2)	119.8
C(1)-C(2)-H(2)	119.8
C(4)-C(3)-C(2)	120.01(18)
C(4)-C(3)-H(3)	120.0
C(2)-C(3)-H(3)	120.0

C(3)-C(4)-C(5)	120.02(18)
C(3)-C(4)-H(4)	120.0
C(5)-C(4)-H(4)	120.0
C(4)-C(5)-C(6)	120.01(19)
C(4)-C(5)-H(5)	120.0
C(6)-C(5)-H(5)	120.0
C(5)-C(6)-C(1)	120.67(18)
C(5)-C(6)-H(6)	119.7
C(1)-C(6)-H(6)	119.7
C(8)-C(7)-C(12)	119.88(17)
C(8)-C(7)-P(1)	119.11(14)
C(12)-C(7)-P(1)	121.01(14)
C(9)-C(8)-C(7)	119.77(19)
C(9)-C(8)-H(8)	120.1
C(7)-C(8)-H(8)	120.1
C(10)-C(9)-C(8)	120.09(19)
C(10)-C(9)-H(9)	120.0
C(8)-C(9)-H(9)	120.0
C(9)-C(10)-C(11)	120.54(18)
C(9)-C(10)-H(10)	119.7
C(11)-C(10)-H(10)	119.7
C(10)-C(11)-C(12)	119.84(19)
C(10)-C(11)-H(11)	120.1
C(12)-C(11)-H(11)	120.1
C(11)-C(12)-C(7)	119.87(18)
C(11)-C(12)-H(12)	120.1
C(7)-C(12)-H(12)	120.1
N(1)-C(13)-C(14)	111.56(15)
N(1)-C(13)-C(20)	109.66(14)
C(14)-C(13)-C(20)	113.69(15)
N(1)-C(13)-H(13)	105.6(12)
C(14)-C(13)-H(13)	109.4(11)
C(20)-C(13)-H(13)	106.5(12)
C(15)-C(14)-C(19)	118.80(17)
C(15)-C(14)-C(13)	119.30(17)
C(19)-C(14)-C(13)	121.86(17)
C(14)-C(15)-C(16)	120.7(2)

C(14)-C(15)-H(15)	119.7
C(16)-C(15)-H(15)	119.7
C(17)-C(16)-C(15)	119.9(2)
C(17)-C(16)-H(16)	120.0
C(15)-C(16)-H(16)	120.0
C(16)-C(17)-C(18)	119.80(19)
C(16)-C(17)-H(17)	120.1
C(18)-C(17)-H(17)	120.1
C(19)-C(18)-C(17)	120.0(2)
C(19)-C(18)-H(18)	120.0
C(17)-C(18)-H(18)	120.0
C(18)-C(19)-C(14)	120.79(18)
C(18)-C(19)-H(19)	119.6
C(14)-C(19)-H(19)	119.6
C(21)-C(20)-C(23)	109.95(15)
C(21)-C(20)-C(13)	110.43(15)
C(23)-C(20)-C(13)	110.68(15)
C(21)-C(20)-H(20)	106.6(11)
C(23)-C(20)-H(20)	108.1(11)
C(13)-C(20)-H(20)	111.0(12)
C(22)-C(21)-C(20)	126.5(2)
C(22)-C(21)-H(21)	116.8
C(20)-C(21)-H(21)	116.8
C(21)-C(22)-H(22A)	117.9(15)
C(21)-C(22)-H(22B)	121.8(16)
H(22A)-C(22)-H(22B)	120(2)
C(24)-C(23)-C(20)	112.22(16)
C(24)-C(23)-H(23A)	109.2
C(20)-C(23)-H(23A)	109.2
C(24)-C(23)-H(23B)	109.2
C(20)-C(23)-H(23B)	109.2
H(23A)-C(23)-H(23B)	107.9
C(25)-C(24)-C(23)	113.51(17)
C(25)-C(24)-H(24A)	108.9
C(23)-C(24)-H(24A)	108.9
C(25)-C(24)-H(24B)	108.9
C(23)-C(24)-H(24B)	108.9

H(24A)-C(24)-H(24B)	107.7
C(30)-C(25)-C(26)	118.15(18)
C(30)-C(25)-C(24)	120.71(18)
C(26)-C(25)-C(24)	121.11(19)
C(27)-C(26)-C(25)	120.9(2)
C(27)-C(26)-H(26)	119.5
C(25)-C(26)-H(26)	119.5
C(28)-C(27)-C(26)	120.1(2)
C(28)-C(27)-H(27)	119.9
C(26)-C(27)-H(27)	119.9
C(29)-C(28)-C(27)	119.4(2)
C(29)-C(28)-H(28)	120.3
C(27)-C(28)-H(28)	120.3
C(28)-C(29)-C(30)	120.4(2)
C(28)-C(29)-H(29)	119.8
C(30)-C(29)-H(29)	119.8
C(25)-C(30)-C(29)	120.96(19)
C(25)-C(30)-H(30)	119.5
C(29)-C(30)-H(30)	119.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for $C_{30}H_{30}NOP$. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	17(1)	11(1)	19(1)	0(1)	0(1)	-1(1)
O(1)	26(1)	12(1)	28(1)	-1(1)	1(1)	-2(1)
N(1)	19(1)	8(1)	21(1)	-1(1)	2(1)	1(1)
C(1)	20(1)	13(1)	21(1)	3(1)	3(1)	-1(1)
C(2)	24(1)	26(1)	26(1)	-5(1)	0(1)	-1(1)
C(3)	20(1)	29(1)	35(1)	-5(1)	2(1)	0(1)
C(4)	27(1)	20(1)	31(1)	3(1)	12(1)	2(1)
C(5)	34(1)	28(1)	19(1)	0(1)	6(1)	2(1)
C(6)	26(1)	26(1)	21(1)	3(1)	-1(1)	0(1)

C(7)	16(1)	18(1)	19(1)	1(1)	2(1)	1(1)
C(8)	23(1)	19(1)	26(1)	2(1)	0(1)	1(1)
C(9)	24(1)	28(1)	28(1)	5(1)	-2(1)	6(1)
C(10)	17(1)	39(1)	23(1)	-1(1)	-2(1)	-1(1)
C(11)	23(1)	28(1)	29(1)	-2(1)	-2(1)	-8(1)
C(12)	21(1)	19(1)	26(1)	2(1)	-1(1)	-1(1)
C(13)	18(1)	12(1)	22(1)	-2(1)	2(1)	2(1)
C(14)	20(1)	20(1)	16(1)	-4(1)	3(1)	1(1)
C(15)	22(1)	23(1)	24(1)	-3(1)	0(1)	2(1)
C(16)	20(1)	37(1)	29(1)	-2(1)	-2(1)	7(1)
C(17)	18(1)	40(1)	30(1)	-9(1)	3(1)	-4(1)
C(18)	28(1)	25(1)	29(1)	-2(1)	5(1)	-7(1)
C(19)	21(1)	20(1)	28(1)	0(1)	2(1)	2(1)
C(20)	21(1)	18(1)	18(1)	-1(1)	1(1)	-1(1)
C(21)	25(1)	40(1)	27(1)	-6(1)	2(1)	-1(1)
C(22)	37(1)	74(2)	29(1)	-4(1)	6(1)	-15(1)
C(23)	22(1)	22(1)	21(1)	0(1)	1(1)	-4(1)
C(24)	24(1)	29(1)	29(1)	6(1)	-3(1)	-2(1)
C(25)	22(1)	23(1)	21(1)	7(1)	-3(1)	0(1)
C(26)	27(1)	25(1)	26(1)	2(1)	1(1)	4(1)
C(27)	24(1)	41(1)	28(1)	7(1)	3(1)	3(1)
C(28)	29(1)	42(1)	25(1)	9(1)	-8(1)	-12(1)
C(29)	40(1)	34(1)	25(1)	-3(1)	-6(1)	-5(1)
C(30)	25(1)	35(1)	24(1)	1(1)	2(1)	4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for $C_{30}H_{30}NOP$

	x	y	z	U(eq)

H(1N)	-151(17)	-1087(16)	5655(18)	19
H(2)	2426	151	5014	30
H(3)	4072	-658	3992	34
H(4)	3708	-1446	2116	31
H(5)	1695	-1459	1264	32
H(6)	54	-624	2269	29
H(8)	-1786	2371	3273	27
H(9)	-3597	2112	2083	32
H(10)	-4427	-1	1738	32
H(11)	-3495	-1866	2616	32
H(12)	-1696	-1623	3826	26
H(13)	-895(17)	1196(15)	6627(17)	21
H(15)	-2958	1512	5970	27
H(16)	-5011	787	5649	34
H(17)	-5524	-1423	6015	35
H(18)	-3977	-2915	6673	33
H(19)	-1930	-2195	6971	28
H(20)	-127(17)	-1158(16)	7911(18)	23
H(21)	-1489	1065	8744	37
H(22A)	-790(20)	-1370(20)	9850(20)	56
H(22B)	-1780(20)	-140(30)	10363(18)	56
H(23A)	1464	435	7305	26
H(23B)	881	1506	8140	26
H(24A)	1306	8	9739	33
H(24B)	1974	-976	8888	33
H(26)	3973	-222	8069	31
H(27)	5826	930	8435	37
H(28)	5958	2602	9837	39
H(29)	4252	3058	10901	40
H(30)	2426	1844	10593	33

Table 6. Torsion angles [°] for $C_{30}H_{30}NOP$

O(1)-P(1)-N(1)-C(13)	49.52(15)

C(1)-P(1)-N(1)-C(13)	171.68(13)
C(7)-P(1)-N(1)-C(13)	-74.41(15)
O(1)-P(1)-C(1)-C(6)	-112.97(16)
N(1)-P(1)-C(1)-C(6)	125.88(16)
C(7)-P(1)-C(1)-C(6)	7.95(18)
O(1)-P(1)-C(1)-C(2)	60.64(17)
N(1)-P(1)-C(1)-C(2)	-60.51(17)
C(7)-P(1)-C(1)-C(2)	-178.45(15)
C(6)-C(1)-C(2)-C(3)	-0.5(3)
P(1)-C(1)-C(2)-C(3)	-174.31(16)
C(1)-C(2)-C(3)-C(4)	0.2(3)
C(2)-C(3)-C(4)-C(5)	-0.4(3)
C(3)-C(4)-C(5)-C(6)	0.9(3)
C(4)-C(5)-C(6)-C(1)	-1.2(3)
C(2)-C(1)-C(6)-C(5)	1.0(3)
P(1)-C(1)-C(6)-C(5)	174.51(16)
O(1)-P(1)-C(7)-C(8)	10.78(17)
N(1)-P(1)-C(7)-C(8)	135.36(14)
C(1)-P(1)-C(7)-C(8)	-111.86(15)
O(1)-P(1)-C(7)-C(12)	-170.18(14)
N(1)-P(1)-C(7)-C(12)	-45.60(17)
C(1)-P(1)-C(7)-C(12)	67.18(16)
C(12)-C(7)-C(8)-C(9)	-1.0(3)
P(1)-C(7)-C(8)-C(9)	178.07(14)
C(7)-C(8)-C(9)-C(10)	-0.2(3)
C(8)-C(9)-C(10)-C(11)	1.0(3)
C(9)-C(10)-C(11)-C(12)	-0.6(3)
C(10)-C(11)-C(12)-C(7)	-0.6(3)
C(8)-C(7)-C(12)-C(11)	1.4(3)
P(1)-C(7)-C(12)-C(11)	-177.65(15)
P(1)-N(1)-C(13)-C(14)	85.70(17)
P(1)-N(1)-C(13)-C(20)	-147.44(13)
N(1)-C(13)-C(14)-C(15)	-103.98(19)
C(20)-C(13)-C(14)-C(15)	131.38(17)
N(1)-C(13)-C(14)-C(19)	73.6(2)
C(20)-C(13)-C(14)-C(19)	-51.1(2)
C(19)-C(14)-C(15)-C(16)	0.4(3)

C(13)-C(14)-C(15)-C(16)	178.03(17)
C(14)-C(15)-C(16)-C(17)	0.3(3)
C(15)-C(16)-C(17)-C(18)	-0.6(3)
C(16)-C(17)-C(18)-C(19)	0.2(3)
C(17)-C(18)-C(19)-C(14)	0.5(3)
C(15)-C(14)-C(19)-C(18)	-0.8(3)
C(13)-C(14)-C(19)-C(18)	-178.38(18)
N(1)-C(13)-C(20)-C(21)	-175.90(16)
C(14)-C(13)-C(20)-C(21)	-50.2(2)
N(1)-C(13)-C(20)-C(23)	62.1(2)
C(14)-C(13)-C(20)-C(23)	-172.23(16)
C(23)-C(20)-C(21)-C(22)	-98.5(2)
C(13)-C(20)-C(21)-C(22)	139.1(2)
C(21)-C(20)-C(23)-C(24)	70.2(2)
C(13)-C(20)-C(23)-C(24)	-167.56(16)
C(20)-C(23)-C(24)-C(25)	-175.36(17)
C(23)-C(24)-C(25)-C(30)	97.6(2)
C(23)-C(24)-C(25)-C(26)	-80.7(2)
C(30)-C(25)-C(26)-C(27)	0.1(3)
C(24)-C(25)-C(26)-C(27)	178.41(19)
C(25)-C(26)-C(27)-C(28)	-1.4(3)
C(26)-C(27)-C(28)-C(29)	1.1(3)
C(27)-C(28)-C(29)-C(30)	0.3(3)
C(26)-C(25)-C(30)-C(29)	1.4(3)
C(24)-C(25)-C(30)-C(29)	-176.93(19)
C(28)-C(29)-C(30)-C(25)	-1.6(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{30}H_{30}NOP$ [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(1)#1	0.854(15)	1.932(16)	2.779(2)	171(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x,y-1/2,-z+1

X-ray Crystal Structure of 1.32

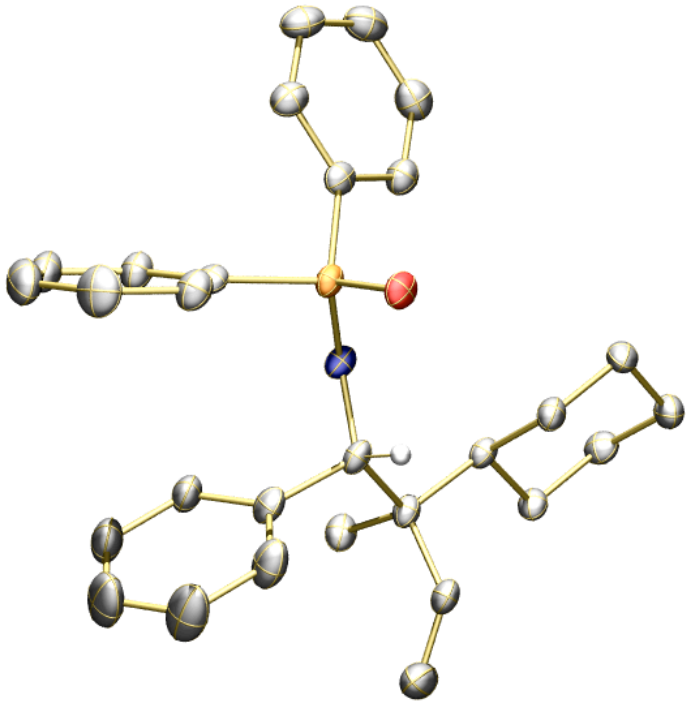


Table 1. Crystal data and structure refinement for $C_{29}H_{34}NOP$

Identification code	$C_{29}H_{34}NOP$	
Empirical formula	$C_{29}H_{34}NOP$	
Formula weight	443.54	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 22.5726(15) Å	α= 90°
	b = 20.6585(13) Å	β= 119.094(4)°
	c = 23.0355(15) Å	γ = 90°
Volume	9386.5(11) $Å^3$	
Z	12	
Density (calculated)	0.942 Mg/m^3	
Absorption coefficient	0.104 mm^{-1}	
F(000)	2856	
Crystal size	0.15 x 0.06 x 0.05 mm^3	

Theta range for data collection	1.41 to 28.81°
Index ranges	-30<=h<=26, -27<=k<=27, 0<=l<=31
Reflections collected	48686
Independent reflections	48686 [R(int) = 0.0000]
Completeness to theta = 28.81°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9948 and 0.9845
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	48686 / 1 / 1729
Goodness-of-fit on F^2	0.998
Final R indices [I>2sigma(I)]	R1 = 0.0492, wR2 = 0.1165
R indices (all data)	R1 = 0.0702, wR2 = 0.1245
Absolute structure parameter	-0.04(3)
Extinction coefficient	na
Largest diff. peak and hole	0.458 and -0.341 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for $C_{29}H_{34}NOP$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	20(1)	2748(1)	29(1)	18(1)
O(1)	-106(1)	3419(1)	180(1)	22(1)
N(1)	24(1)	2228(1)	570(1)	20(1)
C(1)	809(1)	2687(1)	20(1)	21(1)
C(2)	1116(1)	3246(1)	-40(1)	27(1)
C(3)	1714(1)	3207(1)	-69(1)	34(1)
C(4)	2002(1)	2616(1)	-46(1)	34(1)
C(5)	1701(1)	2052(1)	14(1)	32(1)
C(6)	1104(1)	2086(1)	47(1)	26(1)
C(7)	-622(1)	2507(1)	-790(1)	20(1)
C(8)	-493(1)	2454(1)	-1323(1)	26(1)
C(9)	-1020(1)	2356(1)	-1965(1)	30(1)
C(10)	-1675(1)	2312(1)	-2080(1)	31(1)
C(11)	-1813(1)	2358(1)	-1554(1)	29(1)

C(12)	-1293(1)	2457(1)	-918(1)	24(1)
C(13)	-22(1)	2444(1)	1156(1)	21(1)
C(14)	-751(1)	2391(1)	1025(1)	22(1)
C(15)	-1164(1)	1865(1)	695(1)	29(1)
C(16)	-1833(1)	1850(1)	558(1)	35(1)
C(17)	-2102(1)	2353(1)	749(1)	35(1)
C(18)	-1697(1)	2878(1)	1078(1)	33(1)
C(19)	-1027(1)	2898(1)	1213(1)	26(1)
C(20)	514(1)	2112(1)	1819(1)	23(1)
C(21)	337(1)	1400(1)	1832(1)	28(1)
C(22)	507(1)	2493(1)	2378(1)	28(1)
C(23)	402(1)	2263(1)	2857(1)	42(1)
C(24)	1232(1)	2165(1)	1867(1)	29(1)
C(25)	1800(1)	1867(1)	2513(1)	43(1)
C(26)	2485(1)	1890(1)	2533(2)	54(1)
C(27)	2683(1)	2570(1)	2452(1)	49(1)
C(28)	2129(1)	2874(1)	1813(1)	40(1)
C(29)	1442(1)	2860(1)	1801(1)	30(1)
P(2)	10484(1)	10148(1)	10524(1)	20(1)
O(2)	10410(1)	10866(1)	10490(1)	27(1)
N(2)	10115(1)	9825(1)	9779(1)	22(1)
C(30)	11363(1)	9912(1)	10986(1)	26(1)
C(31)	11572(1)	9279(1)	11010(1)	30(1)
C(32)	12242(1)	9111(1)	11377(1)	43(1)
C(33)	12717(1)	9580(2)	11735(2)	64(1)
C(34)	12524(1)	10212(2)	11709(2)	73(1)
C(35)	11848(1)	10390(1)	11340(2)	49(1)
C(36)	10058(1)	9765(1)	10924(1)	20(1)
C(37)	10326(1)	9285(1)	11403(1)	29(1)
C(38)	9943(1)	9022(1)	11667(1)	35(1)
C(39)	9293(1)	9239(1)	11455(1)	33(1)
C(40)	9022(1)	9722(1)	10986(1)	27(1)
C(41)	9402(1)	9985(1)	10720(1)	25(1)
C(42)	10108(1)	10178(1)	9223(1)	21(1)
C(43)	10784(1)	10117(1)	9224(1)	24(1)
C(44)	11049(1)	10648(1)	9058(1)	32(1)
C(45)	11674(1)	10618(1)	9087(1)	41(1)

C(46)	12052(1)	10059(1)	9295(1)	43(1)
C(47)	11796(1)	9523(1)	9461(1)	36(1)
C(48)	11163(1)	9552(1)	9421(1)	27(1)
C(49)	9471(1)	9993(1)	8551(1)	21(1)
C(50)	9561(1)	9310(1)	8351(1)	24(1)
C(51)	9402(1)	10486(1)	8040(1)	27(1)
C(52)	9368(1)	10367(1)	7458(1)	38(1)
C(53)	8820(1)	10020(1)	8632(1)	25(1)
C(54)	8171(1)	9881(1)	7977(1)	34(1)
C(55)	7543(1)	9874(1)	8067(1)	42(1)
C(56)	7465(1)	10507(1)	8360(1)	42(1)
C(57)	8108(1)	10650(1)	9014(1)	35(1)
C(58)	8733(1)	10662(1)	8922(1)	27(1)
P(3)	4815(1)	1138(1)	9976(1)	18(1)
O(3)	4684(1)	486(1)	9662(1)	23(1)
N(3)	4800(1)	1703(1)	9466(1)	19(1)
C(59)	5631(1)	1203(1)	10714(1)	20(1)
C(60)	6209(1)	1363(1)	10680(1)	27(1)
C(61)	6840(1)	1353(1)	11252(1)	33(1)
C(62)	6895(1)	1182(1)	11853(1)	31(1)
C(63)	6325(1)	1019(1)	11889(1)	36(1)
C(64)	5696(1)	1025(1)	11327(1)	29(1)
C(65)	4229(1)	1314(1)	10278(1)	21(1)
C(66)	3818(1)	827(1)	10301(1)	26(1)
C(67)	3402(1)	943(1)	10577(1)	30(1)
C(68)	3399(1)	1544(1)	10839(1)	31(1)
C(69)	3807(1)	2037(1)	10811(1)	30(1)
C(70)	4219(1)	1924(1)	10536(1)	27(1)
C(71)	4388(1)	1600(1)	8743(1)	23(1)
C(72)	3627(1)	1583(1)	8509(1)	25(1)
C(73)	3332(1)	2005(1)	8769(1)	28(1)
C(74)	2641(1)	1998(1)	8536(1)	34(1)
C(75)	2224(1)	1565(1)	8042(1)	35(1)
C(76)	2518(1)	1136(1)	7802(1)	37(1)
C(77)	3218(1)	1142(1)	8044(1)	32(1)
C(78)	4570(1)	2095(1)	8338(1)	25(1)
C(79)	4282(1)	2759(1)	8329(1)	24(1)

C(80)	4282(1)	1821(1)	7644(1)	32(1)
C(81)	3886(1)	2103(1)	7080(1)	47(1)
C(82)	5367(1)	2144(1)	8656(1)	26(1)
C(83)	5595(1)	2600(1)	8277(1)	34(1)
C(84)	6361(1)	2670(1)	8629(1)	41(1)
C(85)	6716(1)	2021(1)	8740(1)	42(1)
C(86)	6491(1)	1568(1)	9114(1)	38(1)
C(87)	5720(1)	1494(1)	8748(1)	33(1)
P(4)	4568(1)	8661(1)	9798(1)	20(1)
O(4)	4827(1)	7984(1)	9934(1)	24(1)
N(4)	5108(1)	9158(1)	9741(1)	21(1)
C(88)	4446(1)	9027(1)	10443(1)	23(1)
C(89)	4998(1)	9302(1)	10996(1)	28(1)
C(90)	4917(1)	9544(1)	11516(1)	34(1)
C(91)	4294(1)	9514(1)	11486(1)	37(1)
C(92)	3741(1)	9247(1)	10936(1)	35(1)
C(93)	3819(1)	9007(1)	10422(1)	28(1)
C(94)	3755(1)	8693(1)	9056(1)	21(1)
C(95)	3413(1)	9279(1)	8830(1)	28(1)
C(96)	2798(1)	9301(1)	8256(1)	34(1)
C(97)	2519(1)	8744(1)	7893(1)	39(1)
C(98)	2858(1)	8158(1)	8112(1)	41(1)
C(99)	3472(1)	8131(1)	8687(1)	29(1)
C(100)	5451(1)	8937(1)	9372(1)	21(1)
C(101)	4997(1)	8986(1)	8622(1)	27(1)
C(102)	4581(1)	9519(1)	8330(1)	30(1)
C(103)	4187(1)	9564(1)	7644(1)	44(1)
C(104)	4191(1)	9069(2)	7244(1)	55(1)
C(105)	4593(1)	8535(2)	7526(1)	55(1)
C(106)	4989(1)	8486(1)	8214(1)	40(1)
C(107)	6147(1)	9296(1)	9618(1)	21(1)
C(108)	6027(1)	9982(1)	9352(1)	27(1)
C(109)	6539(1)	8902(1)	9364(1)	24(1)
C(110)	6687(1)	9044(1)	8897(1)	41(1)
C(111)	6541(1)	9322(1)	10396(1)	20(1)
C(112)	7243(1)	9636(1)	10657(1)	24(1)
C(113)	7614(1)	9695(1)	11416(1)	28(1)

C(114)	7689(1)	9037(1)	11741(1)	29(1)
C(115)	6995(1)	8733(1)	11495(1)	28(1)
C(116)	6618(1)	8668(1)	10735(1)	24(1)
P(5)	9858(1)	1825(1)	4923(1)	19(1)
O(5)	9798(1)	1153(1)	5125(1)	23(1)
N(5)	9598(1)	2369(1)	5267(1)	20(1)
C(117)	9393(1)	1912(1)	4033(1)	22(1)
C(118)	9191(1)	1356(1)	3637(1)	30(1)
C(119)	8839(1)	1414(1)	2952(1)	34(1)
C(120)	8685(1)	2014(1)	2656(1)	35(1)
C(121)	8884(1)	2565(1)	3046(1)	33(1)
C(122)	9234(1)	2517(1)	3732(1)	25(1)
C(123)	10723(1)	2028(1)	5154(1)	24(1)
C(124)	10965(1)	1995(1)	4703(1)	38(1)
C(125)	11641(1)	2093(2)	4909(2)	52(1)
C(126)	12088(1)	2225(1)	5570(2)	49(1)
C(127)	11858(1)	2251(1)	6025(1)	45(1)
C(128)	11182(1)	2160(1)	5823(1)	35(1)
C(129)	9313(1)	2191(1)	5696(1)	22(1)
C(130)	9818(1)	2313(1)	6423(1)	22(1)
C(131)	10225(1)	2861(1)	6633(1)	27(1)
C(132)	10673(1)	2958(1)	7305(1)	32(1)
C(133)	10720(1)	2515(1)	7771(1)	33(1)
C(134)	10330(1)	1962(1)	7567(1)	38(1)
C(135)	9883(1)	1862(1)	6896(1)	31(1)
C(136)	8602(1)	2510(1)	5474(1)	24(1)
C(137)	8687(1)	3235(1)	5649(1)	32(1)
C(138)	8288(1)	2147(1)	5828(1)	34(1)
C(139)	8046(1)	2394(2)	6199(1)	55(1)
C(140)	8138(1)	2433(1)	4701(1)	27(1)
C(141)	7435(1)	2738(1)	4444(1)	42(1)
C(142)	7014(1)	2696(1)	3693(1)	53(1)
C(143)	6932(1)	1999(1)	3445(1)	46(1)
C(144)	7630(1)	1692(1)	3701(1)	36(1)
C(145)	8044(1)	1731(1)	4458(1)	27(1)
P(6)	10247(1)	9399(1)	4945(1)	22(1)
O(6)	10179(1)	8682(1)	4925(1)	29(1)

N(6)	9641(1)	9746(1)	5041(1)	22(1)
C(146)	10146(1)	9732(1)	4177(1)	23(1)
C(147)	9535(1)	9616(1)	3602(1)	28(1)
C(148)	9441(1)	9818(1)	2992(1)	31(1)
C(149)	9949(1)	10144(1)	2943(1)	36(1)
C(150)	10554(1)	10274(1)	3507(1)	42(1)
C(151)	10656(1)	10060(1)	4123(1)	36(1)
C(152)	11079(1)	9646(1)	5571(1)	25(1)
C(153)	11582(1)	9185(1)	5907(1)	36(1)
C(154)	12230(1)	9383(1)	6365(1)	52(1)
C(155)	12377(1)	10026(2)	6487(2)	57(1)
C(156)	11882(1)	10489(1)	6163(1)	44(1)
C(157)	11230(1)	10301(1)	5709(1)	31(1)
C(158)	9414(1)	9418(1)	5466(1)	24(1)
C(159)	9920(1)	9494(1)	6208(1)	26(1)
C(160)	10271(1)	10067(1)	6469(1)	28(1)
C(161)	10730(1)	10111(1)	7145(1)	37(1)
C(162)	10846(1)	9586(2)	7556(1)	45(1)
C(163)	10504(1)	9018(1)	7298(1)	42(1)
C(164)	10048(1)	8969(1)	6629(1)	35(1)
C(165)	8677(1)	9610(1)	5285(1)	26(1)
C(166)	8676(1)	10292(1)	5541(1)	27(1)
C(167)	8441(1)	9118(1)	5615(1)	37(1)
C(168)	8250(2)	9221(2)	6059(1)	54(1)
C(169)	8204(1)	9591(1)	4514(1)	32(1)
C(170)	7464(1)	9752(2)	4306(1)	48(1)
C(171)	7007(1)	9763(2)	3548(1)	58(1)
C(172)	7051(2)	9122(2)	3243(1)	62(1)
C(173)	7784(2)	8976(2)	3440(1)	51(1)
C(174)	8227(1)	8956(1)	4188(1)	41(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{29}H_{34}NOP$

P(1)-O(1)	1.4897(13)
P(1)-N(1)	1.6401(16)
P(1)-C(1)	1.7961(19)

P(1)-C(7)	1.8040(19)
N(1)-C(13)	1.472(2)
N(1)-H(1N)	0.8800
C(1)-C(2)	1.386(3)
C(1)-C(6)	1.397(3)
C(2)-C(3)	1.386(3)
C(2)-H(2A)	0.9500
C(3)-C(4)	1.372(3)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.391(3)
C(4)-H(4A)	0.9500
C(5)-C(6)	1.387(3)
C(5)-H(5A)	0.9500
C(6)-H(6A)	0.9500
C(7)-C(8)	1.394(3)
C(7)-C(12)	1.400(3)
C(8)-C(9)	1.390(3)
C(8)-H(8A)	0.9500
C(9)-C(10)	1.374(3)
C(9)-H(9A)	0.9500
C(10)-C(11)	1.392(3)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.377(3)
C(11)-H(11A)	0.9500
C(12)-H(12A)	0.9500
C(13)-C(14)	1.526(3)
C(13)-C(20)	1.571(3)
C(13)-H(13A)	1.0000
C(14)-C(15)	1.392(3)
C(14)-C(19)	1.392(3)
C(15)-C(16)	1.384(3)
C(15)-H(15A)	0.9500
C(16)-C(17)	1.379(3)
C(16)-H(16A)	0.9500
C(17)-C(18)	1.382(3)
C(17)-H(17A)	0.9500
C(18)-C(19)	1.390(3)

C(18)-H(18A)	0.9500
C(19)-H(19A)	0.9500
C(20)-C(22)	1.516(3)
C(20)-C(21)	1.529(3)
C(20)-C(24)	1.572(3)
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(22)-C(23)	1.325(3)
C(22)-H(22A)	0.9500
C(23)-H(23A)	0.9500
C(23)-H(23B)	0.9500
C(24)-C(29)	1.541(3)
C(24)-C(25)	1.542(3)
C(24)-H(24A)	1.0000
C(25)-C(26)	1.524(4)
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900
C(26)-C(27)	1.515(4)
C(26)-H(26A)	0.9900
C(26)-H(26B)	0.9900
C(27)-C(28)	1.527(4)
C(27)-H(27A)	0.9900
C(27)-H(27B)	0.9900
C(28)-C(29)	1.537(3)
C(28)-H(28A)	0.9900
C(28)-H(28B)	0.9900
C(29)-H(29A)	0.9900
C(29)-H(29B)	0.9900
P(2)-O(2)	1.4899(14)
P(2)-N(2)	1.6415(17)
P(2)-C(30)	1.804(2)
P(2)-C(36)	1.8048(19)
N(2)-C(42)	1.467(2)
N(2)-H(2N)	0.8800
C(30)-C(31)	1.382(3)
C(30)-C(35)	1.404(3)

C(31)-C(32)	1.372(3)
C(31)-H(31A)	0.9500
C(32)-C(33)	1.381(4)
C(32)-H(32A)	0.9500
C(33)-C(34)	1.368(5)
C(33)-H(33A)	0.9500
C(34)-C(35)	1.387(4)
C(34)-H(34A)	0.9500
C(35)-H(35A)	0.9500
C(36)-C(37)	1.386(3)
C(36)-C(41)	1.393(3)
C(37)-C(38)	1.387(3)
C(37)-H(37A)	0.9500
C(38)-C(39)	1.376(3)
C(38)-H(38A)	0.9500
C(39)-C(40)	1.377(3)
C(39)-H(39A)	0.9500
C(40)-C(41)	1.385(3)
C(40)-H(40A)	0.9500
C(41)-H(41A)	0.9500
C(42)-C(43)	1.529(3)
C(42)-C(49)	1.564(3)
C(42)-H(42A)	1.0000
C(43)-C(48)	1.387(3)
C(43)-C(44)	1.389(3)
C(44)-C(45)	1.383(3)
C(44)-H(44A)	0.9500
C(45)-C(46)	1.377(4)
C(45)-H(45A)	0.9500
C(46)-C(47)	1.386(4)
C(46)-H(46A)	0.9500
C(47)-C(48)	1.388(3)
C(47)-H(47A)	0.9500
C(48)-H(48A)	0.9500
C(49)-C(51)	1.505(3)
C(49)-C(50)	1.529(3)
C(49)-C(53)	1.570(3)

C(50)-H(50A)	0.9800
C(50)-H(50B)	0.9800
C(50)-H(50C)	0.9800
C(51)-C(52)	1.328(3)
C(51)-H(51A)	0.9500
C(52)-H(52A)	0.9500
C(52)-H(52B)	0.9500
C(53)-C(54)	1.535(3)
C(53)-C(58)	1.540(3)
C(53)-H(53A)	1.0000
C(54)-C(55)	1.528(3)
C(54)-H(54A)	0.9900
C(54)-H(54B)	0.9900
C(55)-C(56)	1.522(3)
C(55)-H(55A)	0.9900
C(55)-H(55B)	0.9900
C(56)-C(57)	1.530(3)
C(56)-H(56A)	0.9900
C(56)-H(56B)	0.9900
C(57)-C(58)	1.525(3)
C(57)-H(57A)	0.9900
C(57)-H(57B)	0.9900
C(58)-H(58A)	0.9900
C(58)-H(58B)	0.9900
P(3)-O(3)	1.4903(14)
P(3)-N(3)	1.6441(16)
P(3)-C(59)	1.8039(19)
P(3)-C(65)	1.807(2)
N(3)-C(71)	1.476(2)
N(3)-H(3N)	0.8800
C(59)-C(60)	1.385(3)
C(59)-C(64)	1.397(3)
C(60)-C(61)	1.393(3)
C(60)-H(60A)	0.9500
C(61)-C(62)	1.376(3)
C(61)-H(61A)	0.9500
C(62)-C(63)	1.370(3)

C(62)-H(62A)	0.9500
C(63)-C(64)	1.380(3)
C(63)-H(63A)	0.9500
C(64)-H(64A)	0.9500
C(65)-C(66)	1.385(3)
C(65)-C(70)	1.400(3)
C(66)-C(67)	1.388(3)
C(66)-H(66A)	0.9500
C(67)-C(68)	1.381(3)
C(67)-H(67A)	0.9500
C(68)-C(69)	1.394(3)
C(68)-H(68A)	0.9500
C(69)-C(70)	1.376(3)
C(69)-H(69A)	0.9500
C(70)-H(70A)	0.9500
C(71)-C(72)	1.531(3)
C(71)-C(78)	1.569(3)
C(71)-H(71A)	1.0000
C(72)-C(77)	1.368(3)
C(72)-C(73)	1.395(3)
C(73)-C(74)	1.381(3)
C(73)-H(73A)	0.9500
C(74)-C(75)	1.394(3)
C(74)-H(74A)	0.9500
C(75)-C(76)	1.373(3)
C(75)-H(75A)	0.9500
C(76)-C(77)	1.398(3)
C(76)-H(76A)	0.9500
C(77)-H(77A)	0.9500
C(78)-C(80)	1.513(3)
C(78)-C(79)	1.514(3)
C(78)-C(82)	1.580(3)
C(79)-H(79A)	0.9800
C(79)-H(79B)	0.9800
C(79)-H(79C)	0.9800
C(80)-C(81)	1.303(3)
C(80)-H(80A)	0.9500

C(81)-H(81A)	0.9500
C(81)-H(81B)	0.9500
C(82)-C(87)	1.525(3)
C(82)-C(83)	1.536(3)
C(82)-H(82A)	1.0000
C(83)-C(84)	1.517(3)
C(83)-H(83A)	0.9900
C(83)-H(83B)	0.9900
C(84)-C(85)	1.518(3)
C(84)-H(84A)	0.9900
C(84)-H(84B)	0.9900
C(85)-C(86)	1.517(3)
C(85)-H(85A)	0.9900
C(85)-H(85B)	0.9900
C(86)-C(87)	1.527(3)
C(86)-H(86A)	0.9900
C(86)-H(86B)	0.9900
C(87)-H(87A)	0.9900
C(87)-H(87B)	0.9900
P(4)-O(4)	1.4894(14)
P(4)-N(4)	1.6464(16)
P(4)-C(94)	1.8016(19)
P(4)-C(88)	1.804(2)
N(4)-C(100)	1.474(2)
N(4)-H(4N)	0.8800
C(88)-C(93)	1.391(3)
C(88)-C(89)	1.398(3)
C(89)-C(90)	1.389(3)
C(89)-H(89A)	0.9500
C(90)-C(91)	1.376(3)
C(90)-H(90A)	0.9500
C(91)-C(92)	1.389(3)
C(91)-H(91A)	0.9500
C(92)-C(93)	1.374(3)
C(92)-H(92A)	0.9500
C(93)-H(93A)	0.9500
C(94)-C(95)	1.391(3)

C(94)-C(99)	1.398(3)
C(95)-C(96)	1.376(3)
C(95)-H(95A)	0.9500
C(96)-C(97)	1.381(4)
C(96)-H(96A)	0.9500
C(97)-C(98)	1.389(4)
C(97)-H(97A)	0.9500
C(98)-C(99)	1.376(3)
C(98)-H(98A)	0.9500
C(99)-H(99A)	0.9500
C(100)-C(101)	1.523(3)
C(100)-C(107)	1.573(3)
C(100)-H(10B)	1.0000
C(101)-C(102)	1.389(3)
C(101)-C(106)	1.391(3)
C(102)-C(103)	1.388(3)
C(102)-H(10C)	0.9500
C(103)-C(104)	1.378(4)
C(103)-H(10D)	0.9500
C(104)-C(105)	1.375(4)
C(104)-H(10E)	0.9500
C(105)-C(106)	1.394(3)
C(105)-H(10F)	0.9500
C(106)-H(10G)	0.9500
C(107)-C(109)	1.513(3)
C(107)-C(108)	1.514(3)
C(107)-C(111)	1.568(3)
C(108)-H(10H)	0.9800
C(108)-H(10I)	0.9800
C(108)-H(10J)	0.9800
C(109)-C(110)	1.305(3)
C(109)-H(10K)	0.9500
C(110)-H(11B)	0.9500
C(110)-H(11C)	0.9500
C(111)-C(116)	1.528(3)
C(111)-C(112)	1.539(3)
C(111)-H(11E)	1.0000

C(112)-C(113)	1.532(3)
C(112)-H(11F)	0.9900
C(112)-H(11G)	0.9900
C(113)-C(114)	1.522(3)
C(113)-H(11H)	0.9900
C(113)-H(11I)	0.9900
C(114)-C(115)	1.519(3)
C(114)-H(11J)	0.9900
C(114)-H(11K)	0.9900
C(115)-C(116)	1.536(3)
C(115)-H(11L)	0.9900
C(115)-H(11M)	0.9900
C(116)-H(11N)	0.9900
C(116)-H(11O)	0.9900
P(5)-O(5)	1.4915(14)
P(5)-N(5)	1.6398(16)
P(5)-C(117)	1.8002(19)
P(5)-C(123)	1.805(2)
N(5)-C(129)	1.463(2)
N(5)-H(5N)	0.8800
C(117)-C(122)	1.389(3)
C(117)-C(118)	1.398(3)
C(118)-C(119)	1.384(3)
C(118)-H(11P)	0.9500
C(119)-C(120)	1.376(3)
C(119)-H(11Q)	0.9500
C(120)-C(121)	1.382(3)
C(120)-H(12B)	0.9500
C(121)-C(122)	1.383(3)
C(121)-H(12C)	0.9500
C(122)-H(12D)	0.9500
C(123)-C(124)	1.391(3)
C(123)-C(128)	1.403(3)
C(124)-C(125)	1.375(3)
C(124)-H(12E)	0.9500
C(125)-C(126)	1.385(4)
C(125)-H(12F)	0.9500

C(126)-C(127)	1.379(4)
C(126)-H(12G)	0.9500
C(127)-C(128)	1.374(3)
C(127)-H(12H)	0.9500
C(128)-H(12I)	0.9500
C(129)-C(130)	1.521(3)
C(129)-C(136)	1.574(3)
C(129)-H(12J)	1.0000
C(130)-C(135)	1.386(3)
C(130)-C(131)	1.390(3)
C(131)-C(132)	1.391(3)
C(131)-H(13B)	0.9500
C(132)-C(133)	1.375(3)
C(132)-H(13C)	0.9500
C(133)-C(134)	1.378(4)
C(133)-H(13D)	0.9500
C(134)-C(135)	1.391(3)
C(134)-H(13E)	0.9500
C(135)-H(13F)	0.9500
C(136)-C(138)	1.515(3)
C(136)-C(137)	1.538(3)
C(136)-C(140)	1.575(3)
C(137)-H(13G)	0.9800
C(137)-H(13H)	0.9800
C(137)-H(13I)	0.9800
C(138)-C(139)	1.321(4)
C(138)-H(13J)	0.9500
C(139)-H(13K)	0.9500
C(139)-H(13L)	0.9500
C(140)-C(145)	1.532(3)
C(140)-C(141)	1.534(3)
C(140)-H(14A)	1.0000
C(141)-C(142)	1.519(3)
C(141)-H(14B)	0.9900
C(141)-H(14C)	0.9900
C(142)-C(143)	1.528(4)
C(142)-H(14D)	0.9900

C(142)-H(14E)	0.9900
C(143)-C(144)	1.526(3)
C(143)-H(14F)	0.9900
C(143)-H(14G)	0.9900
C(144)-C(145)	1.529(3)
C(144)-H(14H)	0.9900
C(144)-H(14I)	0.9900
C(145)-H(14J)	0.9900
C(145)-H(14K)	0.9900
P(6)-O(6)	1.4880(15)
P(6)-N(6)	1.6515(17)
P(6)-C(152)	1.798(2)
P(6)-C(146)	1.806(2)
N(6)-C(158)	1.472(2)
N(6)-H(6N)	0.8800
C(146)-C(151)	1.392(3)
C(146)-C(147)	1.393(3)
C(147)-C(148)	1.380(3)
C(147)-H(14L)	0.9500
C(148)-C(149)	1.381(3)
C(148)-H(14M)	0.9500
C(149)-C(150)	1.378(3)
C(149)-H(14N)	0.9500
C(150)-C(151)	1.396(3)
C(150)-H(15B)	0.9500
C(151)-H(15C)	0.9500
C(152)-C(153)	1.392(3)
C(152)-C(157)	1.395(3)
C(153)-C(154)	1.386(4)
C(153)-H(15D)	0.9500
C(154)-C(155)	1.366(4)
C(154)-H(15E)	0.9500
C(155)-C(156)	1.382(4)
C(155)-H(15F)	0.9500
C(156)-C(157)	1.383(3)
C(156)-H(15G)	0.9500
C(157)-H(15H)	0.9500

C(158)-C(159)	1.534(3)
C(158)-C(165)	1.558(3)
C(158)-H(15I)	1.0000
C(159)-C(164)	1.388(3)
C(159)-C(160)	1.389(3)
C(160)-C(161)	1.392(3)
C(160)-H(16B)	0.9500
C(161)-C(162)	1.380(4)
C(161)-H(16C)	0.9500
C(162)-C(163)	1.371(4)
C(162)-H(16D)	0.9500
C(163)-C(164)	1.379(3)
C(163)-H(16E)	0.9500
C(164)-H(16F)	0.9500
C(165)-C(167)	1.512(3)
C(165)-C(166)	1.526(3)
C(165)-C(169)	1.567(3)
C(166)-H(16G)	0.9800
C(166)-H(16H)	0.9800
C(166)-H(16I)	0.9800
C(167)-C(168)	1.306(4)
C(167)-H(16J)	0.9500
C(168)-H(16K)	0.9500
C(168)-H(16L)	0.9500
C(169)-C(174)	1.526(3)
C(169)-C(170)	1.534(3)
C(169)-H(16N)	1.0000
C(170)-C(171)	1.536(4)
C(170)-H(17B)	0.9900
C(170)-H(17C)	0.9900
C(171)-C(172)	1.526(5)
C(171)-H(17D)	0.9900
C(171)-H(17E)	0.9900
C(172)-C(173)	1.517(4)
C(172)-H(17F)	0.9900
C(172)-H(17G)	0.9900
C(173)-C(174)	1.514(3)

C(173)-H(17H)	0.9900
C(173)-H(17I)	0.9900
C(174)-H(17J)	0.9900
C(174)-H(17K)	0.9900
O(1)-P(1)-N(1)	111.29(8)
O(1)-P(1)-C(1)	111.77(9)
N(1)-P(1)-C(1)	108.90(9)
O(1)-P(1)-C(7)	110.71(8)
N(1)-P(1)-C(7)	108.61(8)
C(1)-P(1)-C(7)	105.33(9)
C(13)-N(1)-P(1)	121.44(13)
C(13)-N(1)-H(1N)	119.3
P(1)-N(1)-H(1N)	119.3
C(2)-C(1)-C(6)	119.69(18)
C(2)-C(1)-P(1)	119.25(16)
C(6)-C(1)-P(1)	121.02(15)
C(3)-C(2)-C(1)	120.0(2)
C(3)-C(2)-H(2A)	120.0
C(1)-C(2)-H(2A)	120.0
C(4)-C(3)-C(2)	120.4(2)
C(4)-C(3)-H(3A)	119.8
C(2)-C(3)-H(3A)	119.8
C(3)-C(4)-C(5)	120.2(2)
C(3)-C(4)-H(4A)	119.9
C(5)-C(4)-H(4A)	119.9
C(6)-C(5)-C(4)	119.9(2)
C(6)-C(5)-H(5A)	120.1
C(4)-C(5)-H(5A)	120.1
C(5)-C(6)-C(1)	119.80(19)
C(5)-C(6)-H(6A)	120.1
C(1)-C(6)-H(6A)	120.1
C(8)-C(7)-C(12)	118.51(18)
C(8)-C(7)-P(1)	122.49(15)
C(12)-C(7)-P(1)	118.41(15)
C(9)-C(8)-C(7)	120.74(19)
C(9)-C(8)-H(8A)	119.6
C(7)-C(8)-H(8A)	119.6

C(10)-C(9)-C(8)	119.85(19)
C(10)-C(9)-H(9A)	120.1
C(8)-C(9)-H(9A)	120.1
C(9)-C(10)-C(11)	120.2(2)
C(9)-C(10)-H(10A)	119.9
C(11)-C(10)-H(10A)	119.9
C(12)-C(11)-C(10)	120.10(19)
C(12)-C(11)-H(11A)	119.9
C(10)-C(11)-H(11A)	119.9
C(11)-C(12)-C(7)	120.58(18)
C(11)-C(12)-H(12A)	119.7
C(7)-C(12)-H(12A)	119.7
N(1)-C(13)-C(14)	110.40(15)
N(1)-C(13)-C(20)	113.24(15)
C(14)-C(13)-C(20)	114.06(15)
N(1)-C(13)-H(13A)	106.2
C(14)-C(13)-H(13A)	106.2
C(20)-C(13)-H(13A)	106.2
C(15)-C(14)-C(19)	118.30(19)
C(15)-C(14)-C(13)	122.41(18)
C(19)-C(14)-C(13)	119.21(17)
C(16)-C(15)-C(14)	120.7(2)
C(16)-C(15)-H(15A)	119.7
C(14)-C(15)-H(15A)	119.7
C(17)-C(16)-C(15)	120.6(2)
C(17)-C(16)-H(16A)	119.7
C(15)-C(16)-H(16A)	119.7
C(16)-C(17)-C(18)	119.4(2)
C(16)-C(17)-H(17A)	120.3
C(18)-C(17)-H(17A)	120.3
C(17)-C(18)-C(19)	120.1(2)
C(17)-C(18)-H(18A)	119.9
C(19)-C(18)-H(18A)	119.9
C(18)-C(19)-C(14)	120.8(2)
C(18)-C(19)-H(19A)	119.6
C(14)-C(19)-H(19A)	119.6
C(22)-C(20)-C(21)	111.77(17)

C(22)-C(20)-C(13)	106.16(16)
C(21)-C(20)-C(13)	110.65(16)
C(22)-C(20)-C(24)	109.85(16)
C(21)-C(20)-C(24)	109.70(16)
C(13)-C(20)-C(24)	108.63(16)
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(23)-C(22)-C(20)	127.0(2)
C(23)-C(22)-H(22A)	116.5
C(20)-C(22)-H(22A)	116.5
C(22)-C(23)-H(23A)	120.0
C(22)-C(23)-H(23B)	120.0
H(23A)-C(23)-H(23B)	120.0
C(29)-C(24)-C(25)	108.45(18)
C(29)-C(24)-C(20)	114.43(17)
C(25)-C(24)-C(20)	112.66(18)
C(29)-C(24)-H(24A)	107.0
C(25)-C(24)-H(24A)	107.0
C(20)-C(24)-H(24A)	107.0
C(26)-C(25)-C(24)	111.9(2)
C(26)-C(25)-H(25A)	109.2
C(24)-C(25)-H(25A)	109.2
C(26)-C(25)-H(25B)	109.2
C(24)-C(25)-H(25B)	109.2
H(25A)-C(25)-H(25B)	107.9
C(27)-C(26)-C(25)	112.4(2)
C(27)-C(26)-H(26A)	109.1
C(25)-C(26)-H(26A)	109.1
C(27)-C(26)-H(26B)	109.1
C(25)-C(26)-H(26B)	109.1
H(26A)-C(26)-H(26B)	107.9
C(26)-C(27)-C(28)	110.3(2)
C(26)-C(27)-H(27A)	109.6

C(28)-C(27)-H(27A)	109.6
C(26)-C(27)-H(27B)	109.6
C(28)-C(27)-H(27B)	109.6
H(27A)-C(27)-H(27B)	108.1
C(27)-C(28)-C(29)	110.9(2)
C(27)-C(28)-H(28A)	109.5
C(29)-C(28)-H(28A)	109.5
C(27)-C(28)-H(28B)	109.5
C(29)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	108.0
C(28)-C(29)-C(24)	111.82(18)
C(28)-C(29)-H(29A)	109.3
C(24)-C(29)-H(29A)	109.3
C(28)-C(29)-H(29B)	109.3
C(24)-C(29)-H(29B)	109.3
H(29A)-C(29)-H(29B)	107.9
O(2)-P(2)-N(2)	111.27(8)
O(2)-P(2)-C(30)	111.24(9)
N(2)-P(2)-C(30)	111.14(9)
O(2)-P(2)-C(36)	112.89(8)
N(2)-P(2)-C(36)	103.32(9)
C(30)-P(2)-C(36)	106.65(9)
C(42)-N(2)-P(2)	119.67(13)
C(42)-N(2)-H(2N)	120.2
P(2)-N(2)-H(2N)	120.2
C(31)-C(30)-C(35)	119.2(2)
C(31)-C(30)-P(2)	122.37(16)
C(35)-C(30)-P(2)	118.43(18)
C(32)-C(31)-C(30)	121.1(2)
C(32)-C(31)-H(31A)	119.4
C(30)-C(31)-H(31A)	119.4
C(31)-C(32)-C(33)	119.6(3)
C(31)-C(32)-H(32A)	120.2
C(33)-C(32)-H(32A)	120.2
C(34)-C(33)-C(32)	120.3(3)
C(34)-C(33)-H(33A)	119.9
C(32)-C(33)-H(33A)	119.9

C(33)-C(34)-C(35)	120.9(3)
C(33)-C(34)-H(34A)	119.6
C(35)-C(34)-H(34A)	119.6
C(34)-C(35)-C(30)	118.9(3)
C(34)-C(35)-H(35A)	120.6
C(30)-C(35)-H(35A)	120.6
C(37)-C(36)-C(41)	118.90(18)
C(37)-C(36)-P(2)	125.82(15)
C(41)-C(36)-P(2)	115.28(15)
C(36)-C(37)-C(38)	120.3(2)
C(36)-C(37)-H(37A)	119.8
C(38)-C(37)-H(37A)	119.8
C(39)-C(38)-C(37)	120.2(2)
C(39)-C(38)-H(38A)	119.9
C(37)-C(38)-H(38A)	119.9
C(38)-C(39)-C(40)	120.21(19)
C(38)-C(39)-H(39A)	119.9
C(40)-C(39)-H(39A)	119.9
C(39)-C(40)-C(41)	119.8(2)
C(39)-C(40)-H(40A)	120.1
C(41)-C(40)-H(40A)	120.1
C(40)-C(41)-C(36)	120.5(2)
C(40)-C(41)-H(41A)	119.7
C(36)-C(41)-H(41A)	119.7
N(2)-C(42)-C(43)	111.80(16)
N(2)-C(42)-C(49)	110.85(15)
C(43)-C(42)-C(49)	114.71(15)
N(2)-C(42)-H(42A)	106.3
C(43)-C(42)-H(42A)	106.3
C(49)-C(42)-H(42A)	106.3
C(48)-C(43)-C(44)	118.4(2)
C(48)-C(43)-C(42)	121.72(18)
C(44)-C(43)-C(42)	119.75(19)
C(45)-C(44)-C(43)	121.2(2)
C(45)-C(44)-H(44A)	119.4
C(43)-C(44)-H(44A)	119.4
C(46)-C(45)-C(44)	120.0(2)

C(46)-C(45)-H(45A)	120.0
C(44)-C(45)-H(45A)	120.0
C(45)-C(46)-C(47)	119.7(2)
C(45)-C(46)-H(46A)	120.2
C(47)-C(46)-H(46A)	120.2
C(46)-C(47)-C(48)	120.2(2)
C(46)-C(47)-H(47A)	119.9
C(48)-C(47)-H(47A)	119.9
C(43)-C(48)-C(47)	120.6(2)
C(43)-C(48)-H(48A)	119.7
C(47)-C(48)-H(48A)	119.7
C(51)-C(49)-C(50)	111.47(16)
C(51)-C(49)-C(42)	107.72(16)
C(50)-C(49)-C(42)	109.28(15)
C(51)-C(49)-C(53)	108.81(16)
C(50)-C(49)-C(53)	109.77(15)
C(42)-C(49)-C(53)	109.75(15)
C(49)-C(50)-H(50A)	109.5
C(49)-C(50)-H(50B)	109.5
H(50A)-C(50)-H(50B)	109.5
C(49)-C(50)-H(50C)	109.5
H(50A)-C(50)-H(50C)	109.5
H(50B)-C(50)-H(50C)	109.5
C(52)-C(51)-C(49)	126.7(2)
C(52)-C(51)-H(51A)	116.7
C(49)-C(51)-H(51A)	116.7
C(51)-C(52)-H(52A)	120.0
C(51)-C(52)-H(52B)	120.0
H(52A)-C(52)-H(52B)	120.0
C(54)-C(53)-C(58)	109.03(17)
C(54)-C(53)-C(49)	112.18(16)
C(58)-C(53)-C(49)	113.92(16)
C(54)-C(53)-H(53A)	107.1
C(58)-C(53)-H(53A)	107.1
C(49)-C(53)-H(53A)	107.1
C(55)-C(54)-C(53)	111.85(19)
C(55)-C(54)-H(54A)	109.2

C(53)-C(54)-H(54A)	109.2
C(55)-C(54)-H(54B)	109.2
C(53)-C(54)-H(54B)	109.2
H(54A)-C(54)-H(54B)	107.9
C(56)-C(55)-C(54)	111.6(2)
C(56)-C(55)-H(55A)	109.3
C(54)-C(55)-H(55A)	109.3
C(56)-C(55)-H(55B)	109.3
C(54)-C(55)-H(55B)	109.3
H(55A)-C(55)-H(55B)	108.0
C(55)-C(56)-C(57)	110.1(2)
C(55)-C(56)-H(56A)	109.6
C(57)-C(56)-H(56A)	109.6
C(55)-C(56)-H(56B)	109.6
C(57)-C(56)-H(56B)	109.6
H(56A)-C(56)-H(56B)	108.2
C(58)-C(57)-C(56)	111.45(19)
C(58)-C(57)-H(57A)	109.3
C(56)-C(57)-H(57A)	109.3
C(58)-C(57)-H(57B)	109.3
C(56)-C(57)-H(57B)	109.3
H(57A)-C(57)-H(57B)	108.0
C(57)-C(58)-C(53)	111.63(17)
C(57)-C(58)-H(58A)	109.3
C(53)-C(58)-H(58A)	109.3
C(57)-C(58)-H(58B)	109.3
C(53)-C(58)-H(58B)	109.3
H(58A)-C(58)-H(58B)	108.0
O(3)-P(3)-N(3)	111.43(8)
O(3)-P(3)-C(59)	113.29(8)
N(3)-P(3)-C(59)	106.09(8)
O(3)-P(3)-C(65)	111.00(8)
N(3)-P(3)-C(65)	111.62(8)
C(59)-P(3)-C(65)	103.05(9)
C(71)-N(3)-P(3)	119.08(12)
C(71)-N(3)-H(3N)	120.5
P(3)-N(3)-H(3N)	120.5

C(60)-C(59)-C(64)	118.76(18)
C(60)-C(59)-P(3)	121.52(15)
C(64)-C(59)-P(3)	119.40(15)
C(59)-C(60)-C(61)	120.0(2)
C(59)-C(60)-H(60A)	120.0
C(61)-C(60)-H(60A)	120.0
C(62)-C(61)-C(60)	120.4(2)
C(62)-C(61)-H(61A)	119.8
C(60)-C(61)-H(61A)	119.8
C(63)-C(62)-C(61)	119.9(2)
C(63)-C(62)-H(62A)	120.1
C(61)-C(62)-H(62A)	120.1
C(62)-C(63)-C(64)	120.5(2)
C(62)-C(63)-H(63A)	119.7
C(64)-C(63)-H(63A)	119.7
C(63)-C(64)-C(59)	120.4(2)
C(63)-C(64)-H(64A)	119.8
C(59)-C(64)-H(64A)	119.8
C(66)-C(65)-C(70)	119.26(18)
C(66)-C(65)-P(3)	119.92(15)
C(70)-C(65)-P(3)	120.64(15)
C(65)-C(66)-C(67)	120.52(19)
C(65)-C(66)-H(66A)	119.7
C(67)-C(66)-H(66A)	119.7
C(68)-C(67)-C(66)	120.12(19)
C(68)-C(67)-H(67A)	119.9
C(66)-C(67)-H(67A)	119.9
C(67)-C(68)-C(69)	119.6(2)
C(67)-C(68)-H(68A)	120.2
C(69)-C(68)-H(68A)	120.2
C(70)-C(69)-C(68)	120.5(2)
C(70)-C(69)-H(69A)	119.8
C(68)-C(69)-H(69A)	119.8
C(69)-C(70)-C(65)	120.06(19)
C(69)-C(70)-H(70A)	120.0
C(65)-C(70)-H(70A)	120.0
N(3)-C(71)-C(72)	112.62(16)

N(3)-C(71)-C(78)	111.92(15)
C(72)-C(71)-C(78)	112.36(16)
N(3)-C(71)-H(71A)	106.5
C(72)-C(71)-H(71A)	106.5
C(78)-C(71)-H(71A)	106.5
C(77)-C(72)-C(73)	118.25(19)
C(77)-C(72)-C(71)	120.26(18)
C(73)-C(72)-C(71)	121.47(18)
C(74)-C(73)-C(72)	120.7(2)
C(74)-C(73)-H(73A)	119.6
C(72)-C(73)-H(73A)	119.6
C(73)-C(74)-C(75)	120.7(2)
C(73)-C(74)-H(74A)	119.6
C(75)-C(74)-H(74A)	119.6
C(76)-C(75)-C(74)	118.4(2)
C(76)-C(75)-H(75A)	120.8
C(74)-C(75)-H(75A)	120.8
C(75)-C(76)-C(77)	120.6(2)
C(75)-C(76)-H(76A)	119.7
C(77)-C(76)-H(76A)	119.7
C(72)-C(77)-C(76)	121.2(2)
C(72)-C(77)-H(77A)	119.4
C(76)-C(77)-H(77A)	119.4
C(80)-C(78)-C(79)	111.29(17)
C(80)-C(78)-C(71)	106.44(16)
C(79)-C(78)-C(71)	111.24(16)
C(80)-C(78)-C(82)	108.84(17)
C(79)-C(78)-C(82)	109.41(16)
C(71)-C(78)-C(82)	109.55(16)
C(78)-C(79)-H(79A)	109.5
C(78)-C(79)-H(79B)	109.5
H(79A)-C(79)-H(79B)	109.5
C(78)-C(79)-H(79C)	109.5
H(79A)-C(79)-H(79C)	109.5
H(79B)-C(79)-H(79C)	109.5
C(81)-C(80)-C(78)	128.4(2)
C(81)-C(80)-H(80A)	115.8

C(78)-C(80)-H(80A)	115.8
C(80)-C(81)-H(81A)	120.0
C(80)-C(81)-H(81B)	120.0
H(81A)-C(81)-H(81B)	120.0
C(87)-C(82)-C(83)	108.74(17)
C(87)-C(82)-C(78)	114.06(17)
C(83)-C(82)-C(78)	113.34(17)
C(87)-C(82)-H(82A)	106.7
C(83)-C(82)-H(82A)	106.7
C(78)-C(82)-H(82A)	106.7
C(84)-C(83)-C(82)	111.31(19)
C(84)-C(83)-H(83A)	109.4
C(82)-C(83)-H(83A)	109.4
C(84)-C(83)-H(83B)	109.4
C(82)-C(83)-H(83B)	109.4
H(83A)-C(83)-H(83B)	108.0
C(83)-C(84)-C(85)	112.2(2)
C(83)-C(84)-H(84A)	109.2
C(85)-C(84)-H(84A)	109.2
C(83)-C(84)-H(84B)	109.2
C(85)-C(84)-H(84B)	109.2
H(84A)-C(84)-H(84B)	107.9
C(86)-C(85)-C(84)	110.18(19)
C(86)-C(85)-H(85A)	109.6
C(84)-C(85)-H(85A)	109.6
C(86)-C(85)-H(85B)	109.6
C(84)-C(85)-H(85B)	109.6
H(85A)-C(85)-H(85B)	108.1
C(85)-C(86)-C(87)	110.8(2)
C(85)-C(86)-H(86A)	109.5
C(87)-C(86)-H(86A)	109.5
C(85)-C(86)-H(86B)	109.5
C(87)-C(86)-H(86B)	109.5
H(86A)-C(86)-H(86B)	108.1
C(82)-C(87)-C(86)	111.50(18)
C(82)-C(87)-H(87A)	109.3
C(86)-C(87)-H(87A)	109.3

C(82)-C(87)-H(87B)	109.3
C(86)-C(87)-H(87B)	109.3
H(87A)-C(87)-H(87B)	108.0
O(4)-P(4)-N(4)	111.86(8)
O(4)-P(4)-C(94)	110.46(9)
N(4)-P(4)-C(94)	110.72(8)
O(4)-P(4)-C(88)	114.94(9)
N(4)-P(4)-C(88)	102.72(9)
C(94)-P(4)-C(88)	105.77(9)
C(100)-N(4)-P(4)	118.03(13)
C(100)-N(4)-H(4N)	121.0
P(4)-N(4)-H(4N)	121.0
C(93)-C(88)-C(89)	118.96(19)
C(93)-C(88)-P(4)	121.25(16)
C(89)-C(88)-P(4)	119.68(15)
C(90)-C(89)-C(88)	119.9(2)
C(90)-C(89)-H(89A)	120.0
C(88)-C(89)-H(89A)	120.0
C(91)-C(90)-C(89)	120.1(2)
C(91)-C(90)-H(90A)	120.0
C(89)-C(90)-H(90A)	120.0
C(90)-C(91)-C(92)	120.5(2)
C(90)-C(91)-H(91A)	119.8
C(92)-C(91)-H(91A)	119.8
C(93)-C(92)-C(91)	119.6(2)
C(93)-C(92)-H(92A)	120.2
C(91)-C(92)-H(92A)	120.2
C(92)-C(93)-C(88)	121.0(2)
C(92)-C(93)-H(93A)	119.5
C(88)-C(93)-H(93A)	119.5
C(95)-C(94)-C(99)	119.27(18)
C(95)-C(94)-P(4)	120.71(15)
C(99)-C(94)-P(4)	119.98(15)
C(96)-C(95)-C(94)	120.3(2)
C(96)-C(95)-H(95A)	119.8
C(94)-C(95)-H(95A)	119.8
C(95)-C(96)-C(97)	120.3(2)

C(95)-C(96)-H(96A)	119.8
C(97)-C(96)-H(96A)	119.8
C(96)-C(97)-C(98)	119.8(2)
C(96)-C(97)-H(97A)	120.1
C(98)-C(97)-H(97A)	120.1
C(99)-C(98)-C(97)	120.3(2)
C(99)-C(98)-H(98A)	119.8
C(97)-C(98)-H(98A)	119.8
C(98)-C(99)-C(94)	120.0(2)
C(98)-C(99)-H(99A)	120.0
C(94)-C(99)-H(99A)	120.0
N(4)-C(100)-C(101)	112.40(15)
N(4)-C(100)-C(107)	111.05(15)
C(101)-C(100)-C(107)	112.38(16)
N(4)-C(100)-H(10B)	106.9
C(101)-C(100)-H(10B)	106.9
C(107)-C(100)-H(10B)	106.9
C(102)-C(101)-C(106)	118.4(2)
C(102)-C(101)-C(100)	121.74(19)
C(106)-C(101)-C(100)	119.83(19)
C(103)-C(102)-C(101)	120.9(2)
C(103)-C(102)-H(10C)	119.6
C(101)-C(102)-H(10C)	119.6
C(104)-C(103)-C(102)	120.1(2)
C(104)-C(103)-H(10D)	120.0
C(102)-C(103)-H(10D)	120.0
C(105)-C(104)-C(103)	119.9(2)
C(105)-C(104)-H(10E)	120.1
C(103)-C(104)-H(10E)	120.1
C(104)-C(105)-C(106)	120.3(2)
C(104)-C(105)-H(10F)	119.9
C(106)-C(105)-H(10F)	119.9
C(101)-C(106)-C(105)	120.4(2)
C(101)-C(106)-H(10G)	119.8
C(105)-C(106)-H(10G)	119.8
C(109)-C(107)-C(108)	111.77(17)
C(109)-C(107)-C(111)	110.35(15)

C(108)-C(107)-C(111)	108.70(16)
C(109)-C(107)-C(100)	106.05(15)
C(108)-C(107)-C(100)	110.12(15)
C(111)-C(107)-C(100)	109.83(15)
C(107)-C(108)-H(10H)	109.5
C(107)-C(108)-H(10I)	109.5
H(10H)-C(108)-H(10I)	109.5
C(107)-C(108)-H(10J)	109.5
H(10H)-C(108)-H(10J)	109.5
H(10I)-C(108)-H(10J)	109.5
C(110)-C(109)-C(107)	129.0(2)
C(110)-C(109)-H(10K)	115.5
C(107)-C(109)-H(10K)	115.5
C(109)-C(110)-H(11B)	120.0
C(109)-C(110)-H(11C)	120.0
H(11B)-C(110)-H(11C)	120.0
C(116)-C(111)-C(112)	109.50(15)
C(116)-C(111)-C(107)	114.51(15)
C(112)-C(111)-C(107)	111.32(15)
C(116)-C(111)-H(11E)	107.0
C(112)-C(111)-H(11E)	107.0
C(107)-C(111)-H(11E)	107.0
C(113)-C(112)-C(111)	111.52(16)
C(113)-C(112)-H(11F)	109.3
C(111)-C(112)-H(11F)	109.3
C(113)-C(112)-H(11G)	109.3
C(111)-C(112)-H(11G)	109.3
H(11F)-C(112)-H(11G)	108.0
C(114)-C(113)-C(112)	111.05(17)
C(114)-C(113)-H(11H)	109.4
C(112)-C(113)-H(11H)	109.4
C(114)-C(113)-H(11I)	109.4
C(112)-C(113)-H(11I)	109.4
H(11H)-C(113)-H(11I)	108.0
C(115)-C(114)-C(113)	109.77(17)
C(115)-C(114)-H(11J)	109.7
C(113)-C(114)-H(11J)	109.7

C(115)-C(114)-H(11K)	109.7
C(113)-C(114)-H(11K)	109.7
H(11J)-C(114)-H(11K)	108.2
C(114)-C(115)-C(116)	111.12(17)
C(114)-C(115)-H(11L)	109.4
C(116)-C(115)-H(11L)	109.4
C(114)-C(115)-H(11M)	109.4
C(116)-C(115)-H(11M)	109.4
H(11L)-C(115)-H(11M)	108.0
C(111)-C(116)-C(115)	111.53(17)
C(111)-C(116)-H(11N)	109.3
C(115)-C(116)-H(11N)	109.3
C(111)-C(116)-H(11O)	109.3
C(115)-C(116)-H(11O)	109.3
H(11N)-C(116)-H(11O)	108.0
O(5)-P(5)-N(5)	112.21(8)
O(5)-P(5)-C(117)	110.88(9)
N(5)-P(5)-C(117)	109.54(8)
O(5)-P(5)-C(123)	111.93(8)
N(5)-P(5)-C(123)	106.79(9)
C(117)-P(5)-C(123)	105.16(9)
C(129)-N(5)-P(5)	122.21(12)
C(129)-N(5)-H(5N)	118.9
P(5)-N(5)-H(5N)	118.9
C(122)-C(117)-C(118)	119.31(18)
C(122)-C(117)-P(5)	121.60(15)
C(118)-C(117)-P(5)	119.09(15)
C(119)-C(118)-C(117)	119.8(2)
C(119)-C(118)-H(11P)	120.1
C(117)-C(118)-H(11P)	120.1
C(120)-C(119)-C(118)	120.6(2)
C(120)-C(119)-H(11Q)	119.7
C(118)-C(119)-H(11Q)	119.7
C(119)-C(120)-C(121)	119.7(2)
C(119)-C(120)-H(12B)	120.2
C(121)-C(120)-H(12B)	120.2
C(120)-C(121)-C(122)	120.6(2)

C(120)-C(121)-H(12C)	119.7
C(122)-C(121)-H(12C)	119.7
C(121)-C(122)-C(117)	120.0(2)
C(121)-C(122)-H(12D)	120.0
C(117)-C(122)-H(12D)	120.0
C(124)-C(123)-C(128)	118.8(2)
C(124)-C(123)-P(5)	121.90(17)
C(128)-C(123)-P(5)	119.00(16)
C(125)-C(124)-C(123)	120.5(2)
C(125)-C(124)-H(12E)	119.8
C(123)-C(124)-H(12E)	119.8
C(124)-C(125)-C(126)	120.1(2)
C(124)-C(125)-H(12F)	119.9
C(126)-C(125)-H(12F)	119.9
C(127)-C(126)-C(125)	120.1(2)
C(127)-C(126)-H(12G)	120.0
C(125)-C(126)-H(12G)	120.0
C(128)-C(127)-C(126)	120.2(3)
C(128)-C(127)-H(12H)	119.9
C(126)-C(127)-H(12H)	119.9
C(127)-C(128)-C(123)	120.3(2)
C(127)-C(128)-H(12I)	119.8
C(123)-C(128)-H(12I)	119.8
N(5)-C(129)-C(130)	111.22(16)
N(5)-C(129)-C(136)	112.91(15)
C(130)-C(129)-C(136)	112.81(16)
N(5)-C(129)-H(12J)	106.5
C(130)-C(129)-H(12J)	106.5
C(136)-C(129)-H(12J)	106.5
C(135)-C(130)-C(131)	118.28(18)
C(135)-C(130)-C(129)	119.45(18)
C(131)-C(130)-C(129)	122.26(17)
C(130)-C(131)-C(132)	120.33(19)
C(130)-C(131)-H(13B)	119.8
C(132)-C(131)-H(13B)	119.8
C(133)-C(132)-C(131)	120.7(2)
C(133)-C(132)-H(13C)	119.6

C(131)-C(132)-H(13C)	119.6
C(132)-C(133)-C(134)	119.5(2)
C(132)-C(133)-H(13D)	120.2
C(134)-C(133)-H(13D)	120.2
C(133)-C(134)-C(135)	119.9(2)
C(133)-C(134)-H(13E)	120.1
C(135)-C(134)-H(13E)	120.1
C(130)-C(135)-C(134)	121.2(2)
C(130)-C(135)-H(13F)	119.4
C(134)-C(135)-H(13F)	119.4
C(138)-C(136)-C(137)	111.96(18)
C(138)-C(136)-C(129)	106.73(17)
C(137)-C(136)-C(129)	110.21(16)
C(138)-C(136)-C(140)	109.35(16)
C(137)-C(136)-C(140)	108.97(17)
C(129)-C(136)-C(140)	109.59(16)
C(136)-C(137)-H(13G)	109.5
C(136)-C(137)-H(13H)	109.5
H(13G)-C(137)-H(13H)	109.5
C(136)-C(137)-H(13I)	109.5
H(13G)-C(137)-H(13I)	109.5
H(13H)-C(137)-H(13I)	109.5
C(139)-C(138)-C(136)	127.3(3)
C(139)-C(138)-H(13J)	116.4
C(136)-C(138)-H(13J)	116.4
C(138)-C(139)-H(13K)	120.0
C(138)-C(139)-H(13L)	120.0
H(13K)-C(139)-H(13L)	120.0
C(145)-C(140)-C(141)	108.34(18)
C(145)-C(140)-C(136)	114.06(17)
C(141)-C(140)-C(136)	112.79(18)
C(145)-C(140)-H(14A)	107.1
C(141)-C(140)-H(14A)	107.1
C(136)-C(140)-H(14A)	107.1
C(142)-C(141)-C(140)	111.9(2)
C(142)-C(141)-H(14B)	109.2
C(140)-C(141)-H(14B)	109.2

C(142)-C(141)-H(14C)	109.2
C(140)-C(141)-H(14C)	109.2
H(14B)-C(141)-H(14C)	107.9
C(141)-C(142)-C(143)	112.0(2)
C(141)-C(142)-H(14D)	109.2
C(143)-C(142)-H(14D)	109.2
C(141)-C(142)-H(14E)	109.2
C(143)-C(142)-H(14E)	109.2
H(14D)-C(142)-H(14E)	107.9
C(144)-C(143)-C(142)	109.4(2)
C(144)-C(143)-H(14F)	109.8
C(142)-C(143)-H(14F)	109.8
C(144)-C(143)-H(14G)	109.8
C(142)-C(143)-H(14G)	109.8
H(14F)-C(143)-H(14G)	108.2
C(143)-C(144)-C(145)	111.3(2)
C(143)-C(144)-H(14H)	109.4
C(145)-C(144)-H(14H)	109.4
C(143)-C(144)-H(14I)	109.4
C(145)-C(144)-H(14I)	109.4
H(14H)-C(144)-H(14I)	108.0
C(144)-C(145)-C(140)	111.41(17)
C(144)-C(145)-H(14J)	109.3
C(140)-C(145)-H(14J)	109.3
C(144)-C(145)-H(14K)	109.3
C(140)-C(145)-H(14K)	109.3
H(14J)-C(145)-H(14K)	108.0
O(6)-P(6)-N(6)	110.90(9)
O(6)-P(6)-C(152)	111.01(9)
N(6)-P(6)-C(152)	112.32(9)
O(6)-P(6)-C(146)	112.79(9)
N(6)-P(6)-C(146)	104.33(8)
C(152)-P(6)-C(146)	105.23(10)
C(158)-N(6)-P(6)	117.85(13)
C(158)-N(6)-H(6N)	121.1
P(6)-N(6)-H(6N)	121.1
C(151)-C(146)-C(147)	118.64(18)

C(151)-C(146)-P(6)	123.86(16)
C(147)-C(146)-P(6)	117.38(16)
C(148)-C(147)-C(146)	120.4(2)
C(148)-C(147)-H(14L)	119.8
C(146)-C(147)-H(14L)	119.8
C(147)-C(148)-C(149)	120.7(2)
C(147)-C(148)-H(14M)	119.7
C(149)-C(148)-H(14M)	119.7
C(150)-C(149)-C(148)	119.9(2)
C(150)-C(149)-H(14N)	120.0
C(148)-C(149)-H(14N)	120.0
C(149)-C(150)-C(151)	119.7(2)
C(149)-C(150)-H(15B)	120.2
C(151)-C(150)-H(15B)	120.2
C(146)-C(151)-C(150)	120.7(2)
C(146)-C(151)-H(15C)	119.7
C(150)-C(151)-H(15C)	119.7
C(153)-C(152)-C(157)	119.6(2)
C(153)-C(152)-P(6)	120.22(17)
C(157)-C(152)-P(6)	120.14(15)
C(154)-C(153)-C(152)	119.7(2)
C(154)-C(153)-H(15D)	120.2
C(152)-C(153)-H(15D)	120.2
C(155)-C(154)-C(153)	120.3(2)
C(155)-C(154)-H(15E)	119.9
C(153)-C(154)-H(15E)	119.9
C(154)-C(155)-C(156)	120.8(2)
C(154)-C(155)-H(15F)	119.6
C(156)-C(155)-H(15F)	119.6
C(155)-C(156)-C(157)	119.8(2)
C(155)-C(156)-H(15G)	120.1
C(157)-C(156)-H(15G)	120.1
C(156)-C(157)-C(152)	119.8(2)
C(156)-C(157)-H(15H)	120.1
C(152)-C(157)-H(15H)	120.1
N(6)-C(158)-C(159)	112.44(16)
N(6)-C(158)-C(165)	112.12(15)

C(159)-C(158)-C(165)	113.06(16)
N(6)-C(158)-H(15I)	106.2
C(159)-C(158)-H(15I)	106.2
C(165)-C(158)-H(15I)	106.2
C(164)-C(159)-C(160)	118.8(2)
C(164)-C(159)-C(158)	119.19(19)
C(160)-C(159)-C(158)	121.96(18)
C(159)-C(160)-C(161)	119.9(2)
C(159)-C(160)-H(16B)	120.0
C(161)-C(160)-H(16B)	120.0
C(162)-C(161)-C(160)	120.4(2)
C(162)-C(161)-H(16C)	119.8
C(160)-C(161)-H(16C)	119.8
C(163)-C(162)-C(161)	119.8(2)
C(163)-C(162)-H(16D)	120.1
C(161)-C(162)-H(16D)	120.1
C(162)-C(163)-C(164)	120.3(2)
C(162)-C(163)-H(16E)	119.8
C(164)-C(163)-H(16E)	119.8
C(163)-C(164)-C(159)	120.8(2)
C(163)-C(164)-H(16F)	119.6
C(159)-C(164)-H(16F)	119.6
C(167)-C(165)-C(166)	111.10(18)
C(167)-C(165)-C(158)	106.57(17)
C(166)-C(165)-C(158)	109.55(16)
C(167)-C(165)-C(169)	109.89(17)
C(166)-C(165)-C(169)	109.43(17)
C(158)-C(165)-C(169)	110.27(17)
C(165)-C(166)-H(16G)	109.5
C(165)-C(166)-H(16H)	109.5
H(16G)-C(166)-H(16H)	109.5
C(165)-C(166)-H(16I)	109.5
H(16G)-C(166)-H(16I)	109.5
H(16H)-C(166)-H(16I)	109.5
C(168)-C(167)-C(165)	128.0(2)
C(168)-C(167)-H(16J)	116.0
C(165)-C(167)-H(16J)	116.0

C(167)-C(168)-H(16K)	120.0
C(167)-C(168)-H(16L)	120.0
H(16K)-C(168)-H(16L)	120.0
C(174)-C(169)-C(170)	109.05(19)
C(174)-C(169)-C(165)	114.35(19)
C(170)-C(169)-C(165)	112.72(19)
C(174)-C(169)-H(16N)	106.7
C(170)-C(169)-H(16N)	106.7
C(165)-C(169)-H(16N)	106.7
C(169)-C(170)-C(171)	112.6(2)
C(169)-C(170)-H(17B)	109.1
C(171)-C(170)-H(17B)	109.1
C(169)-C(170)-H(17C)	109.1
C(171)-C(170)-H(17C)	109.1
H(17B)-C(170)-H(17C)	107.8
C(172)-C(171)-C(170)	110.7(3)
C(172)-C(171)-H(17D)	109.5
C(170)-C(171)-H(17D)	109.5
C(172)-C(171)-H(17E)	109.5
C(170)-C(171)-H(17E)	109.5
H(17D)-C(171)-H(17E)	108.1
C(173)-C(172)-C(171)	109.8(2)
C(173)-C(172)-H(17F)	109.7
C(171)-C(172)-H(17F)	109.7
C(173)-C(172)-H(17G)	109.7
C(171)-C(172)-H(17G)	109.7
H(17F)-C(172)-H(17G)	108.2
C(174)-C(173)-C(172)	111.6(2)
C(174)-C(173)-H(17H)	109.3
C(172)-C(173)-H(17H)	109.3
C(174)-C(173)-H(17I)	109.3
C(172)-C(173)-H(17I)	109.3
H(17H)-C(173)-H(17I)	108.0
C(173)-C(174)-C(169)	111.9(2)
C(173)-C(174)-H(17J)	109.2
C(169)-C(174)-H(17J)	109.2
C(173)-C(174)-H(17K)	109.2

C(169)-C(174)-H(17K)	109.2
H(17J)-C(174)-H(17K)	107.9

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for $C_{29}H_{34}NOP$. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	23(1)	14(1)	19(1)	-1(1)	12(1)	-1(1)
O(1)	30(1)	14(1)	24(1)	0(1)	15(1)	1(1)
N(1)	31(1)	13(1)	22(1)	0(1)	17(1)	1(1)
C(1)	22(1)	22(1)	22(1)	-2(1)	12(1)	-5(1)
C(2)	26(1)	21(1)	30(1)	6(1)	10(1)	-1(1)
C(3)	24(1)	32(1)	43(1)	13(1)	13(1)	-4(1)
C(4)	22(1)	40(1)	41(1)	3(1)	18(1)	-1(1)
C(5)	28(1)	27(1)	42(1)	-6(1)	19(1)	-2(1)
C(6)	28(1)	19(1)	35(1)	-4(1)	17(1)	-5(1)
C(7)	26(1)	13(1)	21(1)	1(1)	12(1)	-2(1)
C(8)	26(1)	29(1)	26(1)	-2(1)	16(1)	-5(1)
C(9)	37(1)	33(1)	26(1)	-4(1)	19(1)	-5(1)
C(10)	33(1)	32(1)	21(1)	0(1)	8(1)	-3(1)
C(11)	24(1)	32(1)	31(1)	3(1)	13(1)	0(1)
C(12)	28(1)	26(1)	25(1)	0(1)	17(1)	-2(1)
C(13)	29(1)	16(1)	21(1)	-3(1)	14(1)	-2(1)
C(14)	27(1)	23(1)	18(1)	3(1)	13(1)	-2(1)
C(15)	36(1)	23(1)	33(1)	-2(1)	20(1)	-4(1)
C(16)	32(1)	31(1)	40(1)	2(1)	17(1)	-9(1)
C(17)	29(1)	42(1)	41(1)	8(1)	22(1)	-3(1)
C(18)	38(1)	37(1)	33(1)	6(1)	24(1)	7(1)
C(19)	34(1)	27(1)	24(1)	-2(1)	20(1)	-2(1)
C(20)	31(1)	18(1)	19(1)	0(1)	11(1)	2(1)
C(21)	40(1)	20(1)	25(1)	1(1)	16(1)	1(1)
C(22)	40(1)	21(1)	22(1)	-1(1)	13(1)	3(1)

C(23)	68(2)	34(1)	29(1)	1(1)	27(1)	9(1)
C(24)	29(1)	25(1)	29(1)	-2(1)	10(1)	1(1)
C(25)	37(1)	36(1)	39(1)	5(1)	4(1)	3(1)
C(26)	32(1)	47(2)	58(2)	-1(1)	2(1)	4(1)
C(27)	30(1)	46(2)	53(2)	-8(1)	7(1)	-3(1)
C(28)	29(1)	37(1)	52(2)	-10(1)	18(1)	-6(1)
C(29)	28(1)	23(1)	36(1)	-5(1)	13(1)	-3(1)
P(2)	27(1)	16(1)	23(1)	-3(1)	17(1)	-4(1)
O(2)	42(1)	16(1)	31(1)	-3(1)	24(1)	-4(1)
N(2)	31(1)	17(1)	23(1)	-1(1)	18(1)	-6(1)
C(30)	26(1)	31(1)	25(1)	-6(1)	16(1)	-5(1)
C(31)	31(1)	35(1)	30(1)	-5(1)	19(1)	-1(1)
C(32)	32(1)	54(2)	44(1)	-13(1)	20(1)	7(1)
C(33)	25(1)	85(2)	76(2)	-35(2)	19(1)	-1(1)
C(34)	29(1)	74(2)	111(3)	-52(2)	29(2)	-19(1)
C(35)	38(1)	42(2)	68(2)	-28(1)	28(1)	-13(1)
C(36)	25(1)	19(1)	22(1)	-5(1)	16(1)	-6(1)
C(37)	34(1)	30(1)	29(1)	5(1)	20(1)	4(1)
C(38)	52(1)	29(1)	33(1)	4(1)	29(1)	0(1)
C(39)	47(1)	32(1)	35(1)	-10(1)	32(1)	-15(1)
C(40)	26(1)	30(1)	31(1)	-7(1)	17(1)	-5(1)
C(41)	29(1)	22(1)	30(1)	-4(1)	18(1)	-3(1)
C(42)	30(1)	15(1)	23(1)	0(1)	18(1)	-1(1)
C(43)	29(1)	25(1)	20(1)	-4(1)	15(1)	-5(1)
C(44)	40(1)	31(1)	29(1)	-4(1)	21(1)	-11(1)
C(45)	47(1)	53(2)	36(1)	-14(1)	30(1)	-25(1)
C(46)	30(1)	68(2)	37(1)	-22(1)	22(1)	-13(1)
C(47)	31(1)	51(2)	25(1)	-10(1)	12(1)	4(1)
C(48)	30(1)	29(1)	22(1)	-2(1)	13(1)	-1(1)
C(49)	28(1)	14(1)	25(1)	2(1)	16(1)	0(1)
C(50)	30(1)	21(1)	22(1)	-2(1)	14(1)	-2(1)
C(51)	34(1)	20(1)	28(1)	2(1)	16(1)	-2(1)
C(52)	53(1)	31(1)	29(1)	7(1)	19(1)	-6(1)
C(53)	28(1)	19(1)	31(1)	1(1)	17(1)	1(1)
C(54)	34(1)	33(1)	37(1)	-8(1)	18(1)	-3(1)
C(55)	29(1)	45(1)	55(2)	-12(1)	22(1)	-5(1)
C(56)	32(1)	43(1)	52(2)	-6(1)	22(1)	3(1)

C(57)	36(1)	32(1)	43(1)	-3(1)	25(1)	6(1)
C(58)	32(1)	21(1)	32(1)	-1(1)	19(1)	2(1)
P(3)	19(1)	14(1)	21(1)	0(1)	9(1)	-1(1)
O(3)	25(1)	18(1)	25(1)	0(1)	11(1)	0(1)
N(3)	21(1)	12(1)	21(1)	-2(1)	8(1)	-4(1)
C(59)	22(1)	15(1)	21(1)	-1(1)	8(1)	0(1)
C(60)	26(1)	27(1)	29(1)	4(1)	14(1)	2(1)
C(61)	24(1)	34(1)	36(1)	5(1)	11(1)	-1(1)
C(62)	25(1)	27(1)	29(1)	-2(1)	4(1)	-1(1)
C(63)	35(1)	46(1)	22(1)	4(1)	10(1)	-3(1)
C(64)	26(1)	36(1)	25(1)	2(1)	12(1)	-4(1)
C(65)	20(1)	18(1)	26(1)	0(1)	11(1)	1(1)
C(66)	25(1)	21(1)	29(1)	-3(1)	11(1)	-2(1)
C(67)	28(1)	26(1)	40(1)	2(1)	20(1)	-5(1)
C(68)	25(1)	31(1)	44(1)	1(1)	23(1)	4(1)
C(69)	33(1)	20(1)	44(1)	-4(1)	24(1)	1(1)
C(70)	27(1)	18(1)	38(1)	-2(1)	18(1)	-3(1)
C(71)	29(1)	17(1)	24(1)	-2(1)	13(1)	0(1)
C(72)	27(1)	22(1)	26(1)	-1(1)	13(1)	-2(1)
C(73)	27(1)	25(1)	30(1)	-4(1)	13(1)	-1(1)
C(74)	32(1)	29(1)	46(1)	0(1)	23(1)	1(1)
C(75)	24(1)	31(1)	49(1)	6(1)	17(1)	0(1)
C(76)	30(1)	32(1)	41(1)	-8(1)	11(1)	-9(1)
C(77)	29(1)	24(1)	42(1)	-3(1)	16(1)	0(1)
C(78)	30(1)	20(1)	27(1)	-1(1)	16(1)	0(1)
C(79)	26(1)	18(1)	29(1)	6(1)	13(1)	2(1)
C(80)	39(1)	32(1)	28(1)	-3(1)	18(1)	0(1)
C(81)	62(2)	45(2)	25(1)	1(1)	14(1)	3(1)
C(82)	28(1)	22(1)	33(1)	0(1)	19(1)	0(1)
C(83)	40(1)	28(1)	44(1)	5(1)	28(1)	-1(1)
C(84)	42(1)	28(1)	66(2)	3(1)	37(1)	-3(1)
C(85)	43(1)	32(1)	69(2)	4(1)	43(1)	4(1)
C(86)	34(1)	27(1)	63(2)	4(1)	32(1)	3(1)
C(87)	37(1)	21(1)	52(1)	1(1)	30(1)	0(1)
P(4)	17(1)	15(1)	25(1)	1(1)	9(1)	1(1)
O(4)	25(1)	16(1)	32(1)	3(1)	14(1)	3(1)
N(4)	18(1)	15(1)	30(1)	-1(1)	12(1)	-1(1)

C(88)	25(1)	17(1)	29(1)	3(1)	14(1)	2(1)
C(89)	25(1)	25(1)	32(1)	1(1)	13(1)	1(1)
C(90)	41(1)	26(1)	31(1)	-2(1)	15(1)	1(1)
C(91)	50(1)	32(1)	38(1)	0(1)	29(1)	1(1)
C(92)	38(1)	32(1)	46(1)	-1(1)	29(1)	-3(1)
C(93)	28(1)	23(1)	36(1)	-1(1)	18(1)	-2(1)
C(94)	18(1)	19(1)	27(1)	2(1)	13(1)	-4(1)
C(95)	23(1)	24(1)	33(1)	3(1)	10(1)	1(1)
C(96)	23(1)	36(1)	40(1)	13(1)	12(1)	4(1)
C(97)	24(1)	49(2)	33(1)	5(1)	6(1)	-4(1)
C(98)	35(1)	37(1)	39(1)	-11(1)	10(1)	-12(1)
C(99)	24(1)	25(1)	36(1)	-1(1)	12(1)	-3(1)
C(100)	16(1)	17(1)	29(1)	-2(1)	9(1)	2(1)
C(101)	16(1)	30(1)	30(1)	-2(1)	8(1)	-1(1)
C(102)	21(1)	36(1)	30(1)	1(1)	9(1)	7(1)
C(103)	30(1)	59(2)	32(1)	0(1)	7(1)	17(1)
C(104)	38(1)	76(2)	28(1)	-13(1)	-1(1)	12(1)
C(105)	42(1)	64(2)	39(1)	-26(1)	4(1)	9(1)
C(106)	26(1)	42(1)	36(1)	-12(1)	4(1)	3(1)
C(107)	16(1)	19(1)	26(1)	1(1)	8(1)	-1(1)
C(108)	23(1)	22(1)	33(1)	4(1)	10(1)	-2(1)
C(109)	17(1)	26(1)	28(1)	1(1)	8(1)	2(1)
C(110)	39(1)	49(2)	42(1)	10(1)	25(1)	13(1)
C(111)	16(1)	17(1)	27(1)	0(1)	10(1)	0(1)
C(112)	19(1)	23(1)	27(1)	3(1)	10(1)	-2(1)
C(113)	21(1)	32(1)	30(1)	-4(1)	11(1)	-5(1)
C(114)	23(1)	36(1)	24(1)	3(1)	8(1)	1(1)
C(115)	24(1)	32(1)	28(1)	8(1)	13(1)	2(1)
C(116)	19(1)	23(1)	28(1)	3(1)	9(1)	1(1)
P(5)	24(1)	13(1)	19(1)	2(1)	10(1)	1(1)
O(5)	28(1)	14(1)	24(1)	2(1)	11(1)	1(1)
N(5)	32(1)	10(1)	21(1)	1(1)	16(1)	0(1)
C(117)	25(1)	24(1)	17(1)	2(1)	10(1)	6(1)
C(118)	35(1)	23(1)	26(1)	-1(1)	10(1)	6(1)
C(119)	33(1)	41(1)	24(1)	-8(1)	10(1)	4(1)
C(120)	29(1)	50(2)	20(1)	4(1)	8(1)	2(1)
C(121)	29(1)	35(1)	31(1)	15(1)	11(1)	3(1)

C(122)	26(1)	21(1)	29(1)	4(1)	13(1)	2(1)
C(123)	26(1)	17(1)	31(1)	4(1)	14(1)	2(1)
C(124)	33(1)	50(2)	33(1)	13(1)	19(1)	9(1)
C(125)	41(1)	67(2)	63(2)	19(2)	37(1)	13(1)
C(126)	30(1)	44(2)	71(2)	12(1)	24(1)	4(1)
C(127)	32(1)	36(1)	54(2)	-8(1)	10(1)	-5(1)
C(128)	33(1)	31(1)	36(1)	-8(1)	15(1)	-3(1)
C(129)	27(1)	18(1)	21(1)	0(1)	12(1)	-2(1)
C(130)	26(1)	20(1)	21(1)	0(1)	12(1)	1(1)
C(131)	33(1)	21(1)	24(1)	-1(1)	13(1)	-2(1)
C(132)	32(1)	29(1)	26(1)	-9(1)	8(1)	-2(1)
C(133)	27(1)	48(1)	20(1)	-3(1)	8(1)	6(1)
C(134)	38(1)	53(2)	24(1)	13(1)	15(1)	4(1)
C(135)	31(1)	32(1)	28(1)	7(1)	14(1)	-4(1)
C(136)	24(1)	26(1)	24(1)	-1(1)	12(1)	-2(1)
C(137)	33(1)	27(1)	34(1)	-8(1)	15(1)	4(1)
C(138)	28(1)	48(1)	29(1)	-1(1)	14(1)	-8(1)
C(139)	46(2)	86(2)	45(2)	-4(2)	31(1)	-6(1)
C(140)	25(1)	26(1)	24(1)	0(1)	9(1)	-1(1)
C(141)	27(1)	43(1)	40(1)	-8(1)	5(1)	7(1)
C(142)	40(1)	48(2)	44(2)	-3(1)	0(1)	14(1)
C(143)	35(1)	46(2)	34(1)	-3(1)	0(1)	-1(1)
C(144)	36(1)	31(1)	30(1)	-4(1)	8(1)	-7(1)
C(145)	28(1)	24(1)	26(1)	-1(1)	11(1)	-4(1)
P(6)	30(1)	15(1)	18(1)	1(1)	11(1)	3(1)
O(6)	41(1)	16(1)	29(1)	1(1)	17(1)	4(1)
N(6)	31(1)	15(1)	20(1)	4(1)	13(1)	5(1)
C(146)	33(1)	16(1)	20(1)	1(1)	14(1)	7(1)
C(147)	35(1)	22(1)	26(1)	-3(1)	14(1)	-5(1)
C(148)	40(1)	26(1)	21(1)	-3(1)	10(1)	0(1)
C(149)	50(1)	34(1)	26(1)	2(1)	21(1)	0(1)
C(150)	45(1)	51(2)	36(1)	4(1)	23(1)	-10(1)
C(151)	32(1)	46(2)	29(1)	2(1)	14(1)	-2(1)
C(152)	29(1)	25(1)	20(1)	0(1)	9(1)	5(1)
C(153)	42(1)	26(1)	28(1)	1(1)	9(1)	12(1)
C(154)	43(1)	43(2)	41(1)	-2(1)	0(1)	22(1)
C(155)	31(1)	55(2)	54(2)	-15(1)	-3(1)	6(1)

C(156)	37(1)	31(1)	46(1)	-6(1)	6(1)	-1(1)
C(157)	31(1)	22(1)	31(1)	3(1)	8(1)	5(1)
C(158)	38(1)	13(1)	24(1)	2(1)	18(1)	-2(1)
C(159)	35(1)	24(1)	22(1)	6(1)	16(1)	8(1)
C(160)	32(1)	31(1)	23(1)	2(1)	15(1)	3(1)
C(161)	32(1)	51(2)	26(1)	-10(1)	13(1)	-1(1)
C(162)	42(1)	75(2)	17(1)	8(1)	12(1)	26(1)
C(163)	60(2)	45(2)	33(1)	18(1)	30(1)	26(1)
C(164)	56(1)	28(1)	32(1)	10(1)	30(1)	13(1)
C(165)	34(1)	22(1)	25(1)	-2(1)	16(1)	-7(1)
C(166)	27(1)	28(1)	25(1)	-2(1)	12(1)	0(1)
C(167)	43(1)	32(1)	38(1)	-2(1)	22(1)	-11(1)
C(168)	69(2)	52(2)	57(2)	-5(1)	43(2)	-22(1)
C(169)	36(1)	30(1)	25(1)	-2(1)	12(1)	-9(1)
C(170)	36(1)	56(2)	41(1)	-12(1)	11(1)	-12(1)
C(171)	37(1)	83(2)	38(2)	-11(2)	5(1)	-12(1)
C(172)	56(2)	82(2)	35(1)	-17(2)	12(1)	-29(2)
C(173)	64(2)	52(2)	33(1)	-12(1)	22(1)	-22(1)
C(174)	55(2)	36(1)	33(1)	-12(1)	22(1)	-18(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for $C_{29}H_{34}NOP$

	x	y	z	U(eq)
H(1N)	55	1812	508	25
H(2A)	915	3656	-62	32
H(3A)	1925	3591	-105	41
H(4A)	2410	2593	-70	40
H(5A)	1903	1644	32	38
H(6A)	897	1701	89	32
H(8A)	-41	2485	-1245	31
H(9A)	-927	2321	-2324	36
H(10A)	-2036	2248	-2519	37
H(11A)	-2266	2323	-1635	35

H(12A)	-1390	2491	-561	29
H(13A)	90	2916	1208	25
H(15A)	-985	1514	563	35
H(16A)	-2109	1489	330	42
H(17A)	-2560	2339	656	42
H(18A)	-1878	3226	1213	40
H(19A)	-754	3263	1436	31
H(21A)	-113	1369	1796	42
H(21B)	674	1203	2250	42
H(21C)	335	1172	1458	42
H(22A)	587	2945	2385	34
H(23A)	320	1814	2873	51
H(23B)	409	2547	3185	51
H(24A)	1212	1909	1490	35
H(25A)	1831	2106	2899	52
H(25B)	1684	1411	2547	52
H(26A)	2836	1711	2963	65
H(26B)	2467	1613	2174	65
H(27A)	3114	2558	2437	59
H(27B)	2755	2837	2838	59
H(28A)	2093	2634	1426	48
H(28B)	2252	3327	1781	48
H(29A)	1091	3050	1378	36
H(29B)	1470	3128	2170	36
H(2N)	9921	9442	9713	26
H(31A)	11246	8955	10768	36
H(32A)	12379	8675	11386	51
H(33A)	13180	9464	12000	77
H(34A)	12856	10532	11947	88
H(35A)	11716	10829	11327	58
H(37A)	10775	9134	11551	35
H(38A)	10129	8693	11995	42
H(39A)	9030	9054	11633	39
H(40A)	8576	9875	10846	33
H(41A)	9214	10317	10395	30
H(42A)	10057	10646	9300	25
H(44A)	10795	11039	8922	38

H(45A)	11844	10984	8964	50
H(46A)	12487	10040	9325	52
H(47A)	12054	9135	9602	43
H(48A)	10988	9181	9530	32
H(50A)	9966	9297	8297	36
H(50B)	9162	9193	7930	36
H(50C)	9614	9003	8697	36
H(51A)	9381	10927	8145	32
H(52A)	9387	9934	7330	45
H(52B)	9325	10715	7170	45
H(53A)	8865	9669	8950	30
H(54A)	8114	10217	7647	41
H(54B)	8214	9457	7801	41
H(55A)	7135	9800	7631	51
H(55B)	7580	9512	8364	51
H(56A)	7072	10477	8440	51
H(56B)	7378	10864	8042	51
H(57A)	8061	11075	9188	42
H(57B)	8167	10316	9346	42
H(58A)	9141	10741	9357	32
H(58B)	8692	11021	8621	32
H(3N)	5035	2062	9622	23
H(60A)	6176	1480	10266	32
H(61A)	7236	1464	11227	39
H(62A)	7326	1178	12243	37
H(63A)	6363	900	12305	43
H(64A)	5305	908	11358	35
H(66A)	3822	411	10127	31
H(67A)	3117	608	10586	36
H(68A)	3122	1621	11037	37
H(69A)	3800	2453	10984	36
H(70A)	4497	2262	10522	32
H(71A)	4510	1161	8650	28
H(73A)	3610	2300	9110	34
H(74A)	2448	2292	8715	41
H(75A)	1747	1566	7874	42
H(76A)	2242	833	7469	44

H(77A)	3414	833	7882	38
H(79A)	3788	2728	8133	36
H(79B)	4393	3054	8063	36
H(79C)	4477	2924	8784	36
H(80A)	4406	1387	7615	39
H(81A)	3743	2536	7073	57
H(81B)	3739	1874	6675	57
H(82A)	5539	2333	9110	31
H(83A)	5437	2429	7823	41
H(83B)	5386	3032	8235	41
H(84A)	6513	2884	9063	49
H(84B)	6491	2950	8361	49
H(85A)	6608	1827	8307	50
H(85B)	7213	2085	8999	50
H(86A)	6641	1741	9565	46
H(86B)	6704	1139	9160	46
H(87A)	5574	1296	8307	40
H(87B)	5585	1200	9002	40
H(4N)	5189	9544	9926	25
H(89A)	5427	9325	11016	33
H(90A)	5292	9730	11892	41
H(91A)	4242	9676	11845	44
H(92A)	3310	9231	10916	42
H(93A)	3441	8824	10047	34
H(95A)	3606	9665	9074	33
H(96A)	2566	9701	8107	41
H(97A)	2095	8761	7495	47
H(98A)	2666	7775	7863	49
H(99A)	3703	7729	8834	35
H(10B)	5557	8468	9477	25
H(10C)	4567	9857	8602	36
H(10D)	3914	9936	7450	53
H(10E)	3916	9098	6776	66
H(10F)	4601	8197	7250	66
H(10G)	5255	8110	8405	47
H(10H)	6463	10200	9506	41
H(10I)	5759	10217	9514	41

H(10J)	5781	9972	8866	41
H(10K)	6700	8495	9573	29
H(11B)	6542	9444	8667	49
H(11C)	6939	8748	8788	49
H(11E)	6274	9607	10536	24
H(11F)	7518	9372	10518	29
H(11G)	7188	10072	10458	29
H(11H)	8069	9885	11567	34
H(11I)	7358	9989	11553	34
H(11J)	7973	8751	11632	35
H(11K)	7916	9088	12230	35
H(11L)	6724	9004	11634	33
H(11M)	7047	8300	11698	33
H(11N)	6871	8368	10599	29
H(11O)	6164	8479	10589	29
H(5N)	9630	2781	5191	24
H(11P)	9295	940	3837	37
H(11Q)	8703	1036	2684	41
H(12B)	8444	2050	2185	42
H(12C)	8778	2979	2842	40
H(12D)	9367	2897	3996	30
H(12E)	10660	1904	4249	45
H(12F)	11801	2070	4597	63
H(12G)	12554	2298	5710	59
H(12H)	12168	2332	6480	54
H(12I)	11025	2187	6137	42
H(12J)	9235	1713	5647	26
H(13B)	10198	3172	6317	32
H(13C)	10949	3335	7443	38
H(13D)	11018	2590	8230	40
H(13E)	10368	1648	7885	46
H(13F)	9617	1479	6760	37
H(13G)	8976	3288	6129	48
H(13H)	8242	3428	5512	48
H(13I)	8897	3451	5416	48
H(13J)	8262	1689	5778	41
H(13K)	8058	2849	6267	66

H(13L)	7859	2118	6399	66
H(14A)	8366	2669	4485	32
H(14B)	7194	2514	4647	50
H(14C)	7488	3198	4581	50
H(14D)	7235	2954	3489	63
H(14E)	6561	2885	3550	63
H(14F)	6666	1748	3606	55
H(14G)	6684	1992	2953	55
H(14H)	7876	1918	3503	43
H(14I)	7576	1233	3561	43
H(14J)	8494	1530	4608	32
H(14K)	7811	1483	4656	32
H(6N)	9460	10116	4844	26
H(14L)	9180	9395	3630	34
H(14M)	9023	9733	2603	37
H(14N)	9881	10278	2520	43
H(15B)	10900	10507	3476	51
H(15C)	11077	10140	4510	43
H(15D)	11481	8737	5822	43
H(15E)	12574	9069	6595	62
H(15F)	12825	10157	6797	68
H(15G)	11989	10936	6253	53
H(15H)	10887	10618	5492	37
H(15I)	9400	8945	5366	29
H(16B)	10197	10428	6187	34
H(16C)	10965	10506	7324	44
H(16D)	11161	9617	8017	55
H(16E)	10582	8656	7581	51
H(16F)	9819	8571	6454	42
H(16G)	8969	10304	6023	40
H(16H)	8213	10411	5431	40
H(16I)	8845	10599	5331	40
H(16J)	8431	8681	5483	44
H(16K)	8249	9648	6211	65
H(16L)	8112	8868	6230	65
H(16N)	8367	9936	4322	39
H(17B)	7445	10181	4489	57

H(17C)	7288	9427	4500	57
H(17D)	6532	9843	3441	70
H(17E)	7149	10120	3357	70
H(17F)	6865	8769	3399	74
H(17G)	6777	9146	2753	74
H(17H)	7809	8554	3250	61
H(17I)	7955	9313	3255	61
H(17J)	8701	8865	4297	49
H(17K)	8074	8599	4370	49

Table 6. Torsion angles [°] for $C_{29}H_{34}NOP$

O(1)-P(1)-N(1)-C(13)	-5.86(17)
C(1)-P(1)-N(1)-C(13)	117.80(15)
C(7)-P(1)-N(1)-C(13)	-127.98(15)
O(1)-P(1)-C(1)-C(2)	-17.79(19)
N(1)-P(1)-C(1)-C(2)	-141.16(16)
C(7)-P(1)-C(1)-C(2)	102.50(17)
O(1)-P(1)-C(1)-C(6)	164.56(15)
N(1)-P(1)-C(1)-C(6)	41.19(18)
C(7)-P(1)-C(1)-C(6)	-75.15(18)
C(6)-C(1)-C(2)-C(3)	-0.4(3)
P(1)-C(1)-C(2)-C(3)	-178.03(16)
C(1)-C(2)-C(3)-C(4)	0.7(3)
C(2)-C(3)-C(4)-C(5)	-0.7(3)
C(3)-C(4)-C(5)-C(6)	0.3(3)
C(4)-C(5)-C(6)-C(1)	0.1(3)
C(2)-C(1)-C(6)-C(5)	0.0(3)
P(1)-C(1)-C(6)-C(5)	177.62(16)
O(1)-P(1)-C(7)-C(8)	107.14(17)
N(1)-P(1)-C(7)-C(8)	-130.38(17)
C(1)-P(1)-C(7)-C(8)	-13.84(19)
O(1)-P(1)-C(7)-C(12)	-63.94(17)
N(1)-P(1)-C(7)-C(12)	58.54(17)
C(1)-P(1)-C(7)-C(12)	175.08(15)
C(12)-C(7)-C(8)-C(9)	0.2(3)

P(1)-C(7)-C(8)-C(9)	-170.88(16)
C(7)-C(8)-C(9)-C(10)	0.1(3)
C(8)-C(9)-C(10)-C(11)	-0.5(3)
C(9)-C(10)-C(11)-C(12)	0.7(3)
C(10)-C(11)-C(12)-C(7)	-0.4(3)
C(8)-C(7)-C(12)-C(11)	0.0(3)
P(1)-C(7)-C(12)-C(11)	171.42(16)
P(1)-N(1)-C(13)-C(14)	97.76(17)
P(1)-N(1)-C(13)-C(20)	-132.96(15)
N(1)-C(13)-C(14)-C(15)	41.2(2)
C(20)-C(13)-C(14)-C(15)	-87.6(2)
N(1)-C(13)-C(14)-C(19)	-135.59(18)
C(20)-C(13)-C(14)-C(19)	95.6(2)
C(19)-C(14)-C(15)-C(16)	0.0(3)
C(13)-C(14)-C(15)-C(16)	-176.83(19)
C(14)-C(15)-C(16)-C(17)	-0.4(3)
C(15)-C(16)-C(17)-C(18)	0.3(3)
C(16)-C(17)-C(18)-C(19)	0.2(3)
C(17)-C(18)-C(19)-C(14)	-0.6(3)
C(15)-C(14)-C(19)-C(18)	0.5(3)
C(13)-C(14)-C(19)-C(18)	177.42(18)
N(1)-C(13)-C(20)-C(22)	167.21(16)
C(14)-C(13)-C(20)-C(22)	-65.4(2)
N(1)-C(13)-C(20)-C(21)	-71.3(2)
C(14)-C(13)-C(20)-C(21)	56.0(2)
N(1)-C(13)-C(20)-C(24)	49.1(2)
C(14)-C(13)-C(20)-C(24)	176.52(15)
C(21)-C(20)-C(22)-C(23)	3.6(3)
C(13)-C(20)-C(22)-C(23)	124.4(3)
C(24)-C(20)-C(22)-C(23)	-118.4(3)
C(22)-C(20)-C(24)-C(29)	-61.6(2)
C(21)-C(20)-C(24)-C(29)	175.20(17)
C(13)-C(20)-C(24)-C(29)	54.1(2)
C(22)-C(20)-C(24)-C(25)	62.9(2)
C(21)-C(20)-C(24)-C(25)	-60.3(2)
C(13)-C(20)-C(24)-C(25)	178.63(18)
C(29)-C(24)-C(25)-C(26)	-55.4(3)

C(20)-C(24)-C(25)-C(26)	176.9(2)
C(24)-C(25)-C(26)-C(27)	56.4(3)
C(25)-C(26)-C(27)-C(28)	-55.3(3)
C(26)-C(27)-C(28)-C(29)	55.5(3)
C(27)-C(28)-C(29)-C(24)	-57.7(3)
C(25)-C(24)-C(29)-C(28)	56.5(2)
C(20)-C(24)-C(29)-C(28)	-176.81(18)
O(2)-P(2)-N(2)-C(42)	33.75(17)
C(30)-P(2)-N(2)-C(42)	-90.82(16)
C(36)-P(2)-N(2)-C(42)	155.16(14)
O(2)-P(2)-C(30)-C(31)	-170.72(16)
N(2)-P(2)-C(30)-C(31)	-46.1(2)
C(36)-P(2)-C(30)-C(31)	65.80(19)
O(2)-P(2)-C(30)-C(35)	10.1(2)
N(2)-P(2)-C(30)-C(35)	134.69(19)
C(36)-P(2)-C(30)-C(35)	-113.4(2)
C(35)-C(30)-C(31)-C(32)	0.6(3)
P(2)-C(30)-C(31)-C(32)	-178.56(18)
C(30)-C(31)-C(32)-C(33)	0.6(4)
C(31)-C(32)-C(33)-C(34)	-1.8(5)
C(32)-C(33)-C(34)-C(35)	1.8(6)
C(33)-C(34)-C(35)-C(30)	-0.6(5)
C(31)-C(30)-C(35)-C(34)	-0.6(4)
P(2)-C(30)-C(35)-C(34)	178.6(2)
O(2)-P(2)-C(36)-C(37)	-134.23(18)
N(2)-P(2)-C(36)-C(37)	105.46(19)
C(30)-P(2)-C(36)-C(37)	-11.8(2)
O(2)-P(2)-C(36)-C(41)	45.76(17)
N(2)-P(2)-C(36)-C(41)	-74.55(16)
C(30)-P(2)-C(36)-C(41)	168.22(15)
C(41)-C(36)-C(37)-C(38)	0.9(3)
P(2)-C(36)-C(37)-C(38)	-179.15(17)
C(36)-C(37)-C(38)-C(39)	-0.1(3)
C(37)-C(38)-C(39)-C(40)	-0.8(3)
C(38)-C(39)-C(40)-C(41)	0.9(3)
C(39)-C(40)-C(41)-C(36)	-0.2(3)
C(37)-C(36)-C(41)-C(40)	-0.7(3)

P(2)-C(36)-C(41)-C(40)	179.30(15)
P(2)-N(2)-C(42)-C(43)	79.29(18)
P(2)-N(2)-C(42)-C(49)	-151.37(13)
N(2)-C(42)-C(43)-C(48)	35.6(2)
C(49)-C(42)-C(43)-C(48)	-91.7(2)
N(2)-C(42)-C(43)-C(44)	-140.93(18)
C(49)-C(42)-C(43)-C(44)	91.8(2)
C(48)-C(43)-C(44)-C(45)	0.0(3)
C(42)-C(43)-C(44)-C(45)	176.59(19)
C(43)-C(44)-C(45)-C(46)	-1.1(3)
C(44)-C(45)-C(46)-C(47)	1.3(3)
C(45)-C(46)-C(47)-C(48)	-0.4(3)
C(44)-C(43)-C(48)-C(47)	1.0(3)
C(42)-C(43)-C(48)-C(47)	-175.56(18)
C(46)-C(47)-C(48)-C(43)	-0.8(3)
N(2)-C(42)-C(49)-C(51)	165.82(16)
C(43)-C(42)-C(49)-C(51)	-66.4(2)
N(2)-C(42)-C(49)-C(50)	-72.92(19)
C(43)-C(42)-C(49)-C(50)	54.9(2)
N(2)-C(42)-C(49)-C(53)	47.5(2)
C(43)-C(42)-C(49)-C(53)	175.28(16)
C(50)-C(49)-C(51)-C(52)	5.0(3)
C(42)-C(49)-C(51)-C(52)	124.9(2)
C(53)-C(49)-C(51)-C(52)	-116.2(2)
C(51)-C(49)-C(53)-C(54)	59.0(2)
C(50)-C(49)-C(53)-C(54)	-63.2(2)
C(42)-C(49)-C(53)-C(54)	176.68(17)
C(51)-C(49)-C(53)-C(58)	-65.4(2)
C(50)-C(49)-C(53)-C(58)	172.33(17)
C(42)-C(49)-C(53)-C(58)	52.2(2)
C(58)-C(53)-C(54)-C(55)	-55.8(2)
C(49)-C(53)-C(54)-C(55)	177.10(19)
C(53)-C(54)-C(55)-C(56)	56.8(3)
C(54)-C(55)-C(56)-C(57)	-55.6(3)
C(55)-C(56)-C(57)-C(58)	55.9(3)
C(56)-C(57)-C(58)-C(53)	-57.2(2)
C(54)-C(53)-C(58)-C(57)	56.0(2)

C(49)-C(53)-C(58)-C(57)	-177.83(17)
O(3)-P(3)-N(3)-C(71)	27.24(16)
C(59)-P(3)-N(3)-C(71)	150.96(14)
C(65)-P(3)-N(3)-C(71)	-97.50(15)
O(3)-P(3)-C(59)-C(60)	86.49(18)
N(3)-P(3)-C(59)-C(60)	-36.06(18)
C(65)-P(3)-C(59)-C(60)	-153.49(16)
O(3)-P(3)-C(59)-C(64)	-86.94(17)
N(3)-P(3)-C(59)-C(64)	150.50(16)
C(65)-P(3)-C(59)-C(64)	33.08(18)
C(64)-C(59)-C(60)-C(61)	-0.8(3)
P(3)-C(59)-C(60)-C(61)	-174.27(17)
C(59)-C(60)-C(61)-C(62)	0.2(3)
C(60)-C(61)-C(62)-C(63)	0.3(3)
C(61)-C(62)-C(63)-C(64)	-0.2(4)
C(62)-C(63)-C(64)-C(59)	-0.4(4)
C(60)-C(59)-C(64)-C(63)	0.9(3)
P(3)-C(59)-C(64)-C(63)	174.52(18)
O(3)-P(3)-C(65)-C(66)	10.76(19)
N(3)-P(3)-C(65)-C(66)	135.73(16)
C(59)-P(3)-C(65)-C(66)	-110.82(17)
O(3)-P(3)-C(65)-C(70)	-174.08(15)
N(3)-P(3)-C(65)-C(70)	-49.11(18)
C(59)-P(3)-C(65)-C(70)	64.35(18)
C(70)-C(65)-C(66)-C(67)	0.0(3)
P(3)-C(65)-C(66)-C(67)	175.28(16)
C(65)-C(66)-C(67)-C(68)	-0.8(3)
C(66)-C(67)-C(68)-C(69)	1.4(3)
C(67)-C(68)-C(69)-C(70)	-1.2(3)
C(68)-C(69)-C(70)-C(65)	0.4(3)
C(66)-C(65)-C(70)-C(69)	0.2(3)
P(3)-C(65)-C(70)-C(69)	-175.01(17)
P(3)-N(3)-C(71)-C(72)	66.48(19)
P(3)-N(3)-C(71)-C(78)	-165.79(13)
N(3)-C(71)-C(72)-C(77)	-139.0(2)
C(78)-C(71)-C(72)-C(77)	93.5(2)
N(3)-C(71)-C(72)-C(73)	39.8(3)

C(78)-C(71)-C(72)-C(73)	-87.7(2)
C(77)-C(72)-C(73)-C(74)	-3.4(3)
C(71)-C(72)-C(73)-C(74)	177.75(19)
C(72)-C(73)-C(74)-C(75)	0.8(3)
C(73)-C(74)-C(75)-C(76)	1.4(4)
C(74)-C(75)-C(76)-C(77)	-0.8(4)
C(73)-C(72)-C(77)-C(76)	3.9(3)
C(71)-C(72)-C(77)-C(76)	-177.2(2)
C(75)-C(76)-C(77)-C(72)	-1.9(4)
N(3)-C(71)-C(78)-C(80)	163.30(16)
C(72)-C(71)-C(78)-C(80)	-68.8(2)
N(3)-C(71)-C(78)-C(79)	-75.3(2)
C(72)-C(71)-C(78)-C(79)	52.6(2)
N(3)-C(71)-C(78)-C(82)	45.8(2)
C(72)-C(71)-C(78)-C(82)	173.65(16)
C(79)-C(78)-C(80)-C(81)	6.1(3)
C(71)-C(78)-C(80)-C(81)	127.4(3)
C(82)-C(78)-C(80)-C(81)	-114.6(3)
C(80)-C(78)-C(82)-C(87)	-63.3(2)
C(79)-C(78)-C(82)-C(87)	174.91(18)
C(71)-C(78)-C(82)-C(87)	52.7(2)
C(80)-C(78)-C(82)-C(83)	61.9(2)
C(79)-C(78)-C(82)-C(83)	-59.9(2)
C(71)-C(78)-C(82)-C(83)	177.87(17)
C(87)-C(82)-C(83)-C(84)	-56.2(2)
C(78)-C(82)-C(83)-C(84)	175.86(18)
C(82)-C(83)-C(84)-C(85)	56.3(3)
C(83)-C(84)-C(85)-C(86)	-55.3(3)
C(84)-C(85)-C(86)-C(87)	55.8(3)
C(83)-C(82)-C(87)-C(86)	57.6(2)
C(78)-C(82)-C(87)-C(86)	-174.83(19)
C(85)-C(86)-C(87)-C(82)	-58.5(3)
O(4)-P(4)-N(4)-C(100)	42.26(16)
C(94)-P(4)-N(4)-C(100)	-81.41(15)
C(88)-P(4)-N(4)-C(100)	166.05(14)
O(4)-P(4)-C(88)-C(93)	-93.59(18)
N(4)-P(4)-C(88)-C(93)	144.69(17)

