The Use of Reversible Covalent Bonding and Induced Intramolecularity to Achieve Selectivity and Rate Acceleration in Organic Reactions

Author: Amanda D. Worthy

Boston College

The Graduate School of Arts and Sciences

Department of Chemistry

The Use of Reversible Covalent Bonding and Induced Intramolecularity to Achieve Selectivity and Rate Acceleration in Organic Reactions

a dissertation

by

Amanda D. Worthy

submitted in partial fulfillment of the requirements

for the degree of

Doctor of Philosophy

December 2012

Acknowledgements

I would like to thank my advisor, Kian Tan, for being a great mentor, training me to be a thoughtful and productive scientist, and allowing me to contribute to chemistry that I really believe in. I would like to thank my committee members, Professors Jim Morken and Jeff Byers for reading my thesis and for their thoughtful comments. I thank Dr. George Greco for letting me do undergraduate research with him and for being a great teacher and mentor. I also thank my high school chemistry teachers, Mr. Wagner and Mr. Warner for inspiring me to pursue chemistry. I would like to thank my mother, Jan Worthy, for always being supportive and reminding me on the hard days that I could do anything for one day at a time and my father, Robert Worthy, for giving me an interest in science and instilling in me the importance of education. To Ted Lightburn, I appreciate you for being an entertaining mentor who taught me to enjoy applying the scientific method to every day life. To Moriah Gagnon and Omar De Paolis, thank you for your experimental work. To Candice Joe, I appreciate your experimental help on our joint publication and you for being someone I could depend on and trust. I would like to thank Xixi Sun for his experimental help, positive attitude, and insight. To Mike Dombrowski, thank you for experimental work and for being a good friend who helped me to be better. To Jen Dabrowski, thank you for being the best graduate school companion anyone could ask for. To the undergraduates and graduate students that I mentored, I thank you all for reminding me why I decided to study chemistry. I would like to thank all my co-workers for making the Tan lab and Merkert Chemistry Center a great place to work. I would also like to thank all my family and friends for their continuous support.

The Use of Reversible Covalent Bonding and Induced Intramolecularity to Achieve Selectivity and Rate Acceleration in Organic Reactions

Amanda D. Worthy

Thesis Advisor: Professor Kian L. Tan

Abstract

Chapter 1. Catalytic directing group, **I**, which was designed with the ability to form a reversible covalent bond with a substrate and bind a metal, was shown to direct the hydroformylation of allylic amines. The efficient regioselective hydroformylation of a variety of 1,2-disubstituted allylic sulfonamides to form β-amino-aldehydes under mild conditions has been shown.

Chapter 2. Building off of the successful application of **I**, enantioenriched catalytic directing group, **II**, was designed and synthesized. It retained the essential features to direct hydroformylation to obtain good regioselectivity while also providing a chiral environment to induce absolute stereocontrol. Under mild conditions, a variety of disubstituted olefins react to give good yields and excellent enantioselectivites. Thus, the first enantioselective reaction performed with a catalytic directing group was demonstrated.

Chapter 3. A new set of organocatalysts was developed that benefits from reversible covalent bonding and induced intramolecularity. The desymmetrization of meso-1,2-diols was accomplished using organocatalyst **III**, which was synthesized easily and cheaply. Experimental results indicate that the selectivity and increased reactivity are a result of the ability of **III** to pre-organize the substrate through a reversible, covalent bond. A variety of cyclic and acylic substrates were shown to react efficiently with good enantioselectivities under mild conditions. The catalyst's ability to functionalize cis-1,2-diols selectively indicated it might be successfully applied to site selective catalysis. Thus, the selective functionalization of a secondary alcohol in the presence of a primary alcohol was developed using a combination of binding selectivity and stereoselectivity. The (*S*)-enantiomer forms the secondary functionalized product while the (*R*)-enantiomer forms the primary functionalized product with high selectivity. As the enantiomers preferentially form different functionalized products, a regiodivergent reaction on a racemic mixture resulted giving two valuable enriched products.

Table of Contents

List of Abbreviations

Ac	Acetyl
acac	Acetylacetonato
ACS	American Chemical Society
app	Apparent
Ar	Aryl
ATR	Attenuated Total Reflectance
Bn	Benzyl
br	Broad
Bu	Butyl
cat.	Catalytic
CH_2Cl_2	Methylene Chloride
$CHCl_3$	Chloroform
CO	Carbon monoxide
COD	Cyclooctadiene
Cy	Cyclohexyl

d	Doublet
dd	Doublet of doublets
DFT	Density Functional Theory
DIBAL-H	Di-isobutyl aluminum hydride
DIPEA	*N*,*N*-Diisopropylethylamine
DIPEA·HCl	*N*,*N*-Diisopropylethylamine hydrochloride
DMPSCl	Dimethylphenylsilyl chloride
dq	Doublet of quartets
dr	Diastereomeric ratio
dt	Doublet of triplets
DMF	*N*,*N*-Dimethylformamide
DART-TOF	Direct analysis in real time - Time of flight
ee	Enantiomeric excess
Et	Ethyl
Et_2O	Diethylether
EtOAc	Ethyl Acetate

Eq	Equation
equiv	Equivalents
FT	Fourier transform
FID	Flame ionizing detector
GC	Gas chromatography
h	Hours
H_2	Hydrogen gas
Hex	Hexanes
HRMS	High resolution mass spectrometry
I_2	Iodine
i-	Iso
i-PrOH	Isopropanol
IR	Infared
LAH	Lithium aluminum hydride
m	Multiplet
Me	Methyl

MeOH	Methanol
min	Minutes
n-	Normal
$NaBH_4$	Sodium Borohydride
NMI	*N*-methylimidazole
NMR	Nuclear magnetic resonance
o-	Ortho
p-	Para
Ph	Phenyl
PhMe	Toluene
phth	Phthalimide
PMP	*Para*-methoxyphenyl
PMPP	1,2,2,6,6-Pentamethylpiperidine
PMPP·HCl	1,2,2,6,6-Pentamethyl piperidine hydrochloride
ppm	Parts per million
ppt.	Precipitate

PPTS	Pyridinium *para*-toluene sulfonate
p-TsOH	*para*-toluenesulfonic acid
Pr	Propyl
psi	Pounds per square inch
q	Quartet
rr	Regioisomeric ratio
rt	Room temperature
s	Singlet
SFC	Supercritical fluid chromatography
SiO_2	Silica
t	Triplet
t-	tertiary
t-AmylOH	*tertiary*-Amyl alcohol
TBDPS	*tertiary*-Butyldiphenylsilyl
TBDPSCl	*tertiary*-Butyldiphenylsilyl chloride
TBS	*tertiary*-Butyldimethylsilyl

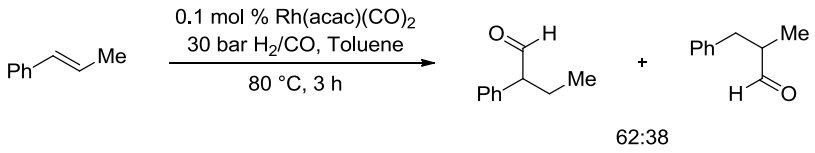
TBSCl	*tertiary*-Butyldimethylsilyl chloride
TES	Triethylsilyl
TESBr	Bromotriethylsilane
TESCl	Chlorotriethylsilane
$TESNO_2$	Triethylsilyl nitrite
TESOTf	Triethylsilyl triflate
THF	Tetrahydrofuran
t-BuOH	*tert*-Butanol
UV	Ultraviolet

Chapter One: Regioselective Hydroformylation

1.1 Directing Groups

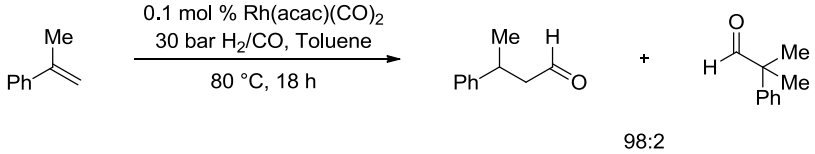
Obtaining selectivity in organic chemistry is a large area of research which scientists have addressed with multiple approaches. In some cases, electronic effects have been used to obtain selectivity. For instance, in hydroformylation, it is known that aryl substrates preferentially form the product with the aldehyde proximal to the phenyl ring (Scheme 1.1).[1] However, selectivity can also be influenced by steric effects. In the case

Scheme 1.1 Hydroformylation of a 1,2-Disubstituted Aryl Olefin.



of the hydroformylation of aryl olefins, the selectivity can be overturned using a 1,1-disubstituted aryl olefin (Scheme 1.2).[1] Another reliable method that has been developed to obtain selectivity is the use of directing groups.[2]

Scheme 1.2 Hydroformylation of a 1,1-Disubstituted Aryl Olefin.



[1]Carrilho, R. M. B.; Neves, A. C. B.; Lourenço, M. A. O.; Abreu, A. R.; Rosado, M. T. S.; Abreu, P. E.; Eusébio, M. E. S.; Kollár, L.; Bayón, J. C.; Pereira, M. M. *J. Organomet. Chem.* **2012**, *698*, 28-34.
[2](a) Hoveyda, A.; Evans, D.; Fu, G. *Chem. Rev.* **1993**, *93*, 1307-1370. (b) Itami, K.; Yoshida, J. *Synlett* **2006**, *2*, 157-180. (c) Oestreich, M. *Eur. J. Org. Chem.* **2005**, *5*, 783-792. (d) Kakiuchi, F.; Chatani, N. *Adv. Syn. Catal.* **2003**, *345*, 1077-1101.

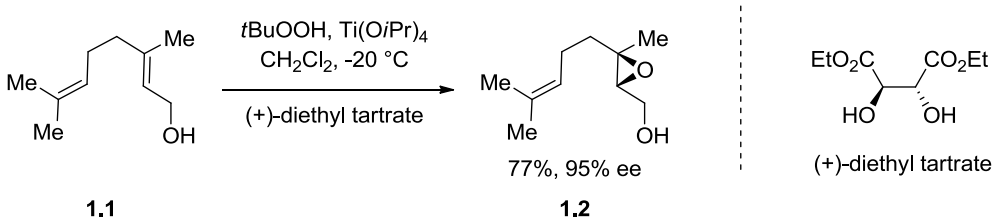
Directing groups are functional groups within a substrate that are able to pre-associate with a reagent in the reaction in order to affect the outcome.[2a] As well as increasing selectivity, sometimes directed reactions are accelerated due to their intramolecular-like reactivity.[3] Thus, directing groups have allowed for some difficult intermolecular reactions to be possible. Directing groups have been used in a variety of transformations such as oxidations, reductions, and C-C bond forming reactions.[2] The directing group can be a common functional group ("useful directing groups") within the substrate (Section 1.2) or a less common group that can be installed prior to the reaction and removed after the desired transformation is complete (Section 1.3)

1.2 Useful Directing Groups

One excellent example of a directed reaction using a common functional group is the Sharpless asymmetric epoxidation.[4] For example, **1.1** is shown to give **1.2** in high yield and enantioselectivity (Scheme 1.3). Although **1.1** has two trisubstituted olefins that can be oxidized, only the olefin proximal to the alcohol reacts. The high site selectivity and enantioselectivity are a result of the alcohol binding to the titanium catalyst and directing oxidation to the top face of the allylic olefin. As a testament to the importance of the reaction, Sharpless received the 2001 Nobel Prize in Chemistry for his work in this area.

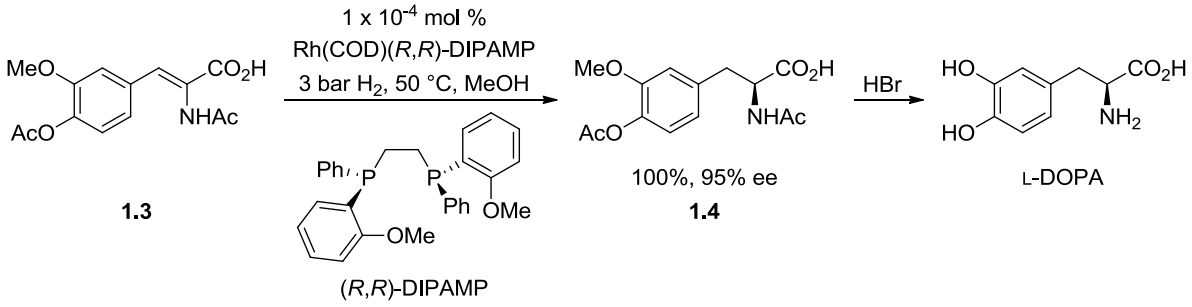
[3]Tan, K. L. *ACS Catal.* **2011**, *1*, 877-886.
[4](a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974-5976. (b) Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 113-126.

Scheme 1.3 Sharpless Asymmetric Epoxidation.



Sharing the 2001 Nobel Prize with Sharpless was Knowles for the asymmetric reduction of enamides, such as **1.3**, using very low catalyst loadings and mild conditions.[5] The reaction proceeds through a chelated intermediate in which the acetamide directs the rhodium catalyst to the top face of the olefin, forming **1.4**. This powerful method was used to synthesize L-DOPA, a drug used in the treatment of Parkinson's disease (Scheme 1.4).

Scheme 1.4 The Monsanto L-DOPA Process.

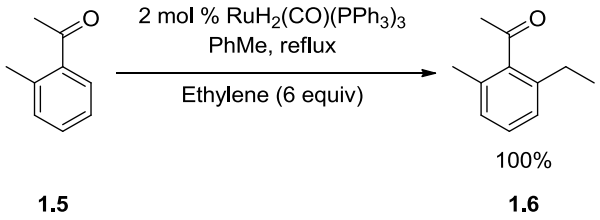


More recently, selective catalytic C-H bond activation is another challenging problem that has interested many researchers. Directing groups have been used effectively to control site selectivity in C-H activation reactions. In an example by Murai, the ketone in **1.5** is able to direct the ruthenium catalyst to activate the *ortho*-C-H bond

[5]Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J. *J. Mol. Cat.* **1983**, *19*, 159-169.

and insert ethylene to obtain **1.6** quantitatively (Scheme 1.5).[6] Subsequently, directing group strategies have become ubiquitous in C-H activation.[7]

Scheme 1.5 Selective *ortho*-C-H Activation.



These examples demonstrate that common functional groups are able to facilitate very powerful and diverse transformations that are sometimes difficult or not possible otherwise.

1.3 Removable Directing Groups

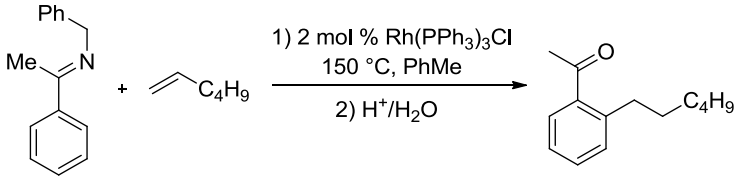
Some reactions cannot be directed by the functional groups that exist in the substrate so a directing group has to be installed prior to the reaction and removed after the desired transformation has occurred. While this is not ideal because it adds additional steps and creates stoichiometric byproducts, it has allowed for the expansion of the scope of reactions that can be directed.[8]

Fortunately, some directing groups can be removed with a simple work-up, such

[6]Murai, S.; Kaiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529-531.
[7]For reviews on directed C-H functionalization, see: (a) Ritleng, V.; Sirlin,C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731-1770. (b) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826-834. (c) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal.* **2003**, *345*, 1077-1101. (d) Dick, A.; Sanford, M. *Tetrahedron* **2006**, *62*, 2439-2463. (e) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879-5918.
[8]Rousseau, G.; Breit, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2450-2494.

as in Scheme 1.6. Jun showed that, in this case, the ketimine is necessary to direct the *ortho*-C-H activation for the selective alkylation of **1.7**. After the reaction, the imine can be cleaved easily with aqueous acid to give **1.8** (Scheme 1.6).[9]

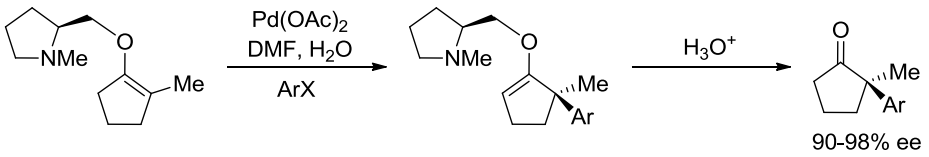
Scheme 1.6 Selective *ortho*-Alkylation by C-H Activation.



1.7 **1.8**

Because amines are known to be ligands in palladium catalysis, Hallberg used a proline based directing group to add aryl groups to the top face of the olefin in **1.9** creating quaternary centers with high enantioselectivities.[10] This group could also be removed easily by acid hydrolysis to give the corresponding ketone **1.10** (Scheme 1.7).

Scheme 1.7 Formation of Quaternary Centers by Heck Reaction.



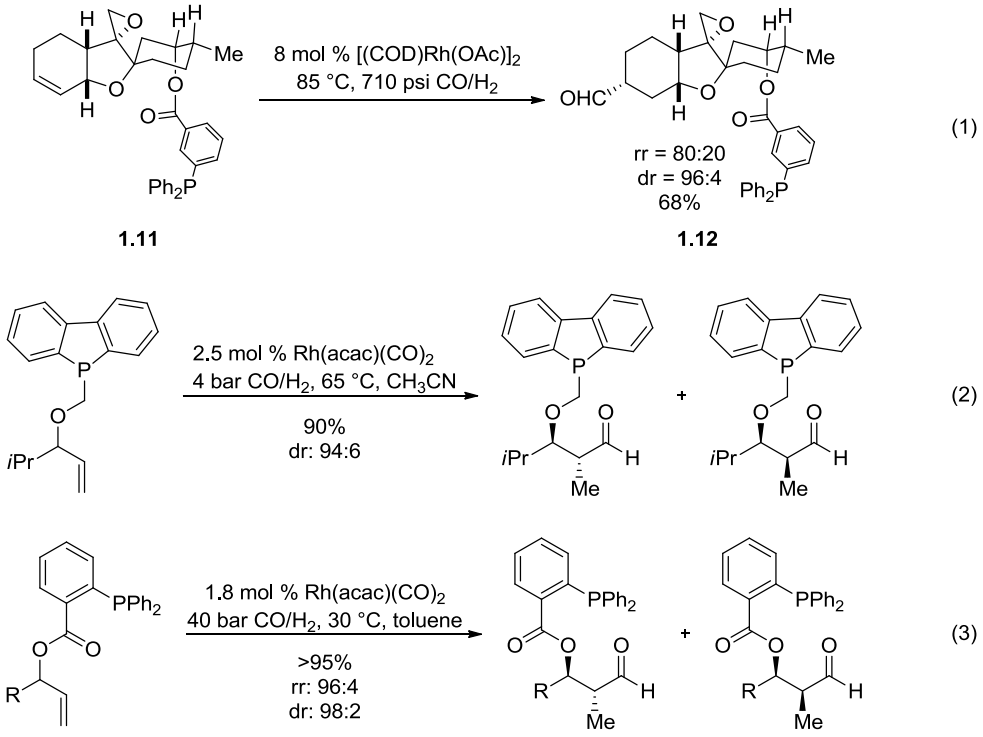
1.9 **1.10**

Designing a practical removable directing group for reactions that typically utilize a phosphine ligand is more challenging. However, during the synthesis of (+)-phyllanthocin, Burke installed a triarylphosphine directing group, using an ester

[9]Jun, C.; Hong, J.; Kim, Y.; Chung, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3440-3442.
[10]Nilsson, P.; Larhed, M.; Hallberg, A. *J. Am. Chem. Soc.* **2003**, *125*, 3430-3431.

linkage.[11] The phosphine was incorporated into the molecule in order to increase the selectivity of the hydroformylation of **1.11**. Impressively, when the phosphine is *meta*, the directing group is able to deliver the rhodium to the bottom face of the olefin resulting in good regio- and diasteroselective ratios for **1.12** (Scheme 1.8, Eq 1).

Scheme 1.8 Examples of Directed Regio- and Diastereoselective Hydroformylation.



Subsequently, Jackson and Perlmutter,[12] Leighton,[13] and Breit[14] demonstrated that phosphorus-based stoichiometric directing groups are successful in the highly regio- and

[11]Burke, S. D.; Cobb, J. E.; Takeuchi, K. *J. Org. Chem.* **1990**, *55*, 2138-2151.
[12]R. W. Jackson, P. Perlmutter and E. E. Tasdelen, J. Chem. Soc., Chem. Commun., 1990, 763-764.
[13]Krauss, I. J.; Wang, C. C. Y.; Leighton, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 11514 – 11515.
[14](a) Breit, B. *Angew. Chem., Int. Ed.* **1996**, *35*, 2835-2837. (b) Breit, B. *Liebigs Ann.* **1997**, 1841-1851. (c) Breit, B.; Heckmann, G.; Zahn, S. K. *Chem. Eur. J.* **2003**, *9*, 425-434. (d) Breit, B.; Demel, P.; Gebert, A. *Chem. Commun.* **2004**, 114 – 115.

diastereoselective hydroformylation of terminal and disubstituted allylic alcohols (Scheme 1.8, Eq 2 and Eq 3).

While it is clear from these examples that removable directing groups are powerful tools, it is at the cost of additional synthetic steps for their installation and removal, as well as the creation of stoichiometric byproducts.

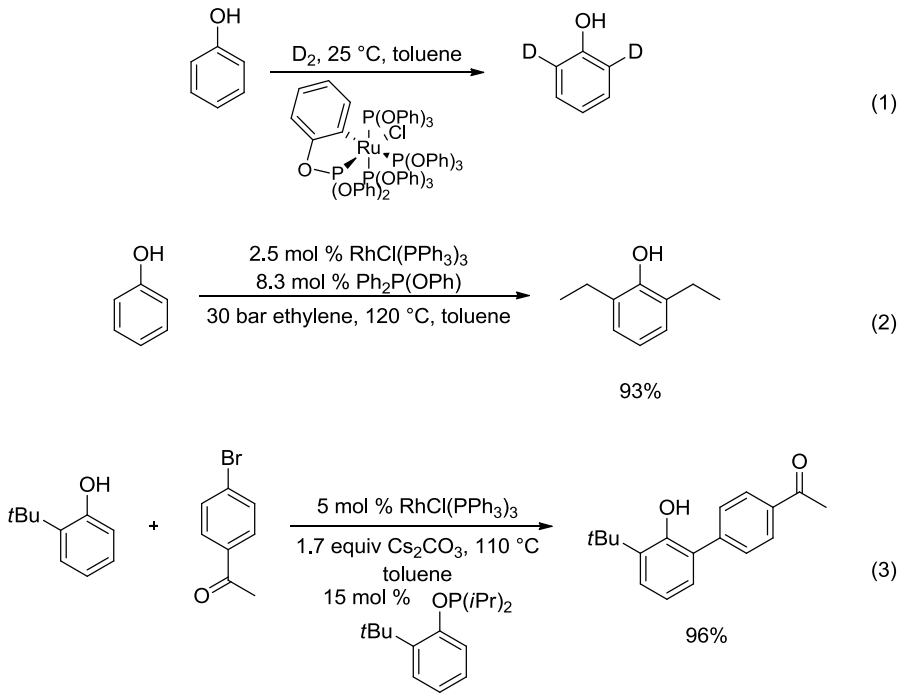
1.4 Developing a Catalytic Directing Group

In order to address the disadvantages of removable directing groups, the Tan group developed a catalytic directing group. Using a directing group catalytically maintains the benefits of a directed reaction while improving the overall efficiency of the process by eliminating installation and removal steps.[8]

Previously, other groups have shown the use of catalytic directing groups. For example, Lewis showed C-H activation and deuterium incorporation into phenol using a catalytic amount of a phosphite (Scheme 1.9, Eq 1).[15a] Lewis and Smith expanded this work to the coupling of olefins to phenol, and Cole-Hamilton developed a more efficient system using a rhodium catalyst (Scheme 1.9, Eq 2).[15b,16] Bedford was able to achieve coupling of phenolic derivatives with aryl halides under similar conditions. (Scheme 1.9, Eq 3).[17]

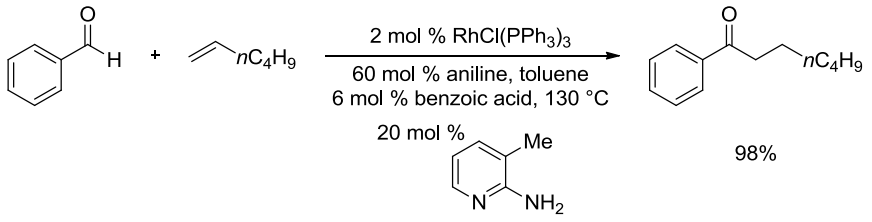
[15](a) Lewis, L. N. *Inorg. Chem.* **1985**, *24*, 4433–4435. (b) Lewis, L. N.; Smith, J. F.; *J. Am. Chem. Soc.* **1986**, *108*, 2728-2735.
[16]Carrion, M. C.; Cole-Hamilton, D. J. *Chem. Commun.* **2006**, *43*, 4527–4529.
[17]Bedford, R. B.; Coles, S. J.; Hursthouse, M. B.; Limmert, M. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 112–114. Bedford, R. B.; Limmert, M. E. *J. Org. Chem.* **2003**, *68*, 8669–8682.

Scheme 1.9 C-H Activation using a Catalytic Directing Group.



Jun and coworkers showed the use of 2-amino-3-picoline as a catalytic directing group to prevent decarbonylation in the hydroacylation of aldehydes with terminal olefins (Scheme 1.10).[18]

Scheme 1.10 Hydroacylation with a Catalytic Directing Group.

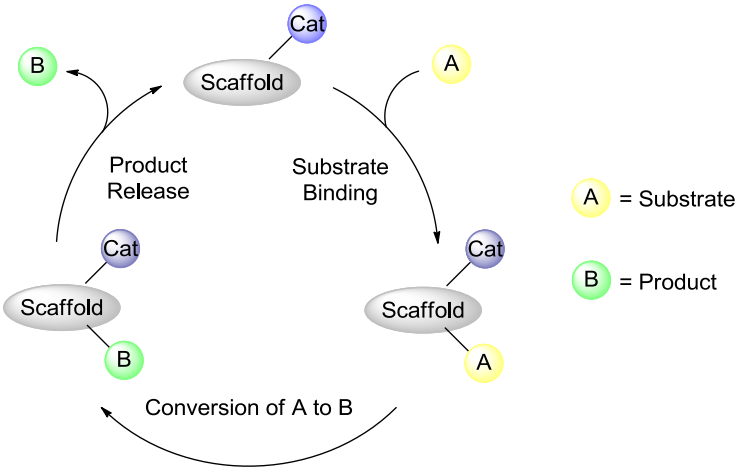


Similar to previous strategies, to maximize efficiency, our catalytic directing group was designed to be an organic scaffold with the ability to bind the substrate

[18]Jun, C. H.; Lee, D. Y.; Lee, H.; Hong, J. B. *Angew. Chem., Int.Ed.* **2000**, *39*, 3070–3072.

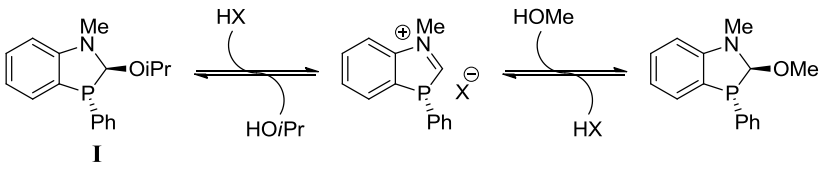
covalently and reversibly under mild conditions while, simultaneously, binding a metal. Thus, under the reaction conditions, the substrate binds to the organic scaffold allowing for a directed reaction to proceed. Upon release of the product, the directing group is regenerated, rendering the process catalytic (Figure 1.1).

Figure 1.1 General Catalytic Directing Group Cycle.



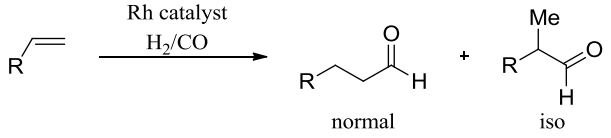
Catalytic directing group **I** was designed with a simple organic backbone and a hemiaminal as the substrate-binding site, in which the lone pair on the amine can assist with alcohol expulsion prior to binding another alcohol (Scheme 1.11). A phosphorus atom was also incorporated into the molecule to act as a metal-binding site.

Scheme 1.11 Alcohol Exchange with **I**.



Taking inspiration from Burke's application of a phosphorus-based removable directing group to hydroformylation,[11] our group decided to use hydroformylation as a testing ground for the feasibility of this concept. Hydroformylation is the efficient addition of hydrogen and carbon monoxide across an olefin yielding valuable aldehyde products.[19] However, two products are possible, the iso and normal isomers (Figure 1.2). In the case of terminal olefins, the normal product is usually favored for steric reasons. For unactivated 1,2-disubstituted olefins, a product mixture of around 1:1 is often obtained.[20]

Figure 1.2 Hydroformylation Reaction.

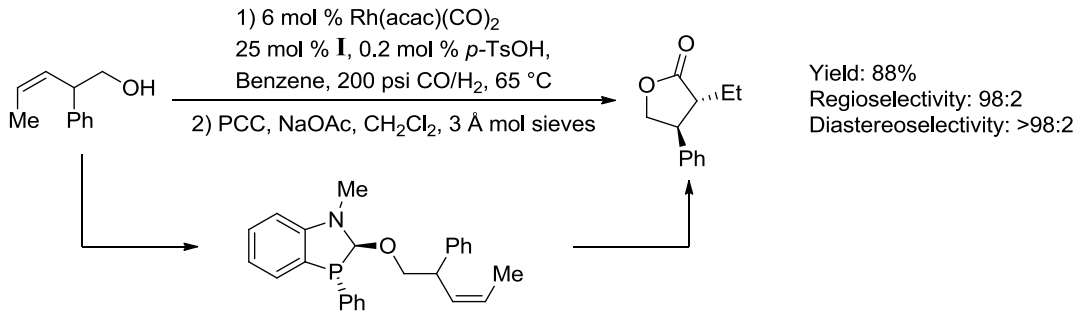


Our group believed that applying a catalytic directing group could alter the reaction's regio- and stereoselectivity. Lightburn applied **I** to the hydroformylation of homoallylic alcohols with good yields, regioselectivities, and diastereoselectivities (Scheme 1.12).[21] It is believed that the reaction is regioselective for the iso product due to the energy difference between the ring sizes (seven vs. eight) of the two chelated intermediates in the hydride insertion step. The seven-membered chelate, **1.13**, is favored

[19](a) *Rhodium Catalyzed Hydroformylation*; Van Leeuwen, P. W. N. M., Claver, C., Eds.; Springer-Verlag: New York, 2002. (b) Frohning, C. D. Kohlpaintner, C. W. Bohnen, H. W. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Eds.; Wiley: Weinheim, Germany, 2002; Vol. 1, p 31.
[20]Breit, B.; Seiche, W. *Synthesis* **2001**, *1*, 1-36.
[21]Lightburn, T. E.; Dombrowski, M. T.; Tan, K. L. *J. Am. Chem. Soc.* **2008**, *130*, 9210-9211.

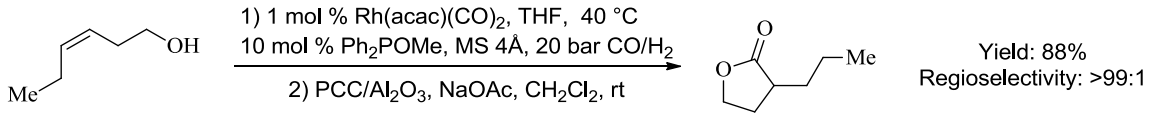
over **1.14** which leads to the iso product being formed (Figure 1.3). The iso product cyclizes under the reaction conditions and was oxidized to the lactone for ease of isolation and characterization.

Scheme 1.12 Tan's Regio- and Diastereoselective Hydroformylation of Homoallylic Alcohols.



At the same time, the Breit group published a paper using a simple phosphinite as a catalytic directing group in the hydroformylation of homoallylic alcohols with good yields and regioselectivities.[22] The phosphinite also reversibly binds alcohols and may achieve selectivity through the energy difference between the two chelated intermediates in the hydride insertion step (Scheme 1.13). Mechanistic studies for both systems need to be performed to verify this hypothesis.

Scheme 1.13 Breit's Regioselective Hydroformylation of Homoallylic Alcohols.

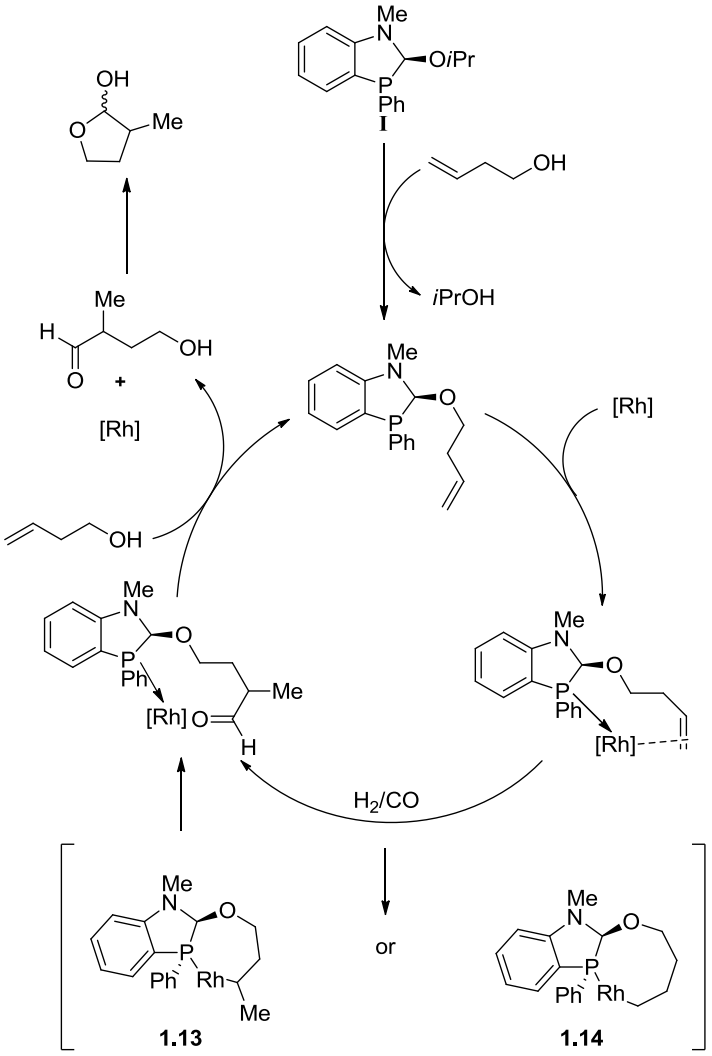


The Breit group has since expanded the use of this phosphinite to other substrates.

[22](a) Grünanger, C. U.; Breit, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 7346-7349. (b) Smejkal, T.; Breit, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 311-315.

The regio- and diastereoselective hydroformylation of bishomoallylic alcohols and cyclic dienes occurs with high yields.[23a,b] The application of this catalytic directing group to the hydroformylation of 1,1-disubstituted olefins also allows the formation of quaternary carbon centers with good yields and regioselectivities.[23c]

Figure 1.3 Catalytic Cycle of the Directed Hydroformylation.



[23](a) Grünanger, C. U.; Breit, B. *Angew. Chem. Int. Ed.* **2010**, *49*, 967 – 970. (b) Usui, I.; Nomura, K.; Breit, B. *Org. Lett.*, **2011**, *13*, 612-615. (c) Ueki, Y.; Ito, H.; Usui, I.; Breit, B. *Chem. Eur. J.* **2011**, *17*, 8555-8558.

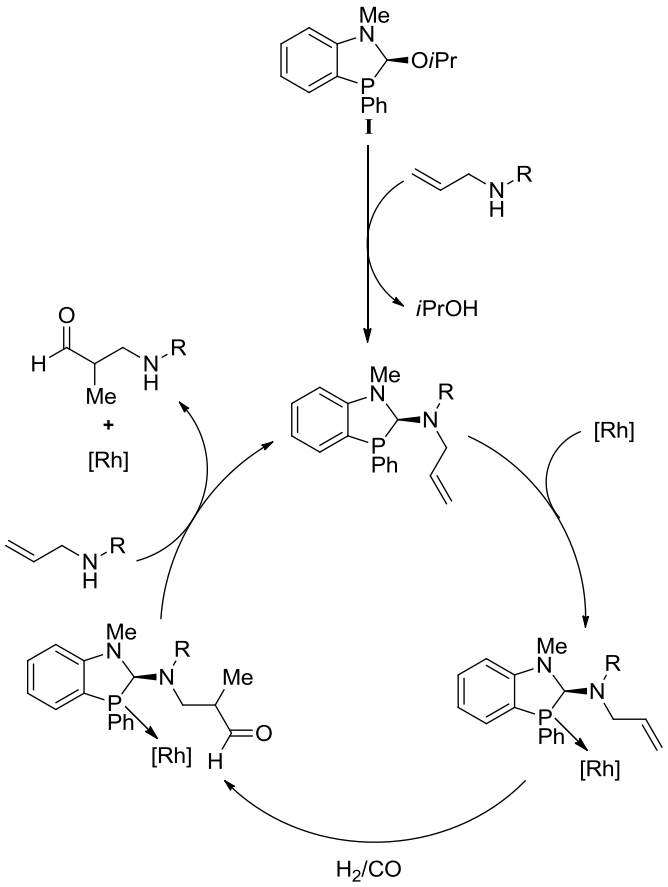
1.5 Regioselective Hydroformylation of Sulfonamides[24]

Since homoallylic alcohols were able to bind **I** and undergo selective hydroformylation,[20] we were interested in expanding the substrates that could bind **I** to undergo directed hydroformylation. In particular, we were interested in applying this methodology to the hydroformylation of allylic amines to form β-amino-aldehydes. Much like the reaction with homoallylic alcohols, the substrate could exchange onto **I** under the reaction conditions, the phosphorus could bind the rhodium catalyst to undergo hydroformylation, and another molecule of substrate could exchange off the product (Figure 1.4).

Investigations began with varying the protecting group on nitrogen. For the reaction to work, the exchange of amines with **I** would need to be faster than the hydroformylation without substrate-bound **I**, which will afford unselective background reaction. It was expected that the protecting group would greatly affect the rate of exchange with **I**. Carbamates and amides were quickly ruled out as potential substrates because they did not exchange with **I**. Sulfonamides, however, exchanged under mild conditions with **I** to give **1.16**. The more electron-withdrawing sulfonamides have greatly increased exchange rates with the 3,5-bis(trifluoromethyl)benzenesulfonamide reaching 69% conversion after 6 hours (Table 1.1). The increased exchange rate is most likely because the electron-withdrawing sulfonamides have lower pK_as.[25]

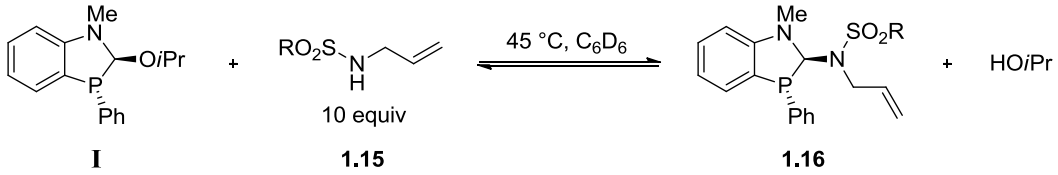
[24]Worthy, A. D.; Gagnon, M. M.; Dombrowski, M. T.; Tan, K. L. *Org. Lett.* **2009**, *11*, 2764-2767.
[25]Eckert, F.; Leito, I.; Kaljurand, I.; Kütt, A.; Klamt, A.; Diedenhofen, M. *J. Comp. Chem.* **2009**, *30*, 799-810.

Figure 1.4 Catalytic Cycle of Allylic Amine Hydroformylation.



The self-exchange between substrates was tested to make sure that the exchange occurring during the reaction would be rapid. First **1.15** was exchanged onto **I** to give **1.16**. When **1.17** was added at room temperature, the exchange was fast showing a ratio of 53:47 (**1.16** to **1.18**) after just 1 hour. An equilibrium ratio of 43:57 (**1.16** to **1.18**) was expected given the steric and electronic similarity of **1.15** and **1.17** (Scheme 1.14).

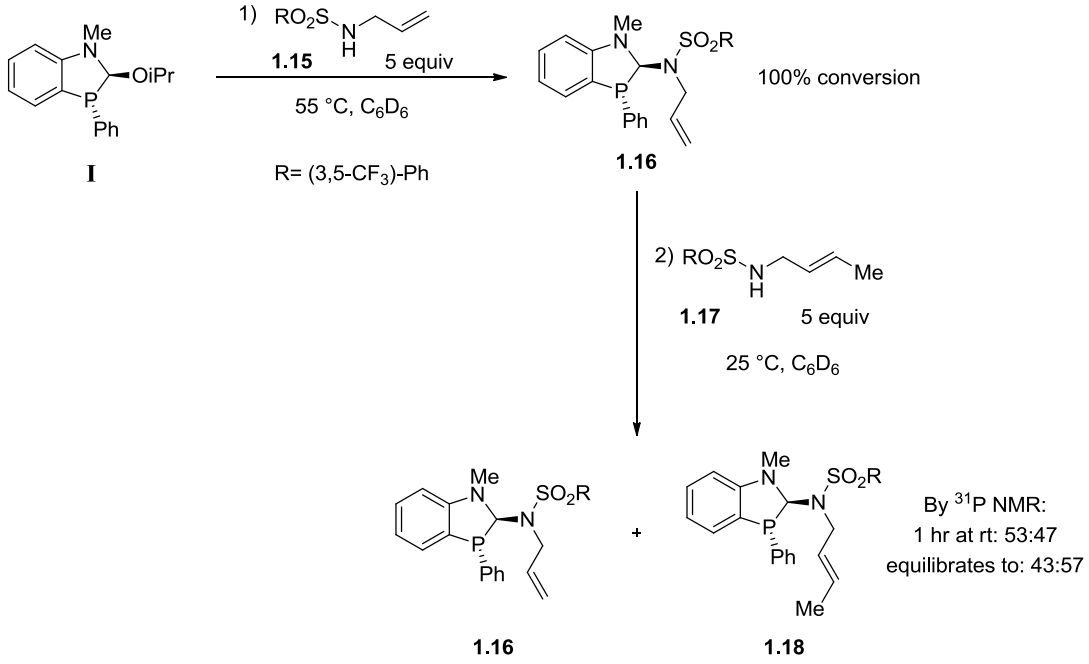
Table 1.1 Sulfonamide Exchange Rates.



R	Conversion at 6 h (%)[a]	pK_a[b]
p-OMe-Ph	0	17
p-Me-Ph	0	16
p-NO_2-Ph	23[c]	14
(3,5-CF_3)-Ph	69[d]	13

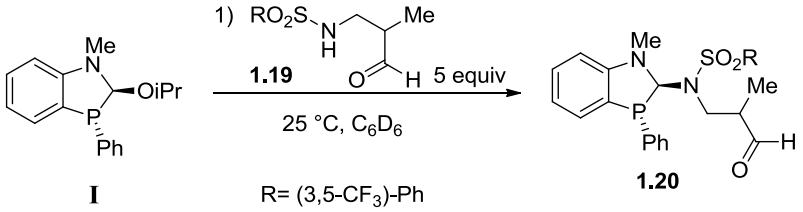
[a]Determined by ^{31}P NMR. [b]Based on ref. 16. [c]>95% conversion reached in 6 days. [d]>95% conversion reached in 13 h.

Scheme 1.14 Exchange Between Substrates.



We were also concerned that the product, **1.19**, may inhibit the reaction. However, when **I** was exchanged with **1.19**, it was found that **1.20** was unfavorable to form and ligand decomposition occurs over time (Table 1.2). Decomposed ligand appears by ^{31}P NMR as oxidation of the phosphorus atom which is believed to occur through the exchange intermediate seen in Scheme 1.11 and 1.15. The iminium ion intermediate is in resonance with the phosphonium ion which can be attacked by water or a molecule of substrate. In the case of an oxygen based nucleophile, protonation of the resulting ylide would give the proposed structure of decomposed ligand, **I-decomp** (Scheme 1.15). A crystal structure of the decomposed ligand confirmed the identity of **I-decomp** (Figure 1.5). During the reaction with **1.15**, however, the decomposition is likely the corresponding sulfonamide derivative.

Table 1.2 Product Exchange with **I**.



Time	**I**[a]	**1.20**[a]	Decomp[a]
5 min	84	12	4
2.5 h	42	48	10
5 h	34	54	12
24 h[b]	6	5	69

[a]Percentages determined by ^{31}P NMR. [b]Multiple unknown peaks appear over time.

Scheme 1.15 Ligand Decomposition Pathway.

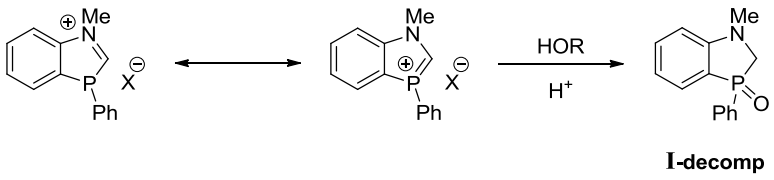
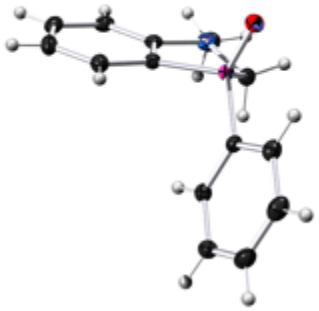
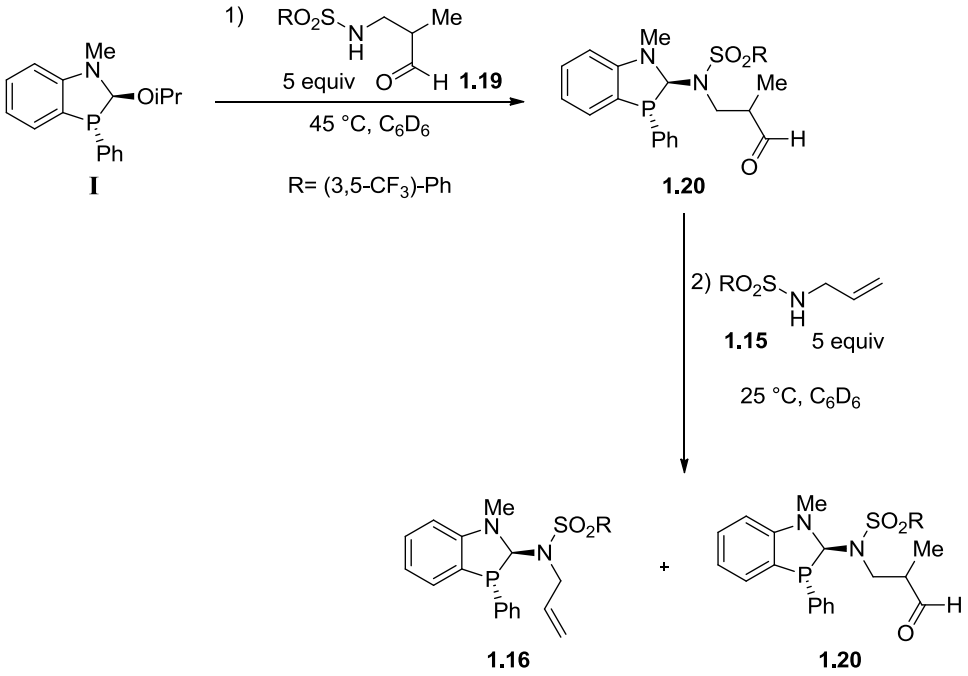


Figure 1.5 Crystal Structure of Decomposed Ligand (CCDC # 837337).



Since **1.20** formed at room temperature over a few hours, a competition experiment between **1.19** and **1.15** was performed to see which would be favored to bind **I**. By first reacting **1.19** and **I** to form **1.20** and then adding **1.15**, it was determined that **1.16** is more stable than **1.20**. Within five minutes of adding **1.15**, **1.20** is no longer detectable by ^{31}P NMR. **1.20** was exchanged completely with **1.15** to form **1.16** (Table 1.3).

Table 1.3 Product vs. Substrate Exchange Competition.



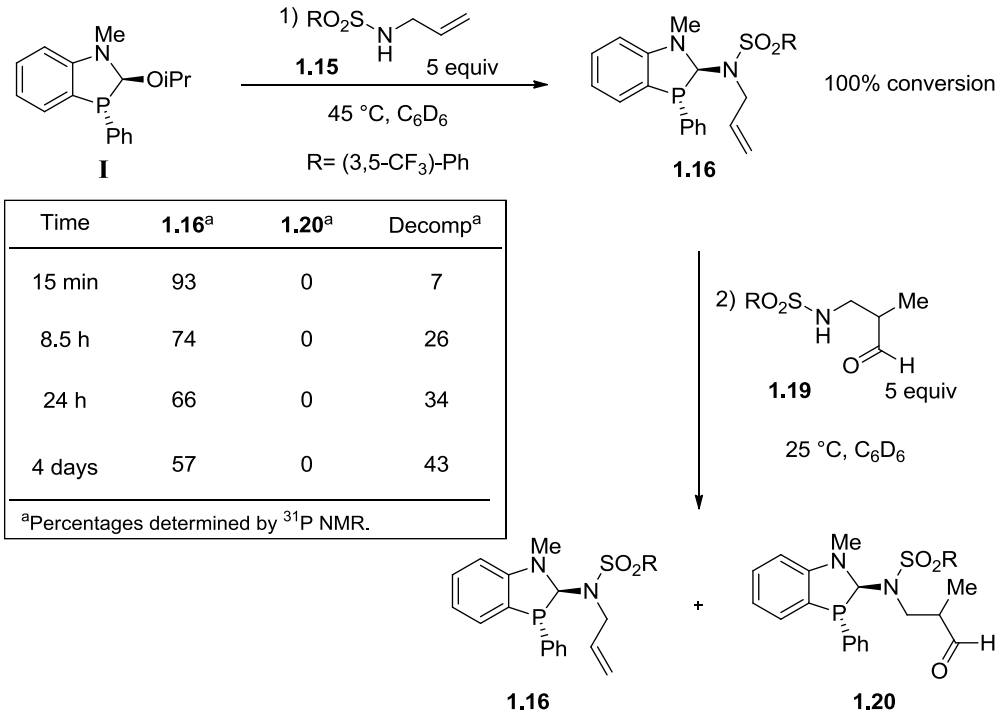
Time	**I**[a]	**1.20**[a]	Decomp[a]	**1.16**[a]
1 h	31	45	24	-
2 h	31	45	24	-
		-added **1.15**-		
5 min[b]	42	0	21	36
20 min	32	0	28	40
4.5 h	23	0	29	48

[a]Percentages determined by ^{31}P NMR. [b]Numbers are slightly off due to low signal:noise ratio in ^{31}P NMR.

In order to be thorough, the experiment was run reversing the addition of **1.15** and **1.19**. By first reacting **1.15** and **I** to form **1.16** and then adding **1.19** (at time=0 min), it was reaffirmed that **1.16** is more stable than **1.20**. **1.20** did not form, and **1.16**

decomposed over time (Table 1.4). We believe the increased sterics of **1.19** compared to **1.15** is the reason for its more unfavorable binding.

Table 1.4 Substrate vs. Product Exchange Competition.



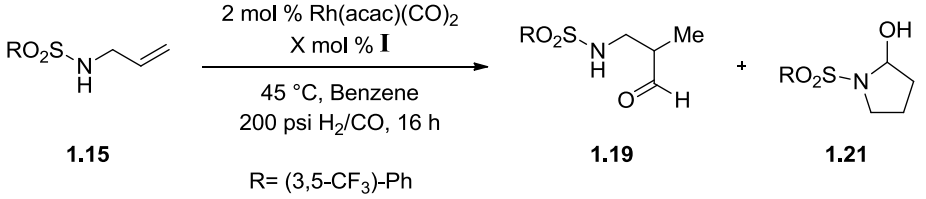
Time	**1.16**[a]	**1.20**[a]	Decomp[a]
15 min	93	0	7
8.5 h	74	0	26
24 h	66	0	34
4 days	57	0	43

[a]Percentages determined by ^{31}P NMR.

After determining that sulfonamides were promising substrates based on exchange data, optimization of the regioselective hydroformylation of **1.15** was started. Hydroformylation of **1.15** using 4% PPh_3 as a ligand gave a 50:50 ratio of iso:normal products. As PPh_3 is incapable of binding the substrate, this gave the inherent selectivity of the hydroformylation of **1.15**. As a terminal substrate usually strongly favors the normal product, we believe the sulfonamide moiety itself can direct the hydroformylation

to some degree.[26] Using 10% of **I** gave a 60:40 of iso:normal products with good conversion. Encouraged by the increase in the ratio of iso product formed using **I**, the ligand loading was increased to 20% and 40% to test if the maximum selectivity had been reached. Fortunately, it was found that increasing the amount of **I** resulted in higher selectivity for the iso product (Table 1.5).

Table 1.5 Ligand Loading Screen.



1.15 **1.19** **1.21**

Ligand (mol %)	Regioselectivity (**1.19**:**1.21**)[a]	Conversion (%)[b]
4[c]	50:50	>95
10	60:40	>95
20	75:25	>95
40	83:17	>95

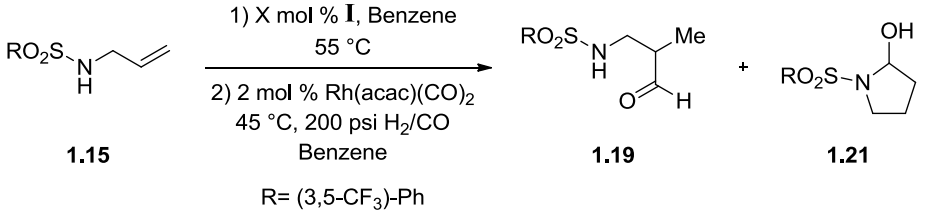
[a]Determined by SFC analysis. [b]Determined by ^{1}H NMR using 1,3,5-trimethoxy-benzene as an internal standard.[c]PPh_3 was used instead of **I**.

However, to develop a practical and efficient methodology, we optimized the conditions at lower ligand loadings. Previous exchange results had showed that while initial exchange of **I** with **1.15** was slow compared to the reaction time (Table 1.1), the exchange between substrate bound ligand, **1.16**, and **1.17** was much faster (Scheme 1.14).

[26] For examples of amide directed hydroformylation see: (a) Ojima, I.; Zhang, Z. *J. Org. Chem.* **1988**, *53*, 4422-4425. (b) Ojima, I.; Zhang, Z. *J. Organomet. Chem.* **1991**, *417*, 253-276. (c) Ojima, I.; Korda, A.; Shay, W. R. *J. Org. Chem.* **1991**, *56*, 2024-2030. (d) Dickson, R. S.; Bowen, J.; Campi, E. M.; Jackson, W. R.; Jonasson, C. A. M.; McGrath, F. J.; Paslow, D. J.; Polas, A.; Renton, P.; Gladiali, S. *J. Mol. Cat. A* **1999**, *150*, 122-146.

Therefore, the exchange of **I** and **1.15** was carried out prior to the hydroformylation reaction. Exchanging 5% of **I** with **1.15** prior to hydroformylation gave similar results to using 20% **I** without the pre-exchange procedure (Table 1.5 and Table 1.6). Impressively, when 10% of **I** was used, a ratio of 90:10 (**1.19**:**1.21**) was obtained with good conversion (Table 1.6).

Table 1.6 Ligand Loading Screen with Pre-exchange of **I** and **1.15**.

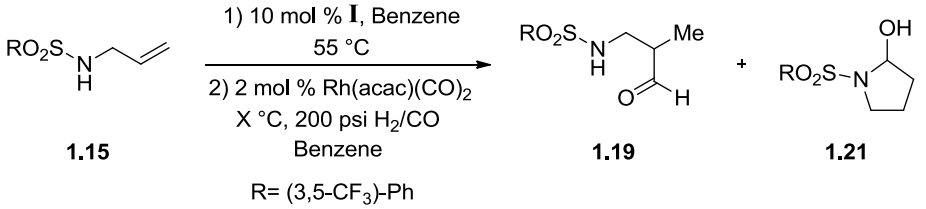


Ligand (mol %)	Regioselectivity (**1.19**:**1.21**)[a]	Conversion (%)[b]
5	77:23	>95
10	90:10	>95

[a]Determined by SFC analysis. [b]Determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Having developed an effective procedure, the temperature of the reaction was screened in order to discover the mildest conditions that would still afford high levels of selectivity. At 35 °C, the conversion and regioselectivity are low. Increasing the temperature to 45 °C increases the conversion as well as the regioselectivity. The increased regioselectivity can be attributed to an increased exchange rate between **I** and **1.15** that occurs with increased temperature. Using 20% **I**, there is no effect to increasing the temperature to 55 °C from 45 °C, as both entries give optimal conversion and selectivities (Table 1.7).

Table 1.7 Temperature Screen.

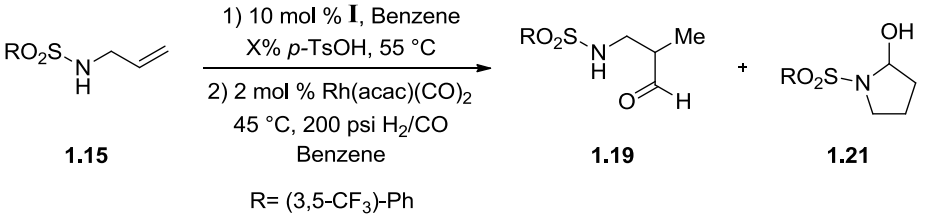


Temperature (°C)	Regioselectivity (**1.19**:**1.21**)[a]	Conversion (%)[b]
35	81:19	65
45	91:9	>95
45[c]	99:1	>95
55[c]	98:2	>95

[a]Determined by SFC analysis. [b]Determined by ^{1}H NMR using 1,3,5-trimethoxy-benzene as an internal standard.[c]Reaction run with 20 mol % **I**.

The effect of adding acid, which was previously shown to accelerate the exchange between **I** and alcohol substrates, was also examined.[13] In this case using 0.2% *p*-toluenesulfonic acid gave lower regioselectivity for **1.19** (Table 1.8). Because **1.15**

Table 1.8 Acid Loading Screen.



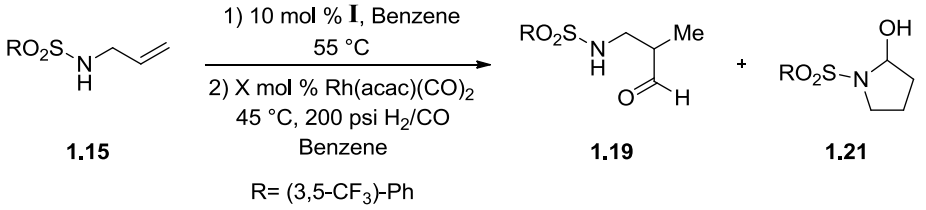
Acid (%)	Regioselectivity (**1.19**:**1.21**)[a]	Conversion (%)[b]
0	84:16	>95
0.2	69:31	>95

[a]Determined by SFC analysis. [b]Determined by ^{1}H NMR using 1,3,5-trimethoxy-benzene as an internal standard.

already contains an acidic proton, adding *p*-TsOH was not necessary. Making the exchange rate faster increases the concentration of the exchange intermediate through which **I** can decompose (Scheme 1.11 and 1.15). The decomposition of **I** results in lower regioselectivities because directed reaction does not occur without **I**.

The amount of rhodium was screened knowing that it would have an effect on the rate of selective reaction with **I**, as well as the unselective, undirected background reaction. At low loadings of rhodium, the directed reaction is able to outcompete the background reaction most effectively, resulting in high regioselectivities; however, the efficiency of the reactions suffers. At 2 mol % rhodium, the balance between complete conversion and high selectivity was reached (Table 1.9).

Table 1.9 Rhodium Loading Screen.



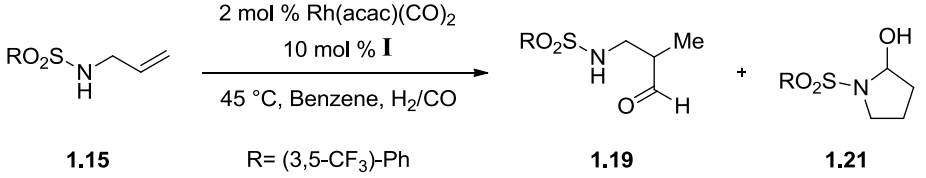
1.15 **1.19** **1.21**

Rhodium (mol %)	Regioselectivity (**1.19**:**1.21**)[a]	Conversion (%)[b]
0.5	91:9	65
1	88:12	84
2	87:13	>95
3	84:16	>95
4	84:16	>95

[a]Determined by SFC analysis. [b]Determined by ^{1}H NMR using 1,3,5-trimethoxy-benzene as an internal standard.

A pressure screen showed the most dramatic effect on selectivity. At 200 psi and above, the conversion is complete. (For a direct comparison of selectivites, reactions with PPh_3 and **I** without the pre-exchange were run at 200 psi.) The regioselectivity shows a strong dependence on pressure, with 400 psi being the optimal pressure (Table 1.10). It is possible that the increased CO pressure inhibits olefin binding to rhodium which would slow the background reaction.[27] Because **1.16** can chelate the metal, the directed reaction would be more competitive under those circumstances. Another possibility is that high H_2/CO pressure changes the rate and selectivity determining step in the reaction.[28]

Table 1.10 Pressure Screen.



1.15 R= (3,5-CF_3)-Ph **1.19** **1.21**

Pressure (psi)	Regioselectivity (**1.19**:**1.21**)[a]	Conversion (%)[b]
200[c]	50:50	>95
200	60:40	>95
200[d]	91:9	>95
100[d]	88:12	83
300[d]	96:4	>95
400[d]	97:3	>95

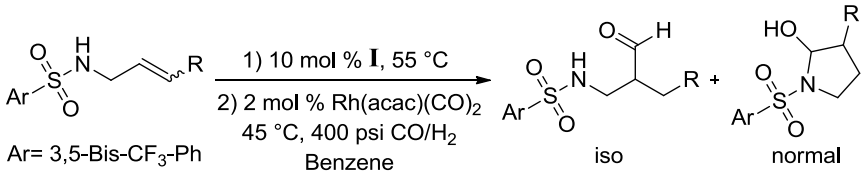
[a]Determined by SFC analysis. [b]Determined by ^{1}H NMR using 1,3,5-trimethoxy-benzene as an internal standard. [c]Reaction run with 4% PPh_3 as the ligand. [d]**1.15** and **I** were exchanged at 55 °C prior to hydroformylation.

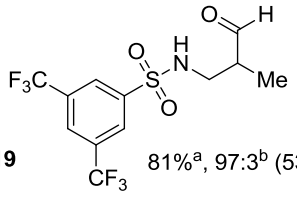
[27](a) van Leeuwen, P. W. N. M.; Casey, C. P.; Whiteker, G. T. *Rhodium Catalyzed Hydroformylation*; Leeuwen, P. W. N. M., Claver, C., Eds.; Kluwer Academic Publishers: Norwell, MA, 2001; Chapter 4, pp 63-106. (b) van Rooy, A.; Orij, E. N.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **1995**, *14*, 34-43.
[28](a) Ghio, C.; Lazzaroni, R.; Alagona, G. *Eur. J. Inorg. Chem.* **2009**, *1*, 98-103. (b) Watkins, A. L.; Landis, C. R. *J. Am. Chem. Soc.* **2010**, *132*, 10306-10317.

With the optimal conditions established, the substrate scope was expanded to 1,2-disubstituted olefins. The more reactive terminal olefin, **1.15**, resulting in a ratio of 97:3 favoring **1.19** indicated that the disubstituted olefins would also be highly regioselective. Accordingly, the alkyl substrates all react with excellent regioselectivities in good yields (Table 1.11, Products **1.19**, **1.22**, and **1.23**). A substrate containing a free alcohol was not successful as the alcohol can also bind to **I**, but the protected alcohol substrate gives similar results to the other alkyl substrates (Table 1.11, **1.24**). In general, styrene substrates prefer to form the aldehyde at the position proximal to the aryl group.[29] Using **I** completely overturned this inherent preference with both electron-withdrawing and donating aryl substrates (Table 1.11, Products **1.25-1.28**). An ester substrate, which yields mostly reduced olefin when PPh_3 is used as the ligand, gives high selectivity for the 1,4 dicarbonyl product, **1.29**, when **I** is used with less than 10% reduced starting material (Table 1.11). The high selectivity is impressive as esters are known to direct hydroformylation.[30] This demonstrates the ability of **I** to overcome a stoichiometric directing group. A skipped diene substrate gives greater than 95:5 selectivity in the presence of **I** leaving the distal olefin untouched. The hydroformylation of this diene with PPh_3 gives a very complex mixture of aldehyde products (Table 11, Product **1.30**).

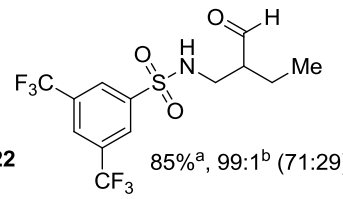
[29](a) Tolman, C. A.; Faller, J. W. In *Homogeneous Catalysis with Metal Phosphine Complexes*; Pignolet, L. H., Ed.; Plenum: New York, 1983; pp 81-109. (b) van der Veen, L. A.; Boele, M. D. K.; Bregman, F. R.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J.; Schenk, H.; Bo, C. *J. Am. Chem. Soc.* **1998**, *120*, 11616-11626.
[30]Neibecker, D.; Réau, R. *Angew. Chem., Int. Ed.* **1989**, *28*, 500-501.

Table 1.11 Substrate Scope of Hydroformylation of Allylic Sulfonamides.

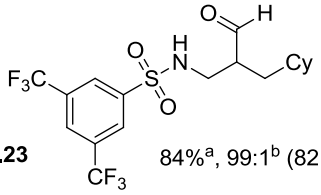




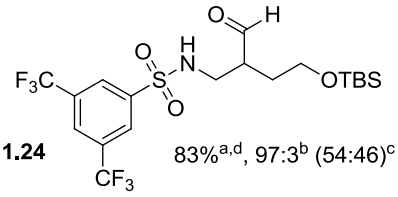
1.19 81%[a], 97:3[b] (53:47)[c]



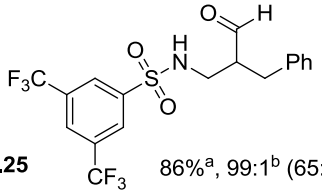
1.22 85%[a], 99:1[b] (71:29)[c]



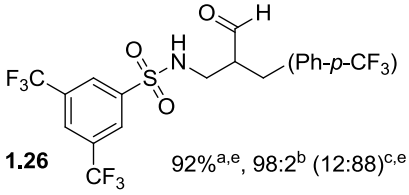
1.23 84%[a], 99:1[b] (82:18)[c]



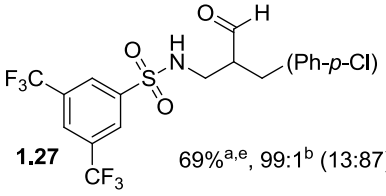
1.24 83%[a,d], 97:3[b] (54:46)[c]



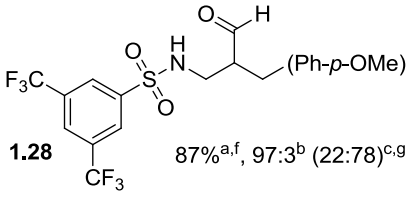
1.25 86%[a], 99:1[b] (65:35)[c]



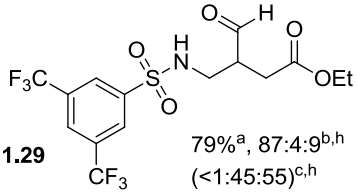
1.26 92%[a,e], 98:2[b] (12:88)[c,e]



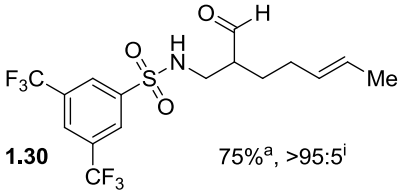
1.27 69%[a,e], 99:1[b] (13:87)[c,e]



1.28 87%[a,f], 97:3[b] (22:78)[c,g]



1.29 79%[a], 87:4:9[b,h] (<1:45:55)[c,h]



1.30 75%[a], >95:5[i]

[a]Isolated yields of the mixture of regioisomers. [b]Regioselectivity of iso:normal products as determined by SFC analysis. [c]Regioselectivity for reactions run with 4% PPh_3 instead of **I**. [d]Hydroformylation performed at 40 °C. [e]Hydroformylation performed in 5% THF/benzene. [f]Hydroformylation performed in 10% THF/benzene with 3 mol % $Rh(acac)(CO)_2$ at 55 °C. [g]Hydroformylation peformed in 10% THF/benzene with 3 mol % $Rh(acac)(CO)_2$ and 6 mol % PPh_3 at 55 °C. [h]Ratio of iso:normal:hydrogenated product. [i]Selectivity determined by analysis of crude ^1H NMR.

1.6 Conclusions

Using catalytic directing group, **I**, the efficient regioselective hydroformylation of substituted allylic sulfonamides to form β-amino-aldehydes under mild conditions has been shown. A complete reversal of the inherent selectivity is obtained in many cases, as well as, excellent site selectivity in the case of **1.30**.

1.7 Experimental

General Considerations

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Lithium reagents were titrated against 2-pentanol or 2,6-di-*tert*-butyl-4-methylphenol (BHT) using 1,10-phenanthroline as the indicator. Flash column chromatography was performed using EMD Silica Gel 60 (230-400 mesh) and ACS grade solvents as received from Fisher Scientific. All experiments were performed in oven or flame-dried glassware under an atmosphere of nitrogen or argon using standard syringe and cannula techniques, except where otherwise noted. All reactions were run with dry, degassed solvents dispensed from a Glass Contour Solvent Purification System (SG Water, USA LLC). ^{1}H, ^{13}C, and ^{31}P NMR were performed on either a Varian Gemini-2000 400 MHz or a Varian Unity 300 MHz instrument. Deuterated solvents were purchased from Cambridge Isotope Labs and stored over 3Å molecular sieves. C_6D_6 was degassed by three successive freeze-pump-thaw cycles and stored over 3Å molecular sieves in a dry box under a nitrogen atmosphere. All NMR chemical shifts are reported in ppm relative to residual solvent for ^{1}H and ^{13}C and external standard (neat H_3PO_4) for ^{31}P

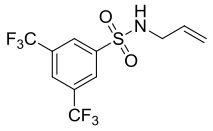
NMR. Coupling constants are reported in Hz. All IR spectra were gathered on a Bruker Alpha FT-IR equipped with a single crystal diamond ATR module and values are reported in cm^{-1}. Analytical supercritical fluid chromatography (SFC) was performed on a Berger Instruments Supercritical Chromatograph equipped with an Alcott auto sampler and a Knauer UV detector using methanol as the modifier. An achiral Princeton SFC 4.6x150 mm silica column (henceforth Silica) with 60Å mesh silica, 6μ particle size was used for analysis of some compounds. All SFC retention times are reported as t_r. HRMS and X-ray crystal structure data were generated in Boston College facilities. Hydroformylation was performed in an Argonaut Technologies Endeavor® Catalyst Screening System using 1:1 H_2/CO supplied by Airgas, Inc.

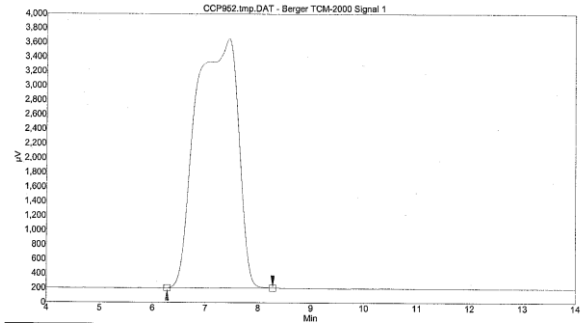
Substrate Syntheses and Characterization

The following compounds were made according to literature procedures and matched reported spectra: (*E*)-ethyl-3-cyclohexylacrylate,[31-33] (*E*)-3-cyclohexyl-2-propen-1-ol,[34-36] (*E*)-but-2-en-1-amine, [37-39] (*E*)-3-phenylprop-2-en-1-amine,[40-41]

[31]Charette, A. B.; Molinaro, C.; Brochu, C. *J. Am. Chem. Soc.* **2001**, *123*, 12168-12175.
[32]Aggarwal, V. K.; Fulton, J. R.; Sheldon, C. G.; de Vicente, J. *J. Am. Chem. Soc*. **2003**, *125*, 6034-6035.
[33]Nishizawa, M.; Hirakawa, H.; Nakagawa, Y.; Yamamoto, H.; Namba, K.; Imagawa, H. *Org. Lett.* **2007**, *9*, 5577-5580.
[34]Takeuchi, R.; Ue, N.; Tanabe, K.; Yamashita, K.; Shiga, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525-9534.
[35]Lombardo, M.; Morganti, S.; Trombini, C. *J. Org. Chem.* **2000**, *65*, 8767-8773.
[36]Chini, M.; Crotti, P.; Flippin, L. A.; Gardelli, C.; Giovani, E.; Macchia, F.; Pineschi, M. *J. Org. Chem.* **1993**, *58*, 1221-1227.
[37]Calsen, P. H. J.; Jorgensen, K. B. *J. Heterocycl. Chem.* **1997**, *34*, 797-806.
[38]Nishikawa, Y.; Nakamura, Y.; Kawaguchi, S. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 155-160.
[39]Hamada, J.; Tsunashima, S.; Sato, S. *Bull. Chem. Soc. Jpn*. **1983**, *56*, 662-666.
[40]Moody, C. J.; Rahimtoola, K. F.; Porter, B.; Ross, B. C. *J. Org. Chem.* **1992**, *57*, 2105-2114.
[41]Bartoli, G.; Di Antonio, G.; Giovannini, R.; Giuli, S.; Lanari, S.; Paoletti, M.; Marcantoni, E. *J. Org. Chem.* **2008**, *73*, 1919-1924.

1,4-but-2-enediol cyclic sulfite,[42-45] 2-isopropoxy-2,3-dihydro-1*H*-benzo[*d*][1,3]azaphosphole (**I**),[21] (*E*)-but-2-en-1-ol,[46] (*E*)-1-bromobut-2-ene,[47] (*E*)-hept-5-en-2-yn-1-ol[48] and (2*E*,5*E*)-hepta-2,5-dien-1-ol.[49]

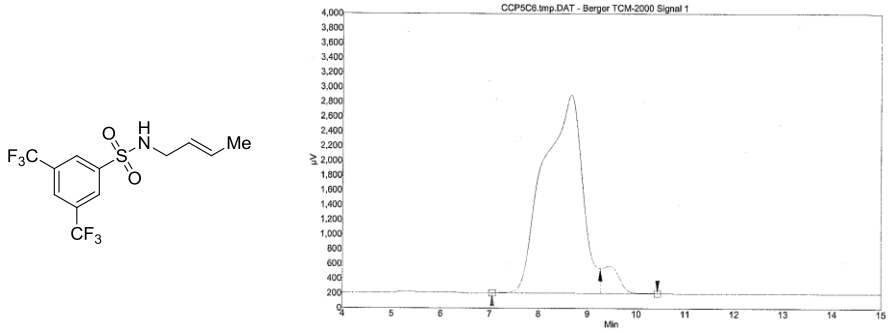




***N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide.**[50] To a flame-dried round-bottom flask was added 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (4.01 g, 12.8 mmol) and CH_2Cl_2 (50 mL). The solution was cooled to 0 °C and allyl amine (4.78 mL, 63.9 mmol) was added dropwise. The solution was allowed to warm to room temperature. The reaction was diluted with CH_2Cl_2 (20 mL) and washed with 1:1 brine/H_2O (2x30 mL) and brine (1x30 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. Chromatography (15% EtOAc/Hex) afforded a white solid (4.15 g, 97%). **SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 7.44 min;

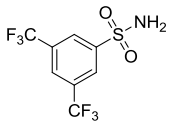
[42]Chaudhari, S. S.; Akamanchi, K. G. *Synlett* **1999**, *11*, 1763-1765.
[43]Shellhamer, D. F.; Anstine, D. T.; Gallego, K. M.; Ganesh, B. R.; Hanson, A. A.; Hanson, K. A.; Henderson, R. D.; Prince, J. M.; Heasley, V. L. *J. Chem. Soc. Perkin Trans. 2* **1995**, *7*, 1569-1570.
[44]Friedrich, M.; Savchenko, A. I.; Wachtler, A.; de Meijere, A. *Eur. J. Org. Chem.* **2003**, *11*, 2138-2143.
[45]Morino, Y.; Hidaka, I.; Oderaotoshi, Y.; Komatsu, M.; Minakata, S. *Tetrahedron* **2006**, *62*, 12247-12251.
[46]Haynes, R. K.; Au-Yeung, T.; Chan, W.; Lam, W.; Li, Z.; Yeung, L.; Chan, A. S. C.; Li, P.; Koen, M.; Mitchell, C. R.; Vonwiller, S. C. *Eur. J. Org. Chem*. **2000**, *18*, 3205-3216.
[47]Loughin, W. A.; Haynes, R. K. *Aust. J. Chem*. **1995**, *48*, 651-661.
[48]Davies, S. G.; Haggitt, J. R.; Ichihara, O.; Kelly, R. J.; Leech, M. A.; Price, M. A. J.; Roberts, P. M.; Smith, A. D. *Org. Biomol. Chem*. **2004**, *2*, 2630-2649.
[49]Pickard, S. T.; Smith, H. E.; Polavarapu, P. L.; Black, T. M.; Rauk, A.; Yang, D. *J. Am. Chem. Soc.* **1992**, *114*, 6850-6857.
[50]Brummond, K. M.; Chen, H.; Mitasev, B.; Casarez, A. D. *Org. Lett.* **2004**, *6*, 2161-2163.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.32 (s, 2H), 8.08 (s, 1H), 5.66-5.75 (m, 1H), 5.13-5.22 (m, 2H), 4.91 (t, 1H, J = 5.9), 3.72 (ddd, 2H, J = 12.0, 6.0, 1.3); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.4, 133.1 (q, J = 34.5), 132.3, 127.5, 126.4, 122.6 (q, J = 273.6), 118.6, 46.0; **IR:** 3274, 3087, 1626, 1430, 1362, 1340, 1281, 1196, 1175, 1160, 1132, 1110, 906, 886, 697, 682, 645, 589, 515 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{10}F_6NO_2S$ $[M+H]^+$: 334.0336, found: 334.0340.



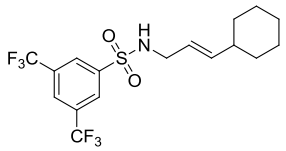
***cis*/*trans*-(1:4.5 mixture)-*N*-(but-2-enyl)-3,5-bis(trifluoromethyl)benzenesulfonamide.** To a flame-dried round-bottom flask was added but-2-en-1-amine hydrochloride (4.11 g, 37.5 mmol), triethylamine (713 μL, 5.12 mmol) and CH_2Cl_2 (150 mL). The solution was cooled to 0 °C and 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (11.7 g, 37.5 mmol) was added. The reaction was allowed to warm to room temperature. The solution was diluted with EtOAc (50 mL) and washed with 1:1 brine/H_2O (2x50 mL) and brine (1x50 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated. Chromatography (CH_2Cl_2) afforded a white solid (5.36 g, 41%). **SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 8.67 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.30 (s, 2H), 8.07 (s, 1H), 5.58-5.67 (m, 1H), 5.27-5.34 (m, 1H), 4.62 (s, 1H), 3.75 (app. t, 0.4H, J = 6.4),

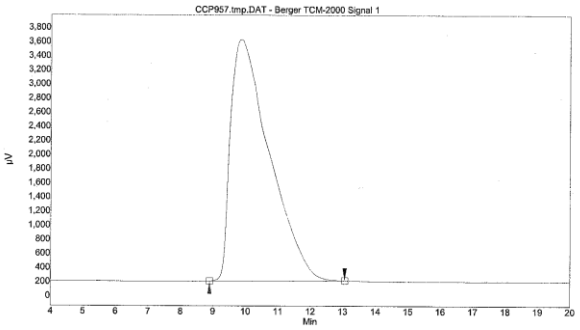
3.65 (ddd, 2H, J = 12.5, 6.2, 1.1), 1.61 (d, 3H, J = 5.3); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.7, 133.1 (q, J = 33.7), 131.1, 127.6, 126.3, 125.0, 122.6 (q, J = 272.8), 45.7, 17.7; **IR**: 3277, 3058, 1626, 1359, 1342, 1279, 1265, 1161, 1141, 1110, 904, 735, 698, 681, 590, 414 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{12}F_6NO_2S$ $[M+H]^+$: 348.0493, found: 348.0502.



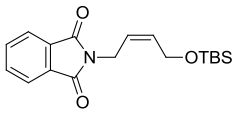
3,5-bis(trifluoromethyl)benzenesulfonamide.[51] 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (1.0 g, 3.2 mmol) was suspended in water in a round-bottom flask. Ammonium hydroxide (1.3 mL, 32 mmol) was added. The mixture was heated to 100 °C. After reaching 100 °C, the reaction was cooled to room temperature and concentrated. Excess water was removed by azeotroping the product with toluene three times to yield a white solid (1.0 g, 100%). **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.39 (s, 2H), 8.09 (s, 1H), 4.99 (s, 2H); **IR**: 3356, 3262, 1323, 1312, 1277, 1266, 1198, 1163, 1131, 907, 731, 699, 682 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_8H_6F_6NO_2S$ $[M+H]^+$: 294.0023, found: 294.0037.

[51]Yuriev, E.; Kong, D. C. M.; Iskander, M. N. *Eur. J. Med. Chem.* **2004**, *39*, 835-847.





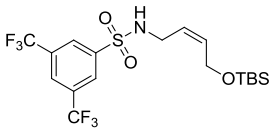
(*E*)-*N*-(3-cyclohexylallyl)-3,5-bis(trifluoromethyl)benzenesulfonamide.[52] 3,5-bis(trifluoromethyl)benzenesulfonamide (658 mg, 4.69 mmol), (*E*)-3-cyclohexyl-2-propen-1-ol (2.75 g, 9.38 mmol) and triphenylphosphine (2.46 g, 9.38 mmol) were dissolved in CH_2Cl_2 (94 mL) in a round-bottom flask. DIAD (1.90 g, 9.38 mmol) was added, and the reaction was stirred at room temperature for 2.5 h. The reaction was concentrated. Chromatography (2-25% EtOAc/Hex) yielded a white solid (371 mg, 19%). **SFC** (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 °C) t_r = 9.87 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.31 (s, 2H), 8.07 (s, 1H), 5.52 (dd, 1H, *J* = 15.5, 6.5), 5.22 (dtd, 1H, *J* = 15.4, 6.4, 1.1), 4.75 (t, 1H, *J* = 5.8), 3.64 (t, 2H, *J* = 6.2), 1.82-1.85 (m, 1H), 1.55-1.69 (m, 5H), 1.03-1.26 (m, 3H), 0.86-0.96 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.6, 141.9, 133.0 (q, *J* = 34.5), 127.5, 126.3, 122.6 (q, *J* = 272.7), 121.2, 45.8, 40.3, 32.6, 26.2, 26.0; **IR**: 3291, 2928, 2855, 1450, 1424, 1360, 1279, 1161, 1142, 1114, 905, 699, 682, 593 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{17}H_{20}F_6NO_2S$ $[M+H]^+$: 416.1119, found: 416.1127.

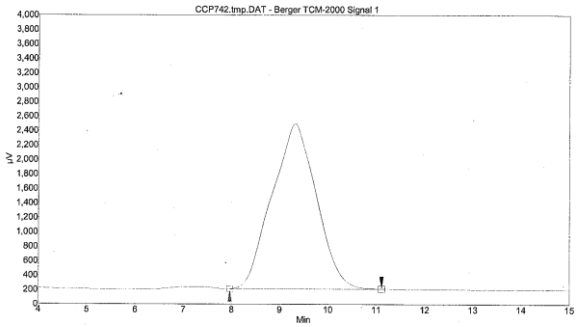


(*Z*)-2-(4-(*tert*-butyldimethylsilyloxy)but-2-enyl)isoindoline-1,3-dione. Potassium

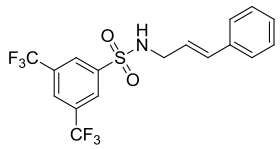
[52]Guisado, C.; Waterhouse, J. E.; Price, W. S.; Jorgensen, M. R.; Miller, A. D. *Org. Biomol. Chem*. **2005**, *3*. 1049-1057.

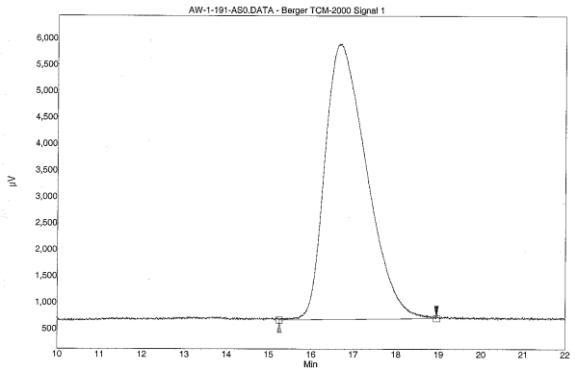
phthalimide (15.2 g, 82.1 mmol) was added to 1,4-but-2-enediol cyclic sulfite (5.51 g, 41.1 mmol) in DMF (22 mL). The suspension was stirred and heated to 100 °C for 1 h. After cooling, the reaction was quenched with H_2O (100 mL). The aqueous phase was extracted with Et_2O (3x50 mL). The combined organic extracts were washed with H_2O (1x50 mL), dried with anhydrous $MgSO_4$, filtered, and concentrated. The resulting white solid was dissolved in CH_2Cl_2 (50 mL) and filtered to remove excess potassium phthalimide. The filtrate was concentrated to give a 3:1 ratio of product to potassium phthalimide and was used without further purification. In a flame-dried 100 mL round bottom flask, the filtrate (6.36 g, 29.3 mmol) was dissolved in CH_2Cl_2 (49 mL) and DMAP (183 mg, 1.50 mmol) was added. The solution was cooled to 0 °C, and triethylamine (4.90 mL, 35.2 mmol) was added. TBSCl (5.32 g, 35.3 mmol) was dissolved in CH_2Cl_2 (10 mL) and added slowly at 0 °C. The solution was allowed to warm to room temperature and stirred overnight at room temperature. Saturated aqueous $NaHCO_3$ (20 mL) was added, and the solution was extracted with CH_2Cl_2 (3x30 mL). The combined organics were washed with brine (1x50 mL), dried over $MgSO_4$, filtered, and concentrated. Chromatography (10% EtOAc/Hex) afforded a white solid (6.63 g, 49% over two steps). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.83-7.86 (m, 2H), 7.70-7.73 (m, 2H), 5.63-5.75 (m, 1H), 5.47-5.55 (m, 1H), 4.45 (d, 2H, *J* = 4.8), 4.33 (d, 2H, *J* = 7.1), 0.92 (s, 9H), 0.11 (s, 6H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 168.0, 134.1, 134.0, 132.3, 123.7, 123.4, 59.6, 35.2, 26.2, 18.6, –4.8; **IR**: 3379, 2955, 2920, 2857, 1773, 1716, 1430, 1089, 838, 779, 716 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{26}NO_3Si$ $[M+H]^+$: 332.1682, found: 332.1675.



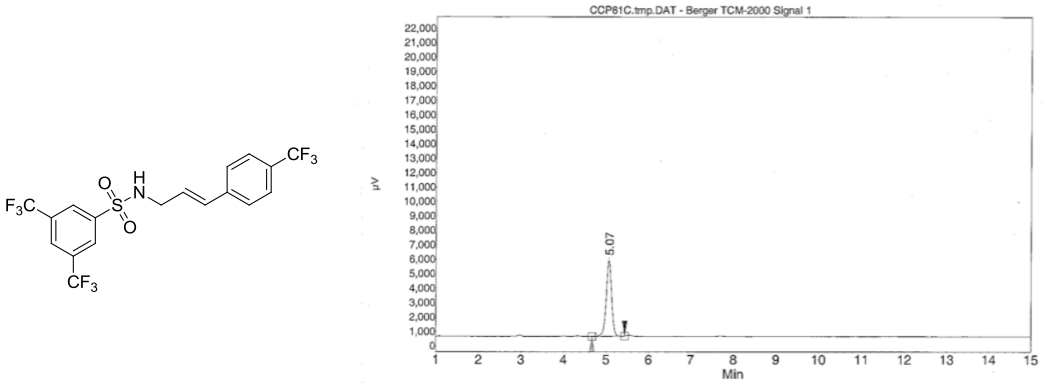


(*Z*)-*N*-(4-(*tert*-butyldimethylsilyloxy)but-2-enyl)-3,5-bis(trifluoromethyl)benzenesulfonamide. (*Z*)-2-(4-(*tert*-butyldimethylsilyloxy)but-2-enyl)isoindoline-1,3-dione (7.71 g, 23.3 mmol) and hydrazine hydrate (2.30 mL, 46.6 mmol) were refluxed in EtOH (23 mL) for 30 minutes. After cooling to room temperature, the mixture was filtered, and the solid was washed with CH_2Cl_2 (3x30 mL). The filtrate was concentrated. The resulting oil (3.42 g, 17.0 mmol) was dissolved in CH_2Cl_2 (57 mL) in a round-bottom flask. The reaction was cooled to 0 °C, and 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (5.29 g, 17.0 mmol) was added. Hunig's base (8.92 mL, 129 mmol) was added slowly, and the reaction was allowed to warm to room temperature. The reaction was diluted with CH_2Cl_2 (20 mL) and washed with 1:1 brine/H_2O (2x30 mL) and brine (1x30 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated. Chromatography (10% EtOAc/Hex) afforded an off-white solid (3.69 g, 39% over two steps). **SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 9.76; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.31 (s, 2H), 8.07 (s, 1H), 5.63-5.73 (m, 1H), 5.38-5.42 (m, 1H), 5.18 (t, 1H, J = 5.7), 4.16 (d, 2H, J = 5.7), 3.76-3.79 (m, 2H), 0.87 (s, 9H), 0.05 (s, 6H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.6, 133.7, 133.1 (q, J = 34.5), 127.5, 126.2, 125.3, 122.6 (q, J = 273.6), 59.6, 40.6, 26.0, 18.4, –5.2; **IR**: 3293, 2956, 2933, 2887, 2859, 1359, 1277, 1137, 1109, 1064, 905, 836, 699, 681, 590, 414; **HRMS** (DART-TOF) calcd. for $C_{18}H_{26}F_6NO_3SSi$ $[M+H]^+$: 478.1307, found: 478.1328.





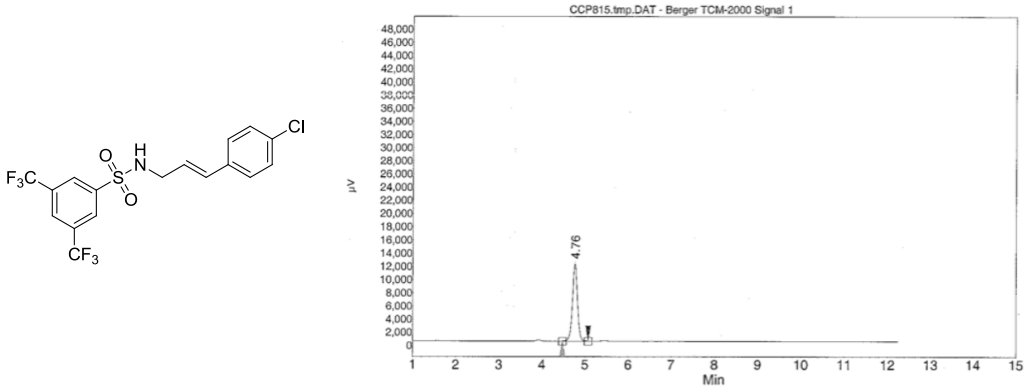
***N*-cinnamyl-3,5-bis(trifluoromethyl)benzenesulfonamide.**[50] The procedure for *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide was followed. Chromatography (15% EtOAc/Hex) afforded a white solid (1.69 g, 50%). **SFC** (AS-H, 2.0 mL/min, 2.0% MeOH, 220 nm, 150 bar, 50 ˚C) t_r = 16.69 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.25 (s, 2H), 7.93 (s, 1H), 7.22-7.13 (m, 5H), 6.38 (d, 1H, *J* = 16.0), 5.91 (dt, 1H, *J* = 15.7, 6.4), 4.85 (t, 1H, *J* = 6.0), 3.79 (dd, 2H, *J* = 6.2, 6.0); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.5, 135.6, 134.2, 133.1 (q, *J* = 34.5), 128.8, 128.4, 127.5, 126.5, 126.3, 123.0, 122.5 (q, *J* = 273.6), 45.8; **IR**: 3281, 3091, 1361, 1340, 1157, 1139, 1110, 970, 907, 749, 696, 682, 590 cm^{-1}; HRMS (DART-TOF) calcd. for $C_{17}H_{13}F_6NO_2S$ $[M]^+$: 409.0571, found: 409.0588.



(*E*)-3,5-bis(trifluoromethyl)-*N*-(3-(4-(trifluoromethyl)phenyl)allyl)benzenesulfonamide.[53] To a flame-dried two-neck round-bottom flask fitted with a reflux condenser was added *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (1.51 g, 4.49 mmol) followed by palladium (II) acetate (50.5 mg, 0.225 mmol) and tri(*o*-tolyl)phosphine (137 mg, 451 μmol). The flask was temporarily placed under vacuum and refilled with nitrogen three times to remove any oxygen followed by addition of acetonitrile (8.4 mL), triethylamine (1.26 mL, 9.01 mmol) and 4-iodobenzotrifluoride (661 μL, 4.51 mmol). The reaction mixture was placed in a preheated oil bath and stirred for 3 h to yield an orange solution. The reaction was cooled below reflux and a second portion of each: palladium (II) acetate (25.3 mg, 0.113 mmol), tri(*o*-tolyl)phosphine (68.5 mg, 0.225 mmol) and 4-iodobenzotrifluoride (278 μL, 1.89 mmol) was added and heated for an additional 16 h. The reaction mixture was diluted with H_2O (28 mL) and extracted with EtOAc (3x20 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated to yield a yellow oil that was dry-loaded (CH_2Cl_2) onto silica gel. Chromatography (15-25% EtOAc/Hex) yielded a light yellow solid (925 mg, 47%). **SFC** (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 5.07 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.24 (s, 2H), 7.96 (s, 1H), 7.46

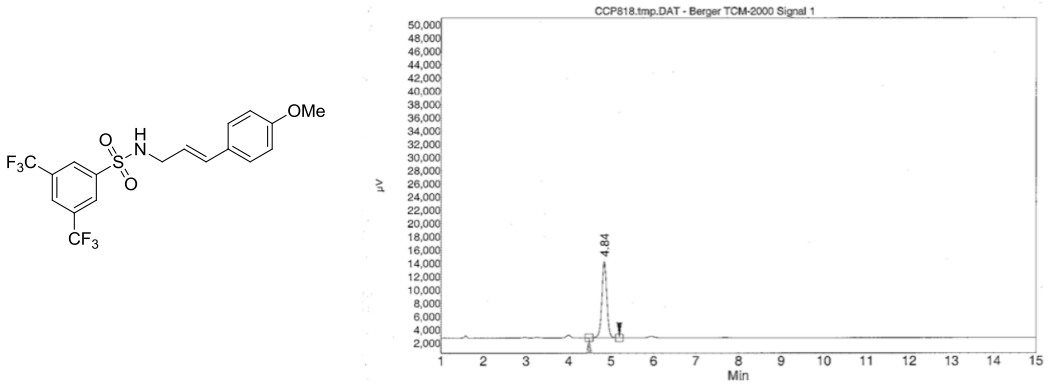
[53]Busacca, C. A.; Dong, Y. *Tet. Lett*. **1996**, *37*, 3947-3950.

(d, 2H, J = 8.4), 7.26 (d, 2H, J = 8.4), 6.45 (d, 1H, J = 16.0), 6.05 (dt, 1H, J = 6.0, 16.0), 4.79 (t, 1H, J = 6.0), 3.83 (t, 2H, J = 6.0); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.5, 139.1, 133.3 (q, J = 34.5), 132.7, 130.4 (q, J = 35.2), 127.5, 126.8, 126.5, 126.0, 125.9, 124.2 (q, J = 275.9), 122.5 (q, J = 273.6), 45.6; **IR**: 3290, 3089, 2925, 2854, 1618, 1416, 1360, 1327, 1279, 1160, 1067, 725, 699, 682 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{12}F_9NO_2S$ $[M]^{+\bullet}$: 477.0445, found: 477.0447.

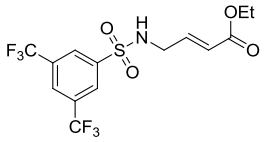


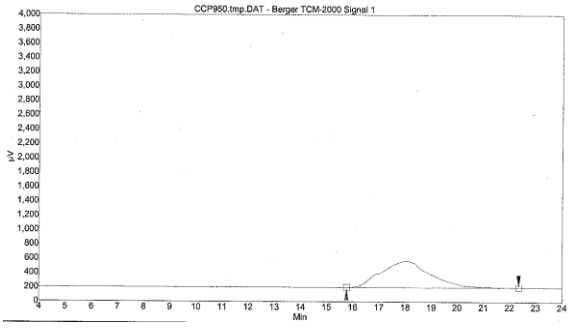
(*E*)-*N*-(3-(4-chlorophenyl)allyl)-3,5-bis(trifluoromethyl)benzenesulfonamide.[53] The procedure for (*E*)-3,5-bis(trifluoromethyl)-*N*-(3-(4-(trifluoromethyl)phenyl)allyl)benzenesulfonamide was followed except that 4-bromochlorobenzene was used instead of 4-iodobenzotrifluoride. Chromatography (25% EtOAc/Hex) yielded a white solid (561 mg, 42%). **SFC** (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 4.8 min; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.32 (s, 2H), 8.04 (s, 1H), 7.27 (d, 2H, J = 8.4), 7.17 (d, 2H, J = 8.4), 6.45 (d, 15.9, J = 15.9), 6.00 (dt, 1H, J = 6.3, 15.9), 4.76 (t, 1H, 5.7), 3.85-3.90 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.5, 134.2, 134.2, 132.7 (q, J = 34.5), 133.0, 129.0, 127.8, 127.6, 122.6 (q, J = 272.8), 126.4, 123.8, 45.7; **IR**: 3159, 3085, 2960, 2924, 2853, 1625, 1593, 1492, 1427, 1318,

1296, 1159, 1096, 926, 698, 681, 592 cm^{-1}; **HRMS** (DART-TOF) calcd. For $C_{17}H_{12}ClF_6NO_2S$ $[M]^+$: 443.0182, found: 443.0190.



(*E*)-*N*-(3-(4-methoxyphenyl)allyl)-3,5-bis(trifluoromethyl)benzenesulfonamide.[53] The procedure for (*E*)-3,5-bis(trifluoromethyl)-*N*-(3-(4-(trifluoromethyl)phenyl)allyl)benzenesulfonamide was followed except that 4-bromoanisole was used instead of 4-iodobenzotrifluoride. Chromatography (10-25% EtOAc/Hex) yielded an off-white solid (925 mg, 47%). **SFC** (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 4.84 min; **^{1}H NMR** (Acetone *d*-6, 400 MHz) δ 8.45 (s, 2H), 8.30 (s, 1H), 7.21 (d, 2H, *J* = 8.8), 6.84 (d, 2H, *J* = 8.8), 6.42 (d, 1H, *J* = 16.0), 5.94 (dt, 1H, *J* = 6.4, 16.0), 3.84 (dd, 2H, *J* = 5.6, 6.4). 3.78 (s, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 160.5, 145.4, 133.2, 133.1 (q, *J* = 33.7), 129.8, 128.5, 128.3, 126.9, 123.8 (q, *J* = 272.8), 122.7, 114.8, 55.7, 46.3; **IR**: 3356, 3262, 2958, 2922, 2851, 1626, 1607, 1364, 1323, 1277, 1163, 1132, 1030, 907, 845, 698 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{16}F_6NO_3S$ $[M+H]^+$: 440.0753, found: 440.0753.



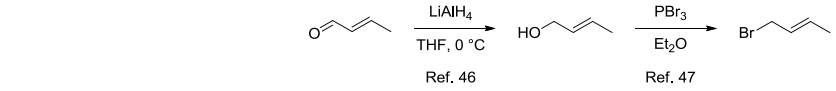


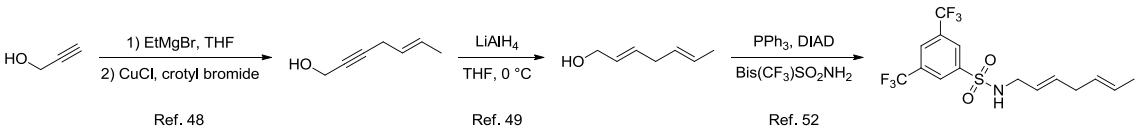
(*E*)-ethyl 4-(3,5-bis(trifluoromethyl)phenylsulfonamido)but-2-enoate.[54] *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (4.1 g, 12 mmol) was dissolved in MeOH (40 mL) and cooled to –78 °C. Ozone was bubbled through the solution until it turned blue. The excess ozone was bubbled out with nitrogen, and dimethyl sulfide (1.3 mL, 18 mmol) was added. The solution was kept at –78 °C for 5 h then slowly allowed to warm to room temperature. The solvent was evaporated. The residue was dissolved in $CHCl_3$ (80 mL), washed with 2% HCl (30 mL) and saturated aqueous $NaHCO_3$ (30 mL), and dried over $MgSO_4$. The organic layer was filtered and concentrated. NaH (314 mg, 13.1 mmol) was suspended in THF (45 mL) and triethylphosphonoacetate (2.67 g, 11.9 mmol) in THF (5 mL) was added. The solution was stirred for 1.5 h. The crude ozonolysis product (4.1 g, 12 mmol) in THF (10 mL) was added, and the solution was stirred at room temperature overnight. The reaction was quenched with H_2O (5 mL) and concentrated. The residue was dissolved in $CHCl_3$ (60 mL), washed with 2% HCl (20 mL) and saturated aqueous $NaHCO_3$ (30 mL), dried over $MgSO_4$, filtered, and concentrated. Chromatography (20% EtOAc/Hex) afforded a white solid. A minor impurity was removed by recrystallization (EtOH/Hex) to give a white solid (590 mg, 12%). **SFC** (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 ˚C) t_r = 17.99 min; **^{1}H**

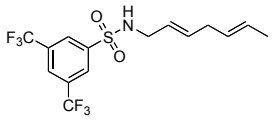
[54]Liu, S.; Hanzlik, R. P. *J. Med. Chem.* **1992**, *35*, 1067-1075.

NMR ($CDCl_3$, 400 MHz) δ 8.31 (s, 2H), 8.09 (s, 1H), 6.73 (dt, 1H, *J* = 15.6, 5.2), 5.93 (dt, 1H, *J* = 16.0, 1.2), 5.11 (t, 1H, *J* = 5.8), 4.17 (q, 2H, *J* = 7.0), 3.87-3.91 (m, 2H,), 1.27 (t, 3H, *J* = 6.8); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 165.5, 143.2, 141.3, 133.3 (q, *J* = 34.5), 127.5, 126.6, 123.8, 122.5 (q, *J* = 274.4), 61.1, 44.1, 14.3; **IR**: 3278, 3089, 2988, 1703, 1360, 1279, 1162, 1139, 1113, 906, 699, 682, 592 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{14}H_{14}F_6NO_4S$ $[M+H]^+$: 406.0548, found: 406.0554.

Synthesis of *N*-((2*E*,5*E*)-hepta-2,5-dienyl)-3,5-bis(trifluoromethyl)benzenesulfonamide:



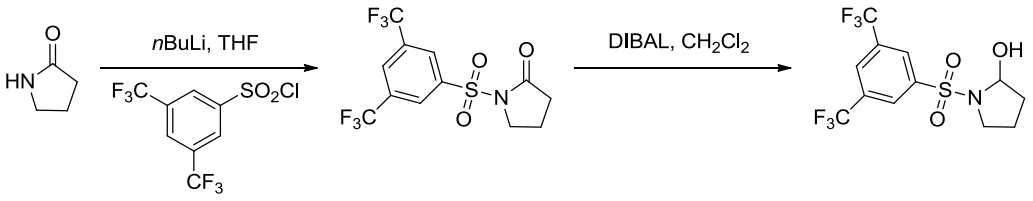


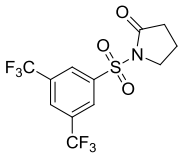


***N*-((2*E*,5*E*)-hepta-2,5-dienyl)-3,5-bis(trifluoromethyl)benzenesulfonamide.**[52] The procedure for (*E*)-*N*-(3-cyclohexylallyl)-3,5-bis(trifluoromethyl)benzenesulfonamide was followed. Chromatography (2-7% EtOAc/Hex) afforded light yellow oil that solidified upon standing to yield a white solid (654 mg, 34%). **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.30 (s, 2H), 8.07 (s, 1H), 5.59 (dt, 1H, *J* = 1.2, 5.1), 5.55-5.63 (m, 3H), 4.56 (t, 1H, *J* = 6.0), 3.67 (dd, 2H, *J* = 1.2, 6.3), 2.59-2,62 (m, 2H), 1.61-1.64 (m, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.7, 134.5, 133.1 (q, *J* = 35.4), 127.9, 127.6, 126.9,

126.3, 124.2, 122.6 (q, J = 273.5), 45.6, 35.1, 18.0; **IR**: 3289, 3088, 2924, 1625, 1426, 1277, 1134, 1109, 969, 904, 843, 698, 680, 631, 589 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{15}H_{16}F_6NO_2S$ $[M+H]^+$: 388.0806, found: 388.0792.

Authentic Linear Hydroformylation Product Synthesis and Characterization

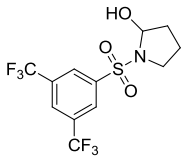




1-(3,5-bis(trifluoromethyl)benzenesulfonyl)pyrrolidin-2-one.[55] Pyrrolidinone (401 mg, 4.69 mmol) was brought up in THF (15 mL) and cooled to 0 °C. *n*BuLi (3.45 mL, 5.17 mmol) was added via syringe. The reaction mixture was stirred at 0 °C for 40 minutes. A cold solution of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (1.48 g, 4.75 mmol) in THF (6 mL) was added via cannula. The reaction was stirred at 0 °C. After ~1 h, the reaction was warmed to room temperature and concentrated. The concentrate was diluted with CH_2Cl_2 (15 mL), washed with H_2O (3x10 mL), dried over $MgSO_4$, filtered, and concentrated. Chromatography (20-100% EtOAc/Hex) yielded a white solid (958 mg, 80%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.52 (s, 2H), 8.15 (s, 1H), 3.97 (t, 2H, J = 7.1), 2.51 (t, 2H, J = 8.1), 2.17 (tt, 2H, J = 7.7, 7.5); **^{13}C NMR** ($CDCl_3$,

[55]Harling, J. D.; Steel, P. G.; Woods, T. M.; Yufit, D. S. *Org. Biomol. Chem.* **2007**, *5*, 3472-3476.

100 MHz) δ 173.6, 140.8, 133.0 (q, J = 34.5), 128.8, 127.7, 122.5 (q, J = 272.8), 47.6, 32.1, 18.6; **IR**: 3095, 2994, 2915, 1750, 1626, 1362, 1279, 1165, 1133, 1109, 965, 906, 696, 682, 634, 593, 540, 415 cm^{-1}; **HRMS** (DART-TOF) cald. for $C_{12}H_{10}F_6NO_3S$ $[M+H]^+$: 362.0256, found: 362.0287.



1-(3,5-bis(trifluoromethyl)benzenesulfonyl)pyrrolidin-2-ol.[56] 1-(3,5-bis(trifluoromethyl)benzenesulfonyl)pyrrolidin-2-one (250 mg, 0.69 mmol) was dissolved in CH_2Cl_2 (3.5 mL) and cooled to –78 °C under Ar. With stirring, the reaction mixture was treated with DIBAL (140 µL, 0.76 mmol) dropwise, stirred for 1 h at –78 °C, and 1 h at room temperature. The reaction was cooled to –78 °C, quenched with MeOH (520 µL) and allowed to warm to room temperature slowly overnight. The reaction was poured on to a 1M aqueous solution of Rochelle's salt (15 mL). This mixture was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were washed with brine (30 mL), dried with $MgSO_4$, filtered, and concentrated. Chromatography (25% EtOAc/Hex) afforded a white solid (160 mg, 64%). **SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 6.48 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.34 (s, 2H), 8.08 (s, 1H), 5.56-5.57 (m, 1H), 3.54 (s, 1H), 3.20 (s, 1H), 3.03 (s, 1H), 2.12-2.21 (m, 1H), 1.90-1.99 (m, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 143.1, 133.9 (q, J = 34.5), 128.3, 127.1, 123.3 (q, J = 272.8), 84.4, 47.6, 34.4, 23.2; **IR**: 3502, 3090,

[56]Unthank, M. G.; Hussain, N.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2006**, *45*, 7066-7069.

2986, 1361, 1280, 1158, 1136, 1114, 907, 731, 700, 682, 652, 600 cm^{-1}; **HRMS** (ESI) calcd. for $C_{12}H_{11}F_6NO_3S$ $[M+Na]^+$: 386.0262, found: 386.0267.

Exchange Reactions with Sulfonamides (Table 1.1)

General Exchange Reaction Procedure: In a dry glovebox, the sulfonamide, **1.15**, (0.10 mmol) was mixed with **I** (0.01 mmol) in benzene (1.0 mL) and heated to 45 °C. The reaction progress was followed by ^{31}P NMR. ^{31}P NMR of **I**: –22.1 ppm.

Table 1.1, Entry 1: *N*-allyl-4-methoxybenzenesulfonamide (23 mg, 1.0 x 10^{-1} mmol) and ligand **I** (2.9 mg, 1.0 x 10^{-2} mmol) were mixed in benzene (1.0 mL) and heated to 45 °C. ^{31}P NMR: –18.7 ppm.

Table 1.1, Entry 2: *N*-allyl-4-methylbenzenesulfonamide (21 mg, 1.0 x 10^{-1} mmol) and ligand **I** (2.9 mg, 1.0 x 10^{-2} mmol) were mixed in benzene (1.0 mL) and heated to 45 °C. ^{31}P NMR: –18.8 ppm.

Table 1.1, Entry 3: *N*-allyl-4-nitrobenzenesulfonamide (24 mg, 1.0 x 10^{-1} mmol) and ligand **I** (2.9 mg, 1.0 x 10^{-2} mmol) were mixed in benzene (1.0 mL) and heated to 45 °C. ^{31}P NMR: –17.9 ppm.

Table 1.1, Entry 4: *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (33 mg, 1.0 x 10^{-1} mmol) and ligand **I** (2.9 mg, 1.0 x 10^{-2} mmol) were mixed in benzene (1.0 mL) and heated to 45 °C. ^{31}P NMR: –17.8 ppm.

Exchange Reaction Between Substrates (Scheme 1.14)

In a dry glovebox, *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (17 mg, 5.0 x 10^{-2} mmol) and **I** (2.9 mg, 1 x 10^{-2} mmol) were mixed in benzene *d*-6 (0.6 mL) and heated to 55 °C. Reaction was followed by ^{31}P NMR. After 48 h, the reaction was complete. The reaction was concentrated and redissolved in benzene *d*-6 (1.0 mL) with (*E*)-*N*-(but-2-en-1-yl)-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.17** (18 mg, 5.0 x 10^{-2} mmol). The reaction was monitored by ^{31}P NMR. After 1 h at room temperature, the ratio between **1.16** and **1.18** was 53:47. At equilibrium (after 22 h), the ratio was 43:57, respectively.

Exchange Reaction with Product (Table 1.2)

In a dry glovebox, *N*-(2-methyl-3-oxopropyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.19**, (18 mg, 5.0 x 10^{-2} mmol) and **I** (2.9 mg, 1.0 x 10^{-2} mmol) were mixed in benzene *d*-6 (0.6 mL). The reaction was monitored by ^{31}P NMR at room temperature for 24 h.

Crystal Structure of **I-decomp** (CCDC # 837337) (Figure 1.5)

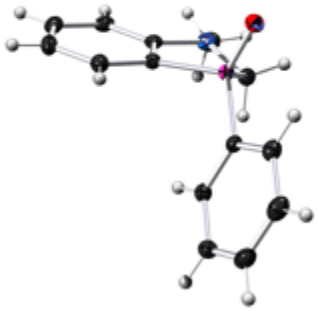


Table 1.12 Crystal data and structure refinement for **I-decomp**.

Identification code	$C_{14}H_{14}NOP$
Empirical formula	$C_{14}H_{14}NOP$
Formula weight	243.23
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	P 1 21/c 1
Unit cell dimensions	a= 9.7934(11) Å a = 90°. b = 10.0938(11) Å b= 108.5370(10)°. c = 12.8098(14) Å g = 90°.
Volume	1200.6(2) $Å^3$
Z	4
Density (calculated)	1.346 Mg/m^3
Absorption coefficient	0.211 mm^{-1}
F(000)	512
Crystal size	0.17 x 0.16 x 0.10 mm^3
Theta range for data collection	2.19 to 28.30°.
Index ranges	-13<=h<=l3, -13<=k<=l3, -16<=1<=17
Reflections collected	14018

Independent reflections	2941 [R(int) = 0.0188]
Completeness to theta = 28 .30°	98.6%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9793 and 0.9651
Refinement method	Full-matrix least-squares on F^2
Data/ restraints/ parameters	2941/ 14/ 196
Goodness-of-fit on F^2	1.065
Final R indices [I>2sigma(I)]	R1 = 0.0362, wR2 = 0.0954
R indices (all data)	R1 = 0.0372, wR2 = 0.0964
Extinction coefficient	na
Largest diff. peak and hole	0.556 and -0.222 e. $Å^{-3}$

Table 1.13 Bond lengths [Å] and angles [°] for **I-decomp**.

P(l)-O(1)	1.4894(9)
P(l)-C(7)	1.7778(11)
P(1)-C(1)	1.7935(12)
P(l)-C(14)	1.8246(12)
N(1)-C(8)	1.3897(15)
N(l)-C(l3)	1.4546(15)
N(1)-C(14)	1.4621(15)
C(1)-C(6)	1.3939(16)
C(l)-C(2)	1.3946(16)
C(2)-C(3)	1.3901(17)
C(2)-H(2)	0.966(13)

C(3)-C(4)	1.3889(19)
C(3)-H(3)	0.960(13)
C(4)-C(5)	1.3834(19)
C(4)-H(4)	0.931(14)
C(5)-C(6)	1.3915(17)
C(5)-H(5)	0.944(13)
C(6)-H(6)	0.937(13)
C(7)-C(12)	1.3910(15)
C(7)-C(8)	1.4069(15)
C(8)-C(9)	1.4036(16)
C(9)-C(10)	1.3873(18)
C(9)-H(9)	0.932(13)

C(10)-C(11)	1.3881(18)
C(10)-H(10)	0.957(13)
C(11)-C(l2)	1.3895(17)
C(11)-H(11)	0.924(13)
C(l2)-H(12)	0.957(13)
C(13)-H(13A)	0.985(14)
C(13)-H(13B)	0.955(14)
C(13)-H(l3C)	0.980(14)
C(l4)-H(l4A)	0.955(13)
C(l4)-H(14B)	0.976(12)
O(1)-P(1)-C(7)	115.94(5)
O(1)-P(1)-C(1)	112.20(5)

C(7)-P(1)-C(l)	109.96(5)
O(1)-P(1)-C(14)	115.89(5)
C(7)-P(1)-C(14)	90.48(5)
C(1)-P(1)-C(14)	110.52(5)
C(8)-N(1)-C(13)	120.06(10)
C(8)-N(1)-C(14)	111.64(9)
C(13)-N(1)-C(14)	115.92(9)
C(6)-C(1)-C(2)	119.78(11)
C(6)-C(1)-P(1)	118.59(9)
C(2)-C(1)-P(1)	121.59(9)
C(3)-C(2)-C(1)	120.12(11)
C(3)-C(2)-H(2)	120.1(10)

C(1)-C(2)-H(2)	119.8(10)
C(4)-C(3)-C(2)	119.71(12)
C(4)-C(3)-H(3)	119.8(10)
C(2)-C(3)-H(3)	120.4(10)
C(5)-C(4)-C(3)	120.49(12)
C(5)-C(4)-H(4)	121.2(11)
C(3)-C(4)-H(4)	118.3(11)
C(4)-C(5)-C(6)	120.03(11)
C(4)-C(5)-H(5)	119.6(10)
C(6)-C(5)-H(5)	120.4(10)
C(5)-C(6)-C(1)	119.88(11)
C(5)-C(6)-H(6)	121.7(10)

C(l)-C(6)-H(6)	118.4(10)
C(12)-C(7)-C(8)	121.12(10)
C(l2)-C(7)-P(l)	130.09(9)
C(8)-C(7)-P(1)	108.38(8)
N(1)-C(8)-C(9)	125.51(11)
N(l)-C(8)-C(7)	114.92(10)
C(9)-C(8)-C(7)	119.52(11)
C(10)-C(9)-C(8)	118.14(11)
C(10)-C(9)-H(9)	120.5(10)
C(8)-C(9)-H(9)	121.3(10)
C(9)-C(10)-C(11)	122.51(11)
C(9)-C(10)-H(10)	119.4(10)

C(11)-C(10)-H(10)	118.0(10)
C(10)-C(11)-C(12)	119.46(11)
C(10)-C(11)-H(11)	118.5(10)
C(12)-C(11)-H(11)	122.0(10)
C(11)-C(12)-C(7)	119.21(11)
C(11)-C(12)-H(12)	122.4(9)
C(7)-C(12)-H(12)	118.4(9)
N(1)-C(13)-H(13A)	111.6(11)
N(1)-C(13)-H(13B)	109.4(11)
H(l3A)-C(13)-H(l3B)	108.0(15)
N(l)-C(l3)-H(13C)	110.6(11)
H(13A)-C(13)-H(13C)	108.4(15)

H(13B)-C(13)-H(l3C)	108.7(15)
N(l)-C(14)-P(l)	103.58(7)
N(l)-C(l4)-H(l4A)	111.5(10)
P(1)-C(14)-H(14A)	111.4(10)
N(1)-C(14)-H(14B)	111.1 (9)
P(1)-C(l4)-H(l4B)	108.1(9)
H(14A)-C(14)-H(14B)	110.9(13)

Exchange Reactions with Product/Substrate (Table 1.3)

In a dry glovebox, *N*-(2-methyl-3-oxopropyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.19**, (18 mg, 5.0 x 10^{-2} mmol) and **I** (2.9 mg, 1.0 x 10^{-2} mmol) were mixed in benzene *d*-6 (0.6 mL) and heat to 45 °C for 2 h. *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (17 mg, 5.0 x 10^{-2} mmol) was added with benzene (0.4 mL). The reaction was monitored by ^{31}P NMR at room temperature for 5 h.

Exchange with Substrate/Product (Table 1.4)

In a dry glovebox, *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (17 mg, 5.0 x 10^{-2} mmol) and **I** (2.9 mg, 1.0 x 10^{-2} mmol) were mixed in benzene *d*-6 (0.6 mL) and heated to 45 °C for 24 h. The reaction was complete. The reaction was concentrated and *N*-(2-methyl-3-oxopropyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.19**, (18 mg, 5.0 x 10^{-2} mmol) was added with benzene (1.0 mL). The reaction was monitored by ^{31}P NMR at room temperature for 4 days.

Optimization of Branch Selective Hydroformylation

General Optimization Procedure. The Endeavor was charged with 500 μL of benzene per reaction well to fill the void volume between reactor wall and reaction tube, and oven-dried glass reaction vials were placed in the Endeavor. The Endeavor was sealed and purged with nitrogen (4x100 psi). The necessary injection(s) were made (see below). The Endeavor was purged with nitrogen (1x100 psi), stirring was started at 250 rpm, and the Endeavor was heated to 45 °C and held for 10 minutes. Stirring was stopped, the Endeavor was charged with H_2/CO, stirring was re-initiated at 700 rpm, and the Endeavor was maintained at a constant temperature of 45 °C and pressure of H_2/CO for 16 h. The Endeavor was vented to ambient pressure and cooled to ambient temperature. The reaction vials were removed from the Endeavor, a solution of 1,3,5-trimethoxybenzene (100 μL, 0.2 M) was added, and the sample was concentrated.

^{1}H NMRs were taken to determine conversion and selectivities. The reaction was chromatographed to determine isolated yield. SFC analysis of the products was used to determine regioselectivities.

Ligand Loading Screen (Table 1.5)

Table 1.5, Entry 1: The General Optimization Procedure was followed. A solution of *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (67 mg, 2.0 x 10^{-1} mmol), triphenylphosphine (4.0 mol %, 2.1 mg, 8.0 x 10^{-3} mmol) and dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) in benzene (1.50 mL) was prepared in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was kept at a constant H_2/CO pressure of 200 psi.

Table 1.5, Entry 2: The General Optimization Procedure was followed. A solution of *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (67 mg, 2.0 x 10^{-1} mmol), ligand **I** (10 mol %, 5.7 mg, 2.0 x 10^{-2} mmol) and dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) in benzene (1.50 mL) was prepared in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was kept at a constant H_2/CO pressure of 200 psi.

Table 1.5, Entry 3: The General Optimization Procedure was followed. *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (67 mg, 2.0 x 10^{-1} mmol 2.0 x 10^{-1} mmol) and ligand **1** (20 mol %, 11 mg, 4.0 x 10^{-2} mmol) in benzene *d*-6 (600 µL) was heated to 55 ˚C for 6 h. The solution was concentrated in a dry box. The resulting white solid, dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) and benzene (1.50 mL) were mixed in a dry box and injected into the Endeavor via syringe. An additional 500 µL of benzene was added to wash the injection port. The Endeavor was kept at a constant H_2/CO pressure of 200 psi.

Table 1.5, Entry 4: The General Optimization Procedure was followed. *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (67 mg, 2.0 x 10^{-1} mmol 2.0 x 10^{-1} mmol) and ligand **1** (40 mol %, 23 mg, 8.0 x 10^{-2} mmol) in benzene *d*-6 (600 µL) was heated to 55 ˚C for 6 h. The solution was concentrated in a dry box. The resulting white solid, dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) and benzene (1.50 mL) were mixed in a dry box and injected into the Endeavor via syringe. An additional 500 µL of benzene was added to wash the injection port. The Endeavor was kept at a constant H_2/CO pressure of 200 psi.

Ligand Loading Screen with Pre-exchange (Table 1.6)

General Pre-exchange Procedure. *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide, **1.15**, (67 mg, 2.0 x 10^{-1} mmol) and **I** (10 mol %, 5.7 mg, 2.0 x 10^{-2} mmol) were dissolved in benzene *d*-6 in a dry box and heated to

55 °C for 6 h. After the solution was concentrated, dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) in benzene (1.50 mL) was added to the residue in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was kept at 45 °C and a constant H_2/CO pressure of 200 psi.

Table 1.6, Entry 1: The General Optimization Procedure and the General Pre-exchange Procedure were followed using 5 mol % **I**. (2.9 mg, 1.0 x 10^{-2} mmol).

Table 1.6, Entry 2: The General Optimization Procedure and the General Pre-exchange Procedure were followed.

Temperature Screen (Table 1.7)

Table 1.7, Entry 1: The General Optimization Procedure and the General Pre-exchange Procedure were followed. The Endeavor was kept at 35 °C during the reaction.

Table 1.7, Entry 2: The General Optimization Procedure and the General Pre-exchange Procedure were followed. The Endeavor was kept at 45 °C during the reaction.

Table 1.7, Entry 3: The General Optimization Procedure and the General Pre-exchange Procedure were followed using 20 mol % **I** (23 mg, 8.0 x 10^{-2} mmol) The Endeavor was kept at 45 °C during the reaction.

Table 1.7, Entry 4: The General Optimization Procedure and the General Pre-exchange Procedure were followed using 20 mol % **I** (23 mg, 8.0 x 10^{-2} mmol). The Endeavor was kept at 55 °C during the reaction.

Acid Loading Screen (Table 1.8)

Table 1.8, Entry 1: The General Optimization Procedure and the General Pre-exchange Procedure were followed.

Table 1.8, Entry 2: The General Optimization Procedure and the General Pre-exchange Procedure were followed adding 0.2% *p*-TsOH (650 μL, 6.21 x 10^{-4} M) to the pre-exchange.

Rhodium Loading Screen (Table 1.9)

Table 1.9, Entry 1: The General Optimization Procedure and the General Pre-exchange Procedure were followed using dicarbonylacetylacetonato rhodium (I) (0.5 mol %, 0.26 mg, 1.0 x 10^{-3} mmol).

Table 1.9, Entry 2: The General Optimization Procedure and the General Pre-exchange Procedure were followed using dicarbonylacetylacetonato rhodium (I) (1.0 mol %, 0.52 mg, 2.0 x 10^{-3} mmol).

Table 1.9, Entry 3: The General Optimization Procedure and the General Pre-exchange Procedure were followed using dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol).

Table 1.9, Entry 4: The General Optimization Procedure and the General Pre-exchange Procedure were followed using dicarbonylacetylacetonato rhodium (I) (3 mol %, 1.5 mg, 6.0 x 10^{-3} mmol).

Table 1.9, Entry 5: The General Optimization Procedure and the General Pre-exchange Procedure were followed using dicarbonylacetylacetonato rhodium (I) (4 mol %, 2.1 mg, 8.0 x 10^{-3} mmol).

Pressure Screen (Table 1.10)

Table 1.10, Entry 1: The General Optimization Procedure was followed. A solution of *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (67 mg, 2.0 x 10^{-1} mmol), triphenylphosphine (4.0 mol %, 2.1 mg, 8.0 x 10^{-3} mmol) and dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) in benzene (1.50 mL) was prepared in a dry box and injected into the Endeavor via

syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was kept at a constant H_2/CO pressure of 200 psi.

Table 1.10, Entry 2: The General Optimization Procedure was followed. A solution of *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (67 mg, 2.0 x 10^{-1} mmol), **I** (10 mol %, 5.7 mg, 2.0 x 10^{-2} mmol) and dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) in benzene (1.50 mL) was prepared in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was kept at a constant H_2/CO pressure of 200 psi.

Table 1.10, Entry 3: The General Optimization Procedure and the General Pre-exchange Procedure were followed. *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (67 mg, 2.0 x 10^{-1} mmol) and ligand **1** (10 mol %, 5.7 mg, 2.0 x 10^{-2} mmol) in benzene *d*-6 (600 μL) was heated to 55 ˚C for 6 h. The solution was concentrated in a dry box. The residue, dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4.0 x 10^{-3} mmol) and benzene (1.50 mL) were mixed in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was kept at a constant H_2/CO pressure of 200 psi.

Table 1.10, Entry 4: The procedure for Table 10, Entry 3 was followed except the Endeavor was kept at a constant H_2/CO pressure of 100 psi.

Table 1.10, Entry 5: The procedure for Table 10, Entry 3 was followed except the Endeavor was kept at a constant H_2/CO pressure of 300 psi.

Table 1.10, Entry 6: The procedure for Table 10, Entry 3 was followed except the Endeavor was kept at a constant H_2/CO pressure of 400 psi.

Hydroformylation Substrate Scope (Table 1.11)

General Hydroformylation Procedure. The Endeavor was charged with 500 μL of benzene per reaction well to fill the void volume between reactor wall and reaction tube, and oven dried glass reaction vials were placed in the Endeavor. The Endeavor was sealed and purged with nitrogen (4x100 psi). The necessary injection(s) were made (see below). The Endeavor was purged with nitrogen (1x100 psi), stirring was started at 250 rpm, and the Endeavor was heated to and held at reaction temperature for 10 minutes. Stirring was stopped, the Endeavor was charged with 400 psi H_2/CO, stirring was reinitiated at 700 rpm, and the Endeavor was maintained at constant reaction temperature of 45 °C and pressure of 400 psi H_2/CO for 16 h. The Endeavor was vented to ambient pressure and cooled to ambient temperature. The reaction vials were removed from the Endeavor and a solution of trimethoxybenzene (100 μL, 0.2 M) was added and the sample was concentrated. ^{1}H NMRs were taken to determine conversion and selectivities. The reaction was chromatographed to determine isolated yield. SFC analysis of the products was used to determine regioselectivities.

Procedure A. A solution of *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (67 mg, 2.0×10^{-1} mmol), triphenylphosphine (4.0 mol %, 2.1 mg, 8.0×10^{-3} mmol), dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.1 mg, 4×10^{-3} mmol), and benzene (1.50 mL) was prepared in a dry box and injected into the Endeavor via syringe. An additional 500 µL of benzene was added to wash the injection port. The Endeavor was heated to 45 °C.

Procedure B. This procedure is identical to Procedure A except the Endeavor was heated to 40 °C.

Procedure C. *N*-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide (67 mg, 2.0×10^{-1} mmol) and ligand **I** (10 mol %, 5.7 mg, 2.0×10^{-2} mmol) in benzene *d*-6 (600 µL) was heated to 45 °C for 6 h. The solution was concentrated in a dry box. The resulting white solid, dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.0 mg, 4×10^{-3} mmol), and benzene (1.50 mL) were mixed in a dry box and injected into the Endeavor via syringe. An additional 500 µL of benzene was added to wash the injection port. The Endeavor was heated to 45 °C.

Procedure D. This procedure is identical to Procedure C except the Endeavor was heated to 40 °C.

Procedure E. A solution of (*E*)-3,5-bis(trifluoromethyl)-*N*-(3-(4-(trifluoromethyl)phenyl)allyl)benzenesulfonamide (95 mg, 2.0×10^{-1} mmol),

triphenylphosphine (4.0 mol %, 2.1 mg, 8.0 x 10^{-3} mmol) and dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.0 mg, 4.0 x 10^{-3} mmol) in tetrahydrofuran (100 μL) and benzene (1.4 mL) was prepared in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was heated to 45 °C.

Procedure F. A solution of (*E*)-*N*-(3-(4-methoxyphenyl)allyl)-3,5-bis(trifluoromethyl)benzenesulfonamide (88 mg, 2.0 x 10^{-1} mmol), triphenylphosphine (6.0 mol %, 3.1 mg, 1.2 x 10^{-2} mmol) and dicarbonylacetylacetonato rhodium (I) (3.0 mol %, 1.3 mg, 6.0 x 10^{-3} mmol) in tetrahydrofuran (200 μL) and benzene (1.3 mL) was prepared in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was heated to 55 °C.

Procedure G. A solution of *N*-((2*E*,5*E*)-hepta-2,5-dienyl)-3,5-bis(trifluoromethyl)benzenesulfonamide (77 mg, 2.0 x 10^{-1} mmol) and ligand **I** (10 mol %, 5.7 mg, 2.0 x 10^{-2} mmol) in benzene *d*-6 (600 μL) was heated to 45 °C for 2 h. The solution was concentrated in a dry box. The resulting white solid, dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.0 mg, 4.0 x 10^{-3} mmol), and benzene (1.50 mL) were mixed in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was heated to 45 °C for 5 h.

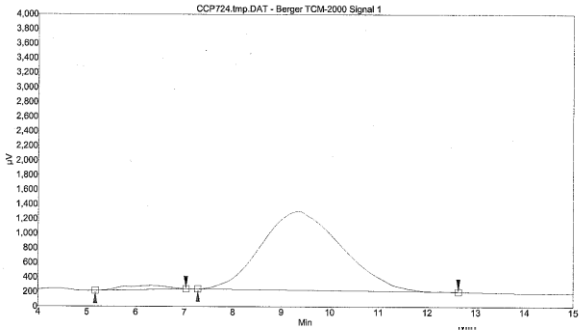
Procedure H. A solution of (*E*)-3,5-bis(trifluoromethyl)-*N*-(3-(4-(trifluoromethyl)phenyl)allyl)benzenesulfonamide (38 mg, 8.0 x 10^{-2} mmol) and ligand **I** (10 mol %, 5.7 mg, 2.0 x 10^{-2} mmol) in benzene *d*-6 (500 μL) and tetrahydrofuran (100 μL) was heated to 55 °C for 16 h. The solution was concentrated in a dry box. The resulting white solid and dicarbonylacetylacetonato rhodium (I) (2.0 mol %, 1.0 mg, 4.0 x 10^{-3} mmol) were dissolved in benzene (1.40 mL) and tetrahydrofuran (100 μL) were mixed in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was heated to 45 °C.

Procedure I. A solution of (*E*)-*N*-(3-(4-methoxyphenyl)allyl)-3,5-bis(trifluoromethyl)benzenesulfonamide (35 mg, 8.0 x 10^{-2} mmol) and ligand **I** (10 mol %, 5.7 mg, 2.0 x 10^{-2} mmol) in benzene *d*-6 (400 μL) and tetrahydrofuran (200 μL) was heated to 55 °C for 16 h. The solution was concentrated in a dry box. The resulting white solid was combined with (*E*)-*N*-(3-(4-methoxyphenyl)allyl)-3,5-bis(trifluoromethyl)benzenesulfonamide (53 mg, 1.2 x 10^{-1} mmol) and dicarbonylacetylacetonato rhodium (I) (3.0 mol %, 1.3 mg, 6.0 x 10^{-3} mmol) were dissolved in benzene (1.30 mL) and tetrahydrofuran (200 μL) were mixed in a dry box and injected into the Endeavor via syringe. An additional 500 μL of benzene was added to wash the injection port. The Endeavor was heated to 55 °C.

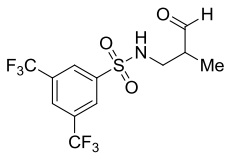
Hydroformylation Results and Product Characterization

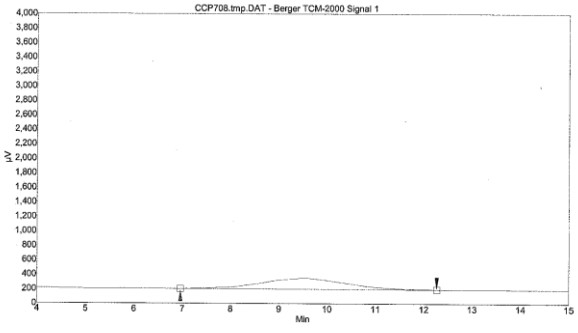
Table 1.11, Entry 1:

N-allyl-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using General Procedure C. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and approximate selectivity. A mixture of normal and iso products was isolated as a white solid (58.2 mg, 80%) and analyzed by SFC (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (97:3).

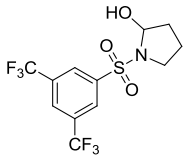


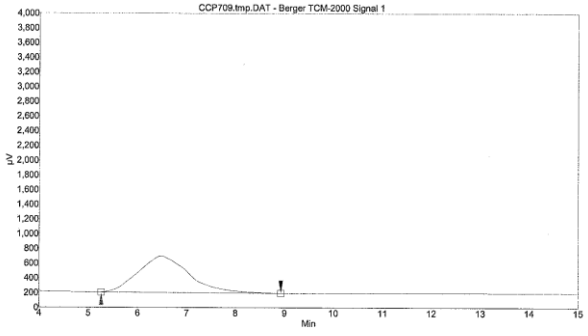
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.17	6.31	7.04	0.00	2.75	55.0	58.5	2.751
2	UNKNOWN	7.28	9.34	12.64	0.00	97.25	1075.6	2067.3	97.249
Total						100.00	1130.5	2125.8	100.000





***N*-(2-methyl-3-oxopropyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.19. SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 9.54 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.63 (s, 1H), 8.30 (s, 2H), 8.09 (s, 1H), 5.22 (t, 1H, *J* = 6.1), 3.10-3.24 (m, 2H), 2.73-2.78 (m, 1H), 1.24 (d, 3H, *J* = 7.5); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 203.5, 143.1, 133.2 (q, *J* = 34.3), 127.4, 126.4, 122.6 (q, *J* = 271.9), 46.7, 43.4, 11.5; **IR:** 3279, 2930, 1721, 1361, 1280, 1163, 1139, 1115, 906, 845, 699, 682, 591 cm^{-1}; **HRMS** (DART-TOF) calcd. For $C_{12}H_{12}F_6NO_3S$ $[M+H]^+$: 364.0442, found: 364.0454.

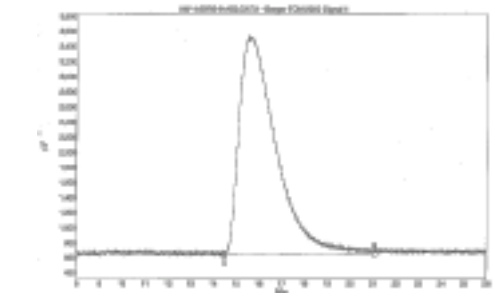




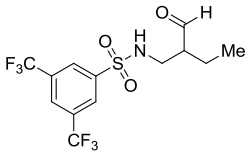
1-(3,5-bis(trifluoromethyl)benzenesulfonyl)pyrrolidin-2-ol. See above for characterization data.

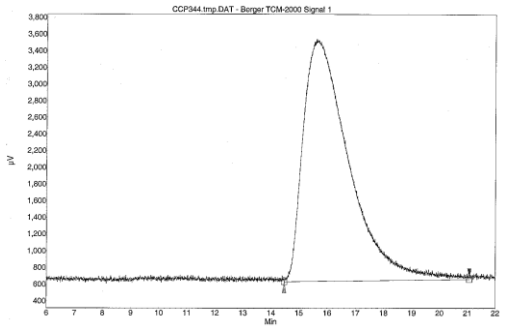
Table 1.11, Entry 2:

(*E*)-*N*-(but-2-enyl)-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using General Procedure C. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid (63.8 mg, 85%) and analyzed by **SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (99:1)

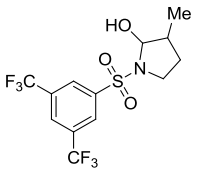


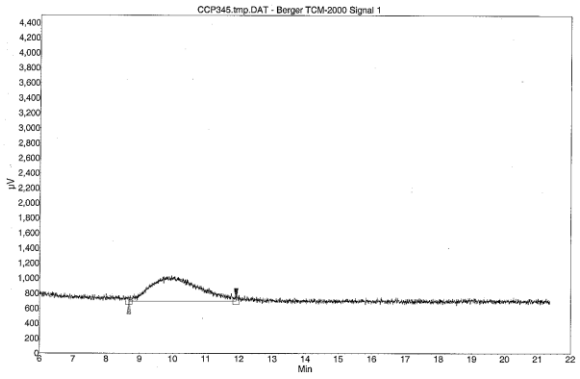
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	14.47	15.65	21.07	0.00	100.00	2878.8	5456.5	100.000
Total						100.00	2878.8	5456.5	100.000





***N*-(2-formylbutyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.22. SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 15.65; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.66 (s, 1H), 8.30 (s, 2H), 8.30 (s, 2H), 8.09 (s, 1H), 5.20 (t, 1H, *J* = 6.6), 3.16-3.24 (m, 2H), 2.55-2.61 (m, 1H), 1.79-1.86 (m, 1H), 1.55-1.62 (m, 1H), 1.05 (t, 3H, *J* = 7.5); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 178.2, 143.2, 133.2 (q, *J* = 34.5), 127.4, 126.4, 122.6 (q, *J* = 272.8), 46.5, 43.4, 22.8, 11.4; **IR:** 3298, 2971, 2931, 1721, 1625, 1460, 1427, 1360, 1279, 1167, 1137, 1114, 906, 844, 699, 682, 591 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{14}F_6NO_3S$ $[M+H]^+$: 378.0599, found: 378.0582.

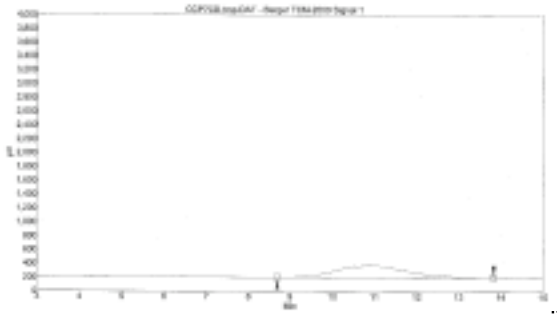




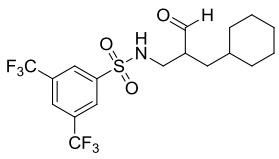
1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-3-methylpyrrolidin-2-ol. SFC (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 9.74 min; **^{1}H NMR** ($CDCl_3$, 400 MHz, 1:1 diastereomer ratio) δ 8.34 (s, 3H), 8.08 (app d, 2H, *J* = 3.8), 5.35 (t, 1H, *J* = 4.2), 5.13 (t, 1H, *J* = 3.5), 3.44-3.52 (m, 2H), 3.29-3.35 (m, 1H), 3.16-3.23 (m, 1H), 3.00 (d, 1H, *J* = 3.1), 2.68 (d, 1H, 4.0), 2.23-2.25 (m, 2H), 1.97-2.07 (m, 3H), 1.81-1.85 (m, 1H), 1.08 (d, 3H, *J* = 6.8), 0.85 (d, 3H, *J* = 7.2); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 142.4, 142.3, 133.1 (q, *J* = 34.5), 127.6, 126.3, 122.6 (q, *J* = 275.1), 90.5, 85.3, 46.9, 46.2, 41.1, 39.5, 30.3, 30.1, 16.1, 13.0; **IR:** 3483, 3092, 2969, 2911, 1626, 1363, 1345, 1286, 1183, 1150, 1130, 1107, 904, 696, 682, 650, 599 cm^{-1}; **HRMS** (ESI) calcd. for $C_{13}H_{13}F_6NO_3SNa$ $[M+Na]^+$: 400.0418 found: 400.0416.

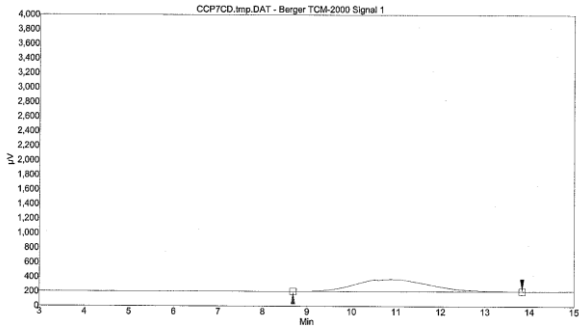
Table 1.11, Entry 3:

(*E*)-*N*-(3-cyclohexylallyl)-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using General Procedure C. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid (74.8 mg, 84%) and analyzed by SFC (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (99:1).



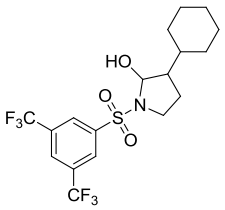
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.85	10.74	14.25	0.00	100.00	172.2	350.5	100.000
Total						100.00	172.2	350.5	100.000

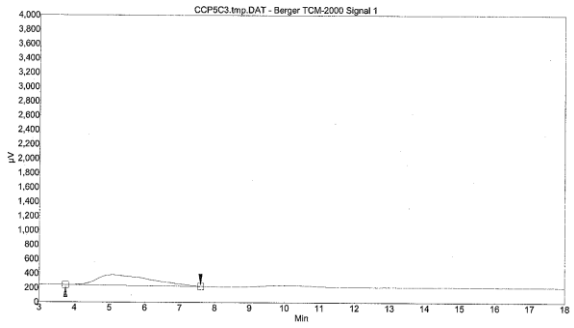




***N*-(3-cyclohexyl-2-formylpropyl)-3,5-bis(trifluoromethyl)benzenesulfonamide,**

1.23. **SFC** (AS-H, 2.0 mL/min, 0.5 % MeOH, 220 nm, 150 bar, 50 °C) t_r = 10.89 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.60 (s, 1H), 8.30 (s, 2H), 8.09 (s, 1H), 5.22 (t, 1H, J = 6.3), 3.08-3.22 (m, 2H), 2.71-2.72 (m, 1H), 1.67-1.74 (m, 4H), 1.52-1.57 (m, 2H), 1.14-1.34 (m, 5H), 0.87-0.96 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 204.0, 143.2, 133.2 (q, J = 34.5), 127.4, 126.4, 122.6 (q, J = 273.6), 49.3, 42.0, 35.1, 33.8, 32.9, 26.5, 26.2; **IR:** 3299, 2926,1723, 1360, 1279, 1163, 1140, 1114, 906, 845, 700, 682, 592 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{22}F_6NO_3S$ $[M+H]^+$: 446.1225, found: 446.1224.

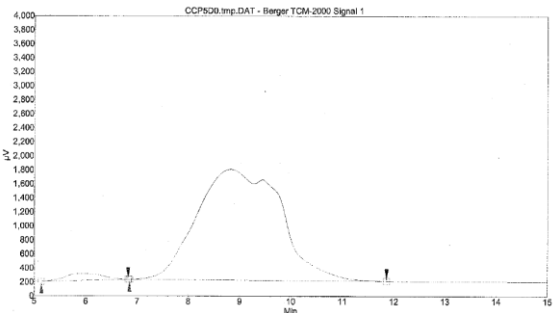




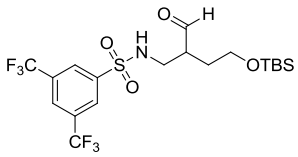
1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-3-cyclohexylpyrrolidin-2-ol. SFC (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 °C) t_r = 5.10; **^{1}H NMR** ($CDCl_3$, 300 MHz, 1:1 diastereomer ratio) δ 8.34 (s, 2H), 8.07 (s, 1H), 5.47-5.49 (m, 1H), 5.33-5.35 (m, 1H), 4.20-4.23 (m, 1H), 3.65-3.66 (m, 1H), 3.47-3.53 (m, 1H), 3.37 (dd, 1H, *J* = 8.3, 8.0), 3.11-3.20 (m, 1H), 3.03-3.07 (m, 1H), 2.57-2.61 (m, 1H), 2.00-2.07 (m, 1H), 1.81-1.88 (m, 2H), 1.60-1.69 (m, 6H), 1.54-1.56 (m, 3H), 1.41-1.47 (m, 3H), 1.09-1.11 (m, 4H), 0.83-0.94 (m, 6H); **IR**: 3511, 2925, 2855, 1724, 1451, 1360, 1280, 1169, 1143, 1061, 1034, 682, 594 cm^{-1}; **LRMS** (DART-TOF) calcd. for $C_{18}H_{22}F_6NO_3S$ $[M+H]^+$: 446.1225; found: 446.1293.

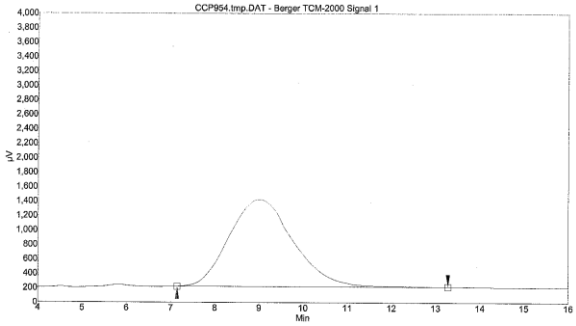
Table 1.11, Entry, 4:

(*Z*)-*N*-(4-(*tert*-butyldimethylsilyloxy)but-2-enyl)-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using General Procedure D. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid (84.2 mg, 83%) and analyzed by SFC (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (97:3).

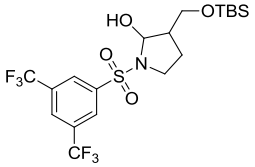


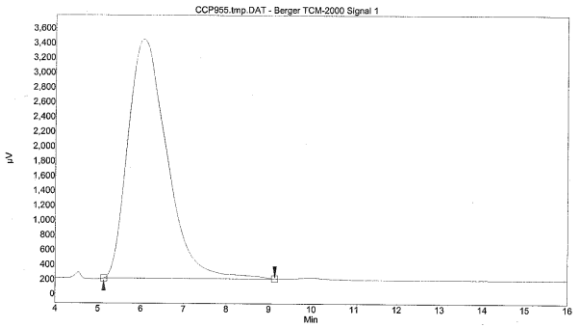
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	5.14	5.86	6.83	0.00	2.64	99.0	81.6	2.636
1	UNKNOWN	6.85	8.83	11.86	0.00	97.36	1582.9	3014.9	97.364
Total						100.00	1681.9	3096.5	100.000





***N*-(4-(*tert*-butyldimethylsilyloxy)-2-formylbutyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.24. SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 9.00 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.65 (s, 1H), 8.30 (s, 2H), 8.07 (s, 1H), 5.70 (s, 1H), 3.73 (t, 2H, J = 5.6), 3.21-3.28 (m, 2H), 2.75-2.78 (m, 1H), 1.96-2.01 (m, 1H), 1.82-1.88 (m, 1H), 0.85 (s, 9H), 0.03 (d, 6H, J = 2.8); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 202.9, 142.9, 132.9 (q, J = 34.5), 127.1, 126.0, 122.3 (q, J = 273.6), 59.9, 49.3, 41.4, 29.5, 25.6, 18.0, –5.7; **IR:** 3286, 3089, 2955, 2932, 2860, 1712, 1359, 1278, 1137, 1108, 905, 835, 809, 777, 699, 681, 589, 413 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{19}H_{28}F_6NO_4SSi$ $[M+H]^+$: 507.1413, found: 508.1429.



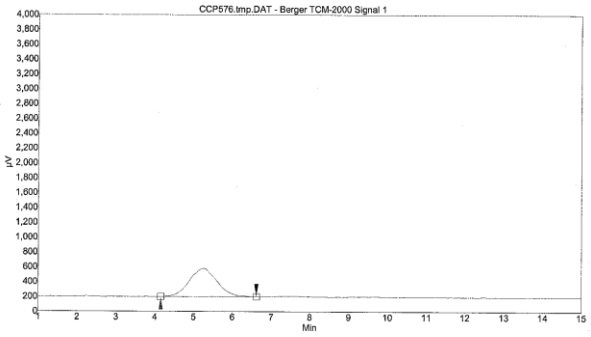


1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-3-((*tert*-butyldimethylsilyloxy)methyl)pyrrolidin-2-ol. **SFC** (AS-H, 1.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 6.06 min; **^{1}H NMR** ($CDCl_3$, 300 MHz, 1.1:1 diastereomer ratio) δ 8.45 (s, 2H), 8.34 (s, 2H), 8.06 (app. d, 2H, *J* = 8.6), 5.65 (t, 1H, *J* = 4.8), 5.40 (t, 1H, *J* = 3.3), 3.97 (d, 1H, *J* = 4.6), 3.89-3.94 (m, 1H), 3.73-3.78 (m, 1H), 3.34-3.48 (m, 6H), 3.10 (d, 1H, *J* = 3.4), 2.24-2.36 (m, 2H), 1.95-2.17 (m, 3H), 1.71-1.80 (m, 1H), 0.83 (app. d, 18H, *J* = 11.3), 0.06 (d, 3H, *J* = 3.6), -0.03 (d, 3H, *J* = 4.1); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 142.6, 142.4, 133.1 (q, *J* = 34.5), 132.7 (q, *J* = 34.5), 128.3, 127.6, 126.4, 126.1, 122.7 (q, *J* = 272.8), 122.6 (q, *J* = 273.6), 86.3, 85.1, 61.8, 61.6, 49.6, 46.7, 46.3, 45.4, 25.9, 25.8, 25.3, 25.0, 18.4, 18.8, –5.4; **IR:** 3514, 2956, 2932, 2859, 1360, 1280, 1169, 1142, 1110, 840, 779, 682, 641, 598 cm^{-1}; **HRMS** (ESI) calcd. for $C_{19}H_{27}F_6NO_4NaSSi$ $[M+Na]^+$: 530.1234, found: 530.1232.

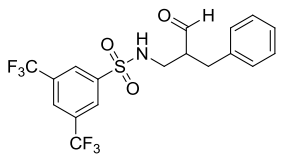
Table 1.11, Entry 5:

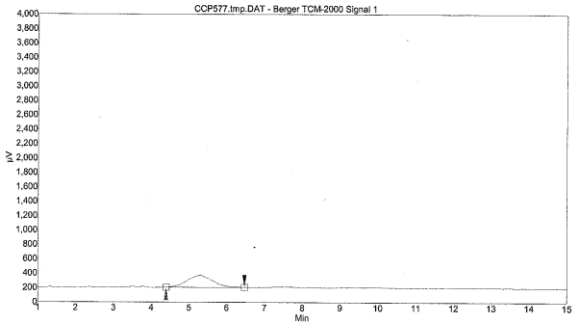
N-cinnamyl-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using General Procedure C. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a

white solid (76.0 mg, 86%) and analyzed by SFC (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (99:1).



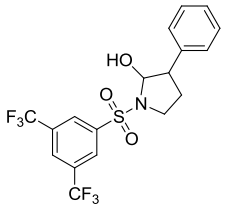
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.15	5.26	6.62	0.00	100.00	381.9	314.5	100.000
Total						100.00	381.9	314.5	100.000

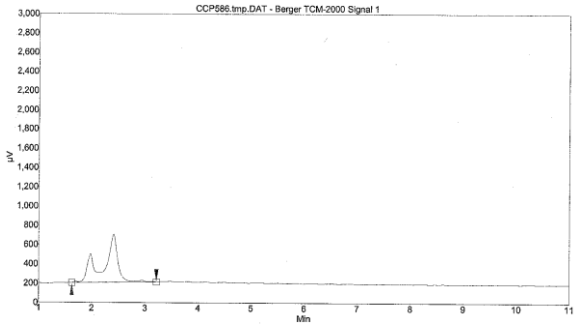




***N*-(2-benzyl-3-oxopropyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.25. SFC** (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50°C) t_r= 5.30 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.72 (s, 1H), 8.23 (s, 2H), 8.06 (s, 1H), 7.26-7.36 (m, 3H), 7.18 (d, 2H, *J* = 7.1), 5.20 (t, 1H, *J* = 6.6), 3.02-3.16 (m, 3H), 2.97-3.02 (m, 1H), 2.79 (dd, 1H, *J* = 14.0, 8.7); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 203.2, 142.8, 136.7, 133.2 (q, *J* = 273.6), 129.1, 128.9, 127.4, 126.5, 122.5 (q, *J* = 34.5), 53.3, 46.3, 41.5, 32.9; **IR:** 3292, 3089,

2889, 1720, 1360, 1280, 1162, 1140, 1114, 906, 844, 699, 682, 591 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{16}F_6NO_3S$ $[M+H]^+$: 440.0755, found: 440.0742.



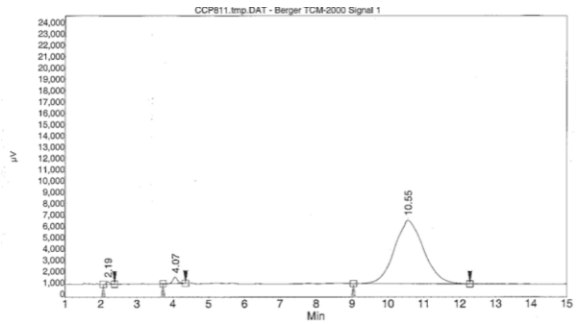


1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-3-phenylpyrrolidin-2-ol. SFC (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50°C) t_r= 2.41 min; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 8.27 (s, 2H), 8.04 (s, 1H), 7.20-7.22 (m, 3H), 7.03-7.06 (m, 2H), 5.51 (t, 1H, *J* = 3.6), 3.54-3.67 (m, 2H), 3.34-3.40 (m, 1H), 3.21 (d, 1H, *J* = 3.2), 2.26-2.52 (m, 1H), 2.06-2.18 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 142.1, 138.8, 133.1 (q, *J* = 33.5), 129.0, 128.7, 127.5, 127.4, 126.8, 126.4, 122.5 (q, *J* = 272.8), 90.5, 84.7, 51.8, 50.3, 47.0, 29.7, 27.0; **IR**: 3488, 3089, 2960, 1625, 1359, 1279, 1162, 1136, 1112, 1017, 699, 682, 644, 596 cm^{-1}; **HRMS** (ESI) calcd. for $C_{18}H_{15}F_6NO_3S$ $[M+Na]^+$: 462.0575, found: 462.0571.

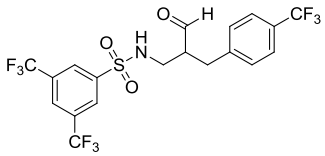
Table 1.11, Entry 6:

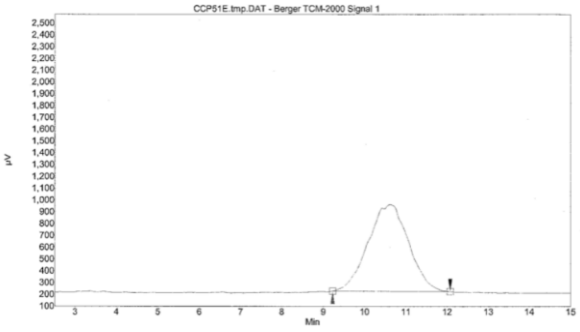
(*E*)-3,5-bis(trifluoromethyl)-*N*-(3-(4-(trifluoromethyl)phenyl)allyl)benzenesulfonamide was hydroformylated using General Procedure H. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid

(92.8 mg, 92%) and analyzed by SFC (Silica, 5.0 mL/min 1.0% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (98:2).



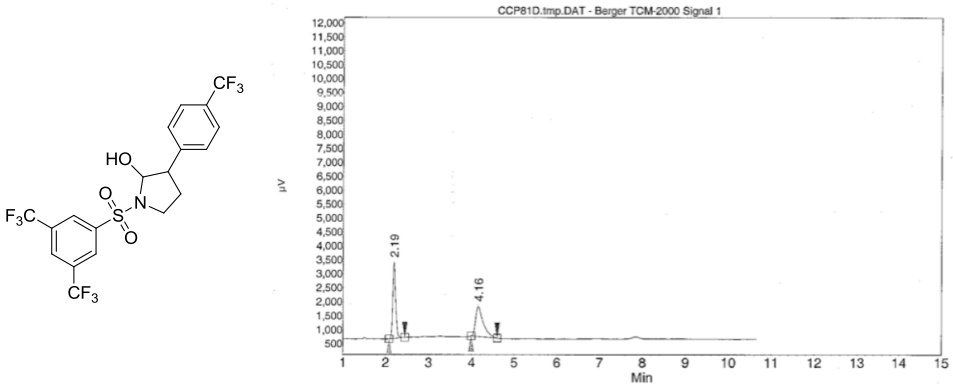
Index	Name	Time	Width	Height	Area	Area
		[min]	[min]	[mAU]	[%]	[mAU*min]
2	FRACTION_	2.19	0.10	231.014	0.466	25.11
1	FRACTION_	4.07	0.14	556.905	1.592	85.82
3	FRACTION_	10.55	0.87	5604.702	97.943	5280.99
Total					100.000	5391.92





***N*-(2-formyl-3-(4-(trifluoromethyl)phenyl)propyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.26. SFC** (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 11.01 min; **^{1}H NMR** (Acetone *d*-6, 400 MHz) δ 9.41 (s, 1H), 8.40 (s, 2H), 8.38 (s, 1H), 7.62 (d, 2H, *J* = 8.0), 7.48 (d, 2H, *J* = 8.4), 7.13 (s, 1H), 3.26-3.37 (m, 2H), 3.21 (dd, 1H, *J* = 6.8, 14.0), 3.03-3.09 (m, 1H), 2.93 (dd, 1H, 7.6, 14.0); **^{13}C NMR** (Acetone *d*-6, 100 MHz) δ 203.1, 144.9, 133.8 (q, *J* = 33.7), 131.3, 129.7 (q, *J* =

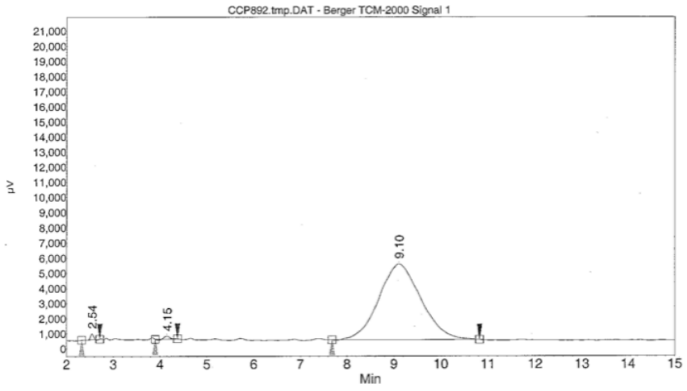
32.1), 129.1, 127.9, 126.8, 126.7, 126.0 (q, J = 270.5), 124.4 (q, J = 272.0), 54.3, 42.8, 33.2; **IR:** 3291, 3090, 2927, 2855, 1724, 1620, 1420, 1360, 1327, 1280, 1162, 1068, 1019, 906, 845, 805, 699, 682, 630 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{19}H_{15}F_9NO_3S$ $[M+H]^+$: 508.0629, found: 508.0628.



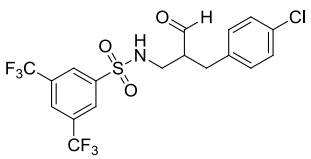
1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-3-(4-(trifluoromethyl)phenyl)pyrrolidin-2-ol. SFC (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 2.2 and 4.2 min (diastereomers); **^{1}H NMR** (Acetone *d*-6, 400 MHz, 46:54 diastereomer ratio) δ 8.55 (s, 1.0H), 8.49 (s, 2.0H), 8.37 (s, 0.6H), 8.34 (s, 1.0H), 7.64 (d, 3.6H, J = 8.1), 7.57 (d, 1.4H, J = 8.1), 7.51 (d, 2.5H, J = 8.1), 5.79-5.84 (m, 1.5H), 5.61 (dd, 1.3H, J = 3.1, 5.9), 5.42 (d, 0.4H, J = 6.2), 3.72-3.80 (m, 1.4H), 3.50-3.63 (m, 2.7H), 3.43-3.49 (m, 1.3H); **^{13}C NMR** (Acetone *d*-6, 100 MHz) δ 145.1, 143.5, 143.4, 142.5, 132.2 (q, J = 34.5), 129.9, 128.7 (q, J = 20.1), 128.4, 128.1, 128.0, 126.3, 125.5, 124.8, 123.1 (q, J = 269.0), 89.9, 84.8, 54.2, 52.9, 49.8, 46.7, 46.1, 27.1; **IR:** 3505, 3089, 2927, 1621, 1360, 1327, 1279, 1163, 1126, 1069, 1046, 907, 844, 700, 682,649, 631 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{19}H_{15}F_9NO_3S$ $[M+H]^+$: 508.0629, found: 508.0647.

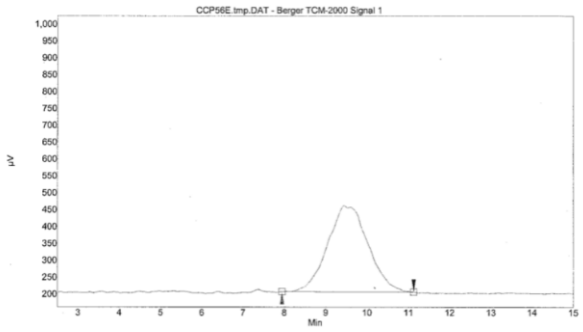
Table 1.11, Entry 7:

(*E*)-*N*-(3-(4-chlorophenyl)allyl)-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using General Procedure H. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid (64.9 mg, 69%) and analyzed by SFC (Silica, 5.0 mL/min 1.0% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (99:1).

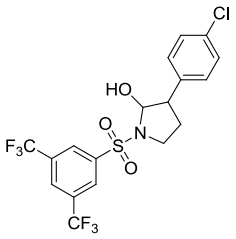


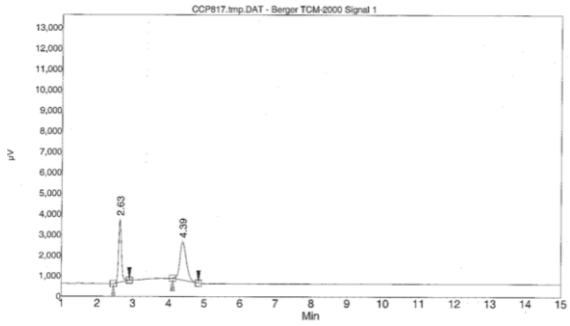
Index	Name	Time [min]	Width [min]	Height [mAU]	Area [%]	Area [mAU*min]
1	FRACTION_	0.05	0.02	4.041	0.002	0.08
2	FRACTION_	0.16	0.02	4.304	0.001	0.06
3	FRACTION_	2.54	0.07	402.117	0.507	26.68
4	FRACTION_	4.15	0.14	190.118	0.409	21.56
5	FRACTION_	9.10	0.96	5023.642	99.081	5219.00
Total					100.000	5267.38





***N*-(2-(4-chlorobenzyl)-3-oxopropyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.27. SFC** (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 9.80 min; **^{1}H NMR** (Acetone *d*-6, 400 MHz) δ 9.72 (s, 1H), 8.41 (s, 2H), 8.38 (s, 1H), 7.23-7.30 (m, 4H), 7.09 (s, 1H), 3.24-3.34 (m, 2H), 3.07-3.12 (m, 1H), 2.95-3.02 (m, 1H), 2.81-2.86 (m, 1H); **^{13}C NMR** (Acetone *d*-6, 100 MHz) δ 203.2, 144.9, 138.7, 133.7 (q, J = 34.5), 133.2, 133.1, 129.2, 130.0, 127.7, 124.3 (q, J = 272.8), 54.4, 42.6, 32.8; **IR:** 3293, 3089, 2929, 1723, 1626, 1493, 1411, 1360, 1318, 1279, 1138, 1112, 906, 844, 722, 699, 630 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{15}ClF_6NO_3S$ $[M+H]^+$: 474.0365, found: 474.0381.



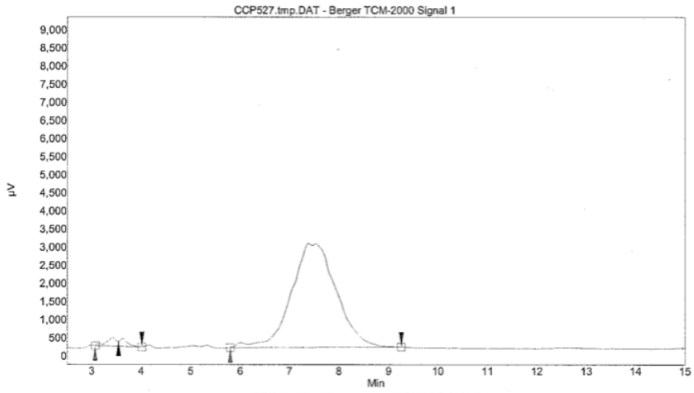


1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-3-(4-chlorophenyl)pyrrolidin-2-ol SFC (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 2.6 and 4.4 min (diastereomers); **^{1}H NMR** ($CDCl_3$, 300 MHz, 10:1 diastereomer ratio) δ 8.41 (s, 0.2H), 8.28 (s, 1.65H), 8.07 (s, 1.0H), 7.32 (d, 0.25H, J = 8.4), 7.19 (d, 2.0H, J = 8.6), 7.01 (d, 1.9H, J = 8.6), 5.64 (dd, 0.1H, J = 3.3, 4.5), 5.47 (dd, 1.0H, J = 2.7, 3.3), 3.57 (dd, 2.0H, J = 2.4, 6.9), 3.46 (d, 1.1H, J = 3.3), 3.33 (dt, 1.2H, J = 3.6, 6.9), 2.57 (app. d, 0.1H, J = 3.0), 2.41-2.52 (m, 1.0H), 2.21-2.30 (m, 0.2H), 2.03-2.14 (m, 1.0H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 142.4, 142.2, 137.3, 134.5, 133.8, 133.5, 133.1 (q, J = 33.7), 132.9 (q, J =

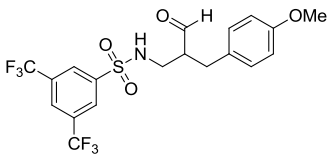
34.5), 130.2, 129.1, 129.0. 128.3, 128.0, 127.5, 126.5, 122.7 (q, J = 273.5), 122.6 (q, J = 272.8), 90.3, 84.5, 51.3, 49.8, 46.9, 46.4, 29.6, 27.5; **IR:** 3493, 3089, 2960, 1625, 1495, 1360, 1279, 1163, 1138, 1015, 907, 844, 721, 699, 660, 626, 595 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{14}ClF_6NO_3SNa$ $[M+Na]^+$: 496.019, found: 496.019.

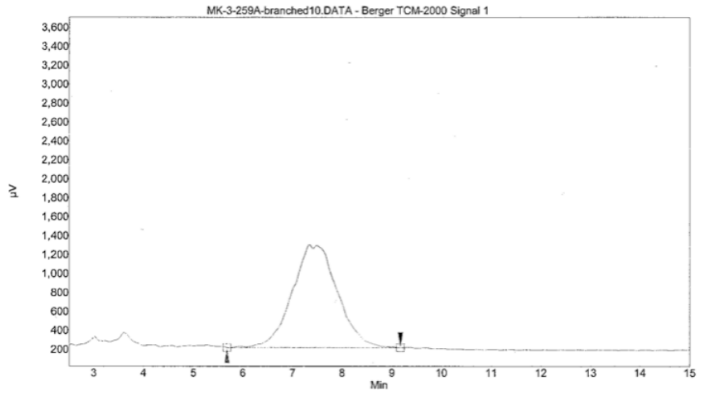
Table 1.11, Entry 8:

(*E*)-*N*-(3-(4-methoxyphenyl)allyl)-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using the corresponding General Procedure I. Analysis of the crude reaction mixture by ^1H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid (81.4 mg, 87%) and analyzed by SFC (Silica, 5.0 mL/min 1.0% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (97:3)

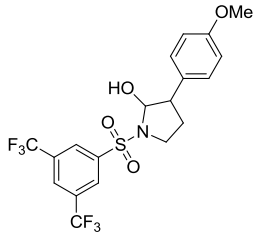


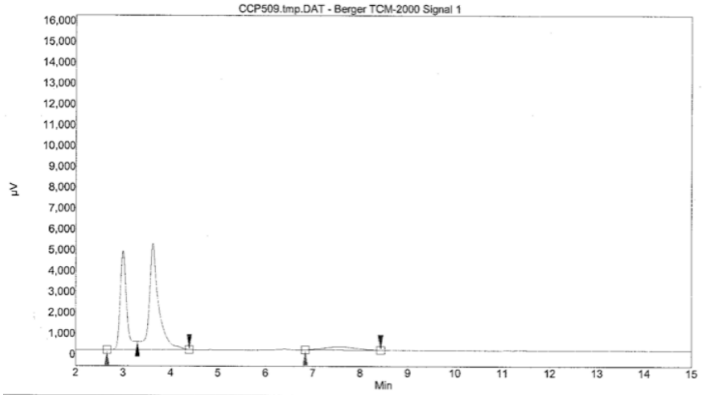
Index	Name	Time [Min]	Area [µV.Min]	Area [%]
1	UNKNOWN	3.42	55.7	1.783
3	UNKNOWN	3.63	38.9	1.246
2	UNKNOWN	7.38	3027.3	96.971
Total			3121.8	100.000





***N*-(2-formyl-3-(4-methoxyphenyl)propyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.28. SFC** (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 8.8 min; **^{1}H NMR** (Acetone *d*-6, 400 MHz) δ 9.69 (s, 1H), 8.25 (s, 2H), 8.07 (s, 1H), 7.08 (d, 2H, *J* = 8.4), 6.85 (d, 2H, *J* = 8.4), 5.43 (t, 1H, *J* = 6.4), 3.79 (s, 3H), 3.08-3.14 (m, 2H), 3.03 (dd, 1H, *J* = 6.4, 14.4), 2.90-2.97 (m, 1H), 2.74 (dd, 1H, *J* = 8.4, 14.4); **^{13}C NMR** (Acetone *d*-6, 100 MHz) δ 203.5, 158.9, 142.9, 133.2 (q, *J* = 34.5), 129.9, 128.6, 127.5, 126.5, 122.6 (q, *J* = 273.6), 114.6, 55.4, 53.5, 41.5, 32.05; **IR:** 3295, 3086, 2936, 2840, 1721, 1613, 1585, 1513, 1422, 1359, 1277, 1248, 1133, 1034, 905, 843, 808, 699, 681, 630, 589 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{19}H_{18}F_6NO_4S$ $[M+H]^+$: 470.0861, found: 470.0844.