C(94)-P(4)-C(88)-C(93)	28.54(19)
O(4)-P(4)-C(88)-C(89)	82.49(18)
N(4)-P(4)-C(88)-C(89)	-39.23(18)
C(94)-P(4)-C(88)-C(89)	-155.38(16)
C(93)-C(88)-C(89)-C(90)	0.7(3)
P(4)-C(88)-C(89)-C(90)	-175.44(16)
C(88)-C(89)-C(90)-C(91)	-0.2(3)
C(89)-C(90)-C(91)-C(92)	-0.5(4)
C(90)-C(91)-C(92)-C(93)	0.6(4)
C(91)-C(92)-C(93)-C(88)	-0.1(3)
C(89)-C(88)-C(93)-C(92)	-0.6(3)
P(4)-C(88)-C(93)-C(92)	175.54(17)
O(4)-P(4)-C(94)-C(95)	-179.96(16)
N(4)-P(4)-C(94)-C(95)	-55.50(18)
C(88)-P(4)-C(94)-C(95)	55.08(18)
O(4)-P(4)-C(94)-C(99)	-2.38(19)
N(4)-P(4)-C(94)-C(99)	122.08(16)
C(88)-P(4)-C(94)-C(99)	-127.34(16)
C(99)-C(94)-C(95)-C(96)	1.0(3)
P(4)-C(94)-C(95)-C(96)	178.64(17)
C(94)-C(95)-C(96)-C(97)	-0.8(3)
C(95)-C(96)-C(97)-C(98)	0.3(4)
C(96)-C(97)-C(98)-C(99)	-0.1(4)
C(97)-C(98)-C(99)-C(94)	0.3(4)
C(95)-C(94)-C(99)-C(98)	-0.8(3)
P(4)-C(94)-C(99)-C(98)	-178.40(18)
P(4)-N(4)-C(100)-C(101)	78.44(18)
P(4)-N(4)-C(100)-C(107)	-154.70(13)
N(4)-C(100)-C(101)-C(102)	41.9(3)
C(107)-C(100)-C(101)-C(102)	-84.3(2)
N(4)-C(100)-C(101)-C(106)	-137.7(2)
C(107)-C(100)-C(101)-C(106)	96.2(2)
C(106)-C(101)-C(102)-C(103)	-2.5(3)
C(100)-C(101)-C(102)-C(103)	178.0(2)
C(101)-C(102)-C(103)-C(104)	1.6(4)
C(102)-C(103)-C(104)-C(105)	-0.8(5)
C(103)-C(104)-C(105)-C(106)	1.0(5)

C(102)-C(101)-C(106)-C(105)	2.6(4)
C(100)-C(101)-C(106)-C(105)	-177.9(2)
C(104)-C(105)-C(106)-C(101)	-1.9(4)
N(4)-C(100)-C(107)-C(109)	163.53(15)
C(101)-C(100)-C(107)-C(109)	-69.60(19)
N(4)-C(100)-C(107)-C(108)	-75.4(2)
C(101)-C(100)-C(107)-C(108)	51.5(2)
N(4)-C(100)-C(107)-C(111)	44.3(2)
C(101)-C(100)-C(107)-C(111)	171.17(15)
C(108)-C(107)-C(109)-C(110)	-10.8(3)
C(111)-C(107)-C(109)-C(110)	-131.9(2)
C(100)-C(107)-C(109)-C(110)	109.3(3)
C(109)-C(107)-C(111)-C(116)	-64.6(2)
C(108)-C(107)-C(111)-C(116)	172.48(16)
C(100)-C(107)-C(111)-C(116)	51.9(2)
C(109)-C(107)-C(111)-C(112)	60.3(2)
C(108)-C(107)-C(111)-C(112)	-62.6(2)
C(100)-C(107)-C(111)-C(112)	176.82(15)
C(116)-C(111)-C(112)-C(113)	-55.4(2)
C(107)-C(111)-C(112)-C(113)	177.01(16)
C(111)-C(112)-C(113)-C(114)	57.2(2)
C(112)-C(113)-C(114)-C(115)	-57.4(2)
C(113)-C(114)-C(115)-C(116)	57.5(2)
C(112)-C(111)-C(116)-C(115)	55.4(2)
C(107)-C(111)-C(116)-C(115)	-178.81(15)
C(114)-C(115)-C(116)-C(111)	-57.5(2)
O(5)-P(5)-N(5)-C(129)	-2.62(17)
C(117)-P(5)-N(5)-C(129)	120.99(15)
C(123)-P(5)-N(5)-C(129)	-125.62(15)
O(5)-P(5)-C(117)-C(122)	164.31(15)
N(5)-P(5)-C(117)-C(122)	39.93(19)
C(123)-P(5)-C(117)-C(122)	-74.52(18)
O(5)-P(5)-C(117)-C(118)	-16.08(19)
N(5)-P(5)-C(117)-C(118)	-140.47(16)
C(123)-P(5)-C(117)-C(118)	105.09(17)
C(122)-C(117)-C(118)-C(119)	0.3(3)
P(5)-C(117)-C(118)-C(119)	-179.32(17)

C(117)-C(118)-C(119)-C(120)	-0.1(3)
C(118)-C(119)-C(120)-C(121)	0.0(3)
C(119)-C(120)-C(121)-C(122)	-0.1(3)
C(120)-C(121)-C(122)-C(117)	0.3(3)
C(118)-C(117)-C(122)-C(121)	-0.4(3)
P(5)-C(117)-C(122)-C(121)	179.19(16)
O(5)-P(5)-C(123)-C(124)	98.62(19)
N(5)-P(5)-C(123)-C(124)	-138.21(18)
C(117)-P(5)-C(123)-C(124)	-21.9(2)
O(5)-P(5)-C(123)-C(128)	-74.83(18)
N(5)-P(5)-C(123)-C(128)	48.35(18)
C(117)-P(5)-C(123)-C(128)	164.69(16)
C(128)-C(123)-C(124)-C(125)	-0.3(4)
P(5)-C(123)-C(124)-C(125)	-173.8(2)
C(123)-C(124)-C(125)-C(126)	0.1(4)
C(124)-C(125)-C(126)-C(127)	0.8(4)
C(125)-C(126)-C(127)-C(128)	-1.5(4)
C(126)-C(127)-C(128)-C(123)	1.2(4)
C(124)-C(123)-C(128)-C(127)	-0.3(3)
P(5)-C(123)-C(128)-C(127)	173.34(19)
P(5)-N(5)-C(129)-C(130)	104.68(17)
P(5)-N(5)-C(129)-C(136)	-127.32(15)
N(5)-C(129)-C(130)-C(135)	-138.55(19)
C(136)-C(129)-C(130)-C(135)	93.4(2)
N(5)-C(129)-C(130)-C(131)	40.9(2)
C(136)-C(129)-C(130)-C(131)	-87.2(2)
C(135)-C(130)-C(131)-C(132)	-1.6(3)
C(129)-C(130)-C(131)-C(132)	178.96(19)
C(130)-C(131)-C(132)-C(133)	0.0(3)
C(131)-C(132)-C(133)-C(134)	1.6(3)
C(132)-C(133)-C(134)-C(135)	-1.5(3)
C(131)-C(130)-C(135)-C(134)	1.7(3)
C(129)-C(130)-C(135)-C(134)	-178.9(2)
C(133)-C(134)-C(135)-C(130)	-0.2(4)
N(5)-C(129)-C(136)-C(138)	164.53(16)
C(130)-C(129)-C(136)-C(138)	-68.3(2)
N(5)-C(129)-C(136)-C(137)	-73.7(2)

C(130)-C(129)-C(136)-C(137)	53.5(2)
N(5)-C(129)-C(136)-C(140)	46.2(2)
C(130)-C(129)-C(136)-C(140)	173.39(16)
C(137)-C(136)-C(138)-C(139)	6.1(3)
C(129)-C(136)-C(138)-C(139)	126.8(3)
C(140)-C(136)-C(138)-C(139)	-114.8(3)
C(138)-C(136)-C(140)-C(145)	-60.4(2)
C(137)-C(136)-C(140)-C(145)	176.98(18)
C(129)-C(136)-C(140)-C(145)	56.3(2)
C(138)-C(136)-C(140)-C(141)	63.8(2)
C(137)-C(136)-C(140)-C(141)	-58.9(2)
C(129)-C(136)-C(140)-C(141)	-179.54(18)
C(145)-C(140)-C(141)-C(142)	-56.5(3)
C(136)-C(140)-C(141)-C(142)	176.3(2)
C(140)-C(141)-C(142)-C(143)	57.0(3)
C(141)-C(142)-C(143)-C(144)	-55.4(3)
C(142)-C(143)-C(144)-C(145)	56.0(3)
C(143)-C(144)-C(145)-C(140)	-58.7(2)
C(141)-C(140)-C(145)-C(144)	57.3(2)
C(136)-C(140)-C(145)-C(144)	-176.22(17)
O(6)-P(6)-N(6)-C(158)	35.89(16)
C(152)-P(6)-N(6)-C(158)	-88.97(16)
C(146)-P(6)-N(6)-C(158)	157.59(14)
O(6)-P(6)-C(146)-C(151)	-116.69(19)
N(6)-P(6)-C(146)-C(151)	122.87(18)
C(152)-P(6)-C(146)-C(151)	4.5(2)
O(6)-P(6)-C(146)-C(147)	59.19(18)
N(6)-P(6)-C(146)-C(147)	-61.25(17)
C(152)-P(6)-C(146)-C(147)	-179.66(15)
C(151)-C(146)-C(147)-C(148)	0.5(3)
P(6)-C(146)-C(147)-C(148)	-175.61(16)
C(146)-C(147)-C(148)-C(149)	-0.5(3)
C(147)-C(148)-C(149)-C(150)	-0.5(4)
C(148)-C(149)-C(150)-C(151)	1.6(4)
C(147)-C(146)-C(151)-C(150)	0.6(3)
P(6)-C(146)-C(151)-C(150)	176.43(19)
C(149)-C(150)-C(151)-C(146)	-1.7(4)

O(6)-P(6)-C(152)-C(153)	7.3(2)
N(6)-P(6)-C(152)-C(153)	132.13(18)
C(146)-P(6)-C(152)-C(153)	-114.98(18)
O(6)-P(6)-C(152)-C(157)	-174.65(17)
N(6)-P(6)-C(152)-C(157)	-49.9(2)
C(146)-P(6)-C(152)-C(157)	63.03(19)
C(157)-C(152)-C(153)-C(154)	-1.2(4)
P(6)-C(152)-C(153)-C(154)	176.8(2)
C(152)-C(153)-C(154)-C(155)	-0.1(4)
C(153)-C(154)-C(155)-C(156)	0.8(5)
C(154)-C(155)-C(156)-C(157)	-0.2(5)
C(155)-C(156)-C(157)-C(152)	-1.1(4)
C(153)-C(152)-C(157)-C(156)	1.8(3)
P(6)-C(152)-C(157)-C(156)	-176.21(19)
P(6)-N(6)-C(158)-C(159)	75.68(18)
P(6)-N(6)-C(158)-C(165)	-155.60(13)
N(6)-C(158)-C(159)-C(164)	-139.86(19)
C(165)-C(158)-C(159)-C(164)	91.9(2)
N(6)-C(158)-C(159)-C(160)	38.2(3)
C(165)-C(158)-C(159)-C(160)	-90.0(2)
C(164)-C(159)-C(160)-C(161)	-1.3(3)
C(158)-C(159)-C(160)-C(161)	-179.45(19)
C(159)-C(160)-C(161)-C(162)	0.8(3)
C(160)-C(161)-C(162)-C(163)	-0.3(3)
C(161)-C(162)-C(163)-C(164)	0.3(4)
C(162)-C(163)-C(164)-C(159)	-0.8(4)
C(160)-C(159)-C(164)-C(163)	1.3(3)
C(158)-C(159)-C(164)-C(163)	179.5(2)
N(6)-C(158)-C(165)-C(167)	164.93(16)
C(159)-C(158)-C(165)-C(167)	-66.7(2)
N(6)-C(158)-C(165)-C(166)	-74.8(2)
C(159)-C(158)-C(165)-C(166)	53.6(2)
N(6)-C(158)-C(165)-C(169)	45.7(2)
C(159)-C(158)-C(165)-C(169)	174.09(16)
C(166)-C(165)-C(167)-C(168)	0.4(4)
C(158)-C(165)-C(167)-C(168)	119.6(3)
C(169)-C(165)-C(167)-C(168)	-120.9(3)

C(167)-C(165)-C(169)-C(174)	-64.6(2)
C(166)-C(165)-C(169)-C(174)	173.13(19)
C(158)-C(165)-C(169)-C(174)	52.6(2)
C(167)-C(165)-C(169)-C(170)	60.7(3)
C(166)-C(165)-C(169)-C(170)	-61.6(2)
C(158)-C(165)-C(169)-C(170)	177.87(19)
C(174)-C(169)-C(170)-C(171)	-54.5(3)
C(165)-C(169)-C(170)-C(171)	177.4(2)
C(169)-C(170)-C(171)-C(172)	55.8(3)
C(170)-C(171)-C(172)-C(173)	-55.8(3)
C(171)-C(172)-C(173)-C(174)	57.5(3)
C(172)-C(173)-C(174)-C(169)	-58.3(3)
C(170)-C(169)-C(174)-C(173)	55.3(3)
C(165)-C(169)-C(174)-C(173)	-177.5(2)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{29}H_{34}NOP$ [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(2)#1	0.88	2.12	2.979(2)	164.7
N(2)-H(2N)...O(1)#2	0.88	2.15	2.907(2)	144.4
N(3)-H(3N)...O(4)#3	0.88	2.11	2.913(2)	151.1
N(4)-H(4N)...O(3)#4	0.88	2.19	2.882(2)	135.5
N(5)-H(5N)...O(6)#5	0.88	1.96	2.833(2)	173.0
N(6)-H(6N)...O(5)#4	0.88	2.26	2.923(2)	131.8

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y-1,z-1 #2 -x+1,y+1/2,-z+1 #3 -x+1,y-1/2,-z+2

#4 x,y+1,z #5 -x+2,y-1/2,-z+1

Absolute Stereochemical Identity of 1.39a

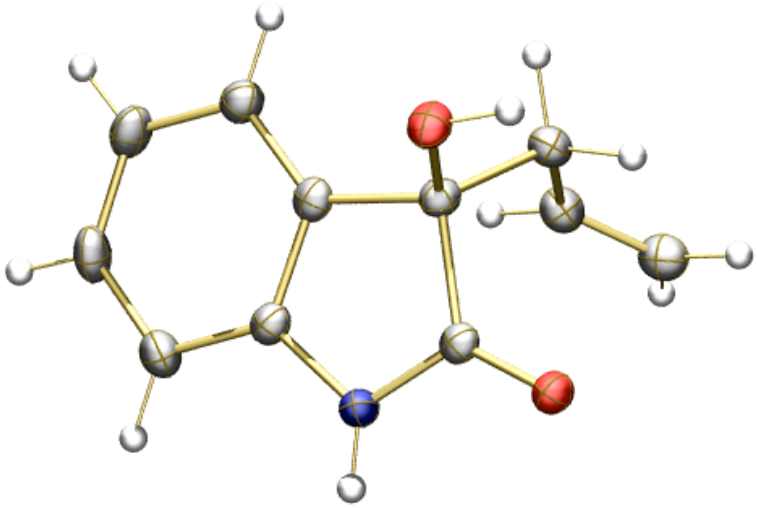


Table 1. Crystal data and structure refinement for $C_{11}H_{11}NO_2$

Identification code	$C_{11}H_{11}NO_2$	
Empirical formula	$C_{11}H_{11}NO_2$	
Formula weight	189.21	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.4763(3) Å	α= 90º
	b = 7.5057(3) Å	β= 90º
	c = 16.9951(7) Å	γ = 90º
Volume	953.68(7) $Å^3$	
Z	4	
Density (calculated)	1.318 Mg/m^3	
Absorption coefficient	0.745 mm^{-1}	
F(000)	400	
Crystal size	0.20 x 0.10 x 0.07 mm^3	
Theta range for data collection	5.20 to 67.32º	
Index ranges	-6<=h<=8, -8<=k<=8, -20<=l<=19	
Reflections collected	5081	
Independent reflections	1626 [R(int) = 0.0390]	
Completeness to theta = 67.32º	97.4 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9497 and 0.8652
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1626 / 0 / 134
Goodness-of-fit on F^2	1.069
Final R indices [I>2sigma(I)]	R1 = 0.0298, wR2 = 0.0746
R indices (all data)	R1 = 0.0308, wR2 = 0.0751
Absolute structure parameter	0.0(2)
Extinction coefficient	0.0093(12)
Largest diff. peak and hole	0.213 and -0.186 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for $C_{11}H_{11}NO_2$ .U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

O(1)	2482(1)	7117(1)	10115(1)	21(1)
O(2)	4795(1)	7911(1)	8720(1)	22(1)
N(1)	616(2)	6638(2)	9063(1)	20(1)
C(1)	2220(2)	6744(2)	9414(1)	18(1)
C(2)	3694(2)	6381(2)	8795(1)	19(1)
C(3)	2590(2)	6138(2)	8062(1)	19(1)
C(4)	3115(2)	5825(2)	7292(1)	23(1)
C(5)	1792(2)	5651(2)	6720(1)	28(1)
C(6)	-3(2)	5773(2)	6921(1)	27(1)
C(7)	-546(2)	6101(2)	7695(1)	24(1)
C(8)	792(2)	6280(2)	8248(1)	20(1)
C(9)	4814(2)	4750(2)	9025(1)	21(1)
C(10)	3789(2)	3043(2)	9088(1)	24(1)
C(11)	3807(2)	1972(2)	9698(1)	28(1)

Table 3. Bond lengths [Å] and angles [°] for $C_{11}H_{11}NO_2$

O(1)-C(1)	1.2390(17)
O(2)-C(2)	1.4187(17)
O(2)-H(2O)	0.86(2)
N(1)-C(1)	1.341(2)
N(1)-C(8)	1.4179(17)
N(1)-H(1N)	0.846(19)
C(1)-C(2)	1.5477(19)
C(2)-C(3)	1.5064(19)
C(2)-C(9)	1.533(2)
C(3)-C(4)	1.3852(19)
C(3)-C(8)	1.386(2)
C(4)-C(5)	1.394(2)
C(4)-H(4)	0.9500
C(5)-C(6)	1.388(2)
C(5)-H(5)	0.9500
C(6)-C(7)	1.398(2)
C(6)-H(6)	0.9500
C(7)-C(8)	1.379(2)
C(7)-H(7)	0.9500
C(9)-C(10)	1.497(2)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.312(2)
C(10)-H(10)	0.9500
C(11)-H(11A)	0.9500
C(11)-H(11B)	0.9500
C(2)-O(2)-H(2O)	108.3(14)
C(1)-N(1)-C(8)	111.26(12)
C(1)-N(1)-H(1N)	120.1(12)
C(8)-N(1)-H(1N)	128.1(12)
O(1)-C(1)-N(1)	125.55(13)
O(1)-C(1)-C(2)	125.49(13)
N(1)-C(1)-C(2)	108.93(11)
O(2)-C(2)-C(3)	109.98(11)

O(2)-C(2)-C(9)	110.65(11)
C(3)-C(2)-C(9)	114.43(11)
O(2)-C(2)-C(1)	109.34(11)
C(3)-C(2)-C(1)	101.16(11)
C(9)-C(2)-C(1)	110.86(11)
C(4)-C(3)-C(8)	120.25(13)
C(4)-C(3)-C(2)	130.28(14)
C(8)-C(3)-C(2)	109.47(11)
C(3)-C(4)-C(5)	118.27(14)
C(3)-C(4)-H(4)	120.9
C(5)-C(4)-H(4)	120.9
C(6)-C(5)-C(4)	120.55(13)
C(6)-C(5)-H(5)	119.7
C(4)-C(5)-H(5)	119.7
C(5)-C(6)-C(7)	121.58(14)
C(5)-C(6)-H(6)	119.2
C(7)-C(6)-H(6)	119.2
C(8)-C(7)-C(6)	116.63(14)
C(8)-C(7)-H(7)	121.7
C(6)-C(7)-H(7)	121.7
C(7)-C(8)-C(3)	122.71(13)
C(7)-C(8)-N(1)	128.16(14)
C(3)-C(8)-N(1)	109.14(13)
C(10)-C(9)-C(2)	114.96(12)
C(10)-C(9)-H(9A)	108.5
C(2)-C(9)-H(9A)	108.5
C(10)-C(9)-H(9B)	108.5
C(2)-C(9)-H(9B)	108.5
H(9A)-C(9)-H(9B)	107.5
C(11)-C(10)-C(9)	125.14(14)
C(11)-C(10)-H(10)	117.4
C(9)-C(10)-H(10)	117.4
C(10)-C(11)-H(11A)	120.0
C(10)-C(11)-H(11B)	120.0
H(11A)-C(11)-H(11B)	120.0

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{11}H_{11}NO_2$. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	21(1)	23(1)	18(1)	-1(1)	0(1)	0(1)
O(2)	24(1)	21(1)	22(1)	2(1)	-1(1)	-6(1)
N(1)	18(1)	25(1)	18(1)	-1(1)	1(1)	2(1)
C(1)	21(1)	14(1)	18(1)	2(1)	1(1)	0(1)
C(2)	19(1)	19(1)	18(1)	0(1)	1(1)	-2(1)
C(3)	24(1)	14(1)	20(1)	1(1)	0(1)	1(1)
C(4)	26(1)	22(1)	21(1)	0(1)	2(1)	3(1)
C(5)	39(1)	26(1)	18(1)	-3(1)	-1(1)	7(1)
C(6)	35(1)	26(1)	22(1)	-4(1)	-10(1)	7(1)
C(7)	24(1)	24(1)	26(1)	0(1)	-4(1)	3(1)
C(8)	23(1)	17(1)	18(1)	0(1)	1(1)	1(1)
C(9)	19(1)	22(1)	23(1)	-1(1)	0(1)	1(1)
C(10)	24(1)	22(1)	26(1)	-3(1)	-2(1)	0(1)
C(11)	29(1)	22(1)	33(1)	0(1)	3(1)	1(1)

Table 5. Hydrogen coordinates ($x\ 10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for $C_{11}H_{11}NO_2$

	x	y	z	U(eq)
H(2O)	5560(30)	7910(30)	9102(11)	33
H(1N)	-320(30)	6910(20)	9315(10)	24
H(4)	4345	5731	7158	28
H(5)	2121	5447	6187	33
H(6)	-885	5630	6523	33
H(7)	-1773	6195	7833	29
H(9A)	5774	4593	8630	26
H(9B)	5394	4991	9538	26
H(10)	3068	2708	8652	29
H(11A)	4510	2259	10146	34

H(11B)	3116	909	9692	34

Table 6. Torsion angles [°] for $C_{11}H_{11}NO_2$

C(8)-N(1)-C(1)-O(1)	176.77(13)
C(8)-N(1)-C(1)-C(2)	-1.54(15)
O(1)-C(1)-C(2)-O(2)	-60.30(18)
N(1)-C(1)-C(2)-O(2)	118.01(12)
O(1)-C(1)-C(2)-C(3)	-176.30(13)
N(1)-C(1)-C(2)-C(3)	2.01(14)
O(1)-C(1)-C(2)-C(9)	61.95(17)
N(1)-C(1)-C(2)-C(9)	-119.74(12)
O(2)-C(2)-C(3)-C(4)	62.35(19)
C(9)-C(2)-C(3)-C(4)	-62.90(19)
C(1)-C(2)-C(3)-C(4)	177.88(15)
O(2)-C(2)-C(3)-C(8)	-117.33(12)
C(9)-C(2)-C(3)-C(8)	117.42(13)
C(1)-C(2)-C(3)-C(8)	-1.80(14)
C(8)-C(3)-C(4)-C(5)	-0.3(2)
C(2)-C(3)-C(4)-C(5)	180.00(14)
C(3)-C(4)-C(5)-C(6)	-0.6(2)
C(4)-C(5)-C(6)-C(7)	1.1(2)
C(5)-C(6)-C(7)-C(8)	-0.6(2)
C(6)-C(7)-C(8)-C(3)	-0.4(2)
C(6)-C(7)-C(8)-N(1)	179.05(14)
C(4)-C(3)-C(8)-C(7)	0.8(2)
C(2)-C(3)-C(8)-C(7)	-179.43(12)
C(4)-C(3)-C(8)-N(1)	-178.67(13)
C(2)-C(3)-C(8)-N(1)	1.05(15)
C(1)-N(1)-C(8)-C(7)	-179.15(14)
C(1)-N(1)-C(8)-C(3)	0.34(16)
O(2)-C(2)-C(9)-C(10)	-177.65(11)
C(3)-C(2)-C(9)-C(10)	-52.74(17)
C(1)-C(2)-C(9)-C(10)	60.87(16)
C(2)-C(9)-C(10)-C(11)	-127.70(16)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for $C_{11}H_{11}NO_2$ [Å and º]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2O)...O(1)#1	0.86(2)	1.96(2)	2.8209(14)	174.0(18)
N(1)-H(1N)...O(1)#2	0.846(19)	2.04(2)	2.8836(16)	173.0(17)

Symmetry transformations used to generate equivalent atoms:

#1 x+1/2,-y+3/2,-z+2 #2 x-1/2,-y+3/2,-z+2

Chapter Two

Enantioselective Additions to Fluorinated Ketones: A Platform for Studying the Interaction Between Organofluorine and a Small Molecule

"Fluorine leaves nobody indifferent; it inflames emotions be that affections or aversions. As a substituent, it is rarely boring, always good for a surprise, but often completely unpredictable."

-Manfred Schlosser, 1998[1]

2.1 Introduction

The element fluorine has been of intense interest to chemists ever since it was proposed to exist in 1810 by Humphrey Davy and André-Marie Ampére.[2] The race to be the first to isolate elemental fluorine claimed the lives of at least two chemists; many others were seriously injured. Fluorine gas proved so difficult to isolate, that some believed it to be what alchemists had termed "the universal solvent", since it seemed to react (often violently) with any material it came in contact with. It wasn't until 76 years after Davy and Ampére's proposal and "after four interruptions caused by serious poisioning" [Weeks pg. 1932] that Henri Moissan was able to isolate fluorine by electrolyzing KHF_2 in liquid HF and trapping the resultant F_2 (g) in a Pt-Ir jar sealed with

(1) Schlosser, M. *Angew. Chem. Int. Ed.* **1998**, *110*, 1496–1513. The quotation is taken from page 1497 in the manuscript.
(2) Weeks, M. E. *J. Chem. Educ.* **1932**, *9,* 1915–1939.

a stopper made of fluorite (CaF_2). Moissan would later win a Nobel Prize partly due to this work.[2]

To this day, there is much interest in the fluorine, particularly because its presence in organic molecules has a myriad of effects that have been utilized by chemists in applications ranging from material science and engineering to pharmaceuticals and agrochemicals. Most of these effects are largely due to the special properties of the C-F bond.[3]

Table 2.1 Selected Pauling Electronegativities

H	C	N	O	F	Cl
2.2	2.6	3.0	3.4	4.0	3.2

Fluorine possesses the highest electronegativity of all the elements in the periodic table (4.0 on the Pauling Scale; the next highest is oxygen with a value of 3.4, Table 2.1),[4] which makes the C-F bond unusually polarized for a covalent bond with carbon. As a result of this polarization, there is a significant electrostatic component to the C-F bond, making it the strongest single bond between carbon and another element (Table 2.2). The difference between the C-O bond strength (86 kcal/mol) and the C-F bond strength (105 kcal/mol)[5] is far higher than can be explained by just a decrease in van der Waals radii from O to F (1.52 Å to 1.47 Å)[6] leading to a stronger bond between carbon and fluorine, so there must be a substantial difference in polarization between C-F and C-O.[4] That oxygen is the second-most electronegative element and does not have nearly the ability to

(3) For an excellent review on organofluorine chemistry that is worth reading for any scholar with an interest in physical organic chemistry, see: O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308–319.
(4) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359–4369.
(5) This value is sometimes cited as 115 kcal/mol, but most sources agree on 105 kcal/mol.
(6) A common misconception is that fluorine is about the same size as hydrogen in organic molecules. While it is true that fluorine is often used as a sterically similar substitute in for hydrogen, a C-F bond is much closer to a C-O bond in size than it is to a C-H bond. See reference 4.

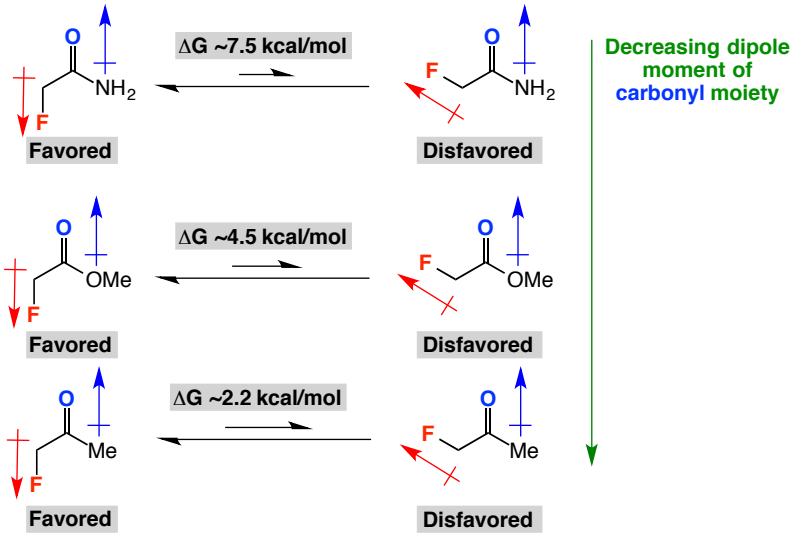
polarize a bond that fluorine does illustrates just how alien fluorine is when compared with any other element that forms covalent bonds with carbon.

Table 2.2 Selected Bond Strengths (kcal/mol) with Carbon

C-H	C-C	C-N	C-O	C-F	C-Cl
99	83	75	86	105	79

Consistent with the polarization of the C-F bond, the dipole moment between carbon and fluorine is large enough to play a noticeable role in dipole-dipole interactions.[3] The computed energetic differences between fluorine and a carbonyl being syn or anti in selected α-fluorocarbonyls is illustrative (Scheme 2.1).[7] While there is undoubtedly some detriment to the syn conformer stemming from electron-electron repulsion between fluorine and the carbonyl oxygen, the observation that the energy difference between syn and anti conformers decreases with decreasing dipole moment of the carbonyl moiety supports the importance of a dipole-dipole interaction.[3]

Scheme 2.1 Conformational Preferences of α-Fluorocarbonyls



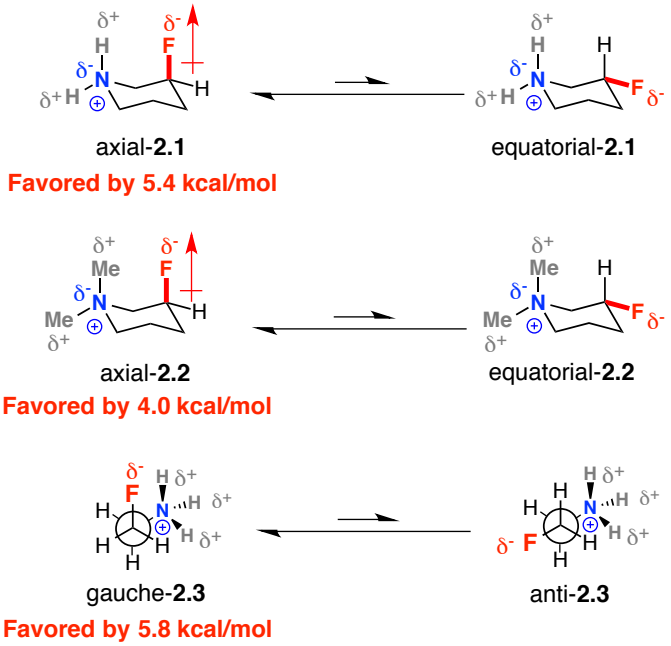
(7) (a) Banks, J. W.; Batsanov, A. S.; Howard, A. K.; O'Hagan, D.; Rzepa, H. S.; Martin-Santamaria, S. *J. Chem. Soc., Perkin Trans 2* **1999**, 2409–2411. (b) van der Veken, B. J.; Truyen, S.; Herrebout, W. A.; Watkins, G. *J. Mol. Struct.* **1993**, *293*, 55–58. (c) Abraham, R. J.; Jones, A. D.; Warne, M. A.; Rittner, R.; Tormena, C. F. *J. Chem. Soc., Perkin Trans 2* **1996**, 533–539.

A surprising consequence of the extreme electronegativity of fluorine is that when it is present in an organic molecule, unlike nitrogen and oxygen, is reluctant to act as a hydrogen-bond acceptor.[8] Whether or not fluorine participates in hydrogen-bonding[9] is currently a controversial topic in chemistry,[8] although most of the controversy seems to stem from differences in how exactly one defines a hydrogen-bond,[10] rather than from anything specifically regarding fluorine. The general consensus is that C-F can occasionally act as a hydrogen-bond acceptor, but the hydrogen bonds it forms do not have a great deal covalent character and are nearly always half or less of the strength of traditional H-bonds (~2-2.5 kcals for an F hydrogen-bond).[3] The rationale for why fluorine in organic molecules is less likely than nitrogen or oxygen to engage in hydrogen-bonding is that lone pairs of fluorine, which are needed for hydrogen-bonding, are held tightly to fluorine due to fluorine's massive electronegativity.[3]

A class of significant interactions that is known for organofluorine to participate in is charge-dipole interactions.[3] In protonated 3-fluoropiperidine **2.1**, the fluorine is observed by NMR to be exclusively in the axial position (axial-**2.1**, Scheme 2.2); the energy difference between axial-**2.1** and equatorial-**2.1**, which mainly is a result of the attraction between the protonated amine and fluorine, is calculated to be 5.4 kcal/mol.[11] Suggesting this observation is not a rare case of organofluorine hydrogen-bonding, the

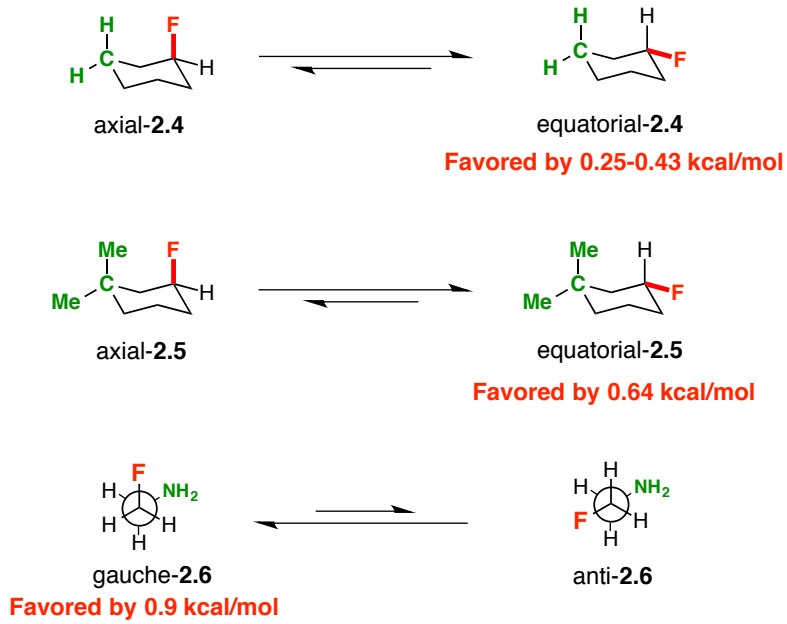
(8) (a) For a review stating that organofluorine is highly unlikely to participate in hydrogen bonding, see: Dunitz, J. D. *ChemBioChem* **2004**, *5*, 614–621. (b) For a review stating it is completely plausible for organofluorine to participate in hydrogen bonding, see: Schneider, H.-J. *Chem. Sci.* **2012**, *3*, 1381–1394.
(9) Specifically, fluorine as it exists in organofluorine compounds. Hydrogen-bonding is widely accepted to be a major interaction between molecules of hydrofluoric acid. Steiner, T. *Angew. Chem. Int. Ed.* **2002**, *41*, 48–76.
(10) A pertinent statement about definitions with regard to hydrogen-bonding has been made by Professor Gautam R. Desiraju in *Acc. Chem. Res.* **2002**, *35*, 565–573. He states, "By definition, a definition cannot be correct or incorrect. It can, however, be useful or have outlived its usefulness. It should never, in any case, hinder the study of a phenomenon because of linguistic limitations and psychological difficulties" (pg. 572).
(11) Sun, A.; Lankin, D. C.; Hardcastle, K.; Snyder, J. P. *Chem. Eur. J.* **2005**, *11*, 1579–1591.

Scheme 2.2 Charge-Dipole Interaction in Organofluorines



dimethyl piperidinium salt **2.2** also displays a large conformational preference for the fluorine to be situated axially (Scheme 2.2).[11] It is worth noting that the large axial preference observed for **2.1** and **2.2** is overcoming the inherent steric bias that similar

Scheme 2.3 Neutral Model Systems for Scheme 2.2



molecules have for the equatorial conformation (see **2.4** and **2.5** in Scheme 2.3). Further evidence for the importance of charge in these interactions is that gauche-**2.3** (Scheme 2.2) is preferred over anti-**2.3** by 5.8 kcal/mol.[12] The neutral form of this molecule (**2.6**, Scheme 2.3) also prefers a gauche conformation, in large part due to the well known gauche-effect,[13] but only by 0.9 kcal/mol.[12] Obtaining a change in magnitude from 0.9 to 5.8 kcal/mol is not consistent with simply a stronger gauche effect upon protonation of **2.6** (thus making the nitrogen substituent more electron withdrawing), indicating significant electrostatic interactions favor gauche-**2.3** over anti-**2.3**.[12] Our laboratory became interested in possibly using such interactions to dictate enantioselectivities in fluorinated substrates.

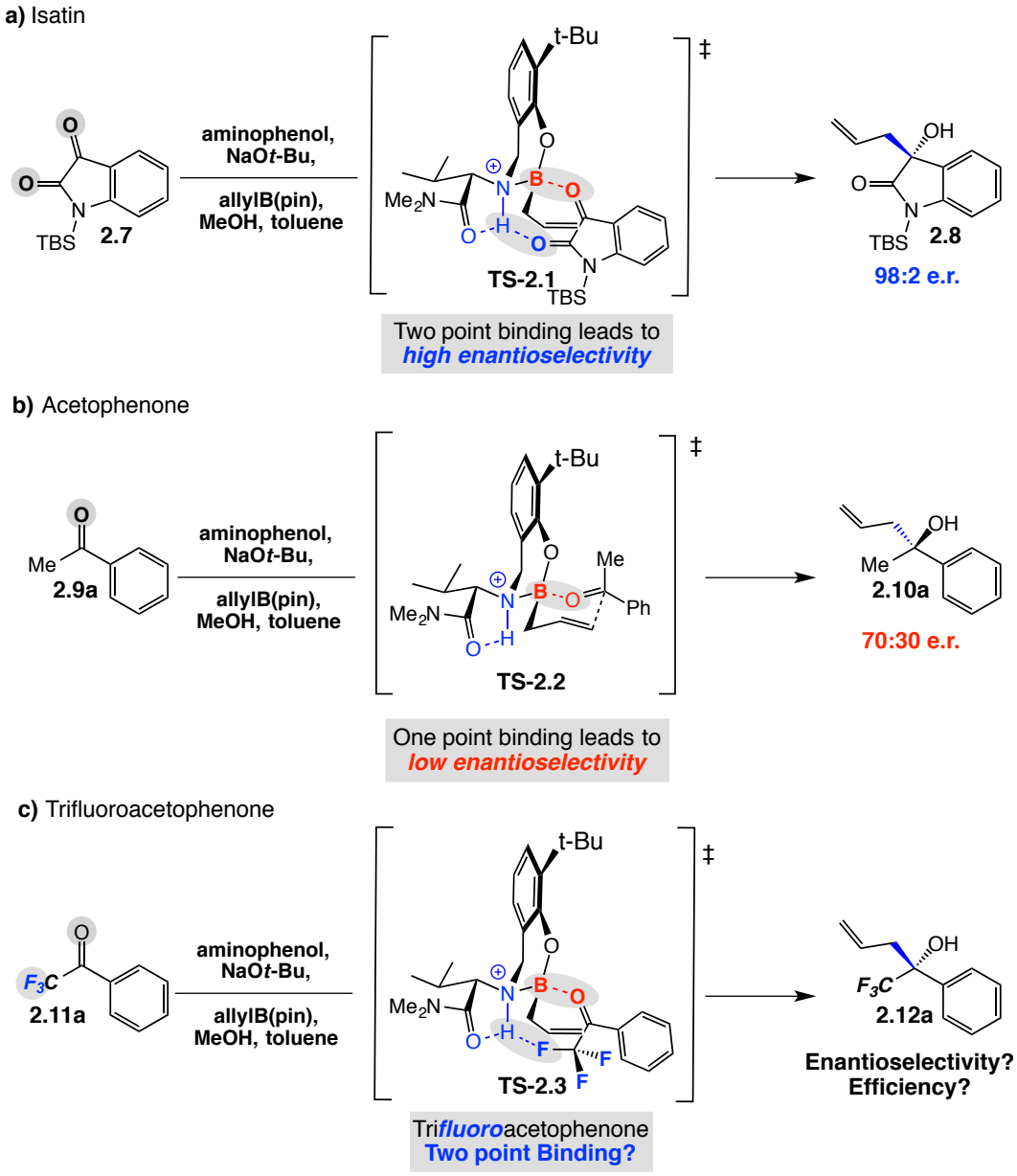
2.2 Background

In a recently published manuscript (see Section 1),[14] our proposed stereochemical model for the allyl-addition to an isatin **2.7** involves a hydrogen bonding interaction between the amide oxygen of the isatin and a proton residing in a protonated aminophenol (Scheme 2.4a). Additional support for this proposal comes from the low enantioselectivity obtained when using substrates that contain only one H-bond acceptor; one example, shown in Scheme 2.4b, is acetophenone (**2.9a**). To further probe this hypothesis, we chose to examine fluorinated substrates such as trifluoroacetophenone **2.11a** (Scheme 2.4c) with the thought that perhaps fluorine will provide the dipole for a cation- dipole interaction. Any increase in the level at which a reaction mechanism is

(12) Briggs, C. R. S.; Allen, M. J.; O'Hagan, D.; Tozer, D. J.; Slawin, A. M. Z.; Goeta, A. E.; Howard, J. A. K. *Org. Biomol. Chem.* **2004**, *2*, 732–740.
(13) For a review of this phenomenon, see: Wolfe, S. *Acc. Chem. Res.* **1972**, *5*, 102–111.
(14) Silverio, D. L.; Torker, S.; Pilyugina, T.; Vieira, E. M.; Snapper, M. L.; Haeffner, F.; Hoveyda, A. H. *Nature* **2013**, *494*, 216–221.

understood not only provides useful information regarding the reaction in question but can also illuminate fundamental principles relevant to the field of chemistry and beyond.

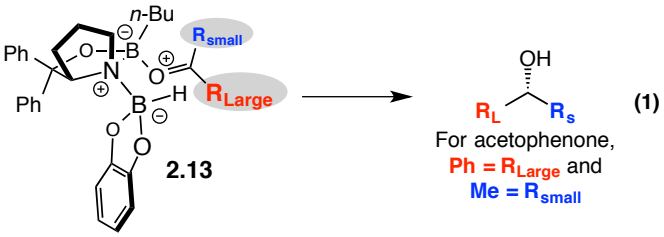
Scheme 2.4 Enantioselectivity Models for Allyl-Additions to Ketones



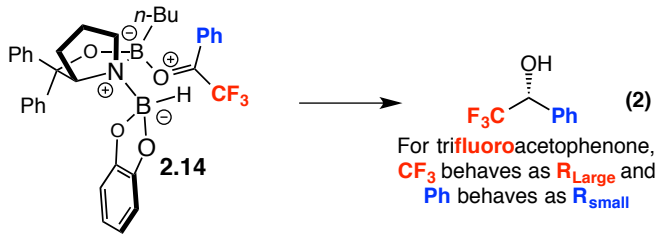
Fluorine in a substrate has been observed (or proposed) in a number of cases to greatly affect the stereoselectivity of a transformation;[15,16] however those that invoke a

(15) For a review involving this subject, see: (a) Cahard, D.; Bizet, V. *Chem. Soc. Rev.* **2014**, *43*, 135–147. For examples not included in the review, see: (b) Ojima, I.; Kwon, H. B. *J. Am. Chem. Soc.* **1988**, *110*,

fluorine-hydrogen interaction are quite scare. A notable example that does not involve such an interaction is the oxazaborolidine-catalyzed reduction of trifluoromethyl ketones.[17] Based on the model for enantioselectivity of the CBS reduction of ketones (**2.13**, Equation 1), the sterically larger substituent on the ketone points down (away from



the catalyst) and the sterically smaller substituent point up (towards the catalyst) to give the enantiomer shown in Equation 1. In the case of acetophenone, as expected by the size difference between a methyl and a phenyl group (A-values of 1.74 and 2.8 kcal/mol respectively; Charton values of 1.66 and 0.52 respectively), the reduction affords the desired product as nearly a single enantiomer of the alcohol shown in Equation 1, with the phenyl group being the large group and the methyl group being the small group. In contrast, reduction of trifluoroacetophenone affords the opposite relative enantiomer to acetophenone (and in high e.r.), implying that now the phenyl group is the small group



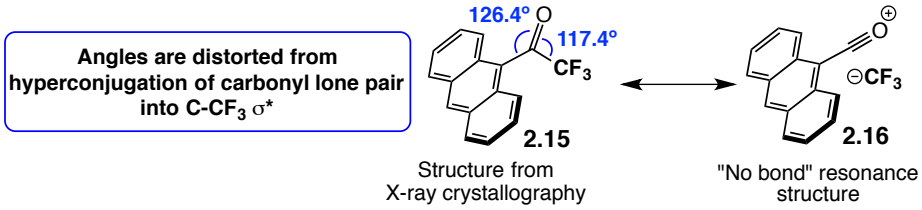
5617–5621. (c) Soloshonok, V. A.; Hayashi, T. *Tetrahedron Lett.*, **1994**, *35*, 2713–2716. (d) Soloshonok, V. A.; Avilov, D. V.; Kukhar, V. P. *Tetrahedron*, **1996**, *38*, 12433–12442. (e) Katagiri, T.; Yamaji, S.; Handa, M.; Irie, M.; Uneyama, K. *Chem. Commun*. **2001**, 2054–2055.

(16) Incorporation of fluorine into a catalyst can also greatly change enantioselectivity. For a review of this growing field, see: Zimmer, L. E.; Sparr, C.; Gilmour, R. *Angew. Chem. Int. Ed.* **2011**, *50*, 11860–11871.

(17) (a) Corey, E. J.; Link, J. O.; Bakshi, R. K. *Tetrahedron Lett.* **1992**, *47*, 7107–7110. (b) Corey, E. J.; Link, J. O.; Sarshar, S.; Shao, Y. *Tetrahedron Lett.* **1992**, *47*, 7103–7106.

and the trifluoromethyl group is the large group (Equation 2).[17a] This result is surprising, since traditional steric parameters suggest that a phenyl substituent is sterically larger group than a trifluoromethyl substituent (A-values of 2.8 and 2.45 kcal/mol respectively; Charton values of 0.91 and 1.66 respectively). Professor Corey explains this anomaly by invoking hyperconjugation from the carbonyl lone pair into the C–CF_3 σ* resulting in a decreased angle between the carbonyl and the CF_3 group (illustrated by the "no bond' resonance structure **2.16** in Figure 2.1), which effectively shields the carbonyl lone pair

Figure 2.1 Rationale for Catalyst Coordination to Lone Pair Anti to CF_3 Group

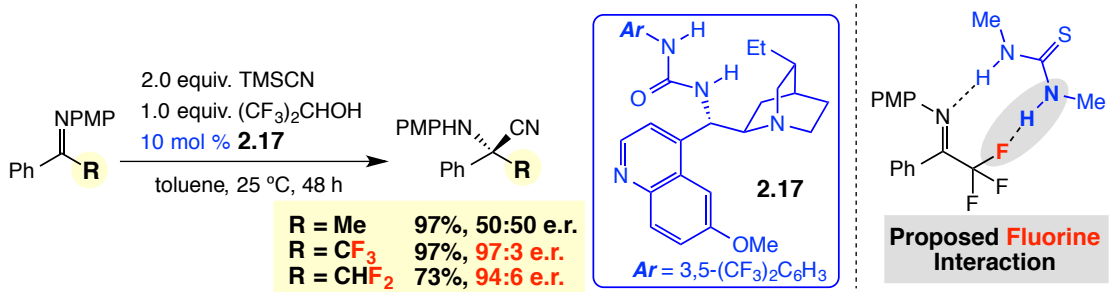


syn to the CF_3 from binding to the catalyst. This hypothesis is supported by the X-ray crystal structure of 9-trifluoroacetyl anthracene **2.15** (a substrate which is undergoes catalytic enantioselective reduction to afford the corresponding tertiary alcohol in 97:3 e.r) that shows a highly distorted angle of 126.4º between the ketone and the anthracene group, as well as a 117.4º angle between the carbonyl and the trifluoromethyl group (Figure 2.1).[18]

A fluorine-hydrogen bond is proposed to explain the large difference between fluorinated and non-fluorinated substrates in a Strecker reaction of ketimines catalyzed

(18) For similar observations that enantioselective reduction of 2,2,2-trifluoromethylacetophenones is highly selective for the opposite relative enantiomer of acetophenone, see: (a) Ramachandran, P. V.; Teodorovic´, A. V.; Gong, B.; Brown, H. C. *Tetrahedron: Asymmetry* **1994**, *5*, 1075–1086. (b) Ramachandran, P. V.; Gong, B.; Teodorovic´, A. V. *J. Fluorine Chem.* **2007**, *128*, 844–850. For a catalytic enantioselective aldol reaction where a major change in stereoselectivity occurs when the substrate is changed from benzaldehyde to pentafluorobenzaldehyde, see reference 15c.

Scheme 2.5 Proposed Fluorine-Hydrogen Interaction in Catalytic Strecker Reaction

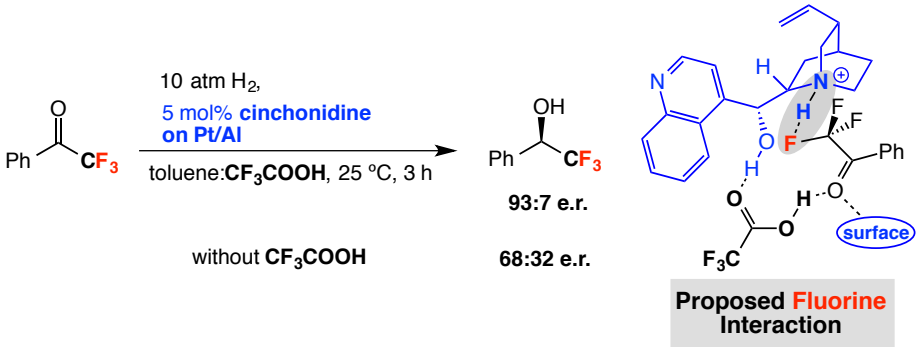


by urea-quinidine containing **2.17** (Scheme 2.5).[19] Ketimines bearing a trifluoro- or difluoromethyl undergo cyanide-addition enantioselectively (>94:6 e.r.), but those without such fluorination afford racemic products under identical conditions. The authors note that thioureas without a Lewis-basic quinidine moiety are not competent catalysts (<5% conv. in five days) for the addition of TMSCN to fluorine containing ketimines (R=CF_3 or CF_2H, Scheme 2.5), but do promote addition to the ketimine where R=Me (48% yield). The authors propose that the Lewis basic nitrogen from the quinidine-derived section of the catalyst is critical for activating the TMSCN. To explain the impact of fluorination, the authors hypothesize one proton of the urea binds to the imine nitrogen while the other binds to the fluorine. Density functional theory (DFT)-based calculations support this rare fluorine-hydrogen bond, but it should be noted that these calculations were performed using a simplified dimethylthiourea catalyst (Scheme 2.5) that, since it does not contain a quinidine moiety, likely will not promote the addition to the fluorinated substrates. As the acidic hexafluoroisopropanol additive does not affect the enantioselectivity of the transformation (it is added to increase conversion), it is unlikely that a protonated catalyst interacting with fluorine through a charge-dipole interaction is significant in determining the stereochemical outcome of the addition.

(19) Liu, Y.-L.; Shi, T.-D.; Zhou, F.; Zhao, X.-L.; Wang, X.; Zhou, J. *Org. Lett.* **2011**, *13*, 3826–3829.

A fluorine-hydrogen interaction has also been speculated to be important in the enantioselective reduction of trifluoroacetophenone catalyzed by a Pt/Al surface impregnated with cinchonidine (Scheme 2.6).[20] When the reduction is carried out in the

Scheme 2.6 Proposed Fluorine-Hydrogen Interaction in Catalytic Hydrogenation



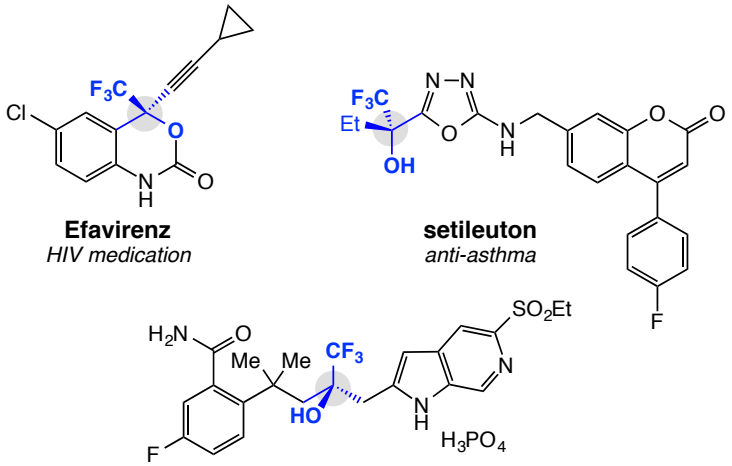
presence of trifluoroacetic acid, the desired alcohol is obtained in 93:7 e.r. Omitting the acid causes the enantiomeric ratio to significantly drop to 68:32. One proposal explaining this change in enantioselectivity is that trifluoroacetic acid protonates the cinchonidine, and this has a charge-dipole interaction with the fluorine of the substrate that favors the observed enantiomer. There are many other proposals for this transformation, and the mechanism is still very much under debate.[21] Even with little precedence, we were interested in examining the possibility of an F-H interaction in our system.

In addition to giving information about the interplay between fluorine and an ammonium cation in the stereochemistry-determining step, developing the enantioselective allyl- and allenyl-addition to fluorinated ketones is a worthwhile synthetic endeavor, in large part due to the utility of fluorine in biologically active molecules. Approximately 20% of all pharmaceuticals, as well as ~30% of all

(20) Szőri, K.; Balázsik, K.; Crerényi, S.; Szőllősi, G.; Bartók, M. *Appl. Catal., A* **2009**, *362* 178–184.
(21) For a reference that summarizes this debate while suggesting this fluorine interaction, while possible, is not the most likely scenario, see: Pereñiguez, R.; Santarossa, G.; Mallat, T.; Baiker, A. *J. Mol. Catal. A: Chem.* **2012**, *365*, 39–49.

agrochemicals, contain fluorine.[22] Compared with nitrogen which appears in ~90% of all pharmaceuticals (see discussion in Section 1.1), this may not seem like a lot, but whereas nitrogen is also ubiquitous in biology (and therefore can be expected to reside in biologically active molecules), there are only thirteen known natural products containing fluorine.[23]

Scheme 2.7 Biologically Active Compounds Containing a Trifluoromethyl Substituted Tertiary Alcohol



Structural incorporation of fluorine is well established to have a variety of beneficial effects in compounds of pharmaceutical significance.[24] In particular, trifluoromethyl[25]-substituted tertiary alcohols are contained in many biologically active molecules, such as HIV medicine Efavirenz,[26] anti-asthma molecule setileuton,[27] and

(22) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881–1886.
(23) Bégué, J.-P.; Delpon-Bonnet, D. *Bioorganic and Medicinal Chemistry of Fluorine*; John C. Wiley and Sons: Hoboken, New Jersey, United States, **2008**.
(24) For reviews/books detailing reasons why fluorine has these effects as well a specific examples, see references 4, 22, and 23 as well as (a) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320–330. (b) *Fluorine in Pharmaceutical and Medicinal Chemistry: From Biophysical Aspects to Clinical Applications*; Gouverneur, V., Müller, K., Eds.; Imperial College Press: London, **2012**. (c) Böhm, H.-J. *et al. ChemBioChem* **2004**, *5*, 637–643. (d) Smart, B. E. *J. Fluorine Chem.* **2001**, *109*, 3–11. (e) Filler, R.; Saha, R. *Future Med. Chem.* **2009**, *1*, 777–791. (f) Wang, J. *et al. Chem. Rev.* **2014**, *114*, 2432–2506.
(25) For a review on the trifluoromethyl group in new pharmaceuticals, see: W. Zhu, et al., J. Fluorine Chem. (2014), http://dx.doi.org/10.1016/j.jfluchem.2014.06.026 *In Press*
(26) Muchiri, J. M., Li, D., Dykes, C., & Bambara, R. A. *Biochemistry* **2013**, *52*, 4981–4990.

non-steroidal anti-inflammatory compound BI 653048 BS H_3PO_4 (Scheme 2.7).[28] In all cases, the stereochemistry of the trifluoromethyl-substituted tertiary alcohol is critical to the biological activity. Allyl and allenyl groups can be reliably transformed into various functional groups[29,30] and therefore, a method for the efficient and practical synthesis of trifluoromethyl-substituted tertiary homoallyl- and homoallenylalcohols is valuable.

Unfortunately, even though many enantioselective allyl-additions to ketones are known,[29] very few of them study 2,2,2-trifluoromethylacetophenone.[31] The three extant reports afford products in ≤ 90:10 e.r. and require 0.3–2.0 equivalents of indium as well as at least that much of the chiral ligand (Schemes 2.8–2.10).[32] Enantioselective allenyl-additions to trifluoromethyl ketones are completely unknown to the best of our knowledge.

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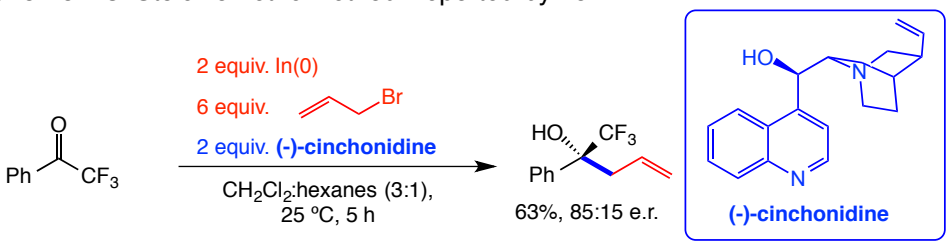
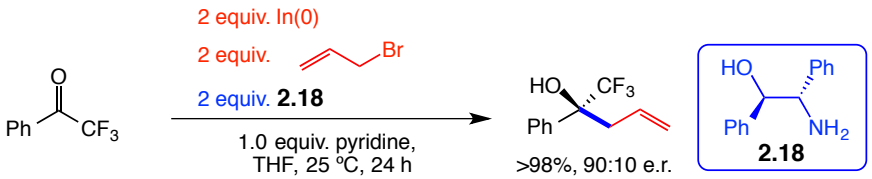
(27) Ducharme, Y. *et al. ACS Med. Chem. Lett.* **2010**, *1*, 170–174.
(28) Reeves, J. T. *et al. J. Org. Chem.* **2013**, *78*, 3616–3635.
(29) For allyl groups, see: (a) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774–7854. (b) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2013**, *113*, 5595–5698.
(30) *Modern Allene Chemistry*, Krause, N., Hashmi, A. S. K., Eds; Wiley−VCH: Weinheim, Germany, **2004**.
(31) There are many more reports of enantioselective ene reactions to generate trifluoromethyl-substituted tertiary homoallylalcohols, but the substrates in these methods are restricted to extremely electrophilic trifluoromethyl pyruvates (a) Mikami, *et al. Tetrahedron: Asymmetry* **2004**, *15*, 3885–3889. (b) Aikawa, K.; Kainuma, S.; Hatano, M.; Mikami, K **2004**, *45*, 183–185. (c) Mikami, K.; Kakuno, H.; Aikawa, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 7257–7260. (d) Aikawa, K.; Miyazaki, Y.; Mikami, K. *Bull. Chem. Soc. Jpn.* **2012**, *85*, 201–218. (e) Doherty, S.; Knight, J. G.; Smyth, C. H.; Harrington, S. W.; Clegg, W. *J. Org. Chem.* **2006**, *71*, 9751–9764. (f) Doherty, S.; Knight, J. G.; Smyth, C. H.; Harrington, S. W.; Clegg, W. *Organometallics* **2007**, *26*, 6453–6461. (g) Doherty, S.; Knight, J. G.; Mehdi-Zodeh, H. *Tetrahedron: Asymmetry* **2012**, *23*, 209–216. (h) Clarke, M. L.; Jones, C. E. S.; France, M. B. *Beilstein J. Org. Chem.* **2007**, *3*, No. 24. (i) Rueping, M.; Theissmann, T.; Kuenkel, A.; Koenigs, R. M. *Angew. Chem. Int. Ed.* **2008**, *47*, 6798–6801. (j) Rueping, M.; Bootwicha, T.; Kambutong, S.; Sugiono, E. *Chem. Asian J.* **2012**, *7*, 1195–1198. (k) Luo, H.-K. *et al. Adv. Synth. Catal.* **2010**, *352*, 1356–1364. (l) Zhao, J. F.; Tan, B. H.; Zhu, M. K.; Tjan, T. B. W.; Loh, T. P. *Adv. Synth. Catal.* **2010**, *352*, 2085–2088. (m) Zheng, K. *et al. Chem. Eur. J.* **2010**, *16*, 9969–9972. (n) Didier, D.; Schulz, E. *ChemCatChem* **2011**, *3*, 1880–1884.
(32) (a) Loh, T.-P.; Zhou, J.-R.; Li, X.-R. *Tetrahedron Lett.* **1999**, *40*, 9333–9336. (b) Zhang, X.; Chen, D.; Liu, X.; Feng, X. *J. Org. Chem.* **2004**, *72*, 5227–5233. (c) Haddad, T. D.; Hirayama, L. C.; Singaram, B. *J. Org. Chem.* **2010**, *75*, 642–649.

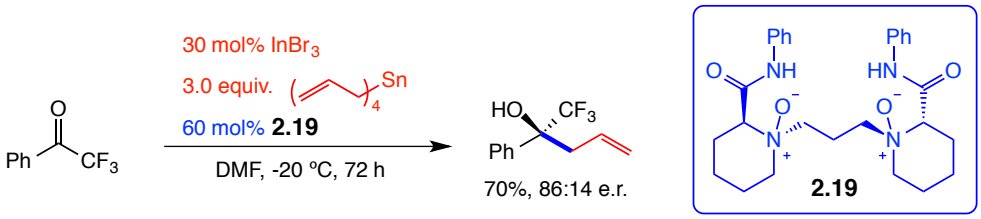
Scheme 2.8 Stoichiometric Method Reported by Loh



Scheme 2.9 Stoichiometric Method Reported by Singaram

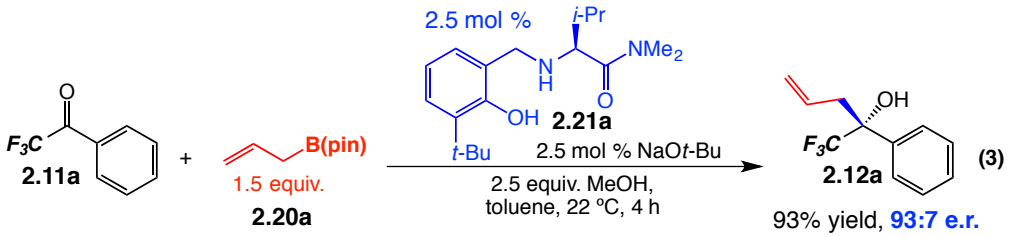


Scheme 2.10 Catalytic Method Reported by Feng



2.3 Development and Scope of Enantioselective Allyl-Additions to Perfluoroalkyl Ketones

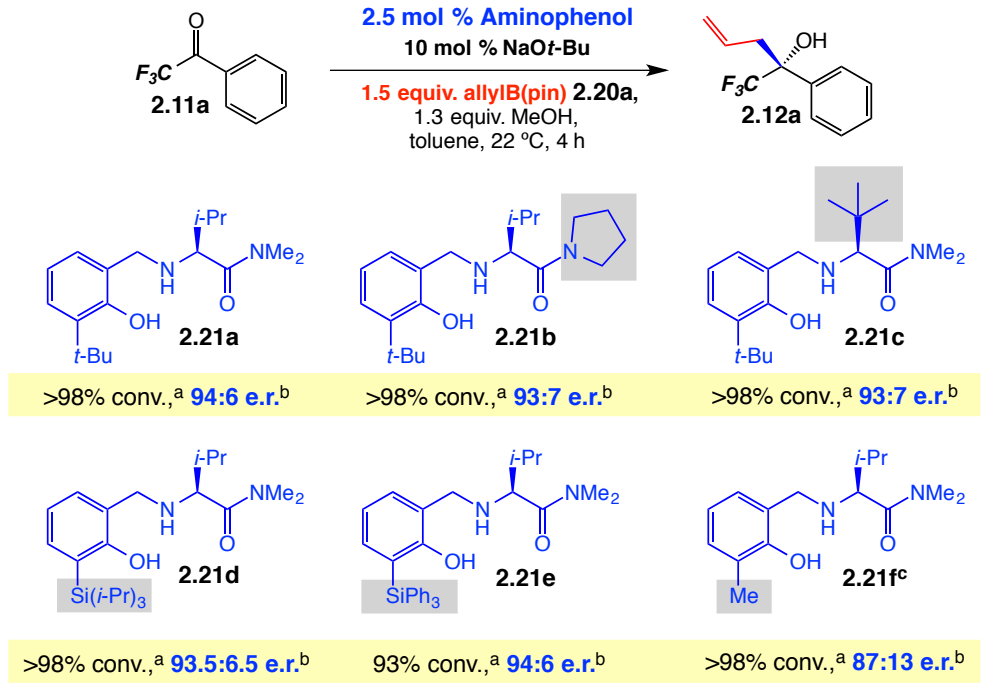
Performing the enantioselective addition of allylboronic acid pinacol ester **2.20** to trifluoroacetophenone **2.11a** under essentially the same conditions employed for additions to aldimines (see Chapter 1) generates chiral tertiary alcohol **2.12a** in 93% yield and 93:7 e.r. (Equation 3). Using what was learned in the synthesis of



homoallylamide **1.21k** (Chapter 1, Section 1.4, Table 1.7), increasing the amount of NaO*t*-Bu to 10 mol % boosts the enantiomeric ratio to 94:6 without causing any

deleterious side effects. Increasing the amount of base further (as high as 20 mol %) did not greatly change the outcome of the reaction. Making the method more practical, reduction in the amount of allylB(pin) to 1.1 equivalents and the amount of methanol to 1.3 equivalents led to no noticeable change in efficiency or enantioselectivity. We next carried out an investigation of the structure of the aminophenol.

Scheme 2.10 Screening of Aminophenols



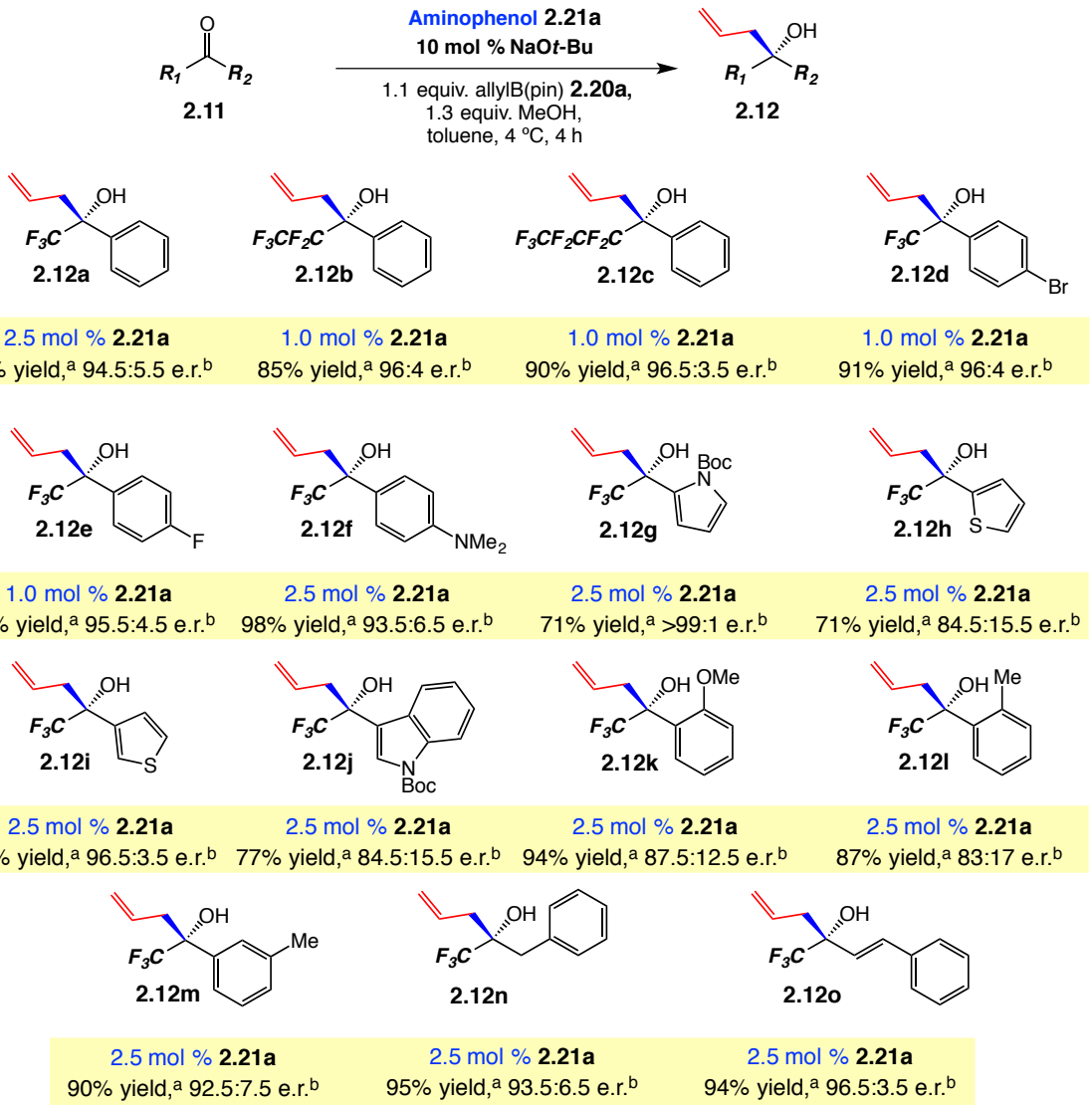
[a]Consumption of starting material as determined by 376 MHz ^{19}F analysis of the unpurified reaction mixture. [b]Determined by HPLC analysis. [c]Reaction performed at 4 °C.

Changing the structure of aminophenol **2.21a** led to no major differences in the resulting transformation, with the exception the shrinking the size of the substituent *ortho* to the phenol from a *tert*-butyl group (**2.21a**) to a methyl group (**2.21f**) afforded the homoallyl alcohol **2.12** in noticeably diminished enantiomeric enrichment (Scheme 2.10). Moving forward with initial aminophenol **2.21a** as optimal, we next cooled the reaction in efforts in increase enantioselectivity. A reaction temperature of 4 °C slightly increased the enantiomeric ratio to 94.5:5.5 while maintaining full conversion to product in only

four hours. Cooling the reaction further to -15 ºC gave the desired product in 95:5 e.r., but the reaction requires 18 hours to reach completion. Following this optimization, we then probed how the transformation behaves as the substrate is modified.

Aminophenol **2.21a** also promotes selective allyl addition to pentafluoroethyl phenyl ketone **2.11b** and heptafluoropropyl phenyl ketone **2.11c** with even greater levels of efficiency and enantioselectivity than to **2.11a** (Scheme 2.11). Both electron

Scheme 2.11 Substrate Scope of Allyl-Addition to Perfluoroalkyl Ketones

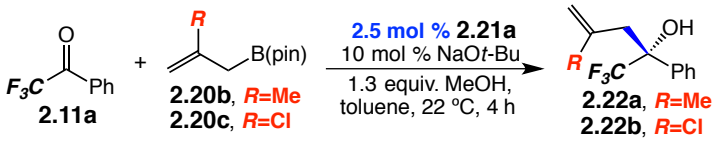


All data are the average of at least two experiments. [a]Yield of isolated product. [b]Determined by HPLC analysis.

withdrawing and donating groups are tolerated (**2.11d–f**) as well as Boc-protected pyrrole **2.11g**.[33] Sterically hindered substrates **2.11j** to **2.11m** afford products in lower levels of enantioselectivity (Scheme 2.11). This drop in selectivity may be due to an increase of the steric repulsion between the aromatic group of the substrate and the *tert*-butyl group of the catalyst in **TS-2.3** (Scheme 2.4) resulting in a TS similar to **TS-2.2** becoming more competitive (see Section 2.5 for a discussion). The increase in selectivity observed for the addition to 3-thiophene trifluoromethyl ketone **2.11i** compared with **2.12h** potentially suggests a sulfur-ammonium interaction competing with the F-H cation-dipole interaction since the sulfur in less selective **2.11h** is well situated to have such an interaction while the sulfur in **2.11i** is much too far away from the ammonium of the catalyst to do so. Trifluoromethyl ketones substituted bearing an α,β-unsaturated or an alkyl group underwent catalytic, enantioselective allyl addition in ≥ 94% yield and ≥93.5:6.5 e.r. to afford homoallyl alcohols **2.12n** and **2.12o**.

To further increase the synthetic scope of the method, we next examined different boronate nucleophiles. Increasing the reaction temperature to 22 ºC (and in the case of

Table 2.3 Enantioselective Additions of Substituted Allylboronates



entry	boronate (equiv.)	conv. (%)[a]; yield (%)[b]	e.r.[c]
1	**2.20b** (1.4)	>98; 85	97.5:2.5
2	**2.20c** (1.1)	>98; 96	96.5:4.5

All data are the average of at least two experiments. [a]Conversion to the desired product as measured by analysis of 376 MHz ^{19}F NMR spectra of unpurified mixtures vs. an internal standard of trifluorotoluene. [b]Yield of isolated product. [c]Determined by HPLC analysis.

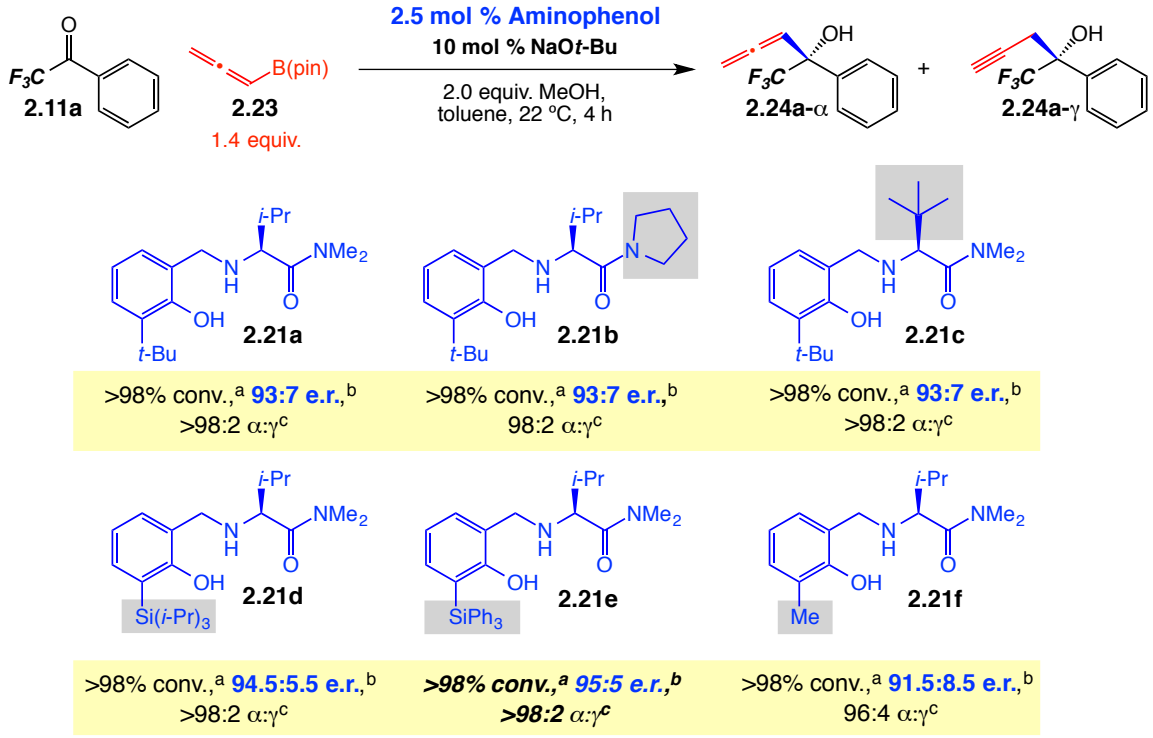
(33) Without the Boc group, the reaction did not proceed (<2% conversion to product).

methallylboronic acid pinacol ester **2.20b**, increasing the amount of **2.20b** to 1.4 equiv.) allows for the addition of 2-substituted allylboronates to trifluoroacetophenone **2.11a** in four hours with at least 96.5:3.5 e.r. (Table 2.3). Even the electron withdrawing and sterically encumbered chloride of boronate **2.20c** did not slow down this transformation (entry 2).

2.4 Development and Scope of Enantioselective Allenyl-Additions to Perfluoroalkyl Ketones

Changing the nucleophile to allenylboronic acid pinacol ester (**2.23**, Scheme 2.12) resulted in a reaction that was more than 98% regioselective for homoallenyl alcohol **2.24a**-α (addition of **2.23** to ketone **2.11a** in an α-selective manner) versus

Scheme 2.12 Screening of Aminophenols for Enantioselective Allene-Addition

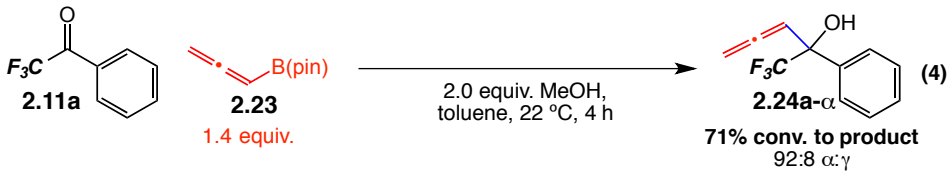


[a]Consumption of starting material as determined by 376 MHz ^{19}F analysis of the unpurified reaction mixture. [b]Determined by HPLC analysis. [c]Determined by 376 MHz ^{19}F analysis of the unpurified reaction mixture.

homopropargyl alcohol **2.24a**-γ (addition of **2.23** to ketone **2.11a** in a γ-selective manner).[34] Efforts to increase the enantioselectivity of this transformation by decreasing the reaction temperature were unsuccessful, so we carried out a screening of aminophenols in an attempt to raise this selectivity (Scheme 2.12).

We first changed the amide terminus of the aminophenol to a more Lewis basic pyrrolidinyl amide **2.21b**, which results in negligible change in the transformation. Use of *tert*-leucine derived **2.21c** also leads to an essentially identical reaction. By increasing the size of the group ortho to the phenol to triphenylsilyl (**2.21d**) and triisoproylsilyl (**2.21e**), the enantioselectivity of the desired product is increased. It is worth noting again that aminophenol **2.21e** does not lead to higher enantioselectivities for the allyl-addition (Scheme 2.10). Exchanging the *tert*-butyl group for a smaller methyl group in **2.21f** produced the product somewhat inferior enantio- and regioselectivity.

Decreasing the amount of methanol and allenylboronic acid pinacol ester **2.23** not only still resulted in >98% conversion after four hours, it also caused a slight increase in the enantiomeric enrichment of **2.24a**-α (Scheme 2.13), possibly due to decreasing the

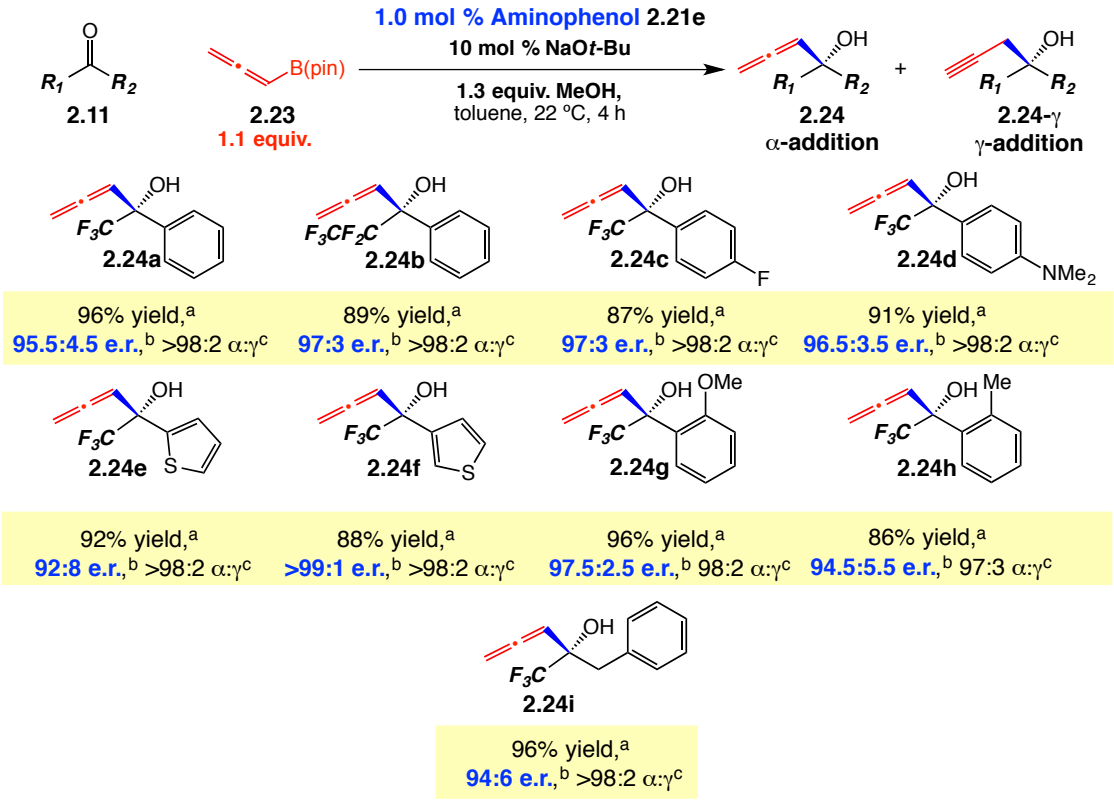


advantageous background reaction (Equation 4). The loading of **2.21e** can be decreased to 1.0 mol % without negatively affecting the transformation.

Examination of a range of substrates (Scheme 2.13) showed that this reaction

(34) It is worth noting that order of addition matters for this regioselectivity. The data shown in this manuscript for allenyl-addition are all performed with the allenylB(pin) being added to the reaction mixture last. When the ketone substrate is added last, α:γ ratio is ~93:7.

Scheme 2.13 Substrate Scope of Allenyl-Addition to Perfluoroalkyl Ketones



All data are the average of at least two experiments. [a]Yield of isolated product. [b]Determined by HPLC analysis.[c]Determined by 400 MHz ^{1}H analysis of the isolated product.

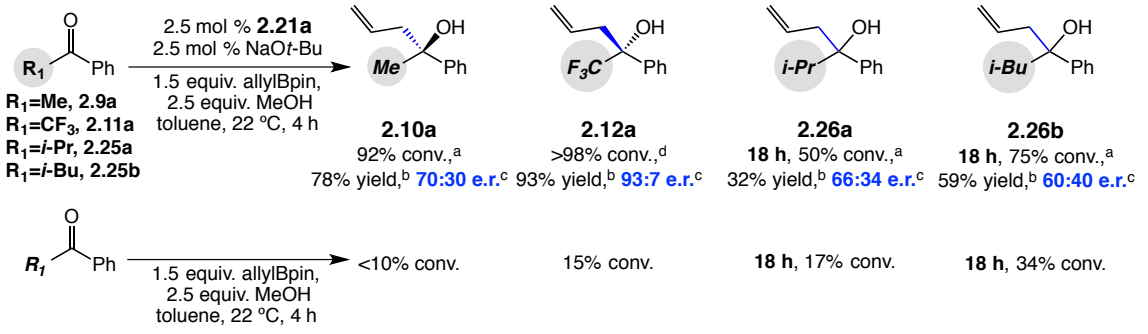
occurs selectively and efficiently to afford pentafluoroethyl-substituted **2.24b** and trifluoromethyl-substituted alcohols containing electronically modified aryl-rings (**2.24c** to **2.24d**). Similar to the allyl additions (Scheme 2.11), a drop in enantioselectivity is observed when 2-trifluoroacetylthiophene is the electrophile (yielding **2.24e** in 92:8 e.r.), but 3-trifluoroacetylthiophene leads to the desired product **2.24f** in >99:1 enantiomeric ratio (Scheme 2.13). Unlike for the enantioselective allyl additions, trifluoromethyl ketones bearing *ortho*-substituents underwent enantioselective allenyl-addition with approximately no drop in selectivity (**2.24g** and **2.24h**, Scheme 2.13). Since the sterically hindered substrates lead to no drop in enantioselectivity, while 2-trifluoroacetylthiophene does lead to such a decrease, the idea is supported that the low enantioselectivity for

observed in **2.24e** (and **2.21h**, Scheme 2.11) is due to an interaction of sulfur with the catalyst rather than unfavorable sterics. Additionally, alkyl-substituted (**2.24i**) homoallenyl alcohol is obtained in 96% yield and 94:6 e.r.

2.5 Mechanistic Investigations

Following the development of methods for enantioselective allyl- and allenyl-addition to perfluoroalkyl-substituted ketones, we focused on studying the mechanism, specifically the proposed charge-dipole interaction between the substrate and the catalyst (Scheme 2.4). The difference in both the sense and magnitude of enantioselectivity between homoallyl alcohols **2.10** (Scheme 2.14) and **2.12a** (Scheme 2.14) led us to consider what impact on molecular properties changing the methyl group in ketone **2.9** for a trifluoromethyl group in **2.11a** has. First, a trifluoromethyl group is sterically much larger (between the size of a isopropyl and isobutyl group)[24d] than a methyl group. We did not believe that this increases in steric demand (and thus, decrease in the steric

Scheme 2.14 Examination of Enantioselectivity Versus Steric Hindrance of the Substrate



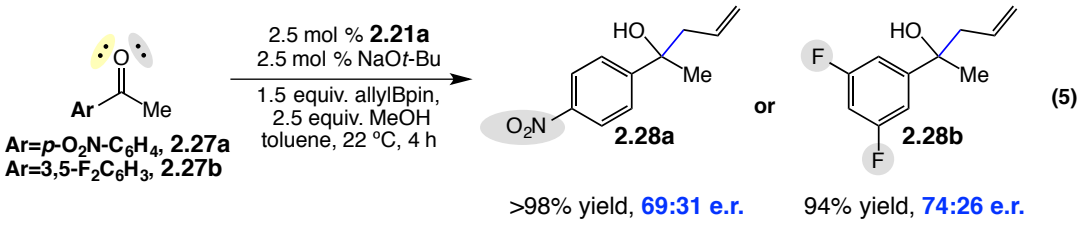
	Ph	Me	CF_3	i-Pr	i-Bu
A-values (kcal/mol):	2.8	1.74	2.45	2.21	n.d.
Charton-values:	1.66	0.52	0.91	0.76	0.98

A more sterically hindered substrate does not lead to higher stereoselectivity.

All data are the average of at least two experiments. [a]Determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture vs. an internal standard of 9-methylanthracene. [b]Yield of isolated product. [c]Determined by HPLC analysis. [d]Determined by 376 MHz ^{19}F analysis of the unpurified reaction mixture vs. an internal standard of α,α,α-trifluorotoluene.

difference between the two substituents of the ketone) was the explanation for the higher stereoselectivity for the allyl-addition to **2.12a**. When we examined the sterically bulky isobutyrophenone **2.25a** or isovalerophenone **2.25b**, we obtained the desired homoallyl alcohols (Scheme 2.14) in at most 66:34 e.r. which suggests increased sterics alone does not explain the high enantioselectivity of **2.12a**. While the lower reactivity of **2.25a** and **2.25b** raises the question of whether the low selectivity is due to a competitive background reaction, control reactions suggest this is not the case (Scheme 2.14, data below the catalytic reactions).

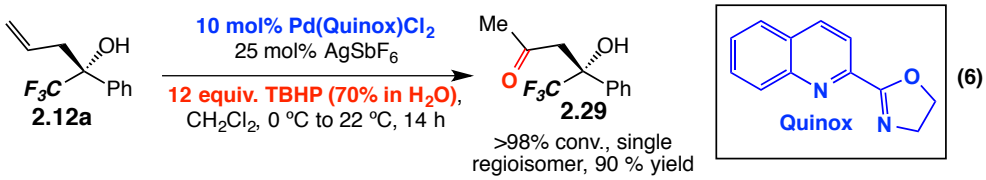
Second, a trifluoromethyl group is more electron withdrawing than a methyl group and therefore allows for better hyperconjugation of the lone pair of the carbonyl into the C-CF_3 σ* orbital. This in turn decreases energy of the lone pair anti to the trifluoromethyl group, which may impact binding of the substrate to the catalyst. Probing whether or not an electron-withdrawing group would affect the enantioselectivity, we performed the enantioselective allyl addition to electron-poor acetophenones **2.27a** and **2.27b** (Equation 5). That the enantiomeric enrichment of the resulting homoallyl alcohols



is not notably different than acetophenone suggests the difference in electronics between CF_3 and Ph is not the major factor in determining enantioselectivity in enantioselective additions to trifluoromethyl acetophenone using an aminophenol-based catalyst.

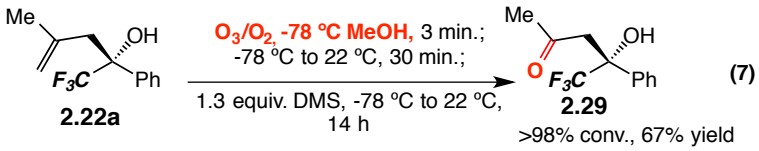
2.5.1 Mechanistic Investigations-Stereochemical Proofs

Critically important to proposing a compelling enantioselectivity model is determining the absolute configuration for the allyl- and allenyl-additions to trifluoroacetophenone **2.11a**. After attempting multiple other derivatizations of the **2.12a**, a Wacker oxidation, using conditions developed by the laboratory of Professor Sigman,[35]



(6)

afforded β-keto alcohol **2.29** in 90% yield (Equation 6). Under other Wacker conditions, a 2:1 ratio of desired ketone **2.29** to the undesired regioisomeric aldehyde is obtained.[36] Comparing both the enantiomerically enriched HPLC trace and the specific rotation of **2.29** with data in the literature[37] proved the stereochemistry of **2.12a** to be (*R*), consistent with the model we propose in Scheme 2.4. The product of methallyl-addition to trifluoroacetophenone, **2.22a**, the relative stereochemistry of which we assume to be the



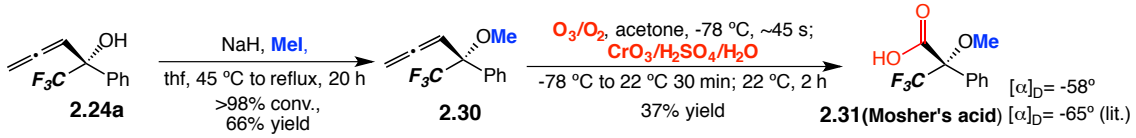
(7)

same as **2.12a**, can be converted to **2.29** (Equation 7). Further supporting our stereochemical assignment of **2.12a**, the methallyl-addition product **2.22a** is also confirmed to be (*R*) by its specific rotation and its enantiomerically enriched HPLC trace.

Determination of the absolute stereochemistry of the allene-addition product **2.24a**-α was accomplished by converting the homoallenyl alcohols to Mosher's acid over

(35) McCombs, J. R.; Michel, B. W.; Sigman, M. S. *J. Org. Chem.* **2011**, *76*, 3609–3613.
(36) Vlad, P., Gorincioi, E.; Aricu, A.; Barba, A.; Manzocchi, A.; Santaniello, E. *Tetreahedron:Asymmetry*, **2010**, *21*, 2108–2116.
(37) Duangdee, N.; Harnying, W.; Rulli, G.; Neudörfl, J.-M.; Gröger, H.; Berkessel, A. *J. Am. Chem. Soc.* **2012**, *134*, 11196–11205.

Scheme 2.15 Proof of Absolute Stereochemistry for **2.24a**



three steps (Scheme 2.15).[38] The large negative value of the specific rotation is consistent with the (*S*) enantiomer of Mosher's acid,[39] which proves the stereochemistry of **2.24a** to be (*R*) and therefore the same relative configuration as allyl-addition product **2.12a**.

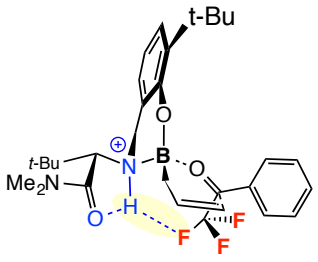
2.5.2 Mechanistic Investigations-Computational Studies

The proposed cation-dipole interaction between the organofluorine of the substrate and the proton of the catalyst was investigated both computationally[40] and by modification of the ketone substrate. The aminophenol derived from L-*tert*-leucine **2.21c** (Scheme 2.10) was modeled instead of **2.21a** due to fewer possible conformers present in **2.21c** (Scheme 2.16). For addition to trifluoroacetophenone, DFT calculations point to transition state **TS-2.4** as the lowest energy transition state for the observed enantiomer (Scheme 2.16a) and **TS-2.6** to be the lowest energy transition state for the minor enantiomer (Scheme 2.16b). Congruent with our hypothesis, the lowest energy transition state **TS-2.4** contains a F-H distance of only 2.06 Å, which is within the van der Waals radius of these nuclei (1.20 Å for H, 1.47 Å for F). Moving the CF_3 group away from the ammonium results in **TS-2.5** which is 4.0 kcal/mol higher in energy than **TS-2.4**, both because of a lack of the stabilizing cation-dipole interaction as well as steric repulsion between the *t*-Bu group *ortho* to the phenol of the catalyst and the phenyl group of the substrate (Scheme 2.16a). Transition state **TS-2.6**, the lowest in energy for the minor

(38) Chong, J. M.; Loewith, R. *Synth. Comm.* **1993**, *23*, 2145–2150.
(39) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.
(40) Calculations were carried out by Dr. Fredrik Haeffner.

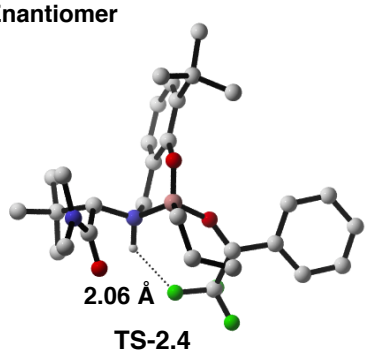
Scheme 2.16 Calculated Stereochemical Models for Allyl-Addition to **2.11a**

a. Transition State Leading to the *R* (Major) Enantiomer

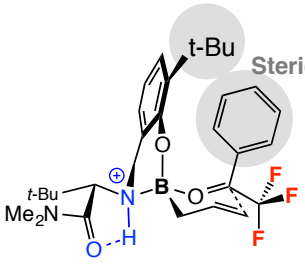


TS-2.4

0.0 kcal/mol



TS-2.4

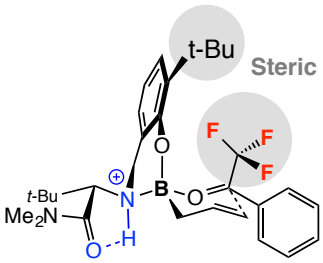


TS-2.5

+4.0 kcal/mol

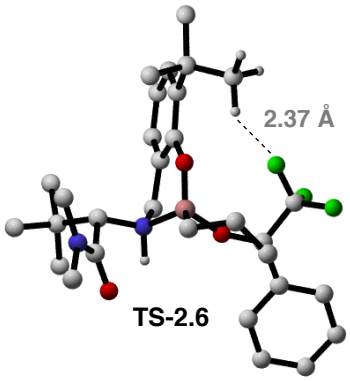
Please Note: The energy of **TS-2.4** is used as a zero point reference

b. Transition States Leading to the *S* (Minor) Enantiomer

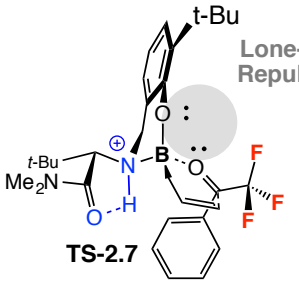


TS-2.6

+2.0 kcal/mol



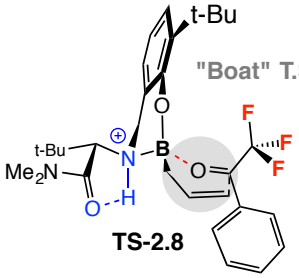
TS-2.6



TS-2.7

Too high in energy

Calculations always relax to **TS-2.8**



TS-2.8

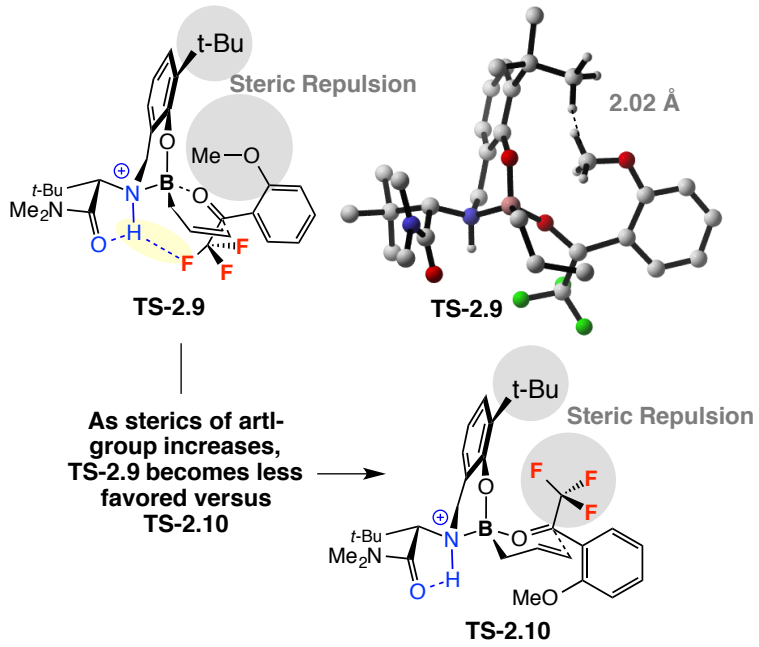
+5.9 kcal/mol

Calculations carried out with b3lyp/6-31G** and pcm=toluene

enantiomer, is disfavored due to the steric clash between the *t*-Bu group *ortho* to the phenol of the catalyst and the CF_3 group of the substrate (2.37 Å between a proton of the *t*-Bu group and a fluorine of the CF_3 group). The steric clash is easier to see in the computer-generated structure of **TS-2.6** (Scheme 2.16b). All attempts to calculate **TS-2.7**, which is **TS-2.4** only with the substituents on the ketones switched, minimize to boat transition state **TS-2.8**. A possible reason for the implausibility of **TS-2.7** is the lone pair lone pair repulsion shown in Scheme 2.16b. This interaction does not seem to be as important in **TS-2.4**, likely because in **TS-2.4** the electron withdrawing CF_3 group absorbing much of the electron density in the lone-pair anti to it, minimizing the repulsion of this substrate lone pair with those on the phenol oxygen of the catalyst.

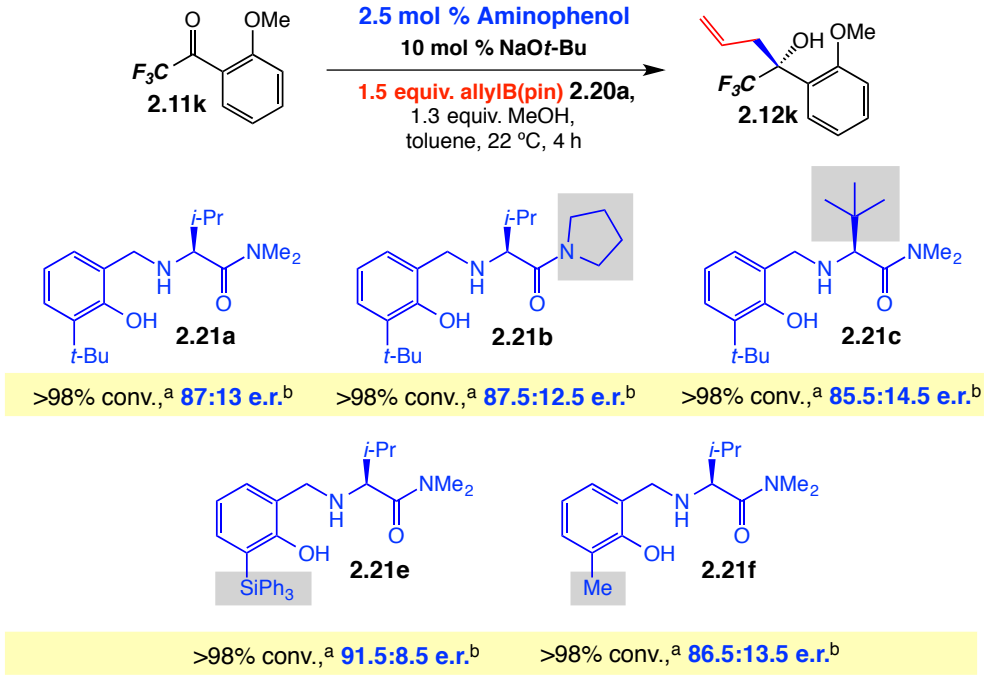
Sterically more hindered substrates, such as trifluoromethyl ketone **2.11k**, lead to lower enantioselectivities in the aminophenol-promoted allyl-addition reaction (Scheme

Scheme 2.17 Rationale for Lower Enantioselectivity with Sterically-Hindered Substrates



2.11). Studying models based on the ones in Scheme 2.16, it becomes clear that a very large aryl-substituent begins to clash with the *tert*-Bu group *ortho* to the phenol of the catalyst in **TS-2.9** (Scheme 2.17). This leads to **TS-2.10** becoming more competitive (Scheme 2.17). A short screening of aminophenols showed a small improvement in the enantioselectivity of the transformation with larger aminophenol **2.21e**, indicating that further increasing the sterics of the group *ortho* to the phenol in the catalyst begins to shift the enantioselectivity back towards the major enantiomer (that is, **TS-2.9**). Sterically less hindered substrates (vs. trifluoroacetophenone), such as alkyl-substituted **2.11n**, undergo addition with similar levels of selectivity to trifluoroacetophenone.

Scheme 2.18 Screening of Aminophenols for Sterically Hindered Ketones

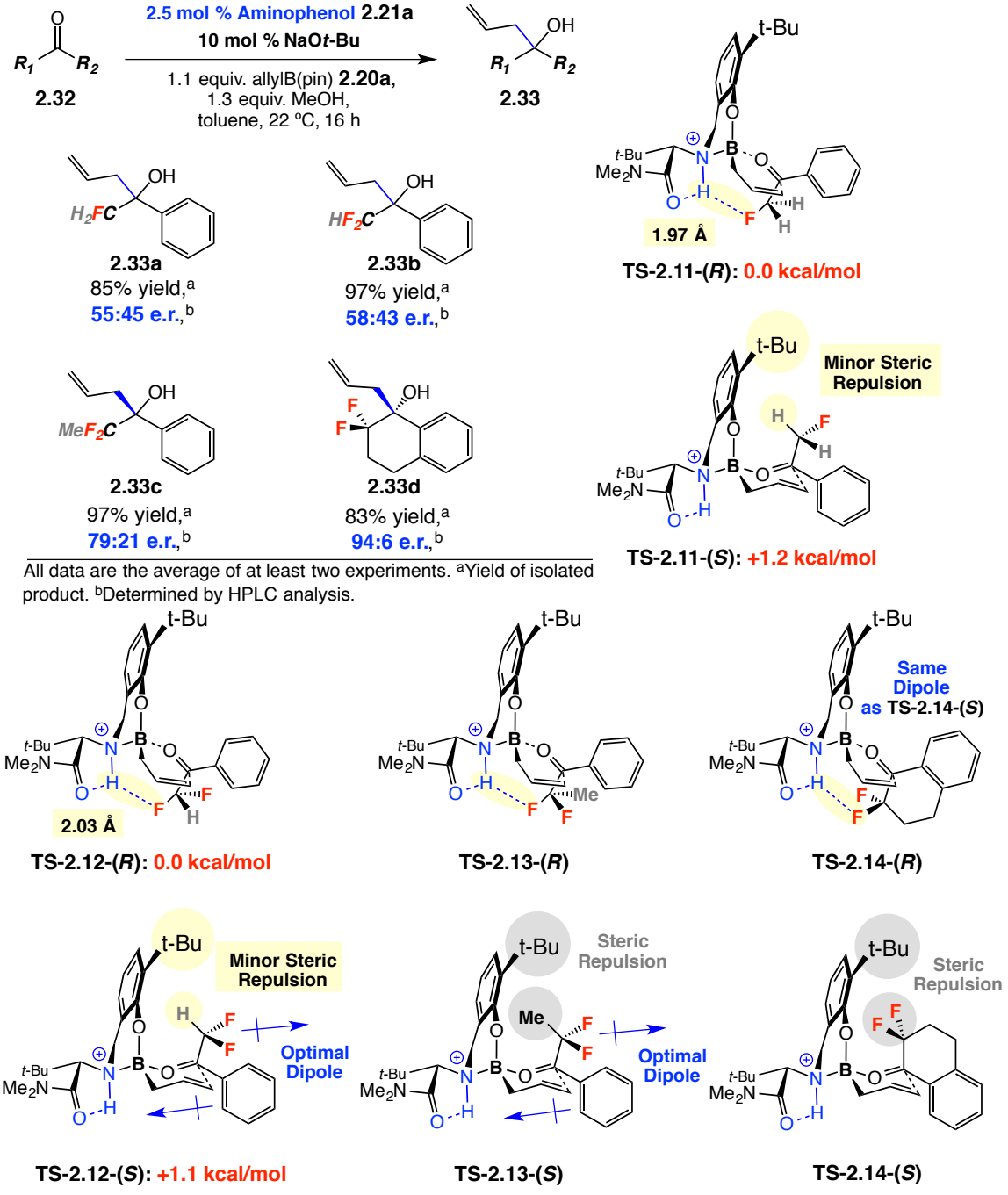


[a]Consumption of starting material as determined by 376 MHz ^{19}F analysis of the unpurified reaction mixture. [b]Determined by HPLC analysis.

The calculated transition states leading to the (*R*) enantiomer for monofluoroacetophenone **2.32a** (**TS-2.11-(*R*)**, Scheme 2.19) and difluoroacetophenone **2.32b** (**TS-2.12-(*R*)**, Scheme 2.19) and contain similar F-H distances and geometries as

TS-2.4 (Scheme 2.16a), suggesting the cation-dipole interaction is plausible for these substrates. A fact worth considering when changing the degree of fluorination on carbon is that, as more fluorines are added to a carbon, the net charge on each fluorine remains

Scheme 2.19 Modifying Substrates to Examine Enantioselectivity



the same, but the C-F bond length is decreasing with increasing fluorination (e.g. 1.38 Å in methyl fluoride to 1.32 Å in carbon tetrafluoride).[41] This decrease in bond length is primarily due to an increased positive charge on carbon with increasing fluorines, and thus, a stronger columbic attraction between C and F.

However, when substrates **2.32a** and **2.32b** are subjected to the catalytic enantioselective allyl-addition conditions, the desired products are afforded with essentially no enantiomeric enrichment (**2.33a** and **2.33b**, Scheme 2.19). The background reaction was not significantly different for **2.32a** and **2.32b** versus trifluoroacetophenone **2.11a**, which minimalizes the possibility that this drop in enantioselectivity is a result of an adventitious uncatalyzed reaction. Additionally, it is worth noting that the proton(s) geminal to fluorine in **2.32a** and **2.32b** are rendered less acidic by the fluorine(s) (rather than more) due to the closely held lone pairs of fluorine, indicating that the change in enantioselectivity is not due to change in the pH of the reaction involving these substrates versus **2.11a**.[3] All these facts taken together imply that the low enantioselectivity observed is due a structural change in the substrates resulting in **TS-2.12-(*S*)** becoming energetically similar to **TS-2.12-(*R*)**.[42] Examining transition state **TS-2.6** in Scheme 2.16 versus **TS-2.12-(*S*)** in Scheme 2.19 and **TS-2.4** versus **TS-2.12-(*R*)** reveals two major differences. First, there is far less steric repulsion disfavoring **TS-2.12-(*S*)** than exists in **TS-2.6**; the same scenario is true for monofluoroacetophenone containing **TS-2.12-(*S*)**. Secondly, in order for a fluorine in in **2.32a** or **2.32b** to form a cation-dipole interaction with the catalyst, as in **TS-2.11-(*R*)** and **TS-2.12-(*R*)**, the substrate must adopt a conformation that is disfavored due to the dipole repulsion

(41) Wiberg, K. *J. Chem. Educ.* **1996**, *73*, 1089–1095.
(42) The same is true for **TS-2.11 (*R*)** and **(*S*)**.

between F–C and O=C. For example, compare the substrate dipole in **TS-2.12-(*R*)** with that of **TS-2.12-(*S*)** in Scheme 2.19. In trifluoroacetophenone **2.11a**, there is no difference in dipole as the trifluoromethyl group is symmetric, which results in there being no conformational preference within the substrate between transitions states **TS-2.4** and **TS-2.6** (Scheme 2.16).

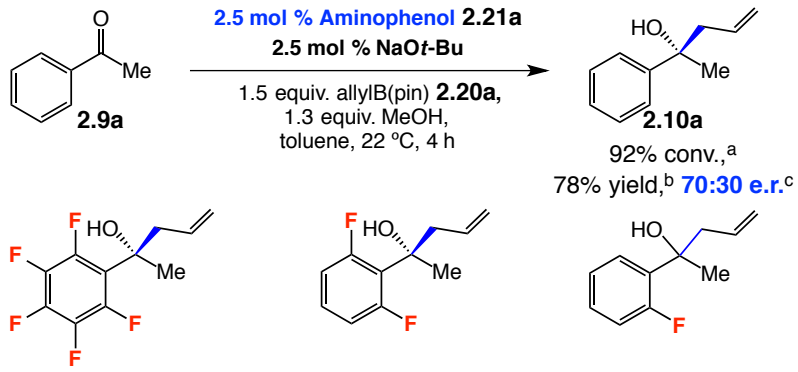
To determine the importance of these two factors, we next employed difluoropropiophenone **2.32c** as a substrate which should restore the aforementioned steric repulsion (disfavoring **TS-2.13-(*S*)**) while maintaining the discrepancy in conformational preference due to dipolar interactions. The desired product **2.33c** is obtained in 79:21 enantiomeric ratio (Scheme 2.19), implying that, while it plays some role, the size difference between the trifluoromethyl group and difluoromethyl group is not exclusively responsible for change in selectivity when comparing **2.11a** as a substrate vs. **2.32b** (or **2.32a**). To support the hypothesis that the conformational preferences within the substrate strongly dictate our enantioselectivity, we synthesized substrate **2.32d** that is conformationally locked and sterically similar to difluoropropiophenone **2.32c** (Scheme 2.19). As expected, due to elimination of the steric and conformational factors mentioned above (cf. **TS-2.14-(*R*)** and **TS-2.14-(*S*)**, Scheme 2.19), the allyl addition to **2.32d** proceeds with nearly identical enantioselectivity to that of trifluoroacetophenone **2.11a**. Importantly, the ability to hyperconjugate with a ketone lone pair is not significantly weaker for the difluoromethyl substituent of difluoropropiophenone **2.32c** than the difluoro substituent of difluorotetralone **2.32d**, meaning that it is unlikely that the tilting of the carbonyl towards the fluorine, proposed by Professor Corey (Figure 2.1) to account for why a trifluoromethyl behaves as the

"large" group in his case, is operative in our case. Additionally, **2.32d** is restricted into a ring, which hinders its ability to make such a tilt. Finally, in the computed lowest energy transitions states in Scheme 2.16, the catalyst coordinates to what, based on Corey's model, would be the more sterically shielded lone pair of the ketone.

2.6 Additions to Ketones Containing an Aryl-Fluoride

Having examined a wide range of ketones that contain an aliphatic organofluorine, we were curious to see if aromatic fluorination *ortho* to the ketone can serve as a controlling element for enantioselectivity. Homoallyl alcohols resulting from allylation of pentafluoroacetophenone **2.9b** and 2,6-difluoroacetophenone **2.9c** are obtained in 95.5:4.5 and 93.5:6.5 e.r. (Scheme 2.20). However, the desired product of

Scheme 2.20 Effect of Fluorination of the Phenyl Group on Enantioselectivity

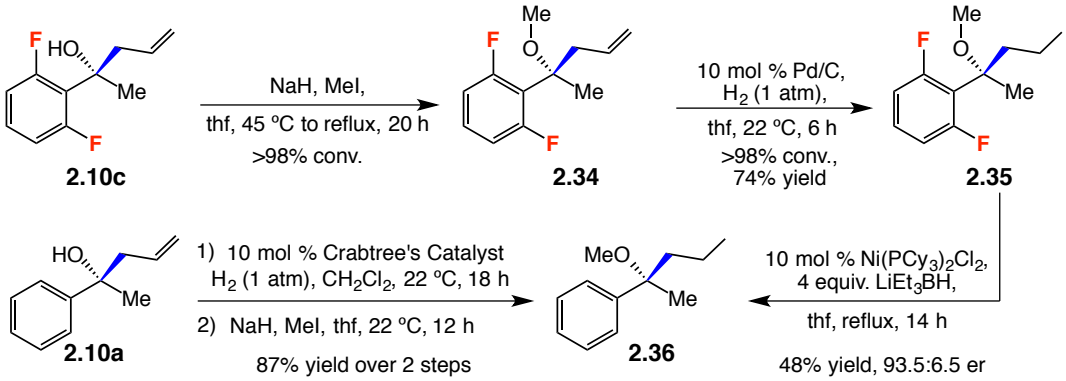


All data are the average of at least two experiments. [a]Conversion to product as determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture versus an internal standard of 9-methylanthracene. [b]Yield of isolated product. [c]Determined by HPLC analysis. [d]Conversion to product as determined by 376 MHz ^{19}F analysis of the unpurified reaction mixture versus an internal standard of monofluorobenzene.

allyl addition to *o*-fluoroacetophenone **2.9d** is afforded nearly racemically. Before devising a stereochemical model, we needed to prove the stereochemistry to **2.10b** and **2.10c**. After many unsuccessful attempts, we were able to establish this stereochemistry through converting **2.10c** to **2.36** by a three-step procedure (Scheme 2.21). The

stereochemistry of **2.36** was then established by converting known (*S*)–**2.10a** to **2.36**. By comparing the HPLC traces of the two samples of **2.36** synthesized by the aforementioned pathway, we established the stereochemistry of **2.10c** (and by correlation, **2.10b** as well) to be (*S*) as shown in Scheme 2.20.

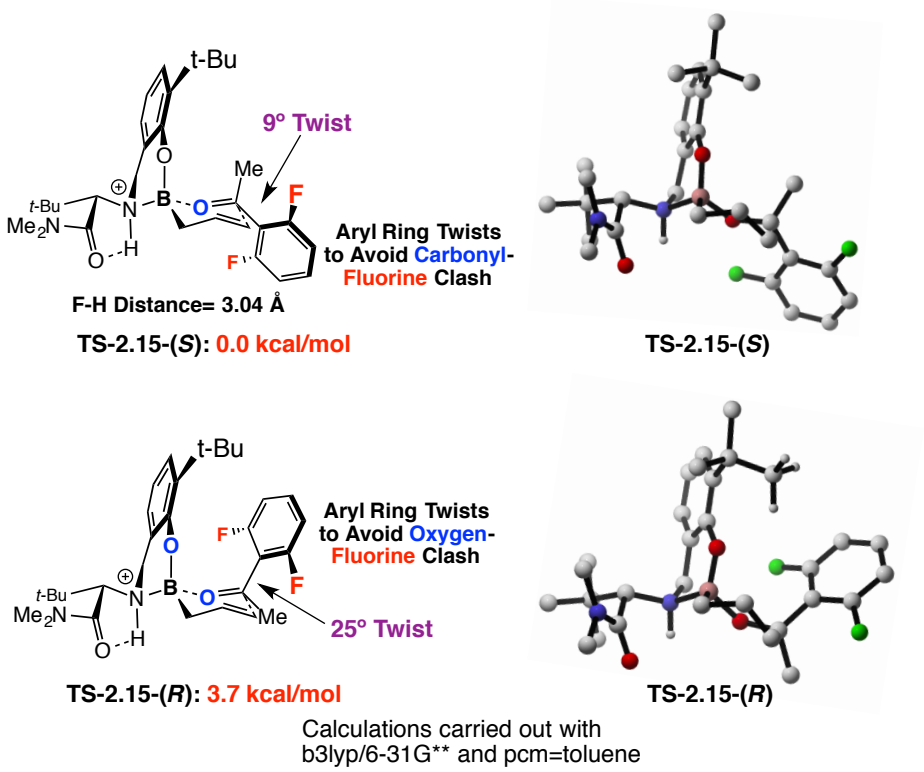
Scheme 2.21 Proof of Absolute Stereochemistry of **2.10c**



We again turned to DFT calculations[43] to get a better understanding of how substrates containing two fluorines at the ortho-position of the aryl ring are noticeably more enantioselective than acetophenone **2.9a**. The lowest locatable transition state for formation of the major enantiomer (**TS-2.14-(*S*)**, Scheme 2.22) shows a large F-H distance of 3.04 Å. Furthermore, the aryl ring twists out of conjugation of the carbonyl by 9º (dihedral angle between the C-C bond of the ring that is directly attached to the carbonyl and the C=O bond of the carbonyl; there are two such C-C bonds, so the number is an average between the two), putting the fluorine even further from the ammonium proton (than it would be if the aryl ring and carbonyl were perfectly coplanar) further suggesting the weakness of this attractive force. Instead of an attractive force, we propose a repulsive steric interaction between the fluorines of the substrate and the catalyst (Scheme 2.22) is behind the enantioselectivities observed in Scheme 2.20, as the

(43) As usual, performed by Dr. Fredrik Haeffner.

Scheme 2.22 Calculated Stereochemical Model for Allyl-Addition to **2.10c**



Calculations carried out with
b3lyp/6-31G** and pcm=toluene

aryl ring in **TS-2.15-(*R*)** twists 25º out of conjugation with the carbonyl, mainly to avoid the phenol oxygen of the catalyst. The observation that **2.10d** is so much less enantiomerically enriched than **2.10b** or **2.10c** also fits this hypothesis, as the aryl group in **2.9d** is sterically much smaller than the aryl group of either **2.9b** or **2.9c** (Scheme 2.20).

2.7 Conclusions

The method disclosed here is valuable not only because it allows access to molecules that are otherwise difficult to obtain, but it also lays the groundwork for future developments in enantioselective catalysis with fluorinated ketones by outlining parameters important for substrate binding, namely that a protonated nitrogen is more likely to be attracted to a fluorine than a neutral nitrogen due to fluorine's propensity for cation-dipole interactions vs. traditional hydrogen bonding.

2.8 Experimental Section

■ **General.** Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, λ_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) or 500 (500 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). Well resolved AB splitting patterns are reported as follows: chemical shift of A and chemical shift of B, integration, multiplicity (AB_q = AB quartet, d of AB_q = doublet of AB quartets, etc), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). Data are reported as follows: chemical shift, multiplicity (singlet unless otherwise noted), and coupling constants (Hz). ^{19}F NMR spectra were recorded on a Varian Unity INOVA 400 (376 MHz). Chemical shifts are reported in ppm with BF_3•OEt_2 as an external standard (BF_3•OEt_2: δ 0.00 ppm). Data are reported as follows: chemical shift, integration, multiplicity, and coupling constants (Hz). High-resolution mass spectrometry was performed on a JEOL AccuTOF-DART (positive mode) or an Advion Expression CMS (ESI+ or ESI-) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios (e.r.) values were determined by HPLC analysis using a Shimadzu LC-2010AHT chromatograph (Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), Chiral

Technologies Chiralcel OJ-H (4.6 x 250 mm), Chiral Technologies Chiralpak AD-H (4.6 x 250 mm). Specific rotations were measured using either an Atago AP-300 Automated Polarimeter or a Rudolph Research Analytical Autopol IV Polarimeter. Melting points were determined using a Thomas Hoover Uni-melt capillary melting point apparatus. Unless otherwise noted, reactions were carried out under an atmosphere of dry N_2 in oven-dried (135 ºC) glassware with the appropriate oven-dried (65 ºC) septa.

■ **Solvents:** Unless otherwise noted, solvents were purged with Ar and purified under a positive pressure of dry Ar by a modified Innovative Technologies purification system. Toluene (Fisher, ACS Grade) was passed successively through activated copper and alumina columns. Dichloromethane (Fisher, ACS Grade) and diethyl ether (Aldrich, Chromasolv®) were passed successively through two activated alumina columns. Tetrahydrofuran was purified by distillation from sodium benzophenone ketyl immediately prior to use. $CDCl_3$ was purchased from Cambridge Isotope Laboratories and stored over activated 4Å molecular sieves prior to use. All work-up and purification procedures were carried out in air with reagent grade solvents (purchased from Fisher). $C_6D_5CD_3$ was purchased from Cambridge Isotope Laboratories and used as received.

■ **Reagents and Catalysts:**

Allenylboronic Acid Pinacol Ester (2.23) was obtained from Frontier Scientific and distilled under vacuum prior to use.

Allylboronates: Allylboronic acid pinacol ester (**2.20a**) was purchased from Aldrich or obtained as a gift from Frontier Scientific, Inc and distilled prior to use. 2-(2-Methylallyl)boronic acid pinacol ester 2.20b) and 2-(2-Chloroallyl)boronic acid pinacol

ester (**2.20c)** were synthesized and purified in accordance with a procedure in the literature.[44]

Bis(tricyclohexylphosphine)Nickel(II) Dichloride was purchased from Aldrich (97%) and used as received.

Crabtree's Catalyst ([Tricyclohexylphosphine] (1,5-Cyclooctadiene) (Pyridine) Iridium(I) Hexafluorophosphate) was purchased from Strem (99%) and used as received.

Fluorobenzene was purchased from Aldrich and used as received.

Hydrogen Gas was purchased from Airgas (industrial grade) and used as received.

Methanol was purchased from Acros (99.8% anhydrous) and distilled at 1 atm from sodium metal prior to use.

Methyl Iodide was purchased from Aldrich and distilled at 1 atm from calcium chloride prior to use.

Palladium, 10% on Activated Carbon was purchased from Strem and used as received.

Sodium *tert*-Butoxide was purchased from Strem (min. 98%) and used as received.

Sodium Hydride was purchased from Aldrich (95%, dry) and used as received.

Super-Hydride® (Lithium Triethylborohydride, 1.0 M in Tetrahydrofuran) was purchased from Aldrich and used as received.

α,α,α-Trifluorotoluene was purchased from Aldrich and used as received.

■ **Substrates (Ketones):**

2.10a (acetophenone): Purchased from Aldrich and distilled under vacuum from calcium hydride prior to use.

(44) Zhang, P.; Roundtree, I. A.; Morken, J. P. *Org. Lett.* **2012**, *14*, 1416–1419.

2.10b (2′,3′,4′,5′,6′-pentafluoroacetophenone): Purchased from Aldrich and distilled under vacuum from calcium chloride prior to use.

2.10c (2′,6′-difluoroacetophenone): Purchased from Oakwood and distilled under vacuum from calcium chloride prior to use.

2.10d (2′-fluoroacetophenone): Purchased from Aldrich and distilled under vacuum from calcium chloride prior to use.

2.11a (2,2,2-trifluoroacetophenone): Purchased from Oakwood and distilled under vacuum from calcium chloride prior to use.

2.11b (**2,2,3,3,3-pentafluoroacetophenone):** Purchased from Matrix and used as received.

2.11c (**4,4,4,4,4,4,4-heptafluoroacetophenone):** Purchased from Alfa Aesar and used as received.

2.11d (**4'-bromo-2,2,2-trifluoroacetophenone):** Purchased from Matrix and used as received.

2.11e (**4'-fluoro-2,2,2-trifluoroacetophenone):** Purchased from Aldrich and used as received.

2.11f (**4'-dimethylamino-2,2,2-trifluoroacetophenone):** Purchased from Aldrich as an orange-yellow solid. Dissolved in hot HPLC grade hexanes (Fisher) and filtered through a hot glass frit to removed dark orange solids. Frit is washed with HPLC grade hexanes and minimal dichloromethane (Fisher, reagent grade) to recover maximum amount of **2.11f**. Concentration *in vacuo* affords **2.11f** as a bright yellow solid.

2.11g (*tert*-butyl 2-(2,2,2-trifluoroacetyl)-1*H*-pyrrole-1-carboxylate): Synthesized in accordance to a procedure in the literature.[45]

2.11h (2-(trifluoroacetyl)thiophene): Purchased from Aldrich and distilled under vacuum from calcium chloride prior to use or used as received (no difference in results are observed).

2.11i (3-(trifluoroacetyl)thiophene): Synthesized in accordance to a procedure in the literature[46] using Knochel's procedure[47] to generate the requisite Grignard.

2.11j (*tert*-butyl 3-(2,2,2-trifluoroacetyl)-1*H*-indole-1-carboxylate): Synthesized in accordance to a procedure in the literature.[45]

2.11k (2'-methoxy-2,2,2-trifluoroacetophenone): Purchased from Oakwood and distilled under vacuum (simple distillation) prior to use or used as received (no difference in results are observed).

2.11l (2'-methyl-2,2,2-trifluoroacetophenone): Synthesized in accordance to a procedure in the literature.[46]

2.11m (3'-methyl-2,2,2-trifluoroacetophenone): Purchased from Oakwood and used as received.

2.11n (1,1,1-Trifluoro-3-phenylacetone): Purchased from Oakwood and distilled under vacuum from calcium chloride or used as received (no difference in results are observed).

2.11o ((*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one): Synthesized in accordance to a procedure in the literature.[48]

(45) Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 1046–1047.
(46) Shaw, D. A.; Tuominen, T. C.; *Synth. Commun.* **1985**, *15*, 1291–1297.
(47) Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 3333–3336.
(48) Kawano, Y.; Kaneko, N.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1133–1145.

2.26a (isobutyrophenone): Purchased from Aldrich and distilled under vacuum from calcium hydride prior to use.

2.26b (isovalerophenone): Purchased from Aldrich and distilled under vacuum from calcium hydride prior to use.

2.28a (4'-nitroacetophenone): Purchased from Aldrich and used as received.

2.28b (3',5'-difluoroacetophenone): Purchased from Oakwood and used as received.

2.33a (2-fluoroacetophenone): Synthesized in accordance to a procedure in the literature.[49]

2.33b (2,2-difluoroacetophenone): Purchased from Alfa Aesar and distilled under vacuum (simple distillation) prior to use.

2.33c (2,2-difluoropropiophenone): Synthesized in accordance to a procedure in the literature.[50]

2.33d (2,2-difluoro-α-tetralone): Synthesized in accordance to a procedure in the literature.[50]

■ **Experimental Procedures and Analytical Data**

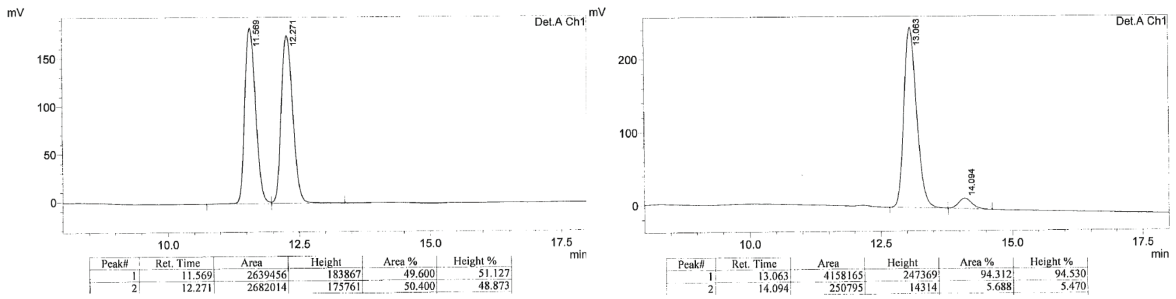
Representative Procedure for Catalytic Enantioselective Allyl Additions to Ketones Bearing a Perfluoroalkyl Group (Scheme 2.11): In a nitrogen-filled glovebox, aminophenol **2.21a** (7.7 mg, 0.025 mmol) is added to a two-dram vial equipped with a stir bar and dissolved in 1.0 mL of toluene. A second stock solution is prepared by dissolving 19.2 mg NaO*t*-Bu in 8.0 mL toluene. A two-dram vial equipped with a stir bar is charged with 200 mmol of the stock solution of **2.21a** (1.5 mg, 5.0 mmol) followed by 800 μL of the stock solution of NaO*t*-Bu (1.9 mg, 20 mmol). This vial is sealed with a

(49) Wei, Z.-L.; Li, Z.-Y.; Lin, G.-Q. *Tetrahedron* **1998**, *54*, 13059–13072.
(50) Pravst, I.; Zupan, M.; Stavber, S. *Synthesis* **2005**, *18*, 3140–3146.

cap (phenolic open top cap with a white PFTE/gray silicone septa) and electrical tape and removed from the glovebox. Methanol (10 μL, 0.25 mmol) and trifluoroacetophenone **2.11a** (28 μL, 0.20 mmol) are added by syringe under N_2 in the stated order. The reaction vessel placed in a 0 ºC ice/water bath and allowed to stir for 15 minutes. Allylboronic acid pinacol ester **2.20a** (42 μL, 0.22 mmol) is added by syringe under N_2 and the reaction mixture is allowed to stir at 4 ºC for 4 h after which time the cap is removed and α,α,α-trifluorotoluene (24.4 μL, 0.199 mmol) is added as an internal standard. Following ^{19}F NMR analysis of the reaction mixture, it is passed through a short plug of silica gel (eluted with Et_2O) and concentrated *in vacuo* being careful not to remove all of the solvent, as the product is volatile. The resulting pale yellow oil is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in pentane and eluted successively with 10 mL pentane, 14 mL 19:1 pentane:Et_2O, and 15 mL 9:1 pentane:Et_2O) to afford desired product **2.12a** (39.9 mg, 0.185 mmol, 92% yield) as a clear, colorless oil.

(*R*)-1,1,1-Trifluoro-2-phenylpent-4-en-2-ol (2.12a, Scheme 2.11): The analytical data are fully consistent with those reported previously.[51] ^1H NMR (500 MHz, $CDCl_3$): δ 7.62–7.54 (2H, m), 7.45–7.32 (3H, m), 5.62–5.50 (1H, m), 5.30–5.18 (2H, m), 2.99 (1H, dd, J = 14.3, 6.6 Hz), 2.85 (1H, dd, J = 14.3, 8.1 Hz), 2.58 (1H, s); HRMS Calcd for $C_{11}H_{10}F_3$ $[M + H - H_2O]^+$: 199.07346; Found: 199.07335; $[\alpha]^{23.3}_D$ = +50.0 (c = 2.20, $CHCl_3$) for a 94:6 e.r. sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 13 min (major) and 14 min (minor).

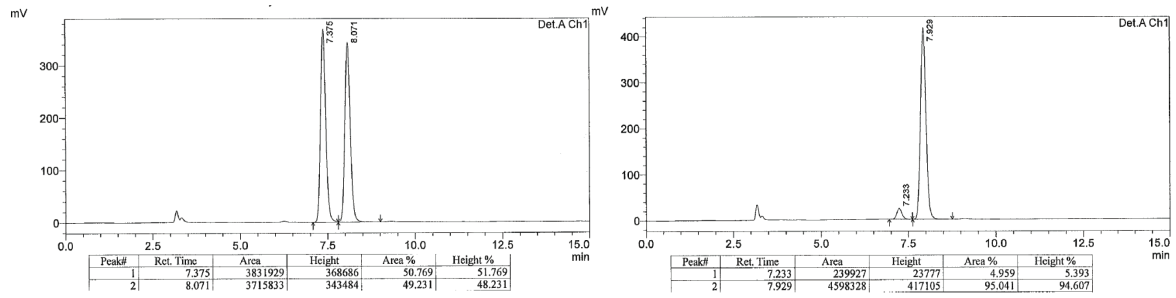
(51) Xie, Z.; Li, G.; Zhao, G.; Wang, J. *Chin. J. Chem.* **2010**, *28*, 1212–1216.



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.5 min	49.600	1	13.1 min	94.312
2	12.3 min	50.400	2	14.1 min	5.688

(*R*)-1,1,1,2,2-Pentafluoro-3-phenylhex-5-en-3-ol (2.12b, Scheme 2.11): The title compound is synthesized analogously to **2.12a** except that the amount of aminophenol **2.21a** is 1.0 mol% (vs. 2.5 mol%). The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 30:1, 10 mL 19:1 pentanes : diethyl ether) affording **2.12b** (45.1 mg, 0.169 mmol, 85% yield) as a clear colorless oil. IR (neat): 3551 (w, br), 3068 (w, br), 3032 (w), 2986 (w), 1450 (w), 1339 (w), 1214 (m), 1173 (s), 1173 (s), 1132 (s), 1057 (m), 1001 (s), 983 (w), 937 (w), 849 (w), 765 (w), 713 (s), 699 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.53 (2H, m), 7.42–7.32 (3H, m), 5.49–5.38 (1H, m), 5.28–5.20 (2H, m), 3.08–3.03 (1H, m), 2.89 (1H, dd, J = 14.2, 8.3 Hz), 2.57 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9 (m), 130.5, 128.6, 128.4, 126.6, 122.5, 119.2 (qt, J = 288.5, 36.6 Hz), 114.5 (tq, J = 261.5, 34.8 Hz), 76.0 (t, J = 23.5 Hz), 40.5 (m); ^{19}F NMR (376 MHz, $CDCl_3$): δ 74.86 (3F, s), 31.76 and 30.56 (2F, ABq, J_{AB} = 276.6 Hz); HRMS Calcd for $C_{12}H_{10}F_5$ $[M + H - H_2O]^+$: 249.07027; Found: 249.06989. $[\alpha]^{23.5}_D$ = +61.7 (c = 1.94, $CHCl_3$) for a 95:5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel

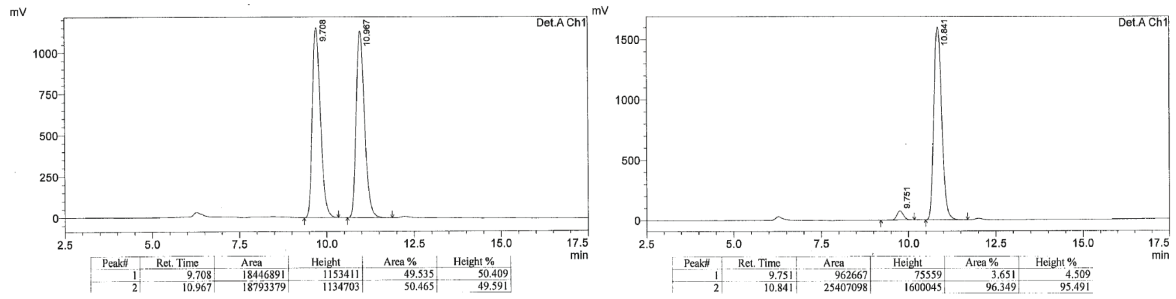
AD-H, 99:1 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R: 7.2 min (minor) and 7.9 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	7.4 min	50.769	1	7.2 min	4.959
2	8.1 min	49.231	2	7.9 min	95.041

(*R*)-5,5,6,6,7,7,7-Heptafluoro-4-phenylhept-1-en-4-ol (2.12c, Scheme 2.11): The title compound is synthesized analogously to **2.12a** except that the amount of aminophenol **2.21a** is 1.0 mol% (vs. 2.5 mol%). The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 30:1, 10 mL 20:1 pentanes:diethyl ether) affording **2.12c** (56.6 mg, 0.179 mmol, 89% yield) as a clear colorless oil. IR (neat): 3553 (w, br), 3068 (w), 1641 (w), 1450 (w), 1341 (m), 1213 (s), 1189 (s), 1116 (s), 1072 (m), 997 (m), 937 (m), 710 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (2H, m), 7.42–7.34 (3H, m), 5.48–5.38 (1H, m), 5.29–5.20 (2H, m), 3.09–3.03 (1H, m), 2.91 (1H, dd, J = 14.1, 8.4 Hz), 2.65 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): Note: Peaks assigned as apparent due to complexity of the spectrum. δ 136.9 (m), 130.4, 128.6, 128.4, 126.7 (m), 122.8–121.9 (m), 122.5, 119.7–118.3 (m), 116.5–115.7 (m), 114.0–112.0 (m), 111.2–109.3 (m), 108.5–106.6 (m), 77.0–76.7 (m), 41.0 (t, 3.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): Note: Peaks assigned as apparent due to complexity of the spectrum. δ 71.87–71.81 (3F, m),

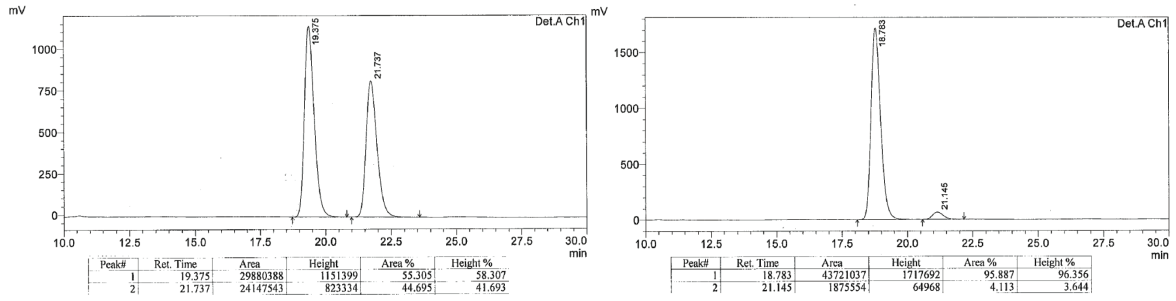
35.62 (1F, app. ddq, J = 283.6, 19.9, 9.9 Hz), 34.24 (1F, app. dp, J = 283.5, 11.8 Hz), 31.33 (1F, app. ddd, J = 289.5, 11.3, 6.2 Hz), 28.59 (1F, app. dd, J = 289.4, 10.9 Hz); HRMS Calcd for $C_{13}H_{10}F_7$ $[M + H - H_2O]^+$: 299.06707; Found: 299.06783. $[\alpha]^{21.4}_D$ = +54.9 (c = 2.55, $CHCl_3$) for a 97:3 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 9.8 min (minor) and 11 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	9.7 min	49.535	1	9.8 min	3.651
2	11.0 min	50.465	2	10.8 min	96.349

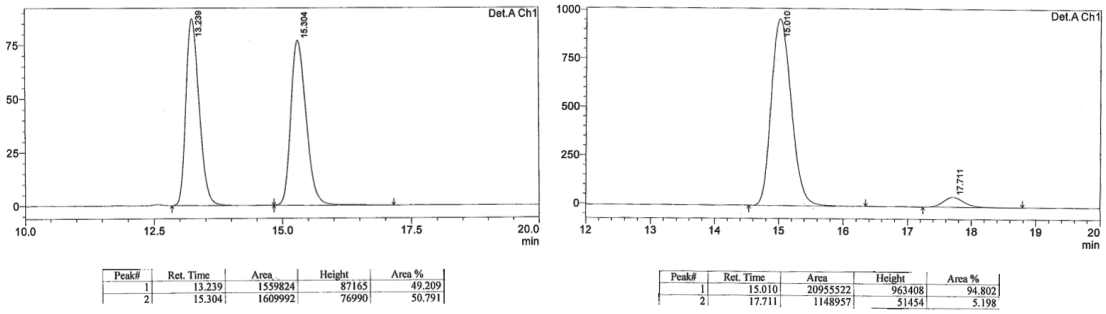
(*R*)-2-(4-Bromophenyl)-1,1,1-trifluoropent-4-en-2-ol (2.12d, Scheme 2.11): The title compound is synthesized analogously to **2.12a** except for the following changes: 1) The substrate is weighed out into the reaction vessel before any other components were added. 2) The amount of aminophenol **2.21a** is 1.0 mol% (vs. 2.5 mol%). The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 30:1, 20 mL 19:1 pentanes : diethyl ether) affording **2.12d** (53.6 mg, 0.182 mmol, 94% yield) as a clear colorless oil. The analytical data are fully consistent with those reported previously.[2] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.52 (2H, m), 7.45 (2H, d, J = 8.4 Hz), 5.60–5.49 (1H,

m), 5.29–5.23 (2H, m), 2.93 (2H, dd, J = 14.4, 6.7 Hz), 2.83 (2H, dd, J = 14.4, 7.9 Hz), 2.61 (1H, s); ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.59 (3F, s); HRMS Calcd for $C_{11}H_9BrF_3$ $[M + H - H_2O]^+$: 276.98397; Found: 276.98282. $[\alpha]^{21.8}_D$ = +71.6 (c = 2.37, $CHCl_3$) for a 96:4 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 19 min (major) and 22 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	19.4 min	55.305	1	18.8 min	95.887
2	21.7 min	44.695	2	21.1 min	4.113

(*R*)-1,1,1-Trifluoro-2-(4-fluorophenyl)pent-4-en-2-ol (2.12e, Scheme 2.11): The analytical data are fully consistent with those reported previously.[51] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68–7.47 (2H, m), 7.17–7.00 (2H, m), 5.66–5.45 (1H, m), 5.37–5.15 (2H, m), 3.02–2.90 (1H, m), 2.89–2.78 (1H, m), 2.61 (1H, br s); HRMS Calculated for $C_{11}H_9F_4$ $[M + H - H_2O]^+$: 217.06387; Found: 217.06404. $[\alpha]^{22}_D$ = +40.4 (c = 0.99, $CHCl_3$) for a 95:5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 15 min (major) and 17 min (minor).

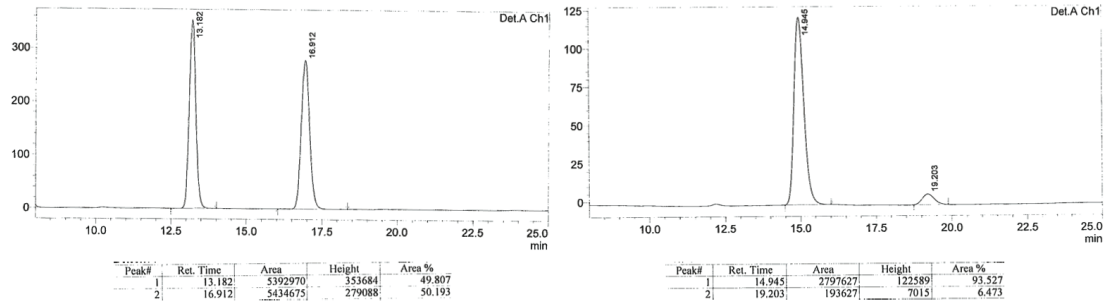


Peak#	Ret. Time	Area	Height	Area %
1	13.239	1559824	87165	49.209
2	15.304	1609992	76990	50.791

Peak#	Ret. Time	Area	Height	Area %
1	15.010	20955522	963408	94.802
2	17.711	1148957	51454	5.198

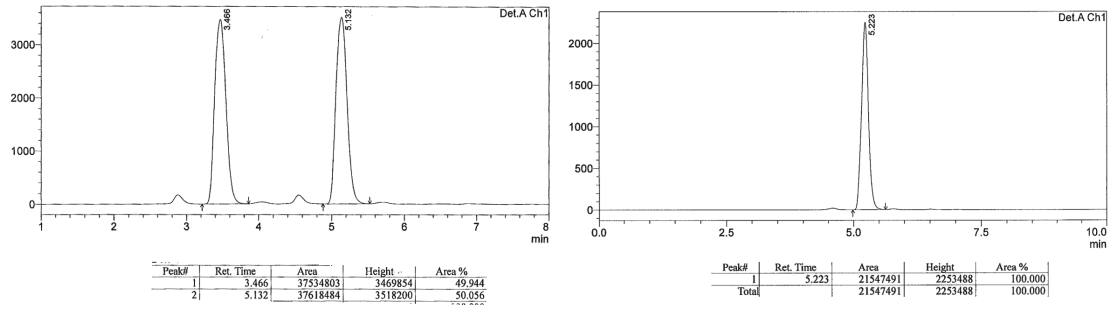
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.2	49.209	1	15.0	94.802
2	15.3	50.791	2	17.7	5.198

(*R*)-2-(4-(Dimethylamino)phenyl)-1,1,1-trifluoropent-4-en-2-ol (2.12f, Scheme 2.11): IR (neat): 3543 (br w), 2921 (br, w), 2854 (br, w), 2807 (br, w), 1614 (m), 1523 (m), 1445 (w), 1358 (w), 1269 (m), 1227 (m), 1145 (s), 994 (m), 944 (m), 814 (s), 710 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (2H, d, J = 8.8 Hz), 6.73–6.70 (2H, m), 5.65–5.54 (1H, m), 5.26–5.18 (2H, m), 3.00–2.95(1H, m,), 2.97 (6H, s), 2.81–2.75 (1H, m), 2.46 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ150.5, 131.1, 127.5 ,125.7 (q, J = 285.4 Hz), 124.1 (s), 121.6 (s), 112.0 (s), 75.7 (q, J =28.2 Hz), 40.4, 40.0; ^{19}F NMR (376 MHz, $CDCl_3$): 79.85 (3F, s); HRMS Calculated for $C_{13}H_{17}F_3NO$ $[M + H]^+$: 260.12622; Found: 260.12544; $[\alpha]^{26}_D$ = +59.8 (c = 1.17, $CHCl_3$) for a 93:7 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AD-H, 97:3 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 15 min (major) and 19 min (minor).



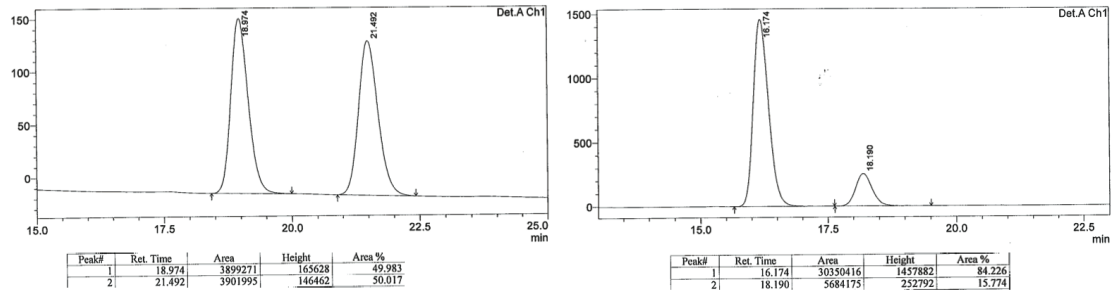
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.2	49.807	1	14.9	93.527
2	16.9	50.193	2	19.2	6.473

***tert*-Butyl-(*R*)-2-(1,1,1-trifluoro-2-hydroxypent-4-en-2-yl)-1*H*-pyrrole-1-carboxylate (2.12g, Scheme 2.11)**: IR (neat): 3299 (br w), 2984 (w), 1718 (m), 1444 (w), 1398 (m), 1373 (m), 1337 (s), 1264 (m), 1145 (s), 1100 (m), 848 (w), 733 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (1H, s), 7.28 (1H, dd, J = 3.6, 1.8 Hz), 6.39 (1H, m), 6.16 (1H, app t, J = 3.5 Hz), 6.06–5.76 (1H, m), 5.27–5.03 (2H, m), 2.90 (2H, m), 1.61 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ151.8, 132.4, 130.3, 125.6 (q, J = 286.9 Hz), 125.4, 118.7, 118.5, 110.4, 86.6, 74.3 (q, J = 28.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.85 (3F, s); HRMS Calculated for $C_{14}H_{19}F_3NO_3$ $[M + H]^+$: 305.12388; Found: 306.13267; $[\alpha]^{23}_D$ = -10.9 (c = 0.92, $CHCl_3$) for a >99:1 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AD-H, 97:3 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 5 min (major) and 3 min (minor).



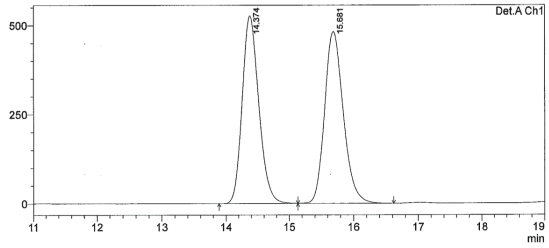
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	3.5	49.944	1	5.2	100
2	5.1	50.056	2	N.A.	0

(*S*)-1,1,1-Trifluoro-2-(thiophen-2-yl)pent-4-en-2-ol (2.12h, Scheme 2.11): : IR (neat): 3531 (w, br), 3083 (w), 2984 (w), 2957 (w), 2929 (w), 1642 (w), 1437 (w), 1274 (m), 1228 (w), 1154 (s, br), 1048 (m), 991 (m), 931 (m), 724 (m), 702 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (1H, dd, J = 5.1, 1.2 Hz), 7.14–7.12 (1H, m), 7.05 (1H, dd, J = 5.1, 3.6 Hz), 5.71–5.60 (1H, m), 5.32–5.26 (2H, m), 2.97–2.91 (1H,m), 2.88–2.82 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 130.1, 127.3, 126.4, 125.9 (q, J = 1.2 Hz), 124.8 (q, J = 285.1 Hz), 122.5, 75.7 (q, J = 29.8 Hz), 41.4 (m); ^{19}F NMR (376 MHz, $CDCl_3$): δ 72.35 (3F, s); HRMS Calculated for $C_9H_8F_3S$ $[M + H - H_2O]^+$: 205.02998; Found: 205.02988. $[\alpha]^{22}_D$ = +52 (c = 0.96, $CHCl_3$) for a 84:16 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 16 min (major) and 18 min (minor).

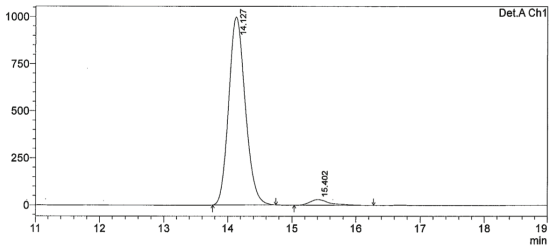


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	19.0	49.983	1	16.2	84.226
2	21.5	50.017	2	18.2	15.774

(*R*)-1,1,1-Trifluoro-2-(thiophen-3-yl)pent-4-en-2-ol (2.12i, Scheme 2.11): IR (neat): 3540 (br, w), 3115 (w), 3083 (w), 2928 (w), 1275 (m), 1226 (m), 1150 (s), 1086 (m), 1019 (m), 920 (m), 853 (s), 785 (s), 724 (s), 688 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (1H, m), 7.38–7.29 (1H, m), 7.14–7.13 (1H, m), 5.65–5.43 (1H, m), 5.26–5.22 (2H, m), 2.92–2.83 (1H, m), 2.83–2.75 (1H, m), 2.63–2.55 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 130.4, 126.4, 126.0, 125.2 (q, J = 284.0 Hz), 123.9, 121.9, 75.4 (q, J = 29.1 Hz), 40.7;^{19}F NMR (376 MHz, $CDCl_3$): δ 73.00 (3F, s); HRMS Calculated for $C_9H_8F_3S$ $[M + H - H_2O]^+$: 205.02998; Found: 205.03052. $[\alpha]^{22}_D$ = +49.4 (c = 1.01, $CHCl_3$) for a 96.5:3.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 14 min (major) and 15 min (minor).



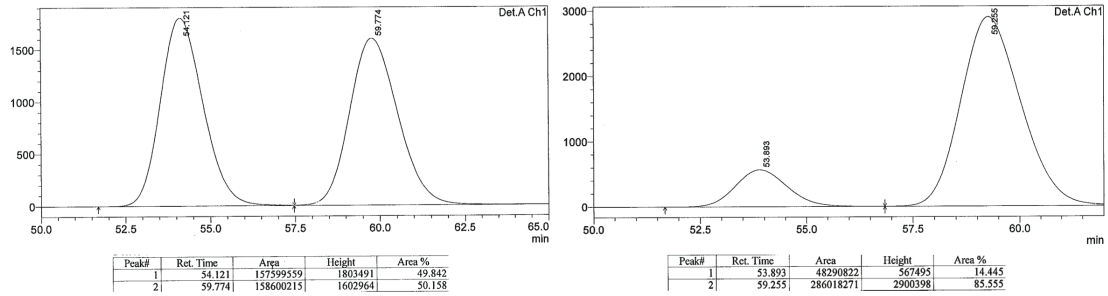
Peak#	Ret. Time	Area	Height	Area %
1	14.374	9623717	526534	49.750
2	15.681	9720323	482105	50.250



Peak#	Ret. Time	Area	Height	Area %
1	14.127	17968129	997355	96.474
2	15.402	656708	30283	3.526

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	14.4	49.750	1	14.1	96.474
2	15.7	50.250	2	15.4	3.526

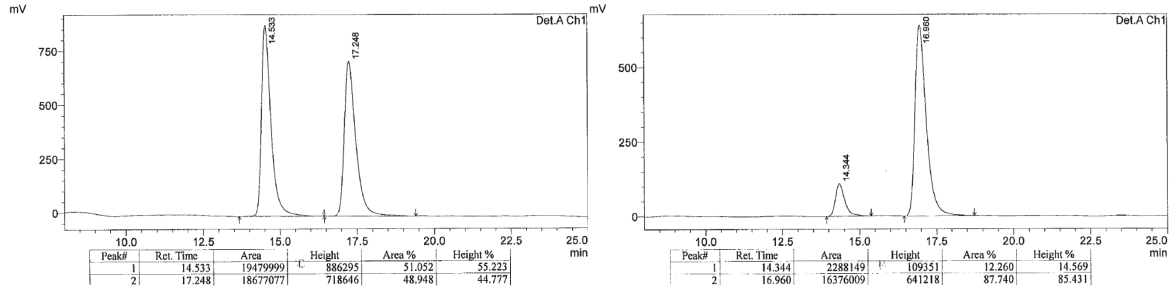
***tert*-Butyl (*R*)-3-(1,1,1-trifluoro-2-hydroxypent-4-en-2-yl)-1*H*-indole-1-carboxylate (2.12j, Scheme 2.11)**: M.p. = 63–65ºC; IR (neat): 3501 (br w), 2981 (w), 1737 (m), 1452 (m), 1372 (s), 1254 (s), 1153 (s), 1078 (m), 1028 (w), 990 (w), 838 (w), 764 (m), 748 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (1H, d, *J* = 8.3 Hz), 7.82 (1H, d, *J* = 8.0 Hz), 7.70 (1H, s), 7.45–7.12 (2H, m), 5.66 (1H, app ddd, *J* = 16.7, 8.7, 8.0 Hz), 5.36–5.10 (2H, m), 3.17–2.86 (2H, m), 2.67 (1H, s), 1.68 (9H, d, *J* = 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6, 136.0, 130.6, 127.9, 125.7, 125.5 (q, *J* = 284.1 Hz), 124.7, 123.0, 122.0, 121.6, 117.4, 115.5, 84.5, 75.0 (q, *J* = 30.0 Hz), 39.6, 28.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.50 (3F, s); HRMS Calculated for $C_{18}H_{20}F_3NO_3$ $[M + H]^+$: 356.14813; Found: 356.14735; $[\alpha]^{22}_D$ = +21.7 (c = 0.92, $CHCl_3$) for a 85.5:14.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 54 min (minor) and 59 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	54.1	49.842	1	53.9	16.364
2	59.8	50.158	2	59.3	83.636

(*R*)-1,1,1-Trifluoro-2-(2-methoxyphenyl)pent-4-en-2-ol (2.12k, Scheme 2.11): The title compound is synthesized analogously to **2.12a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 25 mL 30:1 pentanes : diethyl ether) affording **2.12k** (44.4 mg, 0.180 mmol, 90% yield) as a clear pale yellow oil. IR (neat): 3452 (w, br), 3081 (w), 3015 (w), 2981 (w), 2947 (w), 2845 (w), 1603 (w), 1584 (w), 1438 (m), 1267 (m), 1238 (m), 1182 (m), 1156 (s), 1137 (m), 1022 (m), 912 (m), 753 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.31 (2H, m), 7.05–6.98 (2H, m), 6.07 (1H, s), 5.74 (1H, dddd, J = 17.2, 10.3, 7.2, 6.4 Hz), 5.25–5.06 (2H, m), 3.92–3.91 (3H, m), 3.06 (1H, dd, J = 15.0, 7.2 Hz), 2.85 (1H, dd, J = 14.9, 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 131.9, 130.7, 130.3, 125.9 (q, J = 285.9 Hz), 123.2, 121.5, 119.3, 112.8, 78.4 (q, J = 28.5 Hz), 56.5–56.3 (m), 38.3–38.2 (m); ^{19}F NMR (376 MHz, $CDCl_3$): δ 71.94 (3F, s); HRMS Calcd for $C_{12}H_{12}F_3O$ $[M + H - H_2O]^+$: 229.08402; Found: 229.08451. $[\alpha]^{21.7}_D$ = –0.82 (c = 2.92, $CHCl_3$) for a 88:12 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel

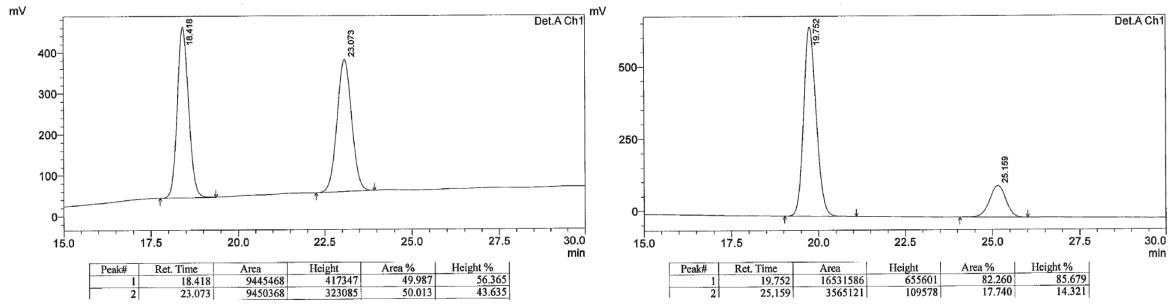
OJ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 14 min (minor) and 17 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	14.5 min	51.052	1	14.3 min	12.260
2	17.2 min	48.948	2	17.0 min	87.740

(*R*)-1,1,1-Trifluoro-2-(*o*-tolyl)pent-4-en-2-ol (2.12l, Scheme 2.11): The title compound is synthesized analogously to **2.12a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 30:1, 15 mL 15:1 pentanes : diethyl ether) affording **2.12l** (40.0 mg, 0.174 mmol, 87% yield) as a clear colorless oil. IR (neat): 3544 (w, br), 1641 (w), 1452 (w), 1296 (w), 1228 (w), 1157 (s), 1011 (w), 994 (w), 941 (w), 912 (w), 761 (w), 731 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.33 (1H, m), 7.19–7.06 (3H, m), 5.62–5.51 (1H, m), 5.22–5.13 (2H, m), 3.10 (1H, dd, J = 14.6, 6.7 Hz), 2.75 (1H, dd, J = 14.6, 7.9 Hz), 2.50–2.45 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5, 134.3, 133.5, 134.0, 128.7 (m), 128.7 (m), 126.0 (q, J = 286.3 Hz), 125.8, 122.4, 78.0 (q, J = 28.3 Hz), 40.8, 23.1 (q, J = 2.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 75.73 (3F, s); HRMS Calcd for $C_{12}H_{12}F_3$ [M + H – H_2O]$^+$: 213.08911; Found: 213.09248. $[\alpha]^{22.4}_D$ = +30.4 (c = 2.30, $CHCl_3$) for a 82:18 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 98:2 hexanes:*i*-PrOH, 0.5

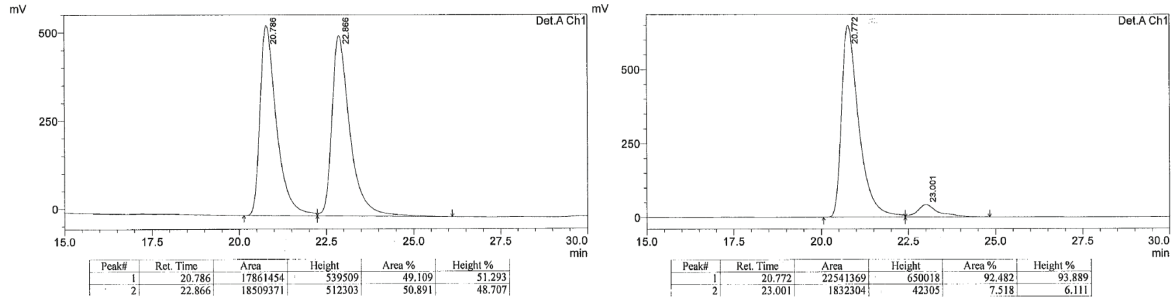
mL/min, 220 nm): t_R: 20 min (major) and 25 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	18.4 min	49.987	1	19.8 min	82.260
2	23.1 min	50.013	2	25.2 min	17.740

(*R*)-1,1,1-Trifluoro-2-(*m*-tolyl)pent-4-en-2-ol (2.12m, Scheme 2.11): The title compound is synthesized analogously to **2.12a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 30:1, 15 mL 15:1 pentanes : diethyl ether) affording **2.12m** (43.1 mg, 0.190 mmol, 94% yield) as a clear colorless oil. IR (neat): 3549 (w, br), 2927 (w), 1642 (w), 1609 (w), 1370 (w), 1269 (m), 1230 (m), 1147 (s), 1023 (m), 993 (m), 785 (m), 708 (s), 646 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.35 (2H, m), 7.30 (1H, app t, J = 7.6 Hz), 7.20–7.17 (1H, m), 5.63–5.53 (1H, m), 5.29–5.22 (2H, m), 2.99 (1H, dd, J = 14.3, 6.5 Hz), 2.85 (1H, dd, J = 14.2, 8.1 Hz), 2.60 (1H, s), 2.40 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 136.9, 130.7, 129.4, 128.4, 127.2, 125.5 (q, J = 285.4 Hz), 123.6, 121.2, 75.9 (q, J = 28.3 Hz), 40.5, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.68 (3F, s); HRMS Calcd for $C_{12}H_{12}F_3$ $[M + H - H_2O]^+$: 213.08911; Found: 213.08958. $[\alpha]^{21.5}_D$ = +61.7 (c = 1.94, $CHCl_3$) for a 92.5:7.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel

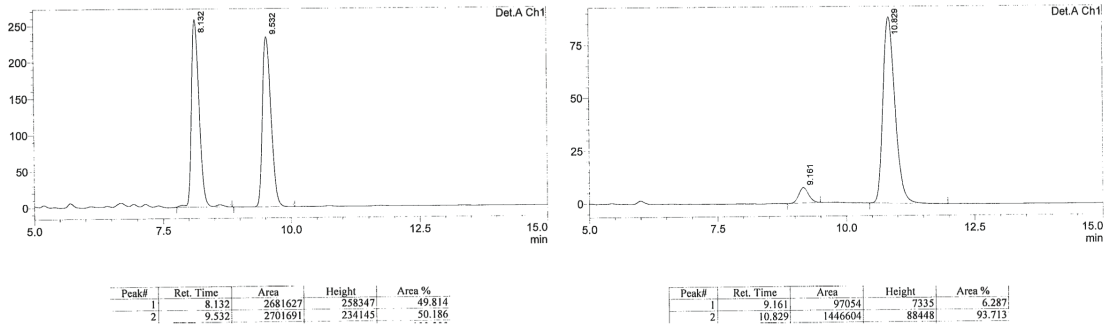
OJ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 21 min (major) and 23 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	20.8 min	49.109	1	20.8 min	92.482
2	22.9 min	50.891	2	23.0 min	7.518

(*R*)-2-Benzyl-1,1,1-trifluoropent-4-en-2-ol (2.12n, Scheme 2.11): The analytical data are fully consistent with those reported previously.[52] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46–7.15 (5H, m), 5.92–5.68 (1H, m), 5.24–5.21 (1H, m), 5.15–5.09 (1H, m), 3.12 and 2.90 (2H, AB_q, J_{AB} = 13.8 Hz), 2.52 (2H, dd, J = 14.4, 6.5 Hz), 2.33–2.23 (2H, m), 2.22 (1H, s); HRMS Calculated for $C_{12}H_{17}F_3N_1O_1$ $[M + NH_4]^+$: 248.12622; Found: 248.12609. $[\alpha]^{22}_D$ = +52.0 (c = 0.96, $CHCl_3$) for a 94:6 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AD-H, 97:3 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 9 min (minor) and 10 min (major).

(52) Felix, C.; Laurent, A.; Mison, P.; *J. Fluorine Chem.*, **1995**, *70*, 71–82

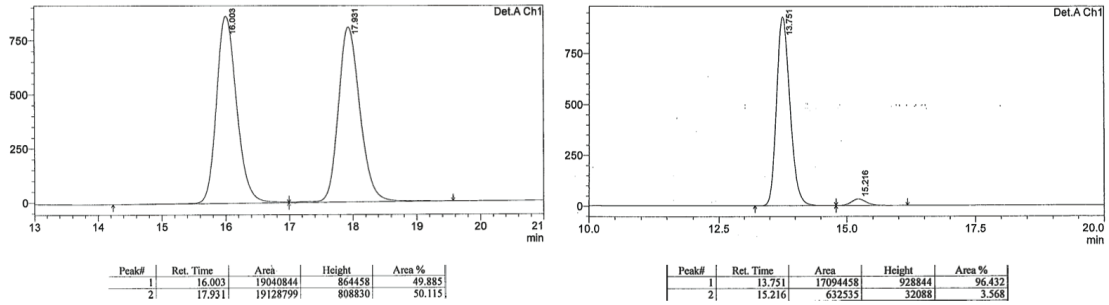


Peak#	Ret. Time	Area	Height	Area %
1	8.132	2681627	258347	49.814
2	9.532	2701691	234145	50.186

Peak#	Ret. Time	Area	Height	Area %
1	9.161	97054	7335	6.287
2	10.829	1446604	88448	93.713

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	8.1	49.814	1	9.2	6.287
2	9.5	50.186	2	10.8	93.713

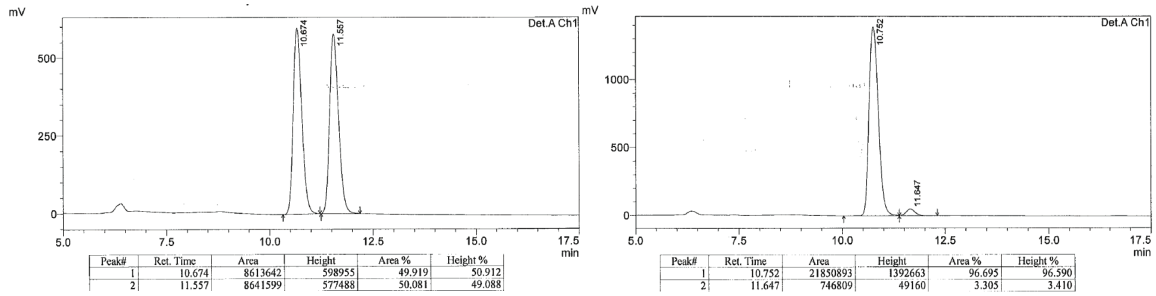
(*S*,*E*)-1-Phenyl-3-(trifluoromethyl)hexa-1,5-dien-3-ol (2.12o, Scheme 2.11): IR (neat): 3543 (br w), 2921 (br, w), 2854 (br, w), 2807 (br, w), 1614 (m), 1523 (m), 1445 (w), 1358 (w), 1269 (m), 1227 (m), 1145 (s), 994 (m), 944 (m), 814 (s), 710 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.40 (2H, m), 7.37–7.35 (2H, m), 7.32–7.26 (1H, m), 6.87 (1H, d, J = 16.0 Hz), 6.21 (1H, d, J = 16.0 Hz), 5.87–5.69 (1H, m), 5.28–5.23 (2H, m), 2.70–2.59 (2H, m), 2.32 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.8, 133.4, 130.5, 128.8, 128.5, 127.0, 125.4 (q, J = 283.7 Hz), 124.8, 121.5, 75.3 (q, J = 28.3 Hz), 39.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ 72.37 (3F, s); HRMS Calculated for $C_{13}H_{12}F_3$ $[M + H - H_2O]^+$: 225.08911; Found: 225.08909. $[\alpha]^{22}_D$ = +19.9 (c = 1.00, $CHCl_3$) for a 96.5:3.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 14 min (major) and 19 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.0	49.885	1	13.7	96.432
2	17.9	50.115	2	15.2	3.568

(*R*)-1,1,1-Trifluoro-4-methyl-2-phenylpent-4-en-2-ol (2.22a, Table 2.3): The title compound is synthesized analogously to **2.12a** except for the following changes: 1) Boronic ester **2.20b** (60 μL, 0.28 mmol) is used instead of **2.20a**. 2) The reaction temperature is 22 ºC. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL of pentanes, 20 mL 30:1 and 15 mL 19:1 pentanes: diethyl ether. Three purifications were needed to obtain analytically pure compound) to afford **2.22a** (41.1 mg, 0.179 mmol, 89% yield) as a pale yellow oil. IR (neat): 3520 (w, br), 3076 (w), 3034 (w), 2973 (w), 2953 (w), 2924 (w), 1645 (w), 1450 (w), 1378 (w), 1265 (m), 1151 (s), 1073 (m), 911 (m), 721 (m), 699 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (2H, d, J = 7.4 Hz), 7.45–7.31 (3H, m), 4.99–4.96 (1H, m), 4.85 (1H, s), 2.97 (1H, app d, J = 13.9 Hz), 2.87–2.83 (1H, m), 2.83 (1H, s), 1.40 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 137.5, 128.6, 128.4, 126.6 (m), 125.5 (q, J = 285.4 Hz), 118.2, 75.3 (q, J = 28.2), 43.5, 23.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.26 (3F, s); HRMS Calcd. for $C_{12}H_{12}F_3$ $[M + H - H_2O]^+$: 213.08911; Found: 213.08958. $[\alpha]^{21.0}_D$ = +88.7 (c = 1.80, $CHCl_3$) for a 97:3 e.r. sample. The

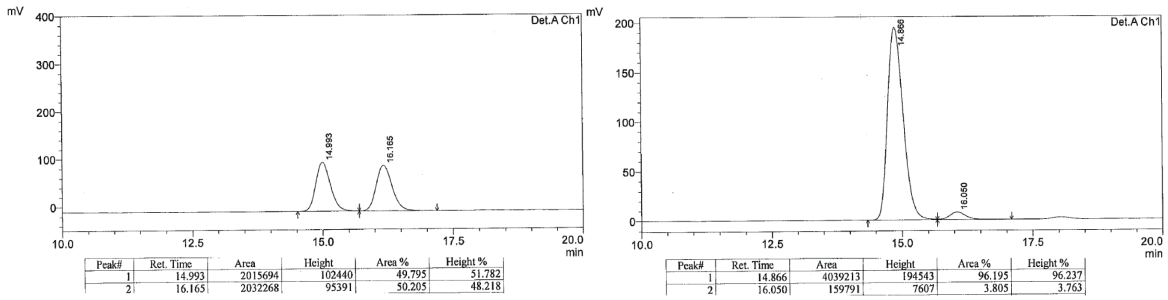
enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 11 min (major) and 12 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	10.7 min	49.919	1	10.8 min	96.695
2	11.6 min	50.081	2	11.6 min	3.305

(*R*)-4-Chloro-1,1,1-trifluoro-2-phenylpent-4-en-2-ol (2.22b, Table 2.3): The title compound is synthesized analogously to **2.12a** except for the following changes: 1) Boronic ester **2.20c** (43 μL, 0.22 mmol) is used instead of **2.20a**. 2) The reaction temperature is 22 ºC. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 30:1, 20 mL 15:1 pentanes: diethyl ether) affording **2.22b** (49.3 mg, 0.197 mmol, 98% yield) as a clear pale yellow oil. IR (neat): 3567 (w, br), 1634 (w), 1451 (w), 1267 (m), 1145 (s), 1074 (m), 1012 (w), 968 (w), 896 (m), 765 (m), 721 (m), 697 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.58 (2H, m), 7.45–7.36 (3H, m), 5.32–5.30 (1H, m), 5.15 (1H, s), 3.31 and 3.13 (2H, ABq, J_{AB} = 15.2), 3.09 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.8, 134.6, 126.9, 128.4, 126.6 (m), 125.1 (q, J = 286.0 Hz), 118.9, 77.0 (q, J = 28.1 Hz, one peak is overlapping with $CDCl_3$), 44.4; ^{19}F NMR (376 MHz,

$CDCl_3$): δ 73.32 (3F, s); HRMS Calcd for $C_{11}H_9ClF_3$ $[M + H - H_2O]^+$: 233.03449; Found: 233.03489. $[\alpha]^{22}_D$ = +36.7 (*c* = 2.18, $CHCl_3$) for a 96.5:3.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 15 min (major) and 16 min (minor).

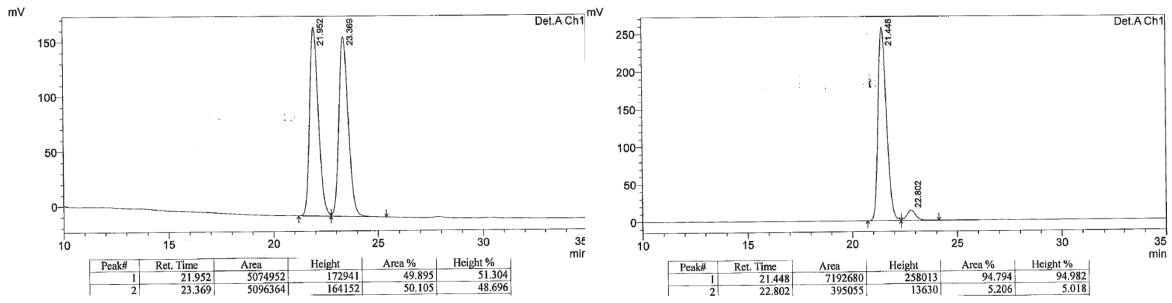


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	15.0 min	49.795	1	14.9 min	96.195
2	16.2 min	50.205	2	16.1 min	3.805

■ **Representative Procedure for Catalytic Enantio- and Regioselective Allenyl Additions to Ketones Bearing a Perfluoroalkyl Group (Scheme 2.13)**: In a nitrogen-filled glovebox, **2.21e** (5.1 mg, 0.010 mmol) is added to a two-dram vial equipped with a stir bar and dissolved in 1.0 mL of toluene. A second stock solution is prepared by dissolving 19.2 mg NaO*t*-Bu in 8.0 mL toluene. A two-dram vial equipped with a stir bar is charged with 200 μmol of the stock solution of **2.21e** (1.5 mg, 20.0 μmol) followed by 800 μL of the stock solution of NaO*t*-Bu (1.9 mg, 5.0 μmol). This vial is sealed with a cap (phenolic open top cap with a white PFTE/gray silicone septa) and electrical tape and removed from the glovebox. Methanol (10. μL, 0.25 mmol), trifluoroacetophenone **2.11a** (28 μL, 0.20 mmol), and allenylboronic acid pinacol ester **2.23** (40. μL, 0.22 mmol) are

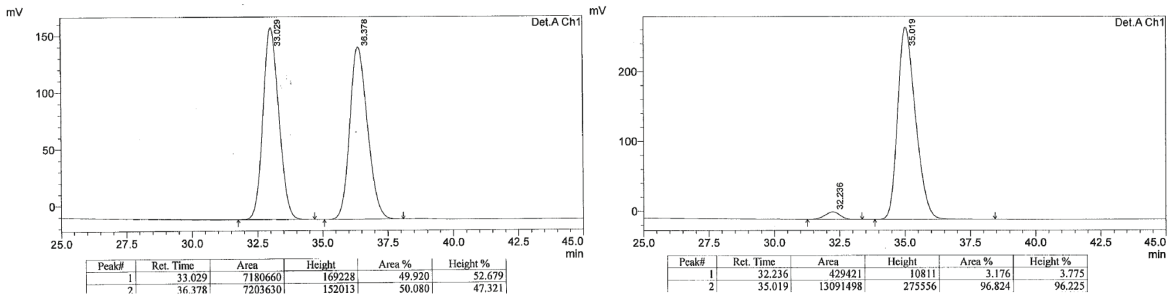
added by syringe under N_2 in the stated order and the reaction mixture is allowed to stir at 22 ºC for 4 h after which time the cap is removed and α,α,α-trifluorotoluene (24.4 μL, 0.199 mmol) is added as an internal standard. Following ^{19}F NMR analysis of the reaction mixture, it is passed through a short plug of silica gel (eluted with Et_2O) and concentrated *in vacuo* being careful not to remove all of the solvent, as the product is volatile. The resulting pale yellow oil is purified by silica gel chromatography (10 mm diameter column slurry packed with 2.5 g of silica gel in pentane and eluted successively with 10 mL of pentanes and 35 mL 11:1 pentanes : diethyl ether) to afford **2.24a** (43.0 mg, 0.201 mmol, >98% yield, >98:2 allene:propargyl) as a pale yellow oil.

(*R*)-1,1,1-Trifluoro-2-phenylpenta-3,4-dien-2-ol (2.24a, Scheme 2.13): IR (neat): 3548 (w, br), 3065 (w), 1959 (w), 1451 (w), 1264 (m), 1154 (s), 1073 (m), 1059 (m), 910 (m), 855 (m), 761 (m), 708 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.66–7.63 (2H, m), 7.44–7.36 (3H, m), 5.87 (1H, t, J = 6.7 Hz), 5.23–5.13 (2H, m), 2.83 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.6, 136.9, 129.0, 128.4, 126.7 (q, J = 1.2 Hz), 124.8 (q, J = 285.9 Hz), 93.1, 82.4, 74.7 (q, J = 29.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.40 (3F, s); HRMS Calcd for $C_{11}H_{10}F_3O$ $[M + H]^+$: 215.06837; Found: 215.06899. $[\alpha]^{21.7}_D$ = +117 (*c* = 1.88, $CHCl_3$) for a 95.5:4.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 99:1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 21 min (major) and 22 min (minor).



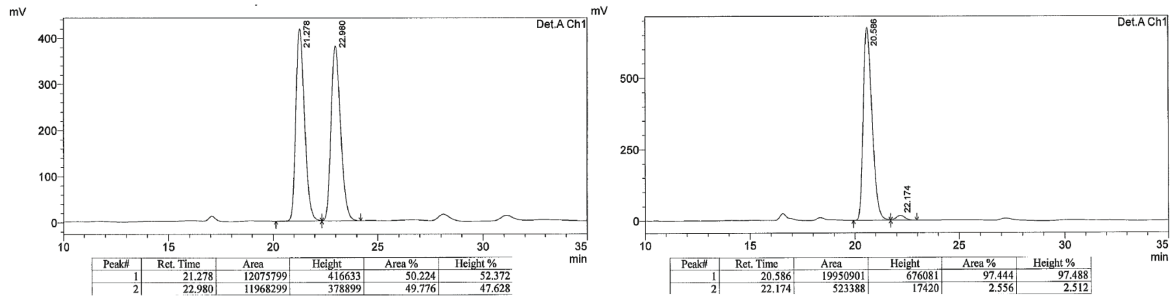
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	22.0 min	49.895	1	21.4 min	94.794
2	23.4 min	50.105	2	22.8 min	5.204

(*R*)-1,1,1,2,2-Pentafluoro-3-phenylhexa-4,5-dien-3-ol (2.24b, Scheme 2.13): The title compound is synthesized analogously to **2.24a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 30:1, 20 mL 15:1 pentanes : diethyl ether) affording **2.24b** (46.3 mg, 0.175 mmol, 88% yield) as a clear pale yellow oil. IR (neat): 3559 (w, br), 1959 (w), 1496 (w), 1451 (w), 1336 (m), 1213 (s), 1172 (s), 1138 (s), 1060 (s), 869 (s), 715 (s), 697 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.61 (2H, m), 7.44–7.35 (3H, m), 5.99 (1H, t, *J* = 6.6 Hz), 5.27–5.22 (1H, m), 5.19–5.14 (1H, m), 2.85 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.9, 137.1, 128.9, 128.4, 126.6 (t, *J* = 1.9 Hz), 119.3 (qt, *J* = 288.4, 36.3 Hz), 113.9 (tq, *J* = 261.9, 34.4 Hz), 93.8–93.7 (m), 83.2, 74.2 (t, *J* = 23.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 75.11 (3F, s), 30.2 and 29.9 (2F, ABq, J_{AB} = 276.8 Hz); HRMS Calcd. for $C_{12}H_{10}F_5O$ $[M + H]^+$: 265.06518; Found: 265.06534. $[\alpha]^{22.0}_D$ = +135 (*c* = 1.99, $CHCl_3$) for a 97:3 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 32 min (minor) and 35 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	33.0 min	49.920	1	32.2 min	3.775
2	36.4 min	50.080	2	35.0 min	96.225

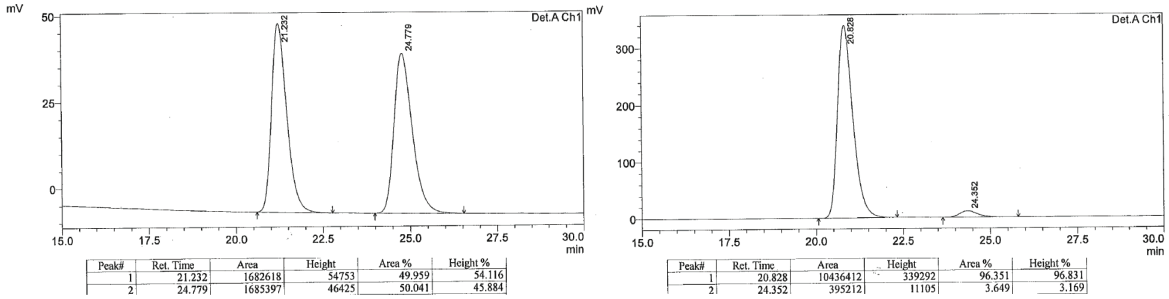
(*R*)-1,1,1-Trifluoro-2-(4-fluorophenyl)penta-3,4-dien-2-ol (2.24c, Scheme 2.13): The title compound is synthesized analogously to **2.24a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 35 mL 11:1) affording **2.24c** (38.7 mg, 0.167 mmol, 83% yield, >98:2 allene:propargyl) as a clear colorless oil. IR (neat): 3568 (w, br), 3490 (w, br), 1958 (w), 1604 (w), 1510 (m), 1235 (m), 1156 (s), 1077 (m), 976 (w), 924 (m), 857 (m), 833 (s), 816 (m), 734 (m), 520 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.59 (2H, m), 7.11–7.06 (2H, m), 5.84–5.81 (1H, m), 5.24–5.13 (2H, m), 2.80–2.79 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.7, 163.1 (d, J = 248.0 Hz), 132.7 (d, J = 3.1 Hz), 128.9–128.6 (m), 124.7 (q, J = 285.2 Hz, most downfield peak of quartet is overlapping with previous multiplet), 115.3 (d, J = 22.1 Hz), 92.9, 82.5, 74.5 (q, J = 29.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.19 (3F, s), 39.7 (1F, m); HRMS Calcd for $C_{11}H_7F_3$ [M + H – H_2O]$^{+}$: 215.04839; Found: 215.04900. $[\alpha]^{22.3}_{D}$ = +124 (c = 2.01, $CHCl_3$) for a 97.5:2.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 99:1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 20 min (major) and 22 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	21.3 min	50.224	1	20.6 min	97.444
2	23.0 min	49.776	2	22.2 min	2.556

(*R*)-2-(4-(Dimethylamino)phenyl)-1,1,1-trifluoropenta-3,4-dien-2-ol (2.24d, Scheme 2.13): The title compound is synthesized analogously to **2.24a** except the substrate is weighed out into the reaction vessel before any other components were added. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL of pentanes, 50 mL 11:1 pentanes : diethyl ether, 20 mL 4:1 pentanes : dichloromethane) to afford **2.24d** (49.6 mg, 0.193 mmol, 96% yield, >98:2 allene:propargyl) as white solid. M.p = 63 – 65 ºC. IR (neat): 3208 (w, br), 3005 (w), 2978 (w), 2894 (w), 2855 (w), 2815 (w), 1976 (w), 1948 (w), 1608 (w), 1515 (w), 1474 (w), 1387 (w), 1313 (w), 1237 (w), 1189 (m), 1151 (s), 1125 (s), 1089 (m), 1047 (w), 076 (w), 924 (m), 859 (m), 826 (m), 815 (m), 740 (w), 699 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.45 (2H, m), 6.74–6.71 (2H, m), 5.84 (1H, t, *J* = 6.7 Hz), 5.20–5.10 (2H, m), 2.97 (6H, s), 2.73 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.6, 150.7, 127.6 (m), 125.0 (q, *J* = 285.8 Hz), 124.2, 111.9, 93.2 (m), 81.9, 74.6 (q, *J* = 29.3 Hz), 40.5, 40.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.11 (3F, s); HRMS Calcd. for $C_{13}H_{15}F_3NO$ $[M + H]^+$: 258.11057; Found: 258.10933; $[\alpha]^{21.8}_D$ = +165 (*c* = 1.70, $CHCl_3$) for a 96:4 er sample. The enantiomeric purity of this compound was determined by

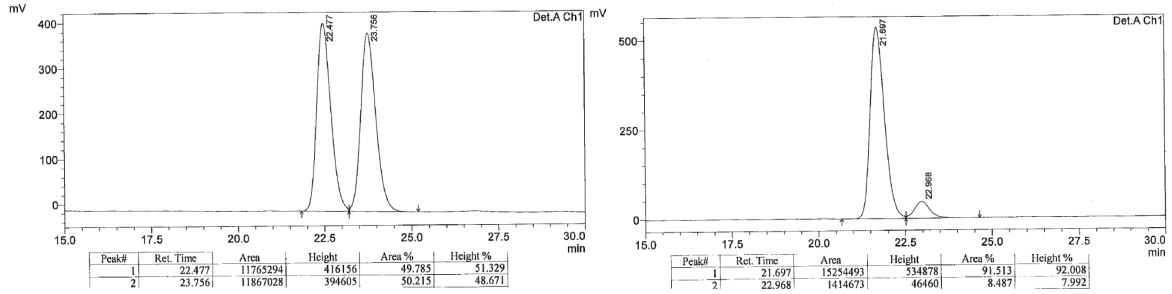
HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 97:3 hexanes:*i*-PrOH, 0.7 mL/min, 220 nm): t_R: 21 min (major) and 24 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	21.2 min	49.959	1	21.4 min	96.351
2	24.8 min	50.041	2	22.8 min	3.649

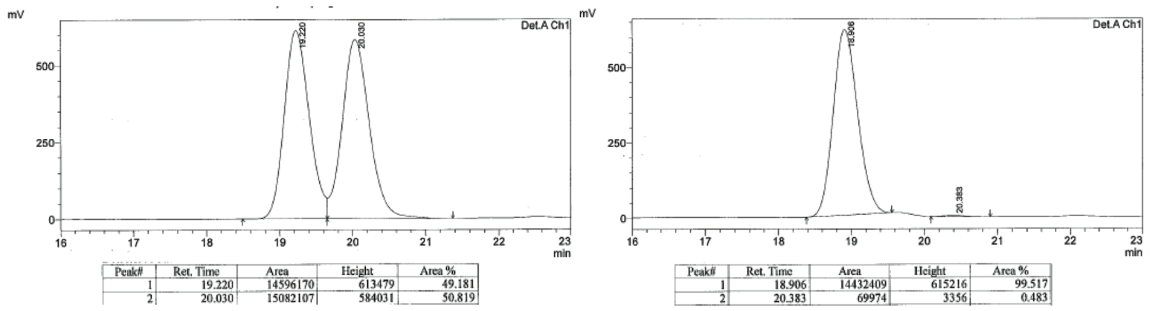
(*S*)-1,1,1-Trifluoro-2-(thiophen-2-yl)penta-3,4-dien-2-ol (2.24e, Scheme 2.13): The title compound is synthesized analogously to **2.24a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL of pentanes and 20 mL 30:1, 25 mL 11:1 pentanes : diethyl ether) to afford **2.24e** (40.3 mg, 0.183 mmol, 92% yield, >98:2 allene:propargyl) as a pale yellow oil. IR (neat): 3534 (w, br), 1980 (w), 1959 (w), 1434 (w), 1267 (w), 1164 (s), 1078 (w), 1047 (w), 996 (w), 890 (w), 853 (m), 716 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.35 (1H, m), 7.22–7.20 (1H, m), 7.06–7.03 (1H, m), 5.82–5.79 (1H, m), 5.27–5.18 (2H, m), 2.99 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.5, 140.6, 127.2, 126.6, 126.5 (m), 124.3 (q, J = 285.6 Hz), 93.0, 82.9, 74.0 (q, J = 31.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 72.80 (3F, s); HRMS Calcd. for $C_9H_6F_3S$ $[M + H - H_2O]^+$: 203.01423; Found: 203.01423; $[\alpha]^{22.4}_D$ = +104 (c = 2.30, $CHCl_3$) for a 93:7 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 22 min

(major) and 23 min (minor).



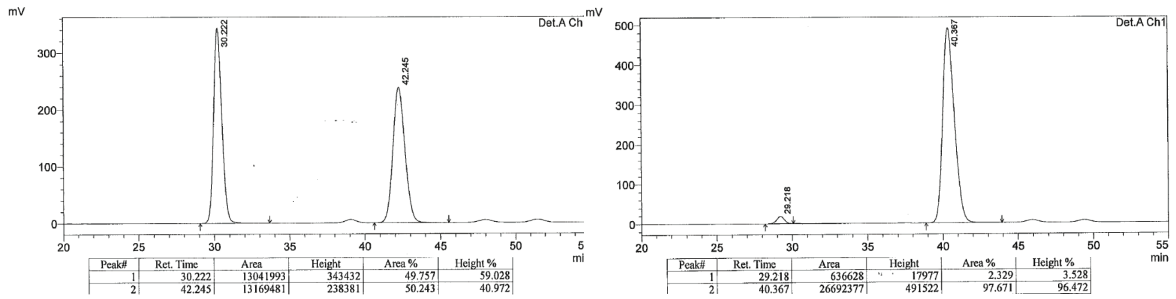
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	22.5 min	49.785	1	21.7 min	91.513
2	23.7 min	50.215	2	23.0 min	8.487

(*R*)-1,1,1-Trifluoro-2-(thiophen-3-yl)penta-3,4-dien-2-ol (2.24f, Scheme 2.13): IR (neat) : 3540 (br w), 3115 (w), 3083 (w), 2928 (w), 1275 (m), 1226 (w), 1150 (s), 1086 (m), 1019 (m), 995(m), 920 (m), 854 (m), 785 (s), 724 (s), 688(s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.42 (1H, m), 7.42–7.29 (1H, m), 7.25–7.13 (1H, m), 5.76 (1H, t, *J* = 6.7 Hz), 5.28–5.05 (2H, m), 2.80 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.6, 138.2, 126.2 (m), 124.6 (q, *J* = 285.5 Hz), 124.1 (m), 92.8–92.7 (m), 82.4, 73.9 (q, *J* = 30.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 72.81; HRMS Calculated for $C_9H_6F_3S$ $[M + H - H_2O]^+$: 203.01423; Found: 203.01483. $[\alpha]^{22}_D$ = +82 (c = 0.97, $CHCl_3$) for a >99:1 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 19 min (major) and 20 min (minor).



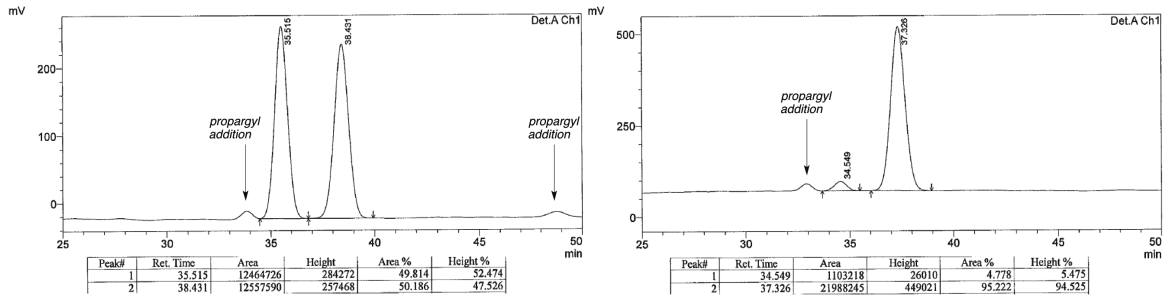
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	19.2 min	49.181	1	18.9 min	99.517
2	20.0 min	50.819	2	20.4 min	0.483

(*R*)-1,1,1-Trifluoro-2-(2-methoxyphenyl)penta-3,4-dien-2-ol (2.24g, Scheme 2.13): The title compound is synthesized analogously to **2.24a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL of pentanes and 35 mL 11:1 pentanes : diethyl ether) to afford **2.24g** (46.3 mg, 0.190 mmol, 95% yield, >98:2 allene:propargyl) as a clear colorless oil. IR (neat): 3442 (w, br), 1961 (w), 1601 (w), 1585 (w), 1491 (w), 1465 (w), 1465 (w), 1239 (s), 1158 (s), 1083 (m), 1050 (m), 1021 (m), 923 (m), 852 (m), 753 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.46 (1H, m), 7.39–7.34 (1H, m), 7.05–6.98 (2H, m), 5.82 (1H, s), 5.79 (1H, t, J = 6.8 Hz), 5.10–4.99 (2H, m), 3.93 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.0, 158.0, 130.5, 130.1 (q, J = 1.2 Hz), 125.1 (q, J = 287.2 Hz), 124.8, 121.4, 112.5, 92.0 (q, J = 1.2 Hz), 79.9, 77.5 (q, J = 29.4 Hz), 56.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ 73.95 (3F, s); HRMS Calcd for $C_{12}H_{10}F_3O$ $[M + H - H_2O]^+$: 227.06837; Found: 227.06884. $[\alpha]^{22}_D$ = +27.9 (c = 1.79, $CHCl_3$) for a 97.5:2.5 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 29 min (minor) and 40 min (major).



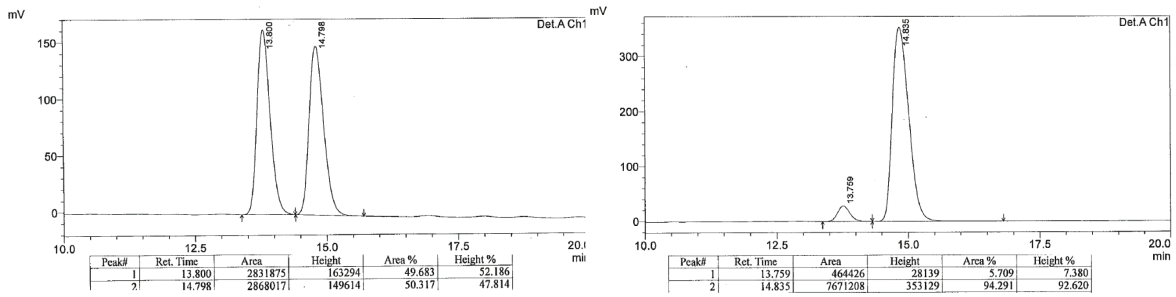
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	30.2 min	49.757	1	29.2 min	2.329
2	42.2 min	50.243	2	40.4 min	97.671

(*R*)-1,1,1-Trifluoro-2-(*o*-tolyl)penta-3,4-dien-2-ol (2.24h, Scheme 2.13): The title compound is synthesized analogously to **2.24a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL of pentanes and 20 mL 12:1 pentanes : diethyl ether) to afford **2.24h** (39.4 mg, 0.173 mmol, 86% yield, 97:3 allene:propargyl) as a clear colorless oil. IR (neat): 3537 (w, br), 1958 (w), 1488 (w), 1458 (w), 1363 (w), 1262 (m), 1156 (s), 1078 (w), 1048 (w), 966 (w), 924 (m), 853 (m), 759 (m), 727 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (1H, d, J = 7.8 Hz), 7.32–7.22 (3H, m), 5.82 (1H, s), 5.86–5.82 (1H, m), 5.22–5.12 (2H, m), 2.79–2.78 (1H, m), 2.60–2.59 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.9, 138.4, 134.5, 133.2, 128.9, 128.0–127.9 (m), 125.6, 125.3 (q, J = 286.6 Hz), 93.4 (m), 81.6, 77.1 (q, J = 29.0 Hz), 22.4 (m); ^{19}F NMR (376 MHz, $CDCl_3$): δ 74.60 (3F, s); HRMS Calcd. for $C_{12}H_{10}F_3$ $[M + H - H_2O]^+$: 211.07346; Found: 211.07439; $[\alpha]^{22.5}_D$ = +63.9 (c = 2.19, $CHCl_3$) for a 95:5 er sample (97:3 ratio of allene to propargyl addition). The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 35 min (minor) and 37 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	35.5 min	49.814	1	34.5 min	4.778
2	38.4 min	50.186	2	37.3 min	95.222

(*S*)-2-Benzyl-1,1,1-trifluoropenta-3,4-dien-2-ol (2.24i, Scheme 2.13): The title compound is synthesized analogously to **2.24a** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL of pentanes and 35 mL 11:1 pentanes : diethyl ether) to afford **2.24i** (42.7 mg, 0.187 mmol, 94% yield, >98:2 allene:propargyl) as a pale yellow oil. IR (neat): 3549 (w, br), 3066 (w), 1959 (w), 1497 (w), 1456 (w), 1273 (m), 1164 (s), 1124 (m), 1088 (m), 1032 (m), 969 (m), 857 (m), 714 (m), 698 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (5H, m), 5.34–5.30 (1H, m), 5.02–4.97 (1H, m), 4.83–4.78 (1H, m), 3.19–3.18 (1H, m), 3.16–3.15 (1H, m), 2.29–2.27 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.9, 134.0, 131.2, 128.2, 127.3, 125.4 (q, J = 285.7 Hz), 91.3 (m), 81.5, 74.1 (q, J = 28.1 Hz), 40.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ 71.86 (3F, s); HRMS Calcd. for $C_{12}H_{12}F_3O$ $[M + H]^+$: 229.08402; Found: 229.08487. $[\alpha]^{22.0}_D$ = +42.6 (c = 1.64, $CHCl_3$) for a 94:6 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 14 min (minor) and 15 min (major).

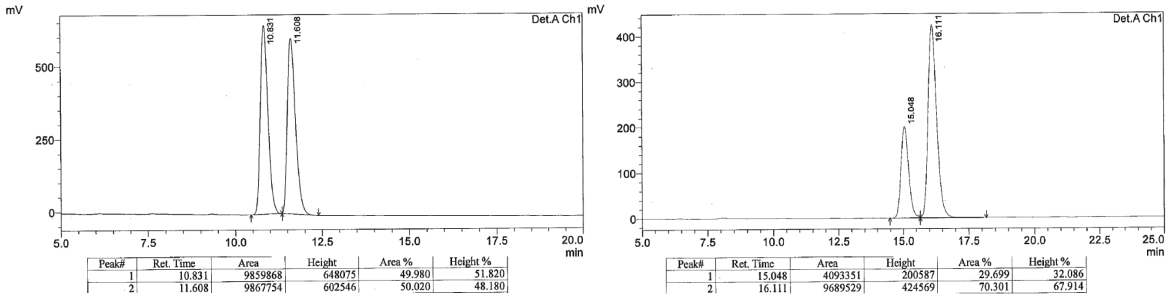


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.8 min	49.683	1	13.8 min	5.709
2	14.8 min	50.317	2	14.8 min	94.291

■ **Representative Procedure for Catalytic Enantioselective Allyl Additions to Ketones in Scheme 2.14**: In a nitrogen-filled glovebox, **2.21a** (7.7 mg, 0.025 mmol) is added to a two-dram vial equipped with a stir bar and dissolved in 1.0 mL of toluene. A second stock solution is prepared by dissolving 4.8 mg NaO*t*-Bu in 8.0 mL toluene. A two-dram vial equipped with a stir bar is charged with 200 μmol of the stock solution of **2.21a** (1.5 mg, 5.0 μmol) followed by 800 μL of the stock solution of NaO*t*-Bu (1.9 mg, 5.0 μmol). This vial is sealed with a cap (phenolic open top cap with a white PFTE/gray silicone septa) and electrical tape and removed from the glovebox. Methanol (20 μL, 0.50 mmol), acetophenone **2.9** (24 μL, 0.20 mmol) and allylboronic acid pinacol ester **2.20a** (56 μL, 0.29 mmol) are added by syringe under N_2 in the stated order. The clear, colorless solution is allowed to stir at 22 ºC for 4 h after which time the cap is removed, and 9-methylanthracene (6.4 mg, 0.033 mmol; stock solution in ethyl acetate) is added as an internal standard for ^{1}H NMR. The solution is passed through a short plug of silica gel (eluted with Et_2O) and concentrated *in vacuo* being careful not to remove all of the solvent, as the product is volatile. The resulting yellow oil is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and

eluted with 10 mL pentanes, 50 mL 98:2, 10 mL 97:3, 20 mL 95:5 pentanes : diethyl ether) affording **2.10** (26.0 mg, 0.160 mmol, 80% yield) as a clear colorless oil.

(*S*)-2-Phenylpent-4-en-2-ol (2.10, Scheme 2.14): The analytical data are fully consistent with those reported previously.[53] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.43 (2H, m), 7.37–7.32 (2H, m), 7.27–7.22 (1H, m), 5.68–5.57 (1H, m), 5.17–5.10 (2H, m), 2.72–2.67 (1H, m), 2.57–2.48 (1H, m), 2.03 (1H, s), 1.55 (3H, s); HRMS Calcd for $C_{11}H_{13}$ $[M + H - H_2O]^+$: 145.10173; Found: 145.10166; $[\alpha]^{23.5}_D$ = –27.8 (*c* = 1.08, $CHCl_3$) for a 70:30 er sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 99:1 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R of: 15 min (minor) and 16 min (major).

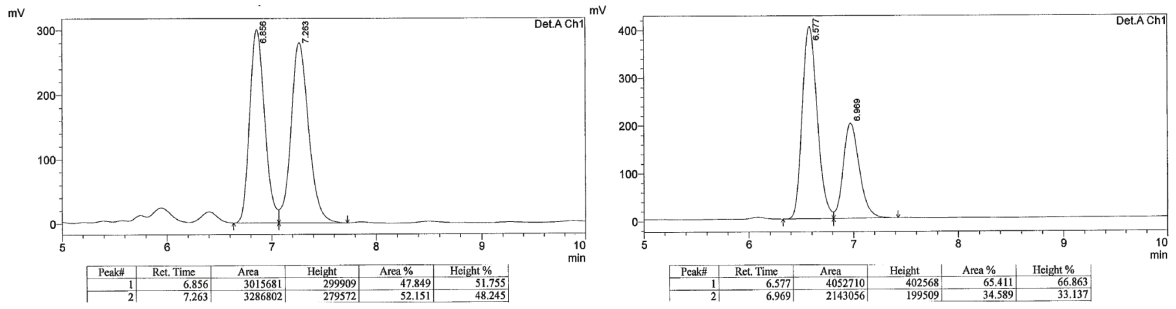


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	10.8 min	49.983	1	15.1 min	29.699
2	11.6 min	50.020	2	16.1 min	70.301

2-Methyl-3-phenylhex-5-en-3-ol (2.26a, Scheme 2.14): The title compound is synthesized analogously to **2.10** except the reaction time was 18 h. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 40 mL 99:1, 10 mL 96:4 pentanes : diethyl ether) affording **2.26a** (12.4 mg, 0.0652 mmol, 33% yield) as a clear colorless oil. The

(53) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 12660–12661.

analytical data are fully consistent with those reported previously.[54] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.31 (4H, m), 7.24–7.21 (1H, m), 5.53–5.42 (1H, m), 5.15–5.05 (2H, m), 2.81 (1H, dd, *J* = 13.8, 5.4 Hz), 2.54 (1H, dd, *J* = 13.8, 9.1 Hz), 2.02 (1H, hept, *J* = 6.9 Hz), 1.93 (1H, s), 0.95 (3H, d, *J* = 6.9 Hz), 0.77 (3H, d, *J* = 6.9 Hz); HRMS Calcd for $C_{13}H_{17}$ $[M + H - H_2O]^+$: 173.13303; Found: 173.13343; $[\alpha]^{23.5}_D$ = +54.5 (*c* = 0.55, $CHCl_3$) for a 65:35 e.r. sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 99:1 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R: 6.6 min (major) and 7.0 min (minor).

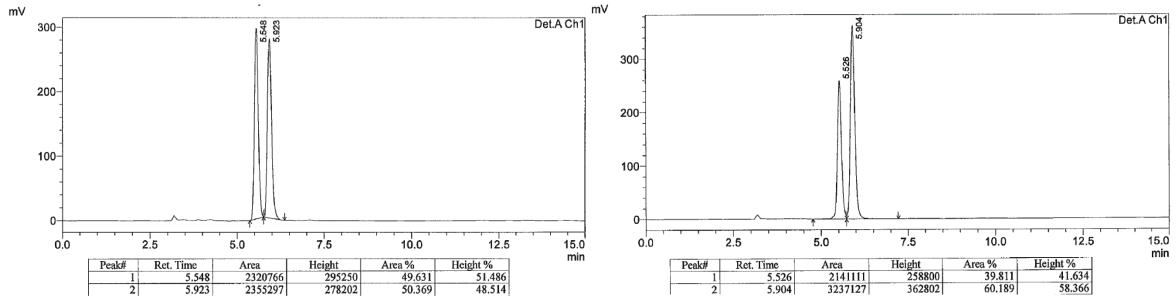


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	6.9 min	47.849	1	6.6 min	65.411
2	7.3 min	52.151	2	7.0 min	34.589

6-Methyl-4-phenylhept-1-en-4-ol (2.26b, Scheme 2.14): The title compound is synthesized analogously to **2.10** except the reaction time was 18 h. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 40 mL 99:1, 10 mL 96:4 pentanes : diethyl ether) affording **2.26b** (25.5 mg, 0.126 mmol, 63% yield) as a clear colorless oil. IR (neat): 3555 (w, br), 3076 (w), 3027 (w), 2952 (w), 2925 (w, br), 2868 (w), 1638 (w),

(54) Uccello-Barretta, G.; Bernardini, R.; Lazzaroni, R.; Salvadori, P. *J. Organomet. Chem.* **2000**, *598*, 174–178.

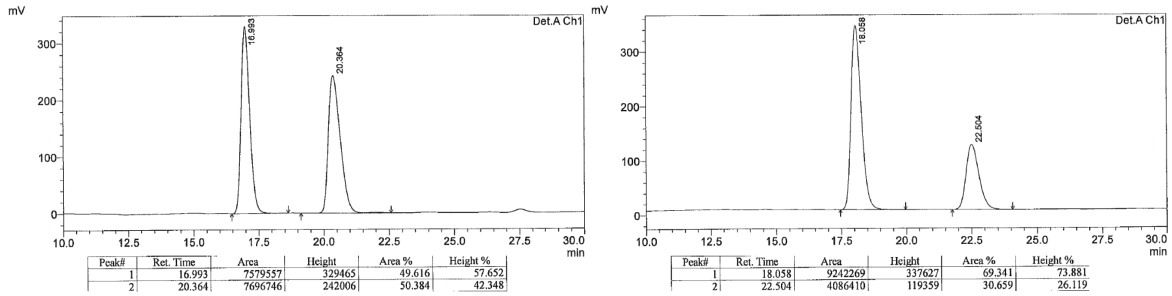
1602 (w), 1494 (w), 1365 (w), 1297 (w), 1259 (w), 1171 (w), 1146 (w), 1061 (w), 1032 (w), 1000 (w), 920 (m), 763 (w), 701 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.32 (4H, m), 7.25–7.20 (1H, m), 5.57–5.47 (1H, m), 5.17–5.09 (2H, m), 2.71 (1H, dd, *J* = 13.6, 5.8 Hz), 2.48 (1H, dd, *J* = 13.6, 8.9 Hz), 2.03 (1H, s), 1.83 (1H, dd, *J* = 14.2, 5.1 Hz), 1.69 (1H, dd, *J* = 14.2, 6.7 Hz), 1.62–1.53 (1H, m), 0.91 (3H, d, *J* = 6.6 Hz), 0.69 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 133.6, 128.1, 126.4, 125.5, 119.9, 76.3, 51.4, 48.8, 24.6, 24.3, 24.3; HRMS Calcd for $C_{14}H_{19}$ $[M + H - H_2O]^+$: 187.14868; Found: 187.14941; $[\alpha]^{21.8}_D$ = –5.77 (*c* = 1.73, $CHCl_3$) for a 60:40 e.r. sample. The enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 99:1 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R: 5.5 min (major) and 5.9 min (minor).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	5.5 min	49.631	1	5.5 min	39.811
2	5.9 min	50.369	2	5.9 min	60.189

(*S*)-2-(4-Nitrophenyl)pent-4-en-2-ol (2.28a, Equation 5): The title compound is synthesized analogously to **2.10** except the substrate was weighed out into the reaction vessel before any other components were added. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 15 mL 1:1 hexanes: dichloromethane, 25 mL dichloromethane) affording

2.28a (41.7 mg, 0.201 mmol, >98% yield) as a clear yellow oil. The analytical data are fully consistent with those reported previously.[55] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20–8.16 (2H, m), 7.63–7.59 (2H, m), 5.64–5.53 (1H, m), 5.17–5.11 (2H, m), 2.70–2.64 (1H, m), 2.56–2.50 (1H, m), 2.21 (1H, s), 1.57 (3H, m); HRMS Calcd for $C_{11}H_{14}N_1O_2$ [M + H]$^+$: 208.09737; Found: 208.09708; $[\alpha]^{21.8}$= –30.6 (*c* = 1.96, $CHCl_3$) for a 70:30 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 95:5 hexanes:*i*-PrOH, 0.8 mL/min, 220 nm): t_R: 18 min (major) and 22 min (minor).

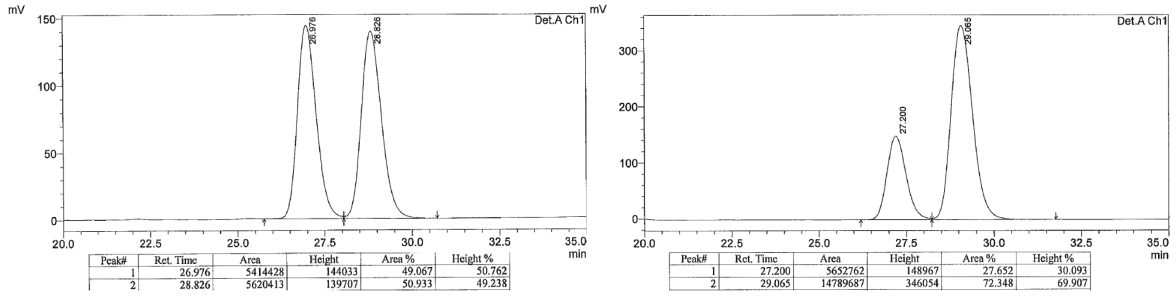


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	17.0 min	49.616	1	18.1 min	69.341
2	20.4 min	50.384	2	22.5 min	30.659

(*S*)-2-(3,5-Difluorophenyl)pent-4-en-2-ol (2.28b, Equation 5): The title compound is synthesized analogously to **2.10** and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 10 mL 30:1, 20 mL 19:1, 10 mL 15:1 pentanes : diethyl ether) affording **2.28b** (33.3 mg, 0.168 mmol, 84% yield) as a clear pale yellow oil. IR (neat): 3432 (w, br), 3081 (w, br), 2980 (w), 2934 (w, br), 1623 (m), 1599 (m), 1433 (m), 1319 (m), 1115 (s), 983 (s), 921 (m), 856 (s), 838 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99–6.93 (2H, m), 6.68 (1H, app

(55)Schneider, U.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2007,** *46*, 5909–5912.

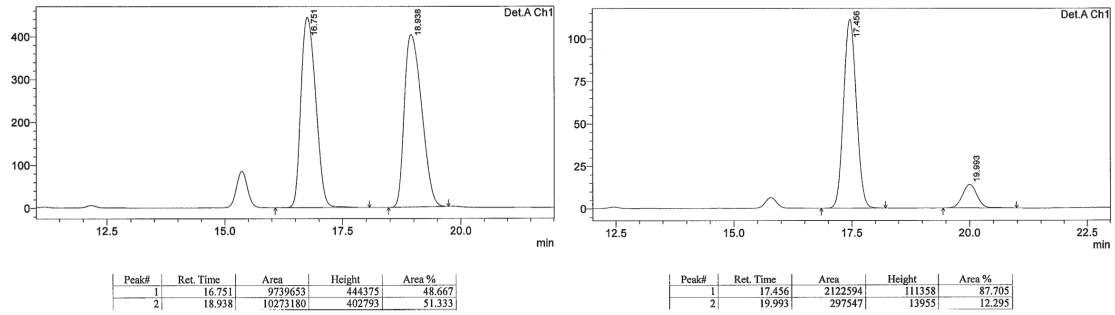
tt, J = 8.8, 2.3 Hz), 5.60 (1H, dddd, J = 16.2, 11.1, 8.3, 6.5 Hz), 5.19–5.13 (2H, m), 2.66–2.60 (1H, m), 2.50–2.44 (1H, m), 2.06 (1H, s), 1.52 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.1 (dd, J = 247.7, 12.7 Hz), 152.2 (t, J = 8.0 Hz), 132.8, 120.5, 108.3–108.0 (m), 102.1 (t, J = 25.4 Hz), 73.5 (t, J = 2.1 Hz), 48.3, 29.9; ^{19}F NMR (376 MHz, $CDCl_3$): 43.01 (2F, s); HRMS Calcd for $C_{11}H_{11}F_2$ $[M + H - H_2O]^+$: 181.08288; Found: 181.08212; $[\alpha]^{23.6}$= –34.0 (c = 1.76, $CHCl_3$) for a 75:25 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 99:1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 27 min (minor) and 29 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	27.0 min	49.067	1	27.2 min	27.652
2	28.8 min	50.933	2	29.1 min	72.348

1-Fluoro-2-phenylpent-4-en-2-ol (2.33a, Scheme 2.19): The title compound is synthesized analogously to **2.12a** except for the following changes: 1) Reaction time is 16 h. 2) Reaction temperature is 22 ºC. Note product is contaminated with ~10% of the starting ketone. IR (neat): 3565 (br w), 3465 (br w), 3064 (w), 2980 (w), 1707 (m), 1640 (w), 1600 (w), 1495 (w), 1448 (m), 1233 (m), 1089 (m), 1071 (s), 998 (m), 967(s), 761 (m), 700 (s), 638 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.46 (2H, m), 7.40–7.36 (2H, m), 7.34–7.27 (1H, m), 5.75–5.52 (1H, m), 5.25–5.05 (2H, m), 4.49 (2H, d, J = 47.7

Hz), 2.74–2.71 (2H, m), 2.44 (1H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.7, 132.4, 129.0, 128.5, 128.0, 125.6, 120.1, 88.6 (d, *J*=178.1 Hz), 75.2 (d, *J*=18.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -224.94 (1F, t, *J* = 47.7 Hz) ; HRMS Calculated for $C_{11}H_{11}F$ [M + H – H_2O]$^+$: 163.09230; Found: 163.09247; $[\alpha]^{23}_D$ = -45.4 (c = 1.10, $CHCl_3$) for a 88:12 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AZ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 17 min (major) and 19 min (minor).



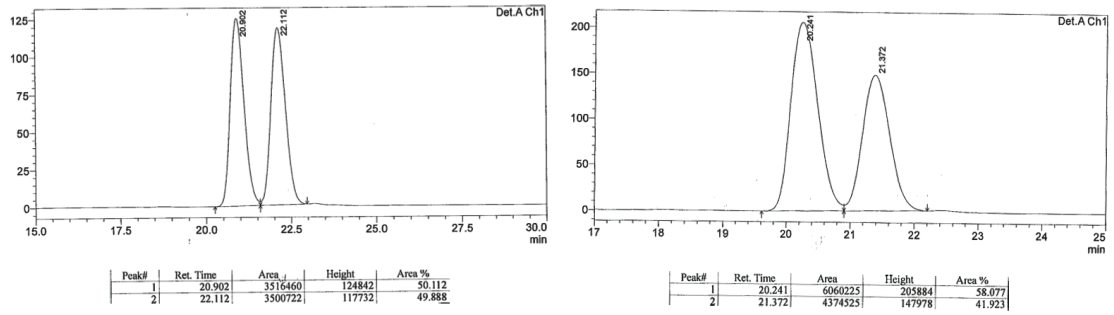
Peak#	Ret. Time	Area	Height	Area %
1	16.751	9739653	444375	48.667
2	18.938	10273180	402793	51.333

Peak#	Ret. Time	Area	Height	Area %
1	17.456	2122594	111358	87.705
2	19.993	297547	13955	12.295

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.8	48.667	1	17.5	87.705
2	19.0	51.333	2	20.0	12.295

1,1-Difluoro-2-phenylpent-4-en-2-ol (2.33b, Scheme 2.19): The title compound is synthesized analogously to **2.12a** except for the following changes: 1) Reaction time is 16 h. 2) Reaction temperature is 22 ºC. IR (neat): 3555 (br w), 3079 (w), 2980 (w), 1641 (w), 1496 (w), 1448 (m), 1346 (m), 1125 (m), 1063 (s), 996 (m), 970 (m), 923 (m), 763 (m), 699 (s), 643 (m), 563 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (2H, dd, *J* = 3.6 Hz. 1.6 Hz), 7.42–7.34 (2H, m), 7.33–7.31 (1H, m); 5.74 (1H, t, *J* = 56.4), 5.67–5.56 (1H, m), 5.25–5.17 (2H, m), 2.90–2.71 (1H, m), 2.42 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9, 131.4, 128.6, 128.3, 126.4, 121.2, 117.0 (t, *J* = 248.9Hz), 75.6 (t, *J* = 21.2Hz), 39.8 (t, *J* = 2.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 23.72 and 22.07 (2F, d of

ABq, $^2J_{F\text{-}F}$ = 277.9 Hz, $^2J_{F\text{-}H}$ = 56.0 Hz); HRMS Calculated for $C_{11}H_{11}F_2$ $[M + H - H_2O]^+$: 181.08277; Found: 181.08288. $[\alpha]^{21}_D$ = +9.88 (c = 1.01, $CHCl_3$) for a 58:42 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with an authentic sample of racemic material (Chiracel AS-H, 99:1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 20 min (major) and 21 min (minor).



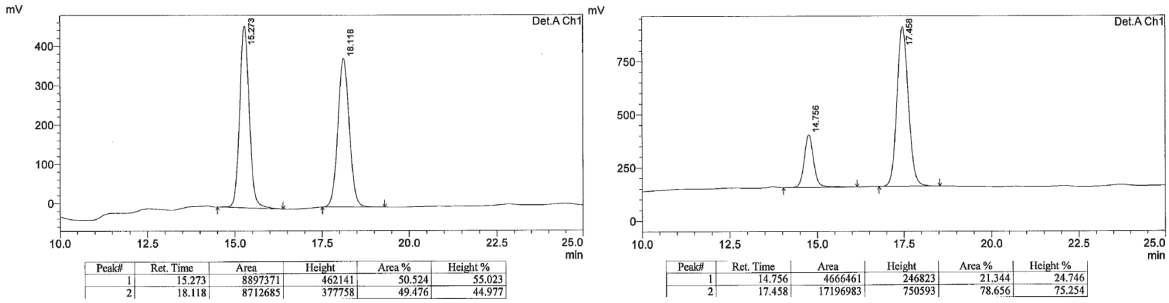
Peak#	Ret. Time	Area	Height	Area %
1	20.902	3516460	124842	50.112
2	22.112	3500722	117732	49.888

Peak#	Ret. Time	Area	Height	Area %
1	20.241	6060225	205884	58.077
2	21.372	4374525	147978	41.923

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	20.9	50.112	1	20.2	58.077
2	22.1	49.888	2	21.4	41.923

(*R*)-2,2-Difluoro-3-phenylhex-5-en-3-ol (2.33c, Scheme 2.19): The title compound is synthesized analogously to **2.12a** except for the following changes: 1) Reaction time is 16 h. 2) Reaction temperature is 22 ºC. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 10 mL 19:1, 10 mL 11:1 pentanes : diethyl ether) affording **2.33c** (42.5 mg, 0.200 mmol, >98% yield) as a clear colorless oil. IR (neat): 3555 (w, br), 3078 (w), 3010 (w), 2982 (w), 2950 (w), 1640 (w), 1497 (w), 1448 (w), 1385 (w), 1203 (m), 1142 (s), 1069 (m), 925 (s), 763 (m), 727 (m), 669 (s), 617 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.54 (2H, m), 7.39–7.29 (3H, m), 5.57–5.46 (1H, m), 5.22–5.12 (2H, m), 3.01 (1H, dd, *J* = 14.2, 6.0 Hz), 2.82 (1H, dd, *J* = 14.4, 8.5 Hz), 2.39 (1H, s), 1.41 (3H, t, *J* = 19.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8 (app d, *J* = 3.8 Hz), 132.4, 128.3,

127.7, 126.6 (m), 124.6 (t, J = 247.6 Hz), 120.7, 77.3 (t, J = 26.2 Hz), 39.8 (t, J = 2.7 Hz), 19.3 (dd, J = 27.4, 25.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): 50.73 and 49.35 (2F, q of ABq, $^2J_{F\text{-}F}$ = 245.2 Hz, $^3J_{F\text{-}H}$ = 19.0 Hz); HRMS Calcd. for $C_{12}H_{13}F_2O$ $[M - H]^-$: 211.09345; Found: 211.09257; $[\alpha]^{22.0}_D$ = +47.2 (c = 2.33, $CHCl_3$) for a 79:21 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R 15 min (minor) and 18 min (major).



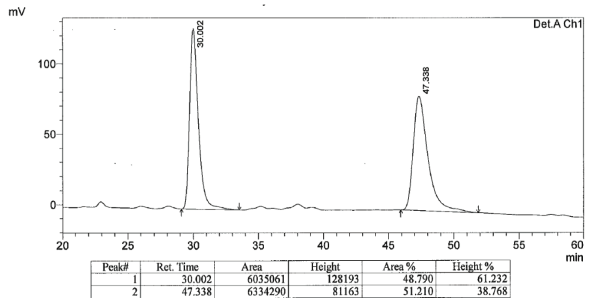
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.273	8897371	462141	50.524	55.023
2	18.118	8712685	377758	49.476	44.977

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.756	4666461	246823	21.344	24.746
2	17.458	17196983	750593	78.656	75.254

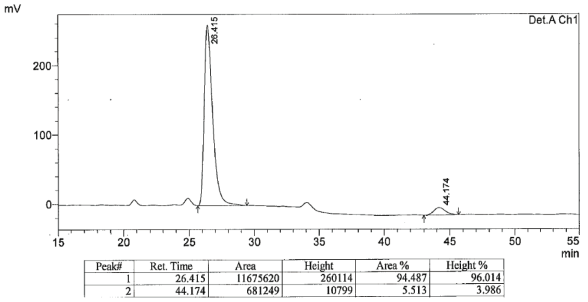
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	15.3 min	50.524	1	14.8 min	21.344
2	18.1 min	49.476	2	17.5 min	78.656

(*R*)-1-Allyl-2,2-difluoro-1,2,3,4-tetrahydronaphthalen-1-ol (2.33d, Scheme 2.19): The title compound is synthesized analogously to **2.12a** except for the following changes: 1) Reaction time is 16 h. 2) Reaction temperature is 22 ºC. 3) The substrate is weighed out into the reaction vessel before any other components were added. The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 20 mL 25:1, 20 mL 19:1, 15 mL 11:1 pentanes : diethyl ether. Three purifications were needed to completely purify the compound) affording **2.33d** (35.1 mg, 0.156 mmol, 78% yield) as a clear colorless oil. IR (neat): 3587 (w, br), 3459 (w, br), 3076 (w), 3023 (w), 2948 (w), 2855 (w), 1640 (w),

1489 (w), 1454 (w), 1364 (w), 1340 (w), 1212 (w), 1146 (m), 1087 (m), 1057 (s), 1001 (m), 959 (s), 915 (m), 758 (s), 731 (s), 655 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.57 (1H, m), 7.29–7.23 (2H, m), 7.13–7.11 (1H, m), 5.78–5.68 (1H, m), 5.13–5.06 (2H, m), 3.12–2.97 (2H, m), 2.78 (1H, dd, *J* = 14.5, 6.1 Hz), 2.65 (1H, dd, *J* = 14.5, 8.5 Hz), 2.55 (1H, app d, *J* = 3.3 Hz), 2.46–2.30 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.7 (app d, *J* = 3.8 Hz), 133.9 (app d, *J* = 1.6 Hz), 133.0, 128.3, 128.1, 127.3 (app d, *J* = 1.5 Hz), 123.2 (dd, *J* = 250.2, 241.9 Hz), 119.3, 74.4 (dd, *J* = 23.7, 21.4 Hz), 28.4 (dd, *J* = 24.8, 23.3 Hz), 26.3 (dd, *J* = 7.6, 3.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 43.27–43.16 and 42.63–42.53 (1F, m), 41.27–41.20 and 40.62–40.58 (1F, m); HRMS Calcd. for $C_{13}H_{13}F_2$ $[M + H - H_2O]^+$: 207.09853; Found: 207.09863; $[\alpha]^{22.0}_D$ = +36.8 (*c* = 1.90, $CHCl_3$) for a 94:6 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 26 min (major) and 44 min (minor).



Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.002	6035061	128193	48.790	61.232
2	47.338	6334290	81163	51.210	38.768

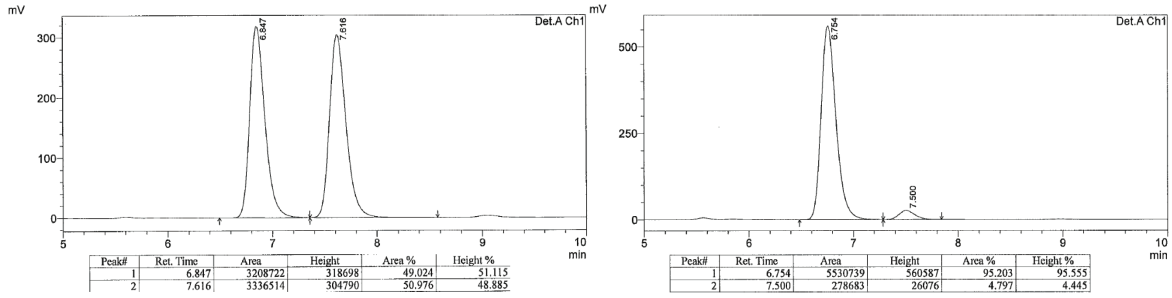


Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.415	11675620	260114	94.487	96.014
2	44.174	681249	10799	5.513	3.986

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	30.0 min	48.790	1	26.4 min	94.487
2	47.3 min	51.210	2	44.2 min	5.513

(*S*)-2-(Perfluorophenyl)pent-4-en-2-ol (2.10b, Scheme 2.20): The title compound is synthesized analogously to **2.10a** and purified by silica gel chromatography (10 mm

diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes and 40 mL 19:1 pentanes : diethyl ether) affording **2.10b** (21.3 mg, 0.0.085 mmol, 85% yield) as a clear colorless oil. IR (neat): 3466 (w, br), 2985 (w), 1650 (w), 1523 (m), 1483 (s), 1348 (w), 1305 (w), 1099 (m), 982 (s), 923 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.74–5.63 (1H, m), 5.20–5.14 (2H, m), 2.84–2.78 (2H, m), 2.59–2.53 (1H, m), 1.72 (3H, t, J = 2.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3–145.9 (m), 143.8–143.5 (m), 141.4–141.1 (m), 139.4–139.0 (m), 138.9–138.5 (m), 136.9–136.6 (m), 132.3, 120.8, 120.1–119.8 (m), 75.5, 47.5 (t, J = 2.6 Hz), 28.9 (t, J = 4.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): 12.33 (2F, d, J = 18.8 Hz); -3.09 (1F, tt, J = 21.1, 2.5 Hz), -9.02 – -9.15 (2F, m); HRMS Calcd. for $C_{11}H_8F_5$ $[M + H - H_2O]^+$: 235.05462; Found: 235.05475; $[\alpha]^{21.5}$= – 6.49 (c = 1.54, $CHCl_3$) for a 95:5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 97.5:2.5 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R of **XX**: 6.5 min (major) and 7.5 min (minor).



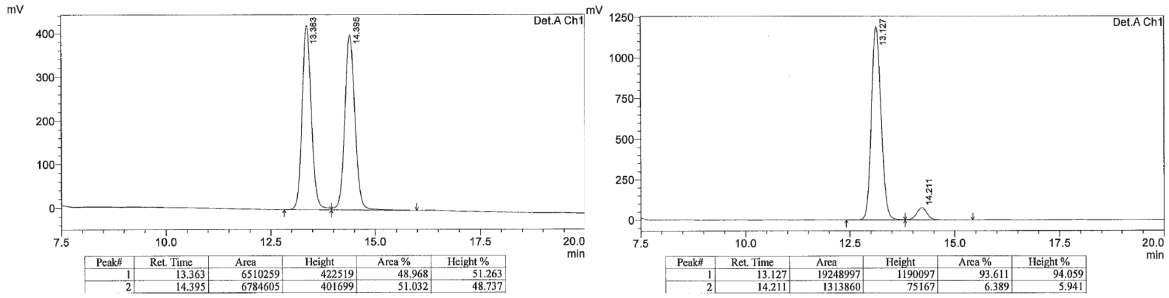
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.847	3208722	318698	49.024	51.115
2	7.616	3336514	304790	50.976	48.885

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.754	5530739	560587	95.203	95.555
2	7.500	278683	26076	4.797	4.445

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	6.8 min	49.024	1	6.8 min	95.203
2	7.6 min	50.976	2	7.5 min	4.797

(*S*)-2-(2,6-Difluorophenyl)pent-4-en-2-ol (2.10c, Scheme 2.20): The title compound is synthesized analogously to **2.10a** and purified by silica gel chromatography (10 mm

diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 15 mL 30:1, 25 mL 19:1 pentanes : diethyl ether) affording **2.10c** (14.6 mg, 0.0737 mmol, 74% yield) as a clear yellow oil. IR (neat): 3629 (w, br), 3484 (w, br), 2981 (w), 2943 (w, br), 1621 (m), 1574 (w), 1462 (s), 1351 (m), 1286 (m), 1262 (m), 1223 (m), 985 (s), 918 (m), 786 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.22–7.15 (1H, m), 6.90–6.82 (2H, m), 5.77–5.66 (1H, m), 5.14–5.09 (2H, m), 3.13–3.10 (1H, m), 2.84–2.79 (1H, m), 2.59–2.53 (1H, m), 1.71–1.70 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7 (dd, J = 247.0, 8.9 Hz), 133.4, 128.6 (t, J = 11.9 Hz), 122.1 (t, J = 13.7 Hz), 116.4, 112.9–112.6 (m), 74.9 (t, J = 2.8 Hz), 47.8 (t, J = 2.7 Hz), 28.8 (t, J = 4.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): 42.75–42.69 (2F, m); HRMS Calcd. for $C_{11}H_{11}F_2$ $[M + H - H_2O]^+$: 181.08288; Found: 181.08301; $[\alpha]^{23.4}$= –79.9 (c=0.25, $CHCl_3$) for a 94.5:5.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 99:1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 13 min (major) and 14 min (minor).



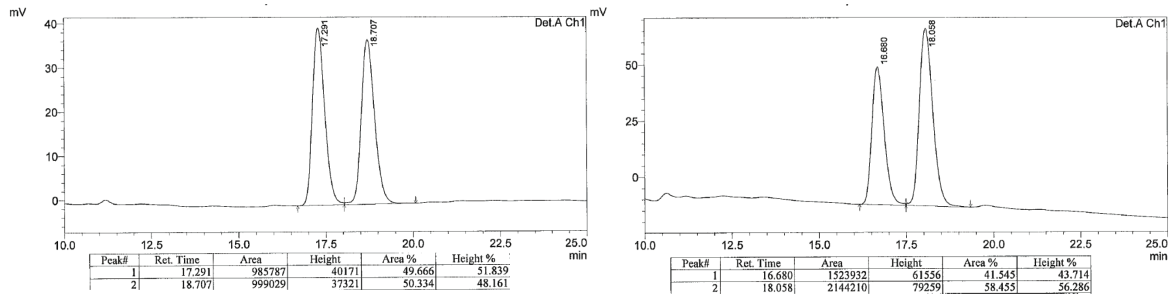
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.363	6510259	422519	48.968	51.263
2	14.395	6784605	401699	51.032	48.737

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.127	19248997	1190097	93.611	94.059
2	14.211	1313860	75167	6.389	5.941

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.4 min	48.986	1	13.1 min	93.611
2	14.4 min	51.032	2	14.2 min	6.389

2-(2-Fluorophenyl)pent-4-en-2-ol (2.10d, Scheme 2.20): The title compound is synthesized analogously to **2.10a** and purified by silica gel chromatography (10 mm

diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 14 mL 49:1, 10 mL 19:1, 25 mL 9:1 pentanes : diethyl ether) affording **2.10d** (36.6 mg, 0.203 mmol, >98% yield) as a clear colorless oil. The analytical data are fully consistent with those reported previously.[55] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.52 (1H, m), 7.27–7.21 (1H, m), 7.15–7.11 (1H, m), 7.02 (2H, ddd, J = 12.2, 8.1, 1.3 Hz), 5.63–5.53 (1H, m), 5.17–5.09 (2H, m), 2.93–2.87 (1H, m), 2.58–2.51 (1H, m), 2.28 (1H, d, J = 1.8 Hz), 1.61 (3H, d, J = 1.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ 39.75 (1F, s); HRMS Calcd. for $C_{11}H_{12}F$ $[M + H - H_2O]^+$: 163.09230; Found: 163.09230; $[\alpha]^{24.0}_D$ = –15.4 (c = 1.30, $CHCl_3$) for a 58:42 er sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD-H, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 17 min (minor) and 19 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	17.3 min	49.666	1	16.7 min	41.545
2	18.7 min	50.334	2	18.1 min	58.455

■■ PROOF of ABSOLUTE STEREOCHEMISTRY of PRODUCTS

Absolute configuration of homoallylalcohol 2.10c:

(*S*)-1,3-Difluoro-2-(2-methoxypentan-2-yl)benzene (2.35, Scheme 2.21): A 10 mL Schlenk flask equipped with a stirbar is charged with **2.34**[56] (25 mg, 0.12 mmol), 10 wt % Pd/C (13 mg, 10 mol% Pd), and tetrahydrofuran (1.5 mL). The flask is purged with N_2 gas followed by H_2 gas, sealed with a rubber septum, and connected to a balloon of H_2 gas by a needle in order to keep the H_2 pressure above the solution at ~ 1 atm. The reaction is allowed to stir at 22 ºC for 6 h after which the balloon is removed and the reaction vessel is purged with N_2 to remove excess H_2 (**IMPORTANT! Opening a Pd/C reduction without first removing H_2 gas can lead to fires)** and the reaction vessel is opened. The cloudy black reaction mixture is passed through a short plug of Celite (eluted with diethyl ether) and carefully concentrated *in vacuo* to minimize loss of volatile **2.35** to afford a clear, colorless oil. This oil is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL pentanes, 30 mL 99:1, 10 mL 49:1 pentanes : diethyl ether) affording **2.35** (19.0 mg, 0.089 mmol, 74% yield) as a clear colorless oil. IR (neat): 2961 (m), 2933 (w), 2874 (w), 2827 (w), 1619 (m), 1460 (s), 1286 (m), 1230 (w), 1087 (m), 986 (m), 789 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.15 (1H, m), 6.88–6.80 (2H, m), 3.16 (3H, m), 1.99 (1H, td, *J* = 12.8, 4.7 Hz), 1.81 (1H, td, *J* = 12.9, 4.6 Hz), 1.70–1.68 (3H, m), 1.43–1.31 (1H, m), 1.24–1.15 (1H, m), 0.89–0.85 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8 (dd, *J* = 250.9, 9.1 Hz), 128.9 (t, *J* = 11.6 Hz), 119.4 (t, *J* = 14.4 Hz), 112.8–112.5 (m), 80.4 (t, *J* = 3.3 Hz), 51.1, 44.5 (t, *J* = 2.4 Hz), 24.2 (t, *J* = 6.3 Hz), 17.8, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$): 44.80–44.75 (2F, m); HRMS Calcd for $C_9H_9F_2O$ $[M - C_3H_7]^+$:

(56) **2.34** is prepared from **2.10c** in accordance to a procedure in the literature, passed through a short plug of silica gel (elute with pentanes), concentrated *in vacuo*, and used without further purification. See: Chong, J. M.; Loewith, R. *Synth. Comm.* **1993**, *23*, 2145–2150.

171.06215; Found: 171.06238; $[\alpha]^{21.6}$= –26.3 (*c* = 0.38, $CHCl_3$) for a 94:6 e.r. sample (based on e.r. of **2.10c**).

(*S*)-(2-methoxypentan-2-yl)benzene (2.36, From 2.35, Scheme 2.21): In a nitrogen-filled glovebox, a 5 mL Schlenk flask equipped with a stirbar is charged with $Ni(PCy_3)_2Cl_2$[57] (2.8 mg, 4.0 μmol), connected to a reflux condenser, and the entire apparatus is sealed with a rubber septum and electrical tape and removed from the glovebox. Nitrogen gas is connected to the apparatus with a needle and tetrahydrofuran (300 μL) is added *via* syringe followed by dropwise addition of a 1.0 M solution of $LiEt_3BH$ (320 μL, 0.32 mmol) in tetrahydrofuran. **2.35** (8.5 mg, 0.040 mmol) is added dropwise as a solution in tetrahydrofuran (200 μL) and the orange solution is heated to reflux and allowed to stir for 14 h during which time the solution darkens from orange to black. The reaction is cooled to 0 ºC, and following removal of the reflux condenser, the reaction mixture is diluted dropwise with diethyl ether (3 mL) followed by water (1 mL) which causes a color change of the solution from black to yellow as well as bubbling. The layers are separated and the aqueous layer is washed with diethyl ether (3 x 5 mL) and the combined organic layers are dried over $MgSO_4$ and carefully concentrated *in vacuo* to minimize loss of volatile **2.36** to afford a yellow oil (>98% consumption of **2.35** by ^{1}H NMR). The product is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted sequentially with 15 mL pentanes, 20 mL 99:1, and 20 mL 49:1 pentanes : diethyl ether) to afford **2.36** (3.3 mg, 0.019 mmol, 46% yield) as a clear, colorless oil.