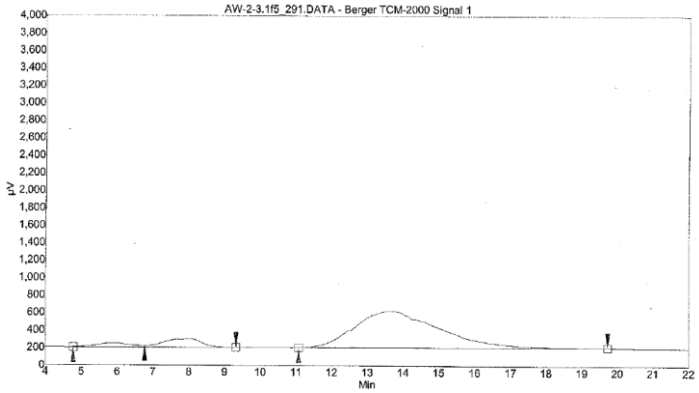




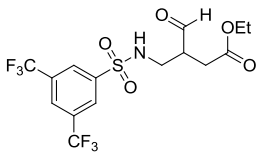
1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-3-(4-methoxyphenyl)pyrrolidin-2-ol SFC (Silica, 5.0 mL/min, 1.0% MeOH, 220 nm, 150 bar, 50 °C) t_r = 4.3 and 5.2 min (diastereomers); **^{1}H NMR** (Acetone *d*-6, 400 MHz, 1:1 diastereomer ratio) δ 8.55 (s, 0.5H), 8.46 (s, 2.0H), 8.33-8.44 (m, 2.3H), 7.23 (d, 0.7H, *J* = 8.2), 7.15 (d, 2.2H, *J* = 8.4), 6.80-6.87 (m, 3.3H), 5.62-5.67 (m, 1.2H), 5.50 (dd, 1.2H, *J* = 3.1, 6.0), 5.17 (d, 0.3H, *J* = 6.4), 3.77 (s, 4.5H), 3.66-3.75 (m, 2.0H), 3.46-3.58 (m, 2.3H), 3.27 (dt, 1.9H, *J* = 2.8, 6.6), 2.35-2.49 (m, 2.1H), 2.07-2.15 (m, 2.1H); **^{13}C NMR** (Acetone *d*-6, 100 MHz) δ 160.2, 144.9, 133.2 (q, *J* = 33.7), 133.2 (q, *J* = 33.7), 131.4, 130.8, 129.8, 129.5, 129.5 (q, *J* = 272.0), 129.1, 127.6, 115.5, 114.9, 91.9, 86.5, 56.1, 53.7, 50.8, 48.1, 47.4, 28.8; **IR:** 3495, 3088, 2959, 2841, 1724, 1613, 1515, 1459, 1359, 1279, 1251, 1163, 1136, 1035, 906, 843, 699, 682, 640, 594 cm^{-1}; **HRMS** (ESI) calcd. for $C_{19}H_{17}F_6NO_4SNa$ $[M+Na]^+$: 492.0680, found: 492.0690.

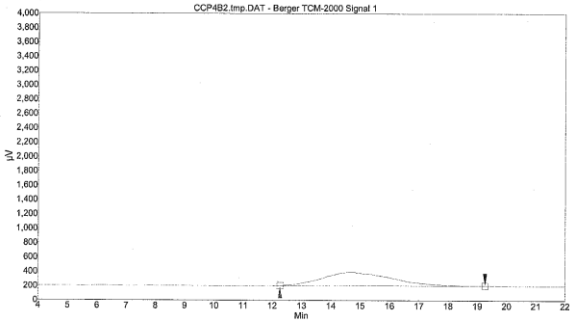
Table 1.11, Entry 9:

(*E*)-ethyl 4-(3,5-bis(trifluoromethyl)phenylsulfonamido)but-2-enoate was hydroformylated using General Procedure C. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid (68.5 mg, 79%) and analyzed by SFC (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 °C) to determine the selectivity (96:4 with 9% hydrogenated starting material).

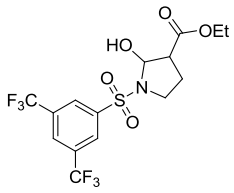


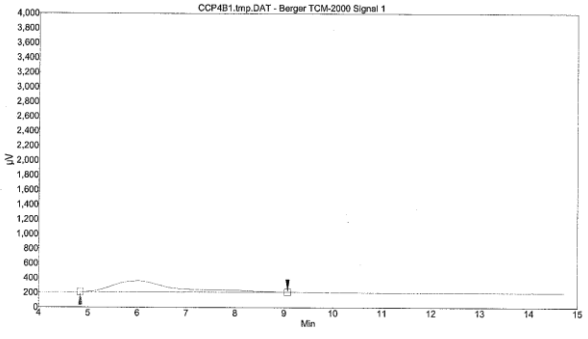
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.77	5.90	6.77	0.00	3.90	45.9	51.2	3.902
3	UNKNOWN	6.77	8.02	9.32	0.00	8.91	98.1	117.0	8.910
2	UNKNOWN	11.08	13.65	19.73	0.00	87.19	415.3	1144.5	87.187
Total						100.00	559.3	1312.7	100.000



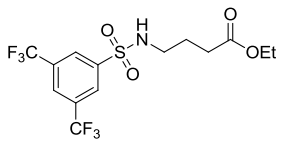


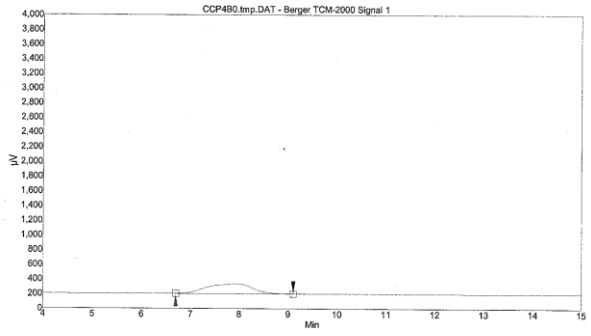
Ethyl 4-(3,5-bis(trifluoromethyl)phenylsulfonamido)-3-formylbutanoate, 1.29. SFC (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 °C) t_r =14.72 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.62 (s, 1H) 8.30 (s, 2H), 8.09 (s, 1H), 5.39 (t, 1H, J = 6.3), 4.19 (q, 2H, J = 7.1), 3.31-3.34 (m, 2H), 3.00-3.06 (m, 1H), 2.66-2.81 (m, 2H), 1.25-1.31 (t, 3H, J = 7.1); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 201.2, 171.3, 142.9, 133.2 (q, J = 34.5), 127.4, 126.5, 122.5 (q, J = 273.6), 61.8, 48.0, 41.7, 31.3, 14.3; **IR:** 3291, 3092, 2987, 1728, 1360, 1280, 1163, 1139, 1114, 906, 844, 699, 682, 591, 414 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{15}H_{16}F_6NO_5S$ $[M+H]^+$: 436.0653, found: 436.0639.





Ethyl 1-(3,5-bis(trifluoromethyl)benzenesulfonyl)-2-hydroxypyrrolidine-3-carboxylate. **SFC** (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 °C) t_r = 6.01 min; **^{1}H NMR** ($CDCl_3$, 300 MHz, 2:1 diastereomer ratio) δ 8.42 (s, 1H), 8.32 (s, 2H), 8.08 (app d, 1.5H, *J* = 4.8), 5.81 (t, 0.5H), 5.69 (s, 1H), 4.21 (q, 1H, *J* = 7.1), 3.98 (q, 2H, *J* = 7.2), 3.56-3.70 (m, 1H), 3.38-3.47 (m, 1H), 3.18-3.27 (m, 2H), 3.04 (app d, 2H, *J* = 7.5), 2.14-2.51 (m, 3H), 1.25-1.31 (m, 3H), 1.14 (t, 3H, *J* = 7.1); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 170.8, 170.6, 142.4, 141.5, 132.8 (q, *J* = 34.5), 128.2, 127.7, 126.5, 120.9 (q, *J* = 271.3), 86.1, 83.0, 61.8, 61.5, 51.3, 49.0, 46.8, 46.0, 26.7, 25.2, 14.3, 14.1; **IR:** 3487, 3089, 2984, 1733, 1625, 1360, 1280, 1165, 1138, 1056, 1033, 906, 845, 682, 640, 596 cm^{-1}; **HRMS** (ESI) calcd. for $C_{15}H_{15}F_6NO_5SNa$ $[M+Na]^+$: 458.0473, found: 458.0481.

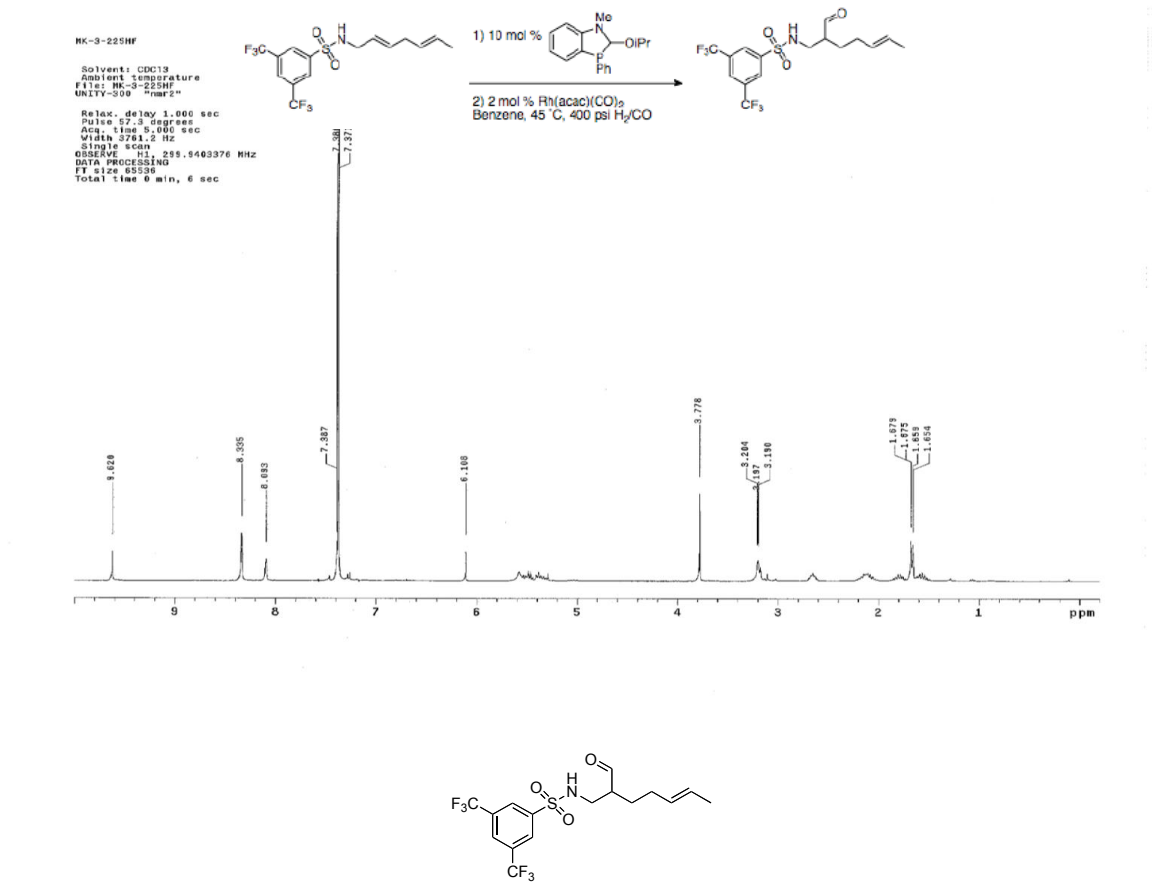




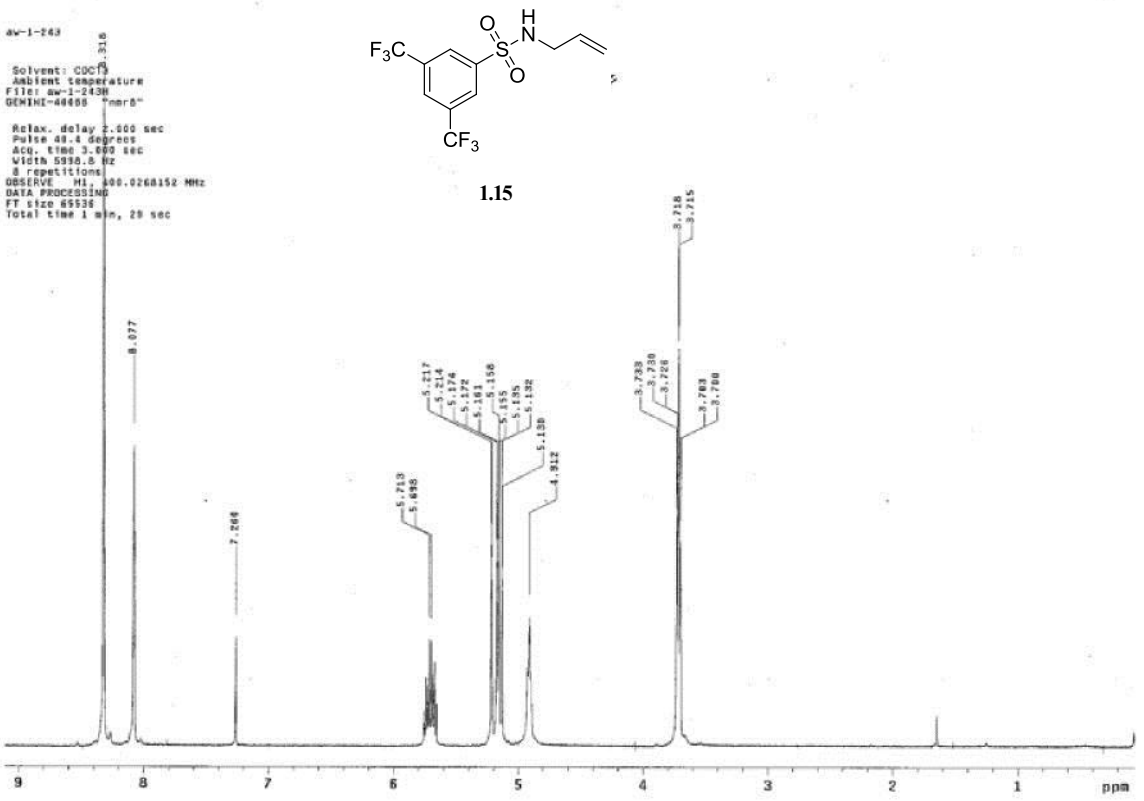
Ethyl 4-(3,5-bis(trifluoromethyl)phenylsulfonamido)butanoate. SFC (AS-H, 2.0 mL/min, 0.5% MeOH, 220 nm, 150 bar, 50 °C) t_r = 7.90 min; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.31 (s, 2H), 8.07 (s, 1H), 5.14 (s, 1H), 4.13 (q, 2H, *J* = 7.1), 3.11 (q, 2H, *J* = 6.4, 6.2), 2.39 (t, 2H, *J* = 6.8), 1.85 (ttt, 2H, *J* = 13.4, 6.8, 6.6), 1.25 (t, 3H, *J* = 7.1); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 173.4, 143.2, 133.1 (q, *J* = 34.5), 127.4, 126.3, 122.6 (q, *J* = 272.8), 61.1, 43.1, 31.5, 24.7, 14.3; **IR:** 3295, 2938, 1733, 1712, 1360, 1279, 1161, 1137, 1114, 905, 682, 591 cm^{-1}; **HRMS** (ESI) calcd. for $C_{14}H_{15}F_6NO_4SNa$ $[M+Na]^+$: 430.0524, found: 430.0525.

Table 1.11, Entry 10:

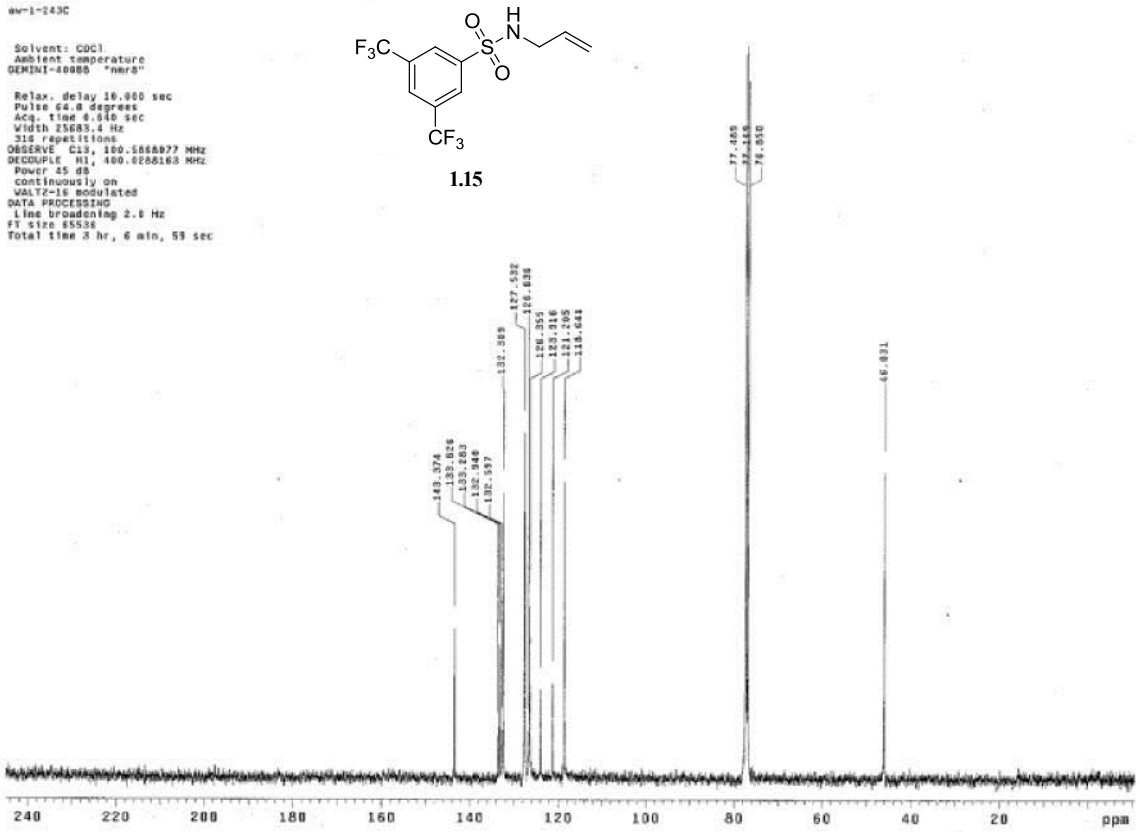
N-((2*E*,5*E*)-hepta-2,5-dienyl)-3,5-bis(trifluoromethyl)benzenesulfonamide was hydroformylated using the corresponding General Procedure G. Analysis of the crude reaction mixture by ^{1}H NMR showed conversion and selectivity. A mixture of normal and iso products was isolated as a white solid (63.4 mg, 76%) with selectivity determined by NMR to be >95:5.



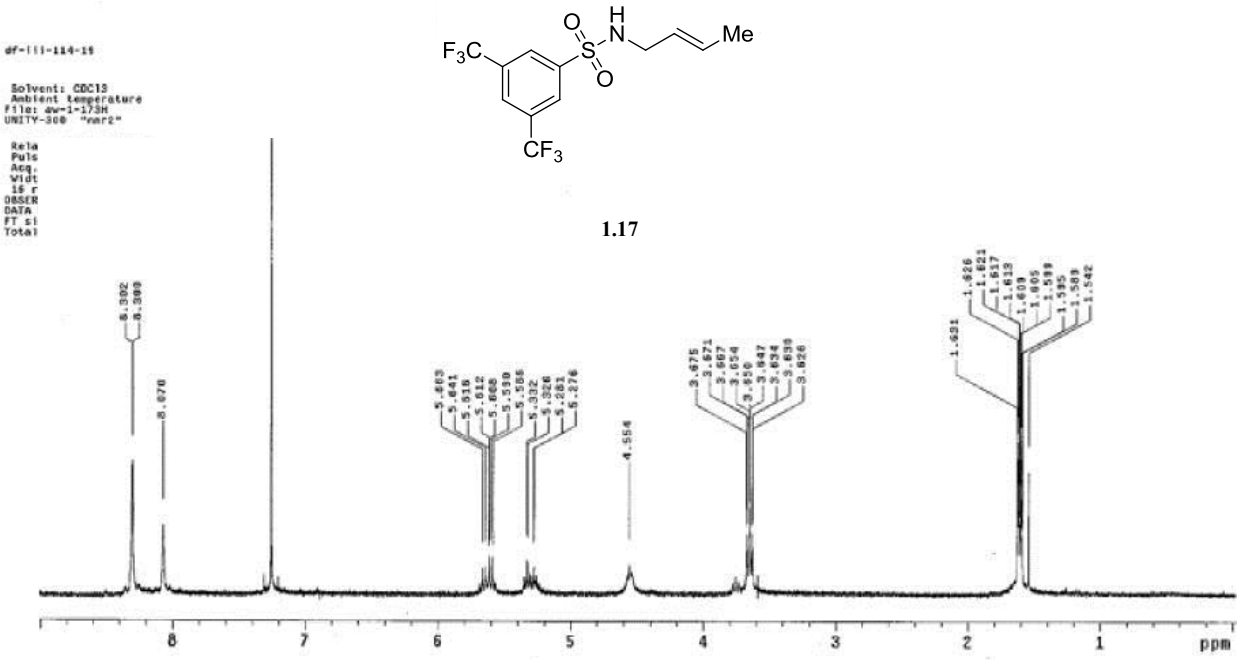
***E*)-*N*-(2-formylhept-5-enyl)-3,5-bis(trifluoromethyl)benzenesulfonamide, 1.30.** **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 9.62 (s, 1H), 8.31 (s, 2H), 8.08 (s, 1H), 5.20-5.60 (m, 2H), 3.09-3.22 (m, 2H), 2.62-2.64 (m, 1H), 2.07-2.20 (m, 2H), 1.67-1.9 (m, 1H), 1.65 (d, 3H, J = 5.99), 1.53-1.60 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 203.9, 143.2, 133.2 (q, J = 34.5), 129.0, 128.2, 127.6, 126.4, 122.6. (q, J = 272.8), 51.0, 41.4, 29.8, 26.1, 18.0; **IR:** 3295, 3087, 3936, 2859, 1721, 1625, 1453, 1359, 1278, 1138, 969, 906, 844, 699, 682, 630 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{18}F_6NO_3S$ $[M+H]^+$: 418.0912, found: 418.0898.


aw-1-243
Solvent: CDCl3
Ambient temperature
File: aw-1-243H
GEMINI-40480 "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
8 repetitions
OBSERVE H1, 400.0268152 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
ppm

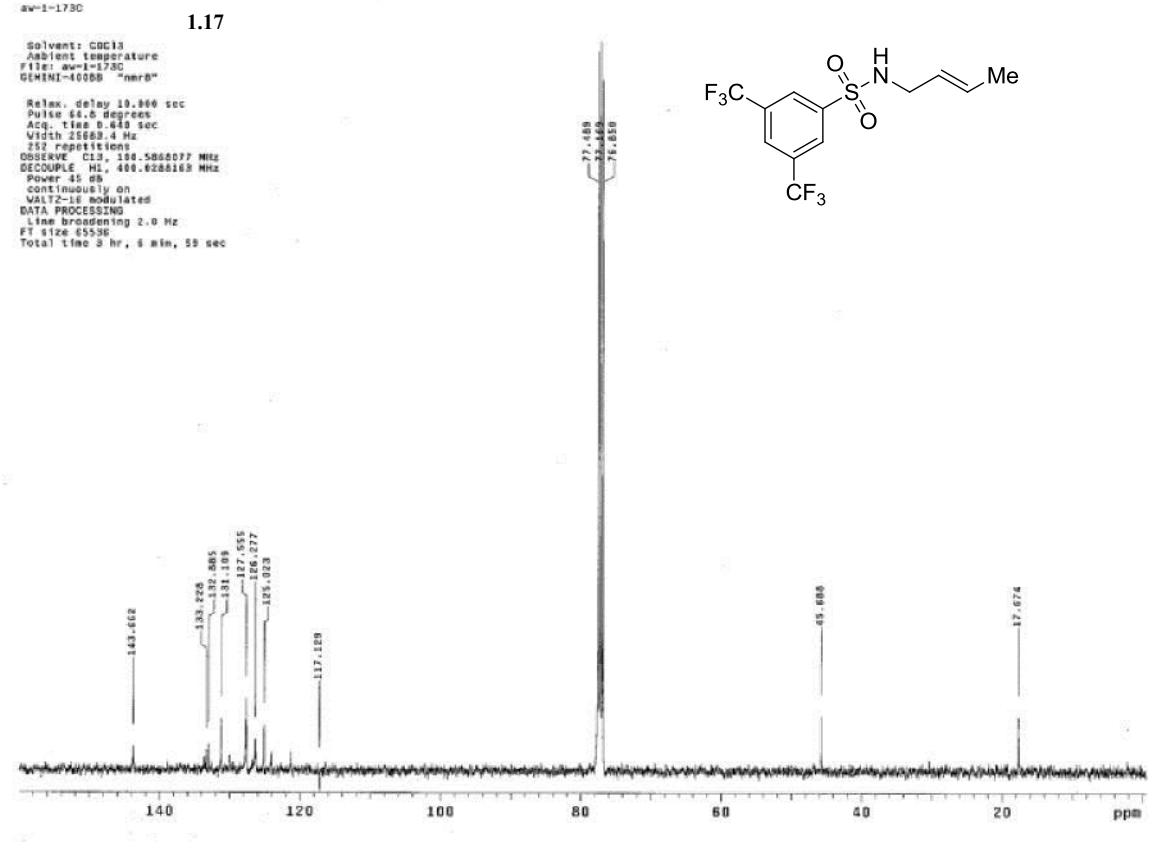
1.15


aw-1-243C
Solvent: CDCl3
Ambient temperature
GEMINI-40880 "nmr8"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25685.4 Hz
316 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.8 Hz
FT size 65536
Total time 3 hr, 6 min, 59 sec
ppm

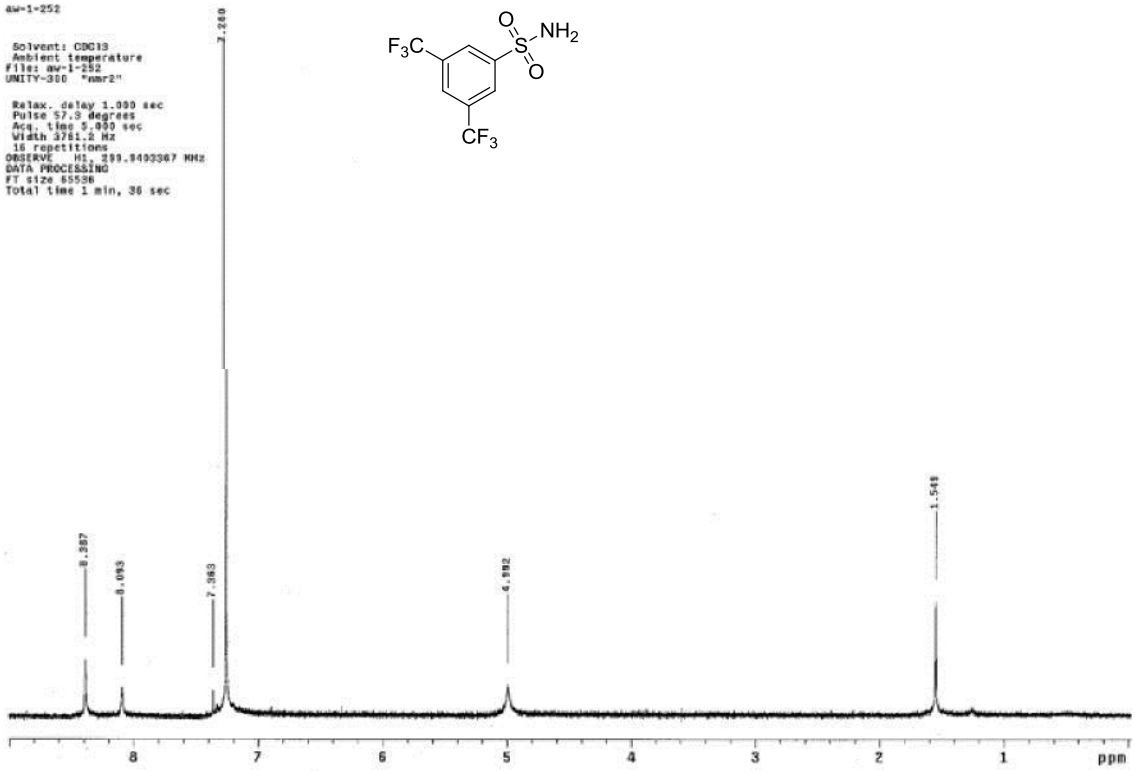
1.15

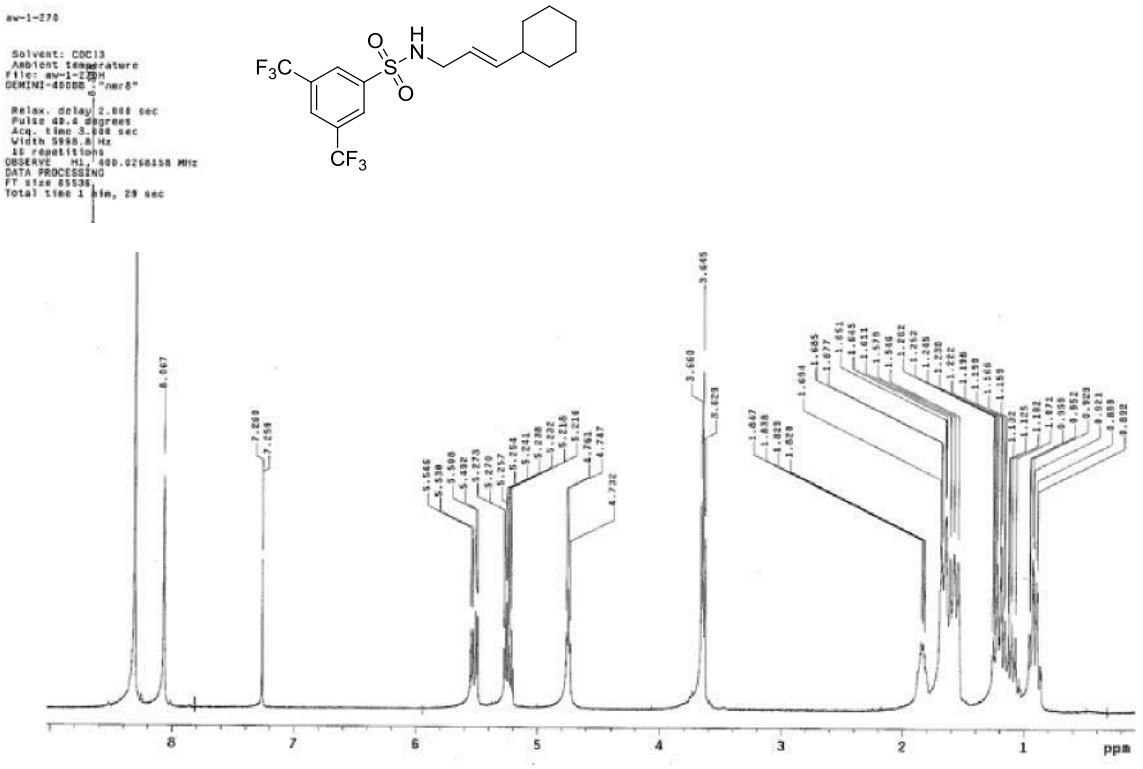

df-(1)-114-1H
Solvent: CDCl3
Ambient temperature
File: aw-1-173H
UNITY-300 "nmr2"
8.302
8.300
8.670
5.603
5.641
5.618
5.612
5.608
5.559
5.556
5.332
5.284
5.283
5.276
4.554
3.675
3.671
3.667
3.654
3.650
3.647
3.634
3.630
3.626
1.631
1.626
1.621
1.617
1.613
1.609
1.605
1.599
1.595
1.589
1.542
8
7
6
5
4
3
2
1
ppm

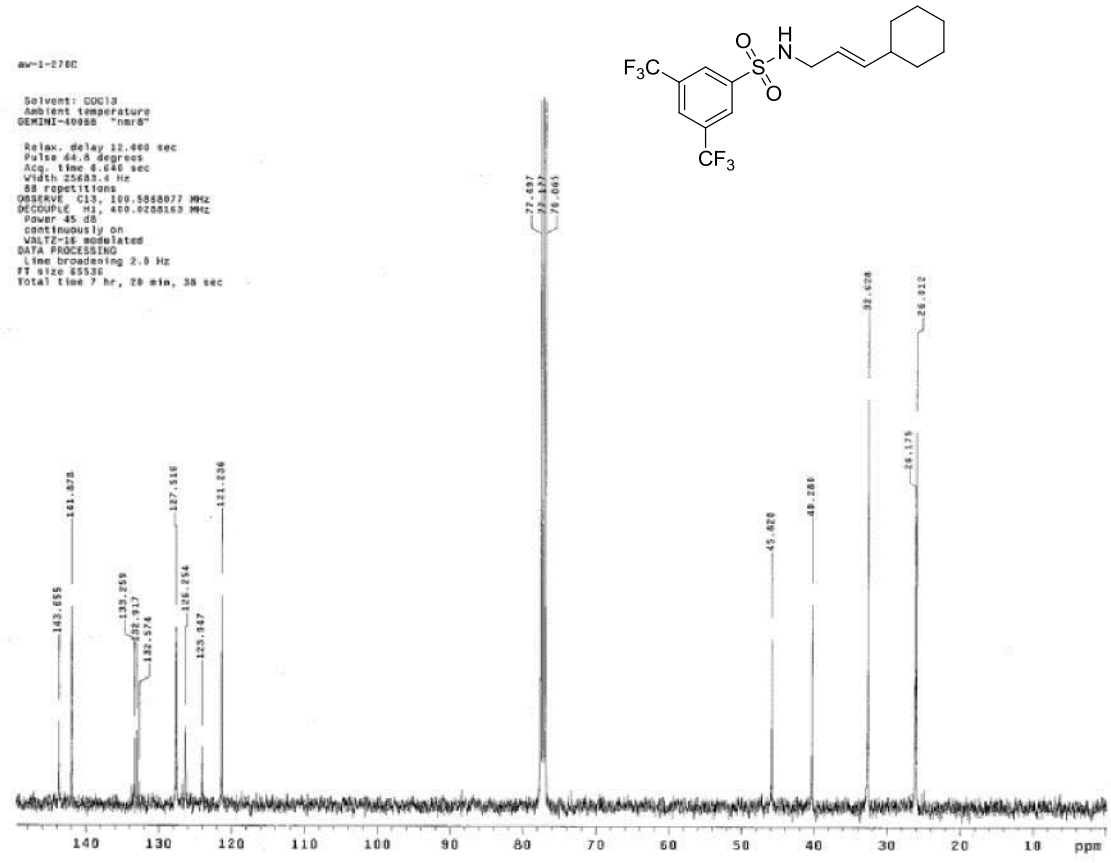
1.17

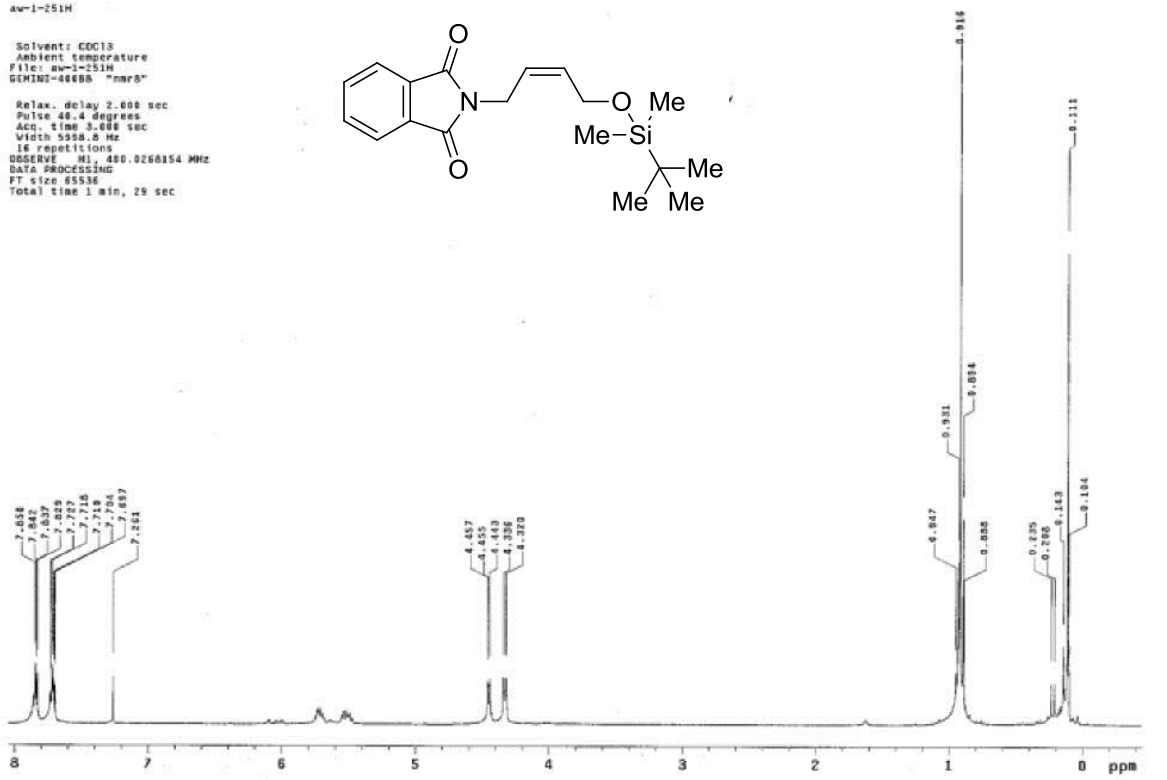

aw-1-173C
Solvent: CDCl3
Ambient temperature
File: aw-1-173C
GEMINI-400BB "nmr8"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.440 sec
Width 25683.4 Hz
252 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 3 hr, 6 min, 58 sec
143.662
133.225
132.865
131.169
127.555
126.277
125.928
117.129
77.489
77.169
76.850
49.688
17.674
140
120
100
80
60
40
20
ppm

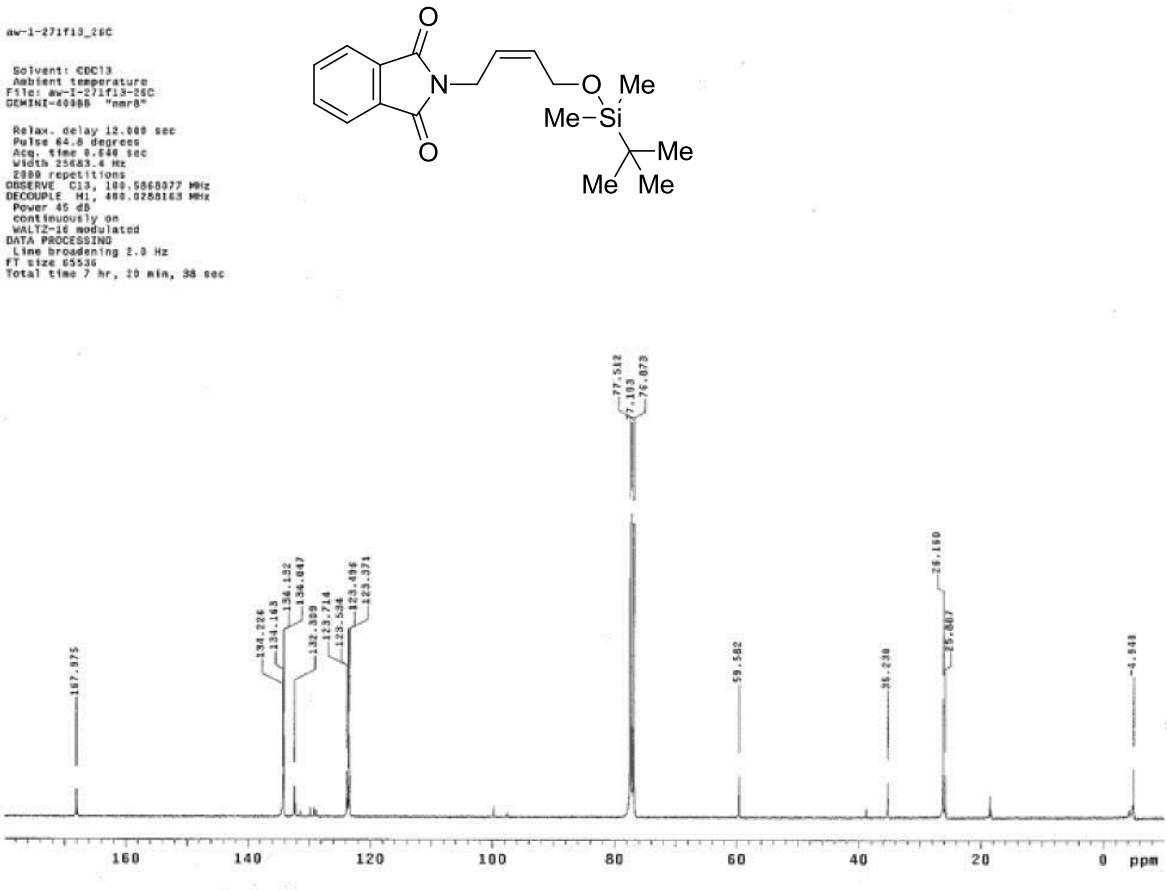
1.17

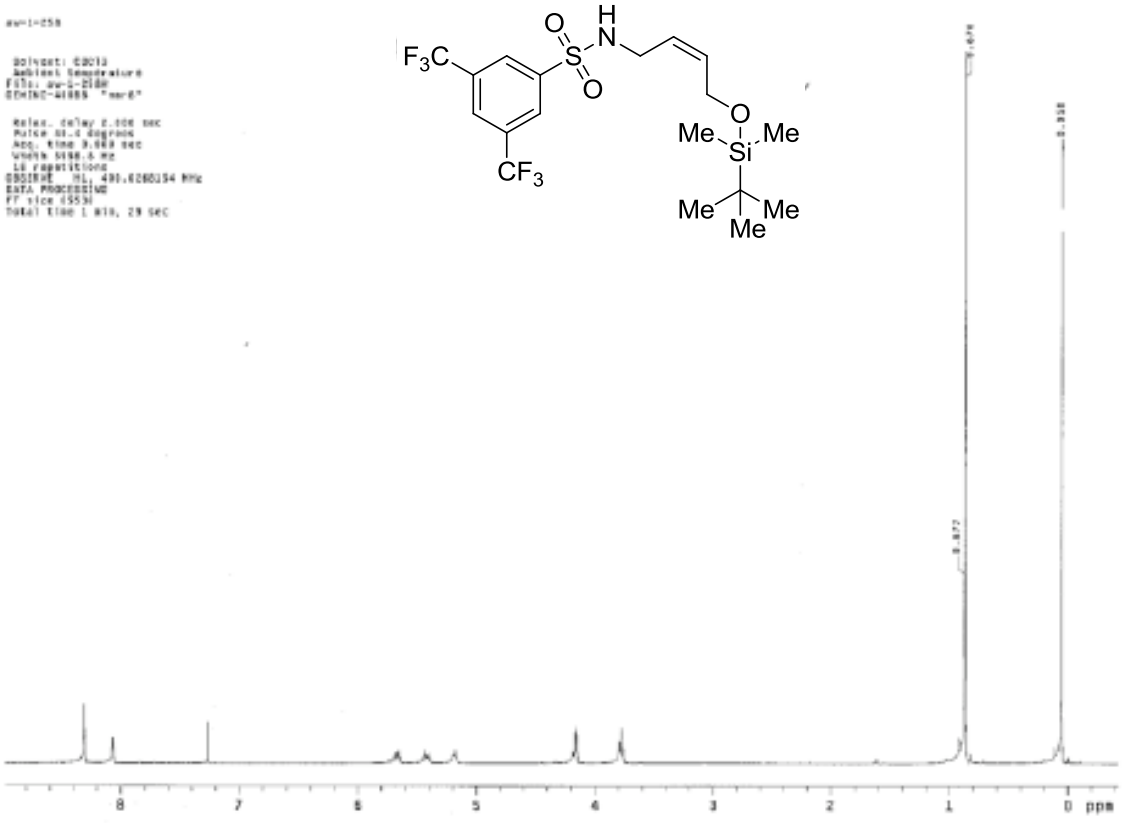

aw-1-252
Solvent: CDCl3
Ambient temperature
File: aw-1-252
UNITY-300 "nmr2"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 399.9493367 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 36 sec
F3C
O
S
NH2
O
CF3
8.287
8.093
7.383
7.269
4.992
1.548
8
7
6
5
4
3
2
1
ppm

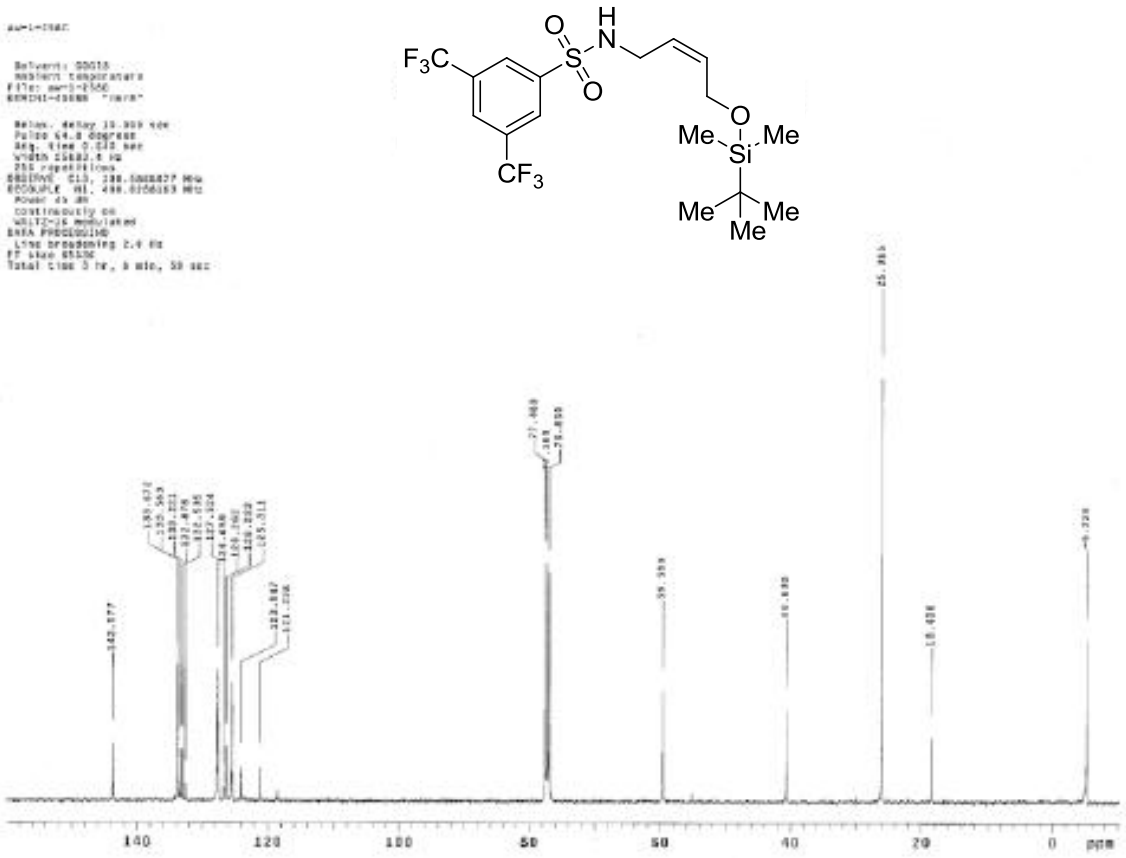

aw-1-278
Solvent: CDCl3
Ambient temperature
File: aw-1-278H
DEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 49.4 degrees
Acq. time 3.004 sec
Width 5988.8 Hz
16 repetitions
OBSERVE H1, 400.0258158 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
F3C
CF3
O
S
N
H
8.067
7.269
7.259
3.660
3.645
8.629
ppm

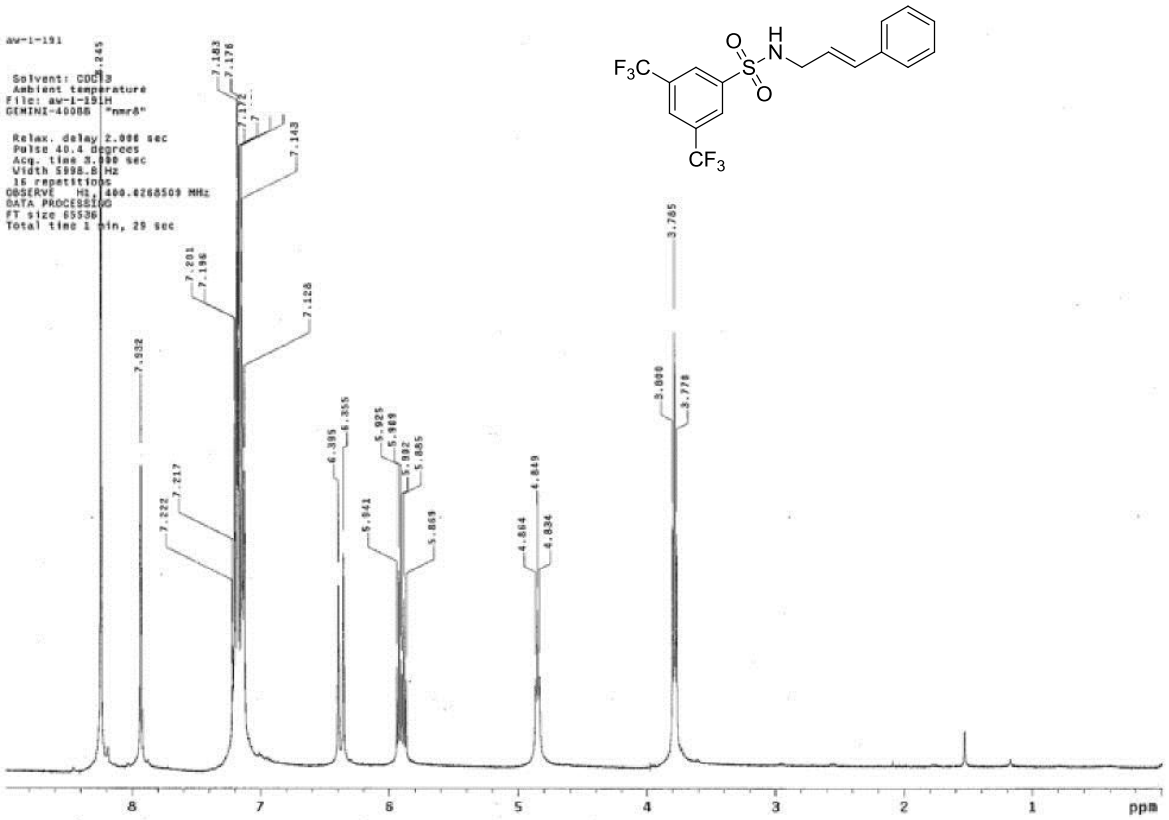

aw-1-278C
Solvent: CDCl3
Ambient temperature
DEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 44.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
88 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0258163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 7 hr, 28 min, 36 sec
F3C
CF3
O
S
N
H
77.497
77.177
76.865
161.878
143.655
133.259
132.917
132.574
127.516
126.254
125.947
121.236
45.628
40.268
32.628
26.012
25.175
ppm

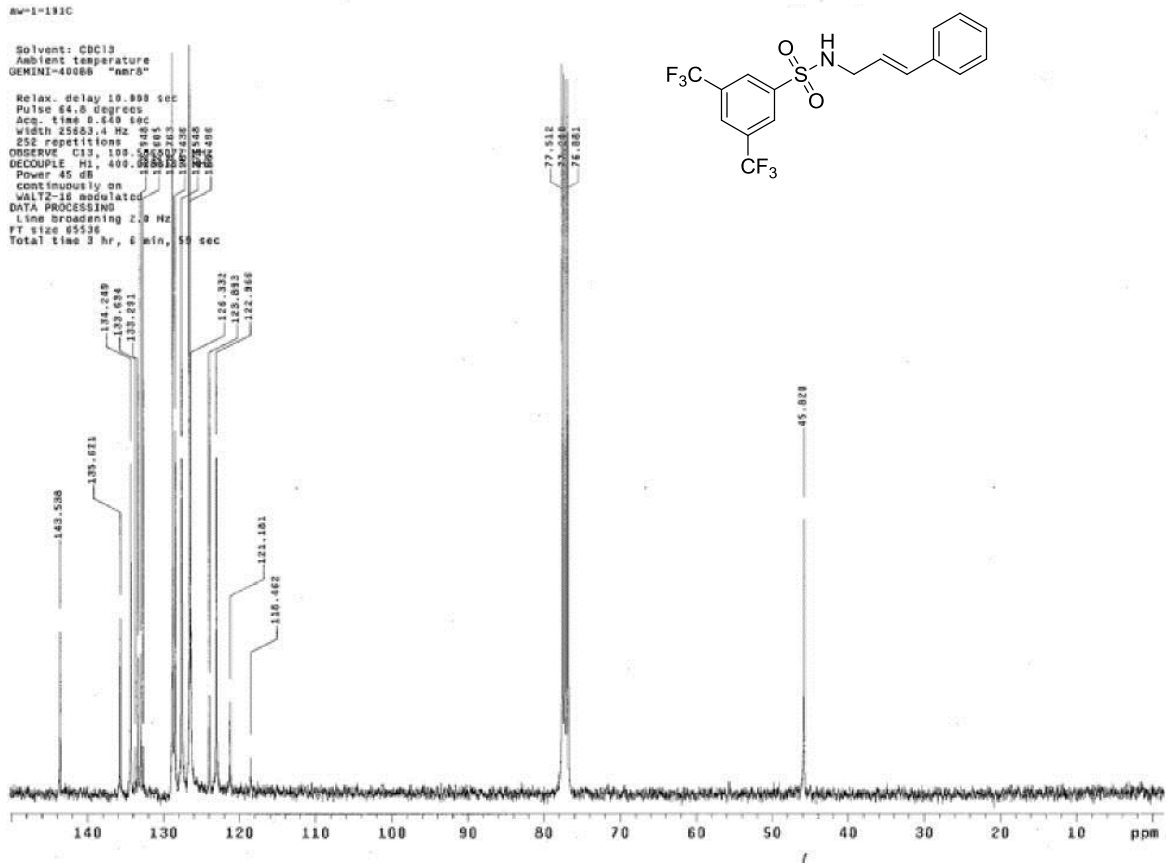

aw-1-251H
Solvent: CDCl3
Ambient temperature
File: aw-1-251H
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5988.8 Hz
16 repetitions
OBSERVE H1, 400.0268154 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
O
N
O
O
Me
Me–Si
Me
Me Me
ppm

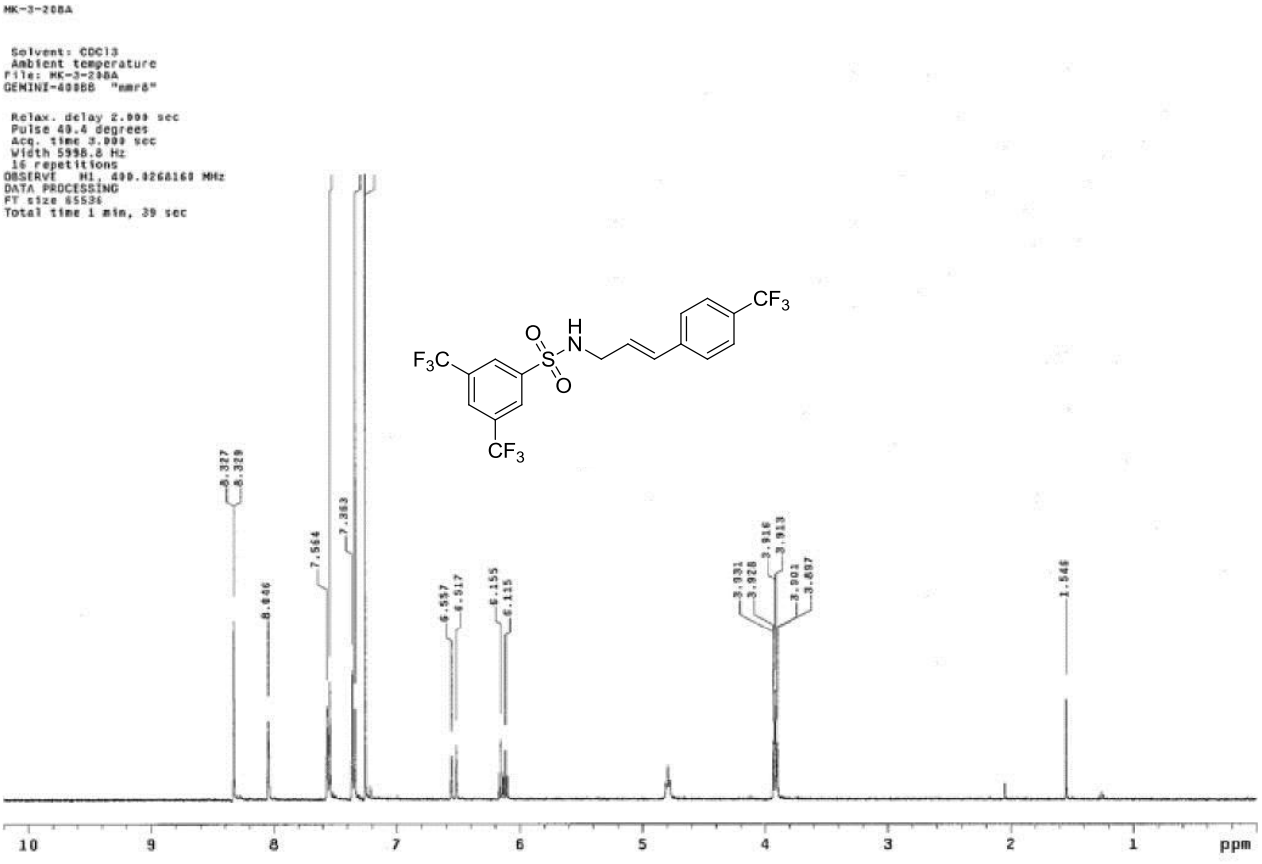

aw-1-271f13_26C
Solvent: CDCl3
Ambient temperature
File: aw-1-271f13-26C
GEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 0.648 sec
Width 25683.4 Hz
2880 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0268163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 7 hr, 20 min, 38 sec
O
N
O
O
Me
Me–Si
Me
Me Me
ppm

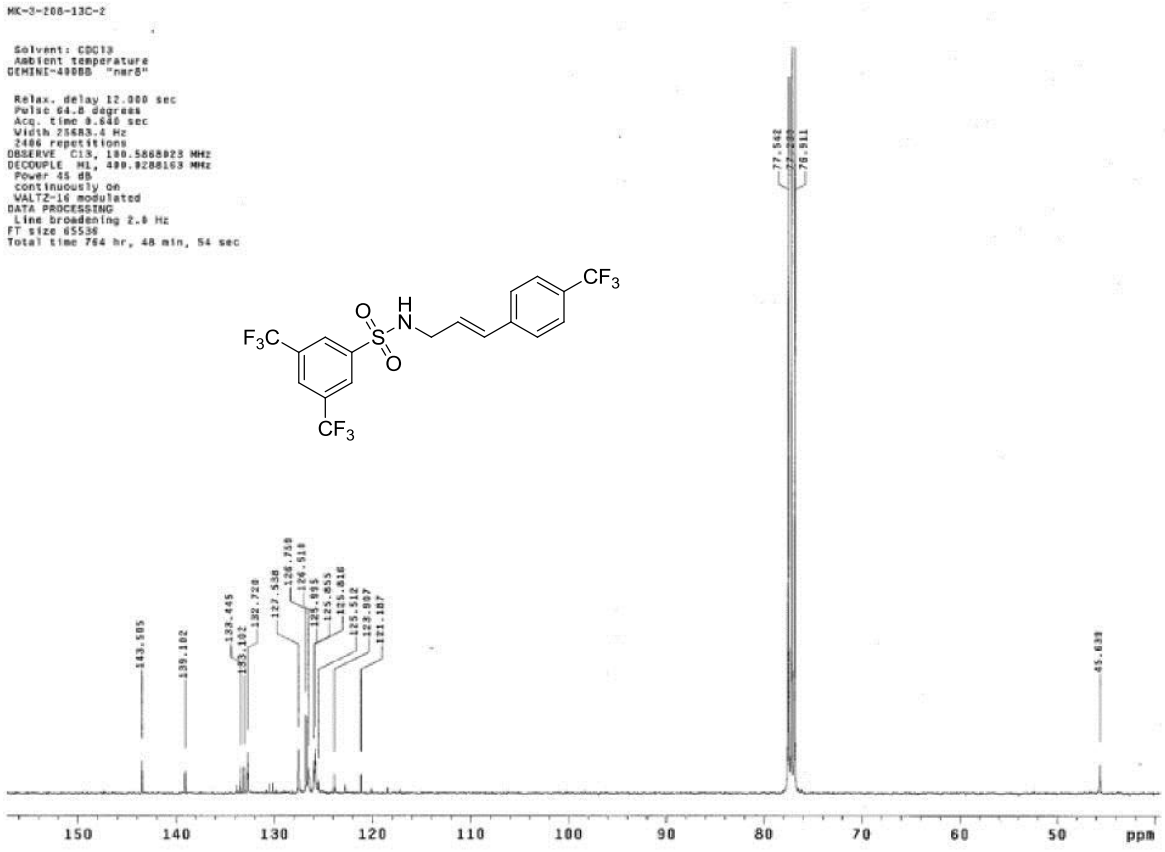

F3C
CF3
O
S
O
H
N
O
Si
Me
Me
Me
Me
Me
8
7
6
5
4
3
2
1
0 ppm

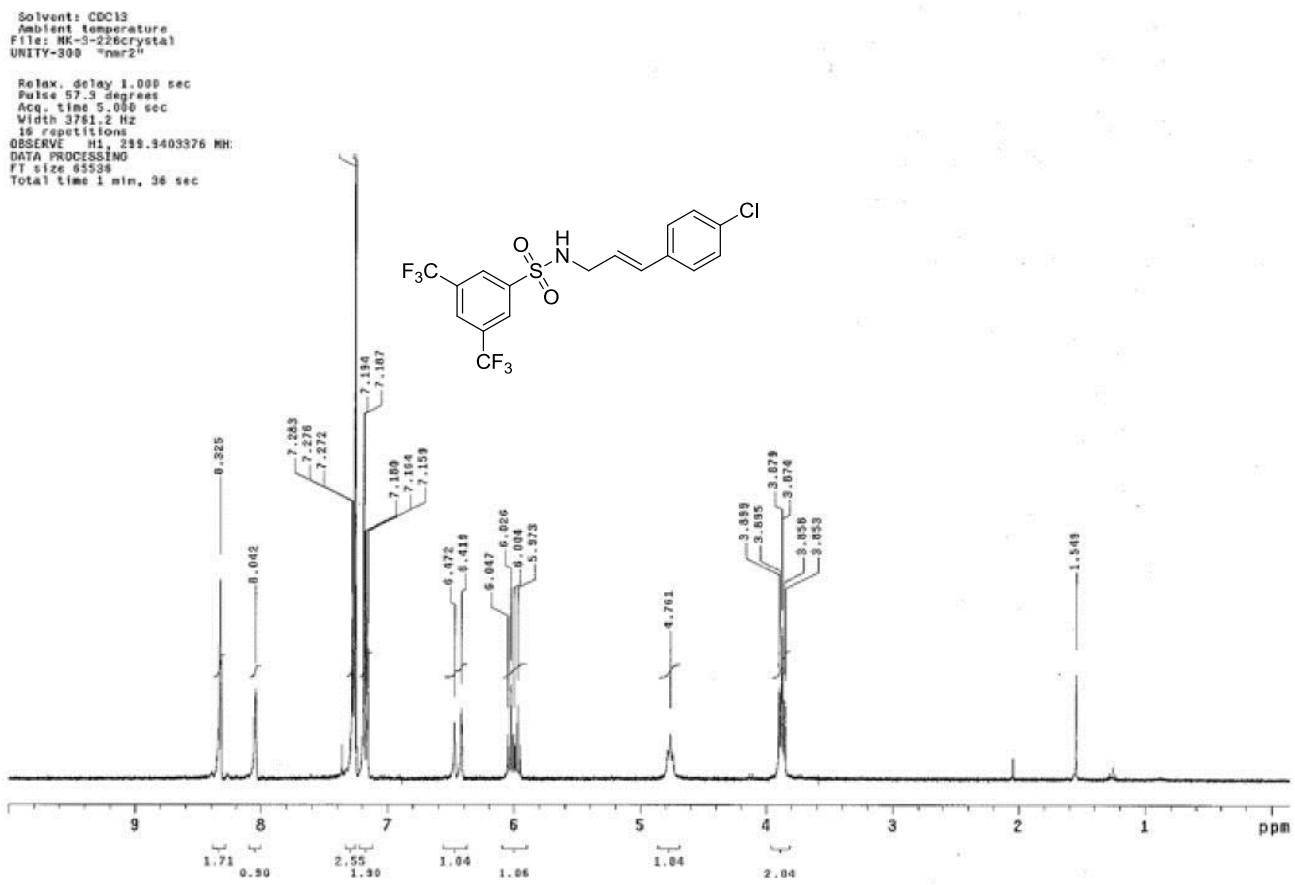

F3C
CF3
O
S
O
H
N
O
Si
Me
Me
Me
Me
Me
140
120
100
80
60
40
20
0 ppm


aw-1-191
Solvent: CDCl3
Ambient temperature
File: aw-1-191H
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0268509 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
7.245
7.183
7.176
7.172
7.143
7.201
7.196
7.128
7.032
7.222
7.217
6.355
6.309
6.041
5.925
5.869
5.865
5.859
4.864
4.849
4.834
3.785
3.030
3.778
8
7
6
5
4
3
2
1
ppm
F3C
CF3
O
S
N
H

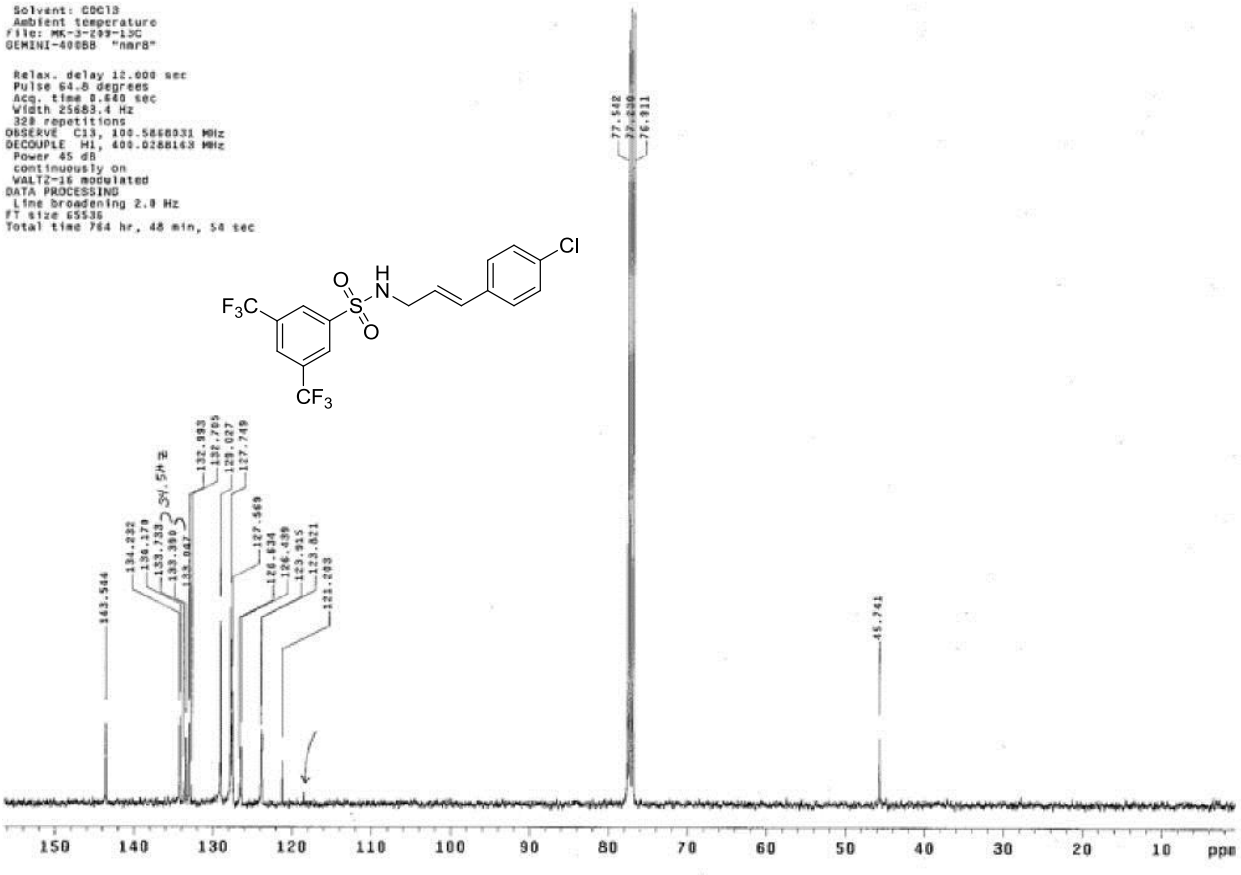

aw-1-191C
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
width 25663.4 Hz
252 repetitions
OBSERVE C13, 100.6
DECOUPLE H1, 400.0
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 3 hr, 6 min, 59 sec
77.512
77.200
76.881
134.249
133.634
133.021
126.332
125.893
122.966
135.671
143.538
121.161
118.462
45.828
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
F3C
CF3
O
S
N
H

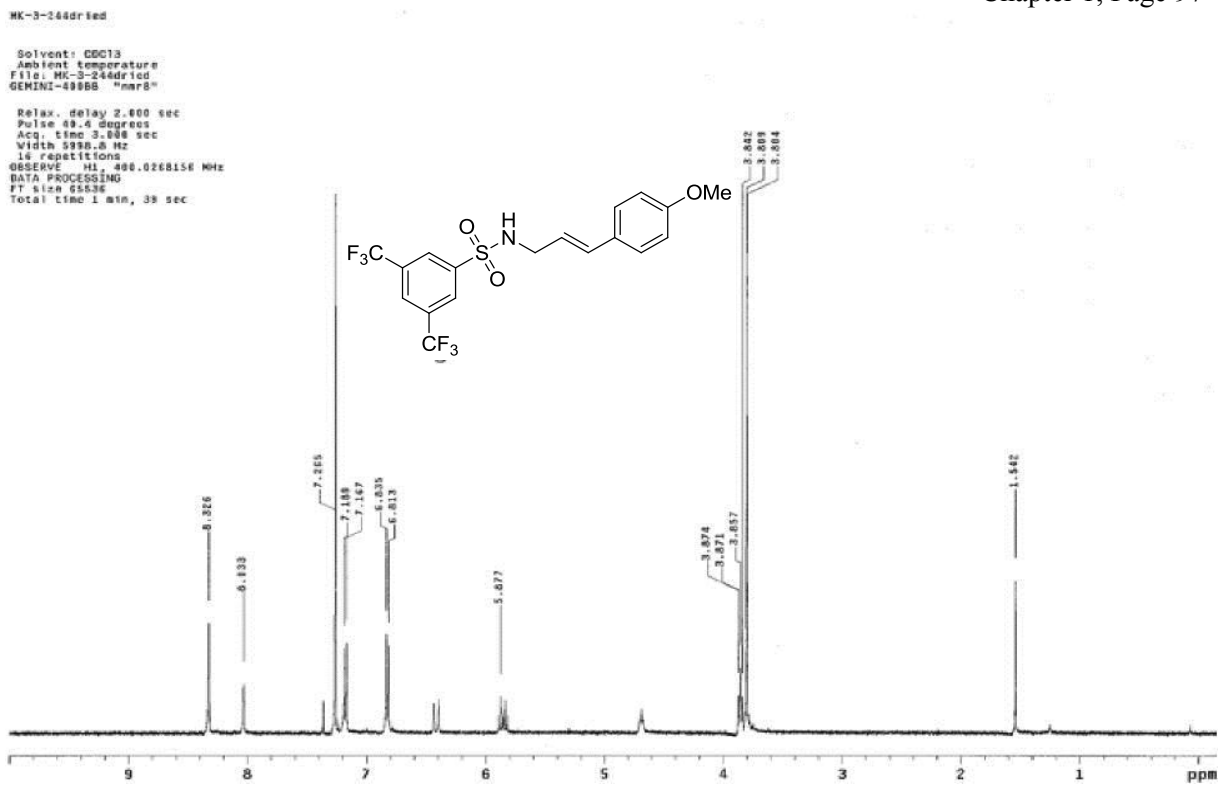

MK-3-208A
Solvent: CDCl3
Ambient temperature
File: MK-3-208A
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0268160 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 39 sec
8.327
8.329
8.046
7.564
7.363
6.597
6.517
6.155
6.115
3.931
3.923
3.916
3.913
3.902
3.887
1.646
F3C
CF3
CF3
O
S
O
H
N
10
9
8
7
6
5
4
3
2
1
ppm

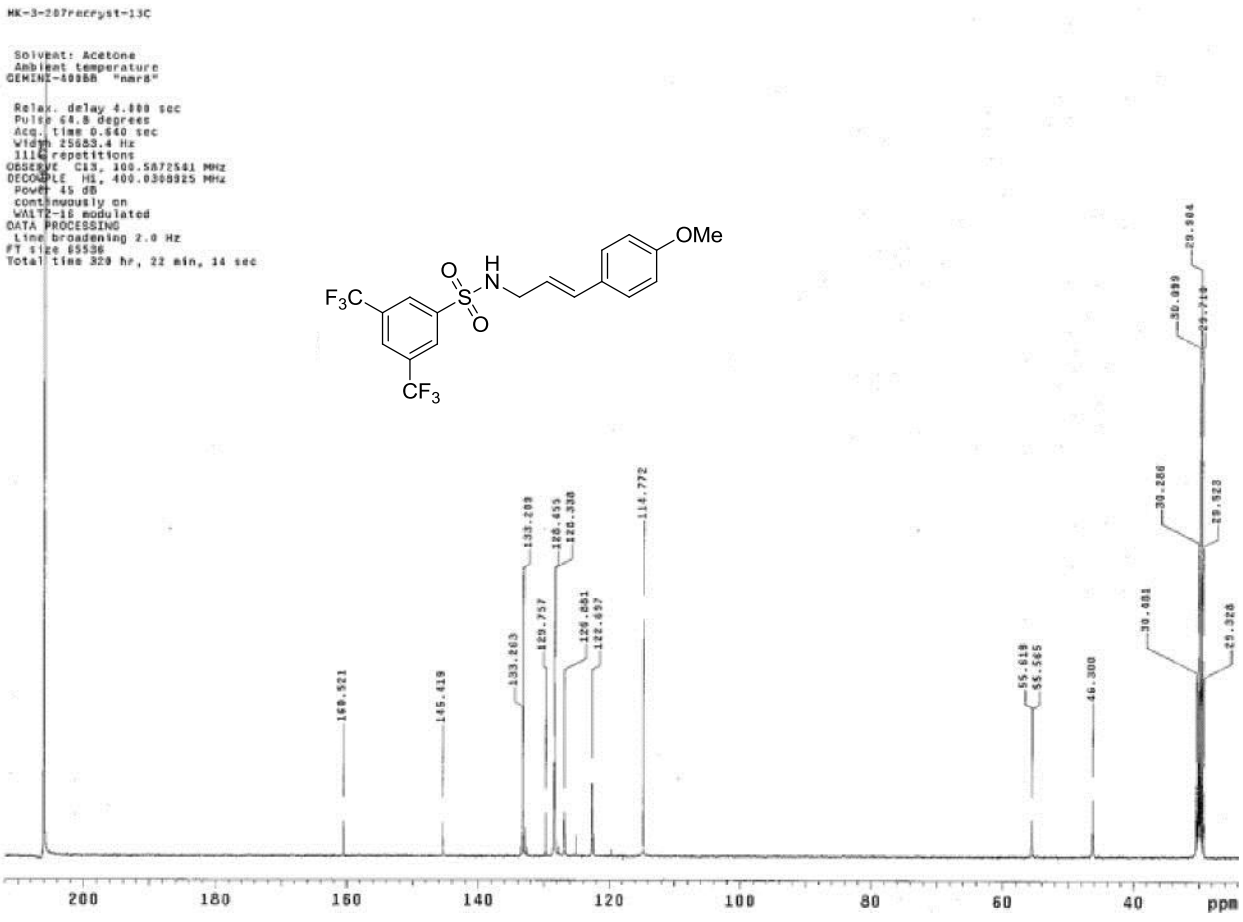

MK-3-208-13C-2
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 0.648 sec
Width 25683.4 Hz
2486 repetitions
OBSERVE C13, 100.5868823 MHz
DECOUPLE H1, 400.9288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 764 hr, 48 min, 54 sec
143.585
139.102
133.445
132.728
127.536
126.758
126.518
125.995
125.855
125.616
125.512
123.907
121.187
77.582
77.260
76.911
45.639
F3C
CF3
CF3
O
S
O
H
N
150
140
130
120
110
100
90
80
70
60
50
ppm

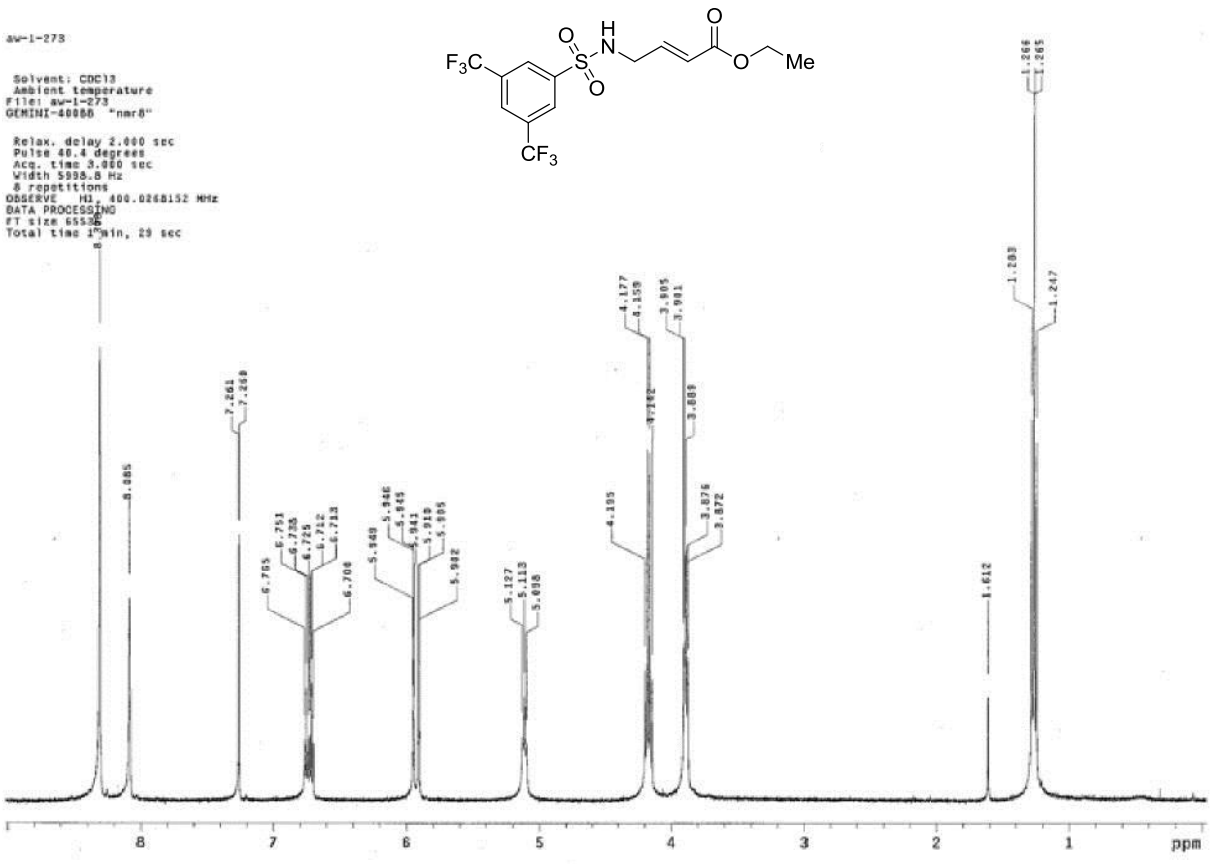

Solvent: CDCl3
Ambient temperature
File: MK-3-226crystal
UNITY-300 "nmr2"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 299.9403376 MH
DATA PROCESSING
FT size 65536
Total time 1 min, 36 sec
Cl
F3C
CF3
ppm

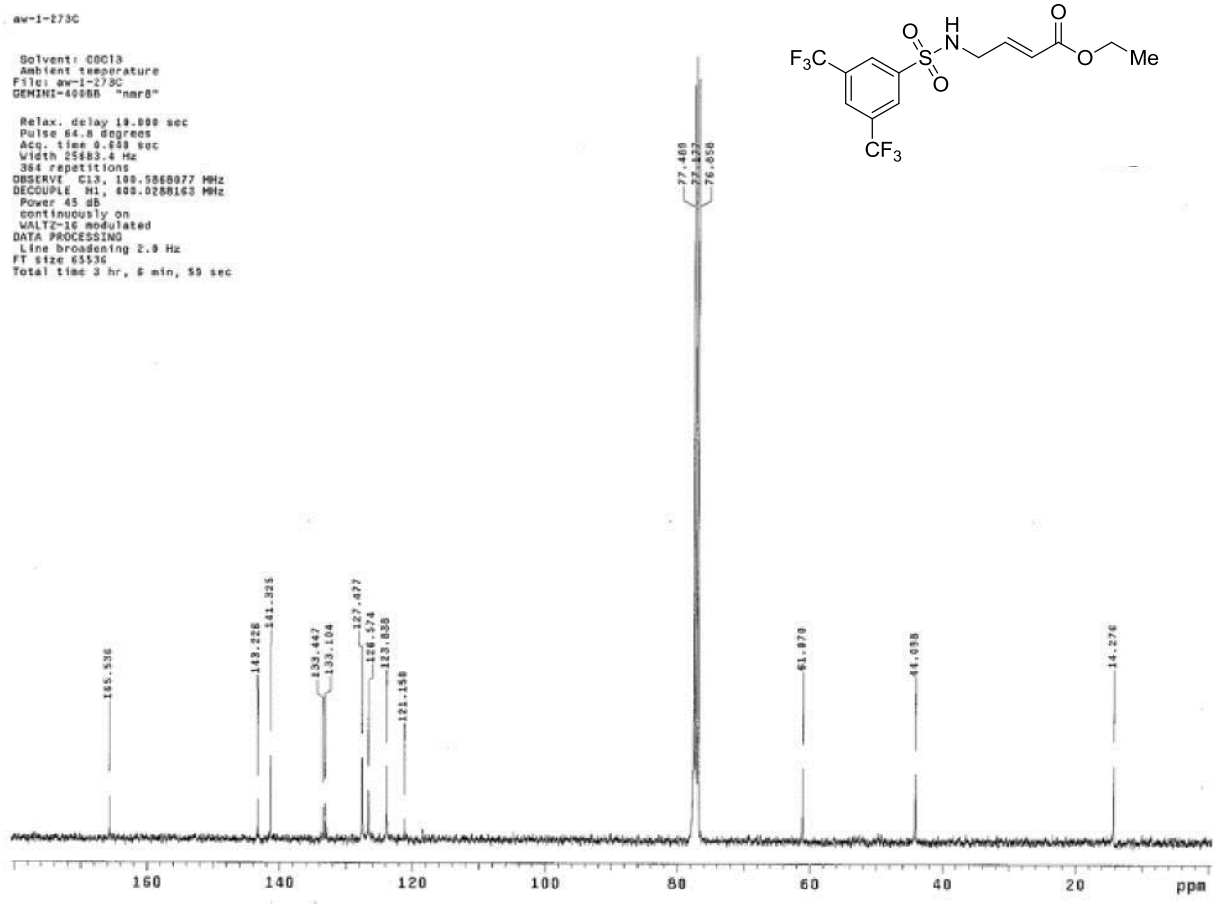
MK-3-289-13C

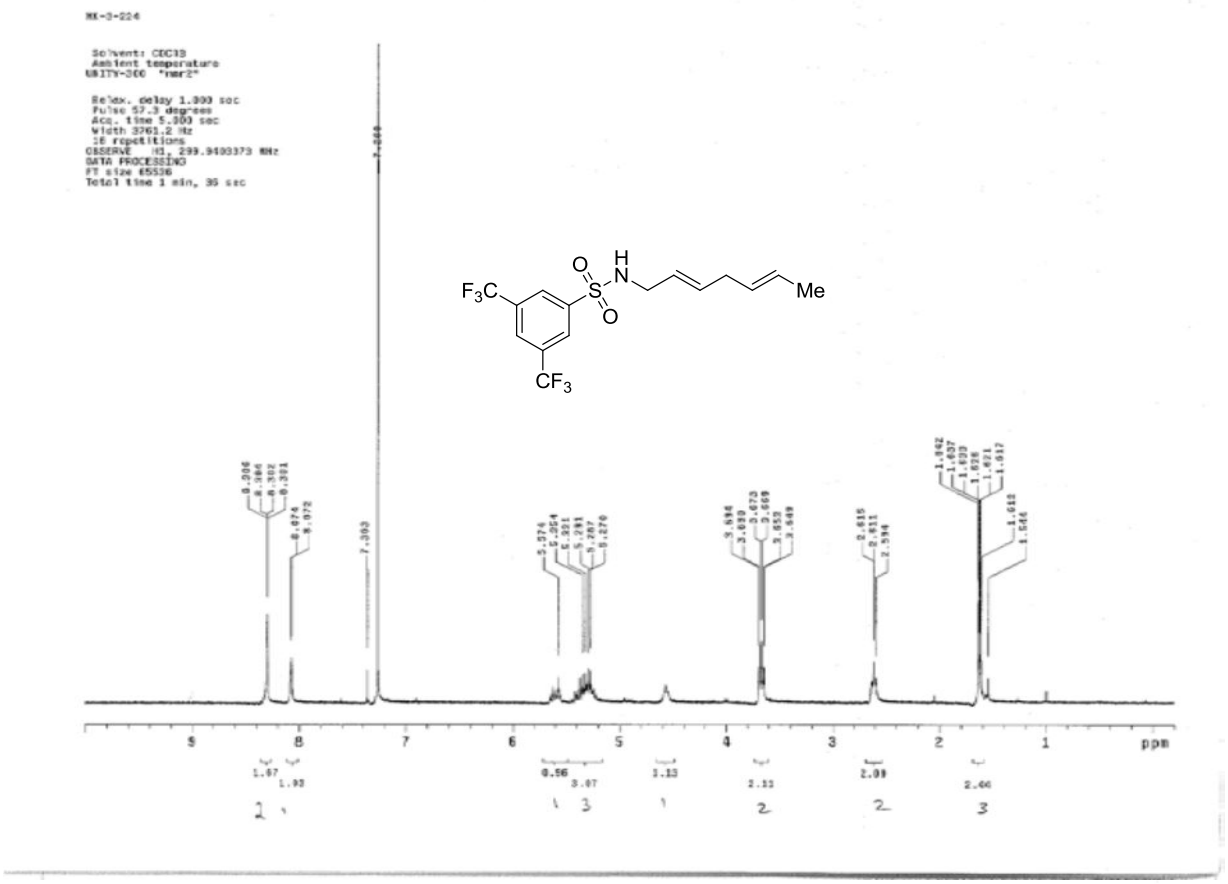

Solvent: CDCl3
Ambient temperature
File: MK-3-289-13C
GEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
328 repetitions
OBSERVE C13, 100.5868031 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 764 hr, 48 min, 54 sec
Cl
F3C
CF3
ppm

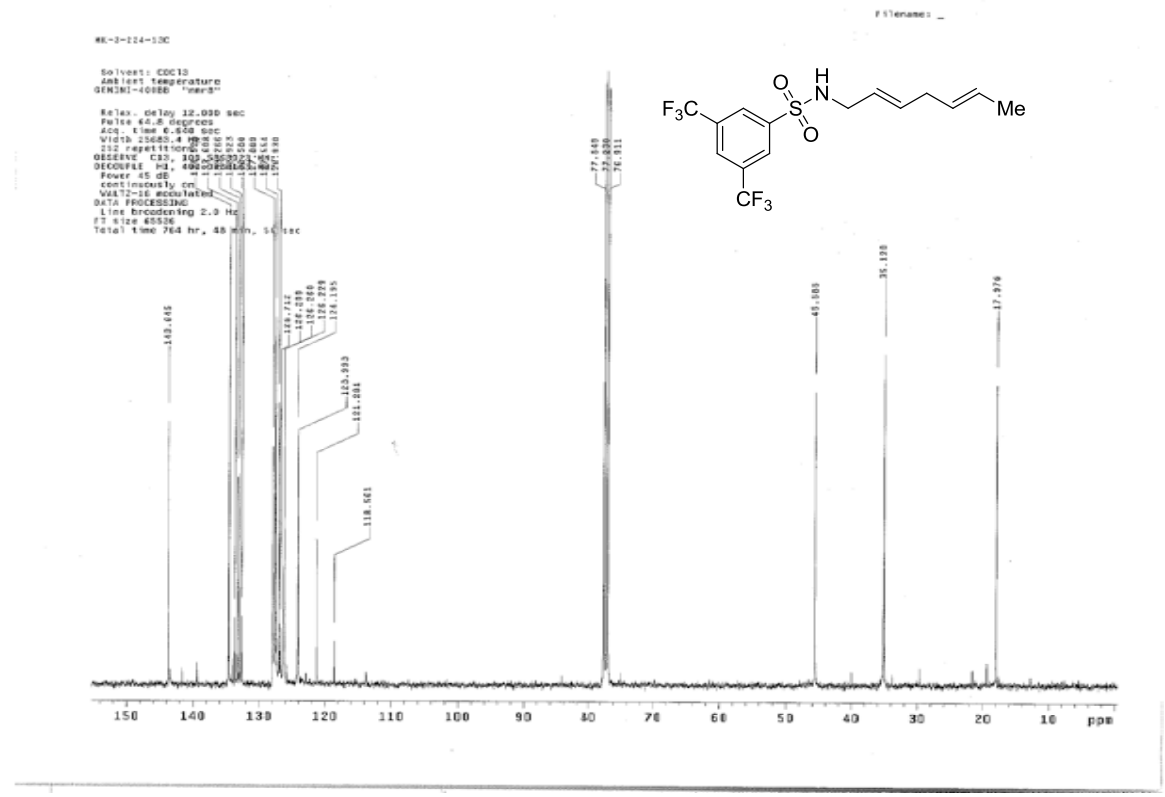

MK-3-244dried
Solvent: CDCl3
Ambient temperature
File: MK-3-244dried
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.008 sec
Width 5996.8 Hz
16 repetitions
OBSERVE H1, 400.0268156 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 39 sec
OMe
F3C
CF3
8.326
8.133
7.265
7.188
7.167
6.835
6.813
5.877
3.874
3.871
3.857
3.842
3.839
3.804
1.542
9
8
7
6
5
4
3
2
1
ppm


MK-3-287recryst-13C
Solvent: Acetone
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 4.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25583.4 Hz
1116 repetitions
OBSERVE C13, 100.5872541 MHz
DECOUPLE H1, 400.0308925 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 320 hr, 22 min, 14 sec
OMe
F3C
CF3
169.521
145.419
133.269
133.203
129.757
126.453
126.338
126.081
122.457
114.772
55.619
55.585
46.300
30.484
30.288
29.864
29.710
29.523
29.326
200
180
160
140
120
100
80
60
40
ppm


aw-1-273
Solvent: CDCl3
Ambient temperature
File: aw-1-273
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
8 repetitions
OBSERVE H1, 400.0268152 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
F3C
CF3
Me
ppm


aw-1-273C
Solvent: CDCl3
Ambient temperature
File: aw-1-273C
GEMINI-400BB "nmr8"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.680 sec
Width 25883.4 Hz
384 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0268163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 3 hr, 6 min, 59 sec
F3C
CF3
Me
ppm

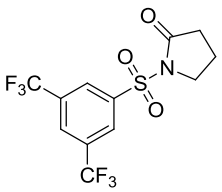

MK-3-224
Solvent: CDCl3
Ambient temperature
UNITY-300 "nmr2"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.300 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 299.9400373 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 36 sec
F3C
CF3
O
S
H
N
Me
ppm

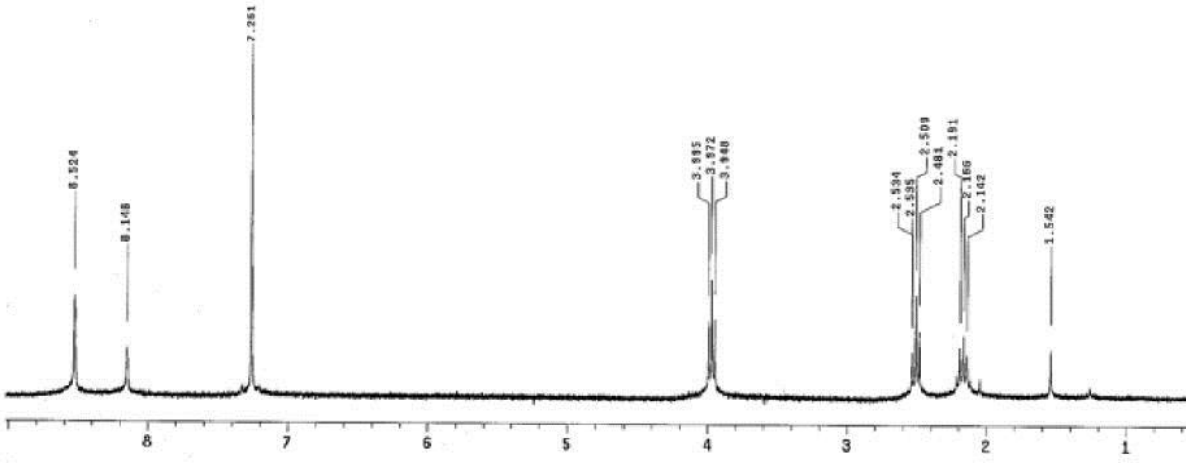

MK-3-224-13C
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr3"
Relax. delay 12.000 sec
Pulse 60.0 degrees
Acq. time 0.500 sec
232 repetitions
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
F3C
CF3
O
S
H
N
Me
ppm

MD-1-247

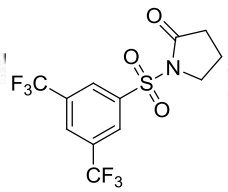
Solvent: CDCl3
Ambient temperature
UNITY-300 "nmr2"

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 299.9493373
DATA PROCESSING
FT size 65536
Total time 1 min, 36 sec



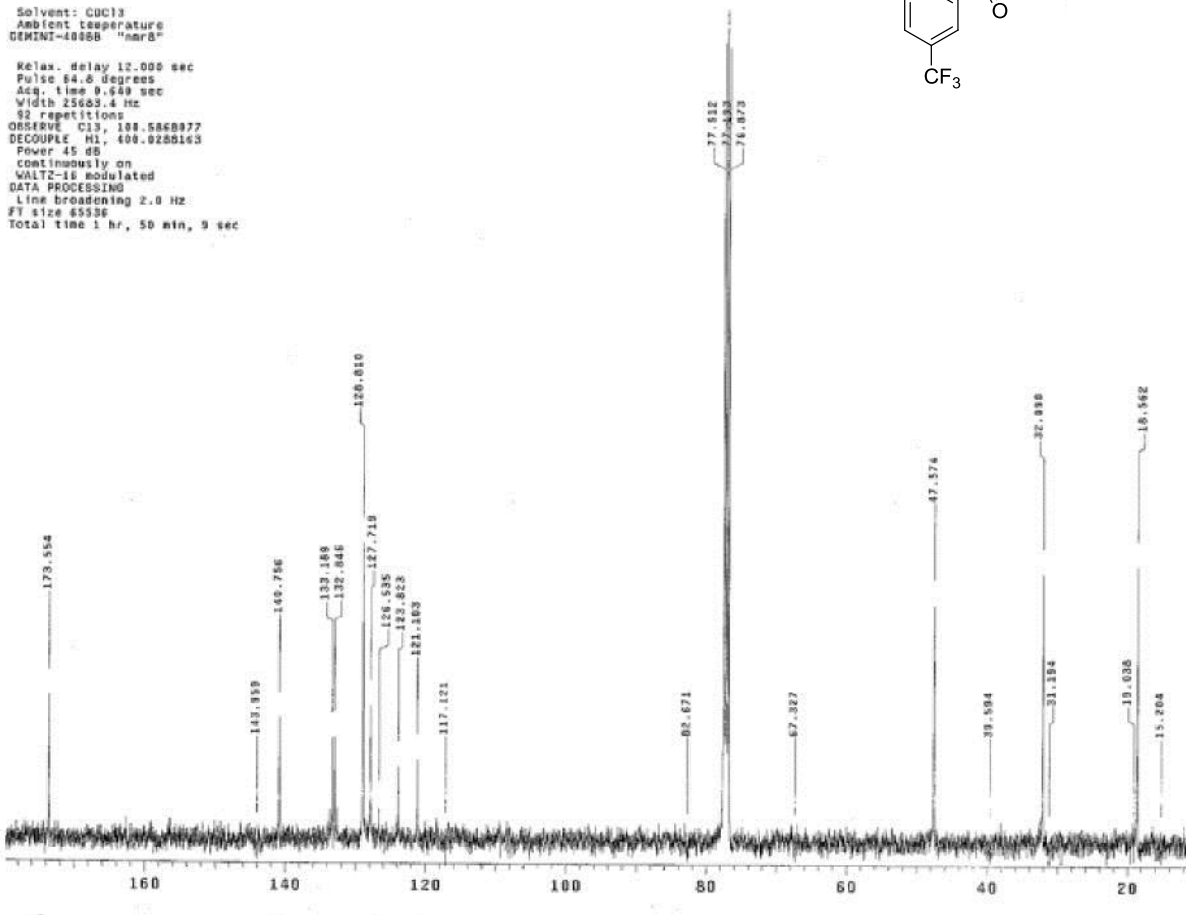


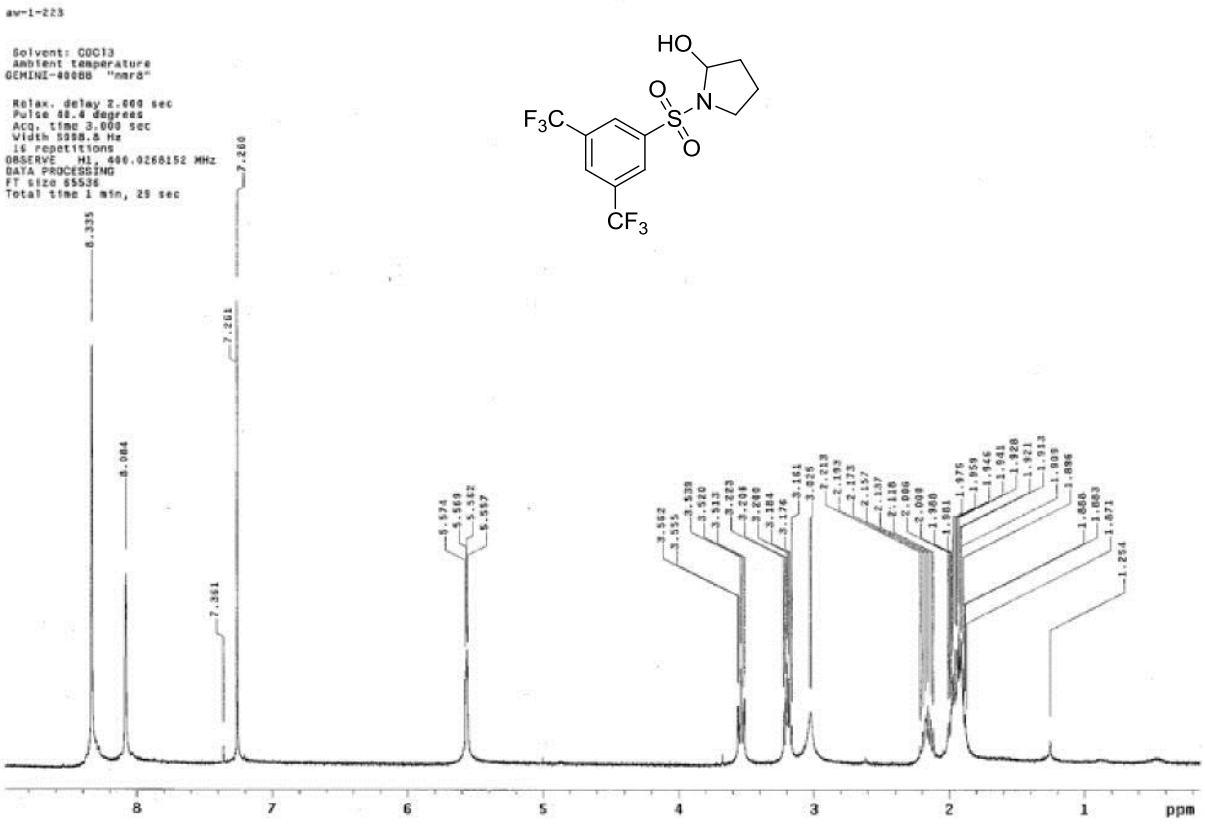
MD-1-247C

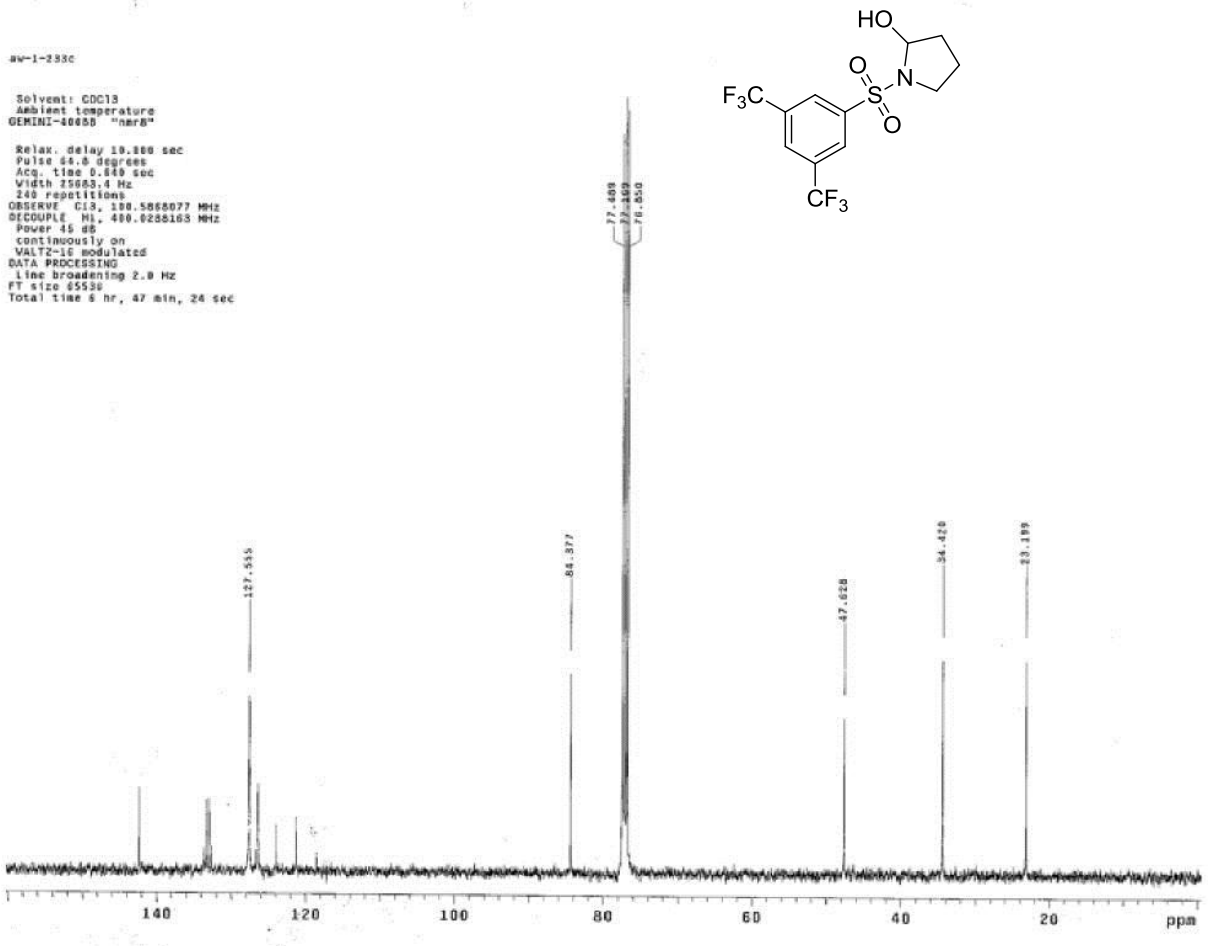


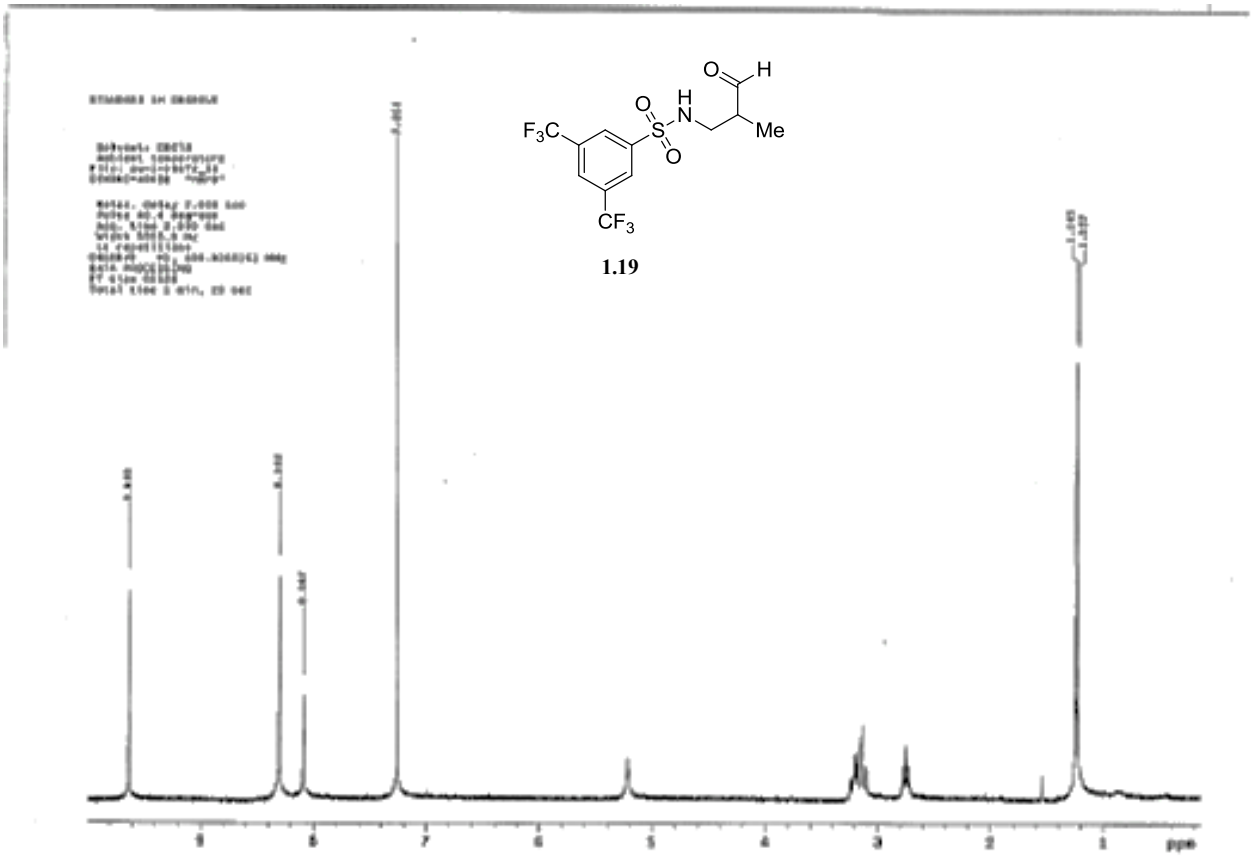
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25663.4 Hz
92 repetitions
OBSERVE C13, 100.5868877
DECOUPLE H1, 400.0288163
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 1 hr, 50 min, 9 sec

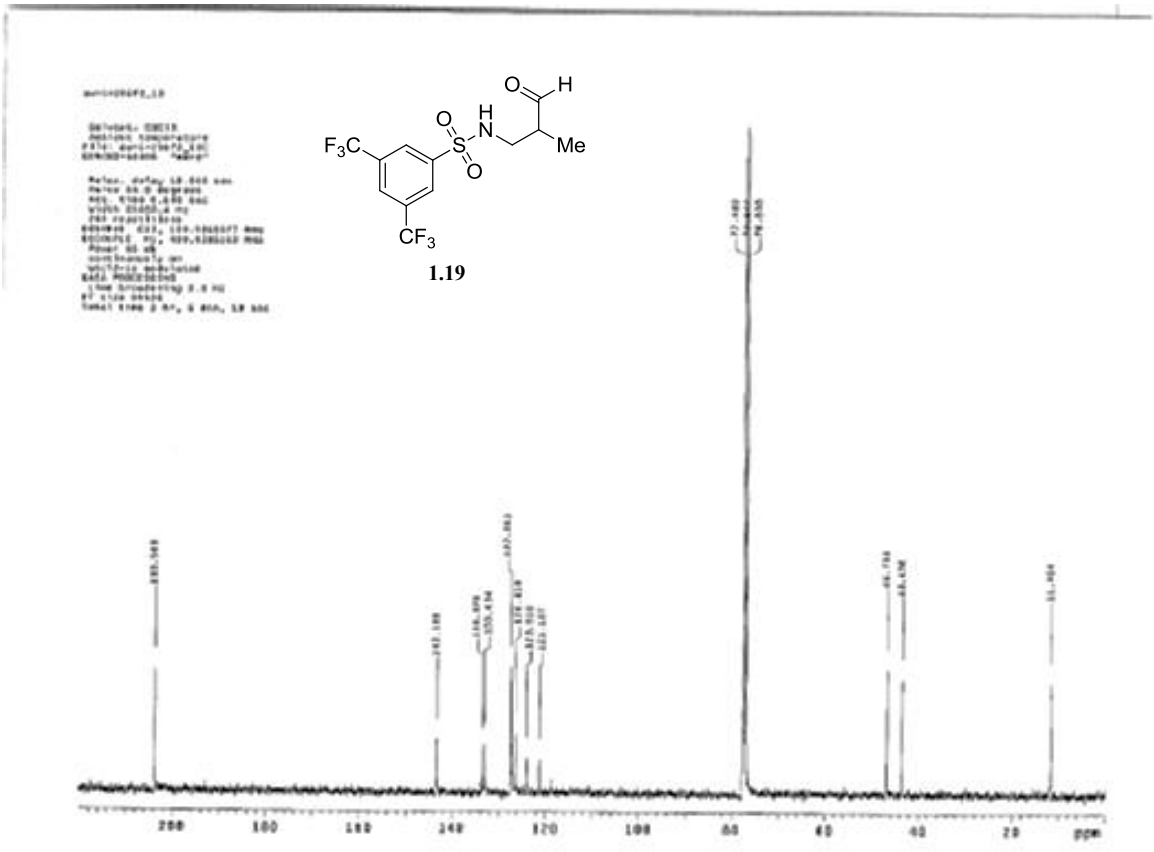



aw-1-223
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 48.4 degrees
Acq. time 3.000 sec
Width 5988.5 Hz
16 repetitions
OBSERVE H1, 400.0268152 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
HO
O
N
S
O
F3C
CF3
8.335
8.084
7.361
7.261
7.260
5.574
5.569
5.562
5.557
3.562
3.555
3.539
3.520
3.513
3.223
3.208
3.200
3.184
3.176
3.161
3.025
2.213
2.193
2.173
2.157
2.137
2.116
2.086
2.008
1.980
1.961
1.976
1.959
1.946
1.941
1.928
1.921
1.913
1.909
1.896
1.868
1.863
1.671
1.254
8
7
6
5
4
3
2
1
ppm


aw-1-233c
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.849 sec
Width 25883.4 Hz
240 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0238163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 2.0 Hz
FT size 65536
Total time 6 hr, 47 min, 24 sec
HO
O
N
S
O
F3C
CF3
77.409
77.189
76.970
76.850
127.535
84.377
47.628
34.428
23.199
140
120
100
80
60
40
20
ppm



1.19



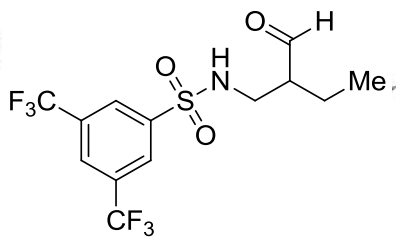
1.19

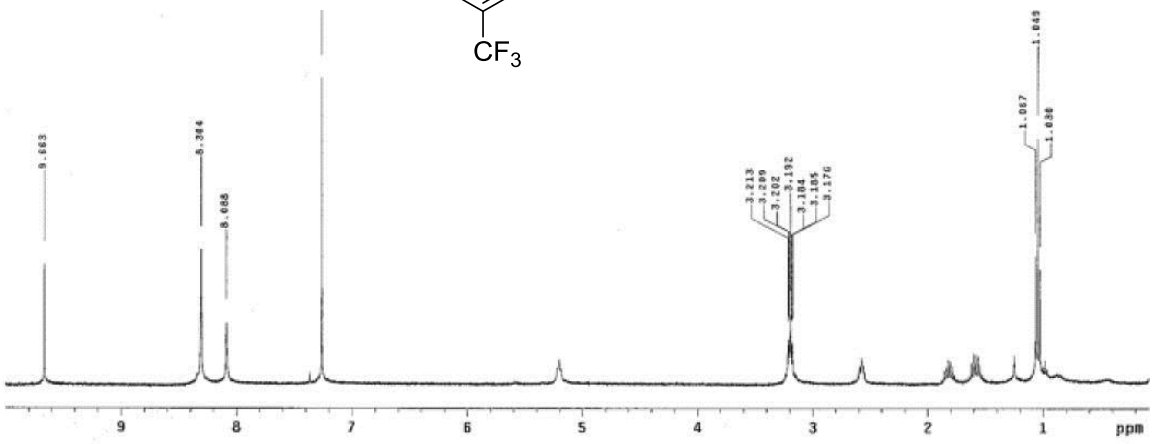
aw-1-281f20_34H

Solvent: CDCl3
Ambient temperature
File: aw-1-281f20_34
GEMINI-400BB "nmr8"

Relax. delay 2.000
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.02
DATA PROCESSING

1.22



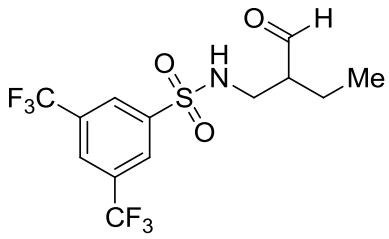


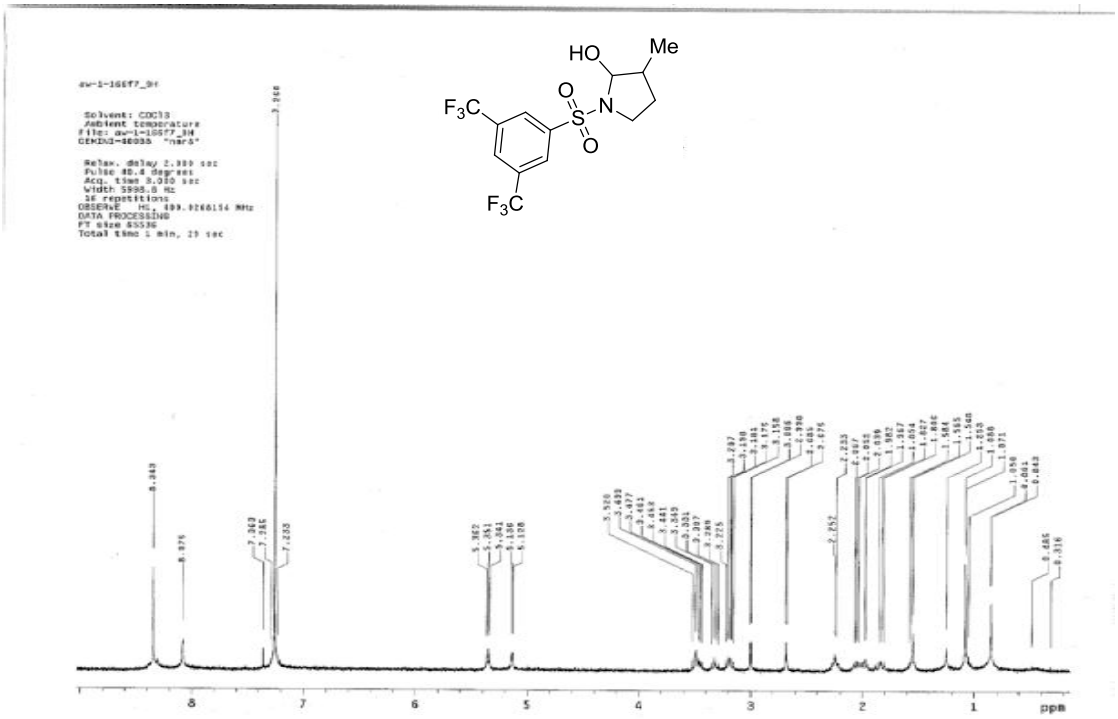
aw-1-281f20_34C2

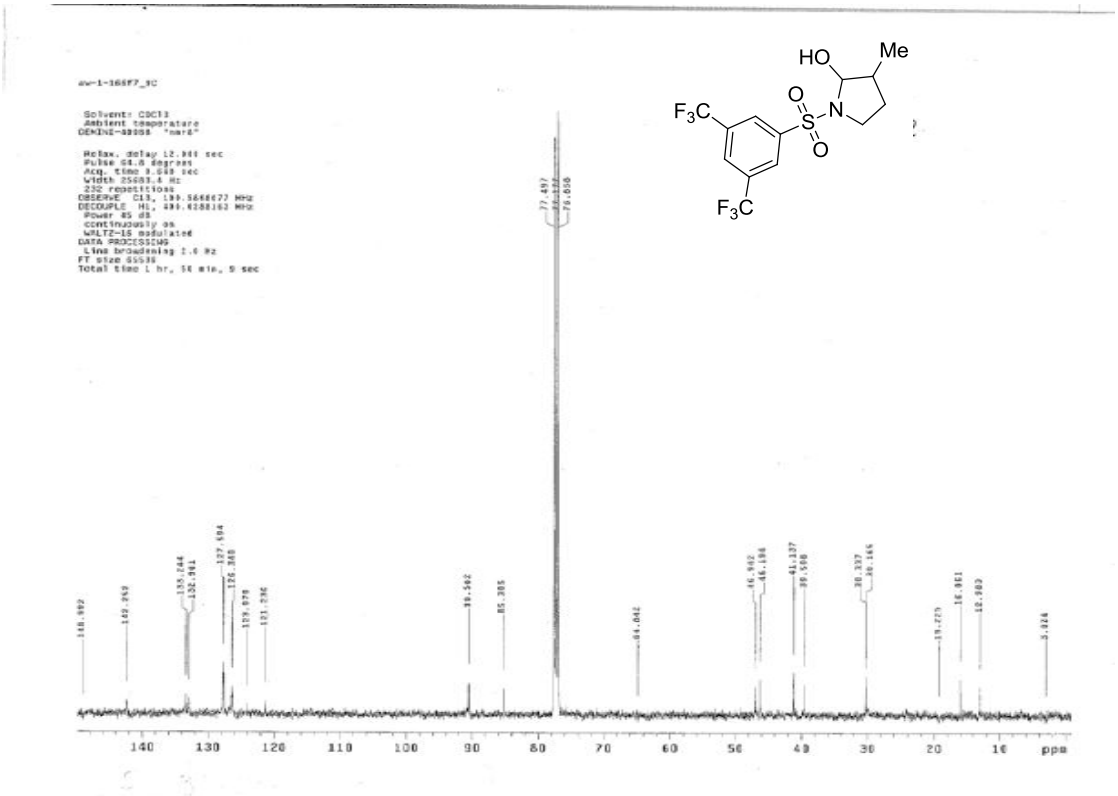
Solvent: CDCl3
Ambient temperature
File: aw-1-281f20_34C2
GEMINI-400BB "nmr8"

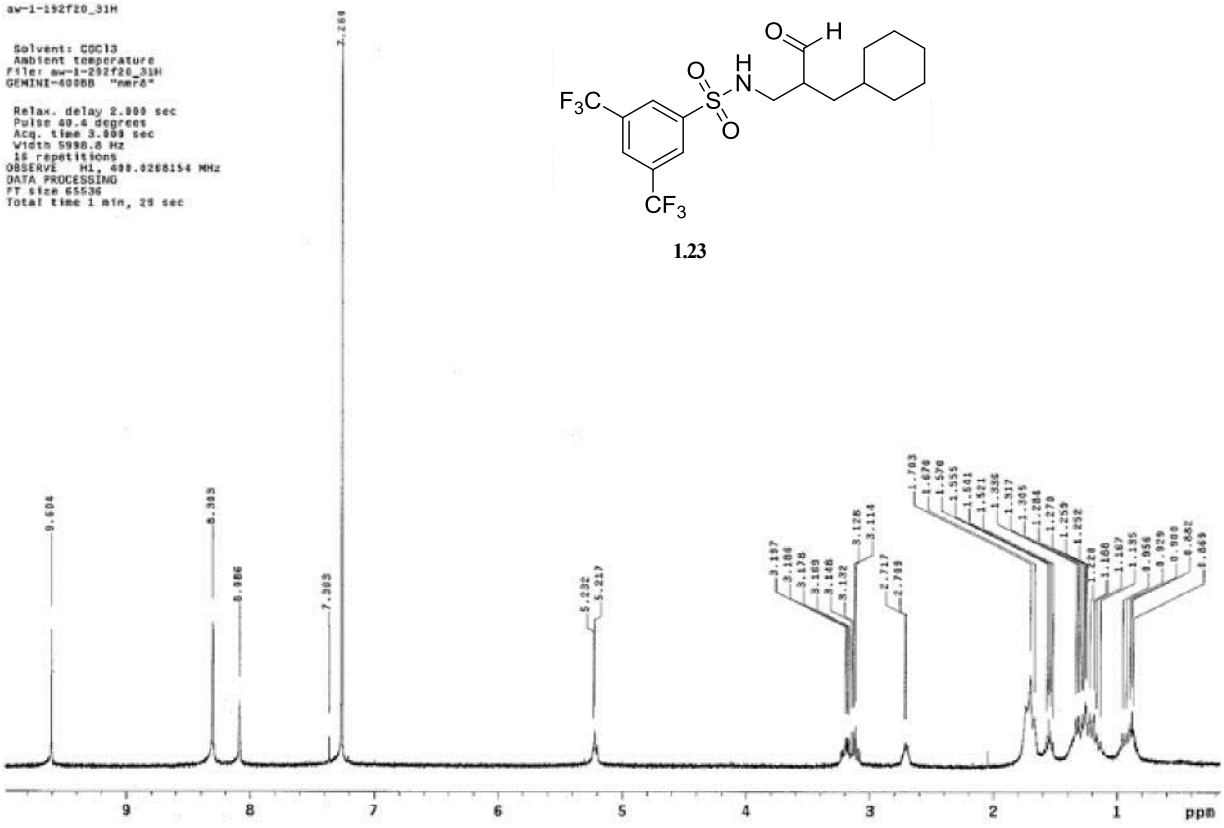
Relax. delay 15.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25603.4 Hz
528 repetitions
OBSERVE C13, 100.5868077
DECOUPLE H1, 400.0288163
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 22 hr, 31 min, 35 sec

1.22

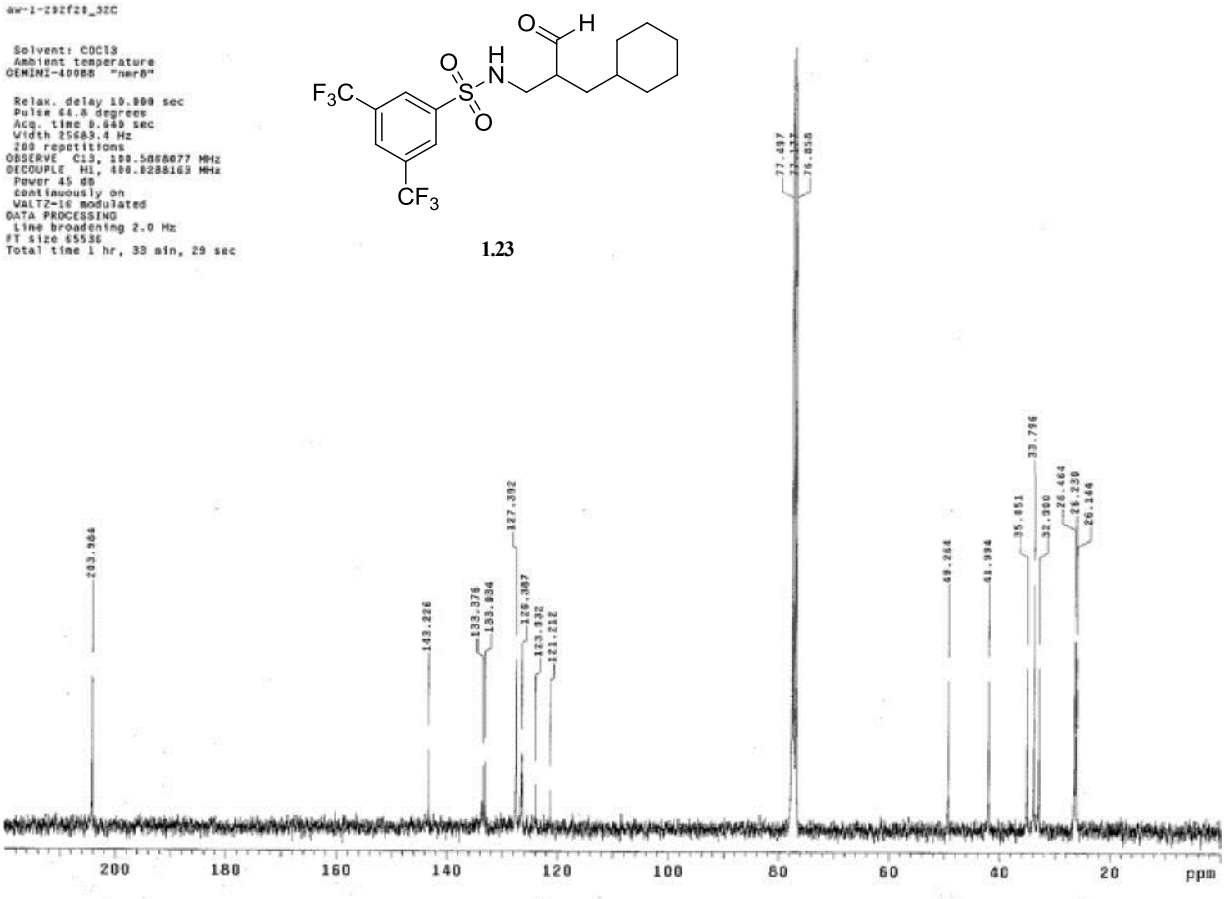



HO
Me
O
S
N
O
F3C
F3C
ppm

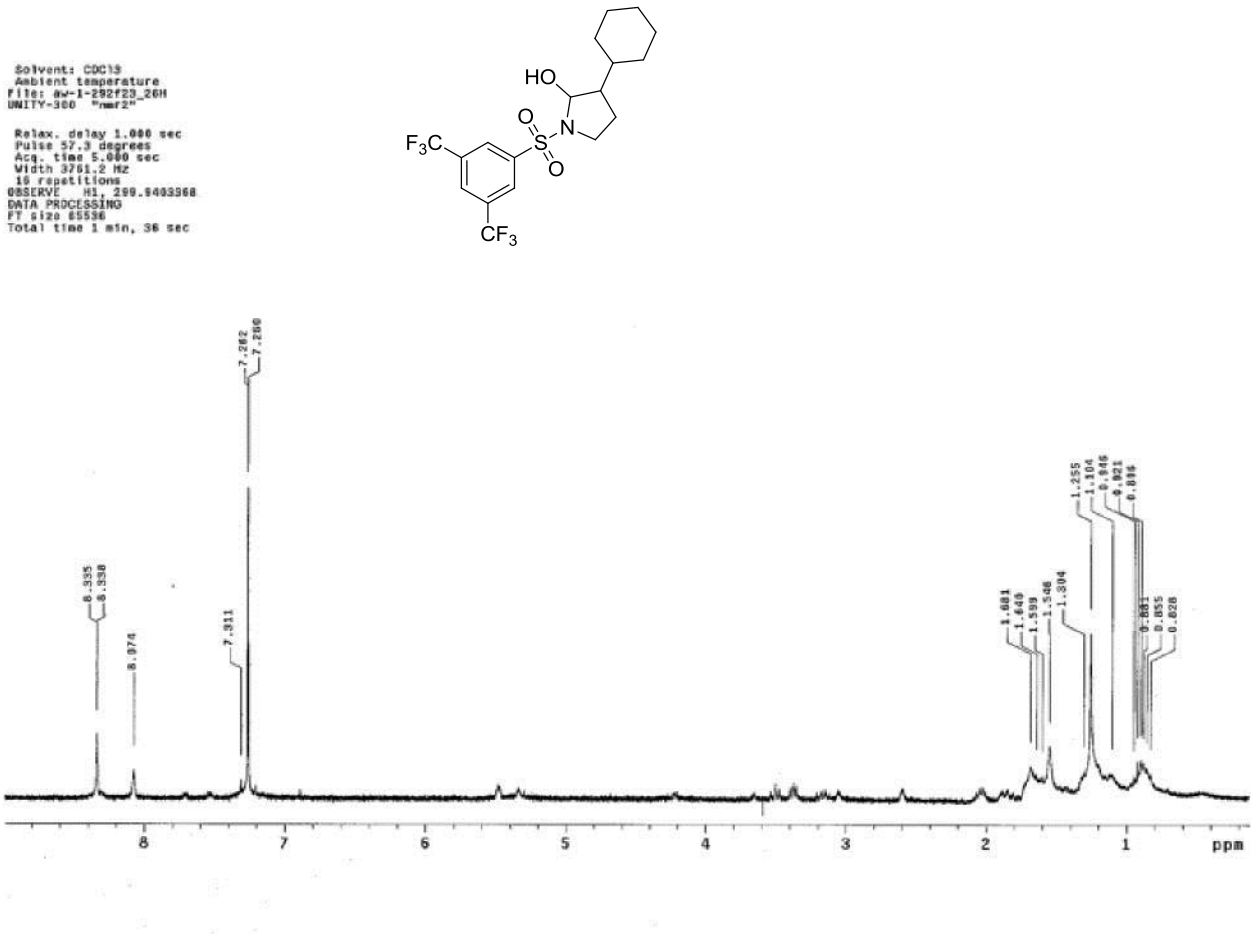

HO
Me
O
S
N
O
F3C
F3C
ppm

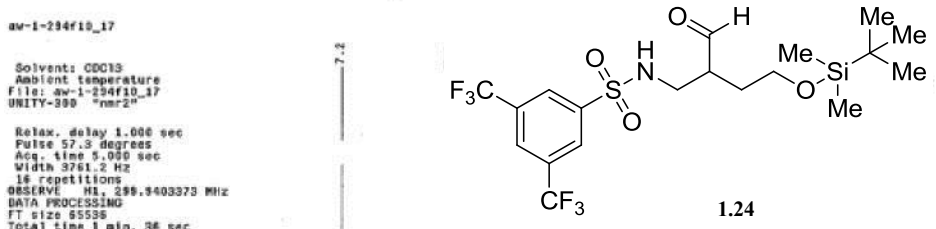

aw-1-192f20_31H
Solvent: CDCl3
Ambient temperature
File: aw-1-292f20_31H
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0268154 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
9.604
8.383
8.066
7.903
7.268
5.232
5.217
3.197
3.188
3.178
3.169
3.146
3.132
3.126
3.114
2.717
2.708
1.703
1.678
1.570
1.555
1.541
1.521
1.336
1.317
1.305
1.284
1.270
1.259
1.252
1.220
1.168
1.167
1.135
0.956
0.929
0.900
0.882
0.869
9
8
7
6
5
4
3
2
1
ppm

1.23


aw-1-292f20_32C
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.649 sec
Width 25683.4 Hz
200 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 1 hr, 33 min, 29 sec
193.984
143.226
133.376
133.034
127.392
126.987
123.932
121.212
77.497
77.172
76.836
69.264
61.994
35.851
33.796
32.300
26.464
26.230
26.144
200
180
160
140
120
100
80
60
40
20
ppm

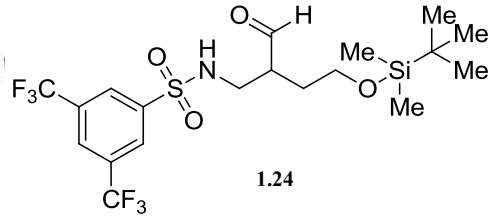
1.23


Solvent: CDCl3
Ambient temperature
File: av-1-292f23_20H
UNITY-300 "rmr2"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 299.9403368
DATA PROCESSING
FT size 65536
Total time 1 min, 36 sec
HO
O
S
N
O
F3C
CF3
8.335
8.330
8.074
7.311
7.282
7.266
1.681
1.649
1.599
1.548
1.304
1.255
1.104
0.946
0.921
0.898
0.881
0.855
0.828
8
7
6
5
4
3
2
1
ppm



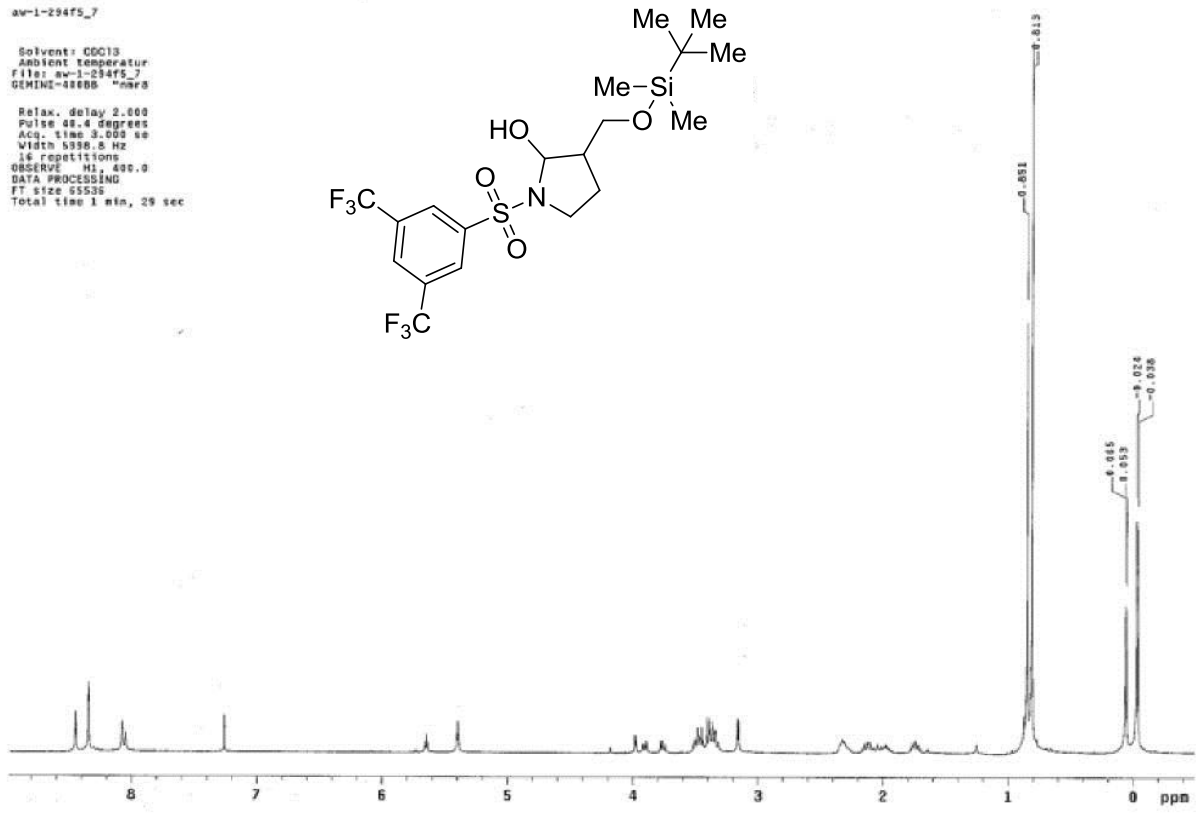
1.24

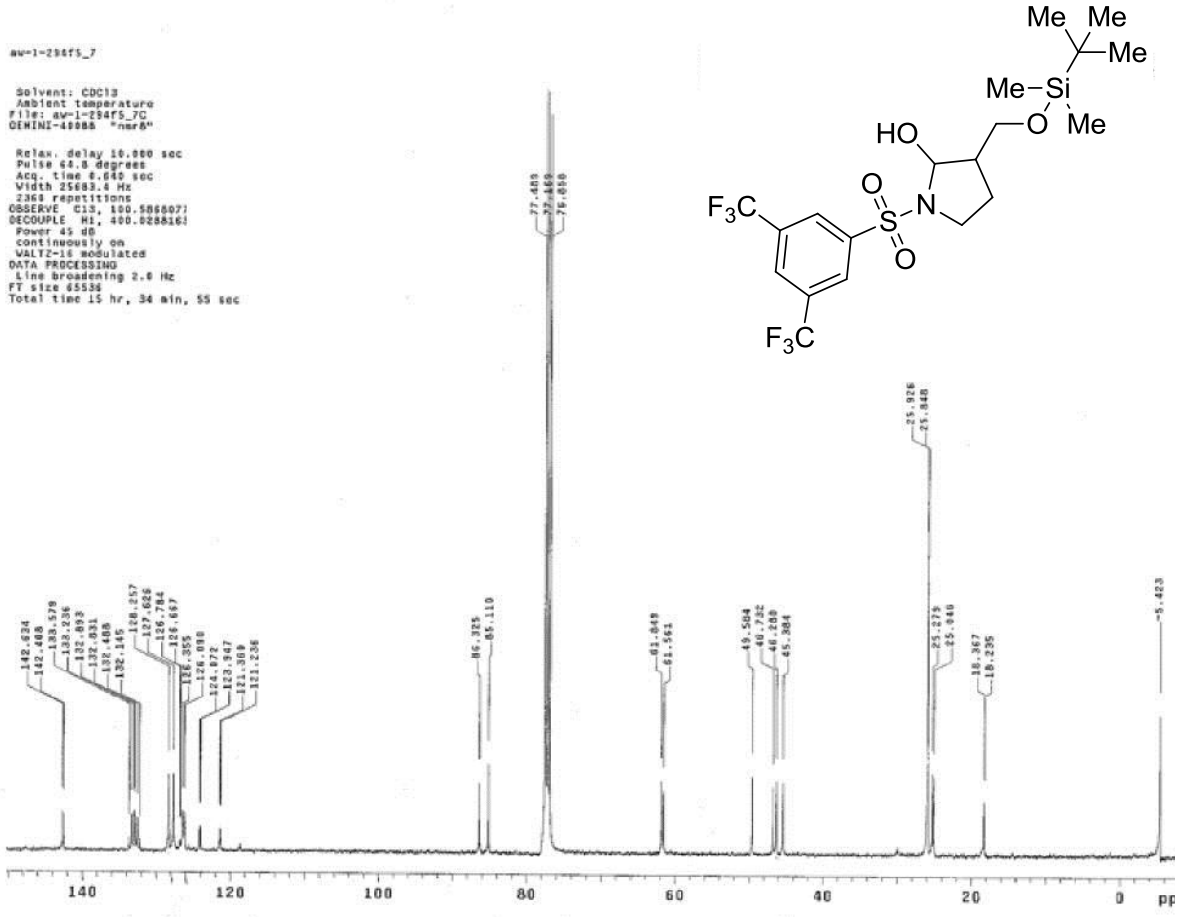
aw-1-294f10_17
Solvent: CDCl3
Ambient temperature
File: aw-1-294f10_17
UNITY-300 "nmr2"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 299.5403373 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 36 sec
9.658
8.293
8.080
7.260
3.752
3.734
3.715
3.254
3.233
0.867
0.847
0.046
0.039
ppm



1.24

aw-1-294f10_17C
Solvent: CDCl3
Ambient temperature
File: aw-1-294f10_17C
GEMINI-400BB "nmr6"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25603.4 Hz
280 repetitions
OBSERVE C13, 100.5868397 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 3 hr, 6 min, 59 sec
77.170
76.851
76.530
25.631
5.703
ppm

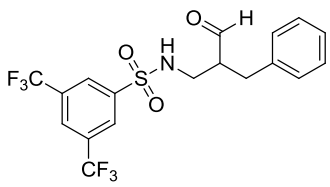

aw-1-294f5_7
Solvent: CDCl3
Ambient temperatur
File: aw-1-294f5_7
GEMINI-400BB "nmr8
Relax. delay 2.000
Pulse 48.4 degrees
Acq. time 3.000 se
Width 5338.8 Hz
16 repetitions
OBSERVE H1, 400.0
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
Me Me
Me
Me–Si
O Me
HO
O
S
N
O
F3C
F3C
8.613
0.691
9.024
0.038
0.065
0.053
8
7
6
5
4
3
2
1
0
ppm


aw-1-294f5_7
Solvent: CDCl3
Ambient temperature
File: aw-1-294f5_7C
GEMINI-400BB "nmr8"
Relax. delay 10.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
2368 repetitions
OBSERVE C13, 100.5868071
DECOUPLE H1, 400.0288161
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 15 hr, 34 min, 55 sec
Me Me
Me
Me–Si
O Me
HO
O
S
N
O
F3C
F3C
77.469
77.149
76.830
25.926
25.848
5.423
140
120
100
80
60
40
20
0
ppm

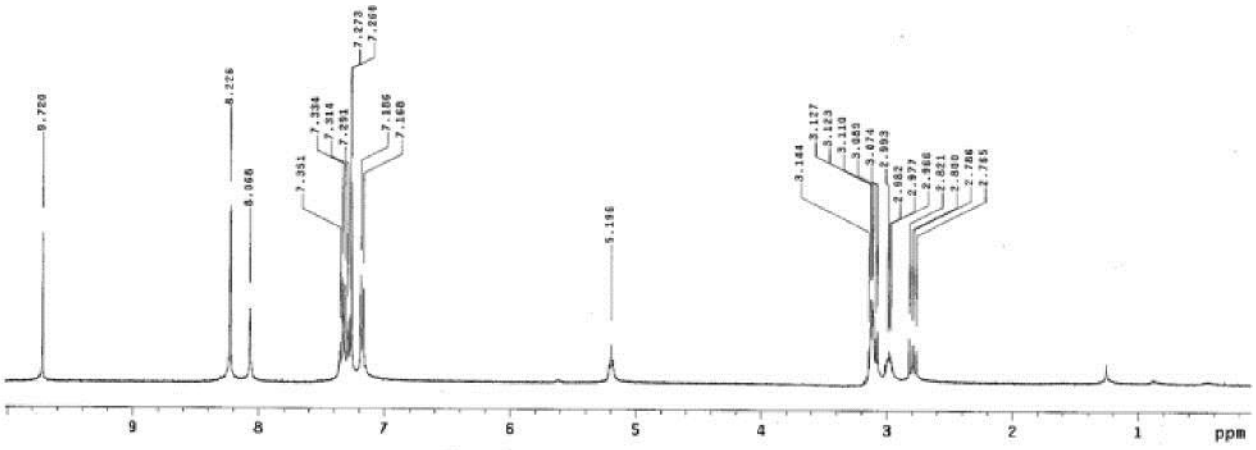
aw-2-1f20_32

Solvent: CDCl3
Ambient temperature
File: aw-2-1f20_32H
GEMINI-400BB "nmr8"

Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5388.8 Hz
16 repetitions
OBSERVE H1, 400.0268156 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec



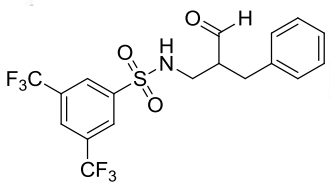
1.25



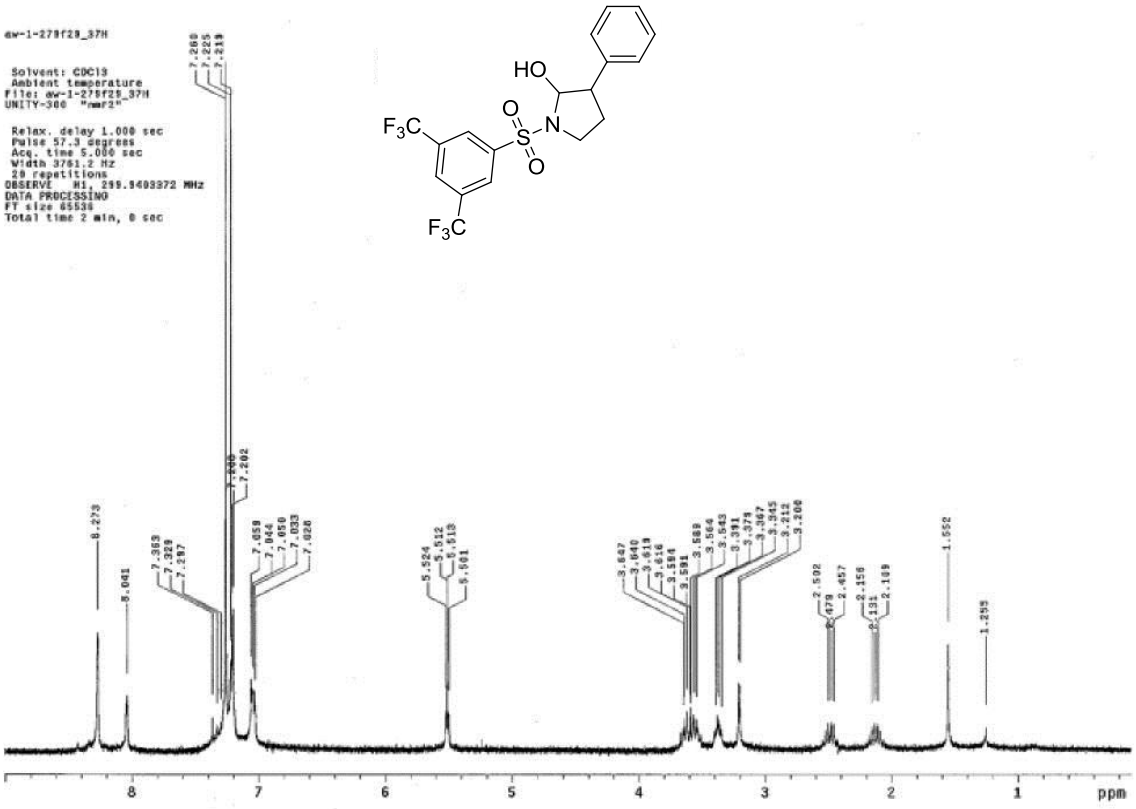
aw-2-1f20_32C

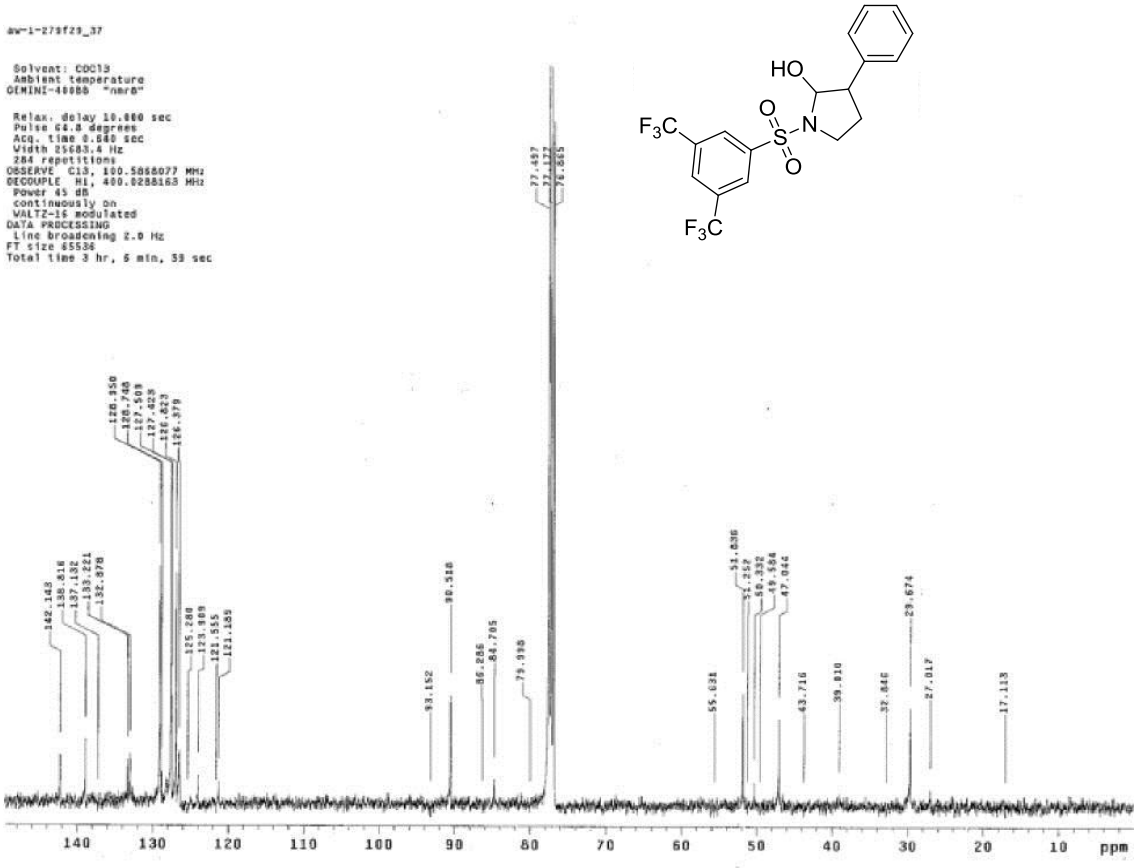
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

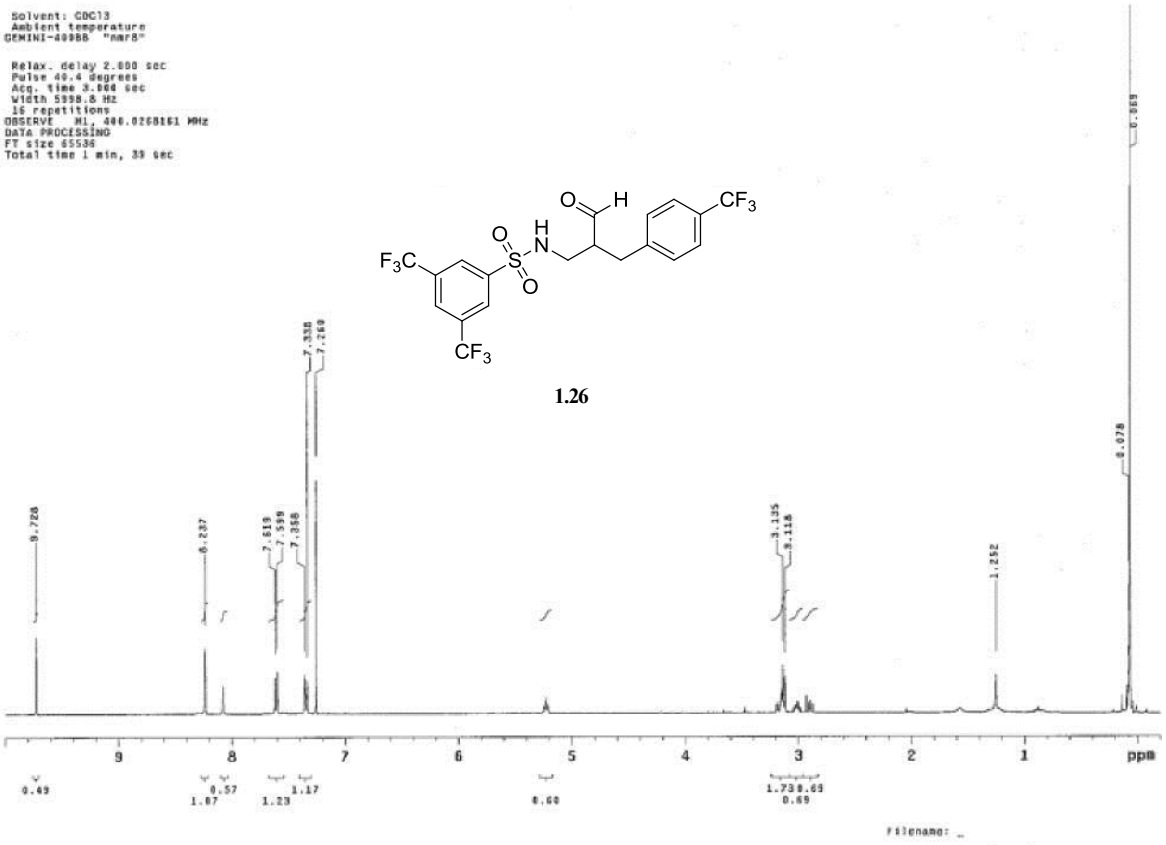
Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 4.640 sec
Width 25683.4 Hz
216 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously On
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 1 hr, 50 min, 9 sec



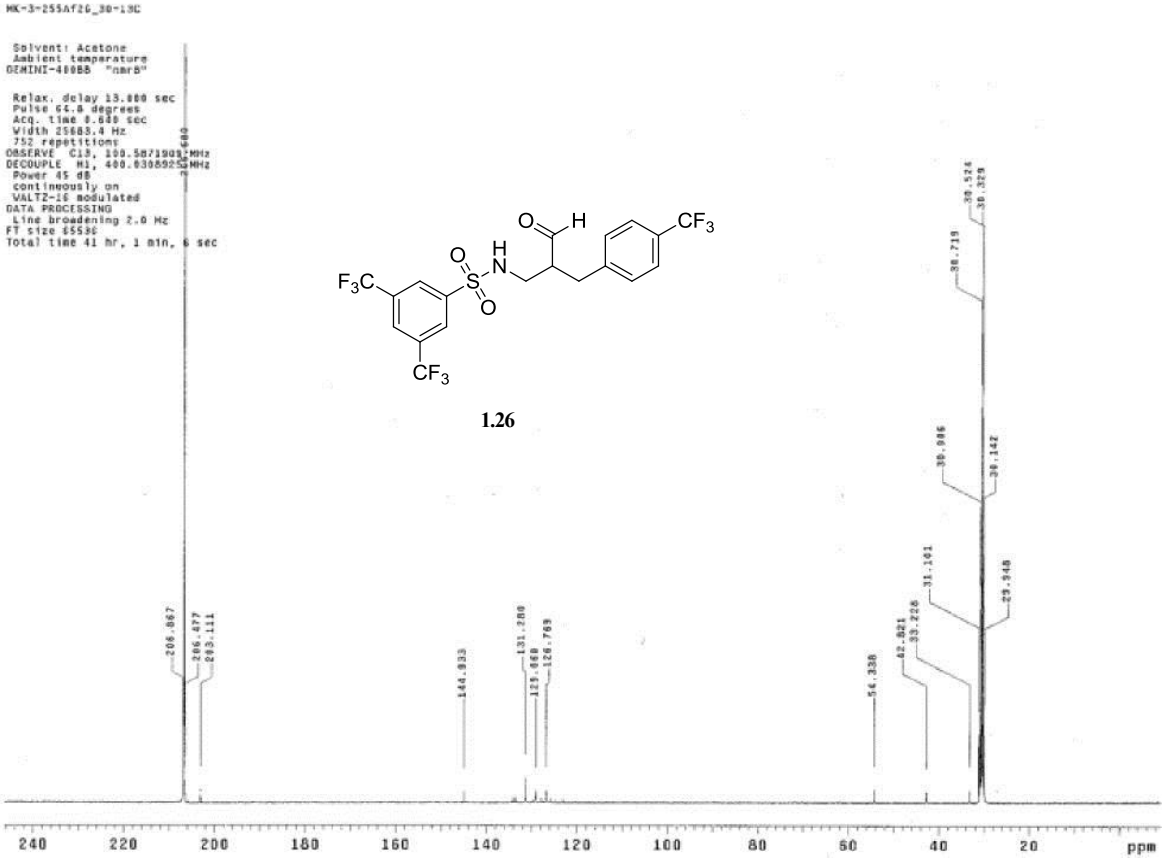
1.25


HO
O
S
N
O
F3C
F3C
ppm

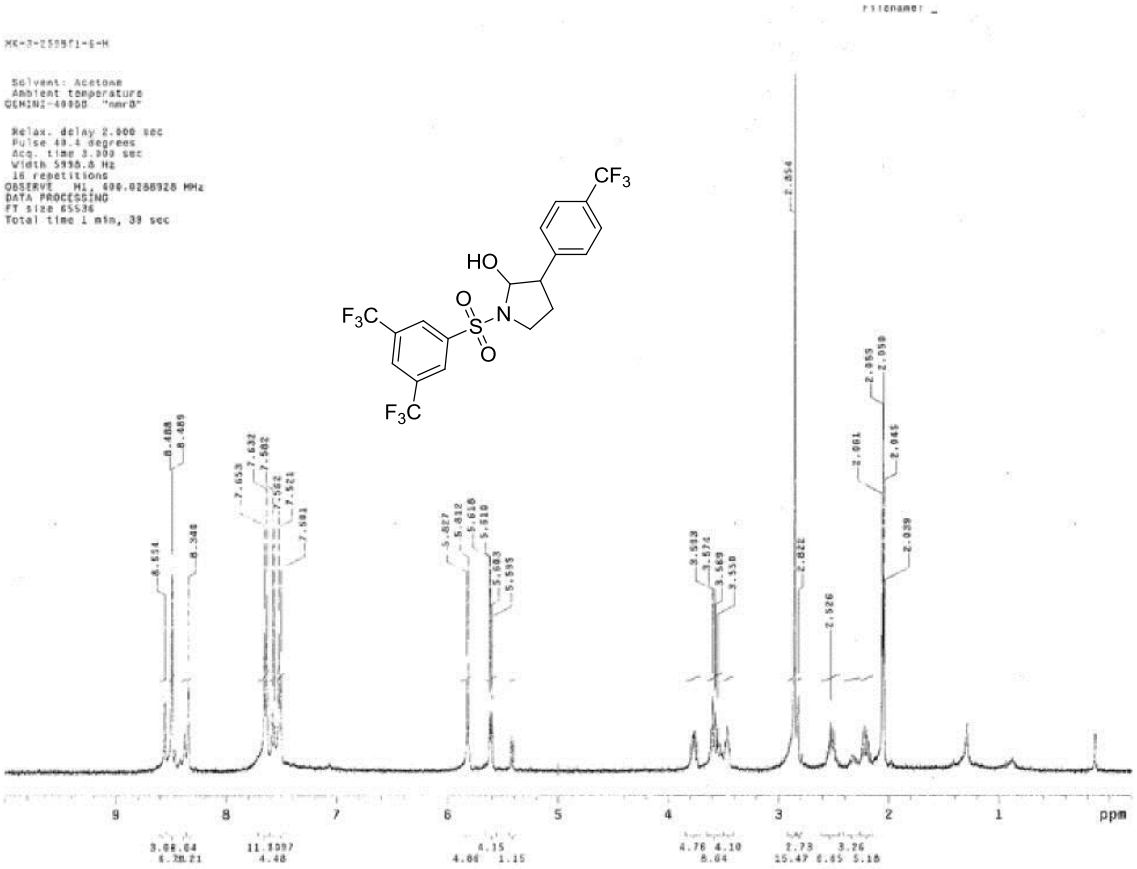

HO
O
S
N
O
F3C
F3C
ppm

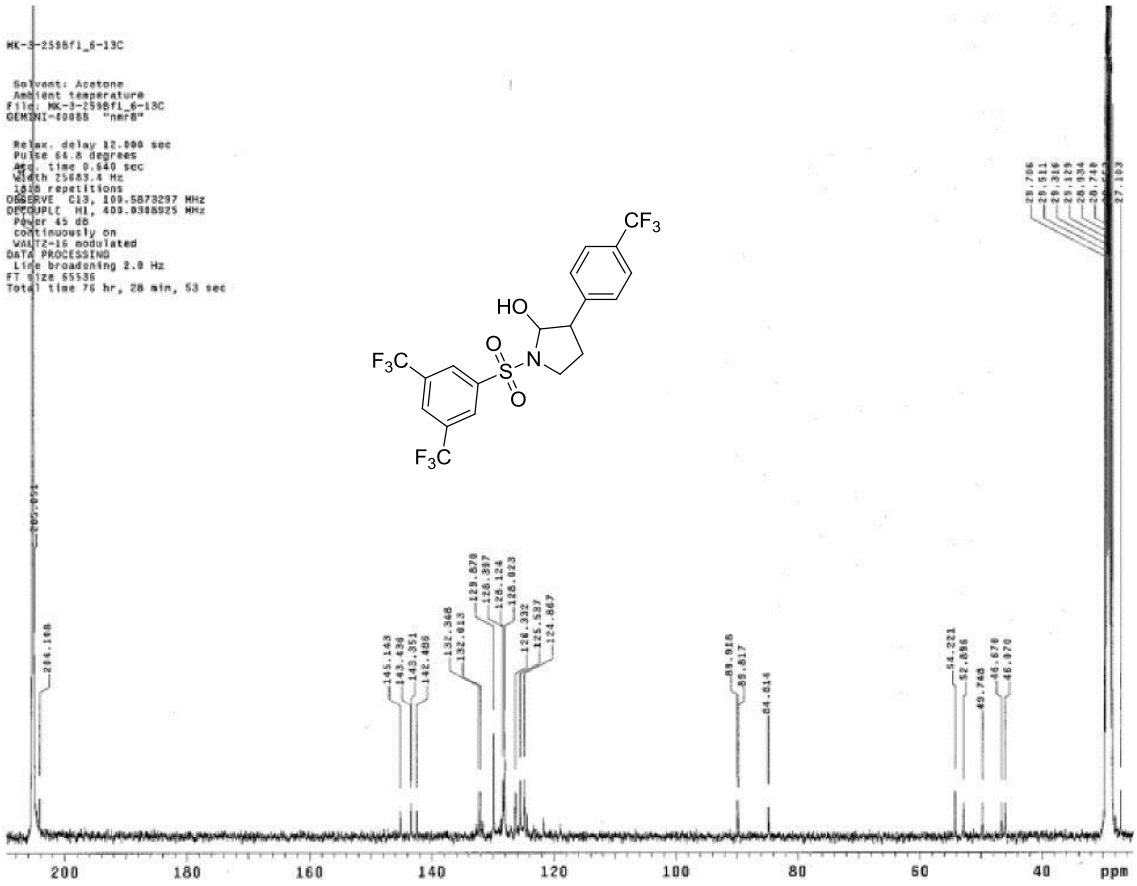

Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0268161 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 39 sec
9.726
8.237
7.818
7.569
7.388
7.338
7.269
3.135
3.118
1.252
0.869
8.078
9
8
7
6
5
4
3
2
1
ppm
0.49
1.87
0.57
1.23
1.17
6.68
1.73
0.69
0.69
Filename:

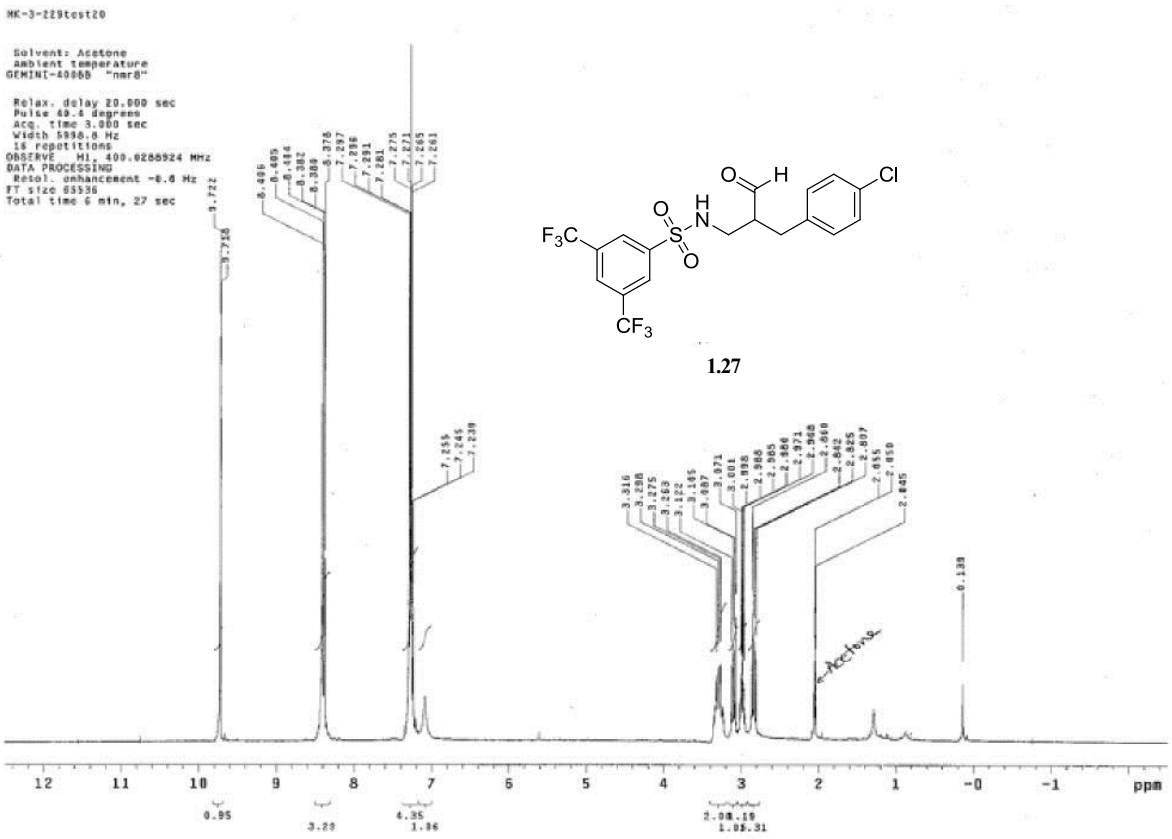
1.26


HK-3-255Af26_30-13C
Solvent: Acetone
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 13.000 sec
Pulse 64.8 degrees
Acq. time 0.680 sec
Width 25683.4 Hz
752 repetitions
OBSERVE C13, 100.5871983 MHz
DECOUPLE H1, 400.0308925 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 41 hr, 1 min, 6 sec
206.867
206.477
205.111
144.933
131.288
129.468
126.769
54.338
42.821
33.228
31.161
30.524
30.329
30.719
30.046
30.142
29.948
240
220
200
180
160
140
120
100
80
60
40
20
ppm

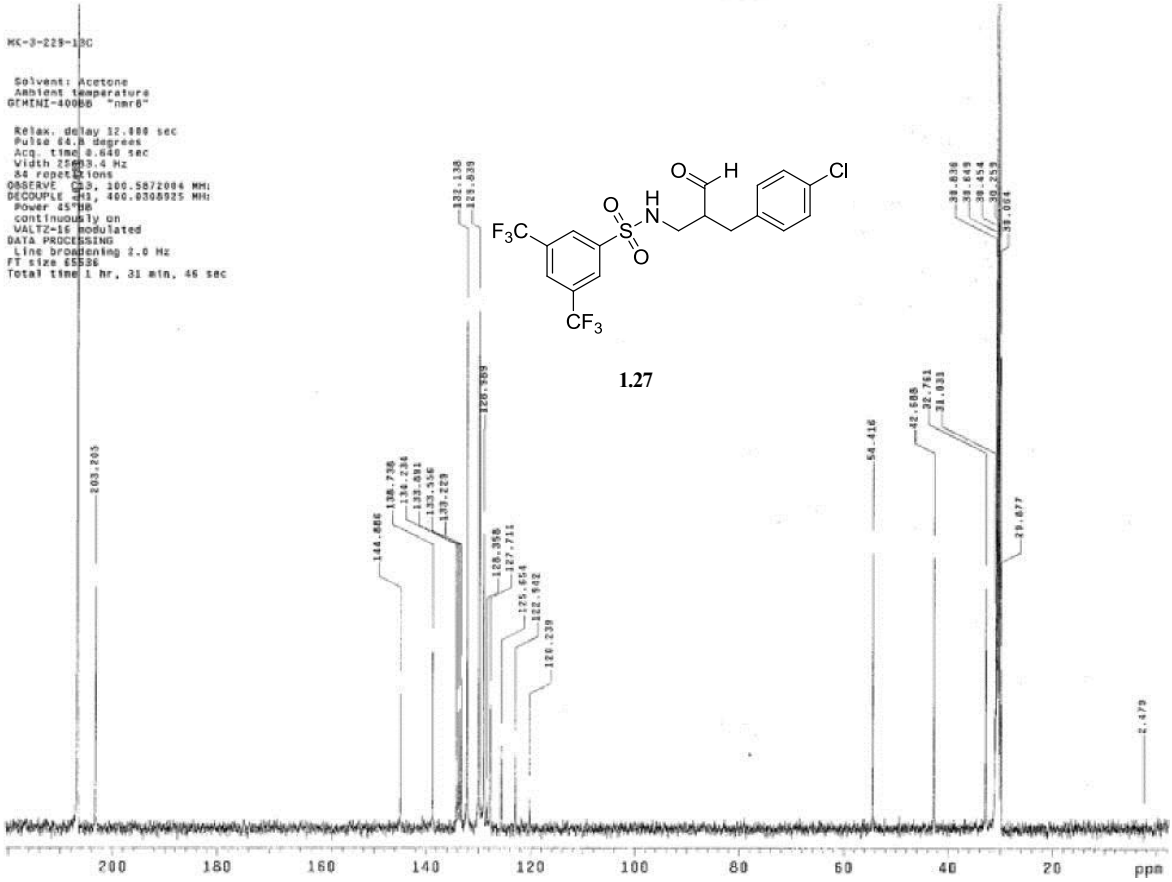
1.26


CF3
HO
O
S
N
O
F3C
F3C
ppm

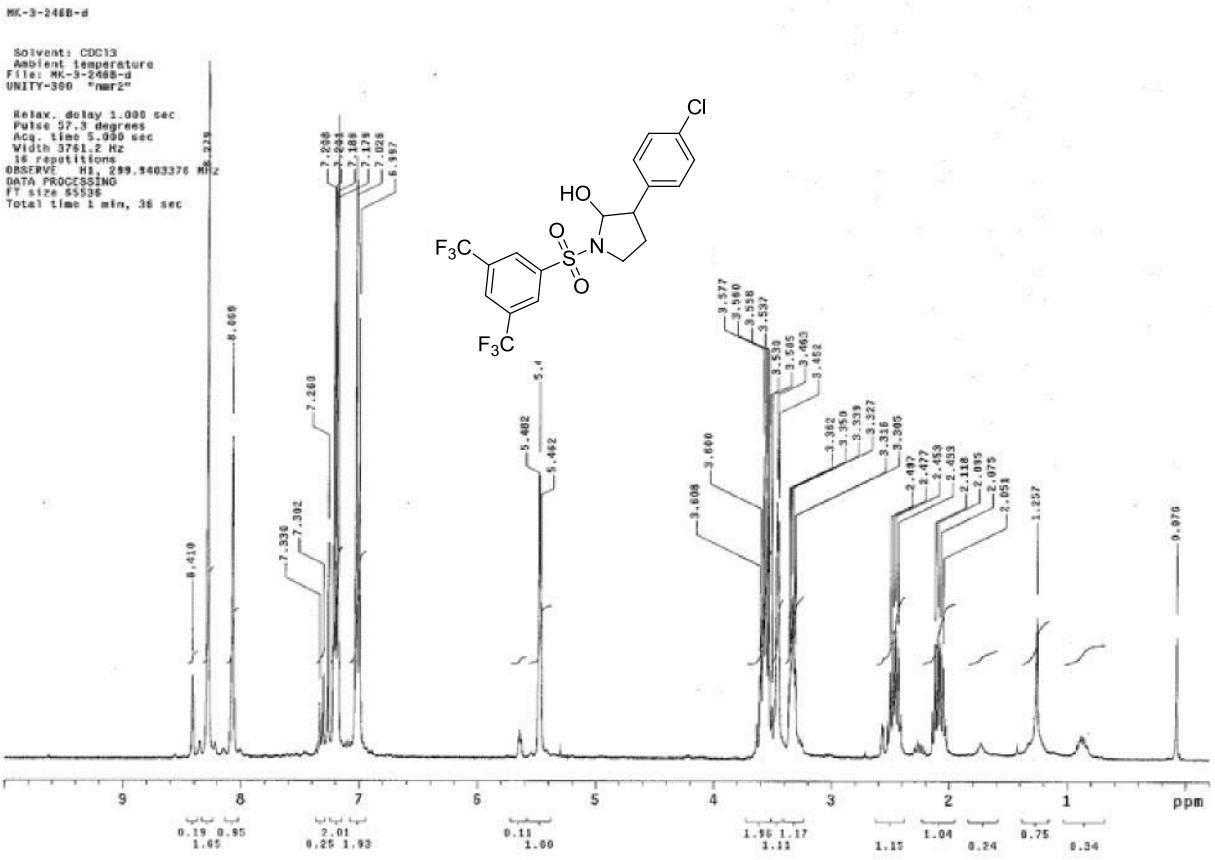

CF3
HO
O
S
N
O
F3C
F3C
ppm

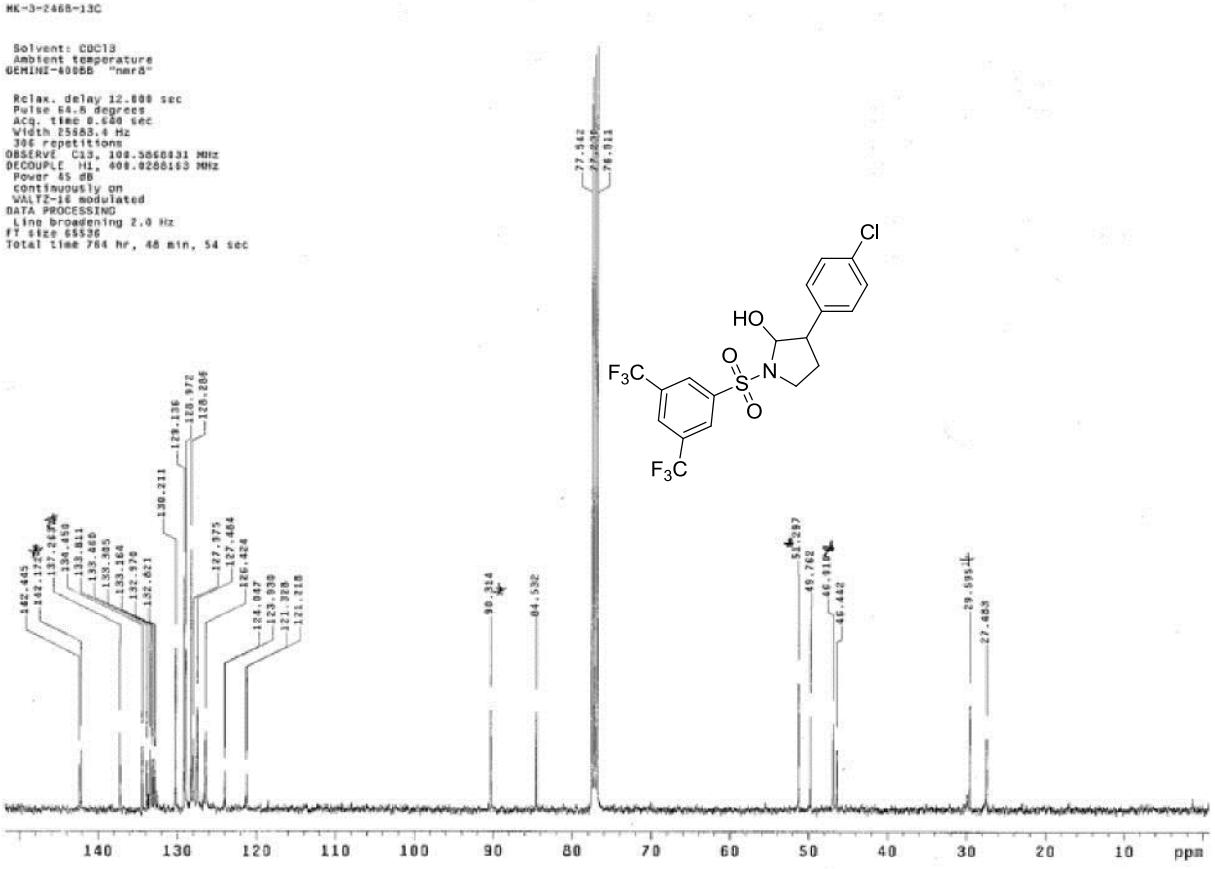

MK-3-229test20
Solvent: Acetone
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 20.000 sec
Pulse 49.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0288924 MHz
DATA PROCESSING
Resol. enhancement -0.6 Hz
FT size 65536
Total time 6 min, 27 sec
Acetone
ppm