(*S*)-(2-methoxypentan-2-yl)benzene (2.36, From 2.10a, Scheme 2.21): In a nitrogen-

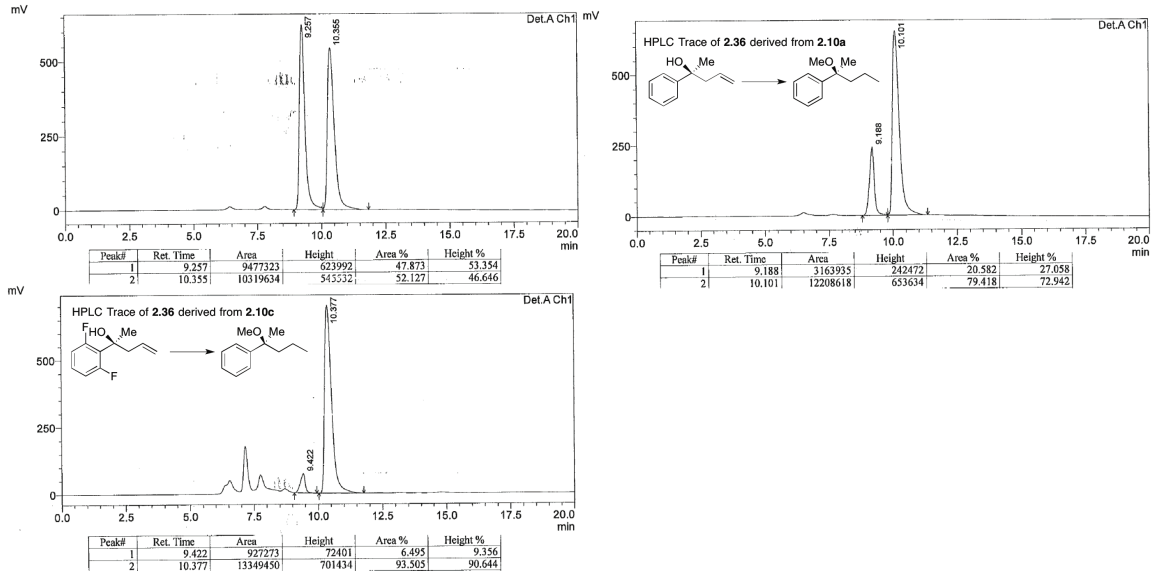
(57) Procedure is based on a report in the literature. See: Zhao, W.; Wu, J.; Cao, S. *Adv. Synth. Catal.* **2012**, *354*, 574–578.

filled glovebox, a 10 mL Schlenk flask equipped with a stirbar is charged with Crabtree's catalyst[58] (32 mg, 0.04 mmol), sealed with a rubber septum and electrical tape, and removed from the glovebox. The reaction vessel is purged with H_2 gas and connected to a balloon of H_2 gas with a needle in order to keep the H_2 pressure above the solution at ~ 1 atm. **2.10a** (65 mg, 0.4 mmol) is added by syringe in a solution of dichloromethane (2.5 mL). The orange solution is allowed to stir at 22 ºC for 18 h after which time the solution is transferred to a 15 mL RBF and concentrated *in vacuo* to afford a green oil. Diethyl ether (5 mL) is added to this, which causes a gummy green precipitate to form. This mixture is passed through a short plug of Celite® (eluted with diethyl ether) and concentrated *in vacuo* to give an olive green oil which was used without further purification.

In a nitrogen-filled glovebox, a RBF equipped with a stirbar is charged with NaH (24.0 mg, 1.00 mmol), sealed with a rubber septum and electrical tape, and removed from the glovebox. Nitrogen gas is connected to the apparatus with a needle and tetrahydrofuran (400 μL) and methyl iodide (100. μL, 1.61 mmol) are added *via* syringe followed by dropwise addition of the olive green oil from the previous step (~0.4 mmol from previous reduction; transferred to reaction vessel with 3 x 200 μL of tetrahydrofuran) *via* syringe with a rate slow enough that the bubbling from H_2 gas production subsides between drops. The cloudy yellow solution is allowed to stir at 22 ºC for 12 h during which time it becomes a cloudy tan solution. The reaction is cooled to 0 ºC, and water is added dropwise *via* syringe with a rate slow enough that the bubbling from H_2 gas production subsides between drops. After no bubbling occurs upon addition

(58) Crabtree, R. H.; Felkin, H.; Morris, G. E. *J. Organomet. Chem.* **1977**, *141*, 205.

of water, the septum and nitrogen line are removed from the flask and the solution is diluted with diethyl ether (3 mL) and water (0.5 mL). The aqueous and organic layers are separated and the organic layer is washed sequentially with a saturated aqueous solution of NH_4Cl (1 mL), an aqueous solution of $Na_2S_2O_3$ (5 wt %, 1 mL), and brine (1 mL). The organic layer is dried over $MgSO_4$, carefully concentrated *in vacuo* to minimize loss of volatile **2.36** to afford a yellow oil which is purified by silica gel chromatography (19 mm diameter column slurry packed with ~6 g of silica gel and eluted with 100 mL of pentanes and 100 mL 99:1 pentanes : diethyl ether) to afford **2.36** (50.5 mg, 0.28 mmol, 71% yield over 2 steps) as a clear pale yellow oil. IR (neat): 2958 (m), 2935 (m), 2872 (w), 2824 (w), 1494 (w), 1446 (m), 1371 (w), 1225 (m), 1167 (m), 1072 (s), 764 (s), 669 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.32 (4H, m), 7.26–7.22 (1H, m), 3.09–3.08 (3H, m), 1.78–1.70 (2H, m), 1.53 (3H, s), 1.33–1.12 (2H, m), 0.86 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 128.2, 126.7, 126.3, 79.2, 50.4, 45.3, 23.1, 17.3, 14.6; HRMS Calcd for $C_{11}H_{15}O$ $[M + H]^+$: 163.11229; Found: 163.11180; $[\alpha]^{21.8}$= –24.8 (c = 2.42, $CHCl_3$) for an 80:20 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 99:1 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 9 min (minor) and 10 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	9.3 min	47.873	1	9.2 min	20.582
2	10.4 min	52.127	2	10.1 min	79.418

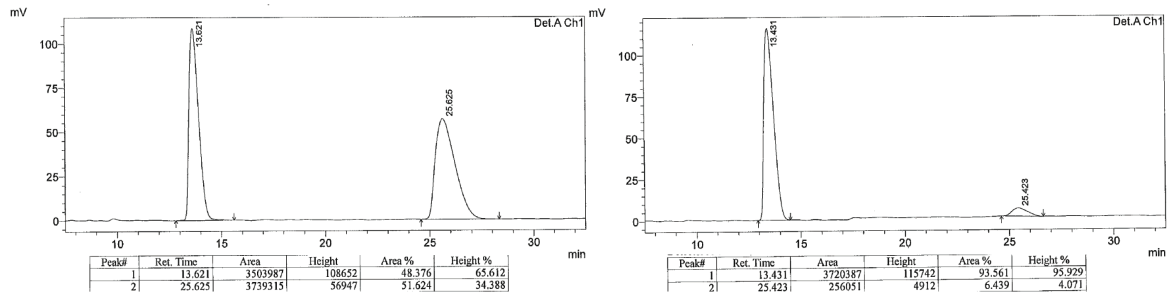
Peak #	Ret. Time	Area %
1	9.4 min	6.495
2	10.4 min	93.505

Absolute configuration of homoallylalcohol 2.12a:

(*R*)-5,5,5-Trifluoro-4-hydroxy-4-phenylpentan-2-one (2.29, Equation 6): **2.12a** is converted to **2.29** in accordance to a procedure in the literature.[59] The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL hexanes, 40 mL 99:1, 50 mL 1:1 hexanes : dichloromethane) affording **2.29** (41.6 mg, 0.179 mmol, 90% yield) as a clear colorless oil. The analytical data are fully consistent with those reported previously and comparison of the specific rotation of **2.29** and its HPLC trace with data in literature

(59) McCombs, J. R.; Michel, B. W.; Sigman, M. S. *J. Org. Chem.* **2011**, *76*, 3609–3613.

establishes the absolute stereochemistry of **2.11a**.[60] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.55 (2H, m), 7.42–7.34 (3H, m), 5.44 (1H, s), 3.37 and 3.21 (2H, ABq, J_{AB} = 17.1 Hz), 2.21 (3H, s); HRMS Calcd for $C_{11}H_{12}F_3O_2$ $[M + H]^+$: 233.07894; Found: 233.07928; $[\alpha]^{23.4}$= –20.0 (*c* = 1.00, $CHCl_3$) for a 95:5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 99:1 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R: 13 min (major) and 25 min (minor).

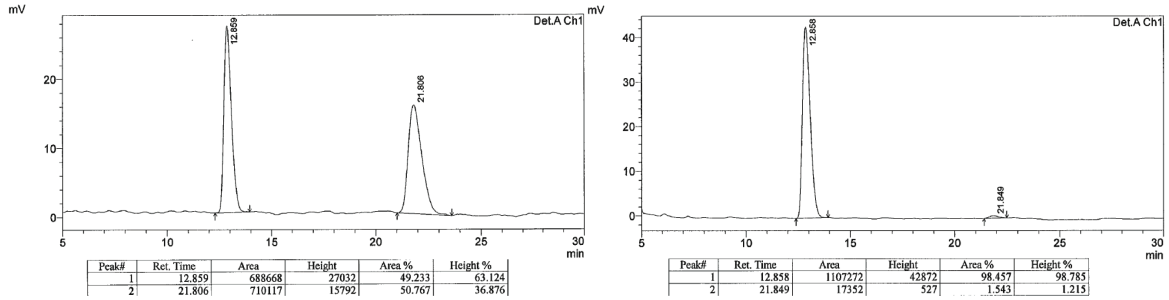


Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.6 min	48.378	1	13.4 min	93.561
2	25.6 min	51.624	2	25.4 min	6.439

Absolute configuration of homoallylalcohol 2.22a:

(*R*)-5,5,5-Trifluoro-4-hydroxy-4-phenylpentan-2-one (2.29, Equation 9): 2.22a is converted to **2.29** in accordance to a procedure in the literature and purified as above to obtain **2.29** (18.8 mg, 0.0810 mmol, 67% yield) as a clear, colorless oil.[61] Comparison of the HPLC trace of **2.29** with data in literature establishes the absolute stereochemistry of **2.22a**.

(60) Duangdee, N.; Harnying, W.; Rulli, G.; Neudörfl, J.-M.; Gröger, H.; Berkessel, A. *J. Am. Chem. Soc.* **2012**, *134*, 11196–11205.
(61) Román, J. G.; Soderquist, J. A. *J. Org. Chem.* **2007**, *72*, 9772–9775.



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	12.9 min	49.233	1	12.9 min	98.457
2	21.8 min	50.767	2	21.8 min	1.543

Absolute configuration of homoallenylalcohol 2.24a:

(*R*)-(1,1,1-Trifluoro-2-methoxypenta-3,4-dien-2-yl)benzene (2.30, Scheme 2.15): The title compound is synthesized in accordance to a procedure in the literature[62] and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 40 mL pentanes, 30 mL 99:1 pentanes : diethyl ether) affording **XX** (33.1 mg, 0.145 mmol, 73% yield as a 95:5 ratio of allene to propargyl product) as a clear pale yellow oil. IR (neat): 2945 (w, br), 2838 (w), 1981 (w), 1958 (w), 1489 (w) 1450 (w), 1276 (m), 1165 (s), 1094 (s), 1094 (s), 1078 (s), 1026 (m), 974 (w), 849 (m), 762 (m), 714 (m), 669 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (2H, m), 7.44–7.36 (3H, m), 5.54 (1H, t, J = 6.8 Hz), 5.06–4.96 (2H, m), 3.38–3.37 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.7, 134.3, 129.1, 128.8 (m), 128.2, 124.5 (q, J = 284.7 Hz, one peak overlaps with m at 128.8), 87.4 (q, J = 1.4 Hz), 82.4 (q, J = 27.7 Hz), 79.1, 52.6; ^{19}F NMR (376 MHz, $CDCl_3$): 75.59 (3F, s); HRMS Calcd for $C_{12}H_{12}OF_3$ $[M + H]^+$: 229.08402; Found: 229.08391; $[\alpha]^{21.8}$= +22.2 (c = 1.35, $CHCl_3$) for a 95:5 e.r. sample (95:5 allene:propargyl).

(62) Chong, J. M.; Loewith, R. *Synth. Comm.* **1993**, *23*, 2145–2150.

(*S*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoic acid (Mosher's Acid) (2.31, Scheme 2.15): The title compound is synthesized in accordance to a procedure in the literature[62] and purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted with 10 mL dichloromethane and 30 mL 99:1 dichloromethane : acetic acid) affording **2.31** (18.4 mg, 0.0786 mmol, 37% yield) as a clear colorless sticky oil. The analytical data are fully consistent with those reported previously; comparison of the specific rotation of **2.31** and its HPLC trace with data in literature establishes the absolute stereochemistry of **2.24a**.[63] ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.27 (1H, br s), 7.59–7.57 (2H, m), 7.46–7.41 (3H, m), 3.57 (3H, s); HRMS Calcd for $C_{10}H_{10}F_3O_3$ $[M + H]^+$: 235.05820; Found: 235.05735; $[\alpha]^{23.7}$= –58.3 (*c* = 1.15, $CHCl_3$) for a 94:6 e.r. sample (based on e.r. of **2.24a**).

■ **DFT Calculations**: All geometry and frequency calculations of the transition states shown in Scheme S2 were carried out employing the hybrid functional B3LYP[64] and the split-valence 6-31G** basis set. The calculations were carried out in toluene, which was simulated by the polarizable dielectric continuum solvation model PCM.[65] Frequency calculations were carried out on the fully optimized geometries. All computed frequencies are real except for the transition state structures, which have one imaginary frequency. Free energies were computed at 298.15 K and 1.0 atm. with harmonic,

(63) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.

(64) (a) Becke, A. D. *J. Chem. Phys*. **1993**, *98*, 5648-5652; Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B*. **1988**, *37*, 785–789. (b) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys*. **1980**, *58*, 1200–1211. (c) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, 98, 11623–11627.

(65) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev*. **2005,** *105*, 2999−3093.

unscaled frequencies. All quantum chemical calculations were carried out with the Gaussian 09 computer program.[66]

Transition State Energy for Complex TS-2.4 (Scheme 2.16a):

Cartesian coordinates (Angstroms):

H	-1.758	4.105	-1.113
C	-0.963	3.718	-1.759
H	-1.099	2.641	-1.869
H	-1.080	4.179	-2.746
C	-6.150	-0.683	0.095
C	-4.907	-1.302	0.178
C	-6.243	0.680	-0.193
C	-3.730	-0.550	-0.019
C	-5.082	1.432	-0.396
C	-3.835	0.826	-0.311
C	3.372	-2.939	-2.850
O	1.909	-2.948	-0.535
N	3.259	-1.785	-1.953
C	2.546	-1.919	-0.808
C	4.906	-1.531	0.701
C	3.927	0.178	2.184
C	3.960	-0.591	-2.421
C	3.580	-1.095	1.378
C	2.508	-0.787	0.244

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(66) Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

C	3.146	-2.252	2.305
B	0.004	-0.158	-0.456
N	1.039	-0.766	0.676
C	0.694	-0.001	1.932
O	0.329	1.212	-0.622
C	0.729	1.493	1.725
C	0.544	2.049	0.450
C	0.923	2.335	2.824
C	0.589	3.446	0.230
C	0.429	4.064	-1.176
C	0.942	3.711	2.645
C	1.544	3.540	-2.115
C	0.786	4.245	1.364
C	0.542	5.602	-1.143
O	-1.391	-0.287	0.116
C	-0.083	-0.871	-1.966
C	-0.867	-2.095	-1.919
C	-2.375	-1.135	0.067
C	-2.238	-2.077	-1.972
H	-7.048	-1.269	0.255
H	-4.862	-2.359	0.396
H	-7.217	1.156	-0.258
H	-5.150	2.493	-0.614
H	-2.934	1.410	-0.454
H	2.867	-2.730	-3.799
H	2.916	-3.805	-2.378
H	4.428	-3.140	-3.055
H	5.664	-1.662	1.478
H	5.284	-0.775	0.007
H	4.816	-2.482	0.171
H	3.107	0.582	2.774
H	4.276	0.977	1.521
H	4.742	-0.052	2.878
H	3.639	-0.365	-3.442
H	5.042	-0.761	-2.431
H	3.750	0.277	-1.801
H	2.714	0.196	-0.174

H	2.277	-2.018	2.925
H	3.966	-2.483	2.991
H	2.920	-3.153	1.731
H	-0.306	-0.339	2.214
H	1.363	-0.296	2.734
H	1.058	1.905	3.813
H	1.089	4.372	3.493
H	2.532	3.814	-1.731
H	1.436	3.989	-3.109
H	1.503	2.456	-2.225
H	0.821	5.321	1.253
H	1.514	5.937	-0.768
H	-0.241	6.061	-0.530
H	0.431	5.991	-2.160
H	0.929	-1.025	-2.340
H	-0.571	-0.092	-2.559
H	-0.351	-3.016	-1.656
C	-2.178	-2.417	0.915
H	-2.749	-1.223	-2.402
H	-2.814	-2.991	-1.885
H	0.820	-1.757	0.821
F	-2.421	-2.105	2.201
F	-0.907	-2.870	0.843
F	-2.975	-3.435	0.566

	1	2	3
	A	A	A
Frequencies --	-196.1530	14.6905	27.5050
Red. masses --	7.1961	3.7800	4.1391

Zero-point correction= 0.675275 (Hartree/Particle)
Thermal correction to Energy= 0.714076
Thermal correction to Enthalpy= 0.715020
Thermal correction to Gibbs Free Energy= 0.605956
Sum of electronic and zero-point Energies= -1826.716932
Sum of electronic and thermal Energies= -1826.678131
Sum of electronic and thermal Enthalpies= -1826.677187
Sum of electronic and thermal Free Energies= -1826.786251

Item	Value	Threshold	Converged?
Maximum Force	0.000013	0.000450	YES
RMS Force	0.000001	0.000300	YES

Transition State Energy for Complex TS-2.5 (Scheme 2.16a):

Cartesian coordinates (Angstroms):

H	2.539	3.355	1.310
C	1.691	3.024	1.917
H	1.662	1.935	1.894
H	1.876	3.342	2.949
C	5.702	-0.215	0.349
C	4.630	-1.100	0.356
C	5.534	1.095	-0.110
C	3.360	-0.677	-0.090
C	4.284	1.517	-0.565
C	3.201	0.642	-0.551
C	-3.874	-2.588	2.694
O	-2.675	-2.724	0.236
N	-3.552	-1.413	1.879
C	-2.995	-1.603	0.659
C	-5.255	-0.477	-0.611
C	-3.954	1.054	-2.043
C	-3.930	-0.141	2.489
C	-3.905	-0.332	-1.361
C	-2.730	-0.413	-0.291
C	-3.839	-1.469	-2.403
B	-0.114	-0.500	0.264
N	-1.325	-0.706	-0.824
C	-0.859	0.064	-2.039
O	0.018	0.883	0.543
C	-0.540	1.503	-1.706
C	-0.144	1.866	-0.409
C	-0.640	2.483	-2.698

C	0.075	3.218	-0.046
C	0.372	3.650	1.408
C	-0.367	3.808	-2.389
C	-0.804	3.222	2.322
C	-0.035	4.159	-1.079
C	0.513	5.181	1.533
O	1.019	-1.175	-0.486
C	-0.218	-1.360	1.698
C	1.128	-1.419	2.243
C	2.206	-1.597	-0.170
C	1.998	-2.433	1.942
H	6.672	-0.549	0.701
H	4.781	-2.111	0.710
H	6.376	1.779	-0.118
H	4.150	2.527	-0.939
H	2.242	0.969	-0.928
H	-3.355	-2.524	3.656
H	-3.561	-3.485	2.166
H	-4.952	-2.626	2.881
H	-6.067	-0.344	-1.330
H	-5.380	0.285	0.163
H	-5.381	-1.464	-0.159
H	-3.112	1.265	-2.699
H	-4.001	1.857	-1.300
H	-4.860	1.117	-2.654
H	-3.478	-0.070	3.484
H	-5.017	-0.081	2.603
H	-3.596	0.712	1.903
H	-2.663	0.545	0.222
H	-2.962	-1.417	-3.055
H	-4.717	-1.407	-3.053
H	-3.841	-2.449	-1.921
H	0.020	-0.475	-2.400
H	-1.611	0.006	-2.819
H	-0.936	2.200	-3.705
H	-0.434	4.574	-3.154
H	-1.736	3.698	2.000

H	-0.608	3.534	3.353
H	-0.947	2.140	2.315
H	0.136	5.205	-0.861
H	-0.397	5.707	1.229
H	1.350	5.568	0.943
H	0.706	5.438	2.579
H	-0.621	-2.351	1.484
H	-0.894	-0.789	2.338
H	1.508	-0.542	2.763
C	2.435	-2.993	-0.811
H	3.013	-2.422	2.321
H	1.614	-3.387	1.597
H	-1.359	-1.708	-1.054
F	2.729	-2.806	-2.110
F	1.322	-3.740	-0.739
F	3.439	-3.686	-0.250

	1	2	3
	A	A	A
Frequencies --	-203.2086	18.4901	19.1728
Red. masses --	6.9236	4.2706	5.0338

Zero-point correction= 0.675795 (Hartree/Particle)
Thermal correction to Energy= 0.714404
Thermal correction to Enthalpy= 0.715349
Thermal correction to Gibbs Free Energy= 0.606904
Sum of electronic and zero-point Energies= -1826.711062
Sum of electronic and thermal Energies= -1826.672452
Sum of electronic and thermal Enthalpies= -1826.671508
Sum of electronic and thermal Free Energies= -1826.779953

Item	Value	Threshold	Converged?
Maximum Force	0.000018	0.000450	YES
RMS Force	0.000002	0.000300	YES

Transition State Energy for Complex TS-2.6 (Scheme 2.16b):

Cartesian coordinates (Angstroms):

H	-0.331	2.950	1.868
H	-1.149	4.342	2.595
C	-0.926	3.834	1.650
H	-0.322	4.512	1.039
C	6.173	-0.703	-0.793
C	5.117	0.075	-0.326
C	5.953	-2.016	-1.210
C	3.813	-0.456	-0.284
C	4.664	-2.556	-1.161
C	3.603	-1.786	-0.703
C	-1.813	-3.996	2.870
O	-0.544	-3.491	0.498
N	-2.198	-2.920	1.953
C	-1.525	-2.787	0.787
C	-3.915	-3.321	-0.655
C	-3.644	-1.422	-2.208
C	-3.293	-2.083	2.438
C	-2.850	-2.455	-1.377
C	-1.957	-1.744	-0.272
C	-2.037	-3.401	-2.286
B	0.090	-0.159	0.377
N	-0.618	-1.159	-0.721
C	-0.564	-0.375	-2.013
O	-0.696	1.015	0.464
C	-1.196	0.989	-1.878
C	-1.278	1.621	-0.628
C	-1.716	1.621	-3.012
C	-1.978	2.841	-0.456
C	-2.245	3.468	0.932
C	-2.330	2.859	-2.889
C	-3.049	2.468	1.800
C	-2.472	3.436	-1.625
C	-3.083	4.760	0.824
O	1.480	-0.095	-0.222
C	0.350	-0.762	1.927

C	1.372	0.090	2.508
C	2.645	0.328	0.182
C	2.712	-0.169	2.344
H	7.171	-0.279	-0.830
H	5.316	1.088	-0.006
H	6.781	-2.619	-1.569
H	4.488	-3.578	-1.481
H	2.607	-2.211	-0.661
H	-1.408	-3.575	3.796
H	-1.061	-4.620	2.394
H	-2.693	-4.598	3.116
H	-4.597	-3.729	-1.406
H	-4.519	-2.734	0.043
H	-3.479	-4.167	-0.118
H	-3.030	-0.773	-2.829
H	-4.250	-0.779	-1.561
H	-4.328	-1.955	-2.876
H	-3.041	-1.702	3.433
H	-4.214	-2.670	2.520
H	-3.480	-1.233	1.787
H	-2.524	-0.915	0.146
H	-1.321	-2.884	-2.931
H	-2.725	-3.935	-2.948
H	-1.489	-4.141	-1.698
H	0.498	-0.307	-2.261
H	-1.042	-0.943	-2.805
H	-1.639	1.135	-3.981
H	-2.727	3.364	-3.763
H	-4.010	2.231	1.330
H	-3.257	2.908	2.781
H	-2.499	1.538	1.954
H	-2.996	4.380	-1.556
H	-4.058	4.584	0.360
H	-2.565	5.541	0.259
H	-3.264	5.150	1.830
H	0.669	-1.802	1.851
H	-0.608	-0.675	2.444

H	1.067	1.048	2.925
C	2.799	1.867	0.280
H	3.462	0.501	2.746
H	3.035	-1.179	2.122
H	-0.024	-1.993	-0.815
F	3.794	2.246	1.105
F	1.675	2.450	0.703
F	3.079	2.336	-0.949

	1	2	3
	A	A	A
Frequencies --	-236.7114	20.4308	27.4711
Red. masses --	7.6378	6.2395	4.6727

Zero-point correction= 0.675817 (Hartree/Particle)
Thermal correction to Energy= 0.714573
Thermal correction to Enthalpy= 0.715517
Thermal correction to Gibbs Free Energy= 0.606617
Sum of electronic and zero-point Energies= -1826.713886
Sum of electronic and thermal Energies= -1826.675130
Sum of electronic and thermal Enthalpies= -1826.674186
Sum of electronic and thermal Free Energies= -1826.783086

Item	Value	Threshold	Converged?
Maximum Force	0.000002	0.000450	YES
RMS Force	0.000000	0.000300	YES

Transition State Energy for Complex TS-2.8 (Scheme 2.16b):

Cartesian coordinates (Angstroms):

H	0.639	-3.364	1.298
H	1.607	-4.608	2.106
C	1.459	-4.067	1.165
H	1.163	-4.797	0.403
C	-6.032	0.099	-1.200
C	-5.003	-0.584	-0.553

C	-5.825	1.386	-1.693
C	-3.738	0.016	-0.408
C	-4.576	1.996	-1.541
C	-3.543	1.318	-0.908
C	1.112	3.945	3.102
O	-0.141	3.223	0.778
N	1.708	3.060	2.097
C	1.012	2.799	0.964
C	3.101	4.024	-0.536
C	3.237	2.217	-2.207
C	3.025	2.540	2.462
C	2.254	2.951	-1.267
C	1.633	1.965	-0.182
C	1.171	3.703	-2.072
B	-0.049	-0.089	0.407
N	0.461	1.098	-0.637
C	0.580	0.380	-1.964
O	0.901	-1.135	0.393
C	1.529	-0.786	-1.890
C	1.659	-1.506	-0.694
C	2.259	-1.173	-3.018
C	2.564	-2.588	-0.570
C	2.770	-3.356	0.755
C	3.122	-2.257	-2.940
C	3.222	-2.383	1.872
C	3.272	-2.935	-1.729
C	3.862	-4.438	0.627
O	-1.401	-0.372	-0.197
C	-0.339	0.284	2.032
C	-1.673	0.814	2.203
C	-2.596	-0.682	0.233
C	-2.773	-0.009	2.308
H	-6.998	-0.382	-1.315
H	-5.194	-1.581	-0.182
H	-6.632	1.916	-2.190
H	-4.410	3.001	-1.916
H	-2.584	1.809	-0.785

H	0.878	3.380	4.011
H	0.203	4.385	2.700
H	1.824	4.735	3.357
H	3.579	4.658	-1.287
H	3.901	3.579	0.063
H	2.501	4.674	0.105
H	2.767	1.514	-2.893
H	3.993	1.666	-1.638
H	3.761	2.958	-2.818
H	2.963	2.064	3.446
H	3.752	3.356	2.520
H	3.386	1.802	1.750
H	2.410	1.281	0.154
H	0.553	3.052	-2.696
H	1.660	4.410	-2.748
H	0.508	4.269	-1.413
H	-0.437	0.054	-2.198
H	0.876	1.082	-2.736
H	2.144	-0.625	-3.949
H	3.690	-2.570	-3.810
H	4.165	-1.896	1.602
H	3.388	-2.938	2.802
H	2.476	-1.611	2.067
H	3.970	-3.761	-1.693
H	4.833	-4.014	0.354
H	3.599	-5.205	-0.108
H	3.980	-4.939	1.592
H	0.445	0.956	2.378
H	-0.220	-0.698	2.498
H	-1.817	1.878	2.025
C	-2.730	-2.193	0.555
H	-2.653	-0.998	2.735
H	-3.772	0.411	2.351
H	-0.309	1.772	-0.698
F	-3.822	-2.493	1.281
F	-1.658	-2.627	1.239
F	-2.796	-2.873	-0.601

	1	2	3
	A	A	A
Frequencies --	-259.2548	12.6420	27.1256
Red. masses --	7.7480	5.2342	4.5174

Zero-point correction= 0.675616 (Hartree/Particle)
Thermal correction to Energy= 0.714487
Thermal correction to Enthalpy= 0.715431
Thermal correction to Gibbs Free Energy= 0.605678
Sum of electronic and zero-point Energies= -1826.706913
Sum of electronic and thermal Energies= -1826.668042
Sum of electronic and thermal Enthalpies= -1826.667098
Sum of electronic and thermal Free Energies= -1826.776851

Item	Value	Threshold	Converged?
Maximum Force	0.000004	0.000450	YES
RMS Force	0.000001	0.000300	YES

Transition State Energy for Complex TS-2.11-(*R*) (Scheme 2.19):

Cartesian coordinates (Angstroms):

H	2.255	3.797	1.176
C	1.464	3.412	1.829
H	1.540	2.324	1.857
H	1.648	3.795	2.838
C	6.172	-1.690	-0.368
C	4.841	-2.095	-0.371
C	6.494	-0.339	-0.218
C	3.809	-1.147	-0.226
C	5.478	0.607	-0.067
C	4.145	0.210	-0.068
C	-3.474	-2.713	2.779
O	-2.048	-2.906	0.450
N	-3.241	-1.586	1.873
C	-2.556	-1.809	0.722
C	-4.847	-1.280	-0.801

C	-3.765	0.387	-2.260
C	-3.806	-0.320	2.335
C	-3.496	-0.918	-1.473
C	-2.405	-0.695	-0.334
C	-3.133	-2.084	-2.416
B	0.165	-0.323	0.378
N	-0.942	-0.787	-0.764
C	-0.551	0.020	-1.979
O	-0.053	1.061	0.623
C	-0.498	1.501	-1.690
C	-0.238	1.968	-0.392
C	-0.676	2.414	-2.733
C	-0.183	3.352	-0.096
C	0.074	3.878	1.333
C	-0.603	3.777	-2.478
C	-1.031	3.374	2.294
C	-0.368	4.225	-1.177
C	0.060	5.420	1.388
O	1.528	-0.537	-0.201
C	0.187	-1.115	1.857
C	0.841	-2.401	1.714
C	2.373	-1.539	-0.256
C	2.213	-2.501	1.676
H	6.958	-2.429	-0.480
H	4.622	-3.153	-0.469
H	7.534	-0.026	-0.216
H	5.724	1.658	0.048
H	3.354	0.942	0.038
H	-2.958	-2.545	3.731
H	-3.102	-3.625	2.319
H	-4.546	-2.809	2.977
H	-5.613	-1.345	-1.577
H	-5.172	-0.514	-0.090
H	-4.817	-2.245	-0.291
H	-2.929	0.736	-2.863
H	-4.041	1.201	-1.582
H	-4.607	0.224	-2.939

H	-3.443	-0.113	3.347
H	-4.899	-0.380	2.368
H	-3.522	0.513	1.698
H	-2.533	0.305	0.075
H	-2.249	-1.895	-3.030
H	-3.963	-2.258	-3.107
H	-2.963	-3.005	-1.852
H	0.431	-0.355	-2.275
H	-1.231	-0.194	-2.797
H	-0.870	2.051	-3.739
H	-0.738	4.493	-3.282
H	-2.015	3.734	1.973
H	-0.848	3.757	3.304
H	-1.059	2.285	2.341
H	-0.330	5.293	-1.006
H	-0.903	5.836	1.074
H	0.846	5.863	0.768
H	0.235	5.742	2.418
H	-0.827	-1.181	2.246
H	0.769	-0.419	2.467
H	0.228	-3.256	1.440
C	2.023	-2.702	-1.173
H	2.817	-1.736	2.152
H	2.694	-3.464	1.534
H	-0.784	-1.780	-0.966
H	2.163	-2.364	-2.207
F	0.695	-3.086	-1.018
H	2.650	-3.576	-0.997

	1	2	3
	A	A	A
Frequencies --	-261.3815	19.0327	27.4182
Red. masses --	7.0765	4.2647	4.2327

Zero-point correction= 0.692049 (Hartree/Particle)

Thermal correction to Energy= 0.729223

Thermal correction to Enthalpy= 0.730167

Thermal correction to Gibbs Free Energy= 0.624954

Sum of electronic and zero-point Energies= -1628.221388

Sum of electronic and thermal Energies= -1628.184214

Sum of electronic and thermal Enthalpies= -1628.183270

Sum of electronic and thermal Free Energies= -1628.288483

Item	Value	Threshold	Converged?
Maximum Force	0.000003	0.000450	YES
RMS Force	0.000001	0.000300	YES

Transition State Energy for Complex TS-2.11-(*S*) (Scheme 2.19):

Cartesian coordinates (Angstroms):

H	-0.049	2.799	1.991
H	-0.708	4.308	2.624
C	-0.538	3.731	1.708
H	0.142	4.309	1.074
C	6.287	-0.133	-0.561
C	5.113	0.407	-0.040
C	6.276	-1.391	-1.167
C	3.906	-0.310	-0.131
C	5.082	-2.113	-1.251
C	3.905	-1.581	-0.734
C	-1.902	-4.091	3.045
O	-0.623	-3.646	0.669
N	-2.241	-2.996	2.131
C	-1.567	-2.896	0.962
C	-3.995	-3.314	-0.463
C	-3.637	-1.442	-2.027
C	-3.289	-2.107	2.623
C	-2.889	-2.509	-1.194
C	-1.954	-1.835	-0.099
C	-2.130	-3.502	-2.100
B	0.177	-0.338	0.508
N	-0.592	-1.318	-0.562
C	-0.507	-0.561	-1.867
O	-0.549	0.889	0.591
C	-1.047	0.844	-1.755

C	-1.083	1.509	-0.519
C	-1.518	1.488	-2.903
C	-1.678	2.788	-0.380
C	-1.885	3.473	0.992
C	-2.034	2.773	-2.811
C	-2.783	2.579	1.882
C	-2.125	3.392	-1.563
C	-2.590	4.838	0.849
O	1.541	-0.321	-0.080
C	0.381	-0.940	2.083
C	1.436	-0.123	2.637
C	2.634	0.264	0.392
C	2.767	-0.369	2.361
H	7.212	0.430	-0.492
H	5.135	1.377	0.439
H	7.193	-1.809	-1.569
H	5.069	-3.091	-1.722
H	2.980	-2.140	-0.803
H	-1.452	-3.692	3.960
H	-1.200	-4.761	2.557
H	-2.812	-4.636	3.312
H	-4.692	-3.700	-1.211
H	-4.572	-2.689	0.224
H	-3.600	-4.171	0.087
H	-2.996	-0.819	-2.648
H	-4.214	-0.774	-1.378
H	-4.344	-1.945	-2.693
H	-3.019	-1.754	3.624
H	-4.242	-2.641	2.694
H	-3.423	-1.239	1.983
H	-2.478	-0.978	0.320
H	-1.386	-3.028	-2.746
H	-2.847	-3.999	-2.760
H	-1.624	-4.268	-1.509
H	0.555	-0.564	-2.126
H	-1.028	-1.111	-2.644
H	-1.481	0.976	-3.861

H	-2.392	3.286	-3.697
H	-3.763	2.430	1.418
H	-2.942	3.059	2.854
H	-2.329	1.601	2.058
H	-2.570	4.378	-1.518
H	-3.578	4.746	0.386
H	-1.998	5.549	0.264
H	-2.734	5.270	1.843
H	0.659	-1.992	2.004
H	-0.573	-0.810	2.595
H	1.169	0.827	3.099
C	2.535	1.786	0.531
H	3.537	0.277	2.766
H	3.070	-1.379	2.108
H	-0.035	-2.178	-0.645
F	3.407	2.282	1.492
H	2.796	2.229	-0.437
H	1.520	2.071	0.798

	1	2	3
	A	A	A
Frequencies --	-279.9058	24.5892	29.9851
Red. masses --	8.2363	4.7956	4.3825

Zero-point correction= 0.692991 (Hartree/Particle)
Thermal correction to Energy= 0.729955
Thermal correction to Enthalpy= 0.730899
Thermal correction to Gibbs Free Energy= 0.626632
Sum of electronic and zero-point Energies= -1628.220284
Sum of electronic and thermal Energies= -1628.183320
Sum of electronic and thermal Enthalpies= -1628.182375
Sum of electronic and thermal Free Energies= -1628.286642

Item	Value	Threshold	Converged?
Maximum Force	0.000021	0.000450	YES
RMS Force	0.000002	0.000300	YES

Transition State Energy for Complex TS-2.12-(*R*) (Scheme 2.19):

Cartesian coordinates (Angstroms):

H	-2.113	3.881	-1.160
C	-1.296	3.532	-1.800
H	-1.361	2.446	-1.883
H	-1.446	3.961	-2.797
C	-6.139	-1.454	0.105
C	-4.820	-1.894	0.154
C	-6.420	-0.097	-0.069
C	-3.760	-0.973	0.034
C	-5.375	0.823	-0.197
C	-4.054	0.391	-0.150
C	3.541	-2.677	-2.853
O	2.057	-2.877	-0.559
N	3.317	-1.563	-1.928
C	2.604	-1.790	-0.797
C	4.889	-1.319	0.773
C	3.799	0.324	2.252
C	3.926	-0.304	-2.350
C	3.531	-0.959	1.431
C	2.461	-0.696	0.282
C	3.143	-2.145	2.340
B	-0.073	-0.246	-0.461
N	0.989	-0.777	0.688
C	0.581	-0.020	1.930
O	0.178	1.138	-0.646
C	0.533	1.472	1.702
C	0.324	1.999	0.418
C	0.671	2.338	2.790
C	0.278	3.394	0.182
C	0.071	3.984	-1.231
C	0.608	3.711	2.594
C	1.216	3.530	-2.170
C	0.421	4.218	1.306
C	0.075	5.526	-1.215
O	-1.462	-0.442	0.088
C	-0.106	-0.983	-1.965

C	-0.782	-2.267	-1.890
C	-2.345	-1.397	0.100
C	-2.151	-2.366	-1.906
H	-6.947	-2.171	0.201
H	-4.633	-2.956	0.273
H	-7.450	0.243	-0.104
H	-5.591	1.878	-0.328
H	-3.242	1.103	-0.238
H	3.054	-2.474	-3.813
H	3.132	-3.588	-2.421
H	4.615	-2.799	-3.026
H	5.641	-1.411	1.561
H	5.235	-0.540	0.087
H	4.858	-2.271	0.238
H	2.949	0.683	2.829
H	4.119	1.144	1.600
H	4.611	0.130	2.959
H	3.599	-0.069	-3.368
H	5.018	-0.390	-2.354
H	3.643	0.525	-1.706
H	2.609	0.310	-0.105
H	2.255	-1.962	2.950
H	3.964	-2.345	3.034
H	2.969	-3.050	1.752
H	-0.401	-0.413	2.202
H	1.254	-0.265	2.745
H	0.826	1.930	3.786
H	0.712	4.390	3.434
H	2.183	3.881	-1.795
H	1.070	3.957	-3.168
H	1.254	2.444	-2.265
H	0.388	5.293	1.182
H	1.023	5.933	-0.850
H	-0.736	5.935	-0.604
H	-0.069	5.894	-2.236
H	0.912	-1.055	-2.345
H	-0.665	-0.254	-2.558

H	-0.183	-3.136	-1.631
C	-2.037	-2.622	0.977
H	-2.746	-1.572	-2.344
H	-2.642	-3.329	-1.805
H	0.823	-1.777	0.844
F	-2.145	-2.202	2.273
F	-0.750	-3.051	0.801
H	-2.701	-3.471	0.820

	1	2	3
	A	A	A
Frequencies --	-210.7181	20.4033	29.0915
Red. masses --	7.2786	4.0317	3.8205

Zero-point correction= 0.683996 (Hartree/Particle)
Thermal correction to Energy= 0.722096
Thermal correction to Enthalpy= 0.723040
Thermal correction to Gibbs Free Energy= 0.615707
Sum of electronic and zero-point Energies= -1727.464615
Sum of electronic and thermal Energies= -1727.426515
Sum of electronic and thermal Enthalpies= -1727.425571
Sum of electronic and thermal Free Energies= -1727.532905

Item	Value	Threshold	Converged?
Maximum Force	0.000005	0.000450	YES
RMS Force	0.000001	0.000300	YES

Transition State Energy for Complex TS-2.12-(*S*) (Scheme 2.19):

Cartesian coordinates (Angstroms):

H	-0.090	2.741	1.937
H	-0.722	4.274	2.534
C	-0.560	3.676	1.631
H	0.131	4.229	0.986
C	6.247	-0.172	-0.649
C	5.073	0.373	-0.137

C	6.238	-1.435	-1.244
C	3.865	-0.343	-0.228
C	5.044	-2.157	-1.331
C	3.866	-1.618	-0.825
C	-1.955	-4.145	2.970
O	-0.668	-3.699	0.598
N	-2.291	-3.051	2.055
C	-1.614	-2.950	0.888
C	-4.038	-3.370	-0.544
C	-3.676	-1.499	-2.108
C	-3.343	-2.163	2.543
C	-2.930	-2.565	-1.272
C	-1.999	-1.891	-0.174
C	-2.168	-3.558	-2.175
B	0.130	-0.400	0.437
N	-0.635	-1.374	-0.635
C	-0.546	-0.615	-1.940
O	-0.581	0.835	0.517
C	-1.089	0.789	-1.827
C	-1.119	1.456	-0.594
C	-1.566	1.430	-2.974
C	-1.711	2.736	-0.453
C	-1.910	3.425	0.917
C	-2.079	2.716	-2.882
C	-2.812	2.538	1.812
C	-2.163	3.338	-1.635
C	-2.607	4.794	0.772
O	1.501	-0.389	-0.149
C	0.341	-1.000	2.007
C	1.386	-0.174	2.575
C	2.590	0.208	0.296
C	2.721	-0.408	2.313
H	7.172	0.392	-0.581
H	5.098	1.352	0.323
H	7.157	-1.857	-1.639
H	5.032	-3.138	-1.793
H	2.941	-2.178	-0.892

H	-1.510	-3.746	3.888
H	-1.250	-4.815	2.485
H	-2.866	-4.692	3.233
H	-4.733	-3.757	-1.294
H	-4.618	-2.745	0.141
H	-3.644	-4.227	0.008
H	-3.034	-0.877	-2.729
H	-4.254	-0.831	-1.462
H	-4.381	-2.003	-2.776
H	-3.079	-1.812	3.546
H	-4.296	-2.698	2.608
H	-3.474	-1.294	1.904
H	-2.524	-1.033	0.242
H	-1.421	-3.085	-2.818
H	-2.883	-4.055	-2.838
H	-1.665	-4.325	-1.582
H	0.516	-0.616	-2.196
H	-1.064	-1.166	-2.718
H	-1.531	0.917	-3.932
H	-2.440	3.228	-3.768
H	-3.795	2.397	1.352
H	-2.963	3.020	2.784
H	-2.365	1.557	1.985
H	-2.605	4.324	-1.591
H	-3.595	4.708	0.311
H	-2.011	5.500	0.185
H	-2.746	5.230	1.766
H	0.629	-2.049	1.929
H	-0.615	-0.882	2.519
H	1.105	0.765	3.049
C	2.454	1.735	0.460
H	3.485	0.242	2.722
H	3.036	-1.411	2.045
H	-0.079	-2.236	-0.718
F	3.344	2.239	1.366
F	2.728	2.296	-0.751
H	1.448	2.018	0.761

	1	2	3
	A	A	A
Frequencies --	-258.6533	23.9815	31.5371
Red. masses --	8.4096	5.0699	4.5318

Zero-point correction= 0.685041 (Hartree/Particle)
Thermal correction to Energy= 0.722819
Thermal correction to Enthalpy= 0.723764
Thermal correction to Gibbs Free Energy= 0.617517
Sum of electronic and zero-point Energies= -1727.463668
Sum of electronic and thermal Energies= -1727.425889
Sum of electronic and thermal Enthalpies= -1727.424945
Sum of electronic and thermal Free Energies= -1727.531191

Item	Value	Threshold	Converged?
Maximum Force	0.000007	0.000450	YES
RMS Force	0.000001	0.000300	YES

Transition State Energy for Complex TS-2.15-(*S*) (Scheme 2.22):

Cartesian coordinates (Angstroms):

H	10.853	-1.832	-4.457
H	9.770	-0.583	-5.111
C	9.966	-1.227	-4.247
H	9.111	-1.875	-4.073
H	12.286	-0.154	-3.222
H	11.303	1.076	-4.038
C	11.377	0.452	-3.141
N	10.200	-0.408	-3.054
H	11.016	-2.193	-1.139
H	12.133	-0.855	-0.795
O	8.314	-1.213	-2.065
C	11.388	-1.526	-0.358
H	11.474	1.107	-2.279
C	9.335	-0.510	-2.017

H	11.905	-2.146	0.380
H	8.741	1.898	-3.305
H	7.337	0.768	-3.138
H	8.793	-2.360	0.075
C	7.707	1.781	-2.980
C	9.589	0.244	-0.691
C	10.251	-0.751	0.357
H	9.791	-2.509	1.529
C	9.254	-1.801	0.892
H	10.241	1.108	-0.807
C	6.825	2.799	-3.482
H	5.030	1.663	-3.429
H	7.244	3.777	-3.713
H	10.572	3.950	-2.048
C	5.447	2.665	-3.410
H	7.573	0.015	-0.524
H	11.428	5.452	-2.435
H	11.673	0.730	1.124
H	11.466	-0.693	2.147
N	8.209	0.802	-0.347
C	10.934	0.020	1.510
H	4.805	3.451	-3.789
B	7.701	2.053	-1.287
H	11.949	4.471	-1.057
C	11.073	4.817	-1.615
H	8.452	-1.376	1.502
O	8.534	3.180	-1.022
O	6.281	2.091	-0.923
H	8.405	5.340	-2.029
H	10.252	0.576	2.151
H	9.284	6.852	-2.287
C	5.318	2.884	-1.369
C	7.972	1.304	1.060
H	8.320	0.563	1.773
C	10.122	5.622	-0.696
F	4.696	0.543	0.286
C	8.930	3.514	0.256

C	8.928	6.152	-1.523
C	3.941	2.330	-1.122
C	3.684	1.207	-0.308
H	11.231	7.447	-1.040
H	6.490	4.701	-1.409
H	6.887	1.364	1.159
C	8.639	2.635	1.312
F	2.938	3.993	-2.493
C	2.789	2.933	-1.664
C	9.646	4.719	0.466
C	2.403	0.737	-0.043
C	5.492	4.373	-1.129
H	11.798	6.567	0.379
C	10.903	6.850	-0.184
H	2.290	-0.124	0.604
H	4.744	4.961	-1.655
C	1.497	2.491	-1.433
C	1.308	1.382	-0.610
H	8.214	6.686	-0.887
H	0.671	3.014	-1.900
H	0.305	1.020	-0.414
C	8.974	2.993	2.621
C	9.950	5.033	1.797
H	5.368	4.541	-0.053
H	10.287	7.497	0.449
H	8.739	2.318	3.440
H	10.478	5.951	2.017
C	9.607	4.203	2.867
H	9.862	4.494	3.881

	1	2	3
	A	A	A
Frequencies --	-325.7913	18.1846	26.7096
Red. masses --	8.4849	4.8842	4.2975

Zero-point correction= 0.682388 (Hartree/Particle)

Thermal correction to Energy= 0.720796

Thermal correction to Enthalpy= 0.721740

Thermal correction to Gibbs Free Energy= 0.613919
Sum of electronic and zero-point Energies= -1727.465578
Sum of electronic and thermal Energies= -1727.427171
Sum of electronic and thermal Enthalpies= -1727.426226
Sum of electronic and thermal Free Energies= -1727.534047

Item	Value	Threshold	Converged?
Maximum Force	0.000005	0.000450	YES
RMS Force	0.000001	0.000300	YES

Transition State Energy for Complex TS-2.15-(*R*) (Scheme 2.22):

Cartesian coordinates (Angstroms):

H	-3.055	2.969	-6.539
H	-2.420	2.072	-5.142
H	-4.102	1.809	-5.680
C	-3.313	2.547	-5.561
H	-8.241	4.273	-8.750
H	-6.642	3.500	-7.022
C	-7.701	4.989	-8.144
C	-6.715	4.558	-7.272
H	-7.603	5.979	-8.578
H	-12.208	2.762	-8.732
H	-2.293	4.987	-5.193
F	-10.568	4.685	-8.939
N	-3.772	3.604	-4.656
H	-5.049	5.132	-6.070
C	-11.664	2.958	-7.816
O	-5.902	2.803	-4.718
H	-1.943	4.069	-3.716
C	-5.999	5.495	-6.455
C	-10.751	3.998	-7.788
C	-2.736	4.565	-4.284
H	-5.869	6.466	-6.939
H	-12.556	1.376	-6.662

C	-11.845	2.194	-6.664
C	-5.072	3.609	-4.269
C	-9.979	4.351	-6.661
H	-9.999	6.691	-8.288
H	-4.137	2.293	-2.306
C	-11.103	2.475	-5.520
C	-9.053	5.539	-6.677
H	-3.130	5.383	-3.687
C	-10.195	3.524	-5.542
H	-11.212	1.900	-4.608
C	-9.595	6.825	-7.288
B	-6.992	5.942	-5.130
H	-6.670	2.138	-2.425
H	-8.814	7.587	-7.293
H	-7.404	4.143	-3.992
O	-8.387	5.759	-5.554
H	-3.353	3.785	-1.740
C	-4.225	3.136	-1.617
C	-5.581	4.613	-3.211
F	-9.510	3.736	-4.392
H	-4.545	8.348	-5.303
N	-6.948	5.028	-3.743
H	-3.900	9.935	-5.755
H	-4.985	5.523	-3.160
H	-6.884	9.122	-6.256
H	-4.184	2.732	-0.602
O	-6.587	7.268	-4.814
H	-10.400	7.172	-6.629
C	-6.695	2.876	-1.620
C	-5.559	3.909	-1.781
C	-4.406	9.374	-4.961
H	-6.150	10.683	-6.662
H	-6.563	2.348	-0.672
C	-6.655	10.117	-5.872
H	-3.744	9.362	-4.088
H	-7.695	3.317	-1.596
H	-8.854	5.711	-3.279

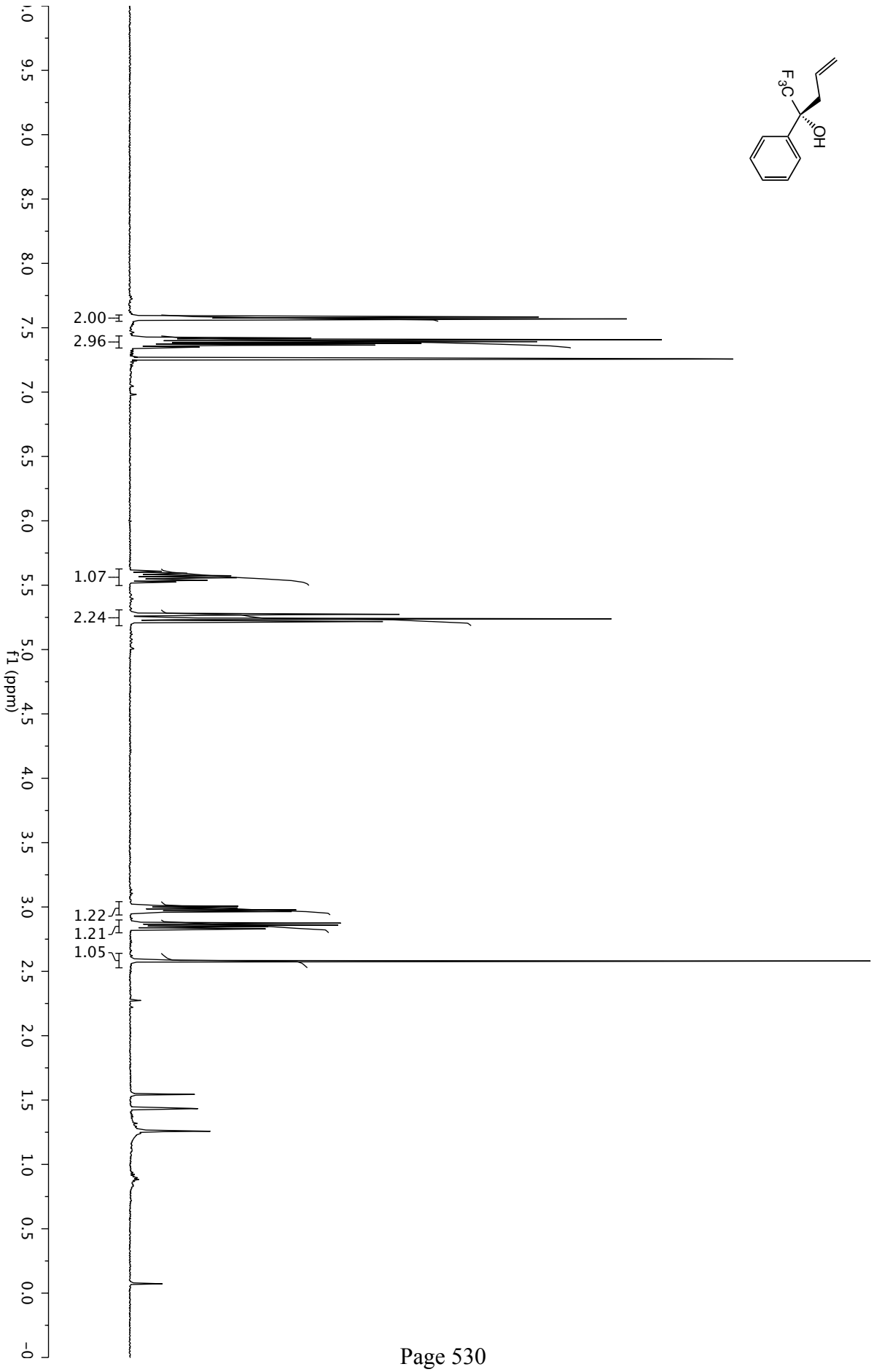
C	-7.874	5.773	-2.804
C	-6.844	7.914	-3.630
C	-5.754	10.052	-4.614
H	-7.598	10.625	-5.646
C	-5.572	4.954	-0.642
H	-4.725	5.641	-0.733
H	-7.945	5.242	-1.860
H	-4.937	12.012	-5.024
C	-7.462	7.205	-2.591
C	-6.465	9.270	-3.488
H	-5.473	4.436	0.317
H	-6.476	5.558	-0.590
C	-5.443	11.504	-4.198
H	-4.781	11.552	-3.328
H	-6.352	12.072	-3.972
C	-7.748	7.851	-1.385
C	-6.775	9.872	-2.260
H	-8.240	7.305	-0.584
H	-6.513	10.910	-2.099
C	-7.411	9.188	-1.223
H	-7.632	9.700	-0.292

	1	2	3
	A	A	A
Frequencies --	-325.9512	19.3307	30.4146
Red. masses --	8.4156	5.1917	3.9396

Zero-point correction= 0.682866 (Hartree/Particle)
Thermal correction to Energy= 0.720969
Thermal correction to Enthalpy= 0.721913
Thermal correction to Gibbs Free Energy= 0.615713
Sum of electronic and zero-point Energies= -1727.456522
Sum of electronic and thermal Energies= -1727.418419
Sum of electronic and thermal Enthalpies= -1727.417475
Sum of electronic and thermal Free Energies= -1727.523674

Item	Value	Threshold	Converged?
Maximum Force	0.000016	0.000450	YES

RMS	Force	0.000002	0.000300	YES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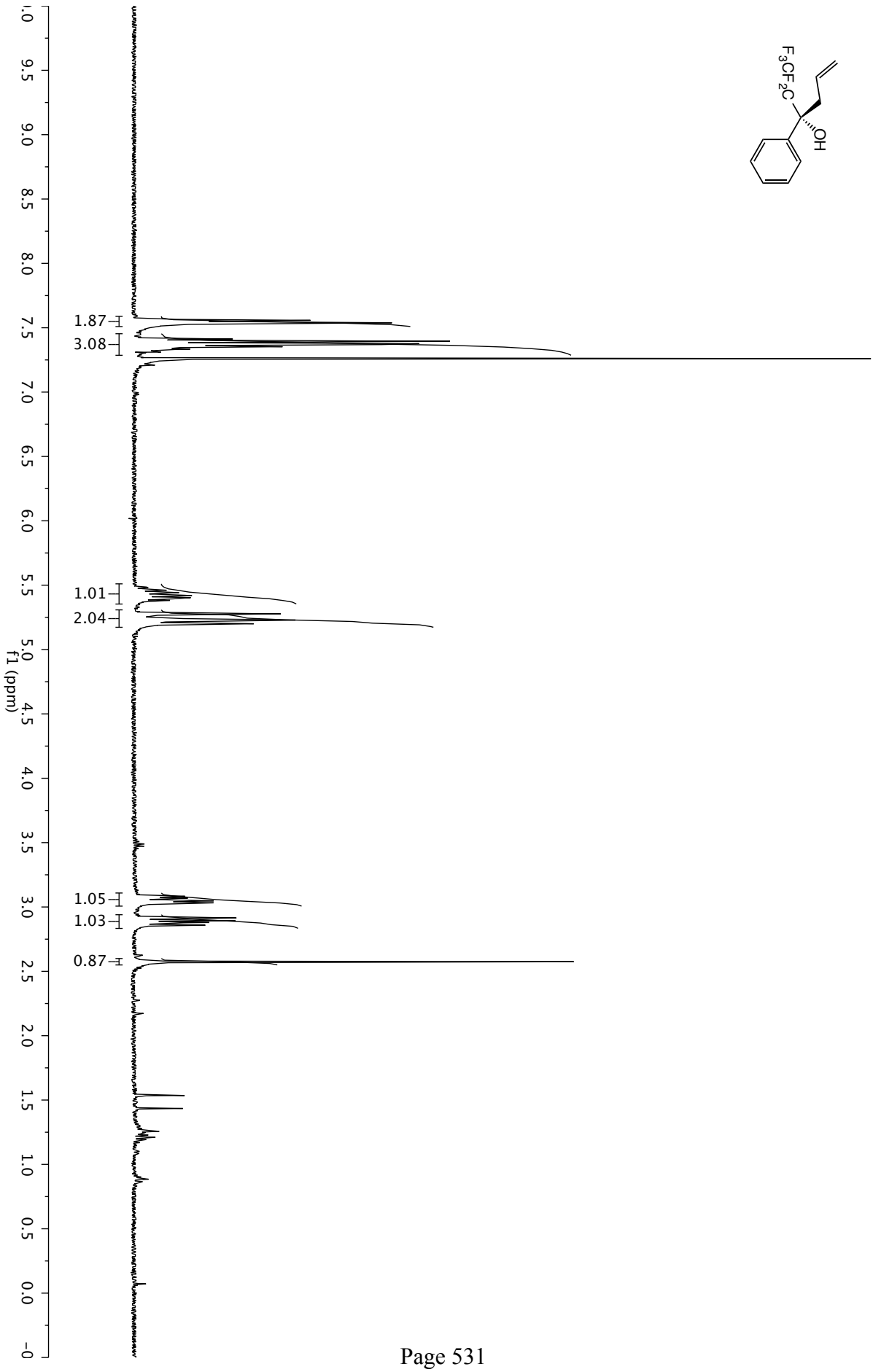
1.07
2.24
1.22
1.21
1.05
f1 (ppm)
F3C
OH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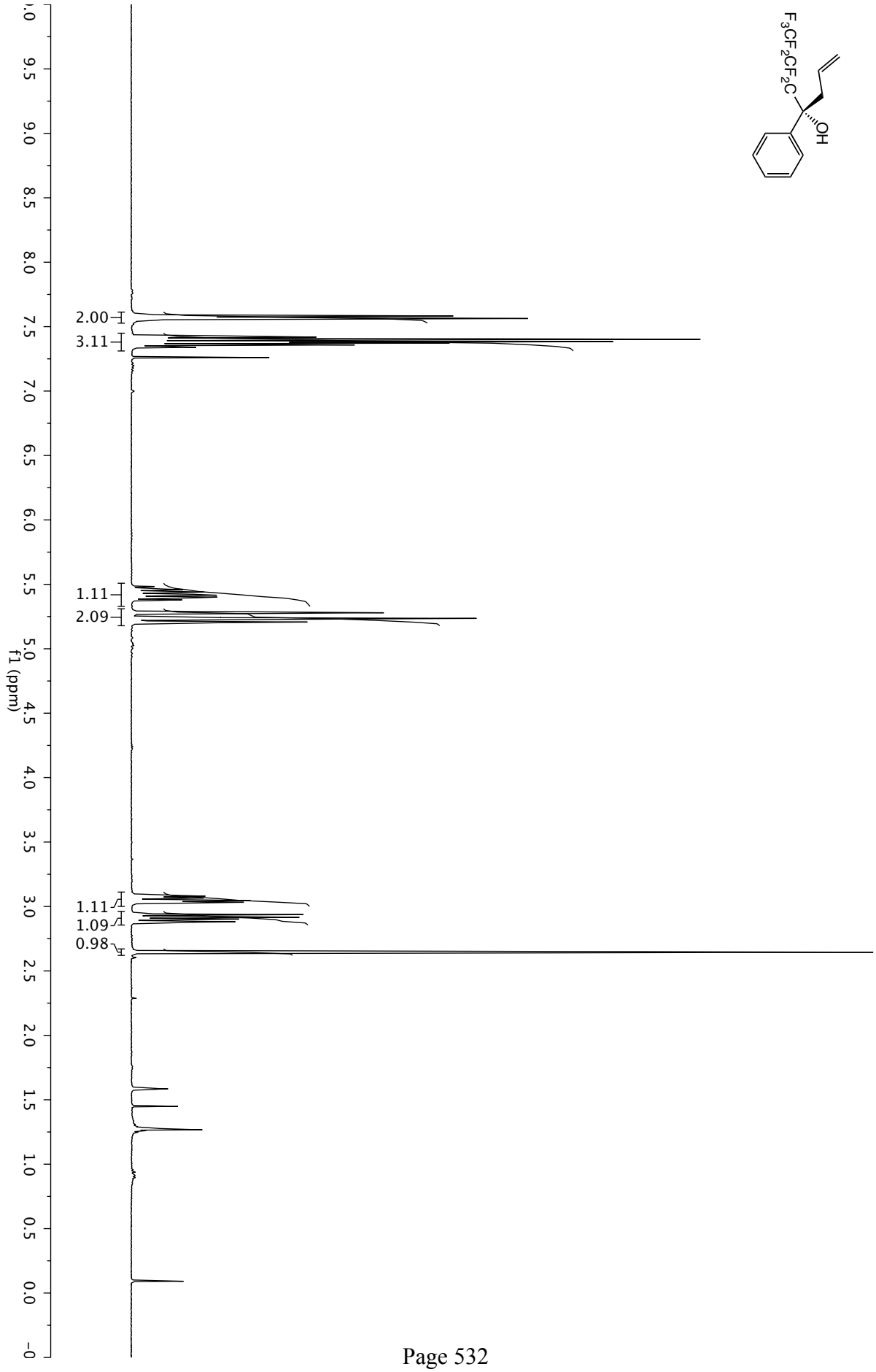
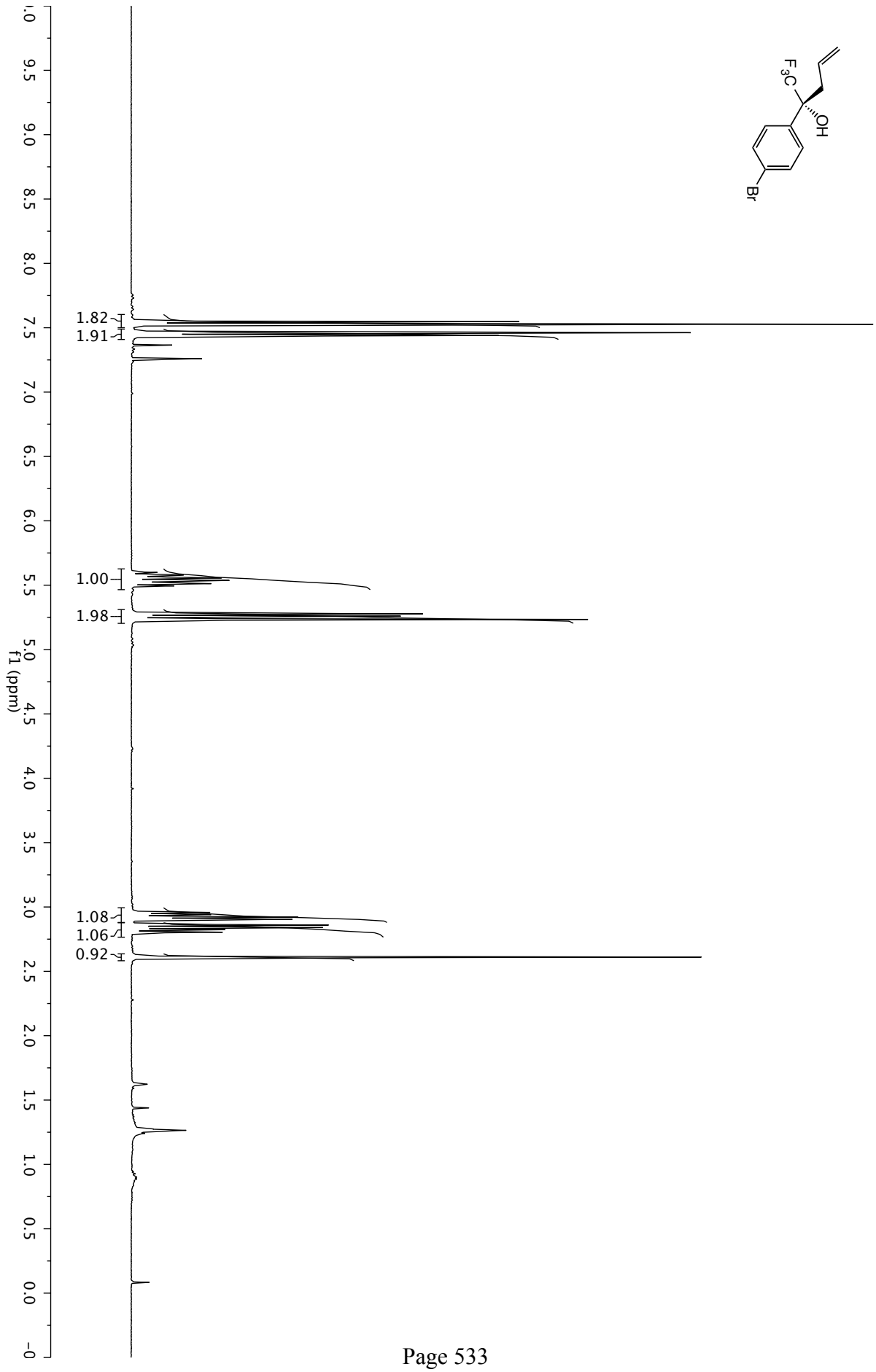
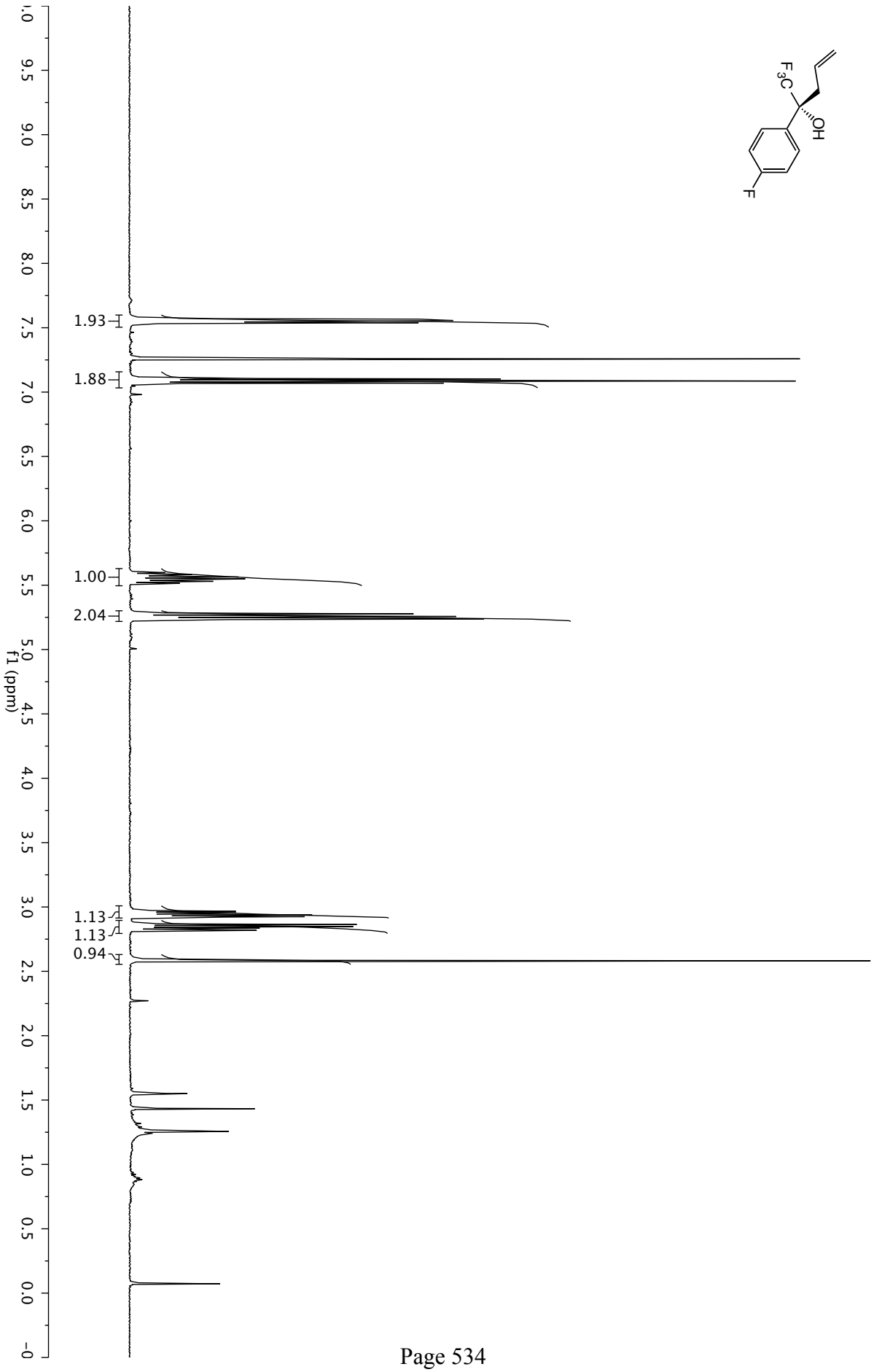
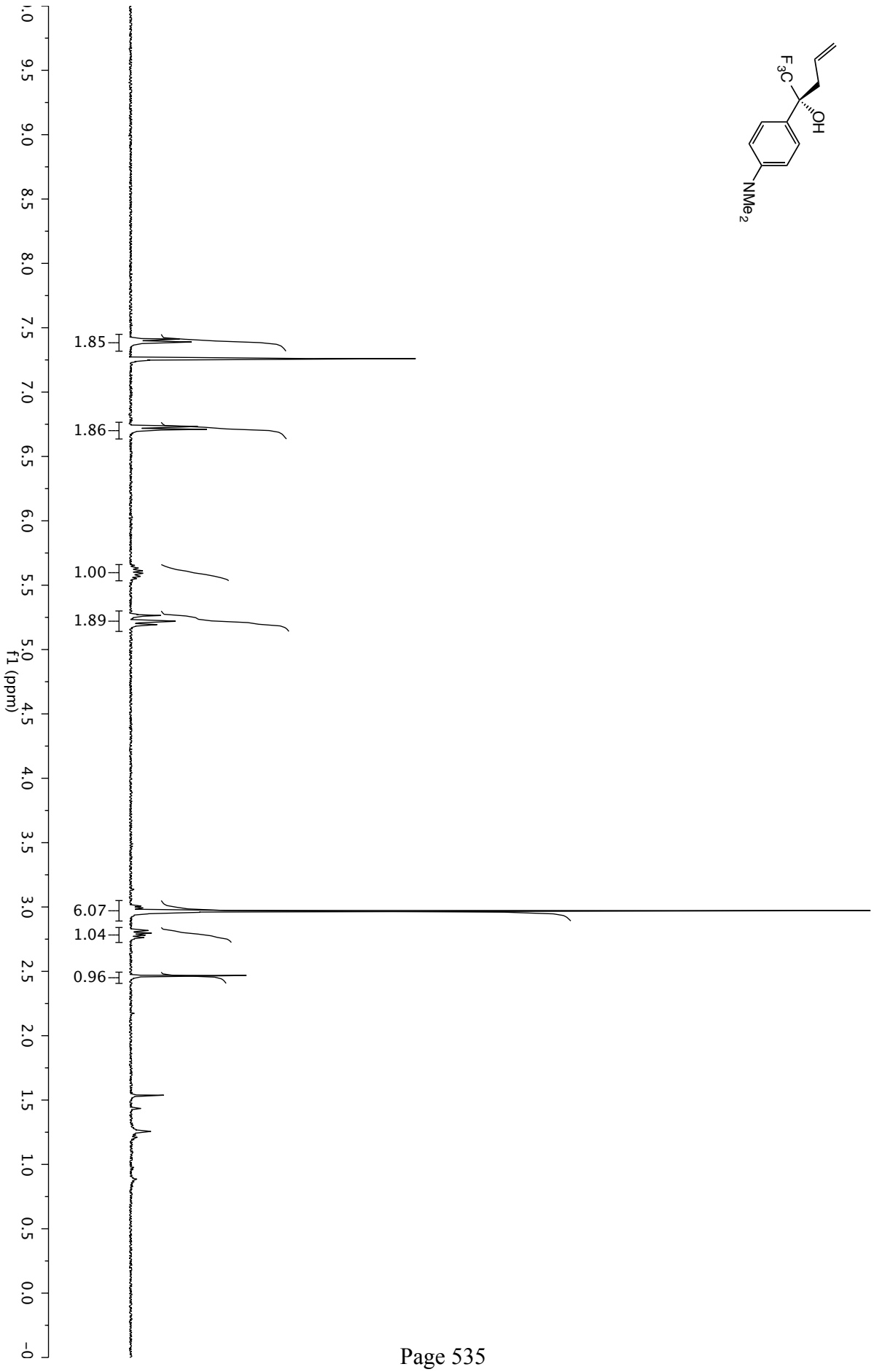
3.08
1.01
2.04
1.05
1.03
0.87
f1 (ppm)
OH


F3CF2CF2C
OH
2.00
3.11
1.11
2.09
1.11
1.09
0.98
f1 (ppm)


1.82
1.91
1.00
1.98
1.08
1.06
0.92
f1 (ppm)
F3C
OH
Br


1.93
1.88
1.00
2.04
1.13
1.13
0.94
f1 (ppm)
F3C
OH
F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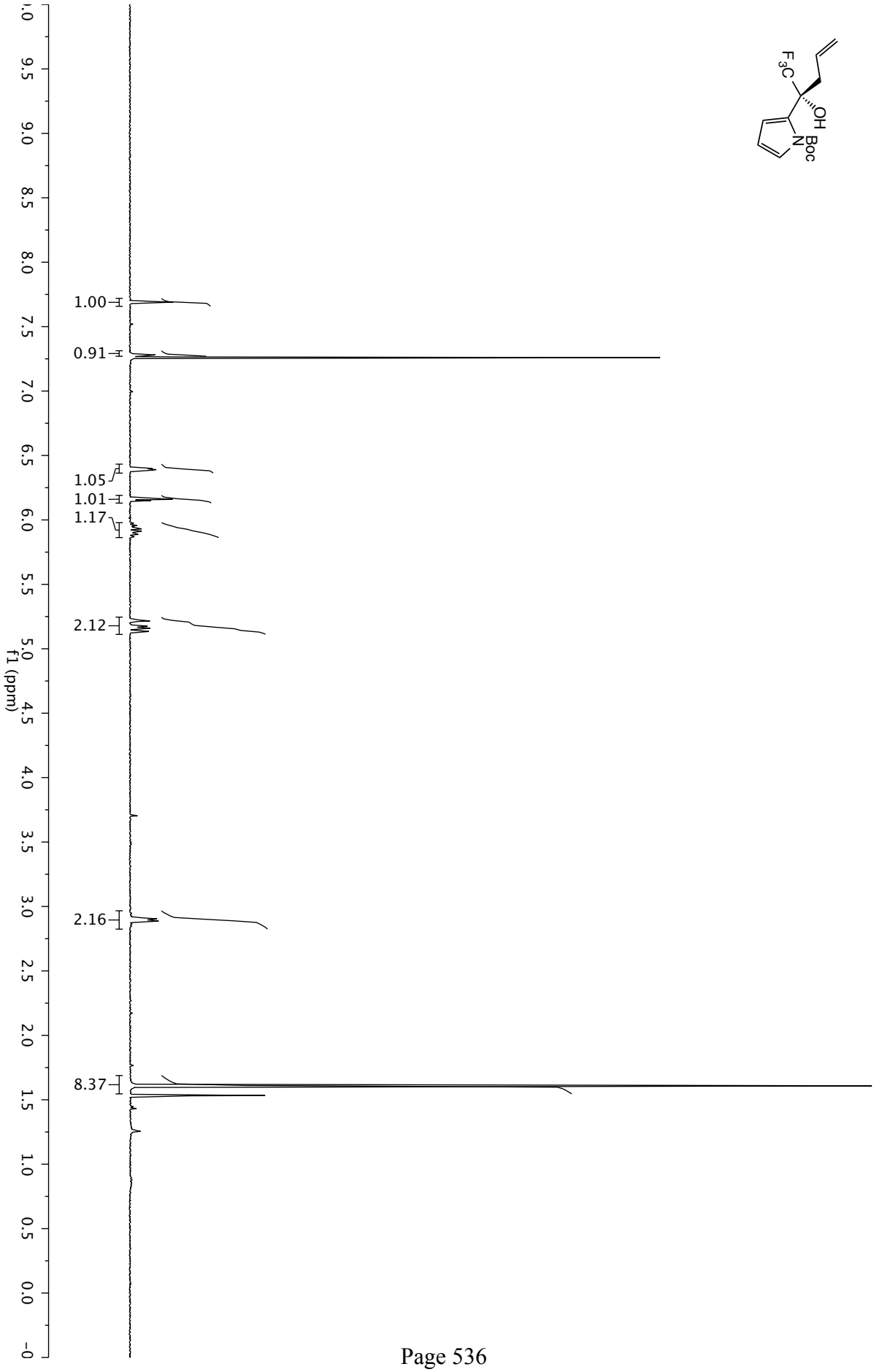
1.00
1.89
6.07
1.04
0.96
f1 (ppm)
F3C
OH
NMe2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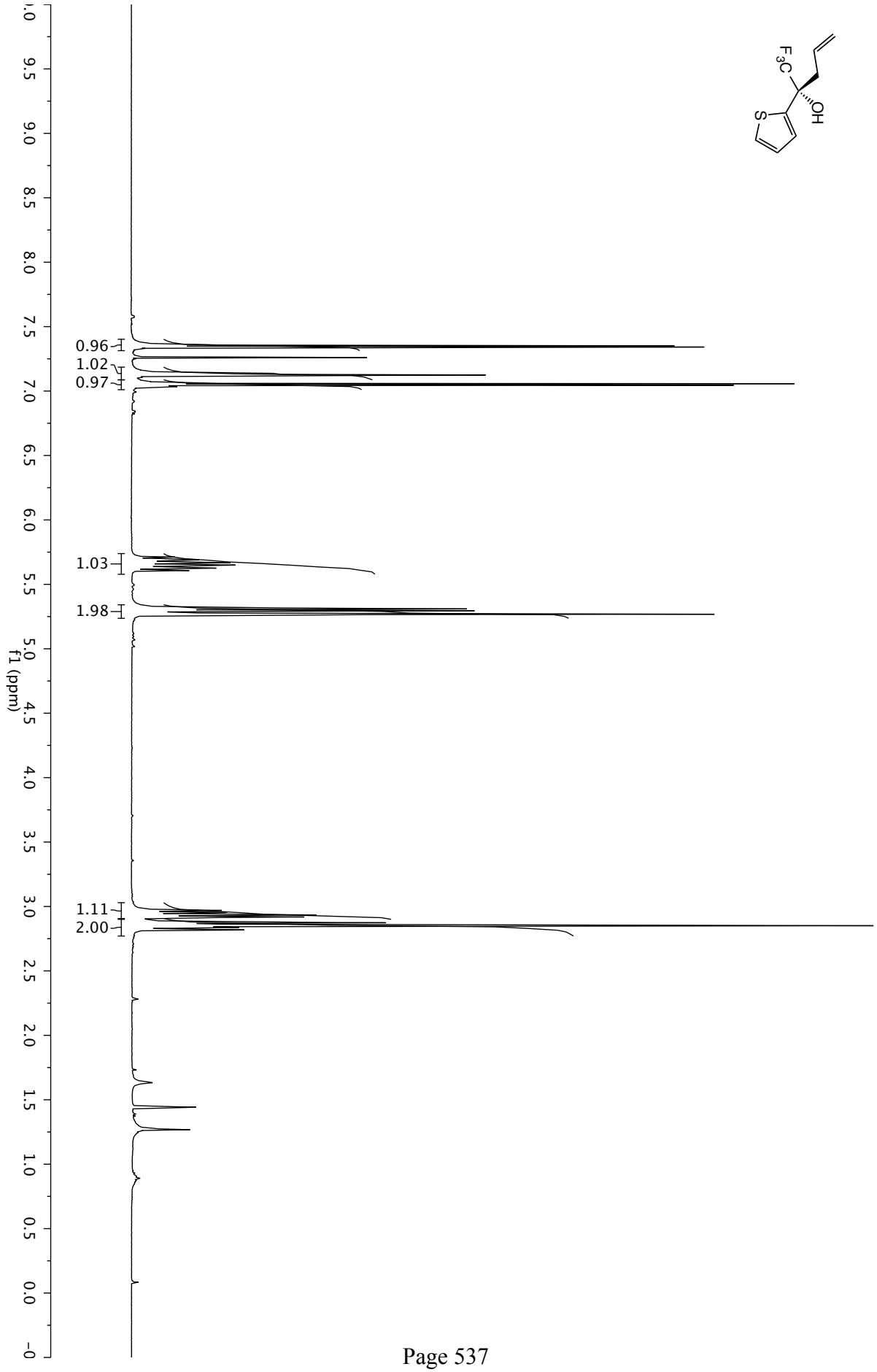
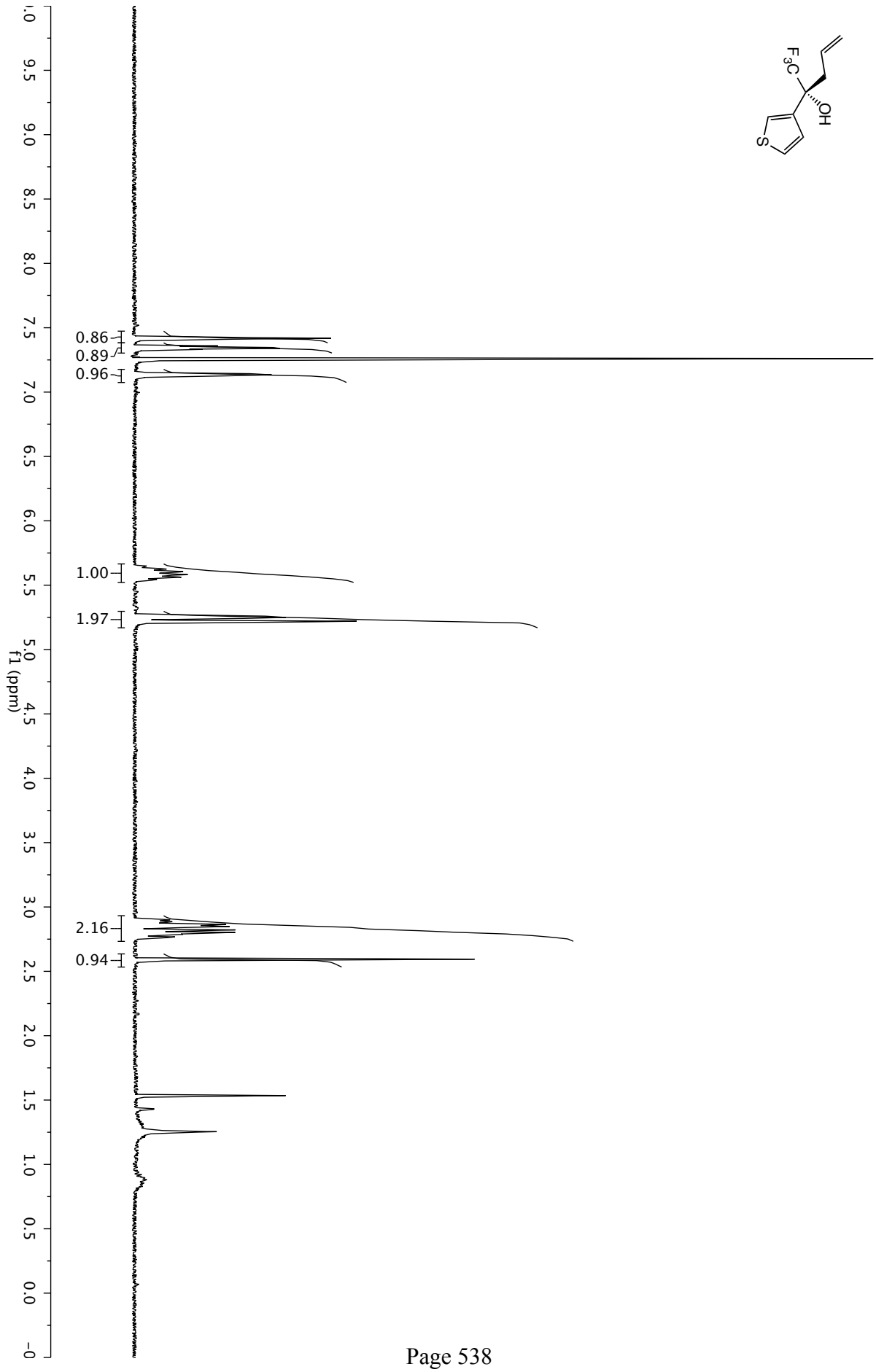
0.91
1.05
1.01
1.17
2.12
2.16
8.37
f1 (ppm)
F3C
OH
N
Boc


0.96
1.02
0.97
1.03
1.98
1.11
2.00
f1 (ppm)
F3C
OH
S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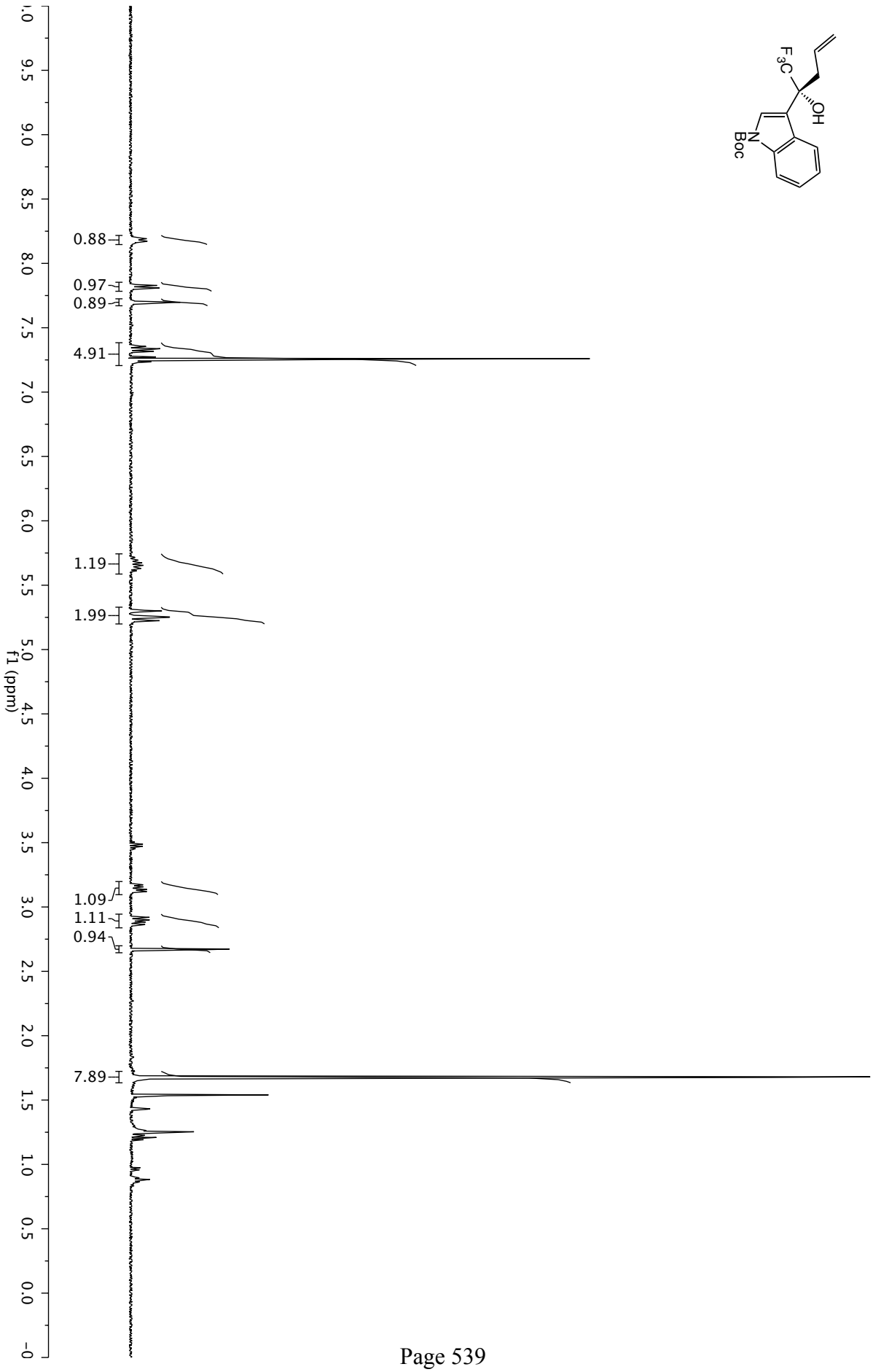
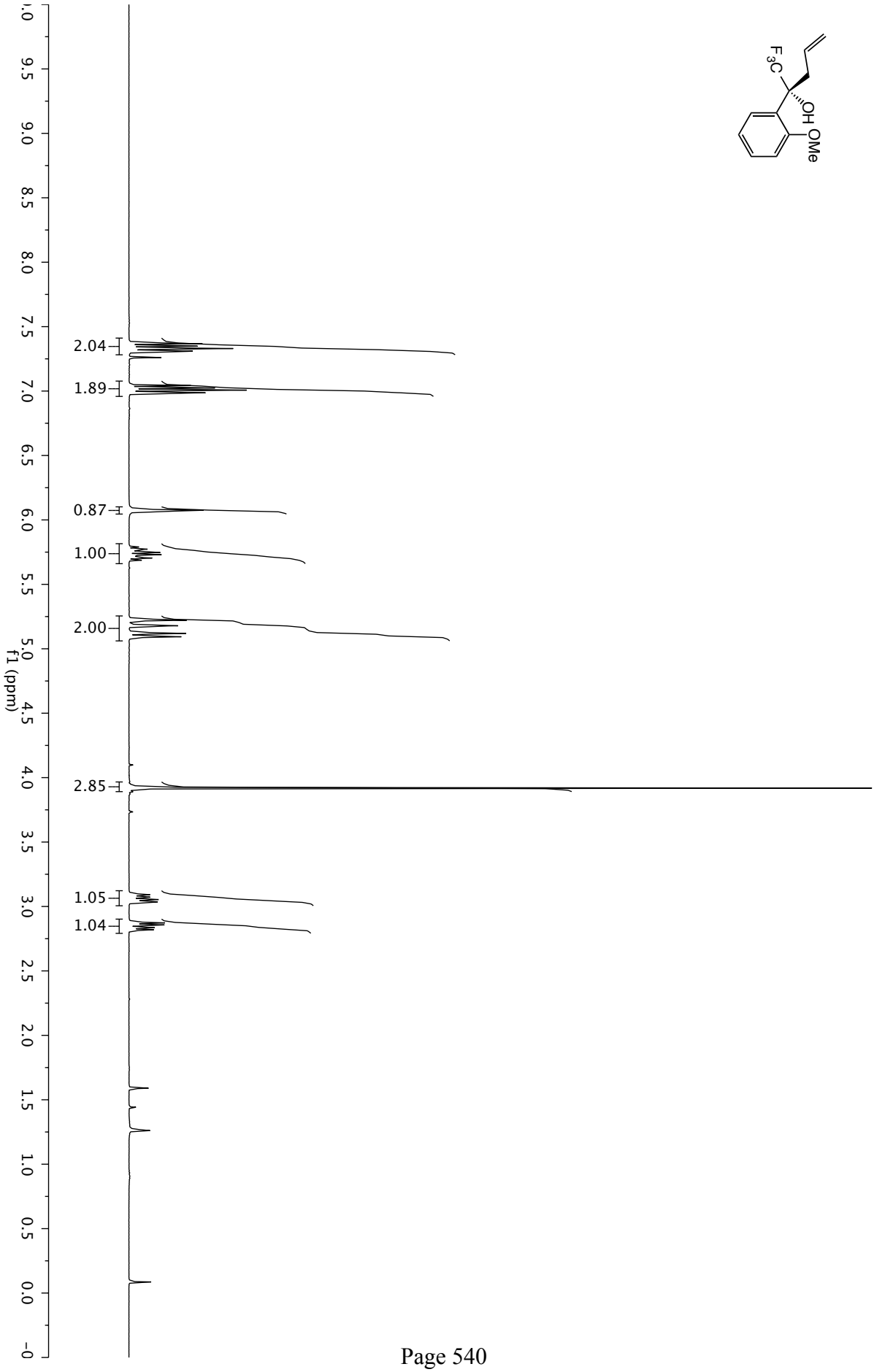
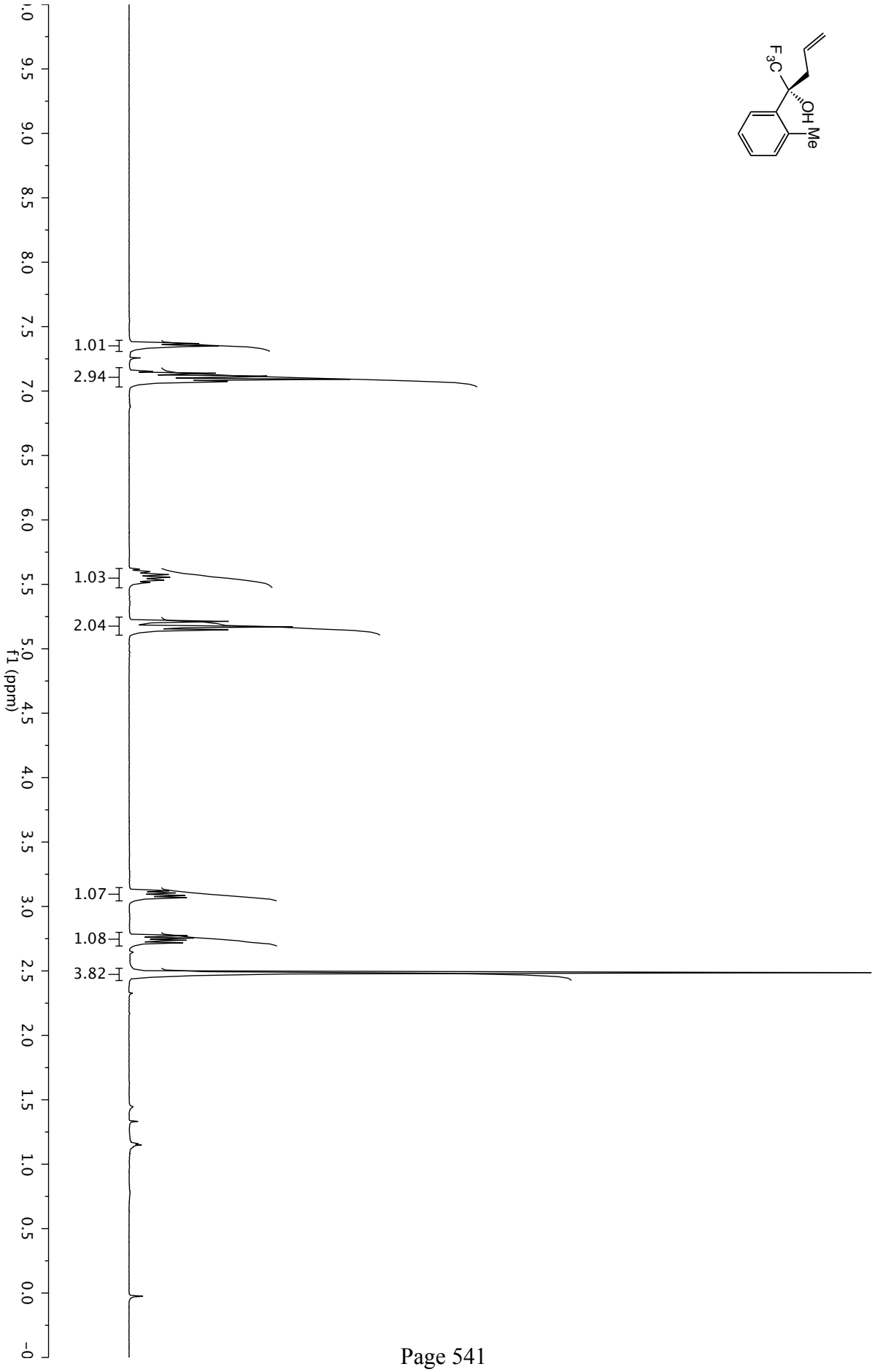
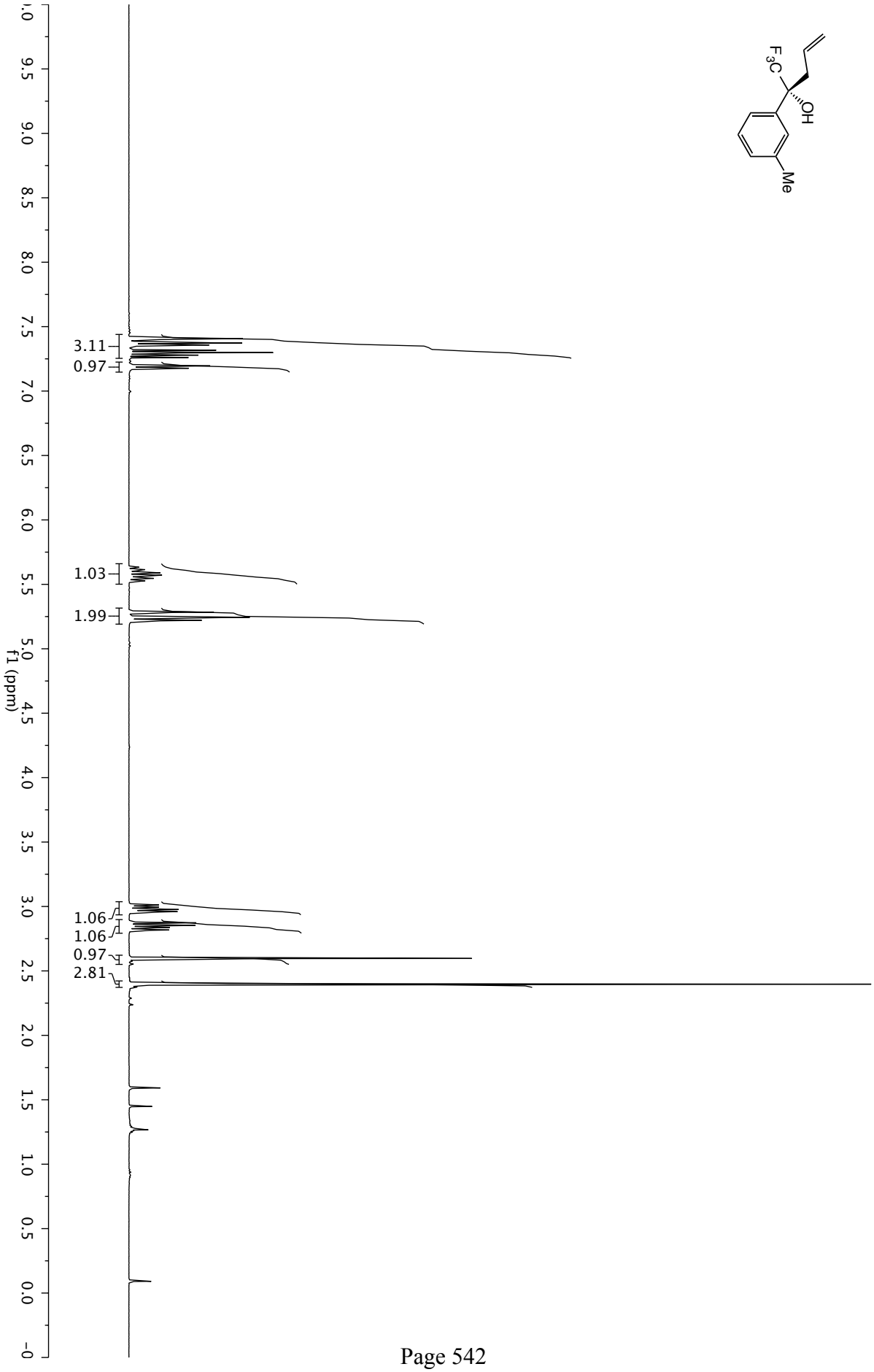
0.89
0.96
1.00
1.97
2.16
0.94
f1 (ppm)
F3C
OH
S


F3C
OH
N
Boc
0.88
0.97
0.89
4.91
1.19
1.99
1.09
1.11
0.94
7.89
f1 (ppm)


F3C
OH
OMe
2.04
1.89
0.87
1.00
2.00
2.85
1.05
1.04
f1 (ppm)


1.01
2.94
1.03
2.04
1.07
1.08
3.82
f1 (ppm)
F3C
OH
Me


3.11
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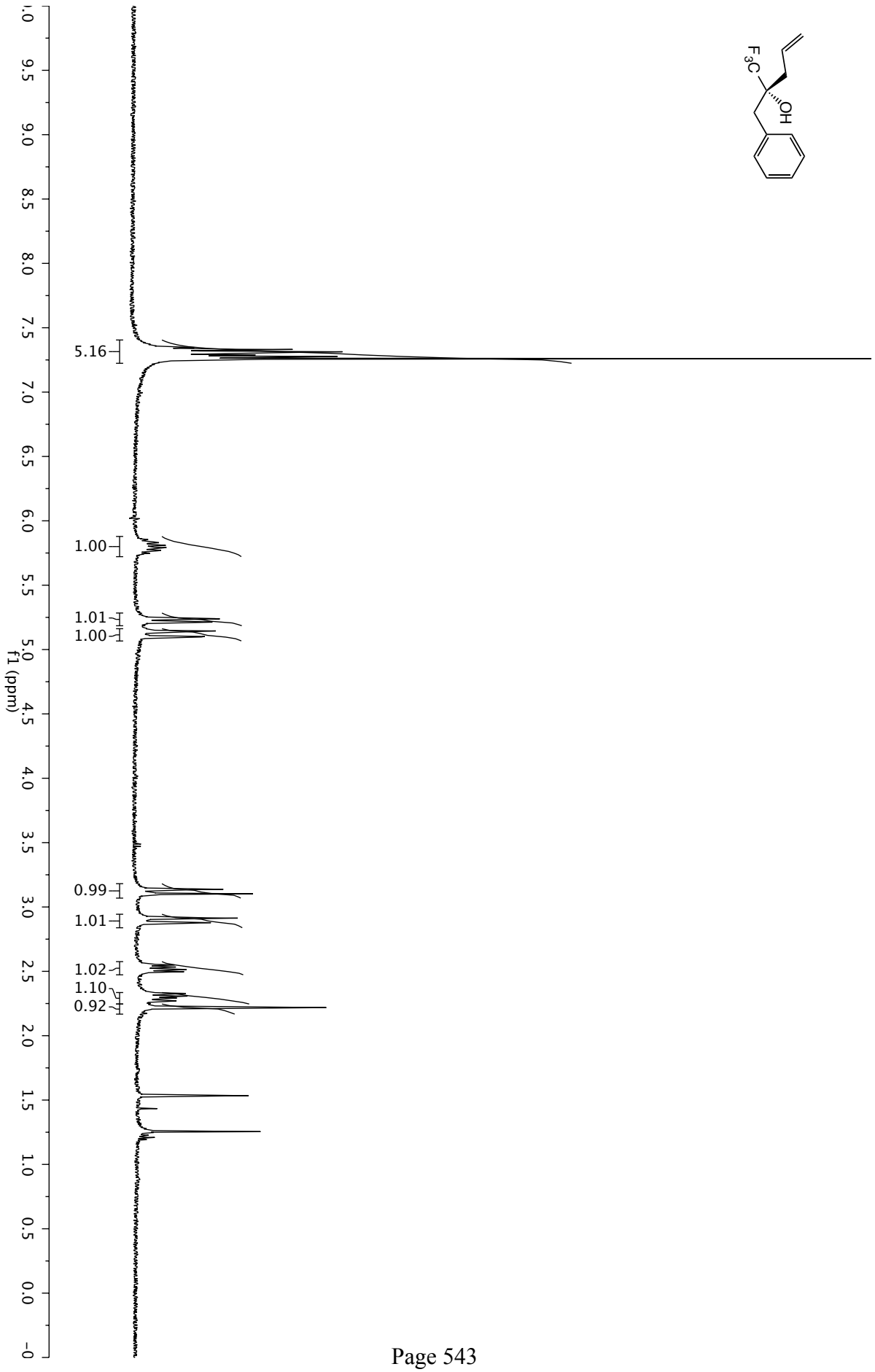
1.03
1.99
1.06
1.06
0.97
2.81
f1 (ppm)
F3C
OH
Me


F3C
OH
5.16
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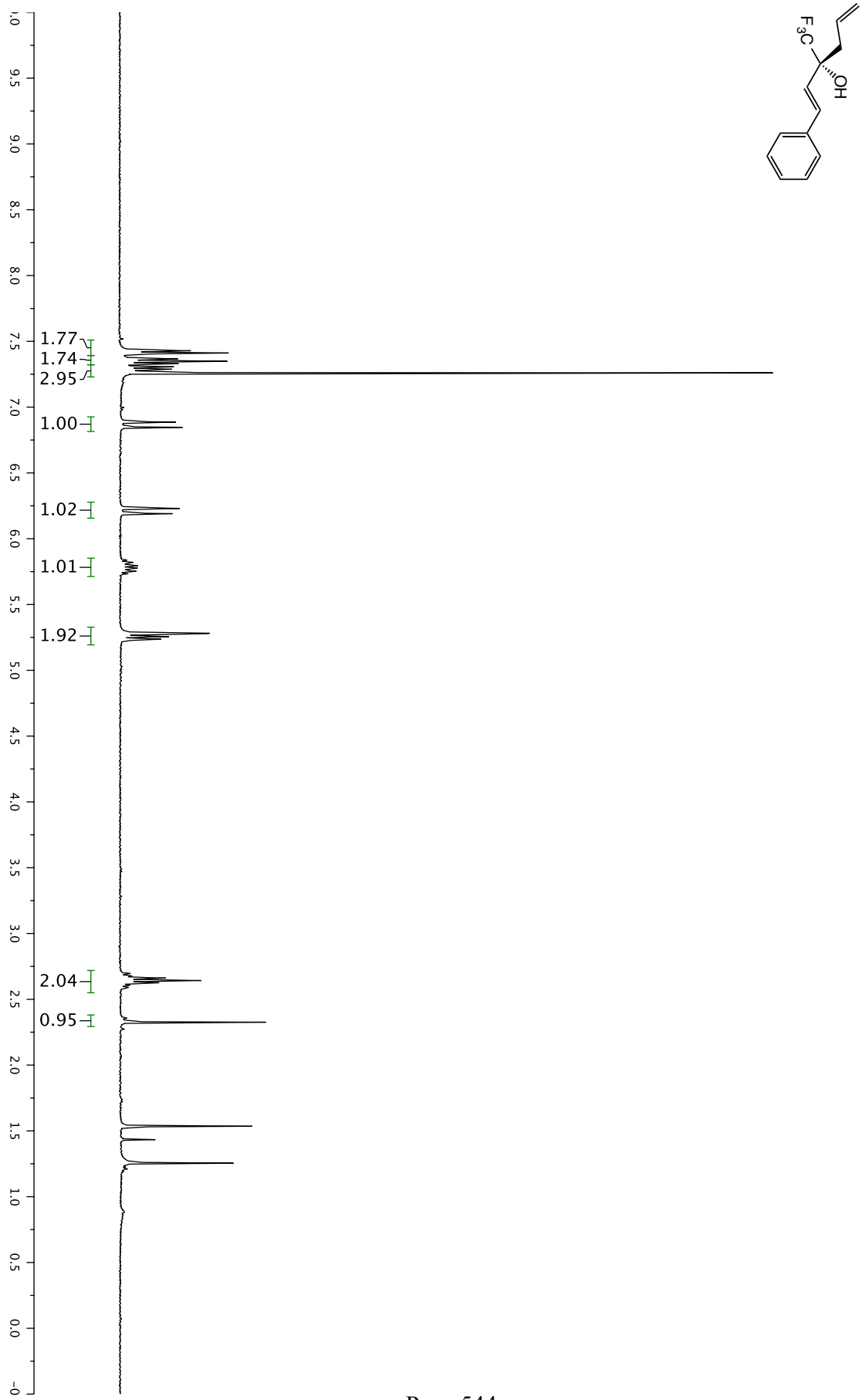
1.01
1.00
0.99
1.01
1.02
1.10
0.92
f1 (ppm)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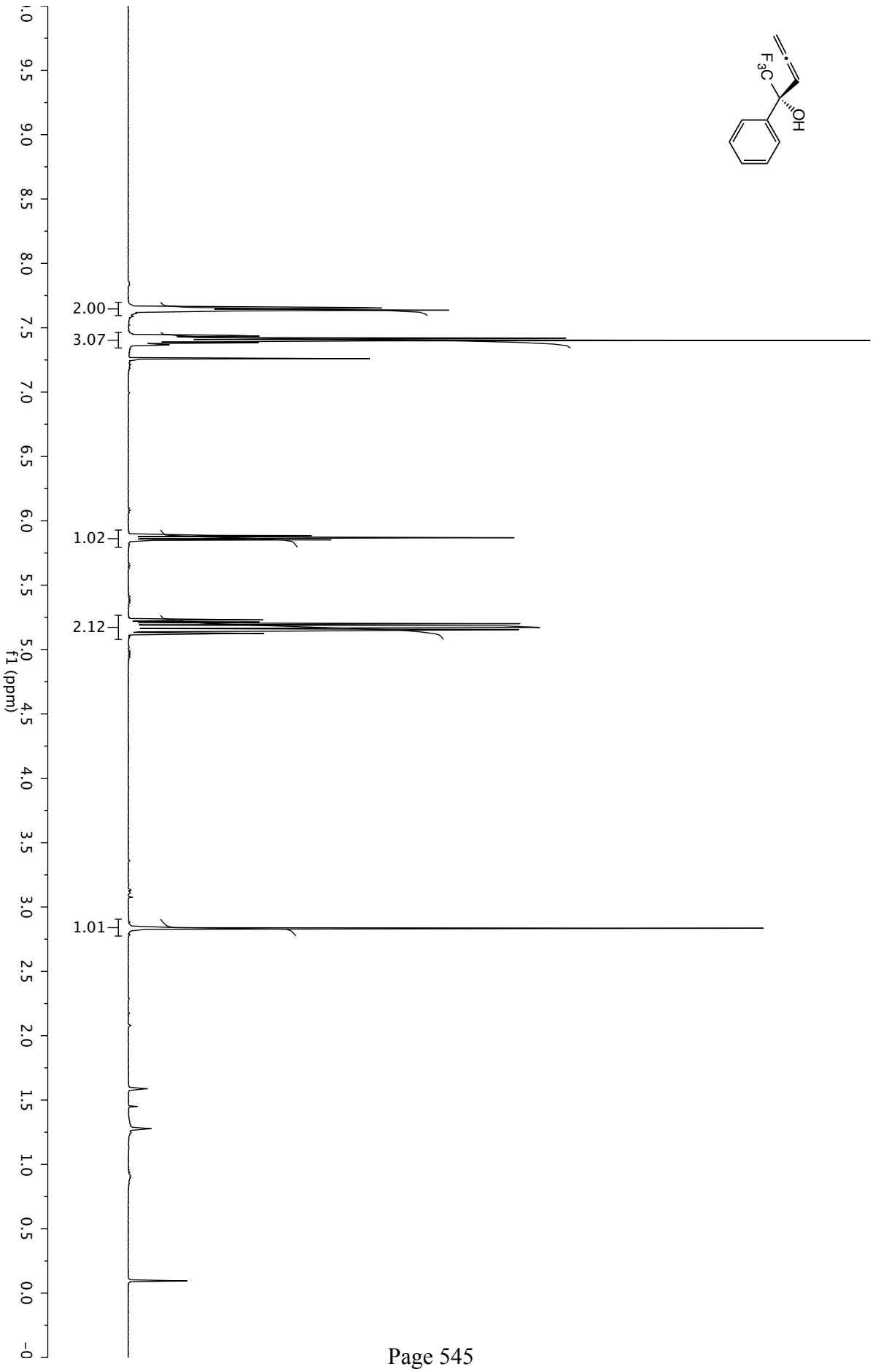
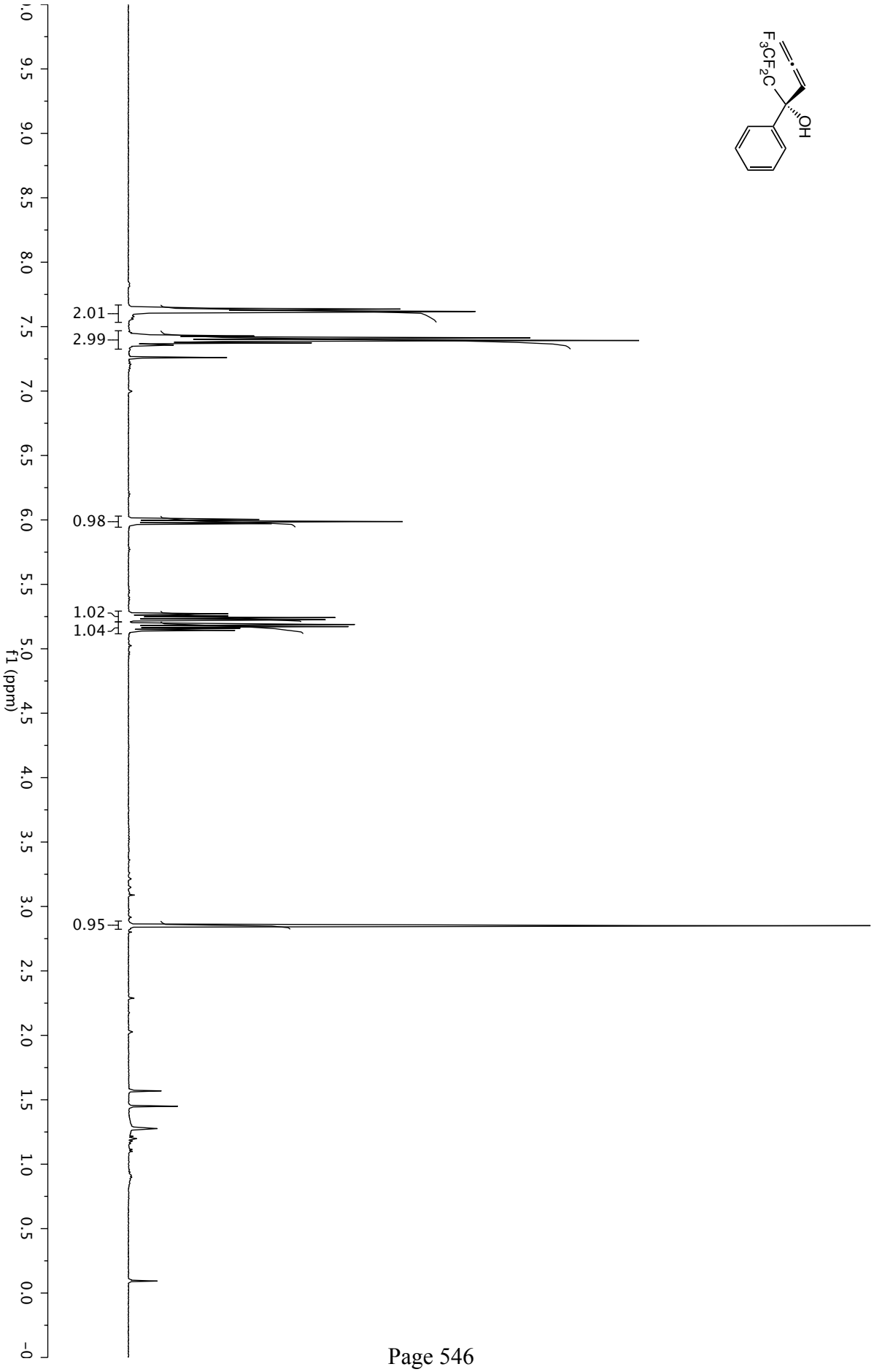
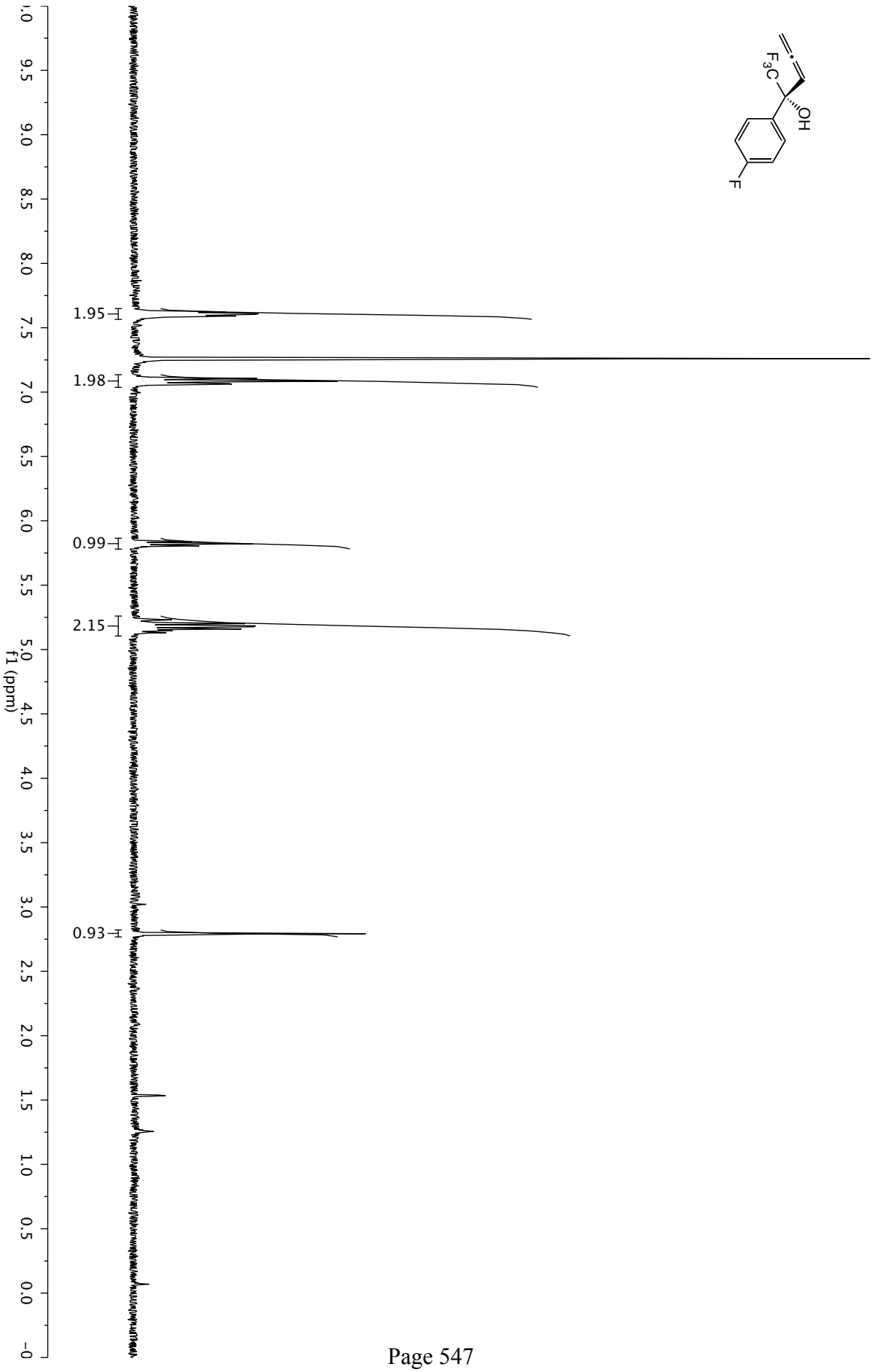
1.00
1.02
1.01
1.92
2.04
0.95
F3C
OH


2.00
3.07
1.02
2.12
1.01
f1 (ppm)
F3C
OH


F3CF2C
OH
2.01
2.99
0.98
1.02
1.04
0.95
f1 (ppm)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2.15
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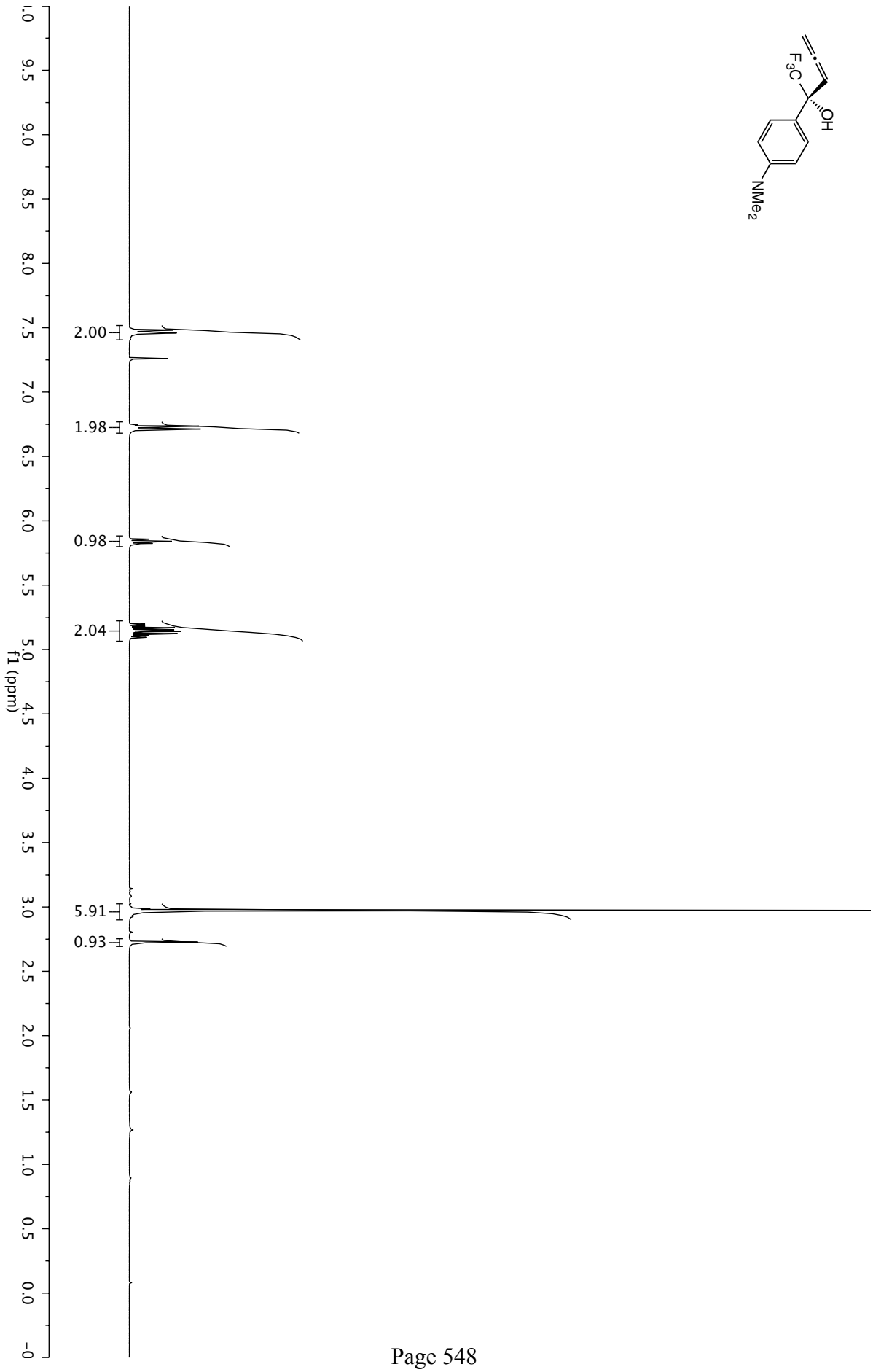
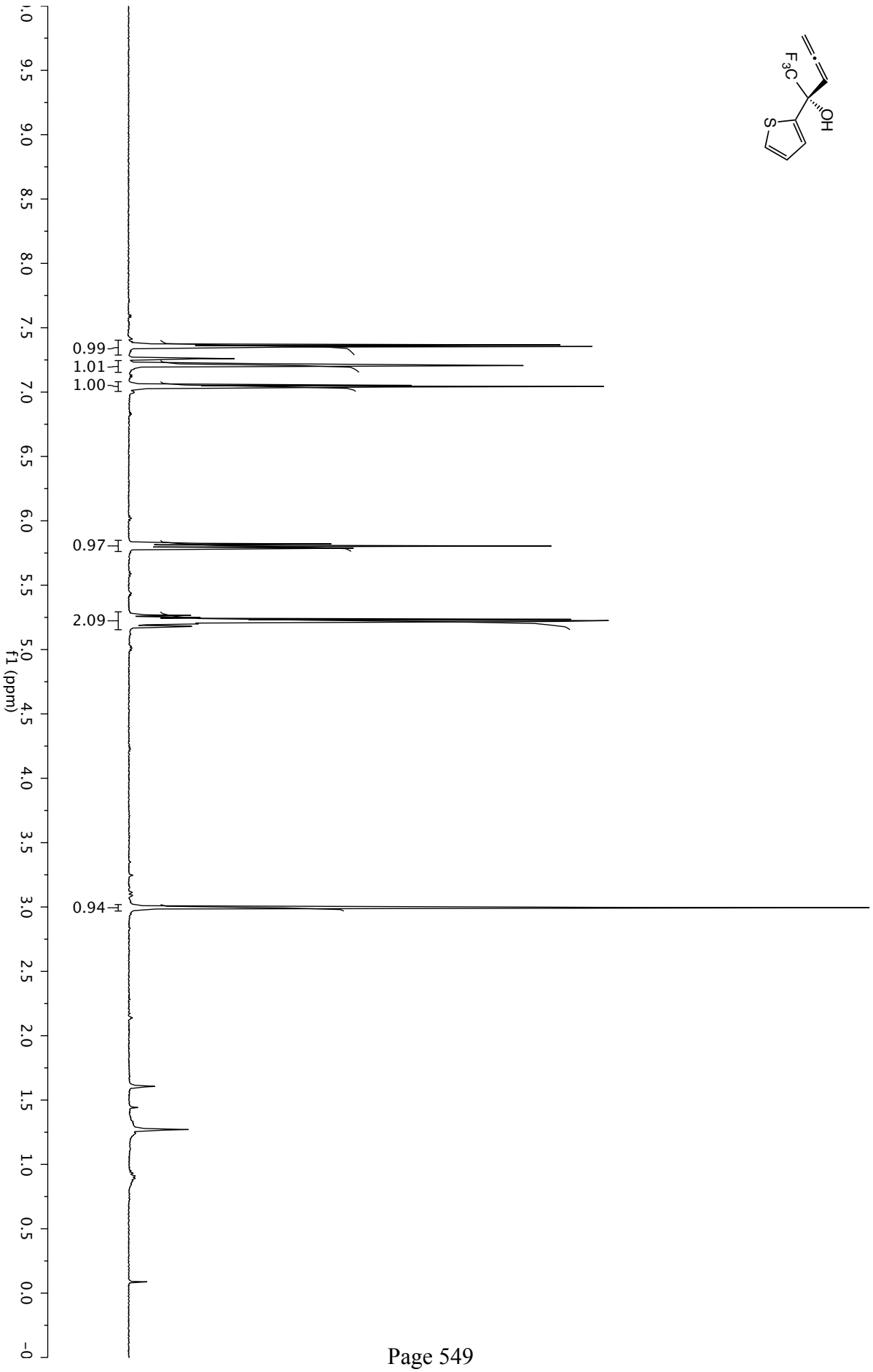
f1 (ppm)
F3C
OH
F


2.00
1.98
0.98
2.04
5.91
0.93
f1 (ppm)
F3C
OH
NMe2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1.01
1.00
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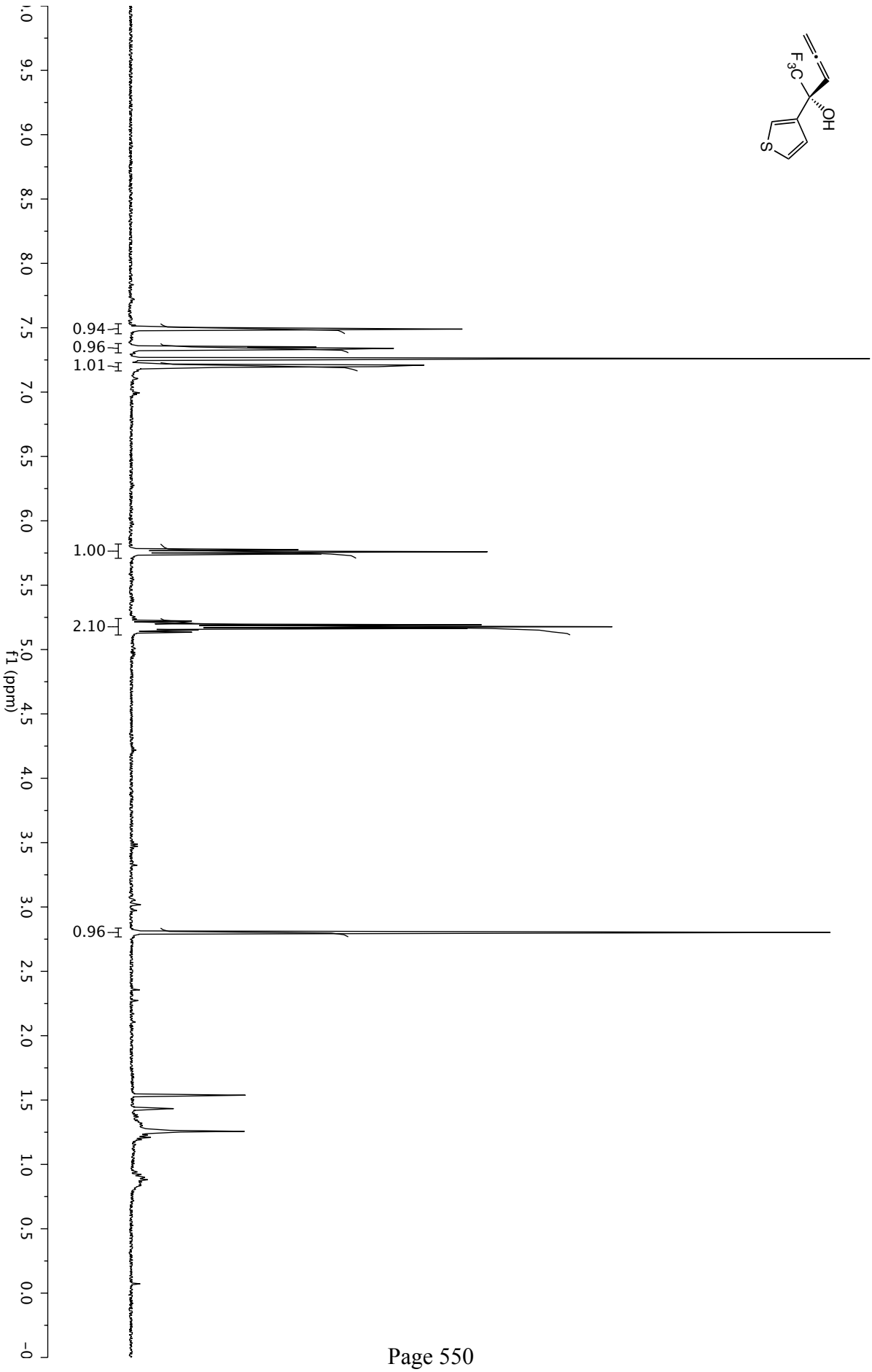
2.09
0.94
f1 (ppm)
F3C
OH
S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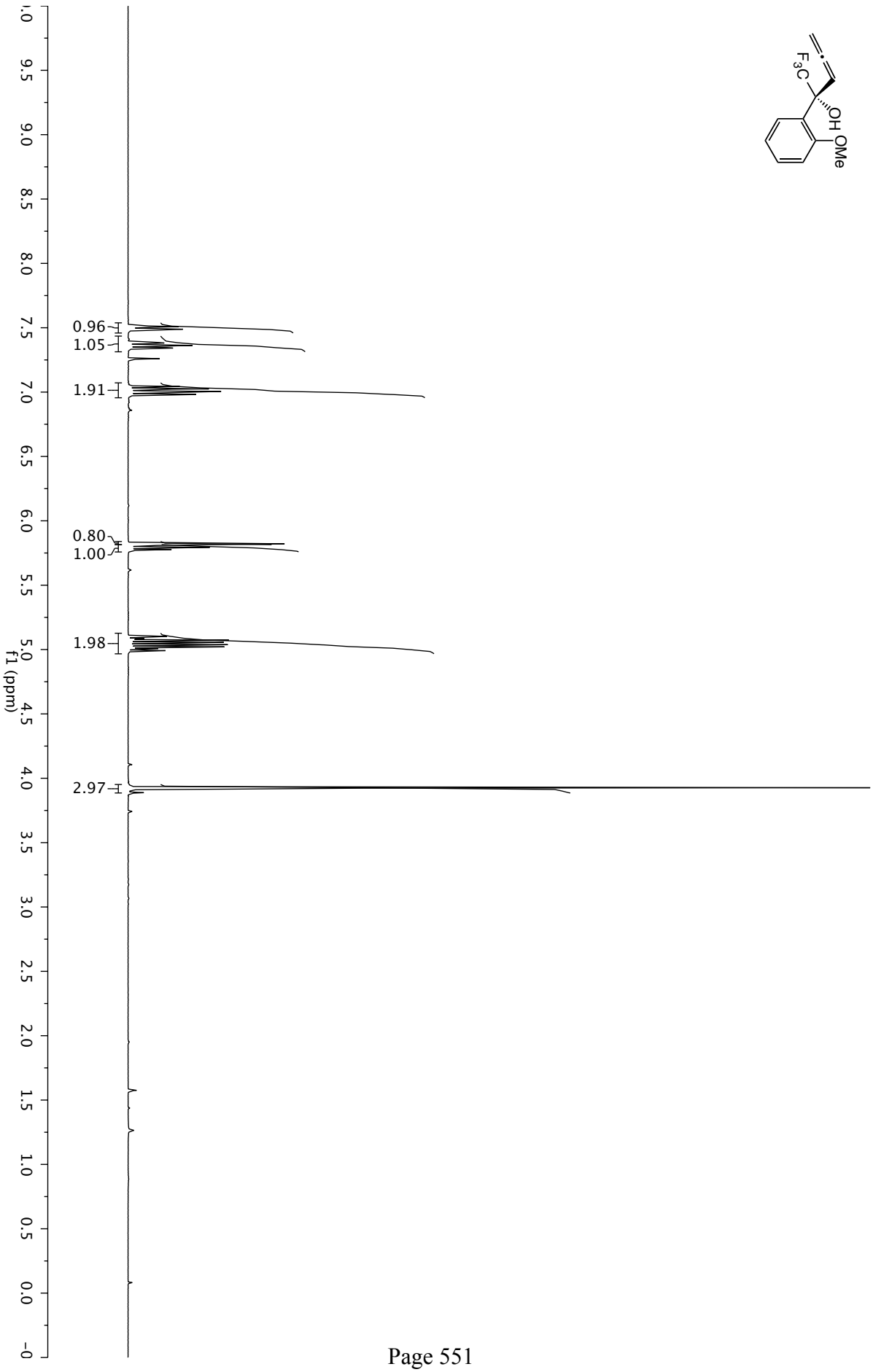
F3C
OH
S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1.98
2.97
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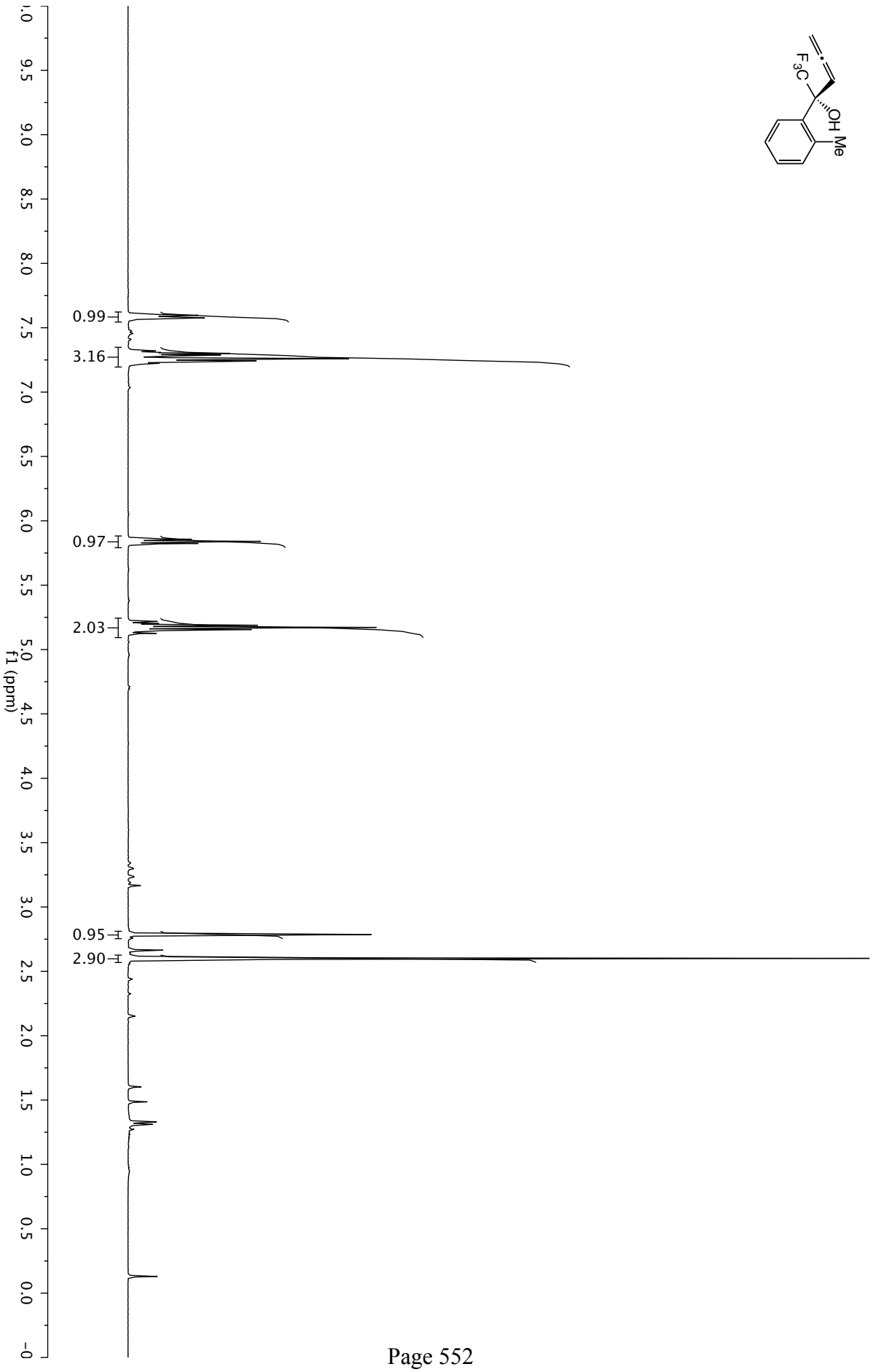
F3C
OH
OMe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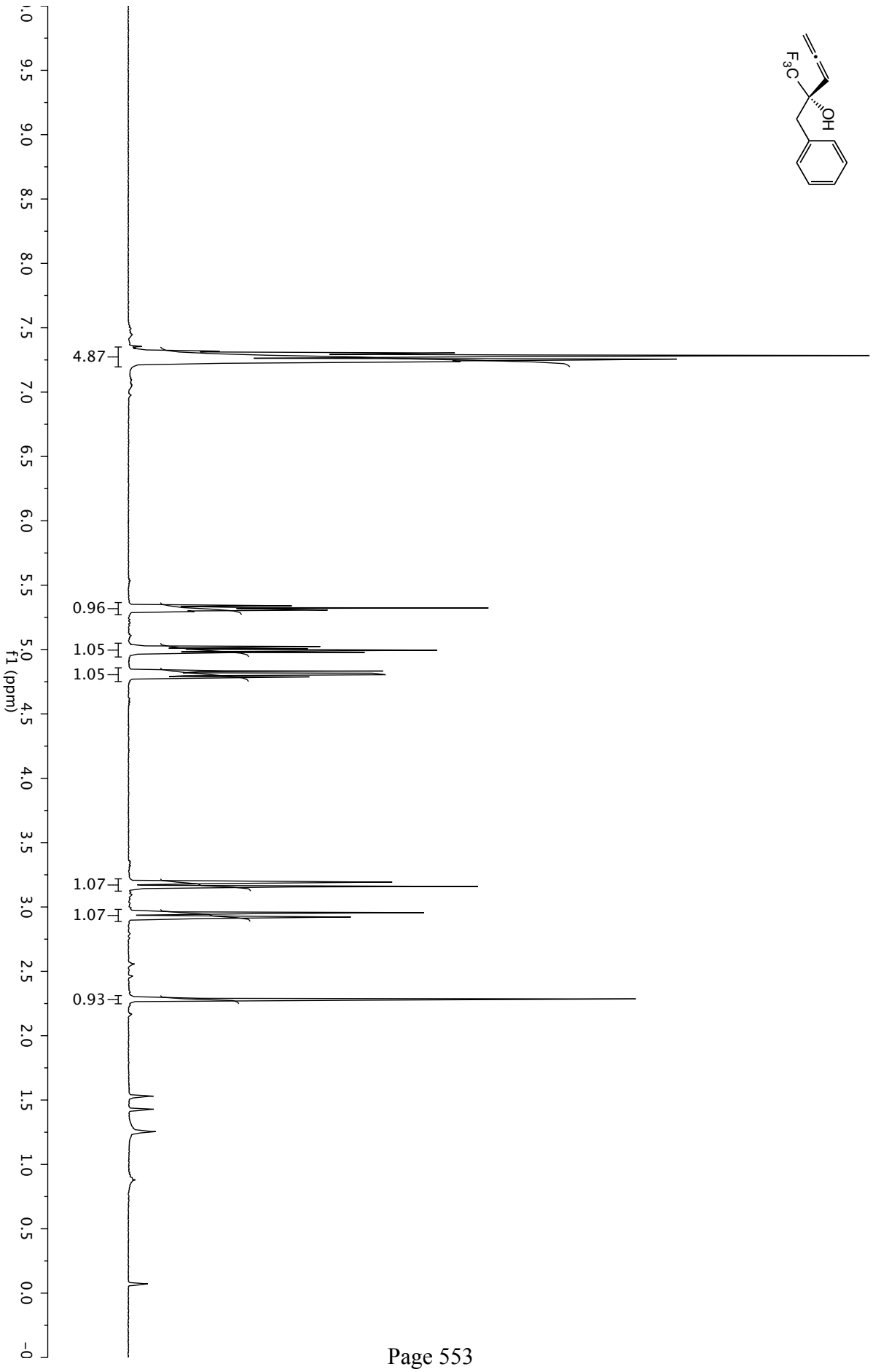
0.95
2.90
f1 (ppm)
F3C
OH
Me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1.07
0.93
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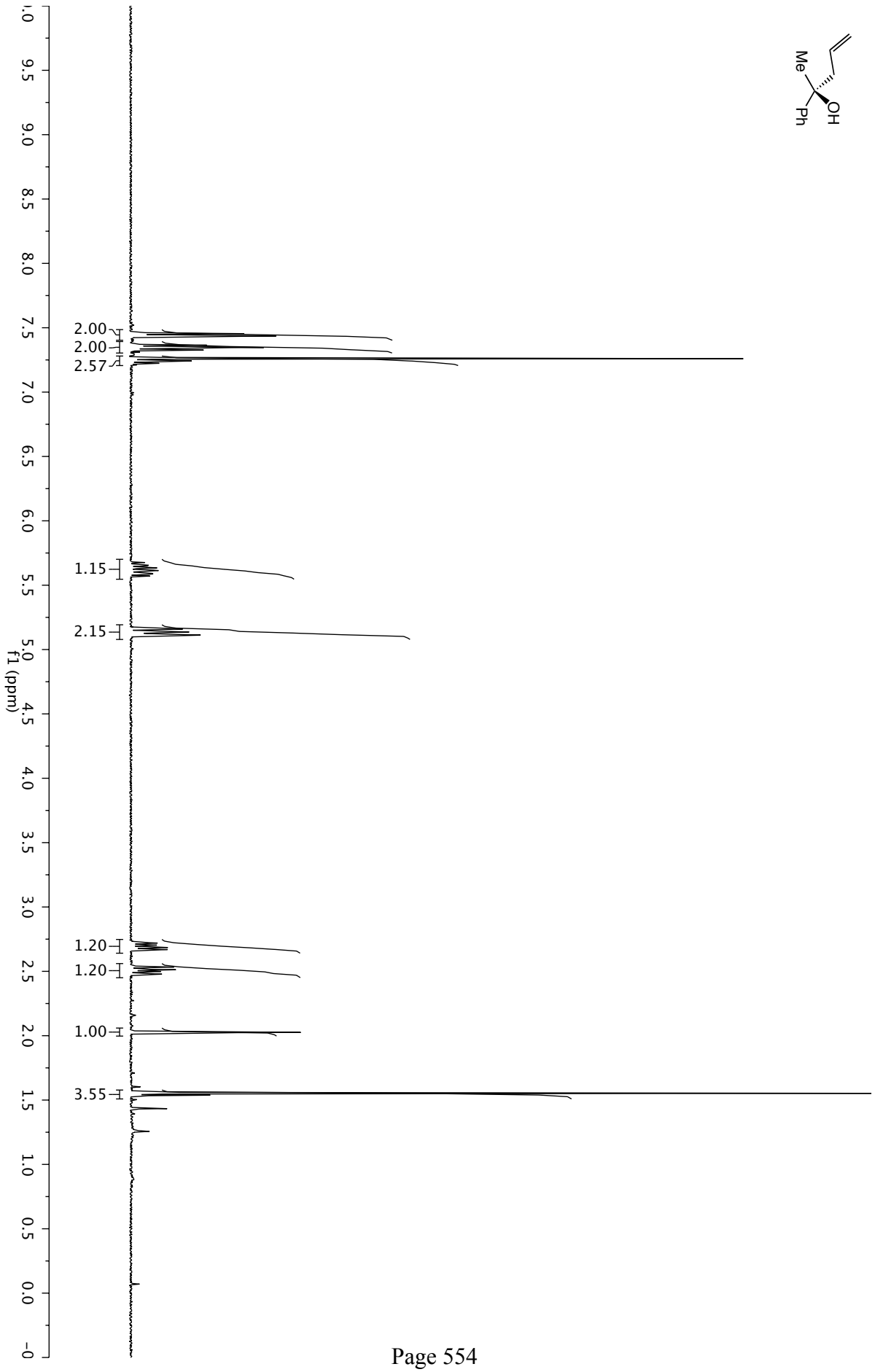
F3C
OH


Me
OH
Ph
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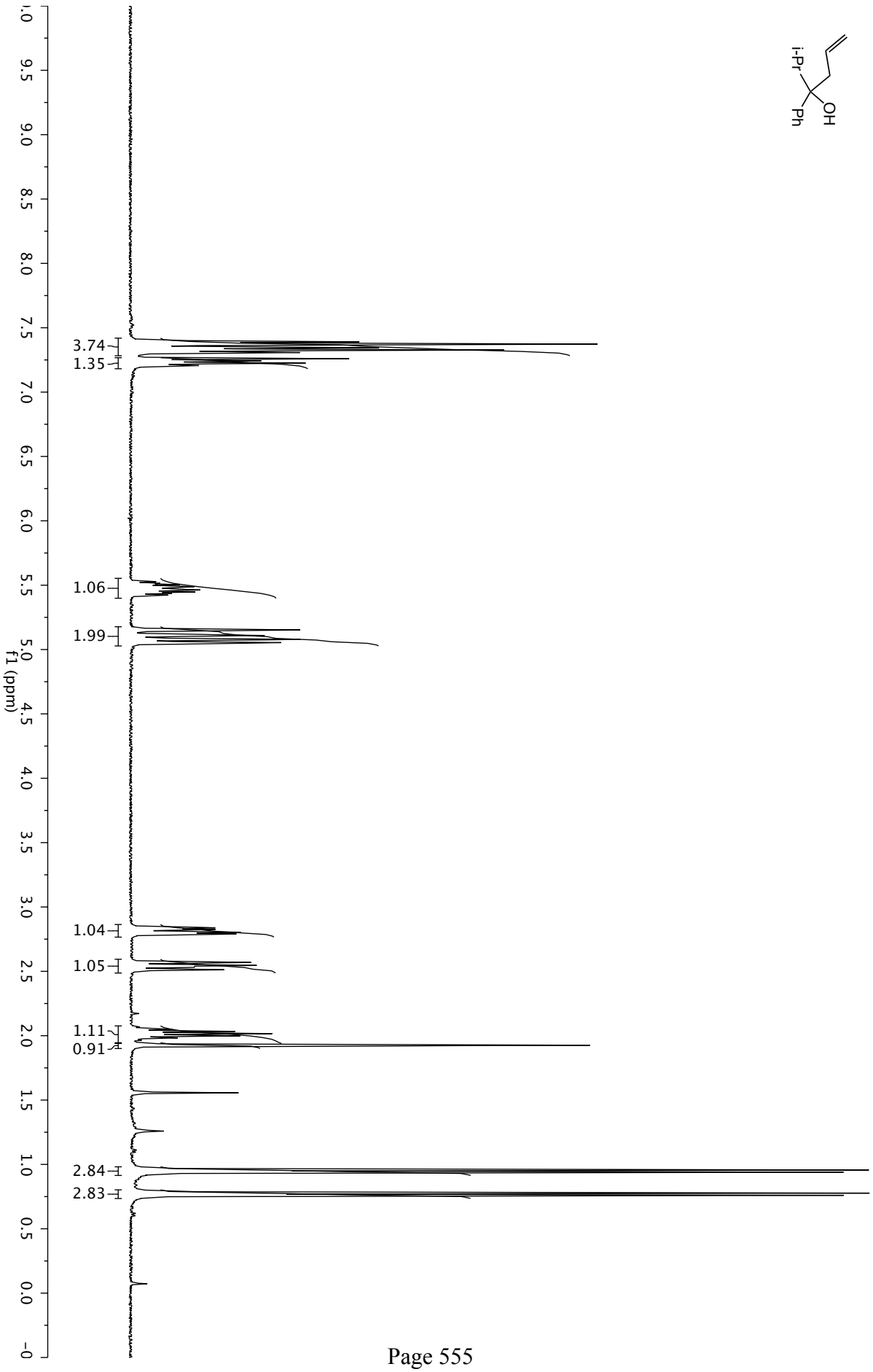
2.15
1.20
1.20
1.00
3.55
f1 (ppm)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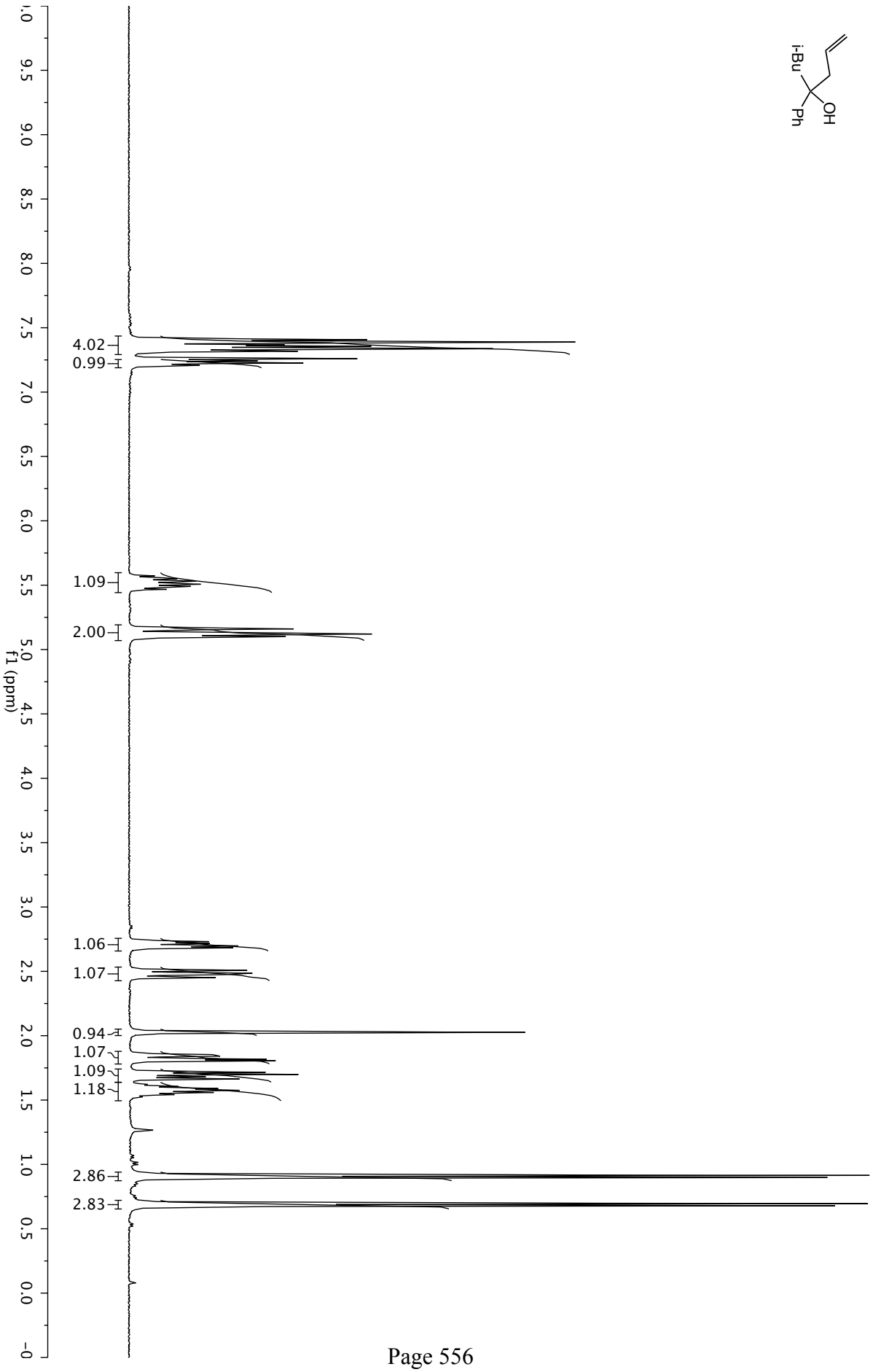
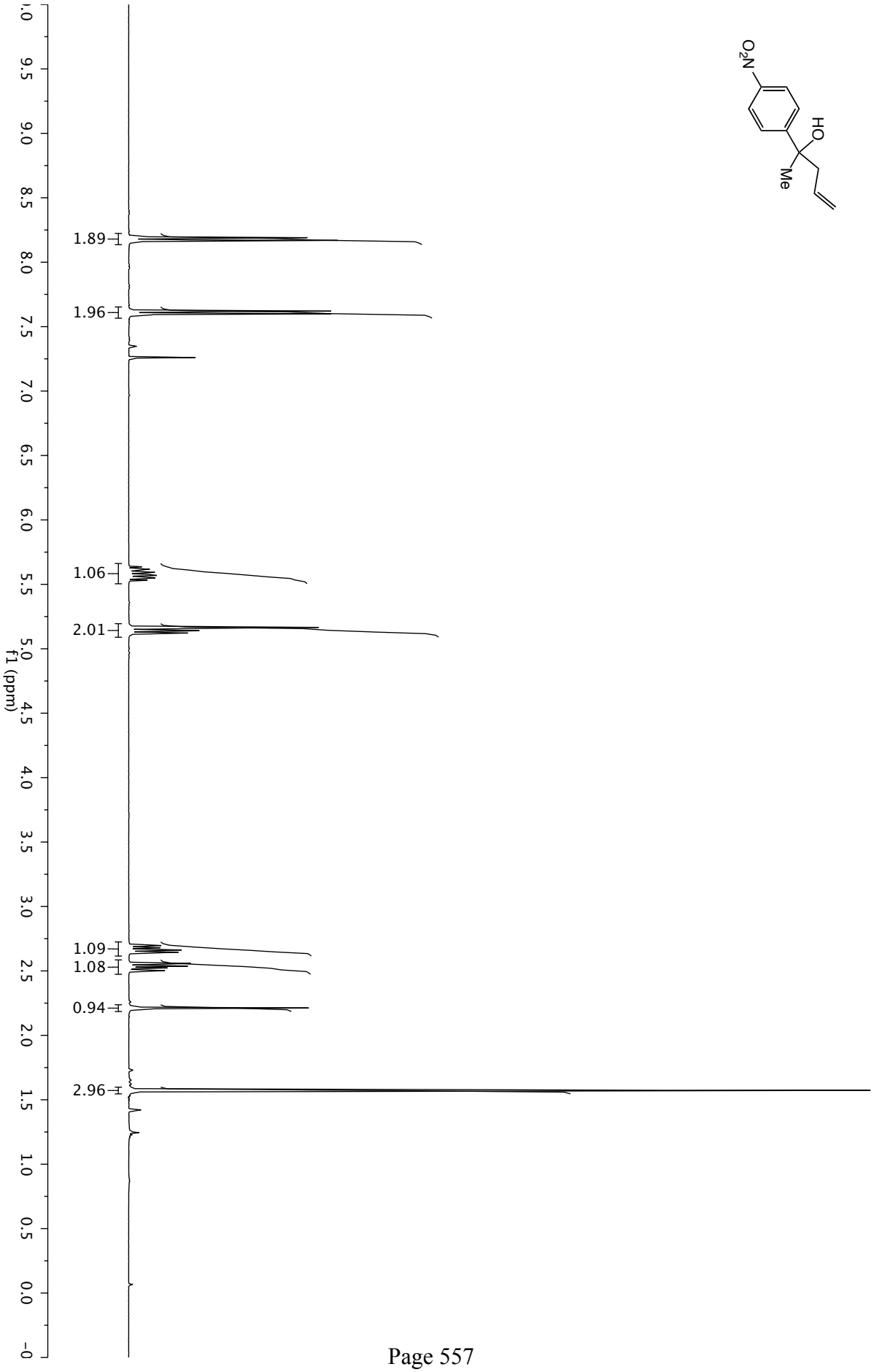
1.05
1.11
0.91
2.84
2.83
f1 (ppm)
i-Pr
OH
Ph


i-Bu
OH
Ph
4.02
0.99
1.09
2.00
1.06
1.07
0.94
1.07
1.09
1.18
2.86
2.83
f1 (ppm)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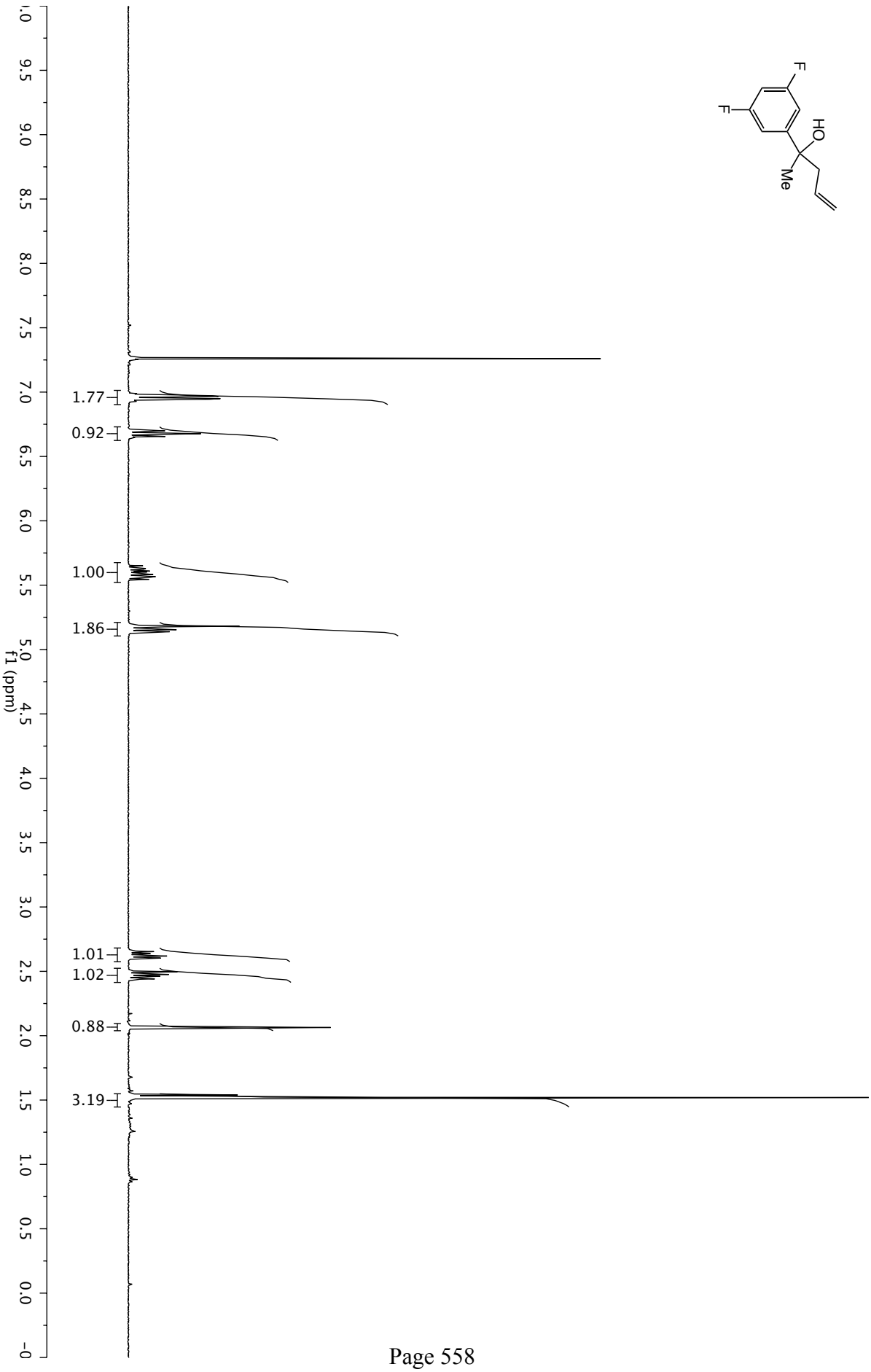
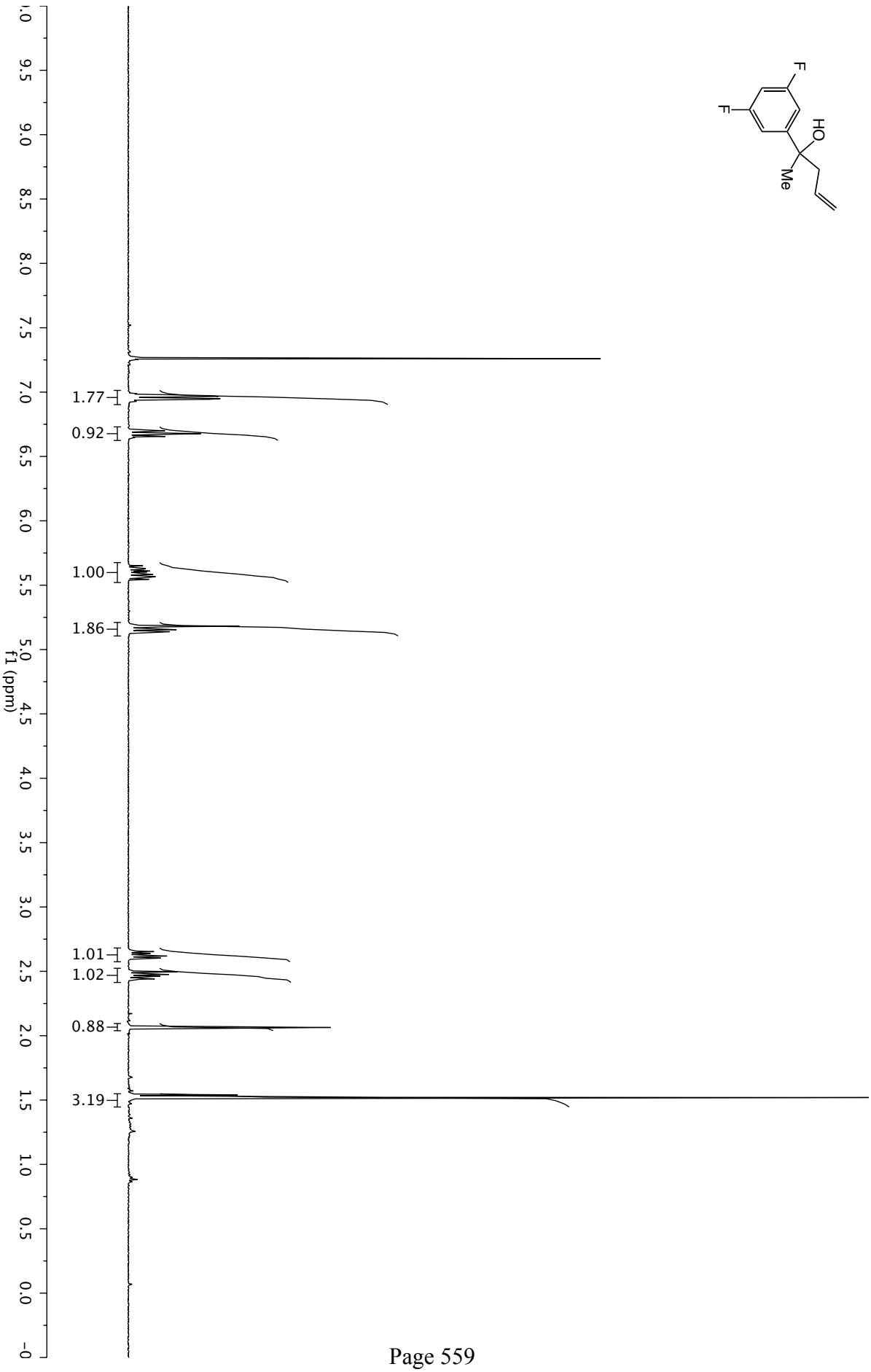
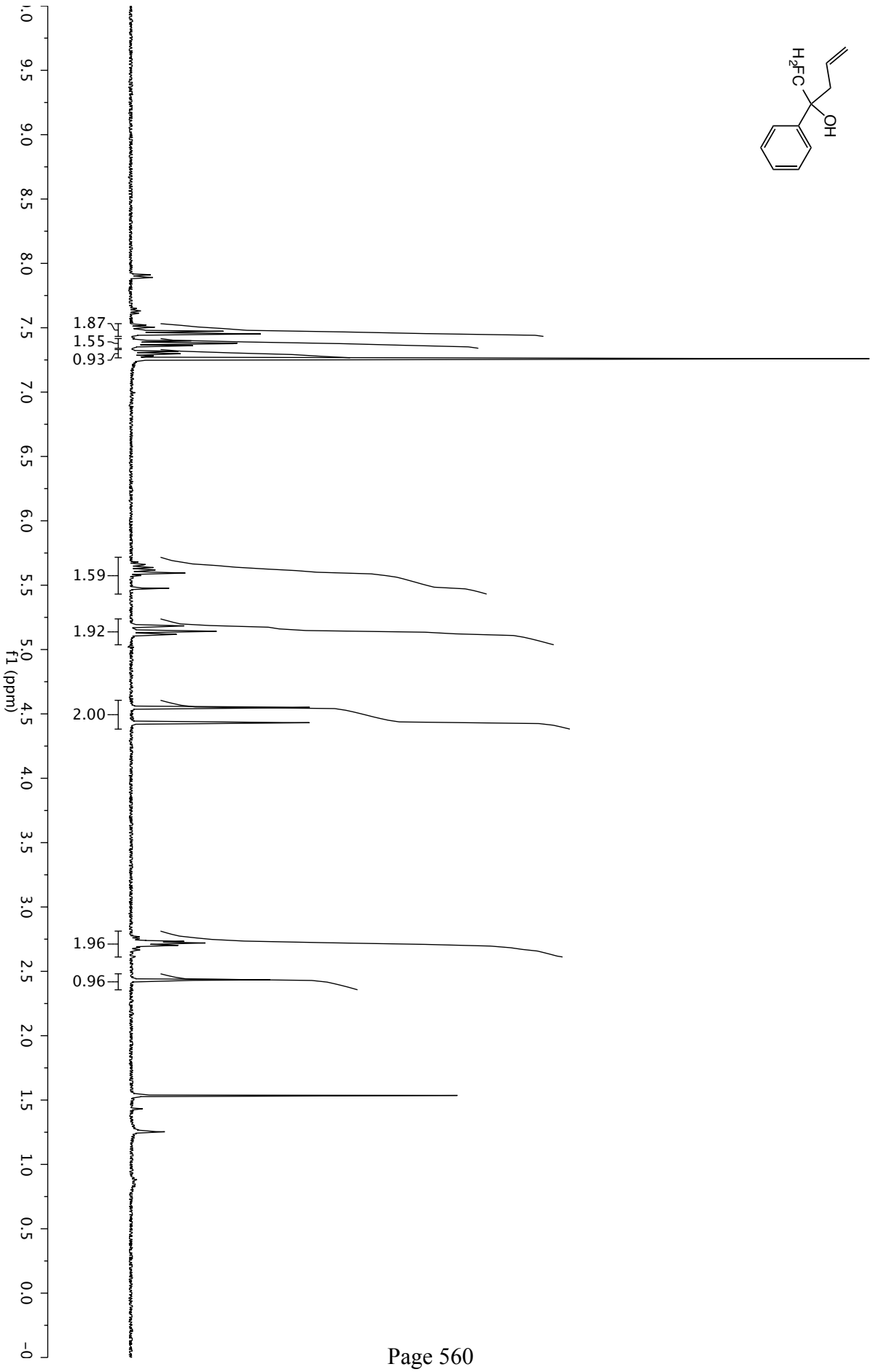
1.96
1.06
2.01
1.09
1.08
0.94
2.96
f1 (ppm)
O2N
HO
Me


F
F
HO
Me
1.77
0.92
1.00
1.86
1.01
1.02
0.88
3.19
f1 (ppm)


F
F
HO
Me
1.77
0.92
1.00
1.86
1.01
1.02
0.88
3.19
f1 (ppm)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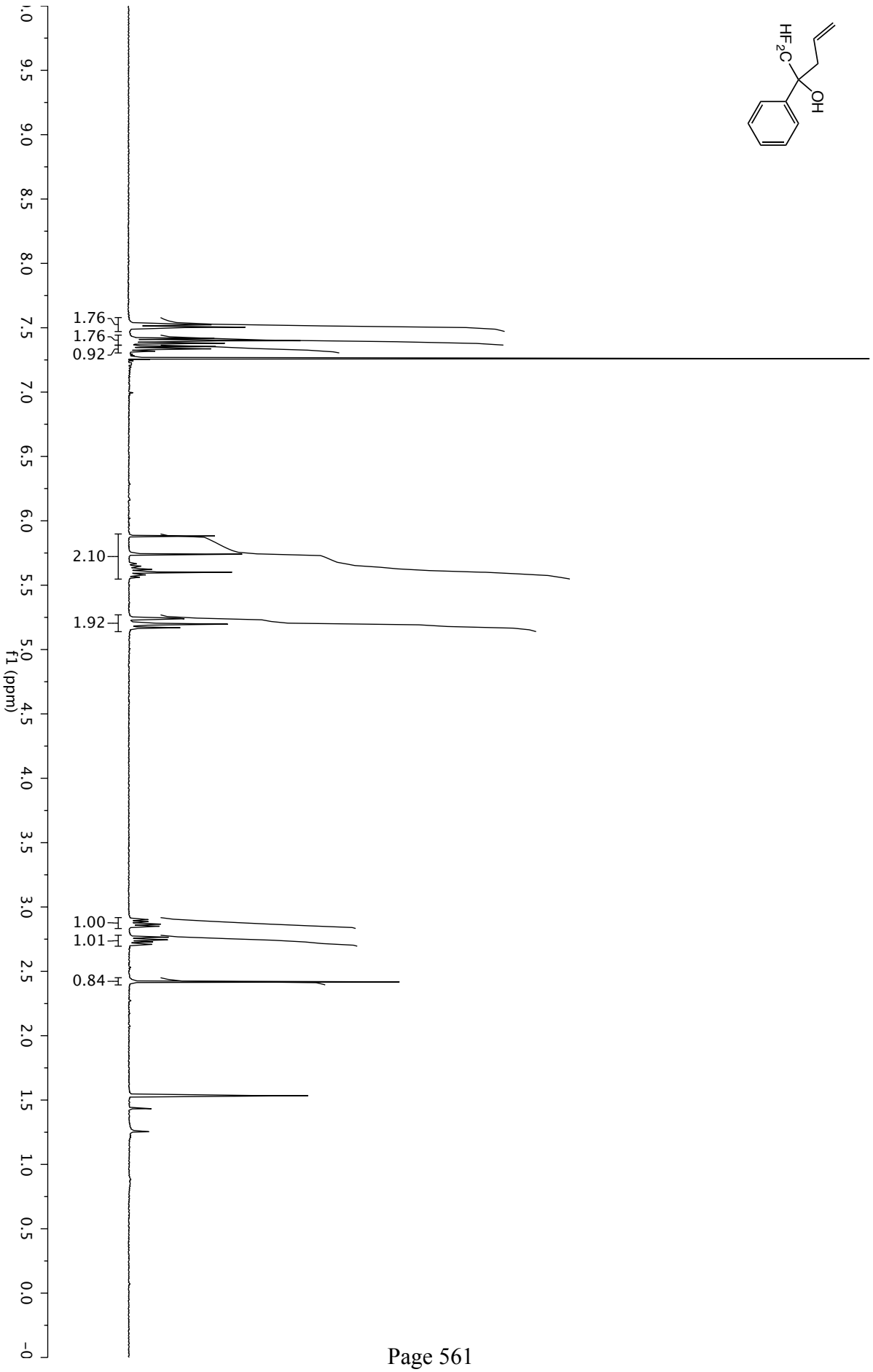
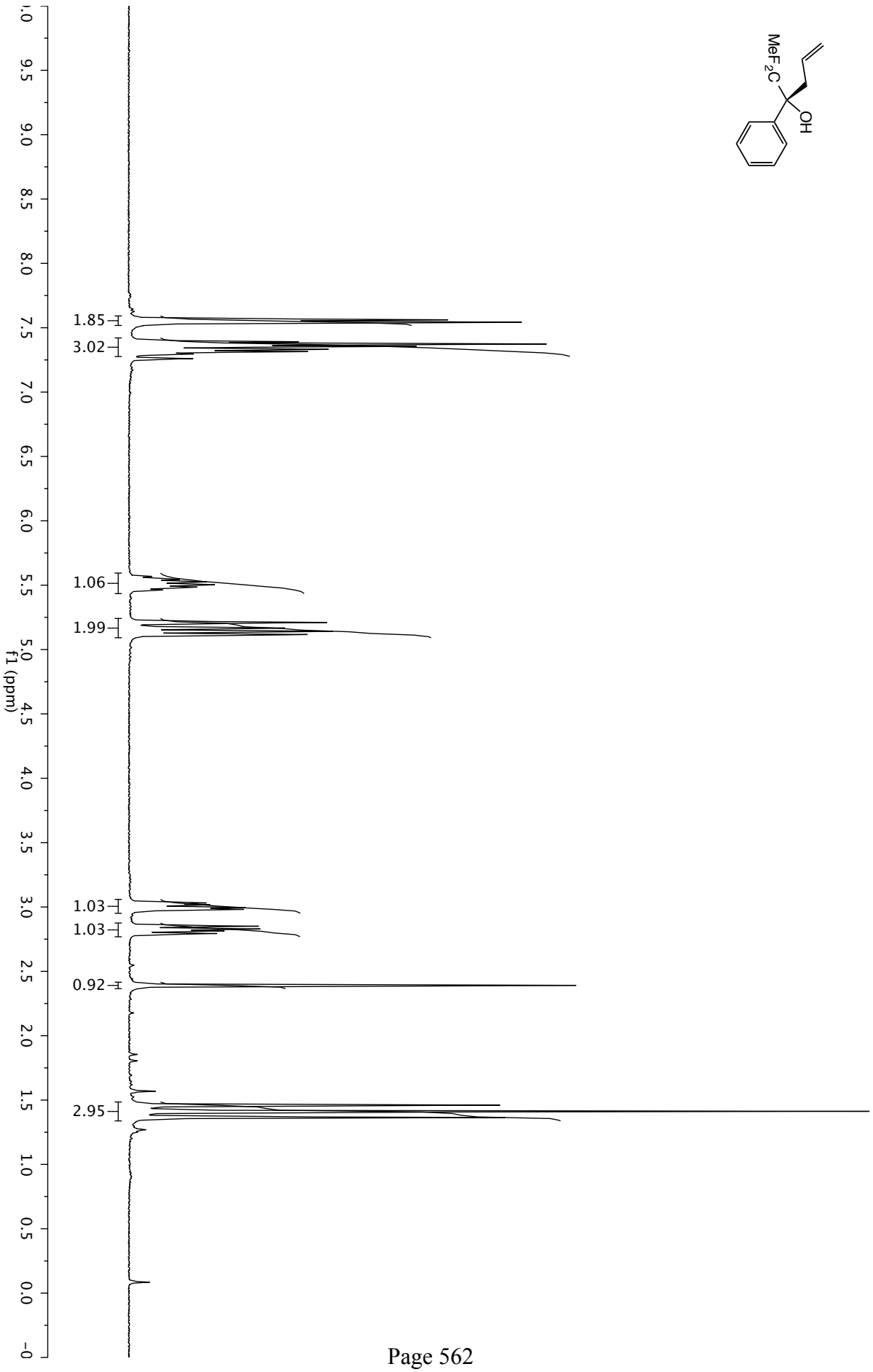
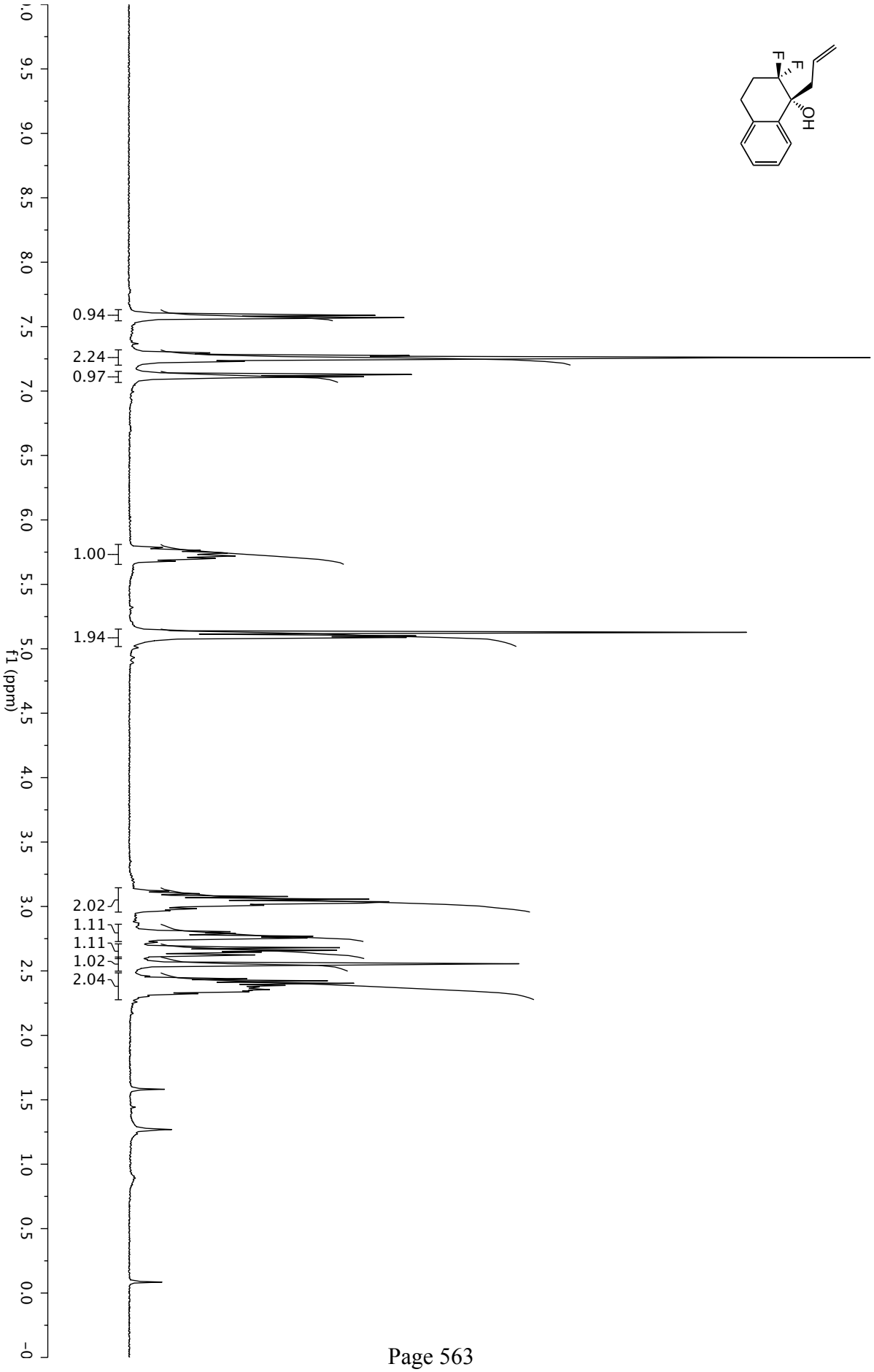
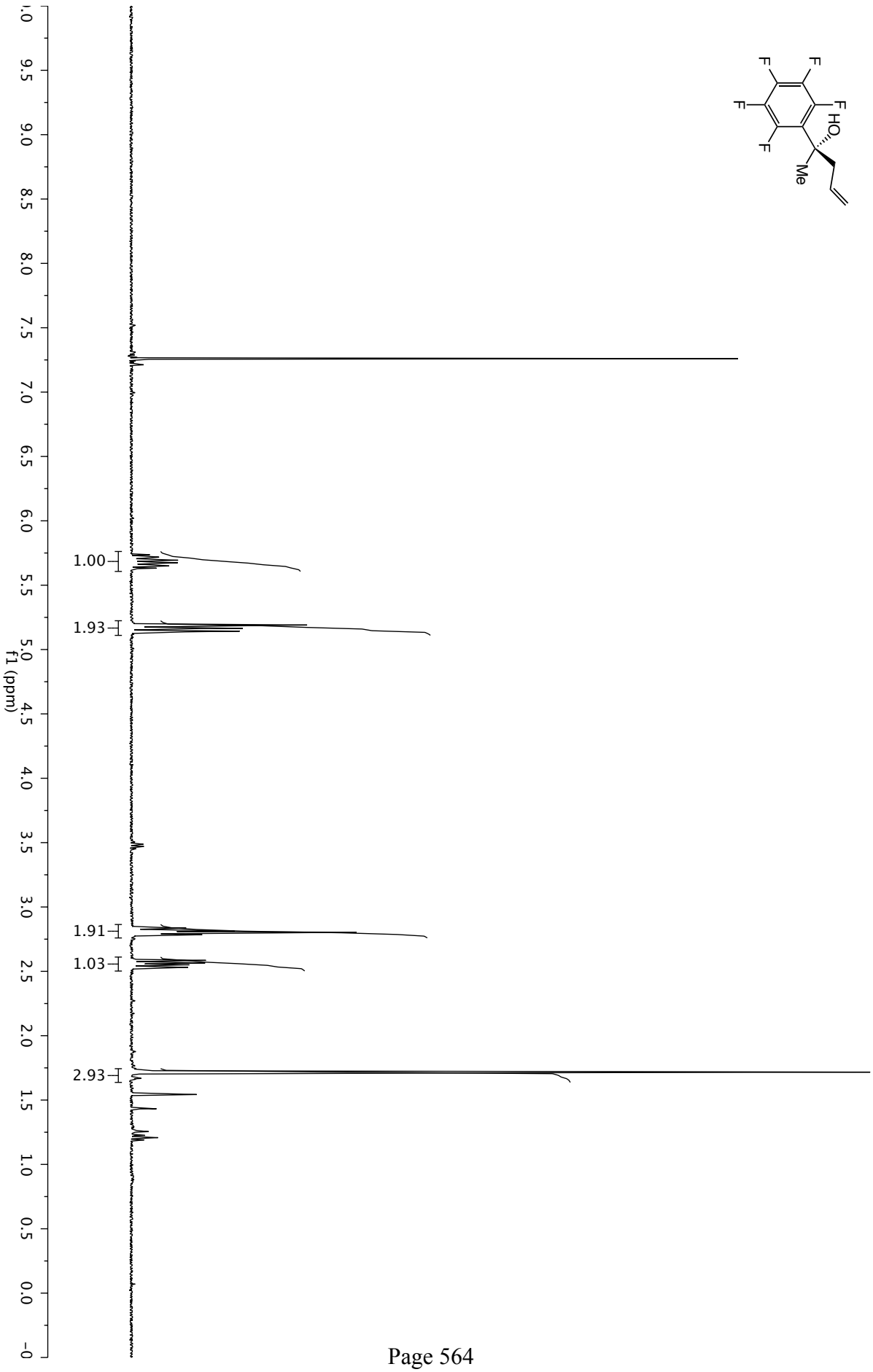
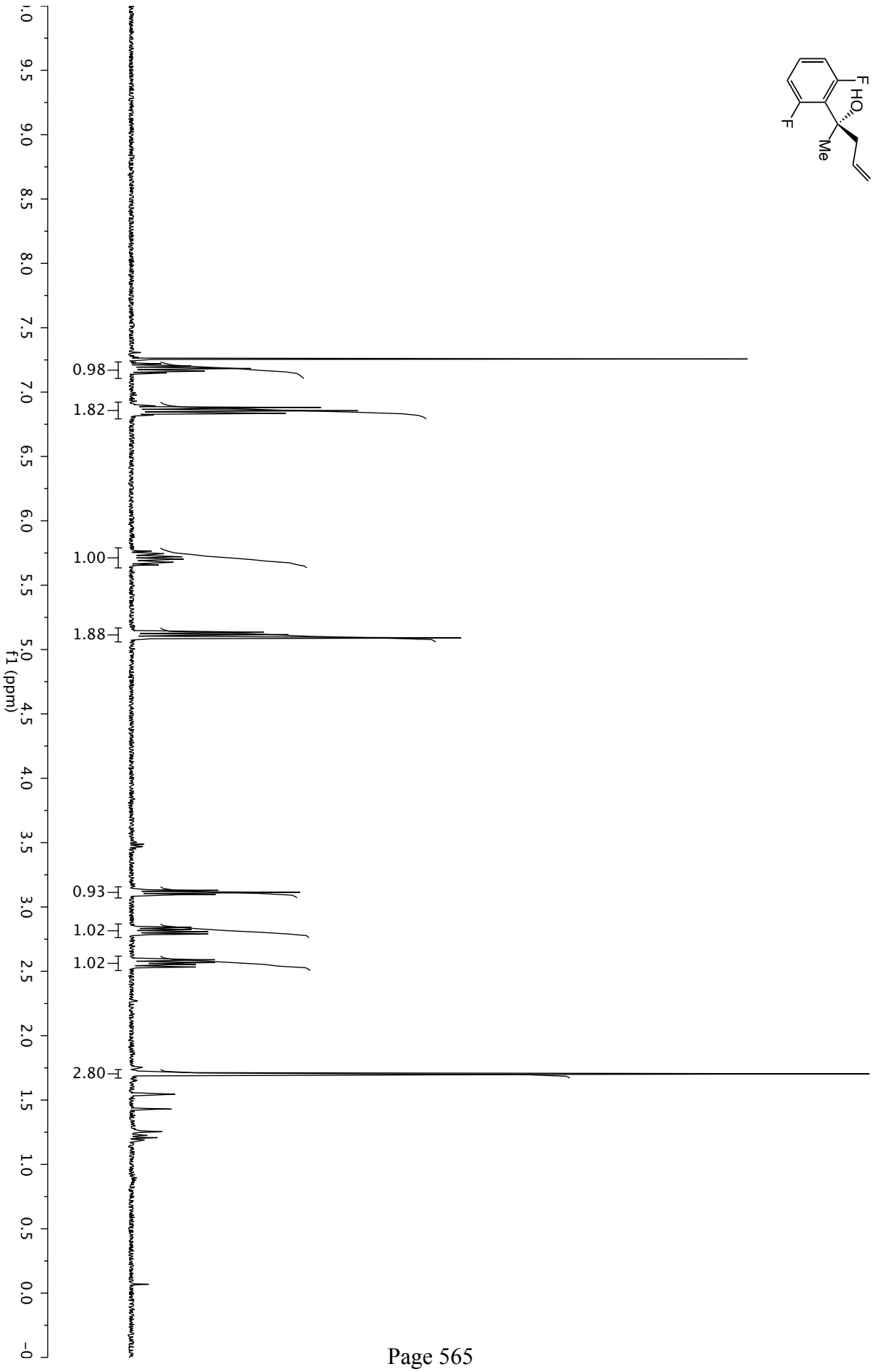
1.55
0.93
1.59
1.92
2.00
1.96
0.96
f1 (ppm)
H2FC
OH

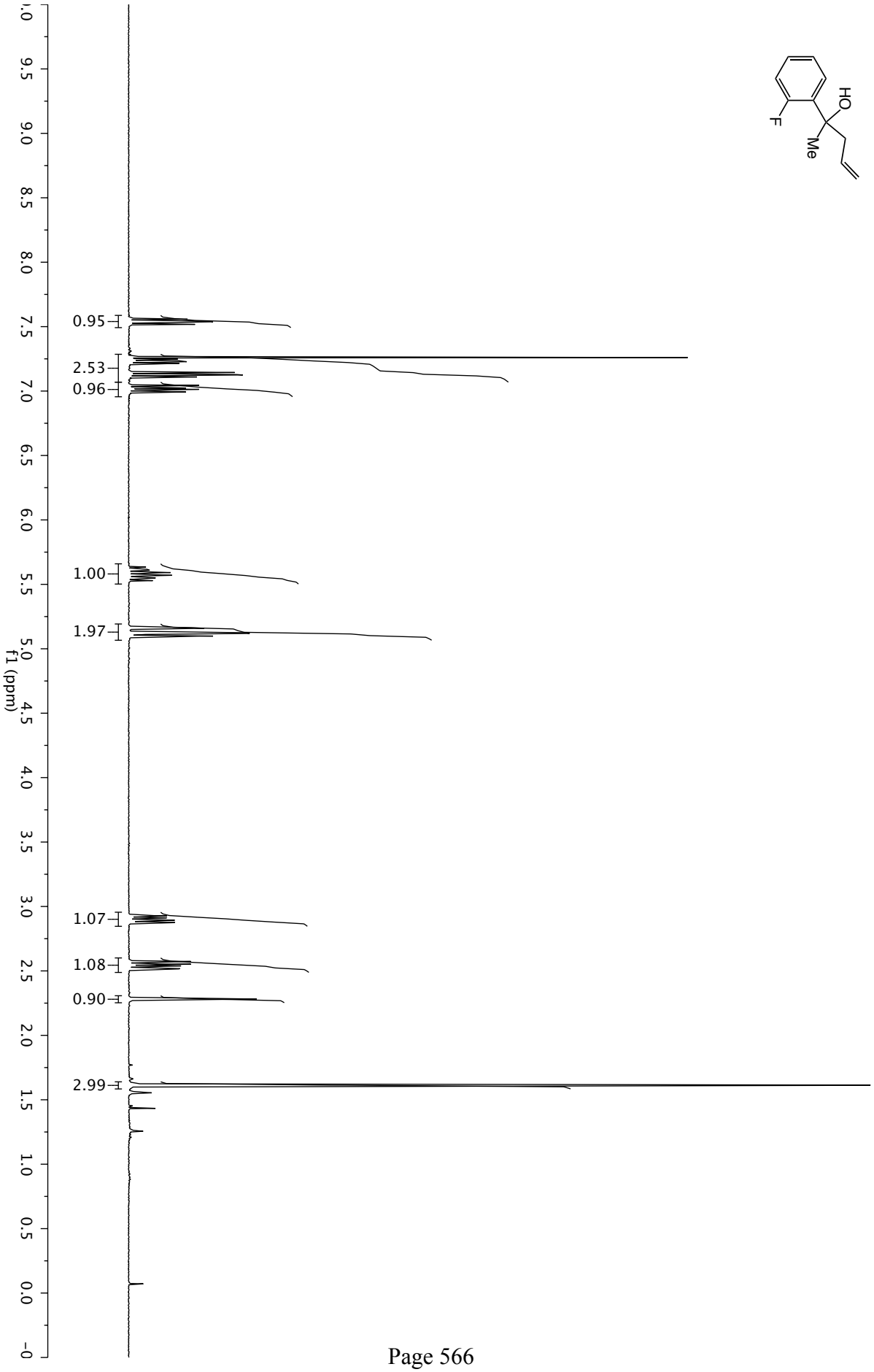

1.76
1.76
0.92
2.10
1.92
1.00
1.01
0.84
f1 (ppm)
HF2C
OH

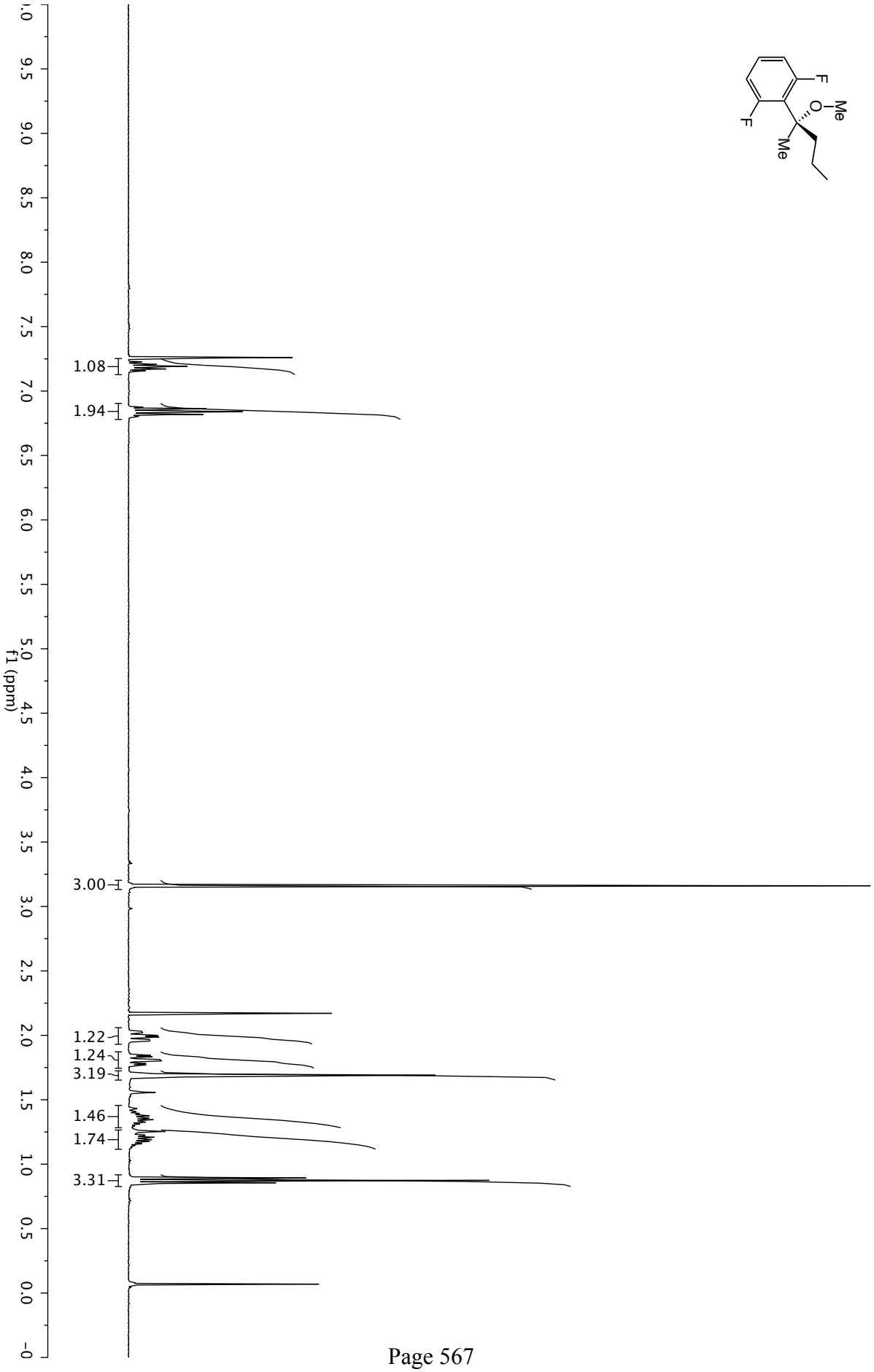

MeF2C
OH
1.85
3.02
1.06
1.99
1.03
1.03
0.92
2.95
f1 (ppm)

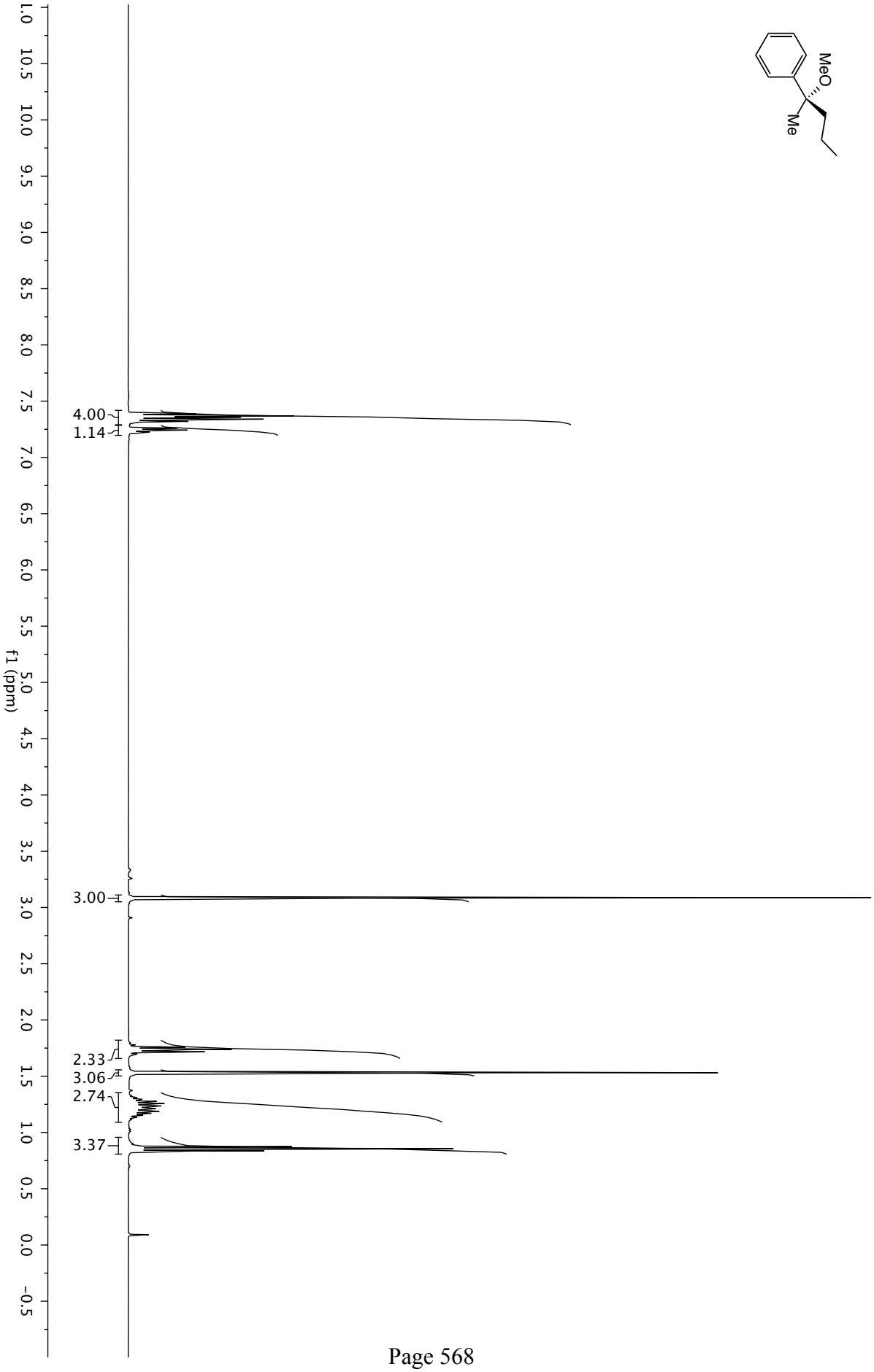

F
F
OH
0.94
2.24
0.97
1.00
1.94
2.02
1.11
1.11
1.02
2.04
f1 (ppm)

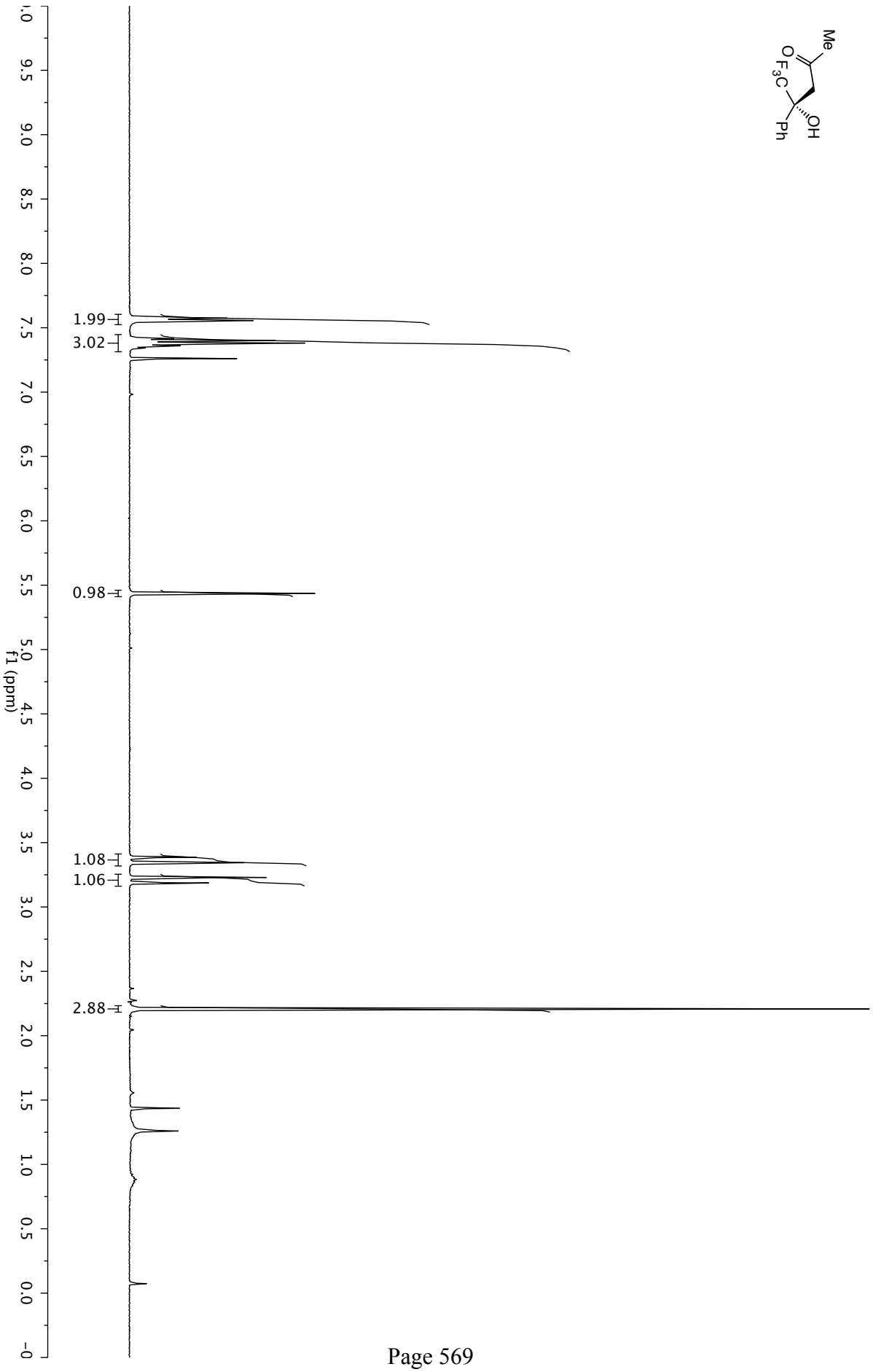

1.00
1.93
1.91
1.03
2.93
f1 (ppm)
F
F
F
F
F
HO
Me

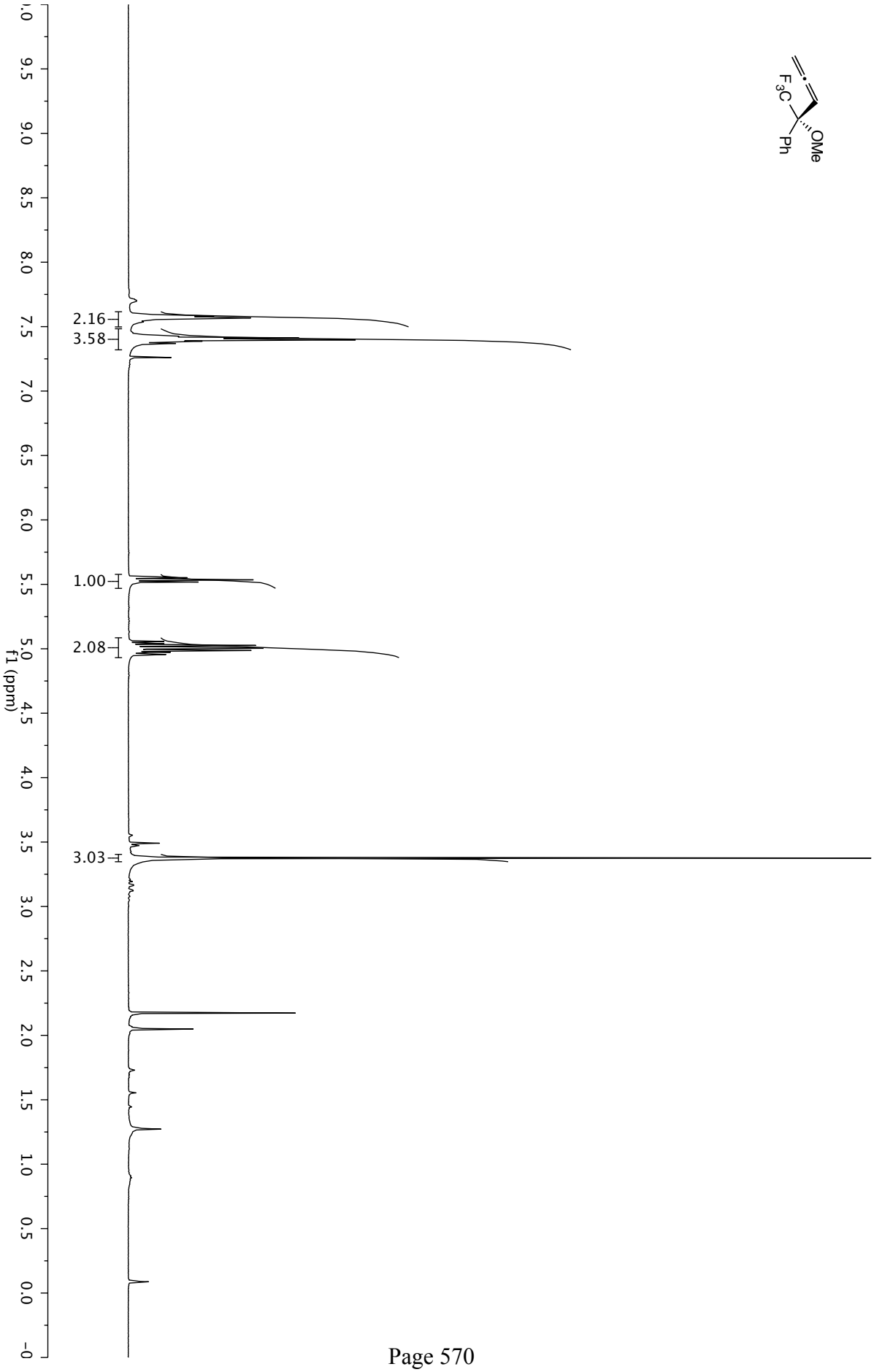

F
HO
F
Me
0.98
1.82
1.00
1.88
0.93
1.02
1.02
2.80
f1 (ppm)

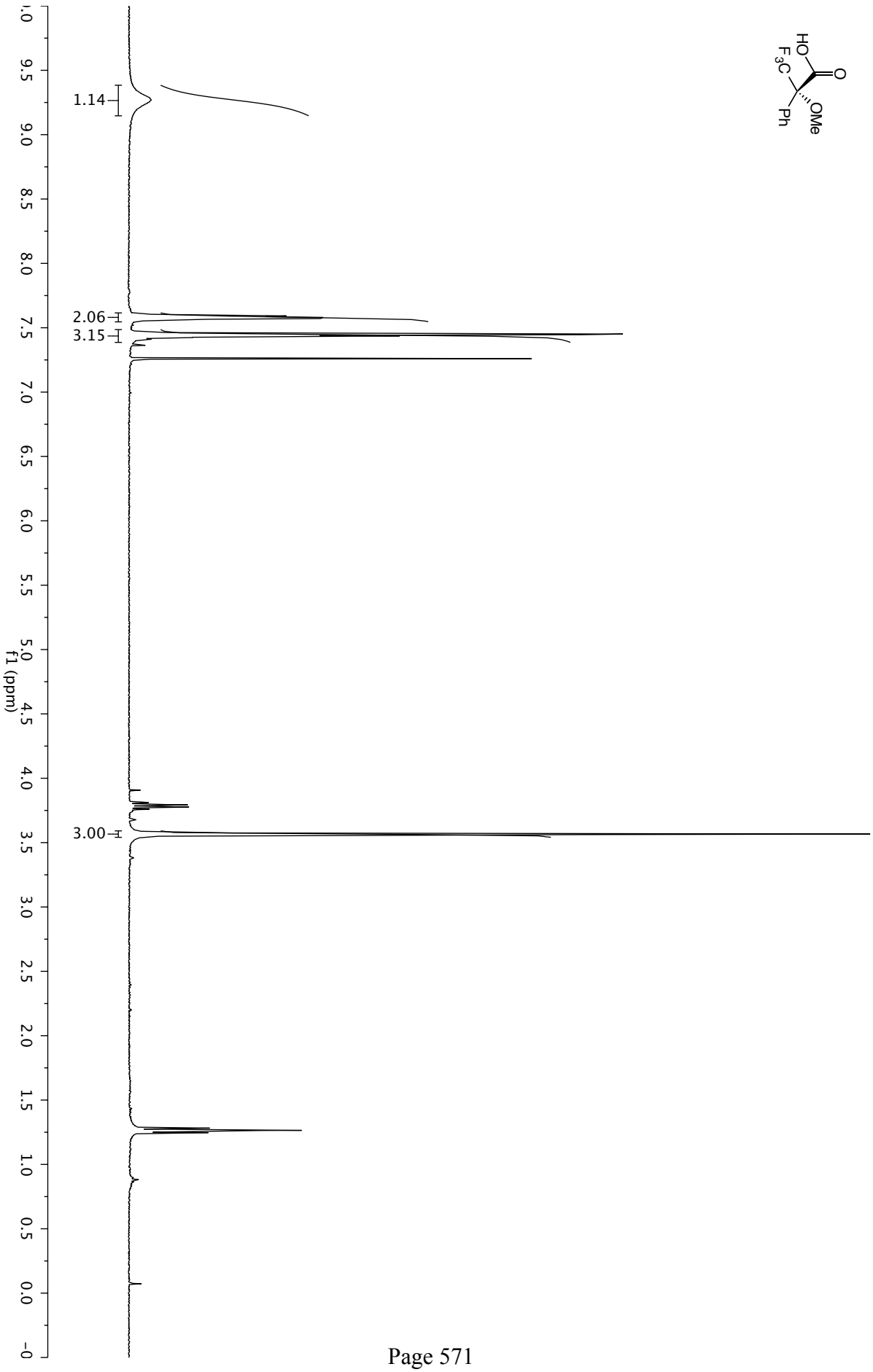

HO
F
Me
0.95
2.53
0.96
1.00
1.97
1.07
1.08
0.90
2.99
f1 (ppm)


F
Me
O
F
Me
1.08
1.94
3.00
1.22
1.24
3.19
1.46
1.74
3.31
f1 (ppm)


MeO
Me
4.00
1.14
3.00
2.33
3.06
2.74
3.37
f1 (ppm)


Me
O
F3C
OH
Ph
1.99
3.02
0.98
1.08
1.06
2.88
f1 (ppm)


2.16
3.58
1.00
2.08
3.03
f1 (ppm)
F3C
Ph
OMe


1.14
2.06
3.15
3.00
f1 (ppm)
HO
O
F3C
OMe
Ph

Chapter Three

Enantioselective Additions of Organoboronates to Ketones and Alphaketoesters Promoted by an Aminophenol Containing Catalyst

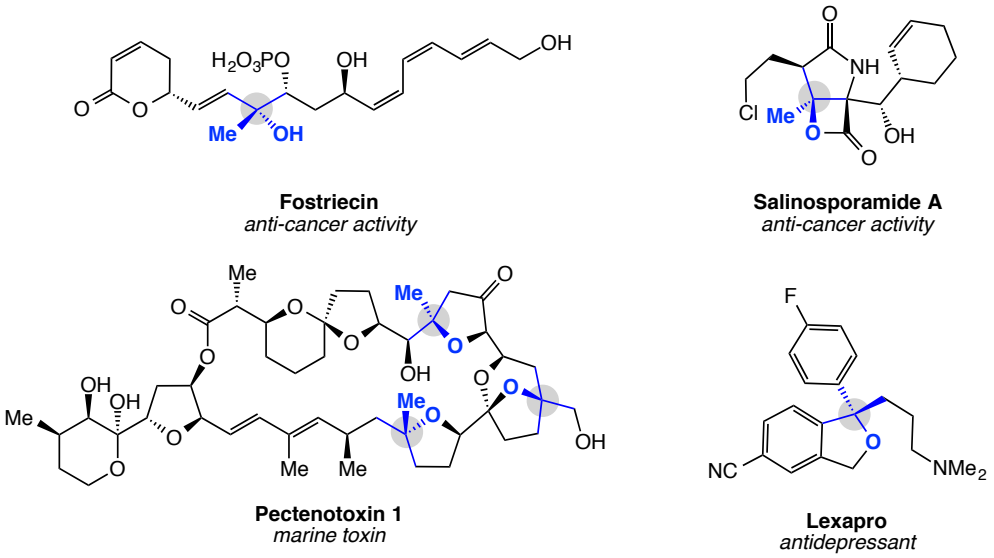
3.1 Introduction

As discussed in Section 1.1, the presence and absolute configuration of stereogenic centers have a substantial impact on the biological activity of organic molecules. Although not as copious as amines and amides, alcohols and/or ethers are found in a significant amount of compounds created by medicinal chemistry programs. Ethers are present in >35% and alcohols are present in ~10% of such molecules surveyed.[1] A subclass of such oxygen-containing functionality is tertiary alcohols and ethers that posses a stereogenic center at the central carbon directly bound to the oxygen. Such moieties are present in the natural products fostriecin[2] and salinosporamide A,[3] both of which exhibit significant ability to destroy myriad cancer cell lines, as well as marine toxin pectenotoxin 1,[4] which is part of a class of molecules implicated in shellfish

(1) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451–3479.
(2) Boger, D. L; Ichikawa, S.; Zhong, W. *J. Am. Chem. Soc.* **2001**, *123*, 4161–4167.
(3) Feling, R. H.; Buchanan, G. O.; Mincer, T. J.; Kauffman, C. A.; Jensen, P. R.; Fenical, W. *Angew. Chem. Int. Ed.* **2003**, *42*, 355–357.
(4) (a) Yasumoto, T.; Murata, M.; Oshima, Y.; Sano, M. *Tetrahedron* **1985**, *41*, 1019–1025. (b) Sasaki, K.; Wright, J. L. C.; Yasumoto, T. *J. Org. Chem.* **1998**, *63*, 2475–2480.

toxicity (Scheme 3.1). The blockbuster antidepressant Lexapro is another example of this functionality in a compound of medical significance. The (*S*) enantiomer of Lexapro,

Scheme 3.1 Biologically Active Molecules Containing an Tertiary Alcohol/Ether Stereogenic Center

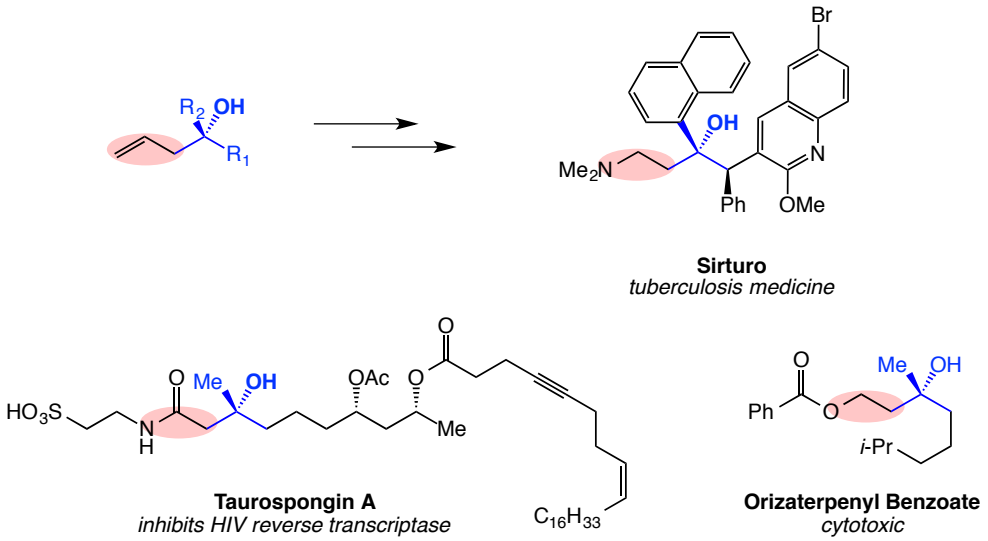


illustrated in Scheme 3.1, is immensely more potent than the (*R*) enantiomer.[5]

As mentioned in Chapters 1 and 2, the allyl group is a useful handle for the installation of diverse functional groups and thus one way to achieve the synthesis of chiral tertiary alcohols/ethers is through the intermediacy of chiral tertiary homoallylic alcohols.[6,7] Examples where such a strategy has been applied are the syntheses of acutumine,[8] an alkaloid with anti-amnesiac properties and selective T-cell toxicity; a fragment of the macrolide spongistatin, a strong antitumor agent;[9] Situro, the first new tuberculosis drug approved in almost 40 years;[10] taurospongin A, an inhibitor of both

(5) Hyttel, J.; Boegesoe, K. P.; Perregaard, J.; Sanchez, C. *J. Neural Transm.: Gen. Sect.* **1992**, *88*, 157–160
(6) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2013**, *113*, 5595–5698.
(7) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774–7854.
(8) For the isolation, see: (a) Tomita, M. *et al. Chem. Pharm. Bull.* **1971**, *19*, 770–791. For the synthesis, see: (b) Li, F.; Tartakoff, S. S.; Castle, S. L *J. Am. Chem. Soc.* **2009**, *131*, 6674–6675.
(9) Allais, F.; Cossy, J. *Org. Lett.* **2006**, *8*, 3655–3657.
(10) Saga, Y.; Motoki, R.; Makino, S.; Shimizu, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 7905–7907.

Scheme 3.2 Chiral Tertiary Alcohols in the Synthesis of Biologically Active Molecules



DNA polymerase and HIV reverse transcriptase,[11] and cytotoxic orizaterpenyl benzoate[12] (Scheme 3.2). A common way to access such molecules, which all syntheses described above utilize, is by a stereoselective allyl-addition to a ketone.

3.2 Background

Whereas there are a large array of methods for the stereoselective allyl-addition to aldehydes, methods applicable to ketones are far less prevalent.[6,7, 13] Like the stereoselective allyl-addition to imines discussed in Section 1.2 of Chapter 1, the methods for stereoselective allyl-addition to ketones can be classified as either stoichiometric[6] or catalytic.[7]

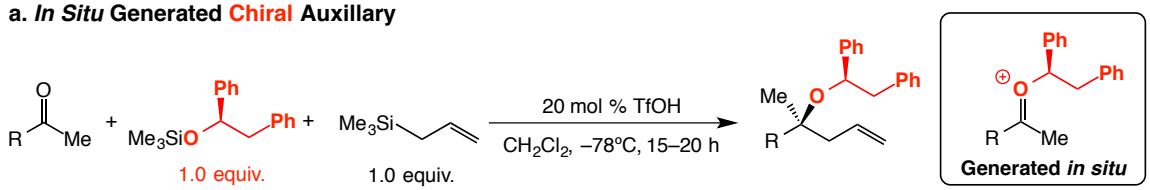
In stoichiometric methods for the stereoselective addition of an allyl-group to a ketone, the chiral compound that controls the stereochemical outcome of a transformation

(11) For the isolation, see: (a) Ishiyama, H.; Ishibashi, M.; Ogawa, A.; Yoshida, S.; Kobayashi, J. *J. Org. Chem.* **1997**, *62*, 3831–3836. For the synthesis, see: (b) Wu, B.; Mallinger, A.; Robertson, J. *Org. Lett.* **2010**, *12*, 2818–2821.
(12) For the isolation, see: Chung, I. M.; Ali, M.; Hahn, S. J.; Siddiqui, N. A.; Lim, Y. H.; Ahmad, A. *Chem. Nat. Comp.* **2005**, *41*, 182–189. For the synthesis, see: (b) Tietze, L. F.; Biller, S.; Wolfram, T. *Synlett*, **2010**, *14*, 2130–2132.
(13) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763–2793.

can have a few different forms. These forms include an *in situ* generated chiral auxillary (Scheme 3.3a)[14] and a chiral acid that activates the ketone.[15] However, the most common stoichiometric methods are those that use a chiral allyl-reagent as the nucleophile. These nucleophiles vary from allylsilane (which are only applicable to ketones containing a 2-hydroxyphenyl ring),[16] allylborons,[17] allylzinc,[18] and allylindiums (Scheme 3.3b).[19]

Scheme 3.3 Representative Stoichiometric Methods

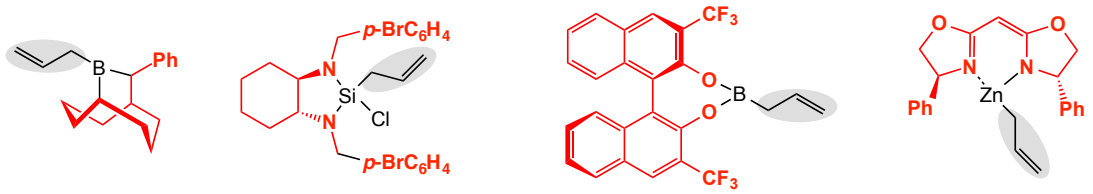
a. *In Situ* Generated Chiral Auxillary



R = Alkyl
R = Ph

79–93%, 86:14–96:4 d.r.
9%, 97:3 d.r.

b. Chiral Reagents



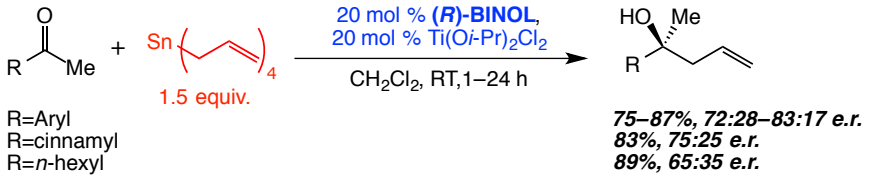
While a method from the Chong group involving a chiral allylboronate allows for the synthesis of a wide range of homoallylalcohols (both aryl- and alkyl-substituted) in high yields (≥80%) and selectivities (≥9:1 e.r),[17b] like all of the aforementioned methods,

(14) (a) Tietze, L. F. *et al*. *Chem. Eur. J.* **2001**, *7*, 1304–1712. (b) Tietze, L. F.; Hölsken, S.; Adrio, J.; Kinzel, T.; Wegner, C. *Synthesis* **2004**, *13*, 2236–2239. (c) Tietze, L. F.; Kinzel, T.; Schmatz, S. *Chem. Eur. J.* **2009**, *15*, 1706–1712. (d) Tietze, L. F.; Kinzel, T.; Wolfram, T. *Chem. Eur. J.* **2009**, *15*, 6199–6210.
(15) (a) Yasuda, M.; Kitahara, N.; Fujibayashi, T.; Baba, A. *Chem. Lett.* **1998**, *27*, 743–744. (b) Yanagisawa, A.; Nakamura, Y.; Arai, N. *Tetrahedron: Asymmetry* **2004**, *15*, 1909–1913.
(16) Burns, N. Z.; Hackman, B. M.; Ng, P. Y.; Powelson, I. A.; Leighton, J. L. *Angew. Chem. Int. Ed.* **2006**, *45*, 3811–3813.
(17) For methods where the chiral allylboron is synthesized prior to the reaction, see: (a) Jadhav, P. K.; Bhat, K. S.; Perumal, T.; Brown, H. C. *J. Org. Chem.* **1986**, *51*, 432–439. (b) Wu, T. R.; Shen, L.; Chong, J. M. *Org. Lett.* **2004**, *6*, 2701–2704. (c) Canales, E.; Prasad, K. G.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 11572–11573. (d) Boshra, R.; Doshi, A.; Jäkle, F. *Angew. Chem. Int. Ed.* **2008**, *47*, 1134–1137. For a method where the allylboron is generated *in situ*, see: (e) Hirayama, L. C.; Haddad, T. D.; Oliver, A. G.; Singaram, B. *J. Org. Chem.* **2012**, *77*, 4342–4353.
(18) Nakamura, M.; Hirai, A.; Sogi, M.; Nakamura, E. *J. Am. Chem. Soc.* **1998**, *120*, 5846–5847.
(19) (a) Loh, T.-P. Zhou, J.-R.; Li, X.-R. *Tetrahedron Lett.* **1999**, *40*, 9333–9336. (b) Thornqvist, V.; Manner, S.; Frejd, T. *Tetrahedron: Asymmetry* **2006**, *17*, 410–415. (c) Haddad, T. D.; Hirayama, L. C.; Taynton, P.; Singaram, B. *Tetrahedron Lett.* **2008**, *49*, 508–511. (d) Haddad, T. D.; Hirayama, L. C.; Singaram, B. *J. Org. Chem.* **2010**, *75*, 642–649.

it requires a stoichiometric amount of the stereocontrolling element, as aspect that is unfavorable when compared to catalytic methods.[20]

In 1999, the Tagliavini group reported the first catalytic enantioselective allylation of ketones (Scheme 3.4).[21a] They used a titanium-based Lewis acidic complex

Scheme 3.4 The First Catalytic, Enantioselective Allyl-Addition to Ketones

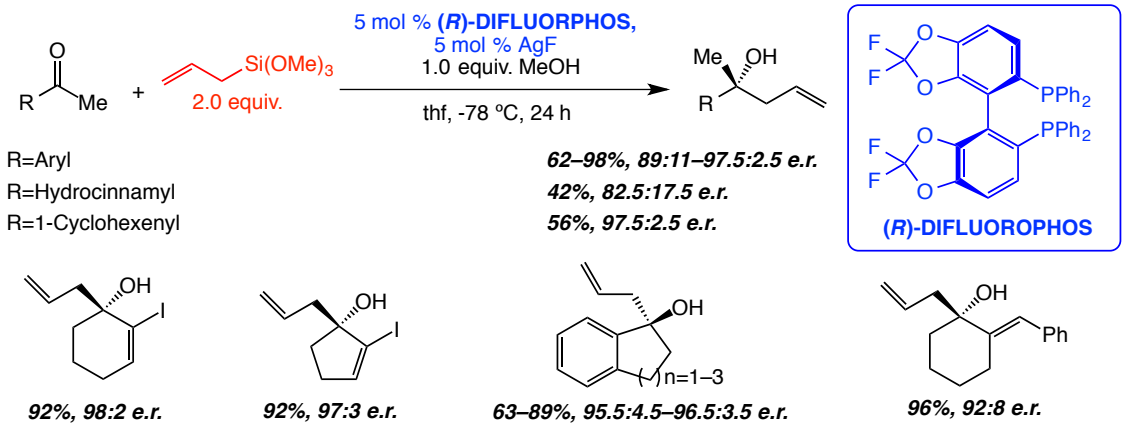


bearing a bidentate BINOL ligand to catalyze the addition of tetraallyltin to selection of ketones, albeit in a maximum of 83:17 e.r. The enantioselectivity of this transformation was subsequently improved by modifications of the ligand[21b-d] and reaction conditions,[21e,f] but these methods all still have the fundamental drawback of involving stoichiometric amounts of highly toxic organotin compounds.[21]

Allylsilanes are attractive to use as the source of the allyl group due to their low cost and low toxicity. The laboratory of H. Yamamoto has developed the only such method utilizing these nucleophiles in a catalytic enantioselective allylation of ketones (Scheme 3.5).[22] Unlike the mostly sluggish methods for imine allylation that employ this

(20) The fundamental advantages and disadvantages of catalytic methods and stoichiometric methods are discussed in greater detail in Section 1.2 of Chapter 2.
(21) (a) Casolari, S.; D'Addario, D.; Tagliavini, E. *Org. Lett.* **1999**, *1*, 1061–1063 (b) Hanawa, H.; Kii, S.; Maruoka, K. *Adv. Synth. Catal.* **2001**, *343*, 57–60. (c) Kii, S.; Maruoka, K. *Chirality*, **2003**, *15*, 68–70. (d) Cunningham, A.; Woodward, S. *Synlett*, **2002**, 43–44. (e) Waltz, K. M.; Gavenonis, J.; Walsh, P. J. *Angew. Chem. Int. Ed.* **2002**, *41*, 3697–3699. (f) Kim, J. G.; Waltz, K. M.; Garcia, I. F.; Kwiatkowski, D.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 12580–12585. For a method that employs allylstannanes, but does not use a Ti-base catalyst, see: (g) Zhang, X.; Chen, D.; Liu, X.; Feng, X. *J. Org. Chem.* **2004**, *72*, 5227–5233.
(22) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 14556–14557.

Scheme 3.5 Silver-Catalyzed Enantioselective Addition of Trimethoxyallylsilane to Ketones



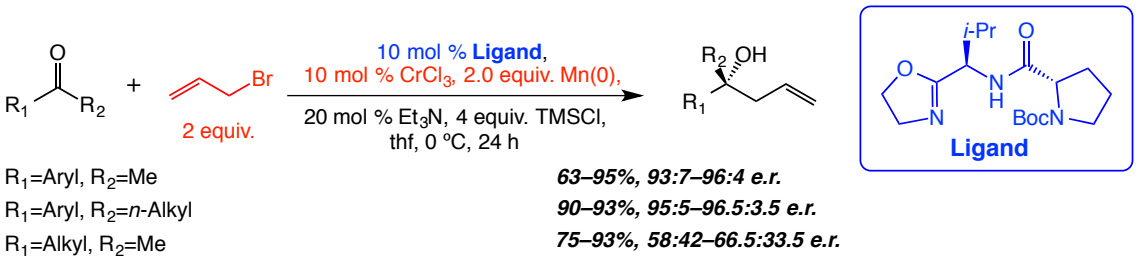
class of nucleophile,[23] the transformation reported by Yamamoto is complete in 24 h at -78 ºC. Promoted by 5 mol % of AgF and the ligand DIFLUOROPHOS, this reaction affords aryl-substituted methyl homoallylalcohols, 1-cyclohexenyl-substituted methyl homoallylalcohols, and cyclic homoallylalcohols in 62 to 98% yields and 89:11 to 97.5:2.5 enantiomeric ratios. A limitation in the scope is acyclic ketones bearing two alkyl substituents, the sole example of which is afforded in only 42% yield and an enantiomeric ratio of 82.5:17.5 (Scheme 3.5). Additionally, there are no examples of substrates bearing functionality that could disrupt the catalyst, such as heterocycles, amines, or thiols. Other flaws of the method include the requirement of very low temperatures to achieve selective transformations as well as the use of the ligand DIFLUOROPHOS which, while commercially available, is quite expensive ($464/mmol from Strem Chemicals).

A different strategy employed in the enantioselective allyl-addition to ketones is to use allylchromiums as the nucleophile. These allylmetals are generated *in situ* from a catalytic amount of chromium and a stoichiometric amount of an allylhalide using

(23) See Section 1.2 of Chapter 1 for a discussion.

Fürstner's modification of the original Nozaki-Hiyama conditions.[24] It is advantageous to utilize allylhalides as the origin of the allyl functionality, since most other common allylic nucleophiles (e.g. allylstannanes, allylsilanes, allylboronates) are synthesized from allylhalides. However, the chromium salts used are toxic, both acutely in humans and chronically in the environment, which keeps this class of protocols from having a wide application.[24] M. S. Sigman reported the best of such methods in 2007 (Scheme 3.6).[25] In that report, 10 mol % of an easily accessible amino acid-derived ligand controls the

Scheme 3.6 Chromium-Catalyzed Enantioselective Addition of Allyl Bromide to Ketones



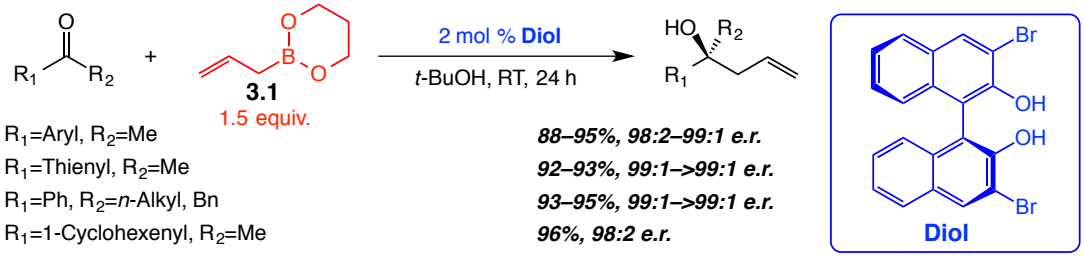
enantioselectivity of the transformation, which occurs in 24 hours at a mild 0 ºC. Four equivalents of TMSCl and 20 mol % of Et_3N are needed to facilitate release of the chromium-ligand complex from the product. The substrate scope of this method is very similar to the one by H. Yamamoto discussed earlier,[22] but it is notable that Sigman's method tolerates aryl-substituted ketones bearing *n*-alkyl groups larger than methyl, affording these products in 90–93% yield and 95:5 to 96.5:3.5 e.r. (Scheme 3.6).

Allylboronates, as mentioned in Section 1.2 of Chapter 1, are useful allyl nucleophiles. Although they react readily with aldehydes, the uncatalyzed addition of allylboronates to ketones is slow. Unique among catalytic, enantioselective allyl-

(24) Fürstner, A. *Chem. Rev.* **1999**, *99*, 991–1045.
(25) (a) Miller, J. J.; Sigman, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 2752–2753. For another method employing allylchromium, see: (b) Huang, X.-R.; Chen, C.; Lee, G.-H.; Peng, S.-M. *Adv. Synth. Catal.* **2009**, *351*, 3089–3095.

additions to ketones since it does not require the use of a metal, the chiral diol catalyst developed in the laboratory of S. E. Schaus is one of the most effective methods for the enantioselective synthesis of tertiary homoallylic alcohols (Scheme 3.7).[26] An improved

Scheme 3.7 Enantioselective Addition of Allylboronates to Ketones Catalyzed by a Chiral Diol



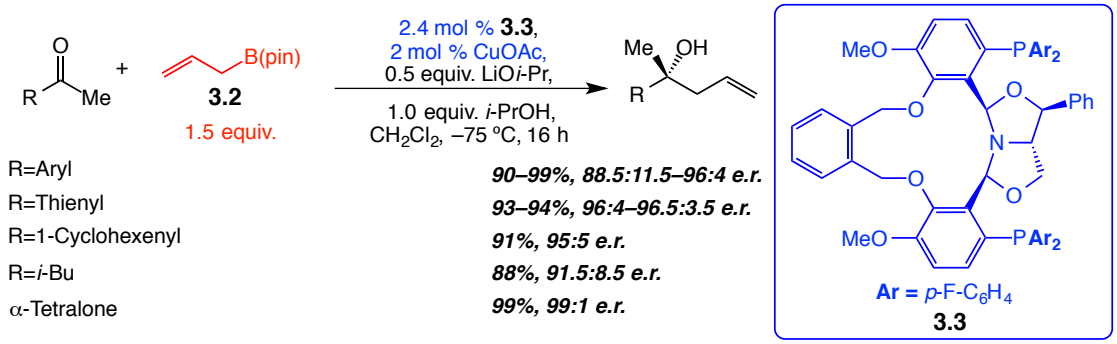
version of an earlier report,[26b] this method uses only 2 mol % of an easily accessed chiral diol to catalyze the addition of allylboronate **3.1** (Scheme 3.7) to ketones in a manner that is exceptionally enantioselective (≥98:2 e.r. in all cases) and high yielding (≥88% yield in all cases). Based on mechanistic studies,[26a] the authors propose the *t*-BuOH solvent (1.0 equiv; the reaction is essentially neat) expedites the regeneration of the active catalyt. Such a role is critical for the significantly higher levels of activity of the catalyst in this method versus the original (15 mol % for 36 hours in the original report).[26b] Notably, this method is applicable to 2- and 3-acetyl thiophene, but no other ketones containing basic functionality (e.g. pyridine) (or acidic functionality , e.g. phenol) were examined. Also, there are no examples of ketones that do not have at least one sp^2-hybridized substituent. Such ketones tend to be difficult substrates in terms of both reactivity and selectivity (See Scheme 3.4 through 3.6). Other than the somewhat limited substrate scope, a drawback of this method is that it requires the commercially unavailable allylboronate **3.1** (Scheme

(26) (a) Barnett, D. S.; Moquist, P. N.; Schaus, S. E. *Angew. Chem. Int. Ed.* **2009**, *48*, 8679–8682. For the original report, see: (b) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 12660–12661. For a related method, see: (c) Zhang, Y. *et al. Org. Lett.* **2013**, *15*, 1710–1713.

3.7). It is true that this reagent is more stable than the allyldiisopropoxyborane used in the initial report, but it is still less stable than allylboronic acid pinacol ester.[27]

Another landmark enantioselective allyl-addition to ketones, this time utilizing commercially available allylB(pin) **3.2**,[28] was achieved by the Shibasaki group by way of the catalytic generation of an allylcopper[29] complex (Scheme 3.8).[30] The modular

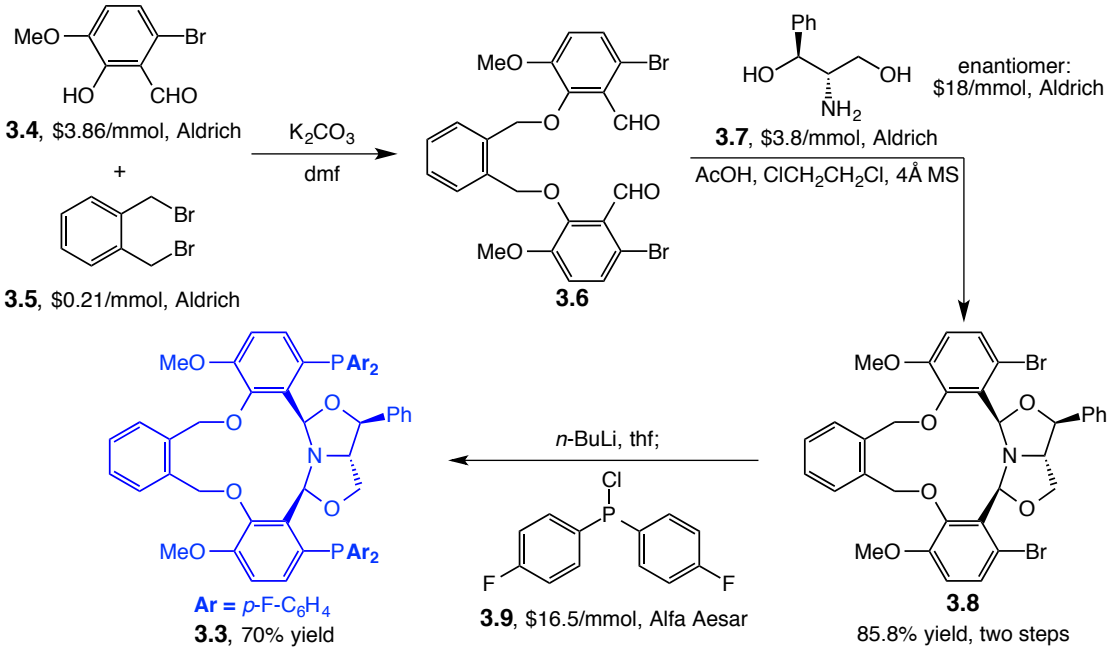
Scheme 3.8 Copper-Catalyzed Addition of Allylboronates to Ketones



enantiopure bisphosphine ligand is accessed in ~60% yield over three easy steps (Scheme 3.9). The substrate scope of this method is very similar to the previously discussed method by Schaus, with the noteworthy exception of the allyl-addition to methyl *iso*-butyl ketone proceeding in 88% yield and 91.5:8.5 e.r. While inferior to the results

(27) (a) *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials, 2nd Edition*; Hall, D. G. Ed.; Wiley-VCH: Weinheim, Germany, **2011**. (b) Roy, C. D.; Brown, H. C. *Monatshefte für Chemie*, **2007**, *138*, 879–887.
(28) A catalytic enantioselective allyl-addition to ketones using this allyl nucleophile and an indium-based catalyst has been reported. The only example in the paper occurs to afford the product in 76:24 e.r. See: Schneider, U.; Ueno, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2008**, *130*, 13824–13825.
(29) Enantioselective methods involving more functionalized allylcopper species, generated catalytically from allenes and allylic nitriles, have been reported. For methods starting with an allene, see: a) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2013**, *52*, 5046–5051. (b) Kawai, J.; Chikkade, P. K.; Shimizu, Y.; Kanai, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 7177–7180. For methods starting with an allylic nitrile, see: (c) Yazaki, R.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 3195–3197. d) Yazaki, R.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 5522–5531.
(30) (a) Yazaki, R.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 5522–5523. For related previous methods, see: (b) Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910–8911. (c) Kanai, M.; Wada, R.; Shibuguchi, T.; Shibasaki, M. *Pure Appl. Chem.* **2008**, *80*, 1055–1062.