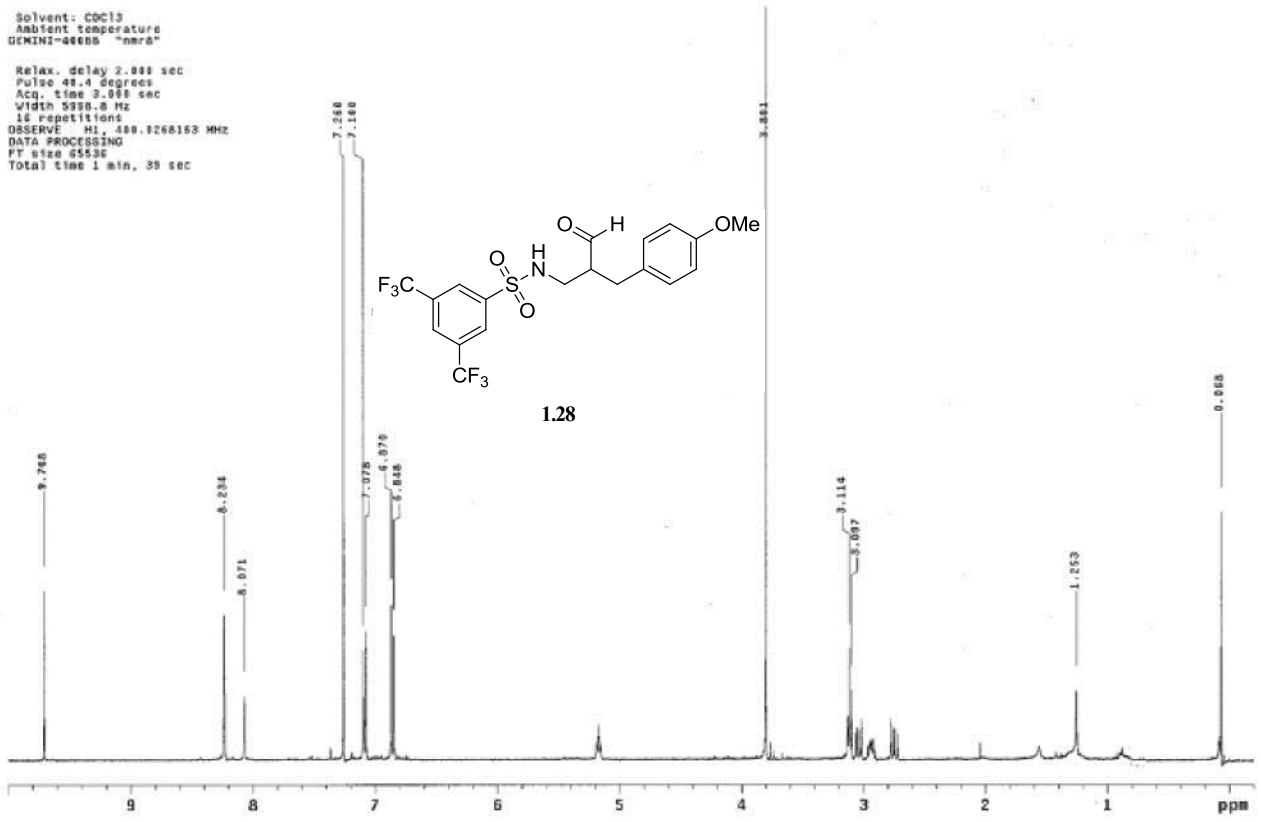
1.27


MK-3-229-13C
Solvent: Acetone
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25063.4 Hz
84 repetitions
OBSERVE C13, 100.5872004 MHz
DECOUPLE H1, 400.0308925 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 1 hr, 31 min, 46 sec
ppm

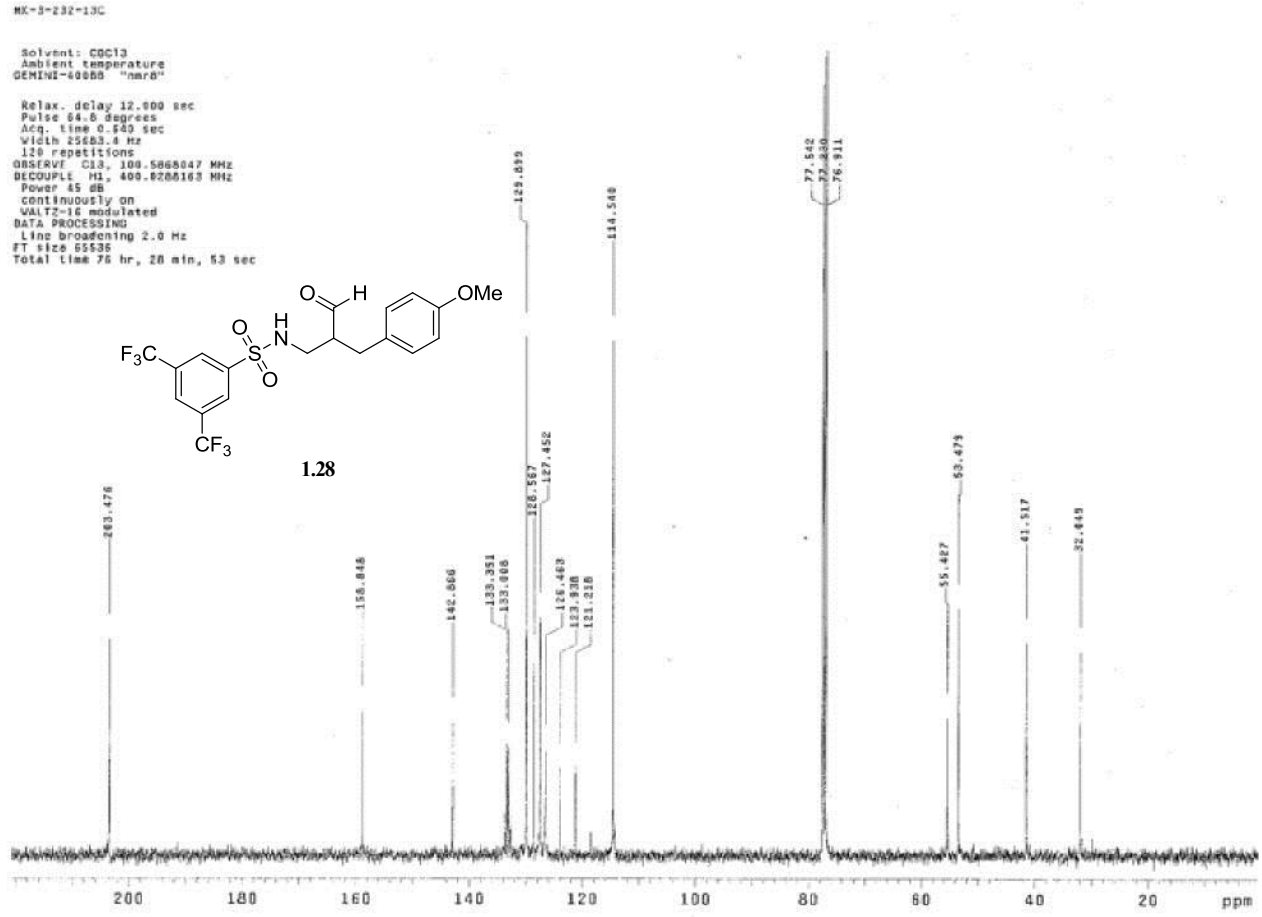
1.27


MK-3-246B-d
Solvent: CDCl3
Ambient temperature
File: MK-3-246B-d
UNITY-300 "nmr2"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 299.9403376 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 36 sec
Cl
HO
N
S
O
F3C
CF3
ppm

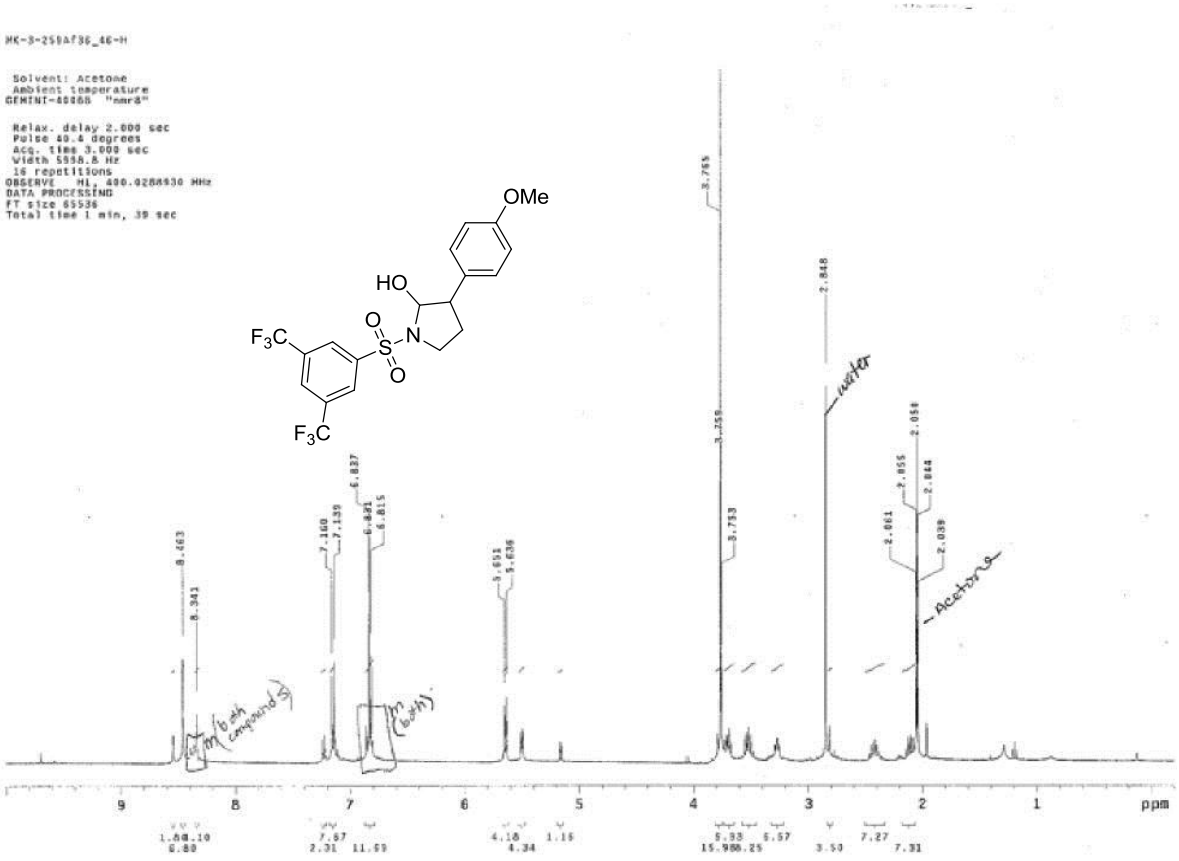

MK-3-246B-13C
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr4"
Relax. delay 12.000 sec
Pulse 64.6 degrees
Acq. time 0.680 sec
Width 25883.4 Hz
386 repetitions
OBSERVE C13, 100.5860431 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 764 hr, 48 min, 54 sec
Cl
HO
N
S
O
F3C
CF3
ppm

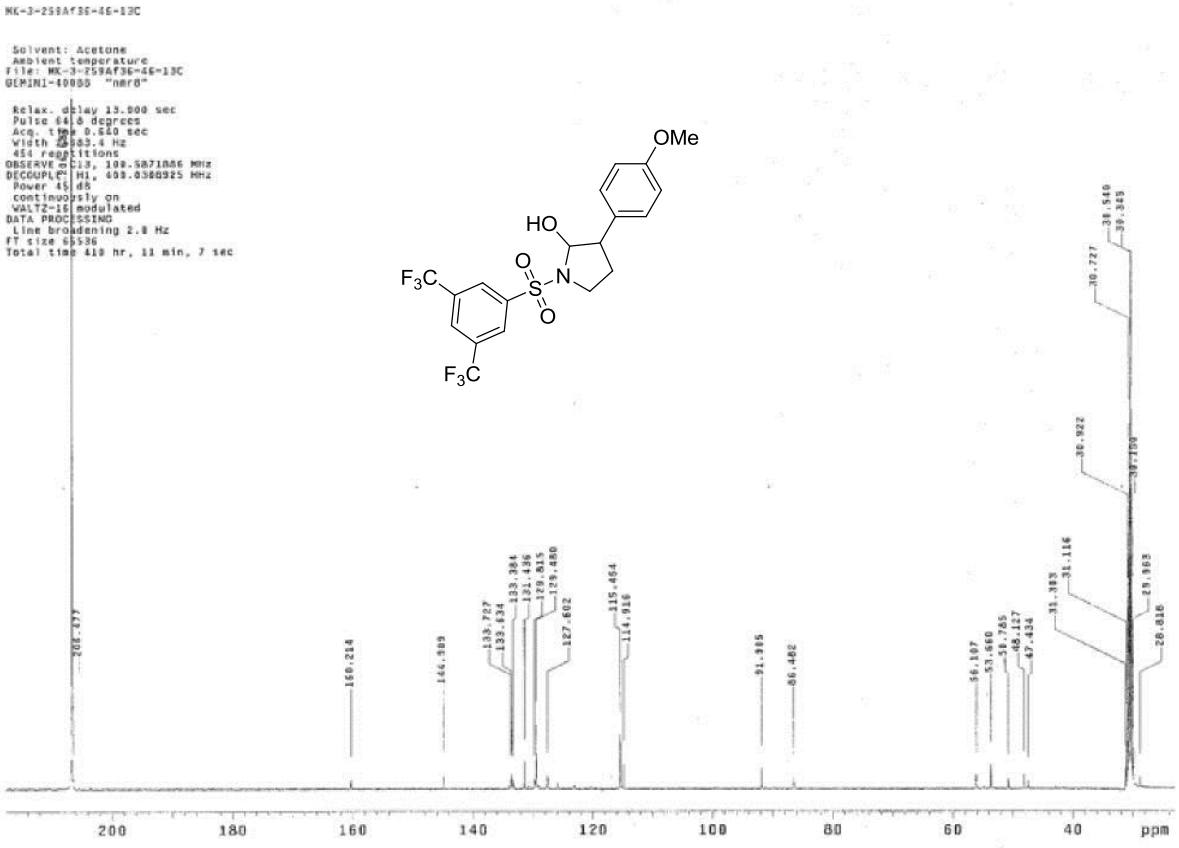

Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 48.4 degrees
Acq. time 3.000 sec
Width 5988.8 Hz
16 repetitions
OBSERVE H1, 400.0268163 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 39 sec
9.748
8.234
8.071
7.268
7.160
7.078
6.870
6.848
3.881
3.114
3.097
1.253
0.868
ppm

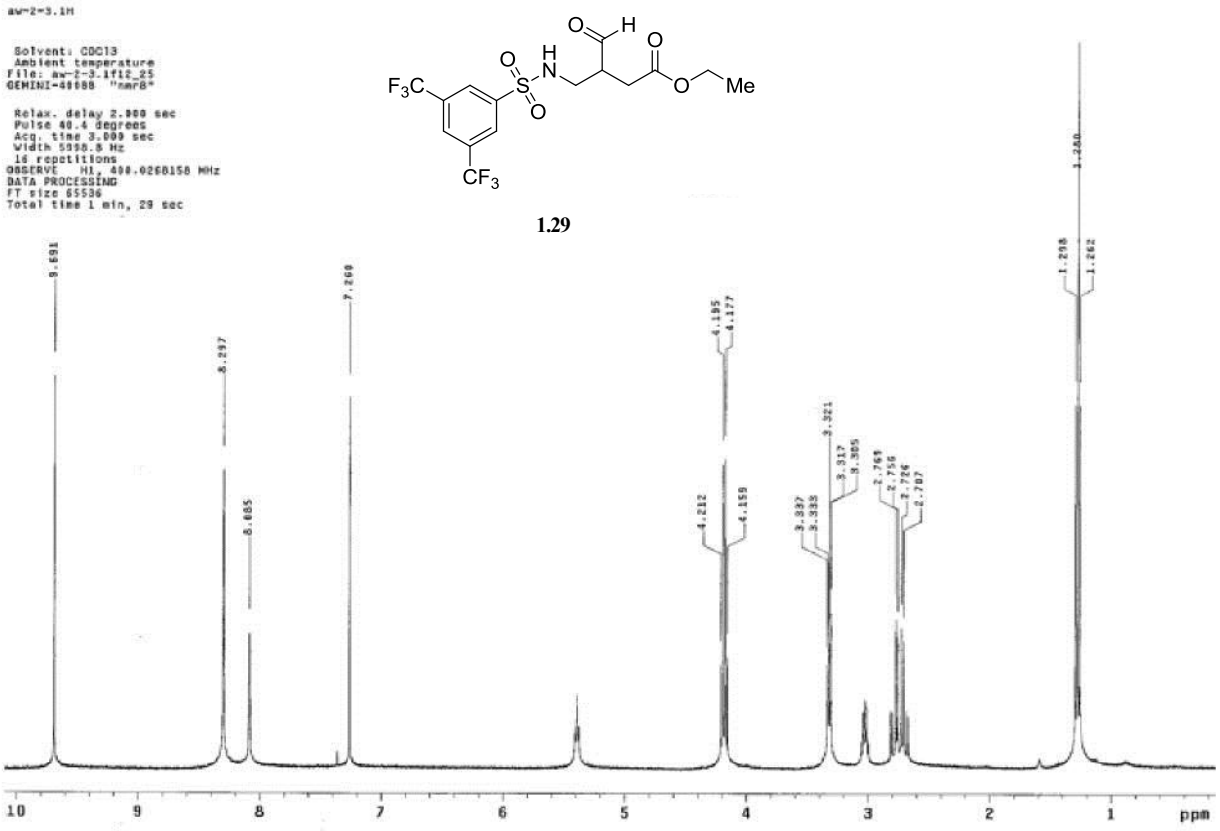
1.28

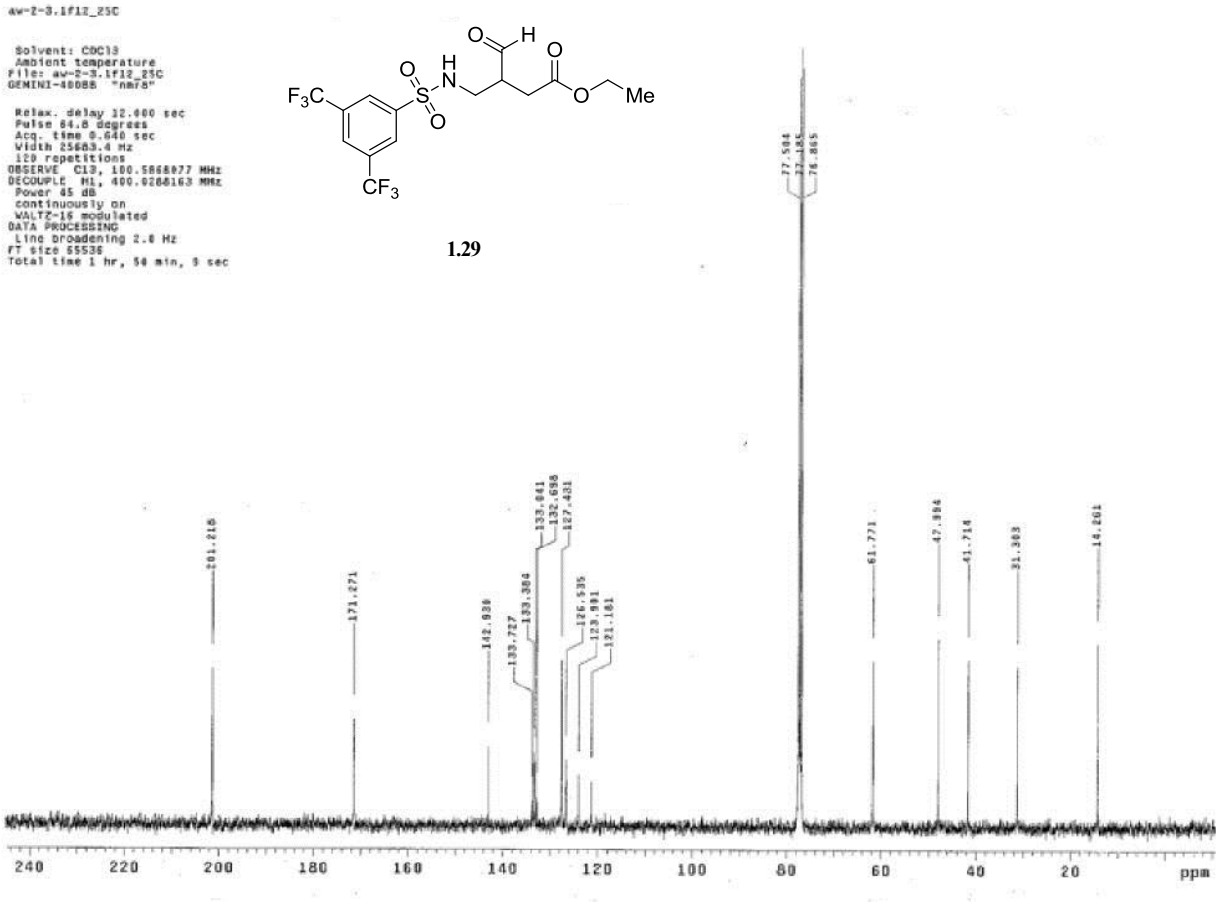

MK-3-232-13C
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 64.6 degrees
Acq. time 0.540 sec
Width 25683.4 Hz
128 repetitions
OBSERVE C13, 100.5868047 MHz
DECOUPLE H1, 400.0268163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 76 hr, 28 min, 53 sec
193.476
158.848
142.666
138.351
133.008
129.899
128.567
127.452
126.463
123.938
121.218
114.548
77.542
77.230
76.911
55.427
53.479
41.517
32.849
ppm

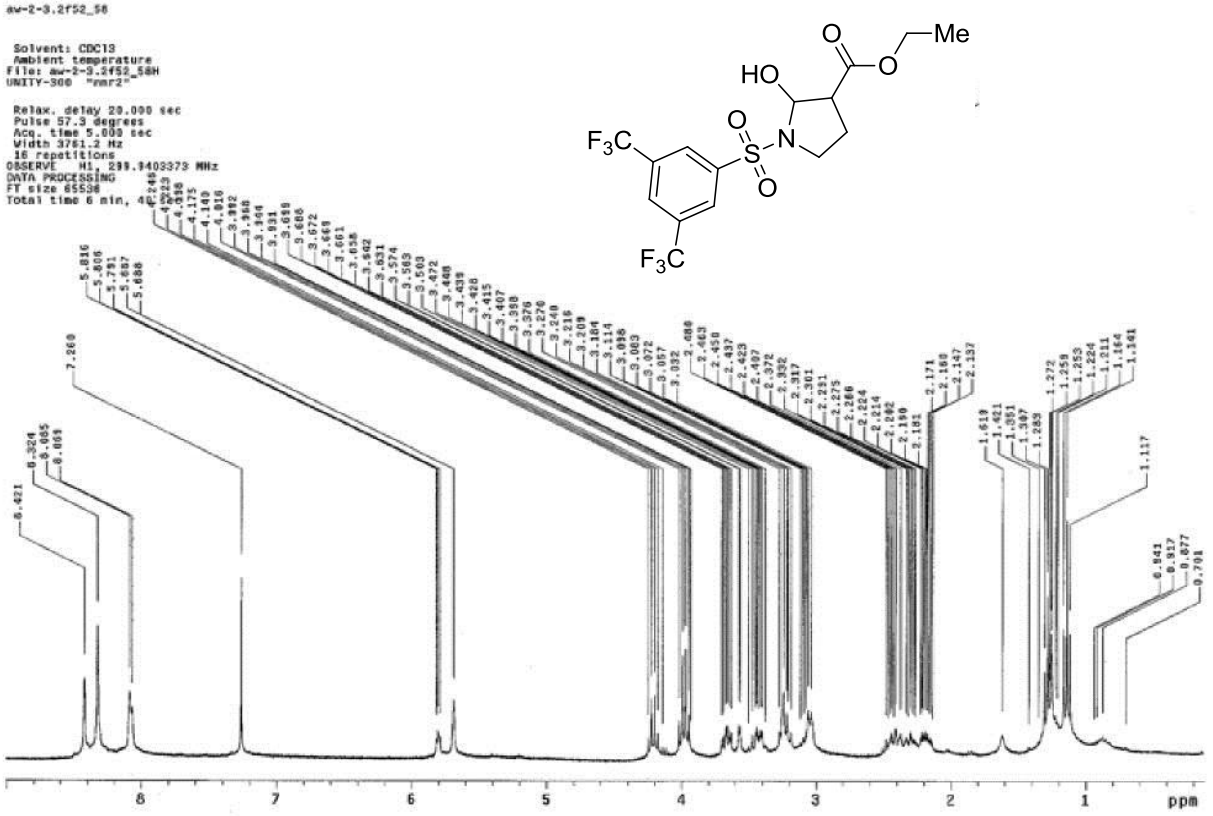
1.28

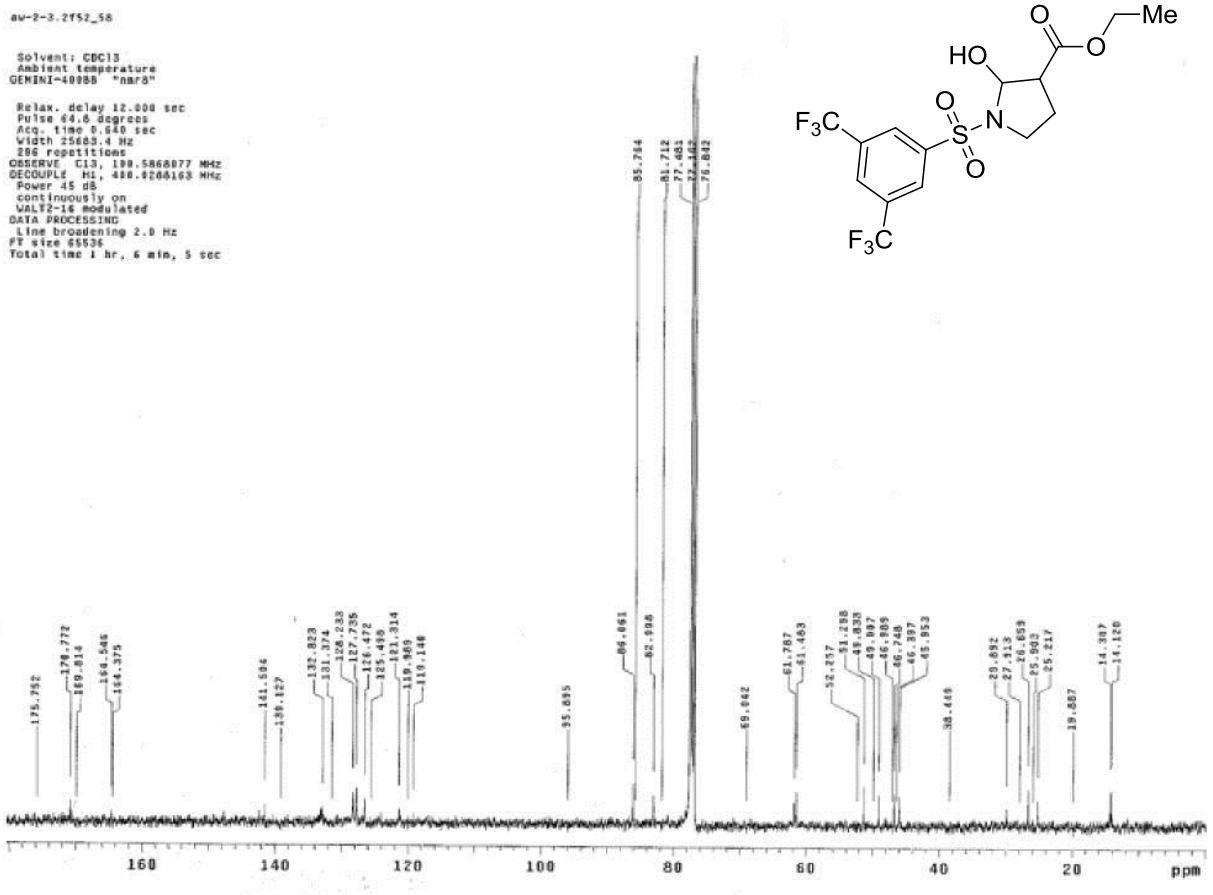

MK-3-259Af36_46-H
Solvent: Acetone
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 49.4 degrees
Acq. time 3.000 sec
Width 5958.8 Hz
16 repetitions
OBSERVE H1, 400.0284930 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 39 sec
OMe
HO
F3C
CF3
water
Acetone
both compounds
ppm


MK-3-259Af36-46-13C
Solvent: Acetone
Ambient temperature
File: MK-3-259Af36-46-13C
GEMINI-400BB "nmr8"
Relax. delay 13.000 sec
Pulse 64.8 degrees
Acq. time 0.660 sec
Width 23583.4 Hz
454 repetitions
OBSERVE C13, 100.5871886 MHz
DECOUPLE H1, 400.0380925 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.8 Hz
FT size 65536
Total time 418 hr, 11 min, 7 sec
OMe
HO
F3C
CF3
ppm


aw-2-3.1H
Solvent: CDCl3
Ambient temperature
File: aw-2-3.1f12_25
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5950.5 Hz
16 repetitions
OBSERVE H1, 400.0268158 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec
1.29
ppm


aw-2-3.1f12_25C
Solvent: CDCl3
Ambient temperature
File: aw-2-3.1f12_25C
GEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
128 repetitions
OBSERVE C13, 100.5868877 MHz
DECOUPLE H1, 400.0268163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.8 Hz
FT size 65536
Total time 1 hr, 54 min, 5 sec
1.29
ppm

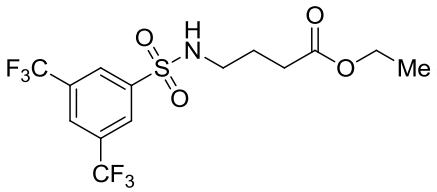

aw-2-3.2f52_58
Solvent: CDCl3
Ambient temperature
File: aw-2-3.2f52_58H
UNITY-300 "nmr2"
Relax. delay 20.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
16 repetitions
OBSERVE H1, 299.9403373 MHz
DATA PROCESSING
FT size 65536
Total time 8 min, 48 sec
ppm

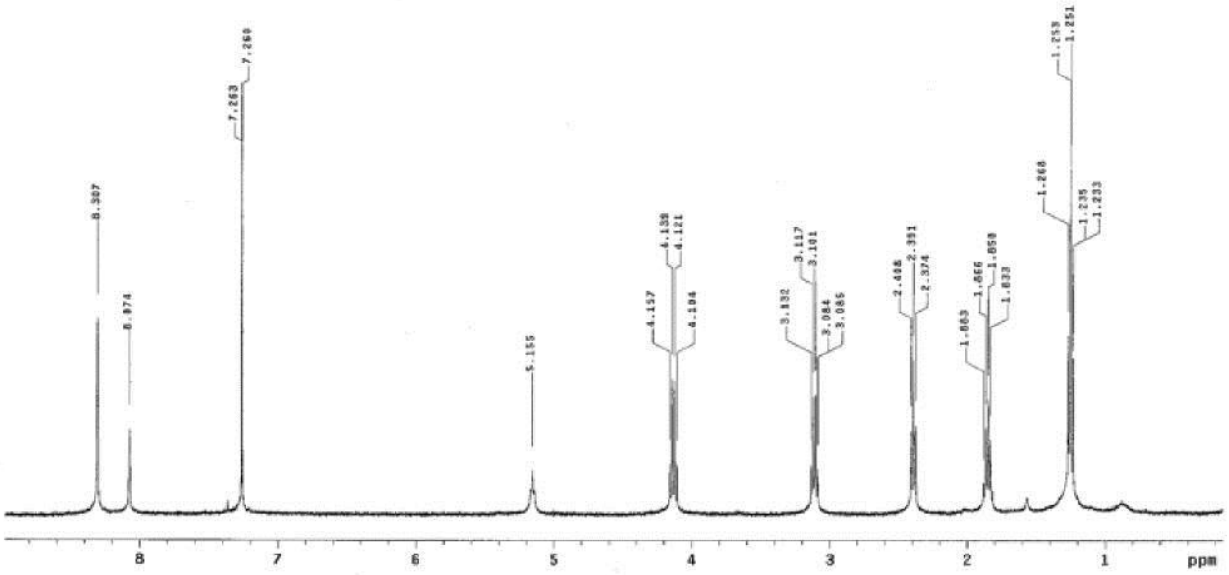

aw-2-3.2f52_58
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"
Relax. delay 12.000 sec
Pulse 64.6 degrees
Acq. time 0.540 sec
Width 25683.4 Hz
296 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0266163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 1 hr, 6 min, 5 sec
ppm

aw-2-3.2f35_40H

Solvent: CDCl3
Ambient temperature
File: aw-2-3.2f35_40H
GEMINI-400BB "nmr8"

Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0288150 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 29 sec

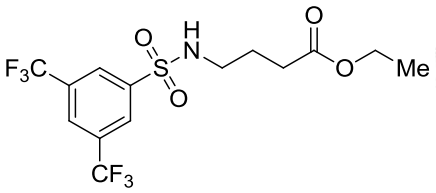


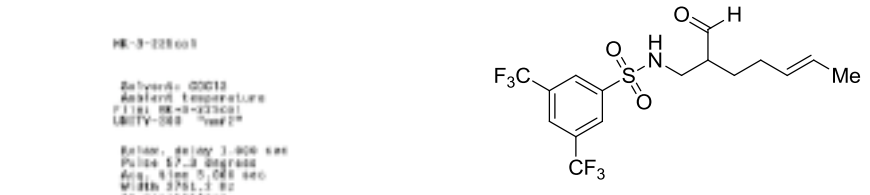


aw-2-3.2f35_40

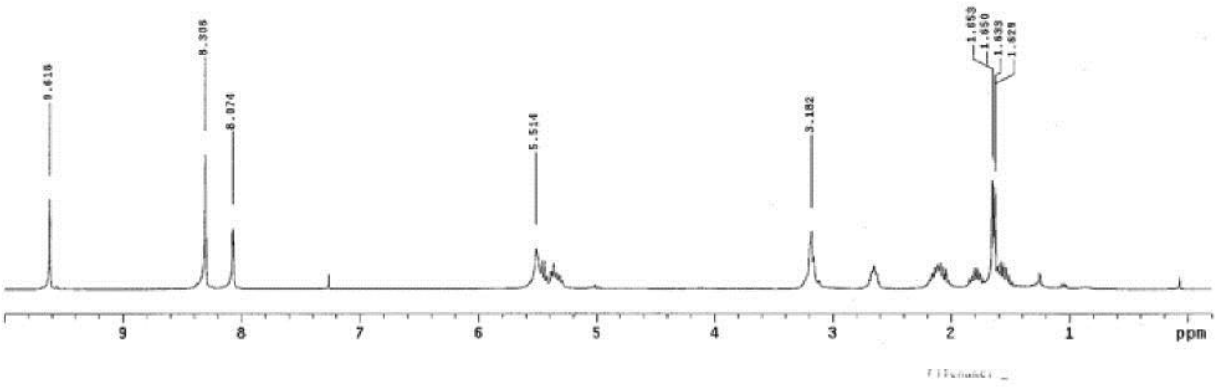
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

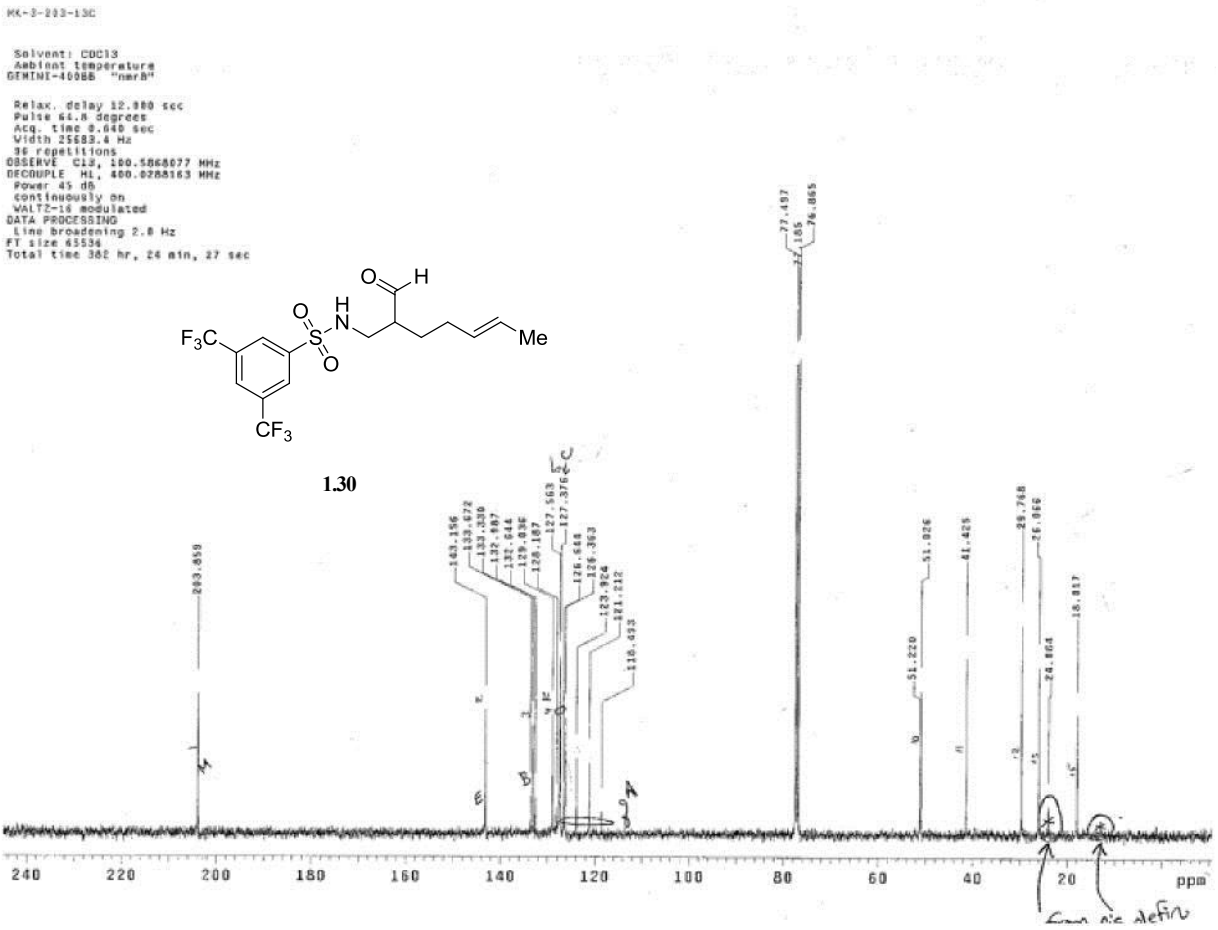
Relax. delay 12.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25083.4 Hz
172 repetitions
OBSERVE C13, 100.5868077 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 1 hr, 54 min, 9 sec





1.30


9.418
9.395
8.074
5.514
3.182
1.653
1.650
1.633
1.629
9
8
7
6
5
4
3
2
1
ppm


Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmrB"
Relax. delay 12.000 sec
Pulse 44.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
96 repetitions
OBSERVE C13, 100.5868677 MHz
DECOUPLE HL, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.8 Hz
FT size 65536
Total time 382 hr, 24 min, 27 sec
77.497
76.865
51.926
41.425
26.748
26.966
24.864
18.817
51.220
203.659
240
220
200
180
160
140
120
100
80
60
40
20
ppm

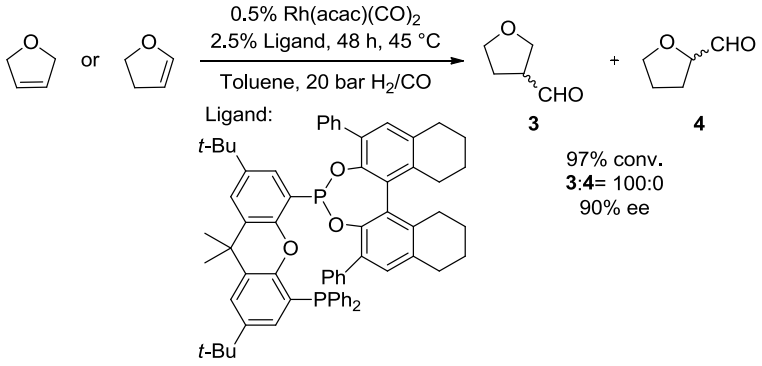
1.30

Chapter Two: Enantioselective Hydroformylation

2.1 Challenges in Enantioselective Hydroformylation

The efficient synthesis of valuable aldehydes through hydroformylation has led many to develop asymmetric methods.[1] A useful method has to first overcome the fundamental challenges of controlling regioselectivity and increasing reactivity of substituted olefins under mild conditions before addressing enantiocontrol in hydroformylation. Numerous groups have used symmetrical (Scheme 2.1)[2h,i] or electronically activated substrates (Scheme 2.2)[2] in order to circumvent the issue of

Scheme 2.1 Reek's Asymmetric Hydroformylation of Dihydrofurans.

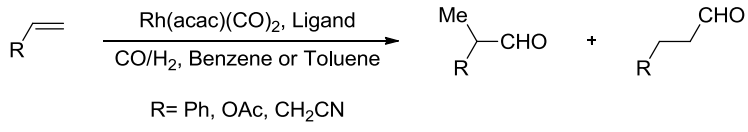


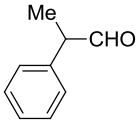
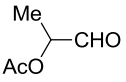
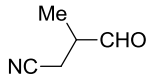
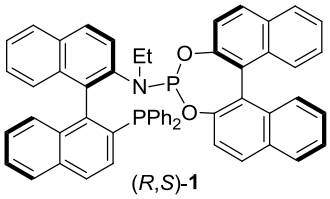
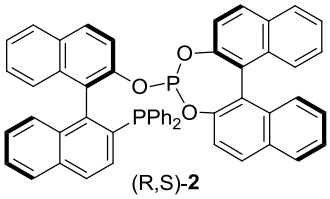
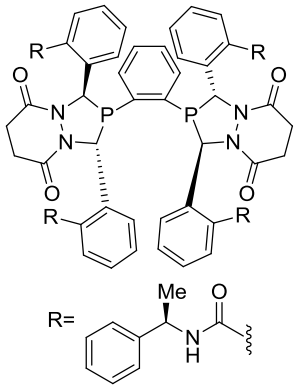
[1]For reviews on asymmetric hydroformylation, see: (a) Agbossou, F.; Carpentier, J. F.; Mortreux, A. *Chem. Rev.* **1995**, *95*, 2485–2506. (b) Dieguez, M.; Pamies, O.; Claver, C. *Tetrahedron: Asymmetry* **2004**, *15*, 2113–2122. (c) Klosin, J.; Landis, C. R. *Acc. Chem. Res.* **2007**, *40*, 1251–1259. (d) Gual, A.; Godard, C.; Castillon, S.; Claver, C. *Tetrahedron: Asymmetry* **2010**, *21*, 1135–1146.

[2](a) Sakai, N.; Mano, S.; Nozaki, K.; Takaya, H. *J. Am. Chem. Soc.* **1993**, *115*, 7033-7034. (b) Whiteker, G. T.; Babin, J. E. WO9393839, 1993. For recent examples, see: (c) Breeden, S.; Cole-Hamilton, D. J.; Foster, D. F.; Schwarz, G. J.; Wills, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 4106–4108. (d) Clark, T. P.; Landis, C. R.; Freed, S. L.; Klosin, J.; Abboud, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 5040–5042. (e) Yan, Y. J.; Zhang, X. M. *J. Am. Chem. Soc.* **2006**, *128*, 7198–7202. (f) Watkins, A. L.; Hashiguchi, B. G.; Landis, C. R. *Org. Lett.* **2008**, *10*, 4553–4556. (g) Zhao, B. G.; Peng, X. G.; Wang, Z.; Xia, C. G.; Ding, K. L. *Chem. Eur. J.* **2008**, *14*, 7847–7857. (h) Mazuela, J.; Coll, M.; Pamies, O.; Dieguez, M. *J. Org. Chem.* **2009**, *74*, 5440–5445. (i) Chikkali, S. H.; Bellini, R.; Berthon-Gelloz, G.; van der Vlugt, J. I.; deBruin, B.; Reek, J. N. H. *Chem. Commun.* **2010**, *46*, 1244–1246. (j) Zhang, X.; Cao, B.; Yan, Y.; Yu, S.; Ji, B.; Zhang, X. *Chem. Eur. J.* **2010**, *16*, 871–877. (k) McDonald, R. I.; Wong, G. W.; Neupane, R. P.; Stahl, S. S.; Landis, C. R. *J. Am. Chem. Soc.* **2010**, *132*, 14027–14029.

regioselectivity and are able to achieve high conversions and good enantioselectivities.[2] In the hydroformylation of activated substrates, Zhang has shown the utility of using mixed phosphine/ phosphoramidite ligands, which make highly active and selective complexes.[2e,j] For comparision, (*R,S*)-BINAPHOS, a similar mixed phosphine/phosphite

Scheme 2.2 Asymmetric Hydroformylation of Activated Substrates.

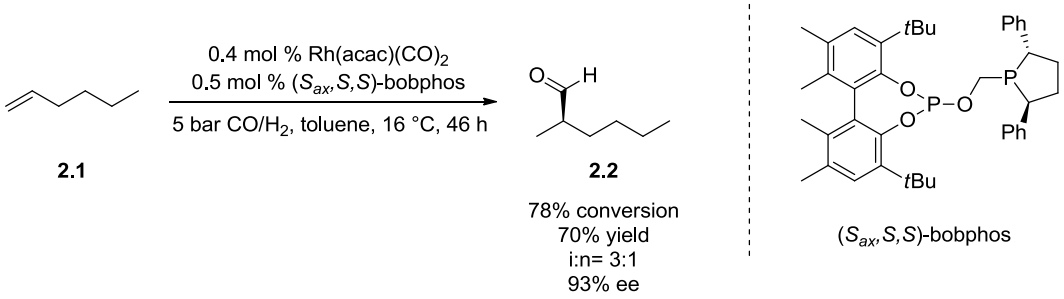


Ligand			
 (*R,S*)-**1**	>99% conv. i:n= 88:12 98% ee	76% conv. i:n= 96:4 96% ee	97% conv. i:n= 80:20 96% ee
 (R,S)-**2**	>99% conv. i:n= 86:14 92% ee	>99% conv. i:n= 88:12 94% ee	>98% conv. i:n= 67:33 72% ee
 **3**	>99% conv. i:n= 86:14 73% ee	>99% conv. i:n= 97:3 91% ee	>99% conv. i:n= 80:20 77% ee

ligand, is often used as a benchmark for reactivity and selectivity in these reactions.[1c,2d,j] Landis and others have developed diazaphospholane ligands which are also react efficiently and selectively (Scheme 2,2).[2d,f,g]

Recently, Clarke and co-workers published a method using another mixed phosphine/phosphite bidentate ligand to achieve iso-selective hydroformylation of alkyl substituted terminal alkenes, such as **2.1**, with good yields and enantioselectivities (Scheme 2.3).[3] The regioselectivity is also quite impressive considering the nature of the substrate. There is no explanation for the observed regioselectivity at this time.

Scheme 2.3 Regioselective Hydroformylation of Unactivated Terminal Alkenes.

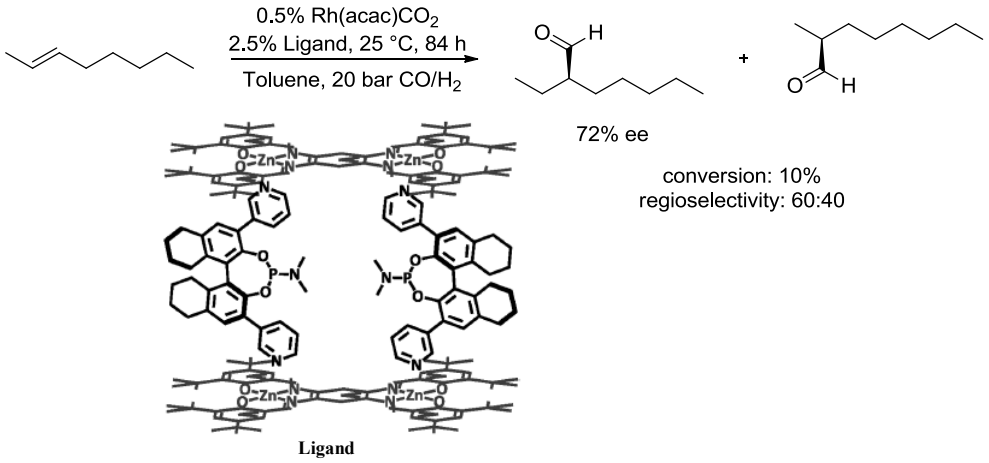


A bidentate phosphoramidite ligand able to supramolecularly control coordination to rhodium was recently developed by Reek. This approach allows for an alternate way to control the activity and selectivity of a hydroformylation catalyst.[4] Hydroformylation of unactivated, substituted olefins has given promising regioselective and enantioselective results (Scheme 2.4). High regio- and enantioselectivites are also obtained when used in

[3]Noonan, G. M.; Fuentes, J. A.; Cobley, C. J.; Clarke, M. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 2477-2480.
[4](a) Bellini, R.; Chikkali, S. H.; Berthon-Gelloz, G.; Reek, J. N. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 7342-7345. (b) Gadzikwa, T.; Bellini, R.; Dekker, H. L.; Reek, J. N. H. *J. Am. Chem. Soc.* **2012**, *134*, 2860-2863. (c) Bellini, R.; Reek, J. N. H. *Chem. Eur. J.* **2012**, *18*, 13510-13519.

the hydroformylation of styrene derivatives.

Scheme 2.4 Supramolecular Ligands in Asymmetric Hydroformylation.



Our group and the Breit group have demonstrated that using a catalytic directing group is an effective solution to both hydroformylation challenges (Chapter 1).[5] In order to expand our method to asymmetric catalysis, we developed an enantioenriched catalytic directing group.

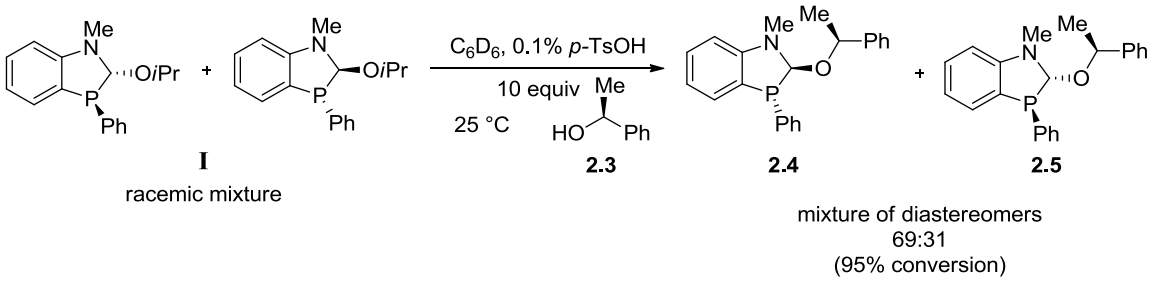
2.2 Developing an Enantioenriched Catalytic Directing Group

First attempts to develop an enantioenriched catalytic directing group were focused on resolving chiral, racemic catalytic directing group **I**. Taking advantage of its ability to bind alcohols, enantiopure alcohol **2.3** was exchanged with **I** with the aim that the resulting diastereomers, **2.4** and **2.5,** would be separable. Surprisingly, a 69:31 mixture of diastereomers resulted from the exchange of **I** with **2.3** (Scheme 2.5).

[5](a) Lightburn, T. E.; Dombrowski, M. T.; Tan, K. L. *J. Am. Chem. Soc.* **2008**, *130*, 9210-9211. (b) Grünanger, C. U.; Breit, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 7346-7349. (c) Smejkal, T.; Breit, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 311-315. (d) Worthy, A. D.; Gagnon, M. M.; Dombrowski, M. T.; Tan, K. L. *Org Lett.* **2009**, *11*, 2764-2767.

Calculations predict structure **2.4** to be 0.64 kcal/mol more stable than **2.5**. That energy difference would translate into a 75:25 ratio of diastereomers, similar to the experimental results that are shown in Scheme 2.5. This indicates that the phosphorus center is inverting under the exchange conditions. Considering that the barrier to phosphorus inversion (MeP(o-tolyl)Ph) is ~30 kcal/mol, this was an unexpected result.[6]

Scheme 2.5 Exchange of **I** with Enantiopure Alcohol **2.3**.



There are two possible mechanisms in which phosphorus inversion might occur under these mild reaction conditions. First, the cationic intermediate that is believed to exist during an exchange reaction is aromatic, which likely lowers the barrier to inversion through stabilization of the planar sp^2 hybridized phosphorus.[7] If the basic phosphorus is protonated, it is possible that the ring can open generating a 2° phosphine which has a lower inversion barrier, especially in the presence of catalytic acid (Figure 2.1).[8,9]

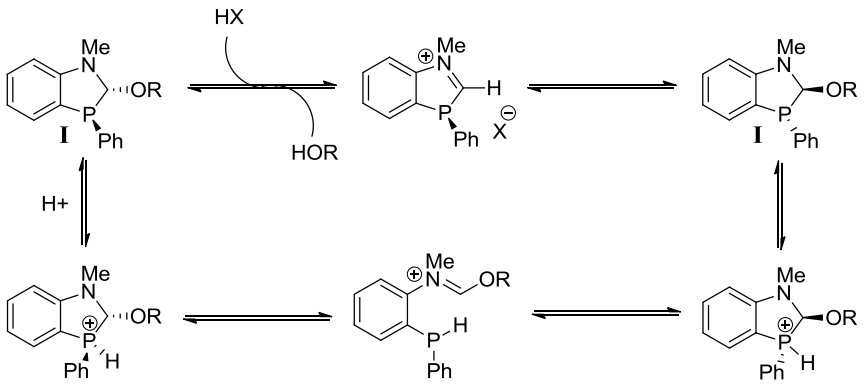
[6]Baechler, R. D.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 3090-3093.

[7](a) Egan, W.; Tang, R.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 1442-1444. (b) Andose, J. D.; Rauk, A.; Mislow, K. *J. Am. Chem. Soc.* **1974**, *96*, 6904-6907. (c) Nyulászi, L. *Tetrahedron* **2000**, *56*, 79-84.

[8](a) Anderson, J. C.; Cubbon, R. J.; Harling, J. D. *Tetrahedron: Asymmetry* **2001**, *12*, 923-935. (b) Neidlein, R.; Greulich, P.; Kramer, W. *Helv. Chim. Acta* **1993**, *76*, 2407-2417. (c) Christoffers, J. *Helv. Chim Acta* **1998**, *81*, 845-852.

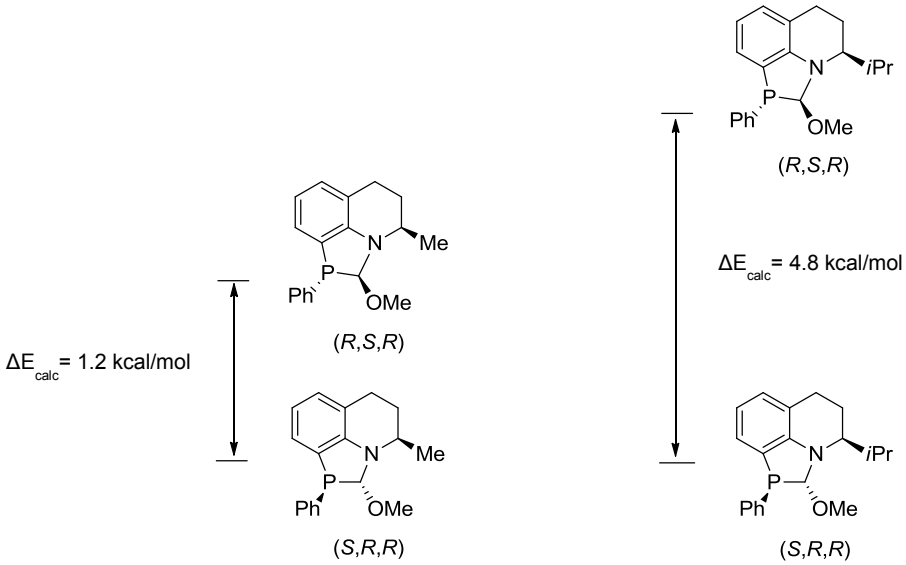
[9](a) Bader, A.; Nullmeyers, T.; Pabel, M.; Salem, G.; Willis, A. C.; Wild, S. B. *Inorg. Chem.* **1995**, *34*, 384-389. (b) Gagnaire, D.; St. Jacques, M. *J. Phys. Chem.* **1969**, *73*, 1678-1684.

Figure 2.1 Possible Mechanisms for Phosphorus Inversion.



We decided to use this interesting characteristic of **I** in the development of an enantioenriched catalytic directing group. If one diastereomer was at least 4 kcal/mol more stable than the others, it should be possible to equilibrate multiple diastereomers to a single stereoisomer. A set of tetrahydroquinoline ligands, which are based on catalytic directing group **I**, were modeled, computationally. The idea was that a set stereocenter next to the nitrogen might be able to gear the other two in the molecule. With a methyl group on the tetrahydroquinoline ring, the energy difference was 1.2 kcal/mol. This would lead to a ~90:10 mixture of the two lowest energy diastereomers in solution. When the group is changed to isopropyl, the energy difference between the two lowest energy diastereomers is 4.8 kcal/mol (Figure 2.2). If the calculations were correct, only one thermodynamically favored diastereomer should be present in solution. It is believed that the isopropyl group is able to gear the methoxy group down to avoid a *syn*-pentane-like interaction. The methoxy group, in turn, gears the phenyl up. Previously, it was seen with **I** that the C-O bond and phenyl group strongly prefer to be *anti*.[5a,d]

Figure 2.2 B3LYP, 6-31g** Energy Calculations.



Compound **II** was synthesized starting from 2-isopropylquinoline. An asymmetric hydrogenation of the quinoline was performed followed by crystallization of the (+)-3-bromocamphor-8-sulfonic acid salt to enrich **2.6** to 98% ee. An *ortho*-lithiation and trap with PPh_2Cl yielded **2.7**. Lithium reduction of the phosphorus to remove a phenyl group followed by a kinetic closure with dichloromethyl methyl ether gave **II-OMe** as a mixture of four diastereomers (visible by ^{31}P NMR). As predicted by calculations, equilibration of the four diastereomers to one, **II-O*i*Pr**, occurred under mild exchange conditions (Scheme 2.6 and Figure 2.3 and 2.4).

Scheme 2.6 Synthesis of **II**.

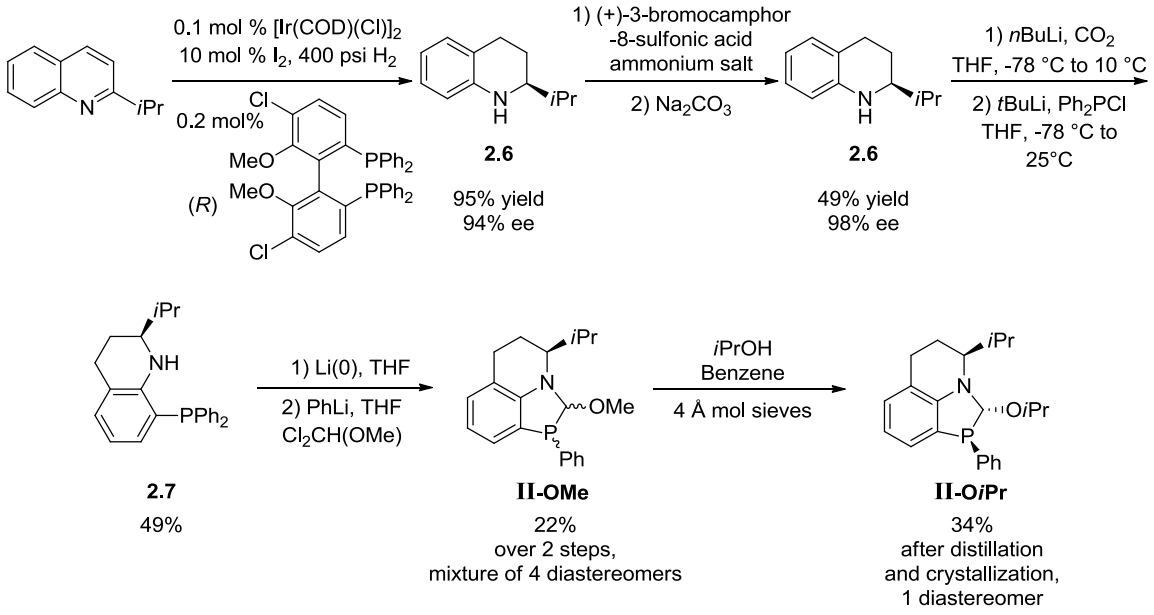


Figure 2.3 Four Diastereomers of **II-OMe** by ^{31}P NMR.

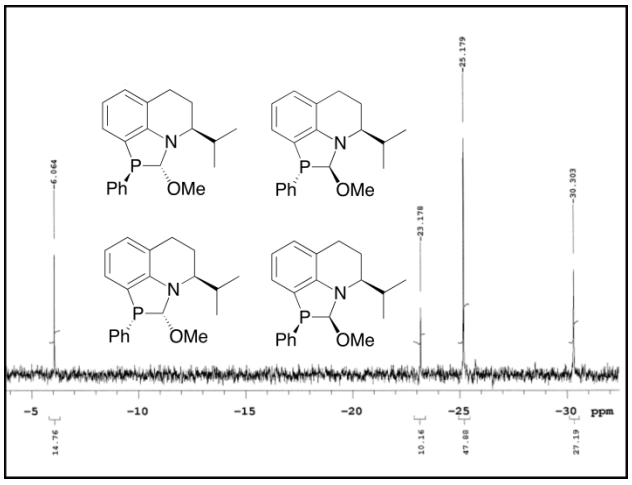
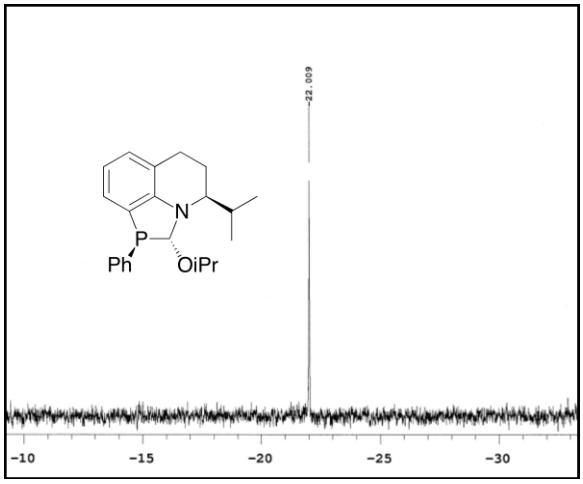
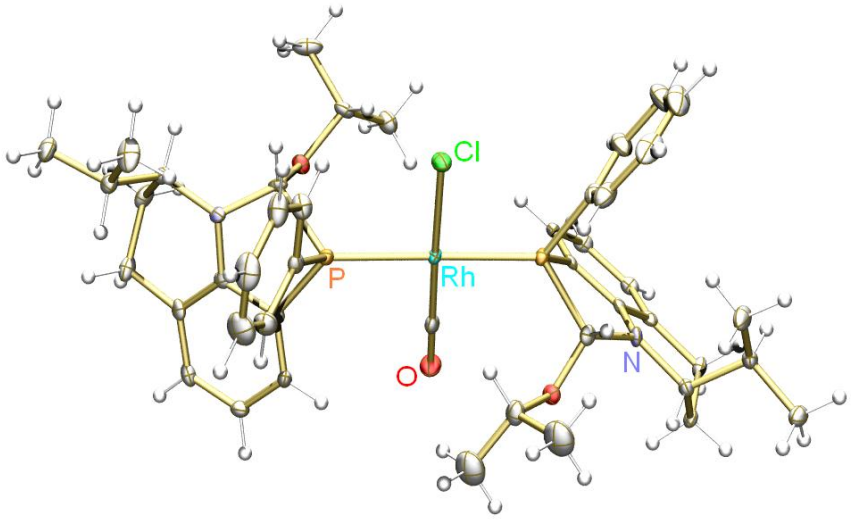


Figure 2.4 Single Diastereomer of **II-O*i*Pr** by ^{31}P NMR.



After complexation of **II** with *trans*-$[Rh(CO)_2Cl]_2$, a crystal structure of the complex was obtained which showed the isopropyl group next to the nitrogen gears the C-O bond down which in turn gears the P-Ph bond up (Figure 2.5), consistent with calculations.

Figure 2.5 Crystal Structure of [(**II**-O*i*Pr)$_2$Rh(CO)Cl].



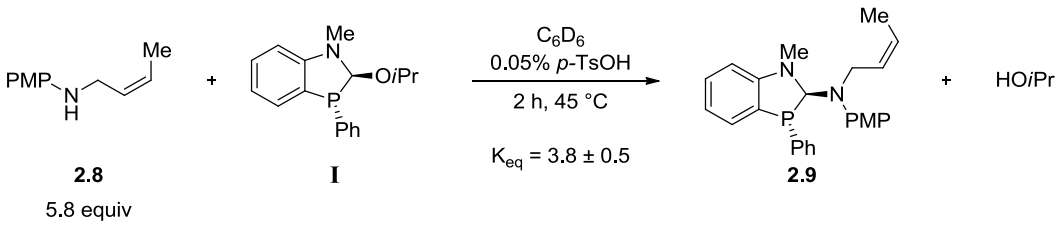
2.3 Enantioselective Hydroformylation of *p*-Methoxyphenyl-protected Allylic Amines[10]

With **II** in hand, focus shifted to developing an enantioselective hydroformylation method. Previously, it was demonstrated that electron-withdrawing sulfonamides undergo efficient exchange and hydroformylation using **I** (Chapter 1).[5d] However, the 3,5-bis(trifluoromethyl)benzenesulfonamide protecting group used was exotic and hard to remove. In order to make this method more useful, anilines were explored as potential substrates. In particular, PMP-protected amines were interesting because they are commonly used and can be deprotected to the free amine without difficulty.[11]

First the exchange of **2.8** with **I** was tested. Equilibrium was reached in 2 h and the K_{eq} was determined to be 3.8 ± 0.5 (Scheme 2.7).

[10]Worthy, A. D.; Joe, C. L.; Lightburn, T. E.; Tan, K. L. *J. Am. Chem. Soc.* **2010**, *132*, 14757-14759.
[11]Carswell, E. L.; Snapper, M. L.; Hoveyda, A. H. *Angew Chem., Int. Ed*. **2006**, *45*, 7230-7233.

Scheme 2.7 Exchange of **2.8** with **I**.



2.8
5.8 equiv

I

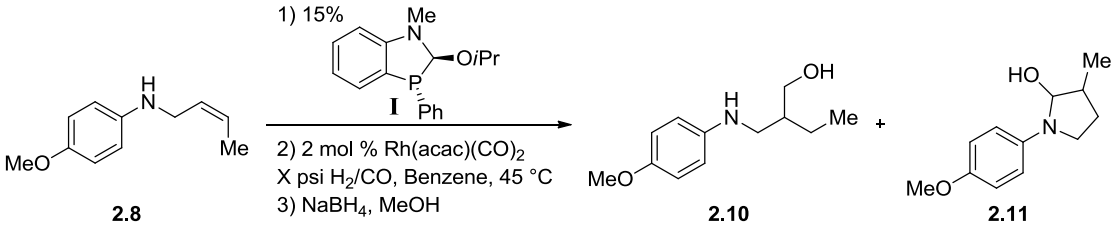
2.9

PMP= *p*-methoxyphenyl

As pre-exchanging amine substrates greatly increased regioselectivity in previous studies (Chapter 1),[5d] **2.8** was pre-exchanged with **I** to form **2.9** prior to hydroformylation. Because it was determined to be unstable and hard to isolate, the aldehyde was reduced to the corresponding alcohol **2.10**, immediately after hydroformylation. The normal product, **2.11**, was never seen in any reaction and attempts to synthesize it independently failed. Thus, it is believed to be unstable under the reaction conditions.

A pressure screen using **I** was first attempted in order to maximize the amount of iso product formed. Running the reaction at a pressure above 50 psi H_2/CO resulted in at least 40% conversion in each case, but **2.10** was not detected in the crude ^{1}H NMR. It is possible that at higher pressures of H_2/CO the reaction was favoring formation of the normal product, **2.11**. At 50 psi, almost 50% conversion was achieved with 37% isolated **2.10** (Table 2.1).

Table 2.1 Pressure Screen with **I**.



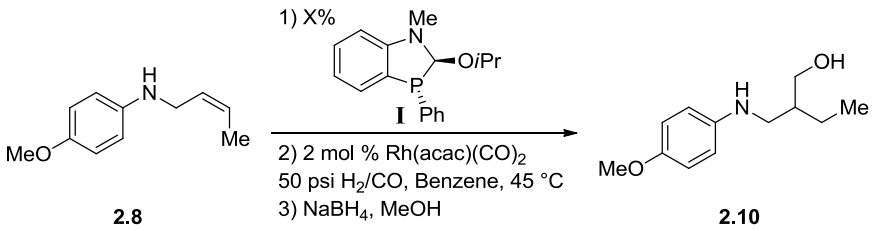
2.8 **2.10** **2.11**

Pressure (psi)	Conversion (%)[a]	**2.10** (%)[a]
25	59	20
50	46	39 (37)[b]
75	43	0
100	40	0

[a]Based on ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b]Isolated yield.

Performing a catalyst loading screen showed that increasing the amount of **I** in the reaction increased the conversion as well as the amount of **2.10** formed. With less amounts of **I**, the unselective background reaction is much more competitive (Table 2.2).

Table 2.2 Catalyst Loading Screen with **I**.

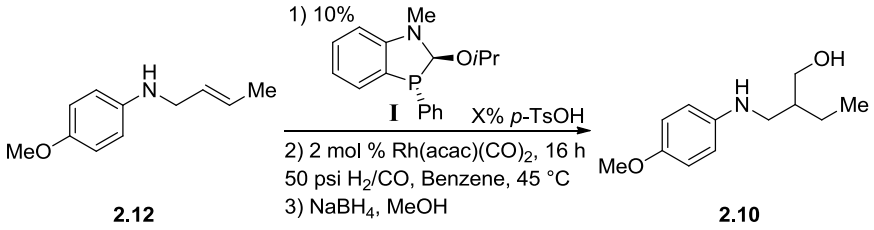


Mol % **I**	Conversion (%)[a]	**2.10** (%)[a]
5	32	12
10	37	18
15	46	39 (37)[b]

[a]Based on ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b]Isolated yield.

At this point, an acid screen was run to ensure that exchange was fast enough during the reaction to achieve iso-selective hydroformylation. The highest amount of **2.10** formed was achieved with 0.05% *p*-toluenesulfonic acid (*p*-TsOH). The difference between conversion and amount of **2.10** formed is low which means that minimal amounts of normal product are being formed (Table 2.3).

Table 2.3 Acid Loading Screen.

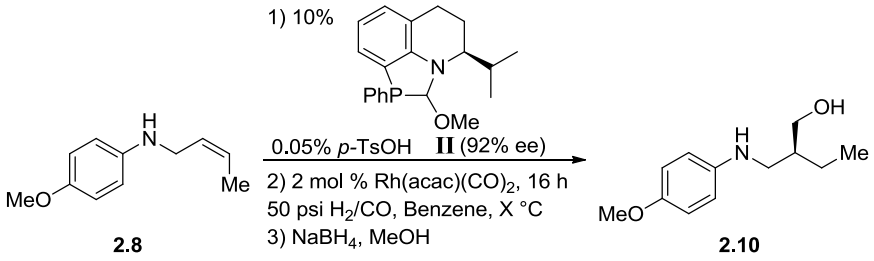


Acid (%)	Conversion (%)[a]	**2.10** (%)[a]
0.02	50	30
0.05	50	40
0.1	55	31
0.2	42	0

[a]Based on ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Eager to test **II**, a temperature screen was performed to optimize the balance between conversion and enantioselectivity. Fortunately, using 10% of **II** resulted in increased conversion and yields of the β-amino alcohol compared to **I**. Larger ligands are known to be more active in hydroformylation due to a higher concentration of the monophosphine complex. Performing the reaction at 55 °C resulted in almost complete conversion, albeit, with moderate enantioselectivites. Decreasing the temperature lowered the conversion of **2.8**, but increased the enantioselectivity of the reaction. The conversion and yield of **2.10** did not change between 45 °C and 35 °C, but 35 °C did give slightly better enantiomeric

Table 2.4 Temperature Screen with **II**.

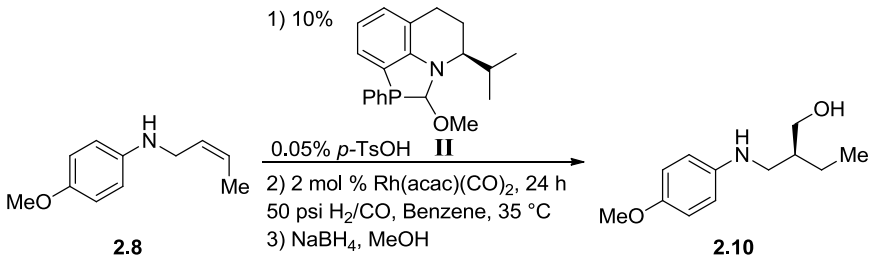


Temperature (°C)	Conversion (%)[a]	**2.10** (%)[a]	ee (%)[b]
55	95	70	76
45	79	71	85
35	77	72	89
30	57	56	89

[a]Based on ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.[b]Separated using supercritical fluid chromatography.

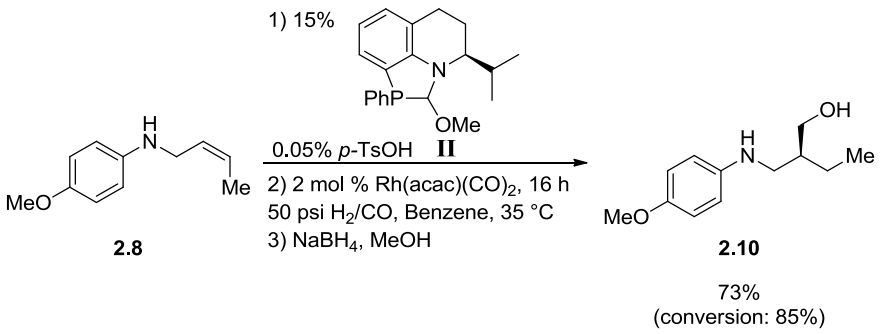
excess for **2.10**. Decreasing to 30 °C did not affect the enantioselectivity but continued to lower the conversion (Table 2.4).

Scheme 2.8 Increasing the Reaction Time.



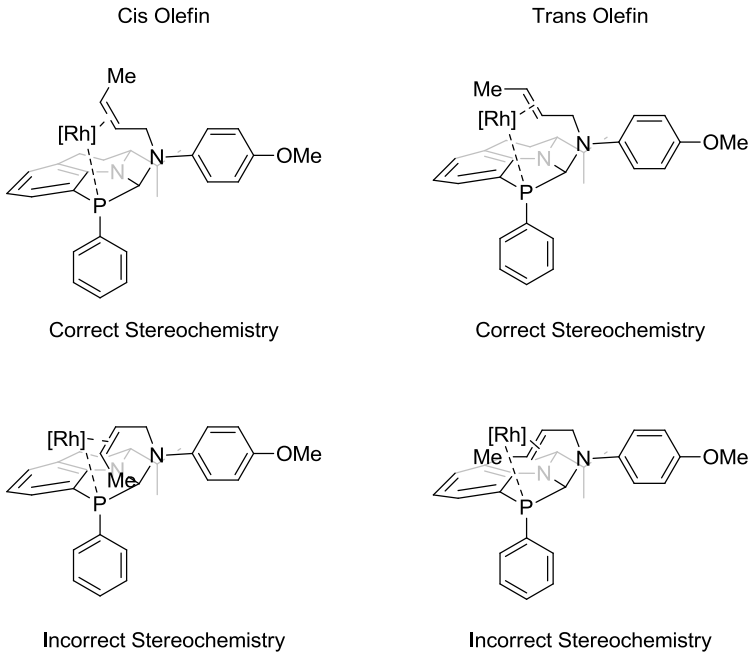
When expanding the substrate scope, the substrates were shown to react under remarkably mild conditions for the hydroformylation of disubstituted olefins. In most cases, however, complete conversion is not achieved which has been attributed to **II** decomposing before the reaction is complete. This is supported by the observation that running the reaction for longer times does not increase the conversion (Scheme 2.8), whereas increasing the amount of **II** improves conversion (Scheme 2.9).

Scheme 2.9 Increasing the Amount of **II**.



Interestingly trans olefins, (Table 2.5, Entries 2 and 4), provide lower enantioselectivities than the corresponding cis olefins (Table 2.5, Entries 1 and 3). Elucidating the reason for this difference has not yet been accomplished. However, using the crystal structure of the ligand and simple modeling, a proposed stereochemical model was developed (Figure 2.6). First to minimize steric interactions with the ligand, the PMP protecting group was oriented out into space. Then by comparing the interaction of the rhodium with each face of the olefin with both the cis and trans substrates, it was obvious that the major enantiomer can come from the two intermediates with less steric interactions. It is interesting to note that in the case of the trans olefin, the model leading

Figure 2.6 Proposed Stereochemical Model.

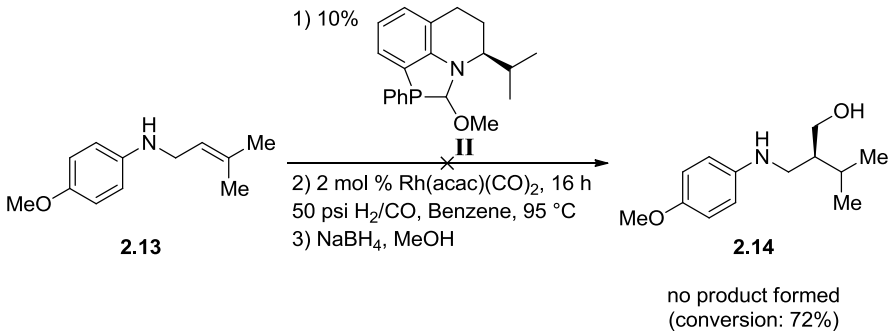


to the minor enantiomer appears more favorable than the corresponding model for the cis olefin. It is possible that in the case of the trans olefin the energy difference between the two faces of the olefin bond to rhodium are closer in energy than the two intermediates possible for the cis olefin. This hypothesis is consistent with the decreased enantioselectivity observed with the trans olefin.

When examining the substrate scope, the phthalimide substrate was the only substrate that showed a significant discrepancy between conversion and amount of iso product (Table 2.5, Entry 8). Amides are known to be able to direct hydroformylation so the phthalimide may be directing formation of the normal isomer which is subsequently

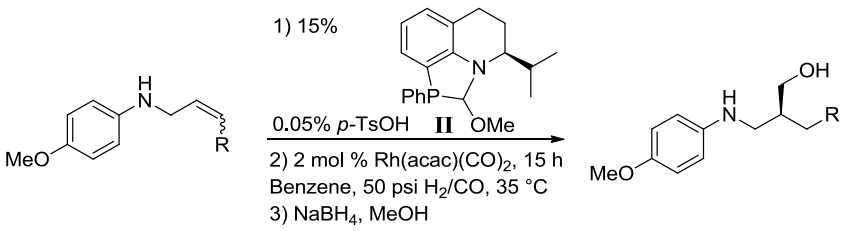
decomposing and causing the mass balance to be skewed.[12] The terminal substrate also likely forms more normal product than the other substrates due to its reactive nature. A trisubstituted olefin was attempted but even at 95 °C, only starting material, **2.13**, and hydrogenated starting material (~20%) were observed (Scheme 2.10).

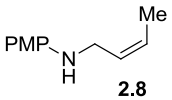
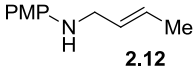
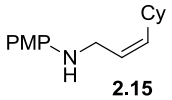
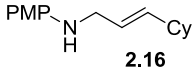
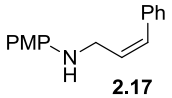
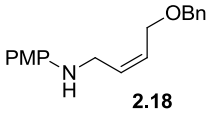
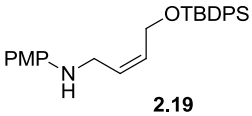
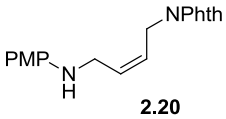
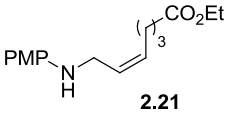
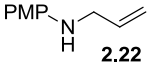
Scheme 2.10 Hydroformylation of 4-methoxy-*N*-(3-methylbut-2-en-1-yl)aniline.



[12]For examples of amide directed hydroformylation see: (a) Ojima, I.; Zhang, Z. *J. Org. Chem.* **1988**, *53*, 4422-4425. (b) Ojima, I.; Zhang, Z. *J. Organomet. Chem.* **1991**, *417*, 253-276. (c) Ojima, I.; Korda, A.; Shay, W. R. *J. Org. Chem.* **1991**, *56*, 2024-2030. (d) Dickson, R. S.; Bowen, J.; Campi, E. M.; Jackson, W. R.; Jonasson, C. A. M.; McGrath, F. J.; Paslow, D. J.; Polas, A.; Renton, P.; Gladiali, S. *J. Mol. Cat. A* **1999**, *150*, 122-146.

Table 2.5 Substrate Scope.



Substrate	Starting Olefin (%)[a]	Product (%)[a]	Isolated Yield (%)	ee (%)[b]
 **2.8**	26	70	69	92
 **2.12**	8	N/A[c]	74	80
 **2.15**	12	N/A[c]	75	86
 **2.16**	20	64	62	76
 **2.17**	45	53	45	79
 **2.18**	11	N/A[c]	70	92
 **2.19**	19	71	66	90
 **2.20**	7	70	55	93
 **2.21**	10	N/A[c]	68	90
 **2.22**	8	77	64	73

[a]Based on ^{1}H NMR with 1,3,5-trimethoxybenzene used as an internal standard. [b]Determined by super-critical fluid chromatography. [c]Amount could not be determined accurately due to peak overlap in ^{1}H NMR.

2.4 Conclusions

Building off of our previously successful catalytic directing group, **I**, enantioenriched catalytic directing group, **II**, was designed and synthesized. It retains the essential features to direct hydroformylation to obtain good regioselectivity while also providing a chiral environment to induce stereoselectivity. Under mild conditions, a variety of disubstituted olefins react to give good yields and excellent enantioselectivites. Thus, the first enantioselective reaction performed with a catalytic directing group was developed.

2.5 Experimental

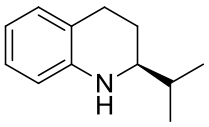
General Considerations

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Lithium reagents were titrated against 2-pentanol using 1, 10-phenanthroline as the indicator. Flash column chromatography was performed using EMD Silica Gel 60 (230-400 mesh) and ACS grade solvents as received from Fisher Scientific. All experiments were performed in oven or flame-dried glassware under an atmosphere of nitrogen or argon using standard syringe and cannula techniques, except where otherwise noted. All reactions were run with dry, degassed solvents dispensed from a Glass Contour Solvent Purification System (SG Water, USA LLC). ^{1}H, ^{13}C, and ^{31}P NMR were performed on either a Varian Gemini 400 MHz or a Varian Unity Inova 500 MHz spectrometers. Deuterated solvents were purchased from Cambridge Isotope Labs and stored over 3Å molecular sieves. C_6D_6 was degassed by three successive freeze-pump-thaw cycles and stored over 3Å molecular sieves in a dry box

under a nitrogen atmosphere. All NMR chemical shifts are reported in ppm relative to residual solvent for ^{1}H and ^{13}C and external standard (neat H_3PO_4) for ^{31}P NMR. Coupling constants are reported in Hz. All IR spectra were gathered on a Bruker Alpha FT-IR equipped with a single crystal diamond ATR module and values are reported in cm^{-1}. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Berger Instruments Supercritical Chromatograph equipped with an Alcott auto sampler and a Knauer UV detector with methanol as the modifier. HRMS and X-ray crystal structure data were generated in Boston College facilities. Analytical chiral high-performance liquid chromatography (HPLC) was performed on a Shimadzu-LC-2010A HT. Hydroformylation was performed in an Argonaut Technologies Endeavor® Catalyst Screening System using 1:1 H_2/CO supplied by Airgas, Inc.

Ligand Synthesis and Characterization

2-isopropyl quinoline[13] was prepared according to a literature procedure and matches reported spectra.



(*S*)-2-isopropyl-1,2,3,4-tetrahydroquinoline, 2.6. $[Ir(COD)Cl]_2$ (68.0 mg, 0.102 mmol) and (*R*)-(+)-5,5'-dichloro-6,6'-dimethoxy-2,2'-bis(diphenylphosphino)-1,1'-biphenyl (132 mg, 0.204 mmol) were dissolved in 5 mL THF in a glovebox and stirred for 20 minutes. The solution was brought out of the box and was added to a solution of 2-isopropyl

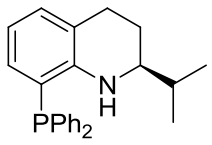
[13]Lachance, N.; Roy, P.; Leblanc, Y. US Patent 20050277644, 2005.

quinoline (8.71 g, 50.9 mmol) and iodine (258 mg, 1.02 mmol) in 50 mL THF. The solution was added to a Parr bomb and cooled to 4 °C (cold room). The system was purged 3 times with hydrogen (charged to 400 psi and then depressurized). The vessel was pressurized to 400 psi hydrogen, and the reaction was stirred for 36 h. The reaction was concentrated and purified on silica (3-5% EtOAc in Hexanes) to yield a yellow oil (8.51 g, 95%). The compound was 94% ee by SFC analysis (OD-H, 1% methanol as modifier, 1.5 mL/min, 150 psi. t_{rminor} = 12.8 min and t_{rmajor} = 13.6 min).

Crystalization to higher ee:

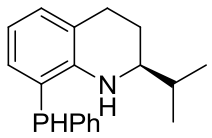
HCl (5.0 mL, conc.) and water (72 mL) were heated to 50 °C and (*S*)-2-isopropyl-1,2,3,4-tetrahydroquinoline (7.18 g, 41.0 mmol) was added followed by (+)-3-bromocamphor-8-sulfonic acid ammonium salt (13.4 g, 40.9 mmol). The temperature was raised to 90 °C. Water (500 mL), ethanol (35 mL), and HCl (25 mL, conc.) were added. The suspension was hot filtered, and the filtrate was allowed to cool overnight. The crystals were collected, and the parent compound was recovered by suspending the crystals in ethyl acetate and washing with 1 M Na_2CO_3 (3×50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated to yield the title compound (3.51 g, 49%) in 98% ee as determined by SFC. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.06-7.02 (m, 2H), 6.68 (ddd, 1H, *J* = 8.0, 7.0, 1.0), 6.54 (dd, 1H, *J* = 7.5, 1.0), 3.82 (br s, 1H), 3.14-3.10 (m, 1H), 2.89-2.80 (m, 2H), 2.02-1.97 (m, 1H), 1.81-1.70 (m, 2H), 1.09 (d, 3H, *J* = 7.0), 1.06 (d, 3H, *J* = 7.0); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 145.1, 129.2, 126.8, 121.5, 116.8, 114.0,

57.3, 32.6, 26.7, 24.6, 18.7, 18.3; **IR**: 3415, 2956, 2870, 2842, 1606, 1483, 1308, 1273, 1253, 741, 713 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{18}N$ $[M+H]^+$: 176.1439, found: 176.1448; $\mathbf{[\alpha]_D^{20}}$ = +65.3 (*c* = 0.915, CH_2Cl_2, *l* = 50 mm).



(*S*)-8-(diphenylphosphino)-2-isopropyl-1,2,3,4-tetrahydroquinoline, 2.7. To a 250 mL, three-neck round-bottom flask was added THF (60 mL) and (*S*)-2-isopropyl-1,2,3,4-tetrahydroquinoline (5.80 g, 33.1 mmol). The solution was cooled to −78 °C and *n*BuLi (18.8 mL, 1.76 M, 33.1 mmol) was added slowly maintaining the internal temperature at or below −70 °C. Upon completion of the *n*BuLi addition, the reaction was warmed in an ice water bath to 0 °C, and CO_2 was bubbled through the solution. The red solution color faded quickly. CO_2 bubbling was continued for 45 min, and the solvent was removed under high vacuum to yield a foamy yellow semi-solid. The residue was redissolved in THF (60 mL) and cooled to −78 °C. *t*BuLi (27.2 mL, 1.40 M, 38.1 mmol) was added, maintaining the internal temperature at or below −70 °C. The solution was warmed to −20 °C for 30 min before being recooled to −78°C. Chlorodiphenylphosphine (6.73 mL, 36.4 mmol) was added as a solution in THF (10 mL) maintaining the internal temperature at or below −70 °C. The solution was stirred overnight, allowing the reaction to warm with the cold bath. HCl was added (52 mL, 6.3 M) and stirred for 45 min. The solution was basified to pH >10 with 10 M NaOH and extracted with EtOAc. The organics were dried over $MgSO_4$, filtered, and concentrated. The unreacted starting material was

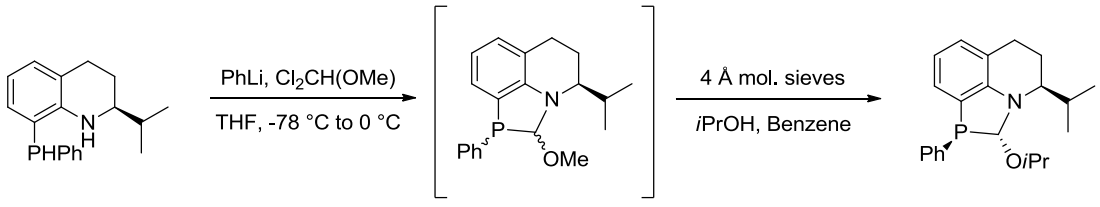
removed by Kugelrohr distillation (120 °C at 0.05 mmHg). The undistilled material was suspended in minimal amount of ethanol, and the product precipitated as a white solid (5.88 g, 49%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.38-7.27 (m, 10H), 6.97 (d, 1H, *J* = 7.0), 6.61 (app t, 1H, *J* = 7.0), 6.50 (app t, 1H, *J* = 7.0), 4.66 (d, 1H, *J* = 7.0), 3.04-3.02 (m, 1H), 2.83-2.74 (m, 2H), 1.90-1.86 (m, 1H), 1.63-1.58 (m, 2H), 0.81 (d, 3H, *J* = 6.5), 0.78 (d, 3H, *J* = 6.5); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 147.7, 147.5, 135.8 (d, *J* = 7.4), 135.6 (d, *J* = 7.4), 133.8 (d, *J* = 7.4), 133.7 (d, *J* = 7.4), 132.14, 132.11, 128.7, 128.6, 128.5, 128.4, 120.99, 120.96, 117.4, 117.3, 116.1, 116.0, 57.6, 57.5, 32.5, 27.0, 24.2, 18.2; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ –20.7; **IR**: 3050, 2955, 2870, 2840, 1586, 1489, 1455, 1433, 1277, 1091, 738, 694, 502 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{24}H_{26}NP$ $[M+H]^+$: 360.1881, found: 360.1870; **$[\alpha]_D^{20}$** = +80.9 (*c* = 0.415, CH_2Cl_2, *l* = 50 mm).



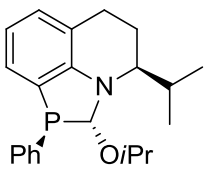
(*S*)-2-isopropyl-8-(phenylphosphino)-1,2,3,4-tetrahydroquinoline. A dry 100 mL round-bottom flask was charged with (*S*)-8-(diphenylphosphino)-2-isopropyl-1,2,3,4-tetrahydroquinoline (2.50 g, 6.96 mmol) and THF (25 mL). The solution was sparged with argon for 30 min, and lithium wire (145 mg, 20.9 mmol) was added. The solution was sparged with argon for an additional 30 min during which time the solution turned orange. (Note: you must use argon for this reaction as lithium metal will react with nitrogen). The solution was stirred overnight under argon. Degassed water (2.5 mL) was added and stirred for 15 min, resulting in a colorless solution. The solvent was removed

under high vacuum, and the residue was quickly extracted with CH_2Cl_2, dried over $MgSO_4$, filtered, and concentrated. Distillation (125 °C at 0.05 mmHg) resulted in an air sensitive clear oil (1.31 g, 66%) as a 1:1 mixture of diastereomers. The compound was stored under argon. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.45-7.41 (m, 2H), 7.37-7.27 (m, 4H), 7.06-7.05 (m, 1H), 6.64-6.58 (m, 1H), 5.10 (d, 1H, *J* = 219), 4.31 (br s, 1H), 3.09-3.05 (m, 0.5H), 2.96-2.92 (m, 0.5H), 2.84-2.74 (m, 2H), 1.91-1.84 (m, 1H), 1.65-1.54 (m, 2H), 0.84 (d, 1.5H, *J* = 7.0), 0.82 (d, 1.5H, *J* = 7.0), 0.78 (d, 1.5H, *J* = 7.0), 0.74 (d, 1.5H, *J* = 7.0); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 147.74, 147.71, 147.2, 147.1, 136.2, 136.1, 136.0, 135.9, 132.3, 132.2, 132.1, 132.0, 131.4, 131.3, 128.70, 128.67, 128.66, 128.64, 128.01, 127.98, 116.2, 116.1, 115.7, 115.6, 57.7, 32.6, 32.5, 32.4, 27.2, 27.1, 24.6, 24.0, 18.4, 18.14, 18.12, 18.0; **^{31}P NMR** ($CDCl_3$, 202 MHz) δ –61.4, –62.1; **IR**: 3421, 2957, 2930, 2871, 2842, 1588, 1490, 1457, 1434, 1285, 759, 737, 695 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{23}NP$ $[M+H]^+$: 284.1568, found: 284.1561; **$[\alpha]_D^{20}$** = +53.4 (*c* = 0.730, CH_2Cl_2, *l* = 50mm)

Synthesis of **II-(O*i*Pr)**



II-OMe **II-O*i*Pr**



(4*S*)-2-isopropoxy-4-isopropyl-1-phenyl-2,4,5,6-tetrahydro-1H-[1,3]azaphospholo[4,5,1-*ij*]quinoline, II-(O*i*Pr). (*S*)-2-isopropyl-8-(phenylphosphino)-1,2,3,4-tetrahydroquinoline (1.30 g, 4.59 mmol) was dissolved in THF (25 mL). The solution was cooled to −78 °C and PhLi (4.89 mL, 1.97 M, 9.64 mmol) was added dropwise. After stirring for 30 min, the flask was transferred to an ice water bath and stirred for an additional 30 min. The dianion solution was added via syringe pump over 1 h to a solution of dichloromethyl methyl ether (448 μL, 5.05 mmol) in THF (150 mL) at 0 °C. The reaction was stirred for 90 min, and the solvent was removed under high vacuum. The resulting residue was brought into a glovebox and extracted with pentane (3×10 mL). The pentane extract was filtered through glass fiber filter paper to remove LiCl. The crude mixture was distilled (150 °C at 0.05 mmHg) to yield a yellow oil (492 mg, 33%) that was a mixture of four diastereomers [**^{31}P NMR** (C_6D_6, 202 MHz) δ −6.0, −23.2, −25.2, −30.3]. To the distillate was added *i*PrOH (3 mL) in benzene (3 mL) over 4Å mol. sieves in a glove box. The solution was allowed to sit for 20 h before being filtered. The sieves were washed with benzene. The filtrate was concentrated and resubjected to *i*PrOH (3 mL) in benzene (3 mL) over 4Å mol. sieves. The filtration/resubjection cycle was repeated. The resulting residue was dissolved in pentane (0.3 mL) and crystallized at −37 °C. More material was recrystallized from the mother liquor, and the white solids were combined (181 mg, 34%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.42-7.40 (m, 1H), 7.38-7.35 (m, 2H), 7.03-7.00 (m, 3H), 6.98-6.96 (m, 2H), 6.73-6.70 (m, 1H), 5.14 (d, 1H, *J* = 13.0), 4.01-3.98 (m, 1H), 3.40-3.37 (m, 1H), 2.44-2.42 (m, 2H), 1.86-1.82 (m, 2H), 1.61-1.55 (m, 2H), 1.17 (d, 3H, *J* = 6.0), 1.08 (d, 3H, *J* = 6.0), 0.64

(d, 3H, J = 7.0), 0.50 (d, 3H, J = 6.5); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 151.3, 136.9, 136.8, 132.1, 132.0, 130.7, 130.6, 130.0, 128.5, 120.0, 119.4, 117.9, 98.3, 67.3, 57.5, 28.8, 24.2, 23.3, 21.6, 21.4, 19.3, 16.0; **^{31}P NMR** (C_6D_6, 202 MHz) δ –22.0 ; **IR** 3052, 2962, 2929, 2870, 1582, 1455, 1383, 1310, 1288, 1183, 1082, 999, 740, 695 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{22}H_{29}NOP$ $[M+H]^+$: 354.1987, found: 354.2000. **$[\alpha]_D^{20}$** = +139.4 (c = 0.340, C_6H_6, l = 50 mm).

Note: Table 2.5 substrates were exchanged with the mixture of four **II-OMe** diastereomers prior to hydroformylation, which effected conversion to one thermodynamically favored diastereomer of substrate-bound ligand.

Ligand, **II-O*i*Pr**, Bound to Rhodium Complex

***trans*-[Rh(1)(CO)$_2$(Cl)]$_2$.** Chlorodicarbonylrhodium (I) dimer (2.7 mg, 6.9 x 10^{-3} mmol) and **II-O*i*Pr** (9.9 mg, 2.8 x 10^{-2} mmol) were weighed out in a glove box, dissolved in benzene-d_6, and allowed to stand for 12 h in a sealed, screw-top NMR tube. The orange solution was concentrated and dissolved in a minimal amount of benzene/pentane (1:1). The solution was placed in a vial with small holes in the cap and was allowed to slowly evaporate in a glovebox, yielding yellow needles suitable for x-ray diffraction analysis. A single crystal was taken and stored under nitrogen until ready for x-ray diffraction analysis.

X-ray Crystallographic Procedures. Single crystals obtained as described above were used for structural determination. The X-ray intensity data were measured at 100(2) K (Oxford Cryostream 700) on a Bruker SMART APEX CCD-based X-ray diffractometer system equipped with a Mo-target X-ray tube (λ = 0.71073Å) operated at 2000 W power.

The crystals were mounted on a goniometer head with silicone oil. The detector was placed at a distance of 6.00 cm from the crystal. For each experiment a total of 2400 frames were collected with a scan width of 0.3° in ω and an exposure time of 20 s/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). The final cell constants are based upon the refinement of the *XYZ*-centroids of several thousand reflections above 20 $\sigma(I)$. 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 F^2 using the Bruker SHELXTL (version 6.12) software package. The coordinates of heavy atoms were found in direct method *E* maps. The remaining atoms were located after an alternative series of least-squares cycles and difference Fourier maps. Hydrogen atoms were included in idealized positions for structure factor calculations. Anisotropic displacement parameters were assigned to all non-hydrogen atoms. Relevant crystallographic data are summarized in Table 2.6. Selected bond lengths are given in Table 2.7.

Crystallographic Tables for CCDC #833149

Table 2.6. Crystal data and structure refinement.

Empirical formula	$C_{45}\ H_{56}\ Cl\ N_2\ O_3\ P_2\ Rh$
Formula weight	873.22

Temperature	100(2) K	
Wavelength	0.71073Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions (Å)	a = 9.199(2)	α= 90°
	b = 14.760(3)	β= 90°
	c = 31.273(7)	γ = 90°
Volume	4246.3(16) $Å^3$	
Z	4	
Density (calculated)	1.366 g/cm^3	
Absorption coefficient	0.582 mm^{-1}	
F(000)	1824	
Crystal size	0.12 x 0.02 x 0.02 mm^3	
Theta range for data collection	2.39 to 28.40.	
Index ranges	-12<=h<=12, -19<=k<=19, -41<=l<=41	
Reflections collected	51112	
Independent reflections	10497 [R(int) = 0.0955]	
Completeness to theta = 28.40°	99.3%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9885 and 0.9335	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10497 / 462 / 481	

Goodness-of-fit on F^2	1.054
Final R indices [I>2sigma(I)]	R1 = 0.0511, wR2 = 0.0858
R indices (all data)	R1 = 0.0706, wR2 = 0.0916
Absolute structure parameter	-0.06(2)
Extinction coefficient	na
Largest diff. peak and hole	0.602 and -0.870 $e^- Å^{-3}$

Table 2.7. Selected bond lengths [Å] and angles [°].

Rh(1)-C(45)	1.811(4)
Rh(1)-P(1)	2.3004(11)
Rh(1)-P(2)	2.3191(11)
Rh(1)-Cl(1)	2.3445(10)
O(3)-C(45)	1.158(4)
C(45)-Rh(1)-P(1)	87.38(12)
C(45)-Rh(1)-P(2)	93.07(12)
P(1)-Rh(1)-P(2)	178.17(4)
C(45)-Rh(1)-Cl(1)	177.31(12)
P(1)-Rh(1)-Cl(1)	90.92(4)
P(2)-Rh(1)-Cl(1)	88.69(3)

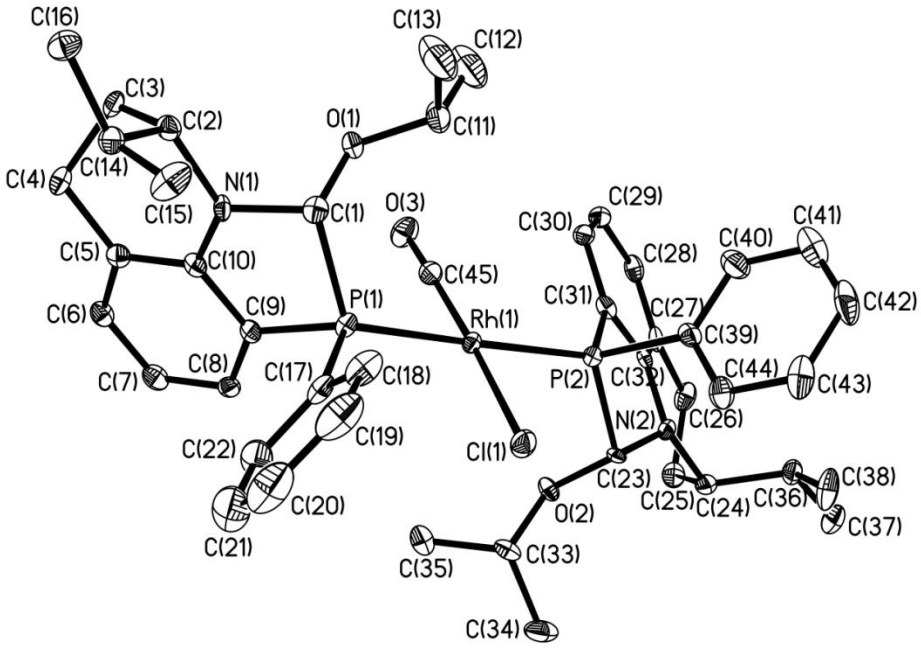
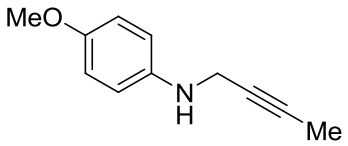


Figure 2.6 Perspective drawing of *trans*-[Rh(**II-O*i*Pr**)$_2$(CO)(Cl)] (CCDC # 833149). Atoms are represented by thermal ellipsoids at the 50% probability level.

Substrate Synthesis and Characterization

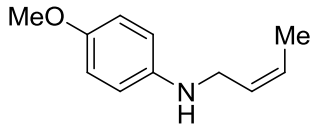
The following compounds were made according to literature procedures and matched reported spectra: (*Z*)-3-phenylprop-2-en-1-ol[14], (*Z*)-(3-chloroprop-1-enyl)benzene[15], 1,4-but-2-enediol cyclic sulfite[16,17], and (*Z*)-3-cyclohexylprop-2-en-1-ol[18], (*Z*)-ethyl 7-hydroxyhept-5-enoate.[19]



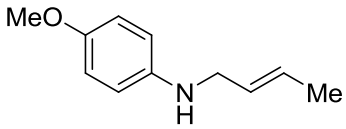
***N*-(but-2-ynyl)-4-methoxyaniline.**[20] To *p*-anisidine (2.80 g, 22.7 mmol) in CH_3CN (13 mL) was added 1-bromo-2-butyne (658 μL, 7.58 mmol). The mixture was stirred overnight at room temperature. Saturated aqueous NH_4Cl (15 mL) was added, and the mixture was separated. The aqueous layer was extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated. Column chromatography (10% EtOAc/Hex) afforded a light yellow oil (855 mg, 64%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.80-6.83 (m, 2H), 6.66 (dd, 2H, J = 9.0, 2.4), 3.83 (q, 2H, J = 2.2), 3.76 (s, 3H), 3.60 (bs, 1H), 1.80-1.81 (m, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 152.6, 141.4, 114.8, 114.6, 78.8, 76.4, 55.6, 34.8, 3.4; **IR**: 3384, 2917, 2932, 1513, 1463, 1235, 1036, 821 cm^{-1}; **HRMS** (DART-TOF) calcd. for

[14]Kim, I. S.; Dong, G. R.; Jung, Y. H. *J. Org. Chem.* **2007**, *72*, 5424-5426.
[15]Bergman, J. M.; Coleman, P. J.; Fraley, M. E.; Garbaccio, R. M.; Hartman, G. D.; Li, C.; Neilson, L. A.; Olson, C. M.; Tasber, E. S. WO 2006007491, 2006.
[16]Chaudhari, S. S.; Akamanchi, K. G. Synlett **1999**, *11*, 1763-1765.
[17]Shellhamer, D. F.; Anstine, D. T.; Gallego, K. M.; Ganesh, B. R.; Hanson, A. A.; Hanson, K. A.; Henderson, R. D.; Prince, J. M.; Heasley, V. L. *J. Chem. Soc. Perkin Trans 2* **1995**, *7*, 1569.
[18]Reed, S. A.; White, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 3316-3318.
[19]Ely, R. J.; Morken, J. P. *J. Am. Chem. Soc.* **2010***, 132*, 2534-2535.
[20]Saito, A.; Oda, S.; Fukaya, H.; Hanzawa, Y. *J. Org. Chem*. **2009**, *74*, 1517-1524.

$C_{11}H_{14}NO$ $[M+H]^+$: 176.1075, found: 176.1069.



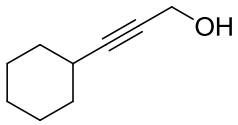
(*Z*)-*N*-(but-2-enyl)-4-methoxyaniline (10% *E* isomer), 2.8.[21] A round-bottom flask was charged with Lindlar's catalyst (121 mg) and purged with argon. *N*-(but-2-ynyl)-4-methoxyaniline (855 mg, 4.88 mmol) in EtOH (9 mL) was added followed by quinoline (46.0 μL, 0.390 mmol). The flask was evacuated and refilled with H_2 four times, fitted with a H_2 balloon, and stirred at room temperature under H_2 for 3.5 h. The reaction was filtered through a plug of silica and concentrated. Column chromatography (20% EtOAc/Hex) yielded a light yellow oil (754 mg, 87%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.79 (app dd, 2H, *J* = 9.0, 2.4), 6.61 (app dd, 2H, *J* = 8.8, 2.4), 5.53-5.69 (m, 2H), 3.76 (s, 3H), 3.73-3.75 (m, 2H), 3.37 (bs, 1H), 1.71 (d, 3H, *J* = 6.3); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.2, 142.6, 127.9, 126.9, 114.8, 114.3, 55.8, 41.8, 13.1; **IR**: 3290, 2934, 2015, 1608, 1512, 1413, 1249, 1032, 837 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{16}NO$ $[M+H]^+$:178.1232, found: 178.1234.



(*E*)-*N*-(but-2-enyl)-4-methoxyaniline, 2.12.[20] To *p*-anisidine (6.13 g, 49.8 mmol) in CH_3CN (29 mL) was added crotyl chloride (1.61 mL, 16.6 mmol). The mixture was

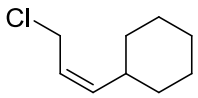
[21]Walters, M. A.; Hoem, A. B.; *J. Org. Chem.* **1994**, *59*, 2645-2647.

stirred overnight at 23 °C. Saturated aqueous NH_4Cl (15 mL) was added, and mixture was separated. The aqueous layer was extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated. Column chromatography yielded a light yellow oil (1.02 g, 35%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 6.79-6.83 (m, 2H), 6.60-6.63 (m, 2H), 5.70-5.75 (m, 1H), 5.59-5.65 (m, 1H), 3.76 (s, 3H), 3.66 (d, 2H, J = 5.9), 3.44 (bs, 1H), 1.73 (dd, 3H, J = 6.4, 1.2); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.1, 142.5, 128.4, 127.7, 114.8, 114.3, 55.8, 47.0, 17.8; **IR**: 3386, 2935, 2832, 1512, 1464, 1235, 1038, 966, 819 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{16}NO$ $[M+H]^+$: 178.1232, found: 178.1230.

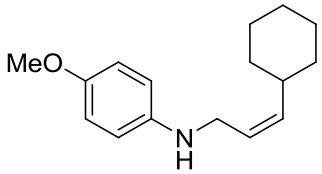


3-cyclohexylprop-2-yn-1-ol.[18] To a solution of cyclohexylacetylene (2.40 mL, 18.5 mmol) in THF (23 mL) at –78 °C was added *n*BuLi as a solution in hexanes (12.5 mL, 1.48 M) dropwise over 10 min. The mixture was stirred at –78 °C for 40 min, and paraformaldehyde (778 mg, 25.9 mmol) was added. The mixture was allowed to warm to 23 °C and stirred for 16 h. Saturated aqueous NH_4Cl (2 mL) was added, followed by Et_2O (70 mL). The mixture was dried over Na_2SO_4, filtered through a plug of Celite, and concentrated. The resulting oil was distilled under vacuum (70 °C at 1.25 mmHg) to yield a colorless oil (2.00 g, 78%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 4.25-4.27 (m, 2H), 2.36-2.40 (m, 1H), 1.78-1.81 (m, 2H), 1.65-1.72 (m, 2H), 1.51-1.58 (m, 2H), 1.37-1.45 (m, 2H), 1.25-1.34 (m, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 90.6, 78.1, 51.4, 32.6, 29.1, 25.8,

24.9; **IR**: 3327 (br), 2929, 2854, 1448, 1148, 1017, 986 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_9H_{15}O$ $[M+H]^+$:139.1123, found: 139.1125.



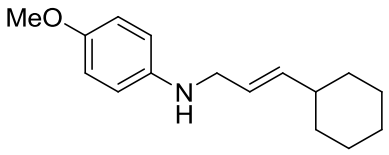
(*Z*)-(3-chloroprop-1-enyl)cyclohexane (10% (*E*)-isomer).[15] (*Z*)-3-cyclohexylprop-2-en-1-ol (642 mg, 4.58 mmol) was dissolved in DMF (3 mL). Collidine (1.11 g, 9.16 mmol), lithium chloride (388 mg, 9.16 mmol), and methanesulfonyl chloride (461 μL, 5.95 mmol) were added. After stirring for 12 h, the reaction was diluted with Et_2O (100 mL), and washed with H_2O, saturated aqueous NH_4Cl, and brine (50 mL each). The organic layer was dried over $MgSO_4$, filtered, and concentrated. Column chromatography (5% EtOAc/Hex) gave a colorless oil (591 mg, 81%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.44-5.56 (m, 2H), 4.11 (dd, 2H, J = 7.0, 2.2), 2.28-2.38 (m, 1H), 1.62-1.76 (m, 5H), 1.05-1.36 (m, 5H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 141.3, 123.2, 39.9, 36.3, 33.0, 25.8, 25.7; **IR**: 2953, 2925, 2853, 2034, 1970, 1511, 1459, 1260, 1032, 798, 410 cm^{-1}.



(*Z*)-*N*-(3-cyclohexylallyl)-4-methoxyaniline (5% (*E*)-isomer), 2.15.[22] K_2CO_3 (289 mg, 7.56 mmol) and *p*-anisidine (1.16 g, 9.45 mmol) were diluted with DMF (8 mL), and (*Z*)-

[22]Correa, A.; Tellitu, I.; Domínguez, E.; SanMartin, R. *J. Org. Chem.* **2006**, *71*, 8316 – 8319.

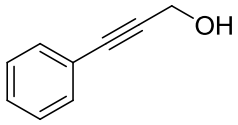
(3-chloroprop-1-enyl)cyclohexane (502 mg, 3.15 mmol) was added. The reaction was heated to 80 °C and stirred overnight. The reaction was cooled and filtered. Water (20 mL) was added, and the mixture was separated. The aqueous layer was extracted with EtOAc (3×30 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated. Column chromatography (10% EtOAc/Hex) yielded a yellow oil (508 mg, 66%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.79 (app dd, 2H, *J* = 9.0, 2.4), 6.61 (app dd, 2H, *J* = 9.0, 2.4), 5.38-5.47 (m, 2H), 3.75 (s, 3H), 3.73 (d, 2H, *J* = 5.1), 3.64 (d, 2H, *J* = 5.9), 3.36 (bs, 1H), 2.29-2.37 (m, 1H), 1.61-1.74 (m, 5H), 1.05-1.35 (m, 5H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 152.2, 142.6, 138.9, 125.0, 114.9, 114.3, 55.8, 42.3, 36.7, 33.3, 26.0, 25.8; **IR**: 2925, 2850, 1512, 1448, 1245, 1179, 1037, 821 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{24}NO$ $[M+H]^+$: 246.1858, found: 246.1860.



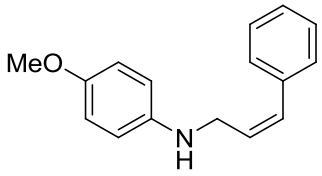
(*E*)-*N*-(3-cyclohexylallyl)-4-methoxyaniline, 2.16.[23] $AuBr_3$ (91.7 mg, 0.210 mmol) was suspended in THF (2 mL), and *p*-anisidine (505 mg, 4.10 mmol) was added. The mixture was stirred under argon at room temperature for 5 min. Cyclohexylallene (298 μL, 2.05 mmol) was added. After 4 h, the mixture was filtered through a silica plug and concentrated. Column chromatography (10% EtOAc/Hex) yielded a slightly yellow oil (189 mg, 38%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.79 (app dd, 2H, *J* = 9.0, 2.4), 6.60 (app dd, 2H, *J* = 9.0, 2.4), 5.66 (dd, 1H, *J* = 15.5, 6.5), 5.54 (dtd, 1H *J* = 15.5, 5.9, 1.0), 3.75

[23]Nishina, N.; Yamamoto, Y. *Tetrahedron* **2009**, *65*, 1799-1808.

(s, 3H), 3.65 (dd, 2H, J = 5.9, 1.0), 3.42 (bs, 1H), 1.92-2.20 (m, 1H), 1.63-1.75 (m, 5H), 1.03-1.32 (m, 5H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.1, 142.5, 139.1, 124.5, 114.8, 114.3, 55.8, 47.2, 40.4, 32.9, 26.1, 26.0; **IR**: 2923, 2845, 1512, 1447, 1234, 1039, 971, 818 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{24}NO$ $[M+H]^+$: 246.1858, found: 246.1860.

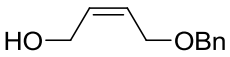


3-phenylprop-2-yn-1-ol.[18] The same procedure as 3-cyclohexylprop-2-yn-1-ol was followed. The resulting oil was distilled under vacuum (93 °C at 1.25 mmHg) to yield a colorless oil (3.64 g, 99%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.42-7.47 (m, 2H), 7.29-7.35 (m, 3H), 4.51 (d, 2H, J = 4.3), 1.69 (bs, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 131.7, 128.5, 128.3, 122.5, 87.1, 85.7, 51.7; **IR**: 3341, 3061, 2866, 1490, 1442, 1032, 953, 756, 691, 524 cm^{-1}; **HRMS** (DART-TOF) calcd. For C_9H_9O $[M+H]^+$: 133.0653, found: 133.0652.



(*Z*)-4-methoxy-*N*-(3-phenylallyl)aniline, 2.17.[20] To *p*-anisidine (1.58 g, 12.8 mmol) in CH_3CN (2 mL) was added (*Z*)-(3-chloroprop-1-enyl)benzene (501 mg, 3.28 mmol). The mixture was stirred overnight at room temperature. Saturated aqueous NH_4Cl (15 mL)

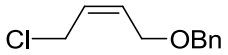
was added, and the mixture was separated. The aqueous layer was extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated. Column chromatography (10% EtOAc/Hex) yielded a yellow oil (369 mg, 47%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.25-7.29 (m, 2H), 7.14-7.21 (m, 3H), 6.68 (app d, 2H, J = 9.0), 6.49-6.56 (m, 1H), 6.47 (dd, 2H, J = 9.0, 2.4), 5.71 (dt, 1H, J = 11.7, 6.5), 3.90 (dd, 2H, J = 6.5, 1.8), 3.64 (s, 3H), 3.46 (bs, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.3, 142.1, 136.7, 131.3, 130.0, 128.8, 128.3, 127.1, 114.9, 114.4, 55.8, 43.2; **IR**: 3388, 3022, 2931, 2832, 1512, 1446, 1237, 1074, 820, 700, 517 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{18}NO$ $[M+H]^+$: 240.1388, found: 240.1390.



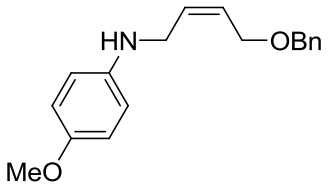
(*Z*)-4-(benzyloxy)but-2-en-1-ol.[24] In a dry box, a flame-dried 250 mL round-bottom flask was charged with sodium hydride (467 mg, 19.5 mmol). The flask was capped with a rubber septum and brought out of the dry box. Dry THF (65 mL) was added via syringe, and the vessel was brought to 0 °C. The commercially available (*Z*)-but-2-ene-1,4-diol (1.64 mL, 20.0 mmol) was added dropwise to the stirring suspension, resulting in vigorous bubbling. Once addition was complete, the reaction was allowed to warm to room temperature over the course of 30 min. Benzyl bromide (16.2 mmol, 1.92 mL) was added to the flask via syringe, and the reaction was allowed to stir overnight. The reaction was concentrated, and the crude residue was diluted with Et_2O (150 mL). The organic layer was washed with H_2O (3×75 mL), dried over $MgSO_4$, filtered, and

[24]Schmidt, B.; Pohler, M.; Costisella, B. *Tetrahedron* **2002**, *58*, 7951-7958.

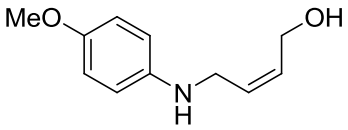
concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography (30% EtOAc/Hex) to yield a pale yellow oil (1.82 g, 48%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.29–7.36 (m 5H), 5.79-5.83 (m, 1H), 5.73-5.77 (m, 1H), 4.53 (s, 2H), 4.16-4.18 (m, 2H), 4.09-4.10 (m, 2H), 1.92 (br s, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 138.1, 132.5, 128.7, 128.5, 128.1, 128.0, 72.7, 65.9, 59.0; **IR**: 3409, 1736, 1241, 1070, 1042, 736, 697 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{15}O_2$ $[M+H]^+$: 179.1072, found: 179.1079.



(*Z*)-(((4-chlorobut-2-en-1-yl)oxy)methyl)benzene.[15] To a 25 mL, flame-dried, round-bottom flask was added LiCl (374 mg, 8.82 mmol), 2,4,6-collidine (1.16 mL, 8.81 mmol), and methanesulfonyl chloride (412 μL, 5.35 mmol). (*Z*)-4-(benzyloxy)but-2-en-1-ol (786 mg, 4.11 mmol) was added to the flask dropwise as a solution in DMF (3.0 mL). The reaction was allowed to stir overnight. The mixture was diluted with Et_2O (100 mL), and the organics were washed with H_2O (3×40 mL), saturated NH_4Cl (3×40 mL), and brine (40 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated. The crude mixture was purified by silica gel chromatography (10% EtOAc/Hex) to yield a pale orange oil (716 mg, 88%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.30–7.37 (m, 5H), 5.82-5.83 (m, 2H), 4.55 (s, 2H), 4.15-4.16 (m, 2H), 4.11-4.12 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 138.1, 131.0, 128.7, 128.6, 128.0, 127.9, 72.6, 65.3, 39.4; **IR**: 2857, 1736, 1453, 1240, 1072, 736, 697 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{17}ClNO$ $[M+NH_4]^+$: 214.0994, found: 214.0999.



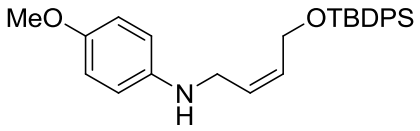
(*Z*)-*N*-(4-(benzyloxy)but-2-en-1-yl)-4-methoxyaniline, 2.18. To a 25 mL, flame-dried, round-bottom flask was added *p*-anisidine (2.54 g, 20.7 mmol). The vessel was charged with (*Z*)-(((4-chlorobut-2-en-1-yl)oxy)methyl)benzene (1.04 g, 5.30 mmol) as a solution in DMF (6 mL). The reaction was allowed to stir overnight. The reaction was diluted with Et_2O (150 mL), washed with H_2O (3×50 mL) and saturated NH_4Cl (3×50 mL), dried over $MgSO_4$, filtered, and concentrated. The crude mixture was purified by silica gel chromatography (15% EtOAc/Hex) to yield a dark orange oil (553 mg, 37%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.29-7.38 (m, 5H), 6.80 (d, 2H, *J* = 9.0), 6.59 (d, 2H, *J* = 8.8), 5.78-5.80 (m, 2H), 4.56 (s, 2H), 4.16 (d, 2H, *J* = 5.1), 3.77 (s, 3H), 3.75 (d, 2H, *J* = 4.9); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 152.6, 142.4, 138.3, 131.1, 128.9, 128.6, 128.0, 127.9, 115.1, 114.6, 72.7, 65.9, 56.0, 42.5; **IR**: 1509, 1232, 1070, 1030, 817, 735, 697 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{18}H_{22}N_1O_2$ $[M+H]^+$: 284.1651, found: 284.1649.



(*Z*)-4-(4-methoxyphenylamino)but-2-en-1-ol.[25] 1,4-but-2-enediol cyclic sulfite (1.50 g, 11.2 mmol) was dissolved in DMF (6 mL). K_2CO_3 (3.72 g, 26.9 mmol) and *p*-anisidine (2.76 g, 22.4 mmol) were added. The reaction was heated to 100 °C for 48 h. The

[25]Friedrich, M.; Savchenko, A. I.; Wachtler, A.; de Meijere, A. *Eur. J. Org. Chem*. **2003**, *11*, 2138-2143.

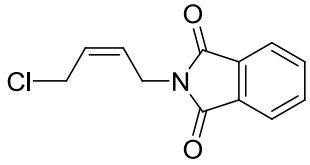
reaction was cooled to room temperature, and H_2O (30 mL) was added. The mixture was separated, and the aqueous layer was extracted with Et_2O (3×25 mL). The combined organic layers were washed with H_2O (25 mL), dried over $MgSO_4$, filtered, and concentrated. Column chromatography (15% EtOAc/Hex) yielded a light yellow oil (1.02 g, 47%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.79 (app dd, 2H, *J* = 9.0, 2.4), 6.61 (app dd, 2H, *J* = 9.0, 2.4), 5.68-5.82 (m, 2H), 4.26 (dd, 2H, *J* = 6.3, 1.2), 3.74-3.75 (m, 5H), 2.78 (bs, 2H); **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 152.6, 141.9, 131.5, 129.5, 114.8, 58.7, 55.7, 42.3; **IR**: 3361, 2939, 2833, 1512, 1235, 1034, 821 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{16}NO_2$ $[M+H]^+$: 194.1181, found: 194.1181.



(*Z*)-*N*-(4-(tert-butyldiphenylsilyloxy)but-2-enyl)-4-methoxyaniline, 2.19.[26] To imidazole (222 mg, 3.30 mmol) and DMF (0.6 mL) in a round-bottom flask was added (*Z*)-4-(4-methoxyphenylamino)but-2-en-1-ol (421 mg, 2.17 mmol) dissolved in DMF (0.6 mL). After stirring for 10 minutes, *tert*-butyldiphenylchlorosilane (610 µL, 2.39 mmol) was added in one portion. After stirring at room temperature for 45 min, H_2O (20 mL) was added. The mixture was separated, and the aqueous phase was extracted with Et_2O (3×15 mL). The combined organic layers were washed with H_2O (25 mL) and brine (25 mL). The resulting organic layer was dried over $MgSO_4$, filtered, and concentrated. Column chromatography (7.5% EtOAc/Hex) yielded a yellow oil (587 mg, 63%). **^{1}H**

[26]Havas, F.; Leygue, N.; Danel, M.; Mestre, B.; Galaup, C.; Picard, C. *Tetrahedron* **2009**, *76*, 7673-7686.

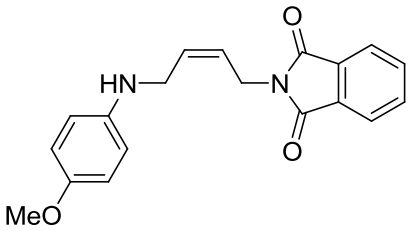
NMR ($CDCl_3$, 400 MHz) δ 7.59-7.62 (m, 4H), 7.27-7.37 (m, 6H), 6.67 (app dd, 2H, *J* = 9.0, 2.4), 6.41 (app dd, 2H, *J* = 9.0, 2.4), 5.65-5.70 (m, 1H), 5.45-5.51 (m, 1H), 4.23 (dt, 2H, *J* = 6.3, 0.8), 3.65 (s, 3H), 3.45 (dt, 2H, *J* = 6.7, 0.8), 3.19 (bs, 1H), 0.97 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.3, 142.2, 135.6, 133.6, 131.4, 129.7, 128.4, 127.7, 114.8, 114.3, 60.2, 55.8, 42.1, 26.8, 19.2; **IR**: 2931, 2857, 1513, 1428, 1236, 1074, 1040, 820, 703, 505 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{27}H_{34}NO_2Si$ $[M+H]^+$: 432.2359 found: 432.2345.



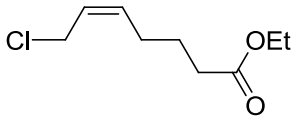
(*Z*)-2-(4-chlorobut-2-en-1-yl)isoindoline-1,3-dione.[27] To a flame-dried round-bottom flask was added potassium phthalamide (2.65 g, 14.3 mmol), followed by DMF (50 mL) under nitrogen. The stirring suspension was charged with (*Z*)-1,4-dichlorobut-2-ene (3.06 mL, 29 mmol). The mixture was allowed to stir at room temperature overnight. The reaction was diluted with EtOAc (200 mL) and extracted with H_2O (6×75 mL). The combined organics were dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude material was purified by silica gel chromatography (20% EtOAc/Hex) to afford the product as a colorless solid (929 mg, 28%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.86 (dd, 2H, *J* = 5.4, 2.9), 7.73 (dd, 2H, *J* = 5.4, 3.2), 5.83-5.89 (m, 1H), 5.69-5.75 (m, 1H), 4.38 (dd, 2H, *J* = 7.3, 1.2), 4.32 (d, 2H, *J* = 7.8) **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 168.0, 134.3, 132.3, 130.1, 127.4, 123.6, 38.8, 34.3; **IR**: 1699, 1429, 1242,

[27]Newman, A.; Grundt, P.; Luedtke, R. R. US Patent 2006106030, 2006.

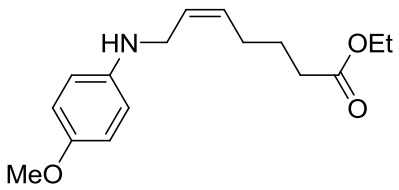
1120, 1065, 764, 711, 530 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{11}ClNO_2$ $[M+H]^+$: 236.0478, found: 236.0485.



(*Z*)-2-(4-((4-methoxyphenyl)amino)but-2-en-1-yl)isoindoline-1,3-dione, 2.20.[20] *p*-Anisidine (3.12 g, 25.4 mmol) was added to a flame-dried, 25 mL, round-bottom flask. The flask was charged with (*Z*)-2-(4-chlorobut-2-en-1-yl)isoindoline-1,3-dione (854 mg, 3.62 mmol) as a solution in CH_3CN (9.1 mL). The reaction mixture was allowed to stir at room temperature overnight. The reaction was diluted with Et_2O (100 mL), and washed successively with H_2O (3×50 mL) and saturated NH_4Cl (3×50 mL). The combined organics were dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude mixture was purified by silica gel chromatography (30% EtOAc/Hex) to yield the title compound as a yellow solid (761 mg, 65%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.85 (dd, 2H, *J* = 6.9, 3.9), 7.72 (dd, 2H, *J* = 6.9, 3.7), 6.80 (d, 2H, *J* = 11.2), 6.68 (d, 2H, *J* = 11.5), 5.79-5.81 (m, 1H), 5.59-5.61 (m, 1H), 4.39 (d, 2H, *J* = 9.1, 1.5), 3.95 (d, 2H, *J* = 8.3), 3.75 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 168.2, 152.6, 142.5, 134.2, 132.4, 131.9, 125.8, 123.5, 115.1, 114.8, 56.0, 42.0, 35.1; **IR**: 1705, 1511, 1390, 1322, 1234, 821, 715 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{19}H_{19}N_2O_3$ $[M+H]^+$: 323.1396, found: 323.1394.

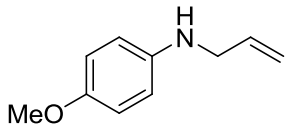


(*Z*)-ethyl-7-chlorohept-5-enoate.[15] To a 25 mL, flame-dried, round-bottom flask was added LiCl (499 mg, 11.0), 2,4,6-collidine (1.45 mL, 11.0 mmol), and methanesulfonyl chloride (552 μL, 7.18 mmol). (*Z*)-4-(benzyloxy)but-2-en-1-ol (951 mg, 5.52 mmol) was added to the flask dropwise as a solution in DMF (3.0 mL). The reaction was allowed to stir overnight. The mixture was diluted with Et_2O (100 mL), and the organics were washed with water (3×40 mL), saturated NH_4Cl (3×40 mL), and brine (40 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated. The crude mixture was purified by silica gel chromatography (3:1 Hex: EtOAc) to afford a pale orange oil (816 mg, 78%). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 5.52-5.63 (m, 2H), 4.12 (q, 2H, *J* = 7.4), 4.07 (d, 2H, *J* = 7.2), 2.25 (t, 2H, *J* = 7.4), 2.08-2.14 (m, 2H), 1.65-1.70 (m, 2H), 1.17-1.21 (m, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 173.6, 135.3, 126.5, 60.5, 39.4, 33.7, 26.6, 24.6, 14.4; **IR**: 2980, 1732, 1375, 1249, 1180, 758, 730 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_9H_{16}ClO_2$ $[M+H]^+$: 191.0839, found: 191.0835.



(*Z*)-ethyl 7-((4-methoxyphenyl)amino)hept-5-enoate, 2.21.[20] A flame-dried, 25 mL, round-bottom flask was charged with *p*-anisidine (3.68 g, 29.9 mmol). (*Z*)-ethyl 7-chlorohept-5-enoate (816 mg, 4.28 mmol) was added to the reaction flask as a solution in

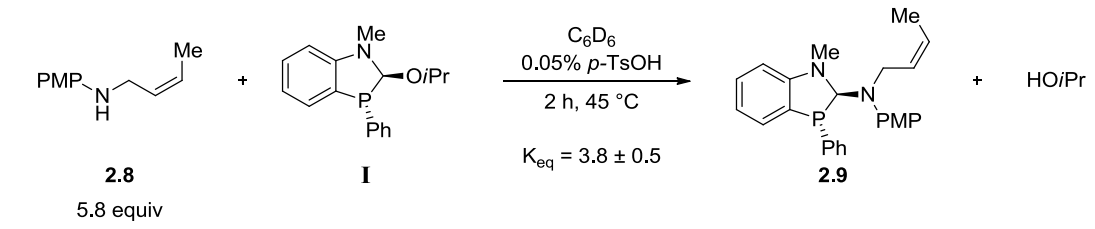
CH_3CN (9.0 mL). The reaction was allowed to stir at room temperature overnight. The reaction was diluted with Et_2O (150 mL) and washed with H_2O (3×50 mL) and saturated aqueous NH_4Cl (3×50 mL). The combined organics were dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude material was purified by silica gel chromatography (20% EtOAc/Hex) to afford an orange oil (684 mg, 57%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 6.77-6.79 (m, 2H), 6.58-6.60 (m, 2H), 5.49-5.61 (m, 2H), 4.13 (q, 2H, *J* = 7.1), 3.74 (s, 3H), 3.70 (dd, 2H, *J* = 6.4), 2.32 (t, 2H, *J* = 7.3), 2.17 (app q, 2H, *J* = 7.3), 1.72-1.75 (m, 2H), 1.25 (t, 3H, *J* = 7.1); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 173.7, 152.4, 142.7, 131.8, 128.4, 115.1, 114.6, 60.5, 56.0, 42.4, 33.9, 27.1, 24.9, 14.5; **IR**: 2936, 1727, 1511, 1234, 1035, 820 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{24}NO_3$ $[M+H]^+$: 278.1756, found: 278.1749.



***N*-allyl-4-methoxyaniline, 2.22.**[22] Allyl chloride (5.29 mL, 65.0 mmol) was added dropwise to a flame-dried 500 mL round-bottom flask containing a solution of 4-methoxyaniline (8.00 g, 65.0 mmol) and potassium carbonate (21.5 g, 156 mmol) in DMF (148 mL). The solution was heated to 80 °C and was stirred at this temperature overnight. The reaction was cooled to room temperature, filtered, and diluted with EtOAc (300 mL). The organic layer was washed with water (4×100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The crude product was purified by silica gel chromatography (5% EtOAc/Hex) to afford an orange oil (7.76 g, 73%). **^{1}H**

NMR ($CDCl_3$, 400 MHz) δ 6.82 (d, 2H, *J* = 8.8), 6.62 (d, 2H, *J* = 8.8), 5.94-6.04 (m, 1H), 5.31 (dd, 1H, *J* = 17.2, 1.6), 5.19 (dd, 1H, *J* = 10.4, 1.6), 3.77 (s, 3H), 3.75 (app. dt, 2H, *J* = 5.6, 1.6), 3.57 (br. s, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.3, 142.5, 136.0, 116.2, 115.0, 114.4, 55.9, 47.6; **IR**: 3396, 1509, 1230, 1178, 1035, 916, 816 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{14}NO$ $[M+H]^+$: 164.1075, found: 164.1077.

Equilibrium Experiment (Scheme 2.7)



2.8
5.8 equiv

I

2.9

PMP= *p*-methoxyphenyl

In a glove box, a solution of *i*PrOH (91 μL, 1.2 mmol) in C_6D_6 (1.67 M) was made. The solution was dispensed into three NMR tubes (see table below for amounts). A second solution of (*Z*)-*N*-(but-2-enyl)-4-methoxyaniline, **2.8**, (71 mg, 0.40 mmol), **I** (19 mg, 6.9 x 10^{-2} mmol), and *p*-TsOH (350 μL, 5.0 × 10^{-4} M in C_6H_6; note C_6H_6 was removed prior to mixing with substrate and **I**) in C_6D_6 (1.4 mL) was made. The solution was dispensed into three NMR tubes (see table below for amounts). An additional amount of C_6D_6 was added to each tube to make the total volume 0.7 mL. ^{31}P NMR were taken immediately, and the NMR tubes were heated to 45 °C. Spectra were acquired at 45 min intervals until equilibrium was reached. All three samples reached equilibrium within 2 h (average K_{eq} = 3.8 with standard deviation = 0.5).

Table 2.8

Experiment	Isopropanol Solution	mmol isopropanol	Substrate Solution	mmol substrate	Ratio **I**:**2.8**	K_{eq}
A	60 μL	0.10	400 μL	0.11	26:74	3.4
B	150 μL	0.25	400 μL	0.11	45:55	3.3
C	300 μL	0.50	400 μL	0.11	53:47	4.5

Optimization Data

General Hydroformylation Optimization Procedure. The Endeavor was charged with 500 μL of benzene per reaction well to fill the void volume between reactor wall and reaction tube, and oven-dried glass reaction vials were placed into the wells. The Endeavor was sealed and purged with nitrogen (4×100 psi). The necessary injection(s) were made (see below). The Endeavor was purged with nitrogen (1×100 psi), stirring was started at 250 rpm, and the Endeavor was heated to and held at the reaction temperature for 10 minutes. Stirring was stopped, the Endeavor was charged with the appropriate pressure of H_2/CO, stirring was re-initiated at 700 rpm, and the Endeavor was maintained at constant reaction temperature and pressure of H_2/CO for 15 h. The Endeavor was vented to ambient pressure and cooled to ambient temperature. The reaction vials were removed from the Endeavor, a solution of trimethoxybenzene in EtOAc (1.00×10^2 μL, 0.2003 M) was added, and the sample was concentrated. The resulting residue was dissolved in MeOH (2 mL) and added to $NaBH_4$ (22.7 mg, 0.600 mmol) in a flame-dried flask. The reaction was stirred for 1.5 h. H_2O (3 mL) was added, and the layers were separated. The organic layer was extracted with EtOAc (3×10 mL), dried over $NaSO_4$, filtered, and concentrated. ^{1}H NMRs were taken to determine conversion. The reaction

was chromatographed (1% MeOH/CH_2Cl_2) to determine isolated yield. SFC or HPLC analysis of the products was used to determine enantioselectivities.

Pressure Screen with **I** (Table 2.1)

(*Z*)-*N*-(but-2-enyl)-4-methoxyaniline, **2.8**, (35 mg, 0.20 mmol) and **I** (7.7 mg, 3.0 x 10^{-2} mmol) were mixed in C_6D_6 (0.6 mL) and heated to 45 °C for 12 h in a sealed NMR tube. The solution was concentrated in a dry glove box to remove MeOH in the solution. During this pre-exchange, **I** converts to **2.9**. The resulting residue was dissolved in benzene (1.5 mL), mixed with 2 mol % Rh(acac)$(CO)_2$ (1.1 mg, 4.0 x 10^{-3} mmol), and injected into the Endeavor followed by 0.5 mL benzene to wash the injection port. The reactions were run at 45 °C at the following pressures: 25, 50, 75 and 100 psi H_2/CO.

Catalyst Loading Screen with **I** (Table 2.2)

(*Z*)-*N*-(but-2-enyl)-4-methoxyaniline, **2.8**, (35 mg, 0.20 mmol) and **I** were mixed in C_6D_6 (0.6 mL) and heated to 45 °C for 12 h in a sealed NMR tube. The solution was concentrated in a dry glove box to remove MeOH in the solution. During this pre-exchange, **I** converts to **2.9**. The resulting residue was dissolved in benzene (1.5 mL), mixed with 2 mol % Rh(acac)$(CO)_2$ (1.1 mg, 4.0 x 10^{-3} mmol), and injected into the Endeavor followed by 0.5 mL benzene to wash the injection port. The reactions were run at 45 °C and 50 psi H_2/CO with the following ligand loadings: 5% (2.6 mg, 1.0 x 10^{-2} mmol), 10% (5.1 mg, 2.0 x 10^{-2} mmol), 15% (7.7 mg, 3.0 x 10^{-2} mmol).

Acid Loading Screen (Table 2.3)

(*E*)-*N*-(but-2-enyl)-4-methoxyaniline, **2.12**, (35 mg, 0.20 mmol), **I** (5.1 mg, 2.0 x 10^{-2} mmol), and the appropriate amount of *p*-toluenesulfonic acid in benzene (7.7 x 10^{-4} M

solution) were mixed in C_6D_6 (0.6 mL) and heated to 45 °C for 12 h in a sealed NMR tube. The solution was concentrated in a dry glove box to remove MeOH in the solution. During this pre-exchange, **I** converts to **2.9**. The resulting residue was dissolved in benzene (1.5 mL), mixed with 2 mol % Rh(acac)$(CO)_2$ (1.1 mg, 4.0 x 10^{-3} mmol), and injected into the Endeavor followed by 0.5 mL benzene to wash the injection port. The reactions were run at 45 °C and 50 psi with the following acid loadings: 0.02% (52 μL, 4.0 x 10^{-5} mmol), 0.05% (130 μL, 1.0 x 10^{-4} mmol), 0.1% (260 μL, 2.0 x 10^{-4} mmol), and 0.2% (520 μL, 4.0 x 10^{-4} mmol).

Temperature Screen with **II** (Table 2.4)

(*Z*)-*N*-(but-2-enyl)-4-methoxyaniline, **2.8**, (35.0 mg, 0.20 mmol), **II-OMe** (6.5 mg, 2.0 x 10^{-2} mmol), and *p*-toluenesulfonic acid in benzene (130 μL, 1.0 x 10^{-4} mmol, 7.7 x 10^{-4} M solution) were mixed in C_6D_6 (0.6 mL) and heated to 45 °C for 12 h in a sealed NMR tube. The solution was concentrated in a dry glove box to remove MeOH in the solution and redissolved in C_6D_6. The solution was heated to 45 °C for 4 h before being concentrated again in a glove box. During this pre-exchange, the four diastereomers of **II-OMe** converge to one substrate-bound ligand peak. The resulting residue was dissolved in benzene (1.5 mL), mixed with 2 mol % Rh(acac)$(CO)_2$ (1.1 mg, 4.0 x 10^{-3} mmol), and injected into the Endeavor followed by 0.5 mL benzene to wash the injection port. The reactions were run with 50 psi H_2/CO at the following temperatures: 30, 35, 45, and 55 °C.

Increasing the Reaction Time (Scheme 2.8)

The procedure for Table 2.4 was followed running substrate **2.8** (0.4 mmol) at 35 °C for 24 hours.

Increasing the Amount of **II** (Scheme 2.9)

The procedure for Table 2.4 was followed running substrate **2.8** (0.4 mmol) at 35 °C with 15 mol % **I** (21 mg, 0.06 mmol).

Reaction of 4-methoxy-*N*-(3-methylbut-2-en-1-yl)aniline (Scheme 2.10)

4-methoxy-*N*-(3-methylbut-2-en-1-yl)aniline (38 mg, 0.20 mmol) and **I** (5.7 mg, 2.0 x 10^{-2} mmol) were mixed in C_6D_6 (0.6 mL) and heated to 45 °C for 12 h in a sealed NMR tube. The solution was concentrated in a dry glove box to remove MeOH in the solution. During this pre-exchange, **I** converts to **2.9**. The resulting residue was dissolved in benzene (1.5 mL), mixed with 2 mol % $Rh(acac)(CO)_2$ (1.1 mg, 4.0 x 10^{-3} mmol), and injected into the Endeavor followed by 0.5 mL benzene to wash the injection port.

Substrate Scope (Table 2.5)

General Hydroformylation Procedure. The Endeavor was charged with 500 μL of benzene per reaction well to fill the void volume between reactor wall and reaction tube, and oven-dried glass reaction vials were placed into the wells. The Endeavor was sealed and purged with nitrogen (4×100 psi). The necessary injection(s) were made (see below). The Endeavor was purged with nitrogen (1×100 psi), stirring was started at 250 rpm, and the Endeavor was heated to and held at 35 ˚C for 10 minutes. Stirring was stopped, the Endeavor was charged with 50 psi H_2/CO, stirring was re-initiated at 700 rpm, and the Endeavor was maintained at constant reaction temperature of 35 °C and pressure of 50

psi H_2/CO for 15 h. The Endeavor was vented to ambient pressure and cooled to ambient temperature. The reaction vials were removed from the Endeavor, a solution of trimethoxybenzene in EtOAc (1.00 x 10^2 μL, 0.2003 M) was added, and the sample was concentrated. The resulting residue was dissolved in MeOH (2 mL) and added to $NaBH_4$ (22.7 mg, 0.600 mmol) in a flame-dried flask. The reaction was stirred for 1.5 h. H_2O (3 mL) was added, and the layers were separated. The organic layer was extracted with EtOAc (3×10 mL), dried over $NaSO_4$, filtered, and concentrated. ^{1}H NMRs were taken to determine conversion. The reaction was chromatographed (1% MeOH/CH_2Cl_2) to determine isolated yield. SFC or HPLC analysis of the products was used to determine enantioselectivities.

Procedure A: (*Z*)-*N*-(but-2-enyl)-4-methoxyaniline, **2.8**, (35 mg, 0.20 mmol), **II-OMe** (9.8 mg, 3.0 x 10^{-2} mmol), and *p*-toluenesulfonic acid in benzene (130 μL, 1.0 x 10^{-4} mmol, 7.70 x 10^{-4} M solution) were mixed in C_6D_6 (0.6 mL) and heated to 45 °C for 12 h in a sealed NMR tube. The solution was concentrated in a dry glove box to remove MeOH in the solution and redissolved in C_6D_6. The solution was heated to 45 °C for 4 h before being concentrated again in a glove box. During this pre-exchange, the four diastereomers of **II-OMe** converge to one substrate-bound ligand peak. The resulting residue was dissolved in benzene (1.5 mL), mixed with 2 mol % Rh(acac)$(CO)_2$ (1.1 mg, 4.0 x 10^{-3} mmol), and injected into the Endeavor followed by 0.5 mL benzene to wash the injection port.

Procedure B: The same procedure as Procedure A using 1.75 mol % Rh(acac)$(CO)_2$ (0.90 mg, 3.5 x 10^{-3} mmol) and 0.03% *p*-TsOH (83 μL, 6.0 × 10^{-5} mmol).

Procedure C: The procedure is the same as Procedure A using 1.5 mol % $Rh(acac)(CO)_2$ (0.77 mg, 3.0 x 10^{-3} mmol).

Procedure D. Same as procedure A except 1.75 mol % $Rh(acac)(CO)_2$ (0.90 mg, 3.5 x 10^{-3} mmol) was used.

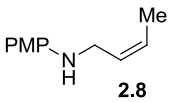
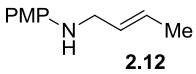
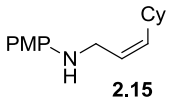
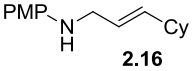
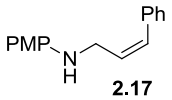
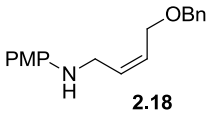
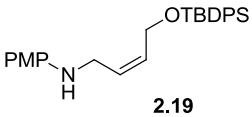
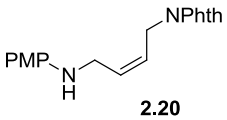
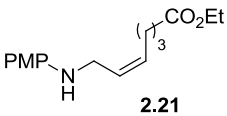
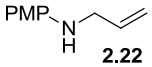
Scale-up Procedure. (*Z*)-*N*-(but-2-enyl)-4-methoxyaniline, **2.8**, (502 mg, 2.83 mmol), **II-OMe** (138 mg, 0.425 mmol), and *p*-toluenesulfonic acid in benzene (1.84 mL, 1.42 x 10^{-3} mmol, 7.7 x 10^{-4} M solution) were mixed in C_6D_6 (9.4 mL) and heated to 45 °C for 3 h in a sealed tube. The solution was concentrated in a dry glove box to remove MeOH in the solution. During this pre-exchange, the four diastereomers of **II-OMe** converge to one substrate-bound ligand peak. The resulting residue was dissolved in benzene (21.3 mL), mixed with 2 mol % $Rh(acac)(CO)_2$ (14.6 mg, 5.60 x 10^{-2} mmol), and 3 mL of the solution was injected into seven Endeavor wells followed by 1.0 mL benzene to wash each injection port.

Hydroformylation Regioselectivities

Under the reaction conditions, the undesired normal products probably cyclize to a *p*-methoxyphenyl protected aminal which could not be detected in crude NMRs or isolated. Trying to make and isolate this product through other methods also failed. The amount of undesired regioisomer was estimated by two calculations: the difference between conversion and yield of iso product by ^1H NMR (Table 2.9, Column 6) and the difference between conversion and isolated yield (Table 2.9, Column 7). The selectivities are generally greater than 4:1. These numbers probably underestimate the actual regioselectitives because it does not account for side reactions or decomposition of the

aldehyde during hydroformylation. Notably, previous work in our group in the hydroformylation of allylic alcohols and sulfonamides afford regioselectivites of >95:5.[5a,d] As mentioned previously, the lower regioselectivity for the phthalimide protected substrate may result from directed hydroformylation from the phthalimide functional group. Similarly the terminal substrate may have a lower regioselectivity due to background reaction that prefers the normal isomer.

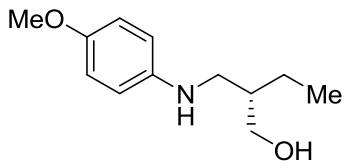
Table 2.9

Substrate	Starting Olefin (%)[a]	Product (%)[a]	Isolated Yield (%)	ee (%)[b]
 **2.8**	26	70	69	92
 **2.12**	8	N/A[c]	74	80
 **2.15**	12	N/A[c]	75	86
 **2.16**	20	64	62	76
 **2.17**	45	53	45	79
 **2.18**	11	N/A[c]	70	92
 **2.19**	19	71	66	90
 **2.20**	7	70	55	93
 **2.21**	10	N/A[c]	68	90
 **2.22**	8	77	64	73

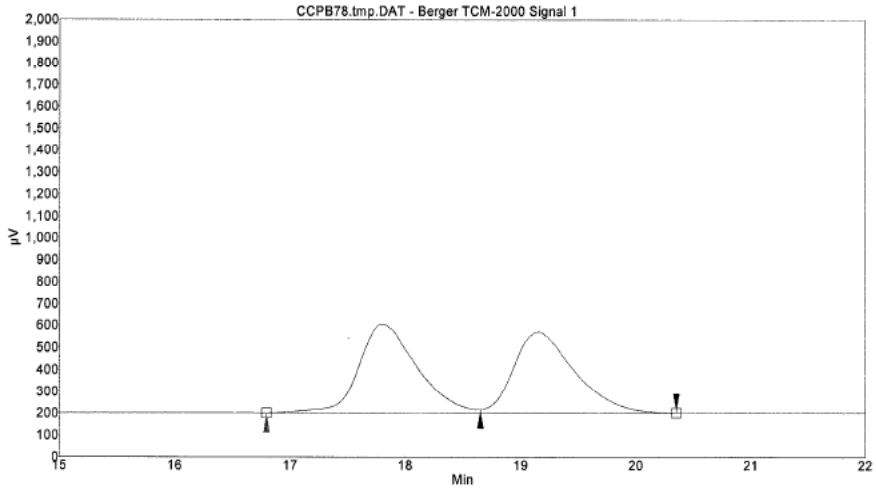
[a]Based on ^{1}H NMR with 1,3,5-trimethoxybenzene used as an internal standard. [b]Determined by super-critical fluid chromatography. [c]Amount could not be determined accurately due to peak overlap in ^{1}H NMR.

Hydroformylation Results and Product Characterization

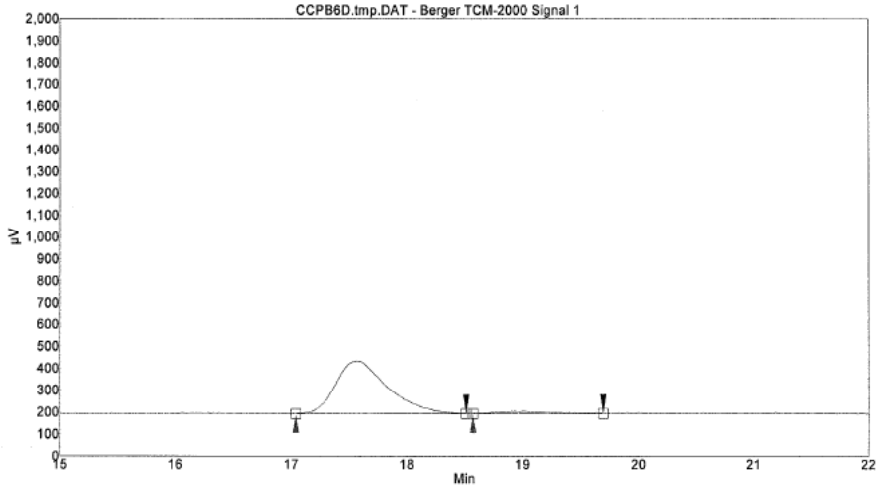
Table 2.5, Entry 1:



(*S*)-2-((4-methoxyphenylamino)methyl)butan-1-ol, 2.10. Procedure A was followed. Chromatography (1% MeOH/CH_2Cl_2) yielded a pale yellow oil (27 mg, 69%). **SFC** (OD-H, 4.0 mL/min, 3.0% MeOH, 220 nm, 150 bar, 35 °C) t_{rmajor} =17.80 min and t_{rminor} =19.16 min, 92% ee; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.78-6.82 (m, 2H), 6.66-6.70 (m, 2H), 3.80 (dd, 1H, *J* = 10.8, 3.9), 3.75 (s, 3H), 3.63-3.68 (m, 1H), 3.30 (bs, 1H), 3.20-3.24 (m, 1H), 3.12 (dd, 1H, *J* = 12.1, 8.4), 1.77-1.82 (m, 1H), 1.39 (q, 2H, *J* = 7.2), 0.96-1.00 (m, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.6, 142.4, 115.1, 114.8, 66.1, 55.8, 48.9, 41.8, 22.3, 11.6; **IR**: 3379, 2961, 2925, 1513, 1464, 1236, 1038, 822 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{20}NO_2$ $[M+H]^+$: 210.1494, found: 210.1498. **$[\alpha]_D^{20}$** = +8.7 (*c* = 0.240, $CHCl_3$, *l* = 50 mm).

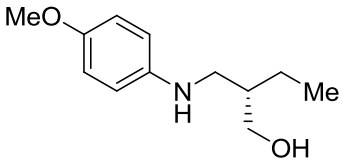


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	16.79	17.80	18.65	0.00	51.19	403.3	236.3	51.190
2	UNKNOWN	18.65	19.16	20.35	0.00	48.81	369.0	225.3	48.810
Total						100.00	772.2	461.6	100.000

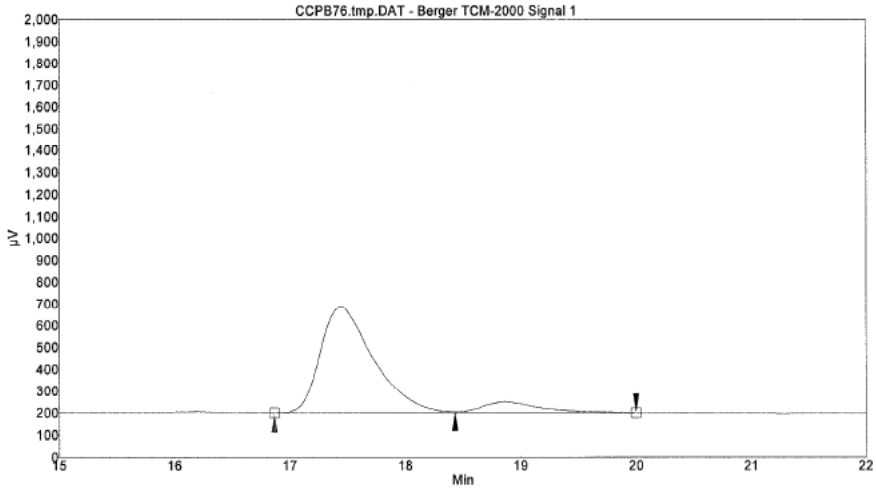


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	17.04	17.57	18.51	0.00	95.83	240.7	125.5	95.829
2	UNKNOWN	18.57	19.01	19.69	0.00	4.17	11.7	5.5	4.171
Total						100.00	252.4	131.0	100.000

Table 2.5, Entry 2:

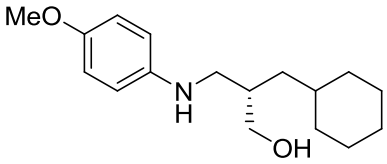


(*S*)-2-((4-methoxyphenylamino)methyl)butan-1-ol. Procedure A was followed. Chromatography (1% MeOH/CH_2Cl_2) yielded a pale yellow oil (28 mg, 74%). **SFC** (OD-H, 4.0 mL/min, 3.0% MeOH, 220 nm, 150 bar, 35 ˚C) 80% ee.

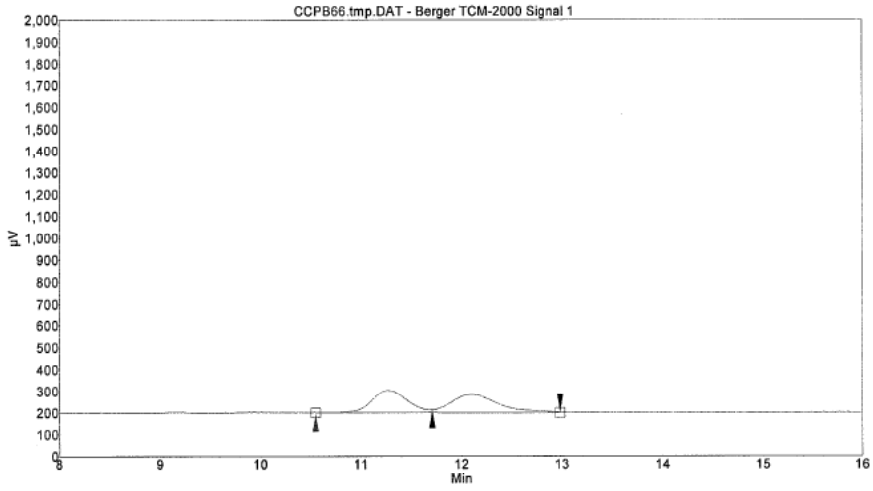


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	16.86	17.44	18.43	0.00	89.79	490.1	258.9	89.789
2	UNKNOWN	18.43	18.86	20.00	0.00	10.21	51.6	29.4	10.211
Total						100.00	541.7	288.3	100.000

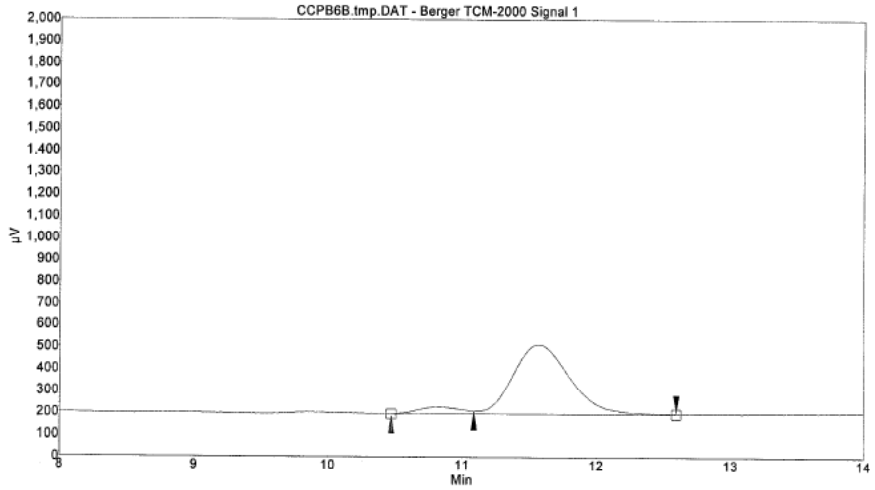
Table 2.5, Entry 3:



(*S*)-3-cyclohexyl-2-((4-methoxyphenylamino)methyl)propan-1-ol. Procedure A was followed. Chromatography (1% MeOH/CH_2Cl_2) yielded a pale yellow oil (42 mg, 75%). **SFC** (OD-H, 1.0 mL/min, 6.0% MeOH, 220 nm, 150 bar, 50 ˚C) t_{rminor} =11.27 min and t_{rmajor} =12.10 min, 86% ee; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 6.80 (dd, 2H, *J* = 6.6, 2.5), 6.64-6.67 (m, 2H), 3.77-3.79 (m, 1H), 3.75 (s, 3H), 3.61 (dd, 1H, *J* = 10.8, 7.3), 3.19 (dd, 1H, *J* = 12.0, 3.9), 3.06 (dd, 1H, *J* = 12.0, 8.6), 1.93-2.20 (m, 1H), 1.64-1.75 (m, 5H), 1.28-1.35 (m, 1H), 1.11-1.28 (m, 5H), 0.84-0.93 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.7, 142.5, 115.2, 114.9, 67.1, 55.8, 49.9, 37.3, 37.1, 35.1, 33.7, 33.6, 26.6, 26.3, 26.3; **IR**: 3376, 2921, 2849, 1512, 1448, 1235, 1037, 819 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{17}H_{28}NO_2$ $[M+H]^+$: 278.2120, found: 278.2117. **$[\alpha]_D^{20}$** = +4.3 (*c* = 0.140, $CHCl_3$, *l* = 50 mm).

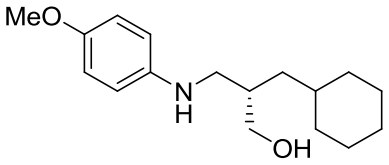


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	10.55	11.27	11.71	0.00	47.94	105.4	42.6	47.936
2	UNKNOWN	11.71	12.10	12.98	0.00	52.06	85.4	46.3	52.064
Total						100.00	190.8	88.8	100.000

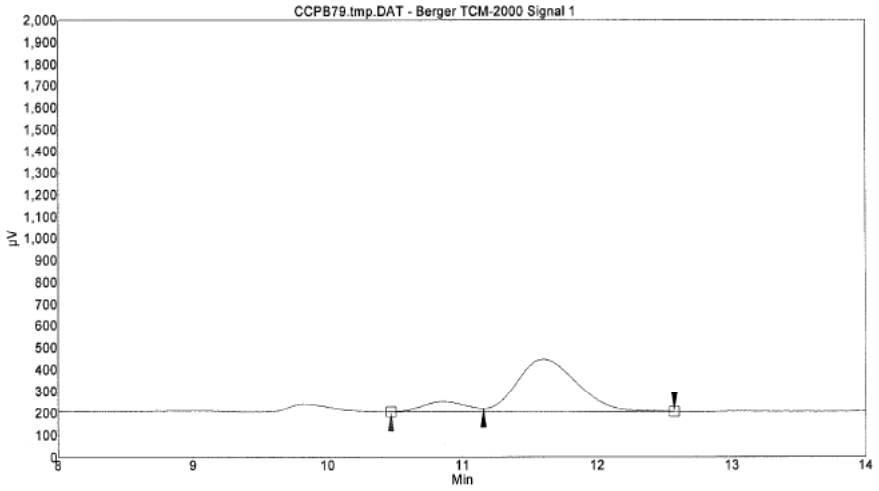


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	10.47	10.83	11.09	0.00	6.87	32.3	11.5	6.866
2	UNKNOWN	11.09	11.56	12.59	0.00	93.13	317.8	155.4	93.134
Total						100.00	350.1	166.9	100.000

Table 2.5, Entry 4:

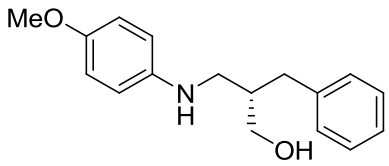


(*S*)-3-cyclohexyl-2-((4-methoxyphenylamino)methyl)propan-1-ol. Procedure A was followed. Chromatography (1% MeOH/CH_2Cl_2) yielded a pale yellow oil (34 mg, 62%). **SFC** (OD-H, 1.0 mL/min, 6.0% MeOH, 220 nm, 150 bar, 50 ˚C) 76 % ee.



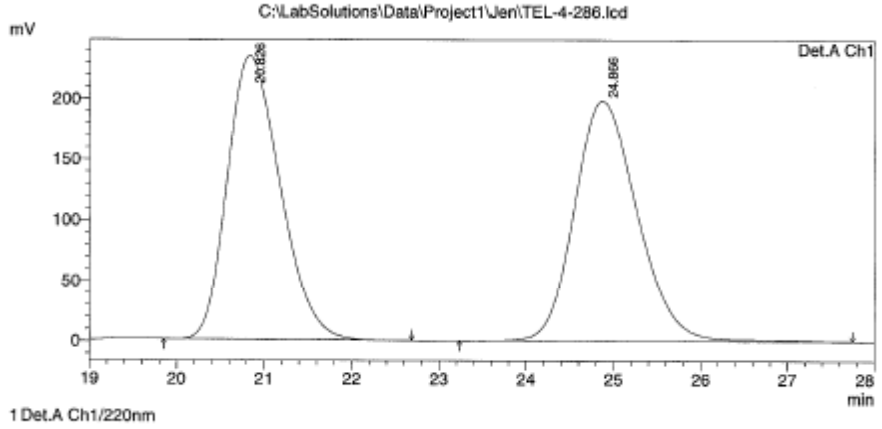
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	10.47	10.85	11.16	0.00	12.15	46.3	17.1	12.146
2	UNKNOWN	11.16	11.60	12.57	0.00	87.85	241.2	123.4	87.854
Total						100.00	287.5	140.4	100.000

Table 2.5, Entry 5:



(*S*)-2-benzyl-3-(4-methoxyphenylamino)propan-1-ol. Procedure A was followed. Column chromatography (1% MeOH/CH_2Cl_2) yielded a pale yellow solid (24 mg, 45%). **SFC** (OD-H, 1.0 mL/min, 5.0% MeOH, 220 nm, 150 bar, 50 ˚C) t_{rmajor}= 20.83 min, t_{rminor}= 24.87 min, 79% ee; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.10-7.28 (m, 5H), 6.69 (d, 2H, *J* = 8.8), 6.49 (d, 2H, *J* = 8.8), 3.70 (dd, 1H, *J* = 3.9, 10.8), 3.67 (s, 3H), 3.58 (dd, 1H, *J* = 6.5, 10.8), 3.05-3.15 (m, 2H), 2.70-3.05 (br s, 2H), 2.50-2.70 (m, 2H), 2.05-2.15 (m, 1H) ; **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.8, 141.8, 139.7, 129.0, 128.5, 126.2, 115.3, 114.8, 65.6, 55.8, 48.6, 41.9, 36.1; **IR**: 3373, 2926, 1510, 1454, 1235, 1033, 820, 743,

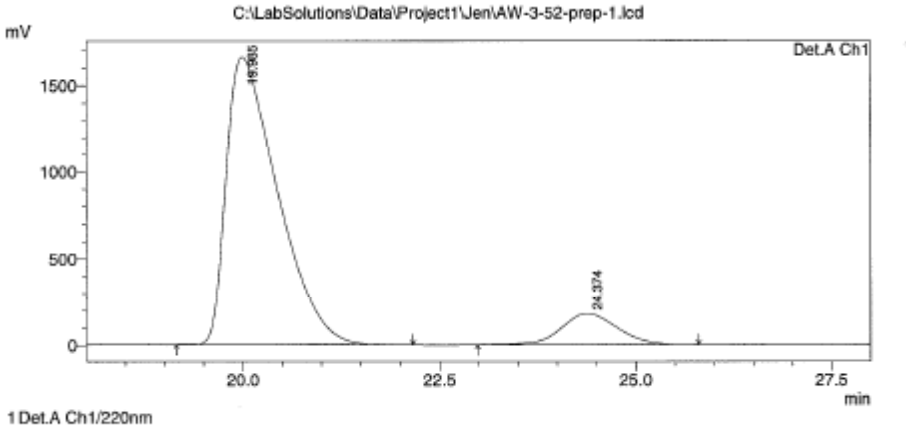
701, 521 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{17}H_{22}NO_2$ $[M+H]^+$: 272.1651, found: 272.1641. $[\alpha]_D^{20}$ = +50.0 (*c* = 0.108, $CHCl_3$, *l* = 50 mm).



PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %
1	20.826	9820286	233924	49.677
2	24.866	9948039	198051	50.323
Total		19768325	431975	100.000

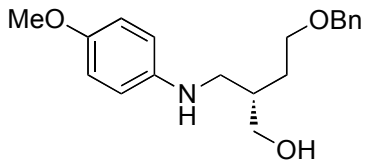


PeakTable

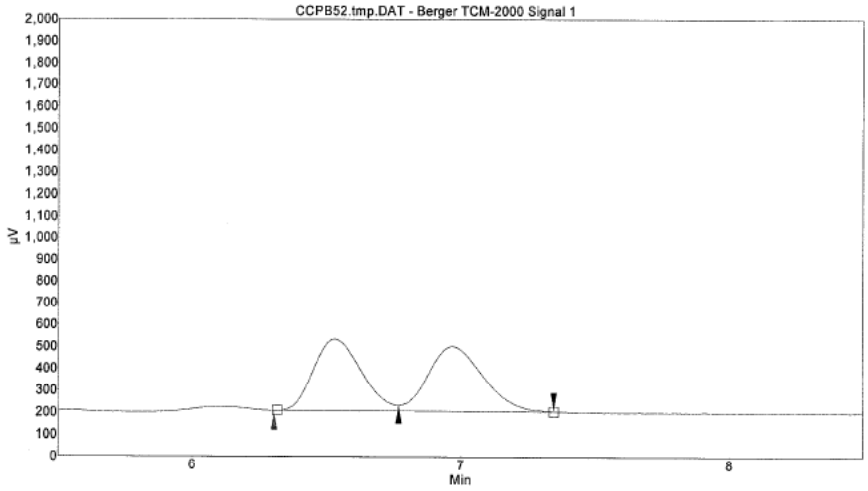
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %
1	19.985	75558073	1658200	89.461
2	24.374	8901186	179526	10.539
Total		84459259	1837727	100.000

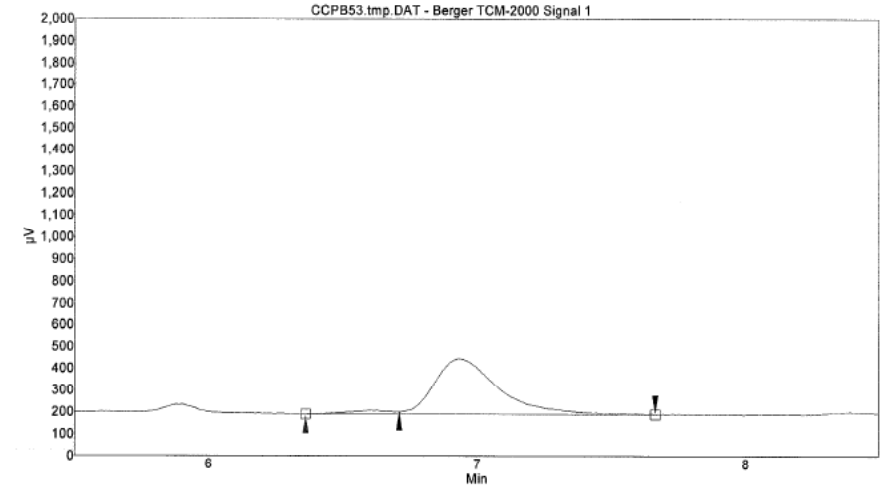
Table 2.5, Entry 6:



(*S*)-4-(benzyloxy)-2-(((4-methoxyphenyl)amino)methyl)butan-1-ol. Procedure B was followed and yielded a light yellow oil (44 mg, 70%). **SFC** (AS-H, 2.0 mL/min, 3.0% MeOH, 240 nm, 150 bar, 50 °C) t_{rminor} =6.53 min and t_{rmajor} =6.96 min, 92% ee; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.30-7.37 (m, 5H), 6.76 (d, 2H, *J* = 9.0), 6.59 (d, 2H, *J* = 9.0), 4.59 (s, 2H), 3.74 (s, 3H), 3.68-3.70 (m, 2H), 3.55-3.62 (m, 2H), 3.13 (d, 2H, *J* = 6.5), 1.99-2.03 (m, 1H), 1.71-1.75 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 152.6, 142.5, 138.1, 128.7, 128.0, 128.0, 115.1, 114.9, 73.5, 68.7, 65.7, 56.0, 48.5, 38.8, 30.3; **IR**: 3362, 1511, 1032, 820, 699 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{19}H_{26}NO_3$ $[M+H]^+$: 316.1919, found: 316.1913. $\mathbf{[\alpha]_D^{20}}$ = +18.0 (*c* = 0.205, $CHCl_3$, *l* = 50 mm).

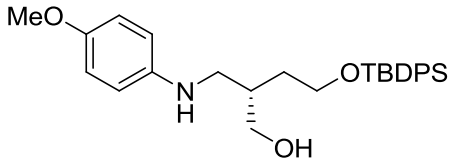


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.30	6.53	6.77	0.00	48.90	325.1	66.8	48.903
2	UNKNOWN	6.77	6.96	7.35	0.00	51.10	295.9	69.8	51.097
Total						100.00	621.0	136.7	100.000

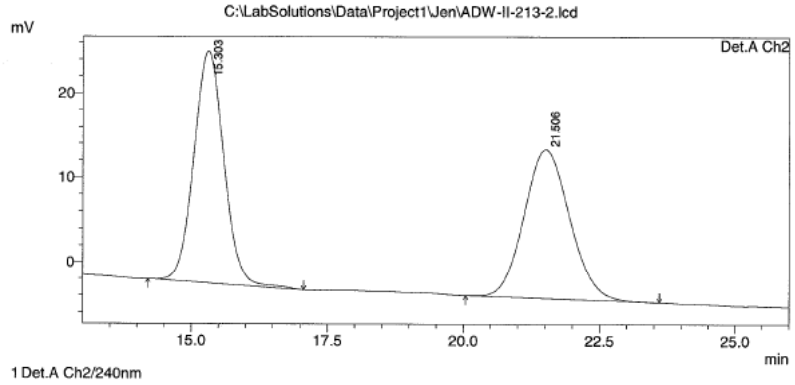


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.36	6.63	6.71	0.00	4.18	16.7	3.1	4.178
2	UNKNOWN	6.71	6.93	7.66	0.00	95.82	254.8	70.4	95.822
Total						100.00	271.6	73.5	100.000

Table 2.5, Entry 7:



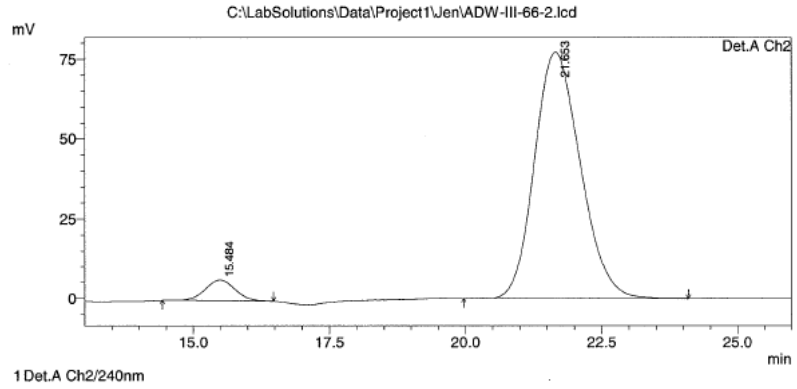
(*S*)-4-(tert-butyldiphenylsilyloxy)-2-((4-methoxyphenylamino)methyl)butan-1-ol. Procedure C was followed. Chromatography (1% MeOH/CH_2Cl_2) yielded a pale yellow oil (62 mg, 67%). **HPLC** (OD-H, 1.0 mL/min, 5.0% *i*PrOH: 95% Hexanes, 240 nm) t_{rminor} = 15.3 min and t_{rmajor} = 21.5, 90% ee; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.67 (dd, 4H, *J* = 8.1, 1.5), 7.37-7.46 (m, 6H), 6.77-6.78 (m, 2H), 6.61 (dd, 2H, *J* = 6.9, 2.2), 3.76-3.81 (m, 2H), 3.75 (s, 3H), 3.67-3.72 (m, 2H), 3.13 (d, 2H, *J* = 6.4), 2.03-2.10 (m, 1H), 1.64 (q, 2H, *J* = 6.1), 1.07 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.4, 142.4, 135.5, 133.4, 129.8, 127.7, 114.9, 114.7, 65.8, 62.2, 55.8, 48.4, 38.0, 32.7, 26.8, 19.1; **IR**: 3352, 2932, 1513, 1236, 1110, 822, 703, 613, 509 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{28}H_{38}NO_3Si$ $[M+H]^+$: 464.2621, found: 464.2622. **$[\alpha]_D^{20}$** = +12.3 (*c* = 0.140, $CHCl_3$, *l* = 50 mm).



PeakTable

Detector A Ch2 240nm

Peak#	Ret. Time	Area	Height	Area %
1	15.303	1059217	27520	50.562
2	21.506	1035662	17623	49.438
Total		2094879	45143	100.000

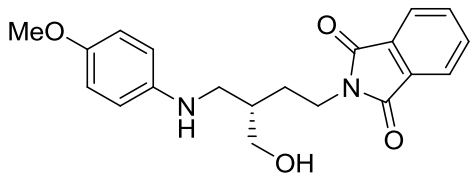


PeakTable

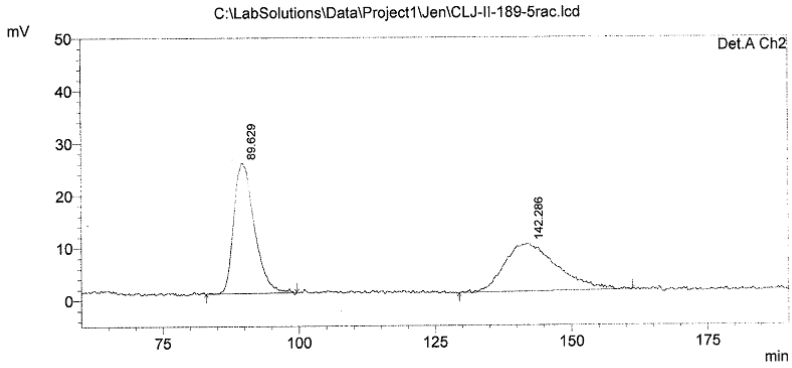
Detector A Ch2 240nm

Peak#	Ret. Time	Area	Height	Area %
1	15.484	245595	6463	5.149
2	21.653	4524475	77193	94.851
Total		4770071	83656	100.000

Table 2.5, Entry 8:



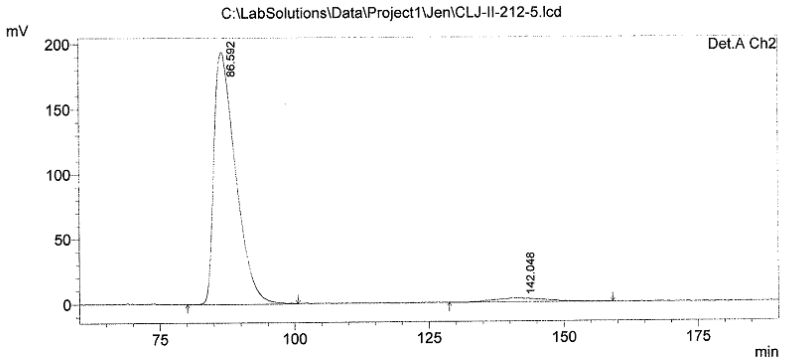
(*S*)-2-(4-hydroxy-3-((4-methoxyphenylamino)methyl)butyl)isoindoline-1,3-dione. Procedure C was followed except only 1 equivalent of $NaBH_4$ was used in reduction to prevent reduction of the phthalimide protecting group. Column chromatography resulted in a pale yellow solid (39 mg, 55%). **HPLC** (AS-H, 1.0 mL/min, 10.0% *i*PrOH: 90% Hexanes, 240 nm) t_{rmajor} = 89.6 and t_{rminor} = 142.3 min, 93% ee; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.82 (dd, 2H, *J* = 5.4, 3.1), 7.70 (dd, 2H, *J* = 5.5, 3.1), 6.73 (d, 2H, *J* = 8.8), 6.61 (d, 2H, *J* = 8.8), 3.76-3.81 (m, 2H), 3.74 (d, 2H, *J* = 6.1), 3.71 (s, 3H), 3.19 (d, 2H, *J* = 6.1), 1.86-1.88 (m, 1H), 1.74-1.78 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) 168.7, 152.7, 142.4, 134.2, 132.2, 123.4, 115.1, 115.0, 65.5, 55.9, 48.4, 37.9, 36.2, 28.7; **IR** : 3378, 2927, 1703, 1512, 1398, 1234, 1037, 720 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{20}H_{23}N_2O_4$ $[M+H]^+$: 355.1658, found: 355.1646. **$[\alpha]_D^{20}$** = +24.0 (*c* = 0.105, $CHCl_3$, *l* = 50 mm).



PeakTable

Detector A Ch2 240nm

Peak#	Ret. Time	Area	Height	Area %
1	89.629	6496666	24897	51.707
2	142.286	6067663	9153	48.293
Total		12564329	34051	100.000

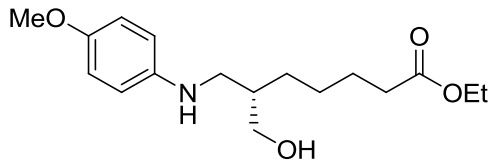


PeakTable

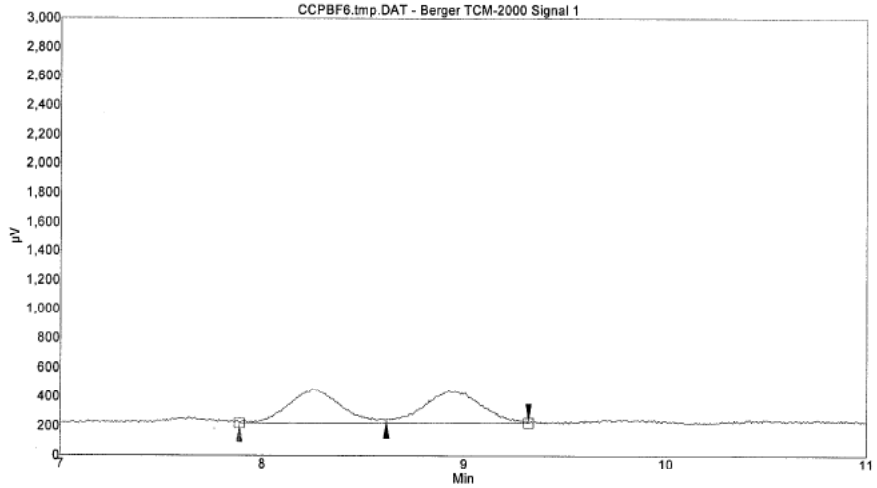
Detector A Ch2 240nm

Peak#	Ret. Time	Area	Height	Area %
1	86.592	54343193	193916	96.559
2	142.048	1936795	3118	3.441
Total		56279987	197034	100.000

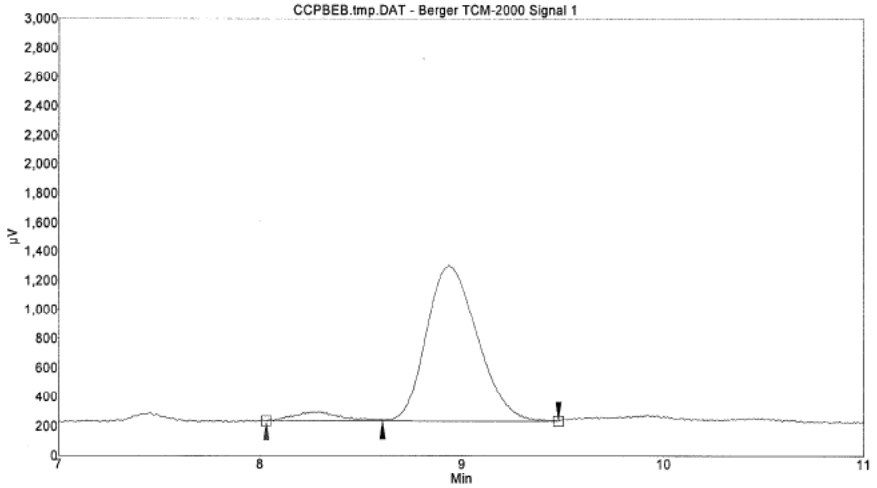
Table 2.5, Entry 9:



(*S*)-ethyl 7-hydroxy-6-((4-methoxyphenylamino)methyl)heptanoate. Procedure A was followed. Column chromatography gave a pale yellow oil (42 mg, 68%). **SFC** (AS-H, 1.0 mL/min, 3.0% MeOH, 240 nm, 150 bar, 50 °C) t_{rminor} =8.25 min and t_{rmajor} =8.95 min, 90% ee; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 6.78-6.80 (m, 2H), 6.65-6.67 (m, 2H), 4.12 (q, 2H, J = 7.2), 3.75 (s, 3H), 3.62-3.78 (m, 2H), 3.10-3.18 (m, 2H), 2.31 (t, 2H, J = 7.4), 1.82-1.92 (m, 1H), 1.61-1.66 (m, 2H), 1.33-1.42 (m, 4H), 1.25 (t, 3H, J = 7.0); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 173.8, 153.0, 142.2, 115.5, 115.0, 66.4, 60.5, 56.0, 49.5, 40.1, 34.3, 29.3, 26.8, 25.3, 14.4; **IR**: 3362, 2933, 1731, 1513, 1251, 1034 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{17}H_{28}NO_4$ $[M+H]^+$: 310.2018, found: 310.2021. **$[\alpha]_D^{20}$** = +18.0 (c = 0.110, $CHCl_3$, l = 50 mm).

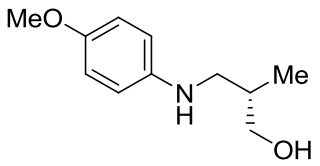


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.89	8.25	8.62	0.00	48.71	234.5	67.9	48.707
2	UNKNOWN	8.62	8.95	9.32	0.00	51.29	213.5	71.5	51.293
Total						100.00	448.0	139.5	100.000

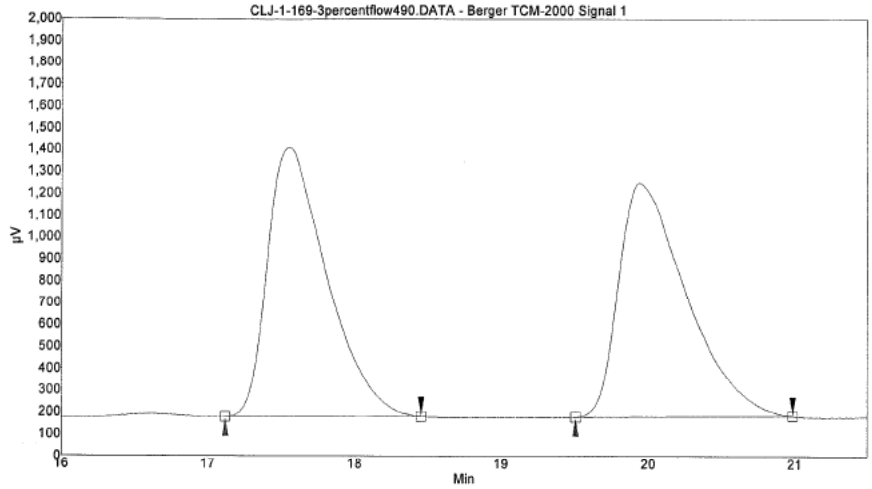


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.03	8.25	8.61	0.00	5.06	61.7	16.6	5.064
2	UNKNOWN	8.61	8.94	9.48	0.00	94.94	1071.3	311.9	94.936
Total						100.00	1133.0	328.5	100.000

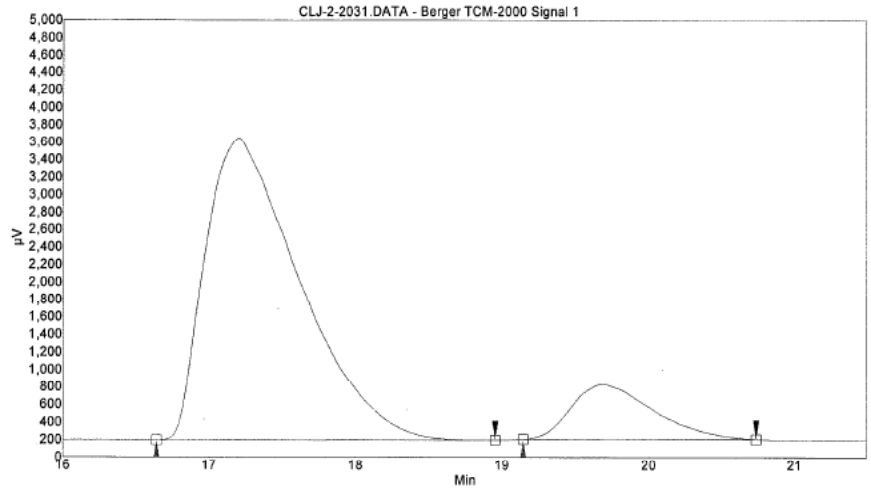
Table 2.5, Entry 10:



(*S*)-3-(4-methoxyphenylamino)-2-methylpropan-1-ol. Procedure C was followed. Column chromatography gave a pale yellow oil (25 mg, 64%). **SFC** (OD-H, 4.0 mL/min, 3.0% MeOH, 220 nm, 150 bar, 50 °C) t_{rmajor} =17.55 min and t_{rminor} =19.94 min, 73% ee; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 6.78 (d, 2H, J = 9.0), 6.63 (d, 2H, J = 8.8), 3.75 (d, 3H), 3.67 (dd, 1H, J = 10.8, 4.7), 3.59 (dd, 1H, J = 10.6, 7.2), 3.08-3.10 (m, 2H), 1.94-2.07 (m, 1H), 0.96 (d, 3H, J = 6.8); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 152.7, 142.6, 115.1, 115.1, 68.2, 56.0, 50.7, 35.5, 15.2; **IR**: 3365, 2929, 1512, 1234, 1034, 819 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{18}NO_2$ $[M+H]^+$: 196.1338, found: 196.1340. **$[\alpha]_D^{20}$** = +2.2 (c = 0.110, $CHCl_3$, l = 50 mm).

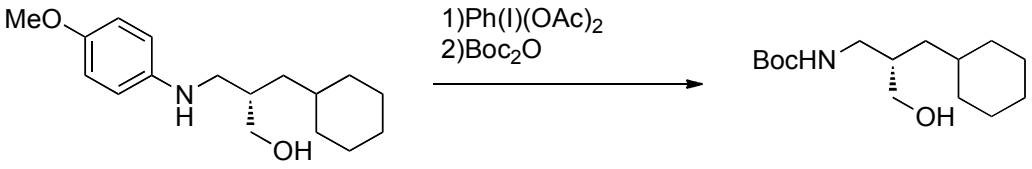


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	17.12	17.55	18.45	0.00	50.09	1227.9	571.9	50.089
2	UNKNOWN	19.51	19.94	20.99	0.00	49.91	1069.8	569.9	49.911
Total						100.00	2297.7	1141.7	100.000



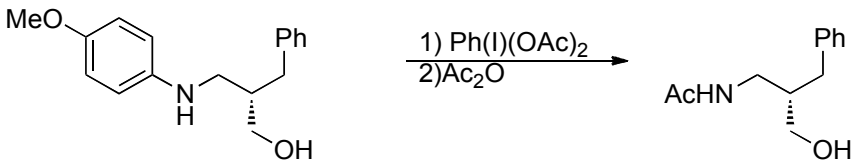
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	16.64	17.20	18.95	0.00	86.43	3446.4	2566.5	86.427
2	UNKNOWN	19.15	19.69	20.74	0.00	13.57	627.8	403.1	13.573
Total						100.00	4074.2	2969.6	100.000

Proof of Stereochemistry



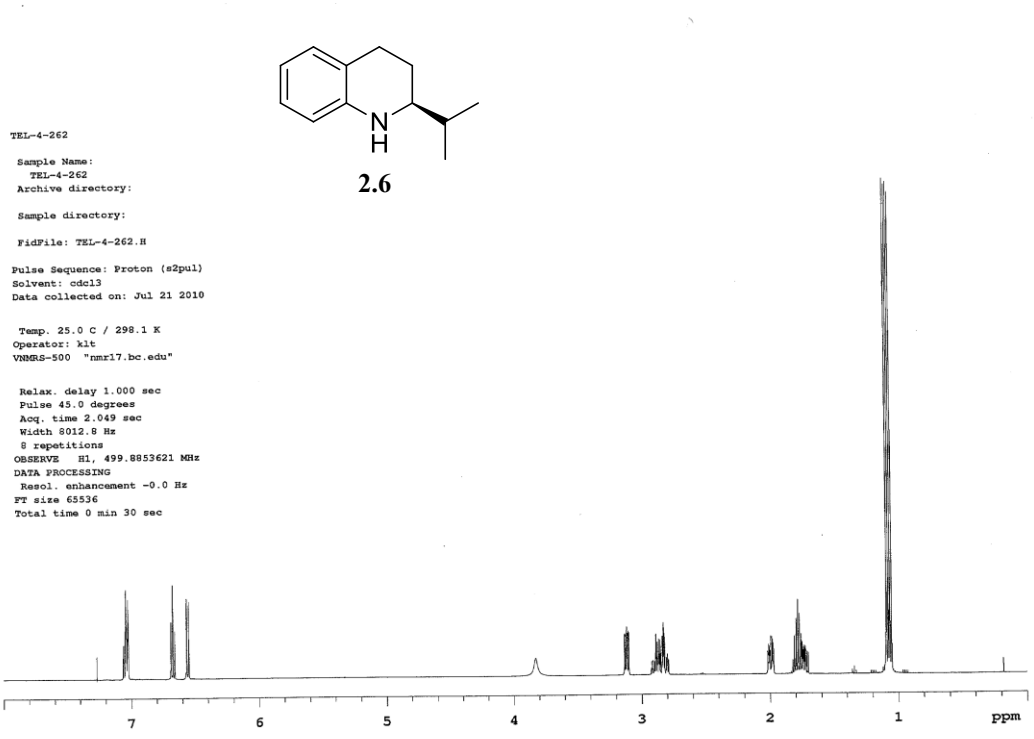
(*S*)-β-Cyclohexylmethyl-γ-Boc-amino alcohol.[11,27] To (*S*)-3-cyclohexyl-2-((4-methoxyphenylamino)methyl)propan-1-ol (136 mg, 0.490 mmol, 86% ee) in 1:1 MeOH/CH_2Cl_2 (7 mL) at 0 °C was added iodobenzene diacetate (632 mg, 1.96 mmol) in MeOH (7 mL). After stirring at 0 °C for 30 min, 1 M HCl (7 mL) was added, and the mixture was stirred for 1 h. The reaction was diluted with CH_2Cl_2 (20 mL), and the layers were separated. The aqueous layer was washed with CH_2Cl_2 (3×20 mL), and the combined organics were washed with 1M HCl (20 mL). The combined aqueous layers were neutralized by adding solid Na_2CO_3 until pH 10 was reached. CH_2Cl_2 (20 mL) and di-*tert*-butyl dicarbonate (0.450 mL, 1.96 mmol) were added, and the mixture was stirred vigorously overnight. The layers were separated, and the aqueous layer was washed with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated. Column chromatography (20-40% EtOAc/Hex) yielded a yellow oil (8.8 mg, 7%). $\mathbf{[\alpha]_D^{20}}$ = +10.5 (*c* = 0.440, $CHCl_3$, *l* = 50 mm). Known compound: (*S*) $\mathbf{[\alpha]_D^{rt}}$ = +23.0 (*c* = 0.50, $CHCl_3$).[27]

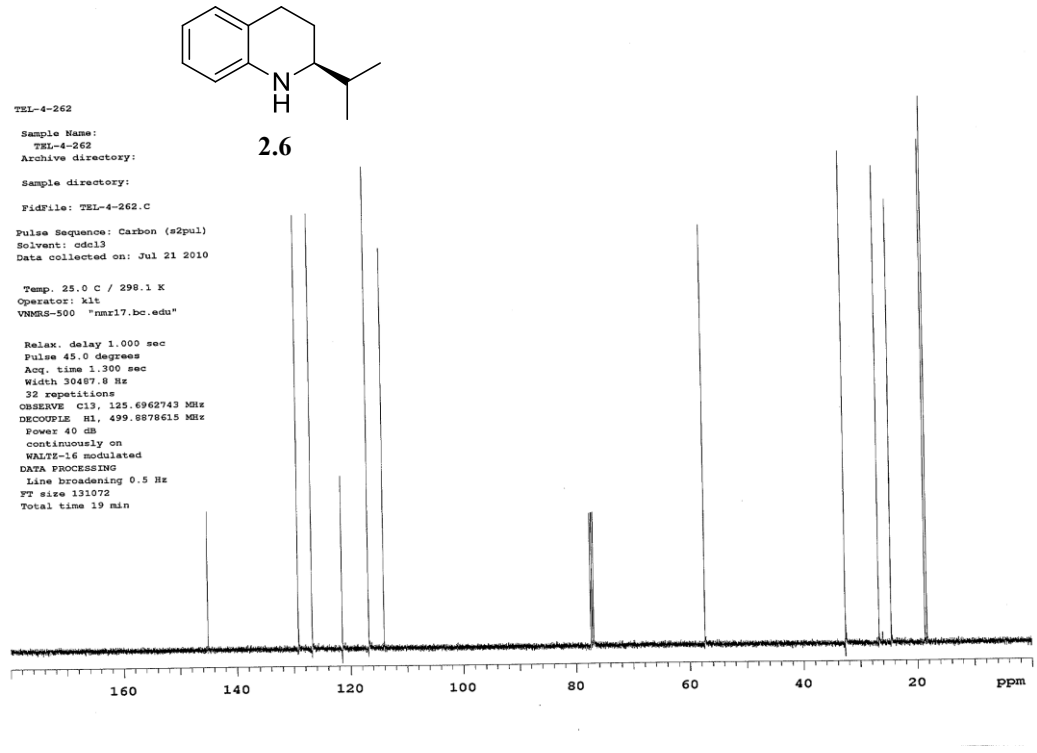
[27]Chi, Y.; English, E. P.; Pomerantz, W. C.; Horne, W. S.; Joyce, L. A.; Alexander, L. R.; Fleming, W. S.; Hopkins, E. A.; Gellman, S. H. *J. Am. Chem. Soc.* **2007**, *129*, 6050-6055.

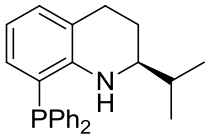


(*S*)-3-(*N*-Acetylamino)-2-benzyl-1-propanol.[11,28] To (*S*)-2-benzyl-3-(4-methoxyphenylamino)propan-1-ol (58.6 mg, 0.220 mmol, 79% ee) in 1:1 MeOH/CH_2Cl_2 (3.2 mL) at 0 °C was added iodobenzene diacetate (268 mg, 0.860 mmol) in MeOH (3.2 mL). After stirring at 0 °C for 30 min, 1 M HCl (3.2 mL) was added, and the mixture was stirred for 1 h. The reaction was diluted with CH_2Cl_2 (10 mL), and the layers were separated. The aqueous layer was washed with CH_2Cl_2 (3×10 mL), and the combined organics were washed with 1 M HCl (10 mL). The combined aqueous layers were neutralized by adding solid Na_2CO_3 until pH 10 was reached. CH_2Cl_2 (5 mL) and acetic anhydride (21.0 μL, 0.220 mmol) were added, and the mixture was stirred vigorously overnight. The layers were separated, and the aqueous layer was washed with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. Column chromatography (5% MeOH/CH_2Cl_2) yielded a yellow oil (2.7 mg, 6%). $\mathbf{[\alpha]_D^{20}}$ = +17.2 (*c* = 0.135, $CHCl_3$, *l* = 50 mm). Known compound: (*R*) $\mathbf{[\alpha]_D^{20}}$ = -24.2 (*c* = 1.59, $CHCl_3$)[28]

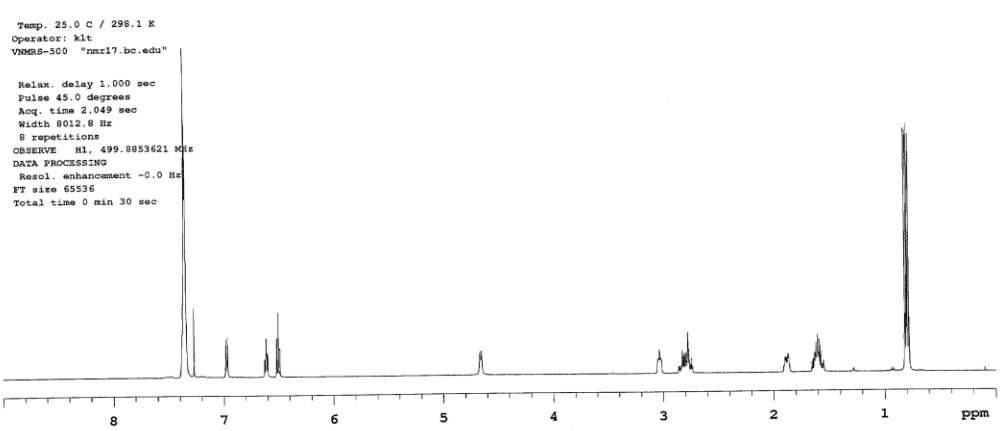
[28]Banfi, L.; Guanti, G.; Riva, R. *Tetrahedron: Asymmetry* **1999**, *10*, 3571-3592.

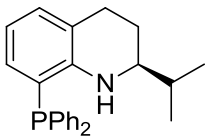

TEL-4-262
Sample Name:
TEL-4-262
Archive directory:
Sample directory:
FidFile: TEL-4-262.H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 21 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8853621 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec
N
H
2.6
7
6
5
4
3
2
1
ppm


TEL-4-262
Sample Name:
TEL-4-262
Archive directory:
Sample directory:
FidFile: TEL-4-262.C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 21 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
32 repetitions
OBSERVE C13, 125.6962743 MHz
DECOUPLE H1, 499.8878615 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min
N
H
2.6
160
140
120
100
80
60
40
20
ppm

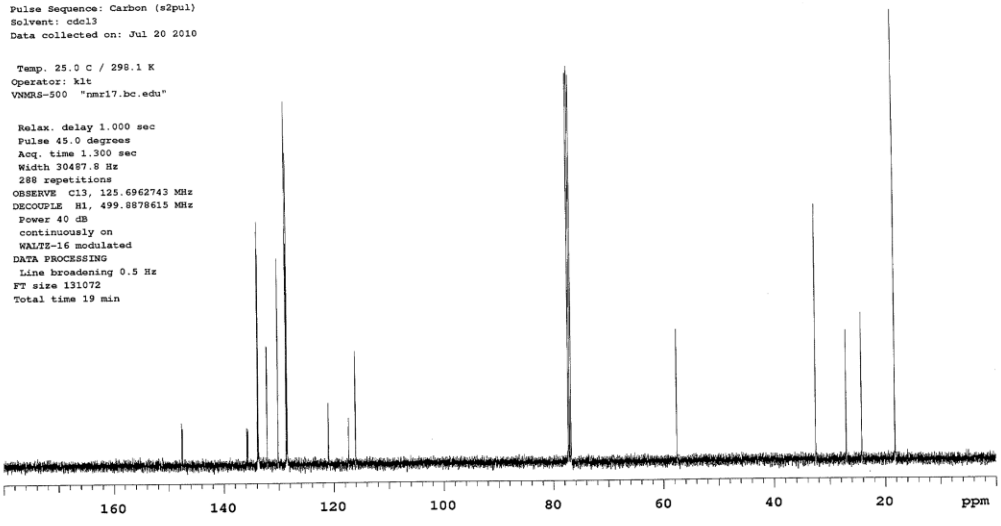

N
H
PPh2

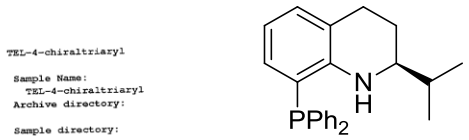
2.7


TEL-4-chiraltriaryl
Sample Name:
TEL-4-chiraltriaryl
Archive directory:
Sample directory:
FidFile: TEL-4-chiral-triaryl.H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8853621 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec
8
7
6
5
4
3
2
1
ppm

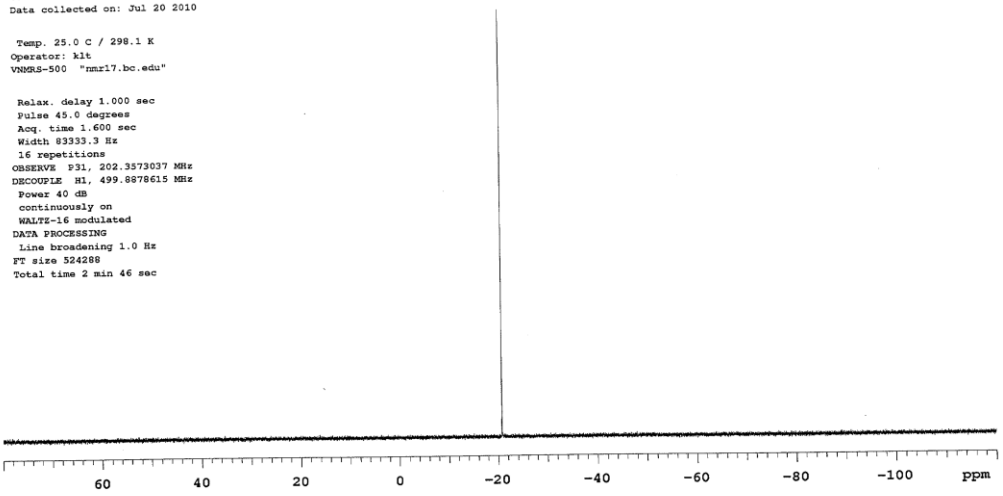

N
H
PPh2

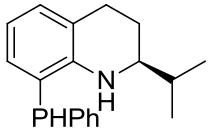
2.7

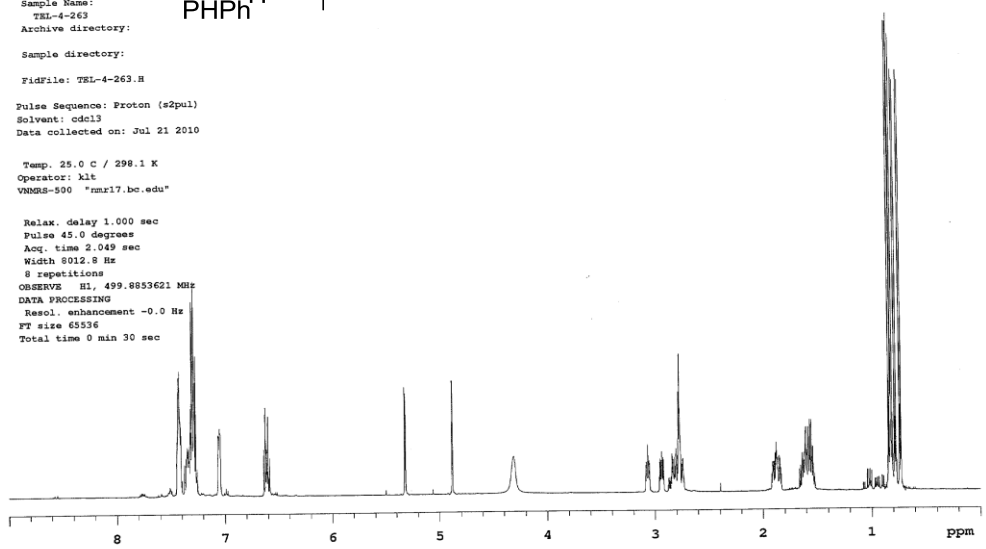

TEL-4-chiraltriaryl
Sample Name:
TEL-4-chiraltriaryl
Archive directory:
Sample directory:
FidFile: TEL-4-chiral-triaryl.C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
288 repetitions
OBSERVE C13, 125.6962743 MHz
DECOUPLE H1, 499.8878615 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min
160
140
120
100
80
60
40
20
ppm

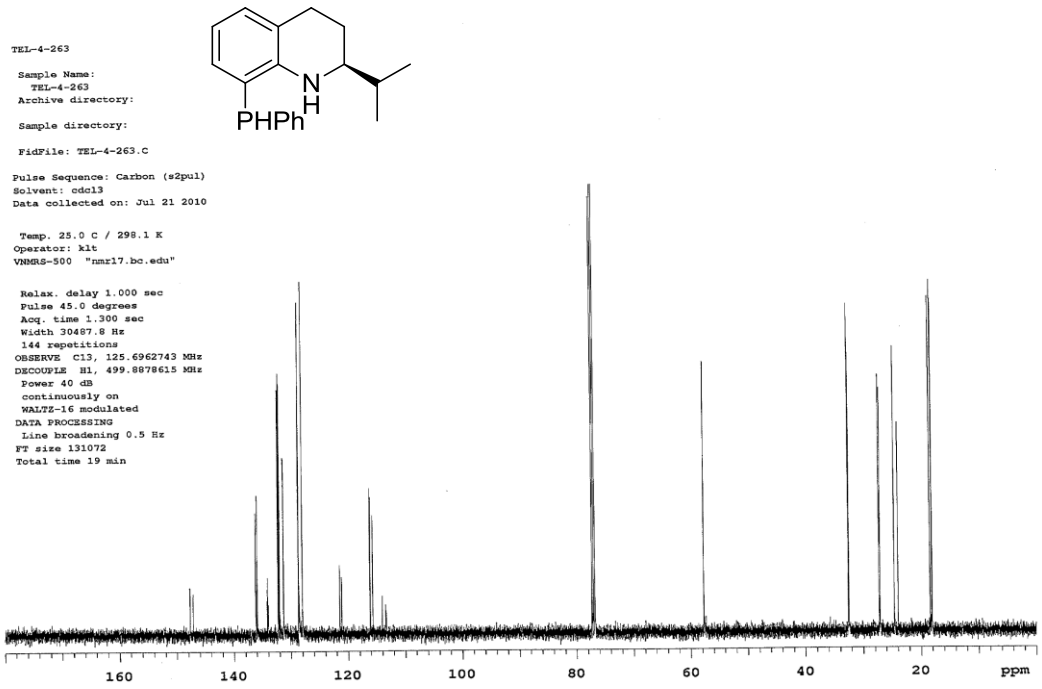

N
H
PPh2

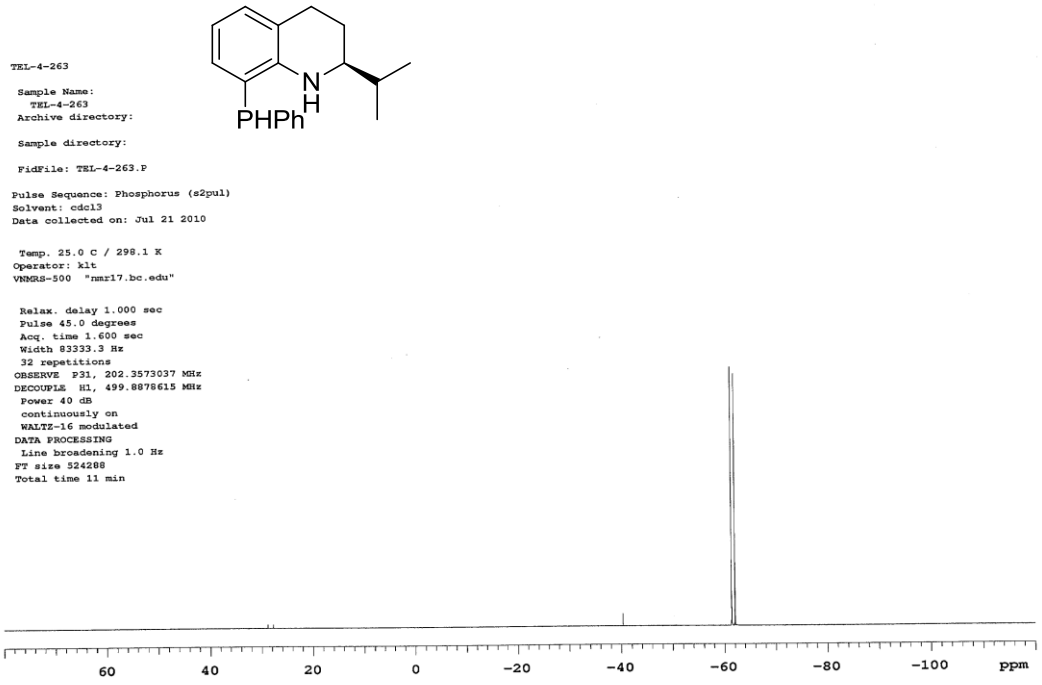
2.7

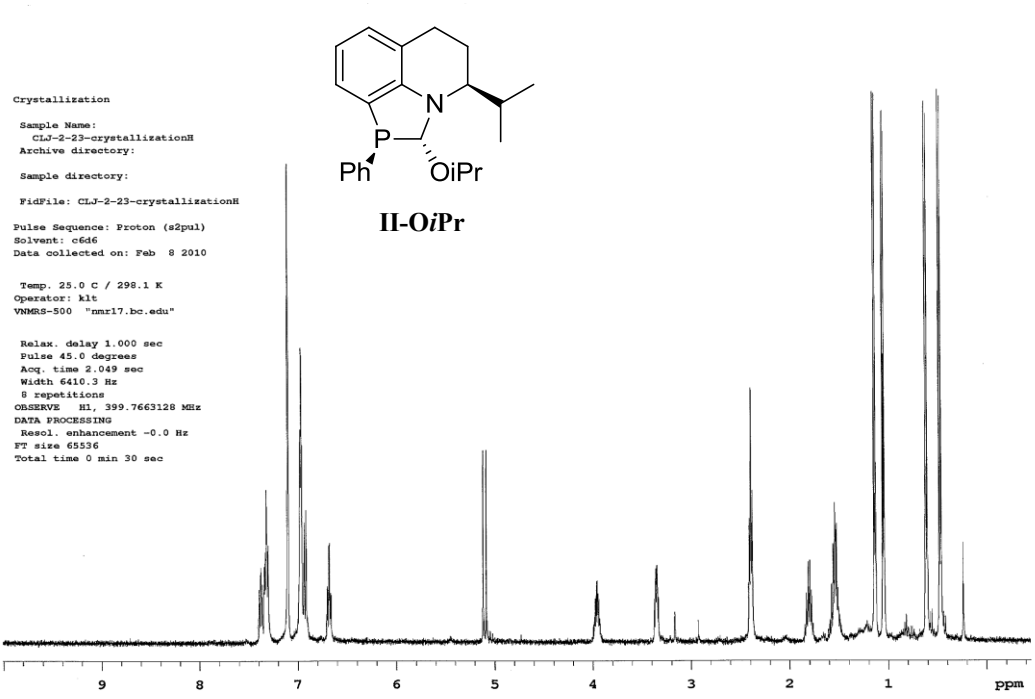

TEL-4-chiraltriaryl
Sample Name:
TEL-4-chiraltriaryl
Archive directory:
Sample directory:
FidFile: TEL-4-chiral-triaryl.P
Pulse Sequence: Phosphorus (s2pul)
Solvent: cdcl3
Data collected on: Jul 20 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.600 sec
Width 83333.3 Hz
16 repetitions
OBSERVE P31, 202.3573037 MHz
DECOUPLE H1, 499.8878615 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 524288
Total time 2 min 46 sec
60
40
20
0
-20
-40
-60
-80
-100
ppm


N
H
PHPh

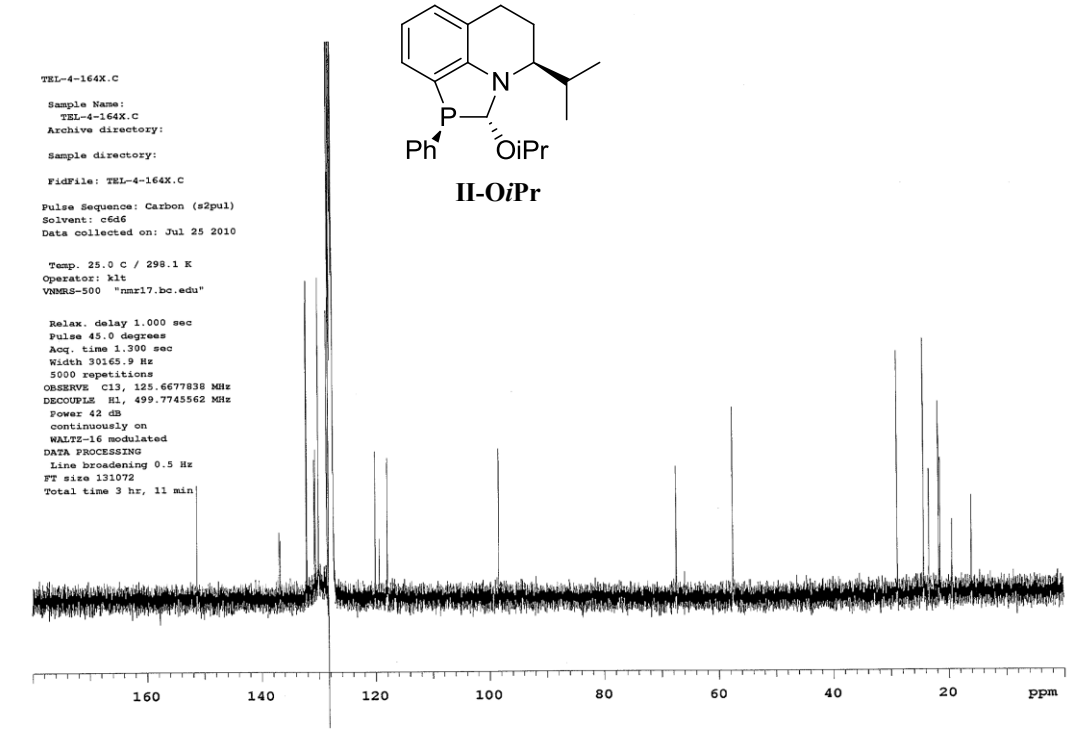

TEL-4-263
Sample Name:
TEL-4-263
Archive directory:
Sample directory:
FidFile: TEL-4-263.H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 21 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8853621 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec
8
7
6
5
4
3
2
1
ppm


TEL-4-263
Sample Name:
TEL-4-263
Archive directory:
Sample directory:
FidFile: TEL-4-263.C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jul 21 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
144 repetitions
OBSERVE C13, 125.6962743 MHz
DECOUPLE H1, 499.8878615 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min
PHPh
N
H
160
140
120
100
80
60
40
20
ppm


TEL-4-263
Sample Name:
TEL-4-263
Archive directory:
Sample directory:
FidFile: TEL-4-263.P
Pulse Sequence: Phosphorus (s2pul)
Solvent: cdcl3
Data collected on: Jul 21 2010
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.600 sec
Width 83333.3 Hz
32 repetitions
OBSERVE P31, 202.3573037 MHz
DECOUPLE H1, 499.8878615 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 524288
Total time 11 min
PHPh
N
H
60
40
20
0
-20
-40
-60
-80
-100
ppm



II-O*i*Pr

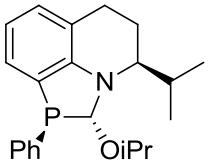


II-O*i*Pr

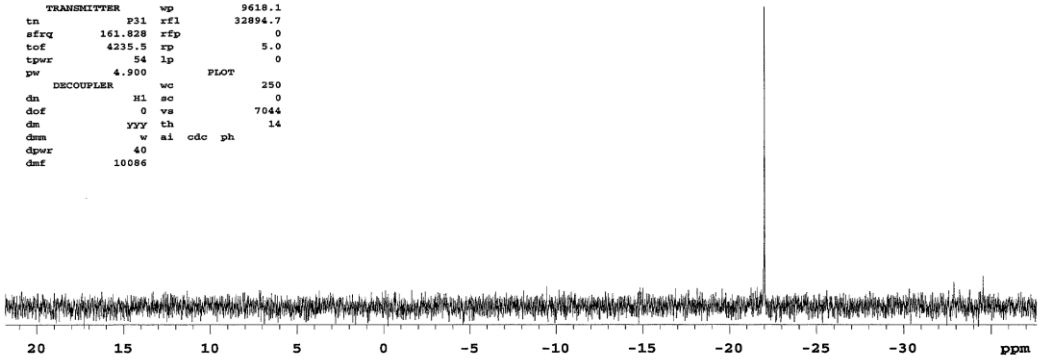
TEL-4-164iproh2

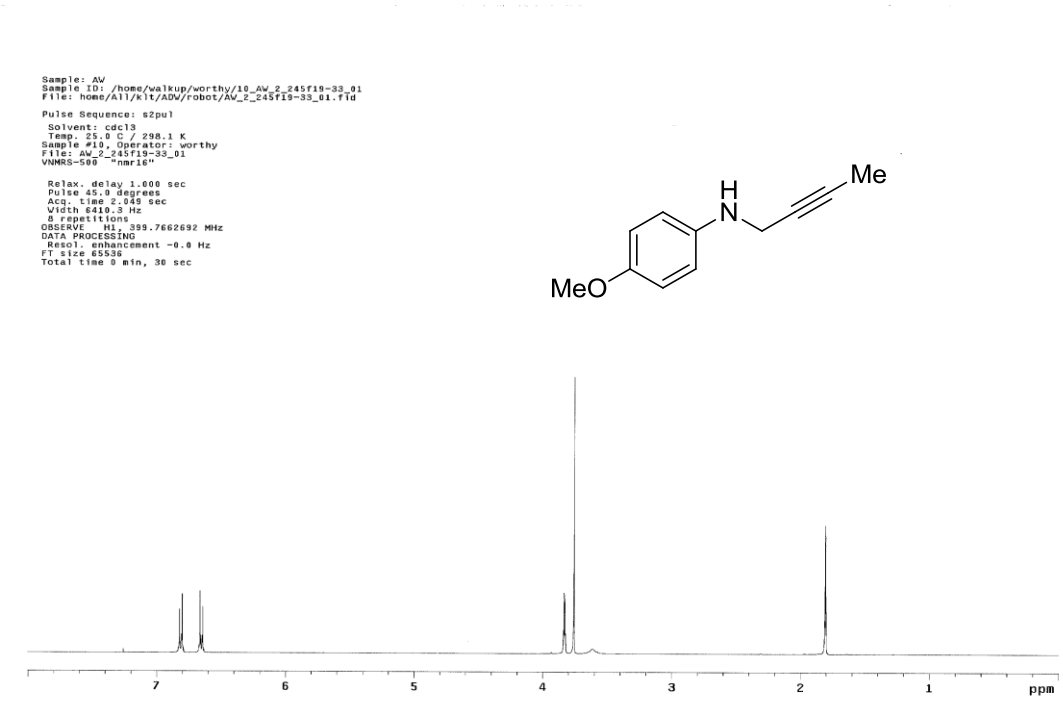
exp3 Phosphorus

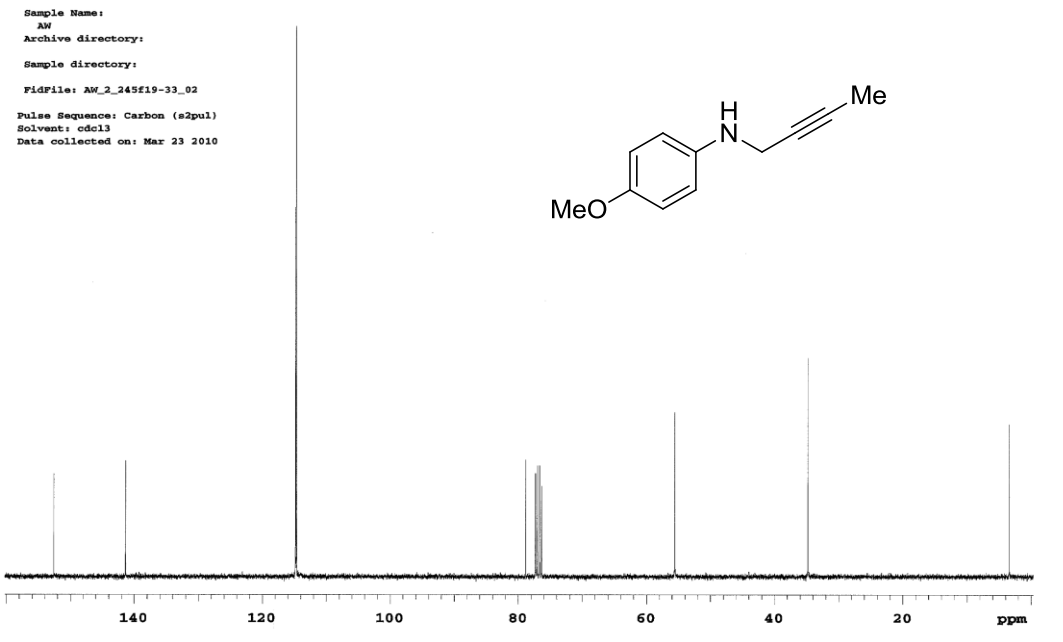
SAMPLE		SPECIAL	
date	Apr 14 2010	temp	25.0
solvent	c6d6	gain	40
file	/home/All/klt~	spin	20
/TEL Backups/TEL-P~		hst	0.008
rocess/TEL-4-164ip~		pw90	9.800
roh2_TEL-4_164ipro~		alfa	10.000
h2_02.fid		FLAGS	
ACQUISITION		il	n
sw	65789.5	in	n
at	1.600	dp	y
np	210530	ha	nn
fb	15000	PROCESSING	
bs	64	lb	1.00
d1	1.000	fn	not used
nt	64	DISPLAY	
ct	64	sp	-6086.9
TRANSMITTER		wp	9618.1
tn	P31	rf1	32894.7
sfrq	161.828	rfp	0
tof	4235.5	rp	5.0
tpwr	54	lp	0
pw	4.900	PLOT	
DECOUPLER		wc	250
dn	H1	sc	0
dof	0	vs	7044
dm	yyy	th	14
dmm	w	ai cdc ph	
dpwr	40		
dmf	10086		



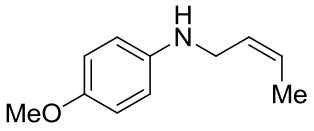
II-O*i*Pr



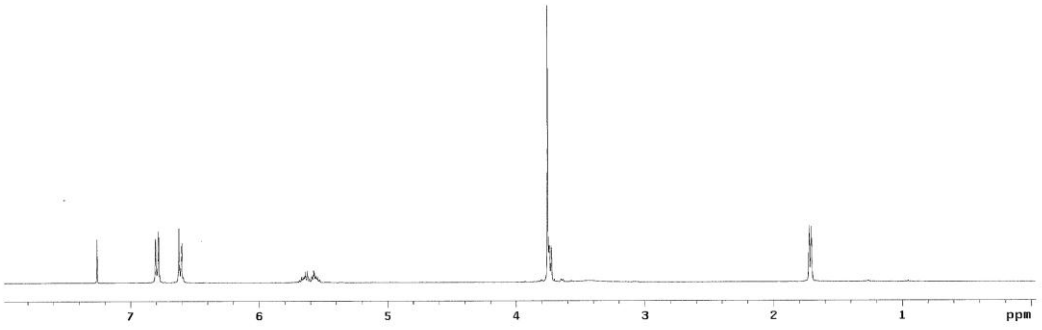

Sample: AW
Sample ID: /home/walkup/worthy/10_AW_2_245f19-33_01
File: home/All/klt/ADW/robot/AW_2_245f19-33_01.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Sample #10, Operator: worthy
File: AW_2_245f19-33_01
VNMRS-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.7662692 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
H
N
Me
MeO
7
6
5
4
3
2
1
ppm


Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_2_245f19-33_02
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Mar 23 2010
H
N
Me
MeO
140
120
100
80
60
40
20
ppm

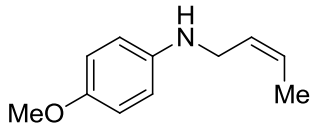
```
AW-2-232

Sample: AW-2-232
Sample ID: s_20100212_03
File: /home/All/klt/ADW/AW-2-232check.fid

Pulse Sequence: s2pul

 Solvent: cdcl3
 Temp. 25.0 C / 298.1 K
Operator: klt
File: AW-2-232check
VNMRS-500  "nmr16"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.049 sec
 Width 6410.3 Hz
 8 repetitions
OBSERVE   H1, 399.7662700 MHz
DATA PROCESSING
 Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
```



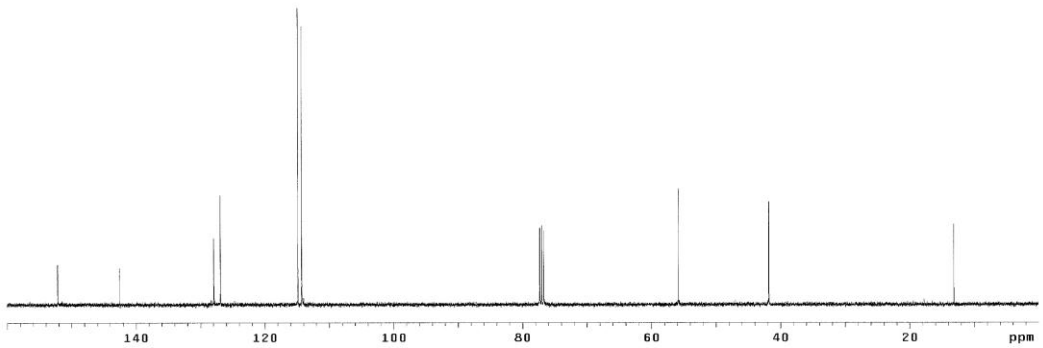
2.8

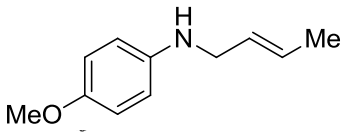



```
expz  Carbon

        SAMPLE                          SPECIAL
date      Feb 23 2010   temp              25.0
solvent       cdcl3     gain                30
file /home/All/klt~     spin                20
/ADW/robot/worthy_~     hst              0.008
   AW_2_131_02.fid      pw90             9.300
    ACQUISITION         alfa            10.000
sw           24509.8            FLAGS
at             1.300     il                  n
np              63750     in                  n
fb              17000     dp                  y
bs                 64     hs                 nn
d1              1.000          PROCESSING
nt                256     lb               0.50
ct                256     fn           not used
   TRANSMITTER                   DISPLAY
tn                C13     sp                2.2
sfrq          100.532     wp            16087.6
tof            1028.1     rfl            1700.2
tpwr               57     rfp                 0
pw              4.650     rp              -136.3
     DECOUPLER          lp                  0
dn                H1               PLOT
dof                0     wc                250
dm               yyy     sc                  0
dmm                w     vs              17292
dpwr              40     th                  5
dmf            10086     al   cdc   ph
```



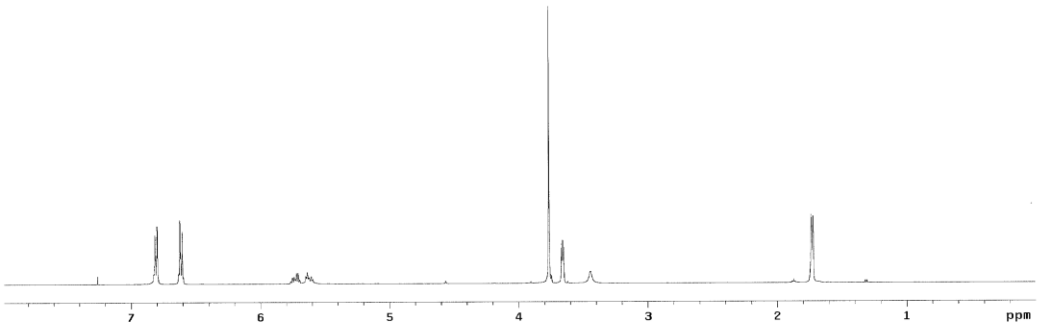
2.8

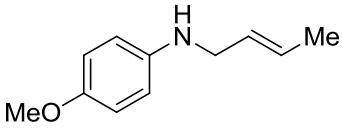




2.12

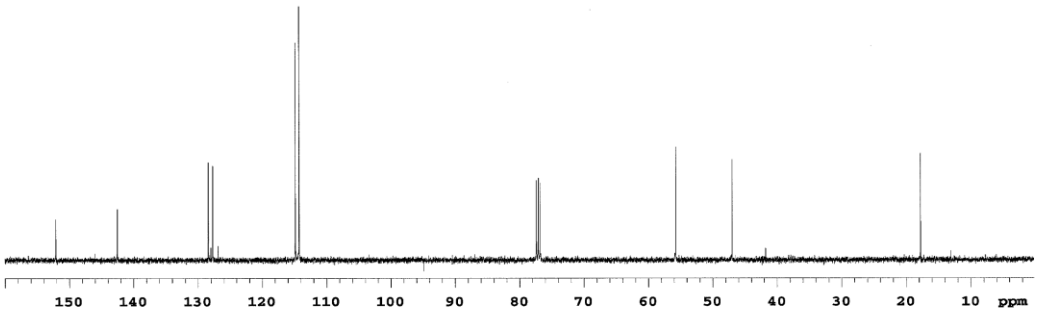
```
AW-2-240f5_21

Sample: AW-2-240
File: /home/All/klt/ADV/AW-2-240f5_21redo.fid

Pulse Sequence: s2pul
 Solvent: cdcl3
  Temp. 25.0 C / 298.1 K
Operator: klt
File: AW-2-240f5_21redo
VNMRS-500  "nmr16"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.049 sec
 Width 8012.8 Hz
 8 repetitions
OBSERVE   H1, 499.8853678 MHz
DATA PROCESSING
 Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
```



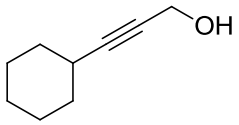


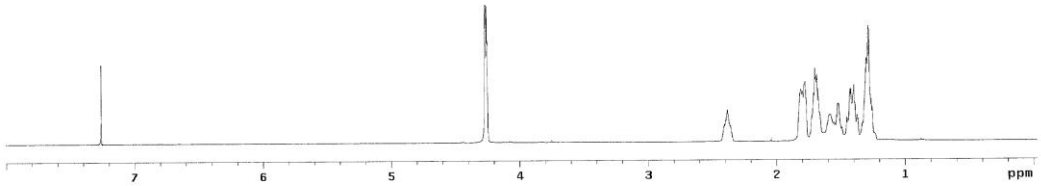
2.12

```
Sample Name:
  AW
Archive directory:

Sample directory:

FidFile: AW_2_240f5_21_02

Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr  1 2010
```

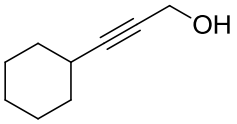


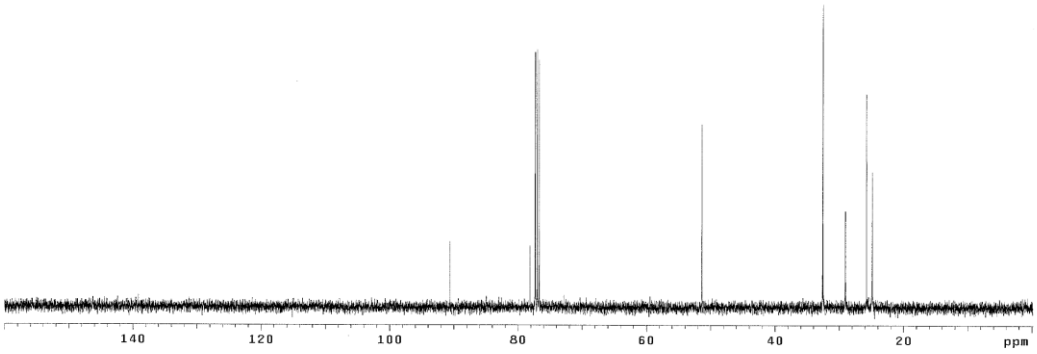
```
AW-2-256

Sample: AW-2-256
Sample ID: s_20100212_03
File: /home/All/klt/ADW/AW-2-256H.fid

Pulse Sequence: s2pul

 Solvent: cdcl3
 Ambient temperature
Operator: klt
File: AW-2-256H
VNMRS-500  "nmr16"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.049 sec
 Width 6410.3 Hz
 8 repetitions
OBSERVE    H1, 399.7662702 MHz
DATA PROCESSING
 Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
```






```
AW-2-256C

Sample: AW-2-256
File: exp

Pulse Sequence: s2pul

 Solvent: cdcl3
 Ambient temperature
Operator: klt
VNMRS-400  "nmr14"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.308 sec
 Width 24509.8 Hz
 112 repetitions
OBSERVE  C13, 100.5213103 MHz
DECOUPLE  H1, 399.7682756 MHz
 Power 40 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.5 Hz
FT size 65536
Total time 19 min, 38 sec
```





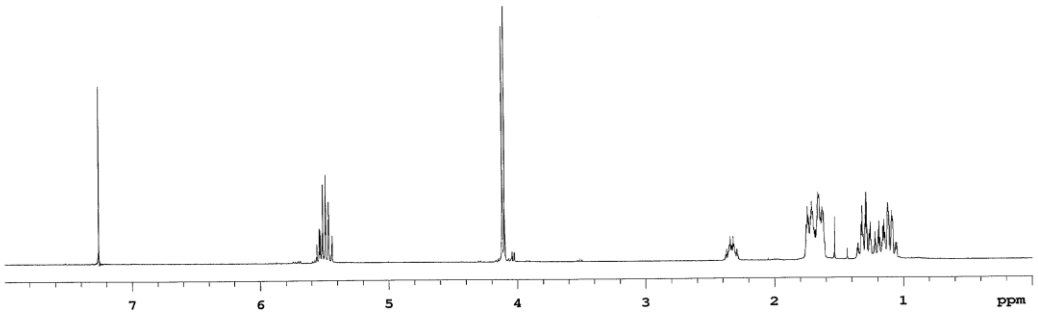
AW-2-270check

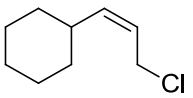
Sample Name:
AW-2-270
Archive directory:

Sample directory:

FidFile: AW-2-270check

Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2010



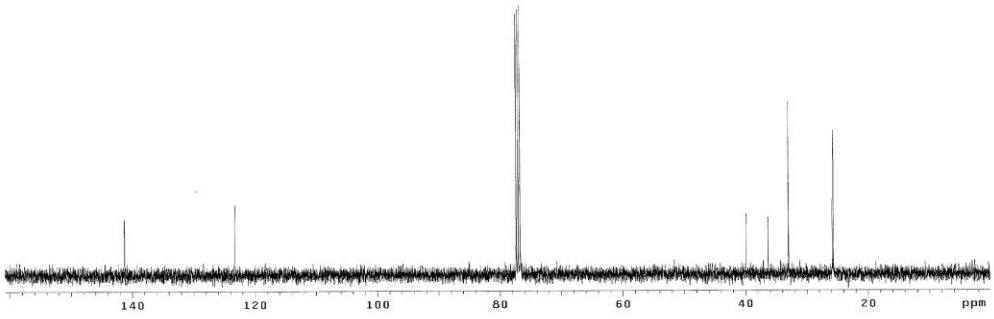


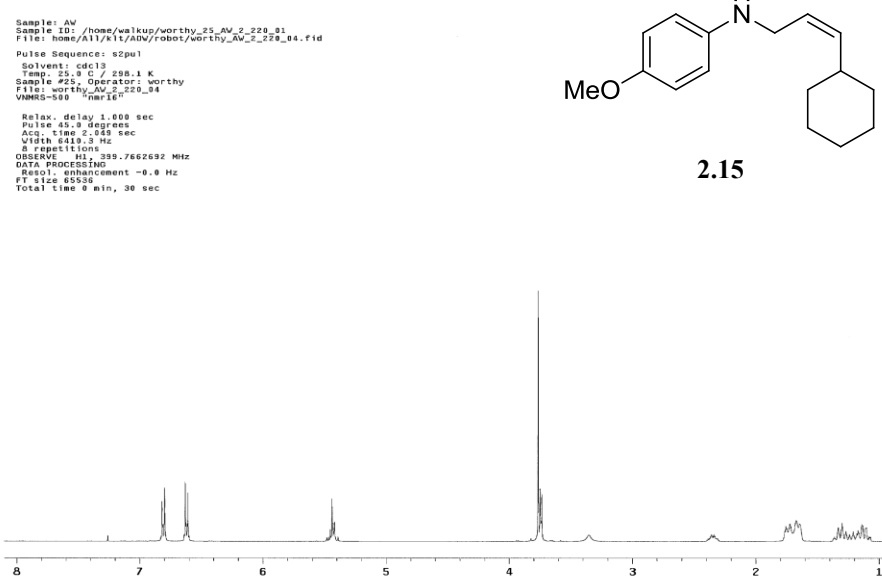
AW-2-270

Sample: AW-2-270
File: exp

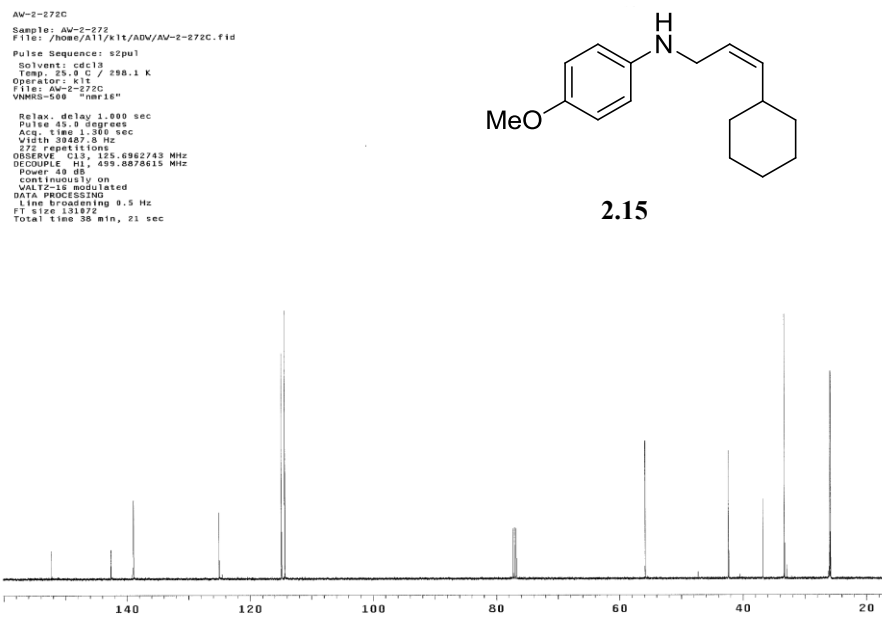
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-400 "nmr14"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
144 repetitions
OBSERVE C13, 100.5213103 MHz
DECOUPLE H1, 399.7682755 MHz
Power 40 dB
continuously On
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 9 min, 49 sec

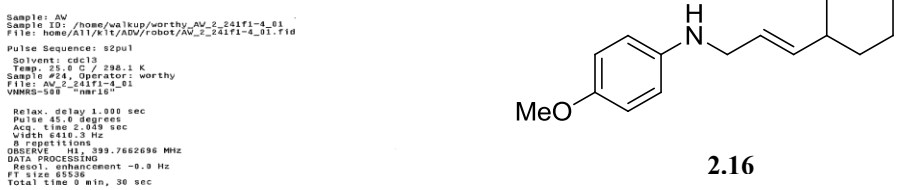



Sample: AW
Sample ID: /home/walkup/worthy_25_AW_2_220_01
File: home/All/klt/ADW/robot/worthy_AW_2_220_04.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Sample #25, Operator: worthy
File: worthy_AW_2_220_04
VNMRS-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.045 sec
Width 6419.3 Hz
8 repetitions
OBSERVE H1, 399.7662692 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
H
N
MeO
8
7
6
5
4
3
2
1
ppm

2.15

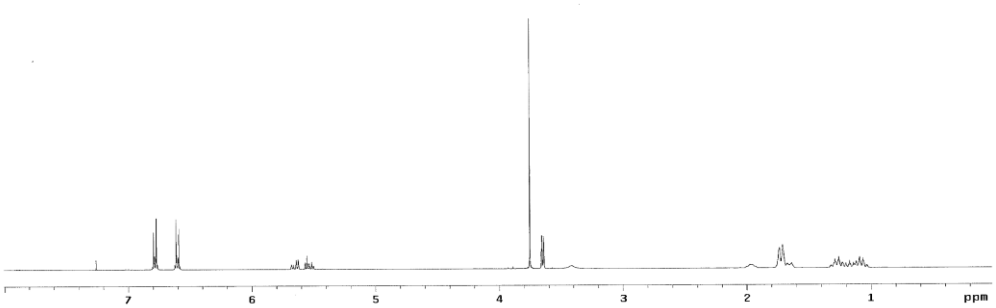

AW-2-272C
Sample: AW-2-272
File: /home/All/klt/ADW/AW-2-272C.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
File: AW-2-272C
VNMRS-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
272 repetitions
OBSERVE C13, 125.6962743 MHz
DECOUPLE H1, 499.8878615 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 38 min, 21 sec
H
N
MeO
140
120
100
80
60
40
20
ppm

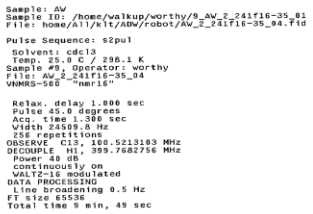
2.15

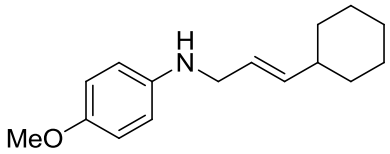

Sample: AV
Sample ID: /home/walkup/worthy_AV_2_241f1-4_01
File: home/All/klt/ADW/robot/AV_2_241f1-4_01.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Sample #24, Operator: worthy
File: AV_2_241f1-4_01
VNMRS-500 "marl8"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.7662696 MHz
DATA PROCESSING
Resol. enhancement -0.9 Hz
FT size 65536
Total time 0 min, 30 sec

H
N
MeO

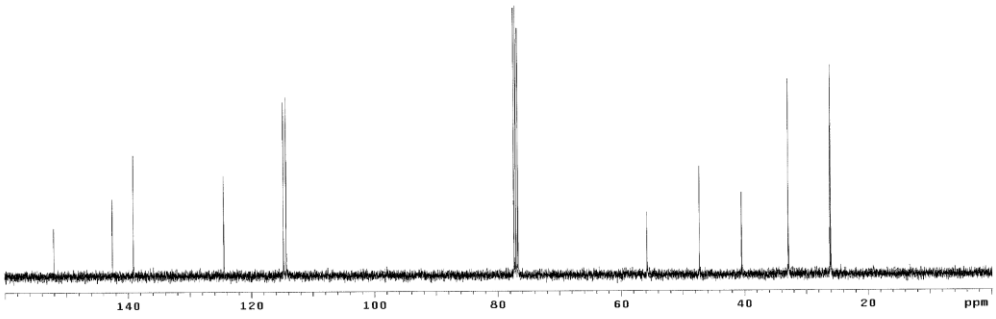
2.16

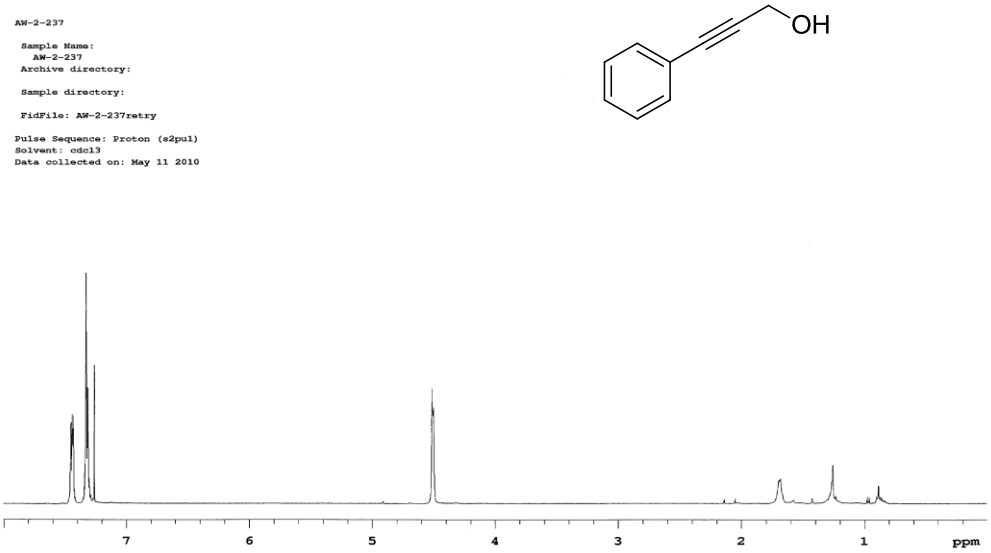

7
6
5
4
3
2
1
ppm

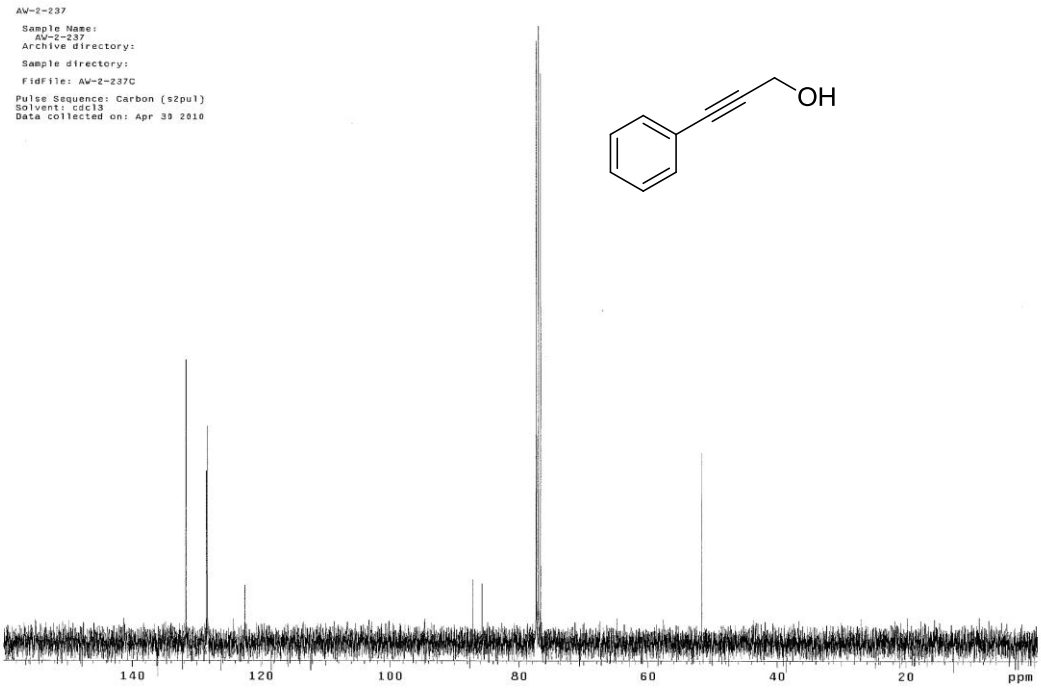

Sample: AV
Sample ID: /home/walkup/worthy/9_AV_2_241f16-35_01
File: home/All/klt/ADW/robot/AV_2_241f16-35_04.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Sample #9, Operator: worthy
File: AV_2_241f16-35_04
VNMRS-500 "marl8"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
256 repetitions
OBSERVE C13, 100.5213103 MHz
DECOUPLE H1, 399.7682756 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 9 min, 49 sec

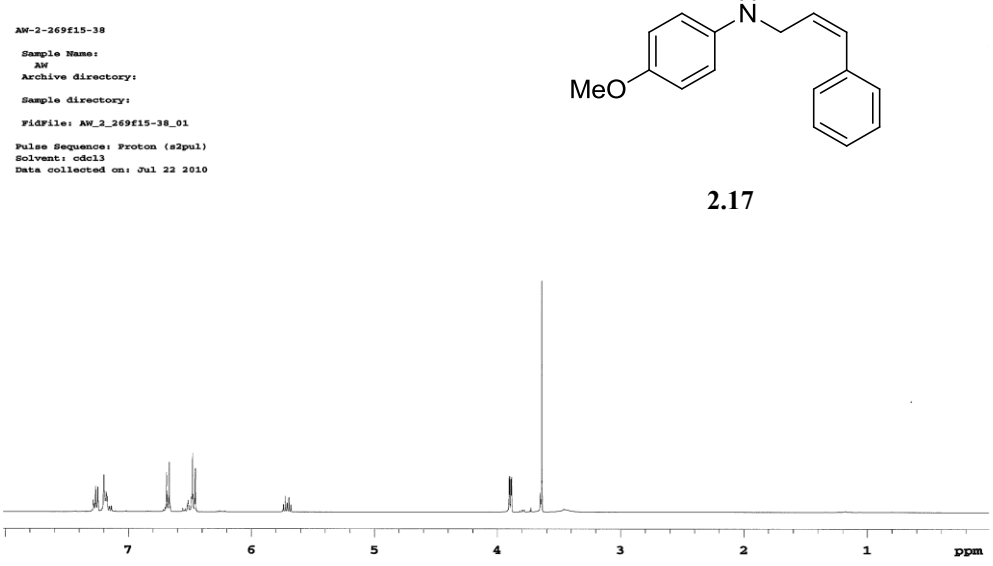

H
N
MeO

2.16

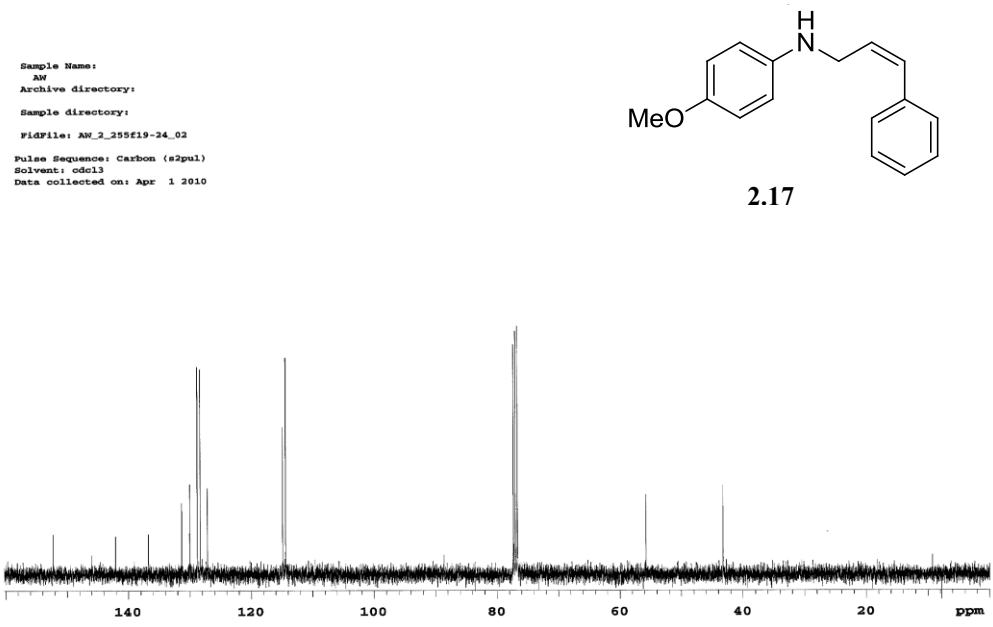

140
120
100
80
60
40
20
ppm


AW-2-237
Sample Name:
AW-2-237
Archive directory:
Sample directory:
FidFile: AW-2-237retry
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: May 11 2010
OH
7
6
5
4
3
2
1
ppm

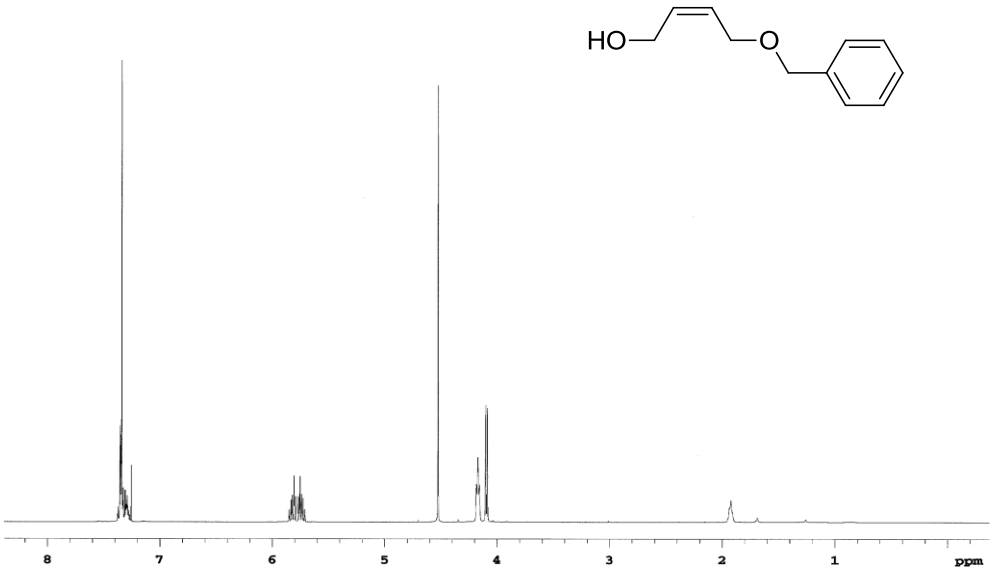

AW-2-237
Sample Name:
AW-2-237
Archive directory:
Sample directory:
FidFile: AW-2-237C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 30 2010
OH
140
120
100
80
60
40
20
ppm

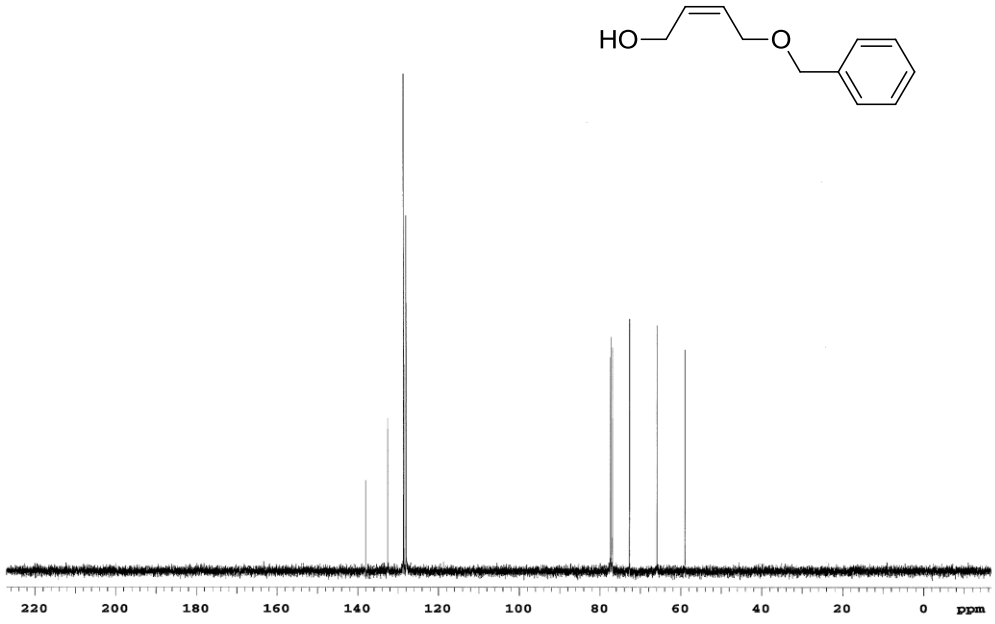

AW-2-269f15-38
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_2_269f15-38_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jul 22 2010
H
N
MeO
7
6
5
4
3
2
1
ppm

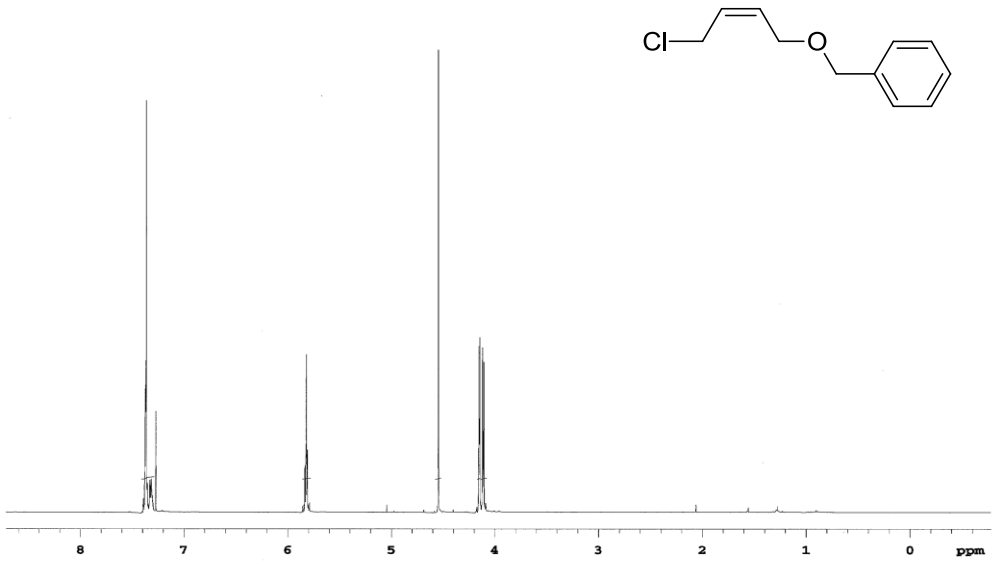
2.17

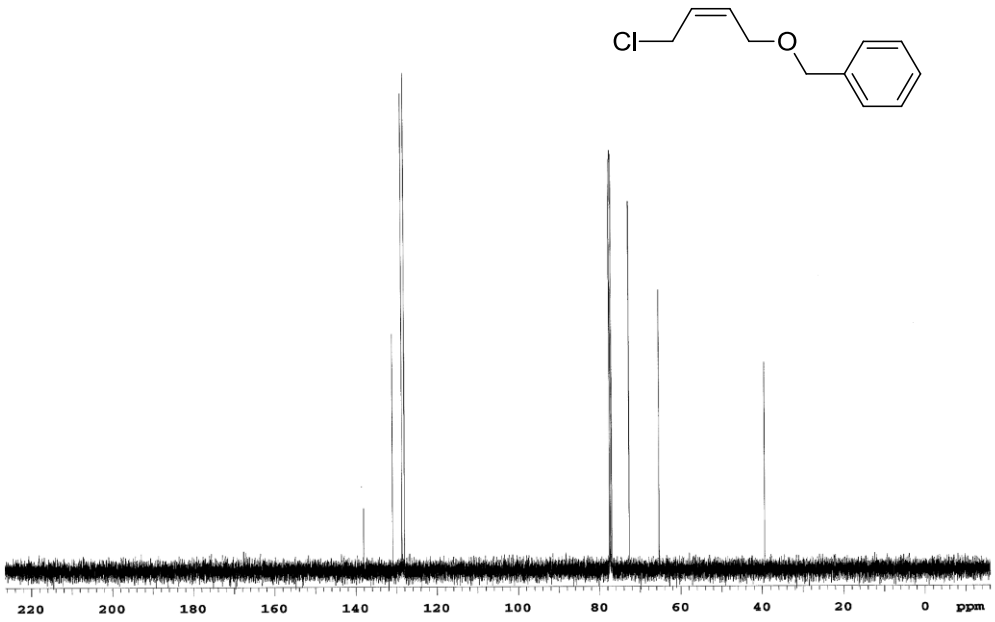

Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_2_255f19-24_02
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 1 2010
H
N
MeO
140
120
100
80
60
40
20
ppm

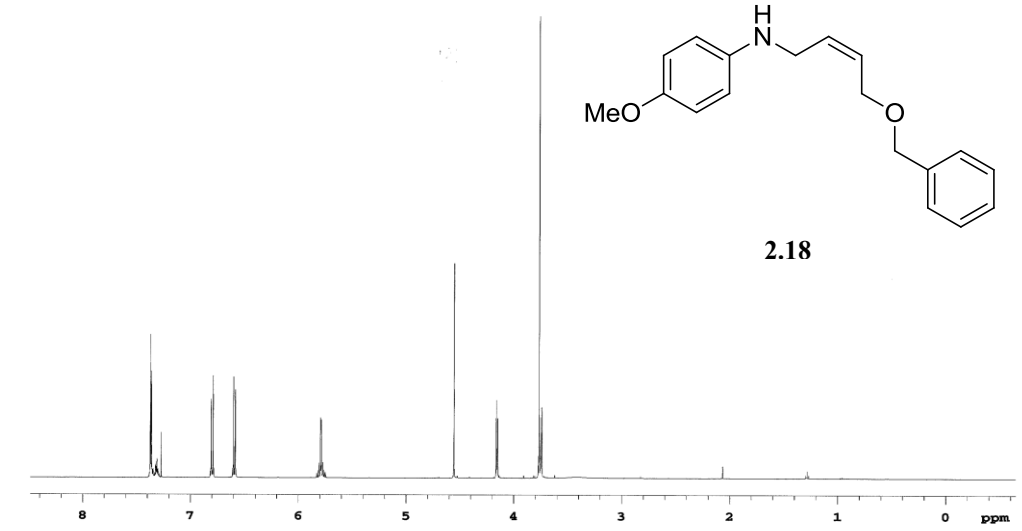
2.17


HO
O
8
7
6
5
4
3
2
1
ppm

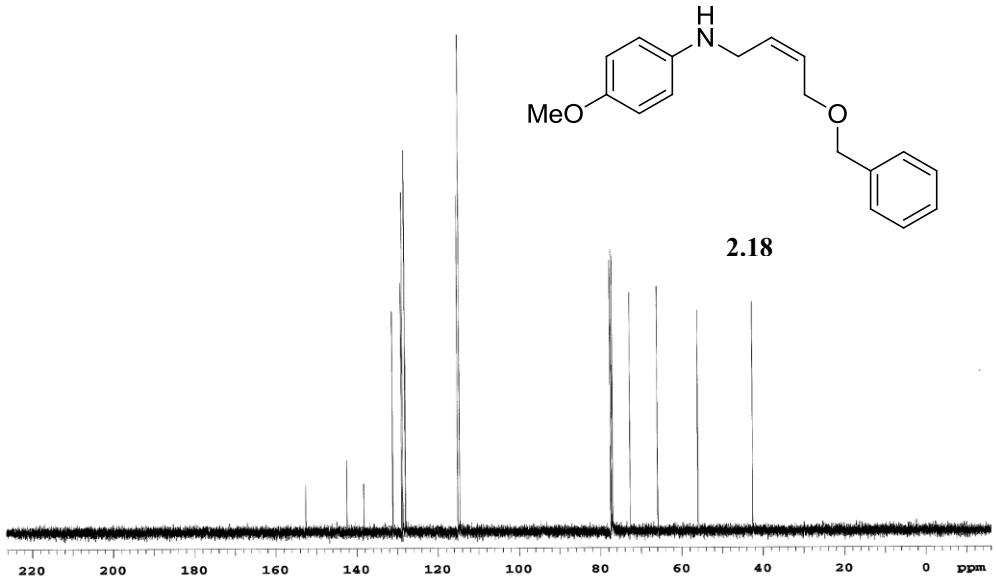

HO
O
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Cl
O
8
7
6
5
4
3
2
1
0
ppm

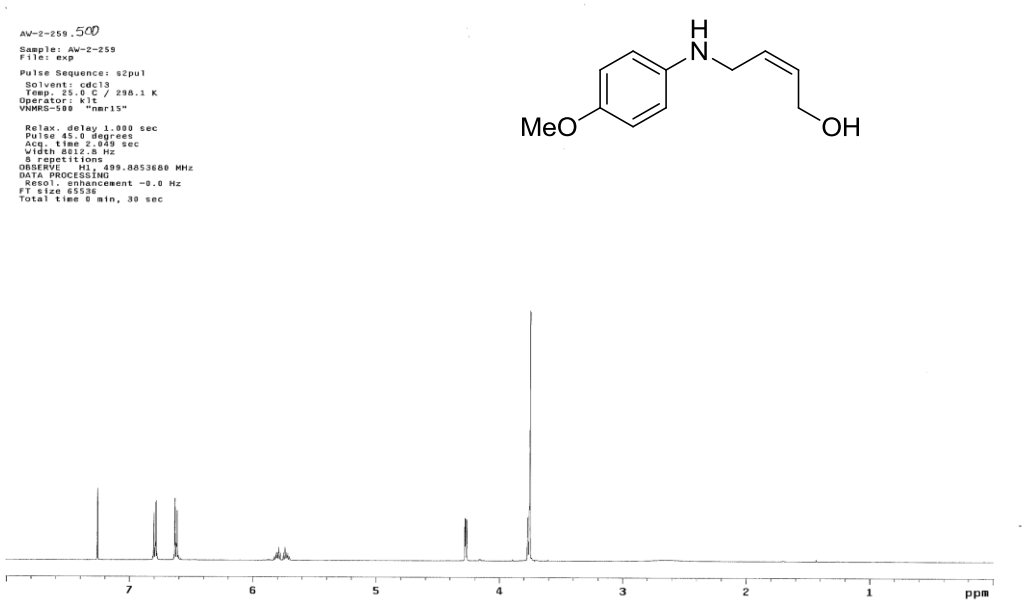

Cl
O
220
200
180
160
140
120
100
80
60
40
20
0
ppm

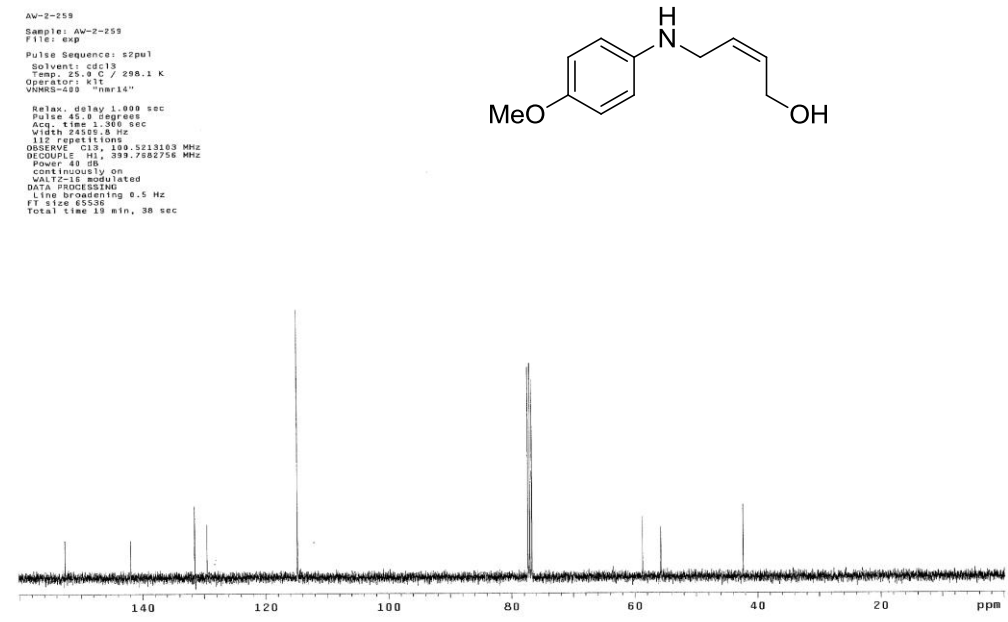

H
N
MeO
O
8
7
6
5
4
3
2
1
0
ppm

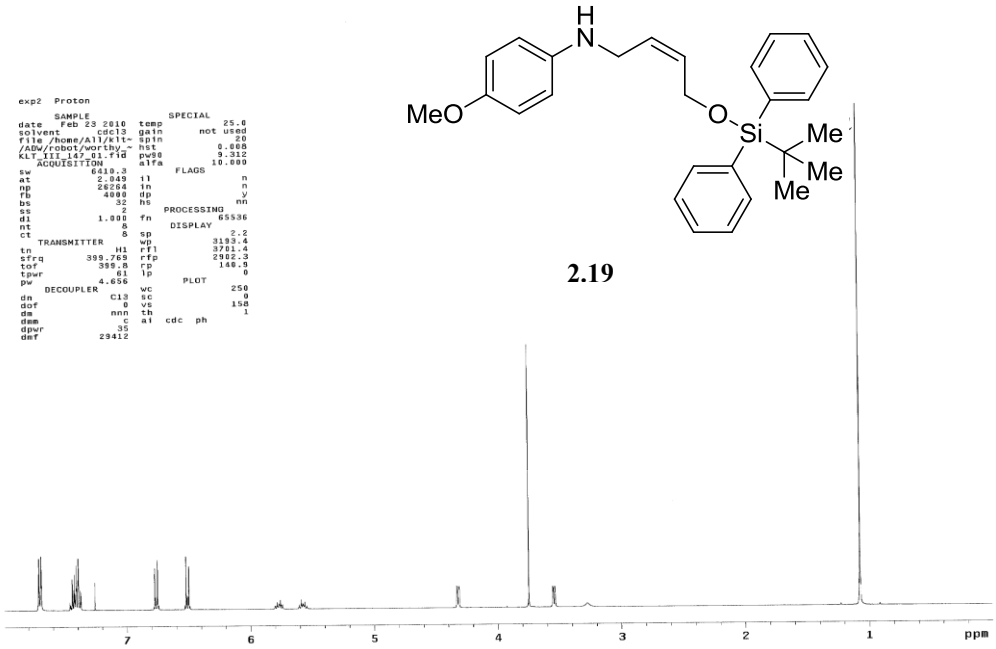
2.18

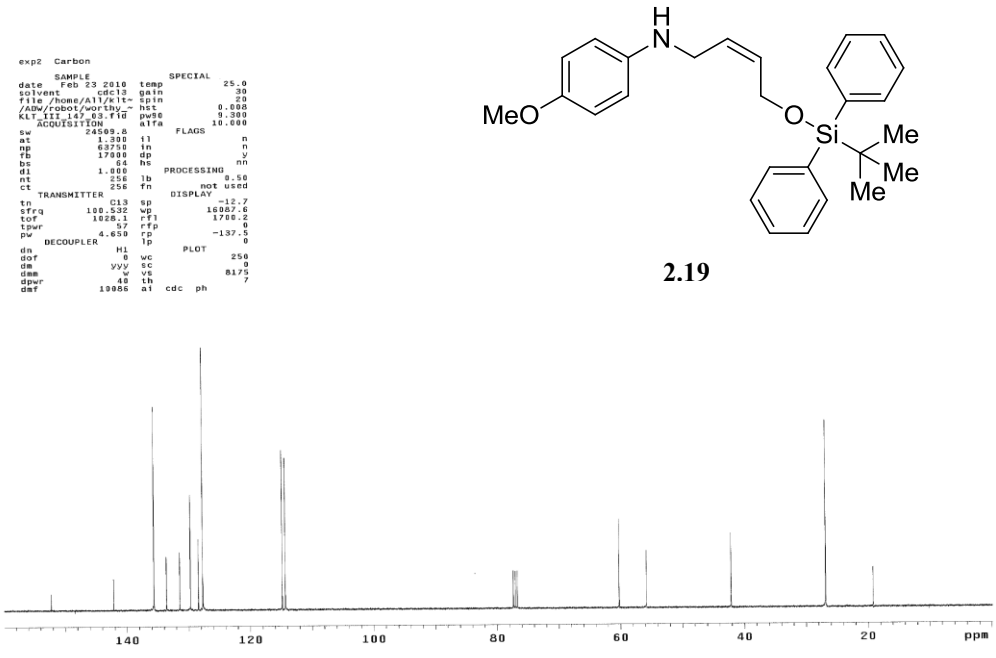

H
N
MeO
O
220
200
180
160
140
120
100
80
60
40
20
0
ppm

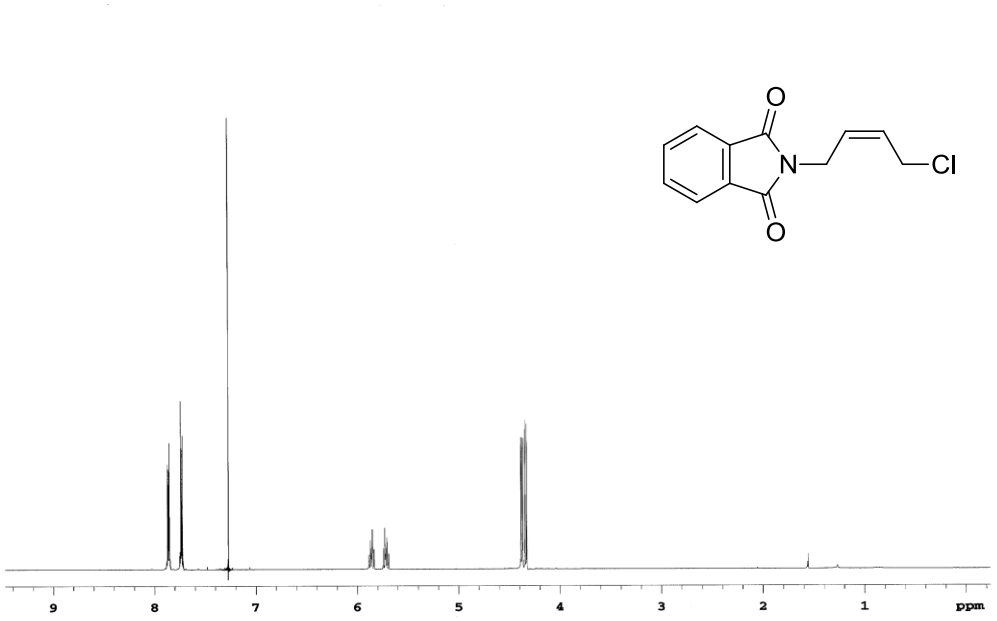
2.18

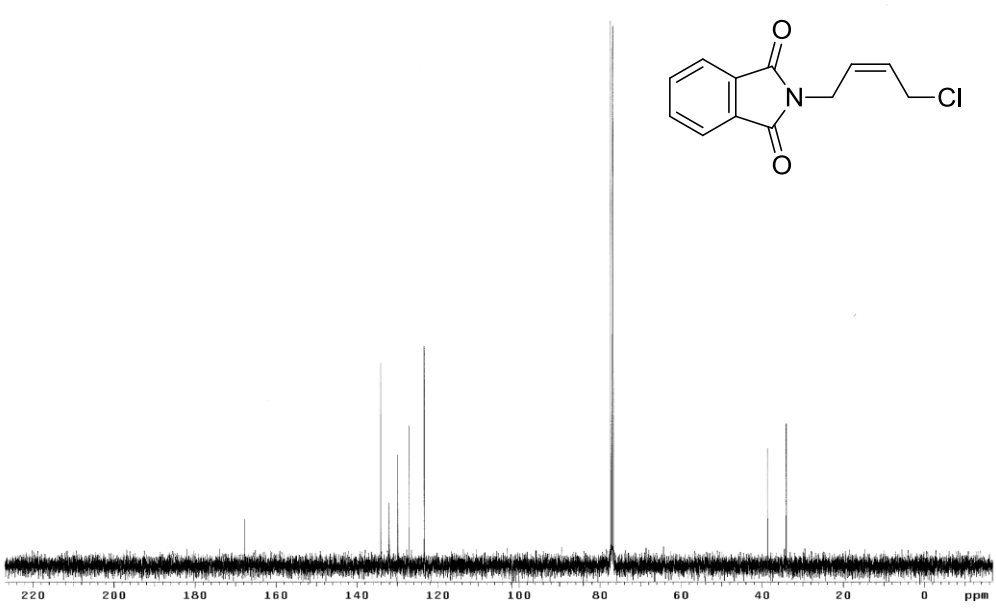

AW-2-259.500
Sample: AW-2-259
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8812.8 Hz
8 repetitions
OBSERVE H1, 499.8853680 MHz
DATA PROCESSING
Resol. enhancement -0.6 Hz
FT size 65536
Total time 0 min, 30 sec
H
N
MeO
OH
7
6
5
4
3
2
1
ppm

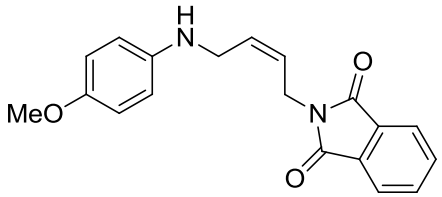

AW-2-259
Sample: AW-2-259
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.9 C / 298.1 K
Operator: klt
VNMRS-600 "nmr14"
Relax. delay 1.900 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
112 repetitions
OBSERVE C13, 199.5213103 MHz
DECOUPLE H1, 399.7582756 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 19 min, 38 sec
H
N
MeO
OH
140
120
100
80
60
40
20
ppm


exp2 Proton
SAMPLE
date Feb 23 2010
solvent cdcl3
file /home/All/klt~
/ADW/robot/worthy_~
KLT_III_147_01.fid
ACQUISITION
sw 6410.3
at 2.049
np 26264
fb 4000
bs 32
ss 2
d1 1.000
nt 8
ct 8
TRANSMITTER
tn H1
sfrq 399.769
tof 399.8
tpwr 61
pw 4.656
DECOUPLER
dn C13
dof 0
dm nnn
dmm c
dpwr 35
dmf 29412
SPECIAL
temp 25.0
gain not used
spin 20
hst 0.008
pw90 9.312
alfa 10.000
FLAGS
PROCESSING
fn 65536
DISPLAY
sp 2.2
wp 3193.4
rf1 3781.4
rfp 2902.3
rp 148.5
lp 0
PLOT
wc 250
sc 0
vs 158
th 1
ai cdc ph
MeO
H
N
O
Si
Me
Me
Me
2.19
7
6
5
4
3
2
1
ppm

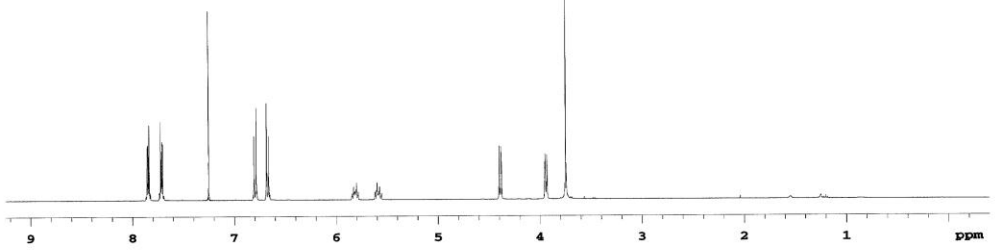

exp2 Carbon
SAMPLE
date Feb 23 2010
solvent cdcl3
file /home/All/klt~
/ADW/robot/worthy_~
KLT_III_147_03.fid
ACQUISITION
sw 24509.8
at 1.300
np 63750
fb 17000
bs 64
d1 1.000
nt 256
ct 256
TRANSMITTER
tn C13
sfrq 100.532
tof 1028.1
tpwr 57
pw 4.650
DECOUPLER
dn H1
dof 0
dm yyy
dmm w
dpwr 48
dmf 19086
SPECIAL
temp 25.0
gain 30
spin 20
hst 0.008
pw90 9.300
alfa 10.000
FLAGS
PROCESSING
lb 0.50
fn not used
DISPLAY
sp -12.7
wp 16087.6
rf1 1708.2
rfp 0
rp -137.5
lp 0
PLOT
wc 250
sc 0
vs 8175
th 7
ai cdc ph
MeO
H
N
O
Si
Me
Me
Me
2.19
140
120
100
80
60
40
20
ppm

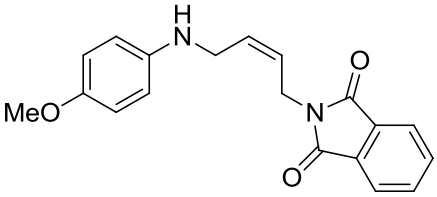

O
N
Cl
O
9
8
7
6
5
4
3
2
1
ppm


O
N
Cl
O
220
200
180
160
140
120
100
80
60
40
20
0
ppm

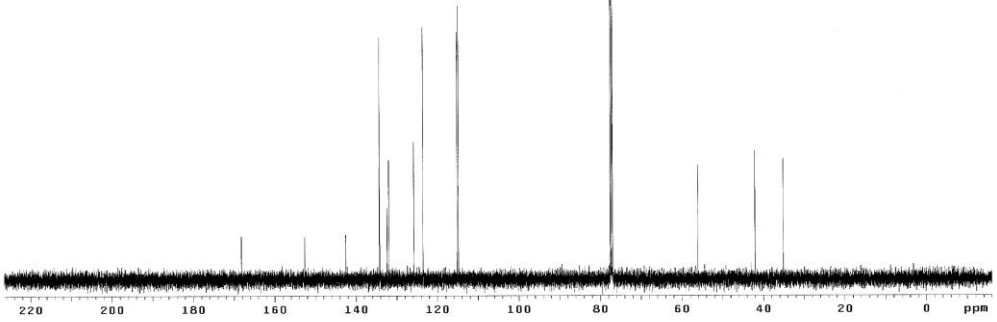

H
N
MeO
O
N
O

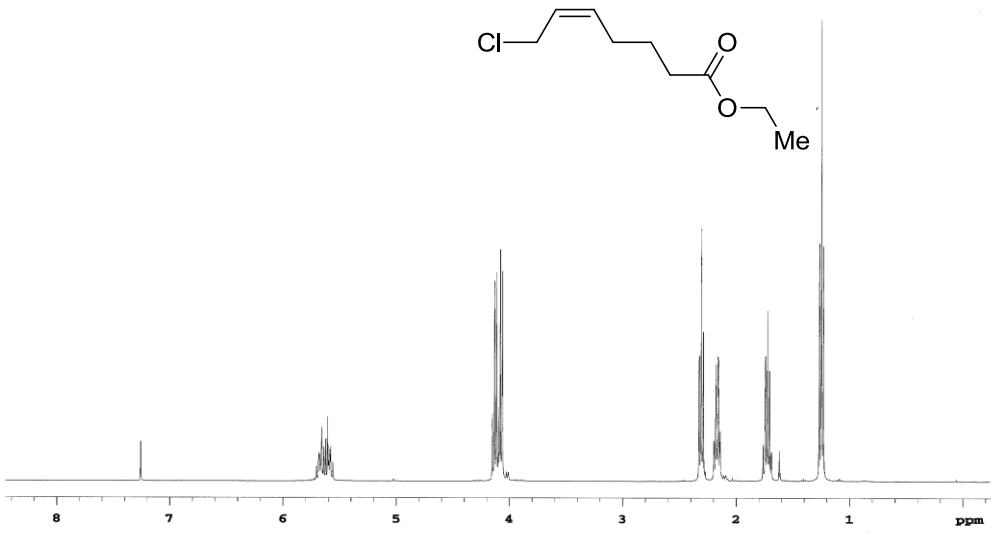
2.20

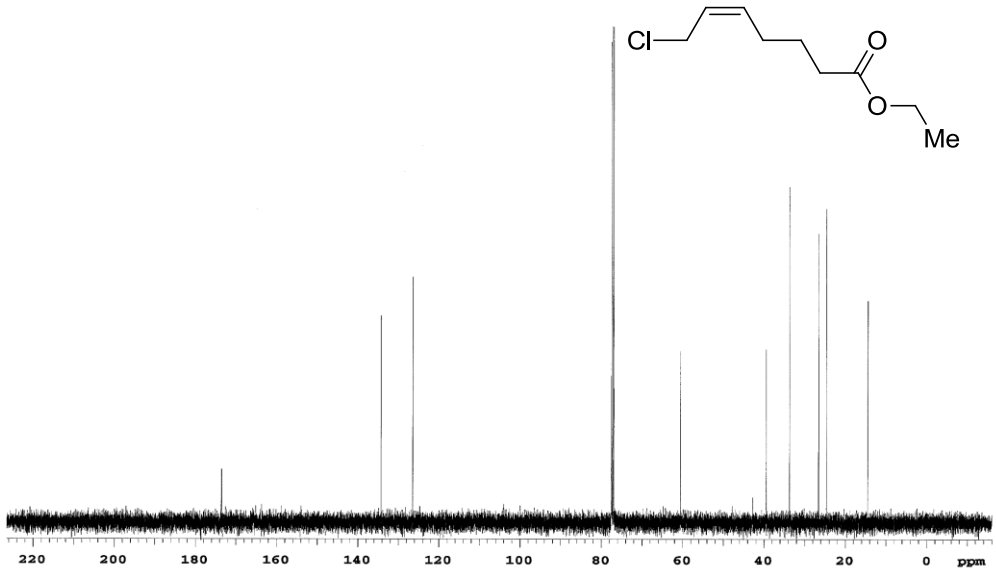

9
8
7
6
5
4
3
2
1
ppm

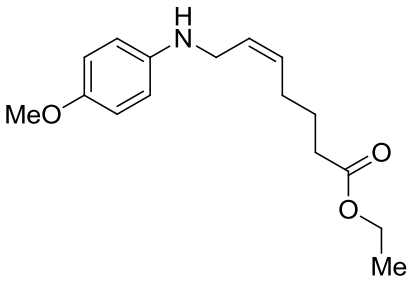

H
N
MeO
O
N
O

2.20


220
200
180
160
140
120
100
80
60
40
20
0
ppm

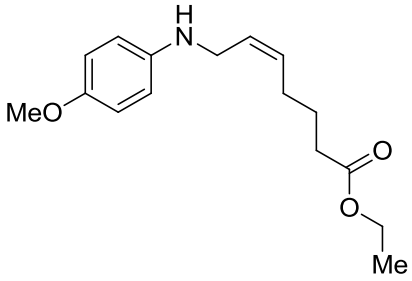

Cl
O
O
Me
8
7
6
5
4
3
2
1
ppm


Cl
O
O
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


H
N
MeO
O
O
Me

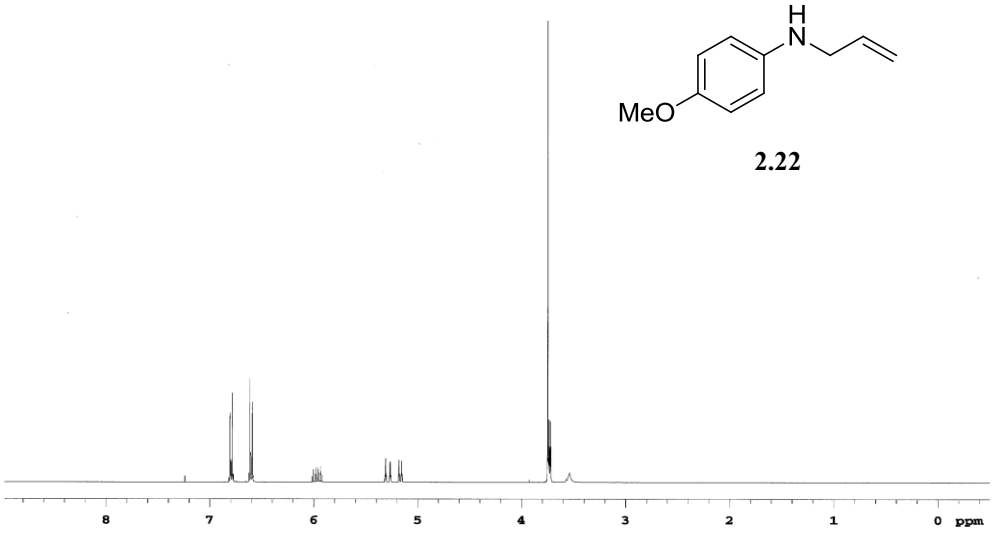
2.21

8
7
6
5
4
3
2
1
0
ppm

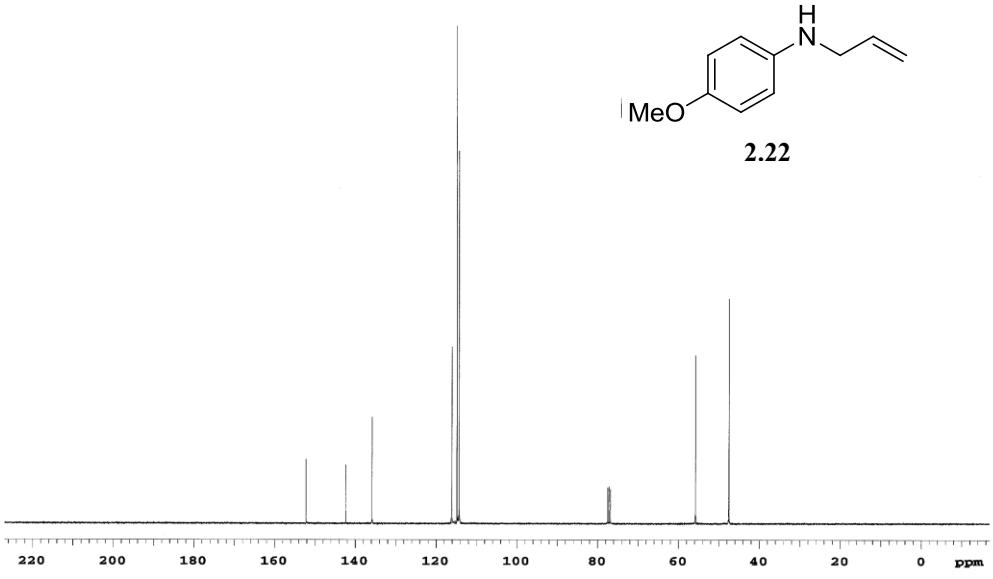

H
N
MeO
O
O
Me

2.21

220
200
180
160
140
120
100
80
60
40
20
0
ppm

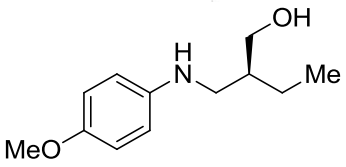

H
N
MeO
8
7
6
5
4
3
2
1
0 ppm

2.22

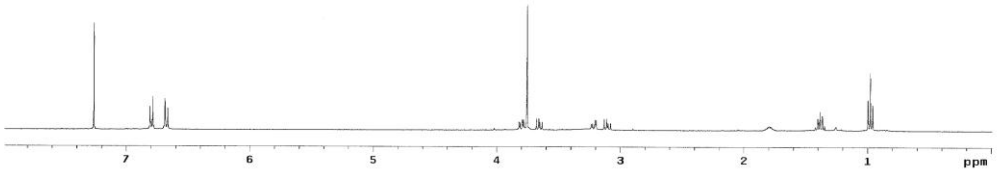

H
N
MeO
220
200
180
160
140
120
100
80
60
40
20
0 ppm

2.22

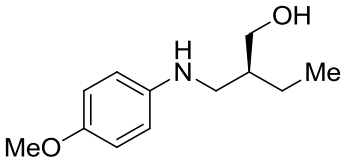

AV-2-268
Sample: AW-2-268
Sample ID: s_20100212_03
File: /home/All/klt/ADW/AW-2-268.fid
Pulse Sequence: s2pul


OH
H
N
Me
MeO

2.10

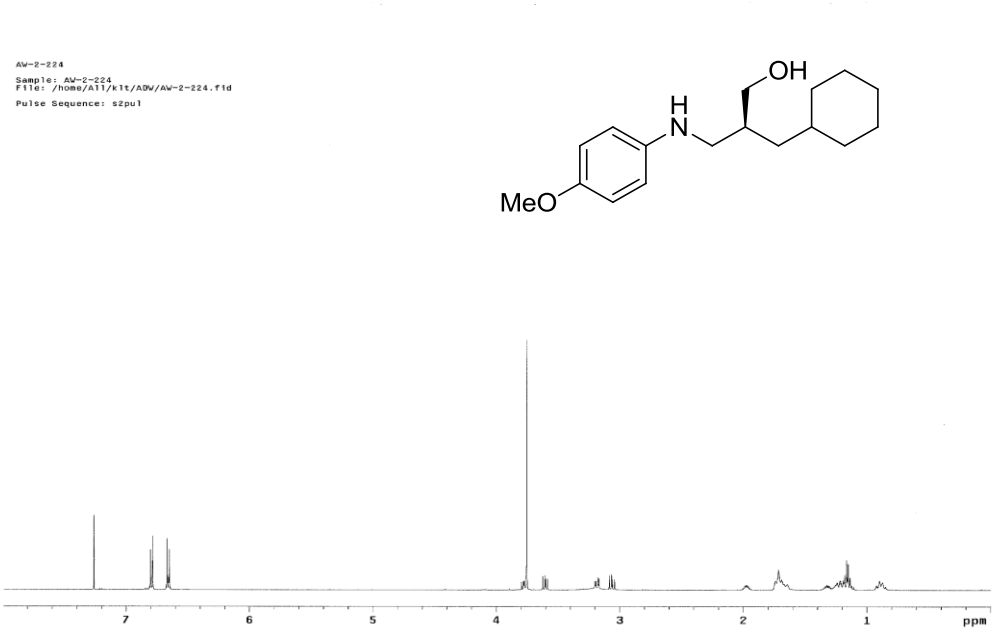

7
6
5
4
3
2
1
ppm

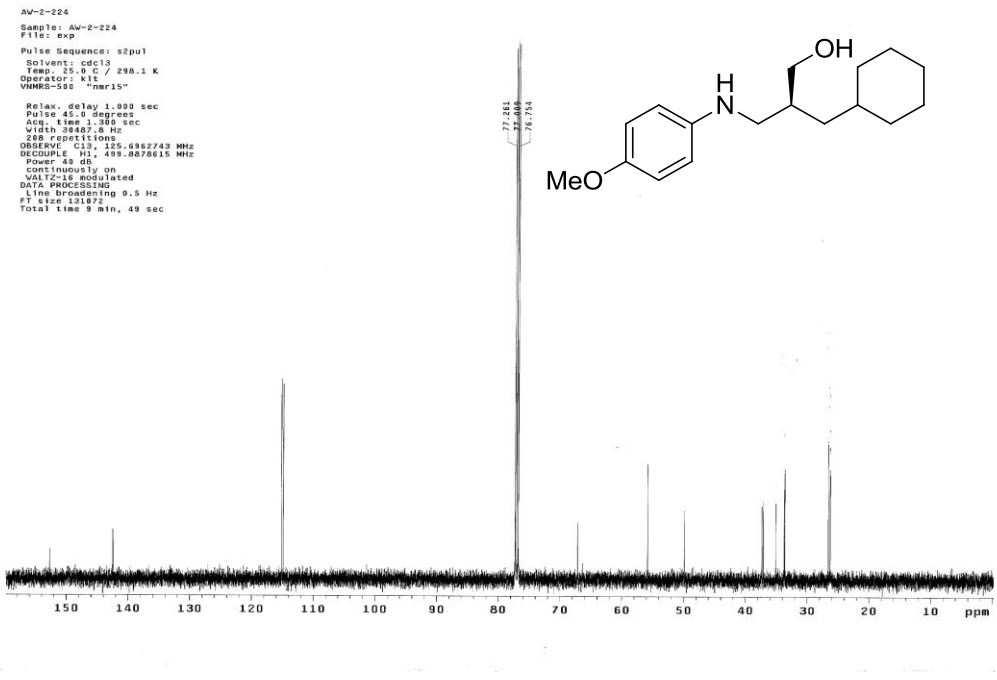

AW-2-223f60_93
Sample: AW
Sample ID: /home/walkup/worthy_20_AW_2_223_01
File: home/All/klt/ADW/robot/worthy_AW_2_223_02.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.9 C / 298.1 K
Sample #20, Operator: worthy
File: worthy_AW_2_223_02
VNMRS-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
256 repetitions
OBSERVE C13, 100.5213103 MHz
DECOUPLE H1, 399.7682756 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 9 min, 49 sec

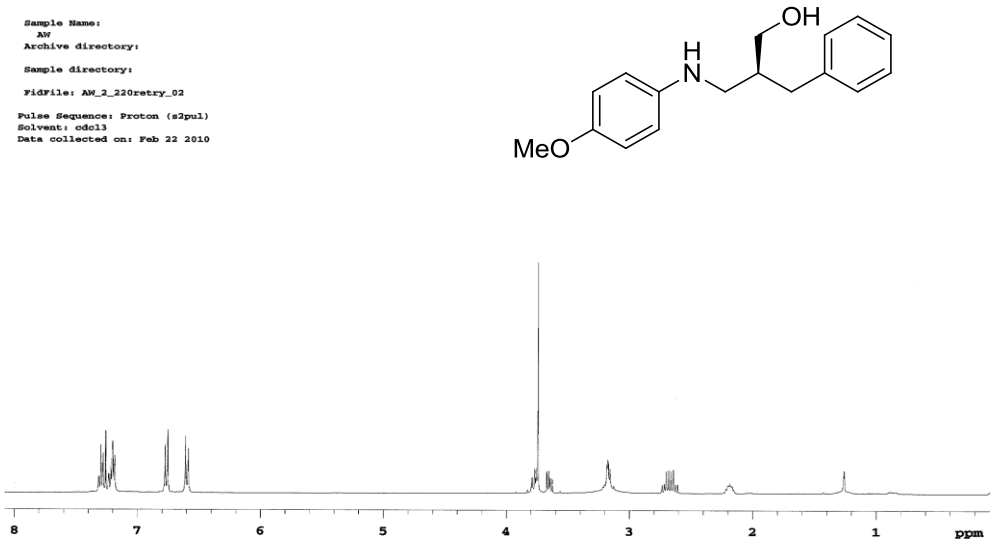

OH
H
N
Me
MeO

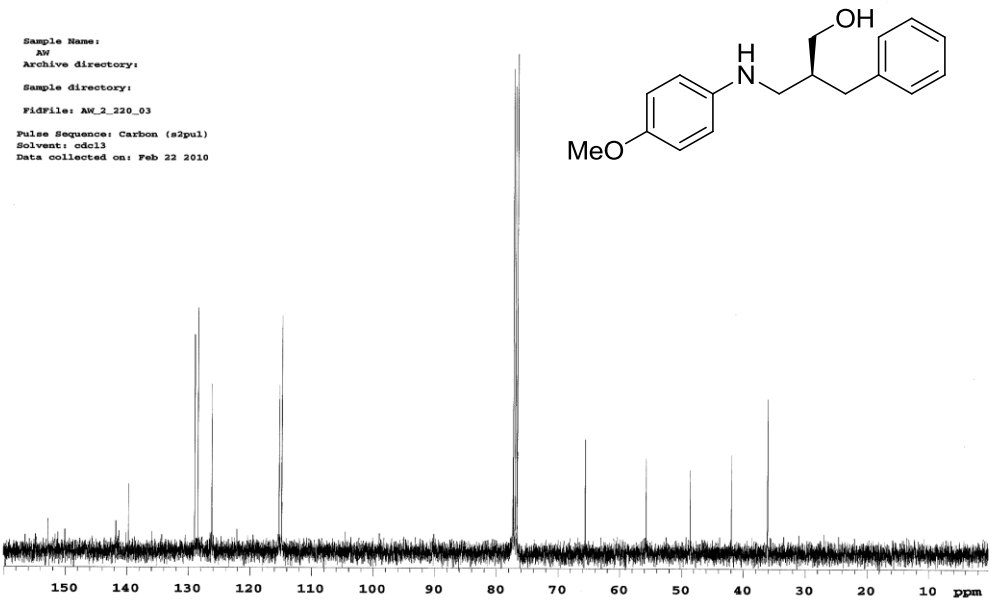
2.10

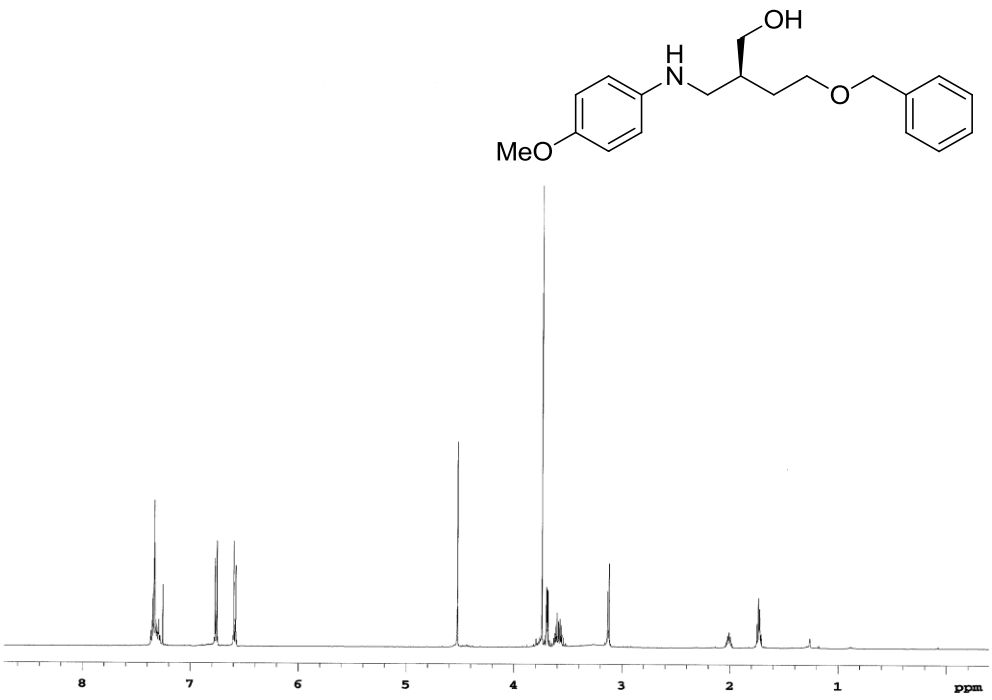
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

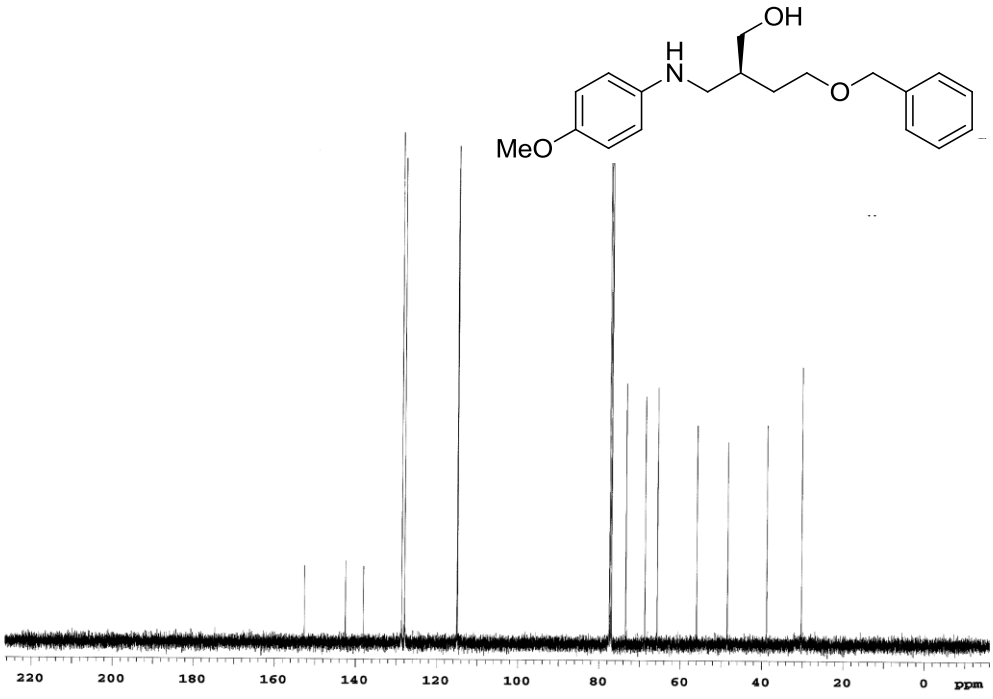

AW-2-224
Sample: AW-2-224
File: /home/All/klt/ADW/AW-2-224.fid
Pulse Sequence: s2pul
OH
H
N
MeO
7
6
5
4
3
2
1
ppm

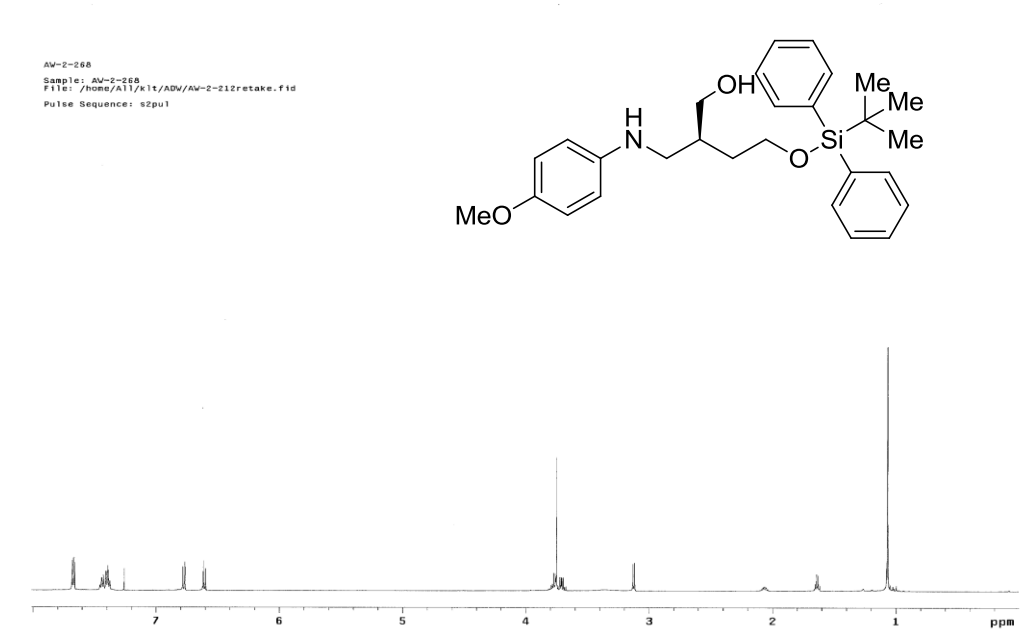

AW-2-224
Sample: AW-2-224
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
208 repetitions
OBSERVE C13, 125.6962743 MHz
DECOUPLE H1, 499.8878615 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
77.261
77.004
76.754
OH
H
N
MeO
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

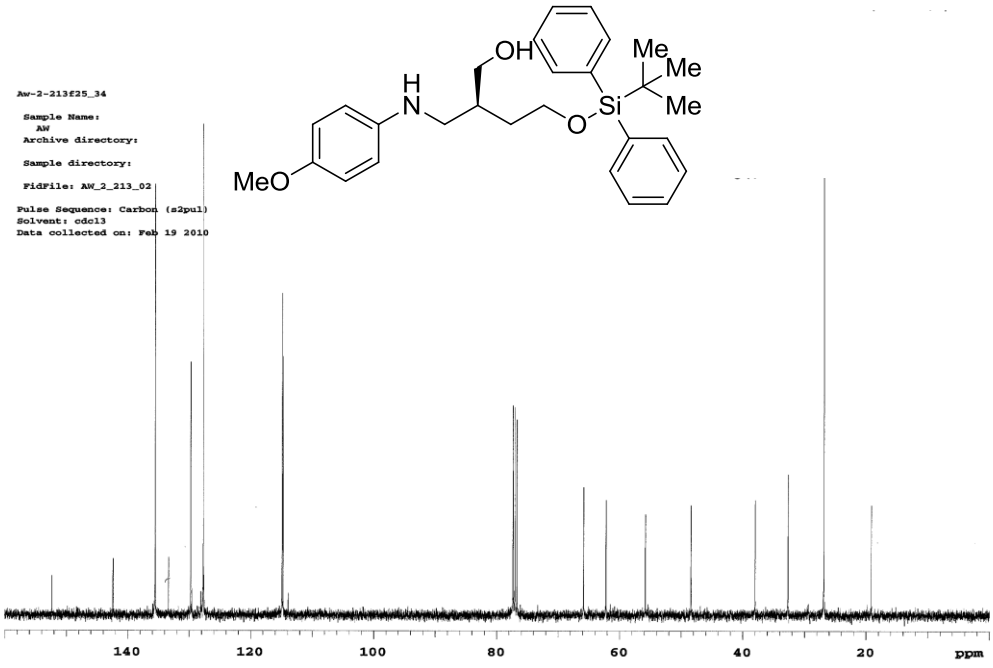

Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_2_220retry_02
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Feb 22 2010
OH
H
N
MeO
8
7
6
5
4
3
2
1
ppm


Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_2_220_03
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 22 2010
OH
H
N
MeO
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


OH
H
N
O
MeO
8
7
6
5
4
3
2
1
ppm


OH
H
N
O
MeO
220
200
180
160
140
120
100
80
60
40
20
0
ppm


AW-2-268
Sample: AW-2-268
File: /home/All/klt/ADW/AW-2-212retake.fid
Pulse Sequence: s2pul
OH
H
N
Me
Me
Me
Si
O
MeO
7
6
5
4
3
2
1
ppm

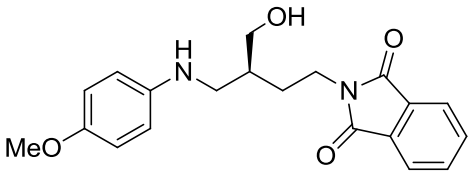

Aw-2-213f25_34
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_2_213_02
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 19 2010
OH
H
N
Me
Me
Me
Si
O
MeO
140
120
100
80
60
40
20
ppm

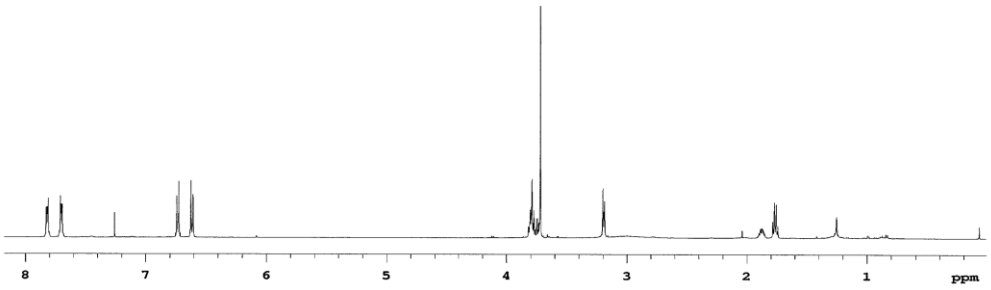
Sample Name:
CLJ-2-206-SI-H
Archive directory:

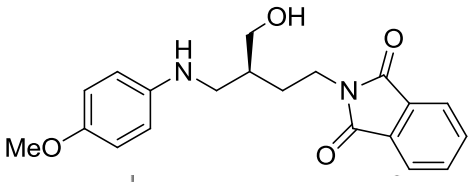
Sample directory:

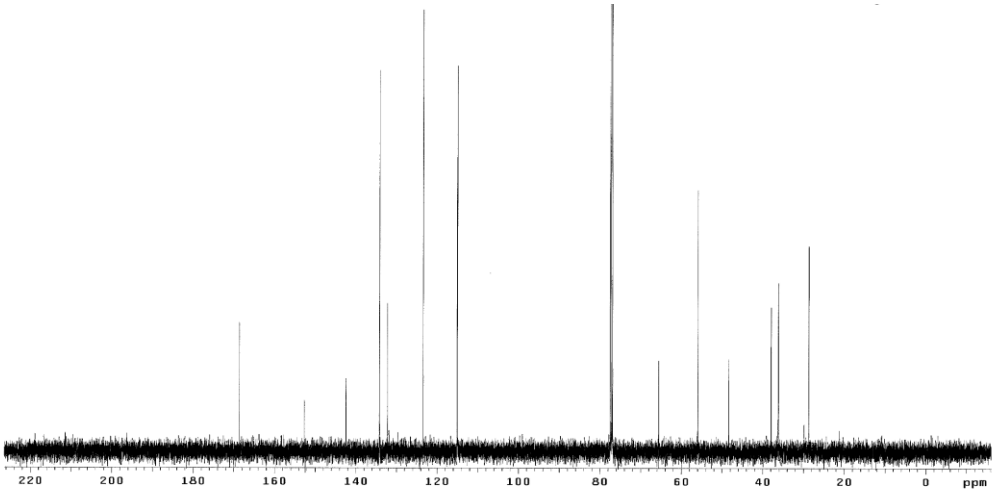
FidFile: CLJ-2-206-SI-H

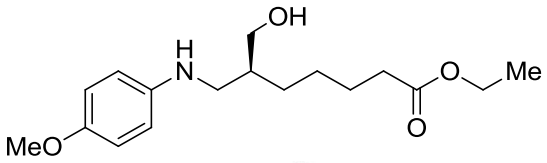
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Aug 9 2010

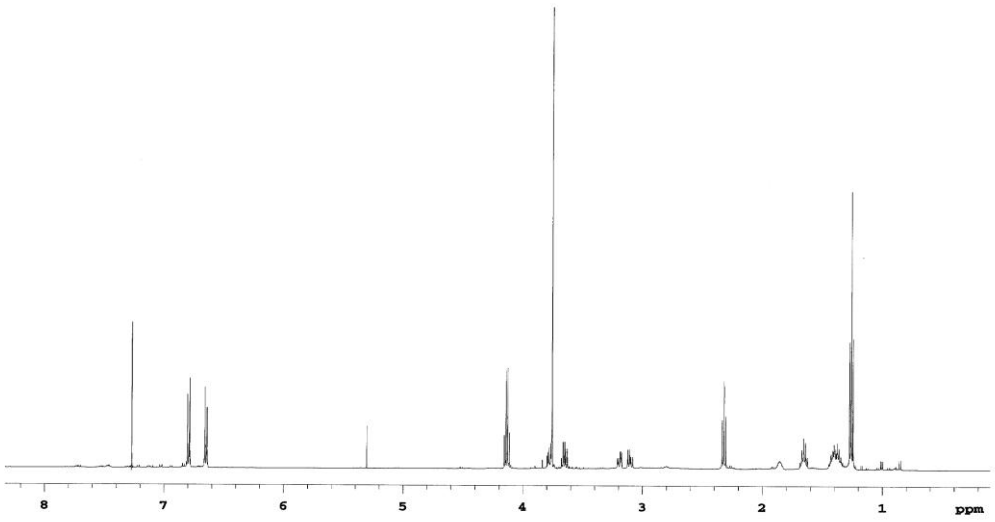


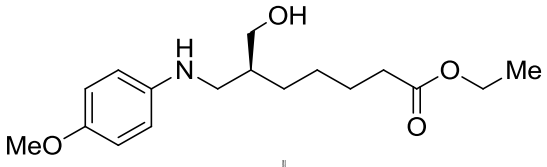


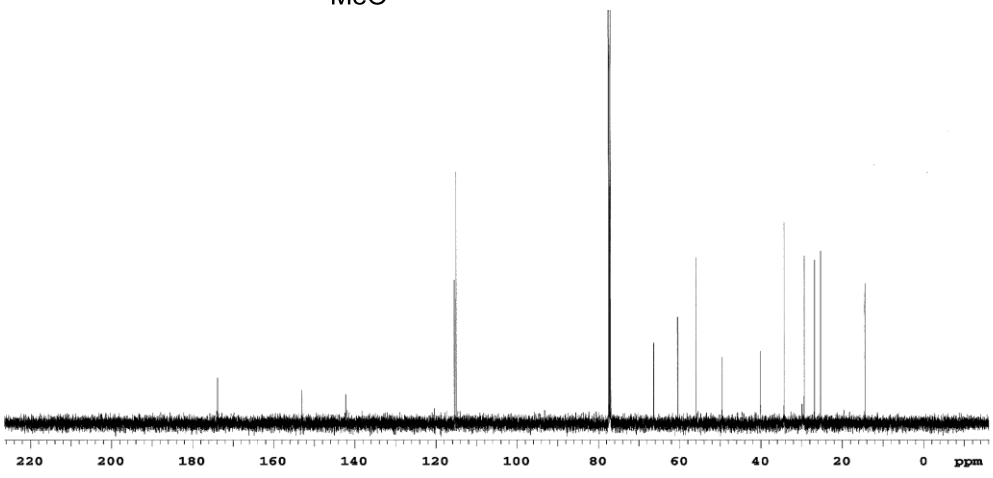


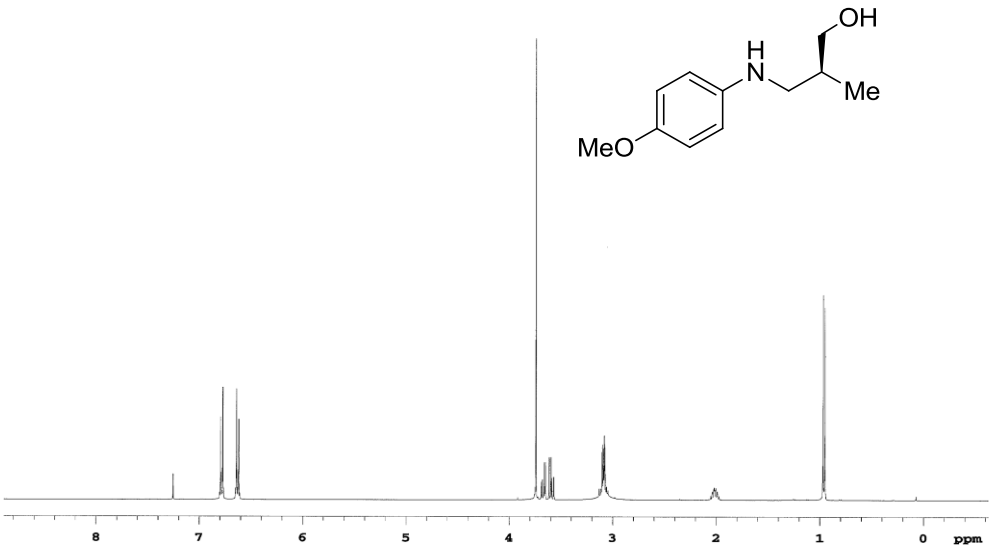


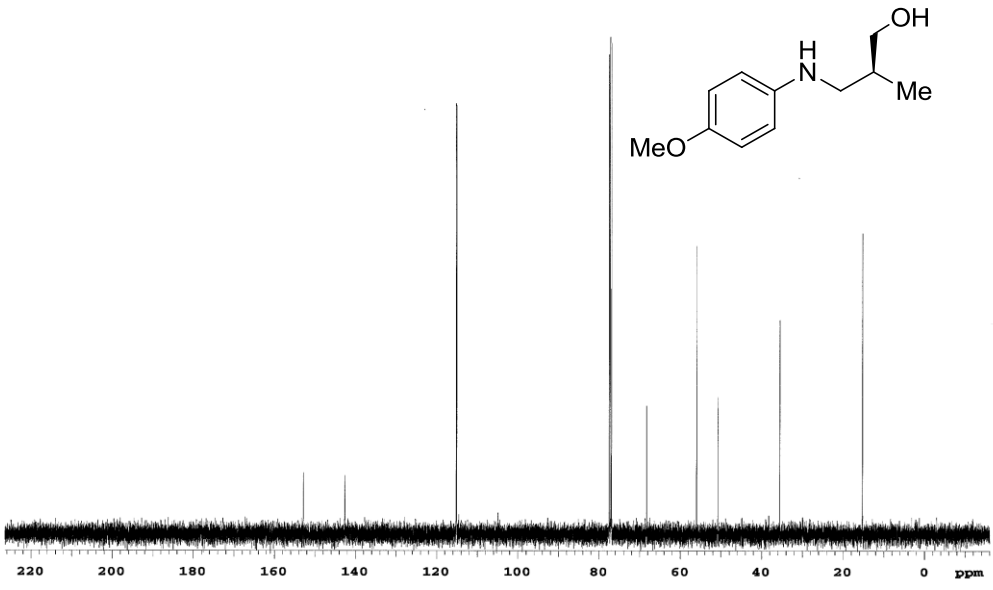

OH
H
N
O
Me
MeO
O

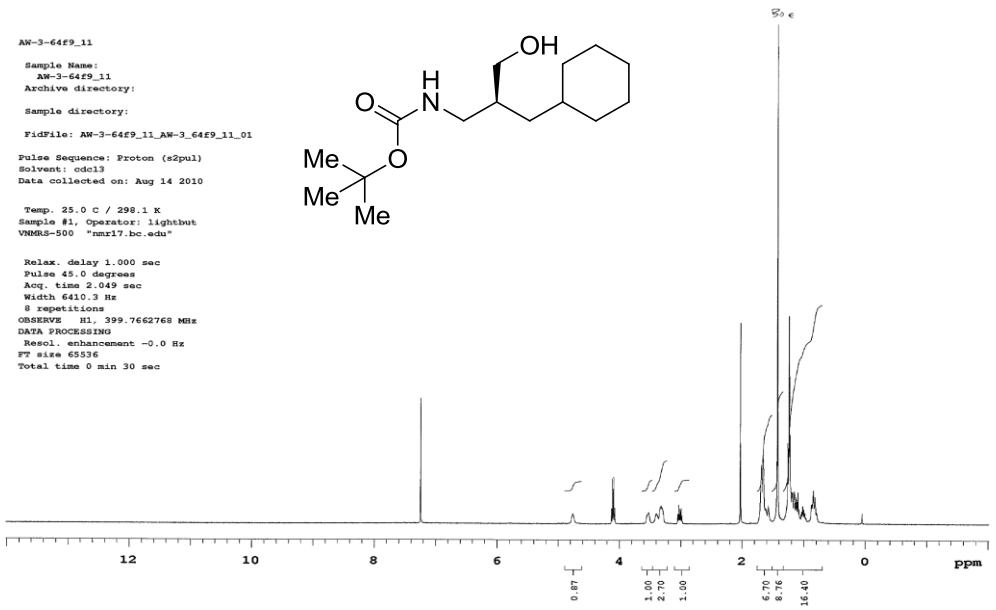

8
7
6
5
4
3
2
1
ppm

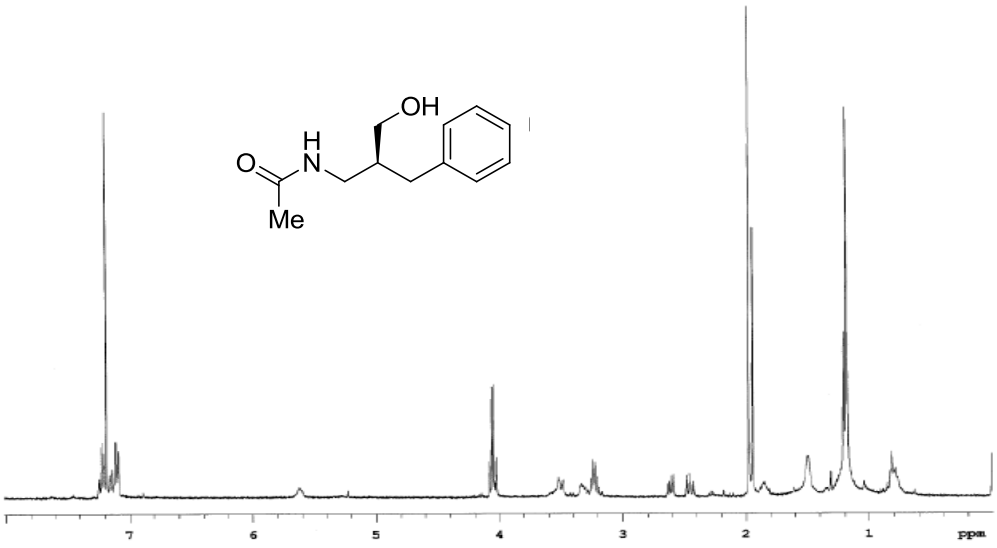

OH
H
N
O
Me
MeO
O


220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
H
N
Me
MeO
8
7
6
5
4
3
2
1
0
ppm


OH
H
N
Me
MeO
220
200
180
160
140
120
100
80
60
40
20
0
ppm


AW-3-64f9_11
Sample Name:
AW-3-64f9_11
Archive directory:
Sample directory:
FidFile: AW-3-64f9_11_AW-3_64f9_11_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Aug 14 2010
Temp. 25.0 C / 298.1 K
Sample #1, Operator: lightbut
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.7662768 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec
OH
H
N
O
O
Me
Me
Me
12
10
8
6
4
2
0
ppm
0.87
1.00
2.70
1.00
6.70
8.76
16.40

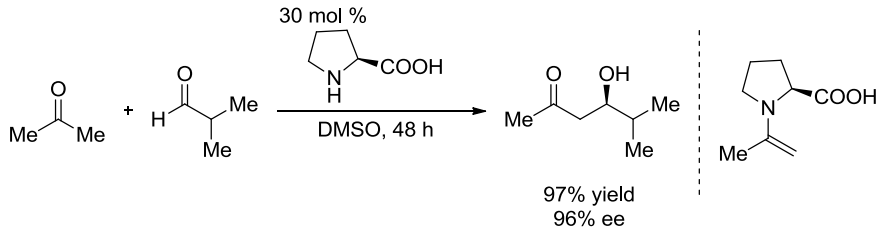

OH
H
N
O
Me
7
6
5
4
3
2
1
ppm

Chapter 3. Selective Functionalization of Diols

3.1 Methods for Accelerating Reaction Rates in Organocatalysis

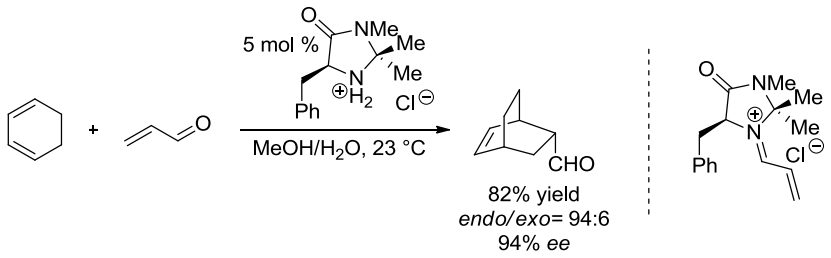
Reversible covalent bonding is a common mode of activation used in organocatalysis. Many methods have focused on making a more active intermediate in order to accelerate the reaction, for example, enamine (Scheme 3.1),[1a,c,e,f] iminium

Scheme 3.1 Enamine Activation Using Proline.[1a]



(Scheme 3.2),[1b,d,e,f] and N-heterocyclic carbene catalysis.[1g] Another approach for accelerating reactions is pre-organization of the substrate via reversible covalent bonding.

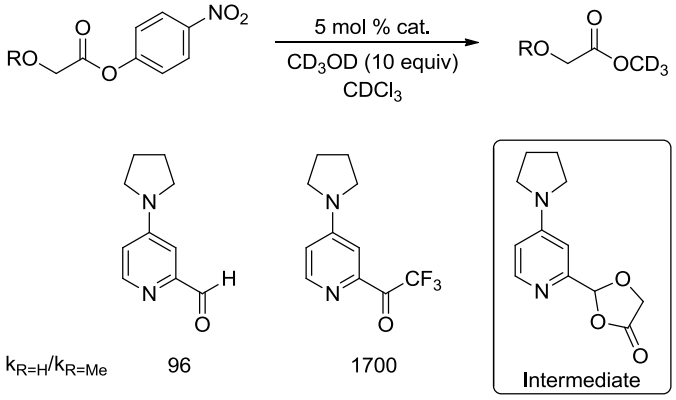
Scheme 3.2 Iminium Activation.[1b]



[1](a) List, B.; Lerner, R. A.; Barbas III, C. F. *J. Am. Chem. Soc.* **2000**, *122*, 2395-2396. (b) Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 4243-4244. (c) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471–5569. (d) Erkkila, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416–5470. (e) Melchiorre, P.; Marigo, M.; Carlone, A.; Bartoli, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 6138–6171. (f) Pihko, P. M.; Majander, I.; Erkkila, A. *Asymmetric Organocatalysis*; Springer-Verlag: Berlin, 2010, pp 29-75. (g) Moore, J. L.; Rovis, T. *Asymmetric Organocatalysis*; Springer-Verlag: Berlin, 2010, 291, pp 77-144.

These reactions achieve rate enhancement through induced intramolecularity.[2] The favorable binding of the substrate to a catalyst comes at a significant entropic cost. However, the subsequent step is accelerated, because it does not have to pay this penalty. For example, Sammakia and co-workers have shown that aldehydes and ketones can be used as intramolecular activation catalysts in the alcoholysis of α–hydroxy esters.[3] The transesterification of α –hydroxy esters occurs up to 1700 times faster than the corresponding methyl ether substrate. The intermediate observed during the reaction demonstrates the importance of the α-hydroxyl group in the reaction (Scheme 3.3).

Scheme 3.3 α-Hydroxy Ester Alcoholysis.

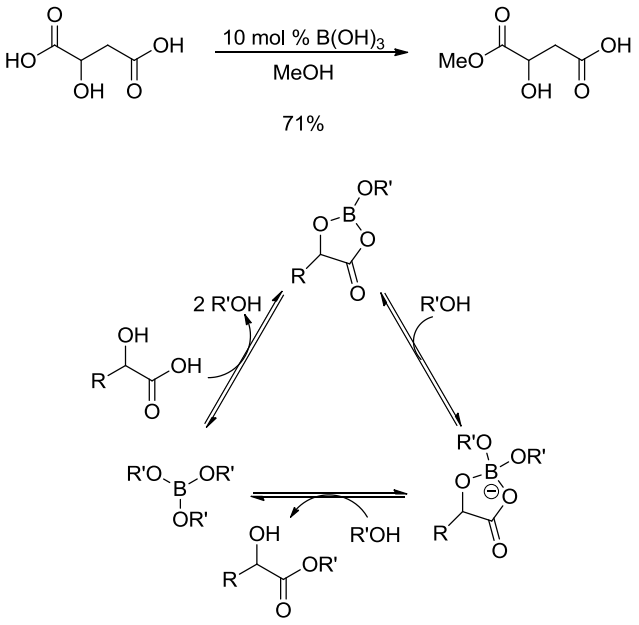


Similarly, boric acid has been shown to be particularly good at catalyzing the site selective esterification of α–hydroxycarboxylic acids.[4] The boric acid initially exchanges with the alcohol allowing the intramolecular cyclization to form the activated ester before

[2]Tan, K. L. *ACS Catal.* **2011**, *1*, 877-886.
[3](a) Sammakia, T.; Hurley, T. B. *J. Am. Chem. Soc.* **1996**, *118*, 8967–8968. (b) Sammakia, T.; Hurley, T. B. *J. Org. Chem.* **1999**, *64*, 4652–4664. (c) Sammakia, T.; Hurley, T. B. *J. Org. Chem.* **2000**, *65*, 974–978.
[4](a) Ishihara, K.; Ohara, S.; Yamamoto, H. *J. Org. Chem.* **1996**, *61*, 4196–4197. (b) Ishihara, K. *Tetrahedron* **2009**, *65*, 1085–1109.

alcoholysis. The order of the steps in the mechanism is what allows for the selective esterification (Scheme 3.4).

Scheme 3.4 Site Selective Boric Acid-Catalyzed Esterification.



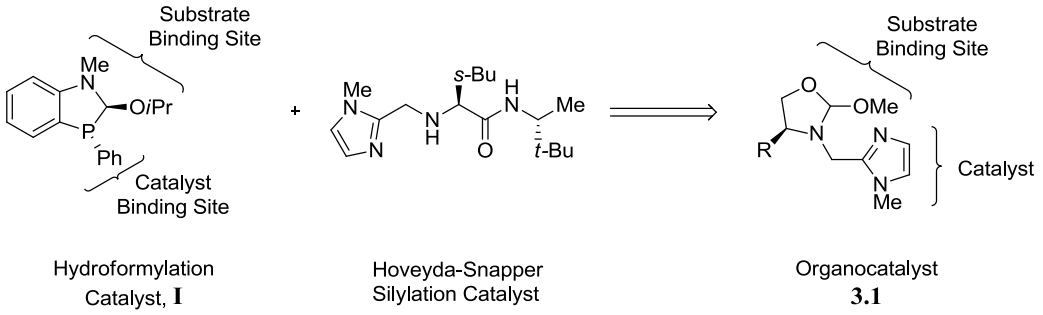
3.2 Development of Organocatalyst **3.1**

Previously, our group has developed catalytic directing groups **I** and **II** for the regio-, diastero-, and enantioselective hydroformylation of olefins (Chapter 1 and 2).[5] These catalytic directing groups use reversible covalent bonding and induced intramolecularity to achieve selectivity and rate acceleration. In order to expand our methodology into electrophile transfer, organocatalyst **3.1** was designed taking into account the features that had made **I** and **II** successful. Therefore, the substrate binding site was retained. A hydrogen-bonding organocatalyst developed by the Hoveyda and

[5](a) For a review of catalytic directing groups: Rousseau, G.; Breit, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2450-2494 and the references within. (b) Worthy, A. D.; Joe, C. L.; Lightburn, T. L.; Tan, K. L. *J. Am. Chem. Soc.* **2010**, *132*, 14757-14759. (c) Lightburn, T. E.; De Paolis, O. A.; Cheng, K. H.; Tan, K. L. *Org. Lett.* **2011**, *13*, 2686-2689.

Snapper groups, which uses *N*-methylimidazole as a catalyst for silylation, was also used as inspiration.[6] Thus, instead of a catalyst binding site, *N*-methylimidazole was built into the molecule. The backbone of the molecule originates from amino alcohols so the source of chirality is cheap, diverse, and readily derivatized (Figure 3.1).

Figure 3.1 Organocatalyst Design.



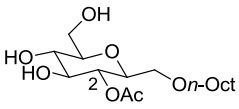
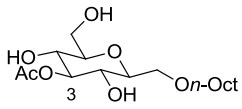
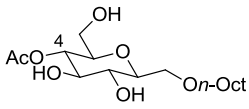
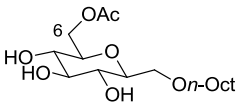
3.3 Application of Organocatalyst **3.1** to Selective Functionalization

In order to show the power of this catalytic directing group, it was important to choose a problem that has been difficult to solve using traditional strategies. While the use of organocatalysts has been successfully applied to many problems in organic synthesis, the functionalization of a less reactive group in the presence of a more reactive one is still a challenge.[7,8] Due to their ability to bind a substrate with the desired

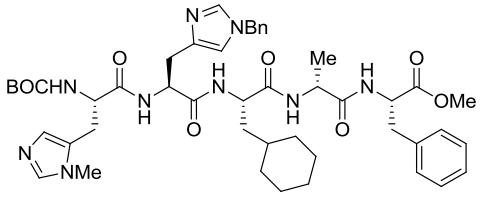
[6]Zhao, Y.; Rodrigo, J.; Hoveyda, A. H.; Snapper, M. L. *Nature* **2006**, *443*, 67-70. [7]*Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A.,Yamamoto, H., Eds.: Springer-Verlag: Berlin Heidelberg, 1999; Vols. I-III. [8](a) Jordan, P. A.; Miller, S. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 2907-2911. (b) Yoshida, K.; Furuta, T.; Kawabata, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 4888-4892. (c) Kawabata, T.; Furuta, T. *Chem. Lett.* **2009**, *38*, 640-647. (d) Ohshima, T.; Iwasaki, T.; Maegawa, Y.; Yoshiyama, A.; Mashima, K. *J. Am. Chem. Soc.* **2008**, *130*, 2944-2945. (e) Lewis, C. A.; Miller, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 5616-5619. (f) Griswold, K. S.; Miller, S. J. *Tetrahedron* **2003**, *59*, 8869-8875. (g) Kurahashi, T.; Mizutani, T.; Yoshida, J. *Tetrahedron* **2002**, *58*, 8669-8677. (h) Hu, G.; Vasella, A. *Helv. Chim. Acta* **2002**, *85*, 4369-4391.

functional group near the catalytically active residue, enzymes are capable of performing site selective catalysis.[9] Taking inspiration from enzymes, Miller discovered a peptide based catalyst through a library screen that is capable of functionalizing a secondary alcohol in the prescence of a primary alcohol in a glucose derived substrate (Table 3.1).[8f] The selectivity is believed to be a result of the catalyst hydrogen bonding to the more accessible primary hydroxyl allowing the 4-O to be acylated. Using similar peptide based catalysts, Miller and co-workers have shown that selective derivitizations of natural products is possible.[10]

Table 3.1 Miller's Selective Functionalization of a Glucose Derivative.

Catalyst				
NMI[a,b]	0	20	16	64
A[a]	9	11	58	22

[a]2 mol % catalyst, Ac_2O (1 equiv), NaOAc, $PhCH_3/CH_2Cl_2$, 0°C, 15 h. [b]Only 14% conversion.



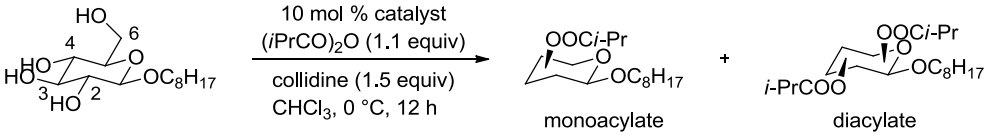
A

[9](a) hi odea Melan o n i *Angew. Chem., Int. Ed.* **2008**, *47* - hi odea Melan o n i *Nature* **2007**, *446*, 1008-1016. (c) Koeller, K. M.; Wong, C.-H. *Chem. Rev.* **2000**, *100*, 4465-4493.

[10](a) Lewis, C. A.; Miller, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 5616-5619. (b) Lewis, C. A.; Merkel, J.; Miller, S. *J. Bioorg. Med. Chem. Lett.* **2008**, *18*, 6007-6011. (c) Lewis, C. A.; Longcore, K. E.; Miller, S. J.; Wender, P. A. *J. Nat. Prod.* **2009**, *72*, 1864-1869. (d) Pathak, T. P.; Miller, S. J. *J. Am. Chem. Soc.* **2012**, *134*, 6120-6123. (e) Fowler, B. S.; Laemmerhold, K. M.; Miller, S. J. *J. Am. Chem. Soc.* **2012**, *134*, 9755-9761.