Scheme 3.9 Synthesis of Ligand **3.3**

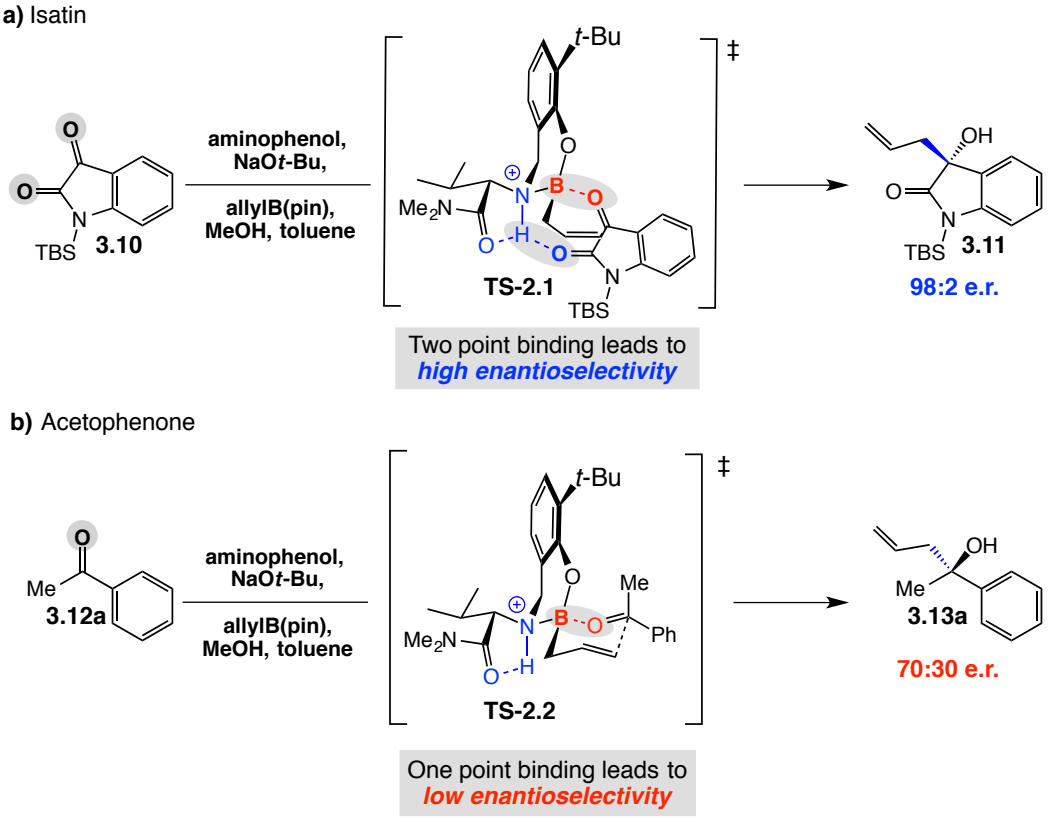


obtained with other substrates, it is one of the best results in the literature for a ketone bearing two alkyl-substituents. As with all methods, there are some deficiencies. In addition to the somewhat limited substrate scope, the reaction requires –75 ºC to achieve high levels of enantioselectivity and an oxygen sensitive Cu(I) salt. Moreover, the synthesis of **3.3**, while efficient, does require some expensive components, such as the two equivalents of phosphinous chloride **3.9** ($16.5/mmol) as well as a source of chirality where one of the enantiomers is far more expensive than the other ($18.0/mmol versus $3.8/mmol). Concerns over the practicality of **3.3** are partially eased by the low catalyst loadings reported.

3.3 Enantioselective Additions to Ketones Achieved through Modifications to the Structure of the Aminophenol Catalyst

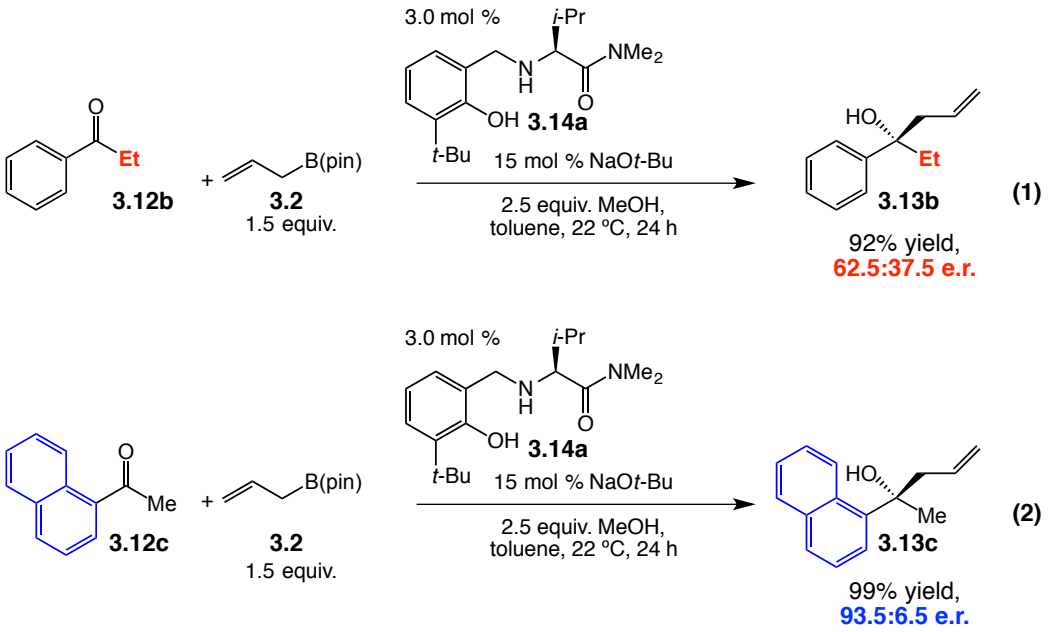
As previously discussed in Chapters 1 and 2, we have proposed two-point binding of the substrate to the catalyst, such as with isatin **3.10** to be important in obtaining products in high levels of enantiomeric enrichment (Scheme 3.10a). Substrates that only

Scheme 3.10 Enantioselectivity Models for Allyl-Additions to Ketones



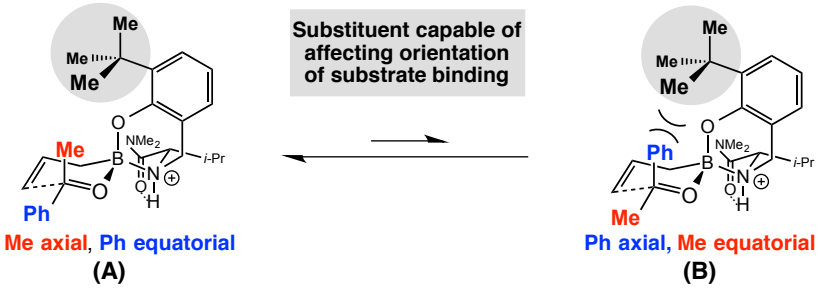
possess one point of binding, such as acetophenone **3.12a**, undergo allyl-addition in lower levels of enantioselectivity (Scheme 3.10b). The value of tertiary homoallylic alcohols led us to consider ways in which the catalyst could be modified to afford products, such as **3.13a**, in higher enantiomeric ratios. We hypothesized that a major source of the minor enantiomer of **3.13a** came from acetophenone binding to the catalyst in such a way that the phenyl group is axial in the transitions state, rather than equatorial (**TS-2.2**, Scheme 3.10). Supporting this hypothesis, the steric difference between the substituents on the ketone plays a major role in enantioselectivity, with substrates bearing

similarly sized groups undergoing less enantioselective additions (Equation 1) and substrates bearing more disparately sized groups undergoing more enantioselective additions (Equation 2).



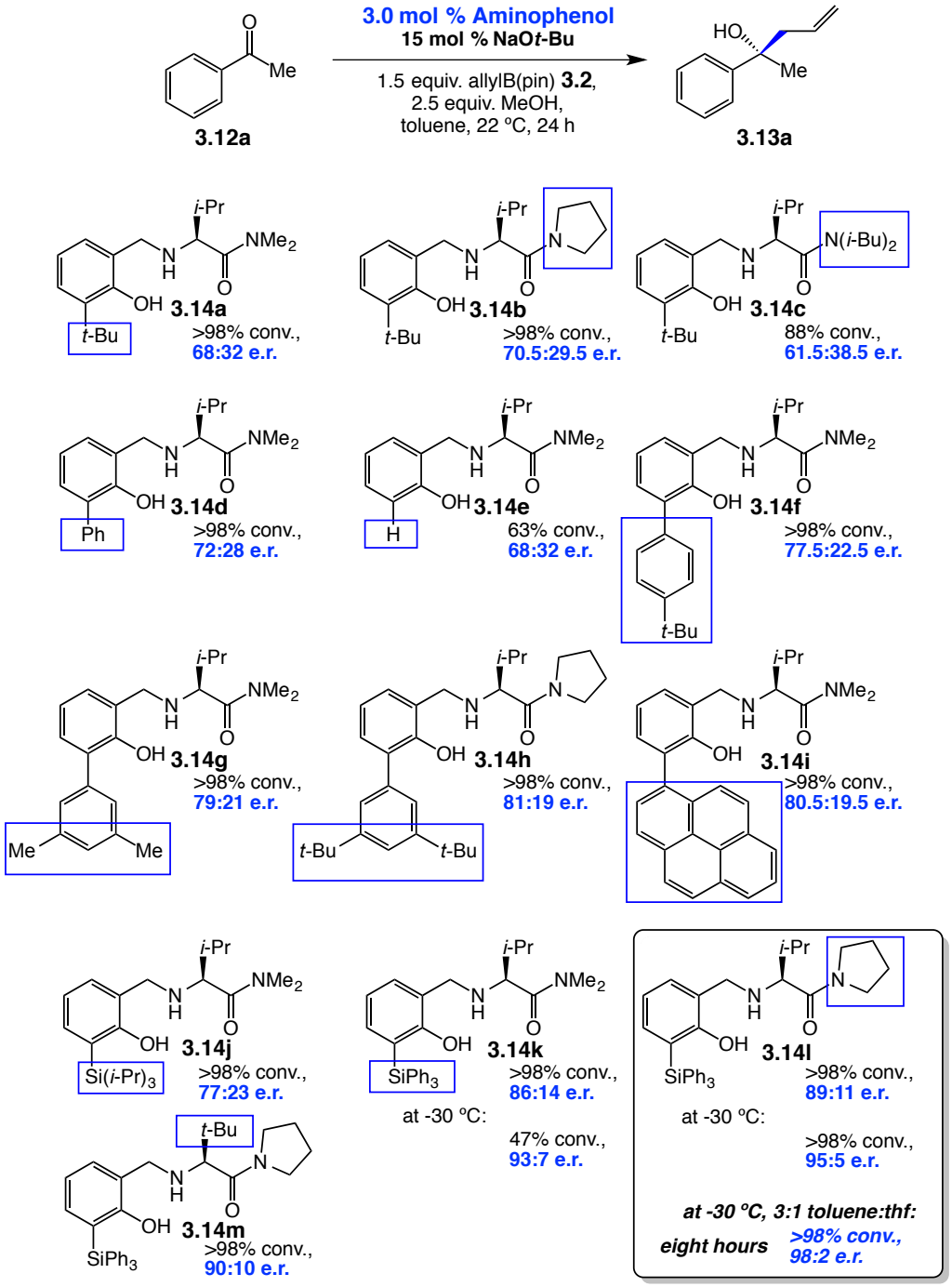
We reasoned that by increasing the size of the group *ortho* to the phenol in the catalyst, we could favor the conformer where the smaller methyl group of acetophenone is axial versus the one where the large phenyl group is axial (Figure 3.1). Based on this rationale, Dr. Daniel Robbins synthesized and screened a variety of modified aminophenols (Scheme 3.11).

Figure 3.1 Impact of Group *ortho* to the Phenol



Changing the size of the group *ortho* to the phenol in the aminophenol by

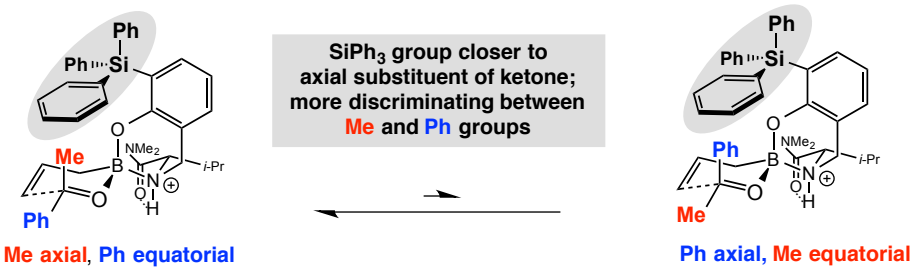
Scheme 3.11 Modification of the Structure of the Aminophenol and Reaction Conditions



installing a variety of sterically modified aryl groups resulted in the increase of the enantioselectivity to a maximum of 81:19 e.r. with aminophenol **3.14h** (Scheme 3.11). Due to synthetic difficulties, installation of aryl rings larger than this was problematic.

I hypothesized that a silane *ortho* to the phenol of the catalyst should be large enough to a interact with the ketone (Figure 3.2), due in part to the C-Si bond length being significantly longer than a C-C bond (1.85 Å versus 1.54 Å). I synthesized **3.14j** and **3.14k**, and when Dr. Robbins tried them in the reaction, he discovered that triphenylsilyl-containing aminophenol **3.14k** afforded the desired product in 86:14 e.r.,

Figure 3.2 Impact of $SiPh_3$

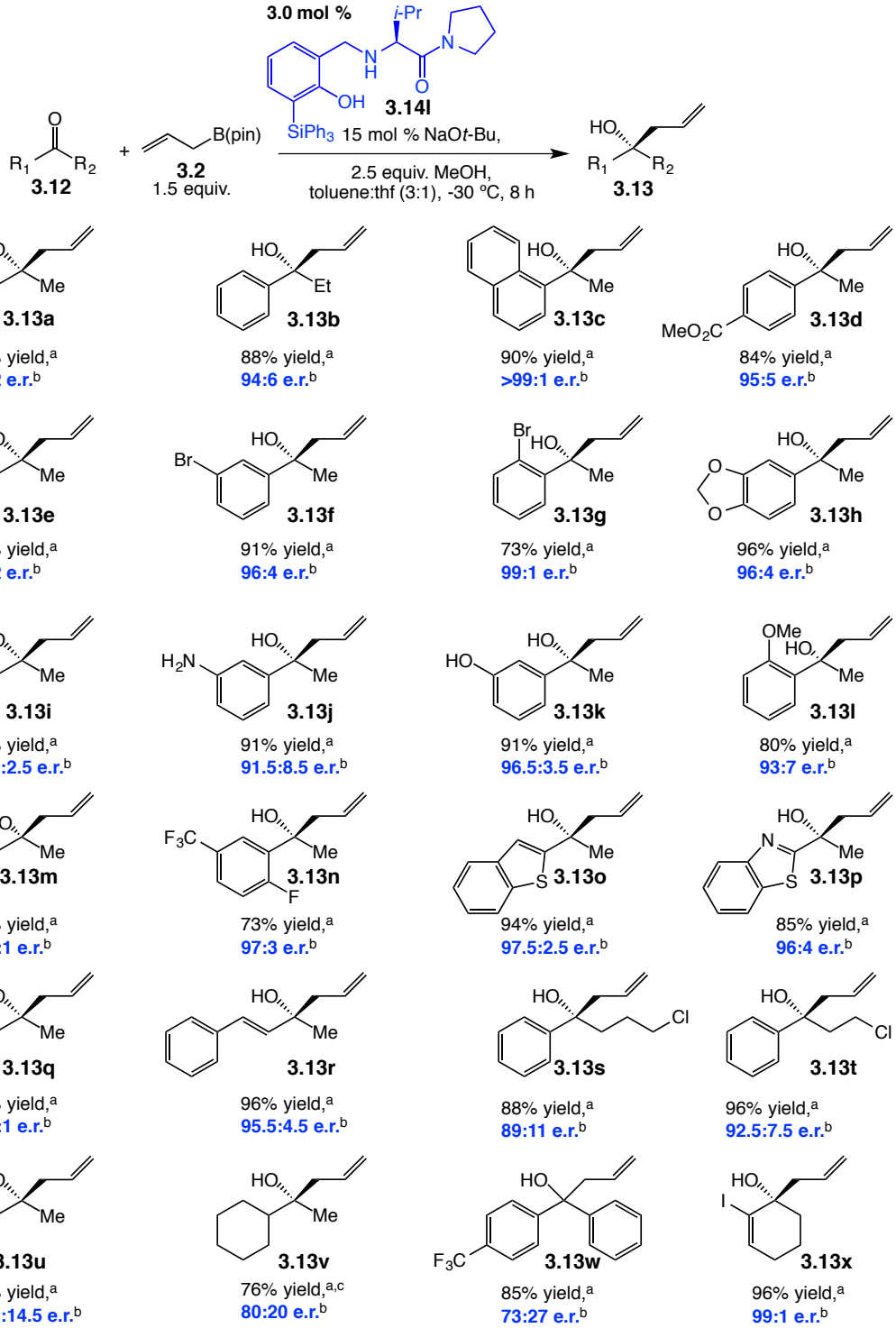


the highest selectivity observed so far (Scheme 3.11). Cooling the reaction led to an increase in the enantioselectivity to 93:7 e.r., but at the cost of reduced reactivity. Hypothesizing that a more Lewis basic amide on the aminophenol could lead to a more efficient transformation, aminophenol **3.14l** was tried and it resulted in a reaction that reached full conversion and proceeded with 95:5 enantioselectivity. Aminophenol **3.14m**, derived from *tert*-leucine, did not behave significantly different than **3.14l**, so Dr. Robbins took the latter to be the optimal aminophenol. Intitially examined to solubilize more polar ketones, he also found that changing the solvent mixture to 3:1 toluene:thf affords a more enantioselective transformation, affording **3.14a** in 98:2 e.r.

Under these optimized conditions, the reaction proceeds to full conversion in eight hours. With these conditions, he examined the substrate scope of the reaction

(Scheme 3.12). Now, propiophenone **3.12b** undergoes catalytic allyl-addition to afford homoallyl alchohol **3.13b** in 94:6 e.r. (up from 62.5:37.5 e.r. in Equation 1) and naphthyl-

Scheme 3.12 Substrate Scope of Allyl-Additions to Ketones



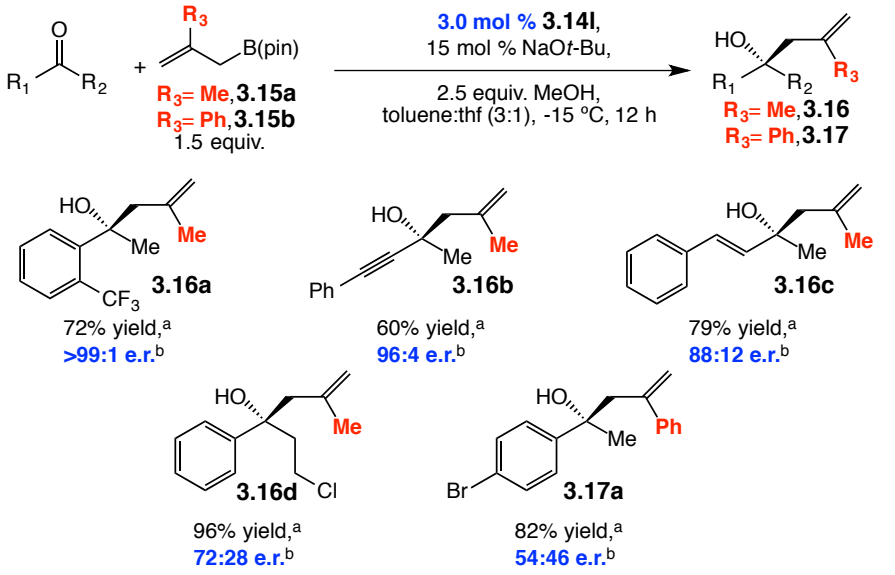
aYield of isolated product. bDetermined by HPLC analysis. cReaction conducted at -15 °C

substituted **3.13c** is afforded in >99:1 e.r. (up from 94:6 e.r. in Equation 2). A wide variety of other substituted ketones, including as those bearing phenyl groups with *ortho*-, *meta-,* and *para*-substituents (e.g. **3.12e** to **3.12f**); those bearing heterocycles (**3.12o** and **3.12p**), alkynyl (**3.12q**), and alkenyl (**3.12r**) groups; and cyclic ketones (**3.12x**) react under these conditions to give the desired products in high yields and enantiomeric enrichment (Scheme 3.12). Compared with the catalytic methods discussed and cited in Section 3.2, one important advantage of this method is that we show it can tolerate functional groups no other method has been reported to, to produce products containing heterocycles (**3.13p**), aryl-substituted esters (**3.13d**), carbamates (**3.13i**), unprotected anilines (**3.13j**), unprotected phenols (**3.13k**), and alkynes (**3.12q**). This is in addition to potentially reactive functionality other methods can tolerate, yielding ethers (**3.13h** and **3.13i**), aryl bromides (**3.12e** to **3.12g**), aryl fluorides (**3.13n**), vinyl iodides (**3.13x**), sulfur-containing heterocycles (**3.13o** and **3.13p**), and alkyl halides **(3.13s** and **3.13t**). One disadvantage of this method compared with some others is that alkyl groups larger than ethyl do result in a diminishment in enantioselectivity (**3.13s** and **3.13t**).[25a,26a] Unfortunately, this protocol does not fair better than other methods with ketones bearing two alkyl substituents, as **3.13u** and **3.13v** are formed in 85.5:14.5 and 80:20 e.r. respectively. Reactivity of these substrates can also be problematic, with **3.12v** requiring a reaction temperature of -15 ºC to reach full conversion. Addition to benzophenone derivative **3.12w** proceeds with a modest selectivity of 73:27 e.r.,[31] but this is a notable level of selectivity for additions to this difficult class of substrates.[32]

(31) The absolute stereochemistry of **3.13w** has not been established, but we believe it is likely that the *para*-trifluoromethyl-containing side acts as the large group.
(32) For a rare example of an enantioselective addition of a carbon nucleophile to benzophenones, see: Kohn, B. L.; Ichiishi, N.; Jarvo, E. R. *Angew. Chem. Int. Ed.* **2013**, *52*, 4414–4417.

To increase the reaction scope, 2-substituted allylboronates were examined (Scheme 3.13).[26c] These transformations are slower than with allylB(pin) **3.2**, and are

Scheme 3.13 Addition of 2-Substituted Allyl Groups to Ketones



[a]Yield of isolated product. [b]Determined by HPLC analysis. [c]Reaction conducted at -15 °C

generally less enantioselective (cf. **3.16b** with **3.13q** and **3.16c** with **3.13r**) and the yields are also lower. Those with 2-phenyl boronate **3.15b** proceed with little to no selectivity. 2-Chloroallylboronate (not shown) does not react under these conditions, even at 23 °C. Having examined a variety of general ketones, we next turned our attention to a more specific class of substrates, α-ketoesters.

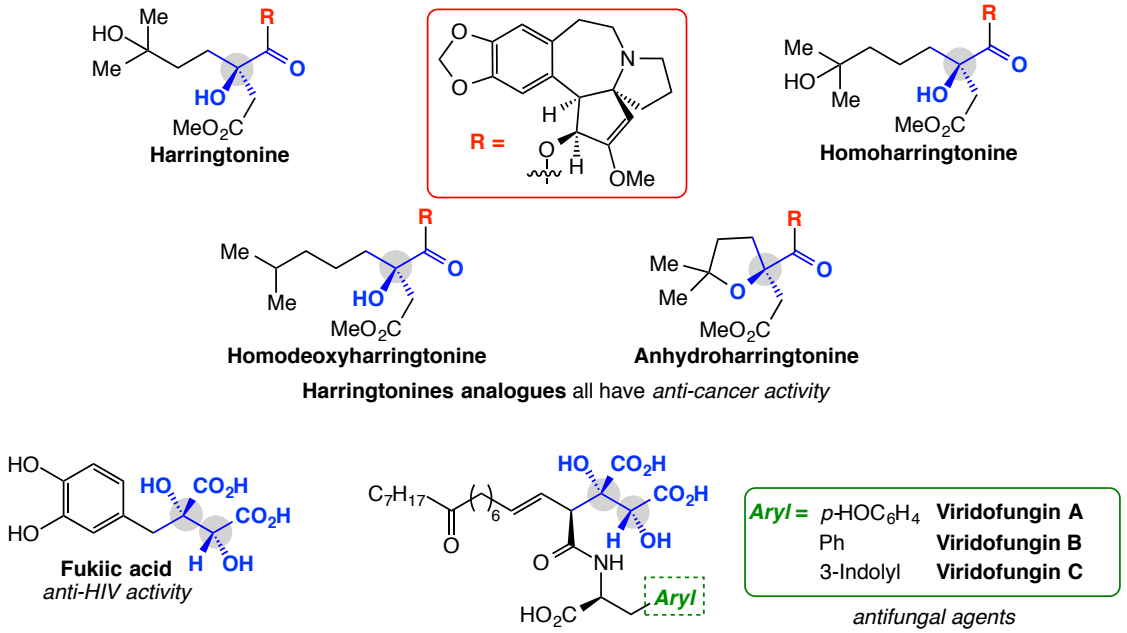
3.4 Catalytic Enantioselective Allyl- and Allenyl-Additions to α-Ketoesters.

The chiral α-hydroxy ester/acid motif is present in a variety of biologically active compounds such as the antiviral compound harringtonine (Scheme 3.14)[33] and its many structurally related natural products, namely homoharringtonine,

(33) Kaur, P.; Thiruchelvan, M.; Lee, R. C. H.; Chen, H.; Chen, K. C.; Ng, M. L.; Chu, J. J. H. *Antimicrob. Agents Chemother*. **2013**, *57*, 155–167.

homodeoxyharringtonine, and anhydroharringtonine, all of which possess anticancer activity.[34]

Scheme 3.14 Biologically Active Compounds Containing an α-Hydroxy Ester or Acid

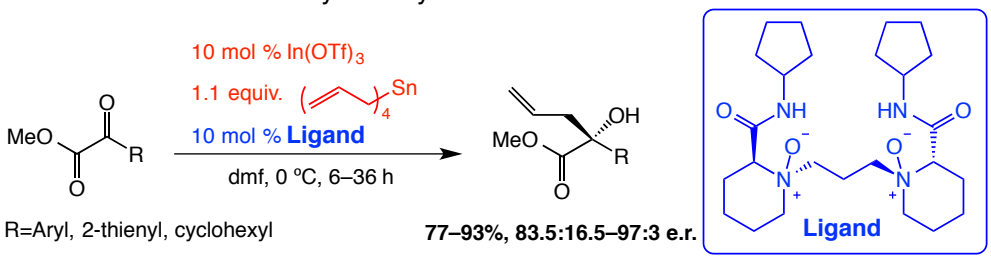


Additional compounds of interest containing this moiety are the anti-HIV fukiic acid,[35] neurotoxic alkaloid dysiherbaine,[36] and the antifugal viridofungin family (Scheme 3.14).[37] One way to access flexible building blocks to this chemical structure is by carrying out an enantioselective allyl- or allenyl-addition to α-ketoesters. This class of homoallylic alcohols has been employed in the synthesis of a variety of the harringtonine derivatives[34] as well as synthetic studies toward dysiherbaine.[36b]

(34) Eckelbarger, J. D.; Wilmot, J. T.; Epperson, M. T.; Thakur, C. S.; Shum, D.; Antczak, C.; Tarassishin, L.; Djaballah, H.; Gin, D. Y. *Chem. Eur. J.* **2008**, *14*, 4293–4306.
(35) Queffélec, C.; Bailly, F.; Mbemba, G.; Mouscadet, J.-F.; Debyser, Z.; Witvrouw, M..; Cotelle, P. *Eur. J. Med. Chem.* **2008**, *43*, 2268–2271.
(36) For the isolation, see: (a) Sakai, R.; Kamiya, H.; Murata, M.; Shimamoto, K. *J. Am. Chem. Soc.* **1997**, *119*, 4112–4116. For an effort towards the synthesis of this molecule that employs a stereoselective allyl-addition to an α-ketoester , see: (b) Huang, J.-M.; Xu, K.-C.; Loh, T.-P. *Synthesis* **2003**, *5*, 755–764.
(37) Goldup, S. M.; Pilkington, C. J.; White, A. J. P.; Burton, A.; Barrett, A. G. M. *J. Org. Chem.* **2006**, *71*, 6185–6191.

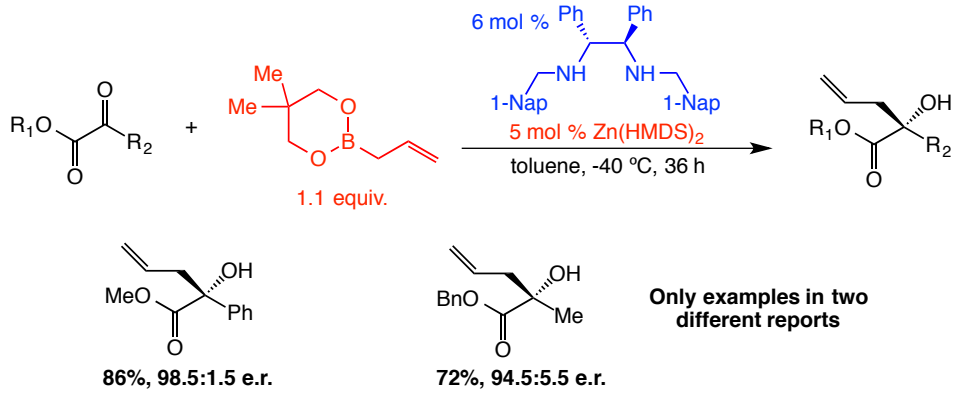
To the best of our knowledge, only two catalytic enantioselective allyl-additions to α-ketoesters exist. The first requires 10 mol % catalyst loading of the costly and precious $In(OTf)_3$ ($4.9/mmol, Strem) as well as stoichiometric organotin (Scheme 3.15).[38] The second, while promoted by 6 mol % an easily accessible diamine ligand

Scheme 3.15 Indium-Catalyzed Allyl-Addition to α-ketoesters



and 5 mol% of a commercially available zinc salt, the reaction takes 36 hours and has very little reported in terms of substrate scope (Scheme 3.16).[39] Additionally $Zn(HMDS)_2$ is quite expensive ($54/mmol from Aldrich). The only catalytic, enantioselective method

Scheme 3.16 Zinc-Catalyzed Allyl-Addition to α-ketoesters

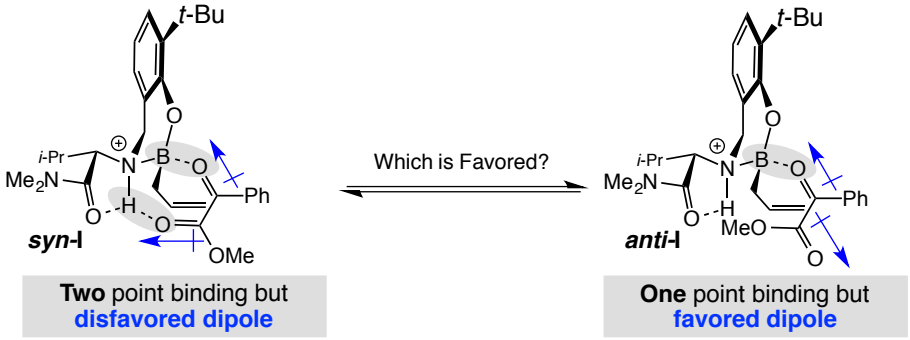


to access the products of allenyl-addition to α-ketoesters is through a rhodium catalyzed reaction between propargyl alcohols and α-diazoesters that is proposed to take place through a oxonium ylide formation followed by a [2,3]-sigmatropic rearrangement.[40]

(38) Zheng, K.; Qin, B.; Liu, X.; Feng, X. *J. Org. Chem.* **2007**, *27*, 8478–8483.
(39) (a) Cui, Y.; Yamashita, Y.; Kobayashi, S. *Chem. Commun.* **2012**, *48*, 10319–10321. (b) Cui, Y.; Li, W.; Sato, T.; Yamashita, Y.; Kobayashi, S. *Adv. Synth. Catal.* **2013**, *355*, 1193–1205.

In addition to the synthetic benefits inherent in developing an efficient and selective method to add allyl and allenyl groups to α-ketoesters, we also wished to use these substrates to learn more about our previously reported enantioselective additions of boronates promoted by an aminophenol.[41] We were curious whether the ester carbonyl of an α-ketoester would have a sufficiently strong interaction with the proton present on the ammonium ion of the proposed catalyst to engender high levels of stereoselectivity (***syn*-I**, Figure 3.3). The α-ketoester should not have as strong a secondary interaction with the

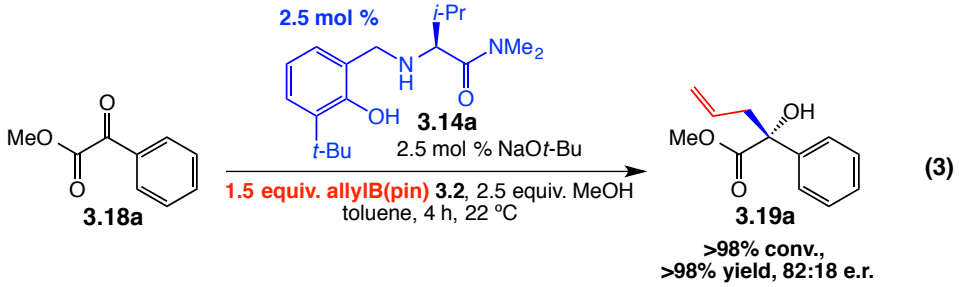
Figure 3.3 Possibility of Two-point Binding with α-Ketoesters



catalyst as the previously reported isatins (cyclic α-ketoamides) for two main reasons: 1) The ester carbonyl in the α-ketoesters is not as strong of a hydrogen bond acceptor as the amide carbonyl of the isatins 2) The isatins are conformationally-locked such that the amide carbonyl is well situated to favorably interact with the catalyst, whereas the ester in the α-ketoesters is free to rotate into a variety of conformations where it is not favorable to interact with the N-H of the catalyst (Figure 3.3).[42] Carrying out the allyl-addition to α-ketoester **3.18a** under conditions similar to those developed for the addition

(40) Li, Z.; Boyarskikh, V.; Hansen, J. H.; Autsback, J.; Musaev, D. G.; Davies, H. M. L. *J. Am. Chem. Soc.* **2012**, *134*, 15497–15504.
(41) Silverio, D. L.; Torker, S.; Pilyugina, T.; Vieira, E. M.; Snapper, M. L.; Haeffner, F.; Hoveyda, A. H. *Nature* **2013**, *494*, 216–221.
(42) Calculations utilizing DFT show ketoester **3.18a** prefers an *anti*-conformation to a *syn*-by 3.5 kcal/mol.

to isatins results in a clean transformation (>98% yield of alcohol **3.19a**) that is promisingly enantioselective (82:18 e.r., see Equation 3).



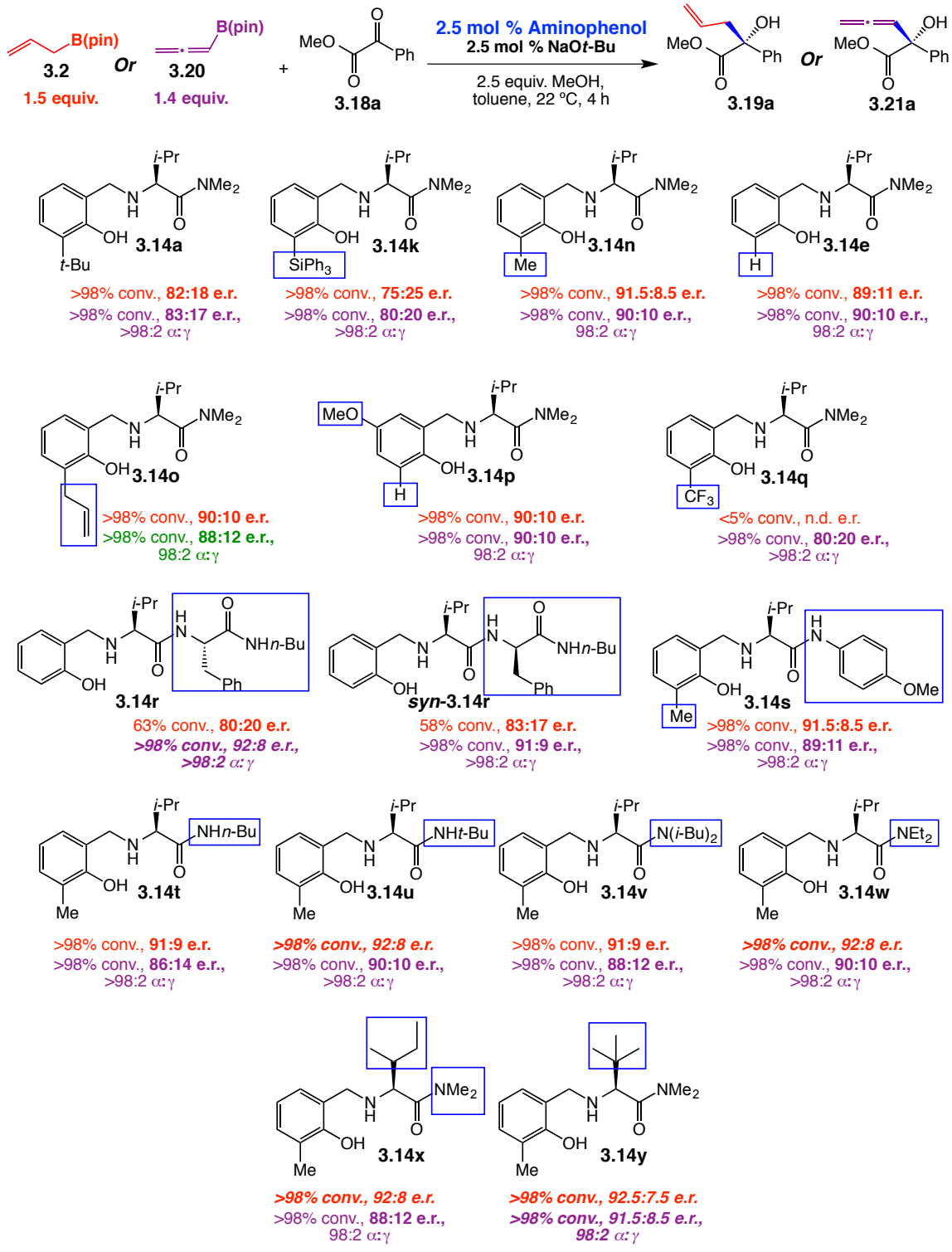
(3)

Modifying the amount of NaO*t*-Bu added (from 1.25 to 20 mol %) does not effect the reaction in either a positive or negative way. Decreasing the reaction temperature does not result in a noticeable increase in the enantioselectivity of the transformation, suggesting that unlike the reaction with ketones (and similar to the reaction with trifluoroacetophenones and aldimines), the stereochemistry is likely determined by entropy rather than enthalpy.

We next screened a variety of aminophenols for the catalytic enantioselective allyl- and allenyl-additions to α-ketoester **3.18a** (Scheme 3.17). In all previous studies utilizing the aminophenol ligands, we have seen that transforming the *t*-Bu group *ortho* to the phenol into a triphenylsilyl group either does not affect the enantioselectivity of the transformation, or it improves the enantioselectivity (See Scheme 3.11 in Section 3.3, Scheme 2.12 in Section 2.4, and Scheme 2.10 in Section 2.3). Interestingly, both additions to substrate **3.18a** proceed in *lower* levels of selectivity when $SiPh_3$ containing aminophenol **3.14k** is employed (Scheme 3.17). With these four data points in hand, we investigated whether decreasing the size of the group *ortho* to the phenol would be beneficial and found a large increase in the enantiomeric ratio of the products when a methyl group (**3.14n**) or a hydrogen (**3.14e**) are used instead of a *t*-Bu group. This is the

first time we have observed aminophenol **3.14n** or **3.14e** to be more selective than **3.14a** in any transformation, and it is especially remarkable that the increase from ~4:1 to ~9:1

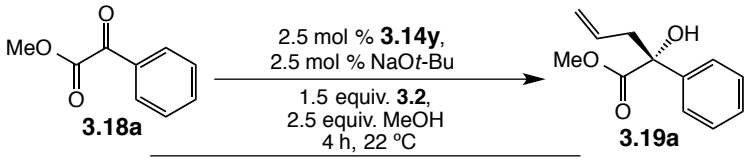
Scheme 3.17 Screening of Aminophenols



e.r. is energetically significant (~0.4 kcal). Thinking that perhaps there is an optimum sized aminophenol between *tert*-butyl-substituted **3.14a** and methyl-substituted **3.14n**, allyl-substituted **3.14o** was examined, but it is slightly worse than **3.14n** in terms of selectivity.

We theorized that perhaps by increasing the polarity of the solvent, the *syn*-conformation of the substrate needed for two point binding (Figure 3.3) could be favored, but increasing solvent polarity (versus pure toluene) resulted in a much less efficient and enantioselective reaction (Table 3.1).[43]

Table 3.1 Solvent Screen



entry	*solvent*	conv. (%)[a]	e.r.[b]
1	1:1 thf:toluene	79	84:16
2	1:3 thf:toluene	69	87:13
3	1:1 CH_2Cl_2:toluene	73	88:12
4	1:3 CH_2Cl_2:toluene	58	86:14

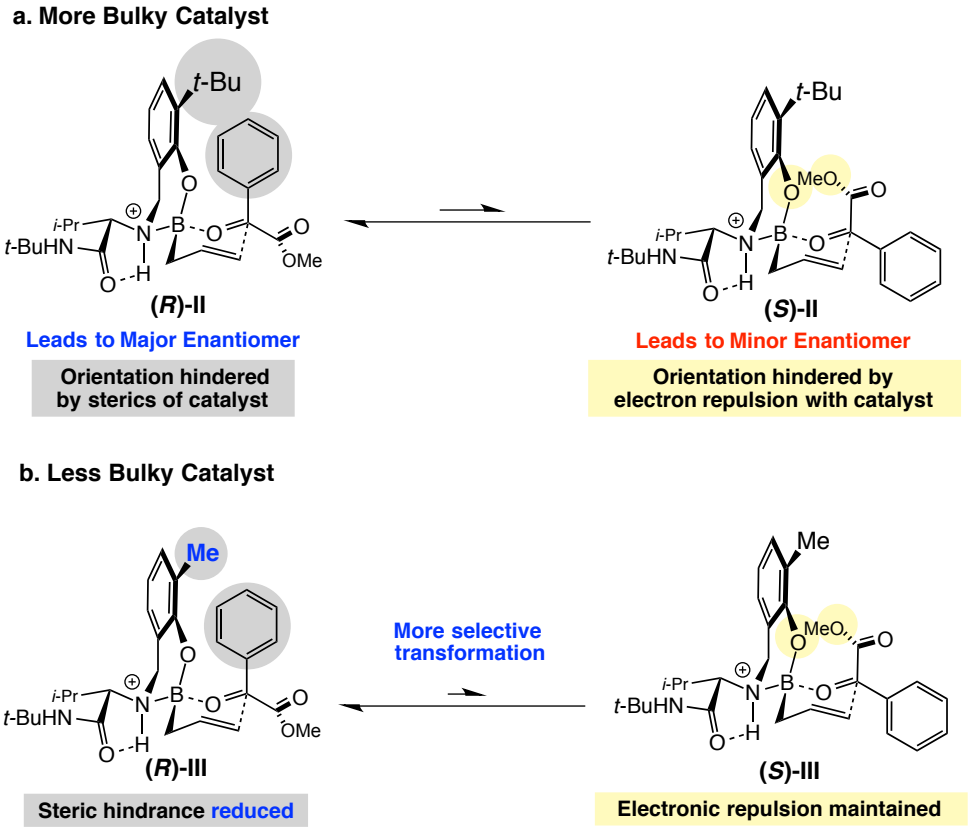
[a]Conversion of starting material to product as determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture. [b]Determined by HPLC analysis.

Since the sterics around the phenol moiety have a profound effect on enantioselectivity, we doubt that the structures in Figure 3.3 play a major role in determining enantioselectivity because the moiety should have little impact in those cases. Instead, we believe that the structures in Figure 3.4 are more important and that the major enantiomer is obtained (**[*R*]-III**, Figure 3.4) due to electronic repulsion disfavoring

(43) This is almost universally the case with reactions promoted by the aminophenol, likely due to increasing the solvent polarity decreasing the importance of electrostatic interactions and H-bonding. For example, performing the allyl-additions to diphenylphosphinoyl aldimines (Chapter 1) in CH_2Cl_2 rather than toluene (3 mol % of aminophenol **3.14a**, 2.5 mol % NaO*t*-Bu, 75 minutes) results in 78% conv. and 91:9 e.r. In toluene, this reaction is >98% conversion and 96.5:3.5 e.r. Why the ketone allyl-addition (section 3.3) is improved by adding tetrahydrofuran as a co-solvent is not fully understood.

(*S*)-III (Figure 3.4). To perhaps increase this electronic repulsion, we examined *p*-methoxycontaining **3.14p**, but this aminophenol also did not lead to a more

Figure 3.4 Rationalization for Enantioselectivity Increase with Less Bulky Catalyst



enantioselective transformation. Next electron poor **3.14q** was tried. Based on previous results regarding the lack of efficiency of aminophenols which contain an acidic phenol (for example, see **1.30e** in Scheme 1.28 in Section 1.5 of Chapter 1), we were not surprised that the formation of homoallylalcohol **3.19a** proceeded in <5% conversion, but we were astonished that the allenyl addition went to full conversion. The marked difference between the efficiency of the allyl- and alleny-additions when promoted by **3.14q** warrants further study and perhaps will shed light on the mechanism for formation of the active catalyst. Continued structural modifications of the aminophenol were carried out this time focusing on the *C* terminus.

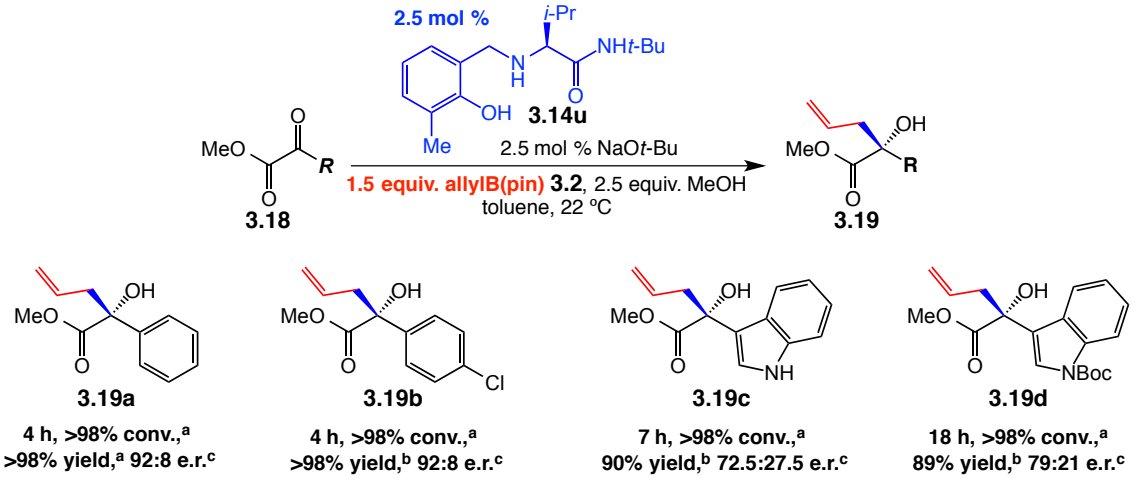
We first tried reactions with bis-amino acid containing aminophenol **3.14r** which affords homoallylalcohol **3.19a** less efficiently and in lower selectivity than the reaction with **3.14n**. Conversely, it affords the homoallenylalcohol **3.21a** in the highest level of enantioselectivity so far which again highlights the difference between allyl- and allenyl-additions. Employing ***syn*-3.14r**, the diastereomer of **3.14r**, leads to essentially the same reaction. We thought that the difference in between reactions promoted by aminophenols **3.14e** versus **3.14r** could be the fact that the former aminophenol contains a tertiary amide while the latter aminophenol contains secondary amides. To probe this, we tried aminophenol **3.14t** in the transformations and discovered that this is unlikely to be the case since the reactivity and enantioselectivity for allyl-addition was restored while the allenyl-addition enantioselectivity dropped noticeably. Thinking that the second amino acid in **3.14r** was simply acting as a sterically large group, we synthesized and studied reactions promoted by **3.14s**–**3.14w**. Interestingly, none of these precatalysts are better than **3.14r** for the allenyl-addition, but **3.14u** and **3.14w** are among the most enantioselective for the allyl-addition. This renders the interesting reactivity and selectivity caused by the second amino acid of **3.14r** poorly understood at this time.

Next, we carried out some modifications of the amino acid in the aminophenol (Scheme 3.17). Switching from valine to isoleucine (**3.14x**) led to a catalyst that was more enantioselective for allylation, but less selective for allenylation. Moving to a *tert*-leucine containing catalyst **3.14y** led to increased enantioselectivities for both transformations.

Moving forward with aminophenols **3.14u** and **3.14r** for allyl and allenyl additions respectively, we carried out a short probe of the substrate scope of these

transformations. Compared with the model methyl benzoylformate **3.18a**, the electron withdrawing *para*-Cl substrate behaves very similarly (Scheme 3.18 and 3.19). The

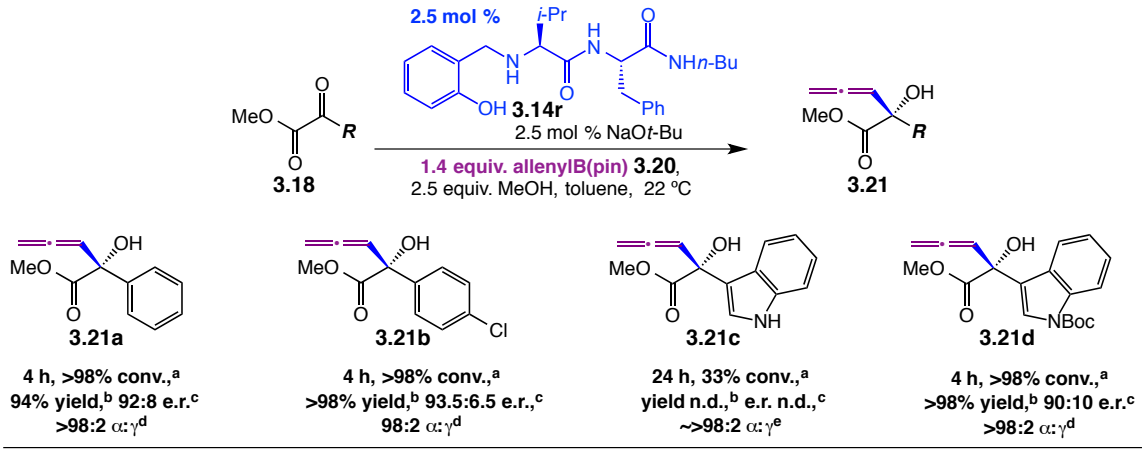
Scheme 3.18 Substrate Scope for Allyl-Addition



4 h, >98% conv.,[a] >98% yield,[a] 92:8 e.r.[c] | **4 h, >98% conv.,[a] >98% yield,[b] 92:8 e.r.[c]** | **7 h, >98% conv.,[a] 90% yield,[b] 72.5:27.5 e.r.[c]** | **18 h, >98% conv.,[a] 89% yield,[b] 79:21 e.r.[c]**

[a]Yield of isolated product. [b]Determined by HPLC analysis. [c]Conversion of starting material to product as determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture.

Scheme 3.19 Substrate Scope for Allenyl-Addition



4 h, >98% conv.,[a] 94% yield,[b] 92:8 e.r.[c] >98:2 α:γ[d] | **4 h, >98% conv.,[a] >98% yield,[b] 93.5:6.5 e.r.,[c] 98:2 α:γ[d]** | **24 h, 33% conv.,[a] yield n.d.,[b] e.r. n.d.,[c] ~>98:2 α:γ[e]** | **4 h, >98% conv.,[a] >98% yield,[b] 90:10 e.r.[c] >98:2 α:γ[d]**

[a]Yield of isolated product. [b]Determined by HPLC analysis. [c]Conversion of starting material to product as determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture. [d]Determined by 400 MHz ^{1}H analysis of the isolated product. [e]Estimated by 400 MHz ^{1}H analysis of the unpurified reaction mixture.

unprotected 3-indolyl substrate **3.18c** is slow to react, but this is in large part due to its low solubility. In the case of the allene-addition to this substrate to form **3.21c** (Scheme 3.19), only 33% conversion is observed even after 24 hours. This stems from the fact that the product is even less soluble than the starting material, and it may be that the methanol in the reaction is being occupied, solvating either the starting material or

product, and therefore cannot enter the catalytic cycle. When protected with a Boc group, the allyl-addition seems to be slowed down, but the allenyl-addition is much faster. As seen before with the trifluoromethylketones, the enantioselectivity of the allylation is more sensitive to sterics than that of the allenylation.

3.5 Conclusions

By employing two aminophenols with opposite steric sizes, the enantioselective addition of an allyl unit to a ketone and an allyl or allenyl unit to an α-ketoester can be promoted. These transformations occur efficiently and tolerate a wide variety of functional groups. The ease of accessibility of the aminophenols coupled with the low catalyst loadings needed contribute to the attractiveness of this method.

3.6 Experimental Section

■ **General.** Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, λ_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) or 500 (500 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). Well resolved AB splitting patterns are reported as follows: chemical shift of A and chemical shift of B, integration, multiplicity (AB_q = AB quartet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal

standard ($CDCl_3$: δ 77.16 ppm). Data are reported as follows: chemical shift, multiplicity (singlet unless otherwise noted), and coupling constants (Hz). ^{19}F NMR spectra were recorded on a Varian Unity INOVA 400 (376 MHz). Chemical shifts are reported in ppm with $BF_3 \bullet OEt_2$ as an external standard ($BF_3 \bullet OEt_2$: δ 0.00 ppm). Data are reported as follows: chemical shift, integration, multiplicity, and coupling constants (Hz). High-resolution mass spectrometry was performed on a JEOL AccuTOF-DART (positive mode) or an Advion Expression CMS (ESI+ or ESI-) at the Mass Spectrometry Facility, Boston College. Enantiomer ratios (e.r.) values were determined by HPLC analysis using a Shimadzu LC-2010AHT chromatograph (Chiral Technologies Chiralcel OD-H (4.6 x 250 mm), Chiral Technologies Chiralcel OJ-H (4.6 x 250 mm), Chiral Technologies Chiralpak AD-H (4.6 x 250 mm), Chiralpak AS-H (4.6 x 250 mm), or GLPC (gas-liquid partition chromatography) with an Agilent chromatograph (Alltech Associated Chiraldex CD-BDM column (30 m x 0.25 mm) or a Hewlett Packard 5890 Series II chromatograph (Alltech Associated Betadex 120 column (30 m x 0.25 m). Specific rotations were measured using either an Atago AP-300 Automated Polarimeter or a Rudolph Research Analytical Autopol IV Polarimeter. Melting points were determined using a Thomas Hoover Uni-melt capillary melting point apparatus. Unless otherwise noted, reactions were carried out under an atmosphere of dry N_2 in oven-dried (135 ºC) glassware with the appropriate oven-dried (65 ºC) septa.

■ **Solvents:** Unless otherwise noted, solvents were purged with Ar and purified under a positive pressure of dry Ar by a modified Innovative Technologies purification system. Toluene (Fisher, ACS Grade) was passed successively through activated copper and alumina columns. Dichloromethane (Fisher, ACS Grade) and diethyl ether (Aldrich,

Chromasolv®) were passed successively through two activated alumina columns. Tetrahydrofuran was purified by distillation from sodium benzophenone ketyl immediately prior to use. $CDCl_3$ was purchased from Cambridge Isotope Laboratories and stored over activated 4Å molecular sieves prior to use. All work-up and purification procedures were carried out in air with reagent grade solvents (purchased from Fisher).

■ **Reagents and Catalysts:**

Allenylboronic Acid Pinacol Ester (3.20) was obtained from Frontier Scientific and distilled under vacuum prior to use.

Allylboronates: Allylboronic acid pinacol ester (**3.2**) was purchased from Aldrich or obtained as a gift from Frontier Scientific, Inc and distilled prior to use. 2-Methylallyl)boronic acid pinacol ester (**3.15a**) was synthesized and purified in accordance with a procedure in the literature.[44] (2-Phenylallyl)boronic acid pinacol ester (**3.15b)** was synthesized and purified in accordance with a procedure in the literature.[45]

Hydrochloric Acid (12 M, 36.5-38.0 wt %) was purchased from Alfa Aesar and used as received.

Magnesium Sulfate was purchased from Fisher and flame-dried under vacuum prior to use.

Methanol was purchased from Acros (99.8% anhydrous) and distilled at 1 atm from sodium metal prior to use.

2-Silylsalicylaldehydes were prepared in accordance to a procedure in the literature and used to make aminophenols, such as **3.14l**, without further purification.[46]

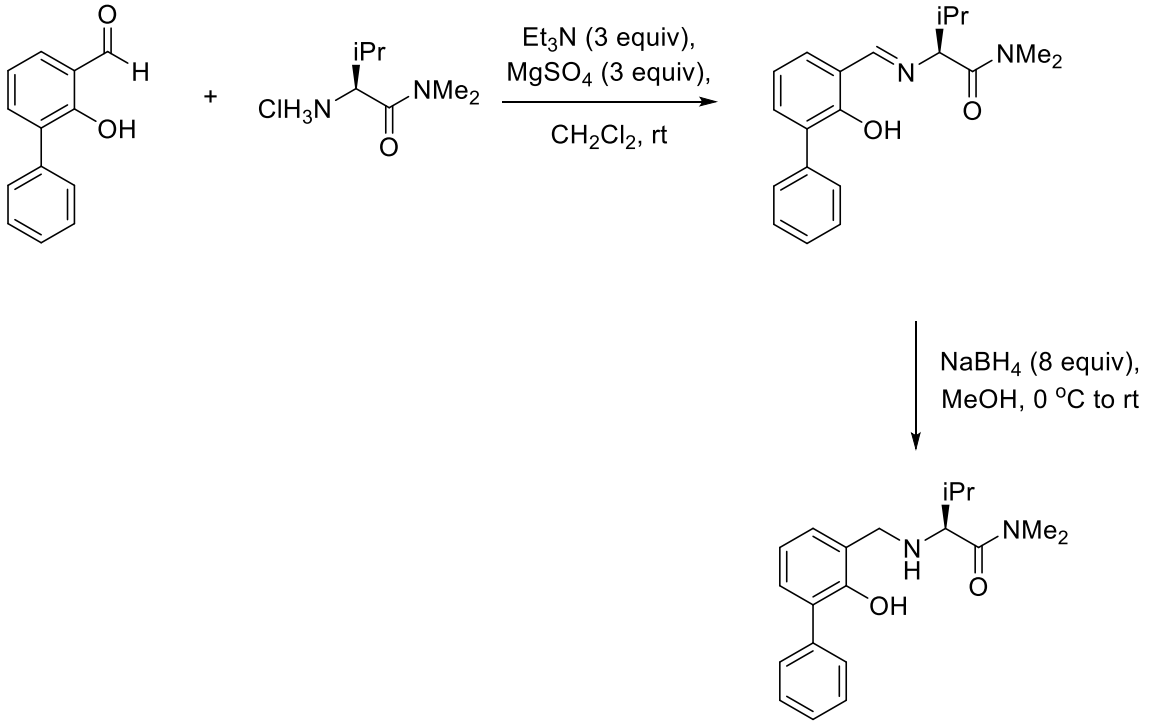
(44) Zhang, P.; Roundtree, I. A.; Morken, J. P. *Org. Lett.* **2012**, *14*, 1416–1419.
(45) Corberan, R.; Mszar, N. W.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2011**, *50*, 7079–7082.
(46) Thadani, A. N.; Huang, Y.; Rawal, V. H. *Org. Lett.* **2007**, *9*, 3873–3876.

Sodium Borohydride was purchased from Aldrich and used as received.

Sodium *tert*-Butoxide was purchased from Strem (min. 98%) and used as received.

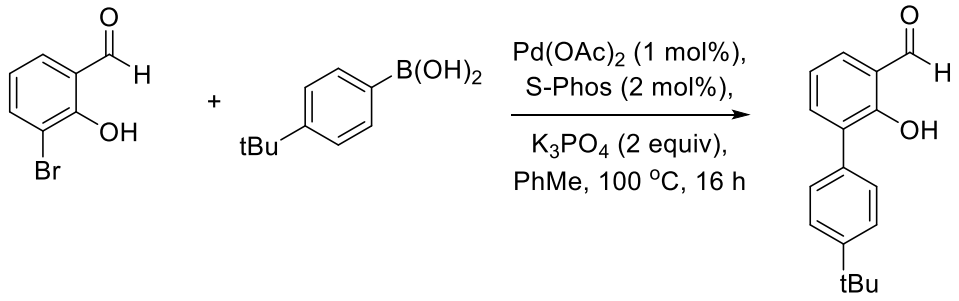
Triethylamine was purchased from Aldrich and distilled from CaH_2 prior to use.

Experimental Procedures



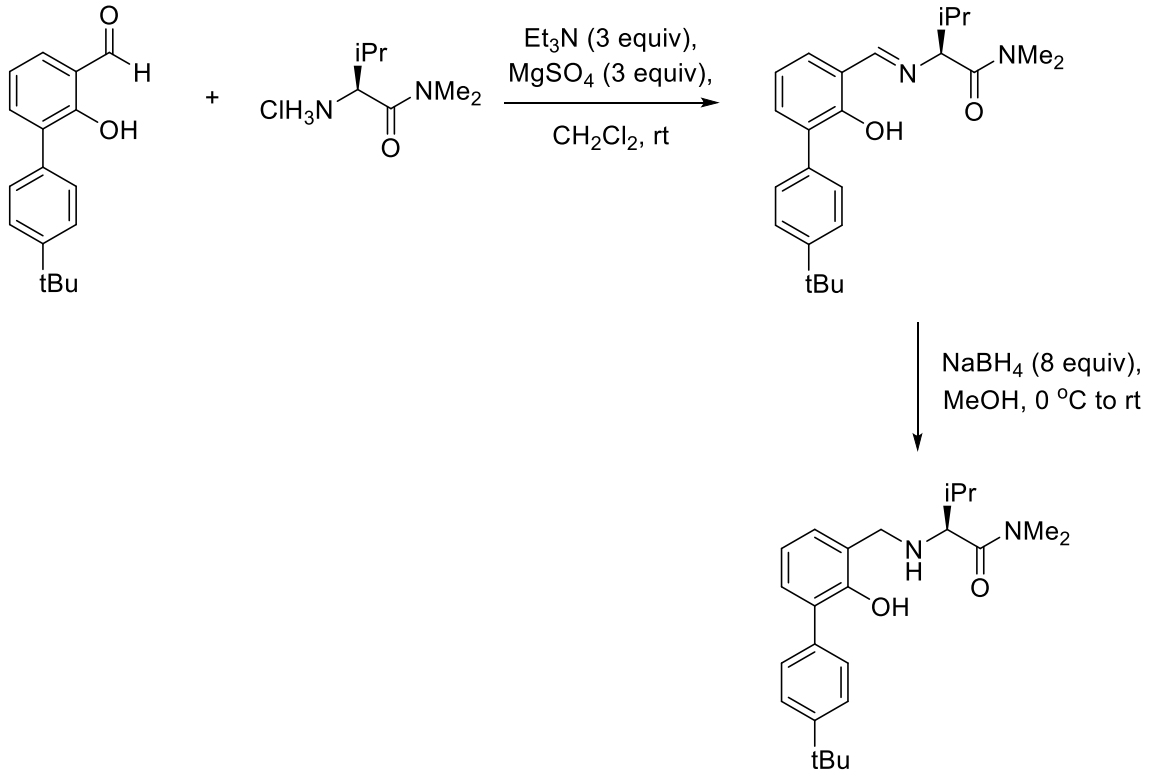
(S)-2-(((2-Hydroxy-[1,1'-biphenyl]-3-yl)methyl)amino)-N,N,3-trimethylbutanamide. 3-phenyl-2-hydroxybenzaldehyde (198 mg, 1.00 mmol, 1.00 equiv), (S)-2-amino-N,N,3-trimethylbutanamide hydrochloride (180 mg, 1.00 mmol, 1.50 equiv), $MgSO_4$ (361 mg, 3.00 mmol, 3.00 equiv), Et_3N (0.42 mL, 3.00 mmol, 3.00 equiv), and CH_2Cl_2 (2 mL) were added to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum and allowed to stir for 16 hours at room temperature. The reaction mixture was filtered through silica gel washing with EtOAc, and concentrated under vacuum. The resulting reaction mixture was dissolved in MeOH (5 mL) and cooled to 0 °C with an ice

bath. $NaBH_4$ (304 mg, 8.00 mmol, 8.00 equiv) and concentrated HCl (1 drop) were added to the reaction mixture, and the ice bath was removed. The reaction mixture was allowed to warm to room temperature for 2 hours. Saturated aqueous $NaHCO_3$ and EtOAc were added, and the layers separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were combined, dried with $MgSO_4$, filtered and concentrated under vacuum. The reaction mixture was purified by column chromatography (2:1 pentane:EtOAc) to give the product (186 mg, 57%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 – 7.56 (m, 2H), 7.48 – 7.35 (m, 2H), 7.36 – 7.20 (m, 2H), 6.97 – 6.88 (m, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 4.07 (d, *J* = 13.6 Hz, 1H), 3.58 (d, *J* = 13.5 Hz, 1H), 3.38 (d, *J* = 5.7 Hz, 1H), 3.04 (s, 3H), 2.94 (s, 3H), 1.98 – 1.75 (m, 1H), 0.96 (dd, *J* = 9.6, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 173.20, 155.17, 138.52, 130.06, 129.35, 129.11, 127.98, 127.87, 126.70, 122.96, 119.06, 61.68, 51.58, 37.03, 35.74, 31.21, 19.99, 17.86. IR (neat): 3291, 2962, 2928, 2872, 1638, 1461, 1429, 1233, 1088, 757, 699. HRMS (ESI$_+$): Calcd for $C_{20}H_{26}N_2O_2$ [M+H]$_+$: 327.1994; Found: 327.2074.



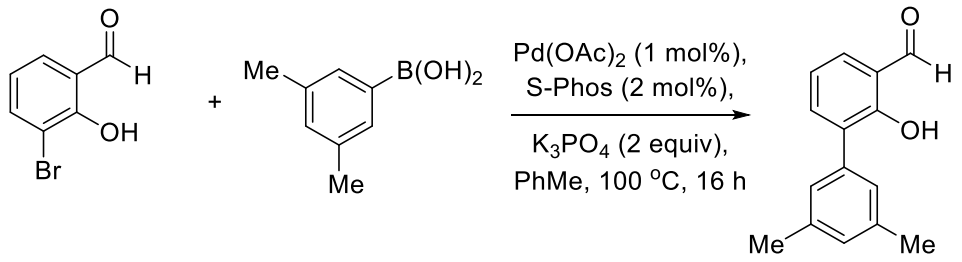
4'-(tert-Butyl)-2-hydroxy-[1,1'-biphenyl]-3-carbaldehyde. Inside an N_2-filled glove box, $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.010 equiv), S-Phos (12.3 mg, 0.03 mmol, 0.020 equiv), K_3PO_4 (639 mg, 3.00 mmol, 2.00 equiv), 3-Bromo-2-hydroxybenzaldehyde (303 mg, 1.50 mmol, 1.00 equiv), 4-*tert*-butylphenylboronic acid (321 mg, 1.80 mmol, 1.20

equiv) and PhMe (4 mL) were added consecutively to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum, removed from the glovebox, equipped with a reflux condenser and allowed to stir for 16 hours in a bath preheated to 100 °C. The reaction mixture was cooled to room temperature, filtered through silica gel washing with Et_2O, and concentrated under vacuum. The reaction mixture was purified by column chromatography (4:1 pentane:Et_2O) to give the product (198 mg, 52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.63 (d, *J* = 0.8 Hz, 1H), 9.93 (d, *J* = 1.1 Hz, 1H), 7.79 – 7.35 (m, 6H), 7.10 (td, *J* = 7.6, 1.0 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 196.89, 158.95, 150.59, 137.72, 133.35, 132.98, 130.34, 128.94, 125.30, 120.87, 119.95, 34.63, 31.40. IR (neat): 2962, 2904, 2866, 1658, 1613, 1439, 1387, 1279, 1217, 1117, 1066, 916, 827, 752, 670, 579.

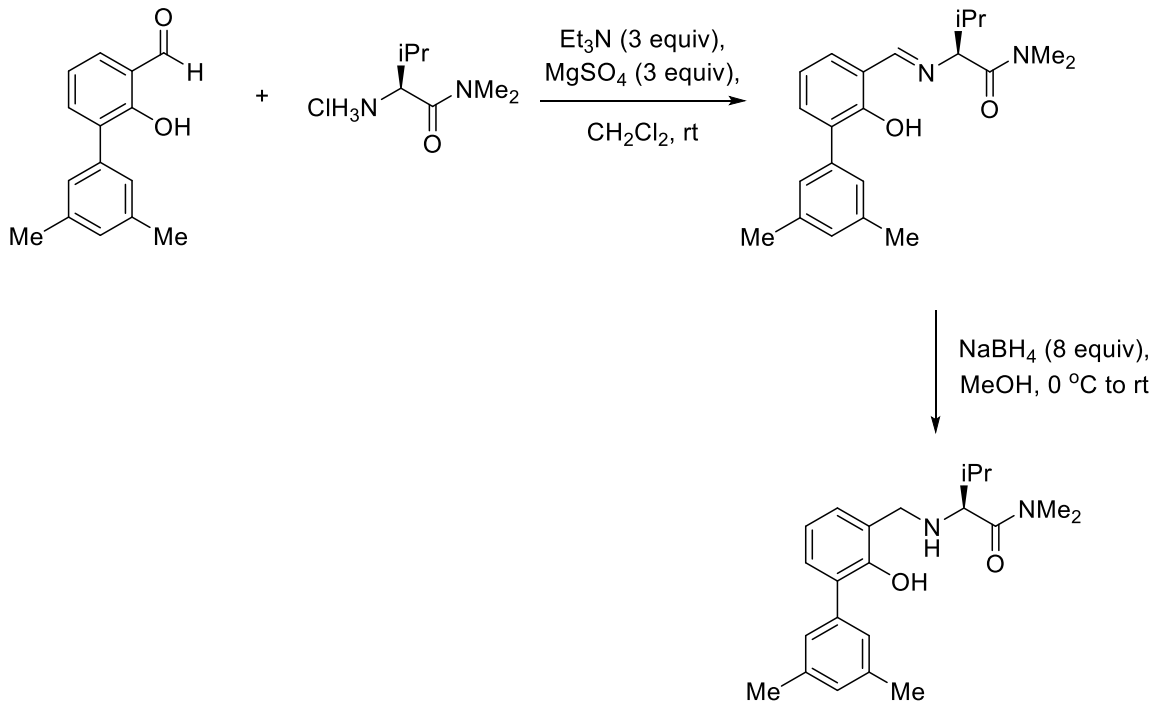


(S)-2-(((4'-(tert-Butyl)-2-hydroxy-[1,1'-biphenyl]-3-yl)methyl)amino)-N,N,3-trimethylbutanamide. 4'-(tert-butyl)-2-hydroxy-[1,1'-biphenyl]-3-carbaldehyde (150 mg, 0.590 mmol, 1.00 equiv), (S)-2-amino-N,N,3-trimethylbutanamide hydrochloride (180 mg, 0.590 mmol, 1.00 equiv), $MgSO_4$ (213 mg, 1.77 mmol, 3.00 equiv), Et_3N (0.25 mL, 1.77 mmol, 3.00 equiv), and CH_2Cl_2 (2 mL) were added to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum and allowed to stir for 16 hours at room temperature. The reaction mixture was filtered through silica gel washing with EtOAc, and concentrated under vacuum. The resulting reaction mixture was dissolved in MeOH (5 mL) and cooled to 0 °C with an ice bath. $NaBH_4$ (183 mg, 4.80 mmol, 8.00 equiv) and concentrated HCl (1 drop) were added to the reaction mixture, and the ice bath was removed. The reaction mixture was allowed to warm to room temperature for 2 hours. Saturated aqueous $NaHCO_3$ and EtOAc were added, and the layers separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were combined, dried with $MgSO_4$, filtered and concentrated under vacuum. The reaction mixture was purified by column chromatography (2:1 pentane:EtOAc) to give the product (111 mg, 49%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.54 (m, 2H), 7.45 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.27 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.96 – 6.88 (m, 1H), 6.82 (td, *J* = 7.5, 1.0 Hz, 1H), 4.07 (d, *J* = 13.7 Hz, 1H), 3.59 (d, *J* = 13.6 Hz, 1H), 3.39 (dd, *J* = 5.8, 1.0 Hz, 1H), 3.04 (s, 3H), 2.94 (s, 3H), 1.97 – 1.73 (m, 1H), 1.36 (s, 9H), 1.05 – 0.91 (m, 6H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 173.18, 155.21, 149.37, 135.55, 130.04, 128.98, 128.94, 127.66, 124.98, 122.93, 119.06, 61.68, 51.64, 37.02, 35.72, 34.50, 31.42, 31.22, 20.00, 17.88. IR (neat): 2960, 2868, 1641, 1456, 1398, 1268,

1118, 824, 750, 579. HRMS (ESI+): Calcd for $C_{24}H_{34}N_2O_2$ $[M+H]^+$: 383.2620; Found: 383.2699.

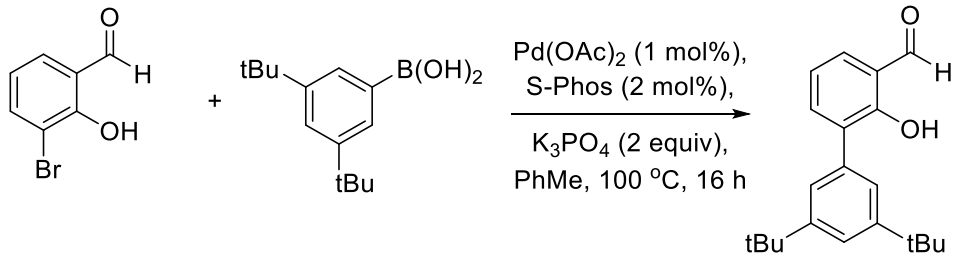


2-Hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-3-carbaldehyde. Inside an N_2-filled glove box, $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.010 equiv), S-Phos (12.3 mg, 0.03 mmol, 0.020 equiv), K_3PO_4 (639 mg, 3.00 mmol, 2.00 equiv), 3-Bromo-2-hydroxybenzaldehyde (303 mg, 1.50 mmol, 1.00 equiv), 3,5-dimethylphenylboronic acid (270 mg, 1.80 mmol, 1.20 equiv) and PhMe (4 mL) were added consecutively to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum, removed from the glovebox, equipped with a reflux condenser and allowed to stir for 16 hours in a bath preheated to 100 °C. The reaction mixture was cooled to room temperature, filtered through silica gel washing with Et_2O, and concentrated under vacuum. The reaction mixture was purified by column chromatography (4:1 pentane:Et_2O) to give the product (185 mg, 55%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.55 (s, 1H), 9.93 (s, 1H), 7.65 – 7.58 (m, 1H), 7.53 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.23 (d, *J* = 0.8 Hz, 2H), 7.15 – 7.00 (m, 2H), 2.41 (s, 6H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 196.83, 158.92, 137.84, 137.77, 136.23, 133.02, 130.80, 129.40, 127.10, 120.81, 119.83, 21.43. IR (neat): 3410, 3025, 2916, 2856, 1649, 1601, 1442, 1385, 1297, 1269, 1223, 851, 751, 700, 667. HRMS (DART+): Calcd for $C_{15}H_{14}O_2$ $[M+H]^+$: 227.1072; Found: 227.1071.



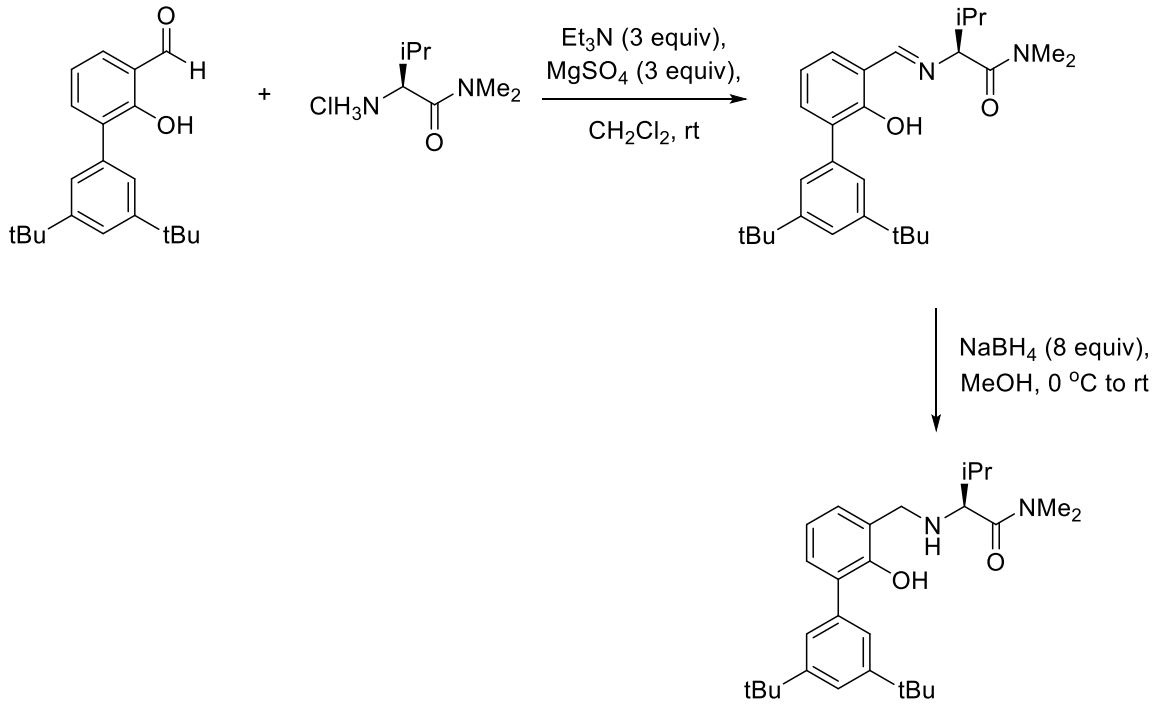
(S)-2-(((2-Hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-3-yl)methyl)amino)-N,N,3-trimethylbutanamide. 2-hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-3-carbaldehyde (95 mg, 0.420 mmol, 1.00 equiv), (S)-2-amino-N,N,3-trimethylbutanamide hydrochloride (76 mg, 0.420 mmol, 1.00 equiv), $MgSO_4$ (152 mg, 1.26 mmol, 3.00 equiv), Et_3N (0.19 mL, 1.26 mmol, 3.00 equiv), and CH_2Cl_2 (2 mL) were added to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum and allowed to stir for 16 hours at room temperature. The reaction mixture was filtered through silica gel washing with EtOAc, and concentrated under vacuum. The resulting reaction mixture was dissolved in MeOH (5 mL) and cooled to 0 °C with an ice bath. $NaBH_4$ (128 mg, 3.36 mmol, 8.00 equiv) and concentrated HCl (1 drop) were added to the reaction mixture, and the ice bath was removed. The reaction mixture was allowed to warm to room temperature for 2 hours. Saturated aqueous $NaHCO_3$ and EtOAc were added, and the layers separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were

combined, dried with $MgSO_4$, filtered and concentrated under vacuum. The reaction mixture was purified by column chromatography (2:1 pentane:EtOAc) to give the product (99 mg, 66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.16 (m, 3H), 6.96 (d, *J* = 1.2 Hz, 1H), 6.92 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 4.06 (d, *J* = 13.5 Hz, 1H), 3.59 (d, *J* = 13.5 Hz, 1H), 3.39 (d, *J* = 5.7 Hz, 1H), 3.05 (s, 3H), 2.95 (s, 3H), 2.37 (s, 6H), 2.01 – 1.72 (m, 1H), 0.97 (dd, *J* = 10.8, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 173.20, 155.15, 138.47, 137.30, 130.14, 129.50, 128.50, 127.71, 127.23, 122.90, 118.95, 61.70, 51.63, 37.02, 35.72, 31.24, 21.46, 19.97, 17.89. IR (neat): 3304, 2961, 2917, 2872, 1636, 1459, 1398, 1234, 1073, 908, 848, 727, 700, 645. HRMS (ESI$_+$): Calcd for $C_{22}H_{30}N_2O_2$ [M+H]$_+$: 355.2307; Found: 355.2379.



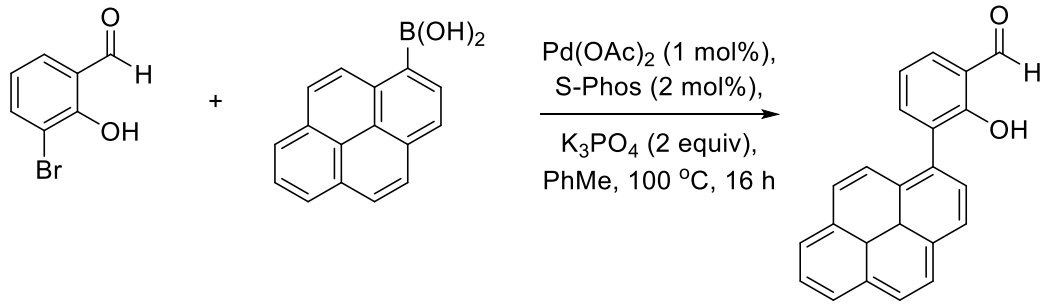
3',5'-Di-tert-butyl-2-hydroxy-[1,1'-biphenyl]-3-carbaldehyde. Inside an N_2-filled glove box, $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.010 equiv), S-Phos (12.3 mg, 0.03 mmol, 0.020 equiv), K_3PO_4 (639 mg, 3.00 mmol, 2.00 equiv), 3-Bromo-2-hydroxybenzaldehyde (303 mg, 1.50 mmol, 1.00 equiv), 3,5-di-*tert*-butylphenylboronic acid (422 mg, 1.80 mmol, 1.20 equiv) and PhMe (4 mL) were added consecutively to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum, removed from the glovebox, equipped with a reflux condenser and allowed to stir for 16 hours in a bath preheated to 100 °C. The reaction mixture was cooled to room temperature, filtered through silica gel washing with Et_2O, and concentrated under vacuum. The reaction

mixture was purified by column chromatography (4:1 pentane:Et_2O) to give the product (308 mg, 66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.68 (s, 1H), 10.00 (d, *J* = 0.5 Hz, 1H), 7.76 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.60 (td, *J* = 3.6, 3.2, 1.7 Hz, 4H), 7.18 (t, *J* = 7.6 Hz, 1H), 1.52 (s, 18H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 196.91, 159.11, 150.58, 138.04, 135.54, 132.98, 131.62, 123.83, 121.84, 120.98, 119.94, 35.06, 31.68. IR (neat): 2960, 2903, 2866, 1655, 1614, 1419, 1384, 1362, 1298, 1249, 1216, 956, 877, 750, 711, 665, 484. HRMS (ESI+): Calcd for $C_{21}H_{26}O_2$ [M+H]+: 333.1825; Found: 333.1831.

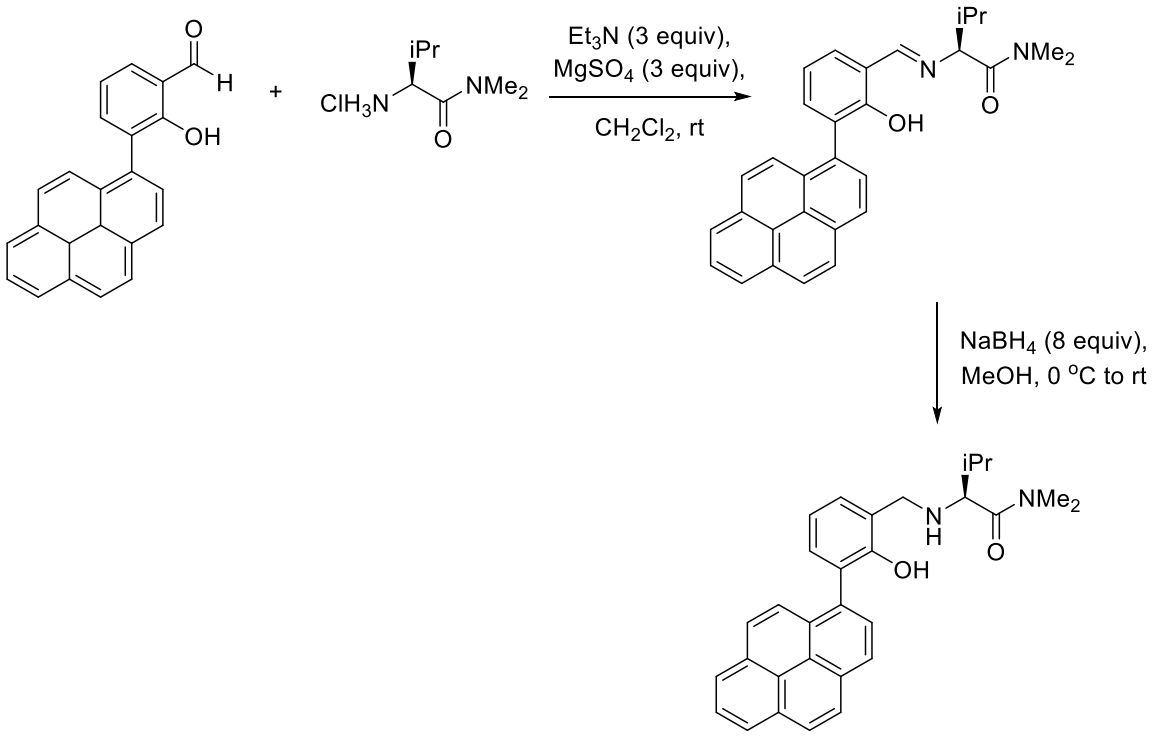


(S)-2-(((3',5'-Di-tert-butyl-2-hydroxy-[1,1'-biphenyl]-3-yl)methyl)amino)-N,N,3-trimethylbutanamide. 3',5'-di-tert-butyl-2-hydroxy-[1,1'-biphenyl]-3-carbaldehyde (308 mg, 1.00 mmol, 1.00 equiv), (S)-2-amino-N,N,3-trimethylbutanamide hydrochloride (181 mg, 1.00 mmol, 1.00 equiv), $MgSO_4$ (361 mg, 3.00 mmol, 3.00 equiv), Et_3N (0.42 mL, 3.00 mmol, 3.00 equiv), and CH_2Cl_2 (2 mL) were added to a dry flask with a magnetic

stir bar. The reaction mixture was sealed with a septum and allowed to stir for 16 hours at room temperature. The reaction mixture was filtered through silica gel washing with Et_2O, and concentrated under vacuum. The resulting reaction mixture was dissolved in MeOH (5 mL) and cooled to 0 °C with an ice bath. $NaBH_4$ (304 mg, 8.00 mmol, 8.00 equiv) and concentrated HCl (1 drop) were added to the reaction mixture, and the ice bath was removed. The reaction mixture was allowed to warm to room temperature for 2 hours. Saturated aqueous $NaHCO_3$ and EtOAc were added, and the layers separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were combined, dried with $MgSO_4$, filtered and concentrated under vacuum. The reaction mixture was purified by column chromatography (2:1 pentane:EtOAc) to give the product (227 mg, 52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 1.8 Hz, 2H), 7.41 (t, *J* = 1.9 Hz, 1H), 7.30 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.94 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.85 (t, *J* = 7.5 Hz, 1H), 4.19 – 4.03 (m, 1H), 3.61 (d, *J* = 13.7 Hz, 1H), 3.42 (d, *J* = 5.7 Hz, 1H), 3.06 (s, 3H), 2.96 (s, 3H), 1.97 – 1.79 (m, 1H), 1.39 (s, 18H), 1.01 (dd, *J* = 10.4, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $cdcl_3$) δ 173.26, 155.23, 149.90, 137.53, 130.27, 130.25, 127.59, 123.85, 122.96, 120.83, 118.95, 61.61, 51.60, 37.04, 35.73, 34.89, 31.58, 31.25, 20.03, 17.86. IR (neat): 2960, 2903, 2868, 1641, 1461, 1416, 1361, 1247, 1122, 876, 748, 712. HRMS (ESI$_+$): Calcd for $C_{28}H_{42}N_2O_2$ $[M+H]_+$: 439.3246; Found: 439.3322.

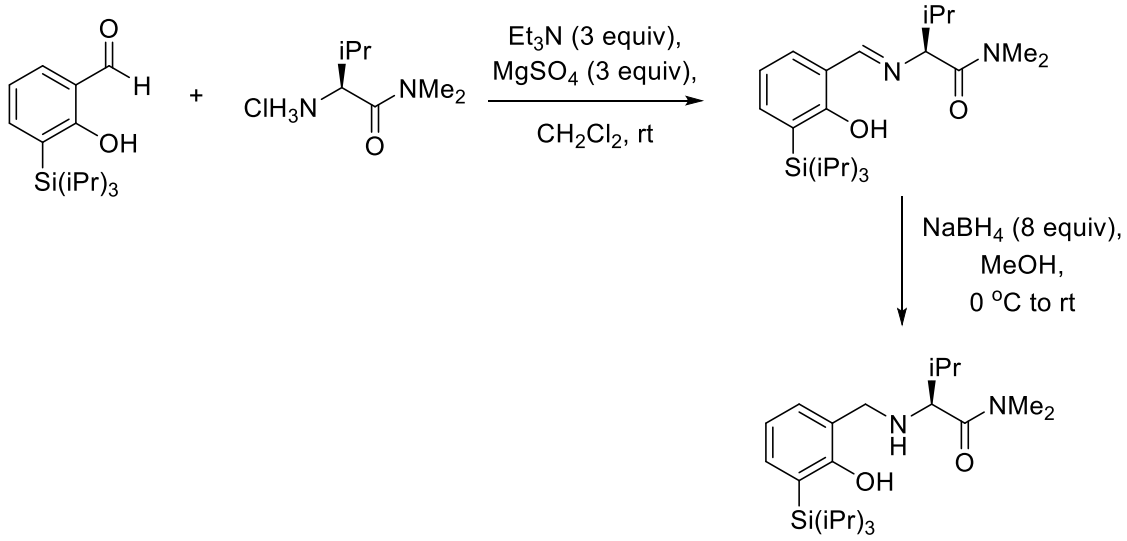


3-(3a1,5a1-Dihydropyren-1-yl)-2-hydroxybenzaldehyde. Inside an N_2-filled glove box, $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 0.010 equiv), S-Phos (12.3 mg, 0.03 mmol, 0.020 equiv), K_3PO_4 (639 mg, 3.00 mmol, 2.00 equiv), 3-Bromo-2-hydroxybenzaldehyde (303 mg, 1.50 mmol, 1.00 equiv), pyrene-1-boronic acid (443 mg, 1.80 mmol, 1.20 equiv) and PhMe (4 mL) were added consecutively to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum, removed from the glovebox, equipped with a reflux condenser and allowed to stir for 16 hours in a bath preheated to 100 °C. The reaction mixture was cooled to room temperature, filtered through silica gel washing with EtOAc, and concentrated under vacuum. The reaction mixture was purified by column chromatography (4:1 pentane:EtOAc) to give the product (290 mg, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.44 (d, *J* = 0.6 Hz, 1H), 9.94 (s, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 8.20 (ddd, *J* = 10.2, 7.6, 1.1 Hz, 2H), 8.11 (s, 2H), 8.09 – 7.97 (m, 3H), 7.91 (d, *J* = 9.2 Hz, 1H), 7.67 (ddd, *J* = 7.5, 1.8, 0.6 Hz, 1H), 7.56 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 196.78, 159.37, 139.52, 133.57, 131.68, 131.37, 131.20, 130.96, 129.91, 129.20, 128.00, 127.70, 127.63, 127.41, 126.05, 125.32, 125.29, 125.14, 124.87, 124.82, 124.66, 120.79, 119.75. IR (neat): 3041, 2844, 1654, 1613, 1438, 1385, 1268, 1217, 845, 755, 720, 675.



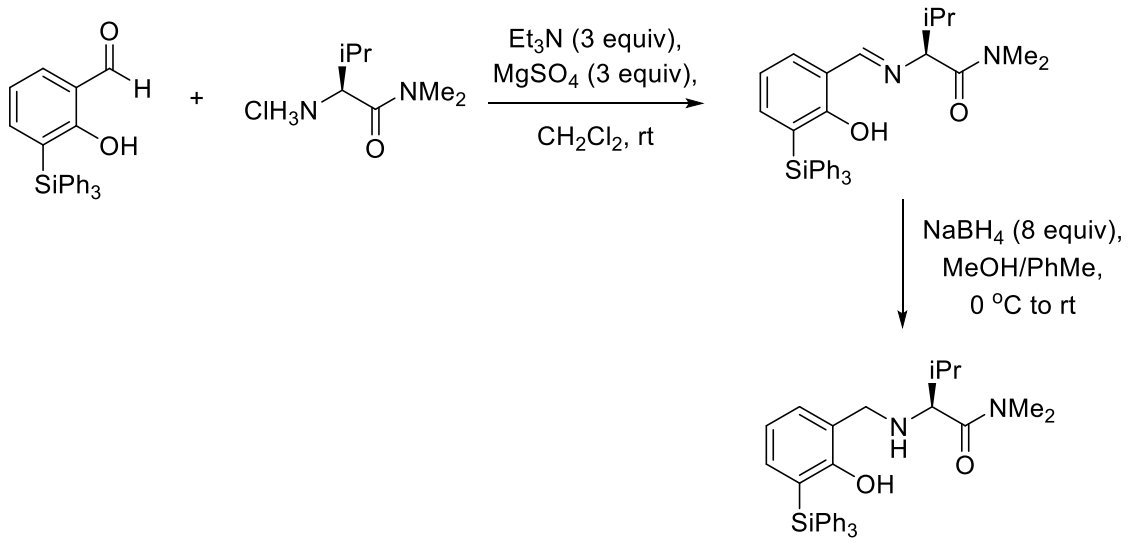
(S)-2-((2-Hydroxy-3-(pyren-1-yl)benzyl)amino)-N,N,3-trimethylbutanamide. 3-(3a1,5a1-dihydropyren-1-yl)-2-hydroxybenzaldehyde (105 mg, 0.324 mmol, 1.00 equiv), (S)-2-amino-N,N,3-trimethylbutanamide hydrochloride (59 mg, 0.32 mmol, 1.0 equiv), $MgSO_4$ (117 mg, 0.970 mmol, 3.00 equiv), Et_3N (0.14 mL, 0.970 mmol, 3.0 equiv), and CH_2Cl_2 (2 mL) were added to a dry flask with a magnetic stir bar. The reaction mixture was sealed with a septum and allowed to stir for 16 hours at room temperature. The reaction mixture was filtered through silica gel washing with Et_2O, and concentrated under vacuum. The resulting reaction mixture was dissolved in MeOH (5 mL) and cooled to 0 °C with an ice bath. $NaBH_4$ (99 mg, 2.6 mmol, 8.0 equiv) and concentrated HCl (1 drop) were added to the reaction mixture, and the ice bath was removed. The reaction mixture was allowed to warm to room temperature for 2 hours. Saturated aqueous $NaHCO_3$ and EtOAc were added, and the layers separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were combined, dried with

$MgSO_4$, filtered and concentrated under vacuum. The reaction mixture was purified by column chromatography (2:1 pentane:EtOAc) to give the product (65 mg, 45%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (dd, *J* = 7.8, 3.4 Hz, 1H), 8.09 – 7.97 (m, 4H), 8.15 – 8.13 (m, 0H), 8.18 (ddt, *J* = 8.8, 7.9, 1.2 Hz, 2H), 8.11 (d, *J* = 5.5 Hz, 2H), 7.39 (dt, *J* = 7.5, 1.8 Hz, 1H), 7.14 (dt, *J* = 7.5, 1.8 Hz, 1H), 7.00 (td, *J* = 7.5, 1.7 Hz, 1H), 4.30 – 4.15 (m, 1H), 3.70 (dd, *J* = 13.8, 5.4 Hz, 1H), 3.46 (dd, *J* = 29.7, 5.7 Hz, 1H), 3.08 (d, *J* = 5.4 Hz, 3H), 2.97 (d, *J* = 13.7 Hz, 3H), 1.88 (dddd, *J* = 13.5, 12.3, 10.0, 6.7 Hz, 1H), 1.07 – 0.84 (m, 6H). IR (neat): 3290, 3039, 2960, 2928, 2872, 1636, 1445, 1398, 1235, 1083, 908, 845, 724. HRMS (ESI+): Calcd for $C_{30}H_{30}N_2O_2$ $[M+H]^+$: 451.2307; Found: 451.2383.

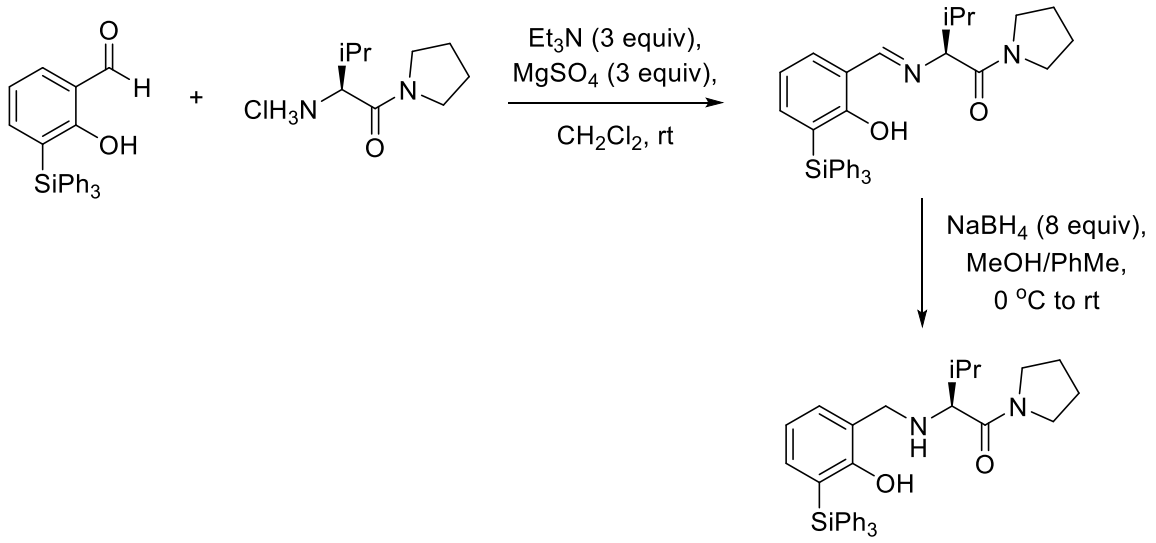


(S)-2-((2-Hydroxy-3-(triisopropylsilyl)benzyl)amino)-N,N,3-trimethylbutanamide. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (dd, *J* = 7.3, 1.7 Hz, 1H), 6.91 (ddd, *J* = 7.3, 1.7, 0.9 Hz, 1H), 6.75 (td, *J* = 7.3, 0.8 Hz, 1H), 4.10 (d, *J* = 13.8 Hz, 1H), 3.46 (d, *J* = 13.8 Hz, 1H), 3.28 (d, *J* = 6.5 Hz, 1H), 3.04 (s, 3H), 2.83 (s, 3H), 1.84 (h, *J* = 6.7 Hz, 1H), 1.65 – 1.40 (m, 3H), 1.19 – 1.02 (m, 18H), 0.94 (ddd, *J* = 19.5, 6.7, 0.8 Hz, 6H). ^{13}C

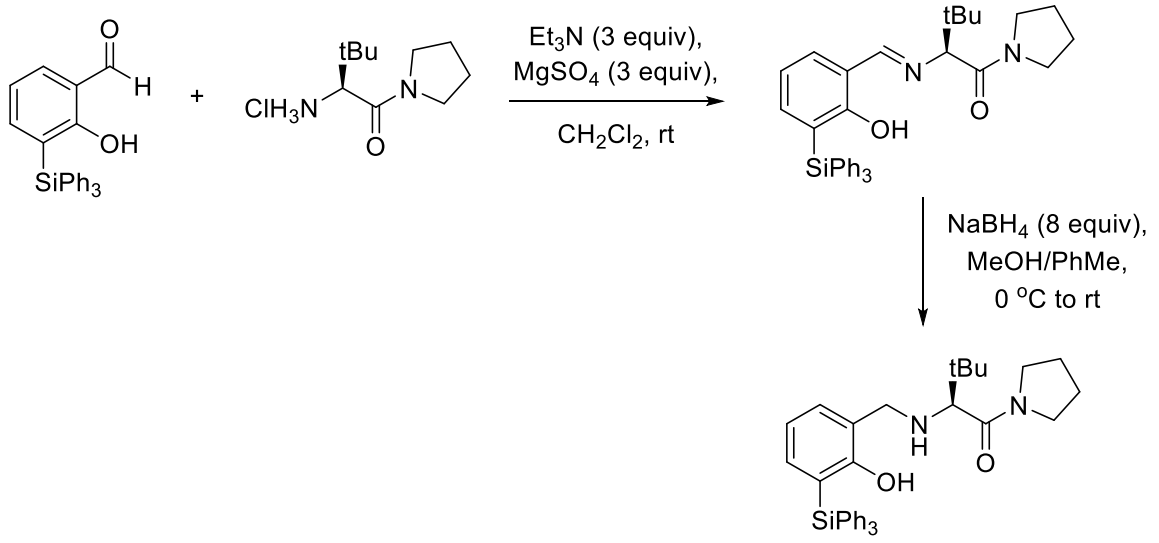
NMR (101 MHz, cdcl$_3$) δ 173.48, 163.32, 136.26, 129.71, 121.60, 121.27, 118.41, 60.61, 51.02, 36.92, 35.64, 31.45, 19.91, 19.04, 18.97, 18.15, 11.68. IR (neat): 3293, 2941, 2888, 2862, 1641, 1461, 1422, 1230, 882, 819, 751, 673. HRMS (ESI+): Calcd for $C_{23}H_{42}N_2O_2Si$ [M+H]+: 407.3016; Found: 407.3092. $[\alpha]^{20}_D$ = -60 (*c* = 1.0, $CHCl_3$).



(S)-2-((2-Hydroxy-3-(triphenylsilyl)benzyl)amino)-N,N,3-trimethylbutanamide. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.55 (m, 6H), 7.44 – 7.28 (m, 9H), 7.10 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.01 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 4.17 (d, *J* = 14.0 Hz, 1H), 3.46 (d, *J* = 14.1 Hz, 1H), 3.23 (d, *J* = 6.4 Hz, 1H), 3.02 (s, 3H), 2.82 (s, 3H), 1.75 (h, *J* = 6.8 Hz, 1H), 0.79 (t, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 173.41, 163.29, 137.80, 136.34, 135.10, 131.22, 129.10, 127.53, 121.69, 120.75, 118.96, 60.53, 50.72, 36.96, 35.66, 31.36, 19.85, 18.02. IR (neat): 3294, 3066, 3047, 2960, 2931, 1642, 1427, 1107, 823, 743, 701, 508. Calcd for $C_{32}H_{36}N_2O_2Si$ [M+H]+: 509.2546; Found: 509.2617. $[\alpha]^{20}_D$ = -80 (*c* = 1.0, $CHCl_3$).



(S)-2-((2-Hydroxy-3-(triphenylsilyl)benzyl)amino)-3-methyl-1-(pyrrolidin-1-yl)butan-1-one. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 – 7.61 (m, 6H), 7.39 (ddd, *J* = 13.9, 7.7, 6.0 Hz, 9H), 7.17 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.04 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.77 (t, *J* = 7.3 Hz, 1H), 4.26 (d, *J* = 14.1 Hz, 1H), 3.77 – 3.40 (m, 4H), 3.38 – 3.13 (m, 1H), 3.05 (d, *J* = 7.1 Hz, 2H), 2.03 – 1.76 (m, 4H), 0.87 (dd, *J* = 6.8, 5.0 Hz, 6H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 171.83, 163.36, 137.83, 136.37, 135.15, 131.14, 129.16, 127.59, 121.66, 120.82, 118.99, 62.83, 50.58, 46.34, 45.69, 31.44, 26.11, 24.21, 19.86, 18.45. IR (neat): 3281, 3066, 3048, 2958, 2873, 1635, 1427, 1107, 742, 701, 508. HRMS (ESI$_+$): Calcd for $C_{34}H_{38}N_2O_2Si$ [M+H]$_+$: 535.2703; Found: 535.2773. $[\alpha]^{20}_D$ = -80 (*c* = 1.0, $CHCl_3$).

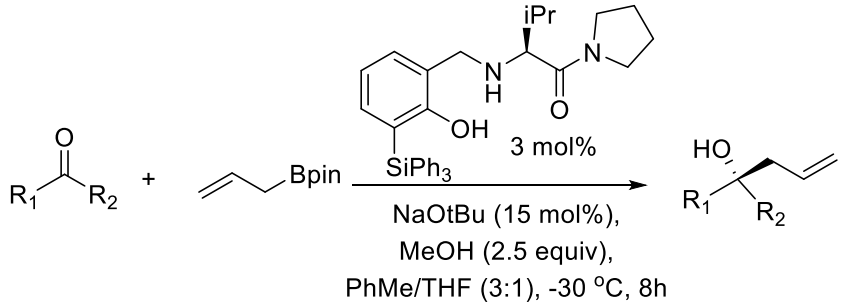


(S)-2-((2-Hydroxy-3-(triphenylsilyl)benzyl)amino)-3,3-dimethyl-1-(pyrrolidin-1-yl)butan-1-one. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.53 (m, 6H), 7.46 – 7.27 (m, 9H), 7.12 (dd, *J* = 7.3, 1.7 Hz, 1H), 6.98 (dd, *J* = 7.3, 1.7 Hz, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 4.22 (d, *J* = 14.0 Hz, 1H), 3.75 – 3.55 (m, 1H), 3.47 (dd, *J* = 13.2, 4.7 Hz, 2H), 3.31 – 3.13 (m, 1H), 3.05 (d, *J* = 9.4 Hz, 2H), 1.87 (q, *J* = 6.2, 5.7 Hz, 4H), 0.86 (s, 9H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 171.25, 163.27, 137.85, 136.32, 135.02, 131.07, 129.10, 127.53, 121.65, 120.79, 118.92, 64.52, 50.54, 47.01, 45.52, 34.21, 26.78, 26.18, 24.19. IR (neat): 3308, 3067, 3047, 2954, 2870, 1632, 1427, 1107, 742, 700, 507. HRMS (ESI$_+$): Calcd for $C_{35}H_{40}N_2O_2Si$ [M+H]$_+$: 549.2859; Found: 549.2934. $[\alpha]^{20}_D$ = -70 (*c* = 1.0, $CHCl_3$).

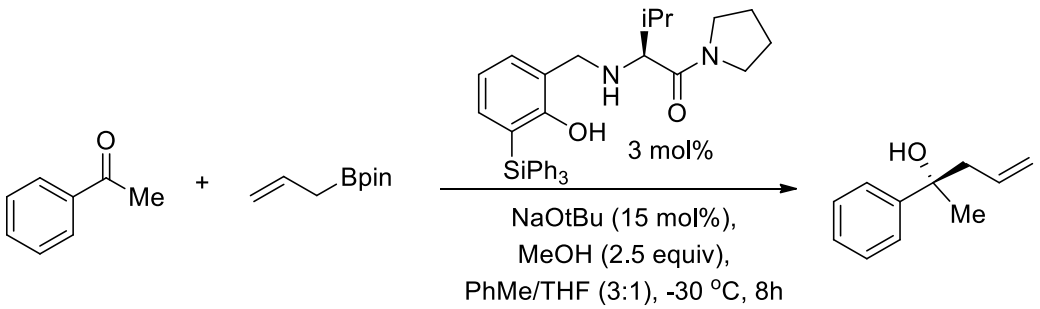
(*S*)-*N*-(*tert*-Butyl)-2-((2-hydroxy-3-methylbenzyl)amino)-3-methylbutanamide (3.14u, Scheme 3.17): Synthesized and purified analogously to the reported procedure to afford a white solid.[47] M.p. = 106–108 ºC. IR (neat): 3366 (w), 3299 (w), 3254 (w), 2965 (w, br), 1671 (m), 1639 (s), 1523 (w), 1467 (m), 1389 (w), 1365 (w), 1268 (w), 1259 (w),

(47) Silverio, D. L.; Torker, S.; Pilyugina, T.; Vieira, E. M.; Snapper, M. L.; Haeffner, F.; Hoveyda, A. H. *Nature* **2013**, *494*, 216–221.

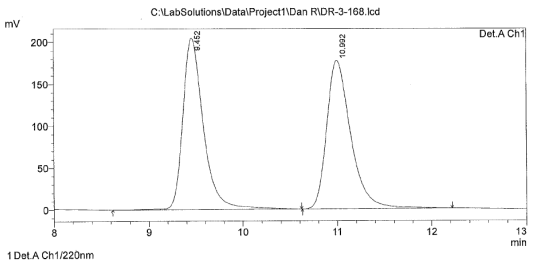
1221 (s), 1082 (m), 828 (m), 764 (s), 741 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 10.71 (1H, s), 7.06 (1H, d, J = 8.0 Hz), 6.80–6.78 (1H, m), 6.69 (1H, t, J = 7.4 Hz), 5.29 (1H, s), 4.07 and 3.64 (2H, AB_q, J_{AB} = 13.8 Hz), 2.51 (1H, d, J = 7.5 Hz), 2.24 (3H, s), 1.90–1.81 (1H, m), 1.39 (9H, s), 1.01 (3H, d, J = 6.8 Hz), 0.93 (3H, d, J = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 156.3, 130.2, 126.4, 125.4, 121.7, 118.8, 67.9, 52.0, 51.0, 31.7, 29.0, 19.8, 19.3, 15.8; HRMS Calcd. for $C_{17}H_{29}N_2O_2$ $[M + H]^+$: 293.22290; Found: 293.22305. $[\alpha]^{23.6}_D$ = –37.7 (c = 1.06, $CHCl_3$) for a >99:1 e.r. (assumed) sample.



General Procedure for Allylation of Ketones. Inside an N_2-filled glove box, aminophenol (8.5 mg, 0.015 mmol, 0.03 equiv), NaOtBu (7.5 mg, 0.075 mmol, 0.15 equiv), (pinacolato)allylboron (126 mg, 0.750 mmol, 1.50 equiv), MeOH (0.050 mL, 1.3 mmol, 2.5 equiv), PhMe (3 mL), and THF (0.5 mL) were added consecutively to a dry vial with a magnetic stir bar. The reaction mixture was sealed with a septum, removed from the glovebox and allowed to stir for 30 minutes in a bath precooled to -30 °C. A solution of the ketone (0.50 mmol, 1.0 equiv) in THF (0.5 mL) was added via syringe and the reaction mixture was allowed to stir at -30 °C for 8 hours. The reaction mixture was warmed to room temperature, filtered through silica gel washing with EtOAc, and concentrated under vacuum. The reaction mixture was purified by column chromatography to give the product.