Similarly, Kawabata and co-workers have demonstrated that very selective 4-O-acylation was possible using their catalyst **B** (Scheme 3.5).[8c] The selectivity is believed to occur through hydrogen bonding to the substrate which orients the 4-hydroxyl near the activated acylating reagent (Figure 3.2).

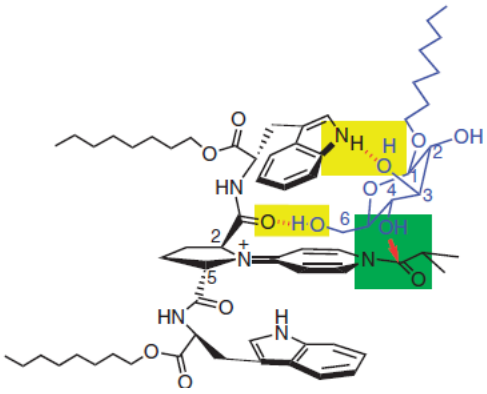
Scheme 3.5 Kawabata Selective Funcationalization of a Glucose Derivative.



Catalyst	Monoacylate (%)	Regioselectivity[a]				Diacylate (%)
		6-O	4-O	3-O	2-O	
DMAP	61	33	24	43	0	21
B	97	0	98	2	0	2

[a]Regioselectivity of monoacylates.

Figure 3.2 Proposed Selectivity Model Using Catalyst **B**.

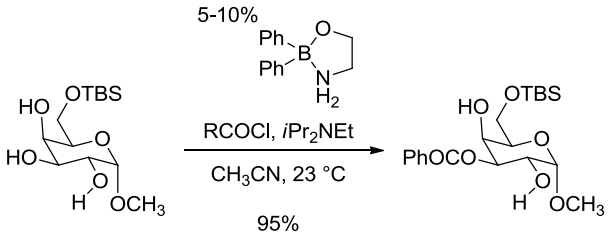


Both of these catalysts are modeled after enzymes in which multiple noncovalent interactions are used to bind a substrate selectively. These catalysts, while smaller than

enzymes, are large compared to most small molecule organic catalysts because of the need for multiple noncovalent interactions.

Taylor has shown selective acylation of sugar derivatives using a commercially available borinate ester which covalently binds cis diols to activate them for functionalization with high selectivitites (Scheme 3.6).[11] Our group believed that we could also be successful in a site selective reaction using a small organocatalyst, **3.1**, which benefits from a reversible covalent bond.

Scheme 3.6 aylor's Borinate ster atalyzed Acylation

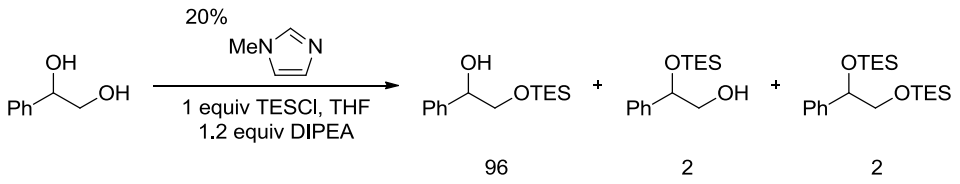


To prove the viability of using **3.1** to functionalize a less reactive group in the presence of a more reactive one, a simple system was tested. The functionalization of a secondary alcohol in the presence of a primary alcohol was interesting since a primary alcohol is about two orders of magnitude more reactive.[12] For example, the silylation of a 1,2-diol with chlorotriethylsilane (TESCl), *N*,*N*-diisopropylethylamine (DIPEA), and catalytic *N*-methylimidazole (NMI) is very selective for the less hindered primary alcohol (Scheme 3.7). In order to reverse this selectivity, an energy difference of >3 kcal/mol

[11]Lee, D.; Taylor, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 3724-3727. Gouliaras, C.; Lee, D.; Chan, L.; Taylor, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 13926-13929. Lee, D.; Williamson, C. L.; Chan, L.; Taylor, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 8260-8267.
[12]Reginato, G.; Ricci, A.; Roelens, S.; Scapecchi, S. *J. Org. Chem.* **1990**, *55*, 5132-5139.

between the two pathways would need to be overcome. Because of this differential reactivity, obtaining the secondary protected product usually requires bis-protection followed by selective deprotection of the primary protected alcohol.[13]

Scheme 3.7 Silylation of a 1,2-Diol.



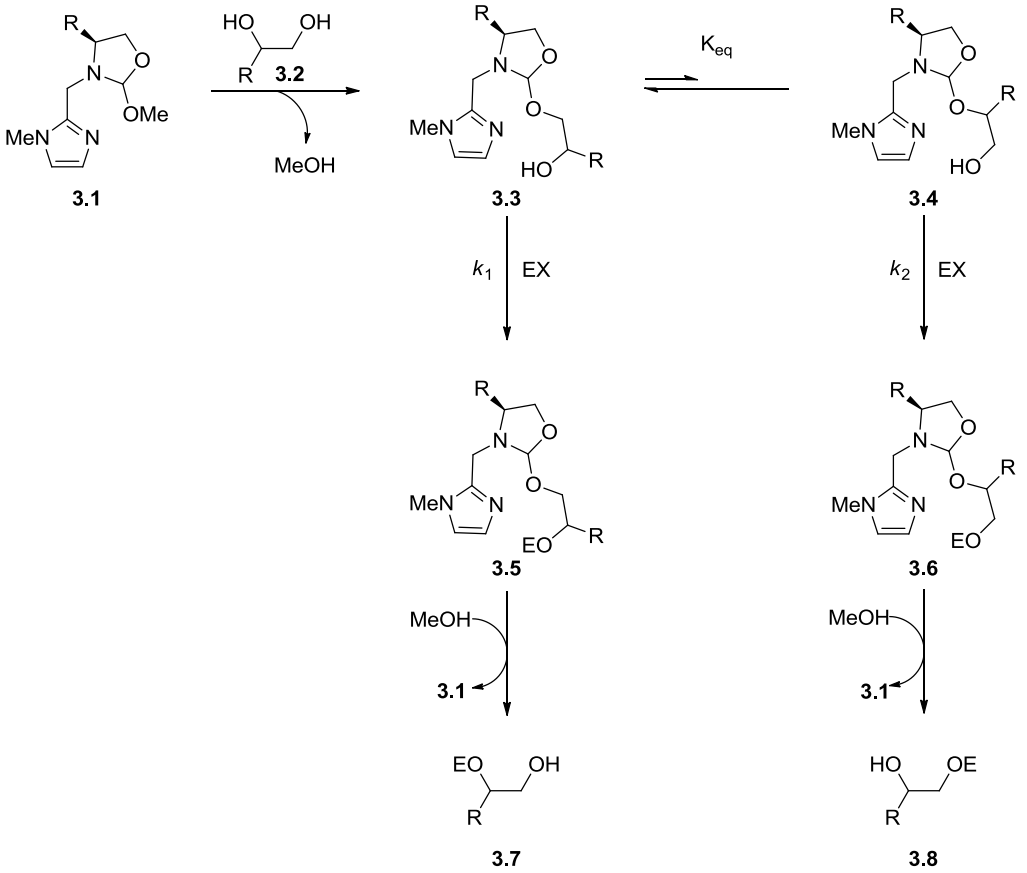
As primary alcohols are more accessible, **3.1** should preferentially bind to the primary alcohol leaving the secondary alcohol free. The catalytic *N*-methylimidazole subunit attached to **3.1** can then facilitate functionalization of the secondary alcohol through activation of an electrophilic reagent and intramolecular delivery.[14] This direct functionalization of a secondary alcohol would eliminate the need for bis-protection and selective deprotection, as well as the byproducts generated from these steps.

Using this strategy, the selectivity of the reaction arises from a combination of the binding selectivity as well as the rate of functionalization (Figure 3.3). Under the reaction conditions, **3.3** and **3.4** should be in equilibrium. As mentioned previously, the primary alcohol bound, **3.3**, should be more favorable. However, k_2 will most likely be greater than k_1 since the primary alcohol is more reactive towards functionalization. To favor the pathway through **3.5**, **3.1** could be designed to decrease the rate of functionalization of

[13]Kobayashi, S.; Alizadeh, B. H.; Sasaki, S. -Y.; Oguri, H.; Hirama, M. *Org. Lett.* **2004**, *6*, 751-754. [14]It is also possible that the *N*-methylimidazole subunit acts as a general base.

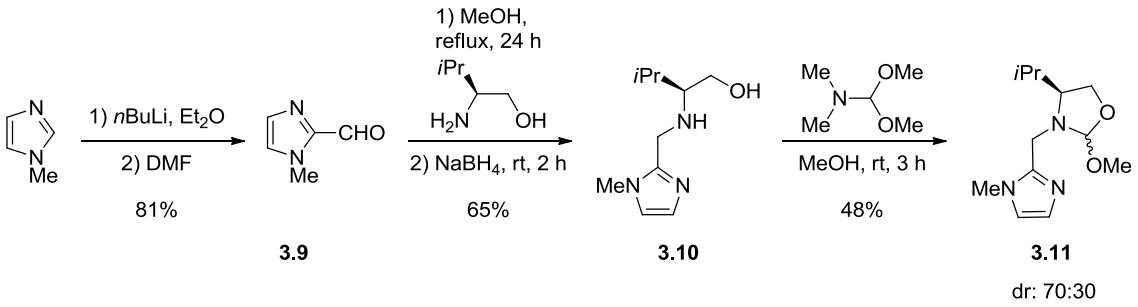
the primary alcohol to form **3.6**, k_2, while increasing the rate of functionalization to form **3.5**, k_1 (mismatched vs matched case, respectively). This matched/ mismatched case could originate from stereoselectivity caused by the rigidness of the covalent bond between **3.1** and **3.2**. After the functionalization step, exchange with methanol would give **3.1** or another molecule of substrate, **3.2**, could exchange on to enter back into the equilibrium between **3.3** and **3.4**.

Figure 3.3 Application of the Curtin-Hammett Principle.



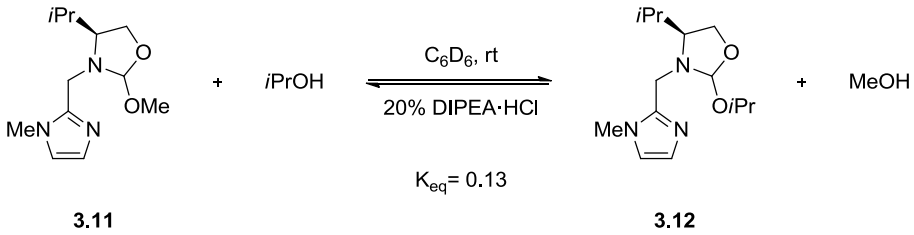
To begin a simple and inexpensive synthesis of catalytic directing group **3.11** was completed starting from L-valinol (Scheme 3.8). First *N*-methylimidazole is lithiated with *n*BuLi and trapped with *N*,*N*-dimethylformamide to yield **3.9**. Reductive amination of **3.9** with valinol gives amino alcohol **3.10**. **3.10** was closed with *N*,*N*-dimethylformamide dimethylacetal in methanol to give catalytic directing group **3.11** in a diastereomeric ratio of 70:30.

Scheme 3.8 Synthesis of **3.11**.



After being synthesized, **3.11** was exchanged with *i*PrOH in the presence of *N*,*N*-diisopropylethylamine hydrochloride as the acid source. A K_{eq} of 0.13 was found which indicates that MeOH has an 8 fold higher binding affinity than *i*PrOH (Scheme 3.9). The reaction reached equilibrium after only 10 minutes at room temperature. (Without acid, it takes 72 h to reach equilibrium.) It was encouraging that the exchange was rapid at room temperature because exchange has to be fast in order to compete with the unselective intermolecular reaction. Also promising and as predicted, there was a large preference to bind the least sterically hindered alcohol. Both of these features of **3.11** are important in order to obtain selectivity.

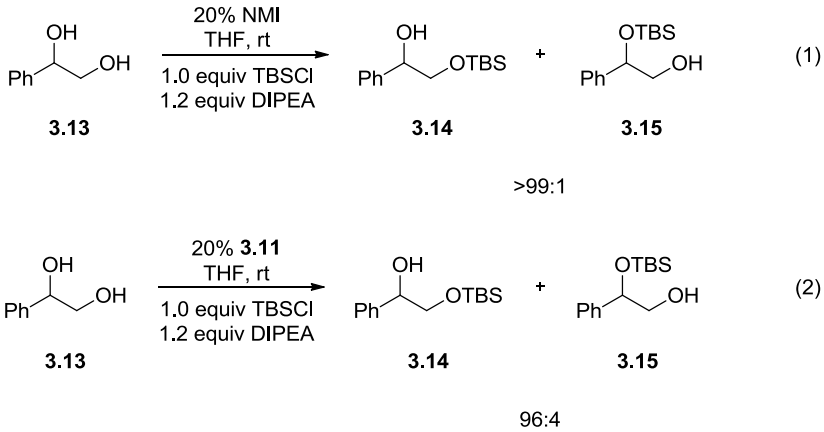
Scheme 3.9 Exchange Study with **3.11**.



3.4 Initial Studies of Selective Functionalization of 1,2-Diols[15]

Initially 1-phenyl-1,2-ethanediol was used as the test substrate and *tert*-butyldimethylsilyl chloride (TBSCl) was used as the electrophile. When NMI was used as the catalyst, there was a strong preference for the primary alcohol to be functionalized resulting in **3.14** (Scheme 3.10, Eq. 1). The secondary product, **3.15**, was not detected by GC. When **3.11** was used as the catalyst, the selectivity for **3.15** increased to 4% (Scheme 3.10, Eq. 2). The low levels of selectivity are most likely due to the large size of the TBS group contributing to a high energetic barrier to secondary alcohol functionalization.

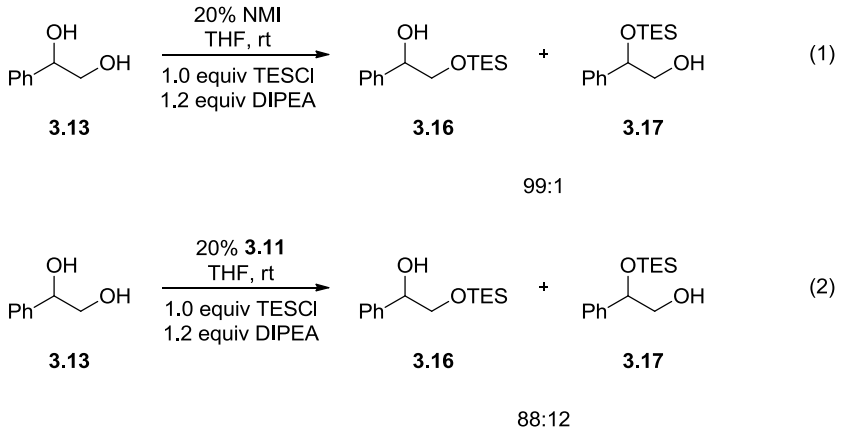
Scheme 3.10 Silylation of **3.13** with TBSCl.



[15]This work was done with Omar De Paolis.

In order to lower this barrier, chlorotriethylsilane (TESCl) was tried under the reaction conditions with NMI. The inherent selectivity was 99:1 for **3.16** (Scheme 3.11, Eq. 1). Although this still represents a strong preference for primary alcohol functionalization, a small amount of the secondary product, **3.17**, was observed. Reaction with **3.11** gave a ratio of 88:12 favoring the primary product, **3.16** (Scheme 3.11, Eq. 2). This change in selectivity represented a 10-fold increase compared to the reaction with NMI. It is important to mention that although bis-silylation is possible, in these initial screens with TESCl, it was always observed to be <5% of the reaction mixture.

Scheme 3.11 Silylation of **3.13** with TESCl.



At this point, there was concern that because **3.11** is a chiral catalyst a matched/mismatched case might be occurring in which the two enantiomers of **3.13** were reacting differently. In order to test this hypothesis, the individual enantiomers of **3.13** were synthesized using Jacobsen's hydrolytic kinetic resolution of epoxides [16] Each of

[16]Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307-1315.

the enantiomers was tested separately in the reaction. Interestingly, while (*S*)-**3.13** gave a 90:10 ratio, strongly favoring formation of the primary functionalized product, **3.16** (Scheme 3.12, Eq. 1), (*R*)-**3.13** gave a ratio of 59:41 (Scheme 3.12, Eq. 2).

Scheme 3.12 Selectivity of Each Enantiomer of **3.13**.

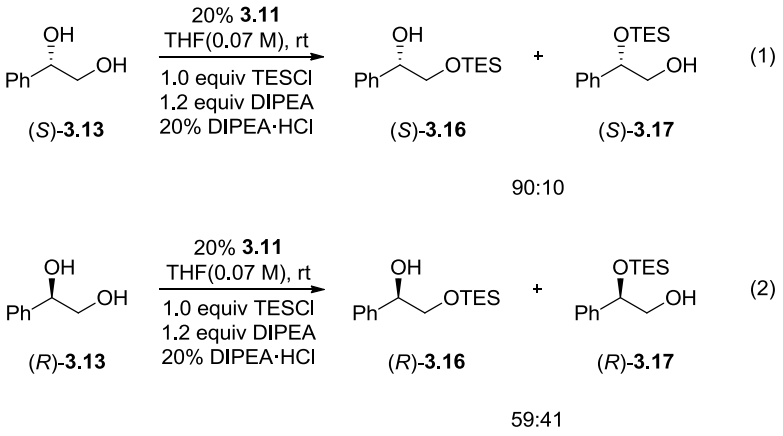
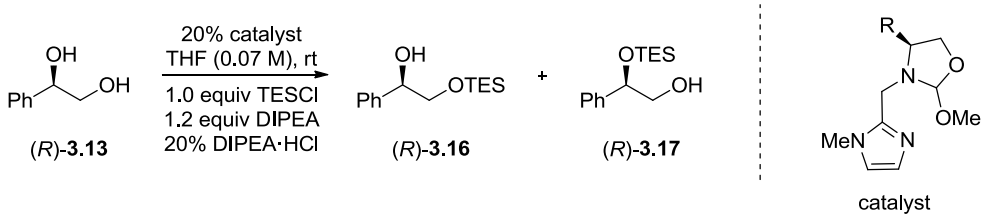


Table 3.2 Variation of Amino Alcohol Backbone.



R	Catalyst dr	Conversion (%)[a]	**3.16**:**3.17**[a]
*t*Bu	85:15	96	55:45
*i*Pr	70:30	98	58:42
*i*Bu	75:25	97	78:22
Me	66:34	95	69:31
H	-	95	83:17
Ph	60:40	97	89:11

[a]Determined by GC analysis.

To increase the selectivity for the secondary product, **3.17**, other catalysts were synthesized to see if any would give improved selectivities. When the catalysts were screened against (*R*)-**3.13**, there was a clear trend that increasing the size of the R group increased the selectivity for **3.17** (Table 3.2).

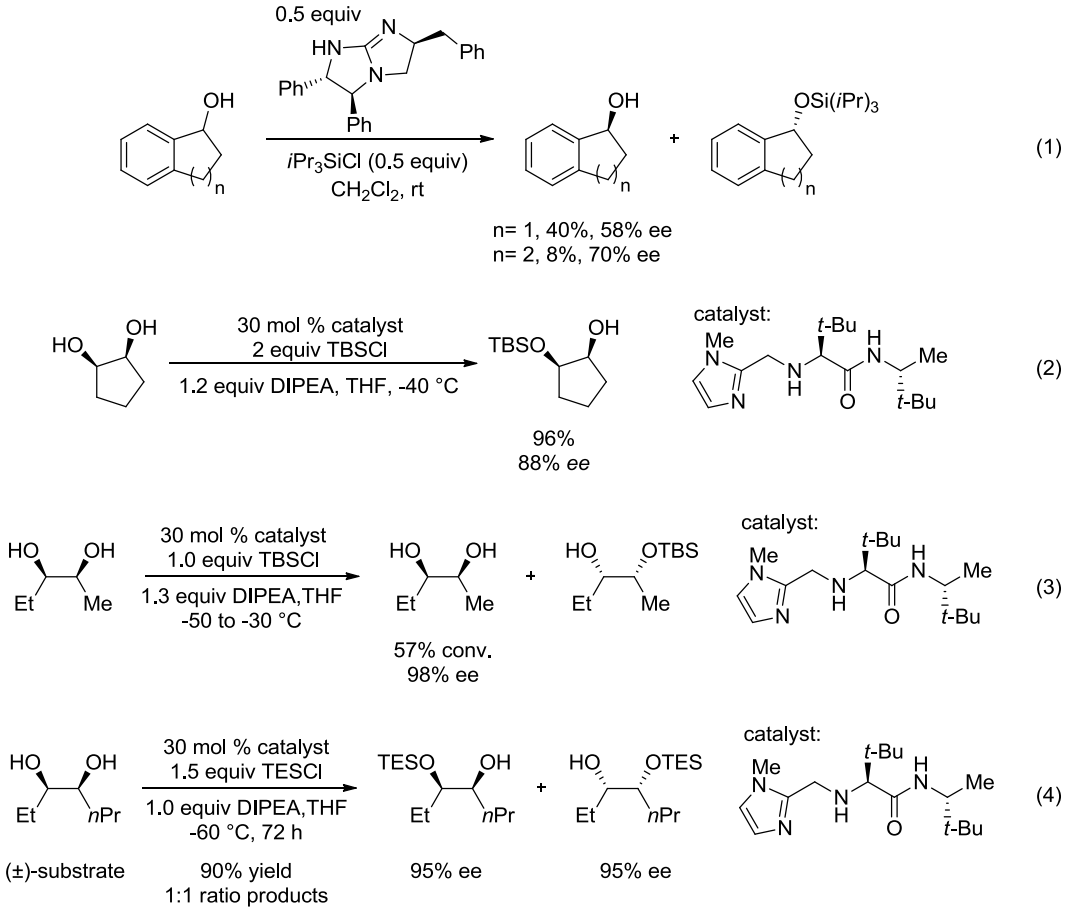
3.5 Stereoselective Functionalization of Diols[17]

Because we predicted that binding selectivity and stereoselectivity would be necessary to obtain site selectivity, we decided to test how effective the catalyst was in an enantioselective reaction. Therefore, an enantioselective desymmetrization reaction was performed. Previously, meso-1,2-diols have been desymmetrized using organocatalysts to catalyze acylation,[18] phosphorylation,[19] sulfonylation,[20] and silylation.[21] Peptide based catalysts that achieve selectivity through non-covalent interactions which pre-organize the substrate and catalyst prior to electrophile transfer have been used for all of these electrophilic transfer reactions. Acylation has also been catalyzed by amine, alcohol, and phosphine organocatalysts.[18a,c] Silyl transfer has been accomplished using a diamine mediator and peptide based catalysts (Scheme 3.13).[21] Ishikawa and co-workers showed

[17]Sun, X.; Worthy, A. D.; Tan, K. L. *Angew. Chem., Int. Ed.* **2011**, *50*, 8167-8171.
[18](a) Oriyama, T.; Imai, K.; Sano, T.; Hosoya, T. *Tet. Lett.* **1998**, *39*, 3529–3532. For reviews on acyl transfer using organocatalysts see the following: (b) Jarvo, E. R.; Miller, S. J. *Tetrahedron* **2002**, *58*, 2481–2495. (c) Spivey, A. C.; Arseniyadis, S. *Top. Curr. Chem.* **2010**, *291*, 233–280. (d) Marinetti, A.; Voituriez, A. *Synlett* **2010**, 174–194 .
[19](a) Sculimbrene, B.; Morgan, A.; Miller, S. *J. Am. Chem. Soc.* **2002**, *124*, 11653–11656. (b) Jordan, P. A.; Kayser-Bricker, K. J.; Miller, S. J. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 20620–20624.
[20]Fiori, K. W.; Puchlopek, A. L. A.; Miller, S. J. *Nat. Chem.* **2009**, *1*, 630–634.
[21](a) Isobe, T.; Fukuda, K.; Araki, Y.; Ishikawa, T. *Chem. Commun.* **2001**, 243–244. (b) Zhao, Y.; Mitra, A. W.; Hoveyda, A. H.; Snapper, M. L. *Angew.Chem., Int. Ed.* **2007**, *46*, 8471–8474. (c) Zhao, Y.; Rodrigo, J.; Hoveyda, A. H.; Snapper, M. L. *Nature* **2006**, *443*, 67–70. (d) You, Z.; Hoveyda, A. H.; Snapper, M. L. *Angew. Chem., Int. Ed.* **2009**, *48*, 547–550. (e) Rodrigo, J. M.; Zhao, Y.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett.* **2011**, *13*, 3778-3781. For a review on asymmetric Si-O coupling of alcohols: (f) Weickgenannt, A.; Mewald, M.; Oestreich, M. *Org. Biomol. Chem.* **2010**, *8*, 1497–1504.

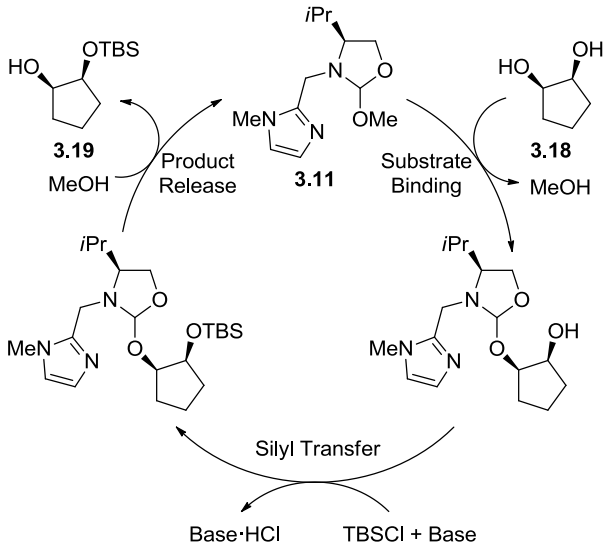
the kinetic resolution of indanol and tetralol with moderate enantioselectivities, but the chiral base used could not be used catalytically (Scheme 3.13, Eq 1).[21a] Hoveyda and Snapper developed a peptide-based catalyst which is able to desymmetrize diols and triols (Scheme 3.12, Eq 2).[21c,d] The chemistry was expanded to kinetic resolutions and regiodivergent reactions on a racemic mixture (Scheme 3.12, Eq 3 and 4).[21b,e] Notably, this is also a site selective reaction; however, the secondary alcohols have to have similar reactivity to achieve high selectivity (Eq 4).

Scheme 3.13 Asymmetric Silyl Transfer Reactions.



It was believed that our catalytic directing group, which pre-organizes the substrate and catalyst using a more rigid covalent bond, could lead to increased reactivity and selectivity.

Figure 3.4 Catalytic Cycle of Desymmetrization of Meso-1,2-Diols.



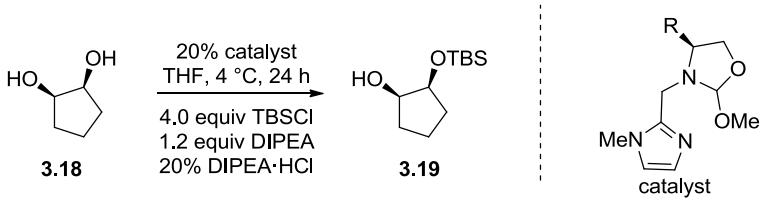
It was imagined that catalytic directing group **3.11** could bind **3.18**, reversibly, and silylation of **3.18** could occur through intramolecular transfer or deprotonation. The release of **3.19** by exchange with methanol regenerates **3.11** (Figure 3.4). Notably, selectivity could come from substrate binding, silyl transfer, or a combination of both.

The reaction was run with TBSCl and 20% catalyst. *N*, *N*-Diisopropylethylamine was chosen to quench the hydrogen chloride generated during the reaction because it is a hindered base that should be slow to promote silylation. DIPEA·HCl, which is generated

during the reaction, was added as an acid to catalyze the initial exchange between substrate and catalyst.

To start, a series of catalysts similar to **3.11** were tested in the reaction. First the R group on the catalyst backbone was varied (Table 3.3). Larger R groups gave increased selectivity. However, the catalysts exist as a mixture of diastereomers, complicating the analysis of selectivity. We were concerned that the two diastereomers might show the opposite sense of absolute stereochemistry. Thus, we wanted to explore catalysts that would exist as a single diastereomer.

Table 3.3 Initial Catalyst Optimization.



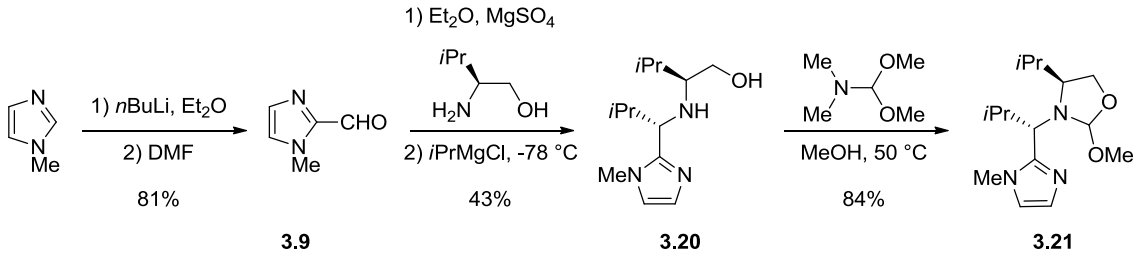
R	dr	Yield (%)[a]	ee (%)[a]
Me	66:34	65	-8
*i*Bu	75:25	42	0
*i*Pr (**3.11**)	70:30	46	42
*t*Bu	85:15	67	41

[a]Determined by GC analysis.

In order to try to force the catalyst to favor one diastereomer, another stereocenter was installed on the methylene linker between the ring and the *N*-methylimidazole subunit. Both the (*S*,*S*) and (*S*,*R*)-catalysts were synthesized. The syntheses of these

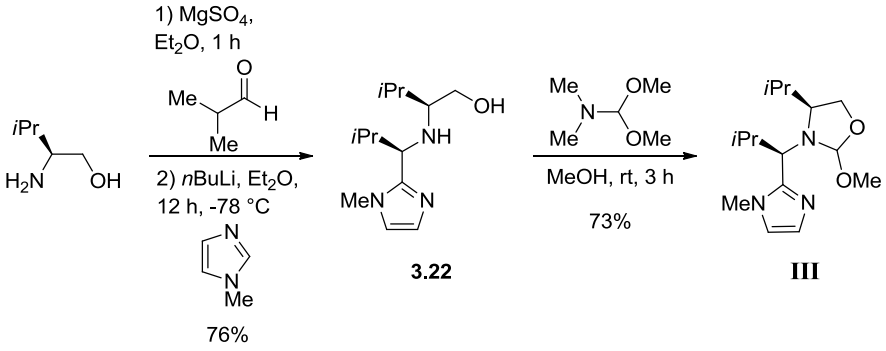
catalysts were similar to the synthesis of **3.11**. To make the (*S*,*S*) series, after **3.9** was condensed with an amino alcohol, the desired nucleophile was added into the imine to obtain **3.20**; cyclization of the amino alcohol gave **3.21** (Scheme 3.14). To obtain the (*S*,*R*)-catalysts, valinol was condensed with the desired aldehyde and lithiated NMI was added to the resulting imine to obtain **3.22** (Scheme 3.15). Closure of **3.22** gave **III**. The syntheses focused on using valinol as the amino acid core since it gave good results in Table 3.3. Catalyst optimization around *tert*-leucine was not pursued because it is much more expensive.

Scheme 3.14 Synthesis of **3.21**.



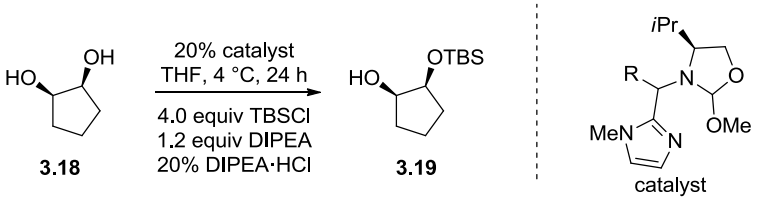
Both of the (*S*,*S*)-catalysts that were synthesized existed as one diastereomer in solution. The yields and enantioselectivities obtained from the reactions with the (*S*,*S*)-catalysts were lower than when **3.11** was used as the catalyst (Table 3.3 and Table 3.4). These results suggest that the addition of this stereocenter improperly gears the imidazole ring making the silylation more difficult.

Scheme 3.15 Synthesis of **III.**



All of the (*S*,*R*)-catalysts gave improved yields compared to the (*S*,*S*)-catalysts. When R= Ph, the diastereomeric ratio was poor along with the enantioselectivity. However, when R was Me, moderate enantioselectivities were achieved. When R was *i*Pr, the catalyst, **III**, is one diastereomer and gives **3.19** in good yield and excellent

Table 3.4 (*S*,*S*) and (*S*,*R*) Catalysts.



R	dr[a]	Yield (%)[b]	ee (%)[b]
(*S*)-Me	99:1	19	-15
(*S*)-*i*Pr	99:1	25	-16
(*R*)-Me	90:10	40	60
(*R*)-Ph	56:44	31	10
(*R*)-*i*Pr (**III**)	99:1	82	96

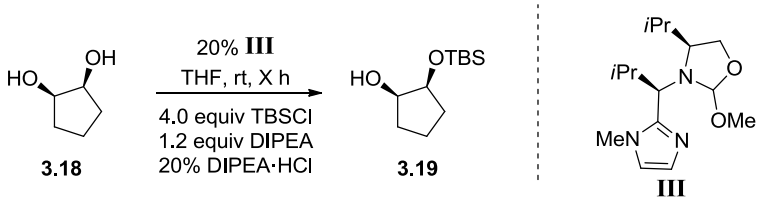
[a]Determined by ^{1}H NMR. [b]Determined by GC analysis.

enantioselectivity (Table 3.4). Attempts to synthesize R= *t*Bu were unsuccessful due to difficulty closing the ring in the last step. It is believed that the steric clash between the two substituents makes the ring closure very unfavorable.

3.6 Desymmetrization of Meso-1,2-Diols

With an effective catalyst developed, the optimal reaction time was explored. The reaction time of 24 h (4 °C) that had been used for catalyst testing was determined to be unnecessary when **III** was used. At room temperature, the reaction reaches completion after 4 h and retains high enantioselectivity (Table 3.5).

Table 3.5 Time Course with **III**.

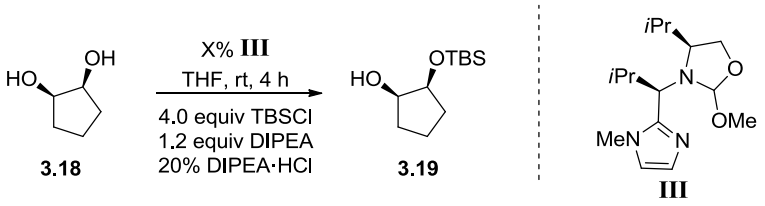


Time	Yield (%)[a]	ee (%)[a]
4	94	94
8	94	94

[a]Determined by GC analysis.

A catalyst loading screen showed that while 5% catalyst resulted in a sluggish reaction and lowered enantioselectivities, 10% gave similar results to using 20% catalyst (Table 3.6).

Table 3.6 Catalyst Loading Screen.

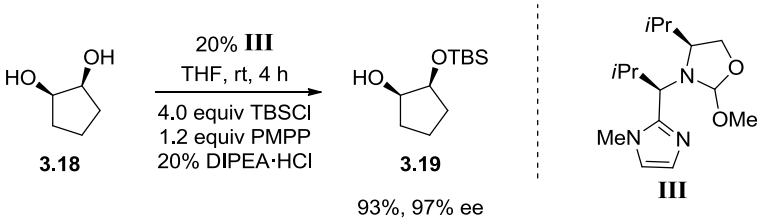


Amount	Yield (%)[a]	ee (%)[a]
5	56	87
10	90	93
20	94	94

[a]Determined by GC analysis.

N,*N*-Diisopropylethylamine was originally chosen as a base because it is hindered and thus, would be slow to promote the silylation by itself. If it were to promote the silylation, it would lead to racemic product which would degrade the enantioselectivity of the reaction. Another hindered base, 1,2,2,6,6-pentamethylpiperidine (PMPP), was also tested in the reaction. Using PMPP, gave a comparable yield with slightly higher enantioselectivies indicating that DIPEA had been promoting some background reaction (Scheme 3.16).

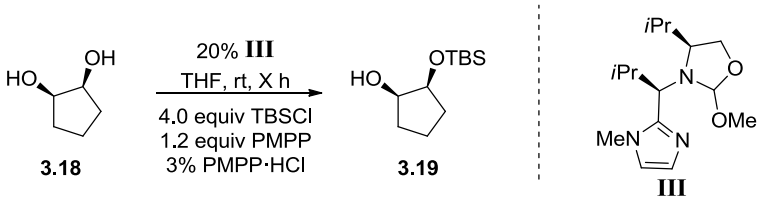
Scheme 3.16 1,2,2,6,6-Pentamethylpiperdine as the Base.



A time course was performed with PMPP·HCl to ensure that this acid would allow the reaction to proceed at a similar rate to the reaction with DIPEA·HCl. At 2 h, the

conversion is not complete, but at 4 h, yields similar to previous reactions are obtained (Table 3.7).

Table 3.7 Time Screen with PMPP and PMPP·HCl.

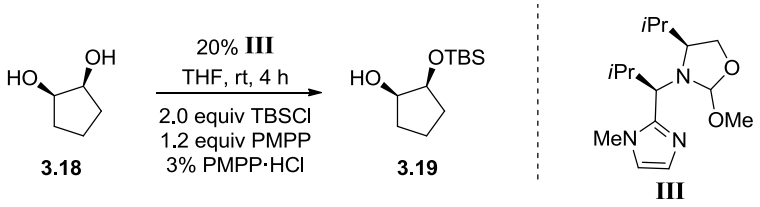


Time	Yield (%)[a]	ee (%)[a]
2	62	97
4	87	97

[a]Determined by GC analysis.

In an effort to decrease the amount of TBSCl necessary for an efficient reaction while still maintaining high enantioselectivity, a concentration screen was run. One concern was that **III** might catalyze the intermolecular reaction in which **3.18** is not bound before functionalization. Decreasing the catalyst concentration could decrease the rate of the intermolecular reaction compared to the intramolecular reaction. With 2 equivalents of TBSCl, a concentration of 0.4 M gave the best enantioselectivities and good yields. Lower concentration resulted in a sluggish reaction; higher concentration started to degrade the enantioselectivity of the reaction (Table 3.8).

Table 3.8 Concentration Screen.

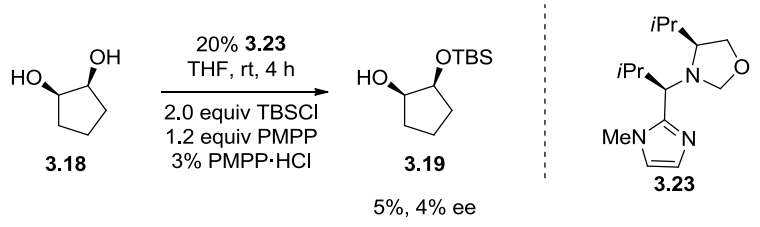


Concentration (M)	Yield (%)[a]	ee (%)[a]
0.2	56	96
0.4	84	97
1.0	87	95

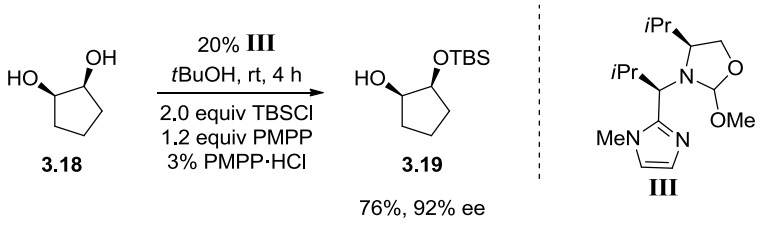
[a]Determined by GC analysis.

With the optimized conditions in place, the reaction was run with control catalyst **3.23** in order to support the hypothesis that covalent bonding is the mode of catalysis that is operating under these conditions. Not only was the enantioselectivity poor, but the conversion was also very low (Scheme 3.17). This implies that **III** is not a good silylation catalyst without the ability to covalently bind the substrate. As further support, running the reaction with **III** in *t*BuOH gave comparable results to the reaction run in THF which is inconsistent with a hydrogen-bonding mechanism (Scheme 3.18).

Scheme 3.17 Reaction with a Control Catalyst.



Scheme 3.18 Reaction Run in *t*BuOH.



The substrate scope was expanded to other cyclic and acyclic meso-1,2-diols. Heteroatoms (**3.24**) and unsaturation (**3.25**) in cyclic substrates were well tolerated (Table 3.9). Medium rings **3.28** and **3.29**, while less reactive, also gave good results. The slower reaction rate for medium rings is believed to be due to ring distortion, which twists the *cis*-diols into more of a *trans* configuration. (Note: *trans*-diols do not react under these conditions.) Due to increased freedom of rotation compared to the cyclic substrates, acyclic substrates, such as **3.30**, are also slower to react. The reaction of (1*R*,2*S*,*Z*)-cyclooct-5-ene-1,2-diol gives **3.32** with low enantioselectivity which is believed to be due to the transannular effect causing the ring to twist the alcohols away from each other (Scheme 3.19).

Scheme 3.19 Reaction of (1*R*,2*S*,*Z*)-cyclooct-5-ene-1,2-diol.

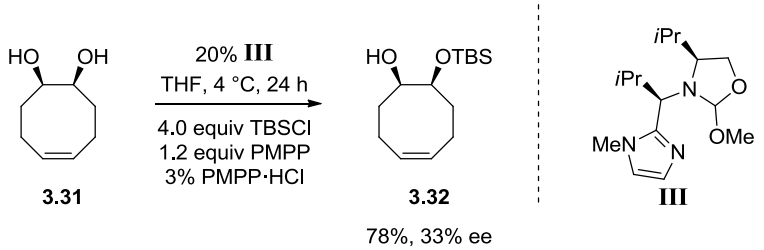
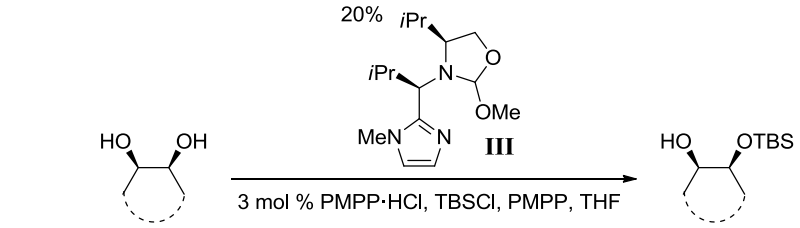
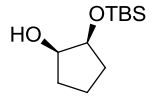
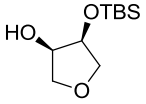
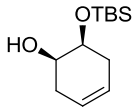


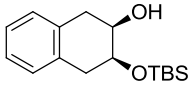
Table 3.9 Substrate Scope.

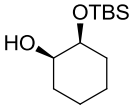


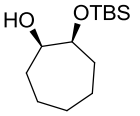
3.19[c]  92%[a], 94% ee[b]

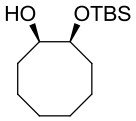
3.24[d]  79%[a], 89% ee[b]

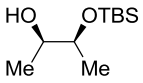
3.25[e]  87%[a], 90% ee[b]

3.26[d]  88%[a], 95% ee[b]

3.27[e]  86%[a], 92% ee[b]

3.28[f]  82%[a], 90% ee[b]

3.29[g]  93%[a], 86% ee[b]

3.30[h]  78%[a], 90% ee[b]

[a]Isolated yields. [b]Enantiomers separated using a chiral GC column.[c]TBSCl (2 equiv), PMPP (1.2 equiv), 0.4 M, 4 h. [d]TBSCl (4 equiv), PMPP (1.2 equiv), 0.2 M, 24 h. [e]TBSCl (2 equiv), PMPP (1.2 equiv), 0.2 M, 12 h. [f]TBSCl (4 equiv), PMPP (2 equiv), 0.2 M, 24 h, 4 °C. [g]TBSCl (4 equiv), PMPP (2 equiv), 0.2 M, 24 h. [h]TBSCl (4 equiv), PMPP (2 equiv), 0.2 M, 36 h, 4 °C. TBSCl = *tert*-butyldimethylsilyl chloride, PMPP = pentamethylpiperidine, THF = tetrahydrofuran

It is also important to note that (1*R*,3*S*)-cyclopentane-1,3-diol, even with 4.0 equivalents of TBSCl, reacts slowly and affords low enantioselectivities (Scheme 3.20). An acyclic 1,3-diol, (2*R*,4*S*)-pentane-2,4-diol, has even worse reactivity than the cyclic diol and gives < % yield his i s most likely d e to the catalyst's ina il ity to transfer the electrophile if the alcohol is not in close proximity to the NMI subunit. While this limits the scope of substrates for this catalyst, it was encouraging because the catalyst was

designed to be a site selective catalyst. A catalyst that is stereoselective and sensitive to proximity effects is less likely to be promiscuous.

Scheme 3.20 Reaction of *cis*-1,3-Diol.

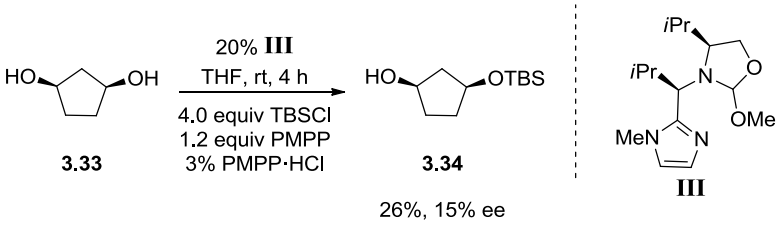
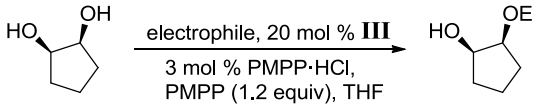


Table 3.10 Silyl Reagent Screen.



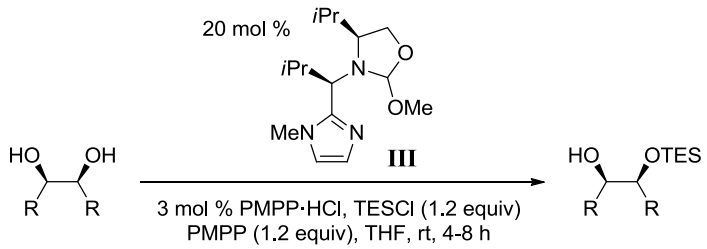
product	electrophile	yield[a]	ee[a]
3.35[b]	TESCl	94	90
3.36[c]	TBDPSCl	75(76)[d]	90(86)[d]
3.37[e]	DMPSCl	71	79

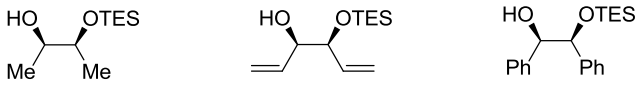
[a]Yields and *ee*s are an average of two runs and were determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard. [b]TESCl (1.2 equiv), 0.2 M, 1 h.[c]TBDPSCl (4 equiv), 0.2 M, 48 h. [d]1.0 M, 24 h.[e]DMPSCl (1.2 equiv), 0.2 M, 1 h. TESCl = triethylsilyl chloride, TBDPSCl = *tert*-butyldiphenylsilyl chloride, DMPSCl = dimethylphenylsilyl chloride.

Other silyl reagents were tested under the reaction conditions with **3.18** to determine if they would also work. Impressively, the smaller and more reactive chlorotriethylsilane (TESCl) gave slightly better yields while still maintaining high

enantioselectivities. The bigger *tert*-butyldiphenylsilyl chloride (TBDPSCl) was less reactive, but also maintained good enantioselectivity. The very reactive dimethylphenylsilyl chloride (DMPSCl) gave only moderate enantioselectivities which may be due to background silylation (Table 3.10).

Table 3.11 Enhancing the Reactivity of Challenging Substrates.





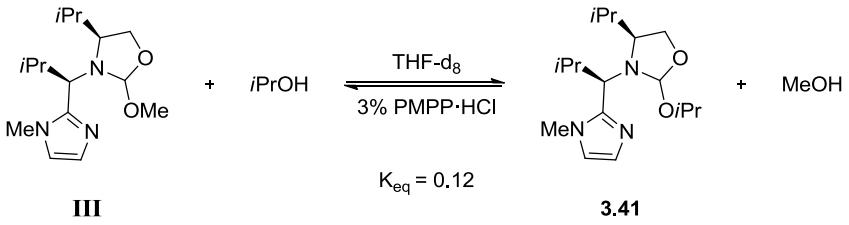
3.38	**3.39**	**3.40**
84% 92% *ee*	82% 92% *ee*	82% 90% *ee*

[a]Yields and *ee*s were determined by GC analysis using trimethoxybenzene as an internal standard.

As TESCl had been shown to be more reactive while still achieving high enantioselectivities, it was used to enhance the reactivity of some challenging substrates. (2*R*,3*S*)-butane-2,3-diol, which previously needed 36 h for complete conversion, showed complete conversion to **3.38** after 4 h. (3*R*,4*S*)-hexa-1,5-diene-3,4-diol and (1*R*,2*S*)-1,2-diphenylethane-1,2-diol are deactivated towards silylation and did not react with TBSCl. When TESCl was used, both were converted to product (**3.39** and **3.40**, respectively) in under 8 h with good enantioselectivities (Table 3.11).

The exchange characteristics of **III** were also studied. Consistent with exchange studies performed with **I** and **3.11**, a K_{eq} of 0.12 was found when **III** was exchanged with *i*PrOH (Scheme 3.21).

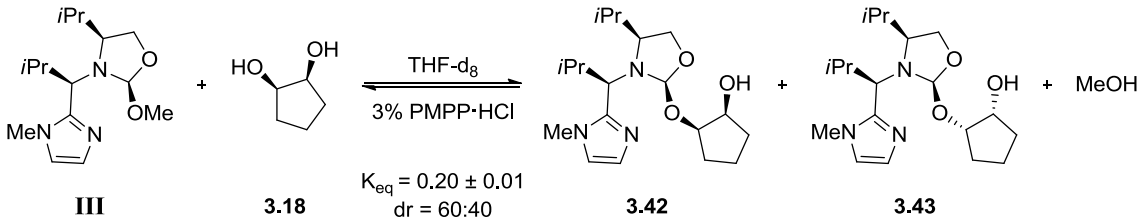
Scheme 3.21 Exchange of **III** with *i*PrOH.



When **III** was exchanged with **3.18**, the K_{eq} was determined to be 0.20 after 2 h. As there are two alcohols in **3.18**, this number was expected. The more interesting piece of data resulting from this exchange was that the two diastereomers, **3.42** and **3.43**, which originate from each alcohol binding to **III**, exist in a 60:40 ratio (Scheme 3.22). Since one diastereomer is not strongly favored over the other, this most likely means that **3.18** binding to **III** is not the selectivity determining step of the reaction. Therefore, selectivity must be arising from the functionalization step. One explanation for the selectivity is if the (*R*)-diol binds **III**, the other alcohol is placed near the NMI subunit so it can be functionalized. In contrast, when the (*S*)-diol binds **III**, the other alcohol may be positioned away from the NMI subunit so it is unable to be functionalized. This is only true, however, if the reaction occurs under exchange conditions at equilibrium. It is possible that one diastereomer is kinetically favored to bind **III**. If silylation is fast and the reaction occurs under kinetic control, it is possible that binding could be the source of selectivity. Based on our observations that the exchange is rapid (Scheme 3.9), while

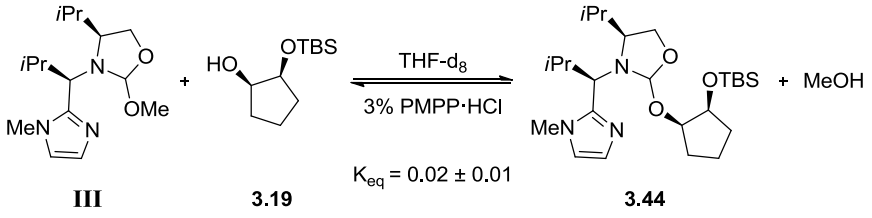
silylation is much slower, we believe that it is not likely that binding is the source of selectivity.

Scheme 3.22 Exchange of **III** with **3.18**.



In order to determine if product exchange onto **III** was competitive, the exchange of **3.19** with **III** was performed. Equilibrium was reached in 2 h with a K_{eq} of 0.02. The K_{eq} of **3.19** was 10 fold less than with **3.18** (Scheme 3.22 and 3.23). This indicates that product inhibition is not a significant problem during the reaction.

Scheme 3.23 Exchange of **III** with **3.19**.



Attempts to crystalize **III** were unsuccessful. However, by taking advantage of its ability to bind alcohols, a crystalline alcohol, **3.45**, was exchanged onto **III** (Scheme 3.24). **3.46** was crystallized, and an X-ray crystal structure was obtained which showed

that the C-O bond was oriented up along with both *i*Pr groups. The NMI subunit was oriented underneath the ring of the catalyst (Figure 3.5).

Scheme 3.24 Exchange of **III** with **3.45**.

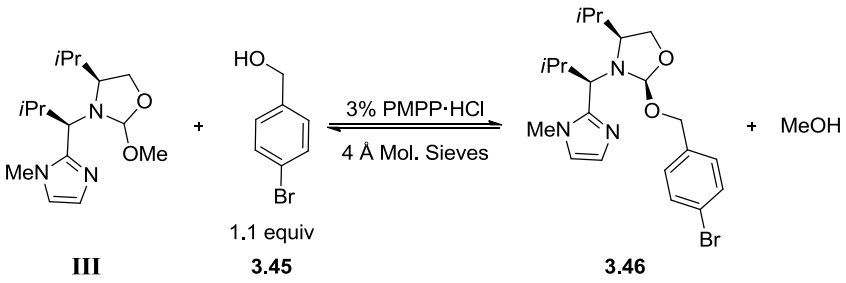
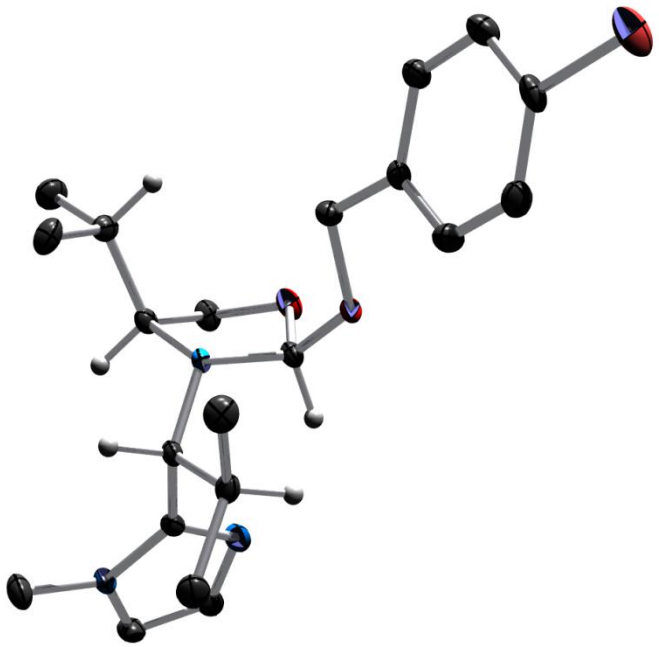
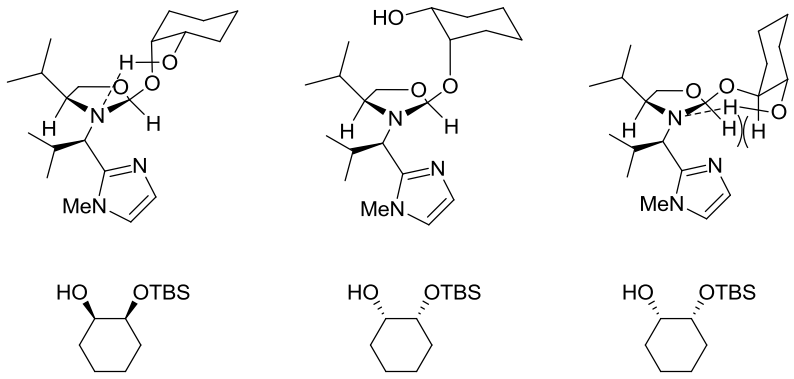


Figure 3.5 Crystal Structure of **3.46** (CCDC # 832192).



The crystal structure allowed us to design models that would rationalize the enantioselectivity of the reaction. In the solid state, the NMI subunit is positioned underneath the ring. Models of the substrate bound catalyst oriented similar to the crystal structure show the hydrogen of the free alcohol could be positioned over the nitrogen in the ring. It is believed that the basic nitrogen in the ring could assist by deprotonating the alcohol before the NMI subunit swings up to transfer the functional group. When the (*R*)-alcohol is bound to the catalyst, the other alcohol is lined up well for this transformation. However, when the (*S*)-alcohol is bound in a conformation in which the other alcohol could be functionalized, there are two eclipsing hydrogens that could make this conformation unfavorable (Figure 3.6).

Figure 3.6 Selectivity Models.

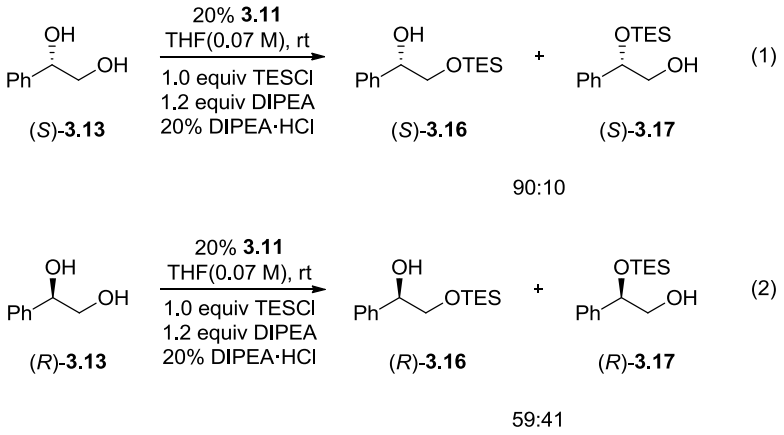


3.7 Developing a Site Selective Functionalization Reaction

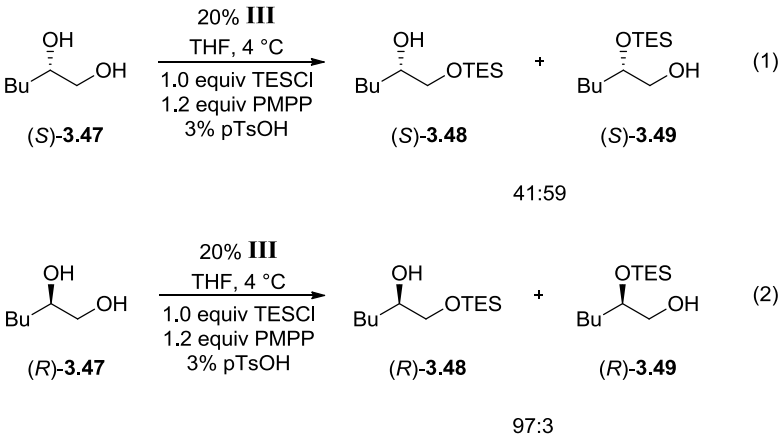
Having shown that **III** was able to catalyze a stereoselective reaction, we returned to developing a site selective reaction. Optimization was approached with the information gained from developing the desymmetrization reaction while remaining cognizant that a

very different problem was being addressed. Because we had seen optimal results with **III** in the desymmetrization reaction, we decided to test it in the site selective reaction (Scheme 3.25).

Scheme 3.12 Reaction of **3.11** with Individual Enantiomers.



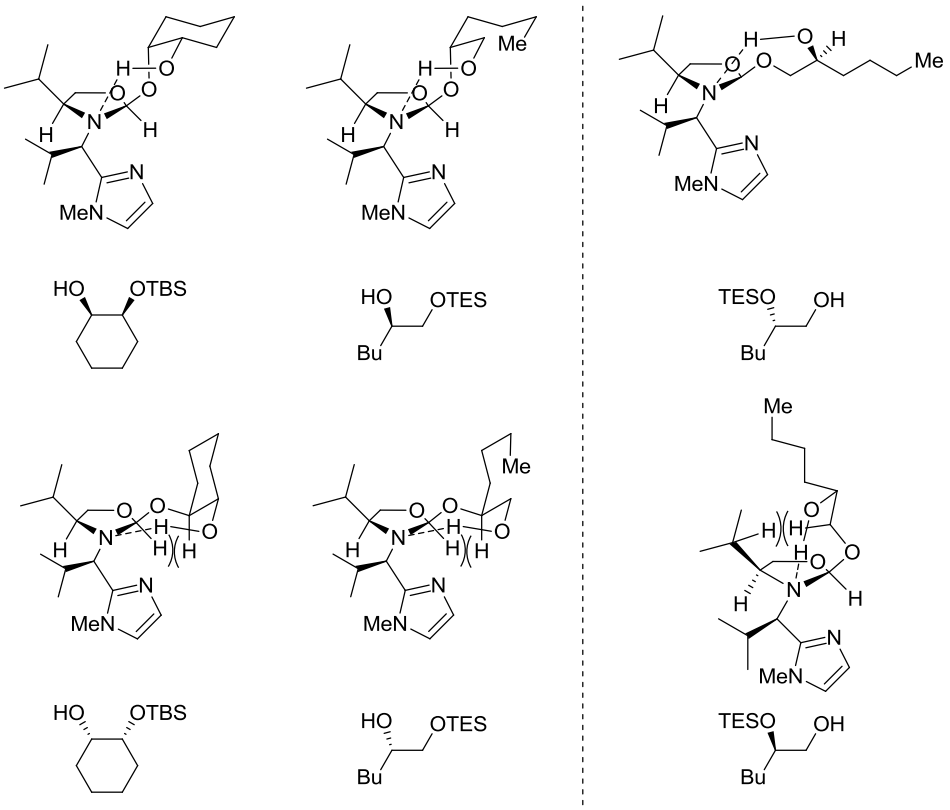
Scheme 3.25 Reaction of **III** with Individual Enantiomers.



Both enantiomers of **3.47** were tested with **III**. When comparing these selectivities with the ones previously seen with catalyst **3.11**, it is interesting to note that the selectivities switch. The catalysts seemed to be matched to different enantiomers of substrate. With **III** and (*S*)-hexane-1,2-diol, the reaction favored the secondary product, **3.49**, in about 59:41 ratio. The (*R*)-hexane-1,2-diol strongly favors the primary product, **3.48** (Scheme 2.25).

The results with **III** are consistent with what was seen in the desymmetrization of meso diols. In that reaction, it was hypothesized that when the (*R*)-alcohol was bound to **III**, the free alcohol was oriented over the amine in the ring allowing it to be deprotonated and subsequently functionalized. However, when the (*S*)-alcohol was bound to **III**, in the only conformation that the free alcohol could possibly be functionalized, two hydrogens are eclipsing each other (Figure 3.6 and 3.7). It is believed this unfavorable interaction causes this conformation to be disfavored so the free alcohol is not functionalized when the (*S*)-alcohol is bound. When the secondary alcohols are bound in the site selective reaction, the desymmetrization models predict that the (*R*)-diol would be able to silylate the primary alcohol easily while the (*S*)-diol would be less favorable. Simple models of the primary alcohols bound show that the secondary alcohol in the (*S*)-diol could be deprotonated similarly. When the (*R*)-diol is in the confirmation in which the nitrogen could deprotonate the alcohol, there are two hydrogens pointing at each other over the ring (Figure 3.7). This unfavorable interaction makes secondary functionalization of the (*R*)-diol disfavored.

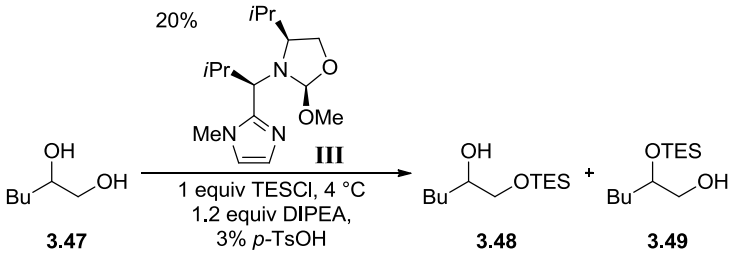
Figure 3.7 Selectivity Models.

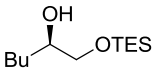
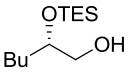
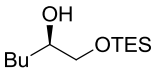
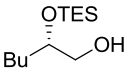
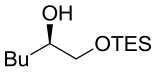
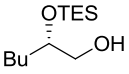
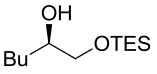
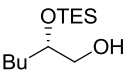
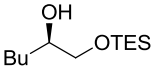
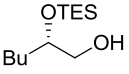
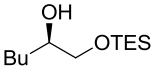
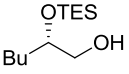


At this point, a solvent screen was run on the racemic substrate to determine if solvent had an effect on the selectivity. By isolating both products and determining their enantioselectivities, the approximate selectivity ratio for each enantiomer can be calculated. Most solvents gave results comparable to THF except for MeO*t*Bu and *t*BuOH. MeOtBu gave very low selectivities for both the enantiomers. Running the reaction in *t*BuOH, however, greatly increased the enantioselectivity of **3.48**. This increase in enantioselectivity corresponds to the (*S*)-enantiomer forming mostly **3.49** (Table 3.12). In this case, the R and S ratios were calculated based on isolated yields so a

loss of small amounts of material during isolation greatly affected these ratios. Future results were calculated based on GC yields and are more correct.

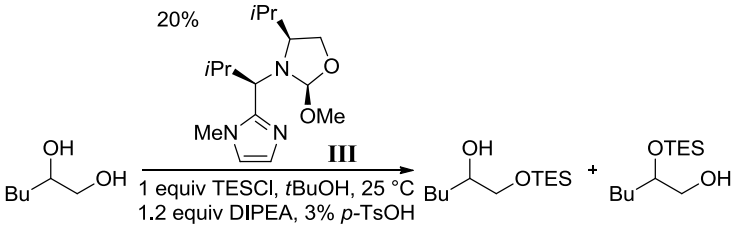
Table 3.12 Solvent Screen.

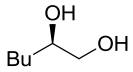
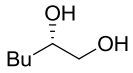
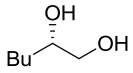


Solvent	**3.48**	**3.49**	**3.48**:**3.49**
THF			R= 95:5 S= 21:79
	59% yield[a] 56% ee[b]	30% yield[a] 90% ee[b]	
EtOAc			R= 95:5 S= 24:76
	32% yield[a] 54% ee[b]	25% yield[a] 90% ee[b]	
MeO*t*Bu			R= 58:42 S= 51:49
	26% yield[a] 16% ee[b]	17% yield[a] 3% ee[b]	
CH_3CN			R= 96:4 S= 28:72
	43% yield[a] 53% ee[b]	27% yield[a] 90% ee[b]	
$ClCH_2Cl$			R= 96:4 S= 23:77
	45% yield[a] 55% ee[b]	35% yield[a] 91% ee[b]	
*t*BuOH[c]			R= 98:2 S= 9:91
	52% yield[a] 88% ee[b]	31% yield[a] 94% ee[b]	

[a]Isolated yield. [b]Determined by GC analysis.[c]Run at rt.

Table 3.13 Individual Enantiomer Selectivity in *t*BuOH.

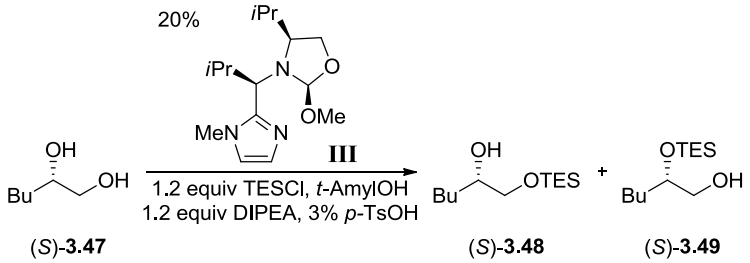


Substrate	**3.48**:**3.49**[a]	Yield(%)[b]
 (*R*)-**3.47**	96:4	72
 (*S*)-**3.47**	17:83	77
 (*S*)-**3.47**	94:6[c]	62[c]

[a]Determined by GC analysis.[b]Isolated yield. [c]Run with *N*-methylimidazole as catalyst.

Each enantiomer was run in *t*BuOH to directly measure the selectivity of each. (*R*)-**3.47** gave similar selectivity to what was previously seen with THF, very high selectivity for **3.48**. (*S*)-**3.47** gave an 83:17 ratio favoring **3.49**. The reaction catalyzed by NMI was also run in *t*BuOH to ensure that the solvent was not changing the inherent selectivity of the reaction, and it was not (Table 3.13).

Table 3.14 Temperature Screen with *t*-Amyl Alcohol.



(*S*)-**3.47** (*S*)-**3.48** (*S*)-**3.49**

Temperature(°C)	**3.48**:**3.49**[a]	Conversion(%)[a]
-6	13:87	>95
4	12:88	>95
25	15:85	>95

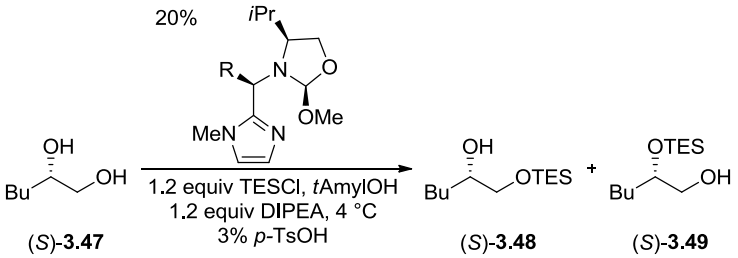
[a]Determined by GC analysis.

In order to test solvents similar to *t*BuOH, *t*-amyl alcohol was tested in the reaction. Less sterically hindered alcoholic solvents, such as *i*PrOH, and MeOH, cannot be used in the reaction as they bind the catalyst and would inhibit exchange. *t*-Amyl alcohol gave slightly better results than *t*-BuOH. The benefit of using *t*-amyl alcohol was that lower temperatures could be explored, whereas, *t*-BuOH would freeze. At 4 °C, the reaction gave almost 90:10 selectivity for **3.49**. Decreasing the temperature to -6 °C did not increase the selectivity further (Table 3.14).

In order to see if fine tuning the group on the methylene linker between NMI and the ring could increase the selectivity further, a few derivatives were synthesized. Previously smaller groups at this position, such as methyl, gave lower selectivities and often existed as multiple diastereomers in solution. Larger groups, such as *t*-butyl, were

unable to be synthesized. A series of catalysts with cyclic alkyl substituents at this position were synthesized. These groups were explored as they are branched like an *i*Pr group, but are tied back making them slightly smaller. The catalyst in which R= cyclopropyl exists as an 80:20 mixture of diastereomers and gives about a 1:1 ratio of **3.48** to **3.49**. When R= cyclopentyl, however, the catalyst gives the same results as **III** (Table 3.15). Unfortunately, the cyclobutyl version of this catalyst could not be made, and the cyclohexyl version did not exchange efficiently.

Table 3.15 Screen of Catalysts with Cyclic R groups.



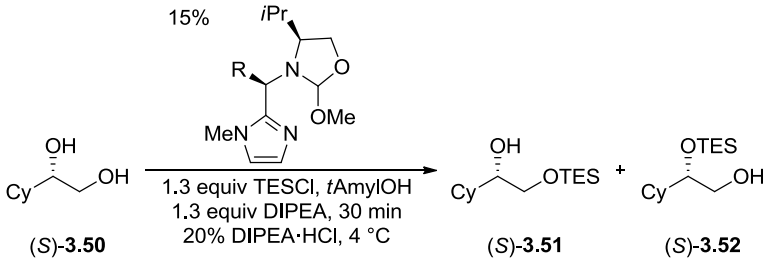
R	**3.48**:**3.49**[a]	Conversion (%)[a]
*i*Pr	12:88	>95
Cyclopropyl (80:20 dr)	49:51	>95
Cyclopentyl (**IV**)	12:88	>95

[a]Determined by GC analysis.

When you compare **IV** and **III** using other substrates, such as (*S*)-1-cyclohexane-1,2-diol, **3.50**, the difference is more obvious. Catalyst **IV** gives almost 90:10 selectivity for **3.52** and much higher yields (Table 3.16, Entry 2 compared with Entry 1). The

reaction with NMI and (*R*)-**3.50** are shown for comparision and are still highly selective for **3.51** (Table 3.16, Entry 1 and 4, respectively).

Table 3.16 Catalyst Screen with (*S*)-Cyclohexylethane-1,2-diol.

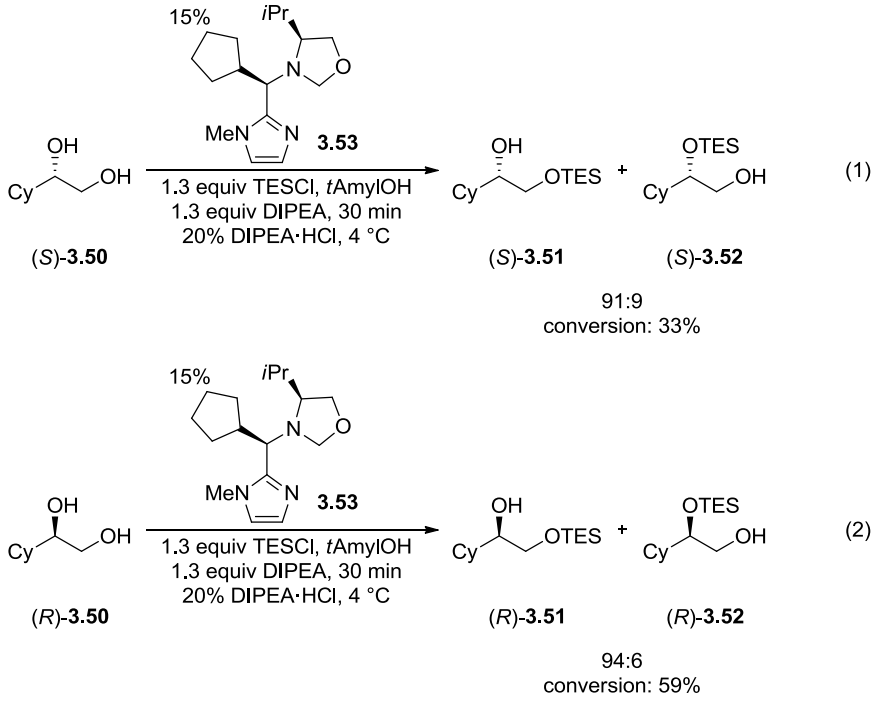


Entry	R	**3.51**:**3.52**[a]	Yield(%)[a]
1[b]	-	98:2	<2
2	*i*Pr	18:82	58
3	Cyp	12:88	76(74)[c]
4[d]	Cyp	>98:2	<1

[a]Based on GC using trimethoxybenzene as an internal standard. [b]Using NMI as catalyst. [c]Isolated yield of **3.47**. [d](*R*)-Cy was used as the substrate.

The control catalyst, **3.53**, which lacks a substrate binding site gives primarily **3.51** with low conversions for both enantiomers of substrate (Scheme 3.26, Eq 1 and 2).

Scheme 3.26 Control Catalyst with (*S*) and (*R*)-1-Cyclohexane-1,2-diol.



With optimized conditions in hand, the substrate scope was expanded. The racemic substrates were run to obtain both valuable enantioenriched products, the primary and the secondary functionalized. This type of reaction is refered to as a regiodivergent reaction on a racemic mixture.[21e,22] If desired, an enantiopure diol can also be run in this reaction to obtain high yields and good selectivities for the secondary functionalized product. When optimizing each substrate, both **III** and **IV** were tested, as they gave similar results with (*S*)-hexane-1,2-diol, **3.47**, but different with (*S*)-1-cyclohexane-1,2-diol, **3.50**. It is important to note that exact reaction times are necessary

[22](a) Miller, L. C.; Sarpong, R. *Chem. Soc. Rev.* **2011**, *40*, 4550-4562.

to prevent conversion of the secondary protected product into bis-protected product over time. Most of the substrates gave good yields and excellent enantioselectivities for the secondary product. The primary product is also obtained with good yields, albeit with slightly lower enantioselectivities. This is because although the (*R*)-enantiomer is extremely selective to form the primary functionalized product, the (*S*)-enantiomer forms the secondary functionalized product in about a 90:10 ratio for most substrates (Table 3.18). Both bulkyl and small alkyl groups are tolerated as well as protected alcohols. The OPh substrate, **3.58**, suffers from bis-silylation being competitive with mono-silylation so the yields are somewhat diminished. The vinyl substrate, **3.59**, is the least selective which has been attributed to its small size and the fact that it deactivates the functionalization of the secondary alcohol (Table 3.17). Similarly, it is believed that the 1-phenyl-1,2-diol substrate was less selective due to deactivation of the secondary alcohol (Scheme 3.27). Notably, a benzyl group in **3.56** still allows for selective secondary alcohol functionalization (Table 3.17).

Scheme 3.27 Reaction Run with 1-Phenyl-1,2-ethanediol.

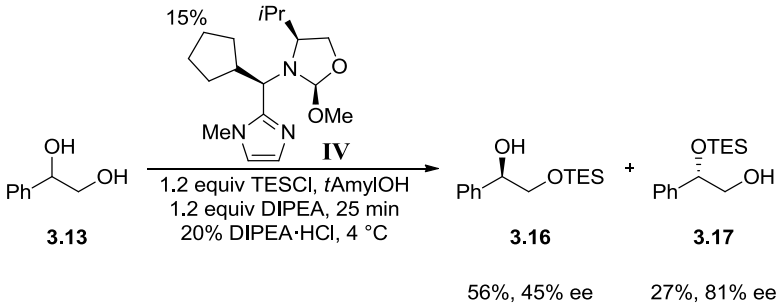
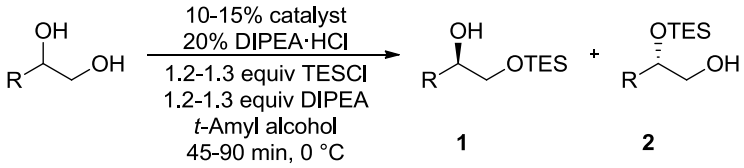
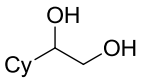
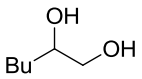
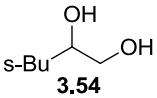
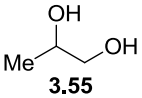
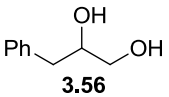
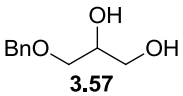
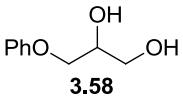
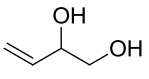
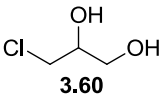
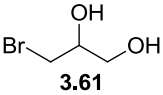


Table 3.17 Substrate Scope.



Substrate	**1**[a,b]	**2**[a,b]
 **3.50**	52%, 81% ee[c]	41%, 97% ee[c]
 **3.47**	54%, 79% ee[d]	40%, 98% ee[d]
 **3.54**	53%, 82% ee[c]	40%, 98% ee[c]
 **3.55**	48%, 70% ee[e]	36%, 92% ee[e]
 **3.56**	46%, 80% ee[f]	40%, 96% ee[f]
 **3.57**	56%, 74% ee[d]	40%, 99% ee[d]
 **3.58**	44%, 78% ee[g]	32%, 96% ee[g]
 **3.59**	53%, 57% ee[e]	37%, 91% ee[e]
 **3.60**	52%, 90% ee[c]	45%, 97% ee[c]
 **3.61**	50%, 91% ee[c]	41%, 98% ee[c]

[a]Isolated yields. [b]ee determined by GC or HPLC analysis. [c]Run with 15% **IV**, 1.3 equiv TESCl and DIPEA. [d]Run with 10% **III**, 1.2 equiv TESCl and DIPEA. [e]Run with 15% **IV**, 1.2 equiv TESCl and DIPEA. [f]Run with 10% **IV**, 1.2 equiv TESCl and DIPEA. [g]Run with 15% **III**, 1.4 equiv TESCl and DIPEA.

When attempting to silylate the bulky 3,3-dimethylbutane-1,2-diol, no secondary silylation product was obtained (Scheme 3.28). The halogenated substrates, **3.60** and **3.61**, were the most selective with the (*S*)-enantiomer forming the secondary product in an impressive 95:5 ratio (Table 3.18).The selectivities for each enantiomer of substrate could be calculated based on the yields and enantioselectivities of each product (Table 3.18).

Scheme 3.28 Reaction of 3,3-dimethylbutane-1,2-diol.

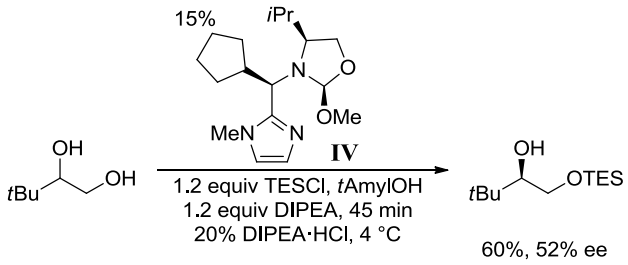


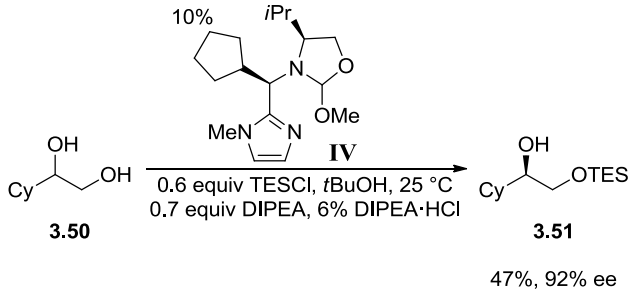
Table 3.18 Calculated Selectivities for Each Enantiomer of Substrate.

Substrate	(*R*)-1[a]	(*R*)-2[a]	(*S*)-1[a]	(*S*)-2[a]
3.13	95	5	41	59
3.50	99	1	12	88
3.47	99	1	13	87
3.54	99	1	11	89
3.55	96	4	17	83
3.56	98	2	10	90
3.57	>99	<1	14	86
3.58	98	2	14	86
3.59	97	3	27	73
3.60	99	1	6	94
3.61	99	1	5	95

[a]Approximate (*R*)-enantiomer and (*S*)-enantiomer selectivities calculated based on isolated yields and ees from Table 3.17.

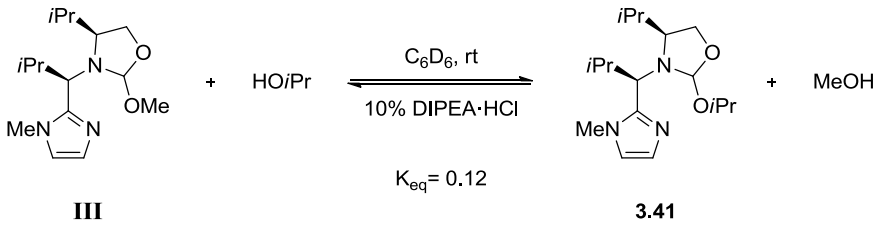
If the reaction is run to low conversion, a kinetic resolution of 1-cyclohexane-1,2-diol is possible to isolate the primary functionalized product, **3.51**, in good yields and higher enantioselectivity (Scheme 3.29). As the rate of functionalization of the (*R*)-diol with **IV** is much faster than the (*S*)-diol, the (R)-diol is most likely matched with the catalyst to silylate the primary alcohol.

Scheme 3.29 Kinetic Resolution of 1-Cyclohexylethane-1,2-diol.



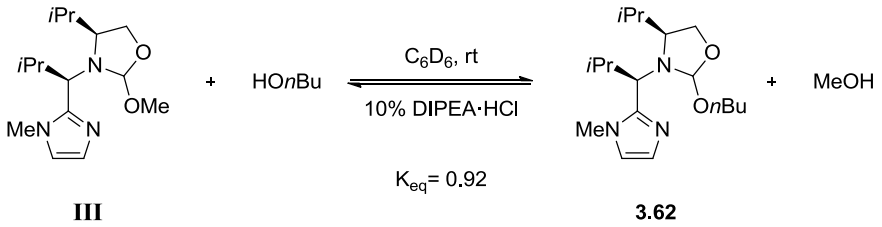
Some exchange reactions were run with **III** to learn more about how binding selectivity may be affecting the reaction. The exchange of **III** with simple alcohols was performed first. The exchange of **III** with HO*i*Pr gave a ratio of 57:43 of **III** to **3.41** at equilibrium which corresponds to a K_{eq} of 0.12 (Scheme 3.30). This K_{eq} is consistent with previous exchange reactions and is expected due to the size difference between a secondary alcohol and MeOH.

Scheme 3.30 Exchange of **III** with HO*i*Pr.



The exchange of **III** with HO*n*Bu gave a ratio of 67:33 (**III** to **3.62**) at equilibrium which gives a K_{eq} of 0.98. As HO*n*Bu is a primary alcohol, the equilibrium was expected to be slightly less than one (Scheme 3.31).

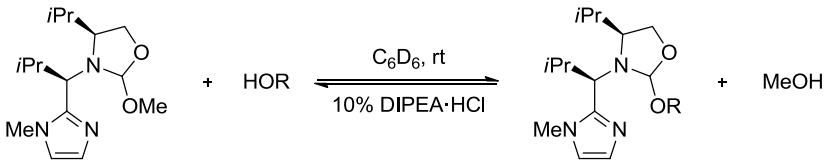
Scheme 3.31 Exchange of **III** with HO*n*Bu.



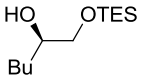
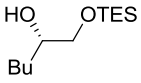
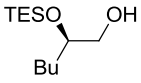
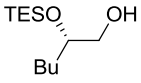
Next the exchange of each product with **III** was studied. As expected for both enantiomers, the free primary alcohols have higher binding affinities than the secondary alcohols. However comparing the individual enantiomers of **3.48** to each other shows some interesting results. The K_{eq} of (*S*)-**3.48** is 1.9 times the K_{eq} of (*R*)-**3.48** (Scheme 3.32, Entry 1 and 2). Because (*R*)-**3.48** is the favored primary product that results from the reaction of **3.47** with **III**, it is interesting that it has a lower binding affinity. The K_{eq}

of (*R*)-**3.49** is 1.2 fold the K_{eq} of (*S*)-**3.49** (Scheme 3.32, Entry 3 and 4). Again the favored product of the reaction has a lower binding affinity than its enantiomer, but the difference is less drastic. Secondary alcohol exchange, which is already less favorable than primary alcohol exchange, appears to be more sensitive to the stereocenter in the molecule.

Scheme 3.32 Product Exchange with **III**.



III **3.63**

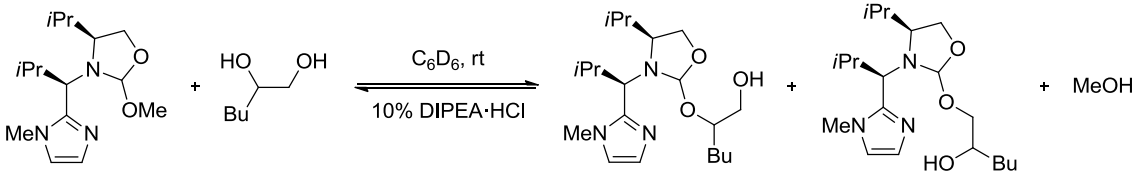
Entry	HOR	Equiv.	**III**:**3.63**	K_{eq}
1	 (*R*)-**3.48**	7.4	92:8	0.012
2	 (*S*)-**3.48**	7.6	87:13	0.023
3	 (*R*)-**3.49**	5	55:45	0.26
4	 (*S*)-**3.49**	5	58:42	0.22

When comparing the primary vs. secondary binding for each enantiomer, another interesting set of data appears. At equilibrium, the K_{eq} of (*S*)-**3.49** is 9.6 times the K_{eq} of

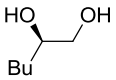
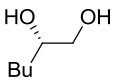
(*S*)-**3.48** (Scheme 3.32, Entry 2 and 4). As methanol has a binding affinity 8 times that of a secondary alcohol, this difference seemed reasonable (Scheme 3.30). In contrast, (*R*)-**3.49** is 21.7 times more favorable to bind than (*R*)-**3.48** (Scheme 3.32, Entry 1 and 3). (*R*)-**3.48** must have a very unfavorable interaction with **III** that causes binding to be much more difficult. Because of the large difference in binding affinity for one enantiomer over the other, we believe it is possible that this catalyst could be developed into a chiral separation technology in the future.

Because the enantiomers of product are sterically and electronically different than the substrates, an exchange reaction with each enantiomer of the hexane-1,2-diol substate, **3.47**, was also performed. (*R*)- and (*S*)-**3.47** led to a similar ratio of **3.64** to **3.65** (Scheme 3.33).

Scheme 3.33 Exchange of **III** with **3.47**.

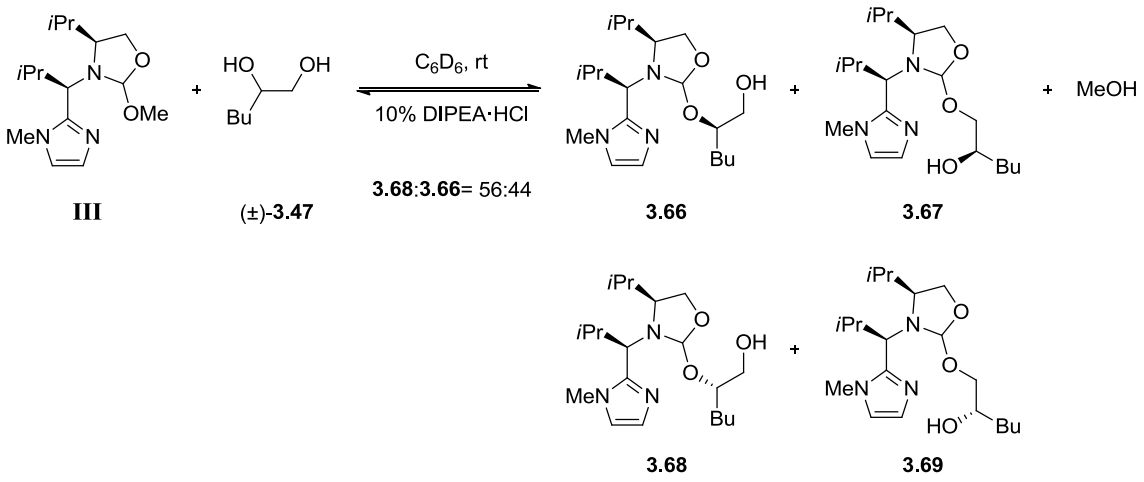


III **3.47** **3.64** **3.65**

Entry	Diol	Equiv.	**3.64:3.65**
1	 (*R*)-**3.47**	5	18:82
2	 (*S*)-**3.47**	5	20:80

Since the two individual enantiomers had been exchanged with **III**, it was possible to identify all of the products of the exchange of racemic **3.47** with **III**. When exchanging racemic **3.47** with **III**, within 10 min, 55% of **III** was converted to the primary alcohol bound to the catalyst. After 24 h, equilibrium was reached with 67% conversion of **III**. The ratio of primary to secondary alcohol bound products was 79:21. This was consistent with the ratio of primary to secondary alcohol bound products seen with the exchange of the individual enantiomers (Scheme 3.33). The ratio of **3.68** to **3.66** was 56:44 (Scheme 3.34). This means that at equilibrium (*S*)-**3.47** is more favorable to bind the secondary alcohol than (*R*)-**3.47**. This is consistent with the exchange data seen with the product exchange but is a less dramatic difference (Scheme 3.32).

Scheme 3.34 Exchange of (±)-**3.47** with **III**.



Consistent with the desymmetrization, the exchange data indicates that the binding of each enantiomer to **III** does not determine the difference in their selectivity.

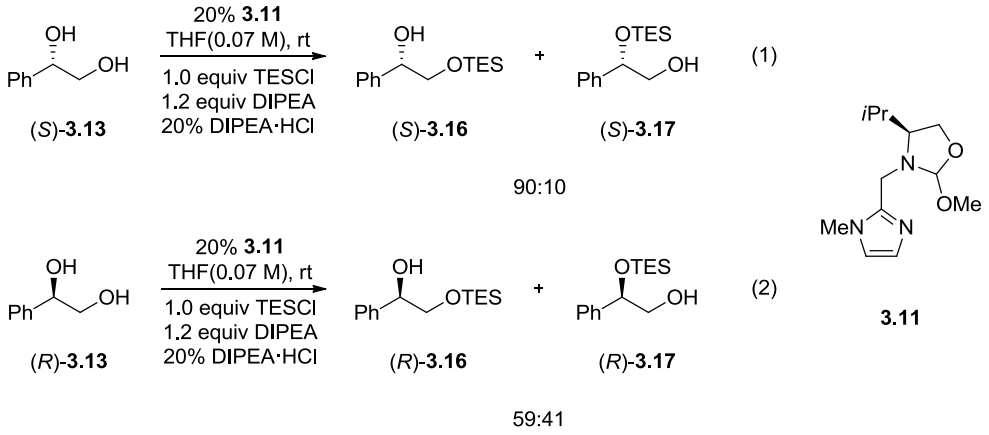
Both enantiomers show that the primary alcohol preferentially binds to **III**. This binding of the primary alcohol preferentially over the secondary alcohol certainly does contribute to the selective functionalization of the secondary alcohol.

The exchange information also corresponds with the optimal reaction conditions that were discovered for each enantiomer. In the beginning of the reaction, before the exchange is at equilibrium, only the primary alcohol has exchanged onto **III**. This is important for the (*S*)-diol to selectively form the secondary functionalized product. Thus, a pre-stir before adding the TESCl does not help the selectivity for the (*S*)-enantiomer. However, when running the reaction under the kinetic resolution conditions, the reaction was pre-stirred for 45 minutes in order to get optimal selectivities for the (*R*)-enantiomer. During this pre-stir, the secondary alcohol exchanges onto the **III** so it can direct the functionalization of the primary alcohol.

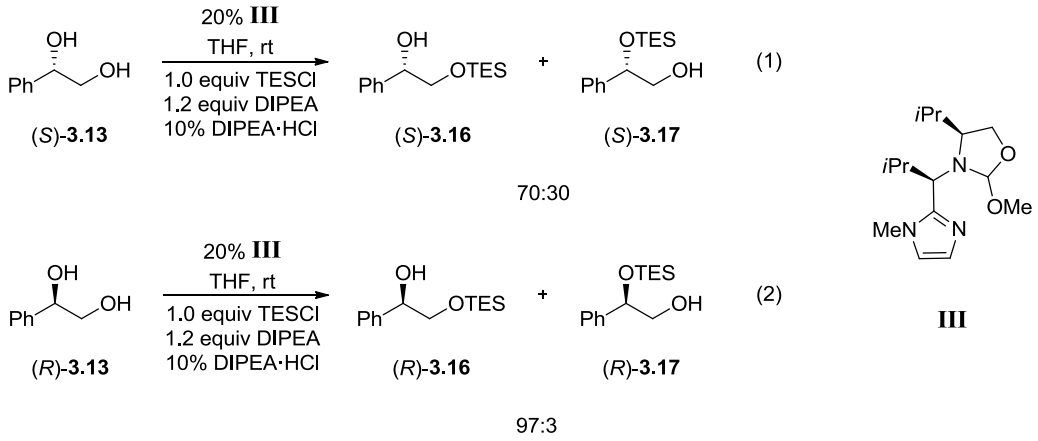
3.8 The Different Selectivities of **3.11** and **III**.[12]

During the optimization of the reaction of **3.13**, the difference in selectivity of **3.11** and **III** was discovered (Scheme 3.12 and 3.35). This difference will be discussed here in the context of the reaction with **3.13**.

Scheme 3.12 Reaction of **3.11** with Individual Enantiomers.



Scheme 3.35 Reaction of **III** with Individual Enantiomers.

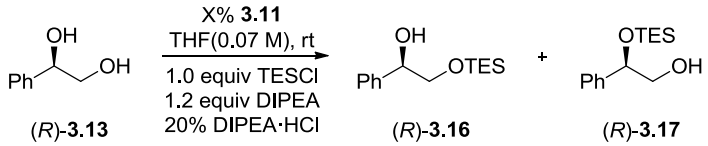


The experimental results which show that the two catalysts are matched to give secondary functionalization with different enantiomers led us to believe that they may be functionalizing the diols through different mechanisms. Remembering that **III** exists as one diastereomer in which the C-O bond is oriented up and that **3.11** exists as two diastereomers, we hypothesized that the diastereomer where the C-O bond is oriented

down may be responsible for the secondary functionalization of the (*R*)-diol in the reaction with **3.11**. Some of the optimization that was done with the 1-phenyl-1,2-diol is important for this discussion. For example, the reaction of **3.13** with **3.11** does not seem to be affected by the catalyst loading (Table 3.19). This is not true of the reactions done with **III**. Increasing the amount of **III**, increased the selectivity.

Intriguingly, this indicates that **3.11** may be matched with the (*R*)-diol and can accelerate the secondary functionalization reaction, whereas, **III** may be acting by decelerating the primary functionalization reaction compared to the secondary functionalization with the (*S*)-diol. This could be due to the steric size difference in the two catalysts and the difference in the freedom of rotation of the *N*-methylimidazole. If **III** is more rigid as well as being sterically hindered, the rate of silylation may be slower for both alcohols.

Table 3.19 Catalyst Loading Screen.



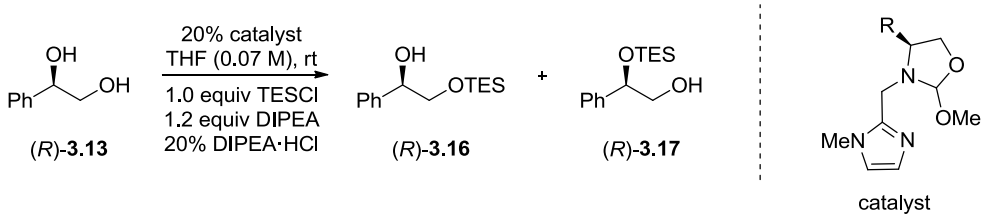
(*R*)-**3.13** (*R*)-**3.16** (*R*)-**3.17**

Entry	**3.11** (%)	**3.16**:**3.17**[a]
1	10	58:42
2	20	58:42
3	50	58:42

[a]Determined by GC analysis.

As shown previously, to increase the selectivity for the secondary product, **3.17**, other catalysts were synthesized to see if any would give improved selectivities. When the catalysts were run with (*R*)-**3.13**, there was a clear trend that increasing the size of the R group corresponded to an increase in the diastereomer ratio of the catalyst and an increase in the selectivity for **3.17** (Table 3.2).

Table 3.2 Variation of Amino Alcohol Backbone.



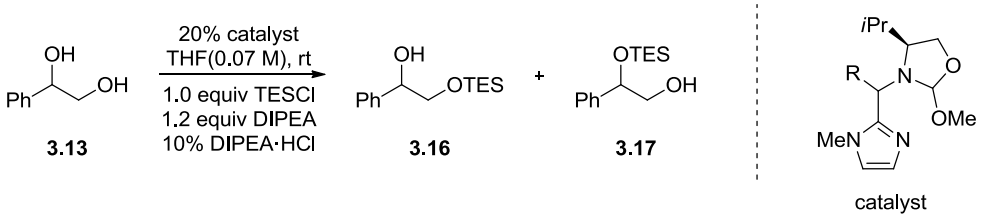
R	dr	Conversion (%)[a]	**3.16**:**3.17**[a]
*t*Bu	85:15	96	55:45
*i*Pr	70:30	98	58:42
*i*Bu	75:25	97	78:22
Me	66:34	95	69:31
H	-	95	83:17
Ph	60:40	97	89:11

[a]Determined by GC analysis.

When trying to optimize the catalyst to force it to be one diastereomer, the (*S*,*S*) and (*S*,*R*) catalysts were tested in the reaction. Unfortunately, the (*S*,*S*)-catalysts gave much worse selectivity in the site selective silylation compared with the simple amino alcohol based catalysts even when one diastereomer was present (Table 3.20 and Table

3.2). Most of the (*S*,*R*)-catalysts did not give good selectivities for **3.17**. However, catalyst **III** was more selective for secondary functionalization than any of the catalysts that were previously tested, but only when the (*S*)-enantiomer of substrate was used (Table 3.20). It was previously rationalized using models why the (*R*)-enantiomer is matched with **III** to form primary functionalized product and does not favor secondary functionalization (Figure 3.7). We believe that during this catalyst optimization we

Table 3.20 (*S*,*S*)- and (*S*,*R*)-Catalysts.



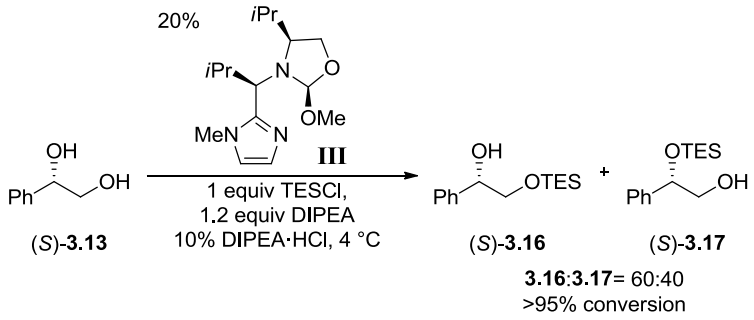
R	dr	**3.13**	Conversion (%)[a]	**3.16**:**3.17**[a]
(*S*)-Me	99:1	(*S*)	78	93:7
		(*R*)	99	91:9
(*S*)-*i*Pr	99:1	(*S*)	92	94:6
		(*R*)	93	95:5
(*R*)-Me	90:10	(*S*)	96	94:6
		(*R*)	95	96:4
(*R*)-*i*Pr (**III**)	99:1	(*S*)	82	70:30
		(*R*)	99	97:3
(*R*)-Ph	56:44	(*S*)	81	95:5
		(*R*)	90	97:3

[a]Determined by GC analysis.

switched the mechanism from acceleration of the secondary functionalization pathway to deceleration of the primary functionalization pathway.

Going forward with catalyst **III**, (*S*)-1-phenyl-1,2-ethanediol was used to optimize the reaction conditions. Simply decreasing the temperature to 4 °C increased the selectivity to 60:40 (Scheme 3.36).

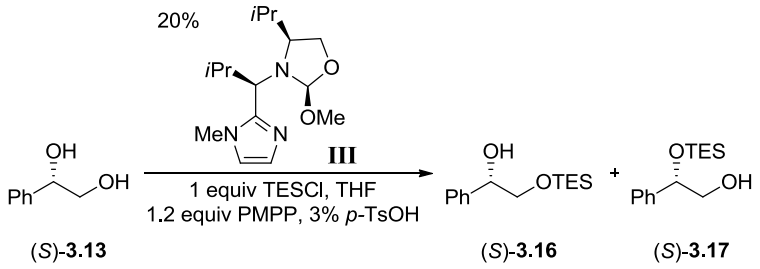
Scheme 3.36 Decreasing the Reaction Temperature.



Next, the base was changed to 1,2,2,6,6-pentamethylpiperidine which in the desymmetrization reaction seemed to catalyze less background reaction than *N*, *N*-diisopropylethylamine. Indeed, as before, the reaction with PMPP gave better selectivity than when DIPEA was used. However, when the reaction temperature was lowered using PMPP as the base, there was no increase in selectivity. This implies that background reaction is sufficiently suppressed using PMPP as the base so decreasing the temperature is not necessary. If DIPEA is used, decreasing the temperature to 4 °C gives approximately the same results as using PMPP. Either reaction condition allows the intramolecular reaction to outcompete the intermolecular reaction. Using crystallized

catalyst, instead of distilled catalyst, also increased the selectivity of the reaction significantly. Clearly, the selectivity is very sensitive to the purity of the **III** (Table 3.21).

Table 3.21 1,2,2,6,6-Pentamethylpiperidine as the Base.



(*S*)-**3.13** (*S*)-**3.16** (*S*)-**3.17**

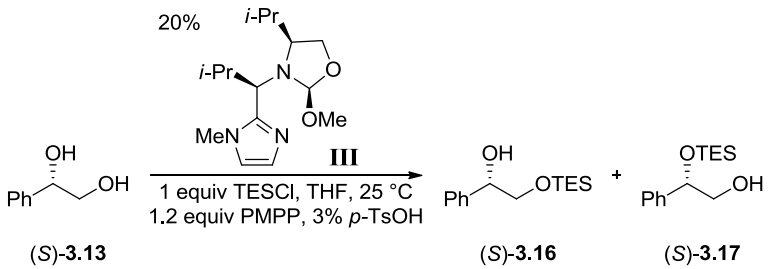
Temperature (°C)	**3.16**:**3.17**[a]	Conversion(%)[a]
4	62:38	>95
25	62:38	>95
25 (crystallized ligand)	53:47	88

[a]Determined by GC analysis.

.

A reagent screen was performed at this point to see if it affected the selectivity. Using TESBr gave similar results to using TESCl. $TESNO_2$ gave much lower selectivities, and the very reactive TESOTf was unselective and gave high amounts of bis silylation. A variety of temperatures were screened with TESOTf, but they all resulted in similar undesirable results (Table 3.22).

Table 3.22 Electrophile Screen.



Reagent	Conversion(%)[a]	**3.16**:**3.17**[a]	Bis(%)[a]
TESBr	80	63:37	4
$TESNO_2$	63	82:18	6
TESOTf	75	89:11	35
TESOTf (4 °C)	74	94:6	33
TESOTf (-60 to 10 °C)	67	82:18	42
TESOTf (60 °C)	68	82:18	31

[a]Determined by GC analysis.

At this point, as shown previously, hexane-1,2-diol was used for further optimization because it was realized that the 1-phenyl-1,2-diol was a less selective substrate in the reaction with **III**. With **III**, 1-phenyl-1,2-diol never acheieved selectivity over 60:40 for secondary functionalization (Table 3.18). In the future, our group will focus on making a catalyst that would exist as one diastereomer in which the C-O bond is oriented down. We believed this may allow for secondary functionalization of the (*R*)-diol with high selectivity.

3.9 Conclusions

A new set of organocatalysts were developed that benefit from reversible covalent bonding and induced intramolecularity. The desymmetrization of meso-1,2-diols was accomplished using organocatalyst **III**, which was synthesized easily and cheaply. Experimental results indicate that the selectivity and increased reactivity are a result of the ability of **III** to pre-organize the substrate through a reversible, covalent bond. A variety of cyclic and acylic substrates were shown to react efficiently with good enantioselectivities under mild conditions. Other silylating reagents were also shown to be effective under the reaction conditions. he catalyst's a il ity to f nc tionalize cis-1,2-diols selectively indicated it might be successfully applied to site selective catalysis. Thus, the selective functionalization of a secondary alcohol in the presence of a primary alcohol was developed using a combination of binding selectivity and stereoselectivity. The (*S*)-enantiomer forms the secondary functionalized product while the (*R*)-enantiomer forms the primary functionalized product with high selectivity. As the enantiomers preferentially form different functionalized products, a regiodivergent reaction on a racemic mixture resulted giving two valuable enantioenriched products.

3.10 Experimental

General Considerations

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Lithium reagents were titrated against 2-pentanol using 1,10-phenanthroline as the indicator. Flash column chromatography was performed

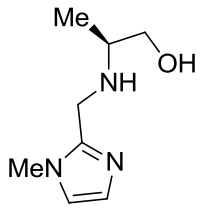
using EMD Silica Gel 60 (230-400 mesh) and ACS grade solvents as received from Fisher Scientific. All experiments were performed in oven or flame-dried glassware under an atmosphere of nitrogen or argon using standard syringe and cannula techniques, except where otherwise noted. All reactions were run with dry, degassed solvents dispensed from a Glass Contour Solvent Purification System (SG Water, USA LLC). ^{1}H and ^{13}C NMR were performed on either a Varian Gemini 400 MHz, Varian Gemini 500 MHz or a Varian Unity Inova 500 MHz spectrometer. Deuterated solvents were purchased from Cambridge Isotope Labs and stored over 3Å molecular sieves. C_6D_6 was degassed by three successive freeze-pump-thaw cycles and stored over 3Å molecular sieves in a dry box under a nitrogen atmosphere. All NMR chemical shifts are reported in ppm relative to residual solvent for ^{1}H and ^{13}C NMR. Coupling constants are reported in Hz. All IR spectra were gathered on a Bruker Alpha FT-IR equipped with a single crystal diamond ATR module and values are reported in cm^{-1}. All GC analyses were performed on an Agilent Technologies 7890A GC System. HRMS and X-ray crystal structure data were generated in Boston College facilities. Analytical chiral high-performance liquid chromatography (HPLC) was performed on a Shimadzu-LC-2010A HT.

Initial Studies of Selective Functionalization of 1,2-Diols

Catalyst Synthesis

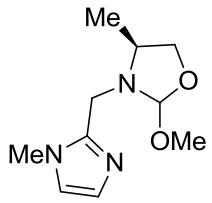
N-methyl-imidazole-2-carboxaldehyde, **3.9**, [23] was made following literature procedures and matched reported spectra.

[23]Plater, M. J.; Barnes, P.; McDonald, L. K.; Wallace, S.; Archer, N.; Gelbrich, T.; Horton, P. N.; Hursthouse, M. B. *Org. Biomol. Chem.* **2009**, *7*, 1633-1641.



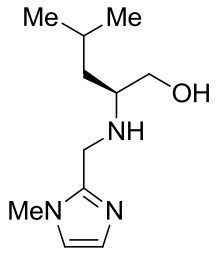
(*S*)-2-((1-methyl-1H-imidazol-2-yl)methylamino)propan-1-ol.[24] To a solution of *N*-methyl-imidazole-2-carboxaldehyde (650 mg, 8.7 mmol) in methanol (17 mL) was added (*S*)-alaninol (960 mg, 8.7 mmol) and 4Å molecular sieves (1.7 g). After refluxing for 24 hours, the reaction was cooled to room temperature, and $NaBH_4$ (340 mg, 8.7 mmol) was added. The reaction was stirred at room temperature for 2 hours, followed by quenching with dropwise addition of concentrated HCl (0.44 mL). The resulting mixture was further neutralized with Na_2CO_3 (1.4 g). The precipitated salts were filtered off, and the filtrate was concentrated. Flash column chromatography (CH_2Cl_2:MeOH = 10:1) afforded pure product as a colorless oil (1.0 g, 70%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 6 7 d *J* = 1.2), 6.78 (d, 1H, *J* = 1.2), 3.91 (d, 1H, *J* = 14.4), 3.76 (d, 1H, *J* = 14.4), 3.60 (s, 3H), 3.53 (dd, 1H, *J* = 11.0, 3.9), 3.26-3.30 (m, 1H), 2.82 (qt, 1H, *J* = 10.3, 3.9), 1.04 (d, 3H, *J* = 6.4); **^{13}C NMR** (C_6D_6 26 M z δ 147.0, 126.9, 121.2, 65.5, 54.9, 42.9, 32.7, 17.3; **IR**: 3201, 2872, 1636, 1499, 1452, 1283, 1048, 736, 662 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_8H_{16}N_3O$ $[M+H]^+$: 170.1293, found: 170.1292. **$[\alpha]_D^{20}$** = +33.0 (*c* = 1.10, $CHCl_3$, *l* = 50 mm).

[24]Suzuki, Y.; Takahashi, H. *Chem. Pharm. Bull*. **1983**, *31*, 2895-2898.



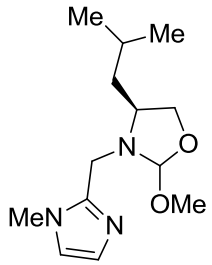
(*4S*)-2-methoxy-4-methyl-3-((1-methyl-1H-imidazol-2-yl)methyl)oxazolidine (66:34 dr). To a solution of (*S*)-2-(((1-methyl-1H-imidazol-2-yl)methyl)amino)propan-1-ol (1.0 g, 6.0 mmol) in anhydrous methanol (24 mL) under argon was added *N,N*-dimethylformamide dimethyl acetal (0.80 mL, 6.0 mmol). The reaction was stirred at room temperature for 2 hours, and the solvent was removed under vacuum. The residue was redissolved in anhydrous methanol (24 mL), and reaction was stirred at room temperature for another 2 hours. ^{1}H NMR analysis showed that all the substrate was consumed and product had formed. The solvent was removed under vacuum. The flask was brought into a dry glove box under nitrogen atmosphere, and the residue was extracted with degassed pentane. The pentane was removed under vacuum, and Kugelrohr distillation (170 °C at 0.05 mmHg) afforded pure product as a colorless oil (330 mg, 26%). **^{1}H NMR** (C_6D_6, 500 M z δ 7 s 0 3 7 3 d 0 66 J = 0.1), 6.37 (s, 0.34H), 6.36 (s, 0.34H), 5.24 (s, 0.66H), 5.17 (s, 0.34H), 3.98 (t, 0.34H, J = 7.3), 3.78 (t, 0.66H, J = 6.8), 3.68-3.72 (m, 2H), 3.36-3.43 (m, 0.66H), 3.32-3.34 (m, 0.34H), 3.28 (s, 0.66H), 3.23 (s, 0.66H), 3.14 (s, 0.34H), 3.07 (s, 0.34H), 2.94-2.96 (m, 1H), 0.74 (d, 1H, J = 6.1), 0.71 (d, 2H, J = 5.9); **^{13}C NMR** (C_6D_6 26 M z δ 7 2 121.7, 114.7, 111.7, 109.0, 73.1, 72.6, 57.9, 54.9, 53.1, 51.4, 47.1, 43.4, 38.3, 32.7, 17.5, 16.8; **IR**: 2928, 1501, 1458, 1284, 1162, 1113, 1066, 1017, 975, 742 cm^{-1}; **HRMS**

(DART-TOF) calcd. for $C_{19}H_{14}N_3O$ [M-OMe]: 180.1137, found: 180.1142. $[\alpha]_D^{20}$ = +11.6 (*c* = 1.09, C_6H_6, *l* = 50 mm).



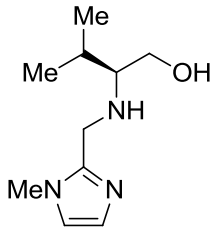
(*S*)-4-Methyl-2-(((1-methyl-1H-imidazol-2-yl)methyl)amino)pentan-1-ol.[24] To a solution of *N*-methyl-imidazole-2-carboxaldehyde (1.65 g, 15.0 mmol) in benzene (30 mL) was added (*S*)-leucinol (1.20 g, 10.0 mmol) and 3Å molecular sieves (1.40 g). After refluxing for 24 hours, the reaction was cooled to room temperature and the solvent was removed in vacuo. The resulting residue was redissolved in MeOH (30 mL), and $NaBH_4$ (570 mg, 15.0 mmol) was added. The reaction was stirred at room temperature for 2 hours, followed by quenching with dropwise addition of concentrated HCl (0.510 mL). The resulting mixture was further neutralized with Na_2CO_3 (1.70 g). The precipitated salts were filtered off, and the filtrate was concentrated. Flash column chromatography (CH_2Cl_2:MeOH = 10:1) afforded the pure product as a yellow oil (1.58 g, 75%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 6 0 d 1 *J* = 1.0), 6.73 (d, lH, *J* = 1.0), 3.84 (d, lH, *J* = 14.5), 3.76 (d, lH, *J* = 14.5), 3.56 (s, 3H), 3.26-3.30 (m, 1H), 2.65-2.69 (m, 1H), 1.58-1.65 (m, 1H), 1.25-1.31 (m, lH), 1.14-1.19 (m, 1H), 0.82 (d, 3H, *J* = 6.5), 0.79 (d, 3H, *J* = 6.5); **^{13}C NMR** ($CDCl_3$ 2 M z δ 6 26 6 2 2 63 7 2 6 32 6 24.8, 22.8, 22.7; **IR**: 3281, 2952, 2867, 1500, 1466, 1051, 735 cm^{-1}; **HRMS** calcd. for

$C_{11}H_{22}N_3O$ $[M+H]^+$: 212.1762, found: 212.1761.



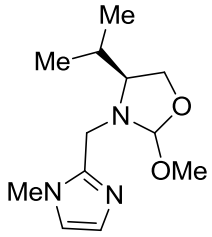
(4*S*)-4-Isobutyl-2-methoxy-3-((1-methyl-1H-imidazol-2-yl)methyl)oxazolidine (75:25 dr). To a solution of (*S*)-4-methyl-2-(((1-methyl-1H-imidazol-2-yl)methyl)amino)pentan-1-ol (0.70 g, 3.3 mmol) in anhydrous methanol (13 mL) under argon was added *N*,*N*-dimethylformamide dimethyl acetal (0.40 mL, 3.3 mmol). The reaction was stirred at room temperature for 2 hours, and the solvent was removed under vacuum. The residue was redissolved in anhydrous methanol (13 mL), and the reaction was again stirred at room temperature for 2 hours until ^{1}H NMR analysis showed all the substrate was consumed. The solvent was removed under vacuum. The flask was brought into a dry glove box under nitrogen atmosphere, and the residue was extracted with degassed pentane. The pentane was removed under vacuum, and Kugelrohr distillation (180 °C at 0.05 mmHg) afforded the pure product as a pale green oil (190 mg, 23%). **^{1}H NMR** (C_6D_6 00 M z δ 7 2 d 0 2 *J* = 1.0), 7.09 (d, 0.75H, *J* = 1.0), 6.34 (d, 0.25H, *J* = 1.0), 6.32 (d, 0.75H, *J* = 1.0), 5.29 (s, 0.75H), 5.17 (s, 0.25H, *J* = 1.0), 3.87-3.92 (m, 0.75H), 3.84-3.86 (m, 0.25H), 3.76-3.81 (m, 0.5H), 3.75 (d, 0.75H, *J* = 13.5), 3.68 (d, 0.75H, *J* = 13.5), 3.49-3.55 (m, 0.75H), 3.40-3.44 (m, 0.25H), 3.19 (s, 0.75H), 3.11 (s, 2.25H), 3.01-3.09 (m, lH), 3.04 (s, 2.25H), 2.97 (s, 0.75H), 1.15-1.28 (m, 2.25H),

1.05-1.11 (m, 0.75H), 0.75 (d, 0.75H, *J* = 6.5), 0.72 (d, 0.25H, *J* = 6.5), 0.70 (d, 0.75H, *J* = 6.5), 0.67 (d, 0.25H, *J* = 6.5); **^{13}C NMR** ($CDCl_3$ 26 M z δ 6 26 7 20 7 114.0, 112.6, 110.6, 71.1, 70.9, 70.5, 70.1, 57.5, 56.1, 52.3, 50.8, 47.2, 42.6, 42.1, 41.5, 37.5, 31.9, 25.5, 23.6, 23.5, 22.1, 21.7; **IR**: 2953, 1500, 1284, 1160, 1076, 1036, 736 cm^{-1}; **HRMS** calcd. for $C_{12}H_{20}N_3O$ [M-OMe]: 222.1606, found: 222.1611.



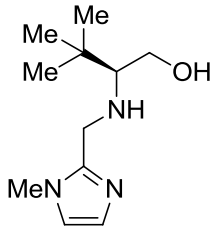
(*S*)-3-methyl-2-((1-methyl-1H-imidazol-2-yl)methylamino)butan-1-ol, 3.10.[24] To a solution of *N*-methyl-imidazole-2-carboxaldehyde (2.1 g, 2.0 x 10^1 mmol) in (40 mL) was added (*S*)-valinol (2.2 g, 2.0 x 10^1 mmol) and 4Å molecular sieves (4.0 g). After refluxing for 24 hours, the reaction was cooled to room temperature, and $NaBH_4$ (760 mg, 2.0 x 10^1 mmol) was added. The reaction was stirred at room temperature for 2 hours, followed by quenching with dropwise addition of concentrated HCl (1.0 mL). The resulting mixture was further neutralized with Na_2CO_3 (3.3 g). The precipitated salts were filtered off, and the filtrate was concentrated. Flash column chromatography (CH_2Cl_2:MeOH = 10:1) afforded the pure product as a colorless oil (2.3 g, 58%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 6.86 (d, 1H, *J* = 1.5), 6.77 (d, 1H, *J* = 1.2), 3.90 (d, 1H, *J* = 14.7), 3.78 (d, 1H, *J* = 14.9), 3.62 (dd, 1H, *J* = 11.2, 3.7), 3.58 (s, 3H), 3.39 (dd, 1H, *J* = 11.0, 7.3), 2.40-2.44 (m, 1H), 1.71-1.78 (m, 1H), 0.92 (d, 3H, *J* = 6.8), 0.87 (d, 3H, *J* =

6.8); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 147.4, 126.9, 121.3, 65.1, 61.6, 44.0, 32.6, 30.0, 19.5, 19.0; **IR**: 3199, 2955, 2871, 1500, 1465, 1283, 1043, 734, 705, 661 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{20}N_3O$ $[M+H]^+$: 198.1606, found:198.1606. **$[\alpha]_D^{20}$** = +19.0 (*c* = 1.0, CH_2Cl_2, *l* = 50 mm).



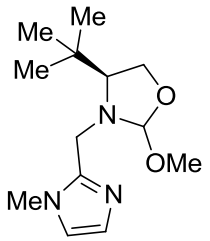
(*4S*)-4-isopropyl-2-methoxy-3-((1-methyl-1H-imidazol-2-yl)methyl)oxazolidine, 3.11 (70:30 dr). To a solution of (*S*)-3-methyl-2-(((1-methyl-1H-imidazol-2-yl)methyl)amino)butan-1-ol (860 mg, 4.4 mmol) in anhydrous methanol (18 mL) under argon was added *N,N*-dimethylformamide dimethyl acetal (580 μL, 4.4 mmol). The reaction was stirred at room temperature for 2 hours, and the solvent was removed under vacuum. The residue was redissolved in anhydrous methanol (18 mL), and the reaction was further stirred at room temperature for 2 more hours until ^{1}H NMR analysis showed complete conversion. The solvent was removed under vacuum. The flask was brought into a dry glove box under nitrogen atmosphere, and the residue was extracted with degassed pentane. The pentane was removed under vacuum, and Kugelrohr distillation (130 °C at 0.05 mmHg) afforded pure product as colorless oil (490 mg, 47%). **^{1}H NMR** (C_6D_6 00 M z δ 7 d 0 3 *J* = 1.2), 7.12 (d, 0.7H, *J* = 1.0), 6.36 (d, 0.3H, *J* = 1.0), 6.35 (d, 0.7H, *J* = 1.2), 5.34 (s, 0.3H), 5.21 (s, 0.7H), 4.02 (d, 0.3H, *J* = 13.9), 3.90 (t,

0.6H, *J* = 8.1), 3.84 (d, 0.3H, *J* = 13.9), 3.79 (t, 0.7H), 3.74 (d, 0.7H, *J* = 13.4), 3.67-3.70 (m, 0.7H), 3.65 (d, 0.7H, *J* = 13.7), 3.17 (s, 0.9H), 3.09 (s, 2.1H), 3.07 (s, 2.1H), 2.98 (s, 09H), 2.82-2.86 (m, 1H), 1.67 (dt, 0.7H, *J* = 20.5, 6.8), 1.58 (ddd, 0.3H, *J* = 13.9, 6.8, 3.7), 0.72 (d, 0.3H, *J* = 6.8), 0.69 (d, 0.7H, *J* = 6.8), 0.65 (d, 0.7H, *J* = 6.8), 0.58 (d, 0.3H, *J* = 7.1); **^{13}C NMR** ($CDCl_3$ 26 M z δ 2 7 2 2 2 6 2 3 111.9, 68.3, 67.1, 65.6, 64.7, 53.0, 51.8, 49.3, 43.9, 32.5, 32.4, 30.7, 28.7, 20.1, 19.9, 17.5, 15.4; **IR**: 2956, 1500, 1466, 1284, 1158, 1123, 1080, 1062, 986, 741 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{18}N_3O$ [M-OMe]: 208.1450, found: 208.1459. **$[\alpha]_D^{20}$** = -7.09 (*c* = 0.71, $CDCl_3$, *l* = 50 mm).



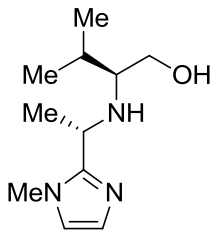
(*S*)-3,3-dimethyl-2-((1-methyl-1H-imidazol-2-yl)methylamino)butan-1-ol.[24] To a solution of *N*-methyl-imidazole-2-carboxaldehyde (750 mg, 6.8 mmol) in methanol (14 mL) was added (*S*)-*tert*-leucinol (0.80 g, 6.8 mmol) and 4Å molecular sieves (1.4 g). After refluxing for 24 hours, the reaction was cooled to room temperature, and $NaBH_4$ (260 mg, 6.8 mmol) was added. The reaction was stirred at room temperature for 2 hours, followed by quenching with dropwise addition of concentrated HCl (0.34 mL). The resulting mixture was further neutralized with Na_2CO_3 (1.1 g). The precipitated salts were filtered off, and the filtrate was concentrated. Flash column chromatography

(CH_2Cl_2:MeOH = 10:1) afforded the pure product as a colorless oil (720 mg, 50%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 6.97 (d, 1H, *J* = 1.5), 6.88 (d, 1H, *J* = 1.0), 4.20 (br s, 2H), 4.15 (d, 1H, *J* = 15.9), 3.97 (d, 1H, *J* = 15.6), 3.82 (dd, 1H, *J* = 11.2, 3.7), 3.45 (s, 3H), 3.51 (dd, 1H, *J* = 11.2, 8.1), 2.45 (dd, 1H, *J* = 8.1, 3.7), 0.94 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 147.7, 126.0, 121.6, 68.7, 62.1, 46.0, 35.1, 32.9, 27.2; **IR**: 3333, 2950, 2868, 1501, 1476, 1283, 1110, 1045, 736 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{22}N_3O$ $[M+H]^+$: 212.1763, found: 212.1764. **$[\alpha]_D^{20}$** = +5.0 (*c* = 1.0, CH_2Cl_2, *l* = 50 mm).



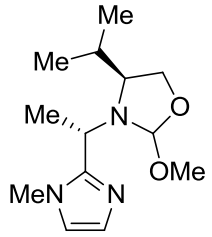
(*4S*)-4-*tert*-butyl-2-methoxy-3-((1-methyl-1H-imidazol-2-yl)methyl)oxazolidine (85:15 dr). To a solution of (*S*)-3,3-dimethyl-2-(((1-methyl-1H-imidazol-2-yl)methyl)amino)butan-1-ol (0.70 g, 3.3 mmol) in anhydrous methanol (13 mL) under argon was added *N,N*-dimethylformamide dimethyl acetal (0.40 mL, 3.3 mmol). The reaction was stirred at room temperature for 2 hours. The residue was redissolved in anhydrous methanol (13 mL), and the reaction was again stirred at room temperature for 2 hours until ^{1}H NMR analysis showed all the substrate was consumed and product had formed. The solvent was removed under vacuum. The flask was brought into a dry glove box under nitrogen atmosphere, and the residue was extracted with degassed pentane. The pentane was removed under vacuum, and Kugelrohr distillation (180 °C at 0.05

mmHg) afforded the pure product as a colorless oil (190 mg, 23%). **^{1}H NMR** (C_6D_6, 500 M z δ 7 2 s 6 3 s s 0 2 s 0 3 d *J* = 13.4), 3.85-3.89 (m, 1H), 3.78-3.81 (m, 1H), 3.65 (d, 1H, *J* = 13.4), 3.15 (s, 0.5H), 3.13 (s, 2.5H), 3.01 (s, 2.5H), 3.00 (s, 0.5H), 2.65-2.68 (m, 1H), 0.85 (s, 1.4H), 0.83 (s, 7.6H); **^{13}C NMR** ($CDCl_3$ 26 M z δ 2 27 3 2 7 20 0 72 3 6 66 3 65.1, 53.2, 52.5, 51.8, 38.1, 34.6, 33.5, 33.3, 26.7, 26.4; **IR**: 2955, 2905, 1499, 1477, 1285, 1147, 1132, 1082, 1066, 993, 740 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{20}N_3O$ [M-OMe]: 222.1606, found: 222.1612. **$[\alpha]_D^{20}$** = -7.09 (*c* = 0.71, $CDCl_3$, *l* = 50 mm).



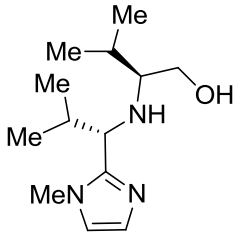
(*S*)-3-Methyl-2-(((*S*)-1-(1-methyl-lH-imidazol-2-yl)ethyl)amino)butan-1-ol.[24] To a solution of *N*-methyl-imidazole-2-carboxaldehyde (3.42 g, 31.0 mmol) in benzene (90 mL) was added (*S*)-valinol (3.20 g, 10.0 mmol) and 3Å molecular sieves (1.40 g). After refluxing for 24 hours, the reaction was cooled to room temperature, and the solvent was removed in vacuo. The resulting residue was redissolved in anhydrous Et_2O (180 mL). The solution was cooled to -78 °C and MeLi (31.0 mL, 3.0 M in dimethoxyethane, 93.0 mmol) was added dropwise. The reaction was allowed to stir for 24 hours before quenching with aqueous NH_4Cl. The organic layer was separated, and the aqueous layer

was extracted with ethyl acetate (3x100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (CH_2Cl_2:MeOH = 10:1) afforded pure product as a yellow oil (2.50 g, 38%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 6.84 (d, 1H, *J* = 1.5), 6.70 (d, 1H, *J* = 1.5), 4.04 (q, 1H, *J* = 6.5), 3.63 (s, 3H), 3.52-3.55 (m, 1H), 3.31 (dd, 1H, *J* = 6.5, 11.0), 2.22-2.25 (m, 1H), 1.61-1.65 (m, 1H), 1.36 (d, 3H, *J* = 6.5), 0.85 (d, 3H, *J* = 7.0), 0.78 (d, 3H, *J* = 7.0); **^{13}C NMR** ($CDCl_3$ 2 M z δ 150.8, 126.8, 120.9, 62.2, 60.7, 47.9, 32.7, 29.3, 21.4, 19.4, 18.8; **IR**: 3311, 2956, 1467, 1280, 1049, 725 cm^{-1}; **HRMS** calcd. for $C_{11}H_{22}N_3O$ $[M+H]^+$: 212.1762, found: 212.1769.



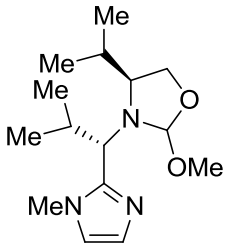
(4*S*)-4-Isopropyl-2-methoxy-3-((*S*)-1-(1-methyl-1H-imidazol-2-yl)ethyl)oxazolidine (99:1 dr). To a solution of (*S*)-3-methyl-2-(((*S*)-1-(1-methyl-lH-imidazol-2-yl)ethyl)amino)butan-1-ol (4.3 g, 18 mmol) in anhydrous methanol (36 mL) under nitrogen atmosphere was added *N*,*N*-dimethylformamide dimethyl acetal (12 mL, 9.0 x 10^1 mmol). The reaction was stirred at 50 °C overnight, concentrated, and redissolved in methanol. After stirring for 2 hours, ^{1}H NMR analysis showed complete conversion to product. The solvent was removed under vacuum, and Kugelrohr distillation (130 °C at 0.05 mmHg) afforded the product as a colorless oil (3.7 g, 73%). **^{1}H NMR** ($CDCl_3$, 500 M z δ 7 0 d H, *J* = 1.5), 6.35 (d, 1H, *J* = 1.5), 5.52 (s, 1H),

3.64-3.75 (m, 3H), 3.11 (s, 3H), 2.81-2.85 (m, 1H), 2.83 (s, 3H), 1.59-1.66 (m, 1H), 1.55 (d, 3H, *J* = 7.0), 0.77 (d, 3H, *J* = 7.0), 0.75 (d, 3H, *J* = 7.0); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 0 26 20 66 6 2 32 0 30 7 6 3 **IR**: 2954, 1281, 1155, 1056, 971, 728 cm^{-1}; **HRMS** calcd. for $C_{12}H_{20}N_3O$ [M-OMe]: 222.1606, found: 222.1615.



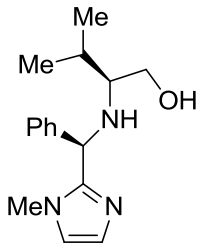
(*S*)-3-methyl-2-((*S*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propylamino)butan-1-ol, 3.20.[24] *N*-methyl-2-imidazolecarboxaldehyde (1.62 g, 14.7 mmol) and (*S*)-valinol (1.52 g, 14.7 mmol) were refluxed in toluene for 3 hours. The solution was concentrated in vacuo. The resulting crude imine was dissolved in tetrahydrofuran (86 mL) and cooled to –78 °C. Isopropyl magnesium chloride (22.8 mL, 45.6 mmol, 2.0 M in THF) was added dropwise. After stirring for 16 hours and allowing the solution to warm to room temperature, the reaction was quenched by slowly adding H_2O (5 mL). The layers were separated, and the organic layer was washed with H_2O (100 mL) and brine (100 mL). The organic layers were concentrated. Column chromatography (1% NEt_3 and 10% MeOH in CH_2Cl_2) yielded a slightly yellow oil (86:14 diastereomer ratio). Rapid stirring of the oil with hexanes (3 mL) resulted in the precipitation of a slightly yellow solid that was one diastereomer (1.50 g, 43%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 6 d *J* = 1.0), 6.76 (d,

1H, *J* = 1.2), 3.61 (s, 3H), 3.57 (dd, 1H, *J* = 11.0, 3.9), 3.43 (d, 1H, *J* = 7.6), 3.34-3.37 (m, 1H), 3.17-3.21 (bs, 1H), 2.07 (dd, 1H, *J* = 11.0, 4.2), 1.99 (dt, 1H, *J* = 21.0, 6.8), 1.55-1.62 (m, 2H), 1.07 (d, 3H, *J* = 6.8), 0.86 (d, 3H, *J* = 6.8), 0.79-0.87 (m, 6H); **^{13}C NMR** ($CDCl_3$ 26 M z δ 0 7 27 20 3 63 2 60 3 3 6 32 2 7 19.0; **IR**: 3219, 2958, 2198, 1467, 1281, 1047, 724, 439 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{26}N_3O$ $[M+H]^+$: 240.2076, found: 240.2079. **$[\alpha]_D^{20}$** = -27.9 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).



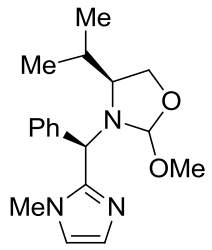
(*4S*)-4-isopropyl-2-methoxy-3-((*S*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine, 3.21 (99:1 dr) . (*S*)-3-methyl-2-((*S*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propylamino)butan-1-ol (1.01g, 4.18 mmol) was dissolved in methanol (17 mL) and sparged with nitrogen for 5 minutes. *N,N*-dimethylformamide dimethyl acetal (2.79 mL, 20.9 mmol) was added in one portion, and the solution was stirred 13 hours at 50 °C. The solution was concentrated under high vacuum. The yellow residue was dissolved in methanol (17 mL) and another portion (2.79 mL, 20.9 mmol) of *N,N*-dimethylformamide dimethyl acetal was added. After 3 hours, the solution was concentrated and stored in a dry glovebox. The yellow residue was distilled (150 °C at 0.25 torr) to yield a slightly yellow oil (994 mg, 84%). **^{1}H NMR** (C_6D_6 00 M z δ 7 20

(s, 1H), 6.37 (s, 0.05H), 6.30 (s, 0.95H), 5.41 (s, 0.05H), 5.35 (s, 0.95H), 3.97 (ddd, 1H, *J* = 13.2, 5.6, 1.2), 3.80 (dd, 1H, *J* = 7.8, 2.2), 3.65 (d, 0.08H, *J* = 10.8), 3.51 (t, 1H, *J* = 7.8), 3.43 (d, 0.92H, *J* = 10.3), 3.33 (s, 2.83H), 3.10 (s, 0.17H), 3.08 (s, 0.17H), 2.88 (s, 2.83H), 2.58-2.65 (m, 1H), 2.16-2.22 (m, 1H), 1.32 (d, 2.7H, *J* = 6.6), 1.25 (d, 0.3H, *J* = 6.6), 1.09 (d, 0.3H, *J* = 6.8), 1.03 (d, 2.7H, *J* = 6.6), 0.95 (d, 2.7H, *J* = 6.9), 0.90-0.92 (m, 0.3H), 0.82 (d, 2.7H, *J* = 6.6), 0.74 (d, 0.3H, *J* = 6.4); **^{13}C NMR** (C_6D_6 26 M z δ 147.5, 128.9, 120.4, 114.9, 66.7, 62.5, 61.6, 51.4, 32.7, 32.3, 31.8, 21.8, 21.0, 20.7, 17.6; **IR**: 2955, 2871, 1473, 1383, 1366, 1282, 1168, 1136, 1054, 959, 727 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{14}H_{24}N_3O$ [M-OMe]: 250.1919, found: 250.1920. **$[\alpha]_D^{20}$** = -12.5 (*c* = 1.20, $CDCl_3$, *l* = 50 mm).



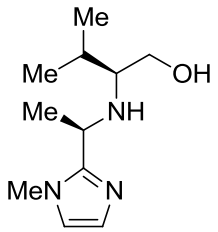
(*S*)-3-Methyl-2-(((*R*)-(1-methyl-1H-imidazol-2-yl)(phenyl)methyl)amino)butan-1-ol.[24] To a solution of benzaldehyde (2.0 mL, 2.0 x 10^1 mmol) in benzene (30 mL) was added (*S*)-valinol (2.0 g, 2.0 x 10^1 mmol) and 3Å molecular sieves (1.4 g). After refluxing for 24 hours, the reaction was cooled to room temperature, and the solvent was removed in vacuo. ^{1}H NMR analysis showed that the imine had formed. The resulting residue was redissolved in Et_2O (20 mL). In another oven-dried glass reaction flask, to a solution of *N*-methylimidazole (5.6 mL, 7.0 x 10^1 mmol) in anhydrous Et_2O (50 mL)

under nitrogen atmosphere was added *n*-butyllithium (7.0 mL, 10 M in hexanes, 7.0 x 10^1 mmol) dropwise at -78 °C. The solution was stirred at -78 °C for 30 minutes, and then slowly cannula transferred into the solution of pre-formed imine at -78 °C. The resulting mixture was stirred at -78 °C for 2 hours and then at room temperature overnight. Aqueous NH_4Cl was added slowly to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3x50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (3:1, Hex/EtOAc to 100% EtOAc) afforded pure product as a yellow oil (3.8 g, 70%). **^{1}H NMR** ($CDCl_3$, 500 M z δ 7 -7.28 (m, 5H), 6.97 (d, 1H, *J* = 1.0), 6.77 (d, 1H, *J* = 1.0), 4.91 (s, 1H), 3.63 (dd, 1H, *J* = 3.5, 11.0), 3.40 (dd, 1H, *J* = 8.0, 11.0), 3.26 (s, 3H), 2.49-2.53 (m, 1H), 1.67-1.71 (m, 1H), 0.96 (d, 3H, *J* = 6.5), 0.90 (d, 3H, *J* = 6.5); **^{13}C NMR** ($CDCl_3$ 2 M z δ 3 0 2 27 27 6 26 121.6, 63.7, 62.9, 59.4, 32.6, 31.7, 19.3; **IR**: 3339, 2955, 2870, 1492, 1281, 1048, 700 cm^{-1}; **HRMS** calcd. For $C_{16}H_{24}N_3O$ $[M+H]^+$: 274.1919, found: 274.1925.



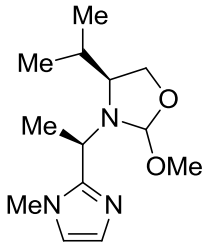
(4*S*)-4-isopropyl-2-methoxy-3-((*R*)-(1-methyl-1H-imidazol-2-yl)(phenyl)methyl)oxazolidine (56:44 dr). To a solution of (*S*)-3-methyl-2-(((*R*)-(1-methyl-1H-imidazol-2-yl)(phenyl)methyl)amino)butan-1-ol (1.0 g, 4.0 mmol) in

anhydrous methanol (16 mL) under nitrogen atmosphere was added *N*,*N*-dimethylformamide dimethyl acetal (0.53 mL, 4.0 mmol). The reaction was stirred at 50 °C overnight, concentrated, and redissolved in MeOH (16 mL). After stirring for 2 hours, ^{1}H NMR analysis showed complete conversion to product. The solvent was removed under vacuum and extraction with degassed pentanes afforded the product as an orange oil (820 mg, 65%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 66-7.96 (m, 1.12H), 7.44-7.47 (m, 0.88H), 6.92-7.12 (m, 3H), 6.29 (d, 0.44H, *J* = 1.5), 6.22 (s, 0.56H), 6.19 (d, 0.56H, *J* = 1.5), 5.88 (s, 0.44H), 5.17 (s, 0.44H), 5.01 (s, 0.56H), 4.00 (t, 0.56H, *J* = 8.0), 3.90 (t, 0.44H, *J* = 8.0), 3.10-3.15 (m, 0.44H), 3.05-3.08 (m, 0.56H), 3.01 (s, 1.32H), 2.86 (s, 1.68H), 2.82 (s, 1.68H), 2.74 (s, 1.32H), 1.70-1.77 (m, 1H), 0.91 (d, 1.68H, *J* = 7.0), 0.81 (d, 1.32H, *J* = 6.5), 0.75 (d, 1.32H, *J* = 6.5), 0.37 (d, 1.68H, *J* = 7.0); **^{13}C NMR** ($CDCl_3$, 2 M z δ 7 6 0 3 2 2 2 2 3 20 6 6 119.5, 112.4, 111.7, 66.7, 65.3, 64.3, 63.9, 59.6, 59.3, 52.3, 51.1, 31.6, 31.5, 30.5, 29.5, 29.4, 29.3, 19.5, 19.2, 19.1, 17.2, 14.3, 14.2; **IR**: 2953, 1490, 1279, 1157, 1055, 962, 700 cm^{-1}; **HRMS** ca1cd. for $C_{17}H_{22}N_3O$ [M-OMe]: 284.1762, found: 284.1748.



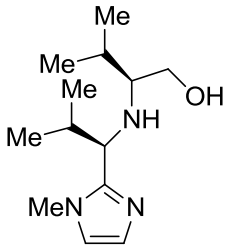
(*S*)-3-Methyl-2-(((*R*)-1-(l-methyl-lH-imidazol-2-yl)ethyl)amino)butan-1-ol.[24] To a stirring solution of (*S*)-valinol (2.0 g, 2.0 x 10^1 mmol) in anhydrous Et_2O (10 mL) under

nitrogen atmosphere was added a solution of acetaldehyde (1.1 mL, 2.0 x 10^1 mmol) in anhydrous Et_2O (10 mL). $MgSO_4$ (4.0 g) was added, and the solution was stirred at room temperature for 1 hour. ^{1}H NMR analysis showed that the imine had formed. In another oven-dried flask, to a solution of *N*-methylimidazole (5.6 mL, 7.0 x 10^1 mmol) in anhydrous Et_2O (50 mL) under nitrogen atmosphere was added *n*-butyllithium (7.0 mL, 10 M in hexanes, 7.0 x 10^1 mmol) dropwise at -78 °C. The solution was stirred at -78 °C for 30 minutes, and then slowly cannula transferred into the solution of pre-formed imine at -78 °C. The resulting mixture was stirred at -78 °C for 2 hours and then at room temperature overnight. Aqueous NH_4Cl was added slowly to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3x50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (3:1 Hex/EtOAc to 100% EtOAc) afforded pure product as a yellow oil (970 mg, 23%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 6 (d, 1H, *J* = 1.2), 6.72 (d, 1H, *J* = 1.2), 3.90 (q, 1H, *J* = 7.0), 3.55 (s, 3H), 3.47 (dd, 1H, *J* = 3.5, 11.0), 3.30 (dd, 1H, *J* = 8.5, 11.0), 2.25-2.29 (m, 1H), 1.56-1.61 (m, 1H), 1.31 (d, 3H, *J* = 7.0), 0.873 (d, 3H, *J* = 6.5), 0.871 (d, 3H, *J* = 6.5); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 7 26 2 2 63 3 62 32 3 2 6 2 **IR**: 3234, 2957, 1492, 1281, 1121, 1052, 725 cm^{-1}; **HRMS** calcd. for $C_{11}H_{22}N_3O$ $[M+H]^+$: 212.1762, found: 212.1764.



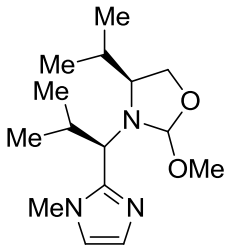
(4*S*)-4-Isopropyl-2-methoxy-3-((*R*)-1-(1-methyl-1H-imidazol-2-yl)ethyl)oxazolidine (90:10 dr). To a solution of (*S*)-3-methyl-2-(((*R*)-1-(1-methyl-lH-imidazol-2-yl)ethyl)amino)butan-1-ol (902 mg, 4.30 mmol) in anhydrous methanol (17 mL) under nitrogen atmosphere was added *N*,*N*-dimethylformamide dimethyl acetal (0.570 mL, 4.30 mmol). The reaction was stirred at room temperature for 2 hours, and the solvent was removed under vacuum. The residue was redissolved in anhydrous methanol (17 mL), and another 0.5 equivalents of *N*,*N*-dimethylformamide dimethyl acetal was added to the mixture. The reaction was again stirred at room temperature for 2 hours until ^{1}H NMR analysis showed all the substrate was consumed. The solvent was removed under vacuum. The flask was brought into a dry glove box under nitrogen atmosphere, and the residue was extracted with degassed pentanes to afford the pure product as a yellow oil (380 mg, 35%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 0 d 0.1H, *J* = 1.5), 7.02 (d, 0.9H, *J* = 1.0), 6.33 (d, 0.1H, *J* = 1.5), 6.31 (d, 0.9H, *J* = 1.0), 5.53 (s, 0.1H), 5.33 (s, 0.9H), 3.97 (q, 0.1H, *J* = 6.5), 3.88 (q, 0.9H, *J* = 6.5), 3.64-3.72 (m, 1.8H), 3.56-3.62 (m, 0.2H), 3.13 (s, 2.7H), 3.08-3.10 (m, 1H), 3.09 (s, 2.7H), 2.95 (s, 0.3H), 2.84 (s, 0.3H), 1.83 (d, 0.3H, *J* = 6.5), 1.51 (d, 2.7H, *J* = 6.5), 1.36-1.43 (m, 1H), 0.59 (d, 2.7H, *J* = 7.0), 0.56 (d, 0.3H, *J* = 7.0), 0.41 (d, 2.7H, *J* = 7.0), 0.38 (d, 0.3H, *J* = 7.0); **^{13}C NMR** ($CDCl_3$, 125 M z δ 7 7 26 20 4, 114.3, 112.0, 107.7. 67.6, 67.0, 61.2, 60.1, 52.2, 51.7, 50.4,

48.7, 46.0, 38.2, 31.4, 30.8, 30.4, 28.7, 19.0, 18.7, 17.1, 15.6, 13.5, 11.3; **IR**: 2954, 1496, 1281, 1153, 1068, 970, 728 cm^{-1}; **HRMS** calcd. for $C_{12}H_{20}N_3O$ [M-OMe]: 222.1606, found: 222.1615.



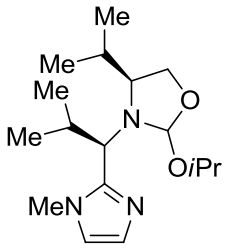
(*S*)-3-methyl-2-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propylamino)butan-1-ol, 3.22.[24] To a stirring solution of (*S*)-valinol (6.8 g, 66 mmol) in anhydrous Et_2O (66 mL) under nitrogen atmosphere was added a solution of isobutyraldehyde (4.8 g, 66 mmol) in anhydrous Et_2O (66 mL). $MgSO_4$ (13 g) was added, and solution was stirred at room temperature overnight. ^1H NMR analysis showed that the imine had formed. In another oven-dried flask, to a solution of *N*-methylimidazole (19 g, 230 mmol) in anhydrous THF (160 mL) under nitrogen atmosphere was added *n*-butyllithium (23 mL, 10 M in hexanes, 230 mmol) dropwise at –78 °C. The solution was stirred at –78 °C for 30 minutes, and then slowly cannula transferred into the solution of pre-formed imine at –78 °C. The resulting mixture was stirred at –78 °C for 2 hours and then at room temperature overnight. Aqueous NH_4Cl was added slowly to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3×100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography (2:1 Hex/EtOAc to 100% EtOAc) afforded pure product as a

colorless oil (12 g, 76%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 6.93 (d, 1H, *J* = 1.2), 6.78 (d, 1H, *J* = 1.2), 3.56-3.57 (m, 4H), 3.35 (d, 1H, *J* = 1.2), 3.34 (d, 1H, *J* = 3.9), 2.13-2.17 (m, 1H), 1.87-1.93 (m, 1H), 1.62-1.68 (m, 1H), 0.98 (d, 3H, *J* = 6.8), 0.93 (d, 3H, *J* = 6.8), 0.88 (d, 3H, *J* = 2.9), 0.87 (d, 3H, *J* = 2.9); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 151.7, 127.0, 121.3, 64.2, 62.9, 60.4, 34.0, 32.9, 31.7, 20.2, 19.5, 19.4, 17.7; **IR**: 2956, 2871, 1488, 1468, 1280, 1045, 725 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{13}H_{26}N_3O$ $[M+H]^+$: 240.2076, found: 240.2087. **$[\alpha]_D^{20}$** = +40.0 (*c* = 1.0, CH_2Cl_2, *l* = 50 mm).



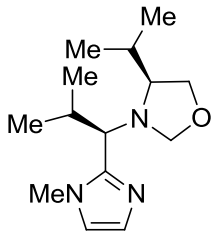
(*4S*)-4-isopropyl-2-methoxy-3-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine, III (99:1 dr). To a solution of (*S*)-3-methyl-2-(((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)amino)butan-1-ol (4.3 g, 18 mmol) in anhydrous methanol (36 mL) under nitrogen atmosphere was added *N,N*-dimethylformamide dimethyl acetal (12 mL, 9.0 x 10^1 mmol). The reaction was stirred at 50 °C overnight, concentrated, and redissolved in methanol. After stirring for 2 hours, ^{1}H NMR analysis showed complete conversion to product. The solvent was removed under vacuum, and Kugelrohr distillation (130 °C at 0.05 mmHg) afforded the product as a colorless oil (3.7 g, 73%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.12 (d, 1H, *J* = 1.2), 6.80 (s, 1H), 6.20 (d, 1H, *J* = 1.2), 3.70 (dd, 1H, *J* = 9.0, 8.1), 3.52 (dd, 1H, *J* = 7.8, 7.1), 3.29 (s, 3H), 3.22 (d, 1H, *J*

= 10.8), 2.78 (s, 3H), 2.55-2.64 (m, 2H), 1.63-1.72 (m, 1H), 1.34 (d, 3H, *J* = 6.4), 0.85 (d, 3H, *J* = 6.8), 0.66 (d, 3H, *J* = 6.8), 0.63 (d, 3H, *J* = 6.6); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 148.8, 128.7, 120.1, 112.4, 66.1, 65.8, 60.5, 52.7, 33.7, 32.2, 29.5, 21.6, 21.0, 20.2, 16.9; **IR**: 2956, 1470, 1281, 1052, 964 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{14}H_{24}N_3O$ [M-OMe]: 250.1919, found: 250.1926. **$[\alpha]_D^{20}$** = -57.0 (*c* = 1.0, CH_2Cl_2, *l* = 50 mm).



(*4S*)-2-isopropoxy-4-isopropyl-3-((*S*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine, 3.41. In a dry glove-box, (*4S*)-4-isopropyl-2-methoxy-3-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine (138 mg, 0.490 mmol) was dissolved in benzene (2.5 mL) in a scintillation vial and *i*PrO 2 μ 7 mmol and 10 molecular sieves (4 Å) were added. After sitting overnight, the sieves were filtered out of the solution and washed with benzene (3x1 mL). The solution was concentrated to obtain a colorless oil (121 mg, 80%). **^{1}H NMR** (C_6D_6 00 M z δ 7 20 d *J* = 1.0), 6.98 (s, 1H), 6.27 (d, 1H, *J* = 1.2), 4.35 (app heptet, 1H, *J* = 6.1), 3.80-3.83 (m, 1H), 3.57-3.60 (m, 1H), 3.28 (d, 1H, *J* = 11.0), 2.85 (s, 3H), 2.66-2.73 (m, 1H), 2.58-2.62 (m, 1H), 1.71-1.77 (m, 1H), 1.48 (d, 3H, *J* = 6.6), 1.30 (d, 3H, *J* = 6.1), 1.24 (d, 3H, *J* = 6.1), 0.94 (d, 3H, *J* = 6.8), 0.75 (d, 3H, *J* = 6.8), 0.72 (d, 3H, *J* = 6.6); **^{13}C NMR** (C_6D_6, 126 M z δ 0 2 20 0 0 7 6 66 6 60 33 7 32 2 2 6 2 6 23 2

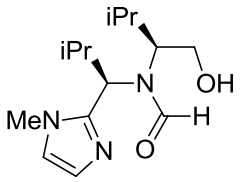
21.6, 21.1, 20.3, 17.0; **IR**: 2958, 2870, 1471, 1380, 1366, 1281, 1139, 1104, 1034, 980, 950, 729 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{14}H_{24}N_3O$ [M-O*i*Pr]: 250.1919, found: 250.1911. $[\alpha]_D^{20}$ = -42.0 (*c* = 0.93, $CDCl_3$, *l* = 50 mm).



(*S*)-4-isopropyl-3-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine, 3.23.[25] To a stirring solution of (*S*)-3-methyl-2-(((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)amino)butan-1-ol (720 mg, 3.0 mmol) and paraformaldehyde (91 mg, 3.0 mmol) in anhydrous toluene (30 mL), *p*-toluenesulfonic acid monohydrate (5.7 mg, 3.0 × 10^{-2} mmol) was added. After refluxing overnight, reaction was cooled to room temperature, and CH_2Cl_2 (30 mL) was added. The resulting solution was concentrated. Flash column chromatography (100% EtOAc) afforded the product as a colorless oil (520 mg, 68%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.00 (d, 1H, *J* = 1.2), 6.73 (d, 1H, *J* = 1.2), 5.01 (d, 1H, *J* = 4.6), 4.34 (d, 1H, *J* = 4.4), 3.61 (s, 3H), 3.40-3.42 (m, 3H), 2.57 (dd, 1H, *J* = 12.7, 6.6), 2.17-2.27 (m, 1H), 1.65-1.75 (m, 1H), 1.12 (d, 3H, *J* = 6.6), 0.93 (d, 3H, *J* = 6.8), 0.86 (d, 3H, *J* = 6.6), 0.66 (d, 3H, *J* = 6.6); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 147.9, 127.9, 120.3, 81.8, 67.6, 67.2, 62.8, 33.1, 33.0, 31.0, 21.1, 20.2, 20.0, 18.1; **IR**: 2955, 2868, 1468, 1279, 1140, 1084, 945, 724 cm^{-1}; **HRMS** (DART-TOF) calcd. for

[25]Agami, C.; Couty, F.; Rabasso, N. *Tet. Lett.* **2002**, *43*, 4633-4636.

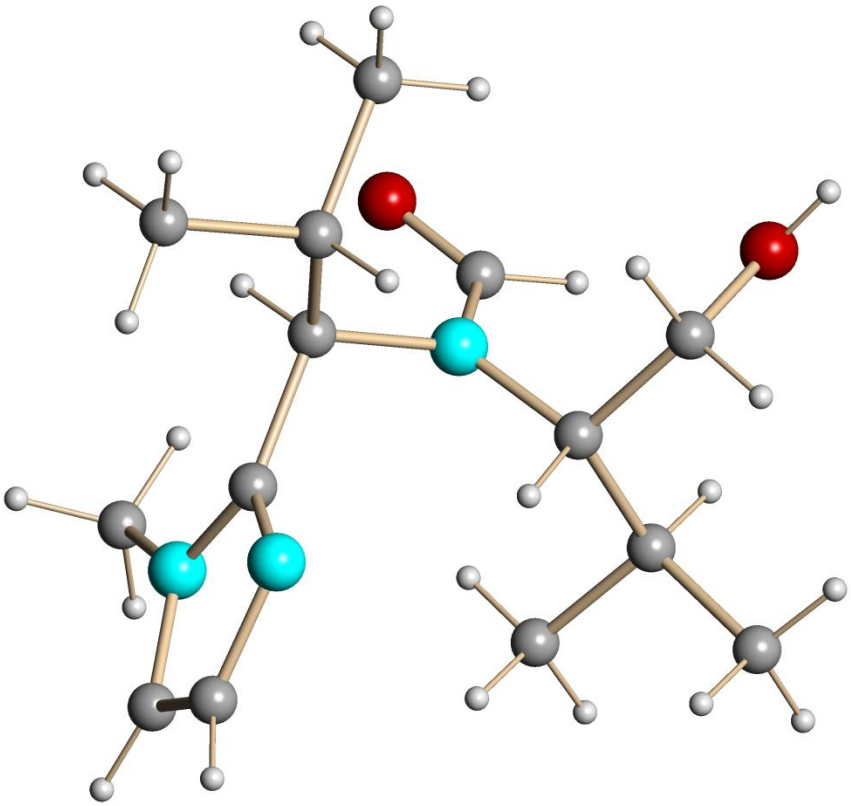
$C_{14}H_{26}N_3O$: $[M+H]^+$: 252.2076, found: 252.2075. $\mathbf{[\alpha]_D^{20}}$ = +32.0 (*c* = 1.0, CH_2Cl_2, *l* = 50 mm).



***N*-((*S*)-1-hydroxy-3-methylbutan-2-yl)-*N*-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)formamide, decomp-III.** Hydrolysis of (*S*)-3-methyl-2-(((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)amino)butan-1-ol, catalyst **III**, (25 mg, 8.9×10^{-2} mmol) by flash column chromatography (40:1, CH_2Cl_2:MeOH) afforded the product as a white solid (21 mg, 88%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.45 (s, 1H), 6.95 (d, 1H, *J* = 1.2), 6.79 (d, 1H, *J* = 1.2), 5.54 (d, 1H, *J* = 11.2), 3.97 (ddd, 1H, *J* = 11.7, 4.4, 2.9), 3.76 (dq, 1H, *J* = 11.7, 2.7), 3.60 (s, 3H), 3.49 (dt, 1H, *J* = 10.3, 2.7), 2.33-2.43 (m, 1H), 2.17 (t, 1H, *J* = 4.9), 1.90-2.00 (m, 1H), 1.06 (d, 3H, *J* = 6.6), 0.83 (d, 6H, *J* = 6.4), 0.08 (d, 3H, *J* = 6.8); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 164.3, 144.9, 127.4, 120.9, 61.6, 60.3, 52.6, 32.9, 29.3, 28.7, 20.3, 20.2, 20.0, 17.7; **IR**: 2963, 1648, 1490, 1248, 1080, 730 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{14}H_{26}N_3O_2$: $[M+H]^+$: 268.2025, found: 268.2034. $\mathbf{[\alpha]_D^{20}}$ = +48.0 (*c* = 1.0, CH_2Cl_2, *l* = 50 mm).

Crystal Structure

In order to get confirmation of the relative stereochemistry, **III** was hydrolyzed to the more crystalline compound **decomp-III**. It was crystallized out of pentanes at 25°C in a glove box.



Equilibrium Experiment of **3.11** with *i*PrOH (Scheme 3.9)

In a glovebox, a solution of catalyst **3.11** (10.0 mg, 4.17 x 10^{-2} mmol) and *N*,*N*-diisopropylethylamine hydrochloride (6.91 mg, 4.17 x 10^{-2} mmol) in anhydrous C_6D_6 00 µ was made and dispensed into an NMR t e *i*PrOH (0.209 mmol, 00 µ 0 7

M solution in C_6D_6, 5 equiv) was added to the NMR tube. The reaction was monitored by ^{1}H NMR. After 15 hours, equilibrium was reached. A ratio of 48:52, **3.11** to **3.12** gave a K_{eq} of 0.126. The equilibrium experiment was repeated with 10 eq *i*PrOH (0.417 mmol) which gave a ratio of 34:66, **3.11** to **3.12**, and a K_{eq} of 0.137. The average K_{eq} was 0.131.

Procedure for the Initial Studies of the Selective Functionalization of 1,2-Diols

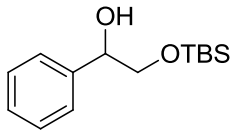
GC Method. An Agilent Technologies 7890A GC System equipped with a 7683B Series Injector was used to introduce samples into a J&W Scientific column (HP-5, 30 m, 0.320 mm ID 0 2 μm film he G wa s r n at 00 ° for 0 mi n tes a nd then the temperature was ramped 8 °C/min. to a final temperature of 180 °C. Compounds were detected by FID and data was analyzed with Agilent Technologies GC Chemstation software. Retention times are reported in minutes.

Scheme 3.10, Eq. 1

In an oven-dried reaction vial, 1-phenyl-1,2-ethanediol, **3.13**, (28 mg, 0.20 mmol) was dissolved in anhydrous THF (0.5 mL). *N*-methylimidazole 3 2 μ 4.0 x 10^{-2} mmol, 20 mol %) was added, and the reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 μ 0 2 mm ol was added followed y addition of a sol ti on of *tert*-butylchlorodimethylsilane (33 mg, 0.20 mmol) in anhydrous THF (0.5 mL). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 μ and methanol μ he mi t re was stirred at room temperature for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the selectivity of the reaction.

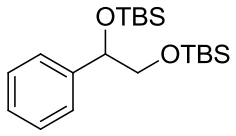
Scheme 3.10, Eq. 2

To an oven-dried reaction vial, a solution of 1-phenyl,-1,2-ethanediol, **3.13**, (28 mg, 0.20 mmol) and **3.11** (9.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (0.5 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 µ 0 2 mm ol was added followed y addition of a sol ti on of *tert*-butylchlorodimethylsilane (33 mg, 0.20 mmol) in anhydrous THF (0.5 mL). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 µ and methanol µ he mi t re was stirred at room temperature for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the selectivity of the reaction.

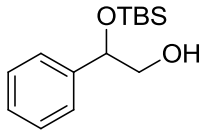


2-((*tert*-Butyldimethylsilyl)oxy)-1-phenylethanol, 3.14. A 100 mL flask was charged with *tert*-butyldimethylsilyl chloride (545 mg, 3.62 mmol) in THF (18 mL). *N*,*N*-Diisopropylethylamine (0.630 mL, 3.62 mmol), *N*-methylimidazole (5.80 x 10^{-2} mL, 0.720 mmol) and 1-phenyl-1,2-ethanediol, **3.13**, (501 mg, 3.62 mmol) in THF was slowly added as a mixture. The reaction was allowed to stir for 48 hours before quenching with MeOH. The resulting mixture was evaporated in vacuo and the crude product was purified on silica gel with 5% EtOAc/Hex to yield 631 mg (69%) of the title compound as a clear oil. **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 2 -7.39 (m, 5H), 4.74-4.77 (m, 1H), 3.78

(dd, lH, *J* = 4.0, 10.0), 3.56 (dd, 1H, *J* = 8.5, 10.0), 3.00 (d, 1H, *J* = 2.0), 0.93 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 0 3 28.3, 127.7, 126.2, 74.4, 68.9, 25.9, 18.3, -5.3, -5.4; **IR**: 3443, 3063, 2953, 2856, 1253, 1103, 833, 698 cm^{-1}; **HRMS** calcd. for $C_{14}H_{25}O_2Si$ $[M-H]^+$: 253.1623, found: 253.1617. **GC Method**: 76.2 min.



2,2,3,3,8,8,9,9-Octamethyl-5-phenyl-4,7-dioxa-3,8-disiladecane. A 100 mL flask was charged with *tert*-butyldimethylsilyl chloride (2.40 g, 15.9 mmol) in THF (18 mL). *N*-methylimidazole (1.30 mL, 15.9 mmol) and 1-phenyl-1,2-ethanediol, **3.13**, (1.01 g, 7.24 mmol) in THF was slowly added as a mixture. The reaction was allowed to stir for 48 hours before quenching with MeOH. The resulting mixture was evaporated in vacuo and the crude product was purified on silica gel with 2% EtOAc/Hex to yield 1.30 g (49%) of the title compound as a clear oil. **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 26-7.38 (m, 5H), 4.73 (dd, 1H, *J* = 5.5, 7.5), 3.70 (dd, 1H, *J* = 7.0, 10.5), 3.58 (dd, 1H, *J* = 5.0, 10.0), 0.92 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.001 (s, 3H), -0.01 (s, 3H), -0.02 (s, 3H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 2 27 27 2 26 76 70 1, 26.0, 25.9, 18.4, 18.3, -4.6, -4.8, -5.4, -5.5; **IR**: 2954, 2928, 2856, 1471, 1253, 1095, 830, 774 cm^{-1}; **HRMS** calcd. for $C_{20}H_{42}NO_2Si_2$ $[M+NH_4]^+$: 384.2763, found: 384.2754. **GC Method**: 91.7 min.



2-((*tert*-Butyldimethylsilyl)oxy)-2-phenylethanol, 3.15. A 100 mL flask was charged with 2,2,3,3,8,8,9,9-octamethyl-5-phenyl-4,7-dioxa-3,8-disiladecane (1.30 g, 3.55 mmol) in ethanol (7 mL), followed by addition of pyridinium *p*-toluenesulfonate (0.892 g, 3.55 mmol). The reaction was allowed to stir for 13 hours before quenching with triethylamine. The crude mixture was evaporated in vacuo and the crude product was purified on silica gel eluting with 5% EtOAc/Hex to yield 647 mg (72%) of the title compound as a colorless oil. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7 26-7.35 (m, 5H), 4.76 (dd, 1H, *J* = 4.5, 7.5), 3.57-3.60 (m, 2H), 2.07 (dd, 1H, *J* = 5.0, 8.5), 0.91 (s, 9H), 0.07 (s, 3H), -0.09 (s, 3H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 2 3 27 7 26 3 7 6 25.8, 25.6, 18.2, -4.5, -5.0; **IR**: 3433, 2953, 2856, 1252, 1098, 912, 776, 698 cm^{-1}; **HRMS** calcd. for $C_{14}H_{25}O_2Si$ $[M+H]^+$: 253.1623, found: 253.1620. GC Method: 61.3 min.

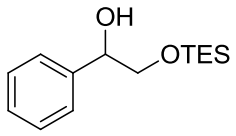
Scheme 3.11, Eq. 1

In an oven-dried reaction vial, 1-phenyl-1,2-ethanediol, **3.13**, (28 mg, 0.20 mmol) was dissolved in anhydrous THF (1.0 mL). *N*-methylimidazole 3 2 μ 4.0 x 10^{-2} mmol, 20 mol %) was added, and the reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 μ 0 2 mm ol was added followed y triethylchlorosilane 36 μ 0 20 mmol After stirring at room temperat re for 2 h o rs the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 μ and methanol μ he mixture was stirred at room temperature for 10 min and filtered through a Pasteur pipette

packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the selectivity of the reaction.

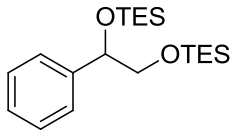
Scheme 3.11, Eq. 2

To an oven-dried reaction vial, a solution of 1-phenyl,-1,2-ethanediol, **3.13**, (28 mg, 0.20 mmol) and **3.11** (9.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (1.0 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 µ 0 2 mm ol was added followed y triethylchlorosilane 36 µ 0 20 mmol A fter stirring at room temperat re for 2 h o rs the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 µ and methanol µ he mixture was stirred at room temperature for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the selectivity of the reaction.

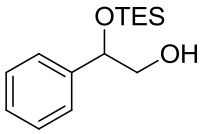


1-phenyl-2-((triethylsilyl)oxy)ethanol, 3.16. A 100 mL flask was charged with triethylchlorosilane (1.09 g, 7.24 mmol) in THF (18 mL). *N*-methylimidazole 7 µ 7.24 mmol) and l-phenyl-1,2-ethanediol, **3.13**, (1.0 g, 7.24 mmol) in THF (18 mL) was slowly added as a mixture. The reaction was allowed to stir for 48 hours before quenching with MeOH. The resulting mixture was evaporated in vacuo and the crude product was purified on silica gel with 2% EtOAc/Hex to yield 898 mg (49%) of the title compound as a clear oil. **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 29-7.42 (m, 5H), 4.77-4.79 (m,

1H), 3.79 (dd, 1H, *J* = 3.5, 10.0), 3.59 (dd, 1H, *J* = 9.0, 10.5), 3.17 (d, 1H, *J* = 2.0), 1.01 (t, 9H, *J* = 8.0), 0.66 (q, 6H, *J* = 8.0); **^{13}C NMR** ($CDCl_3$ 00 M z δ 0 2 3 127.7, 126.2, 74.5, 68.7, 6.7, 4.4; **IR:** 3456, 2954, 2876, 1454, 1104, 1005, 743, 699 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{14}H_{25}O_2Si$ $[M+H]^+$: 253.1623, found: 253.1624. **GC Method:** 88.2 min.



3,3,8,8-Tetraethyl-5-phenyl-4, 7-dioxa-3,8-disiladecane. A 100 mL flask was charged with triethylchlorosilane (2.40 g, 15.9 mmol) in THF (9 mL). *N*-methylimidazole (1.30 g, 15.9 mmol) and 1-phenyl-1,2-ethanediol, **3.13**, (1.01 g, 7.24 mmol) in THF (9 mL) was slowly added as a mixture. The reaction was allowed to stir for 96 hours before quenching with MeOH. The resulting mixture was evaporated in vacuo and the crude product was purified on silica gel with 2% EtOAc/Hex to yield 824 mg (31%) of the title compound as a clear oil. **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 26-7.39 (m, 5H), 4.75 (dd, 1H, *J* = 5.0, 7.0), 3.72 (dd, 1H, *J* = 7.0, 10.0), 3.60 (dd, 1H, 5.0, 10.0), 0.92-0.97 (m, 18H), 0.55-0.65 (m, 12H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 2 27 27 2 26 7 69.6, 6.8, 6.7, 4.9, 4.4; **IR**: 2953, 2876, 1124, 1095, 1004, 723, 697 cm^{-1}; **HRMS** calcd. for $C_{20}H_{39}O_2Si_2$ $[M+H]^+$: 367.2488, found: 367.2495. **GC Method**: 98.4 min.



2-Phenyl-2-((triethylsilyl)oxy)ethanol, 3.17. A 50 mL flask was charged with 3,3,8,8-tetraethyl-5-phenyl-4,7-dioxa-3,8-disiladecane (831 mg, 2.26 mmol) in ethanol (5 mL), followed by addition of pyridinium *p*-toluenesulfonate (572 mg, 2.26 mmol). The reaction was allowed to stir for 14 hours before quenching with triethylamine. The crude mixture was evaporated in vacuo and the crude product was purified on silica gel eluting with 2% EtOAc/Hex to yield 281 mg (49%) of the title compound as a clear oil. **^{1}H NMR** ($CDCl_3$ 00 M z δ 7.26-7.33 (m, 5H), 4.76 (dd, 1H, *J* = 4.5, 7.5), 3.57-3.60 (m, 2H), 2.12 (dd, 1H, *J* = 5.0, 8.5), 0.89 (t, 9H, *J* = 8.5), 0.59 (q, 6H, *J* = 8.5); **^{13}C NMR** ($CDCl_3$, 00 M z δ 128.2, 127.7, 126.2, 75.6, 68.9, 6.7, 4.8; **IR**: 3406, 2953, 2875, 1454, 1098, 1004, 725, 698 cm^{-1}; **HRMS** calcd. for $C_{14}H_{25}O_2Si$ $[M+H]^+$: 253.1623, found: 253.1634. **GC Method**: 85.1 min.