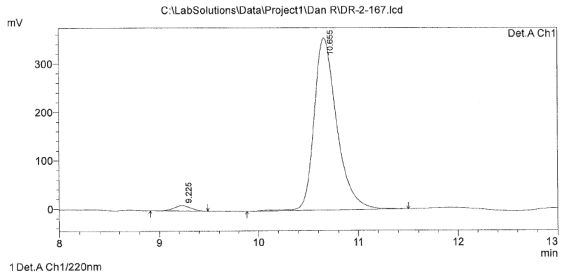
(S)-2-Phenylpent-4-en-2-ol. Based on the general procedure for allylation of ketones, ^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 (m, 2H), 7.25 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.15 (m, 1H), 5.54 (dddd, *J* = 16.8, 10.2, 8.2, 6.5 Hz, 1H), 5.03 (m, 2H), 2.59 (ddt, *J* = 13.7, 6.5, 1.3 Hz, 1H), 2.41 (ddt, *J* = 13.7, 8.2, 1.0 Hz, 1H), 2.05 (s, 1H), 1.45 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 147.64, 133.69, 128.15, 126.60, 124.76, 119.39, 73.62, 48.47, 29.86. IR (neat): 3433, 3060, 2977, 2929, 1445, 1069, 998, 913, 765, 699. HRMS (DART+): Calcd for $C_{11}H_{13}$ [M-OH]+: 145.1017; Found: 145.1019. $[\alpha]^{20}_{D}$ = -60 (*c* = 1.0, $CHCl_3$) for a 98:2 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H, 97% hexanes, 3% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.452	3135260	204050	49.994	53.571
2	10.992	3135980	176847	50.006	46.429
Total		6271241	380897	100.000	100.000

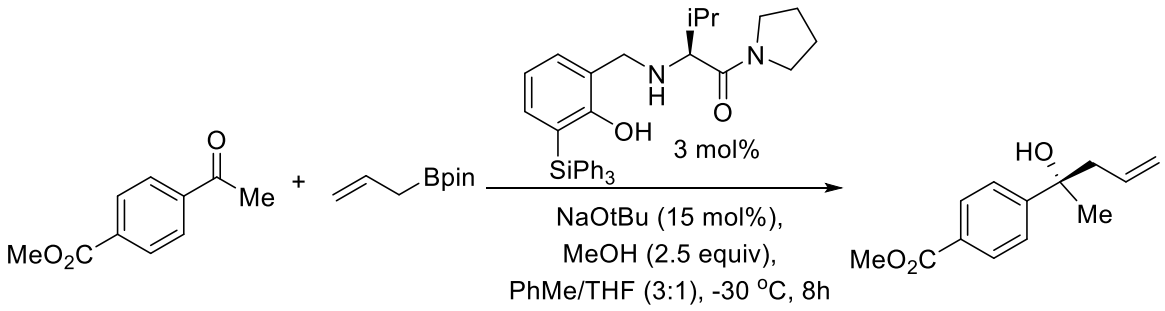


PeakTable

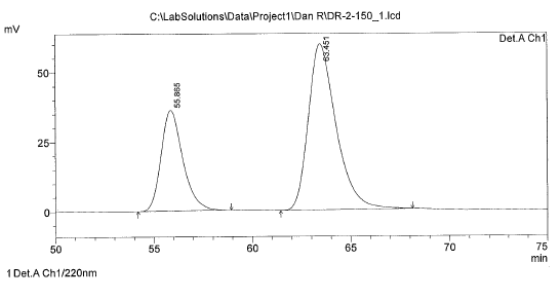
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.225	127712	11013	2.220	2.994
2	10.655	5623838	356809	97.780	97.006
Total		5751550	367822	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	9.5 min	59.994	1	9.2 min	2.220
2	11.0 min	50.006	2	10.7 min	97.780



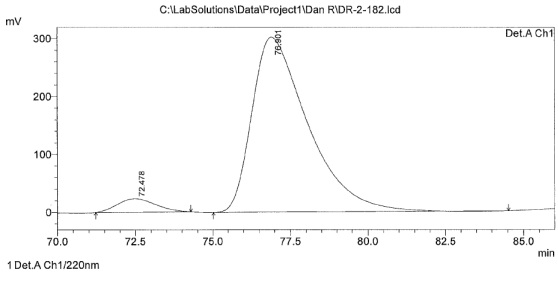
(S)-Methyl 4-(2-hydroxypent-4-en-2-yl)benzoate. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.90 (d, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 7.7 Hz, 2H), 5.51 (m, 1H), 5.02 (m, 2H), 3.81 (s, 3H), 2.57 (m, 1H), 2.42 (m, 1H), 1.47 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 166.98, 152.89, 133.09, 129.46, 128.38, 124.90, 119.68, 73.68, 52.01, 48.30, 29.64. IR (neat): 3481, 2978, 2952, 1722, 1610, 1436, 1280, 1114, 1017, 776, 710. Calcd for $C_{13}H_{15}O_2$ [M-OH]$_+$: 203.1072; Found: 203.1079. $[\alpha]^{20}_D$ = -50 (*c* = 1.0, $CHCl_3$) for a 95:5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H, 97% hexanes, 3% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	55.865	2793104	36076	32.306	37.733
2	63.451	5852658	59533	67.694	62.267
Total		8645762	95609	100.000	100.000

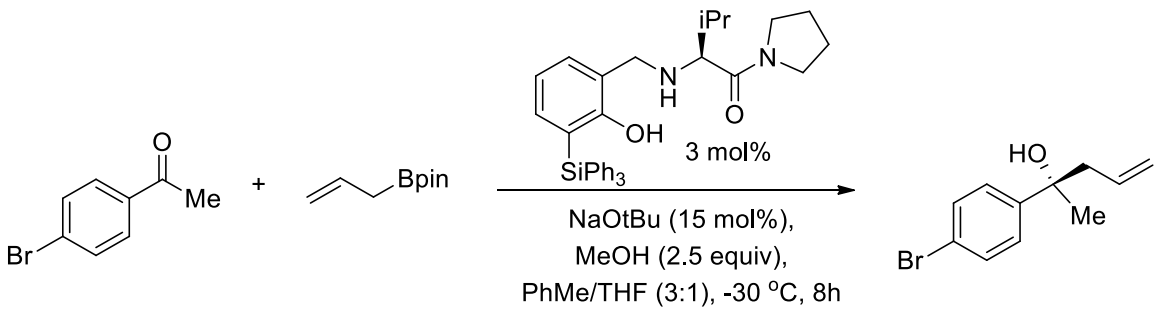


PeakTable

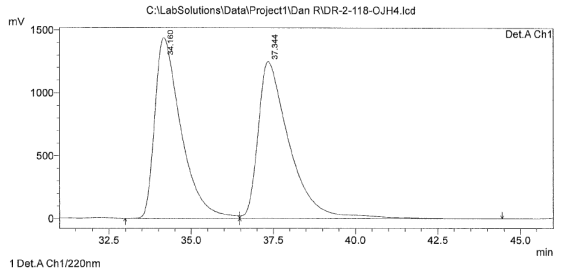
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	72.478	1984017	23298	5.013	7.164
2	76.901	37592629	301890	94.987	92.836
Total		39576646	325188	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	55.9 min	32.306	1	72.5 min	5.013
2	63.5 min	67.694	2	76.9 min	94.987



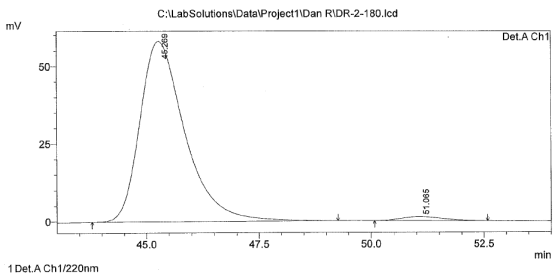
(S)-2-(4-Bromophenyl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 (m, 2H), 7.23 (m, 2H), 5.51 (m, 1H), 5.04 (ddt, *J* = 13.9, 2.3, 1.1 Hz, 2H), 2.54 (m, 1H), 2.38 (ddt, *J* = 13.7, 8.2, 1.0 Hz, 1H), 2.05 (s, 1H), 1.43 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 146.67, 133.17, 131.17, 126.73, 120.53, 119.82, 73.40, 48.31, 29.82. IR (neat): 3421, 3075, 2976, 2929, 1484, 1434, 1075, 1008, 918, 757. HRMS (DART+): Calcd for $C_{11}H_{12}Br$ [M-OH]+: 223.0122; Found: 223.0127. $[\alpha]^{20}_{D}$ = -30 (*c* = 1.0, $CHCl_3$) for a 98:2 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H, 99.5% hexanes, 0.5% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.160	79810048	1436828	49.120	53.559
2	37.344	82668782	1245866	50.880	46.441
Total		162478830	2682694	100.000	100.000

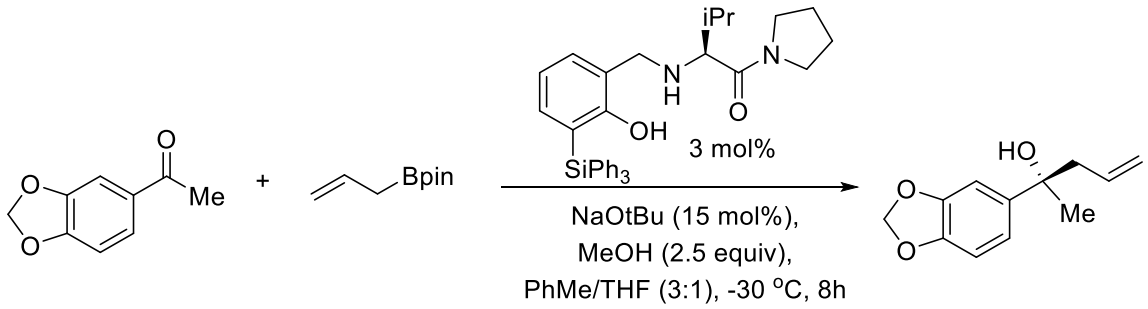


PeakTable

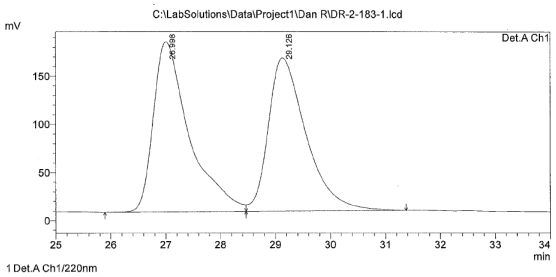
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	45.269	4050296	58142	97.947	97.871
2	51.065	84893	1265	2.053	2.129
Total		4135189	59407	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	34.2 min	49.120	1	45.3 min	97.947
2	37.3 min	50.880	2	51.1 min	2.053



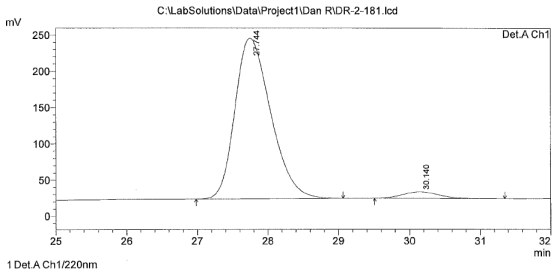
(S)-2-(Benzo[d][1,3]dioxol-5-yl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.94 (s, 1H), 6.88 (dt, *J* = 8.1, 1.5 Hz, 1H), 6.78 – 6.70 (m, 1H), 5.92 (s, 2H), 5.73 – 5.50 (m, 1H), 5.19 – 5.01 (m, 2H), 2.70 – 2.55 (m, 1H), 2.51 – 2.36 (m, 1H), 2.17 (s, 1H), 1.50 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 147.50, 146.04, 141.92, 133.67, 119.29, 117.81, 107.71, 105.90, 100.88, 73.53, 48.53, 29.92. IR (neat): 3450, 3077, 2977, 2897, 1504, 1487, 1434, 1237, 1039, 935, 812. HRMS (DART+): Calcd for $C_{12}H_{13}O_2$ [M-OH]+: 189.0916; Found: 189.0915. $[\alpha]^{20}_D$ = -40 (*c* = 1.0, $CHCl_3$) for a 96:4 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.998	8039105	176742	51.500	52.590
2	29.126	7570718	159331	48.500	47.410
Total		15609824	336073	100.000	100.000

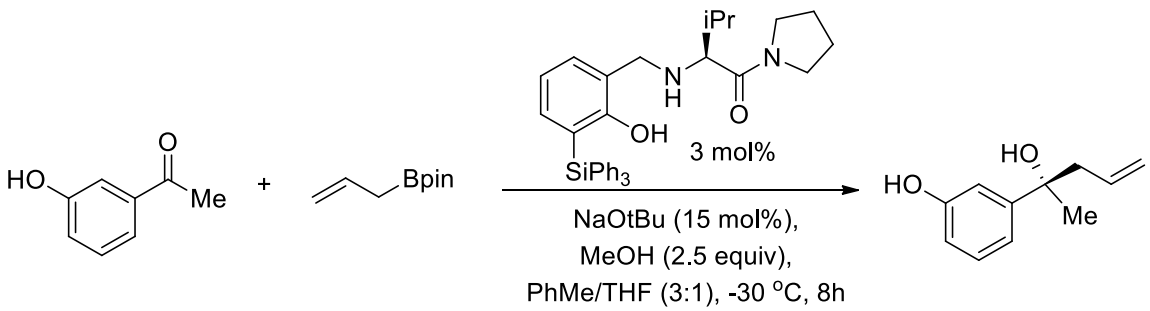


PeakTable

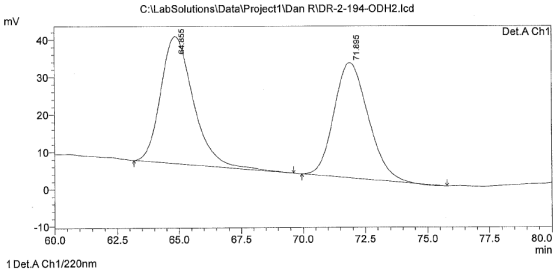
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.744	7833038	221746	96.093	96.122
2	30.140	318512	8947	3.907	3.878
Total		8151550	230692	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	27.0 min	51.500	1	27.7 min	96.093
2	29.1 min	48.500	2	30.1 min	3.907



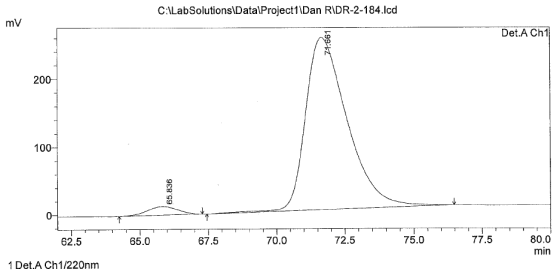
(S)-3-(2-Hydroxypent-4-en-2-yl)phenol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.19 (td, *J* = 7.9, 1.0 Hz, 1H), 7.03 (dt, *J* = 2.6, 1.2 Hz, 1H), 6.92 (m, 1H), 6.72 (dd, *J* = 8.1, 2.6 Hz, 1H), 6.03 (s, 1H), 5.61 (m, 1H), 5.13 (m, 2H), 2.67 (ddt, *J* = 13.8, 6.4, 1.3 Hz, 1H), 2.48 (ddt, *J* = 13.7, 8.3, 1.0 Hz, 1H), 2.40 (s, 1H), 1.53 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 155.75, 149.29, 133.38, 129.46, 119.71, 116.98, 113.70, 112.14, 74.06, 48.18, 29.69. IR (neat): 3371, 2977, 2932, 1589, 1447, 1238, 998, 920, 785, 701. HRMS (DART+): Calcd for $C_{11}H_{13}O$ [M-OH]+: 161.0966; Found: 161.0973. $[\alpha]^{20}_{D}$ = -40 (*c* = 1.0, $CHCl_3$) for a 96.5:3.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 97% hexanes, 3% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	64.855	3128693	34030	51.517	52.394
2	71.895	2944451	30920	48.483	47.606
Total		6073144	64949	100.000	100.000

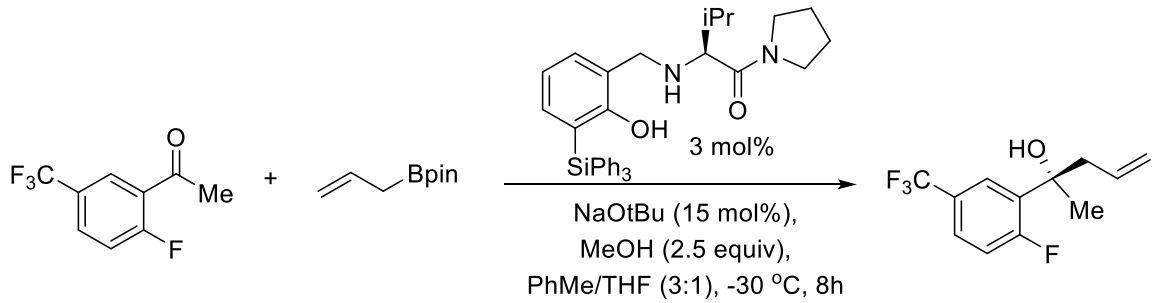


PeakTable

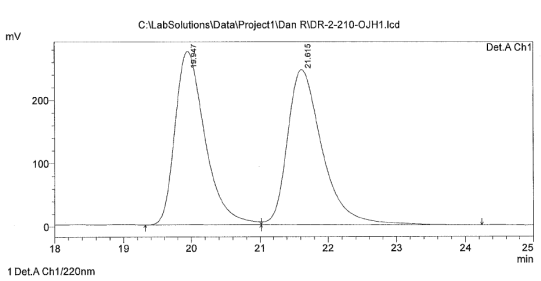
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	65.836	980888	12728	3.517	4.778
2	71.661	26909990	253632	96.483	95.222
Total		27890879	266360	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	64.9 min	51.517	1	65.8 min	3.517
2	71.9 min	48.483	2	71.7 min	96.483



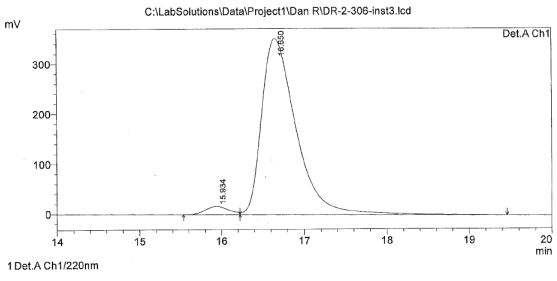
(S)-2-(2-Fluoro-5-(trifluoromethyl)phenyl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (dd, *J* = 7.4, 2.5 Hz, 1H), 7.57 – 7.43 (m, 1H), 7.12 (dd, *J* = 11.2, 8.4 Hz, 1H), 5.68 – 5.45 (m, 1H), 5.22 – 5.04 (m, 2H), 2.88 (ddd, *J* = 14.0, 6.2, 1.6 Hz, 1H), 2.66 – 2.48 (m, 1H), 2.37 (s, 1H), 1.62 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.88 – 159.02 (m), 135.16 (d, *J* = 13.8 Hz), 132.83, 126.59 (dd, *J* = 32.8, 3.4 Hz), 126.08 (dq, *J* = 10.8, 3.8 Hz), 125.38 (dq, *J* = 5.9, 3.7 Hz), 123.89 (q, *J* = 273.2 Hz), 120.20, 116.47 (d, *J* = 25.5 Hz), 72.48 (d, *J* = 4.6 Hz), 46.16 (d, *J* = 4.4 Hz), 28.19 (d, *J* = 3.7 Hz). ^{19}F NMR (376 MHz, cdcl$_3$) δ -61.95, -107.96. IR (neat): 3452, 2981, 2931, 1329, 1267, 1165, 1125, 1078, 917, 828, 619. HRMS (DART+): Calcd for $C_{12}H_{11}F_4$ [M-OH]$^+$: 231.0797; Found: 231.0802. $[\alpha]^{20}_D$ = -50 (*c* = 1.0, $CHCl_3$) for a 97:3 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H, 99.5% hexanes, 0.5% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.947	8363178	274252	49.131	52.773
2	21.615	8659168	245429	50.869	47.227
Total		17022347	519681	100.000	100.000

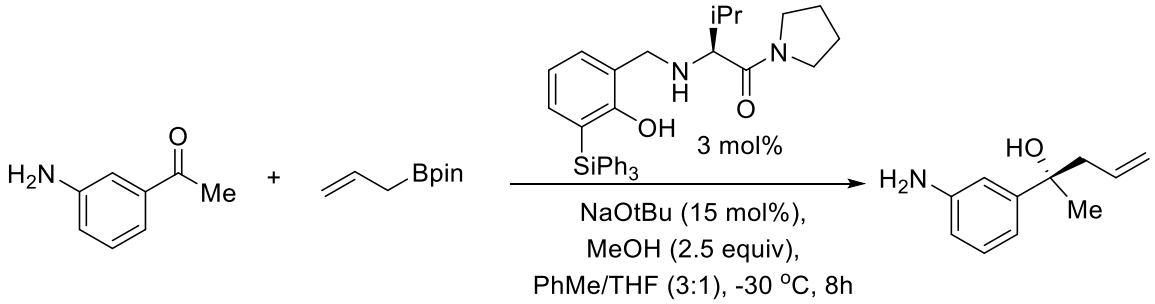


PeakTable

Detector A Ch1 220nm

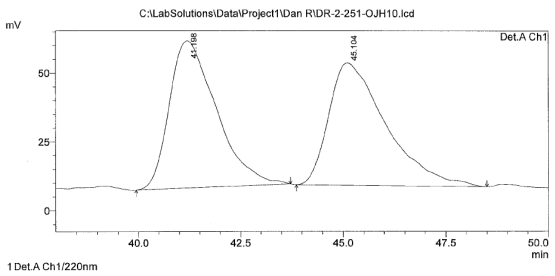
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.934	318444	16017	3.047	4.345
2	16.650	10134045	352588	96.953	95.655
Total		10452489	368605	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	19.9 min	49.131	1	15.9 min	3.047
2	21.6 min	50.869	2	16.7 min	96.953



(S)-2-(3-Aminophenyl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.12 (td, *J* = 7.7, 1.0 Hz, 1H), 6.88 – 6.75 (m, 2H), 6.57 (ddt, *J* = 7.9, 2.3, 1.1 Hz, 1H), 5.77 – 5.50 (m, 1H), 5.22 – 5.05 (m, 2H), 3.67 (s, 2H), 2.67 (ddd, *J* = 13.8, 6.3, 1.3 Hz, 1H), 2.56 – 2.35 (m, 1H), 2.01 (s, 1H), 1.51 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 149.02, 146.22, 133.80, 129.08, 119.30, 115.10, 113.34, 111.71, 73.51, 48.30, 29.83. IR (neat): 3447, 3354, 3234, 3073, 2975, 2929, 1606, 1452, 1372, 1145, 997, 915, 785, 701. HRMS (DART$_+$): Calcd for $C_{11}H_{14}N$ [M-OH]$_+$: 160.1126; Found: 160.1123. $[\alpha]^{20}_D$ = -40 (*c* = 0.5, $CHCl_3$) for a 91.5:8.5 e.r. sample. For determination of enantioselectivity, the product was treated with Boc_2O and guanidinium chloride in EtOH at 50 °C.

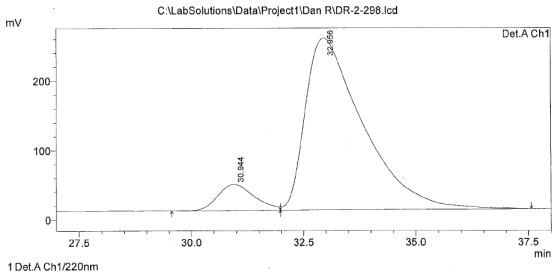
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H, 98% hexanes, 2% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.198	4282602	53427	49.893	54.549
2	45.104	4300887	44516	50.107	45.451
Total		8583489	97942	100.000	100.000

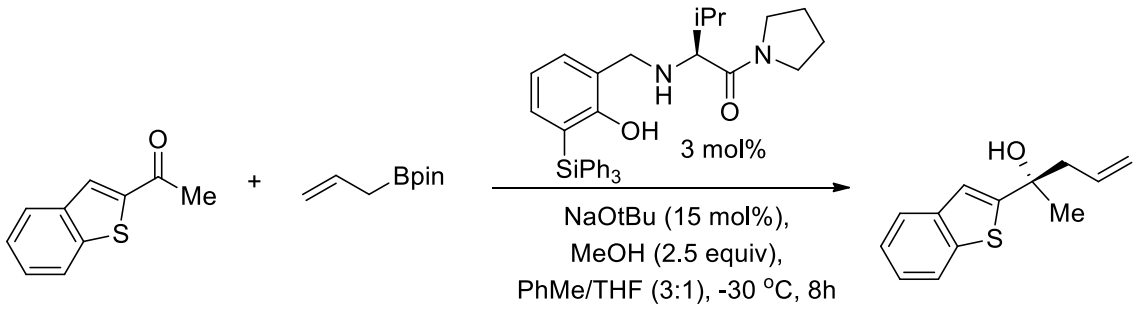


PeakTable

Detector A Ch1 220nm

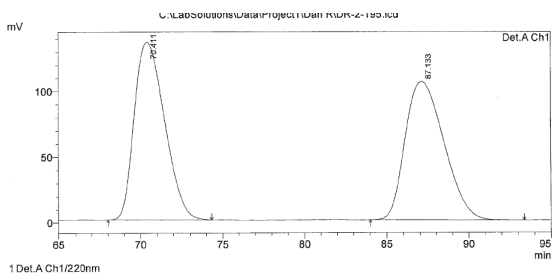
Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.944	2097038	37455	8.655	13.139
2	32.956	22130813	247619	91.345	86.861
Total		24227851	285073	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	41.2 min	49.893	1	30.9 min	8.655
2	45.1 min	50.107	2	33.0 min	91.345



(S)-2-(Benzo[b]thiophen-2-yl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.68 (m, 1H), 7.59 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.20 (m, 2H), 7.02 (s, 1H), 5.65 (dddd, *J* = 16.9, 10.1, 8.1, 6.4 Hz, 1H), 5.07 (m, 2H), 2.65 (m, 1H), 2.50 (ddd, *J* = 13.7, 8.2, 1.0 Hz, 1H), 2.39 (s, 1H), 1.56 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 153.60, 139.88, 139.29, 133.05, 124.21, 123.92, 123.34, 122.29, 119.98, 118.93, 73.15, 48.77, 30.18. IR (neat): 3411, 2976, 1434, 1374, 1111, 997, 920, 829, 745, 726, 607. HRMS (DART+): Calcd for $C_{13}H_{13}S$ [M-OH]+: 201.0738; Found: 201.0741. $[\alpha]^{20}_{D}$ = -70 (*c* = 1.0, $CHCl_3$) for a 97.5:2.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in

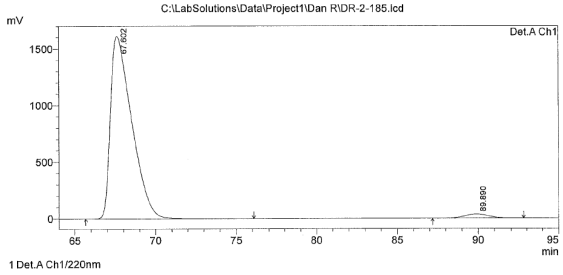
comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	70.411	17388285	135472	50.098	56.215
2	87.133	17320056	105518	49.902	43.785
Total		34708341	240990	100.000	100.000

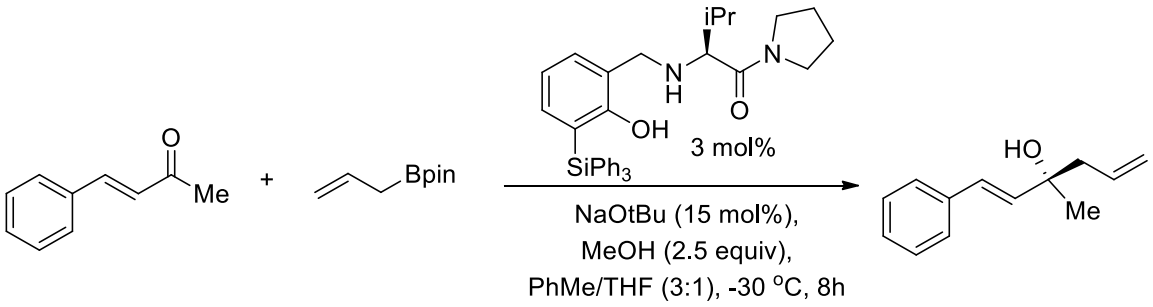


PeakTable

Detector A Ch1 220nm

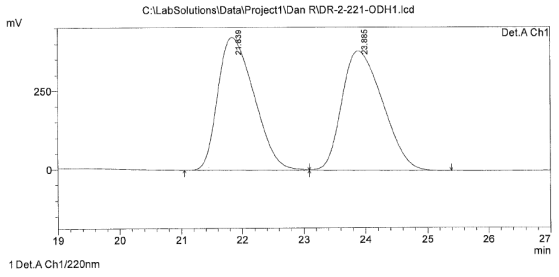
Peak#	Ret. Time	Area	Height	Area %	Height %
1	67.602	148311258	1611745	97.556	97.781
2	89.890	3715452	36584	2.444	2.219
Total		152026710	1648329	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	70.4 min	50.098	1	67.6 min	97.556
2	87.1 min	49.902	2	89.9 min	2.444



(S,E)-3-Methyl-1-phenylhexa-1,5-dien-3-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.28 (d, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.12 (m, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 6.20 (d, *J* = 16.0 Hz, 1H), 5.74 (dddd, *J* = 16.0, 11.3, 8.2, 6.8 Hz, 1H), 5.05 (m, 2H), 2.34 (ddt, *J* = 13.7, 6.7, 1.3 Hz, 1H), 2.26 (ddt, *J* = 13.5, 8.0, 0.9 Hz, 1H), 1.86 (s, 1H), 1.28 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 136.93, 136.25, 133.62, 128.57, 127.41, 126.43, 119.24, 72.37, 47.36, 27.95. IR (neat): 3409, 3077, 3026, 2975, 2928, 1493, 1447, 1102, 969, 916, 747, 693. HRMS (DART+): Calcd for $C_{13}H_{15}$ [M-OH]+: 171.1174; Found: 171.1175. $[\alpha]^{20}_{D}$ = -80 (*c* = 1.0, $CHCl_3$) for a 95.5:4.5 e.r. sample. Enantiomeric purity was

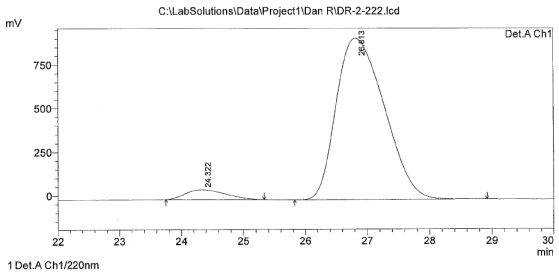
determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 90% hexanes, 10% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.839	17467275	423299	50.124	52.626
2	23.885	17380965	381059	49.876	47.374
Total		34848240	804358	100.000	100.000

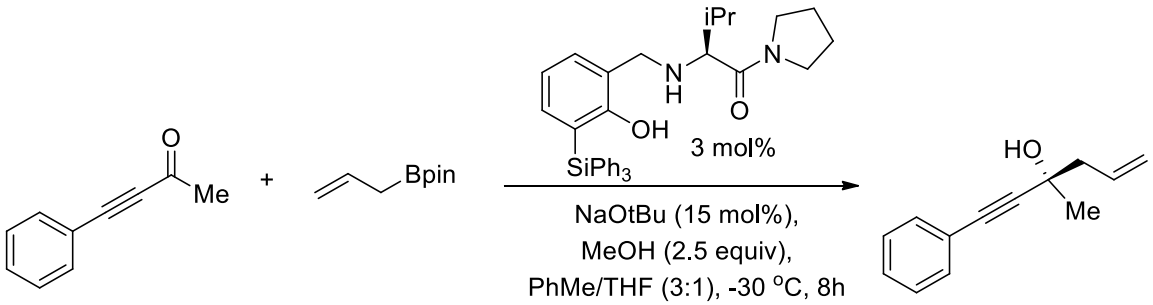


PeakTable

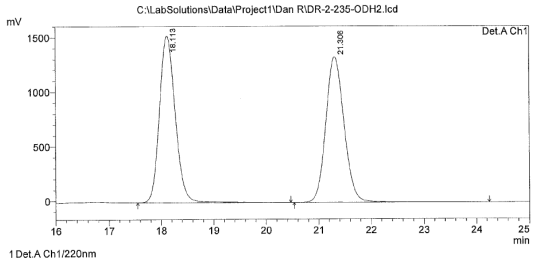
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.322	2462685	55449	4.730	5.642
2	26.813	49606024	927353	95.270	94.358
Total		52068709	982802	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	21.8 min	50.124	1	24.3 min	4.730
2	23.9 min	49.876	2	26.8 min	95.270



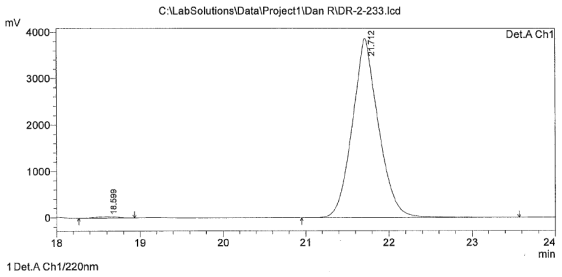
(S)-3-Methyl-1-phenylhex-5-en-1-yn-3-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 6.86 (dd, *J* = 6.6, 3.1 Hz, 2H), 6.73 (dd, *J* = 4.7, 1.9 Hz, 3H), 5.48 (m, 1H), 4.66 (m, 2H), 2.01 (m, 1H), 1.93 (m, 2H), 1.03 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 133.41, 131.66, 128.27, 128.23, 122.68, 119.51, 92.50, 83.59, 67.48, 48.31, 29.30. IR (neat): 3378, 3078, 2980, 2931, 1489, 1369, 1108, 996, 917, 755, 690. HRMS (DART+): Calcd for $C_{13}H_{13}$ [M-OH]+: 169.1017; Found: 169.1012. $[\alpha]^{20}_{D}$ = -40 (*c* = 1.0, $CHCl_3$) for a 99.5:0.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 90% hexanes, 10% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.113	32036417	1527388	49.537	53.352
2	21.306	32635473	1335481	50.463	46.648
Total		64671890	2862870	100.000	100.000

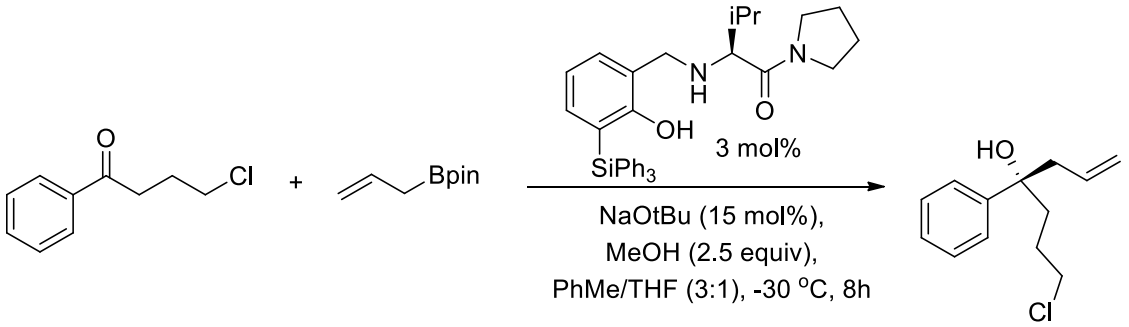


PeakTable

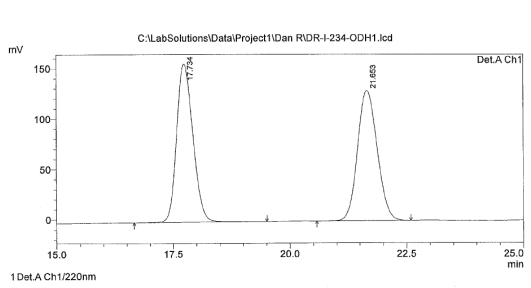
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.599	471967	26773	0.557	0.687
2	21.712	84252555	3869929	99.443	99.313
Total		84724522	3896703	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	18.1 min	49.537	1	18.6 min	0.557
2	21.3 min	50.463	2	21.7 min	99.443



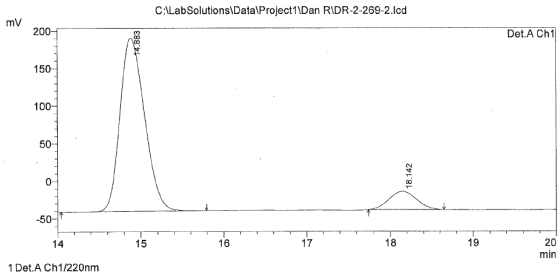
(S)-7-Chloro-4-phenylhept-1-en-4-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 (m, 4H), 7.24 (m, 1H), 5.54 (dddd, *J* = 17.2, 10.1, 8.7, 6.0 Hz, 1H), 5.14 (m, 2H), 3.46 (m, 2H), 2.74 (ddt, *J* = 13.7, 6.0, 1.3 Hz, 1H), 2.50 (dd, *J* = 13.7, 8.8 Hz, 1H), 2.12 (s, 1H), 1.90 (m, 3H), 1.53 (ddtd, *J* = 13.9, 10.7, 6.7, 5.0 Hz, 1H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 145.33, 133.07, 128.23, 126.65, 125.17, 120.12, 75.37, 47.69, 45.54, 39.90, 26.94. IR (neat): 3555, 3443, 3060, 3026, 2957, 1445, 998, 920, 764, 702. HRMS (DART+): Calcd for $C_{13}H_{16}Cl$ [M-OH]+: 207.0941; Found: 207.0941. $[\alpha]^{20}_{D}$ = -40 (*c* = 1.0, $CHCl_3$) for a 89:11 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.734	3841436	157234	50.210	54.832
2	21.653	3809242	129520	49.790	45.168
Total		7650677	286754	100.000	100.000

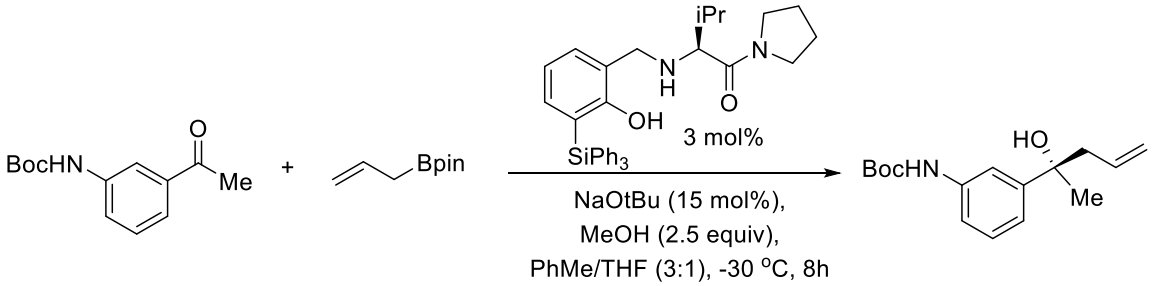


PeakTable

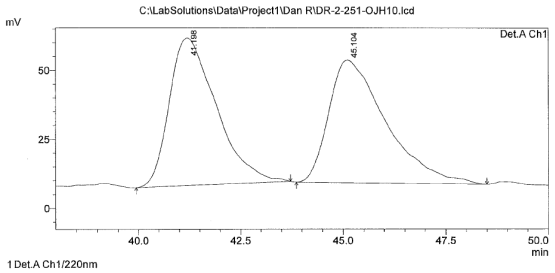
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.883	4701395	230394	89.240	90.383
2	18.142	566854	24515	10.760	9.617
Total		5268249	254908	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	17.7 min	50.210	1	14.9 min	89.240
2	21.7 min	49.790	2	18.1 min	10.760



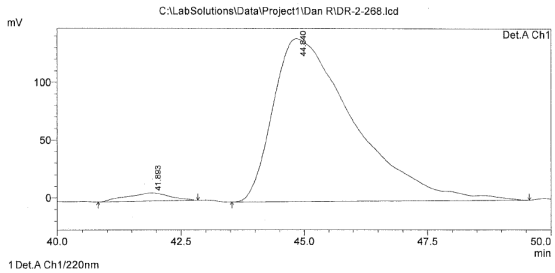
(S)-tert-Butyl (3-(2-hydroxypent-4-en-2-yl)phenyl)carbamate. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.40 (s, 1H), 7.24 (m, 2H), 7.06 (dt, *J* = 7.4, 1.6 Hz, 1H), 6.59 (s, 1H), 5.60 (dddd, *J* = 16.8, 10.2, 8.3, 6.4 Hz, 1H), 5.09 (m, 2H), 2.65 (ddt, *J* = 13.7, 6.4, 1.3 Hz, 1H), 2.46 (ddt, *J* = 13.7, 8.3, 1.0 Hz, 1H), 2.20 (s, 1H), 1.49 (s, 12H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 152.76, 148.73, 138.27, 133.61, 128.75, 119.48, 119.41, 116.81, 115.17, 80.40, 73.59, 48.32, 29.82, 28.33. IR (neat): 3330, 2976, 2931, 1700, 1609, 1542, 1432, 1367, 1240, 1159, 702. HRMS (DART+): Calcd for $C_{16}H_{22}NO_2$ [M-OH]+: 260.1651; Found: 260.1656. $[\alpha]^{20}_D$ = -30 (*c* = 1.0, $CHCl_3$) for a 97.5:2.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H, 98% hexanes, 2% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.198	4282602	53427	49.893	54.549
2	45.104	4300887	44516	50.107	45.451
Total		8583489	97942	100.000	100.000

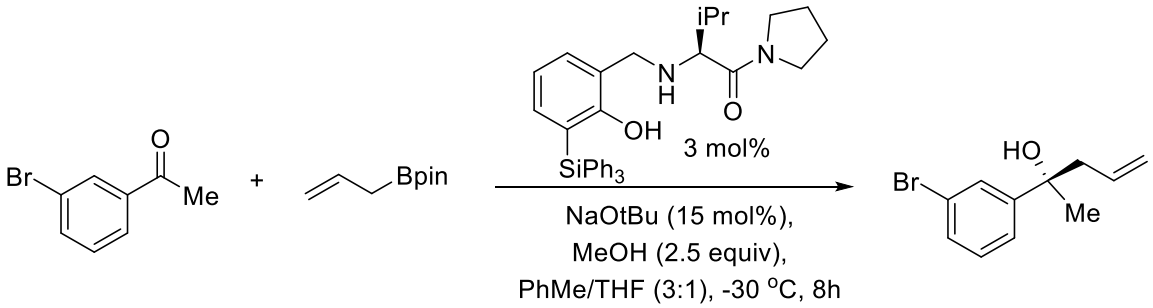


PeakTable

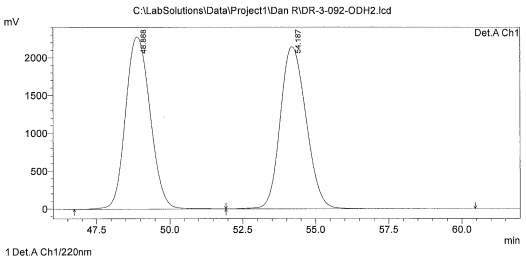
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	41.893	422034	7003	2.554	4.730
2	44.840	16101216	141036	97.446	95.270
Total		16523250	148039	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	41.2 min	49.893	1	41.9 min	2.554
2	45.1 min	50.107	2	44.8 min	97.446



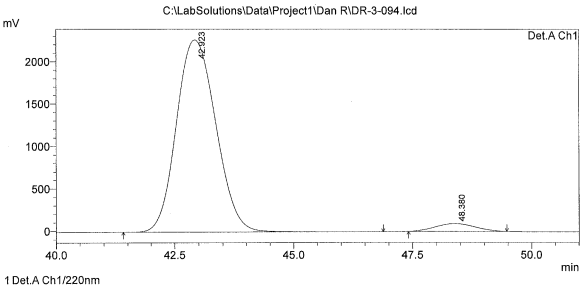
(S)-2-(3-Bromophenyl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (t, *J* = 1.9 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.17 (t, *J* = 7.9 Hz, 1H), 5.67 – 5.49 (m, 1H), 5.10 (dtt, *J* = 13.7, 2.1, 0.9 Hz, 2H), 2.60 (ddt, *J* = 13.8, 6.5, 1.3 Hz, 1H), 2.44 (ddt, *J* = 13.8, 8.2, 1.0 Hz, 1H), 2.33 (s, 1H), 1.49 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 150.09, 133.14, 129.76, 129.68, 128.16, 123.55, 122.52, 119.87, 73.40, 48.32, 29.76. IR (neat): 3433, 2976, 1565, 1415, 1072, 996, 918, 784, 764, 698. HRMS (DART+): Calcd for $C_{11}H_{12}Br$ [M-OH]+: 223.0122; Found: 223.0121. $[\alpha]^{20}_{D}$ = -50 (*c* = 1.0, $CHCl_3$) for a 96:4 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	48.888	132978186	2281009	49.777	51.509
2	54.187	134172210	2147328	50.223	48.491
Total		267150396	4428337	100.000	100.000

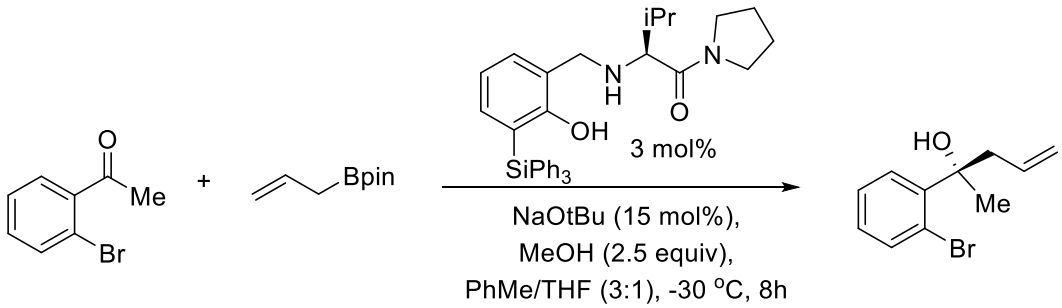


PeakTable

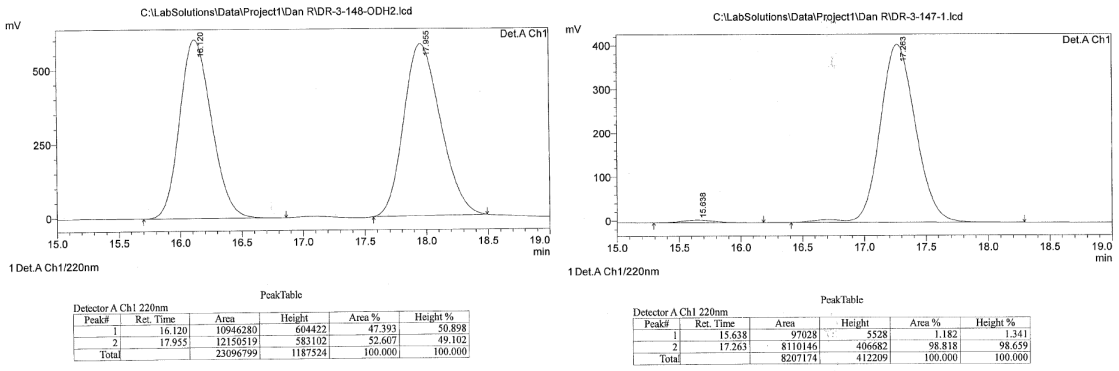
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	42.923	129603990	2266771	96.073	96.081
2	48.380	5297811	92451	3.927	3.919
Total		134901800	2359222	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	48.9 min	49.777	1	42.9 min	96.073
2	54.2 min	50.223	2	48.4 min	3.919



(S)-2-(2-Bromophenyl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.58 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.30 (ddd, *J* = 8.0, 7.2, 1.3 Hz, 1H), 7.09 (ddd, *J* = 7.9, 7.3, 1.8 Hz, 1H), 5.65 – 5.45 (m, 1H), 5.20 – 5.02 (m, 2H), 3.28 (ddt, *J* = 14.0, 6.3, 1.3 Hz, 1H), 2.74 – 2.55 (m, 2H), 1.73 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 144.98, 135.00, 133.58, 128.50, 128.22, 127.38, 119.93, 119.31, 74.61, 45.04, 27.29. IR (neat): 3447, 3091, 2974, 2930, 2196, 2179, 1431, 1374, 1269, 1016, 919, 758, 640, 462, 419. Calcd for $C_{11}H_{12}Br$ [M-OH]$_+$: 223.0122; Found: 223.0118. $[\alpha]^{20}_D$ = -32 (*c* = 1.3, $CHCl_3$) for a 99:1 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

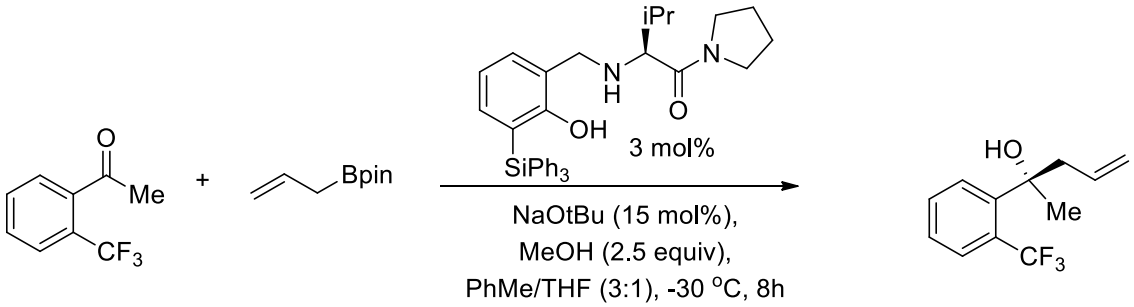
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.120	10946280	604422	47.393	50.898
2	17.955	12150519	583102	52.607	49.102
Total		23096799	1187524	100.000	100.000

PeakTable

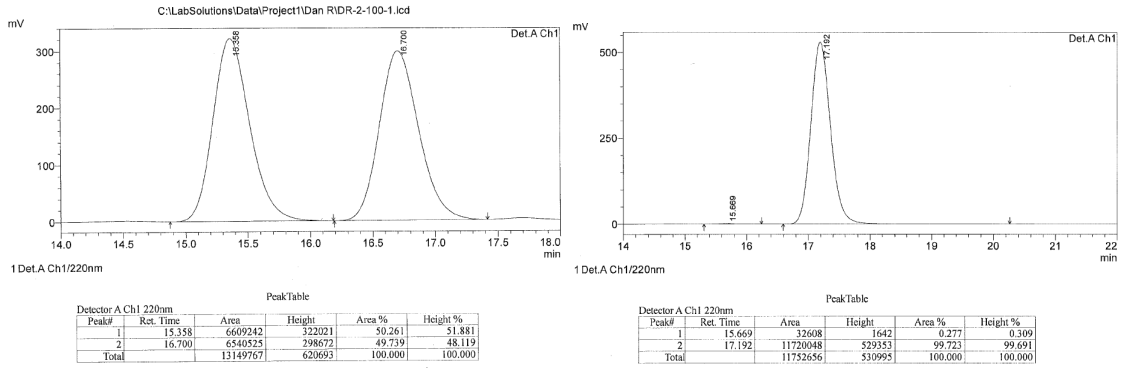
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.638	97028	5528	1.182	1.341
2	17.263	8110146	406682	98.818	98.659
Total		8207174	412209	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	16.1 min	47.393	1	15.6 min	1.182
2	18.0 min	52.607	2	17.3 min	98.818



(S)-2-(2-(Trifluoromethyl)phenyl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.47 (td, *J* = 7.7, 1.5 Hz, 1H), 7.31 (tq, *J* = 7.1, 1.1 Hz, 1H), 5.74 – 5.51 (m, 1H), 5.21 – 5.06 (m, 2H), 2.98 – 2.83 (m, 1H), 2.61 – 2.46 (m, 1H), 2.41 (s, 1H), 1.62 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.69, 133.25, 131.40, 128.50, 127.95 (q, *J* = 7.4 Hz), 127.32 (q, *J* = 30.9 Hz), 126.81, 124.79 (q, *J* = 274.4 Hz), 120.01, 74.57, 48.25, 30.56. ^{19}F NMR (376 MHz, cdcl$_3$) δ -54.07. IR (neat): 3469, 3076, 2980, 2932, 1302, 1271, 1131, 1033, 920, 767. HRMS (DART+): Calcd for $C_{12}H_{12}F_3$ [M-OH]+: 213.0891; Found: 213.0895. $[\alpha]^{20}_D$ = -30 (*c* = 1.0, $CHCl_3$) for a 99.5:0.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel AD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

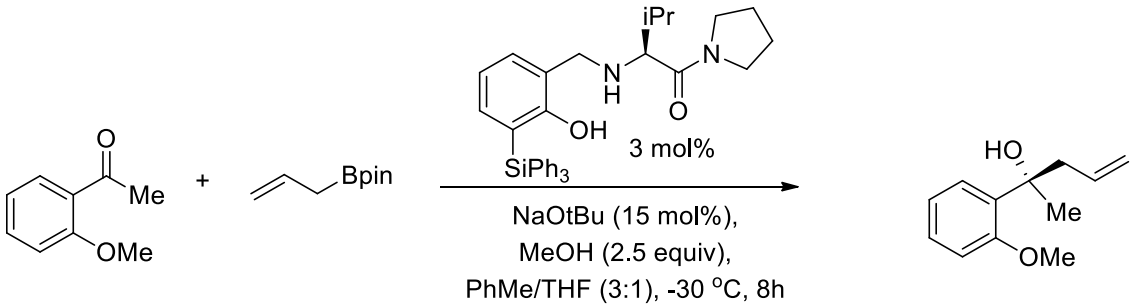
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.358	6609242	322021	50.261	51.881
2	16.700	6540525	298672	49.739	48.119
Total		13149767	620693	100.000	100.000

PeakTable

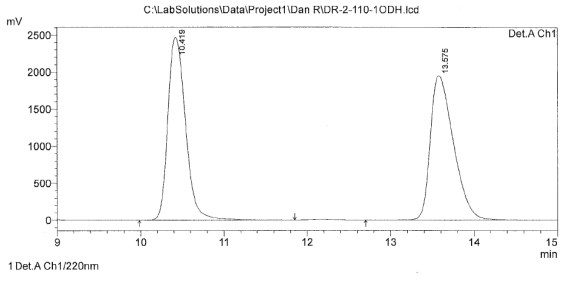
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.669	32608	1642	0.277	0.309
2	17.192	11720048	529353	99.723	99.691
Total		11752656	530995	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	15.4 min	50.261	1	15.7 min	0.277
2	16.7 min	49.739	2	17.2 min	99.723



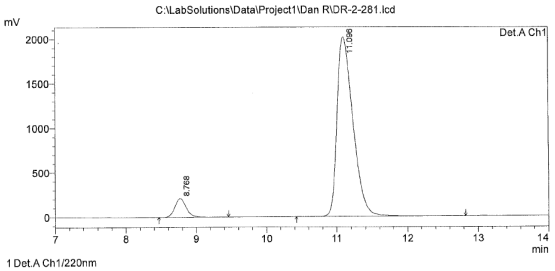
(S)-2-(2-Methoxyphenyl)pent-4-en-2-ol. 1H NMR (400 MHz, Chloroform-*d*) δ 7.32 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.23 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 6.98 – 6.86 (m, 2H), 5.77 – 5.52 (m, 1H), 5.11 – 4.94 (m, 2H), 3.89 (s, 1H), 3.86 (s, 3H), 2.82 (ddt, *J* = 13.7, 6.9, 1.3 Hz, 1H), 2.60 (ddt, *J* = 13.8, 7.7, 1.2 Hz, 1H), 1.57 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 156.60, 134.79, 134.54, 128.18, 126.79, 120.79, 117.71, 111.23, 74.20, 55.25, 46.58, 26.96. IR (neat): 3528, 3073, 2974, 2940, 2838, 1672, 1598, 1486, 1436, 1358, 1291, 1179, 1024, 754, 594. HRMS (DART+): Calcd for $C_{12}H_{15}O$ [M-OH]+: 175.1123; Found: 175.1123. $[\alpha]^{20}_D$ = -20 (*c* = 1.0, $CHCl_3$) for a 93:7 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.419	36467568	2467496	49.223	55.894
2	13.575	37618739	1947117	50.777	44.106
Total		74086307	4414613	100.000	100.000

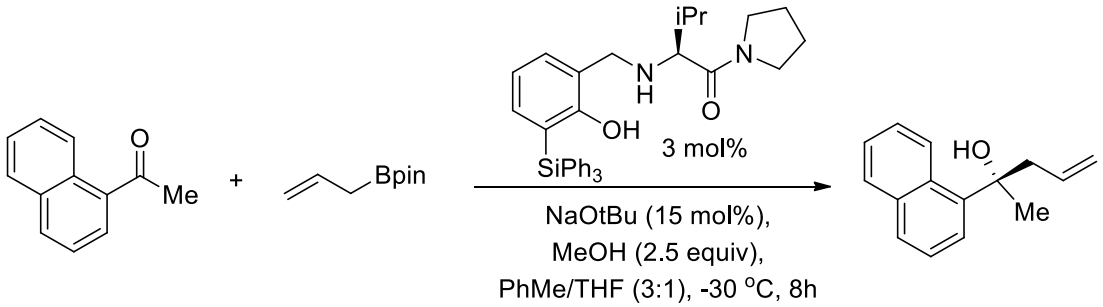


PeakTable

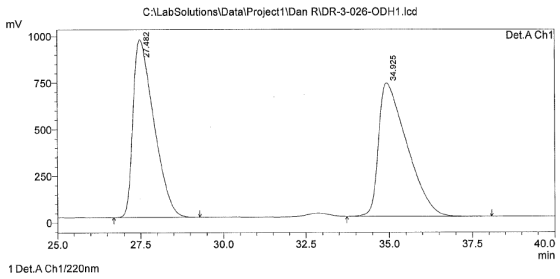
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.768	2359055	209969	7.024	9.414
2	11.096	31226466	2020394	92.976	90.586
Total		33585521	2230363	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	10.4 min	49.223	1	8.8 min	7.024
2	13.6 min	50.777	2	11.1 min	92.976



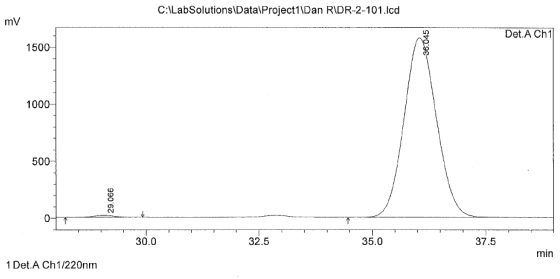
(S)-2-(Naphthalen-1-yl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.78 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.89 (m, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.61 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.49 (m, 3H), 5.69 (dddd, *J* = 17.0, 10.1, 7.9, 6.8 Hz, 1H), 5.15 (m, 2H), 3.13 (ddt, *J* = 13.8, 6.7, 1.2 Hz, 1H), 2.86 (ddt, *J* = 13.9, 8.0, 1.1 Hz, 1H), 2.37 (s, 1H), 1.85 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 142.18, 134.92, 133.93, 130.82, 129.22, 128.60, 126.83, 125.33, 125.13, 124.79, 123.69, 119.23, 75.25, 47.25, 29.61. IR (neat): 3351, 2976, 2202, 2165, 2045, 1971, 1375, 923, 804, 777, 419. HRMS (DART$_+$): Calcd for $C_{15}H_{15}$ [M-OH]$_+$: 195.1174; Found: 195.1176. $[\alpha]^{20}_D$ = -20 (*c* = 1.0, $CHCl_3$) for a 99:1 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H, 95% hexanes, 5% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.482	41530254	953007	49.388	57.079
2	34.925	42560256	716618	50.612	42.921
Total		84090510	1669625	100.000	100.000

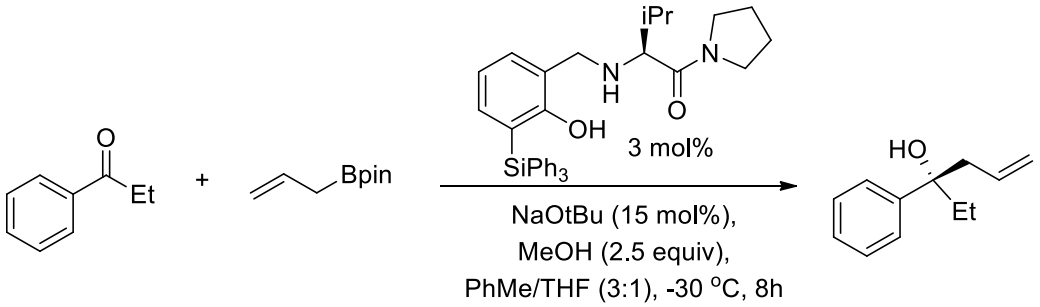


PeakTable

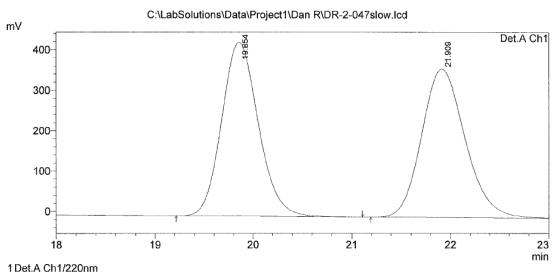
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.066	647349	18169	0.811	1.139
2	36.045	79134934	1577271	99.189	98.861
Total		79782283	1595440	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	27.5 min	49.388	1	29.1 min	0.811
2	34.9 min	50.612	2	36.0 min	99.189



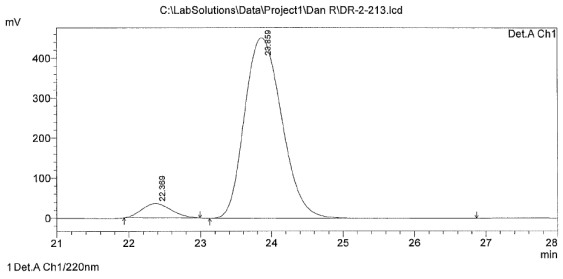
(S)-3-Phenylhex-5-en-3-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.30 (m, 2H), 7.24 (m, 2H), 7.14 (m, 1H), 5.49 (dddd, *J* = 17.1, 10.1, 8.6, 6.1 Hz, 1H), 5.03 (m, 2H), 2.63 (ddt, *J* = 13.7, 6.1, 1.4 Hz, 1H), 2.41 (ddt, *J* = 13.8, 8.7, 0.9 Hz, 1H), 1.95 (s, 1H), 1.76 (m, 2H), 0.68 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 145.74, 133.59, 128.02, 126.39, 125.38, 119.46, 75.99, 46.91, 35.21, 7.82. IR (neat): 3464, 3060, 2974, 1446, 979, 916, 761, 700. HRMS (DART+): Calcd for $C_{12}H_{15}$ [M-OH]+: 159.1174; Found: 159.1168. $[\alpha]^{20}_{D}$ = -60 (*c* = 1.0, $CHCl_3$) for a 94:6 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel AD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.854	11196230	430143	49.870	53.928
2	21.909	11254710	367485	50.130	46.072
Total		22450941	797628	100.000	100.000

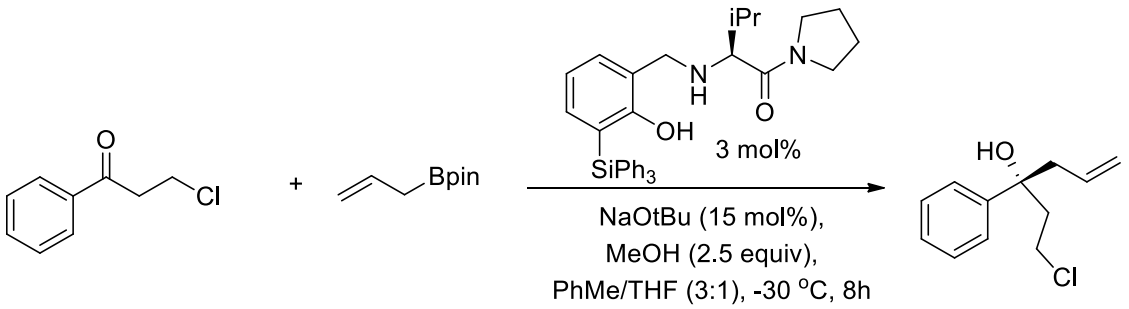


PeakTable

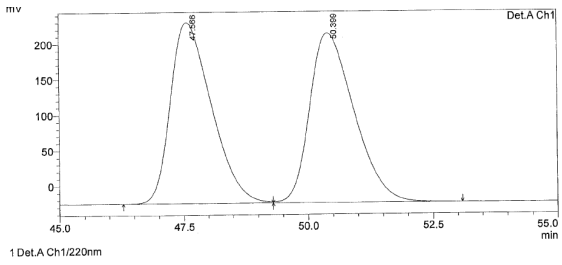
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.369	1019399	35523	5.846	7.294
2	23.859	16418548	451471	94.154	92.706
Total		17437947	486994	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	19.9 min	49.870	1	22.4 min	5.846
2	21.9 min	50.130	2	23.9 min	94.154



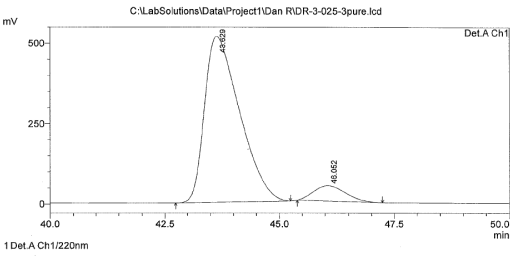
(R)-1-Chloro-3-phenylhex-5-en-3-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 (m, 4H), 7.24 (tdd, *J* = 5.7, 3.2, 2.0 Hz, 1H), 5.51 (ddddd, *J* = 17.2, 10.0, 8.6, 6.0, 1.3 Hz, 1H), 5.15 (m, 2H), 3.55 (m, 1H), 3.20 (m, 1H), 2.72 (m, 1H), 2.50 (dd, *J* = 13.7, 8.7 Hz, 1H), 2.30 (m, 2H), 2.20 (s, 1H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 144.31, 132.47, 128.40, 126.94, 124.96, 120.57, 75.16, 47.75, 45.46, 40.11. IR (neat): 3553, 3462, 3060, 3027, 2976, 2929, 1446, 1059, 998, 923, 701, 668, 584. HRMS (DART^{+}): Calcd for $C_{13}H_{14}Cl$ $[M\text{-}OH]^{+}$: 193.0784; Found: 193.0786. $[\alpha]^{20}_{D}$ = -42 (*c* = 1.2, $CHCl_3$) for a 92.5:7.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99.5% hexanes, 0.5% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	47.566	14738182	254993	49.929	51.622
2	50.399	14780333	238972	50.071	48.378
Total		29518515	493965	100.000	100.000

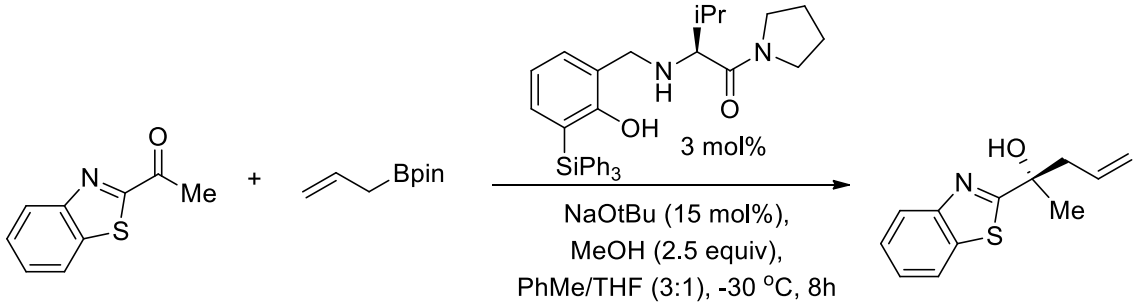


PeakTable

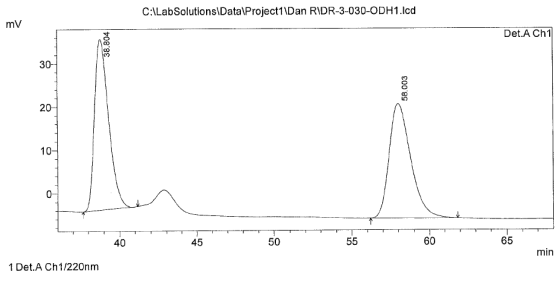
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	43.629	27454156	515936	92.305	91.493
2	46.052	2288810	47973	7.695	8.507
Total		29742966	563909	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	47.6 min	49.929	1	43.6 min	92.305
2	50.4 min	50.071	2	46.0 min	7.695



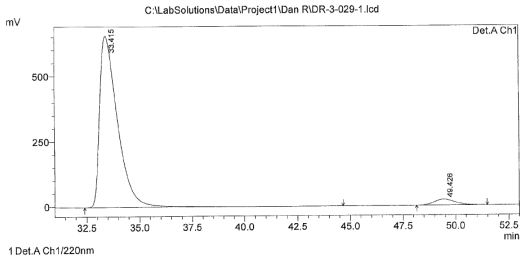
(S)-2-(Benzo[d]thiazol-2-yl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.99 (d, *J* = 8.8 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.47 (m, 1H), 7.37 (t, *J* = 8.2 Hz, 1H), 5.76 (dddd, *J* = 16.8, 10.1, 8.3, 6.4 Hz, 1H), 5.19 (m, 2H), 3.23 (s, 1H), 2.95 (ddt, *J* = 13.7, 6.3, 1.2 Hz, 1H), 2.67 (ddt, *J* = 13.7, 8.3, 1.0 Hz, 1H), 1.71 (s, 3H). ^{13}C NMR (101 MHz, $cdcl_3$) δ 179.29, 153.25, 135.31, 132.40, 125.95, 124.81, 122.86, 121.73, 120.39, 74.98, 47.46, 29.00. IR (neat): 3205, 2927, 2017, 1589, 1499, 1452, 1316, 745. HRMS (DART+): Calcd for $C_{12}H_{14}NOS$ $[M+H]^+$: 220.0796; Found: 220.0792. $[\alpha]^{20}_D$ = -20 (*c* = 1.0, $CHCl_3$) for a 96:4 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99.5% hexanes, 0.5% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	38.804	2456607	39479	48.921	59.760
2	58.003	2564975	26584	51.079	40.240
Total		5021582	66063	100.000	100.000

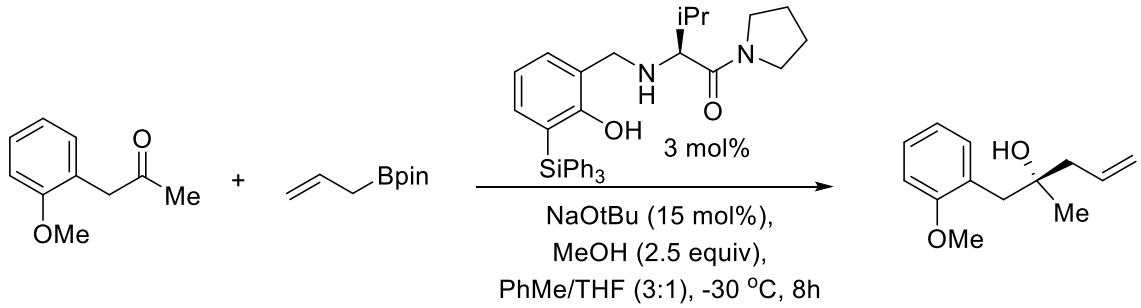


PeakTable

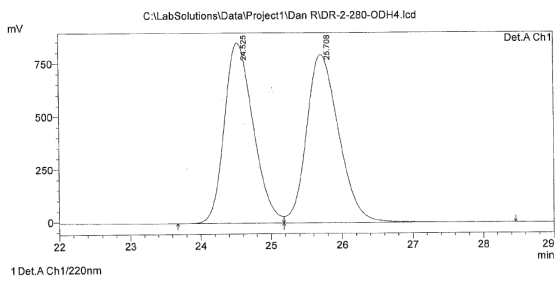
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	33.415	38702980	655495	96.234	96.774
2	49.426	1514612	21853	3.766	3.226
Total		40217592	677347	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	38.8 min	48.921	1	33.4 min	96.234
2	58.0 min	51.079	2	49.4 min	3.766



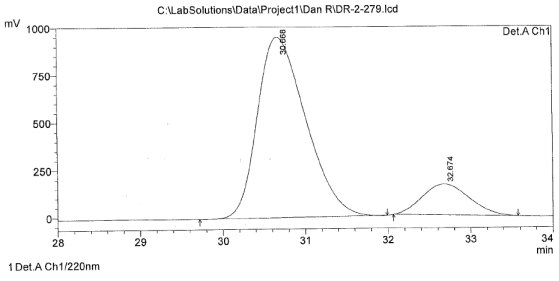
(S)-1-(2-Methoxyphenyl)-2-methylpent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.18 (m, 1H), 7.14 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.99 – 6.82 (m, 2H), 6.05 – 5.83 (m, 1H), 5.20 – 5.01 (m, 2H), 3.81 (s, 3H), 3.00 – 2.71 (m, 4H), 2.35 – 2.17 (m, 1H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 157.56, 134.79, 132.59, 127.88, 126.22, 120.70, 117.86, 110.58, 72.97, 55.28, 47.00, 42.03, 26.58. IR (neat): 3443, 3074, 2973, 2929, 2836, 1492, 1460, 1241, 1125, 1027, 913, 753. HRMS (DART$^+$): Calcd for $C_{13}H_{17}O$ [M-OH]$^+$: 189.1279; Found: 189.1283. $[\alpha]^{20}_D$ = -10 (*c* = 1.0, $CHCl_3$) for a 85.5:14.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99.5% hexanes, 0.5% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.525	24476224	853050	49.459	51.707
2	25.708	25011334	796731	50.541	48.293
Total		49487558	1649781	100.000	100.000

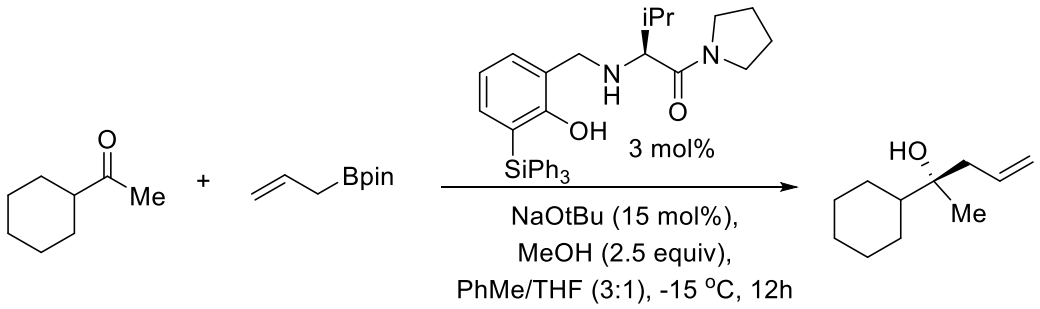


PeakTable

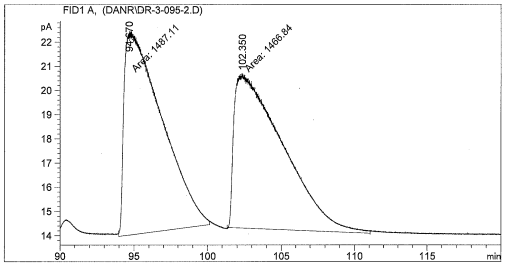
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	30.668	38769112	952624	85.697	85.373
2	32.674	6470528	163213	14.303	14.627
Total		45239639	1115837	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	24.5 min	49.459	1	30.7 min	85.697
2	25.7 min	50.541	2	32.7 min	14.303



(S)-2-Cyclohexylpent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.84 (ddt, *J* = 17.4, 10.2, 7.4 Hz, 1H), 5.14 – 4.98 (m, 2H), 2.28 – 2.07 (m, 2H), 1.88 – 1.53 (m, 5H), 1.36 – 0.82 (m, 9H). IR (neat): 3432, 2976, 2924, 2852, 1450, 1376, 1145, 998, 910. HRMS (DART+): Calcd for $C_{11}H_{19}$ [M-OH]+: 151.1487; Found: 151.1489.



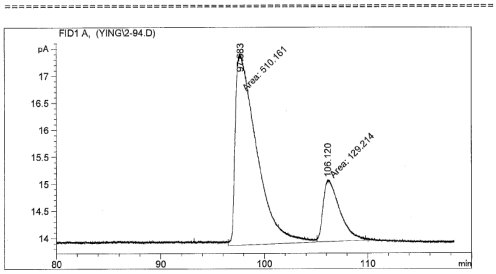
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 7.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	94.670	MM	2.9374	1487.11206	8.43793	50.34315
2	102.350	MM	3.8116	1466.83887	6.41392	49.65685

Totals : 2953.95093 14.85185



Area Percent Report

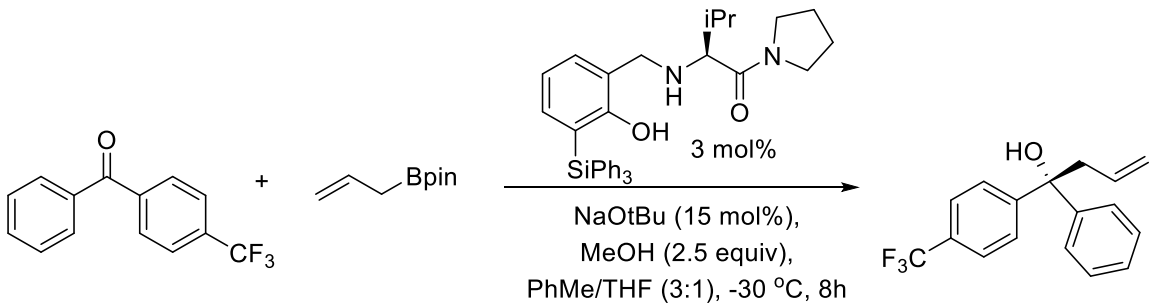
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 7.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	97.683	MF	2.3821	510.16095	3.56938	79.79053
2	106.120	FM	1.8758	129.21437	1.14811	20.20947

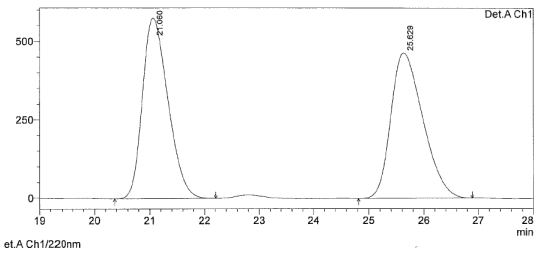
Totals : 639.37532 4.71749

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	94.7 min	50.343	1	97.7 min	79.791
2	102.4 min	49.657	2	106.1 min	20.209



(R)-1-Phenyl-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (s, 4H), 7.50 – 7.39 (m, 2H), 7.33 (ddd, *J* = 7.8, 6.9, 1.3 Hz, 2H), 7.24 (ddt, *J* = 7.8, 6.3, 1.3 Hz, 1H), 5.64 (ddt, *J* = 17.3, 10.1, 7.2 Hz, 1H), 5.36 – 5.09 (m, 2H), 3.08 (qdt, *J* = 13.9, 7.4, 1.2 Hz, 2H), 2.62 (s, 1H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 150.44, 145.66, 132.69, 129.00 (q, *J* = 32.4 Hz), 128.41, 127.28, 126.28, 125.88, 125.11 (q, *J* = 3.8 Hz), 124.13 (q, *J* = 273.3 Hz), 121.14, 76.64, 46.47. ^{19}F NMR (376 MHz,

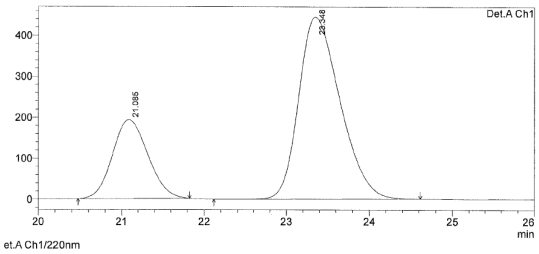
$cdcl_3$) δ -62.49. IR (neat): 3546, 3078, 3028, 2980, 2924, 1409, 1324, 1163, 120, 1067, 1016, 834, 699. Calcd for $C_{17}H_{14}F_3$ [M-OH]+: 275.1048; Found: 275.1047. $[\alpha]^{20}_D$ = +10 (*c* = 1.0, $CHCl_3$) for a 73:27 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.060	18580457	575748	49.551	55.332
2	25.629	18917081	464792	50.449	44.668
Total		37497537	1040539	100.000	100.000

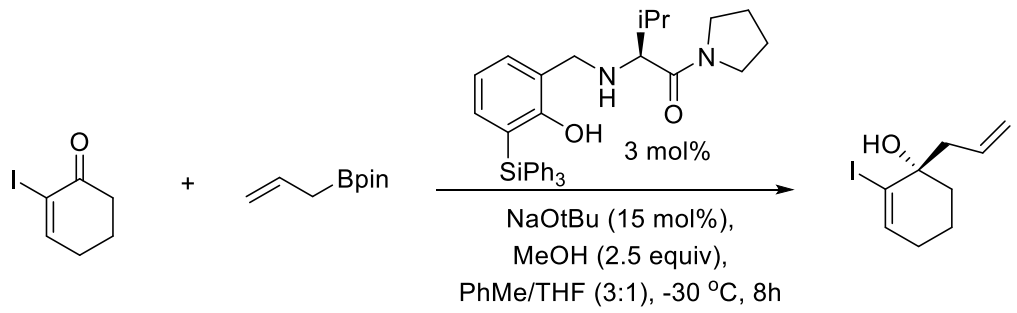


PeakTable

Detector A Ch1 220nm

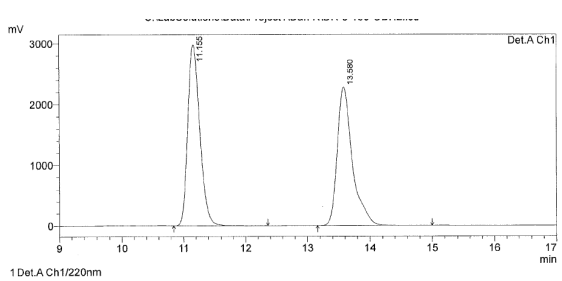
Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.085	5748717	192398	27.139	30.205
2	23.348	15433920	444570	72.861	69.795
Total		21182637	636968	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.3 min	51.407	1	13.3 min	10.149
2	15.1 min	48.593	2	14.8 min	89.851



(S)-1-Allyl-2-iodocyclohex-2-en-1-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.55 (dd, *J* = 4.7, 3.7 Hz, 1H), 5.87 – 5.69 (m, 1H), 5.23 – 5.06 (m, 2H), 2.42 (ddt, *J* = 7.1, 2.2, 1.2 Hz, 2H), 2.19 – 1.96 (m, 3H), 1.93 (s, 1H), 1.91 – 1.82 (m, 1H), 1.81 – 1.61 (m, 2H). ^{13}C NMR (101 MHz, $cdcl_3$) δ 141.82, 132.87, 118.87, 111.75, 72.92, 47.14, 34.17, 29.64, 18.86. IR (neat): 3431, 3073, 2935, 2866, 2829, 1638, 1435, 1328, 1169, 1082, 964, 915, 806, 763, 709, 635. HRMS (DART+): Calcd for $C_9H_{12}I$ [M-OH]+: 246.9984; Found:

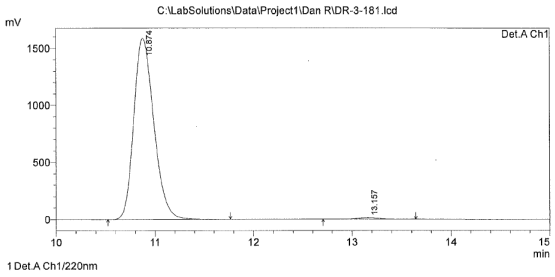
246.9977. $[\alpha]^{20}_D$ = +30 (*c* = 1.0, $CHCl_3$) for a 99:1 e.r. sample. For determination of enantioselectivity, the product was converted to the benzoate for HPLC analysis. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.155	39961393	2981929	51.025	56.649
2	13.580	38356457	2281903	48.975	43.351
Total		78317850	5263832	100.000	100.000

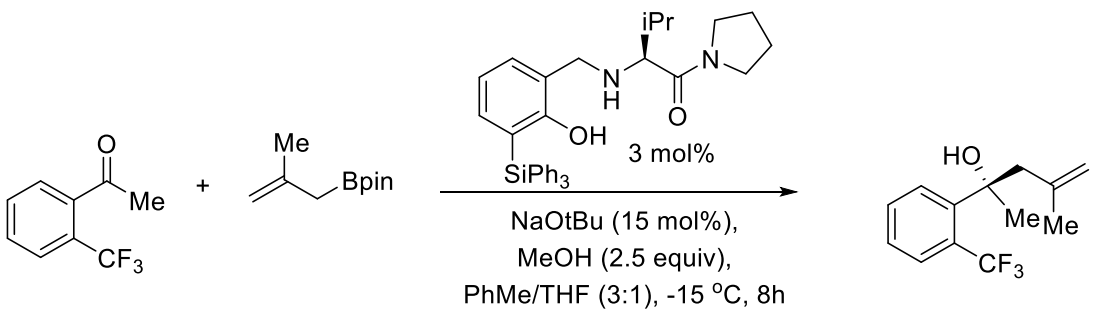


PeakTable

Detector A Ch1 220nm

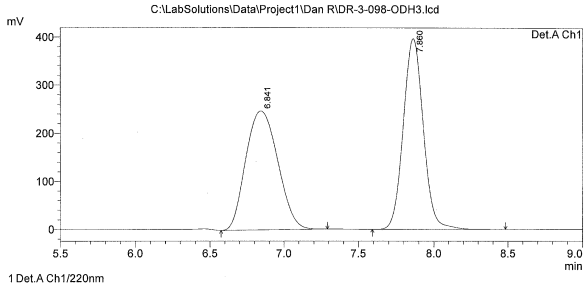
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.874	22305724	1587724	99.174	99.204
2	13.157	185695	12739	0.826	0.796
Total		22491419	1600463	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.2 min	51.025	1	10.9 min	99.174
2	13.6 min	48.975	2	13.2 min	0.826



(S)-4-Methyl-2-(2-(trifluoromethyl)phenyl)pent-4-en-2-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.66 – 7.56 (m, 1H), 7.55 – 7.44 (m, 1H), 7.40 – 7.29 (m, 1H), 5.01 – 4.90 (m, 1H), 4.76 (dd, *J* = 2.1, 1.0 Hz, 1H), 2.86 (dd, *J* = 13.8, 1.0 Hz, 1H), 2.64 (d, *J* = 1.1 Hz, 1H), 2.54 (dd, *J* = 13.8, 0.9 Hz, 1H), 1.67 (s, 3H), 1.48 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.20, 141.99, 131.26, 128.75, 127.89 (q, *J* = 7.5 Hz), 127.02 (q, *J* = 31.0 Hz), 126.73, 124.79 (q, *J* = 274.5 Hz), 116.21,

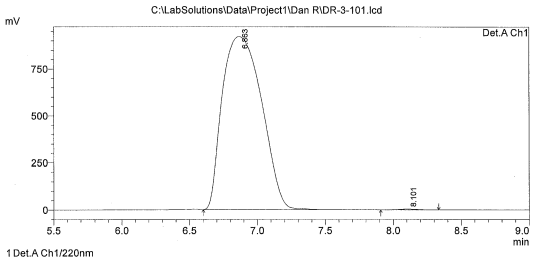
74.18, 51.73 (q, J = 2.0 Hz), 31.56 (q, J = 2.1 Hz), 24.05. ^{19}F NMR (376 MHz, cdcl$_3$) δ -53.75. IR (neat): 3546, 3074, 2978, 2925, 1443, 1303, 1269, 1125, 1034, 898, 767. Calcd for $C_{13}H_{14}F_3$ [M-OH]$^+$: 227.1048; Found: 227.1042. $[\alpha]^{20}_D$ = -30 (c = 1.0, $CHCl_3$) for a 99.5:0.5 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99.5% hexanes, 0.5% i-PrOH, 1.0 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.841	3729774	247432	50.297	38.385
2	7.860	3685746	397178	49.703	61.615
Total		7415520	644610	100.000	100.000

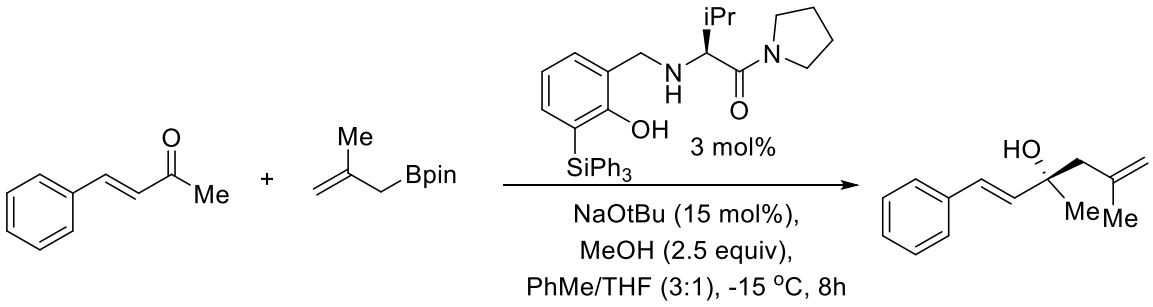


PeakTable

Detector A Ch1 220nm

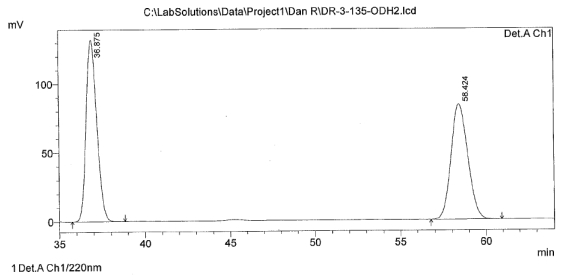
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.863	18689215	921348	99.796	99.568
2	8.101	38249	3997	0.204	0.432
Total		18727464	925346	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	6.8 min	50.297	1	6.9 min	99.796
2	7.9 min	49.703	2	8.1 min	0.204



(S,E)-3,5-Dimethyl-1-phenylhexa-1,5-dien-3-ol. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.42 – 7.33 (m, 2H), 7.30 (ddd, J = 7.7, 6.8, 1.2 Hz, 2H), 7.26 – 7.16 (m, 1H), 6.60 (d, J = 16.0 Hz, 1H), 6.29 (d, J = 16.0 Hz, 1H), 4.94 (dq, J = 2.2, 1.5 Hz, 1H), 4.81 (dq, J = 2.4, 0.9 Hz, 1H), 2.38 (s, 2H), 2.03 (s, 1H), 1.78 (s, 3H), 1.39 (s, 3H). ^{13}C NMR (101 MHz,

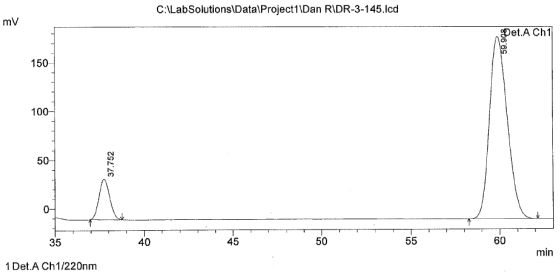
$cdcl_3$) δ 142.30, 137.03, 136.91, 128.54, 127.28, 126.61, 126.34, 115.47, 72.13, 50.86, 28.71, 24.69. IR (neat): 3442, 2971, 2928, 1642, 1493, 1448, 1373, 1091, 970, 893, 748, 692. HRMS (ESI+): Calcd for $C_{14}H_{18}O$ [M+Na]+: 225.1250; Found: 225.1250. $[\alpha]^{20}_D$ = -80 (*c* = 1.0, $CHCl_3$) for a 88:12 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	36.875	5697751	132005	49.939	61.064
2	58.424	5711701	84171	50.061	38.936
Total		11409452	216176	100.000	100.000

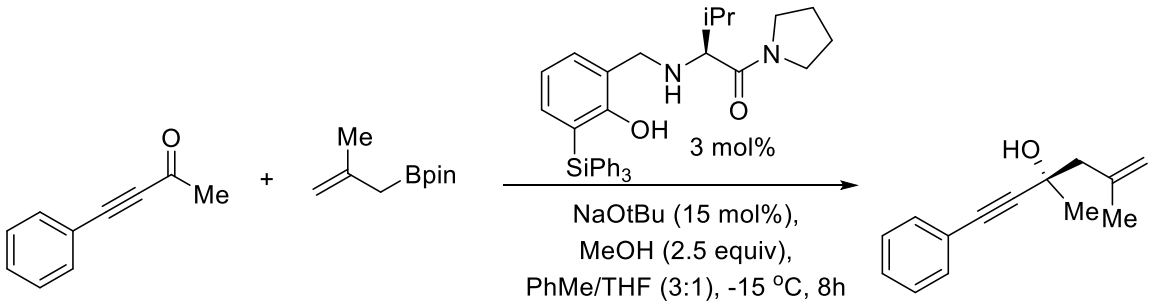


PeakTable

Detector A Ch1 220nm

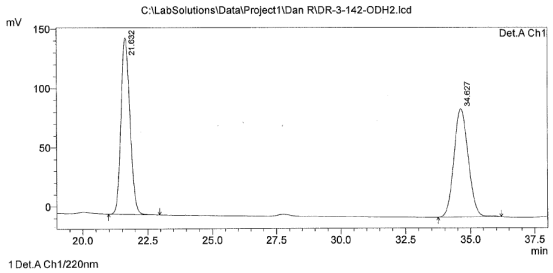
Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.752	1738380	41559	11.756	18.137
2	59.908	13048349	187576	88.244	81.863
Total		14786729	229135	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	36.9 min	49.939	1	37.8 min	11.756
2	58.4 min	50.061	2	59.9 min	88.244



(S)-3,5-Dimethyl-1-phenylhex-5-en-1-yn-3-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.34 (m, 2H), 7.32 – 7.25 (m, 3H), 5.01 (dq, *J* = 2.2, 1.5 Hz, 1H), 4.91 (dt, *J* = 2.3, 0.9 Hz, 1H), 2.63 – 2.39 (m, 3H), 1.98 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (101 MHz, $cdcl_3$) δ 141.88, 131.48, 128.22, 123.52, 122.75, 115.82, 93.12, 83.36, 66.58, 51.35, 30.16, 24.29.

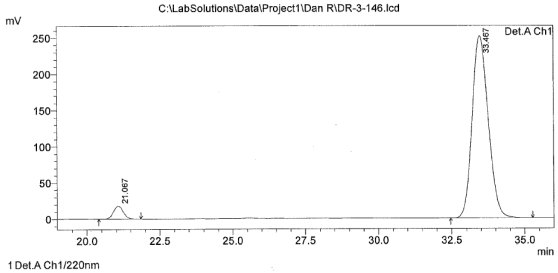
IR (neat): 3403, 3076, 2979, 2934, 1490, 1443, 1372, 1112, 892, 755, 691. HRMS (ESI+): Calcd for $C_{14}H_{16}ONa$ $[M+Na]^+$: 223.1093; Found: 223.1087. $[\alpha]^{20}_D$ = -30 (*c* = 1.0, $CHCl_3$) for a 96:4 e.r. sample. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H, 99% hexanes, 1% i-PrOH, 0.5 mL/min, 220 nm.



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.632	3637345	148839	50.600	61.861
2	34.627	3551035	91765	49.400	38.139
Total		7188380	240604	100.000	100.000

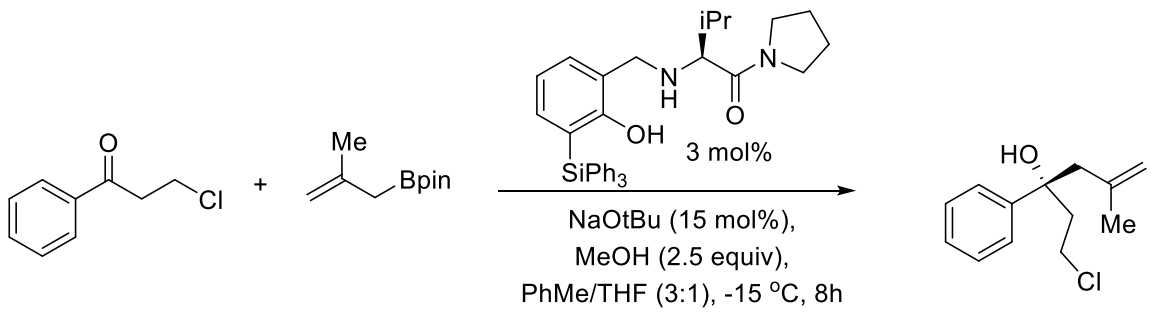


PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.067	417442	17987	4.130	6.654
2	33.467	9688992	252323	95.870	93.346
Total		10106434	270310	100.000	100.000

Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	21.6 min	50.600	1	21.1 min	4.130
2	34.6 min	49.400	2	33.5 min	95.870



(R)-1-Chloro-5-methyl-3-phenylhex-5-en-3-ol. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.28 (m, 4H), 7.27 – 7.16 (m, 1H), 4.91 (dq, *J* = 2.8, 1.5 Hz, 1H), 4.76 (dq, *J* = 1.9, 1.0 Hz, 1H), 3.56 (td, *J* = 10.8, 5.6 Hz, 1H), 3.13 (td, *J* = 10.8, 5.2 Hz, 1H), 2.66 (dd, *J* = 13.4, 0.9 Hz, 1H), 2.58 – 2.49 (m, 2H), 2.44 – 2.19 (m, 2H), 1.28 (s, 3H). ^{13}C NMR (101 MHz, $cdcl_3$) δ 144.54, 141.70, 128.30, 126.87, 125.06, 116.48, 74.45, 51.46, 46.34,

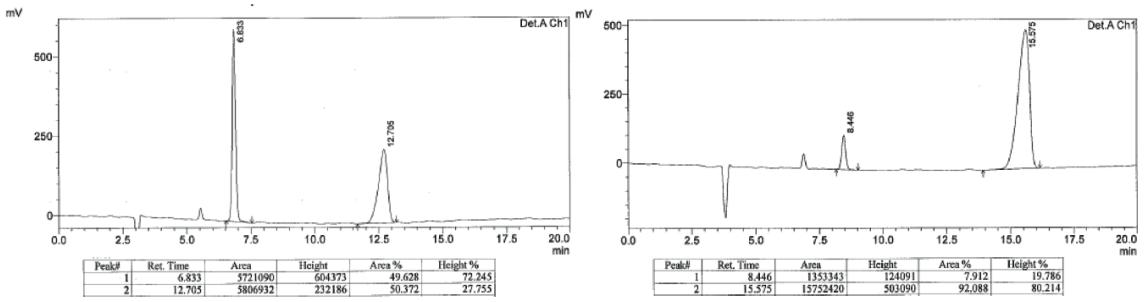
40.19, 24.23. IR (neat): 3534, 3070, 2950, 1446, 1337, 1064, 903, 701, 631. $[\alpha]^{20}_{D}$ = -40 (c = 1.0, $CHCl_3$) for a 72:28 e.r.

■ **Representative Procedure for Catalytic Enantioselective Allyl- or Allenyl-Additions to α-Ketoesters in Scheme 3.18**: In a nitrogen-filled glovebox, aminophenol **3.14u** (7.3 mg, 0.025 mmol) is added to a two-dram vial equipped with a stir bar and dissolved in 1.0 mL of toluene. A second stock solution is prepared by dissolving 4.8 mg NaO*t*-Bu in 8.0 mL toluene. A two-dram vial equipped with a stir bar is charged with 200 mmol of the stock solution of **3.14u** (1.5 mg, 5.0 mmol) followed by 800 mL of the stock solution of NaO*t*-Bu (1.9 mg, 5.0 mmol). This vial is sealed with a cap (phenolic open top cap with a white PFTE/gray silicone septa) and electrical tape and removed from the glovebox. Methanol (20 mL, 0.50 mmol), methyl benzoylformate **3.18a** (28 mL, 0.20 mmol) and allylboronic acid pinacol ester **3.2** (56 mL, 0.29 mmol) are added by syringe under N_2 in the stated order. The clear, colorless solution is allowed to stir at 22 ºC for 4 h after which time the cap is removedand the solution is passed through a short plug of silica gel (eluted with Et_2O) and concentrated *in vacuo*, being careful not to remove all of the solvent, as the product is volatile. The resulting yellow oil is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted sucessively with 10 mL hexanes, 20 mL 30:1 and 20 mL 10:1 hexanes : diethyl ether) affording **3.19a** (41.2 mg, 0.200 mmol, >98% yield) as a clear colorless oil.

(*R*)-2-Hydroxy-2-phenylpent-4-enoate (3.19a, Scheme 3.18): The analytical data are fully consistent with those reported previously.[48] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.60 (2H, m), 7.39–7.35 (2H, m), 7.32–7.28 (1H, m), 5.86–5.75 (1H, m), 5.21–5.13 (2H,

(48) Zheng, K.; Qin, B.; Liu, X.; Feng, X. *J. Org. Chem.* **2007**, *27*, 8478–8483.

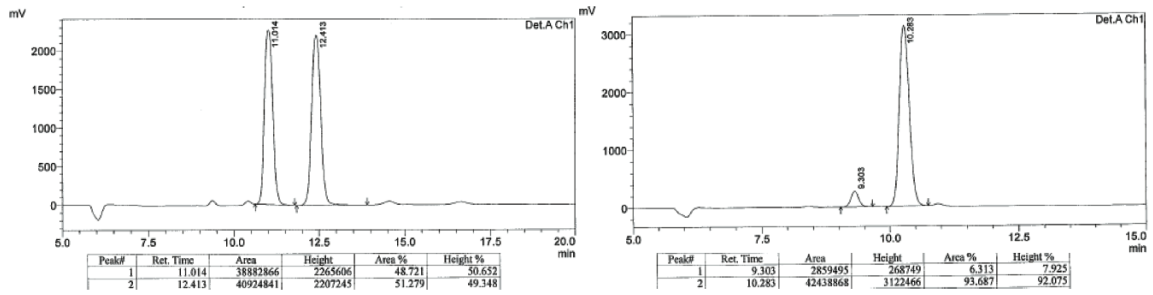
m), 3.78 (3H, s), 3.73 (1H, s), 2.98 (1H, dd, J = 14.0, 7.6 Hz), 2.78 (1H, dd, J = 14.0, 6.5 Hz); HRMS Calcd for $C_{12}H_{13}O_2$ $[M + H - H_2O]^+$: 189.09155; Found: 189.09243; $[\alpha]^{21.7}$= –9.94 (c = 2.01, $CHCl_3$) for a 82:18 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 80:20 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R: 6.9 min (minor) and 12 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	6.8 min	49.628	1	8.4 min	7.912
2	12.7 min	50.372	2	15.6 min	92.088

Methyl (*R*)-2-(4-chlorophenyl)-2-hydroxypent-4-enoate (3.19b, Scheme 3.18): The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted successively with 10 mL hexanes, 20 mL 20:1, 10 mL 10:1 pentanes:ethyl acetate) affording **3.19b** (47.5 mg, 0.197 mmol, >98% yield) as a clear sticky white oil. IR (neat): 3505 (w, br), 3078 (w), 2954 (w), 1728 (s), 1490 (m), 1437 (w), 1227 (s), 1144 (m), 1091 (s), 1033 (m), 921 (m), 830 (m), 760 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.56–7.53 (2H, m), 7.34–7.31 (2H, m), 5.81–5.71 (1H, m), 5.19–5.13 (2H, m), 3.78 (3H, s), 3.73 (1H, s), 2.96–2.90 (1H, m), 2.76–2.70 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 139.8, 134.0, 132.1, 128.6, 127.3, 119.9, 77.9, 53.5, 44.4; HRMS Calcd. for $C_{12}H_{12}Cl_1O_2$ $[M + H - H_2O]^+$: 223.05258; Found:

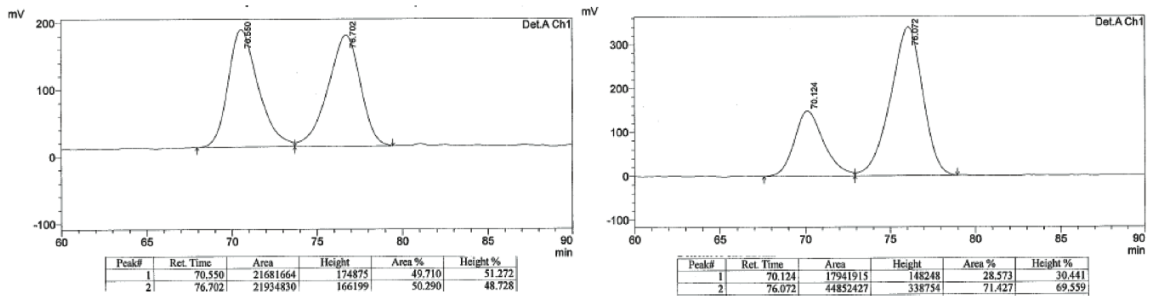
223.05350. $[\alpha]^{24.1}_{D}$ = –24.2 (*c* = 1.65, $CHCl_3$) for a 92:8 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 80:20 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 11 min (minor) and 12 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.0 min	48.721	1	9.3 min	7.925
2	12.4 min	51.279	2	10.3 min	93.687

Methyl (*R*)-2-hydroxy-2-(1*H*-indol-3-yl)pent-4-enoate (3.19c, Scheme 3.18): The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted successively with 10 mL dichloromethane, 25 mL 19:1 dichloromethane:diethyl ether) affording **3.19c** (44.1 mg, 0.180 mmol, 90% yield) as a light tan solid. M.p. = 100–101 ºC. IR (neat): 3486 (w), 3299 (w, br), 1717 (s), 1460 (w), 1334 (m), 1260 (s), 1225 (m), 1138 (m), 1101 (m), 961 (m), 743 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (1H, br s), 7.85–7.82 (1H, d), 7.38–7.35 (1H, m), 7.30–7.29 (1H, m), 7.23–7.18 (1H, m), 7.16–7.11 (1H, m), 5.94–5.83 (1H, m), 5.24–5.15 (2H, m), 3.79–3.78 (1H, m), 3.77–3.76 (3H, m), 3.12–3.07 (1H, m), 3.02–2.96 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.7, 136.9, 132.6, 125.1, 122.4, 120.9, 120.2, 119.4, 117.6, 111.4, 76.1, 53.2, 43.4; HRMS Calcd. for $C_{14}H_{14}N_1O_2$ $[M + H - H_2O]^+$: 228.10245; Found: 228.10211. $[\alpha]^{23.9}_{D}$ = –17.5 (*c* = 1.71, $CHCl_3$) for a 71.5:28.5 e.r. sample. The

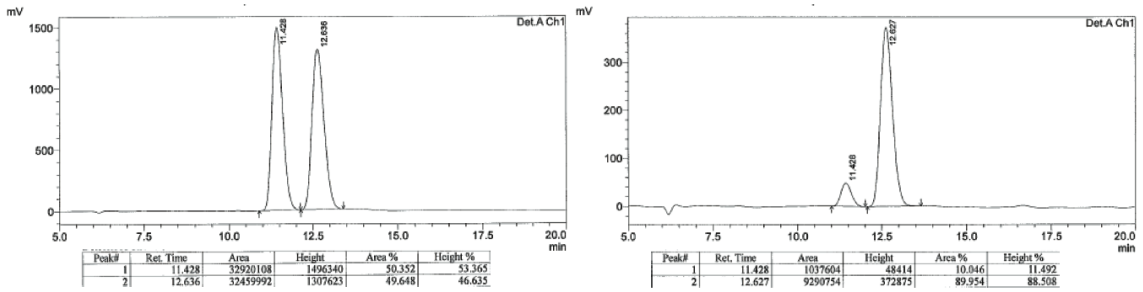
enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 80:20 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 70 min (minor) and 76 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	70.6 min	49.710	1	70.1 min	28.573
2	76.7 min	50.290	2	76.1 min	71.427

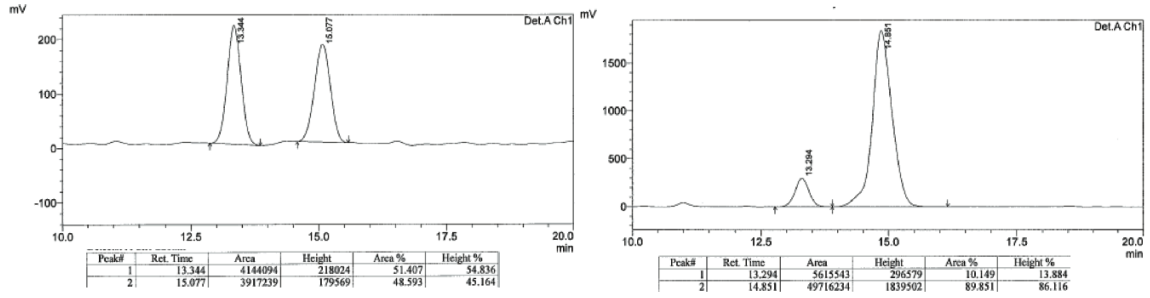
***tert*-Butyl (*R*)-3-(2-hydroxy-1-methoxy-1-oxopent-4-en-2-yl)-1*H*-indole-1-carboxylate (3.19d, Scheme 3.18)**: The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted successively with 10 mL hexanes, 20 mL 20:1, 30 mL 10:1 hexanes:ethyl acetate affording **3.19d** (61.3 mg, 0.177 mmol, 89% yield) as a clear colorless sticky oil. IR (neat): 3503 (w, br), 2980 (w), 1729 (s), 1452 (m), 1369 (s), 1251 (m), 1225 (m), 1152 (s), 1075 (m), 1023 (m), 745 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (1H, d, J = 8.3 Hz), 7.81–7.74 (1H, m), 7.68 (1H, s), 7.31 (1H, m), 7.26–7.20 (1H, m), 5.91–5.81 (1H, m), 5.26–5.14 (2H, m), 3.78 (1H, s), 3.77 (3H, s), 1.67 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 149.7, 136.2, 132.0, 127.9, 124.6, 123.9, 122.9, 121.5, 121.1, 119.9, 115.4, 84.1, 75.6, 53.4, 43.0, 28.3; HRMS Calcd. for $C_{19}H_{22}N_1O_4$ $[M + H - H_2O]^+$: 328.15488; Found: 328.15351. $[\alpha]^{24.3}_D$ = –15.6 (c = 3.19, $CHCl_3$) for a 79:21 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in

comparison with authentic racemic material (Chiracel AS-H, 90:10 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 11 min (minor) and 12 min (major).



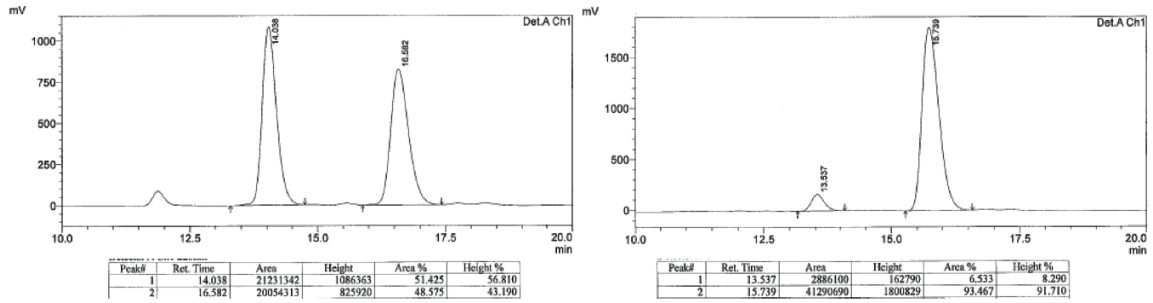
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.4 min	50.352	1	11.4 min	10.046
2	12.6 min	49.648	2	12.6 min	89.954

Methyl (*R*)-2-hydroxy-2-phenylpenta-3,4-dienoate (3.21a, Scheme 3.19): The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted successively with 10 mL hexanes, 10 mL 25:1, 30 mL 10:1 hexanes:ethyl acetate affording **3.21a** (37.6 mg, 0.184 mmol, 92% yield, >98:2 allene:propargyl) as clear colorless oil. IR (neat): 3497 (w, br), 2954 (w), 1958 (w), 1728 (s), 1447 (w), 1436 (w), 1246 (s), 1176 (m), 1151 (m), 1090 (m), 852 (m), 751 (s), 697 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60–7.57 (2H, m), 7.40–7.30 (3H, m), 5.78–5.75 (1H, m), 5.02–5.00 (2H, m), 3.87–3.86 (1H, m), 3.79–3.78 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.1, 174.2, 140.6, 128.4, 128.4, 126.4, 95.5, 79.8, 76.8, 53.5; HRMS Calcd. for $C_{12}H_{21}O_2$ $[M + H - H_2O]^+$: 187.07590; Found: 187.07632. $[\alpha]^{23.8}_D$ = –52.9 (*c* = 1.32, $CHCl_3$) for a 92:8 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OJ-H, 80:20 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 13 min (minor) and 15 min (major).



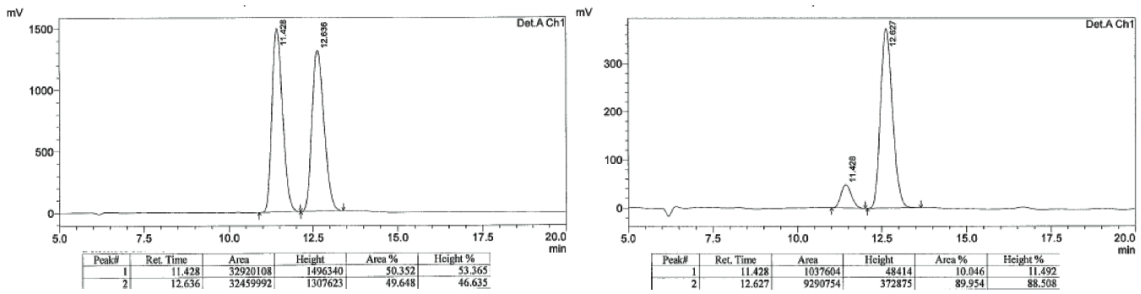
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.3 min	51.407	1	13.3 min	10.149
2	15.1 min	48.593	2	14.8 min	89.851

Methyl (*R*)-2-(4-chlorophenyl)-2-hydroxypenta-3,4-dienoate (3.21b, Scheme 3.19): The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted successively with 10 mL hexanes, 20 mL 20:1, 20 mL 10:1 hexanes:ethyl acetate) affording **3.21b** (47.6 mg, 0.199 mmol, >98% yield, >98:2 allene:propargyl) as a clear sticky white oil. IR (neat): 3497 (w, br), 2954 (w), 1958 (w), 1729 (s), 1489 (m), 1436 (w), 1400 (w), 1246 (s), 1173 (m), 1154 (m), 1079 (s), 1014 (m), 853 (m), 831 (s), 762 (m), 725 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55–7.51 (2H, m), 7.34–7.31 (2H, m), 5.70 (1H, t, J = 6.6 Hz), 5.00 (2H, d, J = 6.6 Hz), 3.88 (1H, s), 3.78 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.2, 173.8, 139.0, 134.3, 128.5, 128.0, 95.3, 80.0, 76.7, 53.7; HRMS Calcd. for $C_{12}H_{21}O_2$ $[M + H - H_2O]^+$: 221.03693; Found: 221.03668. $[\alpha]^{24.2}_D$ = –36.8 (c = 2.17, $CHCl_3$) for a 93.5:6.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AS-H, 90:10 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 14 min (minor) and 16 min (major).

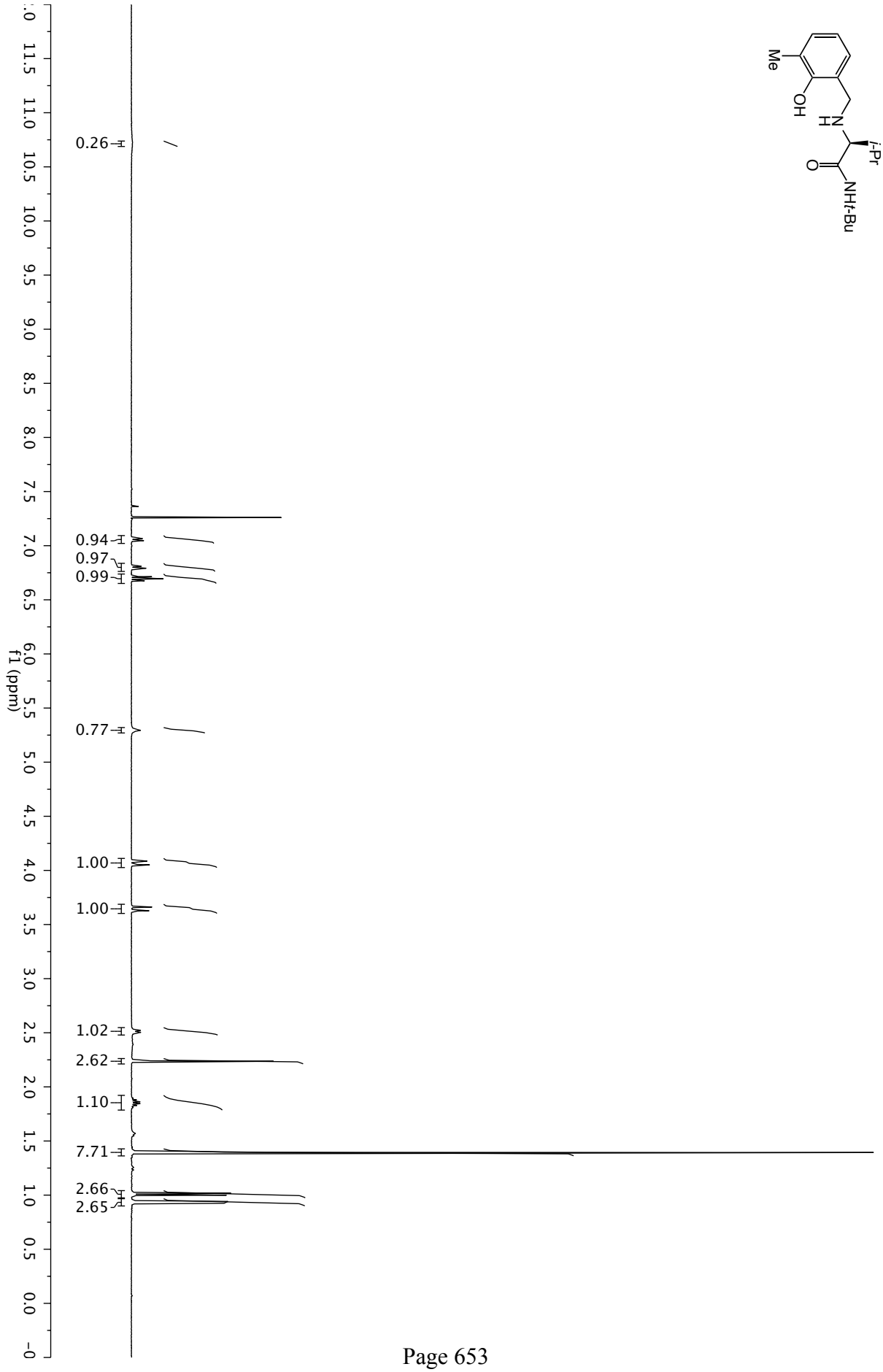


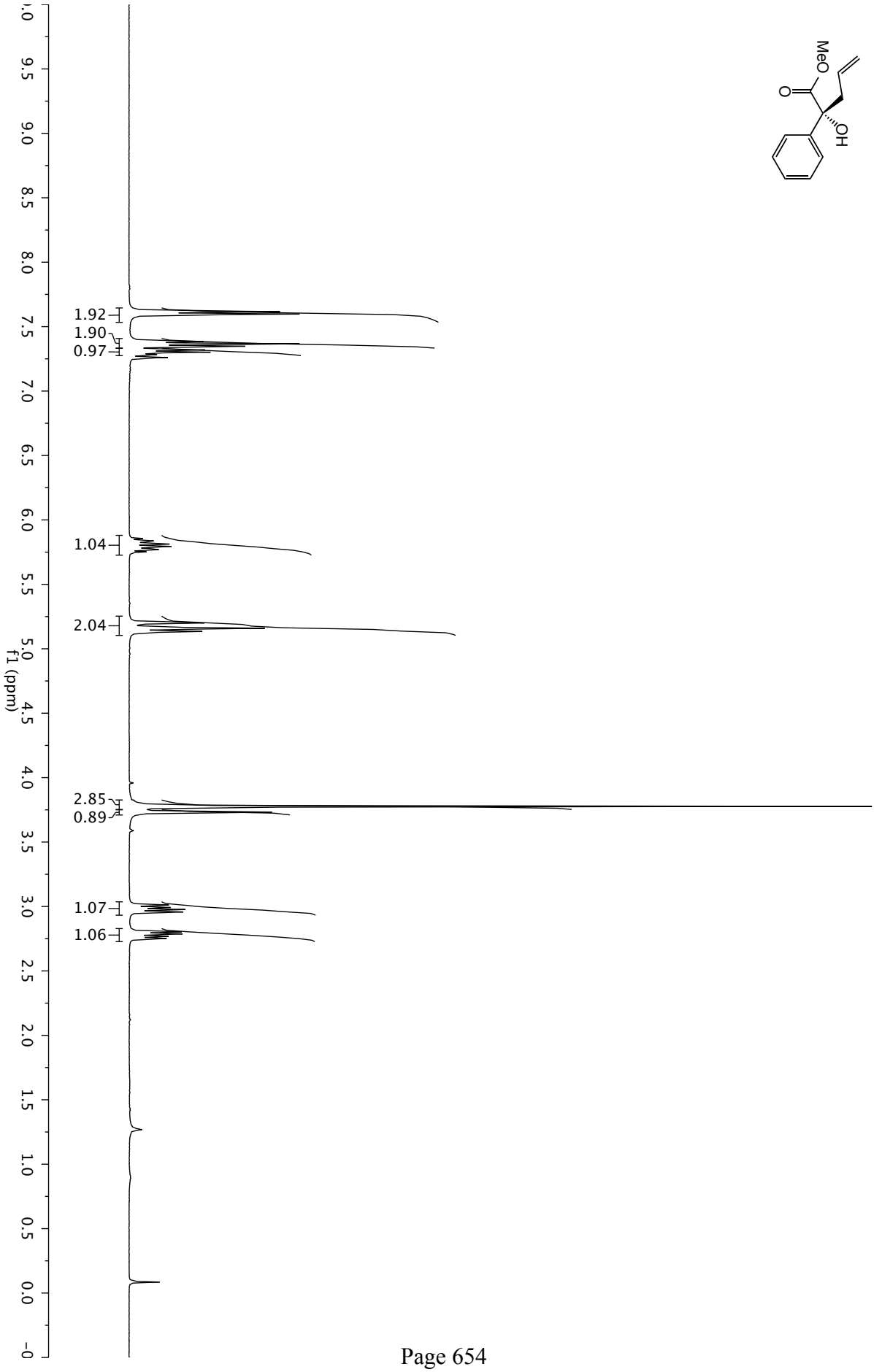
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	14.0 min	51.425	1	13.5 min	6.533
2	16.6 min	48.575	2	15.7 min	93.467

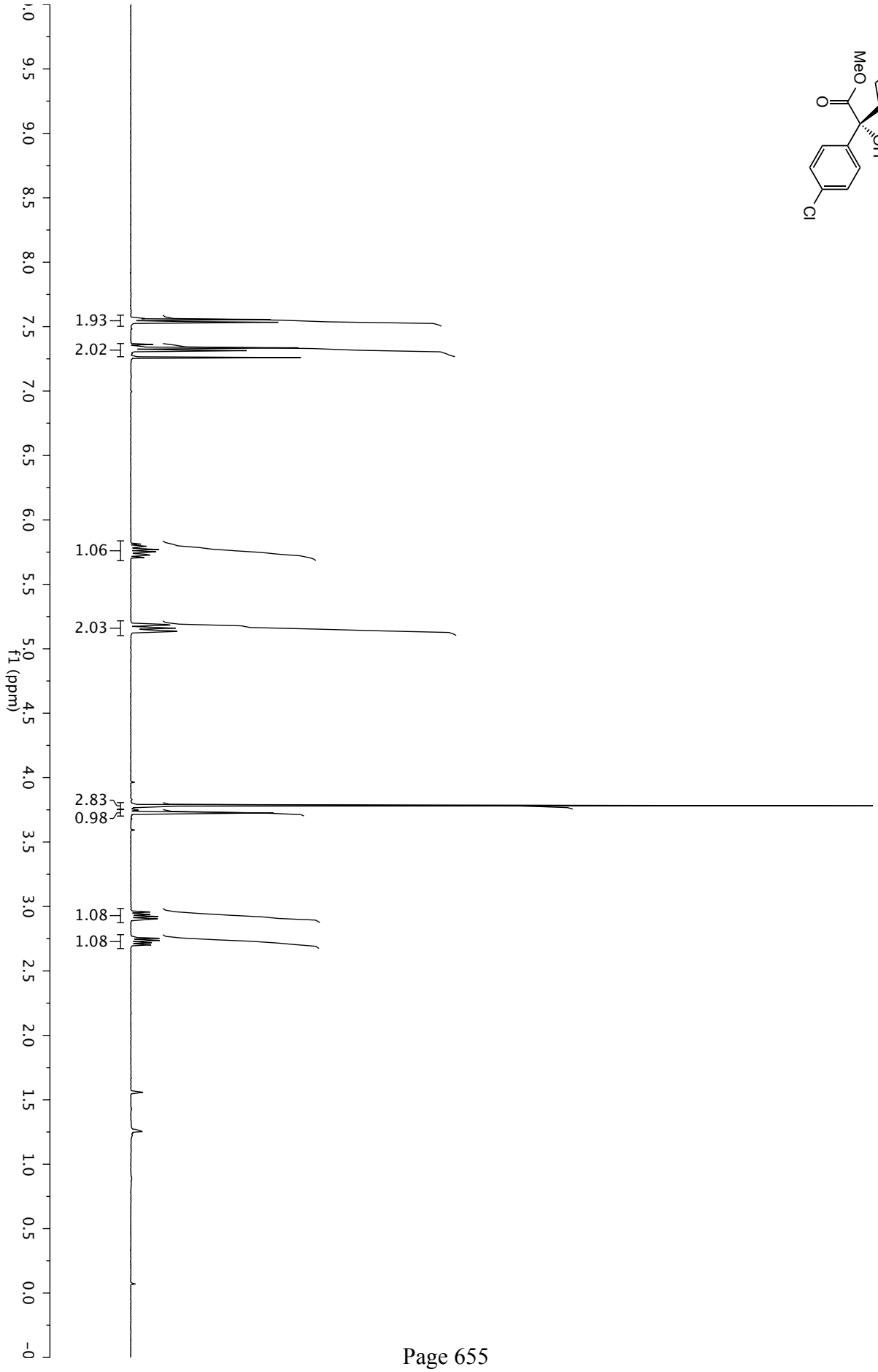
***tert*-Butyl (*R*)-3-(2-hydroxy-1-methoxy-1-oxopenta-3,4-dien-2-yl)-1*H*-indole-1-carboxylate (3.21d, Scheme 3.19)**: The title compound is purified by silica gel chromatography (10 mm diameter column slurry packed with ~2.5 g of silica gel and eluted successively with 10 mL hexanes, 10 mL 20:1, 40 mL 9:1 hexanes:ethyl acetate) affording **3.21d** (71.6 mg, 0.209 mmol, >98% yield, >98:2 allene:propargyl) as a white solid. M.p. = 115–117 ºC. IR (neat): 3504 (w), 1960 (w), 1727 (s), 1453 (w), 1373 (s), 1249 (s), 1225 (m), 1156 (s), 1091 (s), 1020 (m), 853 (m), 831 (s), 776 (m), 744 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (1H, d, J = 8.3 Hz), 7.70 (1H, s), 7.69–7.66 (1H, m), 7.34–7.29 (1H, m), 7.25–7.21 (1H, m), 5.83 (1H, t, J = 6.6 Hz), 5.04 (2H, d, J = 6.6 Hz), 3.84 (1H, s), 3.78 (3H, s), 1.67 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.3, 174.0, 149.7, 136.1, 128.0, 124.7, 122.9, 120.9, 120.8, 115.4, 110.6, 94.5, 84.2, 80.2, 73.8, 53.6, 28.3; HRMS Calcd. for $C_{19}H_{20}N_1O_4$ $[M + H - H_2O]^+$: 326.13923; Found: 326.14036. $[\alpha]^{24.2}_D$ = –47.2 (c = 2.75, $CHCl_3$) for a 90:10 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD-H, 90:10 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 11 min (minor) and 13 min (major).