Reaction of **3.11** with Individual Enantiomers (Scheme 3.12, Eq 1)

To an oven-dried reaction vial, a solution of (*S*)-1-phenyl-1,2-ethanediol, (*S*)-**3.13**, (28 mg, 0.20 mmol), *N*,*N*-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %), and **3.11** (9.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 μ 0 2 mm ol 1.2 equiv) was added, followed by triethylchlorosilane 36 μ 0 20 mmol 0 eq iv). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 μ and methanol μ he mi t re was stirred at room temperature for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Reaction of **3.11** with Individual Enantiomers (Scheme 3.12, Eq 2)

To an oven-dried reaction vial, a solution of (*R*)-1-phenyl-1,2-ethanediol, (*R*)-**3.13**, (28 mg, 0.20 mmol), *N*,*N*-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %), and **3.11** (9.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 µ 0 2 mm ol 2 eq iv) was added, followed by triethylchlorosilane 36 µ 0 20 mmol 0 eq iv). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 µ and methanol µ he mi t re was stirred at room temperat re for 0 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Catalyst Optimization Procedure with **3.13** (Table 3.2)

To an oven-dried reaction vial, a solution of (*R*)-1-phenyl-1,2-ethanediol, (*R*)-**3.13**, (28 mg, 0.20 mmol), *N*,*N*-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %), and catalyst (20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 µ 0 2 mmol, 1.2 equiv) was added, followed by triethylchlorosilane 36 µ 0 20 mmol 0 equiv). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 µ and methanol µ he mi t re was stirred at room temperature for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Table 3.2

R= *t*Bu (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= *i*Pr, **3.11**, (9.6 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= *i*Bu (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= Me (9.1 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= H (8.5 mg, 4.0 x 10^{-2} mmol, 20 mol %)

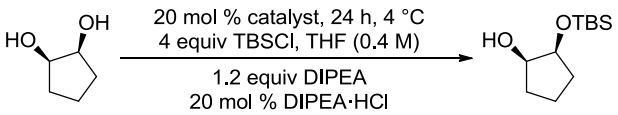
R= Ph (12 mg, 4.0 x 10^{-2} mmol, 20 mol %)

Stereoselective Functionalization of Diols

General Catalyst Optimization Procedure with **3.18**

To an oven-dried glass reaction vial, a solution of *cis*-1,2-cyclopentanediol, **3.18** (2.0 x 10^{1} mg, 0.20 mmol), catalyst (4.0 x 10^{-2} mmol, 20 mol %), and *N*,*N* diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (0.25 mL) was added. The reaction was stirred at 4 °C for 10 minutes. *N*,*N*-diisopropylethylamine (42 μL, 0.24 mmol, 1.2 equiv) was added, followed by addition of a solution of *tert*-butylchlorodimethylsilane (120 mg, 0.80 mmol, 4.0 equiv) in anhydrous THF (0.25 mL). After stirring at 4 °C for 24 hours, the reaction was quenched by addition of *N,N*-diisopropylethylamine (100 μL) and methanol (30 μL). The mixture was stirred for 10 minutes and filtered through a Pasteur pipette packed with silica gel, followed by flush with EtOAc (15 mL). To the combined filtrate, 1,3,5-trimetho y e nzene 0 μ of 0.40M in EtOAc, 0.020 mmol) was added as internal standard. Chiral GLC Analysis (Supelco Beta Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 78 °C for 100 min,

20 °C/min to 180 °C, 180 °C for 20 min, 15 psi.) of crude product afforded yields and enantioselectivities of **3.19**.



3.18 **3.19**

	Major Prod c t na ntiomer	Minor Prod c t na ntiomer	Diol S st rate	Internal Standard
G Ret ime	7 mi n	0 mi n	03 mi n	0 mi n
Response Factor[a]	0 62	0 62	7	00

[a]Response factors were calculated against internal standard on GLC. [b]1,3,5-trimethoxybenzene was used as an internal standard.

Initial Catalyst Optimization (Table 3.3)

R= Me (9.1 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= *i*Bu (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= *i*Pr, **3.11**, (9.6 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= *t*Bu (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

(*S, S*) and (*S, R*)-Catalysts (Table 3.4)

R= (*S*)-Me (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*S*)-*i*Pr (11 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*R*)-Me (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*R*)-Ph (13 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*R*)-*i*Pr, **III**, (11 mg, 4.0 x 10^{-2} mmol, 20 mol %)

General Optimization Procedure:

To an oven-dried glass reaction vial, a solution of *cis*-1,2-cyclopentanediol, **3.18** (2.0 x 10^1 mg, 0.20 mmol), **III** (11 mg, 4.0 x 10^{-2} mmol, 20 mol %), and N,N-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (0.25 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-diisopropylethylamine (42 μL, 0.24 mmol, 1.2 equiv) was added, followed by addition of a solution of *tert*-butylchlorodimethylsilane (120 mg, 0.80 mmol, 4.0 equiv) in anhydrous THF (0.25 mL). After stirring at room temperature for 4 hours, the reaction was quenched by addition of *N,N*-diisopropylethylamine (100 μL) and methanol (30 μL). The mixture was stirred at room temperature for 10 minutes and filtered through a Pasteur pipette packed with silica gel, followed by flush with EtOAc (15 mL). To the combined filtrate, 1,3,5-trimetho y e nzene 0 μ of 0 0M i n tOA c 0 020 mmol was added as internal standard. Chiral GLC Analysis (Supelco Beta Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 78 °C for 100 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi.) of crude product, **3.19**, afforded yields and enantioselectivities.

Time Course with **III** (Table 3.5)

The General Optimization Procedure was followed except the reaction time was 8 hours for entry 2.

Catalyst Loading Screen (Table 3.6)

The General Optimization Procedure was followed using 5 mol % (2.8 mg, 1.0 x 10^{-2} mmol), 10 mol % (5.6 mg, 2.0 x 10^{-2} mmol), and 20 mol % (11 mg, 4.0 x 10^{-2} mmol) of **III**.

1,2,2,6,6-Pentamethylpiperdine as the Base (Scheme 3.16)

The General Optimization Procedure was followed using 1,2,2,6,6-pentamethylpiperidine (44 μL, 0.24 mmol, 1.2 equiv) instead of *N*,*N*-diisopropylethylamine as the base.

Time Screen with PMPP and PMPP·HCl (Table 3.7)

To an oven-dried glass reaction vial, a solution of *cis*-1,2-cyclopentanediol, **3.18** (2.0 x 10^1 mg, 0.20 mmol), **III** (11 mg, 4.0 x 10^{-2} mmol, 20 mol %), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (1.2 mg, 6.0 x 10^{-3} mmol, 3 mol %) in anhydrous THF (0.25 mL) was added. The reaction was stirred at room temperature for 10 minutes. 1,2,2,6,6-pentamethylpiperidine (44 μL, 0.24 mmol, 1.2 equiv) was added, followed by addition of a solution of *tert*-butylchlorodimethylsilane (121 mg, 0.80 mmol, 4.0 equiv) in anhydrous THF (0.25 mL). After stirring at room temperature for 2 or 4 hours, the reaction was quenched by addition of *N,N*-diisopropylethylamine (100 μL) and methanol (30 μL). The mixture was stirred at room temperature for 10 minutes and filtered through a Pasteur pipette packed with silica gel, followed by flush with EtOAc (15 mL). To the combined filtrate, 1,3,5-trimetho y e nzene 0 μ of 0 0M i n tOA c 0 020 mmol was added as internal standard. Chiral GLC Analysis (Supelco Beta Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 78 °C for 100 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi.) of crude product afforded yields and enantioselectivities.

Concentration Screen (Table 3.8)

The procedure for Table 3.7 was followed using 2.0 equiv TBSCl (120 mg, 0.80 mmol), running the reaction for 4 hours, and varying the concentration of the reaction.

Concentrations: 0.2 M (1 mL), 0.4 M 00 μ 0 M 200 μ

Reaction with a Control Catalyst (Scheme 3.17)

The procedure for Table 3.8 was followed using **3.23** (1.0×10^{-1} mg, 4.0×10^{-2} mmol, 20 mol %) as the catalyst in THF (0.4 M).

Reaction Run in *t*BuOH (Scheme 3.18)

The procedure for Table 3.8 was followed using *t*BuOH (0.4 M) as the solvent.

Reaction of (1*R*,2*S*,*Z*)-cyclooct-5-ene (Scheme 3.19)

The procedure for Table 3.7 was followed using (1*R*,2*S*,*Z*)-cyclooct-5-ene, **3.31**, (28 mg, 0.20 mmol), and the reaction was run for 24 h at 4 °C.

Substrate Synthesis

The following compounds were made according to literature procedures and matched reported spectra: (*1R,2S*)-cyclohex-4-ene-1,2-diol[26], (*1R,2S*)-cycloheptane-1,2-diol[26], (*1R,3S*)-cyclopentane-1,3-diol[27].

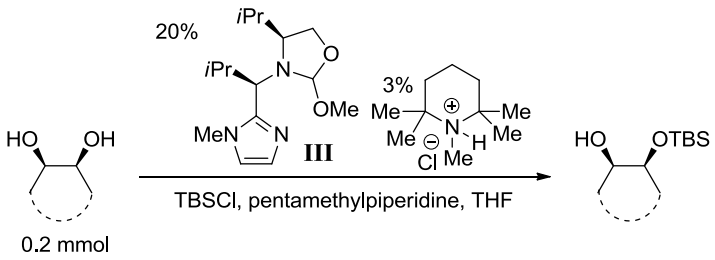
General Procedure for Substrate Scope (Table 3.9)

To an oven-dried glass reaction vial, a solution of *cis*-1,2-cyclopentanediol, **3.18**, (41 mg, 0.40 mmol), catalyst **III** (22 mg, 8.0×10^{-2} mmol, 20 mol %), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (2.3 mg, 1.2×10^{-2} mmol, 3 mol %) in anhydrous THF (0.50 mL) was added. The reaction was stirred at room temperature for 10 minutes. 1,2,2,6,6-pentamethylpiperidine (87 μL, 0.48 mmol, 1.2 equiv) was added, followed by addition of a solution of *tert*-butylchlorodimethylsilane (120 mg, 0.80 mmol, 2.0 equiv) in anhydrous THF (0.50 mL). After stirring at room temperature for 4 hours, the reaction

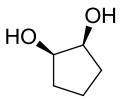
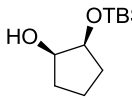
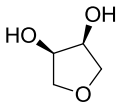
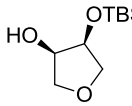
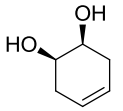
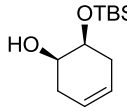
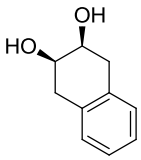
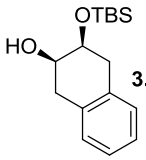
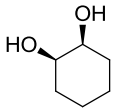
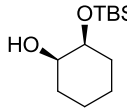
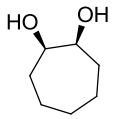
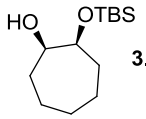
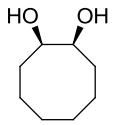
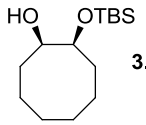
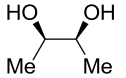
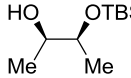
[26]Alvarez, E.; Diaz, M. T.; Perez, R.; Ravelo, J. L.; Regueiro, A.; Vera, J. A.; Zurita, D.; Martin, J. D. *J. Org. Chem.* **1994**, *59*, 2848-2876. [27]Chen, Z.; Halterman, R. L. *Organometallics* **1994**, *13*, 3932-3942.

was quenched by addition of *N,N*-diisopropylethylamine (200 μL) and methanol (60 μL). The mixture was stirred at room temperature for 10 minutes and was concentrated. Flash column chromatography (Hex/EtOAc = 20/1) afforded pure product, **3.19**, as a colorless oil (81 mg, 92%, 94% ee). Chiral GLC Analysis (Supelco Beta Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 78 °C for 100 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi.).

Table 3.9 Substrate Scope



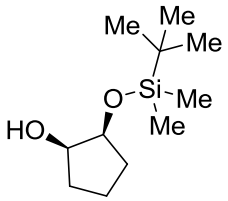
0.2 mmol

entry	substrate	product		yield (%)[a]	ee (%)[b]	yield (%)[a]	ee (%)[b]	ave. yield (2 runs)	ave. ee (2 runs)
1[c]			**3.19**	92[d]	94[d]	84	97	88	96
2[e]			**3.24**	73	92	85	85	79	89
3[g]			**3.25**	85	90	88[d]	90[d]	87	90
4[f]			**3.26**	90	94	85	95	88	95
5[g]			**3.27**	87[d]	92[d]	85	91	86	92
6[h]			**3.28**	83	90	80	90	82	90
7[i]			**3.29**	94	86	91	85	93	86
8[j]			**3.30**	78	91	77	88	78	90

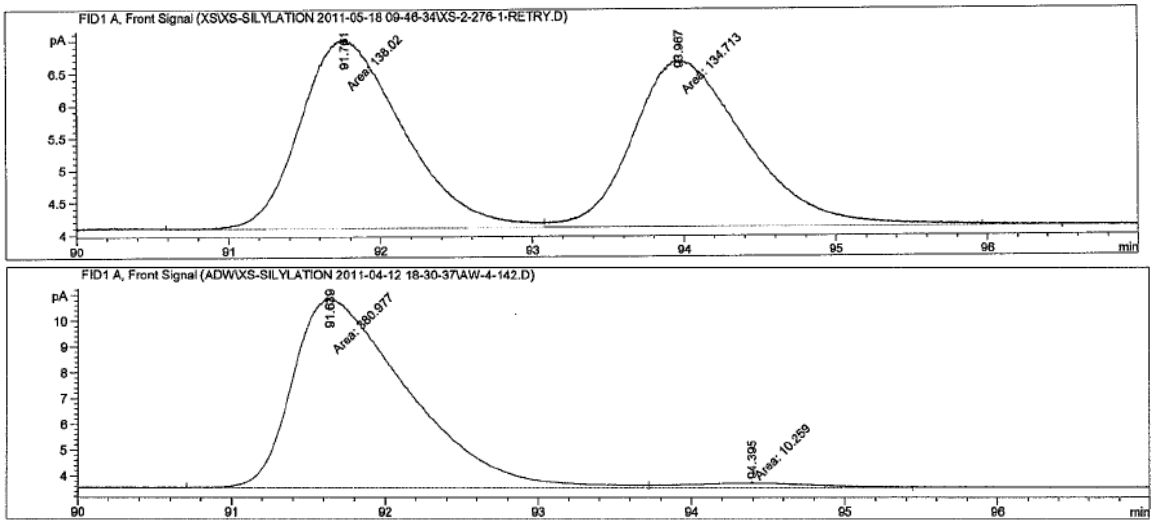
[a]Isolated yields. [b]Ees determined using a chiral GC column. [c]Using 2 equiv TBSCl and 1.2 equiv PMPP at 0.4 M for 4 h. [d]Run on 0.4 mmol substrate. [e]Using 4 equiv TBSCl and 1.2 equiv PMPP at 0.2 M for 24 h. [f]Using 2 equiv TBSCl and 1.2 equiv PMPP at 0.2 M for 8 h.[g]Using 2 equiv TBSCl and 1.2 equiv PMPP at 0.2 M for 12 h. [h]Using 4 equiv TBSCl and 2 equiv PMPP for 24 h at 4 °C. [i]Using 4 equiv TBSCl and 2 equiv PMPP for 24 h at rt. [j]Using 4 equiv TBSCl and 2 equiv PMPP for 36 h at 4 °C.

Desymmetrization Product Characterization

Table 3.9, Entry 1.

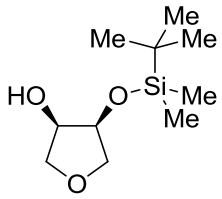


(*1R,2S*)-2-(*tert*-butyldimethylsilyloxy)cyclopentanol, 3.19. The general procedure was followed to yield a colorless oil (81 mg, 92%). **GC** (Supelco Beta Dex 120 (30 m x 0.15 mm 0.2 μm film thickness 7 °C for 100 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi., t_{rmajor} = 91.6 min, t_{rminor} = 94.4 min), 94% ee; **^{1}H NMR** ($CDCl_3$ 00 M z δ 4.02-4.06 (m, 1H), 3.89-3.93 (m, 1H), 2.61 (d, 1H, J = 3.9), 1.59-1.88 (m, 5H), 1.42-1.51 (m, 1H), 0.91 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 7 73.7, 31.6, 31.1, 26.0, 20.2, 18.3, -4.4, -4.8; **$[\alpha]_D^{20}$** = +18.7 (c = 0.52, $CHCl_3$, l = 50 mm).

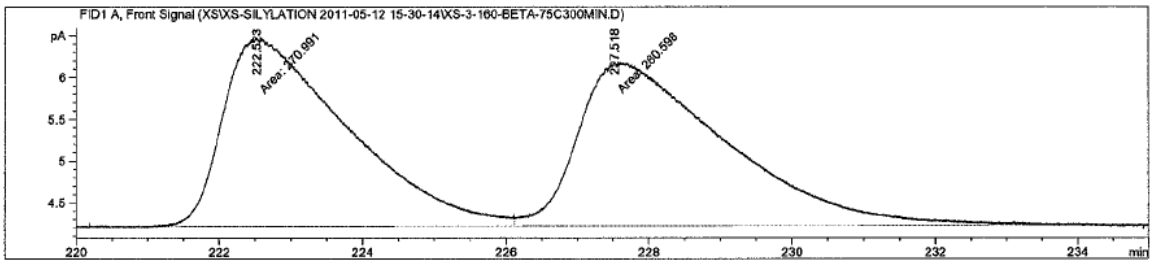


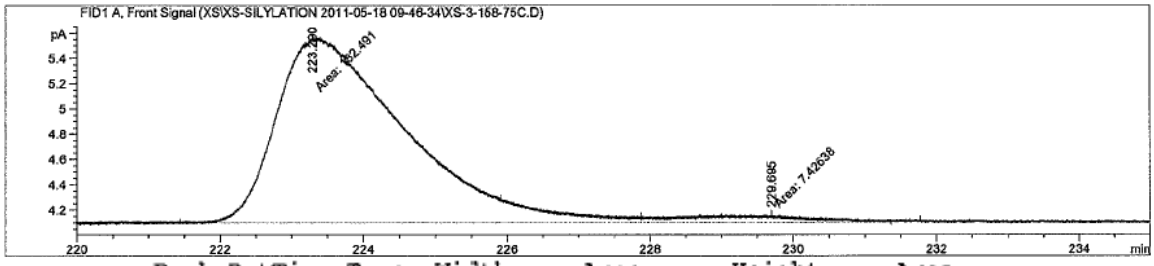
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	91.639	MF	0.8639	380.97656	7.34983	97.37778
2	94.395	FM	0.8785	10.25904	1.94625e-1	2.62222

Table 3.9, Entry 2.



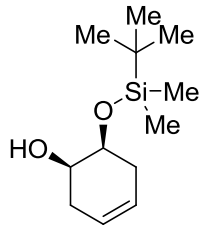
(*3R*,*4S*)-4-((*tert*-butyldimethylsilyl)oxy)tetrahydrofuran-3-ol, 3.24. The general procedure was followed using 4 equivalents of *tert*-butylchlorodimethylsilane at 0.2 M and running 24 hours to yield a colorless oil (32 mg, 73%). **GC** (Supelco Beta Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 75 °C for 260 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi., t_{rmajor} = 223.3 min, t_{rminor} = 229.7 min), 92% ee; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 4.26 (dd, 1H, *J* = 11.5, 5.9), 4.08-4.12 (m, 1H), 3.87-3.92 (m, 2H), 3.71 (dd, 1H, *J* = 9.5, 3.7), 3.57 (dd, 1H, *J* = 9.0, 5.6), 2.81 (d, 1H, *J* = 4.6), 0.90 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 73.6, 72.5, 72.4, 71.2, 26.0, 18.3, -4.5, -4.8; **IR**: 2953, 2930, 2858, 1254, 1131, 1069, 836, 779 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{23}O_3Si$: $[M+H]^+$: 219.1417, found: 219.1421. **$[\alpha]_D^{20}$** = +21.0 (*c* = 1.1, CH_2Cl_2, *l* = 50 mm).



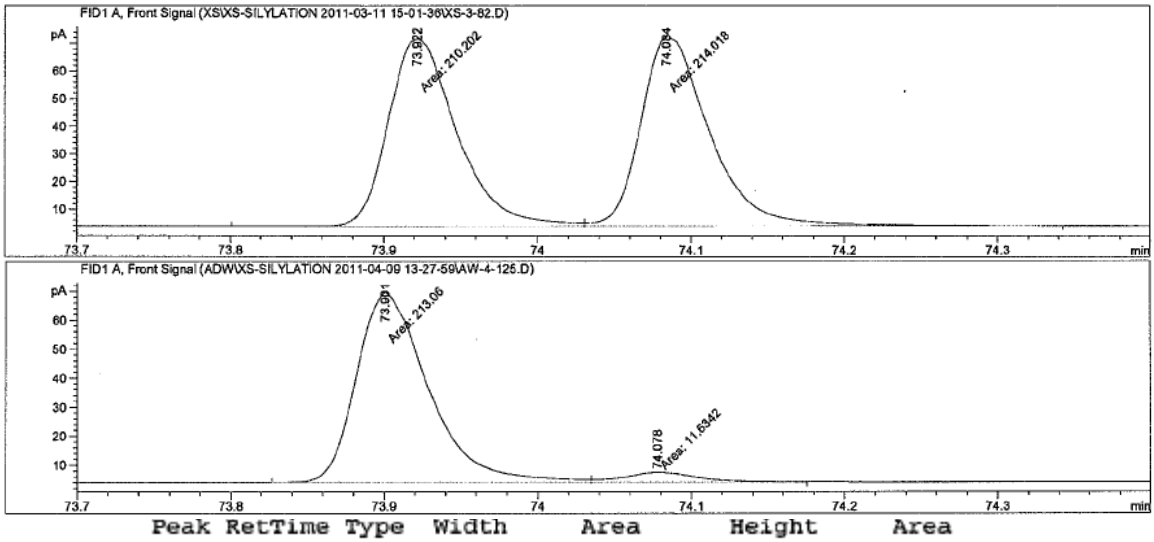


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	223.290	MF	2.0577	182.49138	1.47814	96.08968
2	229.695	FM	1.2953	7.42638	9.55570e-2	3.91032

Table 3.9, Entry 3

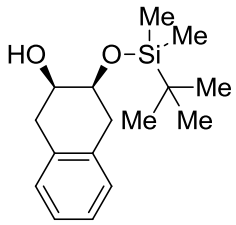


(*1R,6S*)-6-(*tert*-butyldimethylsilyloxy)cyclohex-3-enol, 3.25. The general procedure was followed running at 0.2 M in THF for 12 hours to yield a colorless oil (79 mg, 88%). **GC** S pe lco Beta De 20 30 m 0 mm 0 2 μm film thickness °C for 70 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi., t_{rmajor} = 73.9 min, t_{rminor} = 74.1 min), 90% ee; **^{1}H NMR** ($CDCl_3$ 00 M z δ -5.55 (m, 2H), 3.86-3.92 (m, 2H), 2.28-2.30 (m, 2H), 2.18-2.22 (m, 3H), 0.90 (s, 9H), 0.08 (s, 6H); **^{13}C NMR** ($CDCl_3$ 00 δ 124.0, 123.7, 70.0, 69.3, 31.5, 30.7, 26.0, 18.3, -4.3, -4.6; **$[\alpha]_D^{20}$** = +24.2 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).



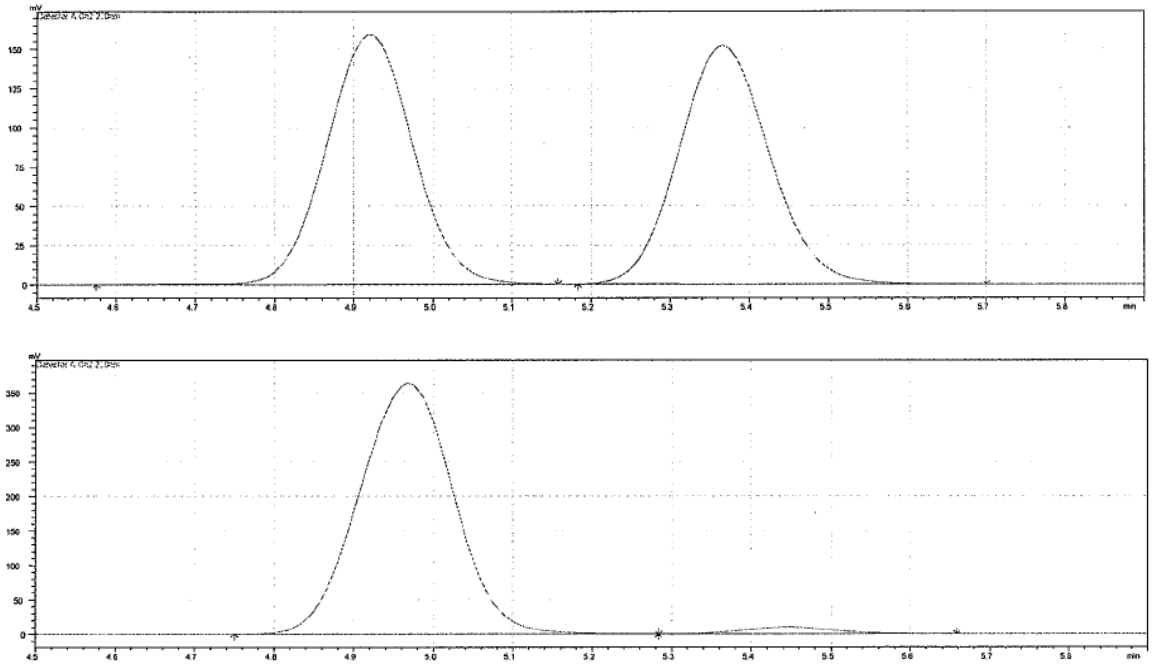
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	73.901	MF	0.0543	213.06021	65.41747	94.82220
2	74.078	FM	0.0559	11.63422	3.46714	5.17780

Table 3.9, Entry 4



(2*R*,3*S*)-3-((*tert*-butyldimethylsilyl)oxy)-1,2,3,4-tetrahydronaphthalen-2-ol, 3.26. The general procedure was followed with (2*R*,3*S*)-1,2,3,4-tetrahydronaphthalene-2,3-diol (99 mg, 0.60 mmol) at 0.2 M in THF for 8 hours to yield a colorless oil (140 mg, 85%). **Chiral HPLC Analysis** (Chiracel AS-H, hexanes/*i*PrOH = 99/1, 1.0 mL/min, 220 nm, t_{rmajor}= 4.9 min and t_{rminor}= 5.4 min) 95% ee; **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 0 -7.26 (m, 4H), 4.08-4.12 (m, 1H), 4.05-4.06 (m, 1H), 3.02 (t, 2H, *J* = 4.2), 2.99 (t, 1H, *J* = 8.3), 2.87 (dd, 1H, *J* = 16.1, 5.4), 2.24 (d, 1H, *J* = 3.4), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); **^{13}C NMR** ($CDCl_3$ 2 M z δ 33 33 2 2 2 0 26 3 26 70 6 .8, 34.9,

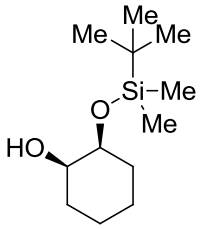
34.5, 26.0, 18.3, -4.2, -4.5; **IR**: 2928, 1253, 1083, 980, 918, 831, 775, 742 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{27}O_2Si$: $[M+H]^+$: 279.1780, found: 279.1781. $[\alpha]_D^{25}$ = +27.0 (*c* = 1.0, MeOH, *l* = 50 mm).



Detector A Ch2 220nm

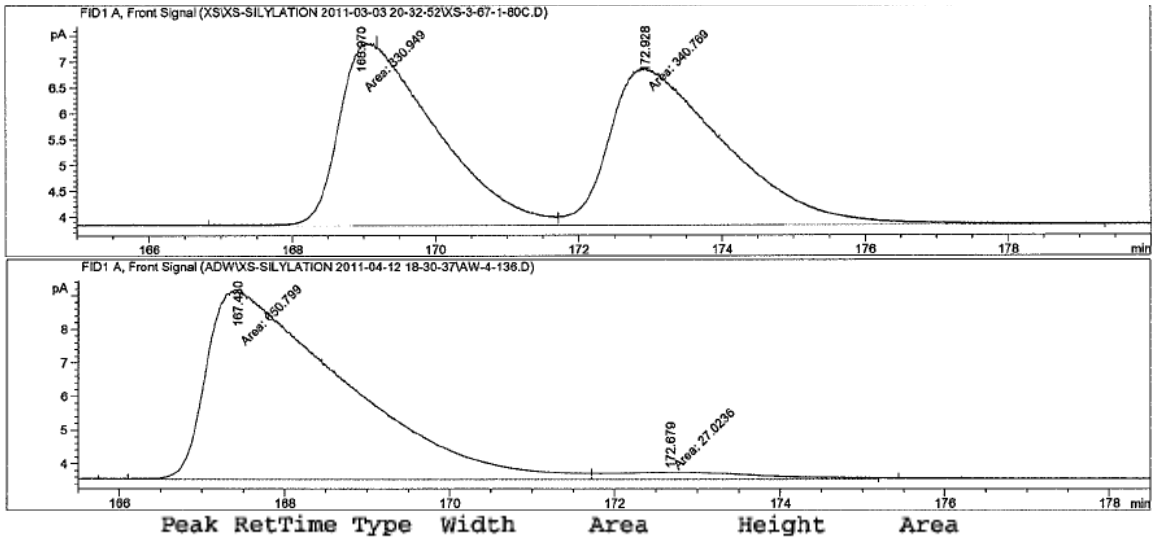
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.964	2990306	364009	97.401	97.372
2	5.441	79785	9824	2.599	2.628
Total		3070091	373833	100.000	100.000

Table 3.9, Entry 5.



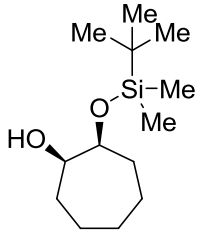
(*1R,2S*)-2-(*tert*-butyldimethylsilyloxy)cyclohexanol, 3.27. The general procedure was followed at 0.2 M in THF for 12 hours to yield a colorless oil (8.0 x 10^1 mg, 87%). **GC**

S pe lco Beta De 20 30 m 0 mm 0 2 μm film thickness 0 °C for 190 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 167.4 min, t_{rminor} = 172.7 min), 92% ee; **^{1}H NMR** ($CDCl_3$ 00 M z δ 3 73-3.76 (m, 1H), 3.63-3.65 (m, 1H), 2.18-2.19 (m, 1H), 1.72-1.79 (m, 2H), 1.65-1.72 (m, 2H), 1.56-1.62 (m, 2H), 1.44-1.51 (m, 1H), 1.21-1.31 (m, 1H), 0.91 (s, 9H), 0.08 (s, 6H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 72 2 70 30.7, 30.3, 26.0, 22.2, 21.3, 18.3, -4.3, -4.7; **$[\alpha]_D^{20}$** = +12.1 (*c* = 1.1, MeOH, *l* = 50 mm).



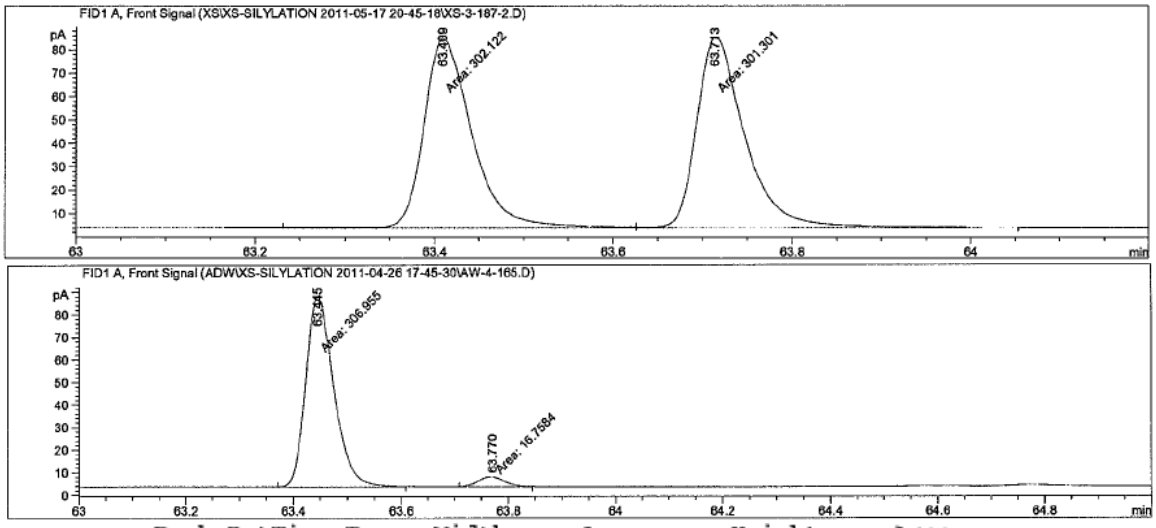
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	167.430	MF	1.9304	650.79871	5.61872	96.01317
2	172.679	FM	2.0692	27.02361	2.17670e-1	3.98683

Table 3.9, Entry 6



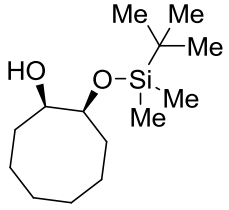
(*1R,2S*)-2-(*tert*-butyldimethylsilyloxy)cycloheptanol, 3.28. The general procedure was followed using 4 equivalents of *tert*-butylchlorodimethylsilane and 2 equivalents of

1,2,2,6,6-pentamethylpiperidine at 4 °C for 24 hours to yield a colorless oil (39 mg, 80%). **GC** S pe lco Beta De 20 30 m 0 mm 0 2 μm film thickness °C for 70 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 63.4 min, t_{rminor} = 63.7 min), 90% ee; **^{1}H NMR** ($CDCl_3$ 00 M z δ 3 0 -3.82 (m, 1H), 3.73-3.75 (m, 1H), 2.55 (d, 1H, J = 4.4), 1.69-1.84 (m, 4H), 1.44-1.62 (m, 4H), 1.26-1.36 (m, 2H), 0.91 (s, 9H), 0.083 (s, 3H), 0.081 (s, 3H); **^{13}C NMR** ($CDCl_3$ 26 M z δ 7 73 7 3 2 3 2 26.0, 22.6, 21.4, 18.3, -4.3, -4.8; **$[\alpha]_D^{20}$** = +6.5 (c = 0.87, $CHCl_3$, l = 50 mm).

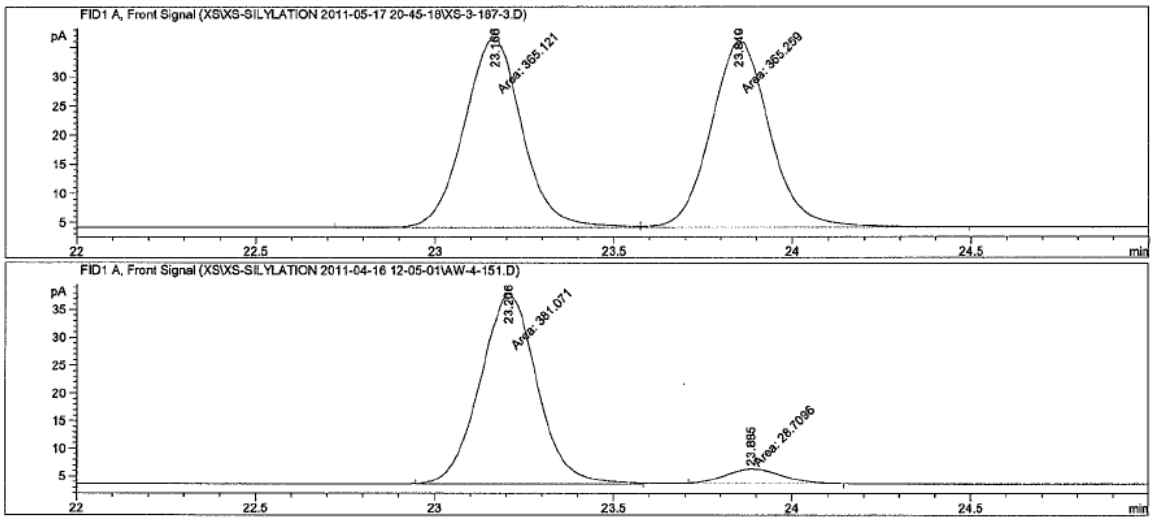


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	63.445	MM	0.0605	306.95523	84.49146	94.82308
2	63.770	MM	0.0598	16.75839	4.66702	5.17692

Table 3.9, Entry 7

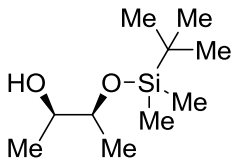


(*1R,2S*)-2-(*tert*-butyldimethylsilyloxy)cyclooctanol, 3.29. The general procedure was followed using 4 equivalents of *tert*-butylchlorodimethylsilane and 2 equivalents of 1,2,2,6,6-pentamethylpiperidine for 24 hours to yield a colorless oil (49 mg, 94%). **GC** S pe lco Beta De 20 30 m 0 mm 0 2 µm film thickness 0 °C for 30 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 23.2 min, t_{rminor} = 23.9 min), 86% ee; **^{1}H NMR** ($CDCl_3$ 00 M z δ 3 2 dt J = 9.0, 3.2), 3.71-3.73 (m, 1H), 2.67-2.68 (m, 1H), 1.97-2.04 (m, 1H), 1.40-1.80 (m, 11H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 7 7 73 7 30 2 2 27 0 26 0 2 7 2 22.8, 18.3, -4.3, -4.7; **$[\alpha]_D^{20}$** = +2.88 (c = 0.83, $CHCl_3$, l = 50 mm).

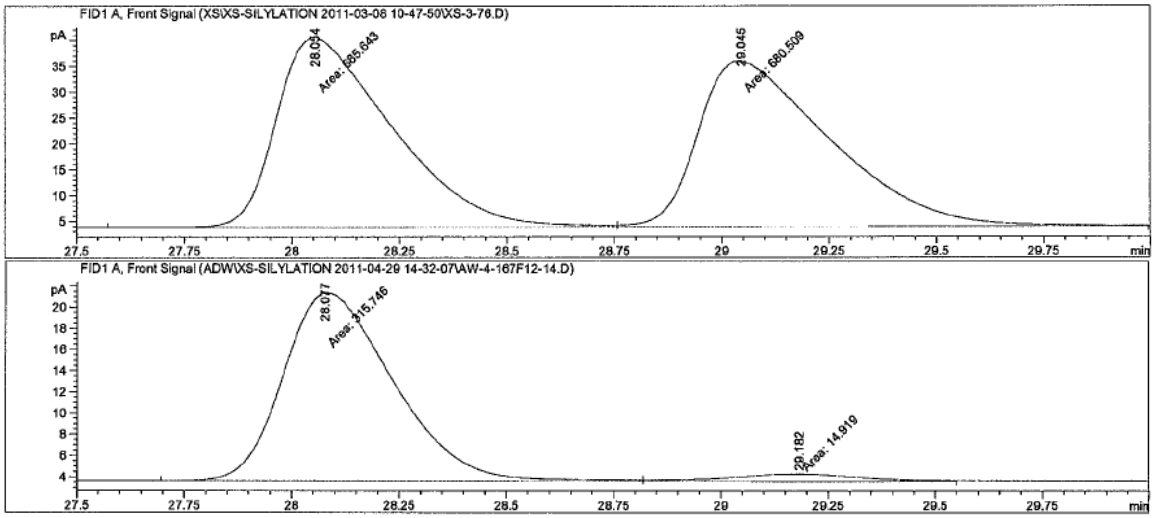


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	23.206	MM	0.1852	381.07095	34.30234	92.99392
2	23.885	MM	0.1837	28.70957	2.60485	7.00608

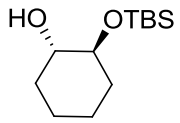
Table 3.9, Entry 8



(*2R,3S*)-3-(*tert*-butyldimethylsilyloxy)butan-2-ol, 3.30. The general procedure was followed using 4 equivalents of *tert*-butylchlorodimethylsilane and 2 equivalents of 1,2,2,6,6-pentamethylpiperidine at 4 °C for 36 hours to yield a colorless oil (32 mg, 78%). **GC** (Supelco Beta Dex 120 (30 m 0 mm 0 2 μm film thickness 0 °C for 35 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 28.1 min, t_{rminor} = 29.1 min), 91% ee; **^{1}H NMR** ($CDCl_3$ 00 M z δ 3 6 -3.78 (m, 2H), 2.12-2.13 (m, 1H), 1.09 (d, 3H, *J* = 5.7), 1.07 (d, 3H, *J* = 5.7), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); **^{13}C NMR** ($CDCl_3$ 00 M z δ 72 7 3 26 0 2 7 7 2 -4.2, -4.7; **$[\alpha]_D^{20}$** = +14.7 (*c* = 0.19, CH_2Cl_2, *l* = 50 mm).

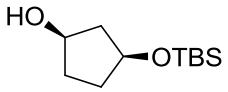


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.077	MF	0.2945	315.74554	17.86900	95.48817
2	29.182	FM	0.3468	14.91901	7.16989e-1	4.51183

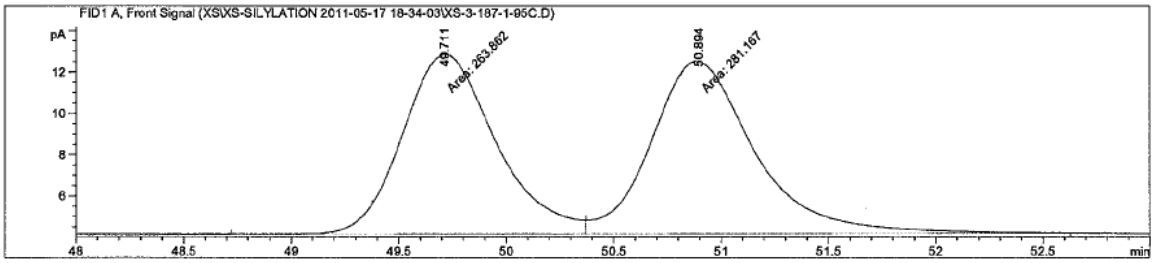


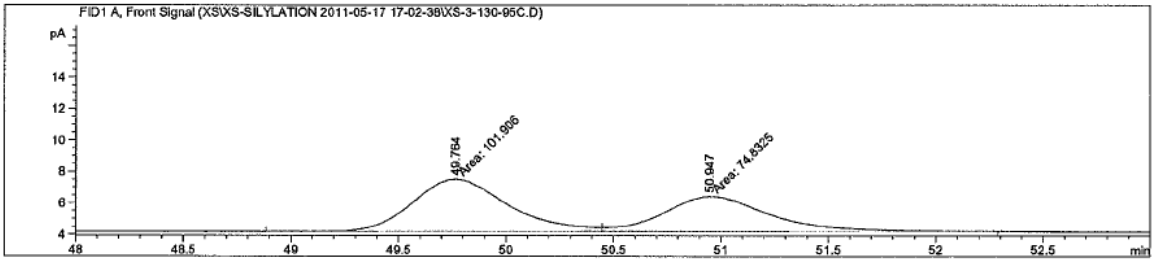
(1*S*,2*S*)-2-((*tert*-butyldimethylsilyl)oxy)cyclohexanol. The general procedure was followed with (±)-trans-1,2-cyclohexanediol (23 mg, 0.20 mmol) and running for 8 hours .The crude reaction was injected into the GC (Supelco Gamma Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 100 °C for 85 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15psi, t_{r1} = 72.2 min, t_{r2} = 78.1 min) to show <5% yield.

Reaction of a *cis*-1,3-Diol (Scheme 3.18)

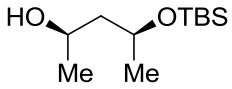


(*1R,3S*)-3-(*tert*-butyldimethylsilyloxy)cyclopentanol, 3.34. The general procedure was followed using 4 equivalents of *tert*-butylchlorodimethylsilane and **3.33** and running for 4 hours. The crude reaction mixture was injected on the GC (Supelco Gamma Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 95 °C for 60 min, 20 °C/min to 180 °C, 180 °C for 20 min, 16 psi, t_{rmajor} = 49.8 min, t_{rminor} = 50.9 min) to obtain a 26% yield and 15% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 4.37-4.39 (m, 1H), 4.24-4.26 (m, 1H), 3.02 (d, 1H, *J* = 10.3), 1.81-1.95 (m, 4H), 1.71-1.78 (m, 1H), 1.63-1.68 (m, 1H), 0.87 (s, 9H), 0.07 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 75.1, 74.2, 44.6, 34.4, 34.3, 26.0, 18.1, -4.7, -4.8.





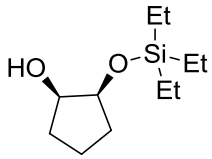
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	49.764	MF	0.5093	101.90605	3.33474	57.65921
2	50.947	FM	0.5546	74.83249	2.24866	42.34079



(*2R,4S*)-4-(*tert*-butyldimethylsilyloxy)pentan-2-ol. The general procedure was followed using 4 equivalents of *tert*-butylchlorodimethylsilane and running for 8 hours. The crude reaction was injected into the GC (Supelco Gamma Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 90 °C for 50 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{r1} = 36.5 min, t_{r2} = 38.0 min) to show <5% yield.

Silyl Reagent Screen (Table 3.10)

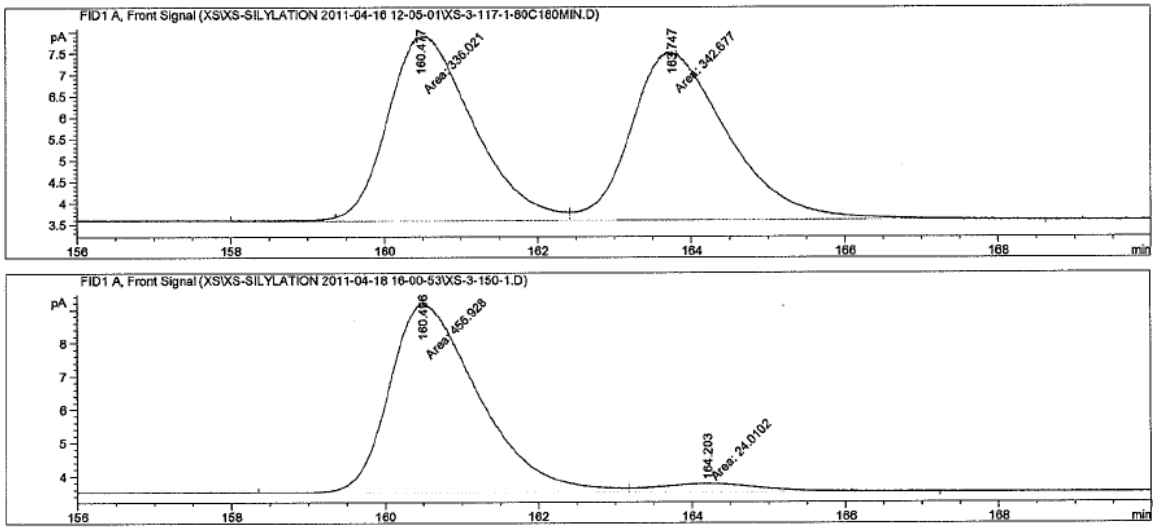
Table 3.10, Entry 1.



(*1R,2S*)-2-((triethylsilyl)oxy)cyclopentanol, 3.35. To an oven-dried glass reaction vial, a solution of *cis*-1,2-cyclopentanediol, **3.18** (61 mg, 0.60 mmol), catalyst **III** (34 mg, 0.12 mmol, 20 mol %), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (3.4 mg, 1.8 x 10^{-2} mmol, 3 mol %) in anhydrous THF (3.0 mL) was added. The reaction was stirred at room

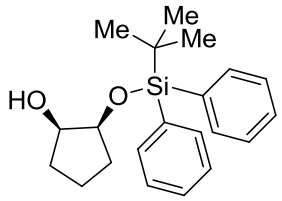
temperature for 10 minutes. 1,2,2,6,6-pentamethylpiperidine (130 μL, 0.72 mmol, 1.2 equiv) was added, followed by addition of triethylchlorosilane (120 μL, 0.72 mmol, 1.2 equiv). After stirring at room temperature for 1 hour, the reaction was concentrated. Flash column chromatography (Hex/EtOAc = 20/1) afforded pure product as a colorless oil (130 mg, 96%). **Chiral GLC Analysis** (Supelco Beta Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 80 °C for 180 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 160.5 min, t_{rminor} = 164.2 min) 90% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 4.01 (dt, 1H, *J* = 8.3, 4.9), 3.89 (dt, 1H, *J* = 8.3, 3.7), 2.65 (d, 1H, *J* = 3.4), 1.55-1.85 (m, 5H), 1.39-1.48 (m, 1H), 0.95 (t, 9H, *J* = 8.0), 0.60 (q, 6H, *J* = 8.0); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 75.1, 73.7, 31.7, 31.2, 20.2, 6.9, 5.0; **IR**: 2955, 2876, 1123, 1096, 1005, 742, 728 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{11}H_{25}O_2Si$: $[M+H]^+$: 217.1624, found: 217.1629. **$[\alpha]_D^{20}$** = +18.0 (c = 1.0, CH_2Cl_2, *l* = 50 mm).

A duplicate reaction of cis-1,2-cyclopentanediol, **3.18** (21 mg, 0.20 mmol) with the same procedure afforded the pure product as colorless oil (39 mg, 92%, 90% ee).



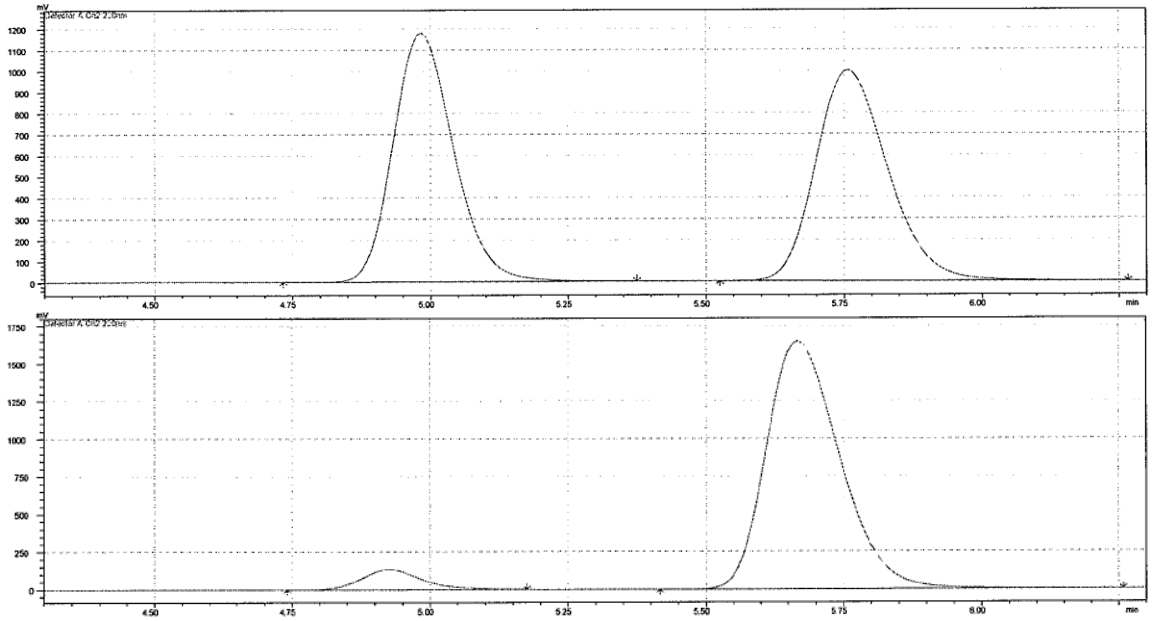
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	160.496	MF	1.3444	456.92770	5.66467	95.00762
2	164.203	FM	1.5778	24.01024	2.53621e-1	4.99238

Table 3.10, Entry 2



(*1R,2S*)-2-((*tert*-butyldiphenylsilyl)oxy)cyclopentanol, 3.36. To an oven-dried glass reaction vial, a solution of *cis*-1,2-cyclopentanediol, **3.18** (61 mg, 0.60 mmol), catalyst **III** (34 mg, 0.12 mmol, 20 mol %), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (3.4 mg, 1.8 x 10^{-2} mmol, 3 mol %) in anhydrous THF (1.5 mL) was added. The reaction was stirred at room temperature for 10 minutes. 1,2,2,6,6-pentamethylpiperidine (130 μL, 0.72 mmol, 1.2 equiv) was added, followed by addition of *tert*-butyl(chloro)diphenylsilane (620 μL, 2.4 mmol, 4.0 equiv). After stirring at room temperature for 48 hours, the reaction was concentrated. Flash column chromatography (Hex/EtOAc = 80/1) afforded pure product as a colorless oil (150 mg, 71%). **Chiral HPLC Analysis** (Chiracel OD-H, Hexanes/*i*PrOH = 99/1, 1.0 mL/min, 220 nm, t_{rminor} = 4.9 min and t_{rmajor} = 5.7 min), 88% ee; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.65-7.69 (m, 4H), 7.42-7.45 (m, 2H), 7.25-7.40 (m, 4H), 4.03-4.07 (m, 1H), 3.86-3.90 (m, 1H), 2.73 (d, 1H, *J* = 2.9), 1.54-1.83 (m, 5H), 1.29-1.38 (m, 1H), 1.08 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 136.0, 135.8, 133.9, 133.6, 130.1, 130.0, 128.0, 127.9, 76.7, 73.6, 31.1, 31.0, 27.2, 20.0, 19.4; **IR**: 2931, 1105, 821, 740, 700, 611, 504 cm^{-1}; **HRMS** (DART-TOF)

calcd. for $C_{21}H_{27}OSi$: $[M\text{-}OH]^+$: 323.1831, found: 323.1822. $[\alpha]_D^{20}$ = +12.0 (c = 1.0, CH_2Cl_2, *l* = 50 mm).

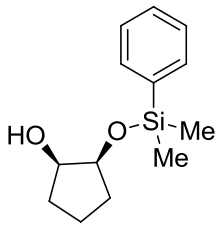


Detector A Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.922	986460	130720	6.097	7.352
2	5.663	15191936	1647199	93.903	92.648
Total		16178396	1777919	100.000	100.000

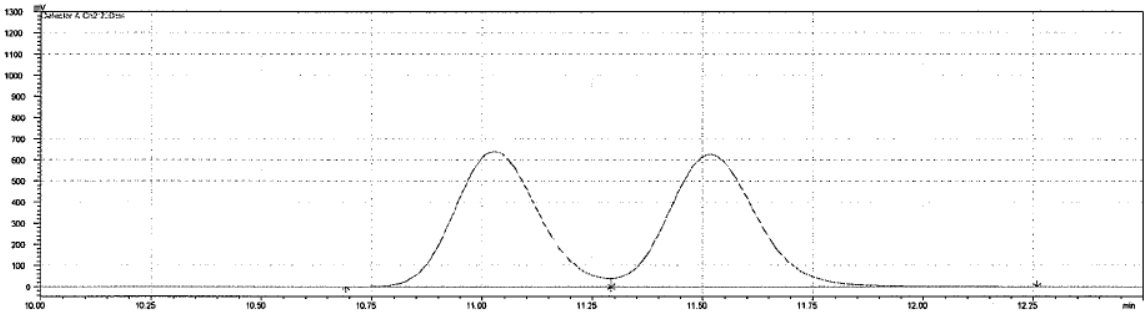
A duplicate reaction of cis-1,2-cyclopentanediol, **3.18** (21 mg, 0.20 mmol) with the same procedure afforded the pure product as colorless oil (53 mg, 78%, 92% ee).

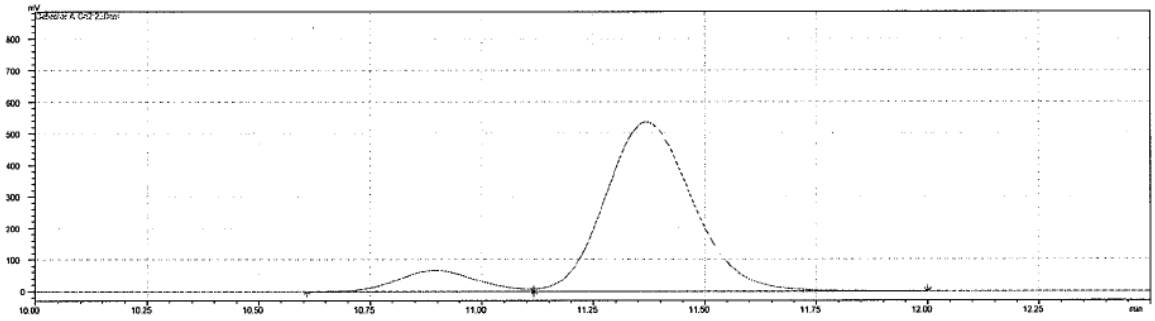
Table 3.10, Entry 3



(*1R,2S*)-2-((dimethyl(phenyl)silyl)oxy)cyclopentanol, 3.37. To an oven-dried glass reaction vial, a solution of *cis*-1,2-cyclopentanediol, **3.18** (21 mg, 0.20 mmol), catalyst

III (11 mg, 4.0×10^{-2} mmol, 20 mol %), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (1.2 mg, 6.0×10^{-3} mmol, 3 mol %) in anhydrous THF (2.0 mL) was added. The reaction was stirred at room temperature for 10 minutes. 1,2,2,6,6-pentamethylpiperidine (44 μL, 0.24 mmol, 1.2 equiv) was added, followed by dropwise addition of a solution of chloro(dimethyl)phenylsilane (0.40 mL, 0.24 mmol, 1.2 equiv) in anhydrous THF (2.0 mL) over 2 hours by syringe pump. The reaction was concentrated. Flash column chromatography (Hex/EtOAc = 20/1) afforded the pure product as a colorless oil (34 mg, 72%). **Chiral HPLC Analysis** (Chiracel OD-H, Hexanes/*i*PrOH = 99.8/0.2, 0.50 mL/min, 220 nm, t_{rminor} = 25.3 min and t_{rmajor} = 27.0 min), 80% ee; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.55-7.57 (m, 2H,), 7.35-7.40 (m, 3H), 3.98-4.02 (m, 1H), 3.85-3.88 (m, 1H), 2.58 (dd, 1H, J = 3.7, 0.5), 1.44-1.82 (m, 5H), 1.35-1.44 (m, 1H), 0.40 (s, 3H), 0.39 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 137.8, 133.6, 130.0, 128.2, 75.7, 73.7, 31.3, 31.0, 20.1, -1.0, -1.1; **IR**: 2961, 1253, 1117, 1093, 891, 830, 787, 741, 700 cm^{-1}; **$[\alpha]_D^{20}$** = +14.0 (c = 1.0, CH_2Cl_2, l = 50 mm).





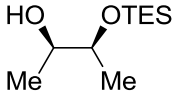
Detector A Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.892	826314	66098	10.197	10.958
2	11.365	7277541	537081	89.803	89.042
Total		8103855	603178	100.000	100.000

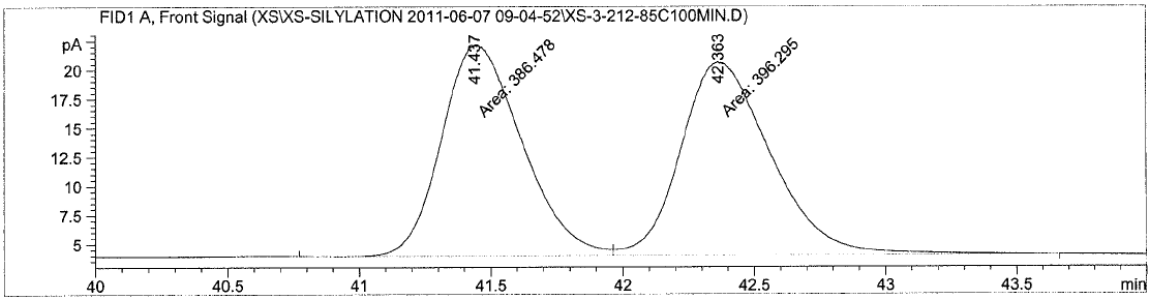
A duplicate reaction of cis-1,2-cyclopentanediol, **3.18** (21 mg, 0.20 mmol) with the same procedure afforded pure product as colorless oil (33 mg, 70%, 79% ee).

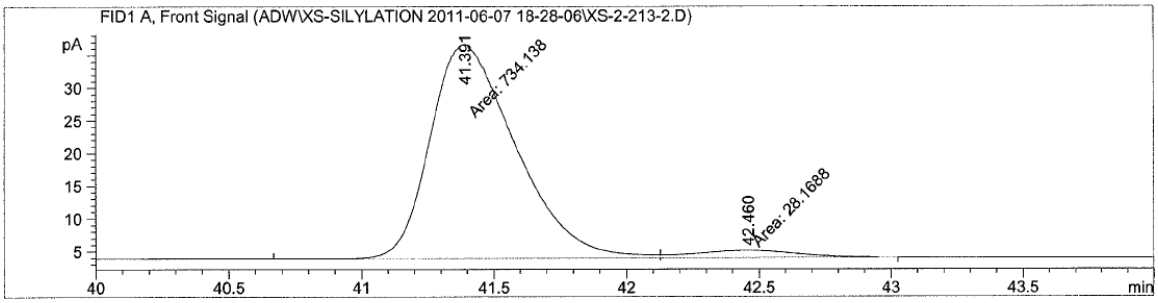
Silylation with TESCl (Table 3.11)

General procedure. To an oven-dried glass reaction vial, a solution of substrate (0.20 mmol), catalyst **III** (11 mg, 4.0 x 10^{-2} mmol, 20 mol %), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (1.2 mg, 6.0 x 10^{-3} mmol, 3 mol %) in anhydrous THF (4.0 mL) was added. The reaction was stirred at room temperature for 10 minutes. 1,2,2,6,6-pentamethylpiperidine (μ 0 2 mm ol 2 eq iv) was added, followed by addition of triethylchlorosilane (0.40 mL, 0.24 mmol, 1.2 equiv). After stirring at room temperature for 4 hours, the reaction was concentrated. Flash column chromatography (Hex/EtOAc = 20/1) afforded the pure product.



(2*R*,3*S*)-3-((triethylsilyl)oxy)butan-2-ol, 3.38. *meso*-2,3-Butanediol (18 mg, 0.20 mmol) was silylated using the general procedure. Pure product was isolated as a colorless oil (34 mg, 83%). **Chiral GLC Analysis** (Supelco Beta Dex 120 (30 m × 0.15 mm × 0.25 μm film thickness), 85 °C for 50 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 41.4 min, t_{rminor} = 42.5 min) 92% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 3.68-3.87 (m, 2H), 2.20 (d, 1H, *J* = 3.9), 1.08 (d, 6H, *J* = 6.1), 0.96 (t, 9H, *J* = 7.8), 0.60 (q, 6H, *J* = 7.8); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 71.8, 71.3, 17.6, 17.1, 7.0, 5.1; **IR**: 2956, 2877, 1239, 1106, 1003, 908, 725 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{25}O_2Si$: $[M+H]^+$: 205.1624, found: 205.1626. **$[\alpha]_D^{20}$** = +12.2 (c = 1.0, CH_2Cl_2, *l* = 50 mm).

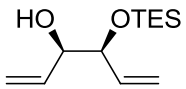




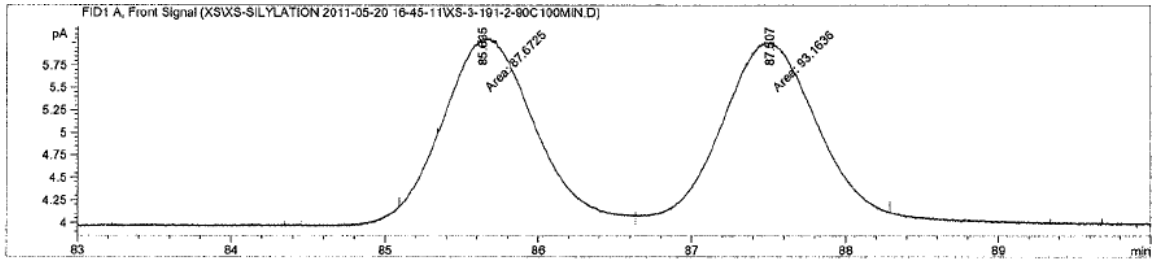
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	41.391	MF	0.3745	734.13788	32.67337	96.30480
2	42.460	FM	0.4290	28.16878	1.09434	3.69520

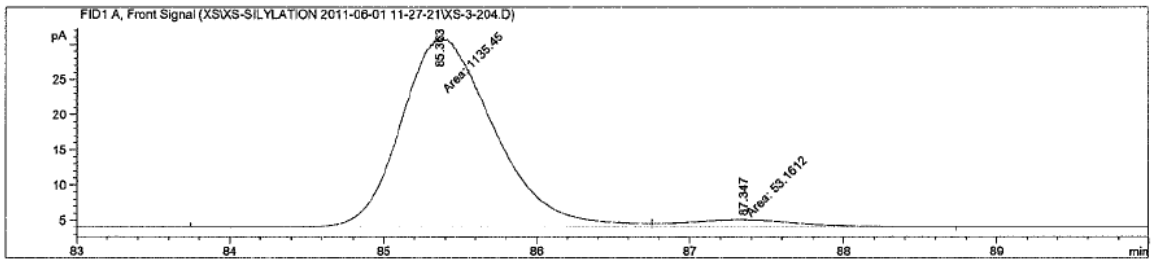
A duplicate reaction of *meso*-2,3-butanediol (54 mg, 0.60 mmol) with the same procedure

afforded the pure product, **3.38**, as a colorless oil (110 mg, 85%, 92% ee).



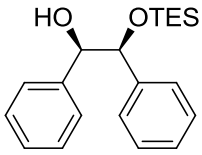
(3*R*,4*S*)-4-((triethylsilyl)oxy)hexa-1,5-dien-3-ol, 3.39. *meso*-1,5-Hexadiene-3,4-diol (23 mg, 0.20 mmol) was silylated using the general procedure. Pure product was isolated as a colorless oil (38 mg, 83%). **Chiral GLC Analysis** (Supelco Beta Dex 120 (30 m × 0.15 mm × 0 2 μ m film thickness 0 ° for 00 mi n 20 °C/min to 180 °C, 180 °C for 20 min, 15psi, t_{rmajor} = 85.4 min, t_{rminor} = 87.4 min) 91% ee. **^{1}H NMR** ($CDCl_3$ 00 M z δ 5.77-5.84 (m, 2H), 5.28 (dt, 1H, *J* = 17.4, 1.5), 5.23 (dt, 1H, *J* = 17.4, 1.5), 5.19-5.20 (m, 1H), 5.16-5.18 (m, 1H), 4.10-4.12 (m, 1H), 4.04-4.08 (m, 1H), 2.32 (d, 1H, *J* = 4.4), 0.94 (t, 9H, *J* = 8.1), 0.60 (q, 6H, *J* = 8.1); **^{13}C NMR** ($CDCl_3$ 2 M z δ 36 36 6 7 3 116.8, 77.1, 76.2, 7.0, 5.1; **IR**: 2955, 2877, 1459, 1416, 1238, 1003, 922, 829, 725 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{23}OSi$: $[M\text{-}OH]^+$: 211.1518, found: 211.1527. **$[\alpha]_D^{20}$** = +4.1 (c = 1.0, CH_2Cl_2, *l* = 50 mm).



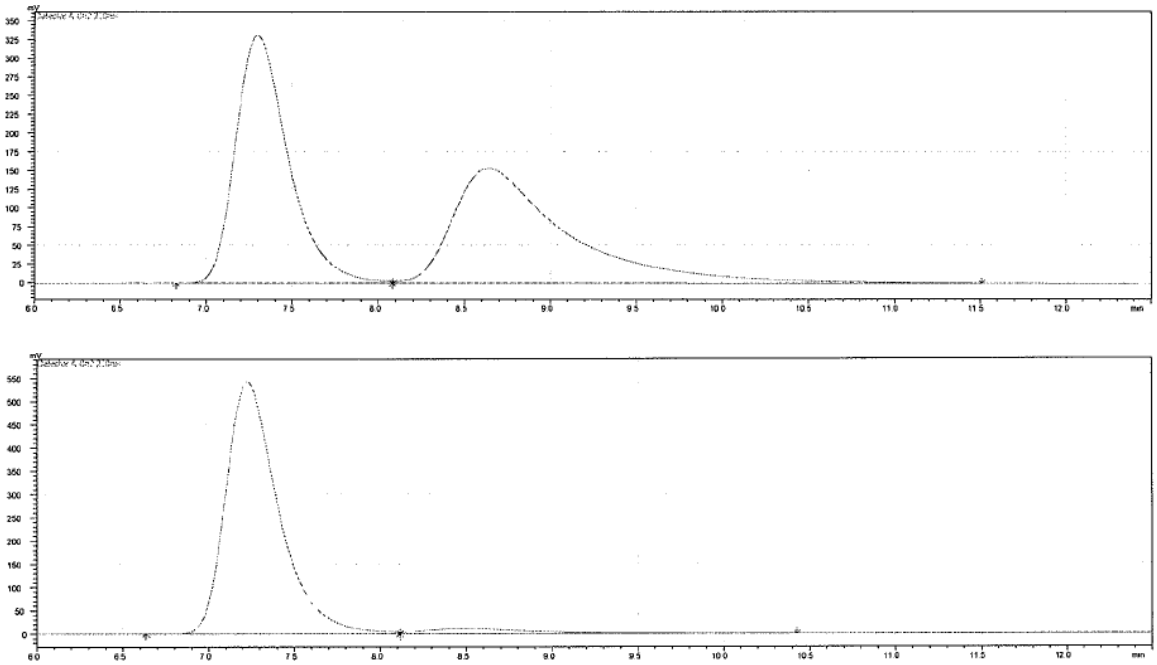


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	85.363	MF	0.7031	1135.45007	26.91563	95.52745
2	87.347	FM	0.8669	53.16124	1.02205	4.47255

A duplicate reaction of *meso*-1,5-Hexadiene-3,4-diol (69 mg, 0.60 mmol) was silylated using the general procedure. Pure product, **3.39**, was isolated as a colorless oil (110 mg, 80%, 92% ee).



(1*R*,2*S*)-1,2-diphenyl-2-((triethylsilyl)oxy)ethanol, 3.40. *meso*-1,2-Diphenylethane-1,2-diol (43 mg, 0.20 mmol) was silylated for 8 hours using the general procedure. Pure product was isolated as a colorless oil (53 mg, 81%). **Chiral HPLC Analysis** (Chiracel OJ-H, Hexanes/*i*PrOH = 99/1, 1.0 mL/min, 220 nm, t_{rmajor} = 7.3 min and t_{rminor} = 8.6 min) 92% ee. **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 6 -7.27 (m, 10H), 4.75 (dd, 1H, *J* = 5.9, 2.9), 4.70 (d, 1H, *J* = 5.9), 2.33 (d, 1H, *J* = 3.2), 0.77 (t, 9H, *J* = 7.8), 0.39 (q, 6H, *J* = 7.8); **^{13}C NMR** ($CDCl_3$ 2 M z δ 0 0 7 27 27 6 27 0 27 7 27 6 27 79.3, 78.9, 6.8, 4.8; **IR**: 2953, 2876, 1097, 1005, 837, 740, 700 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{25}O_2Si$: $[M+H]^+$: 329.1937, found: 329.1926. **$[\alpha]_D^{20}$** = +6.6 (c = 1.0, CH_2Cl_2, *l* = 50 mm).



Detector A Ch2 220nm

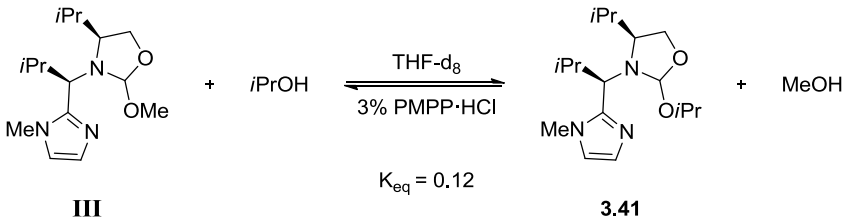
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.221	11612838	541504	96.042	97.949
2	8.484	478613	11342	3.958	2.051
Total		12091450	552846	100.000	100.000

A duplicate reaction of *meso*-1,2-diphenylethane-1,2-diol (130 mg, 0.60 mmol) was silylated using the general procedure. Pure product, **3.40**, was isolated as a colorless oil (160 mg, 83%, 87% ee).

Absolute Stereochemical Proof

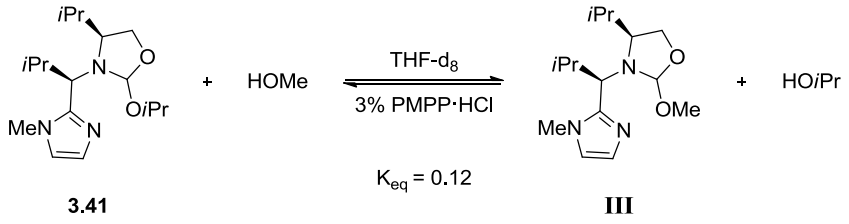
The absolute stereochemistry of the products was determined by comparing the optical rotations to known values. The optical rotations of the silylated products in this paper were determined to be opposite in sign to the optical rotations of the products reported by the Hoveyda and Snapper groups[18]. The absolute stereochemistry of (*1R,2S*)-2-((triethylsilyl)oxy)cyclopentanol, (*1R,2S*)-2-((*tert*-butyldiphenylsilyl)oxy)cyclopentanol, and (*1R,2S*)-2-((dimethyl(phenyl)silyl)oxy)cyclopentanol was assigned by analogy.

Catalyst Equilibrium Experiment with *i*PrOH (Scheme 3.21)



In a glovebox, a solution of catalyst **III** (21 mg, 7.5 x 10^{-2} mmol) and 1,2,2,6,6-pentamethylpiperidine hydrochloride (0.40 mg, 2.0 x 10^{-2} mmol) in anhydrous THF-d_8 2 0 µ was made 00 µ of the sol ti on was added to a NMR t e 2 µ of an internal standard solution of 1,3,5-trimethoxybenzene (5.0 x 10^{-3} mmol, 0.20 M in THF) was added to the NMR tube. *i*PrO 0 2 mm ol 2 µ 2 M sol ti on in F -d_8) and MeOH (5.0 x 10^{-2} mmol 2 µ 2 M sol ti on in F -d_8) was added to the NMR tube. THF-d_8 22 µ was added to the NMR t e to reach a total volume of 0.5 mL. The reaction was monitored by ^{1}H NMR. After 12 hours, equilibrium was reached. A ratio of 70:30, **III** to **3.41** gave a K_{eq} of 0.119.

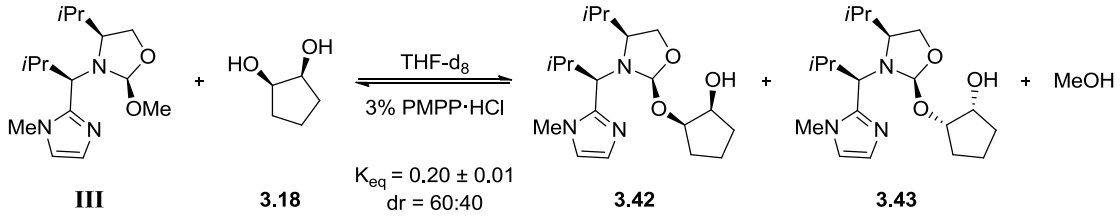
3.41 Equilbrium Experiment with MeOH



An equilibrium experiment in the reverse direction of the above reaction was performed. In a glovebox, a solution of catalyst **3.41** (23 mg, 7.3 x 10^{-2} mmol) and 1,2,2,6,6-

pentamethylpiperidine hydrochloride (0.80 mg, 4.0 x 10^{-3} mmol) in anhydrous THF-d_8 2 0 µ was made 0 µ of the catalyst sol t ion and 0 µ of the acid sol t ion was added to each of two NMR t es µ of an internal standard sol tion of 1,3,5-trimethoxybenzene (3.0 x 10^{-3} mmol, 0.20 M in THF) and *i*PrOH (6.3 x 10^{-2} mmol, 63 µ M sol ti on in F -d_8) was added to each NMR tube as well. MeOH (0.08 mmol, 80 µ M sol ti on in F -d_8) was added to NMR tube 1, and MeOH (0.12 mmol, 120 µ 1M solution in THF-d_8) was added to NMR tube 2, followed by THF-d_8 27 µ and 23 µ respectively to t e a nd 2 to reach a total vol m e of 0 6 m h e reaction was monitored by ^{1}H NMR. After 12 hours, equilibrium was reached. For tube 1, a ratio of 16:84, **3.36** to **III** and gave a K_{eq} of 0.121. For tube 2, a ratio of 10:90, **3.36** to **III** gave a K_{eq} of 0.117. The average K_{eq} for the two runs is 0.119 ± 0.002.

Catalyst Equilibrium Experiment with **3.18** (Scheme 3.22)

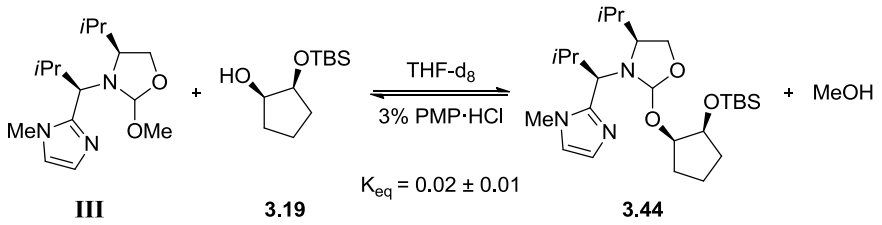


III **3.18** **3.42** **3.43**

In a glovebox, catalyst **III** (5.6 mg, 2.0 x 10^{-2} mmol), 1,2,2,6,6-pentamethylpiperidine hydrochloride (0.60 mg, 3.0 x 10^{-3} mmol), and *cis*-1,2-cyclopentanediol, **3.18**, (1.0 x 10^1 mg, 0.10 mmol) were dissolved in THF-d_8 (0.45 mL) and added to a NMR tube. 1,3,5-Trimethoxybenzene, as an internal standard, (0.050 mL, 1.0 x 10^{-2} mmol, 0.20 M solution in THF) was added to the NMR tube. The exchange reaction was followed by ^{1}H NMR. The reaction reached equilibrium in 3 hours with 40% starting catalyst **III**

remaining and a 60:40 ratio of diastereomers (**3.42** and **3.43**). The K_{eq} was determined to be 0.193. This reaction was repeated to give a K_{eq} of 0.205. The average K_{eq} is 0.199 ± 0.006. The spectrum of the experiment and an NMR of **III** in THF-d_8 are attached in the spectra section.

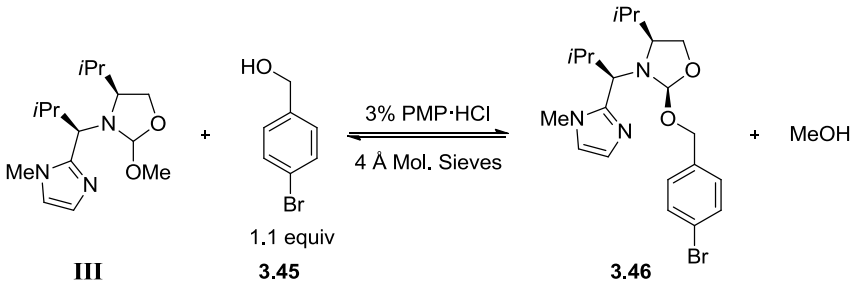
Exchange of **III** with **3.19** (Scheme 3.23)



III **3.19** **3.44**

Catalyst **III** (1.9 mg, 6.8 x 10^{-3} mmol, 20 mol %), **3.19** (7.4 mg, 3.0 x 10^{-2} mmol), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (2.0 x 10^{-1} mg, 1.0 x 10^{-3} mmol, 3 mol %) were mixed in THF-d_8 and monitored by ^{1}H NMR. After 2 h, equilibrium was reached with a ratio of 76:24, **III** to **3.44**, and a K_{eq} of 0.02 ± 0.001.

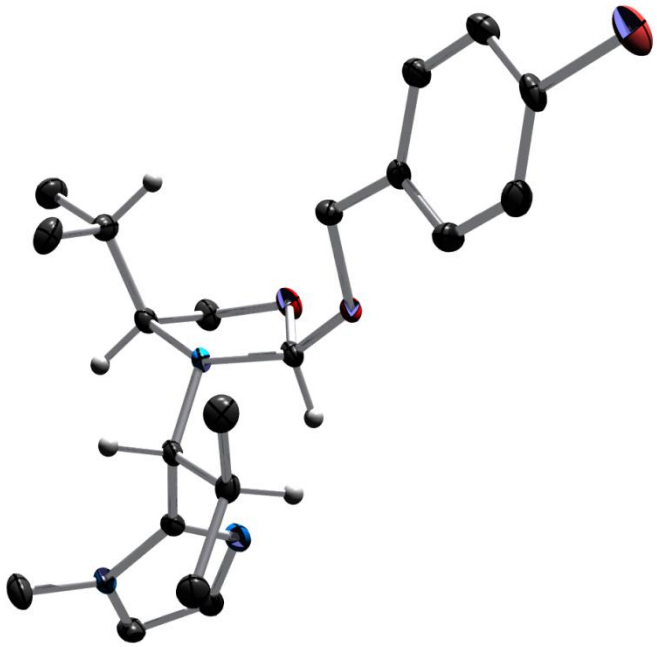
Exchange of **III** with **3.45** (Scheme 3.24)



III **3.45** **3.46**

(2*R*,4*S*)-2-((4-bromobenzyl)oxy)-4-isopropyl-3-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine, 3.46. To an oven-dried reaction vial was added a solution of (4*S*)-4-isopropyl-2-methoxy-3-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine, **III**, (56 mg, 0.20 mmol), 4-bromobenzoyl alcohol, **3.45**, (41 mg, 0.22 mmol, 1.1 equiv.), and 1,2,2,6,6-pentamethylpiperidine hydrochloride (1.2 mg, 6.0 x 10^{-3} mmol, 3 mol %) in 1.0 mL anhydrous THF. After stirring at room temperature for 8 hours, solvent was removed under high vacuum, and the residue was redissolved in 1.0 mL anhydrous THF. Removal and addition of solvent was repeated every 8 hours, until ^{1}H NMR showed complete conversion. Recrystallization of crude product with Et_2O at 4°C afforded pure product **3.46**.

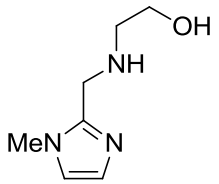
Crystal Structure of **3.46**, CCDC# 832192 (Figure 3.5)



Developing a Site Selective Functionalization Reaction

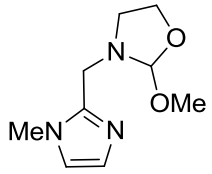
The following compounds were made according to literature procedure: 1-benzyloxy-2,3-propanediol, **3.57**[28], **III**[17],and (*S*)-1-cyclohexylethane-1,2-diol, (*S*)-**3.50**[16].

Catalyst Synthesis

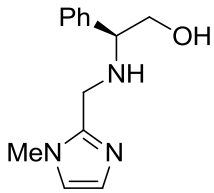


2-(((1-Methyl-l*H*-imidazol-2-yl)methyl)amino)ethanol.[24] To a solution of *N*-methylimidazole-2-carboxaldehyde (2.0 g, 18 mmol) in methanol (40 mL) was added ethanolamine (1.1 mL, 18 mmol) and 3Å molecular sieves (1.4 g). After refluxing for 24 hours, the reaction was cooled to room temperature, and $NaBH_4$ (1.0 g, 27 mmol) was added. The reaction was stirred at room temperature for 2 hours, followed by quenching with dropwise addition of concentrated HCl (0.88 mL). The resulting mixture was further neutralized with Na_2CO_3 (2.9 g). The precipitated salts were filtered off, and the filtrate was concentrated. Flash column chromatography (CH_2Cl_2:MeOH = 9:1) afforded the pure product as a yellow oil (1.9 g, 68%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 6 d *J* = 1.0), 6.74 (d, 1H, *J* = 1.0), 5.79 (s, 2H), 3.89 (s, 2H), 3.62 (t, 2H, *J* = 5.0), 3.58 (s, 3H), 2.82 (t, 2H, *J* = 5.0); **^{13}C NMR** ($CDCl_3$ 2 M z δ 7 26 2 6 0 43.8, 32.9; **IR**: 3280, 2947, 1496, 1282, 1049, 748, 655 cm^{-1}; **HRMS** calcd. for $C_7H_{14}N_3O$ $[M+H]^+$: 156.1136, found: 156.1141.

[28]Tsujigami, T.; Sugai, T.; Ohta, H. *Tet. Asymm.* **2001**, *12*, 2543-2549.

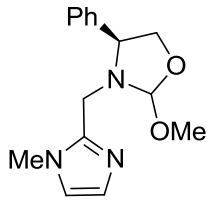


2-Methoxy-3-((1-methyl-1*H*-imidazol-2-yl)methyl)oxazolidine. To a solution of 2-(((1-methyl-1*H*-imidazol-2-yl)methyl)amino)ethanol (0.50 g, 3.2 mmol) in anhydrous methanol (11 mL) under argon was added *N*,*N*-dimethylformamide dimethyl acetal (0.51 mL, 3.8 mmol). The reaction was stirred at room temperature for 2 hours, and the solvent was removed under vacuum. The residue was redissolved in anhydrous methanol (11 mL), and the reaction was again stirred at room temperature for 2 hours. The solvent was removed under vacuum. The flask was brought into a dry glove box under nitrogen atmosphere, and the residue was extracted with degassed pentane to afford the pure product as a colorless oil (320 mg, 51%). **^{1}H NMR** (C_6D_6 00 M z δ 7 0 d H, *J* = 1.0), 6.38 (d, 1H, *J* = 1.0), 5.09 (s, 1H), 3.74 (d, 1H, *J* = 13.0), 3.65 (d, 1H, *J* = 13.0), 3.63-3.67 (m, 1H), 3.53-3.57 (m, 1H), 3.09 (s, 3H), 2.99 (s, 3H), 2.73-2.77 (m, 1H), 2.56-2.60 (m, 1H); **^{13}C NMR** ($CDCl_3$ 26 M z δ 6 20 111.6, 107.1, 64.8, 51.1, 49.1, 46.1, 37.6; **IR**: 2948, 2894, 1500, 1284, 1046, 953, 736 cm^{-1}; **HRMS** calcd. for $C_8H_{12}N_2O$ [M-OMe]: 166.0980, found: 166.0980.



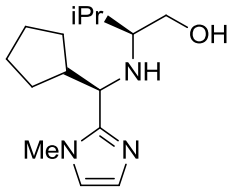
(*S*)-2-(((1-Methyl-1*H*-imidazol-2-yl)methyl)amino)-2-phenylethanol.[24] To a solution of *N*-methyl-imidazole-2-carboxaldehyde (1.37 g, 10.0 mmol) in benzene (30 mL) was

added (*S*)-glycinol (1.10 g, 10.0 mmol) and 3Å molecular sieves (1.40 g). After refluxing for 24 hours, the reaction was cooled to room temperature, and the solvent was removed in vacuo. The resulting residue was redissolved in MeOH (30 mL) and $NaBH_4$ (378 mg, 10.0 mmol) was added. The reaction was stirred at room temperature for 2 hours, followed by quenching with dropwise addition of concentrated HCl (0.51 mL). The resulting mixture was further neutralized with Na_2CO_3 (1.67 g). The precipitated salts were filtered off, and the filtrate was concentrated. Flash column chromatography (CH_2Cl_2:MeOH = 10:1) afforded the pure product as a yellow oil (1.88 g, 81%). **^{1}H NMR** ($CDCl_3$ 00 M z δ 7 2 -7.37 (m, 5H), 6.84 (d, 1H, *J* = 1.0), 6.72 (d, 1H, *J* = 1.0), 3.82-3.86 (m, 1H), 3.66-3.69 (m, 3H), 3.55 (dd, 1H, *J* = 9.5, 11.0), 3.45 (s, 3H); **^{13}C NMR** ($CDCl_3$ 2 M z δ 6 0 2 27 6 27 26 2 0 66 6 3 55.9, 43.3, 32.6; **IR**: 3299, 2914, 2842, 1493, 1283, 1050, 758, 702 cm^{-1}; **HRMS** calcd. for $C_{13}H_{18}N_3O$ $[M+H]^+$: 232.1449, found: 232.1454.



(4*S*)-2-Methoxy-3-((1-methyl-l*H*-imidazol-2-yl)methyl)-4-phenyloxazolidine (60:40 dr). To a solution of (*S*)-2-(((1-methyl-1*H*-imidazol-2-yl)methyl)amino)-2-phenylethanol (1.88 g, 8.10 mmol) in anhydrous methanol (30 mL) under argon was added *N*,*N*-dimethylformamide dimethyl acetal (1.09 mL, 8.10 mmol). The reaction was stirred at room temperature for 2 hours, and the solvent was removed under vacuum. The residue

was redissolved in anhydrous methanol (13 mL), and the reaction was stirred at room temperature for 1 hour. The solvent was removed under vacuum. The flask was brought into a dry glove box under nitrogen atmosphere, and the residue was extracted with degassed pentane to afford the pure product as a pale yellow oil (1.95 g, 88%). **^{1}H NMR** (C_6D_6 00 M z δ 7 2 -7.26 (m, 1.2H), 7.15-7.18 (m, 0.8H), 6.99-7.09 (m, 3H), 6.98 (d, 0.4H, *J* = 1.0), 6.96 (d, 0.6H, *J* = 1.0), 6.22 (d, 0.4H, *J* = 1.0), 6.20 (d, 0.6H, *J* = 1.0), 5.60 (s, 0.6H), 5.39 (s, 0.4H), 4.18 (t, 0.6H, *J* = 8.0), 4.09 (t, 0.4H, *J* = 8.0), 3.95-3.98 (m, 1H), 3.87 (dd, 0.6H, *J* = 7.0, 8.0), 3.72 (dd, 0.4H, *J* = 8.0, 9.5), 3.67-3.70 (m, 0.8H), 3.70 (d, 0.6H, *J*= 14.0), 3.65 (d, 0.6H, *J*= 14.0), 3.20 (s, 0.4H), 3.15 (s, 0.6H), 2.77 (s, 0.6H), 2.72 (s, 0.4H); **^{13}C NMR** ($CDCl_3$ 26 M z δ 2 3 0 6 138.9, 128.2, 127.1, 120.5, 120.4, 113.1, 110.5, 109.1, 106.5, 73.2, 72.3, 66.0, 63.3, 52.7, 50.9, 44.9, 44.0, 41.8, 37.5, 32.0, 31.6; **IR**: 2943, 1498, 1453, 1283, 1155, 1042, 731, 700 cm^{-1}; **HRMS** calcd. for $C_{14}H_{16}N_3O$ [M-OMe]: 242.1293, Found: 242.1308.



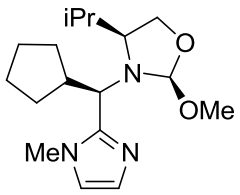
(*S*)-2-(((*R*)-cyclopentyl(1-methyl-1H-imidazol-2-yl)methyl)amino)-3-methylbutan-1-ol (94:6 dr).[24,29] Cyclopentene (7.5 g, 110 mmol) and tris(2,4-di*tert*-butyl-phenyl)phosphite (890 mg, 1.4 mmol) were distributed evenly into five Endeavor® reaction vials that were purged with nitrogen. $Rh(acac)(CO)_2$ (99 mg, 1.8 x 10^{-2} mmol) was dissolved in benzene (22 mL) and also distributed evenly into the five reaction vials.

[29]Trzeciak, A. M.; Ziolkowski, J. J. *J. Organomet. Chem.* **1994**, *479*, 213-216.

The vials were purged 3 times with 1:1 H_2/CO, pressurized to 150 psi, and heated to 80 °C. The reactions were stirred for 6 hours maintaining constant temperature and pressure. Four of the vials containing the crude cyclopentanecarboxaldehyde were combined and used in the next step without purification. To a stirring solution of (*S*)-valinol (9.1 g, 88 mmol) in anhydrous THF (180 mL) under nitrogen atmosphere was added a solution of crude cyclopentanecarboxaldehyde (88 mmol) in benzene (18 mL). $MgSO_4$ (18 g) was added, and the solution was stirred at room temperature for 3 hours to form the imine which closes to the oxazolidine in situ. In another oven-dried flask, to a solution of *N*-methylimidazole (25 g, 310 mmol) in anhydrous THF (180 mL) under nitrogen atmosphere was added *n*-butyllithium (31 mL, 10 M in hexanes, 310 mmol) dropwise at -78 °C. The solution was stirred at -78 °C for 30 minutes, and then was slowly cannula transferred into the solution of formed oxazolidine at -78 °C. The resulting mixture was stirred overnight and gradually warmed to room temperature. Saturated aqueous NH_4Cl solution was added slowly to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3×200 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography (CH_2Cl_2/MeOH = 30:1) afforded the product as colorless oil (12 g, 63%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.77 (d, 0.18H, *J* = 6.8), 0.82 (d, 0.18H, *J* = 6.8), 0.87 (d, 2.82H, *J* = 6.8), 0.91 (d, 2.82H, *J* = 6.8), 1.20-1.32 (m, 0.54H), 1.33-1.74 (m, 8.46H), 2.13-2.22 (m, 1.88H), 2.24-2.27 (m, 0.12H), 3.26 (d, 0.06H, *J* = 7.1), 3.28 (d, 0.94H, *J* = 5.9), 3.30 (d, 0.94H, *J* = 2.9), 3.32 (d, 0.06H, *J* = 4.4), 3.61 (s, 2.82H), 3.62 (s, 0.18H), 3.72 (d, 1H, *J* = 7.6), 6.72 (d, 0.06H, *J* = 1.2), 6.76 (d, 0.94H, *J* = 1.2), 6.93 (d, 0.94H, *J* = 1.2); **^{13}C NMR** ($CDCl_3$, 125

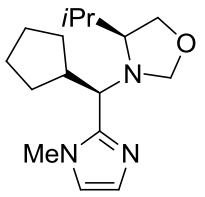
MHz) δ 38.1, 38.3, 38.4, 38.6, 44.4, 44.5, 44.6, 48.6, 48.7, 48.9, 49.8, 50.1, 52.1, 65.0, 77.7, 78.0, 79.3, 81.6, 82.0, 82.7, 139.7, 140.2, 146.1, 146.2, 169.8, 170.6; **IR**: 3201, 2952, 2868, 1486, 1467, 1280, 1107, 1047, 835, 724 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{15}H_{28}N_3O$ $[M+H]^+$: 266.2227, found: 266.2247. $\mathbf{[\alpha]_D^{20}}$ = +46.7 (c = 1.0, CH_2Cl_2, *l* = 50 mm).

Note: The mixture of diastereomers can be taken forward because only one precipitates during purification in the next step.



(2*R*,4*S*)-3-((*R*)-cyclopentyl(1-methyl-1H-imidazol-2-yl)methyl)-4-isopropyl-2-methoxyoxazolidine, IV (99:1 dr). To a solution of (*S*)-2-(((*R*)-cyclopentyl(1-methyl-1H-imidazol-2-yl)methyl)amino)-3-methylbutan-1-ol (7.4 g, 28 mmol) in anhydrous MeOH (56 mL) under nitrogen atmosphere was added *N,N*-dimethylformamide dimethyl acetal (19 mL, 140 mmol). The reaction was stirred at 50 °C overnight. The solvent was removed under vacuum, and the residue was redissolved in anhydrous MeOH (56 mL) in order to convert the small amount of dimethylamine bound catalyst to methanol bound catalyst. The reaction was stirred at 50 °C for 2 hours, and the solvent was removed under vacuum. The residue was moved into a dry box and was dissolved in anhydrous pentane (250 mL). The solution was cooled to -40 °C overnight, and a dark yellow oil formed on the bottom of the flask. The top clear organic layer was decanted off and was

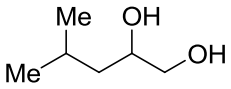
concentrated to approximately 100 mL. The solution was cooled to -40 °C overnight during which the product precipitated as a white solid. The solid was filtered and washed with a small portion of cold pentane to afford pure product (3.9 g, 46%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.69 (d, 3H, *J* = 7.1), 0.73-0.80 (m, 1H), 0.87 (d, 3H, *J* = 6.9), 1.46-1.78 (m, 7H), 2.33-2.40 (m, 1H), 2.75 (ddd, 1H, *J* = 8.8, 6.9, 5.1), 2.92 (s, 3H), 2.97-3.06 (m, 1H), 3.34 (s, 3H), 3.48 (d, 1H, *J* = 11.0), 3.59 (t, 1H, *J* = 7.8), 3.75 (t, 1H, *J* = 8.3), 6.27 (d, 1H, *J* = 1.2), 6.72 (s, 1H), 7.16 (d, 1H, *J* = 1.2); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 16.8, 20.1, 25.6, 26.0, 29.5, 31.8, 32.2, 32.3, 45.1, 52.3, 58.8, 65.4, 66.0, 112.6, 120.2, 128.5, 149.1; **IR**: 2952, 2870, 1650, 1482, 1192, 1174, 1122, 1074, 1052, 962 cm^{-1}**.** **Elemental Anaylsis**: $C_{17}H_{29}N_3O_2$ requires: C = 66.42%, H = 9.51%, N = 13.67%, found: C = 66.51%, H = 9.28%, N = 13.82%. **$[\alpha]_D^{20}$ =** -37.3 (c = 1.0, CH_2Cl_2, *l* = 50 mm).



(*S*)-4-isopropyl-3-((*R*)-2-methyl-1-(1-methyl-1H-imidazol-2-yl)propyl)oxazolidine, 3.53.[25] To a stirring solution of (*S*)-2-(((*R*)-cyclopentyl(1-methyl-1H-imidazol -2-yl)methyl)amino)-3-methylbutan-1-ol (0.50 g, 1.9 mmol) and paraformaldehyde (57 mg, 1.9 mmol) in anhydrous toluene (19 mL), *p*-toluenesulfonic acid monohydrate (3.6 mg, 1.9×10^{-2} mmol) was added. After refluxing overnight, reaction was cooled to room temperature, and CH_2Cl_2 (30 mL) was added. The resulting solution was concentrated. Flash column chromatography (100% EtOAc) afforded the product as colorless oil (280

mg, 54%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.88 (d, 3H, *J* = 6.8), 0.92 (d, 3H, *J* = 6.6), 1.51-1.73 (m, 8H), 2.02-2.07 (m, 1H), 2.57-2.60 (m, 1H), 2.70-2.73 (m, 1H), 3.47 (d, 2H, *J* = 6.3), 3.61 (d, 1H, *J* = 10.5), 3.68 (s, 3H), 4.42 (d, 1H, *J* = 4.6), 5.06 (d, 1H, *J* = 4.4), 6.78 (d, 1H, *J* = 1.0), 7.02 (d, 1H, *J* = 1.2); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 18.1, 19.8, 25.1, 25.4, 30.9, 31.0, 31.7, 33.1, 44.4, 61.5, 66.5, 67.6, 82.3, 120.3, 127.6, 148.4; **IR**: 2953, 2867, 1650, 1479, 1279, 1171, 1133, 1082, 943, 724 cm^{-1}; **$[\alpha]_D^{20}$** = +24.4 (*c* = 0.98, CH_2Cl_2, *l* = 50 mm).

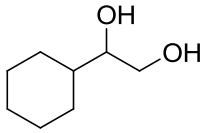
Substrate Synthesis



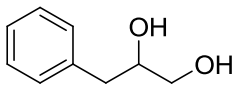
4-methylpentane-1,2-diol, 3.54.[30] Sodium metaperiodate (6.11 g, 28.5 mmol), 4-methyl-1-pentene (6.00 mL, 4.80 x 10^1 mmol), and lithium bromide (1.65 g, 1.90 x 10^1 mmol) were dissolved in acetic acid (79 mL) and heated to 95 °C for 14 hours during which time the solution turned dark red. The reaction was diluted with EtOAc (100 mL) and washed with saturated aqueous $Na_2S_2O_3$ (30 mL), H_2O (30 mL), and saturated aqueous $NaHCO_3$ (30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude oil was dissolved in MeOH (120 mL) and K_2CO_3 (13.1 g, 95 mmol) was added. The mixture was stirred at 25 °C for 15 hours. The methanol was removed under reduced pressure, and the mixture was dissolved in water and extracted with EtOAc (3x50 mL). The combined organic layers were washed with H_2O (50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. Column chromatography

[30]Emmanuvel, L.; Shaikh, T. M.; Sudalai, A. *Org. Lett.* **2005**, *7*, 5071-5074.

was performed (20-50% EtOAc/Hex) resulting in a yellow oil which was distilled (150 °C at 1 mmHg) to yield a colorless oil (2.39 g, 43%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.86 (d, 3H, *J* = 6.6), 0.88 (d, 3H, *J* = 6.6), 1.13 (ddd, 1H, *J* = 18.3, 8.6, 4.4), 1.33 (ddd, 1H, *J* = 19.6, 8.8, 5.6), 1.67-1.75 (m, 1H), 2.30-2.37 (m, 2H), 3.34 (dd, 1H, *J* = 11.0, 7.8), 3.57 (dd, 1H, *J* = 11.0, 2.5), 3.70-3.75 (m, 1H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 22.3, 23.5, 24.7, 42.3, 68.4, 70.6; **IR**: 3341, 2954, 2870, 1468, 1067, 1027, 579 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_6H_{18}N_1O_2$: $[M+NH_4]^+$: 136.1338, found: 136.1341.



1-cyclohexylethane-1,2-diol, 3.50.[30] The same procedure used for 4-methylpentane-1,2-diol was used to yield a colorless oil which solidified upon standing (1.30 g, 49%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 1.00-1.08 (m, 2H), 1.13-1.29 (m, 3H), 1.38-1.45 (m, 1H), 1.63-1.69 (m, 2H), 1.72-1.79 (m, 2H), 1.86-1.89 (m, 2H), 2.00-2.01 (m, 1H), 3.43-3.47 (m, 1H), 3.51-3.55 (m, 1H), 3.69-3.73 (m, 1H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 26.2, 26.3, 26.6, 28.8, 29.1, 40.9, 65.0, 76.7; **IR**: 3339, 2922, 2852, 1449, 1050, 1015, 892, 605 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_8H_{20}N_1O_2$: $[M+NH_4]^+$: 162.1494, found: 162.1490.



3-phenylpropane-1,2-diol, 3.56.[30] The same procedure used for 4-methylpentane-1,2-diol was used to yield a colorless oil (2.98 g, 37%).**^{1}H NMR** ($CDCl_3$, 500 MHz) δ 2.27

(bs, 2H), 2.74-2.83 (m, 2H), 3.51-3.55 (m, 1H), 3.70 (dd, 1H, J = 11.2, 2.4), 3.94-3.98 (m, 1H), 7.23-7.26 (m, 3H), 7.32-7.34 (m, 2H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 39.9, 66.7, 73.2, 126.7, 128.7, 129.5, 138.0; **IR**: 3362, 2925, 1496, 1454, 1089, 1068, 1030, 744, 700, 555 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_9H_{16}N_1O_2$: $[M+NH_4]^+$: 170.1181, found: 170.1189.

Reaction of **III** with Individual Enantiomers (Scheme 3.25)

To an oven-dried reaction vial, a solution of hexane-1,2-diol, **3.47**, (24 mg, 0.20 mmol), *p*-toluenesulfonic acid (1.0 mg, 6.0 x 10^{-3} mmol, 3 mol %), and **III** (12 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred for 10 minutes at 4 °C. 1,2,2,6,6-Pentamethylpiperidine (3 µL, 0.2 mmol, 2 equiv.) was added, followed by triethylchlorosilane (36 µL, 0.20 mmol, 0 equiv.). After stirring at 4 °C for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine (30 µL) and methanol (1 mL). The mixture was stirred for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Scheme 3.25, Eq 1

(*S*)-hexane-1,2-diol, (*S*)-**3.47**, was used as the substrate in the reaction.

Scheme 3.25, Eq 2

(*R*)-hexane-1,2-diol, (*R*)-**3.47**, was used as the substrate in the reaction.

Solvent Screen (Table 3.12)

To an oven-dried reaction vial, a solution of hexane-1,2-diol, **3.47**, (24 mg, 0.20 mmol), *p*-toluenesulfonic acid (1.0 mg, 6.0 x 10^{-3} mmol, 3 mol %), and **III** (12 mg, 4.0 x 10^{-2}

mmol, 20 mol %) in anhydrous solvent (3 mL) was added. The reaction was stirred for 10 minutes at 4 °C. *N*,*N*-Diisopropylethylamine (2 μL, 0.02 mmol, 2 equiv.) was added, followed by triethylchlorosilane (36 μL, 0.20 mmol, 10 equiv.). After stirring at 4 °C for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine (30 μL) and methanol (1 mL). The mixture was stirred for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction. The following solvents were tested in the reaction: THF, EtOAc, MeO*t*Bu, CH_3CN, $ClCH_2Cl$, *t*BuOH (run at room temperature).

Individual Enantiomer Selectivities in *t*BuOH (Table 3.13)

To an oven-dried reaction vial, a solution of hexane-1,2-diol, **3.47**, (24 mg, 0.20 mmol), *p*-toluenesulfonic acid (1.0 mg, 6.0×10^{-3} mmol, 3 mol %), and **III** (12 mg, 4.0×10^{-2} mmol, 20 mol %) in anhydrous *t*BuOH (3 mL) was added. The reaction was stirred for 10 minutes at 25 °C. *N*,*N*-Diisopropylethylamine (2 μL, 0.02 mmol, 2 equiv.) was added, followed by triethylchlorosilane (36 μL, 0.20 mmol, 10 equiv.). After stirring at 25 °C for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine (30 μL) and methanol (1 mL). The mixture was stirred for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Table 3.13, Entry 1

(*R*)-hexane-1,2-diol, (*R*)-**3.47**, was used as the substrate in the reaction.

Table 3.13, Entry 2

(*S*)-hexane-1,2-diol, (*S*)-**3.47**, was used as the substrate in the reaction.

Table 3.13, Entry 3

(*S*)-hexane-1,2-diol, (*S*)-**3.47**, was used as the substrate and *N*-methylimidazole (3.2 µL, 4.0 x 10^{-2} mmol, 20 mol %) was used in the catalyst in the reaction.

t-Amyl Alcohol Temperature Screen (Table 3.14)

To an oven-dried reaction vial, a solution of (*S*)-hexane-1,2-diol, **3.47**, (24 mg, 0.20 mmol), *p*-toluenesulfonic acid (1.0 mg, 6.0 x 10^{-3} mmol, 3 mol %), and **III** (12 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous *t*-amyl alcohol (3 mL) was added. The reaction was stirred for 10 minutes. *N*,*N*-Diisopropylethylamine (2 µL, 0.2 mmol, 2 equiv.) was added, followed by triethylchlorosilane (4.0 x 10^{1} µL, 0.2 mmol, 2 equiv.). After stirring at a constant temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine (30 µL) and methanol (µL). The mixture was stirred for 0 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction. The reaction was run at the following temperatures: -6 °C, 4 °C, and 25 °C.

Screen of Catalysts with Cyclic R Groups (Table 3.15)

To an oven-dried reaction vial, a solution of (*S*)-hexane-1,2-diol, (*S*)-**3.47**, (24 mg, 0.20 mmol), *p*-toluenesulfonic acid (1.0 mg, 6.0 x 10^{-3} mmol, 3 mol %), and catalyst (20 mol %) in anhydrous *t*-amyl alcohol (3 mL) was added. The reaction was stirred for 10 minutes at 4 °C. *N*,*N*-Diisopropylethylamine (2 µL, 0.2 mmol, 2 equiv.) was added, followed by triethylchlorosilane (4.0 x 10^{1} µL, 0.2 mmol, 1.2 equiv). After stirring at 4

°C for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine (30 μ and methanol μ he mi t re was stirred for 0 mi n and filtered thro g h a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

R= *i*Pr, **III**, (12 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= Cyclopropyl (12 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= Cyclopentyl, **IV**, (13 mg, 4.0 x 10^{-2} mmol, 20 mol %)

Catalyst Screen with (*S*)-1-Cyclohexyl-1,2-ethanediol (Table 3.16)

In a dry box, a solution of (*S*)-1-cyclohexylethane-1,2-diol, (*S*)-**3.50**, (29 mg, 0.20 mmol), catalyst, and *N,N*-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous *tert*-amyl alcohol (3.0 mL) was prepared in an oven-dried glass reaction vial. The reaction was stirred at 4 °C for 10 minutes. *N,N*-diisopropylethylamine (45 μL, 0.26 mmol, 1.3 equiv) was added, followed by addition of chlorotriethylsilane (44 μL, 0.26 mmol, 1.3 equiv). The reaction was stirred at 4 °C for 30 minutes. MeOH (100 μL) was added to quench the reaction. The solvent was removed under reduced pressure. 1,3,5-trimethoxybenzene (100 μL, 2M solution in EtOAc, 0.020 mmol) was added as an internal standard. Chiral GC Analysis ((Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 115 °C for 180 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi) of crude product afforded quantitative results of the reaction.

Table 3.16, Entry 1

N-methylimidazole 2 μ 3 0 0 $^{-2}$ mmol, 15 mol %) was used in the catalyst in the reaction.

Table 3.16, Entry 2

Catalyst **III** (8.9 mg, 3.0 x 10^{-2} mmol, 15 mol %) was used in the reaction.

Table 3.16, Entry 3

Catalyst **IV** (8.3 mg, 3.0 x 10^{-2} mmol, 15 mol %) was used in the reaction.

Table 3.16, Entry 4

(*R*)-Cyclohexane-1,2-diol, (*R*)-**3.50**, and catalyst **IV** (8.3 mg, 3.0 x 10^{-2} mmol, 15 mol %) were used in the reaction.

Control Catalyst with (*S*)-Cyclohexane-1,2-diol (Scheme 3.26, Eq 1)

In a dry box, a solution of (*S*)-1-cyclohexylethane-1,2-diol, (*S*)-**3.50**, (29 mg, 0.20 mmol), catalyst **3.53** (8.8 mg, 3.0 x 10^{-2} mmol, 15 mol %), and *N,N*-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous *tert*-amyl alcohol (3.0 mL) was prepared in an oven-dried glass reaction vial. The reaction was stirred at 4 °C for 10 minutes. *N,N*-diisopropylethylamine (45 μL, 0.26 mmol, 1.3 equiv) was added, followed by addition of chlorotriethylsilane (44 μL, 0.26 mmol, 1.3 equiv). The reaction was stirred at 4 °C for 30 minutes. MeOH (100 μL) was added to quench the reaction. The solvent was removed under reduced pressure. 1,3,5-Trimethoxybenzene (100 μL, 2M solution in EtOAc, 0.020 mmol) was added as an internal standard. Chiral GC Analysis ((Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 115 °C for 180 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi) of crude product afforded quantitative results of the reaction.

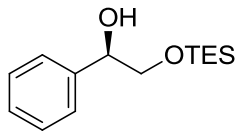
Control Catalyst with (*R*)-Cyclohexane-1,2-diol (Scheme 3.26, Eq 2)

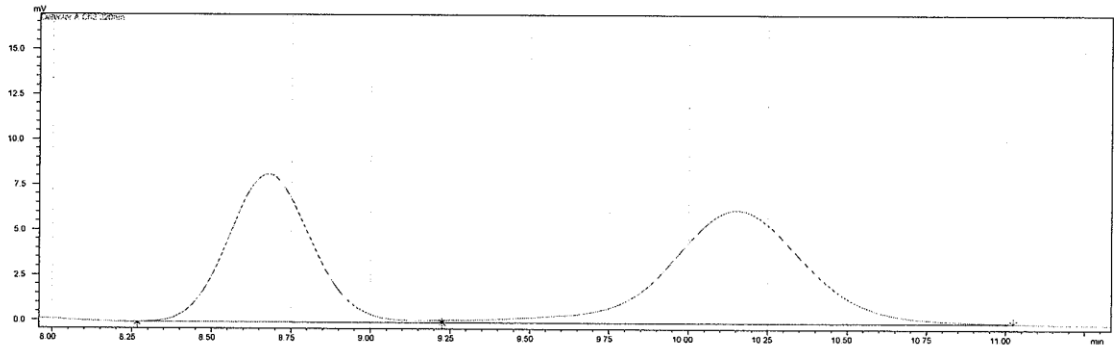
In a dry box, a solution of (*R*)-1-cyclohexylethane-1,2-diol, (*R*)-**3.50**, (29 mg, 0.20 mmol), catalyst **3.53** (8.8 mg, 3.0 x 10^{-2} mmol, 15 mol %), and *N,N*-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous *tert*-amyl alcohol (3.0 mL) was prepared in an oven-dried glass reaction vial. The reaction was stirred at 4 °C for 10 minutes. *N,N*-diisopropylethylamine (45 μL, 0.26 mmol, 1.3 equiv) was added, followed by addition of chlorotriethylsilane (44 μL, 0.26 mmol, 1.3 equiv). The reaction was stirred at 4 °C for 30 minutes. MeOH (100 μL) was added to quench the reaction. The solvent was removed under reduced pressure. 1,3,5-Trimethoxybenzene (100 μL, 2M solution in EtOAc, 0.020 mmol) was added as an internal standard. Chiral GC Analysis ((Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 115 °C for 180 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi) of crude product afforded quantitative results of the reaction.

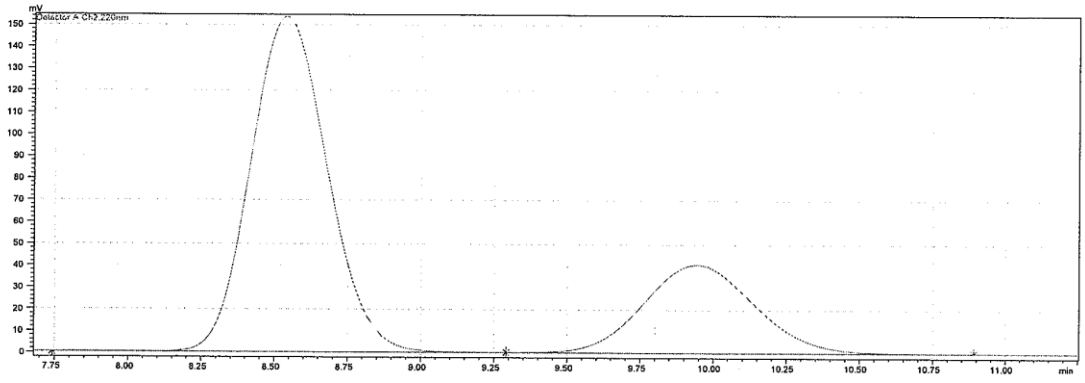
Reaction of 1-Phenyl-1,2-ethanediol (Scheme 3.27)

To an oven-dried reaction vial, a solution of 1-phenyl-1,2-ethane diol, **3.13** (140 mg, 1.0 mmol), *N,N*-diisopropylethylamine hydrochloride (33 mg, 0.20 mmol, 20 mol %), and catalyst **IV** (46 mg, 0.15 mmol, 15 mol %) in anhydrous *t*-amyl alcohol (14 mL) was added. The reaction was stirred for 10 minutes at 4 °C. *N,N*-Diisopropylethylamine (160 μ 2 mmol 2 equiv) was added, followed by triethylchlorosilane 0 μ 2 mmol, 1.2 equiv). After stirring at 4 °C for 25 mins, the reaction was quenched by addition of *N,N*-diisopropylethylamine 200 μ and methanol 0 μ he mi t re was stirred for 10 min and concentrated. Column Chromatography (0 to 20% EtOAc/Hex, using an

ISCO automated purification system) yielded **3.16** (140 mg, 56%) and **3.17** (69 mg, 27%) as colorless oils. **Chiral HPLC Analysis** for **3.16** : (OD-H, 1.0 mL/min, 0.5% *i*PrOH: 95.5% Hexanes, 220 nm, t_{rmajor} = 8.53 min and t_{rminor} = 9.94 min) 45% ee.

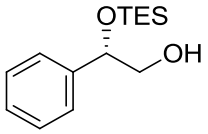




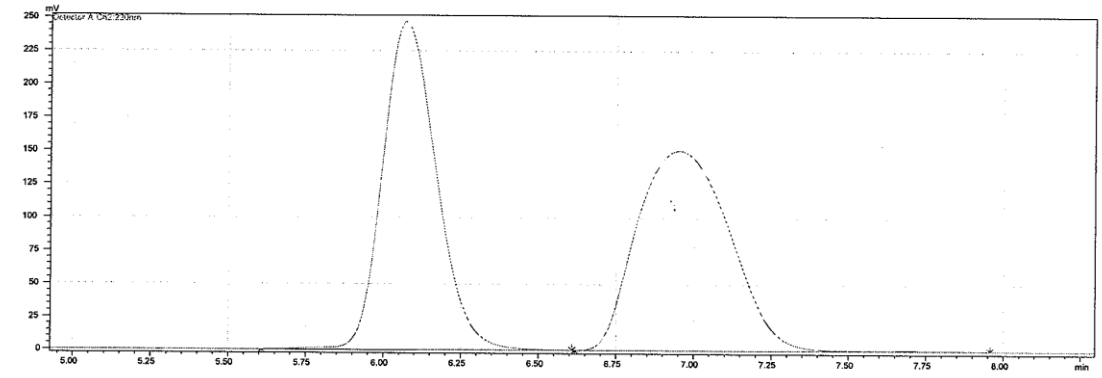


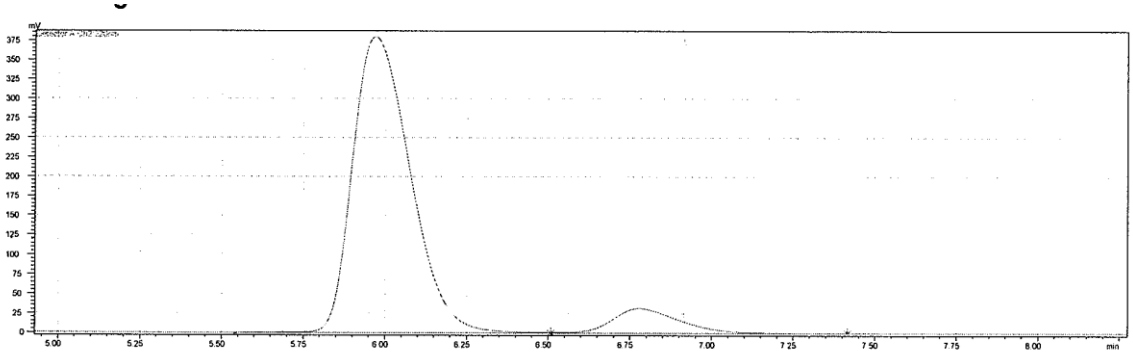
Detector A Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.534	2784397	153185	72.359	79.163
2	9.938	1063652	40322	27.641	20.837
Total		3848050	193507	100.000	100.000



Chiral HPLC Analysis for **3.17**: (OD-H, 1.0 mL/min, 0.5% *i*PrOH: 95.5% Hexanes, 220 nm, t_{rmajor} = 5.97 min and t_{rminor} = 6.78 min) 83% ee.





Detector A Ch2 220nm

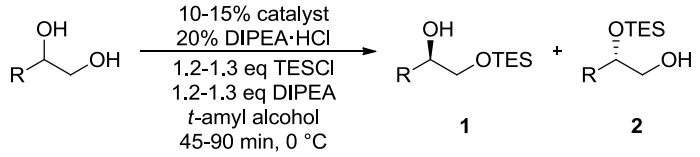
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.966	4635267	379960	91.256	92.315
2	6.775	444137	31631	8.744	7.685
Total		5079404	411591	100.000	100.000

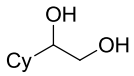
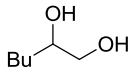
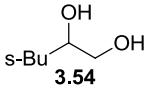
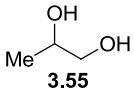
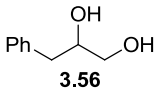
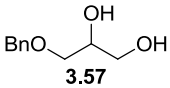
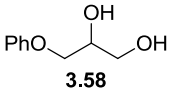
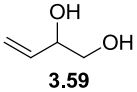
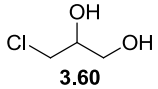
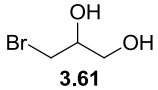
A duplicate reaction gave **3.16** (150 mg, 59%, 45% ee) and **3.17** (57 mg, 23%, 79% ee). The average of the two runs gave **3.16** (57%, 45% ee) and **3.17** (25%, 81% ee). For characterization of both compounds, see above.

General Procedure for Substrate Scope (Table 3.17)

In a dry box, a solution of 1-cyclohexylethane-1,2-diol, **3.50**, (140 mg, 1.0 mmol), catalyst **IV** (46 mg, 0.15 mmol, 15 mol %), and *N,N*-diisopropylethylamine hydrochloride (33 mg, 0.20 mmol, 20 mol %) in anhydrous *tert*-amyl alcohol (14 mL) was prepared in an oven-dried glass reaction vial. The reaction was stirred at 0 °C for 10 minutes. *N,N*-diisopropylethylamine (230 μL, 1.3 mmol, 1.3 equiv) was added, followed by addition of chlorotriethylsilane (220 μL, 1.3 mmol, 1.3 equiv). The reaction was stirred at 0 °C for 45 minutes. MeOH (500 μL) was added to quench the reaction. The solvent was removed under reduced pressure. Column chromatography (0-20% EtOAc in Hexanes, using an ISCO automated purification system) afforded **1** (150 mg, 56%) and **2** (110 mg, 41%) as colorless oils.

Table 3.17 Substrate Scope.



	Run 1		Run 2	
substrate	**1**[a,b]	**2**[a,b]	**1**[a,b]	**2**[a,b]
 **3.50**	47%, 81% ee[c]	41%, 97% ee[c]	56%, 81% ee[c]	41%, 96% ee[c]
 **3.47**	55%, 78% ee[d]	41%, 97% ee[d]	53%, 79% ee[d]	38%, 98% ee[d]
 **3.54**	54%, 82% ee[c]	40%, 98% ee[c]	53%, 82% ee[c]	40%, 98% ee[c]
 **3.55**	46%, 71% ee[e]	35%, 91% ee[e]	51%, 70% ee[e]	36%, 93% ee[e]
 **3.56**	48%, 75% ee[f]	42%, 94% ee[f]	50%, 80% ee[f]	44%, 96% ee[f]
 **3.57**	52%, 75% ee[d]	41%, 99% ee[d]	59%, 73% ee[d]	40%, 99% ee[d]
 **3.58**	42%, 77% ee[g]	31%, 96% ee[g]	47%, 77% ee[g]	34%, 95% ee[g]
 **3.59**	57%, 57% ee[e]	35%, 93% ee[e]	49%, 56% ee[e]	38%, 90% ee[e]
 **3.60**	52%, 90% ee[h]	44%, 97% ee[h]	52%, 90%ee[h]	46%, 98% ee[h]
 **3.61**	49%, 91% ee[c]	41%, 97% ee[c]	50%, 91% ee[c]	41%, 98% ee[c]

[a]Isolated yields. [b]Ee determined by GC or HPLC analysis. [c]Run with 15% **IV**, 1.3 equiv TESCl and DIPEA. [d]Run with 10% **III**, 1.2 equiv TESCl and DIPEA. [e]Run with 15% **IV**, 1.2 equiv TESCl and DIPEA. [f]Run with 10% **IV**, 1.2 equiv TESCl and DIPEA . [g]Run with 15% **III**, 1.4 equiv TESCl and DIPEA.[h]Run with 15% **IV**, 1.3 equiv TESCl and DIPEA .

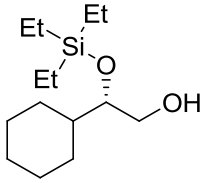
Calculated Selectivities for Each Enantiomer of Substrate (Table 3.18)

Substrate	(*R*)-2a-j[a]	(*R*)-3a-j[a]	(*S*)-2a-j[a]	(*S*)-3a-j[a]
3.13	95	5	41	59
3.50	99	1	12	88
3.47	99	1	13	87
3.54	99	1	11	89
3.55	96	4	17	83
3.56	98	2	10	90
3.57	>99	<1	14	86
3.58	98	2	14	86
3.59	97	3	27	73
3.60	99	1	6	94
3.61	99	1	5	95

[a]Approximate (*R*)-enantiomer and (*S*)-enantiomer selectivities calculated based on isolated yields and ees from Table 3.25.

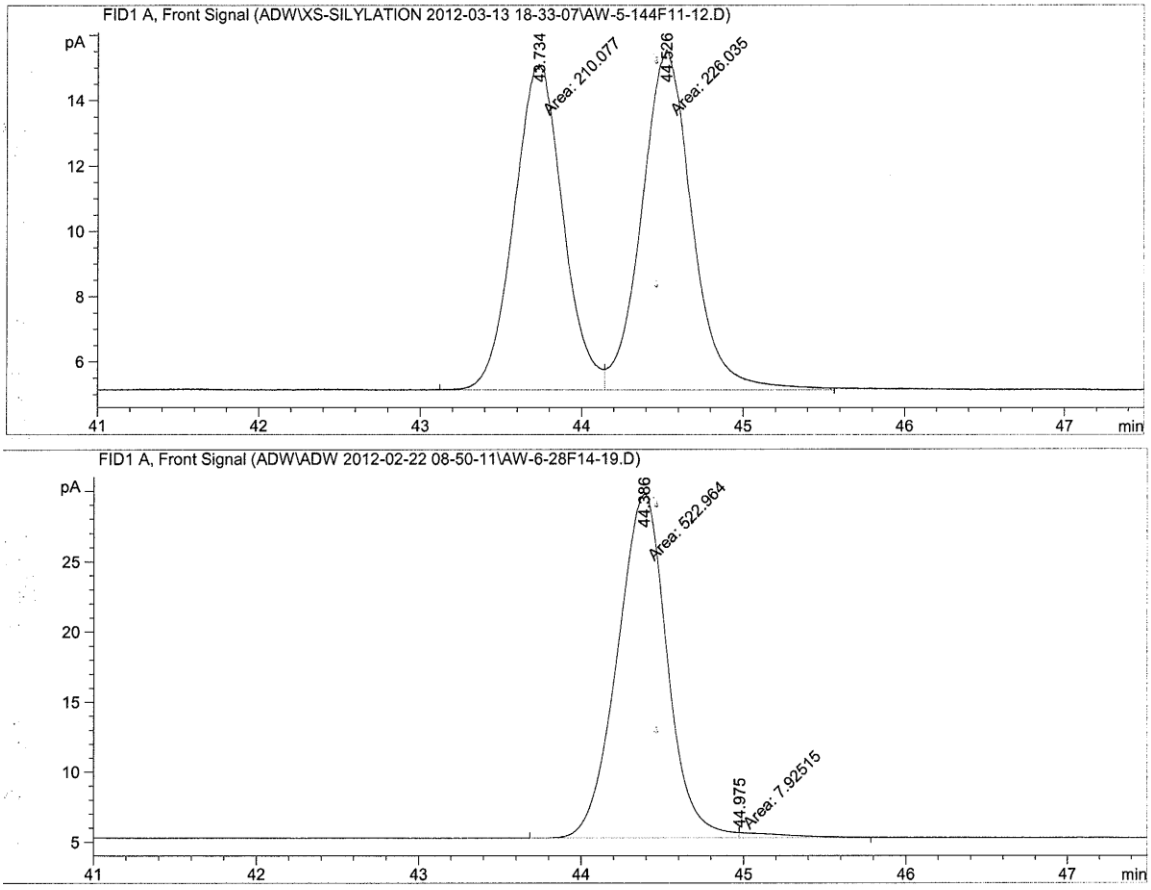
Product Characterization

Table 3.17, Entry 1



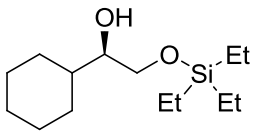
(*S*)-2-cyclohexyl-2-(triethylsilyloxy)ethanol. The general procedure was followed using **3.50** to yield a colorless oil (110 mg, 41%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 145 °C for 100 min, 10 °C/min to 200 °C, 200 °C for 10 min, 15 psi., t_{rmajor} = 44.4 min, t_{rminor} = 45.0 min) 97% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.63 (q, 6H, *J* = 8.1), 0.98 (t, 9H, *J* = 8.1), 1.10-1.25 (m, 4H), 1.46-1.53 (m, 1H), 1.65-1.84 (m, 7H), 3.49 (dt, 1H, *J* = 6.1, 3.7), 3.53-3.59 (m, 2H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 5.3, 7.1, 26.5, 26.6, 26.8, 29.0, 29.3, 41.4, 64.2, 77.4; **IR**: 3421, 2924, 2876, 1450, 1238, 1118, 1006, 739 cm^{-1}; **HRMS** (DART-TOF) calcd. for

$C_{14}H_{31}O_2Si_1$: $[M+H]^+$: 259.2093, found: 259.2099. $[\alpha]_D^{20}$ = +8.7 (*c* = 1.1, CH_2Cl_2, *l* = 50 mm).



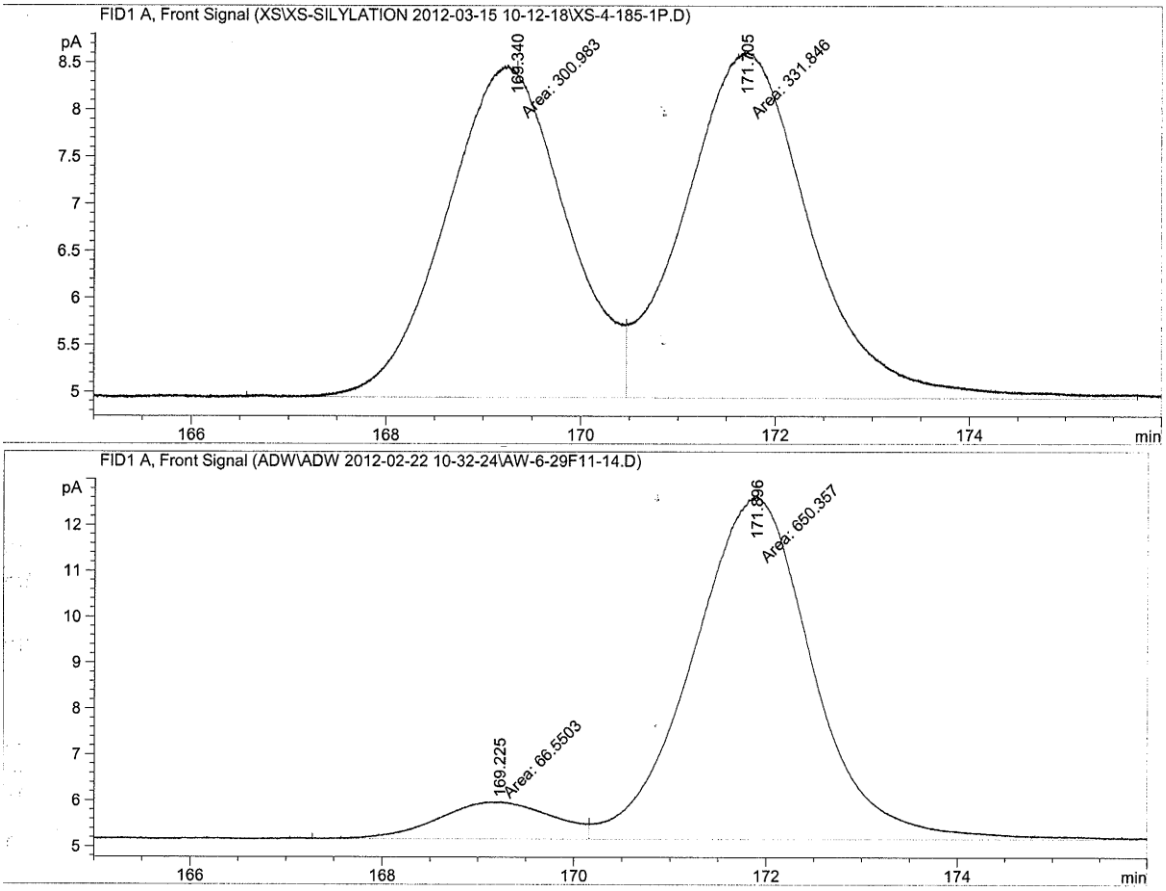
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	44.386	MF	0.3563	522.96381	24.46362	98.50719
2	44.975	FM	0.3433	7.92515	3.84790e-1	1.49281

Table 3.17, Entry 1



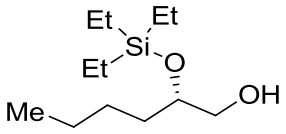
(*R*)-1-cyclohexyl-2-((triethylsilyl)oxy)ethanol. The general procedure was followed using **3.50** to yield the product as a colorless oil (120 mg, 47%). **Chiral GC Analysis**

(Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 115 °C for 180 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 172.2 min, t_{rminor} = 169.2 min) 81% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.59 (q, 6H, *J* = 7.8), 0.94 (t, 9H, *J* = 7.8), 0.98-1.06 (m, 2H), 1.10-1.25 (m, 3H), 1.33-1.40 (m, 1H), 1.57-1.65 (m, 2H), 1.69-1.75 (m, 2H), 1.87-1.91 (m, 1H), 2.48 (d, 1H, *J* = 2.9), 3.34-3.38 (m, 1H), 3.44 (dd, 1H, *J* = 9.8, 8.3), 3.67 (dd, 1H, *J* = 9.8, 3.2); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 26.3, 26.4, 26.7, 29.0, 29.1, 40.7, 65.2, 76.0; **IR**: 2921, 2875, 2852, 1450, 1112, 1079, 1004, 817, 726 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{14}H_{30}O_2NaSi$: $[M+Na]^+$: 281.1907, found: 281.1915. **$[\alpha]_D^{20}$** = -6.4 (c = 1.3, CH_2Cl_2, *l* = 50 mm).

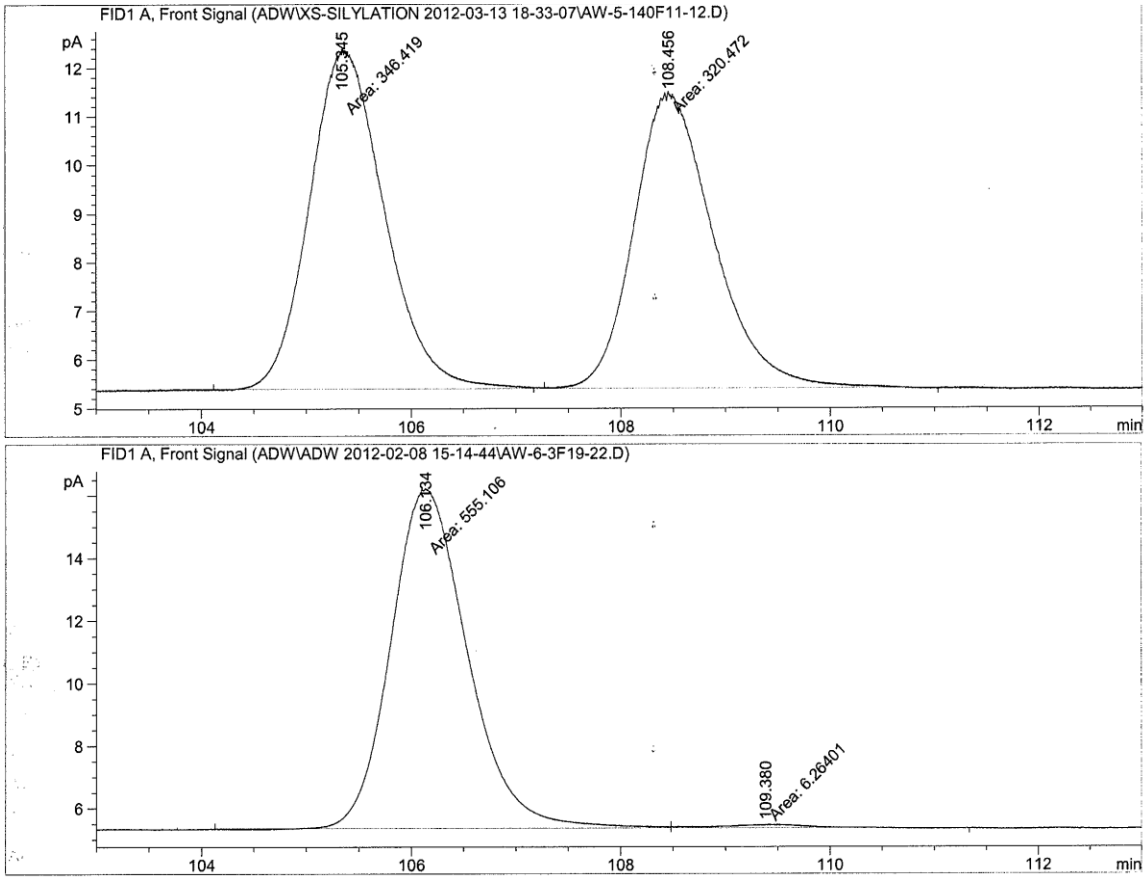


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	169.225	MF	1.3614	66.55033	8.14710e-1	9.28297
2	171.896	FM	1.4520	650.35730	7.46509	90.71703

Table 3.17, Entry 2

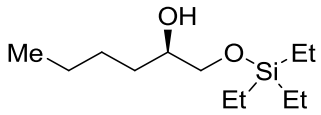


(*S*)-2-(triethylsilyloxy)hexan-1-ol. The general procedure was followed using **3.47** and 1.2 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine, 10 mol % **III**, and a reaction time of 1.5 hours to yield a colorless oil (88 mg, 38%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 95 °C for 120 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi., t_{rmajor} = 106.1 min, t_{rminor} = 109.4 min) 98% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.63 (q, 6H, J = 7.8), 0.88-0.91 (m, 3H), 0.98 (t, 9H, J = 7.8), 1.23-1.34 (m, 4H), 1.47-1.52 (m, 2H), 1.91 (t, 1H, J = 6.4), 3.42-3.46 (m, 1H), 3.54-3.59 (m, 1H), 3.71-3.76 (m, 1H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 5.3, 7.0, 23.0, 23.3, 24.7, 43.5, 66.8, 71.4; **IR**: 3408, 2955, 2876, 1459, 1239, 1097, 1007, 727 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{29}O_2Si_1$: $[M+H]^+$: 233.1937, found: 233.1934. **$[\alpha]_D^{20}$** = +11.4 (*c* = 1.1, CH_2Cl_2, *l* = 50 mm).



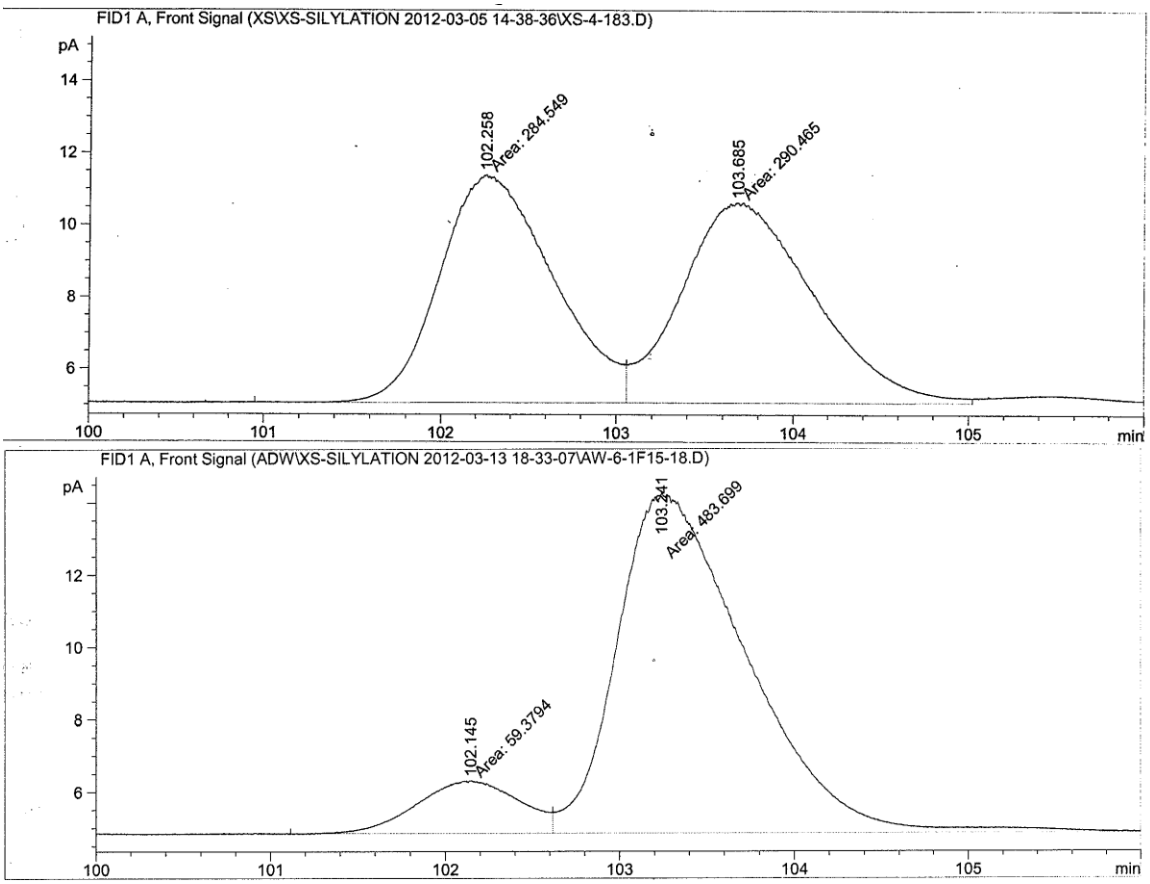
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	106.134	MF	0.8505	555.10553	10.87751	98.88416
2	109.380	FM	0.8242	6.26401	1.26669e-1	1.11584

Table 3.17, Entry 2



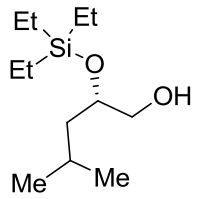
(*R*)-1-((triethylsilyl)oxy)hexan-2-ol. The general procedure was followed using **3.47** and 1.2 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine, 10 mol % **III**, and a reaction time of 1.5 hours to yield a colorless oil (130 mg, 55%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 µm film thickness), 95 °C for 120 min,

20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 103.2 min, t_{rminor} = 102.1 min) 78% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.60 (q, 6H, J = 7.8), 0.89 (t, 3H, J = 7.1), 0.94 (t, 9H, J = 7.8), 1.22-1.45 (m, 6H), 2.44 (d, 1H, J = 3.2), 3.36 (dt, 1H, J = 2.0, 8.8), 3.59-3.64 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 14.2, 23.0, 28.0, 32.7, 67.2, 72.1; **IR**: 2955, 2934, 2913, 2876, 1459, 1095, 1004, 803, 726 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{12}H_{28}O_2NaSi$: $[M+Na]^+$: 255.1751, found: 255.1745. **$[\alpha]_D^{20}$** = -3.6 (c = 1.1, CH_2Cl_2, l = 50 mm).

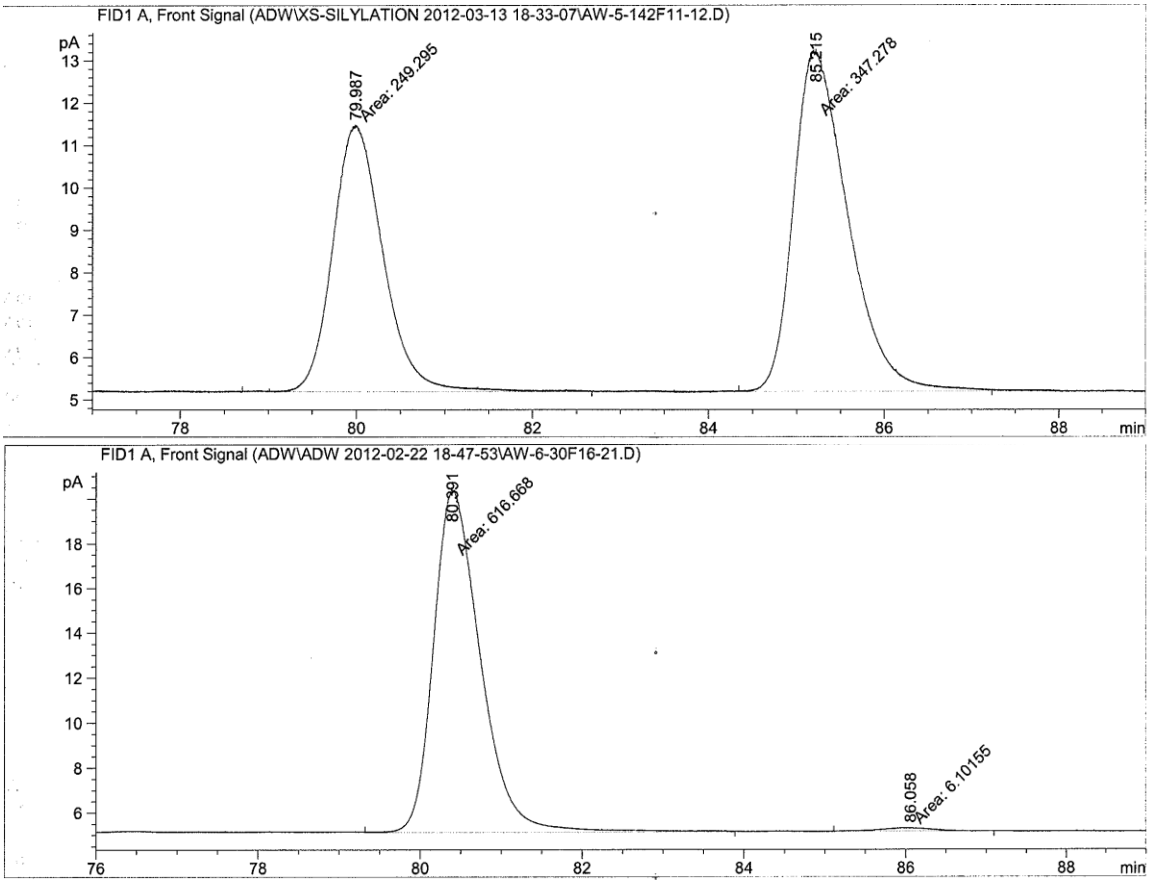


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	102.145	MF	0.6779	59.37944	1.45996	10.93386
2	103.241	FM	0.8584	483.69888	9.39185	89.06614

Table 3.17, Entry 3

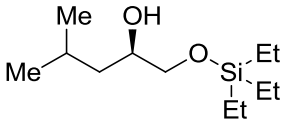


(*S*)-4-methyl-2-(triethylsilyloxy)pentan-1-ol. The general procedure was followed using **3.54** to yield a colorless oil (94 mg, 40%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 95 °C for 120 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi., t_{rmajor} = 80.4 min, t_{rminor} = 86.1 min) 98% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.63 (q, 6H, *J* = 8.1), 0.90 (d, 3H, *J* = 6.6), 0.91 (d, 3H, *J* = 6.6) 0.98 (t, 9H, *J* = 8.1), 1.38 (t, 2H, *J* = 6.8), 1.59-1.67 (m, 1H), 1.92 (t, 1H, *J* = 6.4), 3.39-3.44 (m, 1H), 3.57 (ddd, 1H, *J* = 11.0, 6.1, 3.7), 3.82 (ddt, 1H, *J* = 9.8, 5.4, 1.2); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 5.2, 7.0, 14.2, 23.0, 27.7, 40.0, 66.5, 73.1; **IR**: 3418, 2955, 2876, 1466, 1087, 1046, 742 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{29}O_2Si_1$: $[M+H]^+$: 233.1937, found: 233.1943. **$[\alpha]_D^{20}$** = +10.3 (*c* = 1.1, CH_2Cl_2, *l* = 50 mm).



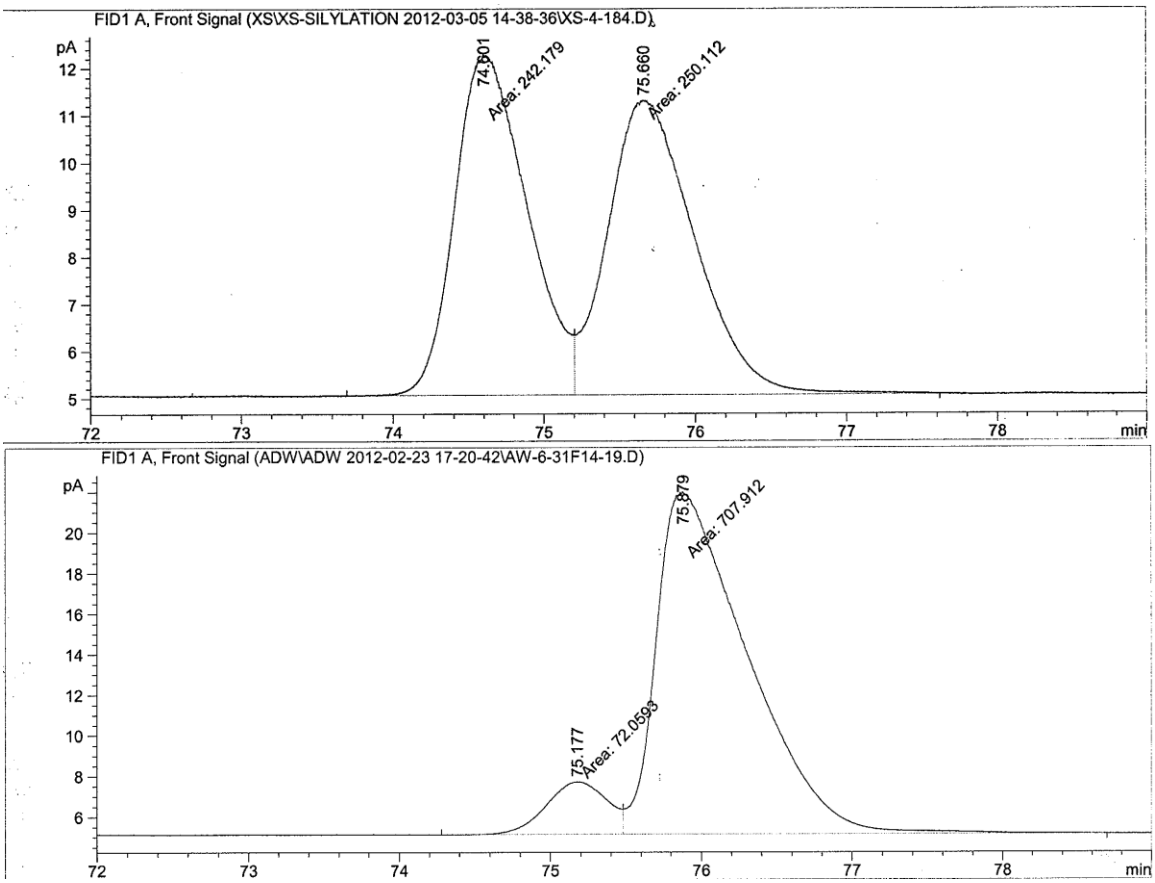
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	80.391	MM	0.6715	616.66846	15.30581	99.02026
2	86.058	MM	0.6070	6.10155	1.67528e-1	0.97974

Table 3.17, Entry 3



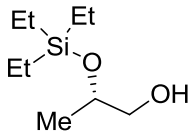
(*R*)-4-methyl-1-((triethylsilyl)oxy)pentan-2-ol. The general procedure was followed using **3.54** to yield the product as a colorless oil (125 mg, 54%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 95 °C for 90 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 75.9 min, t_{rminor} = 75.1 min) 82% ee.

^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.60 (q, 6H, *J* = 7.8), 0.90 (d, 3H, *J* = 6.6), 0.92 (d, 3H, *J* = 6.6), 0.95 (t, 9H, *J* = 7.8), 1.11 (ddd, 1H, *J* = 13.5, 8.5, 4.2),1.36 (ddd, 1H, *J* = 14.2, 8.8, 5.9), 1.74-1.82 (m, 1H), 2.40 (d, 1H, *J* = 3.2), 3.33 (dd, 1H, *J* = 9.8, 7.8), 3.58 (dd, 1H, *J* = 9.8, 3.2), 3.71 (ddd, 1H, *J* = 16.4, 7.8, 3.2); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 22.4, 23.6, 24.8, 42.0, 67.6, 70.3; **IR**: 2954, 2912, 2876, 1096, 1049, 1004, 789, 726 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{12}H_{28}O_2NaSi$: $[M+Na]^+$: 255.1751, found: 255.1763. **$[\alpha]_D^{20}$** = +0.94 (c = 1.2, CH_2Cl_2, *l* = 50 mm).

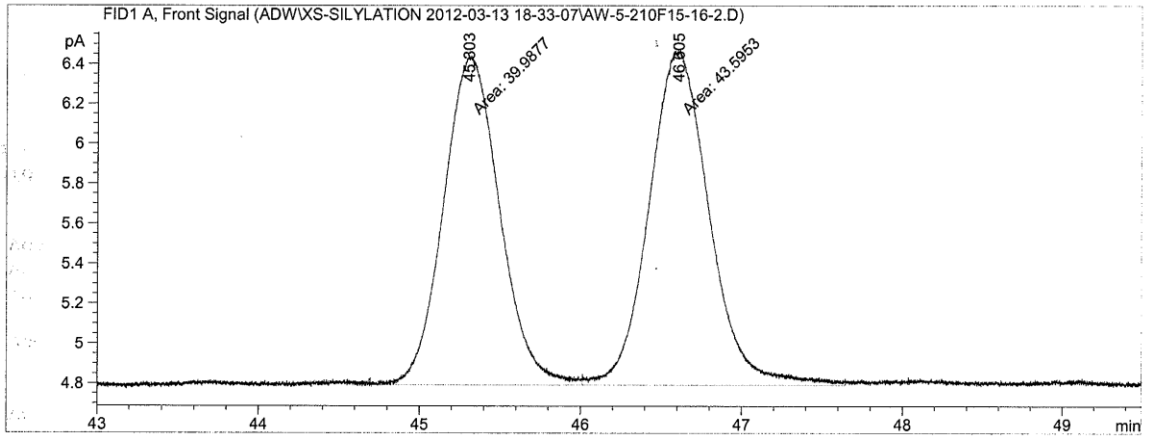


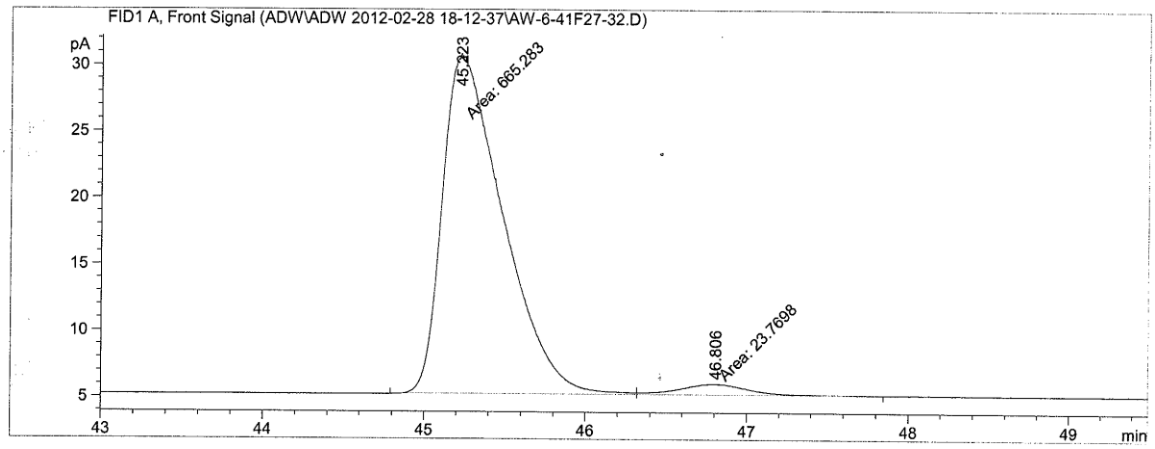
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	75.177	MF	0.4641	72.05933	2.58757	9.23872
2	75.879	FM	0.7002	707.91193	16.85016	90.76128

Table 3.17, Entry 4



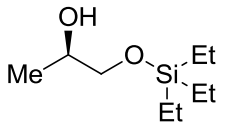
(*S*)-2-(triethylsilyloxy)propan-1-ol. The general procedure was followed using **3.55** and 1.2 equiv chlorotriethylsilane and *N,N*-diisopropylethylamine with a reaction time of 25 minutes. Column chromatography (3-20% Et_2O in Hexanes) yielded a colorless oil (69 mg, 36%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 80 °C for 100 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi., t_{rmajor} = 45.2 min, t_{rminor} = 46.8 min) 93% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.63 (q, 6H, J = 7.8), 0.97 (t, 9H, J = 7.8), 1.14 (d, 3H, J = 6.4), 1.96 (dd, 1H, J = 7.6, 5.1), 3.37 (ddd, 1H, J = 11.7, 6.6, 1.5), 3.48-3.53 (m, 1H), 3.89-3.95 (m, 1H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 5.1, 7.0, 20.1, 68.4, 69.1; **IR**: 3408, 2955, 2877, 1459, 1238, 1005, 741 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{12}H_{29}O_2Si_1$: $[M+H]^+$: 233.1937, found: 233.1934. **$[\alpha]_D^{20}$** = +18.6 (c = 1.0, CH_2Cl_2, l = 50 mm).





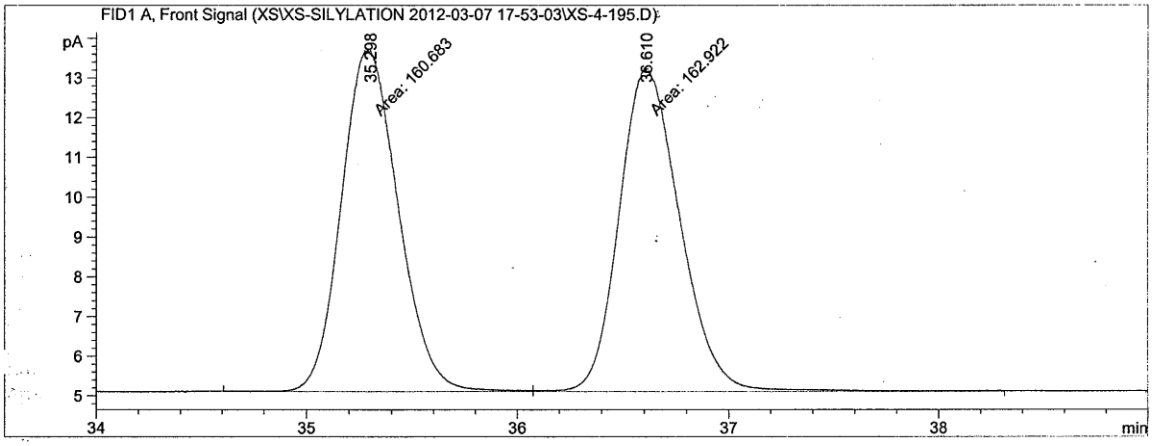
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	45.223	MF	0.4332	665.28326	25.59389	96.55036
2	46.806	FM	0.4828	23.76983	8.20552e-1	3.44964

Table 3.17, Entry 4



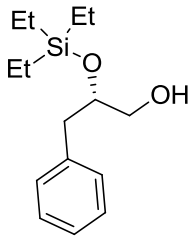
(*R*)-1-((triethylsilyl)oxy)propan-2-ol. The general procedure was followed using **3.50** and 1.2 equiv chlorotriethylsilane and *N,N*-diisopropylethylamine with a reaction time of 25 minutes. Column chromatography (3-20% Et_2O in Hexanes) yielded a colorless oil (97 mg, 51%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm

film thickness), 80 °C for 45 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 36.8 min, t_{rminor} = 35.6 min) 70% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.60 (q, 6H, *J* = 7.8), 0.94 (t, 9H, *J* = 7.8), 1.10 (d, 3H, *J* = 6.4), 2.48 (d, 1H, *J* = 3.0), 3.32 (dd, 1H, *J* = 9.8, 7.8), 3.57 (dd, 1H, *J* = 9.8, 3.4), 3.77-3.84 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 18.4, 68.2, 68.4; **IR**: 2955, 2911, 2877, 1459, 1239, 1087, 1006, 801, 724 cm^{-1}; **HRMS** (ESI+) calcd. for $C_9H_{22}O_2NaSi$: $[M+Na]^+$: 213.1281, found: 213,1271. **$[\alpha]_D^{20}$** = -8.2 (c = 1.1, CH_2Cl_2, *l* = 50 mm).

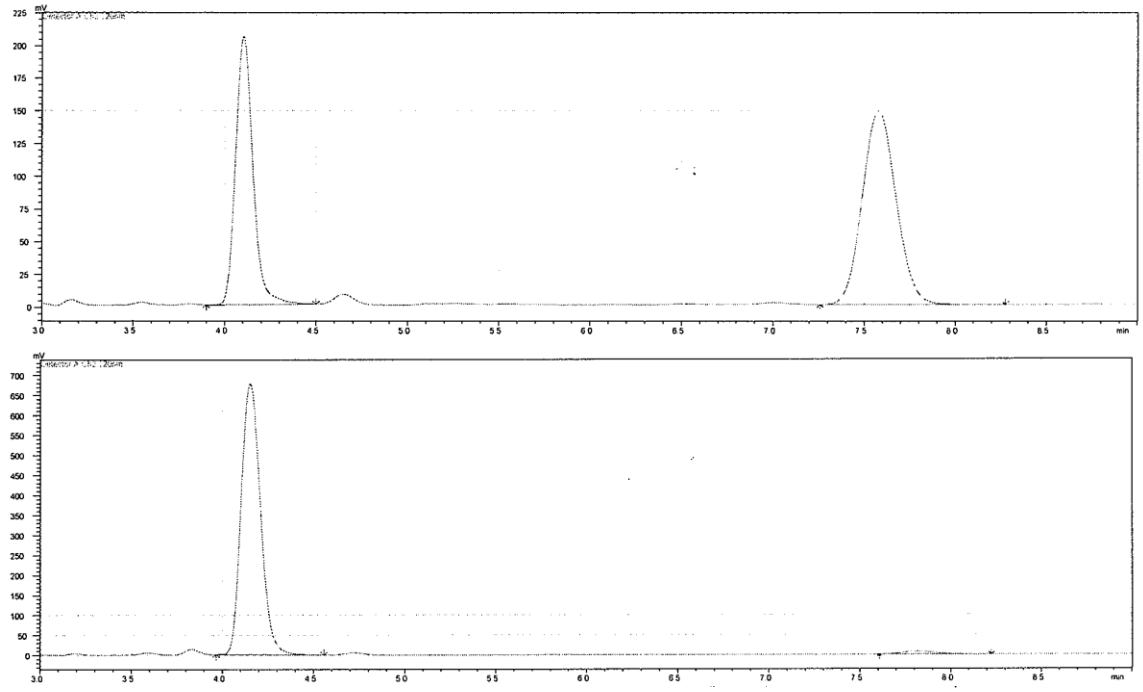


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.627	MM	0.3035	89.41690	4.90958	15.15284
2	36.788	MM	0.3412	500.68295	24.45822	84.84716

Table 3.17, Entry 5



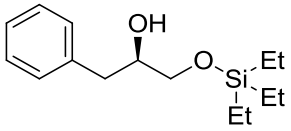
(*S*)-3-phenyl-2-(triethylsilyloxy)propan-1-ol. The general procedure was followed using **3.56** with 1.2 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine and 10 mol % **III** to yield a colorless oil (120 mg, 44%). **Chiral HPLC Analysis** (OD-H, 1.0 mL/min, 10% *i*PrOH: 90% Hexanes, 220 nm, t_{rmajor} = 4.1 and t_{rminor} = 7.8 min) 96% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.53 (dq, 6H, *J* = 16.1, 3.4), 0.90-0.93 (m, 9H), 1.91 (dd, 1H, *J* = 7.0, 5.6), 2.80 (ddd, 2H, *J* = 19.6, 13.5, 6.1), 3.40-3.45 (m, 1H), 3.48-3.53 (m, 1H), 3.92 (dddd, 1H, *J* = 13.7, 7.3, 4.6, 0.98), 7.16-7.20 (m, 3H), 7.24-7.28 (m, 2H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 5.1, 7.0, 40.8, 65.8, 79.2, 126.5, 128.6, 129.8, 138.4; **IR**: 2953, 2912, 2876, 1455, 1238, 1103, 1004, 724, 698, 505 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{15}H_{27}O_2Si_1$: $[M+H]^+$: 267.1780, found: 267.1777. **$[\alpha]_D^{20}$** = -12.6 (*c* = 1.0, CH_2Cl_2, *l* = 50 mm).



Detector A Ch2 220nm

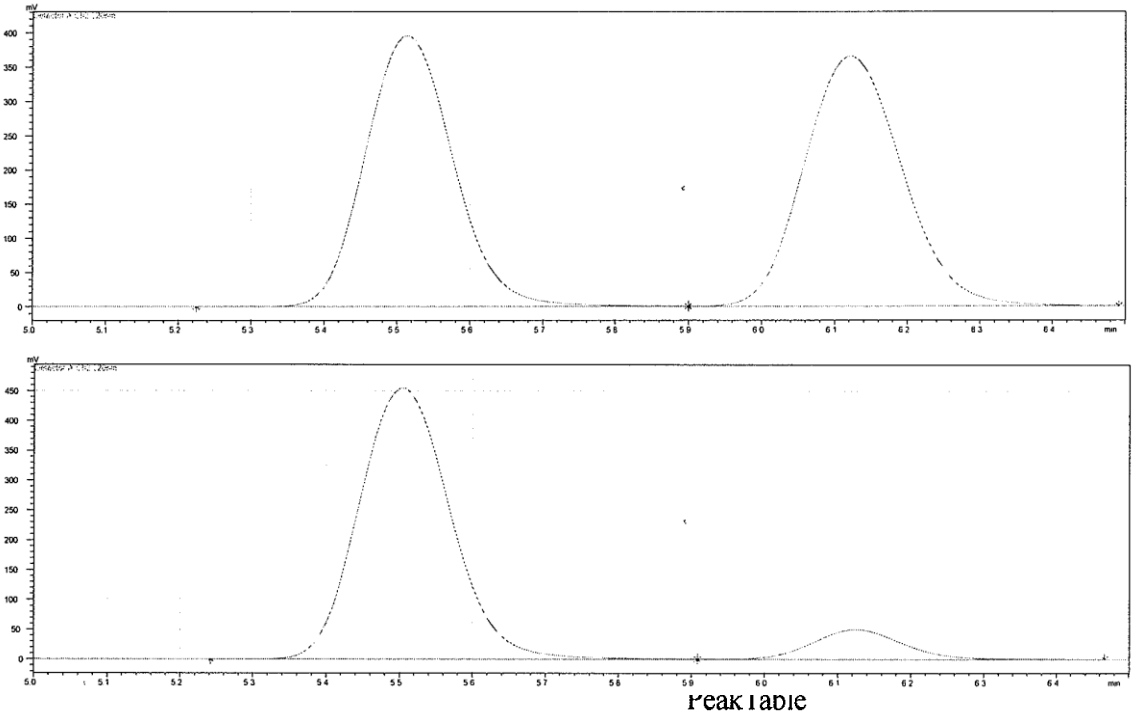
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.148	5003831	677512	98.072	98.873
2	7.816	98366	7723	1.928	1.127
Total		5102197	685235	100.000	100.000

Table 3.17, Entry 5



(*R*)-1-phenyl-3-((triethylsilyl)oxy)propan-2-ol. The general procedure was followed using **3.56**, 1.2 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine, and 10 mol % **III** to yield the product as a colorless oil (130 mg, 50%). **Chiral HPLC Analysis** (OD-H, 1.0 mL/min, 2% *i*PrOH: 98% Hexanes, 220 nm, t_{rmajor} = 5.50 min and t_{rminor} = 6.12 min) 80% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.59 (q, 6H, *J* = 7.8), 0.94 (t, 9H, *J* = 7.8), 2.42 (d, 1H, *J* = 3.9), 2.74 (dd, 1H, *J* = 13.7, 6.4), 2.78 (dd, 1H, *J* = 13.7, 7.1), 3.46 (dd, 1H, *J* = 9.8, 6.8), 3.60 (dd, 1H, *J* = 10.0, 3.7), 3.85-3.90 (m, 1H), 7.18-7.22 (m, 3H),

7.27-7.30 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 39.8, 66.2, 73.0, 126.5, 128.6, 129.5, 138.5; **IR**: 2953, 2911, 2876, 1239, 1111, 1031, 792, 727, 698 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{15}H_{26}O_2NaSi$: $[M+Na]^+$: 289.1594, found: 289.1600. **$[\alpha]_D^{20}$** = +2.6 (c = 1.0, CH_2Cl_2, *l* = 50 mm).

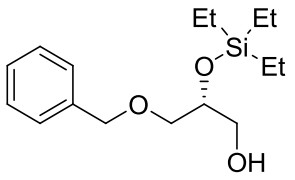


Peak Table

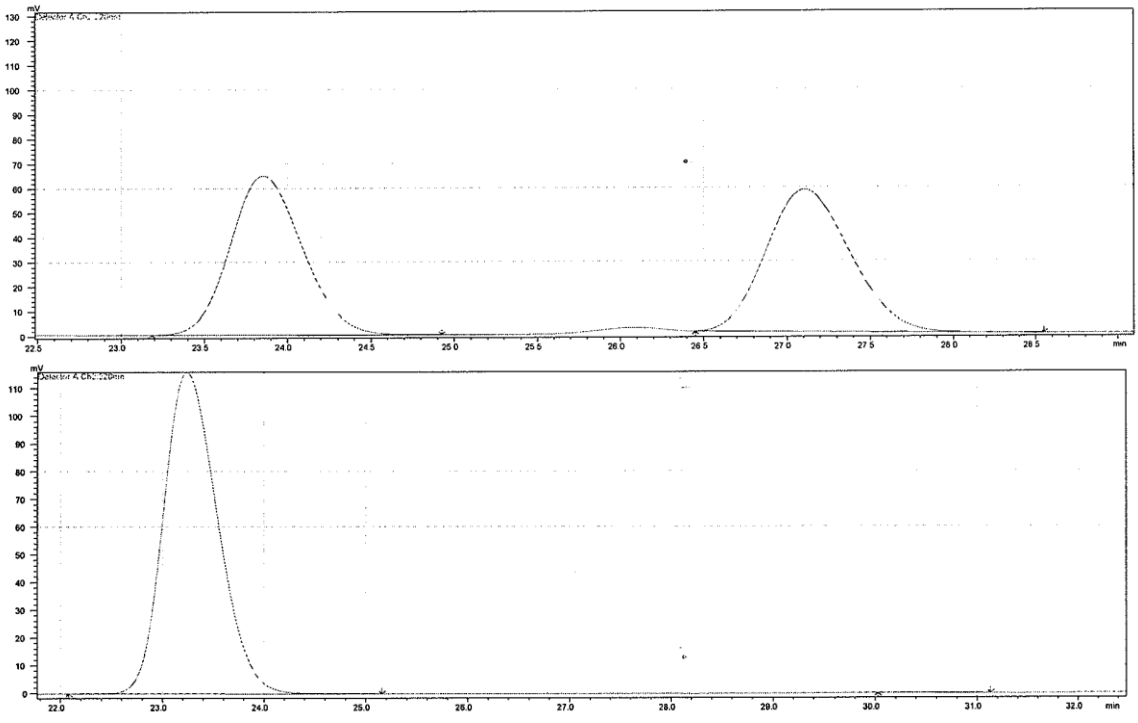
Detector A Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.500	3936878	454367	90.185	90.102
2	6.120	428456	49916	9.815	9.898
Total		4365334	504283	100.000	100.000

Table 3.17, Entry 6



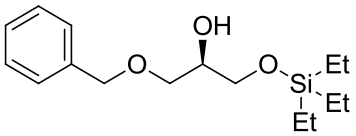
(*R*)-3-(benzyloxy)-2-(triethylsilyloxy)propan-1-ol. The general procedure was followed using **3.57**, 1.2 equiv chlorotriethylsilane and *N,N*-diisopropylethylamine, 10 mol % **III**, and a reaction time of 1.5 hours to yield a colorless oil (120 mg, 40%).**Chiral HPLC Analysis** (OD-H, 1.0 mL/min, 0.5% *i*PrOH: 99.5% Hexanes, 240 nm, t_{rmajor} = 23.2 and t_{rminor} = 30.5 min) 99% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.57-0.63 (q, 6H, J = 8.0), 0.91-0.95 (m, 9H), 2.04-2.08 (m, 1H), 3.44-3.51 (m, 2H), 3.57-3.68 (m, 2H), 3.88-3.93 (m, 1H), 4.51 (s, 2H), 7.25-7.35 (m, 5H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 4.8, 6.7, 64.9, 71.0, 71.9, 73.5, 127.6, 127.7, 128.4, 138.0; **IR**: 3439, 2954, 2876, 1455, 1239, 1098, 1005, 739, 698 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{16}H_{29}O_3Si_1$: $[M+H]^+$: 297.1886, found: 297.1881. **$[\alpha]_D^{20}$** = +21.4 (c = 1.1, CH_2Cl_2, l = 50 mm).