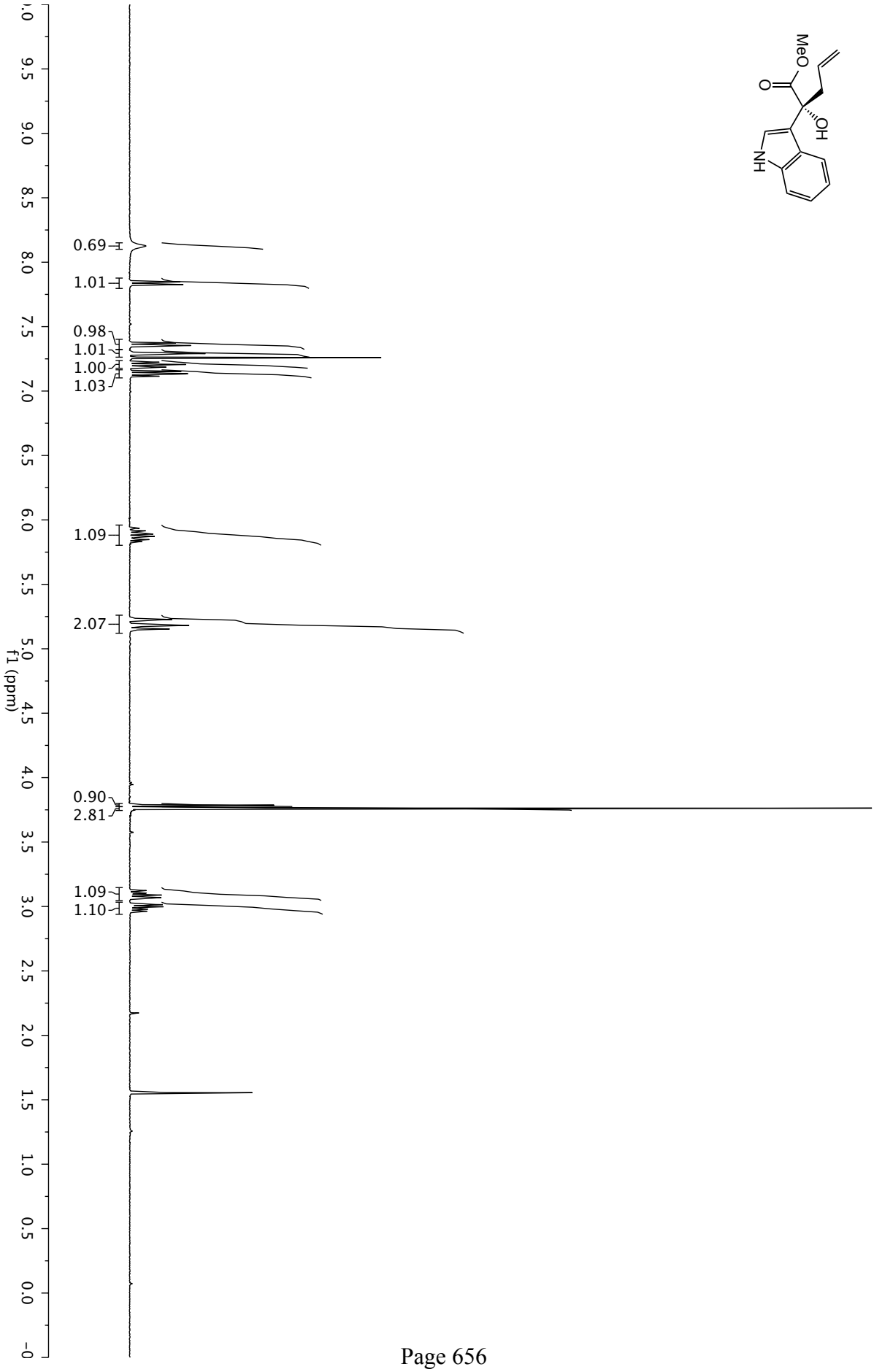


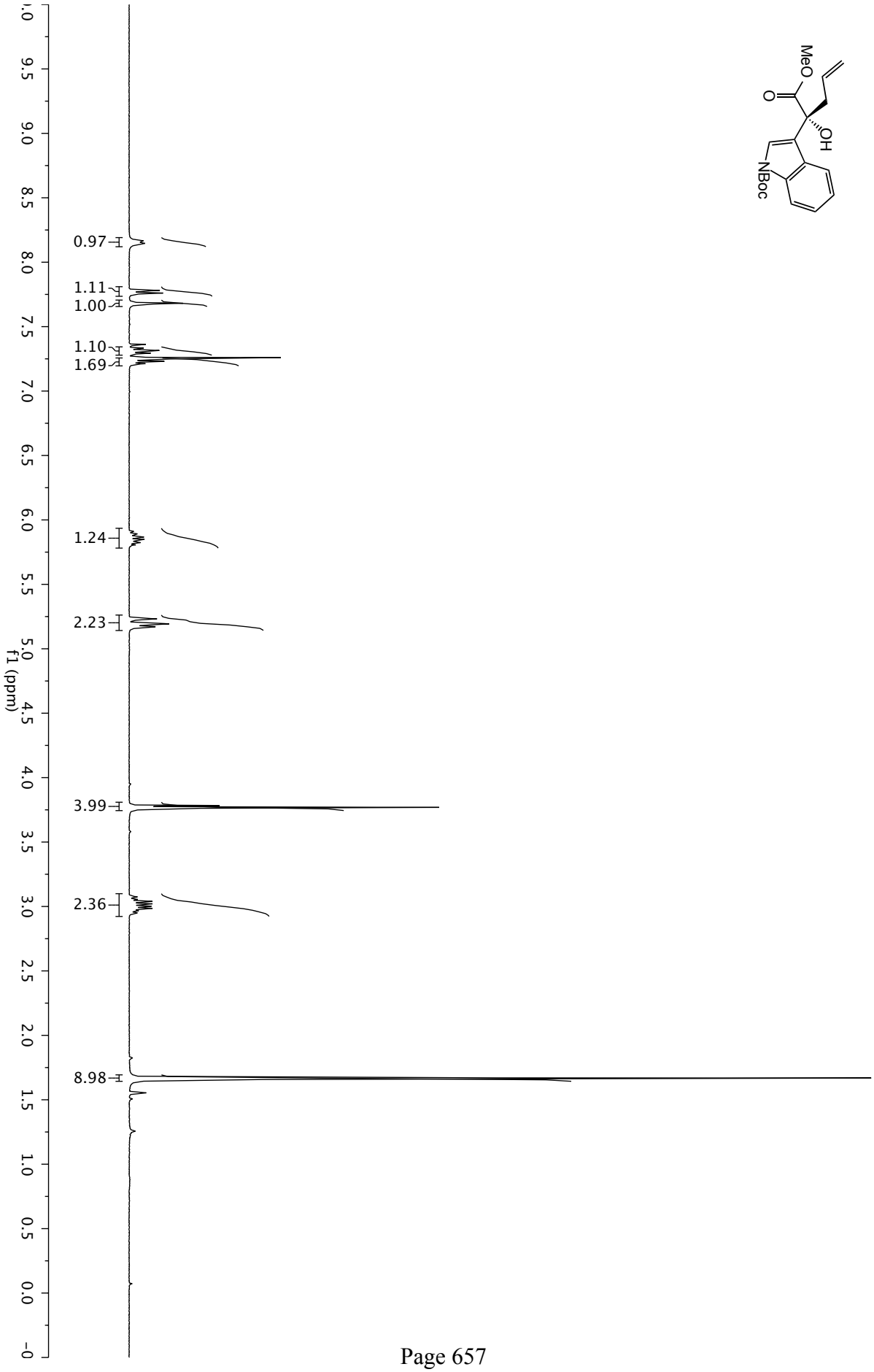
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.4 min	50.352	1	11.4 min	10.046
2	12.6 min	49.648	2	12.6 min	89.954

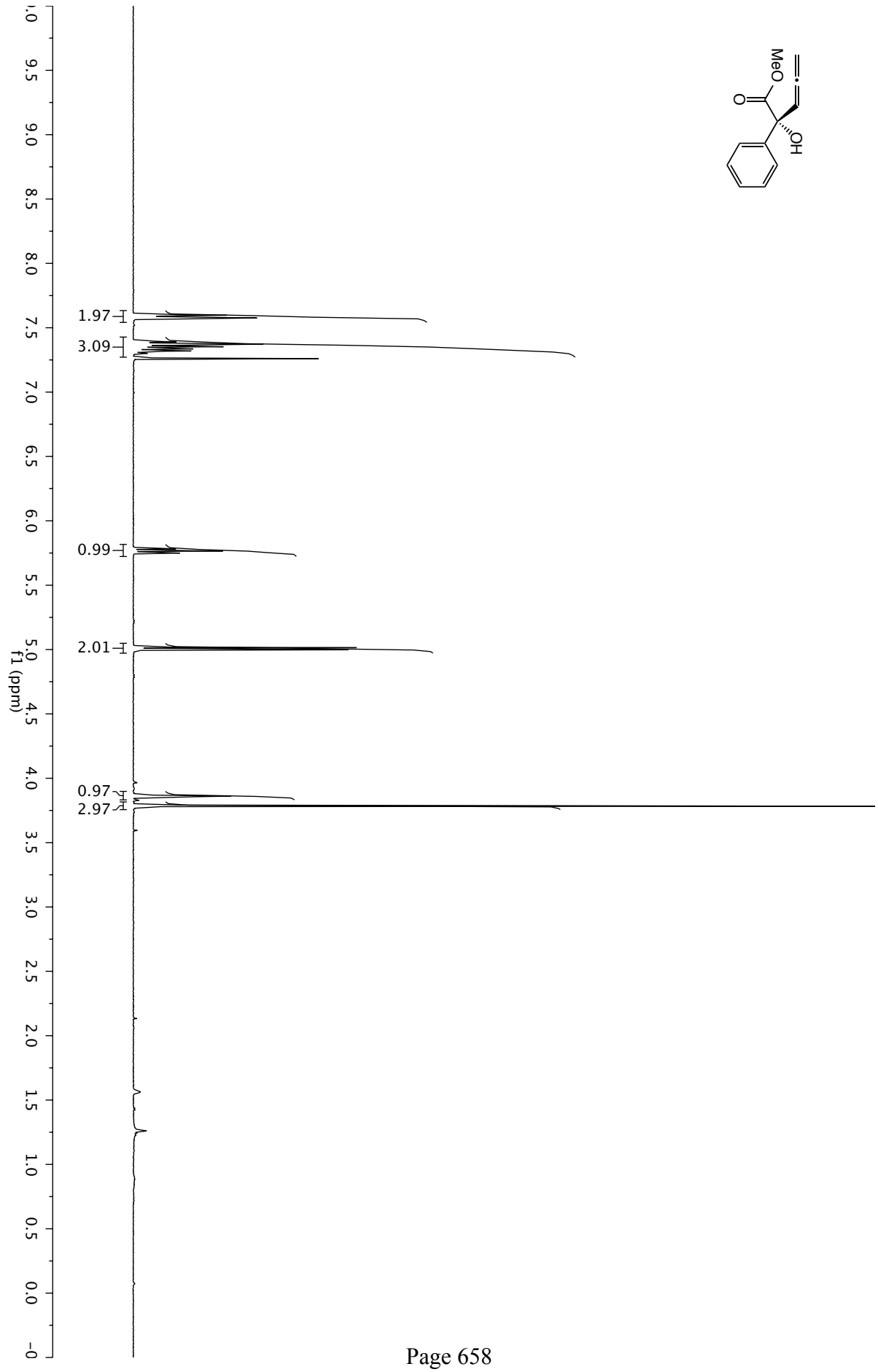

Me
OH
N
H
i-Pr
O
NHt-Bu
0.26
0.94
0.97
0.99
0.77
1.00
1.00
1.02
2.62
1.10
7.71
2.66
2.65
f1 (ppm)

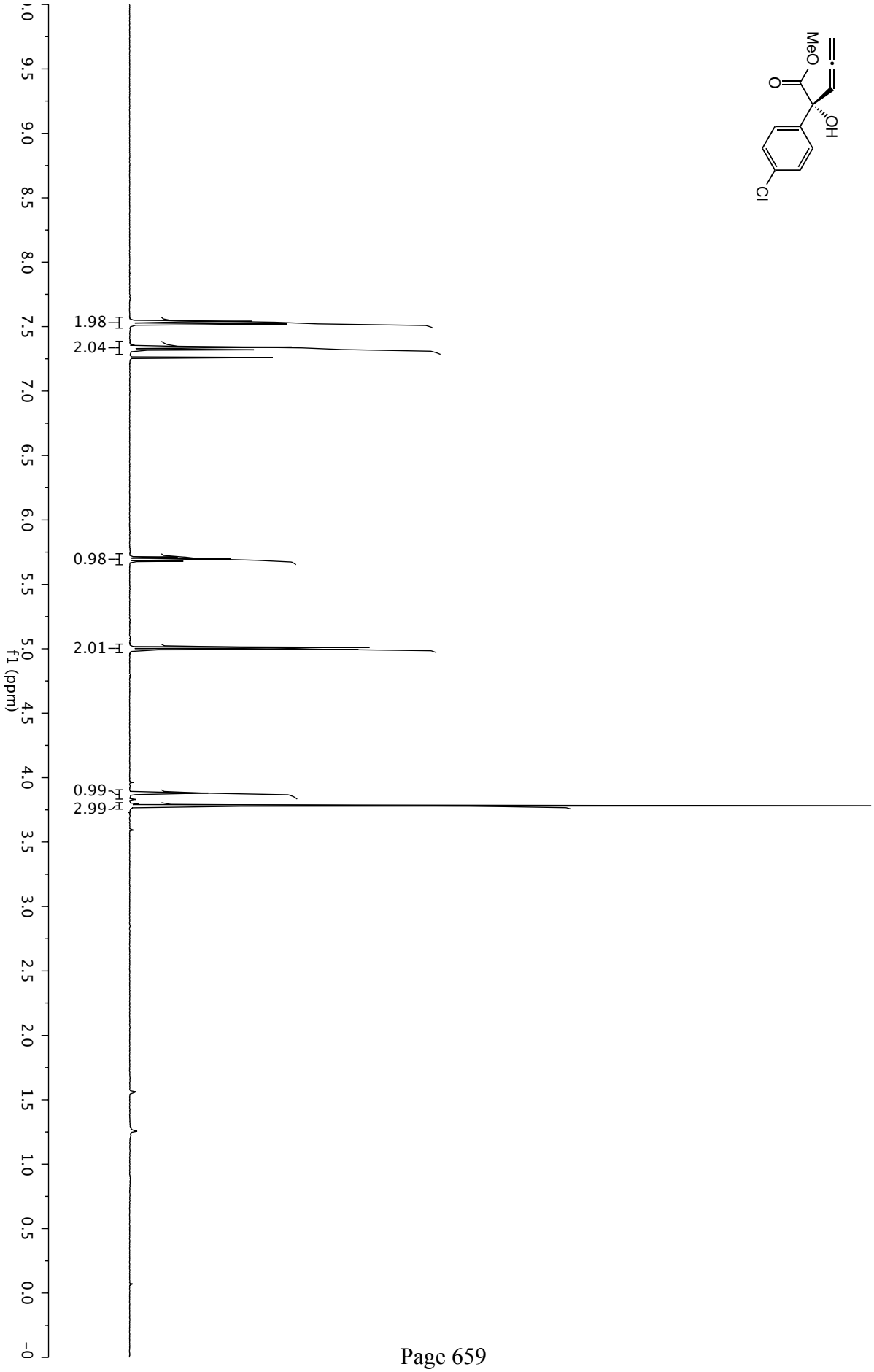

MeO
O
OH
1.92
1.90
0.97
1.04
2.04
2.85
0.89
1.07
1.06
f1 (ppm)

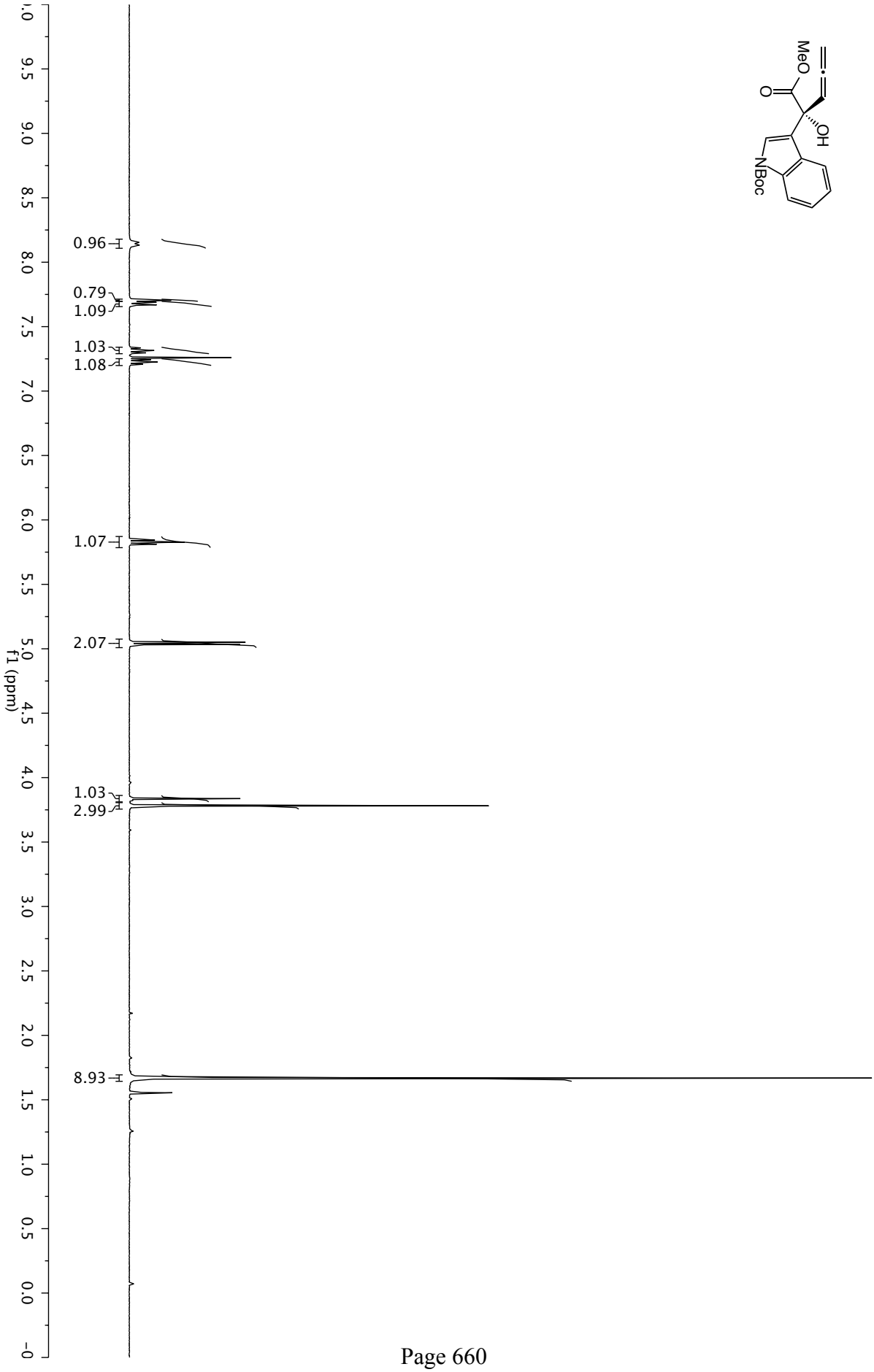

MeO
O
OH
Cl
1.93
2.02
1.06
2.03
2.83
0.98
1.08
1.08
f1 (ppm)


MeO
O
OH
NH
0.69
1.01
0.98
1.01
1.00
1.03
1.09
2.07
0.90
2.81
1.09
1.10
f1 (ppm)


MeO
O
OH
NBoc
0.97
1.11
1.00
1.10
1.69
1.24
2.23
3.99
2.36
8.98
f1 (ppm)


MeO
O
OH
1.97
3.09
0.99
2.01
0.97
2.97
f1 (ppm)


MeO
O
OH
Cl
1.98
2.04
0.98
2.01
0.99
2.99
f1 (ppm)


MeO
O
OH
NBoc
0.96
0.79
1.09
1.03
1.08
1.07
2.07
1.03
2.99
8.93
f1 (ppm)

Chapter Four

Ag-Catalyzed Enantioselective Vinylogous Mannich Reactions of γ-Substituted Siloxyfurans with Aldimines

4.1 Introduction

The Mannich reaction is one of the most popular approaches, in both nature and the work of humankind, to create nitrogen-containing compounds.[1] In general terms, it is a reaction between an enol and an iminium ion to afford a β-amino carbonyl (Equation 1), although modern variants also include a variety of enolates and enol ethers

(1)

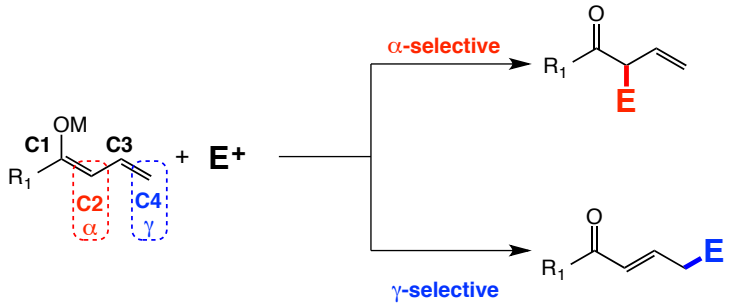
(e.g. silyl enol ethers) as the nucleophile and imines as the electrophile.[1] The vinylogous Mannich reaction,[2] in which a dienol (or its equivalent) is the nucleophile (Equation 2), has proven to be a powerful method to access chiral amines.[3] Harnessing the power of

(2)

(1) For a review on the Mannich reaction and its modern variants, see: Arend, M.; Westermann, B.; Risch, N. *Angew. Chem. Int. Ed.* **1998**, *37*, 1044–1070.
(2) For recent reviews covering the vinylogous Mannich reaction, see: (a) Bur, S. K.; Martin, S. F. *Tetrahedron* **2001**, *57*, 3221–3242. (b) Martin, S. F. *Acc. Chem. Res.* **2002**, *35*, 895–904. (c) Casiraghi, G.; Battistini, L.; Curti, C.; Rassu, G.; Zanardi, F. *Chem. Rev.* **2011**, *111*, 3076–3154.
(3) For a discussion on the importance to medicine of stereochemical pure compounds in general and chiral amines in particular, see Section 1.1 of Chapter 1 of this dissertation.

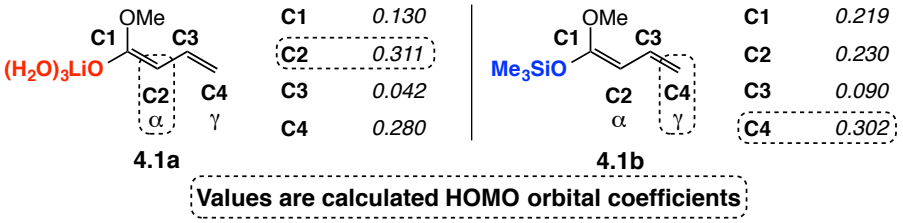
vinylogous[4] nucleophiles can come with a price. As illustrated in Scheme 4.1, when adding to an electrophile, these molecules can potentially react from the α-position (C2 carbon) or the γ-position (C4 carbon). Much of the selectivity obtained hinges on the structure of the nucleophile.[5] Electronically, lithium dienolates preferentially react from

Scheme 4.1 Vinylogous Nucleophiles can React from the α- or γ-Position



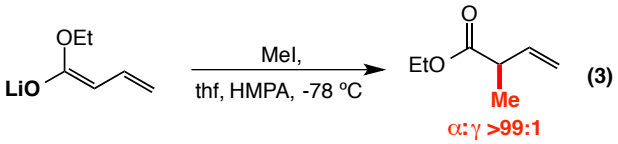
the α-position and silyl ketene acetals (and siyl enol ethers) preferentially react from the γ-position. Calculation of the Fukui orbital densities shows the highest HOMO coefficient resides on the C2 carbon (α-position) for lithium dienolate **4.1a** and on the C4 carbon (γ-position) for silyl ketene acetal **4.1b** (Figure 4.1).[5] Under the conditions shown in equation 3, a lithium dienolate reacts with methyl iodide to exclusively form the α-addition product.[6] In the Mukaiyama aldol in Equation 4, a silyl enol ether reacts to

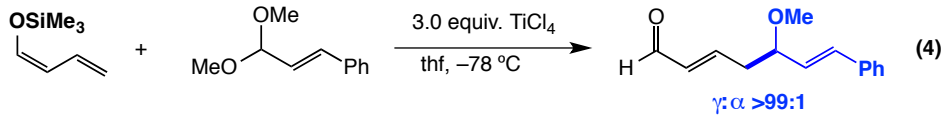
Figure 4.1 HOMO Coefficients of Two Different Vinylogous Nucleophiles



(4) Krishnamurthy, S. J. *J. Chem. Educ.* **1982**, *59*, 543–547.
(5) For a review on catalytic enantioselective vinylogous aldol reaction that skillfully discusses the issue of γ- to α-selectivity, see: Denmark, S. E.; Heemstra, J. R.; Beutner, G. L. *Angew. Chem. Int. Ed.* **2005**, *44*, 4682–4698.
(6) Rathke, M. W.; Sullivan, D. *Tetrahedron Lett.* **1972**, *13*, 4249–4252.

exclusively form the α-addition product.[7] While the electronic features discussed in Figure 4.1 certainly play a role in determining the selectivities shown in Equations 3 and 4, steric effects should not be ignored. In equation 4, the C4 carbon that the nucleophile adds from is less sterically hindered than the competing C2 carbon. Key to data discussed later in this Chapter, substitution at the C4 carbon (γ-position) of these nucleophiles can lead to competitive formation of the α-addition product.





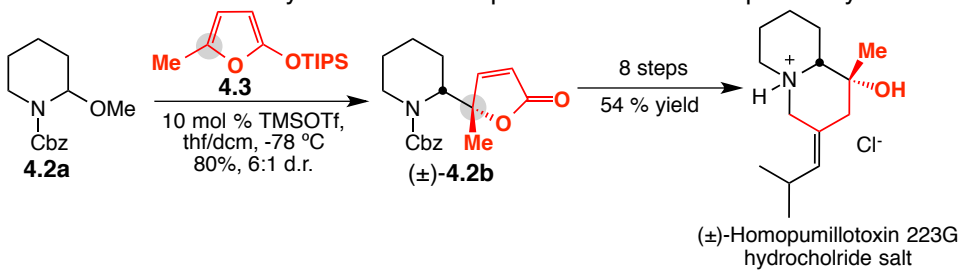
4.2 Background

Enantioselective vinylogous Mannich (EVM) reaction of siloxyfurans[8] gives rise to formation of two contiguous stereogenic centers and the generation of a C-C bond. Substitution at the γ-position of such nucleophiles (e.g. **4.3**, Scheme 4.2) allows for the generation of a quaternary stereogenic center adjacent to a tertiary stereogenic center. This transformation was pioneered by Professor S. F. Martin and has been exploited in synthesis of a variety of amine-containing targets.[9] Such an approach was used in a key

(7) Mukaiyama, T.; Ishida, A. *Chem. Lett.* **1975**, 319–322.
(8) For a review encompassing this class vinylogous nucleophiles, see: Rassu, G.; Zanardi, F.; Battistini, L.; Casiraghi, G. *Chem. Soc. Rev.* **2000**, *29*, 109–118.
(9) For representative examples, see: (a) Martin, S. F.; Barr, K. J.; Smith, D. W.; Bur, S. K. *J. Am. Chem. Soc.* **1999**, *121*, 6990–6997. (b) Liras, S.; Davoren, J. E.; Bordner, J. *Org. Lett.* **2001**, *3*, 703–706. (c) Liras, S.; Lynch, C. L.; Fryer, A. M.; Vu, B. T.; Martin, S. F. *J. Am. Chem. Soc.* **2001**, *123*, 5918–5924. (d) Reichelt, A.; Bur, S. K.; Martin, S. F. *Tetrahedron*, **2002**, *58*, 6323–6328. (e) Bardají, G. G. *et al. J. Org. Chem.* **2008**, *73*, 7657–7662.

step by Pilli and co-workers in the synthesis of the alkaloid (±)-homopumiliotoxin 223G (Scheme 4.2).[10]

Scheme 4.2 Racemic Synthesis of Homopumiliotoxin 223G Reported by Pilli



Although the process of combining **4.3** with the *in situ*-generated iminium ion in Scheme 4.2 is diastereoselective (6:1), it does not afford enantiomerically enriched products. Development of a catalytic enantioselective method to access such quaternary stereogenic centers would represent a notable advance in enantioselective catalysis.

Our group became interested in this challenge from our reports (in collaboration with Prof. M. L. Snapper) of using highly modular amino acid-derived ligands in enantioselective syntheses of amines,[11] specifically in Ag-catalyzed[12] Mannich-type reactions. Under similar conditions and with the same bidentate phosphine ligand **4.4a** (Scheme 4.2), siloxy-containing nucleophiles[13] such as Danishefsky's diene,[14] silyl enol

(10) (a) Santos, L. S.; Pilli, R. A. *Tetrahedron Lett.* **2001**, *42*, 6999–7001. For an earlier enantioselective formal synthesis of this molecule using a similar key step, see: (b) Martin, S. F.; Bur, S. F. *Tetrahedron* **1999**, *55*, 8905–8914.

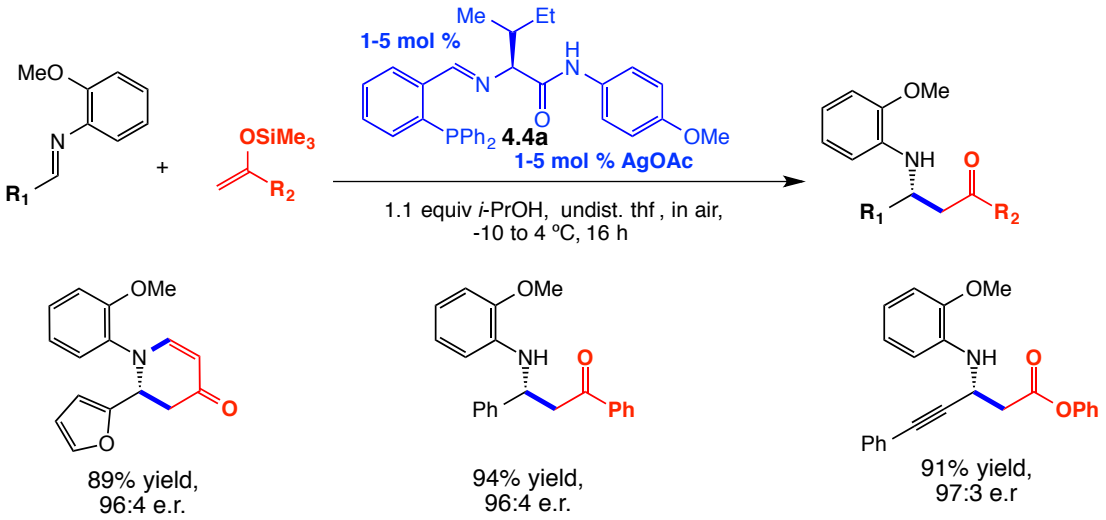
(11) For representative examples, see: (a) Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1668–1671. (b) Shimizu, K. D.; Cole, B. M.; Krueger, C. A.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1703–1707. (c) Krueger, C. A.; Kuntz, K. W.; Dzierba, C. D.; Wirschun, W. G.; Gleason, J. D.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 4284–4285. (d) Porter, J. R.; Wirschun, W. G.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 2657–2658. (e) Josephsohn, N. S.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 11594–11599. (f) Deng, H.; Isler, M. P.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2002**, *41*, 1009–1012. (g) Akullian, L. C.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2003**, *42*, 4244–4247.

(12) For a review of Ag-catalyzed enantioselective transformations, see: (a) Naodovic, M.; Yamamoto, H. *Chem. Rev.* **2008**, *108*, 3132–3148. For a review specific to those that involve chiral Ag-phosphine complexes, see: (b) Yanagisawa, A.; Arai, T. *Chem. Commun.* **2008**, 1165–1172.

(13) For a study of the relative nucleophilicities of various silyl and alkyl enol ethers, see: Burfeindt, J.; Patz, M.; Müller, M.; Mayr, H. *J. Am. Chem. Soc.* **1998**, *120*, 3629–3634.

ethers,[15] and silyl ketene acetals[16] can all be added to aldimines containing an *o*-anisidyl protecting group in high (≥95:5 e.r.) levels of selectivity. The *o*-anisidine group is critical to the enantioselectivity of these transformations, but not their efficiency.[14] We propose this group allows for the substrate to act as a bidentate ligand (involving the anisidyl oxygen and imine nitrogen) for chelation of the Lewis acidic silver species.

Scheme 4.2 Ag-Catalyzed Enantioselective Mannich Reactions with Ligand **4.4a**

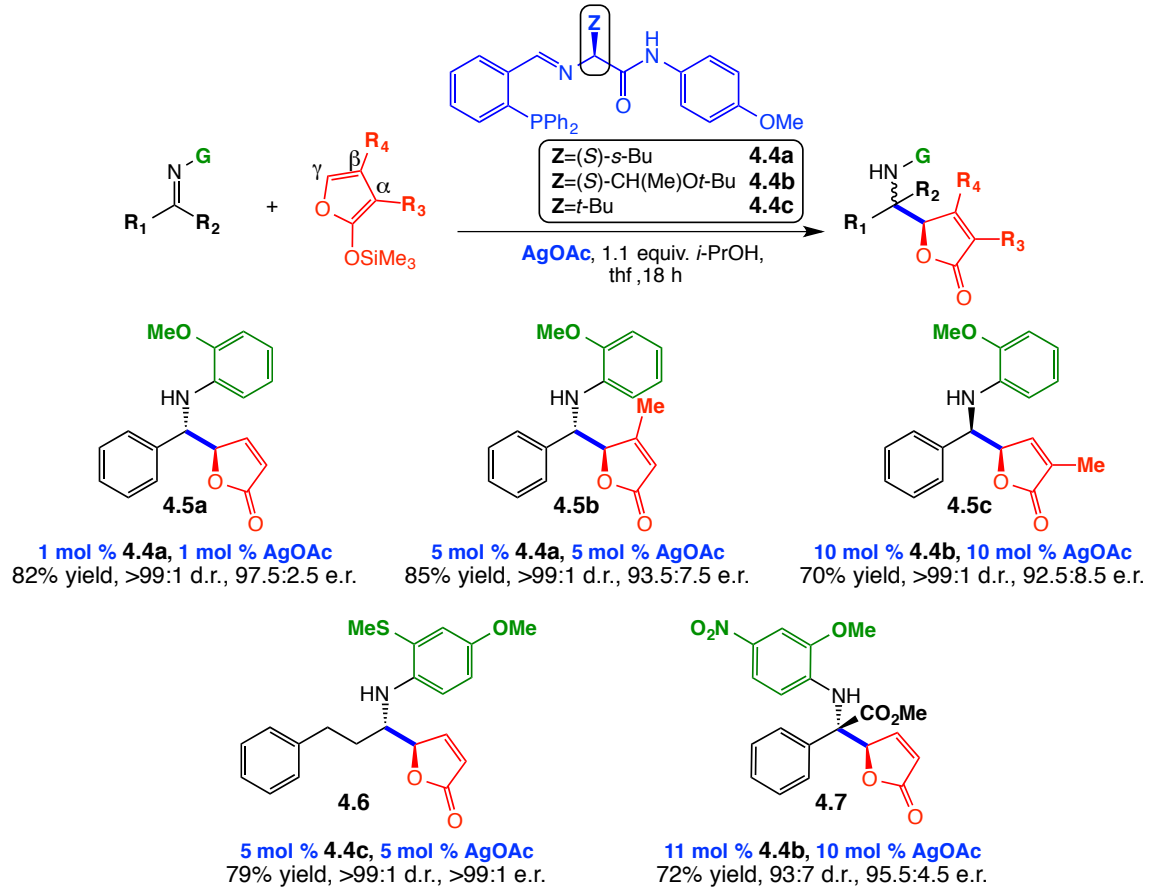


Our group subsequently investigated the Ag-catalyzed EVM reaction promoted by chiral phosphine ligands with three different classes of siloxyfurans (Scheme 4.3); transformations proceed to afford the desired compounds in >99:<1 d.r. and >89.5:<10.5 e.r. (**4.5a-c**, Scheme 4.3).[17] The substrate scope of this method was expanded to allow for additions to alkyl-substituted imines (generated *in situ*), which yield products such as **4.6**

(14) Josephsohn, N. S.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 4018–4019.
(15) Josephsohn, N. S.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 3734–3735.
(16) Josephsohn, N. S.; Carswell, E. L.; Snapper, M. L.; Hoveyda, A. H. *Org. Lett.* **2005**, *7*, 2711–2713.
(17) Carswell, E. L.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2006**, *41*, 6355–6359.

(Scheme 4.3),[18] and ester-substituted ketimines, which yield products such as **4.7** (Scheme 4.3).[19]

Scheme 4.3 Ag-Catalyzed Enantioselective Vinylogous Mannich Reactions

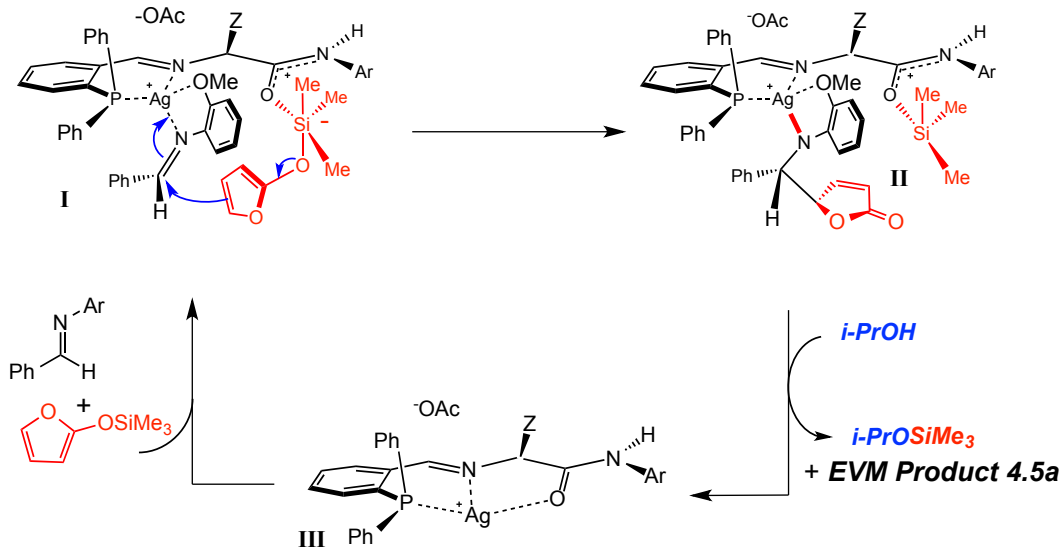


Regarding the transformations shown in Schemes 4.2 and 4.3, further points that merit discussion are: (1) With the exception of the report involving ketimines,[19] all other transformations are performed in undistilled solvent under an atmosphere of air. (2) The protic *i*-PrOH additive is required for high conversions; for example, the reaction to afford **4.5a** in Scheme 4.3 only goes to 43% conversion without this additive versus 91% conversion with 1.1 equivalents of *i*-PrOH (**4.5a** obtained without the use of *i*-PrOH has

(18) (a) Mandai, H.; Mandai, K.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 17961–17969. For an example using the same conditions only with a siloxypyrrole as the nucleophile, see: (b) Ranieri, B.; Curti, C.; Battistini, L.; Sartori, A.; Pinna, L.; Casiraghi, G.; Zanardi, F. *J. Org. Chem.* **2011**, *76*, 10291–10298.
(19) Wieland, L. C.; Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 570–576.

an enantiomeric ratio of 96.5:3.5 e.r., which is very similar to the 97.5:2.5 e.r. observed for the reaction containing *i*-PrOH).[17] We propose the alcohol eases catalytic turnover by facilitating removal of silyl-groups from the catalyst (**II→III**, Scheme 4.4). (3) As shown

Scheme 4.4 Proposed Mechanism for Ag-Catalyzed EVM of Siloxyfurans

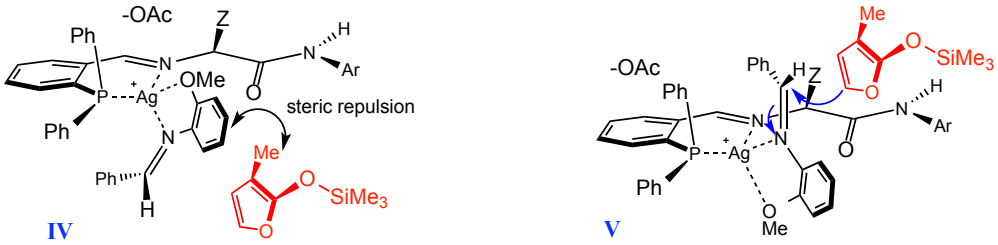


in **I** of Scheme 4.4, we propose the active catalyst is bifunctional.[20] The bidentate phosphine-Schiff base acts as a binding site for the Lewis acidic silver, and the amide acts as a Lewis base to raise the nucleophilicity of the siloxyfuran. Catalysts containing a less Lewis basic methyl ester (versus an amide) are less efficient and enantioselective (though the transformation is still diastereoselective).[17] (4) The modified protecting groups on products **4.6** and **4.7** facilitate their respective transformations in two different ways. Since the alkyl-substituted imines were formed *in situ* (due to their instability), the more electron- donating (versus *ortho*-anisidine) *para*-methoxy-*ortho*-thiomethyl aniline

(20) We have proposed bifunctional catalysis for many other reactions involving amino acid derived-ligands and catalysts. For representative examples, see: Reference 11e, (a) Fu, P.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 5530–5541. (b) Friel, D. K.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 9942–9951. (c) Manville, N.; Alite, H.; Haeffner, F.; Hoveyda, A. H.; Snapper, M. L. *Nature Chem.* **2013**, *5*, 768–774. For reviews, see: (d) Paull, D. H.; Abraham, C. J.; Scerba, M. T.; Alden-Danforth, E.; Lectka, T. *Acc. Chem. Res.* **2008**, *41*, 655–663. (e) Shibasaki, M.; Kanai, M.; Matsunaga, S.; Kumagai, N. *Acc. Chem. Res.* **2009**, *42*, 1117–1127.

in **4.6** (Scheme 4.3) condensed with the aldehydes to form aldimines much faster than *o*-anisidine (at 22 ºC in ten minutes, 90% versus 42% conversion).[18a] The exchange of a methoxy-group for a thiomethyl-group not only increases the nucleophilicity of this aniline, we propose sulfur binds to silver better than oxygen due to the more diffuse electron cloud on sulfur versus oxygen. Additionally, the lone pairs of electrons on the oxygen are more delocalized into the aryl-ring than those of sulfur due to the better orbital overlap between oxygen and carbon. The more electron-withdrawing (versus *o*-anisidine) *para*-nitro-*ortho*-methoxy aniline in **4.7** (Scheme 4.3) is needed to enhance the electrophilicity of the ketimine. The nitro-group also serves as a handle for facile removal of the protecting group.[19] (5) Unlike additions of unsubstituted and β-substituted siloxyfurans, addition of α-methyl substituted siloxyfuran affords the *syn*-diastereomer **4.5c** (>98:<2 d.r. versus >98:<2 d.r. *anti* for the products **4.5a** and **4.5b** and unsubstituted nucleophiles, Scheme **4.3**). We propose this reversal comes from a steric interaction between the methyl group and the *o*-anisidine group (see **IV**) that causes the imine to bind in the *anti*-conformation in the reactive conformer (**V**).

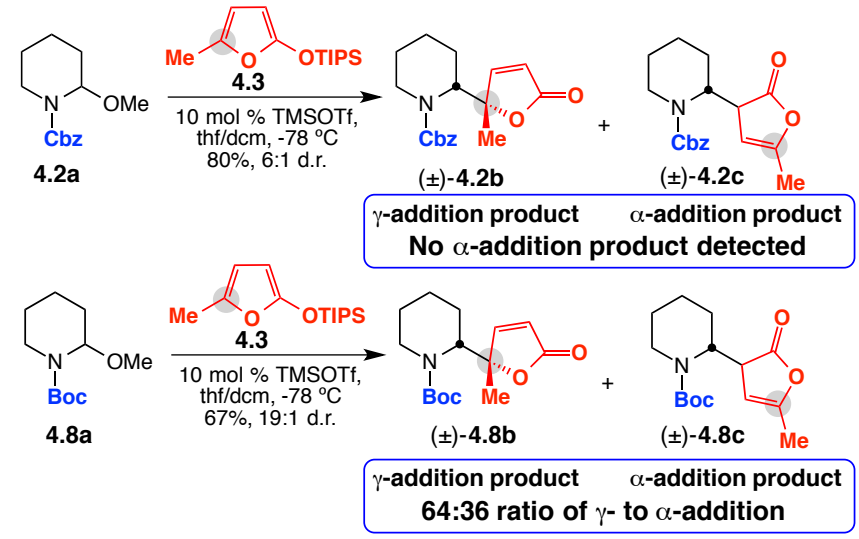
Figure 4.2 Proposal for Reversal of Diastereoselectivity with α-Methyl Siloxyfuran



To extend the scope of the Ag-catalyzed EVM reaction of siloxyfurans, our group began to investigate γ-substituted siloxyfurans as nucleophiles. As mentioned earlier, due to the increased sterics on the γ-position of the nucleophile, complications can arise

including competitive addition from the α-position of the nucleophile as well as overall decreased reactivity. Examples where complete γ-selectivity is observed with these nucleophiles have been reported, but they are almost exclusively additions to iminium or ammonium ions bearing minimal steric encumbrance.[21] Indicative of the important role that sterics play in regioselectivity is the vinylogous Mannich reaction in Pilli's synthesis of (±)-homopumiliotoxin 223G (discussed earlier, Scheme 4.2). Changing the nitrogen-protecting group from Cbz (**4.2a**, Scheme 4.5) to the more sterically bulky Boc (**4.8a**, Scheme 4.5) results in a change from complete γ-selectivity to obtaining a 64:36 ratio of γ- to α-addition products.[10b] Some additional reactions utilizing γ-substituted siloxyfurans show even lower amounts of γ-selectivity and sometimes

Scheme 4.5 Increase Substrate Sterics Increases α-Addition

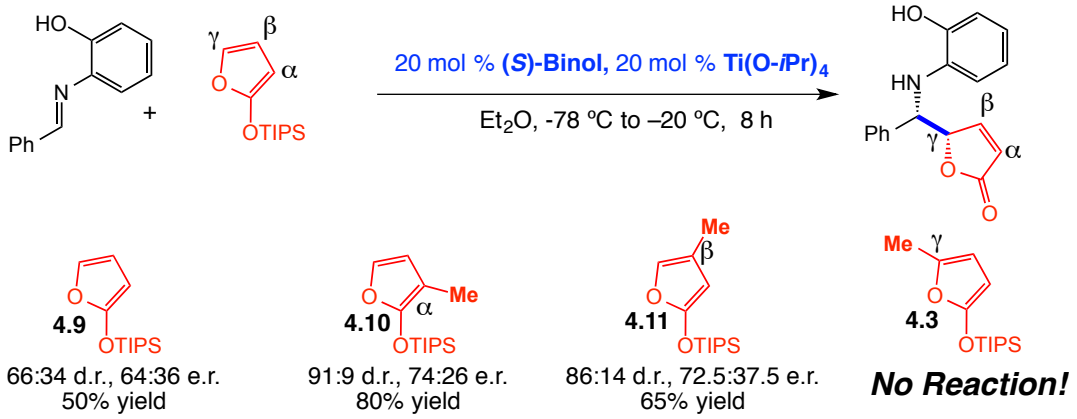


(21) Many of these reports do not mention the possible regiochemical issues when using these nucleophiles, and we infer that they did not observe the α-addition product. It is possible that α-addition did occur in some of these reports, but was relegated to the status of an uncharacterized side product. For examples of vinylogous Mannich reactions, see: References contained in footnotes 9 and 10. For catalytic, enantioselective Michael additions that occur through a catalytically generated iminium intermediate, see: (a) Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192–1194. (b) Huang, Y.; Walji, A. M.; Larsen, C. H.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 15051–15053. (c) Quintard, A.; Lefranc, A.; Alexakis, A. *Org. Lett.* **2011**, *13*, 1540–1543. For a catalytic, enantioselective allylc alkylation occurring through a catalytically generated allylic ammonium, see: (d) Cui, H.-L. *et al.* *Org. Lett.* **2010**, *12*, 720–723.

exclusively form the α-addition product.[22] Of all reported methods for the catalytic EVM reaction with dienolfuran nucleophiles,[23] only two involve γ-substituted nucleophiles.

The first is a Ti-catalyzed reaction of 2-aminophenol-derived aldimines with siloxyfurans (Scheme 4.6).[24] Compared with α- (**4.10**), β- (**4.11**), and unsubstituted (**4.9**) siloxyfurans, all of which react to give the desired product in 50 to 80% yield, γ-substituted siloxyfuran **4.3** does not add to the aldimine, even at -20 ºC. The authors note that at temperatures warmer than this, some product is formed, but it is in low yield and low selectivity (thy do not specify what type of selectivity is meant).

Scheme 4.6 Ti-Catalyzed EVM Reactions of Siloxyfurans



The second method, which came out while we were waiting to publish our report, is a Sc-catalyzed EVM reaction that proceeds in exclusive γ-selectivity to yield products in usually greater than 9:1 diastereomeric ratios and >95:5 enantiomeric ratios (Scheme

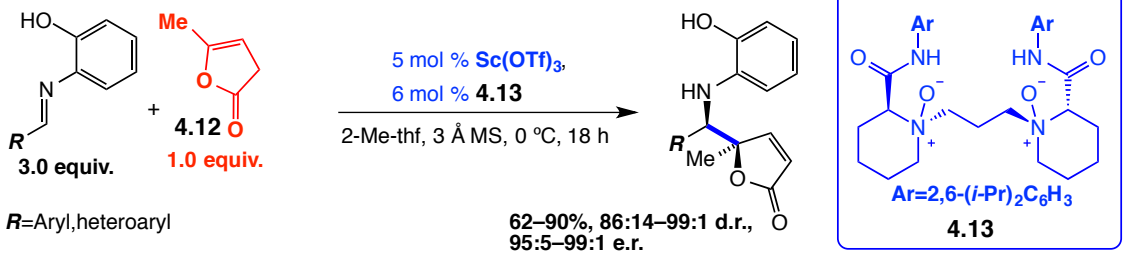
(22) (a) Asaoka, M.; Sugimura, N.; Takei, H. *Bull. Chem. Soc. Jpn*. **1979**, *52*, 1953–1956. (b) Redero, E.; Sandoval, C.; Bermejo, F. *Tetrahedron* **2001**, *57*, 9597–9605. (c) Kong, K.; Romo, D. *Org. Lett.* **2006**, *8*, 2909–2912.

(23) For examples from outside of our laboratory that do not involve γ-substituted nucleophiles, see: (a) Akiyama, T.; Honma, Y.; Itoh, J.; Fuchibe, K. *Adv. Synth. Catal.* **2008**, *350*, 399–402. (b) Yamaguchi, A.; Matsunaga, S.; Shibasaki, M. *Org. Lett.* **2008**, *10*, 2319–2322. (c) Yuan, Z.-L.; Jiang, J.-J.; Shi, M. *Tetrahedron*, **2009**, *65*, 6001–6007. (d) Deng, H.-P.; Wei, Y.; Shi, M. *Adv. Synth. Catal.* **2009**, *351*, 2897–2902.

(24) Martin, S. F.; Lopez, O. D. *Tetrahedron Lett.* **1999**, *40*, 8949–8953.

4.7).[25] Notably this method does not require a preformed siloxyfuran; the nucleophilic scandium dienolate is generated catalytically from α-angelica lactone **4.12** (the starting material used to synthesize γ-substituted siloxyfurans such as **4.3**). Another strong point

Scheme 4.7 Sc-Catalyzed EVM Reaction of α-Angelica Lactone



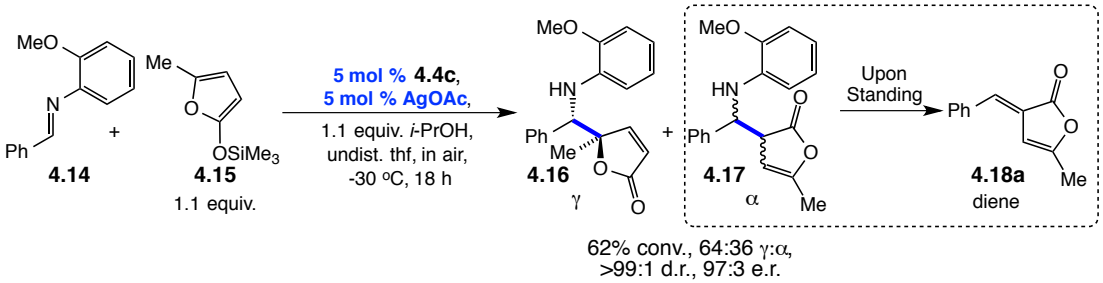
R=Aryl,heteroaryl

of this protocol is ligand **4.13** is accessed in four steps from readily available Boc-pipecolic acid (<$1.50/mmol for either enantiomer). The main drawback of this transformation is that it uses the expensive precious metal salt $Sc(OTf)_3$ ($16.9/mmol from Strem).

4.3 Development and Scope of the Ag-Catalyzed EVM Reaction with γ-Methylsiloxyfuran

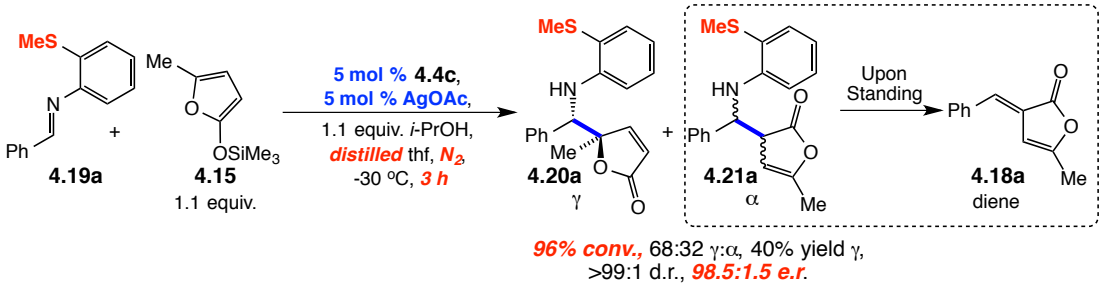
Under conditions similar to those developed for the Ag-catalyzed EVM reaction of siloxyfurans, Dr. Emma Carswell discovered the transformation with γ-substituted siloxyfuran is quite stereoselective (Equation 5), but sluggish (no conversion observed at -78 ºC). However, the main drawback is that it affords a 64:36 mixture of regioisomeric γ-addition and α-addition products. The α-addition product **4.17**, which is obtained in ~55:45 e.r., eliminates to diene **4.18a** upon standing.

(25) Zhou, L.; Lin, L.; Ji, J.; Xie, M.; Liu, X.; Feng, X. *Org. Lett.* **2011**, *13*, 3056–3059.



(5)

Graduate student Peng Fu optimized this further by changing the protecting group of the imine to *o*-thiomethyl-containing **4.19a** (Equation 6) and using more rigorously dry conditions. The conversion greatly improved under these conditions, but the γ:α ratio remained essentially the same.

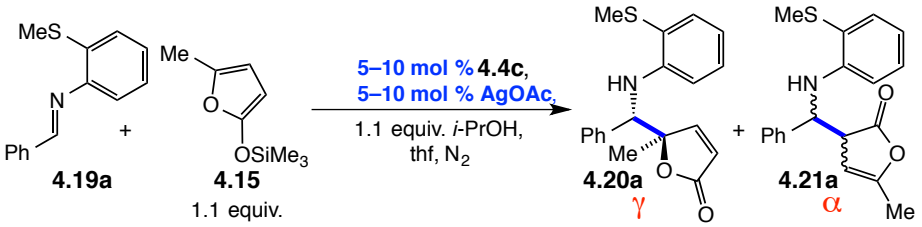


(6)

Around this time, I began to work on this project with the task of finding a way to improve the regioselectivity. Screening various ligand modifications proved unsuccessful, as did screening metal salts (other silver salts behaved the same or worse than AgOAc; copper (I) and copper (II) salts not only gave about the same γ:α ratio, but also decreased the diastereomeric ratio to ~1:1 and afforded a substantial amount of unidentified side products). Changing silyl-groups of the nucleophile also did not lead to increased selectivity; the reaction with the triethylsilyl analog of **4.15** went to 51% conversion and with a γ:α ratio of 62:38; reactions with the TBS and TIPS analogs did not proceed at all. Spurred by a hypothesis that protic additives catalyze α-addition, basic additives were screened, but no improvement was discovered. One parameter that did

prove impactful was temperature. By decreasing the temperature to -78 ºC, the γ:α ratio increased from 68:32 to 85:15 (Scheme 4.8). We next decided to examine *N*-activating groups to determine whether the selectivity and efficiency could be further improved (Table 4.1). Although the enantioselectivity of the products with alternative *N*-activating groups is maintained, conversion and yield suffers (Table 4.1). Therefore, *o*-thiomethylaniline was retained as the *N*-activating group.

Scheme 4.8 Decreasing Temperature Increases Regioselectivity



***-30 ºC,* 3 h,**

95% conv., **68:32** γ:α,
40% yield γ,
>99:1 d.r., 98.5:1.5 e.r.

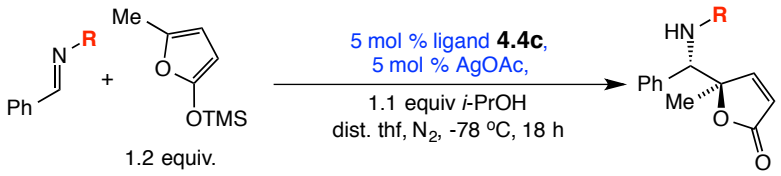
***-50 ºC,* 12 h,**

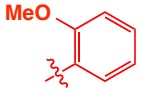
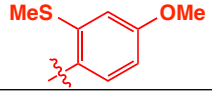
95% conv., **75:25** γ:α,
61% yield γ,
>99:1 d.r., >99:1 e.r.

***-78 ºC,* 18 h,**

81% conv., ***85:15*** *γ:α,*
64% yield γ,
>99:1 d.r., >99:1 e.r.

Table 4.1 Different *N*-Protecting Groups



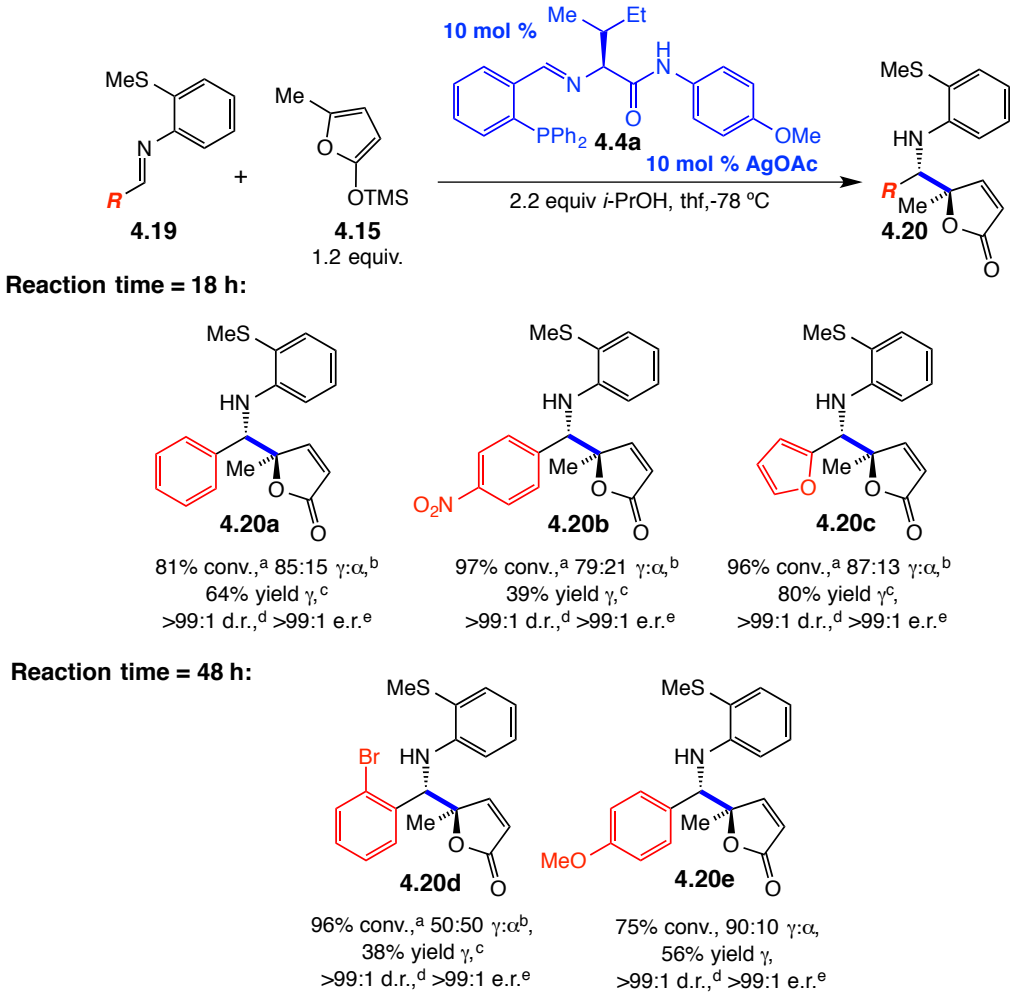
entry	R	conv. (%)[a]	γ:α addition[a]	yield γ (%)[b]	e.r (%)[c]
1		51	74:26	32	97
2		49	83:17	31	>98

Diastereomeric ratio is >99:1 in both cases. [a] Determined by 400 MHz ^{1}H NMR analysis of unpurified reaction mixture. [b] Yield of isolated product [c] Determined by HPLC analysis.

Before investigating the substrate scope, a few final modifications were made. *tert*-Leucine-derived ligand **4.4c** was changed *iso*-leucine-derived **4.4a** since they both

lead to an identical EVM reaction and **4.4a** is more easily accessible.[26] The catalyst loading was also increased to 10 mol % in an effort to increase reproducibility of the reaction.

Scheme 4.9 Additions to Aryl-Substituted Aldimines



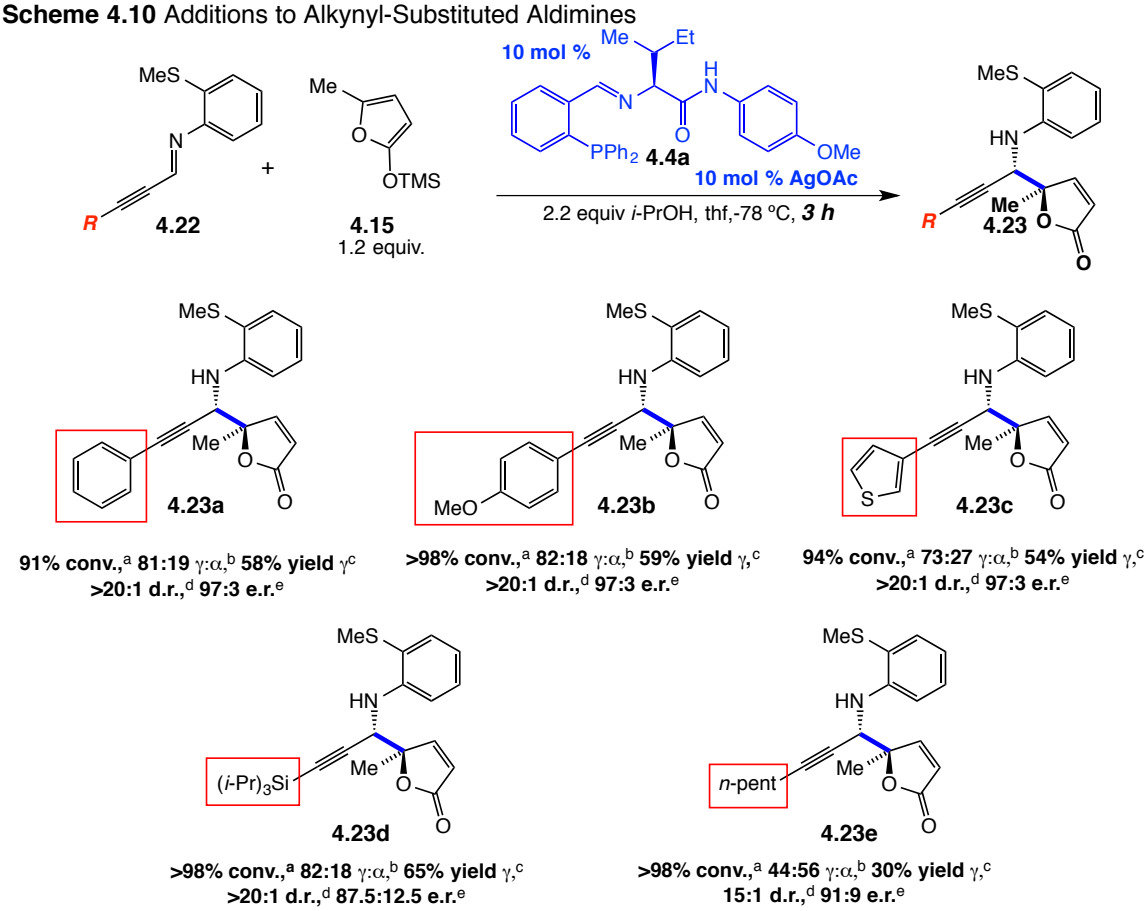
[a]Conversion of starting material to products as determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture. [b] Determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture. [c]Yield of isolated γ-addition product. [d]Determined by 400 MHz ^{1}H analysis of isolated γ-addition product. [e]Determined by HPLC analysis.

The Ag-catalyzed EVM reaction proceeds more efficiently, but with lower regioselectivity with an electron-poor aldimine (**4.20b**, Scheme 4.9). The reaction with electron rich *para*-methoxy aldimine is notably slower, requiring 48 hours to reach 75%

(26) The identity of the amino-acid will not greatly impact the cost of these ligands since 2-(diphenylphosphino)benzaldehyde, needed in the synthesis of these ligands, is $17.4/mmol (Aldrich).

conversion, although it more selective for γ-addition product **4.20e**. Sterically unhindered 2-furyl aldimine **4.19c** undergoes addition more efficiently and with about the same levels of regioselectivity as benzaldehyde-derived aldimine **4.19a**, affording **4.20c** in 80% yield. The decreased γ:α ratio (50:50) observed in the synthesis of **4.20d** is likely due to the increased sterics of the *ortho*-Br benzaldehyde-derived aldimine. In all cases, the γ-addition products are obtained in >99:1 d.r. and e.r.

Scheme 4.10 Additions to Alkynyl-Substituted Aldimines



[a]Conversion of starting material to products as determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture. [b] Determined by 400 MHz ^{1}H analysis of the unpurified reaction mixture. [c]Yield of isolated γ-addition product. [d]Determined by 400 MHz ^{1}H analysis of isolated γ-addition product. [e]Determined by HPLC analysis.

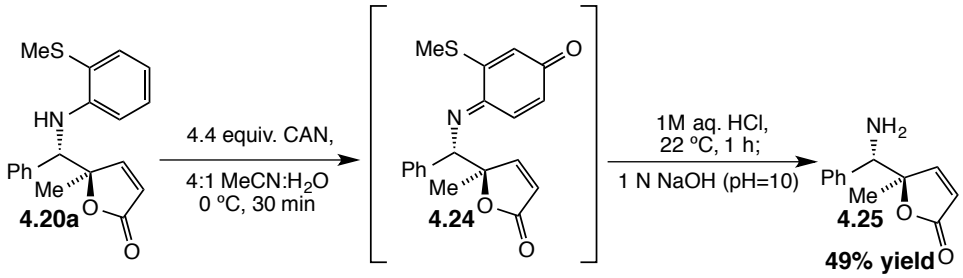
Next, we examined reactions of alkynyl-substituted aldimines (Scheme 4.10). We hypothesized that an unfavorable steric interaction is the cause of the undesired α-addition in the EVM reaction with γ-substituted siloxyfuran **4.15**, therefore, employing

the less sterically encumbered alkynyl-aldimine substrates should favor the formation of desired γ-addition product. However, we obtain similar results to aryl-substituted aldimines in terms of γ-selectivity (Scheme 4.10). The smaller size of the aldimine substituent (and/or its increased electronegativity) did, however, lead to a more efficient reaction with 94 to 98% conversions being obtained in three hours (as opposed to 63 to 97% conversions in 18 hours with aryl-substituted aldimines).

Another noteworthy difference in EVM reactions with alkynyl-substituted aldimines compared with that of aryl-substituted aldimines, is that in certain cases, lower levels of diastereoselectivity are observed with alkynyl-substituted aldimines. (Scheme 4.10 versus Scheme 4.9). Aldimines derived from aryl- and heterocycle-substituted alkynyl aldehydes afford high site-, diastereo-, and enantioselectivities (**4.23a** to **4.23c**, Scheme 4.10). Reaction with an imine substrate bearing a silyl-substituted alkyne yields high site- and diastereoselectivities but decreased enantioselectivities (**4.23d**, Scheme 4.10). EVM reactions with alkynylimines bearing an alkyl group result in a decrease both in diastereoselectivity and the ratio of γ- to α-addition product (**4.23e**, Scheme 4.10).

In order to increase the utility of the EVM reaction with γ-substituted siloxyfurans, an efficient method for the removal of the 2-thiomethylaniline *N*-protecting group must be developed. Employing $PhI(OAc)_2$, which cleanly removes the *o*-anisidyl group from similar products (e.g. **4.5a** in Scheme 4.3),[17] only results in oxidation of the sulfur in **4.20a**. Following extensive optimization, the best result is obtained with cerric ammonium nitrate (CAN) as an oxidant (Scheme 4.11). Following hydrolysis of **4.24**, the free amine **4.25** is afforded in a modest 49% yield.

Scheme 4.11 Removal of 2-Thiomethylaniline *N*-protecting Group



4.3 Conclusions

The EVM reaction with γ-substituted siloxyfuran **4.15** can be promoted by a Ag-phosphine complex. Key to obtaining high yields of the desired γ-addition product is performing the reaction at low temperature to minimize the formation of competing α-addition product. In order to obtain acceptable conversions at such temperatures, use of a 2-thiomethylaniline *N*-protecting group is employed.

4.4 Experimental Section

■ **General.** Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, λ_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) or 500 (500 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). Data are reported as follows: chemical shift, multiplicity

(singlet unless otherwise noted), and coupling constants (Hz). High-resolution mass spectrometry was performed on a JEOL AccuTOF-DART (positive mode) or an Advion Expression CMS (ESI+ or ESI-) or a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College and at the University of Illinois Mass Spectrometry Laboratories (Urbana, Illinois). Elemental microanalyses were performed at Robertson Microlit Laboratories (Madison, NJ). Enantiomer ratios (e.r.) values were determined by HPLC analysis using a SCL-10AVP chromatograph (Chiral Technologies Chiralcel OD (4.6 x 250 mm), Chiral Technologies Chiralcel OJ (4.6 x 250 mm), Chiral Technologies Chiralpak AD (4.6 x 250 mm). Specific rotations were measured using a Rudolph Research Analytical Autopol IV Polarimeter. Melting points were determined using a Thomas Hoover Uni-melt capillary melting point apparatus. Selected single crystals suitable for X-ray crystallographic analysis were used for structural determination. The X-ray intensity data were measured at 100(2) K (Oxford Cryostream 700) on a Bruker Kappa APEX Duo diffractometer system equipped with a sealed Mo-target X-ray tube (λ = 0.71073 Å) and a high brightness IμS copper source (λ = 1.54178 Å). The crystals were mounted on agoniometer head with paratone oil. The detector was placed at a distance of 5.000 or 6.000 cm from the crystal. For each experiment, data collection strategy was determined by APEX software package and all frames were collected with a scan width of 0.5° in ω and φ with an exposure time of 10 or 20s/frame. The frames were integrated with the Bruker SAINT Software package using a narrow-frame integration algorithm to a maximum 2θ angle of 56.54° (0.75 Å resolution) for Mo data and of 134° (0.84 Å resolution) for Cu data. The final cell constants are based upon the refinement of the XYZcentroids of several thousand reflections above 20 σ(I).

Analysis of the data showed negligible decay during data collection. Data were corrected for absorption effects using the empirical method (SADABS). The structures were solved and refined by full-matrix least squares procedures on ||F2|| using the Bruker SHELXTL (version 6.12) software package. All hydrogen atoms were included in idealized positions for structure factor calculations except for those forming hydrogen bonds or on a chiral center. Anisotropic displacement parameters were assigned to all non-hydrogen atoms, except those disordered. Unless otherwise noted, reactions were carried out under an atmosphere of dry N_2 in oven-dried (135 ºC) glassware with the appropriate oven-dried (65 ºC) septa.

■ **Solvents:** Unless otherwise noted, solvents were purged with Ar and purified under a positive pressure of dry Ar by a modified Innovative Technologies purification system. Toluene (Fisher, ACS Grade) was passed successively through activated copper and alumina columns. Dichloromethane (Fisher, ACS Grade) and diethyl ether (Aldrich, Chromasolv®) were passed successively through two activated alumina columns. Tetrahydrofuran was purified by distillation from sodium benzophenone ketyl immediately prior to use. $CDCl_3$ was purchased from Cambridge Isotope Laboratories and stored over activated 4Å molecular sieves prior to use. All work-up and purification procedures were carried out in air with reagent grade solvents (purchased from Fisher). Acetonitrile (HPLC grade) was purchased from Aldrich and used as received.

■ **Reagents:**

Aldehydes (for the Synthesis of Aldimines): The requisite aldehydes to access aldimines **4.19a–e** and **4.22e** were purchased from Aldrich and used as received. The alknyl-substituted aldehydes used in the synthesis of aldimines **4.22a** to **4.22d** were

synthesized from the corresponding alkynes in accordance to a procedure in the literature.[27]

Cerric Ammonium Nitrate (CAN): Purchased from Aldrich (98.5%) and used as received.

Isopropanol: Purchased from Fisher and distilled from CaH_2 and stored over activated 4Å MS prior to use.

Magnesium Sulfate was purchased from Fisher and flame-dried under vacuum prior to use.

Phosphine Ligands 4.4a–4.4c: Synthesized in accordance to a procedure in the literature.[28]

2-(Methylthio)aniline: was purchased from Aldrich and used as received.

Trimethyl((5-methylfuran-2-yl)oxy)silane (4.15): Synthesized in accordance to a procedure in the literature[29] and purified by Kügel–Röhr distillation (~1 Torr, 50 ºC).

Silver Acetate: was purchased from Aldrich (99.99% purity) and used as received.

■ Representative Procedure for the Synthesis of *o*-Thiomethyl Aldimines (4.19a, Equation 6):

A 200 mL round bottom flask equipped with a stirbar is charged with MgSO4 (11.6 g, 96.5 mmol) then sealed with a rubber septum and connected to an atmosphere of N_2 *via* a needle. Dichloromethane (30 mL), benzaldehyde (2.0 mL, 19.3 mmol), and 2-(methylthio)aniline (2.4 mL, 19.5 mmol) are added sequentially and the reaction is allowed to stir at 22 ºC for 20 hours, during which time solution becomes bright yellow. The reaction mixture is passed through a fritted-glass funnel to remove the $MgSO_4$ and

(27) Journet, M.; Cai, D.; DiMichele, L. M.; Larsen, R. D. *Tetrahedron Lett.* **1998**, *39*, 6427–6428.
(28) Carswell, E. L.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2006**, *41*, 6355–6359.
(29) Simmons, B.; Walji, A. M.; ManMillan, D. W. C. **2009**, *48*, 4349–4353.

the resulting solution is concentrated to give a cloudy orange oil. The desired product is purified by trituration from ice-cold hexanes/diethyl ether to afford **4.19a** (3.28g, 14.4 mmol, 74.7% yield) as a bright yellow powder. If purification of the aldimine is not possible by recrystallization or trituration, then it can be purified by silica gel chromatography (columnmust be slurry-packed with ~95:5 hexanes:triethylamine or the substrate will decompose.

Benzylidene-(2-methylsulfanyl-phenyl)-amine (4.19a, Scheme 4.9): M. p. = 44–46 °C. IR (neat): 3058 (m), 2918 (m), 1626 (s), 1575 (m), 1465 (m), 1437 (m), 1190 (s), 1072 (m), 1042 (m), 761 (m) 690 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (1H, s), 7.97-7.95 (2H, m), 7.50–7.48 (3H, m), 7.23–7.22 (2H, m), 7.19–7.15 (1H, m), 7.00–6.98 (1H, m), 2.47 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 149.2, 136.2, 134.1, 131.6, 129.1, 128.9, 126.5, 125.3, 124.6, 117.6, 14.9. Elemental analysis for $C_{14}H_{13}NS$, Calcd: C, 73.97; H, 5.76; N, 6.16; found: C, 74.0; H, 5.94; N, 5.93.

(2-Methylsulfanyl-phenyl)-(4-nitro-benzylidene)-amine (4.19b, Scheme 4.9): Orange solid. M. p. = 134–136 °C. IR (neat): 1595 (m), 1514 (s), 1464 (m), 1434 (m), 1338 (s), 851 (m), 756 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (1H, s), 8.34–8.32 (2H, m), 8.14–8.10 (2H, m), 7.30–7.23 (2H, m), 7.21–7.16 (1H, m), 7.05–7.02 (1H, m), 2.49 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 149.5, 147.9, 141.6, 135.2, 129.7, 127.7, 125.3, 124.8, 124.2, 117.2, 14.8; Elemental analysis for $C_{14}H_{12}N_2OS$, calcd.: C, 61.75; H, 4.44; N, 10.29; found: C, 61.47; H, 4.36; N, 10.09.

Furan-2-ylmethylene-(2-methylsulfanyl-phenyl)-amine (**4.19c, Scheme 4.9):** Yellow solid. M. p. = 69-71 °C. IR (neat): 3117 (m), 3055 (m), 2979 (m), 2918 (m), 1624 (s), 1573 (s), 1482 (m), 1460 (s), 1438 (m), 1393 (m), 1346 (m), 1267 (m), 1199 (m), 1154

(m), 1077 (m), 1042 (m), 1018 (s), 934 (s), 883 (m), 782 (m), 745 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (1H, s), 7.62 (1H, d, *J* = 1.6 Hz), 7.21–7.20 (2H, m), 7.16–7.12 (1H, m), 7.01 (1H, d, *J* = 3.6 Hz), 6.96–6.94 (1H, m), 6.55 (1H, dd, *J* = 3.2, 1.6 Hz), 2.46 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 149.1, 147.9, 145.9, 134.2, 126.6, 125.3, 124.9, 117.5, 116.2, 112.3, 15.0; Elemental analysis for $C_{12}H_{11}NOS$, calcd.: C, 66.33; H, 5.10; N, 6.45; found: C, 66.24; H, 5.03; N, 6.31.

(2-Bromo-benzylidene)-(2-methylsulfanyl-phenyl)-amine (4.19d, Scheme 4.9): Yellow solid. M. p. = 72–74 °C. IR (neat): 3057 (m), 2982 (m), 2917 (m), 1616 (s), 1570 (m), 1471 (s), 1437 (s), 1360 (m), 1271 (s), 1192 (m), 1069 (m), 1042 (s), 1024 (s), 967 (m), 880 (s), 757 (s), 728 (s), 668 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (1H, s), 8.33 (1H, dd, *J* = 8.0, 1.6 Hz), 7.63–7.61 (1H, m), 7.44–7.40 (1H, m), 7.35–7.30 (1H, m), 7.26–7.16 (3H, m), 7.05–7.02 (1H, m), 2.48 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 148.8, 134.7, 134.6, 133.3, 132.6, 129.6, 127.9, 127.0, 126.2, 125.4, 124.7, 117.8, 14.9. Elemental analysis for $C_{14}H_{12}BrNS$, calcd.: C, 54.91; H, 3.95; N, 4.57; found: C, 55.05; H, 3.88; N, 4.41.

(4-Methoxy-benzylidene)-(2-methylsulfanyl-phenyl)-amine (4.19e, Scheme 4.9): Yellow solid. M. p. = 71–73 °C. IR (neat): 2917 (m), 2836 (m), 1622 (s), 1603 (m), 1573 (m), 1511 (s), 1465 (m), 1438 (m), 1308 (m), 1252 (s), 1163 (m), 1069 (m), 1030 (m), 833 (s), 826 (s), 748 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (1H, s), 7.92–7.88 (2H, m), 7.21–7.17 (2H, m), 7.16–7.13 (1H, m), 7.00–6.95 (3H, m), 3.88 (3H, s), 2.46 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 159.4, 149.5, 134.0, 130.8, 129.4, 126.1, 125.3, 124.5, 117.6, 114.3, 55.6, 14.9. Elemental analysis for $C_{15}H_{15}NOS$, calcd.: C, 70.01; H, 5.87; N, 5.44; found: C, 70.05; H, 5.74; N, 5.28.

(2-Methylsulfanyl-phenyl)-(3-phenyl-prop-2-ynylidene)-amine (4.22a, Scheme 4.10): Yellow solid. m. p. = 74–76 °C. IR (neat): 3054 (m), 2980 (m), 2918 (m), 2856 (m), 2197 (s), 1597 (s), 1585 (s), 1572 (s), 1488 (m), 1462 (m), 1435 (s), 1351 (m), 1320 (m), 1265 (m), 1200 (m), 1178 (m), 1160 (m), 1068 (m), 1017 (s), 949 (m), 848 (m), 754 (s), 742 (s), 686 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (1H, s), 7.57–7.55 (1H, m), 7.38–7.32 (3H, m), 7.22-7.18 (2H, m), 7.12–7.08 (1H, m), 6.86 (1H, dd, *J* = 7.6; 0.8 Hz), 2.43 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 144.0, 134.4, 132.6, 130.0, 128.6, 127.5, 125.4, 125.2, 121.6, 117.5, 95.5, 87.8, 15.2; Elemental analysis for $C_{16}H_{13}NS$, calcd.: C, 76.46; H, 5.21; N, 5.57; found: C, 76.44; H,4.89; N, 5.43.

[3-(4-Methoxy-phenyl)-prop-2-ynylidene]-(2-methylsulfanyl-phenyl)-amine (4.22b, Scheme 4.10): Yellow solid. M. p. = 102–104 °C. IR (neat): 2915 (w), 2837 (w), 2197 (s), 1602 (s), 1584 (s), 1559 (s), 1505 (s), 1459 (s), 1439 (s), 1352 (m), 1267 (s), 1169 (s), 1032 (s), 830 (s), 761 (s), 732 (m), 669 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (1H, s), 7.55 (1H, d, *J* = 9.2 Hz), 7.26–7.20 (2H, m), 7.17-7.12 (1H, m), 6.92–6.88 (3H, m), 3.84 (3H, s), 2.43 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 149.2, 144.2, 134.4, 134.3, 127.3, 125.4, 125.2, 117.5, 114.4, 113.5, 96.3, 87.3, 55.5, 15.2; HRMS Calcd for $C_{17}H_{16}N_1OS$ $[M + H]^+$: 282.09526; Found: 282.09572.

***N*-(2-(Methylthio)phenyl)-3-(thiophen-3-yl)prop-2-yn-1-imine (4.22c, Scheme 4.10):** Yellow solid. ~95:5 E:Z M. p. = 91–93 °C. IR (neat): 3105 (w), 2201 (m), 1586 (m), 1560 (w), 1070 (s), 798 (s), 754 (s), 694 (s), 626 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (1H,s), 7.73 (1H, m), 7.35 (1H, dd, *J* = 5.0, 3.0 Hz), 7.30–7.21 (m, 2H), 7.19–7.15 (1H, m), 6.92 (1H, d, *J* = 8.0 Hz), 2.49 (3H, s). ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0,

143.6, 134.4, 132.1, 130.2, 127.5, 125.9, 125.4, 125.2, 120.8, 117.5, 90.7, 87.8, 15.2; HRMS Calcd for $C_{14}H_{12}N_1S_2$ $[M + H]^+$: 258.04112; Found: 258.04106.

(2-Methylsulfanyl-phenyl)-(3-triisopropylsilanyl-prop-2-ynylidene)-amine (4.22d): Yellow oil. 2:1 mixture of E:Z isomers. IR (neat): 3057 (w), 2942 (s), 2890 (m), 2864 (s), 2726 (w), 1590 (s), 1574 (m), 1461 (s), 1437 (m), 1384 (m), 1076 (m), 1057 (s), 1018 (m), 996 (m), 920 (m), 881 (s), 752 (s), 734 (m), 703 (m), 664 (s), 597 (m), 583 (m), 532 (m), 460 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (0.5H, s), 7.67 (1H, s), 7.25-7.19 (3H, m), 7.14–7.08 (1.5H, m), 7.03–7.01 (0.5H, m), 6.86–6.84 (1H, m), 2.45 (3H, s), 2.45 (1.5H, s), 1.18–1.09 (21H, m), 1.01-0.93 (10.5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 148.8, 144.0, 143.3, 134.2, 130.9, 127.4, 126.1, 126.0, 125.3, 125.1, 125.1, 119.4, 117.5, 104.2, 102.7, 99.9, 99.8, 18.7, 18.5, 15.7, 15.1, 11.3, 11.1; HRMS Calcd for $C_{19}H_{30}N_1SiS$ $[M + H]^+$: 332.18682; Found: 332.18749.

***N*-(2-(Methylthio)phenyl)oct-2-yn-1-imine (4.22e):** Orange oil. ~85:15 mixture of E:Z (or Z:E) isomers. IR (neat): 3056 (w), 2925 (m), 2890 (m), 2859 (w), 2213 (m), 1592 (s), 1463 (m), 1437 (m), 1157 (m), 747 (s), cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (1H, t, J = 1.7 Hz), 7.23–7.18 (2H, m), 7.14–7.07 (1H, m), 6.88 – 6.79 (1H, m), 2.44 (5H, d, J = 4.4 Hz), 1.73–1.56 (2H, m), 1.50–1.29 (4H, m), 0.92 (3H, t, J = 7.2 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 144.7, 133.9, 127.1, 125.3, 125.0, 117.5, 98.5, 79.7, 31.2, 27.8, 22.3, 19.7, 15.1, 14.0; HRMS Calcd for $C_{15}H_{20}NS$ $[M + H]^+$: 246.13164; Found: 246.13116.

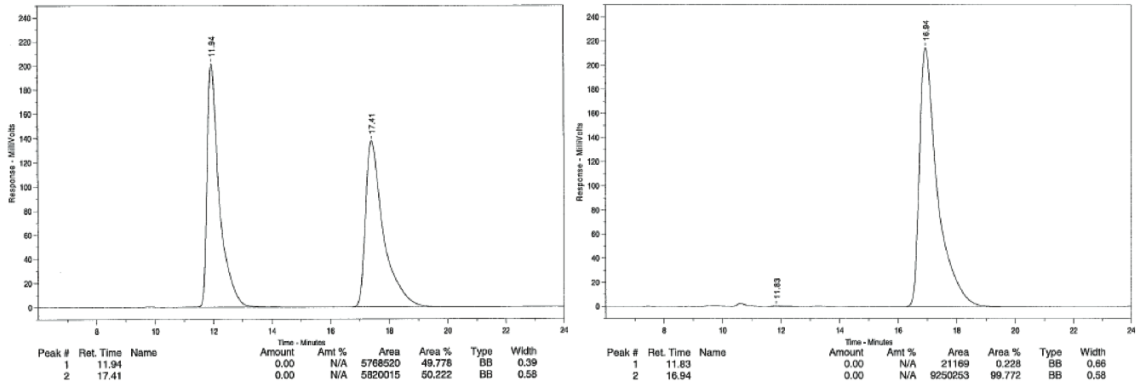
■ **Representative experimental procedure for the EVM reaction:**

To a 10 mL round-bottomed flask equipped with a stirbar, 3.4 mg (0.02 mmol, 0.1 equivalents) AgOAc, 10.1 mg (0.02 mmol, 0.1 equivalents) of ligand **4.4a**, and 45.5 mg

(0.2 mmol, 1.0 equivalents) of benzaldehyde-derived imine **4.19a** is added and a septum is attached. While covered in aluminum foil to prevent exposure to light, the vessel is purged with nitrogen for 15 minutes. 2.0 mL of a stock solution of distilled *i*-PrOH in distilled THF (33.4 μL *i*-PrOH [2.2 equivalents]/ 2 mL THF) is added through a syringe. The solution is allowed to stir for 10 minutes. The solution is allowed to cool to -78 ºC for 15 minutes after which time 45 μL (40.5, .24 mmol, 1.2 equivalents) of siloxyfuran **4.15** is added to the reaction. After 18 hours, 1.0 mL of acetic acid in methanol (22 μL HOAc, 23.1 mg, 0.38 mmol) is added dropwise, and the mixture is allowed to stir at -78 ºC for three hours before being allowed to warm to 23 ºC. The solution is diluted with ethyl acetate, passed through a plug of silica, and concentrated in vacuo. The resulting yellow oil is purified by silica gel chromatography (9 mm column, 10 mL 9:1 hexanes:ethyl acetate, 48 mL 5:1 hexanes:ethyl acetate) to afford the desired product (41.4 mg 0.127 mmol, 64 % yield, >99:1 e.r) as a pale yellow solid.

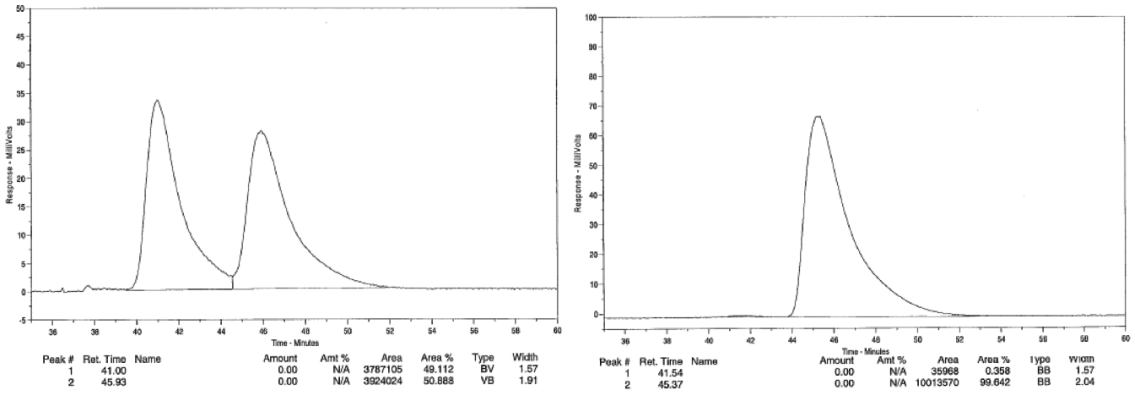
5-Methyl-5-[(2-methylsulfanyl-phenylamino)-phenyl-methyl]-5H-furan-2-one (4.20a): M.p. = 125–127 °C. IR (neat): 3368 (w), 3064 (w), 2986 (w), 2921 (w), 1760 (s), 1587 (s), 1499 (s), 1451 (m), 1426 (w), 1319 (m), 1279 (m), 1235 (m), 1195 (m), 1163 (m), 1140 (m), 1104 (m), 1072 (m), 1038 (s), 965 (m), 947 (m), 911 (m), 818 (m), 778 (m), 748 (m), 702 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.38 (2H, m), 7.30-7.24 (5H, m), 7.03-6.99 (1H, m), (6.64-6.60 (1H, m), 6.40 (1H, d, *J* = 8.0 Hz), 5.94 (1H, d, *J* = 5.6 Hz), 5.89 (1H, d, *J* = 8.4 Hz), 4.68 (1H, d, *J* = 8.4 Hz), 2.36 (3H, s), 1.64 (3H, s). ^{13}C NMR (400 MHz, $CDCl_3$): δ 171.8, 158.1, 146.8, 137.9, 134.4, 129.4, 128.8, 128.4, 127.7, 121.9, 121.0, 118.0, 111.2, 90.2, 63.5, 22.5, 18.7. Elemental analysis for $C_{19}H_{19}NO_2S$, calculated.: C, 70.12; H, 5.88; N, 4.30; found: C, 70.32; H, 5.77; N, 4.08.

Optical rotation: $[\alpha]_D^{22\,°C}$ 0.734 (*c* 1.18, $CHCl_3$) for a 97:3 e.r. sample. The enantiomeric purity was determined by HPLC analysis (OD, 90:10 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm) t_R 11 min (minor) and t_R 16 min (major).



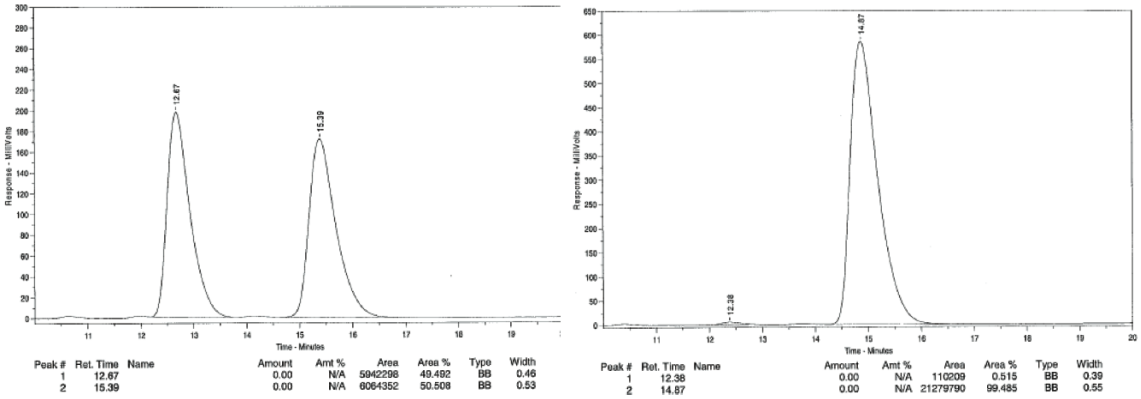
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	11.9	49.778	1	11.8	0.228
2	17.4	50.222	2	16.9	99.772

(5*R*)-5-Methyl-5-(((2-(methylthio)phenyl)amino)(4-nitrophenyl)methyl)furan-2(5*H*)-one (4.20b, Scheme 4.9): Bright yellow oil. IR (neat): 3359 (br), 3107(w), 2923 (w), 1758 (s), 1586 (m), 1519 (s), 1498 (s), 1344 (s), 1314 (m), 1139 (m), 1103 (m), 910 (m), 818 (s), 729 (s), 697 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.15 (2H, dd, *J* = 9.0, 2.1 Hz), 7.52–7.35 (4H, m), 7.07–6.95 (1H, m), 6.73–6.62 (1H, m), 6.29 (1H, d, *J* = 8.0), 5.98 (1H, d, *J* = 8.5 Hz), 5.94 (1H, d, *J* = 5.7 Hz), 4.78 (1H, d, *J* = 8.5 Hz), 2.40 (3H, s), 1.70 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 157.7, 147.9, 145.9, 145.4, 134.4, 129.4, 128.8, 124.0, 122.3, 121.5, 118.9, 111.1, 89.4, 63.1, 22.3, 18.8; HRMS calcd for $C_{19}H_{19}N_2O_4S$ (M+H): 316.10655, Found: 316.10753. Optical rotation: $[\alpha]_D^{20}$ –4.6 (*c* = 0.40, $CHCl_3$) for a >99:1 e.r. sample. The enantiomeric purity was determined by chiral HPLC analysis (OD, 90:10 hexanes:*i*-PrOH, 1.0 mL/min, 254 nm) t_R 41 min (minor) and t_R 46 min (major).



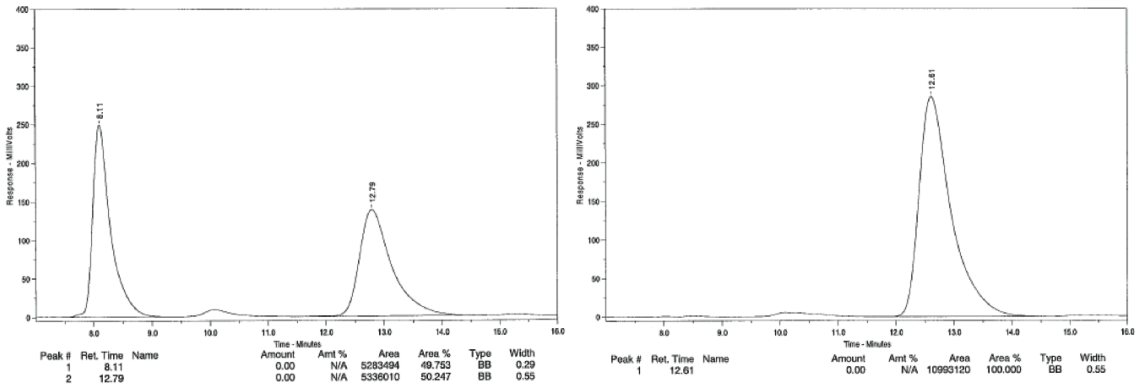
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	41.0	49.112	1	11.8	0.358
2	45.9	50.888	2	16.9	99.642

5-[Furan-2-yl-(2-methylsulfanyl-phenylamino)-methyl]-5-methyl-5H-furan-2-one (4.20c, Scheme 4.9): Pale yellow oil. IR (neat): 3350 (br), 3072 (m), 2984 (m), 2922 (m), 2854 (m), 1752 (s), 1586 (s), 1497 (s), 1450 (m), 1426 (m), 1377 (m), 1314 (m), 1276 (m), 1233 (m), 1147 (m), 1105 (m), 1069 (m), 1050 (m), 1038 (m), 1011 (m), 966 (m), 950 (m), 916 (m), 900 (m), 884 (m), 861 (m), 815 (s), 739 (s), 684 (m), 597 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (2H, d, *J* = 6.0 Hz), 7.39 (1H, dd, *J* = 7.6; 1.6 Hz), 7.35-7.34 (1H, m), 7.14–7.10 (1H, m), 6.70–6.66 (1H, m), 6.57 (1H, d, *J* = 8.4 Hz), 6.29–6.26 (2H, m), 6.08 (1H, d, *J* = 6.0 Hz), 5.54 (1H, d, *J* = 9.2 Hz), 4.81 (1H, d, *J* = 9.2 Hz), 2.28 (3H, s), 1.59 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 157.5, 151.2, 146.8, 142.4, 134.6, 129.6, 122.3, 121.4, 118.6, 114.2, 111.3, 110.8, 108.8, 89.9, 57.8, 21.9, 18.6; HRMS calcd for $C_{17}H_{18}NO_3S$ (M+H): 316.10074, Found: 316.09947. Optical rotation: $[\alpha]_D^{20}$ 109.6 (*c* 0.62, $CHCl_3$) for a 97:3 e.r. sample. The enantiomeric purity was determined by chiral HPLC analysis (OD, 95:5 hexanes:*i*-PrOH, 1.0 mL/min, 254 nm) t_R 18 min (minor) and t_R 23 min (major).



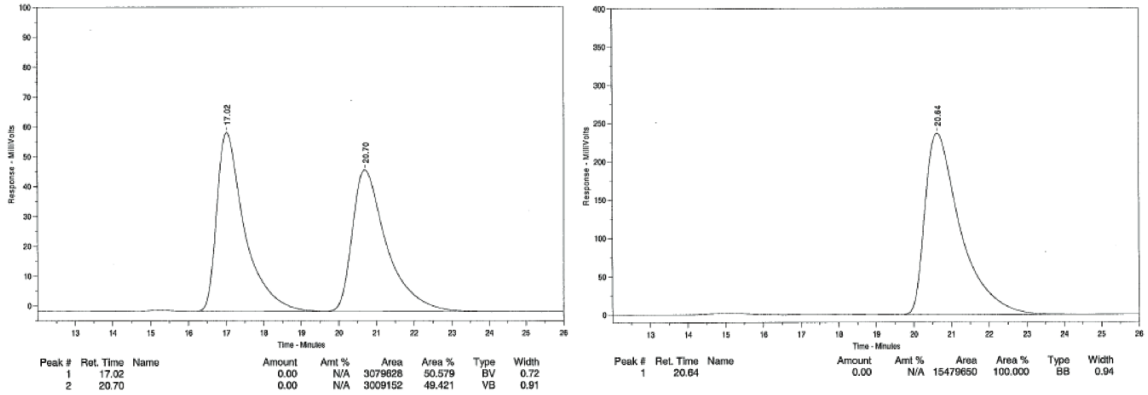
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	12.7	49.492	1	12.4	0.515
2	15.4	50.508	2	14.9	99.485

(5*R*)-5-((2-Bromophenyl)((2-(methylthio)phenyl)amino)methyl)-5-methylfuran-2(5*H*)-one (4.20d, Scheme 4.9): Pale yellow solid. M. p. = 170–172 ºC. IR (neat): 3398 (w), 2922 (w), 1763 (s), 1752 (s), 1500 (s), 1456 (s), 1321 (s), 1303 (m), 1109 (m), 924 (s), 816 (s), 734 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (1H, d, *J* = 5.7 Hz), 7.48 (1H, dd, *J* = 8.0, 1.3 Hz), 7.39 (1H, dd, *J* = 7.6, 1.6 Hz), 7.35 (1H, dd, *J* = 7.8, 1.7 Hz), 7.23–7.18 (1H, m), 7.16–7.01 (2H, m), 6.64 (1H, td, *J* = 7.5, 1.2 Hz), 6.42 (1H, dd, *J* = 8.3, 1.0 Hz), 6.16 (1H, d, *J* = 9.4 Hz), 5.75 (1H, d, *J* = 5.7 Hz), 5.30 (1H, d, *J* = 9.4 Hz), 2.40 (3H, s), 1.79 (3H, s); ^{13}C NMR (400 MHz, $CDCl_3$): δ 171.8, 157.5, 146.5, 134.0, 134.5, 132.7, 129.9, 129.7, 128.6, 128.4, 124.4, 121.8, 121.0, 118.3, 111.2, 90.4, 61.0, 22.8, 18.8; HRMS calcd for $C_{19}H_{19}N^{81}BrO_2S$ (M+H): 406.02994, Found: 406.02972. Optical rotation: $[\alpha]_D^{20}$ –144 (*c* = 0.88, $CHCl_3$) for a >99:1 e.r. sample. The enantiomeric purity was determined by chiral HPLC analysis (OD, 90:10 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm) t_R 8 min (minor) and t_R 13 min (major).



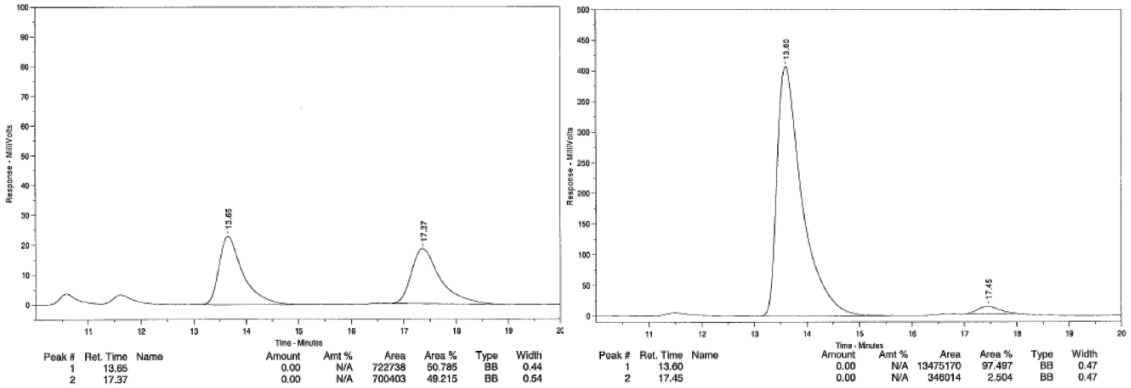
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	8.1	49.753	1	-n.d.-	-n.d.-
2	12.8	50.247	2	12.6	100.000

5-[(4-Methoxy-phenyl)-(2-methylsulfanyl-phenylamino)-methyl]-5-methyl-5H-furan-2-one (4.20e) White solid. M. p. = 134–136 °C. IR (neat): 3343 (w), 2958 (m), 2923 (s), 2853 (m), 1755 (s), 1610 (m), 1586 (s), 1510 (s), 1500 (s), 1453 (m), 1305 (m), 1278 (m), 1246 (s), 1177 (m), 1139 (m), 1101 (m), 1032 (m), 965 (m), 947 (m), 917 (m), 841 (s), 818 (m), 747 (m), 723 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.37 (2H, m), 7.21-7.19 (2H, m), 7.04–6.99 (1H, m), 6.83-6.81 (2H, m), 6.64–6.60 (1H, m), 6.39 (1H, d, J = 8.0 Hz), 5.95 (1H, d, J = 6.0 Hz), 5.83 (1H, d, J = 8.0 Hz), 4.63 (1H, d, J = 8.4 Hz), 3.76 (3H, s), 2.36 (3H, s), 1.62 (3H, s); ^{13}C NMR (400 MHz, $CDCl_3$): δ 171.9, 159.5, 158.2, 146.9, 134.4, 129.8, 129.5, 121.9, 121.0, 118.0, 114.2, 111.3, 90.5, 63.0, 55.3, 22.5, 18.7; HRMS calcd for $C_{20}H_{22}NO_3S$ (M+H): 356.13204, Found: 356.13402. Optical rotation: $[\alpha]_D^{20}$ 13.54 (*c* 0.32, $CHCl_3$) for a 99:1 e.r. sample. The enantiomeric purity was determined by chiral HPLC analysis (OD, 95:5 hexanes:*i*-PrOH, 1.0 mL/min, 254 nm) t_R 29 min (minor) and t_R 35 min (major).



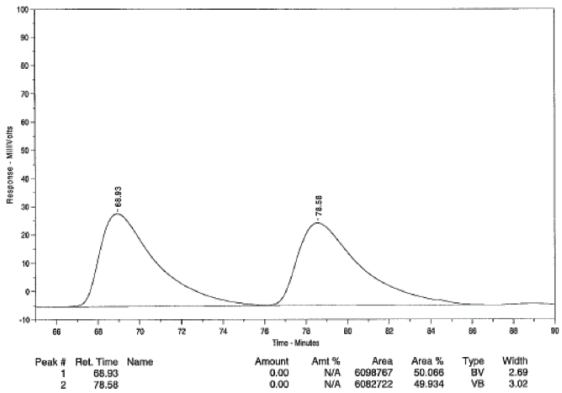
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	17.0	50.579	1	-n.d.-	-n.d.-
2	20.7	49.421	2	20.6	100.000

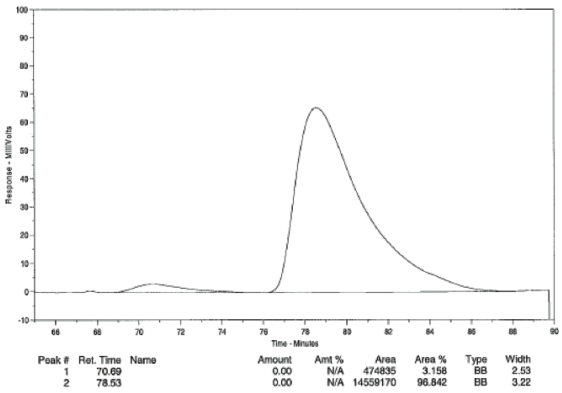
5-Methyl-5-[1-(2-methylsulfanyl-phenylamino)-3-phenyl-prop-2-ynyl]-5H-furan-2-one (4.23a): Yellow oil; IR (neat): 3340 (br), 3064 (w), 2984 (w), 2922 (w), 1758 (s), 1586 (m), 1491 (s), 1450 (m), 1425 (m), 1375 (m), 1313 (m), 1277 (m), 1234 (m), 1163 (m), 1140 (m), 1107 (m), 1071 (s), 1038 (m), 990 (m), 960 (m), 910 (s), 816 (m), 729 (s), 690 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (1H, d, J = 6.0 Hz), 7.45–7.42 (1H, m), 7.38–7.36 (2H, m), 7.33–7.29 (3H, m), 7.23–7.21 (1H, m), 6.82 (1H, d, J = 8.0 Hz), 6.79-6.75 (1H, m), 6.26 (1H, d, J = 6.0 Hz), 5.20 (1H, d, J = 9.2 Hz), 4.64 (1H, d, J = 9.2 Hz), 2.31 (3H, s), 1.79 (3H, s); ^{13}C NMR (400 MHz, $CDCl_3$): δ 171.7, 157.2, 146.7, 134.5, 131.9, 129.6, 128.9, 128.5, 123.2, 122.1, 119.2, 112.1, 89.8, 86.2, 85.1, 53.3, 29.8, 21.4, 18.7. HRMS calcd for $C_{21}H_{20}NO_2S$ (M+H): 350.12147, Found: 350.12270. $[\alpha]_D^{20}$ = +194 (c = 1.29, $CHCl_3$) for a >20:1 d.r. and 96.5:3.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 9:1 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm): t_R: 14 min (major) and 17 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	13.7	50.785	1	13.6	97.497
2	17.4	49.215	2	17.5	2.504

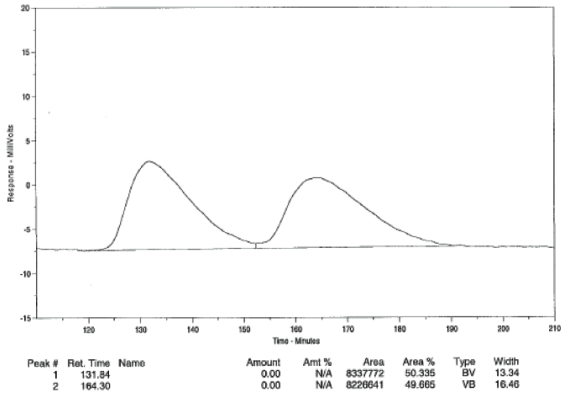
5-[3-(4-Methoxy-phenyl)-1-(2-methylsulfanyl-phenylamino)-prop-2-ynyl]-5-methyl-5H-furan-2-one (4.23b): Yellow oil; IR (neat): 2922 (w), 1763 (s), 1605 (m), 1587 (m), 1509 (s), 1452 (m), 1291 (m), 1249 (s), 1173 (m), 1139 (m), 1108 (m), 1031 (m), 960 (m), 917 (m), 834 (m), 818 (m), 748 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (1H, d, J = 5.6 Hz), 7.42 (1H, dd, J = 7.6, 1.6 Hz), 7.31–7.29 (2H, m), 7.24–7.20 (1H, m), 6.82–6.80 (3H, m), 6.77–6.73 (1H, m), 6.25 (1H, d, J = 5.6 Hz), 5.17 (1H, d, J = 9.2 Hz), 4.62 (1H, d, J = 9.2 Hz), 3.80 (3H, s), 2.30 (3H, s), 1.78 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 160.1, 157.3, 146.8, 134.5, 133.3, 129.6, 123.1, 122.0, 119.1, 114.1, 112.1, 90.0, 86.2, 83.8, 55.4, 53.4, 29.8, 21.5, 18.7; HRMS calcd for $C_{22}H_{22}NO_3S$ (M+H): 380.13204, Found: 380.13422; $[\alpha]_D^{20}$ = +194 (c = 0.74, $CHCl_3$) for a >20:1 d.r. and 96.5:3.5 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 95:5 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 69 min (major) and 79 min (major).

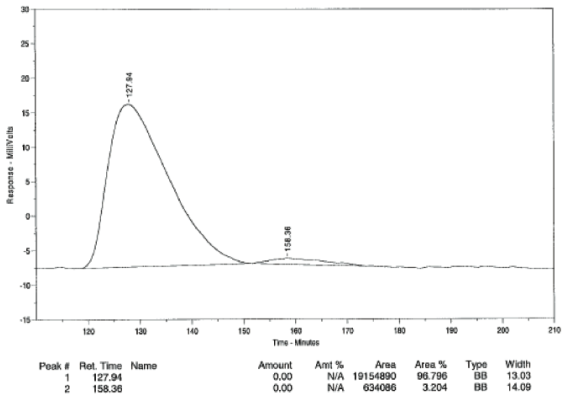




Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	68.9	50.066	1	70.7	3.158
2	78.6	49.934	2	78.5	96.842

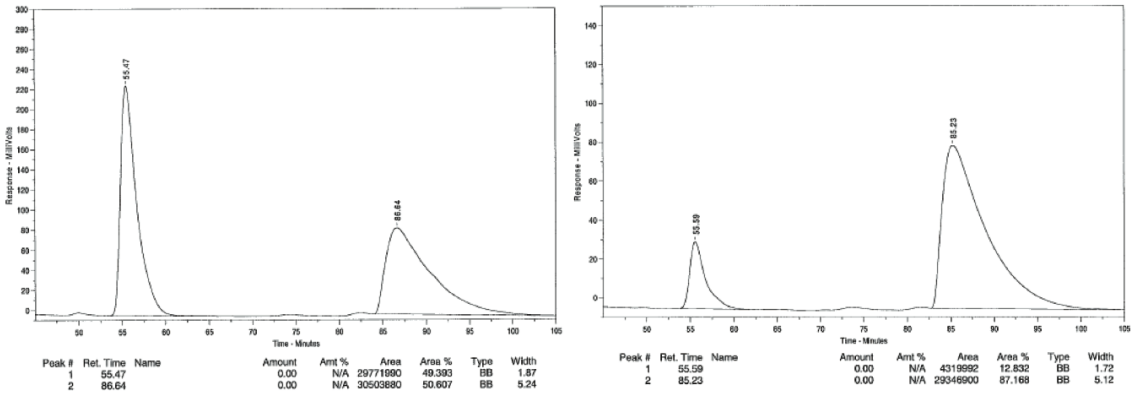
(*R*)-5-Methyl-5-((*S*)-1-((2-(methylthio)phenyl)amino)-3-(thiophen-3-yl)prop-2-yn-1-yl)furan-2(5*H*)-one (4.23c, Scheme 4.10): Yellow oil; IR (neat): 3338 (w, br), 3105 (w), 2920 (w), 2225 (w), 1755 (s), 1586 (m), 1494 (s), 1138 (m), 815 (m), 783 (m), 744 (s), 625 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (1H, d, J = 5.7 Hz), 7.47–7.37 (2H, m), 7.29–7.17 (2H, m), 7.05–7.03 (1H, m), 6.84–6.72 (2H, m), 6.25 (1H, d, J = 5.6 Hz), 5.18 (1H, d, J = 9.3 Hz), 4.61 (1H, d, J = 9.2 Hz), 2.30 (3H, s), 1.77 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 157.2, 146.7, 134.5, 129.9, 239.7, 129.6, 125.7, 123.2, 122.0, 121.0, 119.2, 112.1, 89.8, 84.8, 81.379, 53.3, 21.5, 18.8; HRMS calcd for $C_{19}H_{18}NO_2S_2$ (M+H): 356.07789, Found: 356.07842; $[\alpha]_D^{20}$ = +166 (c = 0.613, $CHCl_3$) for a >20:1 d.r. and 97:3 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel AD, 99:1 hexanes:*i*-PrOH, 0.4 mL/min, 220 nm): t_R: 131 min (major) and 164 min (minor).





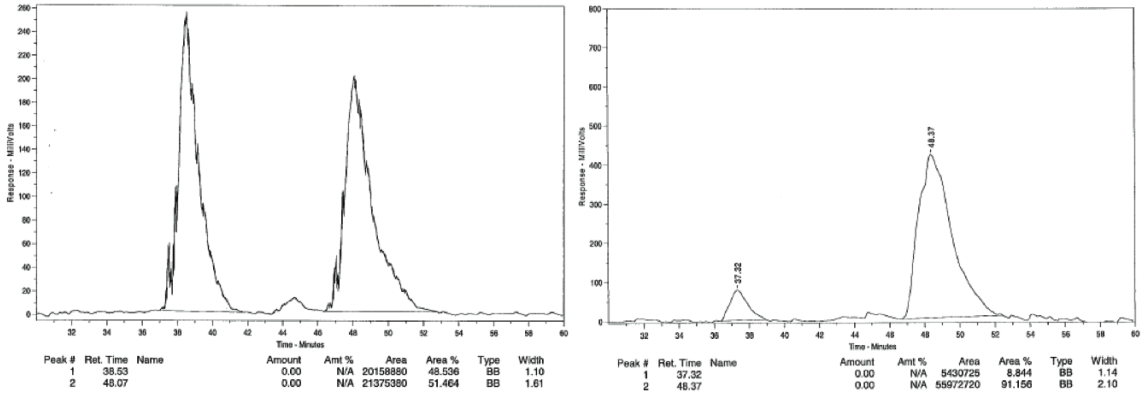
Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	131.8	50.335	1	127.9	96.796
2	164.3	49.665	2	158.4	3.204

(5*R*)-5-Methyl-5-(1-((2-(methylthio)phenyl)amino)-3-(triisopropylsilyl)prop-2-yn-1-yl)furan-2(5*H*)-one (4.23d, Scheme 4.10): Yellow oil; IR (neat): 2941 (w), 2863 (m), 1763 (s), 1588 (w), 1495 (m), 1452 (w), 1107 (m), 1019 (m), 882 (m), 816 (s), 745 (m), 675 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (1H, d, J = 5.6 Hz), 7.41 (1H, dd, J = 7.6, 1.6 Hz), 7.22–7.16 (1H, m), 6.78 (1H, d, J = 8.0 Hz), 6.76–6.70 (1H, m), 6.22 (1H, d, J = 5.6 Hz), 5.12 (1H, d, J = 9.2 Hz), 4.45 (1H, d, J = 9.2 Hz), 2.27 (3H, s), 1.75 (3H, s), 1.01 (21H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 157.0, 146.9, 134.5, 129.6, 123.3, 122.0, 119.2, 112.4, 103.3, 89.6, 88.0, 53.6, 21.6, 18.8, 18.6, 11.2; HRMS calcd for $C_{24}H_{36}NO_2SSi$ (M+H): 430.22360, Found: 430.22409; $[\alpha]_D^{20}$ = +123 (c = 1.53, $CHCl_3$) for a >20:1 d.r. and 88:12 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 98:2 hexanes:*i*-PrOH, 0.3 mL/min, 220 nm): t_R: 56 min (major) and 85 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	55.5	49.393	1	55.6	12.853
2	86.6	50.607	2	85.2	87.168

(5*R*)-5-Methyl-5-(1-((2-(methylthio)phenyl)amino)non-2-yn-1-yl)furan-2(5*H*)-one (4.23e, Scheme 4.10): Orange oil; IR (neat): 3353 (w, br), 2927 (w), 1761 (s), 1587 (m), 1496 (s), 1107 (m), 816 (s), 744 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (1H, d, J = 5.6 Hz), 7.41 (1H, dd, J = 7.5, 1.6 Hz), 7.22–7.17 (1H, m), 6.75–6.71 (2H, m), 6.20 (1H, d, J = 5.6 Hz), 5.04 (1H, d, J = 9.1 Hz), 4.38 (1H, dt, J = 8.8, 2.1 Hz), 2.28 (3H, s), 2.15 (2H, td, J = 7.1, 2.1 Hz), 1.71 (3H, s), 1.52–1.38 (2H, m), 1.37–1.20 (4H, m), 0.93–0.82 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 157.4, 147.0, 134.5, 129.6, 123.0, 121.7, 118.9, 112.0, 90.0, 87.1, 76.3, 52.8, 31.1, 28.3, 22.2, 21.5, 18.7, 18.7, 14.1; HRMS calcd for $C_{20}H_{26}NO_2S$ (M+H): 344.16842, Found: 344.16827; $[\alpha]_D^{20}$ = +101 (c = 1.07, $CHCl_3$) for a >20:1 d.r. and 88:12 e.r. sample. The enantiomeric purity of this compound was determined by HPLC analysis in comparison with authentic racemic material (Chiracel OD, 98:2 hexanes:*i*-PrOH, 0.5 mL/min, 220 nm): t_R: 38 min (minor) and 48 min (major).



Peak #	Ret. Time	Area %	Peak #	Ret. Time	Area %
1	38.5	48.536	1	37.3	8.844
2	48.1	51.464	2	48.4	91.156