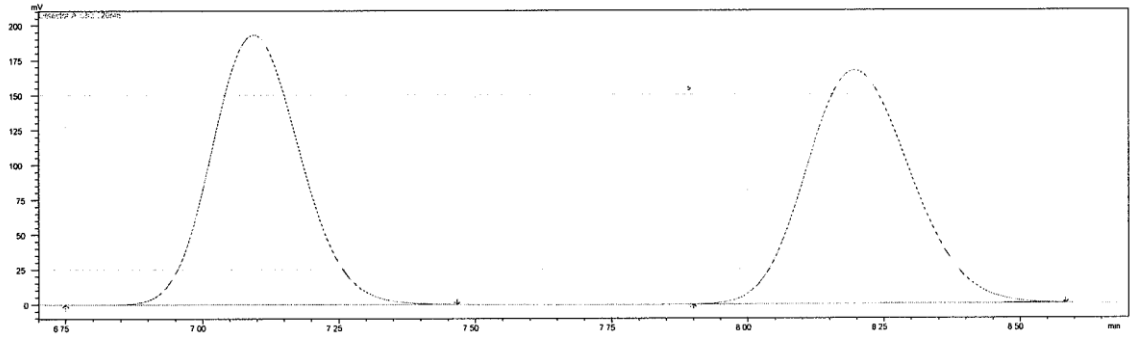
Detector A Ch2 220nm

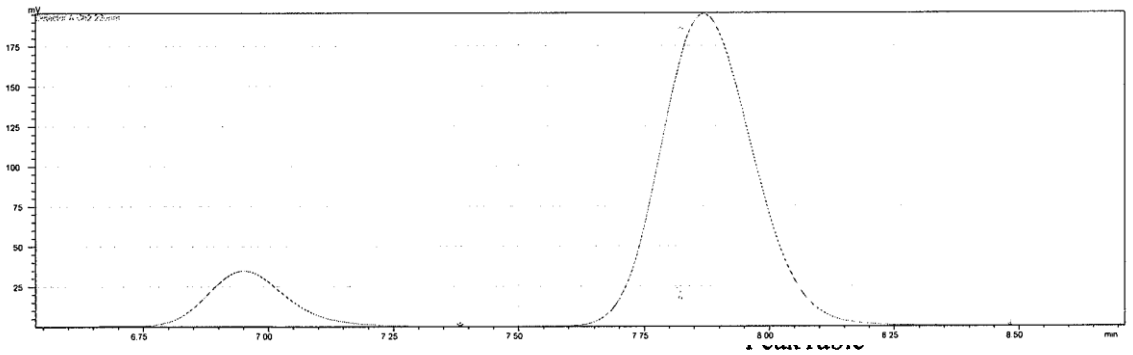
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.237	4280721	116130	99.838	99.838
2	30.476	6947	188	0.162	0.162
Total		4287669	116318	100.000	100.000

Table 3.17, Entry 6



(*R*)-1-(benzyloxy)-3-((triethylsilyl)oxy)propan-2-ol. The general procedure was followed using **3.57**, 1.2 equiv chlorotriethylsilane and *N,N*-diisopropylethylamine, 10 mol % **III**, and a reaction time of 1.5 hours to yield product as a colorless oil (170 mg, 59%). **Chiral HPLC Analysis** (OD-H, 1.0 mL/min, 5% *i*PrOH: 95% Hexanes, 220 nm, t_{rmajor} = 7.87 min and t_{rminor} = 6.95 min) 73% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.59 (q, 6H, *J* = 7.8), 0.94 (t, 9H, *J* = 7.8), 2.48 (d, 1H, *J* = 4.9), 3.49 (dd, 1H, *J* = 9.5, 5.9), 3.53 (dd, 1H, *J* = 9.5, 4.9), 3.62 (dd, 1H, *J* = 10.0, 5.9), 3.66 (dd, 1H, *J* = 10.0, 4.9), 3.82-3.87 (m, 1H), 4.54 (s, 2H), 7.26-7.35 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 64.0, 71.0, 71.3, 73.7, 127.9, 128.0, 128.6, 138.4; **IR**: 2953, 2910, 2875. 1089, 1004, 804, 728, 696 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{16}H_{28}O_3NaSi$: $[M+Na]^+$: 319.1700, found: 319.1697. **$[\alpha]_D^{20}$** = 0.53 (c = 1.1, CH_2Cl_2, *l* = 50 mm).

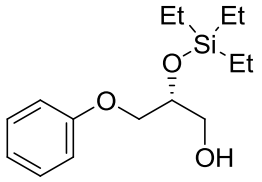




Detector A Ch2 220nm

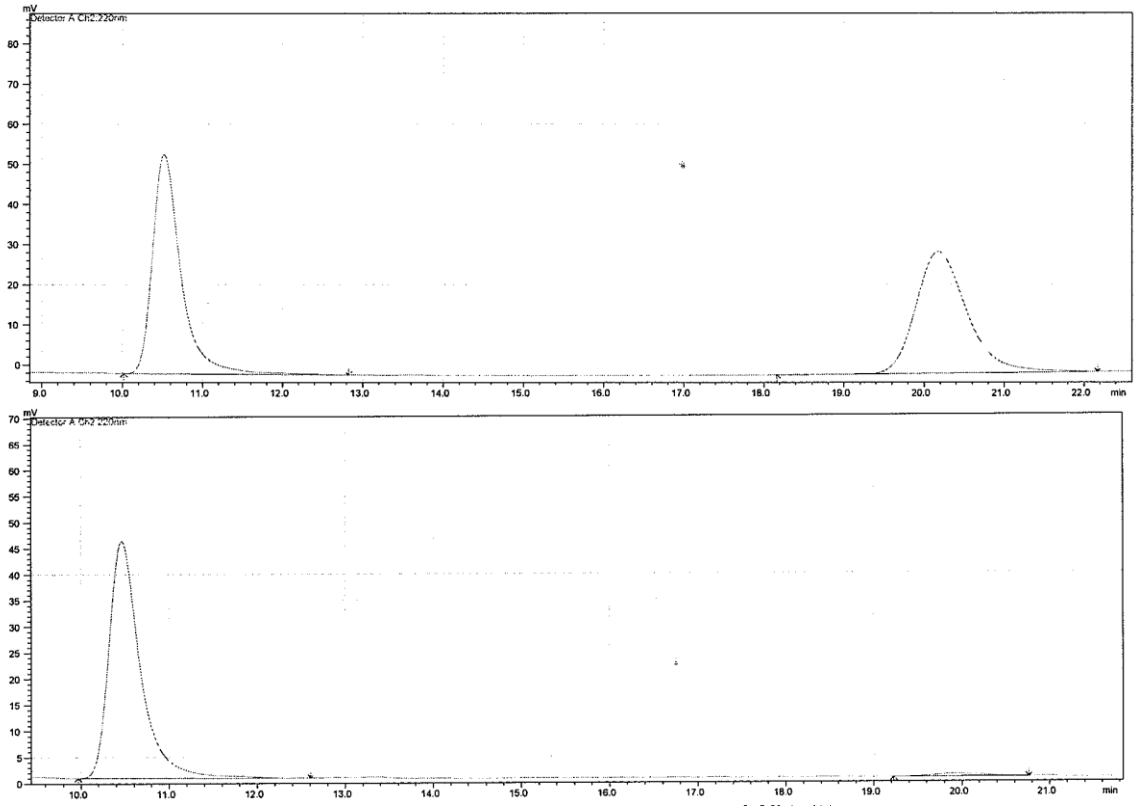
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.947	389411	34575	13.384	15.076
2	7.865	2520112	194761	86.616	84.924
Total		2909523	229336	100.000	100.000

Table 3.17, Entry 7



(*R*)-3-phenoxy-2-(triethylsilyloxy)propan-1-ol. The general procedure was followed using **3.58**, 1.4 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine, and 15 mol % **III** to yield a colorless oil (87 mg, 31%). **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.68 (q, 6H, *J* = 7.8), 0.99 (t, 9H, *J* = 7.8), 2.00 (dd, 1H, *J* = 7.6, 5.4), 3.69 (dd, 1H, *J* = 11.3, 7.3), 3.75 (ddd, 1H, *J* = 11.2, 5.4, 4.2), 3.94 (dd, 1H, *J* = 9.3, 6.1), 3.99 (dd, 1H, *J* = 9.3, 5.9), 4.11-4.15 (m, 1H), 6.90 (dt, 2H, *J* = 8.8, 0.98), 6.96 (tt, 1H, *J* = 7.3, 0.98), 7.26-7.30 (m, 2H); **^{13}C NMR** ($CDCl_3$, 120 MHz) δ 5.1, 7.0, 64.6, 69.2, 71.3, 114.6, 121.1, 129.7, 158.5; **IR**: 3415, 2954, 2876, 1600, 1497, 1244, 1130, 1048, 749, 690 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{15}H_{27}O_2Si_1$: $[M+H]^+$: 283.1730, found: 283.1730. **$[\alpha]_D^{20}$** = +15.4 (*c* = 0.99, CH_2Cl_2, *l* = 50 mm).

Derivitization for ee[31]: The product (15 mg, 9.0 x 10^{-2} mmol) was dissolved in 300 µL of CH_3CN and treated with 100 µL of hydrogen fluoride in pyridine. After 12 hours, column chromatography (1-10% MeOH in CH_2Cl_2) gave the known diol, (*R*)-3-phenoxypropane-1,2-diol. Characterization of the diol matched known literature values. Absolute configuration was confirmed by comparison with a previous literature report.[32] **Chiral HPLC Analysis** (OD-H, 1.0 mL/min, 15% *i*PrOH: 85% Hexanes, 240 nm) t_{rmajor} = 10.5 and t_{rminor} = 20.0 min) 96% ee (as diol).

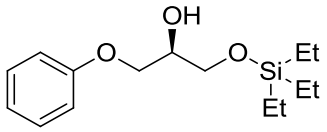


Detector A Ch2 220nm

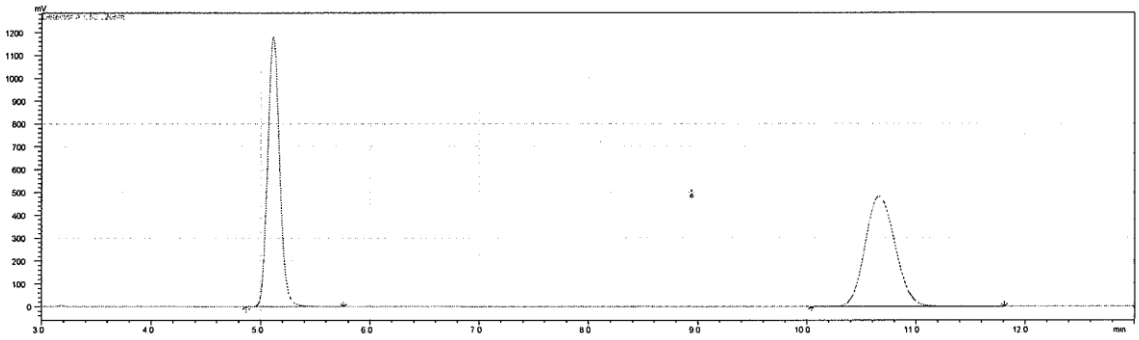
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.461	1116404	45418	98.116	98.791
2	19.971	21443	556	1.884	1.209
Total		1137846	45973	100.000	100.000

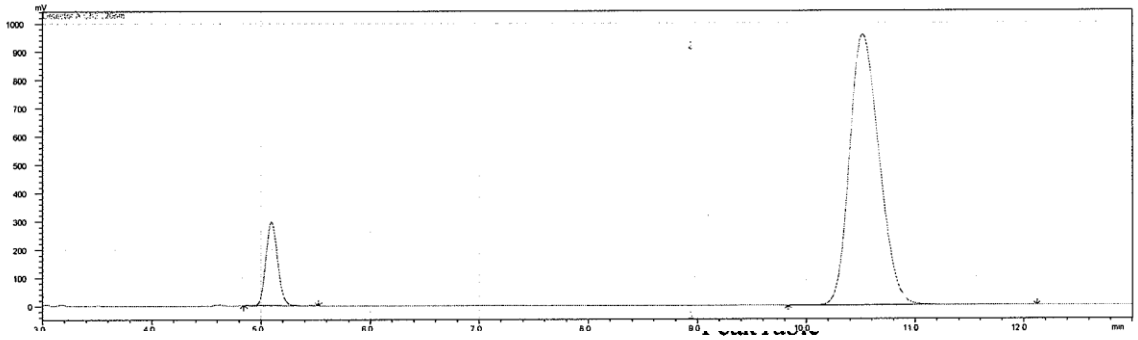
[31]Boschelli, D.; Takemasa, T.; Nishitani, Y.; Masamune, S. *Tet. Lett*. **1985**, *26*, 5239-5242. [32]Turgut, Y.; Aral, T.; Karakaplan, M.; Deniz, P.; Hosgoren, H. *Syn Comm.* **2010**, *40*, 3365-3377.

Table 3.17, Entry 7



(*R*)-1-phenoxy-3-((triethylsilyl)oxy)propan-2-ol. The general procedure was followed using **3.58**, 1.4 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine and 15 mol % **III** to yield product as a colorless oil (131 mg, 47%). **Chiral HPLC Analysis** (OD-H, 1.0 mL/min, 10% *i*PrOH: 90% Hexanes, 220 nm, t_{rmajor} = 10.5 min and t_{rminor} = 5.09 min) 78% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.61 (q, 6H, *J* = 7.8), 0.94 (t, 9H, *J* = 7.8), 2.55 (d, 1H, *J* = 5.1), 3.74 (dd, 1H, *J* = 10.3, 5.1), 3.78 (dd, 1H, *J* = 10.3, 4.6), 3.99-4.05 (m, 3H), 6.89-6.91 (m, 2H), 6.92-6.96 (m, 1H), 7.25-7.28 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 63.7, 68.7, 70.5, 114.8, 121.2 129.7, 158.9; **IR**: 2953, 2876, 1599, 1495, 1458, 1242, 1079, 1043, 1005, 802, 745, 727, 689 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{15}H_{26}O_3NaSi$: $[M+Na]^+$: 305.1543, found: 305.1552. **$[\alpha]_D^{20}$** = -0.19 (c = 1.1, CH_2Cl_2, *l* = 50 mm).

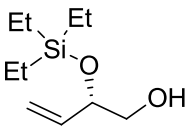




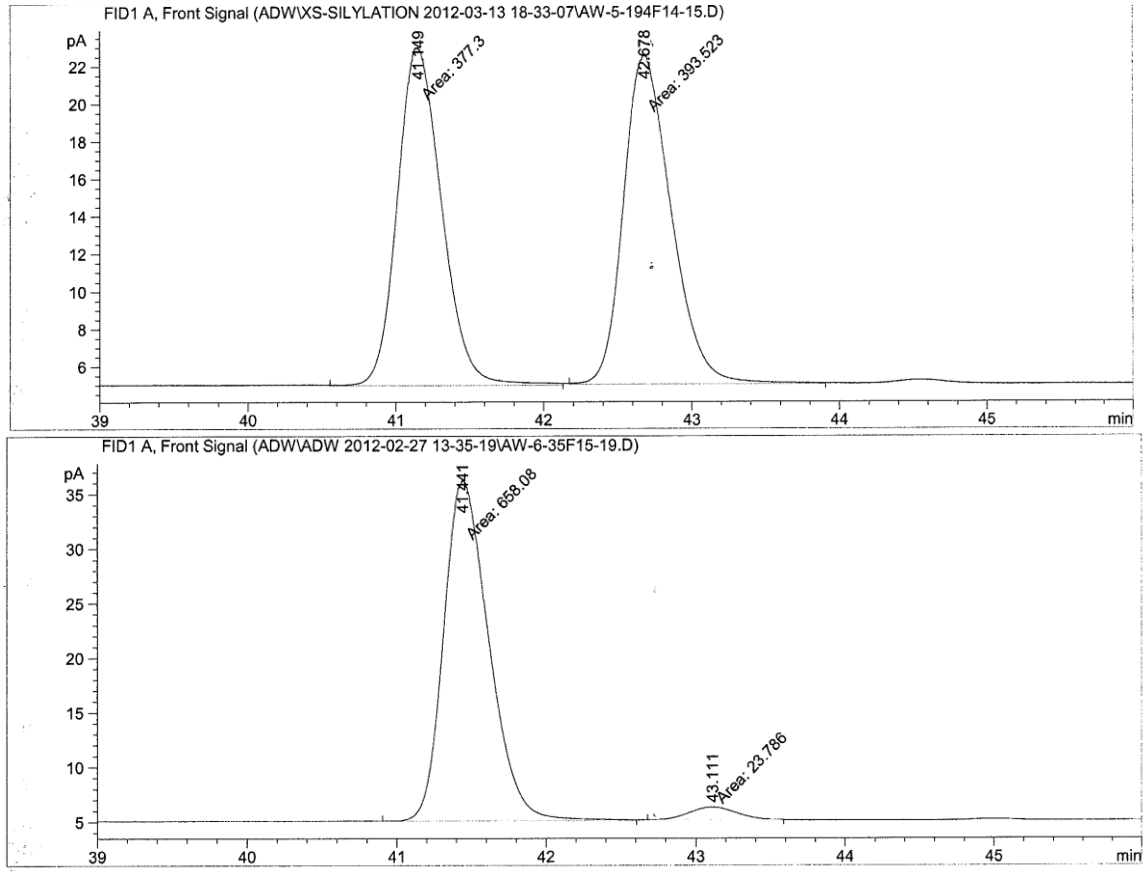
Detector A Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.092	2207486	297754	10.822	23.692
2	10.515	18191300	959009	89.178	76.308
Total		20398787	1256763	100.000	100.000

Table 3.17, Entry 8

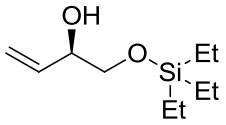


(*S*)-2-(triethylsilyloxy)but-3-en-1-ol. The general procedure was followed using **3.59** with 1.2 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine and a reaction time of 25 minutes to yield a colorless oil (71 mg, 35%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 90 °C for 100 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi., t_{rmajor} = 41.4 min, t_{rminor} = 43.1 min) 93% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.63 (q, 6H, *J* = 7.8), 0.97 (t, 9H, *J* = 7.8), 1.96-1.99 (m, 1H), 3.43-3.55 (m, 2H), 4.20-4.24 (m, 1H), 5.17 (ddd, 1H, *J* = 10.5, 2.9, 1.2), 5.28 (ddd, 1H, *J* = 17.4, 2.9, 1.7), 5.81 (dddd, 1H, *J* = 23.5, 10.5, 6.4, 1.7); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 5.1, 6.9, 67.0, 74.6, 116.5, 138.2; **IR**: 3415, 2955, 2877, 1459, 1098, 1007, 925, 743 cm^{-1}; **HRMS** (DART-TOF) calcd. for $C_{10}H_{23}O_2Si_1$: $[M+H]^+$: 203.1467, found: 203.1475. **$[\alpha]_D^{20}$** = +7.4 (*c* = 0.82, CH_2Cl_2, *l* = 50 mm).



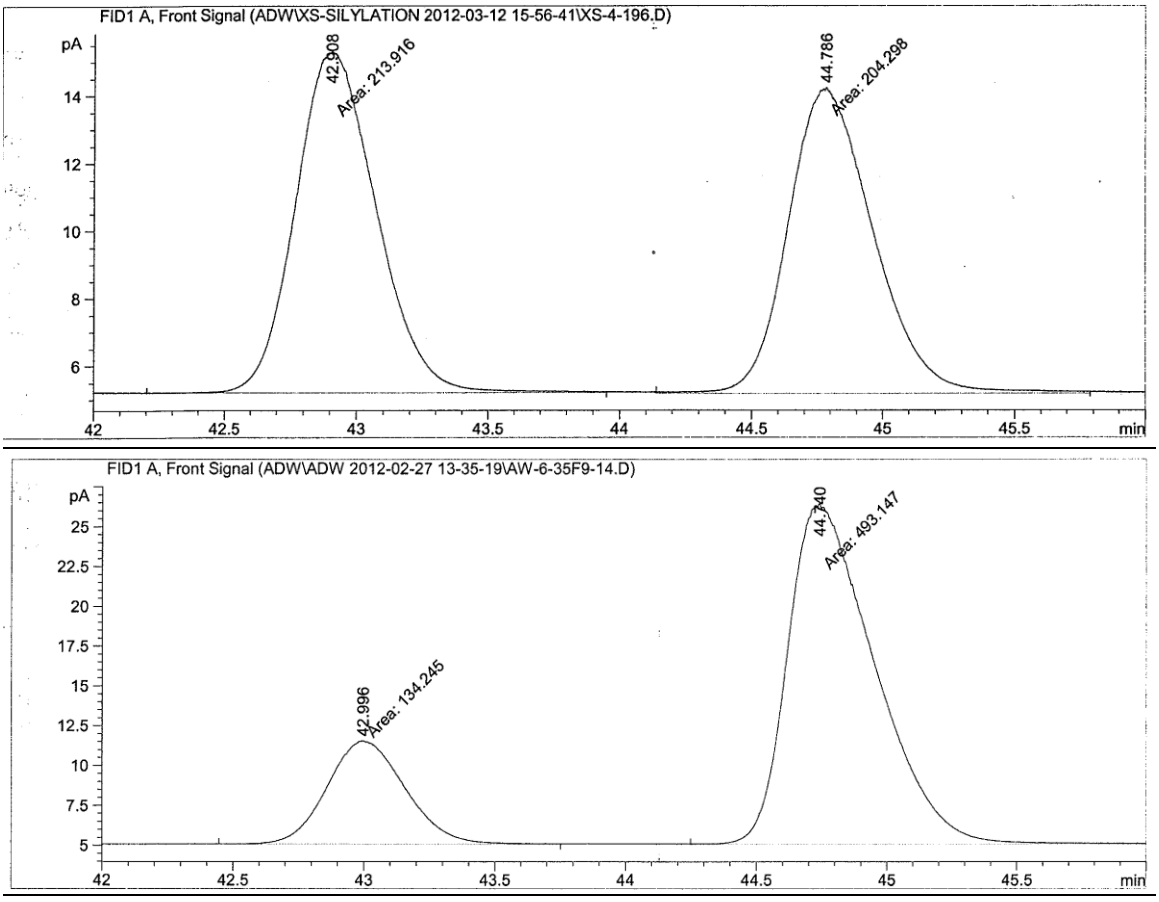
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	41.441	MM	0.3519	658.07965	31.16927	96.51162
2	43.111	MM	0.3485	23.78604	1.13745	3.48838

Table 3.17, Entry 8



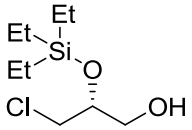
(*R*)-1-((triethylsilyl)oxy)but-3-en-2-ol. The general procedure was followed using **3.59**, 1.2 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine and a reaction time of 25 minutes to yield product as a colorless oil (120 mg, 57%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 90 °C for 50 min, 20 °C/min

to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 44.7 min, t_{rminor} = 43.0 min) 57% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.60 (q, 6H, *J* = 7.8), 0.95 (t, 9H, *J* = 7.8), 2.57 (d, 1H, 3.4), 3.42 (dd, 1H, *J* = 10.0, 7.8), 3.64 (dd, 1H, *J* = 10.0, 3.7), 4.13-4.18 (m, 1H), 5.17 (dt, 1H, *J* = 10.5, 1.5), 5.33 (dt, 1H, *J* = 17.4, 1.5), 5.80 (ddd, 1H, *J* = 17.1, 10.5, 5.6); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.6, 6.9, 66.9, 73.3, 116.7, 136.8; **IR**: 2955, 2912, 2877, 1238, 1102, 1004, 923, 795, 725 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{10}H_{22}O_2NaSi$: $[M+Na]^+$: 225.1281, found: 225.1285. **$[\alpha]_D^{20}$** = +0.84 (c = 1.2, CH_2Cl_2, *l* = 50 mm).

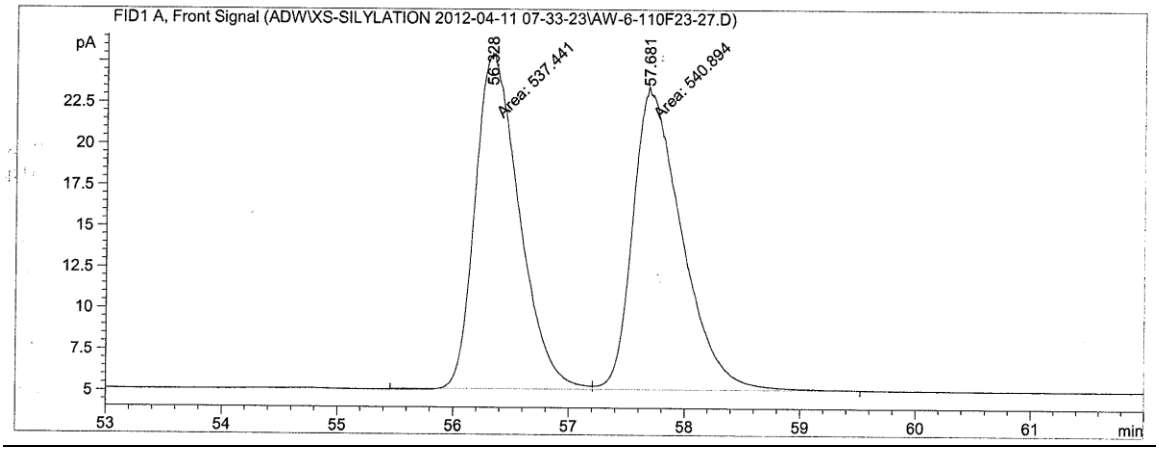


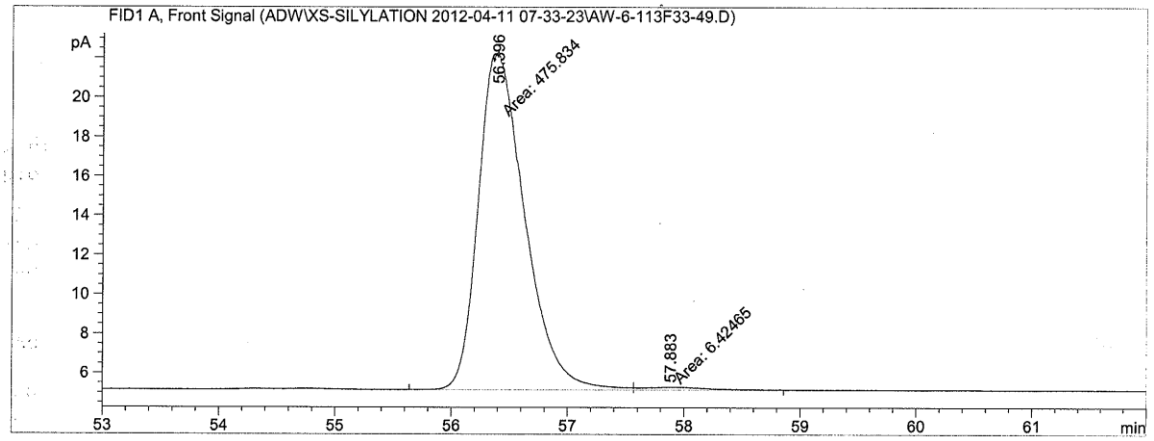
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	42.996	MM	0.3452	134.24469	6.48144	21.39726
2	44.740	MM	0.3844	493.14737	21.37935	78.60274

Table 3.17, Entry 9



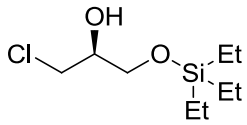
(*R*)-3-chloro-2-(triethylsilyloxy)propan-1-ol. The general procedure was followed using **3.60** with a reaction time of 50 minutes to yield product as a colorless oil (99 mg, 44%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 110 °C for 105 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi, t_{rmajor} = 56.4 min, t_{rminor} = 57.9 min) 97% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.65 (q, 6H, J = 7.8), 0.95-1.00 (m, 9H), 1.85 (t, 1H, J = 6.4), 3.46 (dd, 1H, J = 10.8, 5.1), 3.58 (dd, 1H, J = 11.0, 7.1), 3.68-3.70 (m, 2H), 3.89-3.93 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 5.0, 6.9, 44.7, 64.0, 72.8; **IR**: 3397, 2956, 2878, 1459, 1240, 1120, 1046, 1006, 742 cm^{-1}; **HRMS** (ESI+) calcd. for $C_9H_{22}ClO_2Si$: $[M+H]^+$: 225.1078, found: 225.1071. $\mathbf{[\alpha]_D^{20}}$ = +8.3 (c = 1.1, CH_2Cl_2, l = 50 mm).





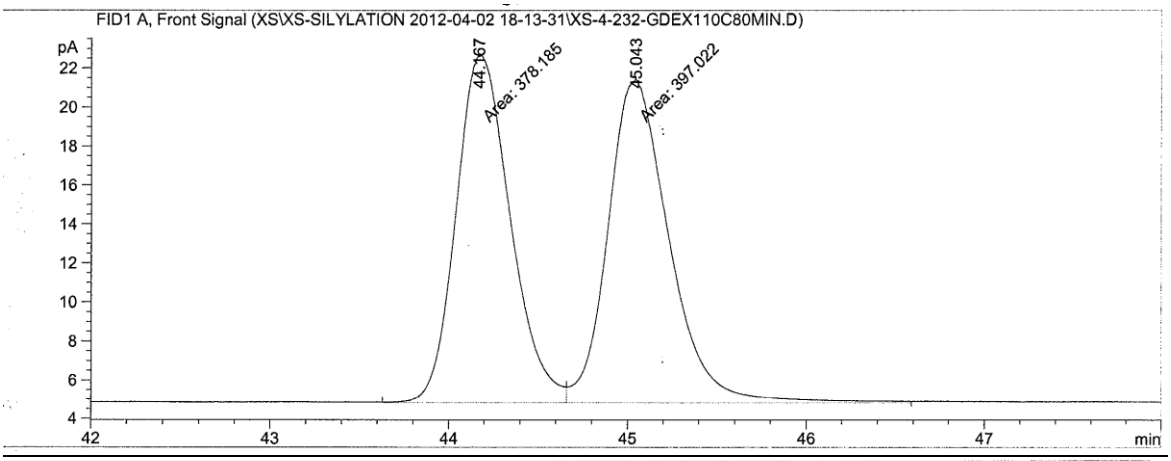
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	56.396	MF	0.4610	475.83353	17.20364	98.66780
2	57.883	FM	0.6492	6.42465	1.64933e-1	1.33220

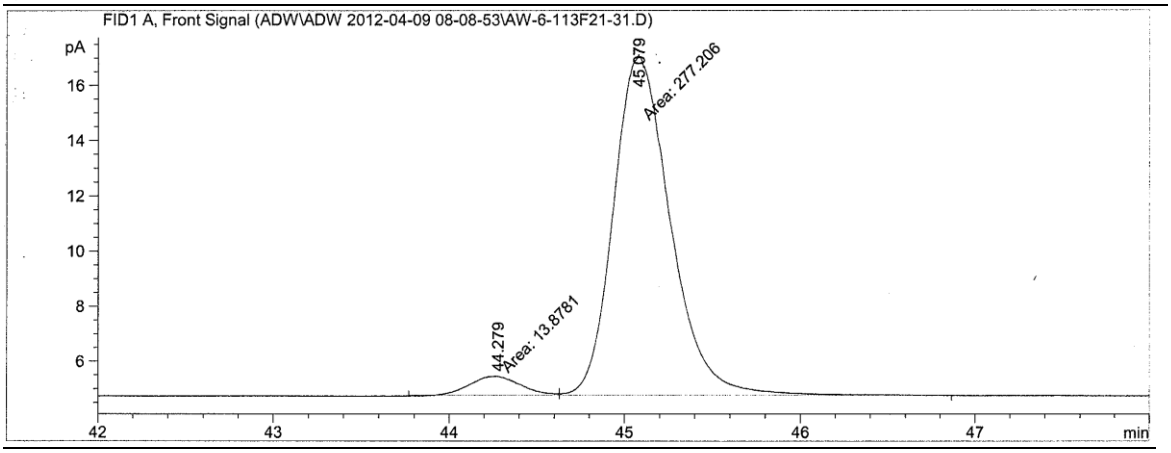
Table 3.17, Entry 9



(*S*)-1-chloro-3-(triethylsilyloxy)propan-2-ol. The general procedure was followed using **3.60** with a reaction time of 50 minutes to yield product as a colorless oil (120 mg, 52%). **Chiral GC Analysis** (Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 110 °C for 50 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi, t_{rmajor} =

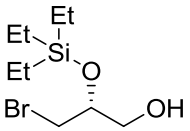
45.1 min, t_{rminor} = 44.3 min) 90% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.61 (q, 6H, *J* = 8.1), 0.93-0.96 (m, 9H), 2.54 (d, 1H, *J* = 6.4), 3.54-3.61 (m, 2H), 3.66-3.72 (m, 2H), 3.80-3.86 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.5, 6.9, 45.6, 63.3, 71.6; **IR**: 3425, 2955, 2877, 1459, 1240, 1111, 1006, 804, 740 cm^{-1}; **HRMS** (ESI+) calcd. for $C_9H_{22}ClO_2Si$: $[M+H]^+$: 225.1070, found: 225.1078. **$[\alpha]_D^{20}$** = -1.5 (c = 1.1, CH_2Cl_2, *l* = 50 mm).



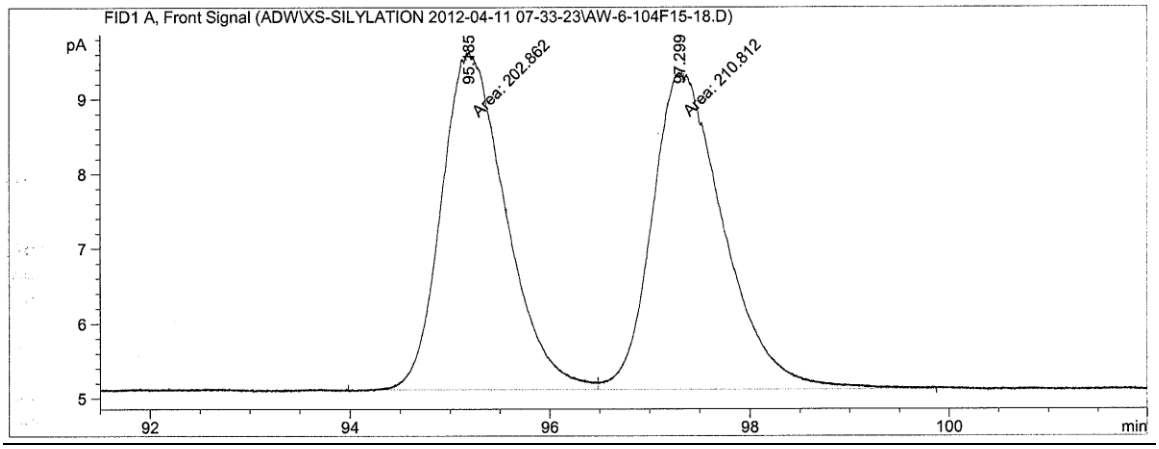


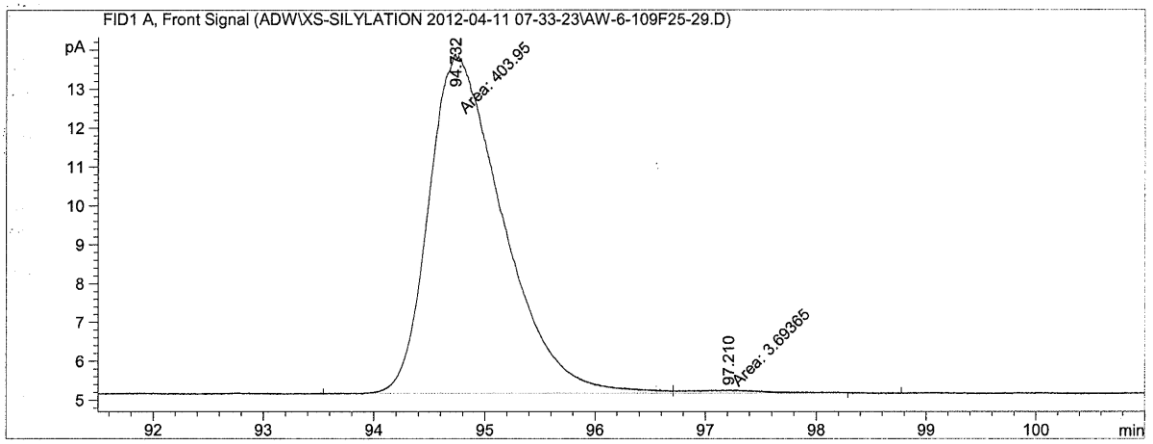
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	44.279	MF	0.3280	13.87813	7.05245e-1	4.76774
2	45.079	FM	0.3738	277.20621	12.36126	95.23226

Table 3.17, Entry 10



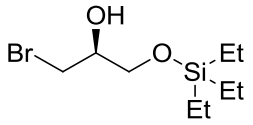
(*R*)-3-bromo-2-(triethylsilyloxy)propan-1-ol. The general procedure was followed using **3.61** to yield product as a colorless oil (110 mg, 41%). **Chiral GC Analysis** (Supelco Beta Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 110 °C for 105 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi, t_{rmajor} = 94.7 min, t_{rminor} = 97.2 min) 98% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.65 (q, 6H, *J* = 8.1), 0.96-0.99 (m, 9H), 1.85 (t, 1H, *J* = 6.4), 3.30-3.33 (m, 1H), 3.43-3.64 (m, 1H), 3.71 (dd, 2H, *J* = 6.1, 4.2), 3.92-3.96 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 4.8, 6.7, 33.0, 64.3, 72.2; **IR**: 3382, 2955, 2971, 2877, 1459, 1240, 1118, 1006, 969, 742, 728 cm^{-1}; **HRMS** (ESI+) calcd. for $C_9H_{22}BrO_2Si$: $[M+H]^+$: 269.0572, found: 269.0573. **$[\alpha]_D^{20}$** = +6.1 (c = 1.1, CH_2Cl_2, *l* = 50 mm).



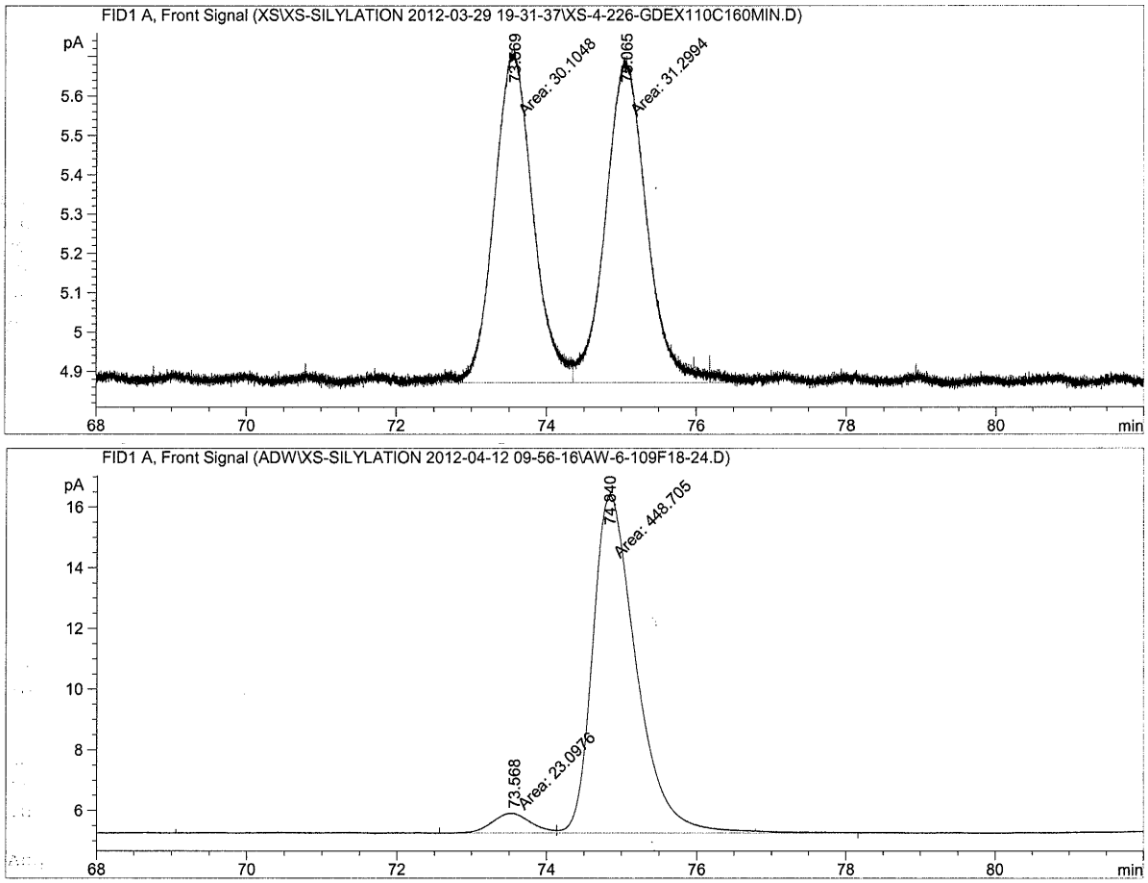


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	94.732	MF	0.7725	403.95001	8.71494	99.09390
2	97.210	FM	0.7345	3.69365	8.38134e-2	0.90610

Table 3.17, Entry 10

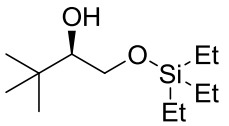


(*S*)-1-bromo-3-(triethylsilyloxy)propan-2-ol. The general procedure was followed using **3.61** to yield product as a colorless oil (140 mg, 50%). **Chiral GC Analysis** (Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 110 °C for 80 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi, t_{rmajor} = 74.8 min, t_{rminor} = 73.6 min) 90% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.61 (q, 6H, J = 7.8), 0.93-0.96 (m, 9H), 2.56 (d, 1H, J = 6.4), 3.41-3.49 (m, 2H), 3.68 (dd, 1H, J = 10.0, 4.9), 3.72 (dd, 1H, J = 10.0, 4.9), 3.80-3.85 (m, 1H); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 4.5, 6.9, 34.7, 64.0, 71.3; **IR**: 2955, 2876, 1459, 1240, 1108, 1006, 799, 727, 671 cm^{-1}; **HRMS** (ESI+) calcd. for $C_9H_{22}BrO_2Si$: $[M+H]^+$: 269.0572, found: 269.0576. **$[\alpha]_D^{20}$** = -0.99 (c = 1.2, CH_2Cl_2, l = 50 mm).



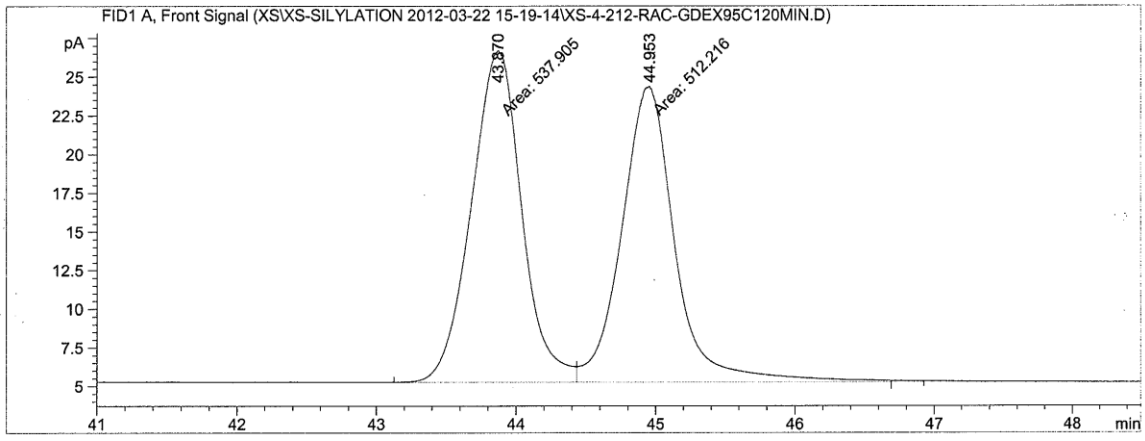
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	73.568	MF	0.5851	23.09759	6.57894e-1	4.89560
2	74.840	FM	0.6665	448.70508	11.21993	95.10440

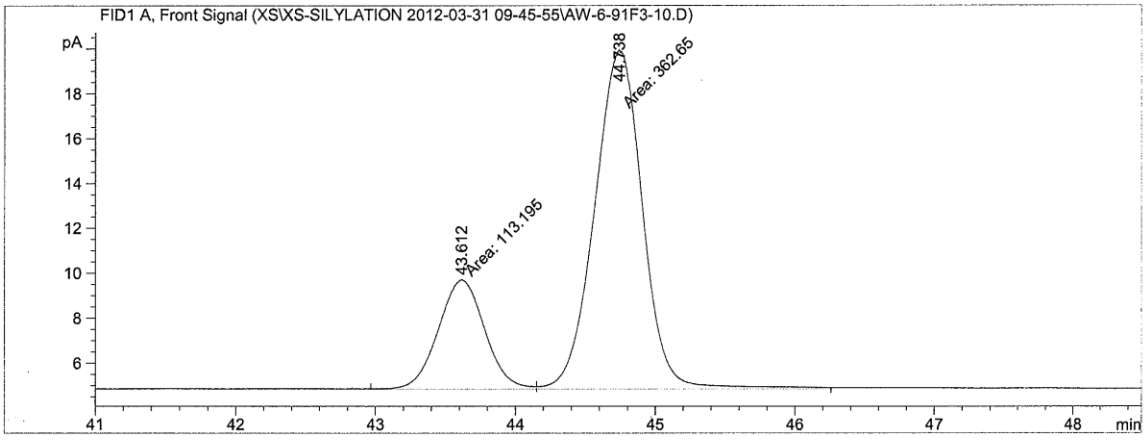
Reaction of 3,3-dimethylbutane-1,2-diol (Scheme 3.28)



(*R*)-3,3-dimethyl-1-(triethylsilyloxy)butan-2-ol.The general procedure was followed using 1.2 equiv of chlorotriethylsilane and *N,N*-diisopropylethylamine and a reaction time of 45 minutes to yield only this product as a colorless oil (140 mg, 60%). **Chiral GC Analysis** (Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 95 °C

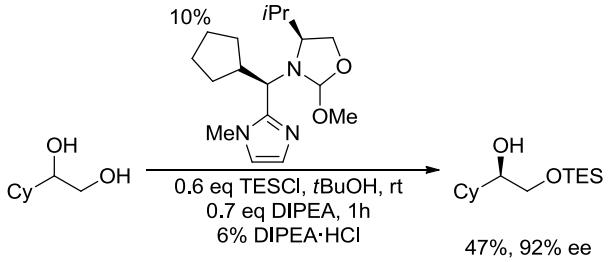
for 50 min, 20 °C/min to 200 °C, 200 °C for 20 min, 15 psi, t_{rmajor} = 44.7 min, t_{rminor} = 43.6 min) 52% ee. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 0.60 (q, 6H, *J* = 8.1), 0.90 (s, 9H), 0.93-0.96 (m, 9H), 2.65 (d, 1H, *J* = 2,2), 3.29-3.32 (m, 1H), 3.41-3.45 (m, 1H), 3.69 (dd, 1H, *J* = 9.8, 3.2); **^{13}C NMR** ($CDCl_3$, 126 MHz) δ 4.6, 6.9, 26.2, 33.4, 63.5, 78.9; **IR**: 2954, 2877, 1460, 1239, 1108, 1067, 1003, 817, 726 cm^{-1}; **HRMS** (ESI+) calcd. for $C_{12}H_{29}O_2Si$: $[M+H]^+$: 233.1937, found: 233.1940. **$[\alpha]_D^{20}$** = -10.0 (c = 1.1, CH_2Cl_2, *l* = 50 mm).



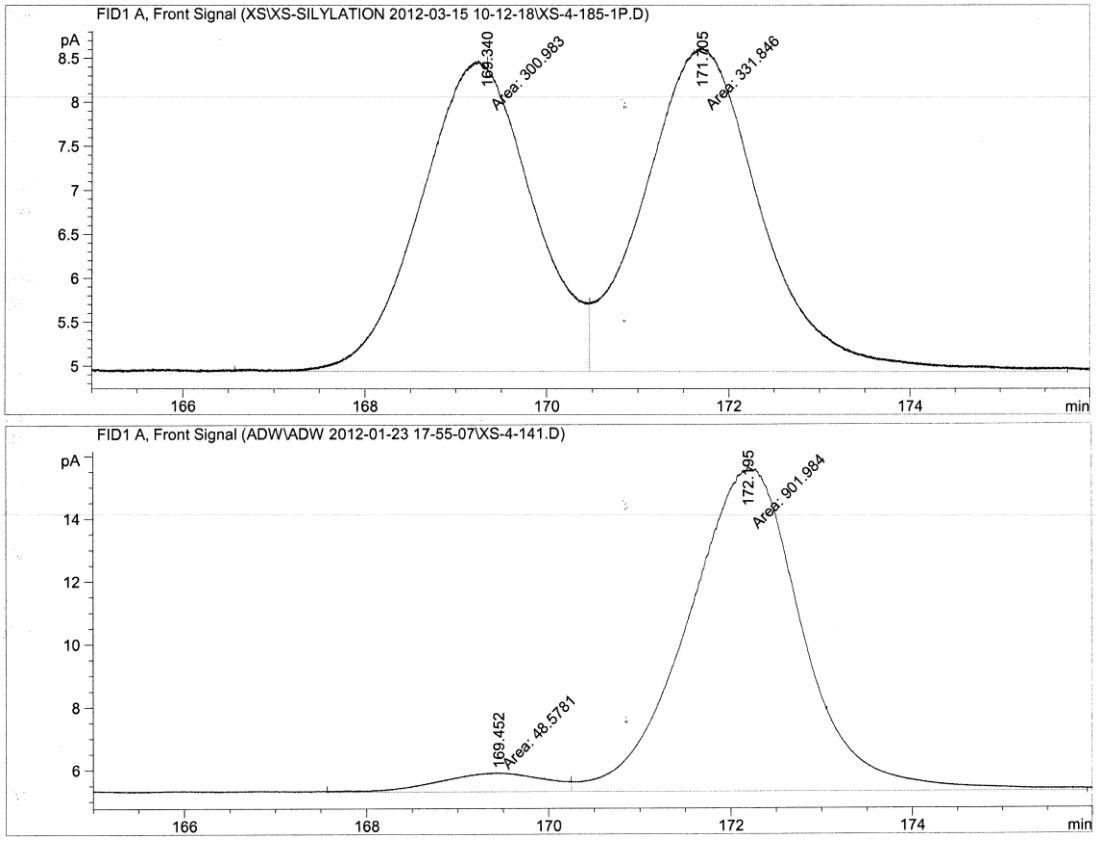


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	43.612	MF	0.3856	113.19453	4.89254	23.78811
2	44.738	FM	0.3993	362.65048	15.13735	76.21189

Kinetic Resolution of 1-Cyclohexylethane-1,2-diol (Scheme 3.29)



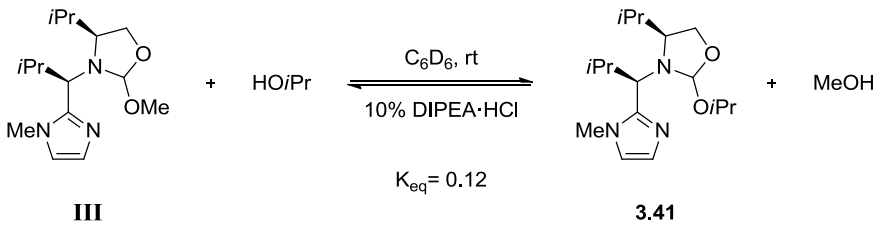
In a dry box, a solution of 1-cyclohexylethane-1,2-diol, **3.50**, (140 mg, 1.0 mmol), catalyst **IV** (31 mg, 0.10 mmol, 10 mol %), and *N,N*-diisopropylethylamine hydrochloride (11 mg, 6.0 x 10^{-2} mmol, 6 mol %) in anhydrous *tert*-butanol (15 mL) was prepared in an oven-dried glass reaction vial. The reaction was stirred at room temperature for 45 minutes. *N,N*-diisopropylethylamine (120 μL, 0.70 mmol, 0.70 equiv) was added, followed by addition of chlorotriethylsilane (100 μL, 0.60 mmol, 0.60 equiv) in 4 portions every 15 minutes (dropwise addition was performed for each portion added). The reaction was stirred at room temperature for 1 hour (starting from the first addition of chlorotriethylsilane). Methanol (150 μL) was added to quench the reaction. The solvent was removed under reduced pressure, Flash column chromatography (hexanes:EtOAc = 60:1) afforded pure product as a colorless oil (120 mg, 48%). **Chiral GC Analysis** (Supelco Gamma Dex 120 (30 m × 0.25 mm × 0.25 μm film thickness), 115 °C for 180 min, 20 °C/min to 180 °C, 180 °C for 20 min, 15 psi, t_{rmajor} = 172.2 min, t_{rminor} = 169.5 min) 90% ee. $\mathbf{[\alpha]_D^{20}}$ = -7.4 (c = 1.0, CH_2Cl_2, *l* = 50 mm).



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	169.452	MF	1.3195	48.57809	6.13608e-1	5.11046
2	172.195	FM	1.4545	901.98389	10.33563	94.88954

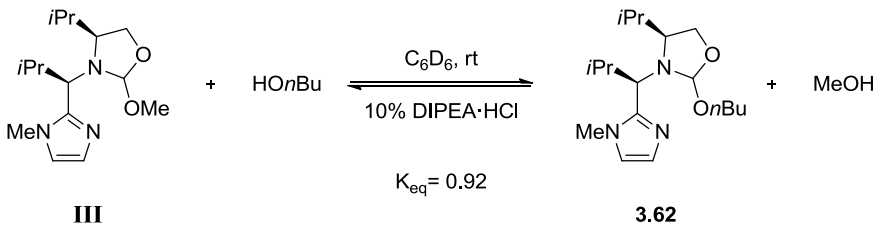
Note: Making the racemic secondary products by literature methods requires multi-step reactions which are very low yielding in many cases. Therefore, the racemic secondary products were prepared by reacting the two enantiomers of catalyst **III** in the regiodivergent resolution and then mixing the reactions together to isolate the products.

Exchange of **III** with *i*PrOH (Scheme 3.30)



In a glovebox, a solution of catalyst **III** (35 mg, 0.13 mmol) and *N,N*-diisopropylethylamine hydrochloride (2.1 mg, 1.3 x 10^{-2} mmol) in anhydrous C_6D_6 (500 µ was made 200 µ of the sol t ion was added to a NMR t e *i*PrOH (0.25 mmol, 130 µ 2 M sol ti on in $_6D_6$) and MeOH (5.0 x 10^{-2} mmol 2 µ 2 M sol ti on in $_6D_6$) was added to the NMR tube. C_6D_6 0 µ was added to the NMR t e to reach a total volume of 0.5 mL. The reaction was monitored by ^{1}H NMR. After 24 hours, equilibrium was reached. A ratio of 68:32, **III** to **3.41**, gave a K_{eq} of 0 Anothe r 200 µ of the catalyst and acid solution was added to another NMR tube. *i*PrOH (5.0 x 10^{-1} mmol, 250 µ 2 M sol ti on in $_6D_6$) and MeOH (5.0 x 10^{-2} mmol 2 µ 2 M sol ti on in $_6D_6$) was added to the NMR tube. C_6D_6 2 µ was added to the NMR t e to reach a total volume of 0.5 mL. The reaction was monitored by 1H NMR. After 24 hours, equilibrium was reached. A ratio of 57:43, **III** to **3.36**, gave a K_{eq} of 0.12. The average Keq for the two runs is 0.12 ± 0.01.

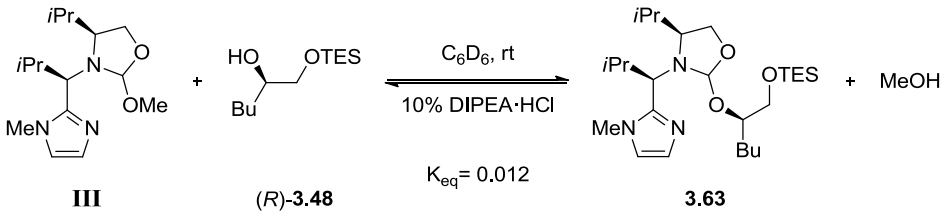
Exchange of **III** with *n*BuOH (Scheme 3.31)



III **3.62**

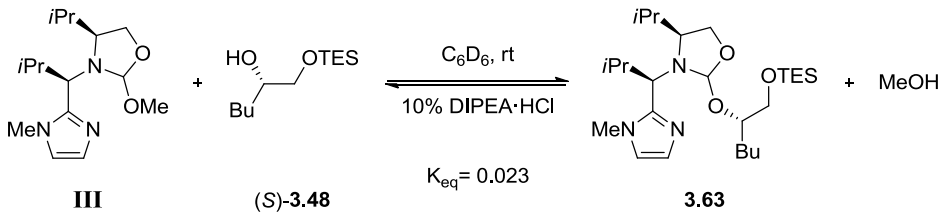
In a glovebox, a solution of catalyst **III** (35 mg, 0.13 mmol) and *N,N*-diisopropylethylamine hydrochloride (2.1 mg, 1.3 x 10^{-2} mmol) in anhydrous C_6D_6 (500 µ was made 200 µ of the sol t ion was added to a NMR t e *n*BuOH (0.15 mmol, 75 µ 2 M sol ti on in C_6D_6) and MeOH (5.0 x 10^{-2} mmol 2 µ 2 M sol ti on in $_6D_6$) was added to the NMR tube. C_6D_6 200 µ was added to the NMR t e to reach a total volume of 0.5 mL. The reaction was monitored by ^{1}H NMR. After 24 hours, equilibrium was reached. A ratio of 67:33, **III** to **3.62**, gave a K_{eq} of 0 Anothe r 200 µ of the catalyst and acid solution was added to another NMR tube. *n*BuOH (5.0 x 10^{-2} mmol, 25 µ 2 M sol ti on in $_6D_6$) and MeOH (5.0 x 10^{-2} mmol 2 µ 2 M sol ti on in $_6D_6$) was added to the NMR tube. C_6D_6 2 0 µ was added to the NMR t e to reach a total volume of 0.5 mL. The reaction was monitored by ^{1}H NMR. After 24 hours, equilibrium was reached. A ratio of 43:57, **III** to **3.62**, gave a K_{eq} of 0.86. The average K_{eq} for the two runs is 0.92 ± 0.06.

III Exchange with (*R*)-**3.48** (Scheme 3.32, Entry 1)



In a glovebox, a solution of catalyst **III** (7.0 mg, 2.5 x 10^{-2} mmol) and *N*,*N*-diisopropylethylamine hydrochloride (4.0 x 10^{-1} mg, 2.5 x 10^{-3} mmol, 10 mol %) in anhydrous C_6D_6 00 µ was made and dispensed into an NMR t e *R*)-**3.48** (44 mg, 0.19 mmol, 7.6 equiv in 2 0 µ $_6D_6$ was added to the NMR t e MeO 2 µ 2 10^{-2} mmol, 1 M in C_6D_6, 1 equiv was added to the NMR t e 2 µ of $_6D_6$ was added. The reaction was monitored by ^{1}H NMR. After 23 hours, equilibrium was reached. A ratio of 8:92, **3.63** to **III** gave a K_{eq} of 0.012.

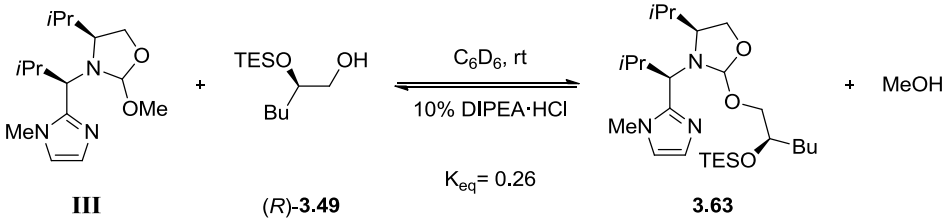
III Exchange with (*S*)-**3.48** (Scheme 3.32, Entry 2)



In a glovebox, a solution of catalyst **III** (7.0 mg, 2.5 x 10^{-2} mmol) and *N*,*N*-diisopropylethylamine hydrochloride (4.0 x 10^{-1} mg, 2.5 x 10^{-3} mmol, 10 mol %) in anhydrous C_6D_6 00 µ was made and dispensed into an NMR t e *S*)-**3.48** (43 mg, 0.19 mmol, 7.4 equiv in 2 0 µ $_6D_6$ was added to the NMR t e MeO 2 µ 2

10^{-2} mmol, 1 M in C_6D_6, 1 equiv was added to the NMR t e 2 µ of $_6D_6$ was added. The reaction was monitored by ^{1}H NMR. After 23 hours, equilibrium was reached. A ratio of 13:87, **3.63** to **III** gave a K_{eq} of 0.023.

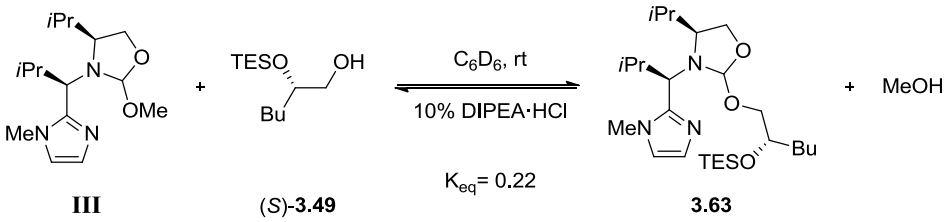
III Exchange with (*R*)-**3.49** (Scheme 3.32, Entry 3)



III (*R*)-**3.49** **3.63**

In a glovebox, a solution of catalyst **III** (14 mg, 5.0 x 10^{-2} mmol) and *N*,*N*-diisopropylethylamine hydrochloride (8.0 x 10^{-1} mg, 5.0 x 10^{-3} mmol, 10 mol %) in anhydrous C_6D_6 00 µ was made and dispensed into an NMR t e *R*)-**3.49** (58 mg, 0.25 mmol, 5 equiv in 2 0 µ $_6D_6$ was added to the NMR t e MeO 0 µ 0 10^{-2} mmol, 1 M in C_6D_6, 1 equiv was added to the NMR t e 00 µ of $_6D_6$ was added. The reaction was monitored by ^{1}H NMR. After 23 hours, equilibrium was reached. A ratio of 45:55, **3.63** to **III** gave a K_{eq} of 0.26.

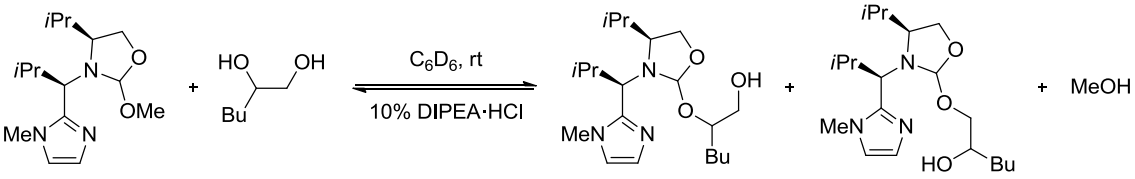
III Exchange with (*S*)-**3.49** (Scheme 3.32, Entry 4)



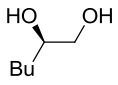
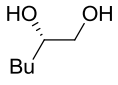
III (*S*)-**3.49** **3.63**

In a glovebox, a solution of catalyst **III** (14 mg, 5.0 x 10^{-2} mmol) and *N*,*N*-diisopropylethylamine hydrochloride (8.0 x 10^{-1} mg, 5.0 x 10^{-3} mmol, 10 mol %) in anhydrous C_6D_6 00 µ was made and dispensed into an NMR t e *S*)-**3.49** (58 mg, 0.25 mmol, 5 equiv in 2 0 µ $_6D_6$ was added to the NMR t e MeO 0 µ 0 10^{-2} mmol, 1 M in C_6D_6, 1 equiv was added to the NMR t e 00 µ of $_6D_6$ was added. The reaction was monitored by ^{1}H NMR. After 23 hours, equilibrium was reached. A ratio of 42:58, **3.63** to **III** gave a K_{eq} of 0.22.

III Exchange with (*R*)- and (*S*)-**3.47** (Scheme 3.33)



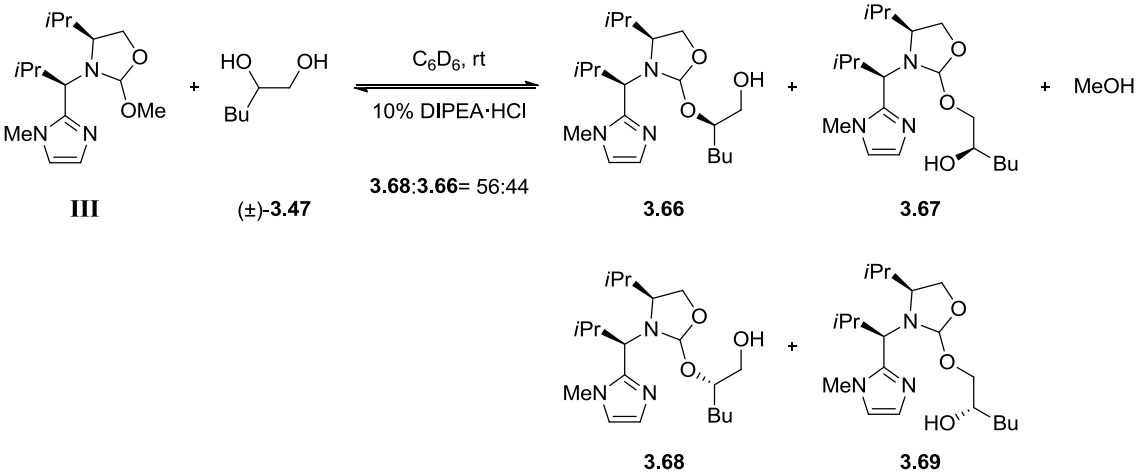
III **3.47** **3.64** **3.65**

Entry	Diol	Equiv.	**3.64:3.65**
1	 (*R*)-**3.47**	5	18:82
2	 (*S*)-**3.47**	5	20:80

In a glovebox, a solution of catalyst **III** (8.4 mg, 3.0 x 10^{-2} mmol) and *N*,*N*-diisopropylethylamine hydrochloride (5.0 x 10^{-1} mg, 3.0 x 10^{-3} mmol, 10 mol %) in anhydrous C_6D_6 00 µ was made and dispensed into an NMR t e (*R*)-**3.47** (18 mg, 0.15 mmol, 3 equiv in 2 0 µ $_6D_6$ was added to the NMR t e MeO 2 µ 0

10^{-2} mmol, 2 M in C_6D_6, 1 equiv) was added to the NMR t e 2 µ of $_6D_6$ was added. The reaction was monitored by ^{1}H NMR. After 24 hours, equilibrium was reached and 57% of **III** had converted to products. A ratio of 18:82 of **3.64** to **3.65** resulted. The reaction was repeated using (*S*)-**3.42**. At equilibrium, a ratio of 20:80 of **3.64** and **3.65** was reached with 56% conversion of **III**.

Exchange of (±)-**3.47** with **III** (Scheme 3.34)



In a glovebox, a solution of catalyst **III** (14 mg, 5.0 x 10^{-2} mmol) and *N*,*N*-diisopropylethylamine hydrochloride (8.0 x 10^{-1} mg, 5.0 x 10^{-3} mmol, 10 mol %) in anhydrous C_6D_6 00 µ was made and dispensed into an NMR t e **3.47** (18 mg, 0.15 mmol, 3 equiv) in 2 0 µ $_6D_6$ was added to the NMR t e MeO 2 µ 0 0 $^{-2}$ mmol, 2 M in C_6D_6, 1 equiv) was added to the NMR t e 2 µ of $_6D_6$ was added. The reaction was monitored by ^{1}H NMR. After 24 hours, equilibrium was reached. A ratio of 56:44, products to **III** gave a K_{eq} of 0.70. The ratio of secondary to primary alcohols bound was 21:79. The ratio of **3.68** to **3.66** was 56:44. The reaction was repeated

using 5 equiv of **3.47** (3.0×10^1 mg, 0.25 mmol). At equilibrium, a ratio of 67:33 of products to **III** corresponds to a K_{eq} of 0.78. The ratio of secondary to primary bound alcohols was 18:82. The average K_{eq} was calculated to be 0.74 ± 0.06.

The Difference in Selectivity of **3.11** and **III**

GC Method for Selective Functionalization of **3.13**

GC Method. An Agilent Technologies 7890A GC System equipped with a 7683B Series Injector was used to introduce samples into a J&W Scientific column (HP-5, 30 m, 0.320 mm ID 0 2 μm film he G wa s r n at 00 ° for 0 mi n tes a nd then the temperature was ramped 8 °C/min. to a final temperature of 180 °C. Compounds were detected by FID and data was analyzed with Agilent Technologies GC Chemstation software. Retention times are reported in minutes.

Reaction of **III** with Individual Enantiomers (Scheme 3.35, Eq 1)

To an oven-dried reaction vial, a solution of (*S*)-1-phenyl-1,2-ethanediol, (*S*)-**3.13**, (28 mg, 0.20 mmol), *N*,*N*-diisopropylethylamine hydrochloride (3.3 mg, 2.0×10^{-2} mmol, 10 mol %), and **III** (11 mg, 4.0×10^{-2} mmol, 20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 μ 0 2 mmol, 1.2 equiv) was added, followed by triethylchlorosilane 36 μ 0 20 mmol 0 eq iv). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 μ and methanol μ he mi t re was stirred at room temperature for 10 min and filtered

through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Reaction of III with Individual Enantiomers (Scheme 3.35, Eq 2)

The procedure for Scheme 3.33, Eq 1 was followed using (*R*)-**3.13** (28 mg, 0.20 mmol).

Catalyst Loading Screen (Table 3.19)

To an oven-dried reaction vial, a solution of (*R*)-1-phenyl-1,2-ethanediol, (*R*)-**3.13**, (28 mg, 0.20 mmol), *N*,*N*-diisopropylethylamine hydrochloride (6.6 mg, 4.0 x 10^{-2} mmol, 20 mol %), and **3.11** in anhydrous THF (3 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 µ 0 2 mm ol 2 eq iv) was added, followed by triethylchlorosilane 36 µ 0 20 mmol 0 eq iv). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 µ and methanol µ he mi t re was stirred at room temperature for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Table 3.19, Entry 1

10 mol % **3.11** (5.1 mg, 2.0 x 10^{-2} mmol) was used in the reaction.

Table 3.19, Entry 2

20 mol % **3.11** (10.2 mg, 4.0 x 10^{-2} mmol) was used in the reaction.

Table 3.19, Entry 3

50 mol % **3.11** (25.4 mg, 0.10 mmol) was used in the reaction.

(*S*,*S*) and (*S*,*R*)-Catalysts Table (3.20)

To an oven-dried reaction vial, a solution of (*R*)-1-phenyl-1,2-ethanediol, (*R*)-**3.13**, (28 mg, 0.20 mmol), *N*,*N*-diisopropylethylamine hydrochloride (3.3 mg, 2.0 x 10^{-2} mmol, 10 mol %), and catalyst (20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred at room temperature for 10 minutes. *N*,*N*-Diisopropylethylamine 2 µ 0 2 mmol, 1.2 equiv) was added, followed by triethylchlorosilane 36 µ 0 20 mmol 0 equiv). After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 µ and methanol µ he mi t re was stirred at room temperature for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction. Each reaction was repeated with (*S*)-**3.13**.

Table 3.20

R= (*S*)-Me (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*S*)-*i*Pr (11 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*R*)-Me (1.0 x 10^{-1} mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*R*)-*i*Pr, **III**, (11 mg, 4.0 x 10^{-2} mmol, 20 mol %)

R= (*R*)-Ph (13 mg, 4.0 x 10^{-2} mmol, 20 mol %)

Decreasing the Reaction Temperature (Scheme 3.36)

To an oven-dried reaction vial, a solution of (*S*)-1-phenyl-1,2-ethanediol, (*S*)-**3.13**, (28 mg, 0.20 mmol), *N*,*N*-diisopropylethylamine hydrochloride (3.3 mg, 2.0 x 10^{-2} mmol, 10 mol %), and **III** (12 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred at 4 °C for 10 minutes. *N*,*N*-Diisopropylethylamine (42

μ 0 2 mm ol 2 eq iv) was added, followed by triethylchlorosilane 36 μ 0 20 mmol, 1.0 equiv). After stirring at 4 °C for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 μ and methanol μ he mi t re was stirred at 4 °C for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

1,2,2,6,6-Pentamethylpiperidine as the Base (Table 3.21)

To an oven-dried reaction vial, a solution of (*S*)-1-phenyl-1,2-ethanediol, (*S*)-**3.13**, (28 mg, 0.20 mmol), *p*-toluenesulfonic acid (1.0 mg, 6.0 x 10^{-3} mmol, 3 mol %), and **III** (12 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred for 10 minutes. 1,2,2,6,6-Pentamethylpiperidine 3 μ 0 2 mm ol 2 eq iv) was added, followed by triethylchlorosilane 36 μ 0 20 mmol 0 eq iv). After stirring at a constant temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 μ and methanol μ he mi t re was stirred for 0 mi n and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Table 3.21, Entry 1

The reaction was run at 4 °C.

Table 3.21, Entry 2

The reaction was run at 25 °C.

Table 3.21, Entry 3

The reaction was run at 25 °C using crystallized **III**.

Electrophile Screen (Table 3.22)

To an oven-dried reaction vial, a solution of (*S*)-1-phenyl-1,2-ethanediol, (*S*)-**3.13**, (28 mg, 0.20 mmol), *p*-toluenesulfonic acid (1.0 mg, 6.0 x 10^{-3} mmol, 3 mol %), and **III** (12 mg, 4.0 x 10^{-2} mmol, 20 mol %) in anhydrous THF (3 mL) was added. The reaction was stirred for at room temperature for 10 minutes. 1,2,2,6,6-Pentamethylpiperidine 3 µ 0.24 mmol, 1.2 equiv) was added, followed by the electrophile. After stirring at room temperature for 12 hours, the reaction was quenched by addition of *N*,*N*-diisopropylethylamine 30 µ and methanol µ The mixture was stirred for 10 min and filtered through a Pasteur pipette packed with silica gel, followed by a flush with EtOAc (10 mL). GC analysis afforded the yield and selectivity of the reaction.

Table 3.22, Entry 1

SB r 3 µ 0 20 mmol, 1.0 equiv) was used as the electrophile.

Table 3.22, Entry 2

$TESNO_2$ was used as the electrophile and the reaction was run in dimethylformamide (3 mL). $TESNO_2$ was made in situ from TES 1 3 µ 0 20 mmol 0 eq iv) and NH_4NO_3 (48 mg, 0.60 mmol, 3.0 equiv)

Table 3.22, Entry 3

TESO f µ 0 20 mmol 0 e q iv) was used as the electrophile.

Table 3.22, Entry 4

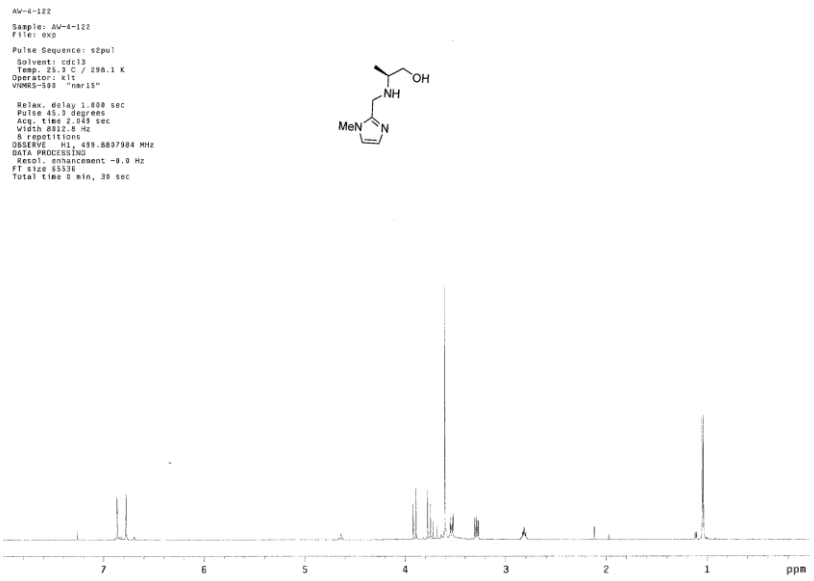
TESO f µ 0 20 mmol 0 e q iv) was used as the electrophile at 4 °C.

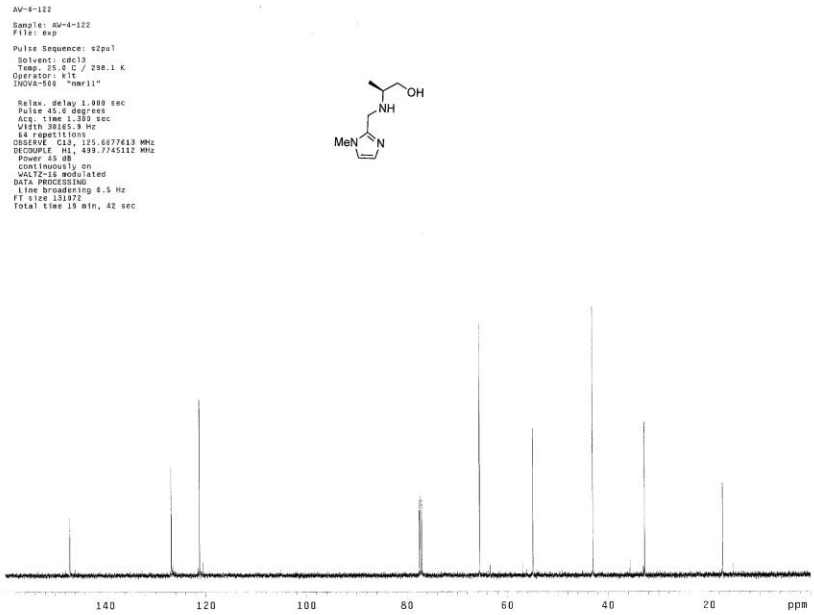
Table 3.22, Entry 5

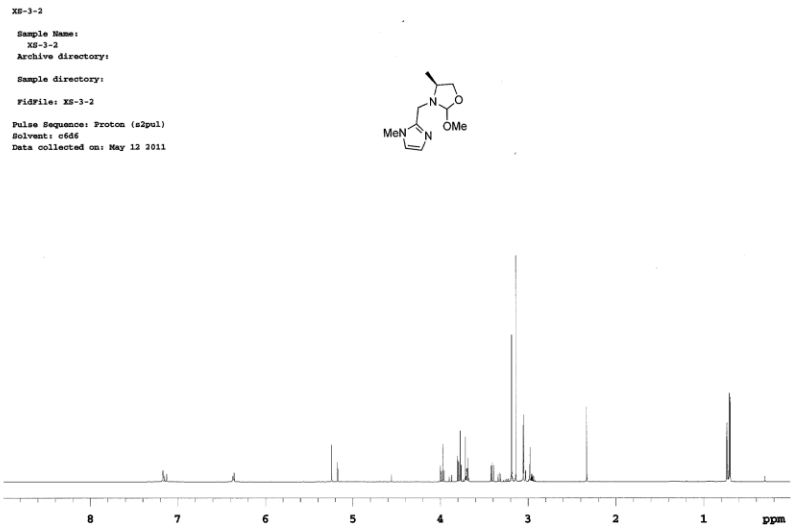
TESO f μ 0 20 mmol 0 e q iv) was used as the electrophile at -60 to 10 °C.

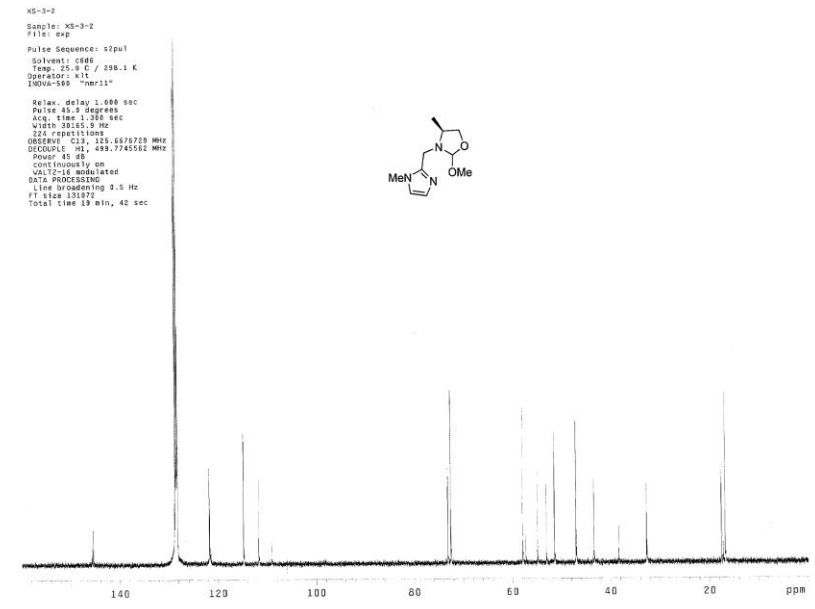
Table 3.22, Entry 6

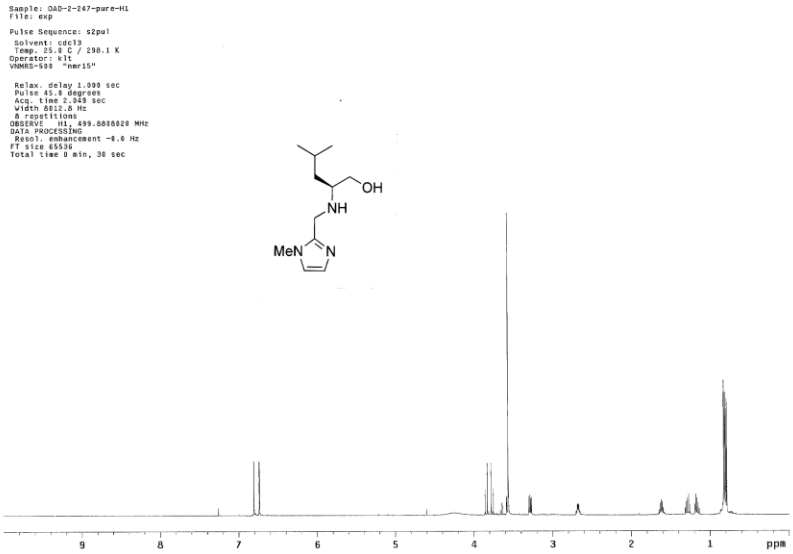
TESO f μ 0 20 mmol 0 e q iv) was used as the electrophile at 60 °C.

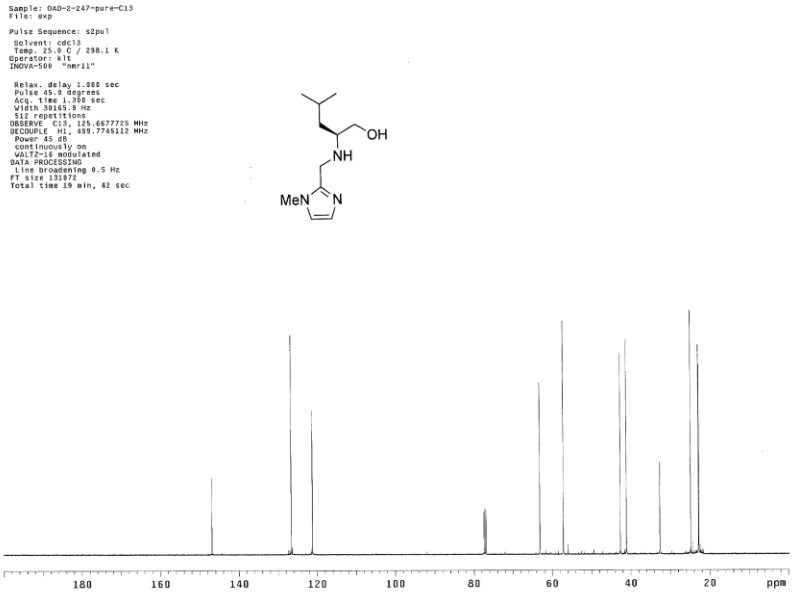

AV-4-122
Sample: AV-4-122
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.3 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.3 degrees
Acq. time 2.949 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8897984 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 39 sec
OH
NH
MeN
N
7
6
5
4
3
2
1
ppm

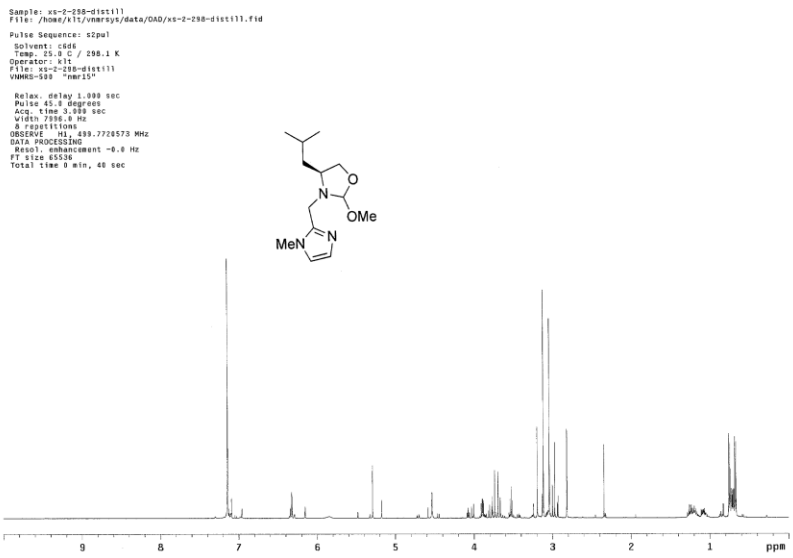

AV-4-122
Sample: AV-4-122
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
64 repetitions
OBSERVE C13, 125.6677613 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
NH
MeN
N
140
120
100
80
60
40
20
ppm

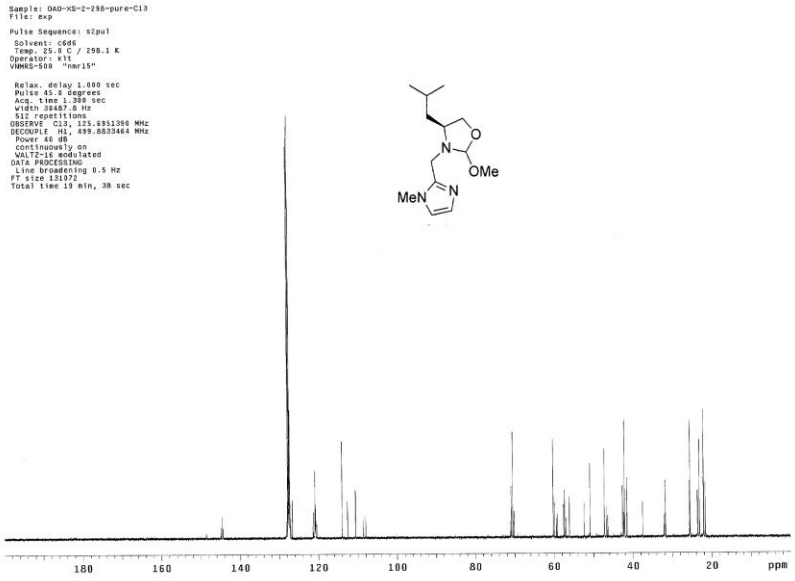

XS-3-2
Sample Name:
XS-3-2
Archive directory:
Sample directory:
FidFile: XS-3-2
Pulse Sequence: Proton (s2pul)
Solvent: c6d6
Data collected on: May 12 2011
MeN
N
O
OMe
8
7
6
5
4
3
2
1
ppm


XS-3-2
Sample: XS-3-2
File: exp
Pulse Sequence: s2pul
Solvent: c6d6
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.380 sec
Width 20165.9 Hz
224 repetitions
OBSERVE C13, 125.6878729 MHz
DECOUPLE H1, 499.7745562 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
MeN
N
O
OMe
140
120
100
80
60
40
20
ppm


Sample: OAD-2-247-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8888020 MHz
DATA PROCESSING
Resol. enhancement -0.6 Hz
FT size 65536
Total time 0 min, 30 sec
OH
NH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

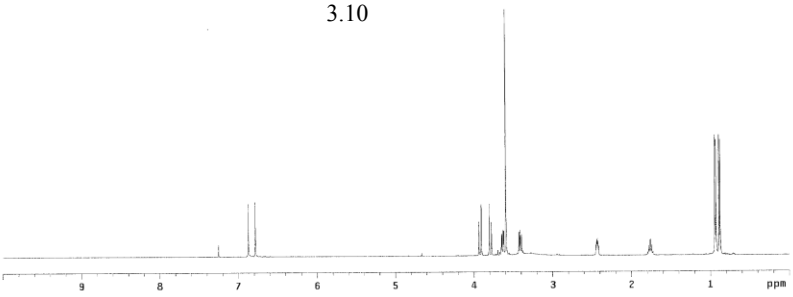

Sample: OAD-2-247-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
NH
MeN
N
180
160
140
120
100
80
60
40
20
ppm


Sample: xs-2-298-distill
File: /home/klt/vnmrsys/data/OAD/xs-2-298-distill.fid
Pulse Sequence: s2pul
Solvent: c6d6
Temp. 25.0 C / 298.1 K
Operator: klt
File: xs-2-298-distill
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.999 sec
Width 7996.0 Hz
8 repetitions
OBSERVE H1, 499.7720573 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 48 sec
O
N
OMe
MeN
N
9
8
7
6
5
4
3
2
1
ppm

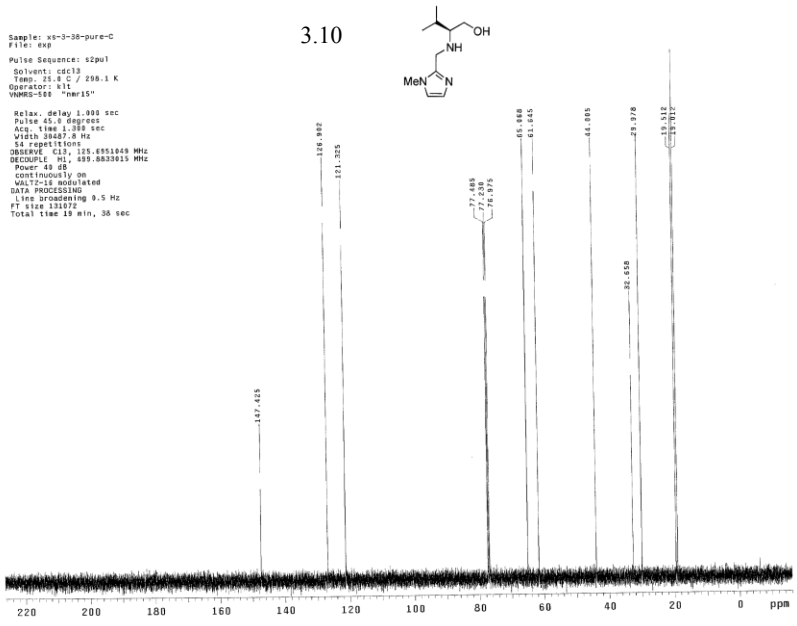

Sample: OAD-XS-2-298-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: c6d6
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 38467.8 Hz
512 repetitions
OBSERVE C13, 125.6951386 MHz
DECOUPLE H1, 499.8833464 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
O
N
OMe
MeN
N
180
160
140
120
100
80
60
40
20
ppm


Sample: xs-3-38-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808029 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
OH
NH
MeN
N

3.10

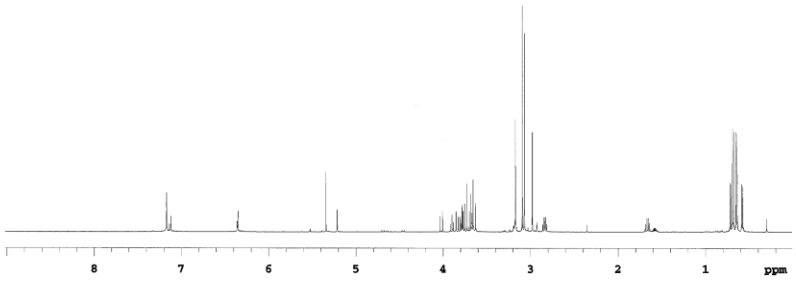

9
8
7
6
5
4
3
2
1
ppm

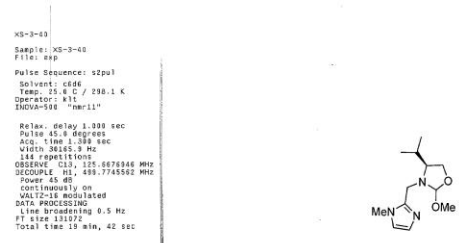
3.10


Sample: xs-3-38-pure-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.366 sec
Width 30487.8 Hz
54 repetitions
OBSERVE C13, 125.6551049 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
OH
NH
MeN
N
147.425
126.982
121.325
77.485
77.230
76.975
65.868
61.645
41.005
29.978
25.658
19.512
19.012
220
200
180
160
140
120
100
80
60
40
20
0
ppm

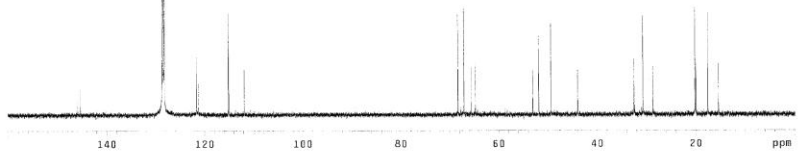

XS-3-40
Sample Name:
XS-3-40
Archive directory:
Sample directory:
FidFile: XS-3-40
Pulse Sequence: Proton (s2pul)
Solvent: c6d6
Data collected on: May 12 2011
MeN
N
O
OMe

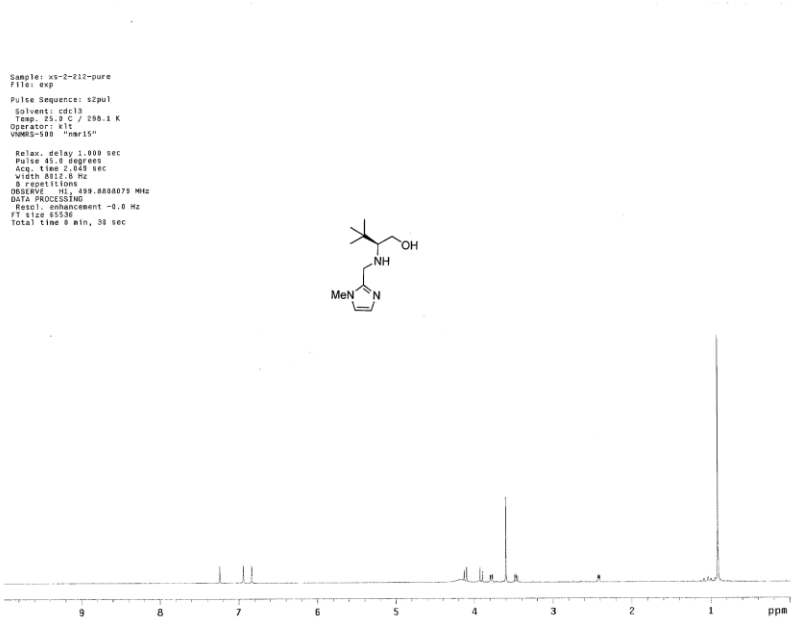
3.11

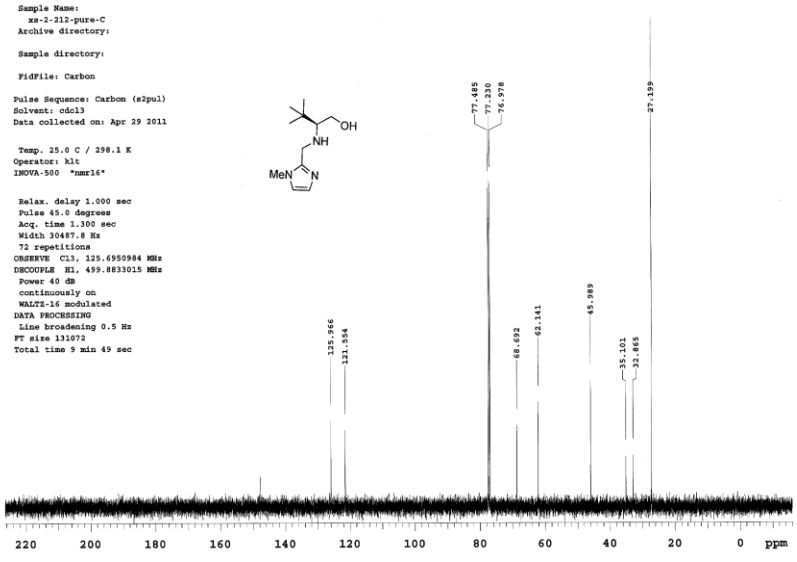

8
7
6
5
4
3
2
1
ppm

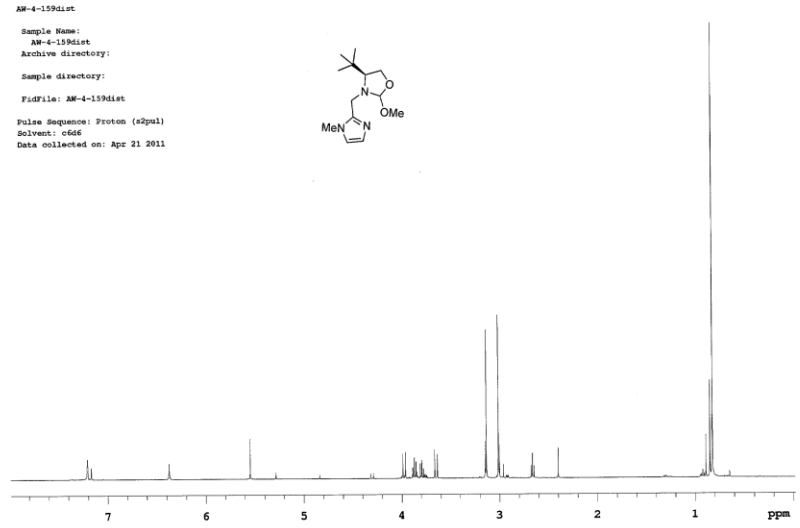

XS-3-40
Sample: XS-3-40
File: exp
Pulse Sequence: s2pul
Solvent: c6d6
Temp. 25.6 C / 298.1 K
Operator: kit
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.589 sec
Width 36185.9 Hz
144 repetitions
OBSERVE C13, 125.6676946 MHz
DECOUPLE H1, 499.7745562 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
MeN
N
O
OMe

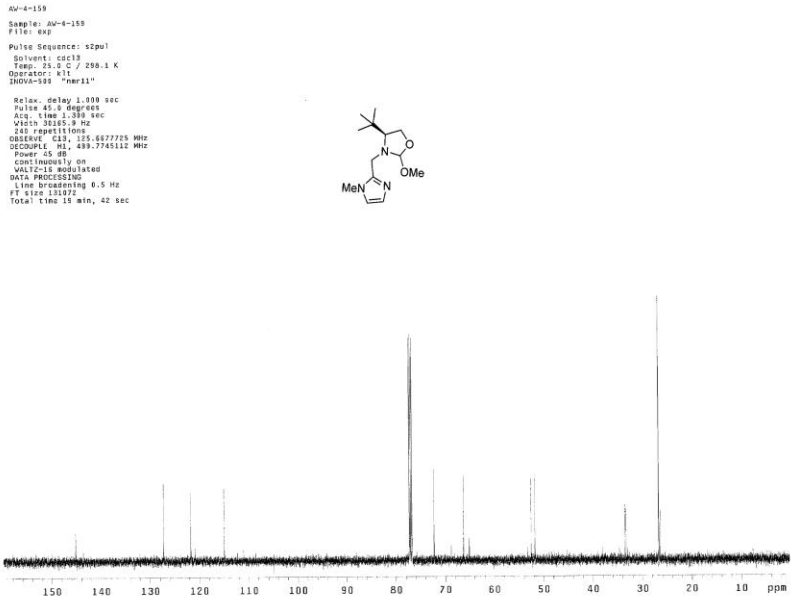
3.11

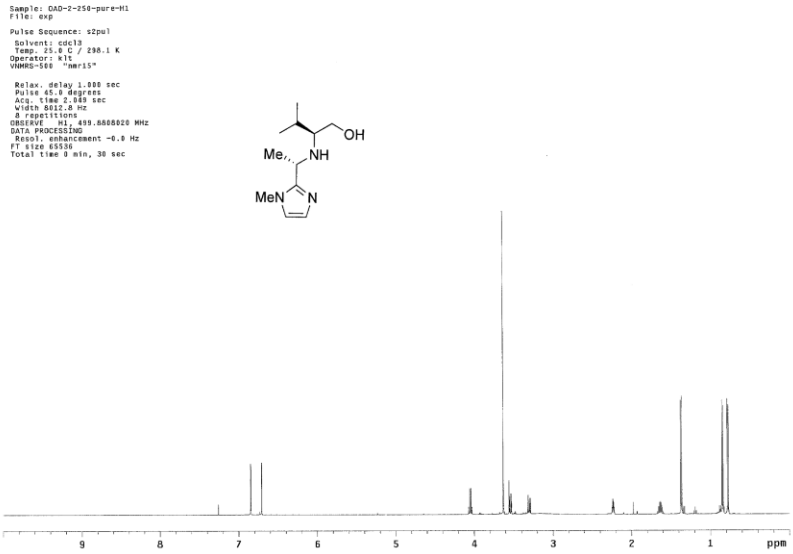

140
120
100
80
60
40
20
ppm

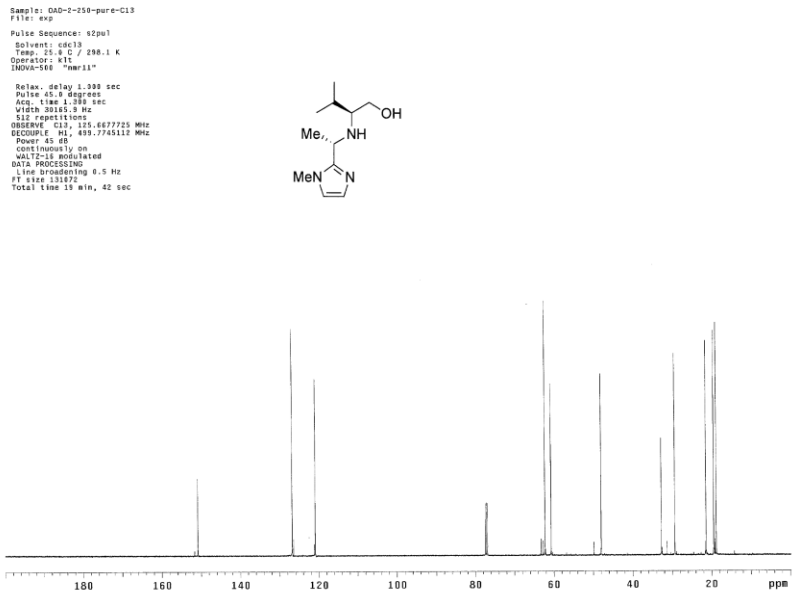

Sample: xs-2-212-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8888079 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
OH
NH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

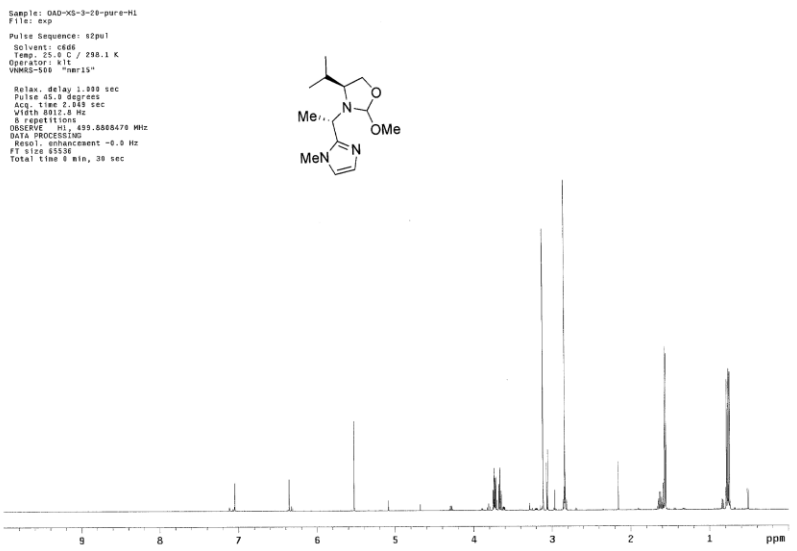

Sample Name:
xs-2-212-pure-C
Archive directory:
Sample directory:
FidFile: Carbon
Pulse Sequence: Carbom (s2pul)
Solvent: cdcl3
Data collected on: Apr 29 2011
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
72 repetitions
OBSERVE C13, 125.6950984 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min 49 sec
OH
NH
MeN
N
77.485
77.230
76.978
27.199
125.966
121.554
68.692
62.141
45.989
35.101
32.865
220
200
180
160
140
120
100
80
60
40
20
0
ppm

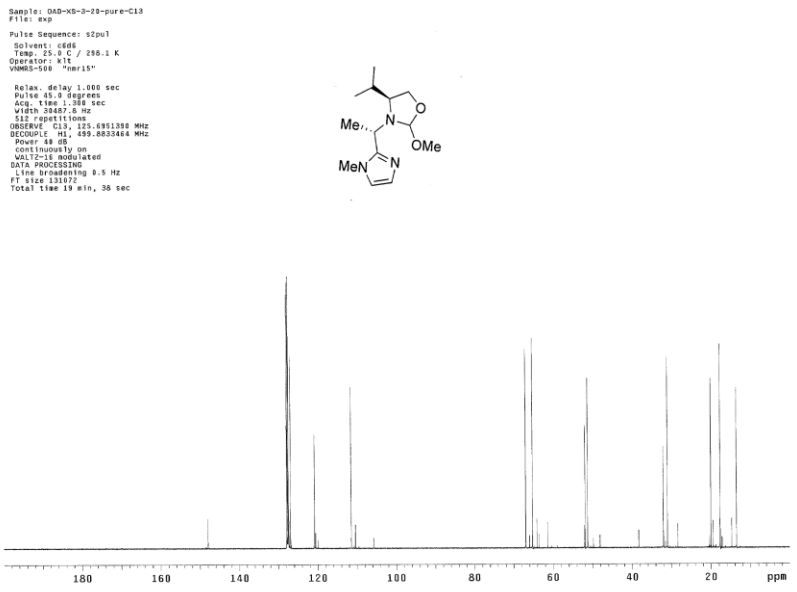

AW-4-159dist
Sample Name:
AW-4-159dist
Archive directory:
Sample directory:
FidFile: AW-4-159dist
Pulse Sequence: Proton (s2pul)
Solvent: c6d6
Data collected on: Apr 21 2011
MeN
N
O
OMe
7
6
5
4
3
2
1
ppm

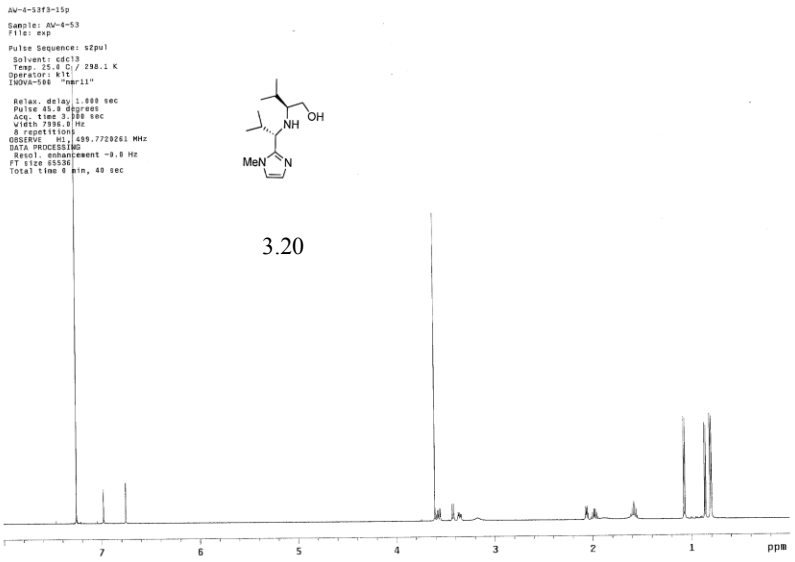

AW-4-159
Sample: AW-4-159
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
240 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 15 min, 42 sec
MeN
N
O
OMe
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


Sample: OAD-2-250-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.849 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808020 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
OH
Me
NH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

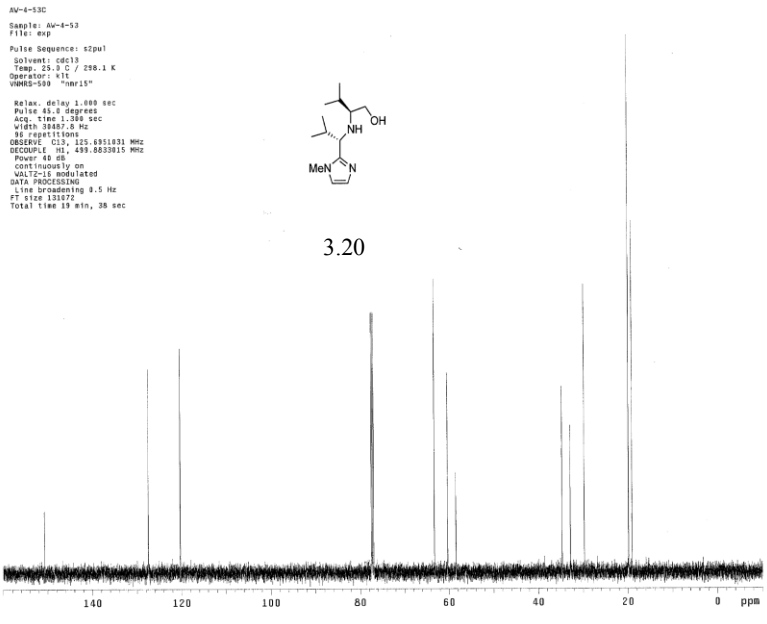

Sample: OAD-2-250-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.998 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
Me
NH
MeN
N
180
160
140
120
100
80
60
40
20
ppm


Sample: OAD-XS-3-28-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8868478 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
Me
N
O
OMe
MeN
N
9
8
7
6
5
4
3
2
1
ppm

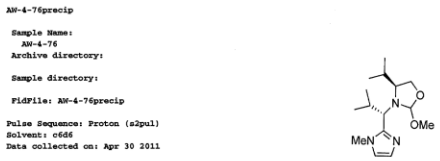

Sample: OAD-XS-3-28-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 39487.8 Hz
512 repetitions
OBSERVE C13, 125.6951398 MHz
DECOUPLE H1, 499.8833464 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 36 sec
Me
N
O
OMe
MeN
N
180
160
140
120
100
80
60
40
20
ppm


AV-4-53f3-15p
Sample: AV-4-53
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.300 sec
Width 7396.0 Hz
8 repetitions
OBSERVE H1, 499.7729261 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 48 sec
NH
OH
MeN
N
7
6
5
4
3
2
1
ppm

3.20

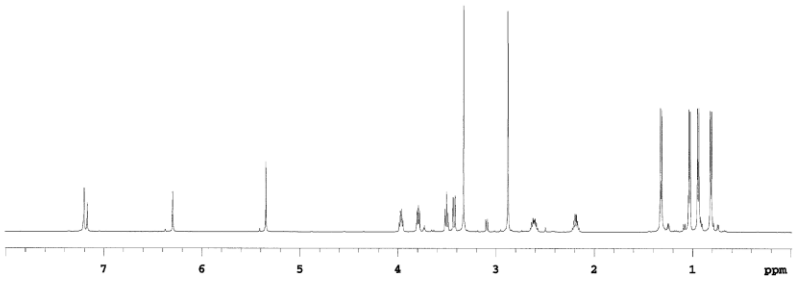

AV-4-53C
Sample: AV-4-53
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
96 repetitions
OBSERVE C13, 125.6951831 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 36 sec
NH
OH
MeN
N
140
120
100
80
60
40
20
0
ppm

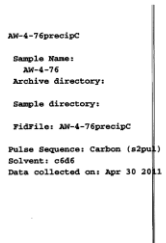
3.20

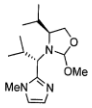

AW-4-76precip
Sample Name:
AW-4-76
Archive directory:
Sample directory:
FidFile: AW-4-76precip
Pulse Sequence: Proton (s2pul)
Solvent: c6d6
Data collected on: Apr 30 2011

MeN
N
O
OMe

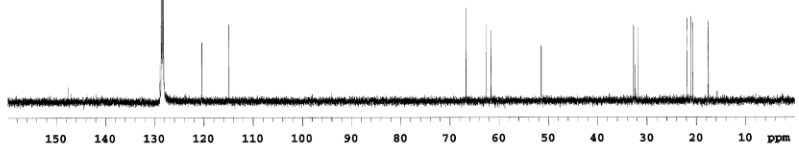
3.21

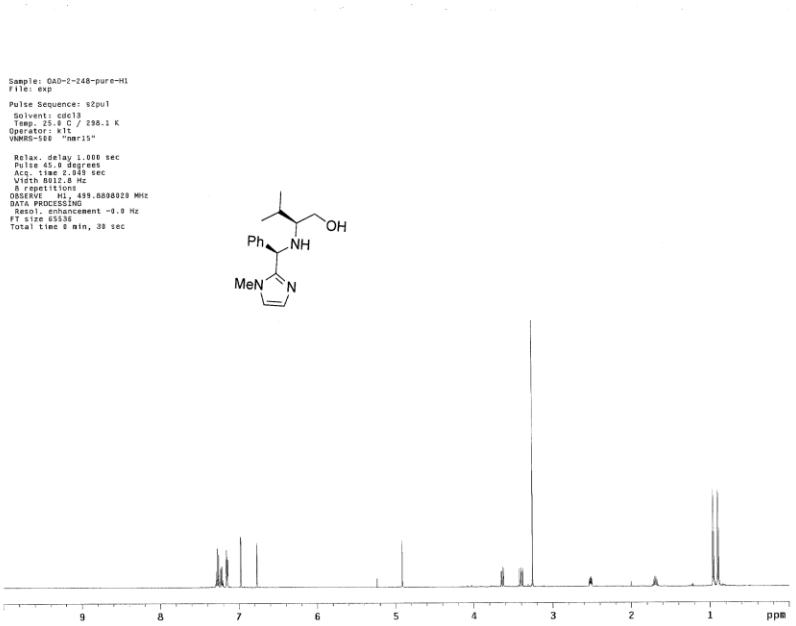

7
6
5
4
3
2
1
ppm

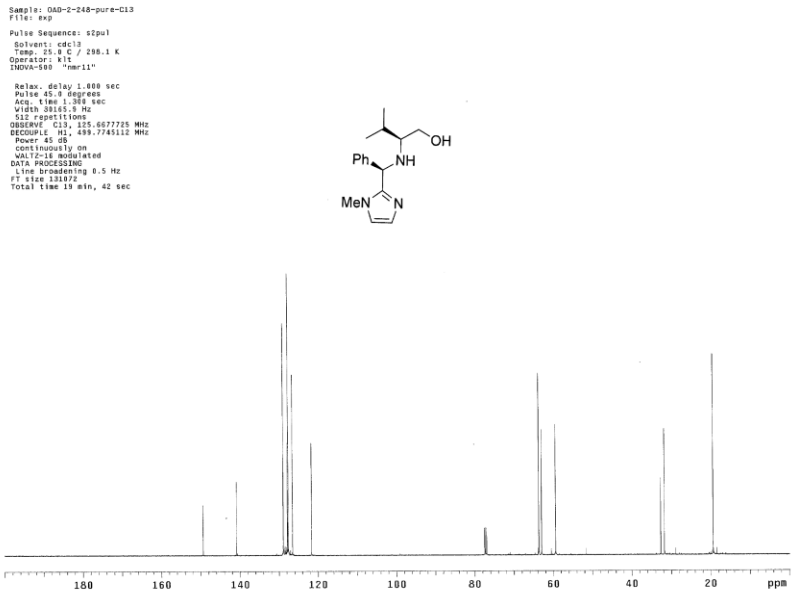

AW-4-76precipC
Sample Name:
AW-4-76
Archive directory:
Sample directory:
FidFile: AW-4-76precipC
Pulse Sequence: Carbon (s2pul)
Solvent: c6d6
Data collected on: Apr 30 2011

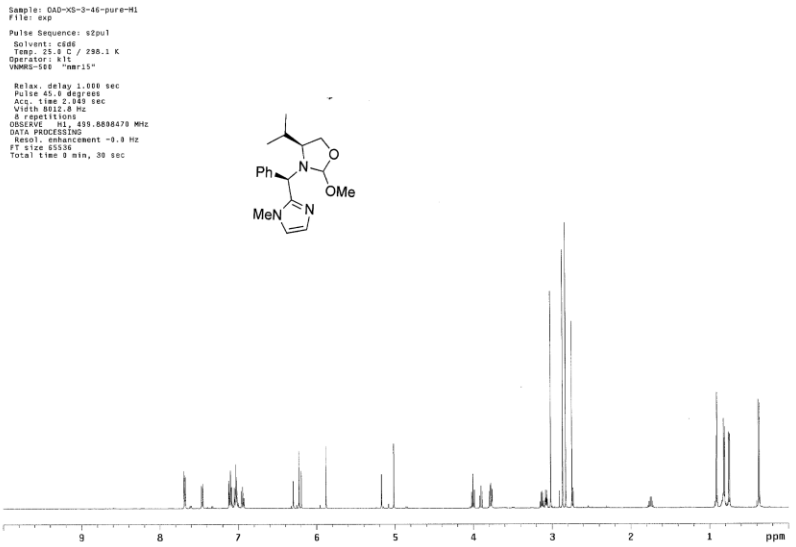

MeN
N
O
OMe

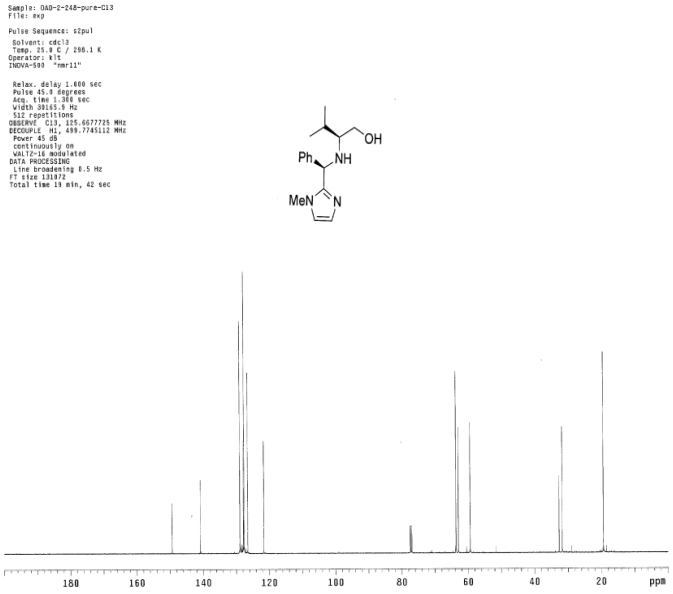
3.21

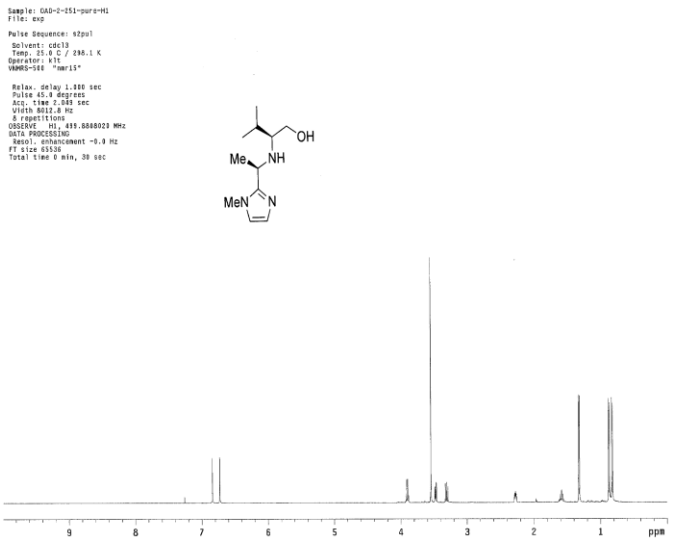

150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

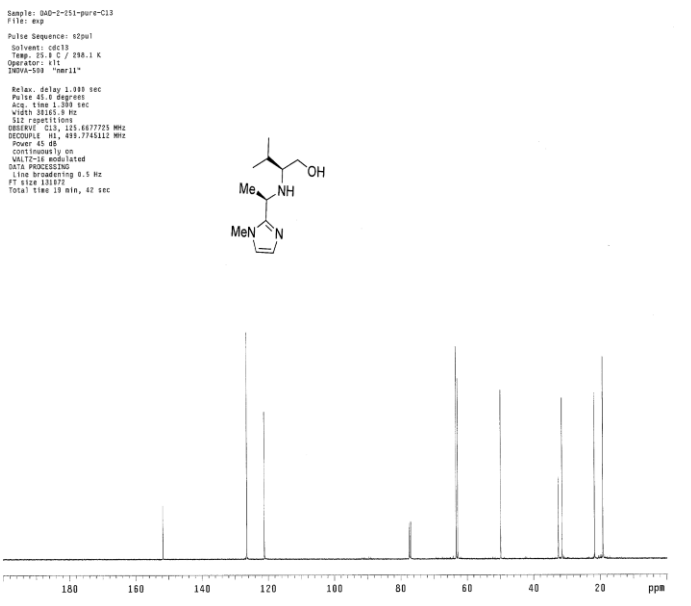

Sample: OAD-2-248-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808929 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 38 sec
OH
Ph
NH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

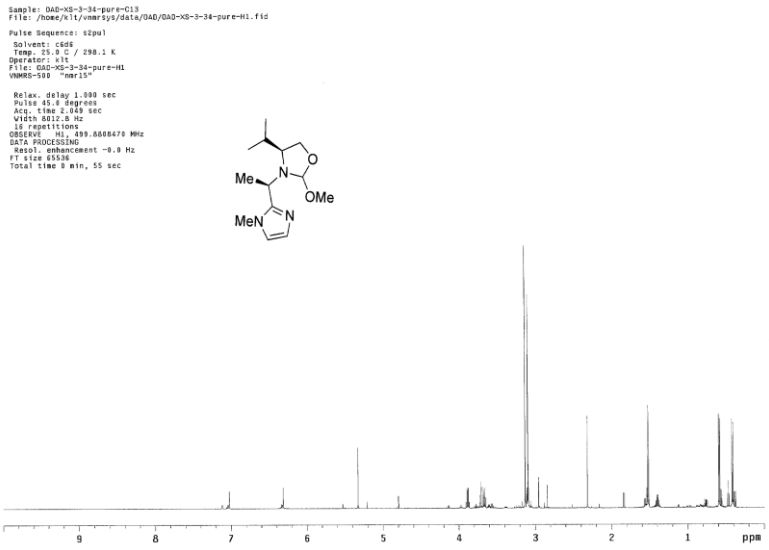

Sample: OAD-2-248-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
Ph
NH
MeN
N
180
160
140
120
100
80
60
40
20
ppm

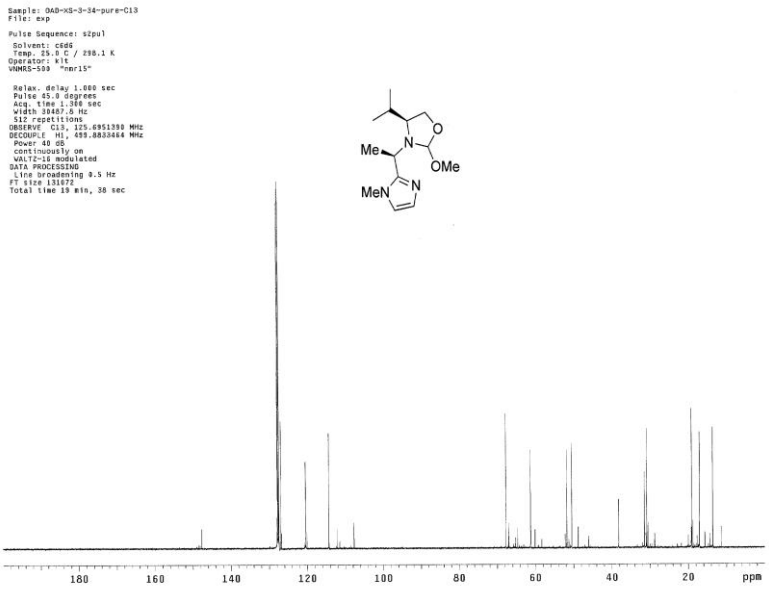

Sample: OAD-XS-3-46-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-568 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.849 sec
Width 8812.8 Hz
8 repetitions
OBSERVE H1, 499.8808478 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
Ph
N
O
OMe
MeN
N
9
8
7
6
5
4
3
2
1
ppm

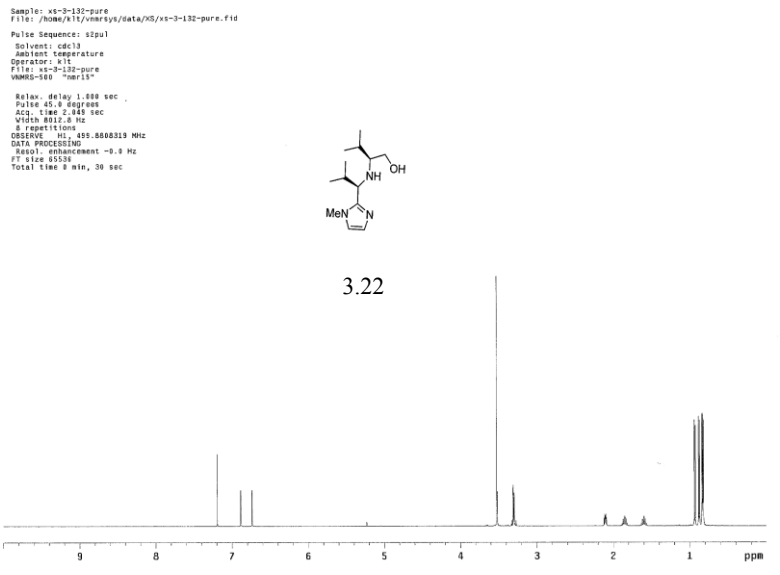

Sample: OAD-2-248-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.366 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
Ph
NH
MeN
N
180
160
140
120
100
80
60
40
20
ppm


Sample: GAD-2-251-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8868029 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
OH
Me
NH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

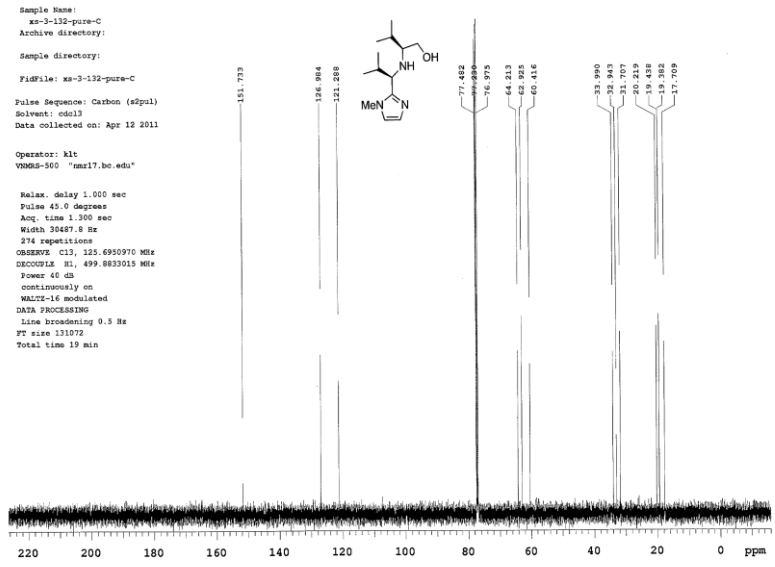

Sample: DAD-2-251-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
Me
NH
MeN
N
180
160
140
120
100
80
60
40
20
ppm

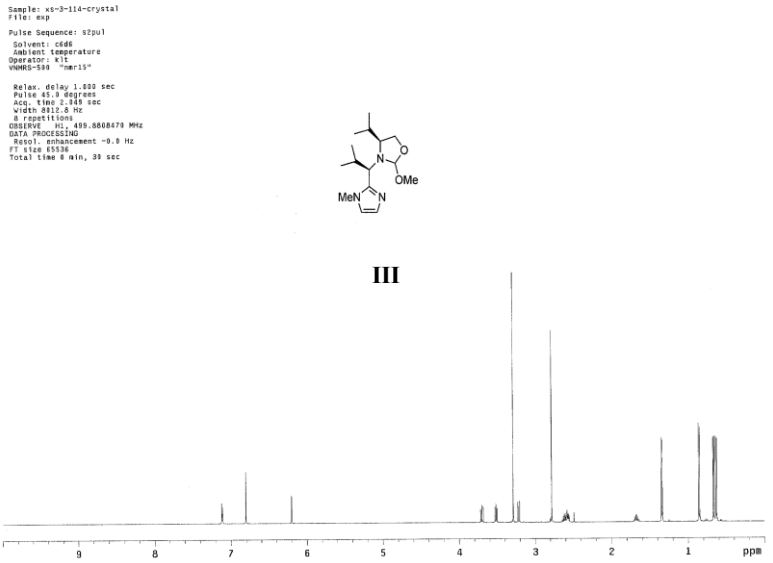

Sample: OAD-XS-3-34-pure-C13
File: /home/klt/vnmrsys/data/OAD/OAD-XS-3-34-pure-H1.fid
Pulse Sequence: s2pul
Solvent: c6d6
Temp. 25.0 C / 298.1 K
Operator: klt
File: OAD-XS-3-34-pure-H1
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
16 repetitions
OBSERVE H1, 499.8808470 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 55 sec
Me
OMe
MeN
N
O
9
8
7
6
5
4
3
2
1
ppm

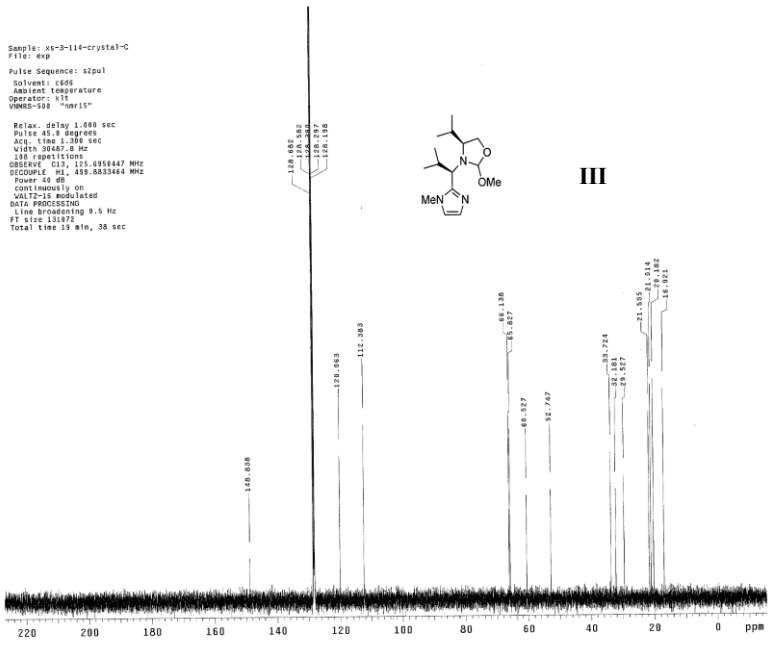

Sample: OAD-XS-3-34-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: c6d6
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.368 sec
Width 30487.8 Hz
512 repetitions
OBSERVE C13, 125.6951398 MHz
DECOUPLE H1, 499.8833464 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
Me
OMe
MeN
N
O
180
160
140
120
100
80
60
40
20
ppm

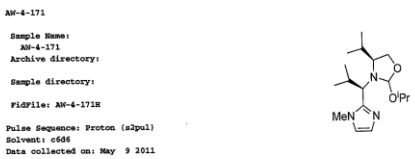

Sample: xs-3-132-pure
File: /home/klt/vnmrsys/data/XS/xs-3-132-pure.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: klt
File: xs-3-132-pure
VNMRS-500 "nmr15"
Relax. delay 1.888 sec
Pulse 45.0 degrees
Acq. time 2.045 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808319 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 8 min, 30 sec
NH
OH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

3.22


Sample Name:
xs-3-132-pure-C
Archive directory:
Sample directory:
FidFile: xs-3-132-pure-C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 12 2011
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
274 repetitions
OBSERVE C13, 125.6950970 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min
151.733
126.904
121.288
77.482
77.060
76.975
64.213
62.925
60.416
33.990
32.943
31.707
20.219
19.438
19.382
17.709
NH
OH
MeN
N
220
200
180
160
140
120
100
80
60
40
20
0
ppm

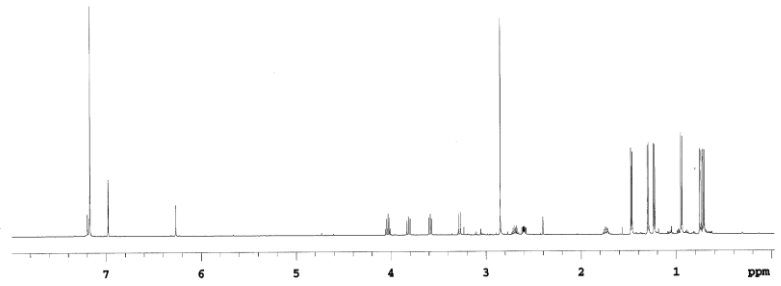

Sample: xs-3-114-crystal
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Ambient temperature
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.949 sec
Width 8812.8 Hz
8 repetitions
OBSERVE H1, 499.8808478 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
OMe
MeN
N
III
9
8
7
6
5
4
3
2
1
ppm

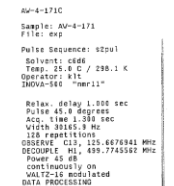

Sample: xs-3-114-crystal-C
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Ambient temperature
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.366 sec
Width 30487.8 Hz
180 repetitions
OBSERVE C13, 125.6956447 MHz
DECOUPLE H1, 499.8833464 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
126.682
126.582
126.397
126.196
140.838
120.663
112.383
66.138
65.827
60.527
52.747
33.724
32.741
25.527
21.595
21.014
20.586
18.924
OMe
MeN
N
III
220
200
180
160
140
120
100
80
60
40
20
0
ppm

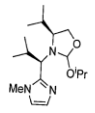

AW-4-171
Sample Name:
AW-4-171
Archive directory:
Sample directory:
FidFile: AW-4-171H
Pulse Sequence: Proton (s2pul)
Solvent: c6d6
Data collected on: May 9 2011

MeN
N
O
O'Pr

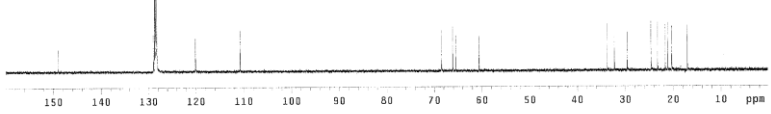
3.41

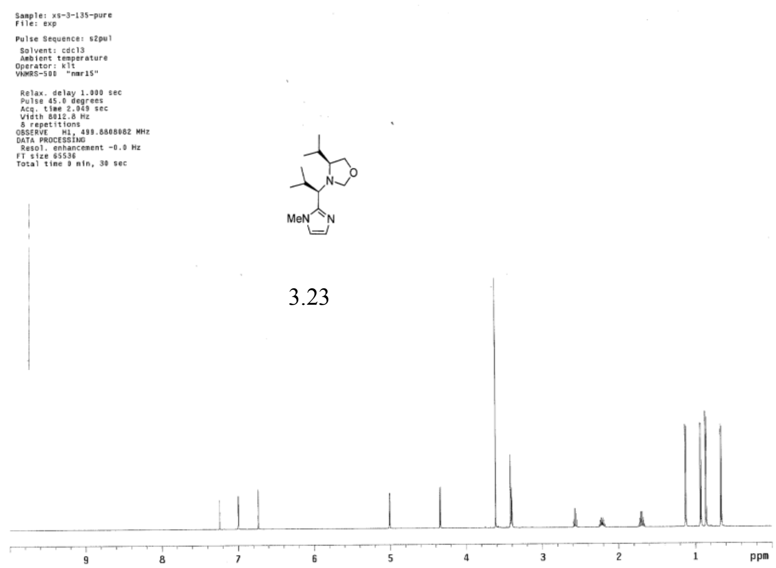

7
6
5
4
3
2
1
ppm


AW-4-171C
Sample: AW-4-171
File: exp
Pulse Sequence: s2pul
Solvent: c6d6
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr1"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.380 sec
Width 30165.9 Hz
128 repetitions
OBSERVE C13, 125.6676941 MHz
DECOUPLE H1, 499.7745562 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec

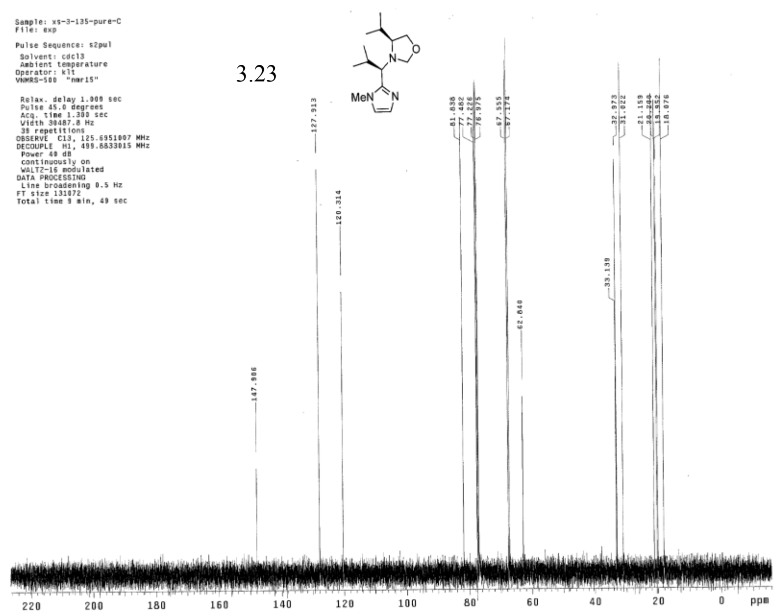

MeN
N
O
O'Pr

3.41


150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

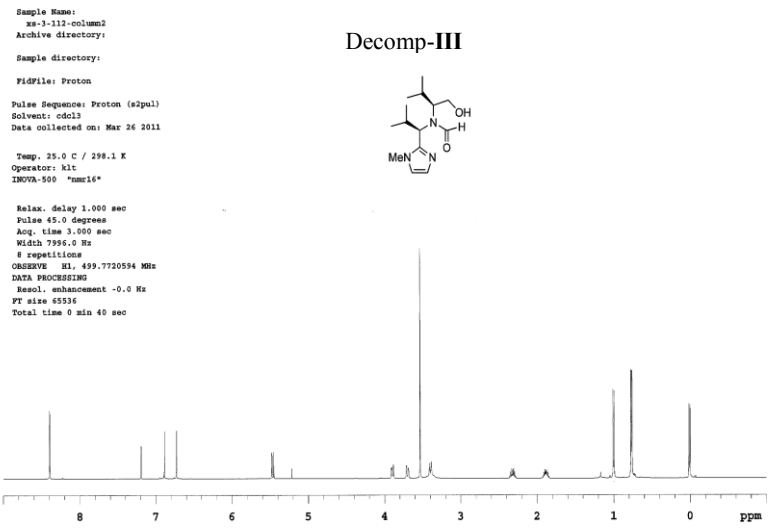


3.23

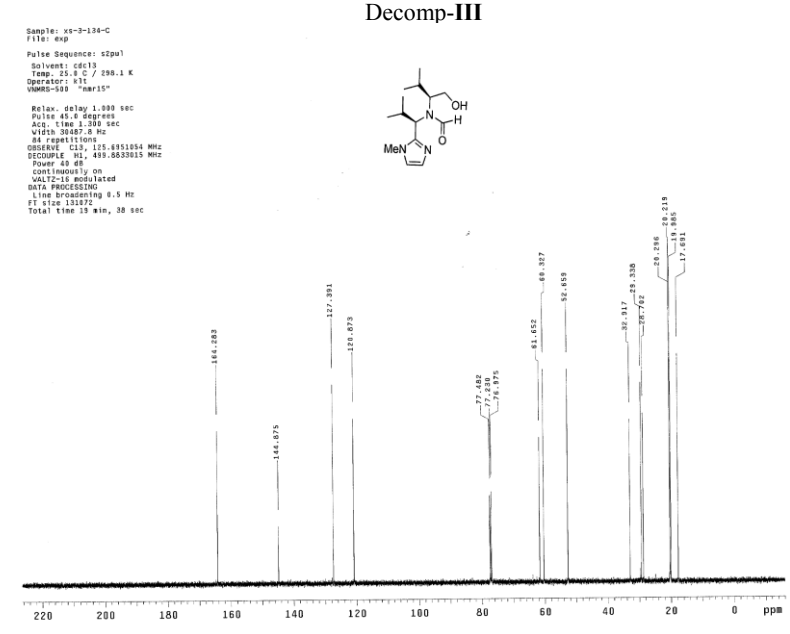


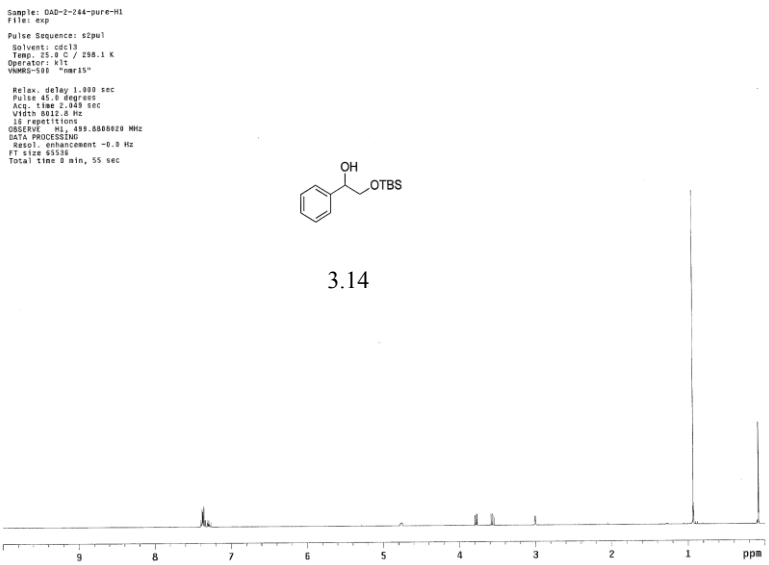
3.23

Decomp-**III**

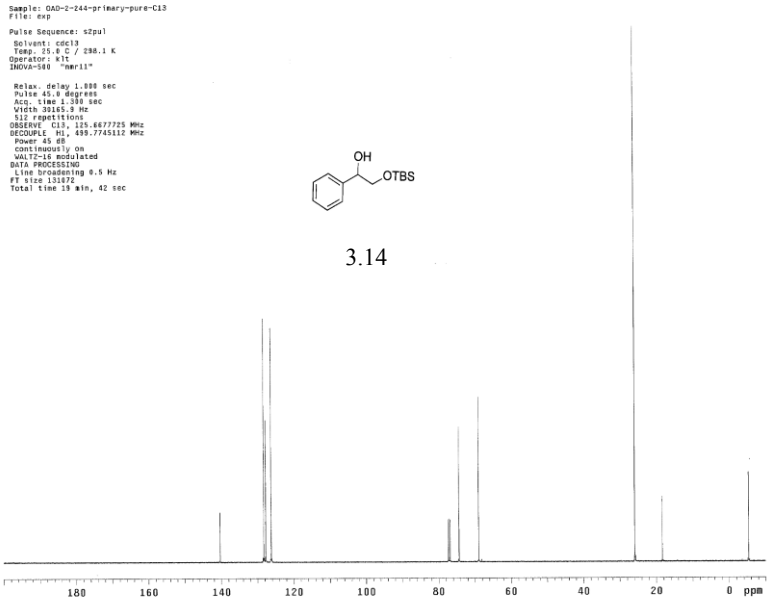


Decomp-**III**

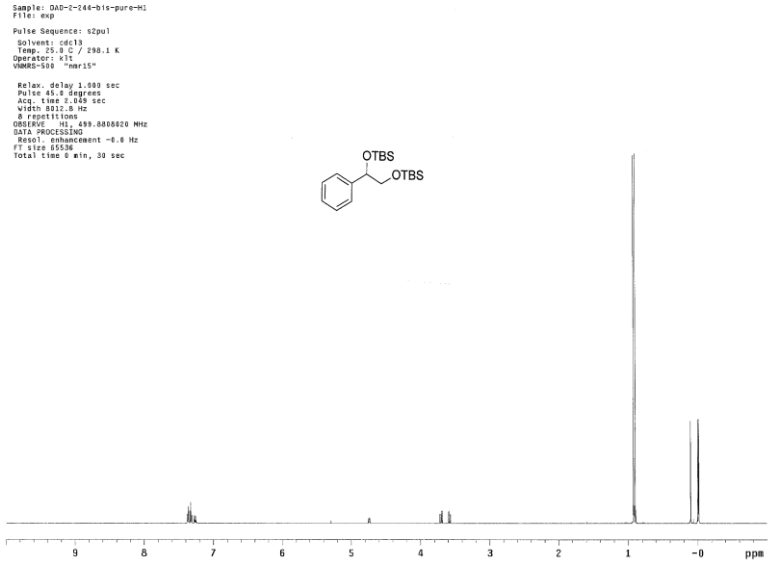


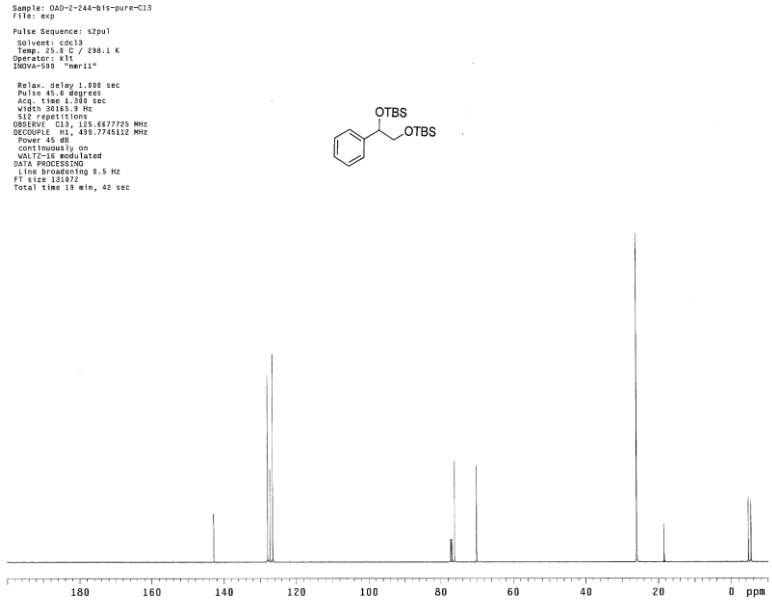

Sample: OAD-2-244-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8012.8 Hz
16 repetitions
OBSERVE H1, 499.8868820 MHz
DATA PROCESSING
Resol. enhancement -0.9 Hz
FT size 65536
Total time 0 min, 55 sec
OH
OTBS
9
8
7
6
5
4
3
2
1
ppm

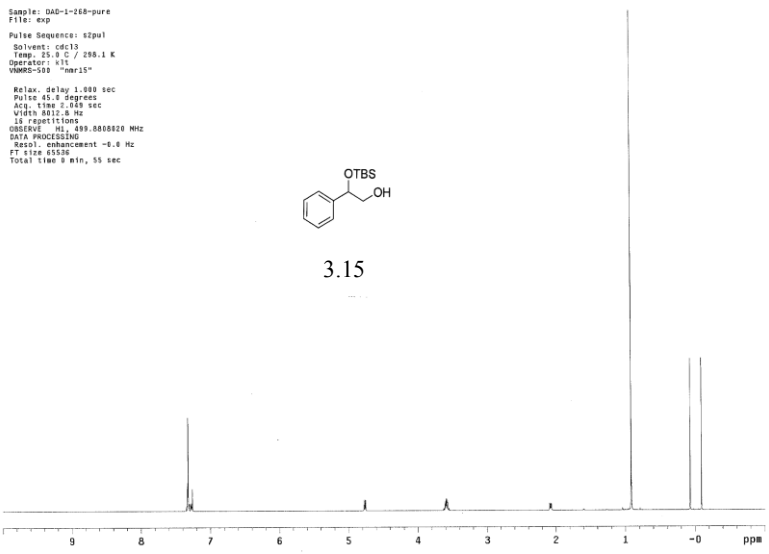
3.14


Sample: OAD-2-244-primary-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
OTBS
180
160
140
120
100
80
60
40
20
0 ppm

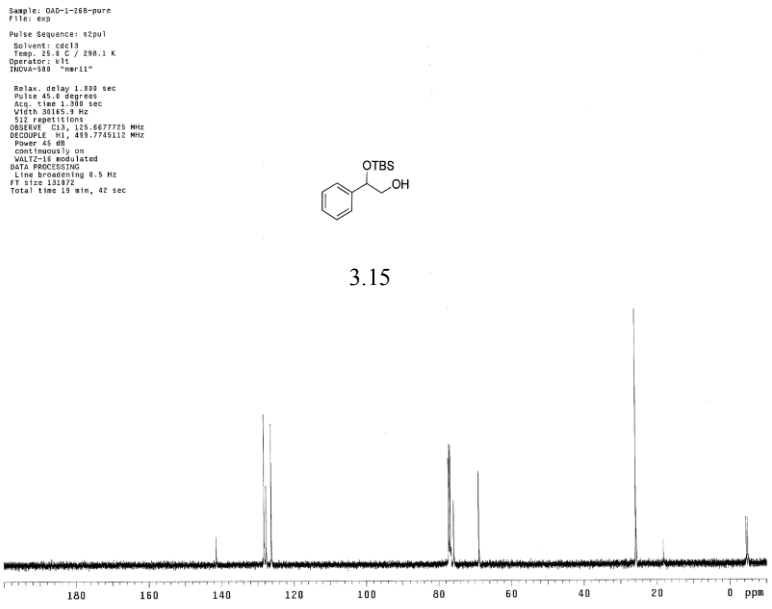
3.14


Sample: OAD-2-244-bis-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808820 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
OTBS
OTBS
9
8
7
6
5
4
3
2
1
-0
ppm

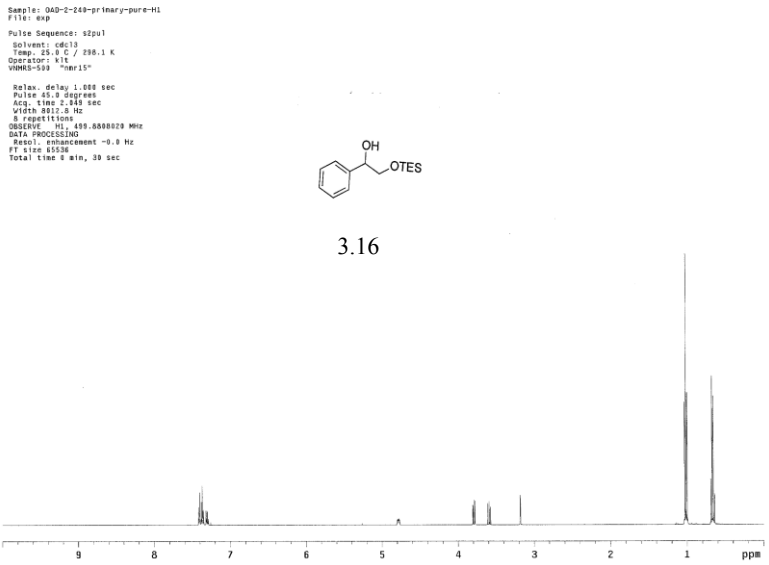

Sample: OAD-2-244-bis-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.398 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OTBS
OTBS
180
160
140
120
100
80
60
40
20
0 ppm

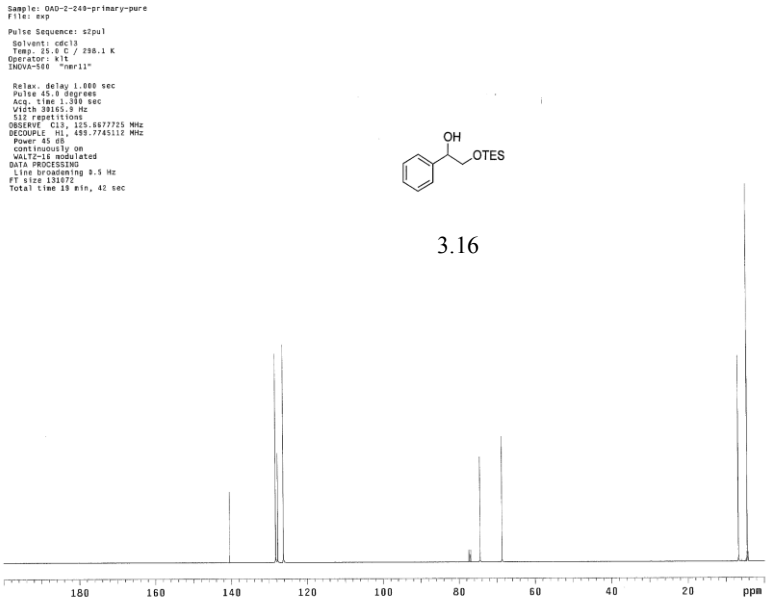

Sample: OAD-1-268-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
16 repetitions
OBSERVE H1, 499.8808820 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 55 sec
OTBS
OH
9
8
7
6
5
4
3
2
1
-0
ppm

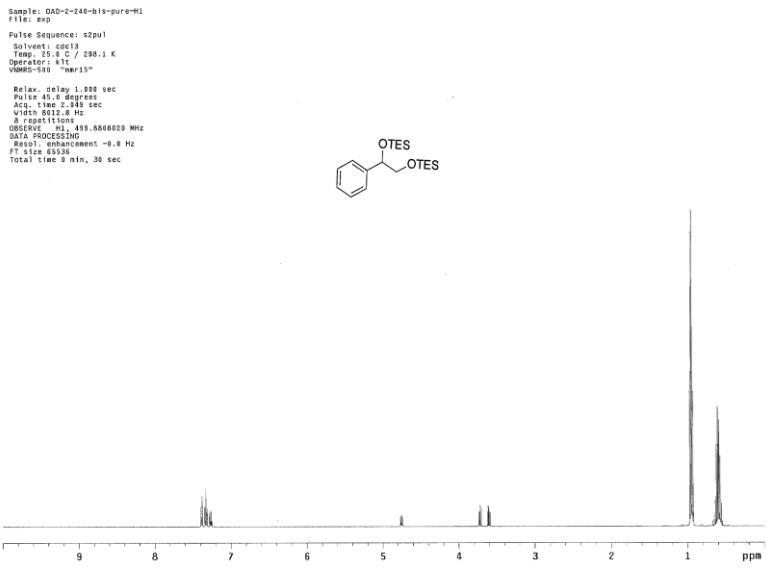
3.15

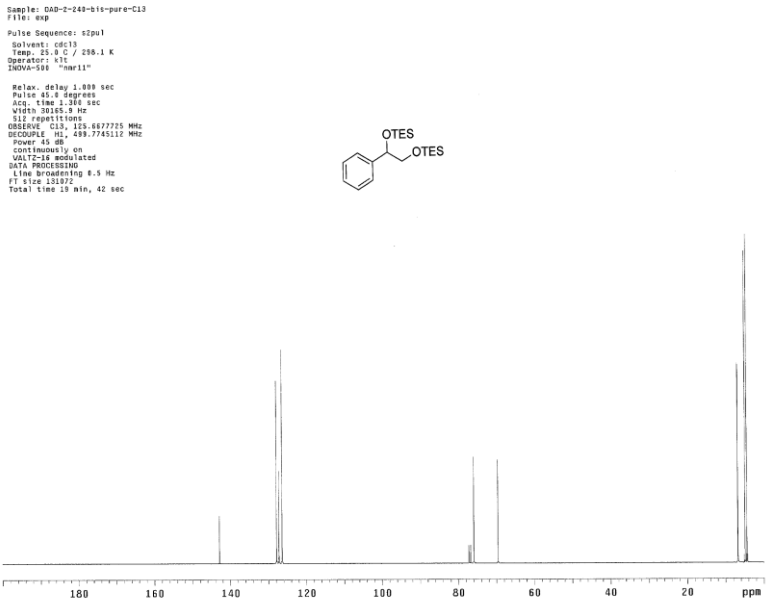

Sample: OAD-1-268-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OTBS
OH
180
160
140
120
100
80
60
40
20
0 ppm

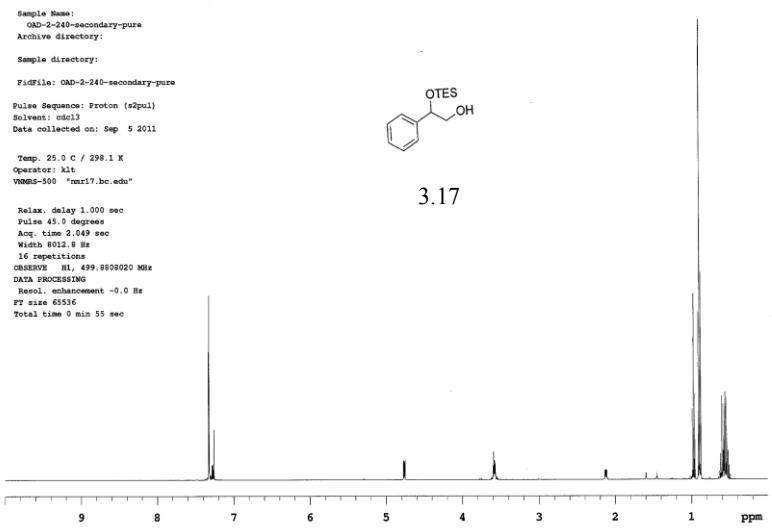
3.15

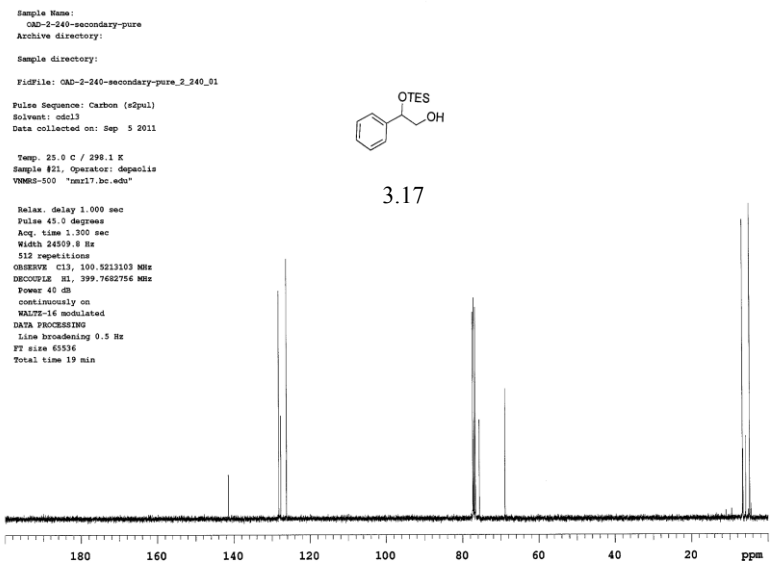

Sample: OAD-2-249-primary-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.849 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808029 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
OH
OTES
3.16
9
8
7
6
5
4
3
2
1
ppm

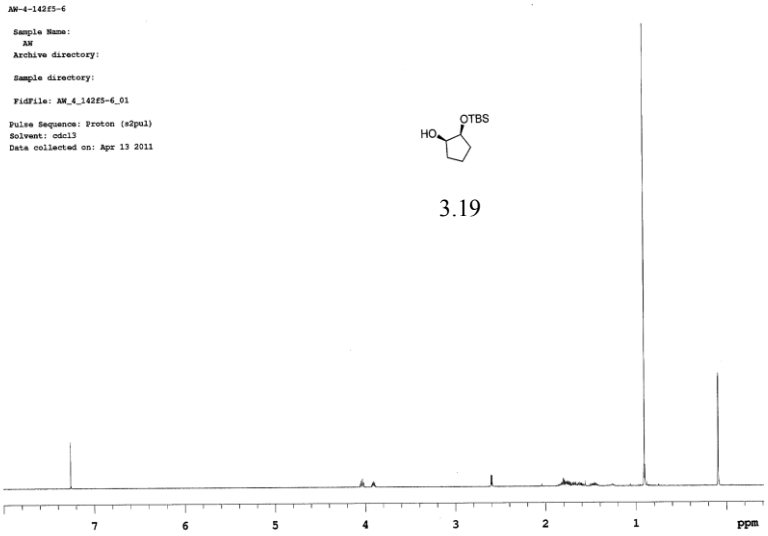

Sample: OAD-2-249-primary-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.359 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
OTES
3.16
180
160
140
120
100
80
60
40
20
ppm


Sample: OAD-2-248-bis-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: k1t
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.045 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808020 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
OTES
OTES
9
8
7
6
5
4
3
2
1
ppm

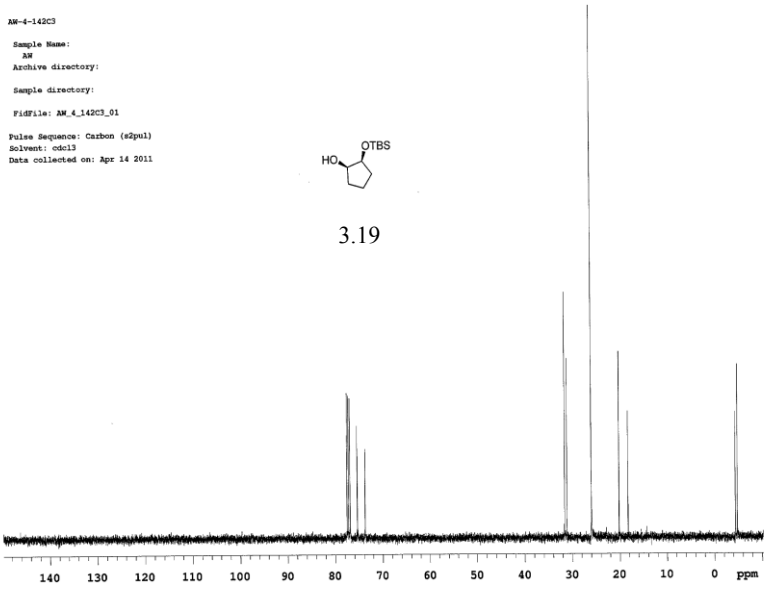

Sample: OAD-2-248-bis-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: k1t
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.360 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OTES
OTES
180
160
140
120
100
80
60
40
20
ppm


Sample Name:
OAD-2-240-secondary-pure
Archive directory:
Sample directory:
FidFile: OAD-2-240-secondary-pure
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Sep 5 2011
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
16 repetitions
OBSERVE H1, 499.8838020 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 55 sec
OTES
OH
3.17
9
8
7
6
5
4
3
2
1
ppm

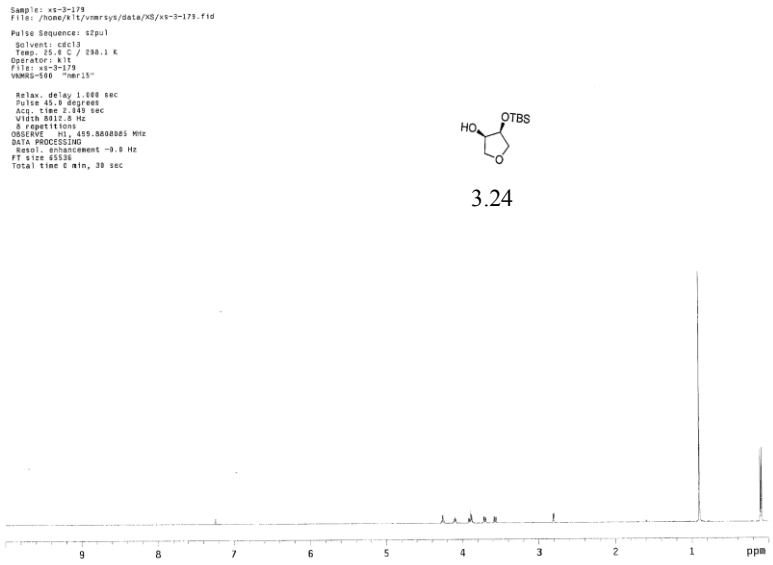

Sample Name:
OAD-2-240-secondary-pure
Archive directory:
Sample directory:
FidFile: OAD-2-240-secondary-pure_2_240_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Sep 5 2011
Temp. 25.0 C / 298.1 K
Sample #21, Operator: Gepaolis
VNMRS-500 "nmr17.bc.edu"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
512 repetitions
OBSERVE C13, 100.5213103 MHz
DECOUPLE H1, 399.7682756 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 19 min
OTES
OH
3.17
180
160
140
120
100
80
60
40
20
ppm

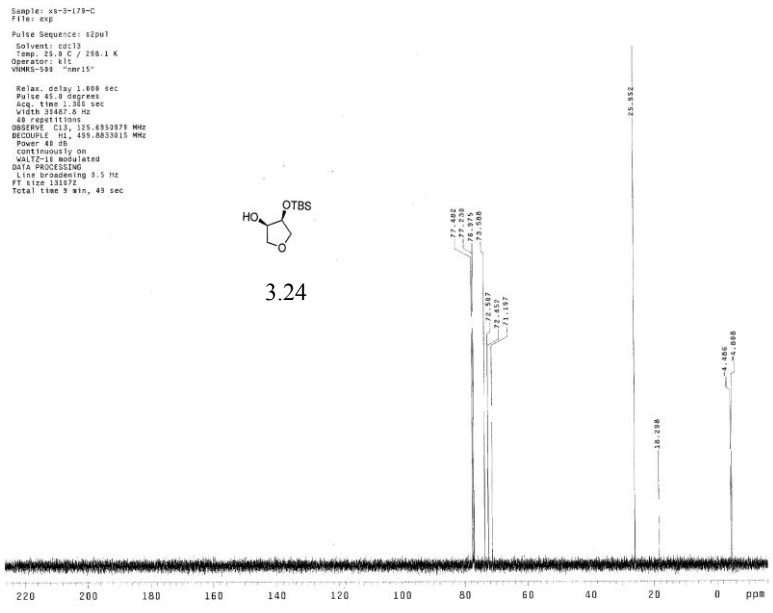

AW-4-142f5-6
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_142f5-6_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 13 2011
OTBS
HO
7
6
5
4
3
2
1
ppm

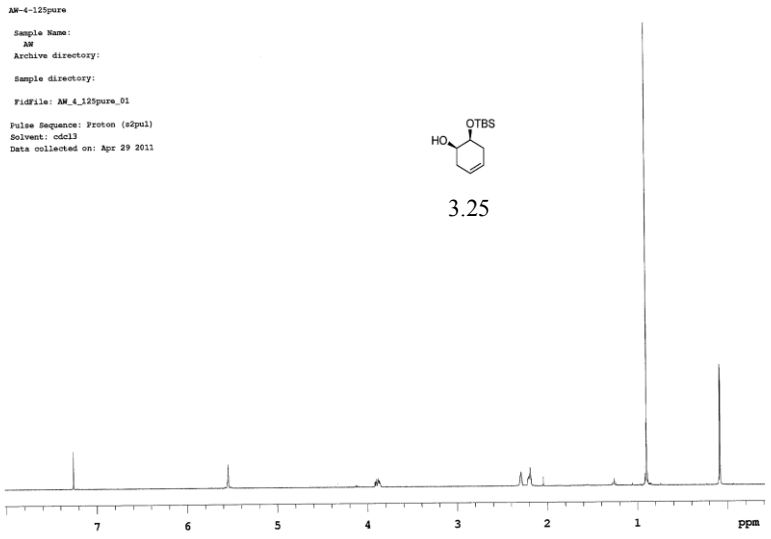
3.19


AW-4-142C3
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_142C3_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 14 2011
OTBS
HO
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

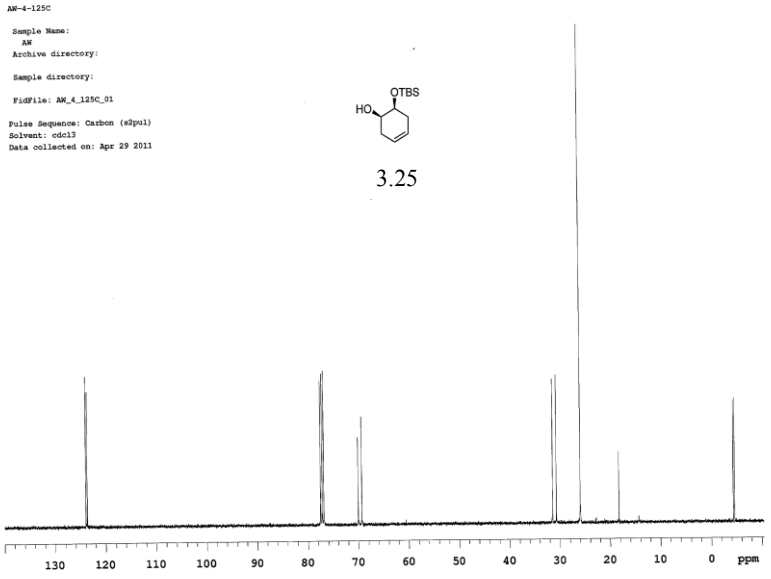
3.19


Sample: xs-3-179
File: /home/klt/vnmrsys/data/XS/xs-3-179.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
File: xs-3-179
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808885 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
OTBS
HO
3.24
9
8
7
6
5
4
3
2
1
ppm

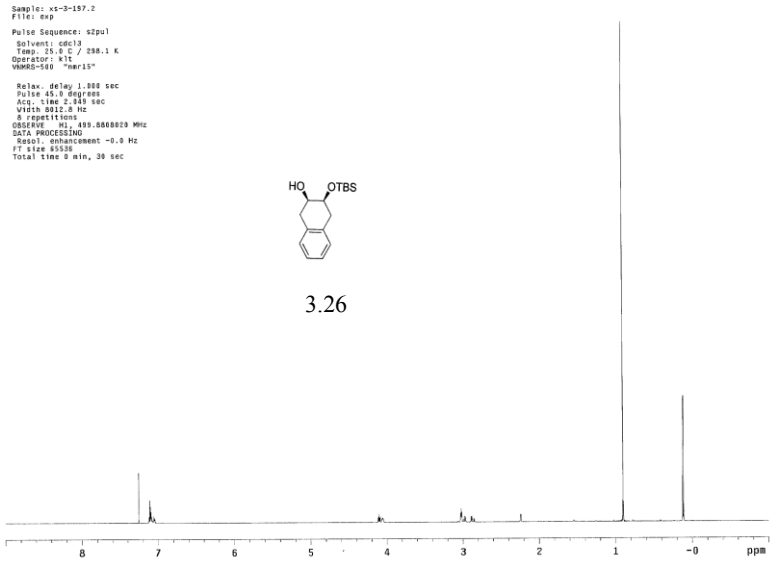

Sample: xs-3-179-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.365 sec
Width 31467.8 Hz
48 repetitions
OBSERVE C13, 125.6959979 MHz
DECOUPLE H1, 499.8833915 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 3.5 Hz
FT size 131072
Total time 9 min, 49 sec
OTBS
HO
3.24
77.488
77.170
76.975
76.566
72.597
72.457
71.197
25.952
18.238
-4.486
-4.888
220
200
180
160
140
120
100
80
60
40
20
0
ppm


AW-4-125pure
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_125pure_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 29 2011
OTBS
HO
7
6
5
4
3
2
1
ppm

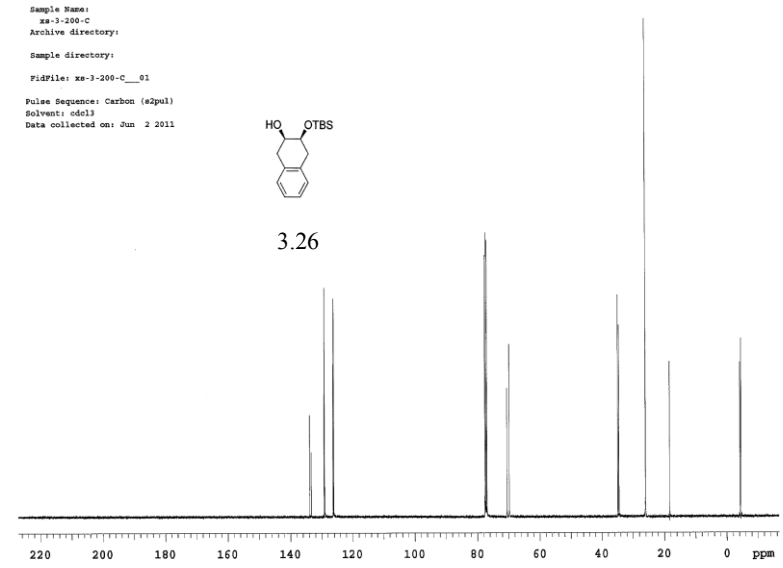
3.25


AW-4-125C
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_125C_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 29 2011
OTBS
HO
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

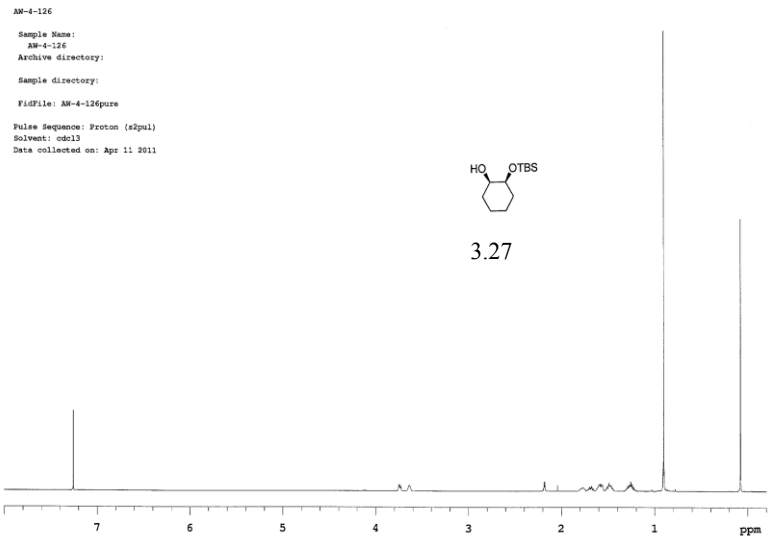
3.25

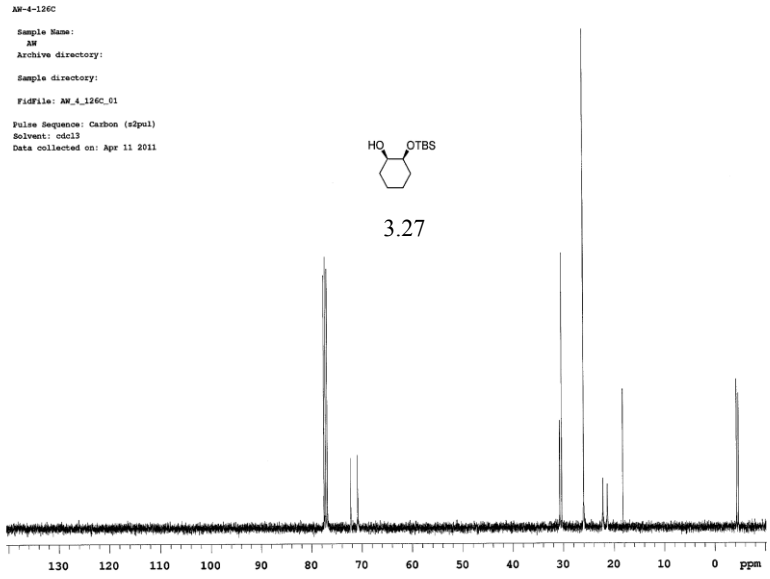

Sample: xt-3-157.2
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: Kit
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.849 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8868829 MHz
DATA PROCESSING
Resol. enhancement -0.9 Hz
FT size 65536
Total time 0 min, 30 sec
HO
OTBS
8
7
6
5
4
3
2
1
-0
ppm

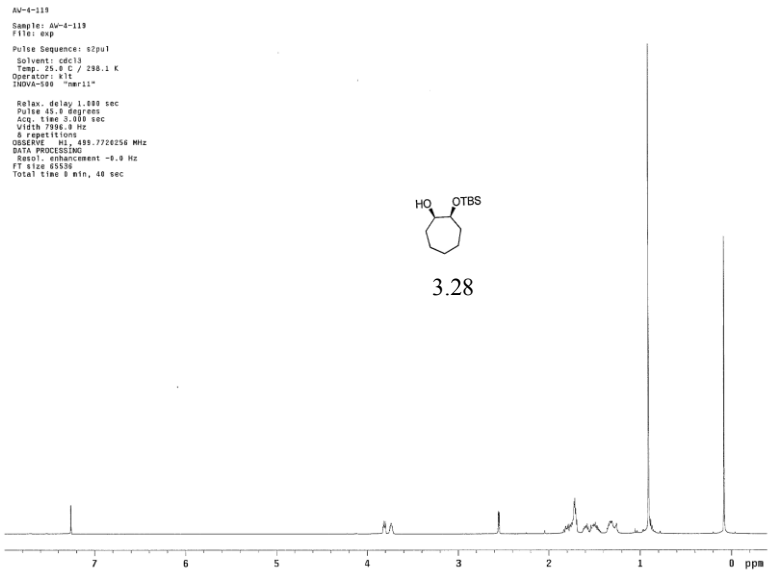
3.26


Sample Name:
xs-3-200-C
Archive directory:
Sample directory:
FidFile: xs-3-200-C___01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jun 2 2011
HO
OTBS
220
200
180
160
140
120
100
80
60
40
20
0
ppm

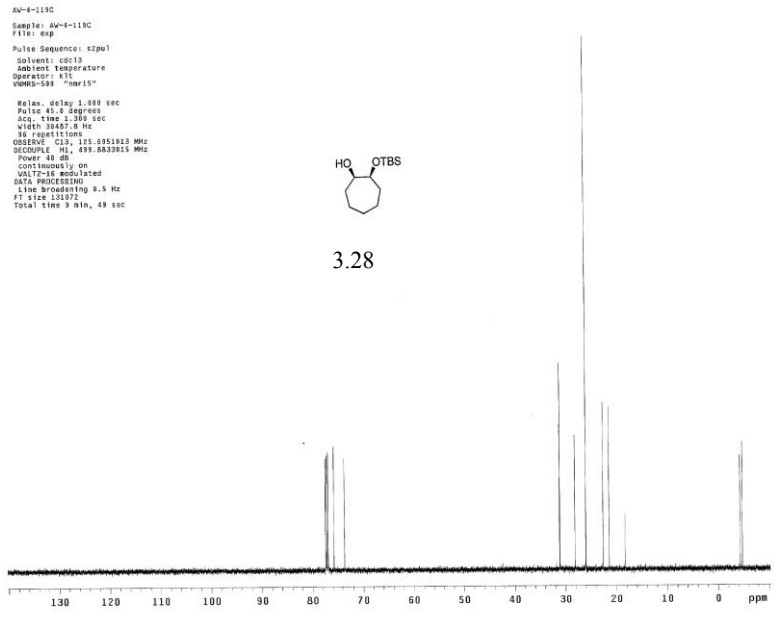
3.26


AW-4-126
Sample Name:
AW-4-126
Archive directory:
Sample directory:
FidFile: AW-4-126pure
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2011
HO
OTBS
3.27
7
6
5
4
3
2
1
ppm

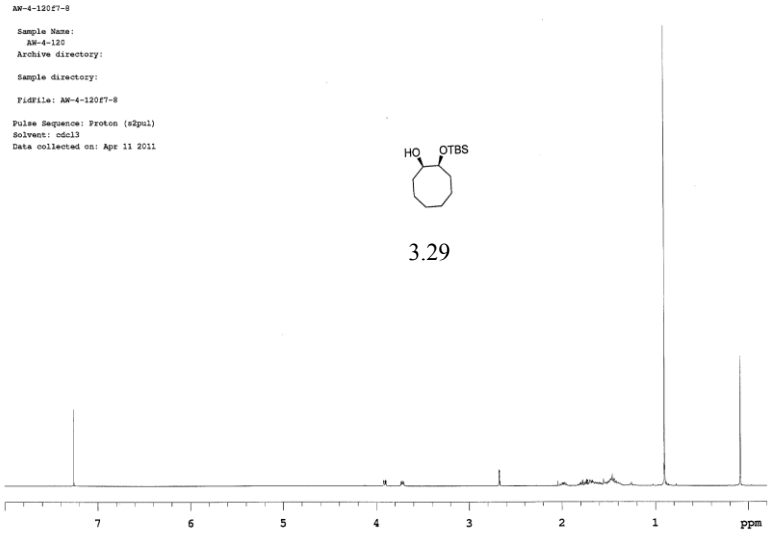

AW-4-126C
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_126C_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2011
HO
OTBS
3.27
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


AV-4-119
Sample: AV-4-119
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "mar11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7906.8 Hz
8 repetitions
OBSERVE H1, 499.7726256 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 40 sec
HO
OTBS
7
6
5
4
3
2
1
0 ppm

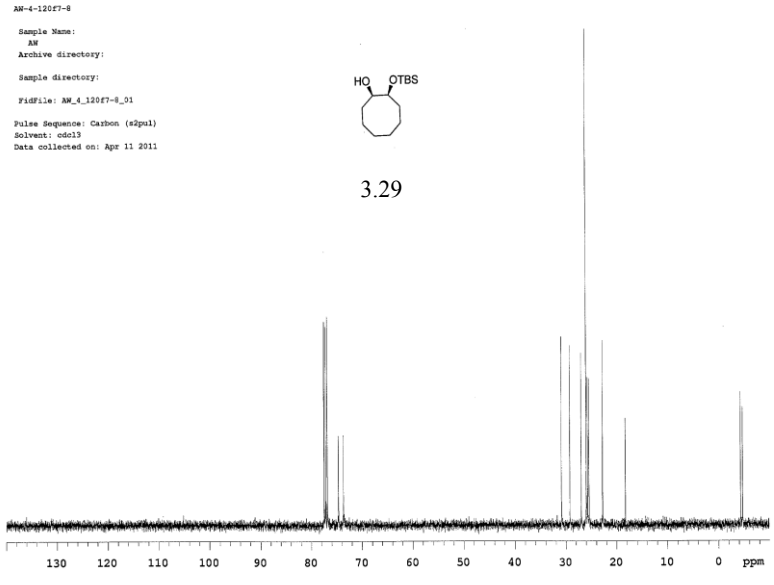
3.28


AV-4-119C
Sample: AV-4-119C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
Operator: klt
VNMRS-500 "mar15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
96 repetitions
OBSERVE C13, 125.6951813 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
HO
OTBS
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

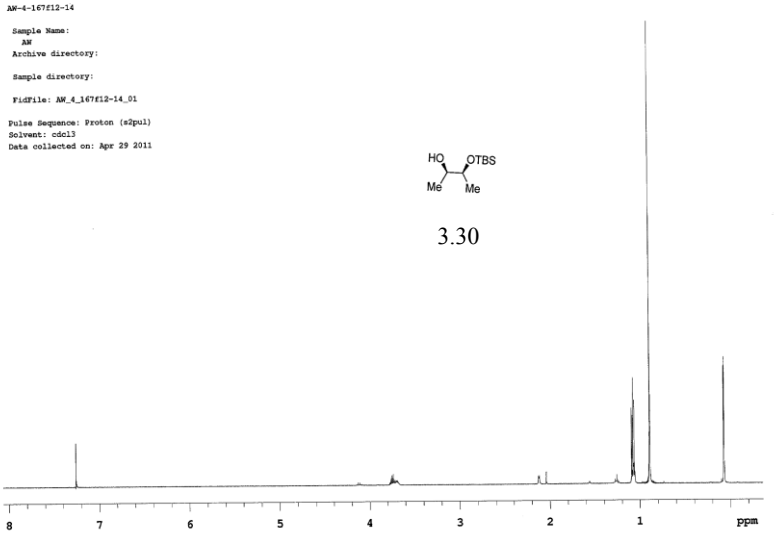
3.28


AW-4-120f7-8
Sample Name:
AW-4-120
Archive directory:
Sample directory:
FidFile: AW-4-120f7-8
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2011
HO
OTBS
7
6
5
4
3
2
1
ppm

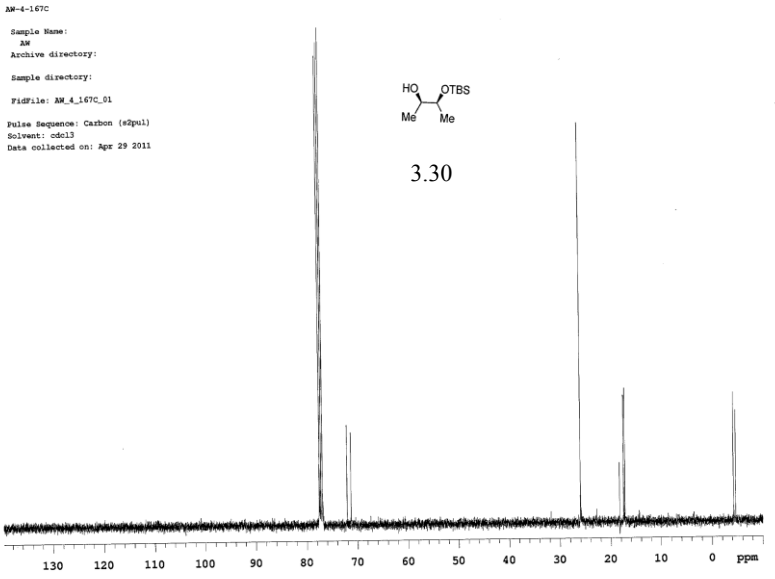
3.29


AW-4-120f7-8
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_120f7-8_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 11 2011
HO
OTBS
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

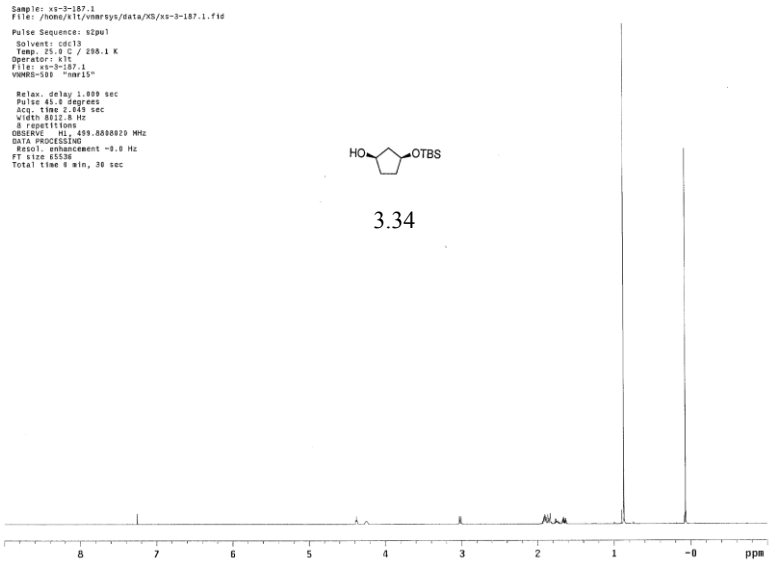
3.29


AW-4-167f12-14
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_167f12-14_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 29 2011
HO
OTBS
Me
Me
8
7
6
5
4
3
2
1
ppm

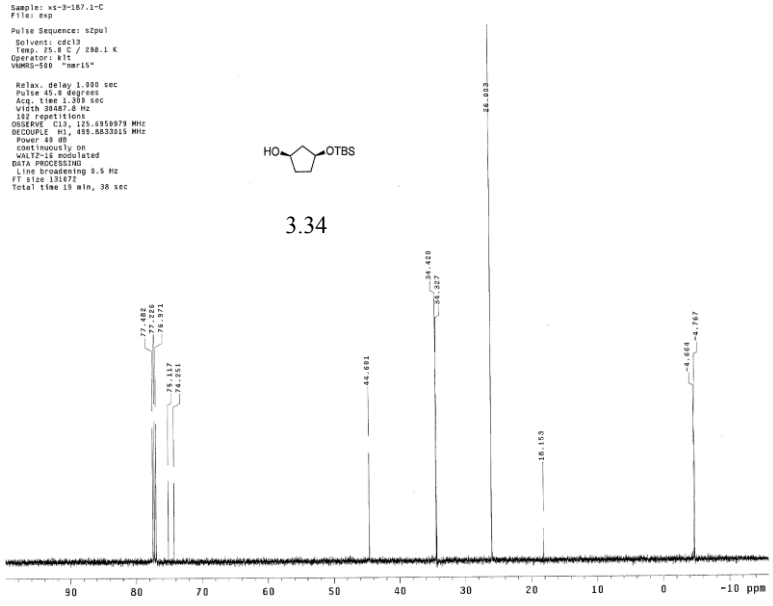
3.30


AW-4-167C
Sample Name:
AW
Archive directory:
Sample directory:
FidFile: AW_4_167C_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 29 2011
HO
OTBS
Me
Me
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

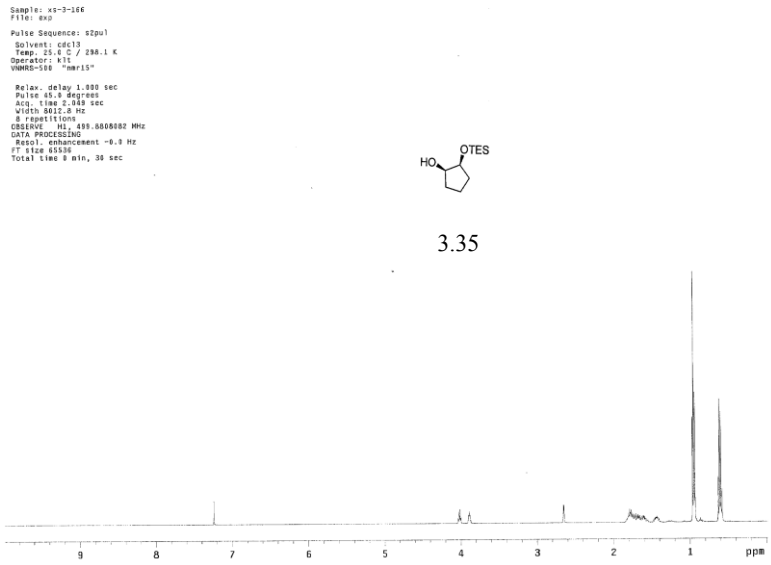
3.30


Sample: xs-3-187.1
File: /home/klt/vnmrsys/data/XS/xs-3-187.1.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
File: xs-3-187.1
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8888020 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
HO
OTBS
8
7
6
5
4
3
2
1
-0
ppm

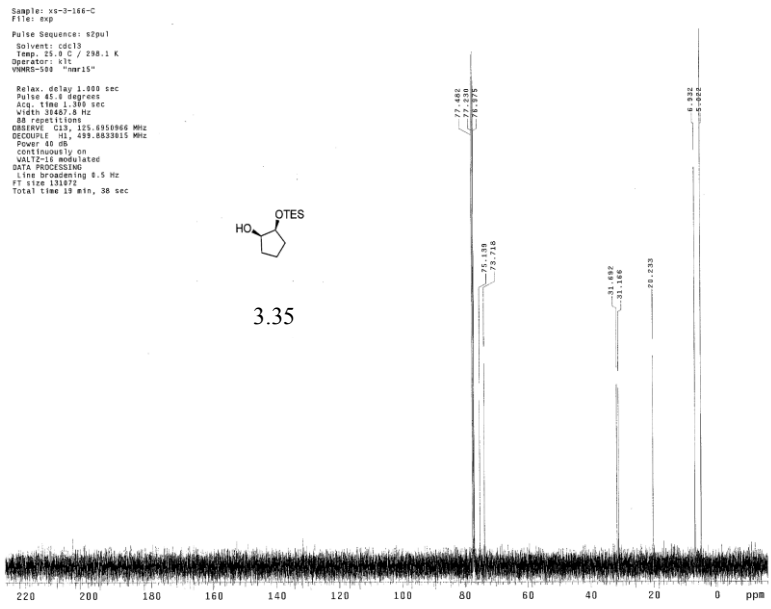
3.34


Sample: xs-3-187.1-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.309 sec
Width 30487.8 Hz
182 repetitions
OBSERVE C13, 125.6959979 MHz
DECOUPLE H1, 499.8833915 MHz
Power 49 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
HO
OTBS
77.488
77.326
76.971
75.117
74.251
44.691
34.420
34.327
26.053
18.153
-4.684
-4.767
90
80
70
60
50
40
30
20
10
0
-10 ppm

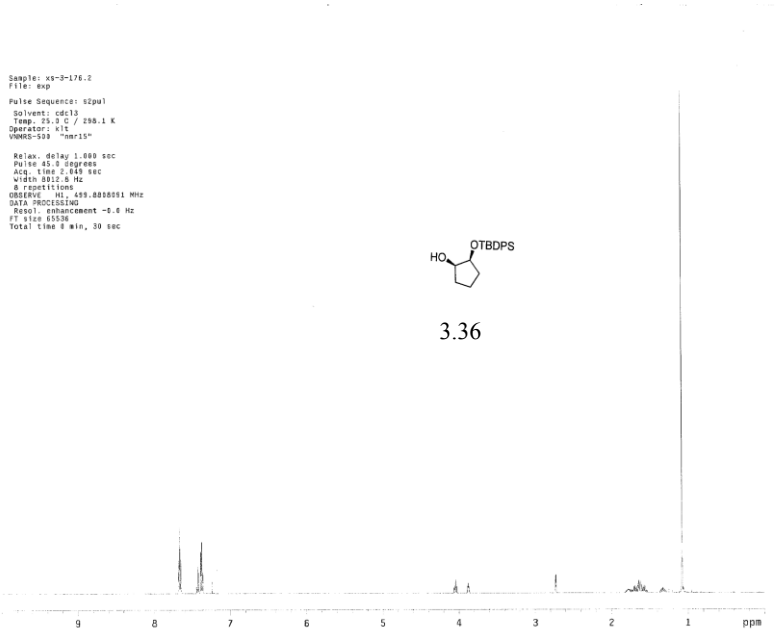
3.34


Sample: xs-3-166
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.6 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6012.8 Hz
8 repetitions
OBSERVE H1, 499.8808882 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 38 sec
HO
OTES
9
8
7
6
5
4
3
2
1
ppm

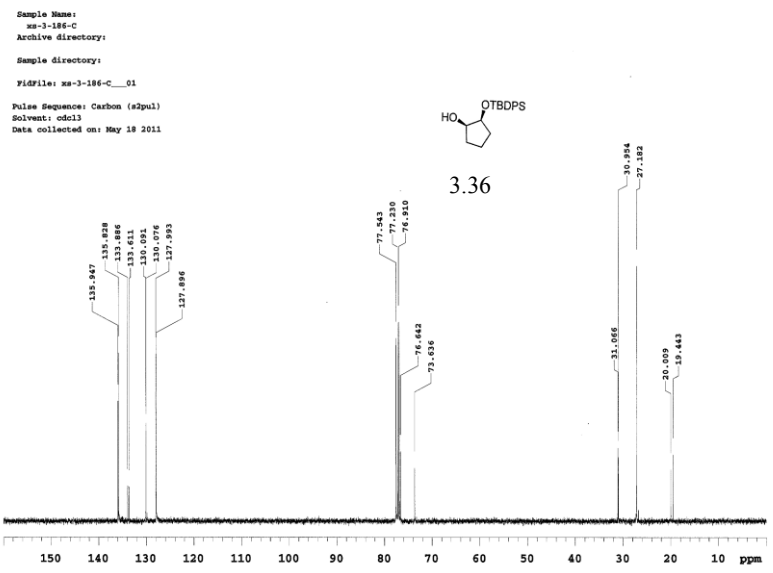
3.35


Sample: xs-3-166-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
88 repetitions
OBSERVE C13, 125.6950966 MHz
DECOUPLE H1, 499.8833815 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
77.482
77.270
76.970
75.189
75.710
31.697
31.166
28.233
6.932
5.922
HO
OTES
220
200
180
160
140
120
100
80
60
40
20
0
ppm

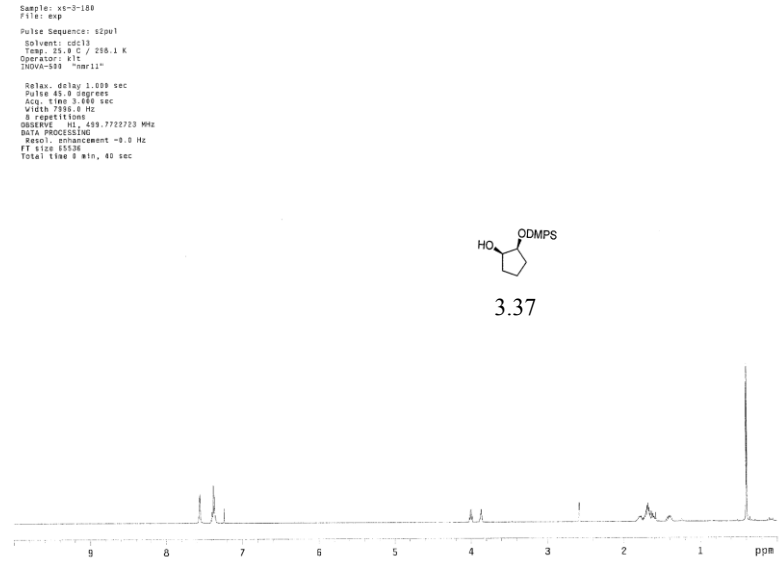
3.35

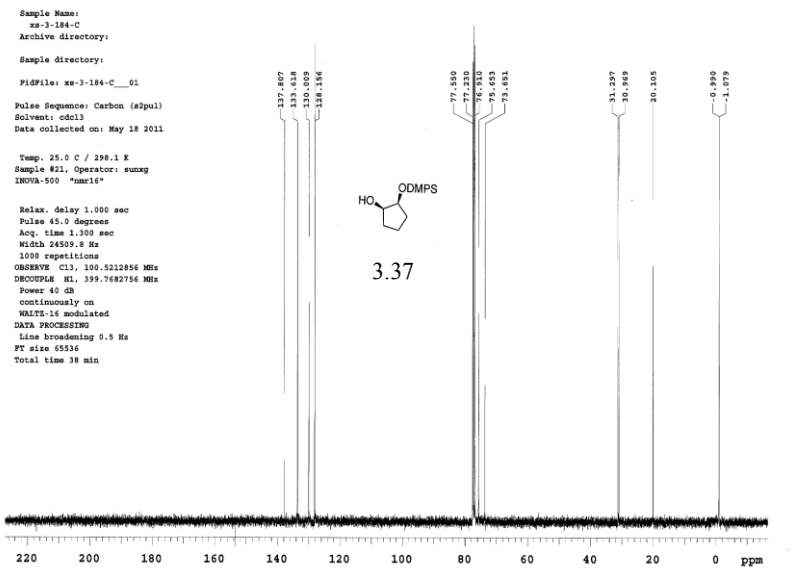

Sample: xs-3-176.2
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.3 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.649 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8888891 MHz
DATA PROCESSING
Resol. enhancement -0.6 Hz
FT size 65536
Total time 8 min, 30 sec
OTBDPS
HO
9
8
7
6
5
4
3
2
1
ppm

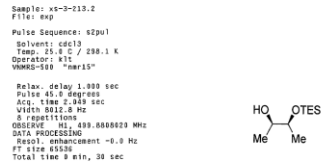
3.36


Sample Name:
xs-3-186-C
Archive directory:
Sample directory:
FidFile: xs-3-186-C___01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: May 18 2011
OTBDPS
HO
135.947
135.828
133.686
133.451
130.091
130.076
127.993
127.896
77.543
77.330
76.910
76.642
73.636
30.954
27.182
31.068
20.009
19.443
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

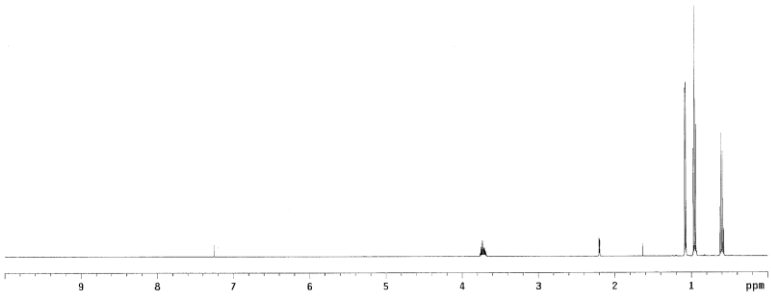
3.36

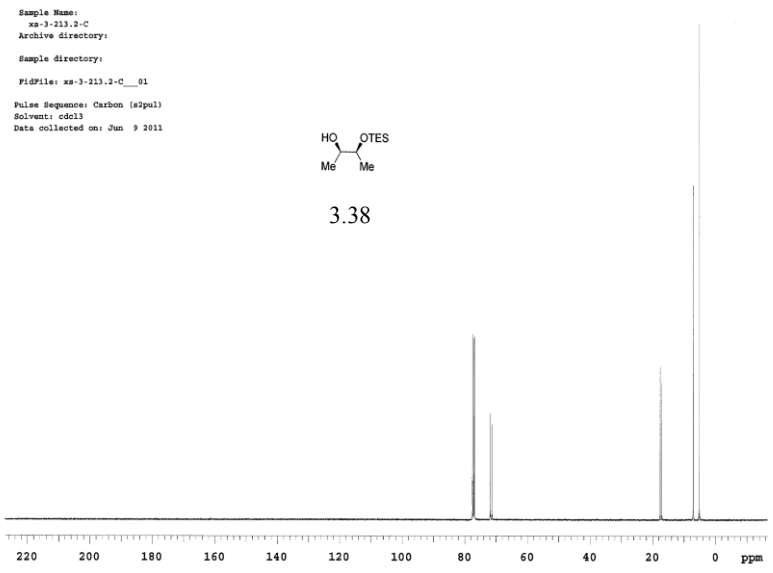

Sample: xs-3-180
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.880 sec
Width 7996.8 Hz
8 repetitions
OBSERVE H1, 499.7722723 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 8 min, 40 sec
HO
ODMPS
3.37
9
8
7
6
5
4
3
2
1
ppm


Sample Name:
xs-3-184-C
Archive directory:
Sample directory:
FidFile: xs-3-184-C___01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: May 18 2011
Temp. 25.0 C / 298.1 K
Sample #21, Operator: sunxg
INOVA-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
1000 repetitions
OBSERVE C13, 100.5212856 MHz
DECOUPLE H1, 399.7682756 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 38 min
137.807
133.618
130.069
128.196
77.590
77.230
76.910
75.653
73.651
31.297
30.969
20.105
-0.990
-1.079
HO
ODMPS
3.37
220
200
180
160
140
120
100
80
60
40
20
0
ppm

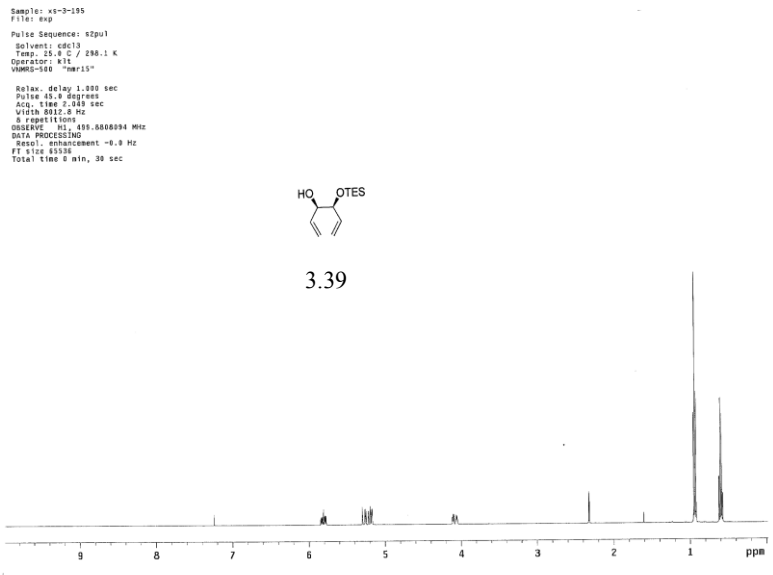

Sample: xs-3-213.2
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.949 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808020 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
HO
OTES
Me
Me

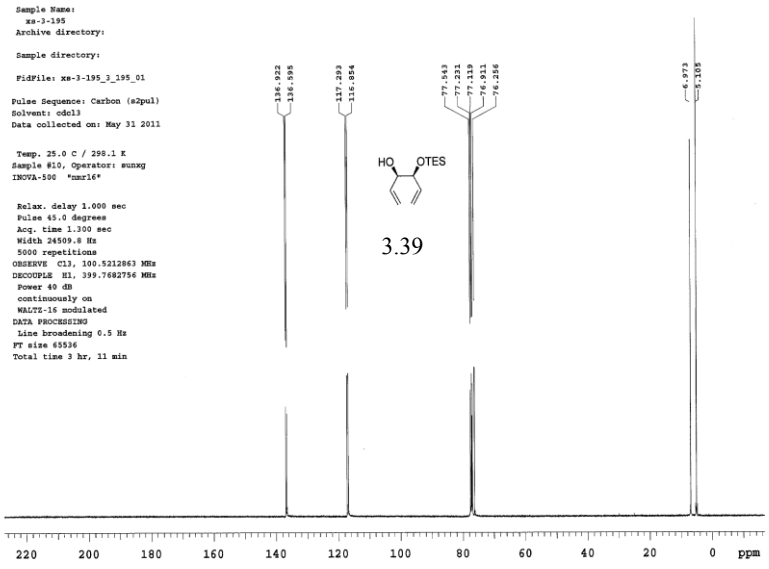
3.38

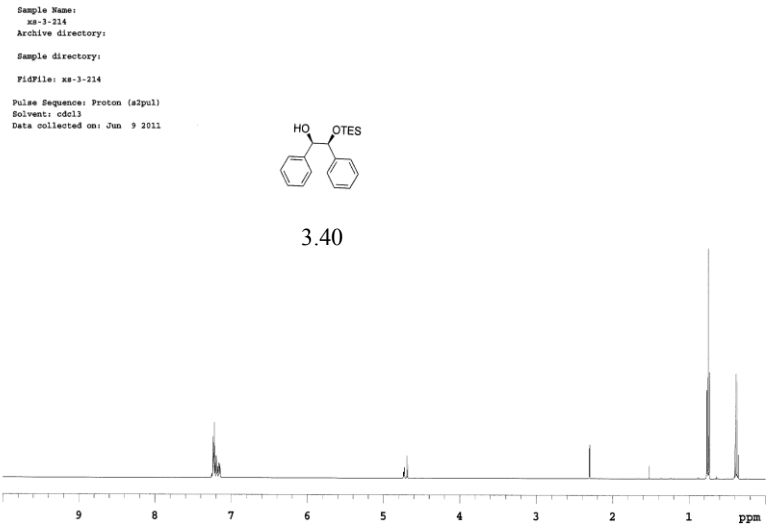

9
8
7
6
5
4
3
2
1
ppm


Sample Name:
xs-3-213.2-C
Archive directory:
Sample directory:
FidFile: xs-3-213.2-C___01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jun 9 2011
HO
OTES
Me
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm

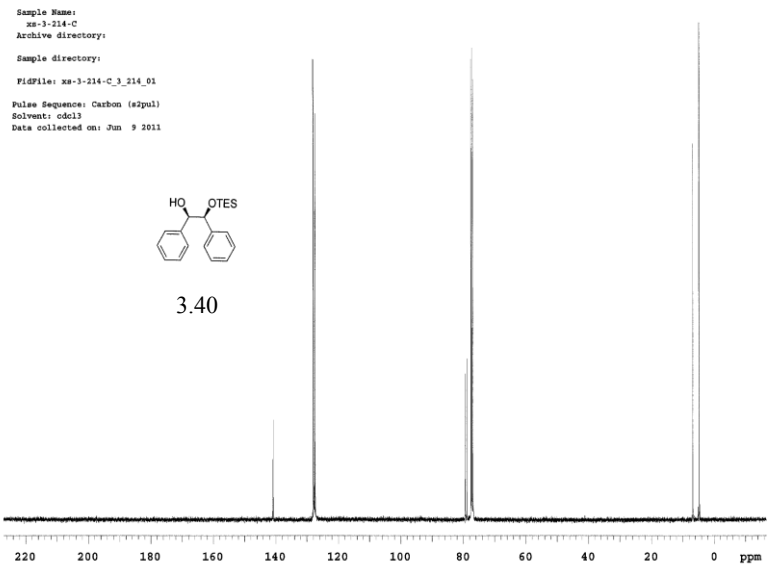
3.38


Sample: xs-3-195
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: ktl
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808894 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
HO
OTES
3.39
9
8
7
6
5
4
3
2
1
ppm


Sample Name:
xs-3-195
Archive directory:
Sample directory:
FidFile: xs-3-195_3_195_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: May 31 2011
Temp. 25.0 C / 298.1 K
Sample #10, Operator: sunxg
INOVA-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
5000 repetitions
OBSERVE C13, 100.5212863 MHz
DECOUPLE H1, 399.7682756 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 3 hr, 11 min
136.922
136.595
117.293
116.854
77.543
77.231
77.119
76.911
76.256
6.973
6.185
HO
OTES
3.39
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Sample Name:
xs-3-214
Archive directory:
Sample directory:
FidFile: xs-3-214
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jun 9 2011
HO
OTES
9
8
7
6
5
4
3
2
1
ppm

3.40


Sample Name:
xs-3-214-C
Archive directory:
Sample directory:
FidFile: xs-3-214-C_3_214_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jun 9 2011
HO
OTES
220
200
180
160
140
120
100
80
60
40
20
0
ppm

3.40

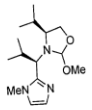
XS-3-165 in THF

Sample Name:
XS-3-165
Archive directory:

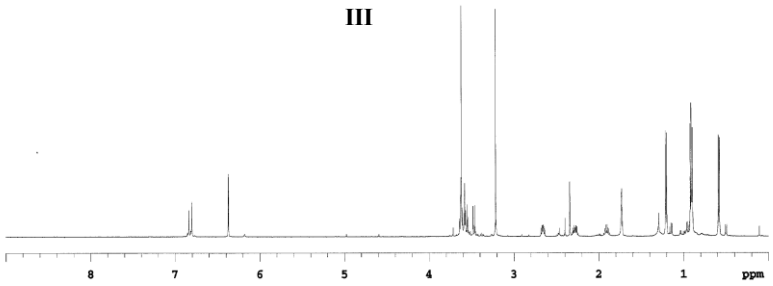
Sample directory:

FidFile: XS-3-165inTHF

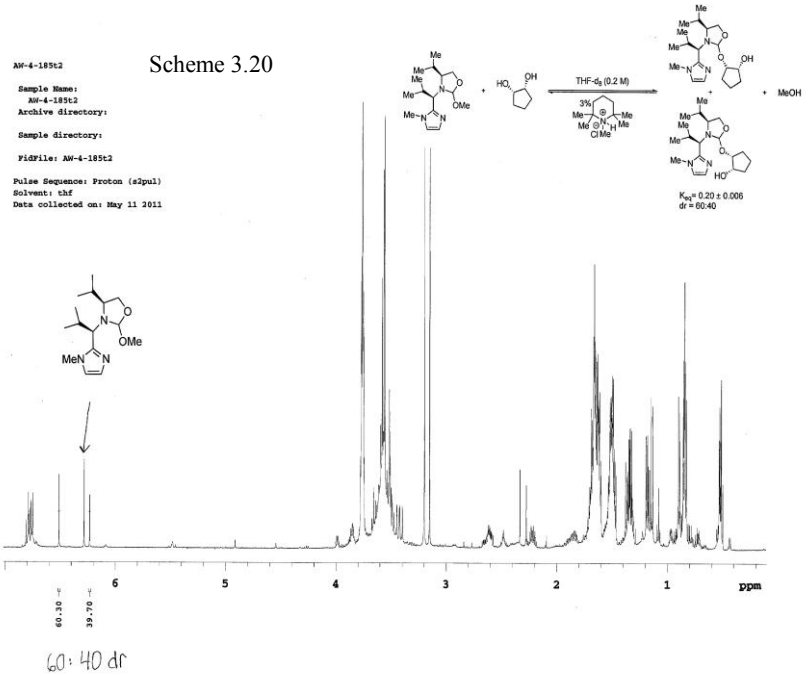
Pulse Sequence: Proton (s2pul)
Solvent: thf
Data collected on: May 12 2011

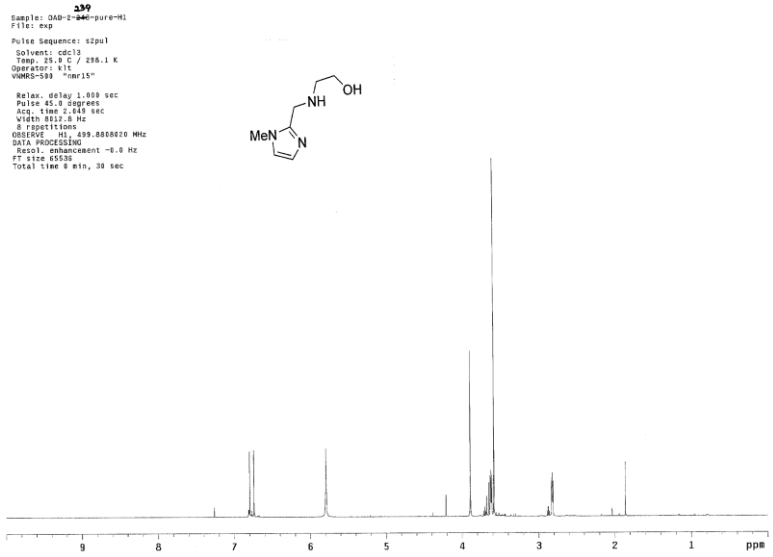


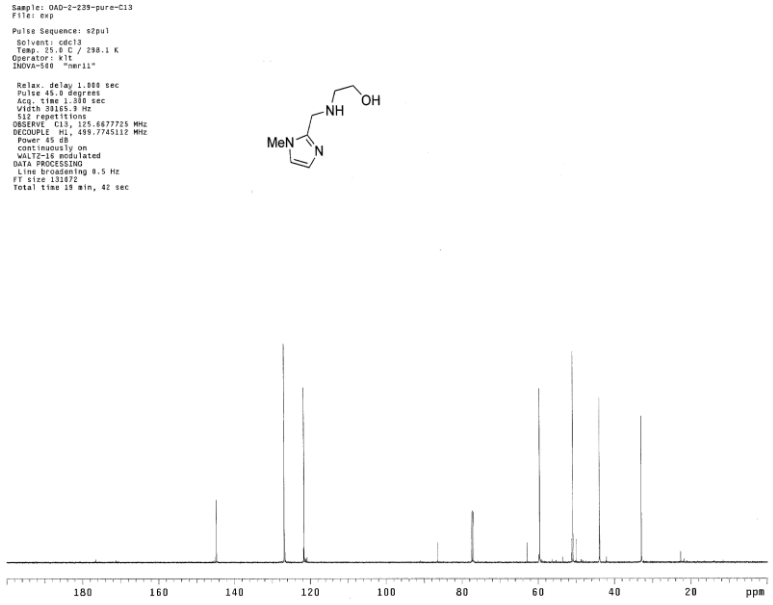
III

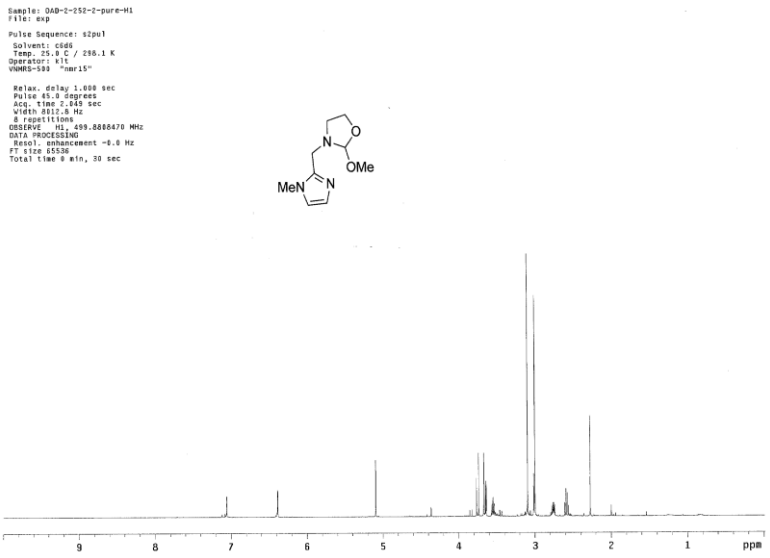


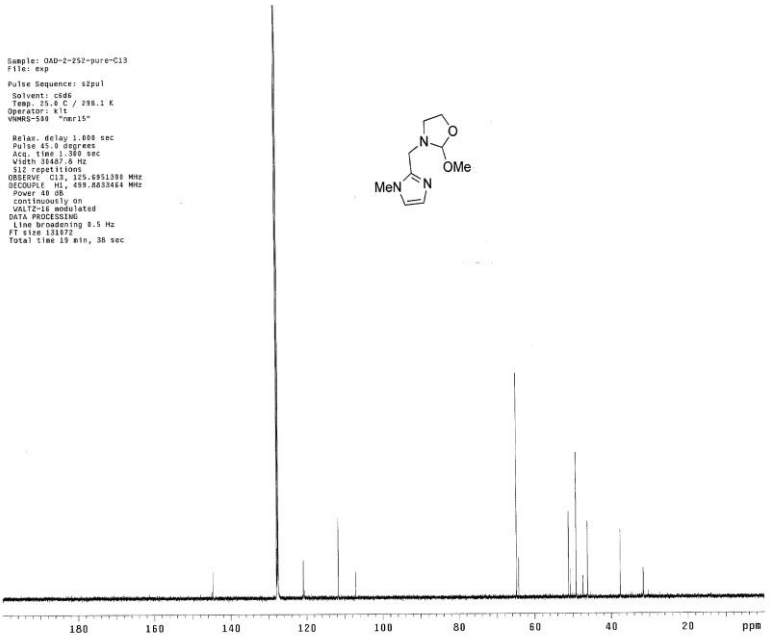
Scheme 3.20

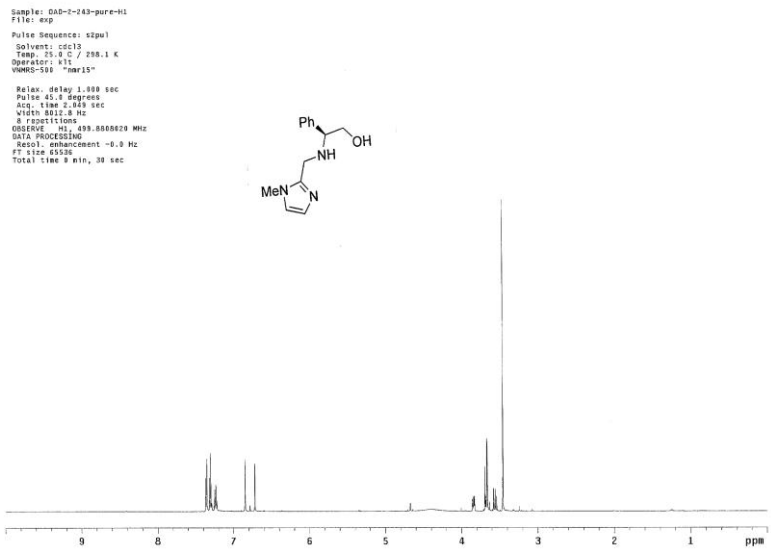


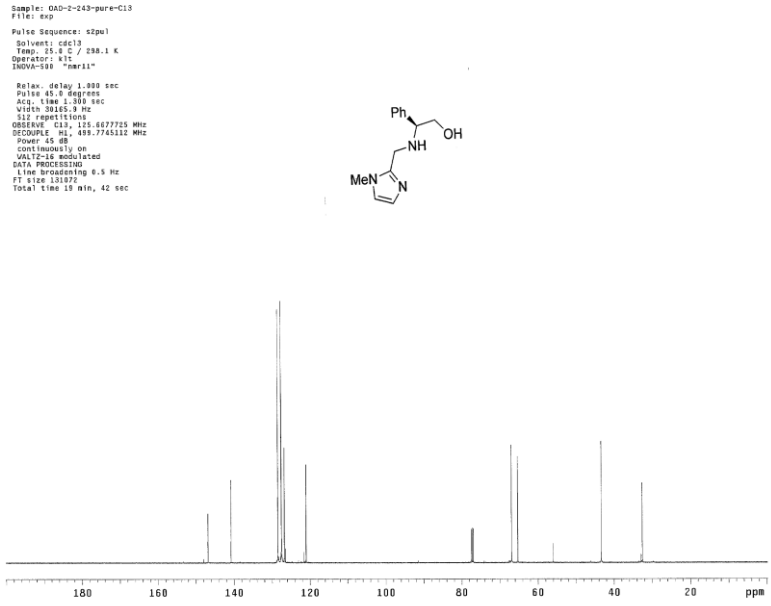

Sample: OAD-2-239-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.649 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808020 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 30 sec
NH
OH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

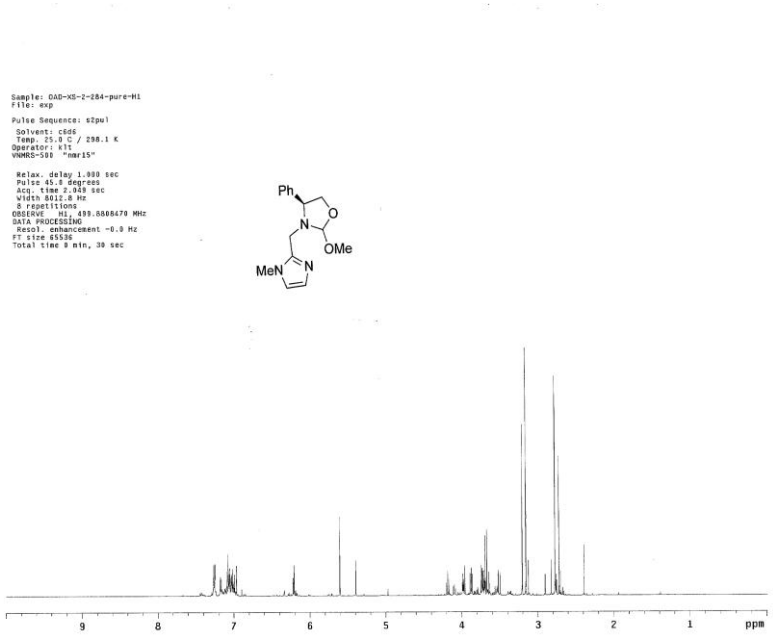

Sample: OAD-2-239-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.398 sec
Width 39165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
NH
OH
MeN
N
180
160
140
120
100
80
60
40
20
ppm

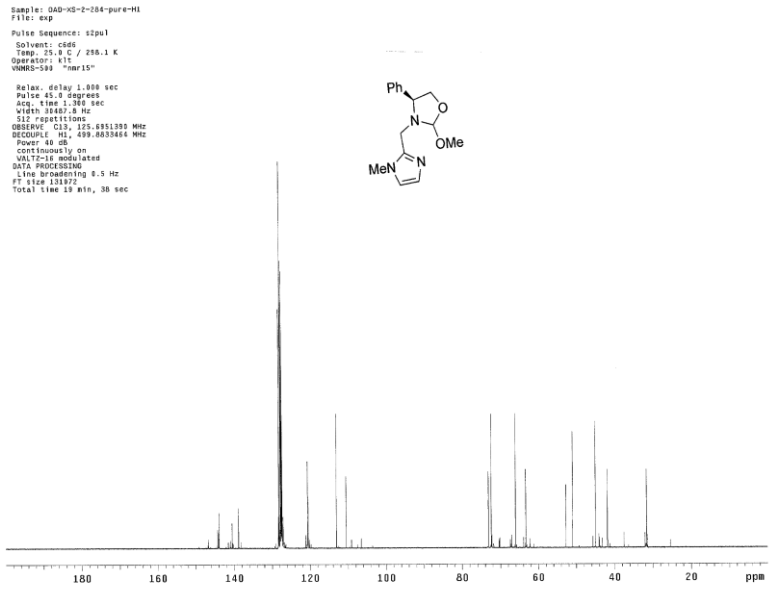

Sample: OAD-2-252-2-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.045 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8868470 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
MeN
N
O
N
OMe
9
8
7
6
5
4
3
2
1
ppm

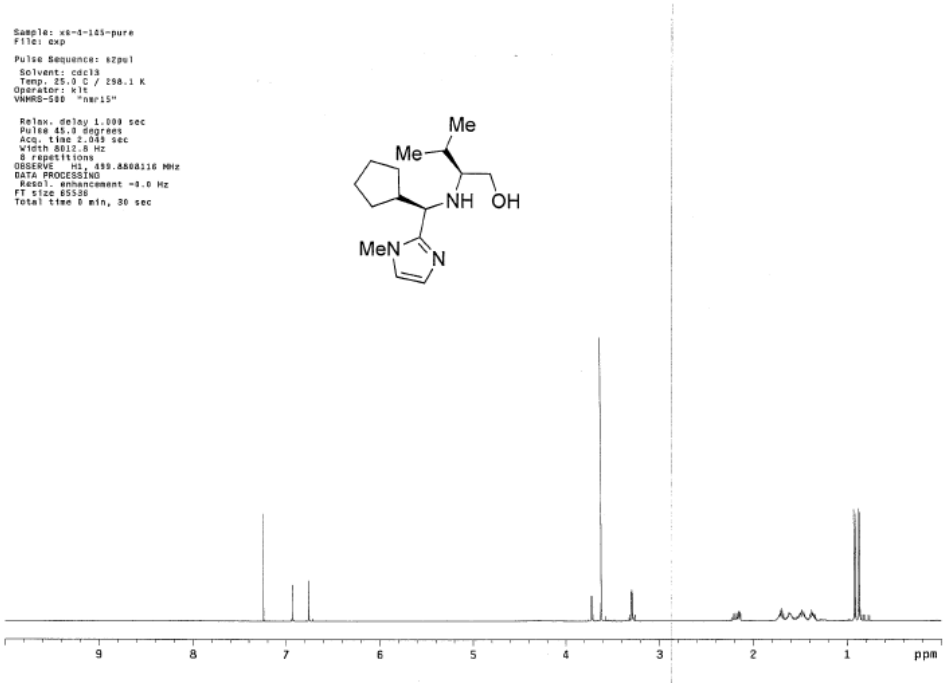

Sample: OAD-2-252-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.360 sec
Width 30487.8 Hz
512 repetitions
OBSERVE C13, 125.6951398 MHz
DECOUPLE H1, 499.8833464 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
MeN
N
O
N
OMe
180
160
140
120
100
80
60
40
20
ppm

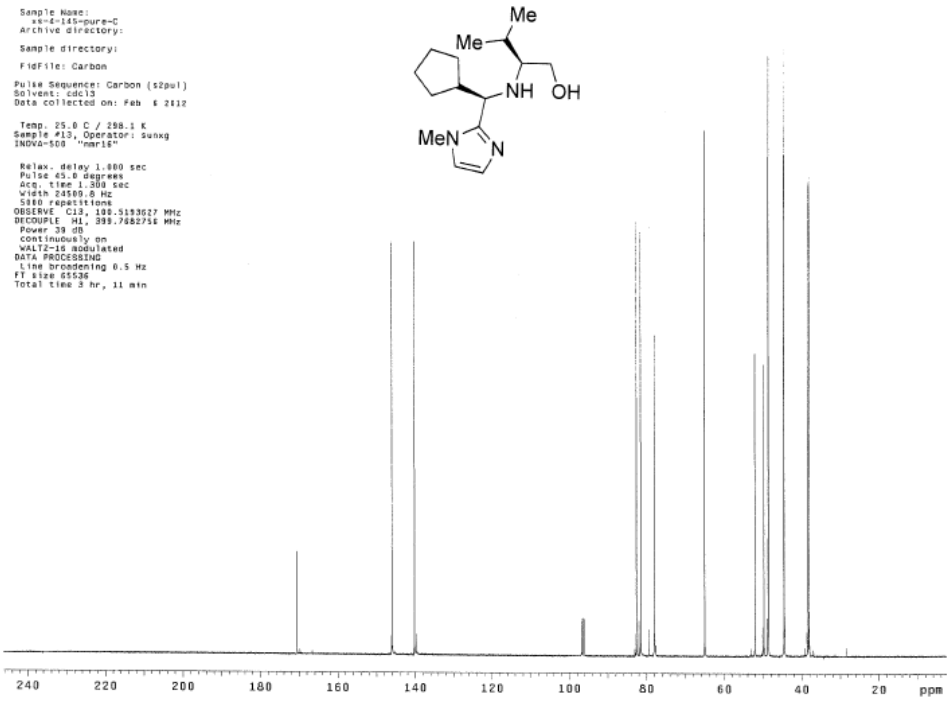

Sample: OAD-2-243-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.849 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8868020 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
Ph
OH
NH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

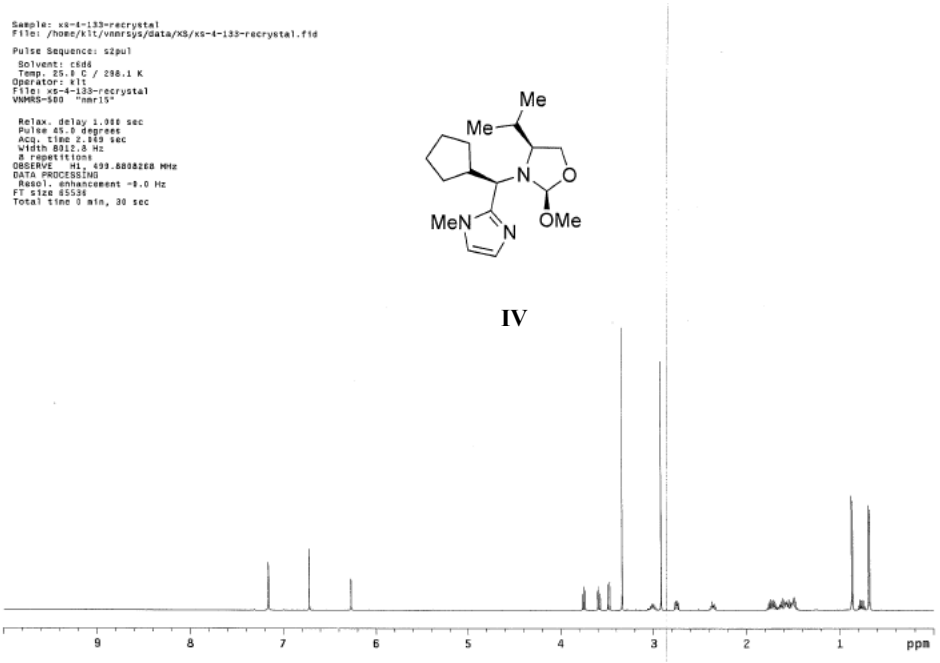

Sample: OAD-2-243-pure-C13
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "nmr11"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.9 Hz
512 repetitions
OBSERVE C13, 125.6677725 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
Ph
OH
NH
MeN
N
180
160
140
120
100
80
60
40
20
ppm


Sample: OAD-XS-2-284-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.949 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8806470 MHz
DATA PROCESSING
Resol. enhancement -0.9 Hz
FT size 65536
Total time 0 min, 39 sec
Ph
O
N
OMe
MeN
N
9
8
7
6
5
4
3
2
1
ppm

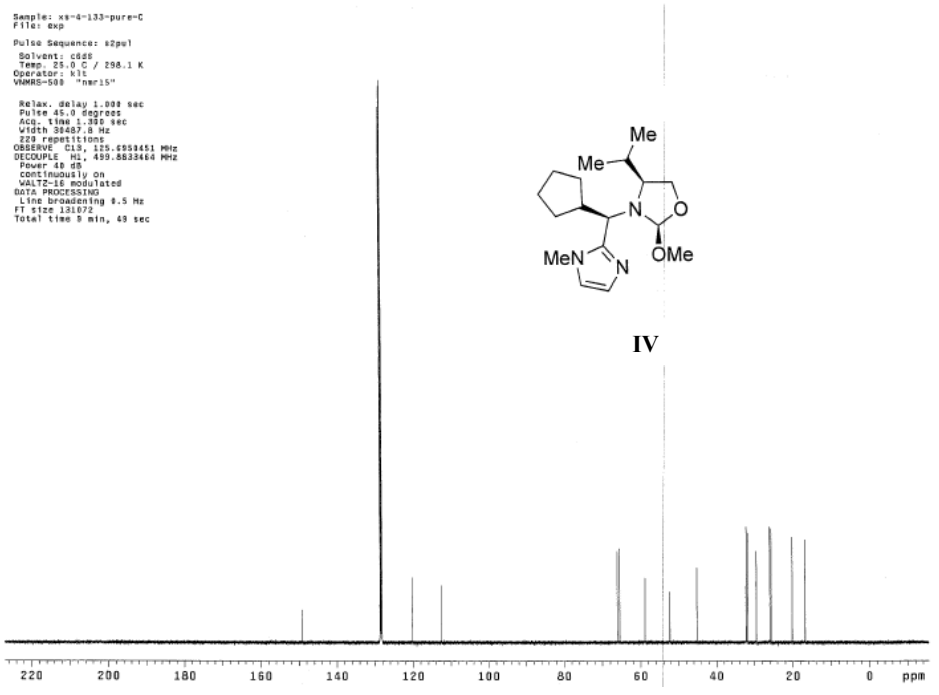

Sample: OAD-XS-2-284-pure-H1
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.360 sec
Width 30487.8 Hz
512 repetitions
OBSERVE C13, 125.6951393 MHz
DECOUPLE H1, 499.8833464 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
Ph
O
N
OMe
MeN
N
180
160
140
120
100
80
60
40
20
ppm


Sample: xs-4-145-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808116 MHz
DATA PROCESSING
Resol. enhancement -4.0 Hz
FT size 65536
Total time 0 min, 30 sec
Me
Me
NH
OH
MeN
N
9
8
7
6
5
4
3
2
1
ppm

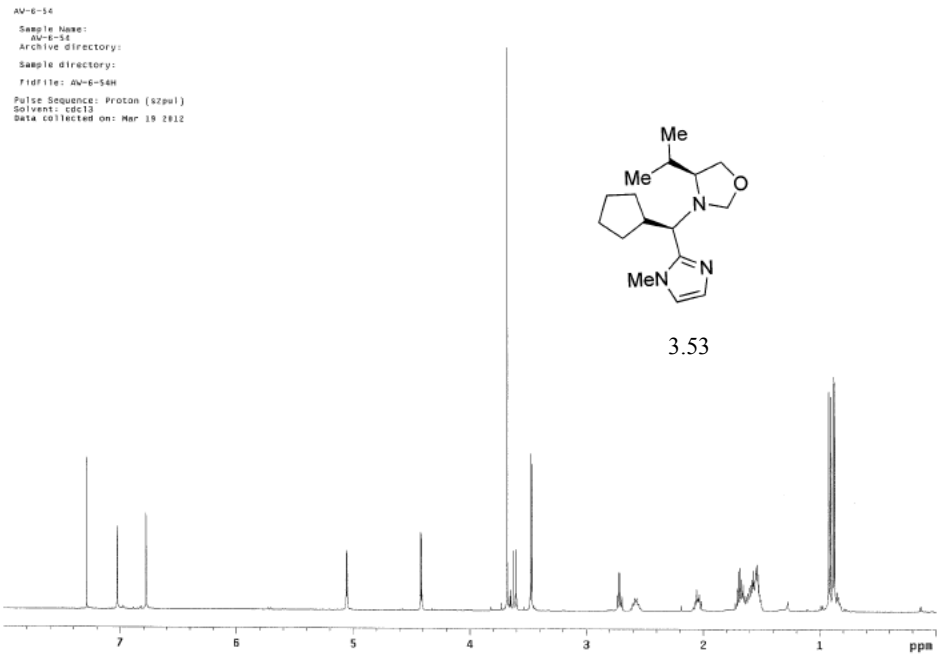

Sample Name:
xs-4-145-pure-C
Archive directory:
Sample directory:
FidFile: Carbon
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Feb 6 2012
Temp. 25.0 C / 298.1 K
Sample #13, Operator: sunkg
INOVA-500 "nmr16"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24509.8 Hz
5980 repetitions
OBSERVE C13, 100.5153627 MHz
DECOUPLE H1, 399.7882756 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 3 hr, 11 min
Me
Me
NH
OH
MeN
N
240
220
200
180
160
140
120
100
80
60
40
20
ppm


Sample: xs-4-133-recrystal
File: /home/klt/vnmrsys/data/XS/xs-4-133-recrystal.fid
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: klt
File: xs-4-133-recrystal
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 65.0 degrees
Acq. time 2.949 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808268 MHz
DATA PROCESSING
Resol. enhancement -8.0 Hz
FT size 65536
Total time 0 min, 30 sec
Me
Me
N
O
MeN
N
OMe
9
8
7
6
5
4
3
2
1
ppm

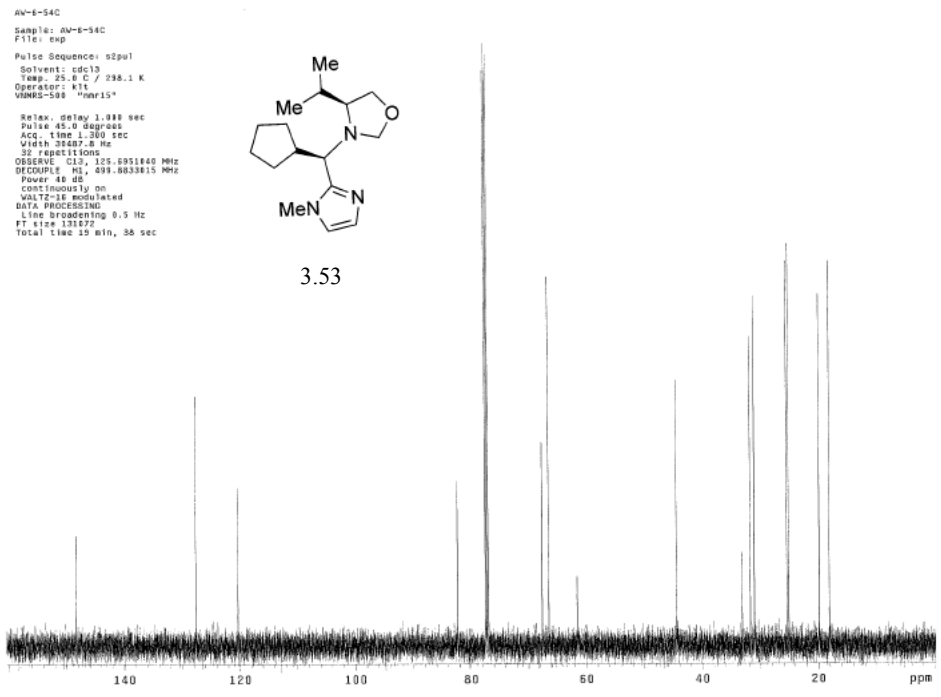
IV


Sample: xs-4-133-pure-C
File: exp
Pulse Sequence: s2pul
Solvent: cdd6
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.360 sec
Width 30487.8 Hz
220 repetitions
OBSERVE C13, 125.6953451 MHz
DECOUPLE H1, 499.8833464 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
Me
Me
N
O
MeN
N
OMe
220
200
180
160
140
120
100
80
60
40
20
0
ppm

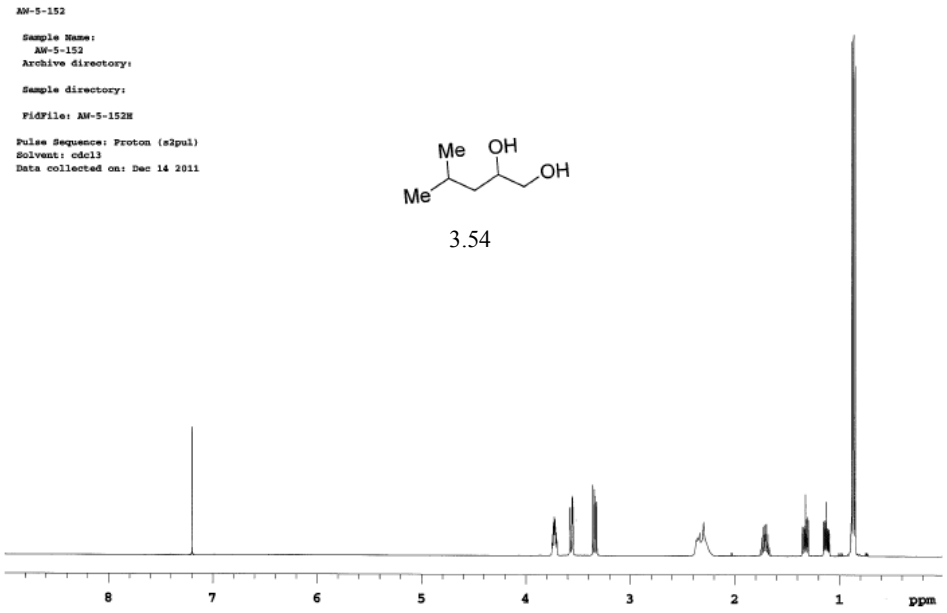
IV


AV-6-54
Sample Name:
AV-6-54
Archive directory:
Sample directory:
FidFile: AV-6-54H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Mar 19 2012
Me
Me
O
N
MeN
N
7
6
5
4
3
2
1
ppm

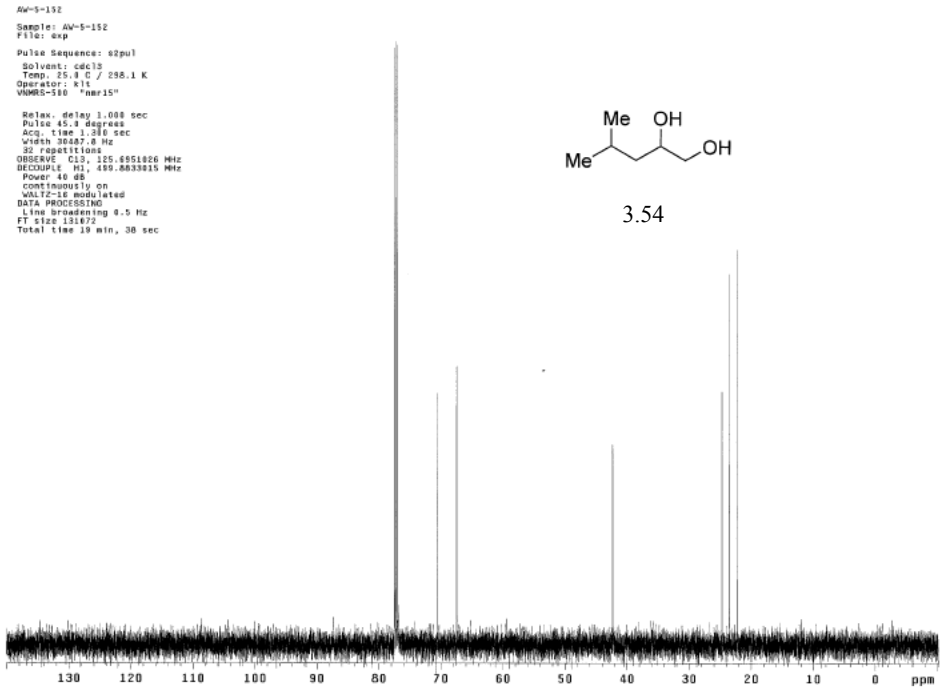
3.53


AV-6-54C
Sample: AV-6-54C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
32 repetitions
OBSERVE C13, 125.6951840 MHz
DECOUPLE H1, 499.8833815 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 15 min, 38 sec
Me
Me
O
N
MeN
N
140
120
100
80
60
40
20
ppm

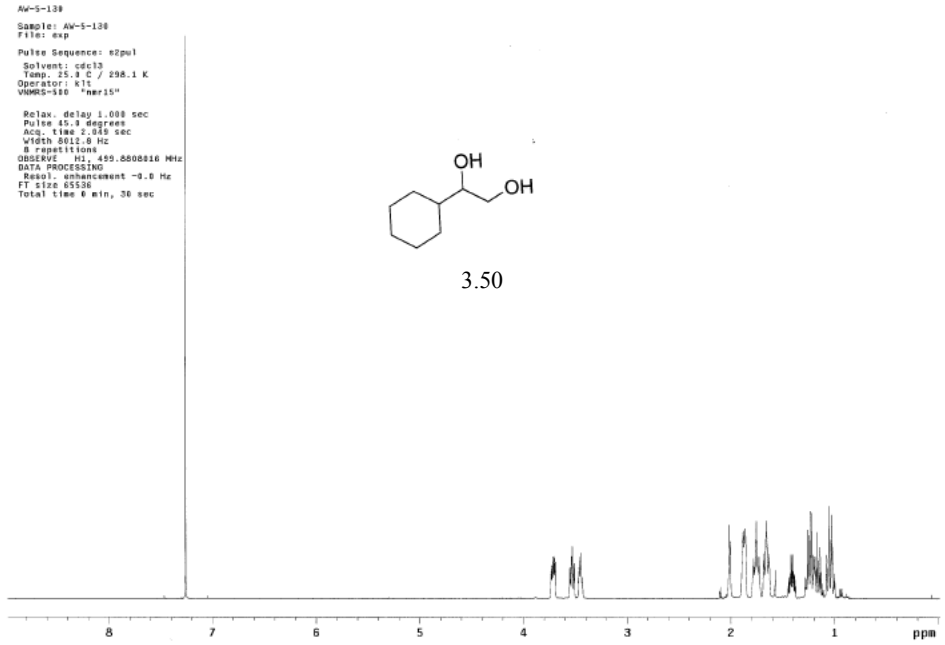
3.53


AW-5-152
Sample Name:
AW-5-152
Archive directory:
Sample directory:
FidFile: AW-5-152H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 14 2011
Me
OH
OH
Me
8
7
6
5
4
3
2
1
ppm

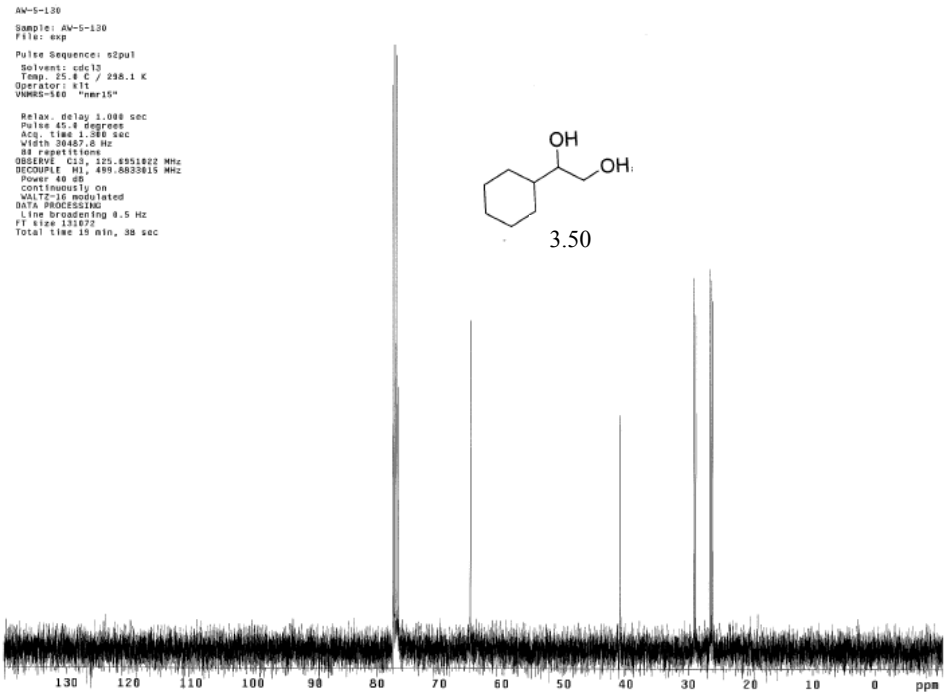
3.54


AW-5-152
Sample: AW-5-152
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-510 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.380 sec
Width 30487.8 Hz
32 repetitions
OBSERVE C13, 125.6551026 MHz
DECOUPLE H1, 499.8833815 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
Me
OH
OH
Me
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

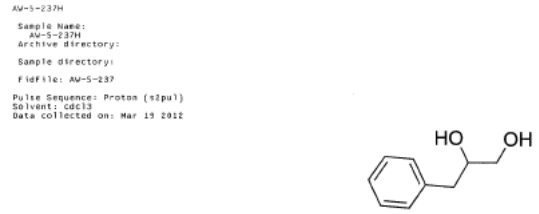
3.54


AW-S-130
Sample: AW-S-130
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808816 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
OH
OH
8
7
6
5
4
3
2
1
ppm

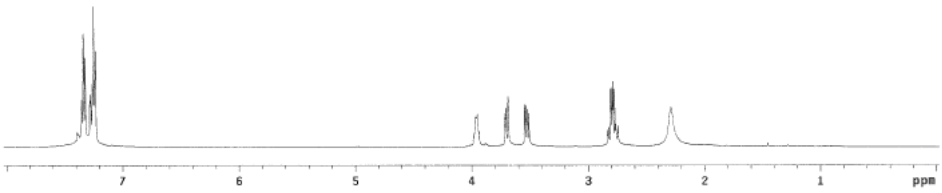
3.50

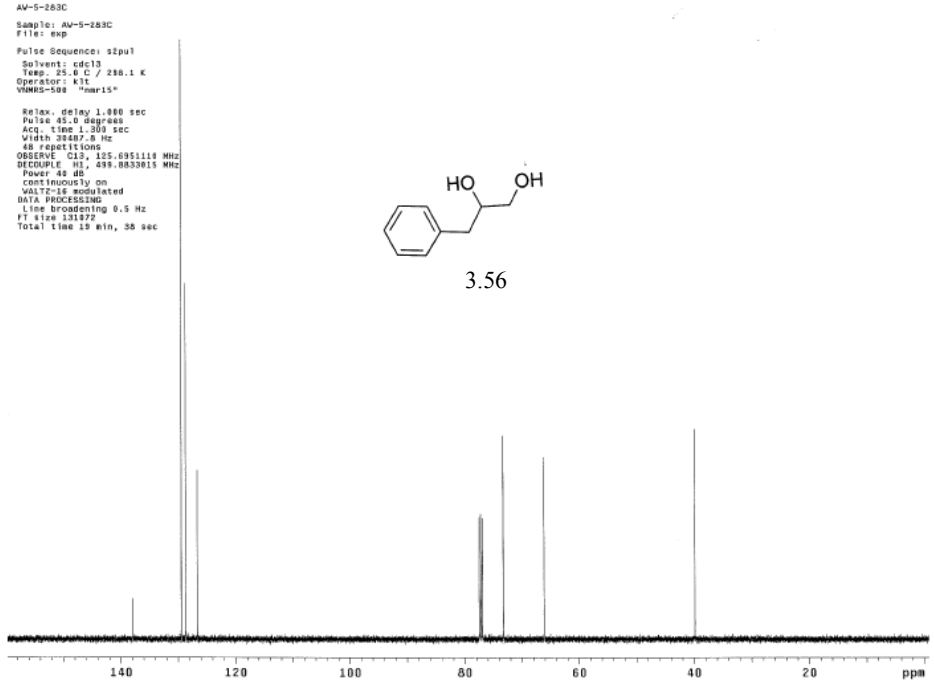

AW-S-130
Sample: AW-S-130
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.4 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.4 degrees
Acq. time 1.380 sec
Width 30487.8 Hz
88 repetitions
OBSERVE C13, 125.6551822 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 15 min, 38 sec
OH
OH
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

3.50

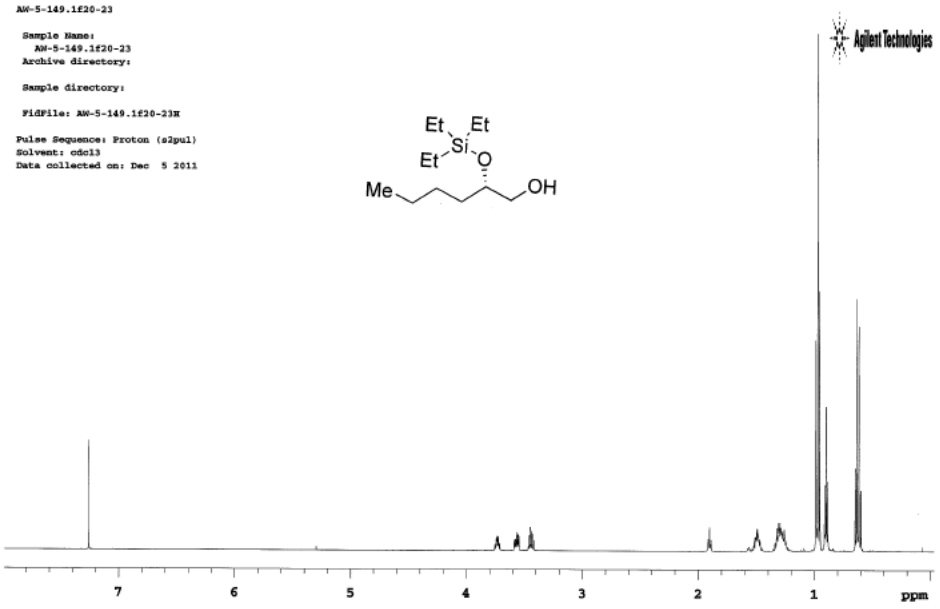

AW-S-237H
Sample Name:
AW-S-237H
Archive directory:
Sample directory:
FidFile: AW-S-237
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Mar 19 2012
HO
OH

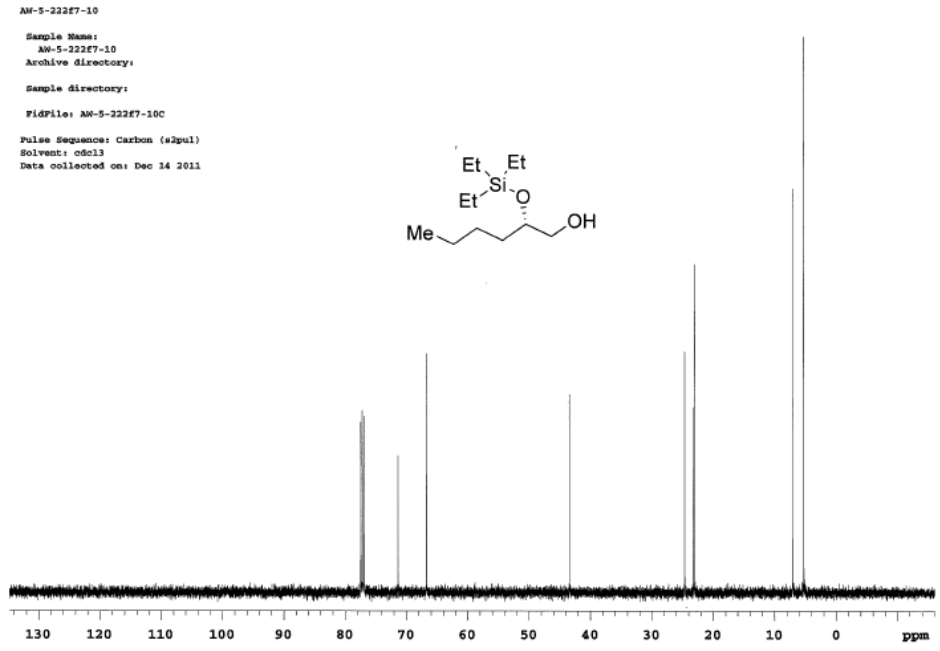
3.56

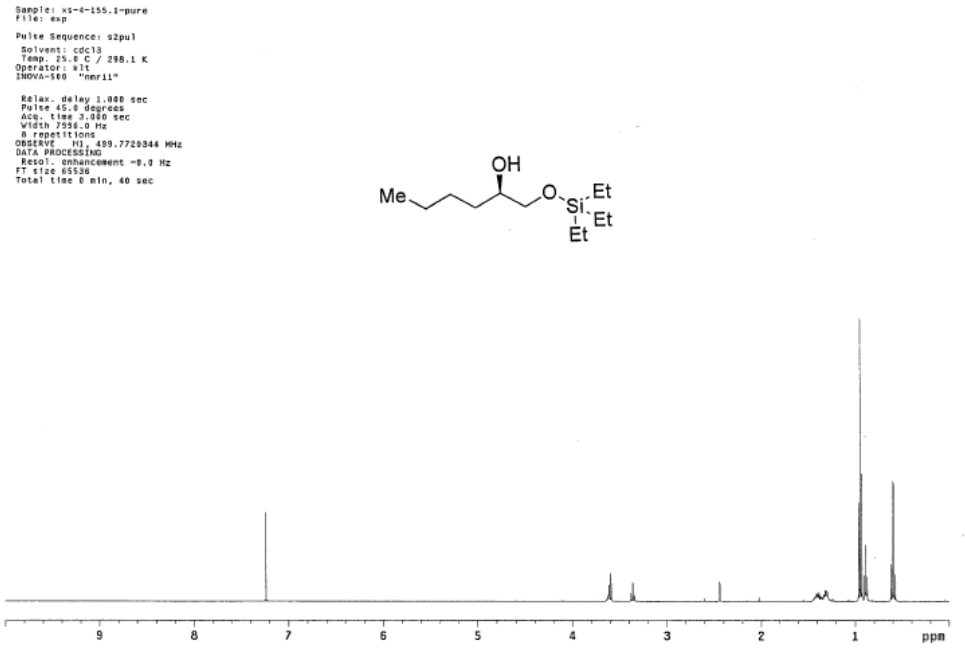

7
6
5
4
3
2
1
ppm

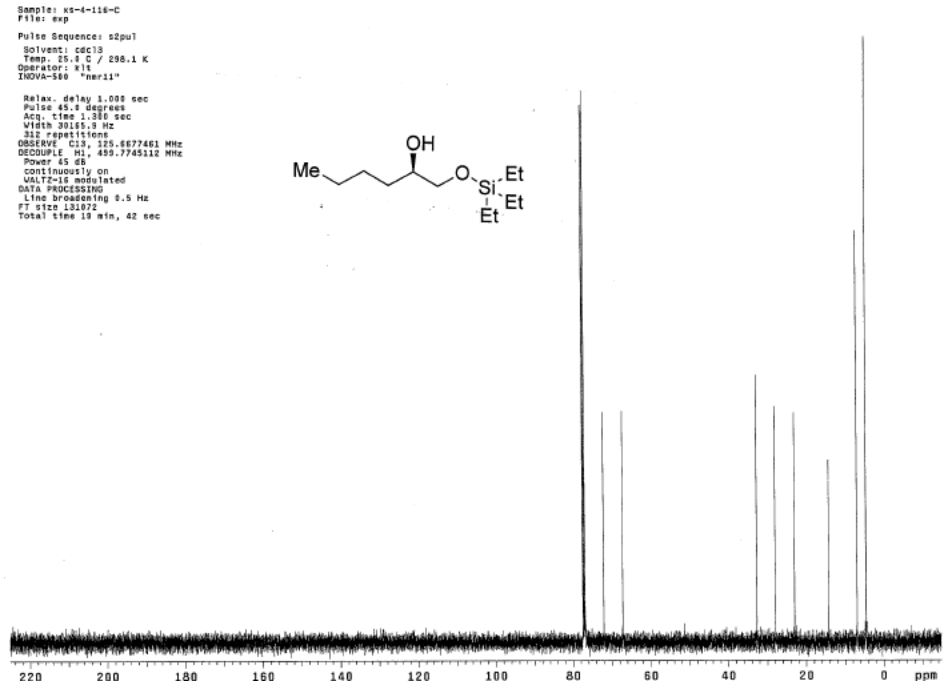

AW-S-283C
Sample: AW-S-283C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.309 sec
Width 29487.6 Hz
48 repetitions
OBSERVE C13, 125.6951118 MHz
DECOUPLE H1, 499.8833015 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
HO
OH
140
120
100
80
60
40
20
ppm

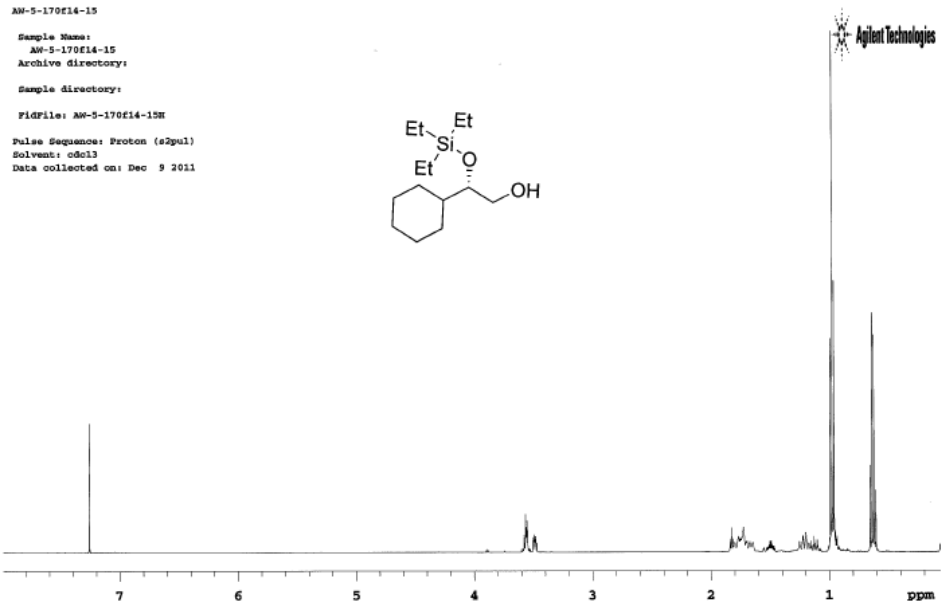
3.56

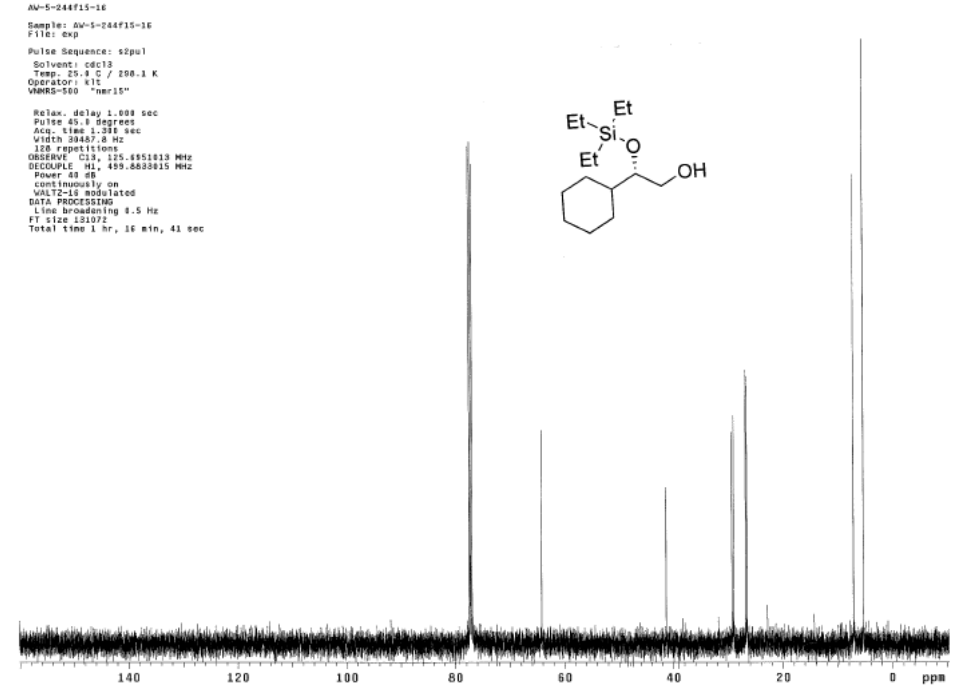

AW-5-149.1f20-23
Sample Name:
AW-5-149.1f20-23
Archive directory:
Sample directory:
FidFile: AW-5-149.1f20-23H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 5 2011
Agilent Technologies
Et
Et
Si
Et
O
Me
OH
7
6
5
4
3
2
1
ppm

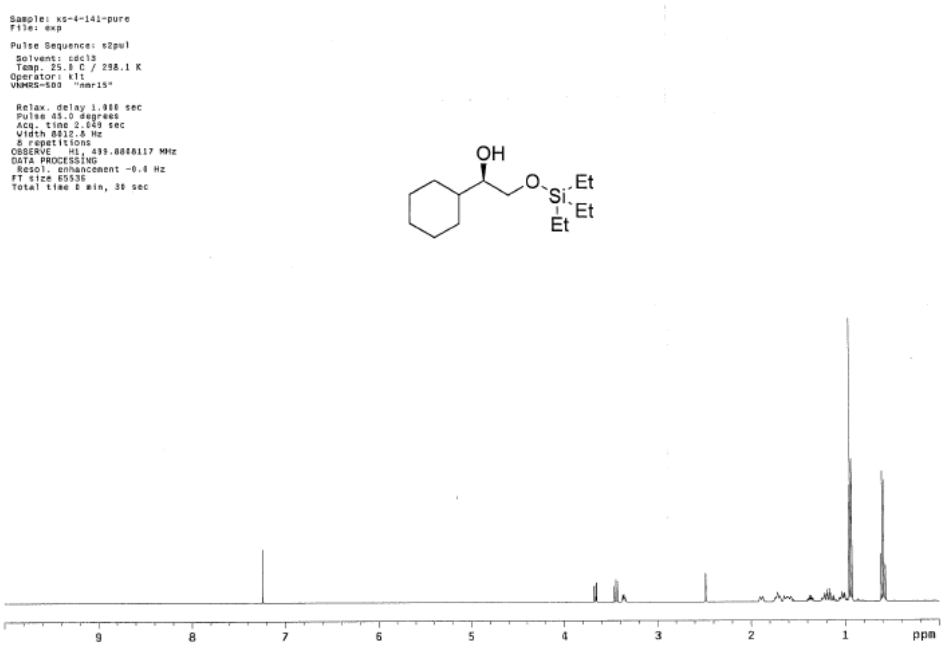

AW-5-222f7-10
Sample Name:
AW-5-222f7-10
Archive directory:
Sample directory:
FidFile: AW-5-222f7-10C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Dec 14 2011
Et
Et
Si
Et
O
Me
OH
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

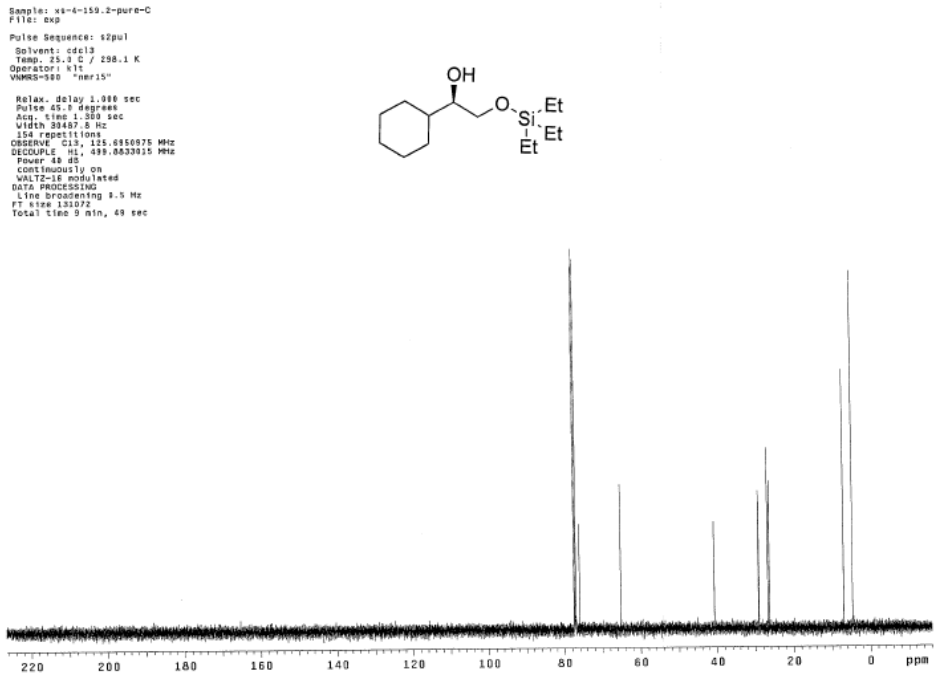

Sample: xs-4-155.1-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "neril"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7556.0 Hz
8 repetitions
OBSERVE H1, 499.7720344 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 40 sec
OH
Me
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

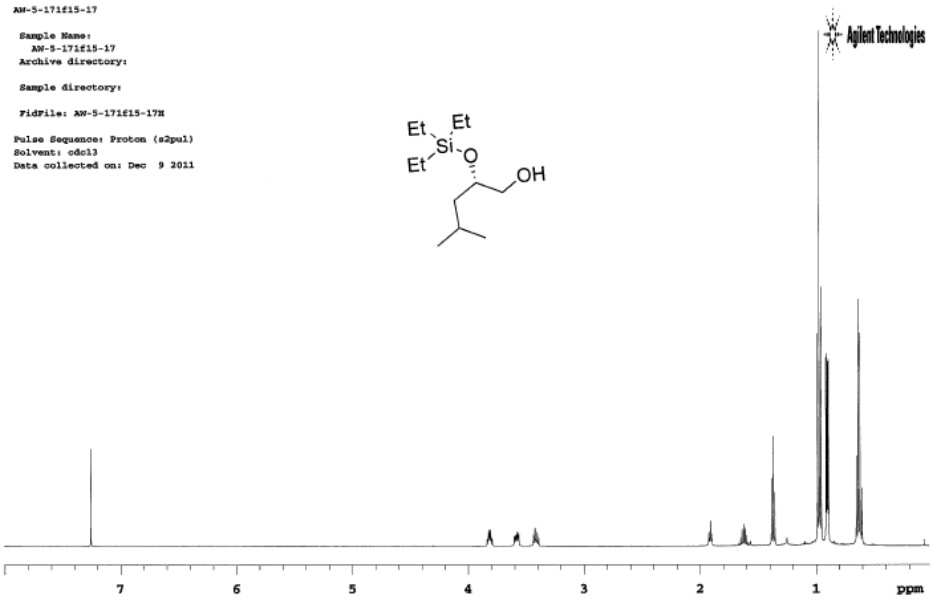

Sample: xs-4-116-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
INOVA-500 "neril"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30165.8 Hz
312 repetitions
OBSERVE C13, 125.6677461 MHz
DECOUPLE H1, 499.7745112 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 42 sec
OH
Me
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm

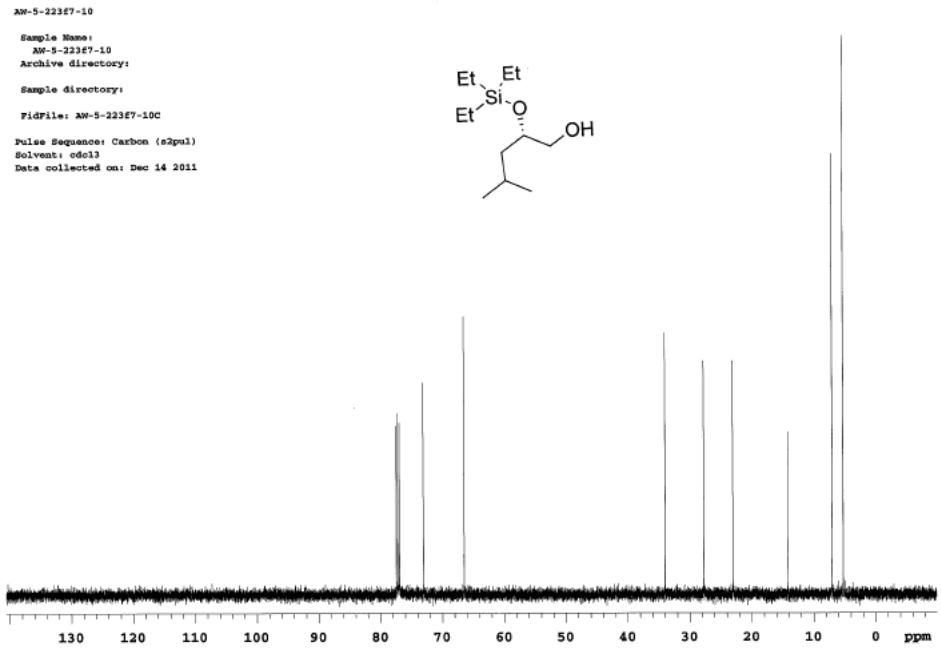

AW-5-170f14-15
Sample Name:
AW-5-170f14-15
Archive directory:
Sample directory:
FidFile: AW-5-170f14-15H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 9 2011
Agilent Technologies
Et
Et
Si
O
Et
OH
7
6
5
4
3
2
1
ppm

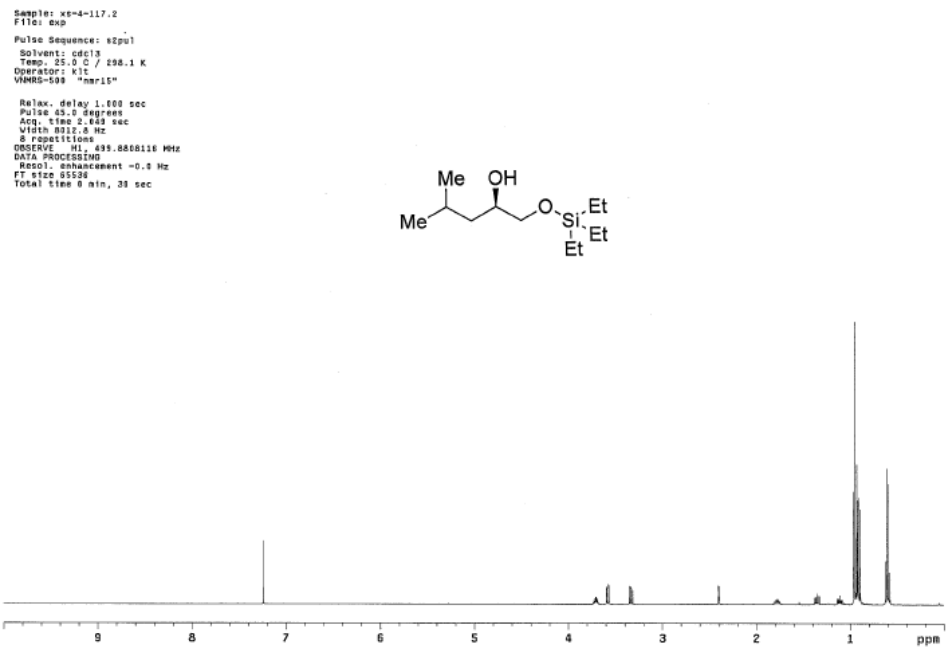

AW-5-244f15-16
Sample: AW-5-244f15-16
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.9 C / 299.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 30487.8 Hz
128 repetitions
OBSERVE C13, 125.6851813 MHz
DECOUPLE H1, 499.8828815 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 1 hr, 16 min, 41 sec
Et
Et
Si
O
Et
OH
140
120
100
80
60
40
20
0
ppm

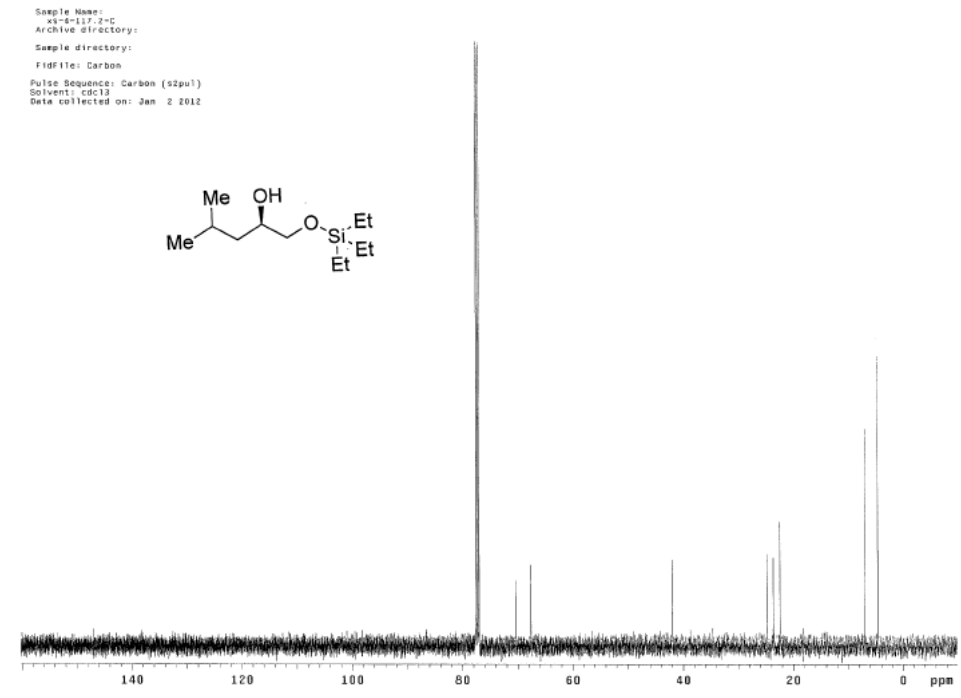

Sample: xs-4-141-pure
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.649 sec
Width 6012.6 Hz
8 repetitions
OBSERVE H1, 499.8868117 MHz
DATA PROCESSING
Resol. enhancement -0.6 Hz
FT size 65536
Total time 0 min, 38 sec
OH
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

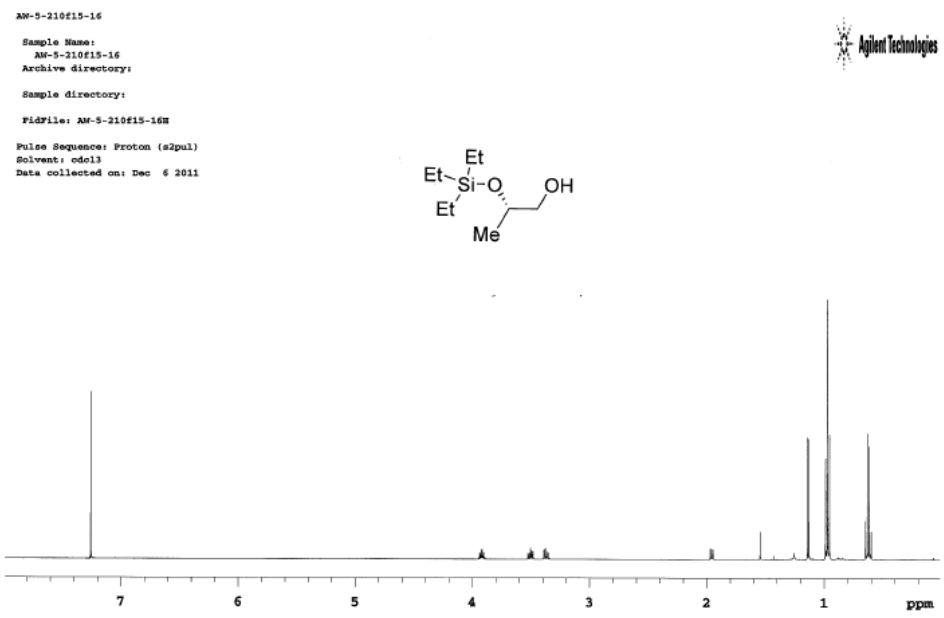

Sample: xs-4-159.2-pure-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.360 sec
Width 30487.8 Hz
154 repetitions
OBSERVE C13, 125.6850975 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
OH
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm

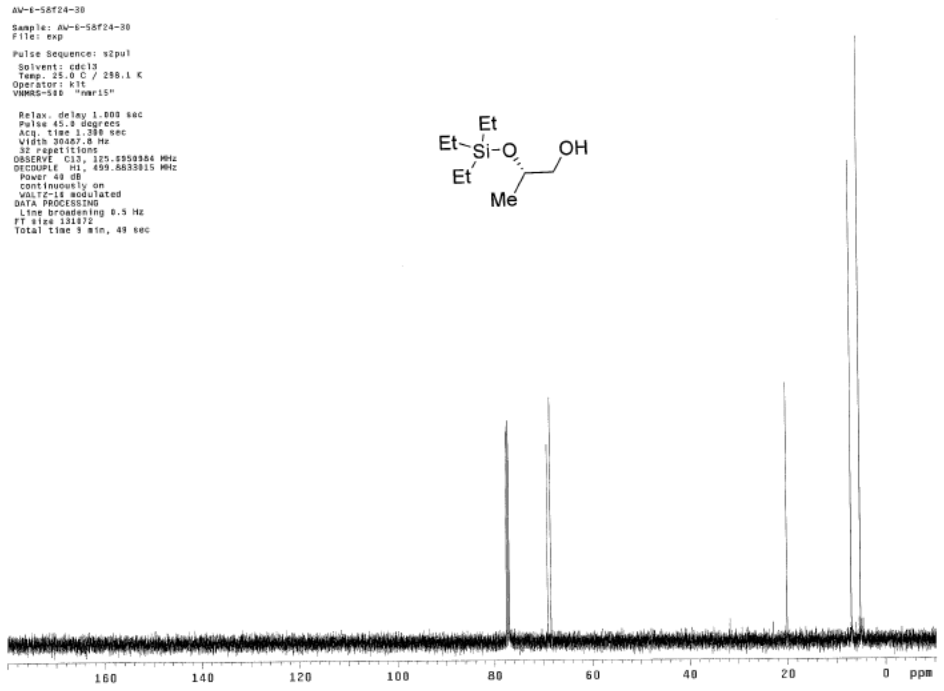

AW-5-171f15-17
Sample Name:
AW-5-171f15-17
Archive directory:
Sample directory:
FidFile: AW-5-171f15-17H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 9 2011
Agilent Technologies
Et
Et
Si
Et
O
OH
7
6
5
4
3
2
1
ppm

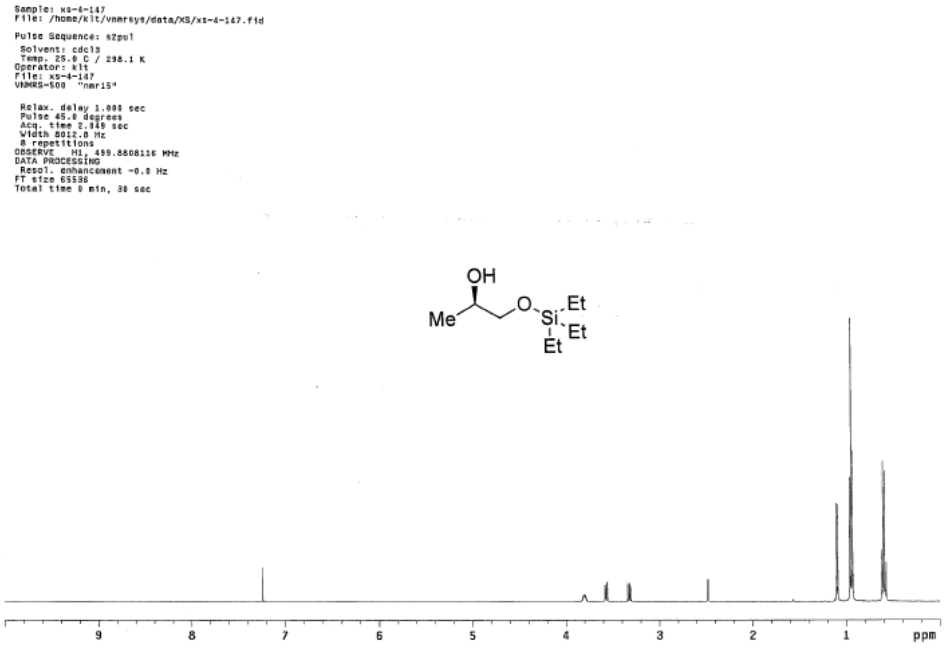

AW-5-223f7-10
Sample Name:
AW-5-223f7-10
Archive directory:
Sample directory:
FidFile: AW-5-223f7-10C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Dec 14 2011
Et
Et
Si
Et
O
OH
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

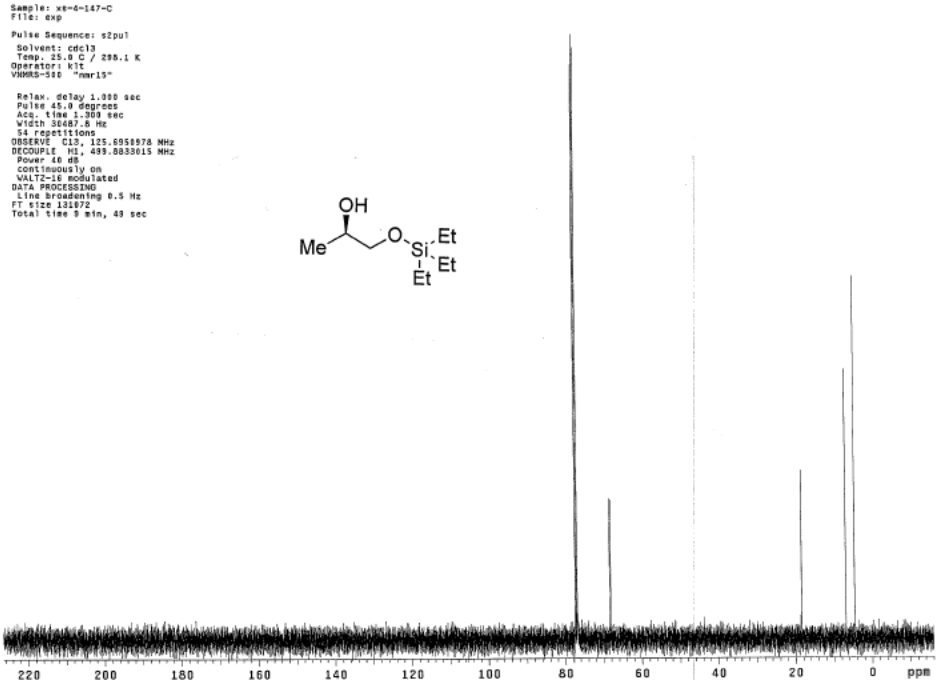

Sample: xs-4-117.2
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.648 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808116 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 38 sec
Me
OH
Me
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

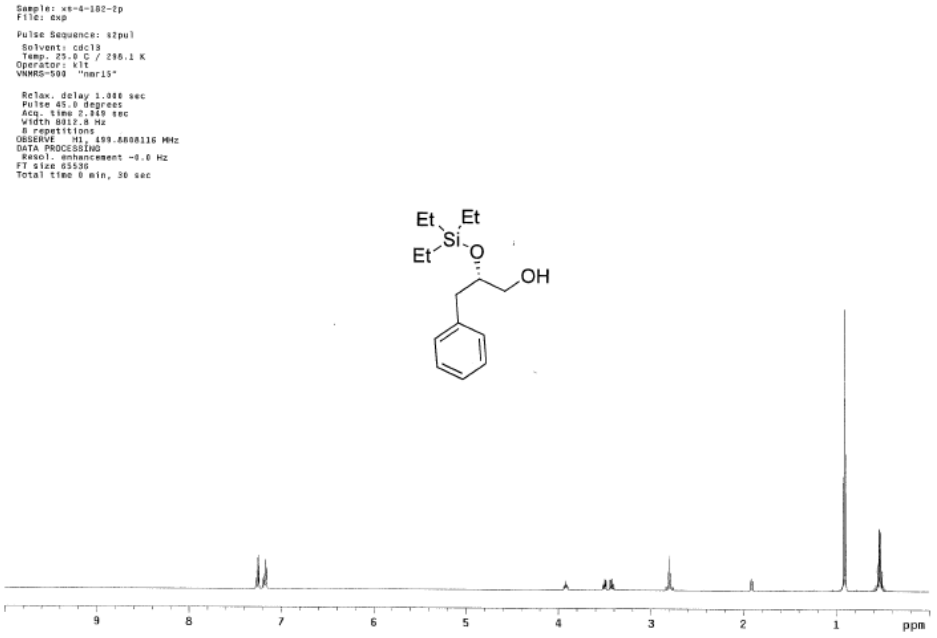

Sample Name:
xs-4-117.2-C
Archive directory:
Sample directory:
FidFile: Carbon
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Jan 2 2012
Me
OH
Me
O
Si
Et
Et
Et
140
120
100
80
60
40
20
0
ppm

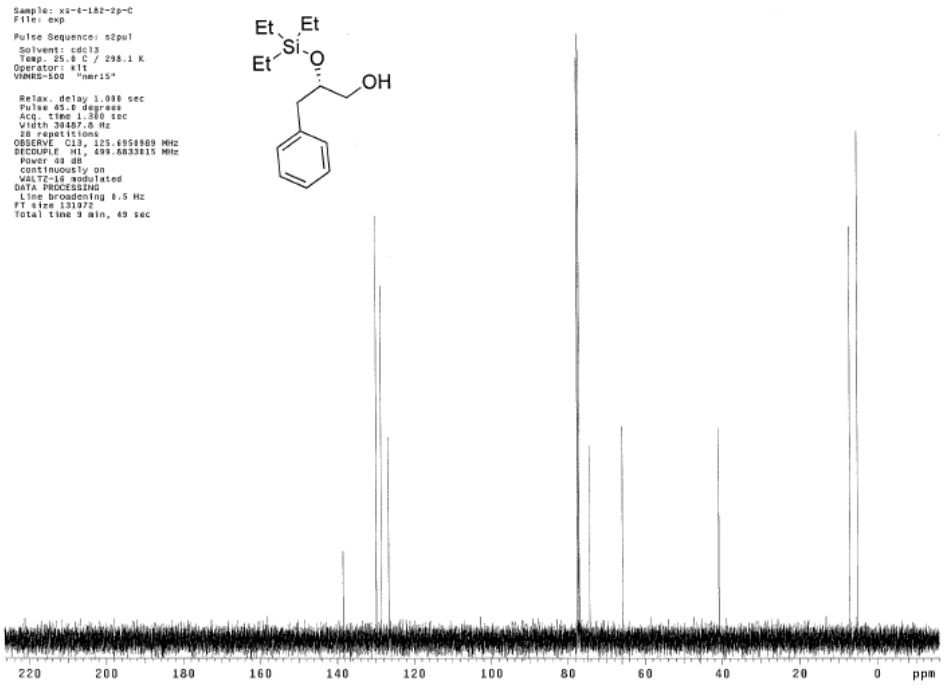

AW-5-210f15-16
Sample Name:
AW-5-210f15-16
Archive directory:
Sample directory:
FidFile: AW-5-210f15-16H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 6 2011
Agilent Technologies
Et
Et
Si
O
OH
Et
Me
7
6
5
4
3
2
1
ppm

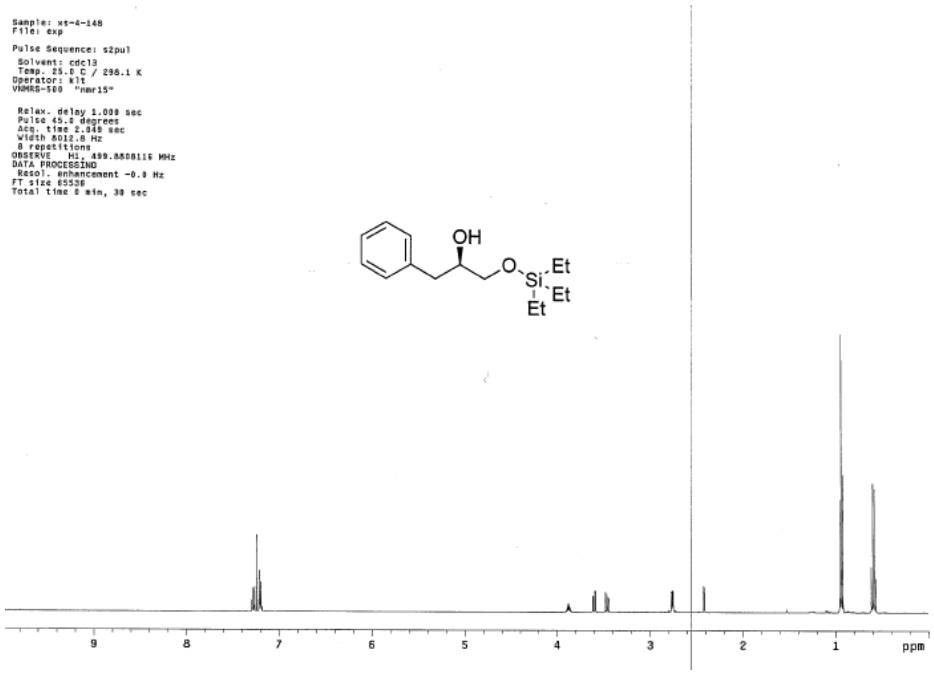

AW-6-58f24-30
Sample: AW-6-58f24-30
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: ktt
VNMRS-5bb "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
32 repetitions
OBSERVE C13, 125.5559364 MHz
DECOUPLE H1, 499.8833815 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
Et
Et
Si
O
OH
Et
Me
160
140
120
100
80
60
40
20
0
ppm

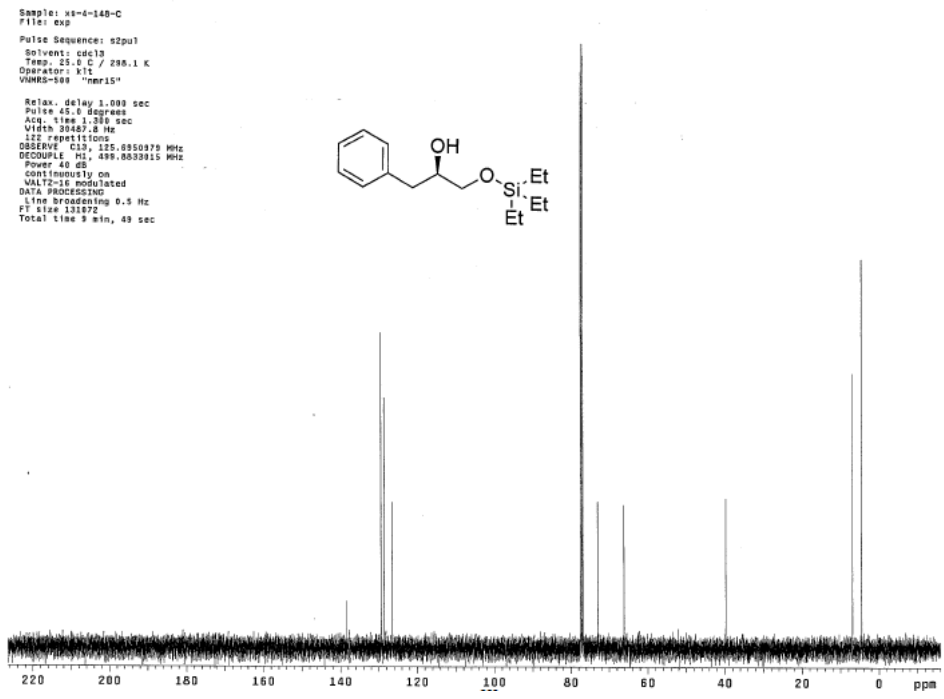

Sample: xs-4-147
File: /home/klt/vnmrsys/data/XS/xs-4-147.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
File: xs-4-147
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.149 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808116 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 38 sec
OH
Me
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

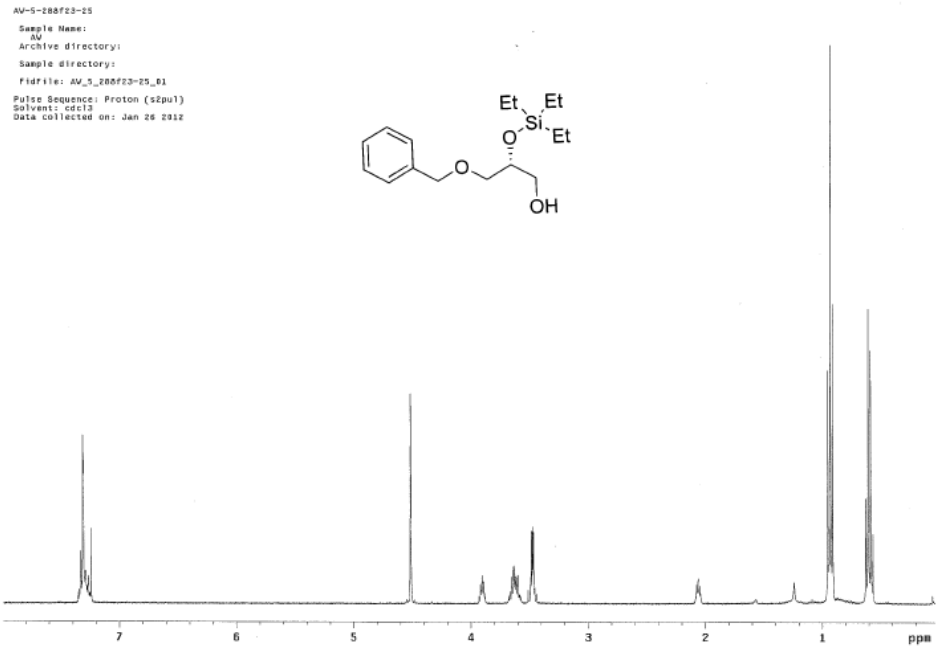

Sample: xs-4-147-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.309 sec
Width 30487.8 Hz
54 repetitions
OBSERVE C13, 125.6958978 MHz
DECOUPLE H1, 499.8833015 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 3 min, 43 sec
OH
Me
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm

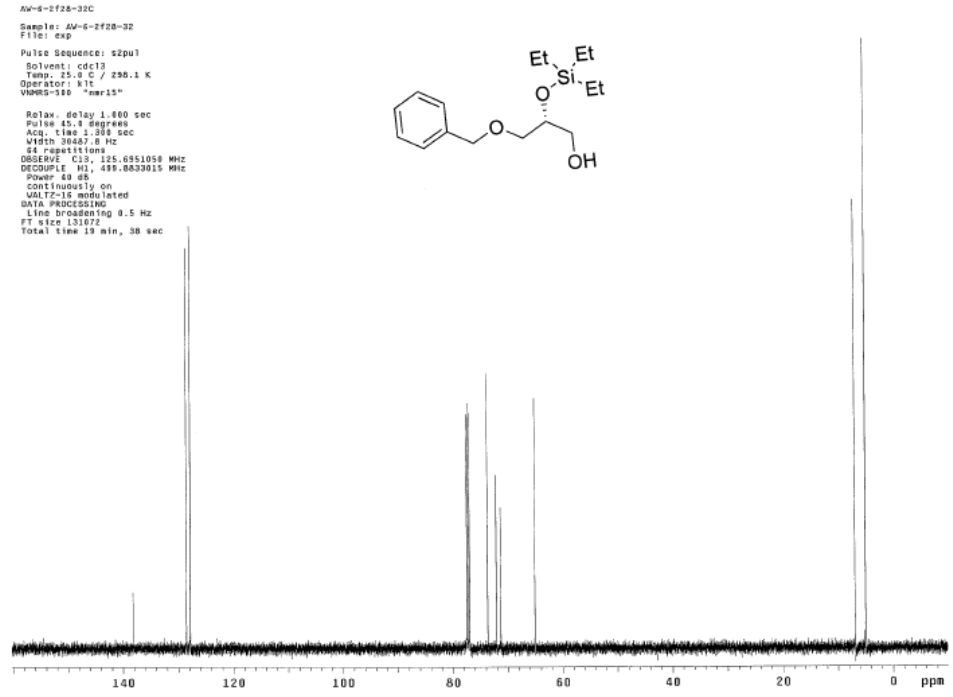

Sample: xs-4-182-2p
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.849 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808116 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
Et
Et
Si
Et
O
OH
9
8
7
6
5
4
3
2
1
ppm

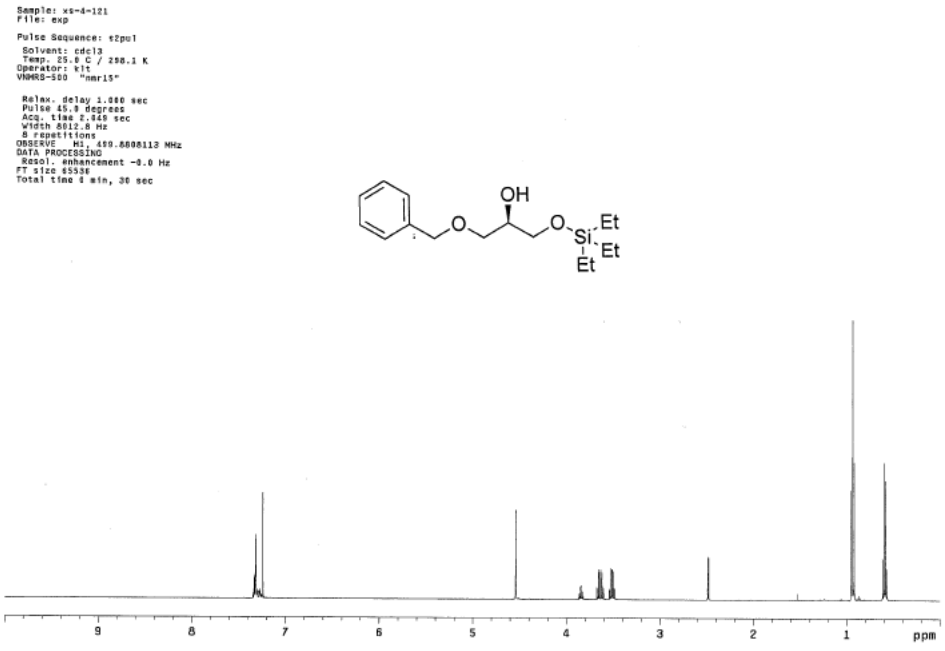

Sample: xs-4-182-2p-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.8 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.380 sec
Width 30487.8 Hz
28 repetitions
OBSERVE C13, 125.6959989 MHz
DECOUPLE H1, 499.8833815 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 3 min, 49 sec
Et
Et
Si
Et
O
OH
220
200
180
160
140
120
100
80
60
40
20
0
ppm

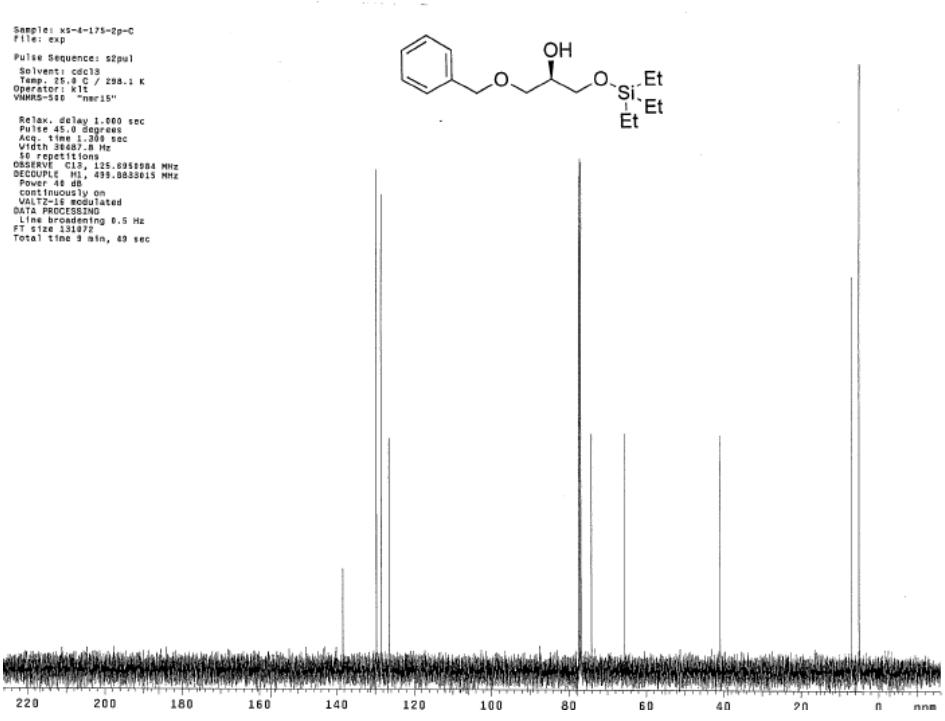

Sample: xs-4-148
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.048 sec
Width 6012.8 Hz
8 repetitions
OBSERVE H1, 499.8808116 MHz
DATA PROCESSING
Resol. enhancement -0.9 Hz
FT size 65536
Total time 0 min, 30 sec
OH
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

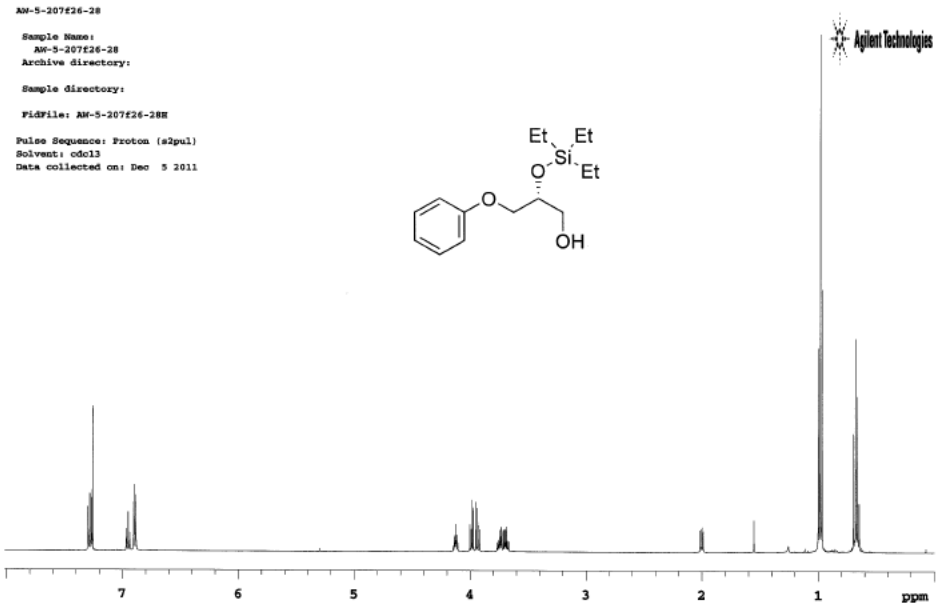

Sample: xs-4-148-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.380 sec
Width 30487.8 Hz
122 repetitions
OBSERVE C13, 125.8850979 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
OH
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm

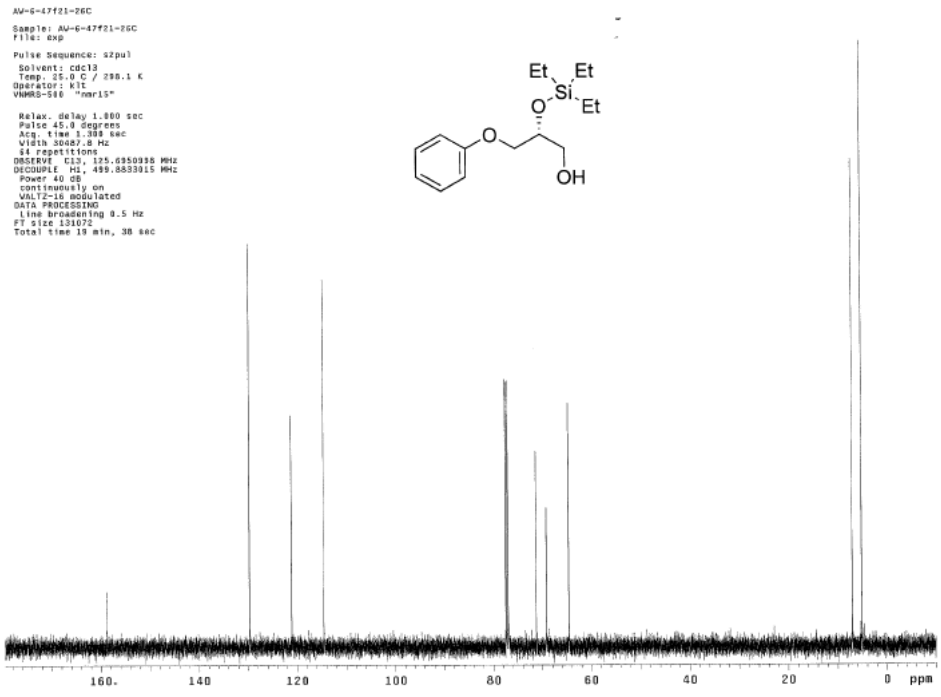

AV-5-288f23-25
Sample Name:
AV
Archive directory:
Sample directory:
Fidfile: AV_5_288f23-25_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Jan 26 2012
Et
Et
Si
Et
O
O
OH
7
6
5
4
3
2
1
ppm

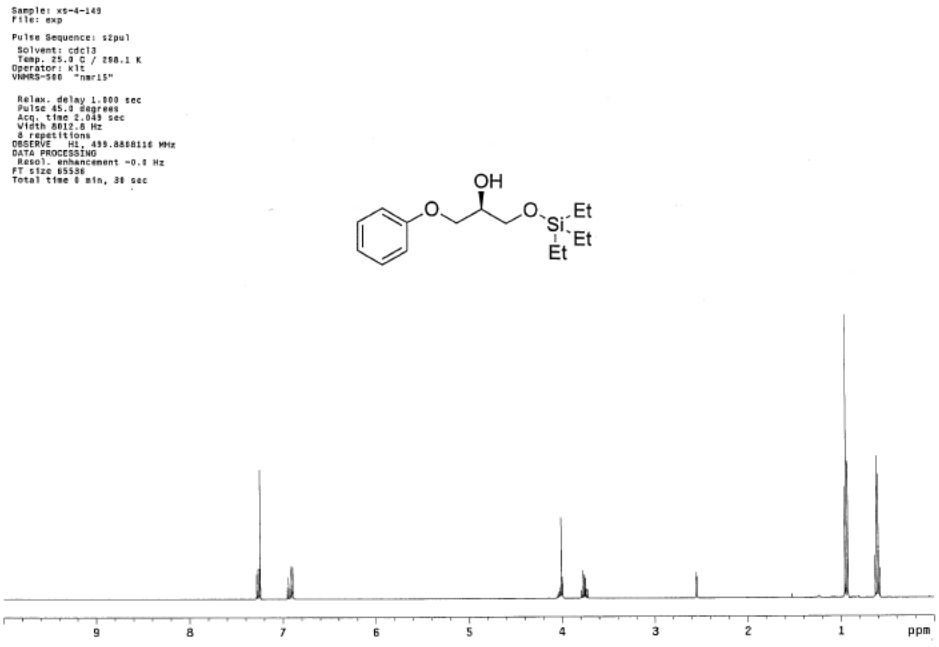

AV-6-2f28-32C
Sample: AV-6-2f28-32
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-510 "mar15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
64 repetitions
OBSERVE C13, 125.6951058 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
Et
Et
Si
Et
O
O
OH
140
120
100
80
60
40
20
0
ppm

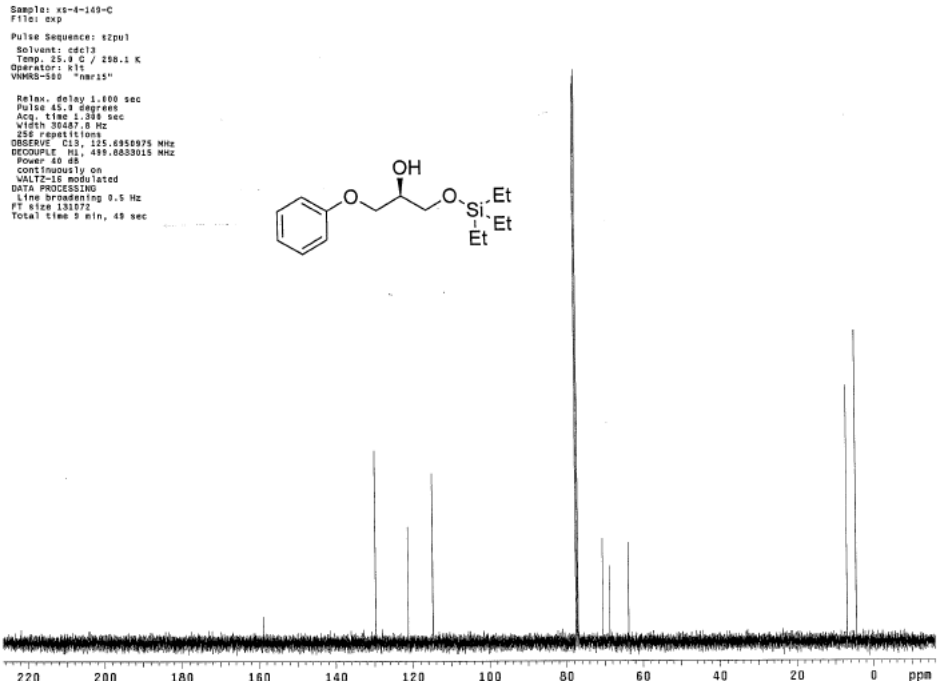

Sample: xs-4-121
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.949 sec
Width 8012.8 Hz
8 repetitions
OBSERVE H1, 499.8808113 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 36 sec
OH
O
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

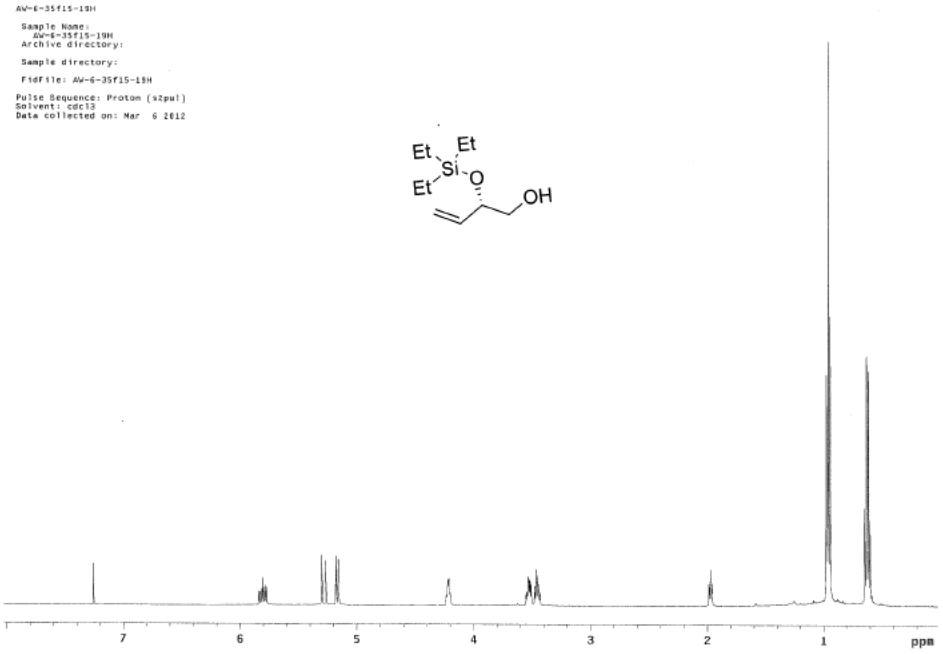

Sample: xs-4-175-2p-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.308 sec
Width 30487.8 Hz
16 repetitions
OBSERVE C13, 125.8958984 MHz
DECOUPLE H1, 499.8833015 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
OH
O
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm

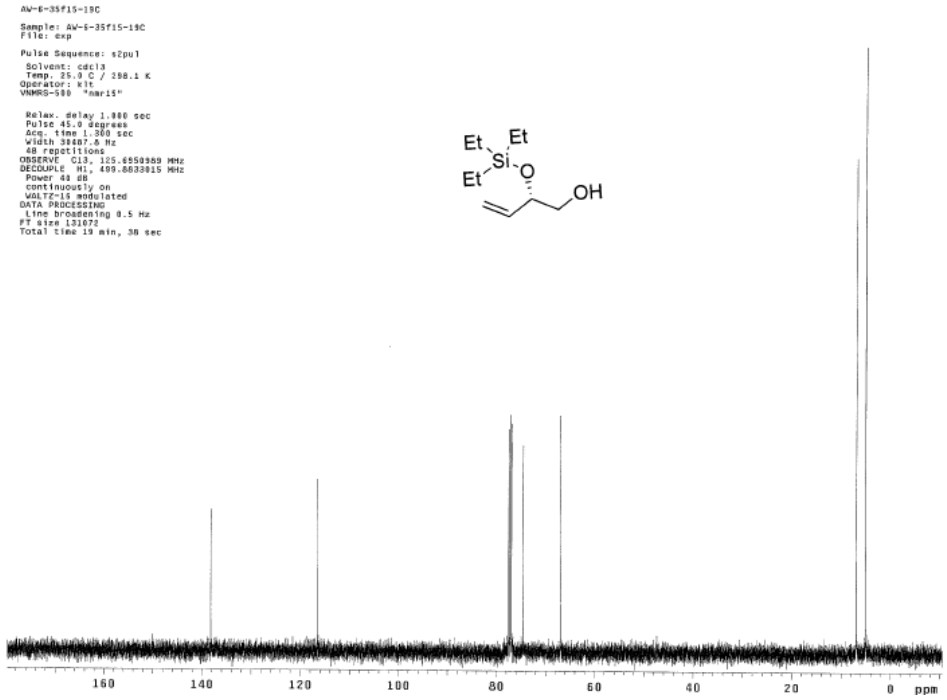

AW-5-207f26-2H
Sample Name:
AW-5-207f26-2H
Archive directory:
Sample directory:
FidFile: AW-5-207f26-2H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 5 2011
Agilent Technologies
Et
Et
Si
Et
O
O
OH
7
6
5
4
3
2
1
ppm

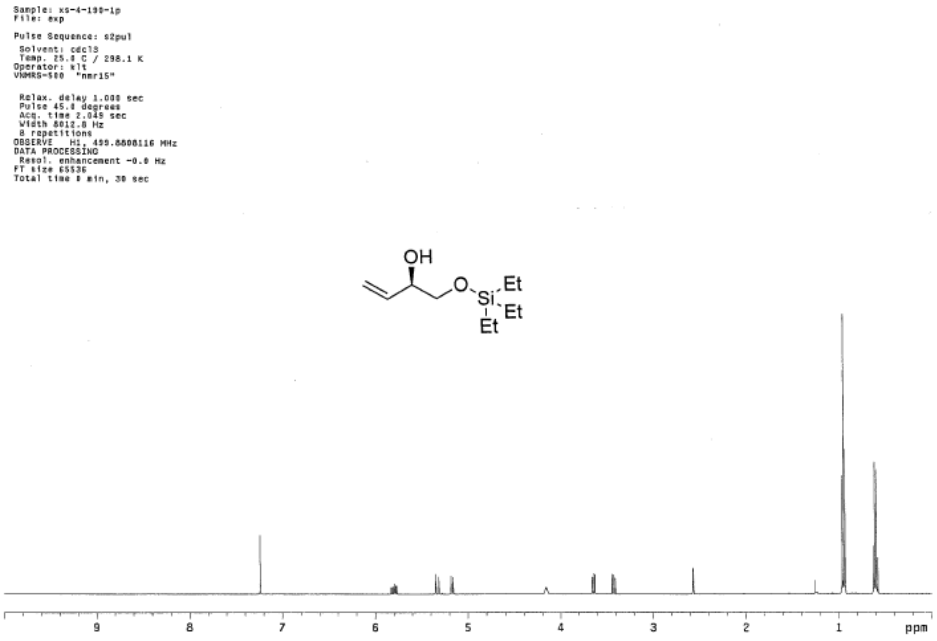

AW-6-47f21-2GC
Sample: AW-6-47f21-2GC
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.388 sec
Width 30487.8 Hz
64 repetitions
OBSERVE C13, 125.6950938 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
Et
Et
Si
Et
O
O
OH
160.
140
120
100
80
60
40
20
0
ppm

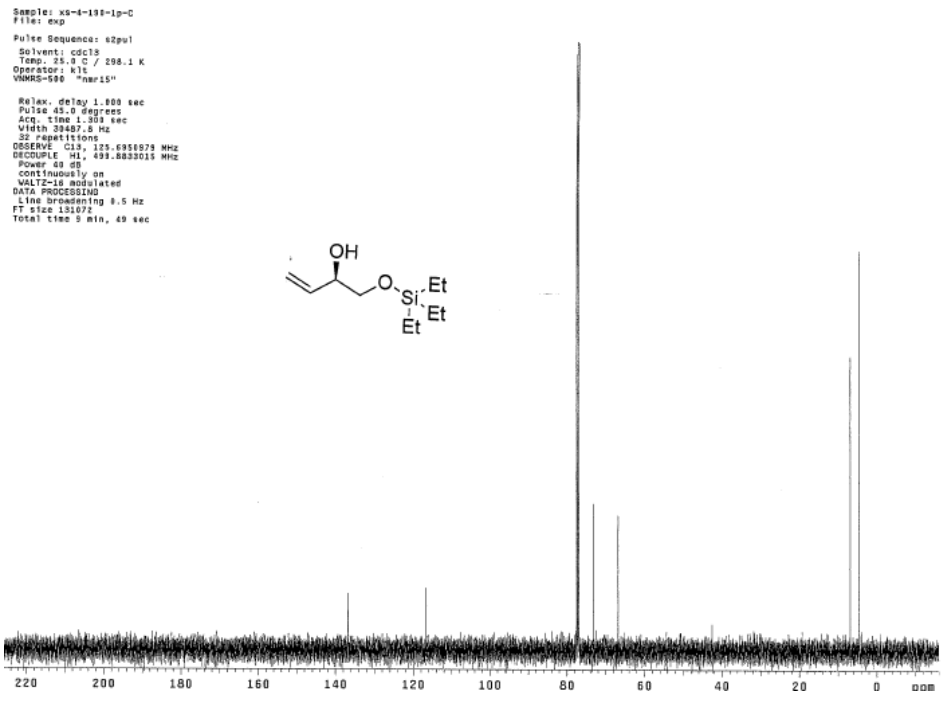

Sample: xs-4-149
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6012.8 Hz
8 repetitions
OBSERVE H1, 499.8868116 MHz
DATA PROCESSING
Resol. enhancement -0.8 Hz
FT size 65536
Total time 0 min, 36 sec
OH
O
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

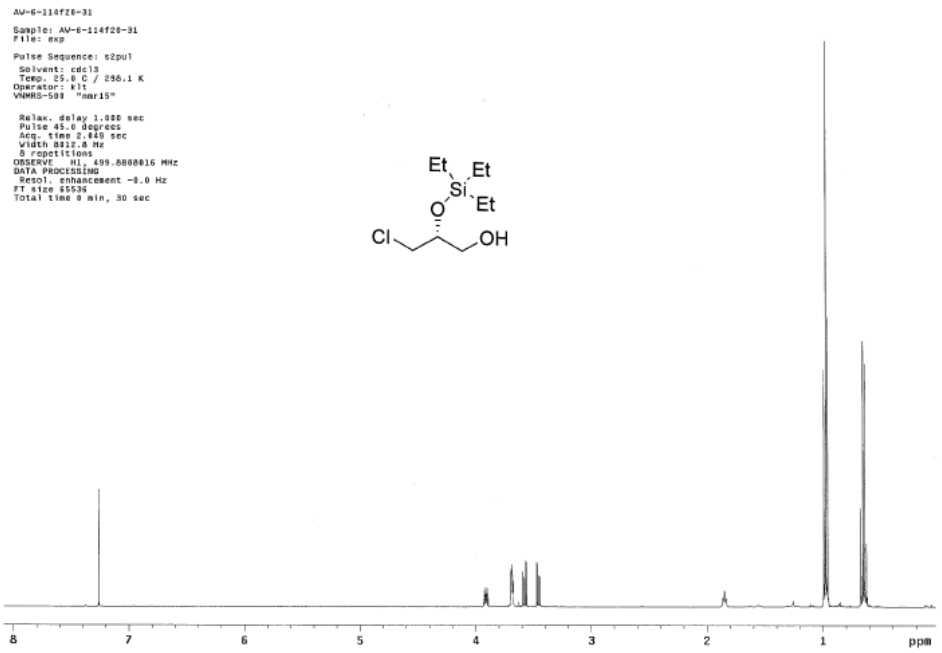

Sample: xs-4-149-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
256 repetitions
OBSERVE C13, 125.6958975 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
OH
O
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm

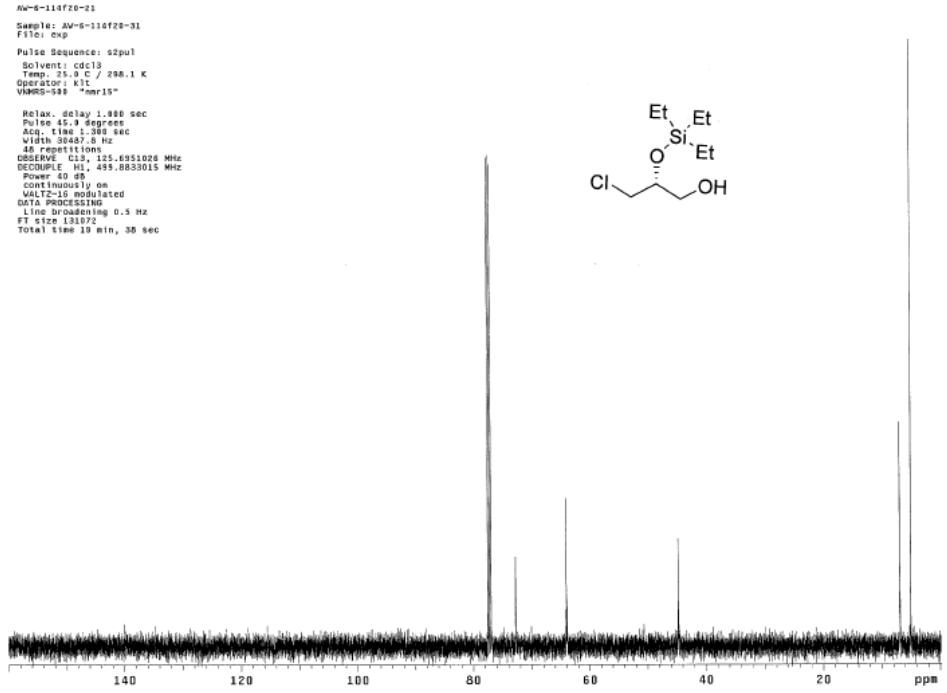

AW-6-35f15-19H
Sample Name:
AW-6-35f15-19H
Archive directory:
Sample directory:
FidFile: AW-6-35f15-19H
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Mar 6 2012
Et
Et
Si
Et
O
OH
7
6
5
4
3
2
1
ppm

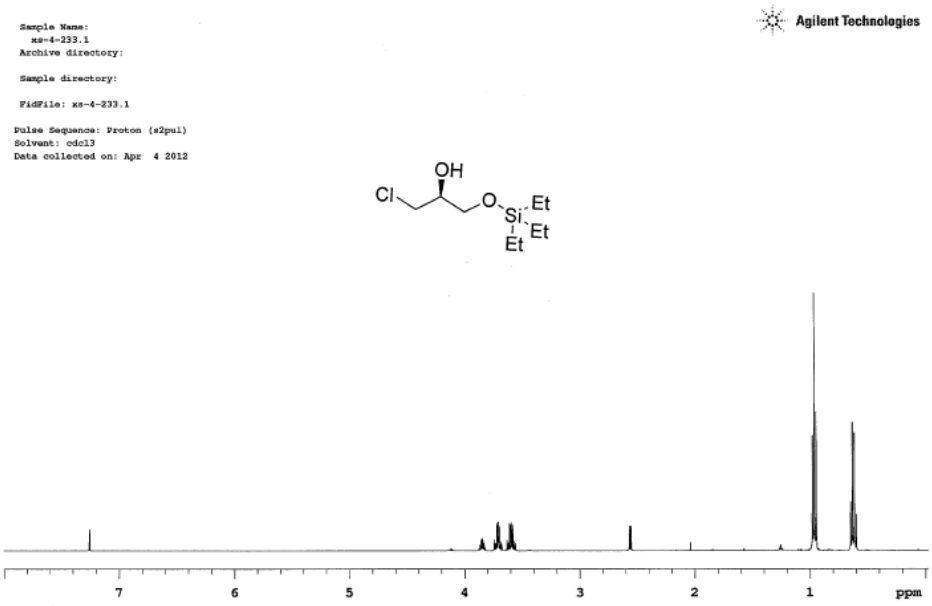

AW-6-35f15-19C
Sample: AW-6-35f15-19C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: kit
VNMRS-580 "mar15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 38407.8 Hz
48 repetitions
OBSERVE C13, 125.6559369 MHz
DECOUPLE H1, 499.8833815 MHz
Power 43 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
Et
Et
Si
Et
O
OH
160
140
120
100
80
60
40
20
0
ppm

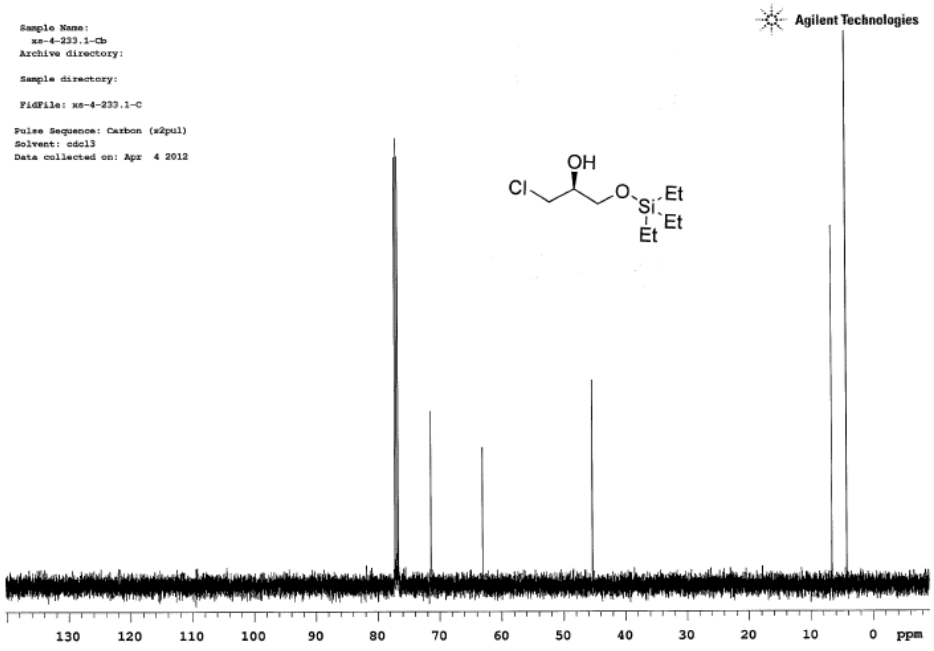

Sample: xs-4-198-1p
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.045 sec
Width 6012.8 Hz
8 repetitions
OBSERVE H1, 499.8808116 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
OH
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm

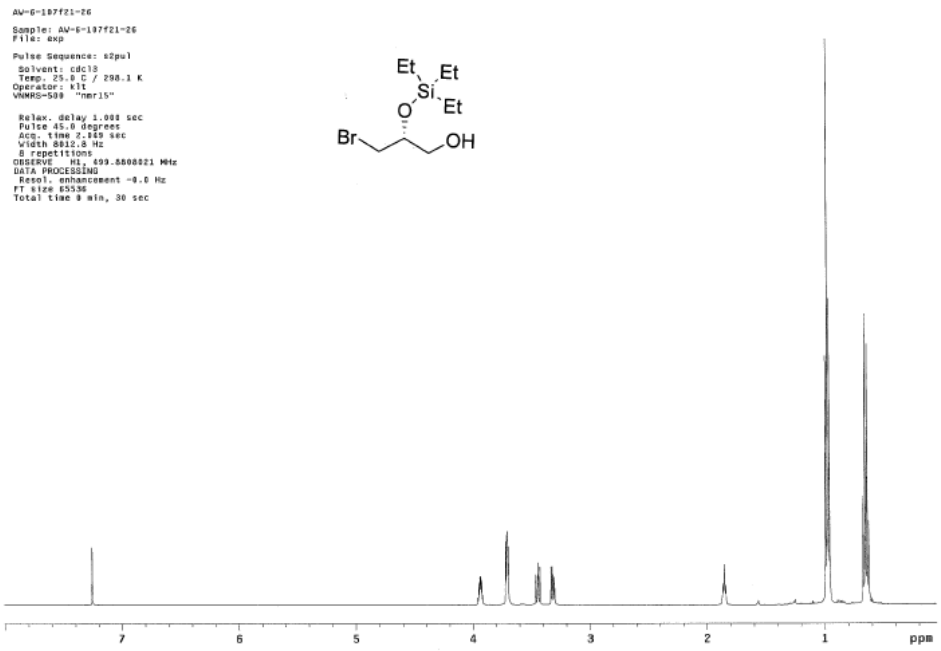

Sample: xs-4-198-1p-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.303 sec
Width 30487.8 Hz
32 repetitions
OBSERVE C13, 125.6958978 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
OH
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm

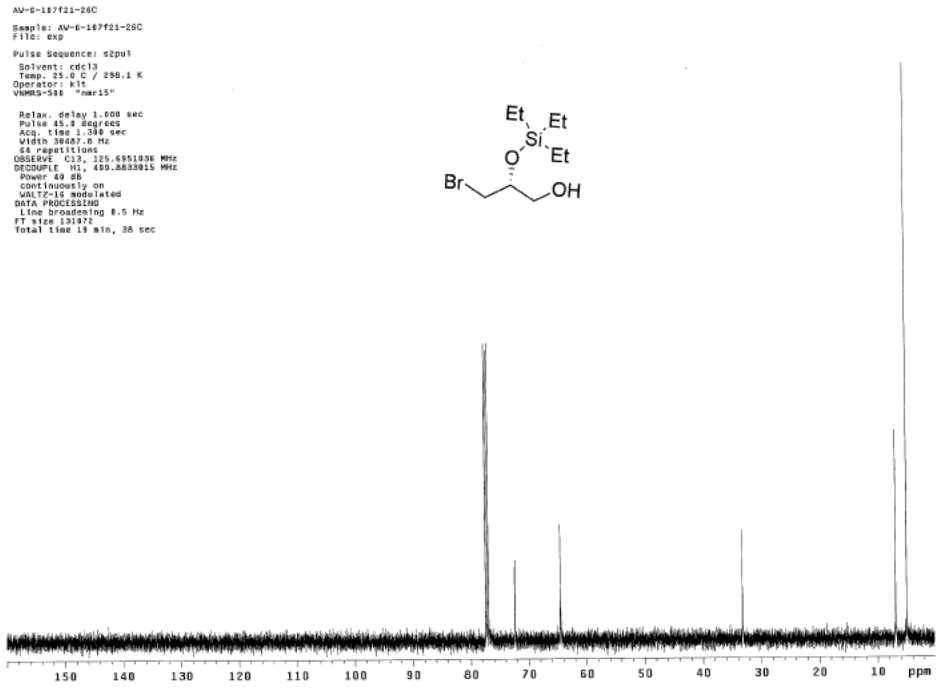

AV-6-114f28-31
Sample: AV-6-114f28-31
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.849 sec
Width 8812.8 Hz
8 repetitions
OBSERVE H1, 499.8808016 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 55536
Total time 0 min, 30 sec
Et
Et
Si
Et
O
Cl
OH
8
7
6
5
4
3
2
1
ppm

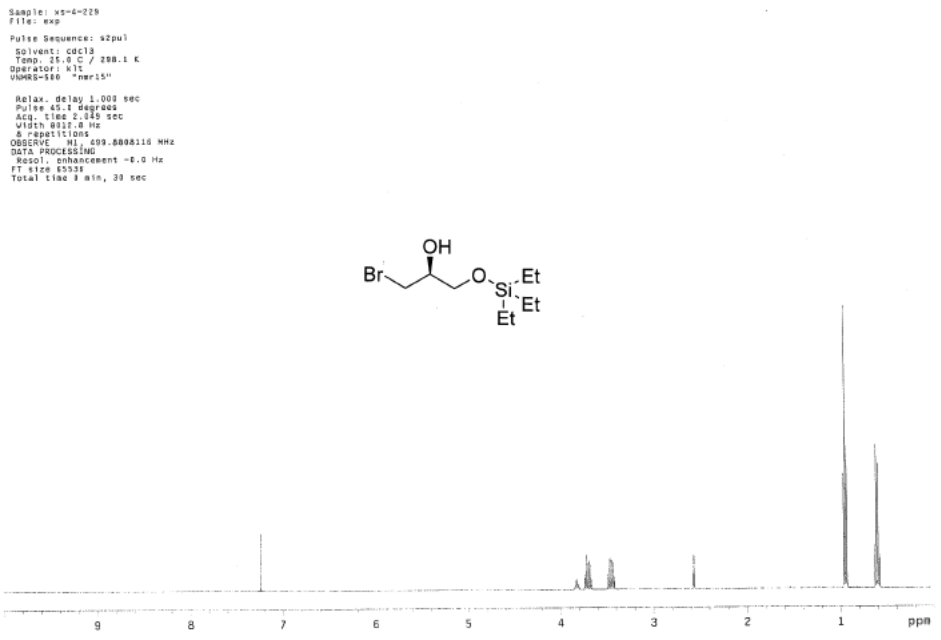

AV-6-114f28-21
Sample: AV-6-114f28-31
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
48 repetitions
OBSERVE C13, 125.6951026 MHz
DECOUPLE H1, 499.8833015 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 36 sec
Et
Et
Si
Et
O
Cl
OH
140
120
100
80
60
40
20
ppm

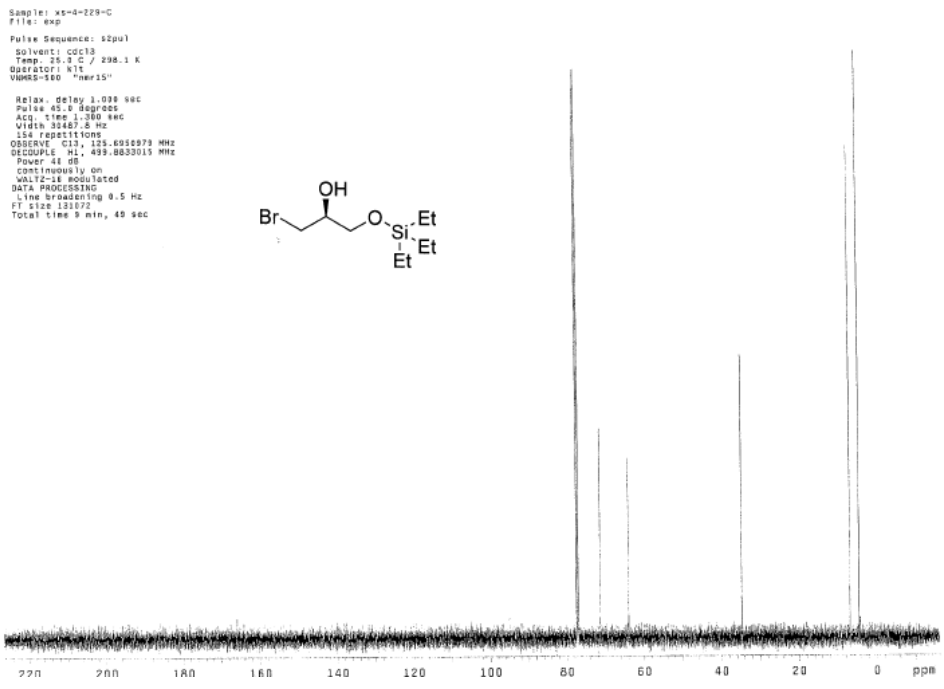

Agilent Technologies
Sample Name:
xs-4-233.1
Archive directory:
Sample directory:
FidFile: xs-4-233.1
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Apr 4 2012
OH
Cl
O
Si
Et
Et
Et
7
6
5
4
3
2
1
ppm

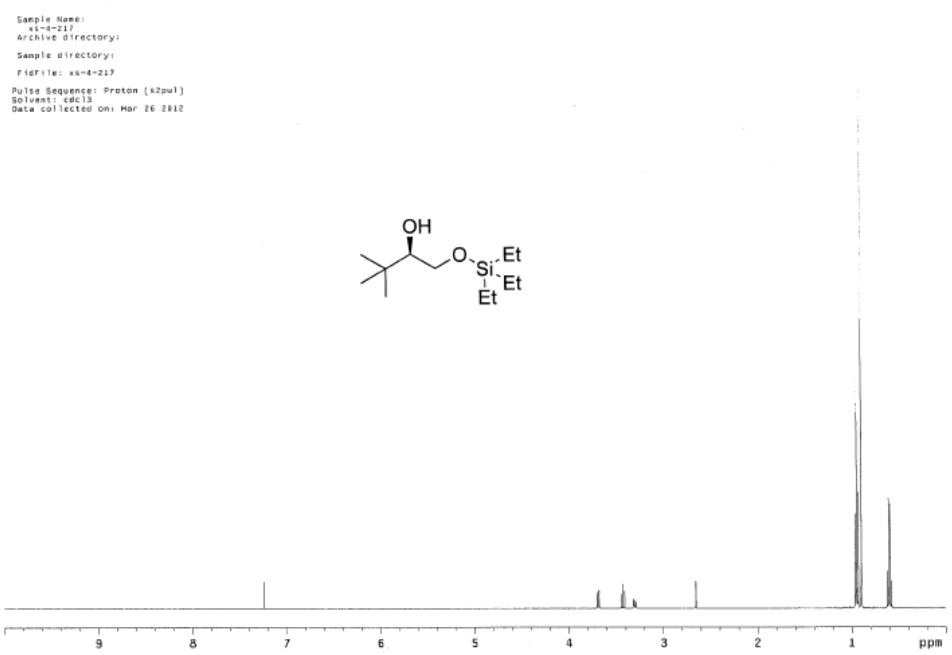

Agilent Technologies
Sample Name:
xs-4-233.1-Cb
Archive directory:
Sample directory:
FidFile: xs-4-233.1-C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Apr 4 2012
OH
Cl
O
Si
Et
Et
Et
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

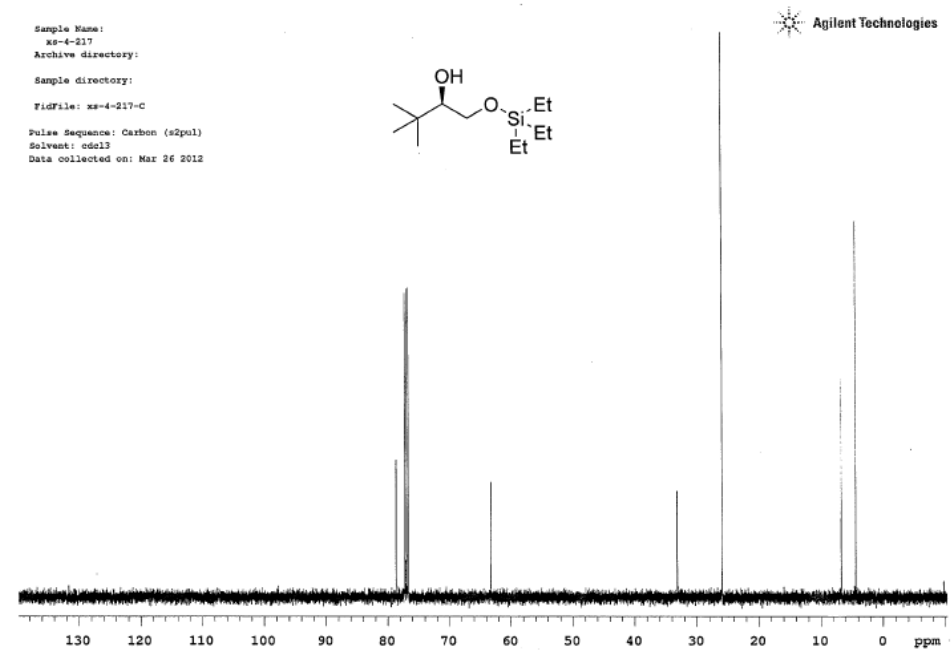

AV-6-187f21-26
Sample: AV-6-187f21-26
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.949 sec
Width 6812.8 Hz
8 repetitions
OBSERVE H1, 499.8808821 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min, 30 sec
Et
Et
Si
Et
O
Br
OH
7
6
5
4
3
2
1
ppm


AV-6-187f21-26C
Sample: AV-6-187f21-26C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
64 repetitions
OBSERVE C13, 125.6951936 MHz
DECOUPLE H1, 499.8833915 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 19 min, 38 sec
Et
Et
Si
Et
O
Br
OH
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


Sample: xs-4-229
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.1 degrees
Acq. time 2.249 sec
Width 8011.8 Hz
8 repetitions
OBSERVE H1, 499.8808118 MHz
DATA PROCESSING
Resol. enhancement -6.0 Hz
FT size 65536
Total time 0 min, 30 sec
OH
Br
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm


Sample: xs-4-229-C
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: klt
VNMRS-500 "nmr15"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 30487.8 Hz
154 repetitions
OBSERVE C13, 125.6956979 MHz
DECOUPLE H1, 499.8833013 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min, 49 sec
OH
Br
O
Si
Et
Et
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Sample Name:
xs-4-217
Archive directory:
Sample directory:
FidFile: xs-4-217
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Mar 26 2012
OH
O
Si
Et
Et
Et
9
8
7
6
5
4
3
2
1
ppm


Agilent Technologies
Sample Name:
xs-4-217
Archive directory:
Sample directory:
FidFile: xs-4-217-C
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Mar 26 2012
OH
O
Si
Et
Et
Et
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm