The Thesis Committee for Nicholas P. Stafford
Certifies that this is the approved version of the following thesis:

Development of Iridium Catalyzed Enantioselective C-C Bond Coupling Reactions

APPROVED BY
SUPERVISING COMMITTEE:

Michael J. Krische, Supervisor

Kami L. Hull

Development of Iridium Catalyzed Enantioselective C-C Bond Coupling Reactions

by

Nicholas P. Stafford

Thesis

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Masters of Art

The University of Texas at Austin

December 2023

Dedication

To my grandfather Larry Spencer

Acknowledgements

I would first like to thank my parents. Mom and Dad, I would not be in the position I am today if it wasn't for the love and encouragement you both have always shown me. There are no words to describe how truly grateful I am for both of you. I would also like to thank my siblings, Chelsea, Jacob, Isiah, and Jesse. You four have always been a constant in my life, and I want to thank you all for the encouragement you have shown me in chasing after my dreams.

I must also thank Grandma Opal and Grandpa Larry. Without you both none of this could have been possible. Because of you both I have been able to achieve goals and dreams I never thought possible.

I would also like to acknowledge my advisor Michael Krische, without his help I would not be in the position I am in now. He is the reason I came to UT Austin, and I am happy to call Austin home now, and for that I will always be grateful.

I must also mention the friendships I have gained from all the members of the Krische group, I would not have made it this far without you all. I especially want to name: Eli, Dana, Zach, Melinda, Cole, Brian, Rosalie, Jon and Kate; you all have always been there when I needed you most, and I will always cherish the friendships we share.

Most importantly I want to thank my wife, Maisie, I am so lucky to have you in my life. You have always been my biggest supporter, and most importantly my best friend throughout this entire process. I am beyond blessed to be able to walk through life with you, and I am excited to see what other journeys we embark on together.

Abstract

Development of Iridium Catalyzed Enantioselective C-C Bond Coupling Reactions

Nicholas P. Stafford, M.A.

The University of Texas at Austin, 2023

Supervisor: Michael J. Krische

Developing new methods to construct enantiomerically enriched higher alcohols via direct C-C bond formation is still a challenge worth pursing in modern synthetic organic chemistry. Enantiomerically enriched alcohols are important due to the abundance of these motifs found in polyketide natural products, a class of molecules widely explored for their bioactive properties. This thesis focuses on the development of iridium catalyzed reductive coupling reactions of allylic acetates with ethanol and symmetric ketones.

Chapter 1 describes the utilization of ethanol, the world's most abundant renewable C-2 feedstock, and its first use as coupling partner in the enantioselective synthesis of higher secondary alcohols. Chapter 2 explains the first systematic study of utilizing symmetric ketones as coupling partners in the synthesis of α-stereogenic tertiary alcohols. Demonstration of the use of these methodologies for the synthesis of pharmacologically inspired molecules is shown through the functional group tolerance of all the top 10 *N*-heterocycles most commonly found in FDA approve drugs.

Table of Contents

List of Tables

List of Figures

Chapter 1: *Exploiting Ethanol as a Renewable C-2 Feedstock in Catalytic Enantioselective C-C Bond Formation*[*1]

1.1 INTRODUCTION

Nonrenewable resources serve as societies leading source for all energy needs, as well as, the primary source of carbon feedstock chemicals utilized in the chemical industry. It was reported in 2017, that of the 20.8 million tons of feedstock chemicals used in organic chemical manufacturing, only 13% were derived from renewable sources. While the remaining 87% originated from nonrenewable sources: crude oil, natural gas, and coal.[1] With societies increasing demands for energy and chemical manufacturing, using nonrenewable sources has become an issue due to the dwindling supplies of these resources, in addition to, the environmental impacts that comes from the increased carbon emissions associated with burning fossil fuels. Ethanol has gained popularity as a renewable replacement to alleviate the need for non-renewable resources. Ethanol is produced at >85 million tons per year, making it the largest volume renewable C-2 feedstock.[2,3] Majority of the worlds production of ethanol is used as a fuel, but its use as a chemical feedstock is widely unexplored. Examples for the potential of ethanol's use in largescale chemical manufacturing have been demonstrated with the Lebedev ethanol to butadiene process, and the process of using ethanol to produce propylene.[4,5] But ethanol's use in the synthesis of fine and commodity chemicals has been limited to synthesis of ethyl halides, ethyl esters, and other achiral compounds.[6-9] There are few examples of ethanol's use in catalytic carbon-carbon bond forming reactions, but these methods only produce achiral or racemic products. [10,11] The use of ethanol in catalytic asymmetric carbon-carbon

*This work is based of previously published work: Meyer, C. C., Stafford, N. P., Cheng, M. J., Krische, M. J. Ethanol: Unlocking an Abundant Renewable C2-Feedstock for Catalytic Enantioselective C−C Coupling. *Angew. Chem. Int. Ed*. **2021**, 60, 10542-10546. **Contributions:** C.C.M (50%), N. P. S. (30%), and M. J. C. (20%)

bond forming reaction remains absent from the literature.[12] Based off prior developed asymmetric catalytic methods of alcohol mediated carbonyl addition,[13] We report the first catalytic asymmetric conversion of ethanol to higher branched alcohols.

1.2 Reaction Development

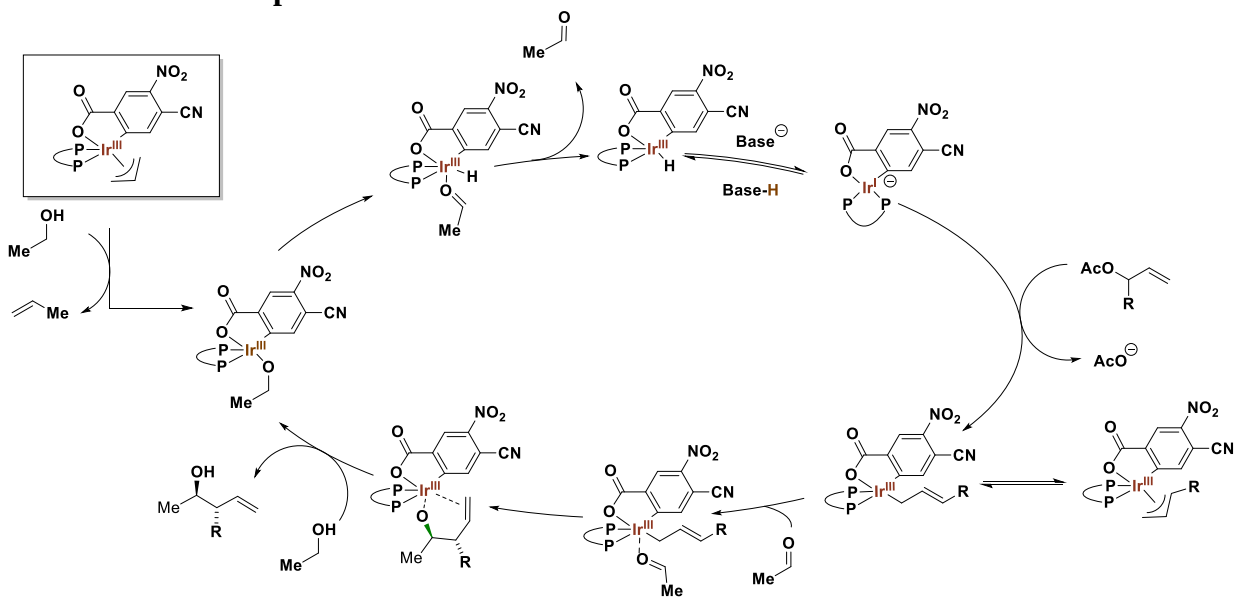
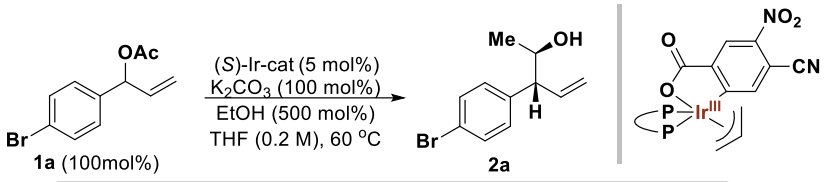


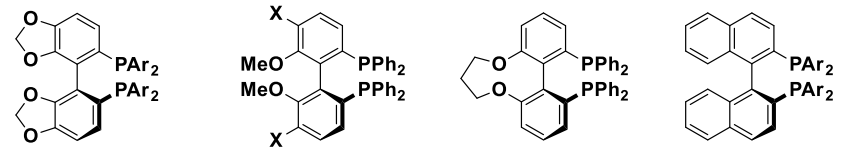
Figure 1.1: Proposed general mechanism of the enantioselective π-allyliridium-C,O-benzoate-catalyzed coupling of ethanol with substituted allylic acetate.

Prior work from the Krische group has pioneered the use of an iridium catalyst used for alcohol meditated asymmetric carbonyl additions of allylic acetate pro-nucleophiles.[15] Based off previous work a mechanism can be proposed for the enantioselective coupling of ethanol with substituted allyl acetates. First the pre-catalyst can be alleviated fof its π-allyl ligand by reacting with ethanol, to give off propene gas, and our reactive iridium-alkoxide. Beta-hydride elimination and ligand dissociation result in an iridium-hydride complex and acetaldehyde. The iridium hydride can then be deprotonated to give a square planar anionic iridium(I) species, that can then do an oxidative addition into the allylic acetate to for an allyliridium complex, which exists in equilibrium with its σ- and π-

haptomeric forms. The σ-allyliridium complex can then react with acetaldehyde to undergo carbonyl addition via a Zimmerman-Traxler like transition state. The resulting carbonyl addition product can be removed from the metal by alkoxide exchange with another molecule of ethanol. This gives off the resulting coupling product and regenerates the catalytic cycle. (Figure 1.1).



Entry	(S)-Ligand	Solvent	Results
1	BINAP	THF (0.2M)	13% Yield, 53% ee
2	DM-SEGPHOS	THF (0.2M)	44% Yield, 76% ee
3	SEGPHOS	THF (0.2M)	51% Yield, 82% ee
4	OMe-BIPHEP	THF (0.2M)	55%Yield, 76% ee
5	Cl,OMe-BIPHEP	THF (0.2M)	61% Yield, 86% ee
6	Cl,OMe-BIPHEP	MTBE (0.2M)	60% Yield, 90% ee
7	**Cl,OMe-BIPHEP**	**MTBE (0.4M)**	**75% Yield, 92% ee**



(*S*)-SEGPHOS, Ar = Ph
(*S*)-DM-DEGPHOS
Ar = 3,5-Me_2Ph

(*S*)-OMe-BIPHEP, X=H
(*S*)-Cl,OMe-BIPHEP, X=Cl

(*S*)-C_3-Tunephos

(*S*)-BINAP, Ar = Ph
(*S*)-tol-BINAP
Ar = 4-MePh

Table 1.1: Selected optimization experiments in the enantioselective π-allyliridium-*C*,*O*-benzoate-catalyzed coupling of ethanol with allylic acetate.[a]

[a]Yields are of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details. **Contributions:** Equal contributions by all authors.

From prior work with the "Krische catalyst," one ubiquitous factor of these reactions is the use of the alcohol pro-electrophile as the limiting reagent. This is an obstacle encountered from the onset of reaction development. We were striving to find conditions where the abundant starting material, ethanol, could be used in excess in comparison to the more

valuable allylic acetate. To implement these ideal reaction conditions, we would need to find a way to inhibit competing degradation side reaction of the allylic acetates, which can occur from protonolysis of the resulting π -allyliridium intermediate.[15b]

By first screening different chiral bidentate phosphine ligands modifying the iridium catalyst, in the reaction of ethanol with allylic acetate **1a** (table 1.1. entries 1-5) The greatest yields of **2a** were obtained using the π -allyliridium-C,O-benzoate catalyst with (S)-Cl,MeO-BIPHEP as its ligand (entry 5). (S)-Cl,MeO-BIPHEP being the most electron-deficient ligand may slow down the rate of π -allyl protonolysis, enabling higher conversion to **2a**. Reactions catalyzed by this ligand also displayed significantly higher enantioselectivity, which due to its electronic properties allows for a more Lewis acidic iridium, which potentially leads to shortened Ir-O and Ir-C bonds. Which in the transition state could enhance asymmetric induction. Further improvements were made by switching solvents to MTBE (entry 6) this increased the enantioselectivity of the reaction with a negligible loss in yield. The optimal reaction conditions were found by increasing concentration of the reaction, resulting in an increased isolated yield of **2a** (entry 7).

1.3 Results and Discussion

To further explore this methodology, the optimized conditions were then applied to the coupling of ethanol with a number of structurally diverse allylic acetates (Table 1.2). It was shown in a survey of U.S. FDA approved drugs, 59% of small molecule drugs incorporate N-heterocycles.[14] To demonstrate the potential utility of this method in the synthesis of small molecules for drug discovery, allylic acetates **1a-1y** incorporated the 10 most frequently encountered N-heterocycles in FDA approved drugs (beyond β-lactams). Products of ethanol-mediated C-C coupling **2a-2y** were formed in good yield with excellent levels of *anti*-diastereoselectivity and enantioselectivity. This includes allylic

acetates substituted by aryl and hetroaryl group, (**2a-2d, 2f-2o**)as well as alkyl (**2s-2y**) and cycloalkyl groups (**2p-2r**).

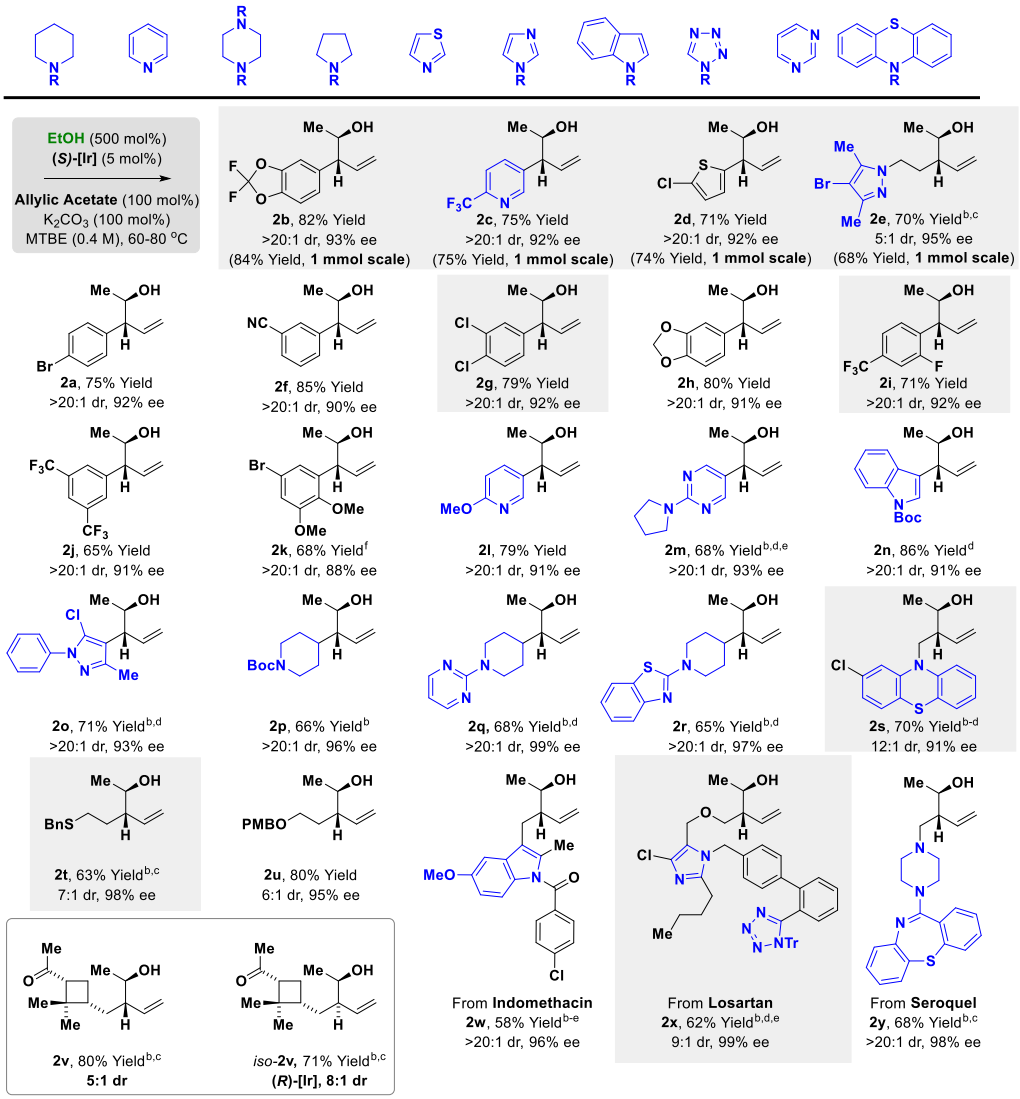


Table 1.2: Diastereo- and enantioselective π-allyliridium-C,O-benzoate-catalyzed coupling of ethanol with allylic acetates **1a-1y** to form homoallylic alcohols **2a-2y**.[a]

[a]Yields are of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details. [b]Acetone (1.0 M), [c](S)-Ir-IV, [d]EtOH (300 mol%), [e]K_2CO_3 (50 mol%), [f]K_2CO_3 (200 mol%). **Contributions**:Nicholas P. Stafford synthesized all highlighted examples

Of particular significance, due to the high functional group tolerance of the catalyst, direct asymmetric coupling of ethanal and allylic acetates derived from the FDA-approved drugs indomethacin (**2w**), losartan (**2x**) and seroquel (**2y**) could be achieved showing potential for this methods utilization for late-stage functionalization of clinical drug candidates.[16] The conversion of chiral allylic acetate **1v**, which is derived from (+)-α-pinene, to form products **2v** and *iso*-**2v** demonstrates how this method proceeds with high levels of catalyst-directed diastereoselectivity.

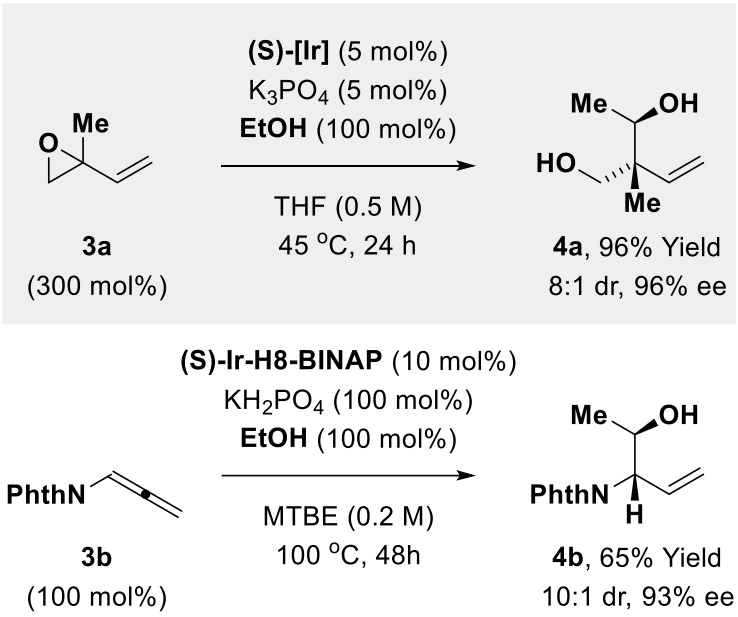


Figure 1.2: Exploring allyl pronucleophiles beyond allylic acetates. [a]

[a]Yields are of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details. **Contributions:** Nicholas P. Stafford synthesis of **4a** (highlighted)**,** Cole C. Meyer synthesis of **4b**.

Further explorations of this method show how aside from allylic acetates, the vinyl epoxide **3a**[17] and allenamide **3b**[18] are capable pronucleophiles, as illustrated by the formation of products **4a** and **4b**.

Another demonstration of this methods potential in drug discovery synthesis was shown, with selected products **2b**, **2c**, **2e**, **2n** and **2o** being converted into *N*-Boc-α-methylamines **5a**-**5f**, (Table 1.3). α-Methylphenethylamines, are bioactive molecules, and

their substructure appears in a number of clinical drug candidates.[19] For example, the FDA-approved drug tamulosin and the clinical candidates talampanel, taranabant and cipargamin all incorporate α-methylphenethylamine substructures, but they are all use to treat different diseases.[20] This functionalization proceeded in two steps. First, under Mitsunobu conditions **2b**, **2c**, **2e**, **2n** and **2o** were exposed to diphenylphosphoryl azide furnishing the corresponding azides with inversion of stereochemistry.[21] A one pot Staudinger reduction and amine protection gave the *N*-Boc α-methylamines **5a-5f.** (Table 1.3)

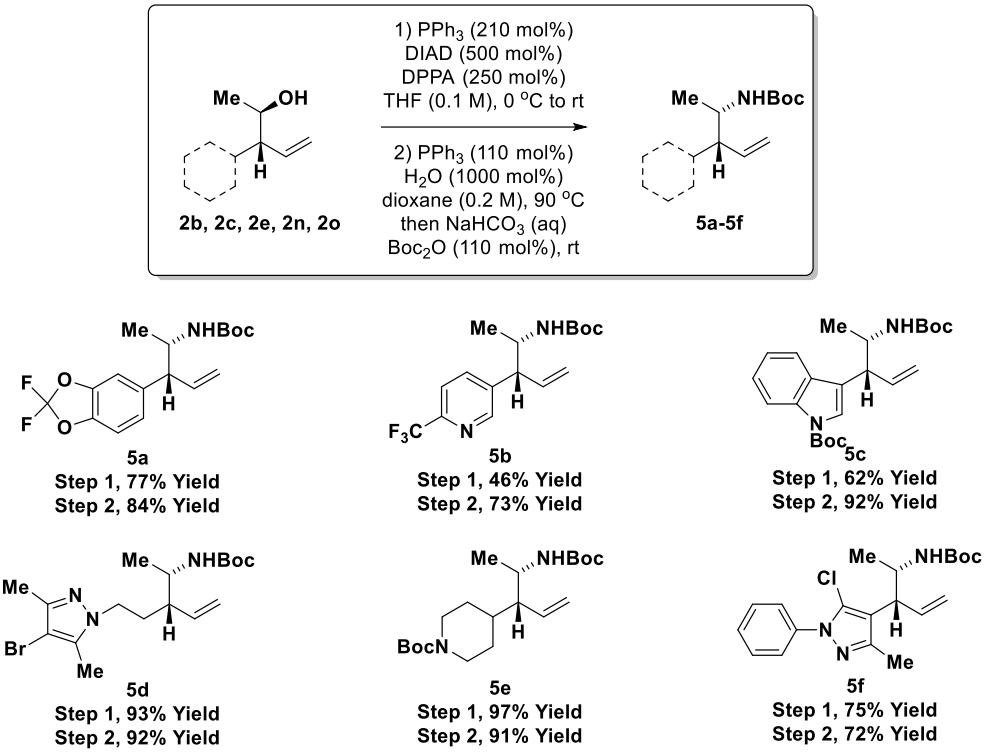


Table 1.3: Representative phenethyl amines and conversion of ethanol adducts to phenethylamines **5a-5f**.[a]

[a]Yields are of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details. **Contributions:** Synthesis of 5a-5f was conducted by Cole C. Meyer. Nicholas P. Stafford and Melinda J. Cheng helped synthesize intermediates and startingmaterialss

1.4 *CONCLUSION*

In conclusion, we report the first catalytic enantioselective C-C couplings of ethanol. The broad scope of this method is demonstrated by couplings with structurally complex, nitrogen-rich allylic acetates that incorporate the top 10 *N*-heterocycles found in FDA-approved drugs. Conversion of selected products to α-methylphenethylamines is described, further highlighting applicability of this method to drug discovery. This method requires no premetalated reagents and generates acetic acid as the sole stoichiometric byproduct. Given the increasing importance of iridium-catalyzed dehydrogenation in process R&D,[23] this work could potentially inspire other "green" catalytic methods for the atom-efficient conversion of renewable feedstocks to value-added products.

Chapter 2: *Synthesis of Chiral Oxetanes and Azetidines via Iridium-Catalyzed 2-Propanol-Mediated Reductive Coupling of Allylic Acetates*[2*]

2.1 INTRODUCTION

The development of catalytic methods for the enantioselective additions of carbon nucleophiles to ketones is still a challenge worth exploring in chemical synthesis.[23,24] The main challenges with these types of methods are due to the enhance stability of ketones when compared to aldehyde electrophiles, and the potential for reversible additions which can diminish kinetic selectivity of the reaction. Traditionally these issues are overcome by the use of premetalated reagents, that give a non-stabilized carbon nucleophile. When it comes to catalytic enantioselective ketone allylations allylmetal reagents incorporating boron, silicon, and tin have most commonly been employed.[25-27] The development of catalytic reductive coupling methods has allowed for the elimination of sacrificial premetalated reagents. Most notably being the Nozaki-Hiyama-Kishi ketone allylation, but even this reaction required the use of stoichiometric amounts of a zero-valent metal reductant.[26] The Buchwald group has developed enantioselective copper-catalyzed ketone allylations using allenes and dienes as pro-nucleophiles, this advancement still requires the use of stoichiometric amounts of a silane reductant.[27] A more ideal improvement to the prior art would be the use of inexpensive feedstock reductants such as hydrogen gas and isopropanol.[28] Unfortunately, applications of such reactions remain limited.[29] The second challenge with these types of reactions is the steric or electronic bias of the groups attached to the ketone leading to the enantioselectivity of these reactions.[24] This enantiodiscrimination is not applicable to symmetric ketones; therefore, requiring the π-

[*]This work is based of previously published work: Stafford, N. P., Cheng, M. J., Nguyen, D. D., Verboom, K.L., Krische, M. J. Chiral α-Stereogenic Oxetanols and Azetidinols via Alcohol-Mediated Reductive Coupling of Allylic Acetates: Enantiotopic π-Facial Selection in Symmetric Ketone Addition. *ACS Catal.* **2022,** *12,* 6172-6179.
Contributions: N. P. S. (50%), M. J. C. (20%), D. D. N. (15%), and K. L. V. (15%)

facial discrimination of the allylmetal nucleophile to solely drive enantioselectivity in these systems.[29] Due to these issues systematic studies of catalytic asymmetric additions to symmetric ketones remain unexplored, with only isolated examples of allylations and aldol additions having been reported.[24,26,30]

In this study we report the first systematic investigation of catalytic enantioselective additions to symmetric ketones, by utilizing the commercially available oxetanone **1a** and N-benzhydryl azetidinone **1b**. This method allows for a simple synthesis of chiral oxetanes and azetidines, which are functional groups commonly employed in pharmaceutical and agrochemical molecules, since these functional groups can serve as bioisosteres.[32-35]

2.2 Reaction Development

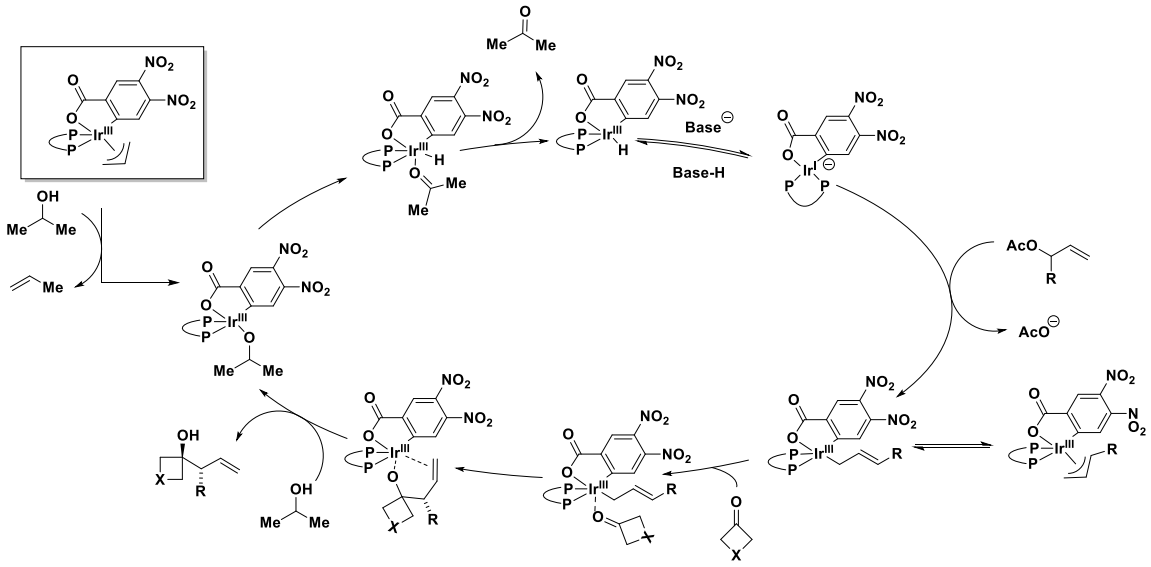
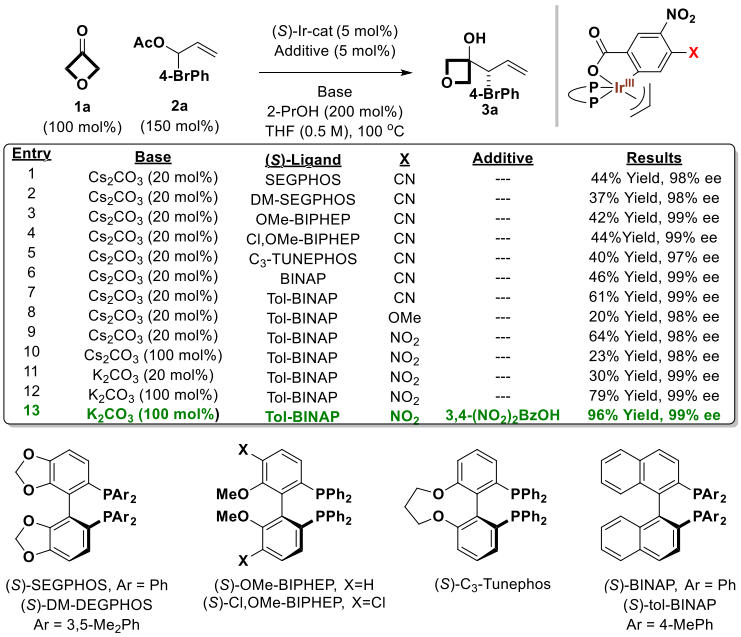


Figure 2.1: Proposed general mechanism of the enantioselective π-allyliridium-C,O-benzoate-catalyzed coupling of symmetric ketones with substituted allylic acetates

Based off prior work in the Krische group, the use of an iridium "Krische" catalyst capable of ketone allylations had been shown, so we believe we could further expand this chemistry into our method.[28] Based off previous work a mechanism can be proposed for

the enantioselective coupling of symmetric ketones with substituted allyl acetates. First the precatalyst can be alleviated for its π-allyl ligand by reacting with isopropanol, to give off propene gas, and our reactive iridium-alkoxide. Beta-hydride elimination and ligand dissociation result in an iridium-hydride complex and acetone. The iridium hydride can then be deprotonated to give a square planar anionic iridium(I) species, that can then do an oxidative addition into the allylic acetate to form an allyliridium complex, which exists in equilibrium with its σ- and π-haptomeric forms. The σ-allyliridium complex can then react with the symmetric ketone to undergo carbonyl addition via a Zimmerman-Traxler like transition state. The resulting carbonyl addition product can be removed from the metal by alkoxide exchange with another molecule of isopropanol. This gives off the resulting coupling product and regenerates the catalytic cycle. (Figure 2.1).



Entry	Base	(*S*)-Ligand	X	Additive	Results
1	Cs_2CO_3 (20 mol%)	SEGPHOS	CN	---	44% Yield, 98% ee
2	Cs_2CO_3 (20 mol%)	DM-SEGPHOS	CN	---	37% Yield, 98% ee
3	Cs_2CO_3 (20 mol%)	OMe-BIPHEP	CN	---	42% Yield, 99% ee
4	Cs_2CO_3 (20 mol%)	Cl,OMe-BIPHEP	CN	---	44%Yield, 99% ee
5	Cs_2CO_3 (20 mol%)	C_3-TUNEPHOS	CN	---	40% Yield, 97% ee
6	Cs_2CO_3 (20 mol%)	BINAP	CN	---	46% Yield, 99% ee
7	Cs_2CO_3 (20 mol%)	Tol-BINAP	CN	---	61% Yield, 99% ee
8	Cs_2CO_3 (20 mol%)	Tol-BINAP	OMe	---	20% Yield, 98% ee
9	Cs_2CO_3 (20 mol%)	Tol-BINAP	NO_2	---	64% Yield, 98% ee
10	Cs_2CO_3 (100 mol%)	Tol-BINAP	NO_2	---	23% Yield, 98% ee
11	K_2CO_3 (20 mol%)	Tol-BINAP	NO_2	---	30% Yield, 99% ee
12	K_2CO_3 (100 mol%)	Tol-BINAP	NO_2	---	79% Yield, 99% ee
13	**K_2CO_3 (100 mol%)**	**Tol-BINAP**	**NO_2**	**3,4-$(NO_2)_2$BzOH**	**96% Yield, 99% ee**

Table 2.1: Selected Optimization Experiments for the enantioselective π-allyliridium-C,O-benzoate-catalyzed coupling of symmetric ketones with substituted allylic acetates

[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further details. **Contribution:** this work was performed by Nicholas P. Stafford.

We first set out to explore the axially chiral chelating phosphine ligands modifying the iridium catalyst in the reaction of oxetanone **1a** with allylic acetate **2a** (Table 2.1, entries 1-7). The best result for this ligand screening was obtained using the cyclometalated π-allyliridium-C,O-benzoate complex derived from 4-cyano-3-nitrobenzoic acid and (S)-tol-BINAP, (S)-Ir-VII, which produced the oxetanol **3a** in 61% yield and 99% ee (Table 2.1, entry 7). By tuning the electronic properties of the C,O-benzoate moiety (Table 2.1, entries 7-9), an improved isolated yield of **3a** was observed using the more electron-deficient 3,4-dinitrobenzoate (Table 2.1, entry 9). The next improvement came from the screening of different bases, which revealed that the reaction using K_2CO_3 (100 mol%) had and improve isolated yield of **3a**, 79% (Table 2.1, entry 12). Finally, with a catalyst decomposition pathway known to occur via loss of the C,O- benzoate ligand, we used 3,4-dinitrobenzoic acid as an additive to potentially extend the lifetime of the catalyst. This proved to be beneficial improving the production of **3a** to 96% yield, while maintaining the 99% ee, giving us our optimized conditions.

2.3 Results and Discussion

With conditions working well for oxetanone **1a**, we set forth to see if the related ketones azetidinone **1b** and cyclobutanone **1c** (Figure 2.2) were competent coupling partners in this reaction. Azetidinone **1b** was subjected to the same conditions and furnished azetidinol **4a** in 65% yield and 98% ee, and with longer reaction times of 36 hours, yield could be improved to a 82% yield. When exploring cyclobutanone **1c**, we found it did not react under any conditions to give cyclobutene **5a.** Intrigued by the lack of reactivity we looked to find a rational for our results. We found that it had been determined by electron transmission spectroscopy, that there is a 10 Kcal/mol difference in LUMO energies between oxetanone **1a** (14 Kcal/mol) and cyclobutanone **1c** (24 Kcal/mol).[36]

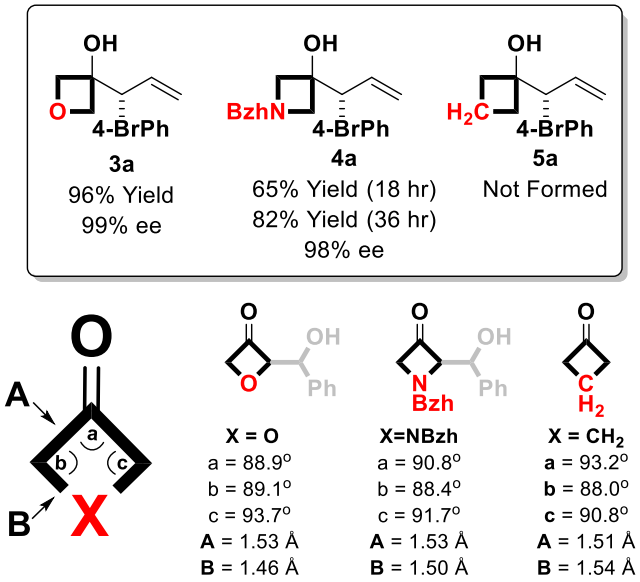


Figure 2.2: Enantioselective iridium-catalyzed reductive coupling of allylic acetate **2a** with oxetanone **1a**, azetidinone **1b** and cyclobutanone **1c,** and selected single crystal X-ray diffraction data[a]

[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further details. **Contributions:** All experiments for 3a, 4a, and 5a where conducted by Nicholas P. Stafford

Further evidence was corroborated by the findings in crystallographic data, the shorter carbon-heteroatom bond lengths of oxetanone **1a** (1.46 Å) and azetidinone **1b** (1.50 Å) compared to cyclobutanone **1c** (1.54 Å) appear to compress the angle between the C-C bonds: 88.9° vs 90.8° vs 93.2°, for **1a**, **1b** and **1c**.[37] We rationalize the change in reactivity towards reductive coupling being due to the increased angle strain and σ-inductive effects associated with heteroatom substitution.

After evaluating potential ketone coupling partners, the scope of allylic acetate coupling partners was explored. Our best conditions identified for the iridium catalyzed reductive coupling of allylic acetate **2a** with oxetanone **1a** or azetidinone **1b** were applied to diversly funcationalized allylic acetates **2a-2v**, these allylic acetates contained the 10 most frequently encountered N-heterocycles in FDA-approved drugs (beyond β-lactams) (Table 2.2).[38]

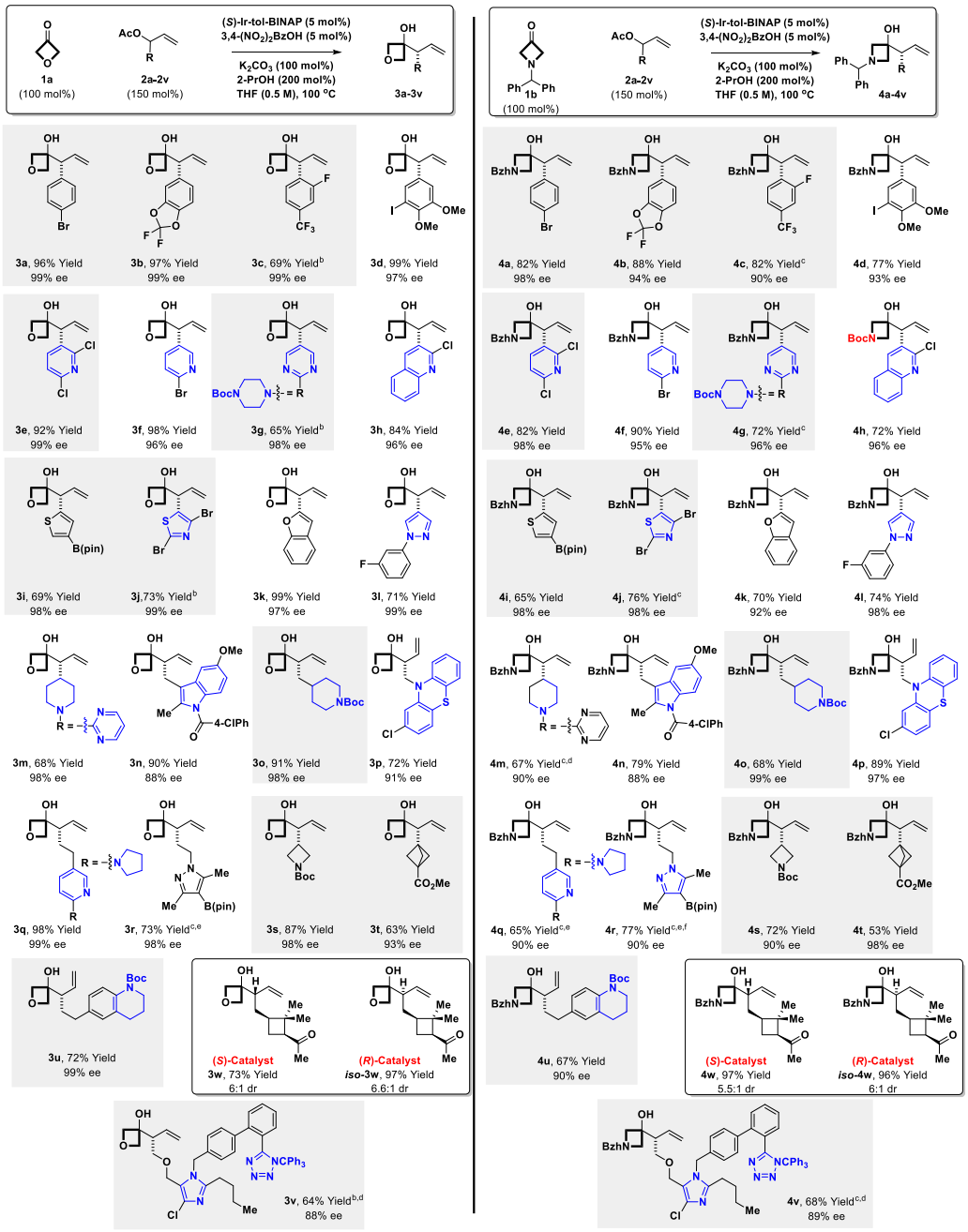


Table 2.2: Enantioselective iridium-catalyzed reductive couplings of allylic acetate **2a-2v** with oxetanone **1a**, and azetidinone **1b.**

[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. Standard conditions: 0.2 mmol scale, 18 h for **1a**, 36 h for **1b**. See Supporting Information for further experimental details. [b]24 h [c]48 h [d](*S*)-Ir-tol BINAP (7.5 mol %), [e](*S*)-Ir-SEGPHOS (5.0 mol%). [f]Derivatizatized as the 3,5-dinitrobenzoate for ee% determination.
Contributions: Nicholas P. Stafford synthesized all highlighted examples

This reaction proved to have a wide array of functional group compatibility, the coupling of oxetanone **1a** and azetidinone **1b** to allylic acetates with substituted aryl (**2a-2d**) and heteroaryl (**2e-2l)** groups, as well as alkyl (**2n-2r, 2u, 2v**) and cycloalkyl (**2m, 2s, 2t**) groups, produced oxetanols **3a-3v** and azetidinols **4a-4v** with high yields and superb levels of enantioselectivity. The synthesis of adducts derived from the FDA approved drugs indomethacin (**3n, 4n**) and losartan (**3v, 4v**) demonstrate promising potential for the use of this method in late-stage functionalization of drug discovery canidates.[39] The absolute stereochemistry of **3a-3v** and **4a-4v** was assigned in analogy to compound **3a** and **4a** which were determined via single-crystal X-ray diffraction. This reaction has also showed its compatibility to work from the alcohol oxidation state, for oxetanol **dihydro-1a** and azetidinol **dihydro-1b**, ketone allylation can be performed via hydrogen auto-transfer to furnish products **3a** and **4a**, but this reaction proved to be less efficient then from the ketone oxidation state (Figure 2.3, eq. 1 & 2).

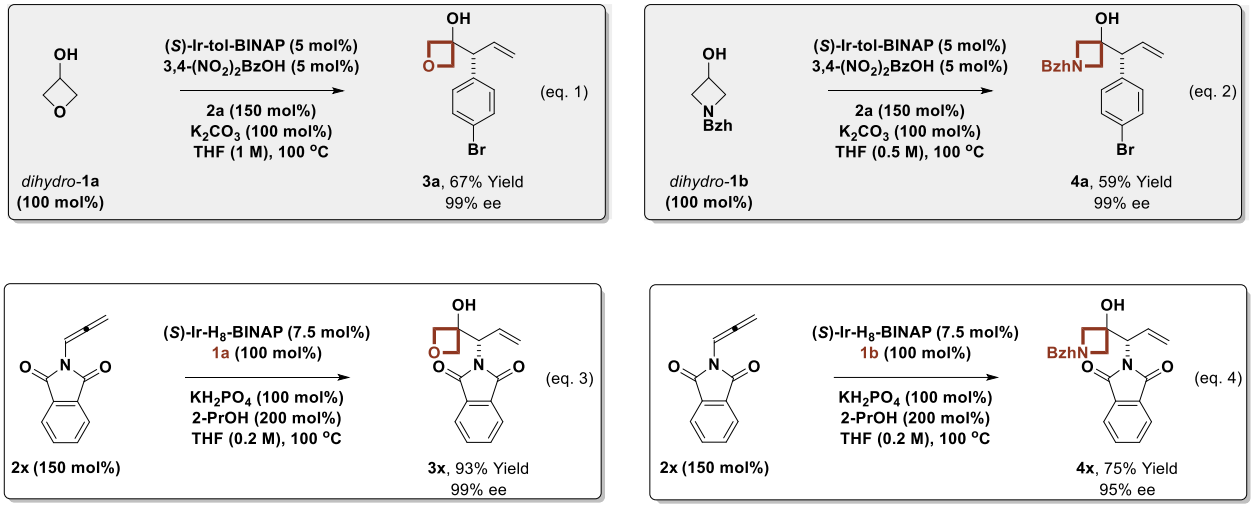


Figure 2.3: Exploring Reactions from the alcohol oxidations state and utilizing alleneamide pro-nucleophiles.

[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. **Contributions**: Nicholas P. Stafford eq. 1 and 2 (highlighted); Duong Nguyen Dinh eq 3 and 4.

When exploring carbon nucleophiles aside from allylic acetates, phthalimidoallene **2x** was found to be a competent pronucleophile, as demonstrated by the enantioselective synthesis of **3x** and **4x** (Figure 2.3, eq. 3 & 4).

2.4 *CONCLUSION*

In summary, we report the first systematic studies on enantioselective additions to symmetric ketones, as illustrated in iridium catalyzed reductive couplings of allylic acetates with oxetanone **1a** and N-benzhydryl azetidinone **1b**. This method provides access to chiral oxetanols and azetidinols containing a wide array of functional groups, especially those rich in nitrogen. Given the importance of oxetanes and azetidines as metabolically stable bioisosteres,[34,35] we believe this method has potential of access pharmacologically relevant motifs useful in drug discovery.[41]

Chapter 3 Supplementary Information

3.1 Chapter 1 Supplementary Information

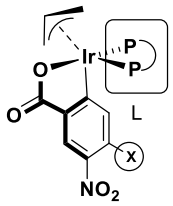
3.1a General Information

All reactions were carried out under inert gas atmosphere (nitrogen or argon) unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were oven dried followed by cooling in a desiccator or under a stream of inert gas prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Fischer Scientific, Sigma Aldrich, and Combi Blocks) without further purification. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still[1] or on a Teledyne Isco Combiflash Rf utilizing Silicycle HP column using a mobile phase composed of either hexanes/ethyl acetate, hexanes/acetone, dichloromethane/methanol, or another suitable solvent system.. Reactions were monitored by analytical thin-layer chromatography (TLC) using 0.25 mm commercial silica gel plates (Dyna.//mic Absorbents F). Visualization was accomplished with UV light followed by dipping in CAM, *p*- Anisaldehyde (PAA), Ninhydrin, or $KMnO_4$ stain solution followed by heating.

3.1b Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer using a diamond ATR unit. High-resolution mass spectra (HRMS) were obtained on a Agilent Technologies 6530 Accurate-Mass Q-TOF spectrometer (ESI) or on a Waters Micromass AutoSpec Ultima spectrometer (CI) and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M^+, $M+H^+$, $M+Na^+$, $M+Ag^+$), or a suitable fragment ion. Nuclear magnetic resonance (^1H, ^{13}C, ^{19}F, ^{31}P NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (400 MHz) or Varian INOVA (500 MHz) spectrometer equipped with a Bruker cryoprobe. The chemical shifts are given as parts per million (ppm) and were referenced to the residual solvent signal ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). Specific optical rotations were recorded on an Azzota Corp AP45 (589 nm) in $CHCl_3$. Solution concentrations are given in the units of 10^{-2} g mL^{-1}. Uncorrected melting points were measured on a Thomas Hoover Capillary Melting Point Apparatus. Absolute and relative configurations of products **2a-2y** were assigned in analogy to the single crystal diffraction data for **2p**.

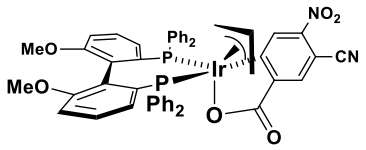
3.1c Detailed Procedure for Preparation of Iridium Complexes



General Procedure A

To a sealed tube equipped with a magnetic stir bar was added Cs_2CO_3 (200 mol%), disubstituted benzoic acid (200 mol%), bisphosphine ligand (100 mol%) and $[Ir(cod)Cl]_2$ (50 mol%). The reaction vessel was purged with argon and THF (0.1 M) was added followed by allyl acetate (250 mol%). The resulting mixture was stirred at room temperature for 30 min, then at 80 ˚C for 90 minutes. After cooling to ambient temperature, the mixture was filtered through celite with the aid of dichloromethane. The combined filtrate was concentrated *in vacuo* and subjected to flash column chromatography (DCM:THF). The resulting gum-like residue was dissolved in THF (2.0 mL). Addition of HPLC grade hexanes (20 mL) led to formation of a precipitate. The product was filtered and washed with HPLC grade hexanes, followed by removal of trace amount of solvent *in vacuo*, to provide a light yellow powder.

Complex (*S*)-Ir-IV



Procedure

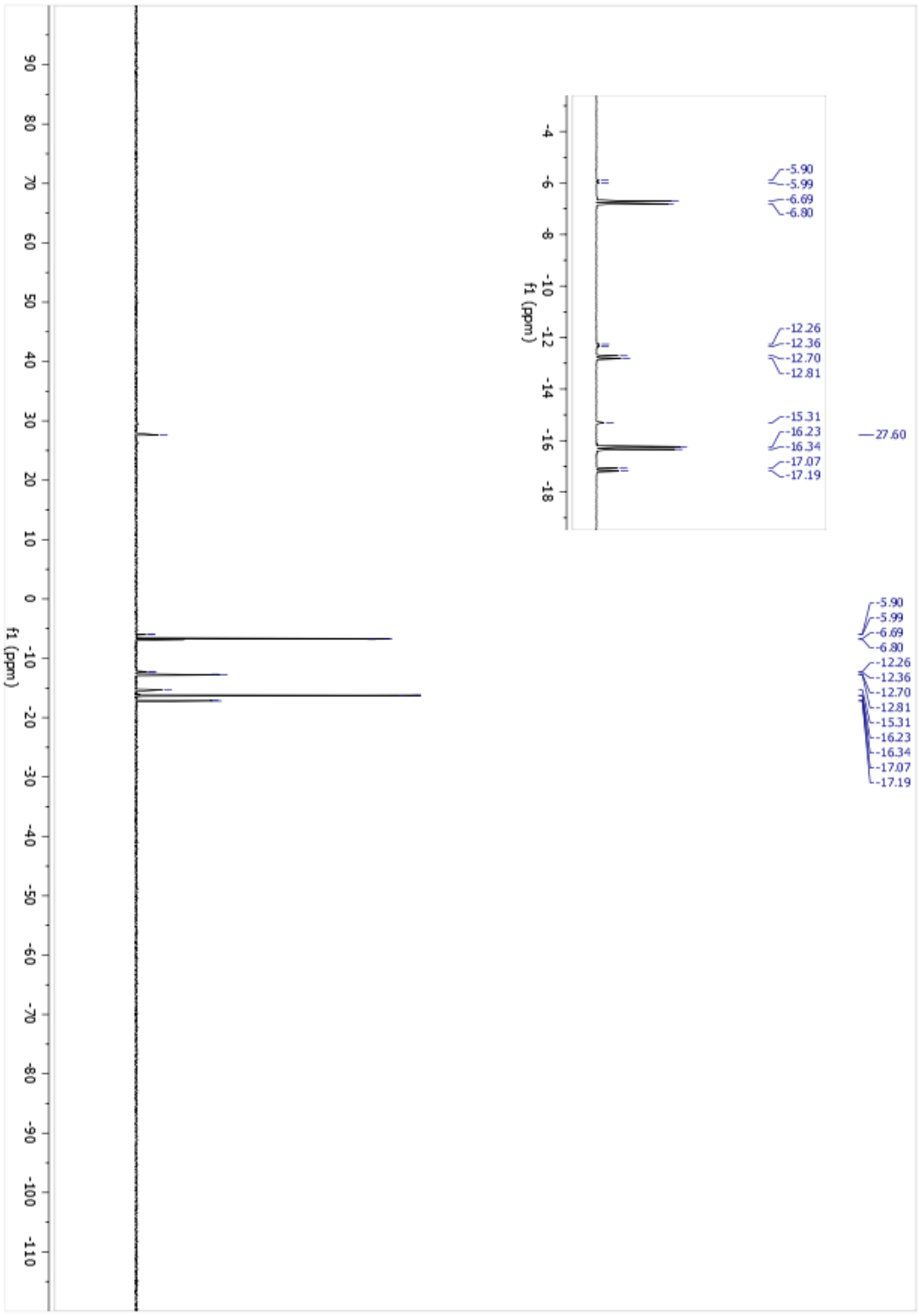
Cs_2CO_3 (401 mg, 1.23 mmol, 200 mol%), 3-cyano-4-nitrobenzoic acid (236 mg, 1.23 mmol, 200 mol%), (*S*)- MeO-BIPHEP (397 mg, 0.610 mmol, 100 mol%), $[Ir(cod)Cl]_2$ (206 mg, 0.310 mmol, 50 mol%), THF (6.1 mL), and allyl acetate (0.166 mL, 1.53 mmol, 250 mol%) were subjected to general procedure A (FCC: DCM:THF = 20:1) to provide **(*S*)-Ir-IV** as a light yellow powder (442 mg, 0.439 mmol) in 72% yield.

^{31}P NMR (202 MHz, $CDCl_3$) δ = 27.6, -5.9 (d, *J* = 18.6 Hz), -6.8 (d, *J* = 21.9 Hz), -12.3 (d, *J* = 18.6 Hz), -12.8 (d, *J* = 23.6 Hz), -15.3, -16.3 (d, *J* = 21.9 Hz), -17.1 (d, *J* = 23.6 Hz).

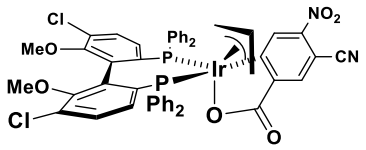
HRMS (ESI): Calculated for $C_{49}H_{39}IrN_2O_6P_2$ [M+Na$^+$] = 1029.1808, Found 1029.1800.

$[\alpha]_D^{28}$= -51.7 (*c* 0.14, $CHCl_3$).

MP: 225-230 °C (decomposes).


f1 (ppm)
-5.90
-5.99
-6.69
-6.80
-12.26
-12.36
-12.70
-12.81
-15.31
-16.23
-16.34
-17.07
-17.19
27.60

Complex (*S*)-Ir-V



Procedure

Cs_2CO_3 (978 mg, 3.00 mmol, 200 mol%), 3-cyano-4-nitrobenzoic acid (576 mg, 3.00 mmol, 200 mol%), (*S*)-Cl,MeO-BIPHEP (977 mg, 1.50 mmol, 100 mol%), $[Ir(cod)Cl]_2$ (504 mg, 0.750 mmol, 50 mol%), THF (15.0 mL), and allyl acetate (0.405 mL, 3.75 mmol, 250 mol%) were subjected to general procedure A (FCC: DCM:THF = 20:1) to provide **(*S*)-Ir-V** as light yellow powder (1.21 g, 1.13 mmol) in 75% yield.

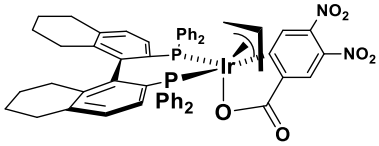
HRMS (ESI): Calculated for $C_{49}H_{37}Cl_2IrN_2O_6P_2$ $[M+H^+]$ = 1075.1179, Found 1075.1195.

$\mathbf{[\alpha]_D^{28}}$**=** -4.2 (*c* 0.24, $CHCl_3$).

MP: 187-192 °C (decomposes).

The spectral data recorded for the compound was in complete agreement with the literature.[45]

Complex (*S*)-Ir-H_8-BINAP

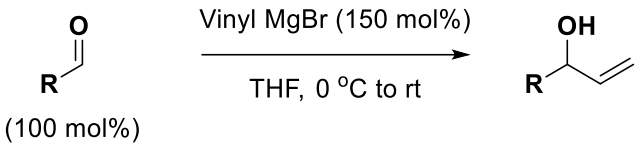


The preformed catalyst **(*S*)-Ir-H_8-BINAP** was prepared following our previously reported literature procedure (75% yield).[3] The spectral data recorded for the compound was in complete agreement with the literature.

3.1d. Procedures and Spectral Data for Synthesis of Allylic Alcohols S1a-S1y

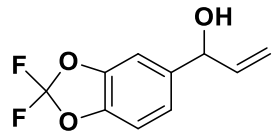
Allylic alcohol precursors **S1a**,[47] **S1g**,[48] **S1h**,[47] **S1j**,[49] **S1l**,[47] **S1n**,[50] **S1p**,[51] **S1t**,[51] and **S1u**[47] were synthesized in the manner previously reported. The obtained products were identical in all respects to the compounds reported the literature.

General Procedure B



An oven-dried round bottom flask equipped with a magnetic stir bar was charged with aldehyde (100 mol%). The flask was purged with argon and anhydrous THF (0.1 M) was added. A solution of vinyl magnesium bromide (1.0 M in THF, 150 mol%) was added at 0 °C via syringe. Following addition, the reaction was allowed to warm to ambient temperature and was monitored by TLC until the starting material was fully consumed. Upon completion of the reaction, the solution was diluted with diethyl ether and was quenched with aqueous saturated NH_4Cl solution. The biphasic mixture was poured into a separatory funnel and mixed thoroughly. The organic layer was separated, and the aqueous layer was extracted three times with diethyl ether. The organics were combined and subjected to sequential washes with water and saturated aqueous brine solution. The organic layer was separated and treated with anhydrous sodium sulfate. The organic solution was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The residue was directly subjected to flash column chromatography to afford allylic alcohols.

1-(2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-ol (S1b)



Procedure

2,2-Difluorobenzo[d][1,3]dioxole-5-carbaldehyde (930 mg, 5.00 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 64% yield (682 mg, 3.18 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.41 (hexanes: ethyl acetate = 4:1).

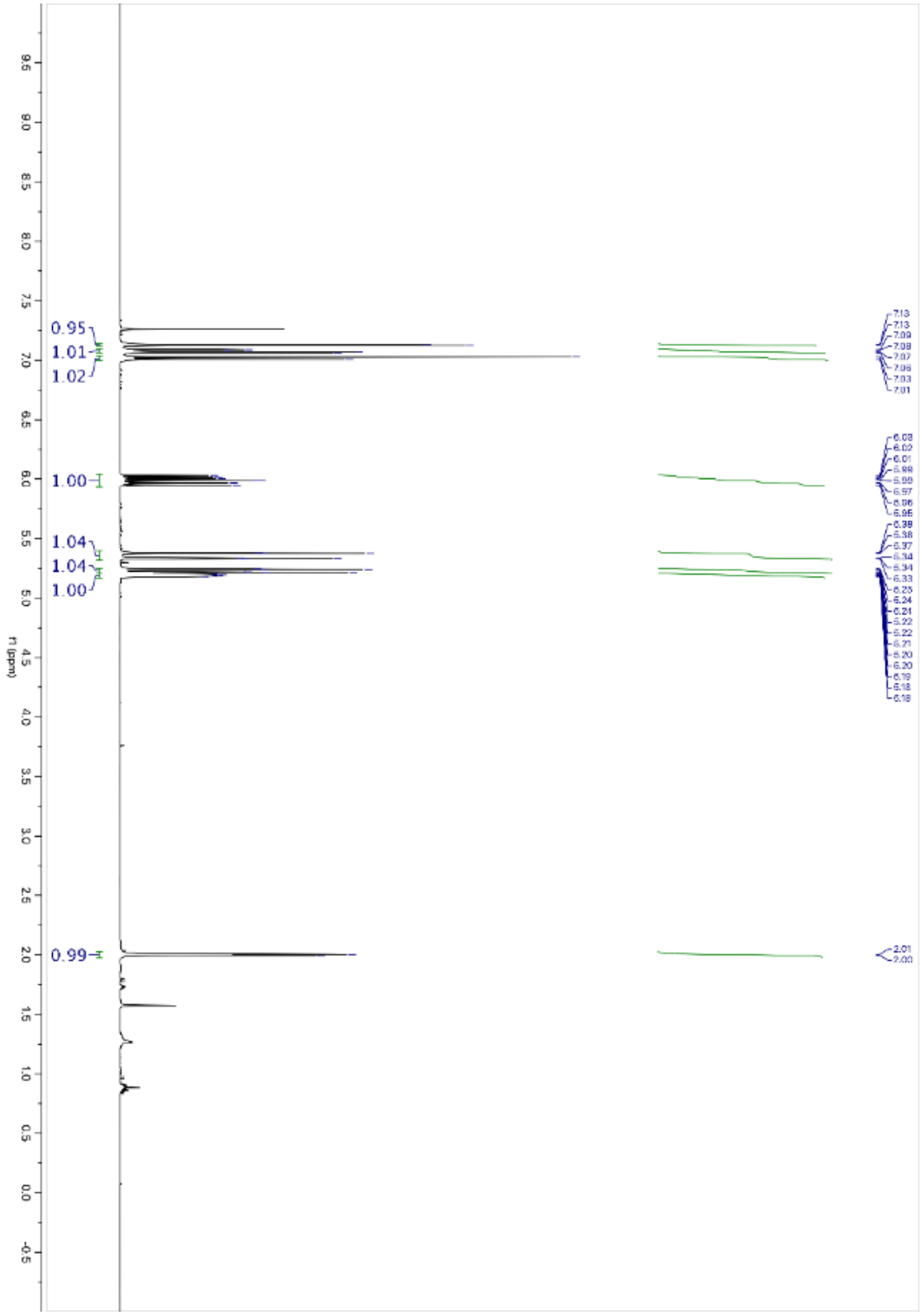
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.13 (d, *J* = 1.7 Hz, 1H), 7.08 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 1H), 5.99 (ddd, *J* = 17.1, 10.3, 6.1 Hz, 1H), 5.36 (dt, *J* = 17.1, 1.3 Hz, 1H), 5.23 (dt, *J* = 10.3, 1.3 Hz, 1H), 5.21 – 5.17 (m, 1H), 2.00 (d, *J* = 3.4 Hz, 1H).

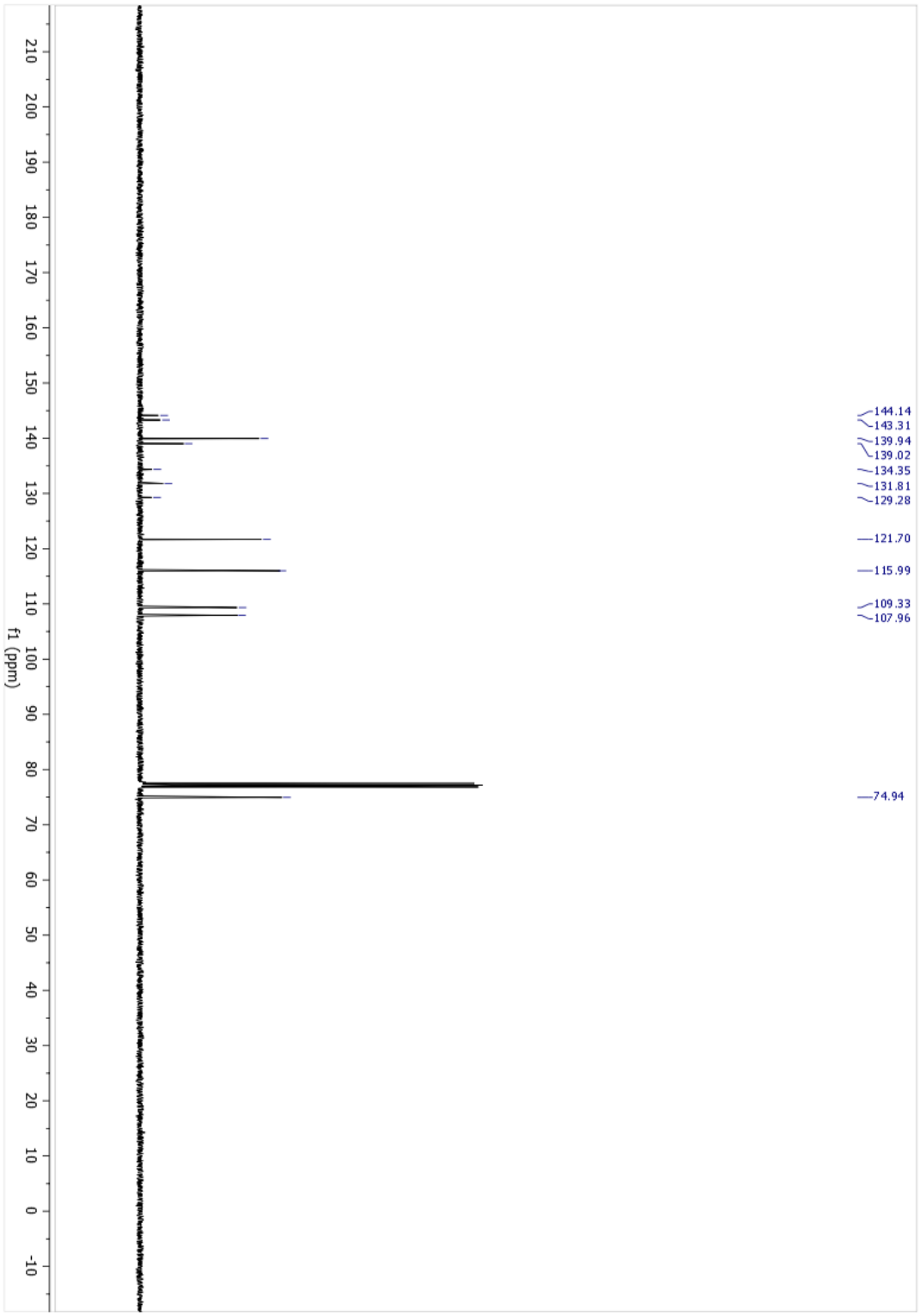
^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.1, 143.3, 139.9, 139.0, 131.8 (t, *J* = 256.5 Hz), 121.7, 116.0, 109.3, 108.0, 74.9.

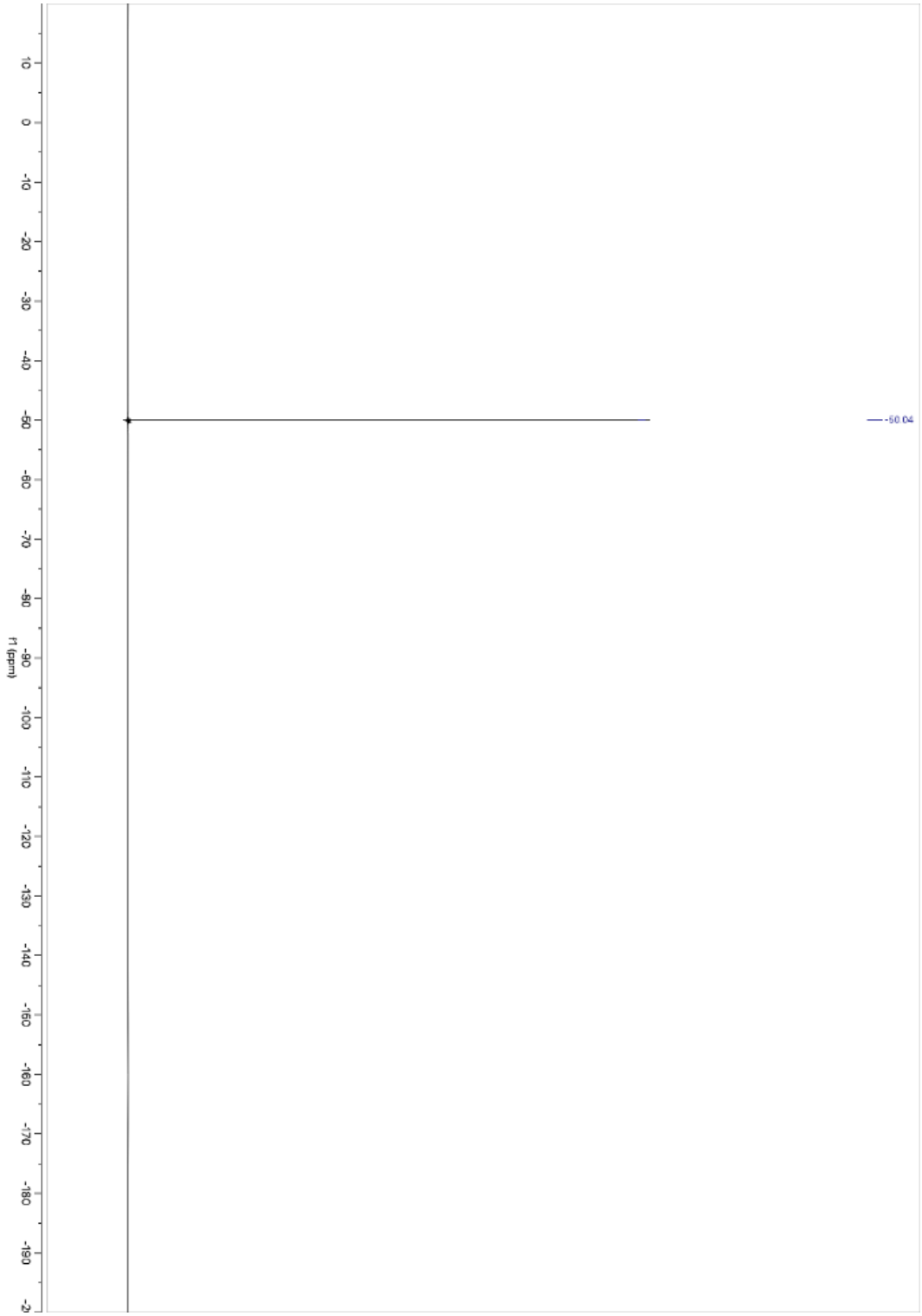
^{19}F NMR (376 MHz, $CDCl_3$) δ = -50.0.

HRMS (CI): Calculated for $C_{10}H_8F_2O_3$ [M+Na^+] = 214.0442, Found 214.0440.

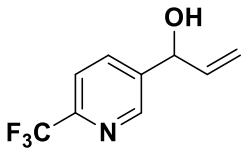
FTIR (neat): 3374, 2981, 1466, 1375, 1275, 1125, 1169, 994, 892, 708, 697, 682 cm^{-1}.


0.95
1.01
1.02
1.00
1.04
1.04
1.00
0.99
f1 (ppm)


144.14
143.31
139.94
139.02
134.35
131.81
129.28
121.70
115.99
109.33
107.96
74.94
f1 (ppm)


10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-2
f1 (ppm)
-50.04

1-(6-(trifluoromethyl)pyridin-3-yl)prop-2-en-1-ol (S1c)



Procedure

6-(Trifluoromethyl)nicotinaldehyde (1.00 g, 5.71 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 54% yield (621 mg, 3.06 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.30 (hexanes: ethyl acetate = 2:1).

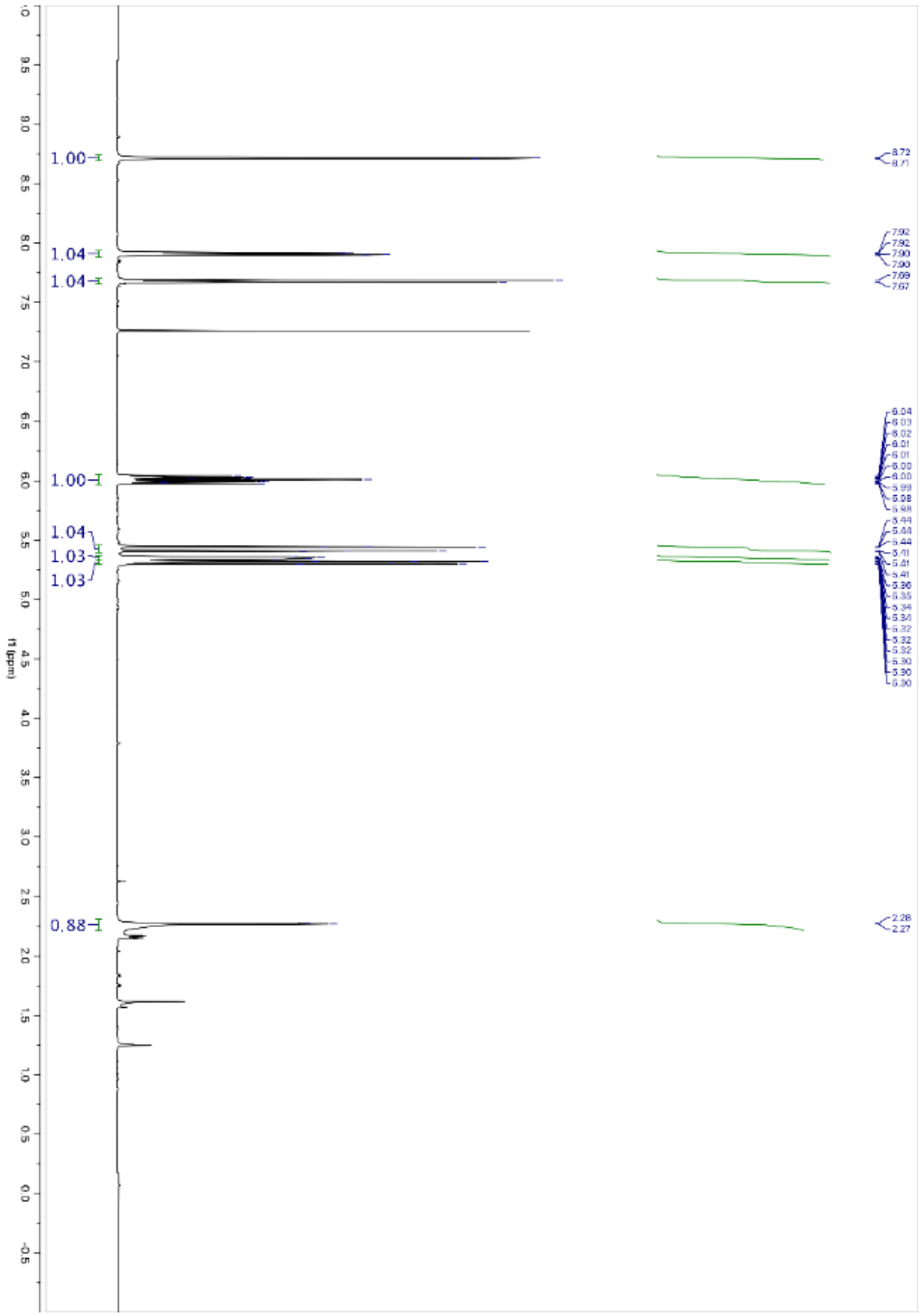
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.71 (d, *J* = 2.3 Hz, 1H), 7.91 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 6.01 (ddd, *J* = 16.8, 10.2, 6.5 Hz, 1H), 5.43 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.35 (dd, *J* = 6.9, 3.1 Hz, 1H), 5.31 (dd, *J* = 10.2, 1.2 Hz, 1H), 2.27 (d, *J* = 3.6 Hz, 1H).

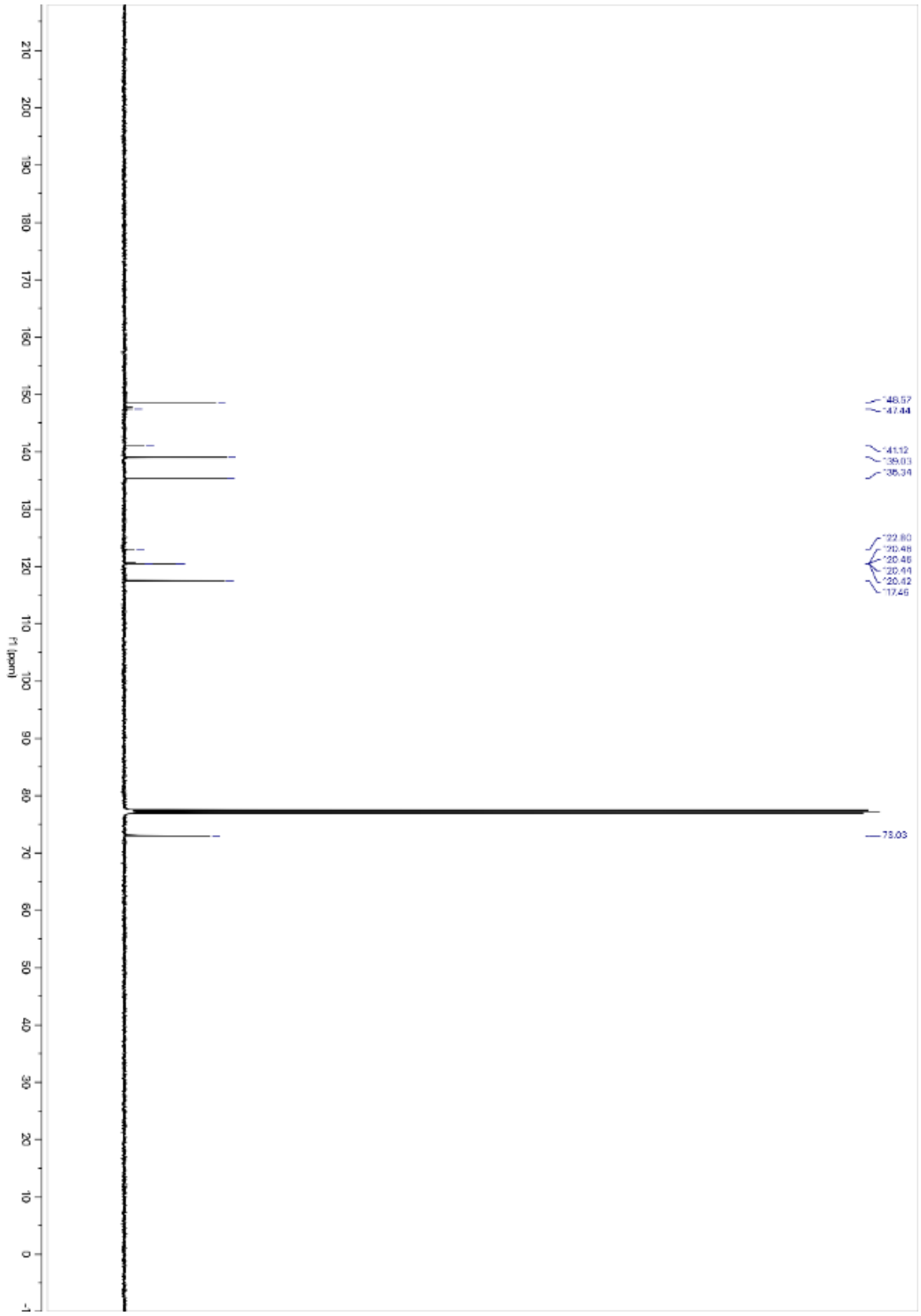
^{13}C NMR (126 MHz, $CDCl_3$) δ = 148.6, 147.4, 141.1, 139.0, 135.3, 122.8, 120.5, 120.5, 120.4, 120.4, 117.5, 73.0.

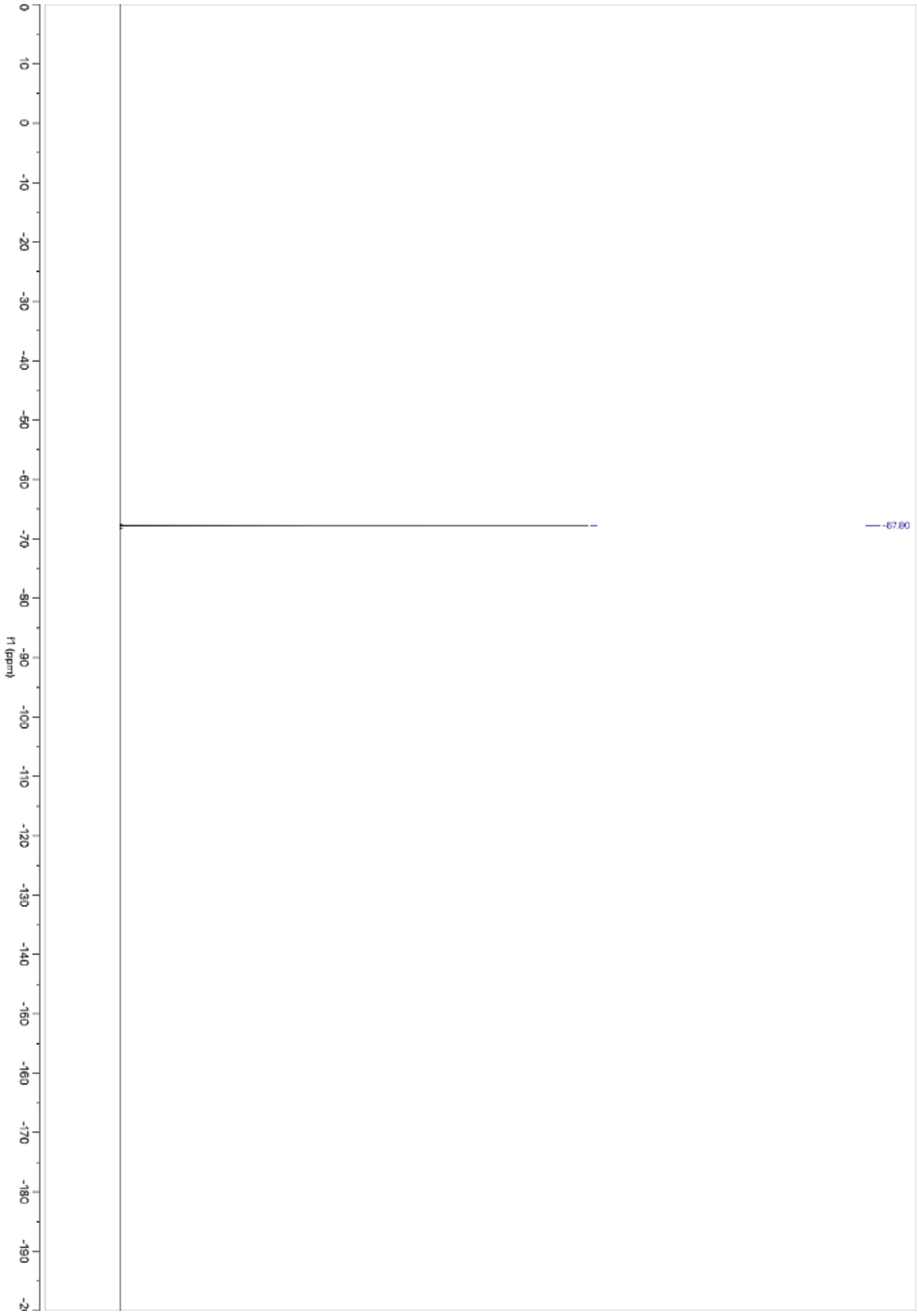
^{19}F NMR (471 MHz, $CDCl_3$) δ -67.8.

HRMS (ESI): Calculated for $C_9H_8F_3NO$ [M+H$^+$] = 204.0631, Found 204.0633.

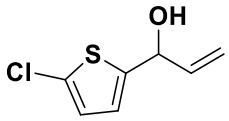
FTIR (neat): 3313, 2359, 1584, 1397, 1334, 1247, 1176, 1132, 1084, 1026, 989, 930, 859, 833, 783, 706 cm^{-1}.


1.00
1.04
1.04
1.00
1.04
1.03
1.03
0.88
f1 (ppm)


f1 (ppm)
148.57
147.44
141.12
139.03
136.34
122.80
120.48
120.45
120.41
120.42
117.46
78.03


-67.80
f1 (ppm)

1-(5-chlorothiophen-2-yl)prop-2-en-1-ol (S1d)



Procedure

5-Chlorothiophene-2-carbaldehyde (1.00 g, 6.82 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 76% yield (904 mg, 5.17 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1-10:1).

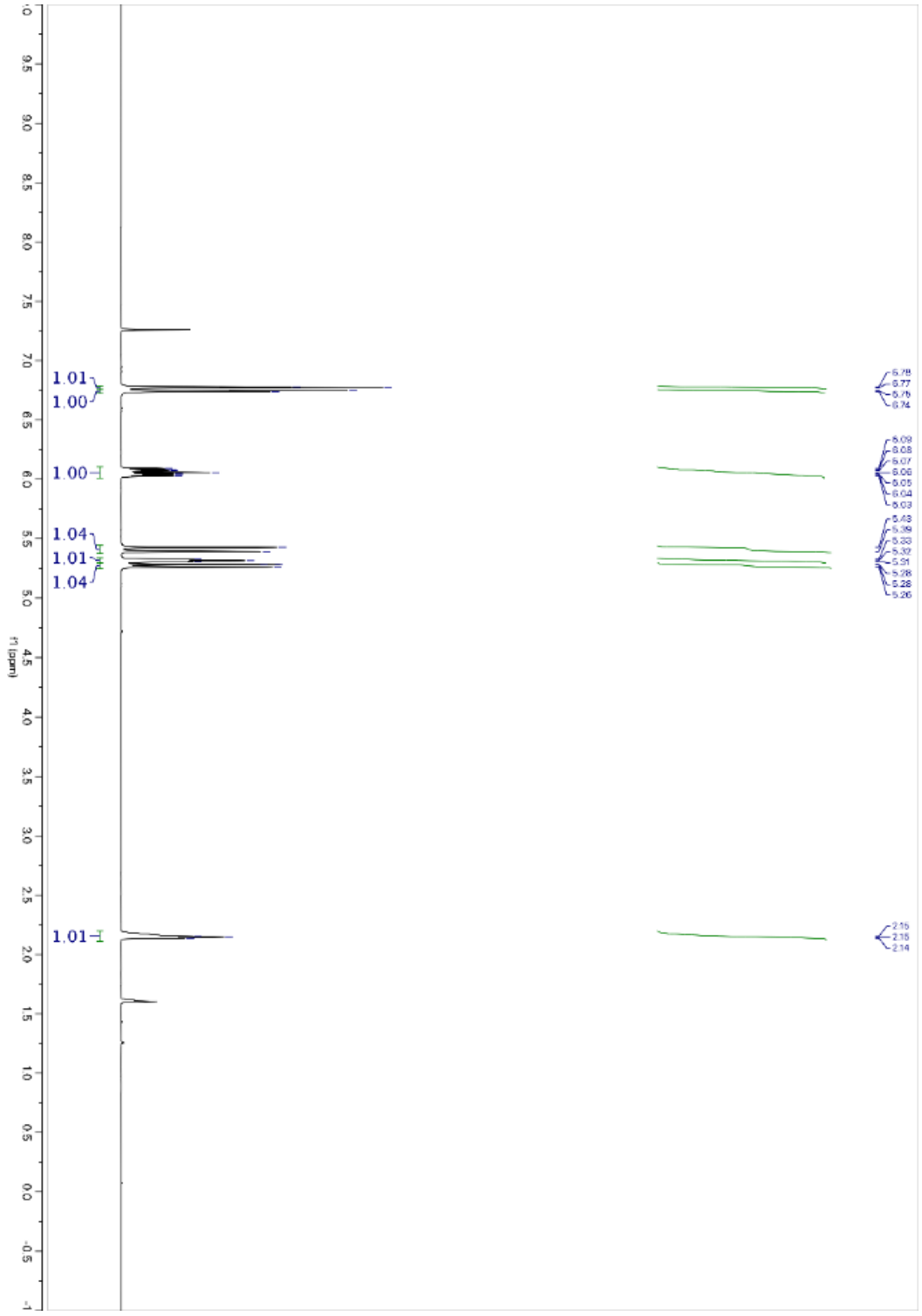
TLC (SiO_2) R_f = 0.54 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.78 (d, *J* = 3.6 Hz, 1H), 6.74 (d, *J* = 3.8 Hz, 1H), 6.06 (ddd, *J* = 16.7, 10.3, 6.0 Hz, 1H), 5.41 (d, *J* = 17.1 Hz, 1H), 5.32 (t, *J* = 5.4 Hz, 1H), 5.29 – 5.23 (m, 1H), 2.15 (t, *J* = 4.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 145.4, 138.8, 130.1, 126.0, 123.9, 116.6, 71.4.

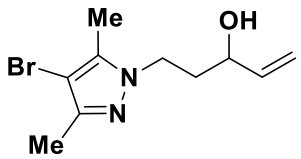
HRMS (EI): Calculated for C_7H_7ClOS [M+] = 173.9906, Found 173.9901.

FTIR (neat): 3321, 2861, 1643, 1449, 1420, 1260, 1212, 1161, 1106, 1060, 1027, 988, 930, 794, 716 cm^{-1}.


1.01
1.00
1.00
1.04
1.01
1.04
1.01
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
145.40
138.82
130.13
125.95
123.85
116.57
71.38

5-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)pent-1-en-3-ol (S1e)



Procedure

3-(4-Bromo-3,5-dimethyl-1H-pyrazol-1-yl)propanal (2.63 g, 11.4 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 34% yield (1.01 g, 3.88 mmol) as a colorless gel after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–2:1).

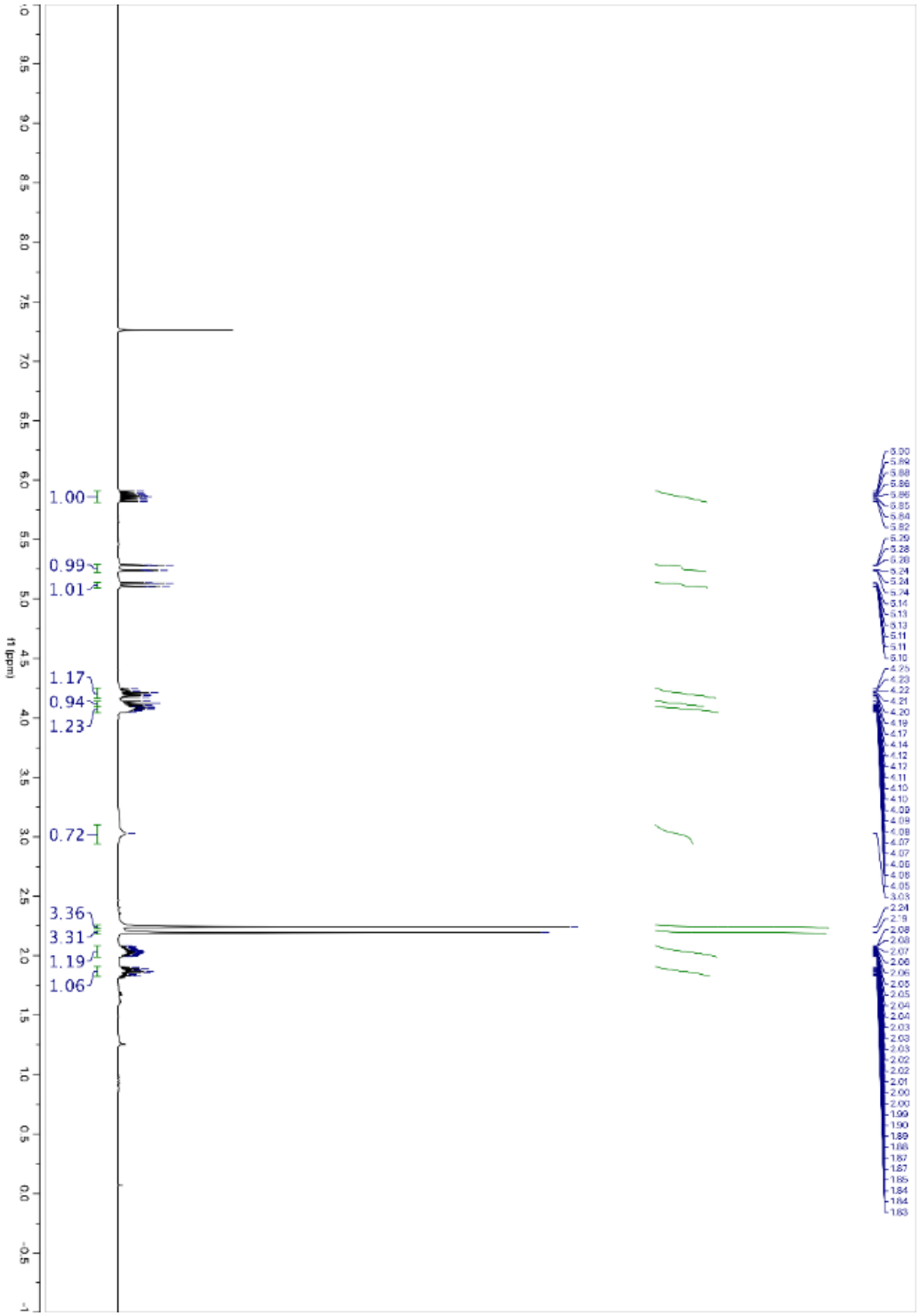
TLC (SiO_2) R_f = 0.27 (hexanes: ethyl acetate = 1:1).

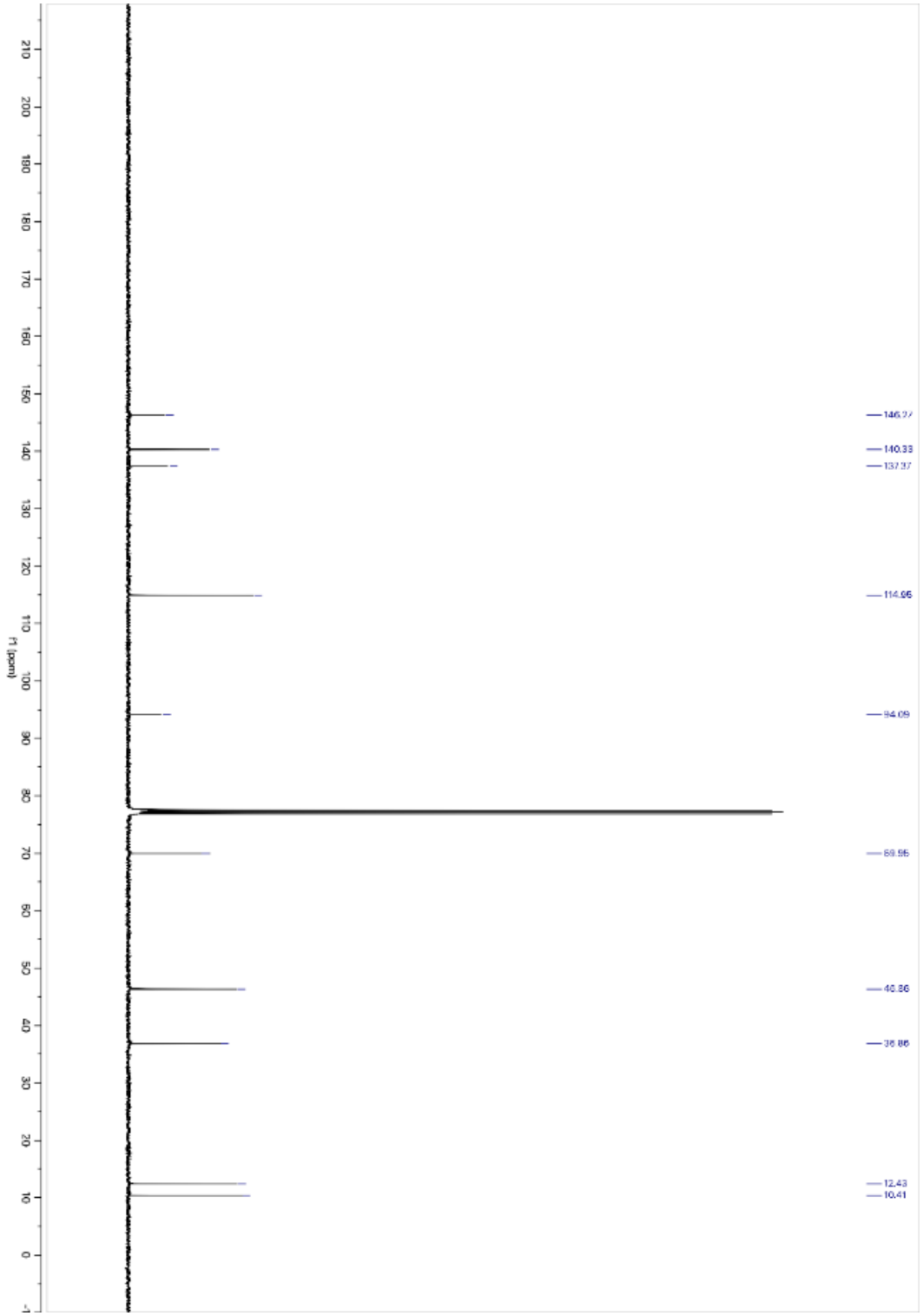
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.86 (ddd, *J* = 17.3, 10.5, 5.5 Hz, 1H), 5.26 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.12 (dt, *J* = 10.5, 1.4 Hz, 1H), 4.21 (ddd, *J* = 14.4, 8.6, 5.9 Hz, 1H), 4.14 – 4.10 (m, 1H), 4.07 (td, *J* = 6.6, 2.3 Hz, 1H), 3.03 (s, 1H), 2.24 (s, 3H), 2.19 (s, 3H), 2.04 (dddd, *J* = 14.2, 8.7, 6.3, 3.7 Hz, 1H), 1.93 – 1.79 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.3, 140.3, 137.4, 115.0, 94.1, 70.0, 46.4, 36.9, 12.4, 10.4.

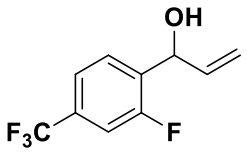
HRMS (ESI): Calculated for $C_{10}H_{15}BrN_2O$ [M+H$^+$] = 259.0441, Found 259.0439.

FTIR (neat): 3242, 2922, 2355, 2343, 1720, 1645, 1579, 1546, 1475, 1424, 1386, 1305, 1070, 994, 925, cm^{-1}.


1.00
0.99
1.01
1.17
0.94
1.23
0.72
3.36
3.31
1.19
1.06
f1 (ppm)


f1 (ppm)
146.27
140.33
137.37
114.96
94.09
69.96
40.86
36.86
12.43
10.41

1-(2-fluoro-4-(trifluoromethyl)phenyl)prop-2-en-1-ol (S1i)



Procedure

2-Fluoro-4-(trifluoromethyl)benzaldehyde (960 mg, 4.99 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 66% yield (791 mg, 3.59 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–15:1).

TLC (SiO_2) R_f = 0.40 (hexanes: ethyl acetate = 4:1).

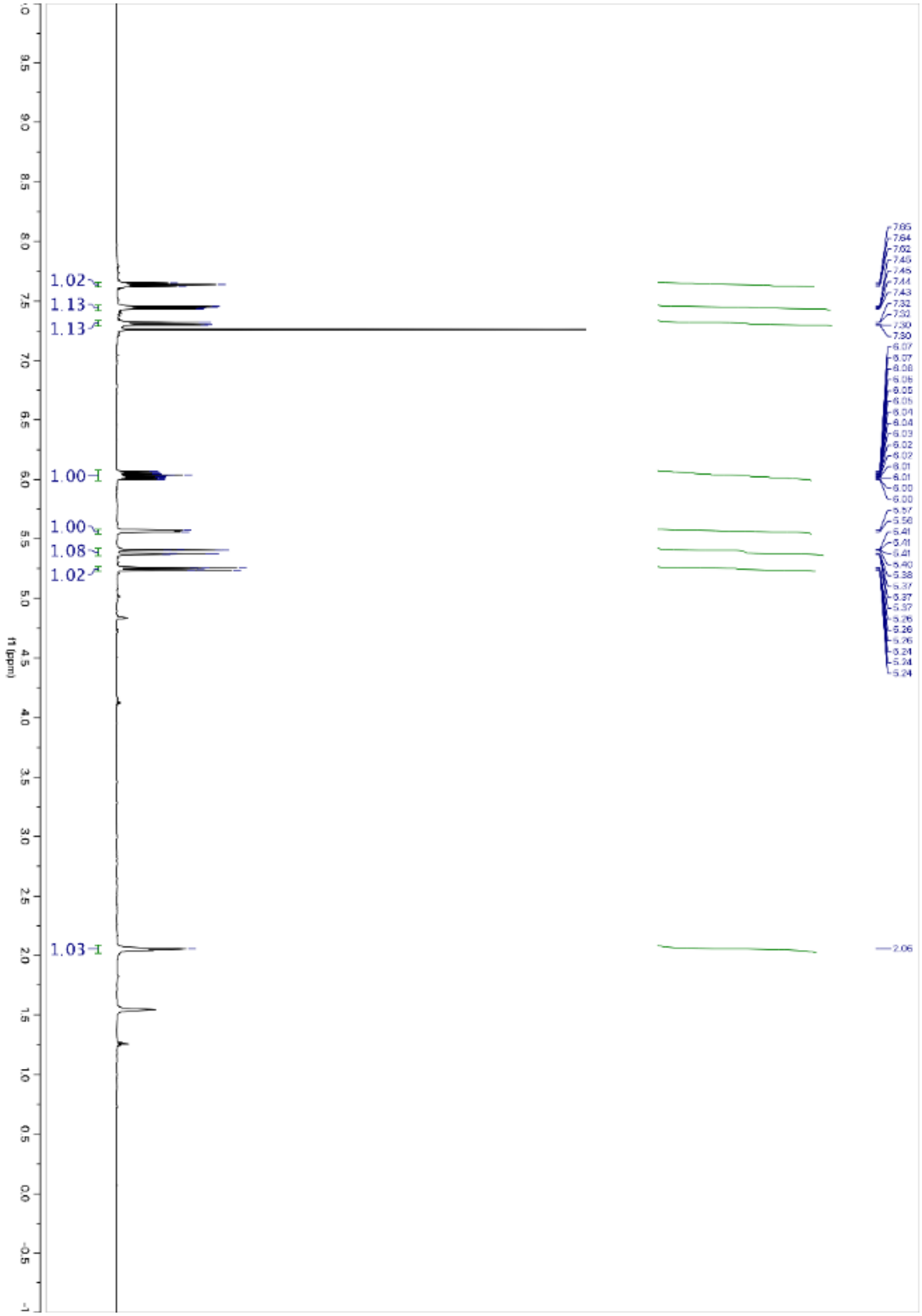
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.64 (t, *J* = 7.6 Hz, 1H), 7.44 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.31 (dd, *J* = 10.1, 1.7 Hz, 1H), 6.04 (dddd, *J* = 17.0, 10.3, 5.8, 0.8 Hz, 1H), 5.57 (d, *J* = 5.8 Hz, 1H), 5.39 (dq, *J* = 17.0, 1.2 Hz, 1H), 5.25 (dt, *J* = 10.3, 1.2 Hz, 1H), 2.06 (s, 1H).

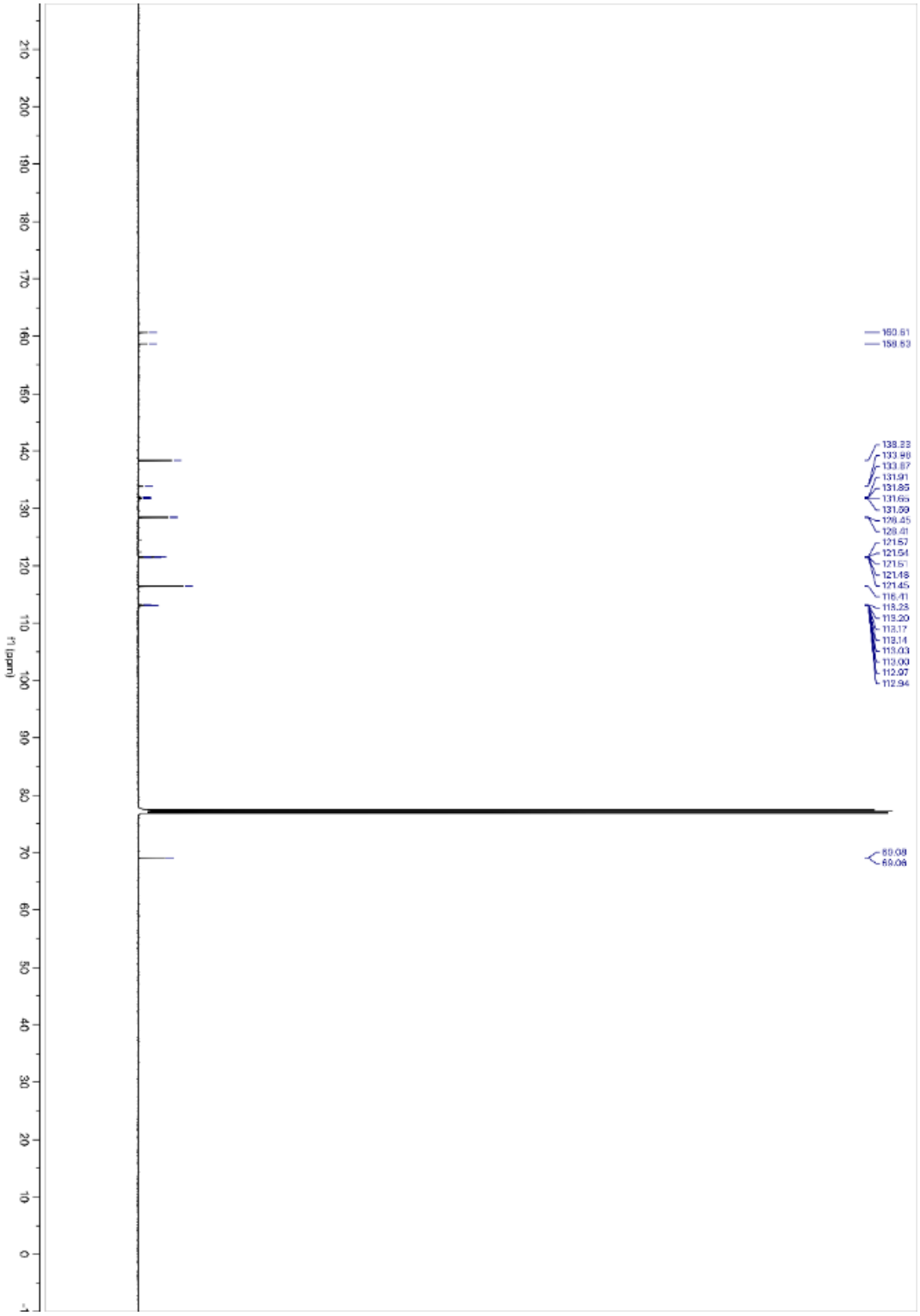
^{13}C NMR (126 MHz, $CDCl_3$) δ = 160.6, 158.6, 138.3, 133.9 (d, *J* = 13.3 Hz), 131.8 (dd, *J* = 33.3, 8.1 Hz), 128.4 (d, *J* = 4.5 Hz), 121.5 (p, *J* = 3.8 Hz), 116.4, 113.1 (dq, *J* = 25.2, 3.8 Hz), 69.1 (d, *J* = 2.7 Hz).

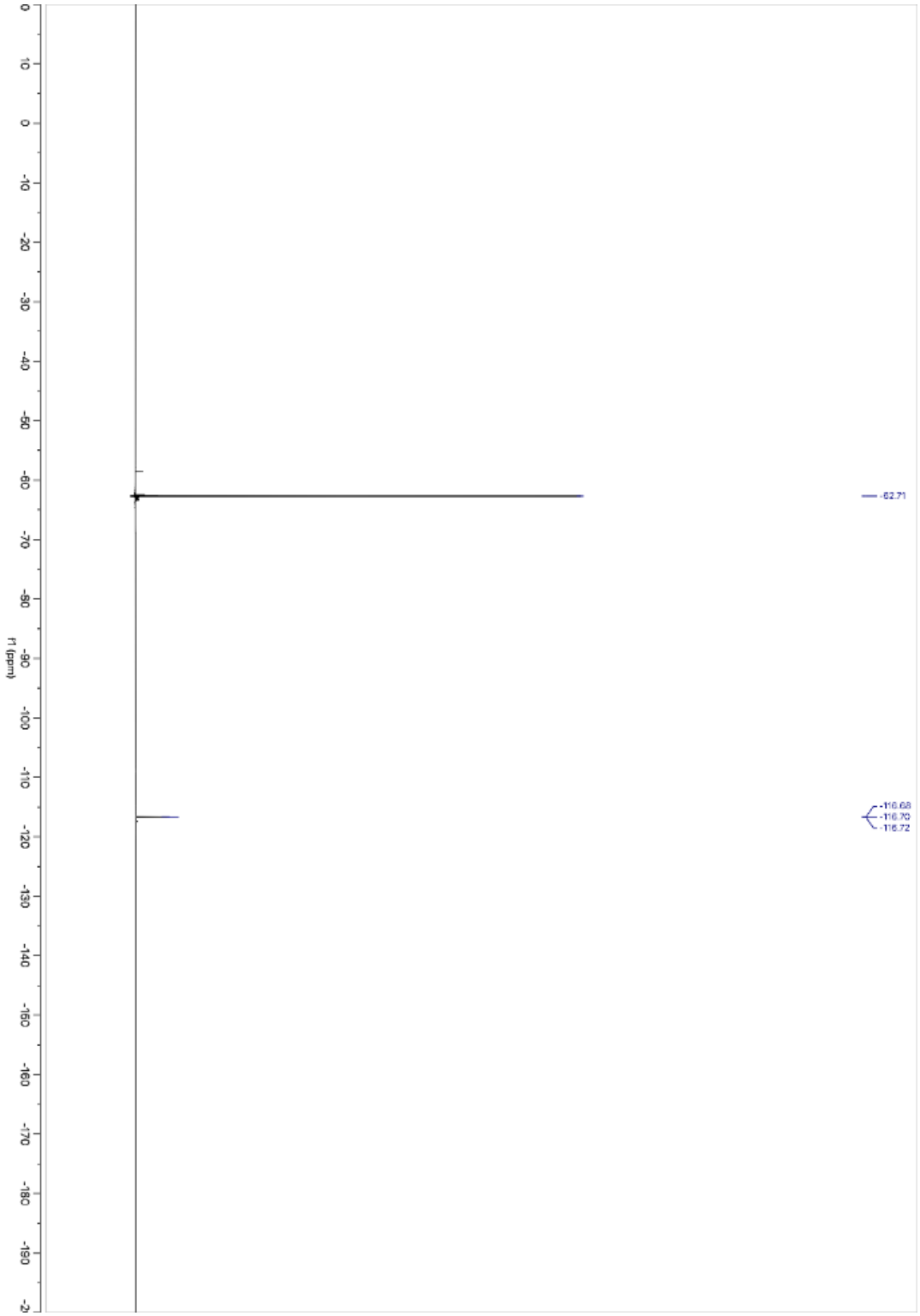
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.7, -116.7 – -116.7 (m).

HRMS (ESI): Calculated for $C_{10}H_8F_4O$ [M+Ag^+] = 326.9557, Found 326.9556.

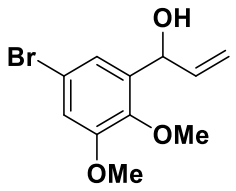
FTIR (neat): 3309, 1588, 1510, 1427, 1328, 1215, 1168, 1125, 1065, 1038, 988, 931, 904, 879, 839, 815, 746 cm^{-1}.


1.02
1.13
1.13
1.00
1.00
1.08
1.02
1.03
f1 (ppm)


f1 (ppm)
160.61
158.63
138.33
133.98
133.87
131.91
131.85
131.65
131.59
129.45
129.41
121.57
121.54
121.51
121.48
121.45
116.41
113.23
113.20
113.17
113.14
113.03
113.00
112.97
112.94
69.09
69.06


-62.71
-116.68
-116.70
-116.72
f1 (ppm)

1-(5-bromo-2,3-dimethoxyphenyl)prop-2-en-1-ol (S1k)



Procedure

5-Bromo-2,3-dimethoxybenzaldehyde (1.23 g, 5.00 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 68% yield (927 mg, 3.39 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–15:1).

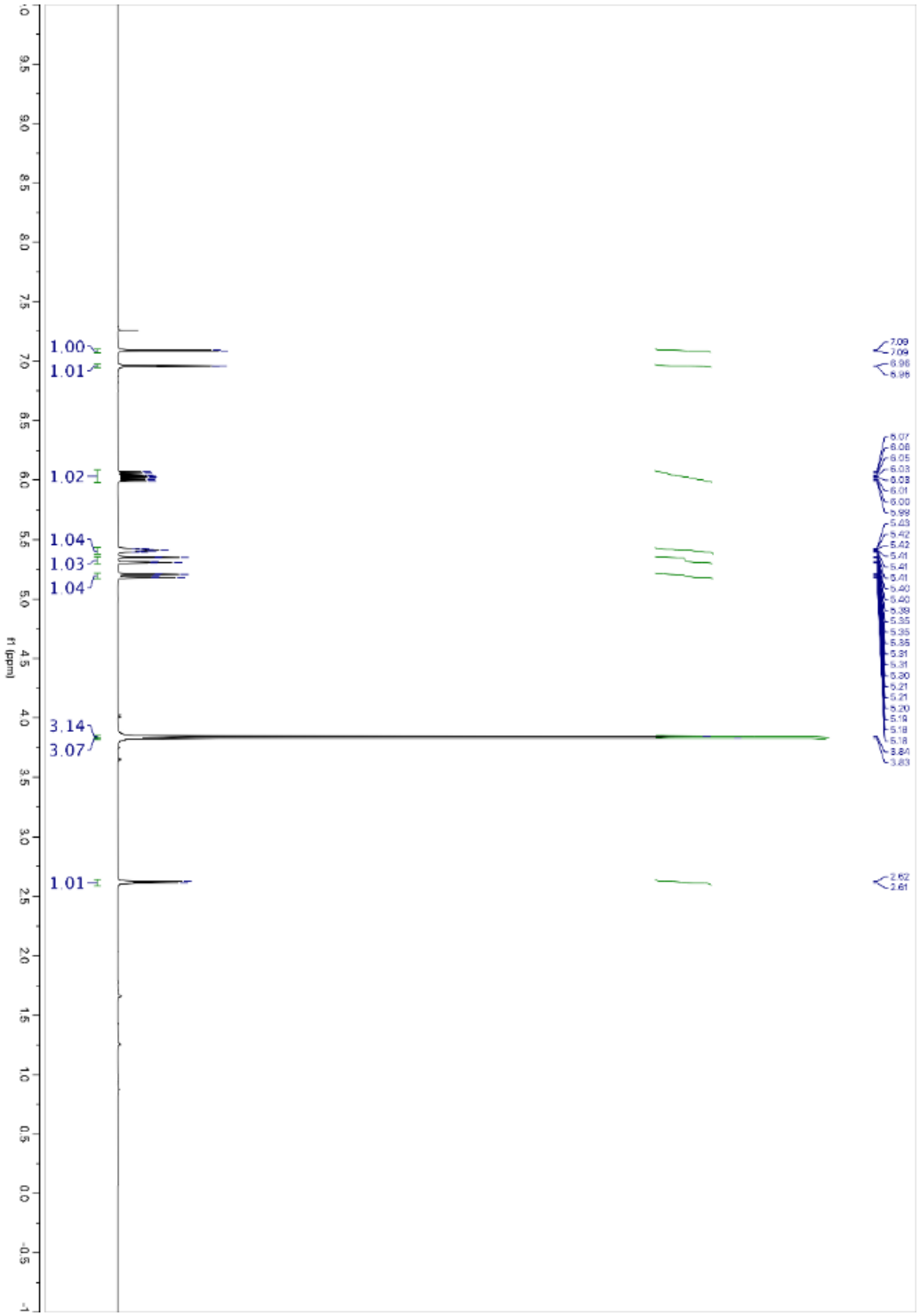
TLC (SiO_2) R_f = 0.30 (hexanes: ethyl acetate = 4:1).

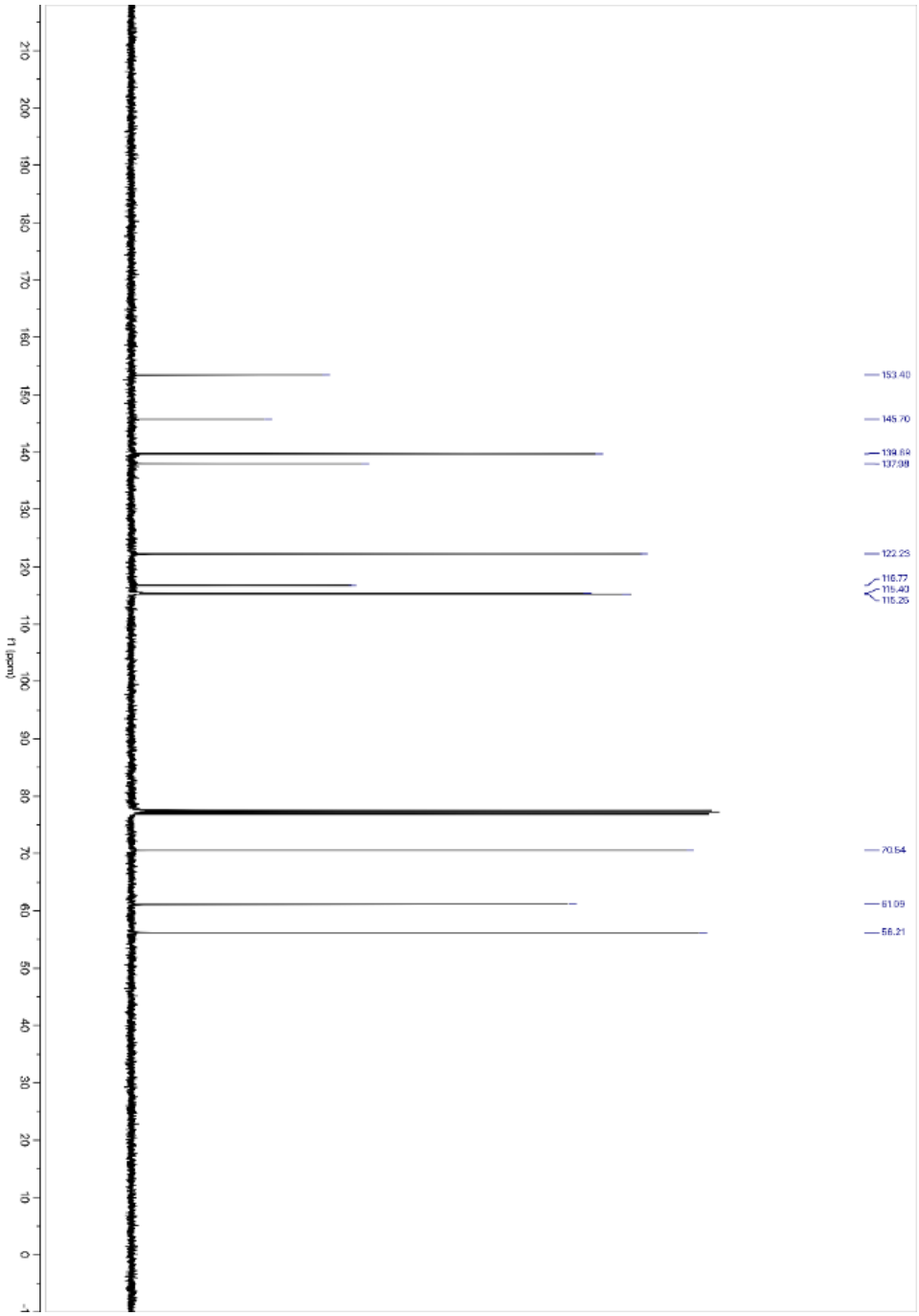
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (d, *J* = 2.3 Hz, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 6.03 (ddd, *J* = 17.1, 10.4, 5.3 Hz, 1H), 5.41 (tt, *J* = 5.4, 1.7 Hz, 1H), 5.33 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.19 (dt, *J* = 10.4, 1.5 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 2.62 (d, *J* = 5.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 153.4, 145.7, 139.7, 138.0, 122.2, 116.8, 115.4, 115.3, 70.5, 61.1, 56.2.

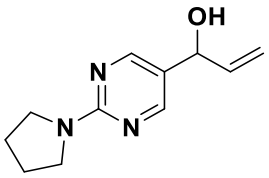
HRMS (ESI): Calculated for $C_{11}H_{13}BrO_3$ [M+Na^+] = 294.9940, Found 294.9938.

FTIR (neat): 3415, 3084, 2938, 2832, 1577, 1478, 1428, 1410, 1291, 1265, 1220, 1169, 1069, 1030, 997, 961, 925, 890, 846, 769, 696 cm^{-1}.


1.00
1.01
1.02
1.04
1.03
1.04
3.14
3.07
1.01
f1 (ppm)


153.40
145.70
139.68
137.98
122.23
116.77
115.40
115.25
70.64
61.09
56.21
f1 (ppm)

1-(2-(pyrrolidin-1-yl)pyrimidin-5-yl)prop-2-en-1-ol (S1m)



Procedure

2-(Pyrrolidin-1-yl)pyrimidine-5-carbaldehyde (660 mg, 3.73 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 78% yield (594 mg, 2.89 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 2:1–1:1).

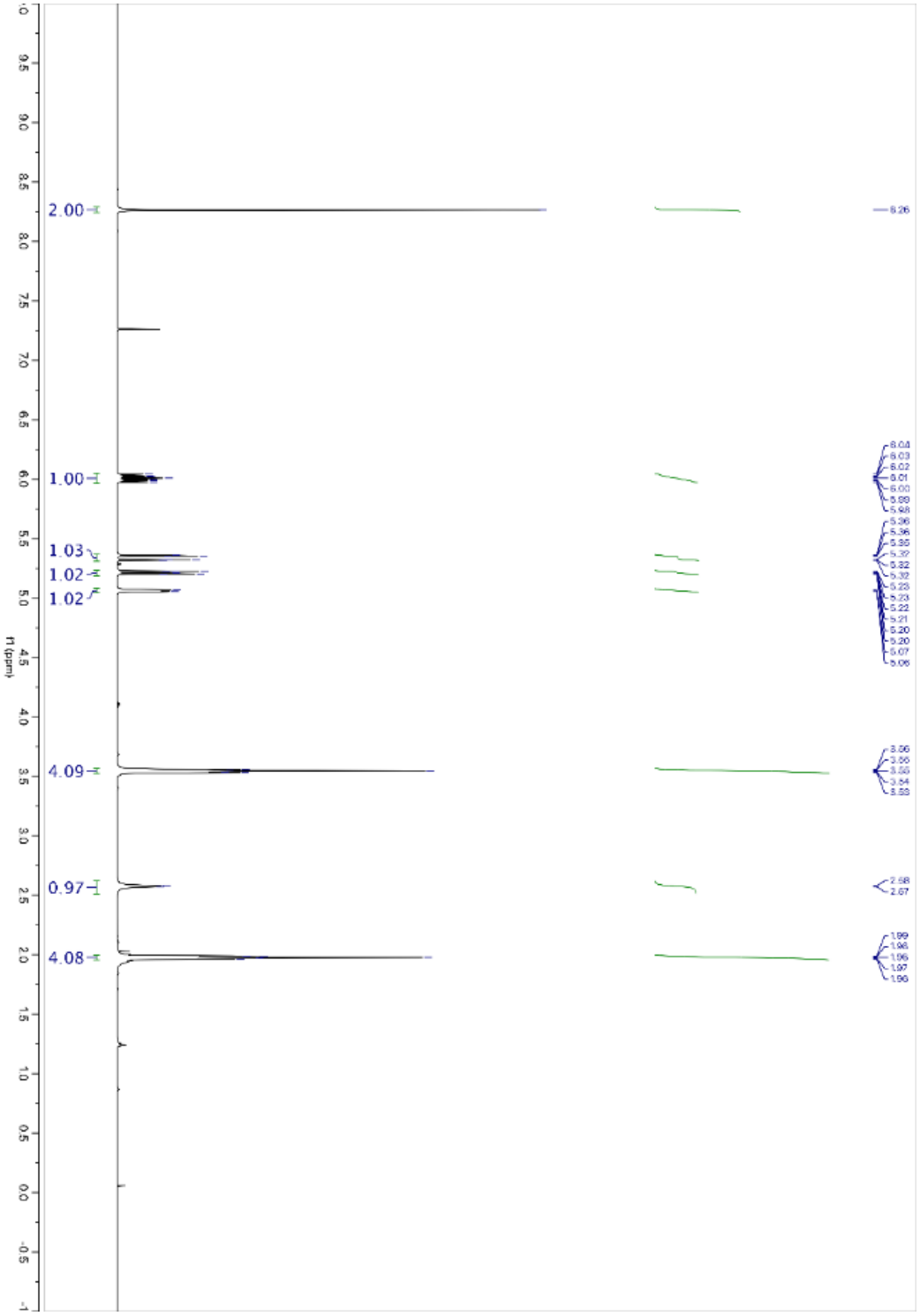
TLC (SiO_2) R_f = 0.12 (hexanes: ethyl acetate = 1:1).

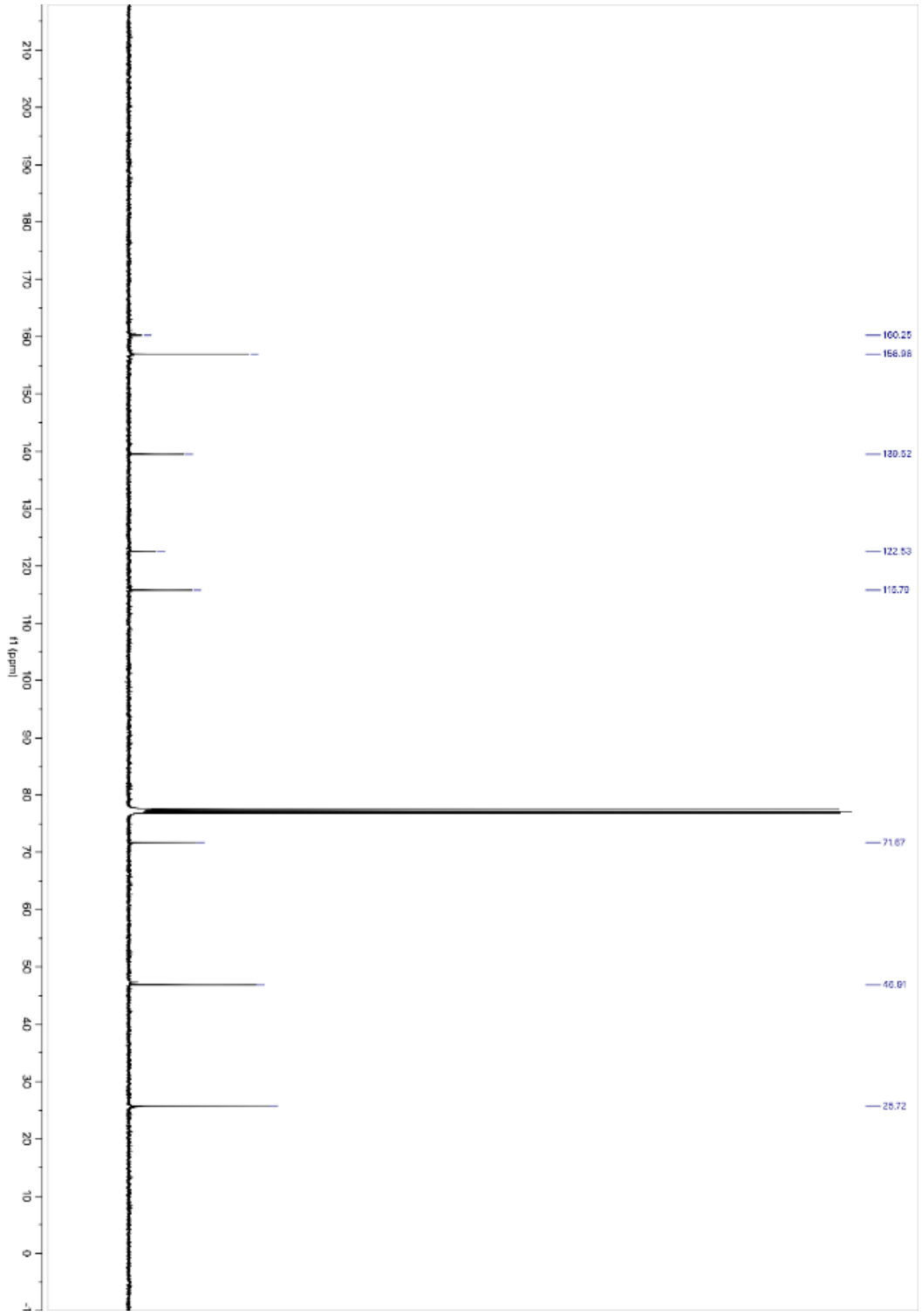
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.26 (s, 2H), 6.01 (ddd, *J* = 16.6, 10.3, 5.7 Hz, 1H), 5.34 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.22 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.06 (d, *J* = 5.6 Hz, 1H), 3.58 – 3.51 (m, 4H), 2.58 (d, *J* = 3.7 Hz, 1H), 2.20 – 1.73 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.3, 157.0, 139.5, 122.5, 115.8, 71.7, 46.9, 25.7.

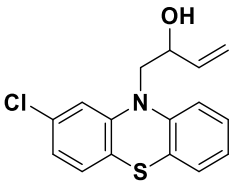
HRMS (ESI): Calculated for $C_{11}H_{15}N_3O$ [M+H$^+$] = 206.1288, Found 206.1287.

FTIR (neat): 3356, 2973, 2870, 1602, 1521, 1485, 1461, 1393, 1336, 1284, 1222, 1177, 1117, 1038, 991, 924, 799 cm^{-1}.


2.00
1.00
1.03
1.02
1.02
4.09
0.97
4.08
f1 (ppm)


160.25
156.98
130.52
122.53
116.70
71.67
46.91
25.72
f1 (ppm)

1-(2-chloro-10*H*-phenothiazin-10-yl)but-3-en-2-ol (S1s)



Procedure

A flame-dried pressure tube was charged with 2-chlorophenothiazine (1.17 g, 5.00 mmol, 100 mol%) and was fit with a rubber septum. The vessel was purged with argon gas. DMF (10 mL, 0.5 M) was added to the tube and the resultant mixture was stirred at room temperature for several minutes. Sodium hydride (60% in mineral oil, 521 mg, 7.50 mmol, 150 mol%) was added in one portion at room temperature. The resulting red solution was allowed to stir at room temperature for 1 hour under an argon balloon. Butadiene monoxide (0.61 mL, 7.5 mmol, 150 mol%) was added in one portion. The septum was replaced with a Teflon pressure cap and the vessel was heated to 90 °C for 16 hours. After the allotted time, the vessel was allowed to cool to room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and diluted with diethyl ether. The biphasic mixture was poured into a separatory funnel and mixed thoroughly. The organic layer was separated, and the aqueous layer was extracted three times with diethyl ether. The organics were combined and subjected to sequential washes with water and saturated aqueous NaCl solution. The organic layer was separated and treated with anhydrous sodium sulfate. The organic solution was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The residue was subjected directly to flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1) to afford the title compound in 36% yield (540 mg, 1.78 mmol) as a pale-yellow oil.

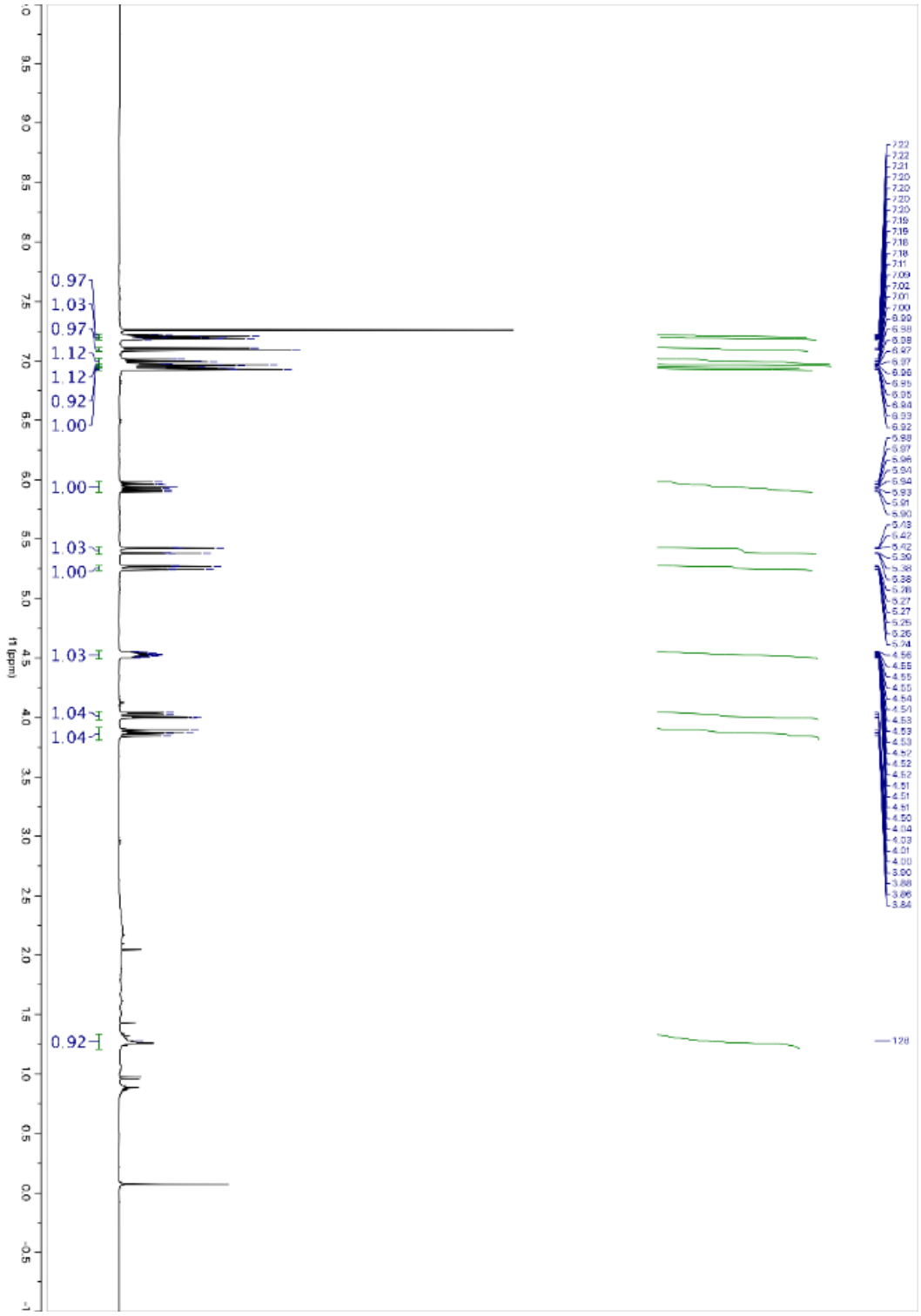
TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 4:1).

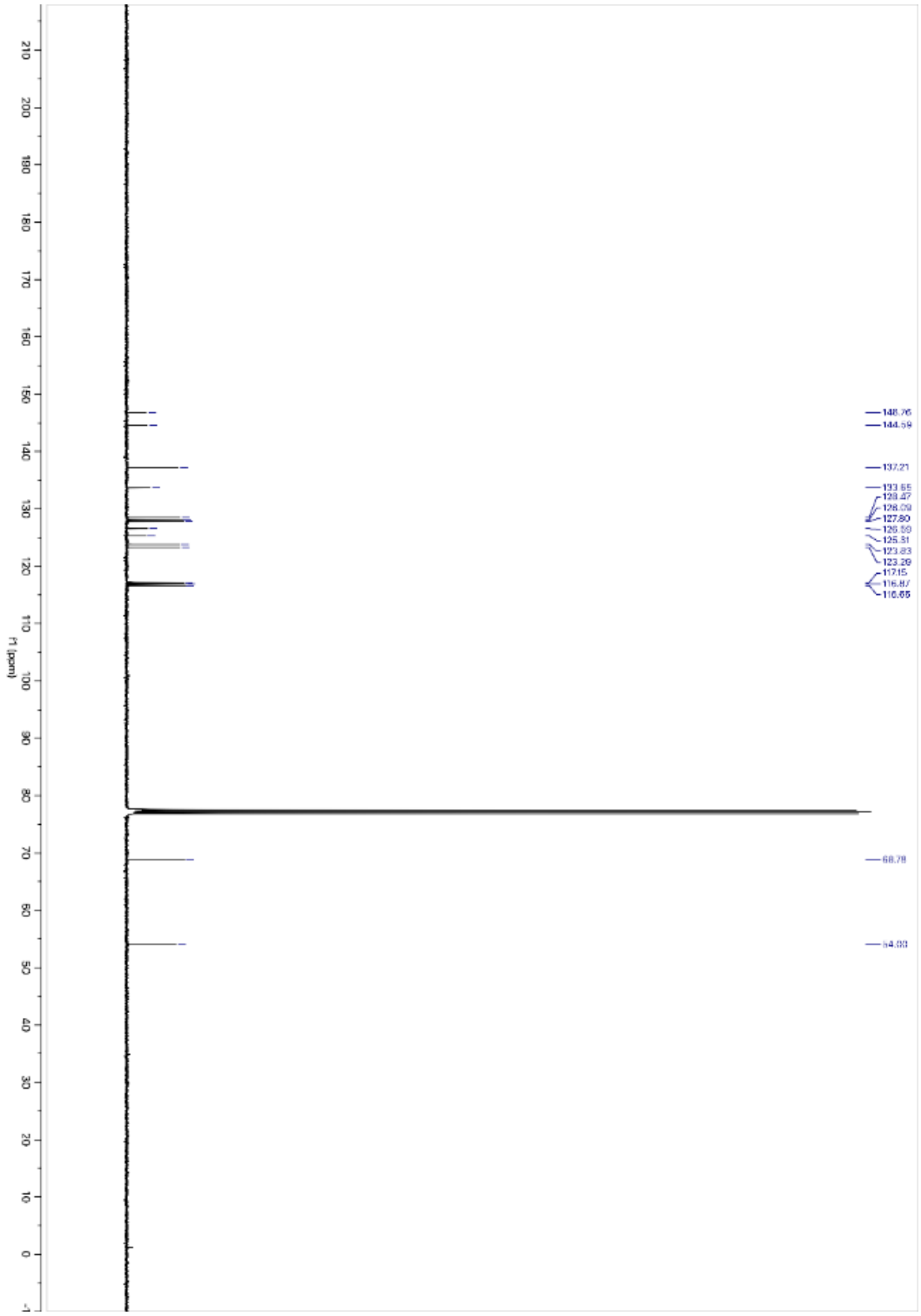
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.23 – 7.20 (m, 1H), 7.20 – 7.17 (m, 1H), 7.10 (d, *J* = 8.1 Hz, 1H), 7.00 (td, *J* = 7.5, 1.2 Hz, 1H), 6.97 (t, *J* = 1.7 Hz, 1H), 6.95 – 6.94 (m, 1H), 6.93 (d, *J* = 2.0 Hz, 1H), 5.94 (ddd, *J* = 17.2, 10.5, 5.8 Hz, 1H), 5.40 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.26 (dt, *J* = 10.6, 1.3 Hz, 1H), 4.53 (dddt, *J* = 8.6, 5.4, 3.9, 1.4 Hz, 1H), 4.02 (dd, *J* = 13.7, 4.0 Hz, 1H), 3.87 (dd, *J* = 13.8, 8.7 Hz, 1H), 1.28 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.8, 144.6, 137.2, 133.7, 128.5, 128.1, 127.8, 126.6, 125.3, 123.8, 123.3, 117.2, 116.9, 116.7, 68.8, 54.0.

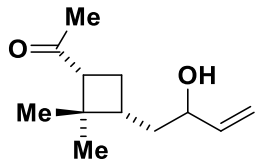
HRMS (ESI): Calculated for $C_{16}H_{14}ClNOS$ [M+Na^+] = 326.0377, Found 326.0374.

FTIR (neat): 3402, 2870, 2360, 2343, 1591, 1567, 1457, 1407, 1323, 1281, 1244, 1217, 1128, 1097, 1038, 992, 906, 855, 801, 752 cm^{-1}.


0.97
1.03
0.97
1.12
1.12
0.92
1.00
1.00
1.03
1.00
1.03
1.04
1.04
0.92
f1 (ppm)


f1 (ppm)
148.76
144.59
137.21
133.65
129.47
128.09
127.80
126.59
125.31
123.83
123.29
117.15
116.87
116.65
68.78
54.83

1-((1*R*,3*R*)-3-(2-hydroxybut-3-en-1-yl)-2,2-dimethylcyclobutyl)ethan-1-one (S1v)



Procedure

2-((1R,3R)-3-acetyl-2,2-dimethylcyclobutyl)acetaldehyde (472 mg, 2.8 mmol, 100 mol%) was subjected to a modified version of general procedure B using vinyl magnesium bromide (1.0 M in THF, 2.8 mmol, 100 mol%) in THF (0.1 M). The title compound was obtained in 40% yield (218 mg, 1.11 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–5:1).

TLC (SiO_2) R_f = 0.32 (hexanes: ethyl acetate = 2:1).

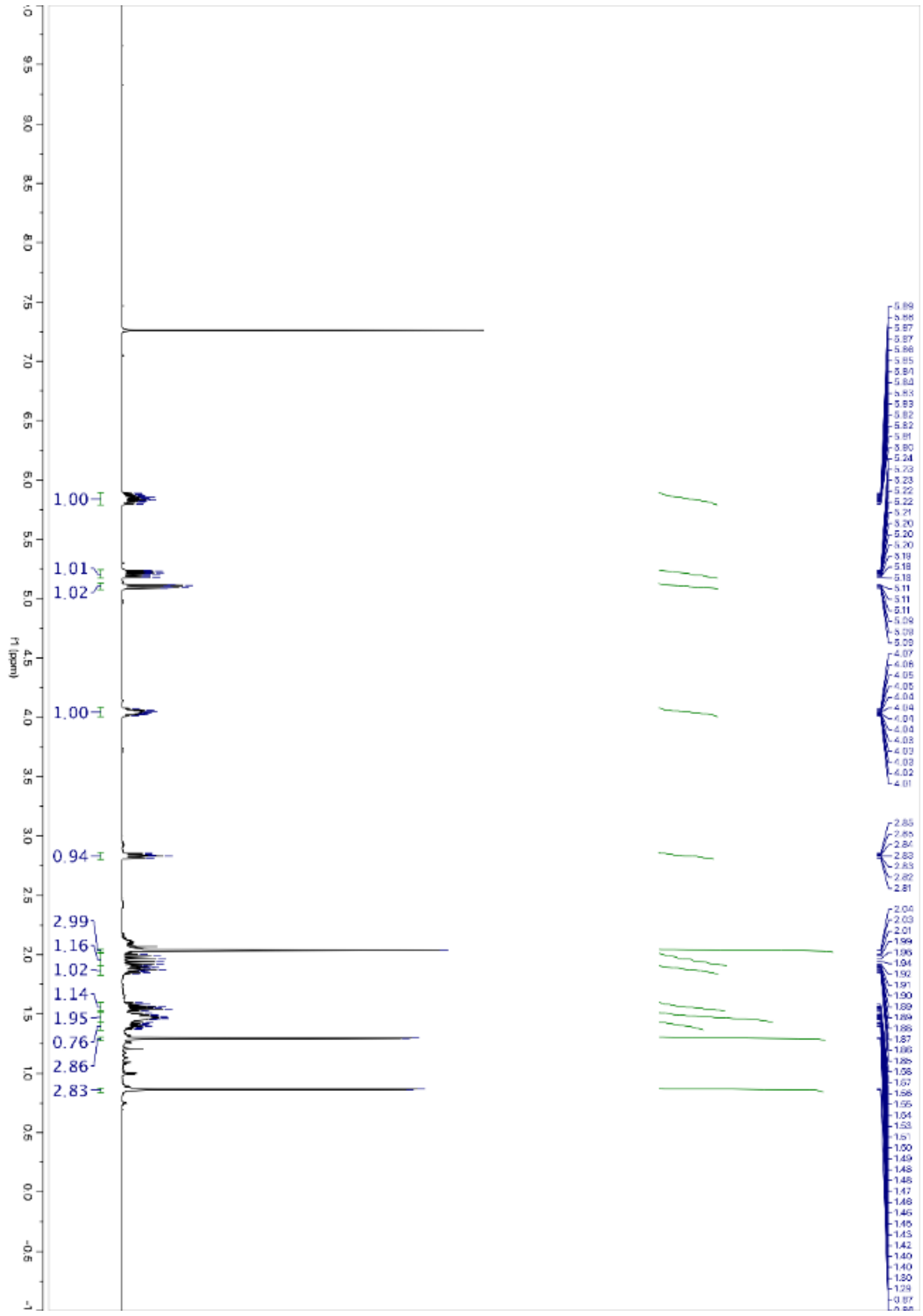
^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.91 – 5.78 (m, 1H), 5.21 (ddt, *J* = 17.2, 7.9, 1.4 Hz, 1H), 5.10 (dt, *J* = 10.4, 1.3 Hz, 1H), 4.09 – 3.99 (m, 1H), 2.83 (ddd, *J* = 9.9, 7.4, 2.3 Hz, 1H), 2.04 (d, *J* = 2.0 Hz, 3H), 2.01 – 1.91 (m, 1H), 1.88 (ddd, *J* = 13.3, 7.4, 3.6 Hz, 1H), 1.60 – 1.52 (m, 1H), 1.51 – 1.43 (m, 2H), 1.40 (ddd, *J* = 13.7, 9.6, 5.5 Hz, 1H), 1.30 (d, *J* = 2.1 Hz, 3H), 0.86 (d, *J* = 1.8 Hz, 3H).

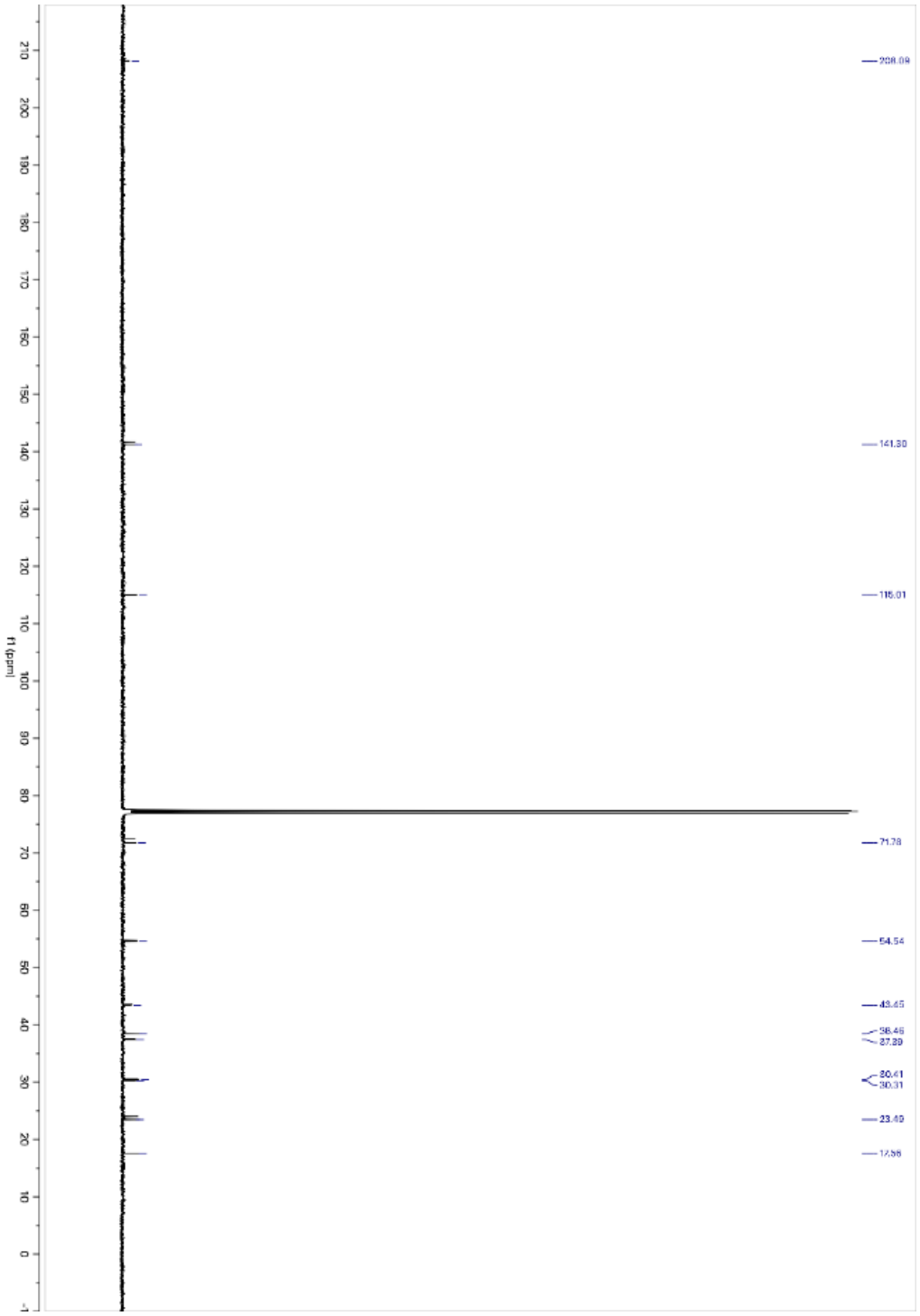
^{13}C NMR (126 MHz, $CDCl_3$) δ = 208.1, 141.3, 115.0, 71.8, 54.5, 43.5, 38.5, 37.4, 30.4, 30.3, 23.5, 17.6.

HRMS (ESI): Calculated for $C_{12}H_{20}O_2$ [M+Na^+] = 219.1356, Found 219.1354.

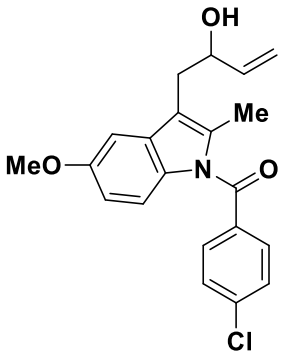
FTIR (neat): 3413, 2953, 1695, 1463, 1424, 1384, 1368, 1224, 1182, 1145, 991, 918 cm^{-1}.

$[\alpha]_D^{28}$= -32.9 (*c* 0.15, $CHCl_3$).


1.00
1.01
1.02
1.00
0.94
2.99
1.16
1.02
1.14
1.95
0.76
2.86
2.83
f1 (ppm)


f1 (ppm)
208.09
141.30
116.01
71.78
54.54
43.45
38.46
37.89
30.41
30.31
23.49
17.86

(4-chlorophenyl)(3-(2-hydroxybut-3-en-1-yl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone (S1w)



Procedure

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetaldehyde (1.00 g, 2.9 mmol, 100 mol%) was subjected to a modified version of general procedure B using vinyl magnesium bromide (1.0 M in THF, 2.9 mmol, 100 mol%) in THF (0.1 M). The title compound was obtained in 37% yield (398 mg, 1.07mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

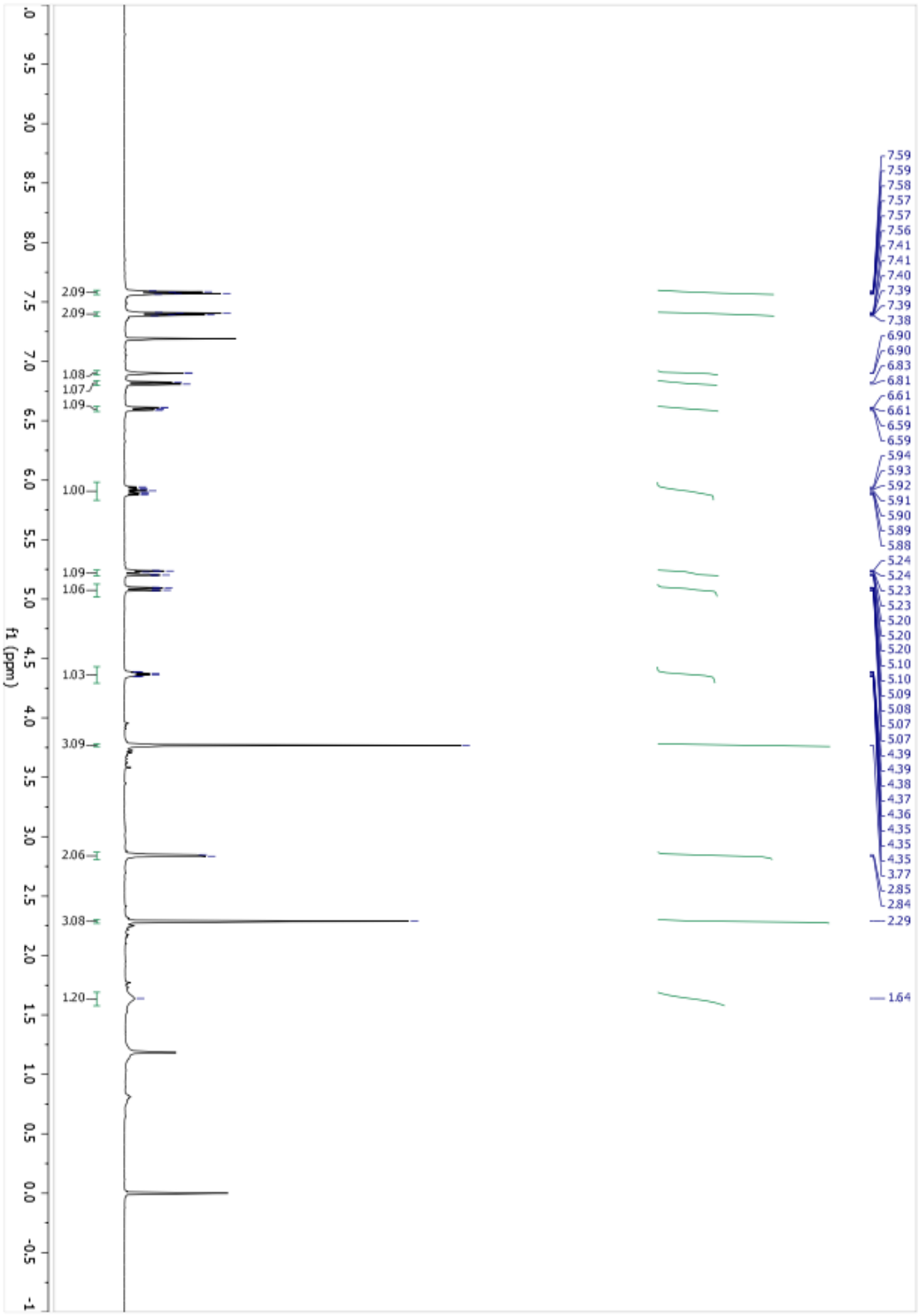
TLC (SiO_2) R_f = 0.4 (hexanes: ethyl acetate = 2:1).

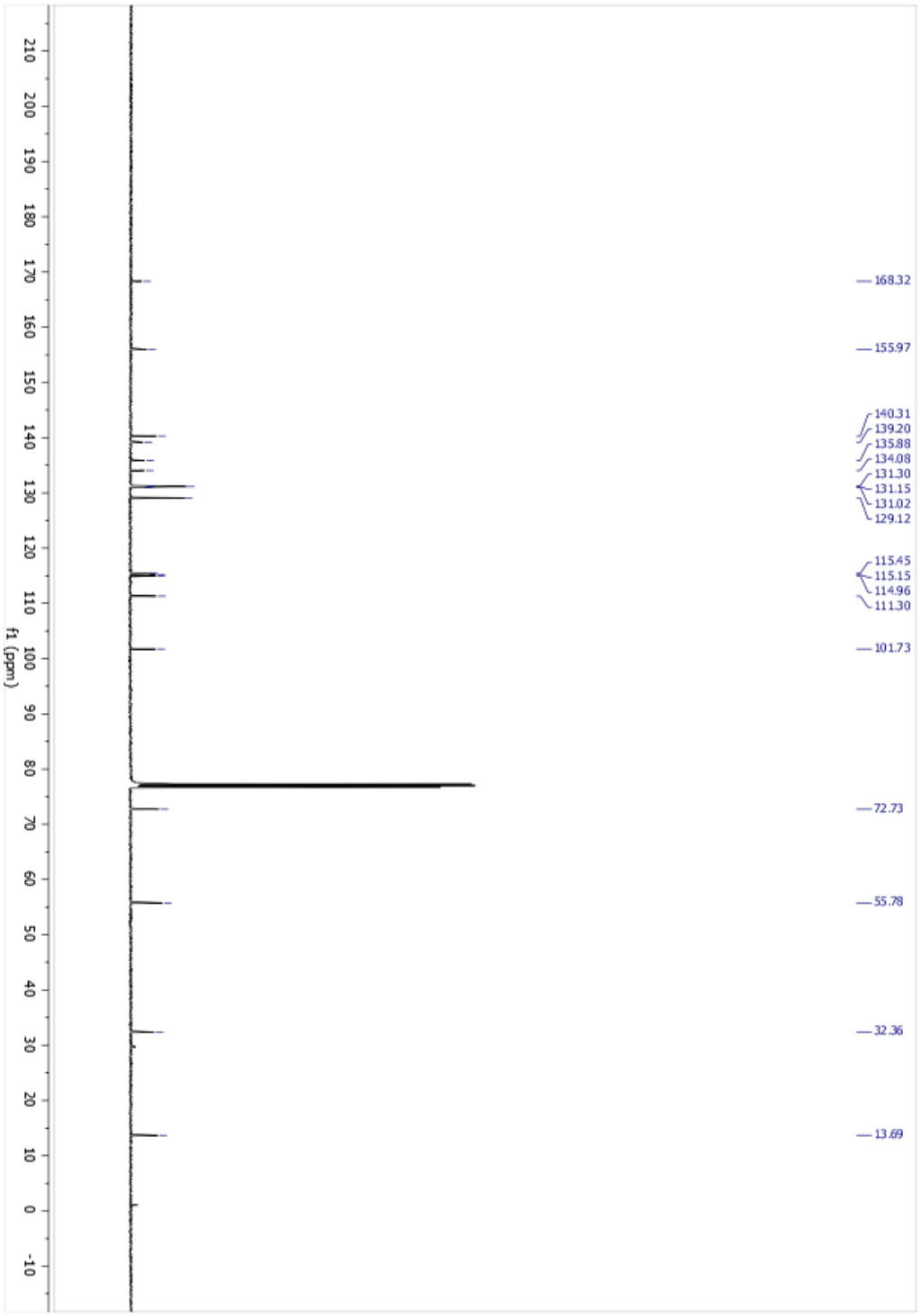
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.60 – 7.56 (m, 2H), 7.41 – 7.38 (m, 2H), 6.90 (d, *J* = 2.5 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 1H), 6.60 (dd, *J* = 9.0, 2.6 Hz, 1H), 5.91 (ddd, *J* = 16.8, 10.4, 5.9 Hz, 1H), 5.22 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.08 (dt, *J* = 10.5, 1.4 Hz, 1H), 4.37 (q, *J* = 6.4 Hz, 1H), 3.77 (s, 3H), 2.84 (d, *J* = 6.5 Hz, 2H), 2.29 (s, 3H), 1.64 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 168.3, 156.0, 140.3, 139.2, 135.9, 134.1, 131.3, 131.2, 131.0, 129.1, 115.5, 115.2, 115.0, 111.3, 101.7, 72.7, 55.8, 32.4, 13.7.

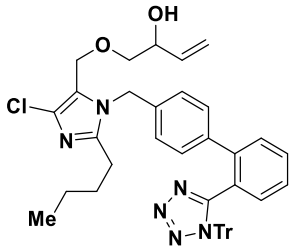
HRMS (ESI): Calculated for $C_{21}H_{20}ClNO_3$ [M+Na^+] = 392.1024, Found 392.1020.

FTIR (neat): 3445, 2927,1675, 1591, 1476, 1358, 1218, 1089, 1038, 1015, 924, 834, 750, 667 cm^{-1}.


f1 (ppm)
2.09
2.09
1.08
1.07
1.09
1.00
1.09
1.06
1.03
3.09
2.06
3.08
1.20
7.59
7.59
7.58
7.57
7.57
7.56
7.41
7.41
7.40
7.39
7.39
7.38
6.90
6.90
6.83
6.81
6.61
6.61
6.59
6.59
5.94
5.93
5.92
5.91
5.90
5.89
5.88
5.24
5.24
5.23
5.23
5.20
5.20
5.20
5.10
5.10
5.09
5.08
5.07
5.07
4.39
4.39
4.38
4.37
4.36
4.35
4.35
4.35
3.77
2.85
2.84
2.29
1.64


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
168.32
155.97
140.31
139.20
135.88
134.08
131.30
131.15
131.02
129.12
115.45
115.15
114.96
111.30
101.73
72.73
55.78
32.36
13.69

1-((2-butyl-4-chloro-1-((2'-(1-trityl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1H-imidazol-5-yl)methoxy)but-3-en-2-ol (S1x)



Procedure

A flame-dried pressure tube was charged with losartan (1.32 g, 1.98 mmol, 100 mol%) and was fit with a rubber septum. The vessel was purged with argon and DMF (3.3 mL, 0.6 M) was added. The vessel was cooled to 0 °C and sodium hydride (60% in mineral oil, 119 mg, 2.98 mmol, 150 mol%) was added in one portion. The resulting solution was allowed to warm to room temperature and was stirred for 20 minutes under an argon balloon. Butadiene monoxide (0.240 mL, 2.98 mmol, 150 mol%) was added in one portion. The septum was quickly replaced with a Teflon pressure cap and the vessel was heated to 60 °C for 16 hours. After the allotted time, the vessel was allowed to cool to room temperature. The reaction solution was quenched with water and diluted with ethyl acetate. The biphasic mixture was poured into a separatory funnel, wherein the pH of the aqueous layer was adjusted to 6 using a saturated aqueous NH_4Cl solution. The layers were mixed vigorously and the organics were separated. The aqueous was extracted three times by ethyl acetate. The combined organics were washed sequentially with water and aqueous saturated brine solution. The organics were dried over anhydrous sodium sulfate, passed through a fritted filter, and concentrated *in vacuo.* The residue was subjected directly to flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1) to afford the title compound in 24% yield (345 mg, 0.470 mmol) as a pale-yellow foam.

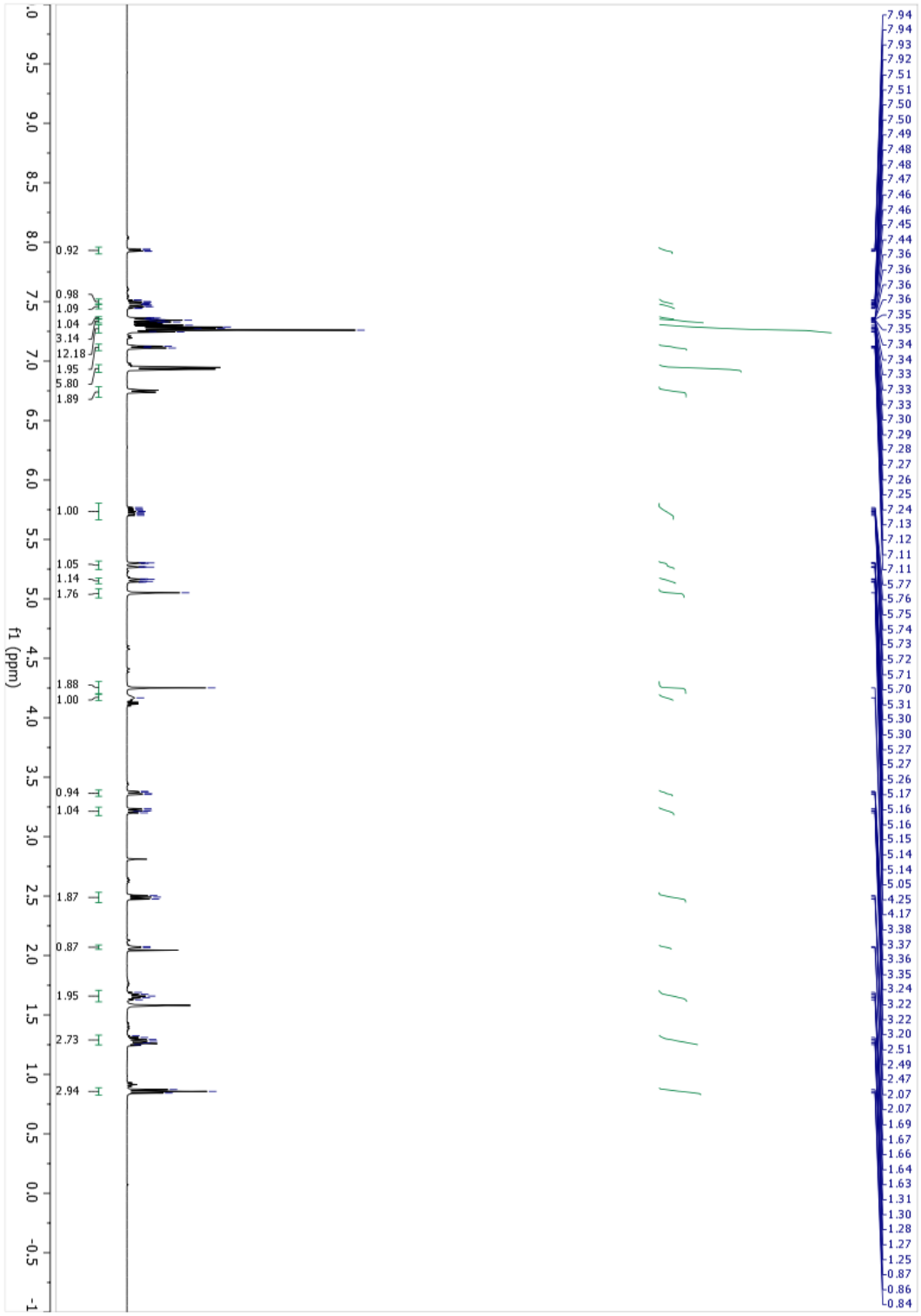
TLC (SiO_2) R_f = 0.44 (hexanes: ethyl acetate = 1:1).

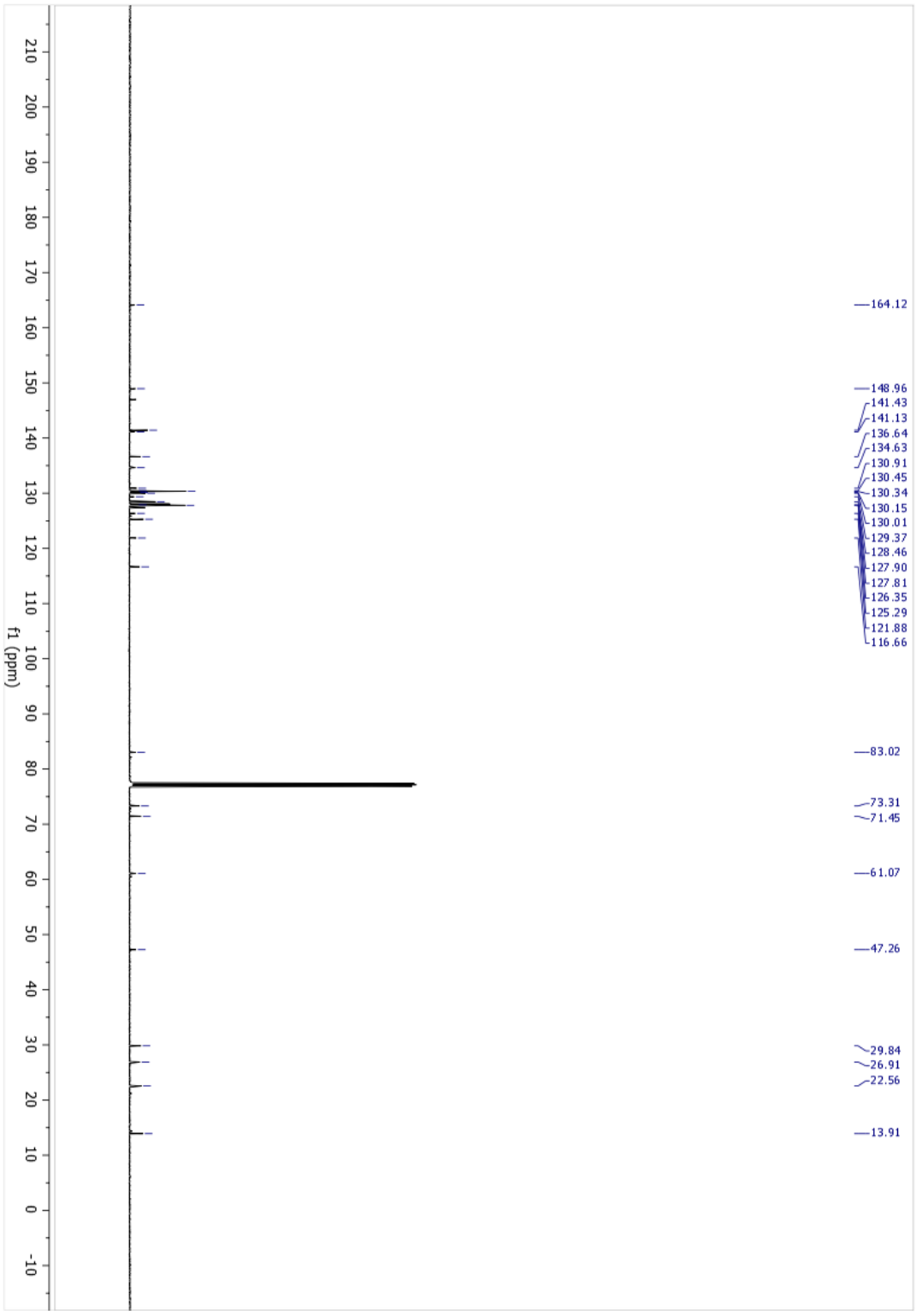
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.50 (td, *J* = 7.5, 1.6 Hz, 1H), 7.46 (td, *J* = 7.5, 1.6 Hz, 1H), 7.37 – 7.35 (m, 1H), 7.35 – 7.32 (m, 3H), 7.31 – 7.24 (m, 6H), 7.14 – 7.09 (m, 2H), 6.97 – 6.90 (m, 6H), 6.75 (d, *J* = 7.9 Hz, 2H), 5.74 (ddd, *J* = 17.2, 10.6, 5.5 Hz, 1H), 5.28 (dt, *J* = 17.1, 1.5 Hz, 1H), 5.15 (dt, *J* = 10.6, 1.5 Hz, 1H), 5.05 (s, 2H), 4.25 (s, 2H), 4.17 (s, 1H), 3.37 (dd, *J* = 9.8, 3.4 Hz, 1H), 3.22 (dd, *J* = 9.8, 7.8 Hz, 1H), 2.53 – 2.45 (m, 2H),

2.07 (d, *J* = 3.7 Hz, 1H), 1.66 (p, *J* = 7.7 Hz, 2H), 1.29 (dq, *J* = 14.7, 7.3 Hz, 2H), 0.86 (t, *J* = 7.4 Hz, 3H).

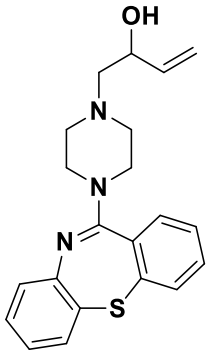
^{13}C NMR (126 MHz, $CDCl_3$): δ = 164.1, 149.0, 141.4, 141.1, 136.6, 134.6, 130.9, 130.5, 130.3, 130.2, 130.0, 129.4, 12856, 127.9, 127.8, 126.4, 125.3, 121.9, 116.7, 83.0, 73.3, 71.5, 61.1, 47.3, 29.8, 26.9, 22.6, 13.9.

HRMS (ESI): Calculated for C47H47ClN6O2 [M+H+] = 753.3209, Found 735.3204.
FTIR (neat): 3312, 3060, 2955, 2929, 2869, 2362, 1493, 1460, 1446, 1426, 1357, 1252, 1189, 1155, 1082, 1029, 1004, 929, 880, 758, 748, 698 cm^{-1}.


f1 (ppm)
0.92
0.98
1.09
1.04
3.14
12.18
1.95
5.80
1.89
1.00
1.05
1.14
1.76
1.88
1.00
0.94
1.04
1.87
0.87
1.95
2.73
2.94


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
164.12
148.96
141.43
141.13
136.64
134.63
130.91
130.45
130.34
130.15
130.01
129.37
128.46
127.90
127.81
126.35
125.29
121.88
116.66
83.02
73.31
71.45
61.07
47.26
29.84
26.91
22.56
13.91

1-(4-(dibenzo[*b,f*][1,4]thiazepin-11-yl)piperazin-1-yl)but-3-en-2-ol (S1y)



Procedure

A flame-dried round-bottom flask was charged with 11-(piperazin-1-yl)dibenzo[b,f][1,4]thiazepine (1.0 g, 3.39 mmol, 100 mol%) and was fit with a rubber septum. The vessel was purged with argon gas. Anhydrous methanol (22.5 mL, 0.15 M), 1,8-diazabicyclo[5.4.0]undec-7-ene (0.57 mL, 3.73 mmol, 110 mol%), and butadiene monoxide (0.63 mL, 7.79 mmol, 230 mol%) were added to the flask at ambient temperature. The resultant mixture was stirred at room temperature for 16 hours. After the allotted time, the solution was concentrated *in vacuo*. The residue was subjected directly to flash column chromatography (SiO_2, dichloromethane: methanol: triethylamine = 1000:100:1–100:100:1) to afford the title compound in 30% yield (375 mg, 1.03 mmol) as a pale-yellow oil.

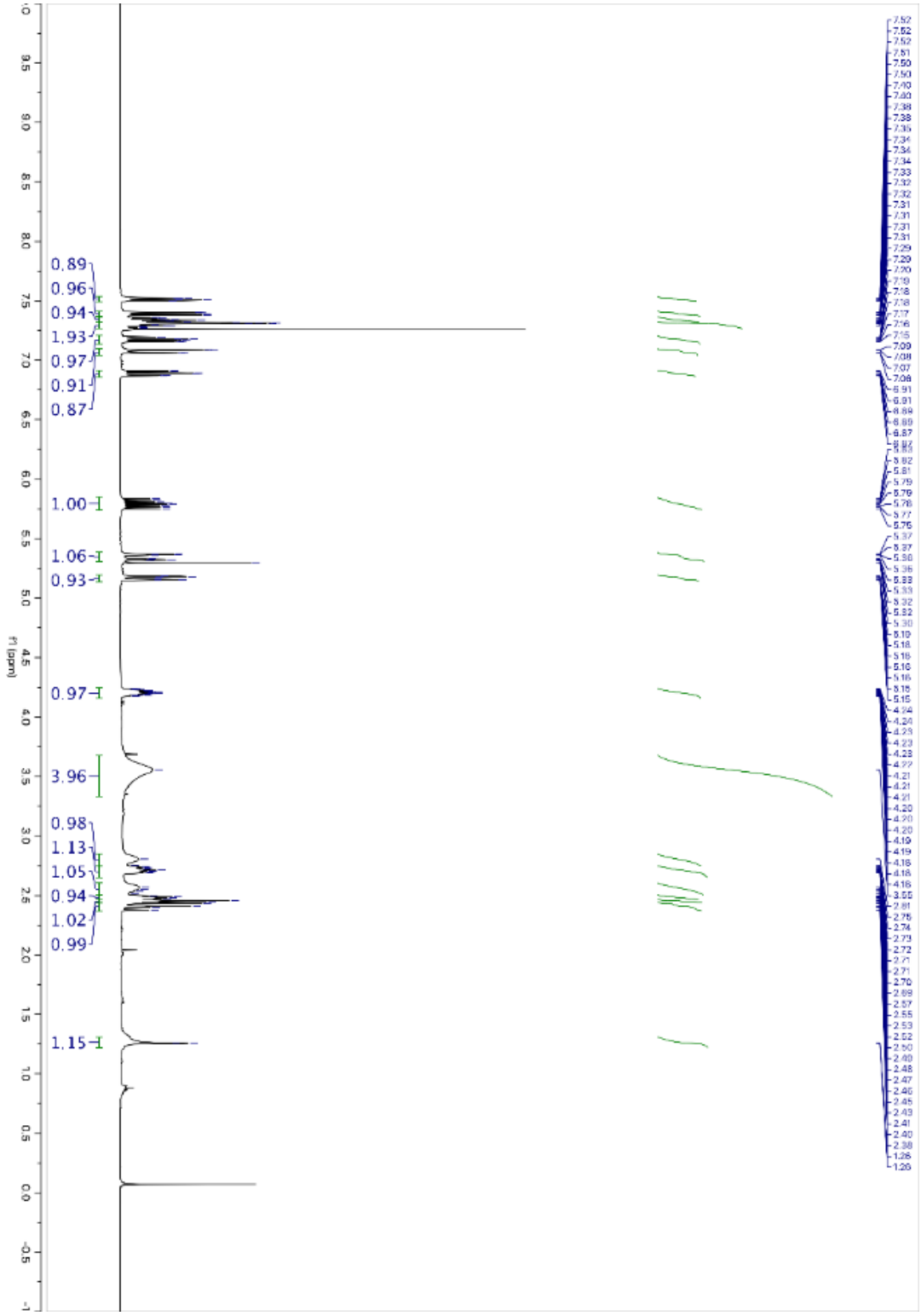
TLC (SiO_2) R_f = 0.43 (dichloromethane: methanol = 9:1).

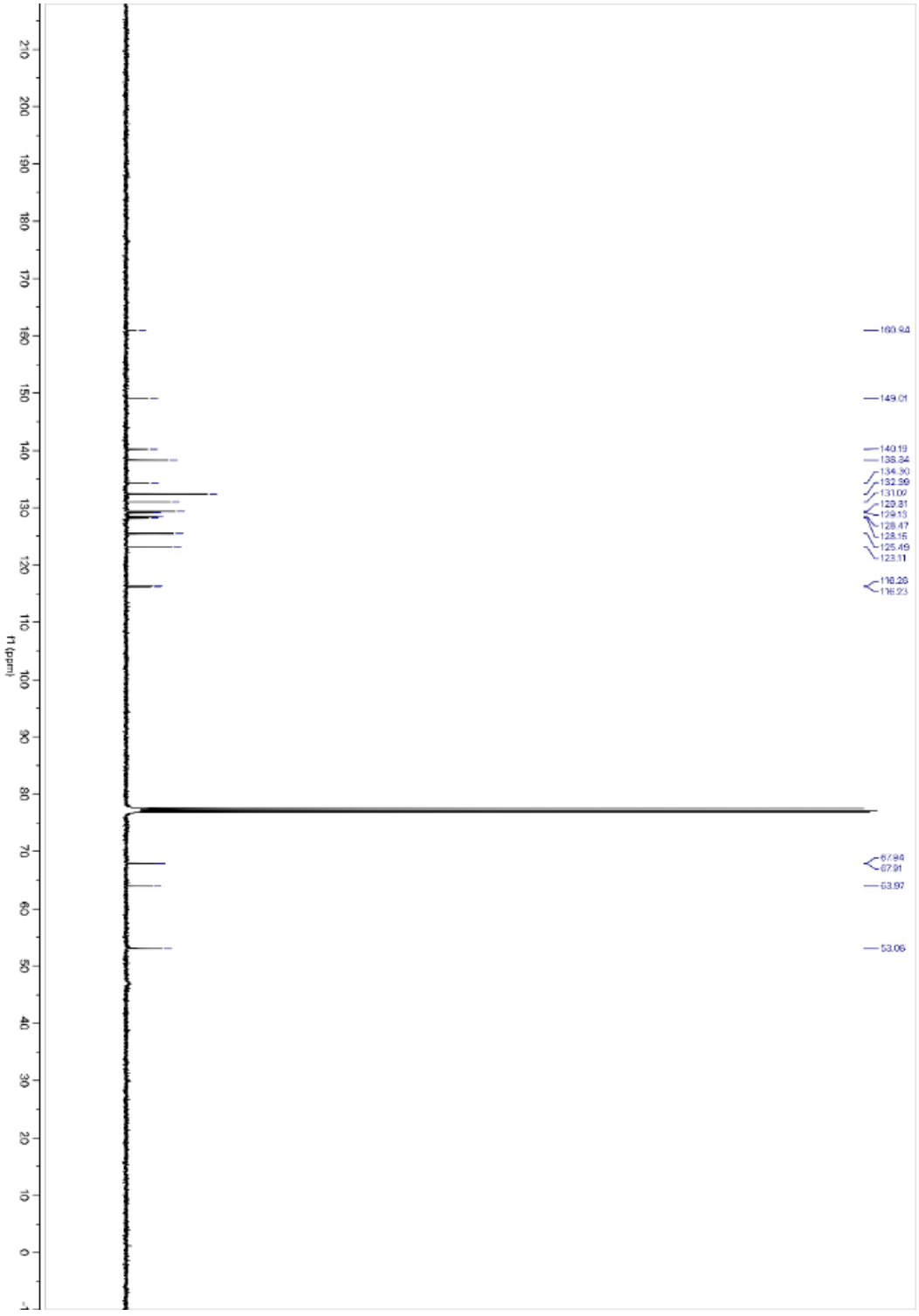
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 (dt, *J* = 7.6, 1.1 Hz, 1H), 7.39 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.36 – 7.32 (m, 1H), 7.32 – 7.27 (m, 2H), 7.18 (ddd, *J* = 8.8, 7.3, 1.5 Hz, 1H), 7.07 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.89 (td, *J* = 7.5, 1.5 Hz, 1H), 5.79 (ddd, *J* = 17.3, 10.5, 5.8 Hz, 1H), 5.34 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.21 – 5.13 (m, 1H), 4.21 (tq, *J* = 5.7, 4.1 Hz, 1H), 3.55 (s, 4H), 2.81 (s, 1H), 2.71 (ddd, *J* = 10.6, 6.9, 3.3 Hz, 1H), 2.57 (s, 1H), 2.50 – 2.47 (m, 1H), 2.46 – 2.43 (m, 1H), 2.42 – 2.36 (m, 1H), 1.26 (d, *J* = 1.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.9, 149.0, 140.2, 138.3, 134.3, 132.4, 131.0, 129.3, 129.1, 128.5, 128.2, 125.5, 123.1, 116.3, 116.2, 67.9, 67.9, 64.0, 53.1.

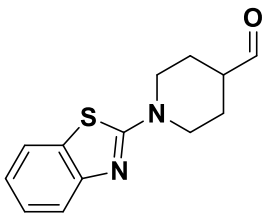
HRMS (ESI): Calculated for $C_{21}H_{23}N_3OS$ $[M+H^+]$ = 366.1635, Found 366.1642.

FTIR (neat): 3345, 2924, 2863, 1646, 1596, 1574, 1556, 1454, 1406, 1305, 1245, 1146, 1002, 925, 762, 744, 669 cm^{-1}.


0.89
0.96
0.94
1.93
0.97
0.91
0.87
1.00
1.06
0.93
0.97
3.96
0.98
1.13
1.05
0.94
1.02
0.99
1.15
f1 (ppm)


160.84
149.01
140.19
138.84
134.30
132.99
131.09
129.81
129.13
128.47
128.15
125.49
123.11
116.28
116.23
67.94
67.91
63.97
53.06
f1 (ppm)

1-(benzo[*d*]thiazol-2-yl)piperidine-4-carbaldehyde



Procedure:

(1-(benzo[d]thiazol-2-yl)piperidin-4-yl)methanol (1.29 g, 5.18 mmol, 100 mol%) was added to a flame-dried round-bottom flask containing a stir bar. The vessel was purged with argon gas and anhydrous dichloromethane (50 mL, 0.1 M) was added. The mixture was stirred at room temperature for several minutes. Sodium bicarbonate (1.74 g, 20 mmol, 400 mol%) was added. Dess-Martin periodinane (2.64 g, 6.22 mmol, 120 mol%) was added in one portion and the reaction was stirred at room temperature until the starting material was consumed. The suspension was diluted with dichloromethane and passed through celite with the aid of dichloromethane. The solution was added to a separatory funnel. The organics were washed sequentially with aqueous saturated solution of sodium carbonate and brine. The organic layer was dried over anhydrous sodium sulfate. The liquid was passed through a fritted filter into a round-bottom flask and was concentrated in vacuo. The residue was directly subjected to flash column chromatography (hexanes: ethyl acetate, 5:1–3:1) to afford the aldehyde as a white solid in 47% yield (601 mg, 2.44 mmol).

TLC (SiO_2) R_f = 0.28 (hexanes: ethyl acetate = 1:1).

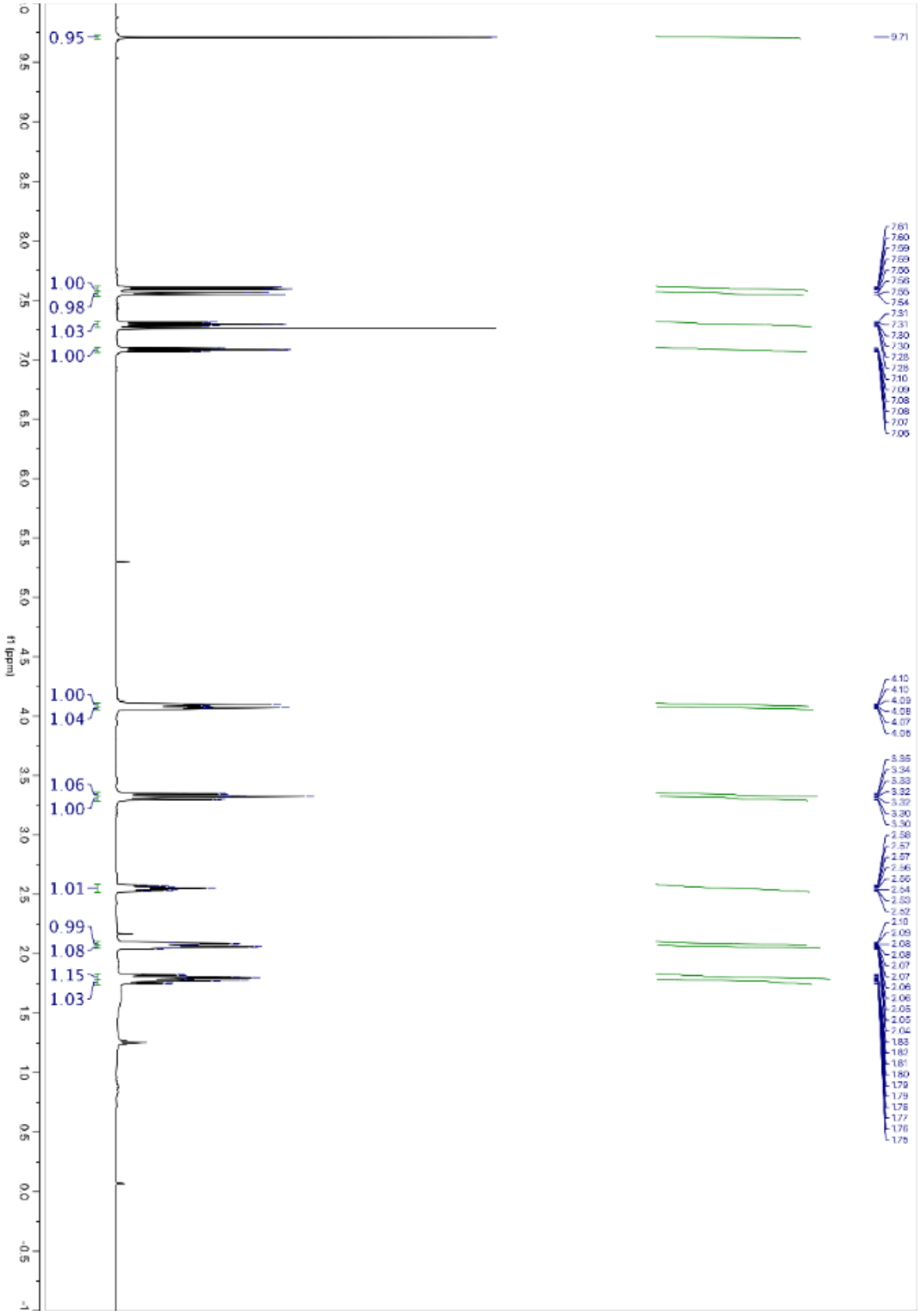
^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.71 (s, 1H), 7.60 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.55 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.30 (td, *J* = 7.7, 1.3 Hz, 1H), 7.08 (td, *J* = 7.6, 1.2 Hz, 1H), 4.10 (t, *J* = 4.3 Hz, 1H), 4.07 (t, *J* = 4.3 Hz, 1H), 3.36 – 3.32 (m, 1H), 3.32 – 3.27 (m, 1H), 2.55 (td, *J* = 10.3, 5.2 Hz, 1H), 2.09 (q, *J* = 4.9, 4.4 Hz, 1H), 2.07 – 2.05 (m, 1H), 1.81 (dd, *J* = 10.5, 4.1 Hz, 1H), 1.79 – 1.74 (m, 1H).

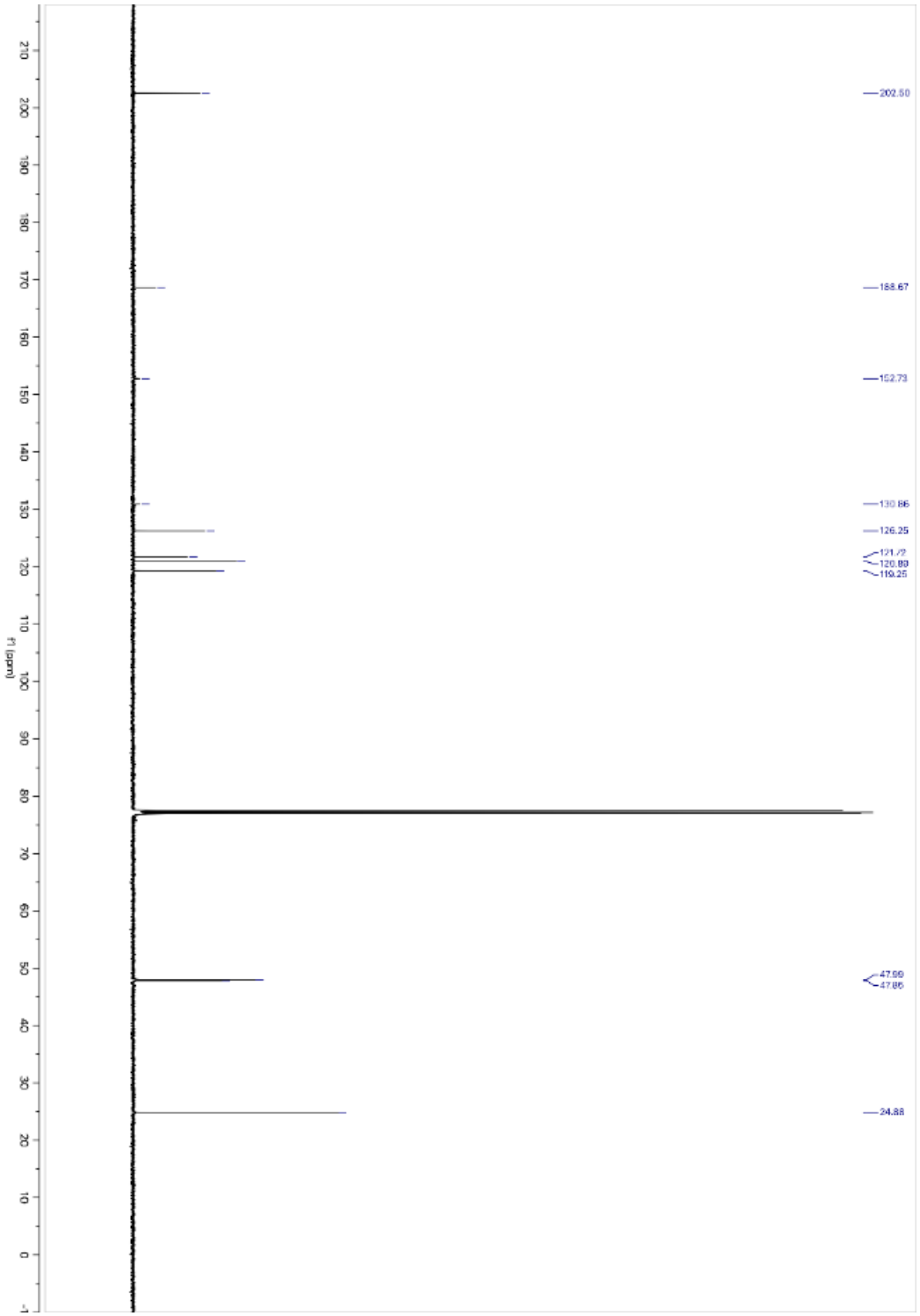
^{13}C NMR (126 MHz, $CDCl_3$) δ = 202.5, 168.7, 152.7, 130.9, 126.3, 121.7, 120.9, 119.3, 48.0, 47.9, 24.9.

HRMS (ESI): Calculated for $C_{13}H_{14}N_2OS$ [M+H$^+$] = 247.0900, Found 247.0904.

FTIR (neat): 2924, 2852, 2714, 1723, 1595, 1564, 1534, 1445, 1385, 1340, 1290, 1211, 1184, 1122, 1070, 1017, 958, 754, 726 cm^{-1}.

MP: 93-95 ^{o}C

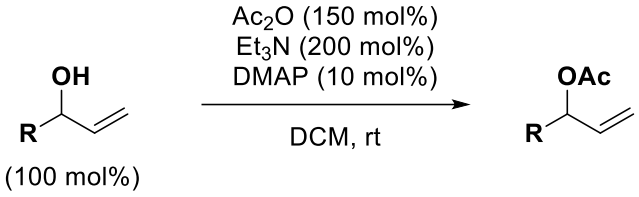

0.95
1.00
0.98
1.03
1.00
1.00
1.04
1.06
1.00
1.01
0.99
1.08
1.15
1.03
f1 (ppm)


202.50
188.67
152.73
130.86
126.25
121.72
120.89
119.25
47.99
47.86
24.88
f1 (ppm)

3.1e. Procedures and Spectral Data for Synthesis of Allyl Acetates 1a-1y

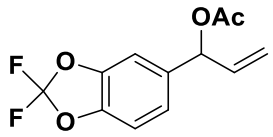
Allyl acetates **1a**,[47] **1h**,[47] **1l**,[47] **1n**,[70] **1t**,[52] and **1u**[47] were synthesized in the manner previously reported. The obtained products were identical in all respects to the compounds reported the literature.

General Procedure C



An oven-dried round bottom flask equipped with a magnetic stir bar was charged with allylic alcohol (100 mol%), triethylamine (200 mol%), acetic anhydride (150 mol%), 4-dimethylaminopyridine (10 mol%), and anhydrous dichloromethane (0.1 M). The reaction was stirred at ambient temperature until starting material was consumed. The reaction solution was diluted with dichloromethane and was washed sequentially with aqueous saturated solutions of ammonium chloride, sodium bicarbonate, distilled water, and brine. The organic layer was separated and dried over anhydrous sodium sulfate. The liquid was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The residue was directly subjected to flash column chromatography to afford allyl acetates **1a-1y**.

1-(2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)allyl acetate (1b)



Procedure

Allylic alcohol **S1b** (640 mg, 3.18 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 86% yield (703 mg, 2.74 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.49 (hexanes: ethyl acetate = 4:1).

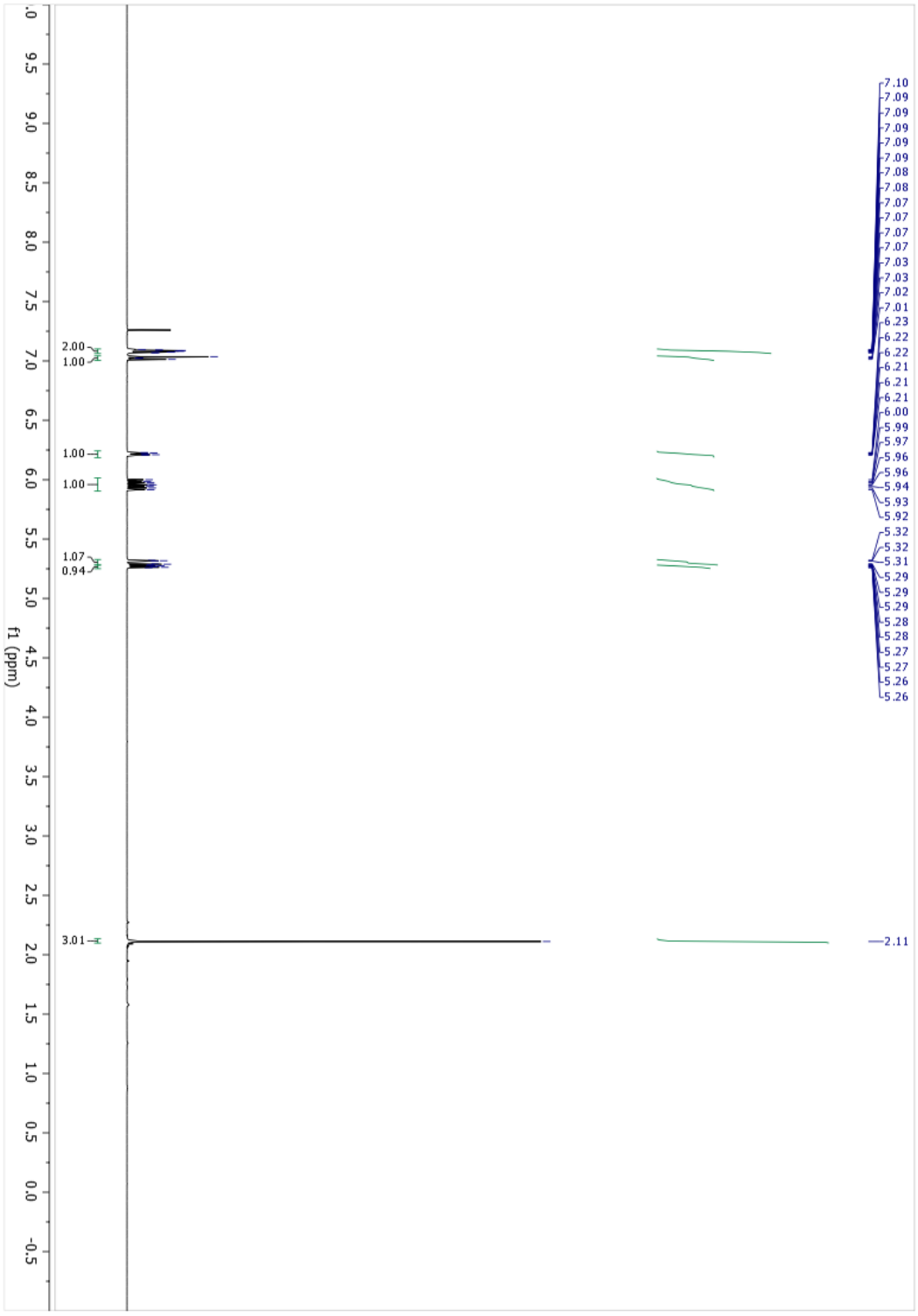
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.10 – 7.06 (m, 2H), 7.02 (d, *J* = 8.6 Hz, 1H), 6.22 (dt, *J* = 5.7, 1.5 Hz, 1H), 5.96 (ddd, *J* = 17.1, 10.5, 5.7 Hz, 1H), 5.30 (dt, *J* = 11.7, 1.2 Hz, 1H), 5.27 (dt, *J* = 5.0, 1.2 Hz, 1H), 2.11 (s, 3H).

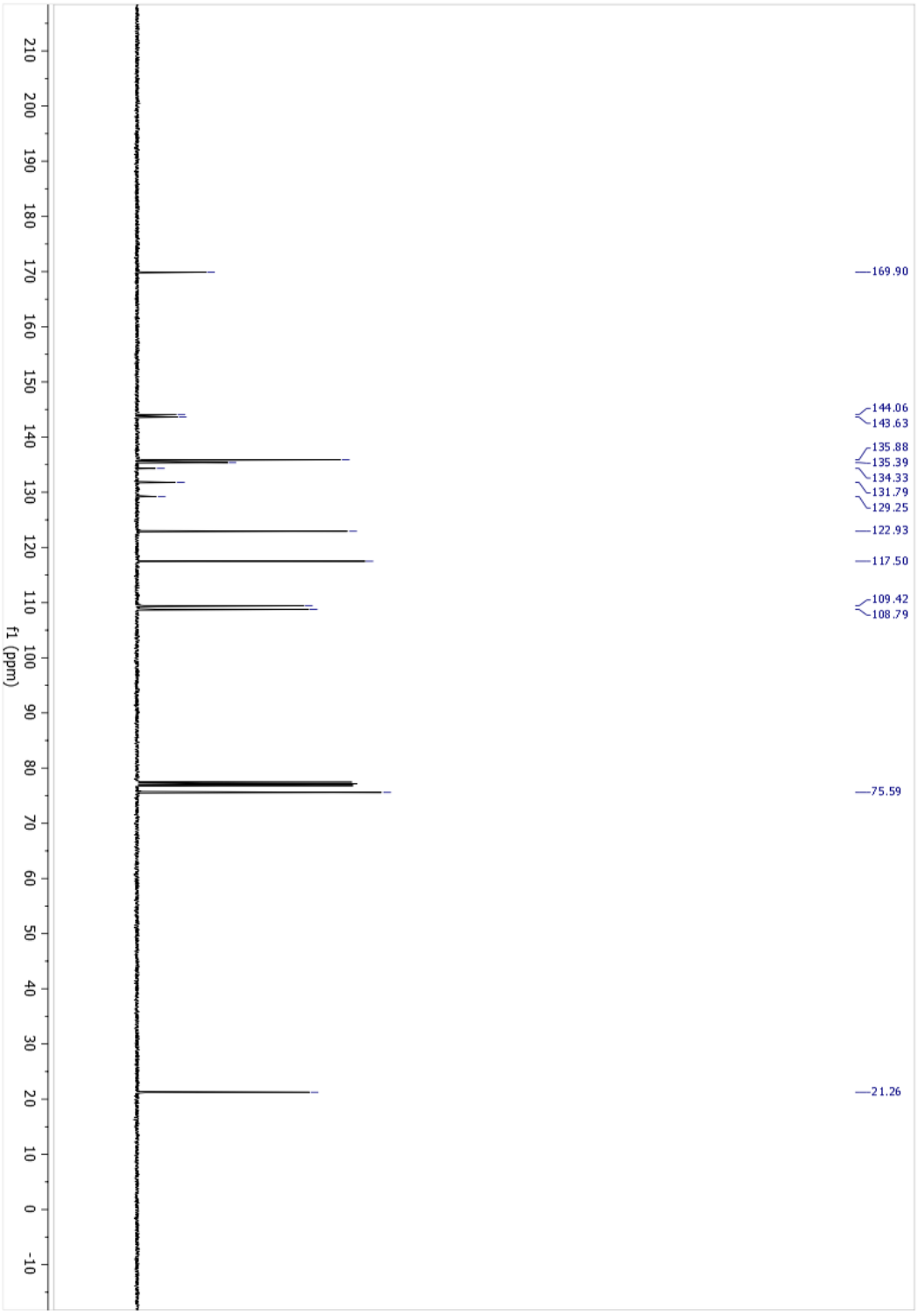
^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.9, 144.1, 143.6, 135.9, 135.4, 131.8 (t, *J* = 255.5 Hz), 122.9, 117.5, 109.4, 108.8, 75.6, 21.3.

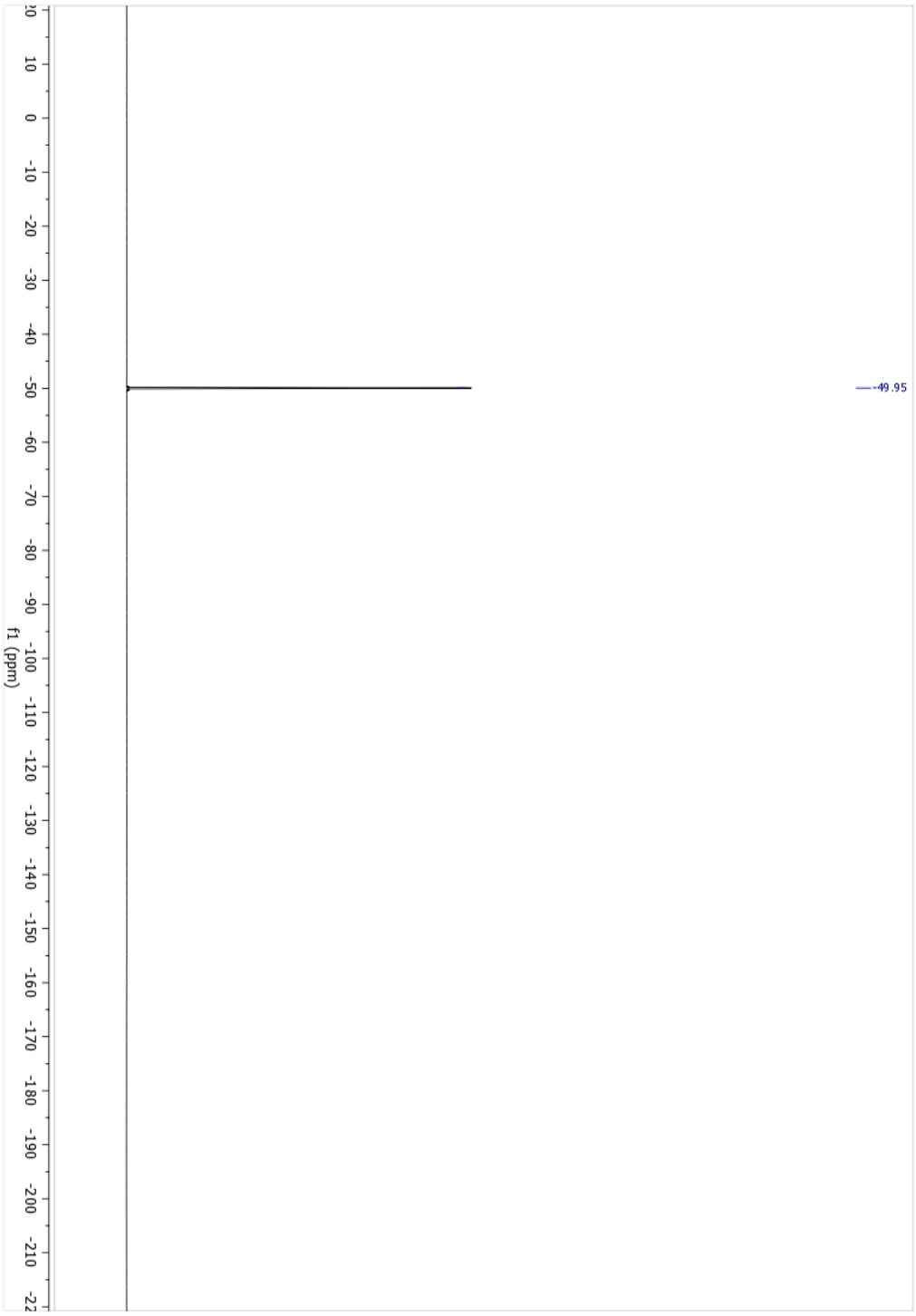
^{19}F NMR (376 MHz, $CDCl_3$) δ = -50.0.

HRMS (ESI): Calculated for $C_{12}H_{10}F_2O_4$ [M+Ag^+] = 362.9593, Found 362.9591.

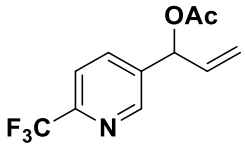
FTIR (neat): 1742, 1644, 1498, 1448, 1372, 1220, 1150, 1035, 985, 930, 810, 706 cm^{-1}.


f1 (ppm)
2.00
1.00
1.00
1.00
1.07
0.94
3.01
7.10
7.09
7.09
7.09
7.09
7.09
7.08
7.08
7.07
7.07
7.07
7.07
7.03
7.03
7.02
7.01
6.23
6.22
6.22
6.21
6.21
6.21
6.00
5.99
5.97
5.96
5.96
5.94
5.93
5.92
5.32
5.32
5.31
5.29
5.29
5.29
5.28
5.28
5.27
5.27
5.26
5.26
2.11


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
169.90
144.06
143.63
135.88
135.39
134.33
131.79
129.25
122.93
117.50
109.42
108.79
75.59
21.26


-49.95
f1 (ppm)

1-(6-(trifluoromethyl)pyridin-3-yl)allyl acetate (1c)



Procedure

Allylic alcohol **S1c** (717 mg, 3.53 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 94% yield (814 mg, 3.32 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1).

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 4:1).

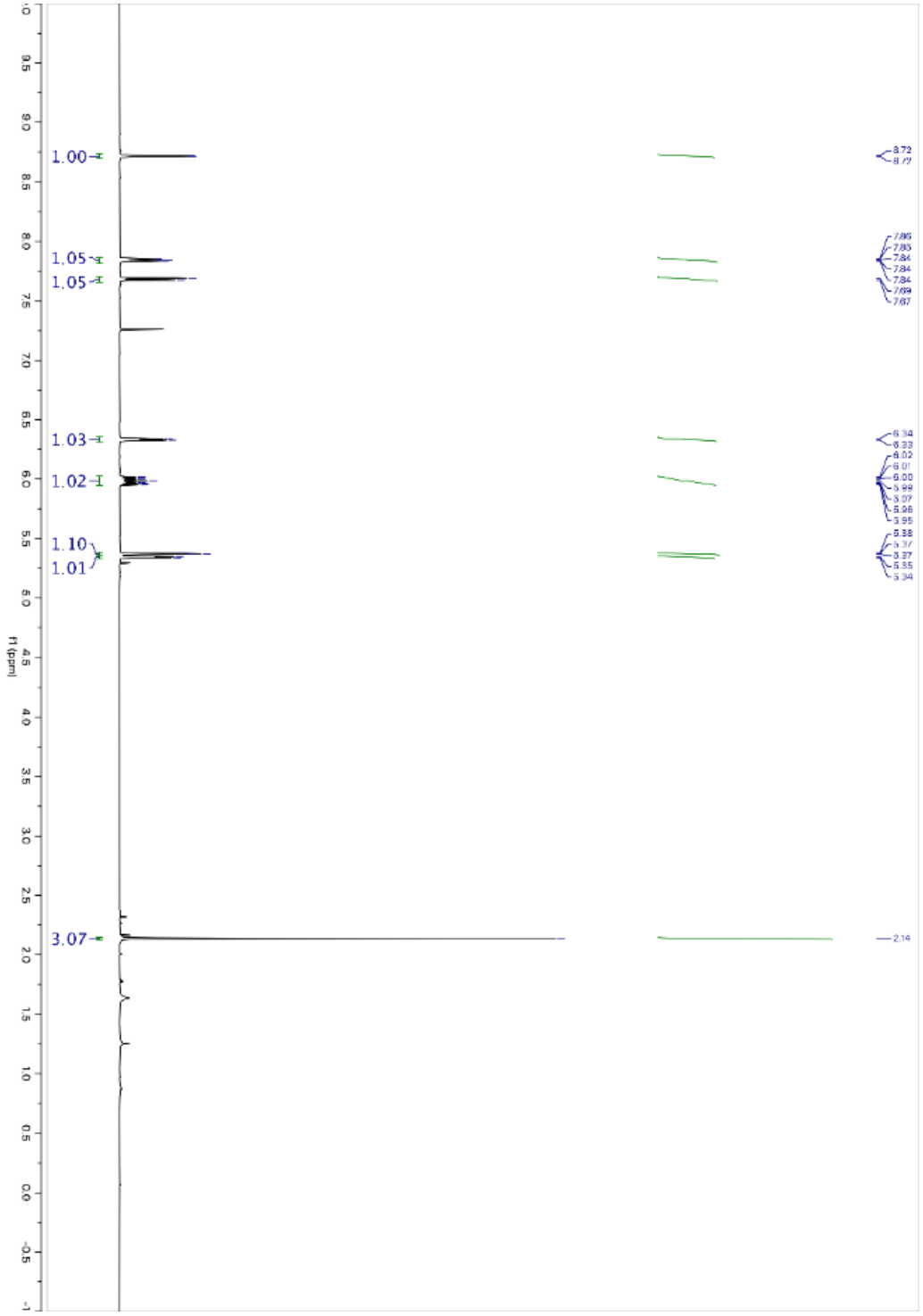
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 2.2 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 6.33 (d, *J* = 6.0 Hz, 1H), 5.99 (ddd, *J* = 16.7, 10.3, 6.0 Hz, 1H), 5.39 – 5.36 (m, 1H), 5.34 (d, *J* = 4.2 Hz, 1H), 2.14 (s, 3H).

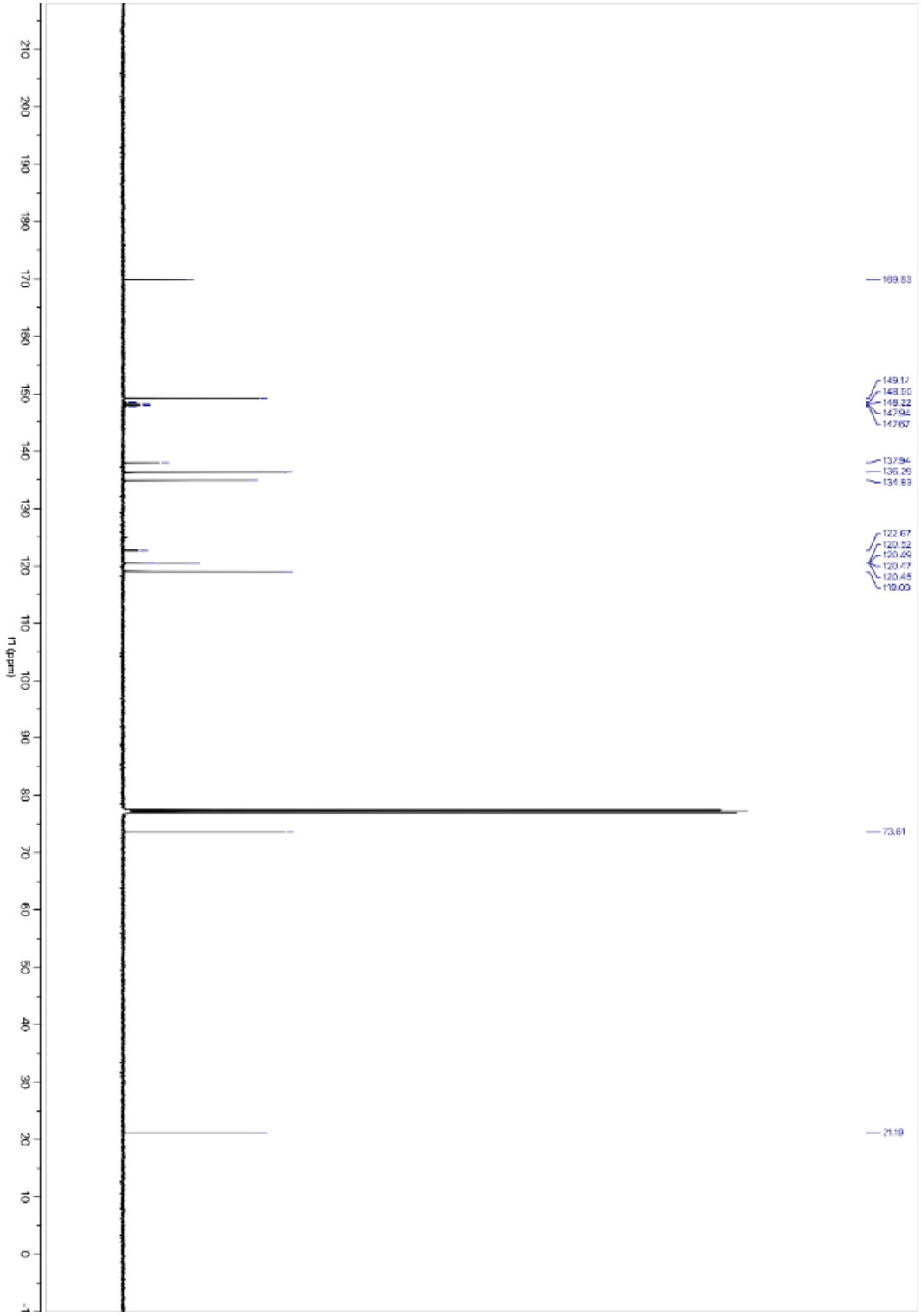
^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.8, 149.2, 148.1 (q, *J* = 34.9 Hz), 137.9, 136.3, 134.8, 122.7, 120.48 (q, *J* = 2.8 Hz), 119.0, 73.6, 21.2.

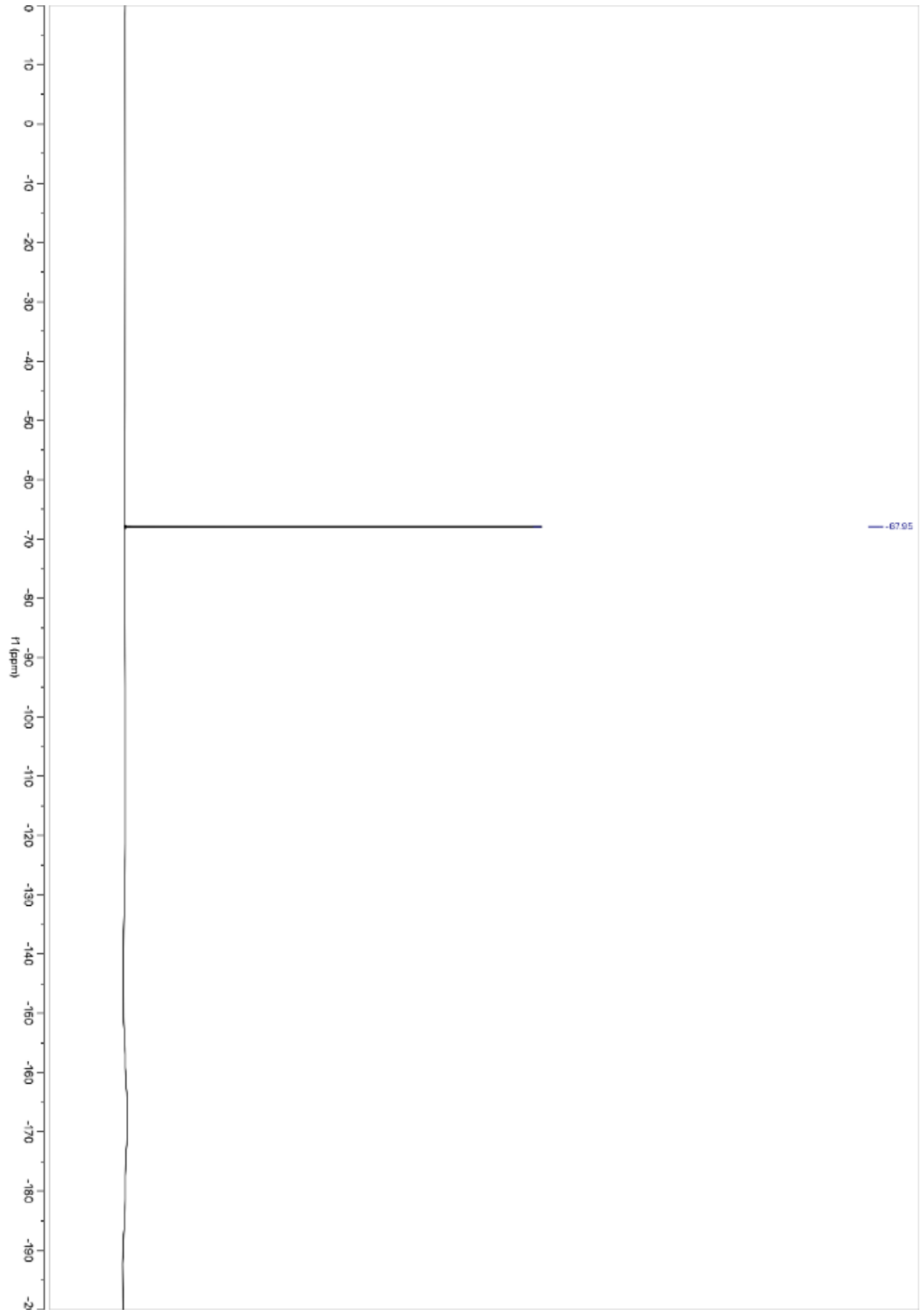
^{19}F NMR (471 MHz, $CDCl_3$) δ = -68.0.

HRMS (ESI): Calculated for $C_{11}H_{10}F_3NO_2$ [M+H$^+$] = 246.0736, Found 246.0735.

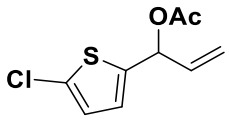
FTIR (neat): 1743, 1372, 1337, 1225, 1174, 1132, 1085, 1021, 985, 938, 841, 772, 702 cm^{-1}.


1.00
1.05
1.05
1.03
1.02
1.10
1.01
3.07
f1 (ppm)


f1 (ppm)
169.83
149.17
148.50
148.22
147.94
147.67
137.94
135.29
134.83
122.67
120.52
120.29
120.07
120.45
119.03
73.61
21.19


-67.95
f1 (ppm)

1-(5-chlorothiophen-2-yl)allyl acetate (1d)



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with allylic alcohol **S1d** (1.71 g, 9.79 mmol, 100 mol%), triethylamine (2.05 mL, 14.7 mmol, 150 mol%), acetic anhydride (1.02 mL, 10.8 mmol, 110 mol%), 4-dimethylaminopyridine (120 mg, 0.98 mmol, 10 mol%), and anhydrous dichloromethane (0.5 M). The reaction was stirred at ambient temperature until starting material was consumed. The reaction solution was quenched with methanol (1.12 mL, 29.4 mmol, 300 mol%) and was diluted with dichloromethane. The organics were washed with an aqueous saturated solution of sodium bicarbonate. The aqueous was extracted three times by dichloromethane. The organics were combined and washed with brine. The organic layer was separated and dried over anhydrous sodium sulfate. The organics were passed through a fritted filter into a round bottom flask and were concentrated *in vacuo*. The title compound was obtained in 71% yield (1.51 g, 6.97 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate: triethylamine 94:5:1). Warning: product is prone to decomposition when exposed to mild acid.

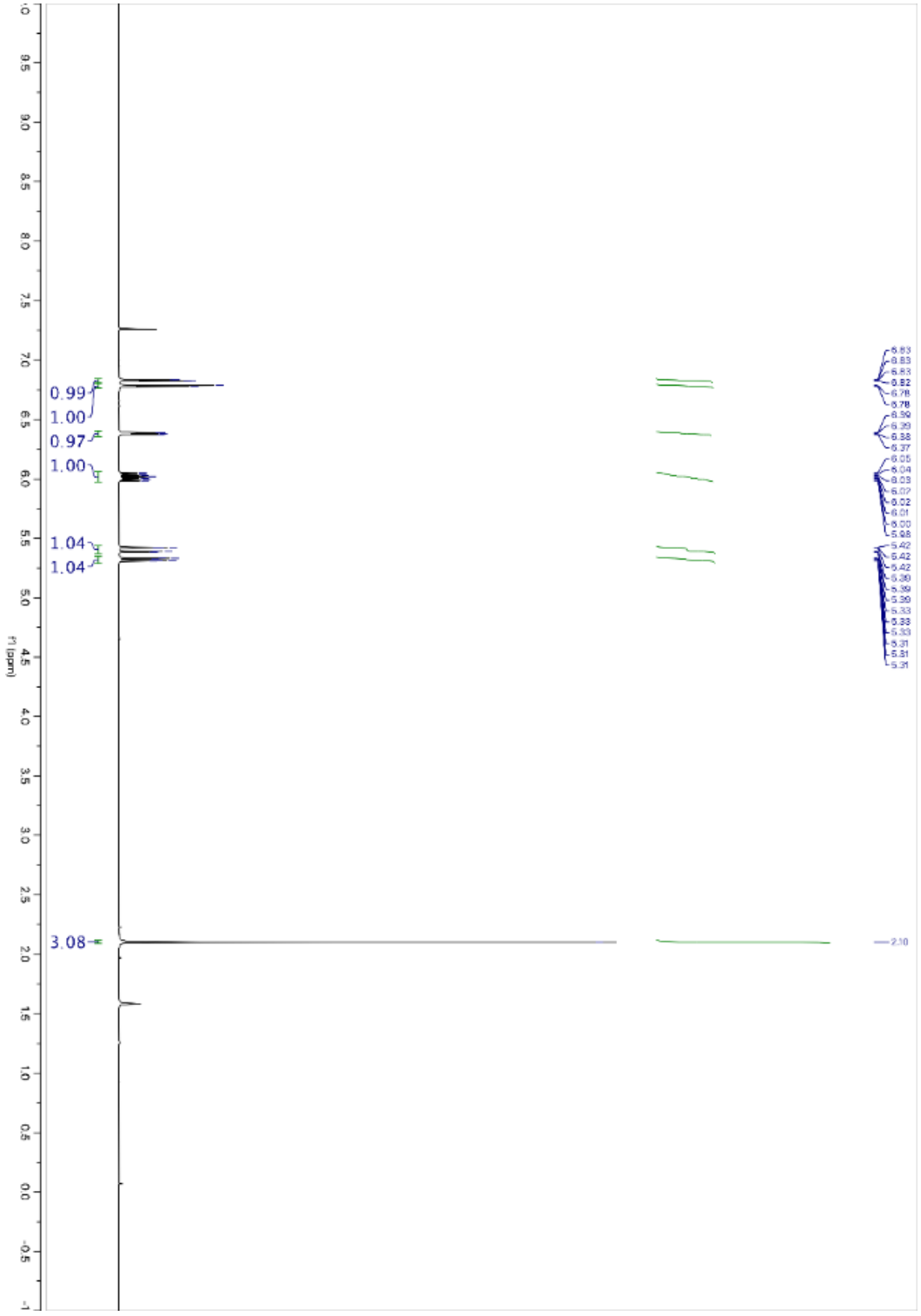
TLC (SiO_2) R_f = 0.75 (hexanes: ethyl acetate = 4:1).

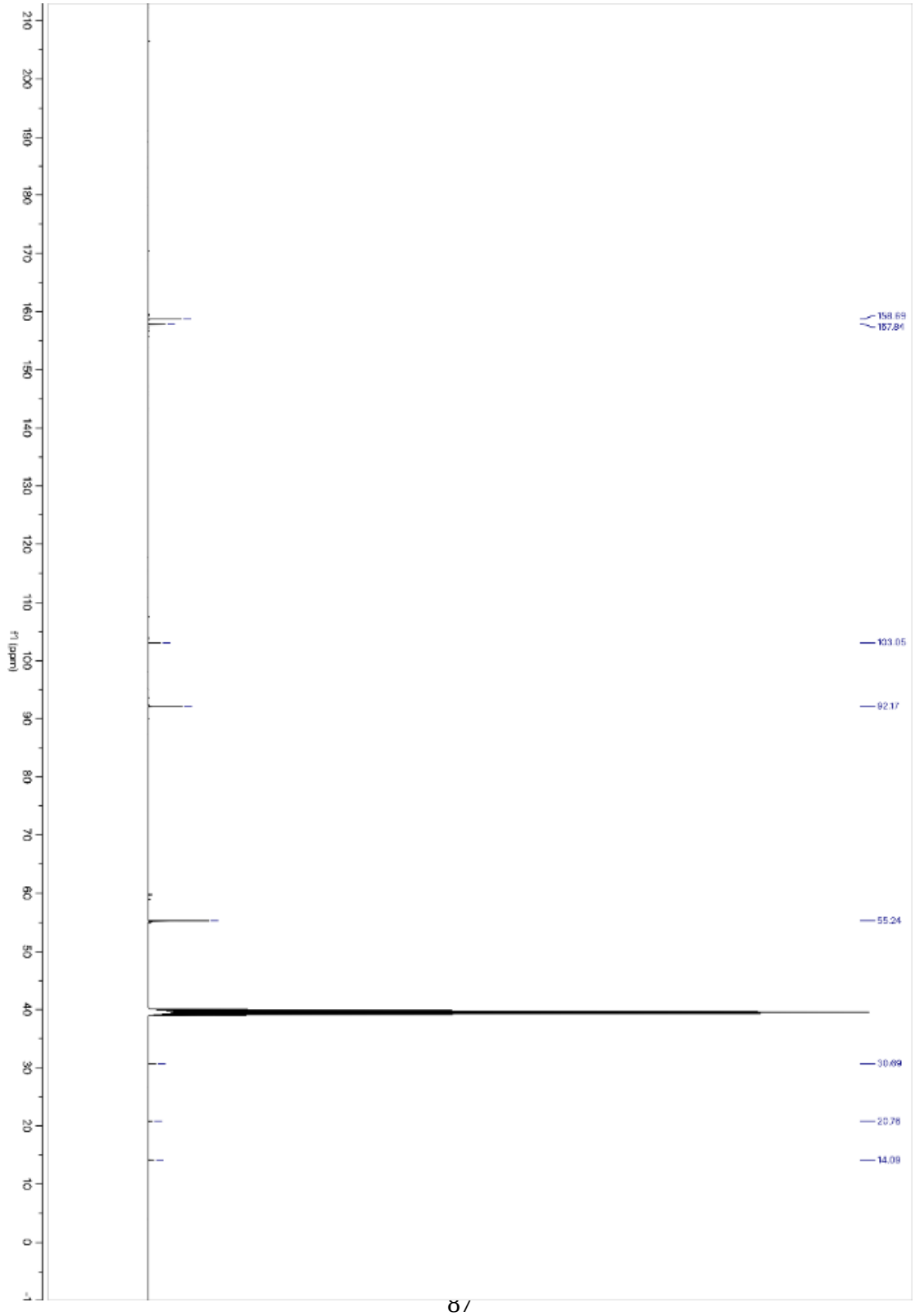
^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.83 (dd, *J* = 3.8, 0.9 Hz, 1 H), 6.78 (d, *J* = 3.8 Hz, 1H), 6.38 (dq, *J* = 5.8, 1.2 Hz, 1H), 6.02 (ddd, *J* = 17.1, 10.4, 5.9 Hz, 1H), 5.40 (dt, *J* = 17.1, 1.2 Hz, 1H), 5.32 (dt, *J* = 10.5, 1.2 Hz, 1H), 2.10 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 158.7, 157.8, 103.1, 92.2, 55.2, 30.7, 20.8, 14.1.

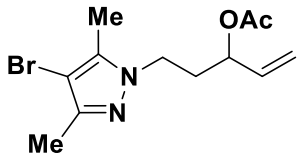
HRMS (ESI): Calculated for $C_9H_9ClO_2S$ [M+Na^+] = 238.9904, Found 238.9907.

FTIR (neat): 1738, 1448, 1369, 1222, 1094, 1062, 1017, 998, 993, 796, 769, 715 cm^{-1}.


0.99
1.00
0.97
1.00
1.04
1.04
3.08
2.10
f1 (ppm)


f1 (ppm)
158.69
157.86
103.05
92.17
55.24
30.69
20.78
14.09

5-(4-bromo-3,5-dimethyl-1*H*-pyrazol-1-yl)pent-1-en-3-yl acetate (1e)



Procedure

Allylic alcohol **S1e** (1.000 g, 3.86 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 82% yield (954 mg, 3.16 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

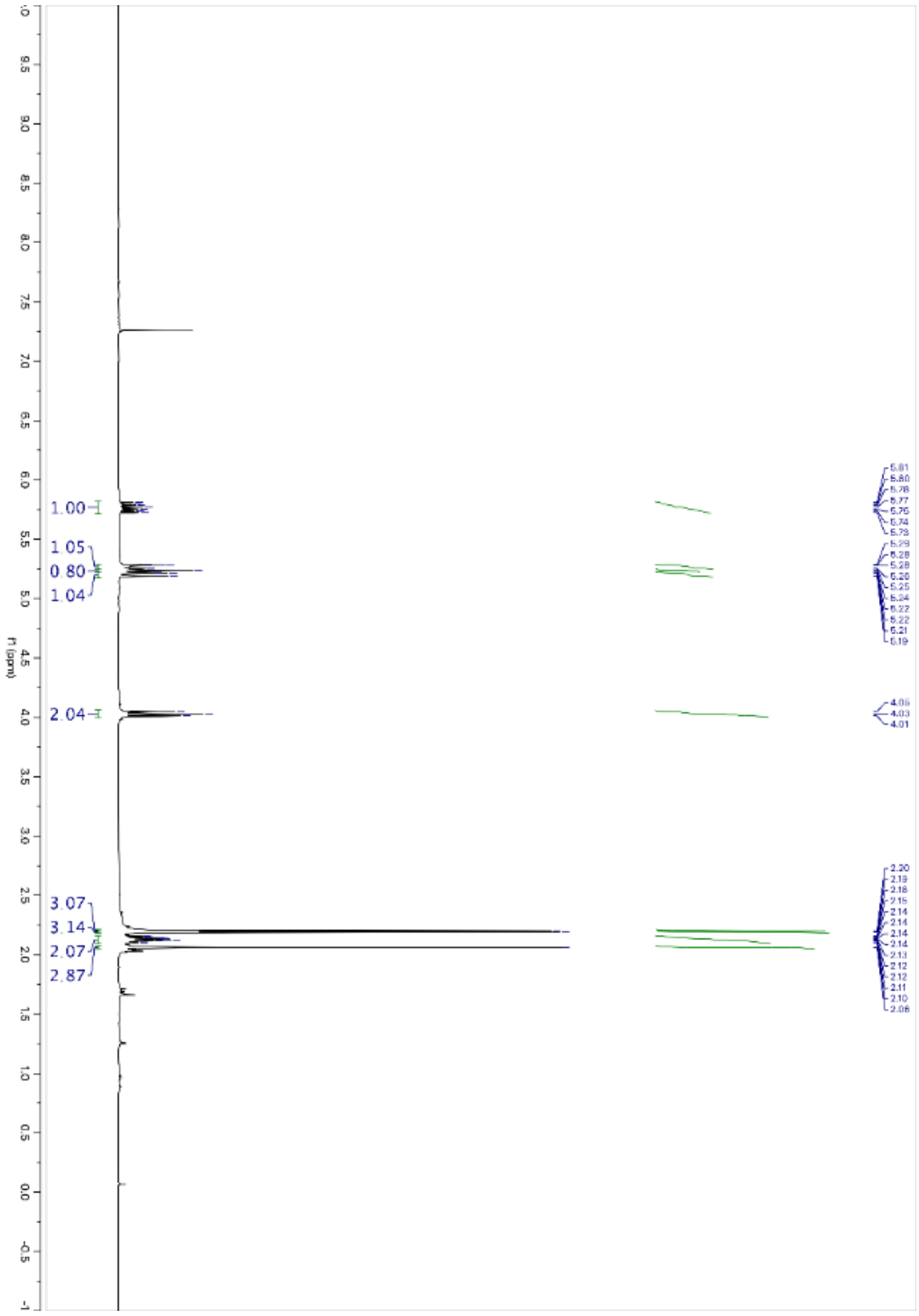
TLC (SiO_2) R_f = 0.61 (hexanes: ethyl acetate = 1:1).

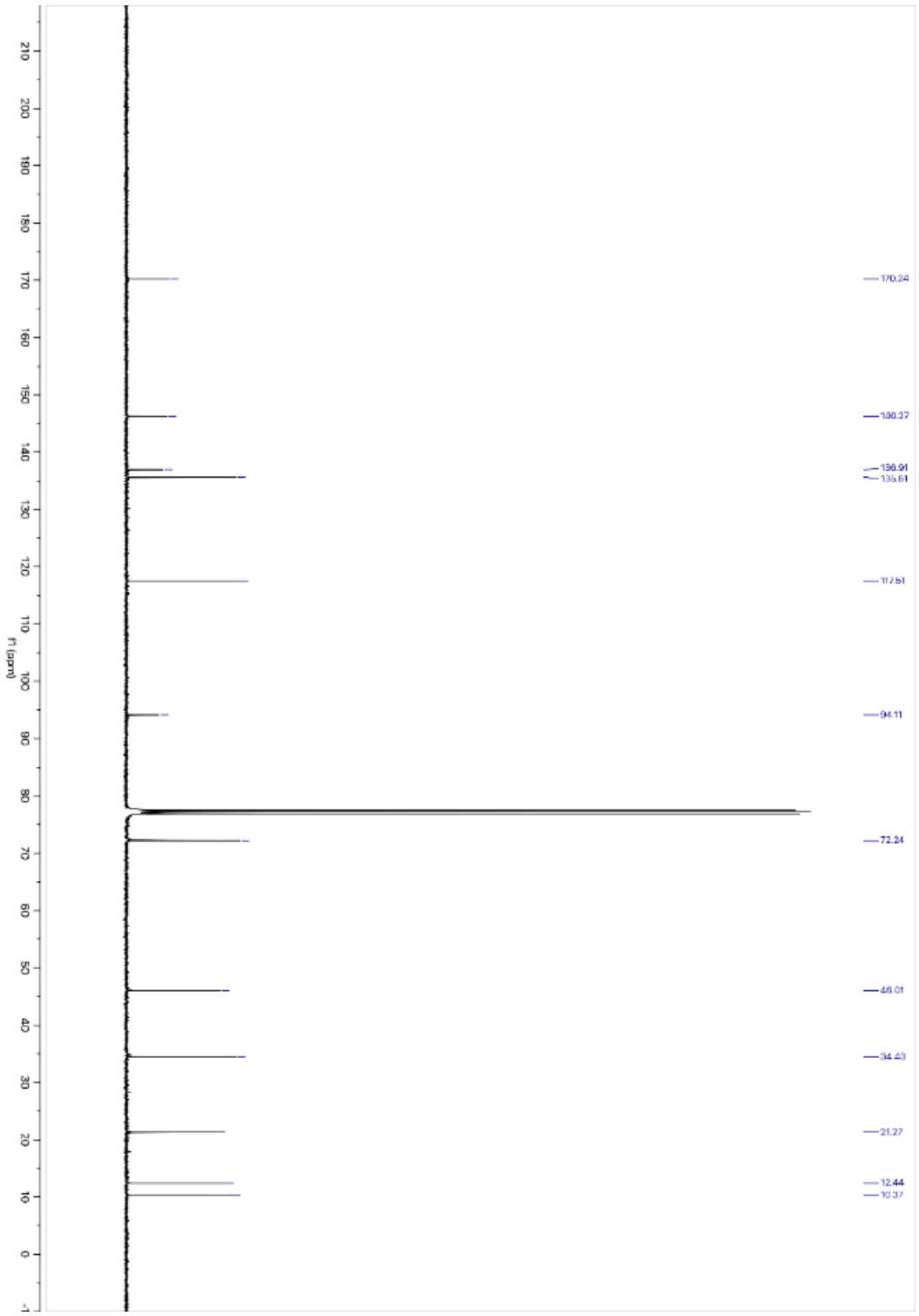
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.77 (ddd, *J* = 17.0, 10.6, 6.0 Hz, 1H), 5.27 (dd, *J* = 10.6, 1.2 Hz, 1H), 5.24 (s, 1H), 5.22 – 5.17 (m, 1H), 4.07 – 3.96 (m, 2H), 2.20 (s, 3H), 2.19 (s, 3H), 2.16 – 2.09 (m, 2H), 2.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.2, 146.3, 136.9, 135.6, 117.5, 94.1, 72.2, 46.0, 34.4, 21.3, 12.4, 10.4.

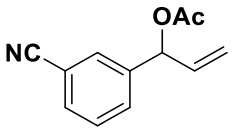
HRMS (ESI): Calculated for $C_{12}H_{17}BrN_2O_2$ [M+H$^+$] = 301.0546, Found 301.0548.

FTIR (neat): 2928, 1736, 1647, 1548, 1475, 1425, 1371, 1231, 1066, 1021, 991, 932 cm^{-1}.


1.00
1.05
0.80
1.04
2.04
3.07
3.14
2.07
2.87
f1 (ppm)


f1 (ppm)
170.24
138.27
136.91
135.61
117.51
94.11
72.24
46.01
34.43
21.27
12.44
10.37

1-(3-cyanophenyl)allyl acetate (1f)



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with 3-cyanobenzaldehyde (262 mg, 2.0 mmol, 100 mol%). The vessel was purged with argon and anhydrous THF (6.5 mL, 0.3 M) was added. A solution of vinyl magnesium bromide (4.0 mL, 1.0 M in THF, 200 mol%) was added at 0 °C. Following addition, the reaction was allowed to reach ambient temperature and was stirred until starting material was consumed. Triethylamine (0.56 mL, 4.0 mmol, 200 mol%) and acetic anhydride (0.28 mL, 3.0 mmol, 150 mol%) were added to the reaction solution via syringe. The reaction was stirred at ambient temperature for one hour. The reaction solution was diluted with dichloromethane and was washed sequentially with aqueous saturated solutions of sodium chloride, sodium bicarbonate, distilled water, and brine. The organic layer was separated and dried over anhydrous sodium sulfate. The organics were passed through a fritted filter into a round bottom flask and concentrated *in vacuo*. The title compound was obtained in 37% yield (147.3 mg, 0.732 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1-15:1).

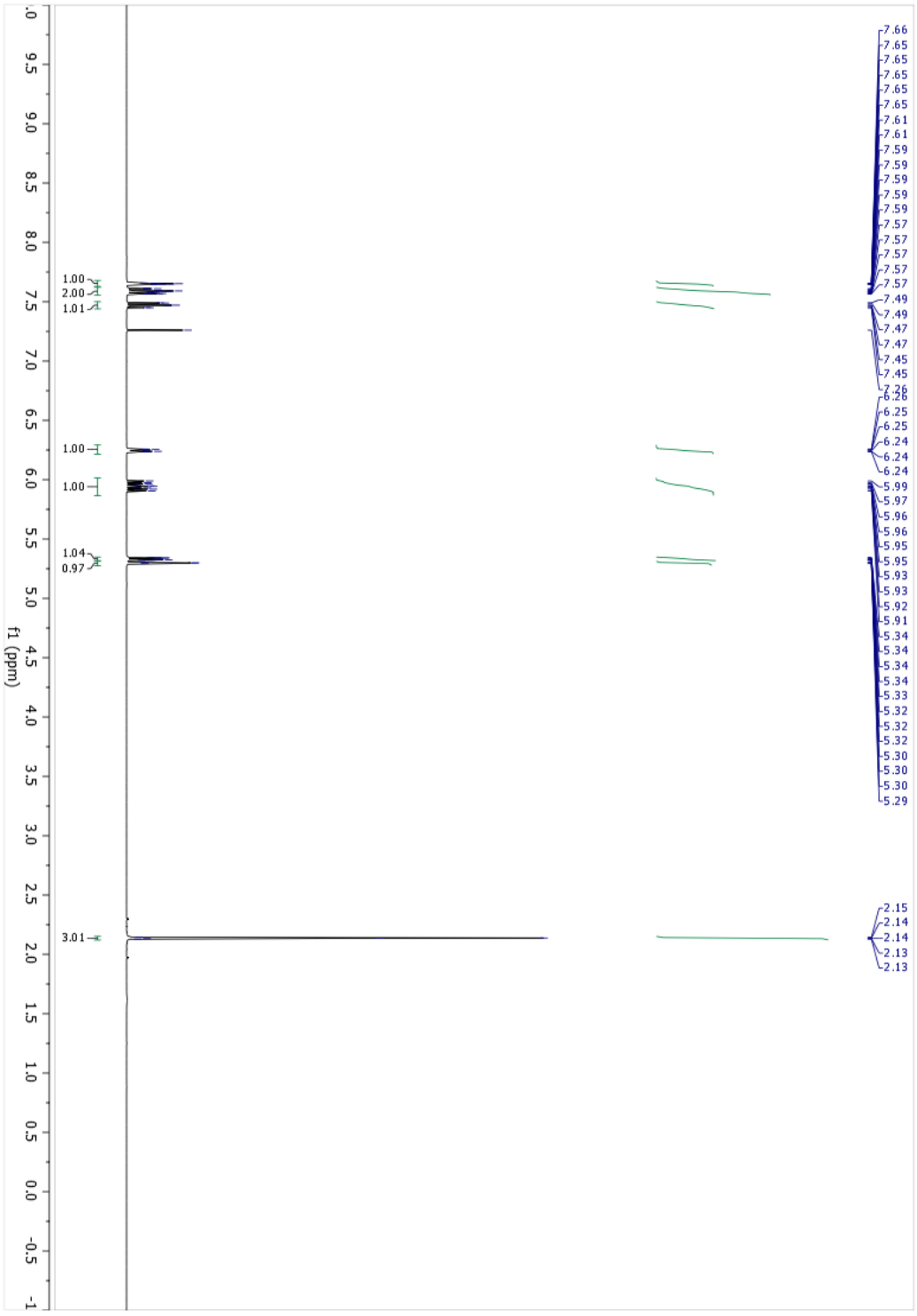
TLC (SiO_2) R_f = 0.44 (hexanes: ethyl acetate = 4:1).

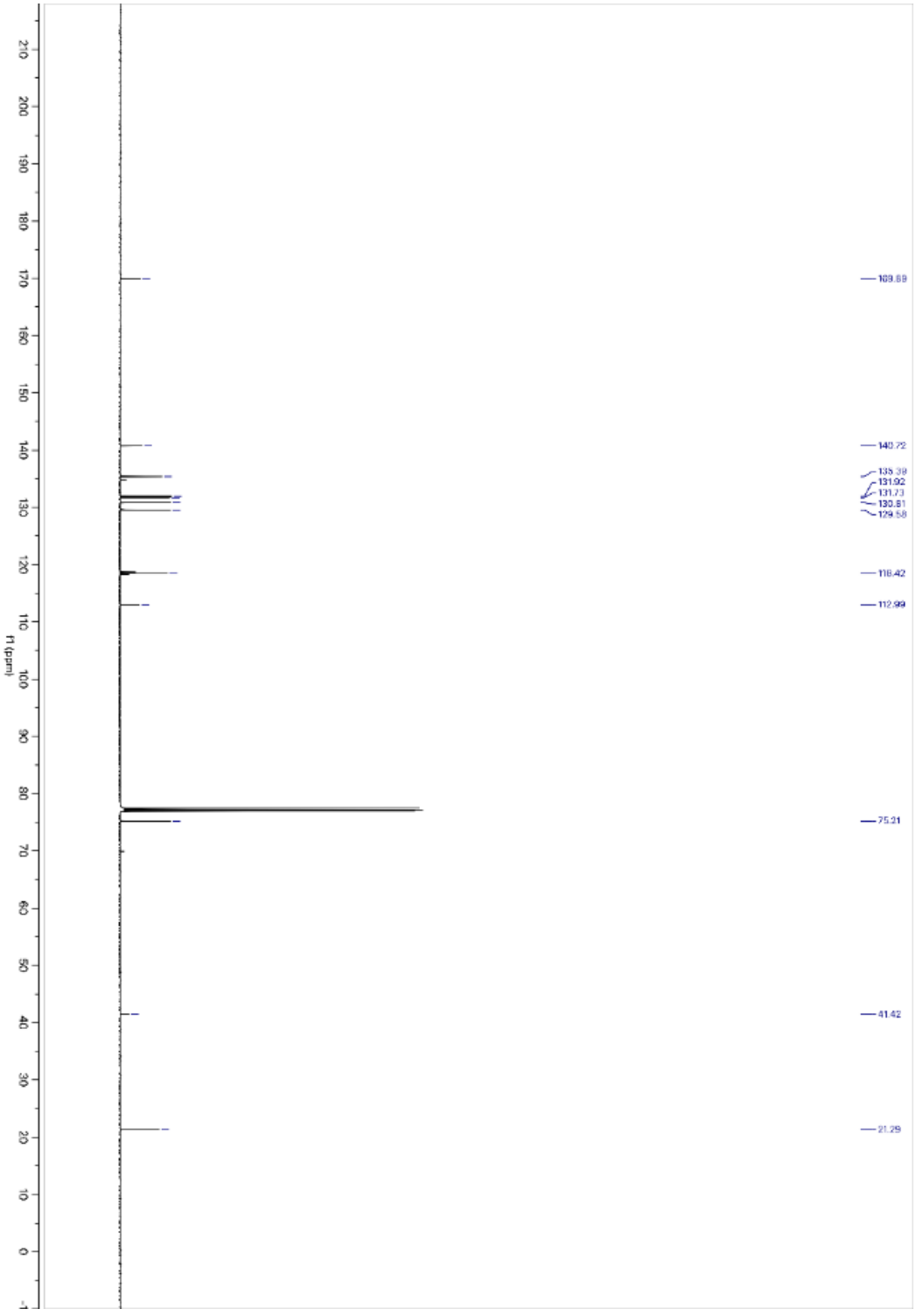
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83 (s, 1H), 7.80 (s, 2H), 6.34 (d, *J* = 6.1 Hz, 1H), 5.97 (dddd, *J* = 17.4, 10.4, 6.1, 0.9 Hz, 1H), 5.39 (dq, *J* = 7.6, 1.0 Hz, 1H), 5.36 – 5.29 (m, 1H), 2.16 (d, *J* = 0.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.9, 140.7, 135.4, 131.9, 131.7, 130.8, 129.6, 118.4, 113.0, 75.2, 41.4, 21.3.

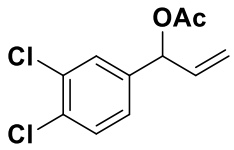
HRMS (ESI): Calculated for $C_{12}H_{11}NO_2$ [M+Na^+] = 224.0682, Found 224.0684.

FTIR (neat): 2932, 2231, 1740, 1483, 1434, 1371, 1224, 1023, 984, 933, 802, 754, 694 cm^{-1}.


f1 (ppm)
1.00
2.00
1.01
1.00
1.00
1.04
0.97
3.01
7.66
7.65
7.65
7.65
7.65
7.65
7.61
7.61
7.59
7.59
7.59
7.59
7.59
7.57
7.57
7.57
7.57
7.57
7.49
7.49
7.47
7.47
7.45
7.45
6.26
6.25
6.25
6.24
6.24
6.24
5.99
5.97
5.96
5.96
5.95
5.95
5.93
5.93
5.92
5.91
5.34
5.34
5.34
5.34
5.33
5.32
5.32
5.32
5.30
5.30
5.30
5.29
2.15
2.14
2.14
2.13
2.13


f1 (ppm)
169.89
140.72
135.38
131.92
131.73
130.81
129.58
118.42
112.99
75.21
41.42
21.29

1-(3,4-dichlorophenyl)allyl acetate (1g)



Procedure

Allylic alcohol **S1g** (656 mg, 3.23 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 68% yield (538 mg, 2.19 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–15:1).

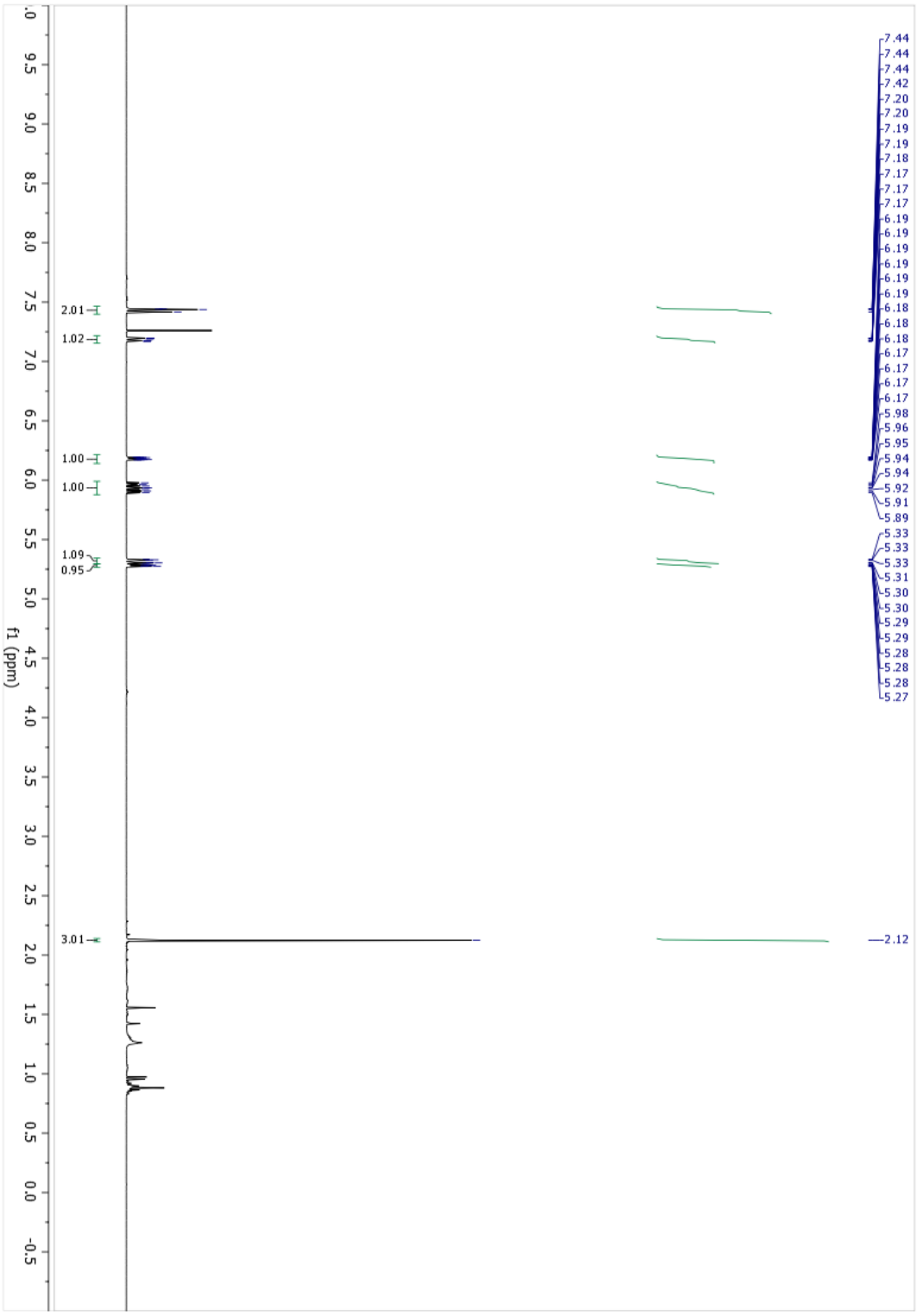
TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 4:1).

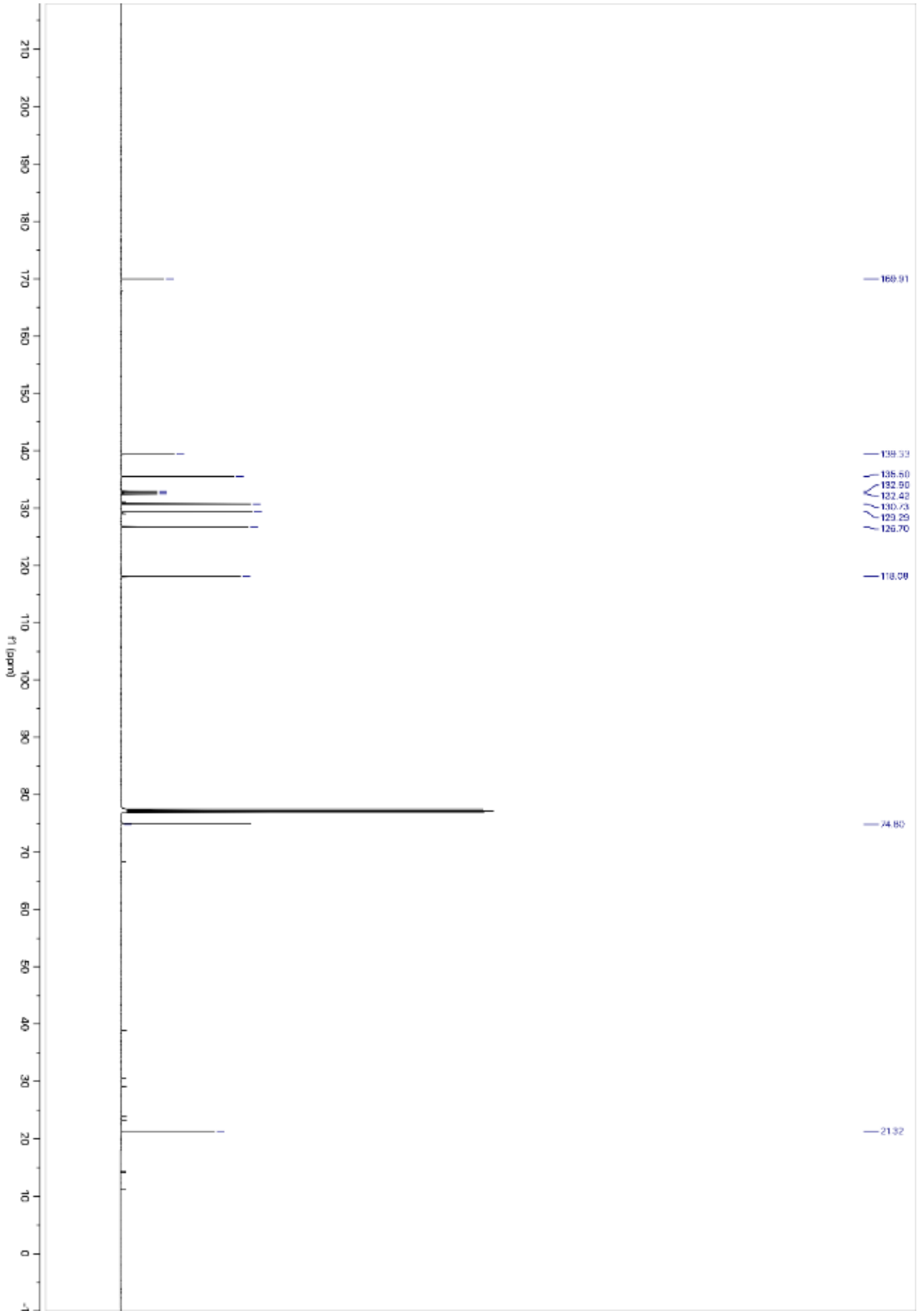
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 2.1 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.18 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.19 (dd, *J* = 5.9, 1.4 Hz, 1H), 5.94 (ddd, *J* = 16.7, 10.4, 5.9 Hz, 1H), 5.33 – 5.29 (m, 1H), 5.29 (dd, *J* = 6.3, 1.6 Hz, 1H), 2.12 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.9, 139.3, 135.5, 132.9, 132.4, 130.7, 129.3, 126.7, 118.1, 74.8, 21.3.

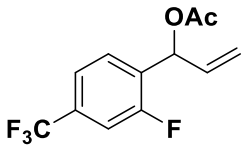
HRMS (ESI): Calculated for $C_{11}H_{10}Cl_2O_2$ [M+Na^+] = 266.9950, Found 266.9954.

FTIR (neat): 3089, 2930, 1740, 1644, 1565, 1471, 1410, 1396, 1370, 1226, 1200, 1132, 1099, 1029, 984, 936, 893, 821, 759, 708 cm^{-1}.


f1 (ppm)
2.01
1.02
1.00
1.00
1.09
0.95
3.01
7.44
7.44
7.44
7.42
7.20
7.20
7.19
7.19
7.18
7.17
7.17
7.17
6.19
6.19
6.19
6.19
6.19
6.19
6.18
6.18
6.18
6.17
6.17
6.17
6.17
5.98
5.96
5.95
5.94
5.94
5.92
5.91
5.89
5.33
5.33
5.33
5.31
5.30
5.30
5.29
5.29
5.28
5.28
5.28
5.27
2.12


f1 (ppm)
169.91
139.33
135.60
132.90
132.42
130.43
129.29
129.70
118.09
74.80
21.32

1-(2-fluoro-4-(trifluoromethyl)phenyl)allyl acetate (1i)



Procedure

Allylic alcohol **S1i** (500 mg, 2.27 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 82% yield (488 mg, 1.86 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.60 (hexanes: ethyl acetate = 4:1).

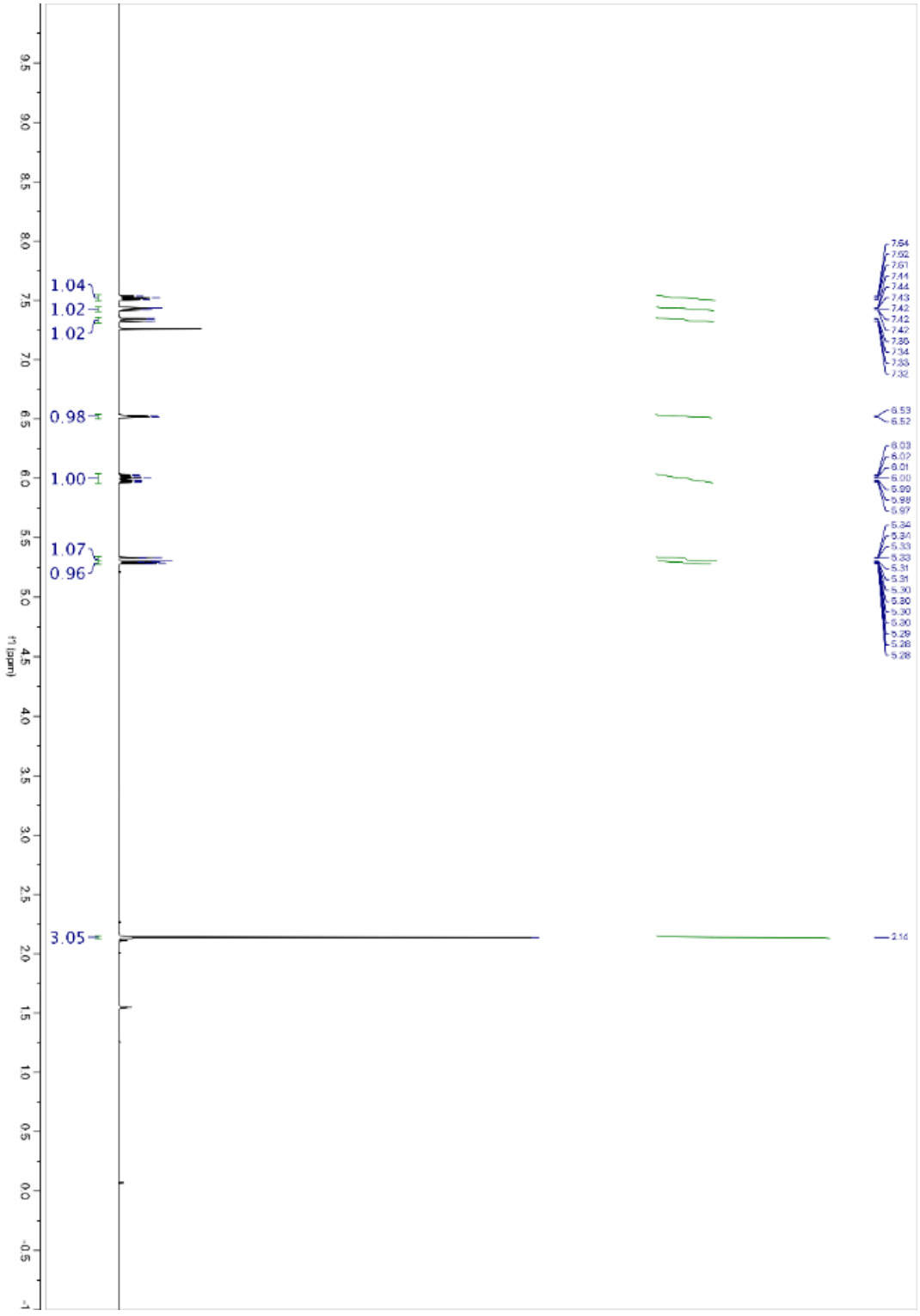
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.52 (t, *J* = 7.4 Hz, 1H), 7.46 – 7.40 (m, 1H), 7.33 (dd, *J* = 9.8, 1.8 Hz, 1H), 6.52 (d, *J* = 5.8 Hz, 1H), 6.00 (ddd, *J* = 16.8, 10.4, 5.9 Hz, 1H), 5.35 – 5.30 (m, 1H), 5.29 (dt, *J* = 7.1, 1.0 Hz, 1H), 2.14 (s, 3H).

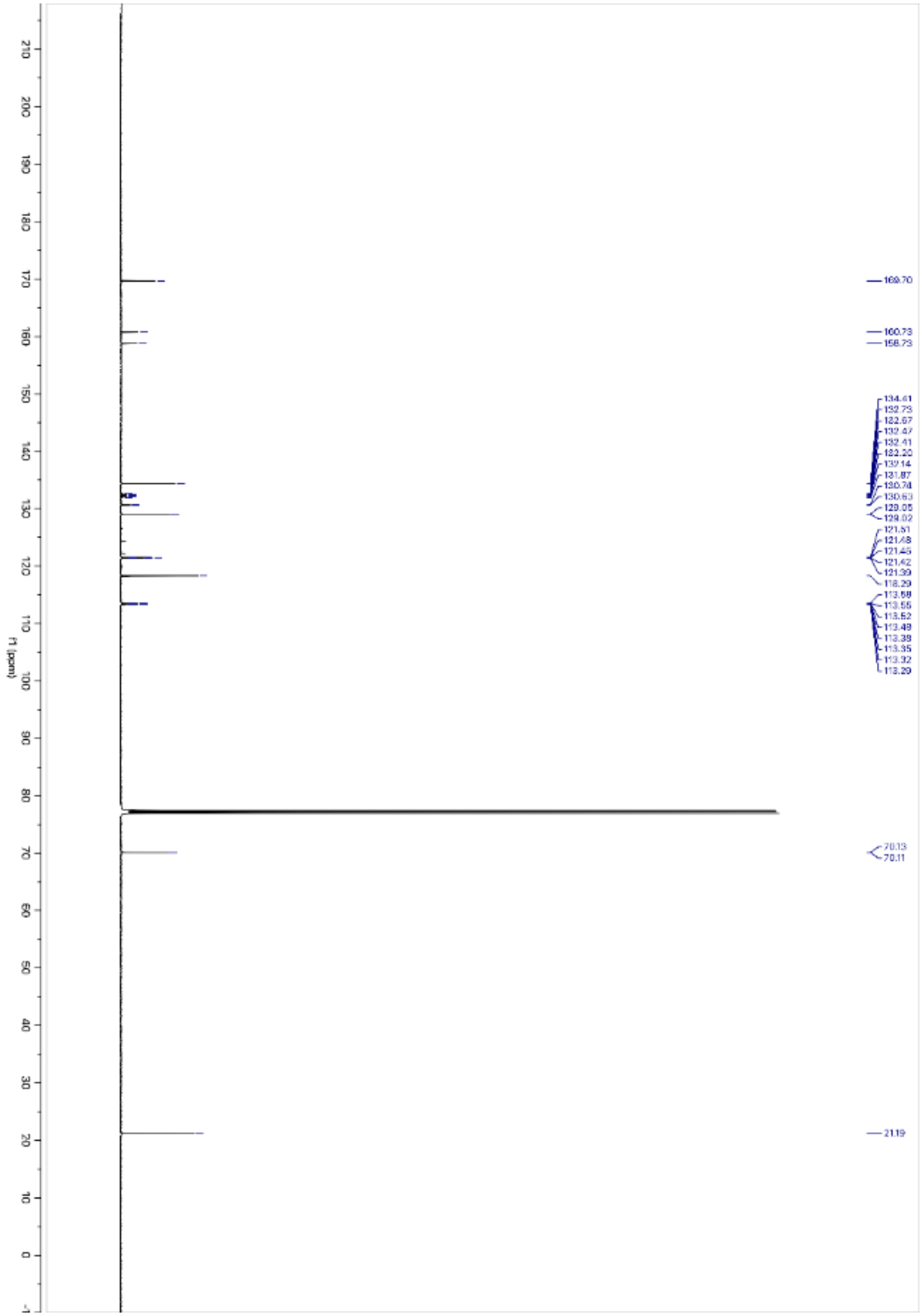
^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.7, 160.7, 158.7, 134.4, 132.9 – 131.8 (m), 130.7 (d, *J* = 13.6 Hz), 129.0 (d, *J* = 4.1 Hz), 121.5 (p, *J* = 3.8 Hz), 118.3, 113.4 (dq, *J* = 25.0, 3.9 Hz), 70.1 (d, *J* = 2.5 Hz), 21.2.

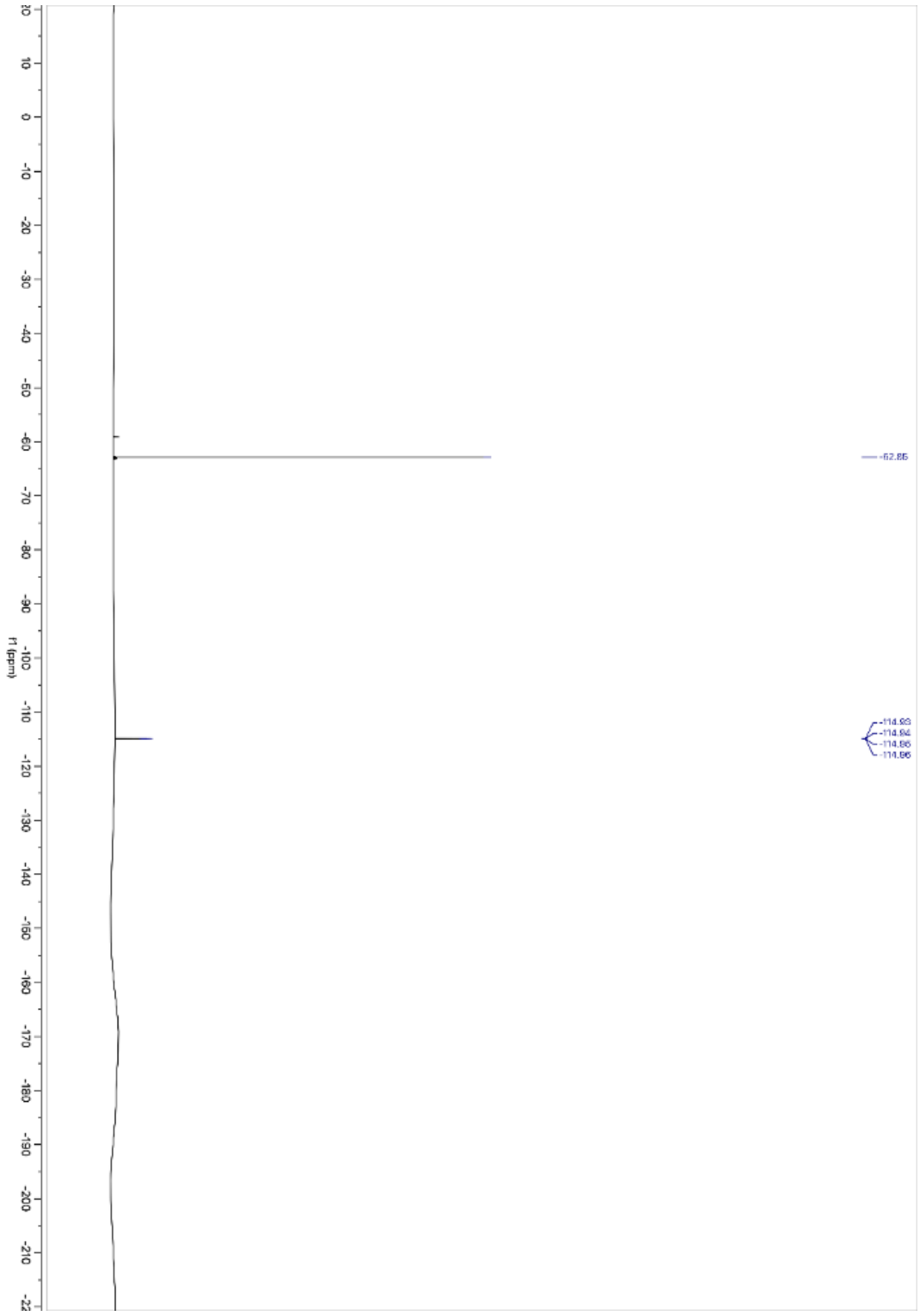
^{19}F NMR (471 MHz, $CDCl_3$) δ = -62.9, -114.9 (dd, *J* = 9.8, 6.8 Hz).

HRMS (ESI): Calculated for $C_{12}H_{10}F_4O_2$ [M+Ag^+] = 368.9662, Found 368.9667.

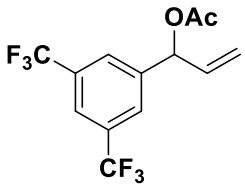
FTIR (neat): 3086, 1746, 1645, 1590, 1512, 1429, 1373, 1329, 1277, 1229, 1215, 1170, 1127, 1065, 1023, 983, 907, 879, 841, 746 cm^{-1}.


1.04
1.02
1.02
0.98
1.00
1.07
0.96
3.05
f1 (ppm)


f1 (ppm)
169.70
160.73
158.73
134.61
132.73
132.67
132.47
132.41
132.20
131.14
131.87
130.74
130.63
129.05
129.02
121.51
121.48
121.45
121.42
121.39
118.29
113.58
113.55
113.52
113.48
113.38
113.35
113.32
113.29
70.13
70.11
21.19


f1 (ppm)
-62.85
-114.93
-114.94
-114.95
-114.96

1-(3,5-bis(trifluoromethyl)phenyl)allyl acetate (1j)



Procedure

Allylic alcohol **S1j** (1.87 g, 6.91 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 77% yield (1.65 g, 5.29 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 60:1).

TLC (SiO_2) R_f = 0.53 (hexanes: ethyl acetate = 4:1).

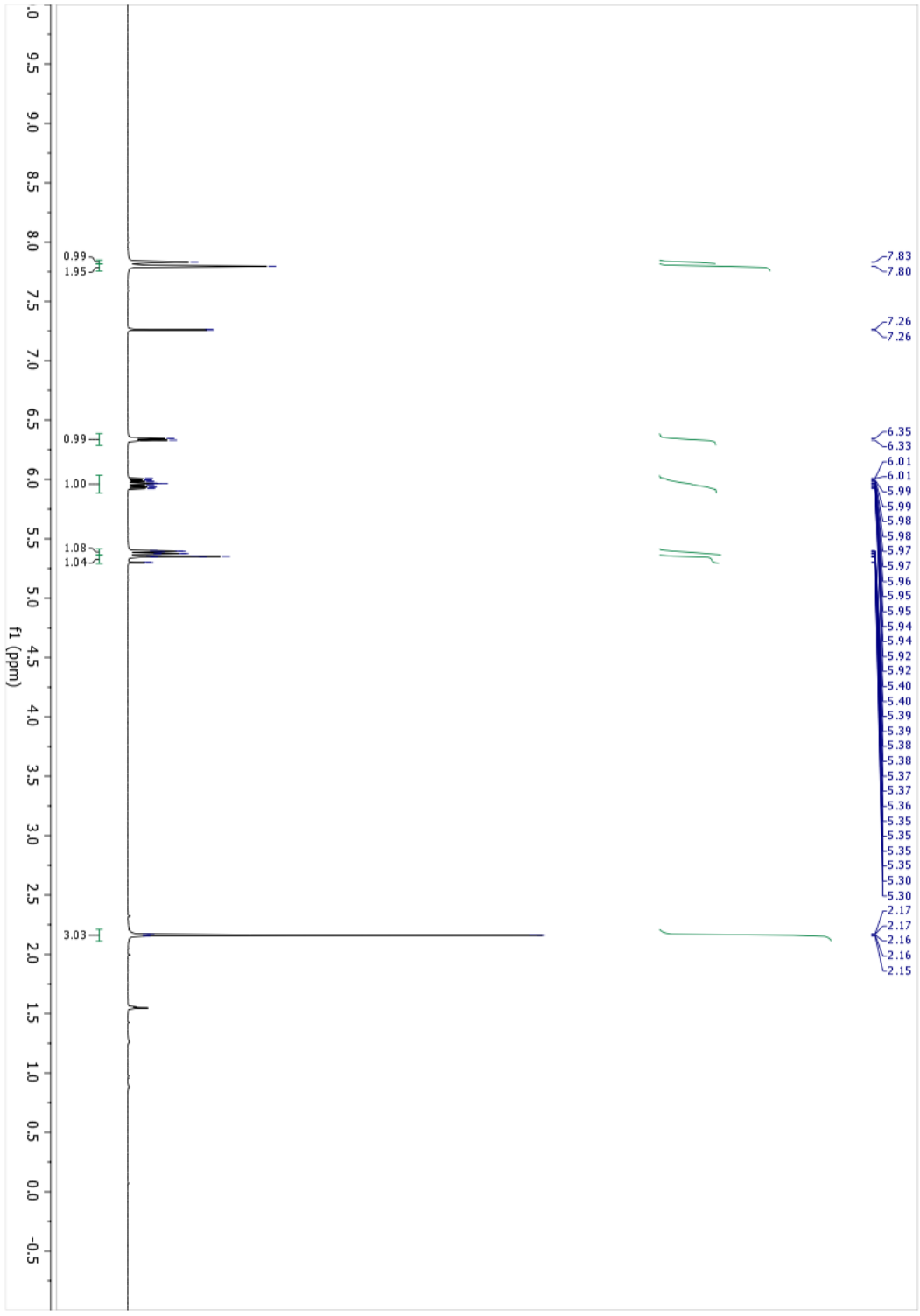
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 2.2 Hz, 1H), 7.80 (d, *J* = 1.8 Hz, 2H), 6.35 – 6.33 (m, 1H), 5.97 (ddd, *J* = 16.8, 10.4, 6.1 Hz, 1H), 5.38 (dt, *J* = 8.7, 1.1 Hz, 1H), 5.35 (p, *J* = 1.0 Hz, 1H), 2.16 (s, 3H).

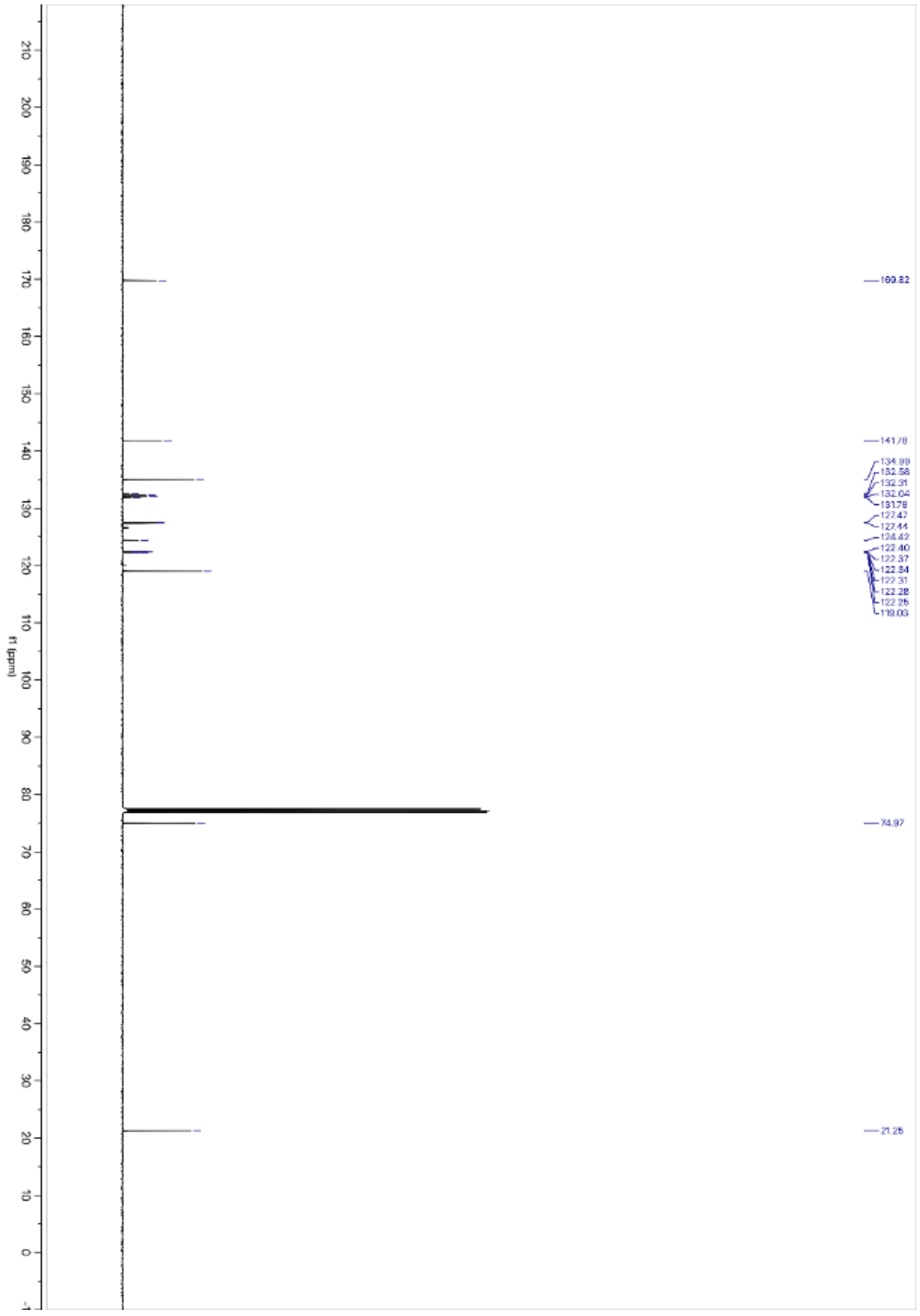
^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.8, 141.8, 135.0, 132.2 (q, *J* = 33.4 Hz), 127.5, 127.4, 124.4, 122.3 (p, *J* = 3.6 Hz), 122.3, 119.0, 75.0, 21.3.

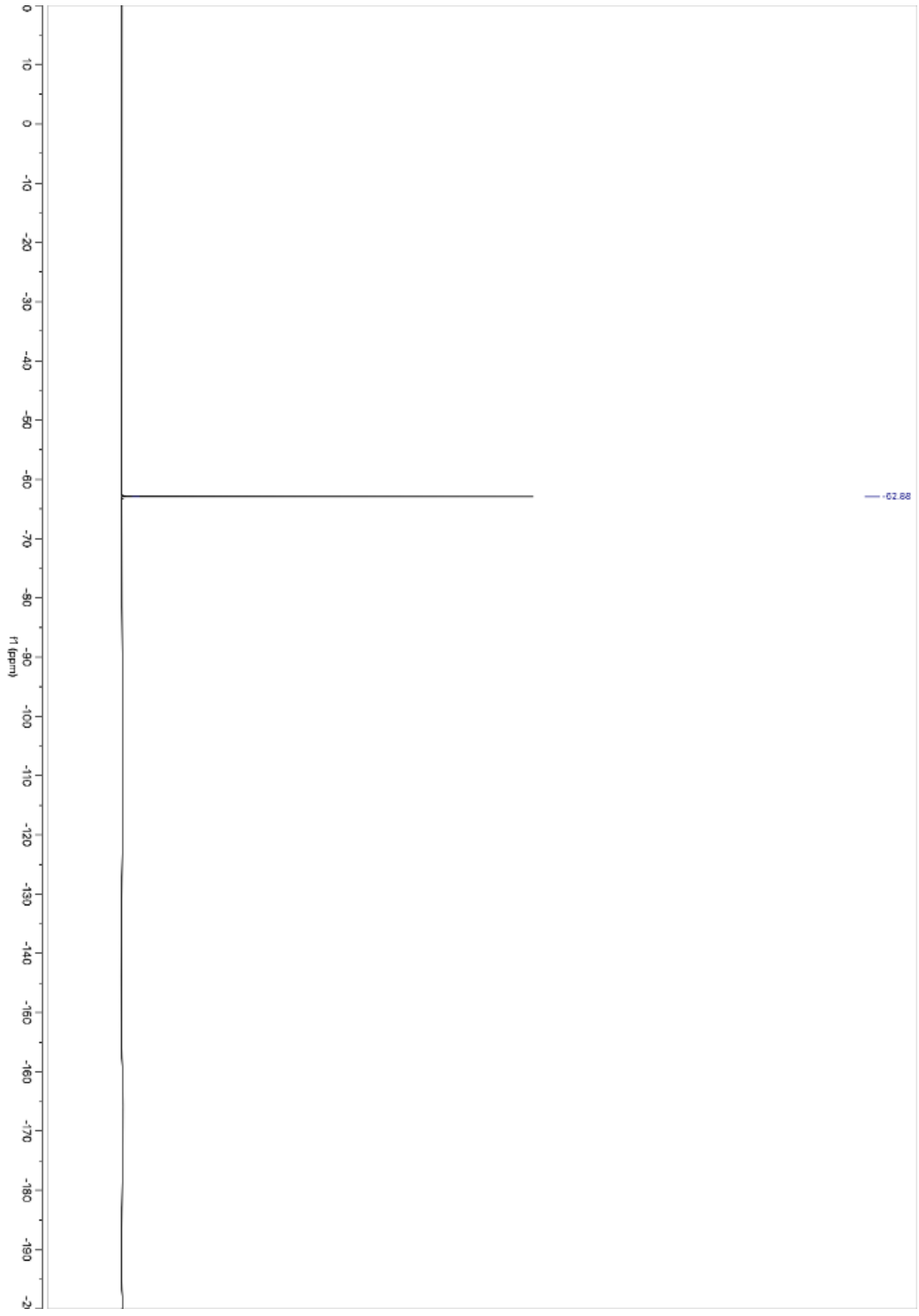
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.9.

HRMS (ESI): Calculated for $C_{13}H_{10}F_6O_2$ [M+Ag^+] = 418.9630, Found 418.9640.

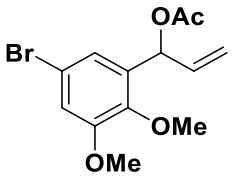
FTIR (neat): 2919, 2849, 2360, 1749, 1380, 1279, 1229, 1174, 1132, 1025, 986, 937, 904, 843, 754, 708, 683 cm^{-1}.


f1 (ppm)
0.99
1.95
0.99
1.00
1.08
1.04
3.03
7.83
7.80
7.26
7.26
6.35
6.33
6.01
6.01
5.99
5.99
5.98
5.98
5.97
5.97
5.96
5.95
5.95
5.94
5.94
5.92
5.92
5.40
5.40
5.39
5.39
5.38
5.38
5.37
5.37
5.36
5.35
5.35
5.35
5.35
5.30
5.30
2.17
2.17
2.16
2.16
2.15


f1 (ppm)
169.82
141.78
134.89
132.58
132.31
132.04
131.78
127.47
127.44
124.42
122.40
122.37
122.34
122.31
122.28
122.25
119.03
74.97
21.25


-62.88
f1 (ppm)

1-(5-bromo-2,3-dimethoxyphenyl)allyl acetate (1k)



Procedure

Allylic alcohol **S1k** (927 mg, 3.39 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 68% yield (495 mg, 1.57 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1–15:1).

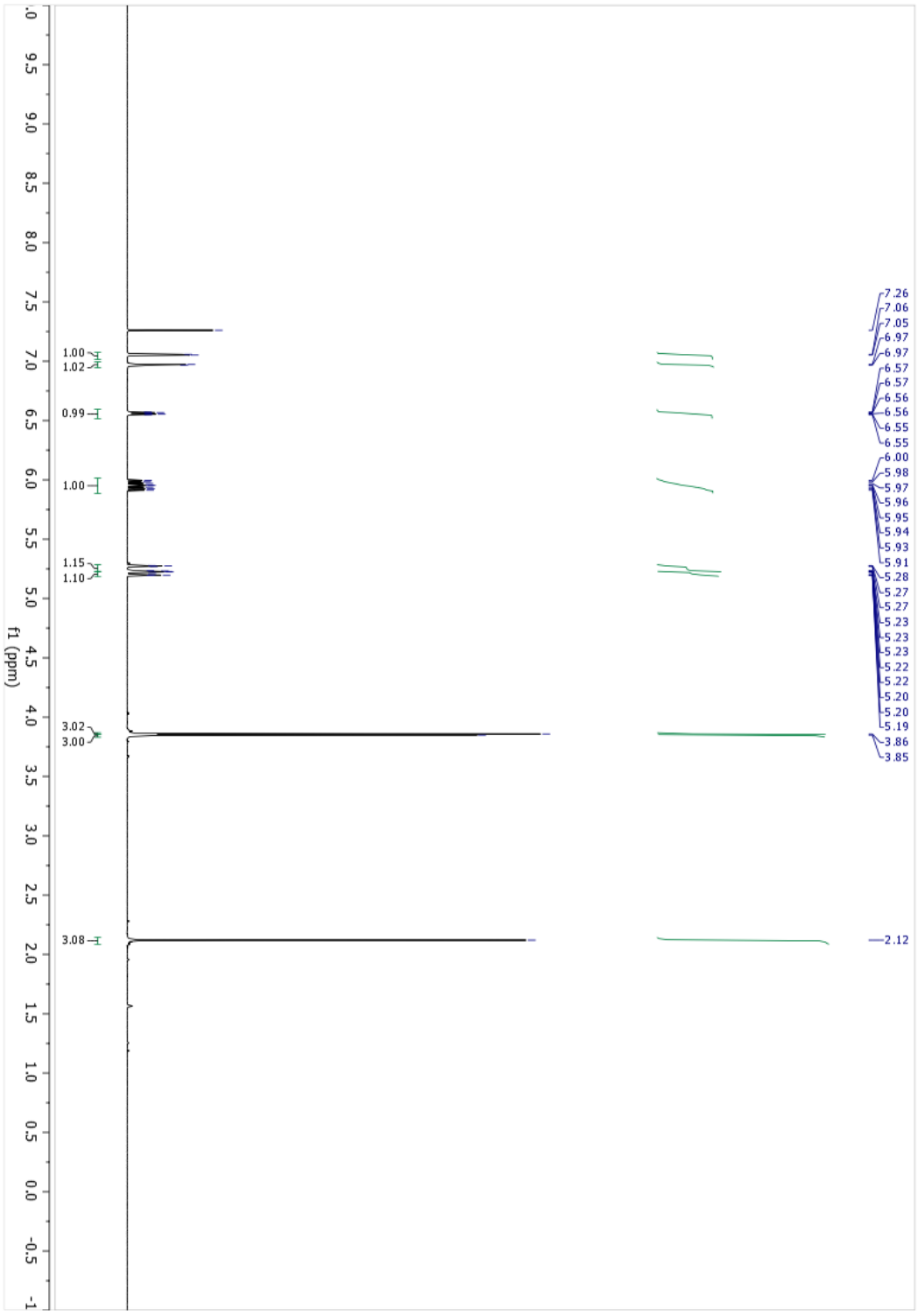
TLC (SiO_2) R_f = 0.42 (hexanes: ethyl acetate = 4:1).

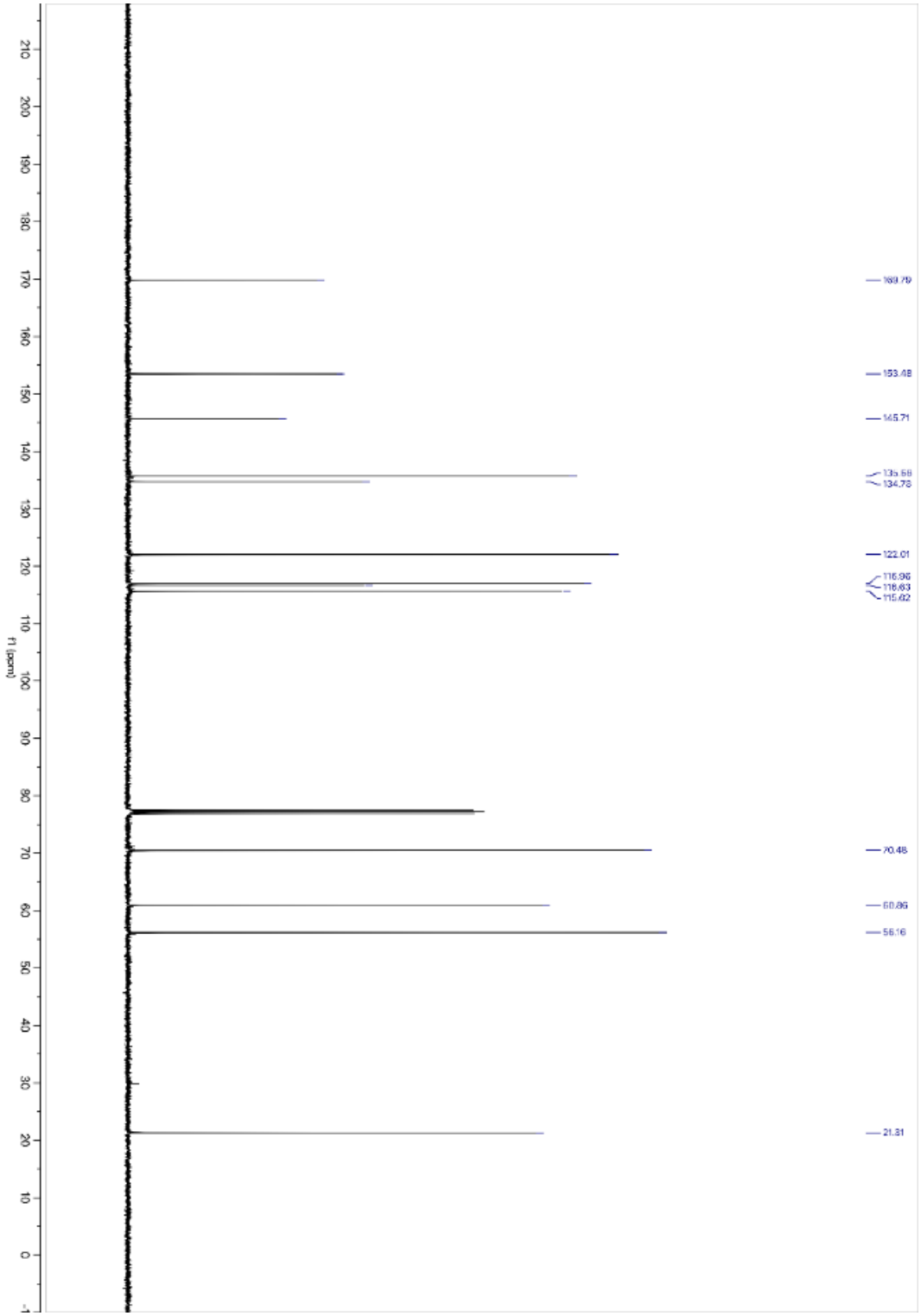
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.05 (d, *J* = 2.3 Hz, 1H), 6.97 (d, *J* = 2.3 Hz, 1H), 6.56 (dt, *J* = 5.7, 1.5 Hz, 1H), 5.95 (ddd, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.25 (dt, *J* = 17.4, 1.5 Hz, 1H), 5.23 – 5.18 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 2.12 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.8, 153.5, 145.7, 135.7, 134.7, 122.0, 117.0, 116.6, 115.6, 70.5, 60.9, 56.2, 21.3.

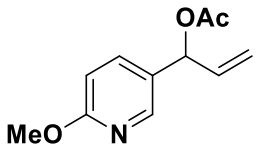
HRMS (ESI): Calculated for $C_{13}H_{15}BrO_4$ [M+Na^+] = 337.0046, Found 337.0051.

FTIR (neat): 2940, 1740, 1578, 1480, 1429, 1412, 1370, 1287, 1261, 1223, 1170, 1102, 1072, 1020, 1001, 983, 930, 850, 784, 697 cm^{-1}.


f1 (ppm)
1.00
1.02
0.99
1.00
1.15
1.10
3.02
3.00
3.08
7.26
7.06
7.05
6.97
6.97
6.57
6.57
6.56
6.56
6.55
6.55
6.00
5.98
5.97
5.96
5.95
5.94
5.93
5.91
5.28
5.27
5.27
5.23
5.23
5.23
5.22
5.22
5.20
5.20
5.19
3.86
3.85
2.12


f1 (ppm)
169.79
153.48
145.71
135.68
134.78
122.01
116.96
116.83
115.62
70.48
60.86
56.16
21.31

1-(6-methoxypyridin-3-yl)allyl acetate (1l)



Procedure

Allylic alcohol **S1l** (819 mg, 4.96 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 50% yield (515 mg, 2.48 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1).

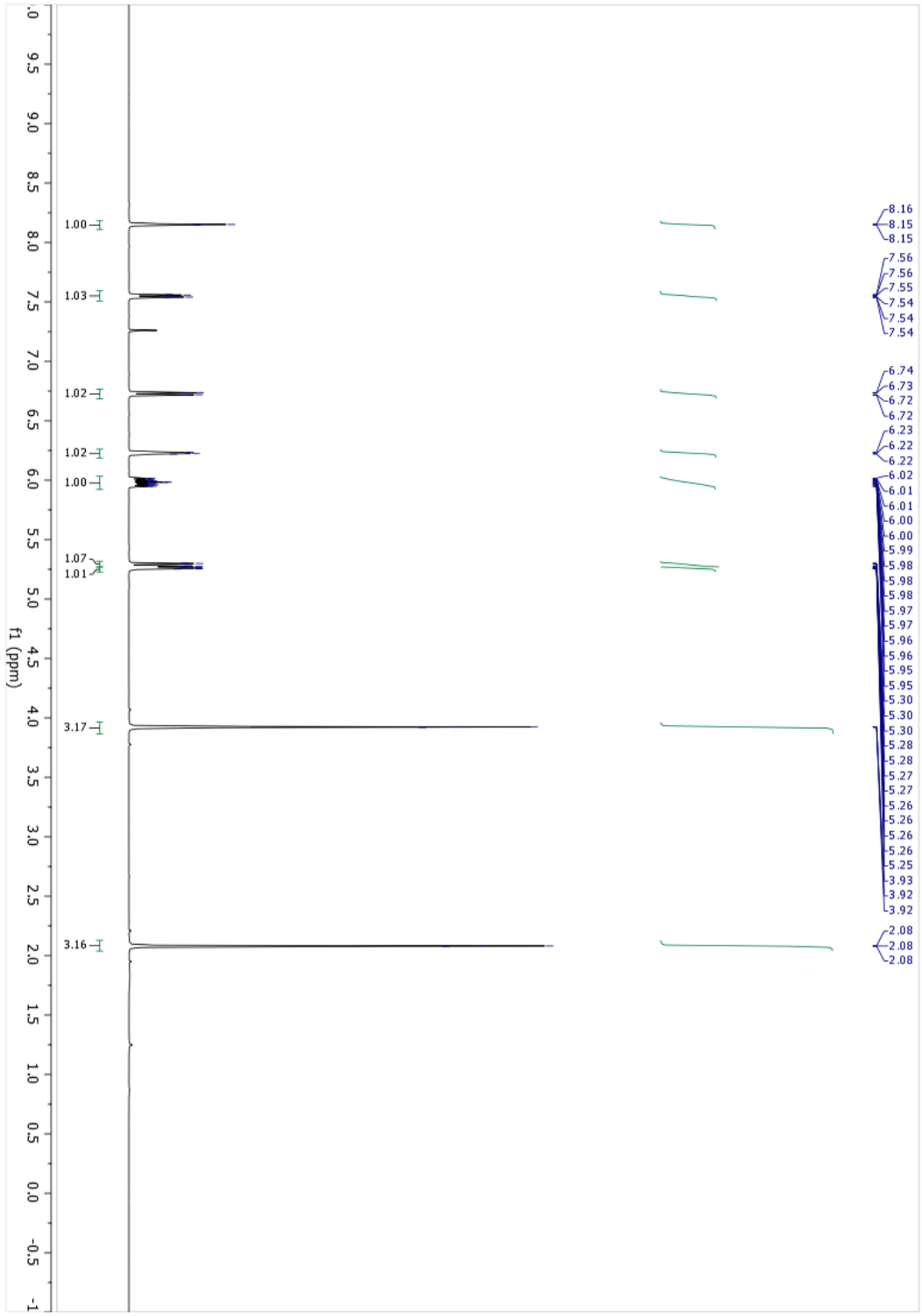
TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 4:1).

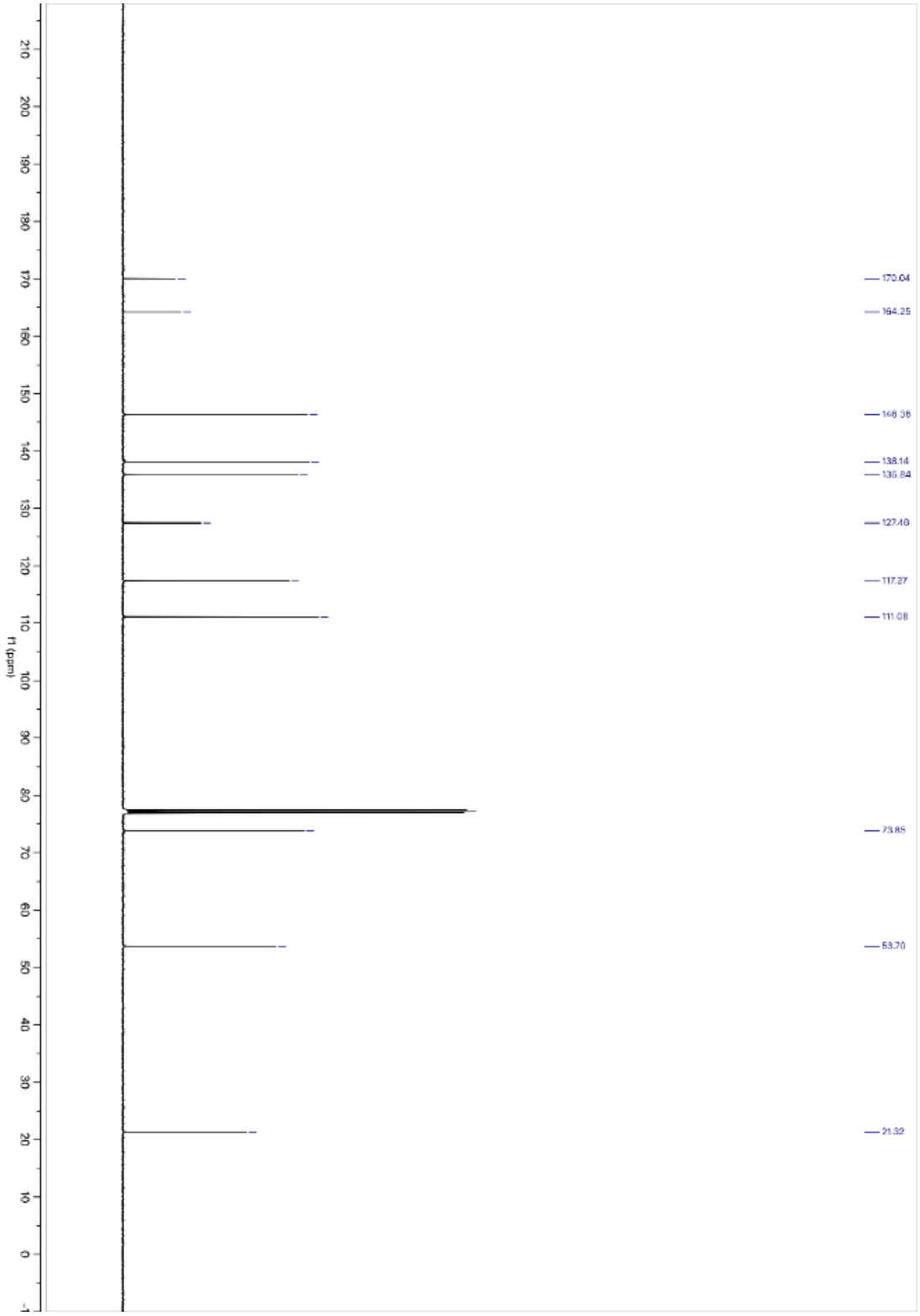
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.15 (t, *J* = 2.0 Hz, 1H), 7.55 (dt, *J* = 8.5, 2.2 Hz, 1H), 6.73 (dd, *J* = 8.6, 1.8 Hz, 1H), 6.23 (t, *J* = 3.7 Hz, 1H), 6.03 – 5.92 (m, 1H), 5.29 (dt, *J* = 11.2, 1.3 Hz, 1H), 5.26 (dt, *J* = 4.5, 1.4 Hz, 1H), 3.92 (t, *J* = 1.5 Hz, 3H), 2.13 – 2.04 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.0, 164.3, 146.4, 138.1, 135.8, 127.5, 117.4, 111.1, 73.9, 53.7, 21.3.

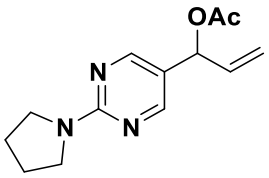
HRMS (ESI): Calculated for $C_{11}H_{13}NO_3$ [M+H$^+$] = 208.0968, Found 208.0968.

FTIR (neat): 2947, 1738, 1644, 1609, 1574, 1493, 1462, 1395, 1370, 1285, 1227, 1126, 1096, 1018, 933, 858, 831, 803, 761, 676 cm^{-1}.


f1 (ppm)
1.00
1.03
1.02
1.02
1.00
1.07
1.01
3.17
3.16
8.16
8.15
8.15
7.56
7.56
7.55
7.54
7.54
7.54
6.74
6.73
6.72
6.72
6.23
6.22
6.22
6.02
6.01
6.01
6.00
6.00
5.99
5.98
5.98
5.98
5.97
5.97
5.96
5.96
5.95
5.95
5.30
5.30
5.30
5.28
5.28
5.27
5.27
5.26
5.26
5.26
5.26
5.25
3.93
3.92
3.92
2.08
2.08
2.08


f1 (ppm)
170.04
164.25
148.38
138.14
136.84
127.49
117.27
111.08
73.85
53.70
21.32

1-(2-(pyrrolidin-1-yl)pyrimidin-5-yl)allyl acetate (1m)



Procedure

Allylic alcohol **S1m** (530 mg, 2.58 mmol, 100 mol%) was subjected to a modified version of general procedure C using triethylamine (522 mg, 5.16 mmol, 200 mol%), acetic anhydride (316 mg, 3.10 mmol, 120 mol%), 4-dimethylaminopyridine (71 mg, 0.26, 10 mol%), and anhydrous dichloromethane (26 mL, 0.1 M). The reaction was stirred at ambient temperature until starting material was consumed. The reaction solution was diluted with dichloromethane and was washed sequentially with water and a saturated aqueous brine solution. The organic layer was separated and dried over anhydrous sodium sulfate. The organics were passed through a fritted filter into a round bottom flask and concentrated *in vacuo* to afford the title compound in 92% yield (587 mg, 2.37 mmol) as a pale-yellow gel. The gel was used without further purification.

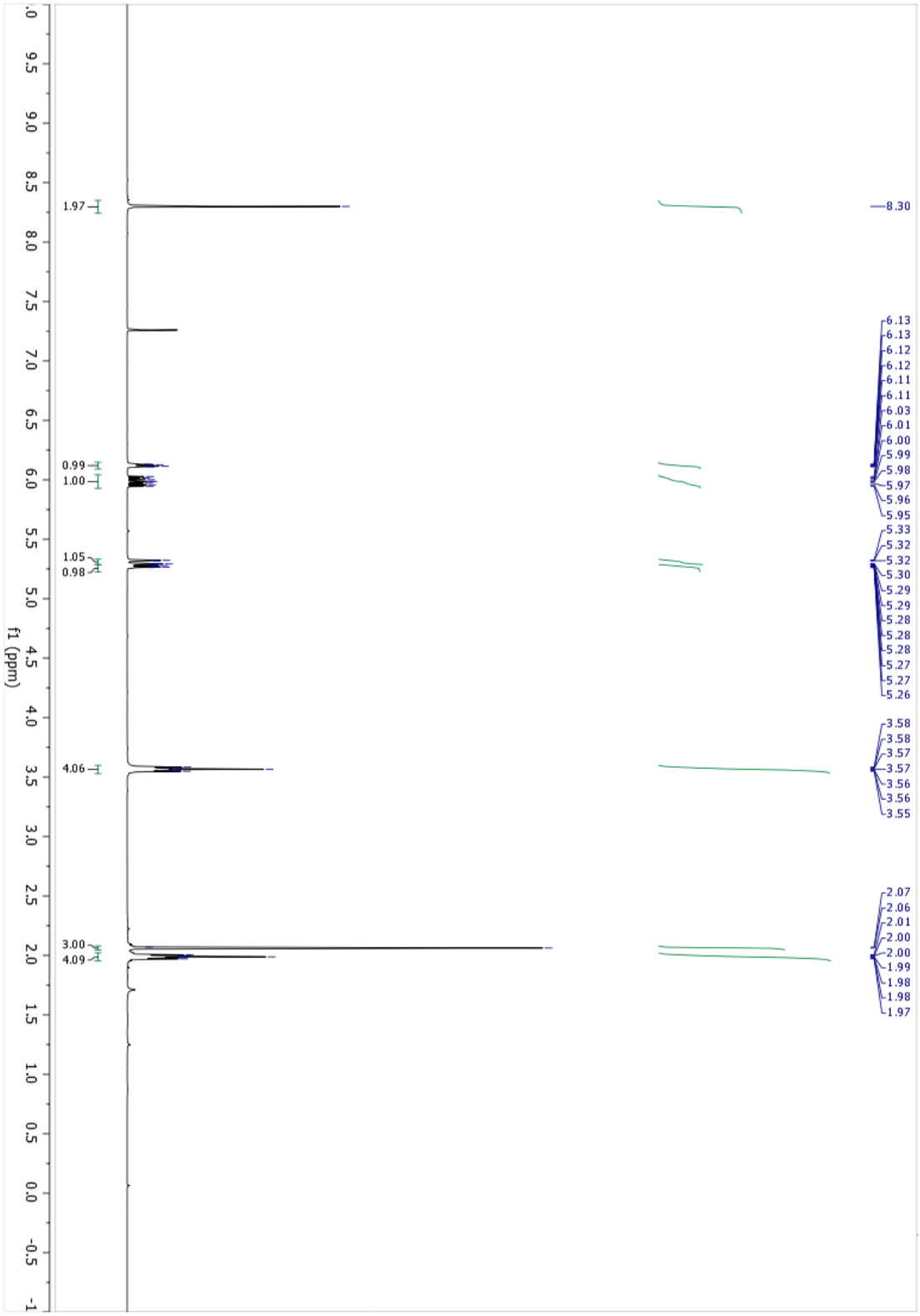
TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 1:1).

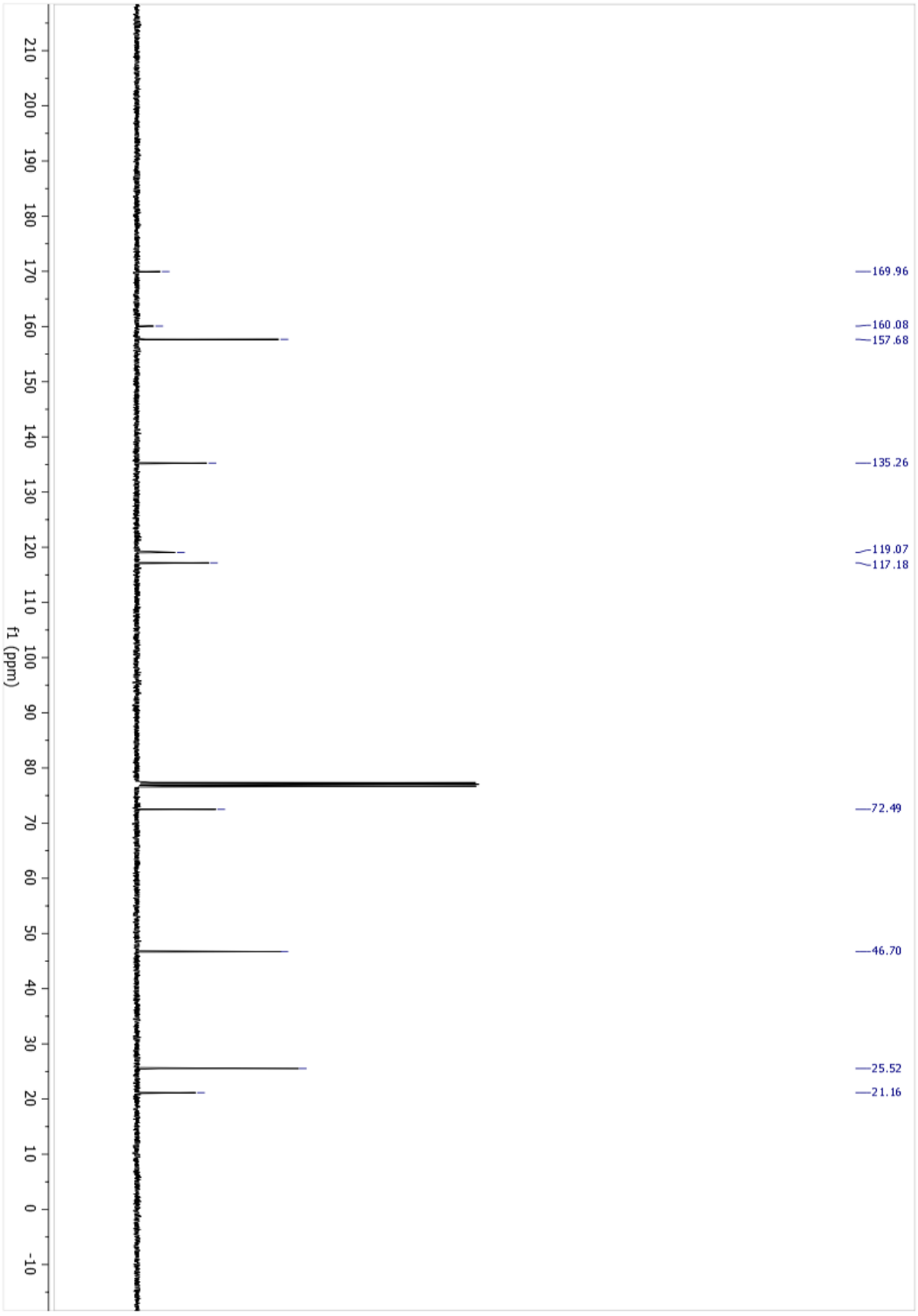
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.30 (s, 2H), 6.12 (dt, *J* = 5.4, 1.6 Hz, 1H), 5.99 (ddd, *J* = 17.2, 10.5, 5.4 Hz, 1H), 5.31 (dt, *J* = 12.0, 1.3 Hz, 1H), 5.27 (dt, *J* = 5.4, 1.3 Hz, 1H), 3.60 – 3.53 (m, 4H), 2.06 (s, 3H), 2.02 – 1.95 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.0, 160.1, 157.7, 135.3, 119.1, 117.2, 72.5, 46.7, 25.5, 21.2.

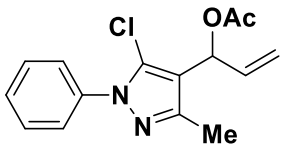
HRMS (ESI): Calculated for $C_{13}H_{17}N_3O_2$ [M+H$^+$] = 248.1394, Found 248.1392.

FTIR (neat): 2968, 2872, 1732, 1599, 1521, 1482, 1460, 1337, 1285, 1224, 927, 800, 773, 698, 652 cm^{-1}.


f1 (ppm)
1.97
0.99
1.00
1.05
0.98
4.06
3.00
4.09
8.30
6.13
6.13
6.12
6.12
6.11
6.11
6.03
6.01
6.00
5.99
5.98
5.97
5.96
5.95
5.33
5.32
5.32
5.30
5.29
5.29
5.28
5.28
5.28
5.27
5.27
5.26
3.58
3.58
3.57
3.57
3.56
3.56
3.55
2.07
2.06
2.01
2.00
2.00
1.99
1.98
1.98
1.97


169.96
160.08
157.68
135.26
119.07
117.18
72.49
46.70
25.52
21.16
f1 (ppm)

1-(5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)allyl acetate (1o)



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with 5-chloro-3-methyl-1-phenyl-1H-pyrazole-4-carbaldehyde (1.00 g, 4.53 mmol, 100 mol%). The vessel was purged with argon and anhydrous THF (23 mL, 0.2 M) was added. A solution of vinyl magnesium bromide (5.44 mL, 1.0 M in THF, 120 mol%) was added at 0 °C. Following addition, the reaction was allowed to reach ambient temperature and was stirred until starting material was consumed. Triethylamine (1.3 mL, 9.1 mmol, 200 mol%) and acetic anhydride (0.64 mL, 6.8 mmol, 150 mol%) were added to the reaction solution via syringe. The reaction was stirred at ambient temperature for one hour. The reaction solution was diluted with diethyl ether and water. The biphasic mixture was poured into a separatory funnel and mixed vigorously. The organics were separated and the aqueous was extracted three times with diethyl ether. The organic layers were combined and washed sequentially with saturated aqueous solutions of sodium bicarbonate and brine. The organics were separated and dried over anhydrous sodium sulfate. The liquid was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The title compound was obtained in 25% yield (330 mg, 1.13 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 100:1–50:1).

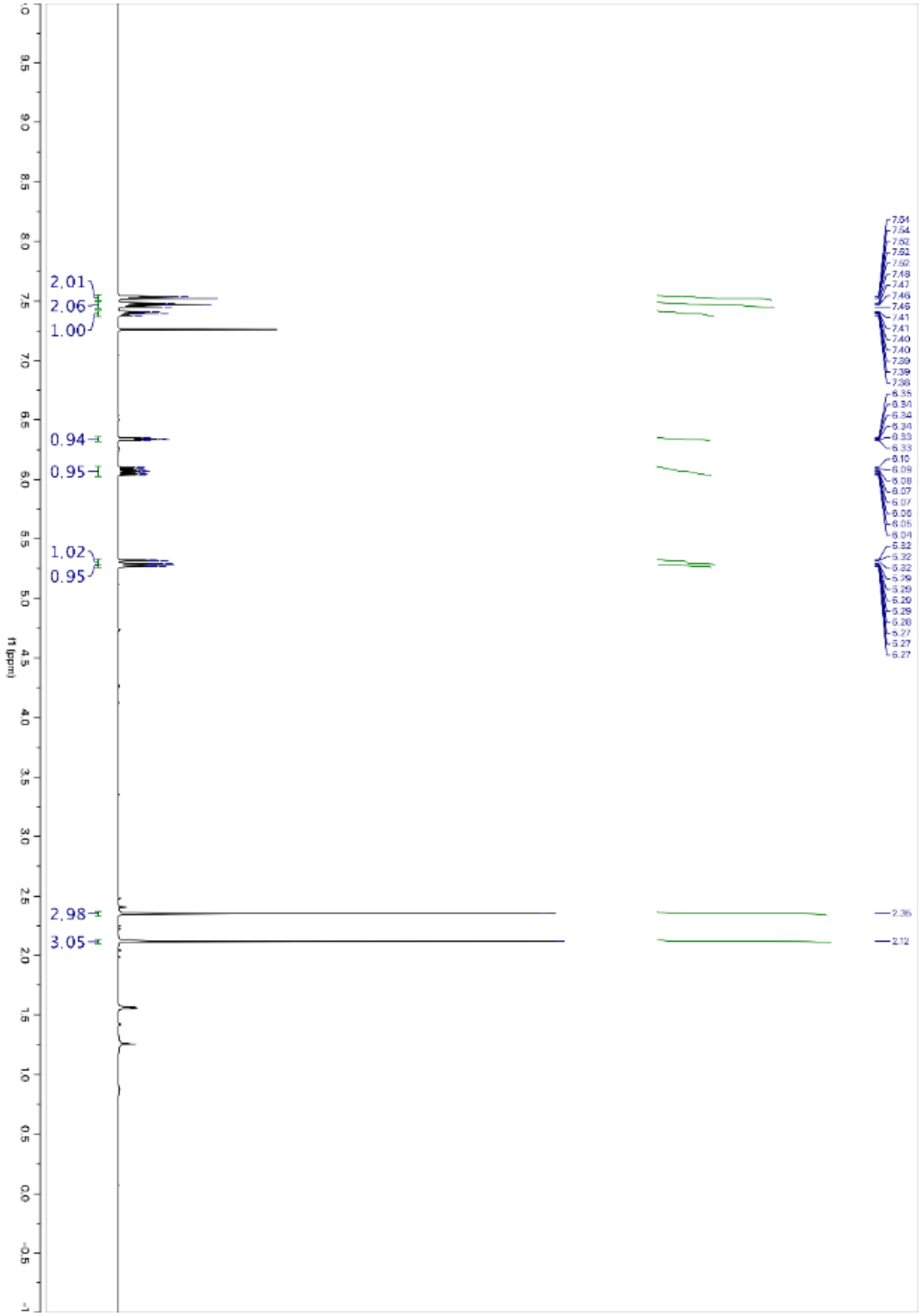
TLC (SiO_2) R_f = 0.59 (hexanes: ethyl acetate = 3:1).

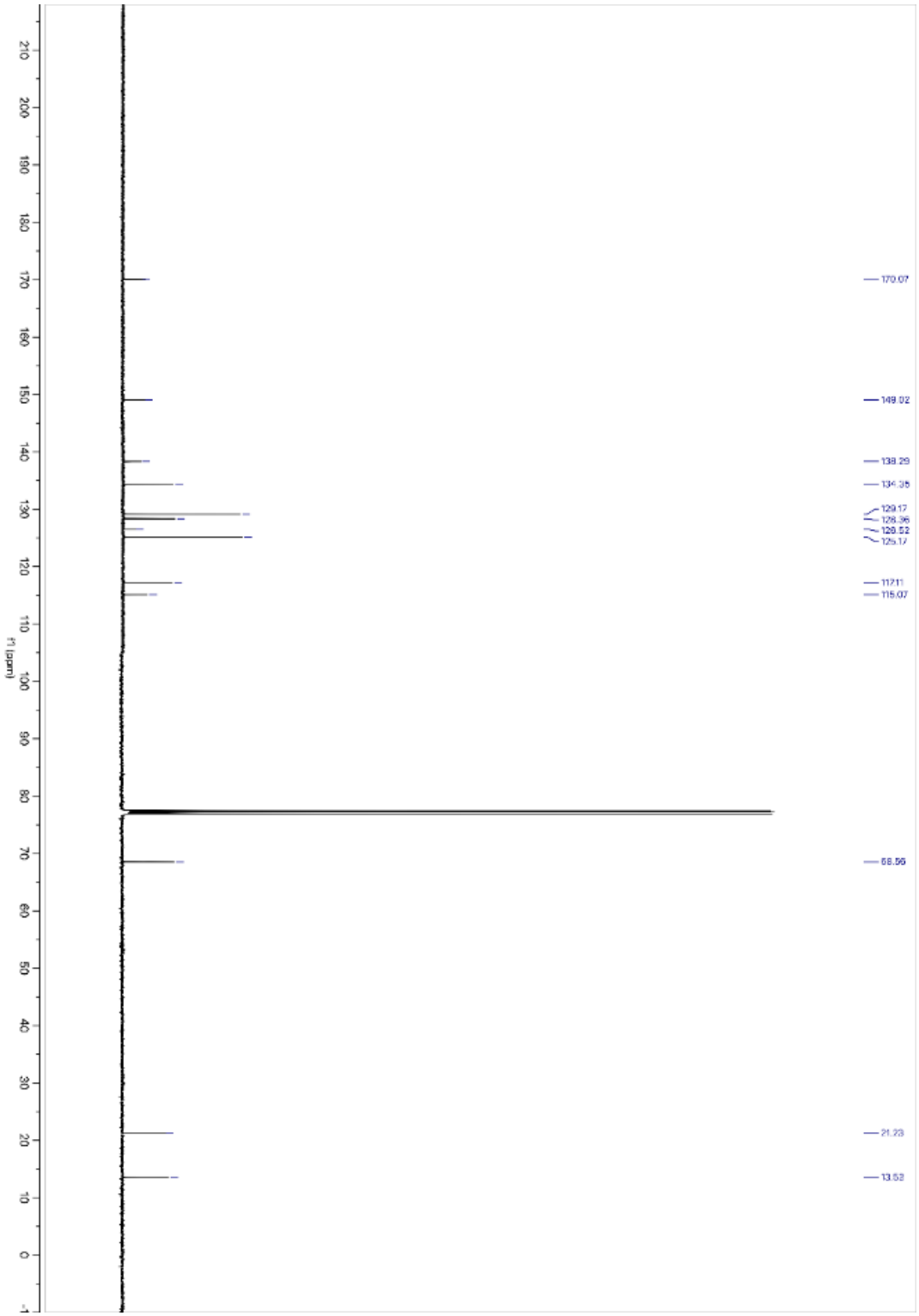
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.55 – 7.51 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.42 – 7.35 (m, 1H), 6.34 (dt, *J* = 5.4, 1.7 Hz, 1H), 6.07 (ddd, *J* = 17.1, 10.4, 5.4 Hz, 1H), 5.31 (dt, *J* = 14.2, 1.3 Hz, 1H), 5.29 – 5.26 (m, 1H), 2.35 (s, 3H), 2.12 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.1, 149.0, 138.3, 134.4, 129.2, 128.4, 126.5, 125.2, 117.1, 115.1, 68.6, 21.2, 13.5.

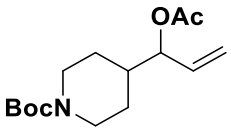
HRMS (ESI): Calculated for $C_{15}H_{15}ClN_2O_2$ $[M+H^+]$ = 291.0895, Found 291.0899.

FTIR (neat): 2918, 2849, 2050, 1652, 1558, 1463 cm^{-1}.


2.01
2.06
1.00
0.94
0.95
1.02
0.95
2.98
3.05
f1 (ppm)


170.07
149.02
138.29
134.35
129.17
128.96
128.52
125.17
117.11
115.07
68.56
21.23
13.52
f1 (ppm)

***tert*-butyl 4-(1-acetoxyallyl)piperidine-1-carboxylate (1p)**



Procedure

Allylic alcohol **S1p** (1.12 g, 4.62 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 48% yield (628.6 mg, 2.22 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1-10:1).

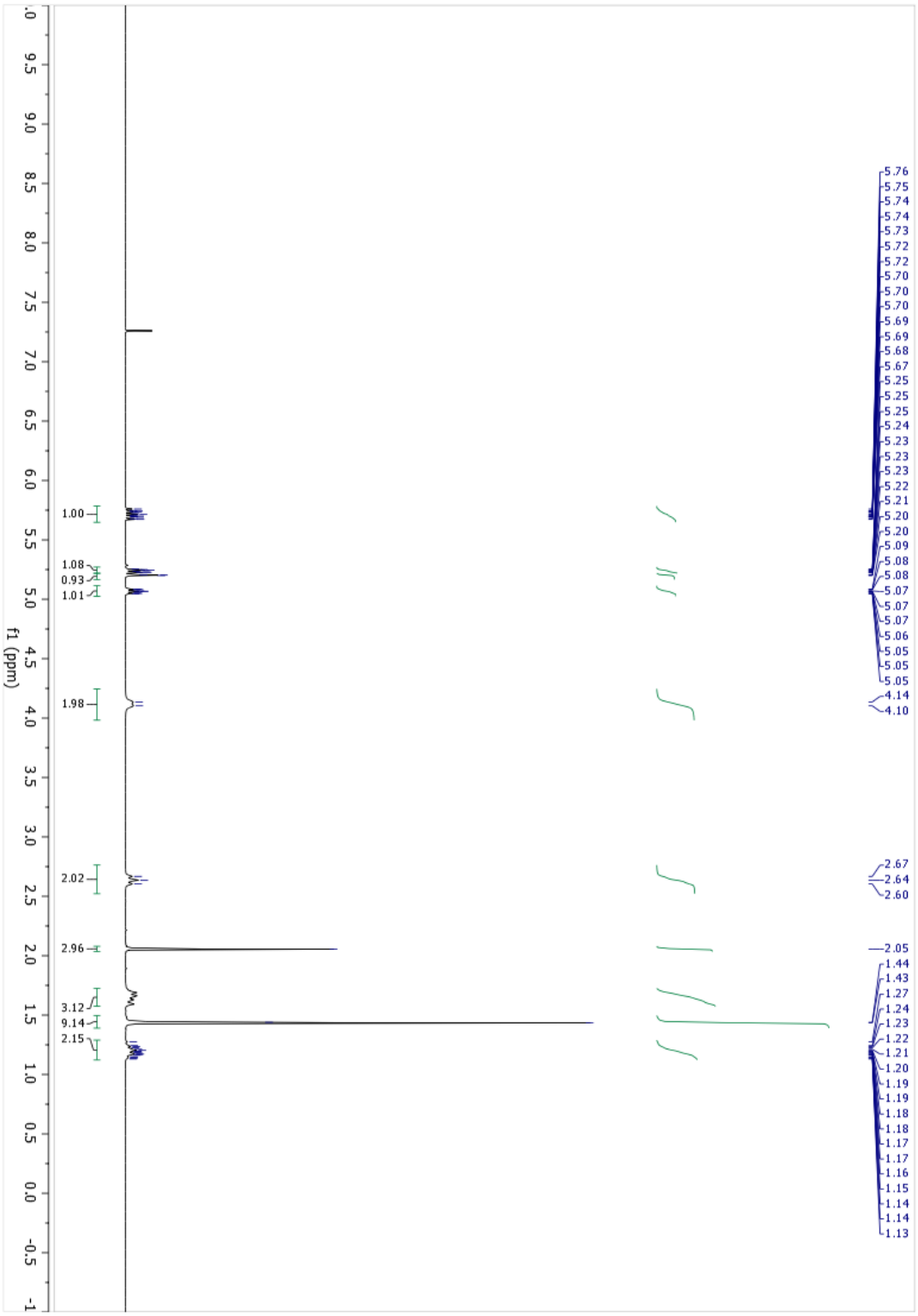
TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 2:1).

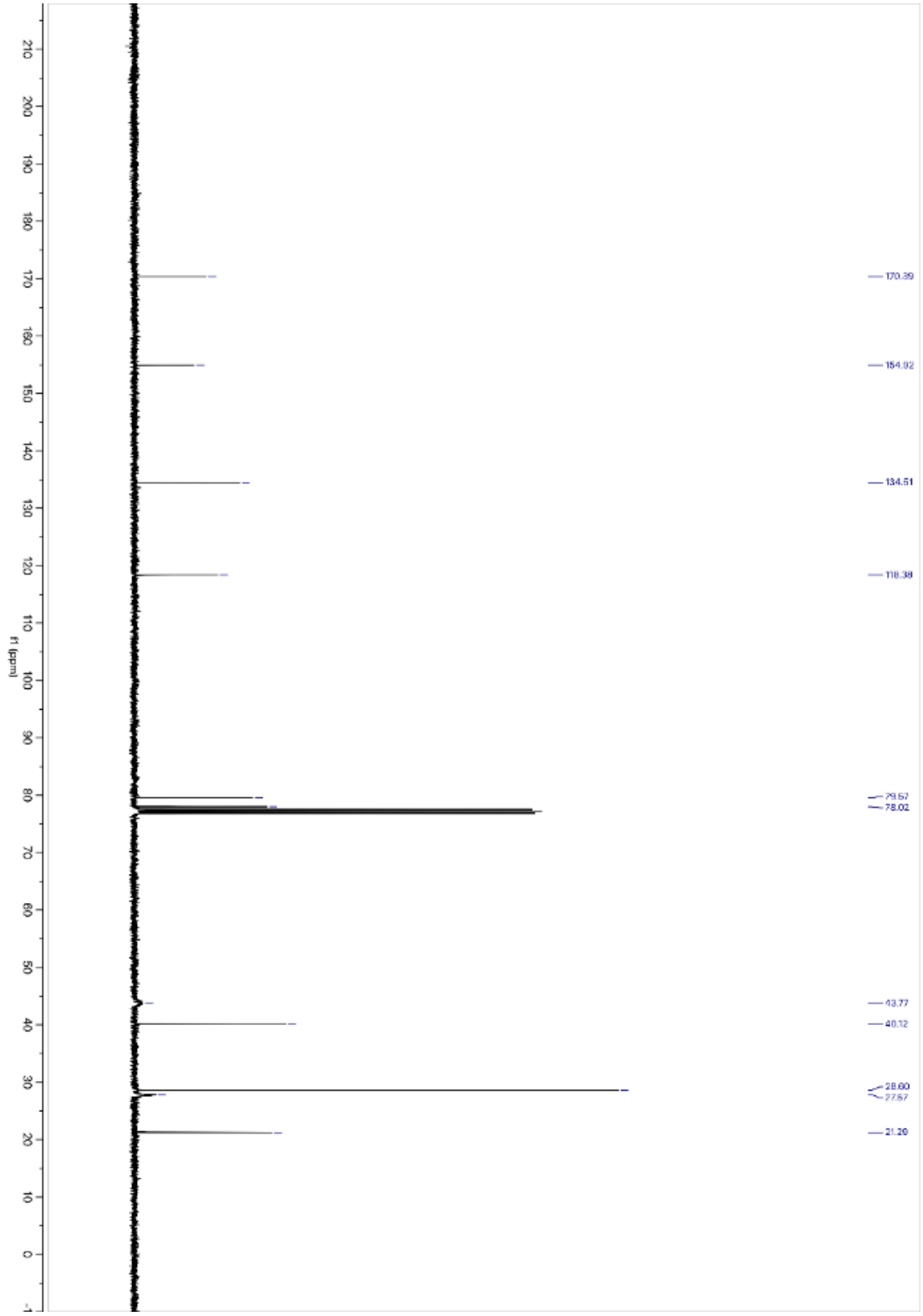
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.78 – 5.65 (m, 1H), 5.24 (dq, *J* = 7.6, 1.5 Hz, 1H), 5.20 (t, *J* = 1.3 Hz, 1H), 5.07 (ddt, *J* = 7.3, 6.2, 1.1 Hz, 1H), 4.12 (d, *J* = 13.2 Hz, 2H), 2.64 (t, *J* = 12.8 Hz, 2H), 2.05 (s, 3H), 1.73 – 1.57 (m, 3H), 1.44 (d, *J* = 1.9 Hz, 9H), 1.29 – 1.12 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 154.9, 134.5, 118.4, 79.6, 78.0, 43.8, 40.1, 28.6, 27.9, 21.3.

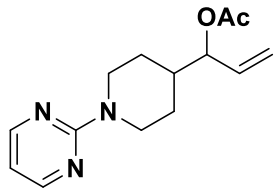
HRMS (ESI): Calculated for $C_{15}H_{25}NO_4$ [M+Na^+] = 306.1676, Found 306.1676.

FTIR (neat): 2975, 2936, 2857, 2364, 1739, 1689, 1422, 1366, 1279, 1231, 1158, 1019, 975, 942, 867, 769 cm^{-1}.


f1 (ppm)
1.00
1.08
0.93
1.01
1.98
2.02
2.96
3.12
9.14
2.15
5.76
5.75
5.74
5.74
5.73
5.72
5.72
5.70
5.70
5.70
5.69
5.69
5.68
5.67
5.25
5.25
5.25
5.24
5.23
5.23
5.23
5.22
5.21
5.20
5.20
5.09
5.08
5.08
5.07
5.07
5.07
5.06
5.05
5.05
5.05
4.14
4.10
2.67
2.64
2.60
2.05
1.44
1.43
1.27
1.24
1.23
1.22
1.21
1.20
1.19
1.19
1.18
1.18
1.17
1.17
1.16
1.15
1.14
1.14
1.13


f1 (ppm)
170.39
154.92
134.51
118.38
79.52
78.02
43.77
40.12
28.60
27.57
21.29

1-(1-(pyrimidin-2-yl)piperidin-4-yl)allyl acetate (1q)



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with 1-(pyrimidin-2-yl)piperidine-4-carbaldehyde (1.91 g, 10.0 mmol, 100 mol%). The vessel was purged with argon and anhydrous THF (100 mL, 0.1 M) was added. A solution of vinyl magnesium bromide (15.0 mL, 1.0 M in THF, 150 mol%) was added at 0 °C. Following addition, the reaction was allowed to reach ambient temperature and was stirred until starting material was consumed. Triethylamine (2.78 mL, 20.0 mmol, 200 mol%) and acetic anhydride (1.42 mL, 15.0 mmol, 150 mol%) were added to the reaction solution via syringe. The reaction was stirred at ambient temperature for one hour. The reaction solution was diluted with diethyl ether and water. The organics were separated and the aqueous was extracted twice with diethyl ether. The organics were combined and washed with an aqueous solution of hydrochloric acid (1.0 M). The organic layer was separated and dried over anhydrous sodium sulfate. The liquid was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The title compound was obtained in 29% yield (750 mg, 2.87 mmol) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–3:1).

TLC (SiO_2) R_f = 0.25 (hexanes: ethyl acetate = 2:1).

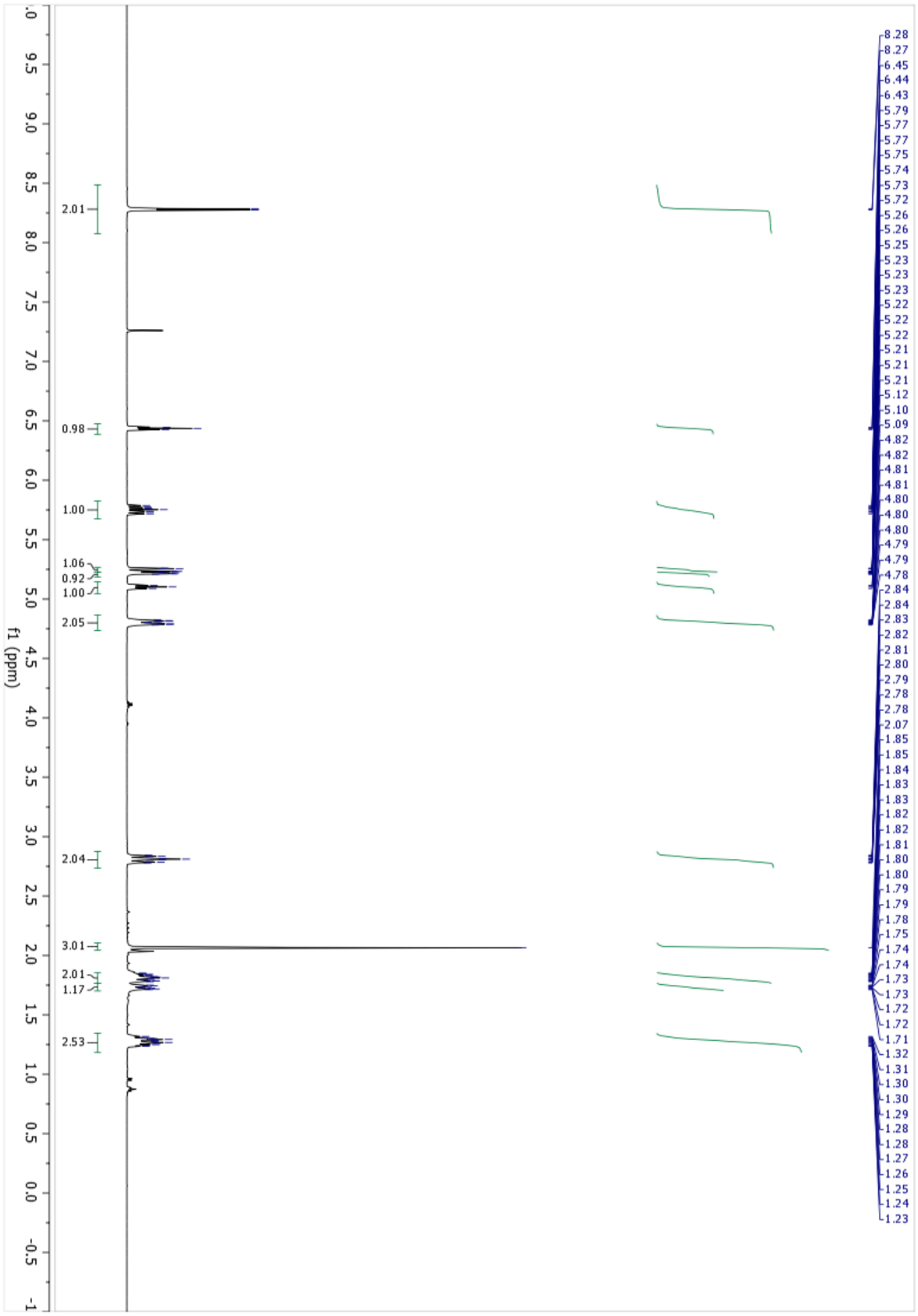
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 4.7 Hz, 2H), 6.44 (t, *J* = 4.7 Hz, 1H), 5.75 (ddd, *J* = 17.3, 10.5, 6.9 Hz, 1H), 5.24 (dt, *J* = 11.7, 1.3 Hz, 1H), 5.22 (dt, *J* = 5.0, 1.3 Hz, 1H), 5.10 (t, *J* = 6.7 Hz, 1H), 4.80 (dq, *J* = 13.5, 2.4 Hz, 2H), 2.81 (tt, *J* = 12.8, 2.9 Hz, 3H), 2.07 (s, 3H), 1.81 – 1.77 (m, 1H), 1.73 (dq, *J* = 13.3, 2.8 Hz, 1H), 1.33 – 1.28 (m, 1H), 1.26 (dt, *J* = 12.2, 4.1 Hz, 2H).

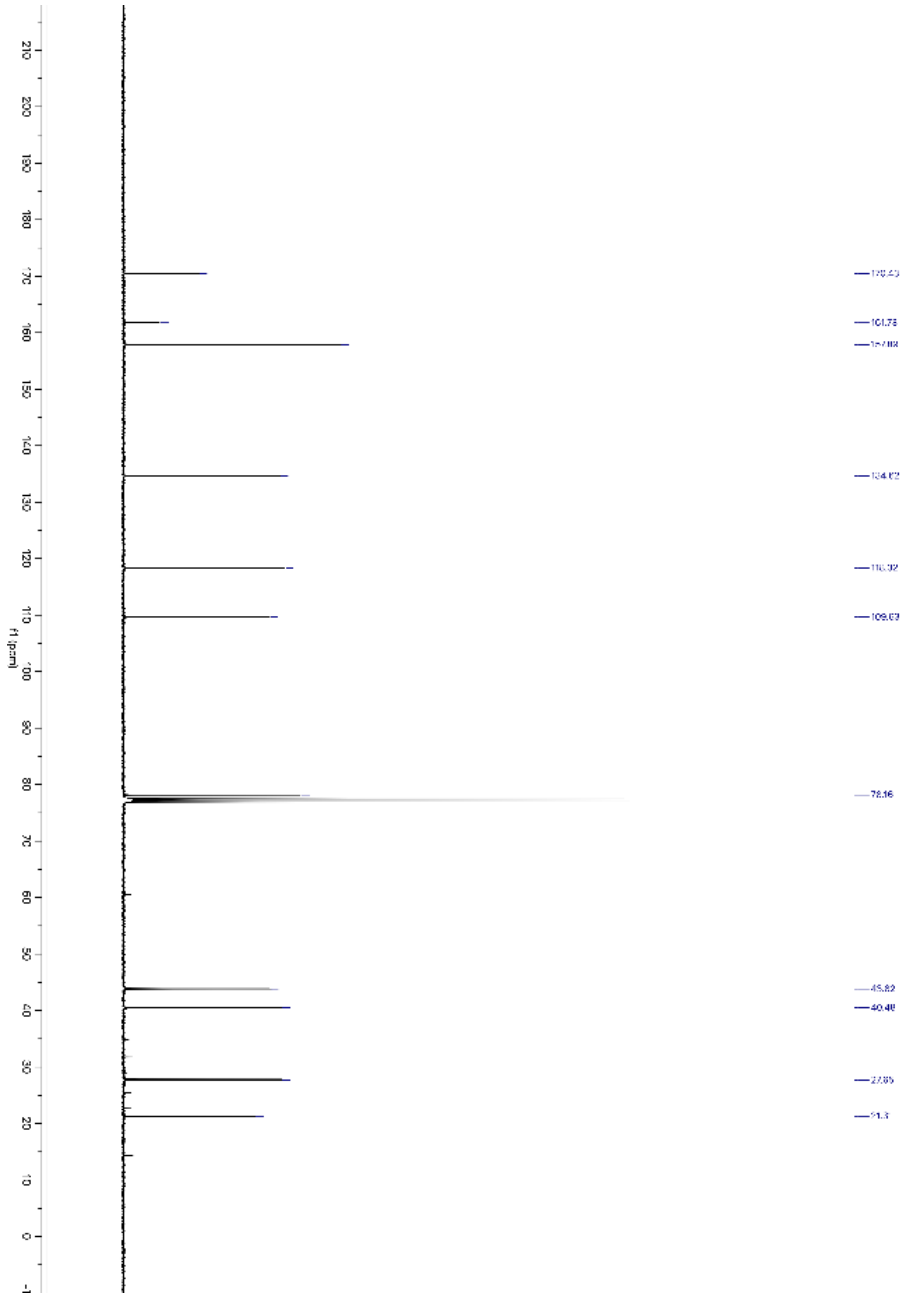
^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.4, 161.7, 157.9, 134.6, 118.3, 109.6, 78.2, 43.8, 40.5, 27.7, 21.3.

HRMS (ESI): Calculated for $C_{14}H_{19}N_3O_2$ [M+H$^+$] = 262.1550, Found 262.1548.

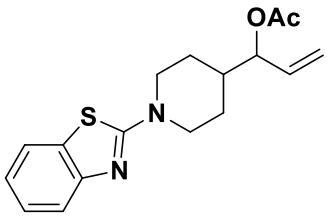
FTIR (neat): 2993, 2939, 2853, 1737, 1584, 1545, 1504, 1448, 1393, 1305, 1231, 1083, 1020, 995, 973, 946, 797, 781 cm^{-1}.

MP: 104-106 °C


f1 (ppm)
2.01
0.98
1.00
1.06
0.92
1.00
2.05
2.04
3.01
2.01
1.17
2.53


f1 (ppm)
78.16
45.82
40.48
27.85

1-(1-(benzo[*d*]thiazol-2-yl)piperidin-4-yl)allyl acetate (1r)



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with 1-(benzo[d]thiazol-2-yl)piperidine-4-carbaldehyde (197 mg, 0.80 mmol, 100 mol%). The vessel was purged with argon and anhydrous THF (8 mL, 0.1 M) was added. A solution of vinyl magnesium bromide (1.2 mL, 1.0 M in THF, 150 mol%) was added at 0 °C. Following addition, the reaction was allowed to reach ambient temperature and was stirred until starting material was consumed. Triethylamine (0.22 mL, 1.6 mmol, 200 mol%) and acetic anhydride (0.11 mL, 1.2 mmol, 150 mol%) were added to the reaction solution via syringe. The reaction was stirred at ambient temperature for one hour. The reaction solution was diluted with diethyl ether and water. The organics were separated and the aqueous was extracted twice with diethyl ether. The organics were combined and washed with an aqueous solution of hydrochloric acid (1.0 M). The organic layer was separated and dried over anhydrous sodium sulfate. The liquid was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The title compound was obtained in 82% yield (210 mg, 0.66 mmol) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–1:1).

TLC (SiO_2) R_f = 0.60 (hexanes: ethyl acetate = 1:1).

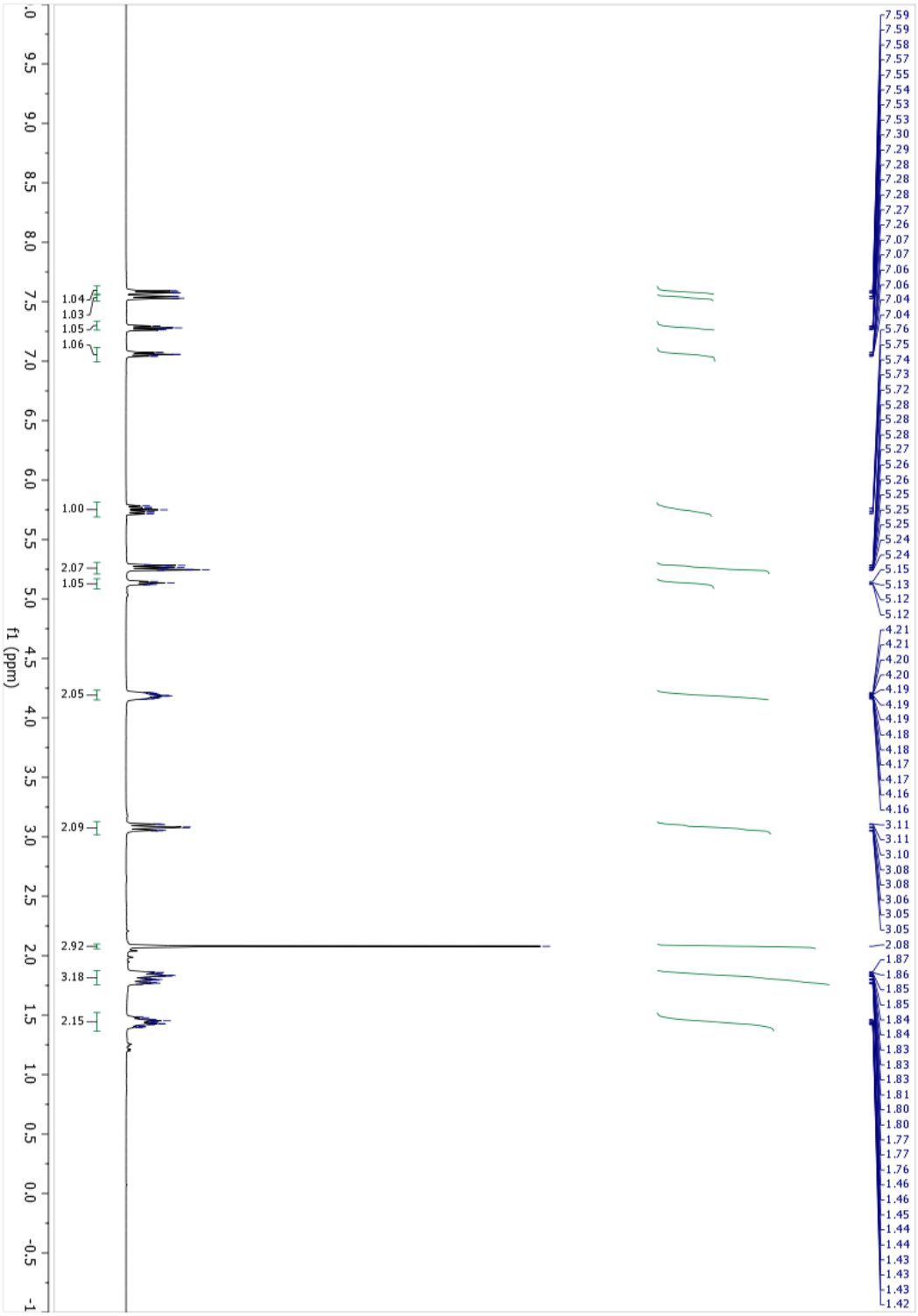
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.58 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.54 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.28 (ddd, *J* = 8.2, 7.2, 1.3 Hz, 1H), 7.06 (td, *J* = 7.6, 1.2 Hz, 1H), 5.75 (ddd, *J* = 17.3, 10.6, 6.9 Hz, 1H), 5.31 – 5.21 (m, 2H), 5.13 (t, *J* = 6.5 Hz, 1H), 4.23 – 4.15 (m, 2H), 3.08 (td, *J* = 12.9, 12.5, 2.9 Hz, 2H), 2.08 (s, 3H), 1.81 (dddt, *J* = 30.2, 16.0, 5.7, 3.0 Hz, 3H), 1.44 (dddd, *J* = 17.5, 12.6, 6.9, 4.0 Hz, 2H).

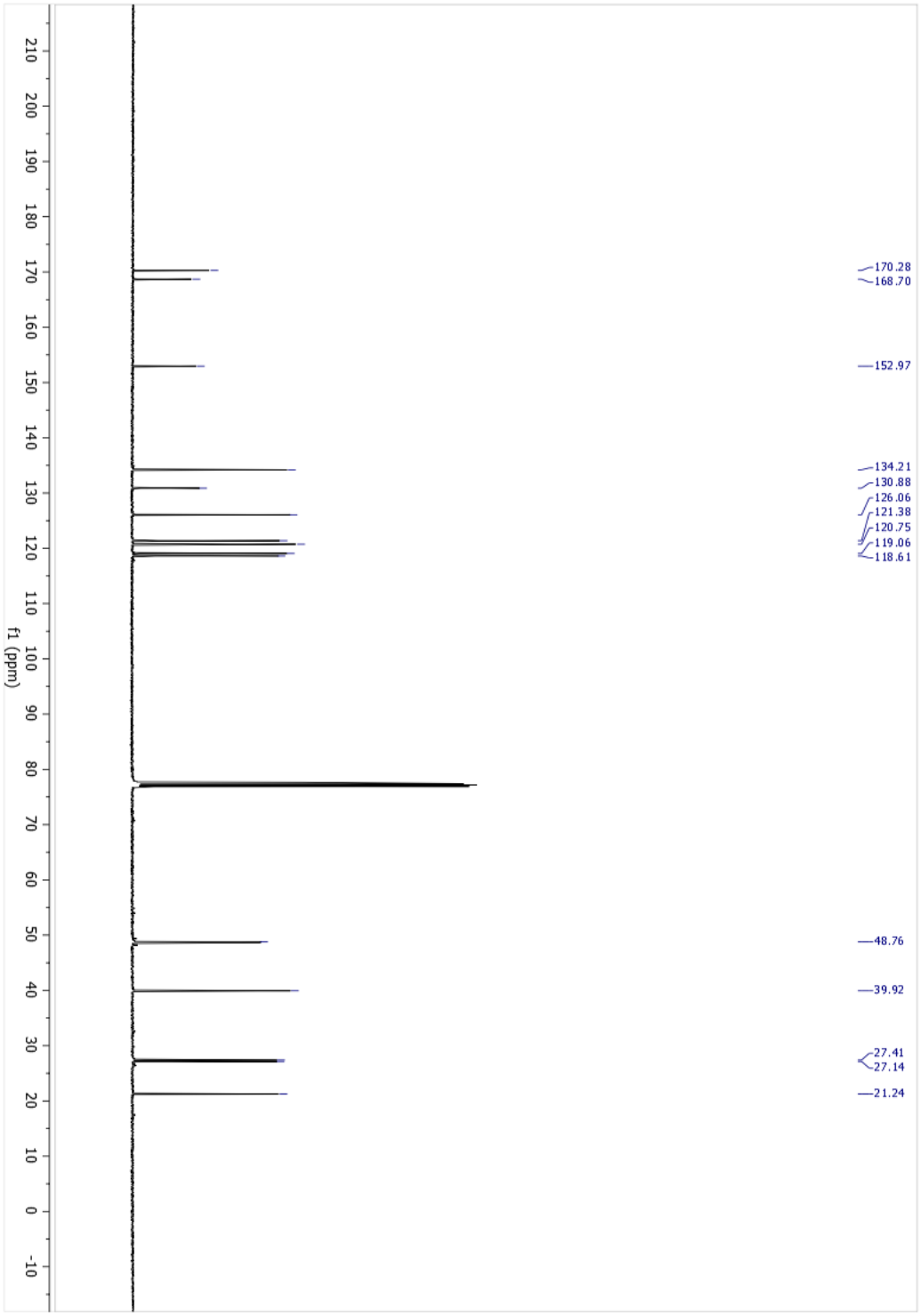
^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.3, 168.7, 153.0, 134.2, 130.9, 126.1, 121.4, 120.8, 119.1, 118.6, 48.8, 39.9, 27.4, 27.1, 21.2.

HRMS (ESI): Calculated for $C_{17}H_{20}N_2O_2S$ [M+H$^+$] = 317.1318, Found 317.1317.

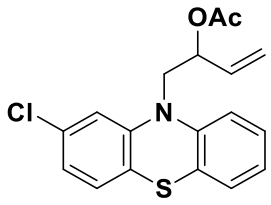
FTIR (neat): 2945, 2855, 1737, 1595, 1531, 1445, 1369, 1289, 1233, 1123, 1018, 980, 926, 753, 726 cm^{1}.

MP: 104-106 °C


f1 (ppm)
1.04
1.03
1.05
1.06
1.00
2.07
1.05
2.05
2.09
2.92
3.18
2.15


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.28
168.70
152.97
134.21
130.88
126.06
121.38
120.75
119.06
118.61
48.76
39.92
27.41
27.14
21.24

1-(2-chloro-10*H*-phenothiazin-10-yl)but-3-en-2-yl acetate (1s)



Procedure

Allylic alcohol **S1s** (540 mg, 1.77 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 80% yield (489 mg, 1.41 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1).

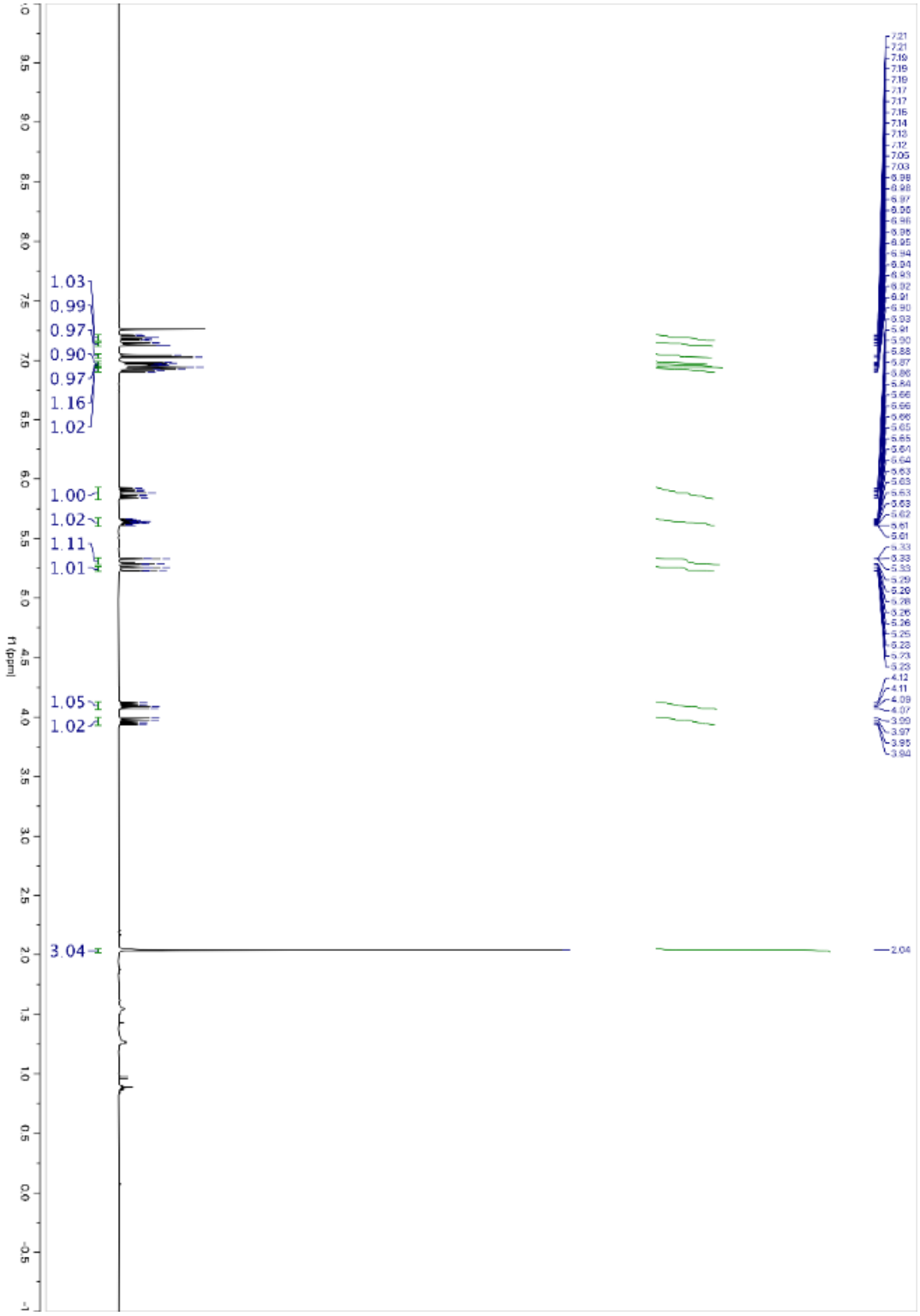
TLC (SiO_2) R_f = 0.7 (hexanes: ethyl acetate = 4:1).

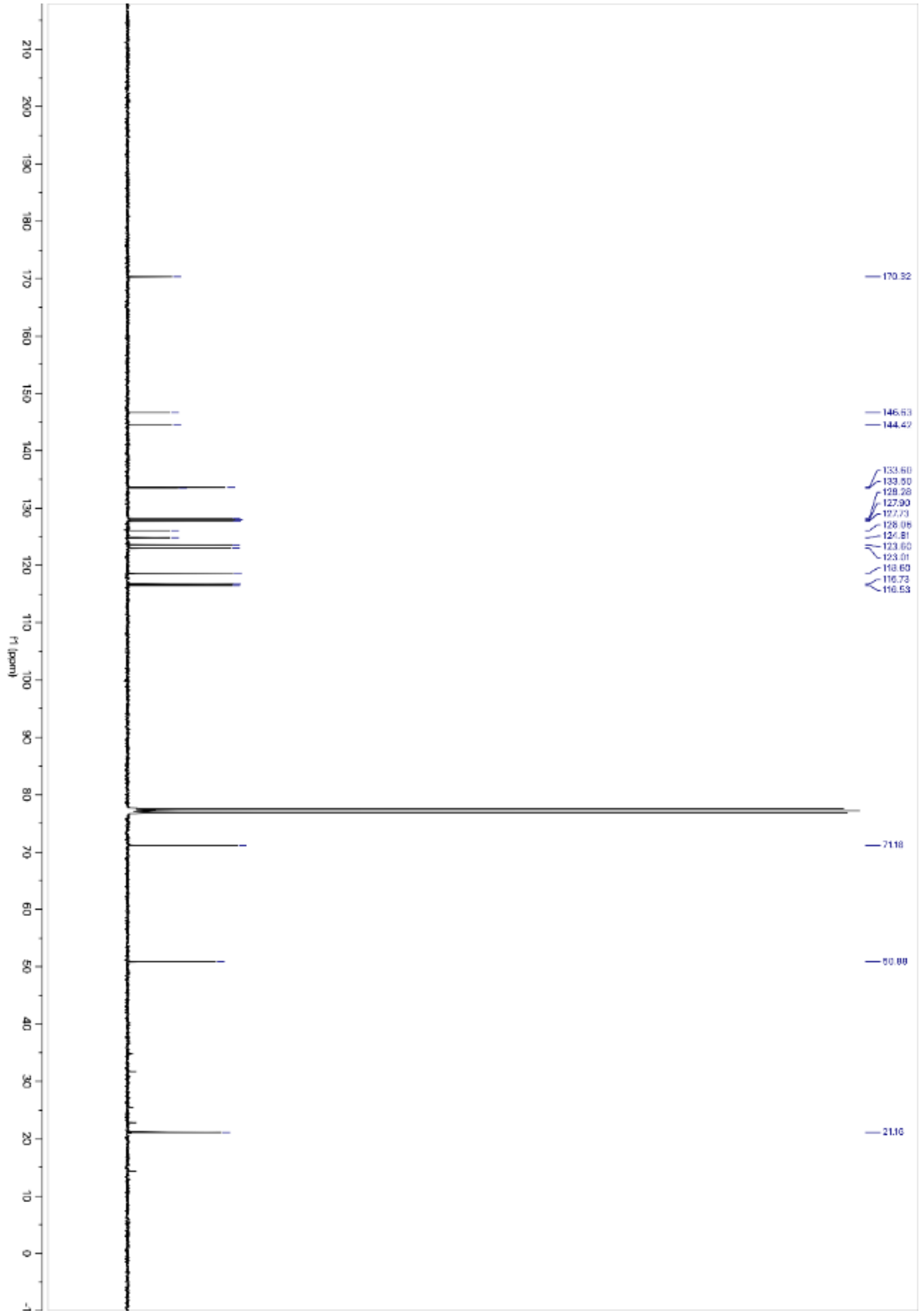
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.21 – 7.16 (m, 1H), 7.14 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 1H), 6.98 – 6.97 (m, 1H), 6.96 (dd, *J* = 2.6, 1.1 Hz, 1H), 6.94 (d, *J* = 2.0 Hz, 1H), 6.92 (dd, *J* = 8.1, 2.0 Hz, 1H), 5.88 (ddd, *J* = 17.0, 10.6, 6.1 Hz, 1H), 5.64 (dtt, *J* = 7.4, 6.3, 1.3 Hz, 1H), 5.31 (dt, *J* = 17.3, 1.3 Hz, 1H), 5.24 (dt, *J* = 10.6, 1.2 Hz, 1H), 4.10 (dd, *J* = 13.8, 7.0 Hz, 1H), 3.96 (dd, *J* = 13.8, 6.3 Hz, 1H), 2.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.3, 146.6, 144.4, 133.6, 133.5, 128.3, 127.9, 127.7, 126.1, 124.8, 123.6, 123.0, 118.6, 116.7, 116.5, 71.2, 50.9, 21.2.

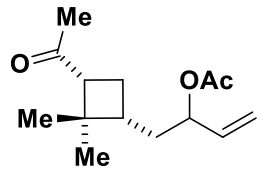
HRMS (ESI): Calculated for $C_{18}H_{16}ClNO_2S$ [M+Na^+] = 368.0482, Found 368.0496.

FTIR (neat): 3059, 2361, 2171, 1739, 1591, 1567, 1457, 1408, 1370, 1325, 1282, 1230, 1128, 1098, 1037, 932, 910, 853, 803, 752 cm^{-1}.


1.03
0.99
0.97
0.90
0.97
1.16
1.02
1.00
1.02
1.11
1.01
1.05
1.02
3.04
2.04
f1 (ppm)


f1 (ppm)
170.32
146.63
144.42
133.60
133.50
128.28
127.90
127.73
126.96
126.81
123.60
123.01
118.60
116.73
116.53
77.16
50.88
21.16

1-((1*R*,3*R*)-3-acetyl-2,2-dimethylcyclobutyl)but-3-en-2-yl acetate (1v)



Procedure

Allylic alcohol **S1v** (214 mg, 1.09 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 85% yield (222 mg, 0.931 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–7:1).

TLC (SiO_2) R_f = 0.53 (hexanes: ethyl acetate = 2:1).

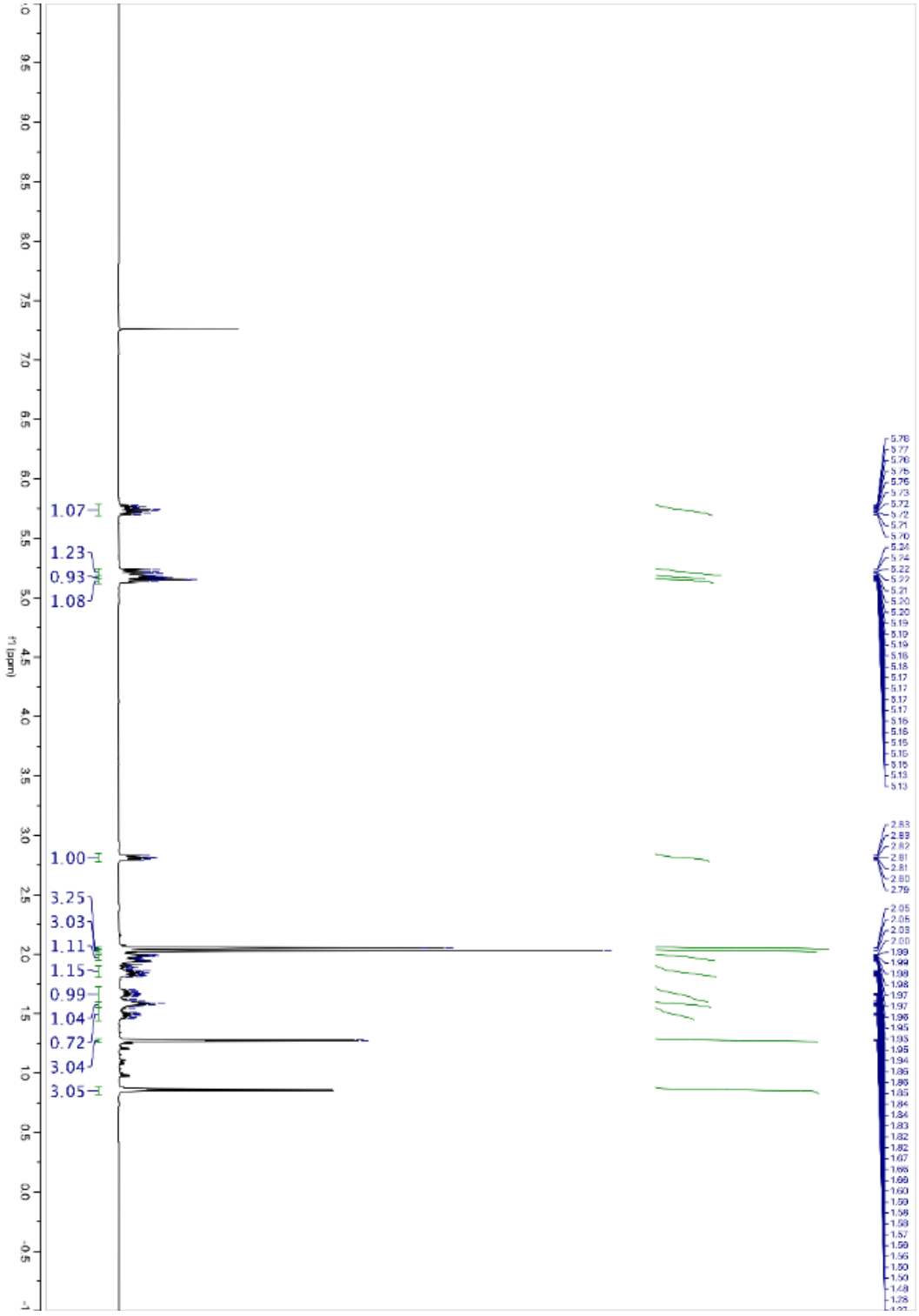
^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.74 (ddt, *J* = 17.1, 10.5, 6.7 Hz, 1H), 5.25 – 5.19 (m, 1H), 5.19 – 5.16 (m, 1H), 5.16 – 5.12 (m, 1H), 2.85 – 2.78 (m, 1H), 2.05 (d, *J* = 2.3 Hz, 3H), 2.03 (s, 3H), 2.00 – 1.95 (m, 1H), 1.91 – 1.79 (m, 1H), 1.71 – 1.60 (m, 1H), 1.60 – 1.55 (m, 1H), 1.55 – 1.44 (m, 1H), 1.27 (d, *J* = 3.8 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H).

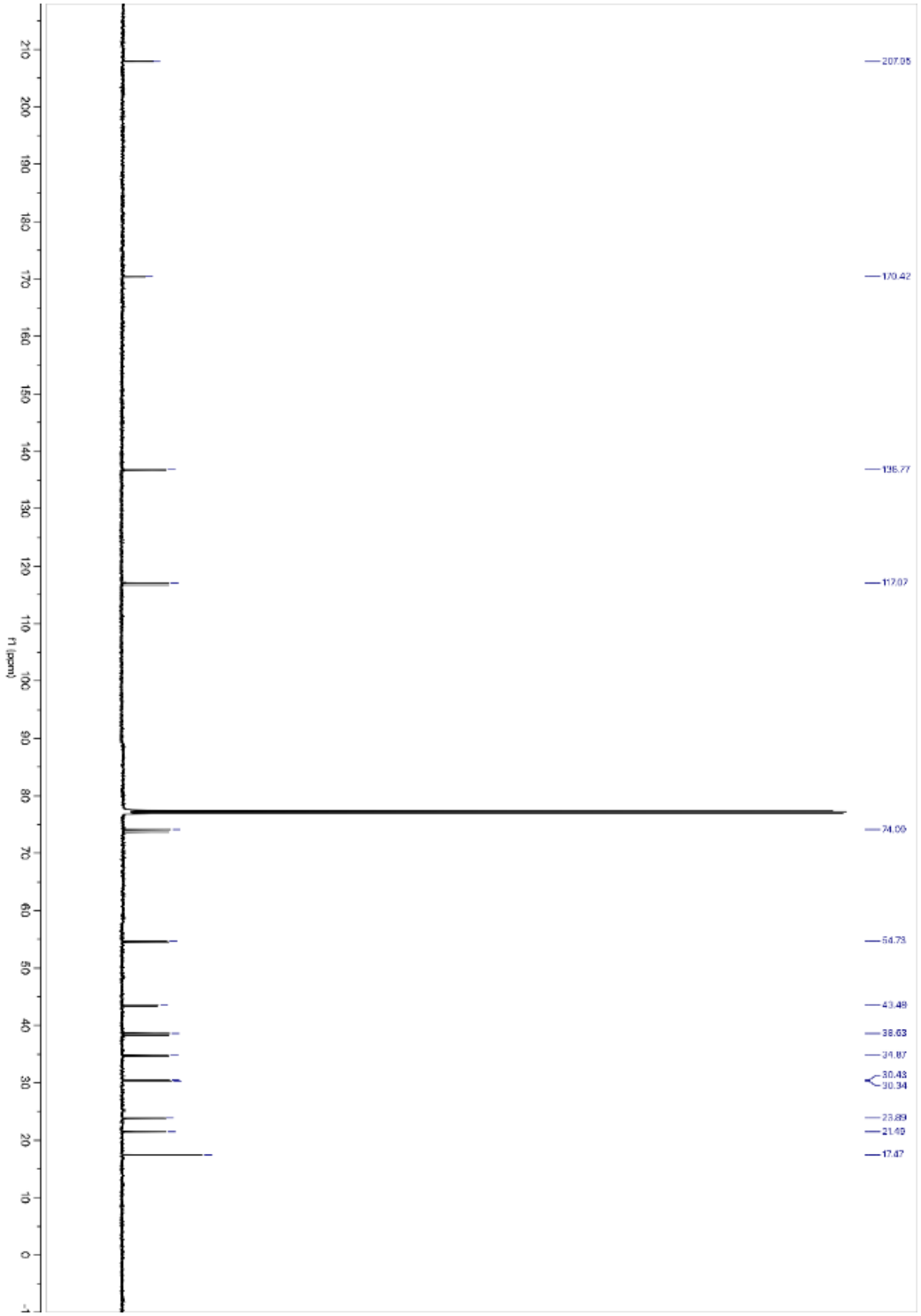
^{13}C NMR (126 MHz, $CDCl_3$) δ = 208.0, 170.4, 136.8, 117.1, 74.1, 54.7, 43.5, 30.4, 30.3, 23.9, 21.5, 17.5.

HRMS (ESI): Calculated for $C_{14}H_{22}O_3$ [M+Na^+] = 261.1461, Found 261.1465.

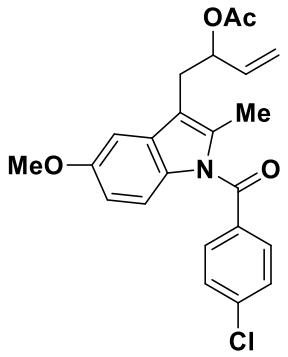
FTIR (neat): 2953, 1736, 1704, 1426, 1369, 1235, 1180, 1099, 1020, 991, 971, 929 cm^{-1}.

$[\alpha]_D^{28}$= -21.4 (*c* 0.14, $CHCl_3$).


1.07
1.23
0.93
1.08
1.00
3.25
3.03
1.11
1.15
0.99
1.04
0.72
3.04
3.05
f1 (ppm)


f1 (ppm)
207.05
170.42
136.77
117.07
74.09
54.73
43.48
38.63
34.87
30.43
30.34
23.89
21.49
17.47

1-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)but-3-en-2-yl acetate (1w)



Procedure

Allylic alcohol **S1w** (298 mg, 0.80 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 76% yield (280 mg, 0.68 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–3:1).

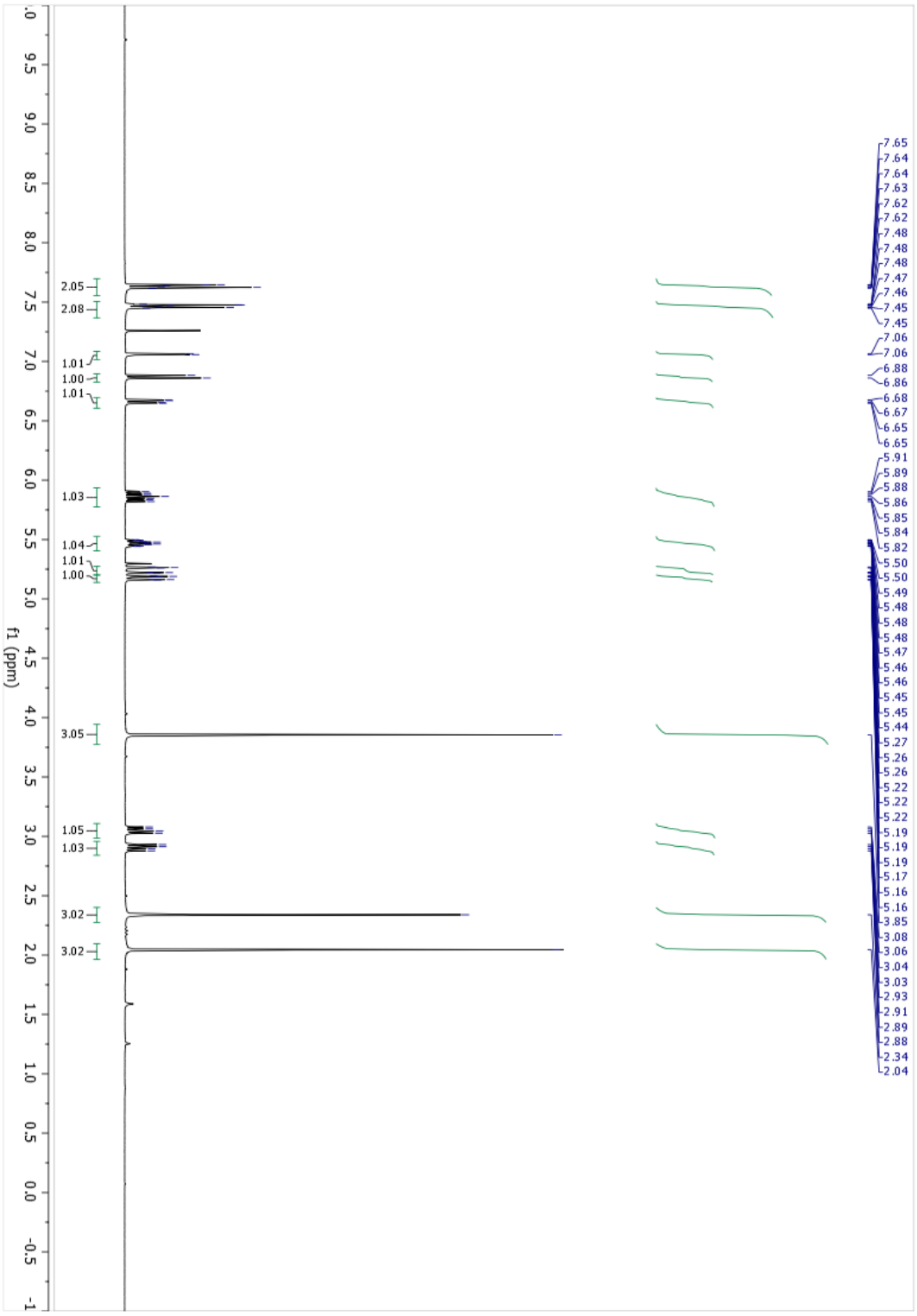
TLC (SiO_2) R_f = 0.34 (hexanes: ethyl acetate = 4:1).

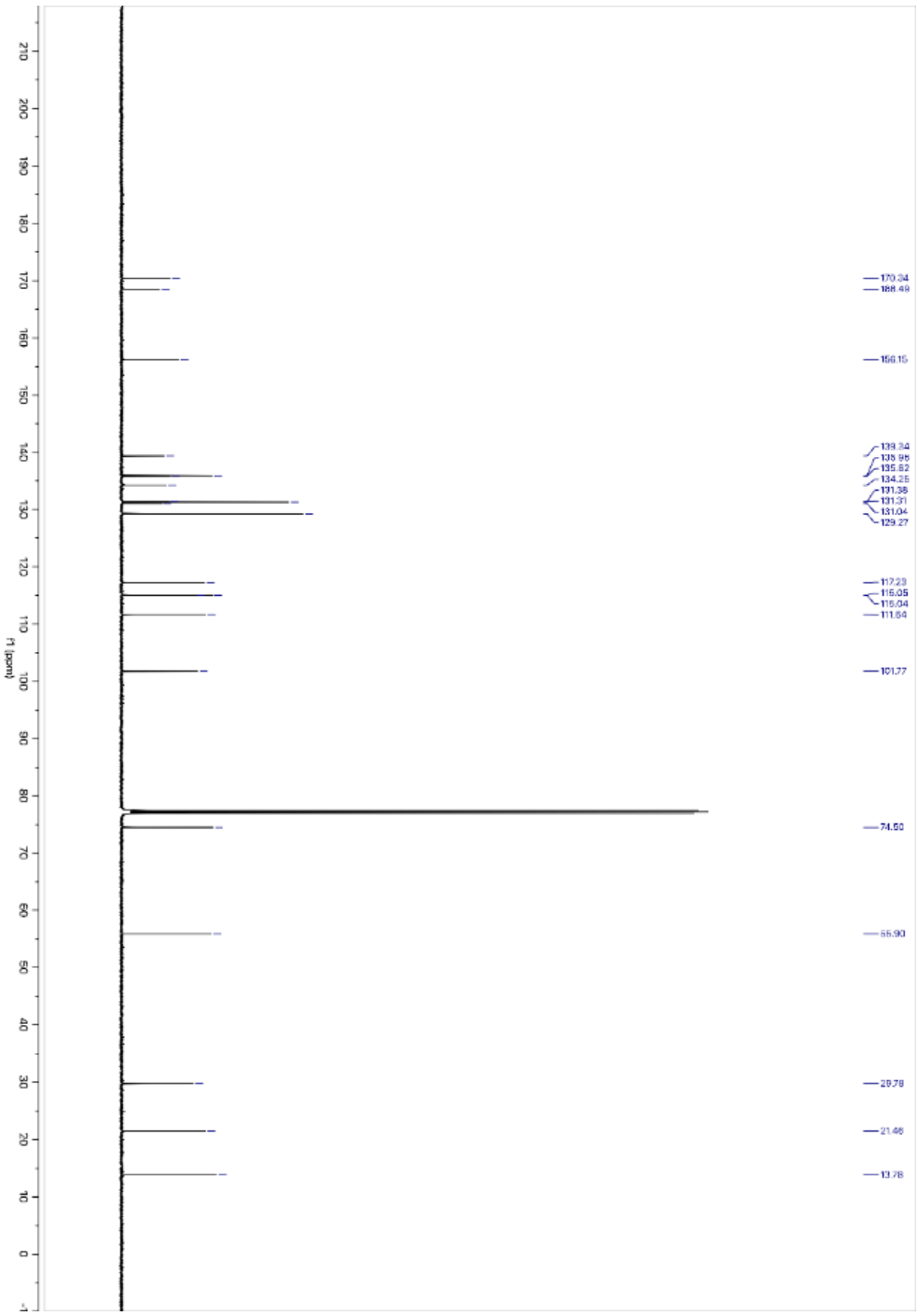
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.70 – 7.55 (m, 2H), 7.51 – 7.37 (m, 2H), 7.06 (d, *J* = 2.5 Hz, 1H), 6.87 (d, *J* = 9.0 Hz, 1H), 6.66 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.86 (ddd, *J* = 17.1, 10.5, 6.4 Hz, 1H), 5.53 – 5.40 (m, 1H), 5.24 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.18 (dt, *J* = 10.6, 1.2 Hz, 1H), 3.85 (s, 3H), 3.05 (dd, *J* = 14.2, 6.5 Hz, 1H), 2.90 (dd, *J* = 14.2, 7.0 Hz, 1H), 2.34 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.3, 168.5, 156.2, 139.3, 136.0, 135.8, 134.3, 131.4, 131.3, 131.0, 129.3, 117.2, 115.1, 115.0, 111.6, 101.8, 74.5, 55.9, 29.8, 21.5, 13.8.

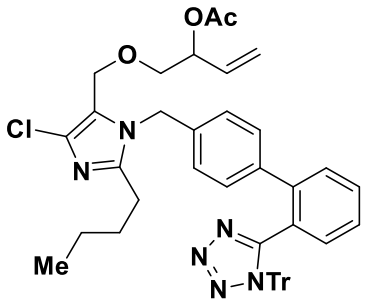
HRMS (ESI): Calculated for $C_{23}H_{22}ClNO_4$ [M+Na^+] = 434.1130, Found 434.1130.

FTIR (neat): 2949, 2930, 2831, 1720, 1674, 1613, 1599, 1480, 1368, 1245, 1229, 1057, 803, 753 cm^{-1}.


f1 (ppm)
2.05
2.08
1.01
1.00
1.01
1.03
1.04
1.01
1.00
3.05
1.05
1.03
3.02
3.02
7.65
7.64
7.64
7.63
7.62
7.62
7.48
7.48
7.48
7.47
7.46
7.45
7.45
7.06
7.06
6.88
6.86
6.68
6.67
6.65
6.65
5.91
5.89
5.88
5.86
5.85
5.84
5.82
5.50
5.50
5.49
5.48
5.48
5.48
5.47
5.46
5.46
5.45
5.45
5.44
5.27
5.26
5.26
5.22
5.22
5.22
5.19
5.19
5.19
5.17
5.16
5.16
3.85
3.08
3.06
3.04
3.03
2.93
2.91
2.89
2.88
2.34
2.04


170.34
168.49
156.15
139.34
135.95
135.82
134.25
131.58
131.31
131.04
129.27
117.23
116.05
115.04
111.84
101.77
74.50
55.90
29.78
21.46
13.78
f1 (ppm)

1-((2-butyl-4-chloro-1-((2'-(1-trityl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1H-imidazol-5-yl)methoxy)but-3-en-2-yl acetate (1x)



Procedure

Allylic alcohol **S1x** (345 mg, 0.47 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 65% yield (237 mg, 0.30 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–3:1).

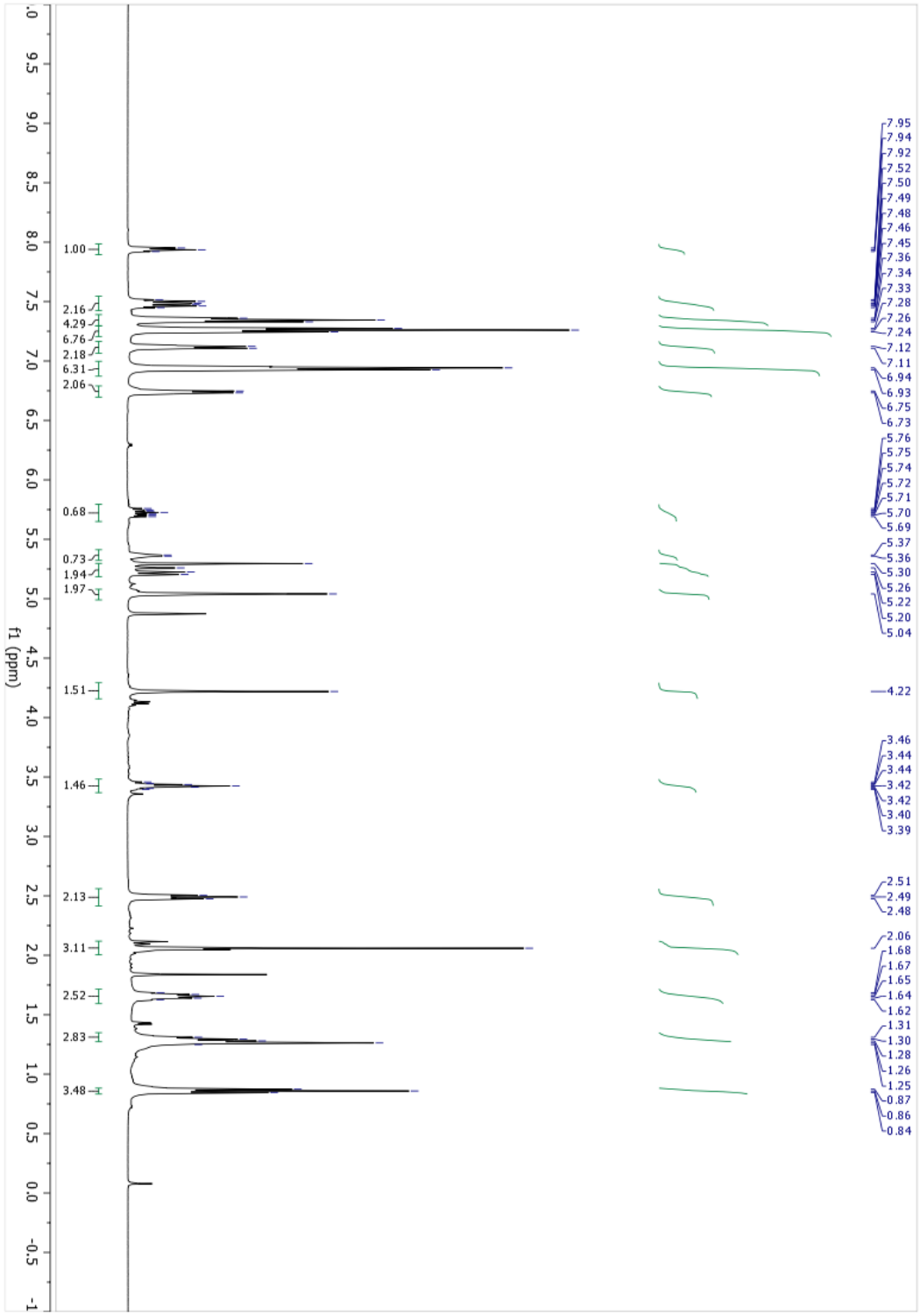
TLC (SiO_2) R_f = 0.60 (hexanes: ethyl acetate = 1:1).

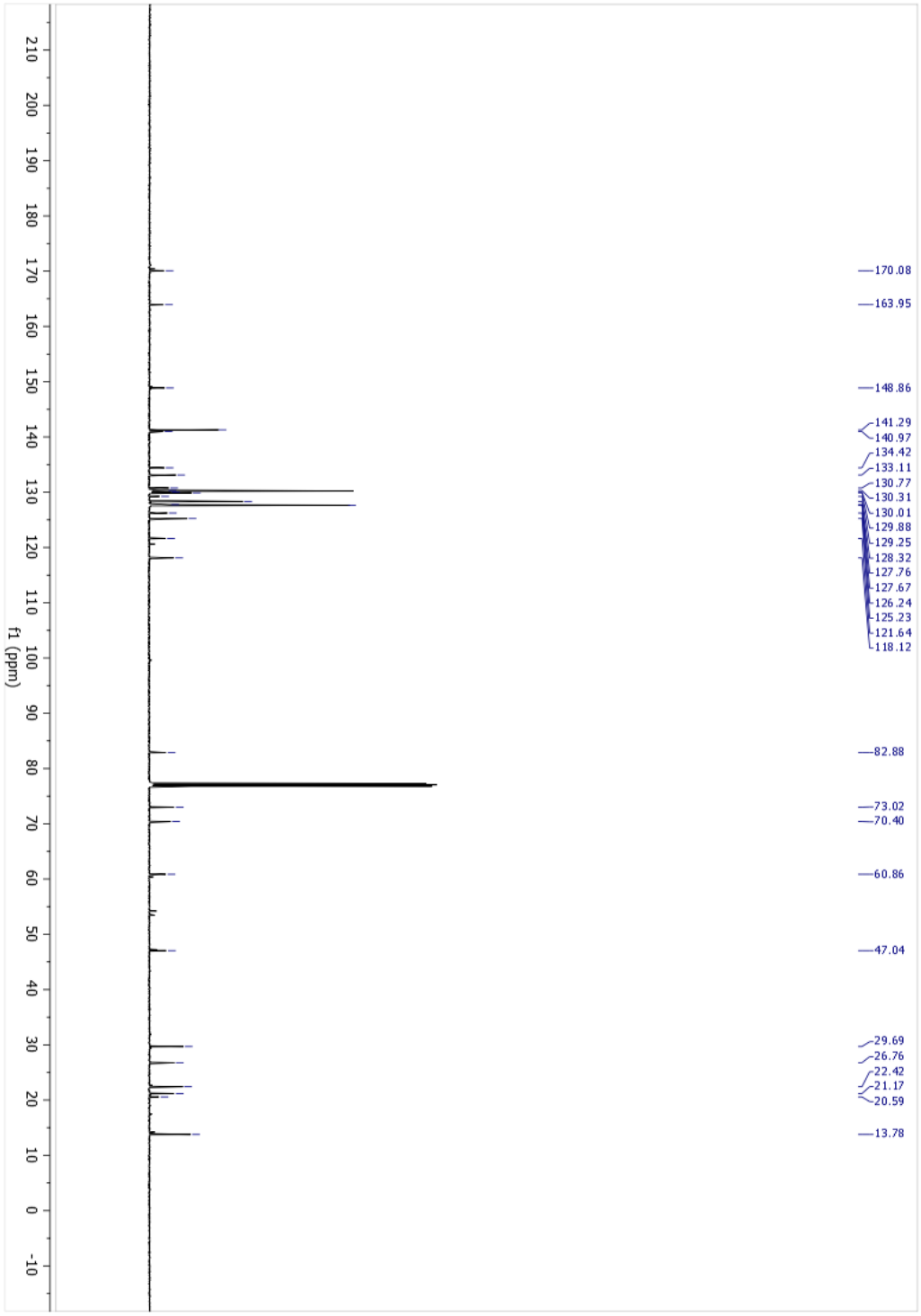
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (t, *J* = 7.3 Hz, 1H), 7.48 (dq, *J* = 14.2, 7.1 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 4H), 7.26 (t, *J* = 7.6 Hz, 7H), 7.11 (d, *J* = 7.8 Hz, 2H), 6.93 (d, *J* = 7.6 Hz, 6H), 6.74 (d, *J* = 7.8 Hz, 2H), 5.72 (ddd, *J* = 17.0, 10.6, 6.0 Hz, 1H), 5.36 (d, *J* = 4.9 Hz, 1H), 5.30 – 5.18 (m, 2H), 5.04 (s, 2H), 4.22 (s, 2H), 3.43 (h, *J* = 6.7 Hz, 1H), 2.49 (t, *J* = 7.8 Hz, 2H), 2.06 (s, 3H), 1.65 (p, *J* = 7.7 Hz, 3H), 1.35 – 1.27 (m, 3H), 0.86 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.1, 164.0, 148.9, 141.3, 141.0, 134.4, 133.1, 130.8, 130.3, 130.0, 129.9, 129.3, 128.3, 127.8, 127.7, 126.2, 125.2, 121.6, 118.1, 82.9, 73.0, 70.4, 60.9, 47.0, 29.7, 26.8, 22.4, 21.2, 20.6, 13.8.

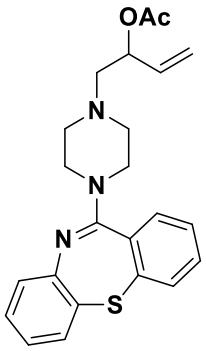
HRMS (ESI): Calculated for C47H47ClN6O2 [M+H+] = 777.3314, Found 777.3315.

FTIR (neat): 2960, 1737, 1584, 1493, 1446, 1372, 1265, 1249, 1028, 993, 881, 733, 699 cm^{-1}.


f1 (ppm)
1.00
2.16
4.29
6.76
2.18
6.31
2.06
0.68
0.73
1.94
1.97
1.51
1.46
2.13
3.11
2.52
2.83
3.48
7.95
7.94
7.92
7.52
7.50
7.49
7.48
7.46
7.45
7.36
7.34
7.33
7.28
7.26
7.24
7.12
7.11
6.94
6.93
6.75
6.73
5.76
5.75
5.74
5.72
5.71
5.70
5.69
5.37
5.36
5.30
5.26
5.22
5.20
5.04
4.22
3.46
3.44
3.44
3.42
3.42
3.40
3.39
2.51
2.49
2.48
2.06
1.68
1.67
1.65
1.64
1.62
1.31
1.30
1.28
1.26
1.25
0.87
0.86
0.84


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.08
163.95
148.86
141.29
140.97
134.42
133.11
130.77
130.31
130.01
129.88
129.25
128.32
127.76
127.67
126.24
125.23
121.64
118.12
82.88
73.02
70.40
60.86
47.04
29.69
26.76
22.42
21.17
20.59
13.78

1-(4-(dibenzo[*b*,*f*][1,4]thiazepin-11-yl)piperazin-1-yl)but-3-en-2-yl acetate (1y)



Procedure

Allylic alcohol **S1y** (375 mg, 1.03 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 89% yield (375 mg, 0.92 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–3:2).

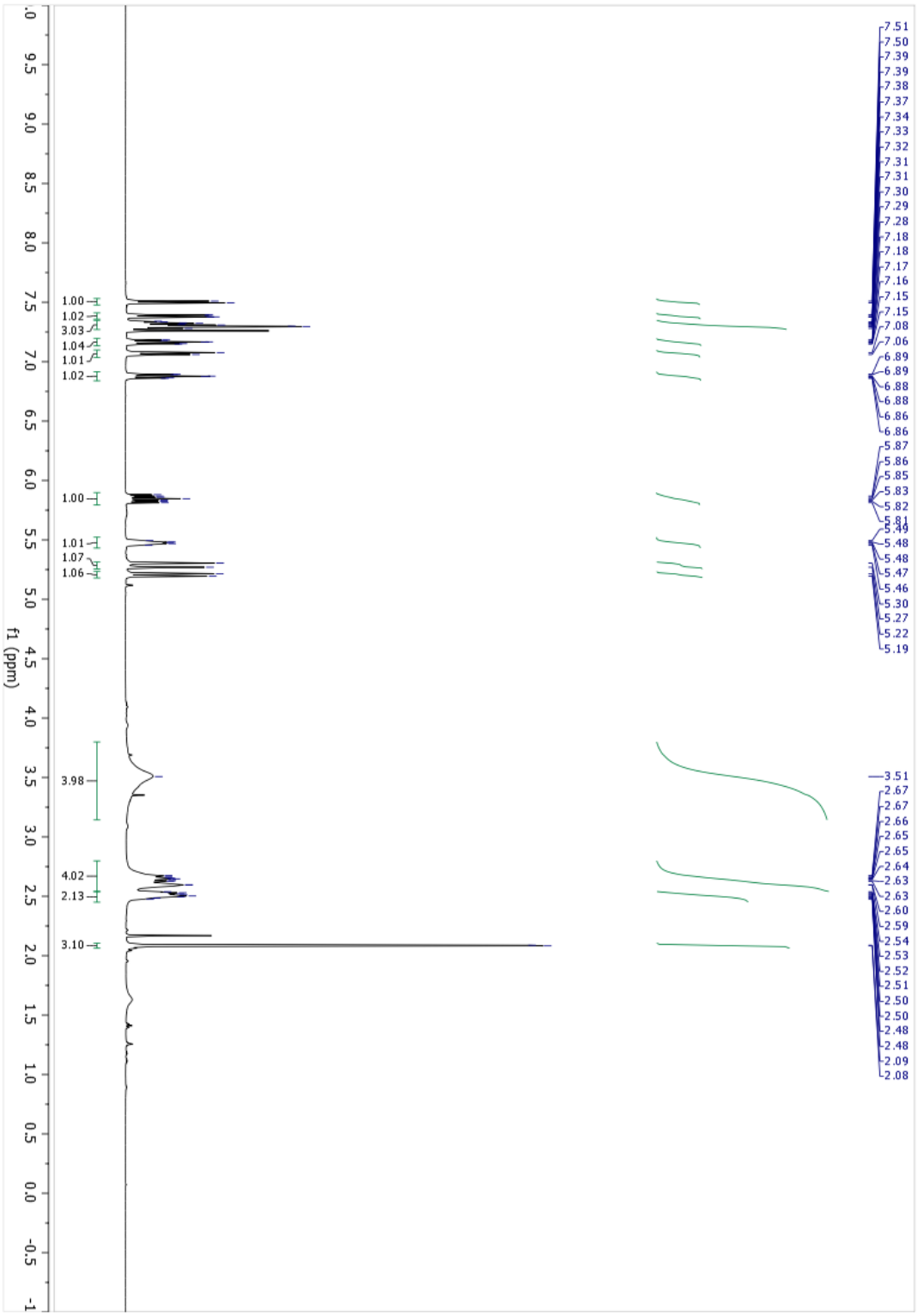
TLC (SiO_2) R_f = 0.50 (hexanes: ethyl acetate = 1:1).

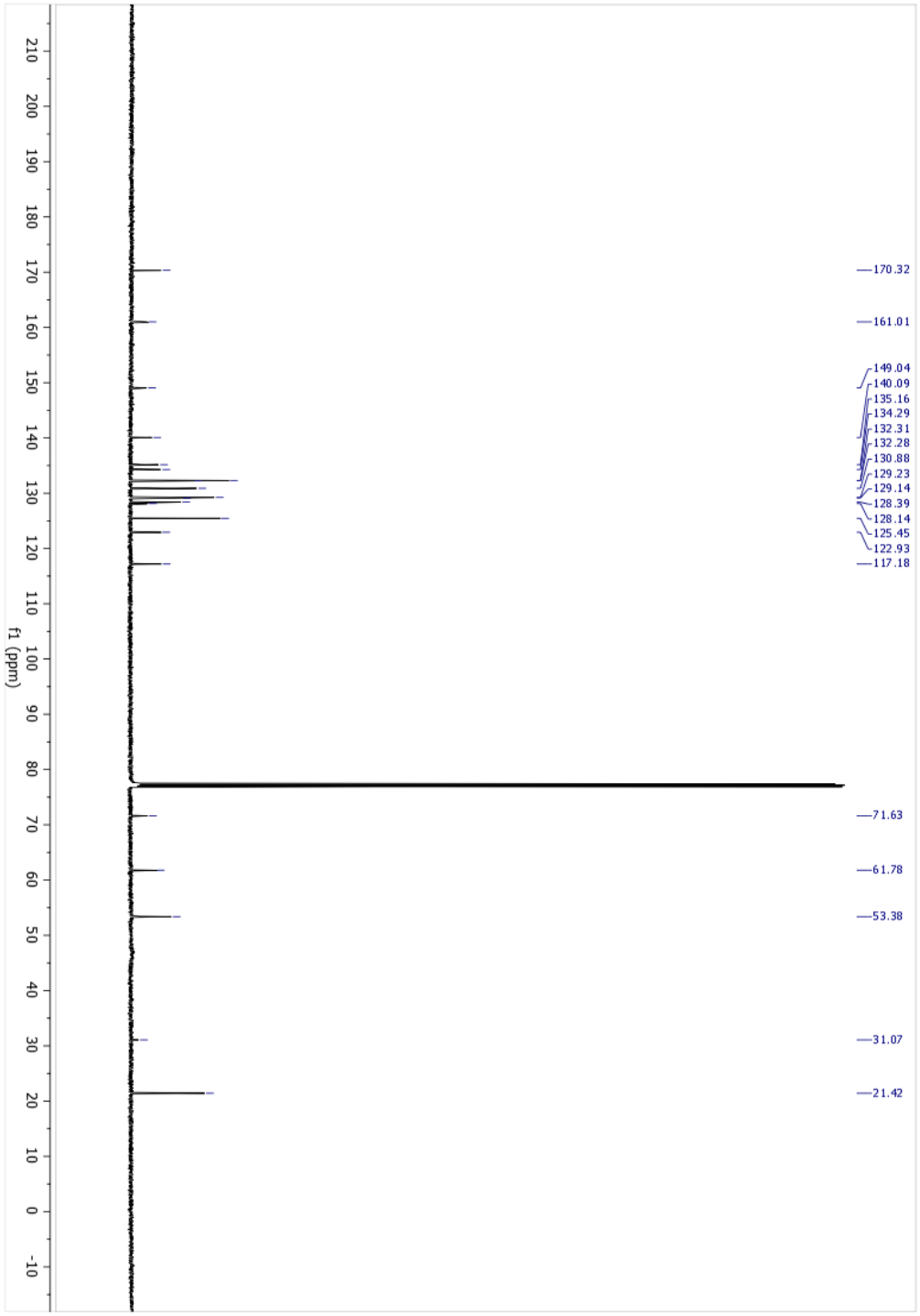
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.50 (d, *J* = 7.5 Hz, 1H), 7.38 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.35 – 7.27 (m, 3H), 7.17 (td, *J* = 7.6, 1.6 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.88 (td, *J* = 7.5, 1.5 Hz, 1H), 5.85 (ddd, *J* = 16.9, 10.6, 5.9 Hz, 1H), 5.48 (q, *J* = 6.1 Hz, 1H), 5.29 (d, *J* = 17.3 Hz, 1H), 5.21 (d, *J* = 10.6 Hz, 1H), 3.51 (s, 4H), 2.80 – 2.54 (m, 4H), 2.51 (ddt, *J* = 13.0, 9.4, 4.1 Hz, 2H), 2.09 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 170.3, 161.0, 149.0, 140.1, 135.2, 134.3, 132.3, 132.3, 130.9, 129.2, 129.1, 128.4, 128.1, 125.5, 122.9, 117.2, 71.6, 61.8, 53.4, 31.1, 21.4.

HRMS (ESI): Calculated for $C_{23}H_{25}N_3O_2S$ [M+H$^+$] = 408.1740, Found 408.1740.

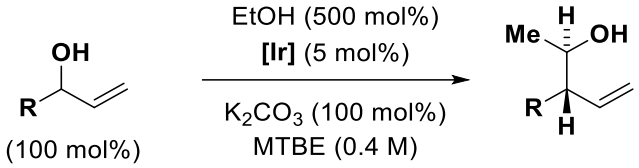
FTIR (neat): 2934, 2812, 1736, 1596, 1574, 1556, 1453, 1410, 1369, 1305, 1235, 1147, 1005, 915, 773, 762, 740 cm^{-1}.


f1 (ppm)
1.00
1.02
3.03
1.04
1.01
1.02
1.00
1.01
1.07
1.06
3.98
4.02
2.13
3.10
7.51
7.50
7.39
7.39
7.38
7.37
7.34
7.33
7.32
7.31
7.31
7.30
7.29
7.28
7.18
7.18
7.17
7.16
7.15
7.15
7.08
7.06
6.89
6.89
6.88
6.88
6.86
6.86
5.87
5.86
5.85
5.83
5.82
5.48
5.48
5.47
5.46
5.30
5.27
5.22
5.19
3.51
2.67
2.67
2.66
2.65
2.65
2.64
2.63
2.63
2.60
2.59
2.54
2.53
2.52
2.51
2.50
2.50
2.48
2.48
2.09
2.08


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.32
161.01
149.04
140.09
135.16
134.29
132.31
132.28
130.88
129.23
129.14
128.39
128.14
125.45
122.93
117.18
71.63
61.78
53.38
31.07
21.42

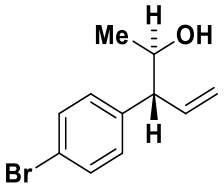
3.1f. Procedures and Spectral Data for Synthesis of Secondary Alcohols 2a-2y

General Procedure D



An oven-dried pressure tube equipped with a magnetic stir bar was charged with allyl acetate (0.200 mmol, 100 mol%), **(*S*)-Ir-V** (10.7 mg, 0.0100 mmol, 5 mol%), and potassium carbonate (27.6 mg, 0.200 mmol, 100 mol%). The tube was purged with argon and ethanol (58 μL, 1.0 mmol, 500 mol%) was added by syringe, followed by *tert*-butyl methyl ether (0.50 mL, 0.40 M). The septum was removed and the tube was sealed with a polytetrafluoroethylene-lined screwcap. The tube was placed in an oil bath at 60 °C and stirred for 24 hours. The vessel was allowed to cool to ambient temperature and the reaction mixture was filtered through celite with the aid of dichloromethane. The filtrate was concentrated *in vacuo* and the residue was directly subjected to flash column chromatography.

(2R,3R)-3-(4-bromophenyl)pent-4-en-2-ol (2a)



Procedure

Allyl acetate **1a** (51.0 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 75% yield (36.2 mg, 0.150 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.32 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.06 (ddd, *J* = 17.1, 10.3, 8.9 Hz, 1H), 5.25 (dd, *J* = 10.2, 1.6 Hz, 1H), 5.21 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.01 – 3.87 (m, 1H), 3.14 (t, *J* = 8.2 Hz, 1H), 1.84 (s, 1H), 1.07 (d, *J* = 6.2 Hz, 3H).

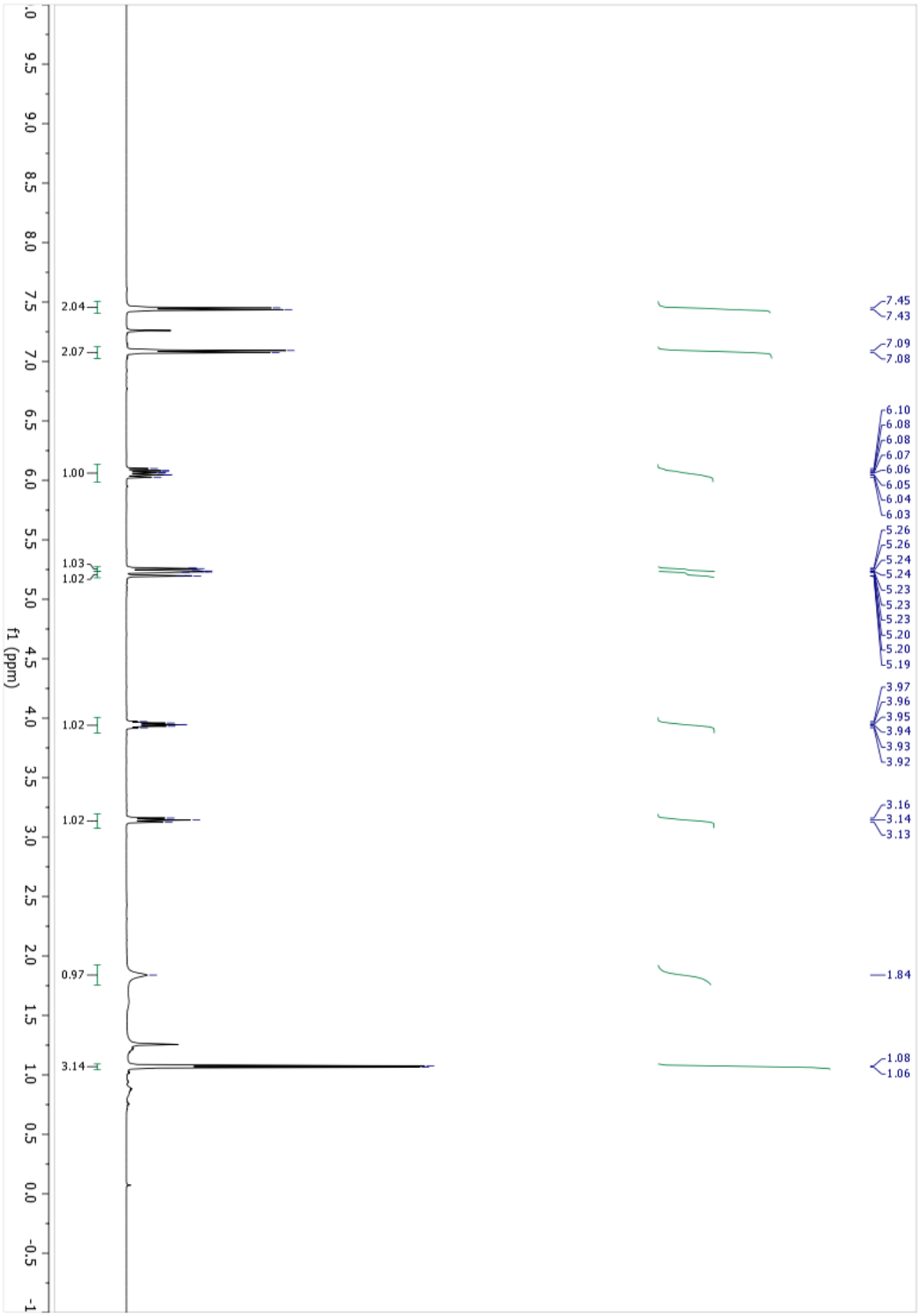
^{13}C NMR (126 MHz, $CDCl_3$) δ = 140.7, 138.0, 131.9, 129.9, 120.7, 118.5, 70.2, 58.5, 20.9.

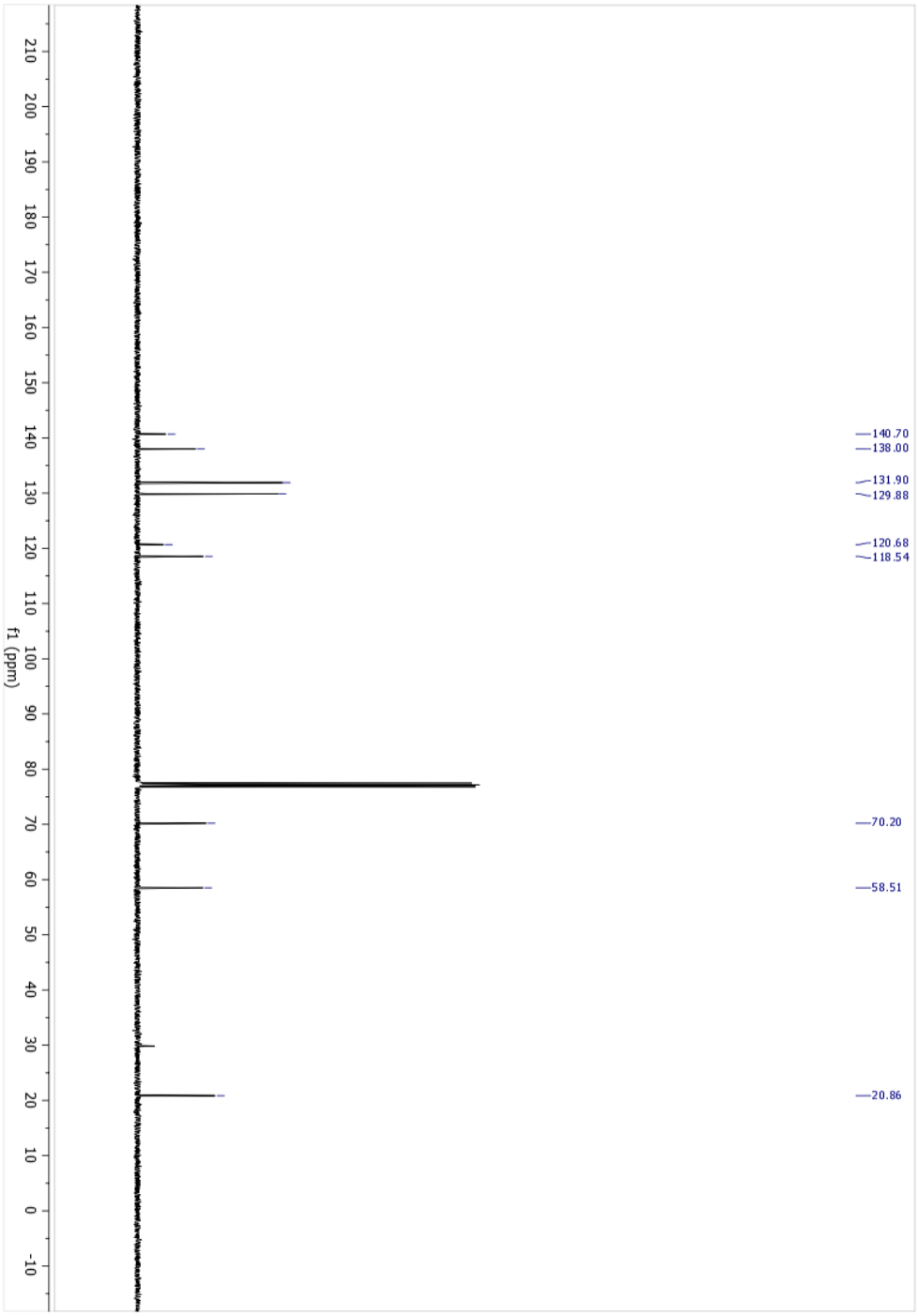
HRMS (ESI): Calculated for $C_{11}H_{13}BrO$ [M+Ag^+] = 346.9195, Found 346.9205.

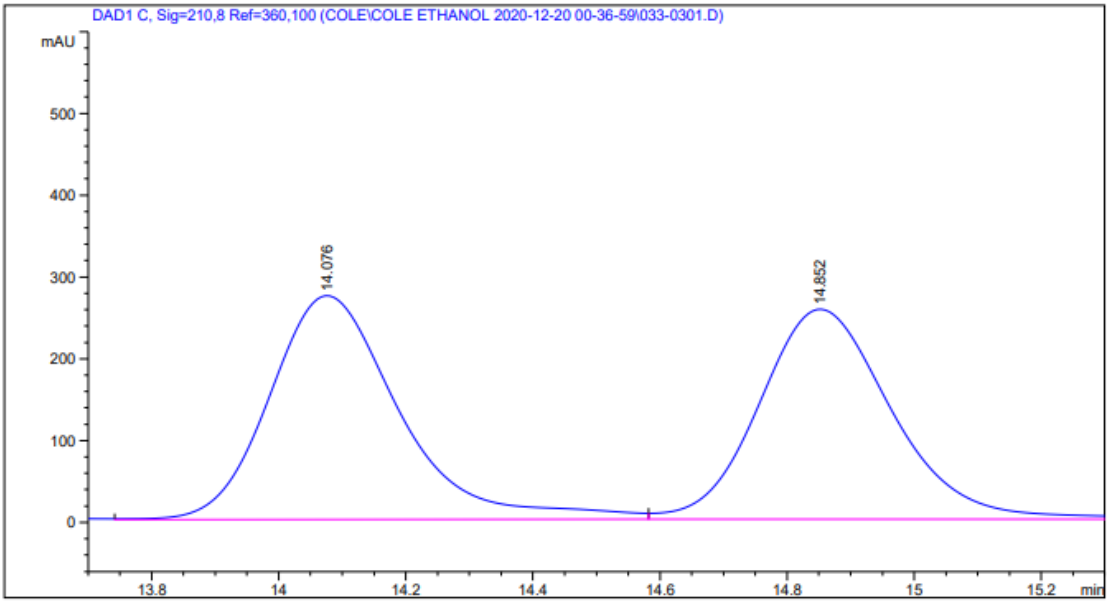
FTIR (neat): 3394, 3077, 2970, 2928, 1637, 1589, 1488, 1455, 1403, 1374, 1262, 1105, 1073, 1010, 920, 869, 816, 718 cm^{-1}.

$[\alpha]_D^{28}$= -67.7 (*c* 0.30, $CHCl_3$).

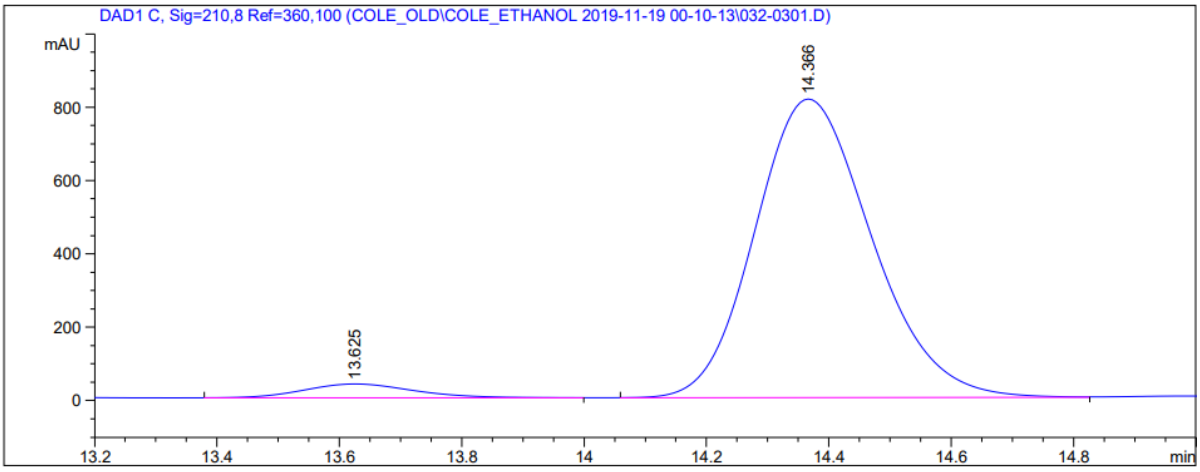
HPLC (Chiralcel OD-H column in series with a Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 230 nm), *ee* = 92%.


f1 (ppm)
2.04
2.07
1.00
1.03
1.02
1.02
1.02
0.97
3.14
7.45
7.43
7.09
7.08
6.10
6.08
6.08
6.07
6.06
6.05
6.04
6.03
5.26
5.26
5.24
5.24
5.23
5.23
5.23
5.20
5.20
5.19
3.97
3.96
3.95
3.94
3.93
3.92
3.16
3.14
3.13
1.84
1.08
1.06


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
140.70
138.00
131.90
129.88
120.68
118.54
70.20
58.51
20.86

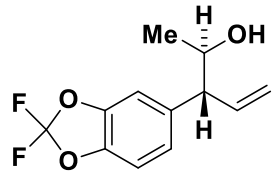


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.076	VV	0.2163	3903.37476	273.89548	51.0942
2	14.852	VV	0.2236	3736.18457	256.95441	48.9058



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.625	BB	0.1947	477.03635	37.94899	4.2171
2	14.366	BV	0.2051	1.08349e4	814.88196	95.7829

(2R,3R)-3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)pent-4-en-2-ol (2b)



Procedures

(0.200 mmol scale) Allyl acetate **1b** (51.2 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 82% yield (39.7 mg, 0.164 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

(1.00 mmol scale) Allyl acetate **1b** (256.2 mg, 1.00 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 84% yield (204 mg, 0.842 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.23 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.00 (d, *J* = 8.2 Hz, 1H), 6.95 (d, *J* = 1.7 Hz, 1H), 6.91 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.05 (ddd, *J* = 17.0, 10.2, 8.8 Hz, 1H), 5.27 (dd, *J* = 10.3, 1.5 Hz, 1H), 5.22 (dt, *J* = 17.0, 1.2 Hz, 1H), 3.94 (dt, *J* = 7.3, 6.1 Hz, 1H), 3.17 (t, *J* = 8.1 Hz, 1H), 1.79 (s, 1H), 1.09 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.1, 142.6, 138.0, 137.8, 131.8 (t, *J* = 253.8 Hz, 1H), 123.2, 118.7, 109.6, 109.3, 70.3, 58.6, 20.9.

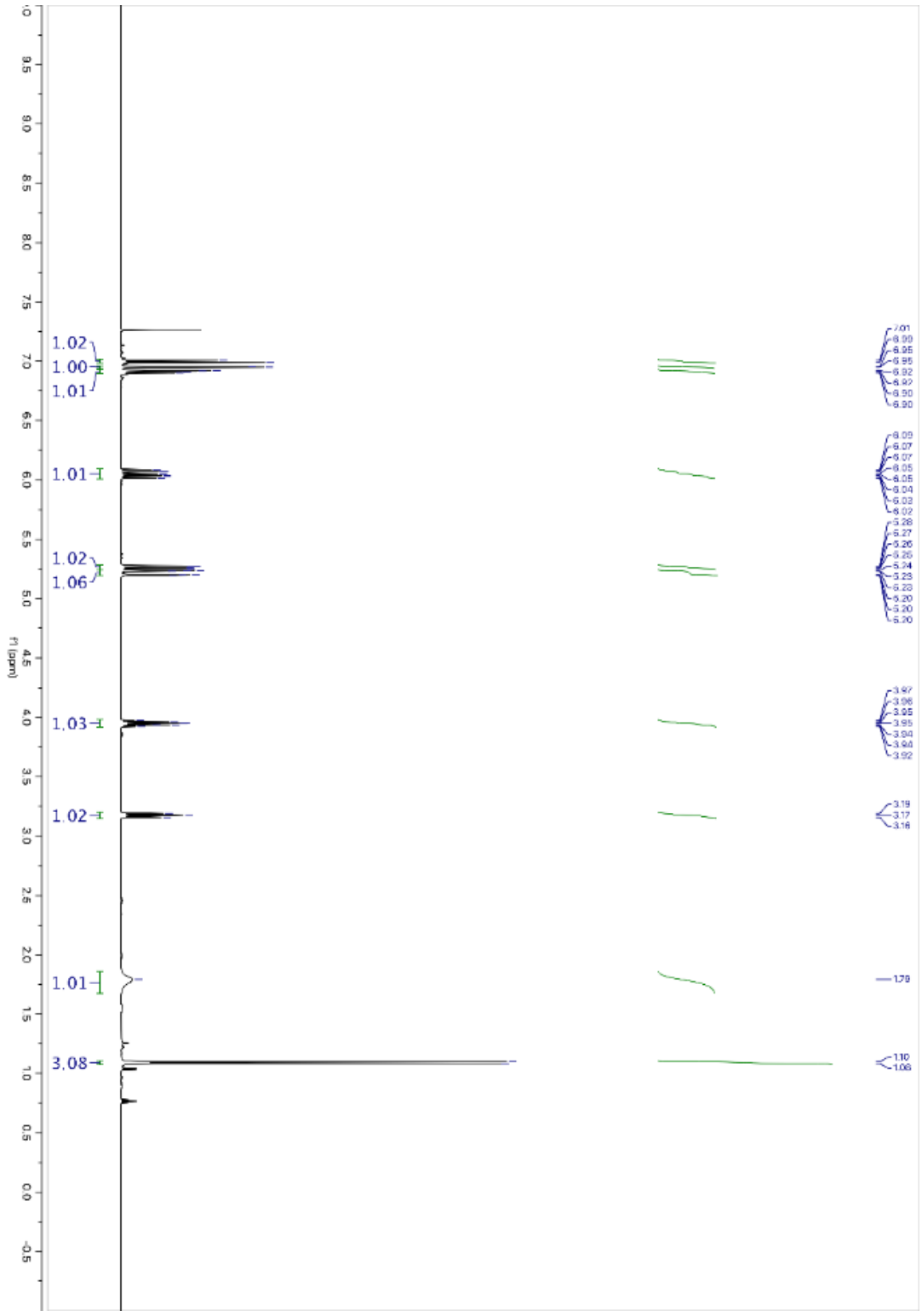
^{19}F NMR (471 MHz, $CDCl_3$) δ -50.0.

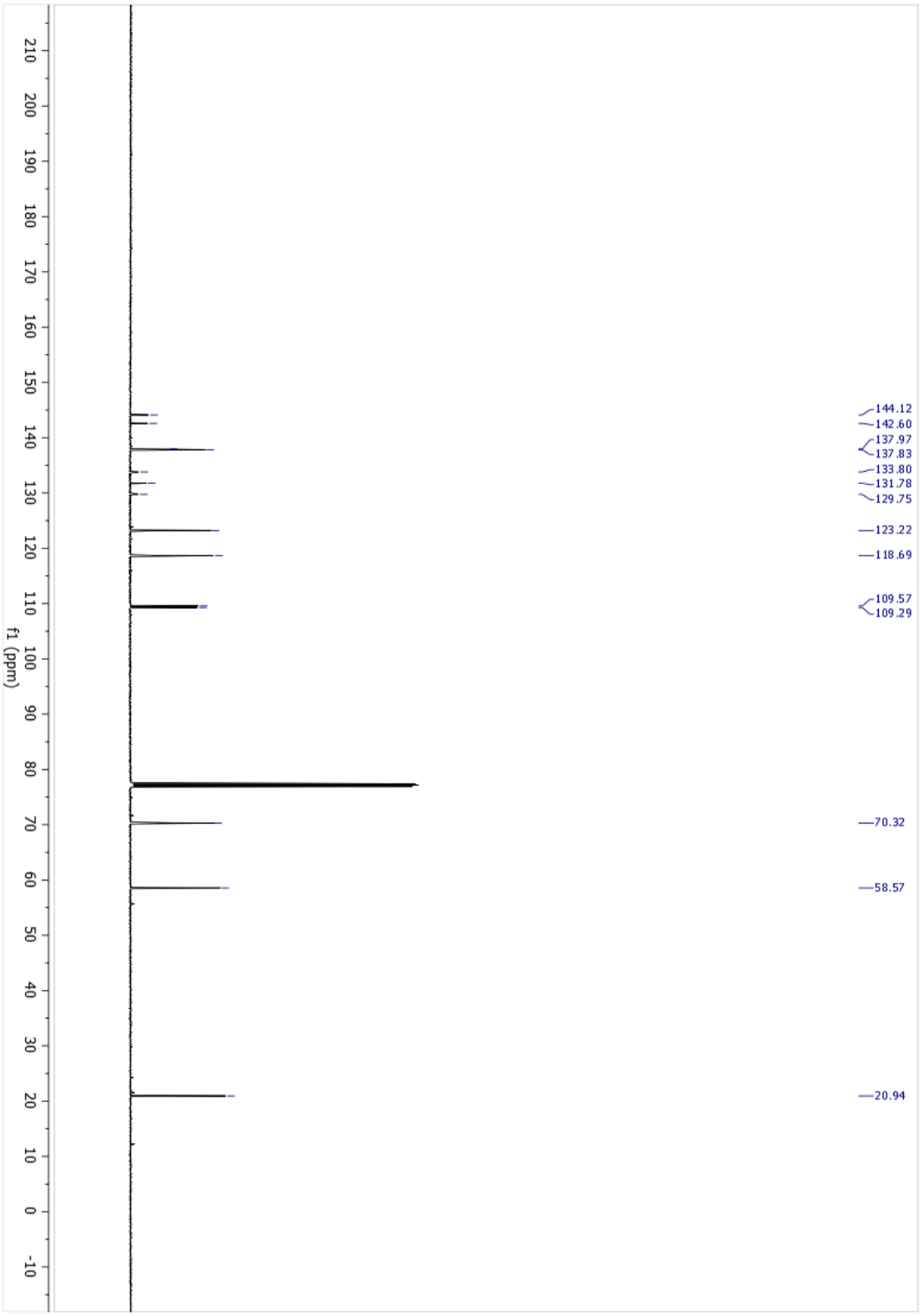
HRMS (ESI): Calculated for $C_{12}H_{12}F_2O_3$ [M+Ag^+] = 348.9800, Found 348.9788.

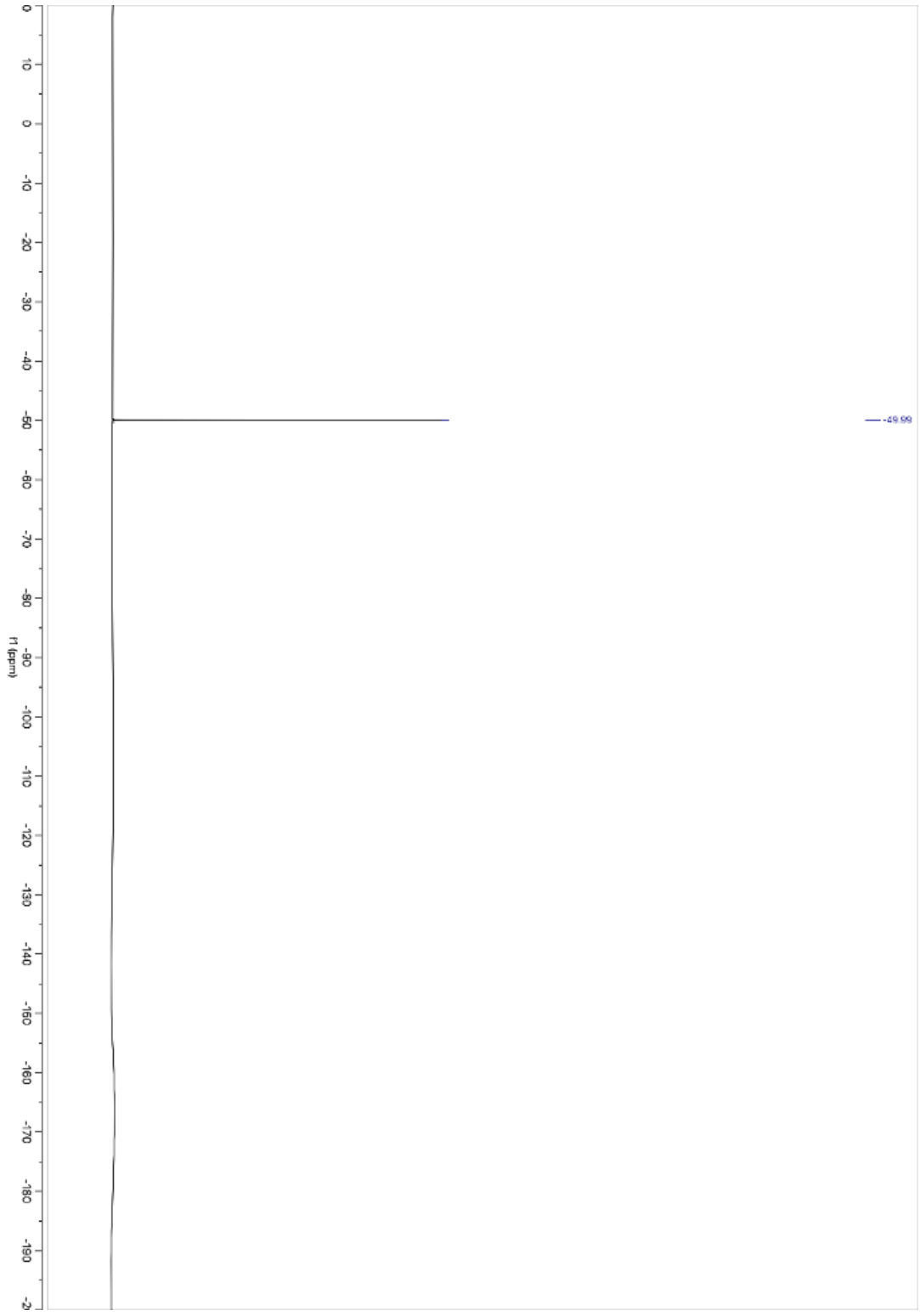
FTIR (neat): 3406, 2976, 1639, 1498, 1446, 1238, 1153, 1034, 952, 924, 901, 873, 811, 705 cm^{-1}.

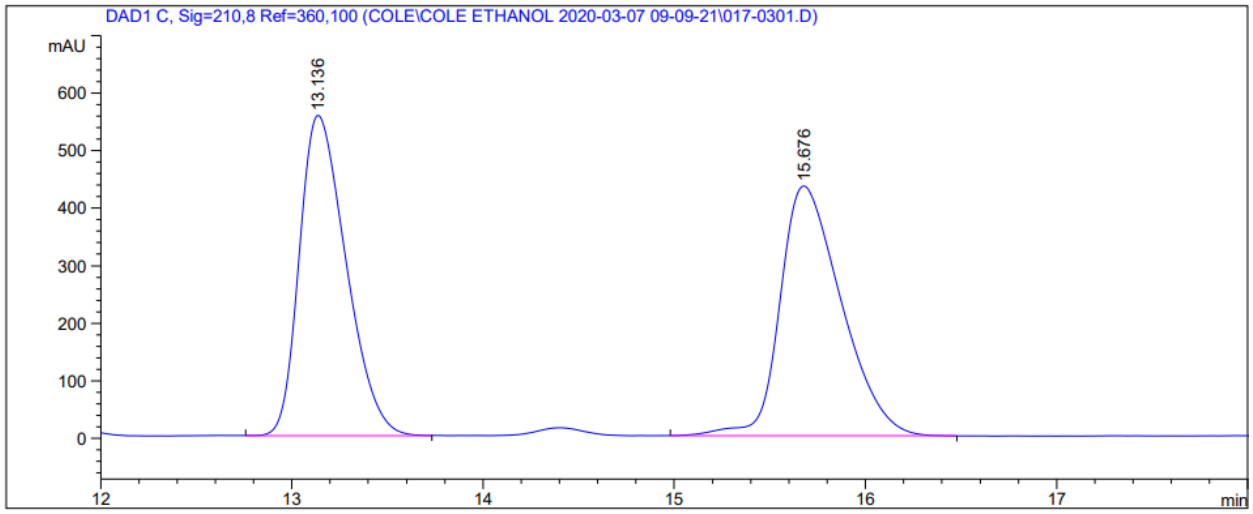
$[\alpha]_D^{25}$= -67.8 (*c* 0.39, $CHCl_3$).

HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 93%.

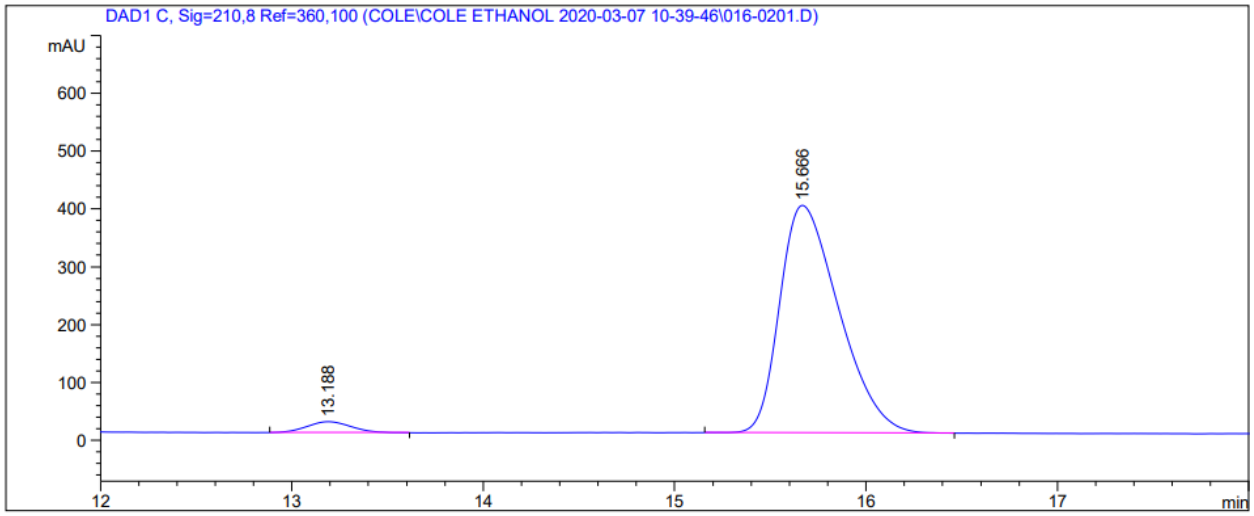

1.02
1.00
1.01
1.01
1.02
1.06
1.03
1.02
1.01
3.08
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
144.12
142.60
137.97
137.83
133.80
131.78
129.75
123.22
118.69
109.57
109.29
70.32
58.57
20.94


-49.99
f1 (ppm)

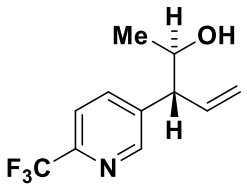


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.136	BB	0.2625	9473.17480	556.82104	49.4154
2	15.676	BB	0.3407	9697.29785	434.00620	50.5846



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.188	BB	0.2436	304.27011	18.92569	3.4703
2	15.666	BB	0.3311	8463.65137	393.17297	96.5297

(2R,3R)-3-(6-(trifluoromethyl)pyridin-3-yl)pent-4-en-2-ol (2c)



Procedures

(0.200 mmol scale) Allyl acetate **1c** (49.0 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 75% yield (34.7 mg, 0.150 mmol, >20:1 dr) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

(1.00 mmol scale) Allyl acetate **1c** (245.2 mg, 1.0 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 75% yield (173 mg, 0.748 mmol, >20:1 dr) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.3 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.59 (d, *J* = 2.0 Hz, 1H), 7.76 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 6.11 (ddd, *J* = 17.1, 10.3, 8.7 Hz, 1H), 5.32 (dd, *J* = 10.3, 1.3 Hz, 1H), 5.27 – 5.18 (m, 1H), 4.05 (p, *J* = 6.3 Hz, 1H), 3.34 (dd, *J* = 8.7, 6.4 Hz, 1H), 2.00 (s, 1H), 1.13 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 150.2, 146.7 (q, *J* = 34.7 Hz), 140.9, 137.0, 136.1, 123.1, 120.4 (dt, *J* = 4.5, 2.3 Hz), 119.8, 70.0, 55.7, 21.3.

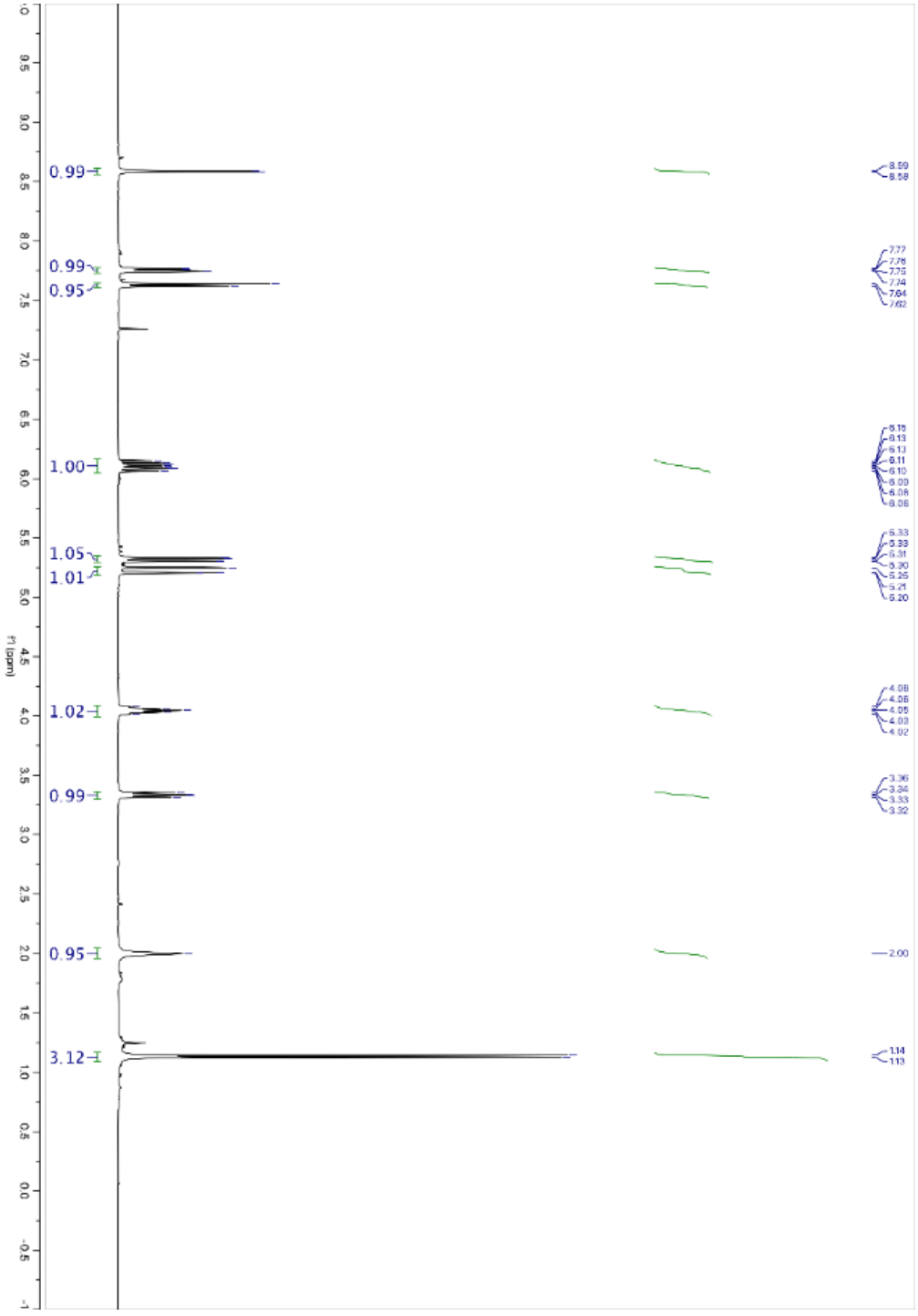
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.8.

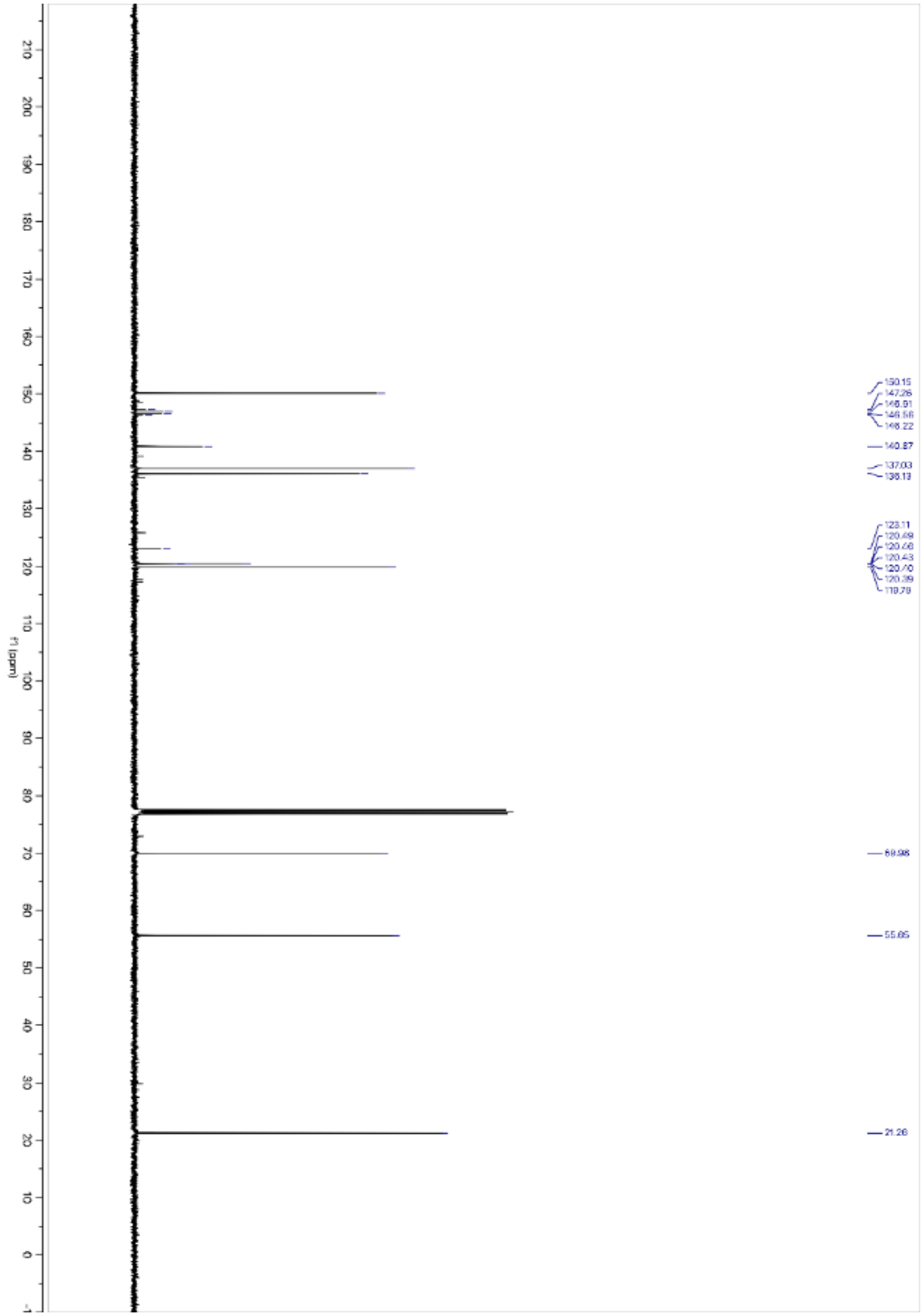
HRMS (ESI): Calculated for $C_{11}H_{12}F_3NO$ [M+H$^+$] = 232.0944, Found 232.0945.

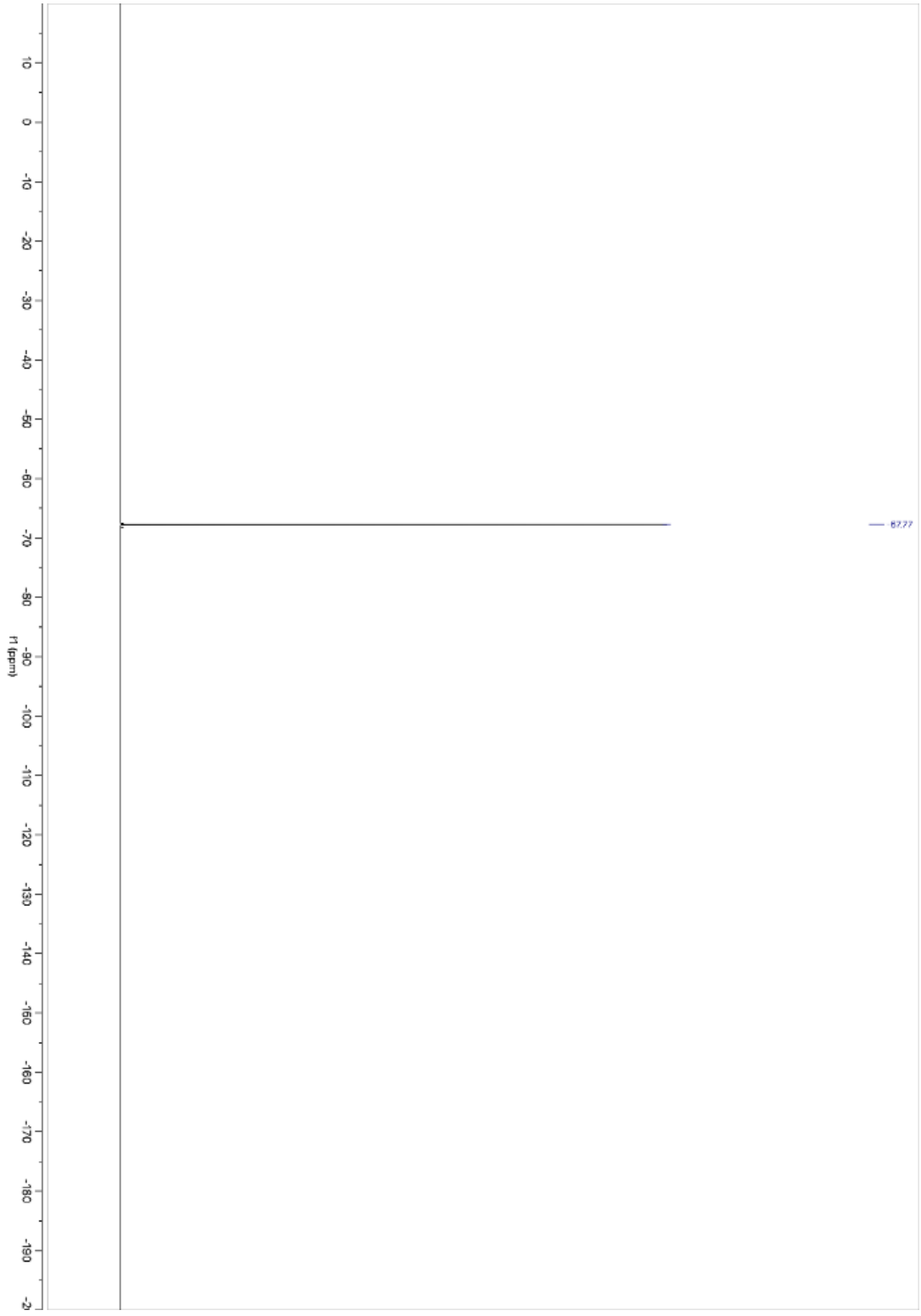
FTIR (neat): 3390, 2970, 1398, 1336, 1241, 1175, 1130, 1085, 1027, 924, 851, 815, 775 cm^{-1}.

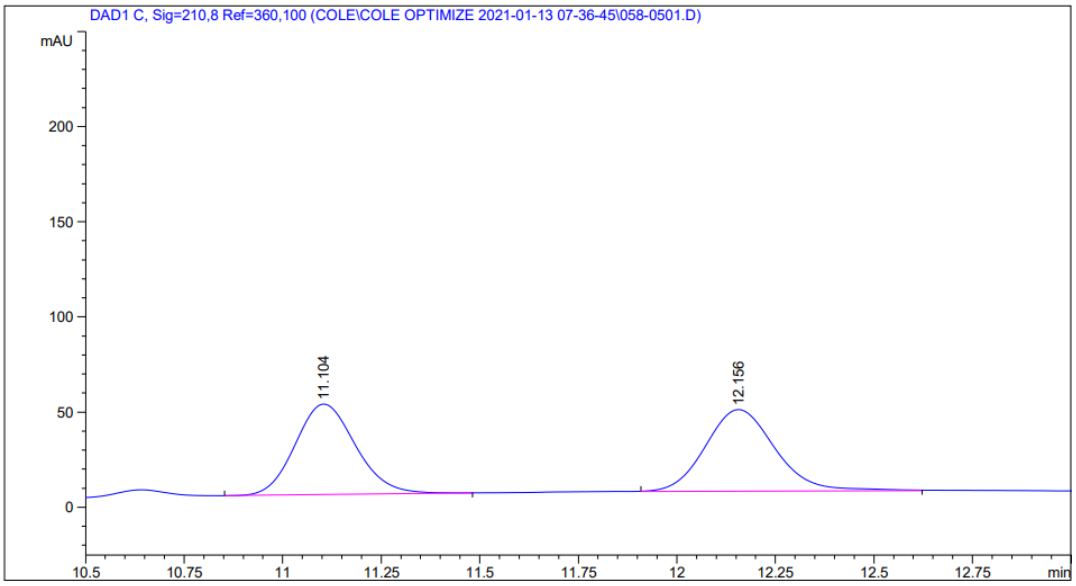
$[\alpha]_D^{28}$= -76.9 (*c* 0.18, $CHCl_3$).

HPLC (Chiralcel AD-H column in series with a Chiracel OD-H column, hexanes:*i*-PrOH = 90:10, 1.00 mL/min, 210 nm), *ee* = 92%.

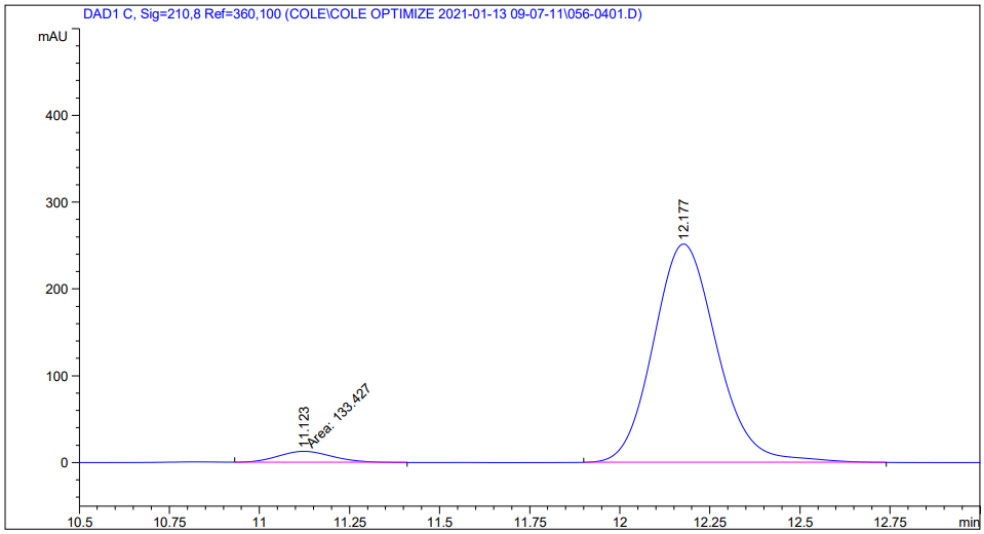

0.99
0.99
0.95
1.00
1.05
1.01
1.02
0.99
0.95
3.12
f1 (ppm)


f1 (ppm)
150.15
147.26
146.91
146.56
146.22
140.87
137.03
136.13
123.11
120.69
120.48
120.43
120.00
120.39
119.79
69.98
55.65
21.26


10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-2
f1 (ppm)
87.77

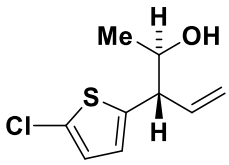


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.104	VB	0.1649	510.50958	47.67224	48.9933
2	12.156	BB	0.1902	531.48926	42.99371	51.0067



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.123	MM	0.1749	133.42749	12.71474	4.1284
2	12.177	BB	0.1895	3098.52148	251.89319	95.8716

(2R,3S)-3-(5-chlorothiophen-2-yl)pent-4-en-2-ol (2d)



Procedures

(0.200 mmol scale) Allyl acetate **1d** (43.3 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 48 hr). The title compound was obtained in 71% yield (28.8 mg, 0.142 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

(1.00 mmol scale) Allyl acetate **1d** (216.7 mg, 1.0 mmol, 100 mol%) was subjected to general procedure D (60 °C, 16 hr). The title compound was obtained in 74% yield (150 mg, 0.740 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

TLC (SiO_2) R_f = 0.49 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.77 (d, *J* = 3.7 Hz, 1H), 6.64 (dd, *J* = 3.7, 0.8 Hz, 1H), 5.98 (ddd, *J* = 17.0, 10.2, 8.8 Hz, 1H), 5.28 (ddd, *J* = 10.2, 1.5, 0.6 Hz, 1H), 5.24 (ddd, *J* = 17.0, 1.5, 0.9 Hz, 1H), 3.96 (p, *J* = 6.2 Hz, 1H), 3.47 – 3.38 (m, 1H), 1.83 (s, 1H), 1.18 (d, *J* = 6.2 Hz, 3H).

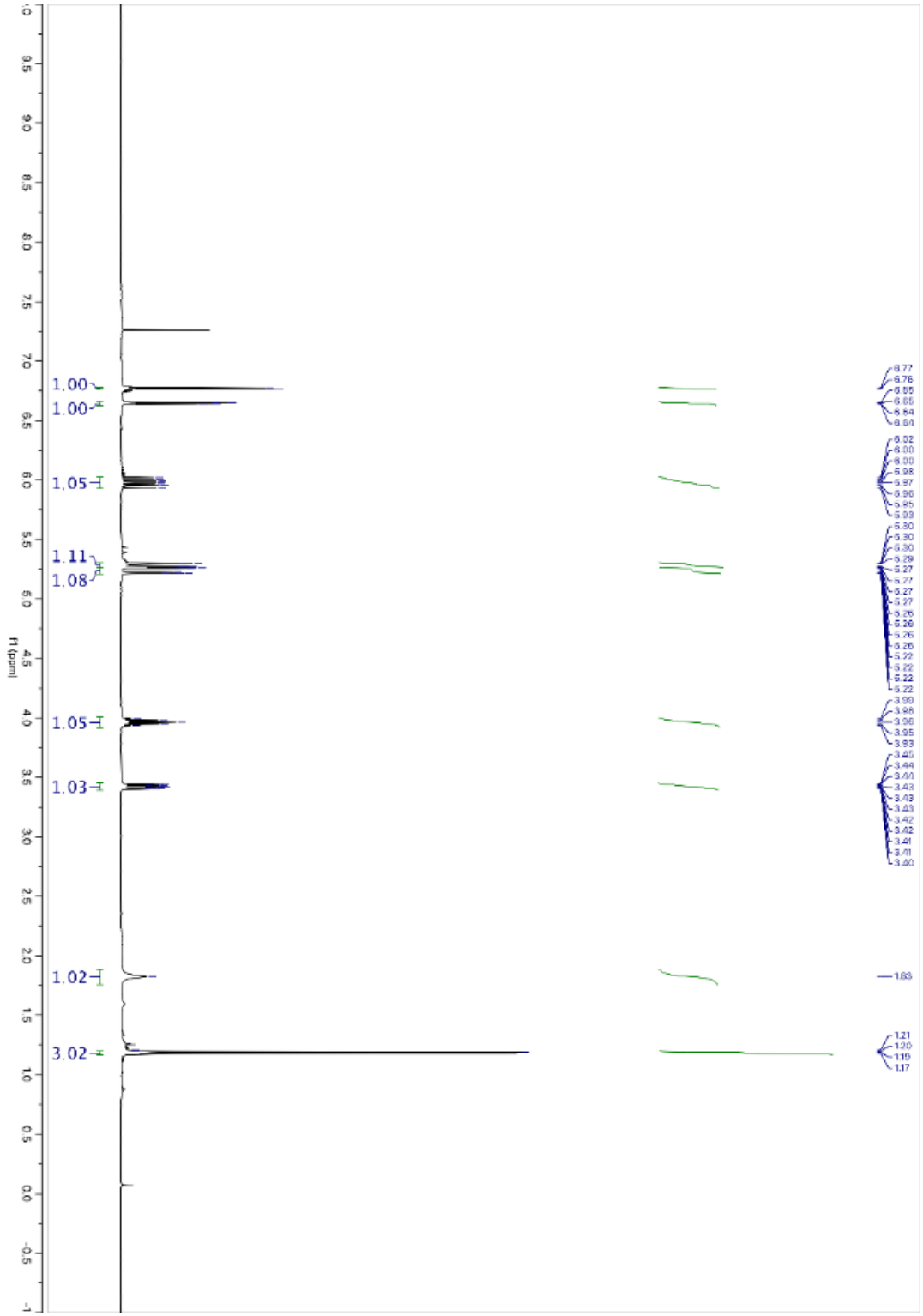
^{13}C NMR (126 MHz, $CDCl_3$) δ = 143.2, 136.6, 128.5, 125.9, 124.1, 119.1, 70.6, 53.9, 20.7.

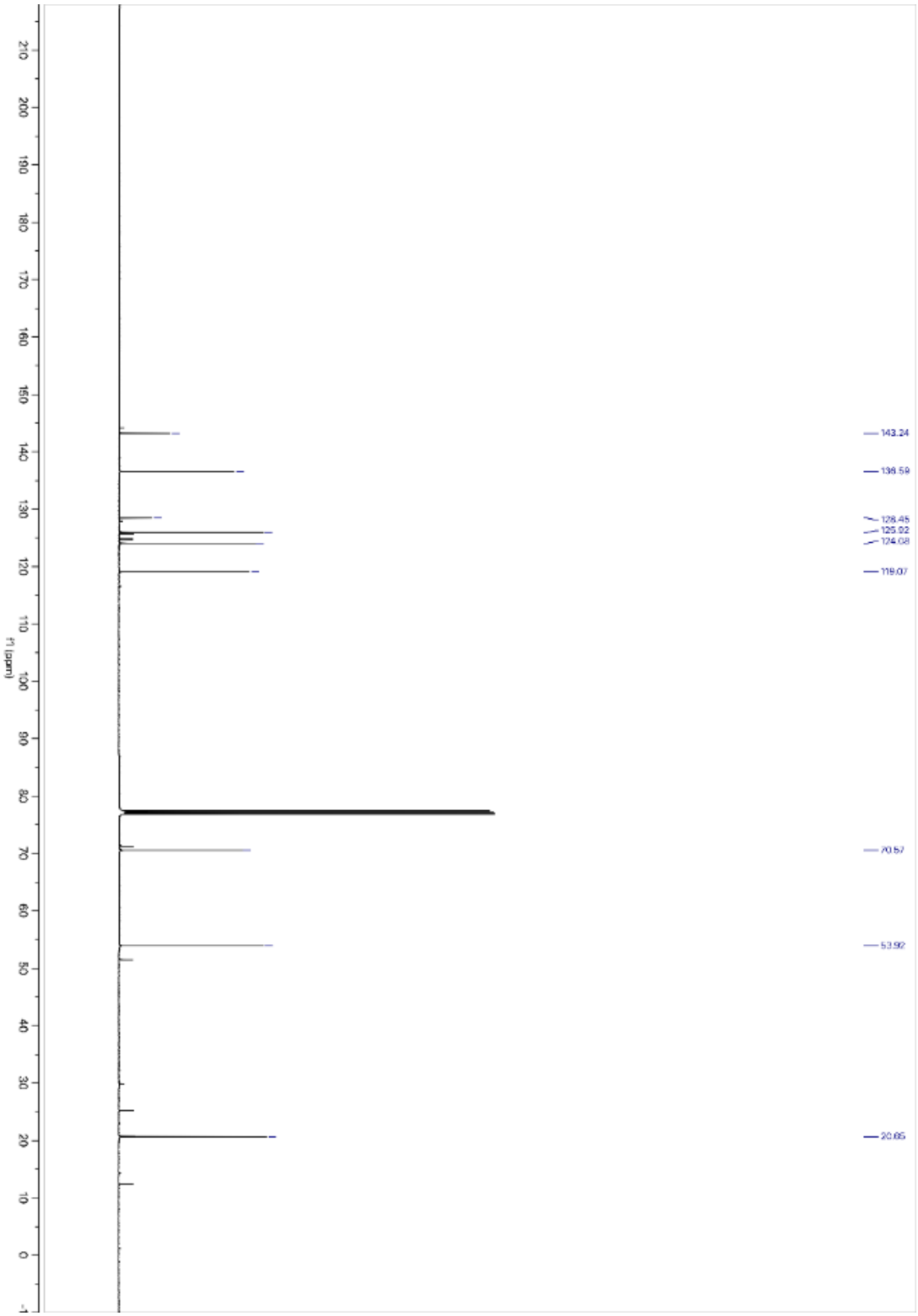
HRMS (ESI): Calculated for $C_9H_{11}ClOS$ [M+Ag^+] = 308.9265, Found 308.9270.

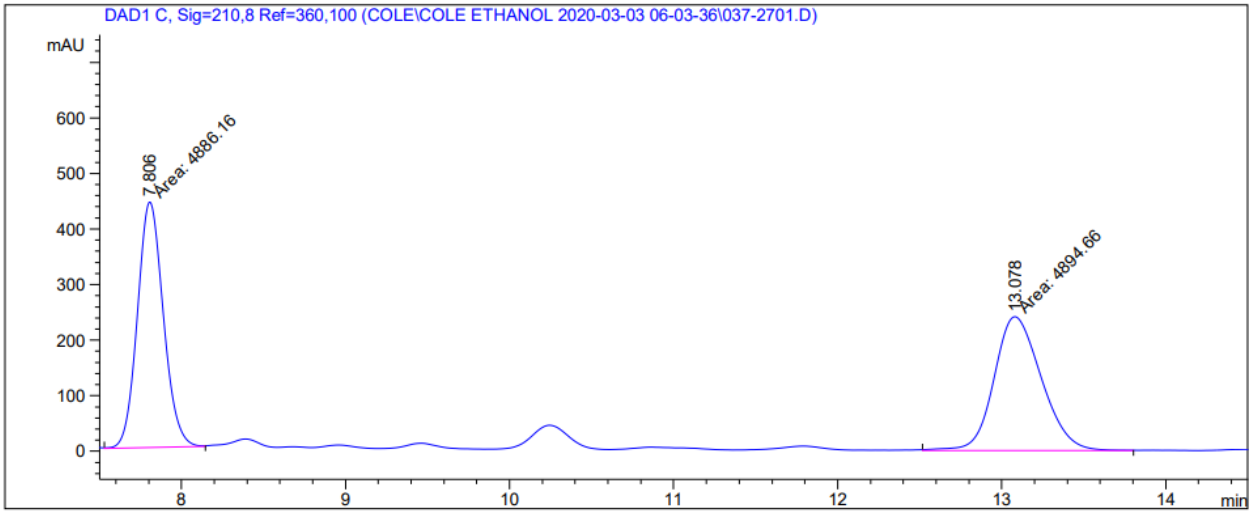
FTIR (neat): 3382, 2976, 1638, 1539, 1450, 1374, 1259, 1215, 1111, 1059, 1015, 989, 922, 792 cm^{-1}.

$[\alpha]_D^{28}$= -18.4 (*c* 0.27, $CHCl_3$).

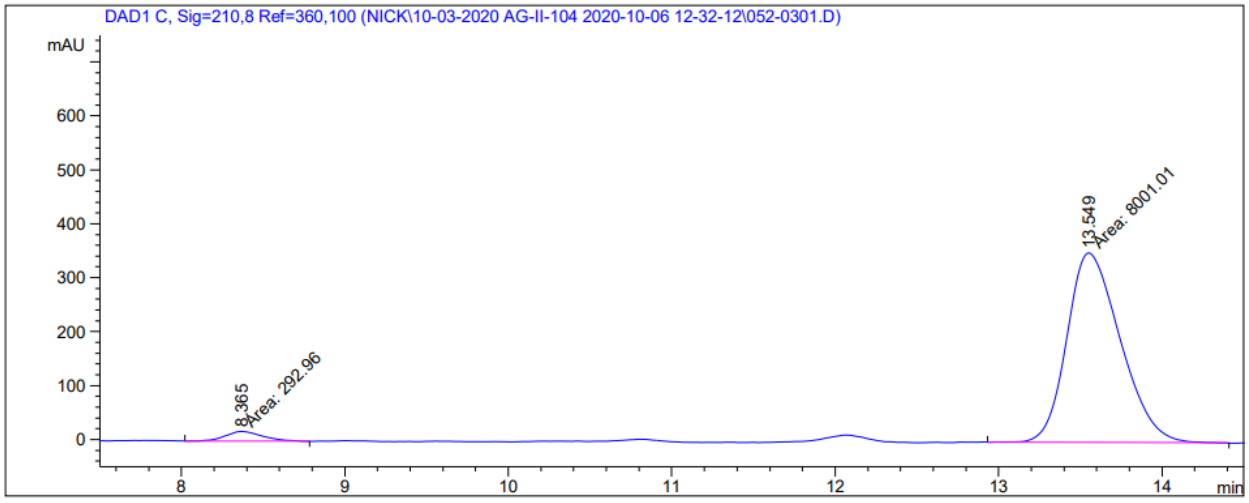
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), *ee* = 92%.


1.00
1.00
1.05
1.11
1.08
1.05
1.03
1.02
3.02
f1 (ppm)


f1 (ppm)
143.24
136.59
128.45
125.02
124.08
119.07
70.57
53.92
20.65

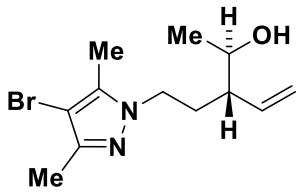


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.806	MM	0.1838	4886.16406	443.02209	49.9566
2	13.078	MM	0.3375	4894.65820	241.69791	50.0434



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.365	MM	0.2686	292.95981	18.17530	3.5322
2	13.549	MM	0.3791	8001.00928	351.72815	96.4678

(2R,3S)-3-(2-(4-bromo-3,5-dimethyl-1H-pyrazol-1-yl)ethyl)pent-4-en-2-ol (2e)



Procedures

(0.200 mmol scale) Allyl acetate **1e** (60.2 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*S*)-Ir-IV** (10.0 mg, 0.0100 mmol) and acetone as solvent (0.2 mL, 1.0M, 60 °C, 24 hr). The title compound was obtained in 70% yield (40.2 mg, 0.142 mmol, 5:1 dr) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–1:1).

(1.00 mmol scale) Allyl acetate **1e** (301.2 mg, 1.00 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*S*)-Ir-IV** (10.0 mg, 0.0100 mmol) and acetone as solvent (1.0 mL, 1.0M, 60 °C, 24 hr). The title compound was obtained in 68% yield (195 mg, 0.679 mmol, 5:1 dr) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–1:1).

TLC (SiO_2) R_f = 0.22 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.67 (ddd, *J* = 17.2, 10.4, 9.1 Hz, 1H), 5.26 (dd, *J* = 10.3, 1.8 Hz, 1H), 5.15 (dd, *J* = 17.3, 1.8 Hz, 1H), 4.01 (ddd, *J* = 14.3, 9.1, 5.3 Hz, 1H), 3.91 (ddd, *J* = 14.0, 8.9, 6.8 Hz, 1H), 3.69 (h, *J* = 6.1 Hz, 1H), 2.20 (s, 3H), 2.19 (s, 3H), 2.10 – 2.04 (m, 1H), 2.00 (dq, *J* = 9.4, 4.5 Hz, 1H), 1.80 (s, 1H), 1.78 – 1.68 (m, 1H), 1.16 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 146.0, 137.8, 136.9, 119.3, 93.9, 69.8, 49.4, 48.2, 31.0, 20.6, 12.4, 10.5.

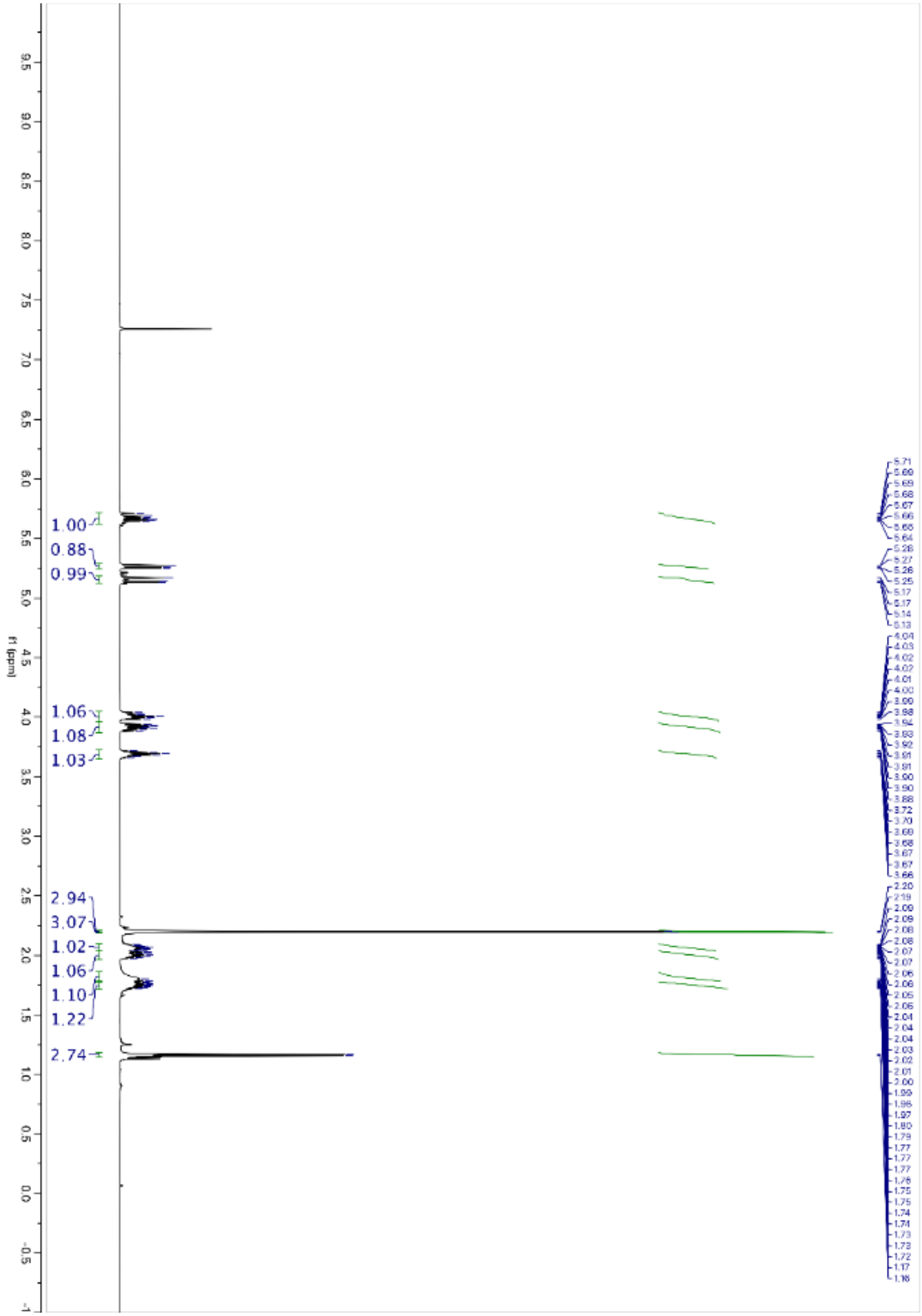
HRMS (ESI): Calculated for $C_{12}H_{19}BrN_2O$ [M+H$^+$] = 287.0754, Found 287.0754.

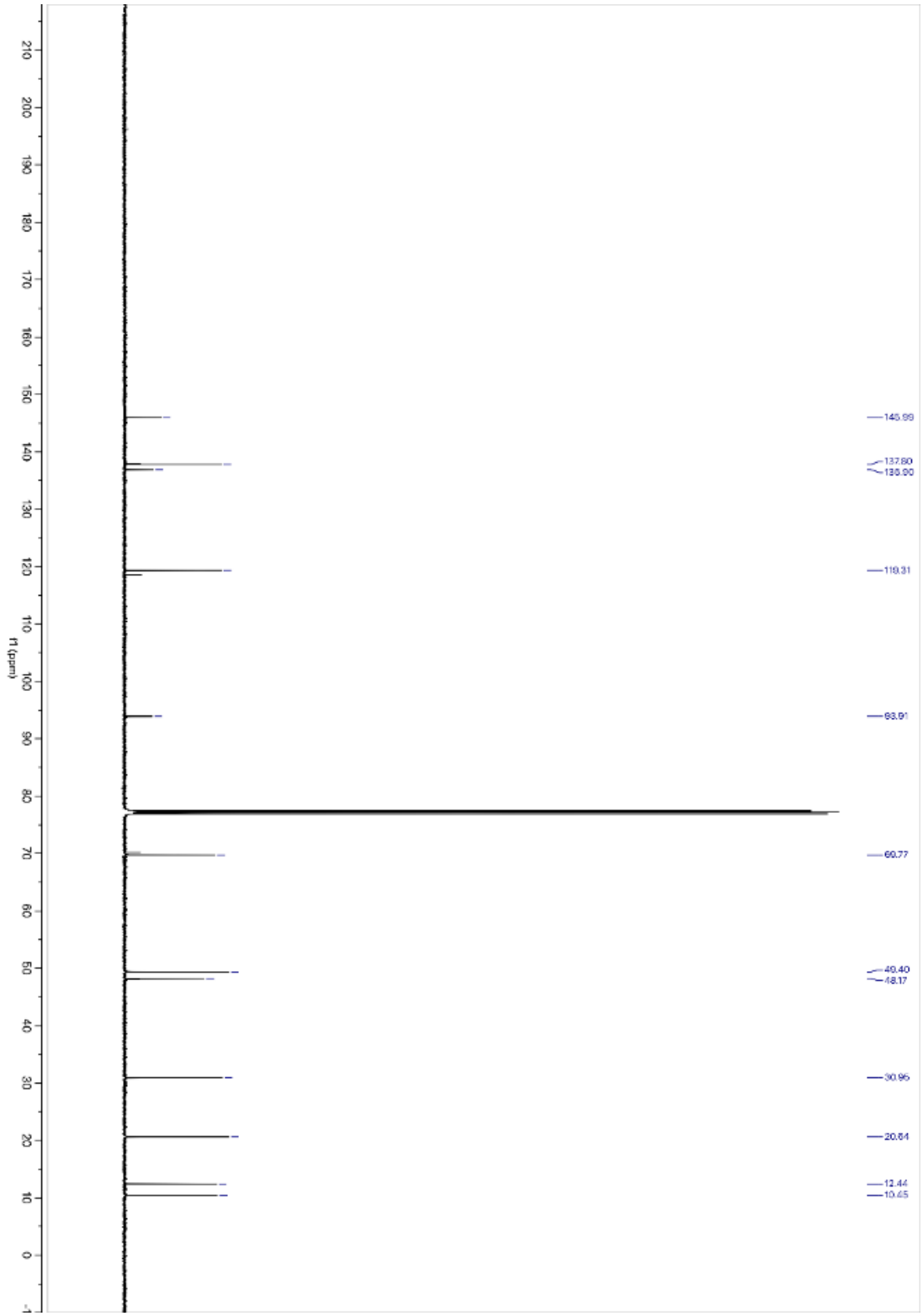
FTIR (neat): 3361, 2969, 2925, 2975, 1740, 1639, 1546, 1475, 1422, 1377, 1315, 1261, 1207, 1130, 1071, 1000, 918, 887, 865, 814, 768, 669 cm^{-1}.

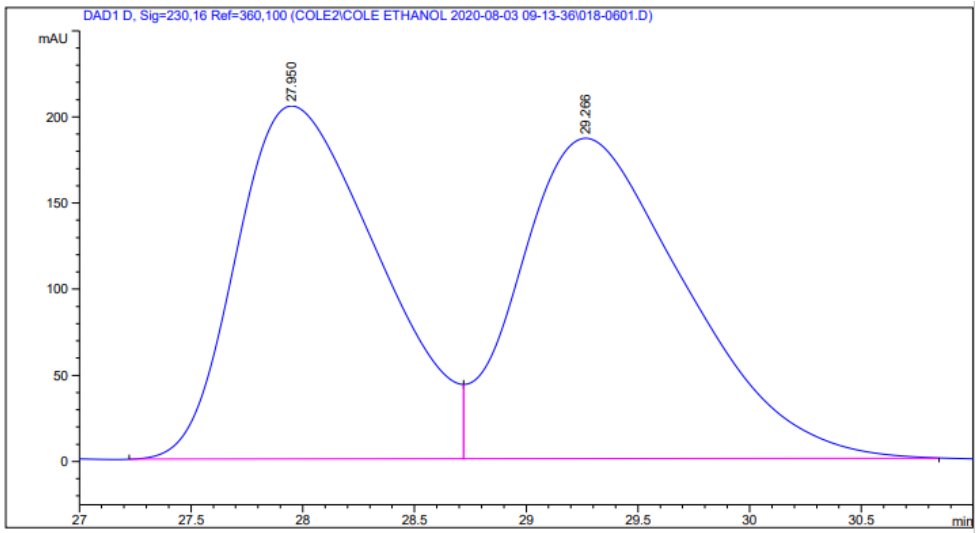
$[\alpha]_D^{28}$= -8.8 (*c* 0.17, $CHCl_3$).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 230 nm), *ee* = 95%.

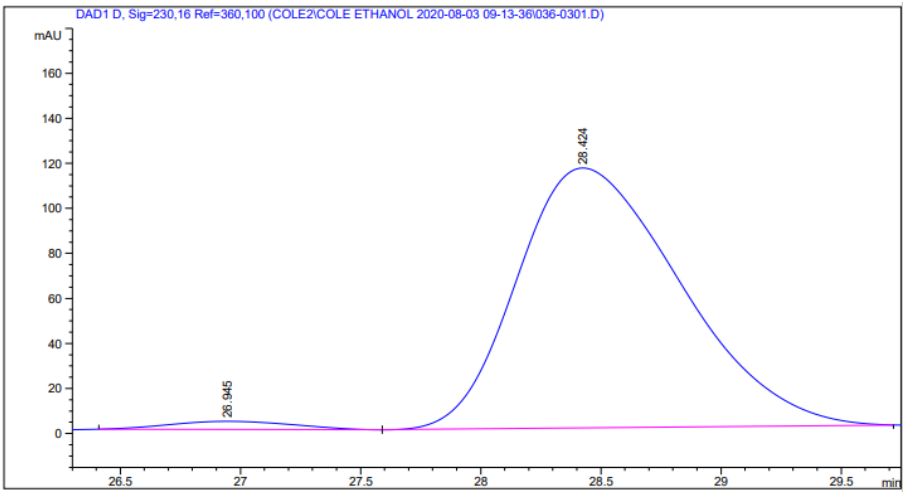
MP: 64-66 °C


1.00
0.88
0.99
1.06
1.08
1.03
2.94
3.07
1.02
1.06
1.10
1.22
2.74
f1 (ppm)


f1 (ppm)
145.99
137.80
135.90
119.31
93.91
69.77
49.40
48.17
30.95
20.84
12.44
10.45

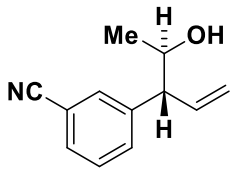


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.950	BV	0.7037	9095.23340	204.95828	48.4645
2	29.266	VB	0.7824	9671.54395	186.08044	51.5355



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.945	BV	0.5130	131.67259	3.66655	2.3500
2	28.424	VB	0.7464	5471.37158	115.54547	97.6500

3-((3R,4R)-4-hydroxypent-1-en-3-yl)benzonitrile (2f)



Procedure

Allyl acetate **1f** (40.2 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 ºC, 36 hr). The title compound was obtained in 85% yield (31.8 mg, 0.142 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.30 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.54 (d, *J* = 7.0 Hz, 1H), 7.52 (s, 1H), 7.47 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.45 – 7.40 (m, 1H), 6.08 (ddd, *J* = 17.0, 10.3, 8.8 Hz, 1H), 5.30 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.23 (dt, *J* = 17.1, 1.3 Hz, 1H), 4.00 (p, *J* = 6.4 Hz, 1H), 3.28 – 3.18 (m, 1H), 1.84 (s, 1H), 1.10 (d, *J* = 6.2 Hz, 3H).

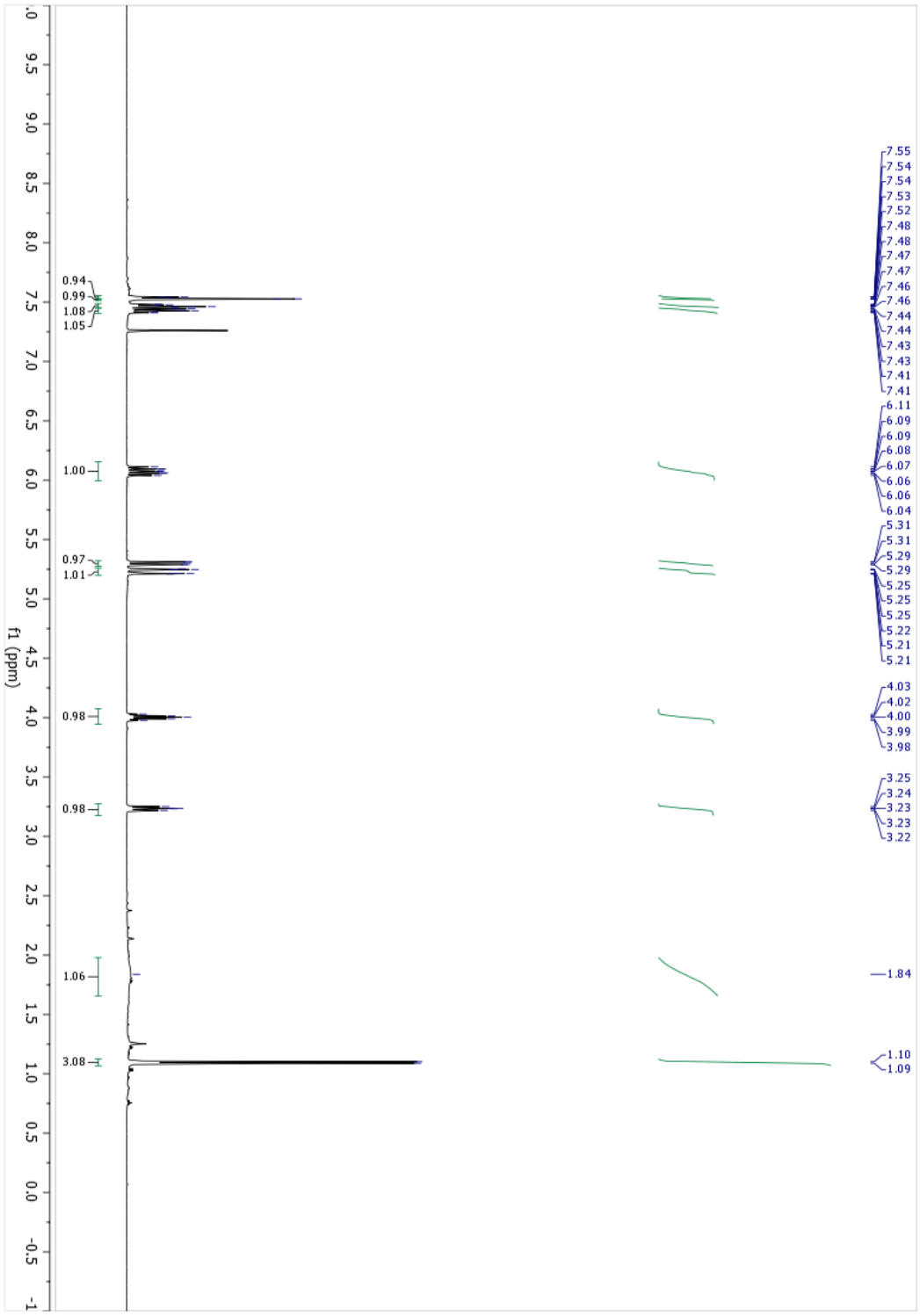
^{13}C NMR (126 MHz, $CDCl_3$) δ = 143.4, 137.1, 132.9, 131.9, 130.6, 129.6, 119.3, 119.0, 112.9, 70.1, 58.3, 21.1.

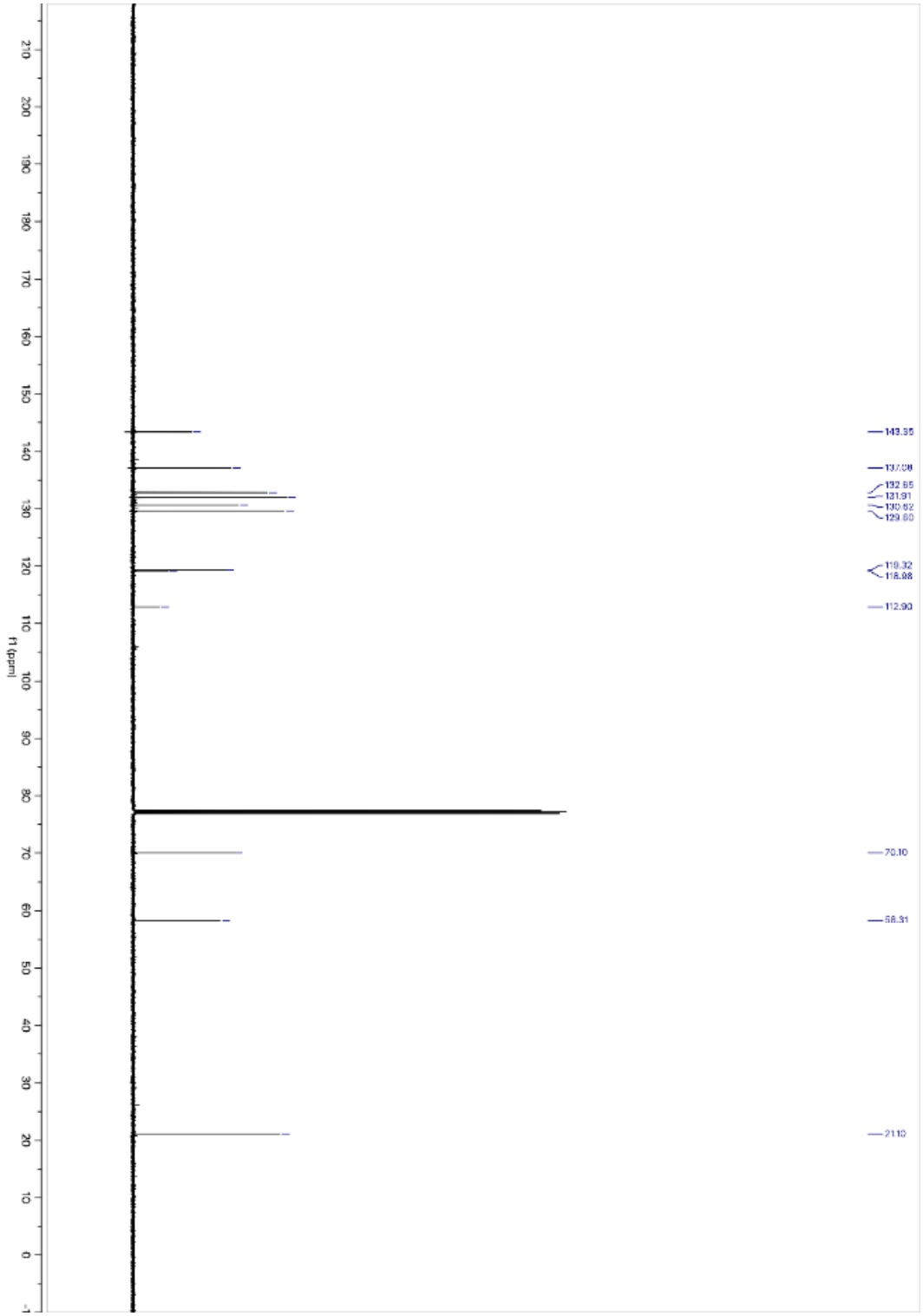
HRMS (ESI): Calculated for $C_{12}H_{13}NO$ [M+Na^+] = 210.0889, Found 210.0884.

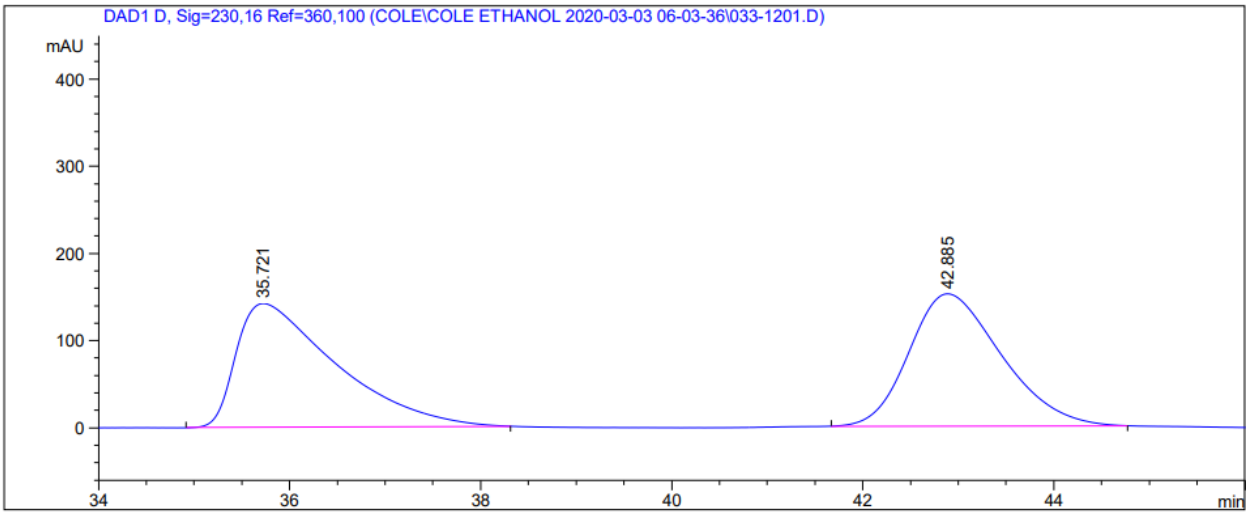
FTIR (neat): 3423, 3078, 2973, 2926, 2229, 2017, 1638, 1599, 1581, 1482, 1454, 1432, 1516, 1375, 1263, 1111, 1073, 998, 972, 921, 797, 752, 737, 697, 673 cm^{-1}.

$[\alpha]_D^{28}$= -47.4 (*c* 0.36, $CHCl_3$).

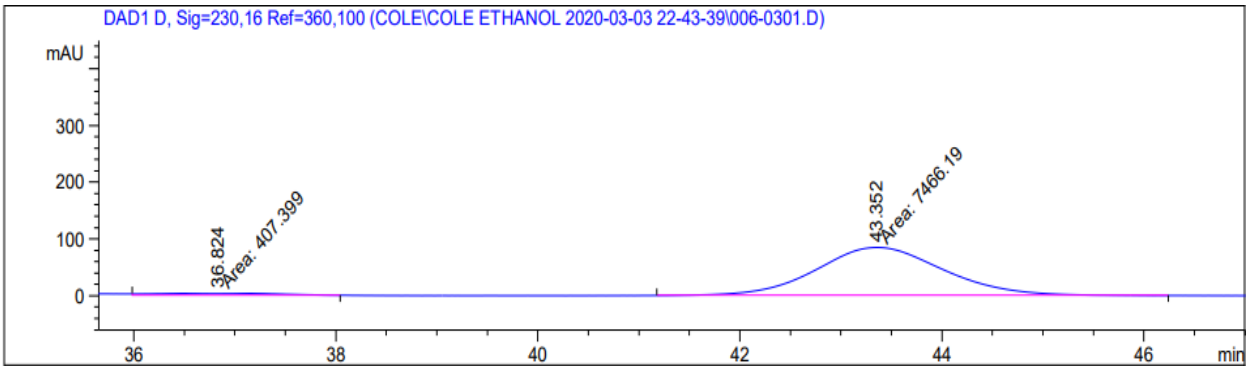
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 230 nm), *ee* = 90%.


f1 (ppm)
0.94
0.99
1.08
1.05
1.00
0.97
1.01
0.98
0.98
1.06
3.08
7.55
7.54
7.54
7.53
7.52
7.48
7.48
7.47
7.47
7.46
7.46
7.44
7.44
7.43
7.43
7.41
7.41
6.11
6.09
6.09
6.08
6.07
6.06
6.06
6.04
5.31
5.31
5.29
5.29
5.25
5.25
5.25
5.22
5.21
5.21
4.03
4.02
4.00
3.99
3.98
3.25
3.24
3.23
3.23
3.22
1.84
1.10
1.09


f1 (ppm)
143.55
137.09
132.65
131.91
130.62
129.60
119.32
118.98
112.93
70.10
58.31
21.10

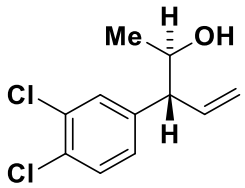


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.721	BB	1.0024	1.03449e4	142.25600	50.2116
2	42.885	BB	1.0031	1.02577e4	152.04002	49.7884



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.824	MF	1.4279	407.39920	4.75518	5.1742
2	43.352	MM	1.4685	7466.19434	84.73927	94.8258

(2*R*,3*R*)-3-(3,4-dichlorophenyl)pent-4-en-2-ol (2g)



Procedure

Allyl acetate **1g** (48.8 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 18 hr). The title compound was obtained in 79% yield (36.3 mg, 0.158 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.33 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.39 (d, *J* = 8.3 Hz, 1H), 7.31 (d, *J* = 2.1 Hz, 1H), 7.06 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.04 (ddd, *J* = 17.0, 10.2, 8.9 Hz, 1H), 5.28 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.22 (dt, *J* = 17.1, 1.2 Hz, 1H), 3.96 (p, *J* = 6.4 Hz, 1H), 3.15 (dd, *J* = 8.9, 7.2 Hz, 1H), 1.79 (s, 1H), 1.09 (d, *J* = 6.3 Hz, 3H).

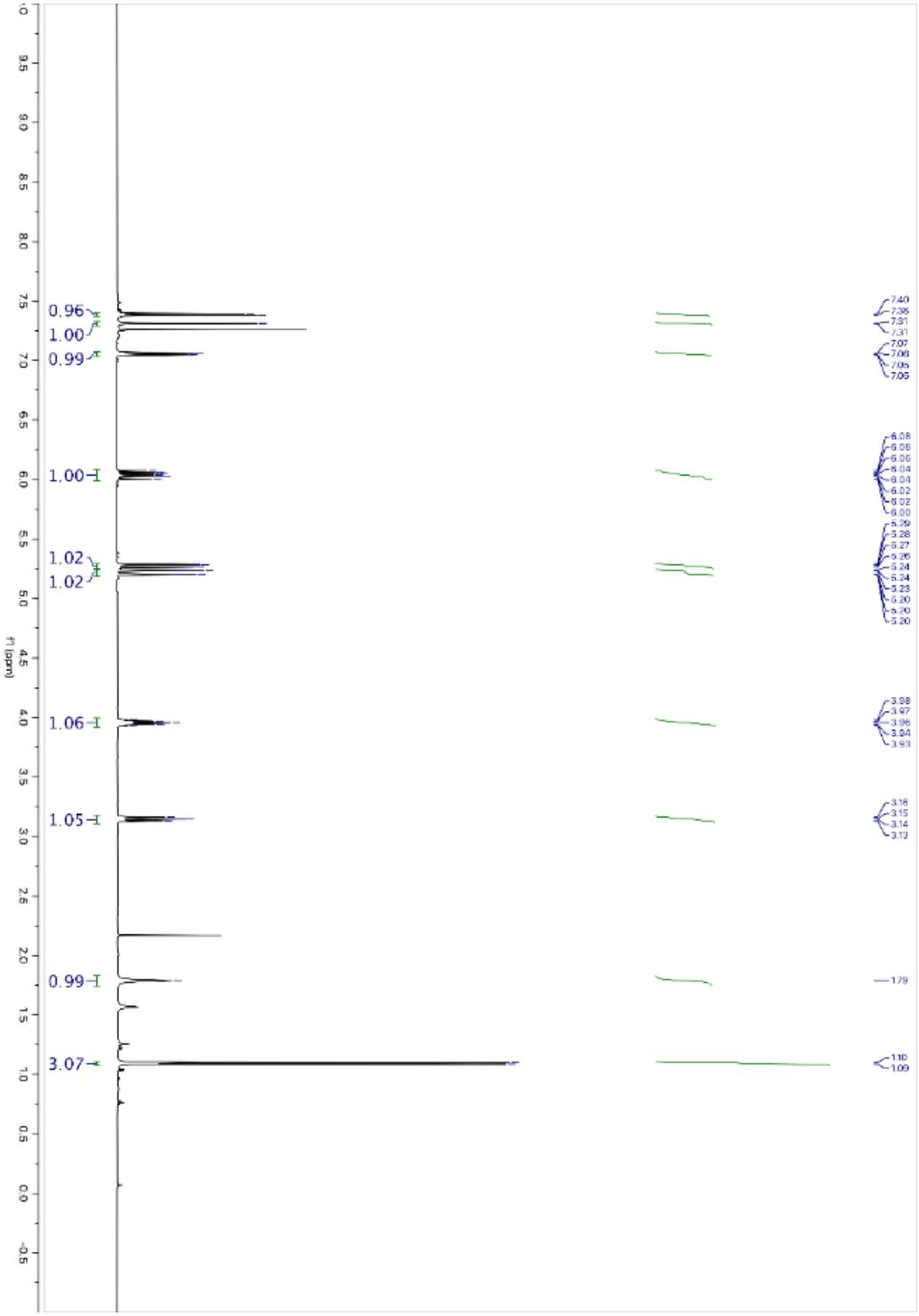
^{13}C NMR (126 MHz, $CDCl_3$) δ = 142.1, 137.4, 132.8, 130.9, 130.7, 130.2, 127.6, 119.1, 70.1, 58.1, 21.0.

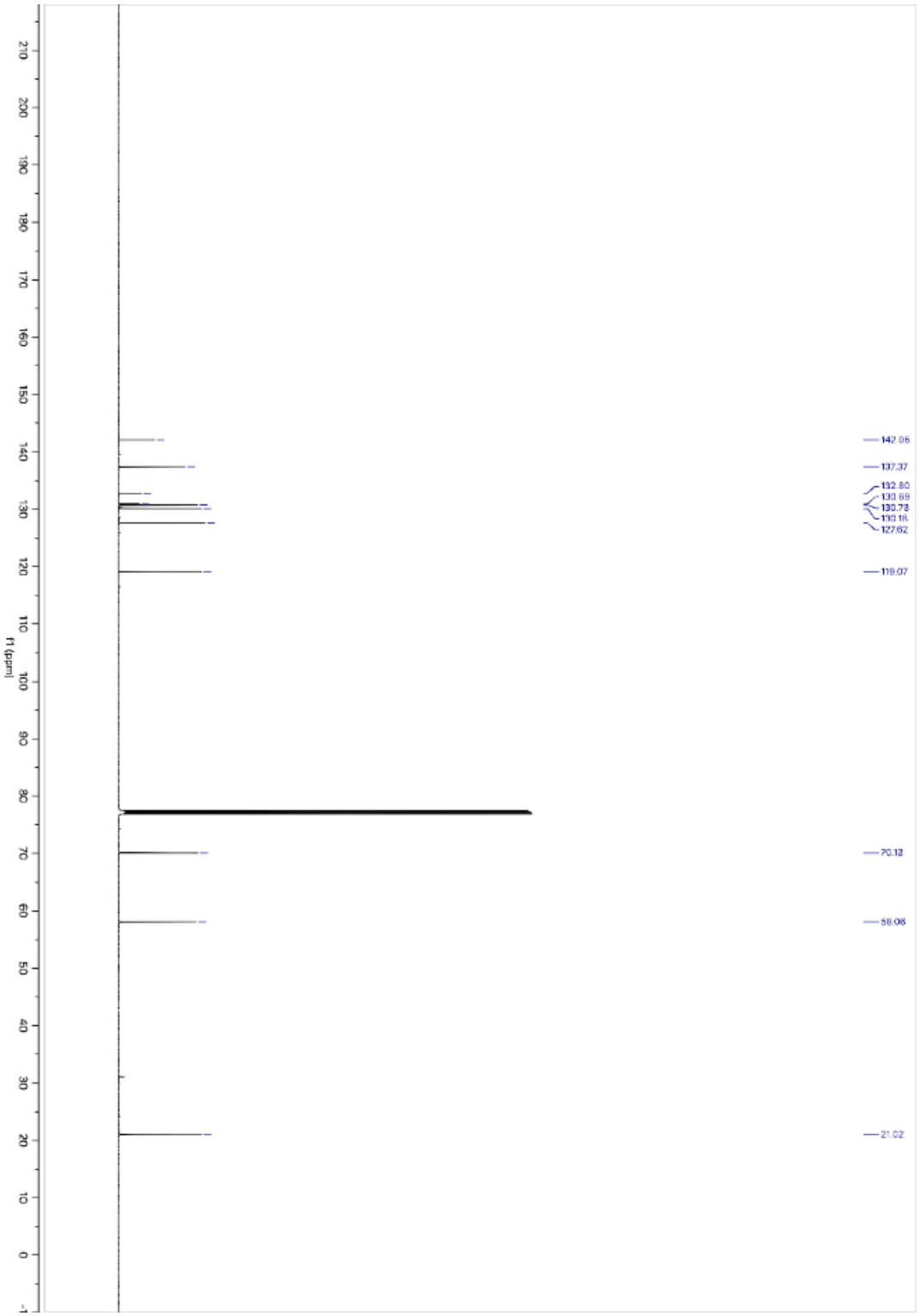
HRMS (ESI): Calculated for $C_{11}H_{12}Cl_2O$ [M+Ag^+] = 336.9311, Found 336.9304.

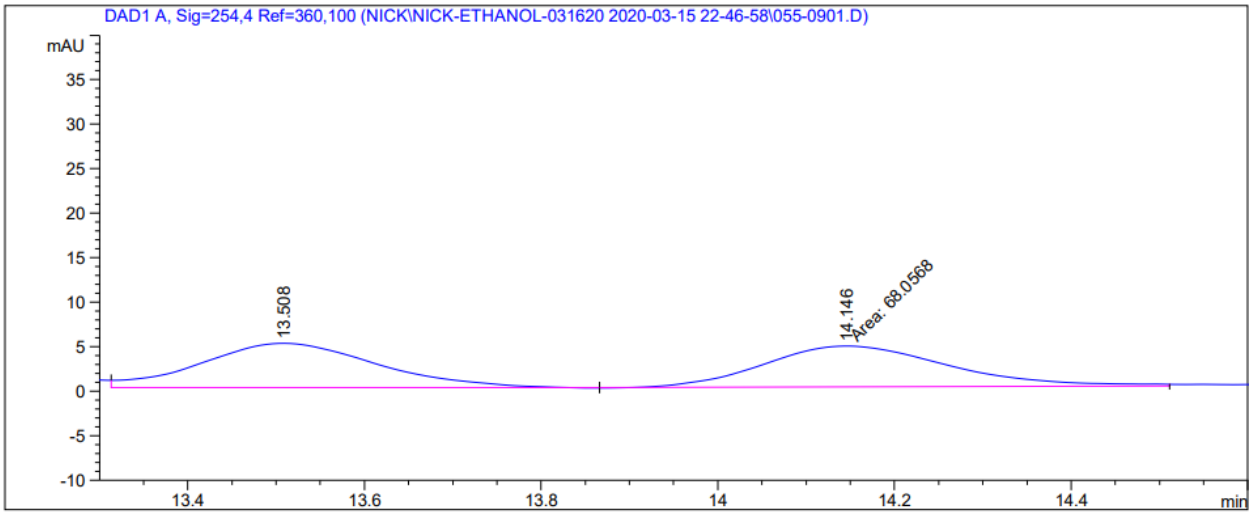
FTIR (neat): 3414, 2972, 2923, 1637, 1560, 1470, 1392, 1261, 1197, 1133, 1075, 1030, 993, 969, 922, 894, 876, 817, 747, 707 cm^{-1}.

$[\alpha]_D^{28}$= -59.3 (*c* 0.27, $CHCl_3$).

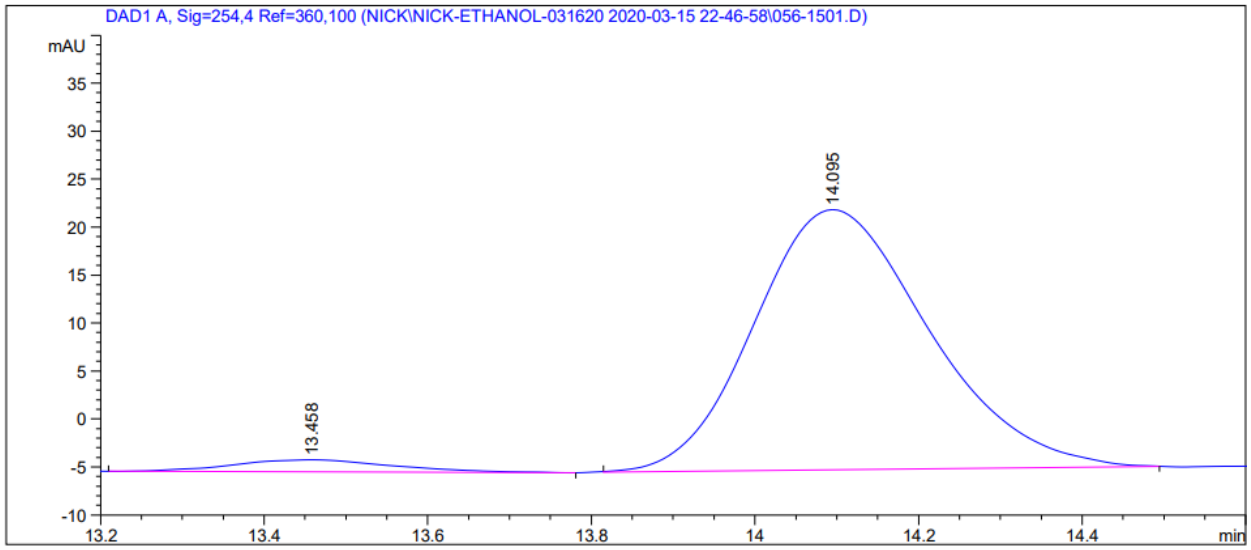
HPLC (Two Chiralcel OD-H columns in series, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 92%.


0.96
1.00
0.99
1.00
1.02
1.02
1.06
1.05
0.99
3.07
f1 (ppm)


f1 (ppm)
142.06
137.37
132.80
130.99
130.73
130.16
127.62
119.07
70.13
58.06
21.02

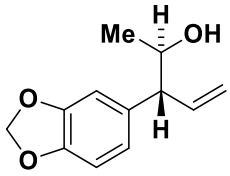


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.508	VV	0.2125	69.88653	5.01749	50.6632
2	14.146	MF	0.2449	68.05678	4.63163	49.3368



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.458	BB	0.1813	17.31525	1.26805	4.1096
2	14.095	BB	0.2315	404.01782	27.16272	95.8904

(2R,3R)-3-(benzo[d][1,3]dioxol-5-yl)pent-4-en-2-ol (2h)



Procedure

Allyl acetate **1h** (44.0 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 80% yield (33.0 mg, 0.160 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

TLC (SiO_2) R_f = 0.33 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.76 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 1.7 Hz, 1H), 6.65 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.05 (ddd, *J* = 16.9, 10.4, 9.0 Hz, 1H), 5.93 (s, 2H), 5.23 (dd, *J* = 3.5, 1.3 Hz, 1H), 5.21 – 5.18 (m, 1H), 3.91 (dq, *J* = 7.7, 6.2 Hz, 1H), 3.09 (t, *J* = 8.3 Hz, 1H), 1.87 (s, 1H), 1.08 (d, *J* = 6.2 Hz, 3H).

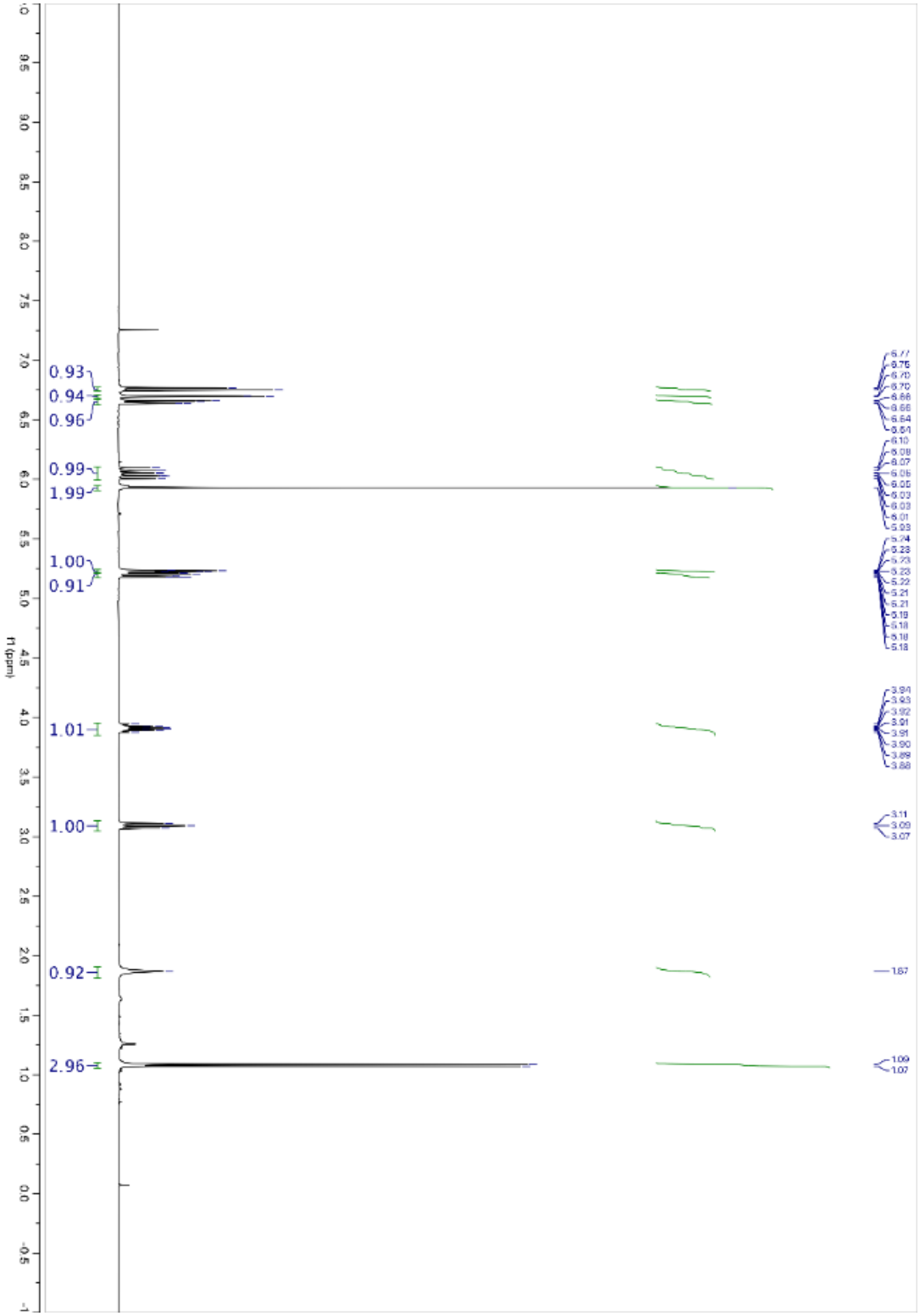
^{13}C NMR (101 MHz, $CDCl_3$) δ = 148.0, 146.4, 138.7, 135.5, 121.2, 118.0, 108.6, 108.4, 101.1, 70.4, 58.8, 20.8.

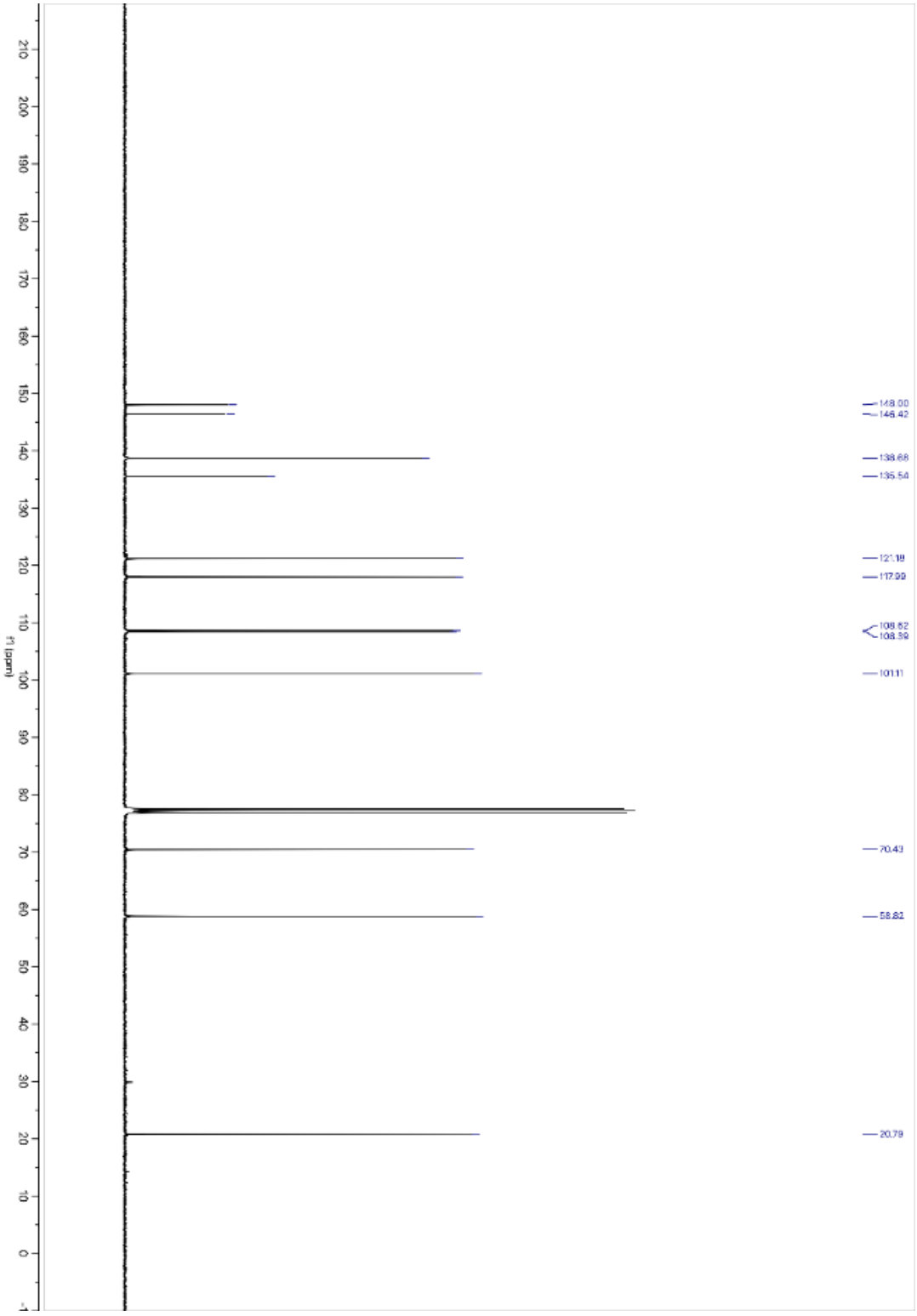
HRMS (ESI): Calculated for $C_{11}H_{11}NO$ [M+Na^+] = 312.9988, Found 312.9982.

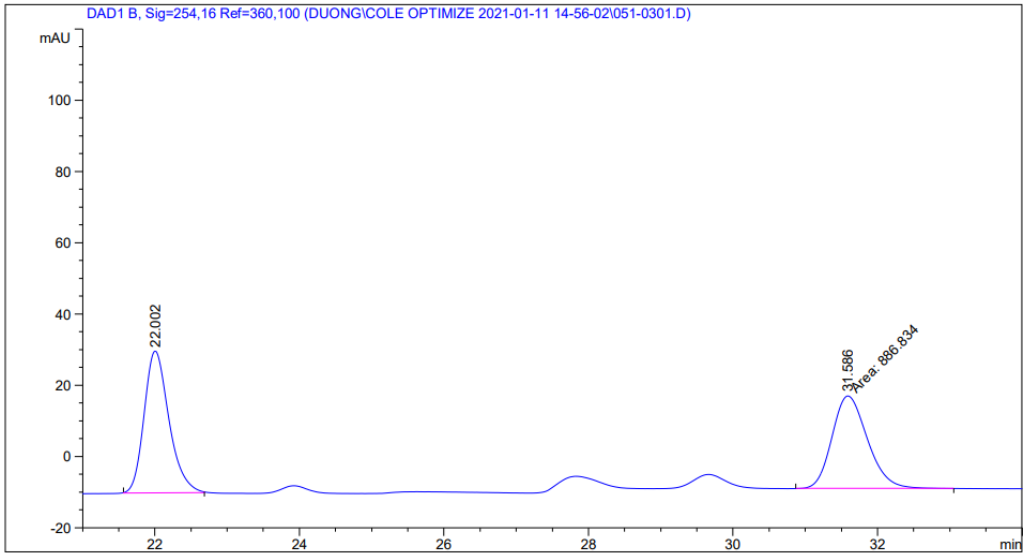
FTIR (neat): 3395, 2972, 2893, 1503, 1485, 1440, 1242, 1152, 1096, 1073, 1037, 929, 806 cm^{-1}.

$[\alpha]_D^{28}$= -39.5 (*c* 0.27, $CHCl_3$).

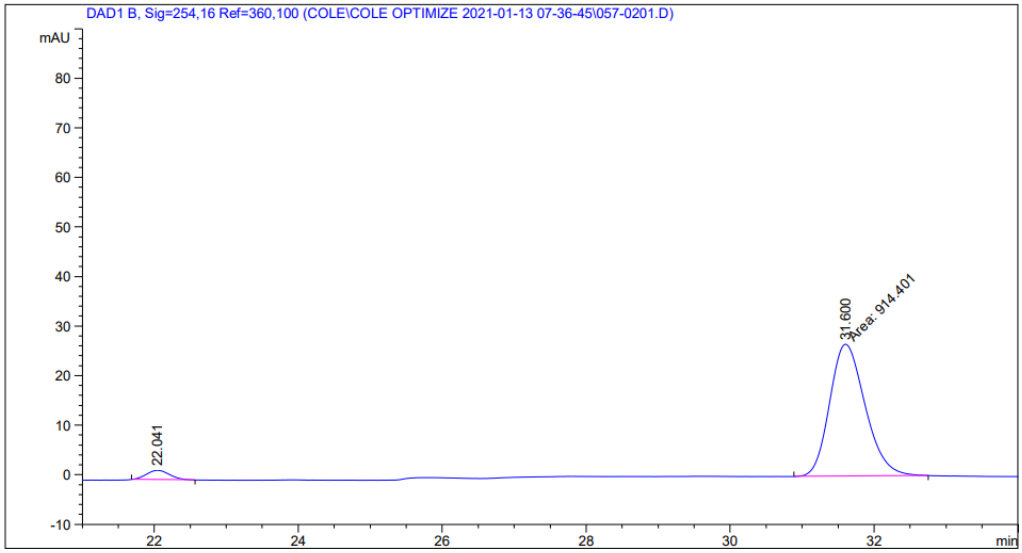
HPLC (Chiralcel AD-H column in series with a Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 91%.


0.93
0.94
0.96
0.99
1.99
1.00
0.91
1.01
1.00
0.92
2.96
f1 (ppm)


148.00
146.42
138.66
135.54
121.19
117.99
108.62
108.39
101.11
70.43
58.82
20.79
f1 (ppm)

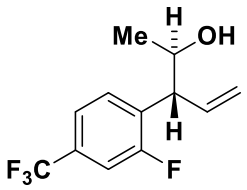


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.002	BB	0.3653	955.88153	39.92601	51.8735
2	31.586	MM	0.5687	886.83362	25.98886	48.1265



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.041	BB	0.2797	42.78994	1.90776	4.4704
2	31.600	MM	0.5723	914.40088	26.63142	95.5296

(2R,3R)-3-(2-fluoro-4-(trifluoromethyl)phenyl)pent-4-en-2-ol (2i)



Procedure

Allyl acetate **1i** (52.4 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 16 hr). The title compound was obtained in 71% yield (35.4 mg, 0.142 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.24 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.43 – 7.36 (m, 2H), 7.36 – 7.28 (m, 1H), 6.13 (dddd, *J* = 17.1, 10.3, 8.9, 1.4 Hz, 1H), 5.30 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.27 (dt, *J* = 17.1, 1.0 Hz, 1H), 4.07 (p, *J* = 6.4 Hz, 1H), 3.57 (t, *J* = 8.2 Hz, 1H), 1.84 (s, 1H), 1.12 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 161.2, 159.2, 136.2, 133.1 (d, *J* = 14.8 Hz), 130.8 (dd, *J* = 33.4, 8.3 Hz), 130.4 (d, *J* = 5.3 Hz), 121.4 (p, *J* = 3.8 Hz), 119.8, 113.4 (dq, *J* = 26.5, 3.9 Hz), 69.4 (d, *J* = 2.1 Hz), 52.2, 21.1.

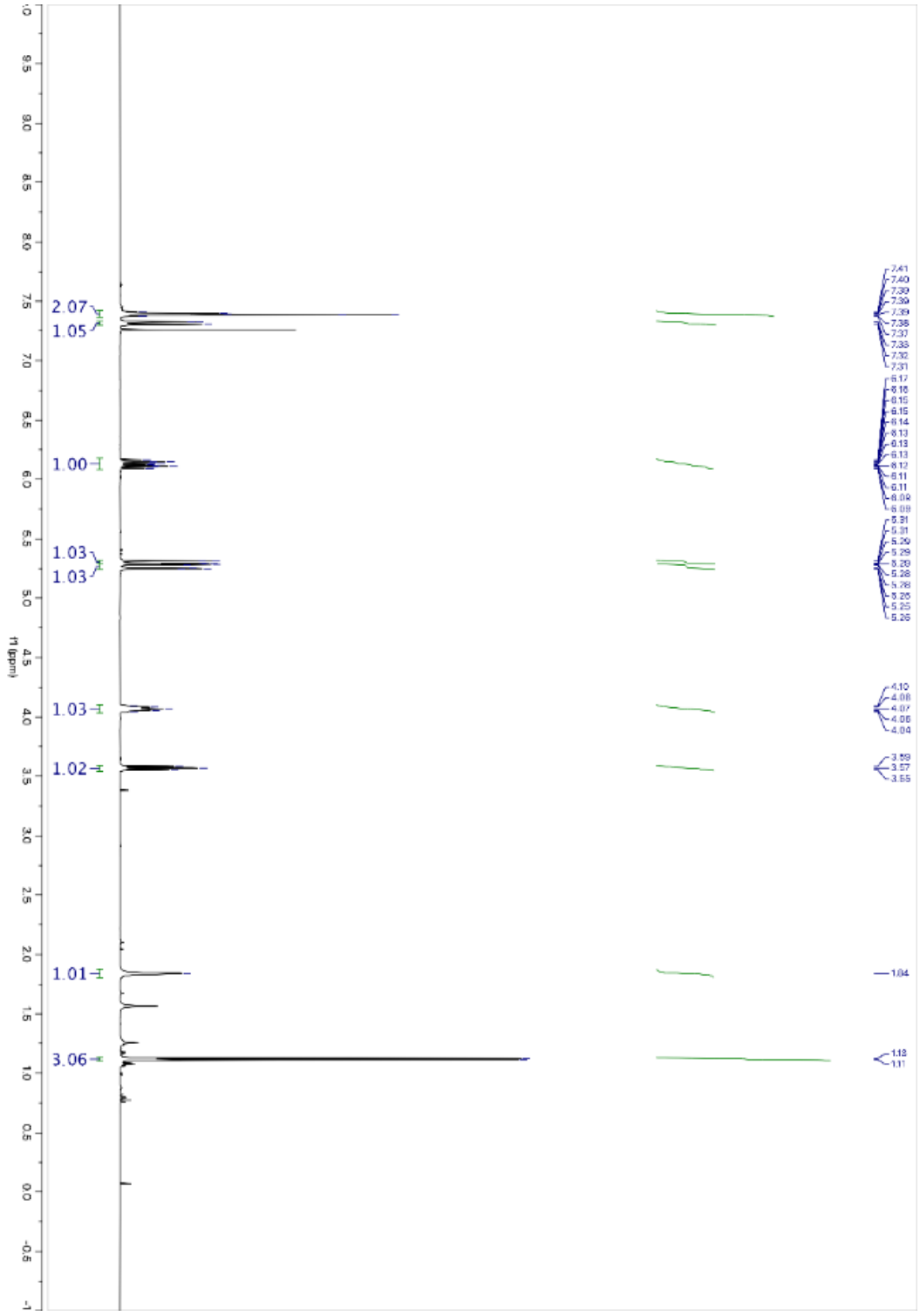
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.7, -114.8 (dd, *J* = 10.5, 4.8 Hz).

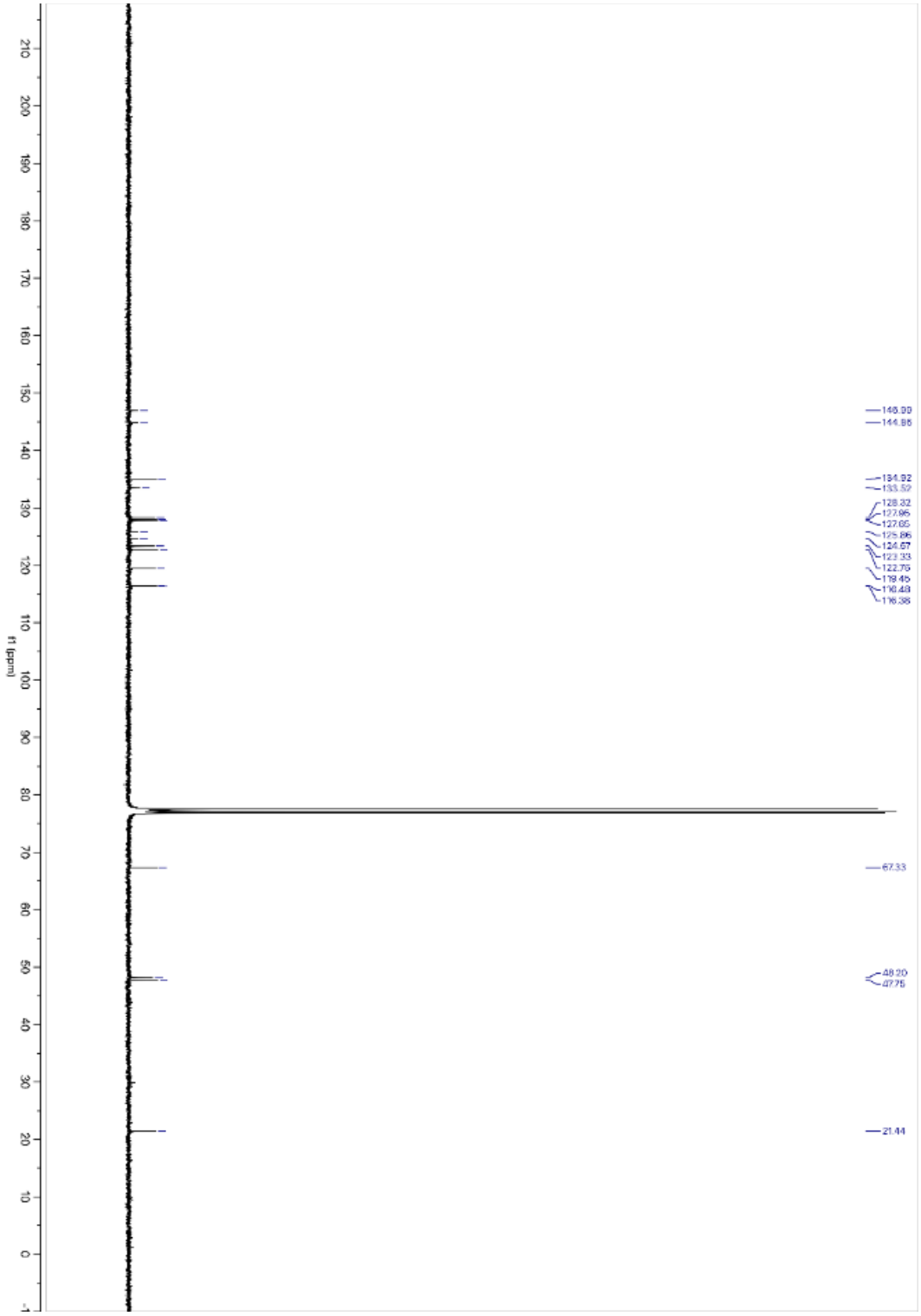
HRMS (ESI): Calculated for $C_{12}H_{12}F_4O$ [M+Ag^+] = 354.9870, Found 354.9866.

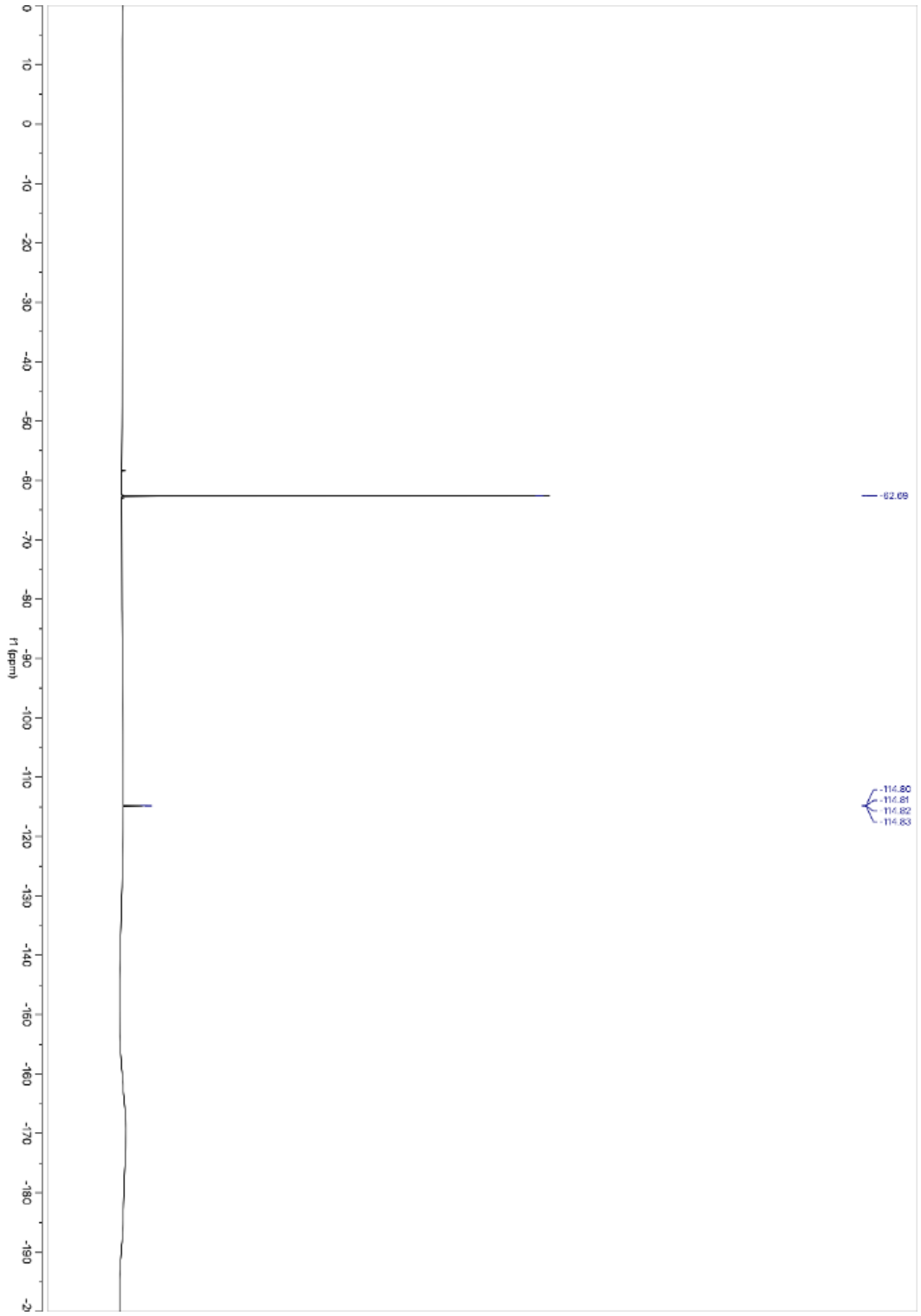
FTIR (neat): 3387, 2978, 1584, 1510, 1429, 1329, 1277, 1217, 1168, 1124, 1067, 994, 970, 923, 904, 879, 830, 744 cm^{-1}.

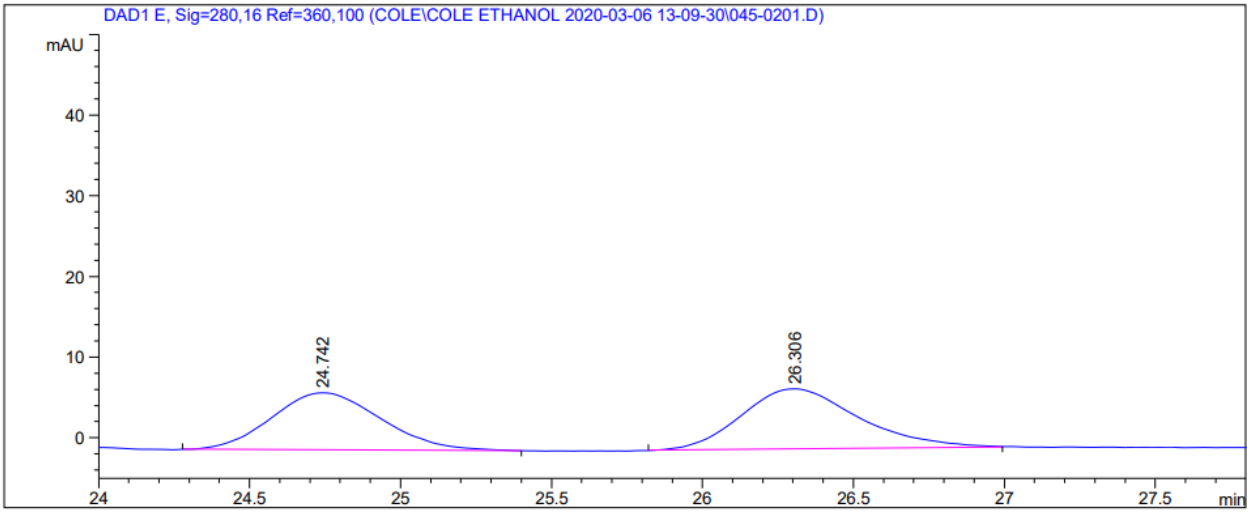
$[\alpha]_D^{28}$= -47 (*c* 0.15, $CHCl_3$).

HPLC (Two Chiralcel OD-H columns in series, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 280 nm), *ee* = 92%.

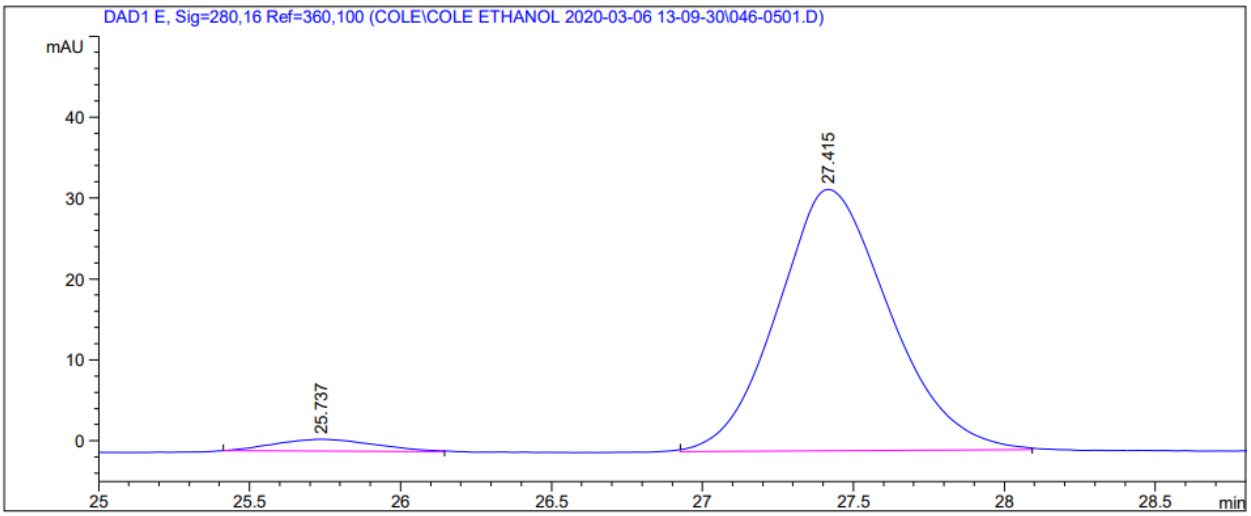

2.07
1.05
1.00
1.03
1.03
1.03
1.02
1.01
3.06
f1 (ppm)


f1 (ppm)
148.00
144.86
134.92
133.52
128.32
127.95
127.65
125.86
124.57
123.33
122.75
118.45
116.48
116.38
67.33
48.20
47.75
21.44


f1 (ppm)
-62.09
-114.80
-114.81
-114.82
-114.83

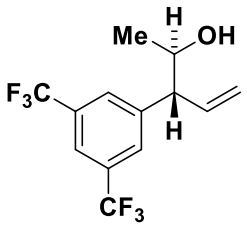


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.742	BB	0.3743	178.67825	7.08254	46.7284
2	26.306	BB	0.3996	203.69766	7.48190	53.2716



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.737	BB	0.2855	34.95705	1.50226	4.0142
2	27.415	BB	0.3797	835.86987	32.32330	95.9858

(2R,3R)-3-(3,5-bis(trifluoromethyl)phenyl)pent-4-en-2-ol (2j)



Procedure

Allyl acetate **1j** (62.4 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 18 hr). The title compound was obtained in 65% yield (39.0 mg, 0.126 mmol, >20:1 dr) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

TLC (SiO_2) R_f = 0.31 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.76 (s, 1H), 7.69 (s, 2H), 6.11 (ddd, *J* = 17.1, 10.3, 8.8 Hz, 1H), 5.34 (dd, *J* = 10.2, 1.4 Hz, 1H), 5.26 (dt, *J* = 17.0, 1.2 Hz, 1H), 4.06 (ddt, *J* = 9.5, 6.5, 3.2 Hz, 1H), 3.36 (dd, *J* = 8.8, 6.5 Hz, 1H), 1.76 (d, *J* = 3.6 Hz, 1H), 1.14 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.5, 136.4, 132.0 (q, *J* = 33.2 Hz), 128.5 (q, *J* = 3.8 Hz), 124.6, 120.9 (dt, *J* = 7.9, 3.9 Hz), 119.9, 70.0, 58.1, 21.3.

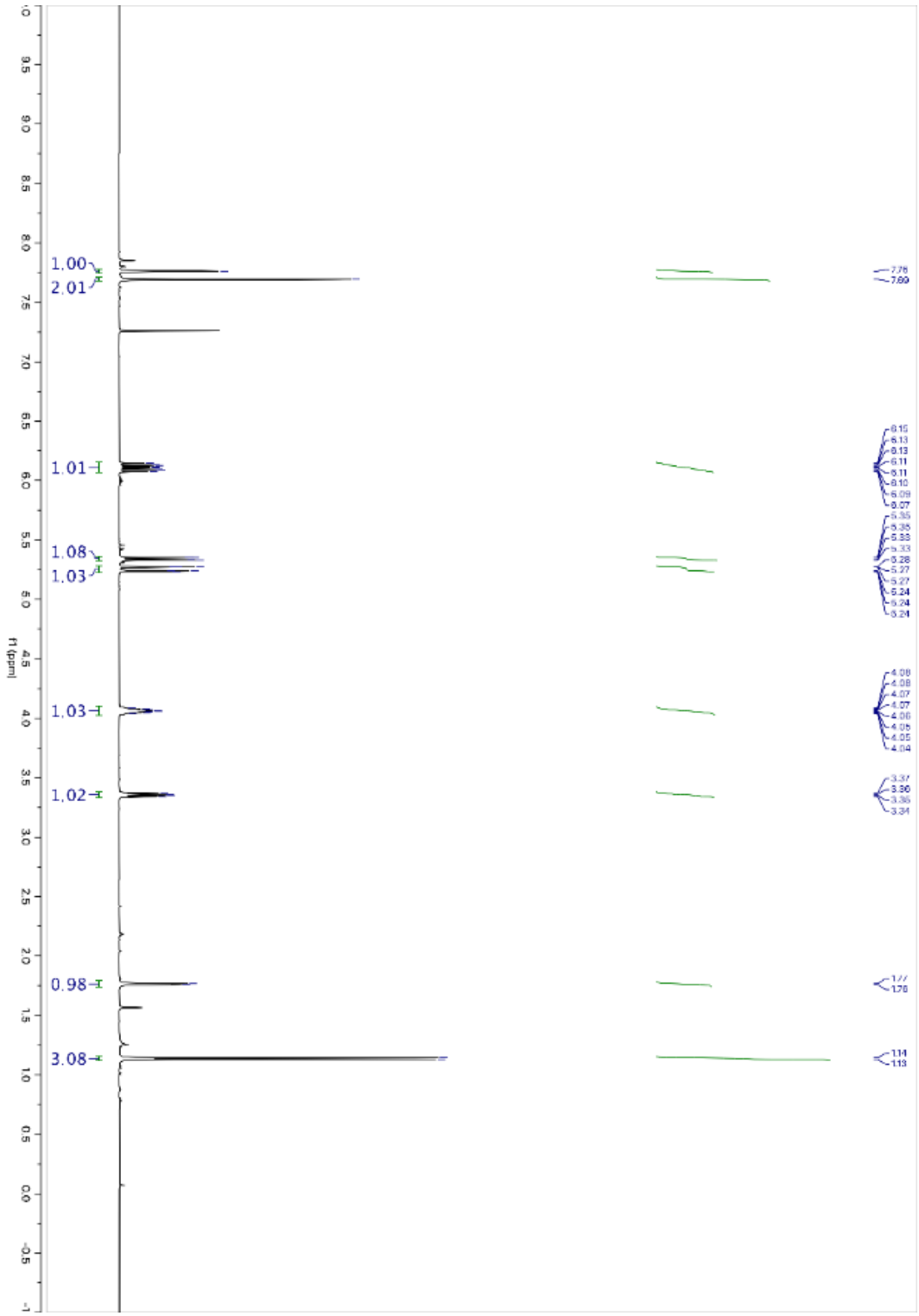
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.8.

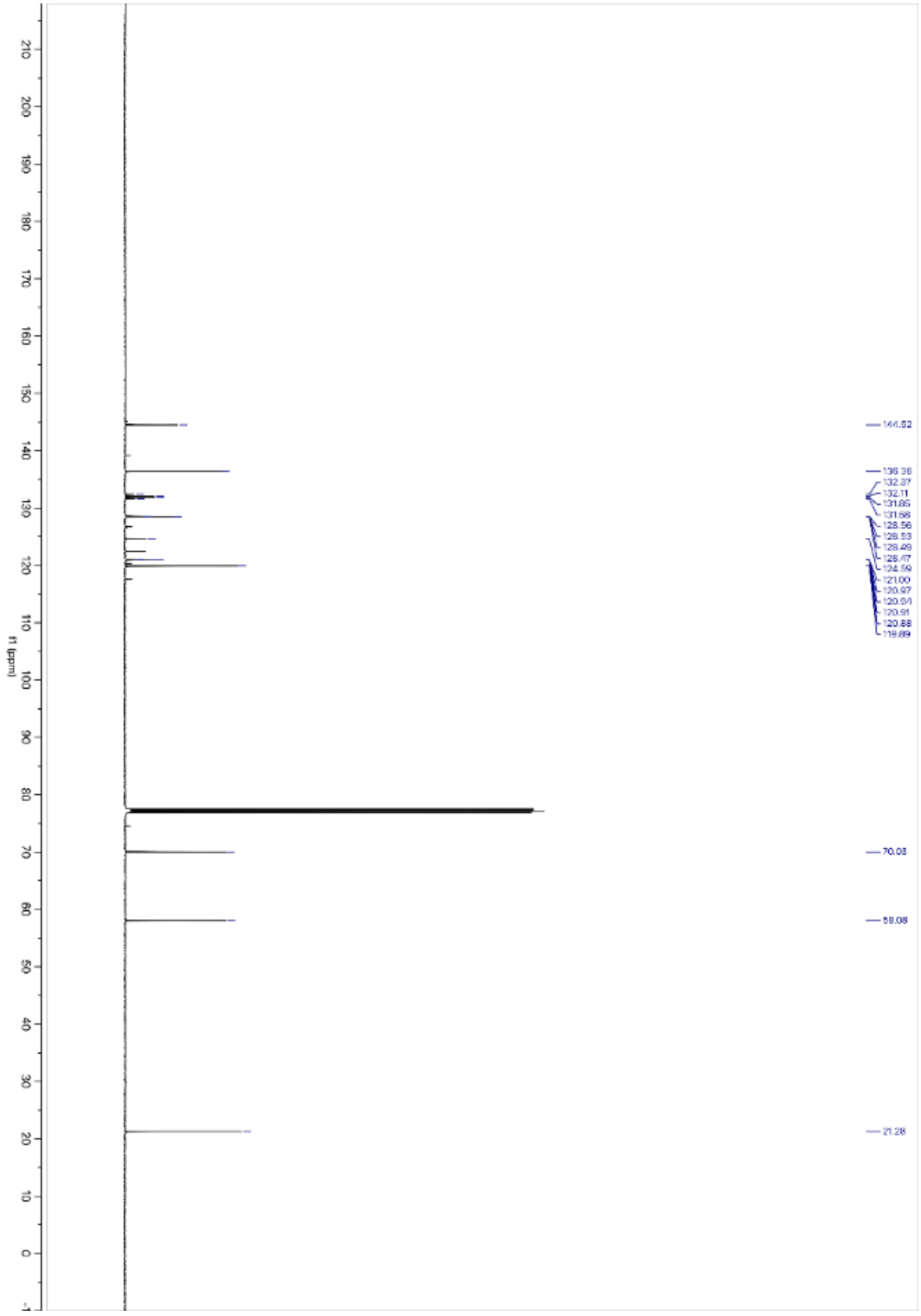
HRMS (ESI): Calculated for $C_{13}H_{12}F_6O$ [M+Ag^+] = 404.9838, Found 404.9849.

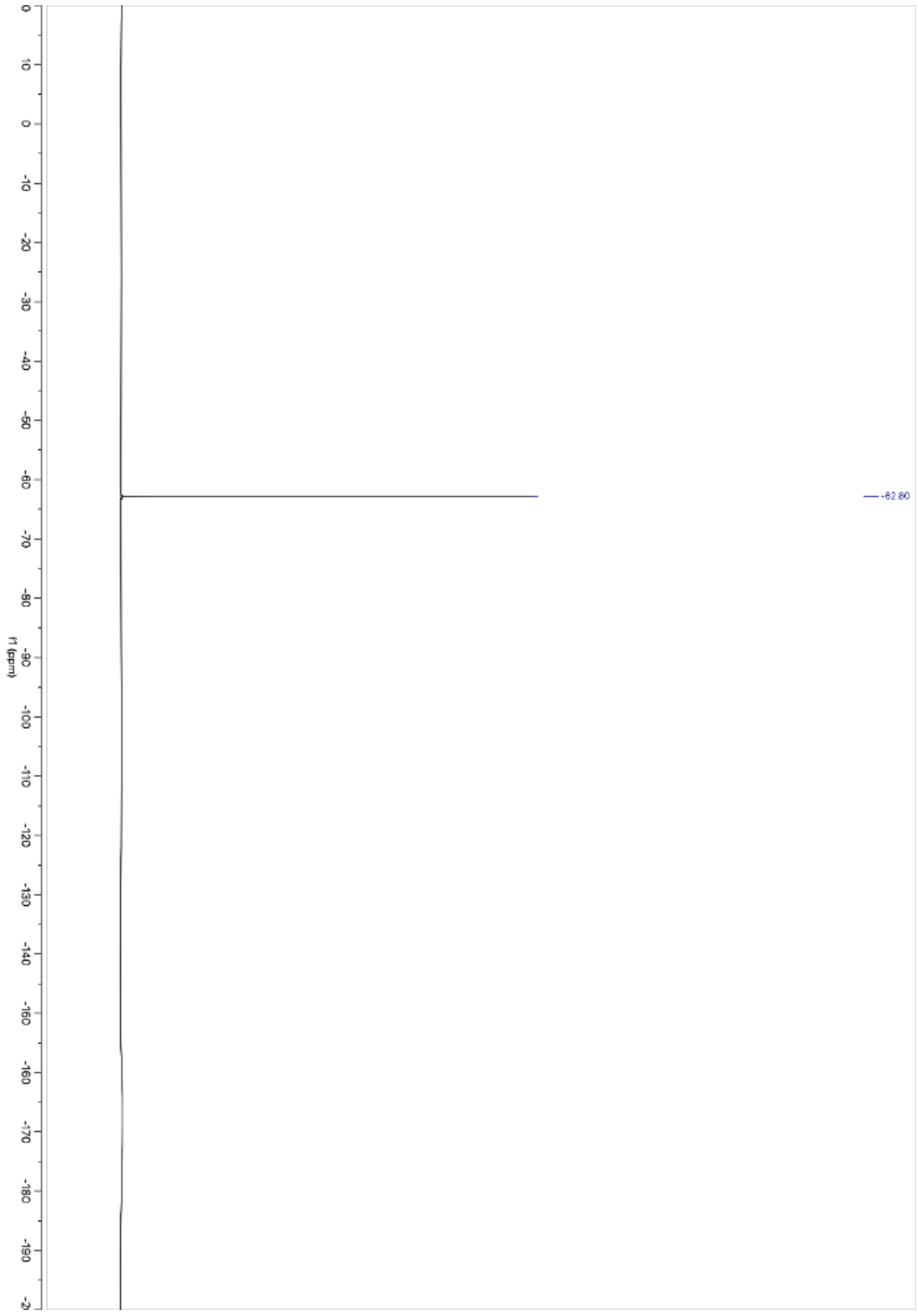
FTIR (neat): 3374, 2981, 1466, 1375, 1275, 1169, 1125, 994, 927, 892, 840, 708, 697, 682 cm^{-1}.

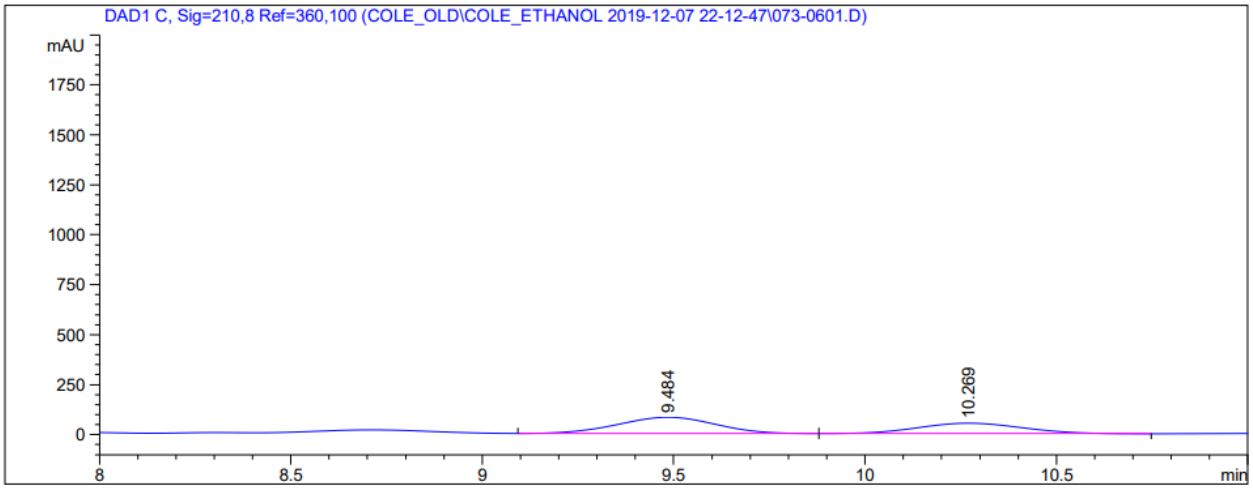
$[\alpha]_D^{28}$= -57 (*c* 0.31, $CHCl_3$).

HPLC (Two Chiralcel OD-H columns in series, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 91%.

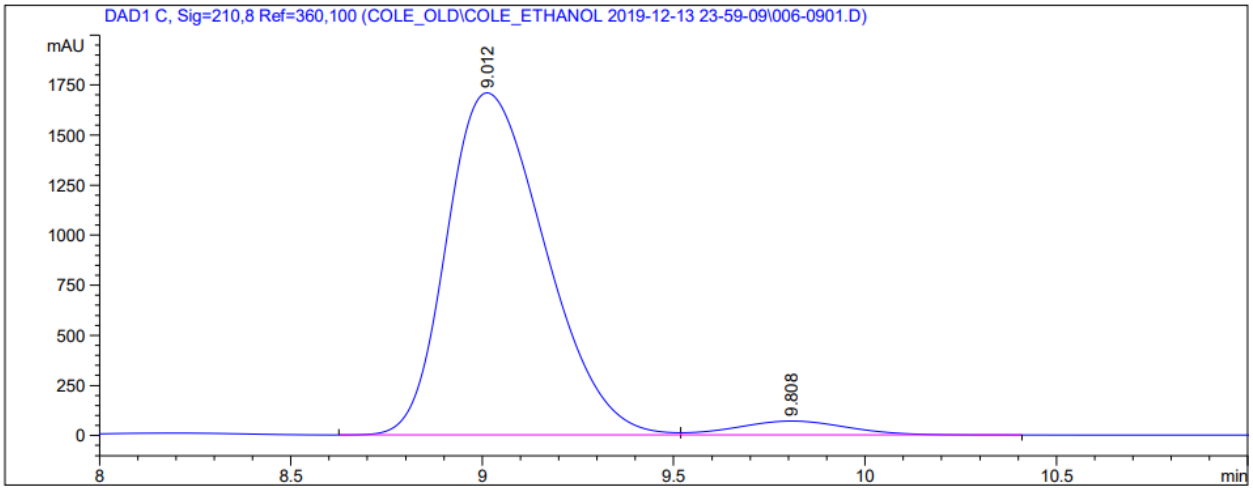

1.00
2.01
1.01
1.08
1.03
1.03
1.02
0.98
3.08
f1 (ppm)


f1 (ppm)
144.52
136.38
132.37
132.11
131.85
131.58
128.56
128.53
128.49
128.47
124.59
121.00
120.97
120.94
120.91
120.88
119.89
70.08
58.08
21.28


-62.80
f1 (ppm)

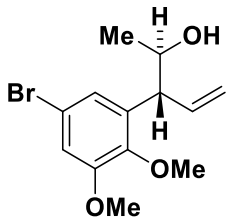


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.484	VV	0.2854	1510.92017	82.62135	59.4689
2	10.269	VV	0.3030	1029.77014	52.92517	40.5311



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.012	VV	0.2799	3.04469e4	1708.90161	95.5901
2	9.808	VB	0.3126	1404.61169	69.85947	4.4099

(2R,3R)-3-(5-bromo-2,3-dimethoxyphenyl)pent-4-en-2-ol (2k)



Procedure

Allyl acetate **1k** (63.0 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D (60 ºC, 20 hr) using an extra equivalent of potassium carbonate (55.3 mg, 0.40 mmol, 200 mol%). The title compound was obtained in 68% yield (41.1 mg, 0.127 mmol, >20:1 dr) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.29 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.95 – 6.88 (m, 2H), 6.12 – 5.98 (m, 1H), 5.26 – 5.23 (m, 1H), 5.23 – 5.19 (m, 1H), 3.95 (ddt, *J* = 12.4, 7.7, 3.8 Hz, 1H), 3.84 (d, *J* = 1.3 Hz, 3H), 3.78 (d, *J* = 1.2 Hz, 3H), 3.67 – 3.58 (m, 1H), 2.05 (s, 1H), 1.07 (dd, *J* = 6.2, 1.2 Hz, 3H).

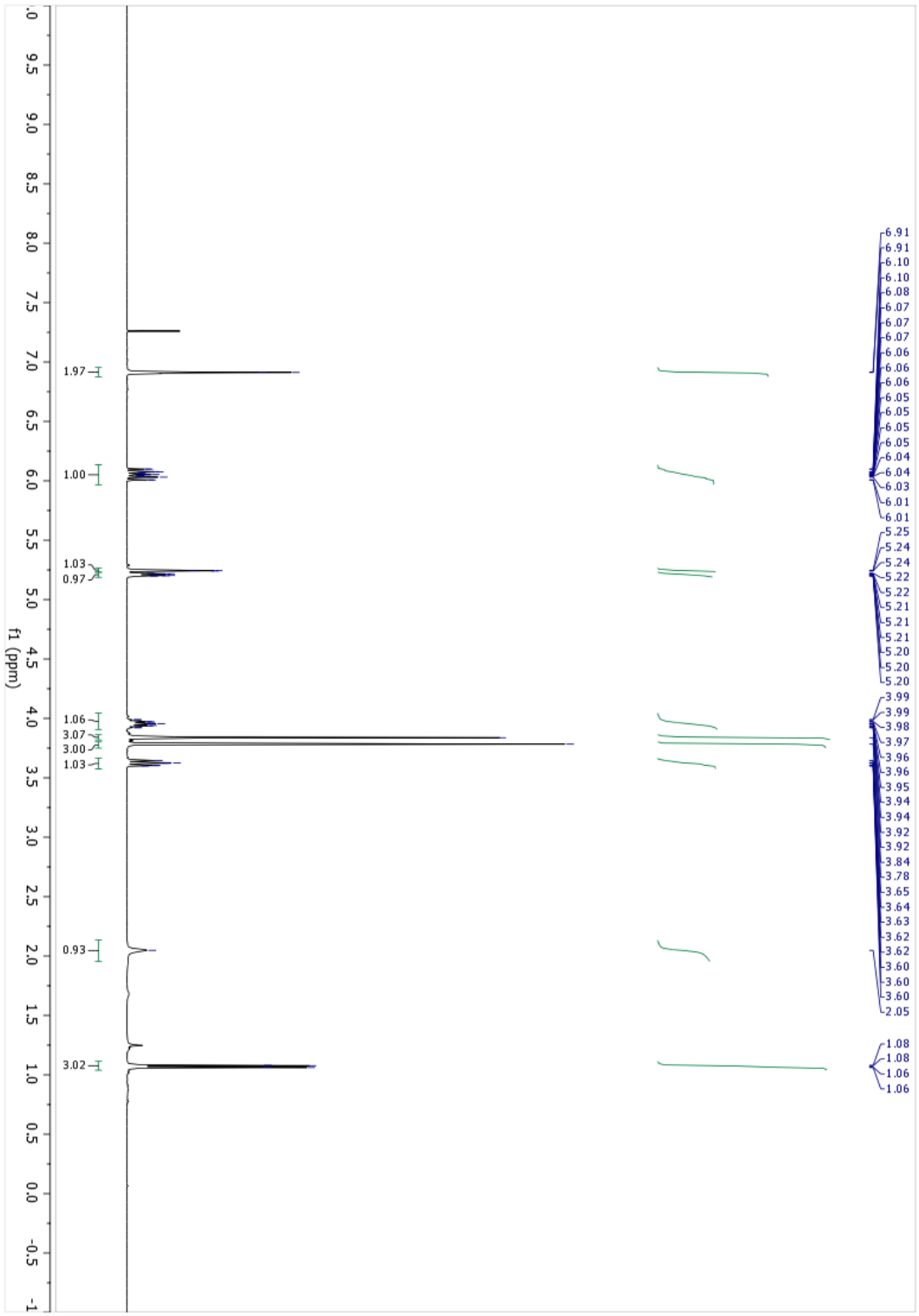
^{13}C NMR (126 MHz, $CDCl_3$): δ = 153.6, 145.9, 138.0, 137.2, 123.0, 118.6, 116.6, 114.1, 69.8, 60.8, 56.0, 55.9, 51.7, 20.7.

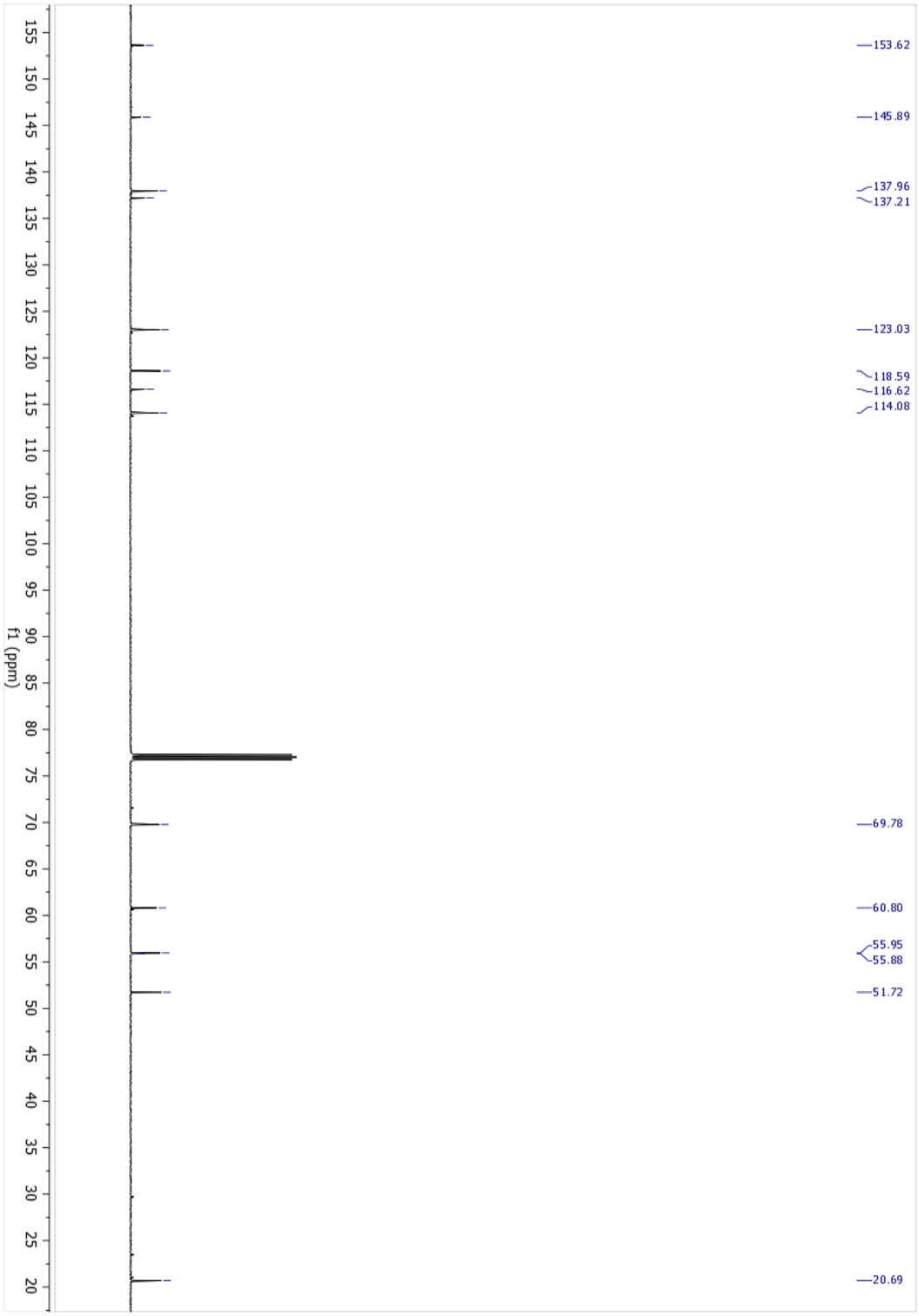
HRMS (ESI): Calculated for $C_{13}H_{17}BrO_3$ [M+Na^+] = 323.0253, Found 323.0246.

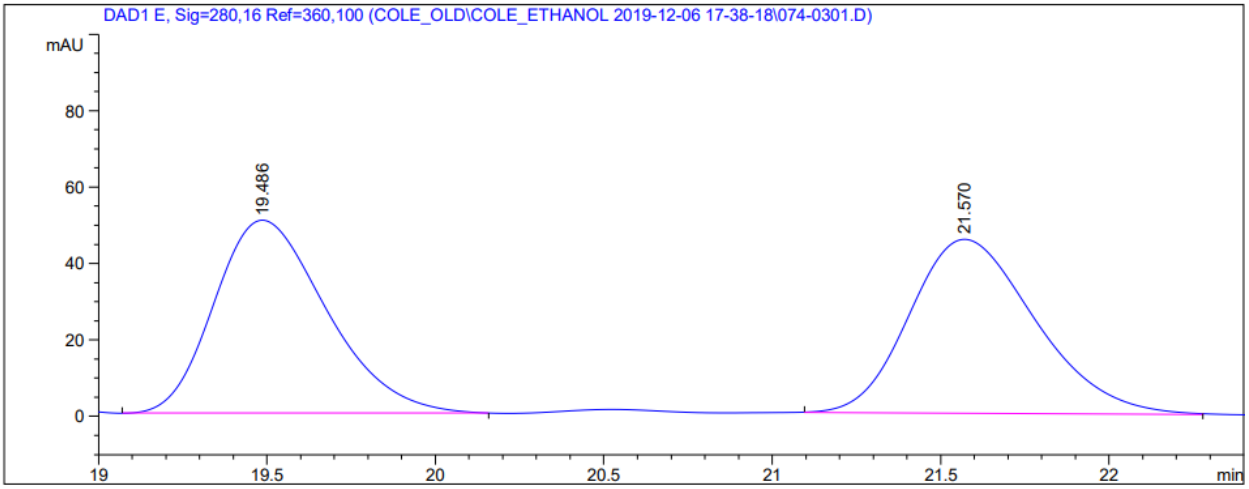
FTIR (neat): 3405, 3081, 2966, 2934, 2832, 2360, 1634, 1573, 1477, 1429, 1410, 1372, 1283, 1216, 1168, 1107, 1064, 1005, 919, 900, 852, 832, 777, 691 cm^{-1}.

$[\alpha]_D^{28}$= -38 (*c* 0.25, $CHCl_3$).

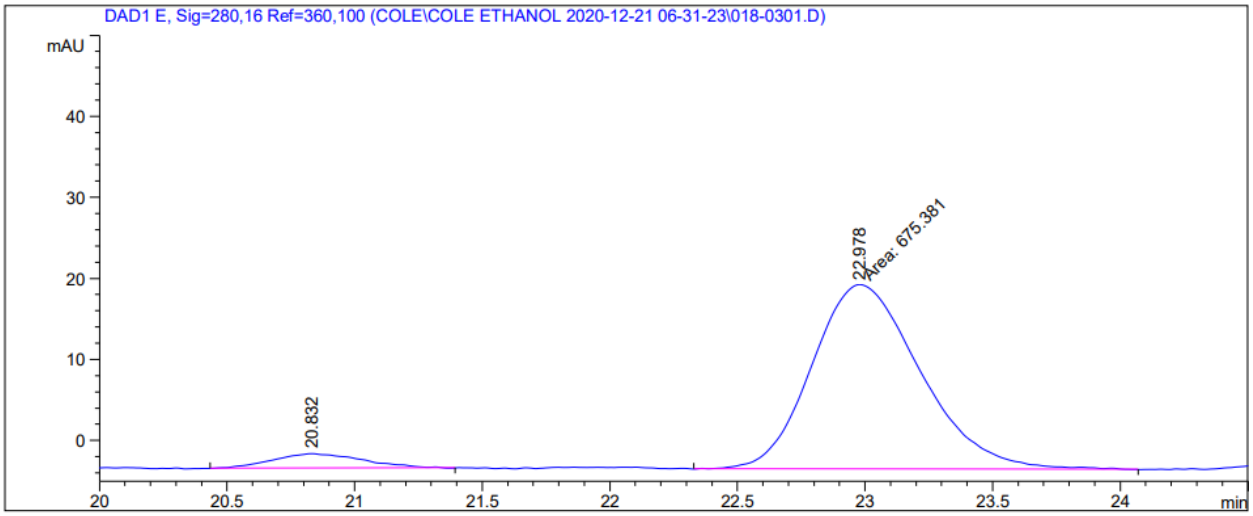
HPLC (Two Chiralcel OD-H columns in series, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 280 nm), *ee* = 88%.


f1 (ppm)
1.97
1.00
1.03
0.97
1.06
3.07
3.00
1.03
0.93
3.02
6.91
6.91
6.10
6.10
6.08
6.07
6.07
6.07
6.06
6.06
6.06
6.05
6.05
6.05
6.05
6.04
6.04
6.03
6.01
6.01
5.25
5.24
5.24
5.22
5.22
5.21
5.21
5.21
5.20
5.20
5.20
3.99
3.99
3.98
3.97
3.96
3.96
3.95
3.94
3.94
3.92
3.92
3.84
3.78
3.65
3.64
3.63
3.62
3.62
3.60
3.60
3.60
2.05
1.08
1.08
1.06
1.06


153.62
145.89
137.96
137.21
123.03
118.59
116.62
114.08
69.78
60.80
55.95
55.88
51.72
20.69
f1 (ppm)

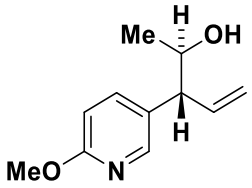


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.486	VB	0.3587	1172.57959	50.54509	49.7430
2	21.570	BB	0.4033	1184.69470	45.57491	50.2570



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.832	BB	0.3012	44.63925	1.80077	6.1997
2	22.978	MM	0.4938	675.38098	22.79760	93.8003

(2R,3R)-3-(6-methoxypyridin-3-yl)pent-4-en-2-ol (2l)



Procedure

Allyl acetate **1l** (41.4 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 79% yield (30.5 mg, 0.158 mmol, >20:1 dr) as a brown oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1—5:1).

TLC (SiO_2) R_f = 0.20 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 2.5 Hz, 1H), 7.43 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 6.06 (ddd, *J* = 17.0, 10.3, 8.7 Hz, 1H), 5.25 (dd, *J* = 10.3, 1.6 Hz, 1H), 5.21 (dt, *J* = 17.1, 1.3 Hz, 1H), 3.99 – 3.91 (m, 1H), 3.92 (s, 3H), 3.15 (t, *J* = 8.1 Hz, 1H), 1.82 (s, 1H), 1.09 (d, *J* = 6.2 Hz, 3H).

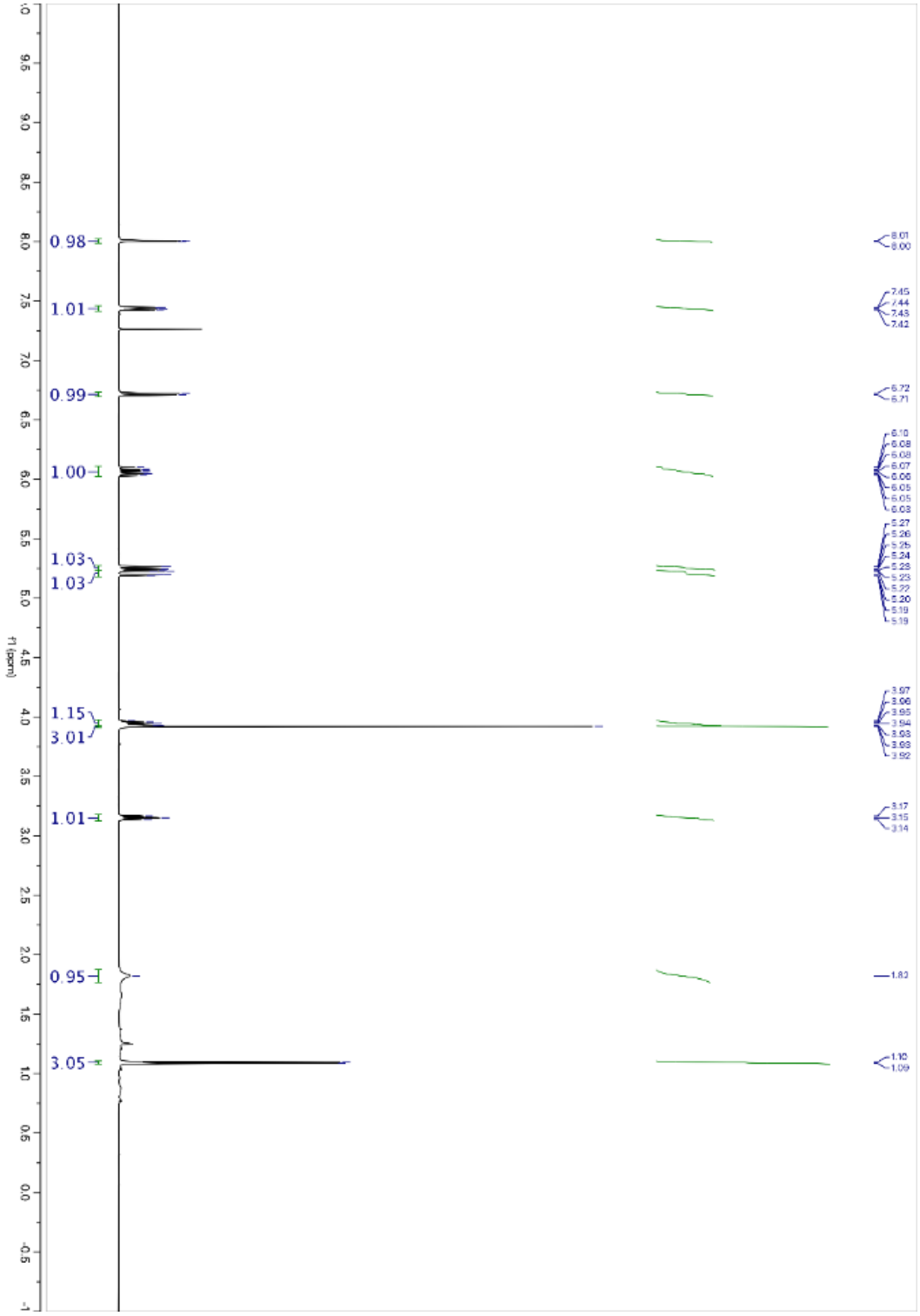
^{13}C NMR (126 MHz, $CDCl_3$) δ = 163.3, 146.3, 138.4, 137.9, 129.8, 118.5, 111.0, 70.3, 55.5, 53.6, 20.9.

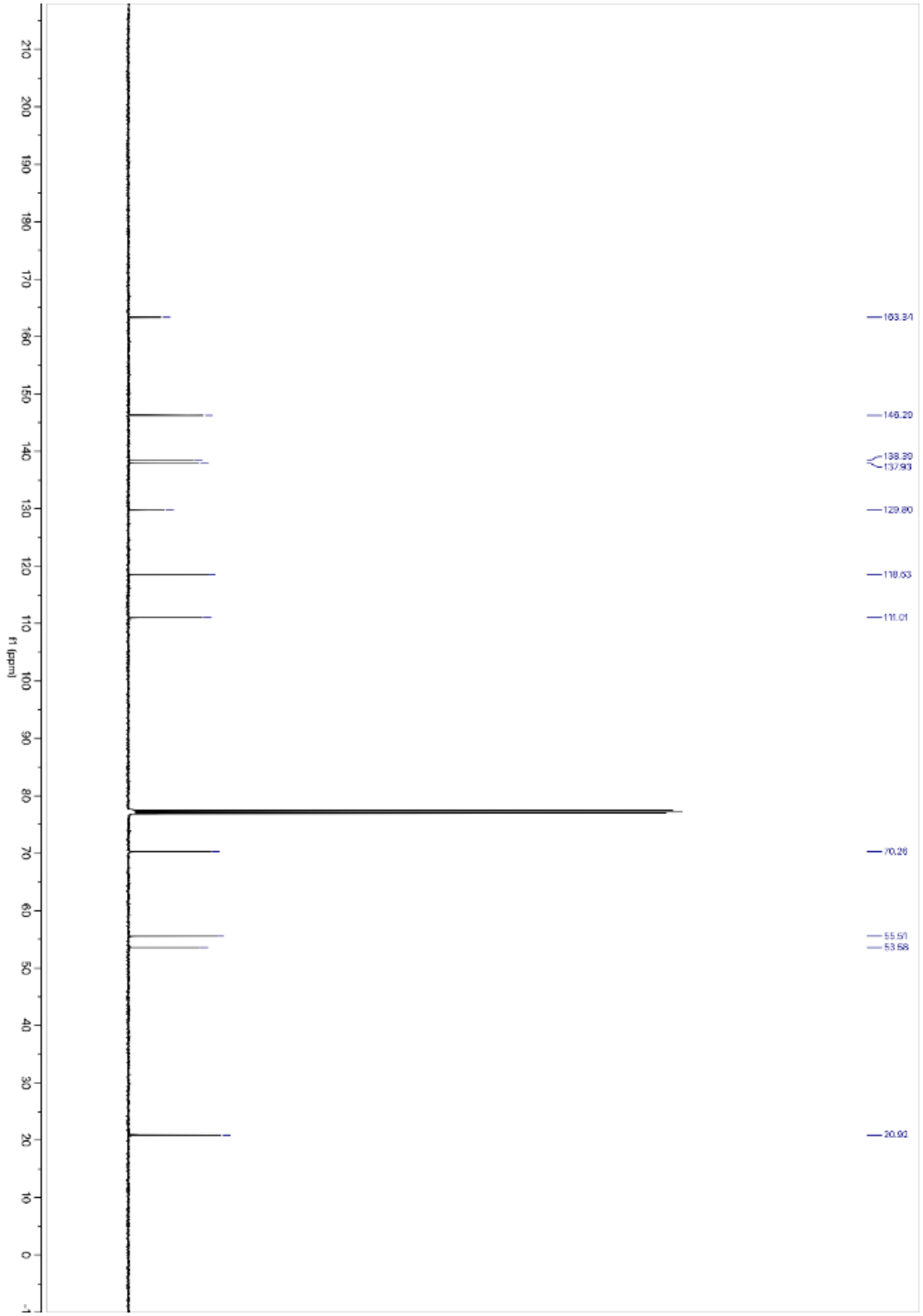
HRMS (ESI): Calculated for $C_{11}H_{15}NO_2$ [M+H$^+$] = 194.1176, Found 194.1175.

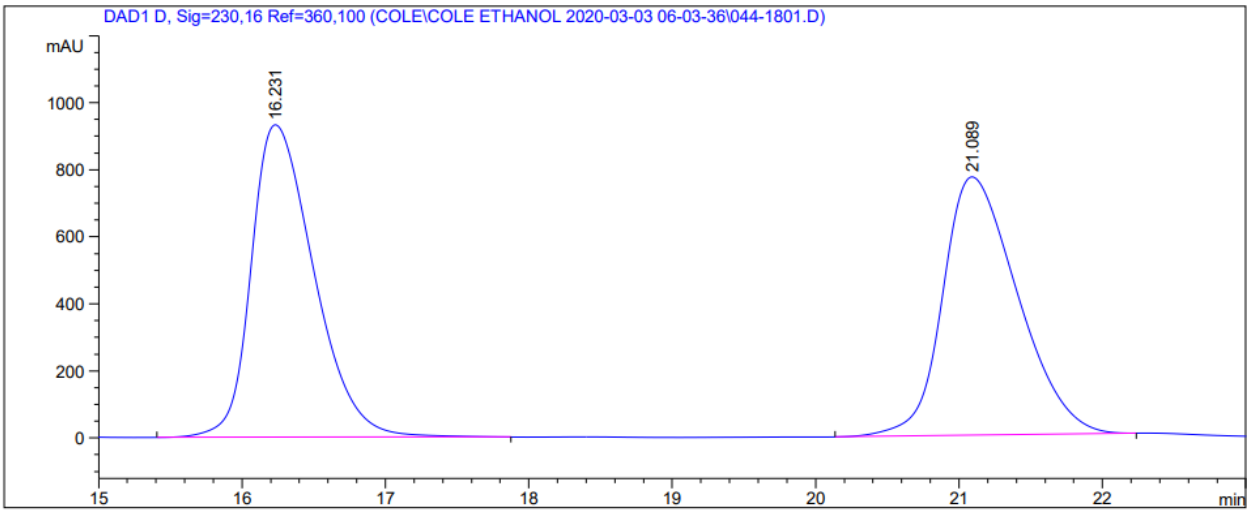
FTIR (neat): 3395, 2973, 2923, 1638, 1605, 1572, 1491, 1462, 1390, 1293, 1275, 1117, 1077, 1027, 919, 873, 829, 759, 699, 664 cm^{-1}.

$[\alpha]_D^{28}$= -85 (*c* 0.20, $CHCl_3$).

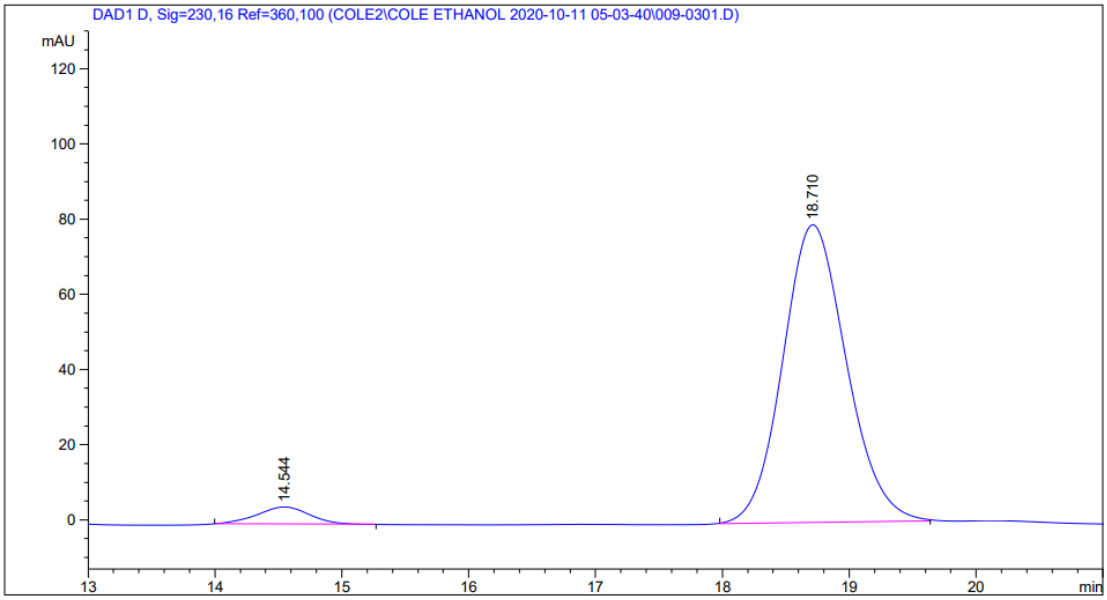
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 230 nm), *ee* = 91%.


0.98
1.01
0.99
1.00
1.03
1.03
1.15
3.01
1.01
0.95
3.05
f1 (ppm)


f1 (ppm)
163.34
146.20
138.30
137.93
129.80
118.53
111.01
70.26
55.51
53.58
20.92

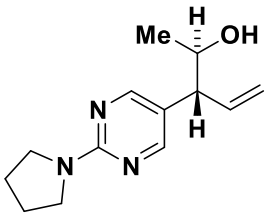


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.231	BB	0.4732	2.83847e4	932.21063	50.2769
2	21.089	BB	0.5629	2.80721e4	770.70575	49.7231



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.544	BB	0.4372	134.21104	4.58967	4.6305
2	18.710	BB	0.5329	2764.22461	79.25741	95.3695

(2R,3R)-3-(2-(pyrrolidin-1-yl)pyrimidin-5-yl)pent-4-en-2-ol (2m)



Procedure

Allyl acetate **1m** (24.7 mg, 0.100 mmol, 100 mol%) was subjected to a modified version of general procedure D using reduced loading of potassium carbonate (6.9 mg, 0.050 mmol, 50 mol%), ethanol (17 μL, 0.30 mmol, 300 mol%), and acetone as solvent (0.10 mL, 1.0 M, 60 °C, 24 hr). The title compound was obtained in 68% yield (15.9 mg, 0.068 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–2:1).

TLC (SiO_2) R_f = 0.15 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.18 (s, 1H), 6.04 (ddd, *J* = 17.2, 10.3, 8.6 Hz, 1H), 5.25 (dd, *J* = 10.2, 1.4 Hz, 1H), 5.20 (dt, *J* = 17.1, 1.3 Hz, 1H), 3.92 (p, *J* = 6.4 Hz, 1H), 3.59 – 3.52 (m, 4H), 3.04 (t, *J* = 7.9 Hz, 1H), 1.99 (p, *J* = 3.6 Hz, 4H), 1.13 (d, *J* = 6.2 Hz, 3H).

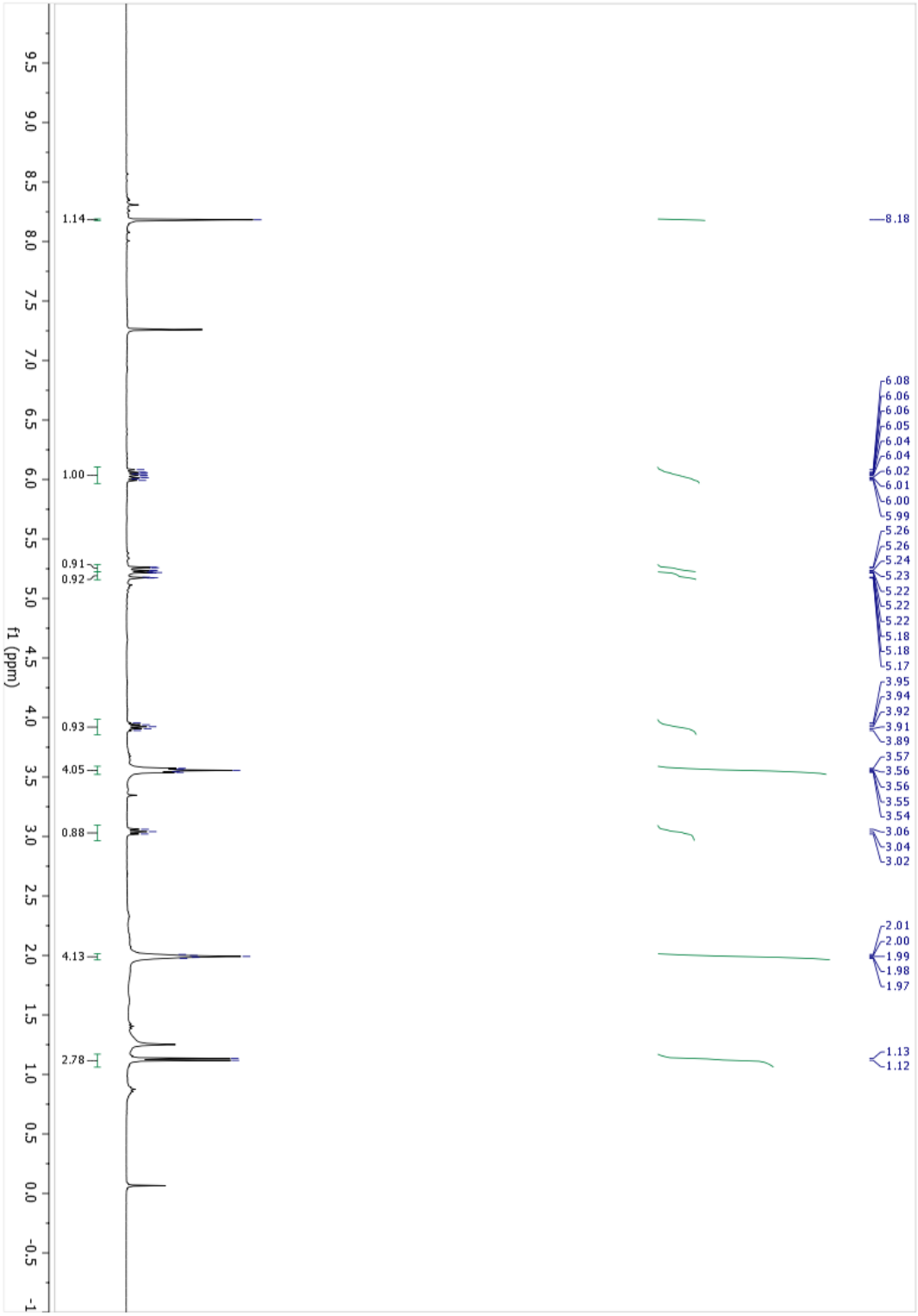
^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.7, 157.6, 137.5, 121.3, 118.4, 70.1, 53.2, 46.8, 25.7, 20.9.

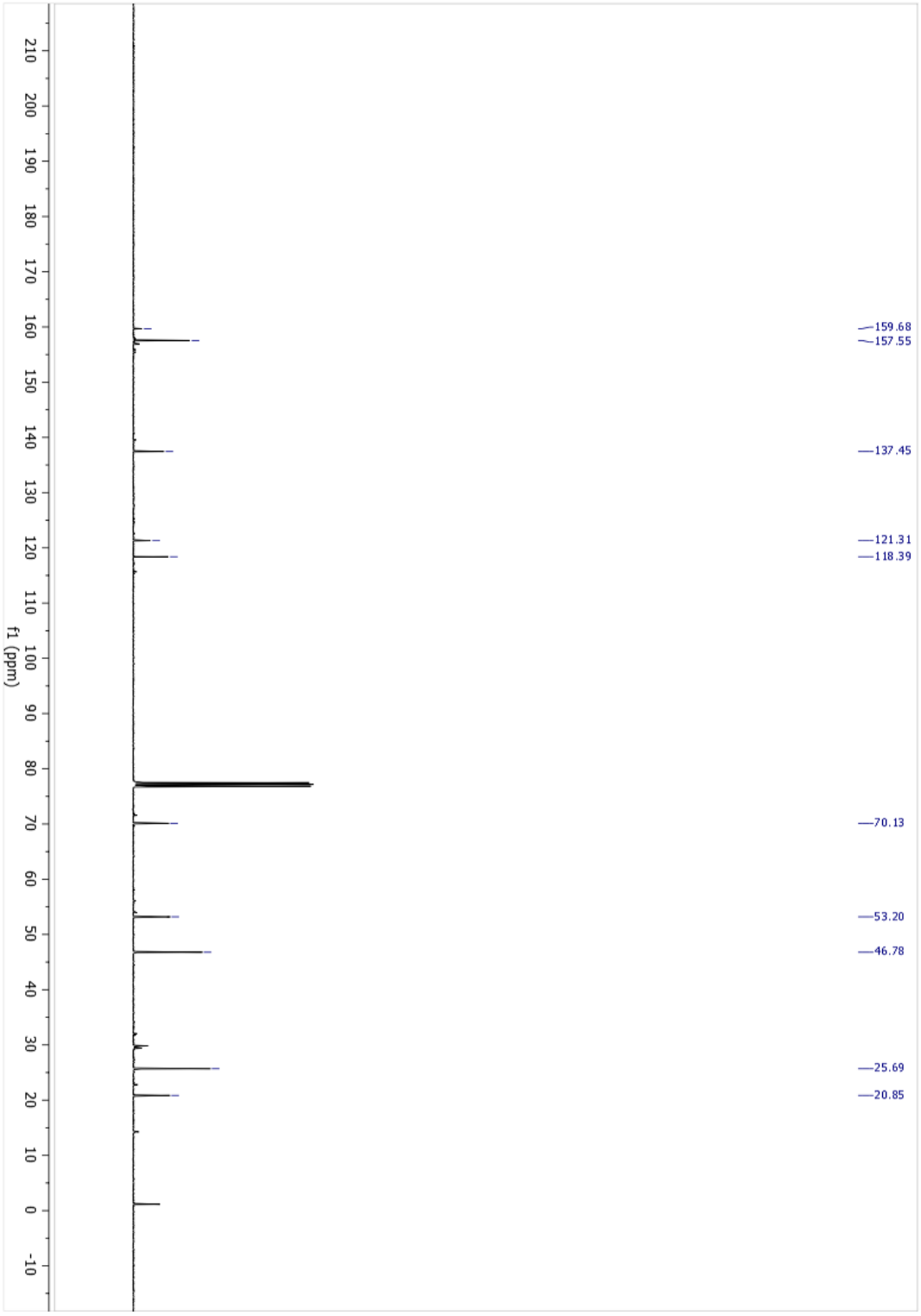
HRMS (ESI): Calculated for $C_{13}H_{19}N_3O$ [M+H$^+$] = 234.1601, Found 234.1607.

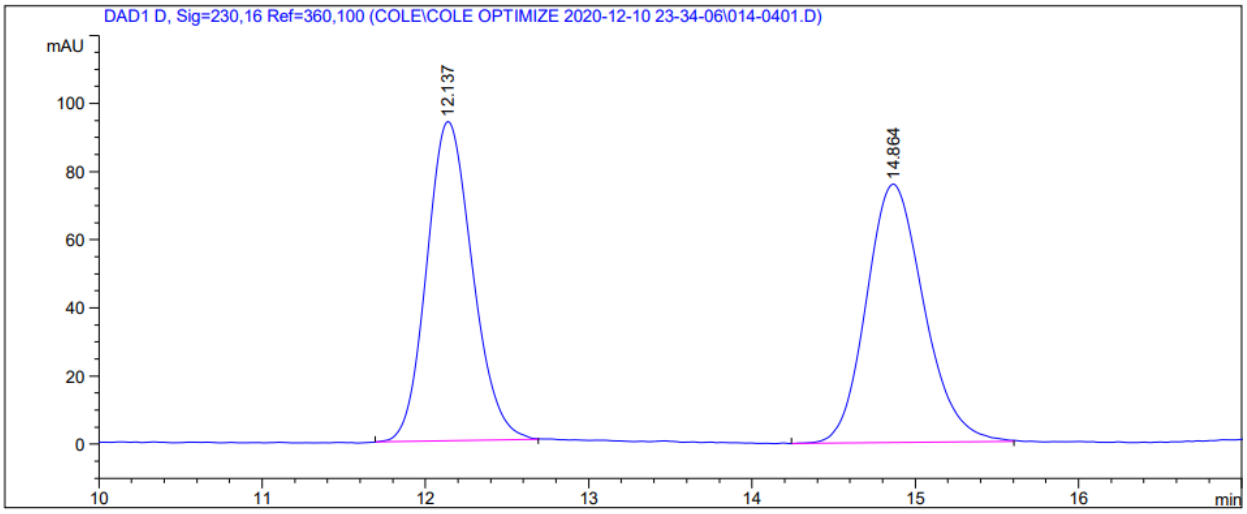
FTIR (neat): 3403, 2959, 2927, 2857, 1735, 1567, 1493, 1447, 1250, 1084, 1028, 880, 785, 698 cm^{-1}.

$[\alpha]_D^{28}$= -30.8 (*c* 0.13, $CHCl_3$).

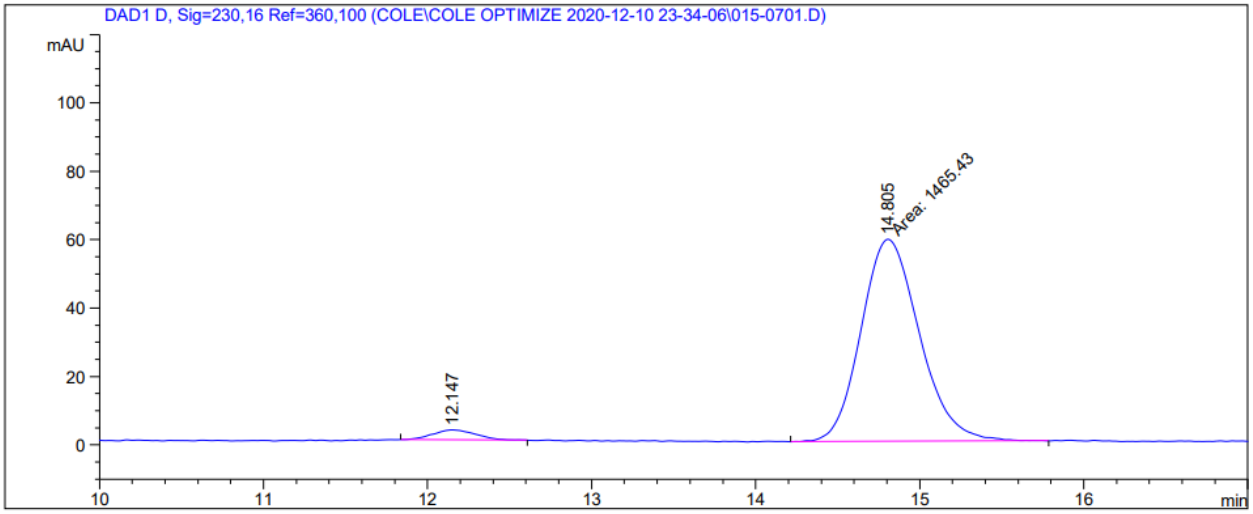
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 93:7, 1.00 mL/min, 230 nm), *ee* = 93%.


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.14
1.00
0.91
0.92
0.93
4.05
0.88
4.13
2.78
8.18
6.08
6.06
6.06
6.05
6.04
6.04
6.02
6.01
6.00
5.99
5.26
5.26
5.24
5.23
5.22
5.22
5.22
5.18
5.18
5.17
3.95
3.94
3.92
3.91
3.89
3.57
3.56
3.56
3.55
3.54
3.06
3.04
3.02
2.01
2.00
1.99
1.98
1.97
1.13
1.12


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
159.68
157.55
137.45
121.31
118.39
70.13
53.20
46.78
25.69
20.85

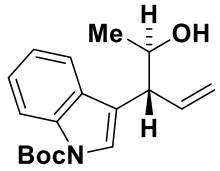


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.137	BB	0.2994	1828.87280	93.80918	49.5619
2	14.864	VB	0.3800	1861.20239	75.92507	50.4381



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.147	BB	0.2273	54.28868	2.94145	3.5723
2	14.805	MM	0.4129	1465.43213	59.14585	96.4277

tert-butyl 3-((3R,4R)-4-hydroxypent-1-en-3-yl)-1H-indole-1-carboxylate (2n)



Procedure

Allyl acetate **1n** (63.1 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D (60 °C, 48 hr) using reduced loading of ethanol (35 μL, 0.60 mmol, 300 mol%). The title compound was obtained in 86% yield (51.8 mg, 0.172 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.14 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.46 (s, 1H), 7.32 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.25 – 7.20 (m, 1H), 6.21 – 6.10 (m, 1H), 5.29 – 5.27 (m, 1H), 5.26 (s, 1H), 4.15 (p, *J* = 6.4 Hz, 1H), 3.50 (dd, *J* = 8.9, 6.6 Hz, 1H), 1.85 (s, 1H), 1.68 (s, 9H), 1.21 (d, *J* = 6.2 Hz, 3H).

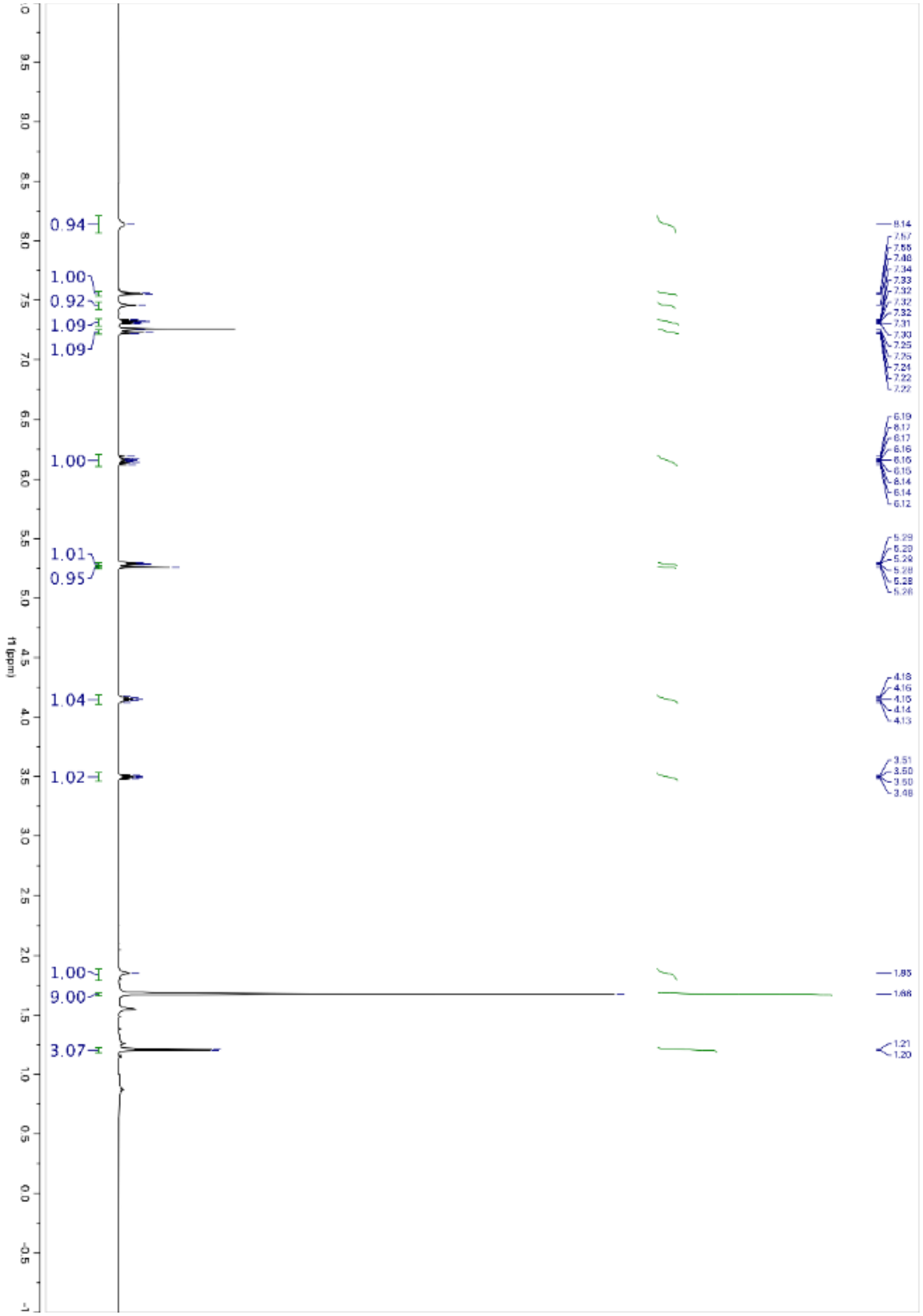
^{13}C NMR (126 MHz, $CDCl_3$): δ = 149.8, 136.8, 129.8, 129.1, 124.6, 122.9, 122.5, 120.6, 119.4, 118.3, 115.4, 83.7, 69.3, 49.6, 28.2, 21.0.

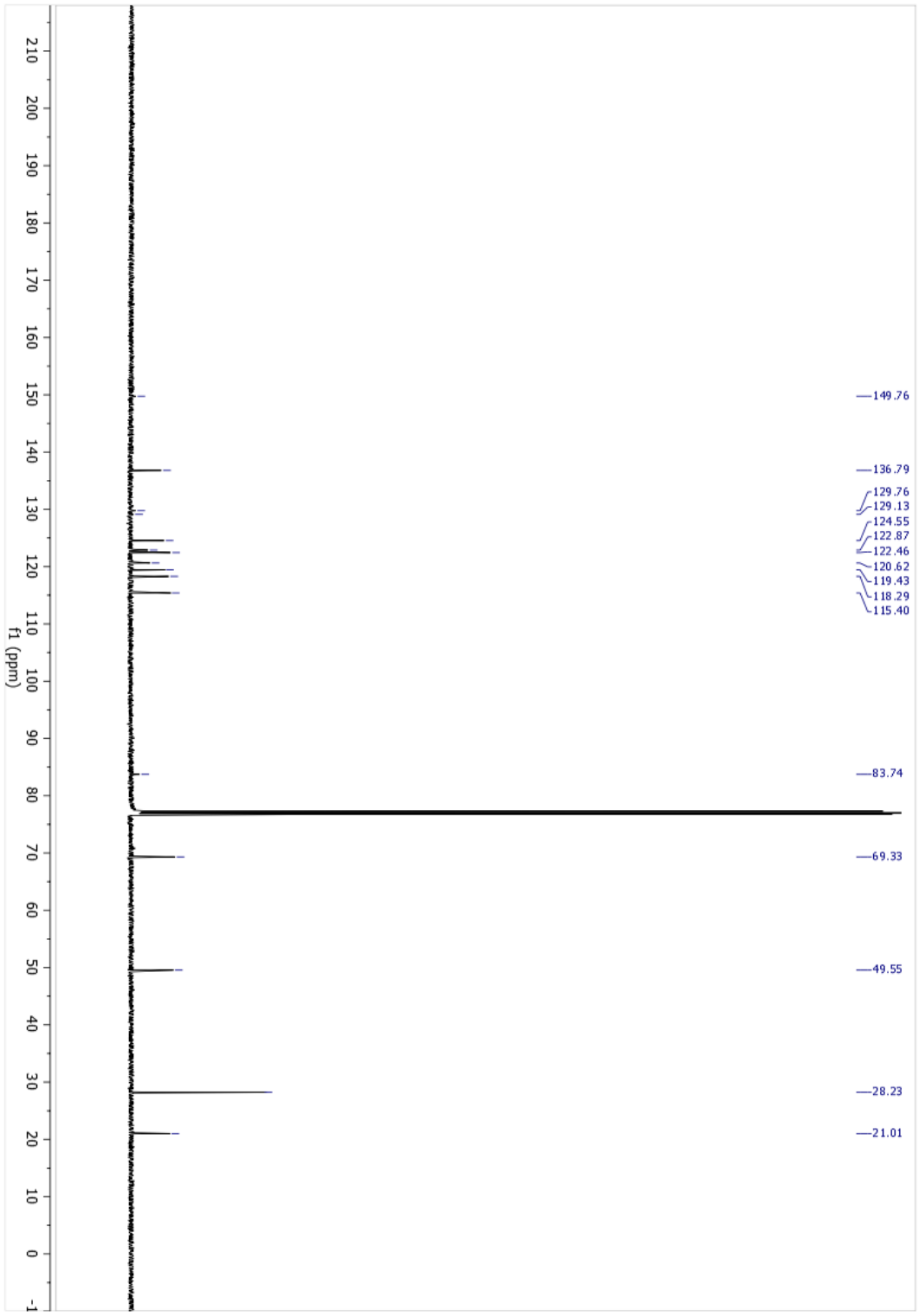
HRMS (ESI): Calculated for $C_{18}H_{23}NO_3$ [M+Na^+] = 324.1570, Found 324.1573.

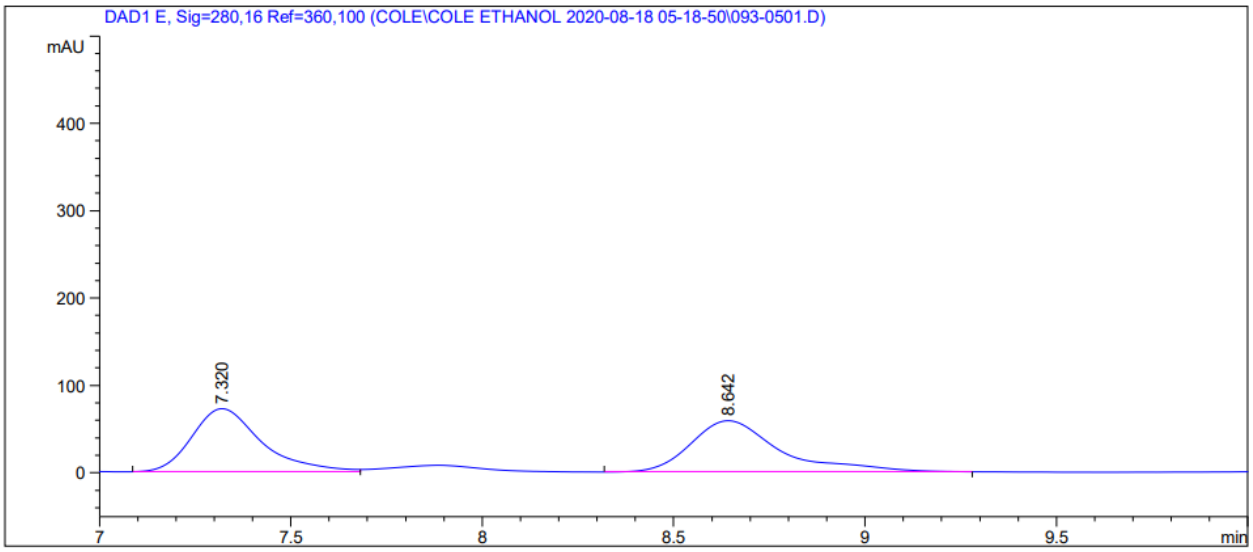
FTIR (neat): 3401, 2977, 2931, 1729, 1608, 1476, 1451, 1368, 1308, 1253, 1216, 1154, 1120, 1073, 1013, 918, 859, 841, 765, 745 cm^{-1}.

$[\alpha]_D^{28}$= -37.5 (*c* 0.27, $CHCl_3$).

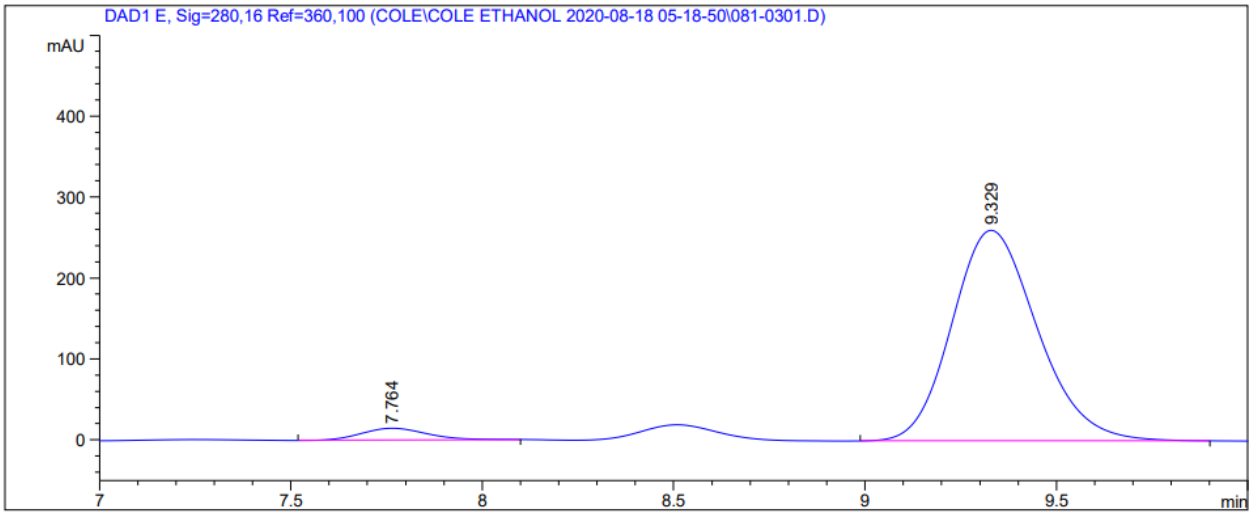
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 280 nm), *ee* = 91%.


0.94
1.00
0.92
1.09
1.09
1.00
1.01
0.95
1.04
1.02
1.00
9.00
3.07
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
149.76
136.79
129.76
129.13
124.55
122.87
122.46
120.62
119.43
118.29
115.40
83.74
69.33
49.55
28.23
21.01

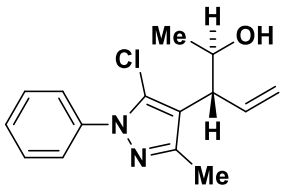


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.320	BV	0.1926	924.40375	72.58103	49.2373
2	8.642	VB	0.2434	953.04260	58.71280	50.7627



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.764	VB	0.1935	186.48053	14.94863	4.4005
2	9.329	BB	0.2415	4051.22778	260.42032	95.5995

(2R,3R)-3-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)pent-4-en-2-ol (2o)



Procedure

Allyl acetate **1o** (58.2 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using reduced loading of ethanol (35 μL, 0.30 mmol, 300 mol%) and acetone as solvent (0.200 mL, 1.0 M, 80 °C, 16 hr). The title compound was obtained in 71% yield (39.5 mg, 0.143 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1 – 4:1).

TLC (SiO_2) R_f = 0.12 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 – 7.50 (m, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.41 – 7.36 (m, 1H), 6.22 (ddd, *J* = 16.7, 10.4, 8.7 Hz, 1H), 5.28 (s, 1H), 5.27 – 5.23 (m, 1H), 4.17 (dq, *J* = 9.0, 6.2 Hz, 1H), 3.25 (t, *J* = 8.9 Hz, 1H), 2.32 (s, 3H), 1.89 (s, 1H), 1.16 (d, *J* = 6.2 Hz, 3H).

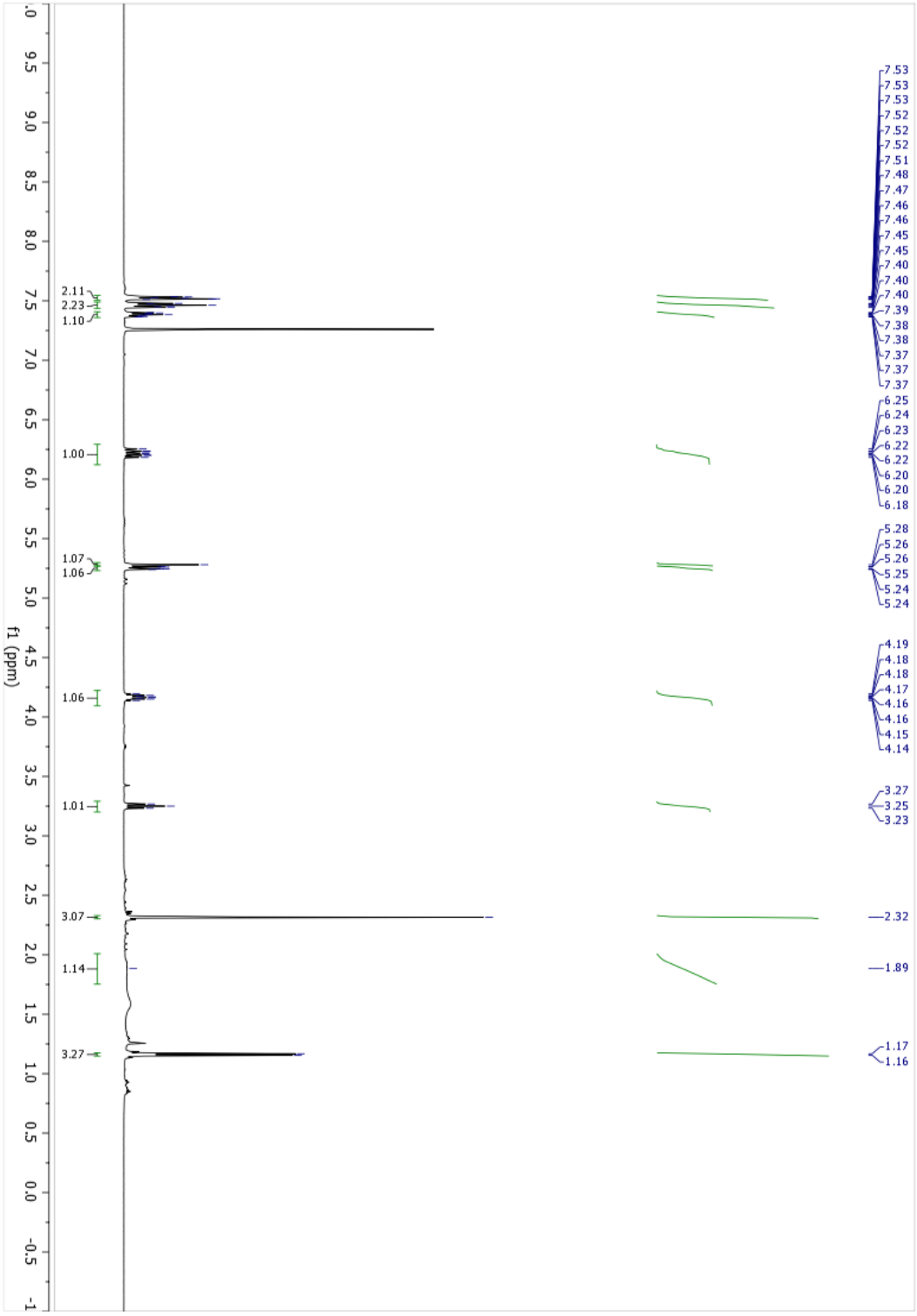
^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.2, 138.5, 136.2, 129.1, 128.1, 125.1, 125.0, 118.6, 116.8, 68.4, 49.7, 21.0, 13.9.

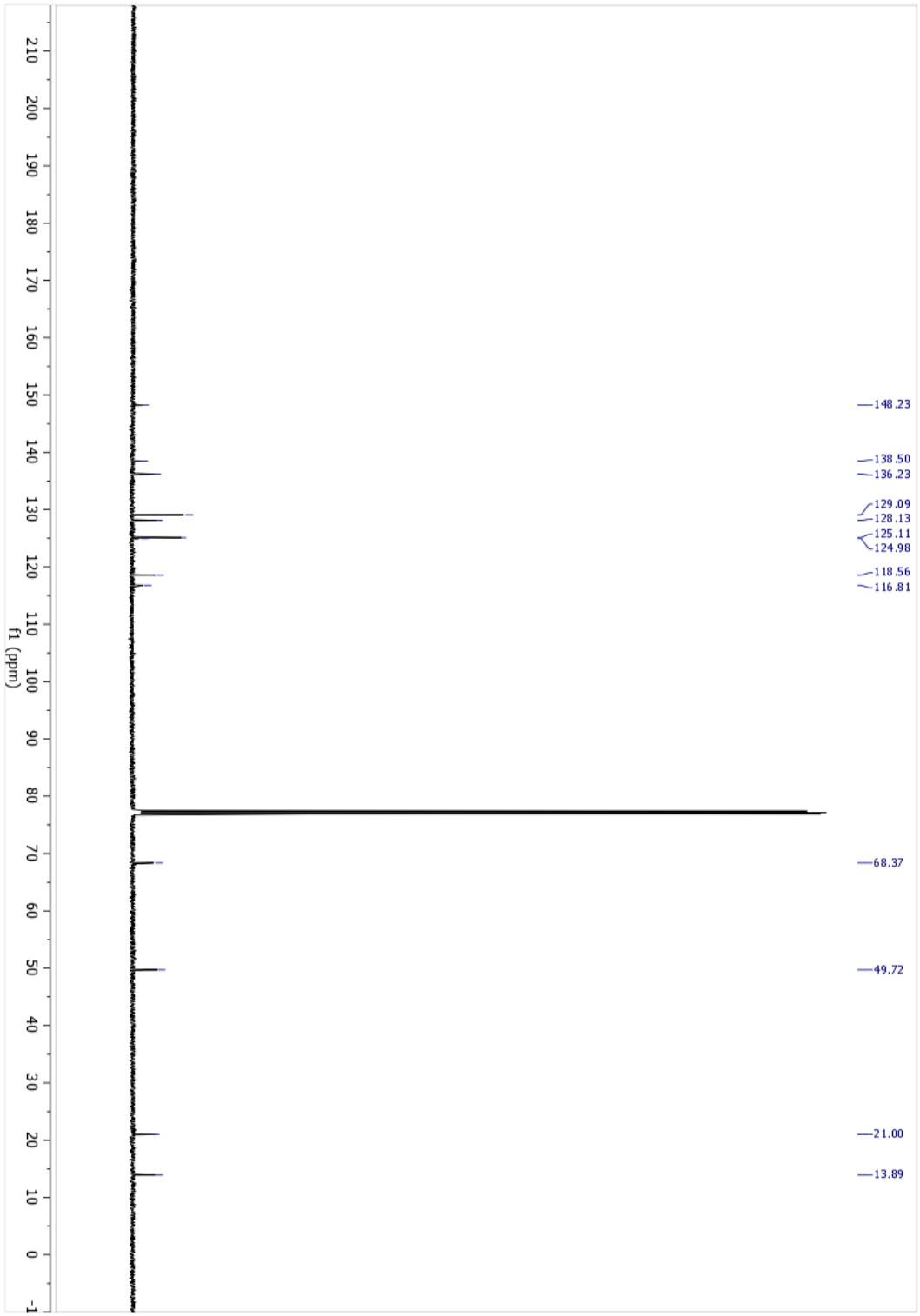
HRMS (ESI): Calculated for $C_{15}H_{17}ClN_2O$ $[M+H^+]$ = 277.1102, Found 277.1106.

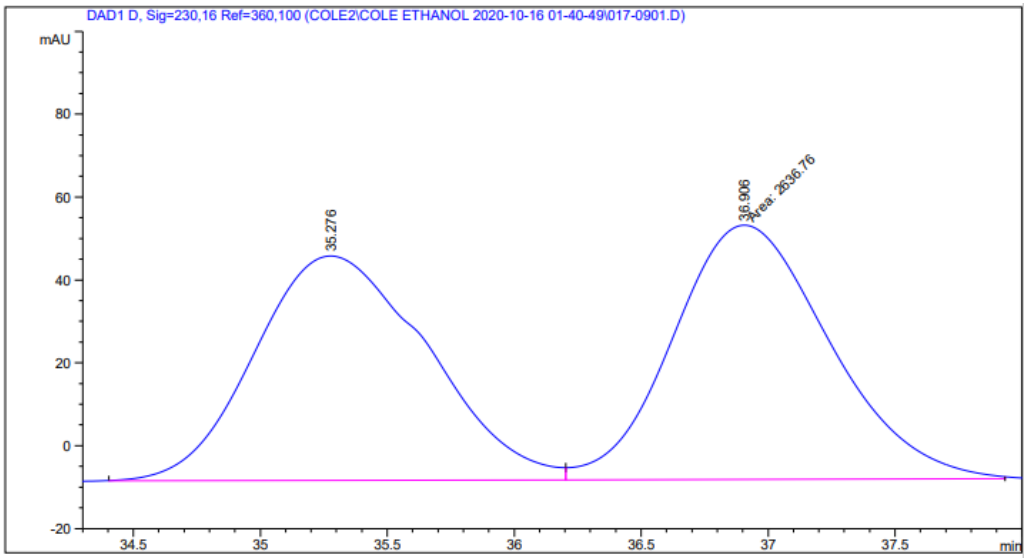
FTIR (neat): 3393, 2965, 2925, 1598, 1550, 1502, 1457, 1411, 1364, 1118, 1076, 1008, 986, 919, 763, 694 cm^{-1}.

$[\alpha]_D^{28}$= -62.9 (*c* 0.58, $CHCl_3$).

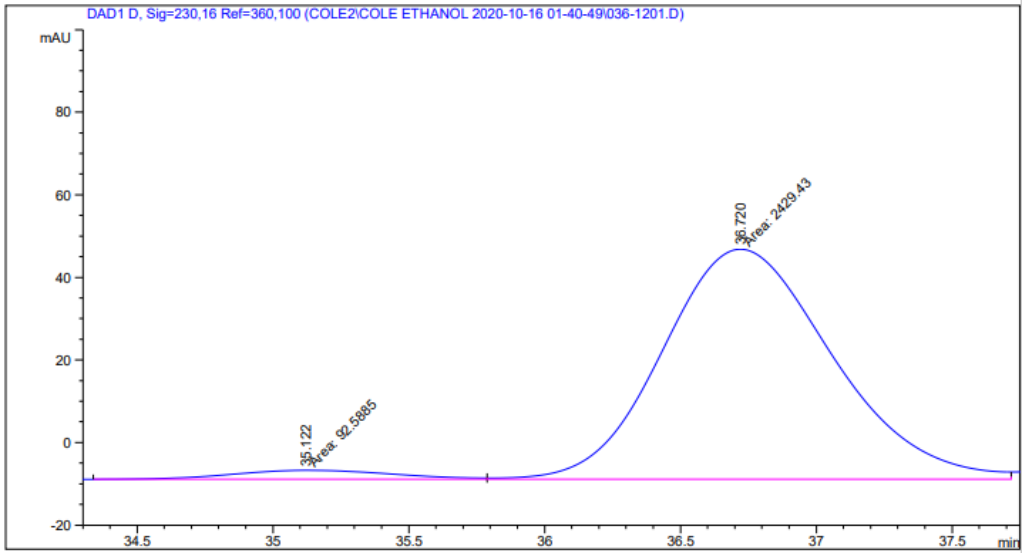
HPLC (Two Chiralcel AD-H columns in series, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 230 nm), *ee* = 93%.


f1 (ppm)
2.11
2.23
1.10
1.00
1.07
1.06
1.06
1.01
3.07
1.14
3.27
7.53
7.53
7.53
7.52
7.52
7.52
7.51
7.48
7.47
7.46
7.46
7.45
7.45
7.40
7.40
7.40
7.39
7.38
7.38
7.37
7.37
7.37
6.25
6.24
6.23
6.22
6.22
6.20
6.20
6.18
5.28
5.26
5.26
5.25
5.24
5.24
4.19
4.18
4.18
4.17
4.16
4.16
4.15
4.14
3.27
3.25
3.23
2.32
1.89
1.17
1.16


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
148.23
138.50
136.23
129.09
128.13
125.11
124.98
118.56
116.81
68.37
49.72
21.00
13.89

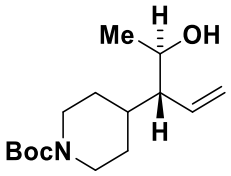


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.276	BV	0.7089	2576.75635	54.17867	49.4245
2	36.906	MF	0.7158	2636.76392	61.39855	50.5755



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.122	MM	0.6962	92.58852	2.21658	3.6712
2	36.720	MM	0.7260	2429.42822	55.77256	96.3288

tert-butyl 4-((3R,4R)-4-hydroxypent-1-en-3-yl)piperidine-1-carboxylate (2p)



Procedure

Allyl acetate **1p** (56.7 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using acetone as solvent (0.200 mL, 1.0 M, 60 °C, 48 hr). The title compound was obtained in 66% yield (35.6 mg, 0.132 mmol, >20:1 dr) as a white crystalline solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–3:1).

TLC (SiO_2) R_f = 0.26 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.68 (dt, *J* = 17.1, 10.1 Hz, 1H), 5.25 (dd, *J* = 10.2, 2.1 Hz, 1H), 5.07 (dd, *J* = 17.3, 2.1 Hz, 1H), 4.12 (d, *J* = 11.4 Hz, 2H), 3.97 – 3.89 (m, 1H), 2.66 (dtd, *J* = 34.4, 12.9, 2.5 Hz, 2H), 1.75 – 1.60 (m, 4H), 1.52 (s, 1H), 1.45 (s, 9H), 1.27 – 1.20 (m, 1H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.16 – 1.06 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 155.0, 136.0, 119.7, 79.4, 66.6, 57.2, 44.3, 36.6, 30.8, 29.3, 28.7, 21.8.

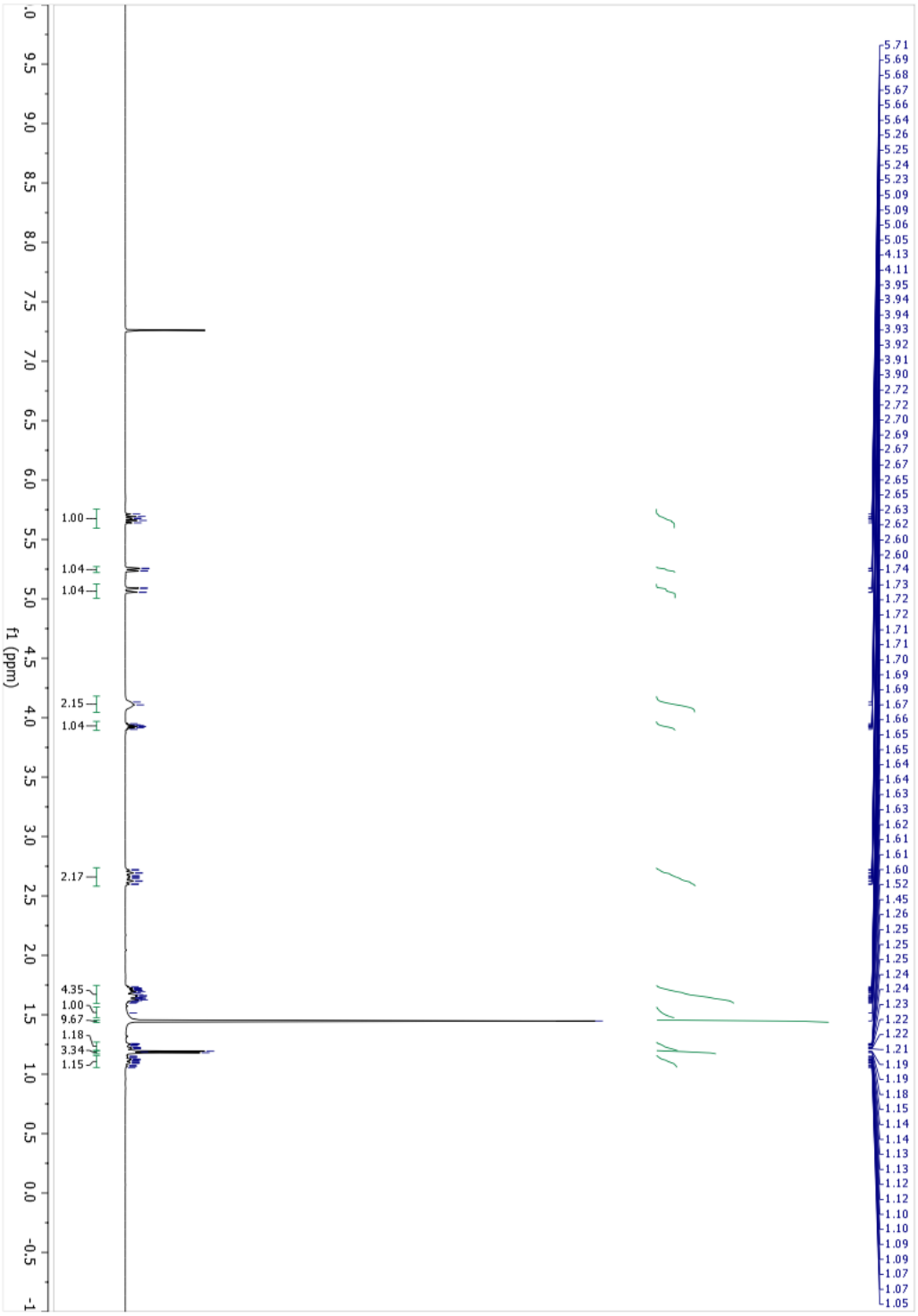
HRMS (ESI): Calculated for $C_{15}H_{27}NO_3$ [M+Na^+] = 292.1883, Found 292.1885.

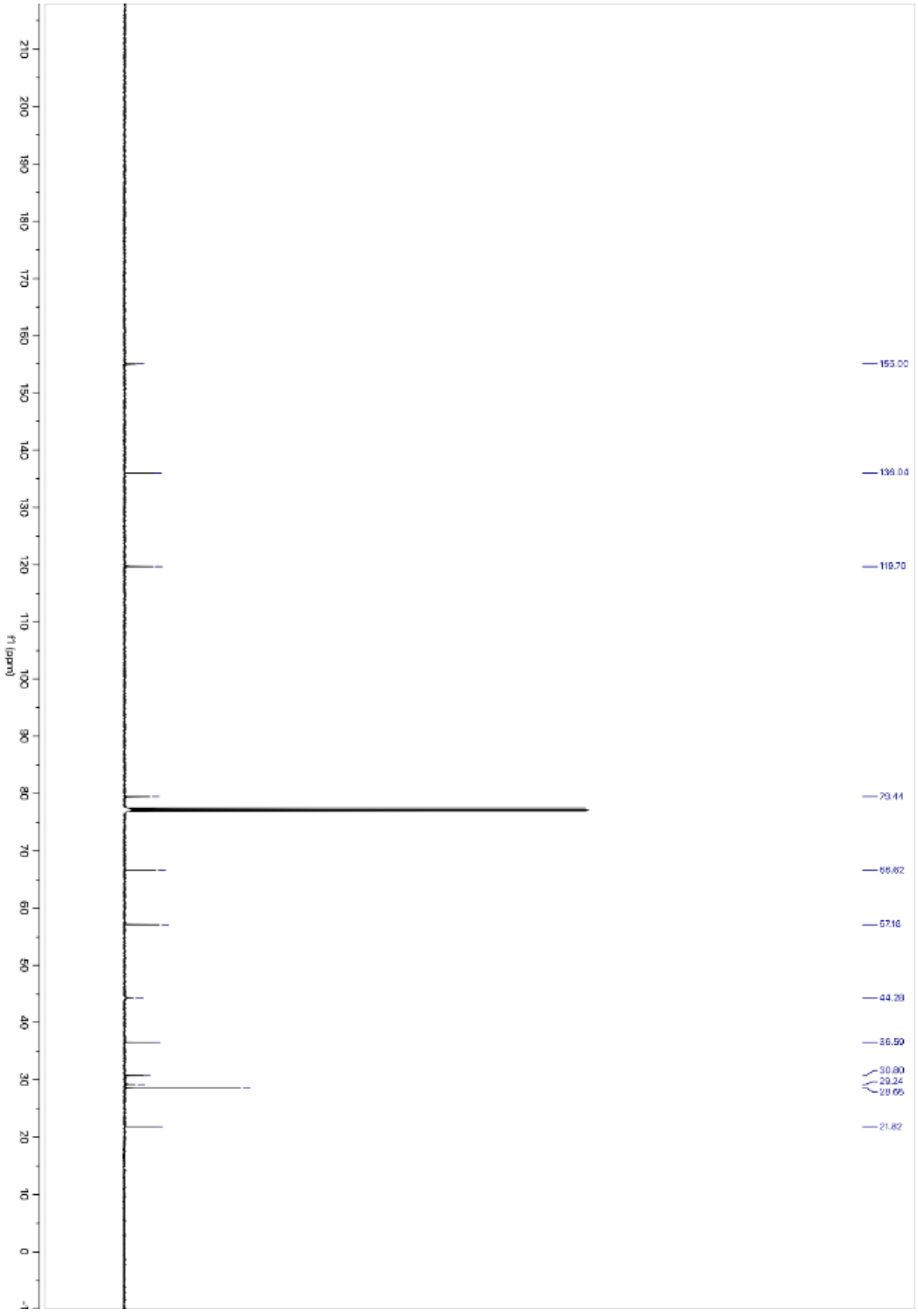
FTIR (neat): 3439, 2974, 2920, 2885, 2851, 2359, 2343, 1695, 1670, 1426, 1366, 1321, 1280, 1250, 1215, 1172, 1155, 1100, 1005, 974, 910, 869, 767 cm^{-1}.

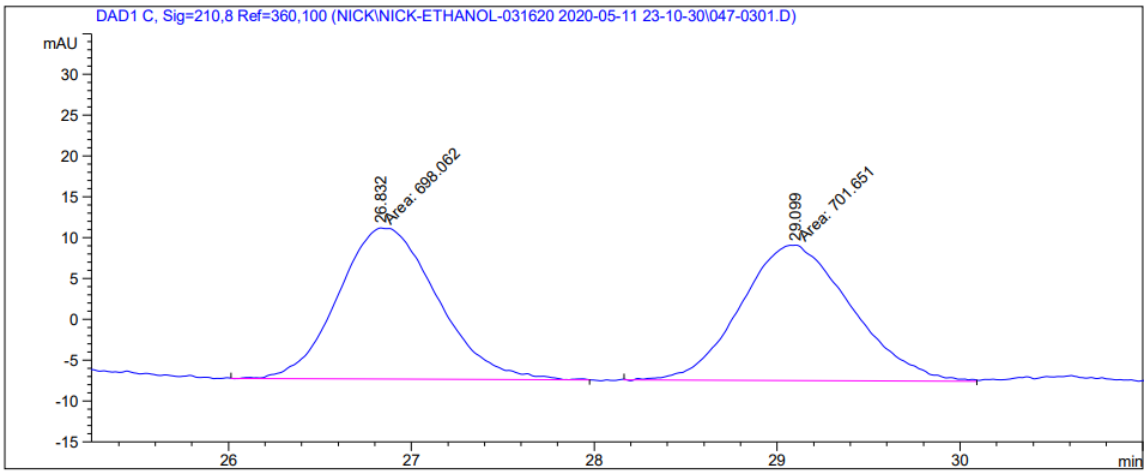
$[\alpha]_D^{28}$= -7.6 (*c* 0.20, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 230 nm), *ee* = 96%.

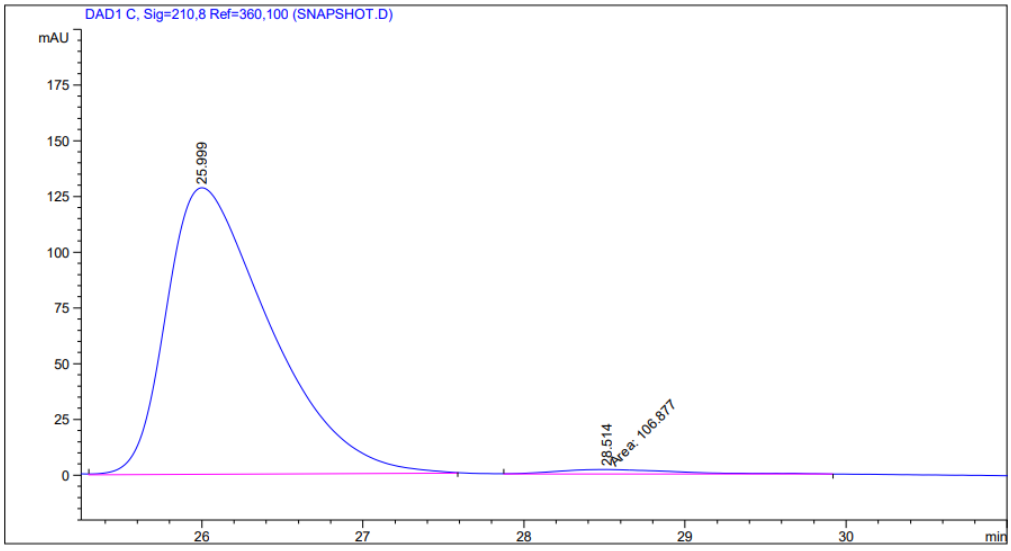
MP: 99-101 °C


f1 (ppm)
1.00
1.04
1.04
2.15
1.04
2.17
4.35
1.00
9.67
1.18
3.34
1.15


f1 (ppm)
153.00
139.04
119.70
79.44
68.62
57.18
44.28
36.59
30.80
29.24
28.65
21.82

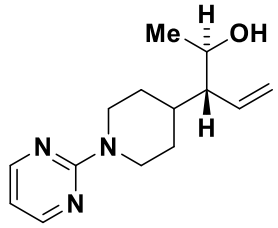


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.832	MM	0.6278	698.06165	18.53064	49.8718
2	29.099	MM	0.7027	701.65125	16.64250	50.1282



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.999	VB	0.6656	5751.09229	128.63985	98.1755
2	28.514	MM	0.8760	106.87740	2.03335	1.8245

(2R,3R)-3-(1-(pyrimidin-2-yl)piperidin-4-yl)pent-4-en-2-ol (2q)



Procedure

Allyl acetate **1q** (52.3 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using reduced loading of ethanol (35 μL, 0.60 mmol, 300 mol%) and acetone as solvent (0.200 mL, 1.0 M, 80 °C, 24 hr). The title compound was obtained in 68% yield (33.8 mg, 0.137 mmol, >20:1 dr) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 7:1–2:1).

TLC (SiO_2) R_f = 0.16 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.28 (d, *J* = 4.7 Hz, 2H), 6.43 (t, *J* = 4.7 Hz, 1H), 5.70 (dt, *J* = 17.1, 9.9 Hz, 1H), 5.24 (dd, *J* = 10.3, 2.1 Hz, 1H), 5.08 (dd, *J* = 17.2, 2.1 Hz, 1H), 4.78 (dddd, *J* = 16.3, 9.3, 4.0, 1.9 Hz, 2H), 3.95 (d, *J* = 7.2 Hz, 1H), 2.83 (dtd, *J* = 33.8, 12.8, 2.4 Hz, 2H), 1.86 – 1.69 (m, 4H), 1.59 (s, 1H), 1.38 (d, *J* = 3.9 Hz, 1H), 1.35 – 1.25 (m, 1H), 1.21 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 157.9, 136.1, 119.7, 109.4, 66.7, 57.3, 44.4, 36.9, 30.8, 29.2, 21.8.

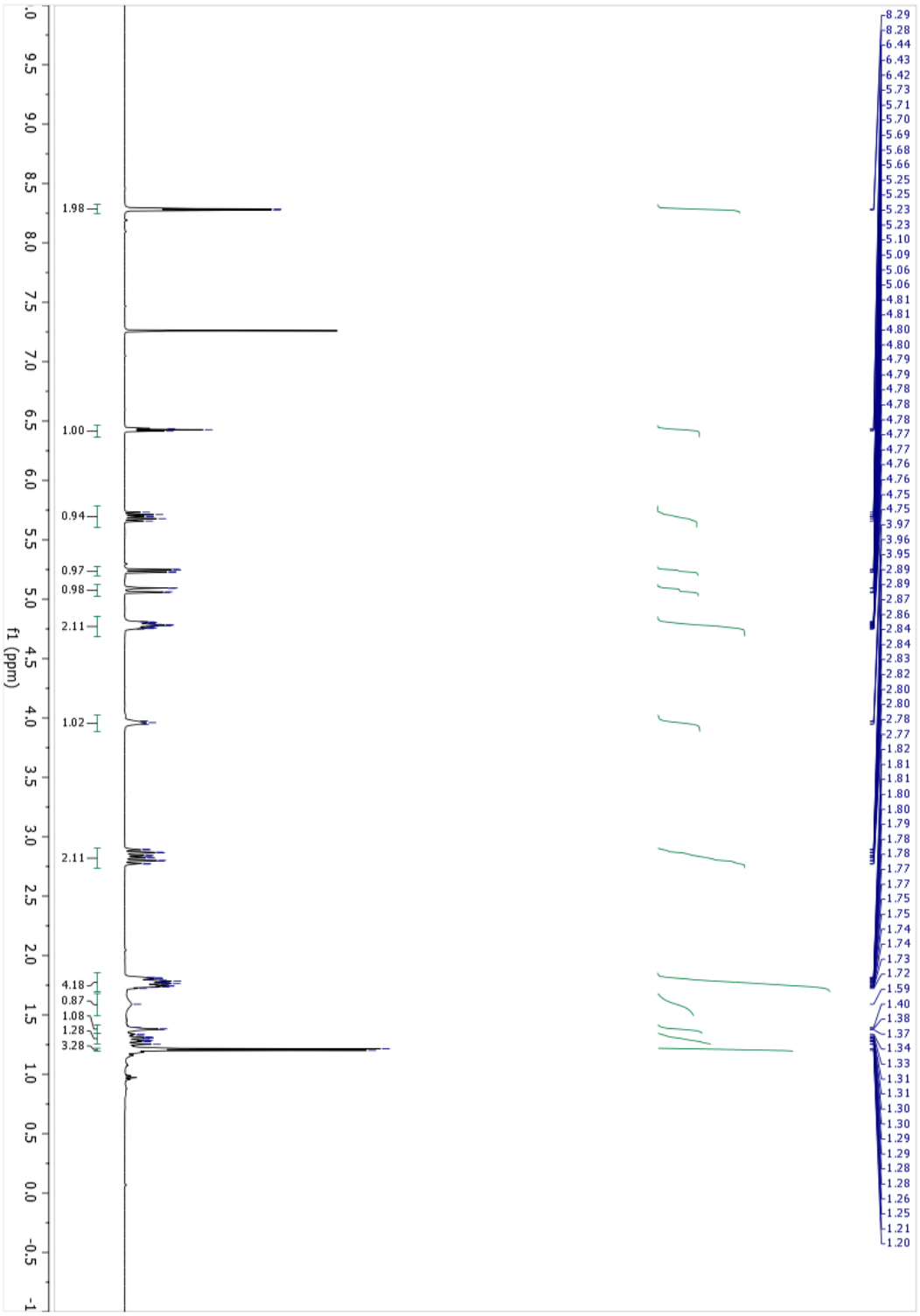
HRMS (ESI): Calculated for $C_{14}H_{21}N_3O$ [M+H$^+$] =248.1757, Found 248.1760.

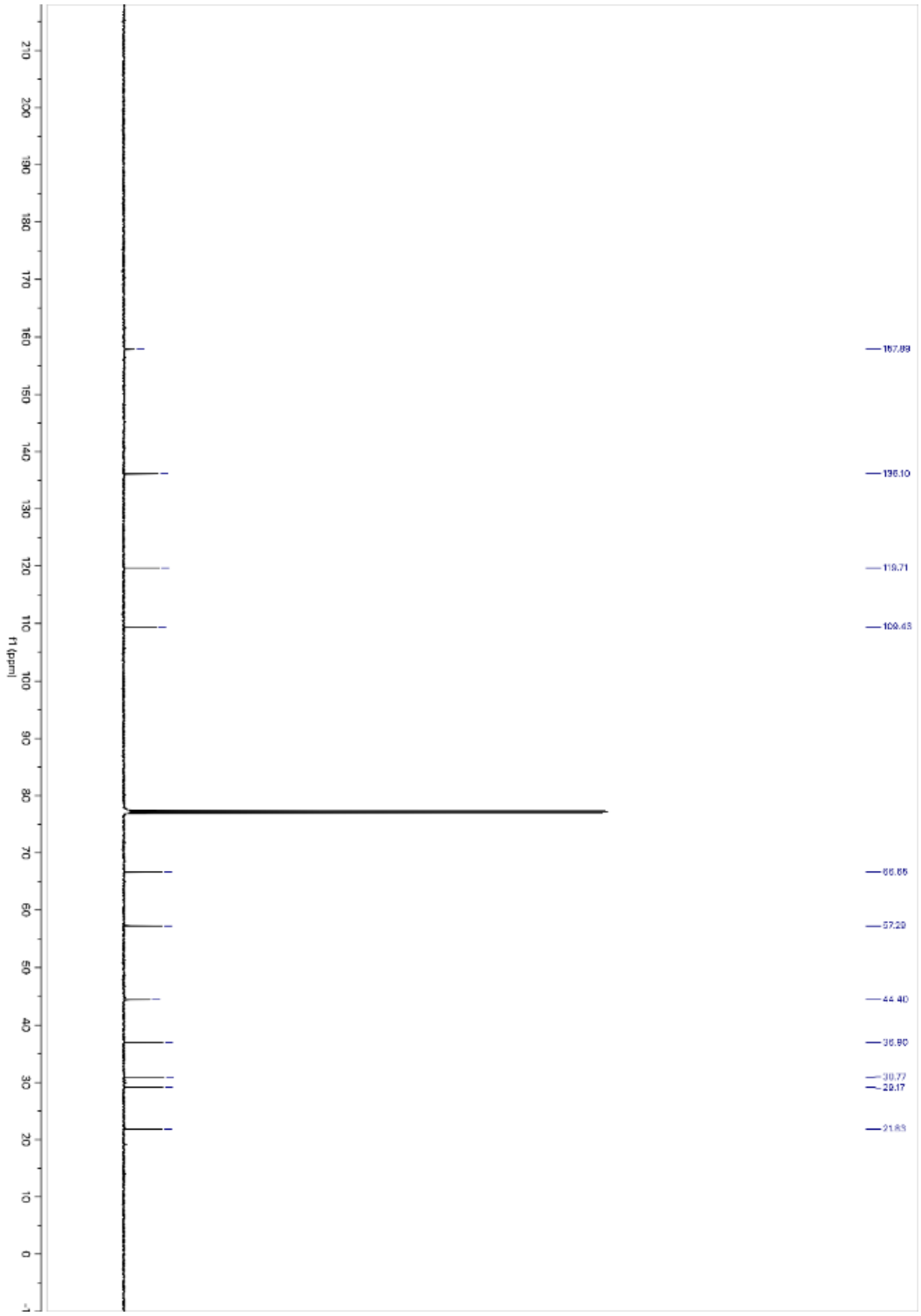
FTIR (neat): 3384, 2904, 1588, 1547, 1517, 1455, 1394, 1363, 1311, 1271, 1214, 1183, 1135, 1054, 1014, 973, 950, 918, 832, 793, 706 cm^{-1}.

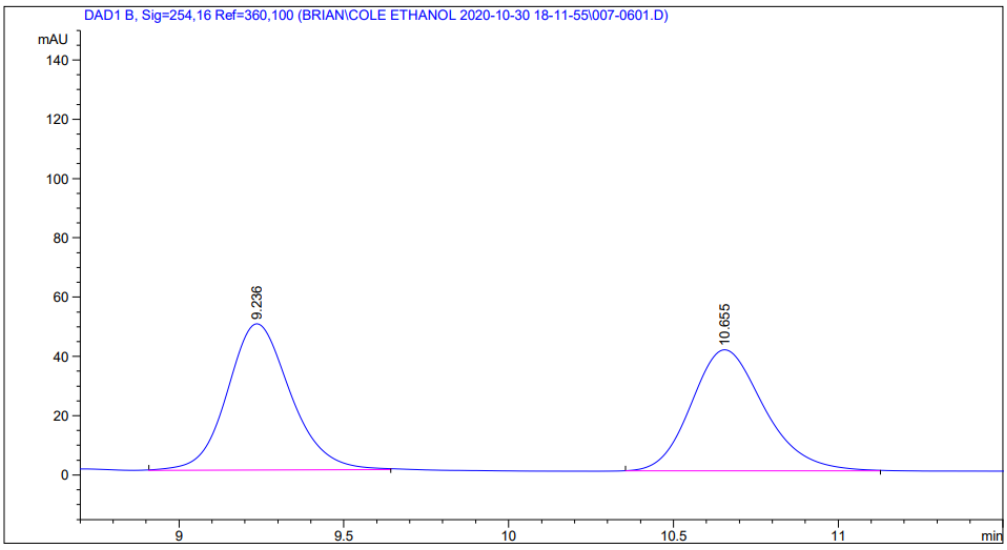
$[\alpha]_D^{28}$ = -27.5 (*c* 0.11, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), *ee* = 99%.

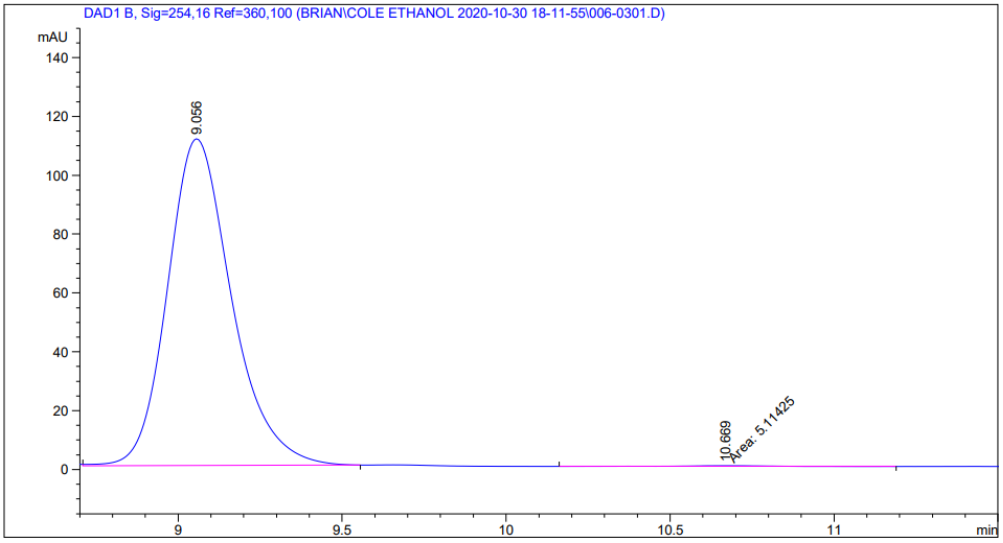
MP: 132-134 °C


f1 (ppm)
1.98
1.00
0.94
0.97
0.98
2.11
1.02
2.11
4.18
0.87
1.08
1.28
3.28


f1 (ppm)
167.89
136.10
119.71
109.48
66.66
57.29
44.40
36.90
30.77
29.17
21.83

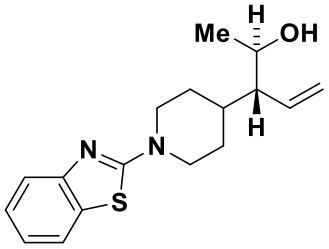


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.236	BB	0.2041	661.39594	49.43079	51.1494
2	10.655	BB	0.2361	631.67151	40.91267	48.8506



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.056	VB	0.2065	1509.00195	111.03948	99.6622
2	10.669	MM	0.3380	5.11425	2.52219e-1	0.3378

(2R,3R)-3-(1-(benzo[d]thiazol-2-yl)piperidin-4-yl)pent-4-en-2-ol (2r)



Procedure

Allyl acetate **1r** (63.3 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using reduced loading of ethanol (35 μL, 0.60 mmol, 300 mol%), acetone as solvent (0.200 mL, 1.0 M, 80 °C, 24 hr). The title compound was obtained in 65% yield (39.3 mg, 0.130 mmol, >20:1 dr) as a pale-yellow powder after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–3:1).

TLC (SiO_2) R_f = 0.28 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 5.70 (dt, *J* = 17.0, 9.9 Hz, 1H), 5.26 (dd, *J* = 10.3, 2.1 Hz, 1H), 5.09 (dd, *J* = 17.2, 2.2 Hz, 1H), 4.16 (dddd, *J* = 19.5, 15.0, 4.5, 2.2 Hz, 2H), 3.97 (q, *J* = 5.9 Hz, 1H), 3.13 (td, *J* = 12.8, 3.0 Hz, 1H), 3.07 (td, *J* = 12.8, 2.7 Hz, 1H), 1.90 – 1.80 (m, 2H), 1.77 (ddt, *J* = 16.4, 11.2, 5.0 Hz, 2H), 1.48 – 1.39 (m, 1H), 1.38 – 1.32 (m, 1H), 1.21 (d, *J* = 6.3 Hz, 3H).

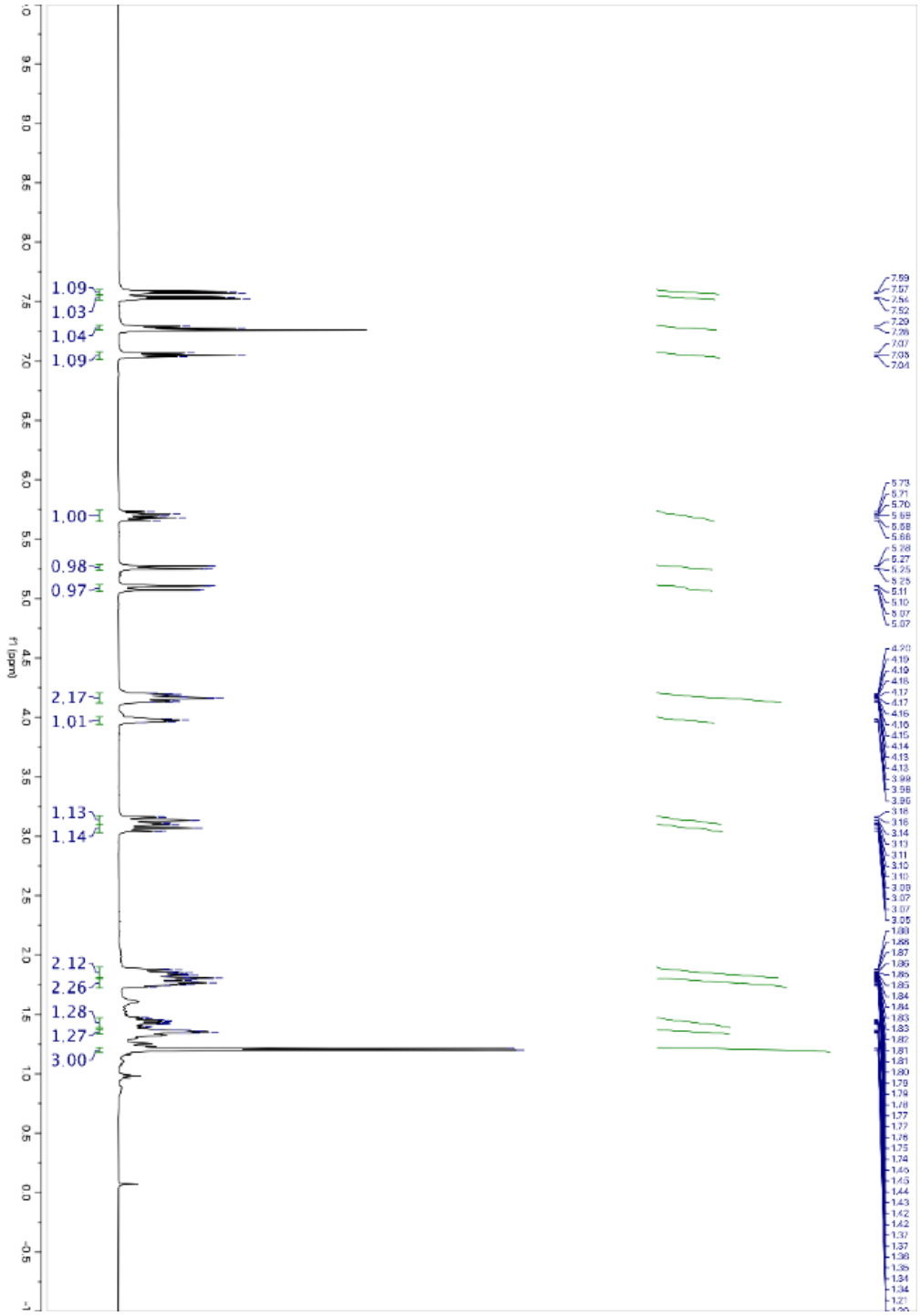
^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.8, 153.1, 135.7, 130.9, 126.1, 121.3, 120.8, 119.9, 119.0, 66.6, 56.9, 49.2, 36.4, 30.2, 29.0, 22.0.

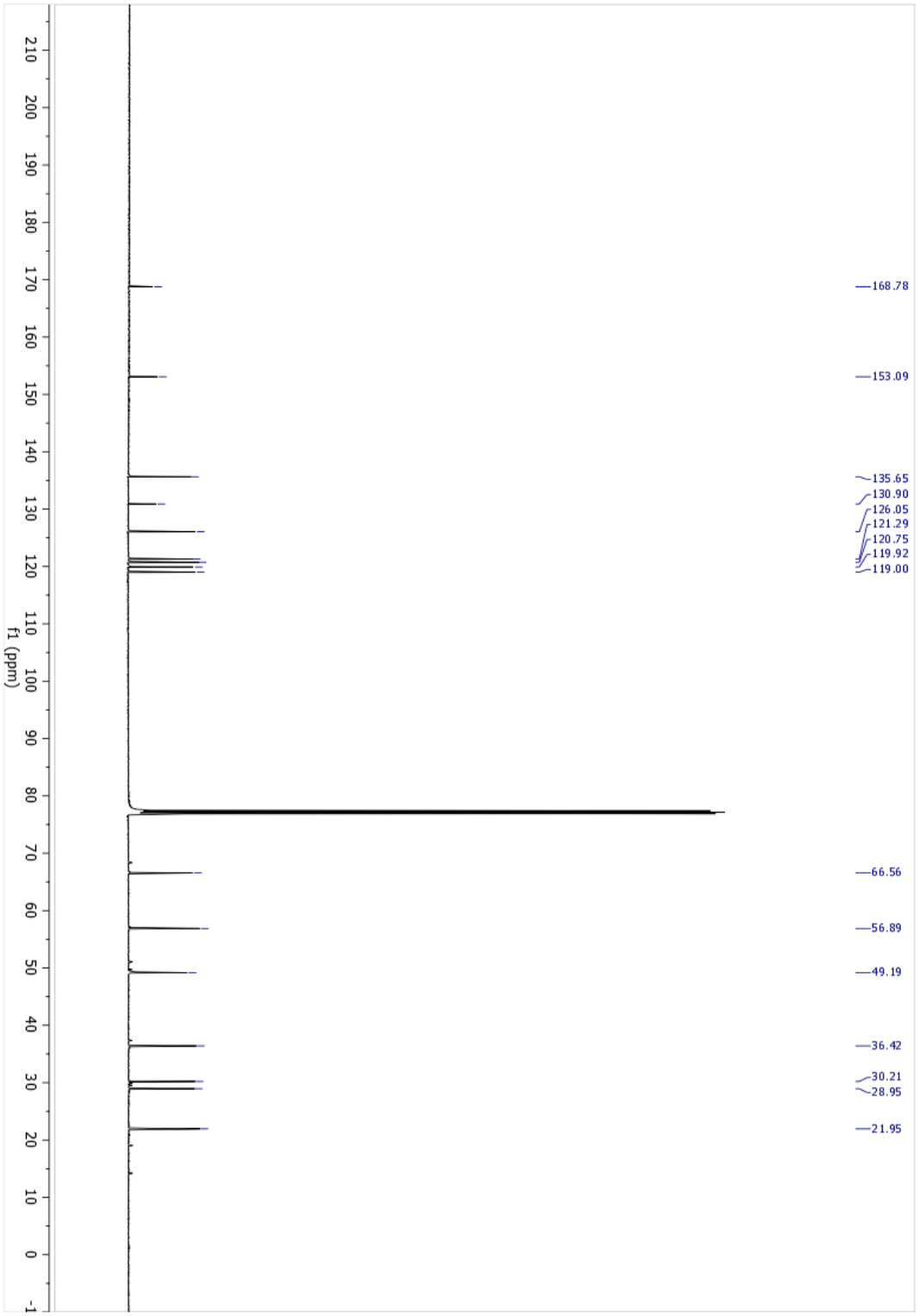
HRMS (ESI): Calculated for $C_{17}H_{22}N_2OS$ [M+H$^+$] = 303.1526, Found 303.1530.

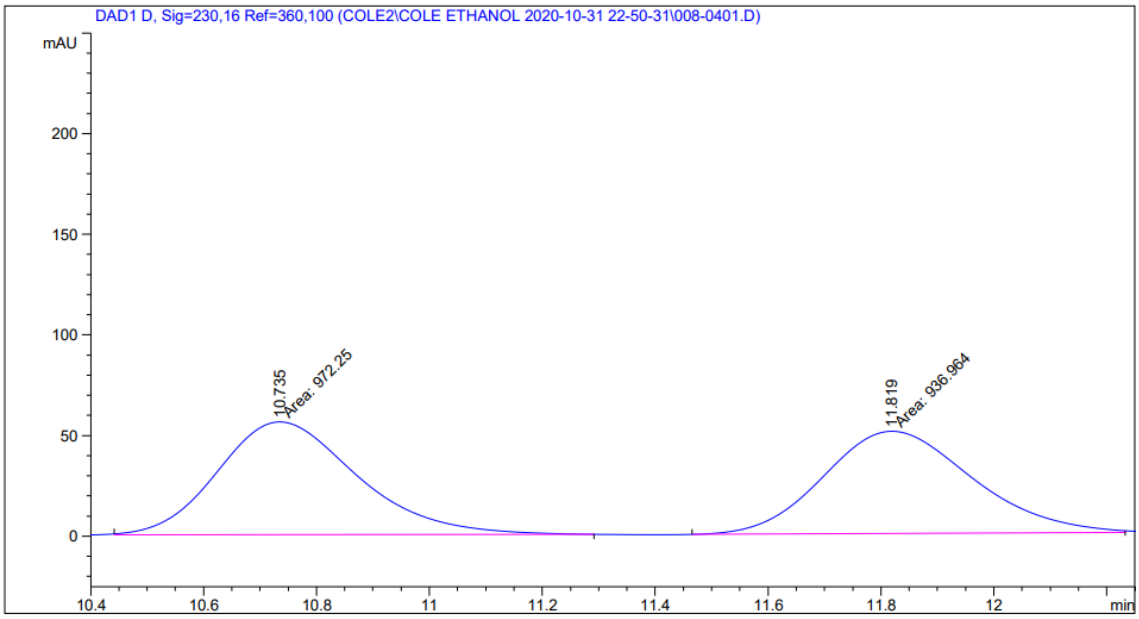
FTIR (neat): 3299, 2953, 2939, 2911, 2847, 2362, 2336, 1592, 1566, 1535, 1451, 1389, 1344, 1314, 1291, 1270, 1248, 1204, 1124, 1052, 1005, 974, 921, 855, 937, 819, 754, 728, 709 cm^{-1}.

$[\alpha]_D^{28}$= +20.8 (*c* 0.1, $CHCl_3$).

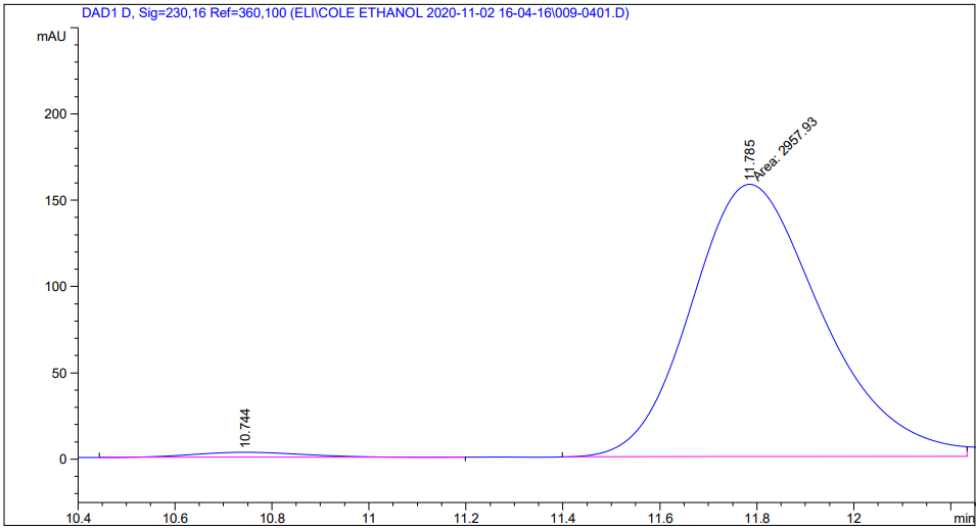
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 97%.


1.09
1.03
1.04
1.09
1.00
0.98
0.97
2.17
1.01
1.13
1.14
2.12
2.26
1.28
1.27
3.00
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
168.78
153.09
135.65
130.90
126.05
121.29
120.75
119.92
119.00
66.56
56.89
49.19
36.42
30.21
28.95
21.95

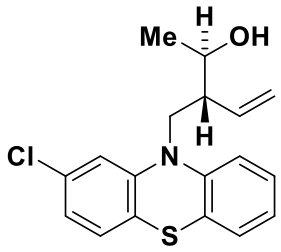


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.735	FM	0.2884	972.25031	56.19202	50.9241
2	11.819	MF	0.3068	936.96429	50.89541	49.0759



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.744	BB	0.2451	47.41357	2.95609	1.5776
2	11.785	MF	0.3123	2957.92603	157.83408	98.4224

(2*R*,3*R*)-3-((2-chloro-10*H*-phenothiazin-10-yl)methyl)pent-4-en-2-ol (2s)



Procedure

Allyl acetate **1s** (69.2 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*S*)-Ir-IV** (10.0 mg, 0.01 mmol), reduced loading of ethanol (35 μL, 0.60 mmol, 300 mol%), and acetone as solvent (0.2 mL, 1.0M, 80 °C, 36 hr). The title compound was obtained in 70% yield (46.4 mg, 0.140 mmol, 12:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.4 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.16 (td, *J* = 7.5, 1.5 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 1H), 6.96 (td, *J* = 7.5, 1.1 Hz, 2H), 6.93 – 6.92 (m, 1H), 6.91 – 6.87 (m, 1H), 5.78 (ddd, *J* = 17.3, 10.4, 8.9 Hz, 1H), 5.26 (dd, *J* = 10.4, 1.8 Hz, 1H), 5.14 (ddd, *J* = 17.2, 1.7, 0.9 Hz, 1H), 4.10 (dd, *J* = 13.7, 8.3 Hz, 1H), 4.02 (qd, *J* = 6.4, 3.4 Hz, 1H), 3.82 (dd, *J* = 13.6, 6.2 Hz, 1H), 2.67 – 2.58 (m, 1H), 1.17 (d, *J* = 6.5 Hz, 3H).

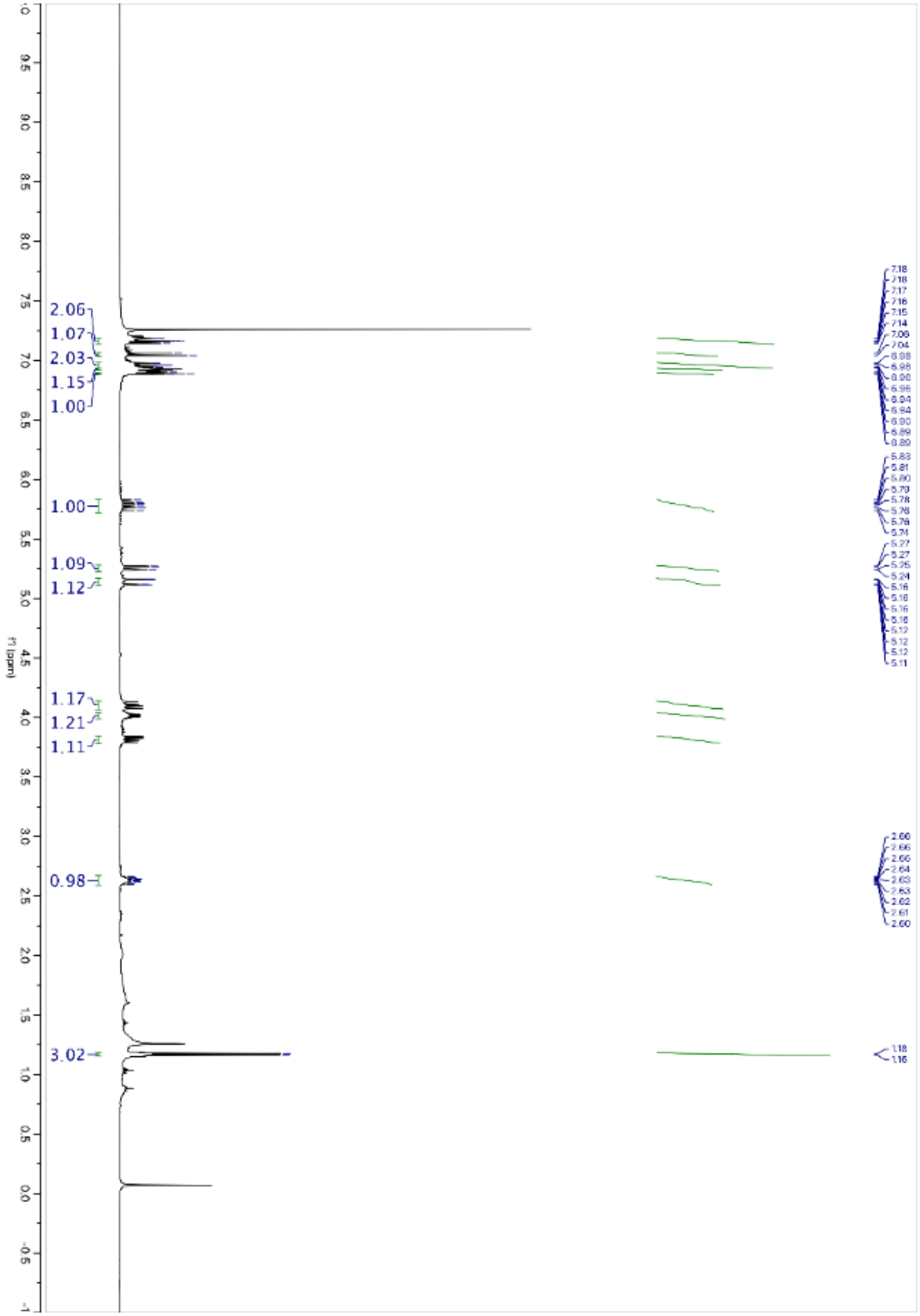
^{13}C NMR (101 MHz, $CDCl_3$) δ = 147.0, 144.9, 134.9, 133.5, 128.3, 128.0, 127.7, 125.9, 124.6, 123.3, 122.8, 119.5, 116.5, 116.4, 67.3, 48.2, 47.8, 21.4.

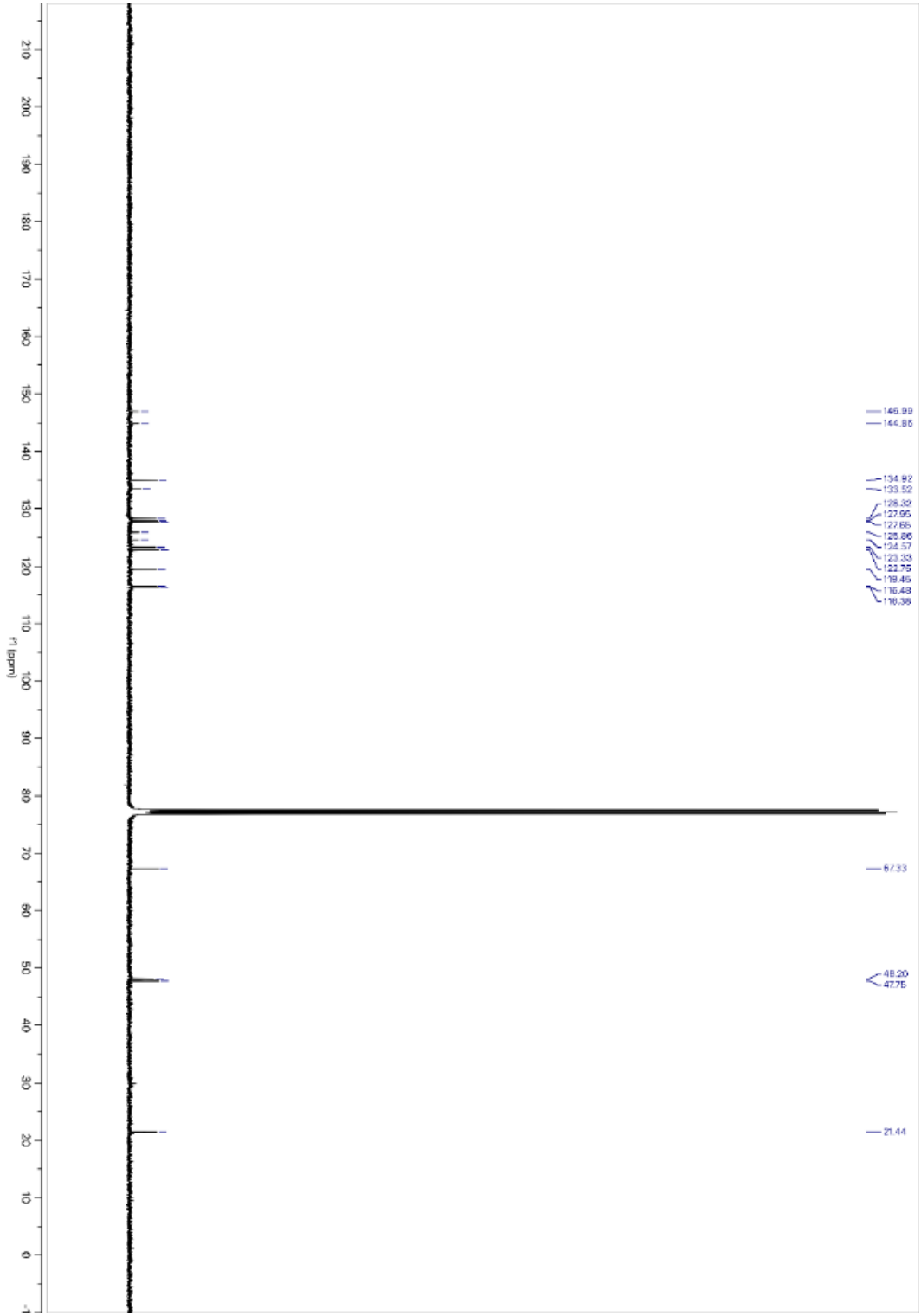
HRMS (ESI): Calculated for $C_{18}H_{18}ClNOS$ [M+H$^+$] = 332.0870, Found 332.0868.

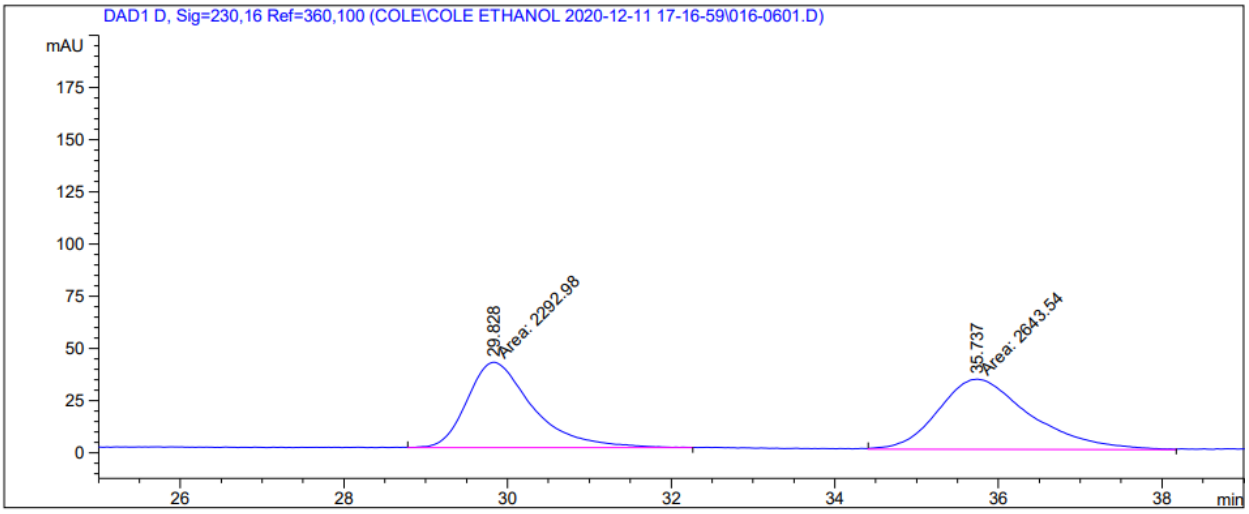
FTIR (neat): 3396, 3050, 2967, 2922, 1738, 1591, 1567, 1456, 1408, 1379, 1319, 1282, 1244, 1218, 1127, 1096, 1039, 907, 851, 802, 752 cm^{-1}.

$[\alpha]_D^{25}$= -8.2 (*c* 0.37, $CHCl_3$).

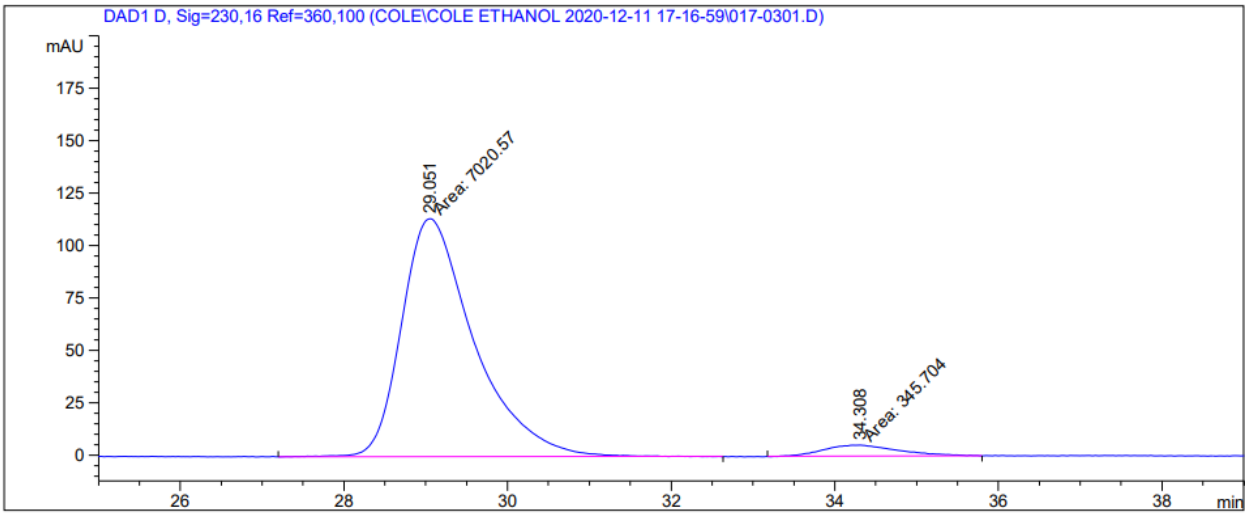
HPLC (Phenomenex Amylose-1 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 230 nm), *ee* = 91%.


2.06
1.07
2.03
1.15
1.00
1.00
1.09
1.12
1.17
1.21
1.11
0.98
3.02
f1 (ppm)


f1 (ppm)
146.99
144.86
134.92
133.52
128.32
127.95
127.66
125.86
124.57
123.33
122.75
119.45
116.48
116.38
64.33
48.20
47.75
21.44

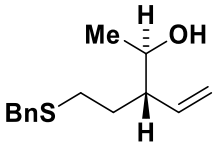


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.828	MM	0.9337	2292.98291	40.93120	46.4494
2	35.737	MM	1.3088	2643.53540	33.66444	53.5506



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.051	MM	1.0317	7020.57275	113.41743	95.3069
2	34.308	MM	1.0800	345.70361	5.33492	4.6931

(2R,3S)-3-(2-(benzylthio)ethyl)pent-4-en-2-ol (2t)



Procedure

Allyl acetate **1t** (50.1 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*S*)-Ir-IV** (10.0 mg, 0.01 mmol) and acetone as solvent (0.2 mL, 1.0M, 60 °C, 72 hr). The title compound was obtained in 63% yield (29.9 mg, 0.126 mmol, 7:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

TLC (SiO_2) R_f = 0.4 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.31 (s, 2H), 7.30 (s, 2H), 7.24 (dt, *J* = 8.8, 4.2 Hz, 1H), 5.55 (ddd, *J* = 17.2, 10.3, 9.2 Hz, 1H), 5.19 (dd, *J* = 10.2, 1.9 Hz, 1H), 5.10 (dd, *J* = 17.0, 2.0 Hz, 1H), 3.70 (s, 2H), 3.62 (p, *J* = 6.0 Hz, 1H), 2.48 (ddd, *J* = 12.9, 8.9, 4.9 Hz, 1H), 2.33 (ddd, *J* = 12.9, 8.9, 7.3 Hz, 1H), 2.11 – 2.01 (m, 1H), 1.70 (dddd, *J* = 13.2, 9.0, 7.3, 3.9 Hz, 1H), 1.54 (dddd, *J* = 13.8, 10.4, 8.7, 4.7 Hz, 2H), 1.15 (d, *J* = 6.2 Hz, 3H).

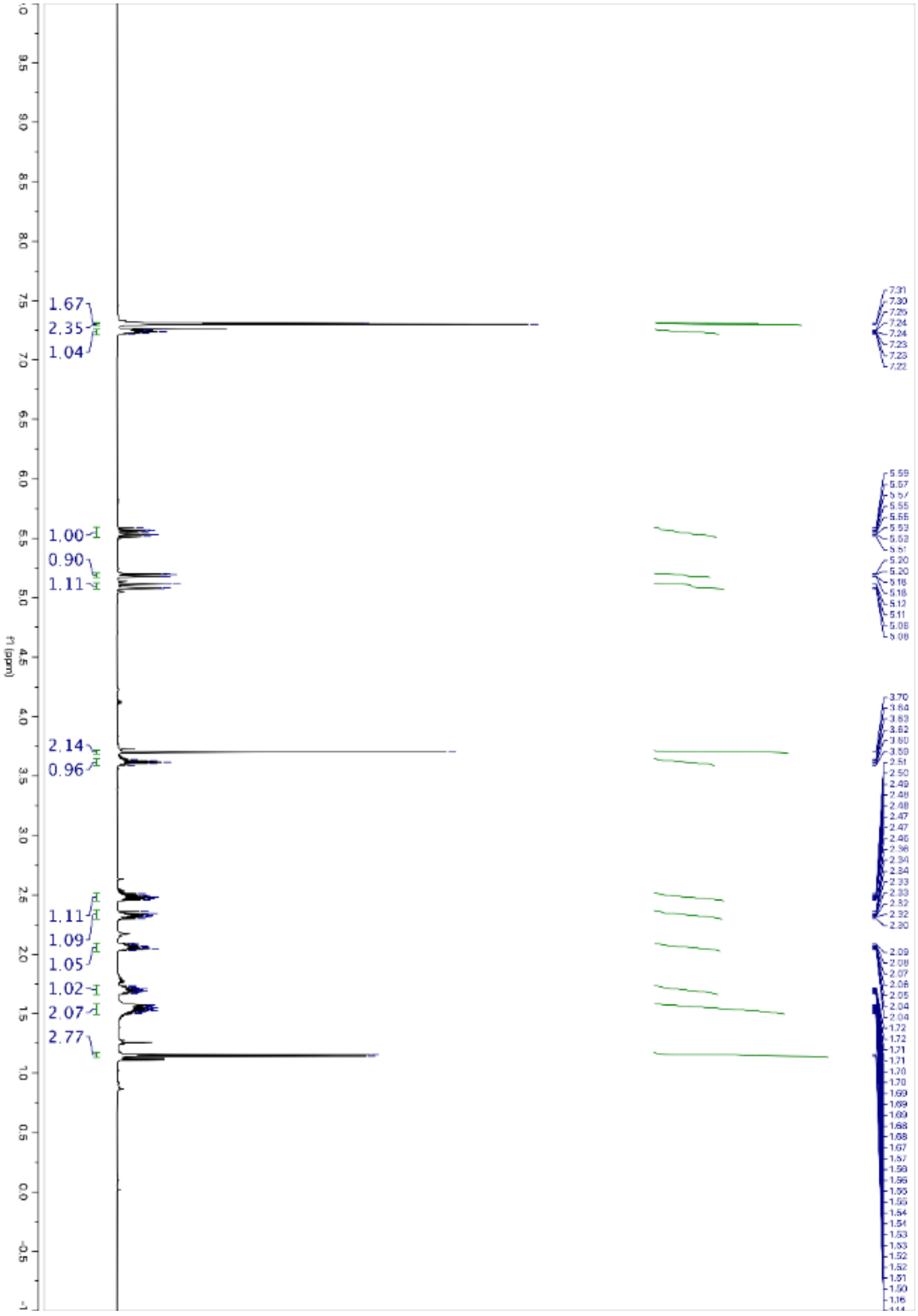
^{13}C NMR (101 MHz, $CDCl_3$) δ = 138.7, 138.0, 129.0, 128.7, 127.1, 119.2, 69.7, 51.4, 36.5, 30.3, 29.5, 20.8.

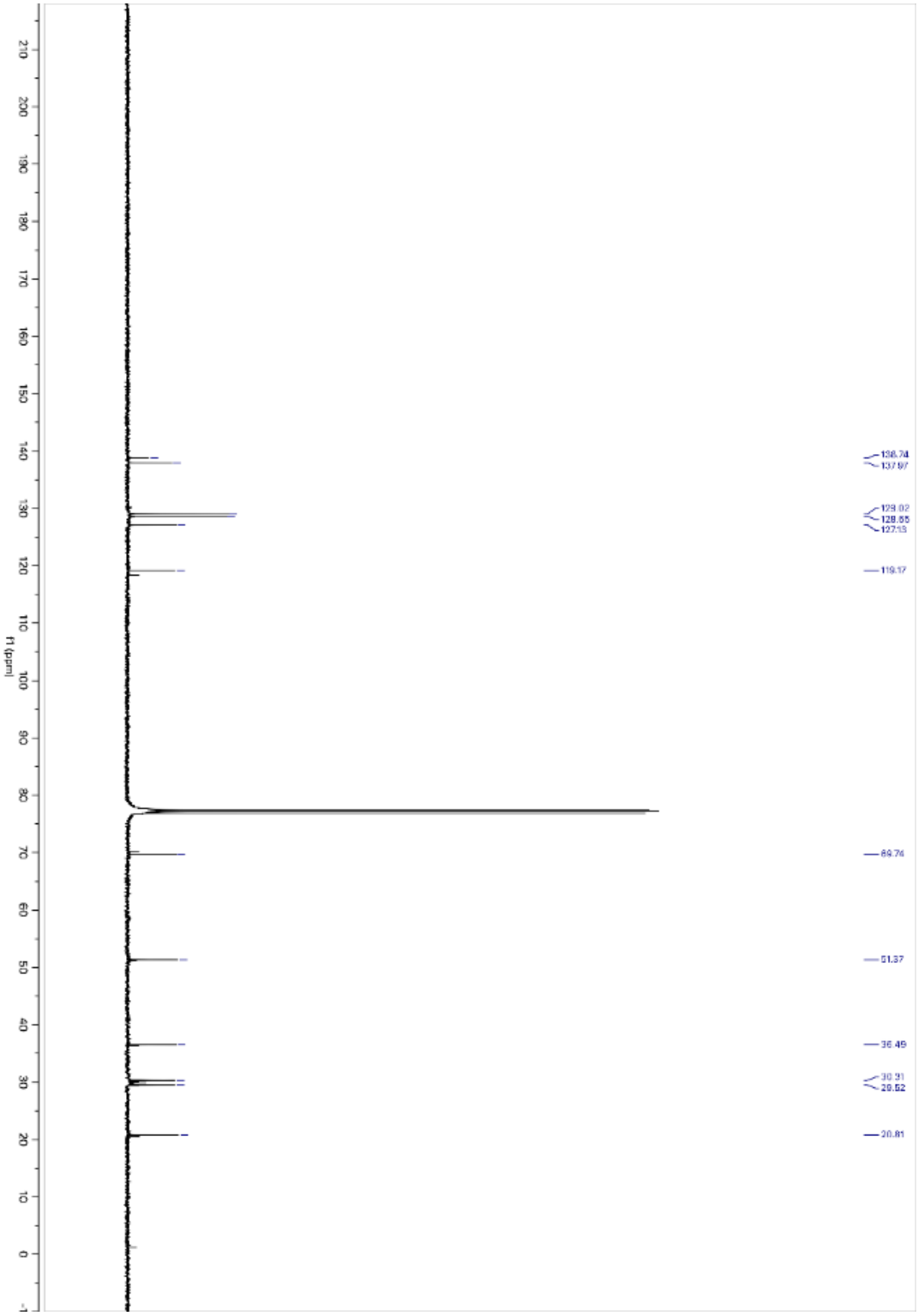
HRMS (ESI): Calculated for $C_{14}H_{20}OS$ [M+Na^+] = 259.1127, Found 259.1127.

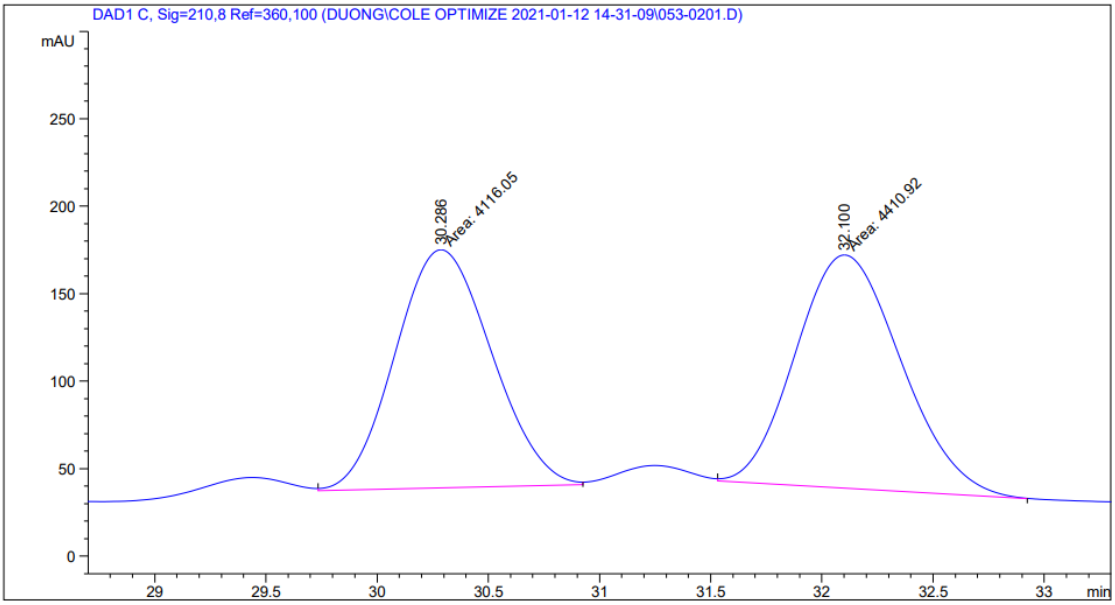
FTIR (neat): 3402, 3027, 2966, 2915, 1639, 1602, 1494, 1453, 1420, 1373, 1259, 1070, 1010, 916, 791 cm^{-1}.

$[\alpha]_D^{28}$= +16.1 (*c* 0.31, $CHCl_3$).

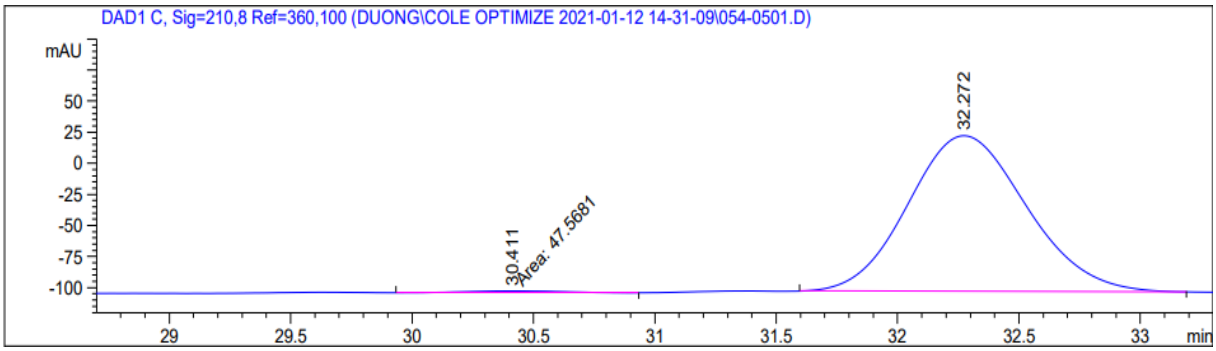
HPLC (Chiralcel AD-H column in series with a Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 98%.


1.67
2.35
1.04
1.00
0.90
1.11
2.14
0.96
1.11
1.09
1.05
1.02
2.07
2.77
f1 (ppm)


f1 (ppm)
138.74
137.97
129.02
128.65
127.13
119.17
69.74
51.37
36.49
30.31
29.52
20.81

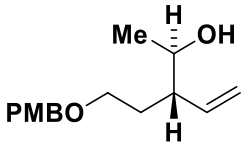


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.286	MM	0.5031	4116.04639	136.34325	48.2709
2	32.100	MM	0.5511	4410.91895	133.40161	51.7291



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.411	MM	0.4986	47.56807	1.59012	1.1031
2	32.272	BB	0.5229	4264.45557	125.34425	98.8969

(2R,3S)-3-(2-((4-methoxybenzyl)oxy)ethyl)pent-4-en-2-ol (2u)



Procedures

Allyl acetate **1u** (52.5 mg, 0.200 mmol, 100 mol%) was subjected to general procedure D (60 °C, 24 hr). The title compound was obtained in 80% yield (40.3 mg, 0.160 mmol, 6:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.15 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.75 – 5.57 (m, 1H), 5.17 (dd, *J* = 10.3, 2.0 Hz, 1H), 5.09 (dd, *J* = 17.1, 2.0 Hz, 1H), 4.47 – 4.38 (m, 2H), 3.80 (s, 3H), 3.69 (t, *J* = 6.0 Hz, 1H), 3.52 (dt, *J* = 9.5, 5.7 Hz, 1H), 3.42 (ddd, *J* = 9.2, 8.0, 5.6 Hz, 1H), 2.18 (dq, *J* = 9.2, 4.8, 4.4 Hz, 1H), 2.11 (s, 1H), 1.85 (ddt, *J* = 13.8, 7.9, 5.6 Hz, 1H), 1.59 (ddt, *J* = 14.5, 9.2, 5.6 Hz, 1H), 1.16 (d, *J* = 6.3 Hz, 3H).

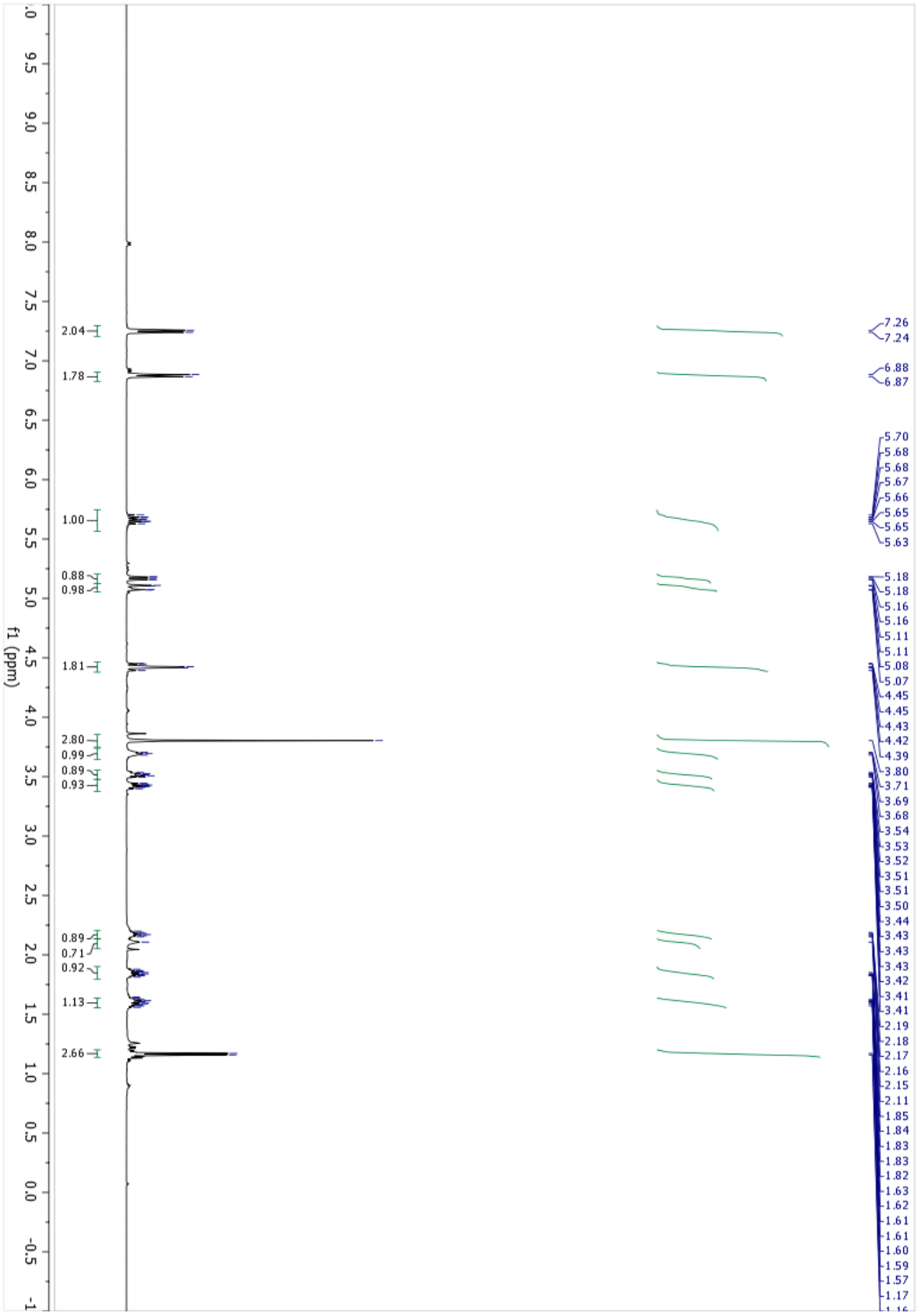
^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.3, 138.3, 130.5, 129.5, 118.2, 113.9, 72.9, 69.7, 68.2, 55.4, 49.2, 31.2, 20.6.

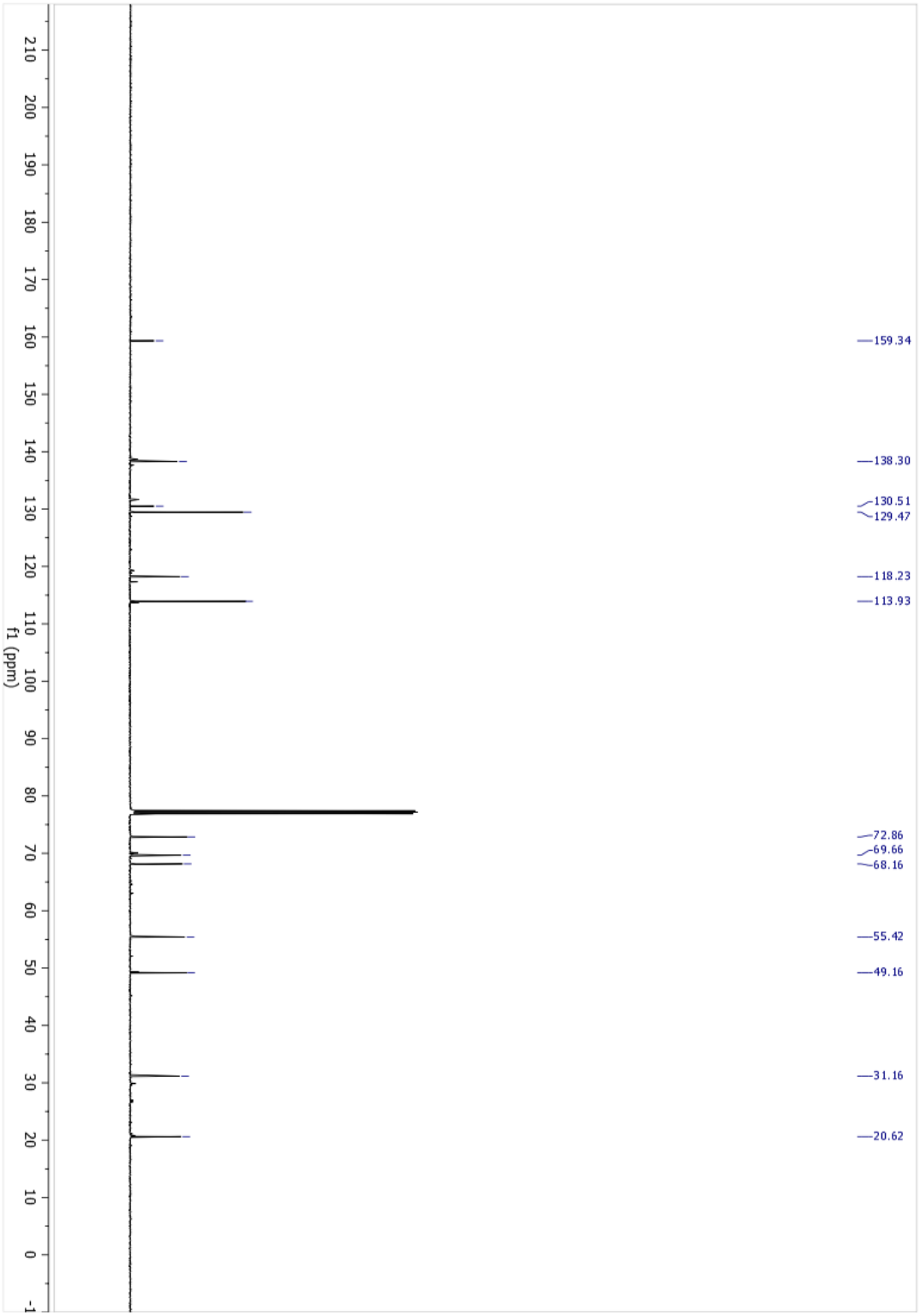
HRMS (ESI): Calculated for $C_{15}H_{22}O_3$ [M+Na^+] = 273.1461, Found 273.1466.

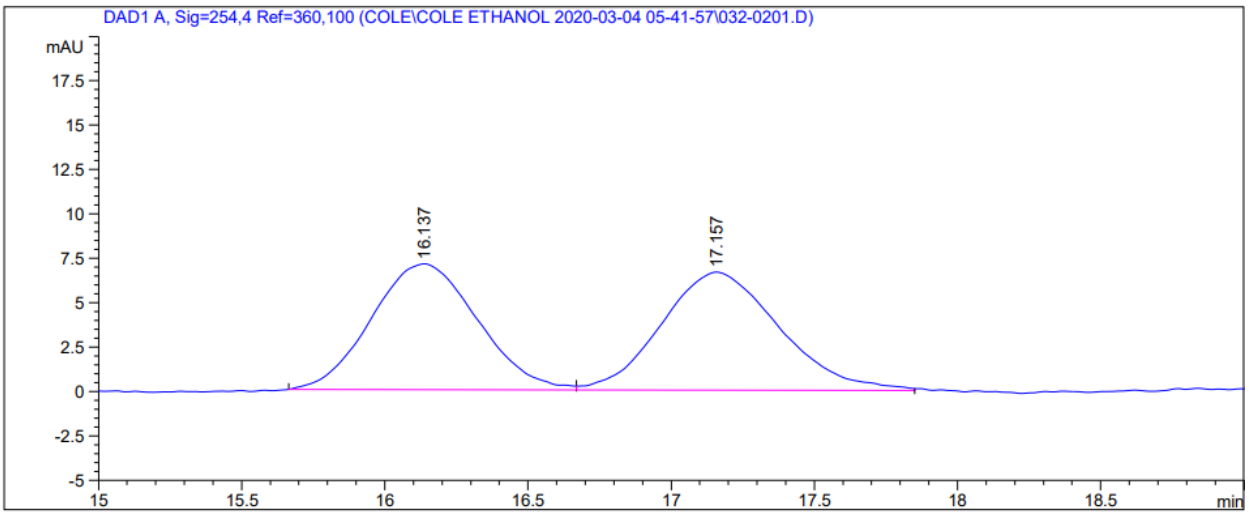
FTIR (neat): 3379, 3072, 2968, 2929, 2868, 1711, 1606, 1513, 1463, 1421, 1367, 1302, 1249, 1170, 1098, 1035, 919, 821, 772, 701 cm^{-1}.

$[\alpha]_D^{28}$= +10.5 (*c* 0.57, $CHCl_3$).

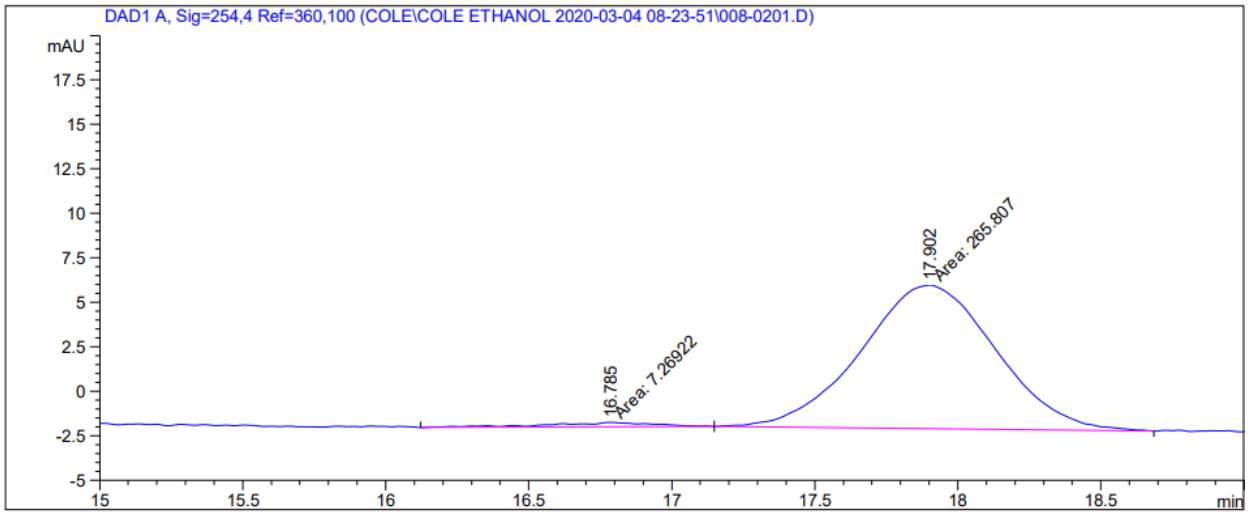
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), *ee* = 95%.


f1 (ppm)
2.04
1.78
1.00
0.88
0.98
1.81
2.80
0.99
0.89
0.93
0.89
0.71
0.92
1.13
2.66
7.26
7.24
6.88
6.87
5.70
5.68
5.68
5.67
5.66
5.65
5.65
5.63
5.18
5.18
5.16
5.16
5.11
5.11
5.08
5.07
4.45
4.45
4.43
4.42
4.39
3.80
3.71
3.69
3.68
3.54
3.53
3.52
3.51
3.51
3.50
3.44
3.43
3.43
3.43
3.42
3.41
3.41
2.19
2.18
2.17
2.16
2.15
2.11
1.85
1.84
1.83
1.83
1.82
1.63
1.62
1.61
1.61
1.60
1.59
1.57
1.17


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
159.34
138.30
130.51
129.47
118.23
113.93
72.86
69.66
68.16
55.42
49.16
31.16
20.62

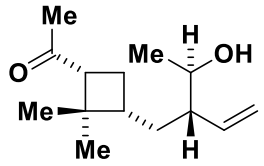


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.137	BV	0.3714	183.67256	7.11071	49.0452
2	17.157	VB	0.3699	190.82394	6.66753	50.9548



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.785	MM	0.4572	7.26922	2.64972e-1	2.6620
2	17.902	MM	0.5475	265.80673	8.09161	97.3380

1-((1R,3S)-3-((S)-2-((R)-1-hydroxyethyl)but-3-en-1-yl)-2,2-dimethylcyclobutyl)ethan-1-one (2v)



Procedure

Allyl acetate **1v** (47.7 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*S*)-Ir-IV** (10.0 mg, 0.01 mmol), reduced loading of ethanol (35 μL, 0.60 mmol, 300 mol%), and acetone as solvent (0.2 mL, 1.0M, 80 °C, 16 hr). The title compound was obtained in 80% yield (36 mg, 0.16 mmol, 5:1 dr) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–5:1).

TLC (SiO_2) R_f = 0.3 (hexanes: ethyl acetate = 2:1).

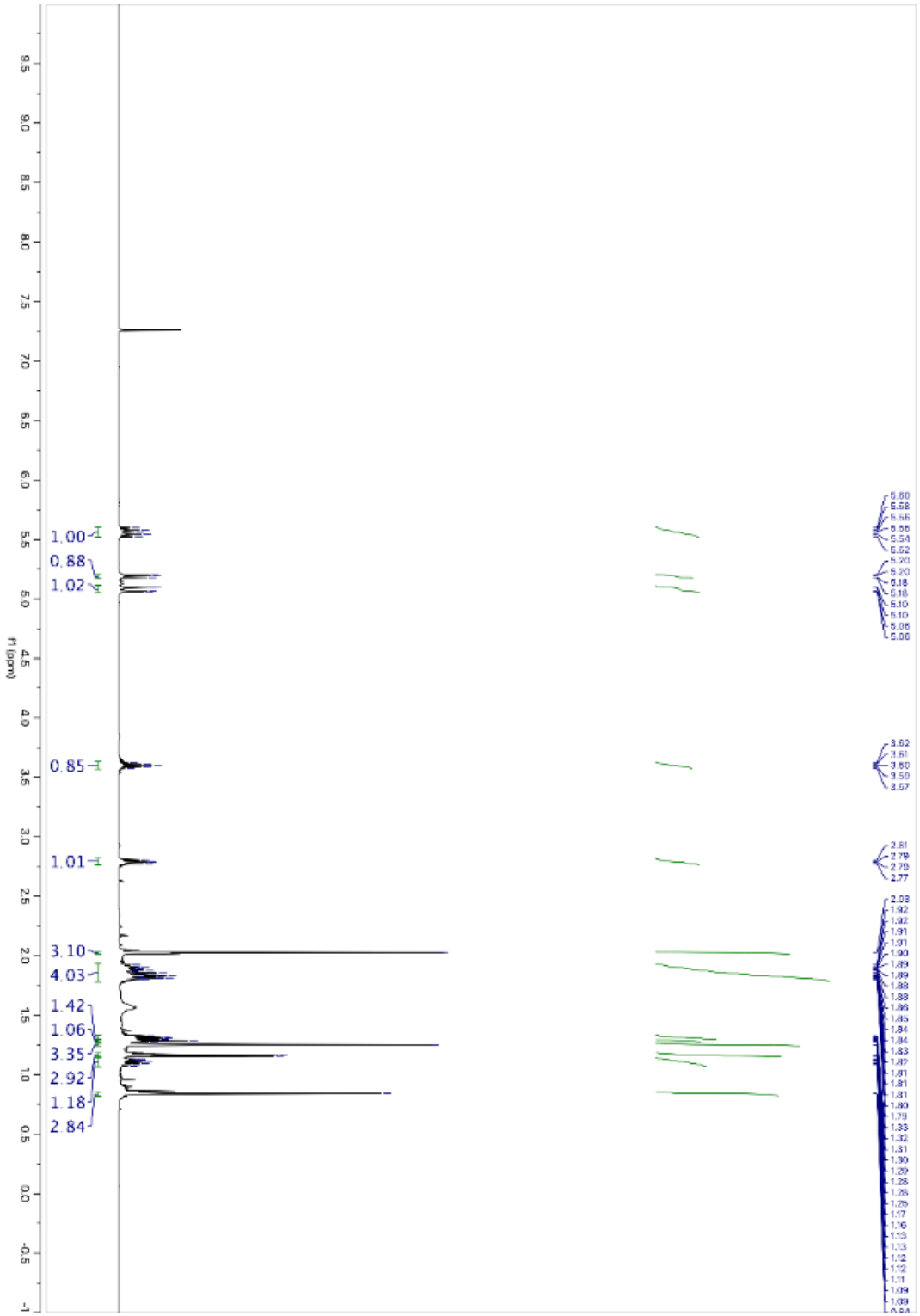
^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.56 (dt, *J* = 17.2, 9.8 Hz, 1H), 5.19 (dd, *J* = 10.3, 2.1 Hz, 1H), 5.08 (dd, *J* = 17.2, 2.1 Hz, 1H), 3.60 (p, *J* = 6.2 Hz, 1H), 2.79 (dd, *J* = 9.7, 7.6 Hz, 1H), 2.03 (s, 3H), 1.94 – 1.78 (m, 4H), 1.31 (dd, *J* = 9.7, 4.5 Hz, 1H), 1.29 – 1.27 (m, 1H), 1.25 (s, 3H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.10 (tt, *J* = 11.8, 5.7 Hz, 1H), 0.84 (s, 3H).

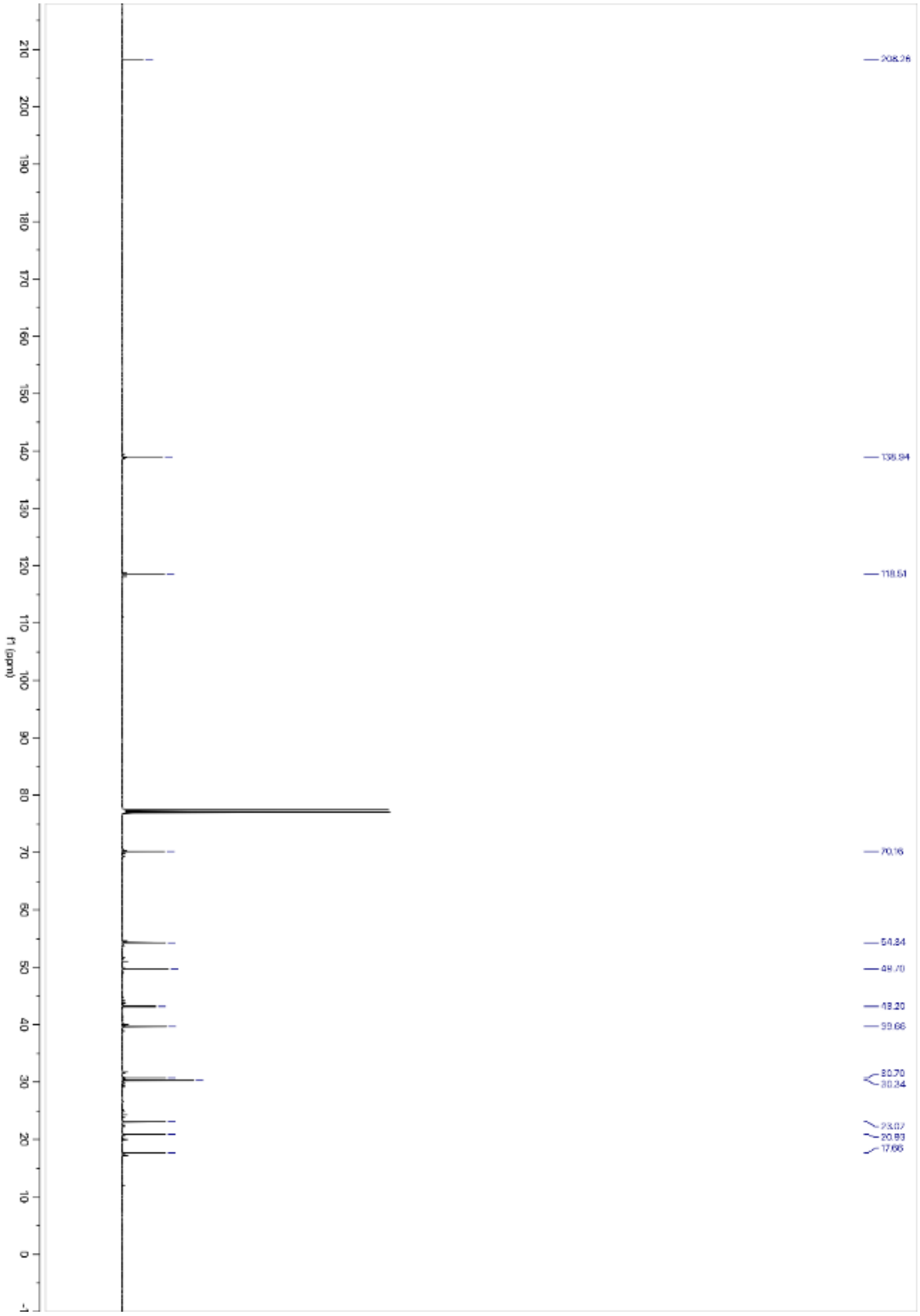
^{13}C NMR (126 MHz, $CDCl_3$) δ = 208.3, 138.9, 118.5, 70.2, 54.3, 49.7, 43.2, 39.7, 30.7, 30.3, 23.1, 20.9, 17.7.

HRMS (ESI): Calculated for $C_{14}H_{24}O_2$ [M+Na^+] = 247.1669, Found 247.1678.

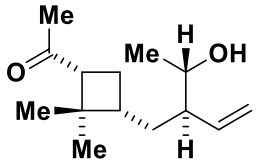
FTIR (neat): 3451, 3069, 2963, 1702, 1639, 1462, 1421, 1385, 1368, 1358, 1287, 1223, 1181, 1153, 1128, 1046, 1002, 941, 911, 704 cm^{-1}.

$[\alpha]_D^{28}$= -10.7 (*c* 0.19, $CHCl_3$).


f1 (ppm)
1.00
0.88
1.02
0.85
1.01
3.10
4.03
1.42
1.06
3.35
2.92
1.18
2.84


f1 (ppm)
208.26
138.94
118.51
70.16
54.84
49.70
43.20
39.66
30.70
30.34
23.07
20.93
17.66

1-((1R,3S)-3-((R)-2-((S)-1-hydroxyethyl)but-3-en-1-yl)-2,2-dimethylcyclobutyl)ethan-1-one (*iso*-2v)



Procedure

Allyl acetate **1v** (47.7 mg, 0.200 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*R*)-Ir-IV** (10.0 mg, 0.01 mmol), reduced loading of ethanol (35 μL, 0.60 mmol, 300 mol%), and acetone as solvent (0.2 mL, 1.0M, 80 °C, 16 hr). The title compound was obtained in 71% yield (31.8 mg, 0.142 mmol, 8:1 dr) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–5:1).

TLC (SiO_2) R_f = 0.29 (hexanes: ethyl acetate = 2:1).

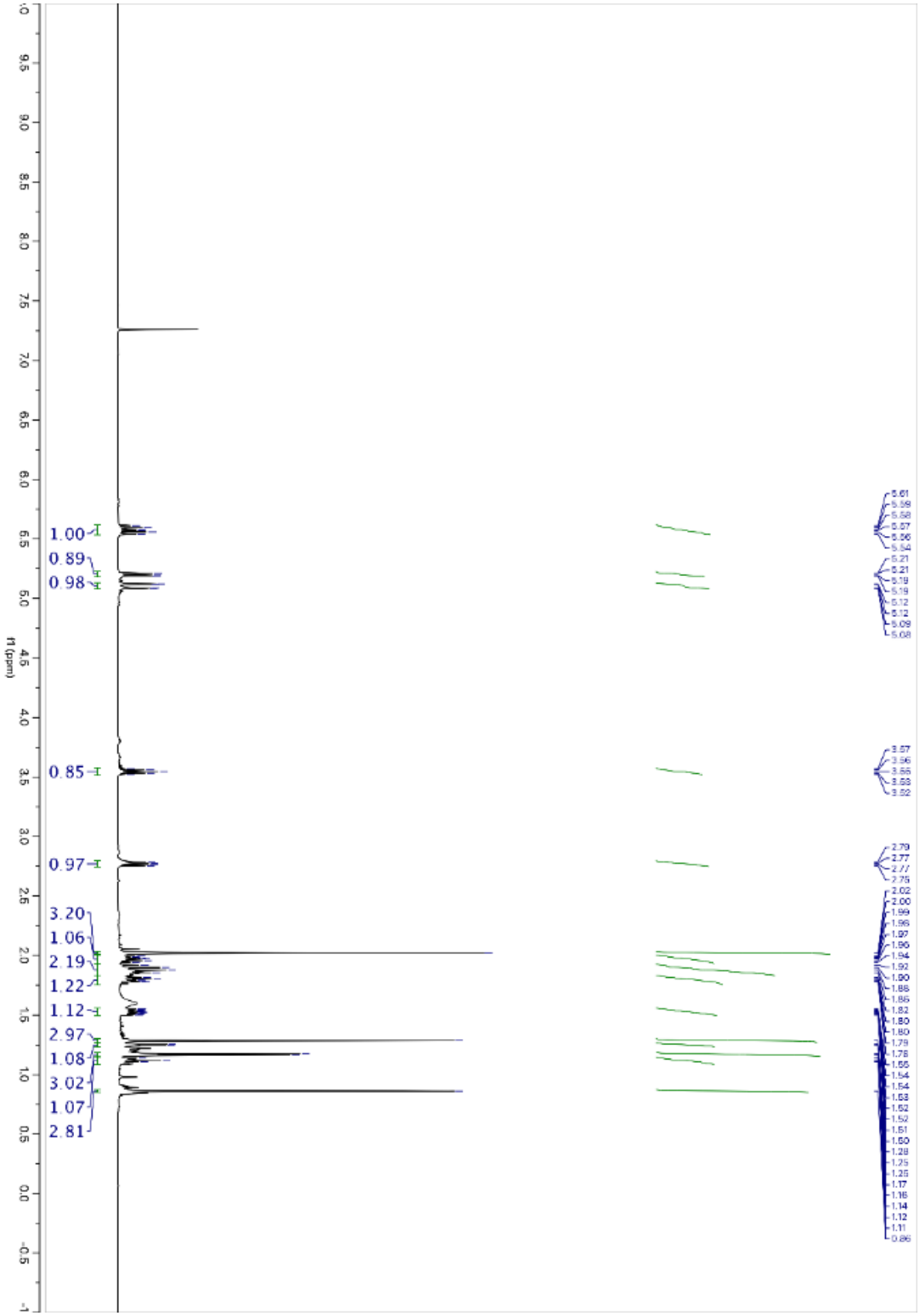
^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.58 (dt, *J* = 17.1, 9.8 Hz, 1H), 5.20 (dd, *J* = 10.3, 2.0 Hz, 1H), 5.10 (dd, *J* = 17.3, 2.0 Hz, 1H), 3.55 (p, *J* = 6.2 Hz, 1H), 2.77 (dd, *J* = 10.2, 7.4 Hz, 1H), 2.02 (s, 3H), 2.01 – 1.93 (m, 1H), 1.89 (m, *J* = 10.6 Hz, 2H), 1.82 – 1.74 (m, 1H), 1.53 (ddd, *J* = 13.7, 7.7, 3.8 Hz, 1H), 1.28 (s, 3H), 1.25 (d, *J* = 1.8 Hz, 1H), 1.17 (d, *J* = 6.2 Hz, 3H), 1.17 – 1.06 (m, 1H), 0.86 (s, 3H).

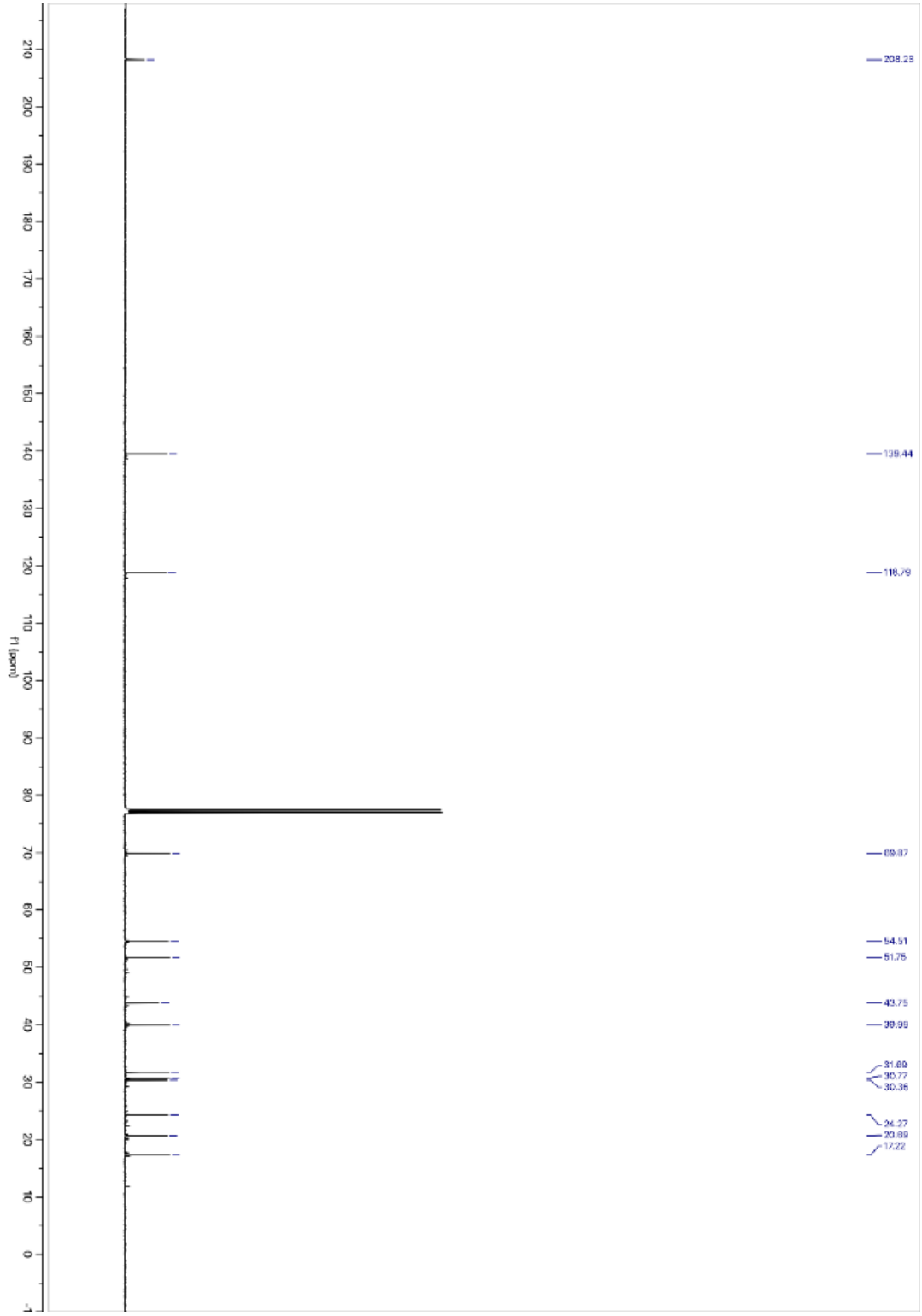
^{13}C NMR (126 MHz, $CDCl_3$) δ = 208.2, 139.4, 118.8, 69.9, 54.5, 51.8, 43.8, 40.00, 31.7, 30.8, 30.4, 24.3, 20.7, 17.2.

HRMS (ESI): Calculated for $C_{14}H_{24}O_2$ [M+Na^+] = 247.1669, Found 247.1673.

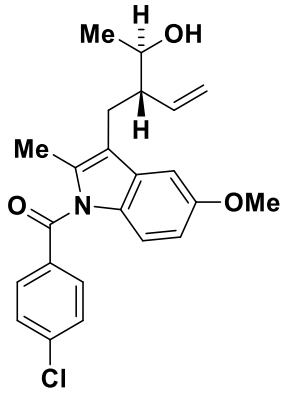
FTIR (neat): 3435, 3076, 2953, 2920, 2358, 1701, 1639, 1453, 1421, 1368, 1357, 1286, 1224, 1181, 1152, 1101, 1034, 1001, 910, 850, 706 cm^{-1}.

$[\alpha]_D^{28}$ = -23.9 (*c* 0.21, $CHCl_3$).


f1 (ppm)
1.00
0.89
0.98
0.85
0.97
3.20
1.06
2.19
1.22
1.12
2.97
1.08
3.02
1.07
2.81


f1 (ppm)
208.23
139.44
118.79
69.87
54.51
51.75
43.75
39.99
31.69
30.77
30.36
24.27
20.89
17.22

(2R,3R)-3-((4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl)methyl)pent-4-en-2-ol (2w)



Procedures

Allyl acetate **1w** (41.2 mg, 0.10 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*S*)-Ir-IV** (5.0 mg, 0.005 mmol), reduced loading of potassium carbonate (6.9 mg, 0.050 mmol, 50 mol%), ethanol (17.5 μL, 0.30 mmol, 300 mol%), and acetone as solvent (0.1 mL, 1.0M, 60 °C, 24 hr). The title compound was obtained in 58% yield (23.3 mg, 0.058 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–3:1).

TLC (SiO_2) R_f = 0.20 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 – 7.61 (m, 2H), 7.48 – 7.44 (m, 2H), 6.95 (d, *J* = 2.5 Hz, 1H), 6.92 (d, *J* = 9.0 Hz, 1H), 6.66 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.82 (ddd, *J* = 17.1, 10.3, 9.0 Hz, 1H), 5.15 (dd, *J* = 10.3, 1.9 Hz, 1H), 5.03 (dd, *J* = 17.2, 1.9 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 1H), 2.94 (dd, *J* = 14.1, 6.9 Hz, 1H), 2.66 (dd, *J* = 14.2, 7.9 Hz, 1H), 2.36 (td, *J* = 7.6, 4.2 Hz, 1H), 2.31 (s, 3H), 1.44 (d, *J* = 4.7 Hz, 1H), 1.25 (d, *J* = 6.3 Hz, 3H).

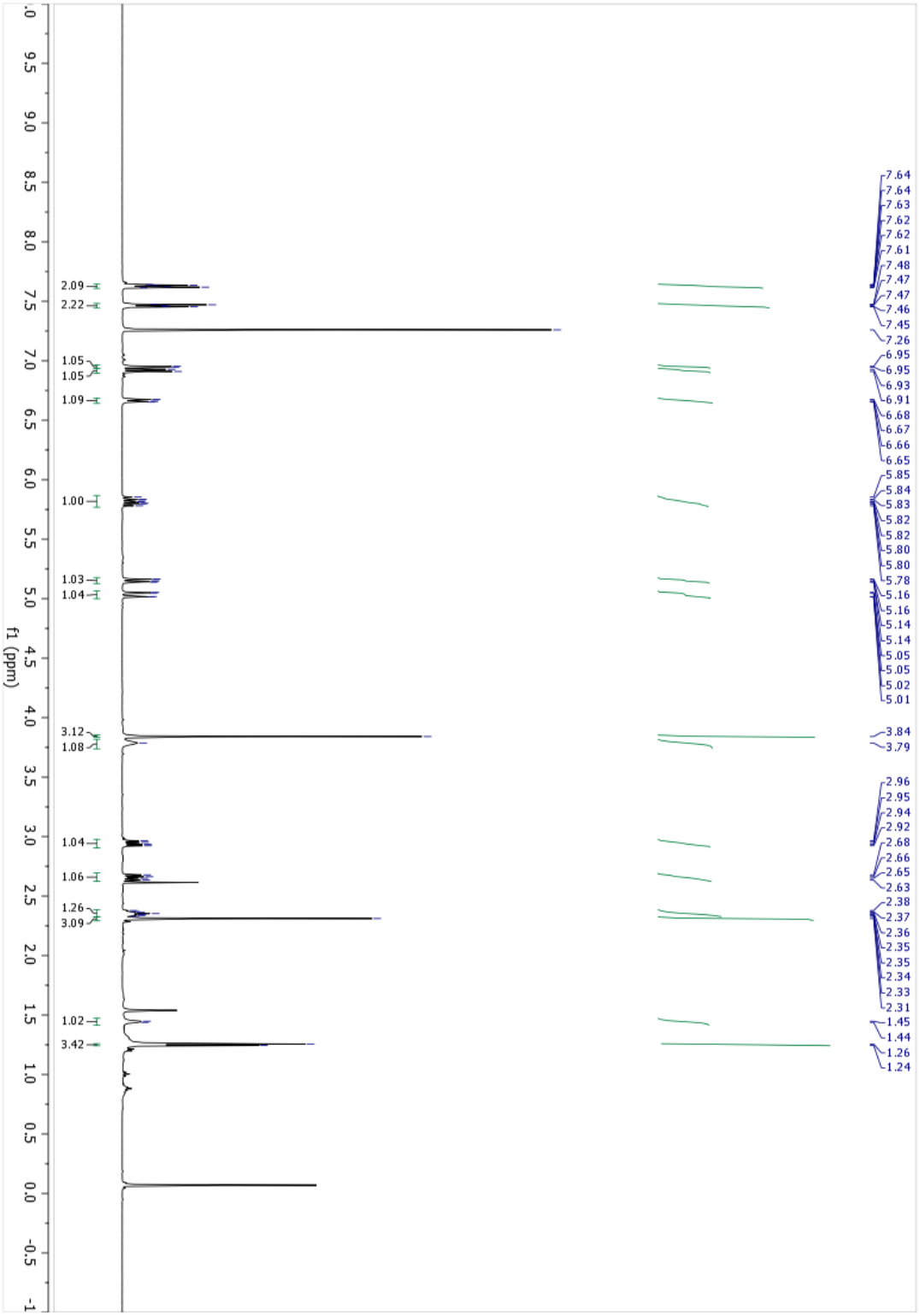
^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.5, 156.0, 139.2, 137.7, 135.0, 134.4, 131.6, 131.2, 129.2, 129.2, 118.4, 118.1, 115.1, 110.9, 102.0, 68.7, 55.9, 51.5, 26.0, 21.6, 13.8.

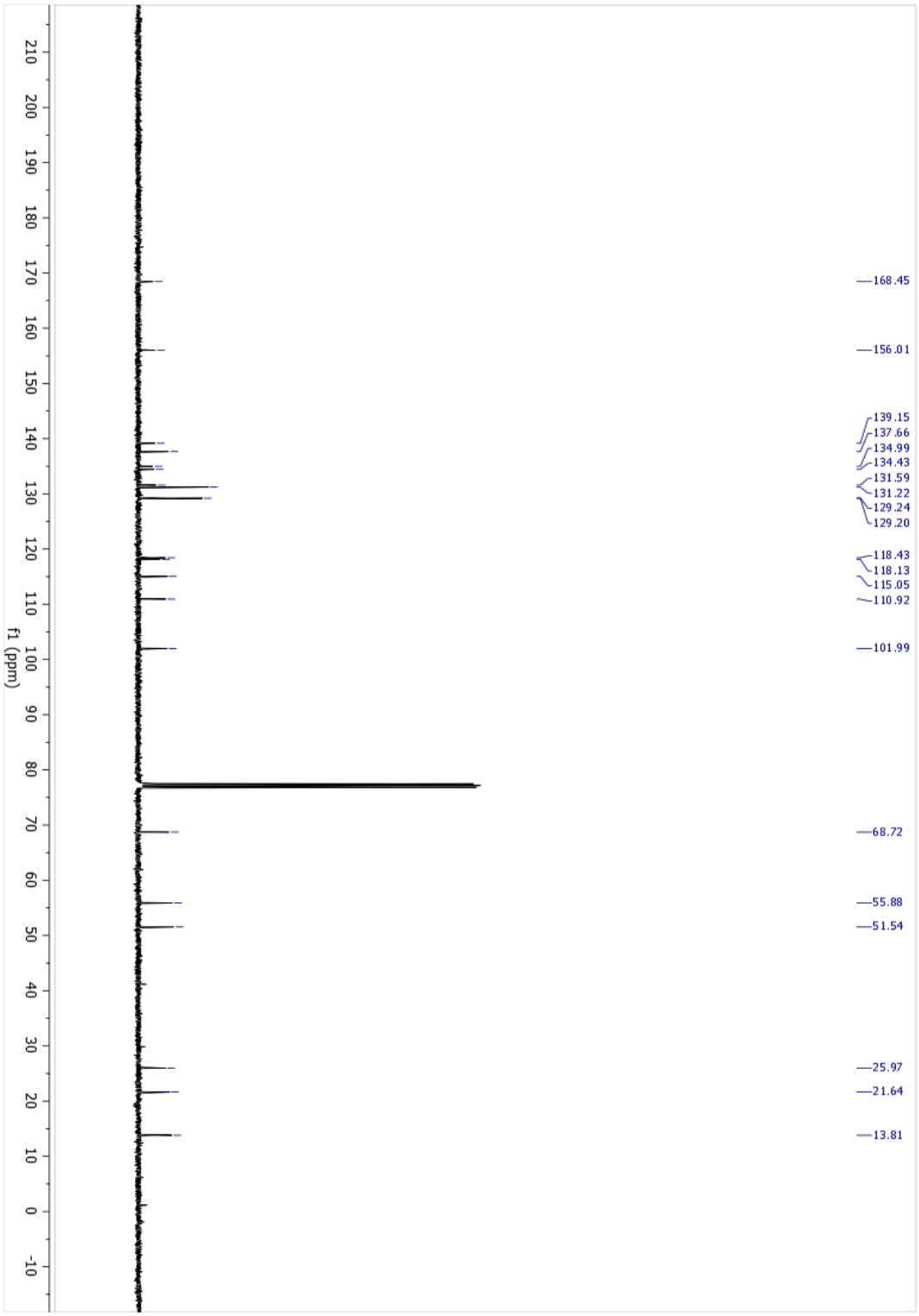
HRMS (ESI): Calculated for $C_{23}H_{24}ClNO_3$ [M+Na^+] = 420.1337, Found 420.1348.

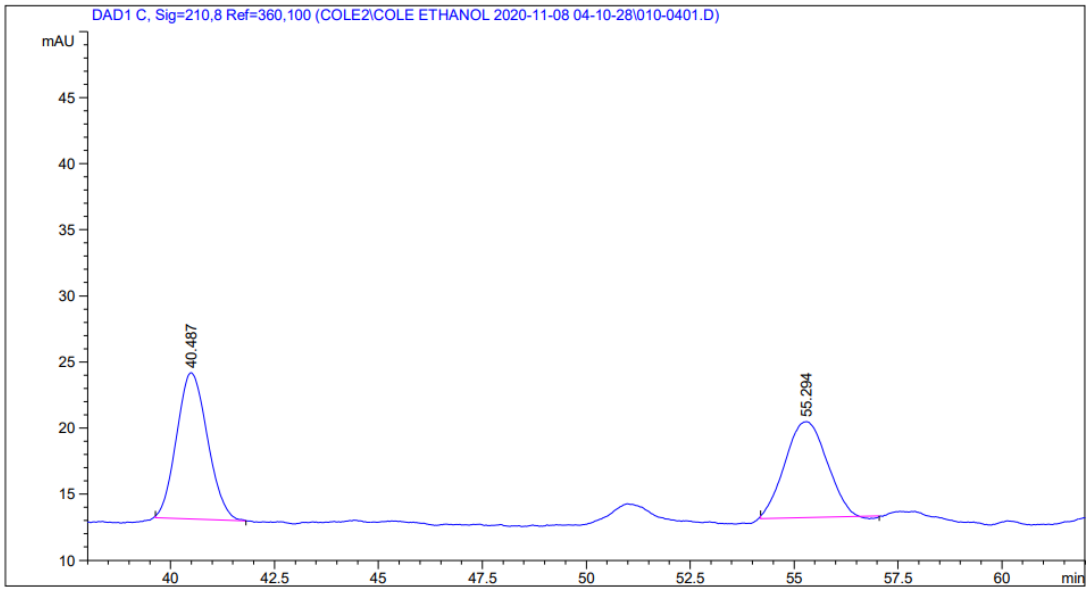
FTIR (neat): 3470, 3076, 2965, 2929, 1678, 1595, 1477, 1455, 1400, 1371, 1358, 1325, 1288, 1261, 1228, 1179, 1154, 1089, 1065, 1035, 1014, 924, 833, 802, 755 cm^{-1}.

$[\alpha]_D^{28}$ = +8.3 (*c* 0.18, $CHCl_3$).

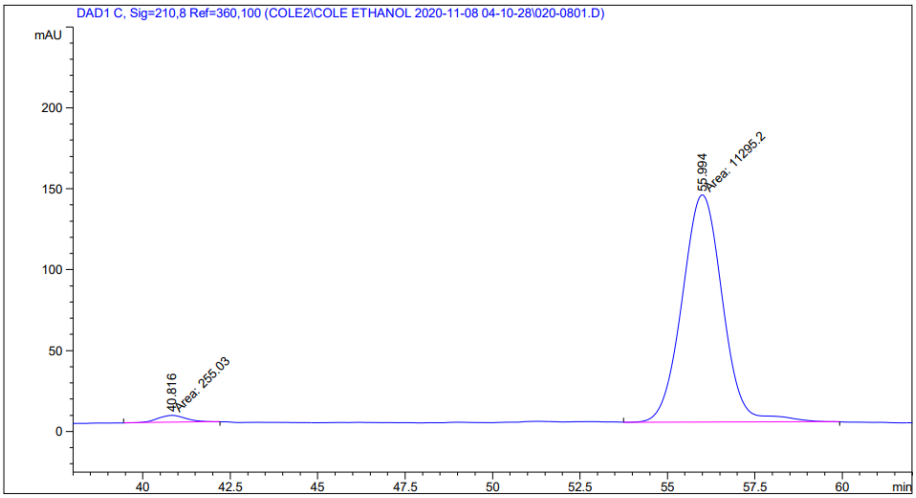
HPLC (Two Chiralcel AD-H columns in series, hexanes:*i*-PrOH = 93:7, 1.00 mL/min, 210 nm), *ee* = 96%


f1 (ppm)
2.09
2.22
1.05
1.05
1.09
1.00
1.03
1.04
3.12
1.08
1.04
1.06
1.26
3.09
1.02
3.42
7.64
7.64
7.63
7.62
7.62
7.61
7.48
7.47
7.47
7.46
7.45
7.26
6.95
6.95
6.93
6.91
6.68
6.67
6.66
6.65
5.85
5.84
5.83
5.82
5.82
5.80
5.80
5.78
5.16
5.16
5.14
5.14
5.05
5.05
5.02
5.01
3.84
3.79
2.96
2.95
2.94
2.92
2.68
2.66
2.65
2.63
2.38
2.37
2.36
2.35
2.35
2.34
2.33
2.31
1.45
1.44
1.26
1.24


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
168.45
156.01
139.15
137.66
134.99
134.43
131.59
131.22
129.24
129.20
118.43
118.13
115.05
110.92
101.99
68.72
55.88
51.54
25.97
21.64
13.81

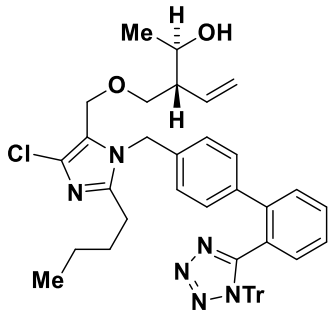


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.487	BB	0.6786	576.38507	11.08601	52.9607
2	55.294	BB	0.8301	511.94180	7.28290	47.0393



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.816	MM	0.9745	255.02982	4.36184	2.2080
2	55.994	MM	1.3411	1.12952e4	140.37448	97.7920

(2R,3R)-3-(((2-butyl-4-chloro-1-((2'-(1-trityl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1H-imidazol-5-yl)methoxy)methyl)pent-4-en-2-ol (2x)



Procedure

Allyl acetate **1x** (77.7 mg, 0.10 mmol, 100 mol%) was subjected to a modified version of general procedure D using reduced loading of potassium carbonate (6.9 mg, 0.050 mmol, 50 mol%), ethanol (17 μL, 0.300 mmol, 300 mol%), and acetone as solvent (0.1 mL, 1.0M, 60 °C, 72 hr). The title compound was obtained in 62% yield (47.2 mg, 0.62 mmol, 9:1 dr) as a colorless gel after isolation by flash column chromatography (SiO2, hexanes: ethyl acetate = 10:1–3:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.50 (td, *J* = 7.4, 1.7 Hz, 1H), 7.46 (td, *J* = 7.5, 1.6 Hz, 1H), 7.36 (q, *J* = 1.4 Hz, 1H), 7.35 – 7.32 (m, 3H), 7.27 (d, *J* = 1.5 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 4H), 7.12 – 7.09 (m, 2H), 6.94 – 6.91 (m, 6H), 6.73 (d, *J* = 8.1 Hz, 2H), 5.74 (ddd, *J* = 17.3, 10.4, 8.6 Hz, 1H), 5.18 (dd, *J* = 10.4, 1.9 Hz, 1H), 5.12 – 5.06 (m, 1H), 5.03 (s, 2H), 4.17 (s, 2H), 3.85 (tq, *J* = 6.5, 3.1, 2.7 Hz, 1H), 3.52 – 3.40 (m, 2H), 2.53 – 2.45 (m, 2H), 2.27 – 2.20 (m, 1H), 2.11 (d, *J* = 4.4 Hz, 1H), 1.65 (tt, *J* = 9.3, 6.9 Hz, 2H), 1.29 (h, *J* = 7.4 Hz, 2H), 1.11 (d, *J* = 6.3 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H).

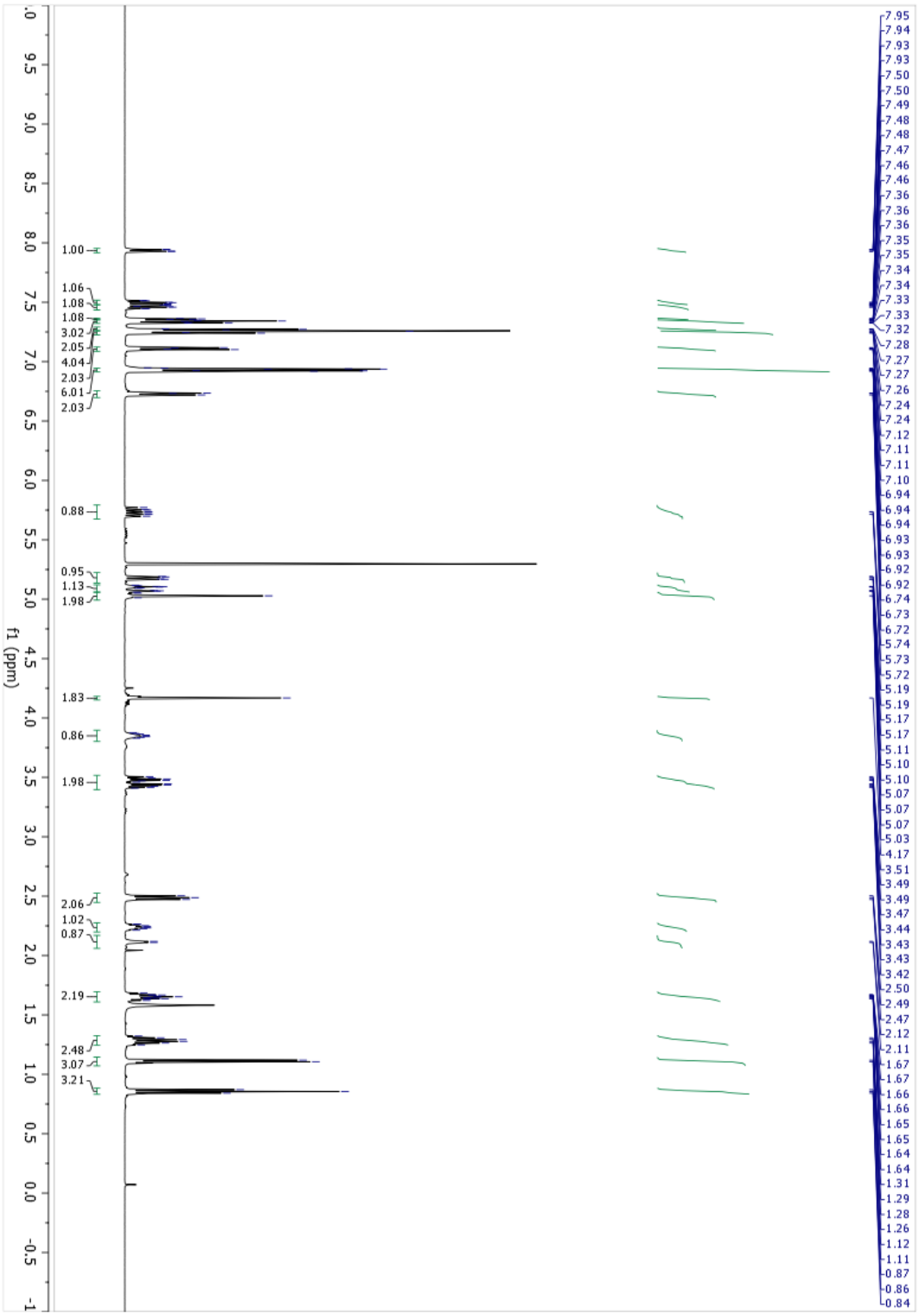
^{13}C NMR (126 MHz, $CDCl_3$): δ = 164.1, 148.9, 141.4, 141.1, 135.4, 134.6, 130.9, 130.5, 130.3, 130.1, 130.0, 129.4, 128.5, 127.9, 127.8, 126.4, 125.3, 125.3, 121.9, 118.7, 83.0, 71.3, 68.4, 61.1, 50.4, 47.2, 29.9, 26.9, 22.5, 20.6, 13.9.

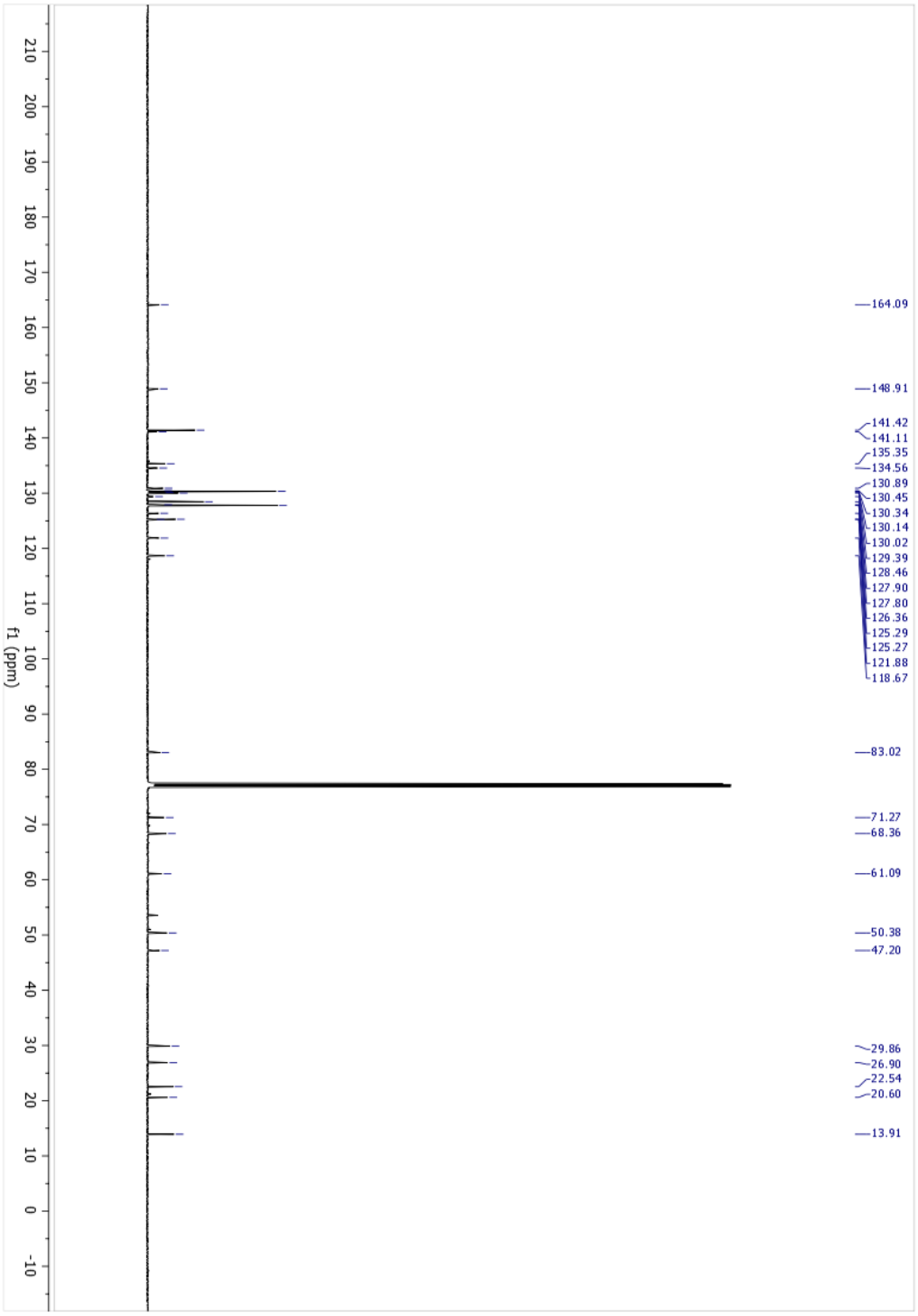
HRMS (ESI): Calculated for C47H47ClN6O2 [M+H+] = 763.3522, Found 763.3511.

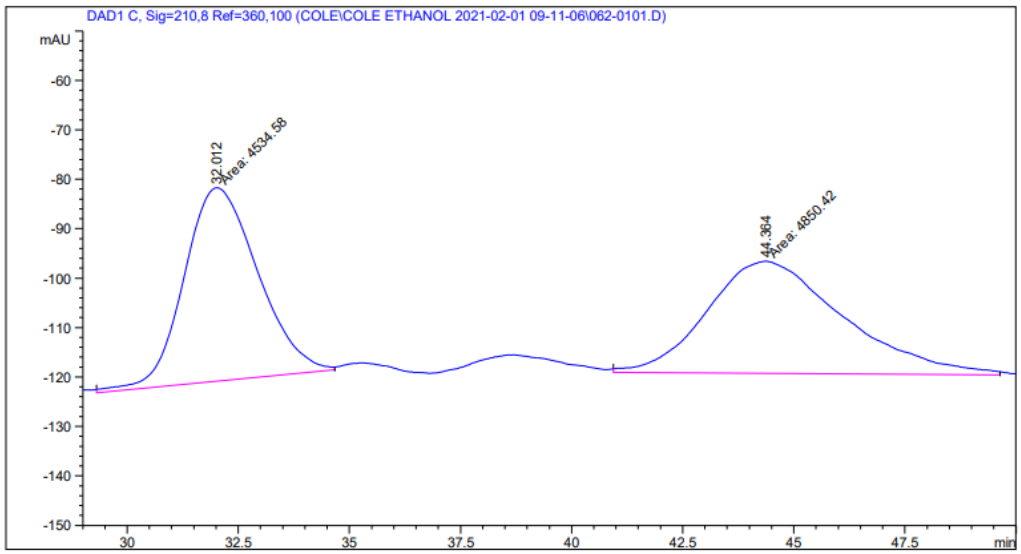
FTIR (neat): 3384, 3071, 2966, 2924, 2870, 2356, 1740, 1584, 1545, 1515, 1492, 1462, 1448, 1430, 1410, 1356, 1334, 1285, 1252, 1188, 1159, 1084, 1029, 1005, 924, 880, 822, 798, 784, 758, 748 cm–1.

$[\alpha]_D^{28}$ = -44.0 (*c* 0.50, $CHCl_3$).

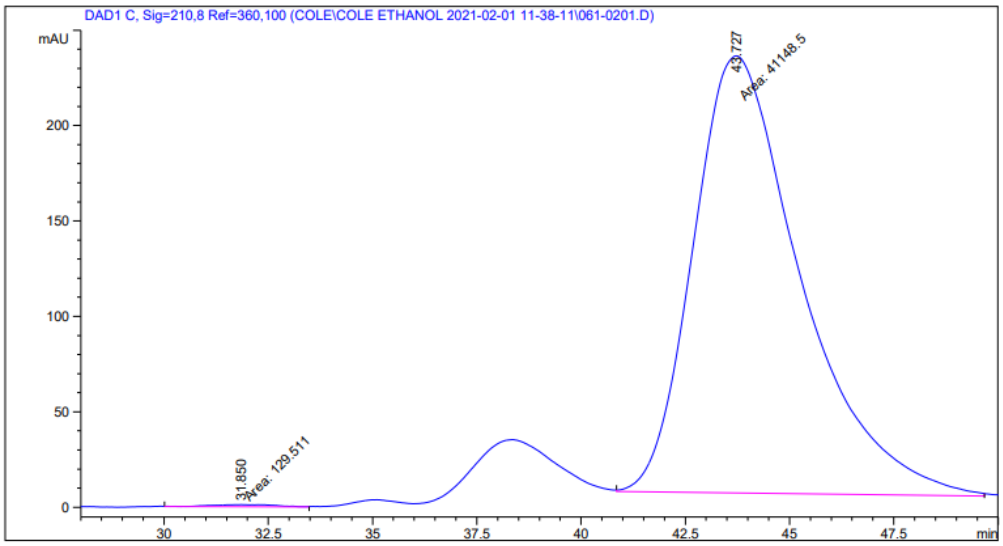
HPLC (Three Chiralcel AD-H columns in series, hexanes:i-PrOH = 8:2, 1.0 mL/min, 230 nm), ee = 99%.


f1 (ppm)
1.00
1.06
1.08
1.08
3.02
2.05
4.04
2.03
6.01
2.03
0.88
0.95
1.13
1.98
1.83
0.86
1.98
2.06
1.02
0.87
2.19
2.48
3.07
3.21


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
164.09
148.91
141.42
141.11
135.35
134.56
130.89
130.45
130.34
130.14
130.02
129.39
128.46
127.90
127.80
126.36
125.29
125.27
121.88
118.67
83.02
71.27
68.36
61.09
50.38
47.20
29.86
26.90
22.54
20.60
13.91

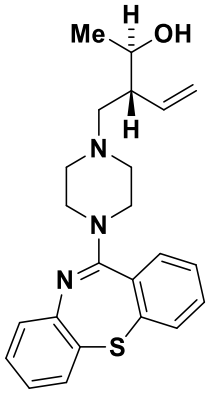


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.012	MM	1.9292	4534.58447	39.17502	48.3173
2	44.364	MM	3.5531	4850.42285	22.75223	51.6827



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.850	MM	1.8658	129.51149	1.15691	0.3138
2	43.727	MF	2.9939	4.11485e4	229.07104	99.6862

(2R,3R)-3-((4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl)methyl)pent-4-en-2-ol (2y)



Procedure

Allyl acetate **1y** (40.8 mg, 0.100 mmol, 100 mol%) was subjected to a modified version of general procedure D using **(*S*)-Ir-IV** (5.0 mg, 0.0050 mmol) and acetone as solvent (0.1 mL, 1.0M, 60 °C, 24 hr). The title compound was obtained in 68% yield (26.7 mg, 0.068 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, dichloromethane: ethyl acetate = 50:1–5:1).

TLC (SiO_2) R_f = 0.15 (dichloromethane: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 – 7.41 (m, 1H), 7.35 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.30 (td, *J* = 5.0, 4.3, 3.0 Hz, 1H), 7.27 (s, 1H), 7.25 – 7.21 (m, 1H), 7.13 (td, *J* = 7.6, 1.5 Hz, 1H), 7.03 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.85 (td, *J* = 7.5, 1.5 Hz, 1H), 5.70 – 5.56 (m, 1H), 5.11 – 4.94 (m, 2H), 3.89 (qd, *J* = 6.4, 3.3 Hz, 1H), 3.83 – 2.95 (b, 5H), 2.83 – 2.59 (m, 4H), 2.59 – 2.37 (m, 3H), 1.13 (d, *J* = 6.4 Hz, 3H).

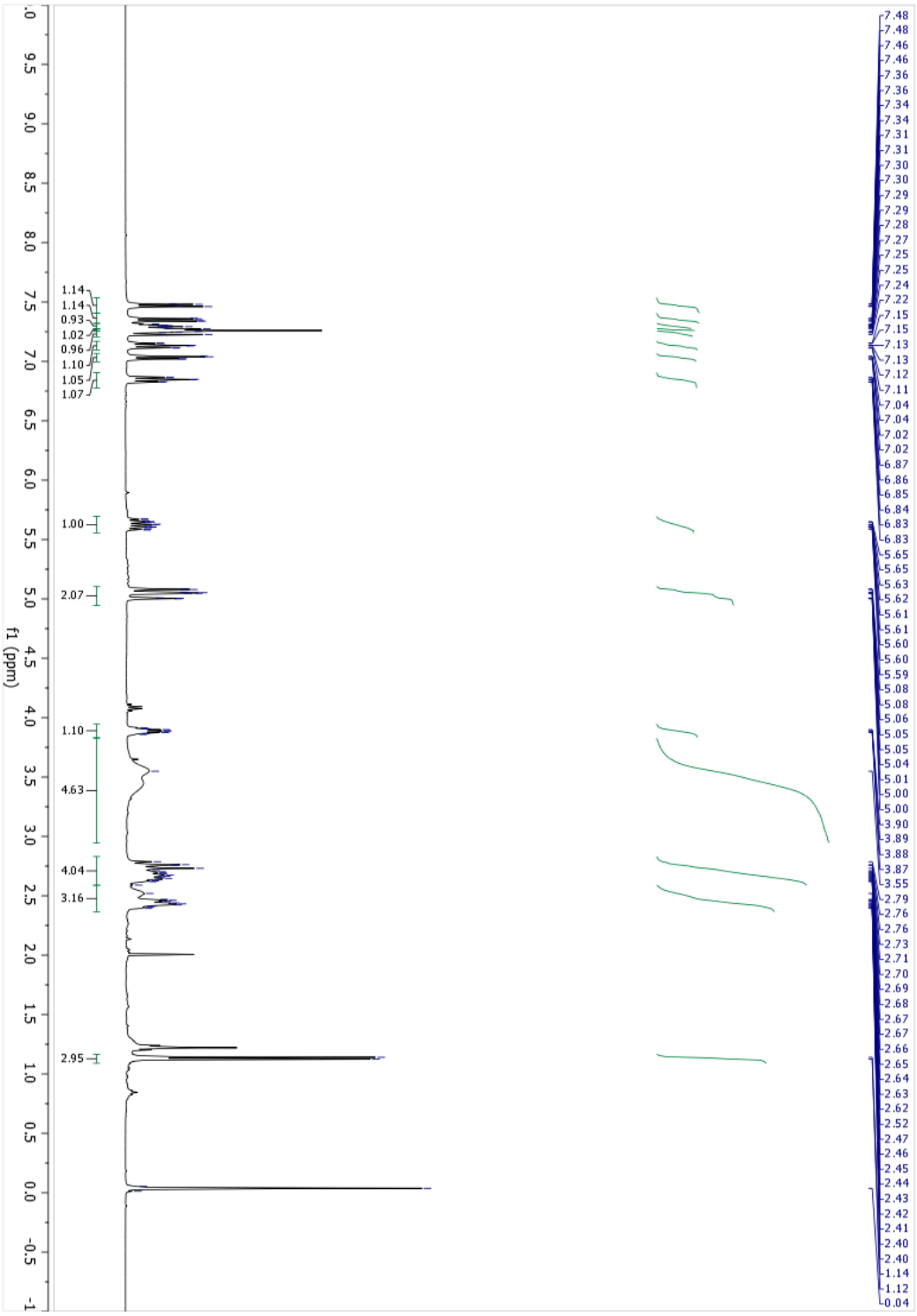
^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.6, 147.8, 138.9, 136.1, 133.0, 131.2, 131.2, 129.8, 128.1, 127.9, 127.3, 127.3, 126.9, 124.3, 121.9, 115.8, 69.8, 58.4, 52.5, 43.8, 17.8.

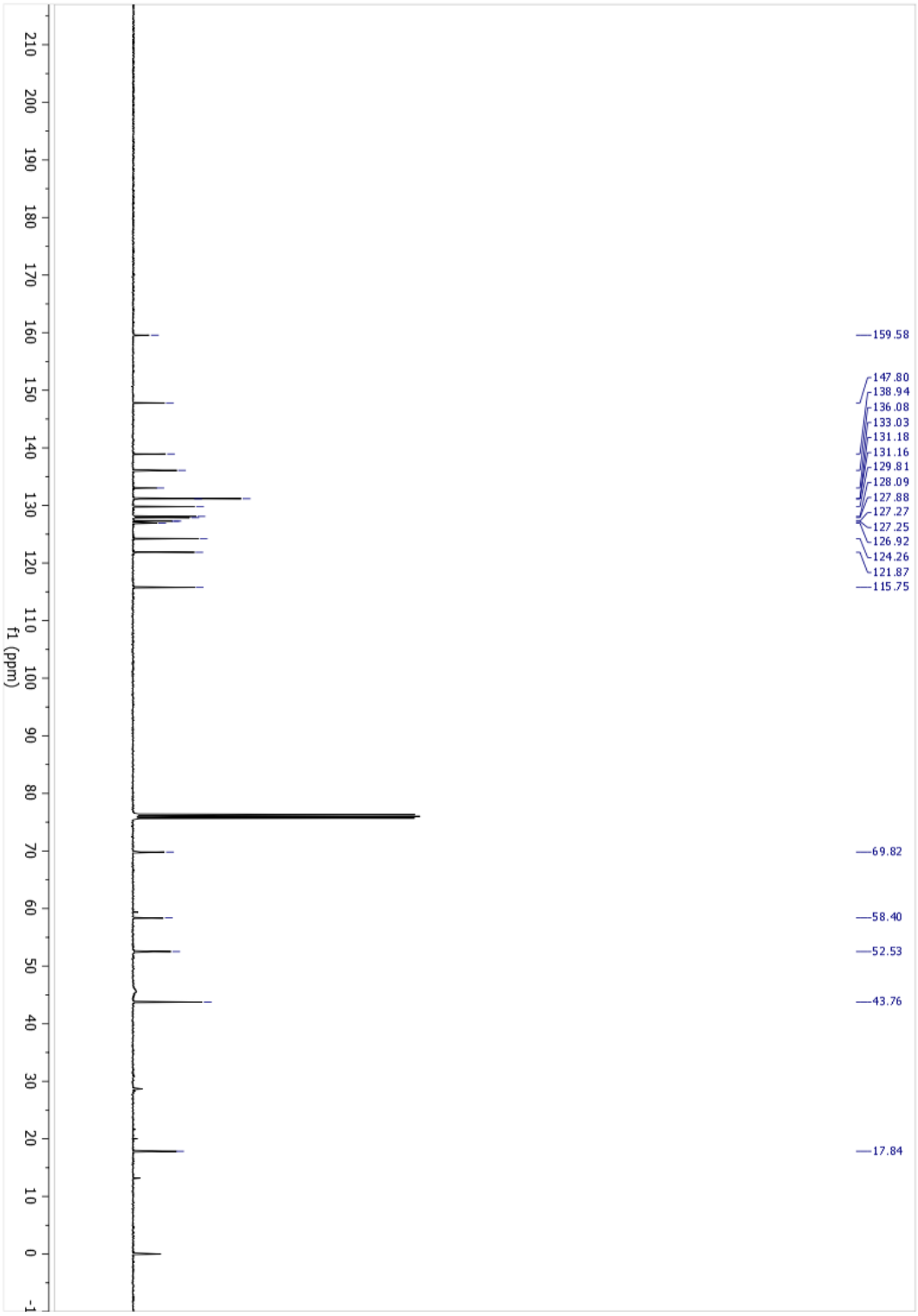
HRMS (ESI): Calculated for $C_{23}H_{27}N_3OS$ [M+H$^+$] = 394.1948, Found 394.1954.

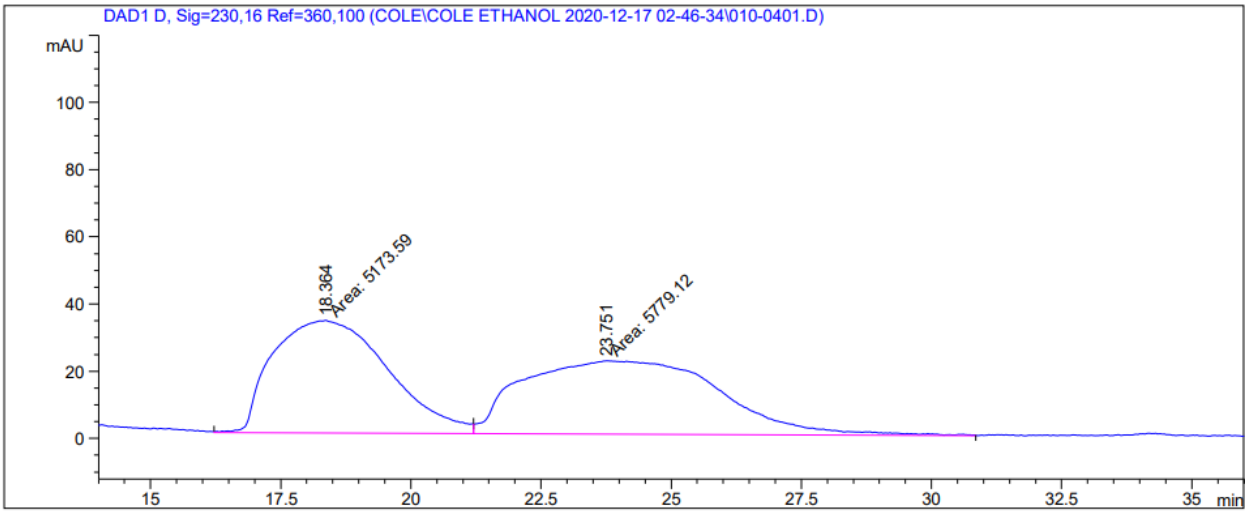
FTIR (neat): 3361, 2933, 2898, 2850, 2361, 2353, 2345, 2332, 2320, 1599, 1575, 1558, 1455, 1403, 1305, 1258, 1246, 1142, 1109, 1014, 919, 801, 762, 741, 701 cm^{-1}.

$[\alpha]_D^{28}$ = -13.3 (*c* 0.15, $CHCl_3$).

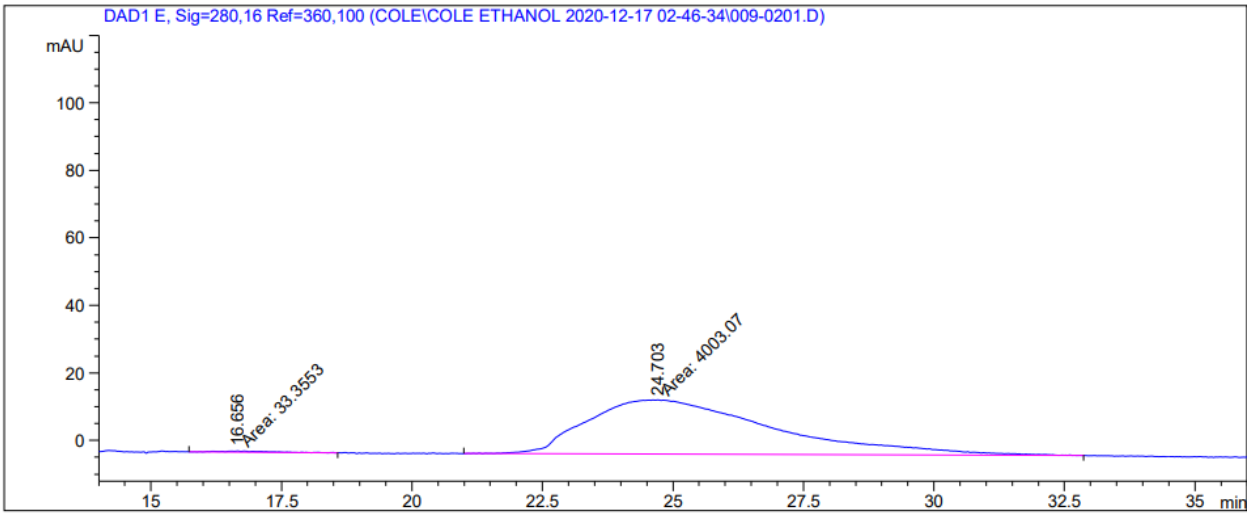
HPLC (Phenomenex cellulose-2 column in series with a Phenomenex cellulose-5 column, hexanes:*i*-PrOH = 80:20, 1.00 mL/min, 230 nm), *ee* = 98%.


f1 (ppm)
1.14
1.14
0.93
1.02
0.96
1.10
1.05
1.07
1.00
2.07
1.10
4.63
4.04
3.16
2.95


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
159.58
147.80
138.94
136.08
133.03
131.18
131.16
129.81
128.09
127.88
127.27
127.25
126.92
124.26
121.87
115.75
69.82
58.40
52.53
43.76
17.84

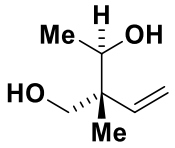


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.364	MF	2.5708	5173.58740	33.54079	47.2357
2	23.751	FM	4.4105	5779.12402	21.83851	52.7643



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.656	MM	1.2776	33.35529	4.35115e-1	0.8264
2	24.703	MM	4.1427	4003.07153	16.10495	99.1736

(2R,3R)-2-methyl-2-vinylbutane-1,3-diol (4a)



Procedure

Isoprene monoxide **3a** (80 μL, 0.600 mmol, 300 mol%), **(*S*)-Ir-V** (10.7 mg, 0.0100 mmol, 5 mol%), K_3PO_4 (2.1 mg, 0.01 mmol, 5 mol%), ethanol (12 μL, 0.200 mmol, 100 mol%) and THF (0.4 mL, 0.5 M) were sealed in an argon-filled pressure tube and stirred at 45 °C for 48 hr. The title compound was obtained in 96% yield (25.0 mg, 0.192 mmol, 8:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–3:1).

TLC (SiO_2) R_f = 0.20 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.99 (dd, *J* = 17.8, 11.1 Hz, 1H), 5.28 (dd, *J* = 11.0, 1.4 Hz, 1H), 5.17 (dd, *J* = 17.8, 1.4 Hz, 1H), 3.82 (q, *J* = 6.4 Hz, 1H), 3.67 (d, *J* = 10.6 Hz, 1H), 3.59 (d, *J* = 10.7 Hz, 1H), 2.30 (d, *J* = 5.6 Hz, 2H), 1.14 (d, *J* = 6.4 Hz, 3H), 0.98 (s, 3H).

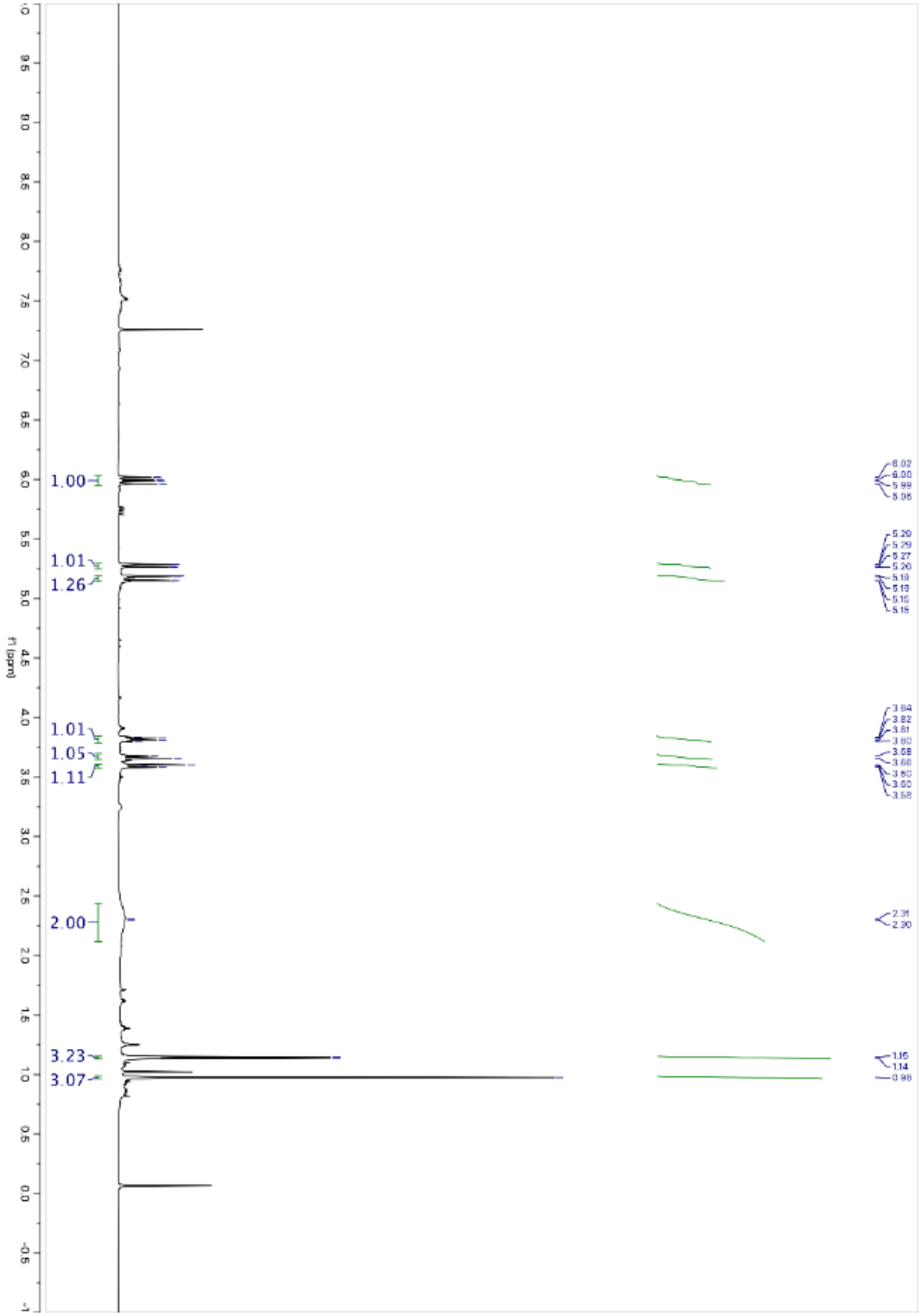
^{13}C NMR (101 MHz, $CDCl_3$) δ = 139.8, 116.3, 73.9, 70.4, 45.9, 18.5, 18.1.

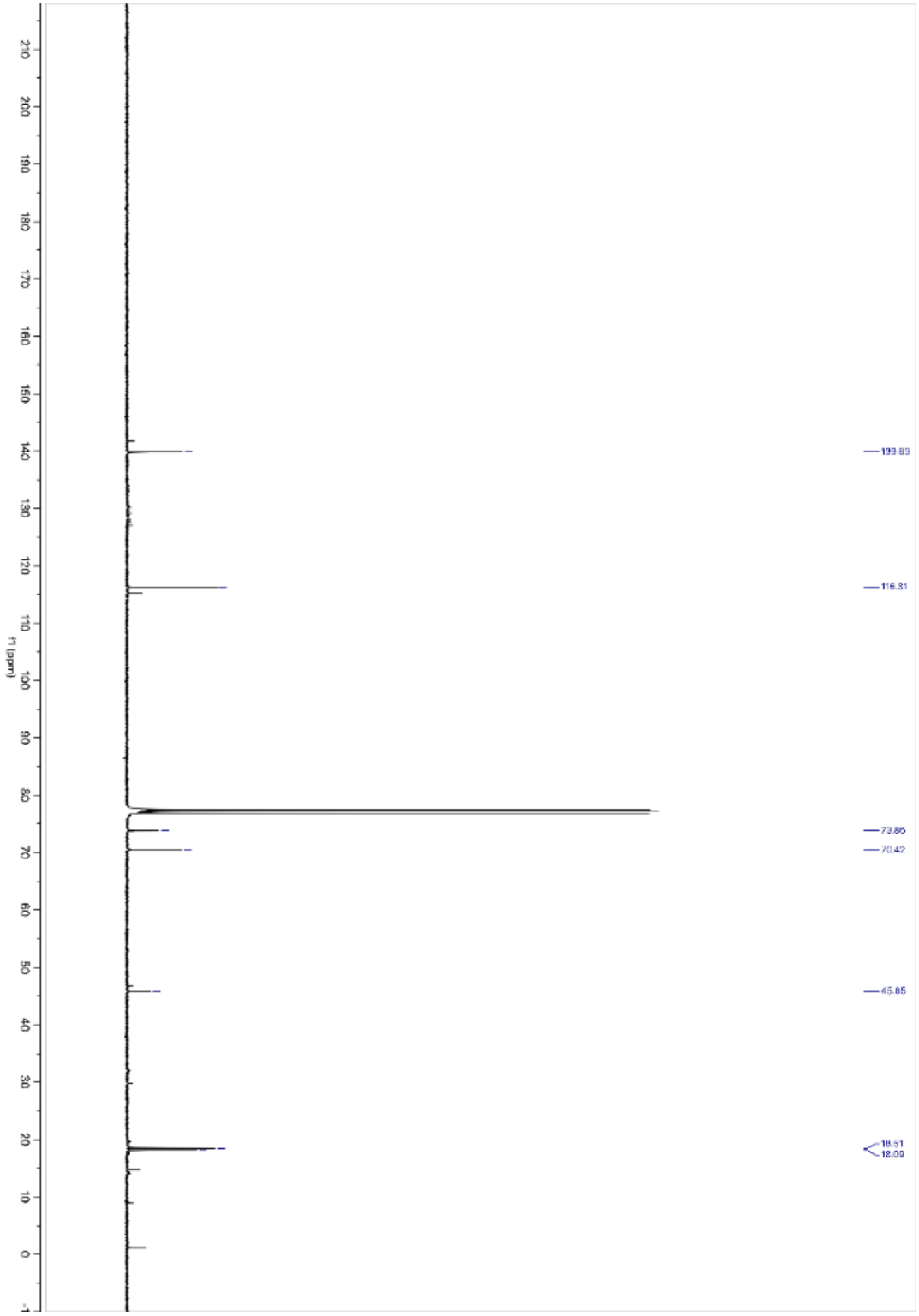
HRMS (CI): Calculated for $C_7H_{15}O_2$ [M+H$^+$] = 131.1069, Found 131.1072.

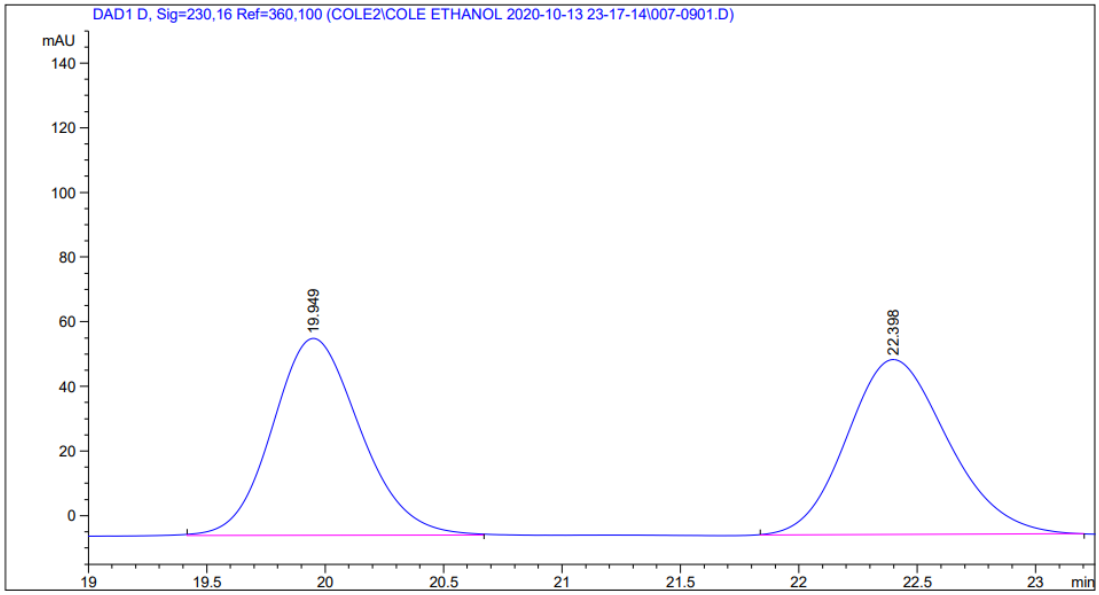
FTIR (neat): 3352, 2973, 2927, 2877, 1638, 1562, 1456, 1415, 1377, 1260, 1165, 1076, 1028, 917, 763 cm^{-1}.

$[\alpha]_D^{28}$= -11.5 (*c* 0.1, $CHCl_3$).

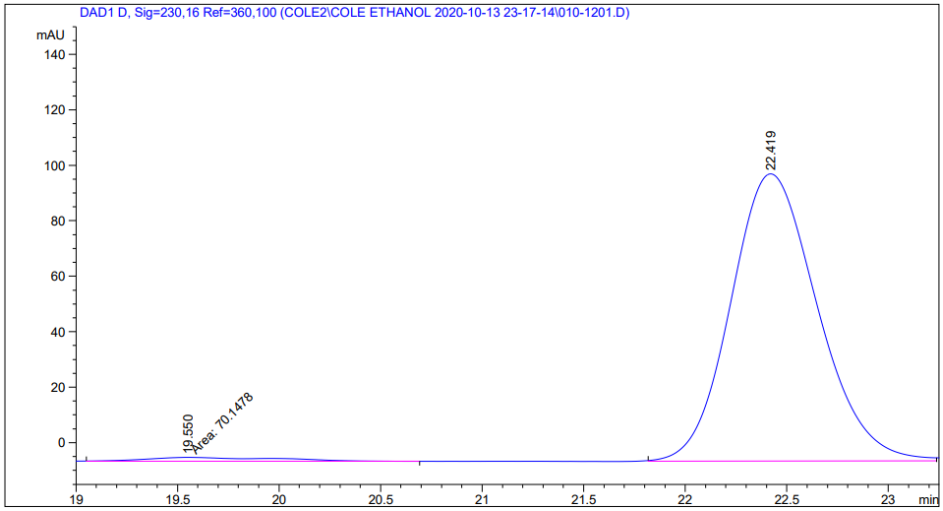
HPLC Analyzed as the mono-tosylated diol. (Two Chiralcel OJ-H columns in series, hexanes:*i*-PrOH = 93:7, 1.00 mL/min, 230 nm), *ee* = 96%.


1.00
1.01
1.26
1.01
1.05
1.11
2.00
3.23
3.07
f1 (ppm)


139.89
116.31
77.85
70.42
45.85
18.51
18.00
f1 (ppm)

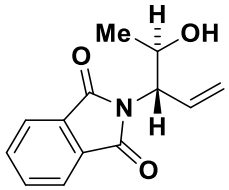


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.949	BB	0.3992	1573.06287	60.93098	49.3715
2	22.398	BB	0.4611	1613.11389	54.22101	50.6285



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.550	MM	0.7892	70.14780	1.48148	2.2331
2	22.419	BB	0.4598	3071.09644	103.60686	97.7669

2-(((3S,4R)-4-hydroxypent-1-en-3-yl)amino)-1H-indene-1,3(2H)-dione (4b)



Procedure

Phthalimidoallene **3b** (37.4 mg, 0.200 mmol, 100 mol%), **(*S*)-Ir-SI** (21.1 mg, 0.0200 mmol, 10 mol%), KH_2PO_4 (27.2 mg, 0.200 mmol, 100 mol%), ethanol (12 μL, 0.200 mmol, 100 mol%) and MTBE (1.0 mL, 0.2 M) were sealed in an argon-filled pressure tube and stirred at 100 °C for 48 hr. The title compound was obtained in 65% yield (23.3 mg, 0.101 mmol, 10:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.30 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.30 (ddd, *J* = 17.1, 10.3, 7.9 Hz, 1H), 5.34 (dt, *J* = 10.4, 1.1 Hz, 1H), 5.29 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.63 (ddt, *J* = 7.9, 4.3, 1.1 Hz, 1H), 4.30 (qd, *J* = 6.4, 4.3 Hz, 1H), 3.49 (s, 1H), 1.26 (d, *J* = 6.4 Hz, 4H).

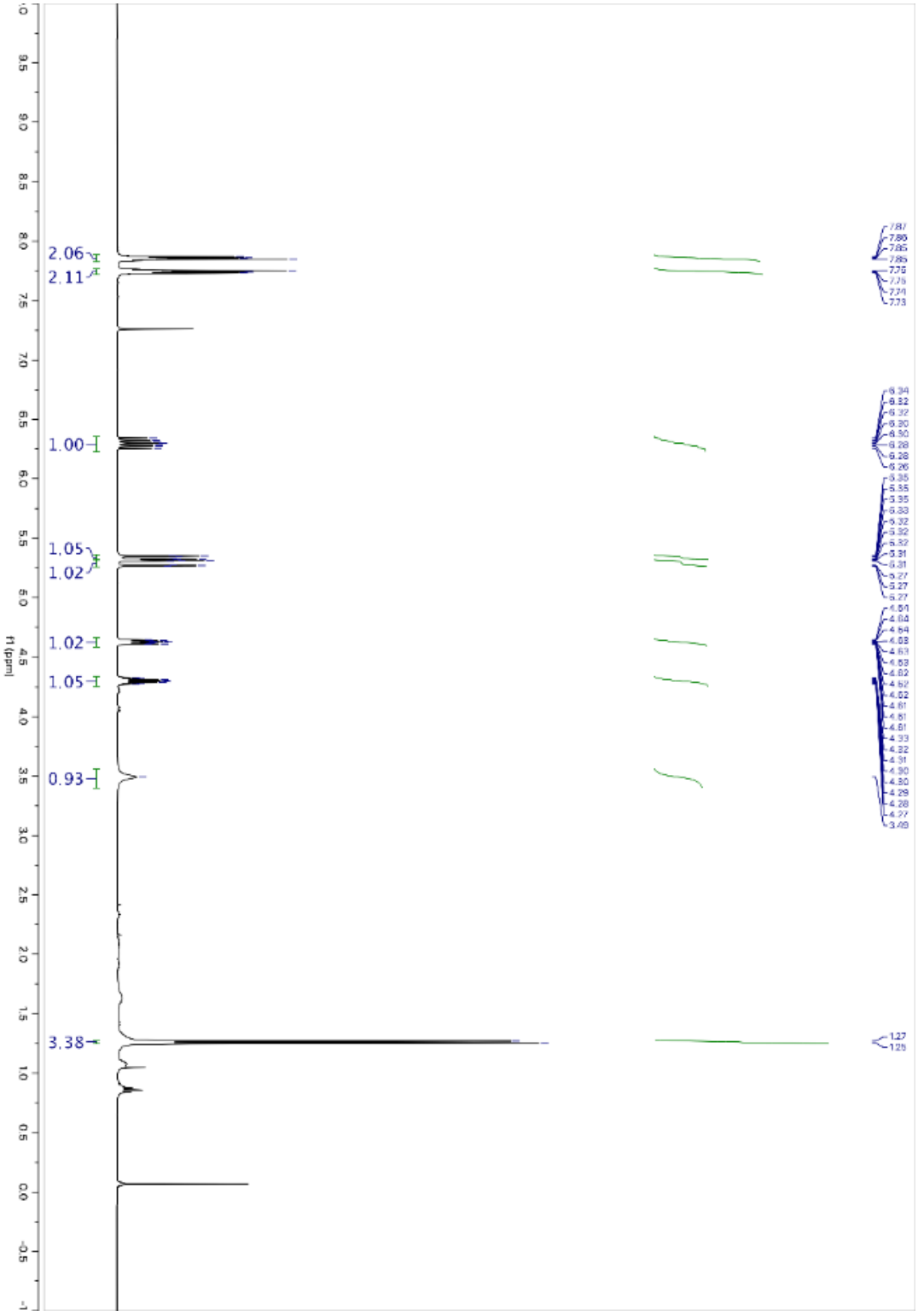
^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.8, 134.5, 131.9, 131.2, 123.7, 120.5, 68.5, 60.7, 20.4.

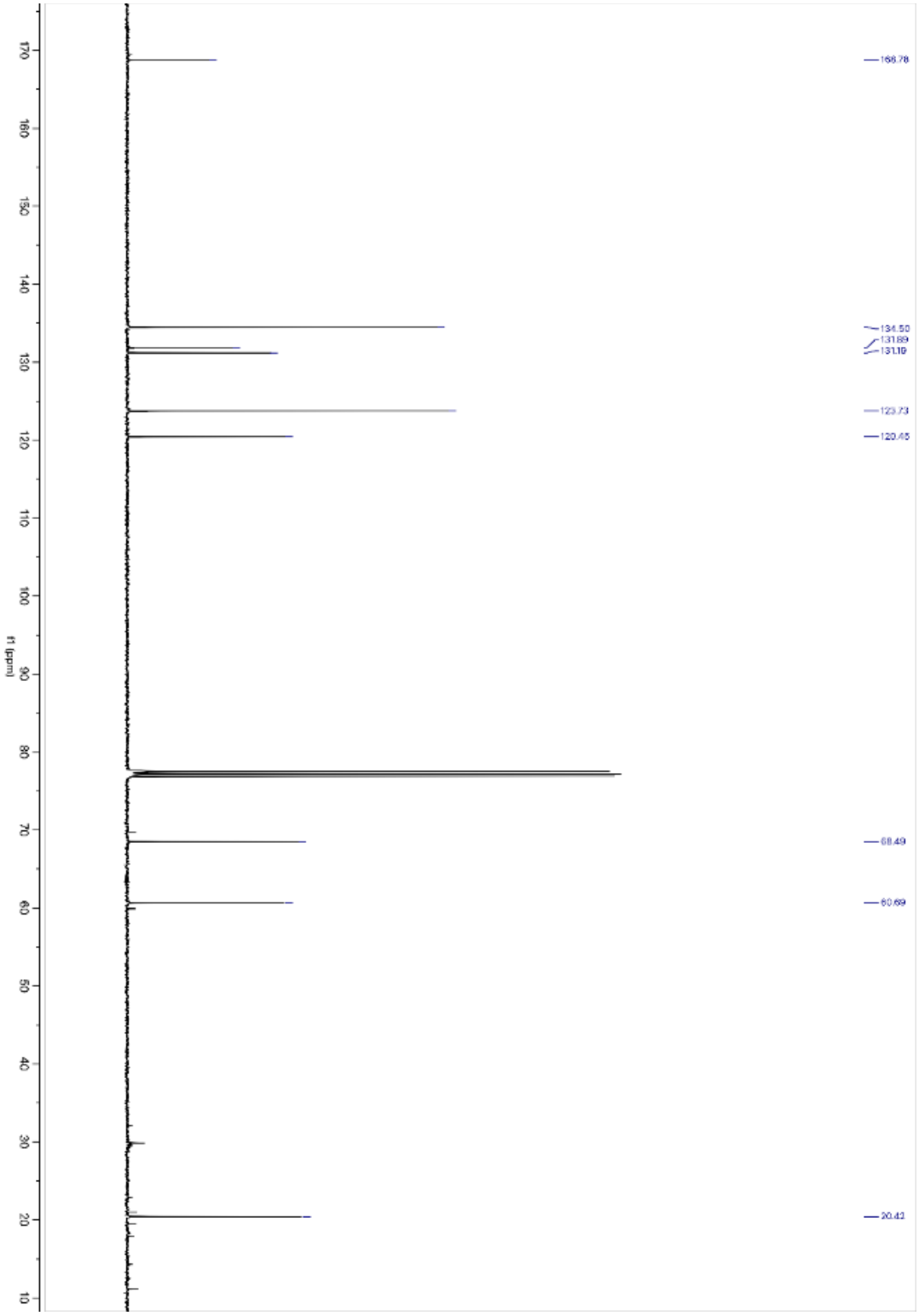
HRMS (ESI): Calculated for $C_{13}H_{13}NO_3$ [M+Na^+] = 254.0788, Found 254.0789.

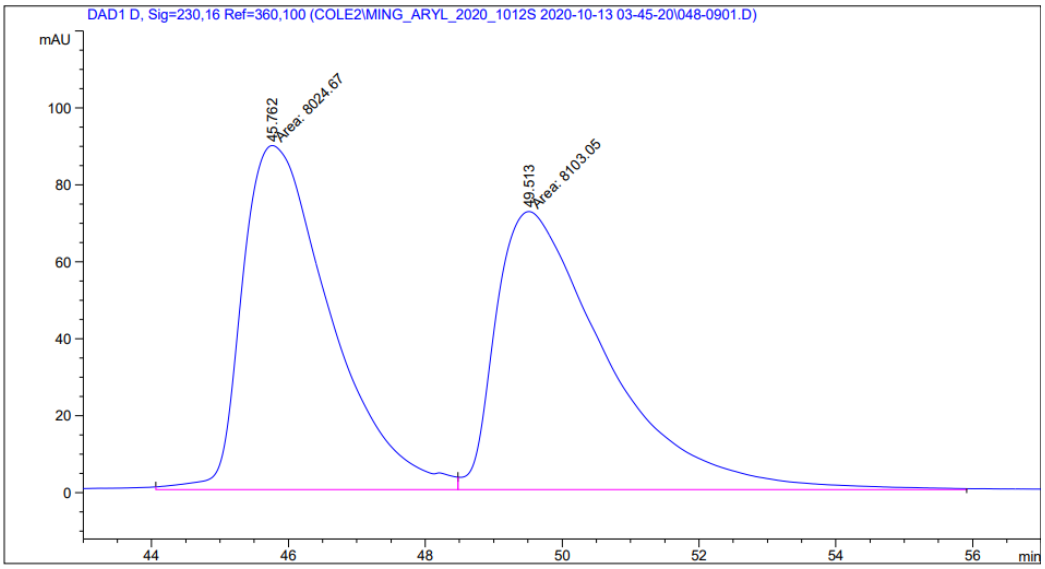
FTIR (neat): 3502, 2920, 2359, 1770, 1711, 1468, 1384, 1334, 1172, 1072, 909, 750, 720 cm^{-1}.

$[\alpha]_D^{28}$= +72.8 (*c* 0.33, $CHCl_3$).

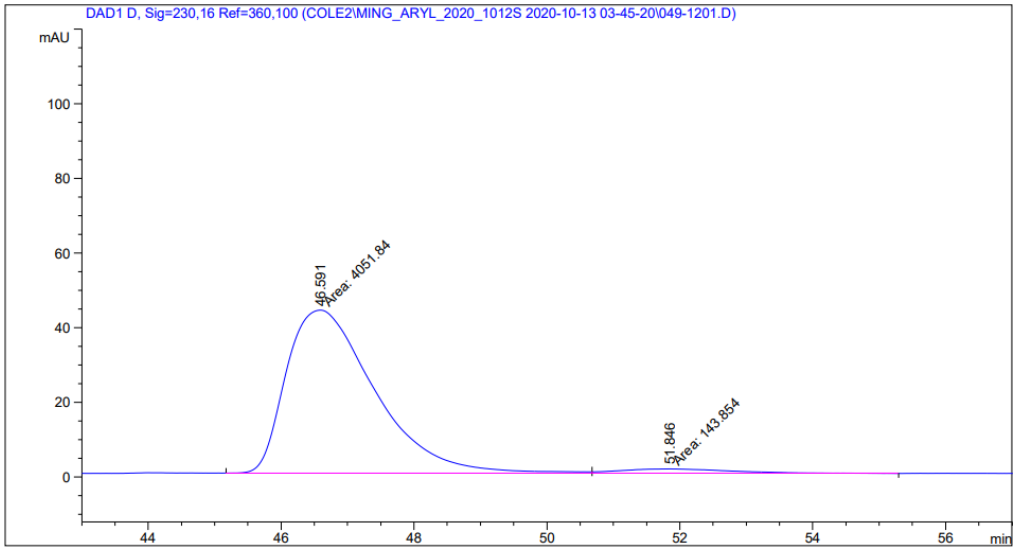
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 230 nm), *ee* = 93%.


2.06
2.11
1.00
1.05
1.02
1.02
1.05
0.93
3.38
f1 (ppm)


f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
168.78
134.50
131.89
131.19
123.73
120.45
68.49
60.69
20.42

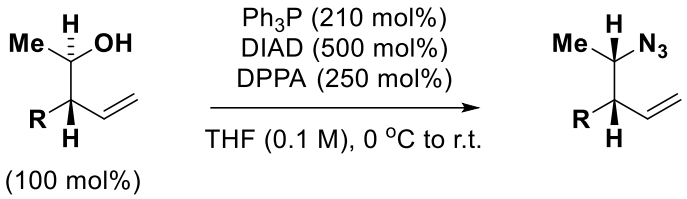


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	45.762	MF	1.4963	8024.66846	89.38510	49.7570
2	49.513	FM	1.8697	8103.05273	72.23315	50.2430



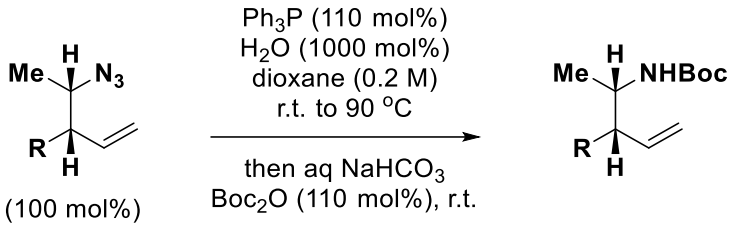
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.591	MF	1.5463	4051.83618	43.67313	96.5714
2	51.846	FM	1.9996	143.85440	1.19906	3.4286

3.1g. Procedures and Spectral Data for Synthesis of N-Boc *α*-Methylamines 5a-5f



General Procedure E

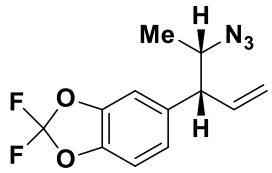
An oven-dried round bottom flask equipped with a magnetic stir bar was charged with homoallylic alcohol (100 mol%) and triphenylphosphine (210 mol%). The vessel was purged with argon and anhydrous THF (0.1 M) was added. The flask was cooled to 0 °C and diisopropyl azodicarboxylate (500 mol%) was added dropwise via syringe. The reaction was stirred for 15 minutes at 0 °C. Diphenylphosphoryl azide (250%) was added to the flask dropwise via syringe. Following addition, the reaction was allowed to reach ambient temperature and was stirred overnight or until the homoallylic alcohol was consumed (monitored by TLC). Once complete, the reaction was concentrated *in vacuo* and the resultant yellow oils were directly subjected to flash column chromatography to afford homoallylic azides **S5a-S5f**.



General Procedure F

An oven-dried pressure tube equipped with a magnetic stir bar was charged with homoallylic azide (100 mol%) and triphenylphosphine (110 mol%). The vessel was fit with a rubber septum and was purged with argon. Dioxane (0.2 M) was added and the reaction was stirred at ambient temperature for 10 minutes before water (1000 mol%) was added in one portion. The septum was removed and the tube was sealed with a PTFE lined cap. The vessel was heated to 90 °C for 2 hours or until full consumption of homoallylic azide (monitored by TLC). The vessel was allowed to cool to ambient temperature and saturated aqueous sodium bicarbonate was added (0.725 mL/mmol homoallylic azide starting material) followed by di-tert-butyl carbonate (110 mol%). The vessel was stirred at room temperature overnight or until full consumption of the amine intermediate (monitored by TLC). Once complete, the reaction mixture was diluted with ethyl acetate and added to a separatory funnel. The organics were washed once with water and separated. The aqueous layer was extracted three times by ethyl acetate. The organics were combined and washed with brine. The organic solution was dried over anhydrous sodium sulfate, passed through a fritted filter, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography to afford N-Boc α-methylamines **5a**-**5f**.

5-((3R,4S)-4-azidopent-1-en-3-yl)-2,2-difluorobenzo[d][1,3]dioxole (S5a)



Procedure

Homoallylic alcohol **2b** (48.4 mg, 0.200 mmol, 100 mol%) was subjected to general procedure E. The title compound was obtained in 77% yield (40.9 mg, 0.153 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 150:1–80:1).

TLC (SiO_2) R_f = 0.70 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.01 (d, *J* = 8.2 Hz, 1H), 6.98 (d, *J* = 1.8 Hz, 1H), 6.94 (dd, *J* = 8.2, 1.8 Hz, 1H), 5.97 (ddd, *J* = 16.9, 10.2, 8.4 Hz, 1H), 5.18 (d, *J* = 10.2 Hz, 1H), 5.14 (dt, *J* = 17.0, 1.2 Hz, 1H), 3.79 – 3.69 (m, 1H), 3.28 (t, *J* = 8.1 Hz, 1H), 1.30 (d, *J* = 6.6 Hz, 3H).

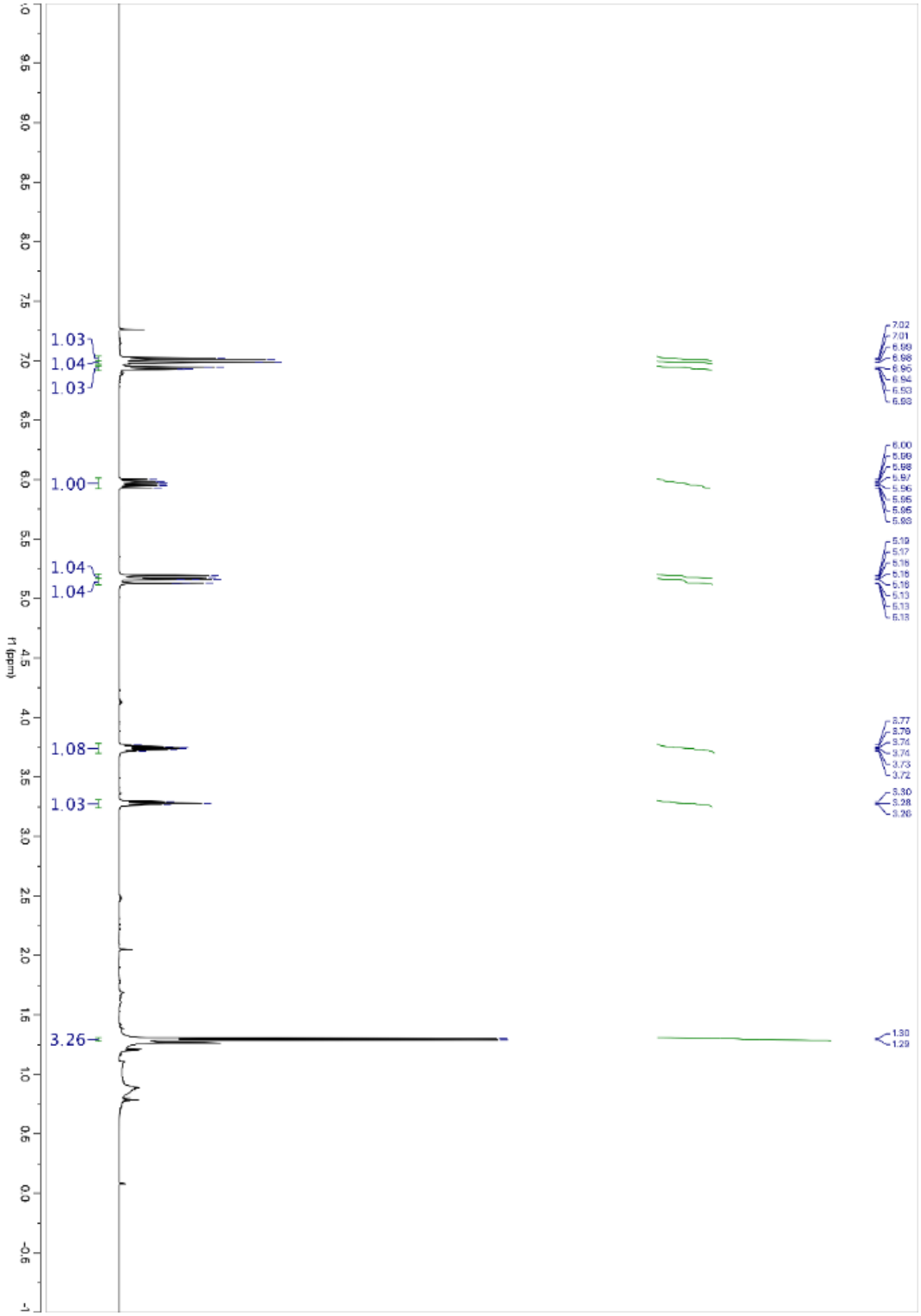
^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.1, 142.8, 137.6, 136.9, 133.8, 131.8, 129.8, 123.6, 118.0, 109.6, 109.5, 61.2, 55.9, 17.9.

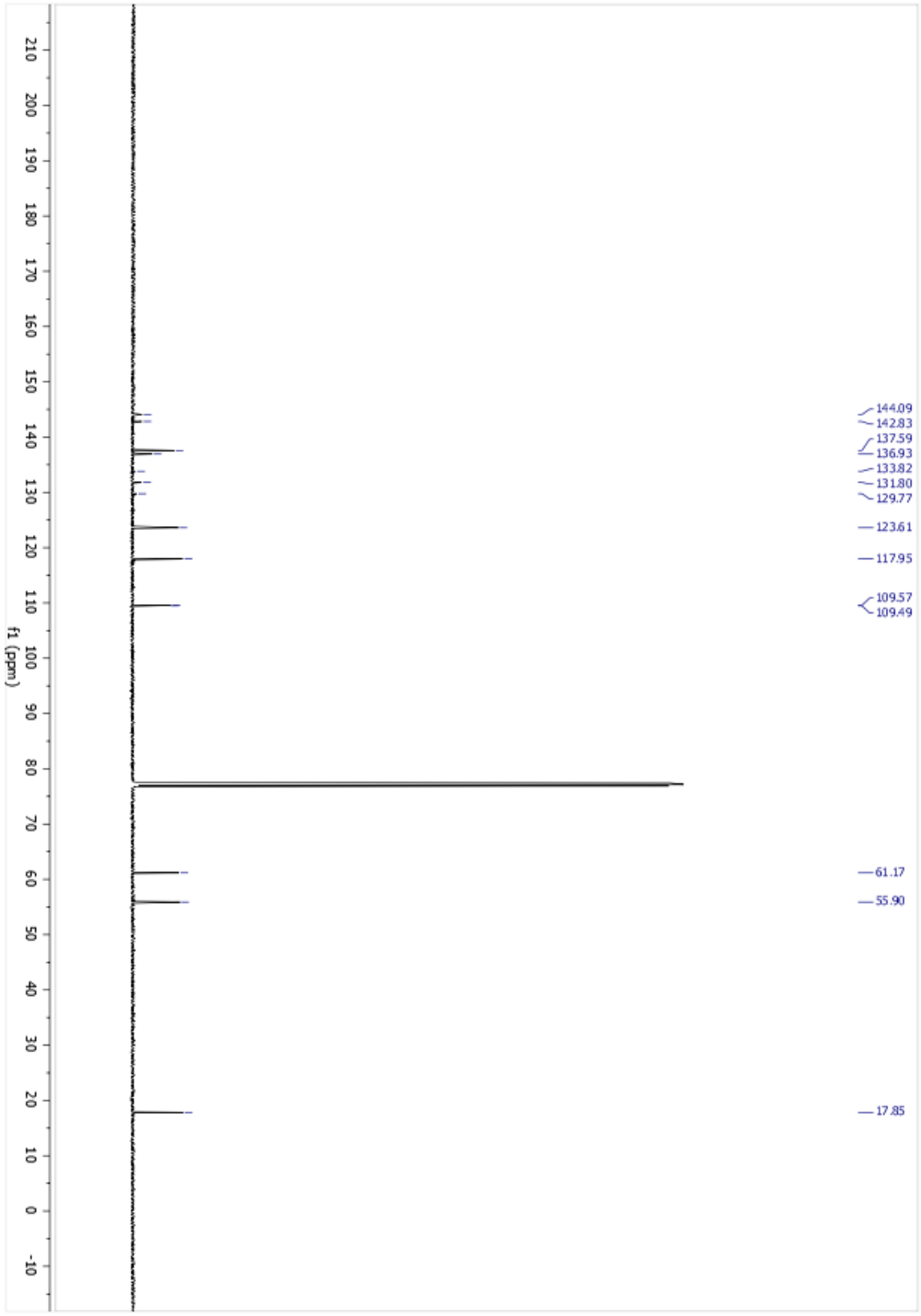
^{19}F NMR (471 MHz, $CDCl_3$) δ = -49.9 (d, *J* = 4.4 Hz).

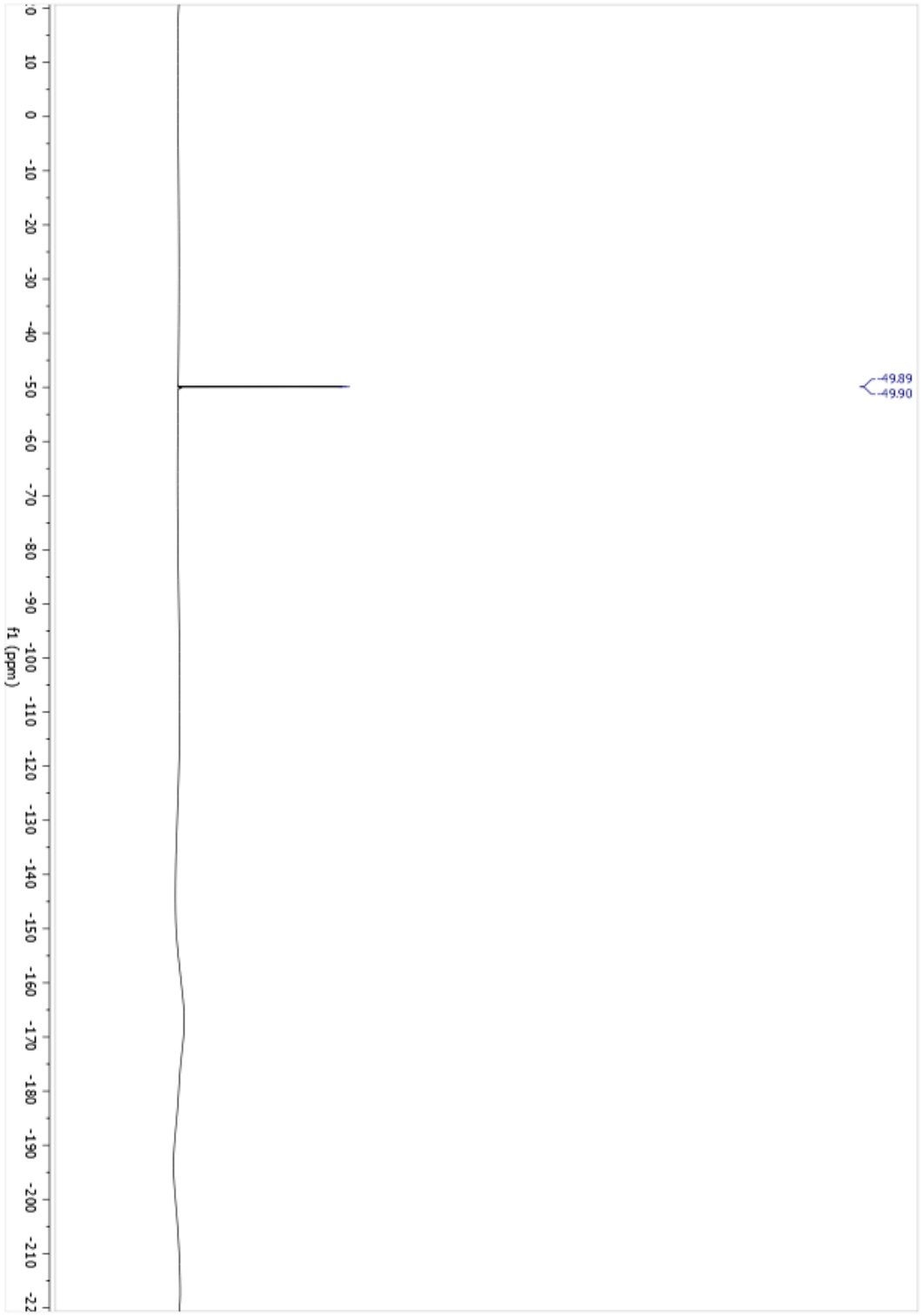
HRMS (ESI): Calculated for $C_{12}H_{11}F_2N_3O_2$ [M+Ag^+] = 373.9865, Found 373.9850.

FTIR (neat): 2924, 2851, 2103, 1719, 1498, 1448, 1380, 1238, 1154, 1119, 1103, 1035, 1019, 991, 924, 903, 874, 813, 732, 705 cm^{-1}.

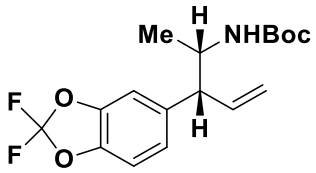
$[\alpha]_D^{28}$= -23.7 (*c* 0.19, $CHCl_3$).


1.03
1.04
1.03
1.00
1.04
1.04
1.08
1.03
3.26
f1 (ppm)


144.09
142.83
137.59
136.93
133.82
131.80
129.77
123.61
117.95
109.57
109.49
61.17
55.90
17.85
f1 (ppm)


-49.89
-49.90
f1 (ppm)

tert-butyl ((2S,3R)-3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)pent-4-en-2-yl)carbamate (5a)



Procedure

Homoallylic azide **S5a** (20.0 mg, 0.075 mmol, 100 mol%) was subjected to general procedure F. The title compound was obtained in 84% yield (21.6 mg, 0.063 mmol, >20:1 dr) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–10:1).

TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.00 – 6.96 (m, 2H), 6.93 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.00 (ddd, *J* = 17.0, 10.3, 9.0 Hz, 1H), 5.21 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.16 (dt, *J* = 17.0, 1.2 Hz, 1H), 4.32 (s, 1H), 3.97 (s, 1H), 3.38 (t, *J* = 8.0 Hz, 1H), 1.37 (s, 10H), 1.10 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 155.2, 144.0, 142.5, 137.8, 136.9, 133.8, 131.8 (t, *J* = 255.8 Hz), 129.8, 123.4, 118.4, 109.5, 109.3, 79.5, 55.7, 50.0, 28.4, 18.3.

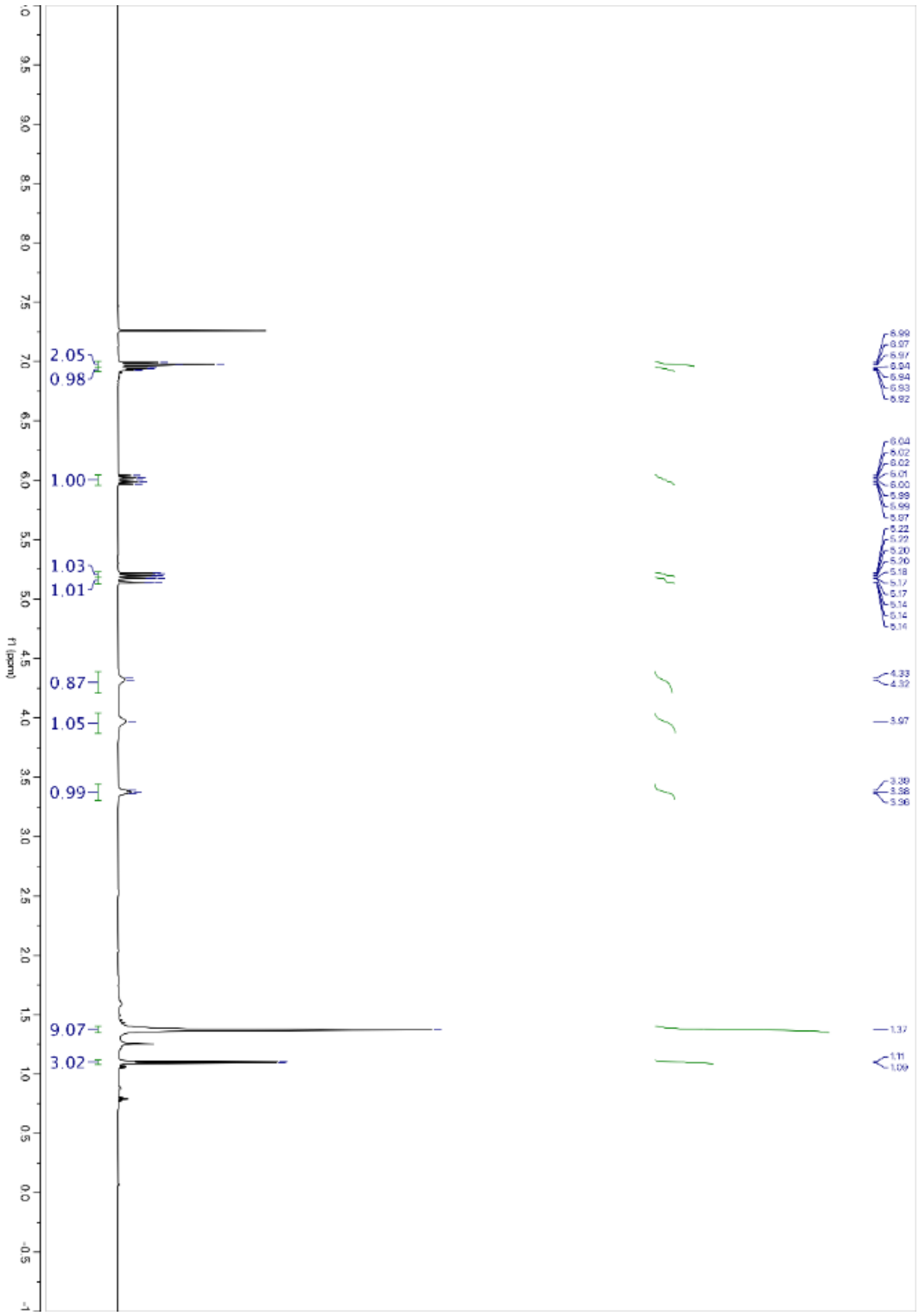
^{19}F NMR (471 MHz, $CDCl_3$) δ = -50.1.

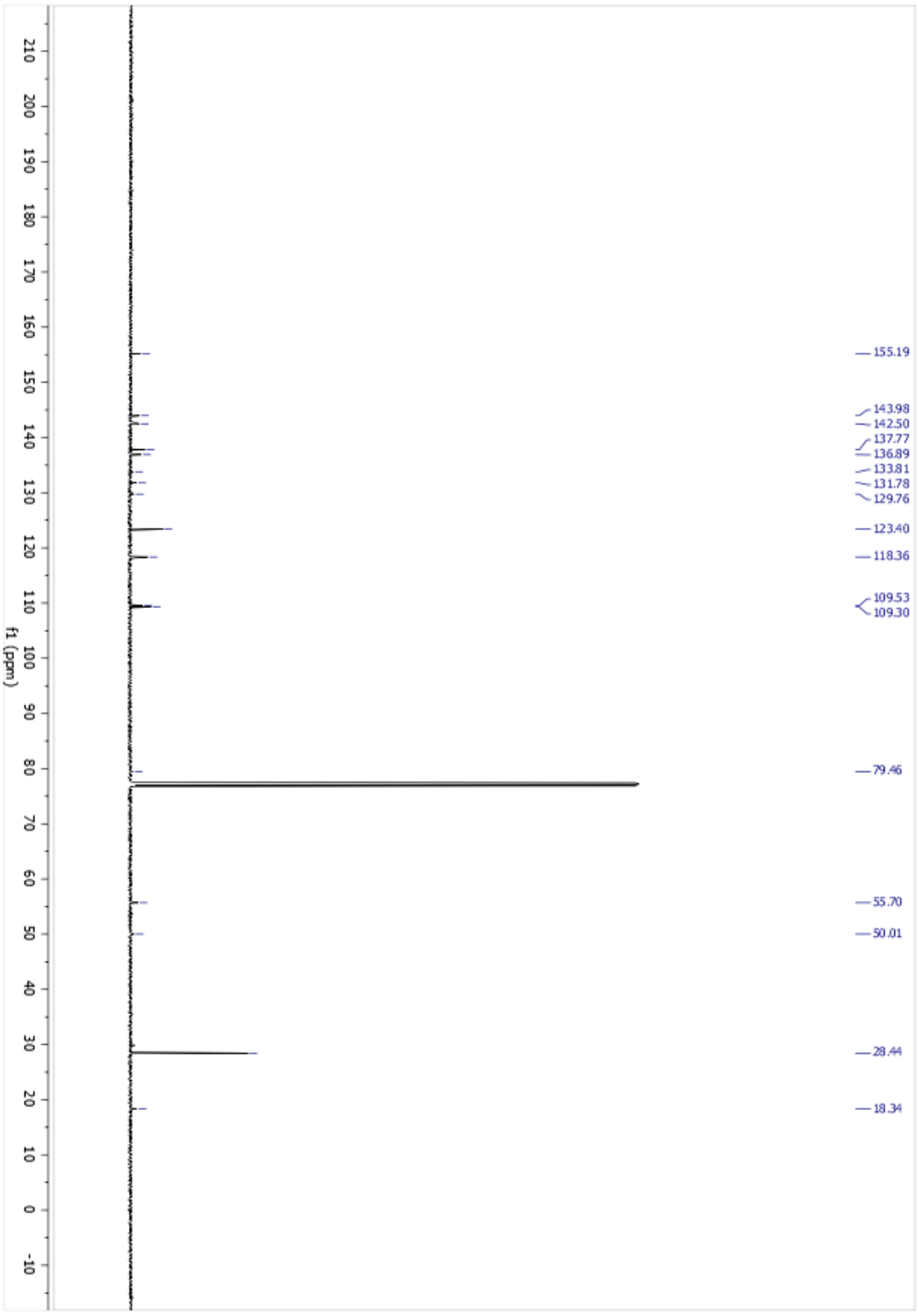
HRMS (ESI): Calculated for $C_{17}H_{21}F_2NO_4$ [M+Na^+] = 364.1331, Found 364.1333.

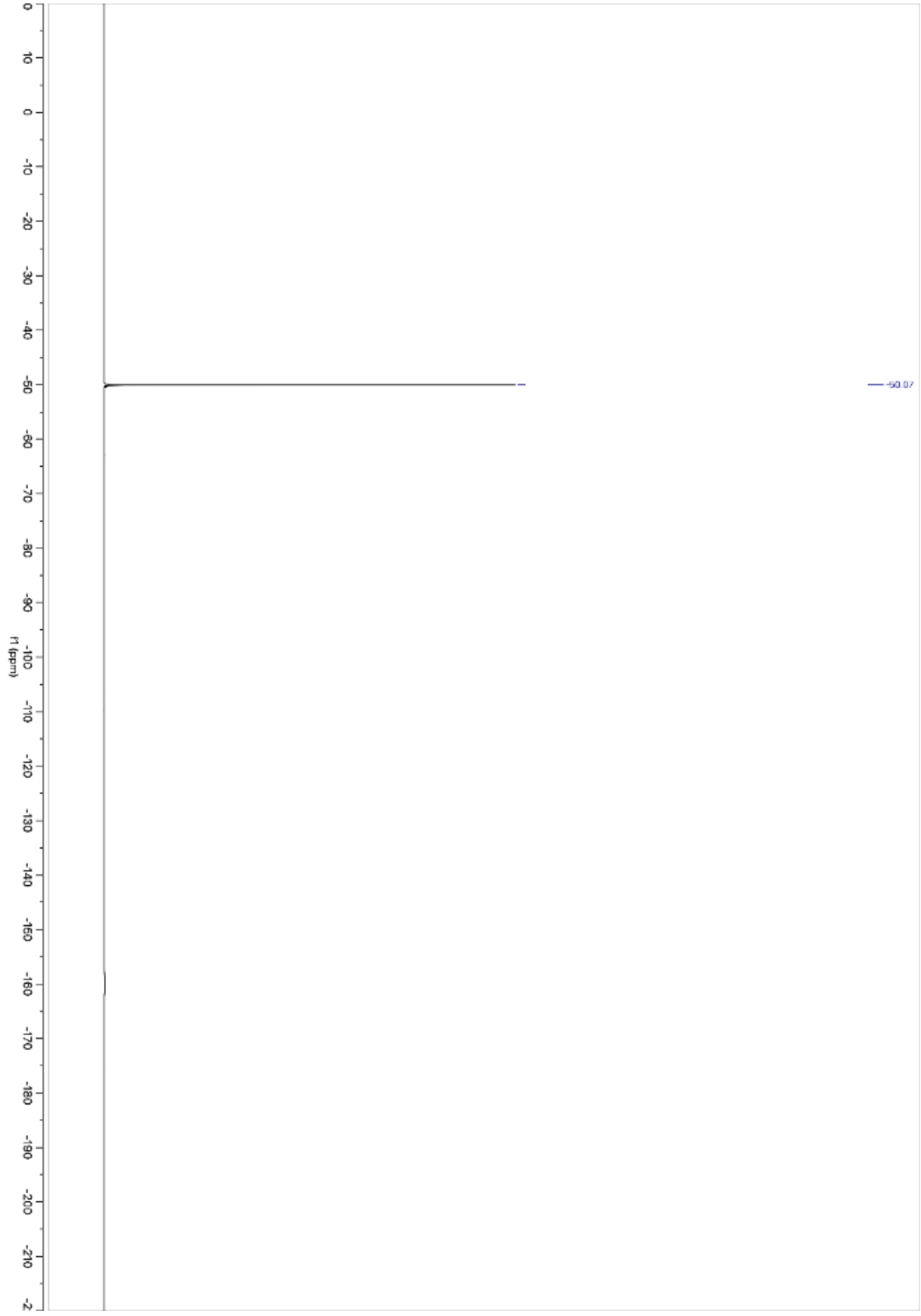
FTIR (neat): 3354, 2978, 2930, 2365, 1695, 1498, 1449, 1392, 1367, 1238, 1159, 1034, 922, 903, 857, 804, 705 cm^{-1}.

$[\alpha]_D^{28}$= -27.4 (*c* 0.20, $CHCl_3$).

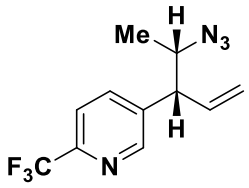
MP: 82-84 °C


2.05
0.98
1.00
1.03
1.01
0.87
1.05
0.99
9.07
3.02
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
155.19
143.98
142.50
137.77
136.89
133.81
131.78
129.76
123.40
118.36
109.53
109.30
79.46
55.70
50.01
28.44
18.34


10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-2
f1 (ppm)
-50.07

5-((3R,4S)-4-azidopent-1-en-3-yl)-2-(trifluoromethyl)pyridine (S5b)



Procedure

Homoallylic alcohol **2c** (46.4 mg, 0.200 mmol, 100 mol%) was subjected to general procedure E. The title compound was obtained in 46% yield (23.8 mg, 0.093 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 100:1–50:1).

TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.59 (s, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 6.09 – 5.90 (m, 1H), 5.25 (d, *J* = 10.2 Hz, 1H), 5.18 (d, *J* = 17.0 Hz, 1H), 3.84 (p, *J* = 6.7 Hz, 1H), 3.39 (t, *J* = 7.9 Hz, 1H), 1.32 (d, *J* = 6.5 Hz, 3H).

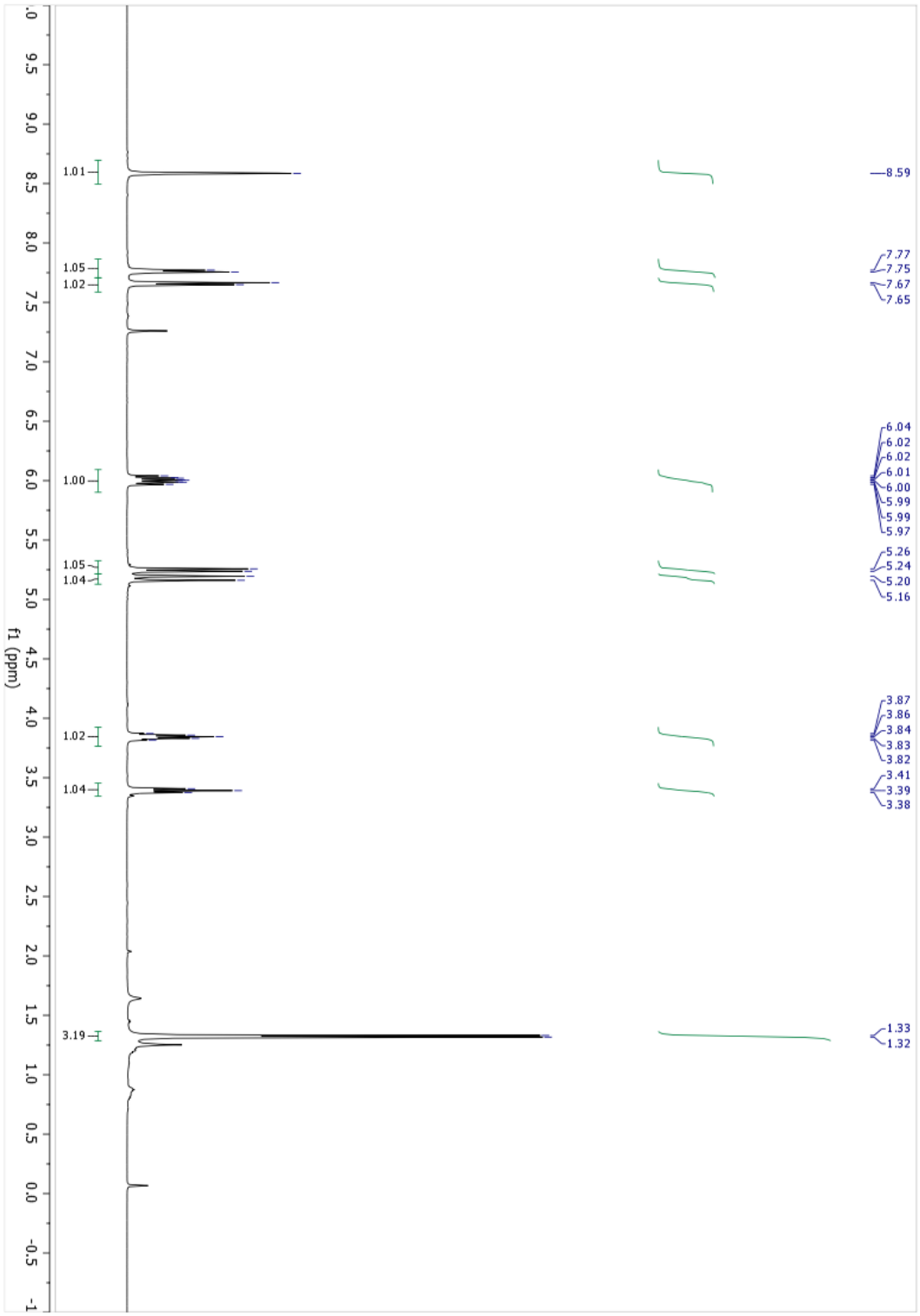
^{13}C NMR (126 MHz, $CDCl_3$): δ = 150.4, 147.1 (q, *J* = 35.3 Hz), 139.5, 137.2, 136.4, 121.7 (q, *J* = 274.4 Hz), 120.4 (q, *J* = 2.5 Hz), 119.1, 60.7, 53.4, 17.9.

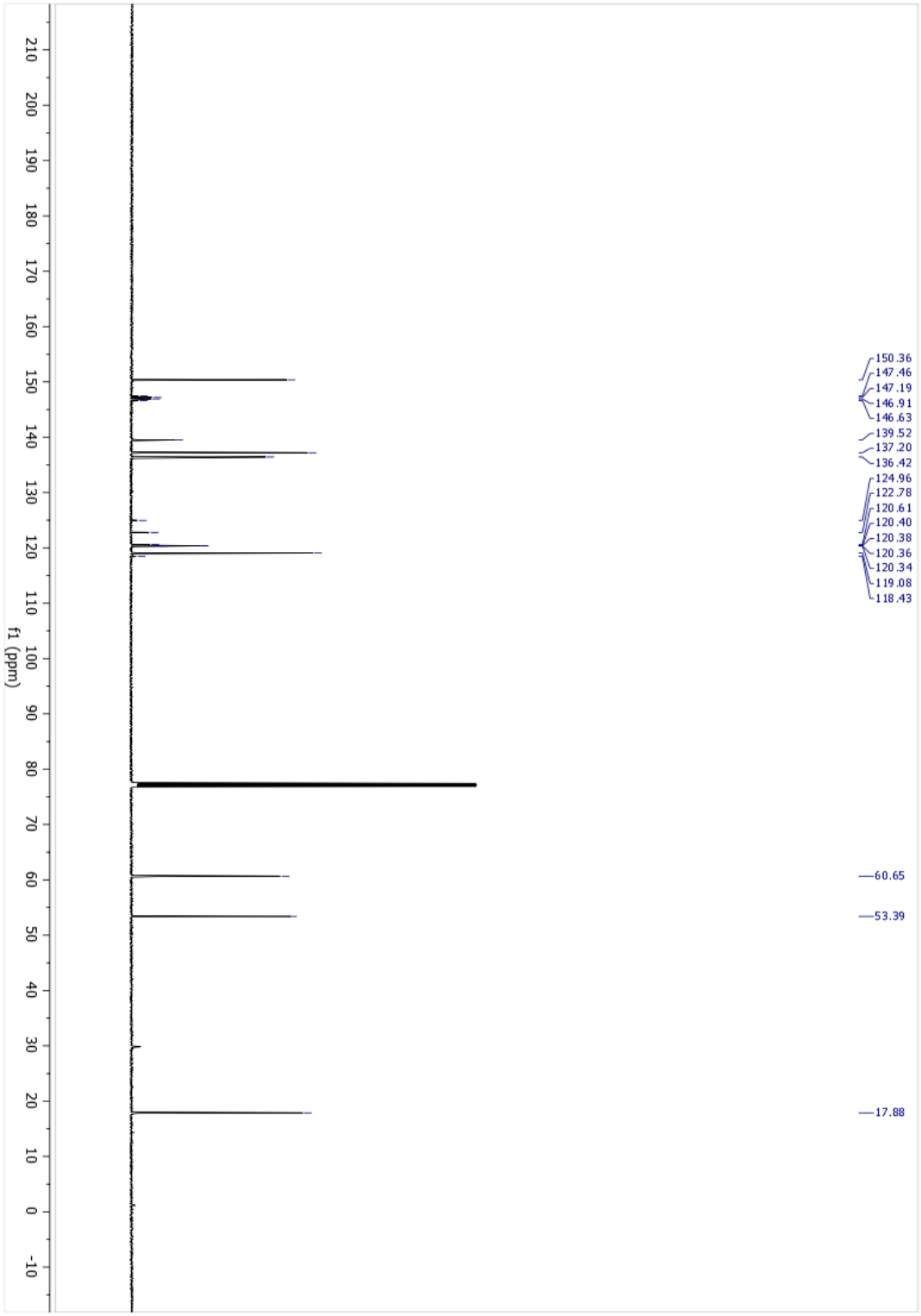
^{19}F NMR (471 MHz, $CDCl_3$) δ = -67.8.

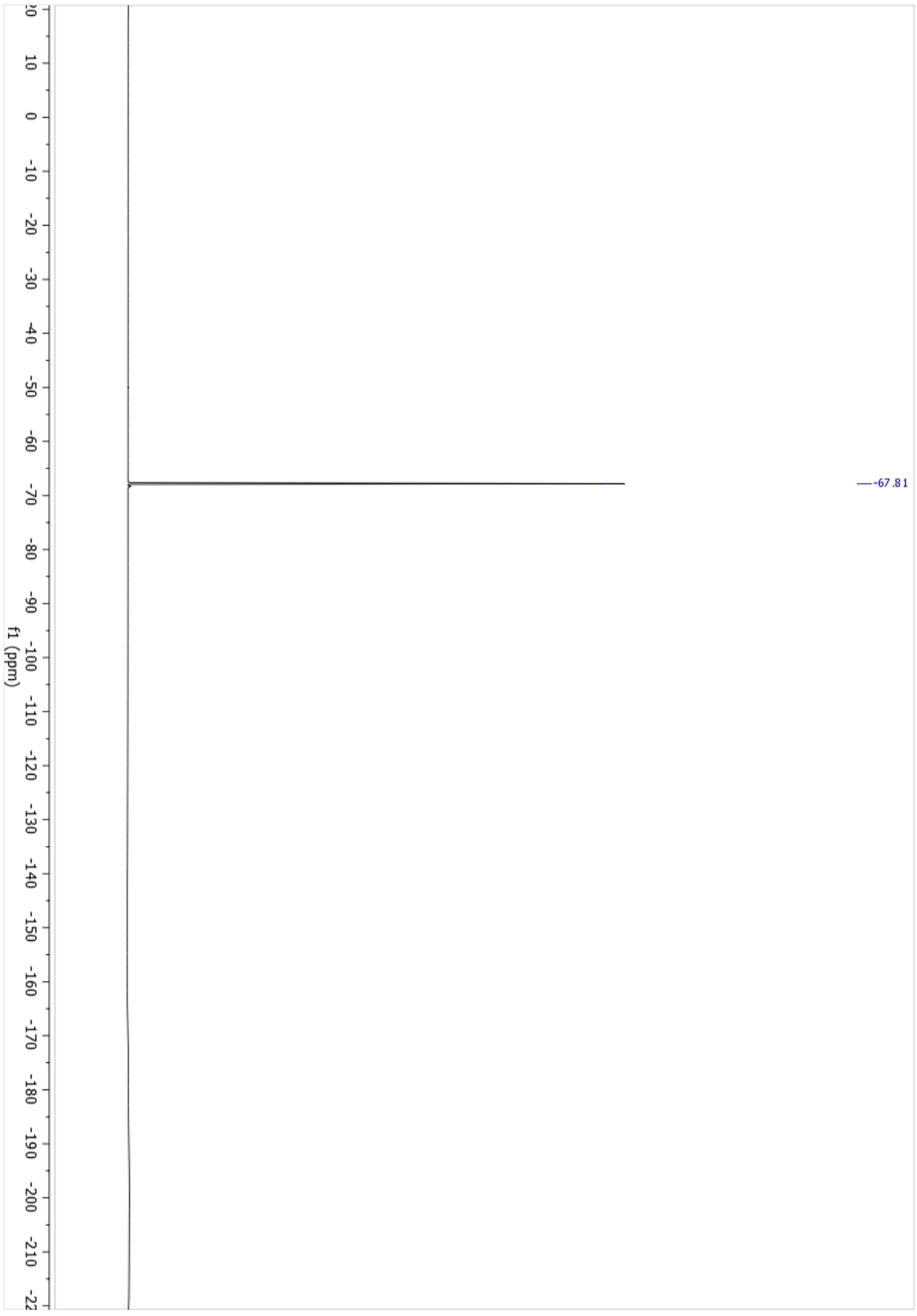
HRMS (ESI): Calculated for $C_{11}H_{11}F_3N_4$ [M+H$^+$] = 257.1009, Found 257.1013.

FTIR (neat): 3104, 2979, 2937, 2170, 2105, 1732, 1639, 1476, 1452, 1371, 1309, 1256, 1217, 1157, 1074, 1016, 922, 859, 766, 746 cm^{-1}.

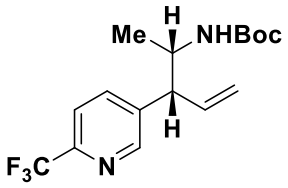
$[\alpha]_D^{28}$= -11.3 (*c* 0.71, $CHCl_3$).


f1 (ppm)
1.01
1.05
1.02
1.00
1.05
1.04
1.02
1.04
3.19
8.59
7.77
7.75
7.67
7.65
6.04
6.02
6.02
6.01
6.00
5.99
5.99
5.97
5.26
5.24
5.20
5.16
3.87
3.86
3.84
3.83
3.82
3.41
3.39
3.38
1.33
1.32


150.36
147.46
147.19
146.91
146.63
139.52
137.20
136.42
124.96
122.78
120.61
120.40
120.38
120.36
120.34
119.08
118.43
60.65
53.39
17.88
f1 (ppm)


-67.81
f1 (ppm)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-22

tert-butyl ((2S,3R)-3-(6-(trifluoromethyl)pyridin-3-yl)pent-4-en-2-yl)carbamate (5b)



Procedure

Homoallylic azide **S5b** (23.8 mg, 0.093 mmol, 100 mol%) was subjected to general procedure F using additional triphenylphosphine (31.7 mg, 0.121 mmol, 130 mol%). The title compound was obtained in 73% yield (22.3 mg, 0.066 mmol, >20:1 dr) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–10:1).

TLC (SiO_2) R_f = 0.48 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.57 (d, *J* = 2.2 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 6.04 (ddd, *J* = 17.0, 10.3, 9.0 Hz, 1H), 5.26 (d, *J* = 10.2 Hz, 1H), 5.20 (dt, *J* = 16.9, 1.2 Hz, 1H), 4.34 (d, *J* = 7.8 Hz, 1H), 4.05 (s, 1H), 3.45 (t, *J* = 8.3 Hz, 1H), 1.57 (s, 1H), 1.31 (s, 9H), 1.16 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 154.9, 150.1, 146.5 (q, *J* = 34.0 Hz), 140.4, 136.9, 135.9, 122.7, 120.1 (d, *J* = 2.5 Hz), 120.1, 119.2, 79.6, 53.4, 49.5, 28.2, 18.6.

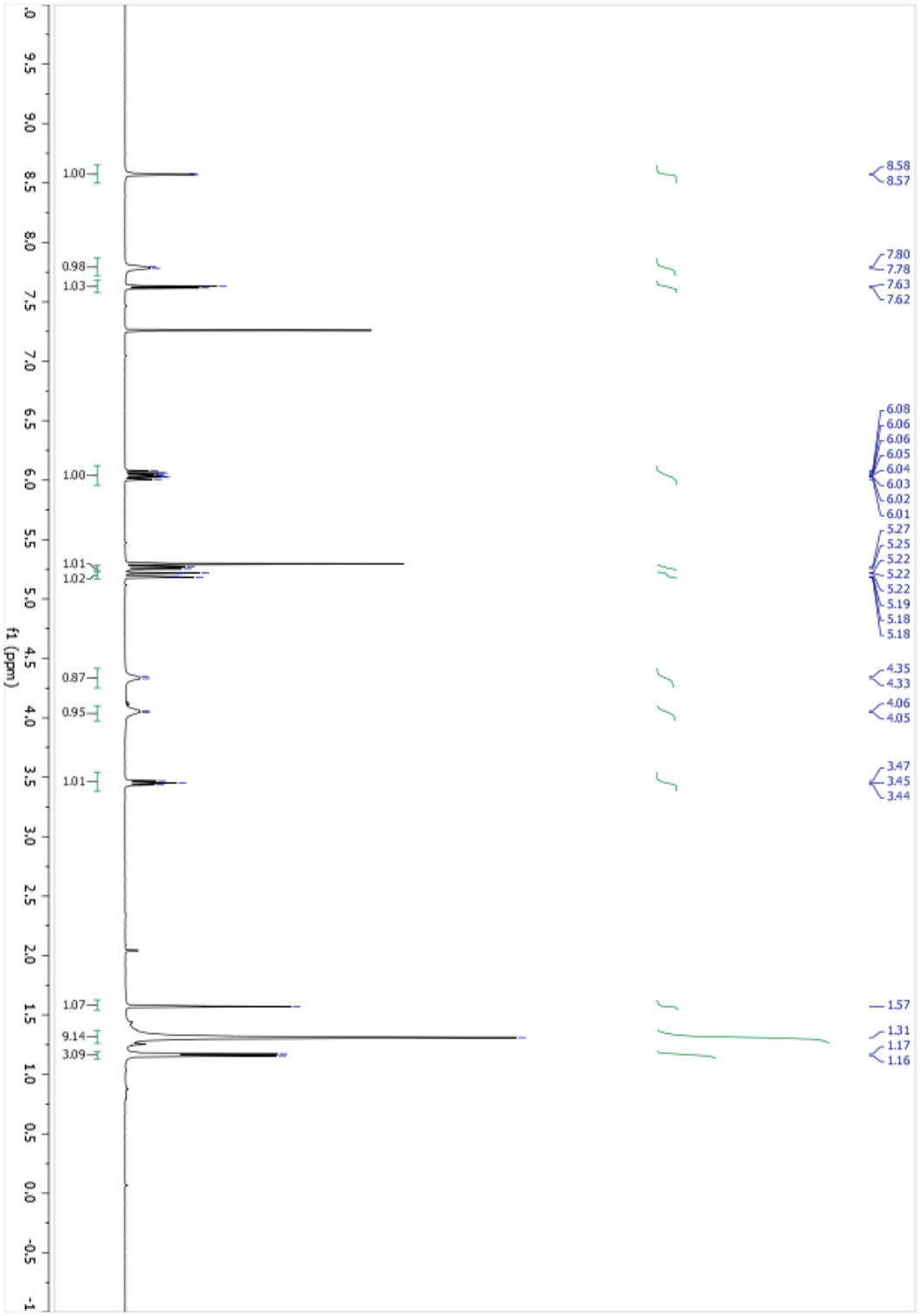
^{19}F NMR (471 MHz, $CDCl_3$) δ = -67.8.

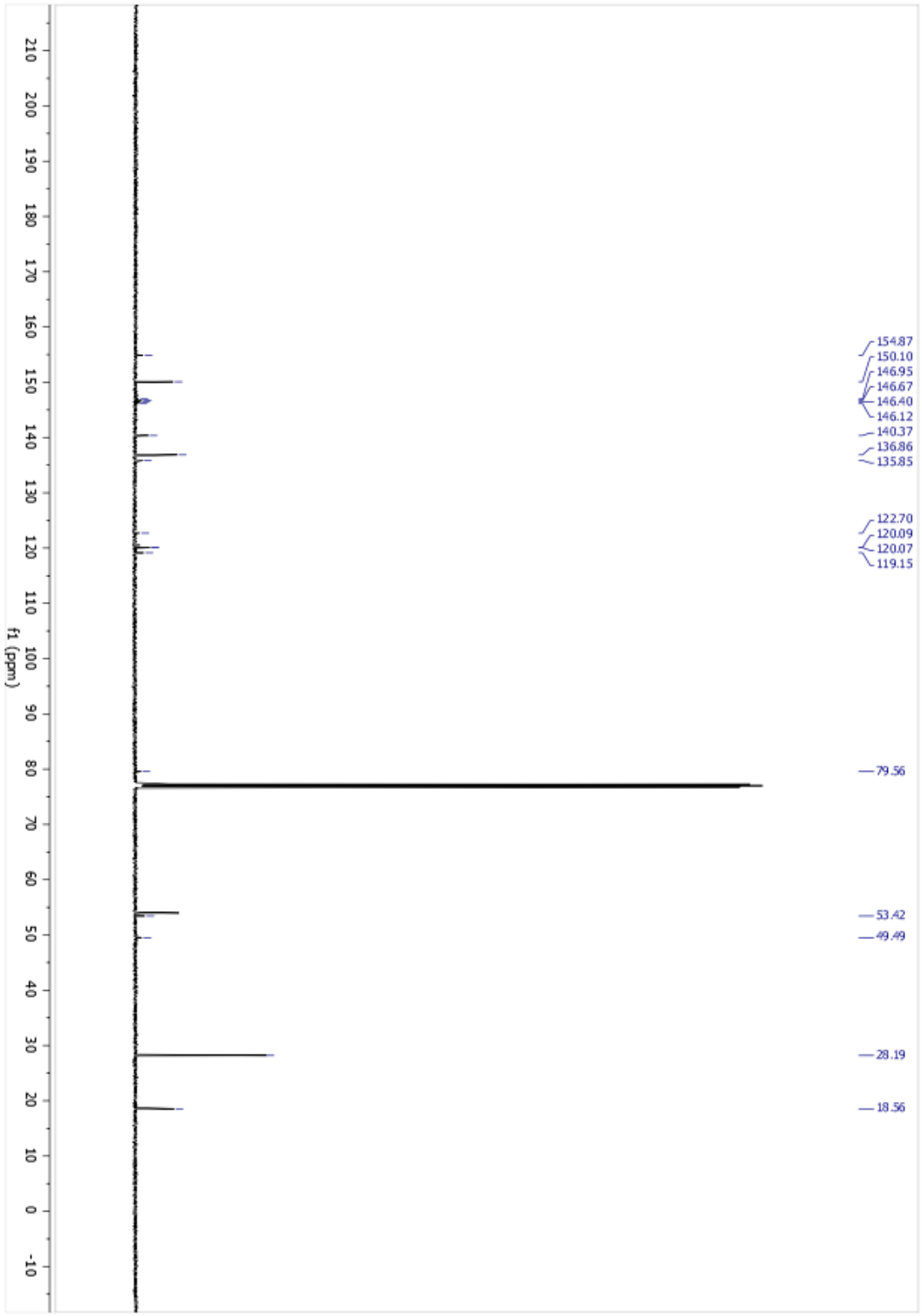
HRMS (ESI): Calculated for $C_{16}H_{21}F_3N_2O_2$ [M+H$^+$] = 331.1628, Found 331.1633.

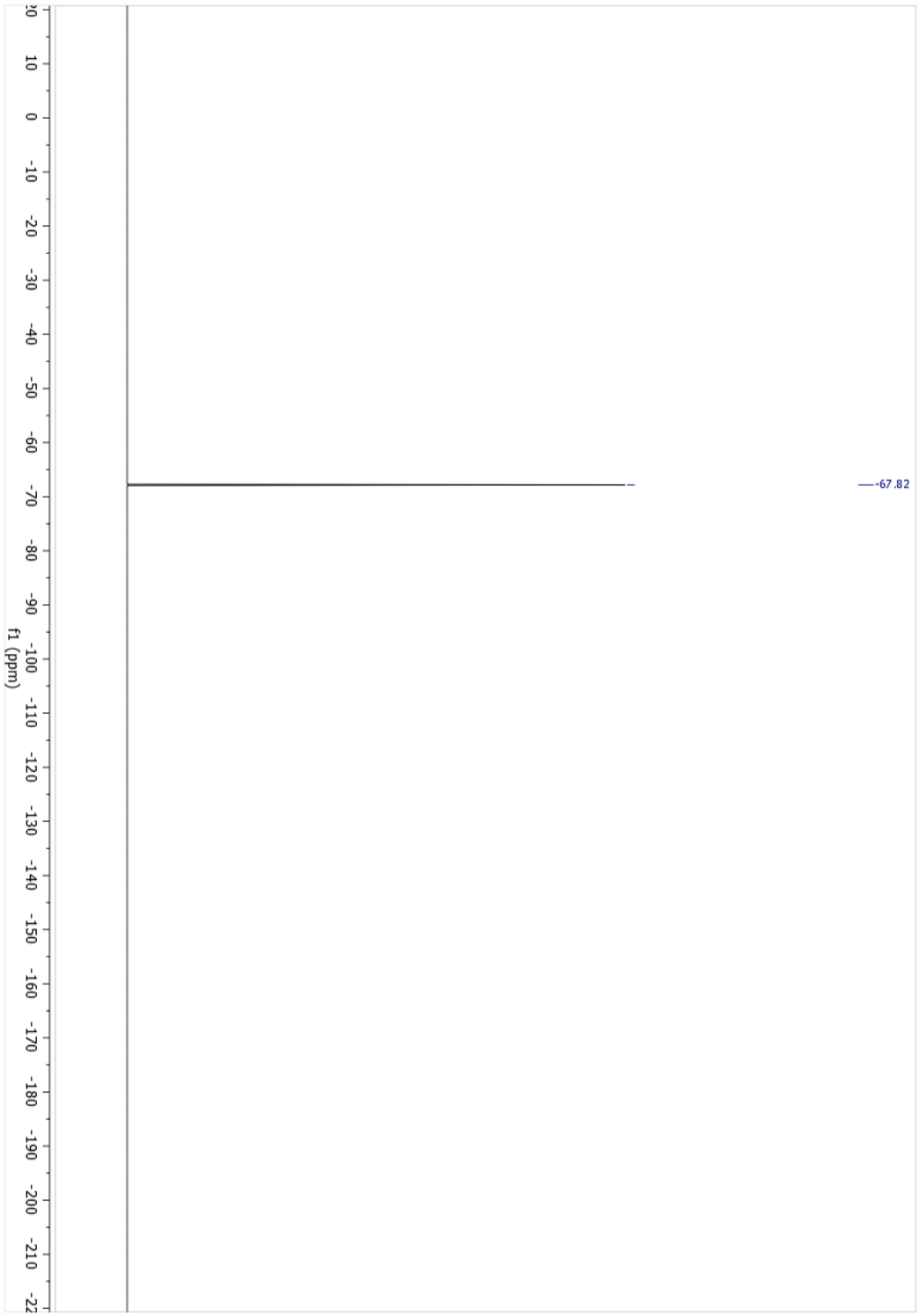
FTIR (neat): 3353, 2977, 2931, 2019, 1701, 1523, 1455, 1392, 1367, 1339, 1252, 1174, 1142, 1087, 1050, 1028, 926, 848 cm^{-1}.

$[\alpha]_D^{28}$ = -78.9 (*c* 0.19, $CHCl_3$).

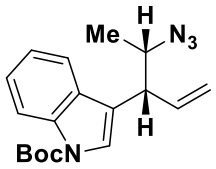
MP: 87-89 °C


f1 (ppm)
1.00
0.98
1.03
1.00
1.01
1.02
0.87
0.95
1.01
1.07
9.14
3.09
8.58
8.57
7.80
7.78
7.63
7.62
6.08
6.06
6.06
6.05
6.04
6.03
6.02
6.01
5.27
5.25
5.22
5.22
5.22
5.19
5.18
5.18
4.35
4.33
4.06
4.05
3.47
3.45
3.44
1.57
1.31
1.17
1.16


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
154.87
150.10
146.95
146.67
146.40
146.12
140.37
136.86
135.85
122.70
120.09
120.07
119.15
79.56
53.42
49.49
28.19
18.56


-67.82
f1 (ppm)

tert-butyl 3-((3R,4S)-4-azidopent-1-en-3-yl)-1H-indole-1-carboxylate (S5c)



Procedure

Homoallylic alcohol **2n** (48.2 mg, 0.160 mmol, 100 mol%) was subjected to general procedure E. The title compound was obtained in 62% yield (32.4 mg, 0.099 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 150:1–50:1).

TLC (SiO_2) R_f = 0.70 (hexanes: ethyl acetate = 3:1).

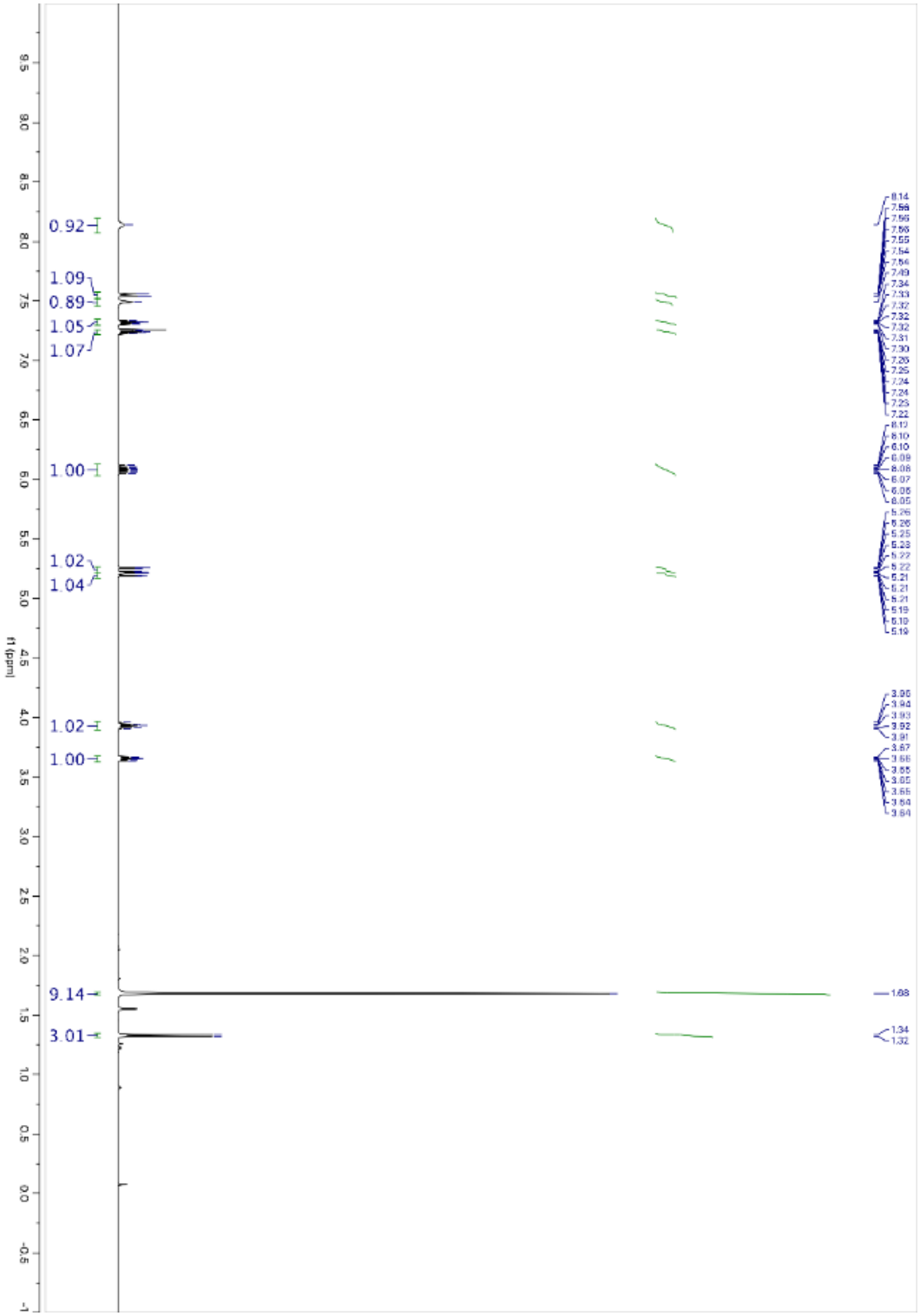
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.14 (s, 1H), 7.55 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.49 (s, 1H), 7.32 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.24 (td, *J* = 7.6, 7.2, 1.2 Hz, 1H), 6.08 (ddd, *J* = 17.0, 10.2, 8.4 Hz, 1H), 5.24 (dt, *J* = 17.0, 1.3 Hz, 1H), 5.20 (dt, *J* = 10.1, 1.1 Hz, 1H), 3.93 (p, *J* = 6.6 Hz, 1H), 3.69 – 3.62 (m, 1H), 1.68 (s, 9H), 1.33 (d, *J* = 6.6 Hz, 3H).

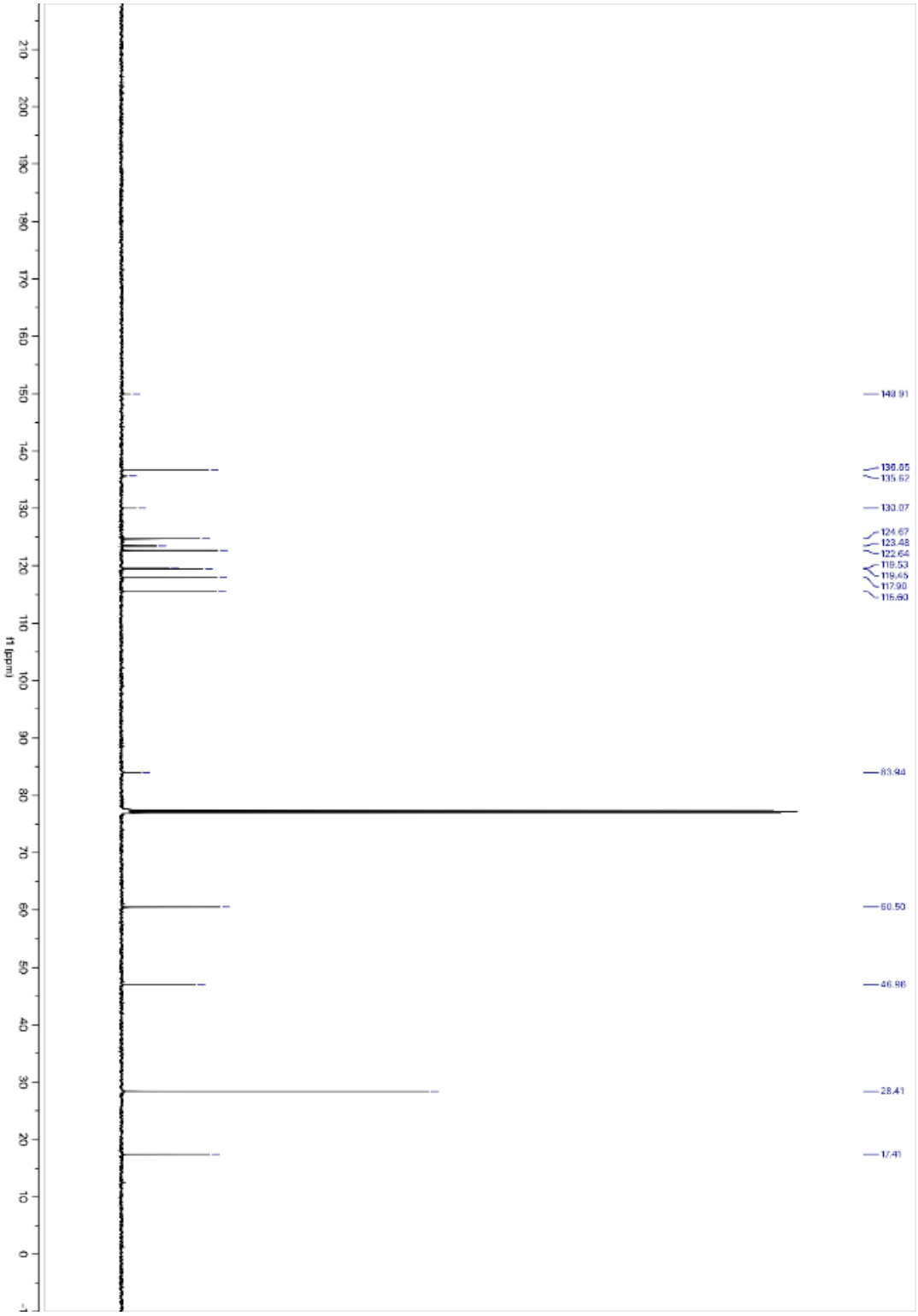
^{13}C NMR (126 MHz, $CDCl_3$) δ = 149.9, 136.7, 135.6, 130.1, 124.7, 123.5, 122.6, 119.5, 119.5, 117.9, 115.6, 83.9, 60.5, 47.0, 28.4, 17.4.

HRMS (ESI): Calculated for $C_{18}H_{22}N_4O_2$ [M+Na$^+$] = 349.1635, Found 349.1635.

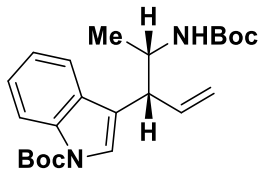
FTIR (neat): 2978, 2928, 2361, 2266, 2105, 1997, 1733, 1476, 1452, 1371, 1309, 1256, 1217, 1157, 1072, 1019, 923, 859, 766, 746 cm^{-1}.

$[\alpha]_D^{28}$= +25 (*c* 0.10, $CHCl_3$).


0.92
1.09
0.89
1.05
1.07
1.00
1.02
1.04
1.02
1.00
9.14
3.01
f1 (ppm)


f1 (ppm)
148.91
136.85
135.62
130.07
124.67
123.48
122.64
119.53
119.45
117.90
116.60
83.94
60.50
46.86
28.41
17.41

tert-butyl 3-((3R,4S)-4-((tert-butoxycarbonyl)amino)pent-1-en-3-yl)-1H-indole-1-carboxylate (5c)



Procedure

Homoallylic azide **S5c** (23.0 mg, 0.070 mmol, 100 mol%) was subjected to general procedure F. The title compound was obtained in 92% yield (25.9 mg, 0.065 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–10:1).

TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 3:1).

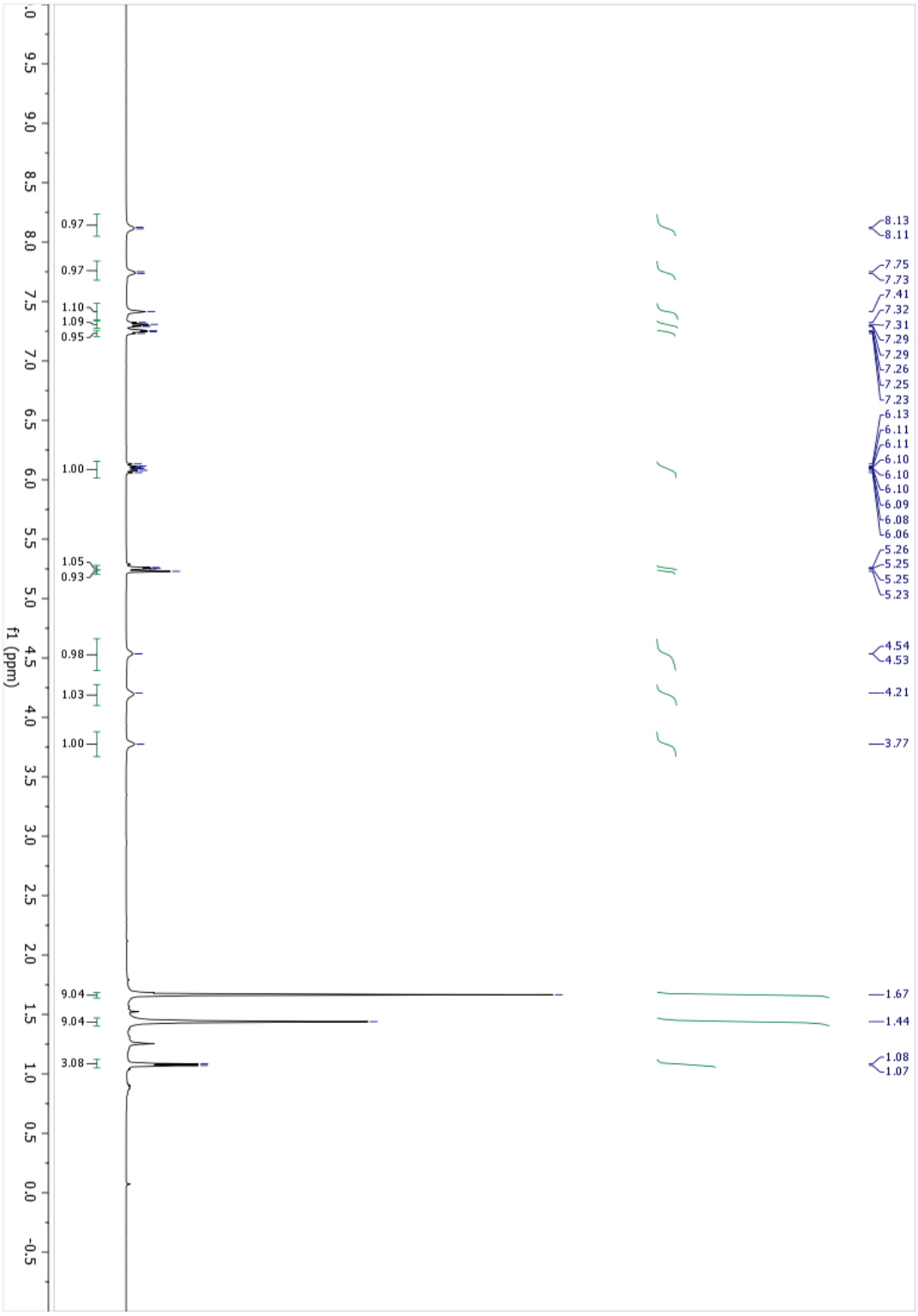
^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.23 – 8.05 (m, 1H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.41 (s, 1H), 7.34 – 7.28 (m, 1H), 7.24 (t, *J* = 6.1 Hz, 1H), 6.15 – 6.02 (m, 1H), 5.28 – 5.24 (m, 1H), 5.23 (s, 1H), 4.66 – 4.39 (m, 1H), 4.21 (s, 1H), 3.77 (s, 1H), 1.67 (s, 9H), 1.44 (s, 9H), 1.08 (d, *J* = 6.8 Hz, 3H).

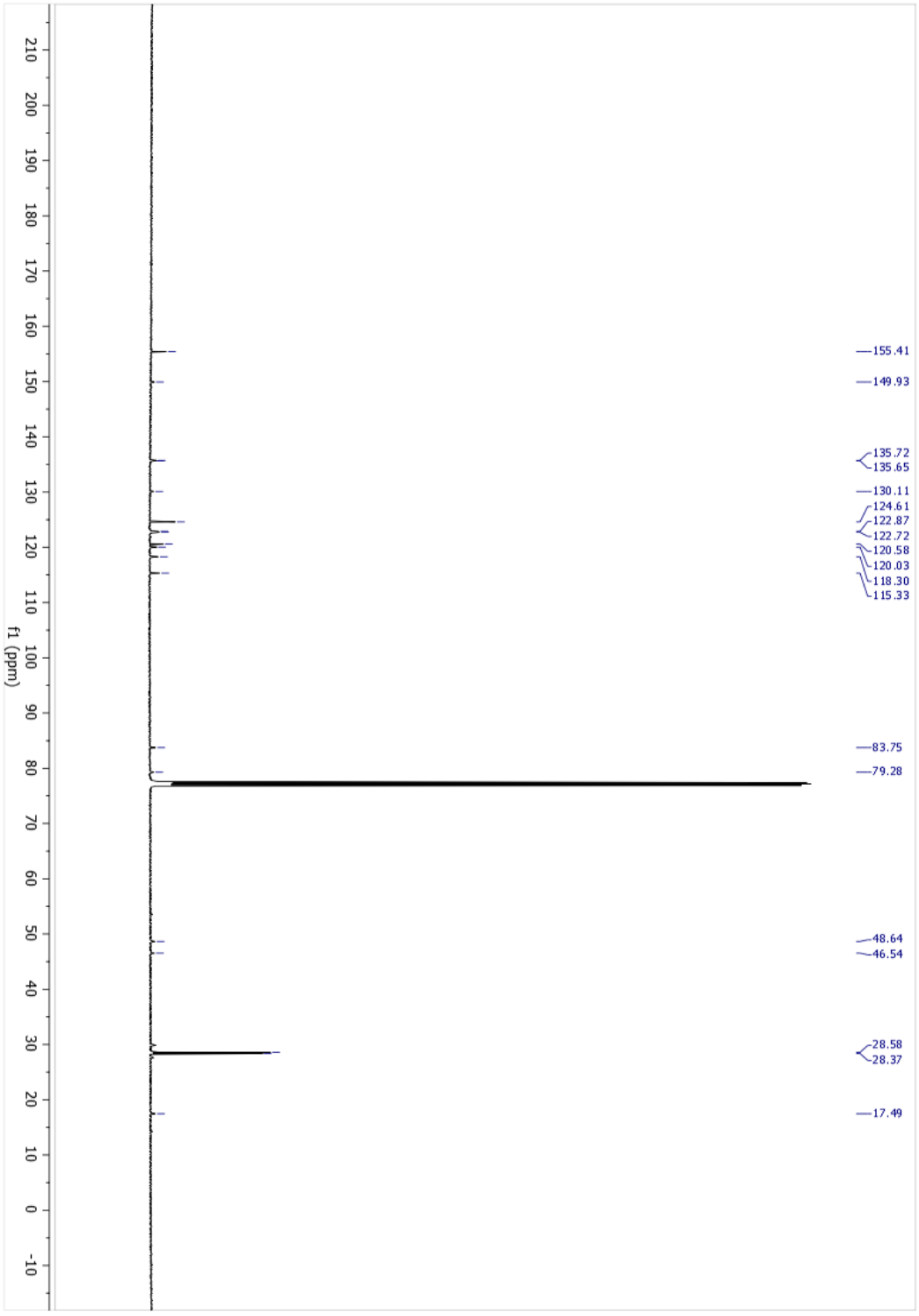
^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.4, 149.9, 135.7, 135.7, 130.1, 124.6, 122.9, 122.7, 120.6, 120.0, 118.3, 115.3, 83.8, 79.3, 48.6, 46.5, 28.6, 28.4, 17.5.

HRMS (ESI): Calculated for $C_{23}H_{32}N_2O_4$ [M+Na$^+$] = 423.2254, Found 423.2253.

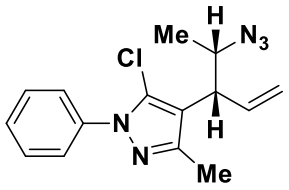
FTIR (neat): 3382, 2977, 2931, 1731, 1708, 1499, 1453, 1368, 1309, 1251, 1219, 1157, 1121, 1074, 1053, 1018, 921, 858, 766, 747 cm^{-1}.

$[\alpha]_D^{28}$= -50.0 (*c* 0.10, $CHCl_3$).


f1 (ppm)
0.97
0.97
1.10
1.09
0.95
1.00
1.05
0.93
0.98
1.03
1.00
9.04
9.04
3.08
8.13
8.11
7.75
7.73
7.41
7.32
7.31
7.29
7.29
7.26
7.25
7.23
6.13
6.11
6.11
6.10
6.10
6.10
6.09
6.08
6.06
5.26
5.25
5.25
5.23
4.54
4.53
4.21
3.77
1.67
1.44
1.08
1.07


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
155.41
149.93
135.72
135.65
130.11
124.61
122.87
122.72
120.58
120.03
118.30
115.33
83.75
79.28
48.64
46.54
28.58
28.37
17.49

4-((3R,4S)-4-azidopent-1-en-3-yl)-5-chloro-3-methyl-1-phenyl-1H-pyrazole (S5d)



Procedure

Homoallylic alcohol **2o** (33.8 mg, 0.122 mmol, 100 mol%) was subjected to general procedure E. The title compound was obtained in 76% yield (27.9 mg, 0.092 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 150:1–50:1).

TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 3:1).

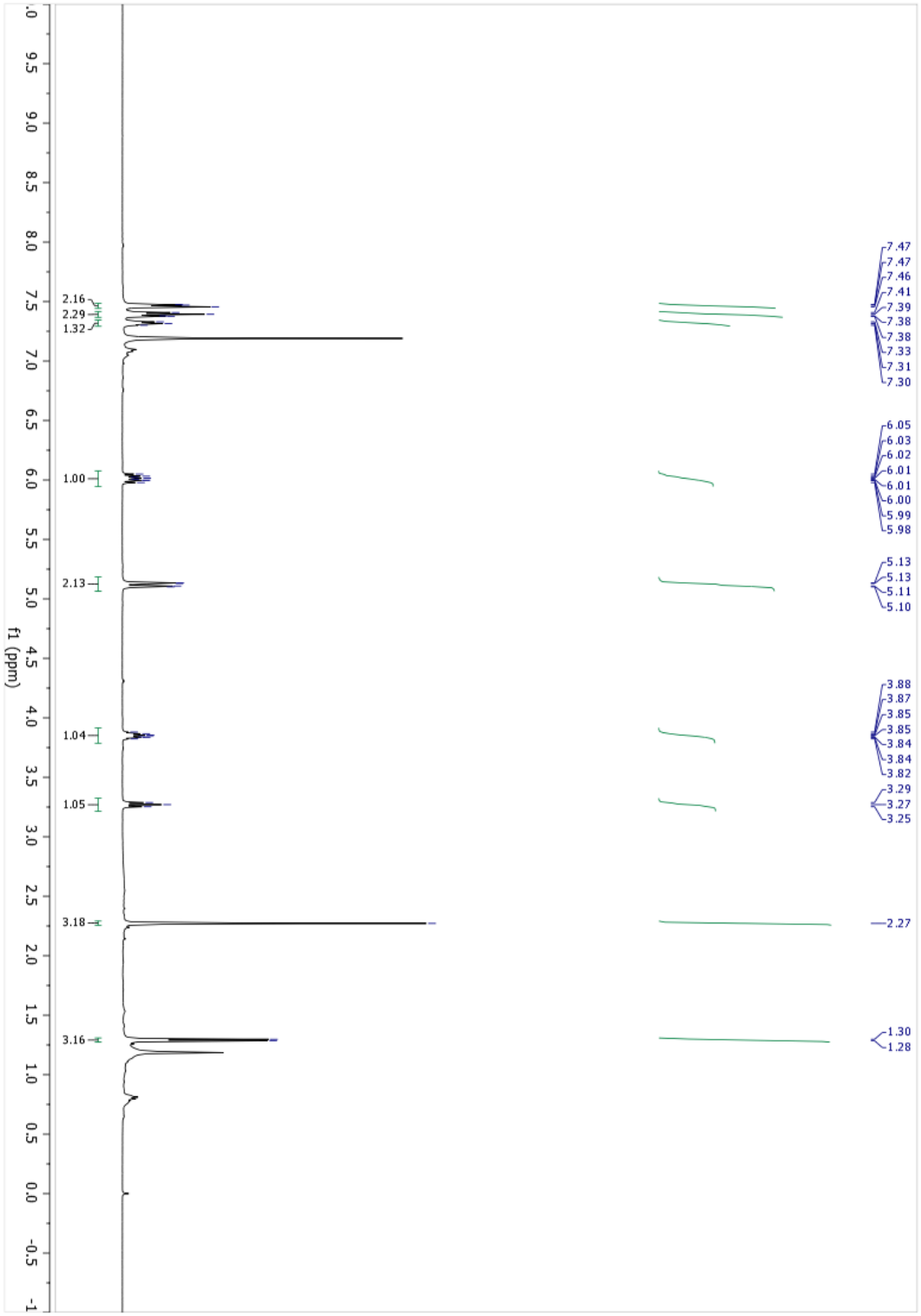
^{1}H NMR (500 MHz, $CDCl_3$): 7.48 – 7.44 (m, 2H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 6.08 – 5.94 (m, 1H), 5.12 (dd, *J* = 13.7, 3.0 Hz, 2H), 3.84 (dt, *J* = 8.6, 6.4 Hz, 1H), 3.27 (t, *J* = 8.8 Hz, 1H), 2.27 (s, 3H), 1.29 (d, *J* = 6.5 Hz, 3H).

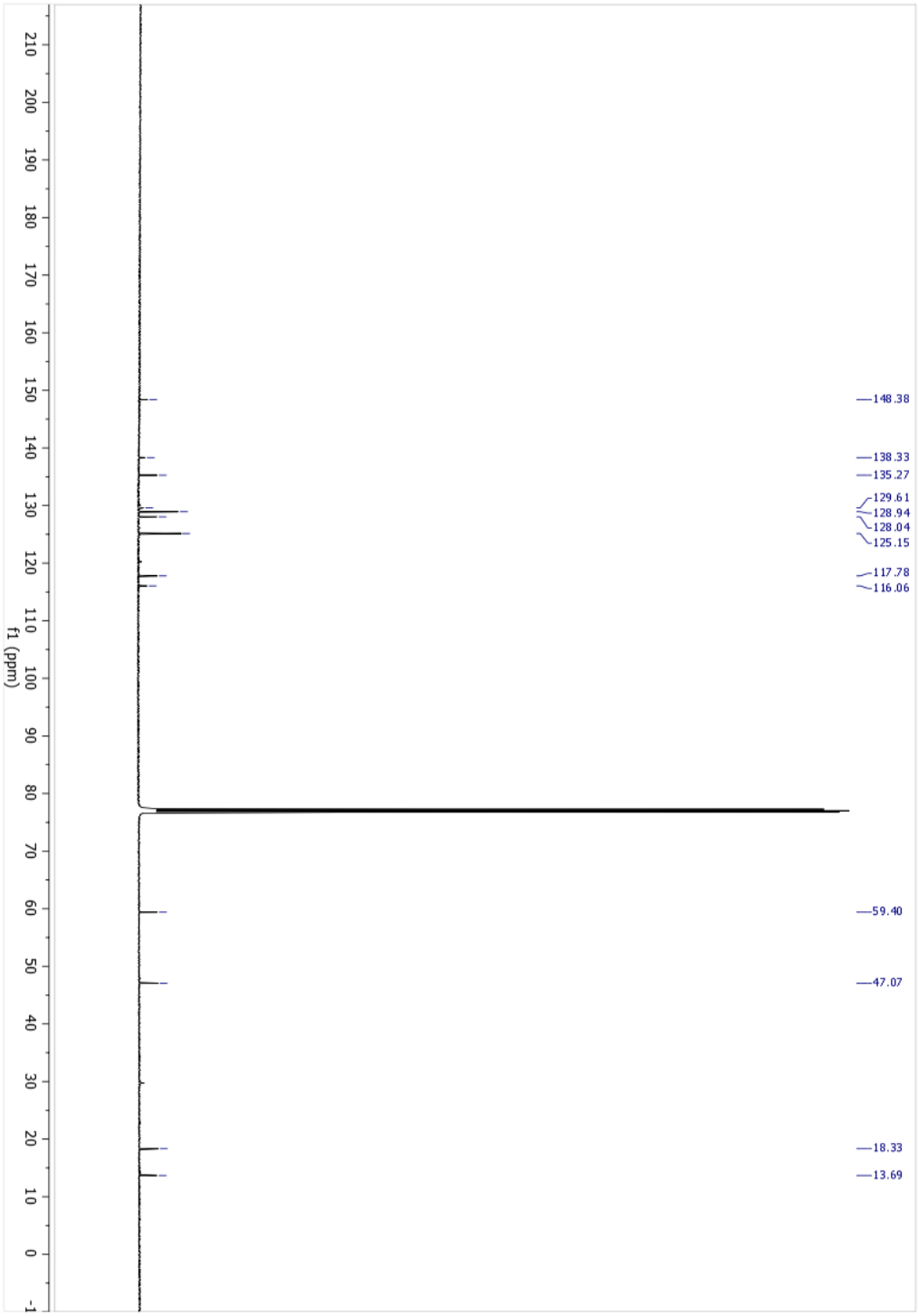
^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.4, 138.3, 135.3, 129.6, 128.9, 128.0, 125.2, 117.8, 116.1, 59.4, 47.0, 18.3, 13.7.

HRMS (ESI): Calculated for $C_{15}H_{16}ClN_5$ $[M+H^+]$ = 302.1167, Found 302.1167.

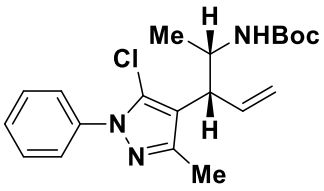
FTIR (neat): 3077, 2972, 2927, 2170, 2105, 2085, 1724, 1639, 1597, 1549, 1502, 1456, 1412, 1379, 1365, 1261, 1204, 1183, 1161, 1114, 1072, 1025, 1009, 988, 966, 921, 762, 693 cm^{-1}.

$[\alpha]_D^{28}$= +20.8 (*c* 0.12, $CHCl_3$).


f1 (ppm)
2.16
2.29
1.32
1.00
2.13
1.04
1.05
3.18
3.16
7.47
7.47
7.46
7.41
7.39
7.38
7.38
7.33
7.31
7.30
6.05
6.03
6.02
6.01
6.01
6.00
5.99
5.98
5.13
5.13
5.11
5.10
3.88
3.87
3.85
3.85
3.84
3.84
3.82
3.29
3.27
3.25
2.27
1.30
1.28


f1 (ppm)
148.38
138.33
135.27
129.61
128.94
128.04
125.15
117.78
116.06
59.40
47.07
18.33
13.69

tert-butyl ((2S,3R)-3-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)pent-4-en-2-yl)carbamate (5d)



Procedure

Homoallylic azide **S5d** (22.6 mg, 0.075 mmol, 100 mol%) was subjected to general procedure F. The title compound was obtained in 72% yield (20.2 mg, 0.054 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–10:1).

TLC (SiO_2) R_f = 0.35 (hexanes: ethyl acetate = 3:1).

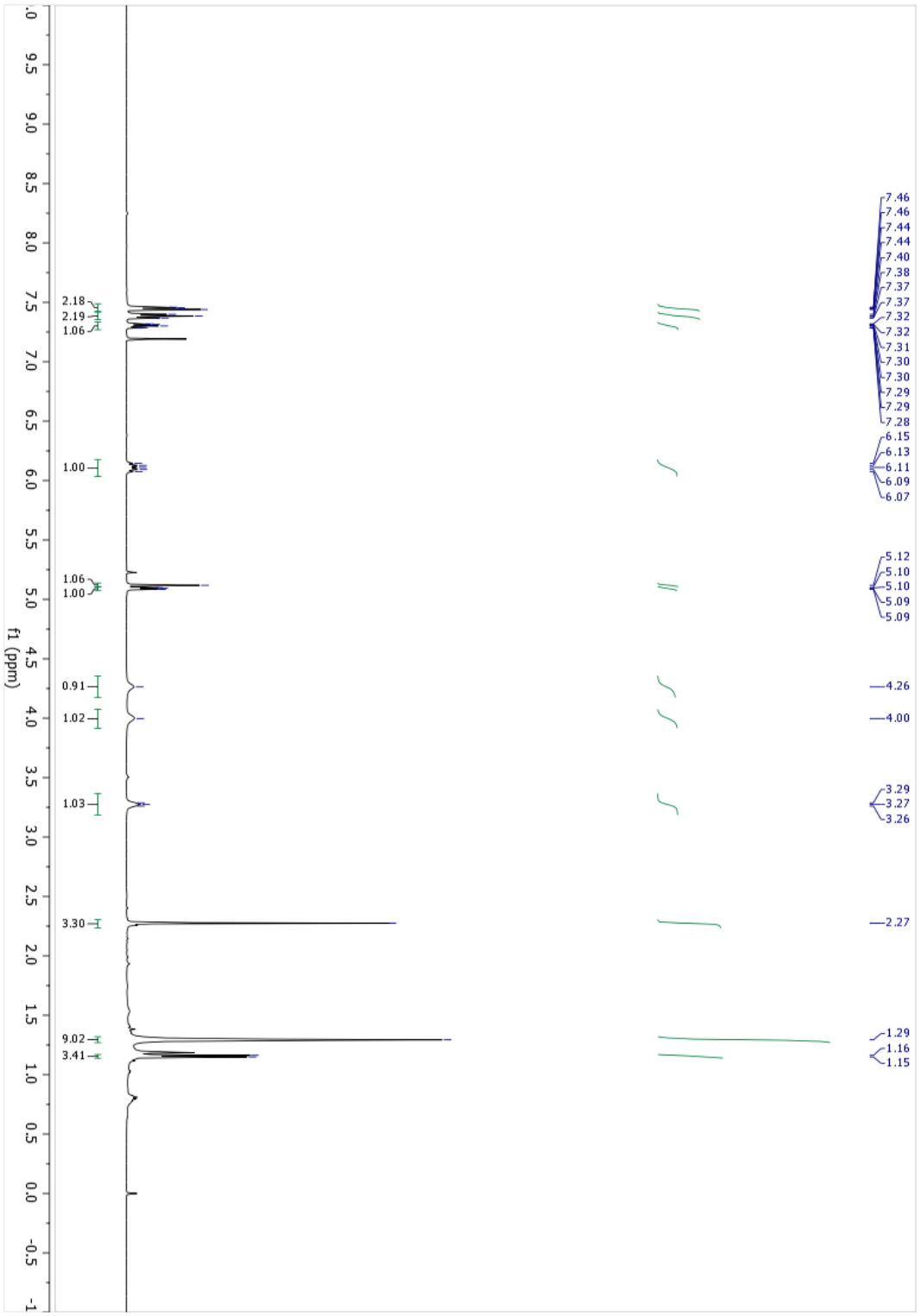
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (dd, J = 7.6, 1.8 Hz, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.33 – 7.27 (m, 1H), 6.11 (dt, J = 17.9, 9.2 Hz, 1H), 5.12 (s, 1H), 5.09 (dd, J = 5.4, 1.4 Hz, 1H), 4.26 (s, 1H), 4.00 (s, 1H), 3.27 (t, J = 6.8 Hz, 1H), 2.27 (s, 3H), 1.29 (s, 9H), 1.16 (d, J = 6.7 Hz, 3H).

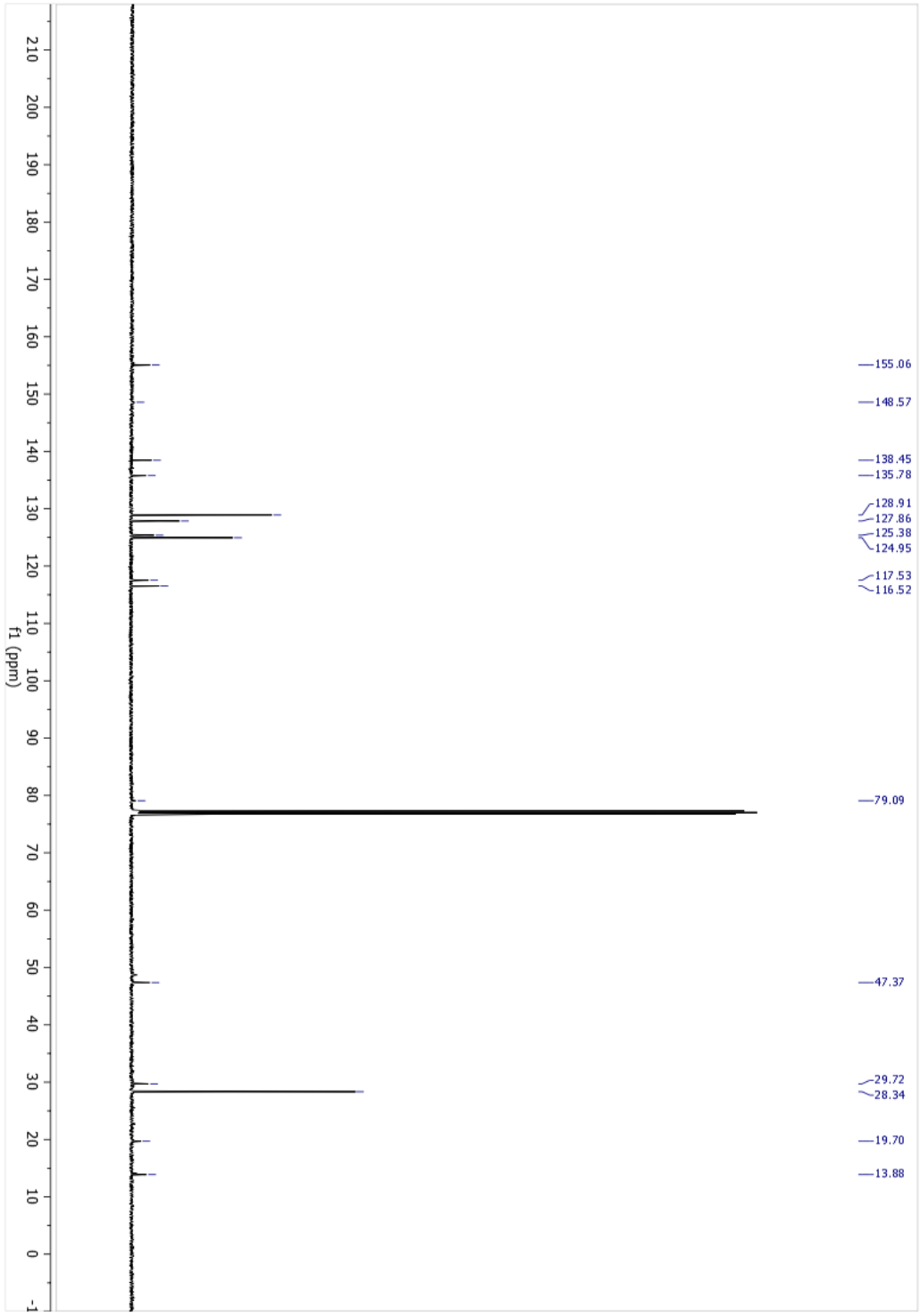
^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.1, 148.6, 138.4, 135.8, 128.9, 127.9, 125.4, 125.0, 117.5, 116.5, 79.1, 47.4, 29.7, 28.3, 19.7, 13.9.

HRMS (ESI): Calculated for $C_{20}H_{26}ClN_3O_2$ $[M+H^+]$ = 376.1786, Found 376.1790.

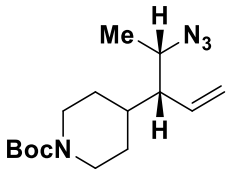
FTIR (neat): 3333, 2977, 2929, 2854, 2357, 2343, 2088, 1711, 1599, 1503, 1452, 1412, 1365, 1251, 1171, 1105, 1049, 1027, 988, 919, 861, 761, 694 cm^{-1}.

$[\alpha]_D^{28}$= -5.0 (*c* 0.1, $CHCl_3$).


f1 (ppm)
2.18
2.19
1.06
1.00
1.06
1.00
0.91
1.02
1.03
3.30
9.02
3.41
7.46
7.46
7.44
7.44
7.40
7.38
7.37
7.37
7.32
7.32
7.31
7.30
7.30
7.29
7.29
7.28
6.15
6.13
6.11
6.09
6.07
5.12
5.10
5.10
5.09
5.09
4.26
4.00
3.29
3.27
3.26
2.27
1.29
1.16
1.15


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
155.06
148.57
138.45
135.78
128.91
127.86
125.38
124.95
117.53
116.52
79.09
47.37
29.72
28.34
19.70
13.88

tert-butyl 4-((3R,4S)-4-azidopent-1-en-3-yl)piperidine-1-carboxylate (S5e)



Procedure

Homoallylic alcohol **2p** (62.5 mg, 0.232 mmol, 100 mol%) was subjected to general procedure E. The title compound was obtained in 97% yield (66.4 mg, 0.226 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 150:1–40:1).

TLC (SiO_2) R_f = 0.65 (hexanes: ethyl acetate = 3:1).

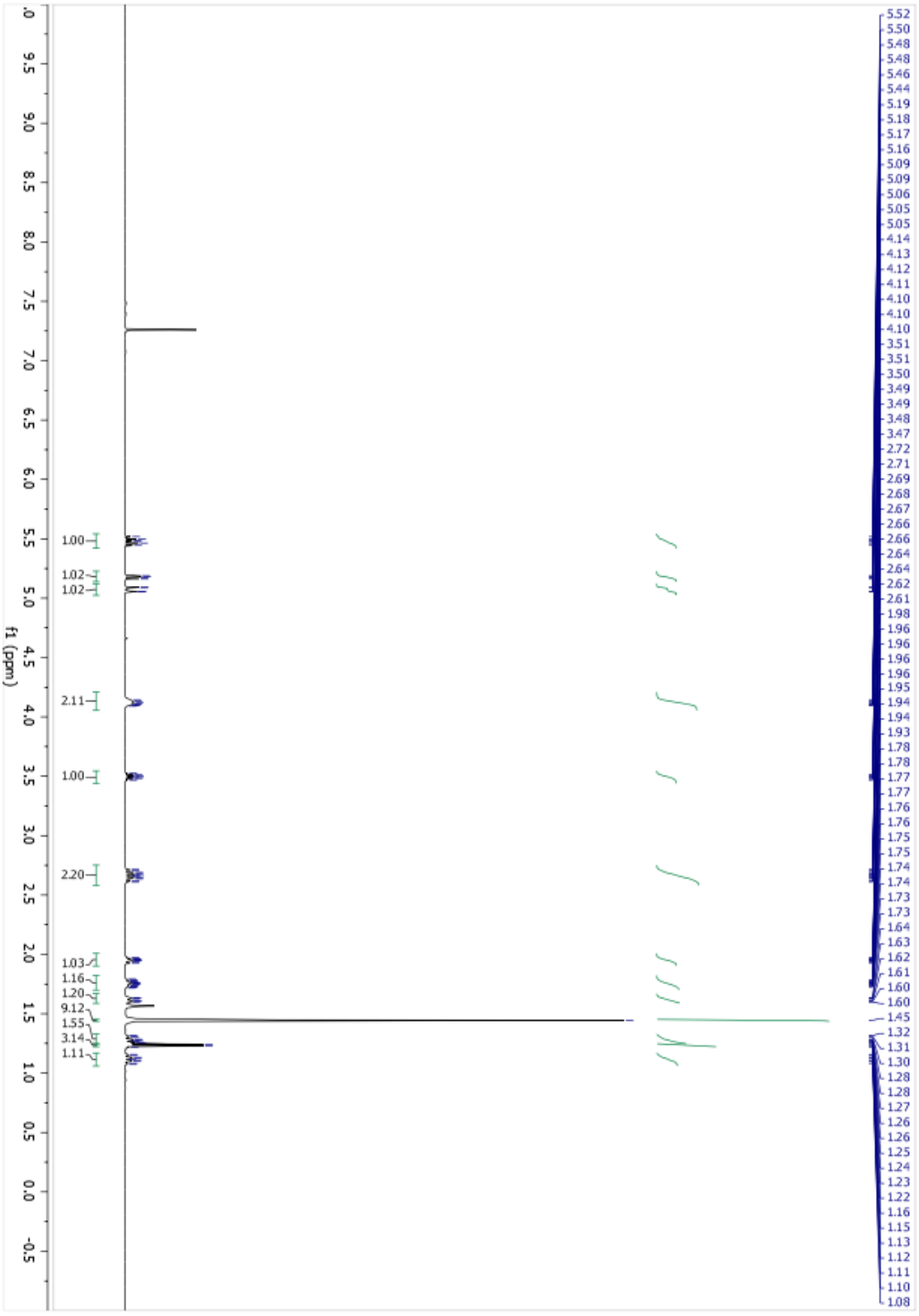
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.48 (dt, *J* = 17.0, 10.1 Hz, 1H), 5.18 (dd, *J* = 10.2, 1.9 Hz, 1H), 5.12 – 5.02 (m, 1H), 4.21 – 4.05 (m, 2H), 3.50 (dq, *J* = 8.4, 6.6 Hz, 1H), 2.66 (dtd, *J* = 23.1, 12.9, 2.9 Hz, 2H), 2.01 – 1.90 (m, 1H), 1.76 (dddd, *J* = 12.0, 8.6, 4.9, 2.5 Hz, 1H), 1.62 (dt, *J* = 13.1, 2.8 Hz, 1H), 1.45 (s, 9H), 1.33 – 1.21 (m, 2H), 1.24 (d, *J* = 6.5 Hz, 3H), 1.12 (qd, *J* = 12.5, 4.4 Hz, 1H).

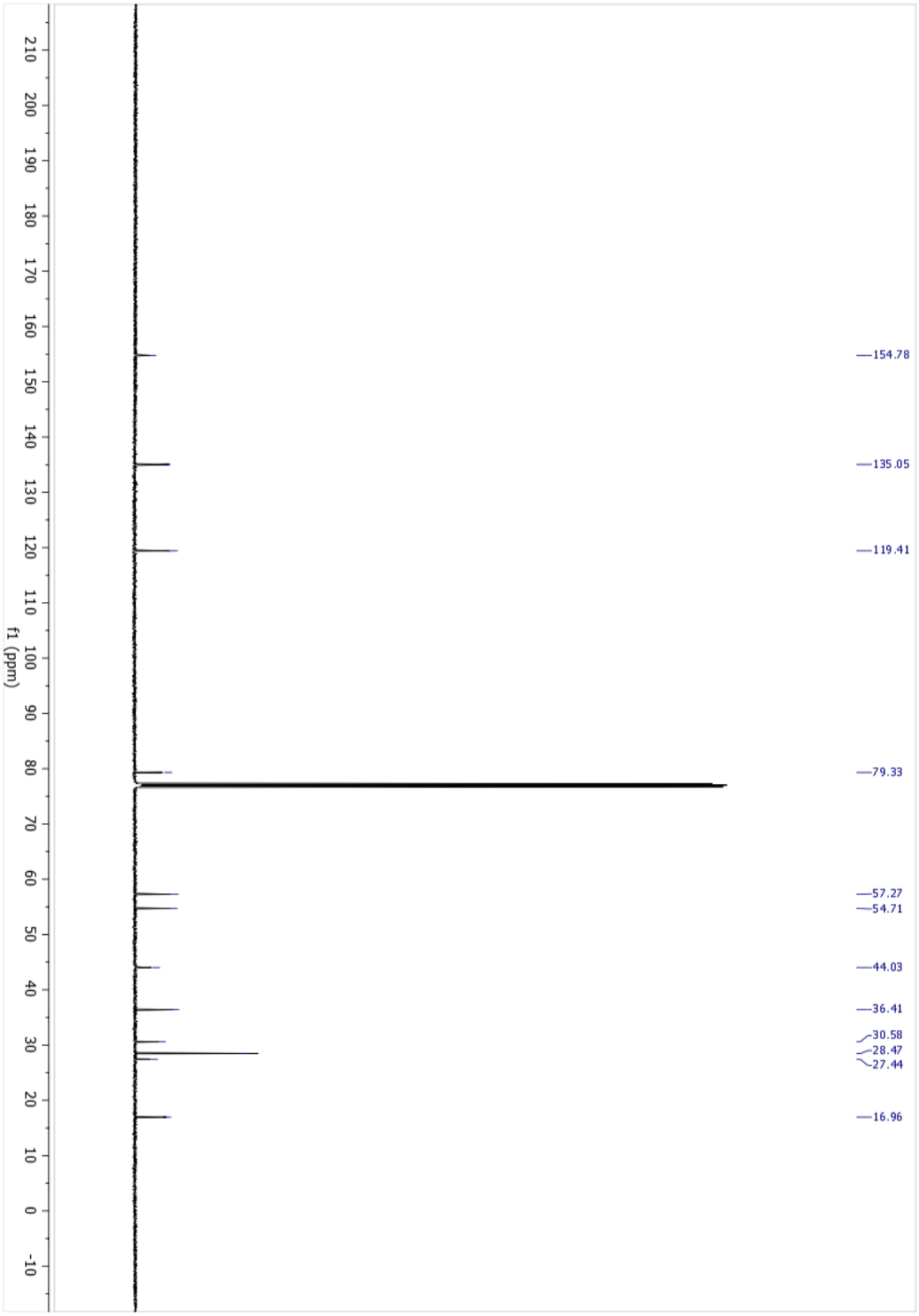
^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.1, 148.6, 138.5, 135.8, 128.9, 127.9, 125.4, 125.0, 117.5, 116.5, 79.1, 47.4, 29.7, 28.3, 19.7, 13.9.

HRMS (ESI): Calculated for $C_{15}H_{26}N_4O_2$ [M+Na$^+$] = 317.1948, Found 317.1949.

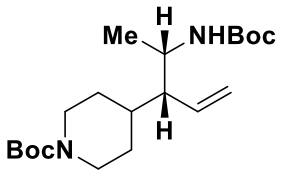
FTIR (neat): 2928, 2855, 2087, 1721, 1691, 1449, 1422, 1391, 1365, 1267, 1250, 1234, 1173, 1153, 1103, 1040, 1019, 1001, 921, 867, 769, 732 cm^{-1}.

$[\alpha]_D^{28}$ = +25.0 (*c* 0.1, $CHCl_3$).


f1 (ppm)
1.00
1.02
1.02
2.11
1.00
2.20
1.03
1.16
1.20
9.12
1.55
3.14
1.11


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
154.78
135.05
119.41
79.33
57.27
54.71
44.03
36.41
30.58
28.47
27.44
16.96

tert-butyl 4-((3R,4S)-4-((tert-butoxycarbonyl)amino)pent-1-en-3-yl)piperidine-1-carboxylate (5e)



Procedure

Homoallylic azide **S5e** (63.0 mg, 0.214 mmol, 100 mol%) was subjected to general procedure F. The title compound was obtained in 91% yield (71.7 mg, 0.195 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–10:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 3:1).

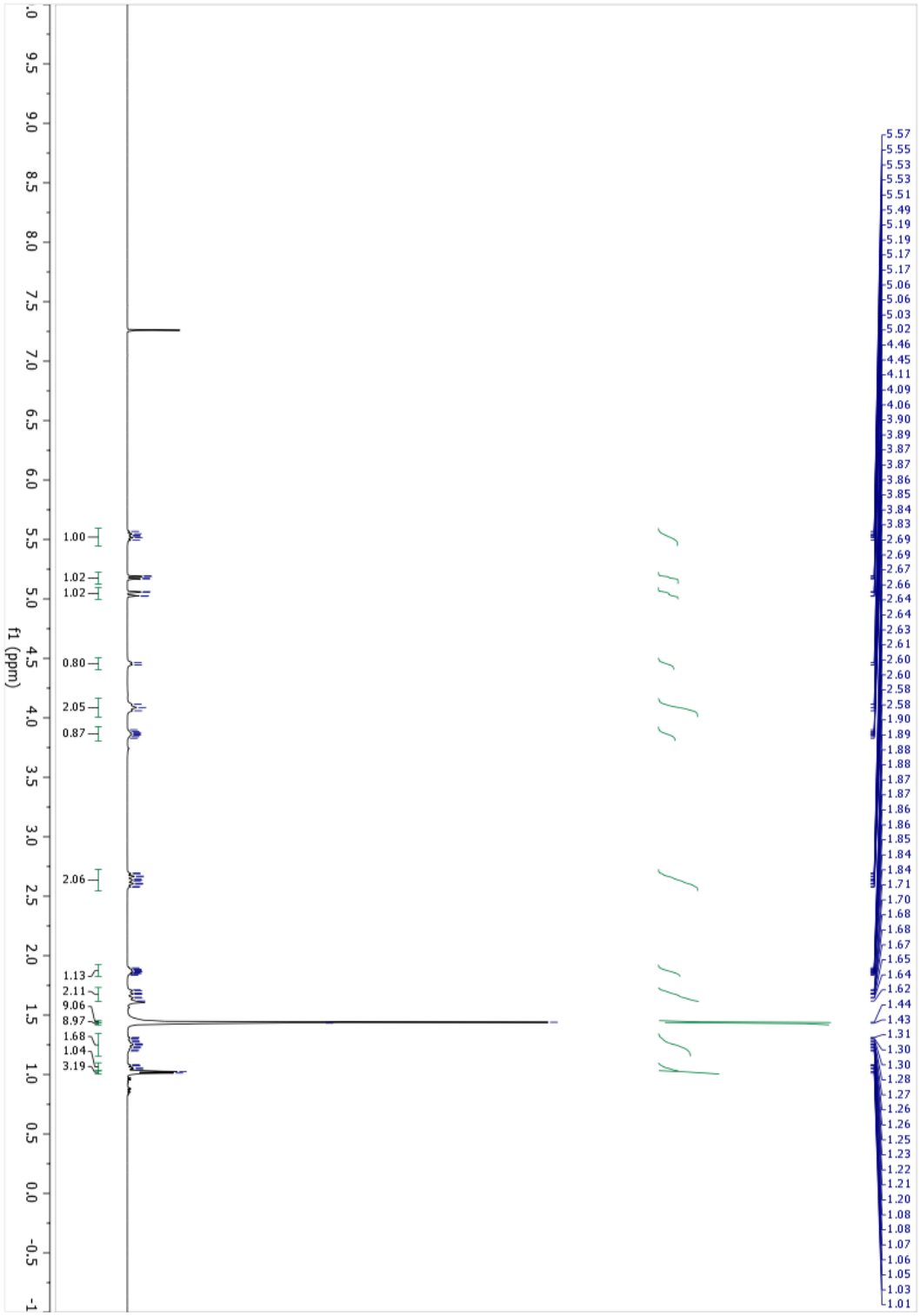
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.53 (dt, J = 17.0, 10.1 Hz, 1H), 5.18 (dd, J = 10.2, 2.1 Hz, 1H), 5.04 (dd, J = 17.1, 2.1 Hz, 1H), 4.46 (d, J = 9.3 Hz, 1H), 4.09 (t, J = 13.6 Hz, 2H), 3.86 (dt, J = 9.3, 6.4 Hz, 1H), 2.73 – 2.54 (m, 2H), 1.92 – 1.82 (m, 1H), 1.73 – 1.61 (m, 2H), 1.44 (s, 9H), 1.43 (s, 9H), 1.34 – 1.15 (m, 2H), 1.07 (dd, J = 12.5, 4.4 Hz, 1H), 1.02 (d, J = 6.8 Hz, 3H).

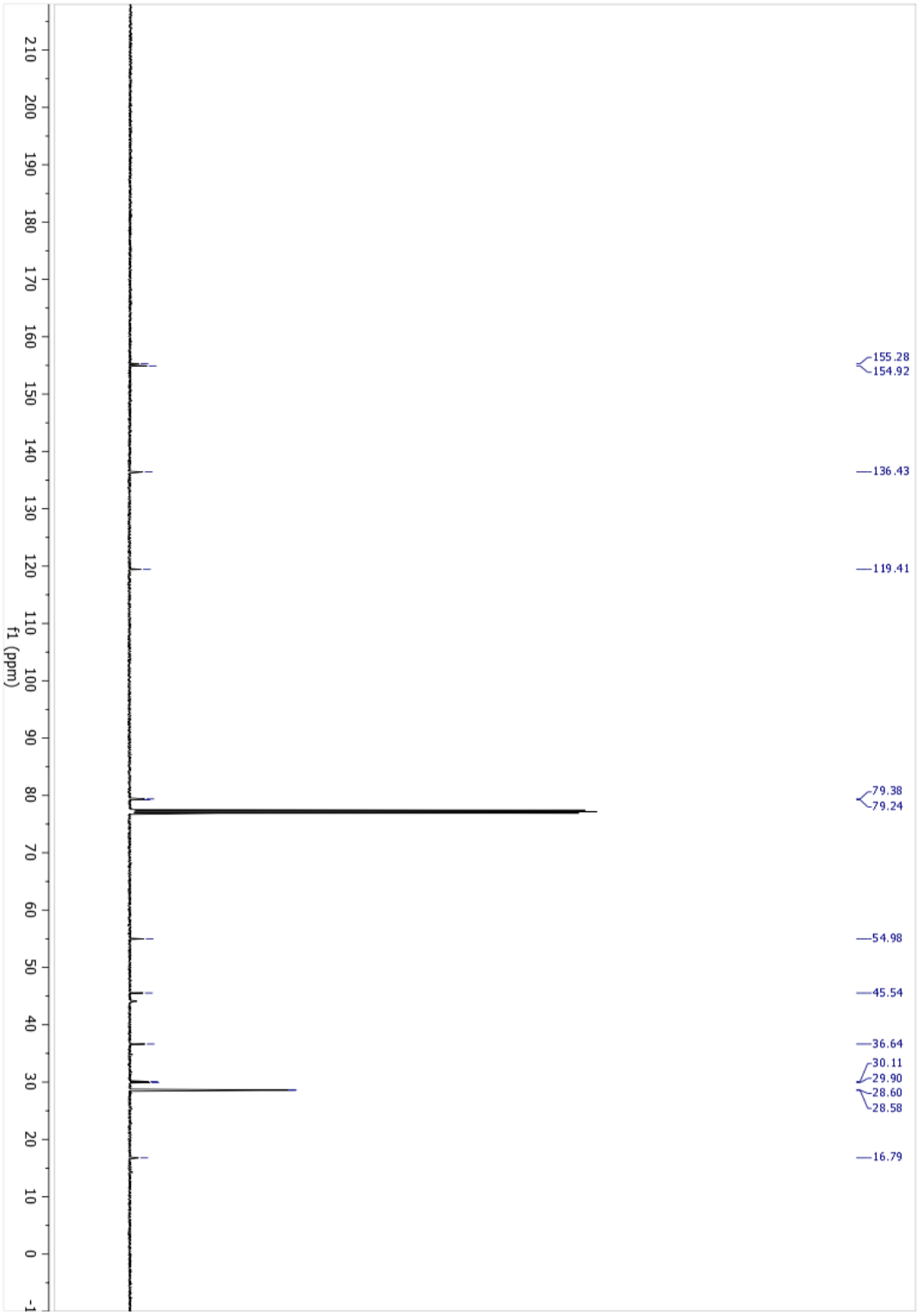
^{13}C NMR (126 MHz, $CDCl_3$) δ = 155.1, 154.8, 136.3, 119.3, 79.3, 79.1, 54.8, 45.4, 44.0, 36.5, 30.0, 29.8, 28.5, 28.5.

HRMS (ESI): Calculated for $C_{20}H_{36}N_2O_4$ [M+Na$^+$] = 391.2567, Found 391.2566.

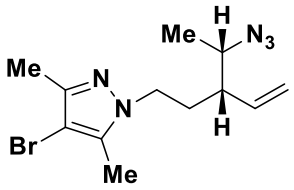
FTIR (neat): 3336, 2976, 2932, 2855, 1693, 1676, 1524, 1449, 1424, 1365, 1277, 1234, 1166, 1097, 1045, 1030, 976, 916, 868, 769 cm^{-1}.

$[\alpha]_D^{28}$= -7.6 (*c* 0.13, $CHCl_3$).


f1 (ppm)
1.00
1.02
1.02
0.80
2.05
0.87
2.06
1.13
2.11
9.06
8.97
1.68
1.04
3.19


f1 (ppm)
155.28
154.92
136.43
119.41
79.38
79.24
54.98
45.54
36.64
30.11
29.90
28.60
28.58
16.79

1-((S)-3-((S)-1-azidoethyl)pent-4-en-1-yl)-4-bromo-3,5-dimethyl-1H-pyrazole (S5f)



Procedure

Homoallylic alcohol **2e** (57.4 mg, 0.200 mmol, 100 mol%) was subjected to general procedure E. The title compound was obtained in 93% yield (57.8 mg, 0.185 mmol, >20:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 150:1–40:1).

TLC (SiO_2) R_f = 0.51 (hexanes: ethyl acetate = 3:1).

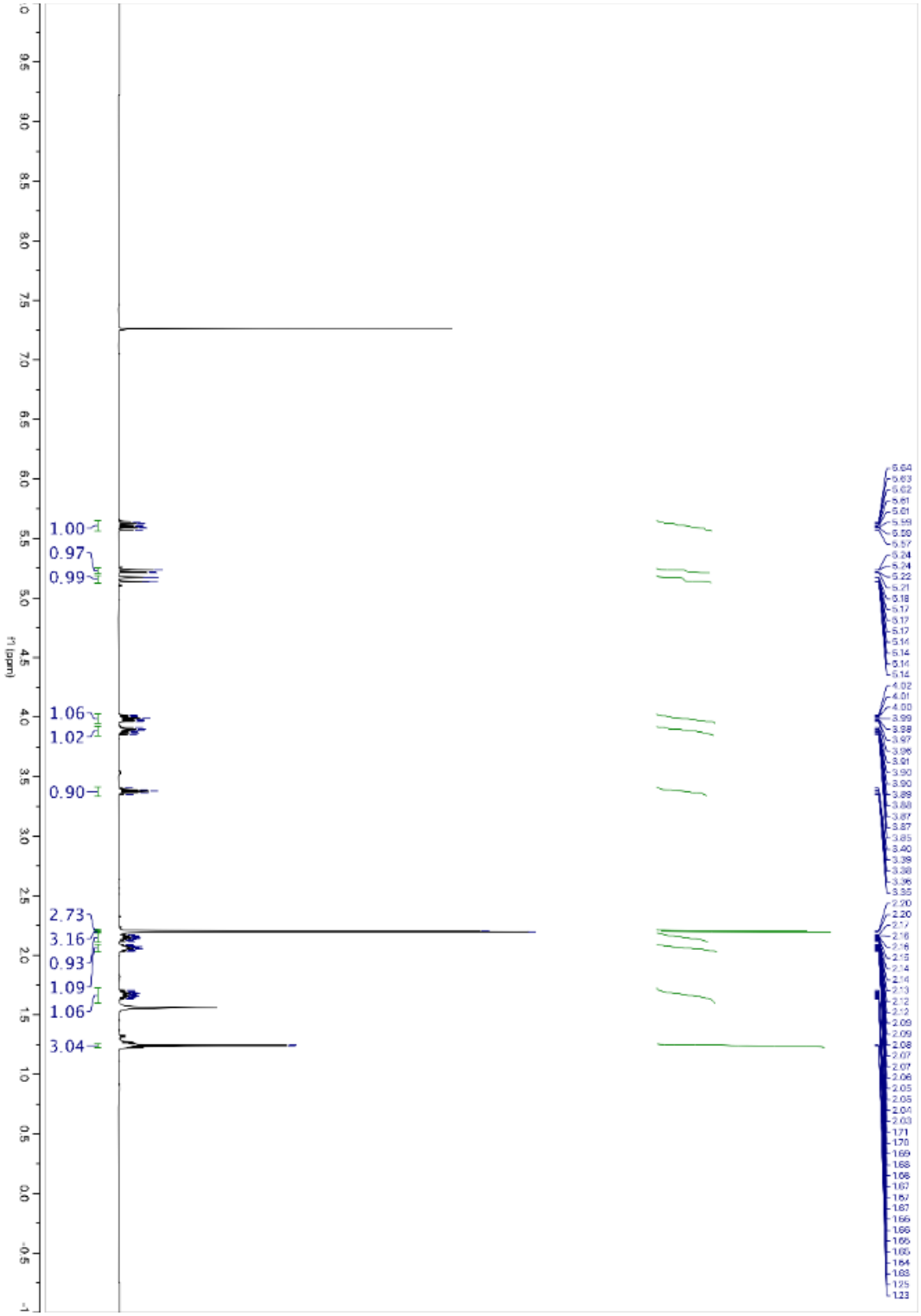
^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.61 (ddd, *J* = 17.1, 10.3, 9.1 Hz, 1H), 5.23 (dd, *J* = 10.3, 1.6 Hz, 1H), 5.16 (ddd, *J* = 17.1, 1.6, 0.8 Hz, 1H), 3.99 (ddd, *J* = 14.3, 9.5, 5.0 Hz, 1H), 3.88 (ddd, *J* = 13.9, 9.2, 7.0 Hz, 1H), 3.38 (p, *J* = 6.7 Hz, 1H), 2.20 (s, 3H), 2.20 (s, 3H), 2.14 (dtd, *J* = 9.8, 7.0, 6.5, 3.0 Hz, 1H), 2.06 (tdd, *J* = 9.7, 6.7, 3.1 Hz, 1H), 1.67 (dddd, *J* = 13.7, 10.6, 9.2, 4.9 Hz, 1H), 1.24 (d, *J* = 6.7 Hz, 3H).

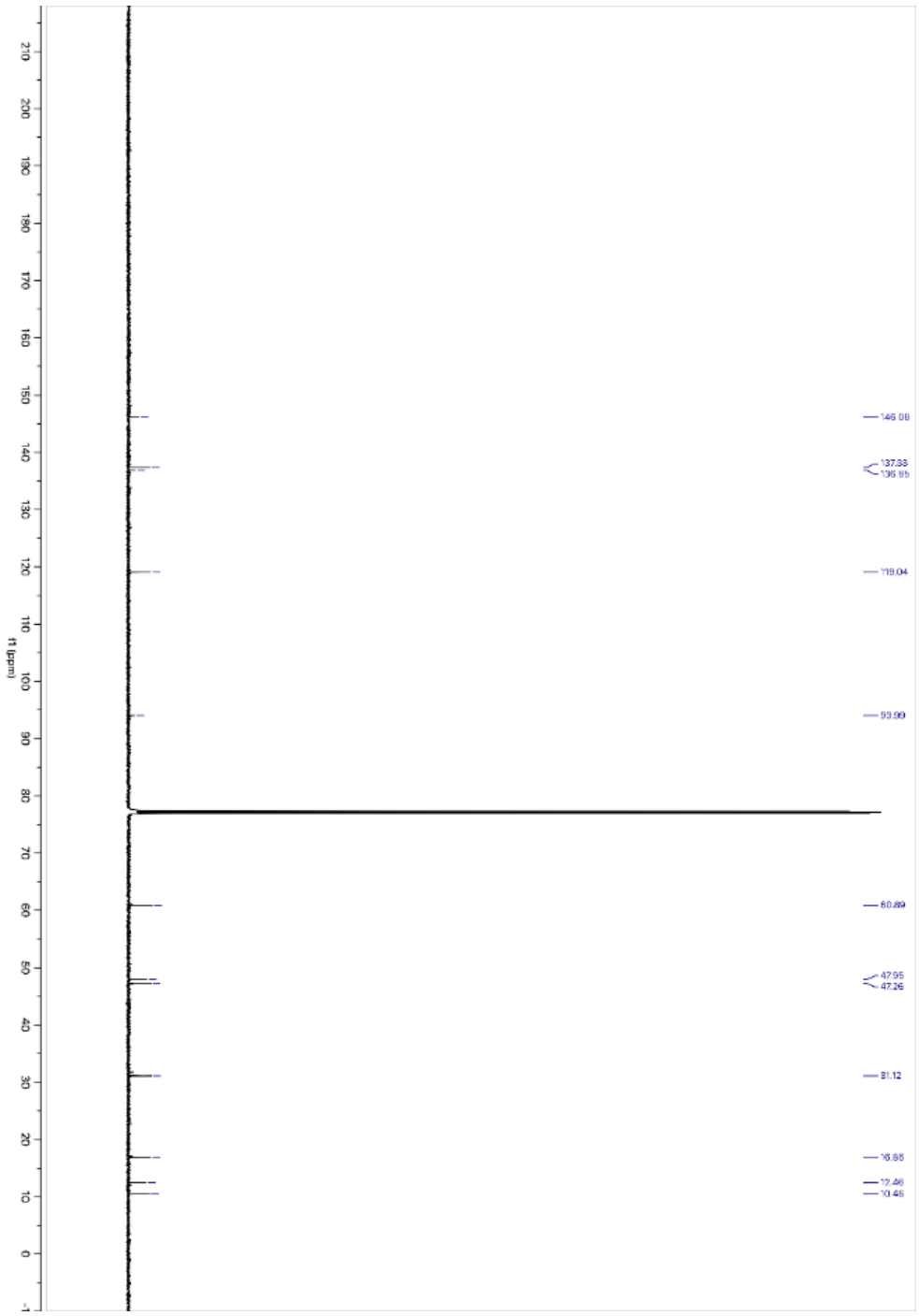
^{13}C NMR (126 MHz, $CDCl_3$) δ = 146.1, 137.3, 136.9, 119.0, 94.0, 60.9, 48.0, 47.3, 31.1, 16.9, 12.5, 10.5.

HRMS (ESI): Calculated for $C_{12}H_{18}BrN_5$ [M+H$^+$] = 312.0818, Found 312.0819.

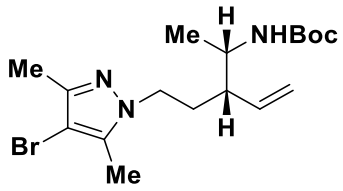
FTIR (neat): 2976, 2927, 2177, 2160, 2104, 2021, 1979, 1733, 1641, 1547, 1475, 1456, 1422, 1382, 1315, 1261, 1068, 998, 926, 842, 683 cm^{-1}.

$[\alpha]_D^{28}$= +25.0 (*c* 0.10, $CHCl_3$).


f1 (ppm)
1.00
0.97
0.99
1.06
1.02
0.90
2.73
3.16
0.93
1.09
1.06
3.04


f1 (ppm)
146.08
137.88
136.85
119.04
93.99
80.89
47.95
47.26
31.12
18.85
12.46
10.46

tert-butyl ((2S,3S)-3-(2-(4-bromo-3,5-dimethyl-1H-pyrazol-1-yl)ethyl)pent-4-en-2-yl)carbamate (5f)



Procedure

Homoallylic azide **S5f** (50.5 mg, 0.162 mmol, 100 mol%) was subjected to general procedure F. The title compound was obtained in 92% yield (57.3 mg, 0.148 mmol, >20:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–10:1).

TLC (SiO_2) R_f = 0.34 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.60 (dt, J = 16.7, 9.6 Hz, 1H), 5.21 (d, J = 10.0 Hz, 1H), 5.16 – 5.05 (m, 1H), 4.49 (d, J = 8.6 Hz, 1H), 3.97 (s, 1H), 3.89 (s, 1H), 3.65 (s, 1H), 2.20 (s, 6H), 2.11 (s, 1H), 2.01 (s, 1H), 1.76 – 1.65 (m, 1H), 1.43 (s, 10H), 1.04 (d, J = 6.3 Hz, 3H).

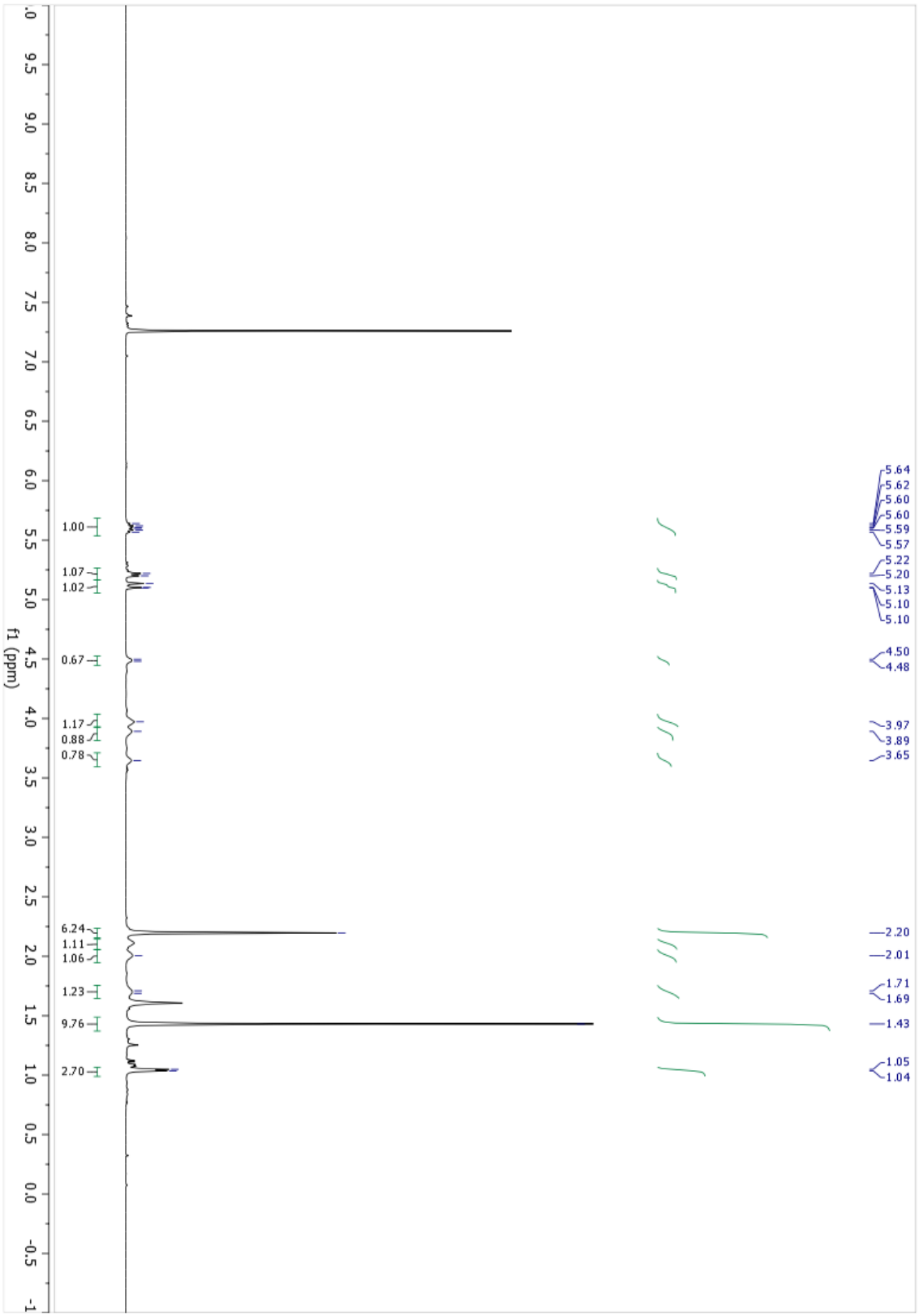
^{13}C NMR (126 MHz, $CDCl_3$): δ = 155.3, 145.8, 137.3, 136.7, 118.9, 93.7, 79.2, 49.1, 48.0, 47.1, 31.7, 28.4, 17.3, 12.3, 10.3, 10.2.

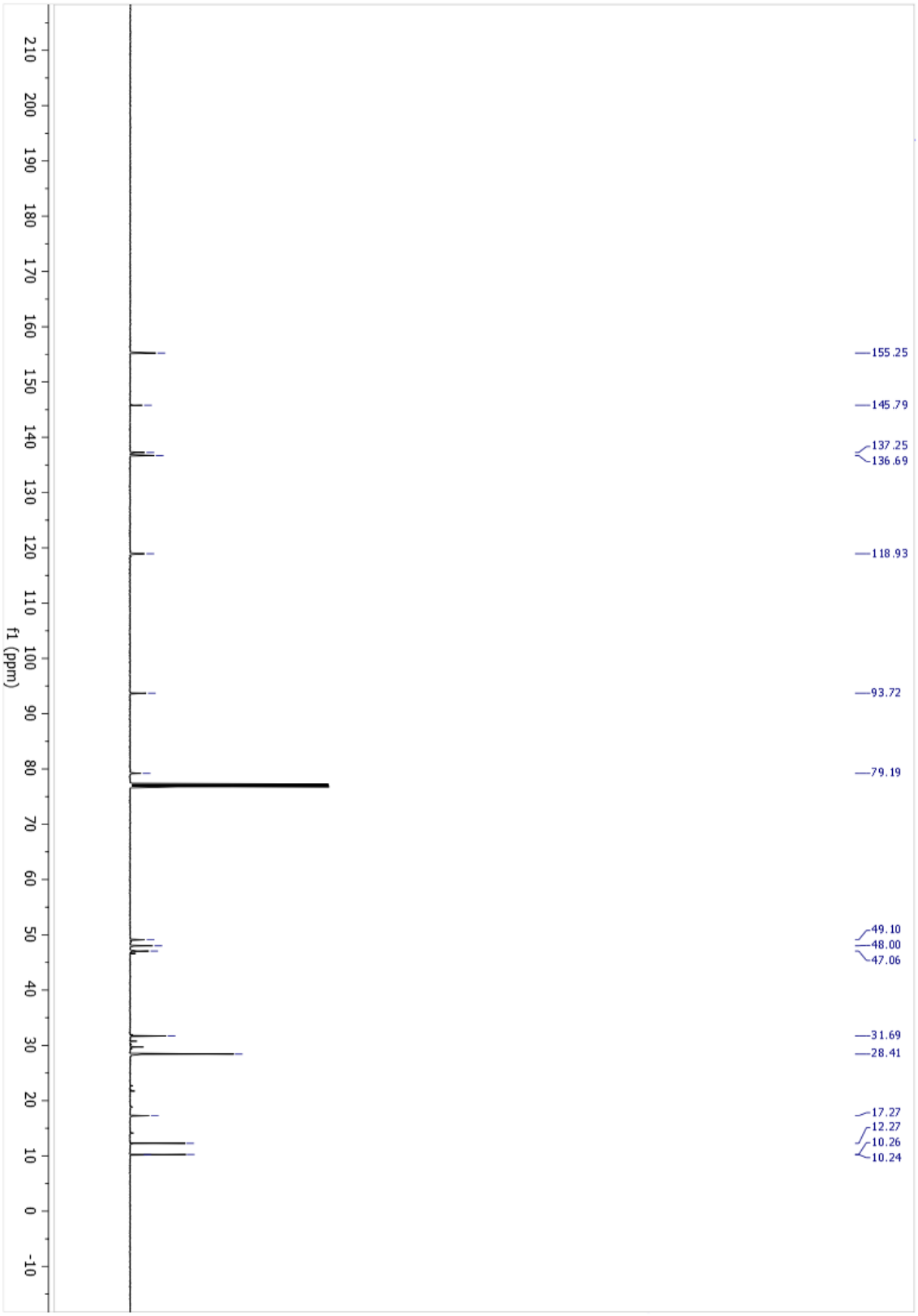
HRMS (ESI): Calculated for $C_{17}H_{28}BrN_3O_2$ $[M+H^+]$ = 386.1438, Found 386.1438.

FTIR (neat): 3319, 2976, 2926, 1708, 1502, 1454, 1389, 1365, 1248, 1167, 1065, 1000, 920, 859, 779

cm^{-1}.

$[\alpha]_D^{28}$= -56.5 (*c* 0.18, $CHCl_3$).


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.00
1.07
1.02
0.67
1.17
0.88
0.78
6.24
1.11
1.06
1.23
9.76
2.70
5.64
5.62
5.60
5.60
5.59
5.57
5.22
5.20
5.13
5.10
5.10
4.50
4.48
3.97
3.89
3.65
2.20
2.01
1.71
1.69
1.43
1.05
1.04

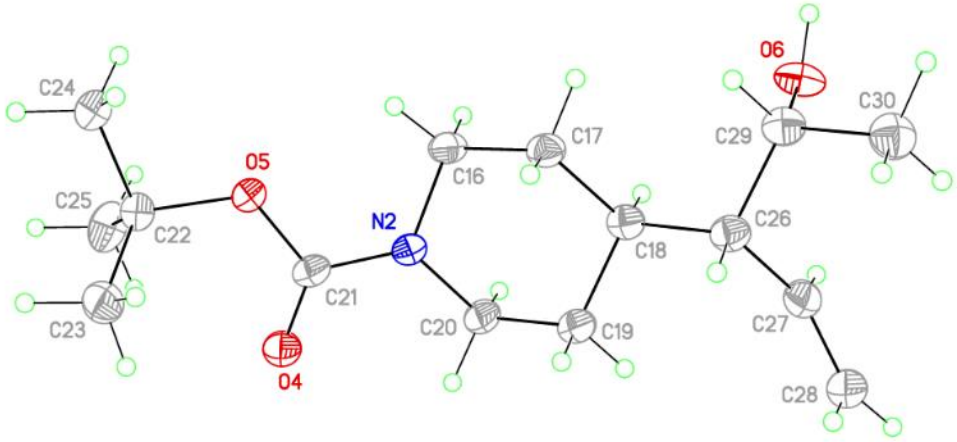

f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
155.25
145.79
137.25
136.69
118.93
93.72
79.19
49.10
48.00
47.06
31.69
28.41
17.27
12.27
10.26
10.24

3.1h. Single Crystal Diffraction Data for Secondary Alcohol 2p

Empirical formula	C15 H27 N O3	
Formula weight	269.37	
Temperature	100.02(12) K	
Wavelength	1.54184 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.99890(10) Å	α= 90°.
	b = 9.46510(10) Å	β= 90°.
	c = 37.2866(3) Å	γ = 90°.
Volume	3175.90(5) $Å^3$	
Z	8	
Density (calculated)	1.127 Mg/m^3	
Absorption coefficient	0.617 mm^{-1}	
F(000)	1184	
Crystal size	0.28 x 0.21 x 0.17 mm^3	
Theta range for data collection	2.370 to 73.220°.	
Index ranges	-11<=h<=11, -11<=k<=11, -45<=l<=45	
Reflections collected	54350	
Independent reflections	6342 [R(int) = 0.0297]	
Completeness to theta = 67.684°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.93770	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6342 / 0 / 375	
Goodness-of-fit on F^2	1.080	
Final R indices [I>2sigma(I)]	R1 = 0.0297, wR2 = 0.0739	
R indices (all data)	R1 = 0.0301, wR2 = 0.0741	

Absolute structure parameter	-0.02(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.113 and -0.176 e.Å^{-3}

Figure 3.1: View of **2p** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



3.2 Chapter 2 Supplementary Information

3.2a. General Information

All reactions were carried out under inert gas atmosphere (nitrogen or argon) unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were oven dried followed by cooling in a desiccator or under a stream of inert gas prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Fischer Scientific, Sigma Aldrich, Ameed and Combi Blocks) without further purification. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still[1] or on a Teledyne Isco Combiflash Rf utilizing Silicycle HP column using a mobile phase composed of either hexanes/ethyl acetate, hexanes/acetone, dichloromethane/methanol, or another suitable solvent system.. Reactions were monitored by analytical thin-layer chromatography (TLC) using 0.25 mm commercial silica gel plates (Dyna.//mic Absorbents F).

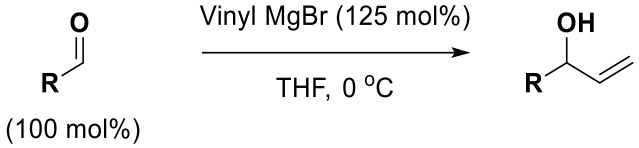
3.2b. Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer using a diamond ATR unit. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M^+, $M+H^+$, $M+Na^+$, $M+Ag^+$), or a suitable fragment ion. Nuclear magnetic resonance (^1H, ^{13}C, ^{19}F, ^{31}P NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (400 MHz) or Varian INOVA (500 MHz) spectrometer equipped with a Bruker cryoprobe. The chemical shifts are given as parts per million (ppm) and were referenced to the residual solvent signal (CDCl3: δ_H = 7.26 ppm, δ_C = 77.16 ppm). Specific optical rotations were recorded on an Azzota Corp AP45 (589 nm) in CDCl3. Solution concentrations are given in the units of 10^{-2} g mL^{-1}.

3.2c. Procedures and Spectral Data for Synthesis of Allylic Alcohols

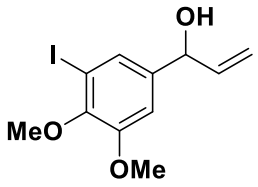
Allylic alcohol precursors **1a**,[47] **1b**,[53] **1c**,[53] **1k**,[54] **1m**,[53] **1n**,[53] **1p**,[53] **1s**,[55] **1u**,[56] and **1v**,[53] were synthesized in the manner previously reported. The obtained products were identical in all respects to the compounds reported the literature.

General Procedure A



An oven-dried round bottom flask equipped with a magnetic stir bar was charged with aldehyde (100 mol%). The flask was purged with argon and freshly distilled THF (0.1 M) was added. A solution of vinyl magnesium bromide (1.0 M in THF, 125 mol%) was added at 0 °C. Following addition, the reaction was allowed to stir for 30 minutes. Upon completion of the reaction, the solution was diluted with diethyl ether and was quenched with aqueous saturated NH_4Cl solution. The biphasic mixture was poured into a separatory funnel and mixed thoroughly. The organic layer was extracted three times with ethyl acetate, then washed with brine, and Na_2SO_4 (dried). After 15 minutes, the organic solution was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The residue was directly subjected to flash column chromatography to afford allylic alcohols.

(1d) 1-(3-iodo-4,5-dimethoxyphenyl)prop-2-en-1-ol



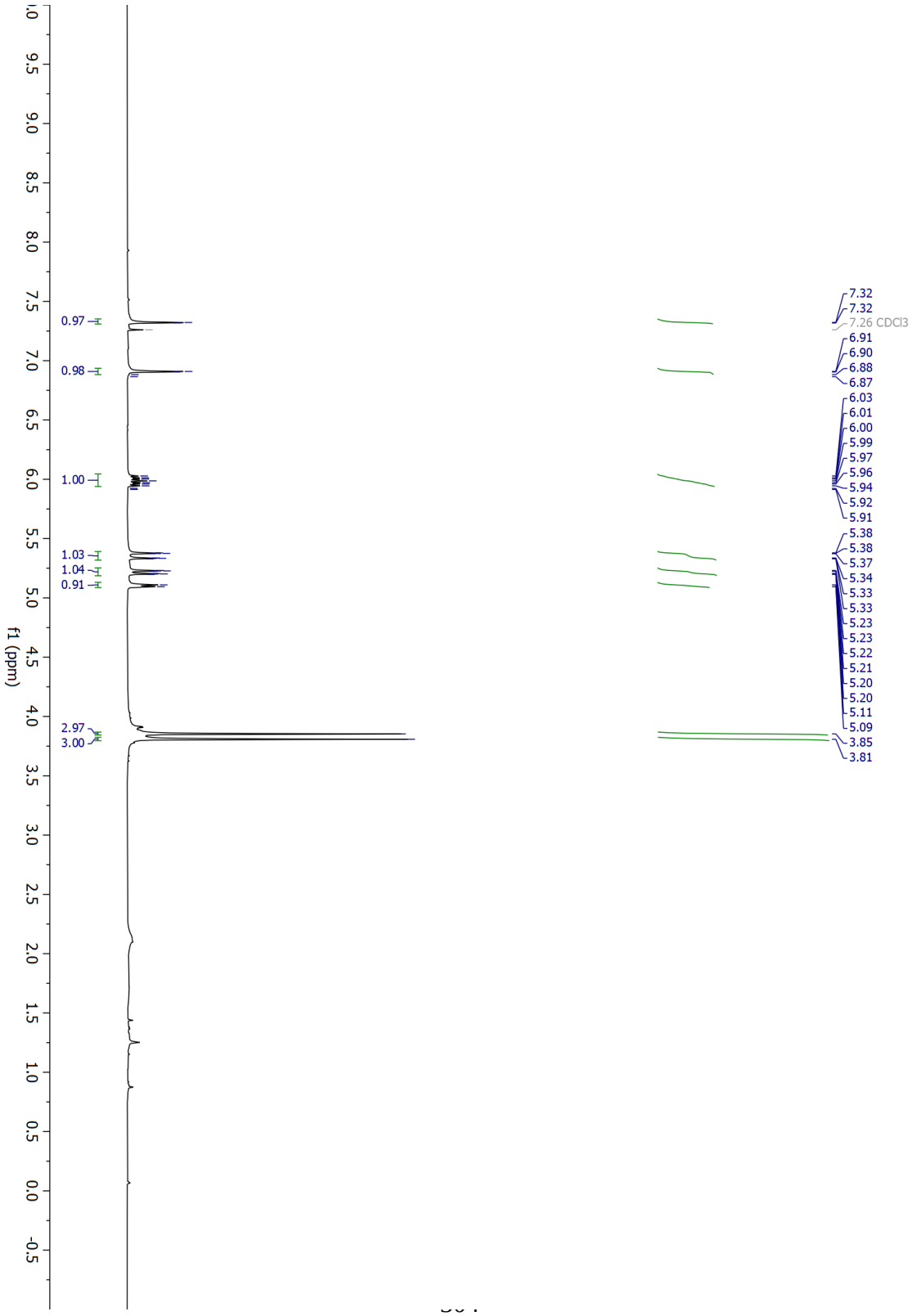
Procedure

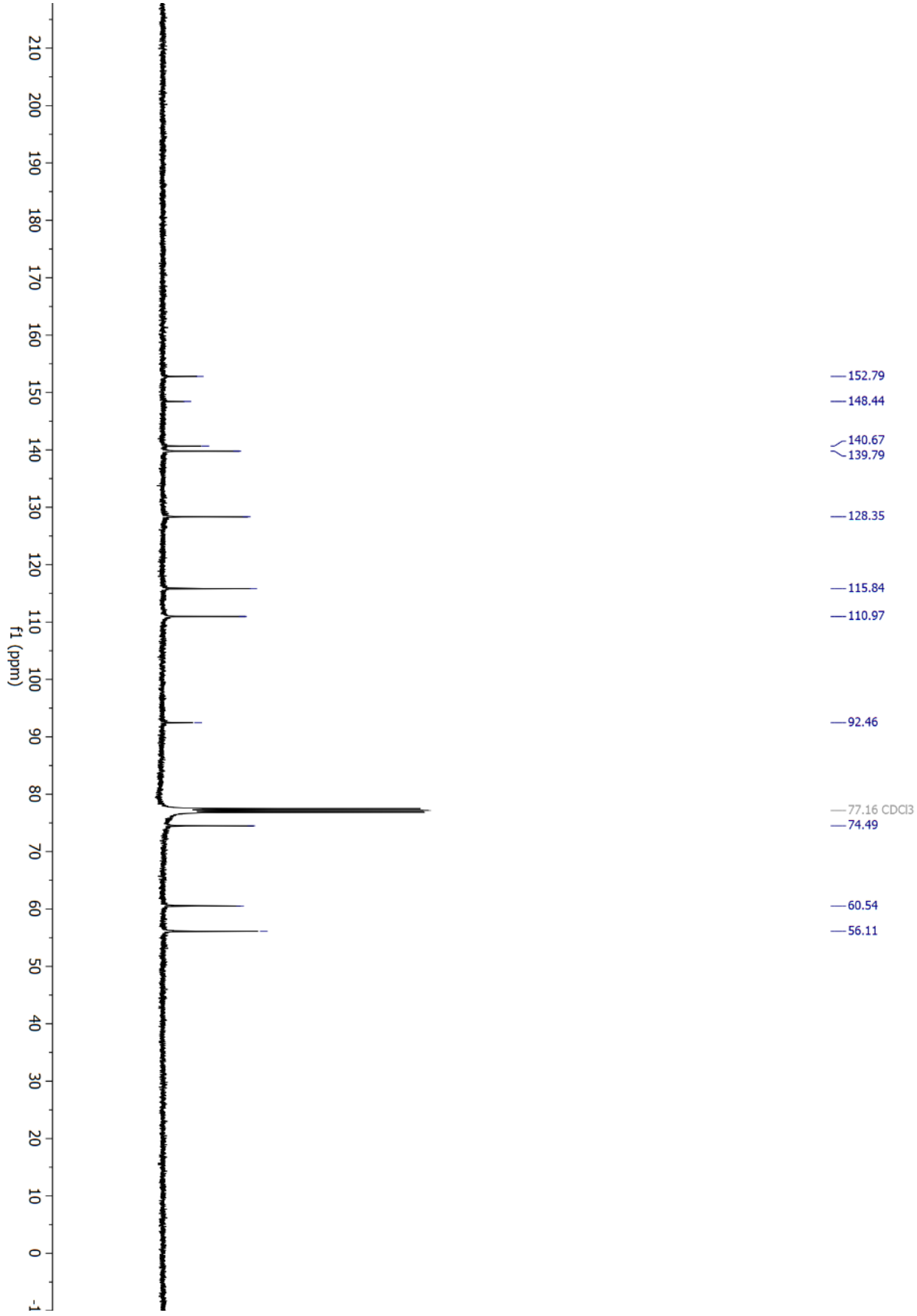
3-iodo-4,5-dimethoxybenzaldehyde (2.00g, 6.80 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 87% yield (1.90g, 5.90 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2): R_f = 0.29 (hexanes: ethyl acetate = 4:1).

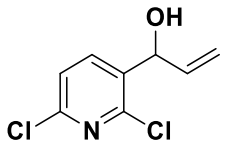
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 1.9 Hz, 1H), 6.91 (d, *J* = 1.9 Hz, 1H), 5.99 (ddd, *J* = 16.8, 10.3, 6.0 Hz, 1H), 5.35 (dt, *J* = 17.0, 1.4 Hz, 1H), 5.21 (dt, *J* = 10.4, 1.3 Hz, 1H), 5.10 (d, *J* = 6.1 Hz, 1H), 3.85 (s, 3H), 3.81 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 152.8, 148.4, 140.7, 139.8, 128.3, 115.8, 111.0, 92.5, 74.5, 60.5, 56.1.
HRMS (ESI): Calculated for $C_{11}H_{13}IO_3$ [M+Na+] = 342.9802, Found 342.9801.

FTIR (neat): 3417, 3010, 2935, 1738, 1590, 1463, 1409, 1269, 1138 cm^{-1}.


f1 (ppm)
0.97
0.98
1.00
1.03
1.04
0.91
2.97
3.00
7.32
7.32
7.26 CDCl3
6.91
6.90
6.88
6.87
6.03
6.01
6.00
5.99
5.97
5.96
5.94
5.92
5.91
5.38
5.38
5.37
5.34
5.33
5.33
5.23
5.23
5.22
5.21
5.20
5.20
5.11
5.09
3.85
3.81


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
152.79
148.44
140.67
139.79
128.35
115.84
110.97
92.46
77.16 CDCl3
74.49
60.54
56.11

(1e) 1-(2,6-dichloropyridin-3-yl)prop-2-en-1-ol



Procedure

2,6-dichloronicotinaldehyde (1.76 g, 10.0 mmol, 100 mol%) was subjected to general procedure A. The title compound was obtained in 62 % yield (1.26 g, 6.16 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

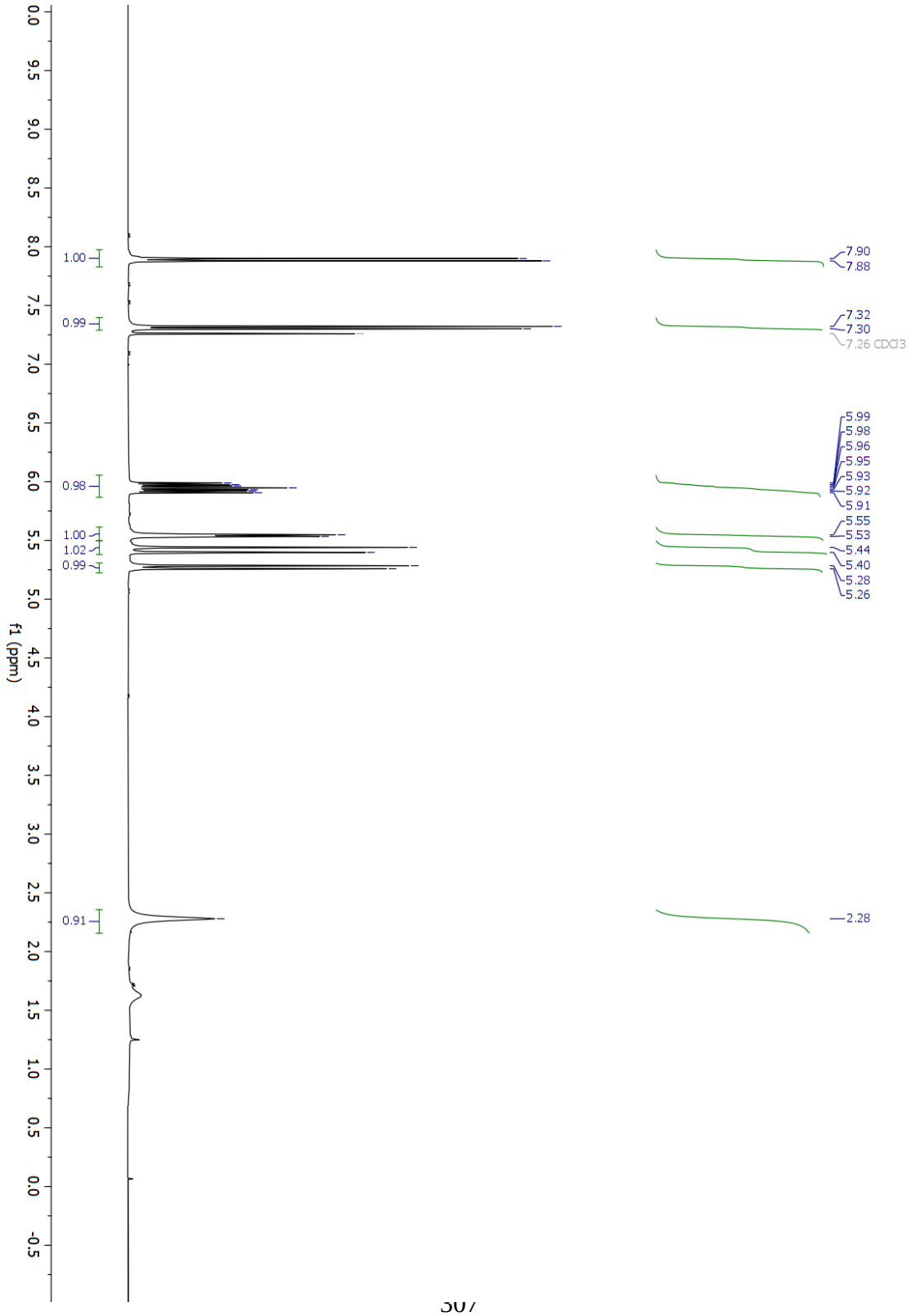
TLC (SiO_2): R_f = 0.22 (hexanes: ethyl acetate = 4:1).

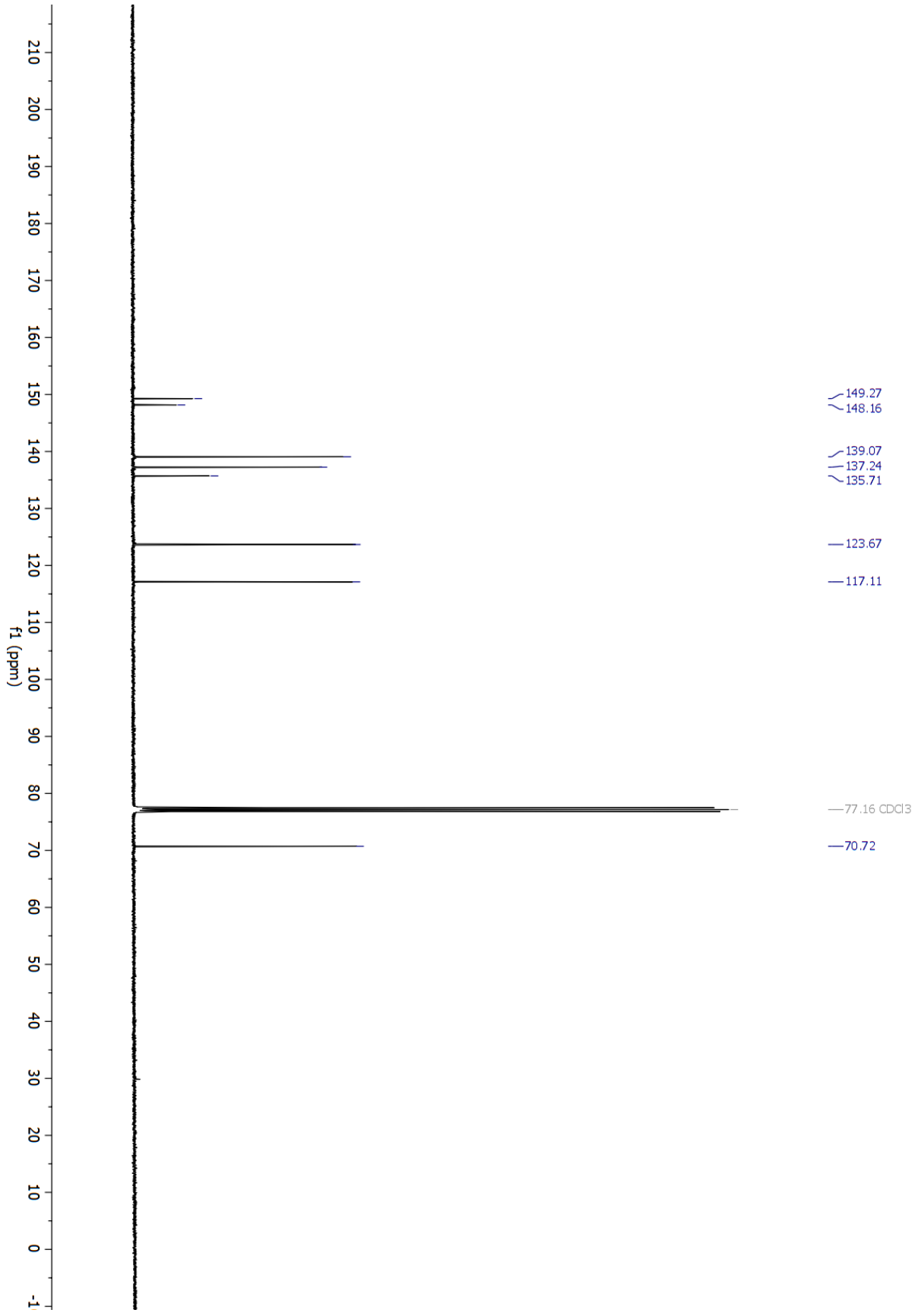
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 5.95 (ddd, J = 16.6, 10.3, 5.7 Hz, 1H), 5.54 (d, J = 5.8 Hz, 1H), 5.42 (d, J = 17.1 Hz, 1H), 5.27 (d, J = 10.3 Hz, 1H), 2.28 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 149.3, 148.2, 139.1, 137.2, 135.7, 123.7, 117.1, 70.7.

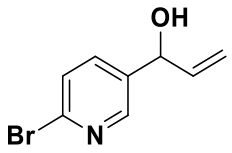
HRMS (ESI): calculated for $C_8H_7Cl_2NO$ [M+H^+]= 203.9972, Found 203.9977

FTIR (neat): 3359, 2923, 1574, 1552, 1422, 989, 855, 781 cm^{-1}.


f1 (ppm)
1.00
0.99
0.98
1.00
1.02
0.99
0.91
7.90
7.88
7.32
7.30
7.26 CDCl3
5.99
5.98
5.96
5.95
5.93
5.92
5.91
5.55
5.53
5.44
5.40
5.28
5.26
2.28


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)
149.27
148.16
139.07
137.24
135.71
123.67
117.11
77.16 CDCl3
70.72

(1f) 1-(6-bromopyridin-3-yl)prop-2-en-1-ol



Procedure

6-bromonicotinaldehyde (1.67 g, 9.00 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 67% yield (1.30 g, 6.10 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

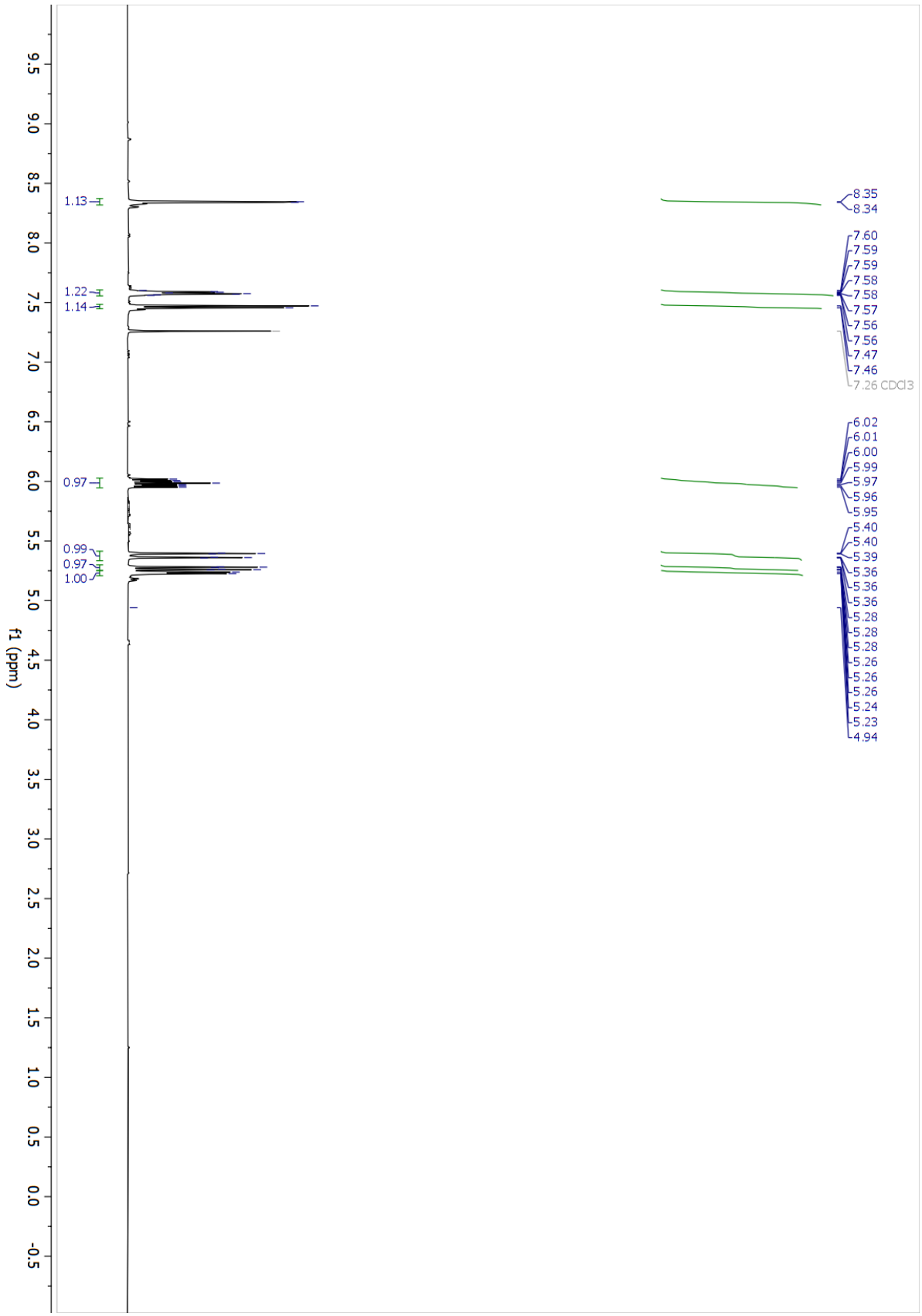
TLC (SiO_2): R_f = 0.15 (hexanes: ethyl acetate = 4:1).

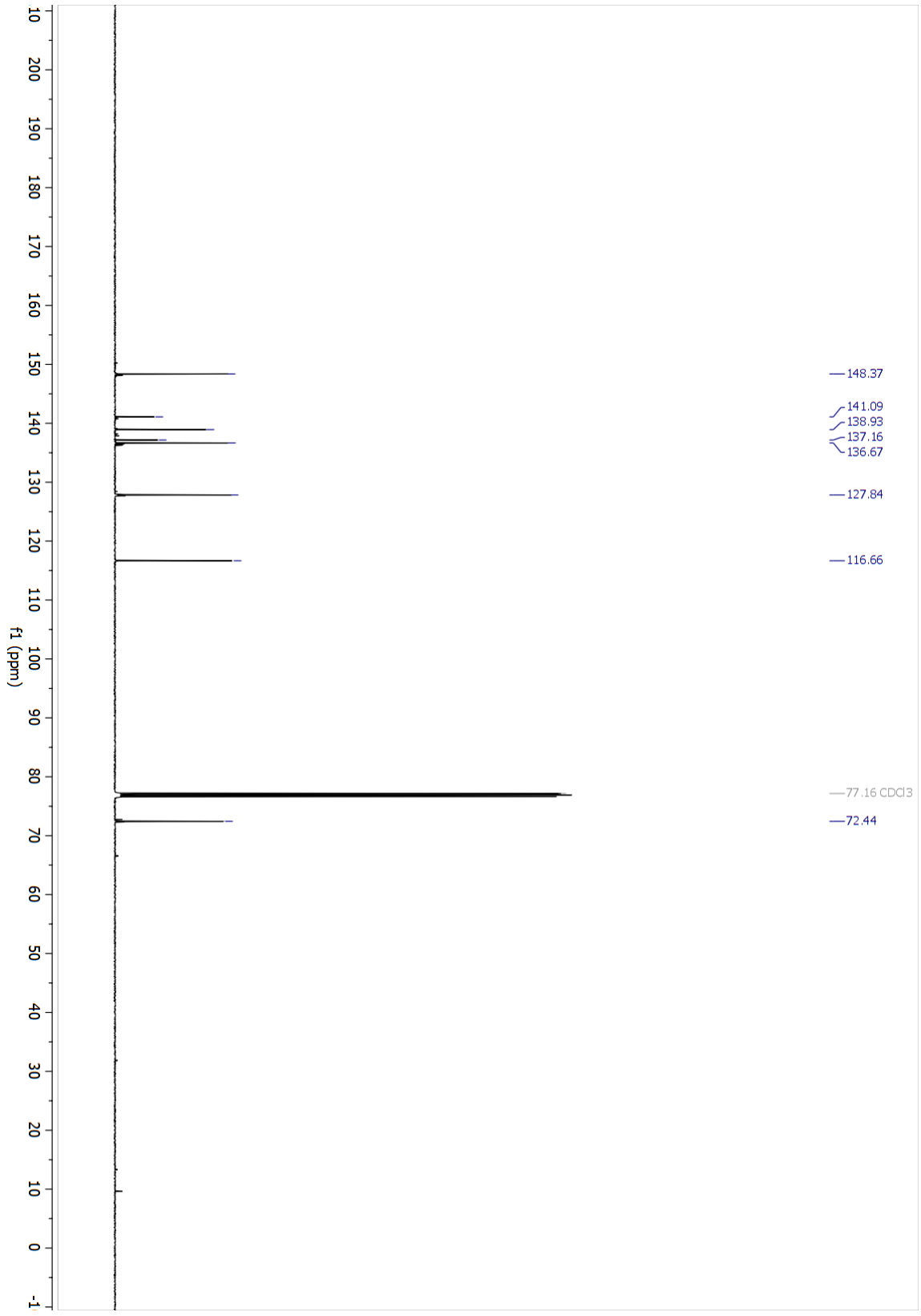
^{1}H NMR (500 MHz, $CDCl_3$): δ: 8.34 (d, *J* = 2.5 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 5.99 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 5.38 (dt, *J* = 17.1, 1.3 Hz, 1H), 5.27 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.23 (d, *J* = 6.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 148.4, 141.1, 138.9, 137.2, 136.7, 127.8, 116.7, 72.4.

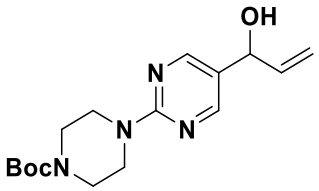
HRMS (ESI): Calculated for C_8H_8BrNO $[M+H^+]$ = 213.9862, Found 213.9865

FTIR (neat): 3303, 1579, 1452, 1085, 1049, 928, 848, 740 cm^{-1}


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.13
1.22
1.14
0.97
0.99
0.97
1.00
8.35
8.34
7.60
7.59
7.59
7.58
7.58
7.57
7.56
7.56
7.47
7.46
7.26 CDCl3
6.02
6.01
6.00
5.99
5.97
5.96
5.95
5.40
5.40
5.39
5.36
5.36
5.36
5.28
5.28
5.28
5.26
5.26
5.26
5.24
5.23
4.94


148.37
141.09
138.93
137.16
136.67
127.84
116.66
77.16 CDCl3
72.44
f1 (ppm)

(1g) tert-butyl 4-(5-(1-hydroxyallyl)pyrimidin-2-yl)piperazine-1-carboxylate



Procedure

tert-butyl 4-(5-formylpyrimidin-2-yl)piperazine-1-carboxylate (1.00 g, 3.42 mmol, 100 mol%) was subjected to general procedure A. The title compound was obtained in 64% yield (701 mg, 2.19 mmol) as a white solid after isolation by flash column chromatography (SiO_2, dichlormethane: ethyl acetate = 20:1–5:1).

TLC (SiO_2): R_f = 0.24 (dichloromethane: ethyl acetate = 4:1).

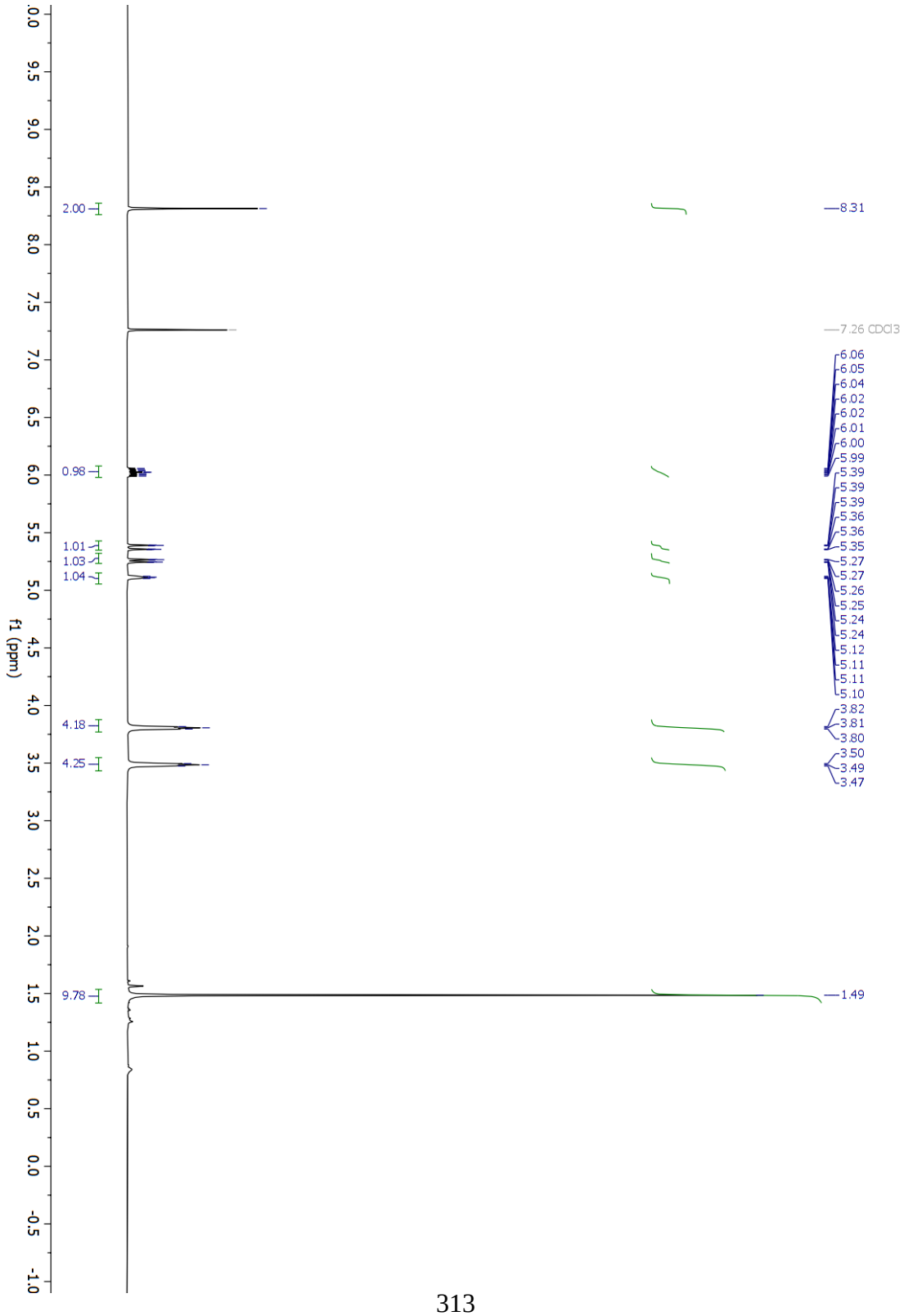
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (s, 2H), 6.02 (ddd, J = 17.0, 10.3, 5.8 Hz, 1H), 5.37 (dt, J = 17.1, 1.3 Hz, 1H), 5.26 (dt, J = 10.4, 1.2 Hz, 1H), 5.11 (dd, J = 5.9, 3.8 Hz, 1H), 3.81 (t, J = 5.2 Hz, 4H), 3.49 (t, J = 5.3 Hz, 4H), 1.49 (s, 9H).

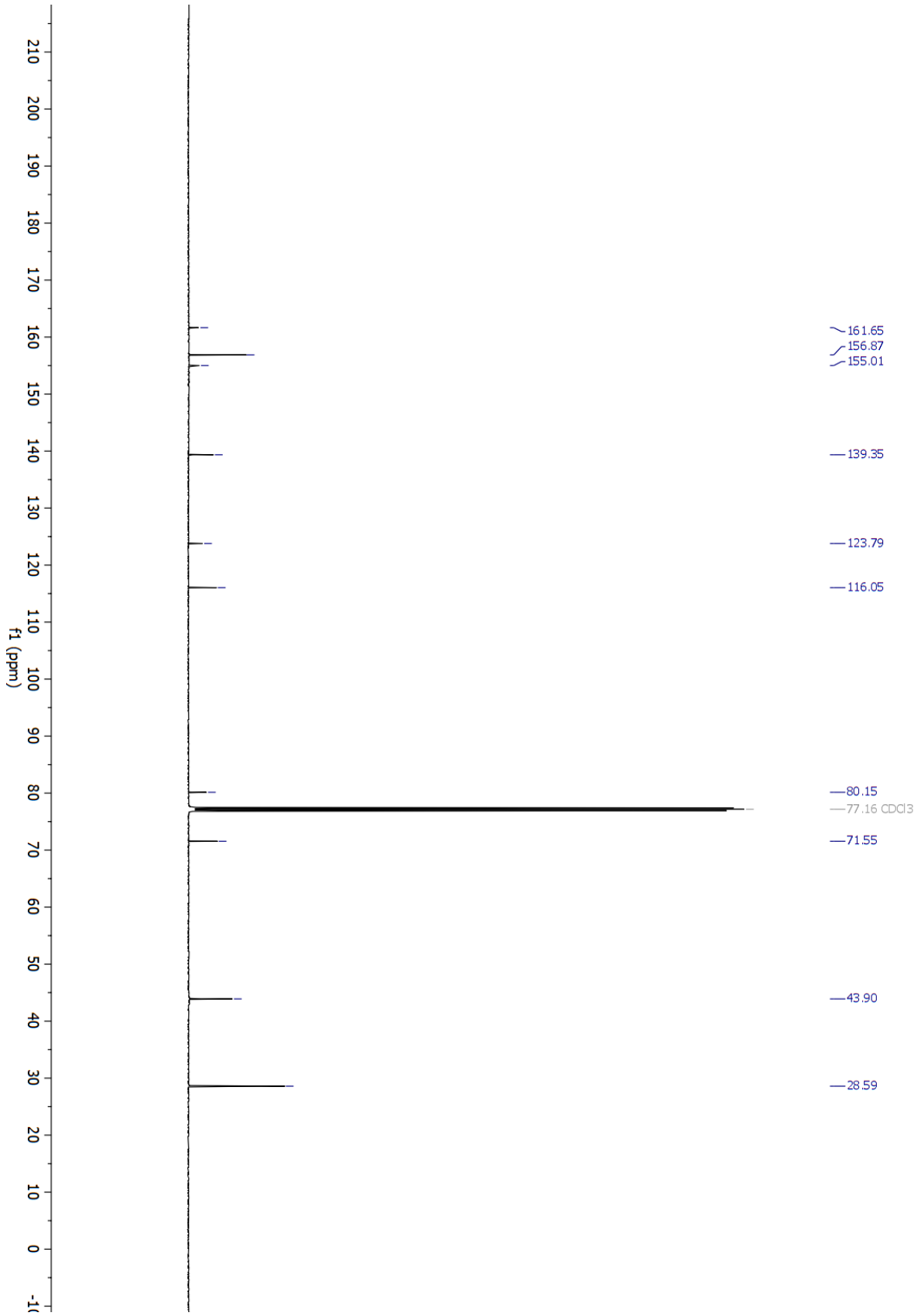
^{13}C NMR (126 MHz, $CDCl_3$): δ 161.7, 156.9, 155.0, 139.3, 123.8, 116.0, 80.1, 71.5, 43.9, 28.6.

HRMS (ESI): calculated for $C_{16}H_{24}N_4O_3$ $[M+H^+]$= 321.1921, Found 321.1928.

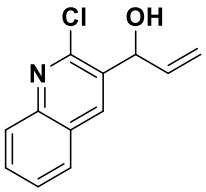
FTIR (neat): 3424, 2972, 2908, 2861, 1654, 1640, 1543, 1460, 1246, 1166, 1119, 863 cm^{-1}.

MP: 135-137 ºC


f1 (ppm)
2.00
0.98
1.01
1.03
1.04
4.18
4.25
9.78
8.31
7.26 CDCl3
6.06
6.05
6.04
6.02
6.02
6.01
6.00
5.99
5.39
5.39
5.39
5.36
5.36
5.35
5.27
5.27
5.26
5.25
5.24
5.24
5.12
5.11
5.11
5.10
3.82
3.81
3.80
3.50
3.49
3.47
1.49


161.65
156.87
155.01
139.35
123.79
116.05
80.15
77.16 CDCl3
71.55
43.90
28.59
f1 (ppm)

(1h) 1-(2-chloroquinolin-3-yl)prop-2-en-1-ol



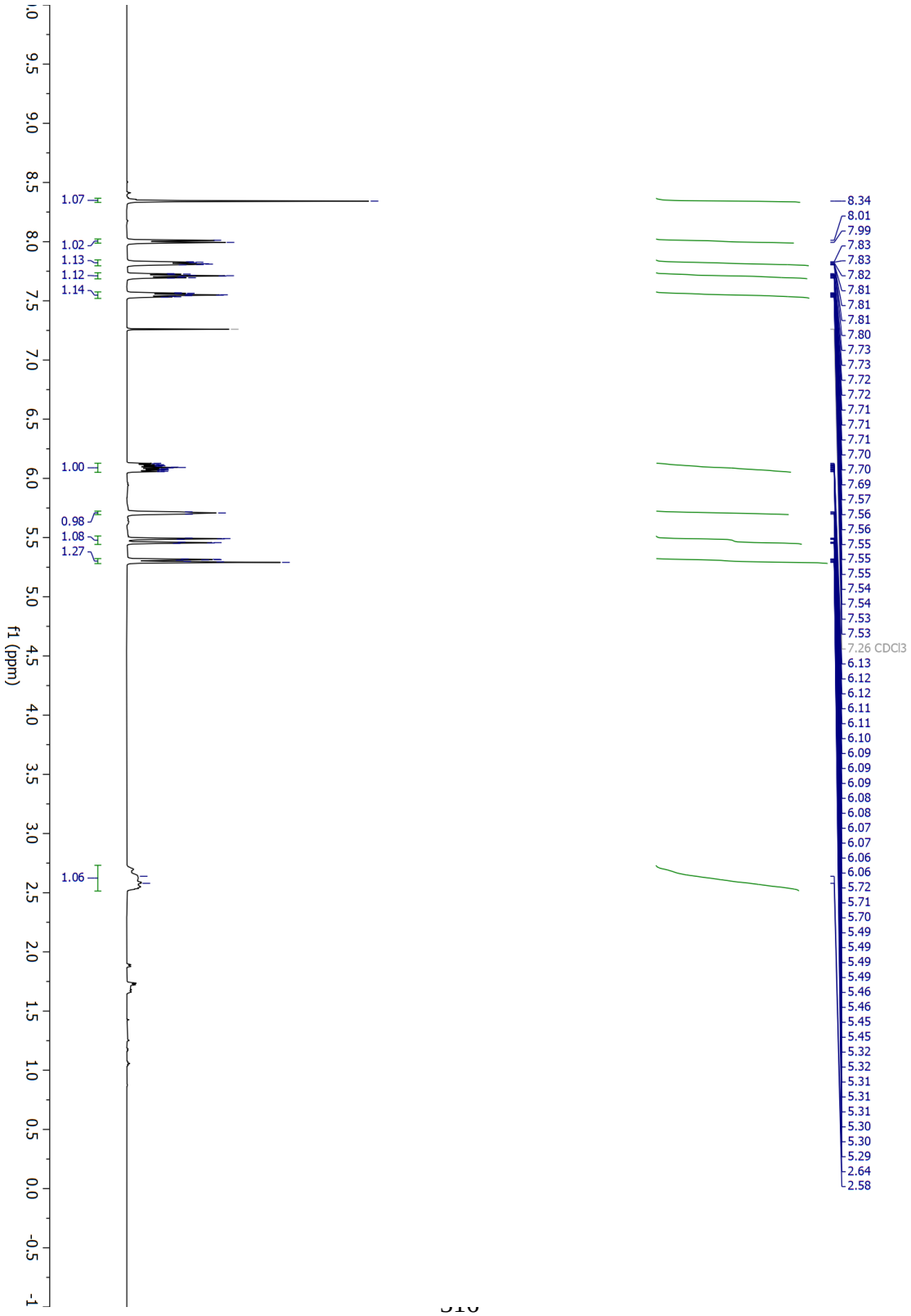
Procedure

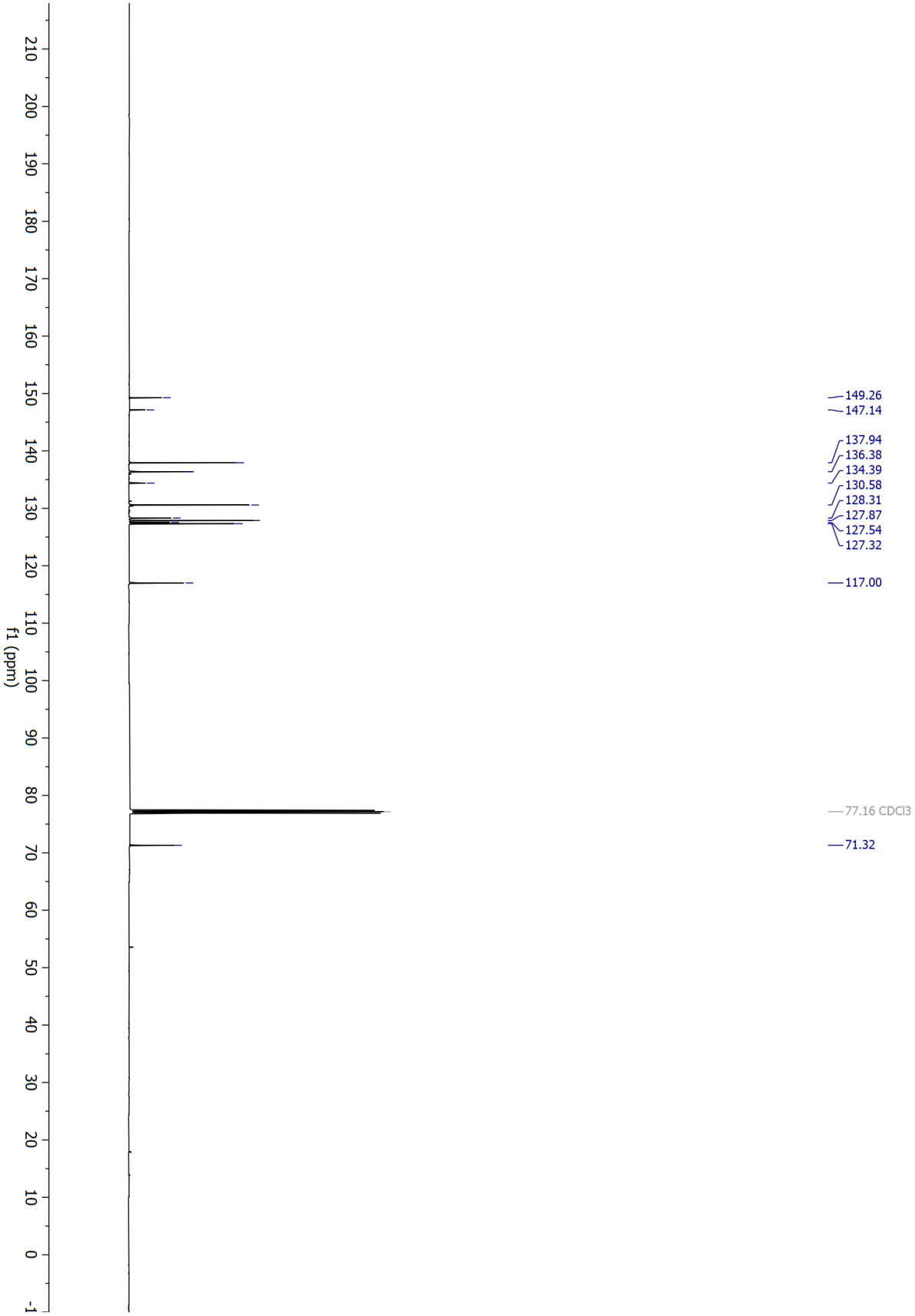
2-chloroquinoline-3-carbaldehyde (2.00g, 10.4 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 75% yield (1.70g, 7.80 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–5:1).

TLC (SiO_2): R_f = 0.19 (hexanes: ethyl acetate = 3:1).

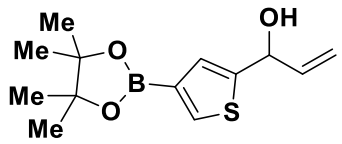
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (s, 1H), 8.00 (d, *J* = 8.6 Hz, 1H), 7.84 – 7.80 (m, 1H), 7.71 (ddt, *J* = 8.5, 6.9, 1.6 Hz, 1H), 7.55 (ddt, *J* = 8.6, 6.9, 1.7 Hz, 1H), 6.09 (dddd, *J* = 17.5, 10.3, 5.6, 1.8 Hz, 1H), 5.71 (t, *J* = 4.8 Hz, 1H), 5.47 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.33 – 5.26 (m, 1H), 2.64 (s, 1H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 149.3, 147.1, 137.9, 136.4, 134.4, 130.6, 128.3, 127.9, 127.5, 127.3, 117.0, 71.3.
HRMS (ESI): Calculated for $C_{12}H_{10}ClNO$ [M+H+] = 220.0524, Found 220.0529.

FTIR (neat): 3336, 3087, 2358, 1587, 1396, 1313, 1262, 1136, 998 cm^{-1}.


f1 (ppm)
1.07
1.02
1.13
1.12
1.14
1.00
0.98
1.08
1.27
1.06
8.34
8.01
7.99
7.83
7.83
7.82
7.81
7.81
7.81
7.80
7.73
7.73
7.72
7.72
7.71
7.71
7.71
7.70
7.70
7.69
7.57
7.56
7.56
7.55
7.55
7.55
7.54
7.54
7.53
7.53
7.26 CDCl3
6.13
6.12
6.12
6.11
6.11
6.10
6.09
6.09
6.09
6.08
6.08
6.07
6.07
6.06
6.06
5.72
5.71
5.70
5.49
5.49
5.49
5.49
5.46
5.46
5.45
5.45
5.32
5.32
5.31
5.31
5.31
5.30
5.30
5.29
2.64
2.58


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
149.26
147.14
137.94
136.38
134.39
130.58
128.31
127.87
127.54
127.32
117.00
77.16 CDCl3
71.32

(1i) 1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)prop-2-en-1-ol



Procedure

4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene-2-carbaldehyde (1.00 g, 4.20 mmol, 100 mol%) was subjected to a modified version of general procedure A using vinyl magnesium bromide (1.0 M in THF, 4.62 mmol, 110 mol%) in THF (0.1 M) at -78°C. Upon completion of the reaction, the solution was diluted with brine and allowed to warm to room temperature. The biphasic mixture was poured into a separatory funnel and mixed thoroughly. The organic layer was extracted 3 times with ethyl acetate. And dried anhydrous sodium sulfate. After 15 minutes, the organic solution was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The title compound was obtained in 51% yield (570 mg, 2.14 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: diethyl ether = 5:1–2:1).

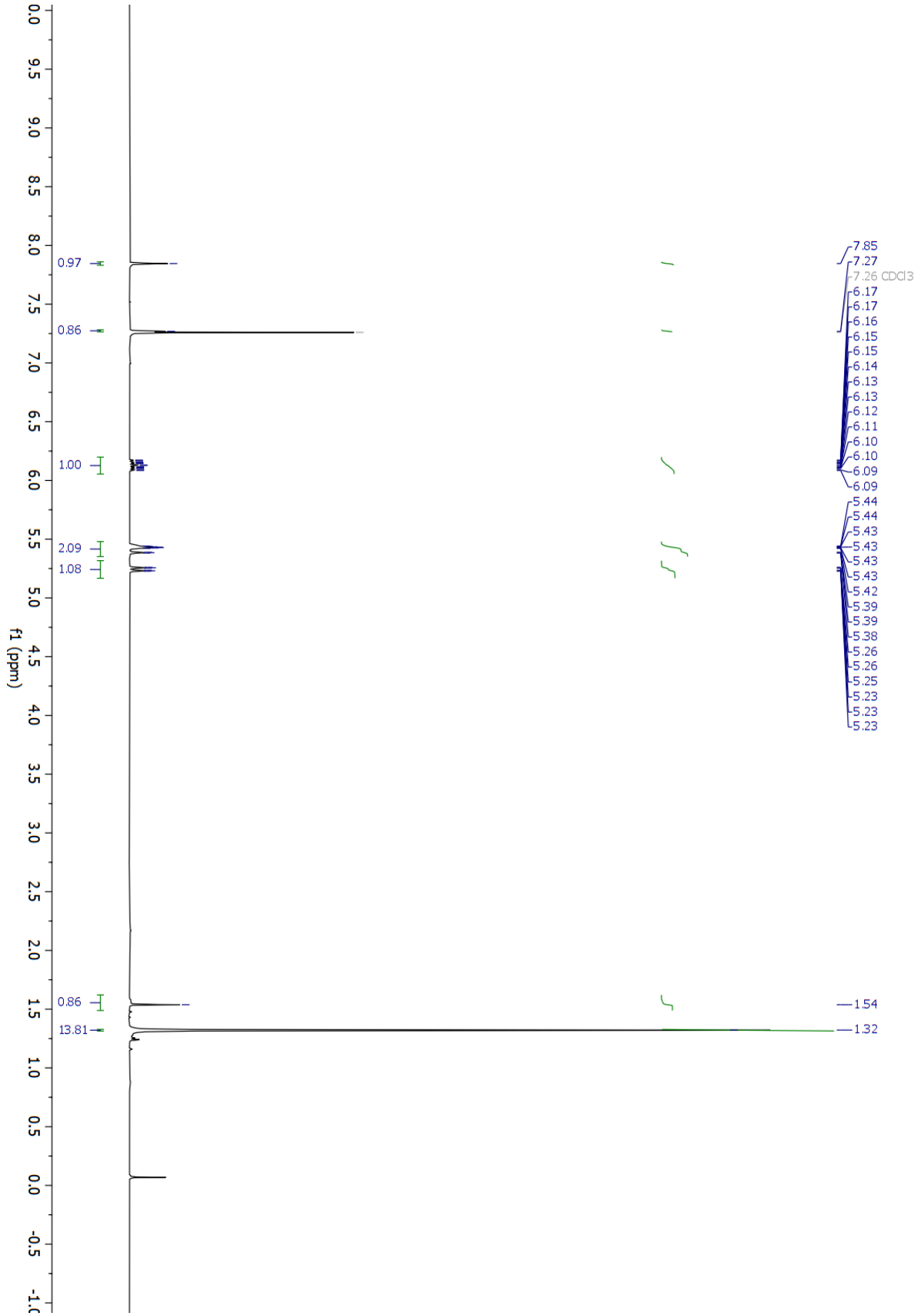
TLC (SiO_2): R_f = 0.35 (hexanes: diethyl ether = 1:1).

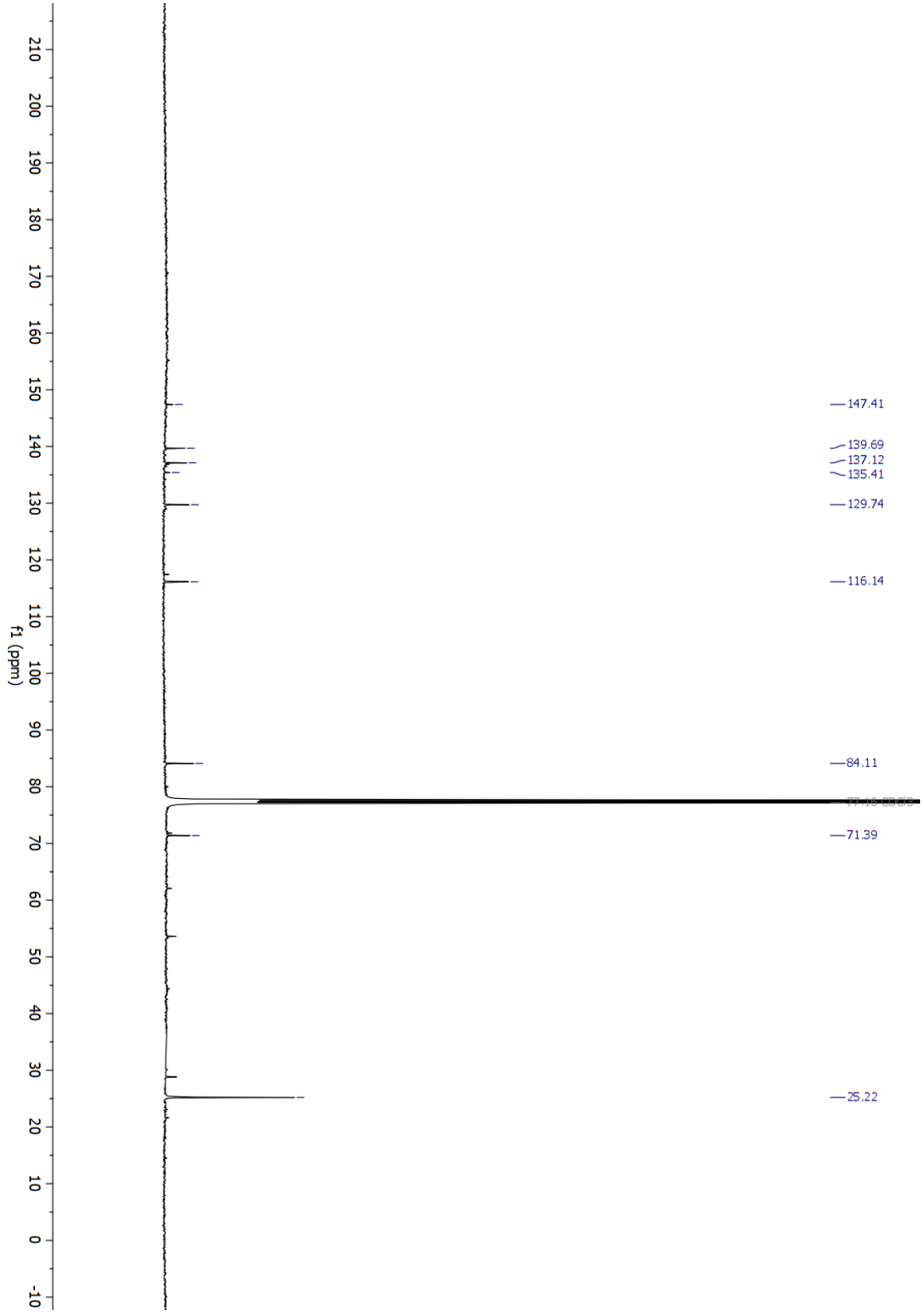
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.27 (s, 1H), 6.13 (dddd, J = 16.7, 10.4, 6.0, 1.7 Hz, 1H), 5.49 – 5.30 (m, 2H), 5.24 (dt, J = 10.3, 1.3 Hz, 1H), 1.54 (s, 1H), 1.32 (s, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 147.2, 139.5, 136.9, 135.2, 129.5, 115.9, 83.9, 71.1, 25.0.

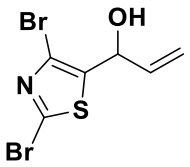
HRMS (ESI): calculated for $C_{16}H_{24}N_4O_3$ $[M+Na^+]$= 289.1043, found= 289.1055.

FTIR (neat): 3439, 2977, 1738, 1671, 1537, 1457, 1371, 1307, 1260, 1139, 965, 703 cm^{-1}


f1 (ppm)
0.97
0.86
1.00
2.09
1.08
0.86
13.81
7.85
7.27
7.26 CDCl3
6.17
6.17
6.16
6.15
6.15
6.14
6.13
6.13
6.12
6.11
6.10
6.10
6.09
6.09
5.44
5.44
5.43
5.43
5.43
5.43
5.42
5.39
5.39
5.38
5.26
5.26
5.25
5.23
5.23
5.23
1.54
1.32


147.41
139.69
137.12
135.41
129.74
116.14
84.11
77.16 CDCl3
71.39
25.22
f1 (ppm)

(1j) 1-(2,4-dibromothiazol-5-yl)prop-2-en-1-ol



Procedure

2,4-dibromothiazole-5-carbaldehyde (1.08 g, 4.00 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 47% yield (562 mg, 1.88 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2): R_f = 0.22 (hexanes: ethyl acetate = 4:1).

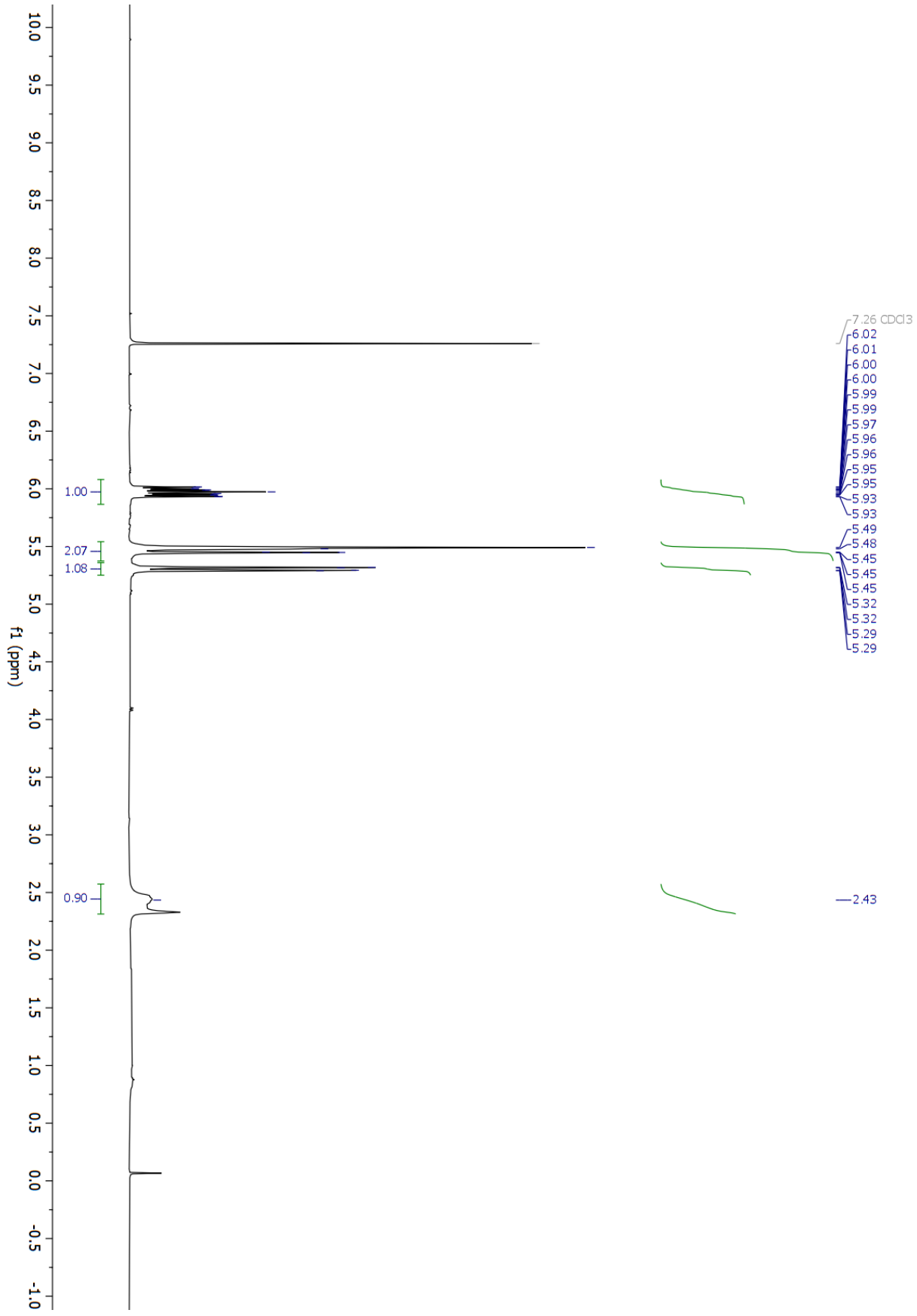
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.02 – 5.93 (m, 1H), 5.49 (s, 1H), 5.48 (d, J = 12.2 Hz, 1H), 5.31 (dd, J = 10.4, 1.5 Hz, 1H), 2.43 (s, 1H).

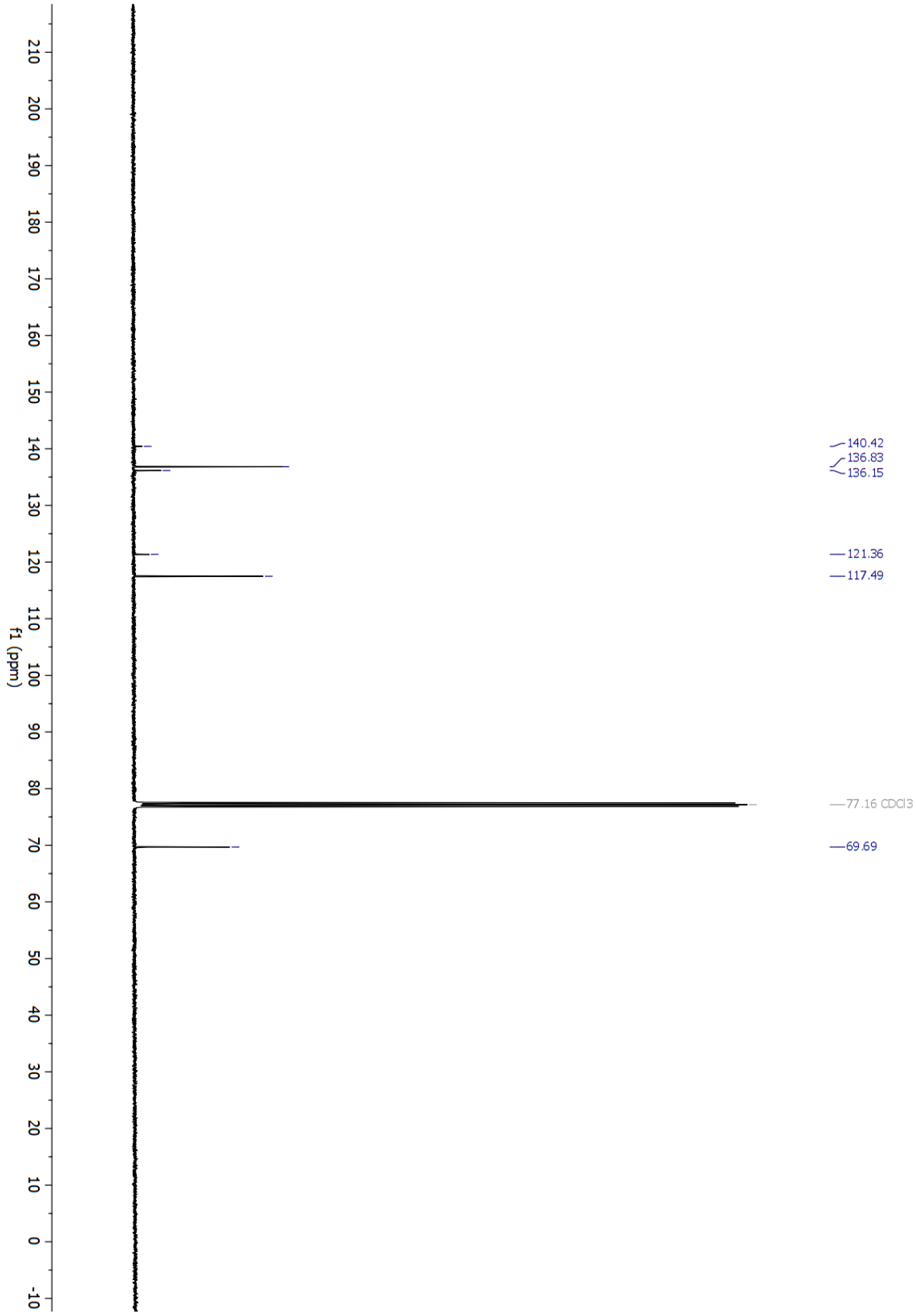
^{13}C NMR (101 MHz, $CDCl_3$): δ 140.4, 136.8, 136.1, 121.4, 117.5, 69.7.

HRMS (ESI): calculated for C_6H_5NOS $[M+H^+]$= 297.8531, found= 297.8528

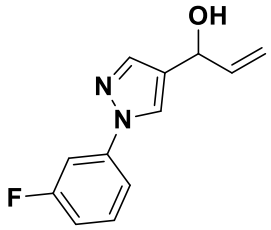
FTIR (neat): 3322, 1393, 1250, 1210, 1021, 983, 932, 846, and 729 cm^{-1}

.


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.00
2.07
1.08
0.90
7.26 CDCl3
6.02
6.01
6.00
6.00
5.99
5.99
5.97
5.96
5.96
5.95
5.95
5.93
5.93
5.49
5.48
5.45
5.45
5.45
5.32
5.32
5.29
5.29
2.43


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
140.42
136.83
136.15
121.36
117.49
77.16 CDCl3
69.69

(1l) 1-(1-(3-fluorophenyl)-1*H*-pyrazol-4-yl)prop-2-en-1-ol



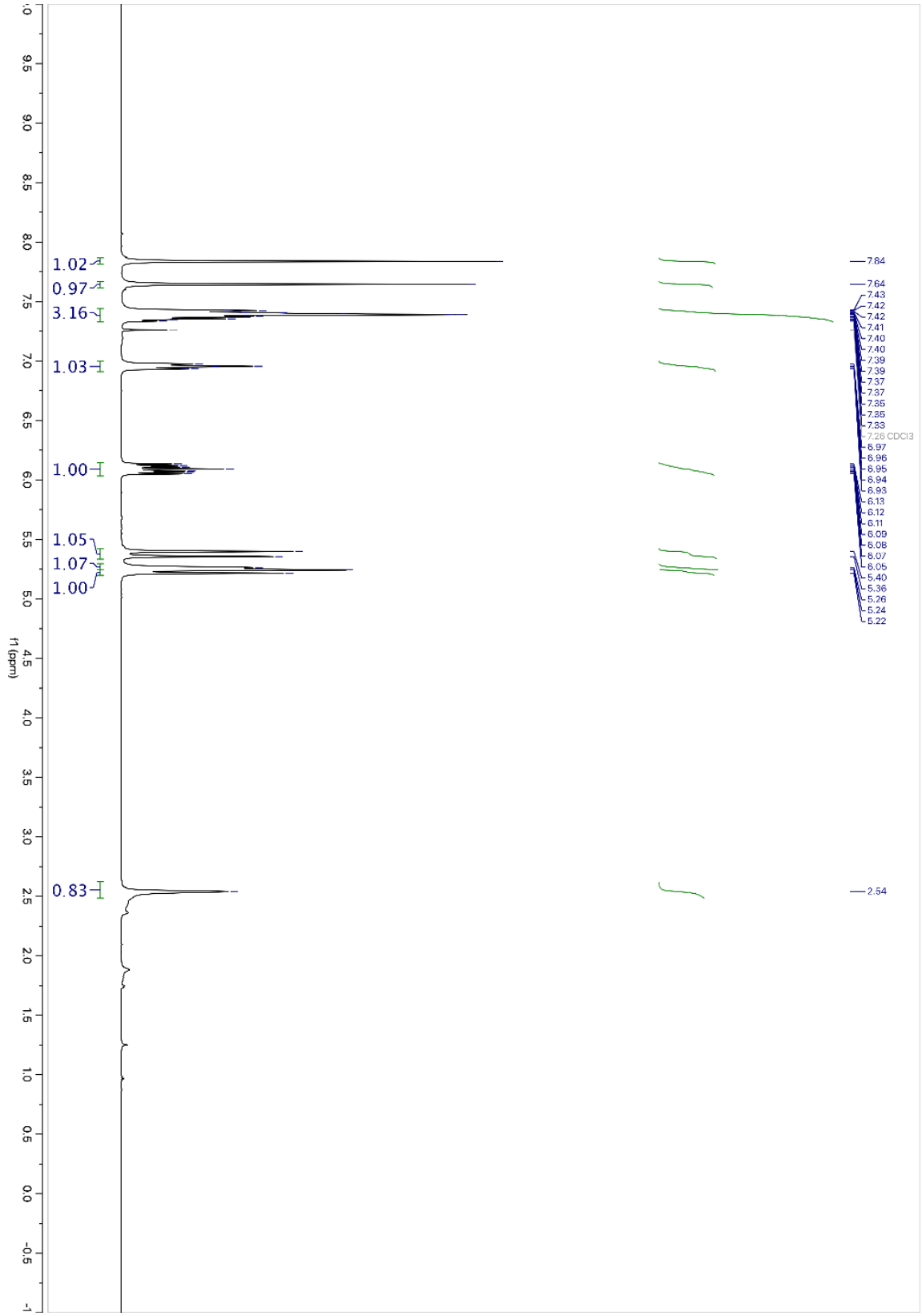
Procedure

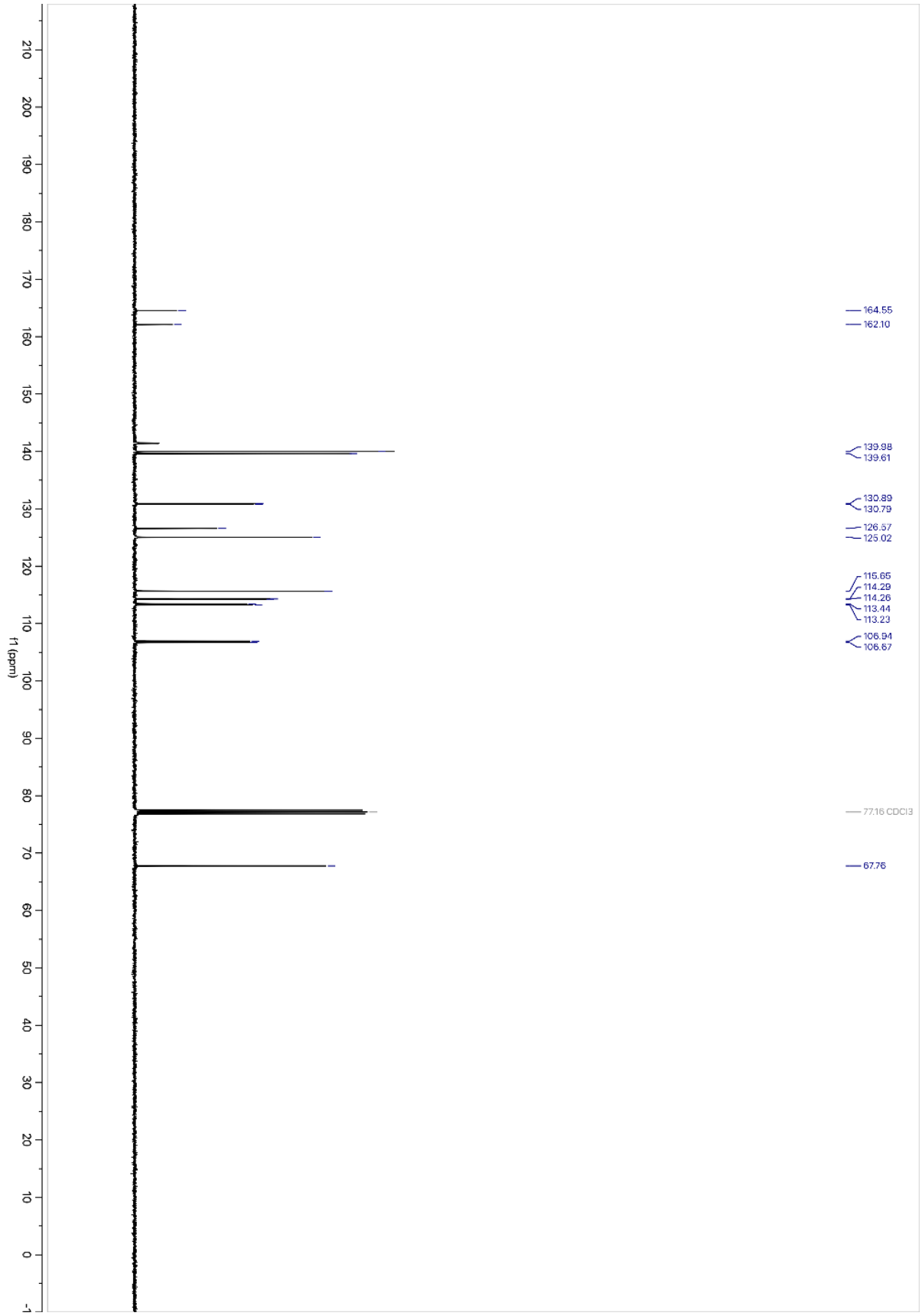
1-(3-fluorophenyl)-1*H*-pyrazole-4-carbaldehyde (2.00 g, 10.5 mmol, 100 mol%) was subjected to general procedure A. The title compound was obtained in 70% yield (1.60 g, 7.33 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–5:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.64 (s, 1H), 7.45 – 7.31 (m, 3H), 7.00 – 6.91 (m, 1H), 6.09 (ddd, *J* = 16.7, 10.2, 6.0 Hz, 1H), 5.38 (d, *J* = 17.1 Hz, 1H), 5.26 (s, 1H), 5.23 (d, *J* = 11.0 Hz, 1H), 2.54 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 163.33 (d, J = 246.7 Hz), 141.43 (d, J = 10.2 Hz), 139.98, 139.61, 130.84 (d, J = 9.4 Hz), 126.57, 125.02, 115.65, 114.27 (d, J = 3.3 Hz), 113.34 (d, J = 21.4 Hz), 106.81 (d, J = 26.5 Hz), 67.76.
^{19}F NMR (376 MHz, $CDCl_3$): δ -110.82.
HRMS (ESI): Calculated for $C_{12}H_{11}FN_2O$ $[M+H^+]$ = 219.0928, Found 219.0934.

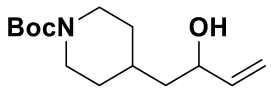
FTIR (neat): 3353, 1613, 1601, 1568, 1498, 1477, 1459, 1395, 1257, 1179, 1151, 1019, 864 cm^{-1}.


1.02
0.97
3.16
1.03
1.00
1.05
1.07
1.00
0.83
7.84
7.64
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.39
7.37
7.37
7.35
7.35
7.33
7.26 CDCl3
6.97
6.96
6.95
6.94
6.93
6.13
6.12
6.11
6.09
6.08
6.07
6.05
5.40
5.36
5.26
5.24
5.22
2.54
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
164.55
162.10
139.98
139.61
130.89
130.79
126.57
125.02
115.65
114.29
114.26
113.44
113.23
106.94
106.67
77.16 CDCl3
67.76

-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)
-110.82

(1o) tert-butyl 4-(2-hydroxybut-3-en-1-yl)piperidine-1-carboxylate



Procedure

tert-butyl 4-(2-oxoethyl)piperidine-1-carboxylate (2.27 g, 10.0 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 71% yield (1.81 g, 7.10 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1–1:1).

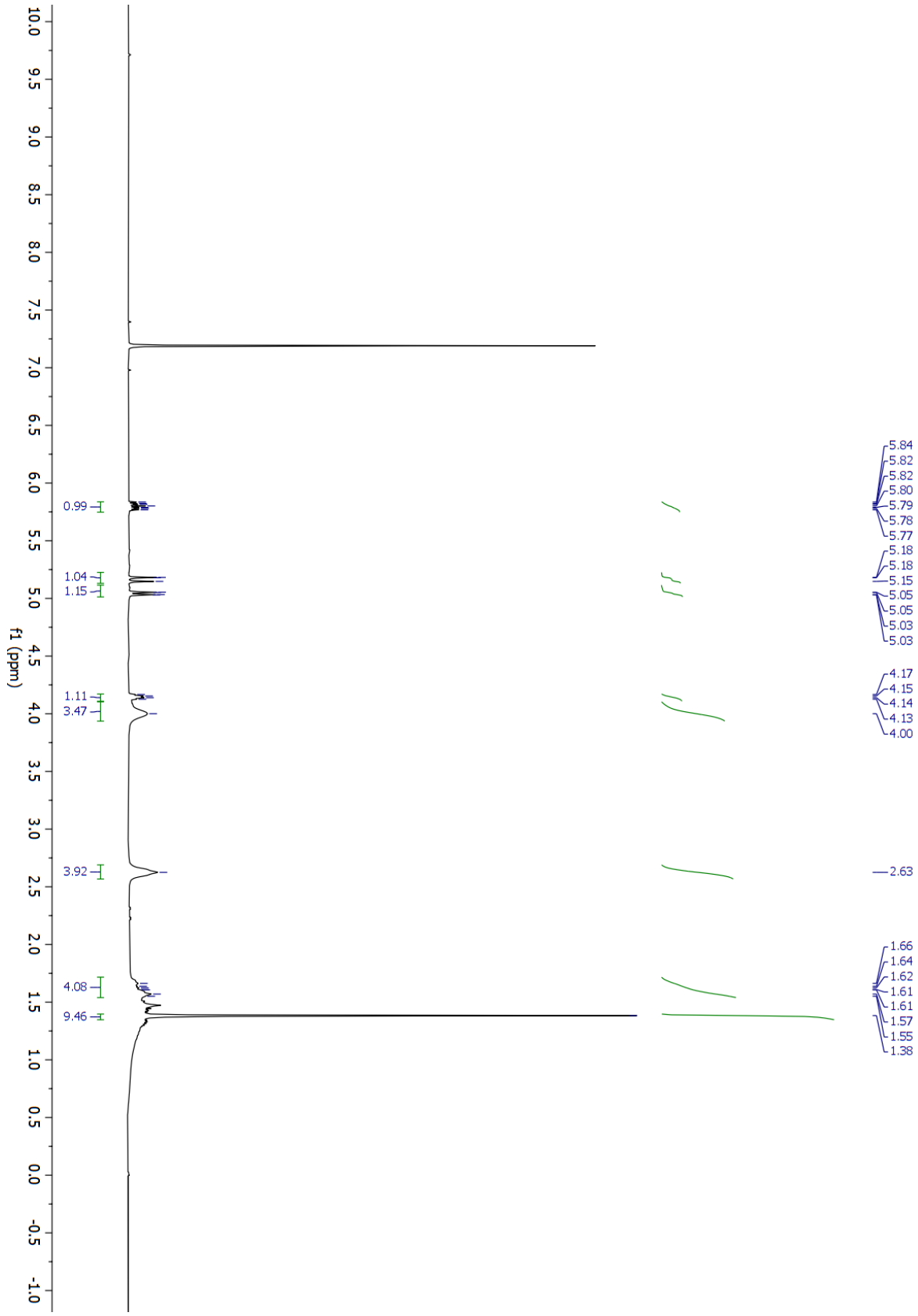
TLC (SiO_2): R_f = 0.35 (hexanes: ethyl acetate = 1:1).

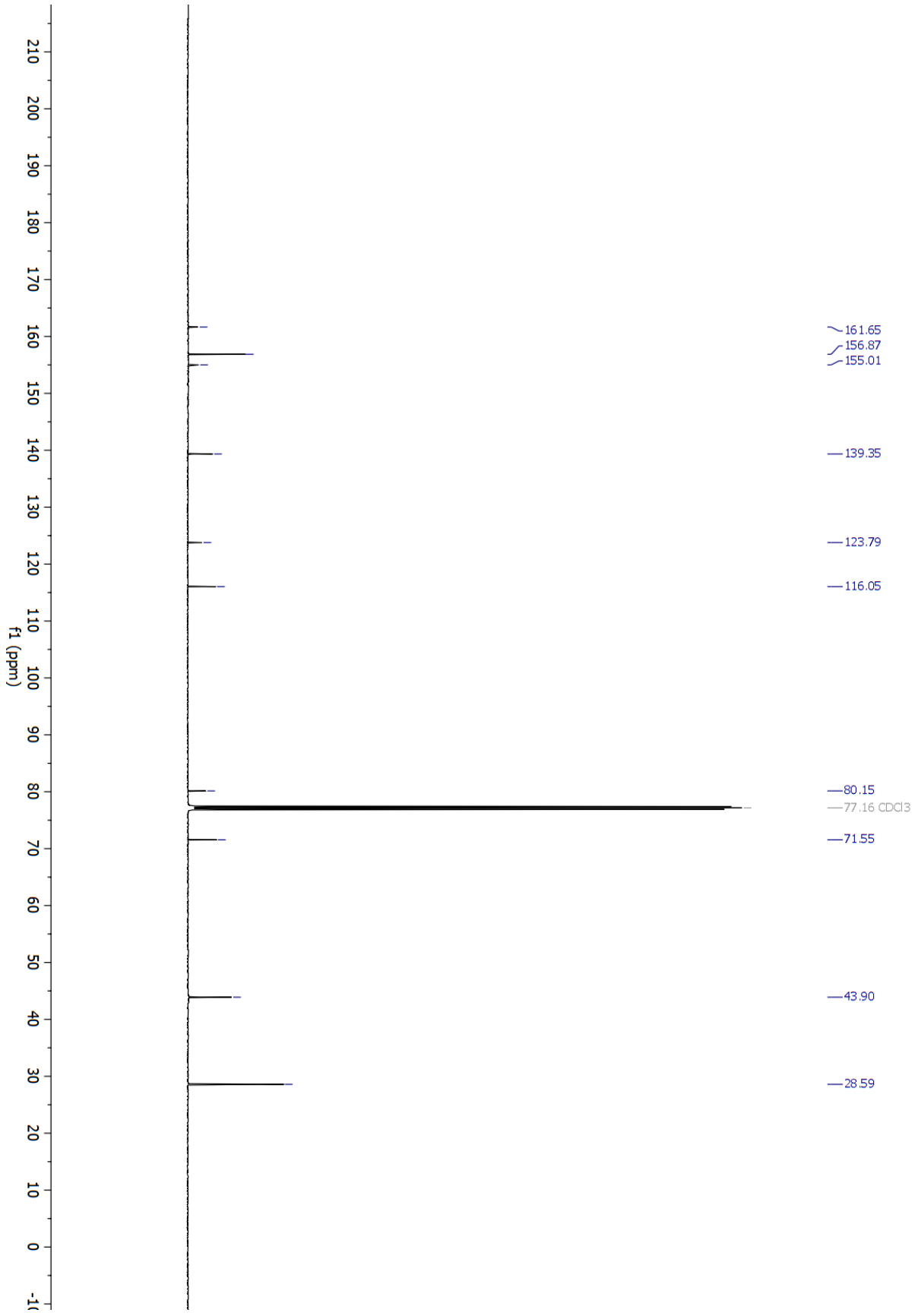
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.80 (ddd, J = 16.9, 10.4, 6.3 Hz, 1H), 5.31 – 5.13 (m, 1H), 5.04 (dd, J = 10.4, 1.4 Hz, 1H), 4.15 (q, J = 6.5 Hz, 1H), 4.00 (s, 4H), 2.63 (s, 4H), 1.74 – 1.51 (m, 4H), 1.38 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 155.3, 141.9, 115.1, 79.6, 71.0, 44.1, 32.8, 28.9, 28.9.

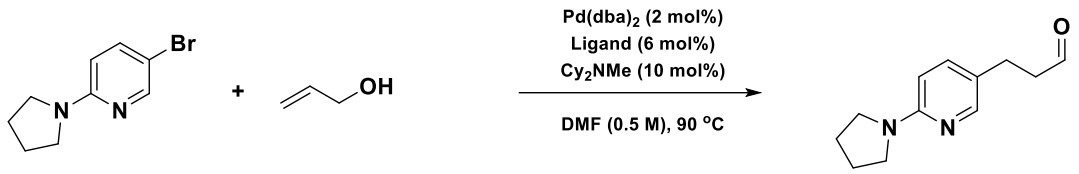
HRMS (ESI): calculated for $C_{14}H_{25}NO_3$ [M+Na^+]= 278.1727, found= 278.1733.

FTIR (neat): 3456, 2975, 2920, 2849, 1691, 1668, 1477, 1365, 1297, 1163, 1085, 993, 918, 768 cm^{-1}.


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.99
1.04
1.15
1.11
3.47
3.92
4.08
9.46
5.84
5.82
5.82
5.80
5.79
5.78
5.77
5.18
5.18
5.15
5.05
5.05
5.03
5.03
4.17
4.15
4.14
4.13
4.00
2.63
1.66
1.64
1.62
1.61
1.61
1.57
1.55
1.38


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
161.65
156.87
155.01
139.35
123.79
116.05
80.15
77.16 CDCl3
71.55
43.90
28.59

(S1q) 3-(6-(pyrrolidin-1-yl)pyridin-3-yl)propanal



Procedure

To an oven-dried round bottom flask equipped with a magnetic stir bar was charged with $Pd(dba)_2$ (287 mg, 0.26 mmol, 2 mol%), 2-[bis(1,1-dimethylethyl)phosphino]-1-phenyl-1H-indole (267.0 mg, 0.792 mmol, 6 mol%), 5 – bromo – 2 - (pyrrolidin-1-yl)pyridine (3.00 g, 13.2 mmol, 100mol%) and purged with argon. Then DMF (24 mL), N,N-dicyclohexylmethylamine (3.2 mL, 1.45 mmol, 10 mol%), allyl alcohol (1.0 mL, 14.5 mmol, 110 mol%) were added under argon balloon, respectively. After stirring for 2 h at 90 ^{0}C, the reaction mixture was cooled to room temperature, and sat. NH_4Cl aq. was poured into the reaction mixture and extracted with Et_2O. The organic layer was washed with water, Na_2SO_4 (dried), and filtered. The filtrate was concentrated in vacuo and the residue was subjected to silica gel flash column chromatography. Silica gel was premixed with dichloromethane : triethylamine = 100:1 then loaded to the column. The products are eluted by dichloromethane: ethyl acetate = 1:1. The title compound was then obtained in 40% yield (1.1 g, 5.28 mmol) as an orange oil.

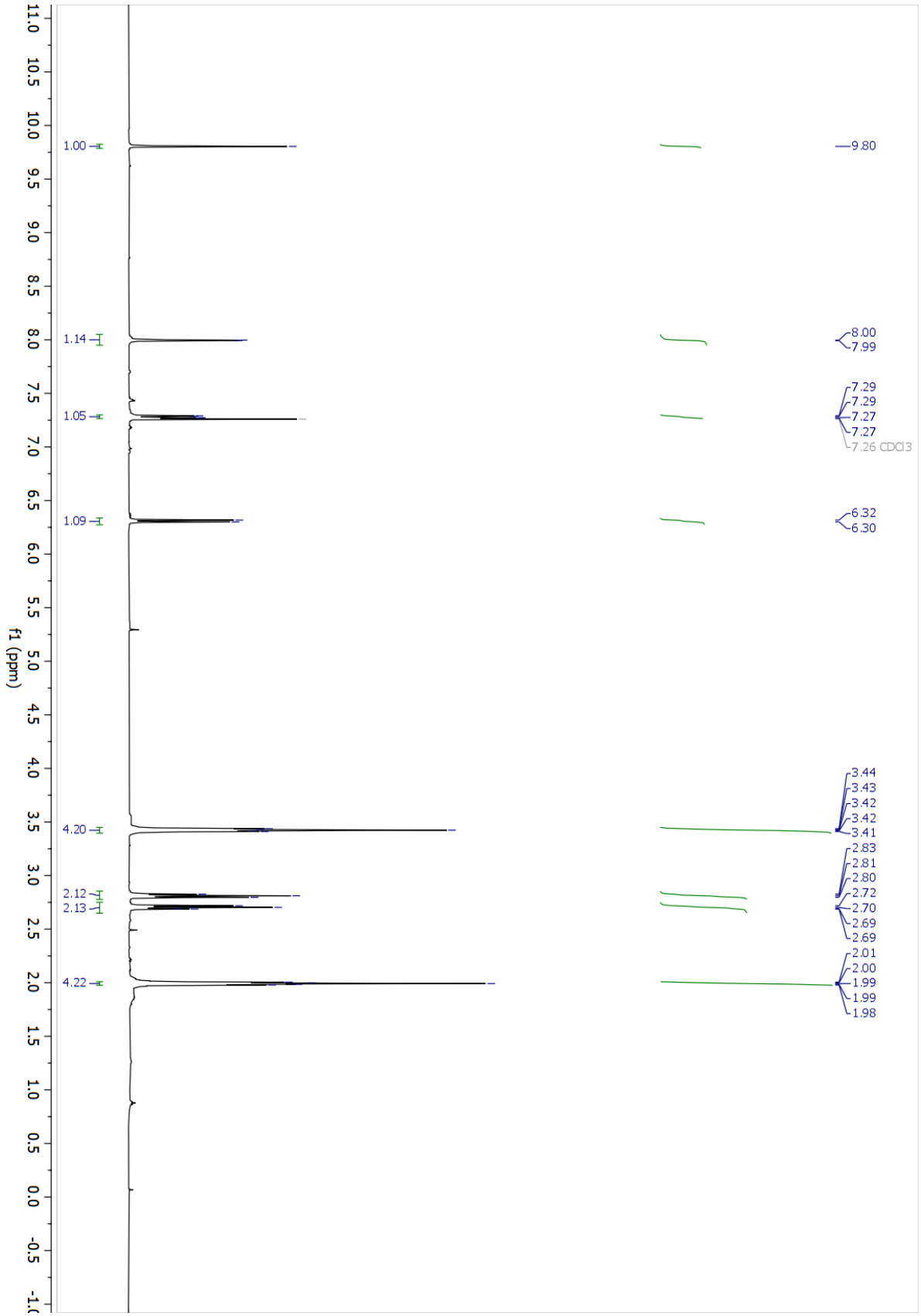
TLC (SiO_2): R_f = 0.43 (dichloromethane: ethyl acetate = 1:1).

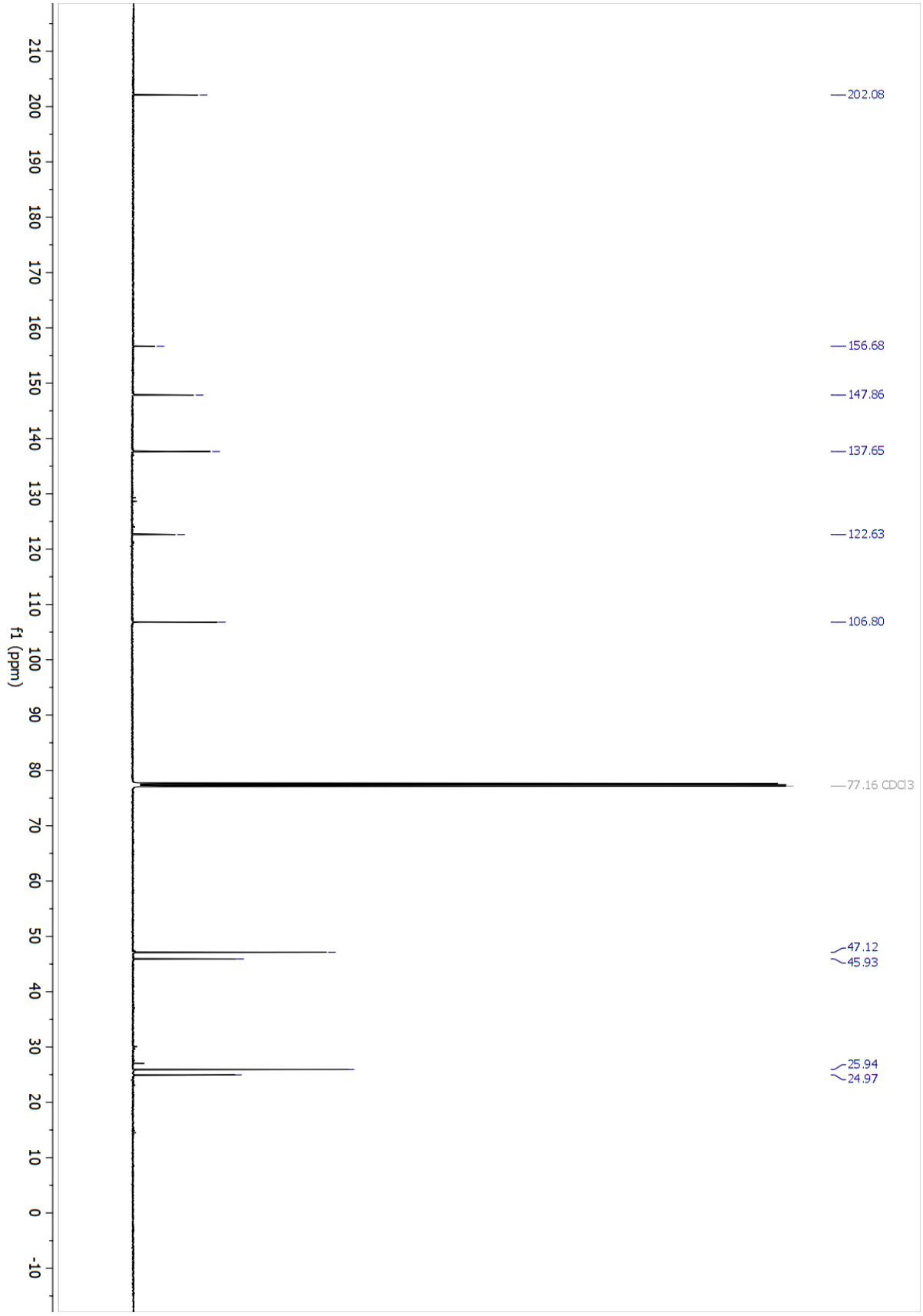
^{1}H NMR (500 MHz, $CDCl_3$): δ: 9.80 (s, 1H), 7.99 (d, *J* = 2.4 Hz, 1H), 7.28 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.31 (d, *J* = 8.6 Hz, 1H), 3.48 – 3.39 (m, 4H), 2.81 (t, *J* = 7.4 Hz, 2H), 2.70 (t, *J* = 7.5 Hz, 2H), 2.02 – 1.95 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 202.1, 156.7, 147.9, 137.7, 122.6, 106.8, 47.1, 45.9, 25.9, 25.0.

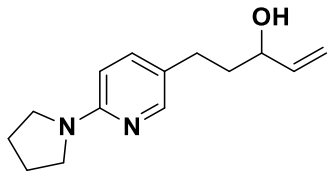
HRMS (ESI): Calculated for $C_{12}H_{16}N_2O$ $[M+H^+]$ = 205.1335, Found 205.1336

FTIR (neat): 2926, 1609, 1506, 1485, 1415, 1162, 804.88 cm^{-1}


f1 (ppm)
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
1.14
1.05
1.09
4.20
2.12
2.13
4.22
9.80
8.00
7.99
7.29
7.29
7.27
7.27
7.26 CDCl3
6.32
6.30
3.44
3.43
3.42
3.42
3.41
2.83
2.81
2.80
2.72
2.70
2.69
2.69
2.01
2.00
1.99
1.99
1.98


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
202.08
156.68
147.86
137.65
122.63
106.80
77.16 CDCl3
47.12
45.93
25.94
24.97

(1q) 5-(6-(pyrrolidin-1-yl)pyridin-3-yl)pent-1-en-3-ol



Procedure

Aldehyde **S1q** (545.0 mg, 2.720 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 40% yield (247.0 mg, 1.080 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, ethyl acetate: dichloromethane: triethylamine = 300:100:1).

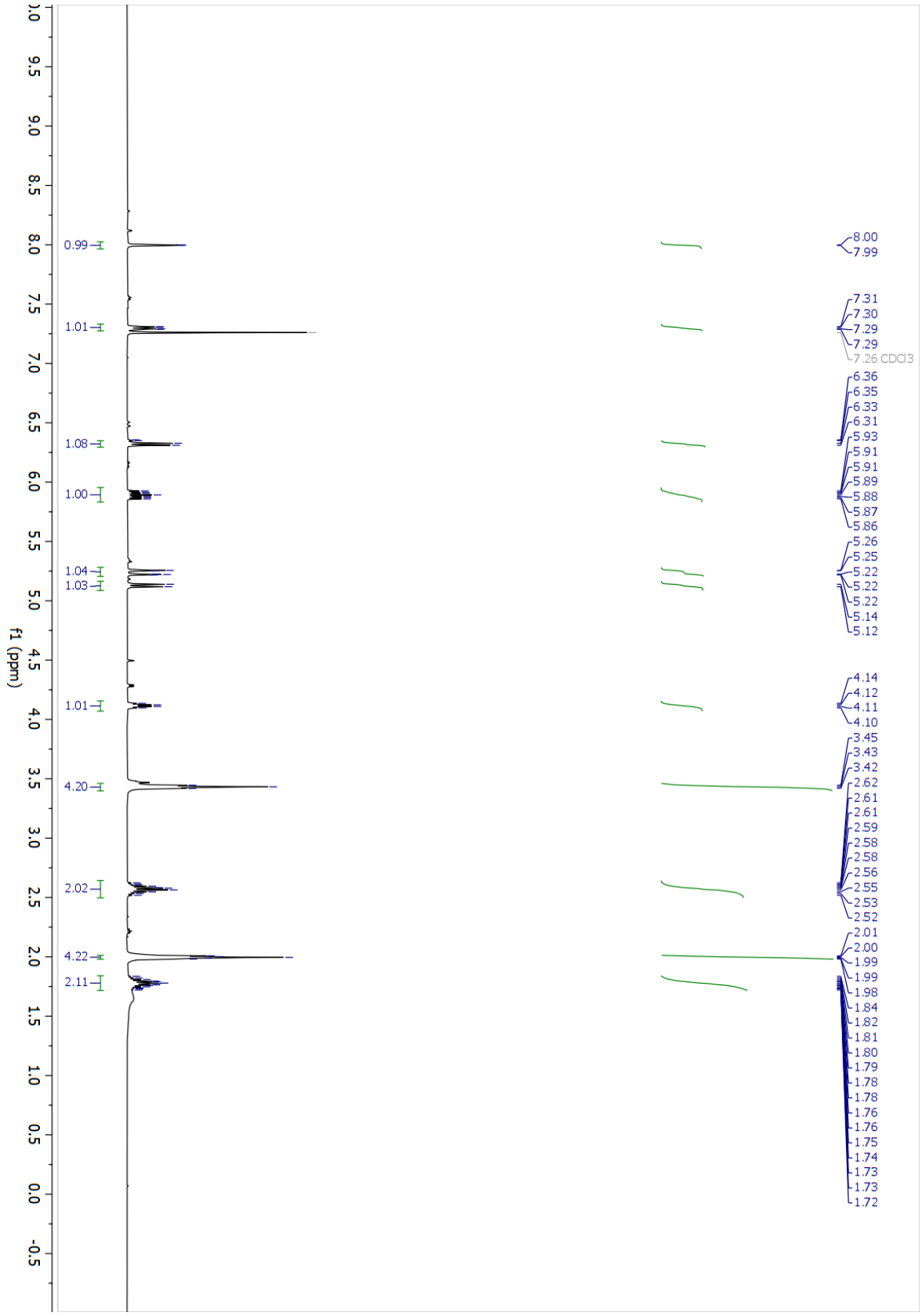
TLC (SiO_2): R_f = 0.4 (ethyl acetate: dichloromethane: triethylamine = 400:100:1).

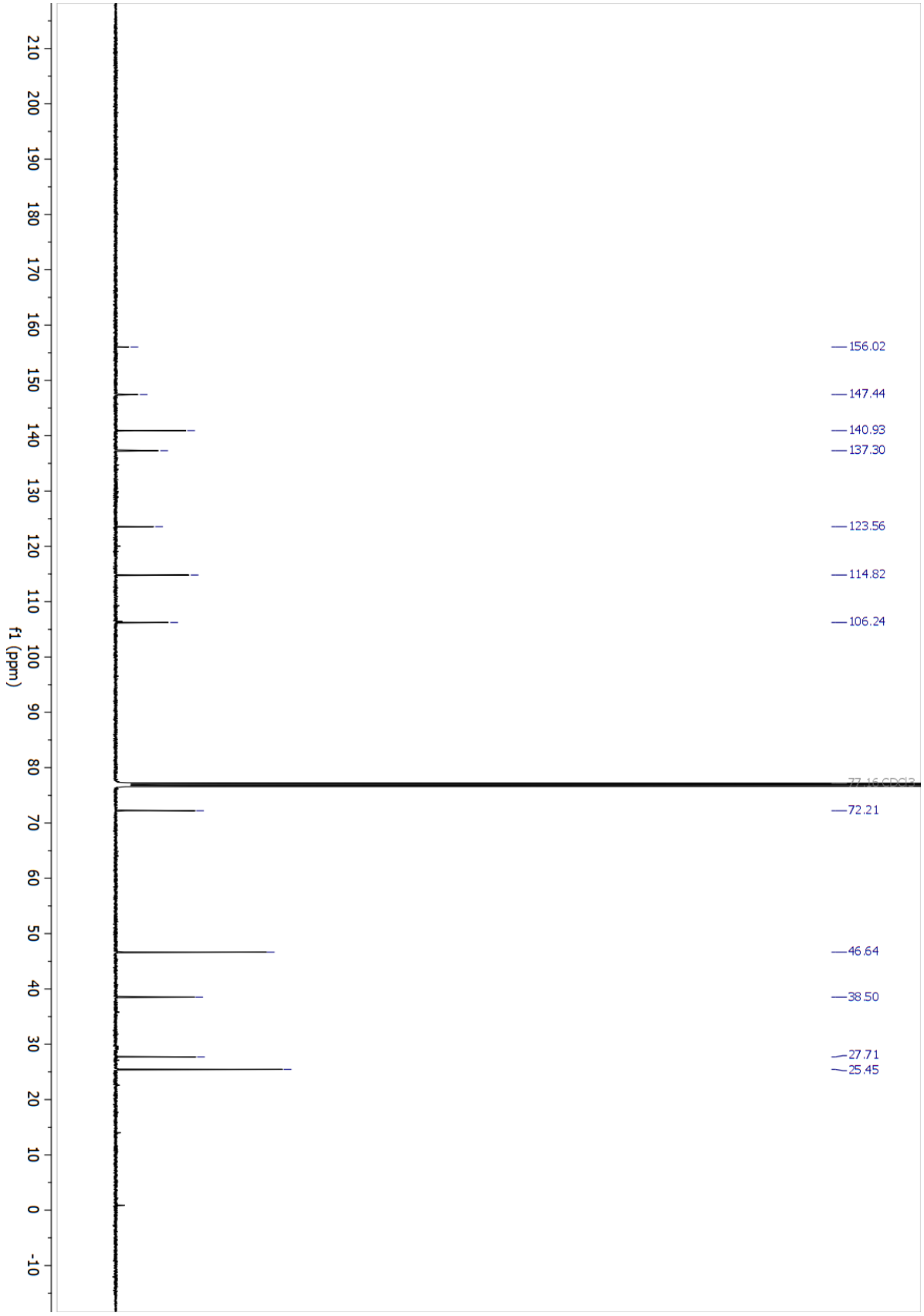
^{1}H NMR (500 MHz, $CDCl_3$): δ: 8.00 (d, *J* = 2.3 Hz, 1H), 7.30 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.32 (d, *J* = 8.6 Hz, 1H), 5.89 (ddd, *J* = 16.9, 10.4, 6.2 Hz, 1H), 5.28 – 5.17 (m, 1H), 5.13 (d, *J* = 10.4 Hz, 1H), 4.12 (q, *J* = 6.4 Hz, 1H), 3.50 – 3.38 (m, 4H), 2.64 – 2.50 (m, 2H), 2.05 – 1.94 (m, 4H), 1.85 – 1.71 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 156.0, 147.4, 140.9, 137.3, 123.6, 114.8, 106.2, 72.2, 46.6, 38.5, 27.7, 25.4.

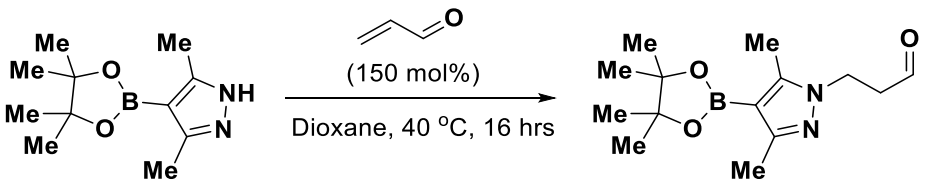
HRMS (ESI): Calculated for $C_{14}H_{20}N_2O$ $[M+H^+]$ = 233.1648, Found 233.1655

FTIR (neat): 3250, 2926, 2852, 1605, 1484, 1418, 1013, 806, 750 cm^{-1}


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0.99
1.01
1.08
1.00
1.04
1.03
1.01
4.20
2.02
4.22
2.11
8.00
7.99
7.31
7.30
7.29
7.29
7.26 CDCl3
6.36
6.35
6.33
6.31
5.93
5.91
5.91
5.89
5.88
5.87
5.86
5.26
5.25
5.22
5.22
5.22
5.14
5.12
4.14
4.12
4.11
4.10
3.45
3.43
3.42
2.62
2.61
2.61
2.59
2.58
2.58
2.56
2.55
2.53
2.52
2.01
2.00
1.99
1.99
1.98
1.84
1.82
1.81
1.80
1.79
1.78
1.78
1.76
1.76
1.75
1.74
1.73
1.73
1.72


156.02
147.44
140.93
137.30
123.56
114.82
106.24
77.16 CDCl3
72.21
46.64
38.50
27.71
25.45
f1 (ppm)

(S1r) 3-(3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)propanal



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with 5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (5.0 g, 22.5 mmol, 100 mol%). The flask was then purged with argon. Anhydrous dioxane (15. mL) and freshly distilled acrolein (2.5 mL, 150 mol%) were added subsequently. The reaction mixture was then heated at 40 ^{0}C for 16 hrs. The reaction mixture was then diluted by dichloromethane and passed through a plug of silica gel. The solution was then concentrated in vacuo at 70^{0}C to obtain in 80% yield (5.0 g, 18 mmol) as a pale yellow oil which is used for next step without any further purification.

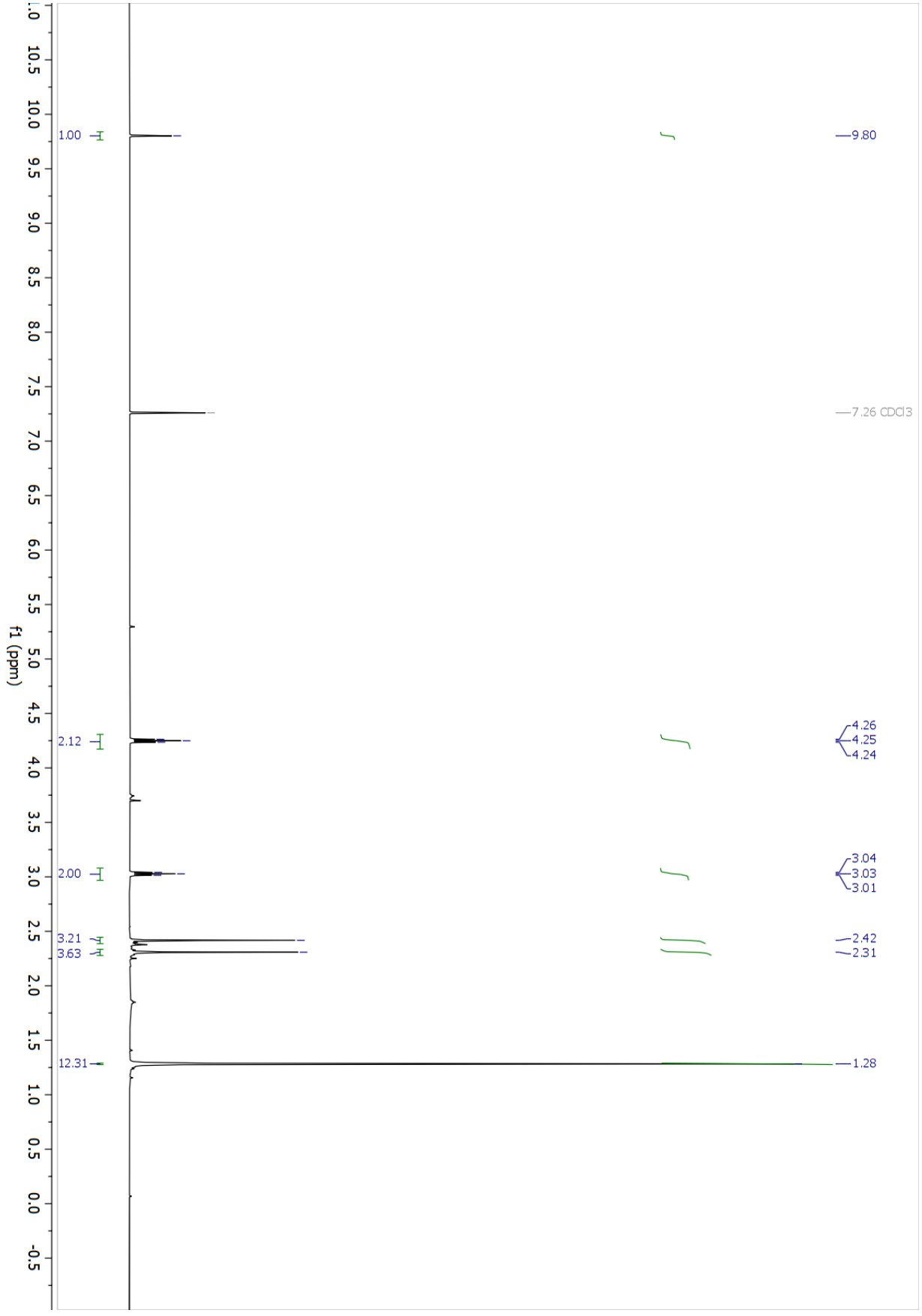
TLC (SiO_2): R_f = 0.50 (dichloromethane: ethyl acetate = 1:1).

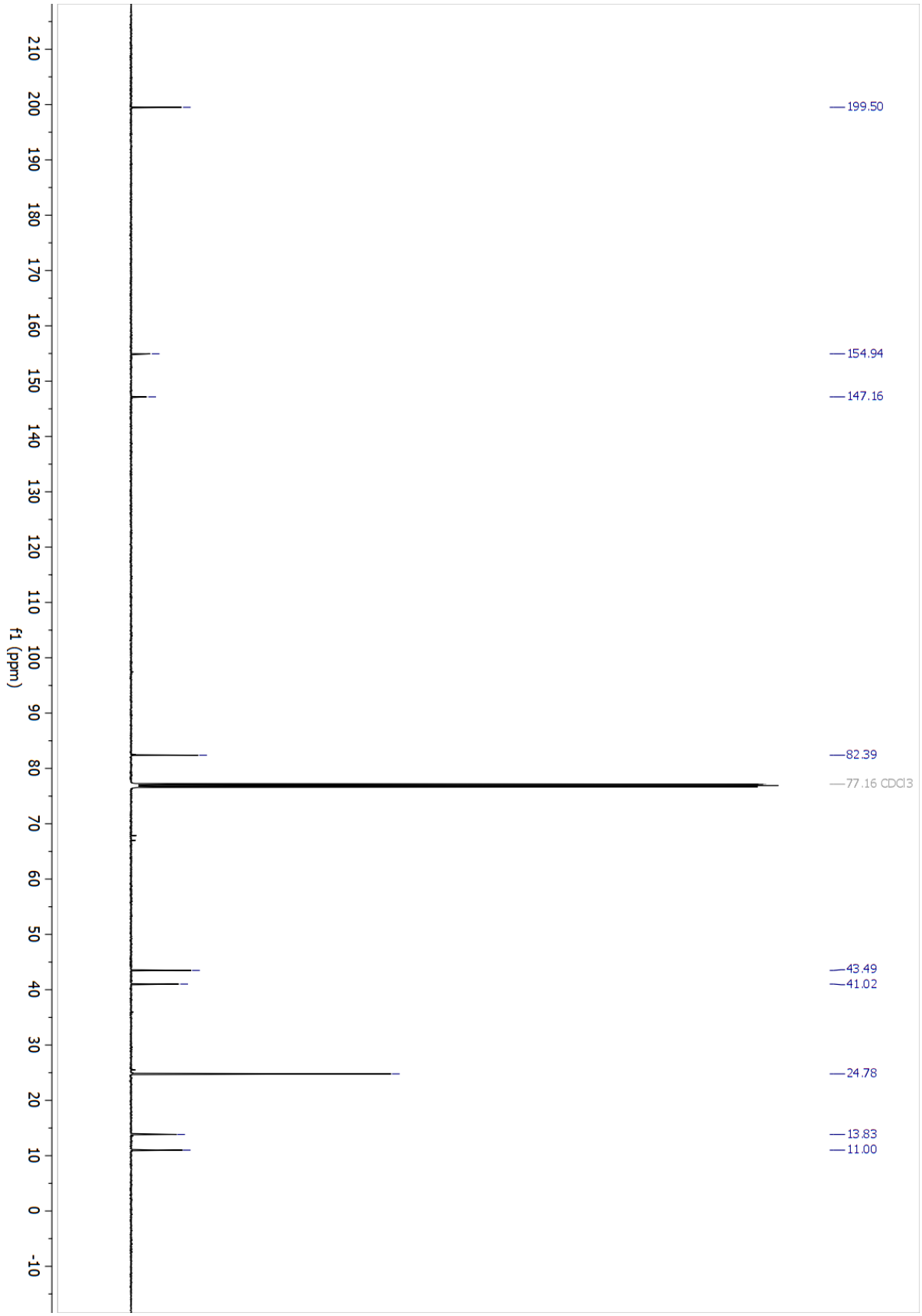
^{1}H NMR (500 MHz, $CDCl_3$): δ: 9.80 (s, 1H), 4.25 (t, *J* = 6.7 Hz, 2H), 3.03 (t, *J* = 6.7 Hz, 2H), 2.42 (s, 3H), 2.31 (s, 3H), 1.28 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 199.5, 154.9, 147.2, 82.4, 43.5, 41.0, 24.8, 13.8, 11.0.

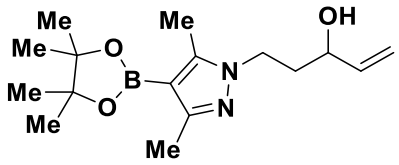
HRMS (ESI): Calculated for $C_{14}H_{23}BN_2O_3$ [M+H$^+$] = 279.1877, found 279.1885

FTIR (neat): 2976, 1547, 1435, 1275, 1147, 1136, 1081, 751, 717 cm^{-1}


f1 (ppm)
1.00
2.12
2.00
3.21
3.63
12.31
9.80
7.26 CDCl3
4.26
4.25
4.24
3.04
3.03
3.01
2.42
2.31
1.28


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
199.50
154.94
147.16
82.39
77.16 CDCl3
43.49
41.02
24.78
13.83
11.00

(1r) 5-(3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)pent-1-en-3-ol



Procedure

Aldehyde **S1r** (3.130 g, 10.200 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 50% yield (0.860 g, 5.100 mmol) as a white solid after isolation by flash column chromatography (SiO_2, dichloromethane: ethyl acetate = 1:1).

TLC (SiO_2): R_f = 0.40 (dichloromethane: ethyl acetate = 1:1).

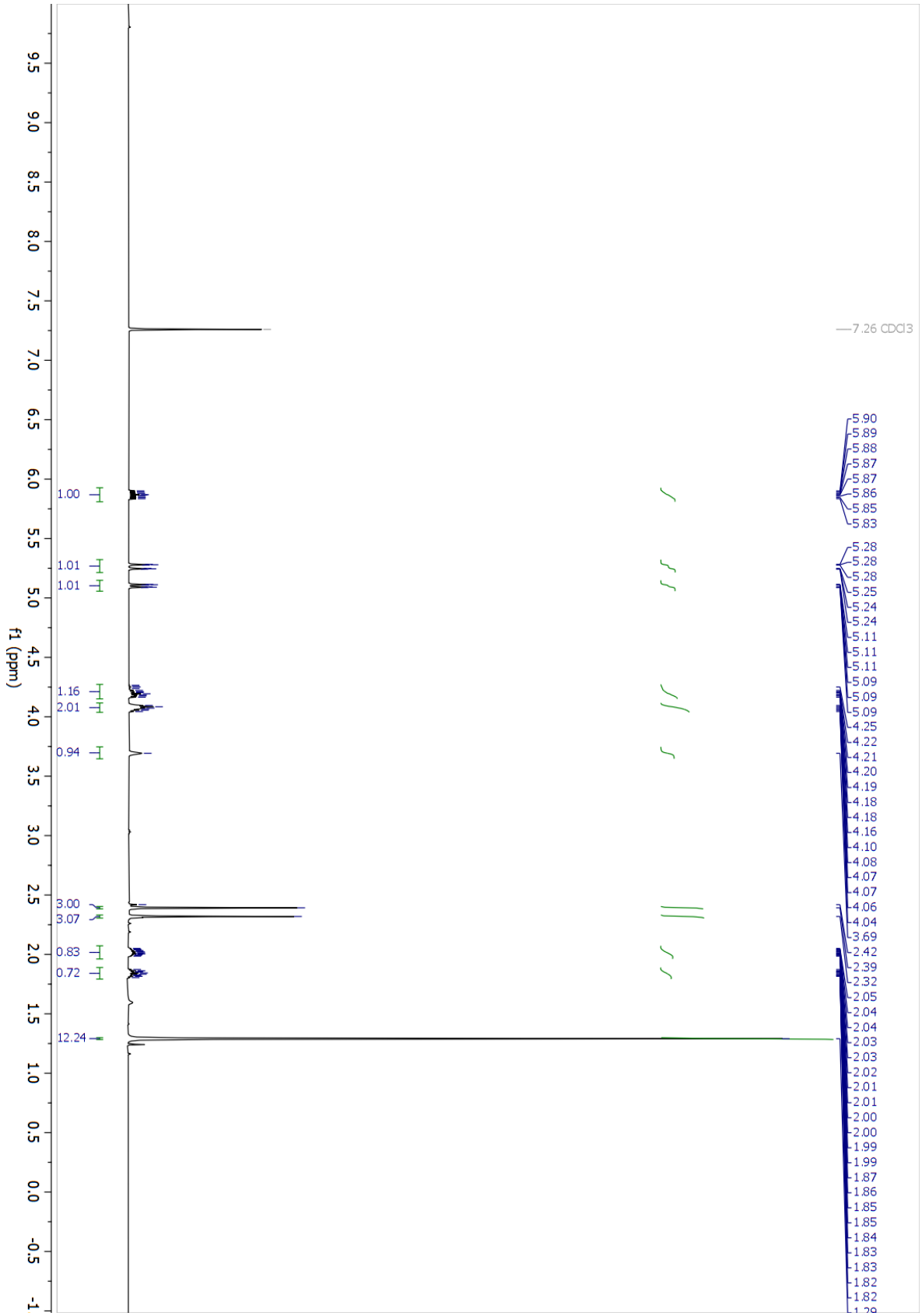
^{1}H NMR (500 MHz, $CDCl_3$): δ: 5.87 (ddd, *J* = 17.1, 10.5, 5.4 Hz, 1H), 5.26 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.10 (dt, *J* = 10.5, 1.5 Hz, 1H), 4.28 – 4.15 (m, 1H), 4.07 (dt, *J* = 14.2, 5.7 Hz, 2H), 3.69 (s, 1H), 2.39 (s, 3H), 2.32 (s, 3H), 2.02 (dddd, *J* = 14.4, 9.2, 5.8, 3.5 Hz, 1H), 1.84 (ddt, *J* = 14.4, 9.0, 5.4 Hz, 1H), 1.29 (s, 12H).

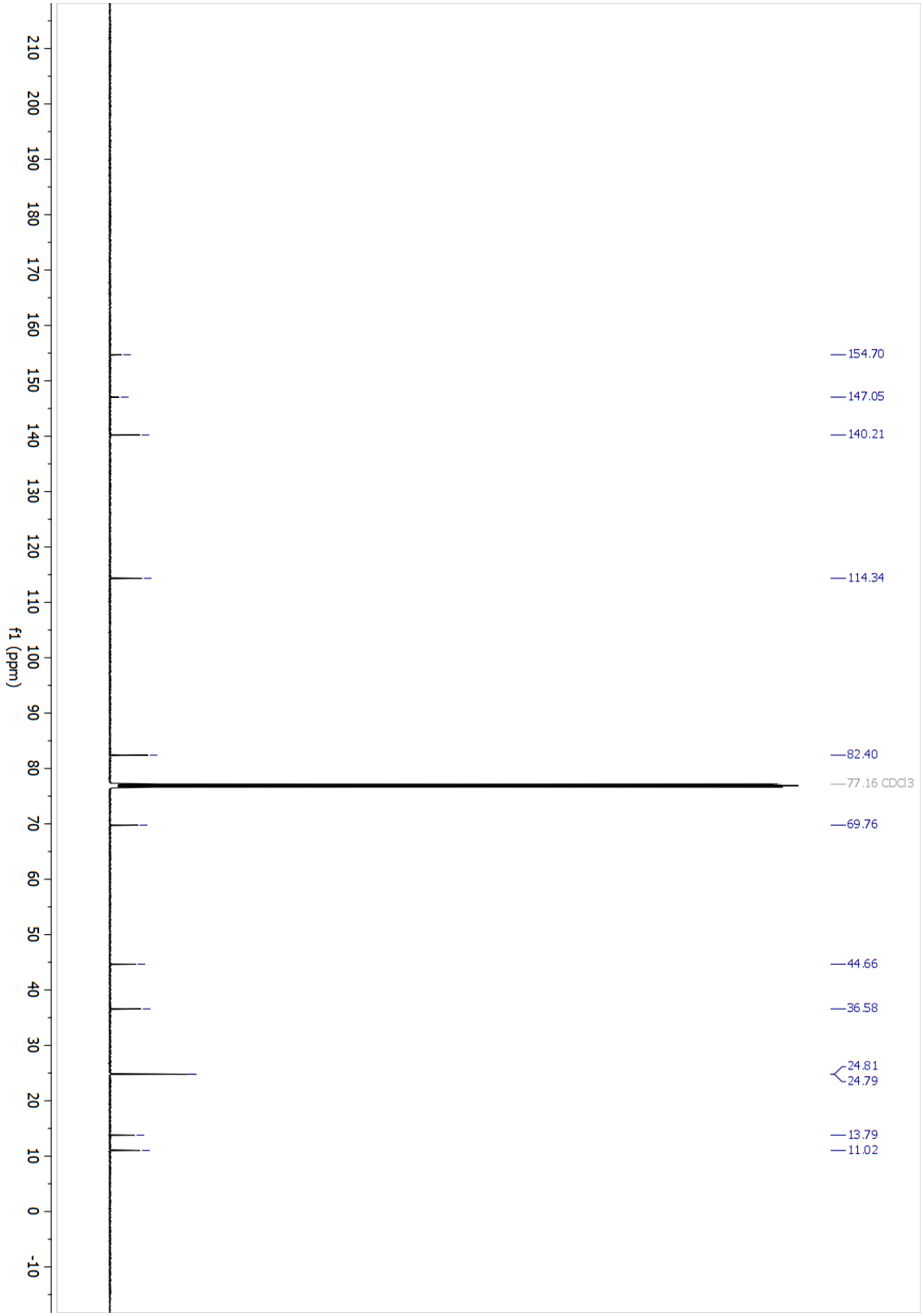
^{13}C NMR (126 MHz, $CDCl_3$): δ: 154.7, 147.0, 140.2, 114.3, 82.4, 69.8, 44.7, 36.6, 24.8, 24.8, 13.8, 11.0.

HRMS (ESI): Calculated for $C_{16}H_{27}BN_2O_3$ [M+H$^+$] = 306.2224, found 306.2231

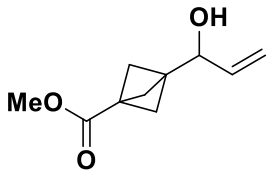
FTIR (neat): 3201, 2978, 1543, 1478, 1283, 1144, 1081, 920, 859, 718 cm^{-1}

MP: 124-130 ^{0}C


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.00
1.01
1.01
1.16
2.01
0.94
3.00
3.07
0.83
0.72
12.24
7.26 CDCl3
5.90
5.89
5.88
5.87
5.87
5.86
5.85
5.83
5.28
5.28
5.28
5.25
5.24
5.24
5.11
5.11
5.11
5.09
5.09
5.09
4.25
4.22
4.21
4.20
4.19
4.18
4.18
4.16
4.10
4.08
4.07
4.07
4.06
4.04
3.69
2.42
2.39
2.32
2.05
2.04
2.04
2.03
2.03
2.02
2.01
2.01
2.00
2.00
1.99
1.99
1.87
1.86
1.85
1.85
1.84
1.83
1.83
1.82
1.82


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
154.70
147.05
140.21
114.34
82.40
77.16 CDCl3
69.76
44.66
36.58
24.81
24.79
13.79
11.02

(1t) methyl 3-(1-hydroxyallyl)bicyclo[1.1.1]pentane-1-carboxylate



Procedure

methyl 3-formylbicyclo[1.1.1]pentane-1-carboxylate (304.0 mg, 1.97 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 68% yield (245.0 mg, 1.34 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–1:1).

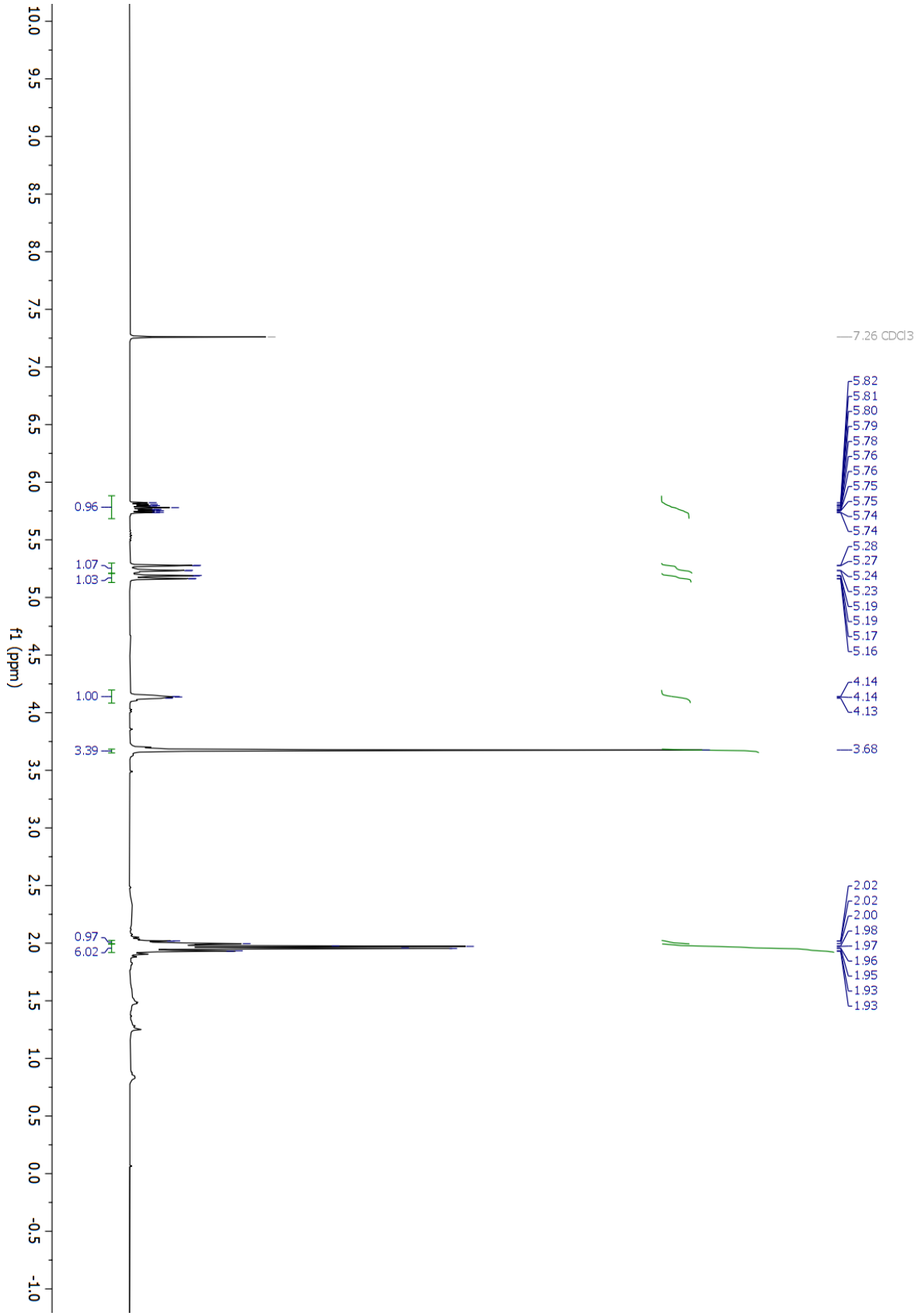
TLC (SiO_2): R_f = 0.26 (hexanes: ethyl acetate = 1:1).

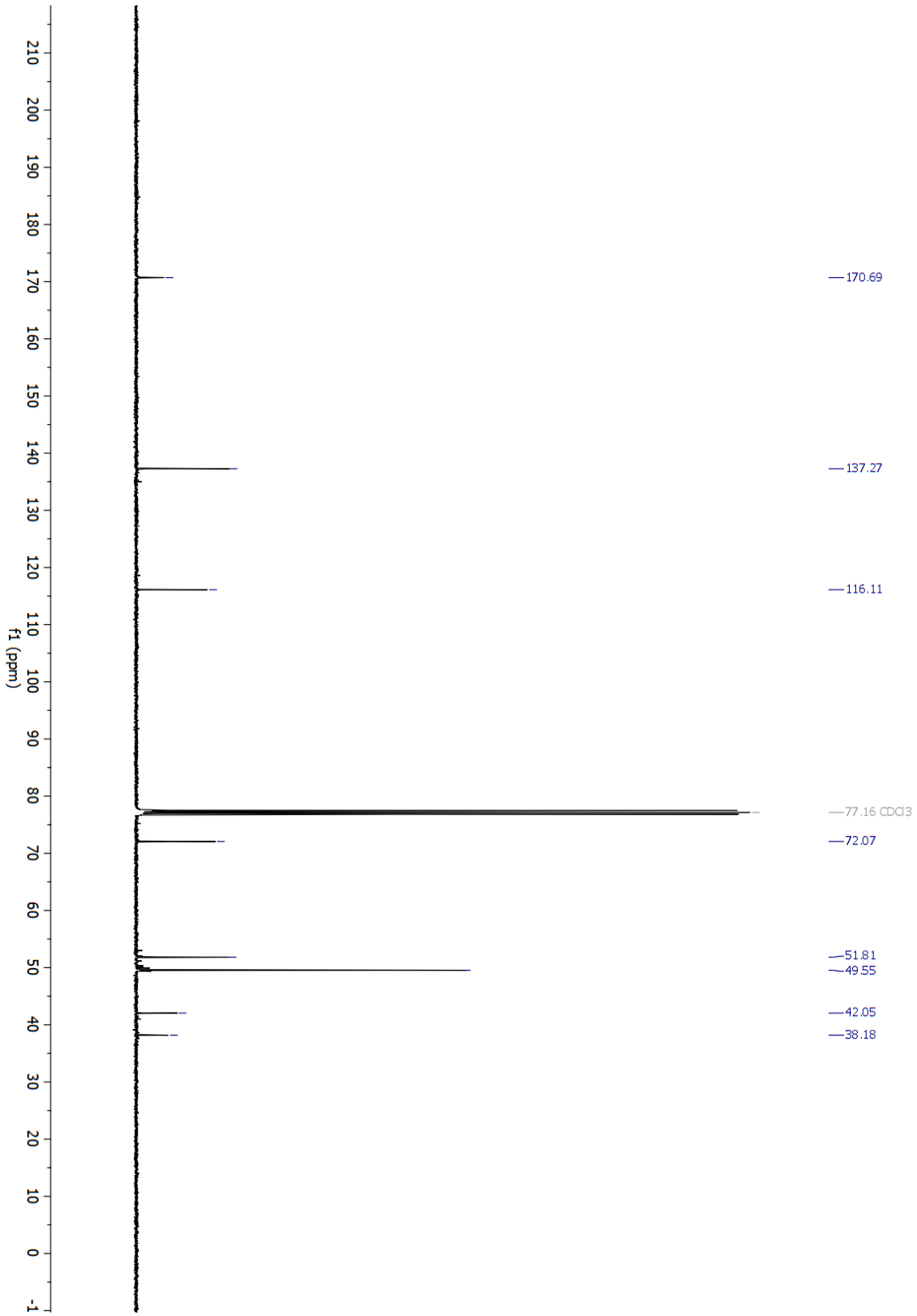
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77 – 5.64 (m, 1H), 5.19 (dd, J = 17.2, 1.4 Hz, 1H), 5.11 (dd, J = 10.4, 1.4 Hz, 1H), 4.10 – 4.04 (m, 1H), 3.61 (s, 3H), 1.95 (s, 1H), 1.90 (q, J = 8.9, 8.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.7, 137.3, 116.1, 72.1, 51.8, 49.5, 42.0, 38.2.

HRMS (ESI): Calculated for $C_{10}H_{14}O_3$ $[M+Na^+]$= 205.0835, found= 205.0837

FTIR (neat): 3465, 2970, 2919, 2882, 2360, 1736, 1437, 1366, 1351, 1203, 1066, 990, 925, 752 cm^{-1}

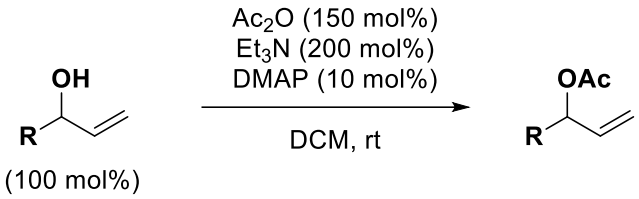

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.96
1.07
1.03
1.00
3.39
0.97
6.02
7.26 CDCl3
5.82
5.81
5.80
5.79
5.78
5.76
5.76
5.75
5.75
5.74
5.74
5.28
5.27
5.24
5.23
5.19
5.19
5.17
5.16
4.14
4.14
4.13
3.68
2.02
2.02
2.00
1.98
1.97
1.96
1.95
1.93
1.93


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
170.69
137.27
116.11
77.16 CDCl3
72.07
51.81
49.55
42.05
38.18

3.2d. Procedures and Spectral Data for Synthesis of Allylic Acetates 2a-2v

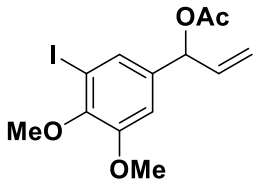
Allylic acetates **2a**,[45] **2b**,[53] **2c**,[53] **2m**,[53] **2n**,[53] **2p**,[53] **2s**,[55] **2u**,[56] and **2v**,[53] were synthesized in the manner previously reported. The obtained products were identical in all respects to the compounds reported the literature.

General Procedure B



An oven-dried round bottom flask equipped with a magnetic stir bar was charged with allylic alcohol (100 mol%), triethylamine (200 mol%), acetic anhydride (150 mol%), 4-dimethylaminopyridine (10 mol%), and anhydrous dichloromethane (0.1 M). The reaction was stirred at ambient temperature for 30 minutes. The reaction solution was diluted with dichloromethane and was washed with aqueous saturated solutions of ammonium chloride, then brine. The organic layer was then separated, Na_2SO_4 (dried), and filtered. The liquid was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The residue was directly subjected to flash column chromatography to afford allyl acetates **2a**-**2v**.

(2d) 1-(3-iodo-4,5-dimethoxyphenyl)allyl acetate



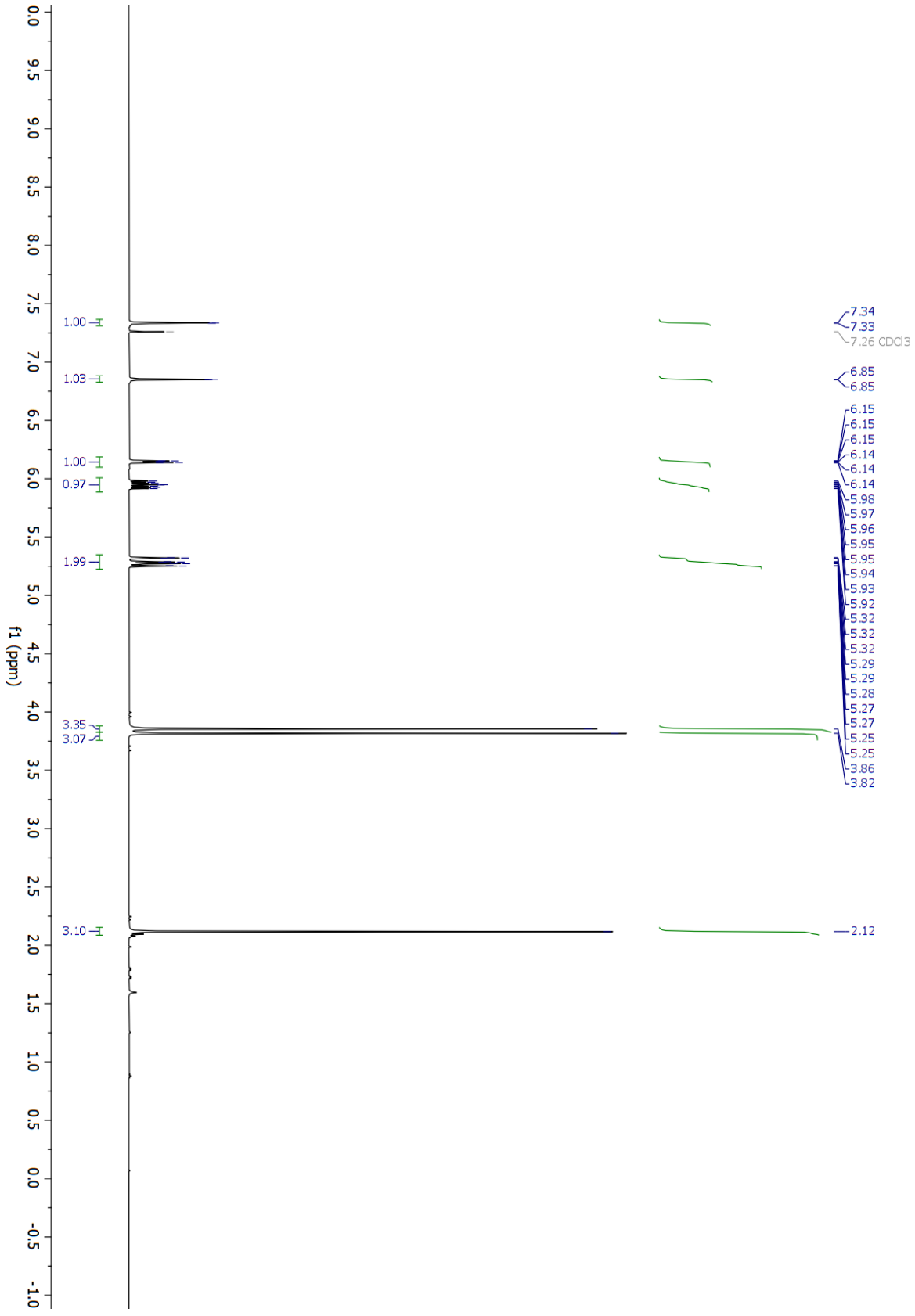
Procedure

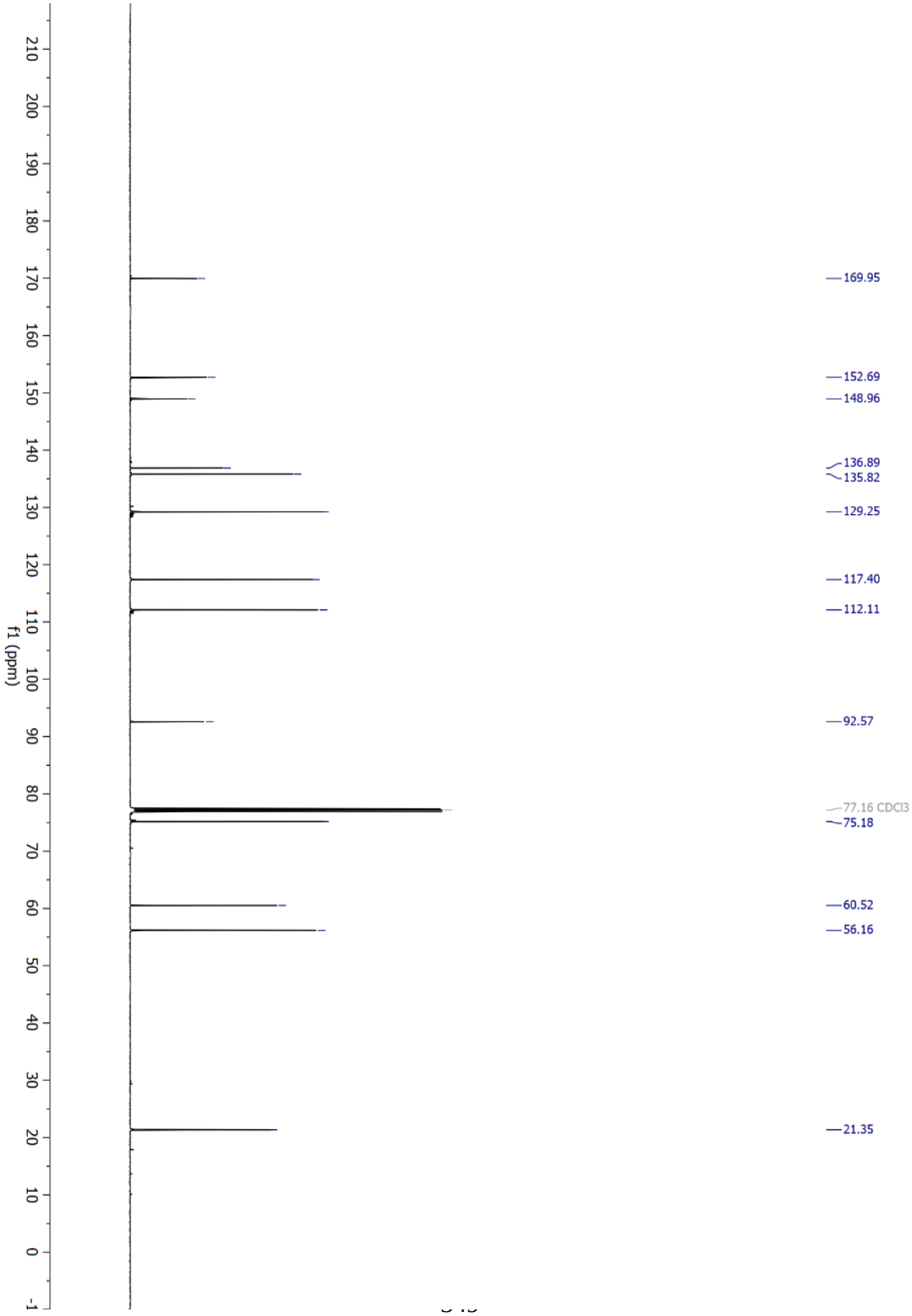
Alcohol **1d** (1.91g, 5.90 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 90% yield (1.91 g, 5.34 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2): R_f = 0.50 (hexanes: ethyl acetate = 4:1).

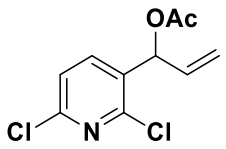
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, *J* = 1.9 Hz, 1H), 6.85 (d, *J* = 2.0 Hz, 1H), 6.15 (dt, *J* = 5.8, 1.5 Hz, 1H), 6.00 – 5.90 (m, 1H), 5.33 – 5.24 (m, 2H), 3.86 (s, 3H), 3.82 (s, 3H), 2.12 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 170.0, 152.7, 149.0, 136.9, 135.8, 129.2, 117.4, 112.1, 92.6, 75.2, 60.5, 56.2, 21.3.
HRMS (ESI): Calculated for $C_{13}H_{15}IO_4$ [M+Na+] = 384.9907, Found 384.9911

FTIR (neat): 3001.85, 2935.00, 1738.10, 1563.55, 1462.96, 1369.5, 1226.47, 1140.62, 1000 cm^{-1}


f1 (ppm)
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.00
1.03
1.00
0.97
1.99
3.35
3.07
3.10
7.34
7.33
7.26 CDCl3
6.85
6.85
6.15
6.15
6.15
6.14
6.14
6.14
5.98
5.97
5.96
5.95
5.95
5.94
5.93
5.92
5.32
5.32
5.32
5.29
5.29
5.28
5.27
5.27
5.25
5.25
3.86
3.82
2.12


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
169.95
152.69
148.96
136.89
135.82
129.25
117.40
112.11
92.57
77.16 CDCl3
75.18
60.52
56.16
21.35

(2e) 1-(2,6-dichloropyridin-3-yl)allyl acetate



Procedure

Alcohol **1e** (1.26 g, 6.16 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 86% yield (1.35 g, 5.28 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

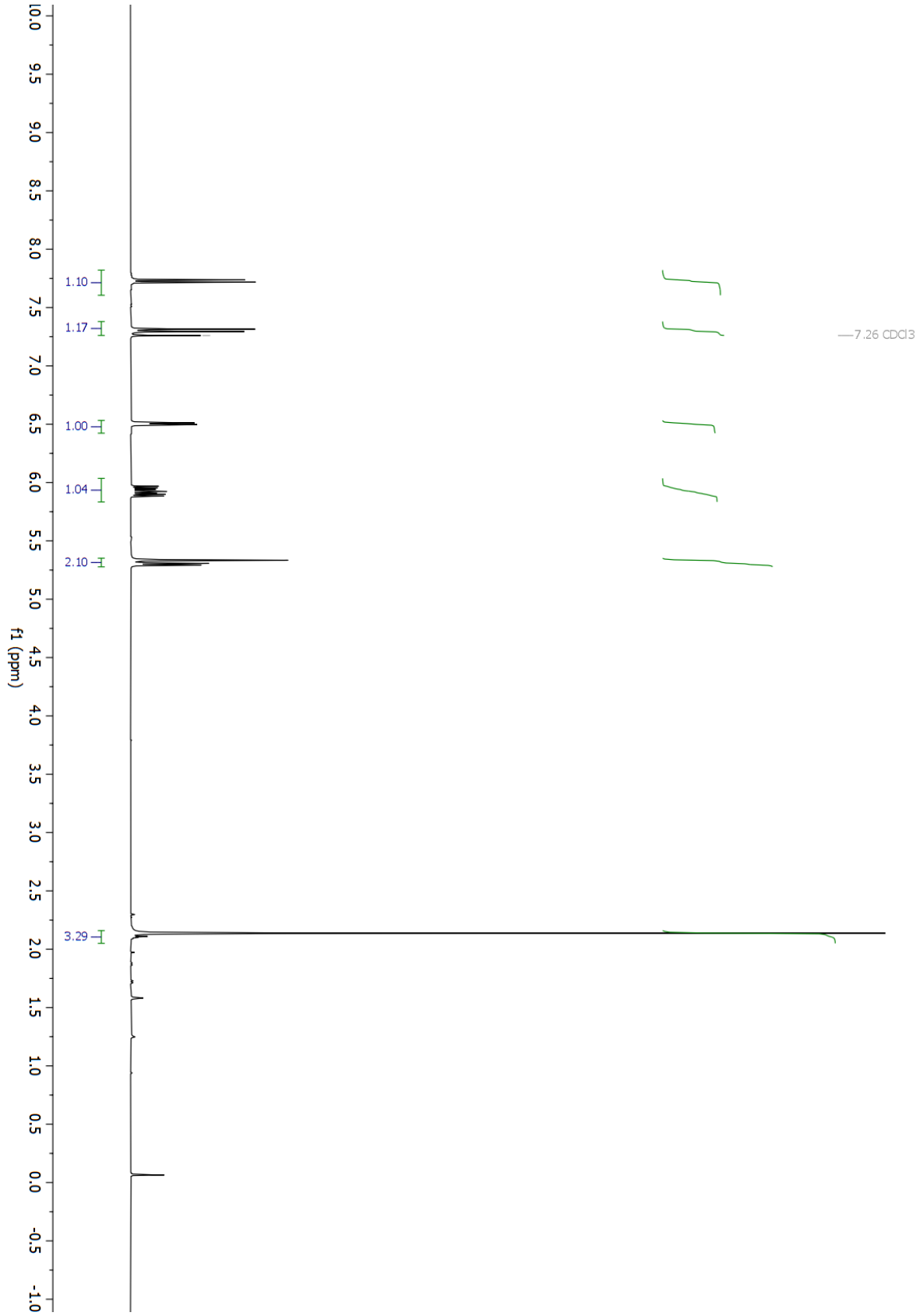
TLC (SiO_2): R_f = 0.45 (hexanes: ethyl acetate = 4:1).

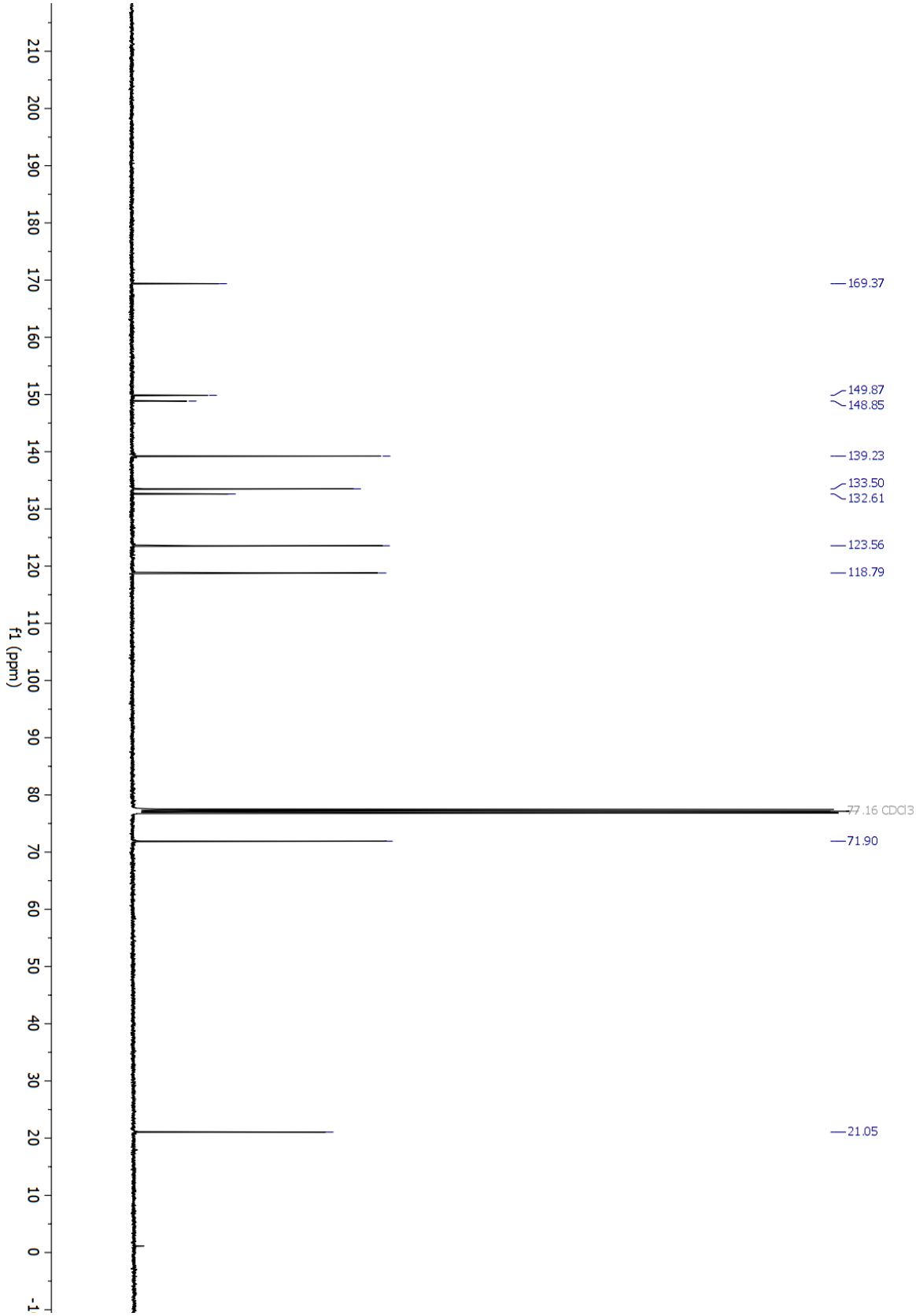
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 8.1 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 6.51 (dd, J = 5.8, 1.5 Hz, 1H), 5.93 (ddd, J = 17.4, 10.2, 5.7 Hz, 1H), 5.33 (d, J = 1.3 Hz, 1H), 5.30 (dd, J = 5.9, 1.2 Hz, 1H), 2.14 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.7, 150.2, 149.2, 139.6, 133.8, 132.9, 123.9, 119.1, 72.2, 21.4.

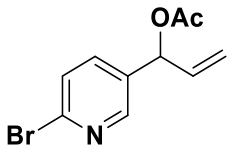
HRMS (ESI): Calculated for $C_{10}H_{14}O_3$ $[M+H^+]$= 246.0083, found= 246.0088

FTIR (neat): 2960, 1737, 1419, 1229, 1217, 1098, 929, 857 cm^{-1}


10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)
1.10
1.17
1.00
1.04
2.10
3.29
7.26 CDCl3


169.37
149.87
148.85
139.23
133.50
132.61
123.56
118.79
77.16 CDCl3
71.90
21.05
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1

(2f) 1-(6-bromopyridin-3-yl)allyl acetate



Procedure

Alcohol **1f** (438 mg, 2.04 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 76% yield (398 mg, 1.55 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexane: ethyl acetate = 10:1–5:1).

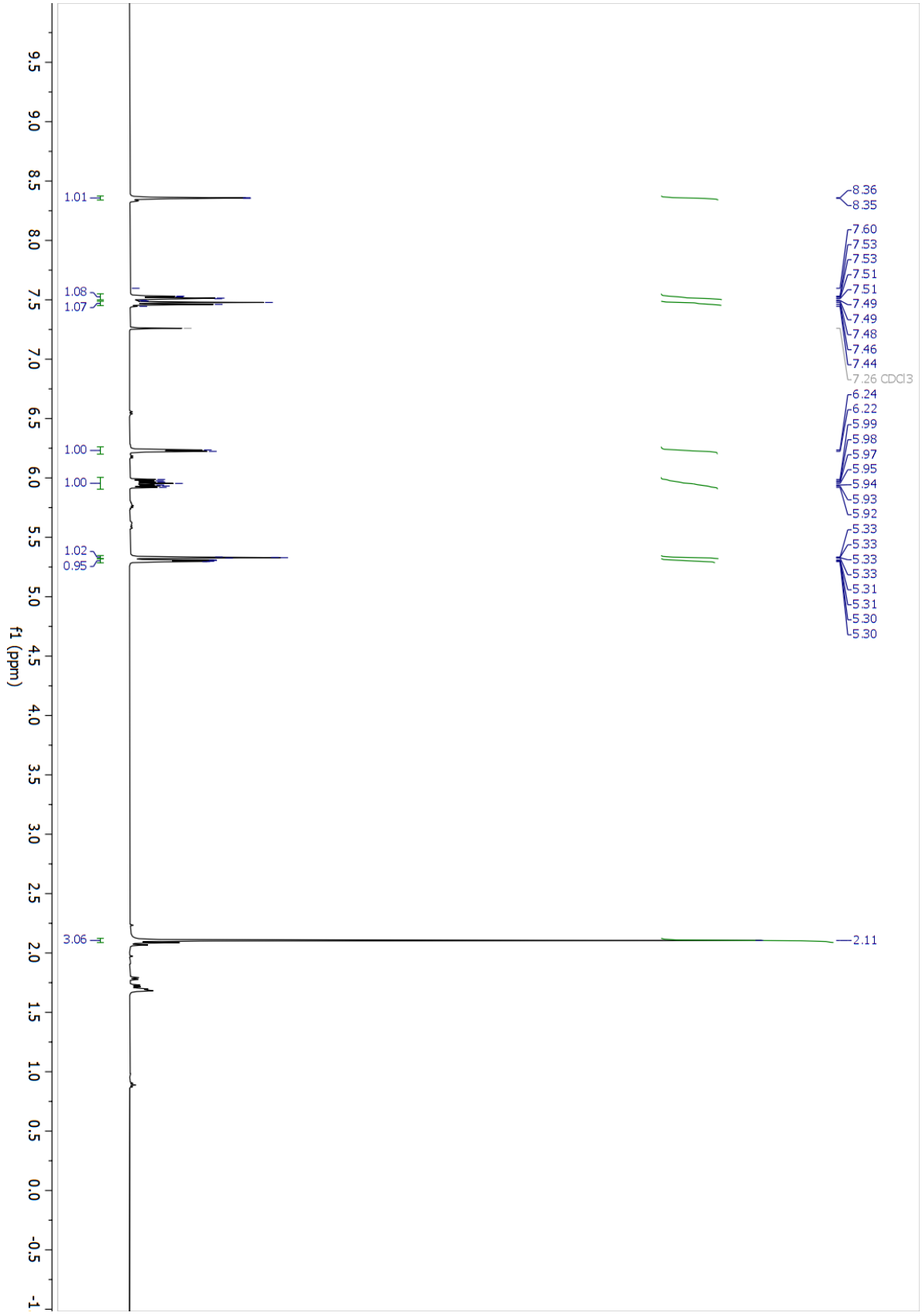
TLC (SiO_2): R_f = 0.40 (hexanes: ethyl acetate = 4:1).

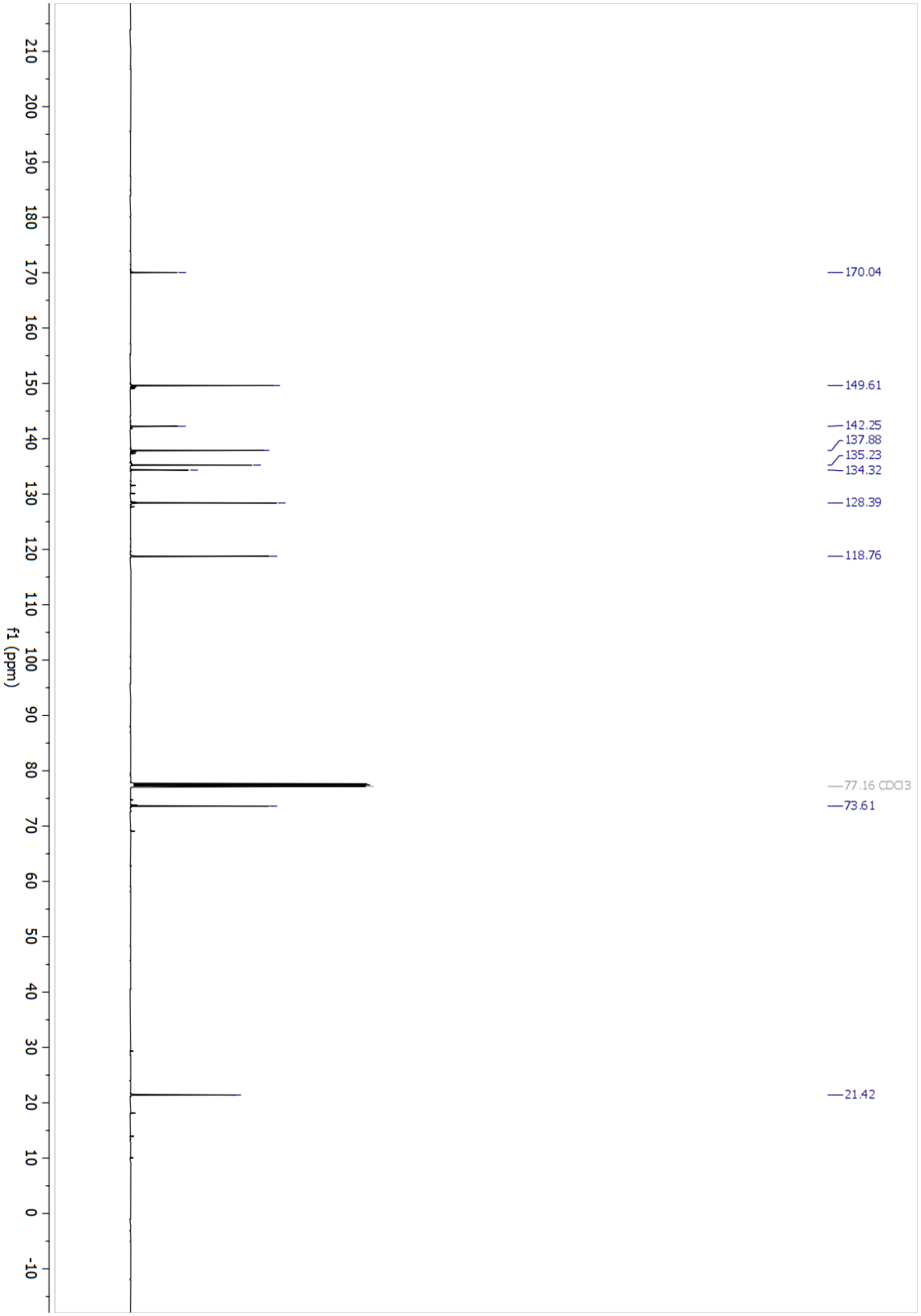
^{1}H NMR (500 MHz, $CDCl_3$): δ: 8.36 (d, *J* = 2.4 Hz, 1H), 7.52 (dd, *J* = 8.3, 2.4 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 6.23 (d, *J* = 5.8 Hz, 1H), 5.95 (ddd, *J* = 16.7, 10.3, 5.9 Hz, 1H), 5.33 (q, *J* = 1.2 Hz, 1H), 5.30 (dd, *J* = 4.9, 1.3 Hz, 1H), 2.11 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 170.0, 149.6, 142.2, 137.9, 135.2, 134.3, 128.4, 118.78, 73.6, 21.4.

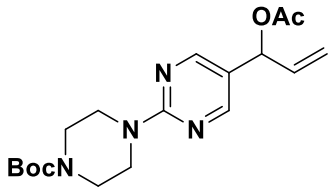
HRMS (ESI): Calculated for $C_{10}H_{10}BrNO_2$ $[M+H^+]$ =255.9968, Found 255.9971

FTIR (neat): 1739, 1224, 1085, 1018, 935, 850, 739 cm^{-1}


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.01
1.08
1.07
1.00
1.00
1.02
0.95
3.06
8.36
8.35
7.60
7.53
7.53
7.51
7.51
7.49
7.49
7.48
7.46
7.44
7.26 CDCl3
6.24
6.22
5.99
5.98
5.97
5.95
5.94
5.93
5.92
5.33
5.33
5.33
5.33
5.31
5.31
5.30
5.30
2.11


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.04
149.61
142.25
137.88
135.23
134.32
128.39
118.76
77.16 CDCl3
73.61
21.42

(2g) tert-butyl 4-(5-(1-acetoxyallyl)pyrimidin-2-yl)piperazine-1-carboxylate



Procedure

Alcohol **1g** (400 mg, 1.25 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 75% yield (339.2 mg, 0.936 mmol) as a pale-yellow solid after isolation by flash column chromatography (Basic Alumina, hexanes: ethyl acetate = 5:1–1:1).

TLC (SiO_2): R_f = 0.61 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 2H), 6.12 (dt, J = 5.4, 1.6 Hz, 1H), 5.98 (ddd, J = 17.4, 10.5, 5.4 Hz, 1H), 5.32 (d, J = 10.6 Hz, 1H), 5.29 (d, J = 4.0 Hz, 1H), 3.81 (dd, J = 6.5, 4.0 Hz, 4H), 3.48 (dd, J = 6.3, 4.1 Hz, 4H), 2.07 (s, 3H), 1.48 (s, 9H).

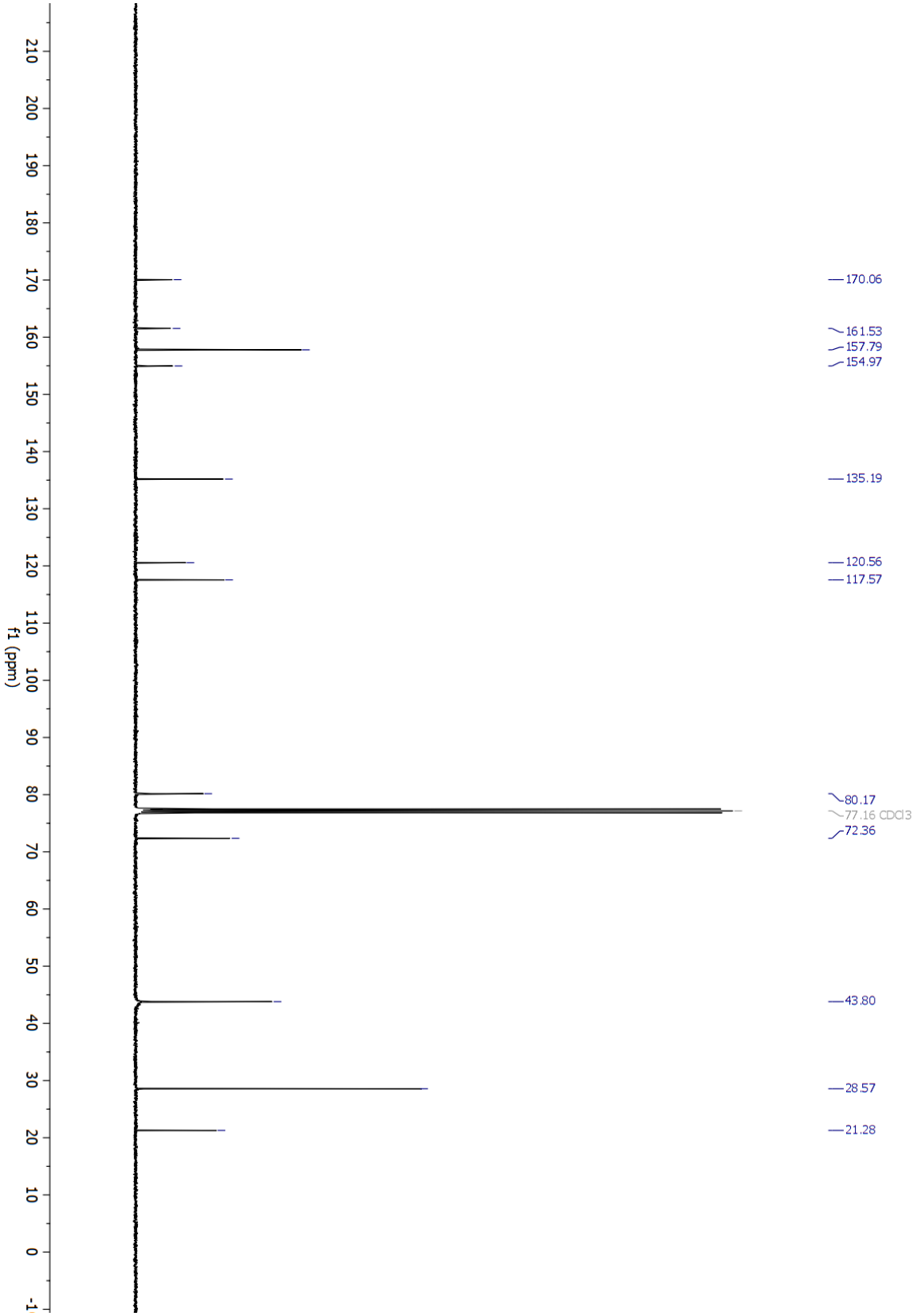
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 161.5, 157.8, 155.0, 135.2, 120.6, 117.6, 80.2, 72.4, 43.8, 28.6, 21.3.

HRMS (ESI): Calculated for $C_{18}H_{26}N_4O_4$ [M+Na^+]= 385.1846, found= 385.1847

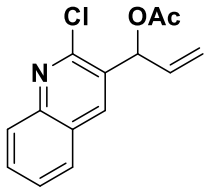
FTIR (neat): 2971, 2922, 2860, 2361, 1739, 1695, 1604, 1542, 1508, 1414, 1243, 1018, and 799 cm^{-1}

MP 140-142°C

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
2.00
1.03
1.09
2.12
4.19
4.29
3.37
9.17
8.30
7.26 CDCl3
6.14
6.13
6.13
6.12
6.12
6.11
6.02
6.01
6.00
5.98
5.98
5.97
5.95
5.94
5.33
5.31
5.29
5.29
5.28
3.82
3.81
3.80
3.80
3.49
3.49
3.48
3.47
2.07
1.48


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
170.06
161.53
157.79
154.97
135.19
120.56
117.57
80.17
77.16 CDCl3
72.36
43.80
28.57
21.28

(2h) 1-(2-chloroquinolin-3-yl)allyl acetate



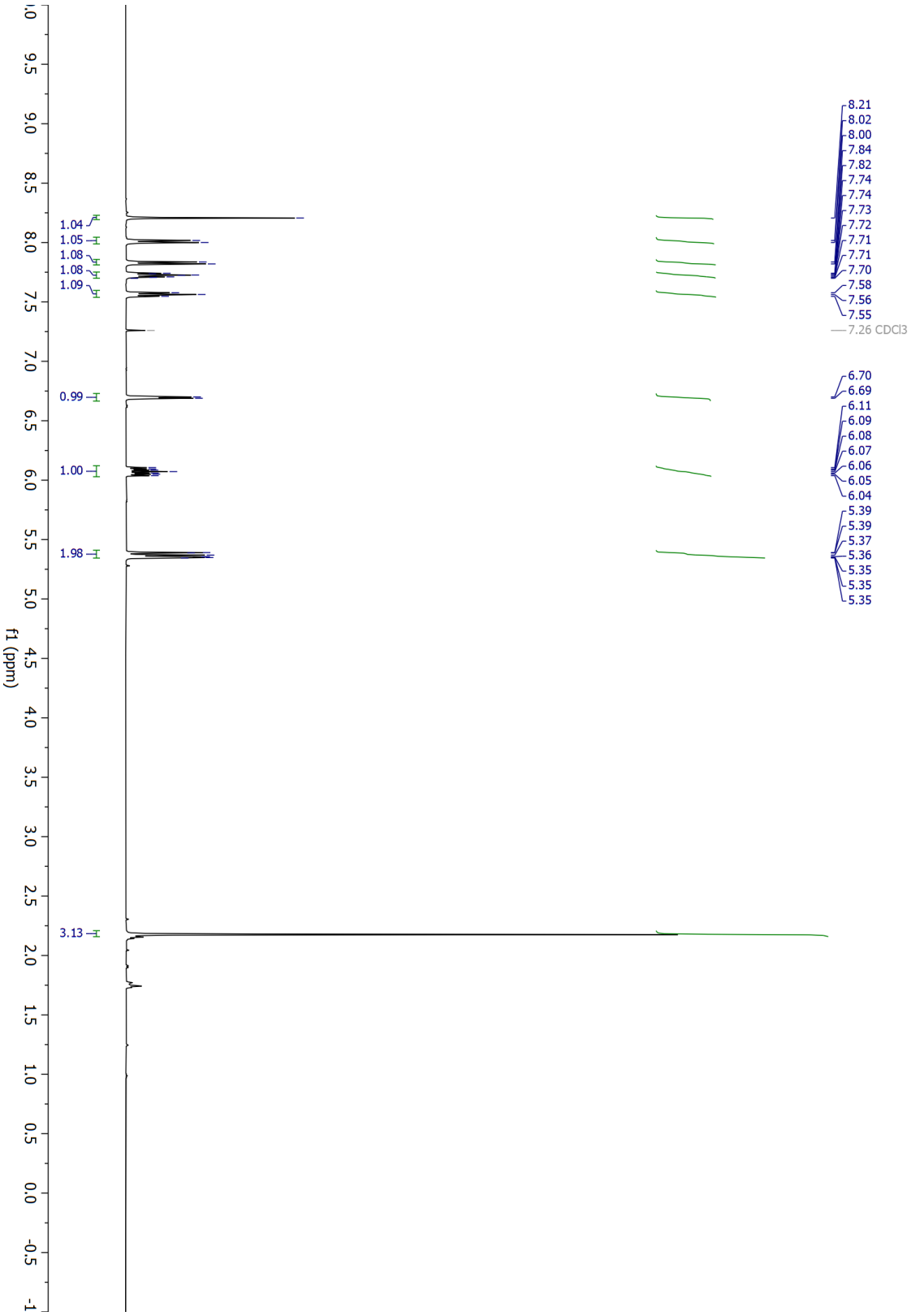
Procedure

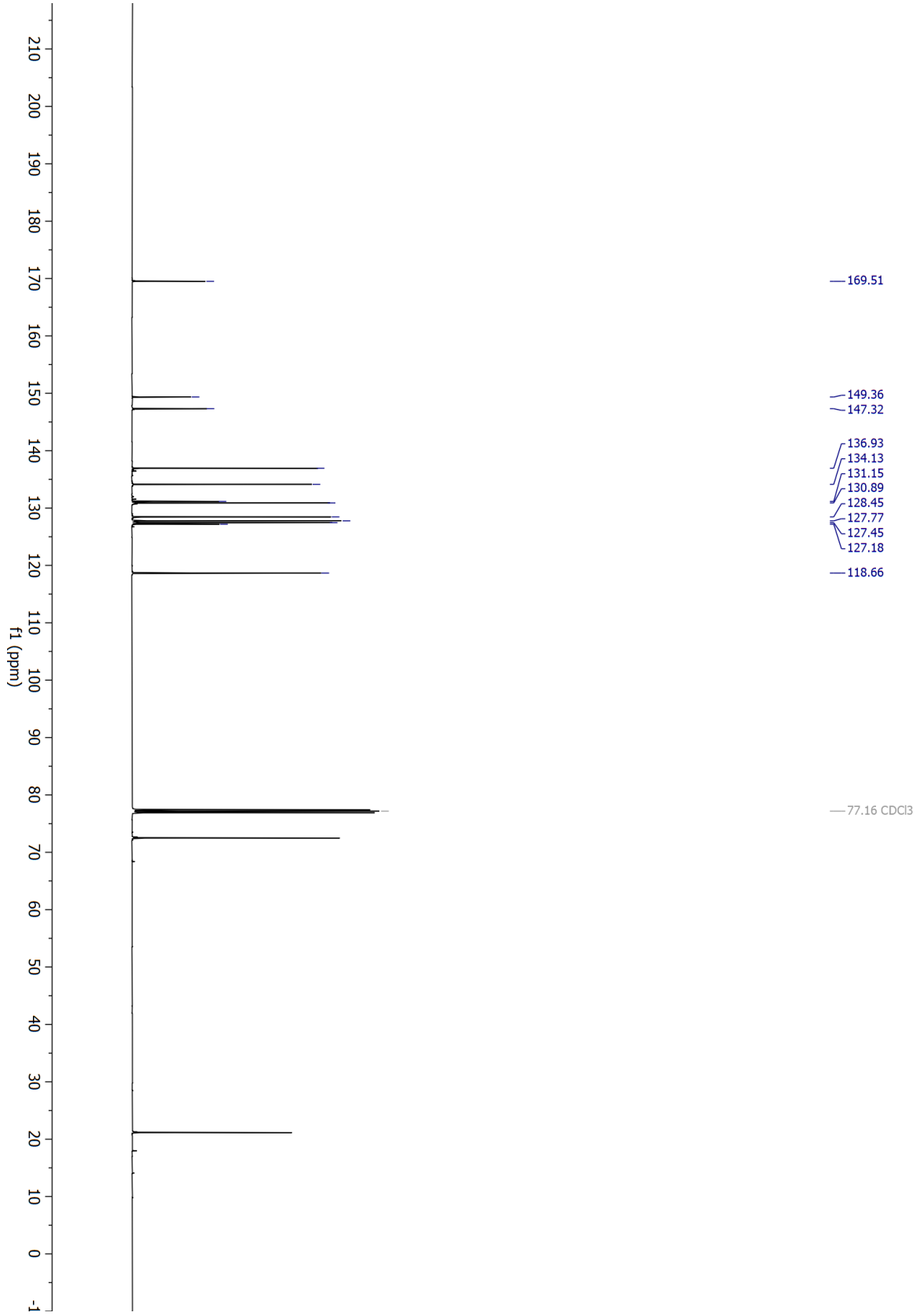
Alcohol **1h** (1.70 g, 7.80 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 93% yield (1.90 g, 7.25 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2): R_f = 0.54 (hexanes: ethyl acetate = 4:1).

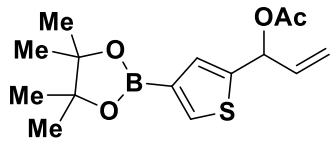
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.73 (dd, *J* = 8.6, 6.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 5.7 Hz, 1H), 6.07 (ddd, *J* = 16.7, 10.4, 5.8 Hz, 1H), 5.45 – 5.30 (m, 2H), 2.18 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 169.5, 149.4, 147.3, 136.9, 134.1, 131.1, 130.9, 128.4, 127.8, 127.4, 127.2, 118.7.
HRMS (ESI): Calculated for $C_{14}H_{12}ClNO_2$ [M+Na^+] = 284.0449, Found 284.0456

FTIR (neat): 3061, 2362, 1740, 1618, 1565, 1490, 1369, 1222, 1099, 1019 cm^{-1}


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.04
1.05
1.08
1.08
1.09
0.99
1.00
1.98
3.13
8.21
8.02
8.00
7.84
7.82
7.74
7.74
7.73
7.72
7.71
7.71
7.70
7.58
7.56
7.55
7.26 CDCl3
6.70
6.69
6.11
6.09
6.08
6.07
6.06
6.05
6.04
5.39
5.39
5.37
5.36
5.35
5.35
5.35


169.51
149.36
147.32
136.93
134.13
131.15
130.89
128.45
127.77
127.45
127.18
118.66
77.16 CDCl3
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1

(2i) 1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)allyl acetate



Procedure

Alcohol **1i** (200 mg, 0.750 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 75% yield (177 g, 0.563 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate: triethylamine = 89:10:1- 79:20:1).

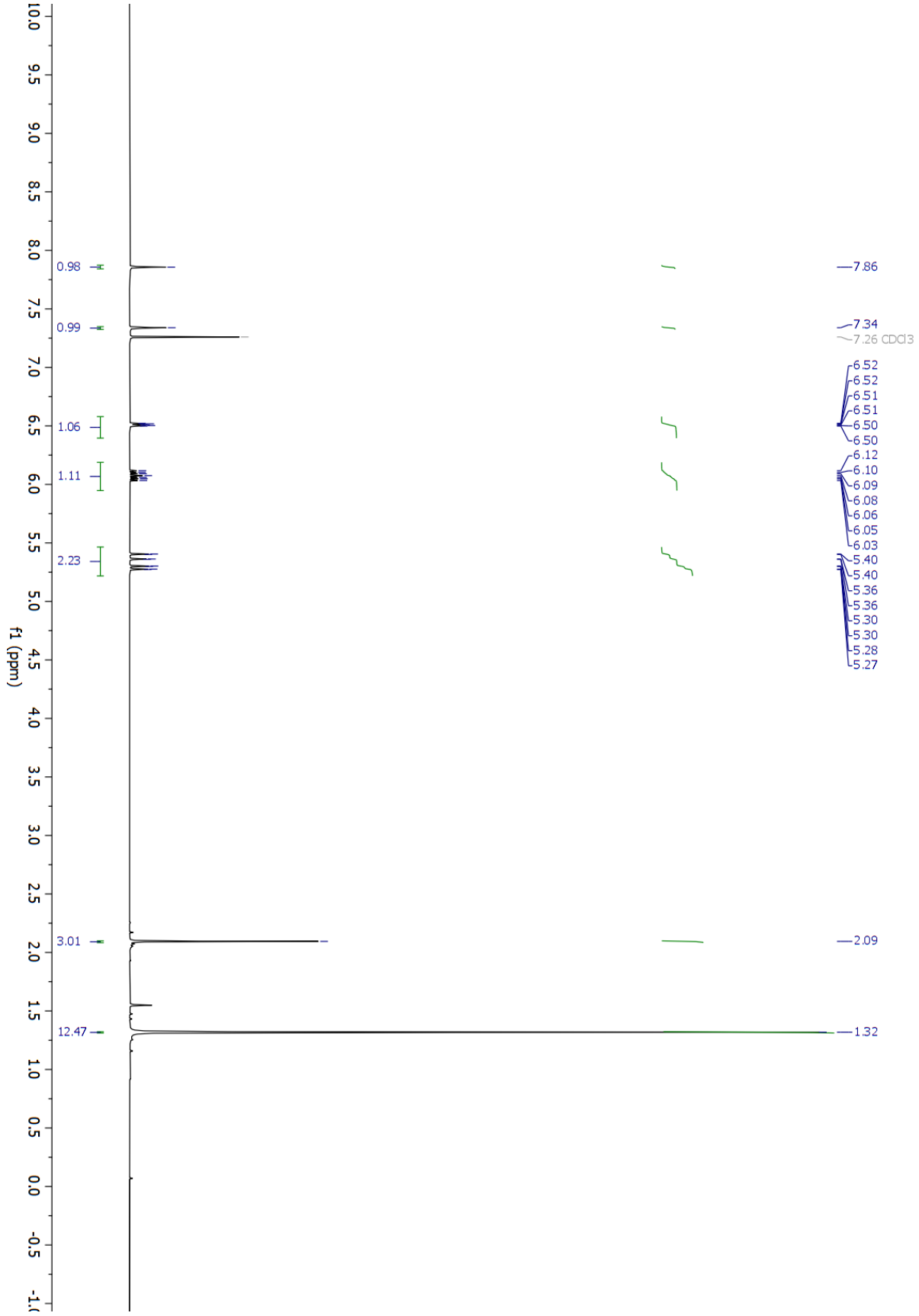
TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 4:1).

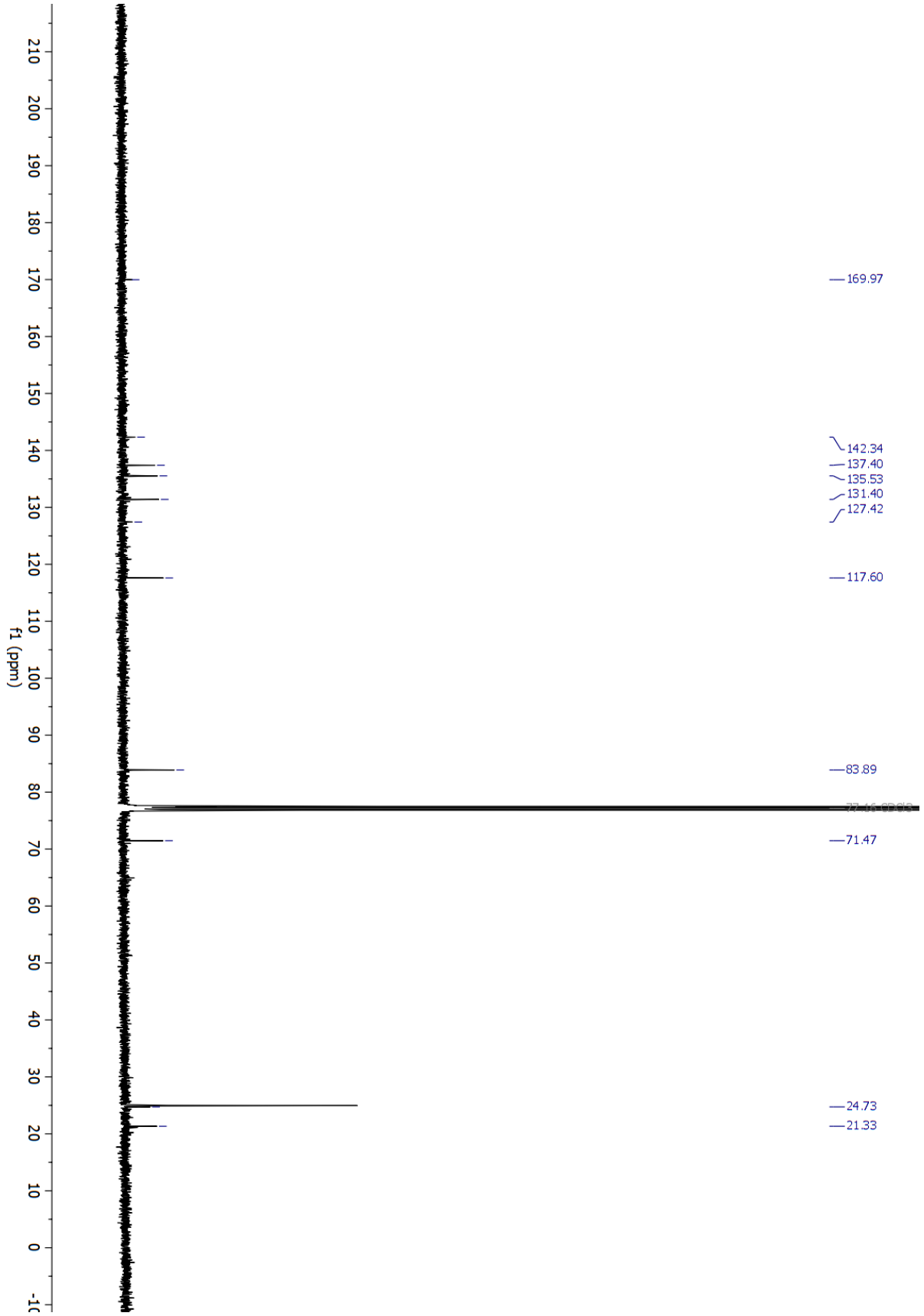
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.34 (s, 1H), 6.51 (dd, J = 6.3, 1.5 Hz, 1H), 6.08 (ddd, J = 16.7, 10.4, 6.0 Hz, 1H), 5.38 (dd, J = 17.1, 1.3 Hz, 1H), 5.29 (dd, J = 10.5, 1.2 Hz, 1H), 2.09 (s, 3H), 1.32 (s, 12H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 142.3, 137.4, 135.5, 131.4, 127.4, 117.6, 83.9, 71.5, 24.7, 21.3.

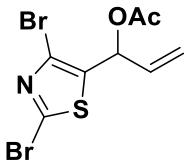
HRMS (ESI): Calculated for $C_{15}H_{21}BO_4S$ [M+Na^+]= 331.1149, found= 331.1156

FTIR (neat): 2973, 2929, 2854, 2362, 2326, 2166,1739, 1538, 1452, 1371, 1309, 1228, 858, 688 cm^{-1}


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0.98
0.99
1.06
1.11
2.23
3.01
12.47
7.86
7.34
7.26 CDCl3
6.52
6.52
6.51
6.51
6.50
6.50
6.12
6.10
6.09
6.08
6.06
6.05
6.03
5.40
5.40
5.36
5.36
5.30
5.30
5.28
5.27
2.09
1.32


169.97
142.34
137.40
135.53
131.40
127.42
117.60
83.89
71.47
24.73
21.33
f1 (ppm)

(2j) 1-(2,4-dibromothiazol-5-yl)allyl acetate



Procedure

Alcohol **1j** (410 mg, 1.37 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 92% yield (429 mg, 1.26 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

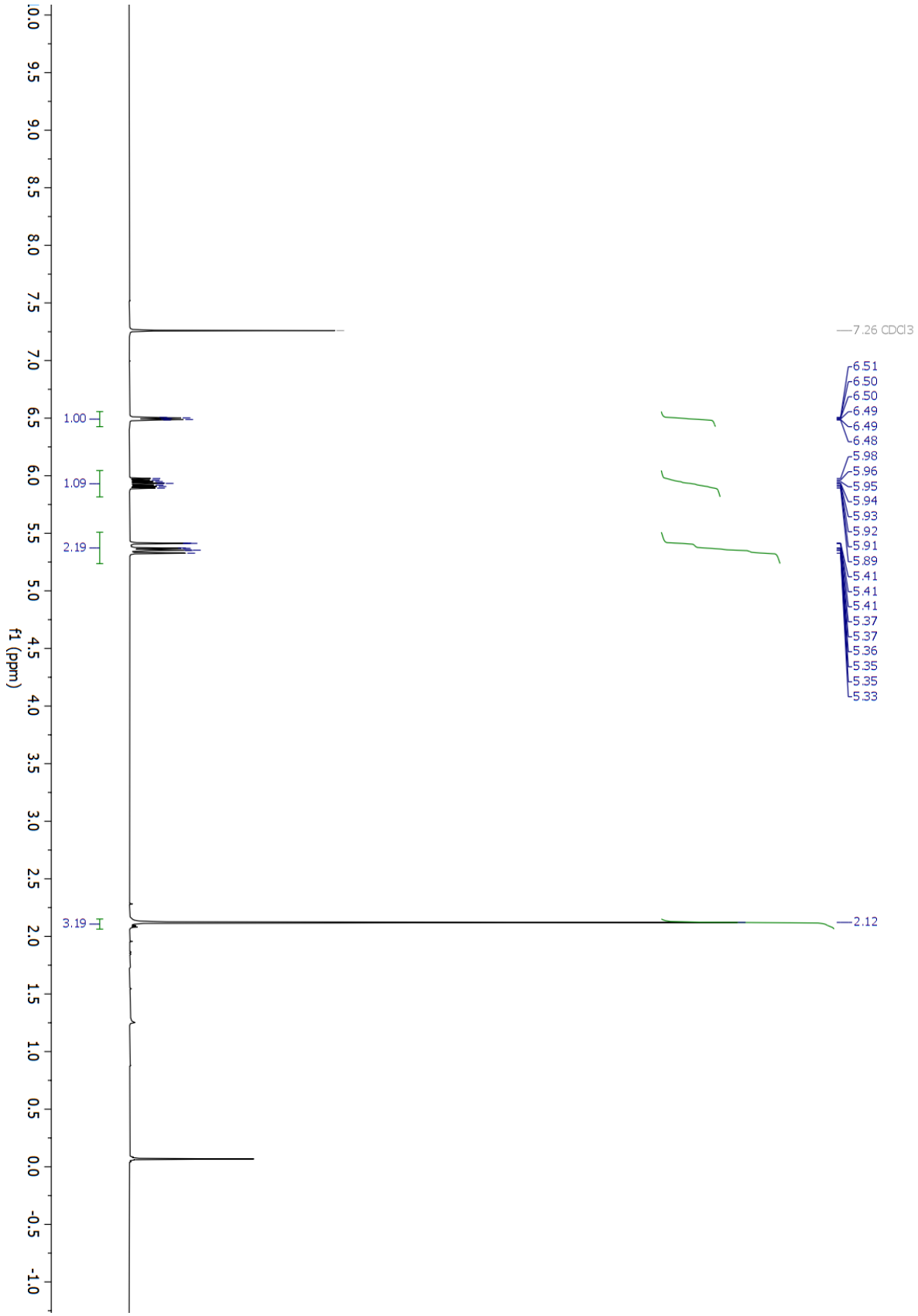
TLC (SiO_2): R_f = 0.55 (hexanes: ethyl acetate = 4:1).

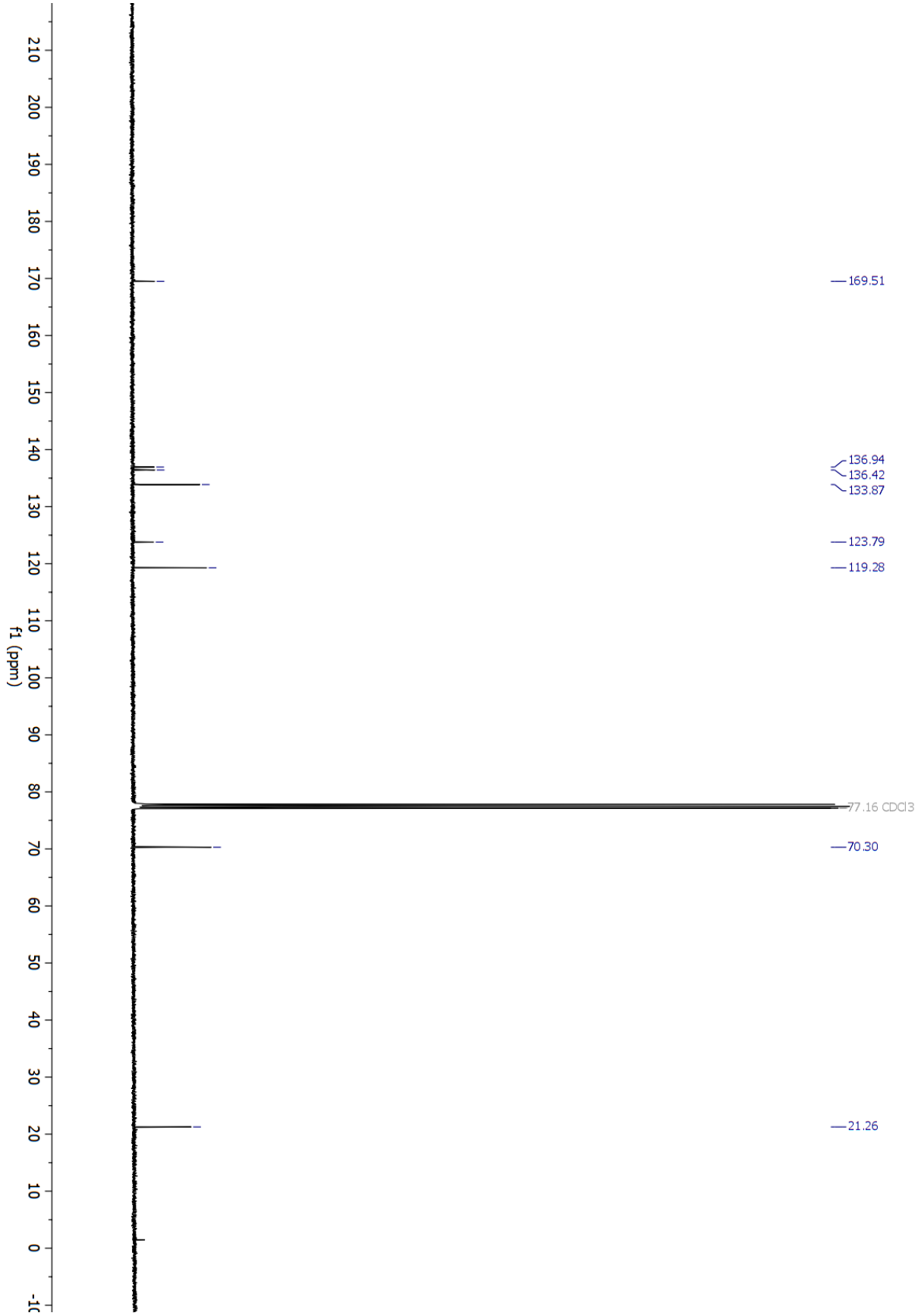
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.50 (dt, J = 5.8, 1.5 Hz, 1H), 5.93 (ddd, J = 17.3, 10.4, 5.7 Hz, 1H), 5.44 – 5.36 (m, 1H), 5.34 (d, J = 10.5 Hz, 1H), 2.12 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.5, 136.9, 136.4, 133.9, 123.8, 119.3, 70.3, 21.3.

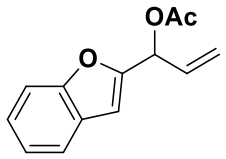
HRMS (ESI): Calculated For $C_8H_7Br_2NO_2S$ $[M+H^+]$= 341.8616, found= 341.8618

FTIR (neat): 1737, 1419, 1229, 1217, 1098, 929, 857, 835 cm^{-1}


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.00
1.09
2.19
3.19
7.26 CDCl3
6.51
6.50
6.50
6.49
6.49
6.48
5.98
5.96
5.95
5.94
5.93
5.92
5.91
5.89
5.41
5.41
5.41
5.37
5.37
5.36
5.35
5.35
5.33
2.12


169.51
136.94
136.42
133.87
123.79
119.28
77.16 CDCl3
70.30
21.26
f1 (ppm)

(2k) 1-(benzofuran-2-yl)allyl acetate



Procedure

Alcohol **1k** (360 mg, 2.06 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 81% yield (360 mg, 1.66 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

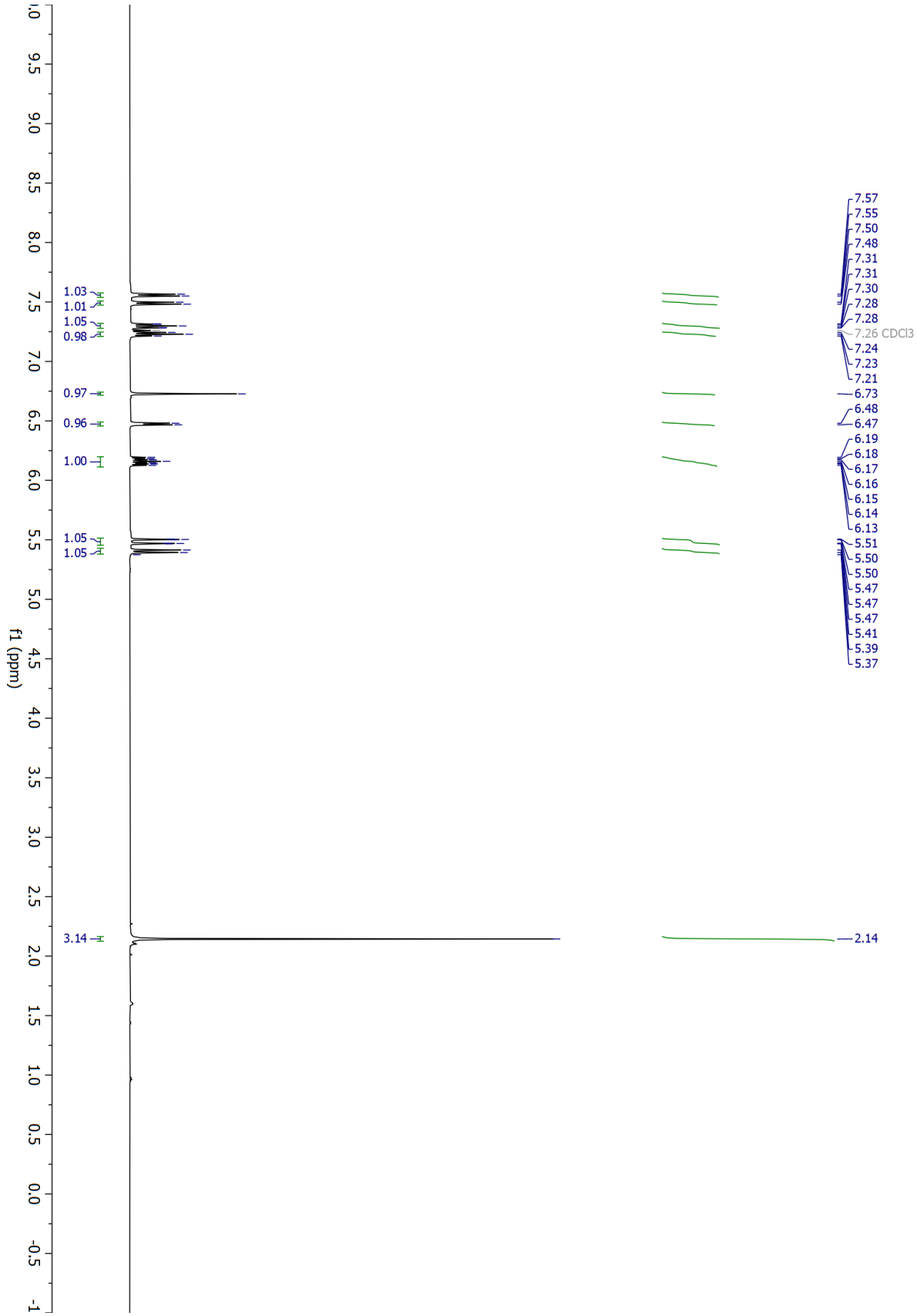
TLC (SiO_2): R_f = 0.61 (hexanes: ethyl acetate = 4:1).

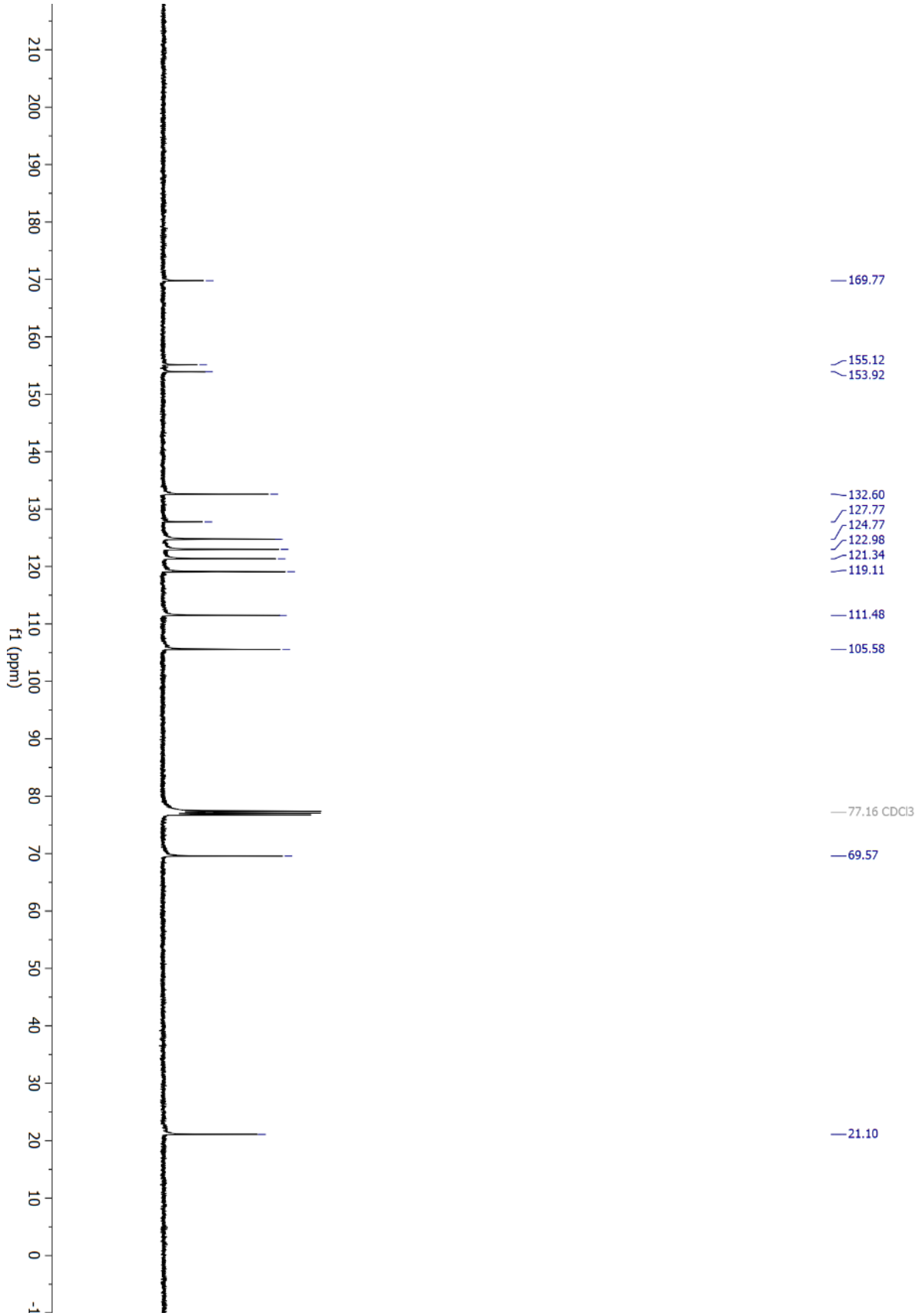
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.73 (s, 1H), 6.47 (d, *J* = 6.3 Hz, 1H), 6.16 (ddd, *J* = 16.9, 10.4, 6.3 Hz, 1H), 5.49 (dt, *J* = 17.2, 1.1 Hz, 1H), 5.40 (d, *J* = 10.4 Hz, 1H), 2.14 (s, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.8, 155.1, 153.9, 132.6, 127.8, 124.8, 123.0, 121.3, 119.1, 111.5, 105.6, 69.6, 21.1.

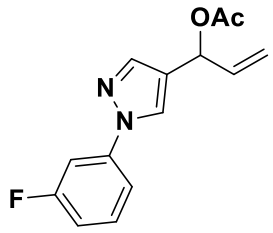
HRMS (ESI): Calculated for $C_{13}H_{12}O_3$ [M+Na^+] = 239.0679, Found 239.0683

FTIR (neat): 3011, 2954, 1741, 1453, 1370, 1223, 1017, 980, 751cm^{-1}


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.03
1.01
1.05
0.98
0.97
0.96
1.00
1.05
1.05
3.14
2.14
7.57
7.55
7.50
7.48
7.31
7.31
7.30
7.28
7.28
7.26 CDCl3
7.24
7.23
7.21
6.73
6.48
6.47
6.19
6.18
6.17
6.16
6.15
6.14
6.13
5.51
5.50
5.50
5.47
5.47
5.47
5.41
5.39
5.37


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
169.77
155.12
153.92
132.60
127.77
124.77
122.98
121.34
119.11
111.48
105.58
77.16 CDCl3
69.57
21.10

(2l) 1-(1-(3-fluorophenyl)-1*H*-pyrazol-4-yl)allyl acetate



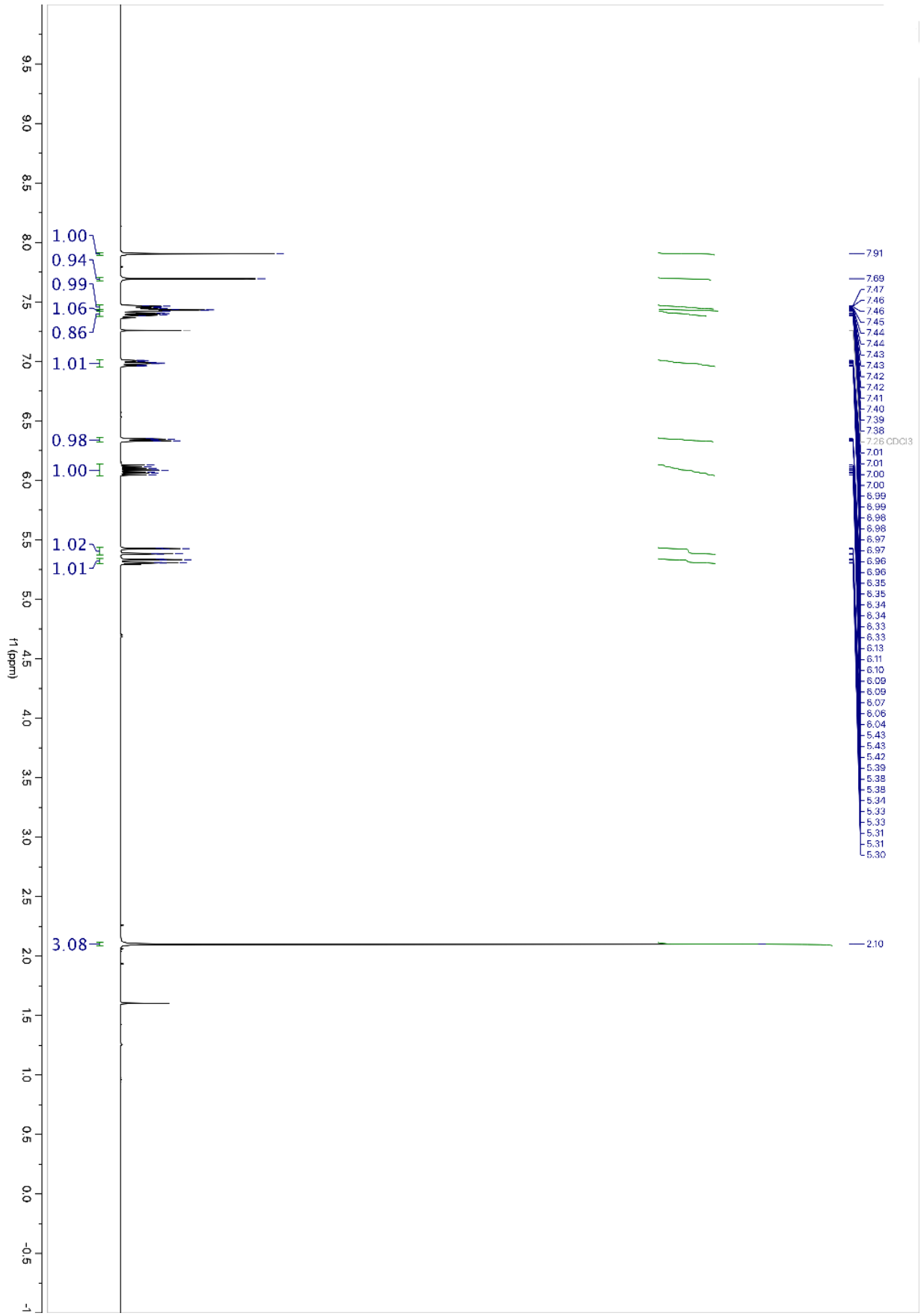
Procedure

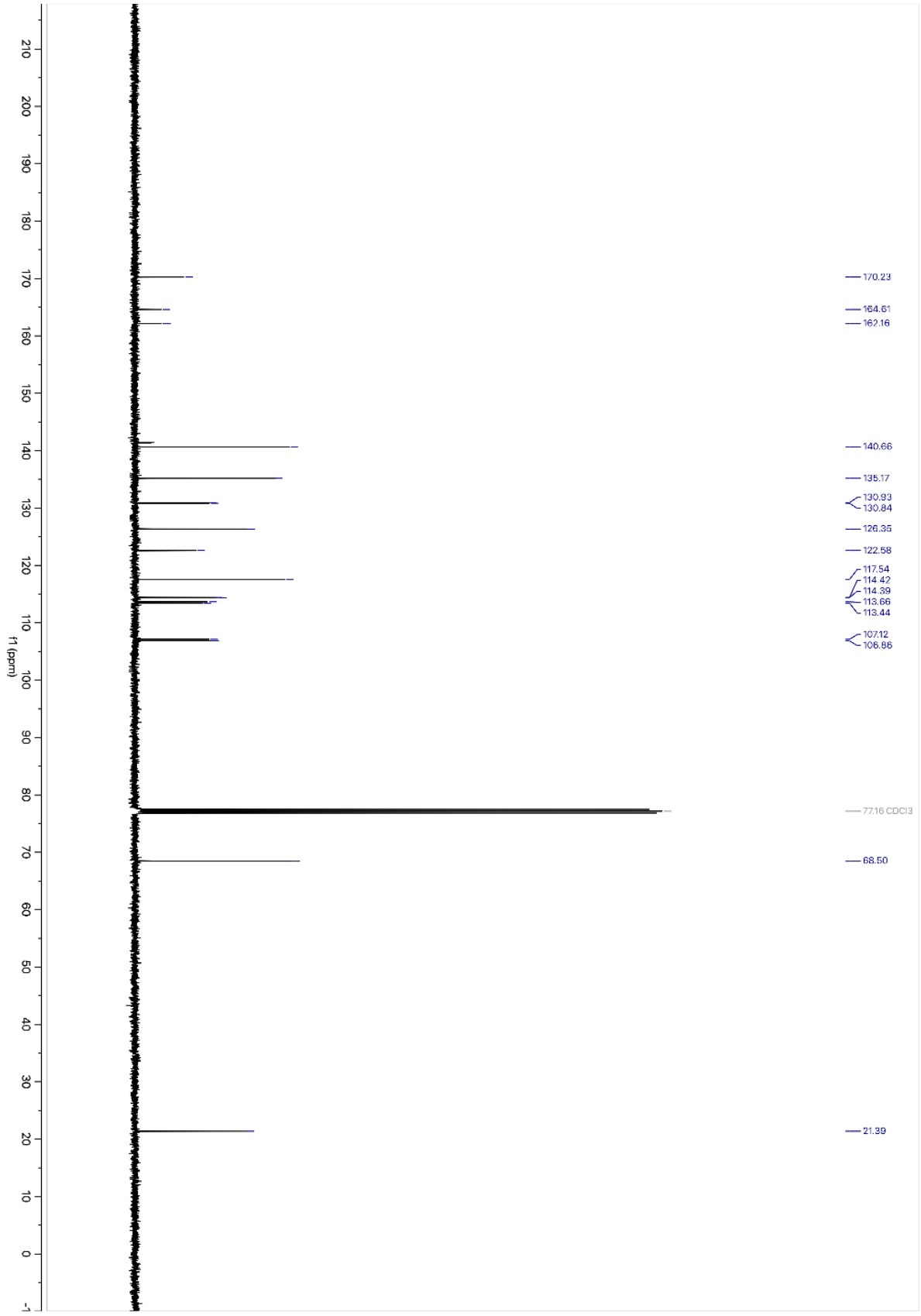
Alcohol **1l** (1.50 g, 6.87 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 82% yield (1.47 g, 5.63 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1–20:1).

TLC (SiO_2): R_f = 0.24 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.69 (s, 1H), 7.45 (dt, *J* = 7.8, 2.2 Hz, 1H), 7.44 – 7.42 (m, 1H), 7.42 – 7.38 (m, 1H), 6.98 (tdd, *J* = 8.1, 2.5, 1.4 Hz, 1H), 6.34 (dt, *J* = 5.9, 1.5 Hz, 1H), 6.09 (ddd, *J* = 17.3, 10.5, 5.9 Hz, 1H), 5.40 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.32 (dt, *J* = 10.3, 1.3 Hz, 1H), 2.10 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 163.2 (d, J = 246.8 Hz), 141.3 (d, J = 10.1 Hz), 140.5, 135.0, 130.8 (d, J = 9.2 Hz), 126.2, 122.4, 117.4, 114.3 (d, J = 3.2 Hz), 113.4 (d, J = 21.3 Hz), 106.9 (d, J = 26.4 Hz), 68.4, 21.3.
^{19}F NMR (376 MHz, $CDCl_3$): δ -110.79.
HRMS (ESI): Calculated for $C_{14}H_{13}FN_2O_2$ [M+H$^+$] = 261.1034, Found 261.1043.

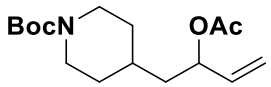
FTIR (neat): 3092, 1732, 1613, 1602, 1568, 1499, 1478, 1460, 1398, 1369, 1229, 1182, 1151, 1095, 1016, 968, 935, 864, 776 cm^{-1}.


f1 (ppm)
1.00
0.94
0.99
1.06
0.86
1.01
0.98
1.00
1.02
1.01
3.08
7.91
7.69
7.47
7.46
7.46
7.45
7.44
7.44
7.43
7.43
7.42
7.42
7.41
7.40
7.39
7.38
7.26 CDCl3
7.01
7.01
7.00
7.00
6.99
6.99
6.98
6.98
6.97
6.97
6.96
6.96
6.35
6.35
6.34
6.34
6.33
6.33
6.13
6.11
6.10
6.09
6.09
6.07
6.06
6.04
5.43
5.43
5.42
5.39
5.38
5.38
5.34
5.33
5.33
5.31
5.31
5.30
2.10


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
170.23
164.61
162.16
140.66
135.17
130.93
130.84
126.35
122.58
117.54
114.42
114.39
113.66
113.44
107.12
106.86
77.16 CDCl3
68.50
21.39

-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)
-110.79

(2o) tert-butyl 4-(2-acetoxybut-3-en-1-yl)piperidine-1-carboxylate



Procedure

Alcohol **1o** (750 mg, 2.94 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 69% yield (600 mg, 2.02 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–2:1).

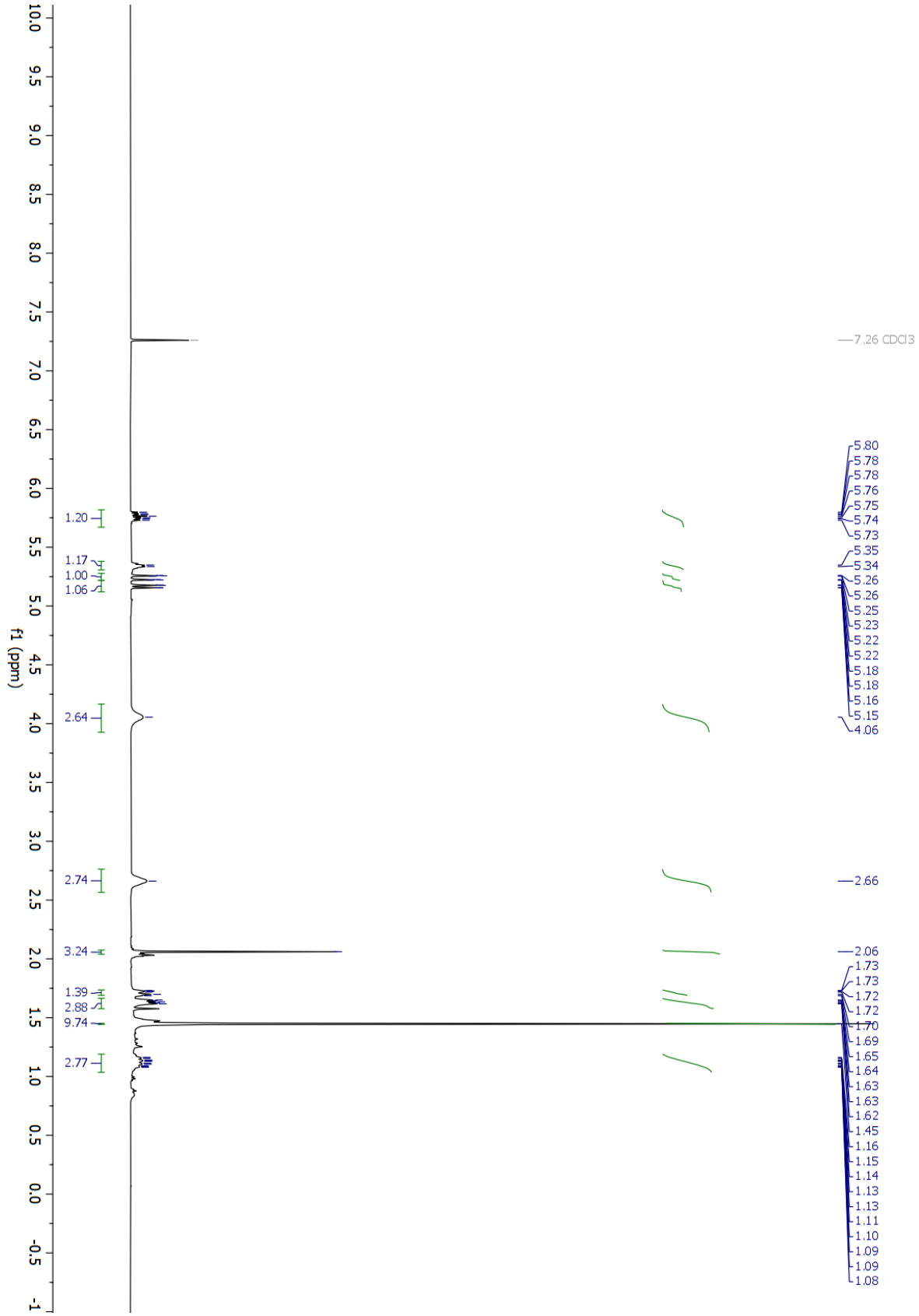
TLC (SiO_2): R_f = 0.64 (hexanes: ethyl acetate = 1:1).

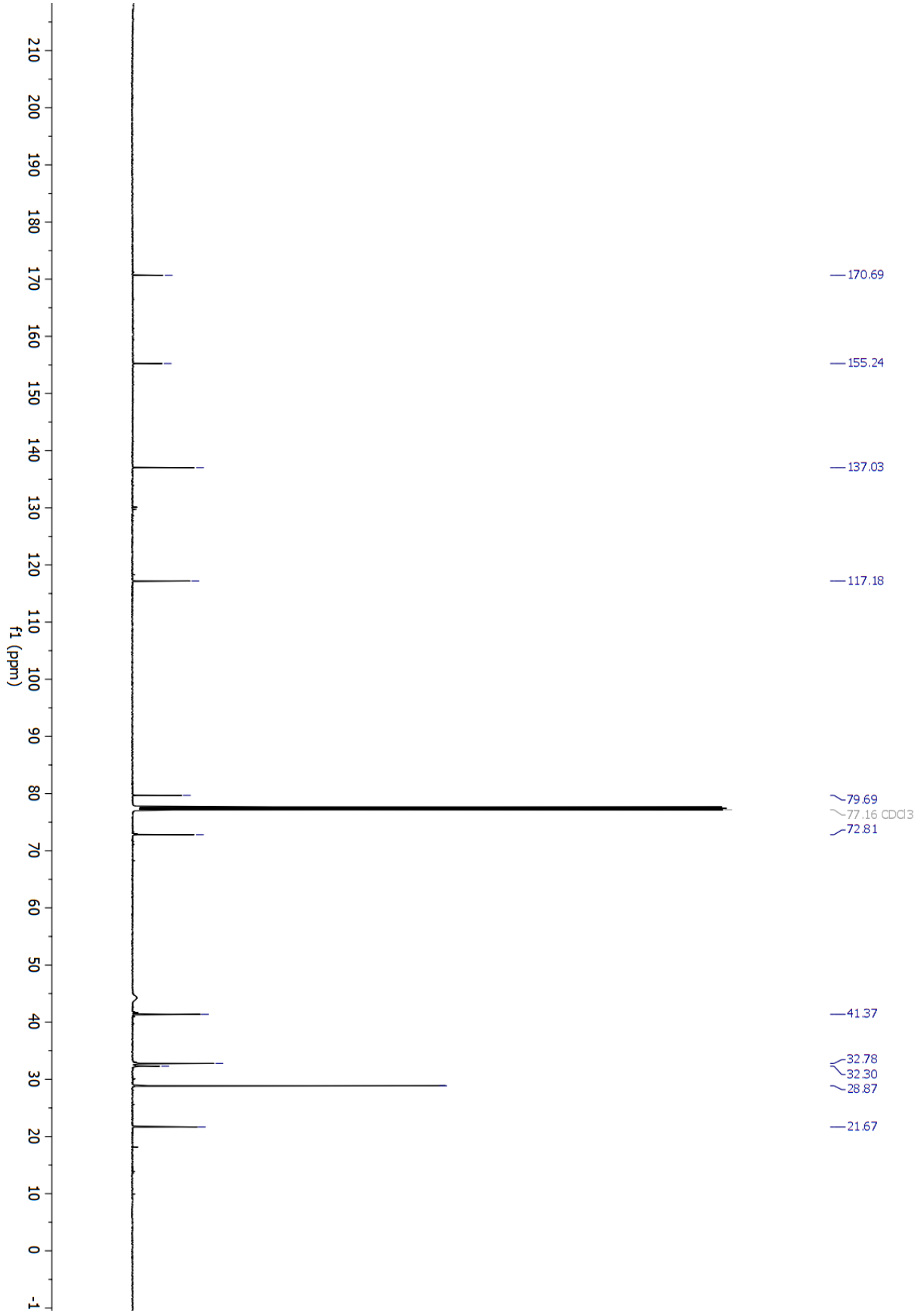
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.76 (ddd, J = 17.1, 10.5, 6.4 Hz, 1H), 5.34 (d, J = 6.4 Hz, 1H), 5.24 (dt, J = 17.2, 1.2 Hz, 1H), 5.20 – 5.14 (m, 1H), 4.06 (s, 2H), 2.66 (d, J = 10.3 Hz, 2H), 2.06 (s, 2H), 1.76 – 1.68 (m, 1H), 1.67 – 1.60 (m, 3H), 1.45 (s, 9H), 1.21 – 1.02 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 170.7, 155.2, 137.0, 117.2, 79.7, 72.8, 41.4, 32.8, 32.3, 28.9, 21.7.

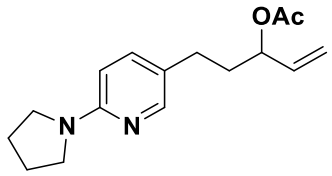
HRMS (ESI): Calculated for $C_{16}H_{27}NO_4$ $[M+Na^+]$= 320.1832, found= 320.1838

FTIR (neat): 3015, 2970, 1738, 1424, 1365, 1229, 1216, 899 cm^{-1}


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.20
1.17
1.00
1.06
2.64
2.74
3.24
1.39
2.88
9.74
2.77
7.26 CDCl3
5.80
5.78
5.78
5.76
5.75
5.74
5.73
5.35
5.34
5.26
5.26
5.25
5.23
5.22
5.22
5.18
5.18
5.16
5.15
4.06
2.66
2.06
1.73
1.73
1.72
1.72
1.70
1.69
1.65
1.64
1.63
1.63
1.62
1.45
1.16
1.15
1.14
1.13
1.13
1.11
1.10
1.09
1.09
1.08


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
170.69
155.24
137.03
117.18
79.69
77.16 CDCl3
72.81
41.37
32.78
32.30
28.87
21.67

(2q) 5-(6-(pyrrolidin-1-yl)pyridin-3-yl)pent-1-en-3-yl acetate



Procedure

Alcohol **1q** (791 mg, 2.58 mmol, 100 mol%) was subjected to a modified version of general procedure B. The reaction was stirred at ambient temperature for 2 hours. The reaction solution was then diluted with dichloromethane and was washed with aqueous saturated sodium bicarbonate, followed by distilled water, and brine. The organic layer was then separated and dried over anhydrous potassium carbonate. The title compound was obtained in 40% yield (359 mg, 1.03 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexane: ethyl acetate: triethylamine = 400:100:1).

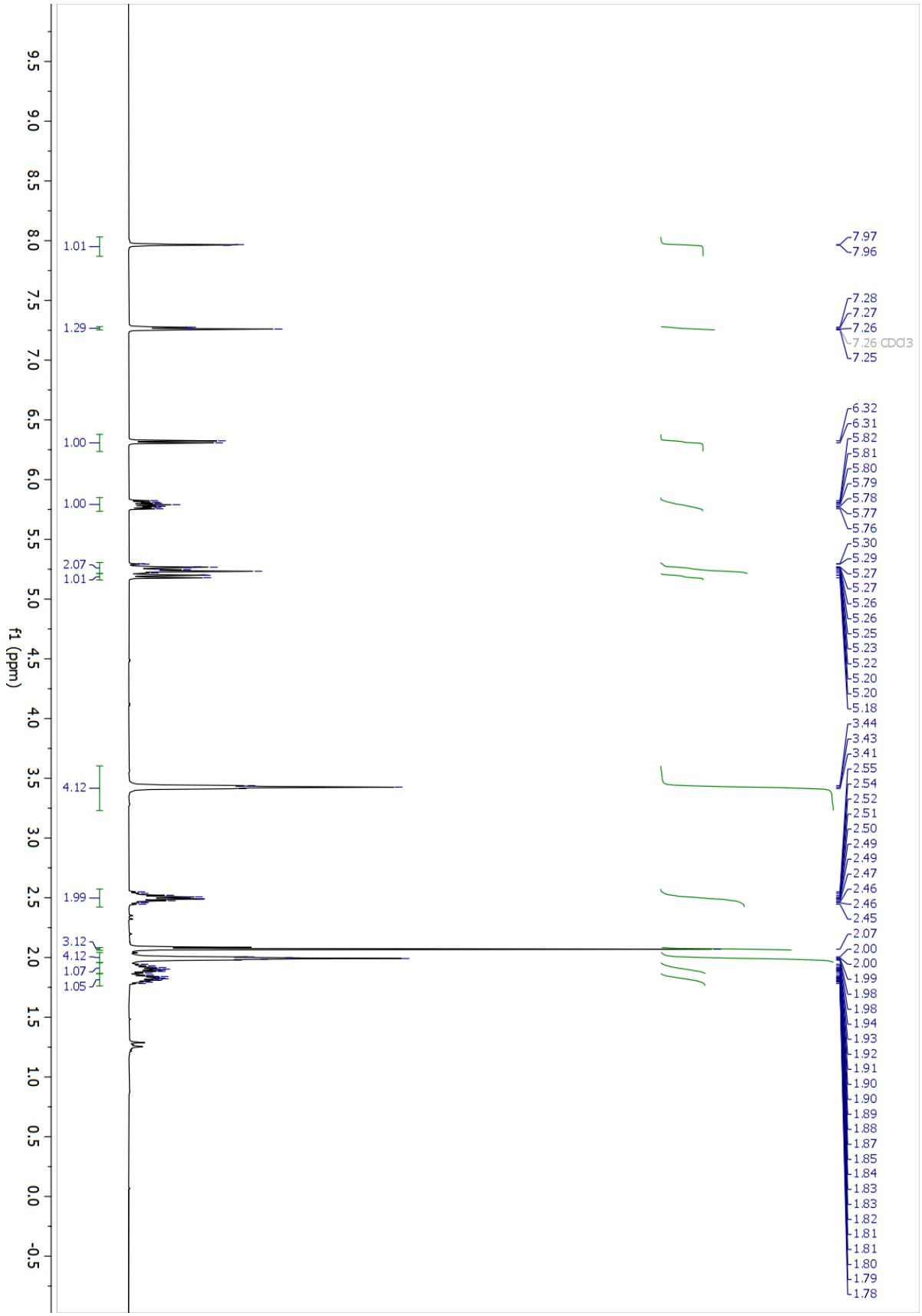
TLC (SiO_2): R_f = 0.45 (hexanes: ethyl acetate = 1:1).

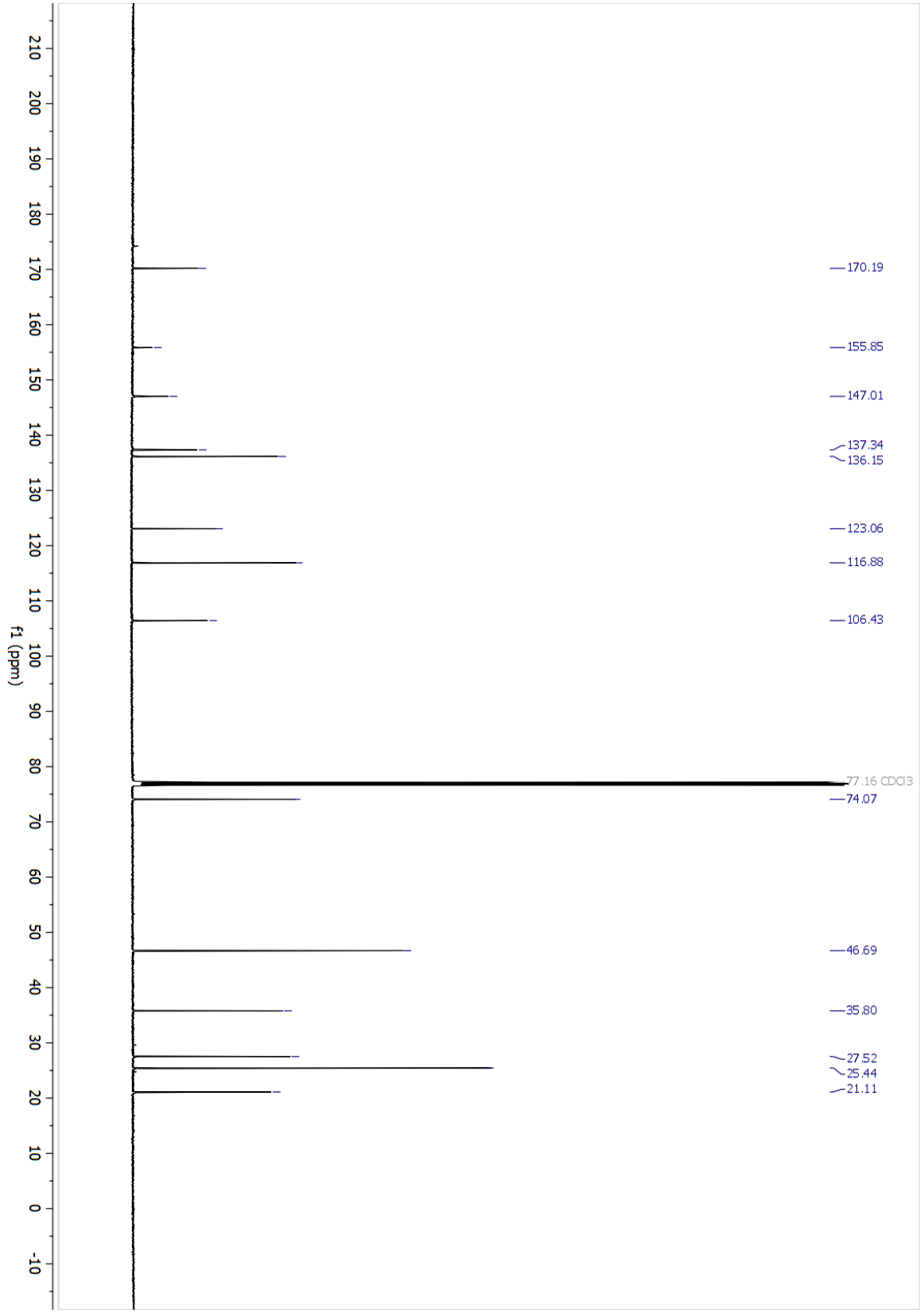
^{1}H NMR (500 MHz, $CDCl_3$): δ: 7.96 (d, *J* = 2.4 Hz, 1H), 7.29 – 7.24 (m, 1H), 6.32 (d, *J* = 8.6 Hz, 1H), 5.79 (ddd, *J* = 17.1, 10.5, 6.4 Hz, 1H), 5.31 – 5.21 (m, 2H), 5.21 – 5.16 (m, 1H), 3.46 – 3.38 (m, 4H), 2.57 – 2.43 (m, 2H), 2.07 (s, 3H), 2.02 – 1.96 (m, 4H), 1.91 (ddt, *J* = 13.5, 9.1, 6.8 Hz, 1H), 1.82 (ddt, *J* = 13.3, 9.1, 6.2 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 170.2, 155.9, 147.0, 137.3, 136.1, 123.1, 116.9, 106.4, 74.1, 46.7, 35.8, 27.5, 25.4, 21.1.

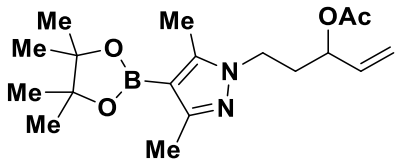
HRMS (ESI): Calculated for $C_{16}H_{22}N_2O_2$ $[M+H^+]$ =275.1754, Found 275.1759

FTIR (neat): 2946, 2854, 1734, 1608, 1484, 1414, 1232, 1017, 805 cm^{-1}


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.01
1.29
1.00
1.00
2.07
1.01
4.12
1.99
3.12
4.12
1.07
1.05
7.97
7.96
7.28
7.27
7.26
7.26 CDCl3
7.25
6.32
6.31
5.82
5.81
5.80
5.79
5.78
5.77
5.76
5.30
5.29
5.27
5.27
5.26
5.26
5.25
5.23
5.22
5.20
5.20
5.18
3.44
3.43
3.41
2.55
2.54
2.52
2.51
2.50
2.49
2.49
2.47
2.46
2.46
2.45
2.07
2.00
2.00
1.99
1.98
1.98
1.94
1.93
1.92
1.91
1.90
1.90
1.89
1.88
1.87
1.85
1.84
1.83
1.83
1.82
1.81
1.81
1.80
1.79
1.78


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.19
155.85
147.01
137.34
136.15
123.06
116.88
106.43
77.16 CDCl3
74.07
46.69
35.80
27.52
25.44
21.11

(2r) 5-(3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)pent-1-en-3-yl acetate



Procedure

Alcohol **1r** (791 mg, 2.58 mmol, 100 mol%) was subjected to general procedure C. The title compound was obtained in 60% yield (539 mg, 1.55 mmol) as a colorless oil after isolation by flash column chromatography (SiO_2, hexane: ethyl acetate = 4:1).

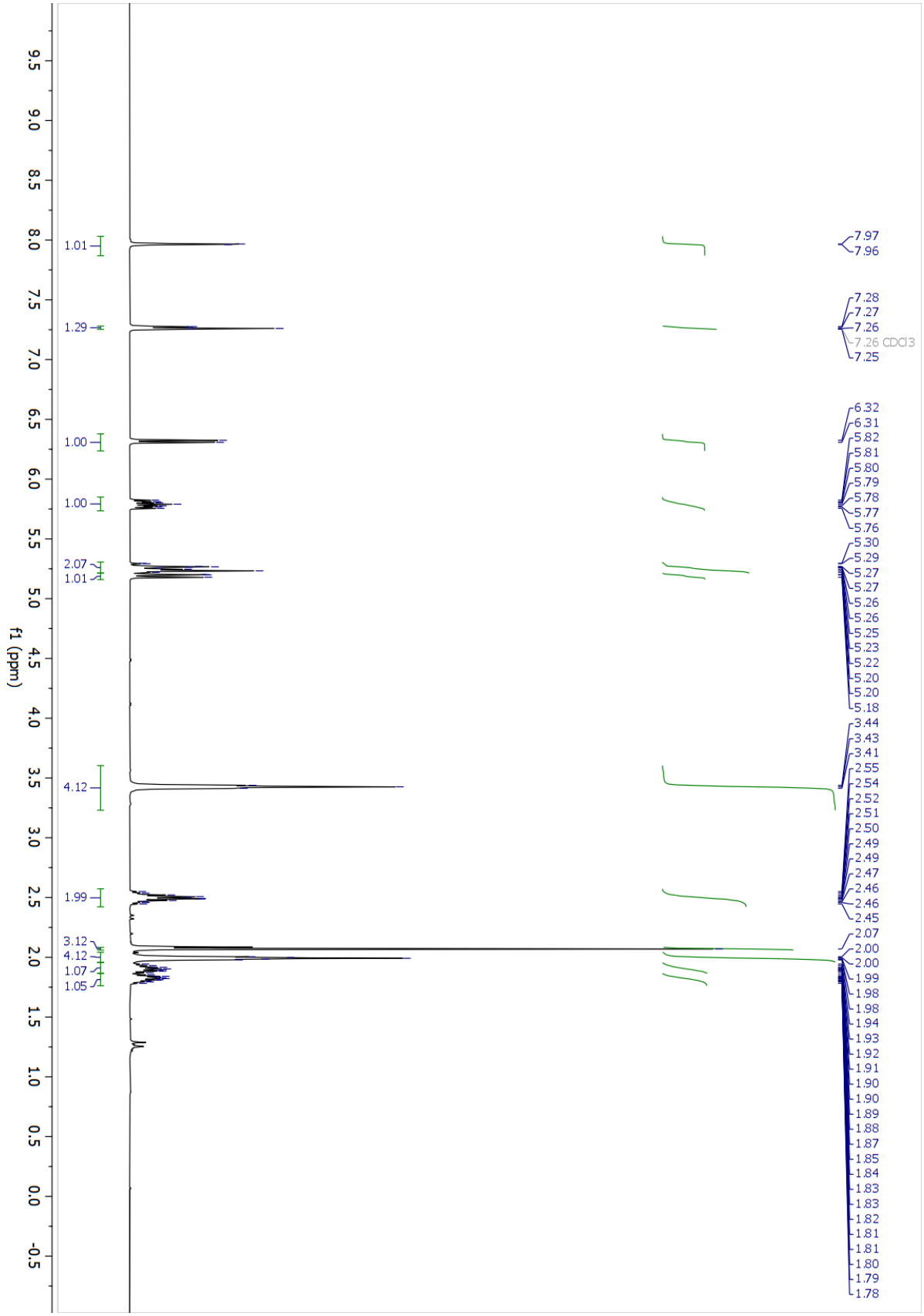
TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 4:1).

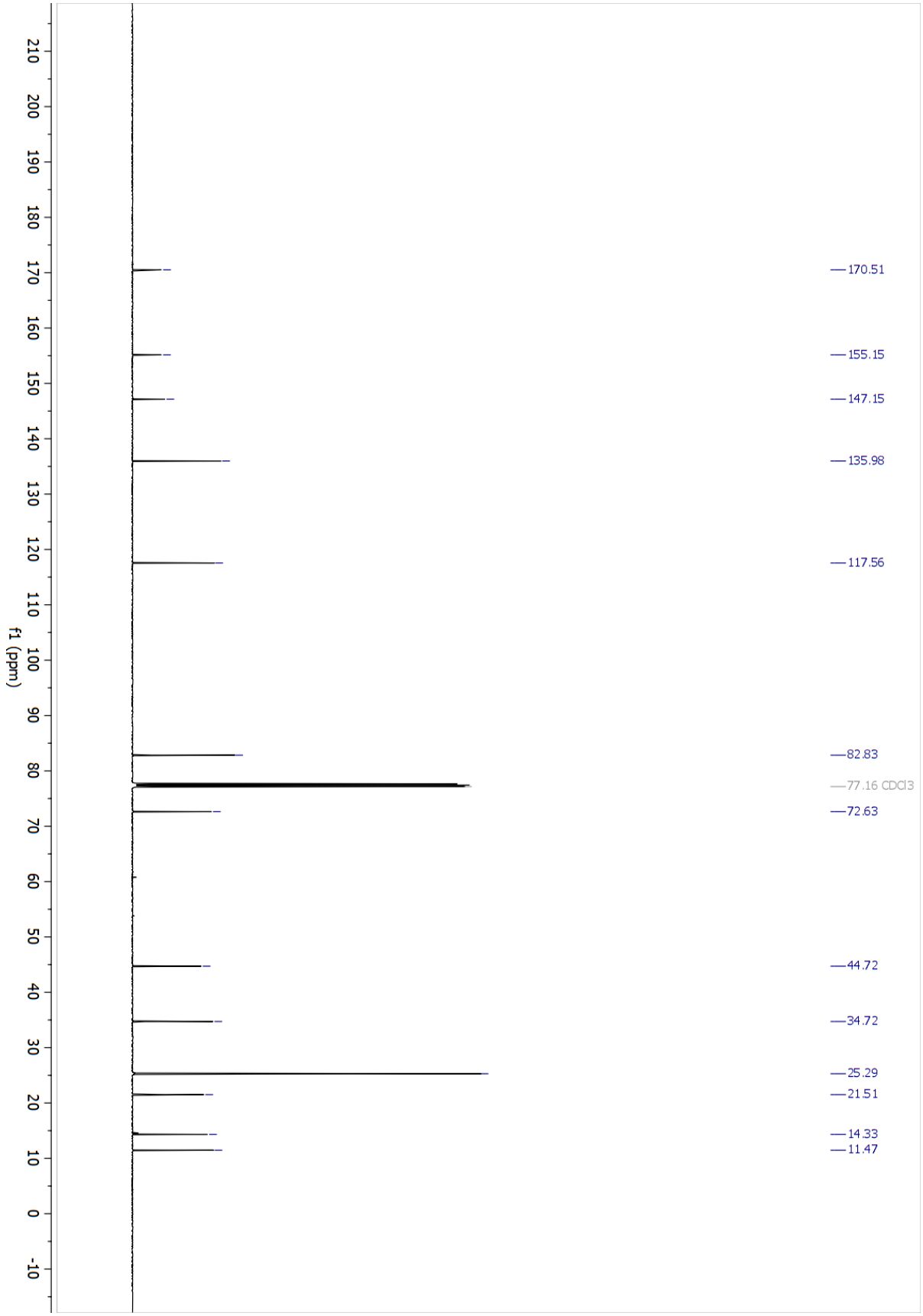
^{1}H NMR (500 MHz, $CDCl_3$): δ: 5.83 – 5.71 (m, 1H), 5.30 – 5.22 (m, 2H), 5.19 (dt, *J* = 10.6, 1.6 Hz, 1H), 3.99 (td, *J* = 7.6, 2.1 Hz, 2H), 2.35 (s, 3H), 2.32 (s, 3H), 2.17 – 2.09 (m, 2H), 2.06 (s, 3H), 1.28 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 170.5, 155.1, 147.1, 136.0, 117.6, 82.8, 72.6, 44.7, 34.7, 25.3, 21.5, 14.3, 11.5.

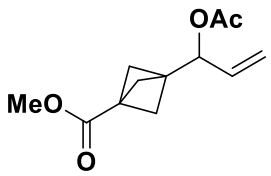
HRMS (ESI): Calculated for $C_{18}H_{29}BN_2O_4$ [M+H$^+$] =348.2329, Found 348.2337

FTIR (neat): 2977, 1738, 1546, 1232, 1078, 862, 727 cm^{-1}


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.01
1.29
1.00
1.00
2.07
1.01
4.12
1.99
3.12
4.12
1.07
1.05
7.97
7.96
7.28
7.27
7.26
7.26 CDCl3
7.25
6.32
6.31
5.82
5.81
5.80
5.79
5.78
5.77
5.76
5.30
5.29
5.27
5.27
5.26
5.26
5.25
5.23
5.22
5.20
5.20
5.18
3.44
3.43
3.41
2.55
2.54
2.52
2.51
2.50
2.49
2.49
2.47
2.46
2.46
2.45
2.07
2.00
2.00
1.99
1.98
1.98
1.94
1.93
1.92
1.91
1.90
1.90
1.89
1.88
1.87
1.85
1.84
1.83
1.83
1.82
1.81
1.81
1.80
1.79
1.78


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.51
155.15
147.15
135.98
117.56
82.83
77.16 CDCl3
72.63
44.72
34.72
25.29
21.51
14.33
11.47

(2t) methyl 3-(1-acetoxyallyl)bicyclo[1.1.1]pentane-1-carboxylate



Procedure

Alcohol **1t** (250 mg, 1.37 mmol, 100 mol%) was subjected to general procedure B. The title compound was obtained in 82% yield (237 mg, 1.12 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–2:1).

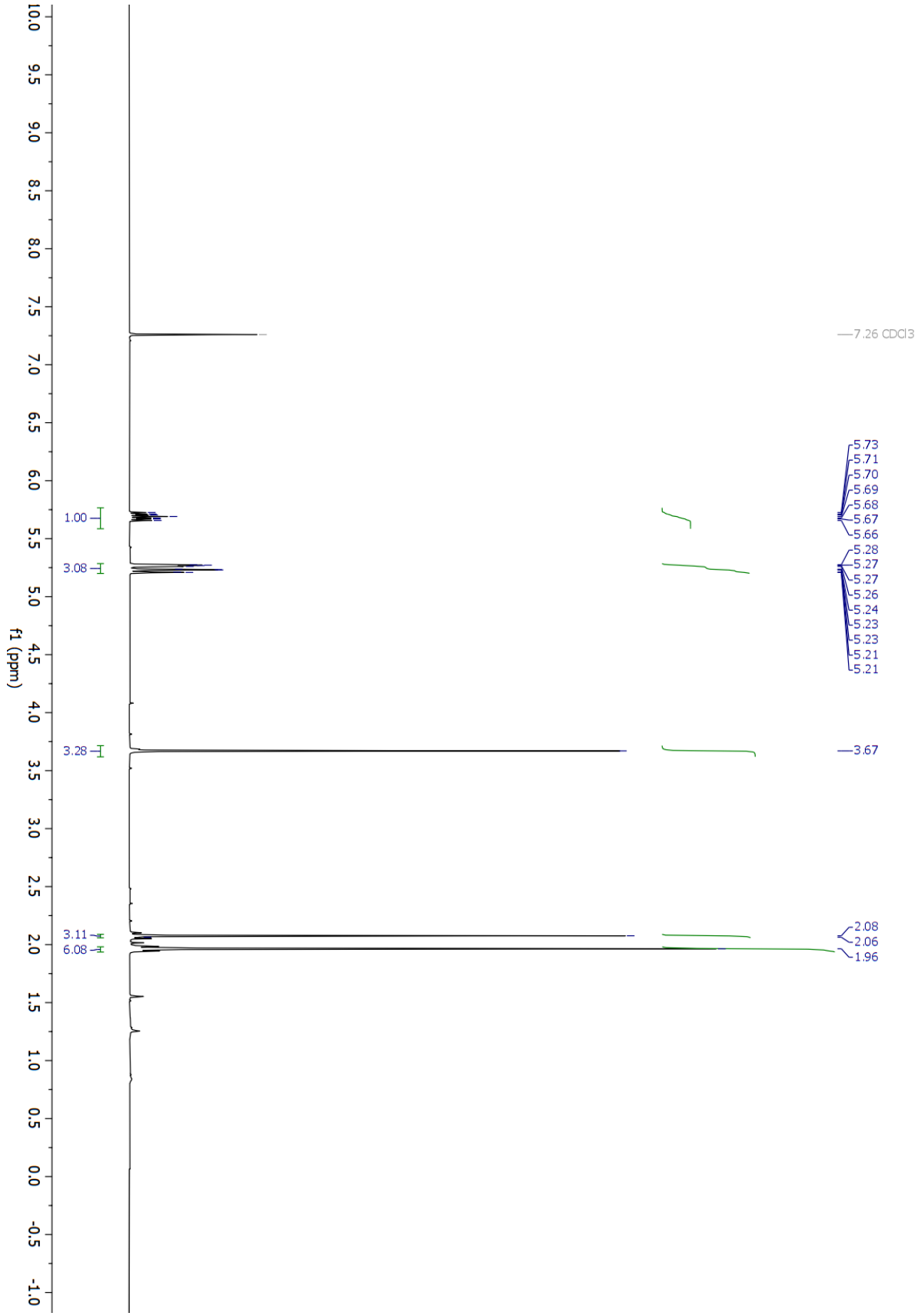
TLC (SiO_2): R_f = 0.54 (hexanes: ethyl acetate = 1:1).

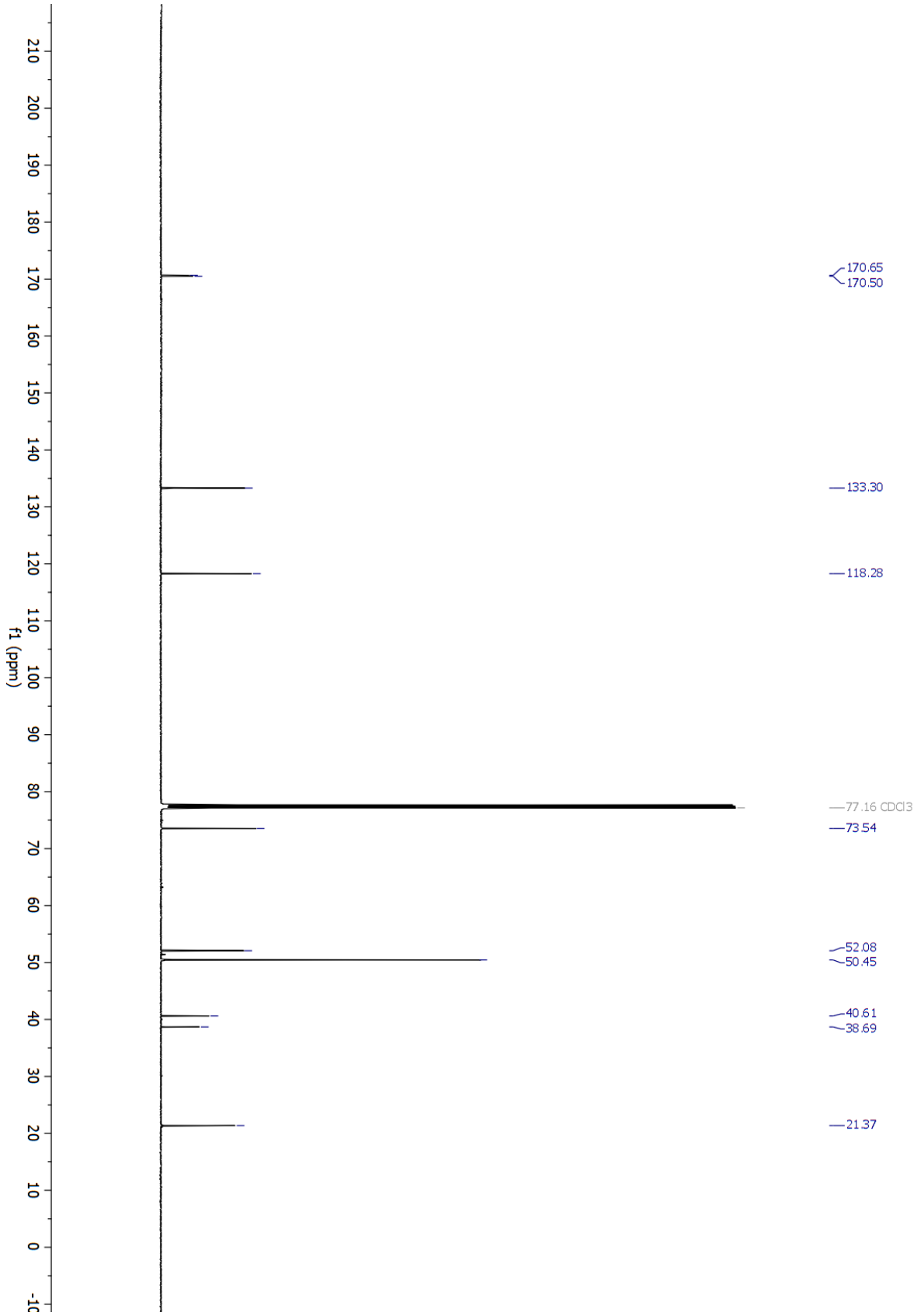
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.69 (ddd, J = 17.3, 10.5, 6.7 Hz, 1H), 5.27 (dd, J = 4.4, 2.6 Hz, 2H), 5.22 (dd, J = 10.9, 1.3 Hz, 1H), 3.67 (s, 3H), 2.08 (s, 3H), 1.96 (s, 6H).

^{13}C NMR 13C NMR (126 MHz, $CDCl_3$): δ 170.7, 170.5, 133.3, 118.3, 73.5, 52.1, 50.4, 40.6, 38.7, 21.4.

HRMS (ESI): Calculated for $C_{12}H_{16}O_4$ $[M+Na^+]$= 247.0941, found= 247.0946

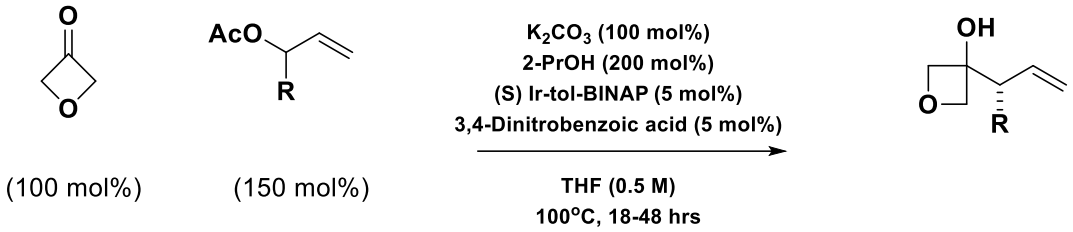
FTIR (neat): 2988, 2920, 2882, 1735, 1426, 1370, 1335, 1232, 1202, 1181, 1067, 1021, 790 cm^{-1}


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
7.26 CDCl3
5.73
5.71
5.70
5.69
5.68
5.67
5.66
5.28
5.27
5.27
5.26
5.24
5.23
5.23
5.21
5.21
3.67
2.08
2.06
1.96
1.00
3.08
3.28
3.11
6.08


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.65
170.50
133.30
118.28
77.16 CDCl3
73.54
52.08
50.45
40.61
38.69
21.37

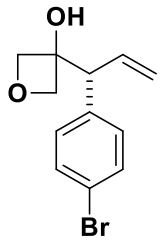
3.2e Procedures and Spectral Data for Synthesis of Oxetanols 3a-3v

General Procedure C



An oven-dried pressure tube equipped with a magnetic stir bar was charged allylic acetate (0.300 mmol, 150 mol%), (*S*)-Ir-tol-BINAP (11.2 mg, 0.010mmol, 5 mol%), 3,4-dinitrobenzoic acid (2.12 mg, 0.010 mmol, 5 mol%) and potassium carbonate (27.6 mg, 0.200 mmol, 100 mol%). The tube was purged with argon and 3-oxetanone (14.8 mg 0.200 mmol, 100 mol%) was added by syringe, followed by 2-propanol (30 µL, 0.400 mmol, 200 mol%), and THF (0.40 mL, 0.50 M). The septum was removed, and the tube was sealed with a polytetrafluoroethylene-lined screwcap. The tube was placed in an oil bath at 100 ^{o}C and stirred for 18-48 hours. The vessel was allowed to cool to ambient temperature. Upon cooling, the reaction mixture was concentrated onto silica gel and purified by flash chromatography to furnish products **3a-3v**.

(3a) (R)-3-(1-(4-bromophenyl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2a** (76.5 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 °C, 18 hr). The title compound was obtained in 96% yield (51.6 mg, 0.192 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.5 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.11 – 5.98 (m, 1H), 5.22 (d, *J* = 10.3 Hz, 1H), 5.12 (d, *J* = 17.1 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.51 (d, *J* = 6.9 Hz, 1H), 4.47 (d, *J* = 7.1 Hz, 1H), 4.38 (d, *J* = 7.1 Hz, 1H), 3.75 (d, *J* = 8.0 Hz, 1H), 2.25 (s, 1H).
^{13}C NMR 126 MHz, $CDCl_3$): δ 137.9, 135.4, 132.1, 130.9, 121.7, 119.5, 83.4, 82.8, 76.30, 55.8.

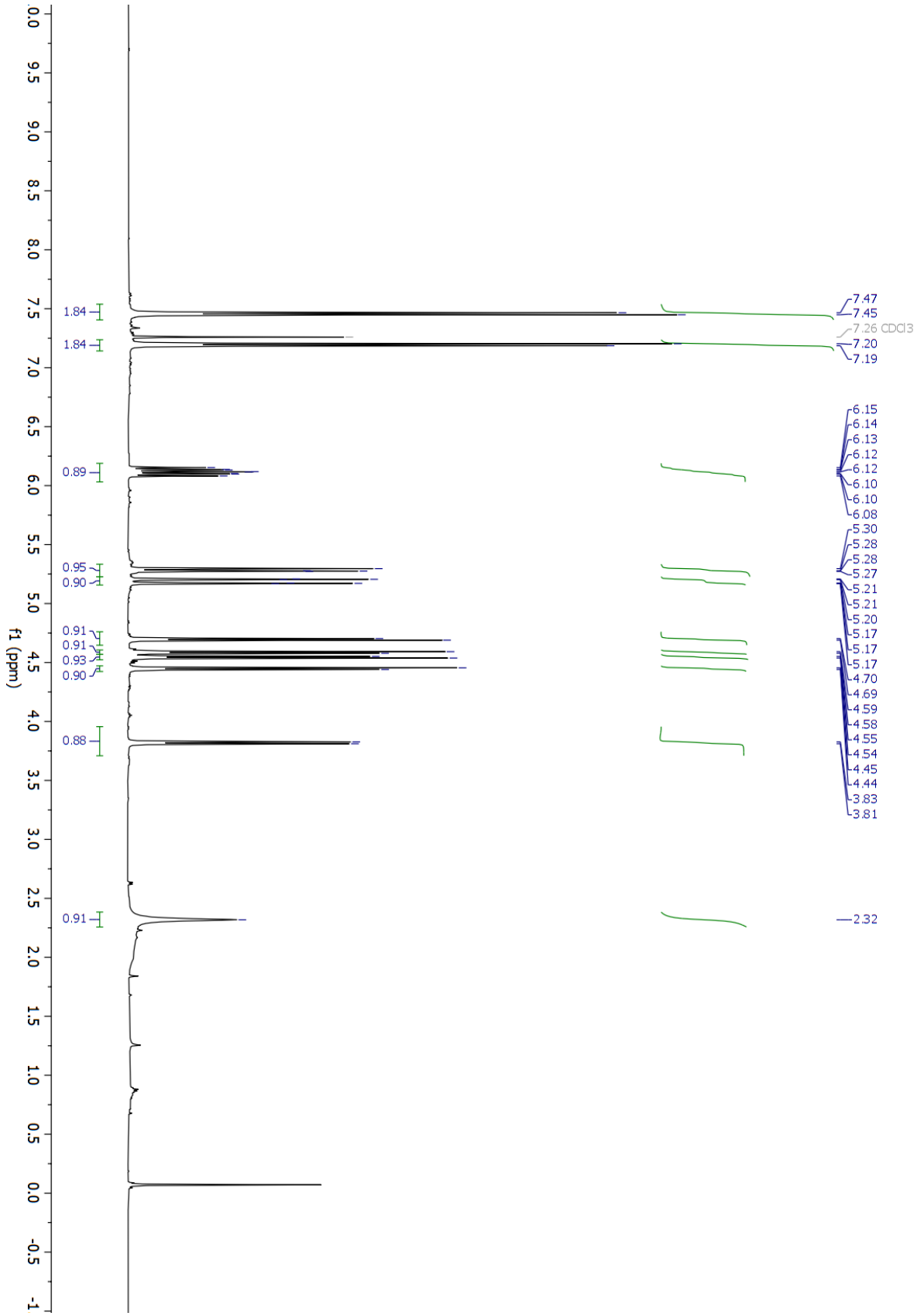
HRMS (ESI): calculated for $C_{12}H_{13}BrO_2$ [M+Na^+]= 290.9991, found= 290.9991

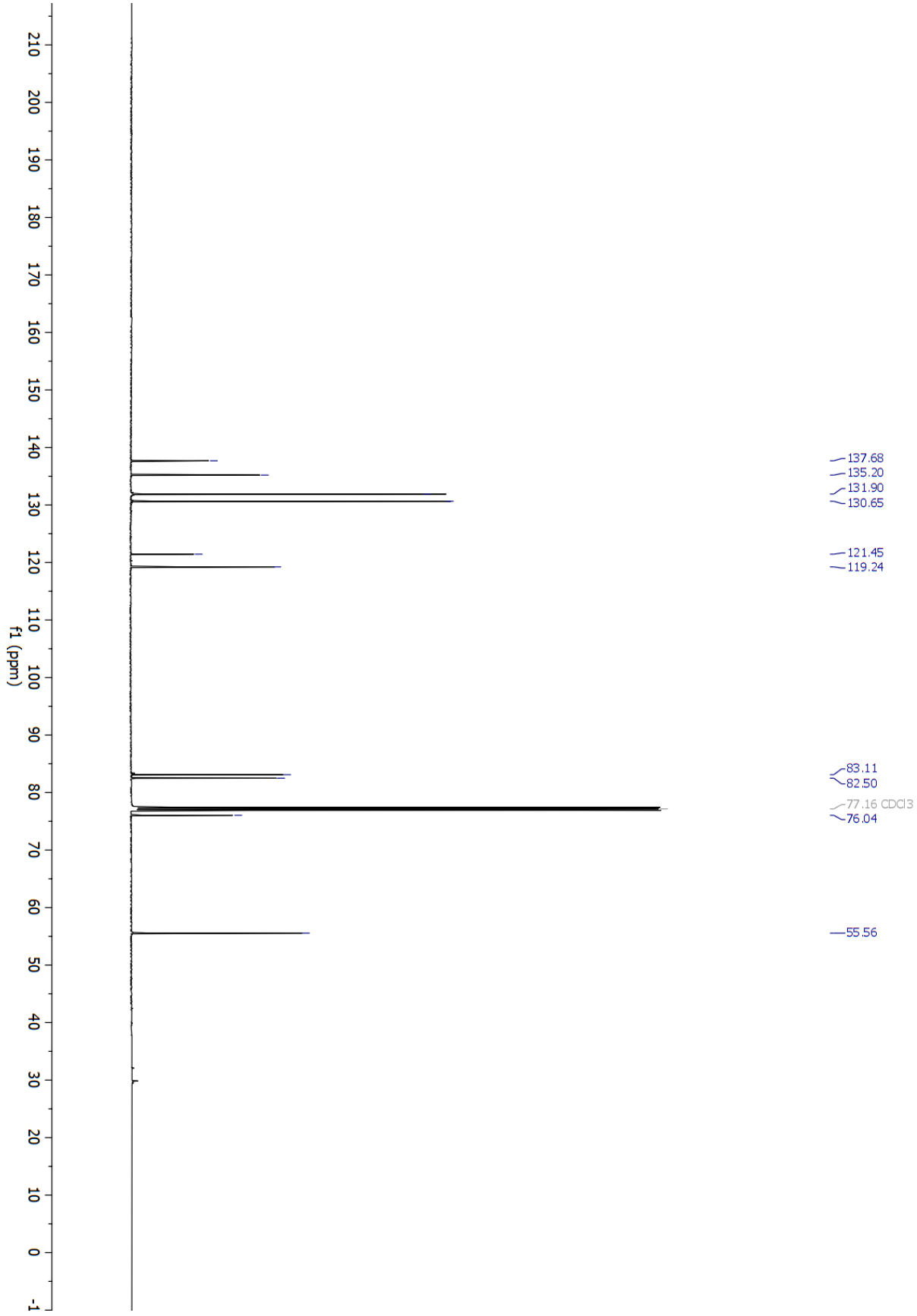
FTIR (neat): 3361, 2946, 2876, 1635, 1413, 966, 944, 813, 777 cm^{-1}

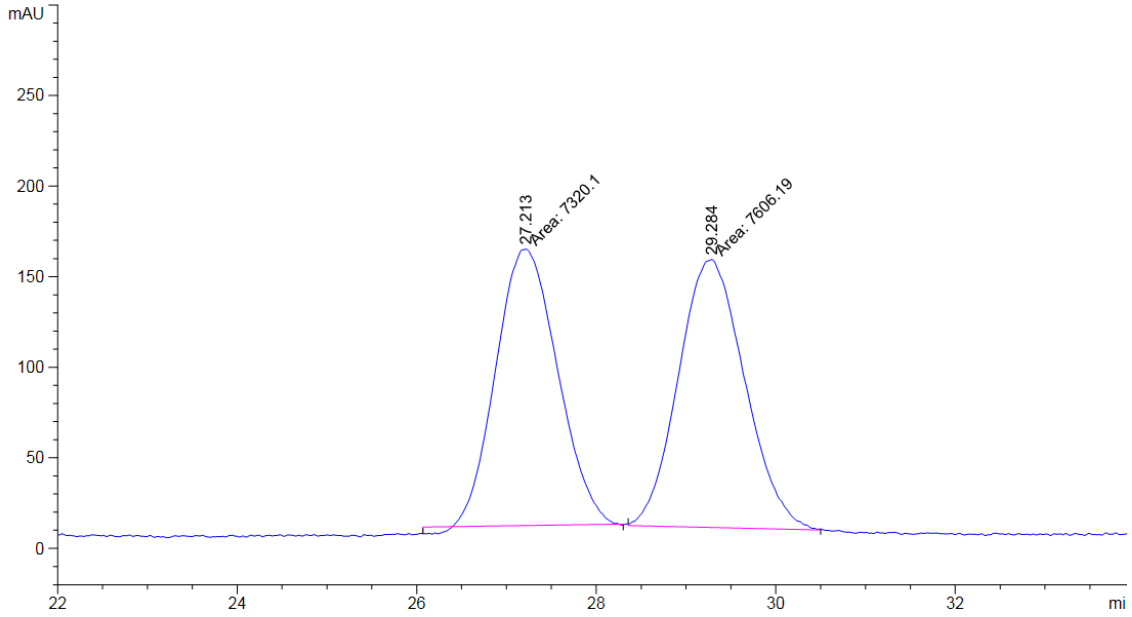
$[\alpha]_D^{28}$= -20.0 (*c* 0.10, $CHCl_3$).

MP: 155-157°C

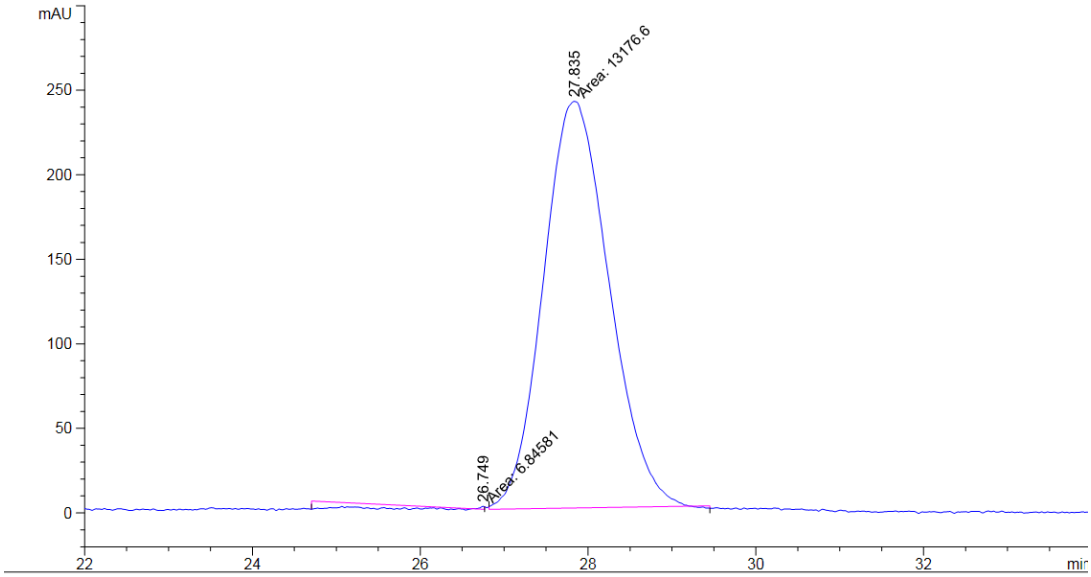
HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm): ee = 99%.


f1 (ppm)
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.84
1.84
0.89
0.95
0.90
0.91
0.91
0.93
0.90
0.88
0.91
7.47
7.45
7.26 CDCl3
7.20
7.19
6.15
6.14
6.13
6.12
6.12
6.10
6.10
6.08
5.30
5.28
5.28
5.27
5.21
5.21
5.20
5.17
5.17
5.17
4.70
4.69
4.59
4.58
4.55
4.54
4.45
4.44
3.83
3.81
2.32


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
137.68
135.20
131.90
130.65
121.45
119.24
83.11
82.50
77.16 CDCl3
76.04
55.56

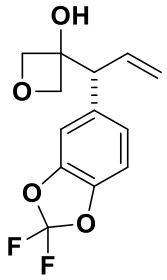


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.213	MM	0.7987	7320.10352	152.74689	49.0417
2	29.284	MM	0.8564	7606.18994	148.03404	50.9583



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.749	MM	0.0654	6.84581	1.74368	0.0519
2	27.835	MM	0.9128	1.31766e4	240.59981	99.9481

(3b) (R)-3-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2b** (76.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 18 hr). The title compound was obtained in 97% yield (52.4 mg, 0.194 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.31 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, CDCl3) δ 7.12 (s, 1H), 7.00 (d, J = 1.8 Hz, 2H), 6.09 (ddd, J = 17.8, 10.3, 8.0 Hz, 1H), 5.28 (d, J = 10.3 Hz, 1H), 5.19 (d, J = 17.2 Hz, 1H), 4.69 (d, J = 6.8 Hz, 1H), 4.57 (d, J = 7.0 Hz, 1H), 4.53 (d, J = 7.1 Hz, 1H), 4.44 (d, J = 7.0 Hz, 1H), 3.83 (d, J = 8.0 Hz, 1H), 2.62 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.3, 143.2, 135.6, 135.2, 132.0 (t, J = 255.2 Hz), 124.4, 119.4, 110.4, 109.7, 83.6, 82.8, 76.4, 56.1.

^{19}F NMR (471 MHz, $CDCl_3$): δ -49.95.

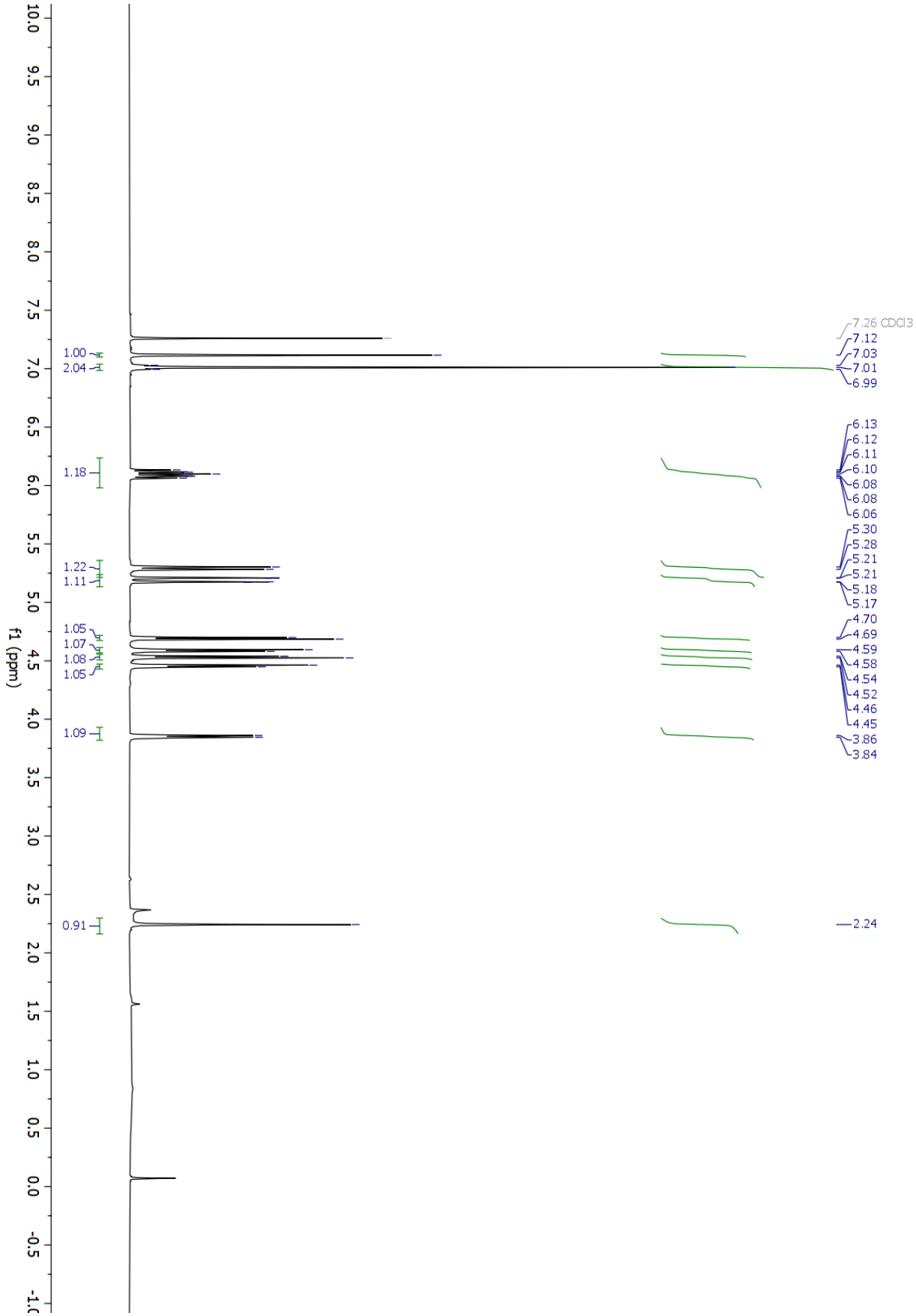
HRMS (CI): Calculated for $C_{13}H_{12}F_2O_4$ $[M+H^+]$= 271.0766, found= 271.0772.

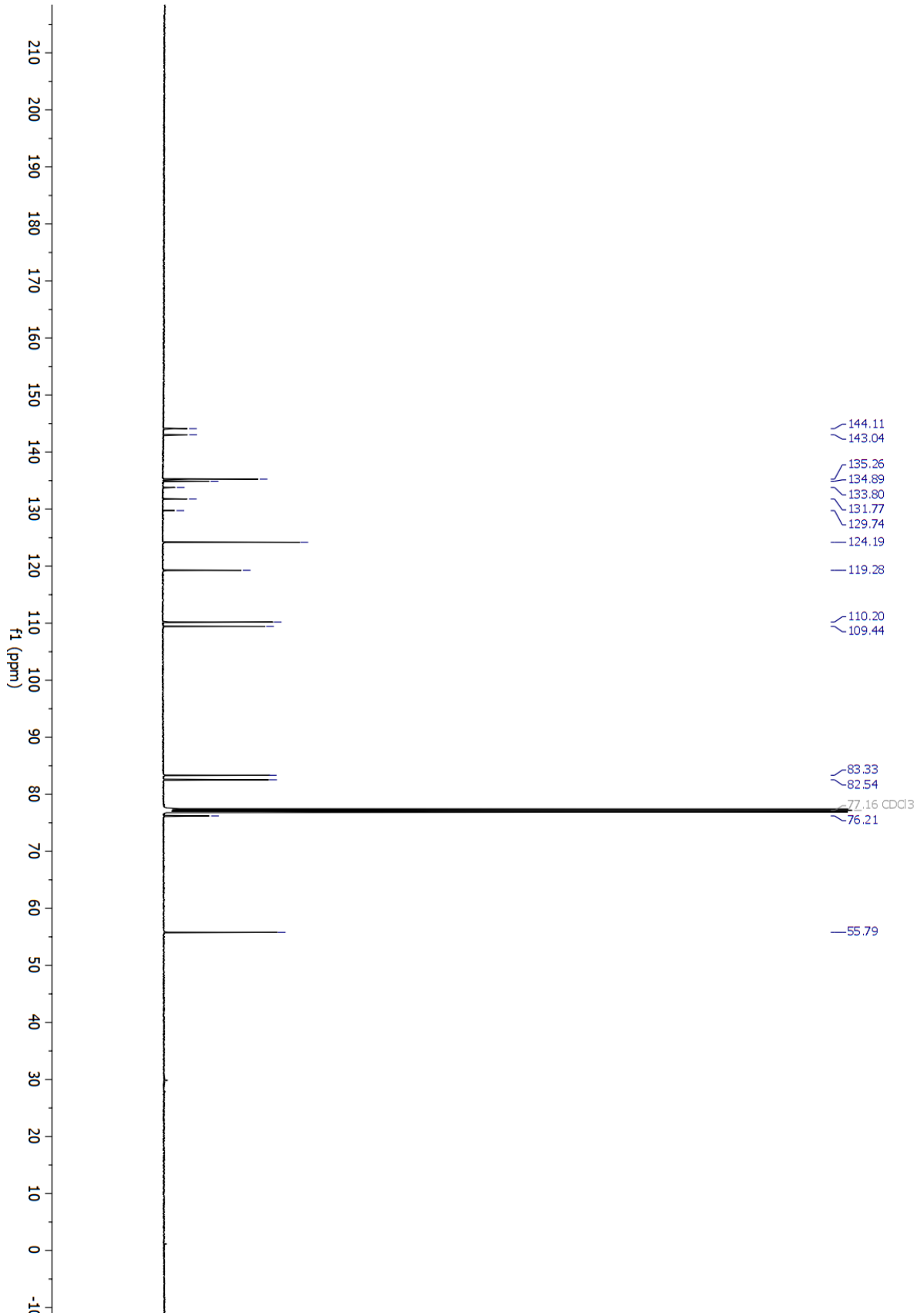
FTIR (neat): 3368, 2960, 2890, 1642, 1498, 1486, 1421, 1134, 990 , 934, 871, 791, 717, 700 cm^{-1}

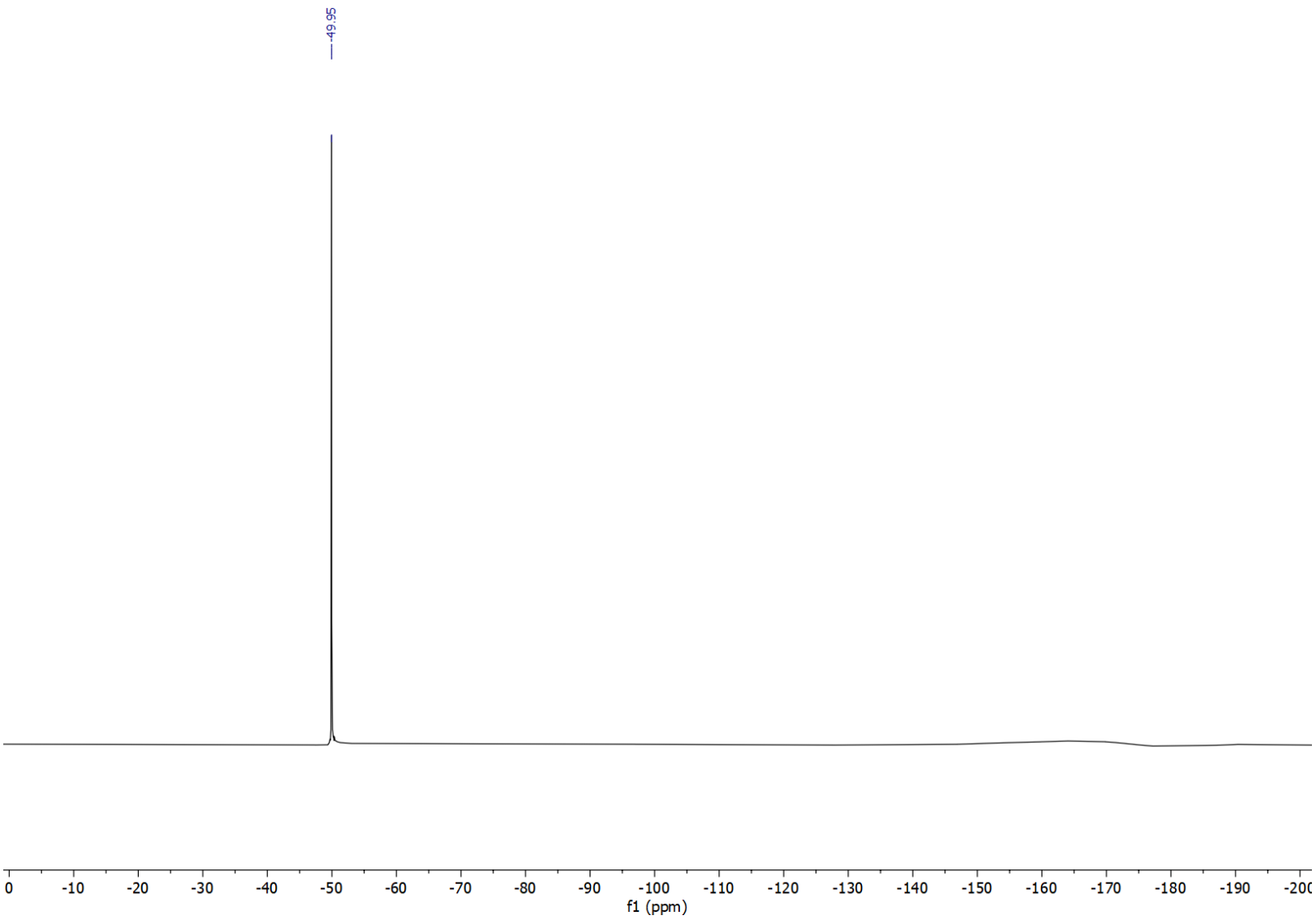
$[\alpha]_D^{28}$= -15.0 (*c* 0.10, $CHCl_3$).

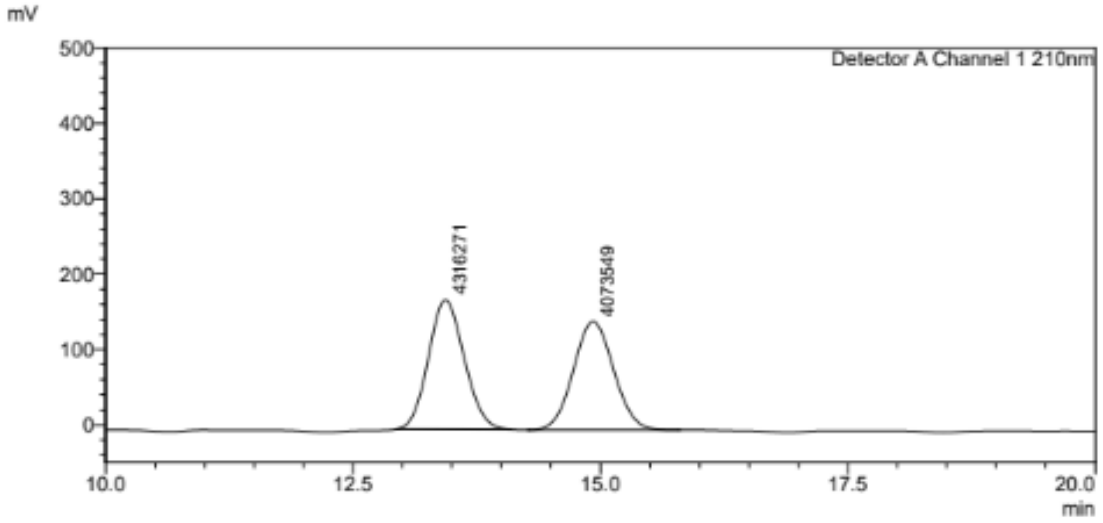
HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 97:2, 1.00 mL/min, 210 nm): *ee* = 99%

.


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
2.04
1.18
1.22
1.11
1.05
1.07
1.08
1.05
1.09
0.91
7.26 CDCl3
7.12
7.03
7.01
6.99
6.13
6.12
6.11
6.10
6.08
6.08
6.06
5.30
5.28
5.21
5.21
5.18
5.17
4.70
4.69
4.59
4.58
4.54
4.52
4.46
4.45
3.86
3.84
2.24

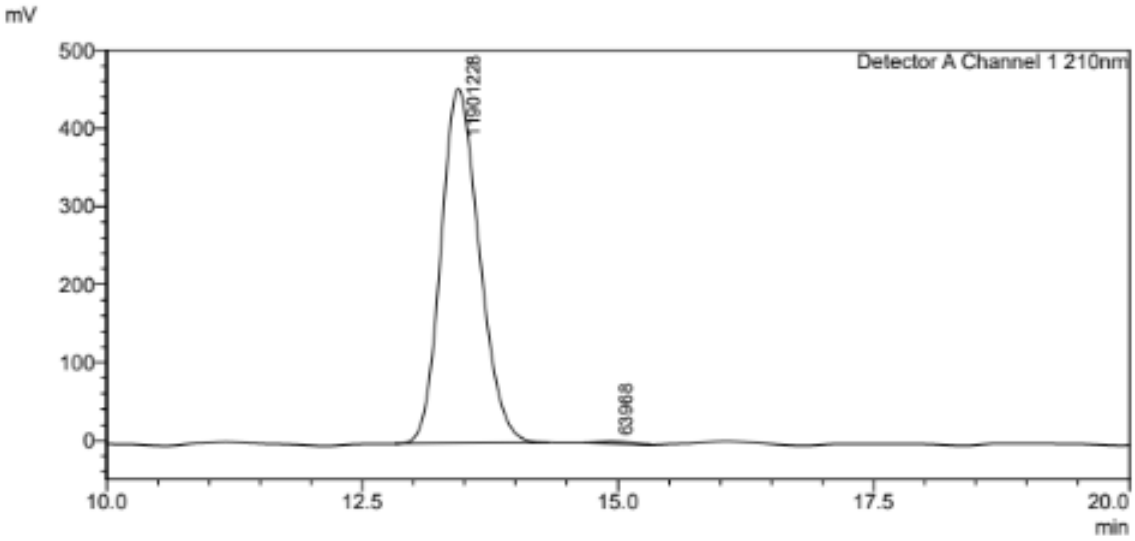

144.11
143.04
135.26
134.89
133.80
131.77
129.74
124.19
119.28
110.20
109.44
83.33
82.54
77.16 CDCl3
76.21
55.79
f1 (ppm)


-49.95
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)



Detector A Channel 1 210nm

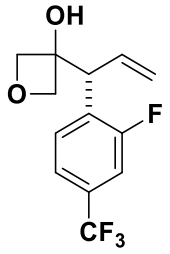
Ret. Time	Height	Area	Area%
13.435	171322	4316271	51.447
14.926	143758	4073549	48.553
	315080	8389819	100.000



Detector A Channel 1 210nm

Ret. Time	Height	Area	Area%
13.439	454103	11901228	99.465
14.932	3137	63968	0.535
	457241	11965196	100.000

(3c) (R)-3-(1-(2-fluoro-4-(trifluoromethyl)phenyl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2c** (78.6 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 24 hr). The title compound was obtained in 69% yield (38.1 mg, 0.138 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.34 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (t, J = 7.6 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.34 (dd, J = 9.9, 1.8 Hz, 2H), 6.12 (ddd, J = 17.7, 10.2, 7.9 Hz, 2H), 5.33 (d, J = 10.2 Hz, 2H), 5.22 (d, J = 17.1 Hz, 2H), 4.74 (d, J = 7.1 Hz, 2H), 4.60 (d, J = 7.0 Hz, 2H), 4.53 (d, J = 7.2 Hz, 2H), 4.48 (d, J = 7.1 Hz, 2H), 4.33 (d, J = 8.1 Hz, 2H), 2.38 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 160.3 (d, J = 247.6 Hz), 146.9, 133.7, 131.1 (d, J = 4.2 Hz), 130.1 (d, J = 14.3 Hz), 127.4, 127.3, 121.1 – 120.9 (m), 119.9, 113.3 – 112.9 (m), 83.2, 82.4, 76.1, 47.9.

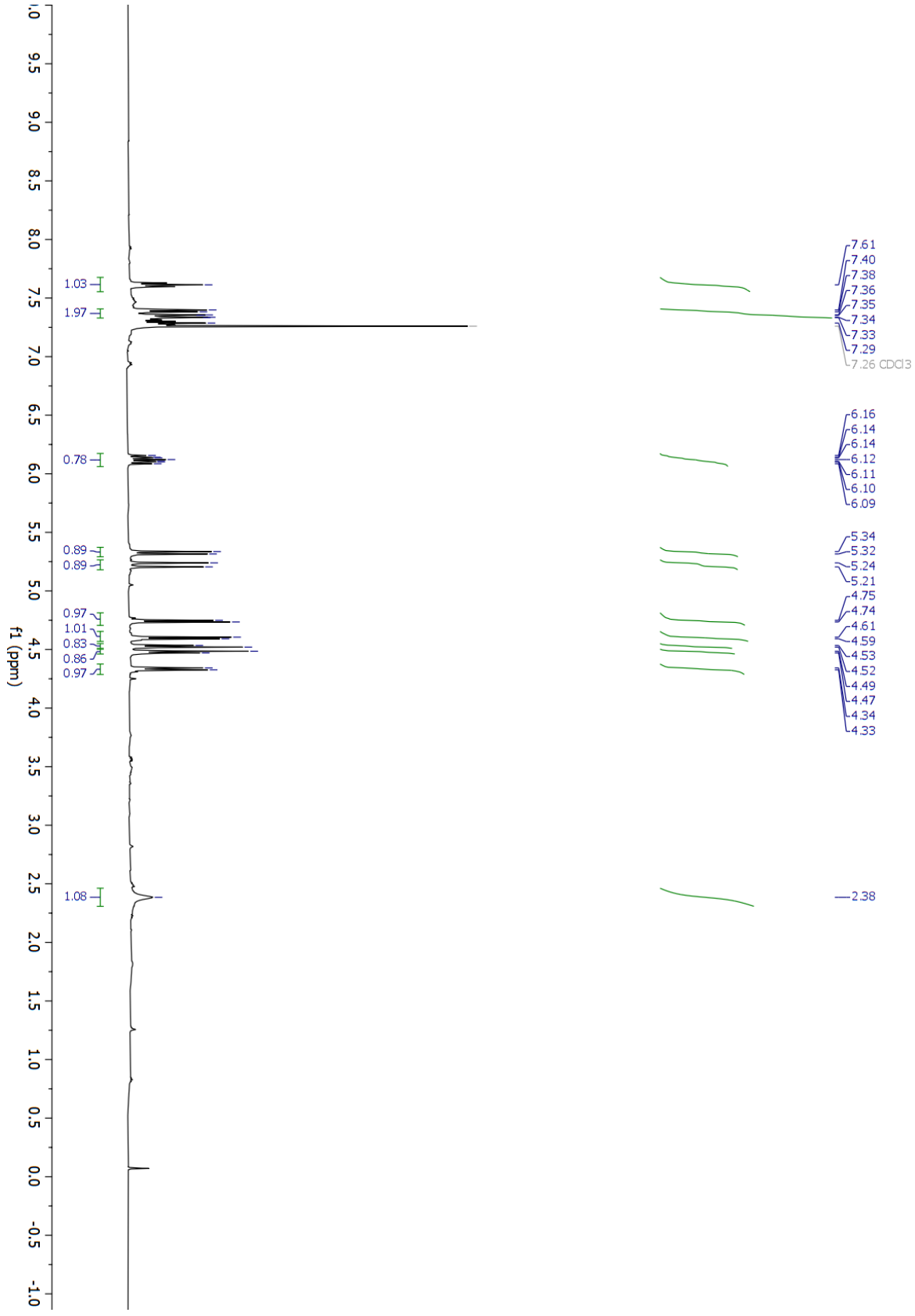
^{19}F NMR (471 MHz, $CDCl_3$): δ -62.80, -108.98 – -119.56 (m).

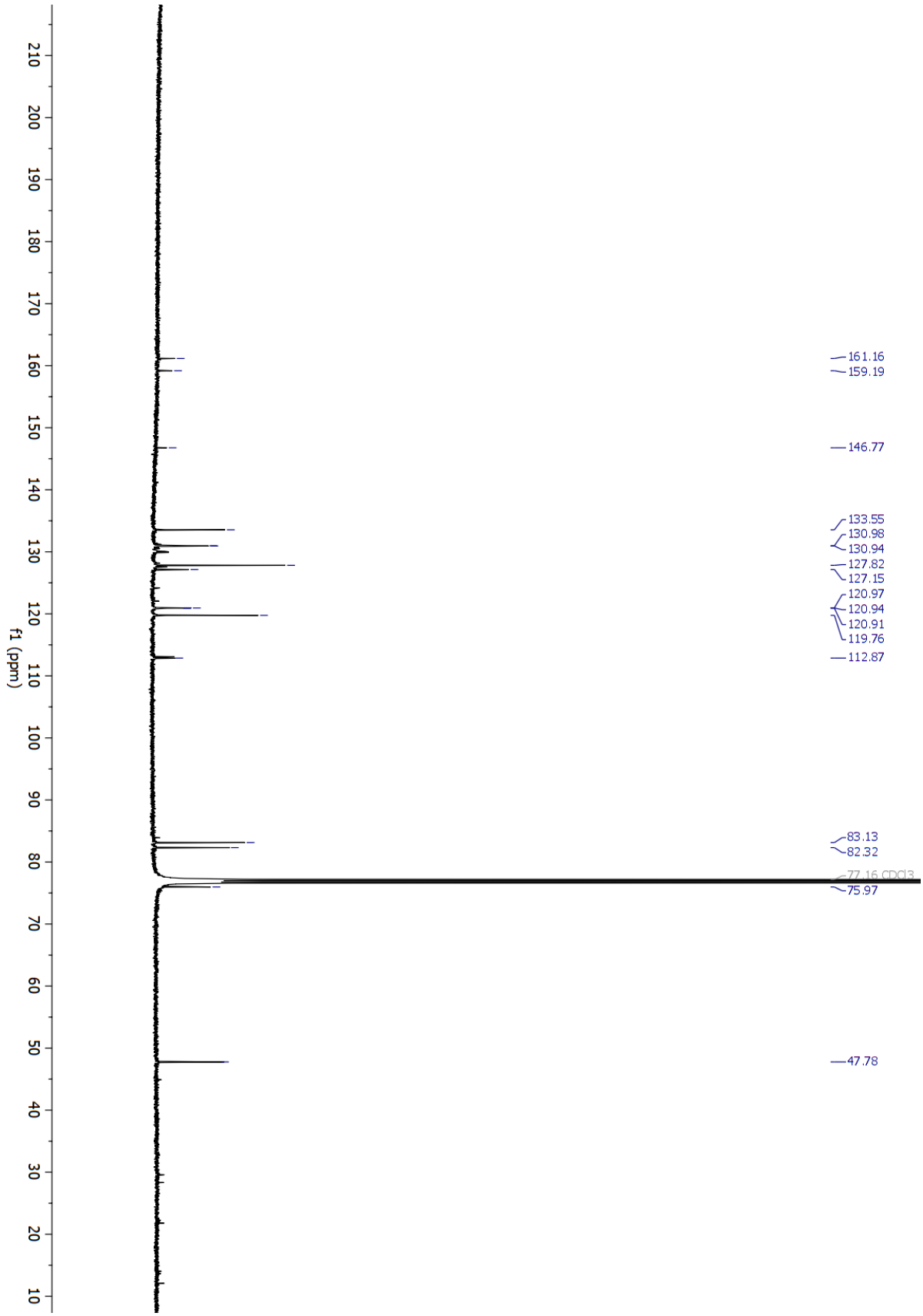
HRMS (ESI): Calculated for $C_{13}H_{12}F_4O_3$ [M+H$^+$]= 277.0773, found= 277.0777

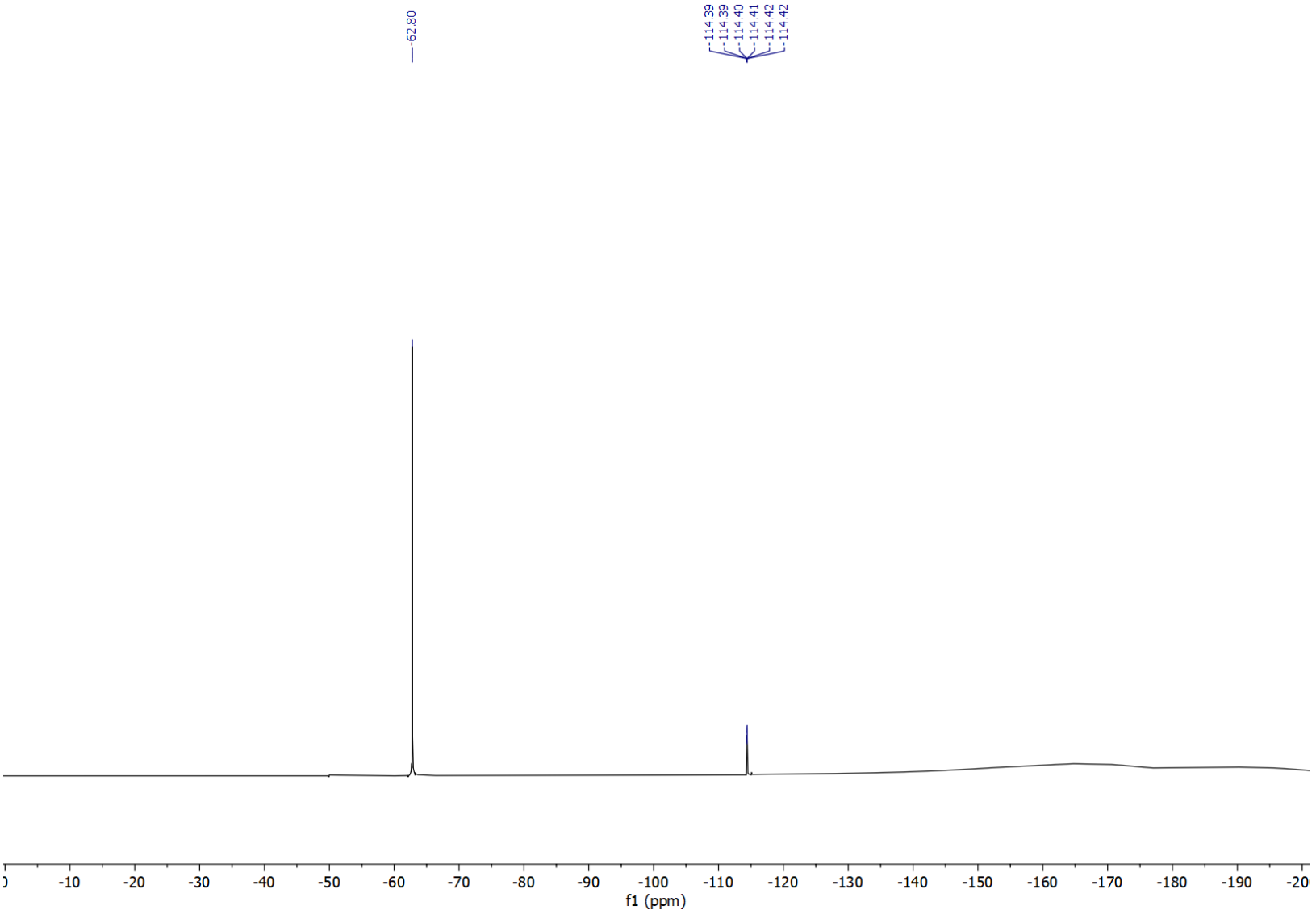
FTIR (neat): 3368, 2960, 2890, 1642, 1498, 1486, 1445, 1421, 1226, 1134, 990, 934, 927, 717, 700 cm^{-1}

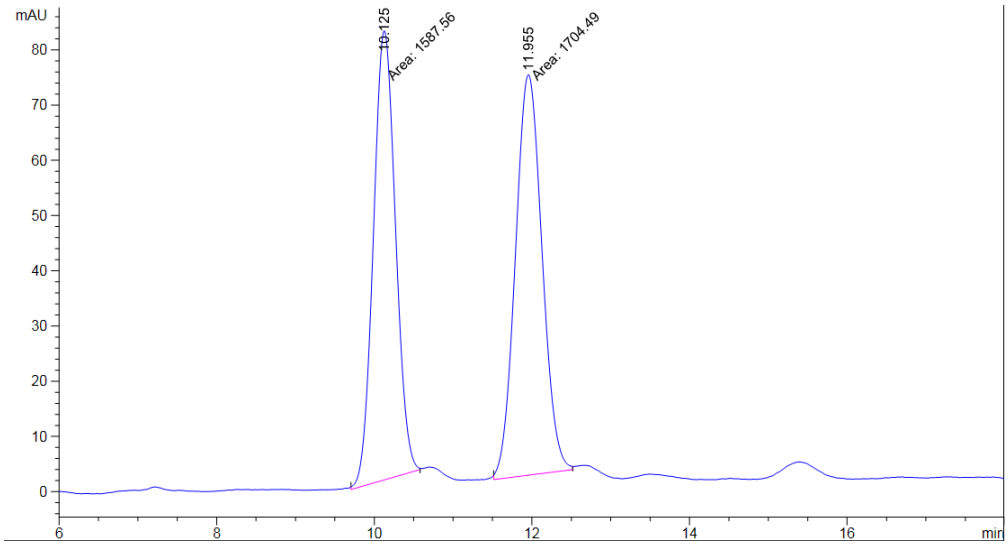
$[\alpha]_D^{28}$= -12.1 (*c* 0.10, $CHCl_3$)

HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210nm): *ee* = 99%

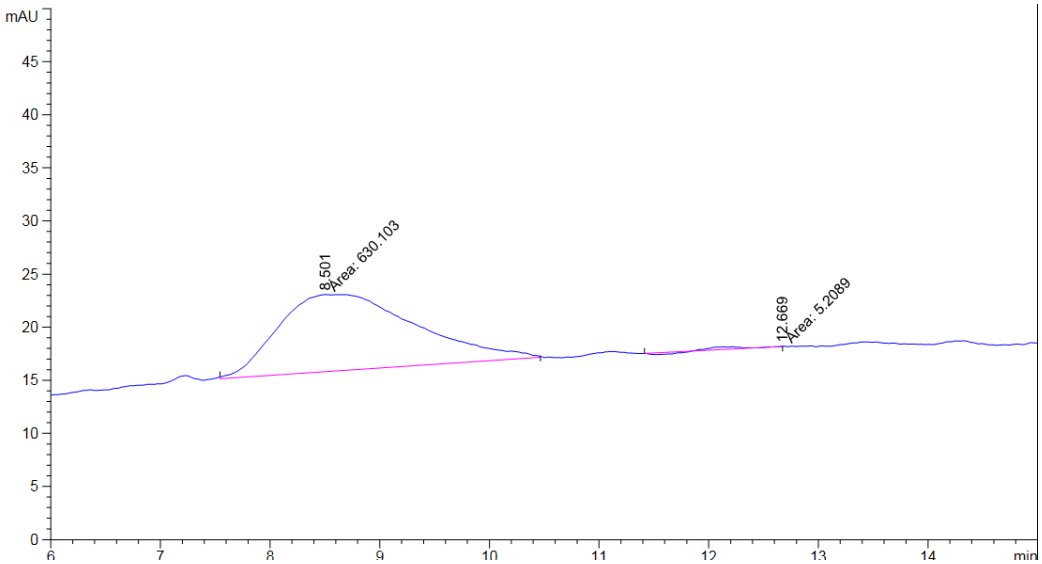

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.03
1.97
0.78
0.89
0.89
0.97
1.01
0.83
0.86
0.97
1.08
7.61
7.40
7.38
7.36
7.35
7.34
7.33
7.29
7.26 CDCl3
6.16
6.14
6.14
6.12
6.11
6.10
6.09
5.34
5.32
5.24
5.21
4.75
4.74
4.61
4.59
4.53
4.52
4.49
4.47
4.34
4.33
2.38


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
161.16
159.19
146.77
133.55
130.98
130.94
127.82
127.15
120.97
120.94
120.91
119.76
112.87
83.13
82.32
77.16 CDCl3
75.97
47.78


-62.80
-114.39
-114.39
-114.40
-114.41
-114.42
-114.42
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)

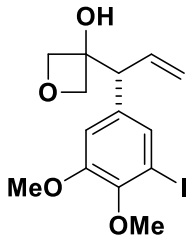


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.125	MM	0.3250	1587.56213	81.40942	48.2241
2	11.955	MM	0.3914	1704.48950	72.57436	51.7759



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.501	MM	1.4440	630.10278	7.27277	99.1801
2	12.669	MM	2.7989	5.20890	3.10181e-2	0.8199

(3d) (R)-3-(1-(3-iodo-4,5-dimethoxyphenyl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2d** (108.0 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 ^{o}C, 18 hr). The title compound was obtained in 99% yield (74.5mg, 0.190 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.23 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 1.9 Hz, 1H), 6.85 (d, *J* = 1.9 Hz, 1H), 6.18 – 6.11 (m, 1H), 5.95 (ddd, *J* = 16.6, 10.4, 5.8 Hz, 1H), 5.35 – 5.23 (m, 2H), 3.86 (s, 3H), 3.82 (s, 3H), 2.12 (s, 4H).

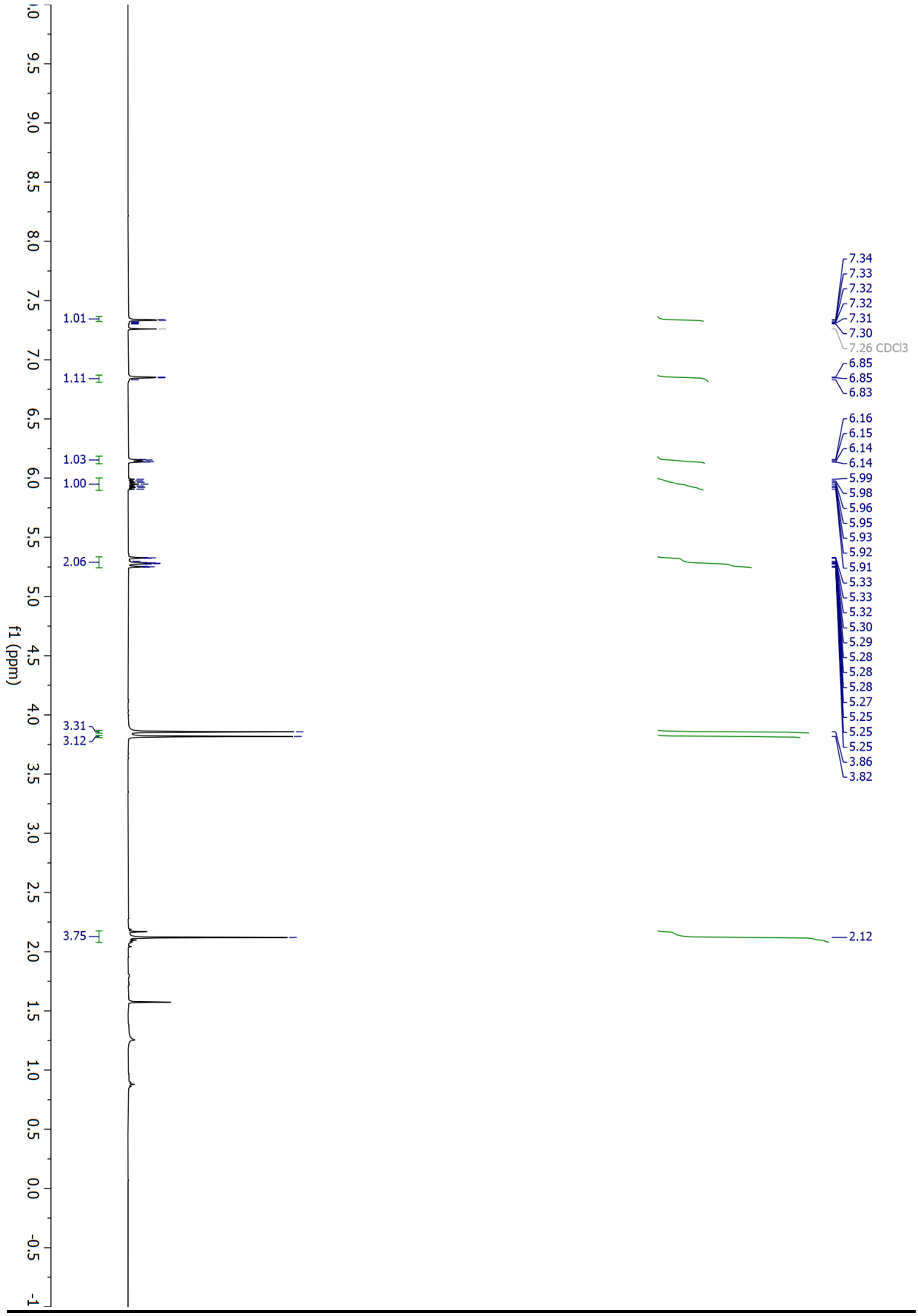
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 152.7, 148.96, 136.9, 135.8, 129.3, 117.4, 112.1, 92.6, 75.2, 60.5, 56.2, 21.4.

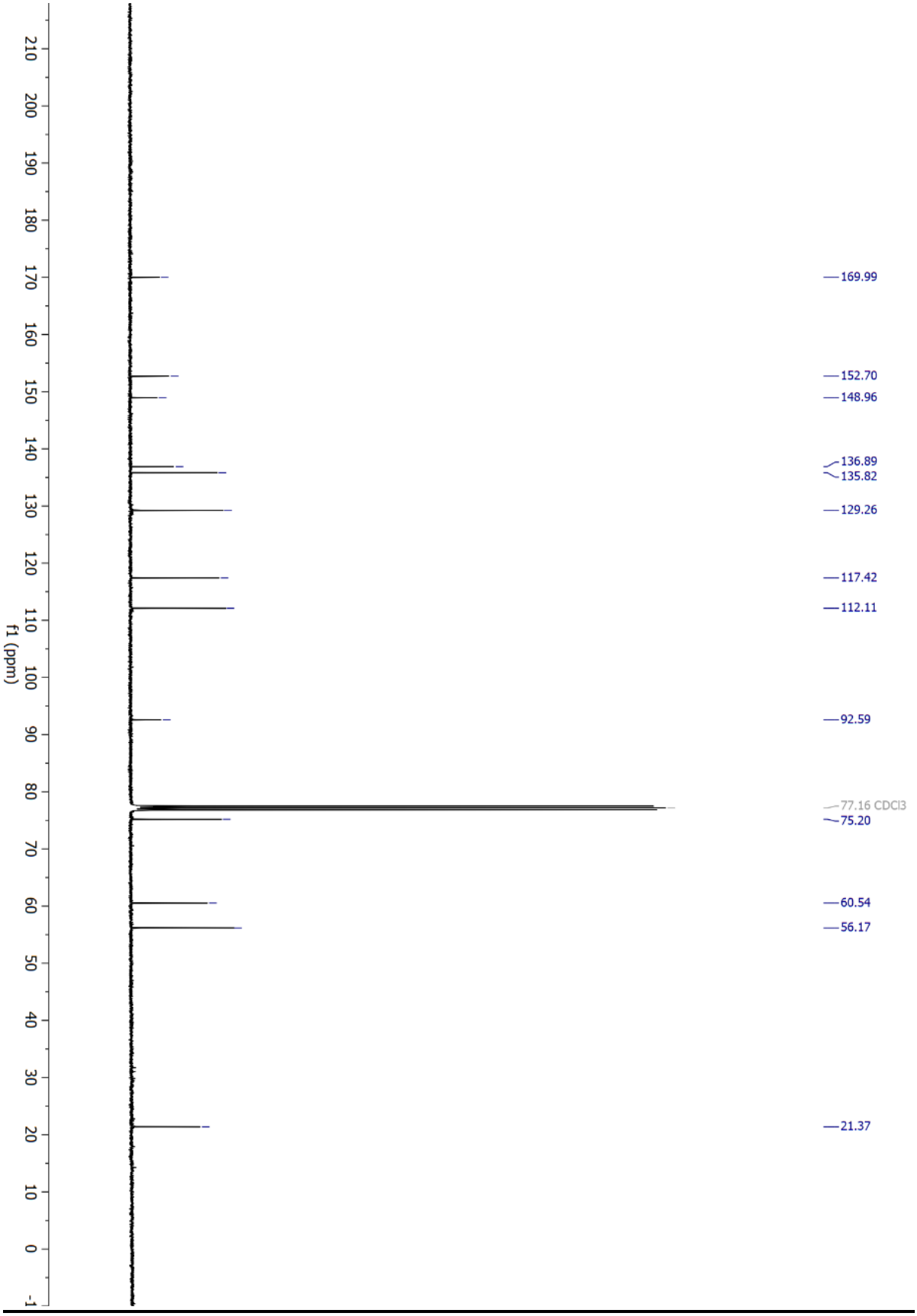
HRMS (ESI): Calculated for $C_{14}H_{17}IO_4$ [M+Na^+] = 399.0064, Found 399.0058

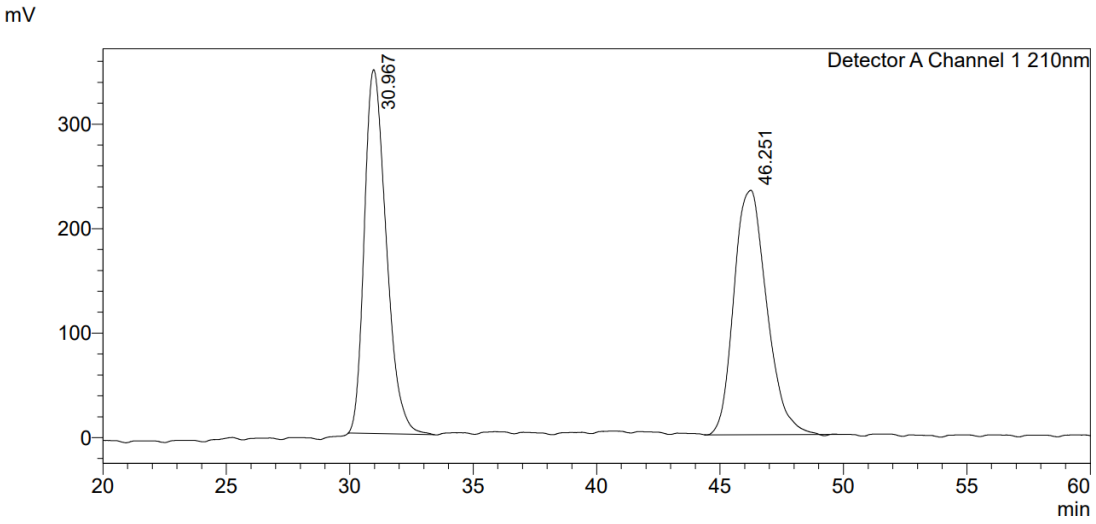
FTIR (neat): 3409, 2969, 2947, 2872, 1738, 1558, 1365., 1272, 1229, 1042cm^{-1}

$[\alpha]_D^{28}$= -19.0 (c 0.1, $CHCl_3$)

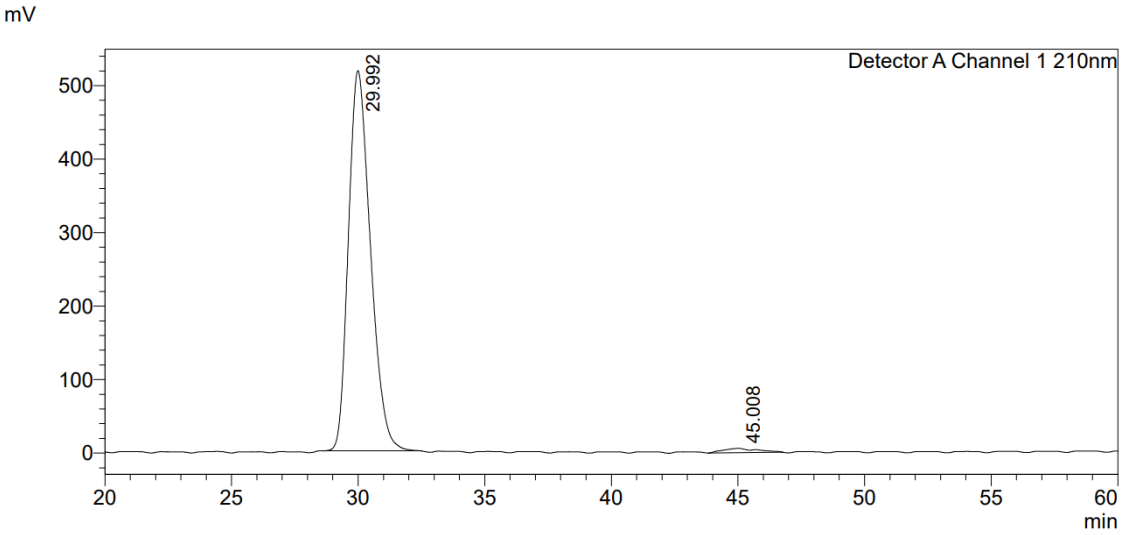
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 97%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.01
1.11
1.03
1.00
2.06
3.31
3.12
3.75
2.12
7.34
7.33
7.32
7.32
7.31
7.30
7.26 CDCl3
6.85
6.85
6.83
6.16
6.15
6.14
6.14
5.99
5.98
5.96
5.95
5.93
5.92
5.91
5.33
5.33
5.32
5.30
5.29
5.28
5.28
5.28
5.27
5.25
5.25
5.25
3.86
3.82


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
169.99
152.70
148.96
136.89
135.82
129.26
117.42
112.11
92.59
77.16 CDCl3
75.20
60.54
56.17
21.37

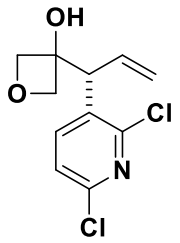


Peak#	Ret. Time	Area	Height	Conc.	Area%
1	30.967	21484372	348242	49.790	49.790
2	46.251	21665932	233973	50.210	50.210
Total		43150304	582215		100.000



Peak#	Ret. Time	Area	Height	Conc.	Area%
1	29.992	31323310	517309	98.357	98.357
2	45.008	523249	5804	1.643	1.643
Total		31846560	523114		100.000

(3e) (R)-3-(1-(2,6-dichloropyridin-3-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2e** (73.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 18 hr). The title compound was obtained in 92% yield (47.8 mg, 0.184 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.25 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 8.2 Hz, 1H), 7.24 (d, J = 8.2 Hz, 1H), 5.99 (ddd, J = 17.6, 10.3, 7.6 Hz, 1H), 5.33 (d, J = 10.3 Hz, 1H), 5.18 (dd, J = 17.1, 1.6 Hz, 1H), 4.74 (d, J = 7.1 Hz, 1H), 4.59 (d, J = 7.1 Hz, 1H), 4.51 (d, J = 7.3 Hz, 1H), 4.48 (d, J = 3.6 Hz, 1H), 4.46 (d, J = 3.7 Hz, 1H), 2.39 (s, 1H).

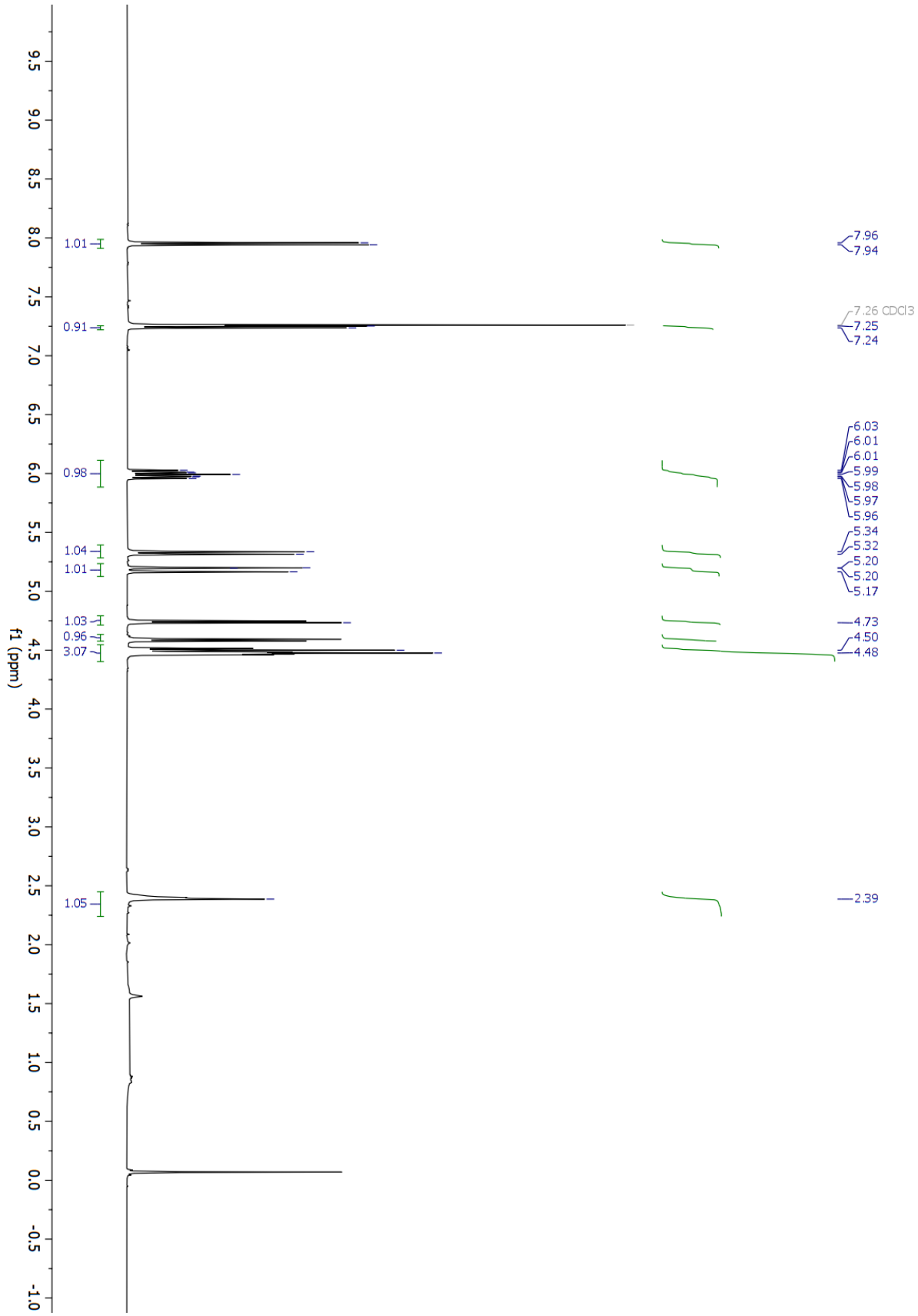
^{13}C NMR (126 MHz, $CDCl_3$): δ 150.34, 148.73, 141.18, 133.22, 132.06, 122.99, 120.11, 83.77, 82.25, 76.05, 50.40.

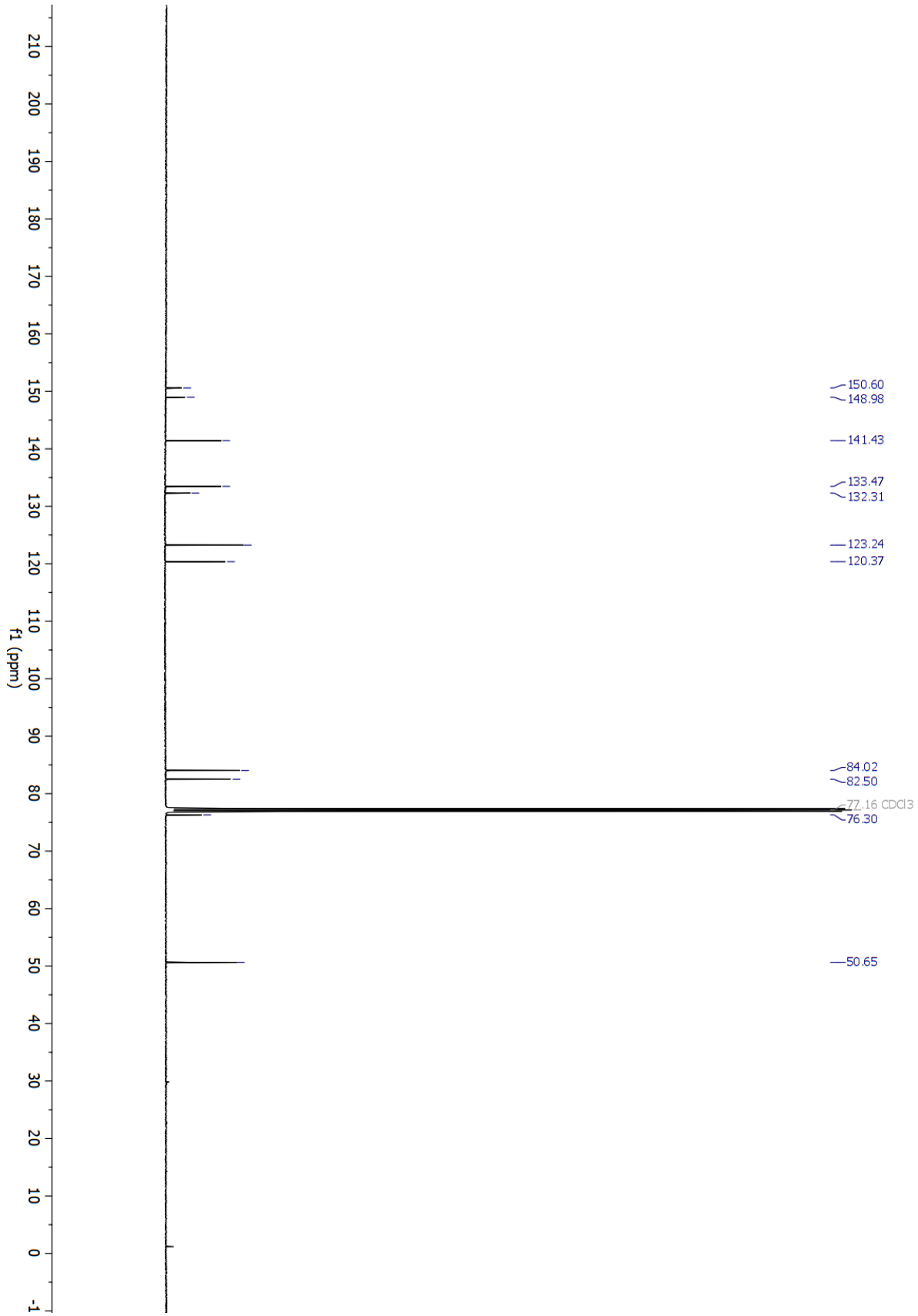
HRMS (ESI): Calculated for $C_{11}H_{11}Cl_2NO_3$ $[M+H^+]$= 260.0240, found= 260.0247.

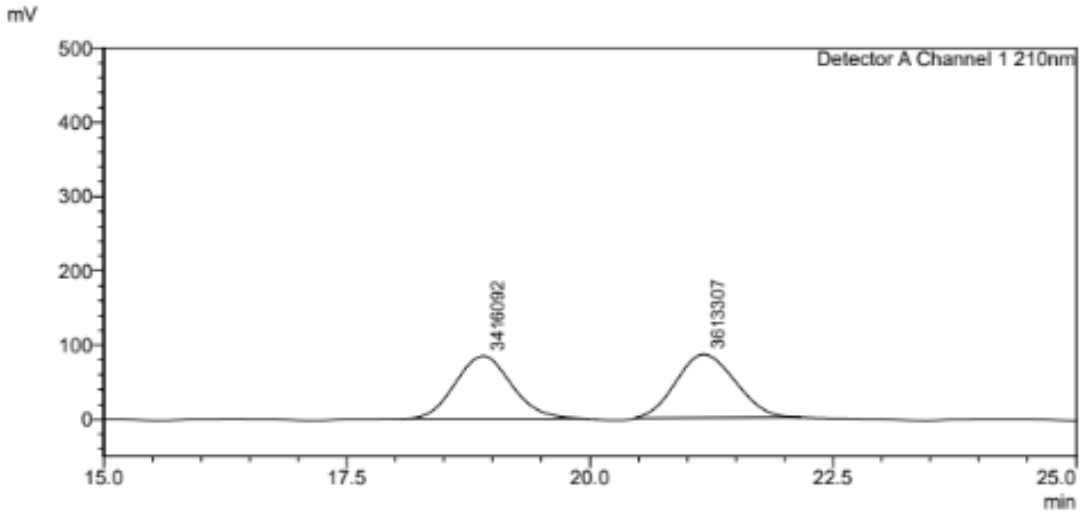
FTIR (neat): 3293, 3058, 2969, 2881, 2360, 1634, 1570, 1545. 1420, 1098, 990, 928, 857, 842 cm^{-1}.

$\mathbf{[\alpha]_D^{28}}$= -68.1 (*c* 0.10, $CHCl_3$)

HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 98%

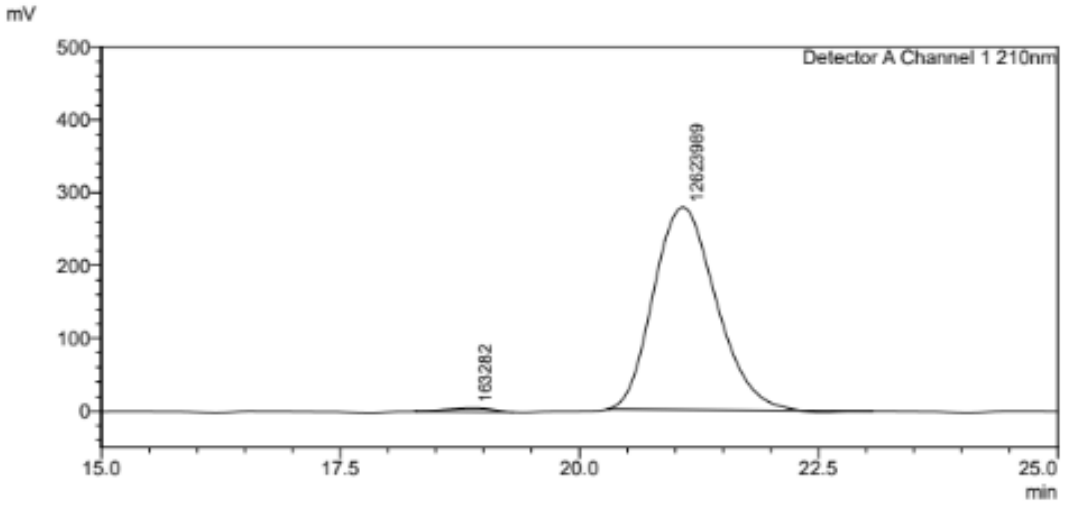

f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.01
0.91
0.98
1.04
1.01
1.03
0.96
3.07
1.05
7.96
7.94
7.26 CDCl3
7.25
7.24
6.03
6.01
6.01
5.99
5.98
5.97
5.96
5.34
5.32
5.20
5.20
5.17
4.73
4.50
4.48
2.39


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
150.60
148.98
141.43
133.47
132.31
123.24
120.37
84.02
82.50
77.16 CDCl3
76.30
50.65



Detector A Channel 1 210nm

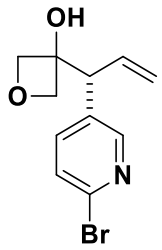
Ret. Time	Height	Area	Area%
18.904	84532	3416092	48.597
21.170	85306	3613307	51.403
	169839	7029399	100.000



Detector A Channel 1 210nm

Ret. Time	Height	Area	Area%
18.870	4892	163282	1.277
21.082	277880	12623989	98.723
	282773	12787271	100.000

(3f) (R)-3-(1-(6-bromopyridin-3-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2f** (76.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 18 hr). The title compound was obtained in 98% yield (52.9 mg, 0.196 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1–2:1).

TLC (SiO_2): R_f = 0.36 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 8.31 (d, *J* = 2.5 Hz, 1H), 7.59 (dd, *J* = 8.2, 2.6 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 6.09 (ddd, *J* = 17.2, 10.3, 8.1 Hz, 1H), 5.30 (d, *J* = 10.3 Hz, 1H), 5.20 (dd, *J* = 17.1, 1.4 Hz, 1H), 4.68 (d, *J* = 7.0 Hz, 1H), 4.58 (d, *J* = 7.1 Hz, 1H), 4.45 (q, *J* = 36.0 Hz, 2H), 3.83 (d, *J* = 8.1 Hz, 1H), 3.12 (s, 1H).

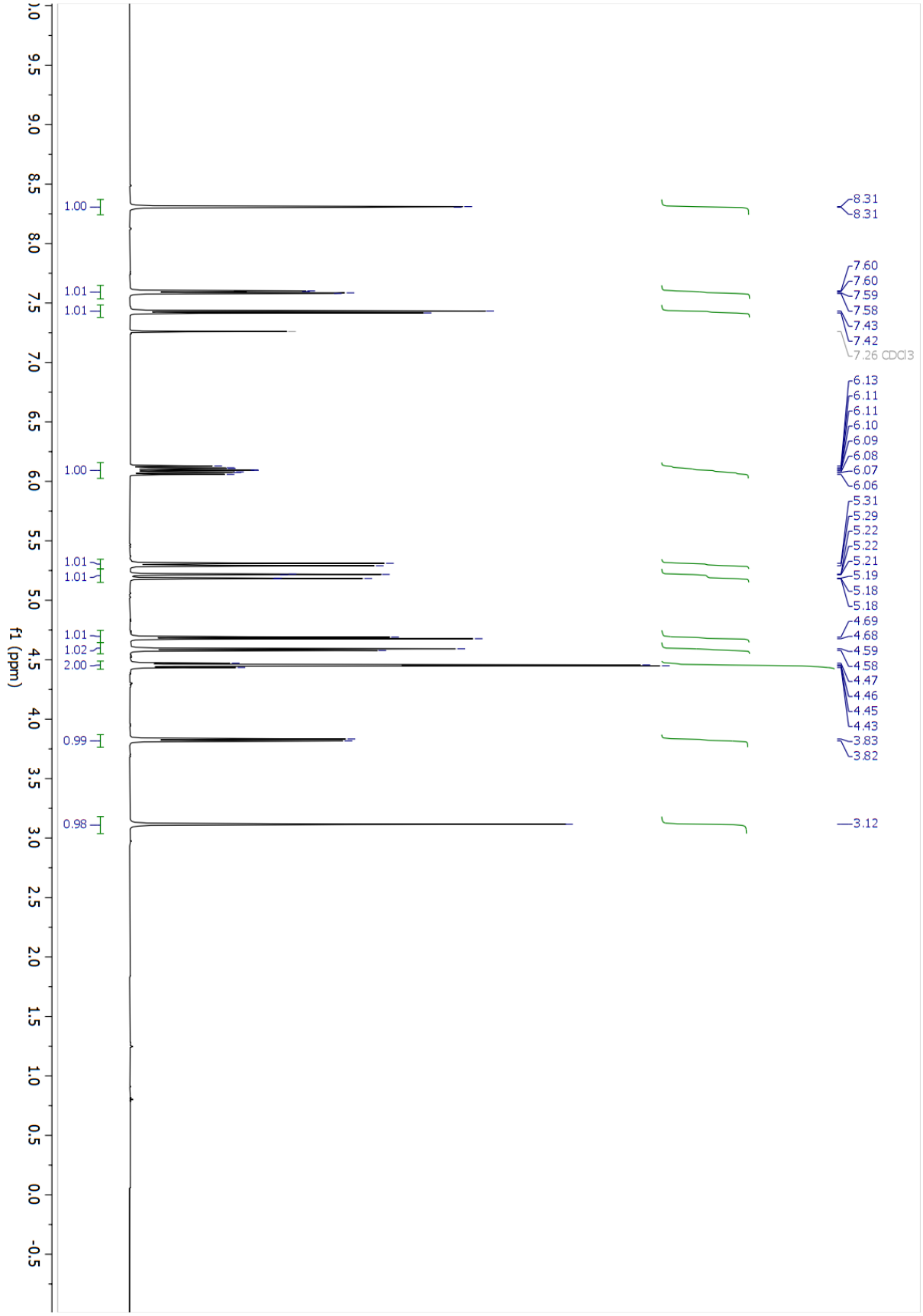
^{13}C NMR (126 MHz, $CDCl_3$): δ: 150.5, 140.9, 139.4, 134.5, 134.1, 128.0, 119.8, 83.4, 82.6, 75.8, 53.1.

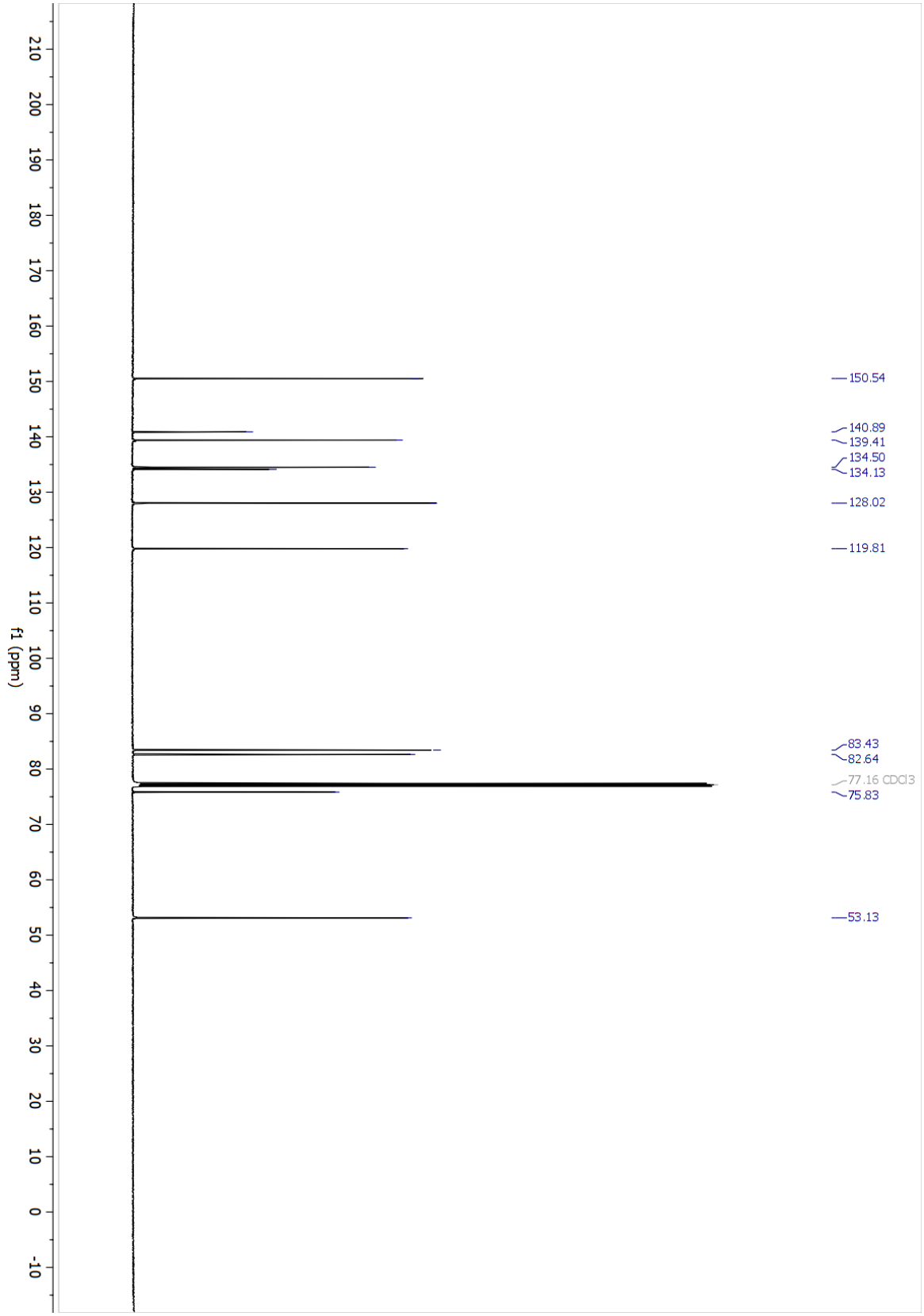
HRMS (ESI): Calculated for $C_{11}H_{12}BrNO_2$ $[M+H^+]$ =270.0124, Found 270.0126

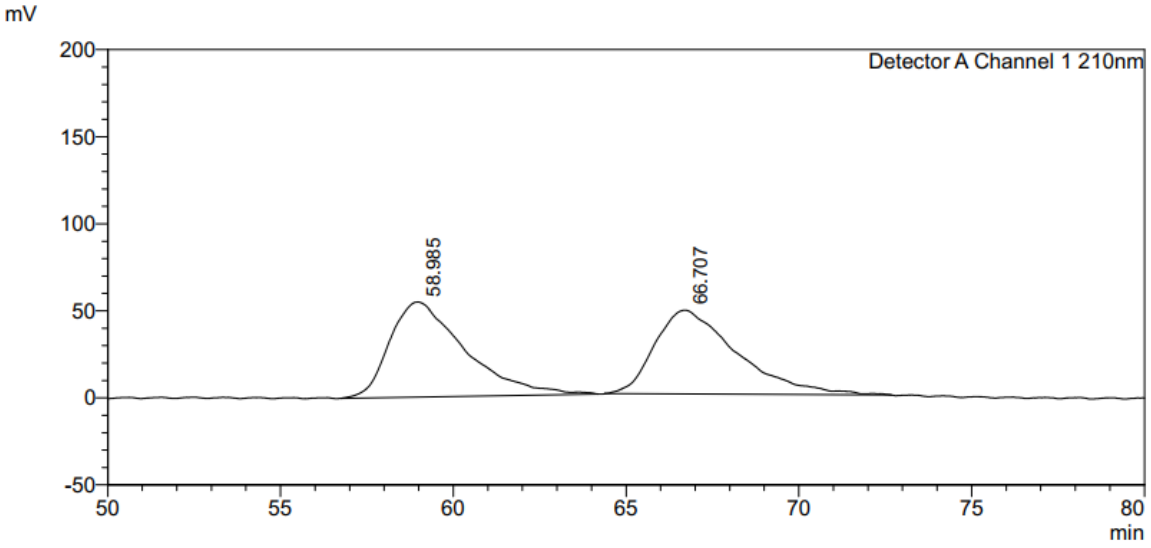
FTIR (neat): 3345, 1452, 1087, 969, 926, 854, 765 cm^{-1}

$[\alpha]_D^{28}$= -93.3^0 (c = 1.07, $CHCl_3$)

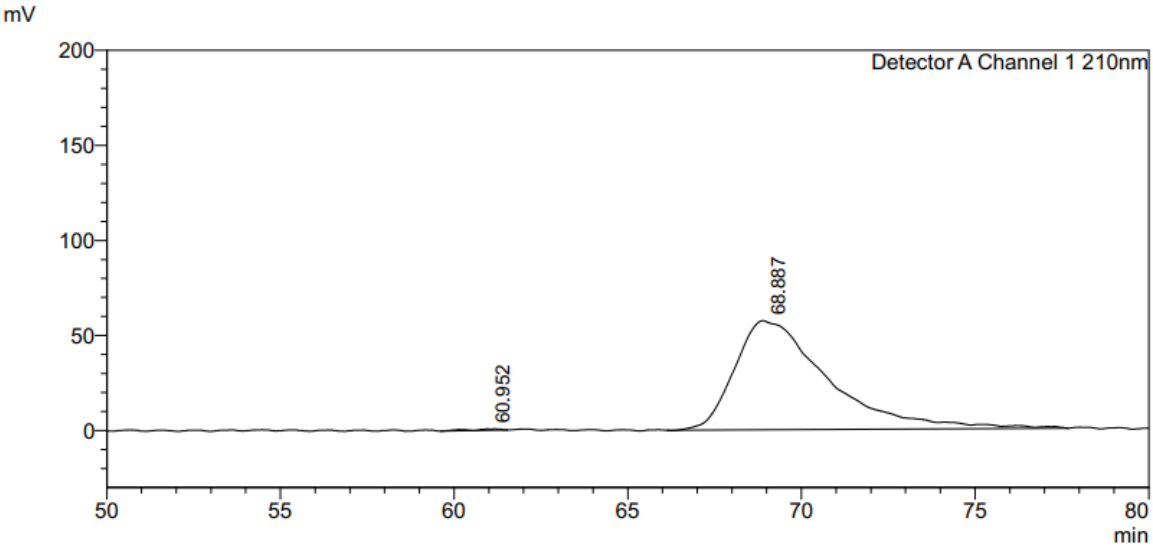
HPLC (Phenomenex Cellulose Column , Hexane:*i*-PrOH = 95:05, 1.0 mL/min, 210 nm): ee= 99%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
1.01
1.01
1.00
1.01
1.01
1.01
1.02
2.00
0.99
0.98
8.31
8.31
7.60
7.60
7.59
7.58
7.43
7.42
7.26 CDCl3
6.13
6.11
6.11
6.10
6.09
6.08
6.07
6.06
5.31
5.29
5.22
5.22
5.21
5.19
5.18
5.18
4.69
4.68
4.59
4.58
4.47
4.46
4.45
4.43
3.83
3.82
3.12


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
150.54
140.89
139.41
134.50
134.13
128.02
119.81
83.43
82.64
77.16 CDCl3
75.83
53.13

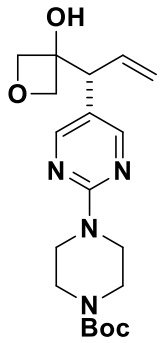


Peak#	Ret. Time	Area	Height	Area%
1	58.985	8259443	54534	50.863
2	66.707	7979204	48142	49.137
Total		16238646	102676	100.000



Peak#	Ret. Time	Area	Height	Area%
1	60.952	46387	791	0.429
2	68.887	10766718	57430	99.571
Total		10813106	58222	100.000

(3g) tert-butyl (R)-4-(5-(1-(3-hydroxyoxetan-3-yl)allyl)pyrimidin-2-yl)piperazine-1-carboxylate



Procedure

Allyl acetate **2g** (108.7 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 °C, 24 hr). The title compound was obtained in 65% yield (48.9 mg, 0.130 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

TLC (SiO_2): R_f = 0.15 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 2H), 6.08 (ddd, J = 17.6, 10.3, 7.8 Hz, 1H), 5.27 (d, J = 10.3 Hz, 1H), 5.19 (d, J = 17.1 Hz, 1H), 4.67 (d, J = 7.0 Hz, 1H), 4.57 (d, J = 7.0 Hz, 1H), 4.50 – 4.41 (m, 2H), 3.77 (dd, J = 6.5, 4.1 Hz, 4H), 3.67 (d, J = 7.8 Hz, 1H), 3.48 (dd, J = 6.5, 4.0 Hz, 4H), 2.84 (s, 1H), 1.48 (s, 9H).

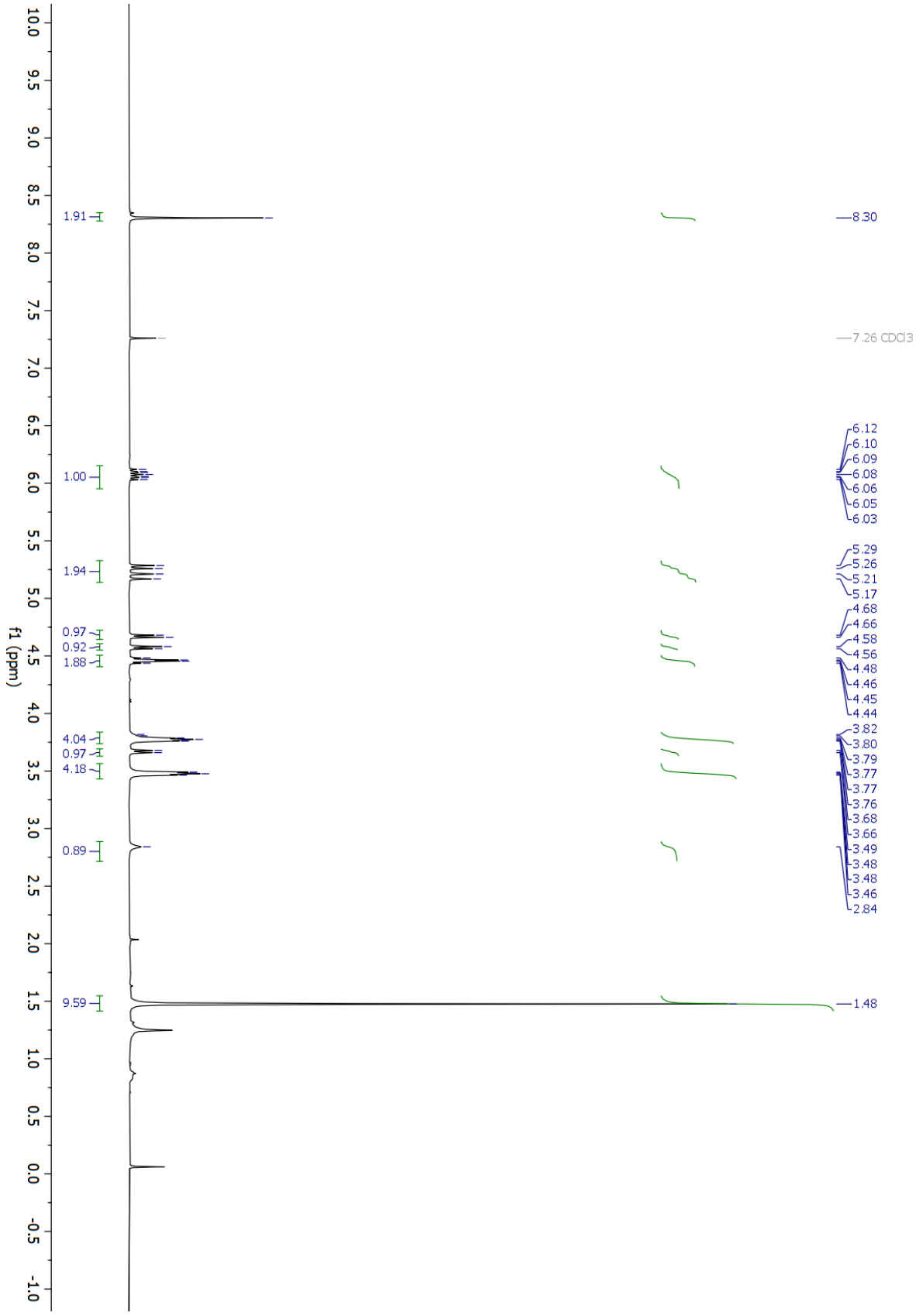
^{13}C NMR (101 MHz, $CDCl_3$): δ 161.1, 158.2, 155.0, 134.9, 120.2, 119.1, 83.3, 82.7, 80.2, 76.0, 51.1, 43.8, 28.6.

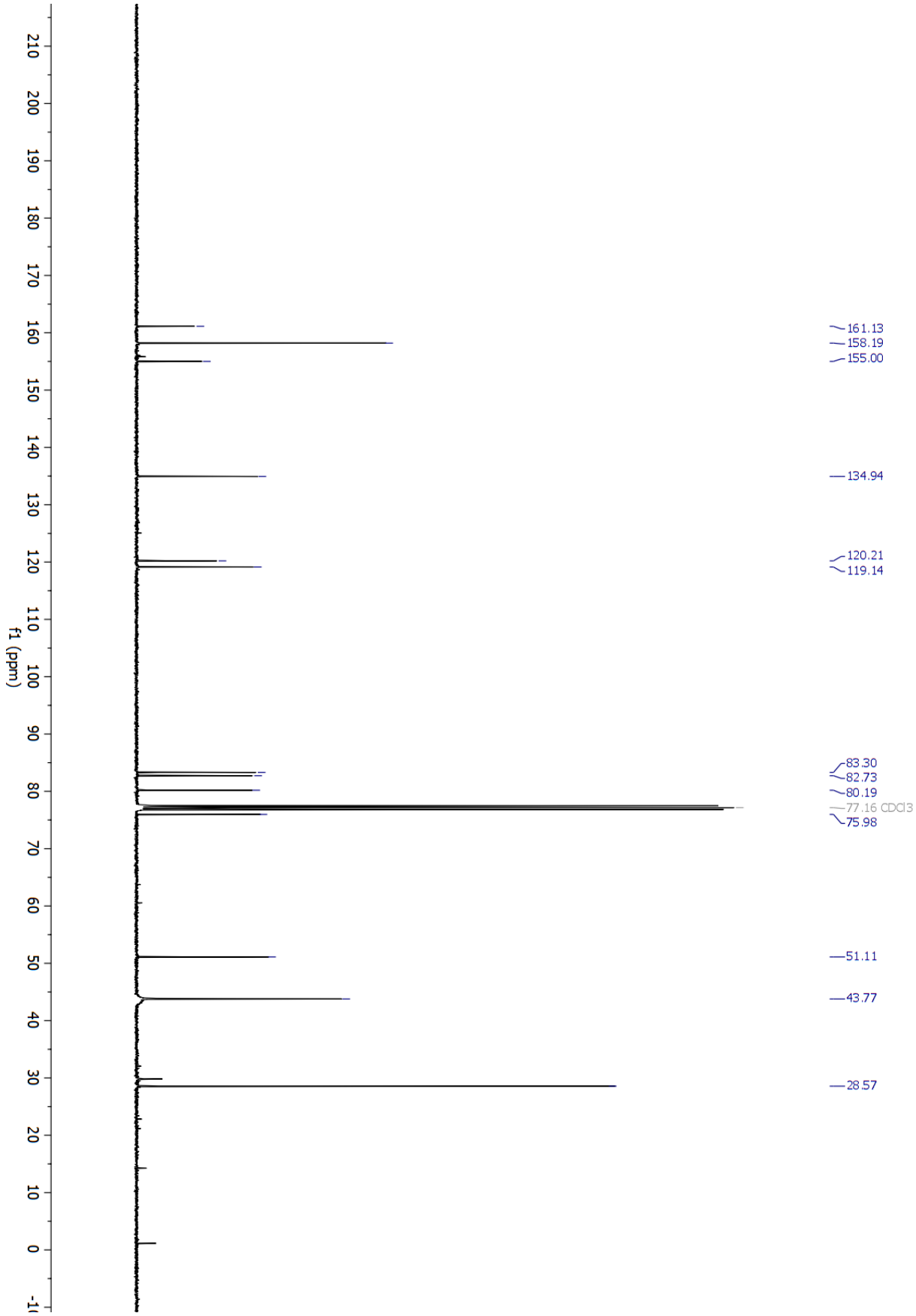
HRMS (ESI): Calculated for $C_{19}H_{28}N_4O_4$ [M+Na^+]= 399.2003, found= 399.2012

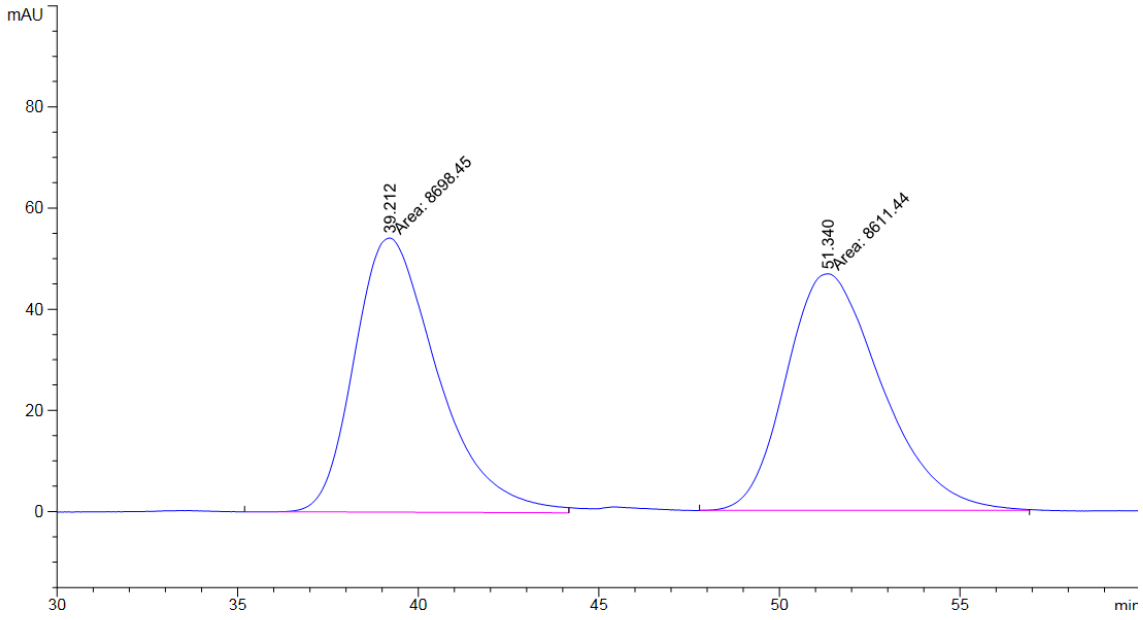
FTIR (neat): 3374, 2929, 2870. 2362, 1696, 1671, 1600, 1538, 1450, 1422, 1363, 1245, 1167, 1130, 998, 951, 798, 770, 667cm^{-1}.

$[\alpha]_D^{28}$= -22.0 (*c* 0.10, $CHCl_3$)

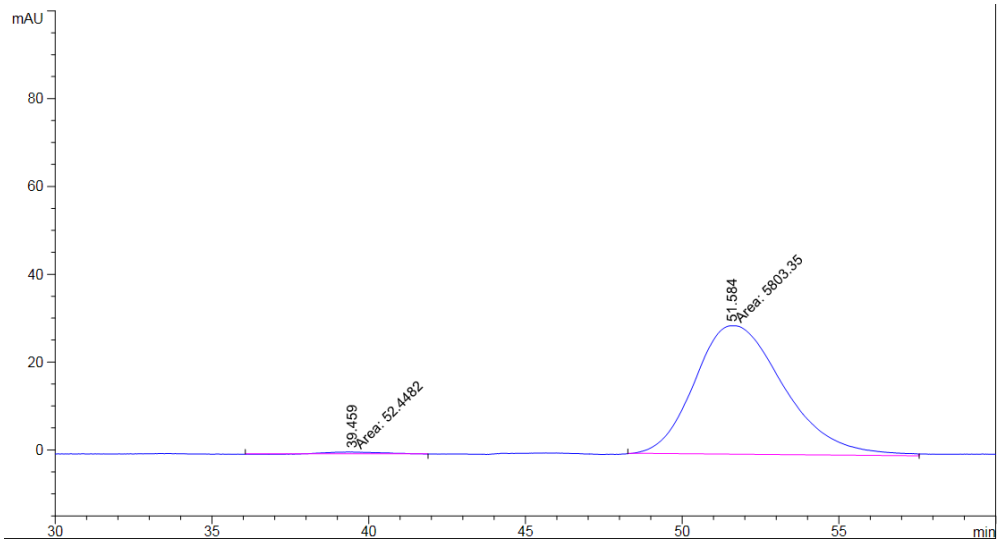
HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 98%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.91
1.00
1.94
0.97
0.92
1.88
4.04
0.97
4.18
0.89
9.59
8.30
7.26 CDCl3
6.12
6.10
6.09
6.08
6.06
6.05
6.03
5.29
5.26
5.21
5.17
4.68
4.66
4.58
4.56
4.48
4.46
4.45
4.44
3.82
3.80
3.79
3.77
3.77
3.76
3.68
3.66
3.49
3.48
3.48
3.46
2.84
1.48


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
161.13
158.19
155.00
134.94
120.21
119.14
83.30
82.73
80.19
77.16 CDCl3
75.98
51.11
43.77
28.57

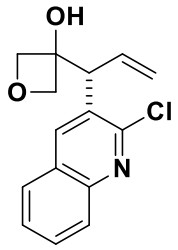


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.212	MM	2.6735	8698.45313	54.22733	50.2513
2	51.340	MM	3.0684	8611.44141	46.77451	49.7487



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.459	MM	2.0776	52.44817	4.20753e-1	0.8957
2	51.584	MM	3.3071	5803.34717	29.24699	99.1043

(3h) (R)-3-(1-(2-chloroquinolin-3-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2h** (79.0 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 18 hr). The title compound was obtained in 84% yield (46.3 mg, .0170 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

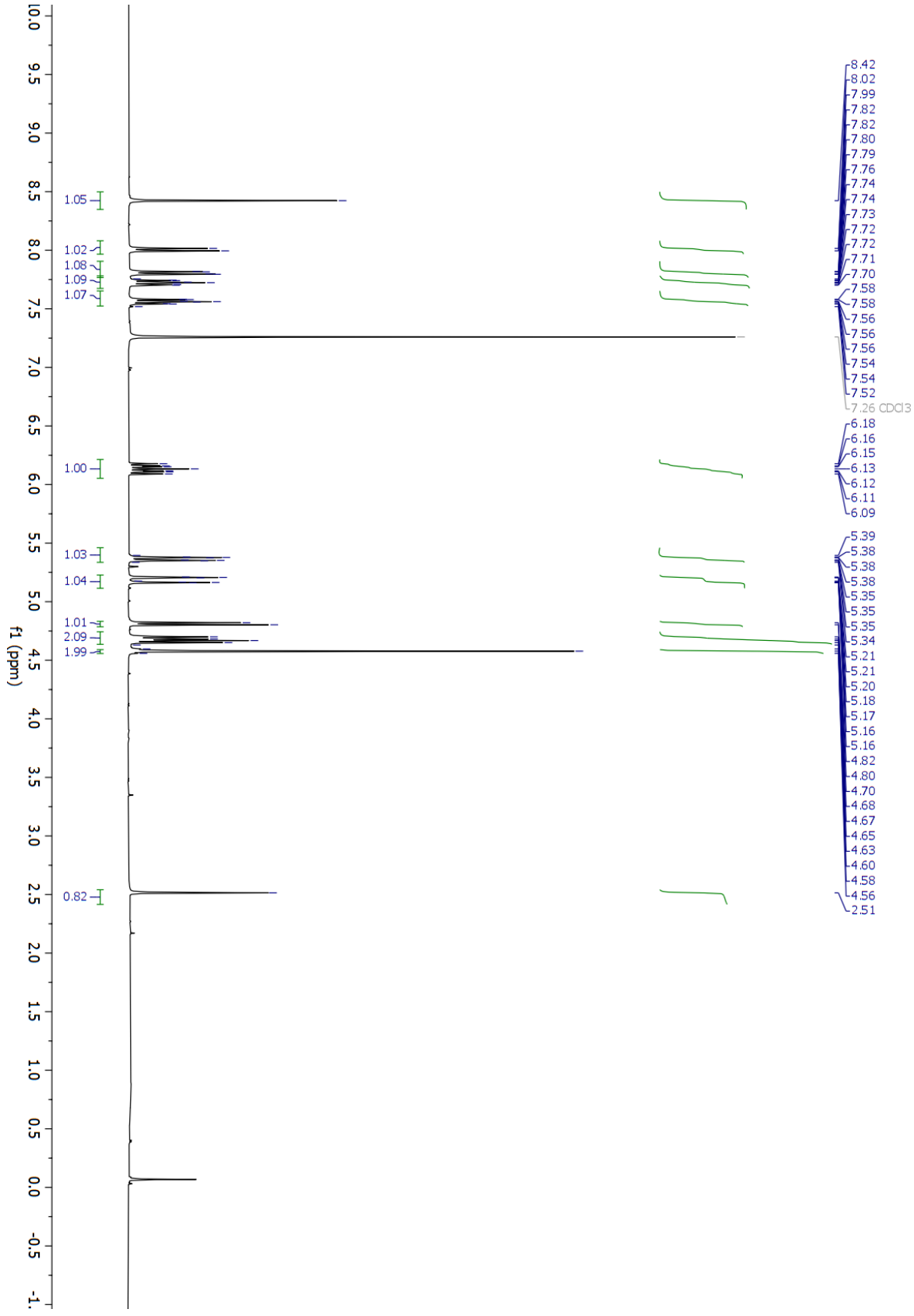
TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 2:1).

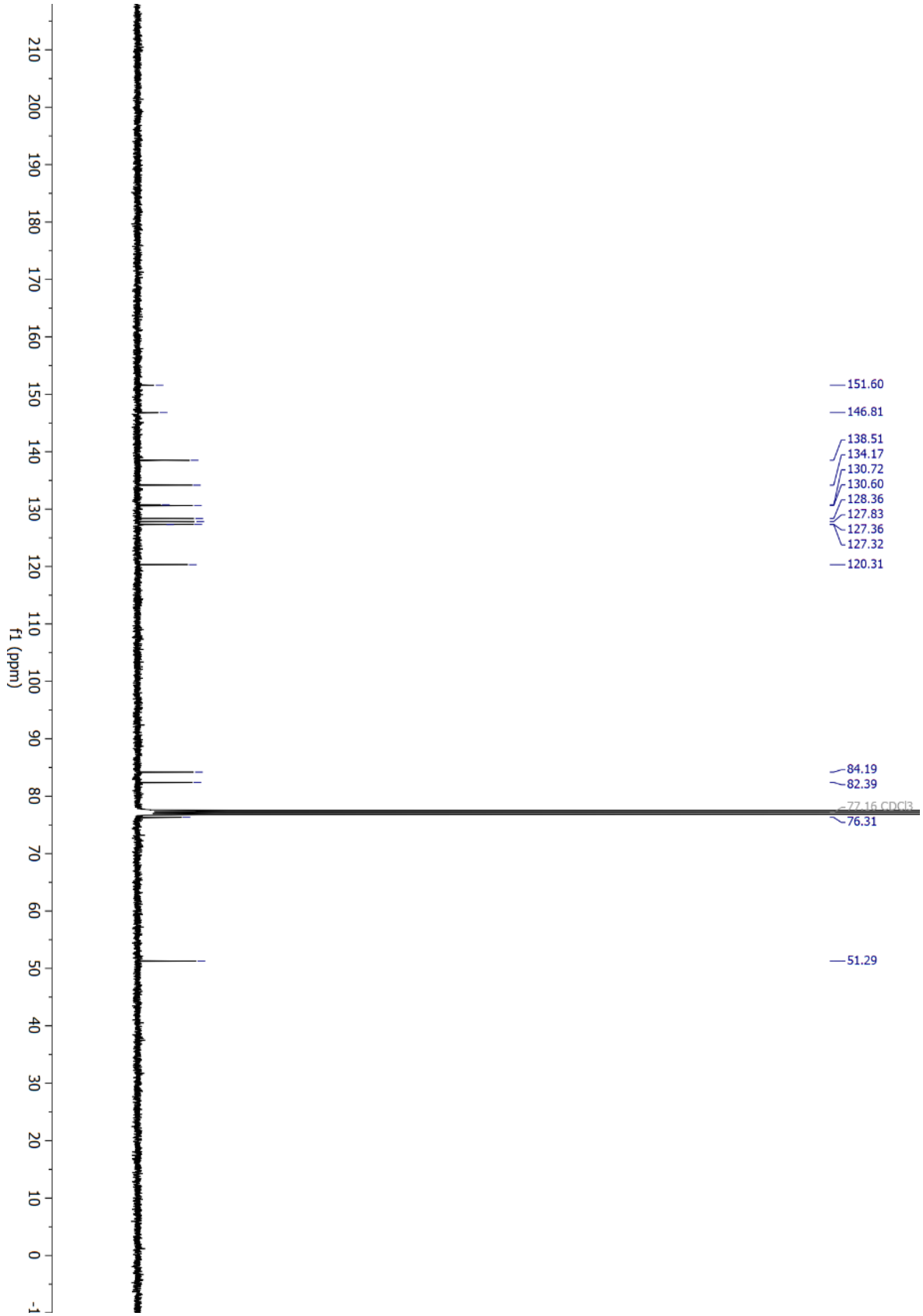
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.81 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.72 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.56 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.13 (ddd, *J* = 17.4, 10.3, 7.4 Hz, 1H), 5.36 (dt, *J* = 10.3, 1.0 Hz, 1H), 5.19 (dt, *J* = 17.2, 1.2 Hz, 1H), 4.81 (d, *J* = 7.0 Hz, 1H), 4.67 (dd, *J* = 12.5, 7.2 Hz, 2H), 4.58 (s, 2H), 2.51 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 151.6, 146.8, 138.5, 134.2, 130.7, 130.6, 128.4, 127.8, 127.4, 127.3, 120.3, 84.2, 82.4, 76.3, 51.3.
HRMS (ESI): Calculated for $C_{15}H_{14}ClNO_2$ [M+H+] = 276.0786, Found 276.0791

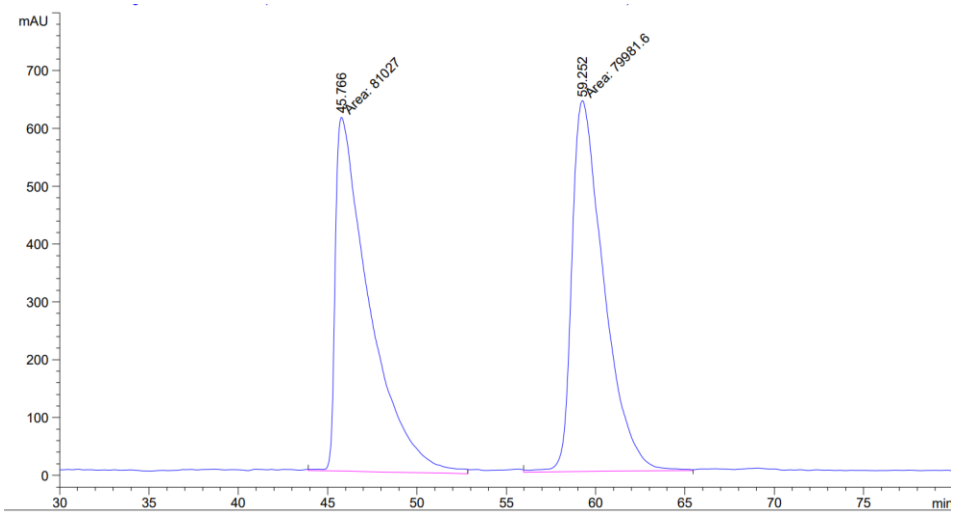
FTIR (neat): 3350, 3064, 2952, 2874, 1635, 1488, 1331, 1137, 1034, 968 cm^{-1}.

$[\alpha]_D^{28}$ = -46.0 (c 0.1, $CHCl_3$)

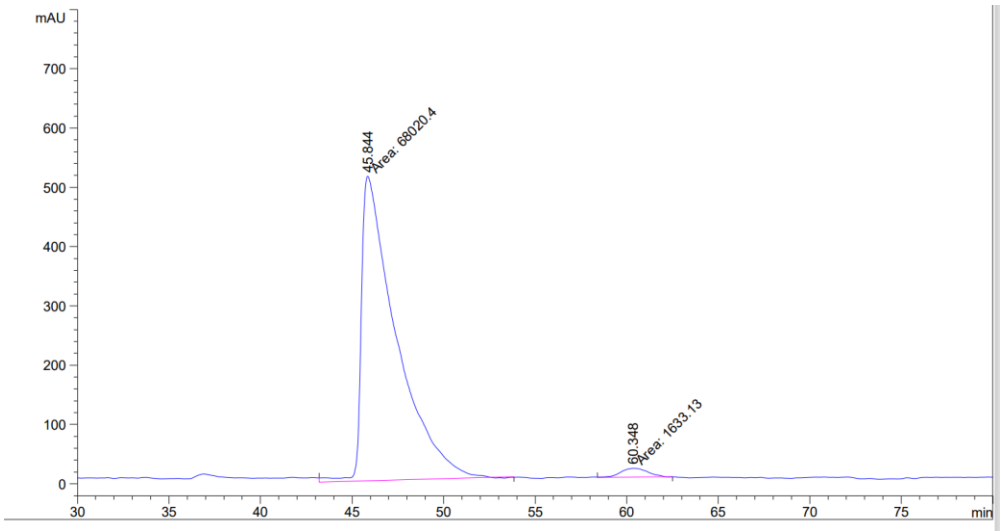
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm): *ee* = 96%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
1.05
1.02
1.08
1.09
1.07
1.00
1.03
1.04
1.01
2.09
1.99
0.82
8.42
8.02
7.99
7.82
7.82
7.80
7.79
7.76
7.74
7.74
7.73
7.72
7.72
7.71
7.70
7.58
7.58
7.56
7.56
7.56
7.54
7.54
7.52
7.26 CDCl3
6.18
6.16
6.15
6.13
6.12
6.11
6.09
5.39
5.38
5.38
5.38
5.35
5.35
5.35
5.34
5.21
5.21
5.20
5.18
5.17
5.16
5.16
4.82
4.80
4.70
4.68
4.67
4.65
4.63
4.60
4.58
4.56
2.51


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
151.60
146.81
138.51
134.17
130.72
130.60
128.36
127.83
127.36
127.32
120.31
84.19
82.39
77.16 CDCl3
76.31
51.29

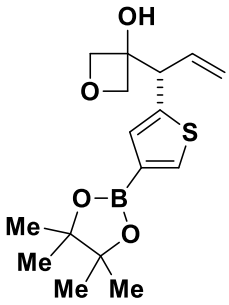


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	45.766	MM	2.2075	8.10270e4	611.76801	50.3247
2	59.252	MM	2.0787	7.99816e4	641.29346	49.6753



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	45.844	MM	2.2062	6.80204e4	513.84814	97.6554
2	60.348	MM	1.7756	1633.12781	15.32931	2.3446

(3i) (S)-3-(1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2i (**92.5 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 ^{o}C, 18 hr). The title compound was obtained in 69% yield (44.5 mg, 0.138 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.25 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 1.1 Hz, 1H), 7.14 (s, 3H), 6.03 (ddd, J = 16.9, 10.2, 8.3 Hz, 2H), 5.28 – 5.16 (m, 3H), 4.60 (t, J = 6.5 Hz, 3H), 4.53 (d, J = 7.0 Hz, 1H), 4.47 (d, J = 7.0 Hz, 1H), 4.08 (d, J = 8.1 Hz, 1H), 1.50 (s, 1H), 1.26 (s, 12H).

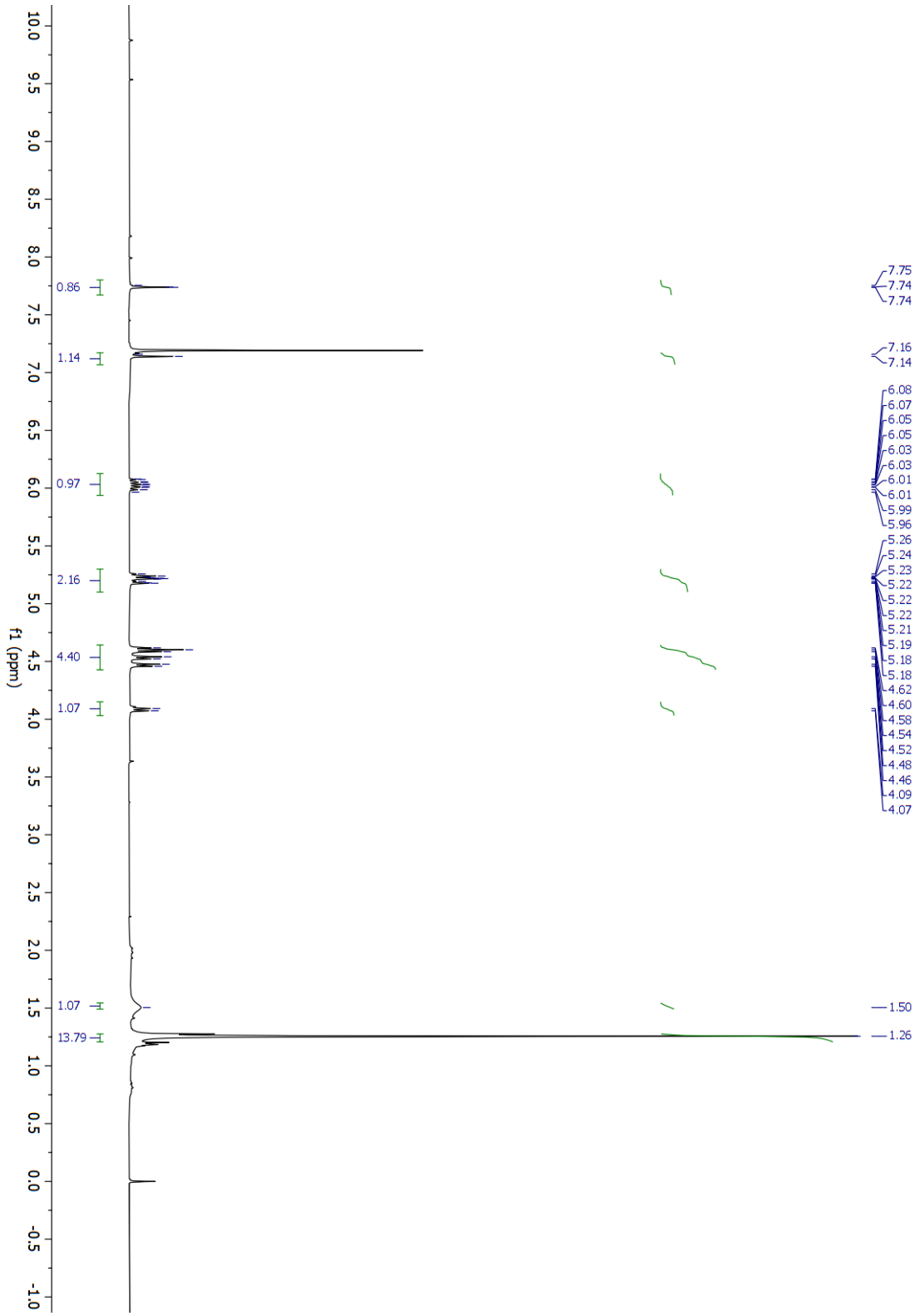
^{13}C NMR (126 MHz, $CDCl_3$): δ 140.9, 136.5, 135.1, 131.0, 119.3, 83.9, 82.5, 81.8, 75.9, 52.0, 28.6, 25.0.

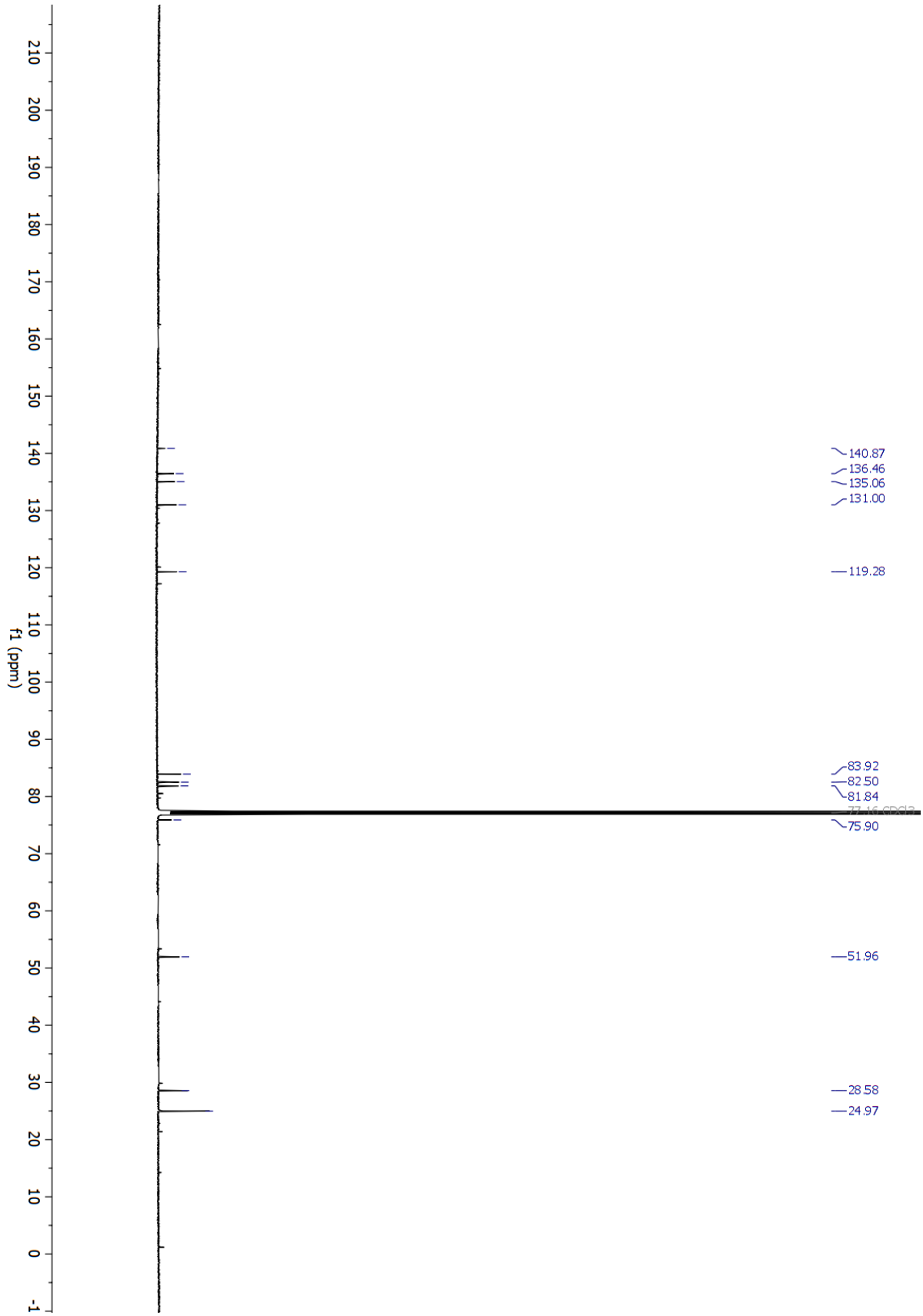
HRMS (ESI): Calculated for $C_{16}H_{23}BO_4S$ [M+Na^+]= 345.1305, found= 345.1311

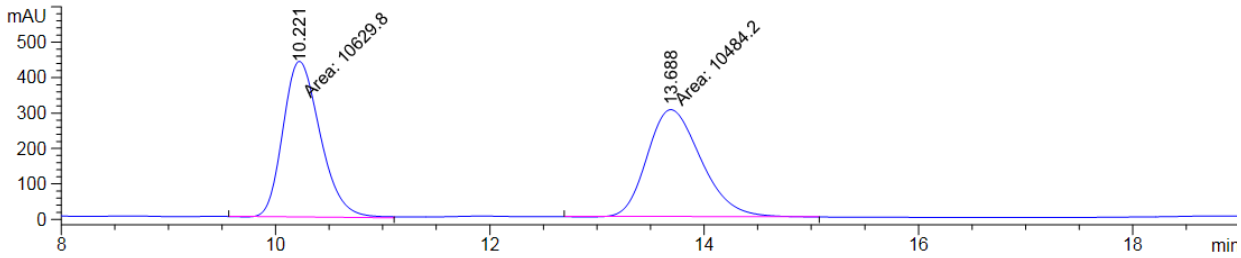
FTIR (neat): 3417, 2978, 2956, 2876, 1537, 1453, 1372, 1310, 1261, 1143, 1110, 966, 885, 687 cm^{-1}

$[\alpha]_D^{28}$= -33.0 (*c* 0.10, $CHCl_3$)

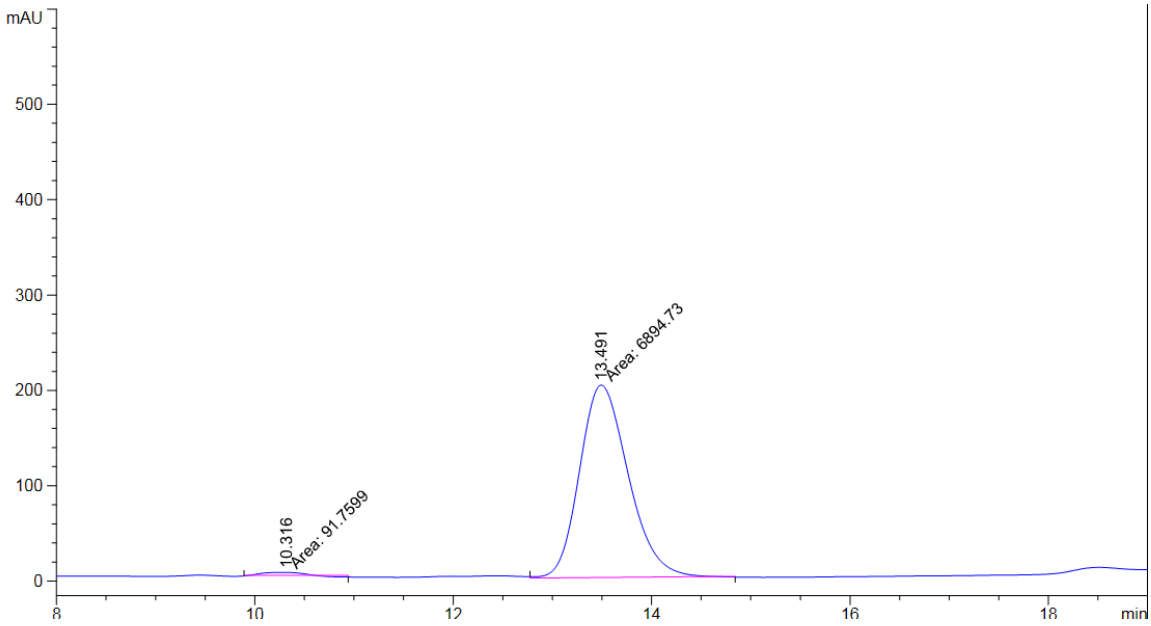
HPLC (Chiralcel AS-H hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm): *ee* = 98%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.86
1.14
0.97
2.16
4.40
1.07
1.07
13.79
7.75
7.74
7.74
7.16
7.14
6.08
6.07
6.05
6.05
6.03
6.03
6.01
6.01
5.99
5.96
5.26
5.24
5.23
5.22
5.22
5.22
5.21
5.19
5.18
5.18
4.62
4.60
4.58
4.54
4.52
4.48
4.46
4.09
4.07
1.50
1.26


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
140.87
136.46
135.06
131.00
119.28
83.92
82.50
81.84
77.16 CDCl3
75.90
51.96
28.58
24.97

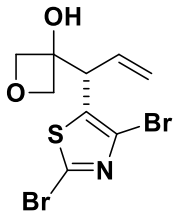


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.221	MM	0.4035	1.06298e4	439.10687	50.3448
2	13.688	MM	0.5796	1.04842e4	301.46143	49.6552



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.316	MM	0.4689	91.75986	3.26146	1.3134
2	13.491	MM	0.5690	6894.72949	201.97038	98.6866

(3j) (S)-3-(1-(2,4-dibromothiazol-5-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2j (**102.3 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 ^{o}C, 24 hr). The title compound was obtained in 73% yield (51.8 mg, 0.146 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.31 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85 (ddd, J = 17.3, 10.2, 7.4 Hz, 1H), 5.32 (d, J = 10.2 Hz, 1H), 5.29 – 5.15 (m, 1H), 4.70 (d, J = 7.5 Hz, 1H), 4.58 (d, J = 7.3 Hz, 1H), 4.48 (d, J = 7.3 Hz, 1H), 4.44 (d, J = 0.8 Hz, 1H), 4.41 (d, J = 7.5 Hz, 1H), 2.55 – 2.50 (m, 1H).

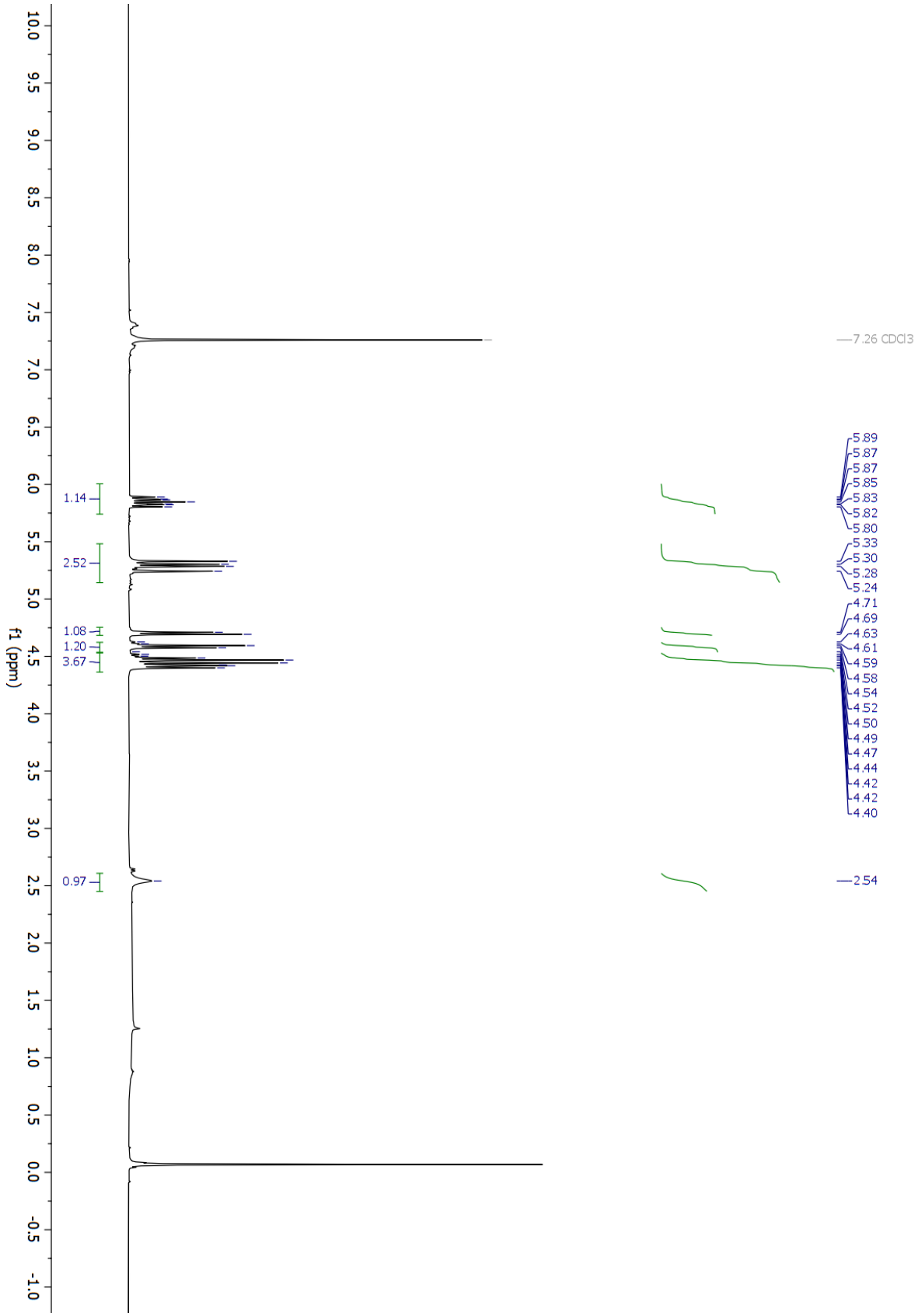
^{13}C NMR (101 MHz, $CDCl_3$): δ 134.2, 133.0, 124.9, 120.8, 82.9, 82.8, 51.1, 30.2.

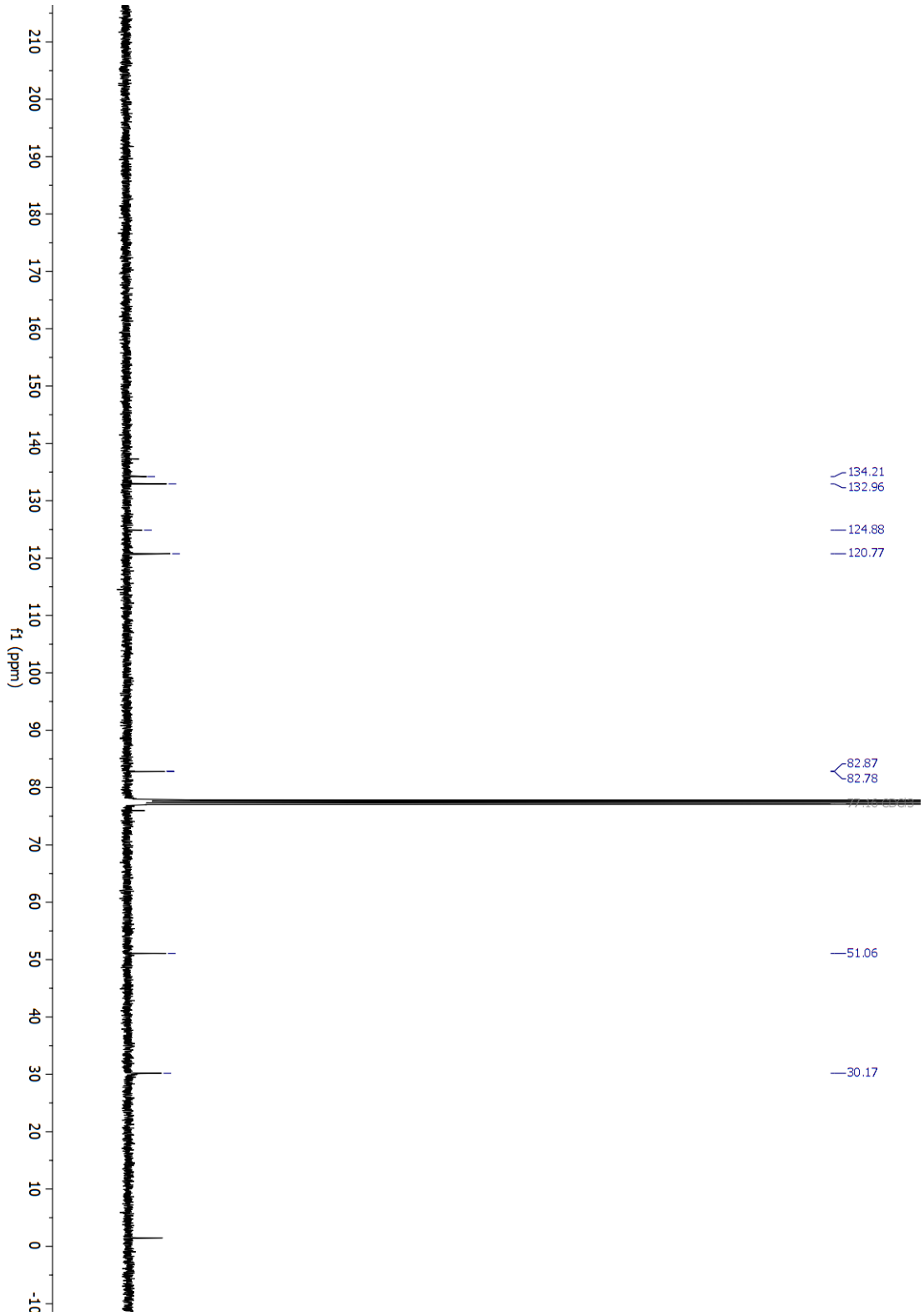
HRMS (ESI): Calculated for $C_{10}H_{14}O_3$ [M+Na^+]= 355.8773, found= 355.8776

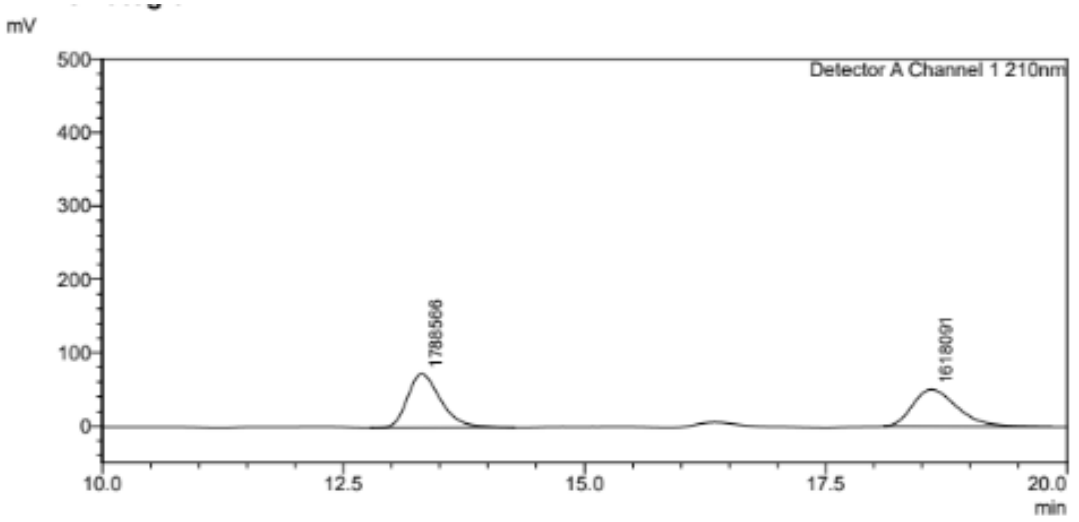
FTIR (neat): 3330, 3017, 2970, 2953, 1635, 1575, 1407, 1365, 1229, 1216, 1109, 1021, 885, 668 cm^{-1}

$[\alpha]_D^{28}$= -54.2 (*c* 0.10, $CHCl_3$)

HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 99%

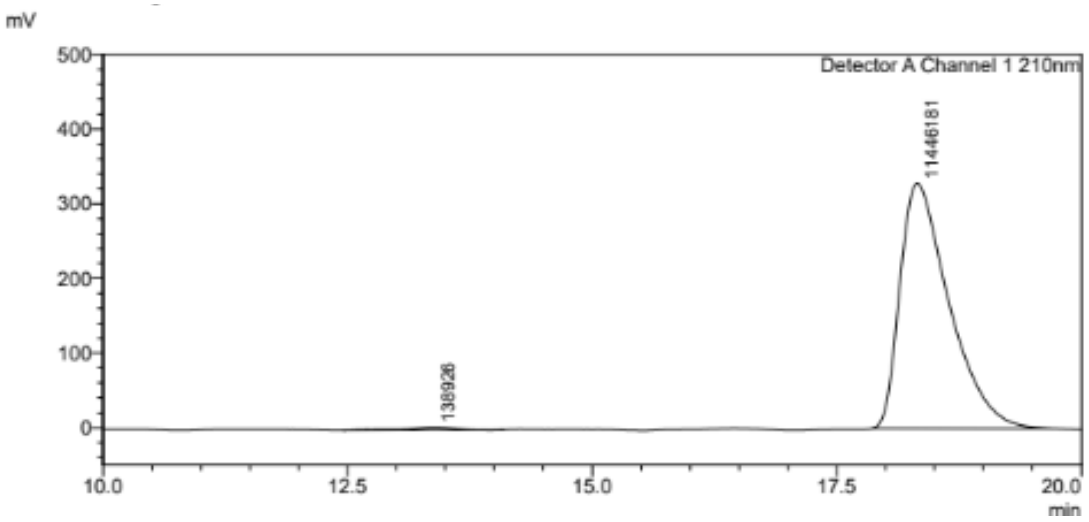

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.14
2.52
1.08
1.20
3.67
0.97
7.26 CDCl3
5.89
5.87
5.87
5.85
5.83
5.82
5.80
5.33
5.30
5.28
5.24
4.71
4.69
4.63
4.61
4.59
4.58
4.54
4.52
4.50
4.49
4.47
4.44
4.42
4.42
4.40
2.54


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
134.21
132.96
124.88
120.77
82.87
82.78
51.06
30.17



Detector A Channel 1 210nm

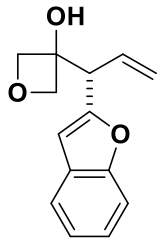
Ret. Time	Height	Area	Area%
13.312	73522	1788566	52.502
18.595	50154	1618091	47.498
	123676	3406657	100.000



Detector A Channel 1 210nm

Ret. Time	Height	Area	Area%
13.382	4411	138926	1.199
18.323	328176	11446181	98.801
	332588	11585107	100.000

(3k) (S)-3-(1-(benzofuran-2-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2k** (64.9 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 °C, 18 hr). The title compound was obtained in 99% yield (45.6 mg, 0.190 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

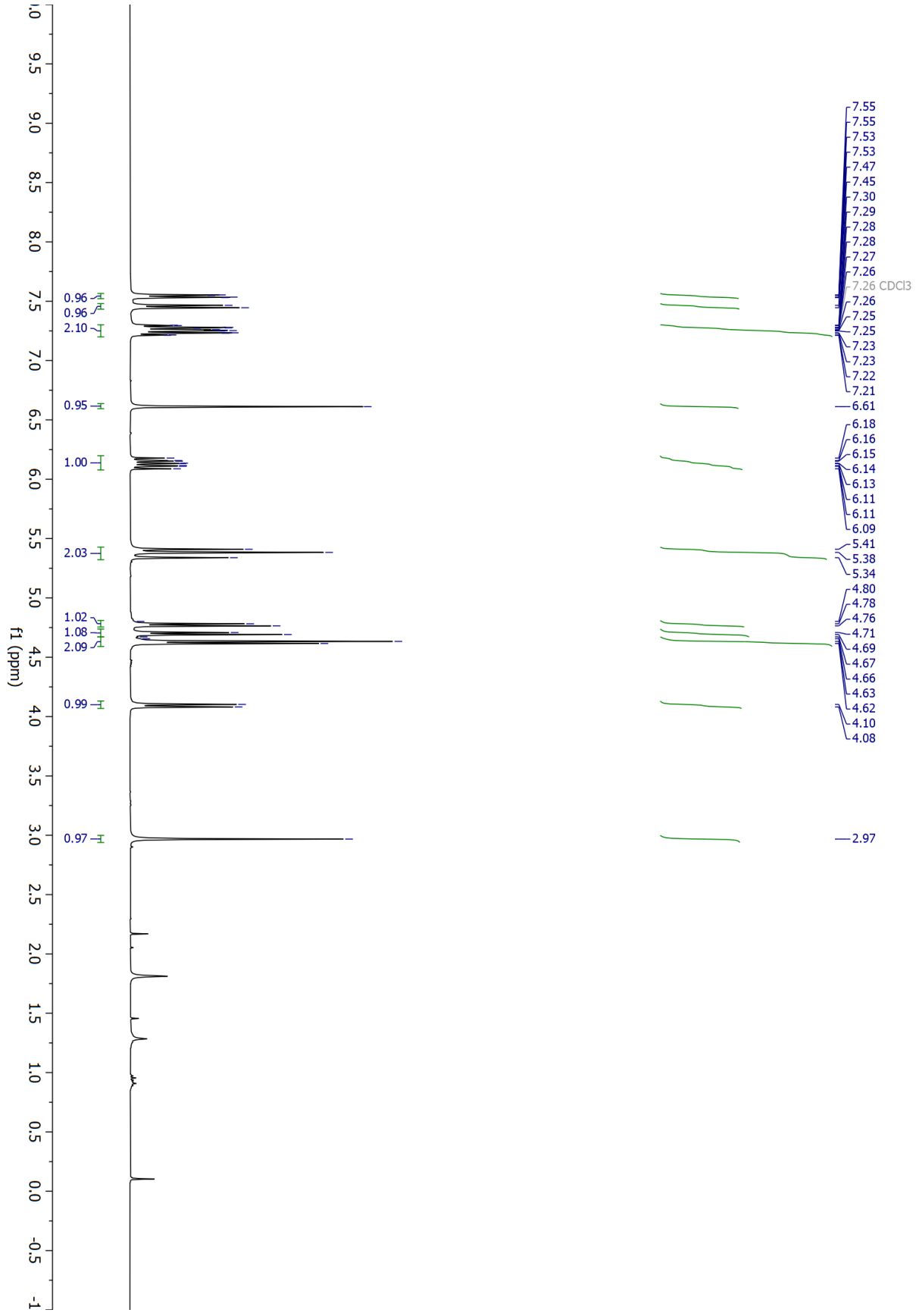
TLC (SiO_2): R_f = 0.21 (hexanes: ethyl acetate = 4:1).

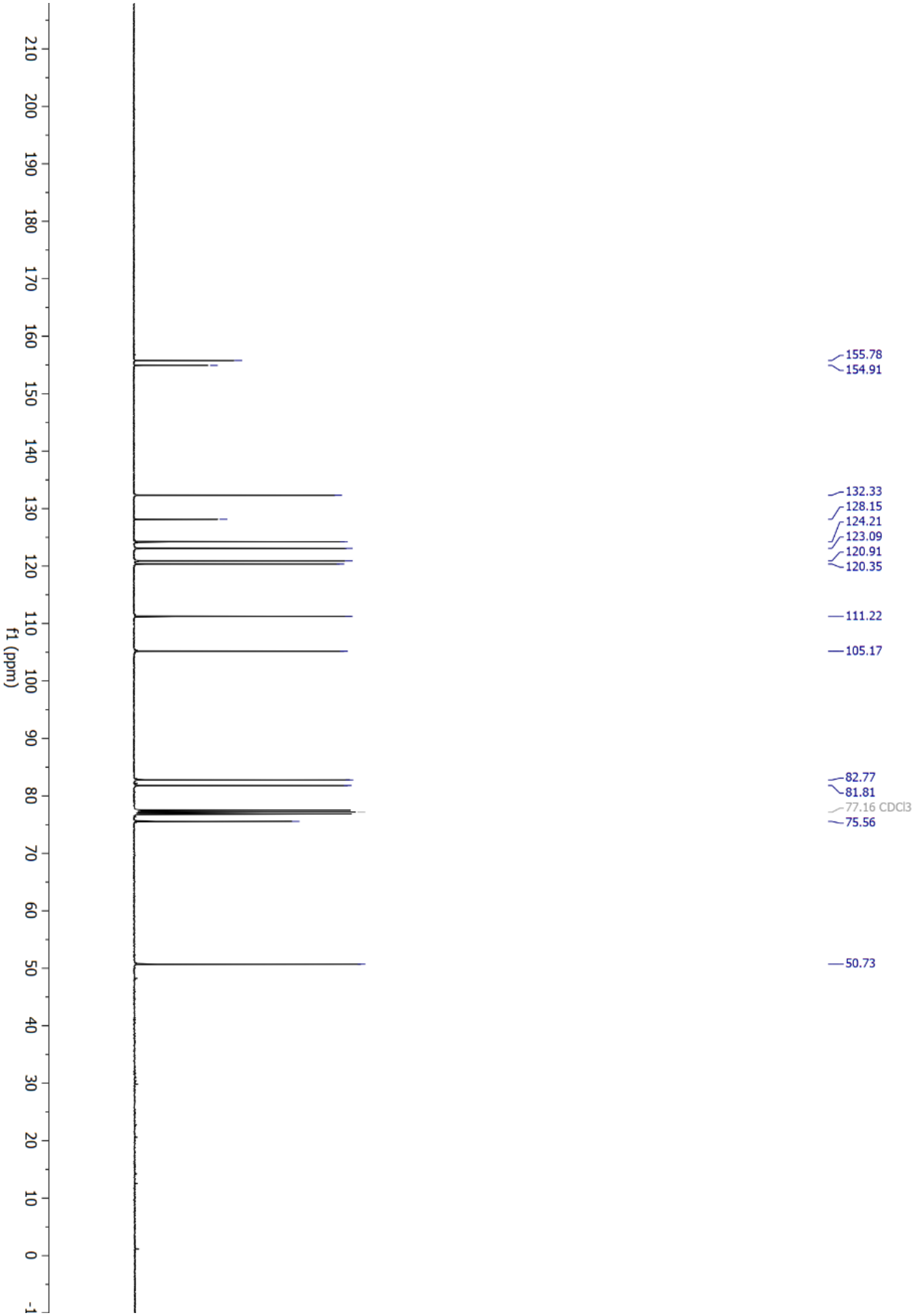
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.32 – 7.19 (m, 2H), 6.61 (s, 1H), 6.13 (ddd, *J* = 17.0, 10.3, 8.4 Hz, 1H), 5.43 – 5.32 (m, 2H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.70 (d, *J* = 7.0 Hz, 1H), 4.62 (d, *J* = 7.1 Hz, 2H), 4.09 (d, *J* = 8.4 Hz, 1H), 2.97 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 155.8, 154.9, 132.3, 128.1, 124.2, 123.1, 120.9, 120.3, 111.2, 105.2, 82.8, 81.8, 75.6, 50.7.
HRMS (ESI): (ESI): Calculated for $C_{14}H_{14}O_3$ [M+Na^+] = 253.0835, Found 253.0843

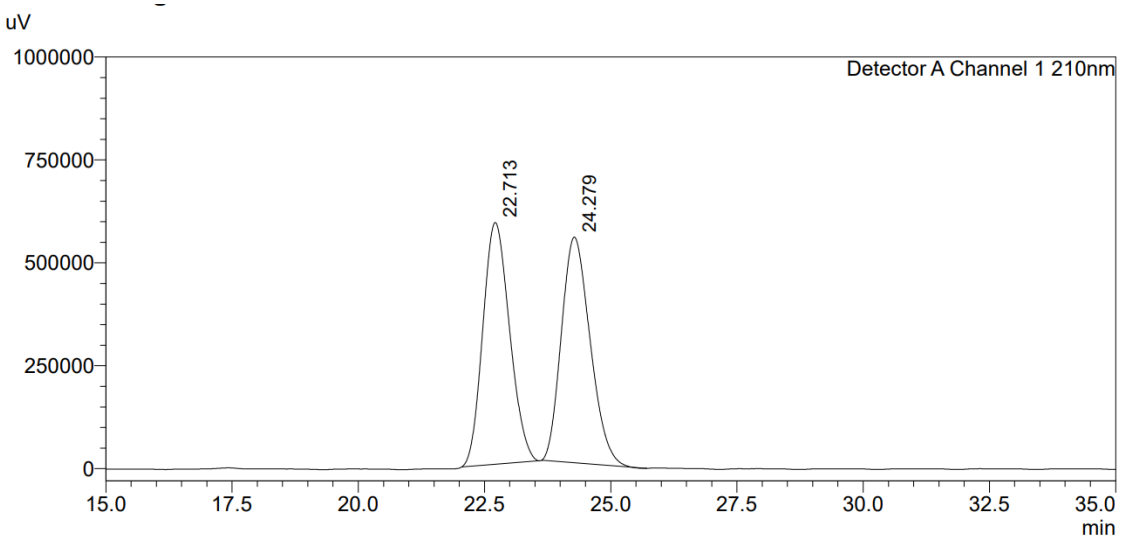
FTIR (neat): 3364, 2951, 2876, 1738, 1582, 1453, 1365, 1254, 1171cm^{-1}

$[\alpha]_D^{28}$= -34.0 (c 0.1, CDCl3)

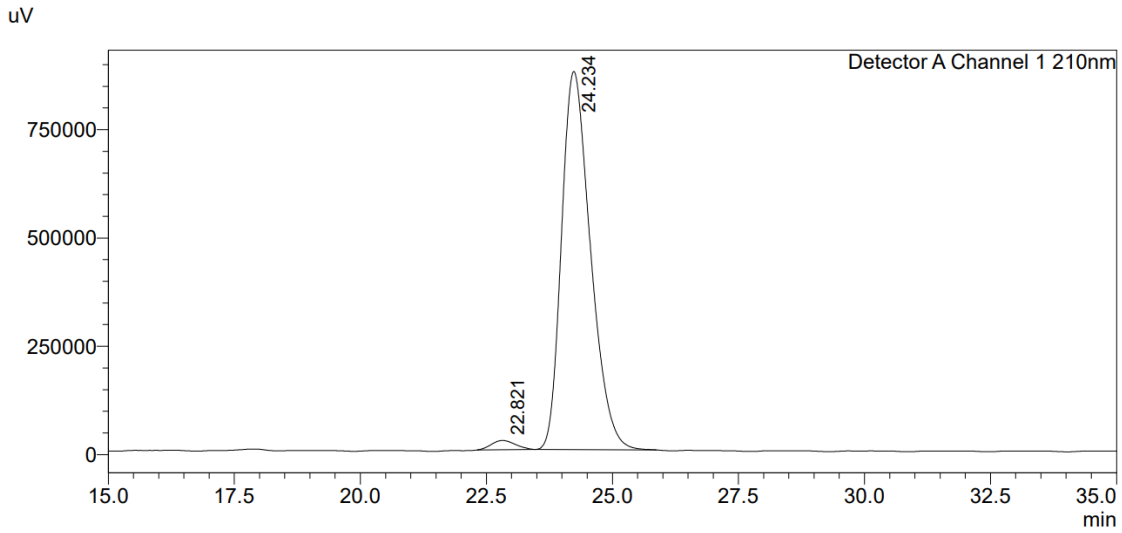
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 96%.


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
0.96
0.96
2.10
0.95
1.00
2.03
1.02
1.08
2.09
0.99
0.97
7.55
7.55
7.53
7.53
7.47
7.45
7.30
7.29
7.28
7.28
7.27
7.26
7.26 CDCl3
7.26
7.25
7.25
7.23
7.23
7.22
7.21
6.61
6.18
6.16
6.15
6.14
6.13
6.11
6.11
6.09
5.41
5.38
5.34
4.80
4.78
4.76
4.71
4.69
4.67
4.66
4.63
4.62
4.10
4.08
2.97


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
155.78
154.91
132.33
128.15
124.21
123.09
120.91
120.35
111.22
105.17
82.77
81.81
77.16 CDCl3
75.56
50.73

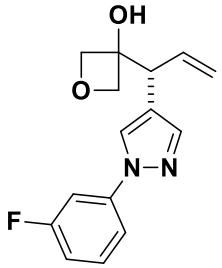


Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.713	21654153	587147	49.937	49.937
2	24.279	21708372	548058	50.063	50.063
Total		43362525	1135205		100.000



Peak#	Ret. Time	Area	Height	Conc.	Area%
1	22.821	699476	21309	1.965	1.965
2	24.234	34898791	872672	98.035	98.035
Total		35598266	893981		100.000

(3l) (*R*)-3-(1-(1-(3-fluorophenyl)-1*H*-pyrazol-4-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2l** (78.0 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 °C, 18 hr). The title compound was obtained in 71% yield (38.7 mg, 0.141 mmol) as a brown oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1—2:1).

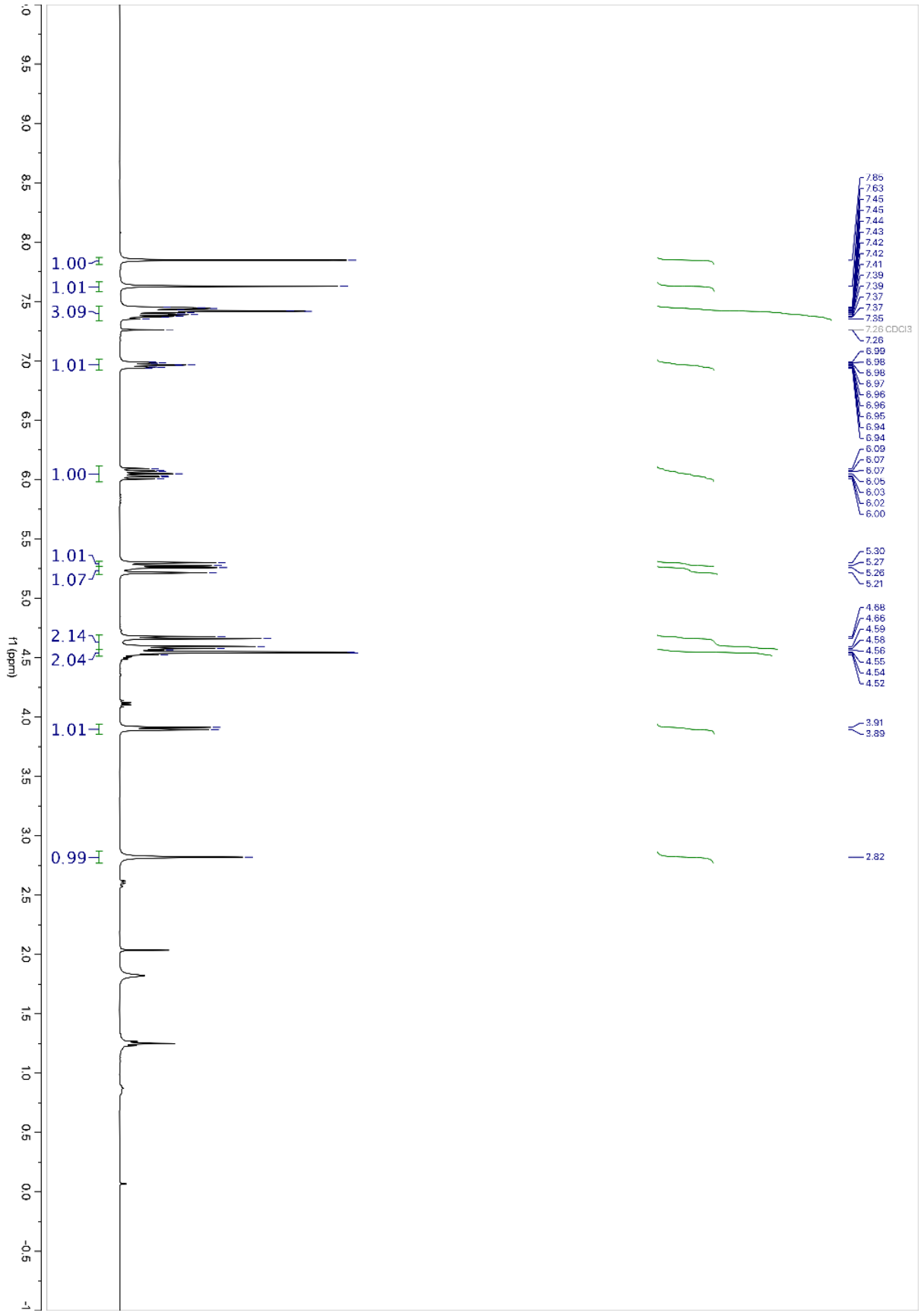
TLC (SiO_2): R_f = 0.35 (hexanes: ethyl acetate = 1:1).

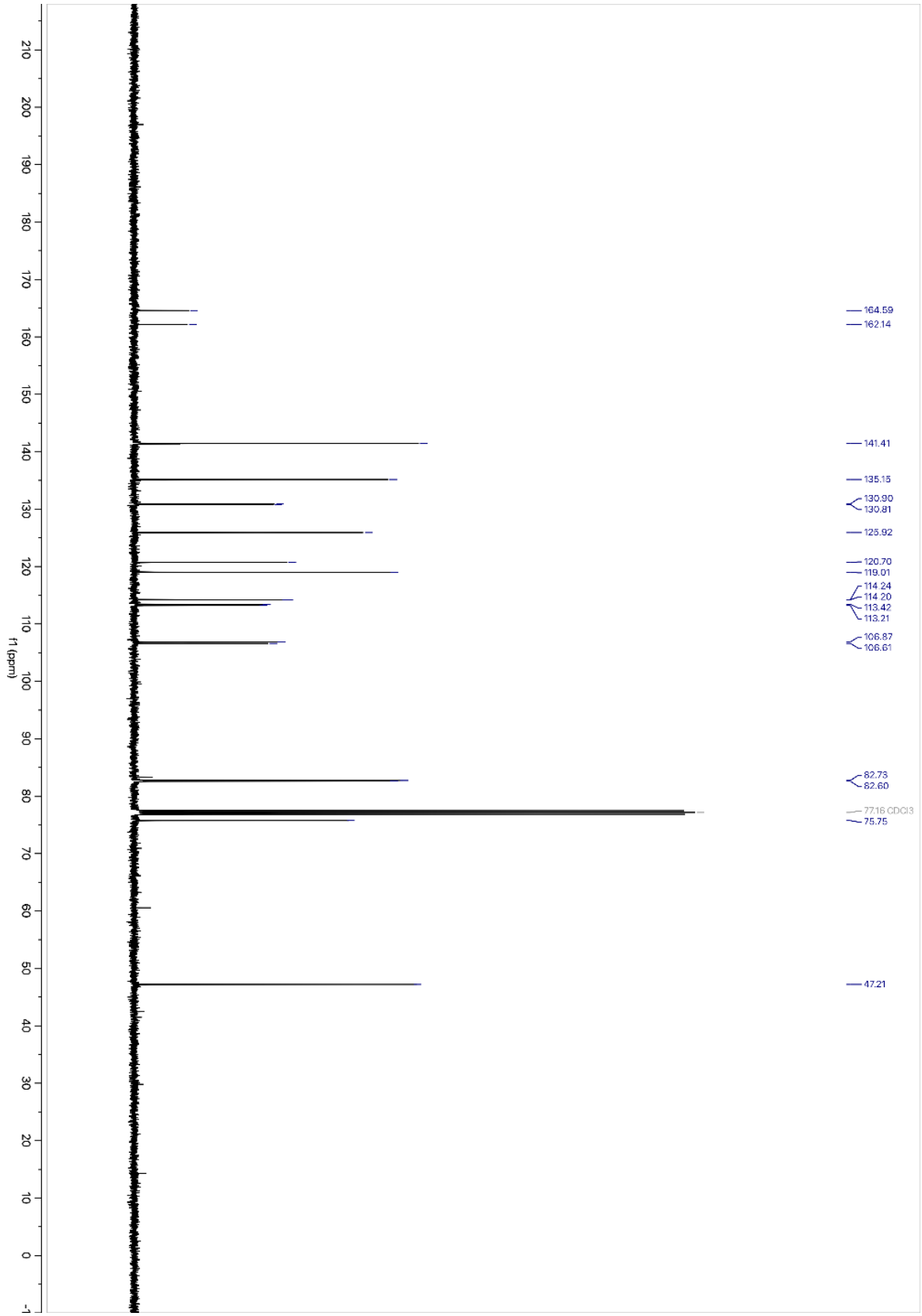
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.63 (s, 1H), 7.48 – 7.33 (m, 3H), 6.96 (tt, *J* = 8.5, 1.9 Hz, 1H), 6.05 (ddd, *J* = 17.6, 10.2, 7.9 Hz, 1H), 5.29 (d, *J* = 10.1 Hz, 1H), 5.24 (d, *J* = 17.1 Hz, 1H), 4.69 – 4.57 (m, 2H), 4.57 – 4.51 (m, 2H), 3.90 (d, *J* = 7.9 Hz, 1H), 2.82 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 163.4 (d, J = 246.6 Hz), 141.4, 135.1, 130.9 (d, J = 9.1 Hz), 125.9, 120.7, 119.0, 114.2 (d, J = 3.0 Hz), 113.3 (d, J = 21.3 Hz), 106.7 (d, J = 26.3 Hz), 82.7, 82.6, 75.8, 47.1.
^{19}F NMR (376 MHz, $CDCl_3$): δ -110.82.
HRMS (ESI): Calculated for $C_{15}H_{15}FN_2O_2$ [M+H$^+$] = 275.1190, Found 275.1193

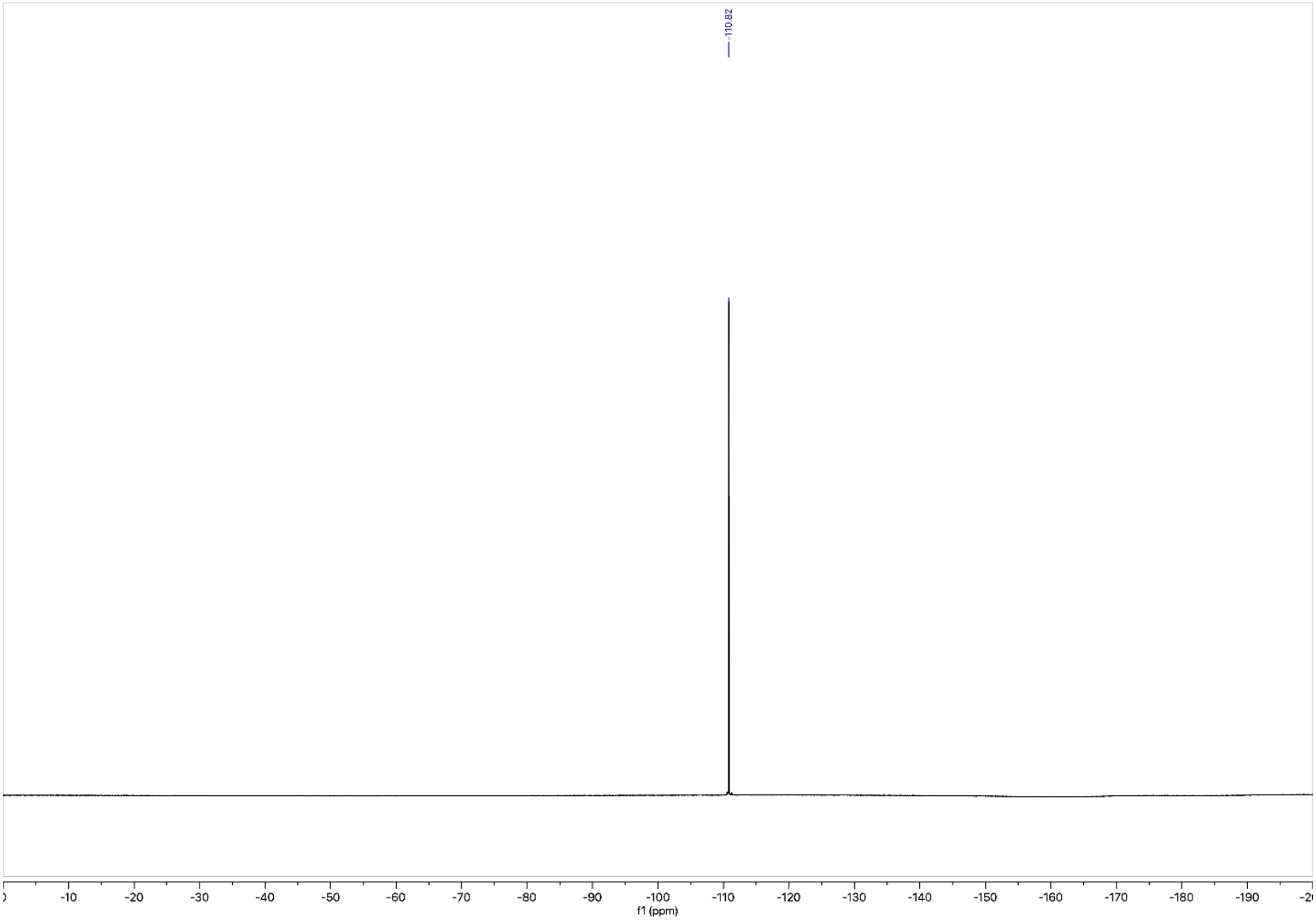
FTIR (neat): 3380, 2952, 2877, 1614, 1601, 1567, 1500, 1395, 1258, 1184, 1152, 969, 866, 662 cm^{-1}

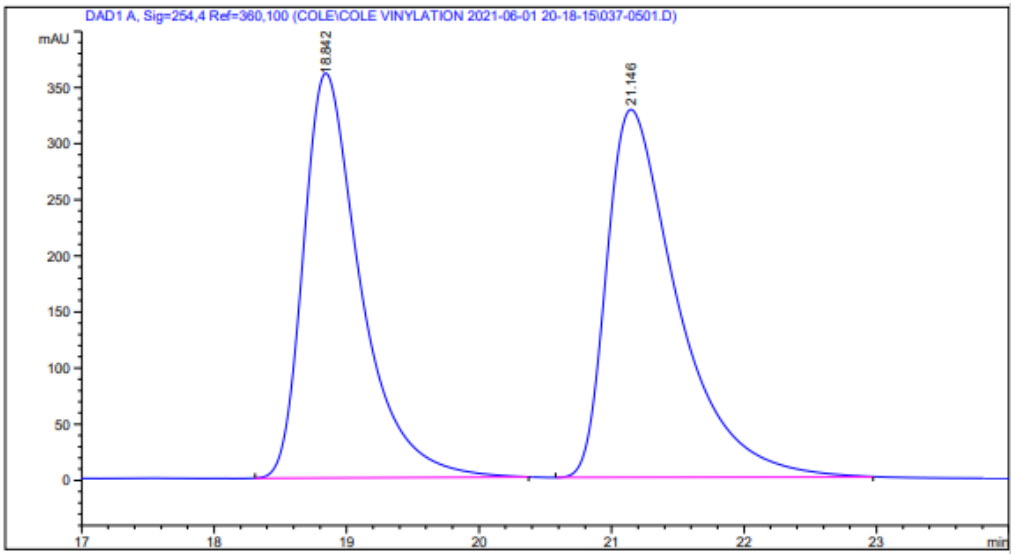
$[\alpha]_D^{28}$ = -45.0(*c* 0.10, $CHCl_3$).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): ee = 99%

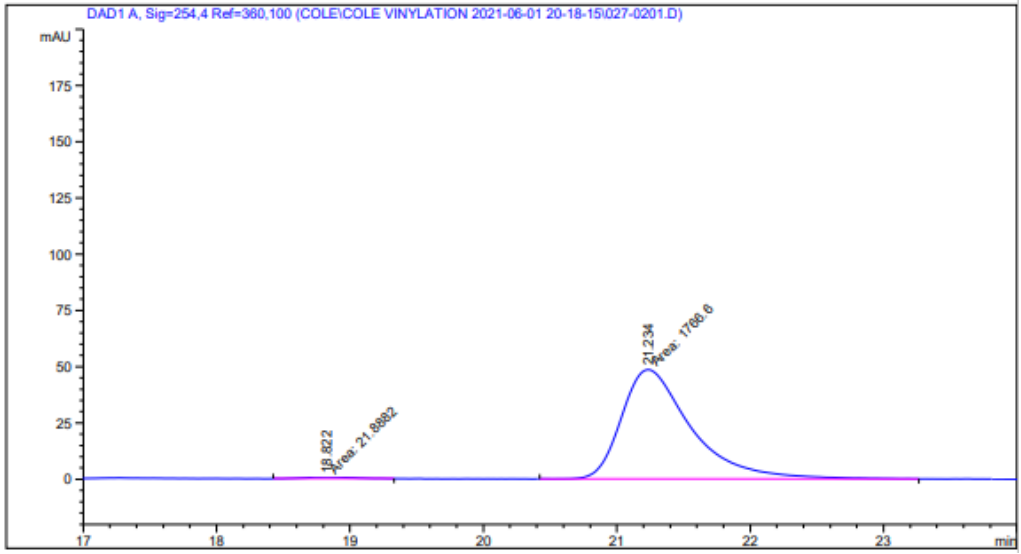

1.00
1.01
3.09
1.01
1.00
1.01
1.07
2.14
2.04
1.01
0.99
f1 (ppm)
7.85
7.63
7.45
7.45
7.44
7.43
7.42
7.42
7.41
7.39
7.39
7.37
7.37
7.35
7.26 CDCl3
7.26
6.99
6.98
6.98
6.97
6.96
6.96
6.95
6.94
6.94
6.09
6.07
6.07
6.05
6.03
6.02
6.00
5.30
5.27
5.26
5.21
4.68
4.66
4.59
4.58
4.56
4.55
4.54
4.52
3.91
3.89
2.82


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
164.59
162.14
141.41
135.15
130.90
130.81
125.92
120.70
119.01
114.24
114.20
113.42
113.21
106.87
106.61
82.73
82.60
77.16 CDCl3
75.75
47.21


-110.82
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

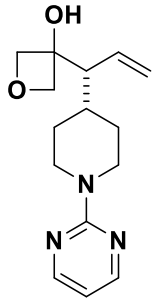


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.842	BB	0.4506	1.08369e4	360.57532	47.1051
2	21.146	BB	0.5554	1.21689e4	327.60324	52.8949



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.822	MM	0.4747	21.88818	7.68422e-1	1.2238
2	21.234	MM	0.6057	1766.59619	48.60963	98.7762

(3m) (*R*)-3-(1-(1-(pyrimidin-2-yl)piperidin-4-yl)allyl)oxetan-3-ol



Procedure

Allyl acetate **2m** (78.4 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 ^{o}C, 18 hr). The title compound was obtained in 68% yield (37.5 mg, 0.136 mmol) as a brown oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 2:1—1:1).

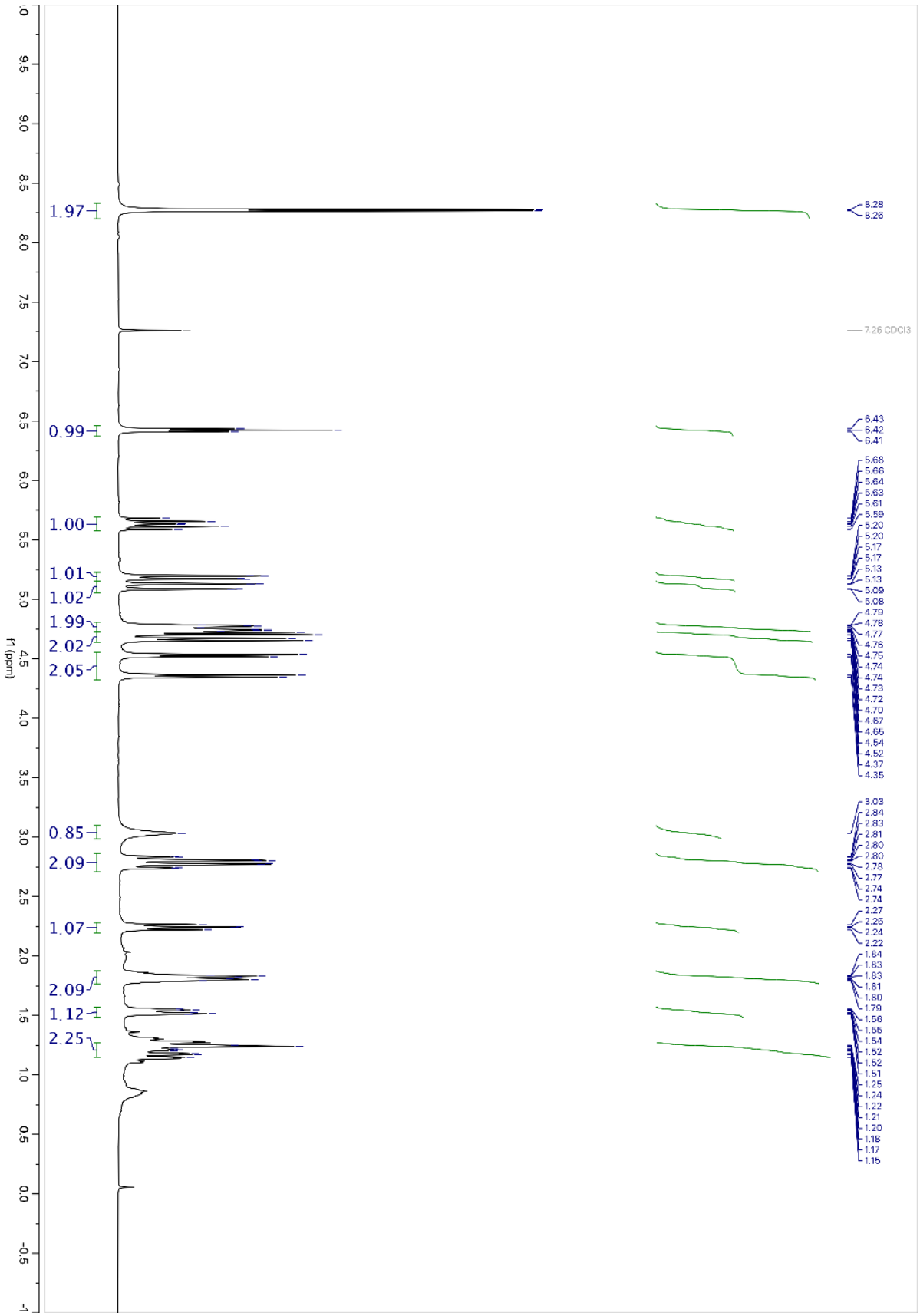
TLC (SiO_2): R_f = 0.13 (hexanes: ethyl acetate = 1:1).

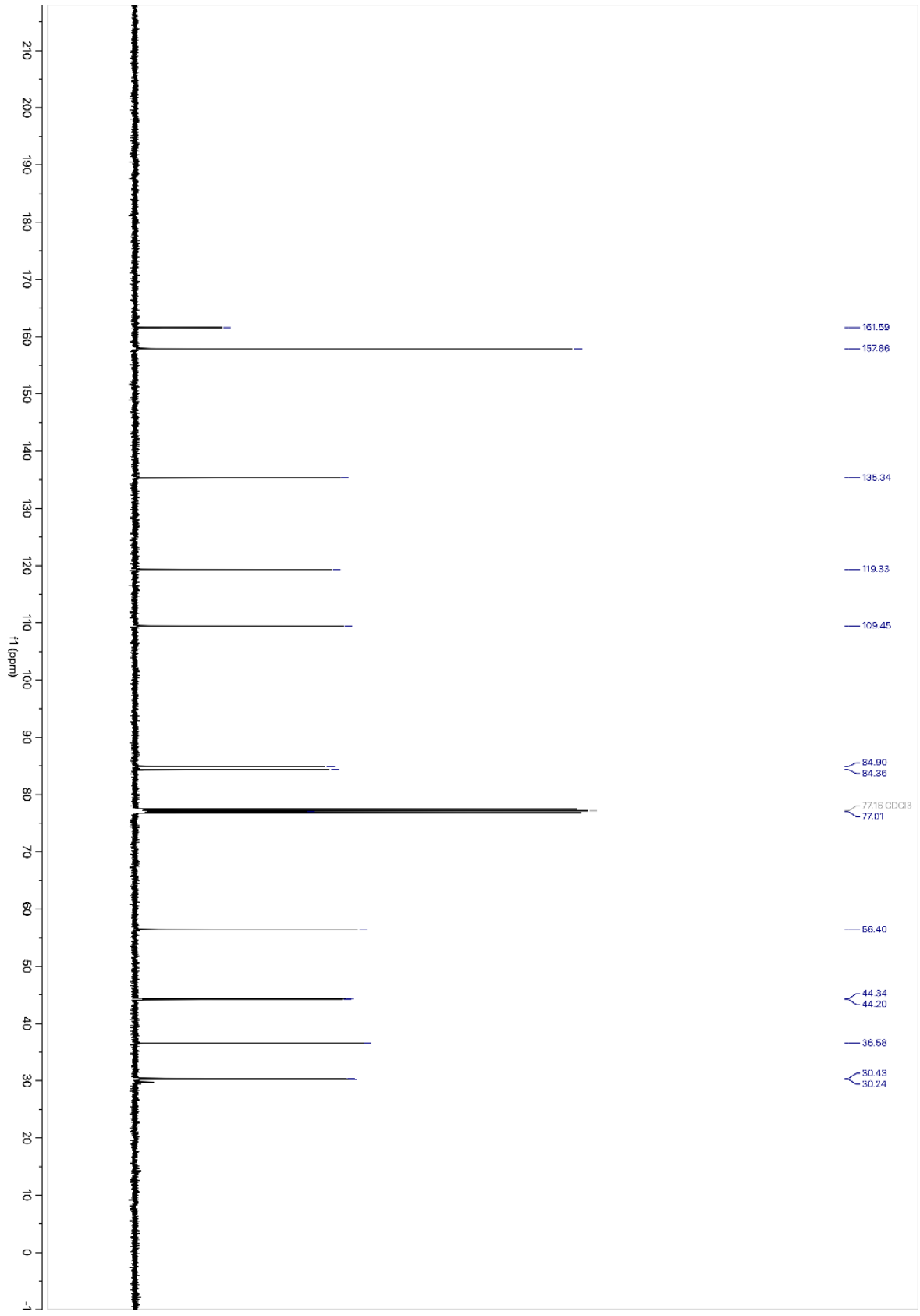
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 4.7 Hz, 2H), 6.42 (t, *J* = 4.7 Hz, 1H), 5.63 (dt, *J* = 17.1, 10.0 Hz, 1H), 5.19 (dd, *J* = 10.3, 1.9 Hz, 1H), 5.11 (dd, *J* = 17.2, 1.9 Hz, 1H), 4.80 – 4.73 (m, 2H), 4.69 (dd, *J* = 20.3, 7.3 Hz, 2H), 4.44 (dd, *J* = 68.5, 7.3 Hz, 2H), 3.03 (s, 1H), 2.86 – 2.69 (m, 2H), 2.24 (dd, *J* = 9.8, 7.9 Hz, 1H), 1.82 (dt, *J* = 13.8, 3.5 Hz, 2H), 1.53 (dt, *J* = 12.6, 3.0 Hz, 1H), 1.27 – 1.14 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 161.6, 157.9, 135.3, 119.3, 109.4, 84.9, 84.4, 77.0, 56.4, 44.3, 44.2, 36.6, 30.4, 30.2.
HRMS (ESI): Calculated for $C_{15}H_{21}N_3O_2$ [M+H$^+$] = 276.1707, Found 276.1712

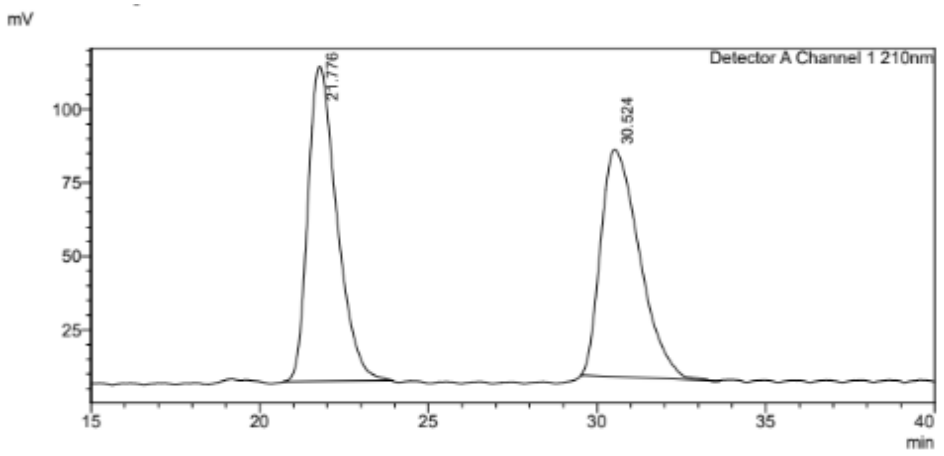
FTIR (neat): 3369, 2942, 2871, 1586, 1545, 1509, 1458, 1394, 1363, 1306, 1269, 1245, 1224, 1083, 976, 949,, 921, 840, 796 cm^{-1}

$[\alpha]_D^{28}$= -25.0 (*c* 0.20, $CHCl_3$)

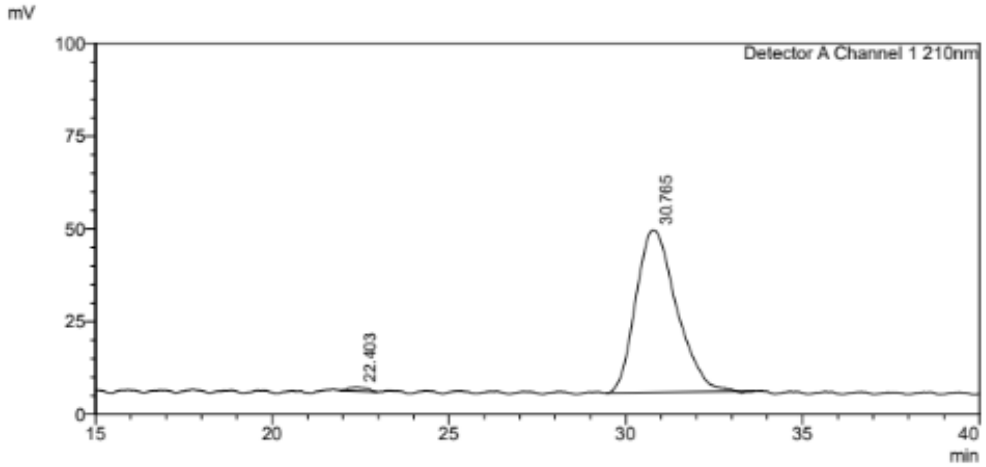
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm): *ee* = 98%


1.97
0.99
1.00
1.01
1.02
1.99
2.02
2.05
0.85
2.09
1.07
2.09
1.12
2.25
f1 (ppm)
8.28
8.26
7.26 CDCl3
6.43
6.42
6.41
5.68
5.66
5.64
5.63
5.61
5.59
5.20
5.20
5.17
5.17
5.13
5.13
5.09
5.08
4.79
4.78
4.77
4.76
4.75
4.74
4.74
4.73
4.72
4.70
4.67
4.65
4.54
4.52
4.37
4.35
3.03
2.84
2.83
2.81
2.80
2.80
2.78
2.77
2.74
2.74
2.27
2.25
2.24
2.22
1.84
1.83
1.83
1.81
1.80
1.79
1.56
1.55
1.54
1.52
1.52
1.51
1.25
1.24
1.22
1.21
1.20
1.18
1.17
1.15


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
161.59
157.86
135.34
119.33
109.45
84.90
84.36
77.16 CDCl3
77.01
56.40
44.34
44.20
36.58
30.43
30.24

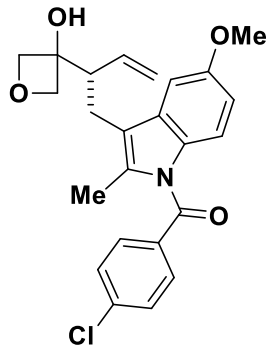


Peak#	Ret. Time	Area	Area%
1	21.776	6403147	50.851
2	30.524	6188948	49.149
Total		12592095	100.000



Peak#	Ret. Time	Area	Area%
1	22.403	37051	1.049
2	30.765	3496515	98.951
Total		3533566	100.000

(3n) (*S*)-(4-chlorophenyl)(3-(2-(3-hydroxyoxetan-3-yl)but-3-en-1-yl)-5-methoxy-2-methyl-1*H*-indol-1-yl)methanone



Procedure

Allyl acetate **2n** (123.6 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 °C, 18 hr). The title compound was obtained in 95% yield (81.3 mg, 0.191 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1—3:1).

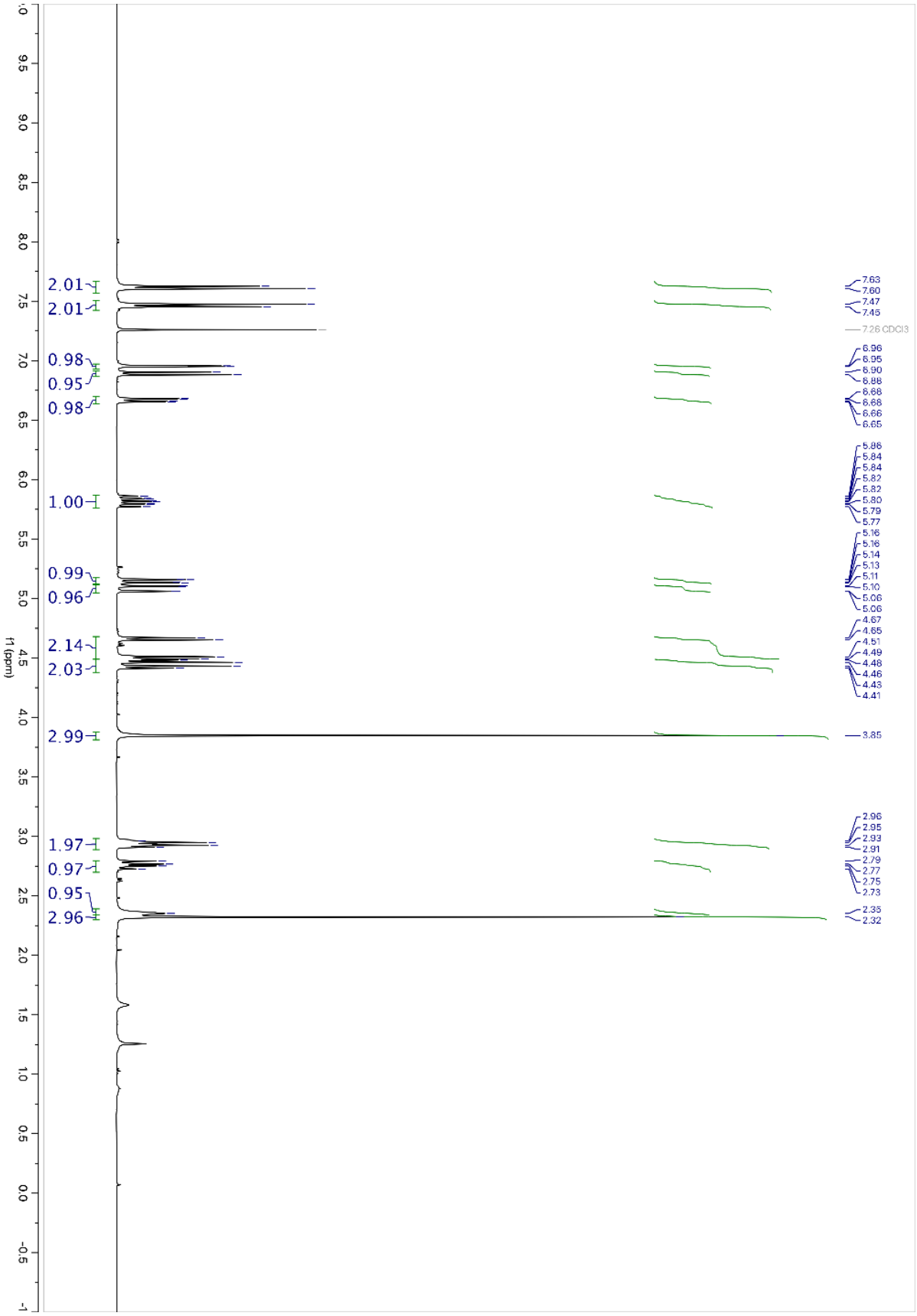
TLC (SiO_2): R_f = 0.36 (hexanes: ethyl acetate = 1:1).

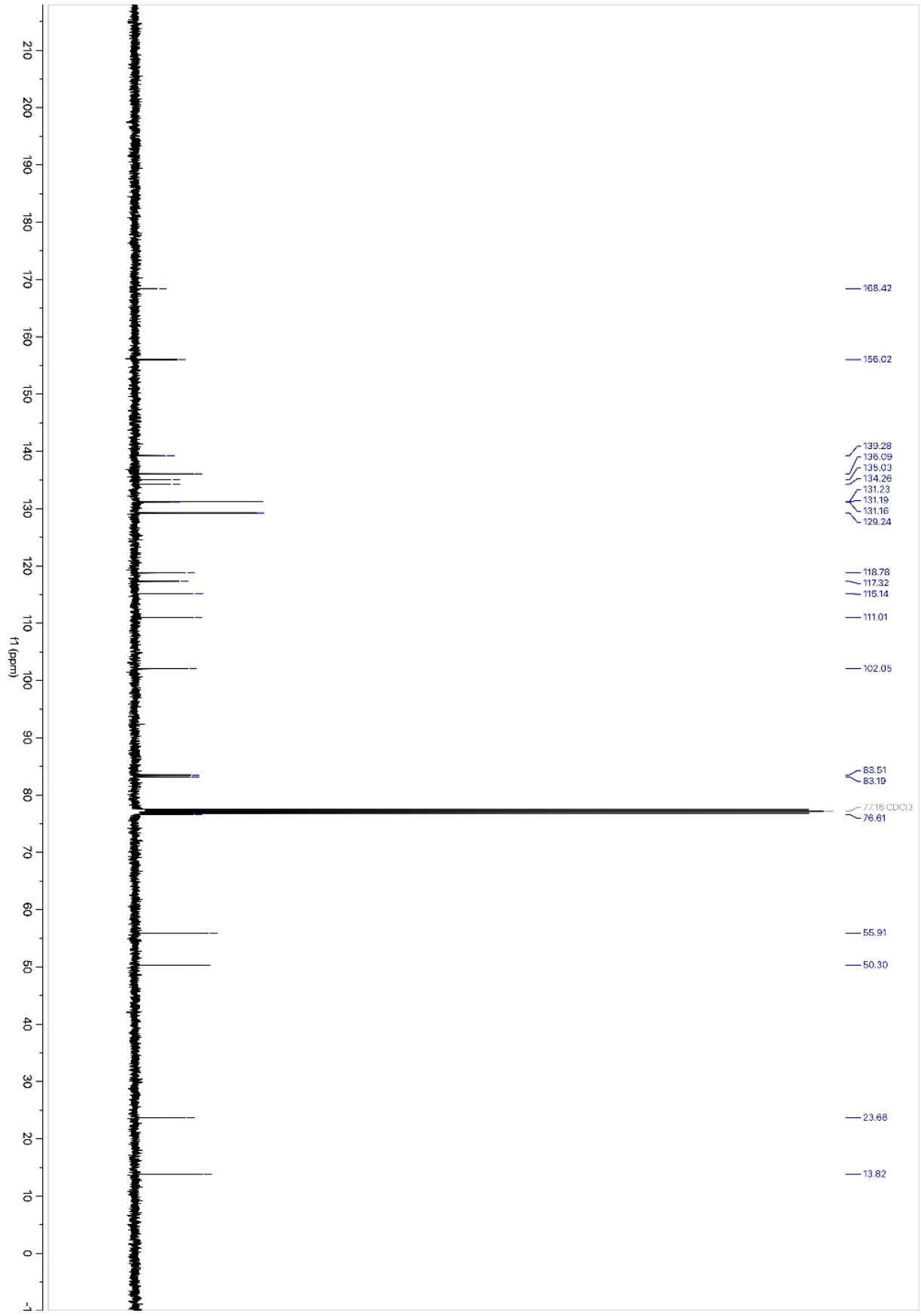
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 2.5 Hz, 1H), 6.89 (d, *J* = 9.0 Hz, 1H), 6.67 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.82 (ddd, *J* = 17.3, 10.3, 8.2 Hz, 1H), 5.15 (dd, *J* = 10.3, 1.6 Hz, 1H), 5.08 (dd, *J* = 17.2, 1.6 Hz, 1H), 4.58 (dd, *J* = 63.8, 7.2 Hz, 2H), 4.49 – 4.38 (m, 2H), 3.85 (s, 3H), 2.99 – 2.89 (m, 2H), 2.76 (dd, *J* = 16.1, 10.1 Hz, 1H), 2.35 (s, 1H), 2.32 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 168.4, 156.0, 139.3, 136.1, 135.0, 134.3, 131.2, 131.2, 131.2, 129.2, 118.8, 117.3, 115.1, 111.0, 102.0, 83.5, 83.2, 76.6, 55.9, 50.3, 23.7, 13.8.
HRMS (APCI): Calculated for $C_{24}H_{24}ClNO_4$ [M+H$^+$] = 426.1467, Found 426.1477.

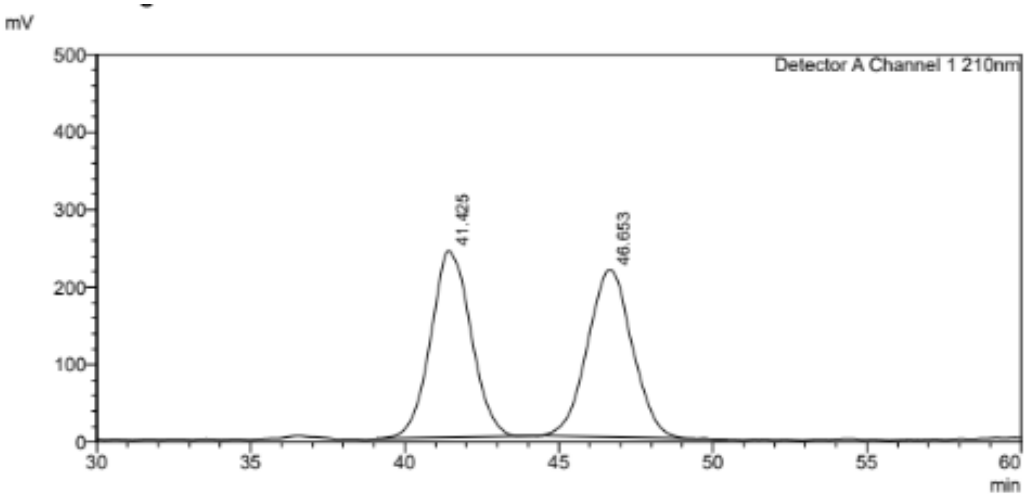
FTIR (neat): 3415, 3073, 2950, 2873, 2364, 1678, 1591, 1288, 1262, 1217, 1179, 1157, 691 cm^{-1}

$[\alpha]_D^{28}$ = -5.0 (*c* 0.10, $CHCl_3$)

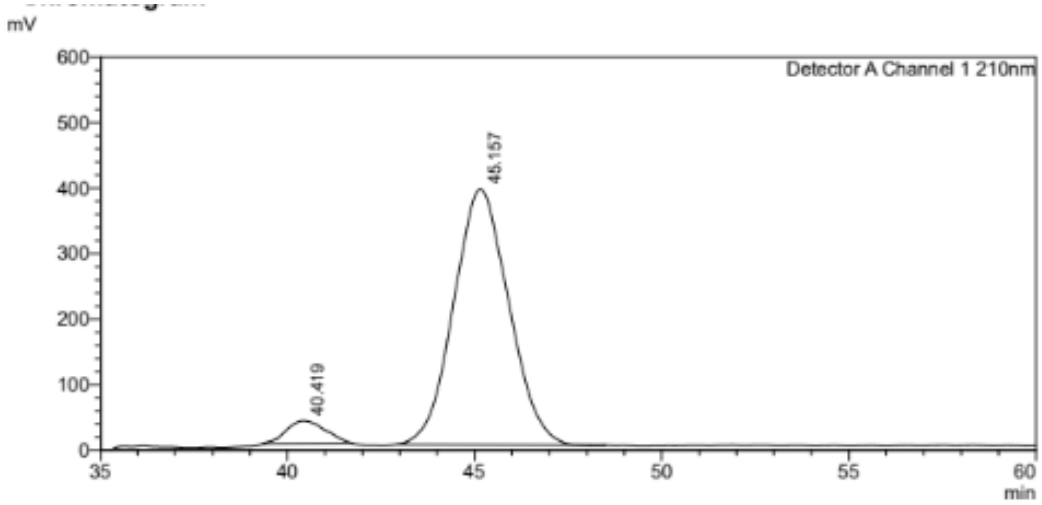
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm): *ee* = 88%


2.01
2.01
0.98
0.95
0.98
1.00
0.99
0.96
2.14
2.03
2.99
1.97
0.97
0.95
2.96
7.63
7.60
7.47
7.45
7.26 CDCl3
6.96
6.95
6.90
6.88
6.68
6.68
6.66
6.65
5.86
5.84
5.84
5.82
5.82
5.80
5.79
5.77
5.16
5.16
5.14
5.13
5.11
5.10
5.06
5.06
4.67
4.65
4.51
4.49
4.48
4.46
4.43
4.41
3.85
2.96
2.95
2.93
2.91
2.79
2.77
2.75
2.73
2.35
2.32
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
168.42
156.02
139.28
136.09
135.03
134.26
131.23
131.19
131.16
129.24
118.78
117.32
115.14
111.01
102.05
83.51
83.19
77.16 CDCl3
76.61
55.91
50.30
23.68
13.82

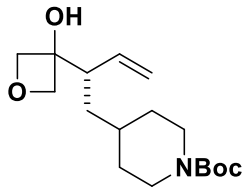


Peak#	Ret. Time	Area	Area%
1	41.425	21972534	50.199
2	46.653	21798260	49.801
Total		43770793	100.000



Peak#	Ret. Time	Area	Area%
1	40.419	2491732	5.862
2	45.157	40011710	94.138
Total		42503441	100.000

(3o) tert-butyl (S)-4-(2-(3-hydroxyoxetan-3-yl)but-3-en-1-yl)piperidine-1-carboxylate



Procedure

Allyl acetate **2o** (89.2 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 °C, 18 hr). The title compound was obtained in 91% yield (56.7 mg, 0.182 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

TLC (SiO_2): R_f = 0.35 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.65 (ddd, J = 17.1, 10.3, 9.2 Hz, 1H), 5.24 (dd, J = 10.3, 1.7 Hz, 1H), 5.19 (dd, J = 16.9, 1.8 Hz, 1H), 4.56 (d, J = 7.0 Hz, 1H), 4.52 (s, 2H), 4.49 (d, J = 7.0 Hz, 1H), 4.07 (t, J = 13.5 Hz, 2H), 2.73 – 2.60 (m, 2H), 2.56 (ddd, J = 11.6, 9.2, 2.7 Hz, 1H), 2.04 (s, 1H), 1.74 (d, J = 12.6 Hz, 1H), 1.56 (q, J = 15.8, 15.0 Hz, 4H), 1.45 (s, 10H), 1.29 – 1.23 (m, 1H), 1.17 (qd, J = 12.5, 4.4 Hz, 1H), 1.01 (qd, J = 12.5, 4.3 Hz, 1H).

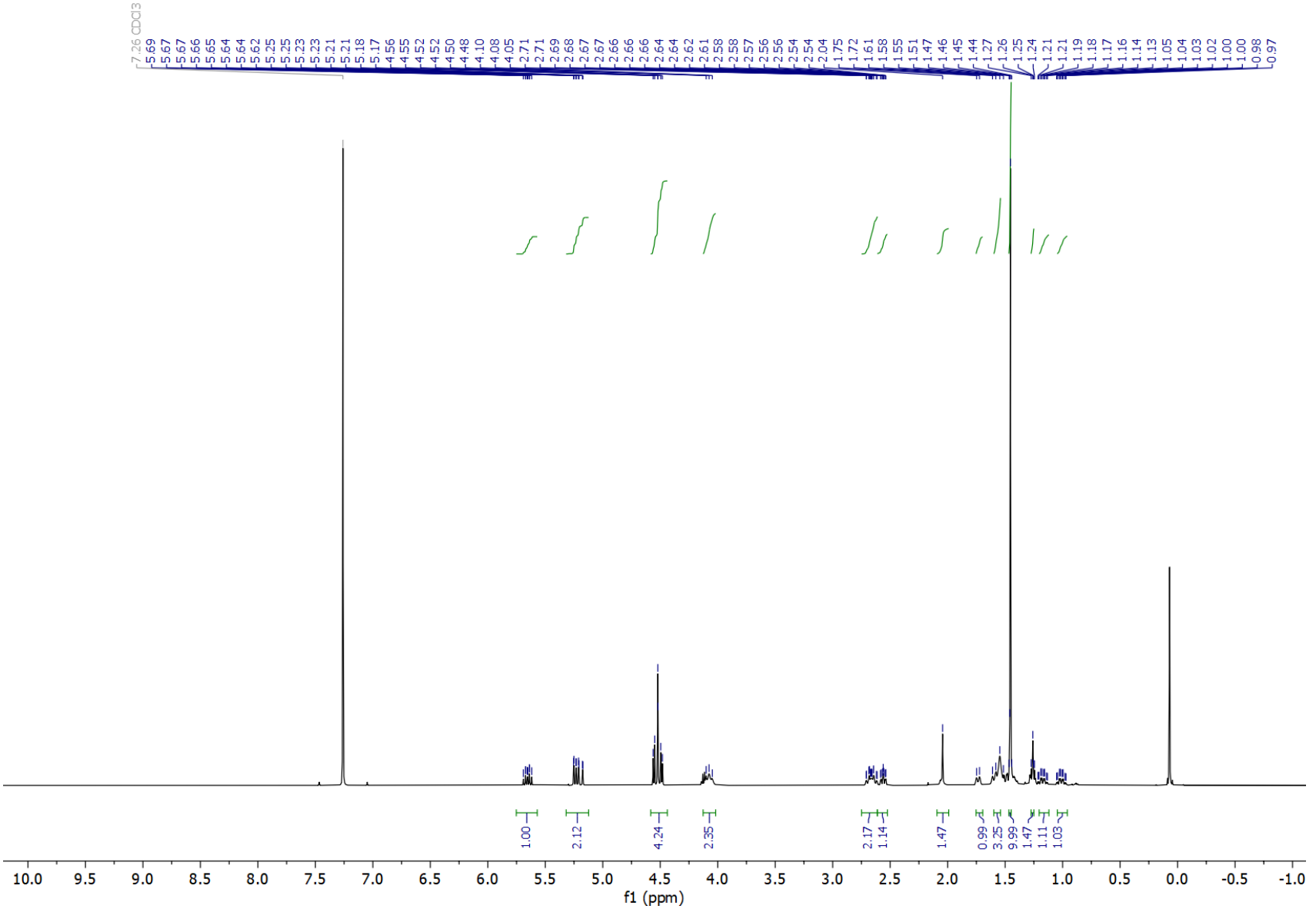
^{13}C NMR (101 MHz, $CDCl_3$): δ 154.8, 136.3, 119.1, 82.5, 79.3, 77.2, 76.3, 47.6, 34.3, 33.3, 28.5.

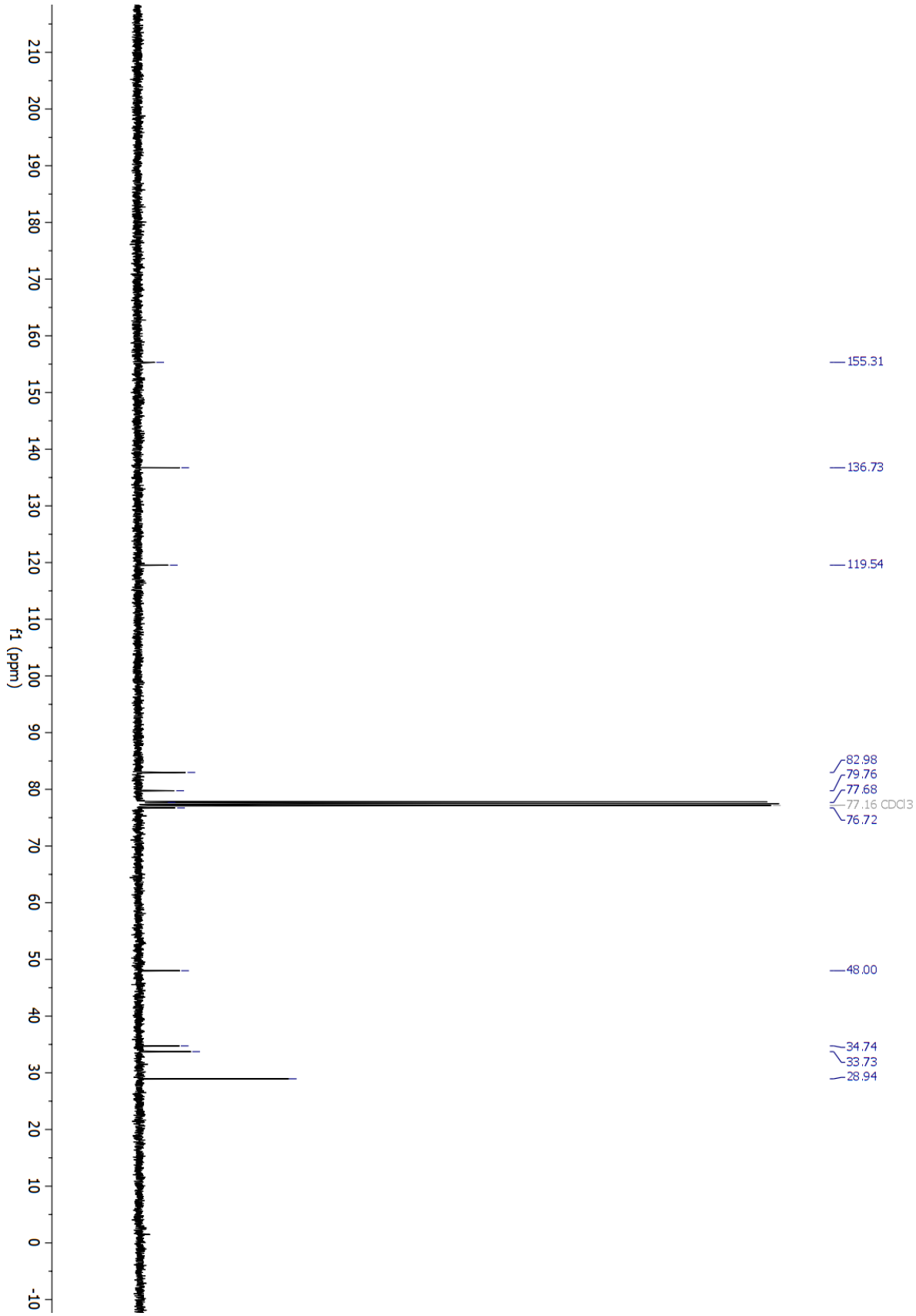
HRMS (ESI): Calculated for $C_{17}H_{29}NO_4$ $[M+H^+]$ = 311.2097, found= 311.2101

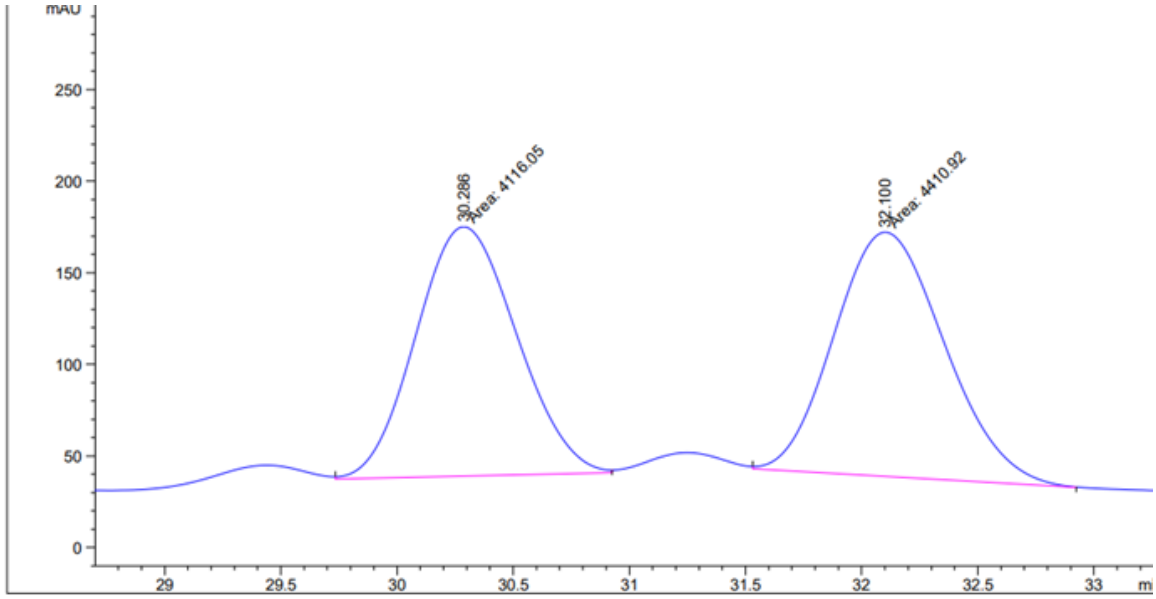
FTIR (neat): 33387, 2970, 2934, 2868, 1737, 1690, 1663, 1047, 1003, 972, 923, 854, 827, and 768 cm^{-1}

$[\alpha]_D^{28}$= -17.3 (c 0.1 $CHCl_3$)

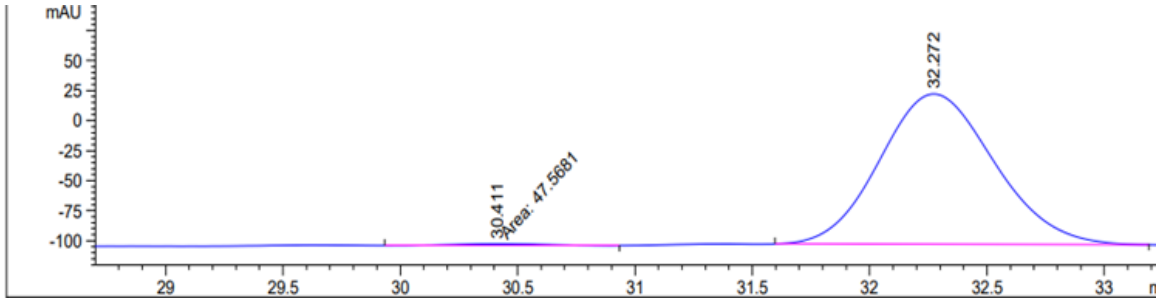
HPLC (Chiralcel AD-H column in series with a Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 98%


7.26 CDCl3
5.69 5.67 5.67 5.66 5.65 5.64 5.64 5.62 5.25 5.25 5.23 5.23 5.21 5.21 5.18 5.17 4.56 4.55 4.52 4.52 4.50 4.48 4.10 4.08 4.05 2.71 2.71 2.69 2.68 2.67 2.67 2.66 2.66 2.66 2.64 2.64 2.62 2.61 2.58 2.58 2.57 2.56 2.56 2.54 2.54 2.04 1.75 1.72 1.61 1.58 1.55 1.51 1.47 1.46 1.45 1.44 1.27 1.26 1.25 1.24 1.21 1.21 1.19 1.18 1.17 1.16 1.14 1.13 1.05 1.04 1.03 1.02 1.00 1.00 0.98 0.97
1.00 2.12 4.24 2.35 2.17 1.14 1.47 0.99 3.25 9.99 1.47 1.11 1.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
155.31
136.73
119.54
82.98
79.76
77.68
77.16 CDCl3
76.72
48.00
34.74
33.73
28.94

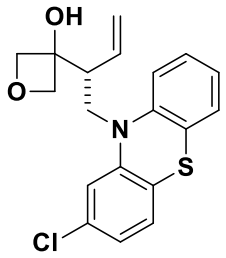


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.286	MM	0.5031	4116.04639	136.34325	48.2709
2	32.100	MM	0.5511	4410.91895	133.40161	51.7291



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.411	MM	0.4986	47.56807	1.59012	1.1031
2	32.272	BB	0.5229	4264.45557	125.34425	98.8969

(3p) (R)-3-(1-(2-chloro-10H-phenothiazin-10-yl)but-3-en-2-yl)oxetan-3-ol



Procedure

Allyl acetate **2p** (93.3 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 ^{o}C, 18 hr). The title compound was obtained in 72% yield (51.7 mg, 0.114 mmol) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–4:1).

TLC (SiO_2): R_f = 0.50 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 7.25 – 7.16 (m, 2H), 7.09 (d, *J* = 8.2 Hz, 1H), 7.02 – 6.97 (m, 1H), 6.97 – 6.93 (m, 2H), 6.90 (d, *J* = 2.1 Hz, 1H), 5.78 (ddd, *J* = 16.9, 10.3, 8.9 Hz, 1H), 5.31 – 5.23 (m, 2H), 4.66 (d, *J* = 7.5 Hz, 1H), 4.60 (d, *J* = 7.3 Hz, 1H), 4.56 (d, *J* = 7.5 Hz, 1H), 4.43 (d, *J* = 7.3 Hz, 1H), 4.18 (dd, *J* = 13.8, 8.6 Hz, 1H), 3.80 (dd, *J* = 13.8, 5.3 Hz, 1H), 3.21 (td, *J* = 8.7, 5.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 147.0, 144.8, 134.0, 133.9, 128.7, 128.4, 128.0, 126.3, 125.0, 123.9, 123.3, 120.2, 116.6, 116.4, 83.7, 83.4, 76.0, 47.2, 46.7.

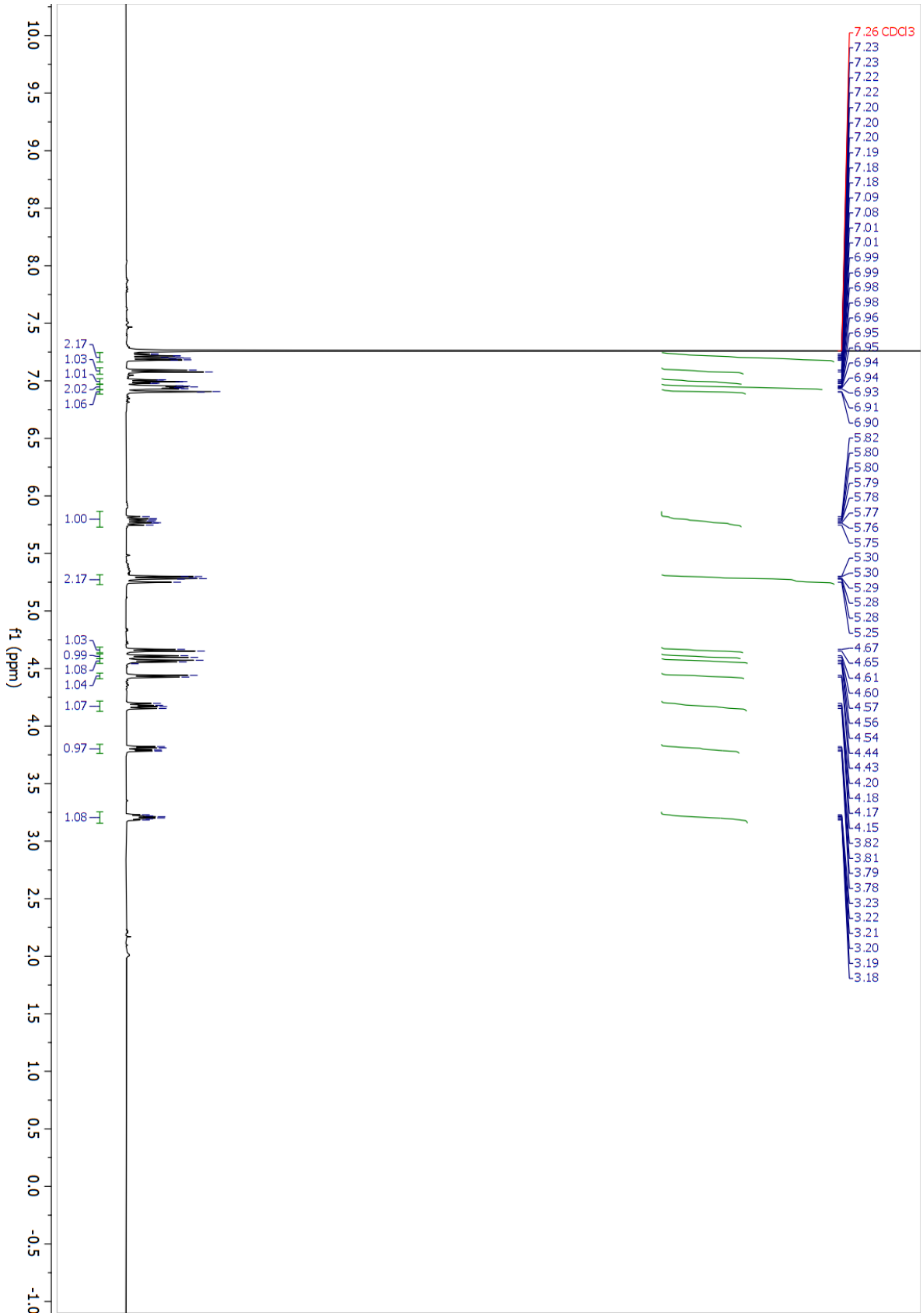
HRMS (ESI): Calculated for $C_{19}H_{18}ClNO_2S$ $[M+H^+]$ =360.0820, Found 360.0820

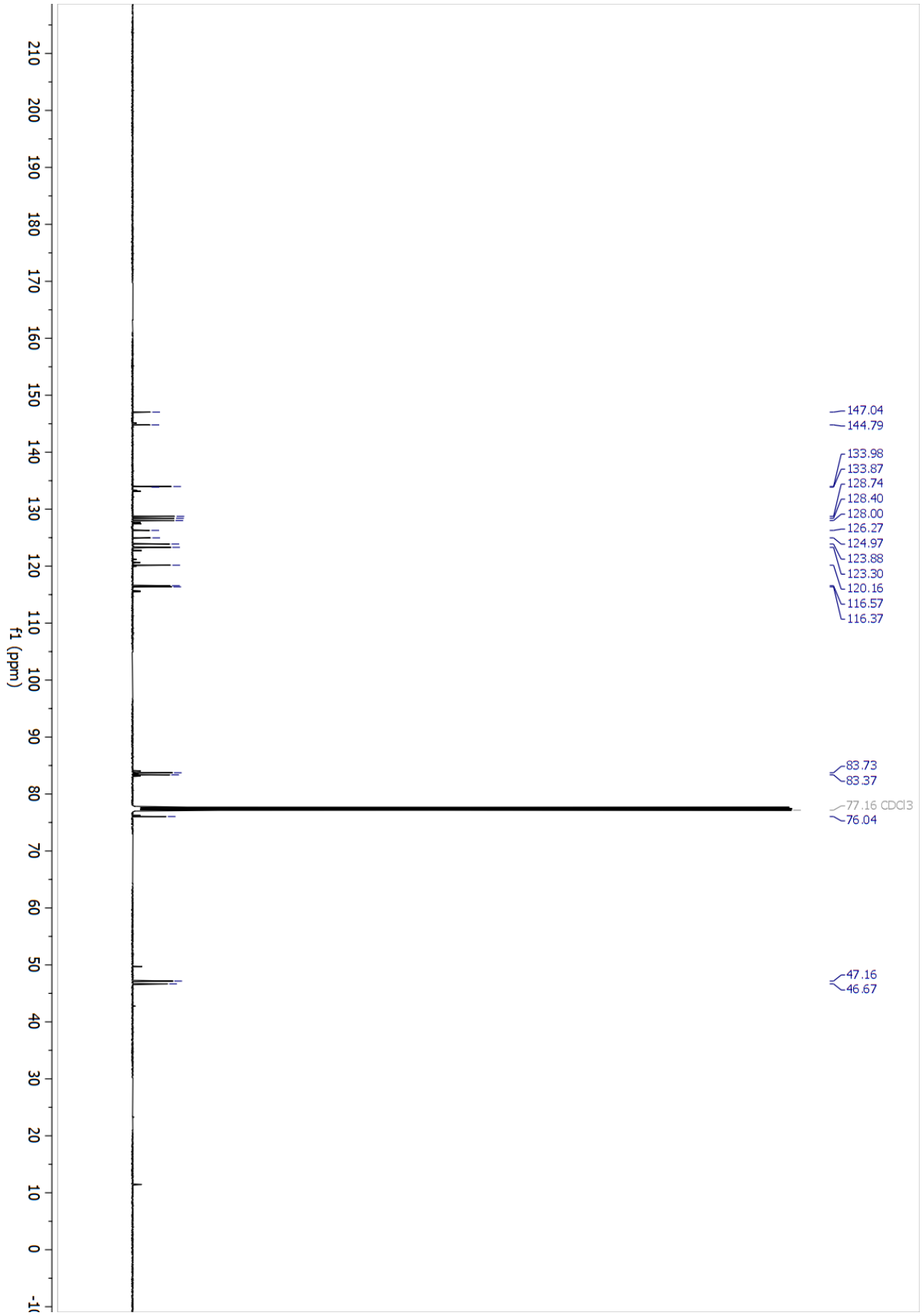
FTIR (neat): 3349, 1454, 1225, 931, 799, 743 cm^{-1}

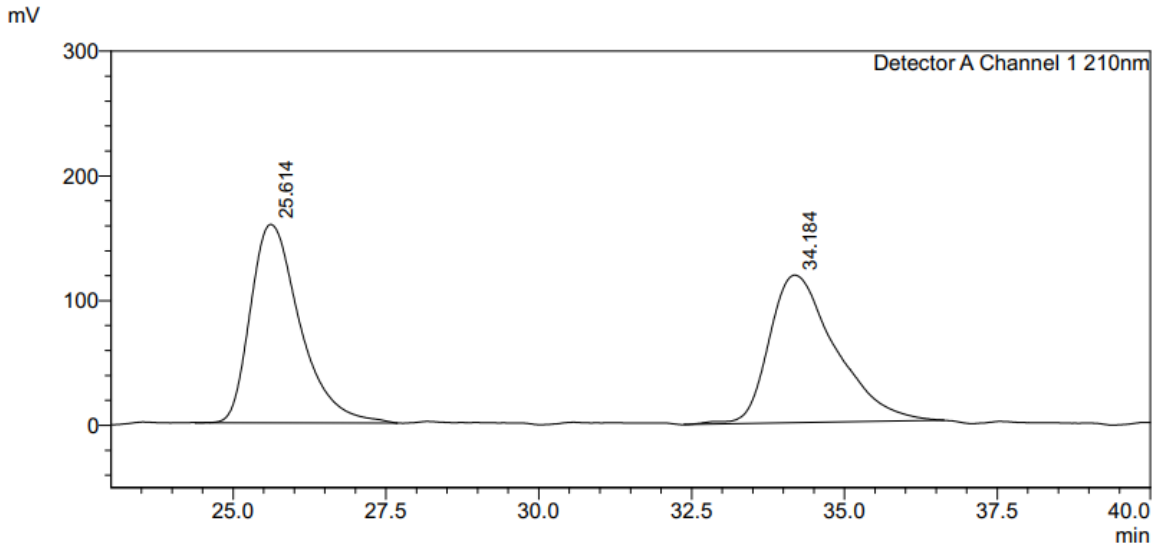
$\mathbf{[\alpha]_D^{28}}$= -8.8^{0} (c = 0.68, $CHCl_3$)

MP: 121-128 ^{0}C

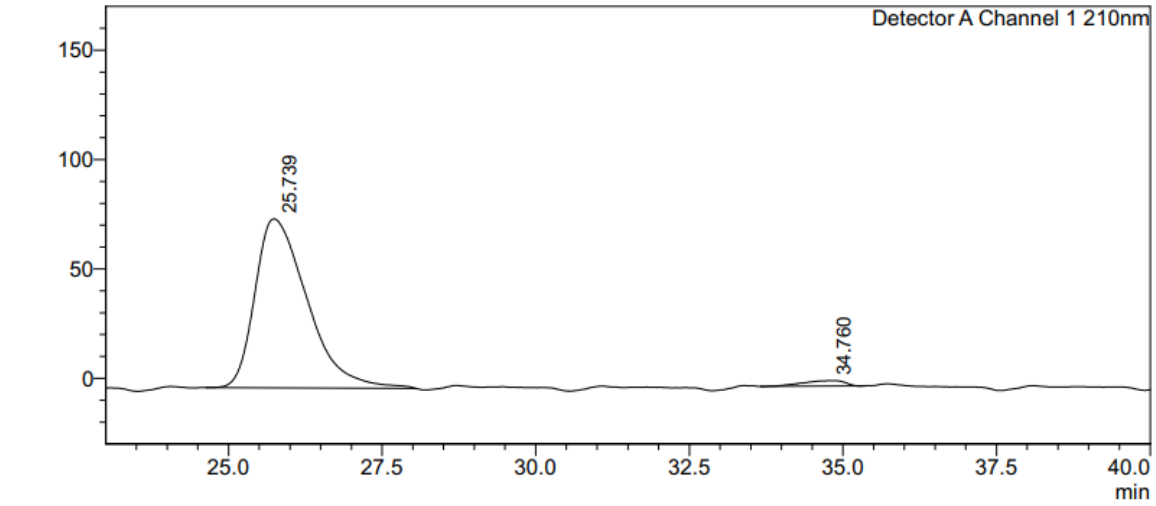
HPLC (Phenomenex column Cellulose 5, hexane:*i*-PrOH = 98:02, 1.0 mL/min, 210 nm): *ee*= 95%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
2.17
1.03
1.01
2.02
1.06
1.00
2.17
1.03
0.99
1.08
1.04
1.07
0.97
1.08
7.26 CDCl3
7.23
7.23
7.22
7.22
7.20
7.20
7.20
7.19
7.18
7.18
7.09
7.08
7.01
7.01
6.99
6.99
6.98
6.98
6.96
6.95
6.95
6.94
6.94
6.93
6.91
6.90
5.82
5.80
5.80
5.79
5.78
5.77
5.76
5.75
5.30
5.30
5.29
5.28
5.28
5.25
4.67
4.65
4.61
4.60
4.57
4.56
4.54
4.44
4.43
4.20
4.18
4.17
4.15
3.82
3.81
3.79
3.78
3.23
3.22
3.21
3.20
3.19
3.18


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
147.04
144.79
133.98
133.87
128.74
128.40
128.00
126.27
124.97
123.88
123.30
120.16
116.57
116.37
83.73
83.37
77.16 CDCl3
76.04
47.16
46.67

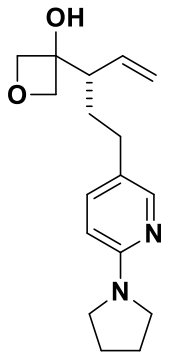


Peak#	Ret. Time	Area	Height	Area%
1	25.614	8973007	159054	50.108
2	34.184	8934208	118429	49.892
Total		17907215	277483	100.000



Peak#	Ret. Time	Area	Height	Area%
1	25.739	4572275	77297	97.506
2	34.760	116951	2447	2.494
Total		4689226	79744	100.000

(3q) (S)-3-(5-(6-(pyrrolidin-1-yl)pyridin-3-yl)pent-1-en-3-yl)oxetan-3-ol



Procedure

Allyl acetate **2q** (82.3 mg, 0.300 mmol, 150 mol%) was subjected to a modified version of general procedure C using (S)-Ir-SEGPHOS (11.8 mg, 0.01 mmol, 5 mol%, 100 ºC, 48 hr). The title compound was obtained in 98% yield (56.5 mg, 0.196 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, dichloromethane: acetone = 10:1–2:1).

TLC (SiO_2): R_f = 0.20 (dichloromethane: acetone: = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 7.95 (d, *J* = 2.3 Hz, 1H), 7.28 – 7.25 (m, 1H), 6.32 (d, *J* = 8.5 Hz, 1H), 5.69 (dt, *J* = 17.0, 9.7 Hz, 1H), 5.29 (dd, *J* = 10.2, 1.8 Hz, 1H), 5.22 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.59 – 4.38 (m, 4H), 3.53 – 3.33 (m, 4H), 2.61 (dt, *J* = 13.8, 6.6 Hz, 1H), 2.44 – 2.32 (m, 2H), 2.03 – 1.96 (m, 4H), 1.69 (qd, *J* = 8.2, 7.5, 3.5 Hz, 2H).

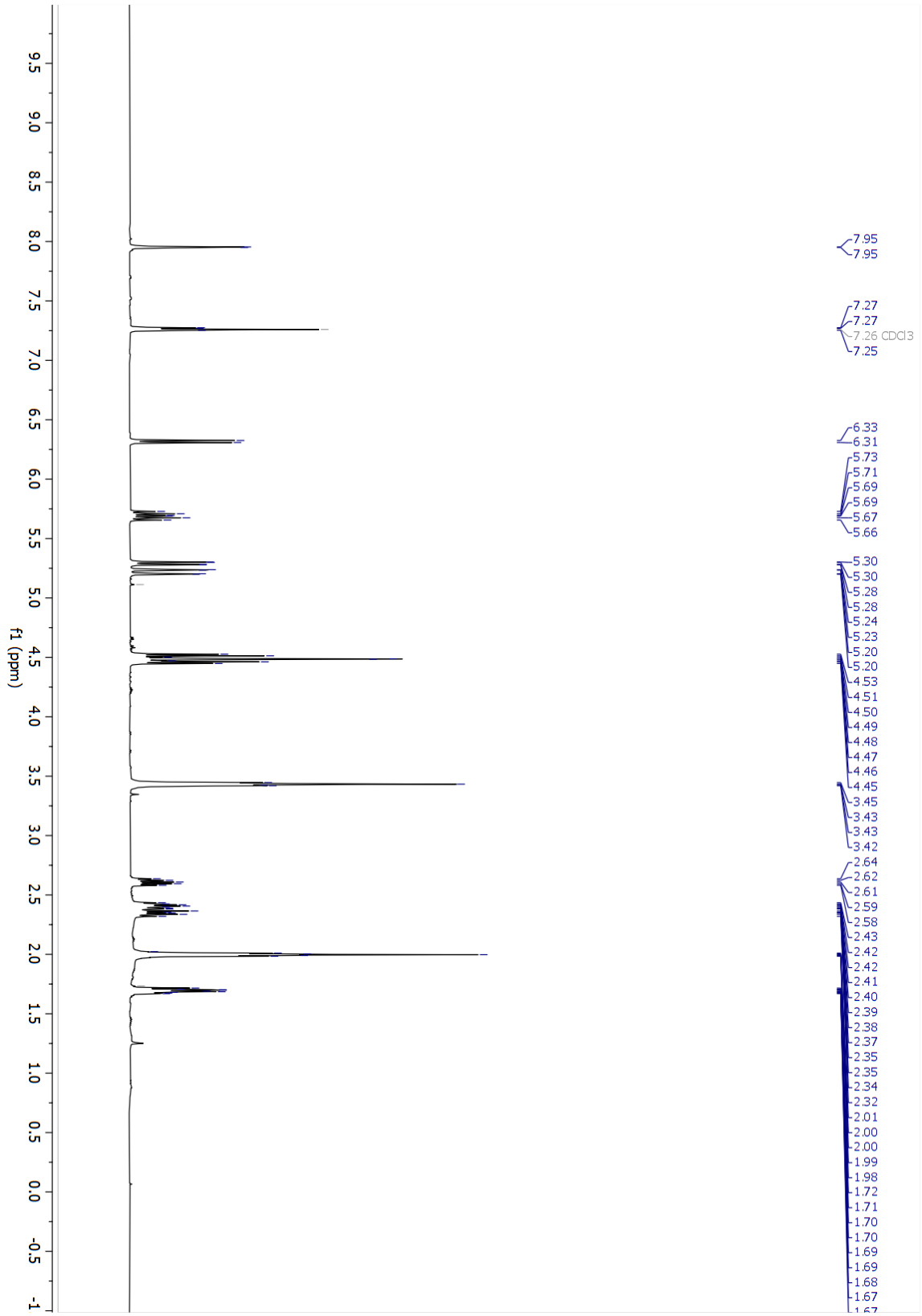
^{13}C NMR (126 MHz, $CDCl_3$): δ:156.5, 147.9, 137.7, 136.4, 124.0, 119.9, 106.9, 83.0, 82.9, 76.6, 50.0, 47.2, 29.9, 29.8, 26.0.

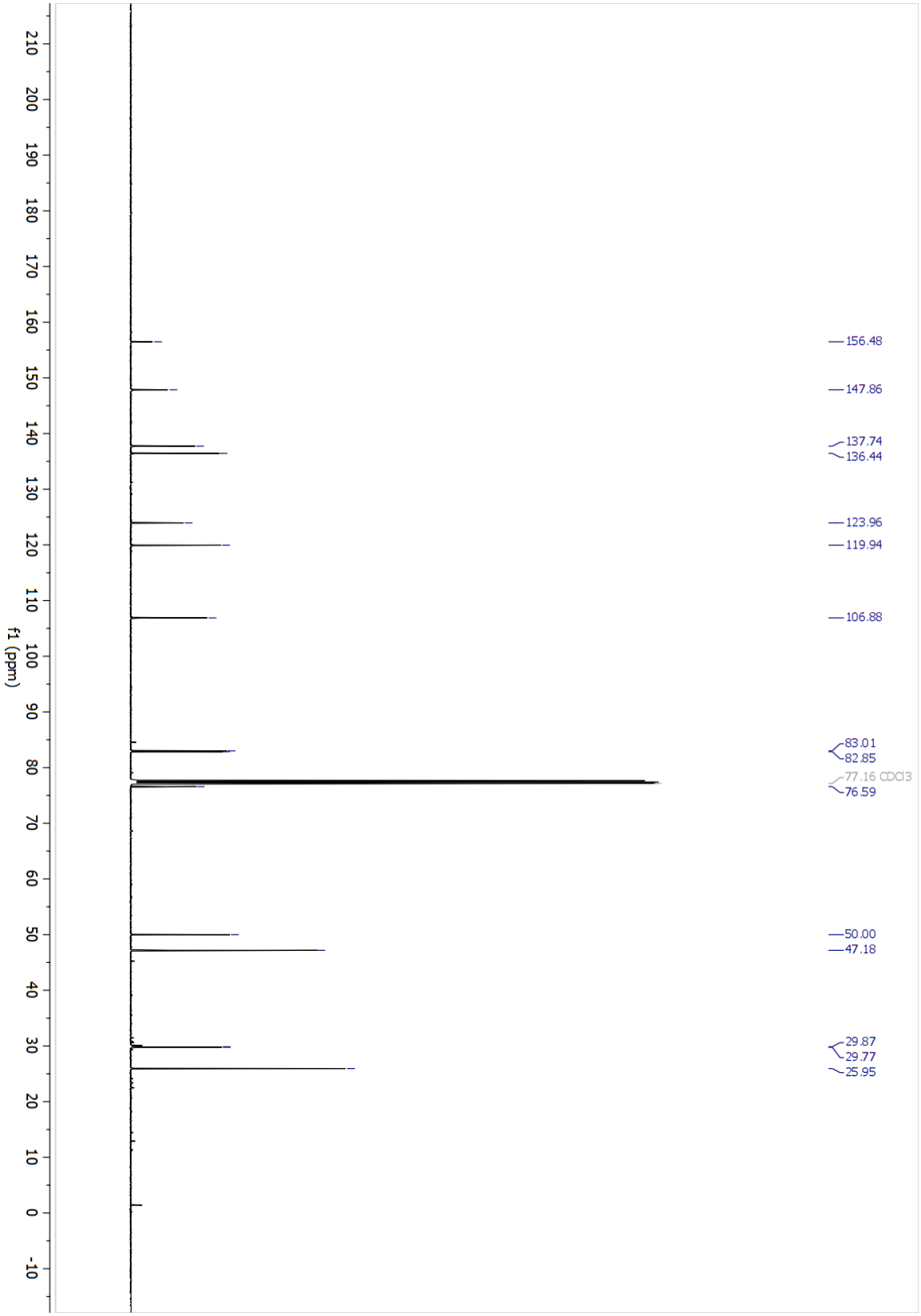
HRMS (ESI): Calculated for $C_{17}H_{24}N_2O_2$ [M+H$^+$] =289.1911, Found 289.1914

FTIR (neat): 3400, 2946, 2866, 1507, 1416, 974, 917, 808cm^{-1}

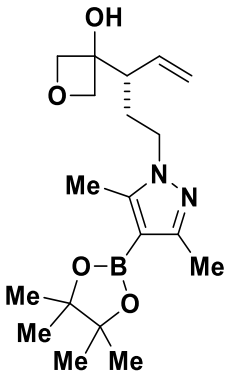
$[\alpha]_D^{28}$= -37.7 ^{0} (c = 0.27, $CHCl_3$)

Enantiomeric excess was determined from derivative **5q.**


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
7.95
7.95
7.27
7.27
7.26 CDCl3
7.25
6.33
6.31
5.73
5.71
5.69
5.69
5.67
5.66
5.30
5.30
5.28
5.28
5.24
5.23
5.20
5.20
4.53
4.51
4.50
4.49
4.48
4.47
4.46
4.45
3.45
3.43
3.43
3.42
2.64
2.62
2.61
2.59
2.58
2.43
2.42
2.42
2.41
2.40
2.39
2.38
2.37
2.35
2.35
2.34
2.32
2.01
2.00
2.00
1.99
1.98
1.72
1.71
1.70
1.70
1.69
1.69
1.68
1.67


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
156.48
147.86
137.74
136.44
123.96
119.94
106.88
83.01
82.85
77.16 CDCl3
76.59
50.00
47.18
29.87
29.77
25.95

(3r) (S)-3-(5-(3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)pent-1-en-3-yl)oxetan-3-ol



Procedure

Allyl acetate **2r** (104.5 mg, 0.300 mmol, 150 mol%) was subjected to modified version of general procedure C using (S)-Ir-SEGPHOS (11.8 mg, 0.01 mmol, 5 mol%, 100 ^{o}C, 48 hr).The title compound was obtained in 73% yield (52.3 mg, 0.146 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1).

TLC (SiO_2): R_f = 0.12 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.80 (dt, *J* = 17.1, 9.8 Hz, 1H), 5.27 (dd, *J* = 10.4, 1.7 Hz, 1H), 5.21 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.53 (d, *J* = 7.0 Hz, 1H), 4.51 – 4.44 (m, 3H), 4.00 (ddd, *J* = 12.9, 7.3, 5.2 Hz, 1H), 3.89 (ddd, *J* = 14.3, 8.4, 7.0 Hz, 1H), 3.44 (s, 1H), 2.43 (dt, *J* = 9.4, 4.8 Hz, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 2.23 – 2.13 (m, 1H), 1.83 (dddd, *J* = 14.3, 9.5, 6.9, 5.1 Hz, 1H), 1.29 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 155.1, 147.5, 136.5, 119.7, 83.1, 82.9, 82.5, 76.3, 48.3, 46.2, 28.7, 25.3, 25.3, 14.3, 11.5.

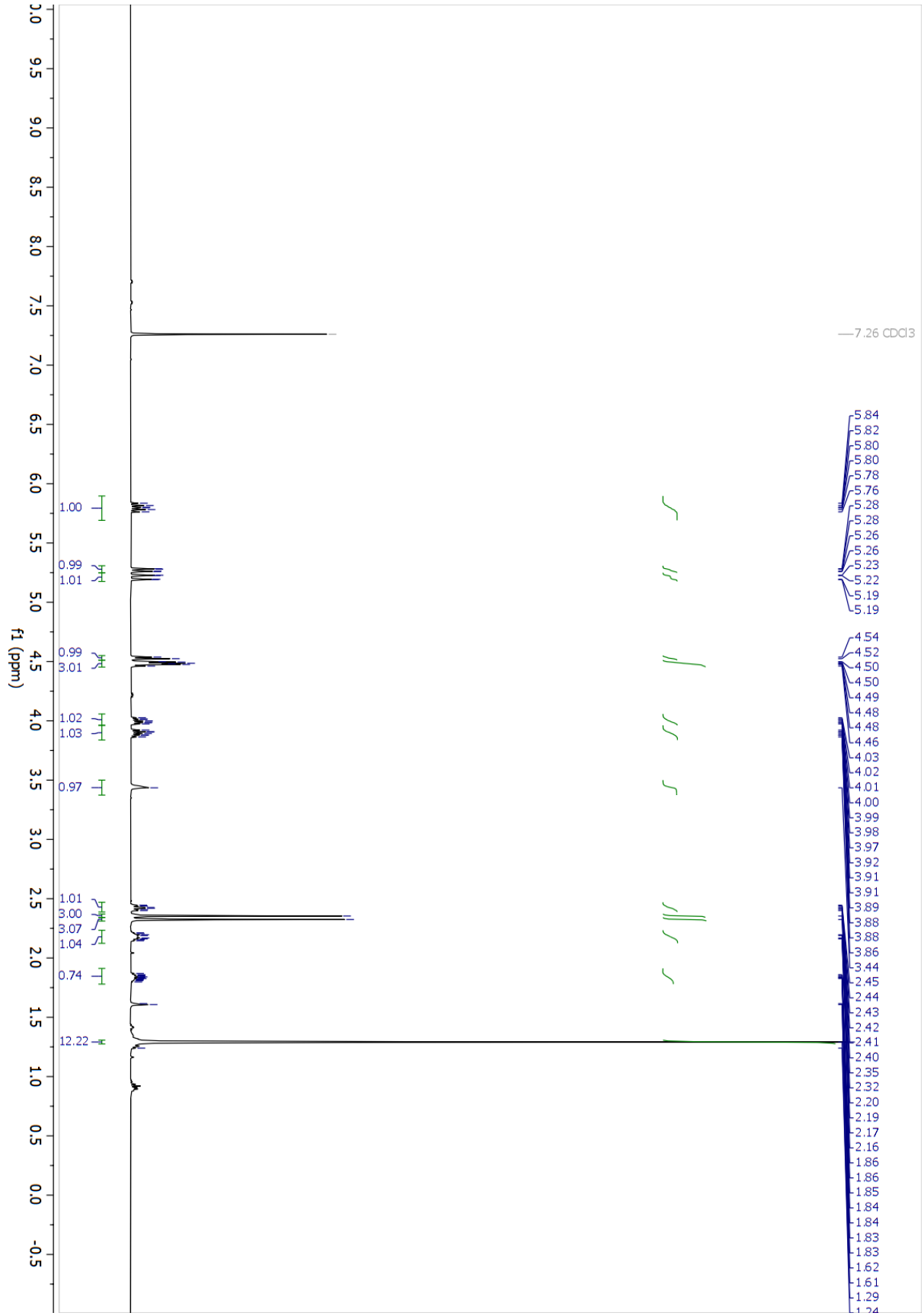
HRMS (ESI): Calculated for $C_{19}H_{31}BN_2O_4$ [M+H$^+$] =362.2486, Found 362.2492

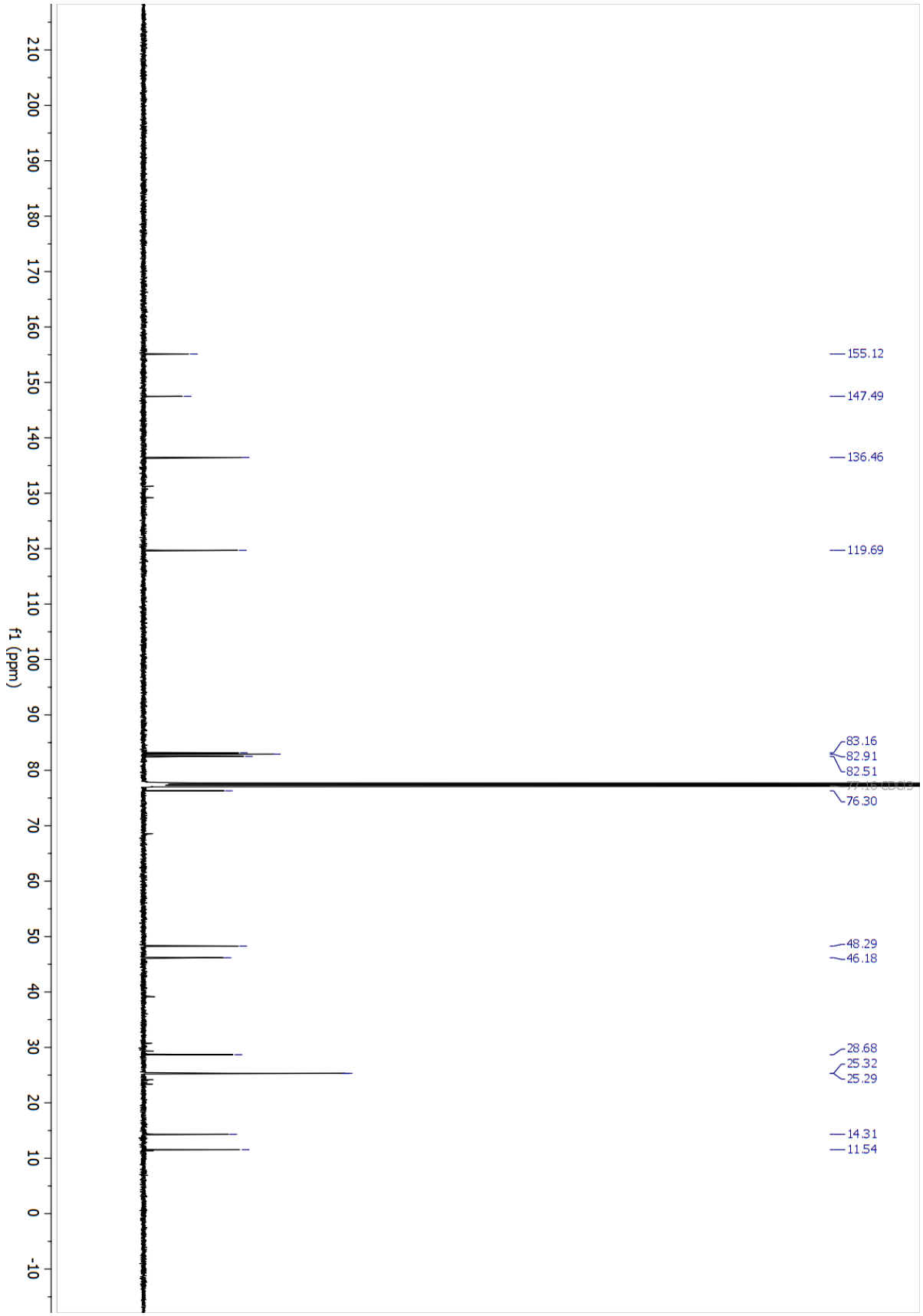
FTIR (neat) 3352, 2976, 1545, 1146, 1082, 963, 855, 727 cm^{-1}

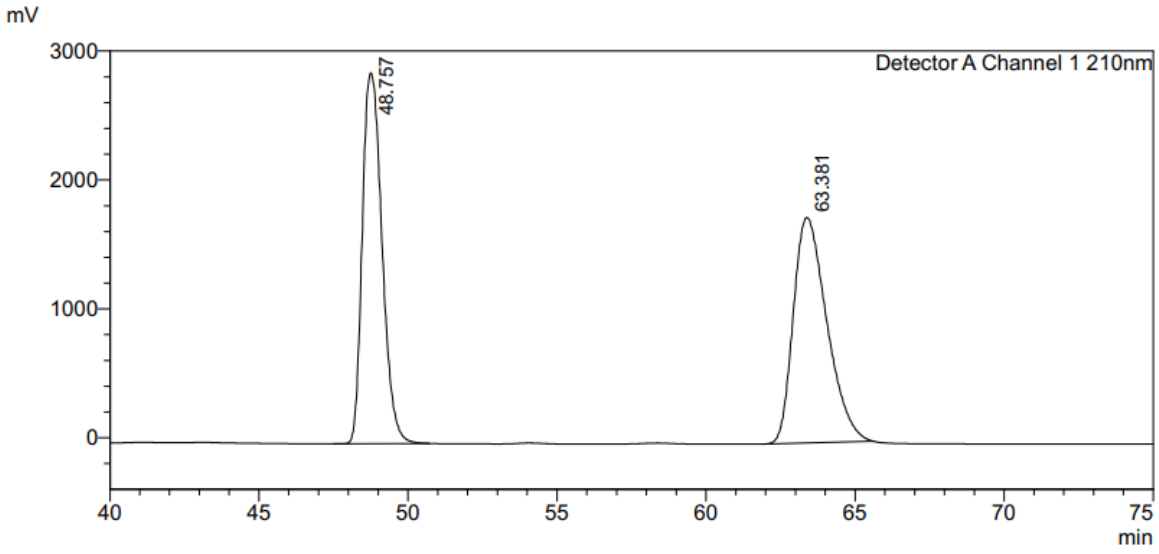
$[\alpha]_D^{28}$= -5.3^0 (c = 0.94, $CHCl_3$)

MP: 111-117 ^{0}C

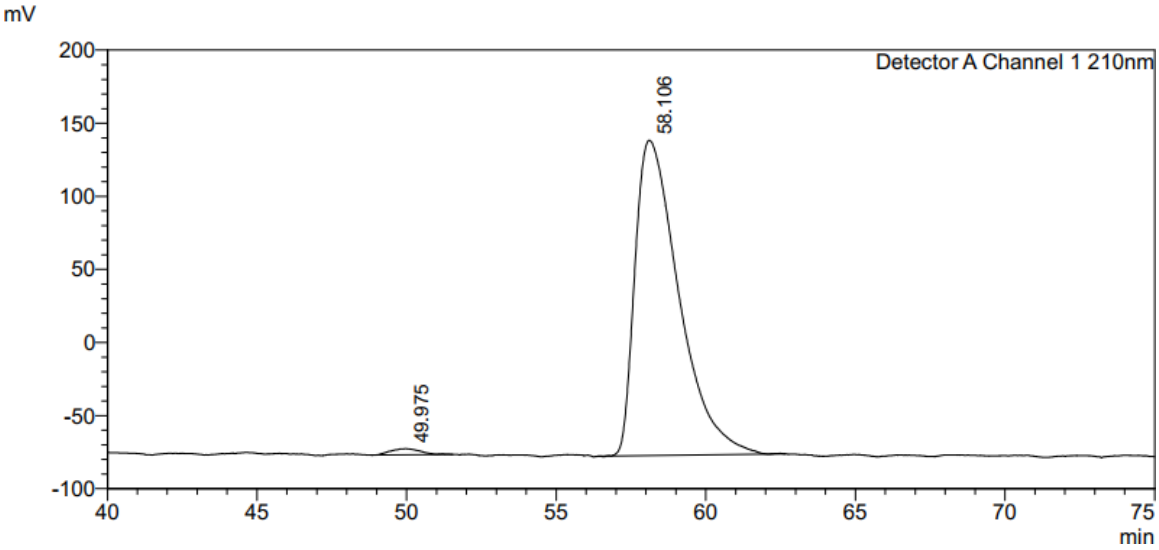
HPLC (Phenomenex Cellulose Column, hexane:*i*-PrOH = 95:05, 0.5 mL/min, 210 nm): ee =98%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
0.99
1.01
0.99
3.01
1.02
1.03
0.97
1.01
3.00
3.07
1.04
0.74
12.22
7.26 CDCl3
5.84
5.82
5.80
5.80
5.78
5.76
5.28
5.28
5.26
5.26
5.23
5.22
5.19
5.19
4.54
4.52
4.50
4.50
4.49
4.48
4.48
4.46
4.03
4.02
4.01
4.00
3.99
3.98
3.97
3.92
3.91
3.91
3.89
3.88
3.88
3.86
3.44
2.45
2.44
2.43
2.42
2.41
2.40
2.35
2.32
2.20
2.19
2.17
2.16
1.86
1.86
1.85
1.84
1.84
1.83
1.83
1.62
1.61
1.29


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
155.12
147.49
136.46
119.69
83.16
82.91
82.51
77.16 CDCl3
76.30
48.29
46.18
28.68
25.32
25.29
14.31
11.54

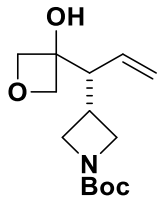


Peak#	Ret. Time	Area	Height	Area%
1	48.757	131976989	2875784	49.105
2	63.381	136789593	1748888	50.895
Total		268766582	4624672	100.000



Peak#	Ret. Time	Area	Height	Area%
1	49.975	283031	4227	1.269
2	58.106	22013646	215590	98.731
Total		22296676	219818	100.000

(3s) tert-butyl (R)-3-(1-(3-hydroxyoxetan-3-yl)allyl)azetidine-1-carboxylate



Procedure

Allyl acetate **2s** (76.6 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 18 hr). The title compound was obtained in 87% yield (47.0 mg, 0.174mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–2:1).

TLC (SiO_2): R_f = 0.31 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (dt, J = 17.1, 9.8 Hz, 1H), 4.59 (dd, J = 11.5, 7.1 Hz, 2H), 4.47 (dd, J = 15.6, 7.1 Hz, 2H), 3.97 (t, J = 8.5 Hz, 1H), 3.88 (t, J = 8.7 Hz, 1H), 3.74 (dt, J = 8.9, 6.5 Hz, 2H), 2.80 (ddd, J = 15.0, 7.5, 1.9 Hz, 1H), 2.64 (t, J = 2.0 Hz, 2H), 1.43 (s, 9H).

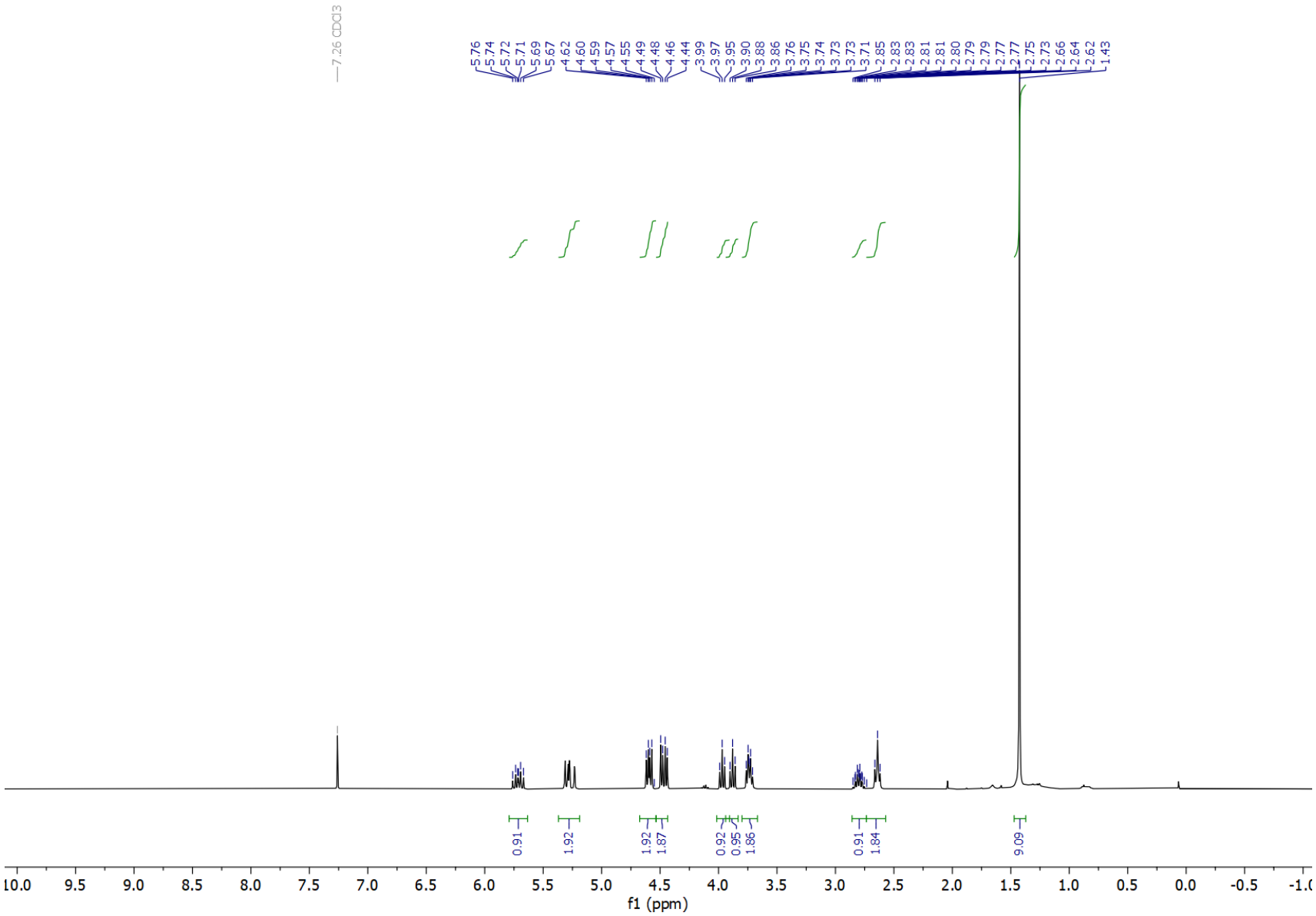
^{13}C NMR (101 MHz, $CDCl_3$): δ 156.8, 133.4, 121.0, 83.4, 83.3, 79.9, 76.9, 53.4, 28.9, 28.6.

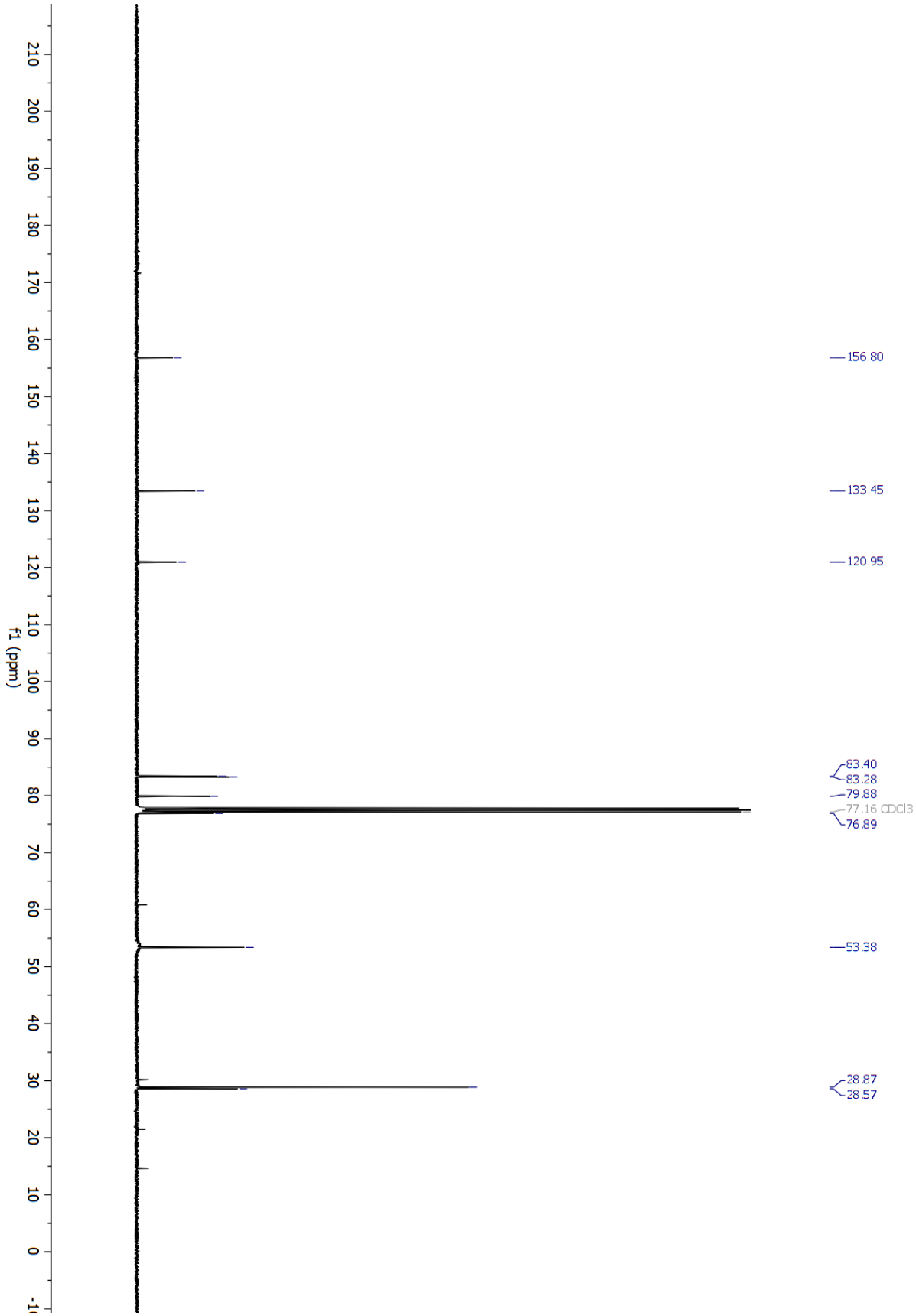
HRMS (ESI): Calculated for $C_{14}H_{23}NO_4$ [M+Na^+]= 292.1519, found= 292.1526

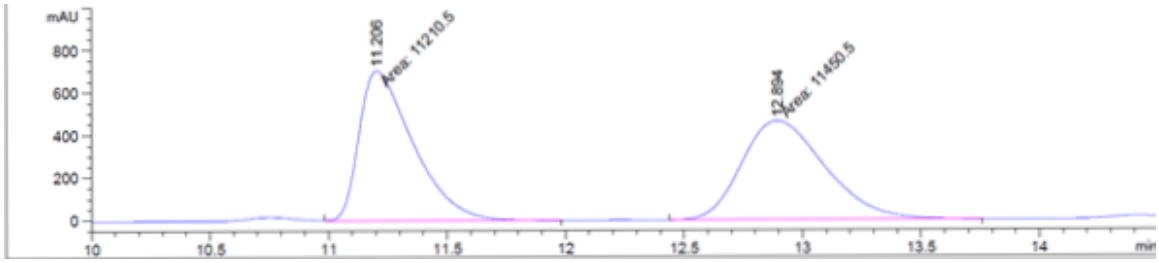
FTIR (neat): 3416, 2953, 2870, 1663, 1457, 1480, 1414, 1362, 1130, 996, 971, 942, 853, 770, 707 cm^{-1}

$[\alpha]_D^{28}$= -44.0 (c 0.1, $CHCl_3$)

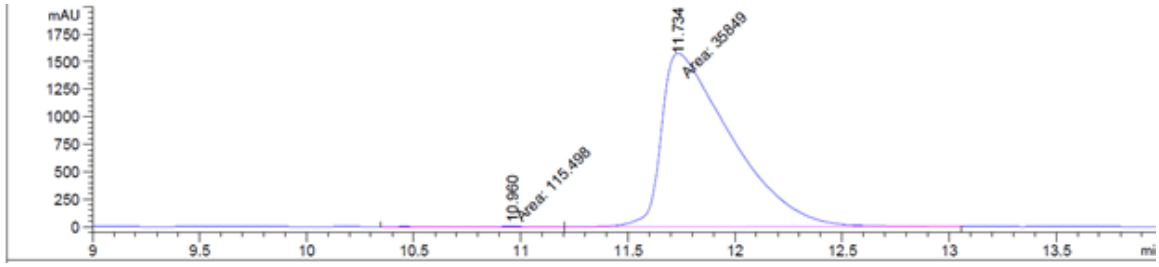
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 98%


7.26 CDCl3
5.76
5.74
5.72
5.71
5.69
5.67
4.62
4.60
4.59
4.57
4.55
4.49
4.48
4.46
4.44
3.99
3.97
3.95
3.90
3.88
3.86
3.76
3.75
3.74
3.73
3.73
3.71
2.85
2.83
2.83
2.81
2.81
2.80
2.79
2.79
2.77
2.77
2.75
2.73
2.66
2.64
2.62
1.43
0.91
1.92
1.92
1.87
0.92
0.95
1.86
0.91
1.84
9.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
156.80
133.45
120.95
83.40
83.28
79.88
77.16 CDCl3
76.89
53.38
28.87
28.57

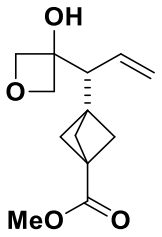


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	11.206	MF	0.2649	1.12105e4	49.4704
2	12.894	MF	0.4099	1.14505e4	50.5296



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	10.960	MM	0.5601	115.49792	0.3211
2	11.734	MM	0.3786	3.58490e4	99.6789

(3t) methyl (R)-3-(1-(3-hydroxyoxetan-3-yl)allyl)bicyclo[1.1.1]pentane-1-carboxylate



Procedure

Allyl acetate **2t** (67.3mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 ^{o}C, 18 hr). The title compound was obtained in 60% yield (28.6 mg, 0.120 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

TLC (SiO_2): R_f = 0.15 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.69 (dt, J = 17.1, 9.8 Hz, 1H), 5.22 (dd, J = 10.3, 1.7 Hz, 1H), 5.16 (dd, J = 17.1, 1.7 Hz, 1H), 4.63 (d, J = 6.9 Hz, 1H), 4.57 (d, J = 7.2 Hz, 1H), 4.54 (d, J = 6.9 Hz, 1H), 4.45 (d, J = 7.1 Hz, 1H), 3.65 (s, 3H), 2.66 (d, J = 9.4 Hz, 1H), 2.31 (s, 1H), 2.34 – 1.96 (m, 6H).

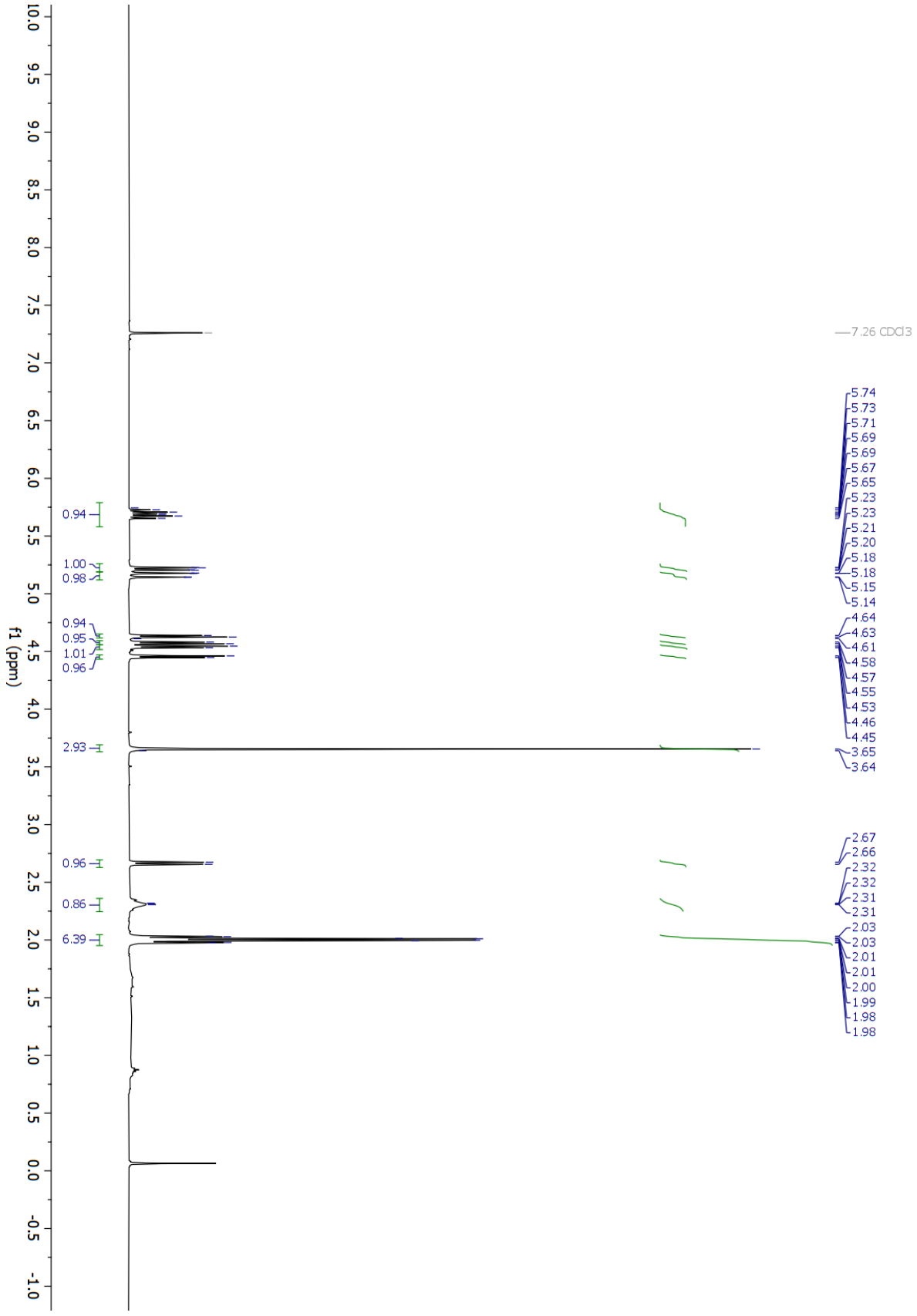
^{13}C NMR (126 MHz, $CDCl_3$): δ 169.2, 132.1, 118.3, 82.5, 82.4, 76.3, 76.0, 75.8, 75.6, 50.9, 50.6, 49.9, 38.5, 37.9.

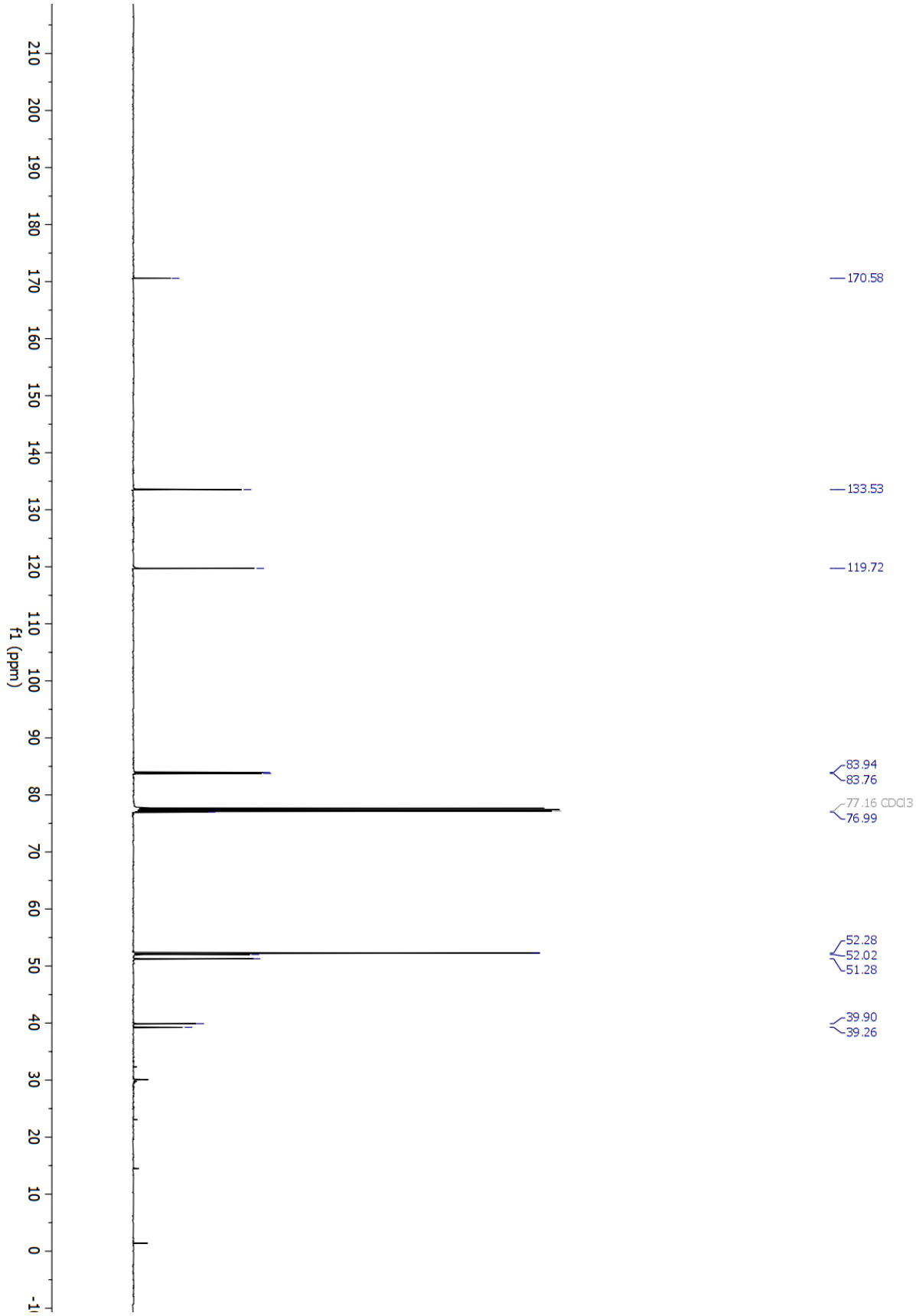
HRMS (ESI): Calculated for $C_{13}H_{18}O_4$ $[M+H^+]$= 239.1205, found= 239.1205

FTIR (neat): 3427, 2932, 1691, 1500, 1452, 1367, 1342, 1307, 1254, 1227, 1137, 1010, 748, 666 cm^{-1}

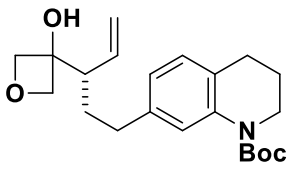
$[\alpha]_D^{28}$= -23.0 (*c* 0.10, $CHCl_3$)

Enantiomeric excess determined from derivative **5t**.


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.94
1.00
0.98
0.94
0.95
1.01
0.96
2.93
0.96
0.86
6.39
7.26 CDCl3
5.74
5.73
5.71
5.69
5.69
5.67
5.65
5.23
5.23
5.21
5.20
5.18
5.18
5.15
5.14
4.64
4.63
4.61
4.58
4.57
4.55
4.53
4.46
4.45
3.65
3.64
2.67
2.66
2.32
2.32
2.31
2.31
2.03
2.03
2.01
2.01
2.00
1.99
1.98
1.98


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
170.58
133.53
119.72
83.94
83.76
77.16 CDCl3
76.99
52.28
52.02
51.28
39.90
39.26

(3u) tert-butyl (S)-7-(3-(3-hydroxyoxetan-3-yl)pent-4-en-1-yl)-3,4-dihydroquinoline-1(2H)-carboxylate



Procedure

Allyl acetate **2u** (107.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure C (100 ^{o}C, 18 hr). The title compound was obtained in 72% yield (53.8 mg, 0.144 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–2:1).

TLC (SiO_2): R_f = 0.32 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, J = 8.4 Hz, 1H), 6.93 (dd, J = 8.5, 2.2 Hz, 1H), 5.76 – 5.65 (m, 1H), 5.30 (dd, J = 10.3, 1.8 Hz, 1H), 5.22 (dd, J = 17.1, 1.8 Hz, 1H), 4.53 (dd, J = 15.1, 6.2 Hz, 3H), 4.47 (d, J = 6.9 Hz, 1H), 3.69 (dd, J = 6.8, 5.3 Hz, 2H), 2.73 (t, J = 6.6 Hz, 2H), 2.68 (ddd, J = 14.3, 9.5, 5.0 Hz, 1H), 2.48 – 2.36 (m, 2H), 1.91 (p, J = 6.5 Hz, 2H), 1.52 (s, 9H).

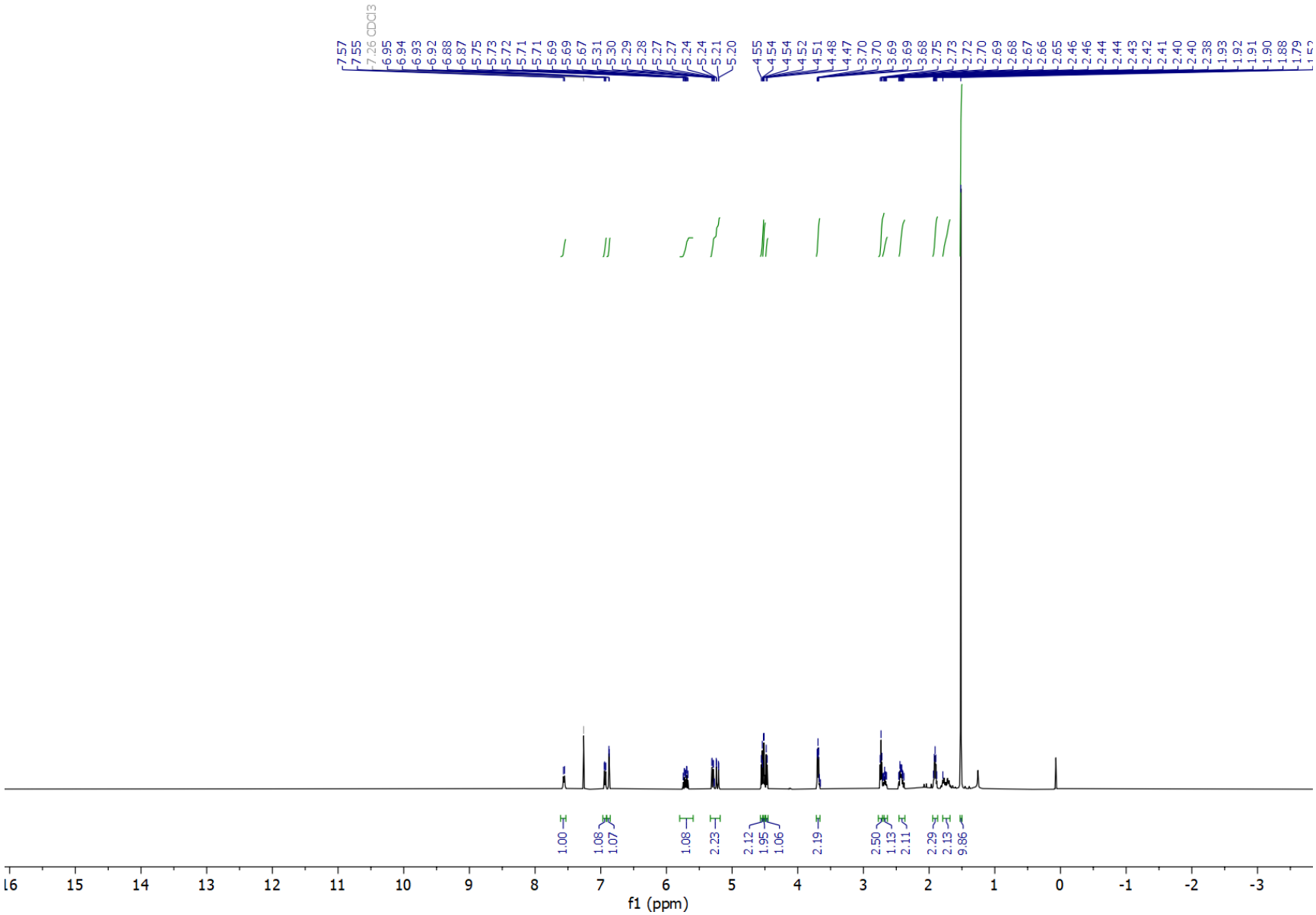
^{13}C NMR (126 MHz, $CDCl_3$): δ 154.1, 136.7, 136.3, 129.9, 128.4, 125.9, 124.3, 119.6, 82.8, 82.6, 80.8 76.4, 50.1, 44.8, 32.9, 29.6, 28.6, 27.7, 23.7.

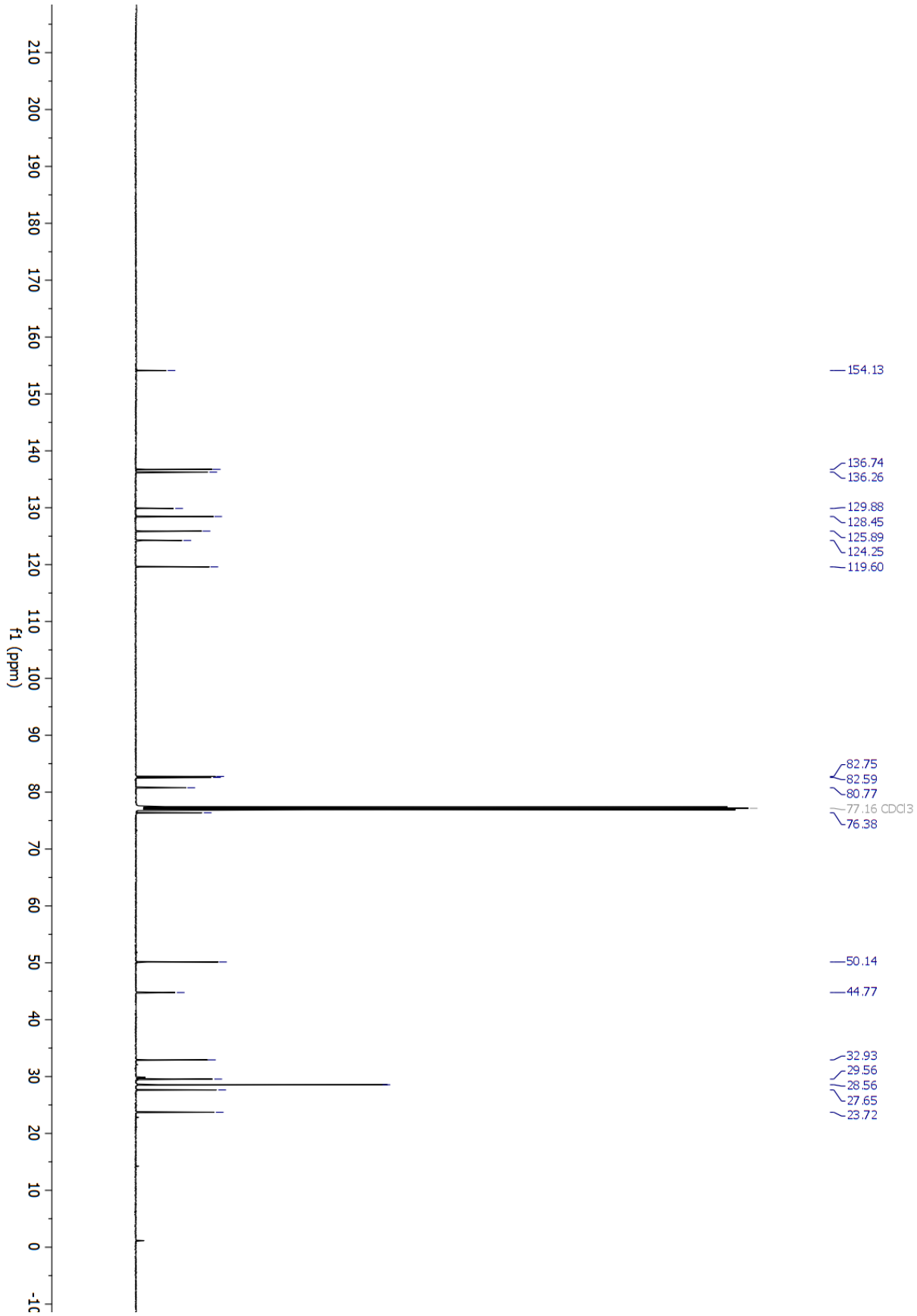
FTIR (neat): 3461, 2970, 2945, 1738, 1537, 1500, 1455, 1366, 1228, 1216, 1163, 824, 766, and 686 cm^{-1}

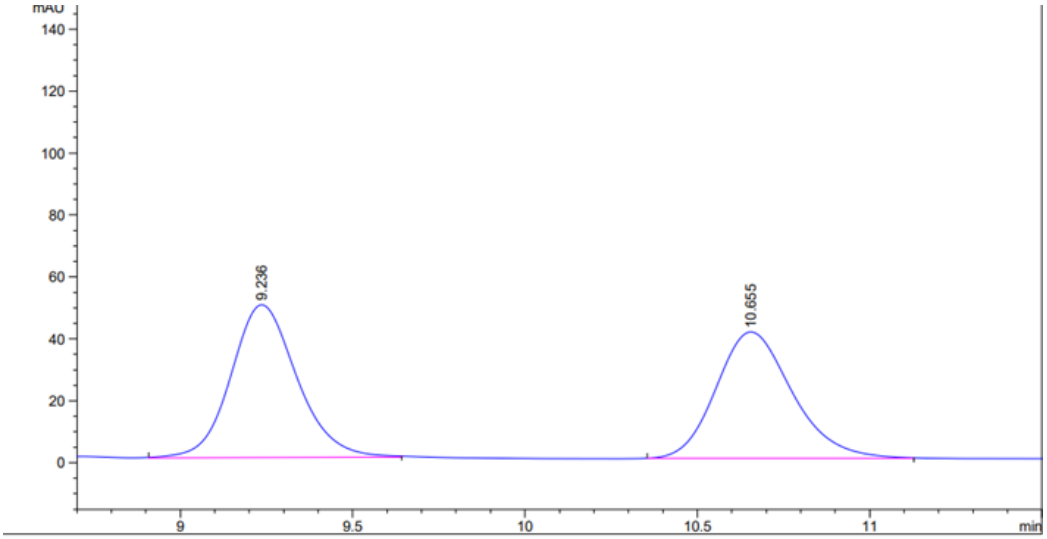
$[\alpha]_D^{28}$= -55.0 (*c* 0.10, $CHCl_3$)

HRMS (ESI): Calculated for $C_{22}H_{31}NO_4$ $[M+Na^+]$= 396.2145, found= 396.2152

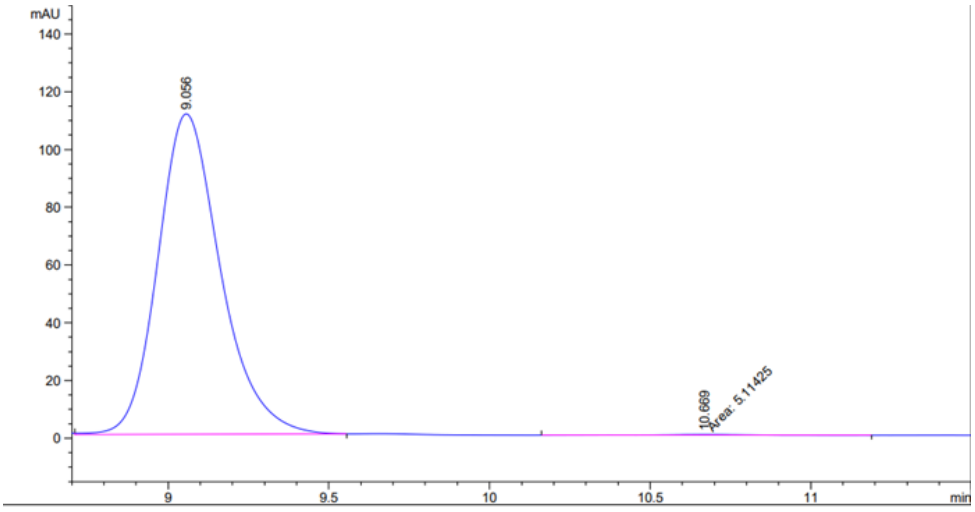
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm): *ee* = 99%


7.57
7.55
7.26 CDCl3
6.95
6.94
6.93
6.92
6.88
6.87
5.75
5.73
5.72
5.71
5.71
5.69
5.69
5.67
5.31
5.30
5.29
5.28
5.27
5.27
5.24
5.24
5.21
5.20
4.55
4.54
4.54
4.52
4.51
4.48
4.47
3.70
3.70
3.69
3.69
3.68
2.75
2.73
2.72
2.70
2.69
2.68
2.67
2.66
2.65
2.46
2.46
2.44
2.44
2.43
2.42
2.41
2.40
2.40
2.38
1.93
1.92
1.91
1.90
1.88
1.79
1.00
1.08
1.07
1.08
2.23
2.12
1.95
1.06
2.19
2.50
1.13
2.11
2.29
2.13
9.86
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
154.13
136.74
136.26
129.88
128.45
125.89
124.25
119.60
82.75
82.59
80.77
77.16 CDCl3
76.38
50.14
44.77
32.93
29.56
28.56
27.65
23.72

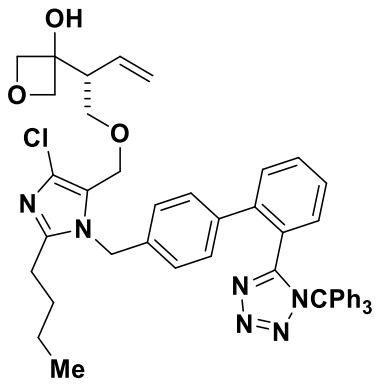


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.236	BB	0.2041	661.39594	49.43079	51.1494
2	10.655	BB	0.2361	631.67151	40.91267	48.8506



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.056	VB	0.2065	1509.00195	111.03948	99.6622
2	10.669	MM	0.3380	5.11425	2.52219e-1	0.3378

(3v) (R)-3-(1-((2-butyl-4-chloro-1-((2'-(1-trityl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1H-imidazol-5-yl)methoxy)but-3-en-2-yl)oxetan-3-ol



Procedure

Allyl acetate **2v** (233.1 mg, 0.300 mmol, 150 mol%) was subjected to modified version of general procedure C using 7.5 mol% (S)-Ir-tol-BINAP (100 °C, 24hr). The title compound was obtained in 64% yield (101.1 mg, 0.128 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1–1:1).

TLC (SiO_2): Rf = 0.12 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (dd, J = 7.2, 1.9 Hz, 1H), 7.49 (pd, J = 7.5, 1.7 Hz, 2H), 7.39 – 7.31 (m, 4H), 7.29 – 7.23 (m, 7H), 7.12 (d, J = 8.0 Hz, 2H), 6.98 – 6.90 (m, 6H), 6.71 (d, J = 7.9 Hz, 2H), 5.78 (ddd, J = 17.2, 10.5, 8.6 Hz, 1H), 5.36 – 5.14 (m, 2H), 5.00 (s, 2H), 4.61 – 4.47 (m, 4H), 4.15 (s, 2H), 3.56 (dd, J = 9.6, 4.5 Hz, 1H), 3.49 (dd, J = 9.6, 6.1 Hz, 1H), 3.43 (s, 1H), 2.71 (dt, J = 9.8, 5.4 Hz, 1H), 2.55 – 2.47 (m, 2H), 1.66 (dq, J = 16.4, 8.7, 8.1 Hz, 4H), 1.34 – 1.24 (m, 3H), 0.87 (t, J = 7.3 Hz, 3H).

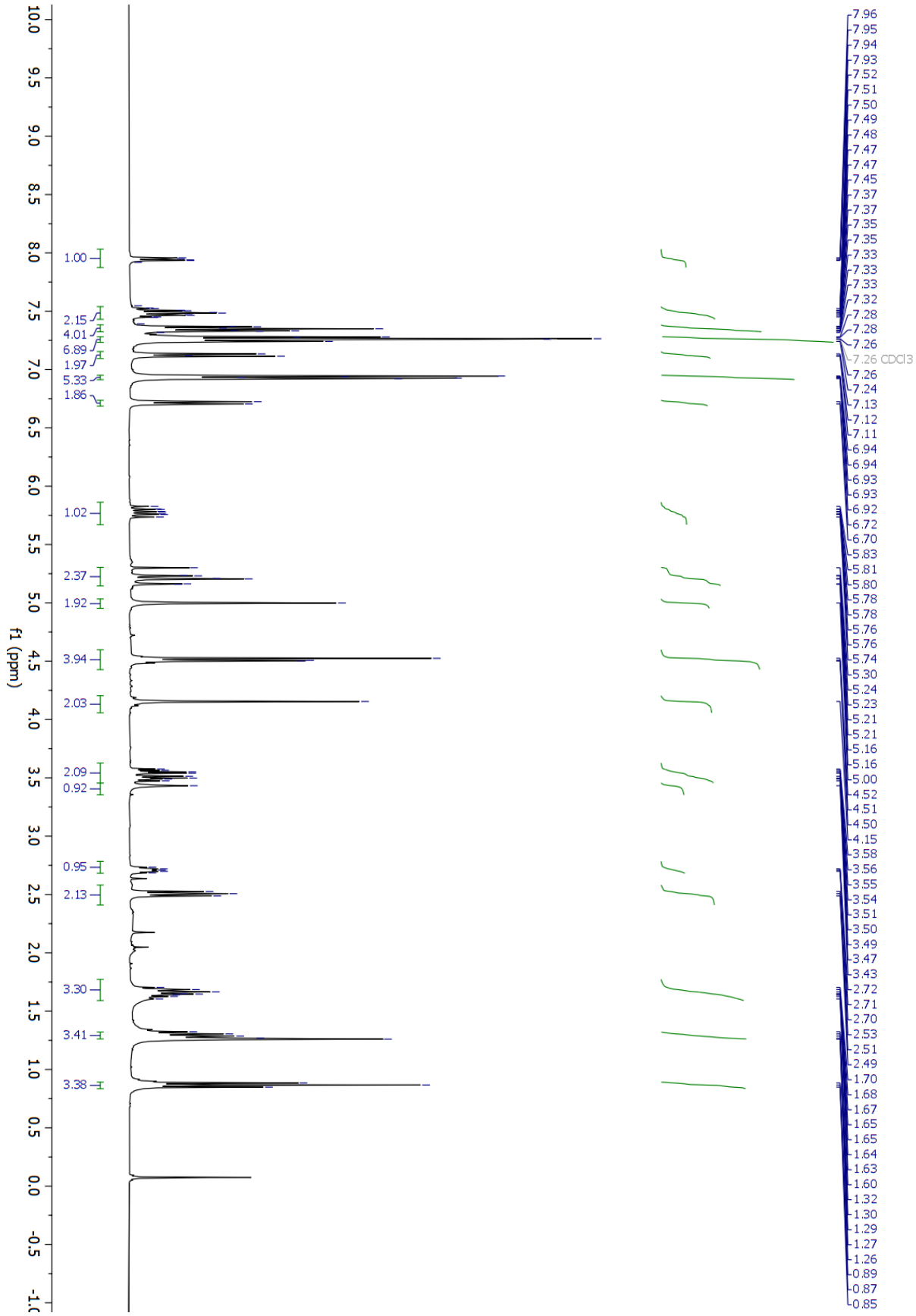
^{13}C NMR (101 MHz, $CDCl_3$): δ 164.1, 149.2, 141.4, 141.3, 134.3, 133.6, 130.9, 130.5, 130.3, 130.2, 130.1, 129.9, 128.5, 128.1, 128.0, 127.8, 126.3, 125.2, 121.3, 119.5, 83.2, 83.0, 82.2, 76.3, 69.7, 61.3, 49.1, 47.2, 29.9, 26.9, 22.5, 13.9.

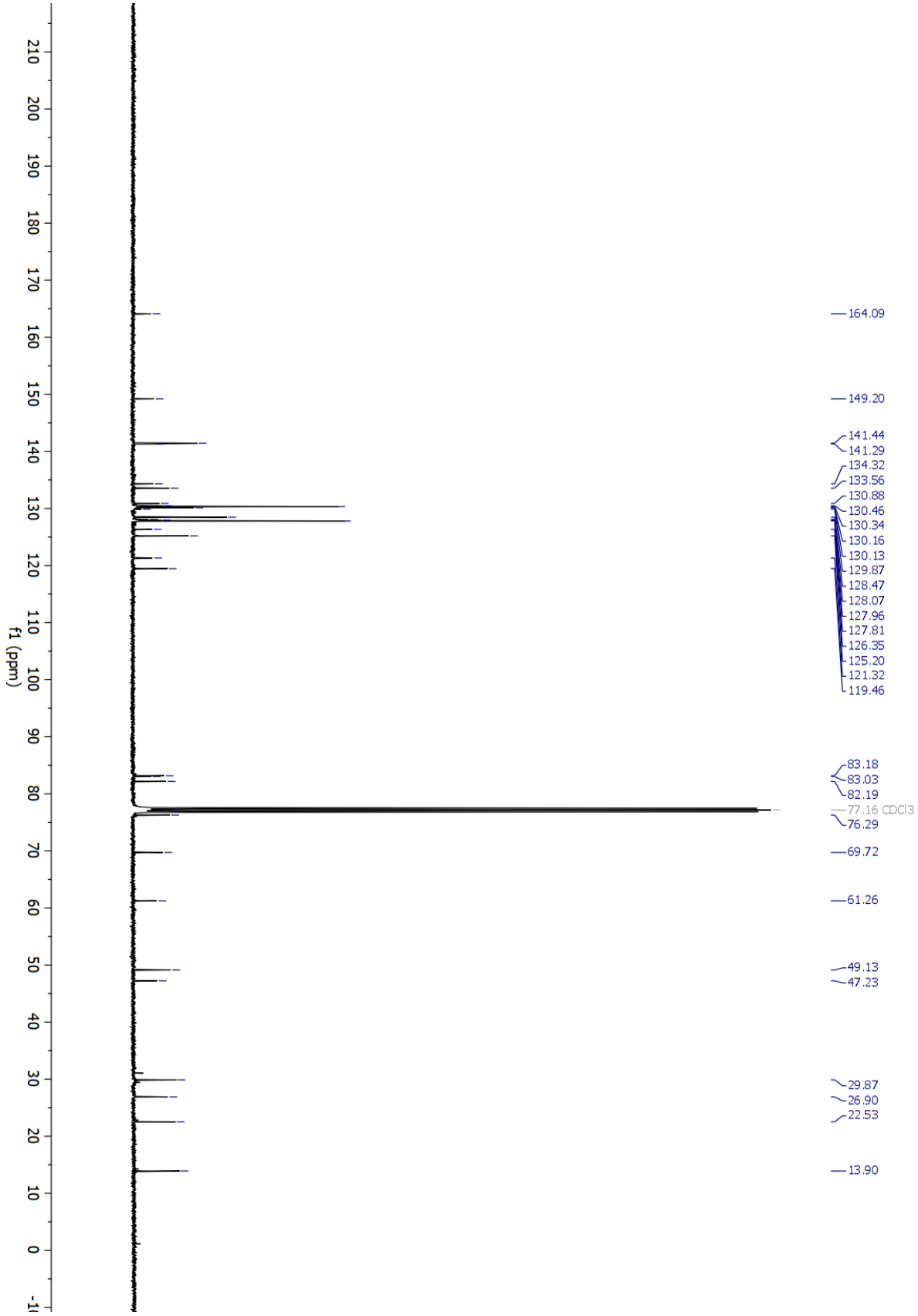
FTIR (neat): 3384, 3071, 2966, 2924, 2870, 2356, 1740, 1430, 1410, 1356,1159, 798, 784, 758, 748 cm^{-1}

$[\alpha]_D^{28}$= -20.0(c 0.10, CDCl3)

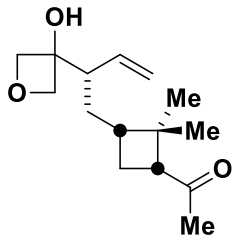
HRMS (ESI): Calculated for $C_{48}H_{47}ClN_6O_3$ $[M+H^+]$= 791.3471, found= 791.3478

Enantiomeric excess determined from derivative **6v.**


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
2.15
4.01
6.89
1.97
5.33
1.86
1.02
2.37
1.92
3.94
2.03
2.09
0.92
0.95
2.13
3.30
3.41
3.38
7.96
7.95
7.94
7.93
7.52
7.51
7.50
7.49
7.48
7.47
7.47
7.45
7.37
7.37
7.35
7.35
7.33
7.33
7.33
7.32
7.28
7.28
7.26
7.26 CDCl3
7.26
7.24
7.13
7.12
7.11
6.94
6.94
6.93
6.93
6.92
6.72
6.70
5.83
5.81
5.80
5.78
5.78
5.76
5.76
5.74
5.30
5.24
5.23
5.21
5.21
5.16
5.16
5.00
4.52
4.51
4.50
4.15
3.58
3.56
3.55
3.54
3.51
3.50
3.49
3.47
3.43
2.72
2.71
2.70
2.53
2.51
2.49
1.70
1.68
1.67
1.65
1.65
1.64
1.63
1.60
1.32
1.30
1.29
1.27
1.26
0.89
0.87
0.85


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
164.09
149.20
141.44
141.29
134.32
133.56
130.88
130.46
130.34
130.16
130.13
129.87
128.47
128.07
127.96
127.81
126.35
125.20
121.32
119.46
83.18
83.03
82.19
77.16 CDCl3
76.29
69.72
61.26
49.13
47.23
29.87
26.90
22.53
13.90

(3w) 1-((1*R*,3*S*)-3-((*S*)-2-(3-hydroxyoxetan-3-yl)but-3-en-1-yl)-2,2-dimethylcyclobutyl)ethan-1-one



Procedure

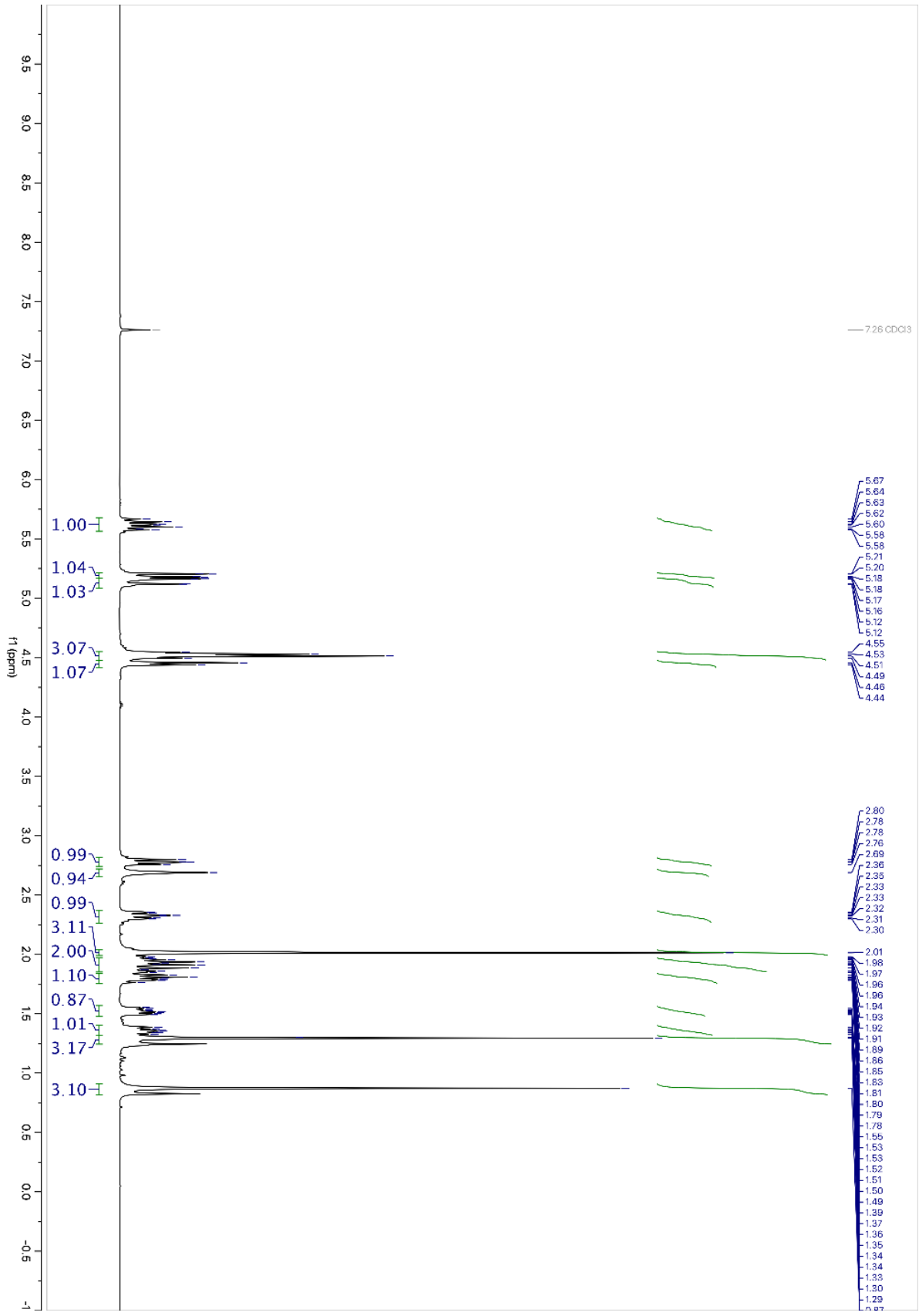
Allyl acetate **2w** (71.5 mg, 0.300 mmol, 150 mol%) was subjected to a modified version of general procedure C using (S)-Ir-Cl, OMe-BIPHEP (10.1 mg, 0.010 mmol, 5 mol%, 100 ^{o}C, 18 hr). The title compound was obtained in 73% yield (36.9 mg, 0.146 mmol, 6:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1—1:1).

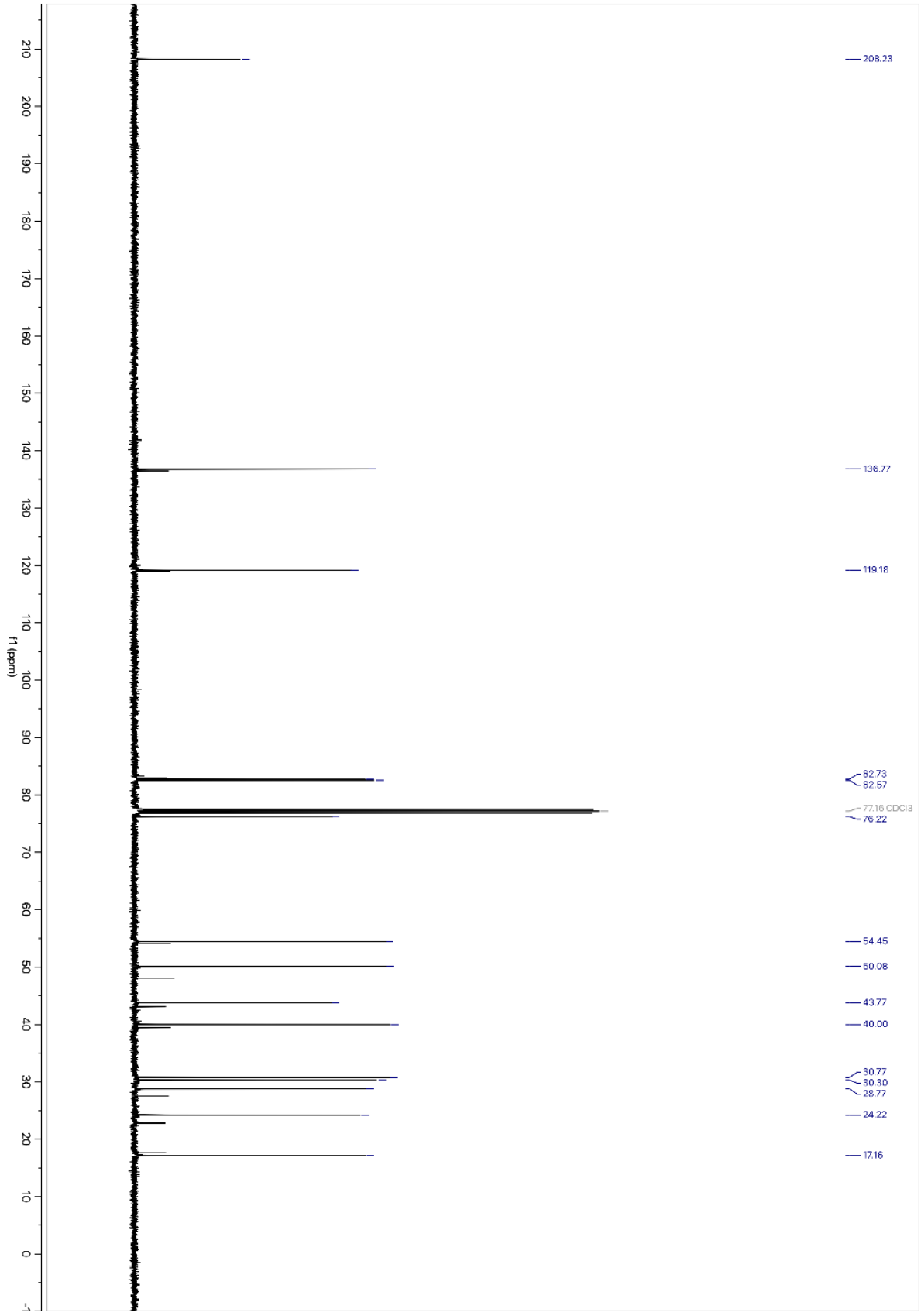
TLC (SiO_2): R_f = 0.31 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.62 (dt, *J* = 17.0, 9.9 Hz, 1H), 5.19 (dd, *J* = 10.3, 1.8 Hz, 1H), 5.14 (dd, *J* = 17.2, 1.8 Hz, 1H), 4.52 (q, *J* = 7.4, 6.8 Hz, 3H), 4.45 (d, *J* = 7.0 Hz, 1H), 2.78 (dd, *J* = 9.7, 7.4 Hz, 1H), 2.69 (s, 1H), 2.33 (ddd, *J* = 11.9, 9.4, 3.0 Hz, 1H), 2.02 (d, *J* = 3.4 Hz, 3H), 1.99 – 1.85 (m, 2H), 1.85 – 1.73 (m, 1H), 1.52 (ddd, *J* = 14.0, 7.5, 3.0 Hz, 1H), 1.40 – 1.31 (m, 1H), 1.29 (s, 3H), 0.87 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 208.2, 136.8, 119.2, 82.7, 82.6, 76.2, 54.4, 50.1, 43.8, 40.0, 30.8, 30.3, 28.8, 24.2, 17.2.
HRMS (APCI): Calculated for $C_{15}H_{24}O_3$ [M+H$^+$] = 253.1798, Found 253.1802

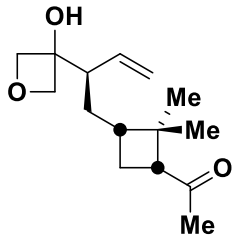
FTIR (neat): 3399, 3074, 2952, 2873, 2363, 1701, 1638, 1463, 1421, 1386, 1368, 1357, 1268, 1242, 1223, 1182, 1153, 1070, 1001, 974, 918, 845, 750 cm^{-1}

$[\alpha]_D^{28}$ = -14.0(*c* 0.10, $CHCl_3$)


f1 (ppm)
7.26 CDCl3
1.00
1.04
1.03
3.07
1.07
0.99
0.94
0.99
3.11
2.00
1.10
0.87
1.01
3.17
3.10


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
208.23
138.77
119.18
82.73
82.57
77.16 CDCl3
76.22
54.45
50.08
43.77
40.00
30.77
30.30
28.77
24.22
17.16

(*iso*-3w) 1-((1*R*,3*S*)-3-((*R*)-2-(3-hydroxyoxetan-3-yl)but-3-en-1-yl)-2,2-dimethylcyclobutyl)ethan-1-one



Procedure

Allyl acetate **2w** (71.5 mg, 0.300 mmol, 150 mol%) was subjected to a modified version of general procedure C using (R)-Ir-Cl, OMe-BIPHEP (10.1 mg, 0.010 mmol, 5 mol%, 100 ^{o}C, 18 hr). The title compound was obtained in 97% yield (49.1 mg, 0.195 mmol, 6.6:1 dr) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1—1:1).

TLC (SiO_2): R_f = 0.31 (hexanes: ethyl acetate = 1:1).

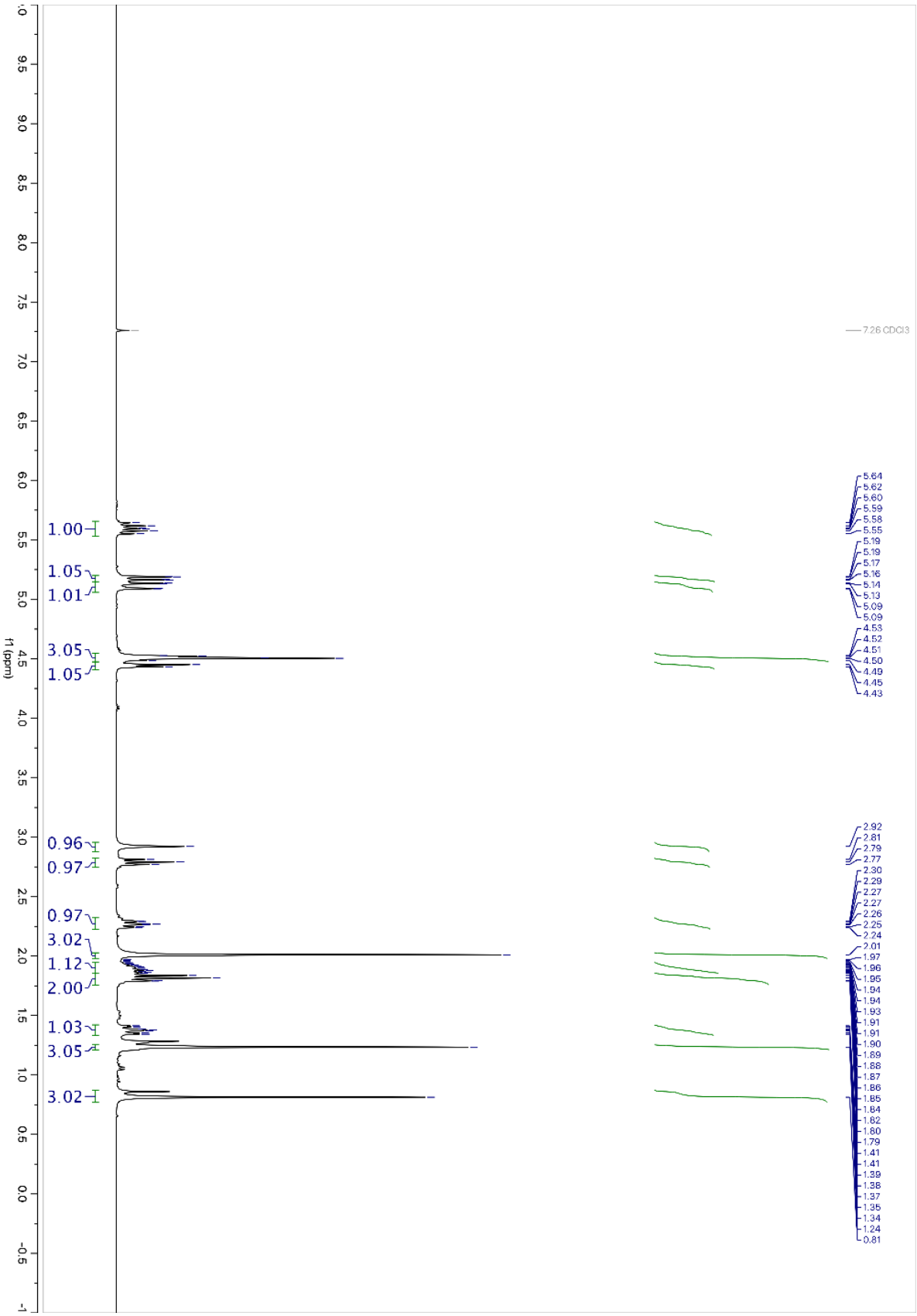
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.60 (dt, *J* = 17.0, 9.8 Hz, 1H), 5.18 (dd, *J* = 10.3, 1.9 Hz, 1H), 5.11 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.57 – 4.48 (m, 3H), 4.44 (d, *J* = 6.9 Hz, 1H), 2.92 (s, 1H), 2.78 (q, *J* = 8.9 Hz, 1H), 2.27 (ddd, *J* = 11.6, 9.3, 2.6 Hz, 1H), 2.01 (s, 3H), 1.90 (dtt, *J* = 17.6, 7.1, 3.5 Hz, 1H), 1.82 (t, *J* = 8.3 Hz, 2H), 1.38 (ddd, *J* = 14.6, 11.2, 3.6 Hz, 1H), 1.24 (s, 3H), 0.81 (s, 3H).

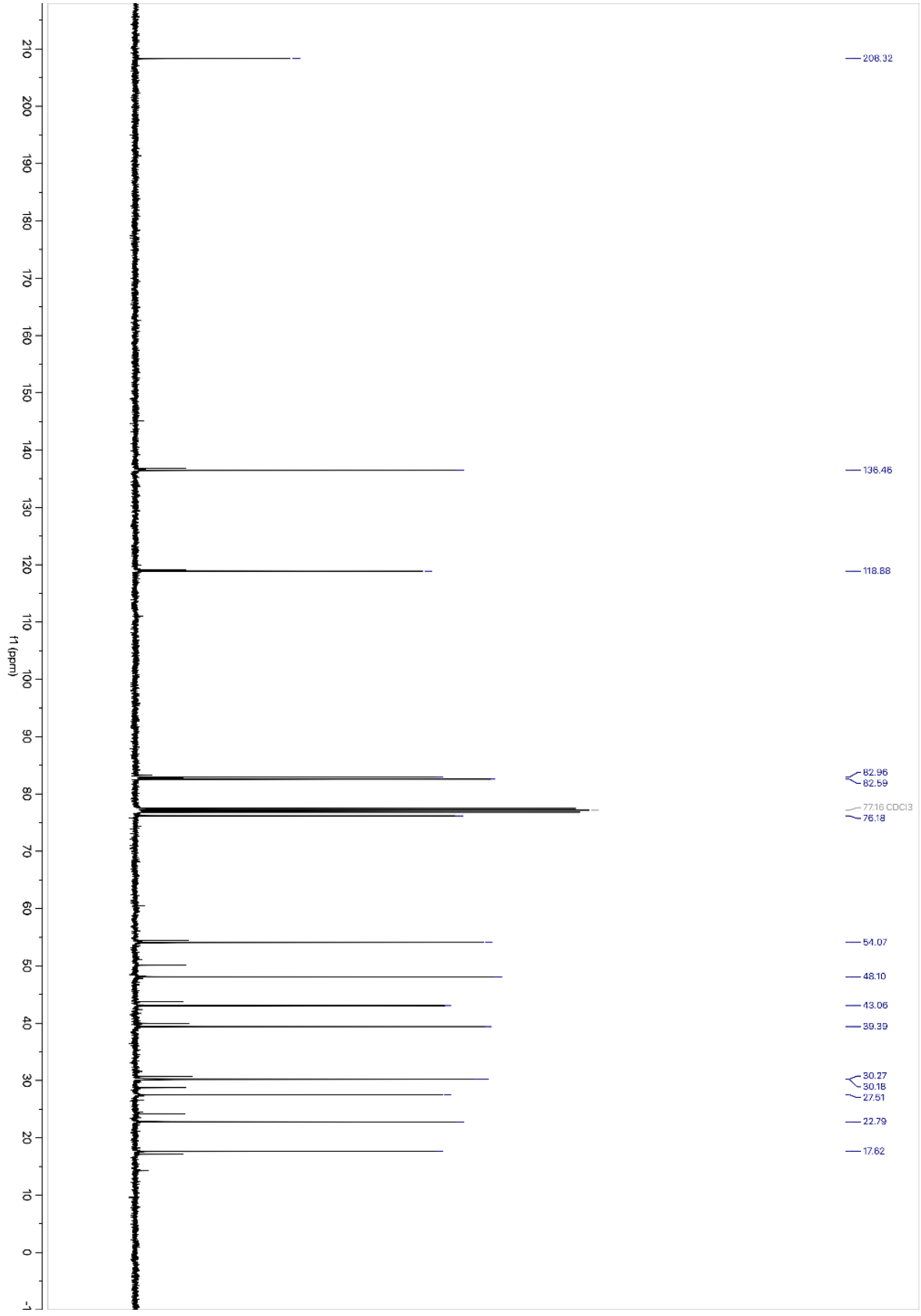
^{13}C NMR (101 MHz, $CDCl_3$): δ 208.32, 136.46, 118.88, 82.96, 82.59, 76.18, 54.07, 48.10, 43.06, 39.39, 30.27, 30.18, 27.51, 22.79, 17.62.

HRMS (ESI): Calculated for $C_{15}H_{24}O_3$ [M+H$^+$] = 253.1798, found 253.1800

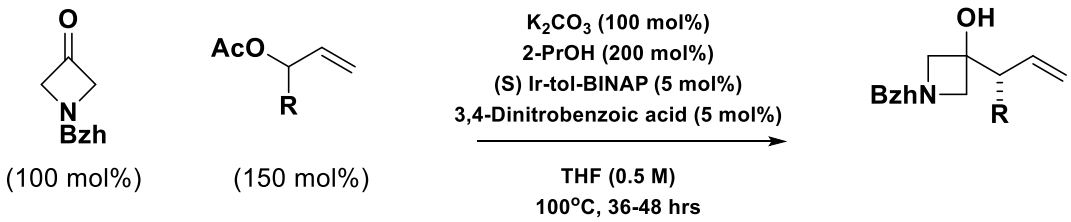
FTIR (neat): 3396, 2951, 2872, 1702, 1638, 1461, 1385, 1280, 1225, , 1097, 1001, 969, 918, 872, cm^{-1}

$[\alpha]_D^{28}$= +19.6 (*c* 0.20, $CHCl_3$)


f1 (ppm)
7.26 CDCl3
1.00
1.05
1.01
3.05
1.05
0.96
0.97
0.97
3.02
1.12
2.00
1.03
3.05
3.02

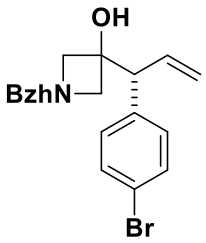

f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
208.32
136.46
118.88
82.96
82.59
77.16 CDCl3
76.18
54.07
48.10
43.06
39.39
30.27
30.18
27.51
22.79
17.62

General Procedure D



An oven-dried pressure tube equipped with a magnetic stir bar was charged allylic acetate (0.30 mmol, 150 mol%), (*S*)-Ir-tol-BINAP (11.2 mg, 0.01 mmol, 5 mol%), 3,4-dinitrobenzoic acid (2.12 mg, 0.010 mmol, 5 mol%) 1-diphenymethyl-3-azetidinone (47.6 mg 0.20 mmol, 100 mol%), and potassium carbonate (27.6 mg, 0.20 mmol, 100 mol%). The tube was purged with argon and *i*-propanol (30 µL, 0.400 mmol, 200 mol%) was added by syringe, followed by THF (0.40 mL, 0.50 M). The septum was removed, and the tube was sealed with a polytetrafluoroethylene-lined screwcap. The tube was placed in an oil bath at 100 °C and stirred for 36-48 hours. The vessel was allowed to cool to ambient temperature. Upon cooling, the reaction mixture was concentrated onto silica gel and purified by flash chromatography to furnish products **4a-4w**.

(4a) (R)-1-benzhydryl-3-(1-(4-bromophenyl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2a** (76.5 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 ºC, 36 hr). The title compound was obtained in 82% yield (71.2 mg, 1.64 mmol) as a pale yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.35 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 7.6 Hz, 3H), 7.25 (s, 2H), 7.23 (d, J = 2.3 Hz, 0H), 7.20 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 3.0 Hz, 0H), 6.15 (ddd, J = 17.8, 10.4, 8.0 Hz, 1H), 5.23 (d, J = 10.3 Hz, 1H), 5.13 (d, J = 17.2 Hz, 1H), 4.37 (s, 1H), 3.67 (d, J = 8.0 Hz, 1H), 3.39 (d, J = 8.2 Hz, 1H), 3.22 (d, J = 8.3 Hz, 1H), 3.02 (d, J = 8.2 Hz, 1H), 2.89 (d, J = 8.3 Hz, 1H), 2.07 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 142.12, 138.7, 131.6, 130.9, 128.6, 127.5, 121.0, 118.7, 77.9, 72.0, 65.4, 64.8, 56.6.

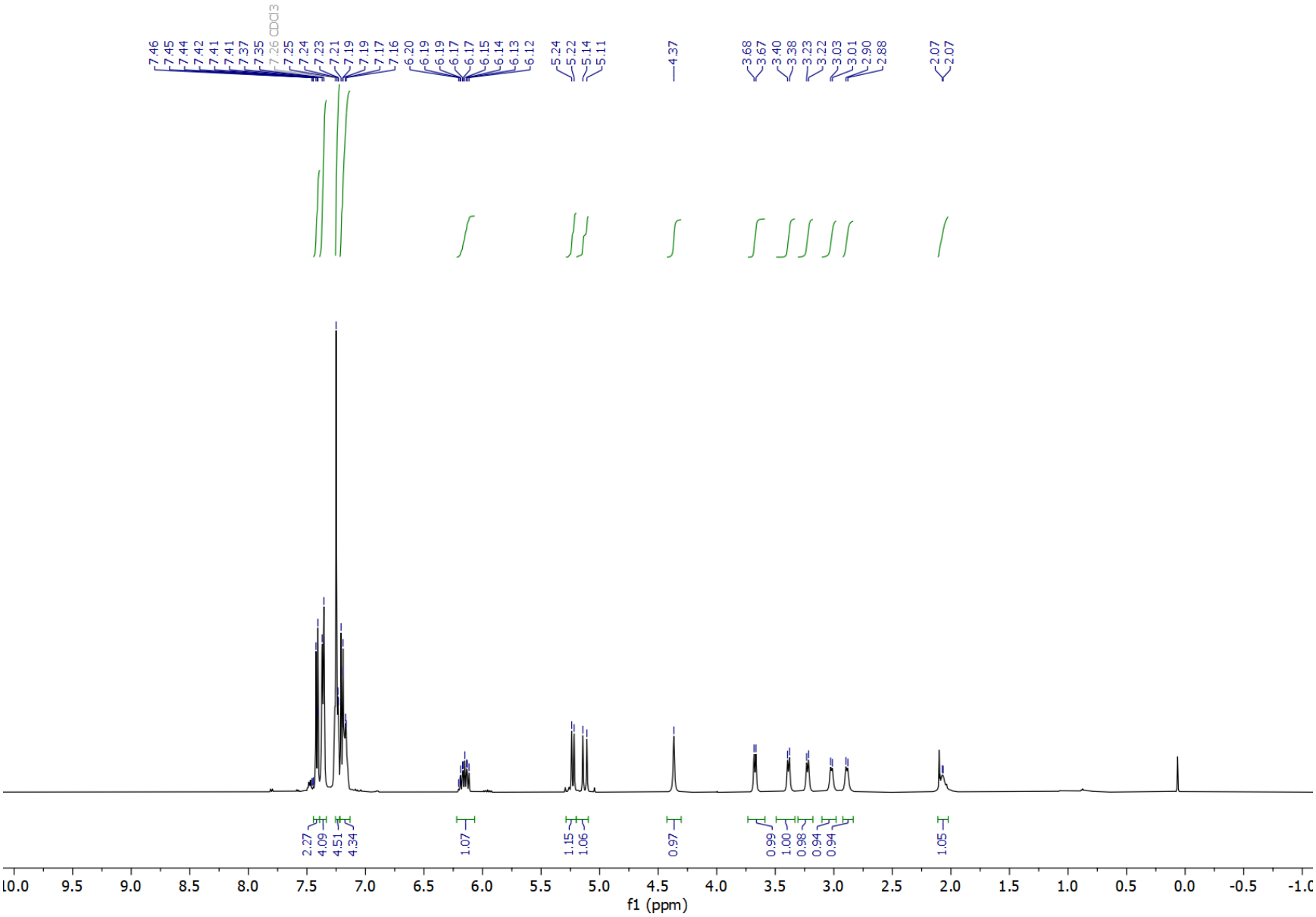
HRMS (ESI): Calculated for $C_{30}H_{40}N_2O_3$ [M+H$^+$]= 477.3112, found= 477.3118

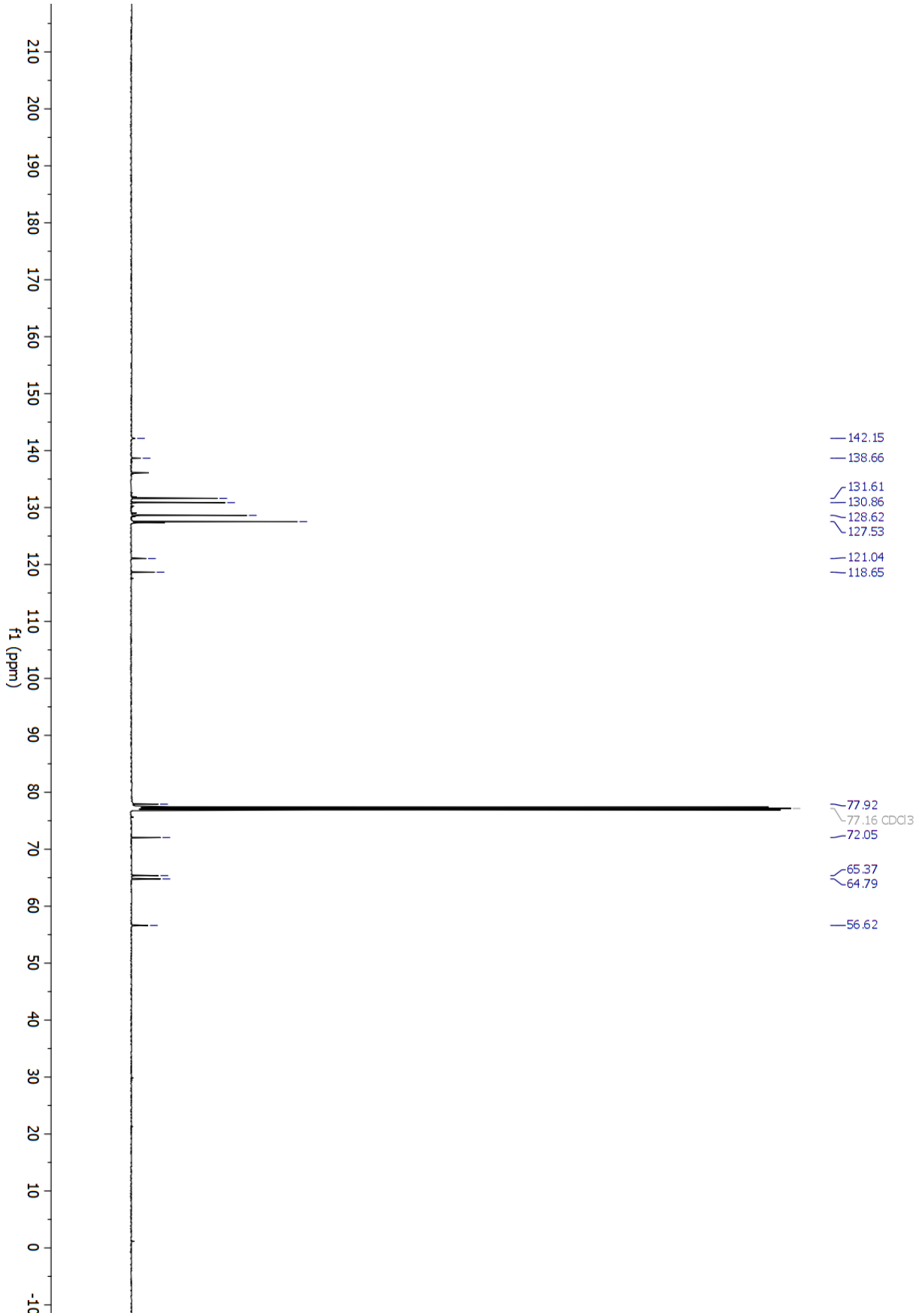
FTIR (neat): 3556, 3060, 3027, 2935, 2850, 1489, 1171, 1073, 993, 794, 701 cm^{-1}

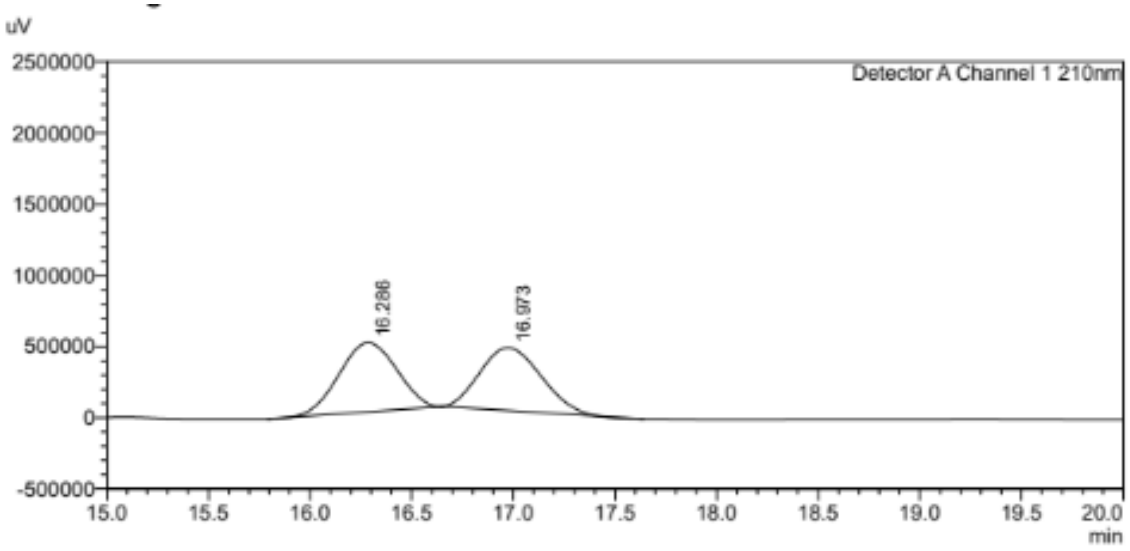
$[\alpha]_D^{28}$= -10.0 (*c* 0.10, $CHCl_3$)

MP: 160-163ºC

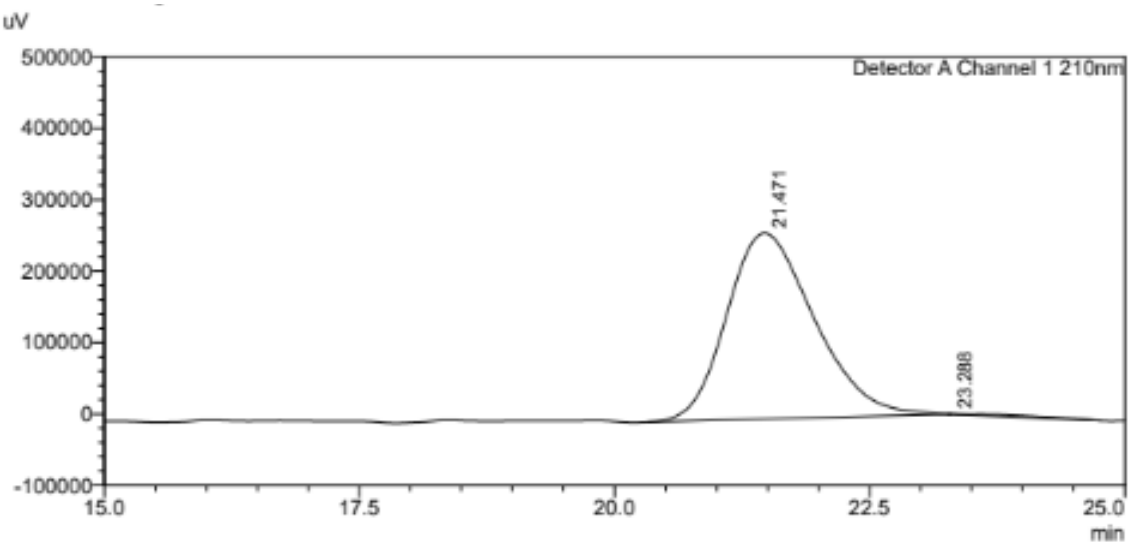
HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm): *ee* = 98%


7.46
7.45
7.44
7.42
7.41
7.41
7.37
7.35
7.26 CDCl3
7.25
7.24
7.23
7.21
7.19
7.19
7.17
7.16
6.20
6.19
6.19
6.17
6.17
6.15
6.14
6.13
6.12
5.24
5.22
5.14
5.11
4.37
3.68
3.67
3.40
3.38
3.23
3.22
3.03
3.01
2.90
2.88
2.07
2.07
2.27
4.09
4.51
4.34
1.07
1.15
1.06
0.97
0.99
1.00
0.98
0.94
0.94
1.05
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
142.15
138.66
131.61
130.86
128.62
127.53
121.04
118.65
77.92
77.16 CDCl3
72.05
65.37
64.79
56.62

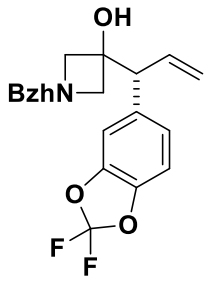


Peak#	Ret. Time	Area	Height	Area%
1	16.286	9566439	484750	50.955
2	16.973	9207922	441616	49.045
Total		18774361	926367	100.000



Peak#	Ret. Time	Area	Height	Area%
1	21.471	15526675	259954	99.101
2	23.288	140910	37	0.899
Total		15667585	259992	100.000

(4b) (R)-1-benzhydryl-3-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2b** (76.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 ºC, 36 hr). The title compound was obtained in 88% yield (76.1 mg, 0.176 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.31 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 7.6 Hz, 4H), 7.26 – 7.19 (m, 5H), 7.17 (dt, J = 7.3, 3.7 Hz, 2H), 7.11 (d, J = 1.7 Hz, 1H), 7.01 (dd, J = 8.2, 1.7 Hz, 1H), 6.95 (d, J = 8.2 Hz, 1H), 6.12 (ddd, J = 17.6, 10.3, 7.9 Hz, 1H), 5.23 (d, J = 10.3 Hz, 1H), 5.12 (d, J = 17.2 Hz, 1H), 4.37 (s, 1H), 3.69 (d, J = 7.9 Hz, 1H), 3.38 (d, J = 8.2 Hz, 1H), 3.20 (d, J = 8.4 Hz, 1H), 3.02 (d, J = 8.2 Hz, 1H), 2.89 (d, J = 8.3 Hz, 1H), 2.10 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 142.3, 138.7, 136.1, 131.9, 131.6, 130.9, 129.0, 128.6, 127.5, 127.3, 121.0, 118.7, 77.9, 72.1, 65.4, 64.8, 56.6.

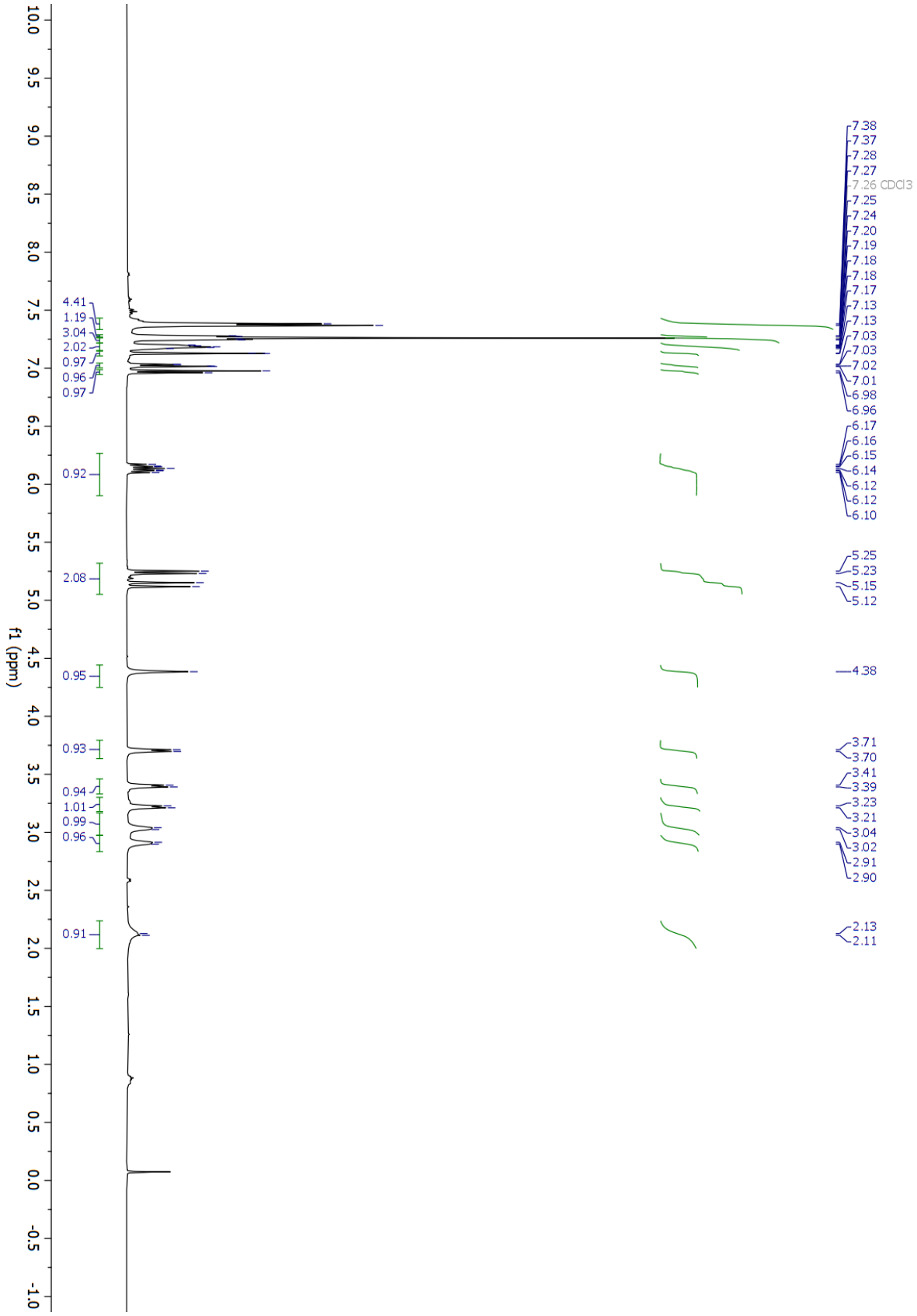
^{19}F NMR (471 MHz, $CDCl_3$): δ -50.03

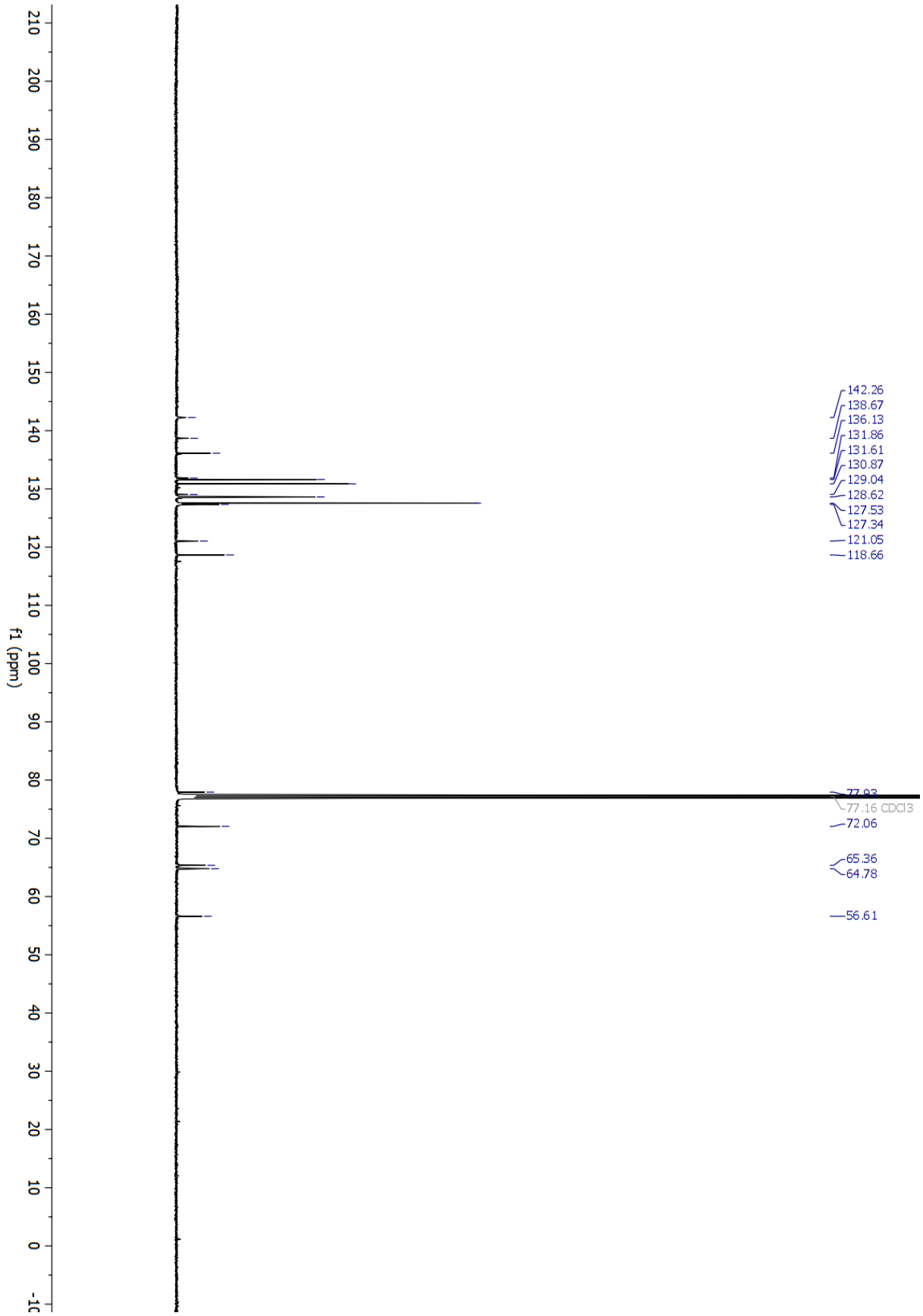
HRMS (ESI): Calculated for $C_{26}H_{23}F_2NO_3$ $[M+H^+]$= 436.1719, found= 436.1725

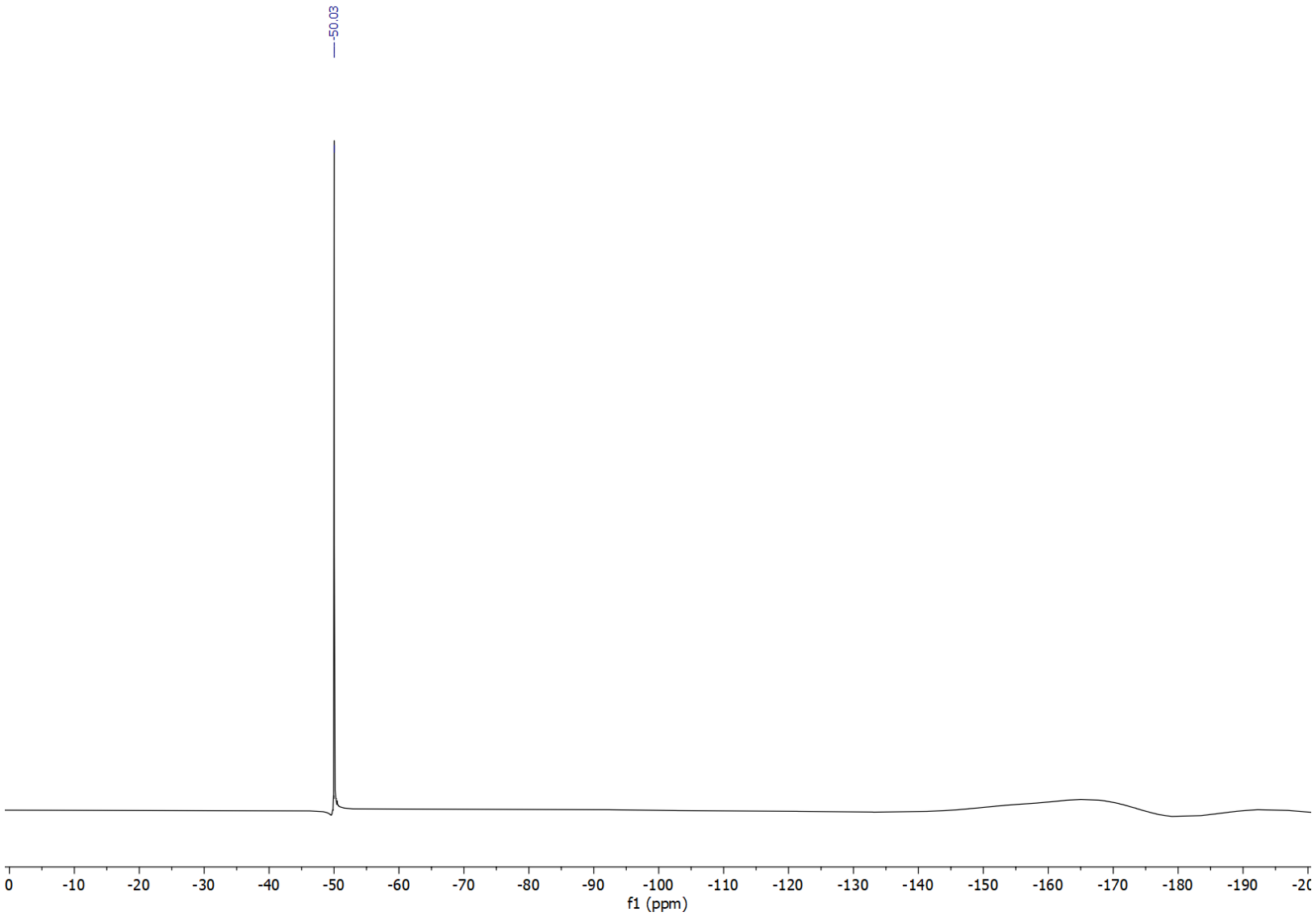
FTIR (neat): 3371, 3021, 2969, 1494, 1470, 1451, 1370, 1238, 1153, 1074, 1035, 812, 703, 668 cm^{-1}

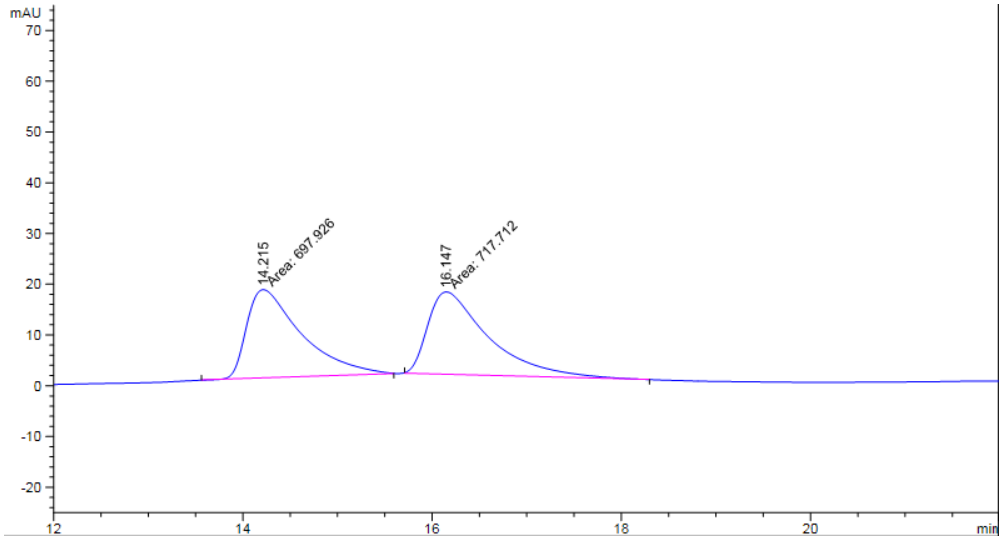
$[\alpha]_D^{28}$= -32.1 (*c* 0.10, $CHCl_3$)

HPLC (Chiralcel AD-H hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 230 nm): *ee* = 94%

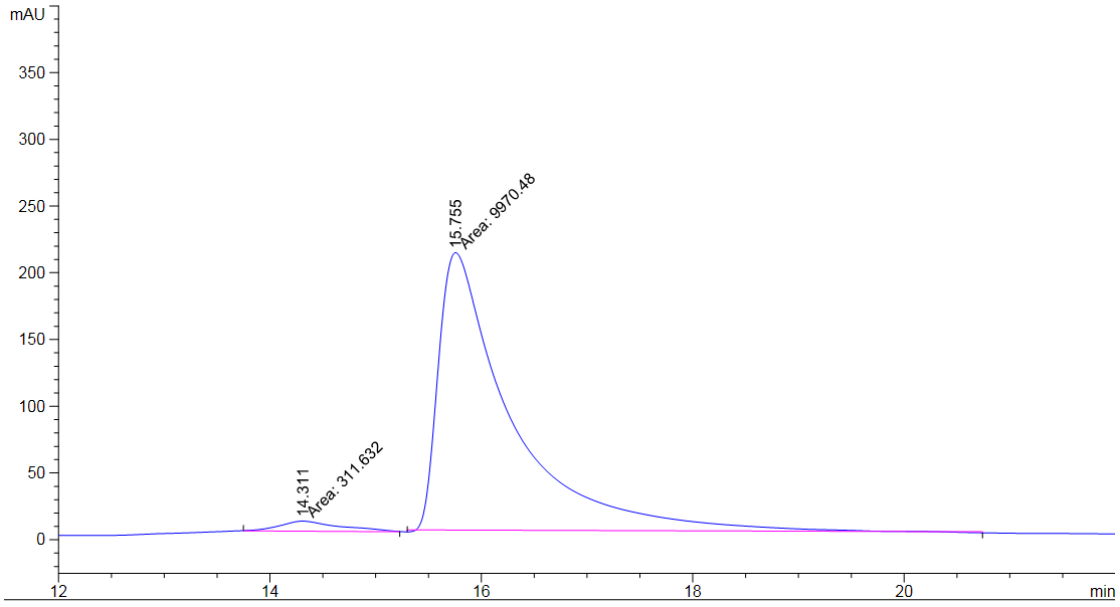

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
4.41
1.19
3.04
2.02
0.97
0.96
0.97
0.92
2.08
0.95
0.93
0.94
1.01
0.99
0.96
0.91
7.38
7.37
7.28
7.27
7.26 CDCl3
7.25
7.24
7.20
7.19
7.18
7.18
7.17
7.13
7.13
7.03
7.03
7.02
7.01
6.98
6.96
6.17
6.16
6.15
6.14
6.12
6.12
6.10
5.25
5.23
5.15
5.12
4.38
3.71
3.70
3.41
3.39
3.23
3.21
3.04
3.02
2.91
2.90
2.13
2.11


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
142.26
138.67
136.13
131.86
131.61
130.87
129.04
128.62
127.53
127.34
121.05
118.66
77.83
77.16 CDCl3
72.06
65.36
64.78
56.61


-50.03
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

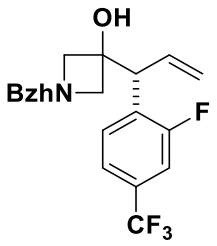


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.215	MM	0.6684	697.92633	17.40407	49.3012
2	16.147	MM	0.7378	717.71216	16.21279	50.6988



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.311	MM	0.6778	311.63248	7.66289	3.0308
2	15.755	MM	0.7992	9970.47852	207.91676	96.9692

(4c) (R)-1-benzhydryl-3-(1-(2-fluoro-4-(trifluoromethyl)phenyl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2c** (78.6 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 48 hr). The title compound was obtained in 82% yield (72.5 mg, 0.164 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.41 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (t, J = 7.6 Hz, 1H), 7.31 (dt, J = 10.9, 5.8 Hz, 5H), 7.21 (t, J = 7.3 Hz, 5H), 7.14 (d, J = 7.3 Hz, 2H), 6.12 (ddd, J = 17.6, 10.2, 7.9 Hz, 1H), 5.22 (d, J = 10.4 Hz, 1H), 5.12 (d, J = 17.1 Hz, 1H), 4.34 (s, 1H), 3.37 (d, J = 8.1 Hz, 1H), 3.15 (d, J = 8.3 Hz, 1H), 3.01 (d, J = 8.1 Hz, 1H), 2.87 (d, J = 8.3 Hz, 1H), 2.54 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 160.5 (d, J = 247.1 Hz), 142.1 (d, J = 3.3 Hz), 134.7, 131.4 (d, J = 4.4 Hz), 128.6, 127.8, 127.5, 127.5, 127.3, 120.9 (t, J = 3.7 Hz), 119.3, 112.9 (dd, J = 27.0, 4.0 Hz), 109.7 (d, J = 121.9 Hz), 77.9, 72.1, 65.8, 64.8, 48.9 (d, J = 1.9 Hz).

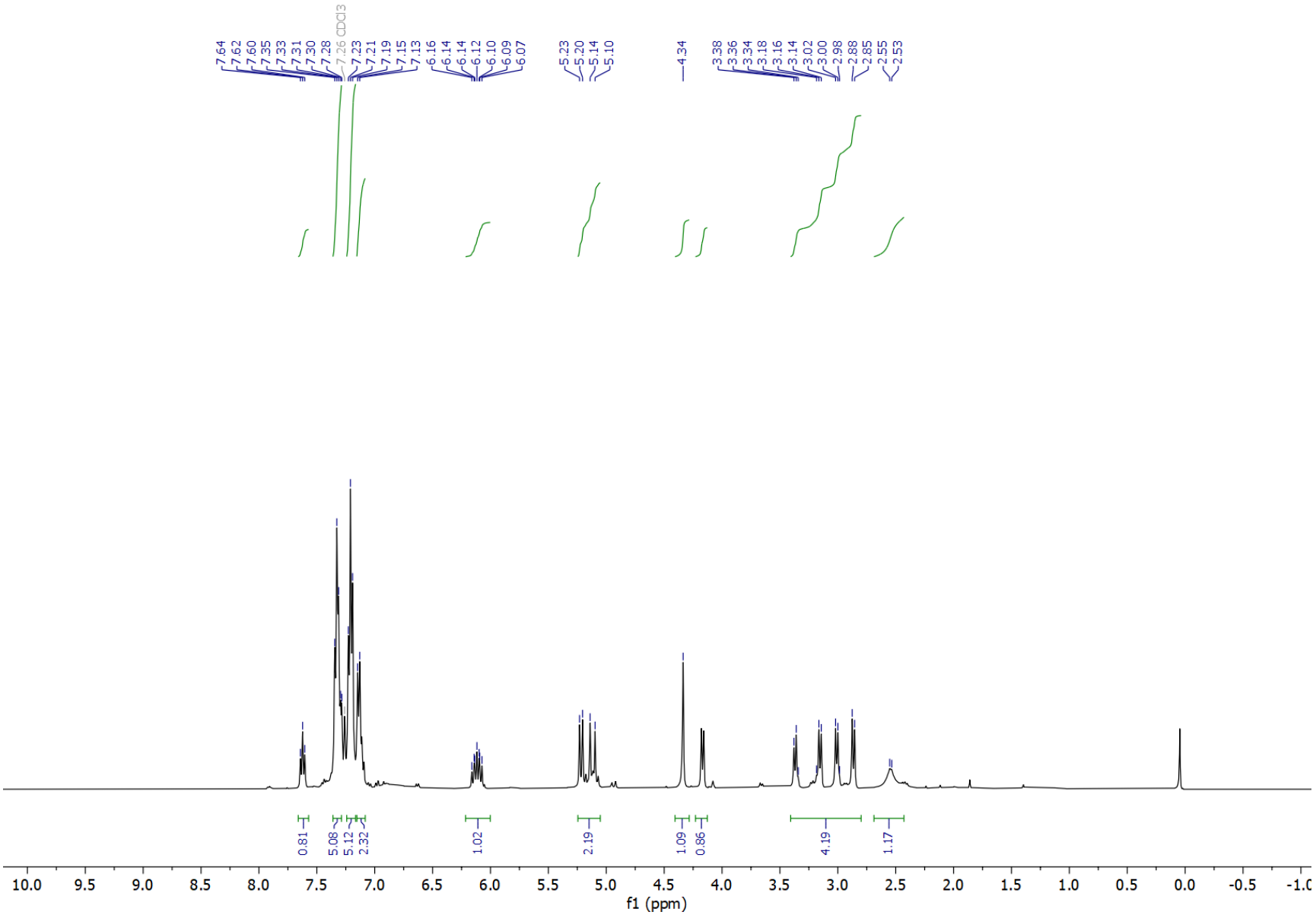
^{19}F NMR (376 MHz, $CDCl_3$): δ -62.66, -114.67 (t, J = 8.4 Hz).

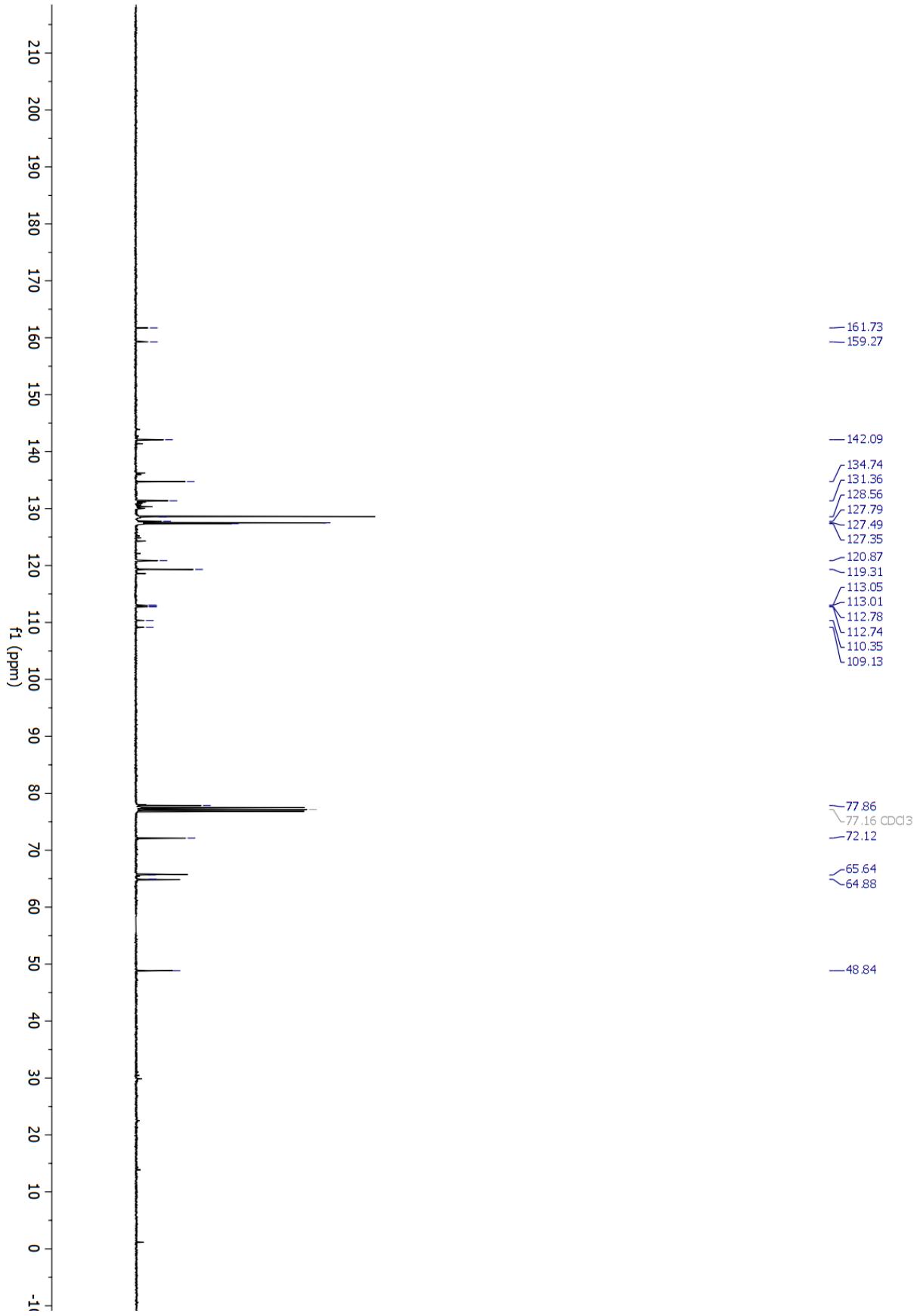
HRMS (ESI): Calculated for $C_{26}H_{23}F_4NO$ $[M+H^+]$= 422.1789, found= 422.1798

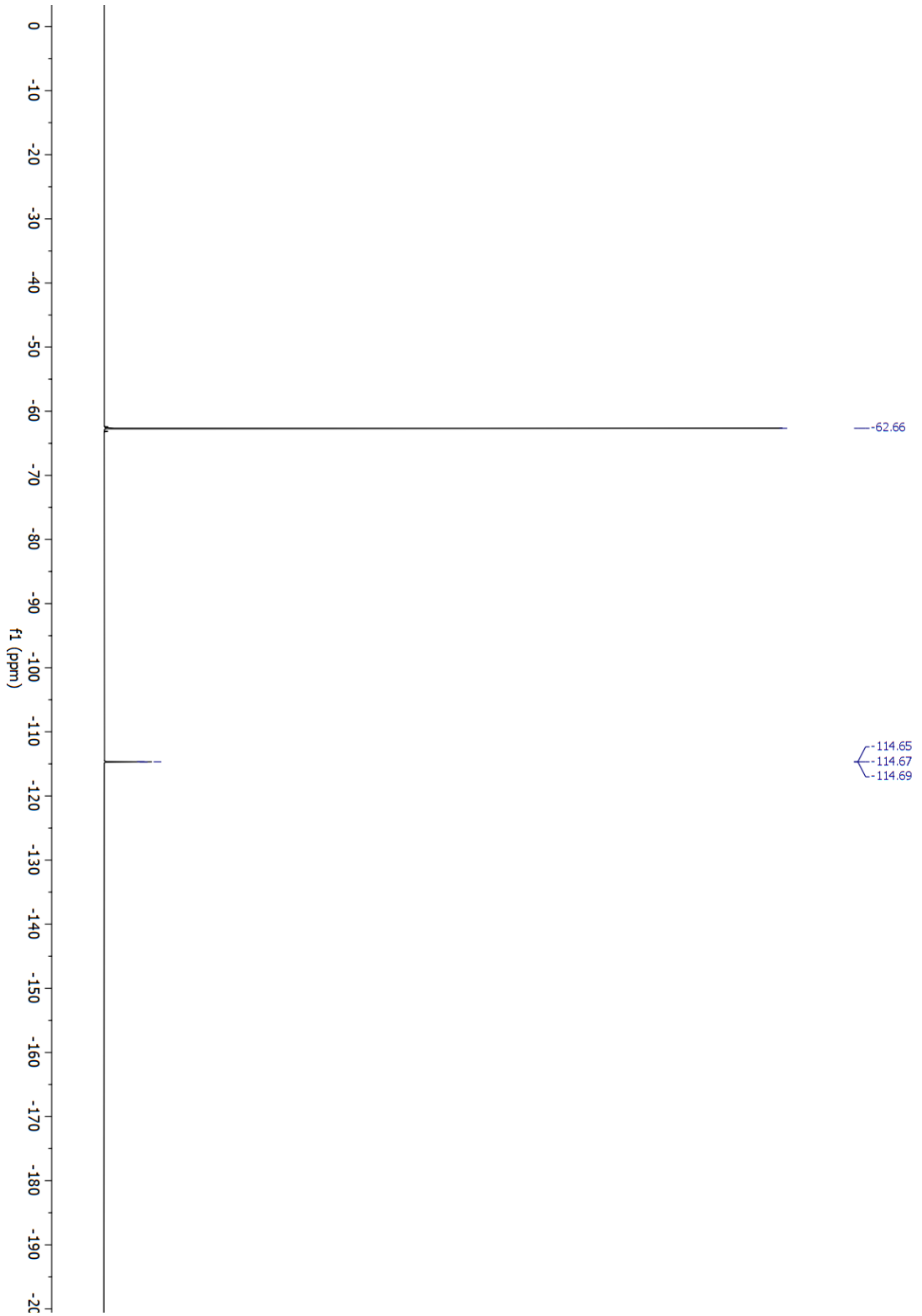
FTIR (neat): 3350, 2962, 2893, 1635, 1501, 1445, 1413, 1211, 1171, 994, 945, 931, 751, 711 cm^{-1}

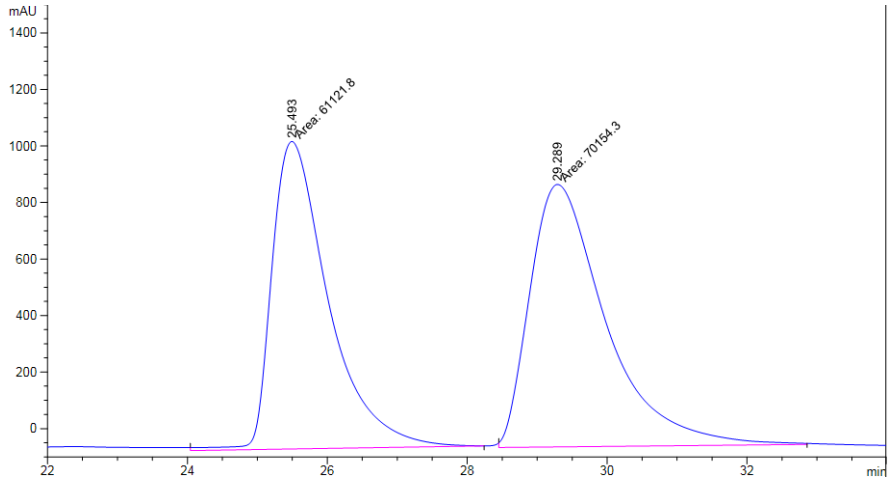
$[\alpha]_D^{28}$= -32.1 (*c* 0.10, $CHCl_3$)

HPLC (Chiralcel OD-H column in series with a Chiralcel AJ-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 90%

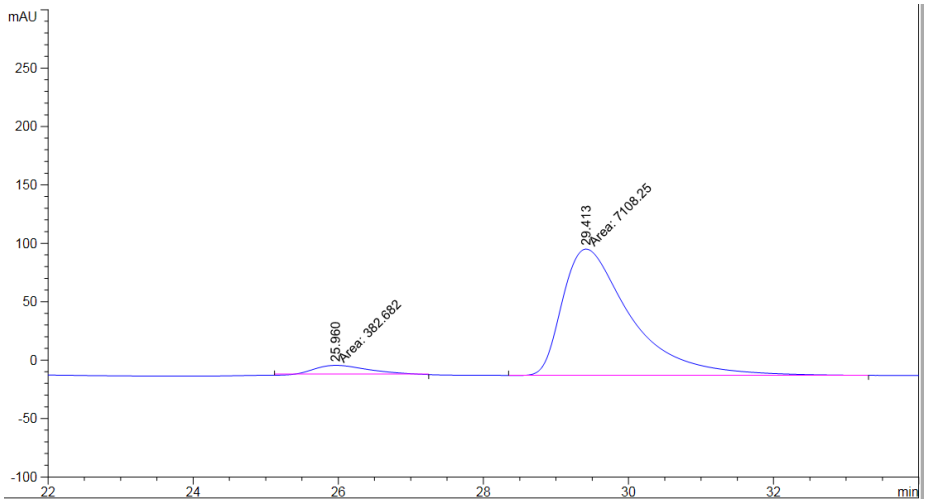

7.64
7.62
7.60
7.35
7.33
7.31
7.30
7.28
7.26 CDCl3
7.23
7.21
7.19
7.15
7.13
6.16
6.14
6.14
6.12
6.10
6.09
6.07
5.23
5.20
5.14
5.10
4.34
3.38
3.36
3.34
3.18
3.16
3.14
3.02
3.00
2.98
2.88
2.85
2.55
2.53
0.81
5.08
5.12
2.32
1.02
2.19
1.09
0.86
4.19
1.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
161.73
159.27
142.09
134.74
131.36
128.56
127.79
127.49
127.35
120.87
119.31
113.05
113.01
112.78
112.74
110.35
109.13
77.86
77.16 CDCl3
72.12
65.64
64.88
48.84


0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-20
f1 (ppm)
-62.66
-114.65
-114.67
-114.69

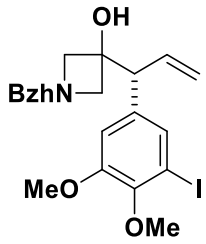


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.493	MM	0.9360	6.11218e4	1088.36633	46.5597
2	29.289	MM	1.2586	7.01543e4	928.99512	53.4403



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.960	MM	0.8412	382.68213	7.58172	5.1086
2	29.413	MM	1.0949	7108.25098	108.20315	94.8914

(4d) (R)-1-benzhydryl-3-(1-(3-iodo-4,5-dimethoxyphenyl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2d** (109.0 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 ^{o}C, 36 hr). The title compound was obtained in 77% yield (82.9 mg, .150 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

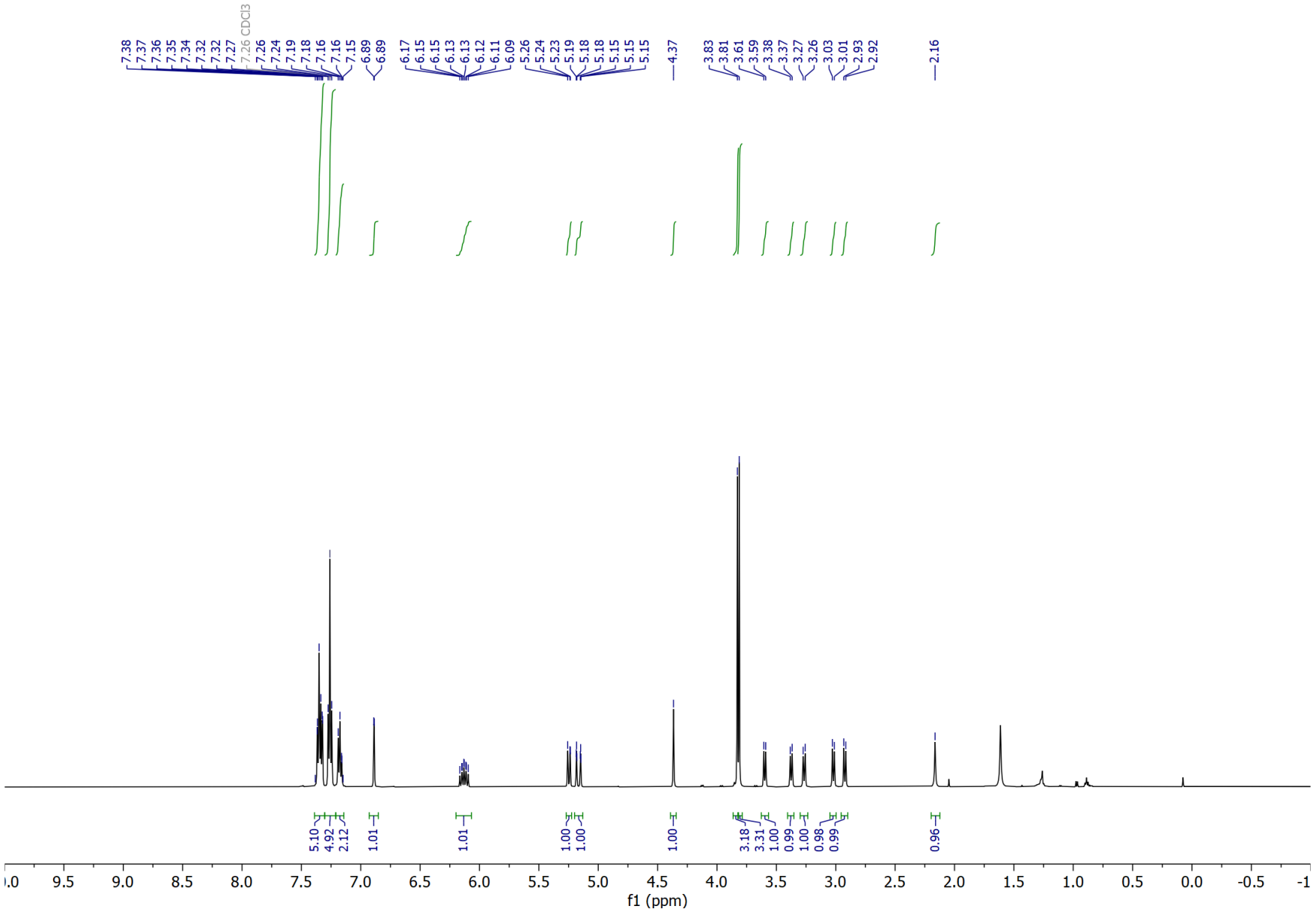
TLC (SiO_2): R_f = 0.33 (hexanes: ethyl acetate = 2:1).

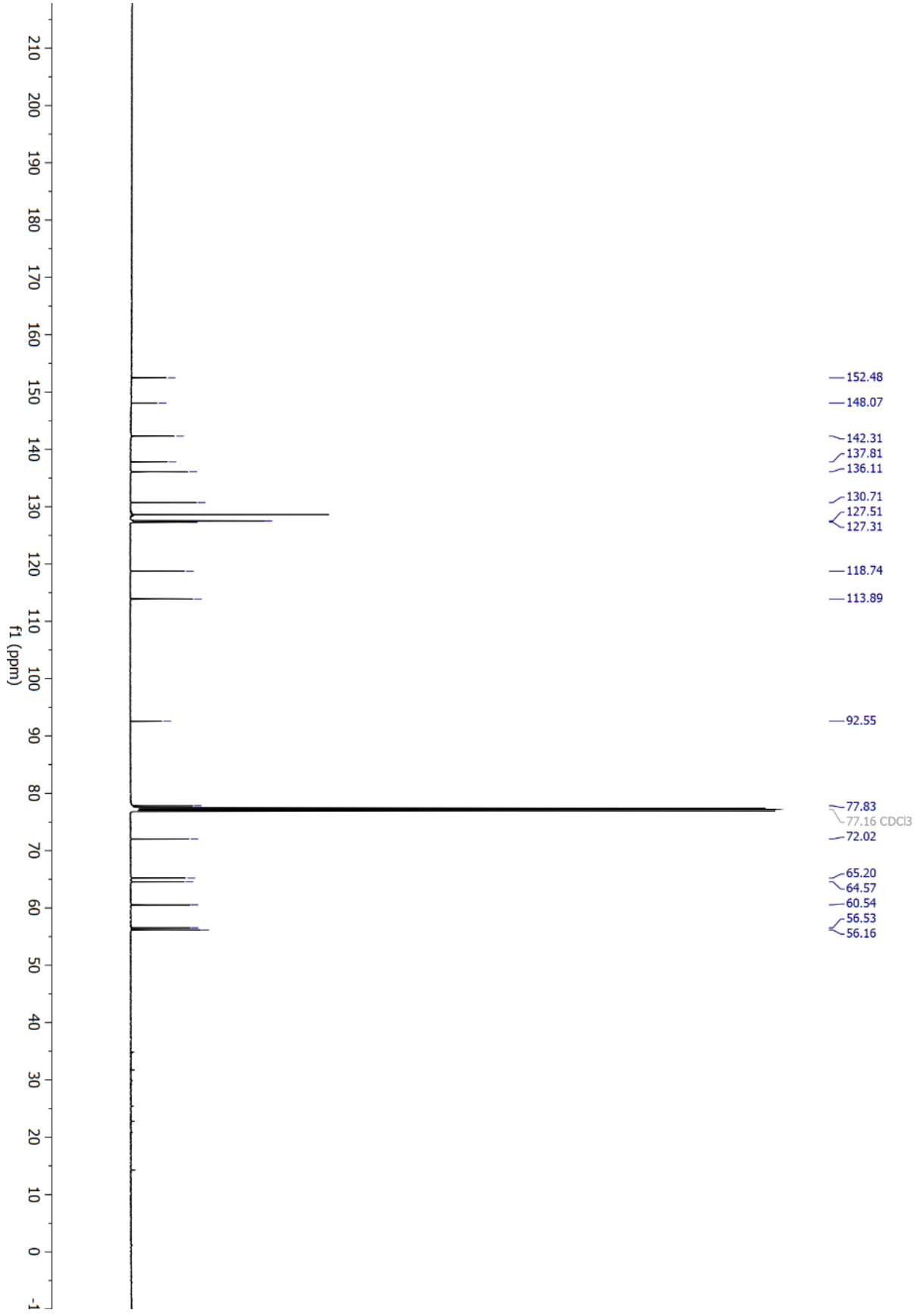
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 – 7.30 (m, 5H), 7.29 – 7.23 (m, 5H), 7.18 (t, *J* = 7.1 Hz, 2H), 6.89 (d, *J* = 1.9 Hz, 1H), 6.13 (ddd, *J* = 17.1, 10.3, 8.2 Hz, 1H), 5.27 – 5.22 (m, 1H), 5.17 (dt, *J* = 17.1, 1.3 Hz, 1H), 4.37 (s, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.60 (d, *J* = 8.2 Hz, 1H), 3.38 (d, *J* = 8.1 Hz, 1H), 3.27 (d, *J* = 8.3 Hz, 1H), 3.02 (d, *J* = 8.1 Hz, 1H), 2.92 (d, *J* = 8.3 Hz, 1H), 2.16 (s, 1H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 152.5, 148.1, 142.3, 137.8, 136.1, 130.7, 127.5, 127.3, 118.7, 113.9, 92.6, 77.8, 72.0, 65.2, 64.6, 60.5, 56.5, 56.2.
HRMS (ESI): Calculated for $C_{27}H_{28}INO_3$ [M+H$^+$] = 542.1187, found 542.1194

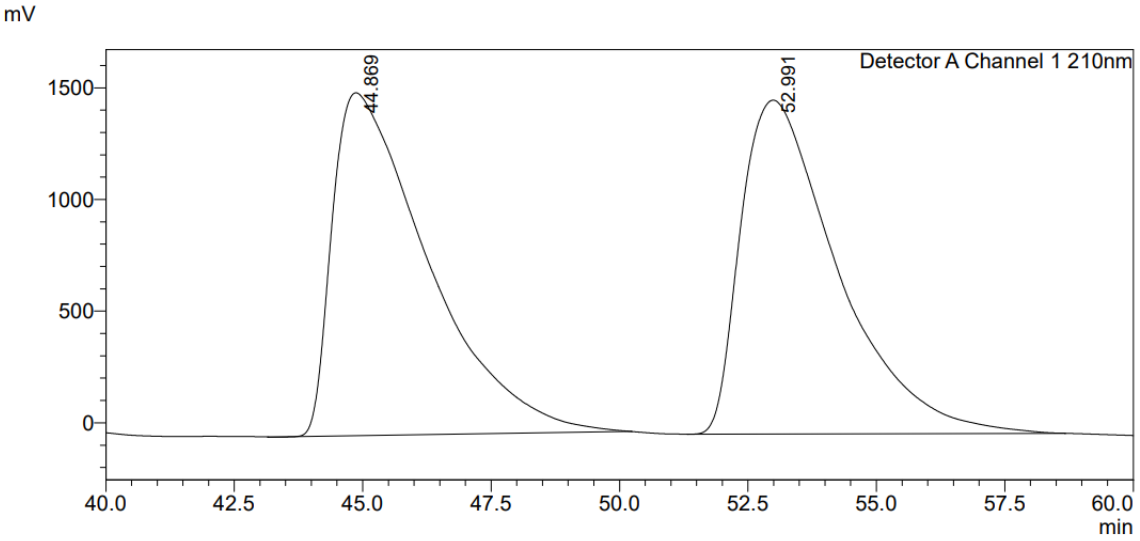
FTIR (neat): 3588.71, 2960.57, 2929.61, 1556.66, 1461.23, 1405.91, 1027.53, 933.19 cm^{-1}

$[\alpha]_D^{28}$= -13.6 (c 0.1, $CHCl_3$)

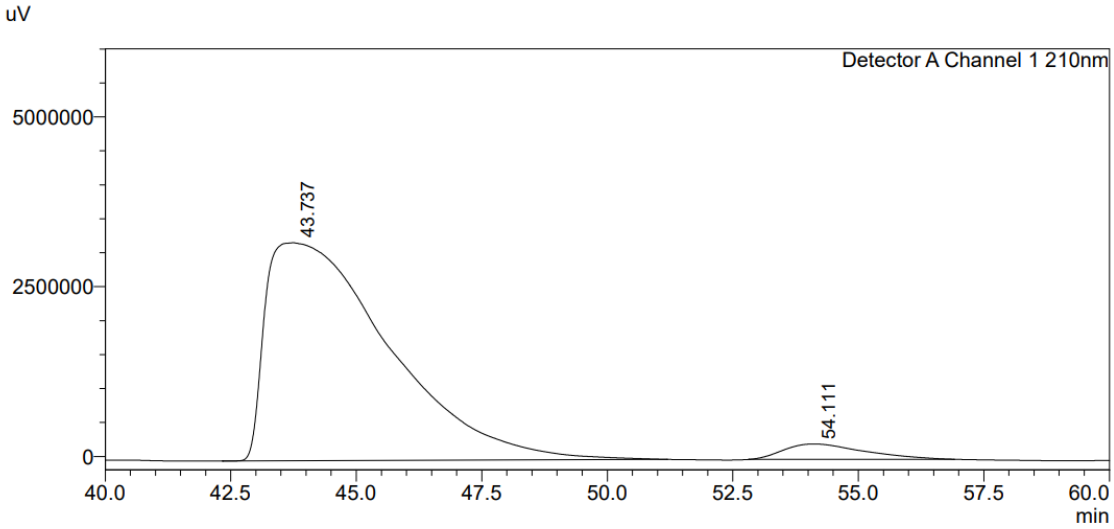
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 96:4, 0.50 mL/min, 210 nm): *ee* = 91%.


7.38
7.37
7.36
7.35
7.34
7.32
7.32
7.27
7.26 CDCl3
7.26
7.24
7.19
7.18
7.16
7.16
7.15
6.89
6.89
6.17
6.15
6.15
6.13
6.13
6.12
6.11
6.09
5.26
5.24
5.23
5.19
5.18
5.18
5.15
5.15
5.15
4.37
3.83
3.81
3.61
3.59
3.38
3.37
3.27
3.26
3.03
3.01
2.93
2.92
2.16
5.10
4.92
2.12
1.01
1.01
1.00
1.00
1.00
3.18
3.31
1.00
0.99
1.00
0.98
0.99
0.96
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
152.48
148.07
142.31
137.81
136.11
130.71
127.51
127.31
118.74
113.89
92.55
77.83
77.16 CDCl3
72.02
65.20
64.57
60.54
56.53
56.16

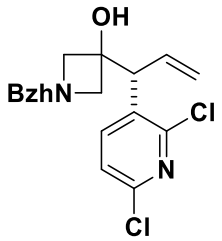


Peak#	Ret. Time	Area	Height	Area%
1	44.869	198840619	1534902	50.341
2	52.991	196148594	1494665	49.659
Total		394989214	3029566	100.000



Peak#	Ret. Time	Area	Height	Area%
1	43.737	551032286	3208994	95.609
2	54.111	25306919	226794	4.391
Total		576339205	3435787	100.000

(4e) (R)-1-benzhydryl-3-(1-(2,6-dichloropyridin-3-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2a** (73.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 36 hr). The title compound was obtained in 82% yield (69.8 mg, 0.164 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.38 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.2 Hz, 1H), 7.65 – 7.46 (m, 1H), 7.40 (t, J = 6.9 Hz, 4H), 7.27 (d, J = 8.2 Hz, 3H), 7.19 (dd, J = 9.9, 6.4 Hz, 3H), 6.03 (ddd, J = 17.4, 10.3, 7.4 Hz, 1H), 5.26 (d, J = 10.3 Hz, 1H), 5.11 (d, J = 17.2 Hz, 1H), 4.43 (s, 1H), 4.33 (d, J = 7.5 Hz, 1H), 3.47 (d, J = 8.3 Hz, 1H), 3.21 (s, 1H), 3.10 (s, 1H), 2.94 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 150.6, 148.6, 141.8, 134.3, 132.6, 130.2, 128.8, 128.4, 127.5, 127.5, 123.1, 119.7, 72.1, 66.4, 64.9, 51.7.

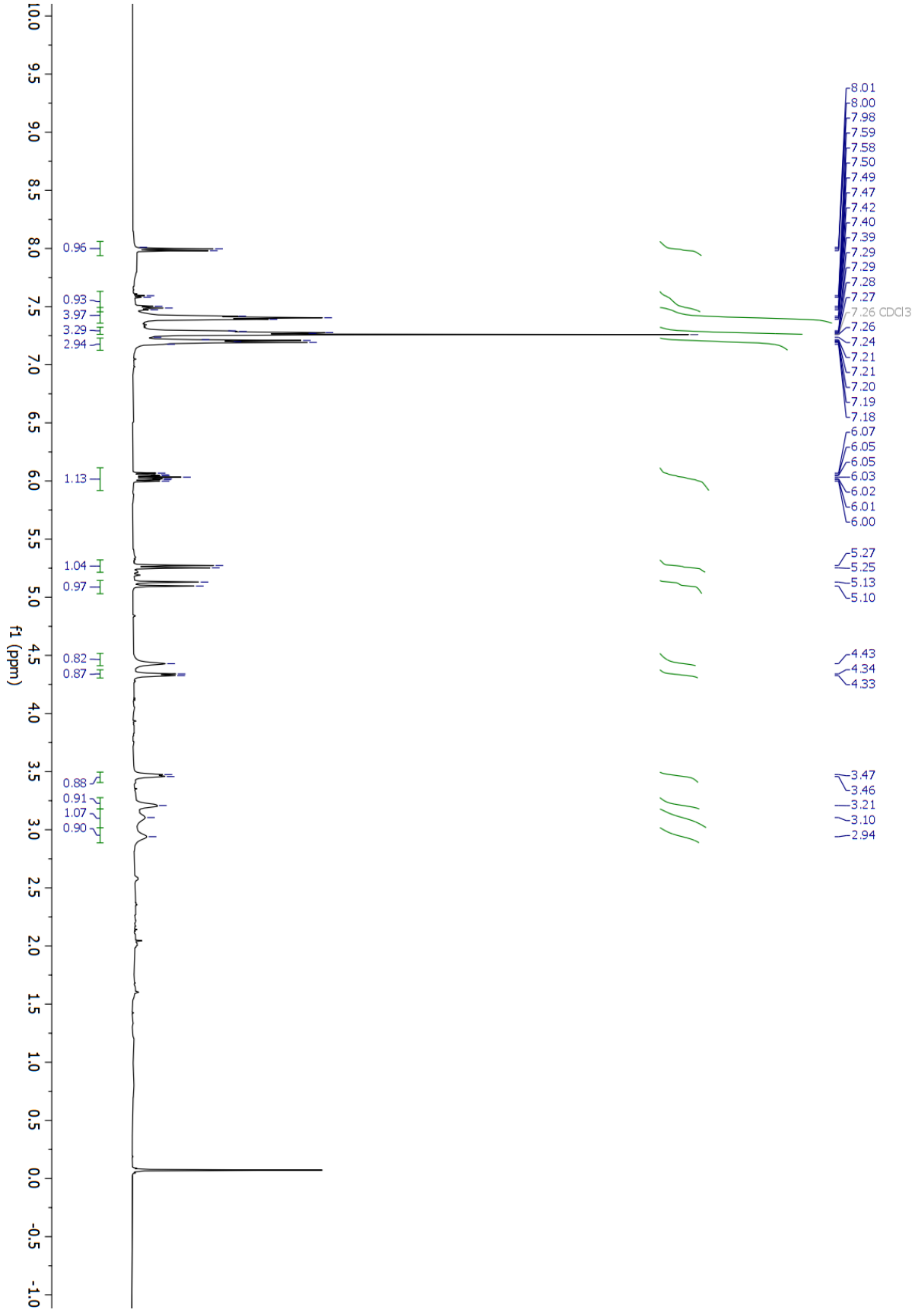
HRMS (ESI): Calculated for $C_{24}H_{22}Cl_2N_2O$ $[M+H^+]$= 425.1182, found= 425.1189

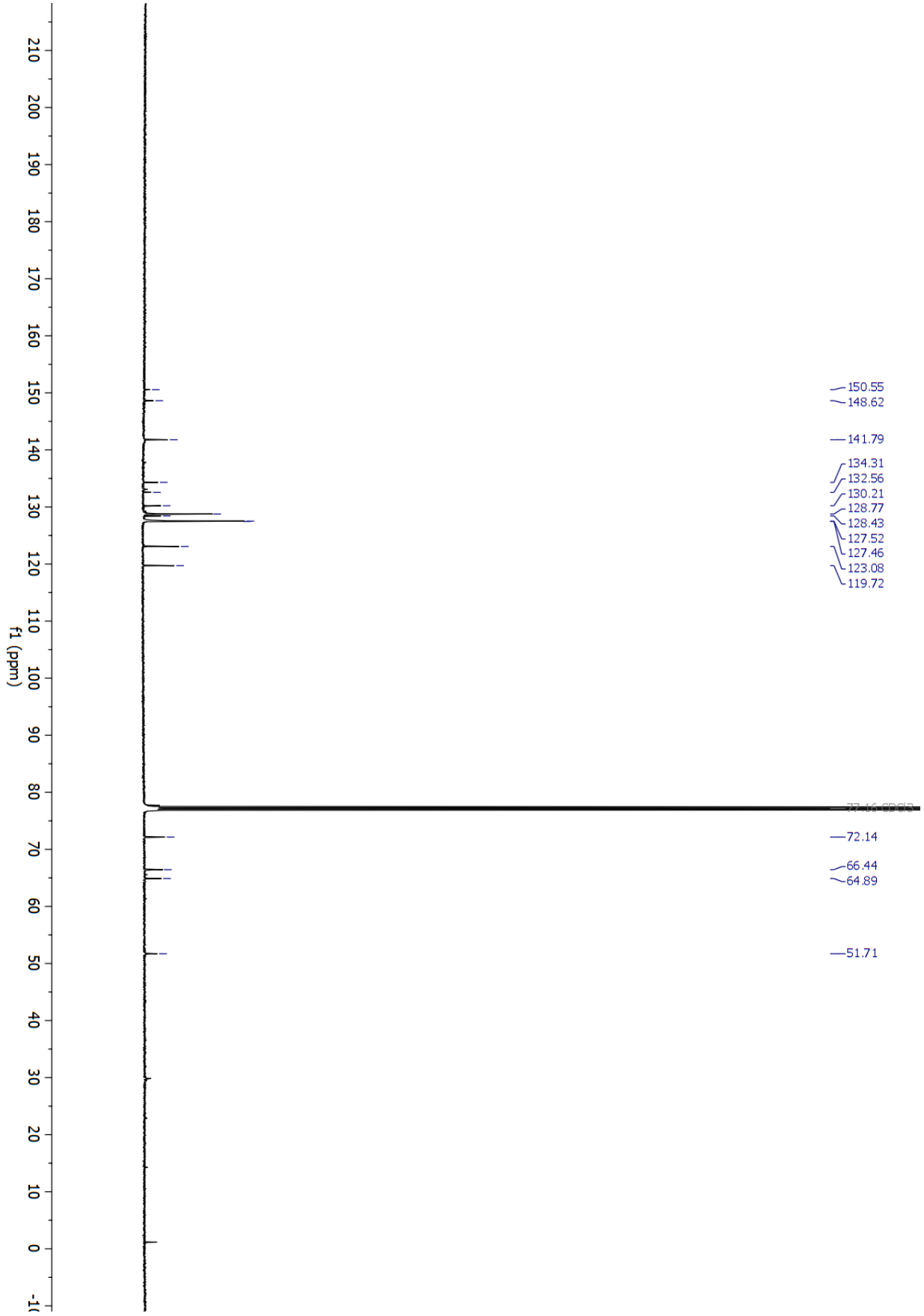
FTIR (neat): 3391, 3064, 2946, 1652, 1575, 1545, 1491, 1451, 1423, 1208, 1056, 923, 785, 667 cm^{-1}

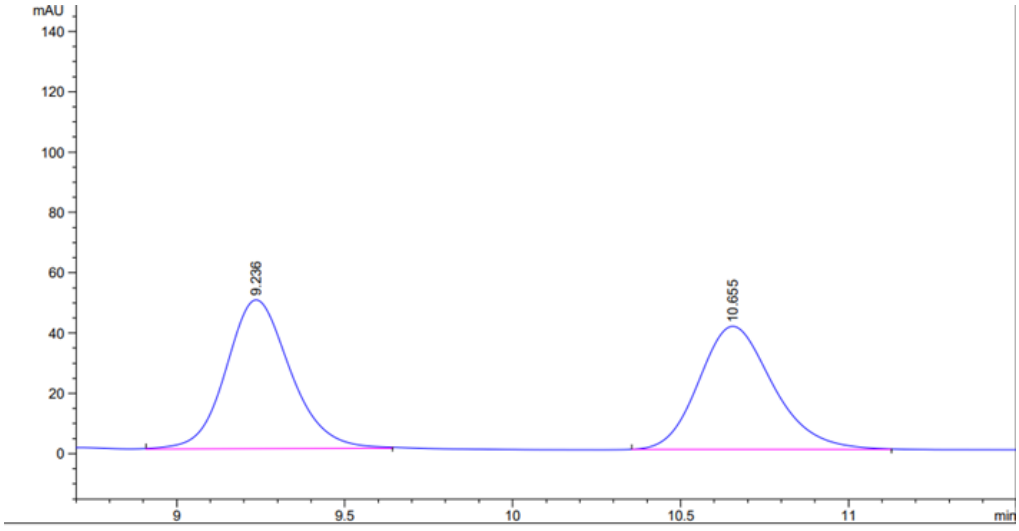
$[\alpha]_D^{28}$= -107.0 (*c* 0.10, $CHCl_3$)

MP 121-122°C

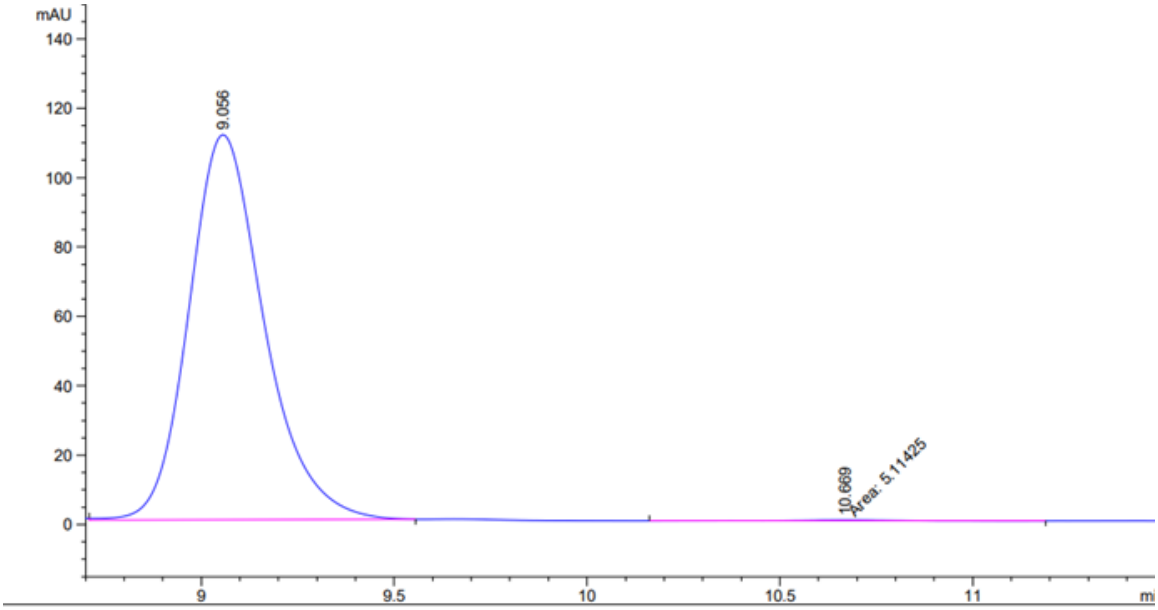
HPLC (Chiralcel OD-H hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 98%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.96
0.93
3.97
3.29
2.94
1.13
1.04
0.97
0.82
0.87
0.88
0.91
1.07
0.90
8.01
8.00
7.98
7.59
7.58
7.50
7.49
7.47
7.42
7.40
7.39
7.29
7.29
7.28
7.27
7.26 CDCl3
7.26
7.24
7.21
7.21
7.20
7.19
7.18
6.07
6.05
6.05
6.03
6.02
6.01
6.00
5.27
5.25
5.13
5.10
4.43
4.34
4.33
3.47
3.46
3.21
3.10
2.94


150.55
148.62
141.79
134.31
132.56
130.21
128.77
128.43
127.52
127.46
123.08
119.72
77.46 CDCl3
72.14
66.44
64.89
51.71
f1 (ppm)

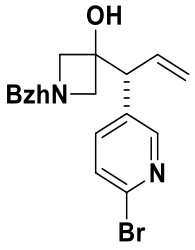


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.236	BB	0.2041	661.39594	49.43079	51.1494
2	10.655	BB	0.2361	631.67151	40.91267	48.8506



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.056	VB	0.2065	1509.00195	111.03948	99.6622
2	10.669	MM	0.3380	5.11425	2.52219e-1	0.3378

(4f) (R)-1-benzhydryl-3-(1-(6-bromopyridin-3-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2f** (76.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 36 hr). The title compound was obtained in 90% yield (78.8 mg, 0.180 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–4:1).

TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 8.33 (d, *J* = 2.4 Hz, 1H), 7.61 (dd, *J* = 8.3, 2.5 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 4H), 7.27 (d, *J* = 3.2 Hz, 2H), 7.24 (d, *J* = 3.5 Hz, 2H), 7.22 – 7.13 (m, 2H), 6.13 (ddd, *J* = 17.6, 10.3, 7.8 Hz, 1H), 5.27 (d, *J* = 10.3 Hz, 1H), 5.14 (d, *J* = 17.2 Hz, 1H), 4.37 (s, 1H), 3.71 (d, *J* = 7.8 Hz, 1H), 3.40 (d, *J* = 8.3 Hz, 1H), 3.16 (d, *J* = 8.4 Hz, 1H), 3.01 (d, *J* = 8.3 Hz, 1H), 2.86 (d, *J* = 8.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ: 150.9, 140.7, 139.3, 135.3, 134.8, 128.7, 128.7, 127.8, 127.5, 127.5, 119.4, 77.9, 71.9, 65.8, 64.9, 53.9.

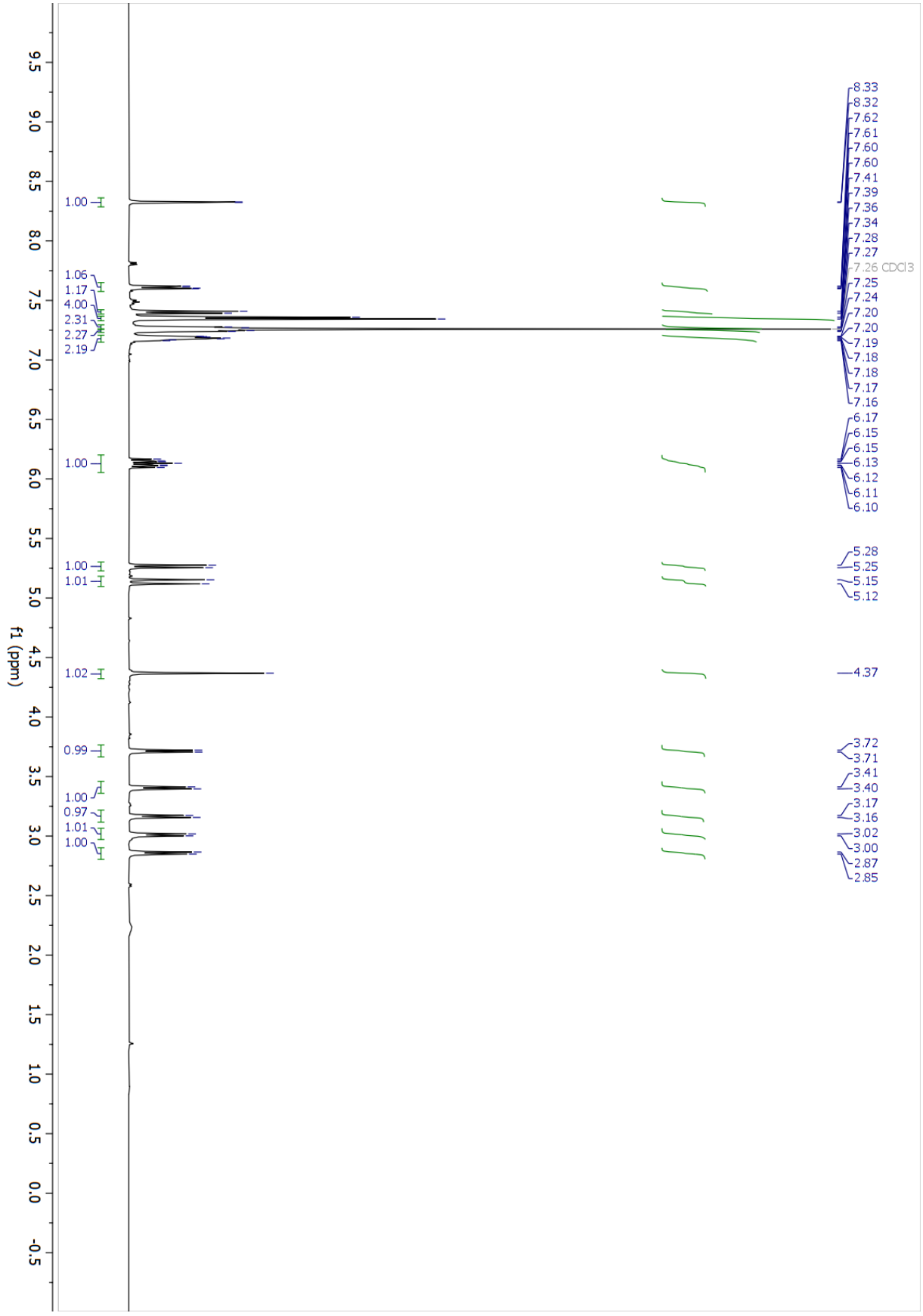
HRMS (ESI): Calculated for $C_{24}H_{23}BrN_2O$ $[M+H^+]$ =435.1067, found 435.1072

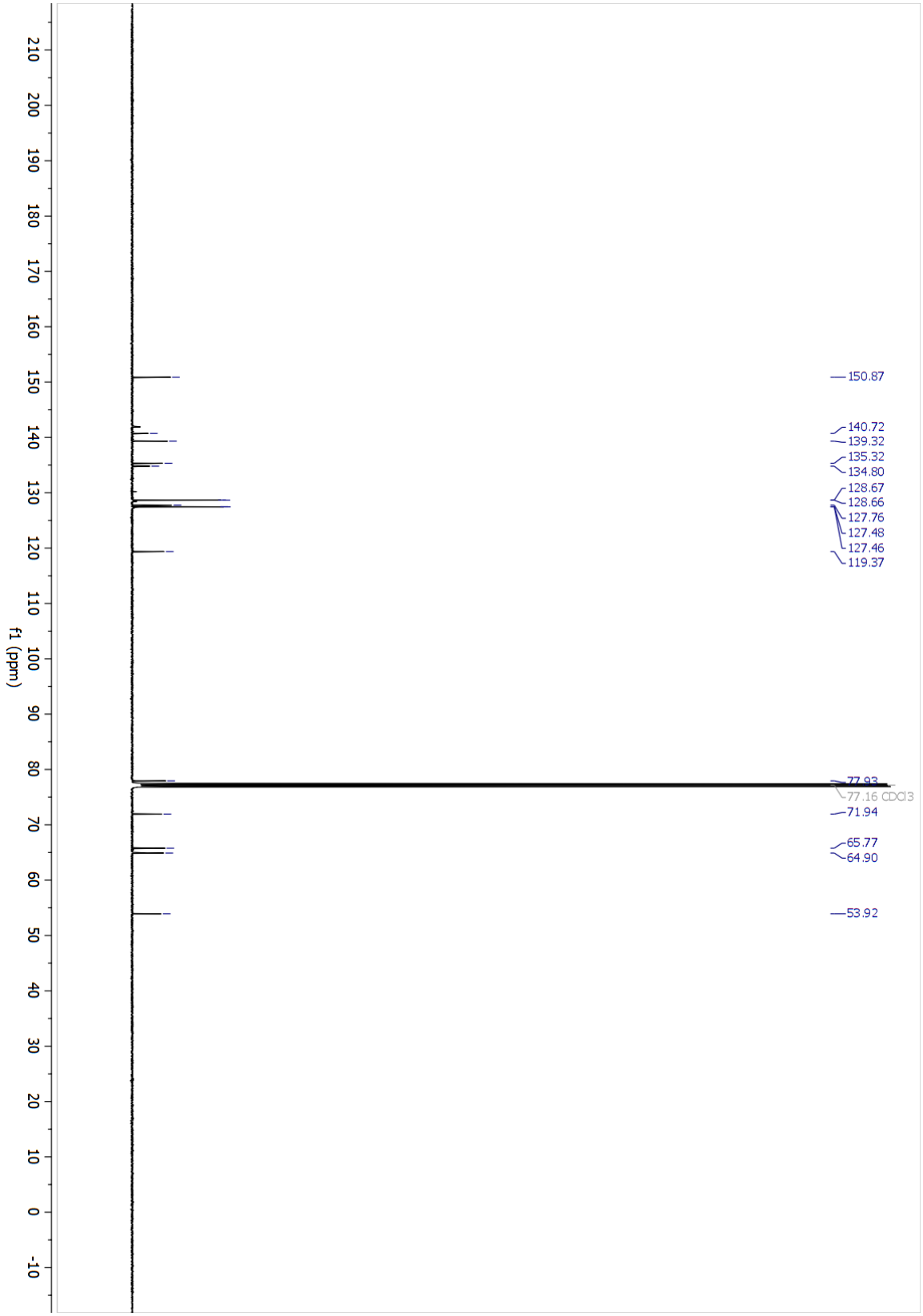
FTIR (neat): 3338, 1451, 1087, 1027, 922, 742, 702 cm^{-1}

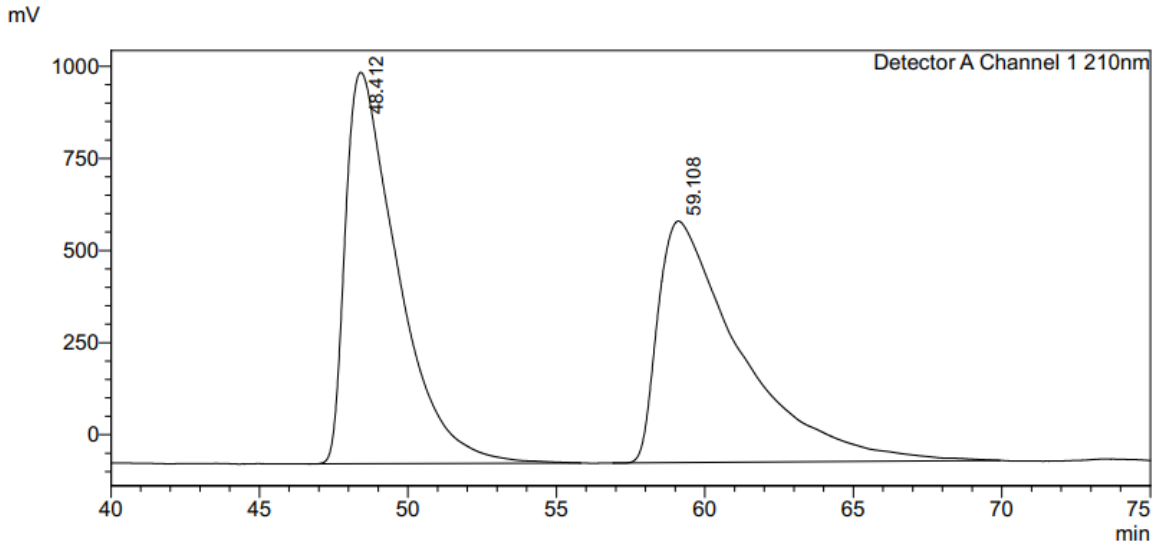
$\mathbf{[\alpha]_D^{28}}$**=** -19.8^0 (c = 1.24, $CHCl_3$)

MP: 75-80 ^{0}C

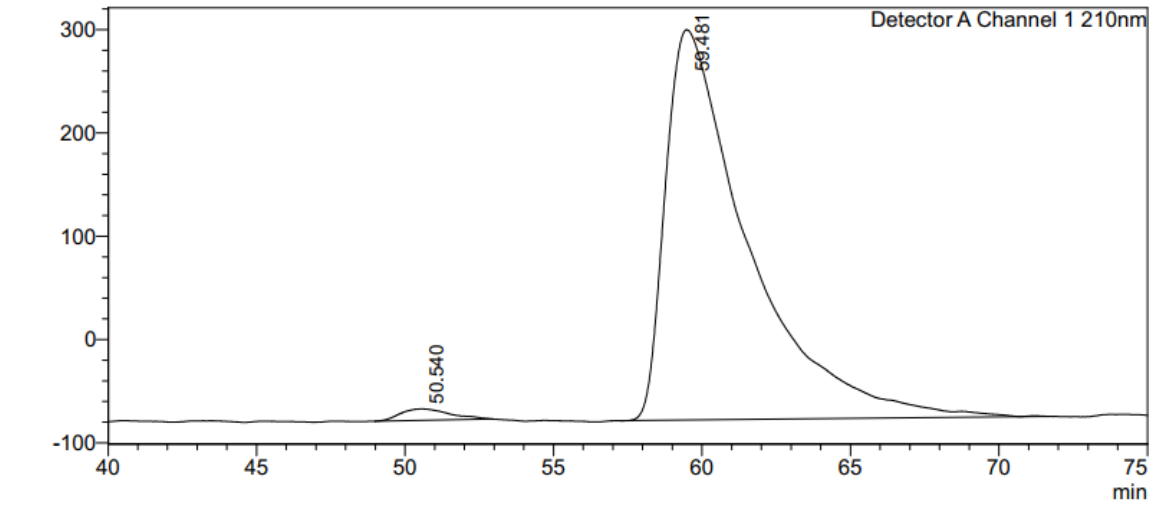
HPLC (Chiracel column OD-H, hexane:*i*-PrOH = 96:4, 0.5 mL/min, 210 nm): *ee*= 96%


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
1.06
1.17
4.00
2.31
2.27
2.19
1.00
1.00
1.01
1.02
0.99
1.00
0.97
1.01
1.00
8.33
8.32
7.62
7.61
7.60
7.60
7.41
7.39
7.36
7.34
7.28
7.27
7.26 CDCl3
7.25
7.24
7.20
7.20
7.19
7.18
7.18
7.17
7.16
6.17
6.15
6.15
6.13
6.12
6.11
6.10
5.28
5.25
5.15
5.12
4.37
3.72
3.71
3.41
3.40
3.17
3.16
3.02
3.00
2.87
2.85


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
150.87
140.72
139.32
135.32
134.80
128.67
128.66
127.76
127.48
127.46
119.37
77.93
77.16 CDCl3
71.94
65.77
64.90
53.92

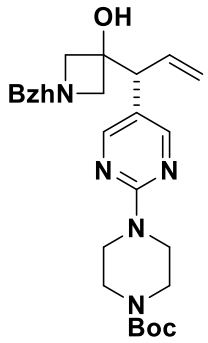


Peak#	Ret. Time	Area	Height	Area%
1	48.412	130146645	1062265	50.588
2	59.108	127122012	655337	49.412
Total		257268657	1717602	100.000



Peak#	Ret. Time	Area	Height	Area%
1	50.540	1260533	11118	1.692
2	59.481	73243014	377862	98.308
Total		74503547	388980	100.000

(4g) tert-butyl (R)-4-(5-(1-(1-benzhydryl-3-hydroxyazetidin-3-yl)allyl)pyrimidin-2-yl)piperazine-1-carboxylate



Procedure

Allyl acetate **2g** (108.7 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 48 hr). The title compound was obtained in 72% yield (78.0 mg, 0.144 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–2:1).

TLC (SiO_2): R_f = 0.35 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, J = 5.1 Hz, 2H), 7.42 – 7.32 (m, 5H), 7.25 – 7.11 (m, 5H), 6.13 (ddd, J = 17.4, 10.2, 7.4 Hz, 1H), 5.25 (d, J = 10.3 Hz, 1H), 5.15 (d, J = 17.4 Hz, 1H), 4.36 (s, 1H), 3.78 (q, J = 6.9, 5.2 Hz, 4H), 3.55 (t, J = 7.4 Hz, 1H), 3.48 (q, J = 5.4 Hz, 4H), 3.19 (d, J = 8.4 Hz, 1H), 2.99 (d, J = 8.2 Hz, 1H), 2.85 (d, J = 8.5 Hz, 1H), 1.56 (s, 2H), 1.48 (s, 8H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 161.4, 158.5, 155.3, 142.4, 135.9, 128.9, 128.9, 127.8, 121.3, 119.0, 80.4, 78.2, 72.3, 65.8, 60.8, 52.2, 44.1, 28.9, 21.5.

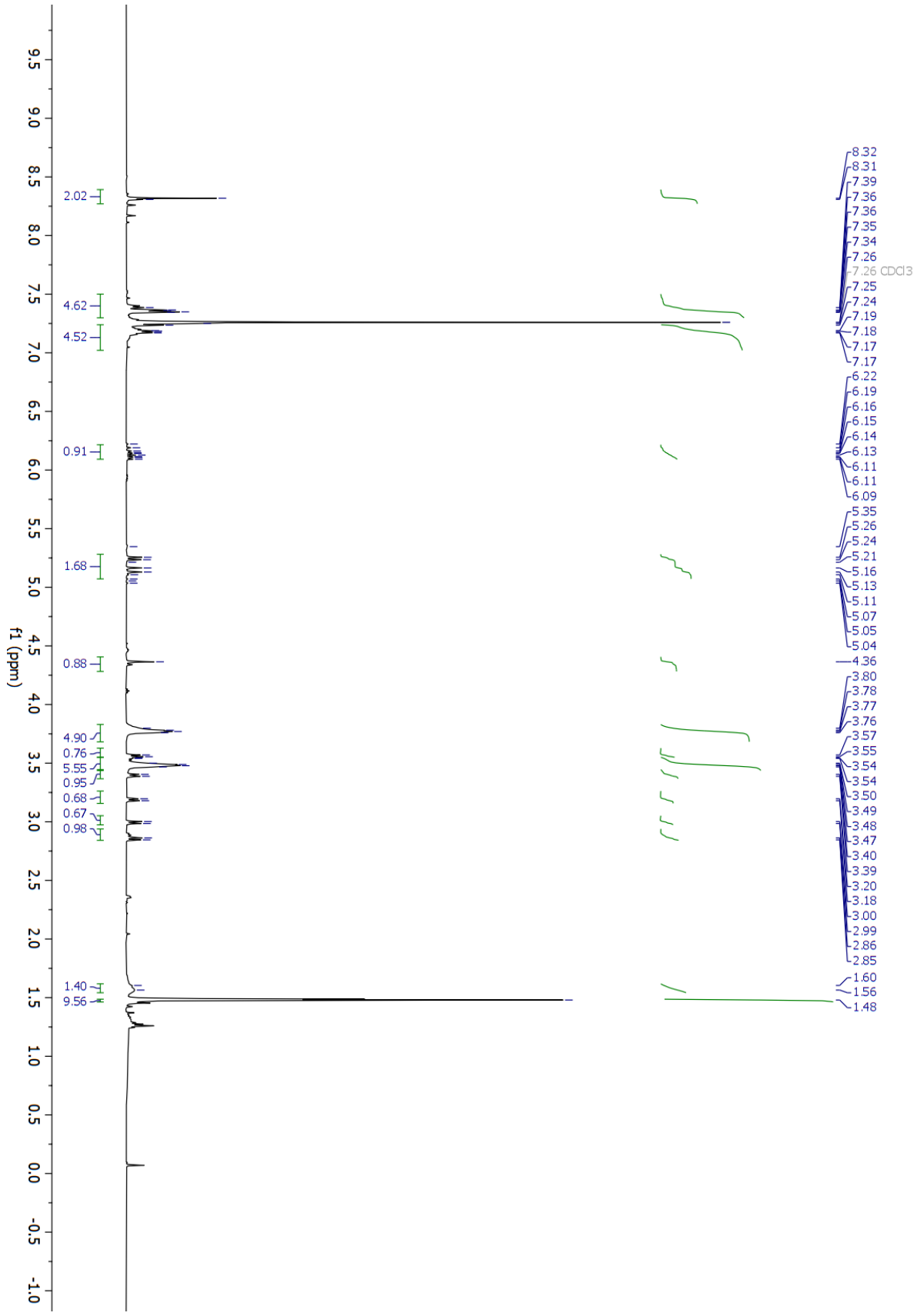
HRMS (ESI): Calculated for $C_{32}H_{39}N_5O_3$ [M+H$^+$]= 542.3126, found= 542.3133

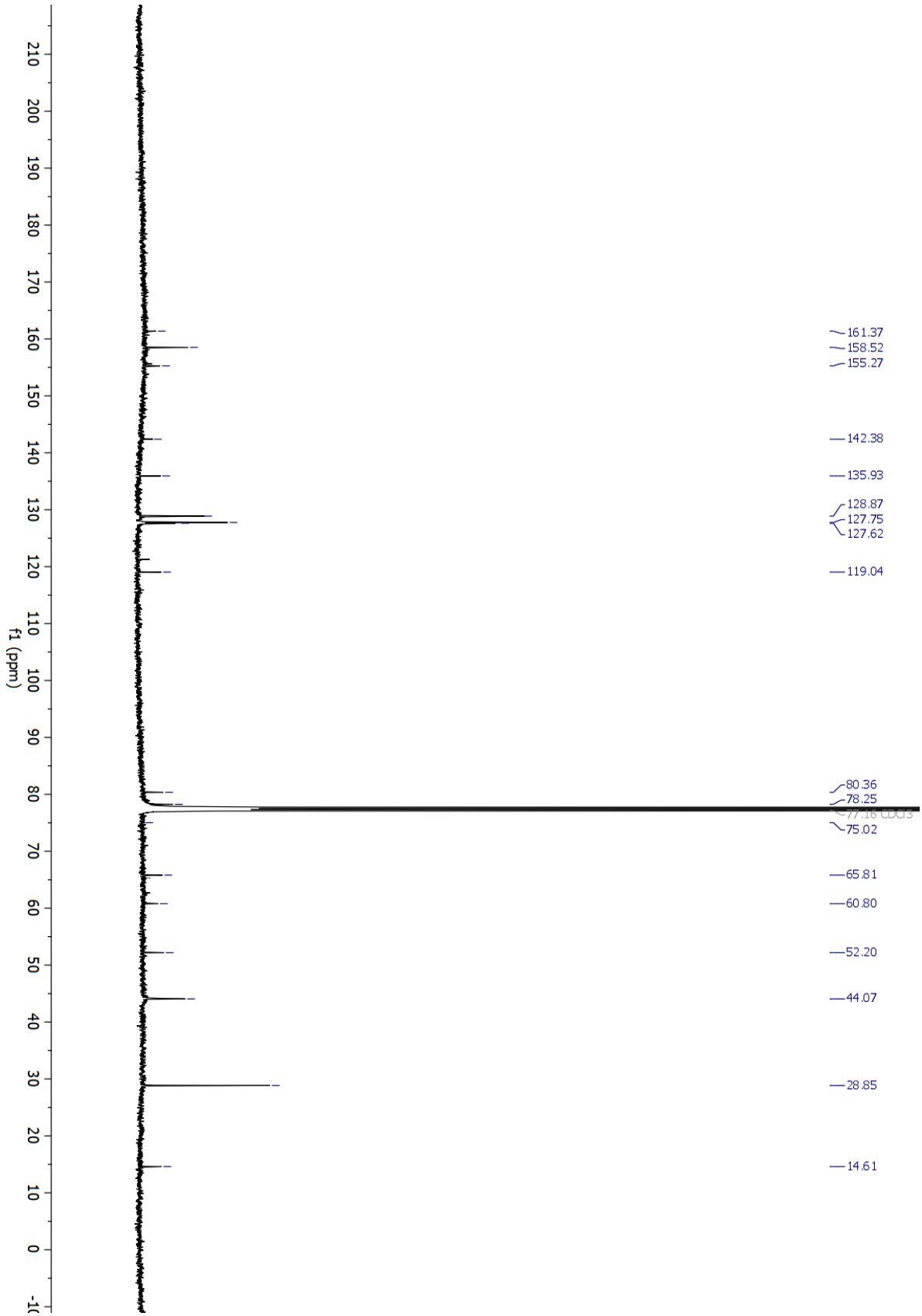
FTIR (neat): 3434, 3001, 2925, 2851, 1694, 1634, 1598, 1538, 1494, 1417, 1362,, 1083, 948, 797, cm^{-1}

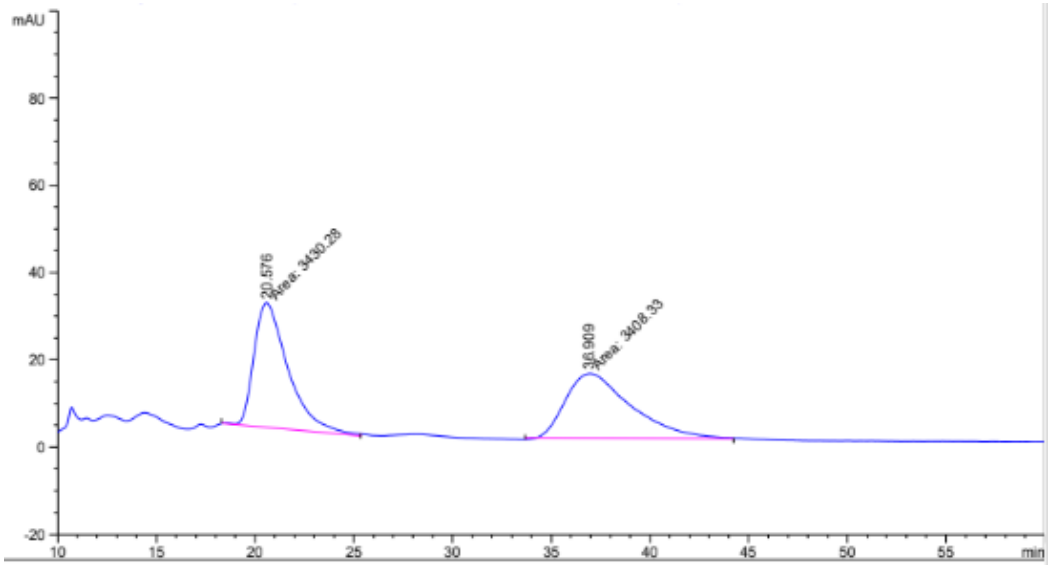
$[\alpha]_D^{28}$= -69.4 (*c* 0.10, $CHCl_3$)

MP: 145-147°C

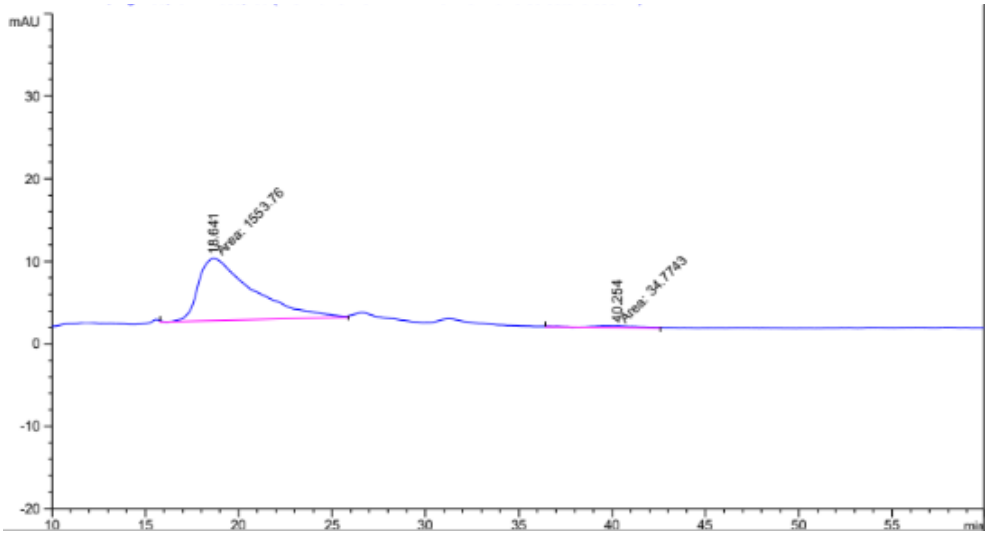
HPLC (Chiralcel AD-H hexanes:*i*-PrOH = 93:7, 1.00 mL/min, 210 nm): *ee*= 96%


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
2.02
4.62
4.52
0.91
1.68
0.88
4.90
0.76
5.55
0.95
0.68
0.67
0.98
1.40
9.56
8.32
8.31
7.39
7.36
7.36
7.35
7.34
7.26
7.26 CDCl3
7.25
7.24
7.19
7.18
7.17
7.17
6.22
6.19
6.16
6.15
6.14
6.13
6.11
6.11
6.09
5.35
5.26
5.24
5.21
5.16
5.13
5.11
5.07
5.05
5.04
4.36
3.80
3.78
3.77
3.76
3.57
3.55
3.54
3.54
3.50
3.49
3.48
3.47
3.40
3.39
3.20
3.18
3.00
2.99
2.86
2.85
1.60
1.56
1.48


161.37
158.52
155.27
142.38
135.93
128.87
127.75
127.62
119.04
80.36
78.25
77.16 CDCl3
75.02
65.81
60.80
52.20
44.07
28.85
14.61
f1 (ppm)

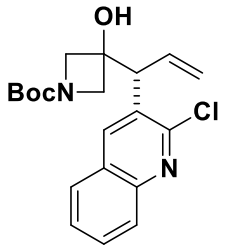


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.576	MM	1.9991	3430.28174	28.59907	50.1605
2	36.909	MM	3.8447	3408.33496	14.77485	49.8395



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.641	MM	3.4308	1553.76062	7.54812	97.8109
2	40.254	MM	2.9248	34.77425	1.98156e-1	2.1891

(4h) tert-butyl (R)-3-(1-(2-chloroquinolin-3-yl)allyl)-3-hydroxyazetidine-1-carboxylate



Procedure

Allyl acetate **2h** (78.5 mg, 0.30 mmol, 150 mol%) was subjected to a modified version of general procedure D using 1-Boc-3-azetidinone (34.2 mg, 0.20 mmol, 100 mol%, 100 °C, 36 hr). The title compound was obtained in 72% yield (54.0 mg, 0.14 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

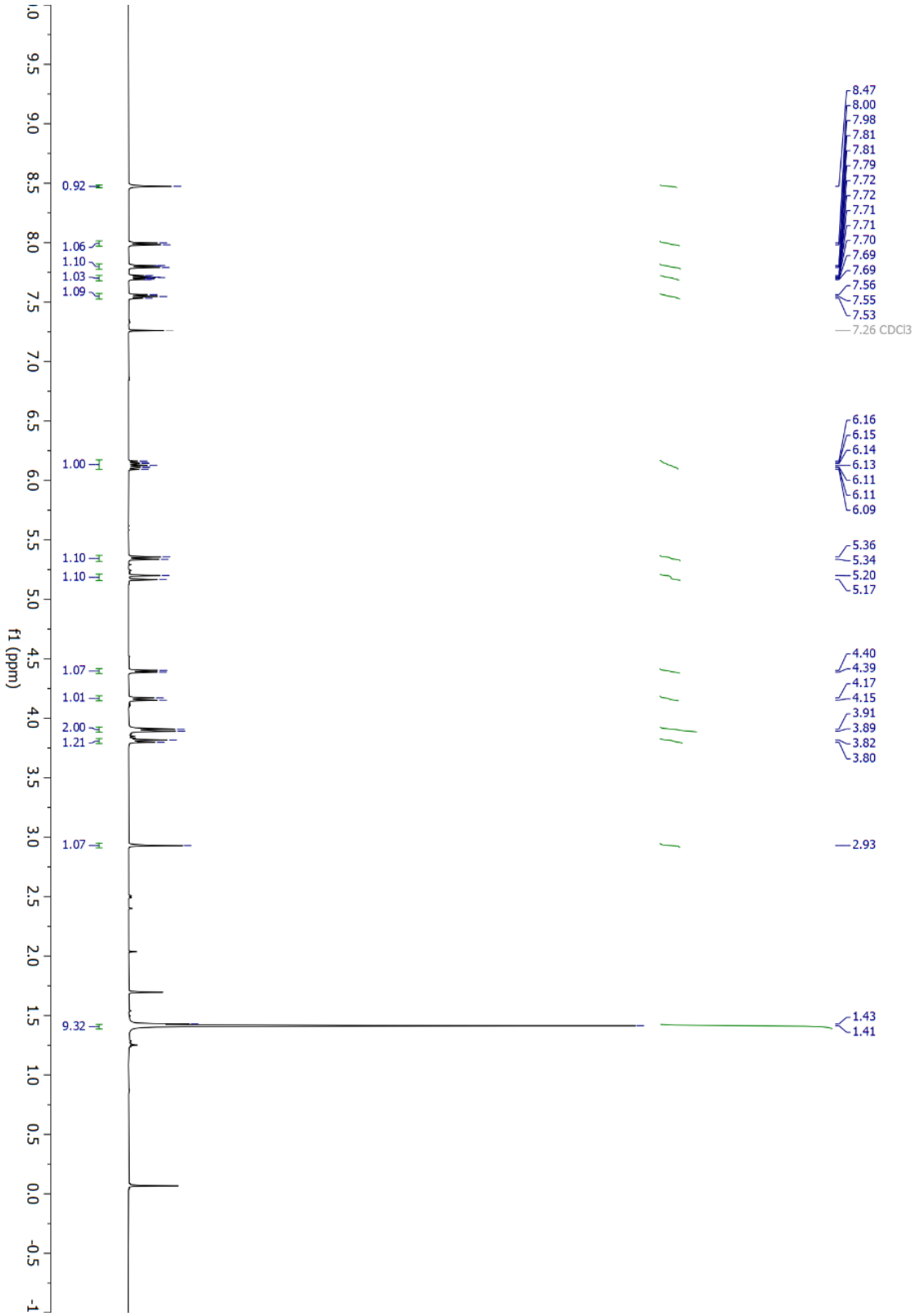
TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 4:1).

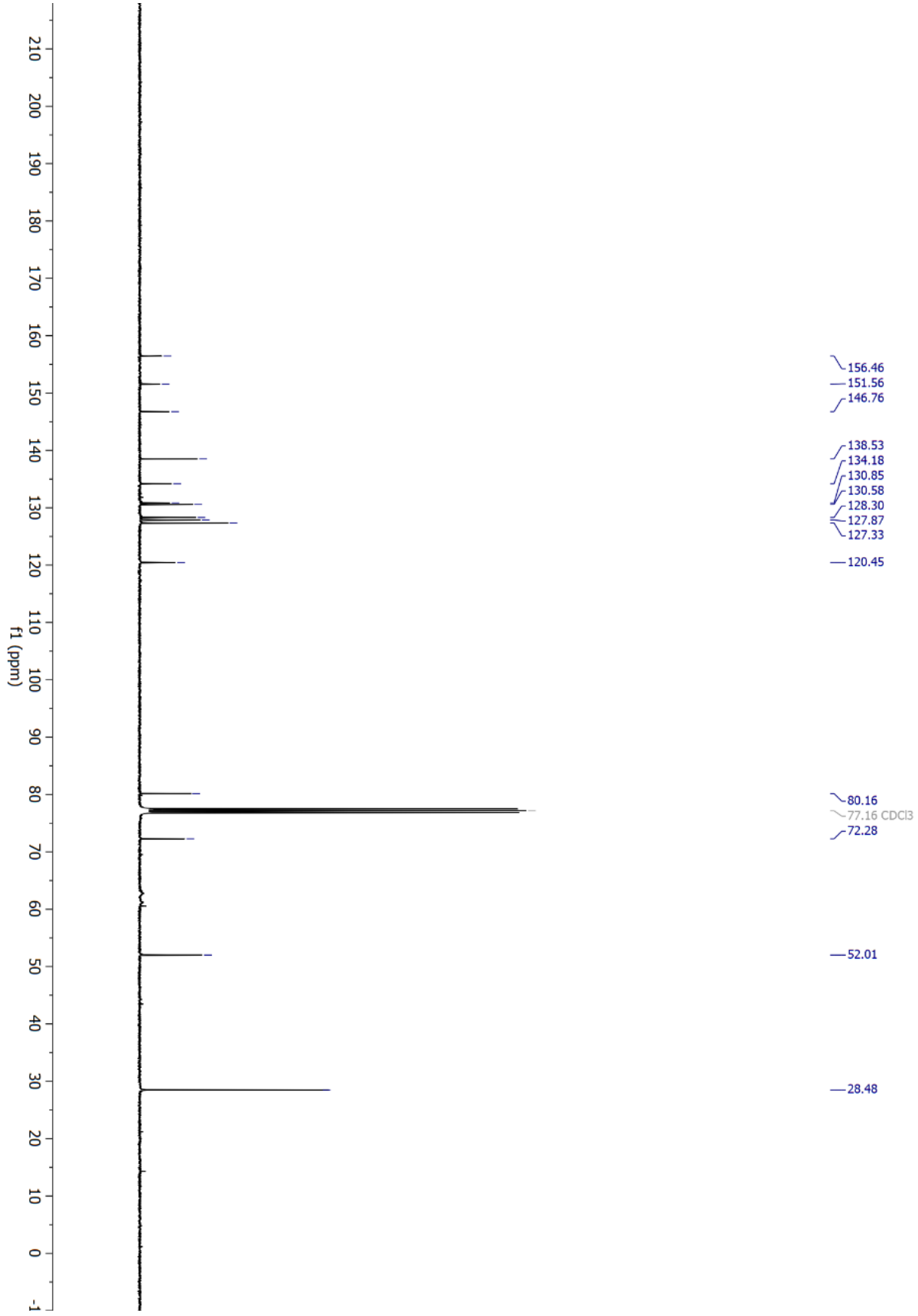
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.83 – 7.77 (m, 1H), 7.71 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 6.13 (ddd, *J* = 17.5, 10.3, 7.5 Hz, 1H), 5.35 (d, *J* = 10.3 Hz, 1H), 5.18 (d, *J* = 17.2 Hz, 1H), 4.39 (d, *J* = 7.5 Hz, 1H), 4.16 (d, *J* = 9.3 Hz, 1H), 3.90 (d, *J* = 9.3 Hz, 2H), 3.81 (d, *J* = 9.5 Hz, 1H), 2.93 (s, 1H), 1.41 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 156.5, 151.6, 146.8, 138.5, 134.2, 130.9 130.6, 128.3, 127.9, 127.3, 120.4, 80.2, 72.3, 52.0, 28.5.
HRMS (ESI): Calculated for $C_{20}H_{23}ClN_2O_3$ [M+Na^+] = 397.1289, found 397.1294

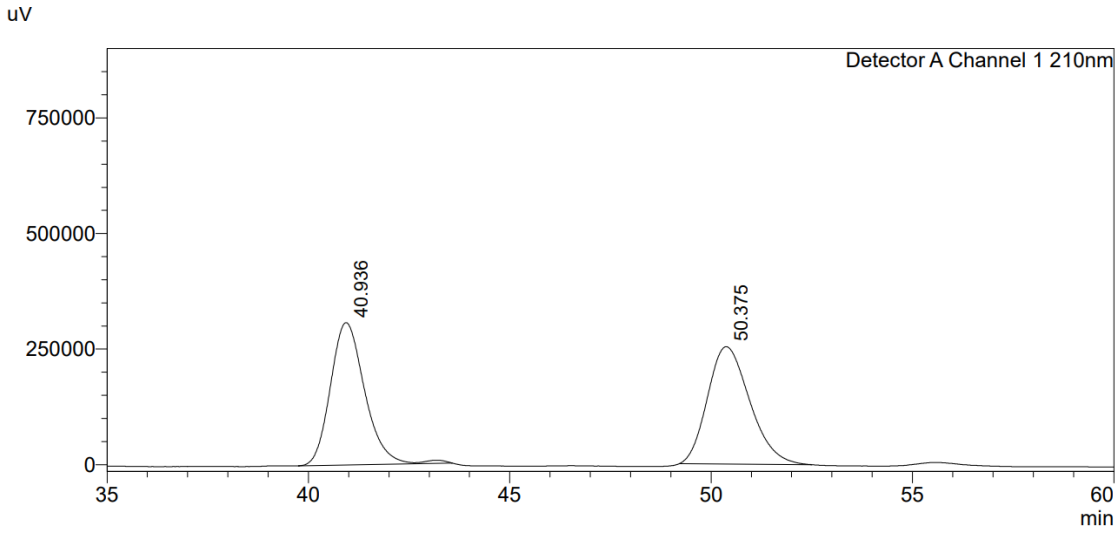
FTIR (neat): 3440.04, 2962.86, 1667.52, 1586.81, 1421.16, 1158.07, 1000.58, 930.34 cm^{-1}

$[\alpha]_D^{28}$= -20.0 (c 0.1, $CHCl_3$).

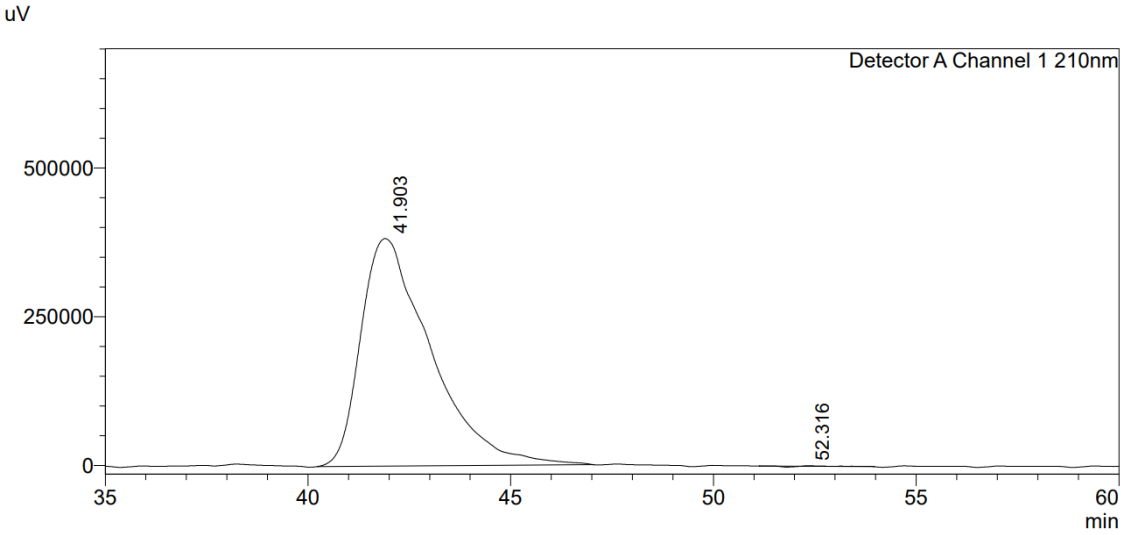
HPLC (Chiralcel OD column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 99%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
0.92
1.06
1.10
1.03
1.09
1.00
1.10
1.10
1.07
1.01
2.00
1.21
1.07
9.32
8.47
8.00
7.98
7.81
7.81
7.79
7.72
7.72
7.71
7.71
7.70
7.69
7.69
7.56
7.55
7.53
7.26 CDCl3
6.16
6.15
6.14
6.13
6.11
6.11
6.09
5.36
5.34
5.20
5.17
4.40
4.39
4.17
4.15
3.91
3.89
3.82
3.80
2.93
1.43
1.41


156.46
151.56
146.76
138.53
134.18
130.85
130.58
128.30
127.87
127.33
120.45
80.16
77.16 CDCl3
72.28
52.01
28.48
f1 (ppm)

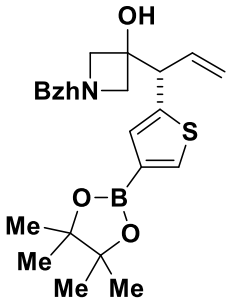


Peak#	Ret. Time	Area	Height	Conc.	Area%
1	40.936	18314738	307904	49.724	49.724
2	50.375	18518228	253702	50.276	50.276
Total		36832966	561607		100.000



Peak#	Ret. Time	Area	Height	Area%	Conc.
1	41.903	45921590	382392	99.977	99.977
2	52.316	10638	853	0.023	0.023
Total		45932228	383245	100.000	

(4i) (S)-1-benzhydryl-3-(1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophen-2-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2i (**92.5 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 36 hr). The title compound was obtained in 65% yield (63.3 mg, 0.130 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2): R_f = 0.42 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.52 – 7.31 (m, 6H), 7.17 (d, J = 20.6 Hz, 5H), 6.14 (dt, J = 17.7, 9.3 Hz, 1H), 5.32 – 5.08 (m, 2H), 4.40 (s, 1H), 4.03 (d, J = 8.3 Hz, 1H), 3.38 (dd, J = 18.7, 8.3 Hz, 2H), 3.02 (dd, J = 36.0, 8.4 Hz, 2H), 1.70 (s, 1H), 1.32 (s, 12H).

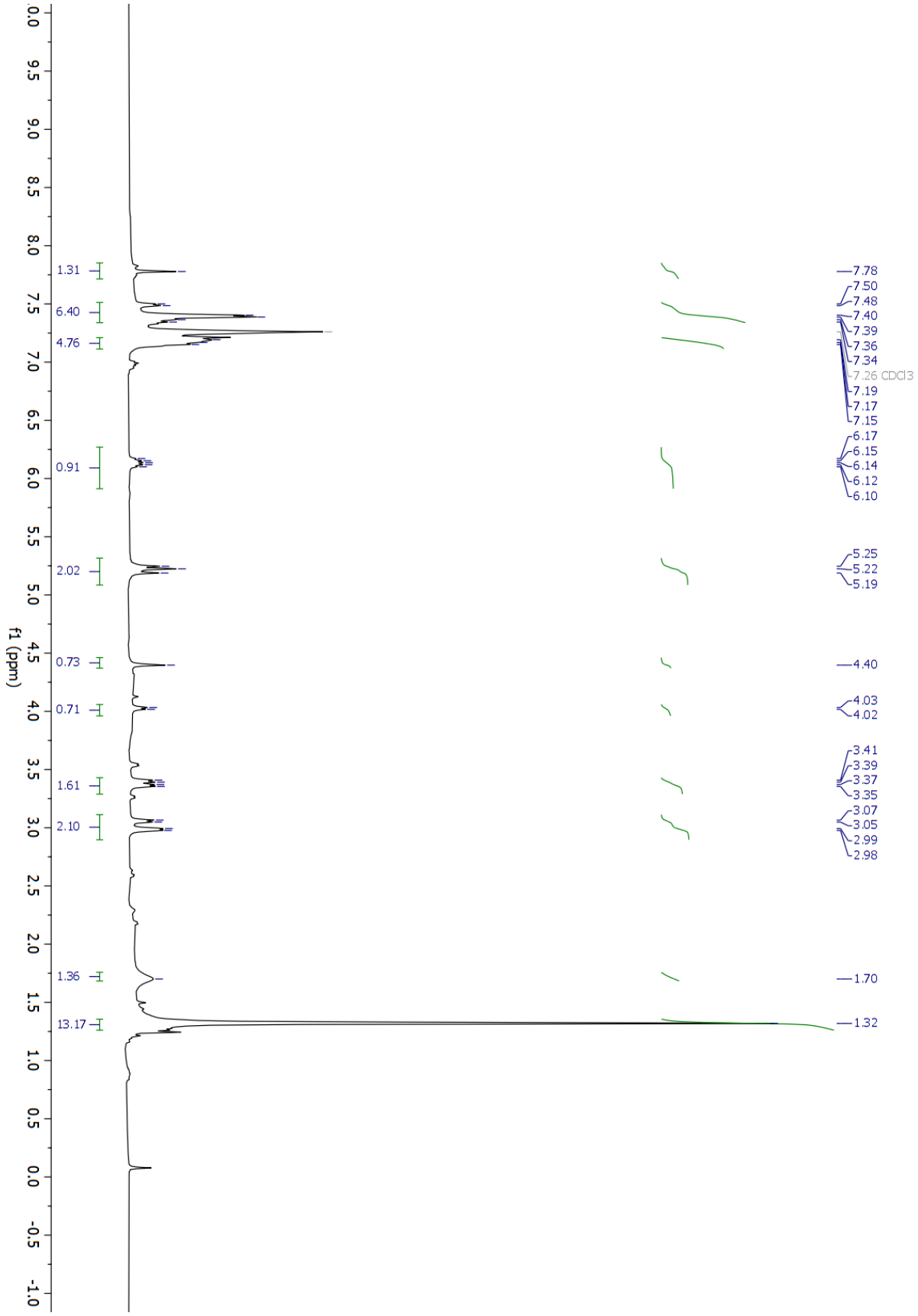
^{13}C NMR (126 MHz, $CDCl_3$): δ 142.4, 141.9, 136.1, 130.8, 129.2, 128.6, 128.3, 127.6, 127.3, 118.5, 83.8, 78.0, 68.7, 64.8, 64.3, 53.0, 25.0.

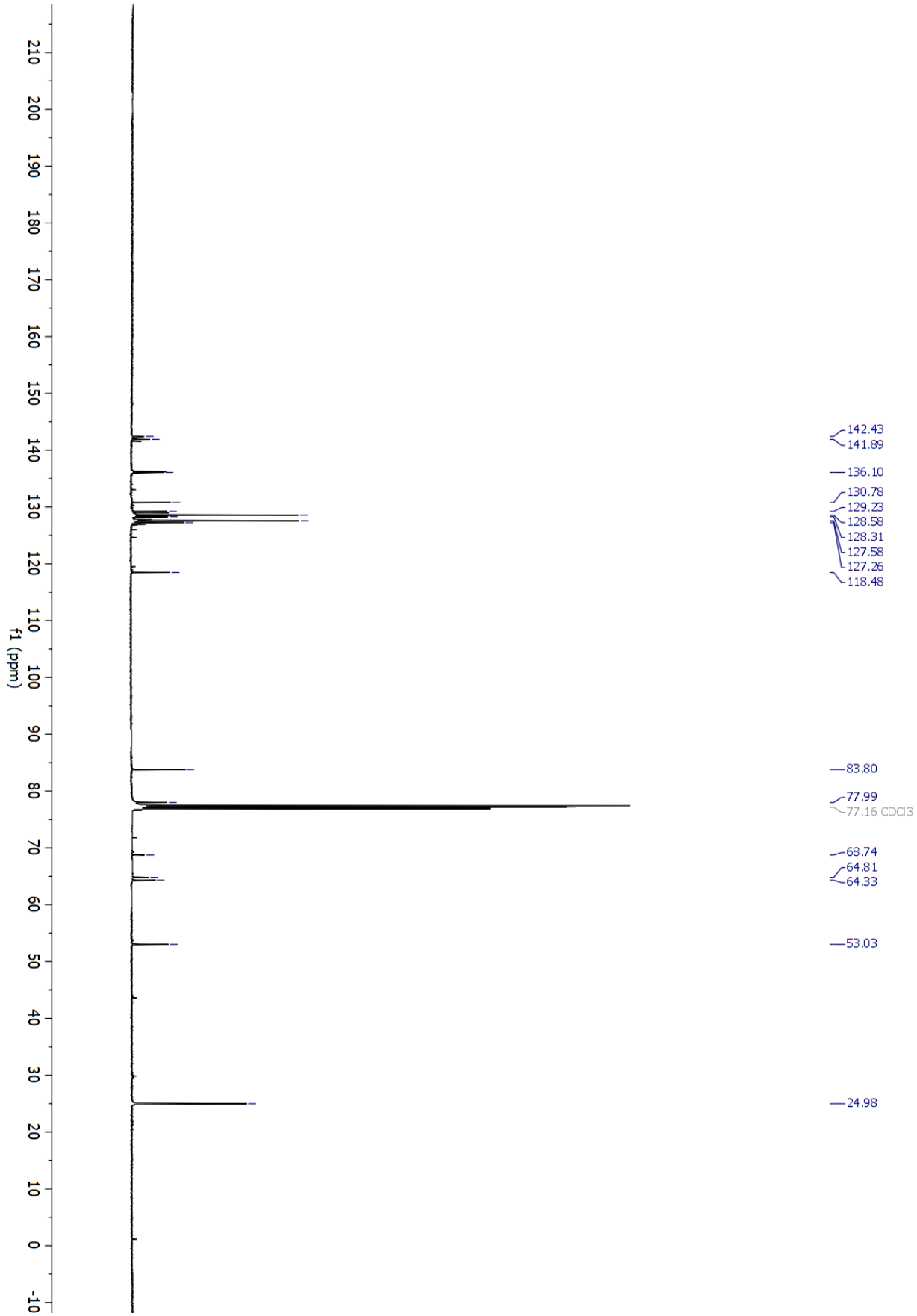
FTIR (neat): 3438, 2970, 2928, 2876, 1668, 1513, 1469, 1386, 1371, 1257, 1194, 1074, 988, 813 $cm^{-1.}$

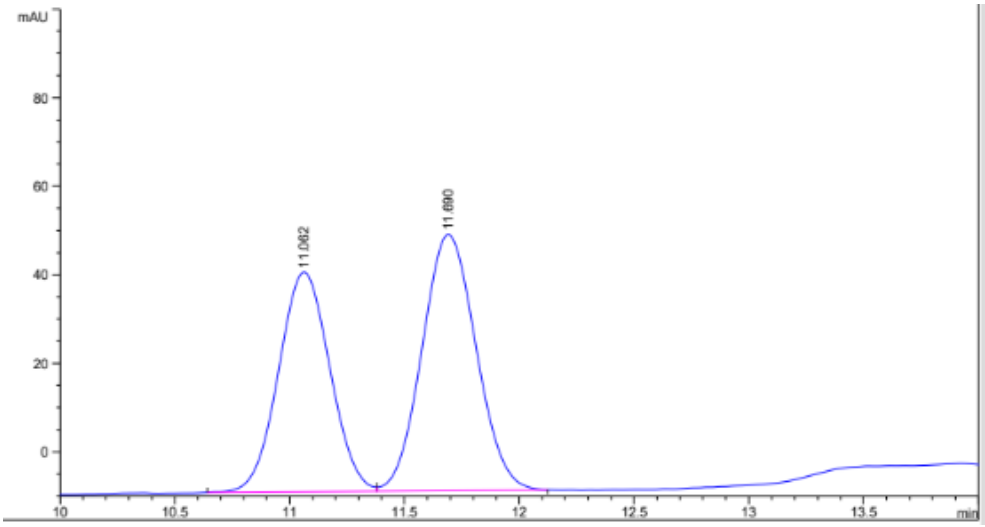
HRMS (ESI): Calculated for $C_{29}H_{34}BNO_3S$ [M+H+] = 488.2352, found 488.2352

$[\alpha]_D^{28}$= -35.2 (*c* 0.10, $CHCl_3$)

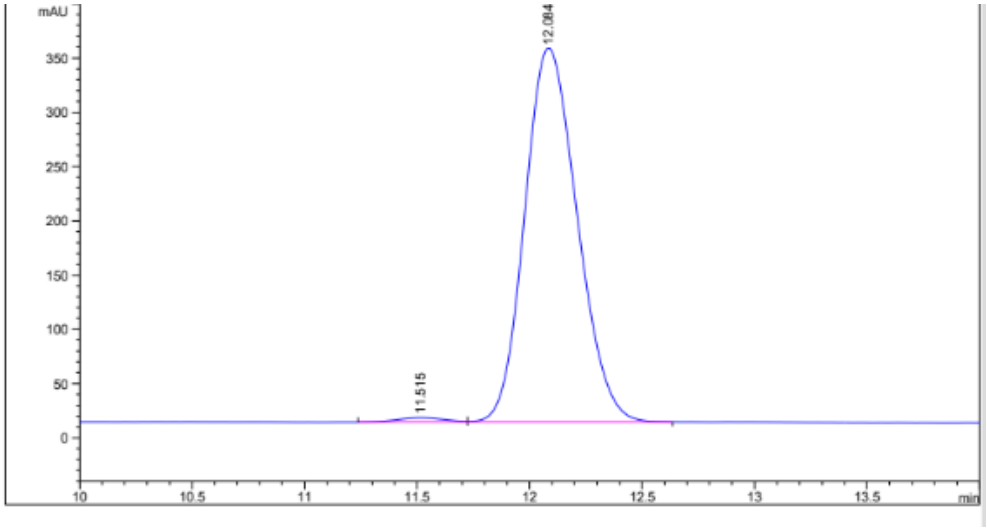
HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 230 nm): *ee* = 98%


f1 (ppm)
1.31
6.40
4.76
0.91
2.02
0.73
0.71
1.61
2.10
1.36
13.17
7.78
7.50
7.48
7.40
7.39
7.36
7.34
7.26 CDCl3
7.19
7.17
7.15
6.17
6.15
6.14
6.12
6.10
5.25
5.22
5.19
4.40
4.03
4.02
3.41
3.39
3.37
3.35
3.07
3.05
2.99
2.98
1.70
1.32


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
142.43
141.89
136.10
130.78
129.23
128.58
128.31
127.58
127.26
118.48
83.80
77.99
77.16 CDCl3
68.74
64.81
64.33
53.03
24.98

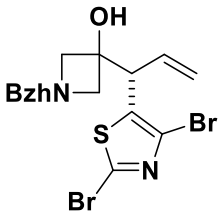


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.062	BV	0.2441	775.45636	49.68894	44.9384
2	11.690	VB	0.2553	950.14325	57.93660	55.0616



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.515	BV	0.2165	59.32895	4.10897	1.0500
2	12.084	VB	0.2532	5591.13477	344.82907	98.9500

(4j) (S)-1-benzhydryl-3-(1-(2,4-dibromothiazol-5-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2j (**102.3 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 48 hr). The title compound was obtained in 76% yield (79.0 mg, 0.152 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.25 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, J = 7.2 Hz, 4H), 7.25 – 7.20 (m, 4H), 7.15 (td, J = 7.2, 4.4 Hz, 2H), 5.86 (ddd, J = 17.2, 10.3, 7.1 Hz, 1H), 5.23 (dd, J = 10.2, 1.1 Hz, 1H), 5.19 – 5.11 (m, 1H), 4.36 (s, 1H), 4.24 (d, J = 7.1 Hz, 1H), 3.39 (d, J = 8.3 Hz, 1H), 3.11 (d, J = 8.4 Hz, 1H), 2.99 (d, J = 8.3 Hz, 1H), 2.85 (d, J = 8.5 Hz, 1H).

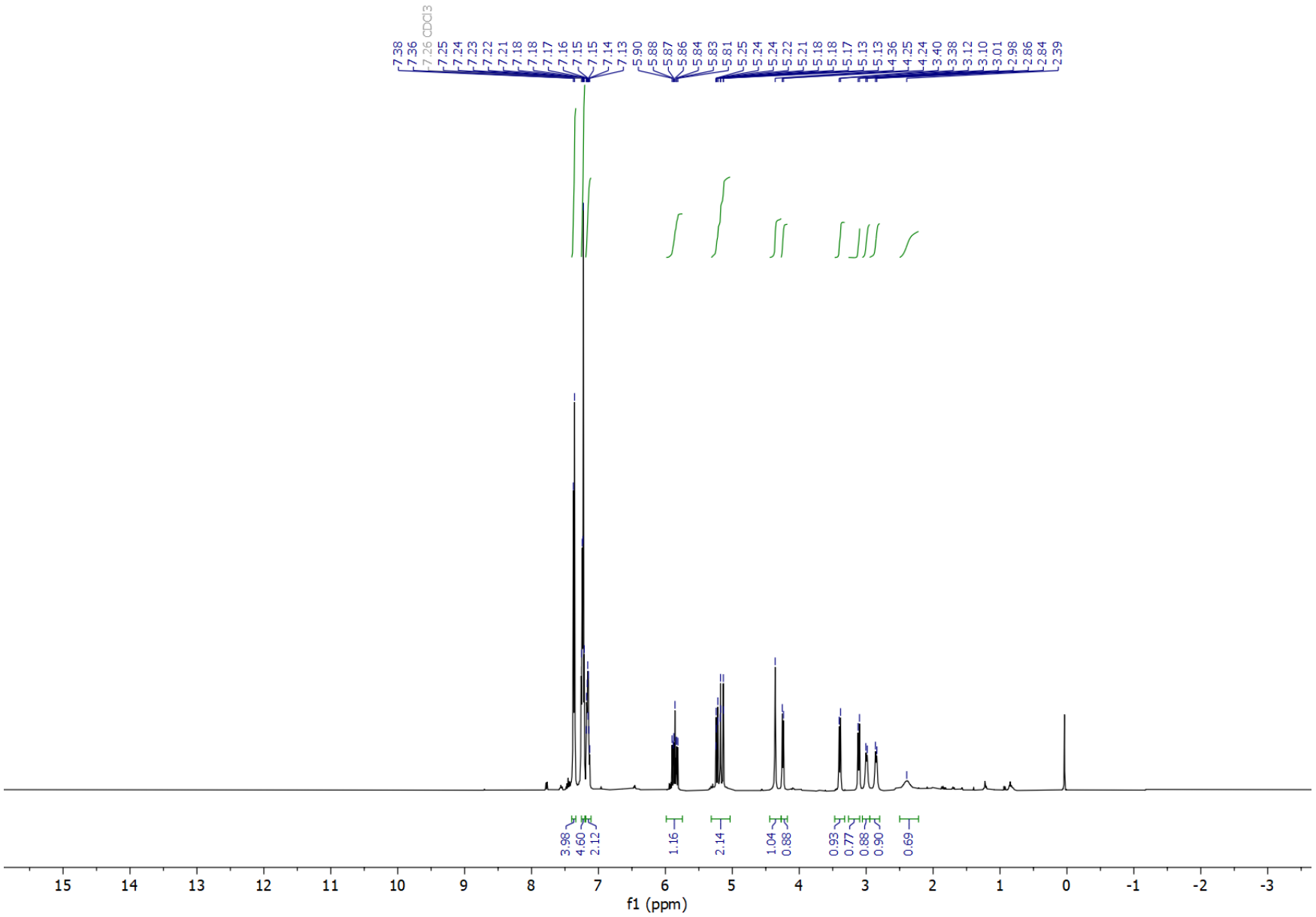
^{13}C NMR (126 MHz, $CDCl_3$): δ 133.0, 130.1, 128.9, 128.5, 128.3, 127.8, 127.3, 127.3, 119.7, 71.3, 65.1, 29.7.

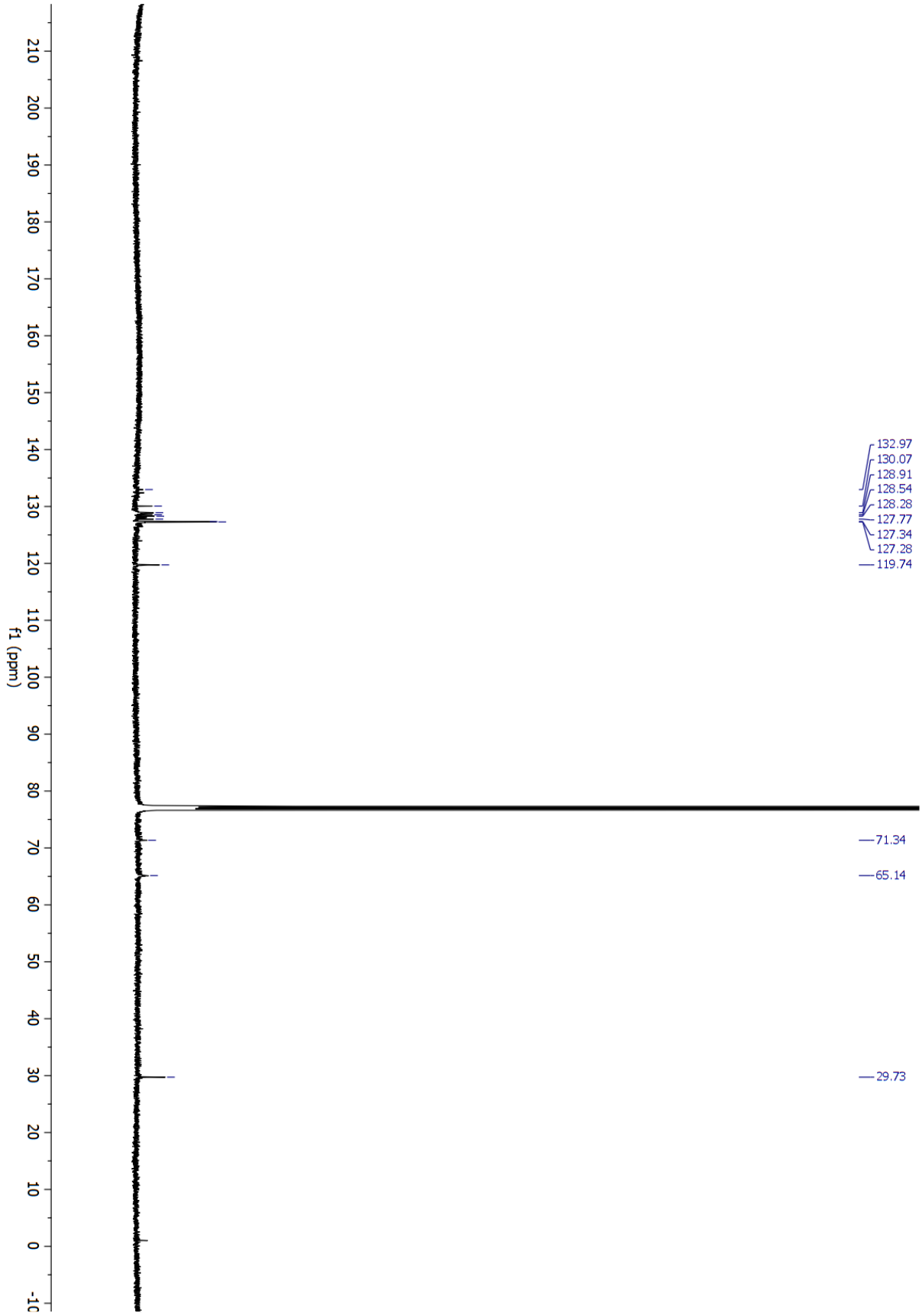
HRMS (ESI): calculated for $C_{22}H_{20}N_2OS$ $[M+H^+]$= 520.9716, found= 520.9721

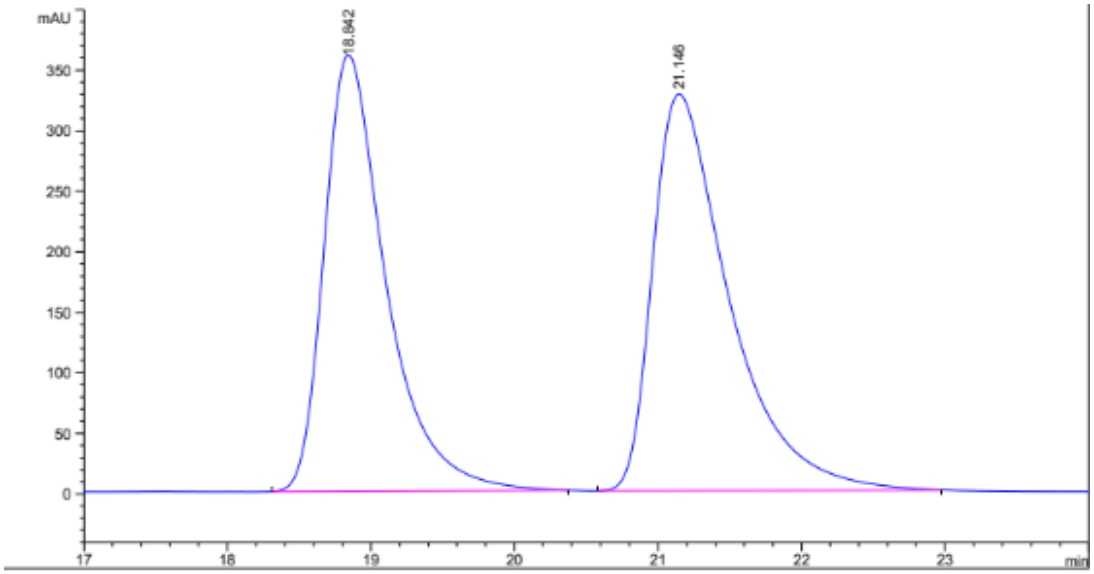
FTIR (neat): 3468, 3006, 2954, 2922, 2852, 1653, 1496, 1455, 1365, 1259, 1164, 1090, 702, 648 cm^{-1}

$[\alpha]_D^{28}$= -44.4 (*c* 0.10, $CHCl_3$)

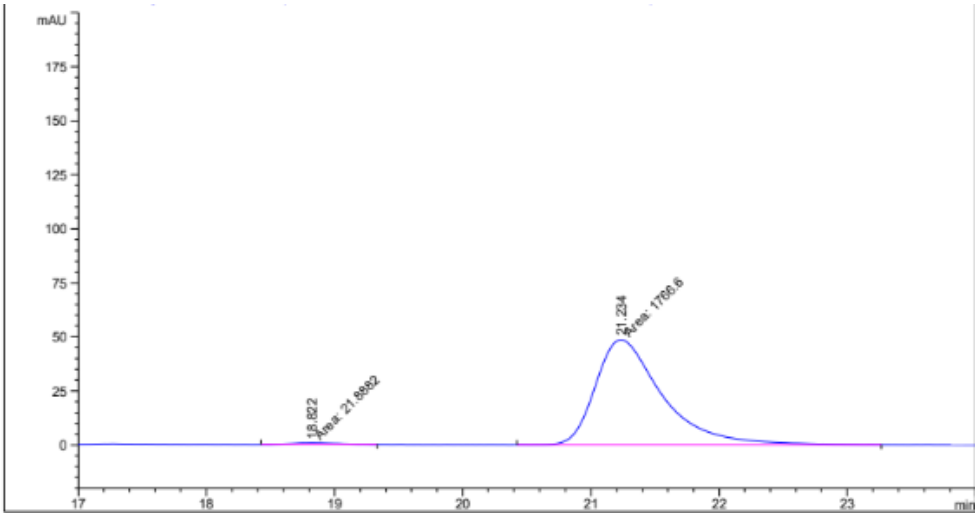
HPLC (Chiralcel AD-H column in series with a Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm): *ee* = 98%


7.38
7.36
7.26 CDCl3
7.25
7.24
7.23
7.22
7.21
7.18
7.18
7.17
7.16
7.15
7.15
7.14
7.13
5.90
5.88
5.87
5.86
5.84
5.83
5.81
5.25
5.24
5.24
5.22
5.21
5.18
5.18
5.17
5.13
5.13
4.36
4.25
4.24
3.40
3.38
3.12
3.10
3.01
2.98
2.86
2.84
2.39
3.98
4.60
2.12
1.16
2.14
1.04
0.88
0.93
0.77
0.88
0.90
0.69
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
132.97
130.07
128.91
128.54
128.28
127.77
127.34
127.28
119.74
71.34
65.14
29.73

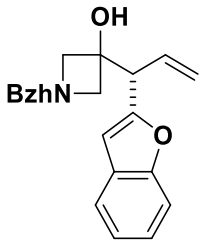


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.842	BB	0.4506	1.08369e4	360.57532	47.1051
2	21.146	BB	0.5554	1.21689e4	327.60324	52.8949



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.822	MM	0.4747	21.88818	7.68422e-1	1.2238
2	21.234	MM	0.6057	1766.59619	48.60963	98.7762

(4k) (S)-1-benzhydryl-3-(1-(benzofuran-2-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2a** (65.0 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 ºC, 36 hr). The title compound was obtained in 70% yield (55.4 mg, .14 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

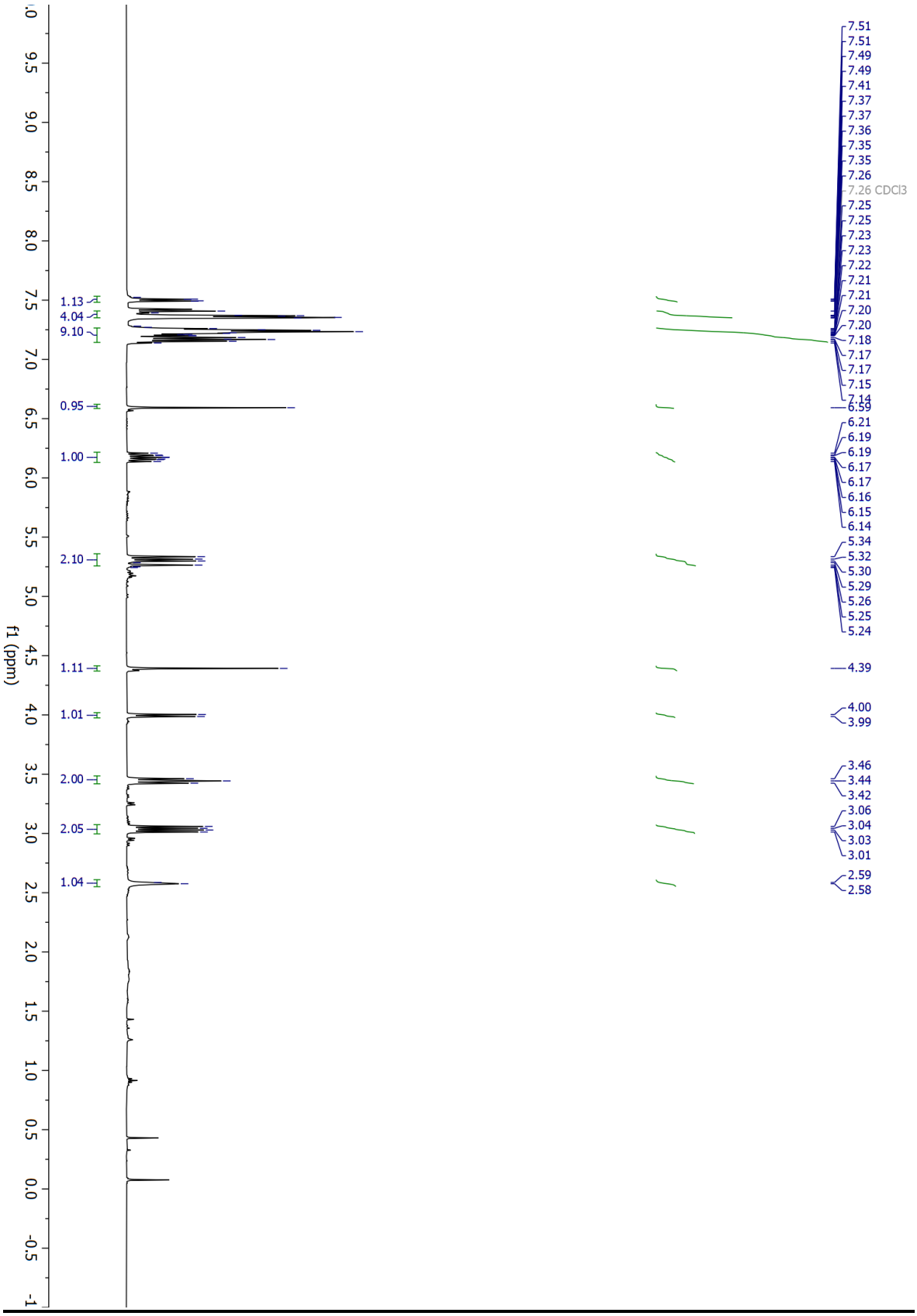
TLC (SiO_2): R_f = 0.25 (hexanes: ethyl acetate = 3:1).

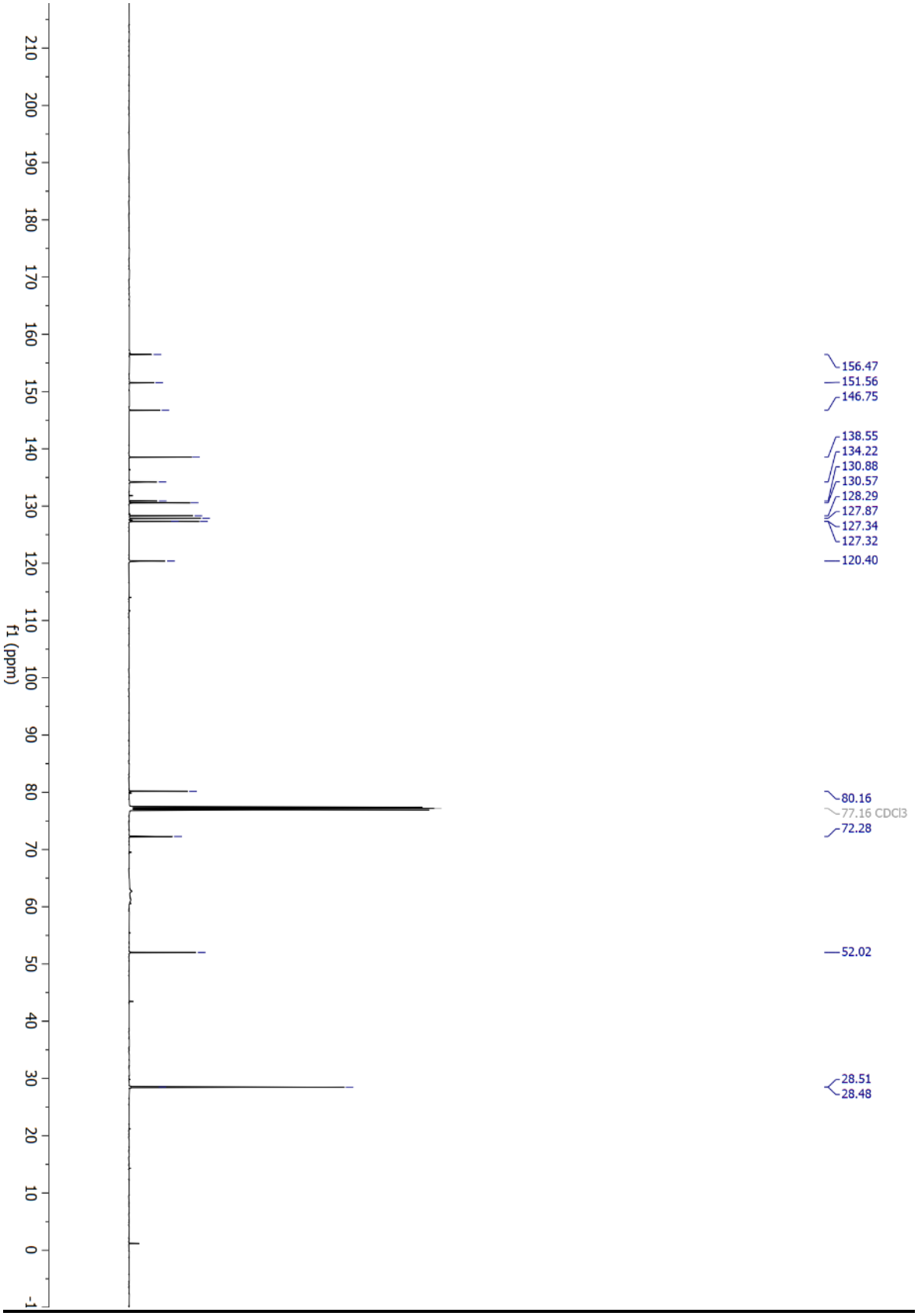
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.41 – 7.33 (m, 4H), 7.30 – 7.12 (m, 9H), 6.59 (s, 1H), 6.17 (ddd, *J* = 17.2, 10.3, 8.2 Hz, 1H), 5.35 – 5.23 (m, 2H), 4.39 (s, 1H), 3.99 (d, *J* = 8.2 Hz, 1H), 3.44 (t, *J* = 9.5 Hz, 2H), 3.04 (dd, *J* = 15.7, 8.1 Hz, 2H), 2.58 (d, *J* = 5.2 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 156.5, 151.6, 146.8, 138.6, 134.2, 130.9, 130.6, 128.3, 127.9, 127.3, 127.3, 120.4, 80.2, 72.3, 52.0, 28.5, 28.5.
HRMS (ESI): Calculated for $C_{27}H_{25}NO_2$ [M+H$^+$] = 396.1958, found 396.1966

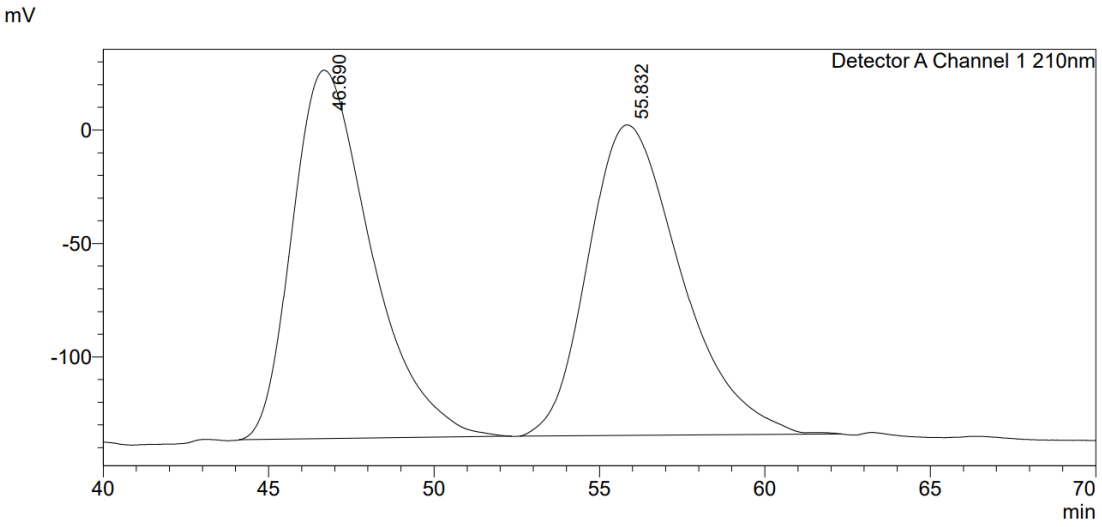
FTIR (neat): 3550.17, 3027.50, 2936.42, 2841.94, 1572.59, 1451.77, 1357.38, 1176.49, 803.73 cm

$[\alpha]_D^{28}$= -22.5 (c 0.1, $CHCl_3$)

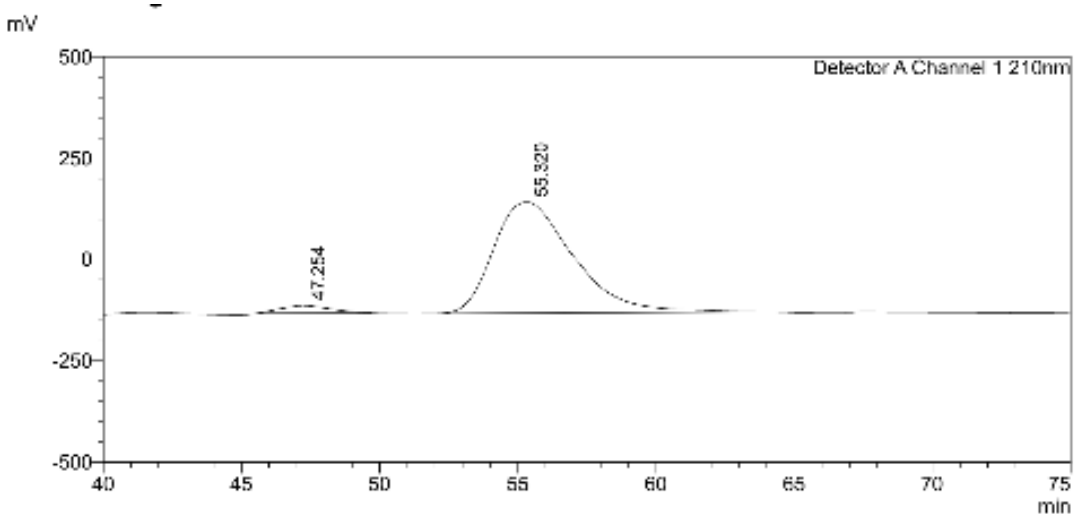
HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 0.50 mL/min, 210 nm): *ee* = 92%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.13
4.04
9.10
0.95
1.00
2.10
1.11
1.01
2.00
2.05
1.04
7.51
7.51
7.49
7.49
7.41
7.37
7.37
7.36
7.35
7.35
7.26
7.26 CDCl3
7.25
7.25
7.23
7.23
7.22
7.21
7.21
7.20
7.20
7.18
7.17
7.17
7.15
7.14
6.59
6.21
6.19
6.19
6.17
6.17
6.16
6.15
6.14
5.34
5.32
5.30
5.29
5.26
5.25
5.24
4.39
4.00
3.99
3.46
3.44
3.42
3.06
3.04
3.03
3.01
2.59
2.58


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
156.47
151.56
146.75
138.55
134.22
130.88
130.57
128.29
127.87
127.34
127.32
120.40
80.16
77.16 CDCl3
72.28
52.02
28.51
28.48

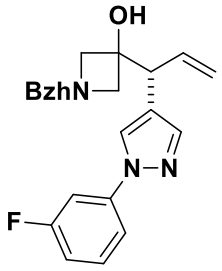


Peak#	Ret. Time	Area	Height	Conc.	Area%
1	46.690	26866480	162381	50.071	50.071
2	55.832	26790348	136812	49.929	49.929
Total		53656829	299193		100.000



Peak#	Ret. Time	Area	Height	Conc.	Area%
1	47.254	2275619	18617	3.978	3.978
2	55.320	54923073	273788	96.022	96.022
Total		57198692	292406		100.000

(4l) (*R*)-1-benzhydryl-3-(1-(1-(3-fluorophenyl)-1*H*-pyrazol-4-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2l** (78.0 mg, 0.30 mmol, 150 mol%) was subjected to general procedure D (100 oC, 36 hr). The title compound was obtained in 74% yield (65.2 mg, 0.148 mmol) as a yellow oil after isolation by flash column chromatography (SiO2, hexanes: ethyl acetate = 10:1—7:1).

TLC (SiO2): Rf = 0.18 (hexanes: ethyl acetate = 4:1).

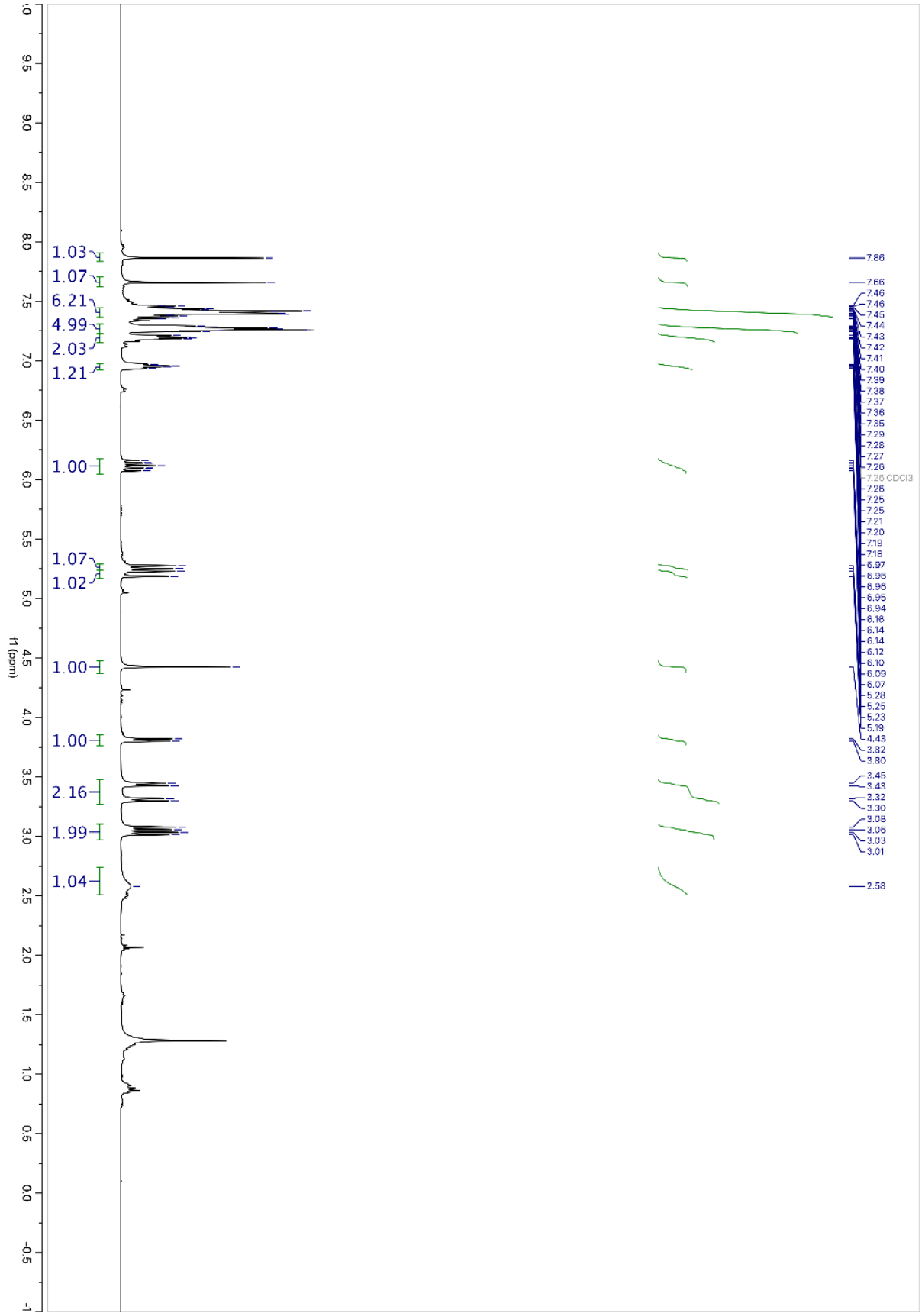
1H NMR (400 MHz, CDCl3): δ 7.86 (s, 1H), 7.66 (s, 1H), 7.41 (pd, *J* = 7.9, 2.4 Hz, 6H), 7.31 – 7.23 (m, 5H), 7.20 (dd, *J* = 7.2, 4.5 Hz, 2H), 6.95 (td, *J* = 8.1, 2.7 Hz, 1H), 6.12 (ddd, *J* = 17.5, 10.3, 7.7 Hz, 1H), 5.26 (d, *J* = 10.2 Hz, 1H), 5.21 (d, *J* = 17.1 Hz, 1H), 4.43 (s, 1H), 3.81 (d, *J* = 7.7 Hz, 1H), 3.37 (dd, *J* = 51.8, 8.2 Hz, 2H), 3.05 (dd, *J* = 17.5, 8.3 Hz, 2H), 2.58 (s, 1H).
13C NMR (101 MHz, CDCl3): δ 163.3 (d, J = 246.5 Hz), 141.8, 136.1, 130.8 (d, J = 9.1 Hz), 128.6, 127.5, 127.3, 125.9, 121.4, 118.4, 114.1 (d, J = 3.1 Hz), 113.1 (d, J = 21.2 Hz), 106.7 (d, J = 26.3 Hz), 78.0, 71.71, 64.9, 48.1, 29.8.
19F NMR (376 MHz, CDCl3): δ -110.97.

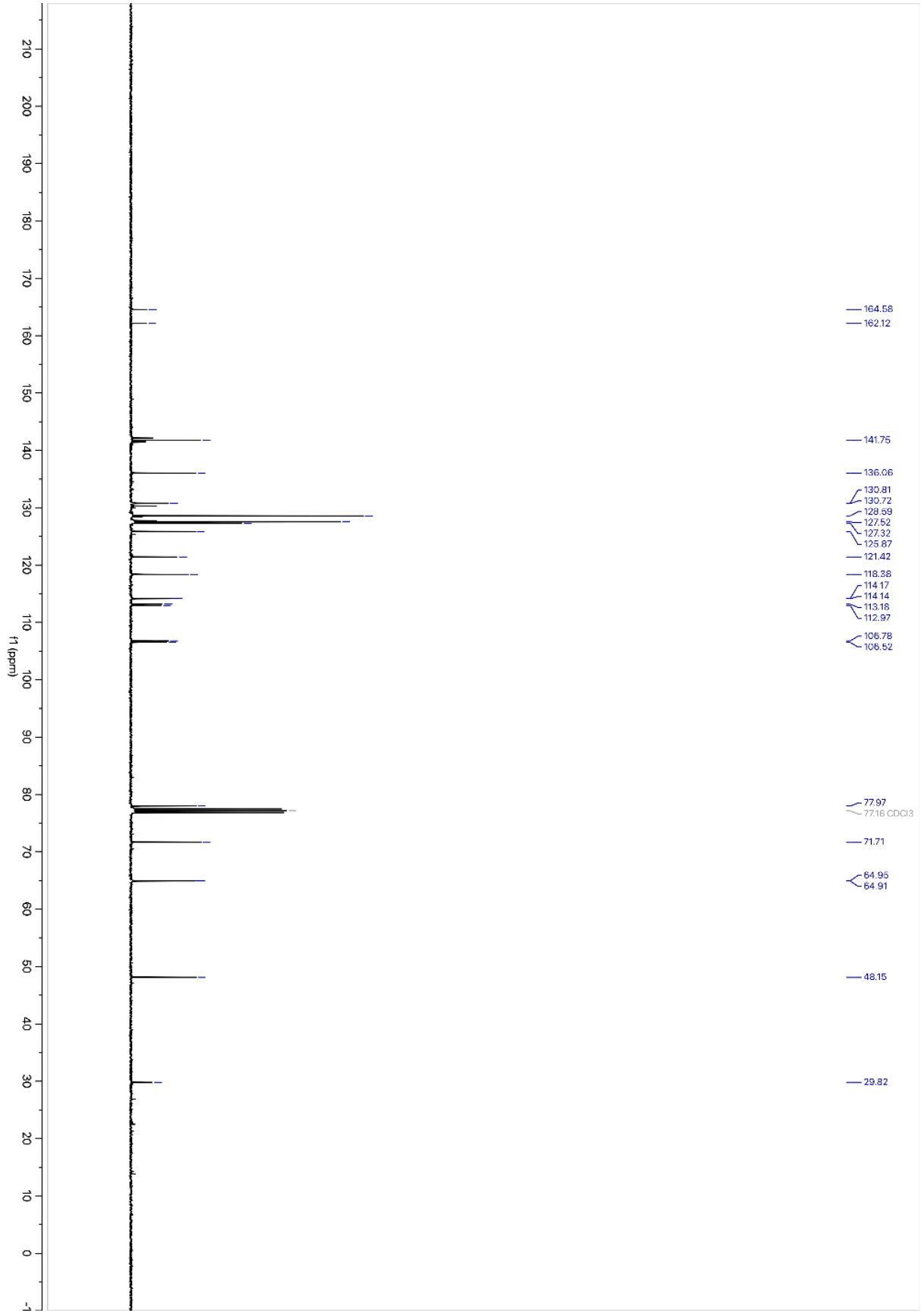
HRMS (ESI): Calculated for C28H26FN3O [M+H+] = 440.2133, found 440.2135

FTIR (neat): 3380, 3063, 3026, 2932, 2834, 1613, 1601, 1565, 1497, 1452, 1393, 1345, 1308, 1259, 1208, 1176, 1152, 1074, 1029, 996, 970, 950, 922 cm–1.

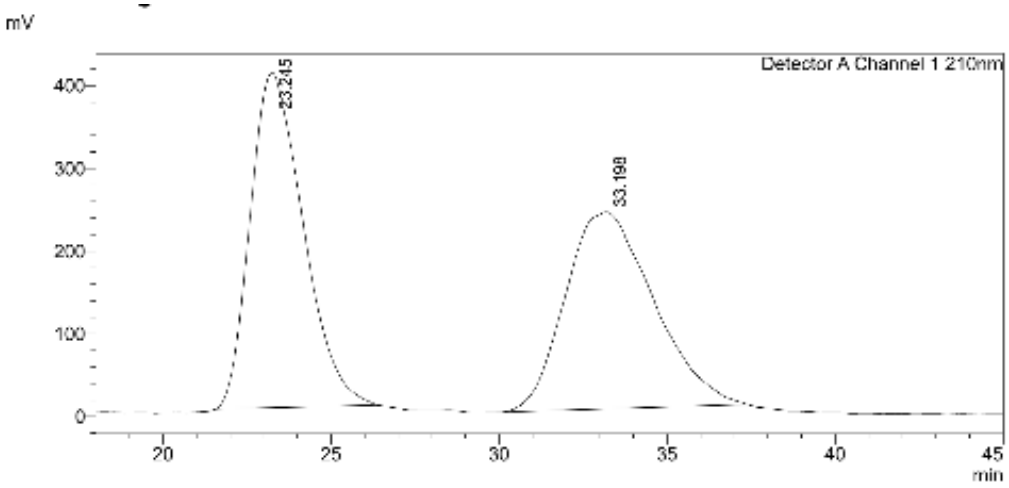
$[\alpha]_D^{28}$= -18.5 (*c* 0.10, CHCl3).

HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm): *ee* = 98%.

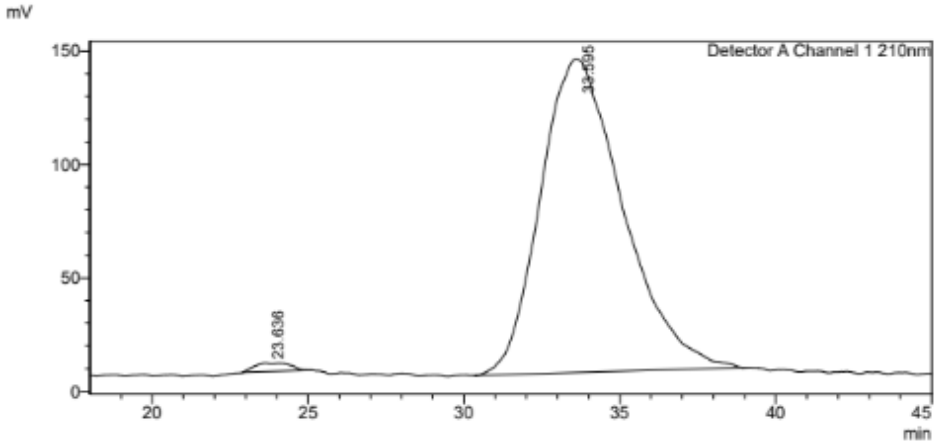

1.03
1.07
6.21
4.99
2.03
1.21
1.00
1.07
1.02
1.00
1.00
2.16
1.99
1.04
f1 (ppm)
7.86
7.66
7.46
7.46
7.45
7.44
7.43
7.42
7.41
7.40
7.39
7.38
7.37
7.36
7.35
7.29
7.28
7.27
7.26
7.26 CDCl3
7.26
7.25
7.25
7.21
7.20
7.19
7.18
6.97
6.96
6.96
6.95
6.94
6.16
6.14
6.14
6.12
6.10
6.09
6.07
5.28
5.25
5.23
5.19
4.43
3.82
3.80
3.45
3.43
3.32
3.30
3.08
3.06
3.03
3.01
2.58


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
164.58
162.12
141.75
136.06
130.81
130.72
128.59
127.52
127.32
125.87
121.42
118.38
114.17
114.14
113.18
112.97
106.78
106.52
77.97
77.16 CDCl3
71.71
64.95
64.91
48.15
29.82

-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)
-110.97

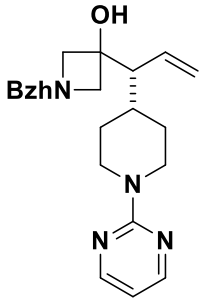


Peak#	Ret. Time	Area	Area%
1	23.245	44459957	50.585
2	33.198	43431584	49.415
Total		87891541	100.000



Peak#	Ret. Time	Area	Area%
1	23.636	286368	1.112
2	33.595	25473630	98.888
Total		25759999	100.000

(4m) (*R*)-1-benzhydryl-3-(1-(1-(pyrimidin-2-yl)piperidin-4-yl)allyl)azetidin-3-ol



Procedure

Allyl acetate **2m** (78.4 mg, 0.30 mmol, 150 mol%) was subjected to a modified version of general procedure D (100 oC, 48 hr). The title compound was obtained in 67% yield (59.2 mg, 0.134 mmol) as a brown oil after isolation by flash column chromatography (SiO2, hexanes: ethyl acetate = 3:1—2:1).

TLC (SiO2): Rf = 0.26 (hexanes: ethyl acetate = 4:1).

1H NMR (500 MHz, CDCl3): δ 8.27 (d, J = 4.7 Hz, 1H), 7.39 (d, J = 7.5 Hz, 2H), 7.19 (dt, J = 7.1, 3.7 Hz, 1H), 6.41 (t, J = 4.7 Hz, 1H), 5.84 – 5.58 (m, 0H), 5.18 – 5.02 (m, 1H), 4.73 (dddt, J = 11.2, 9.0, 4.7, 2.3 Hz, 1H), 4.33 (s, 1H), 3.24 (d, J = 8.6 Hz, 1H), 3.16 (d, J = 8.6 Hz, 1H), 3.06 (q, J = 8.9 Hz, 1H), 2.79 (qd, J = 12.8, 2.6 Hz, 1H), 1.99 (dd, J = 9.8, 7.7 Hz, 1H), 1.94 – 1.80 (m, 1H), 1.67 (dt, J = 13.1, 2.8 Hz, 1H), 1.31 – 1.21 (m, 1H).

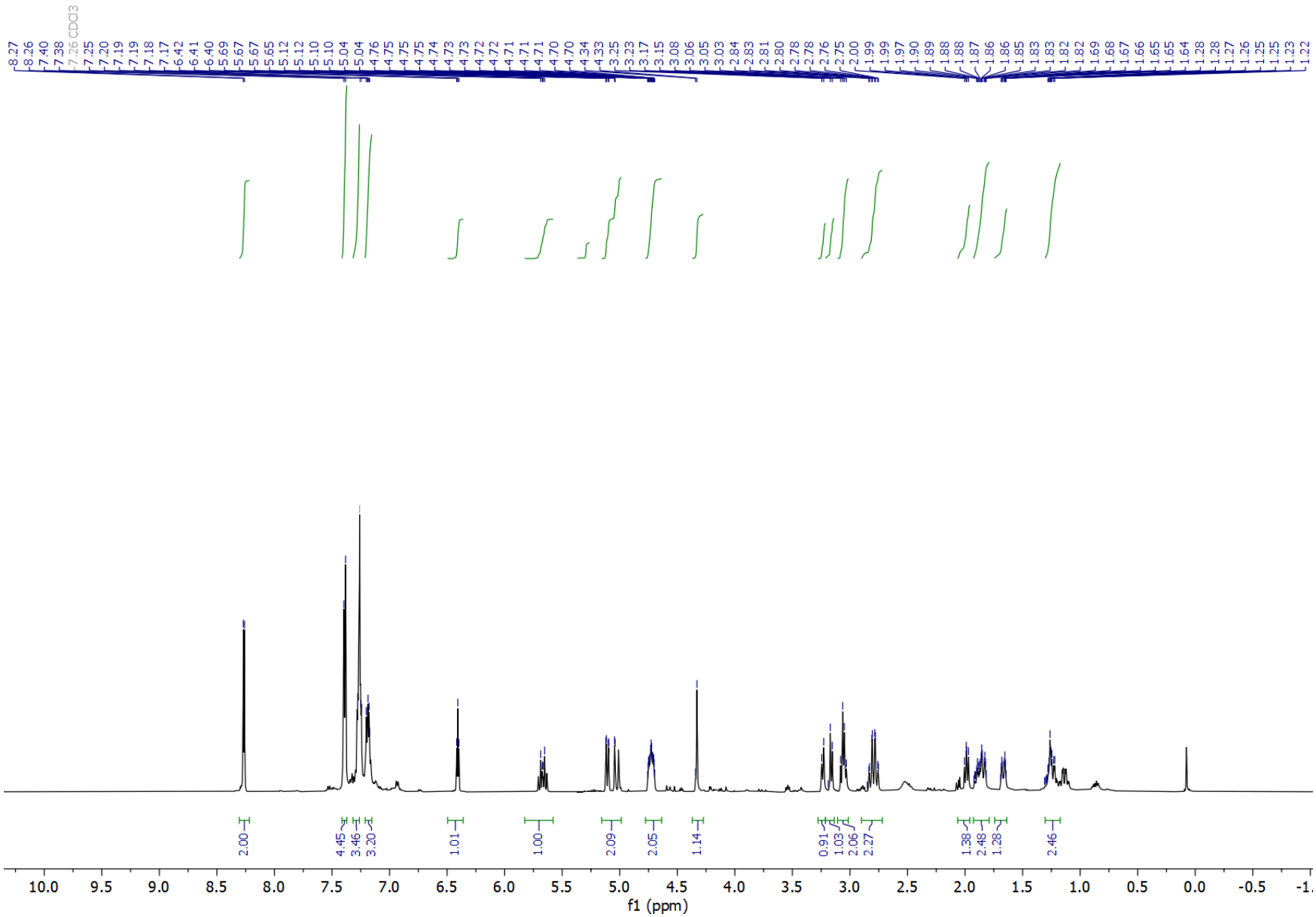
13C NMR (126 MHz, CDCl3): δ 161.7, 157.9, 136.0, 130.3, 128.6, 127.3, 118.5, 109.3, 78.0, 73.2, 67.64, 66.7, 58.2, 44.4, 44.2, 36.5, 30.7, 30.4.

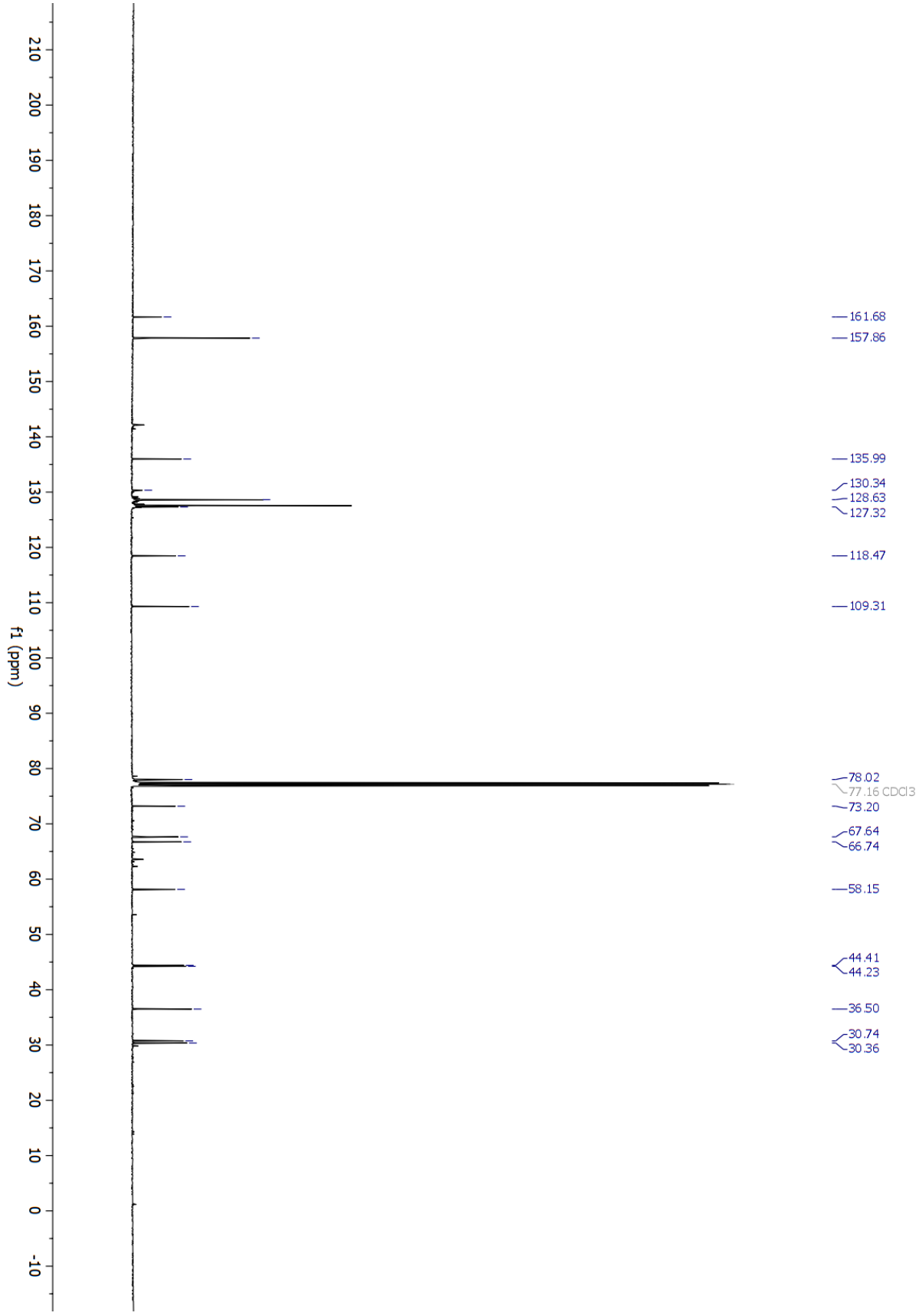
HRMS (APCI): Calculated for C28H32N4O [M+H+] = 441.2649, found 441.2659

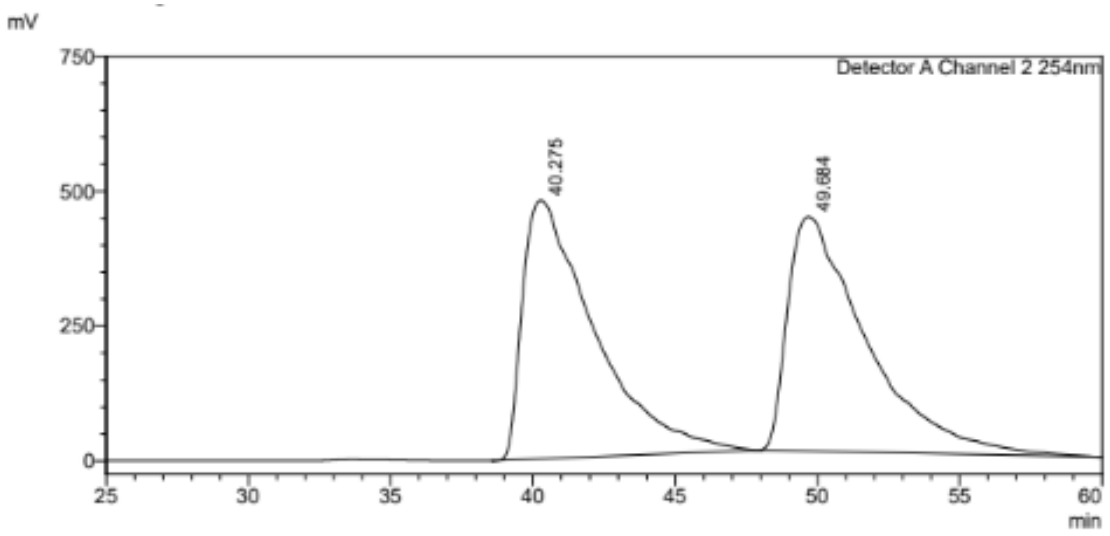
FTIR (neat): 3342, 3026, 2968, 1587, 1546, 1492, 1451, 1393, 1362, 1306, 1271, 1206, 1160, 1128, 1028, 1002, 974, 950, 918, 816, 796, 744, 703 cm–1

$[\alpha]_D^{28}$= -5.0 (*c* 0.20, CHCl3)

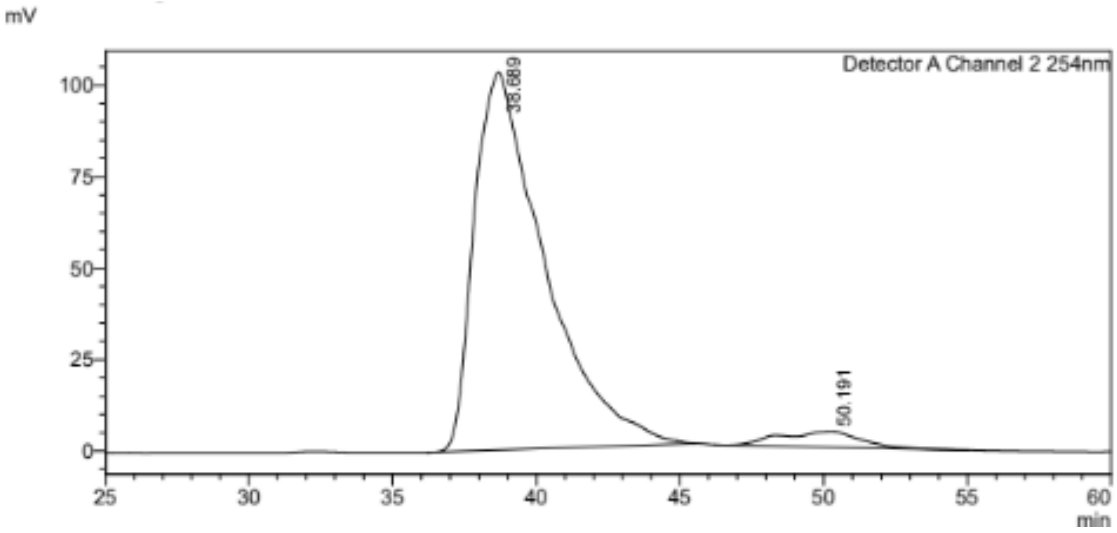
HPLC (Phenonox Cellulose column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm): *ee* = 91%


8.27 8.26 7.40 7.38 7.26 CDCl3 7.25 7.20 7.19 7.19 7.18 7.17 6.42 6.41 6.40 5.69 5.67 5.67 5.65 5.12 5.12 5.10 5.10 5.04 5.04 4.76 4.75 4.75 4.75 4.74 4.73 4.73 4.72 4.72 4.71 4.71 4.71 4.70 4.70 4.34 4.33 3.25 3.23 3.17 3.15 3.08 3.06 3.05 3.03 2.84 2.83 2.81 2.80 2.78 2.78 2.76 2.75 2.00 1.99 1.99 1.97 1.90 1.89 1.88 1.88 1.87 1.86 1.86 1.85 1.83 1.83 1.82 1.82 1.69 1.68 1.67 1.66 1.65 1.65 1.64 1.28 1.28 1.27 1.26 1.25 1.25 1.23 1.22
2.00 4.45 3.46 3.20 1.01 1.00 2.09 2.05 1.14 0.91 1.03 2.06 2.27 1.38 2.48 1.28 2.46
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
161.68
157.86
135.99
130.34
128.63
127.32
118.47
109.31
78.02
77.16 CDCl3
73.20
67.64
66.74
58.15
44.41
44.23
36.50
30.74
30.36

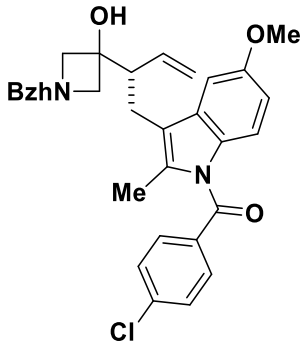


Peak#	Ret. Time	Area	Area%
1	40.275	84309016	50.250
2	49.684	83469644	49.750
Total		167778660	100.000



Peak#	Ret. Time	Area	Area%
1	38.689	17567467	95.490
2	50.191	829646	4.510
Total		18397113	100.000

(4n) (*S*)-(3-(2-(1-benzhydryl-3-hydroxyazetidin-3-yl)but-3-en-1-yl)-5-methoxy-2-methyl-1*H*-indol-1-yl)(4-chlorophenyl)methanone



Procedure

Allyl acetate **2n** (123.6 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 36 hr). The title compound was obtained in 79% yield (93.2 mg, 0.158 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1—3:1).

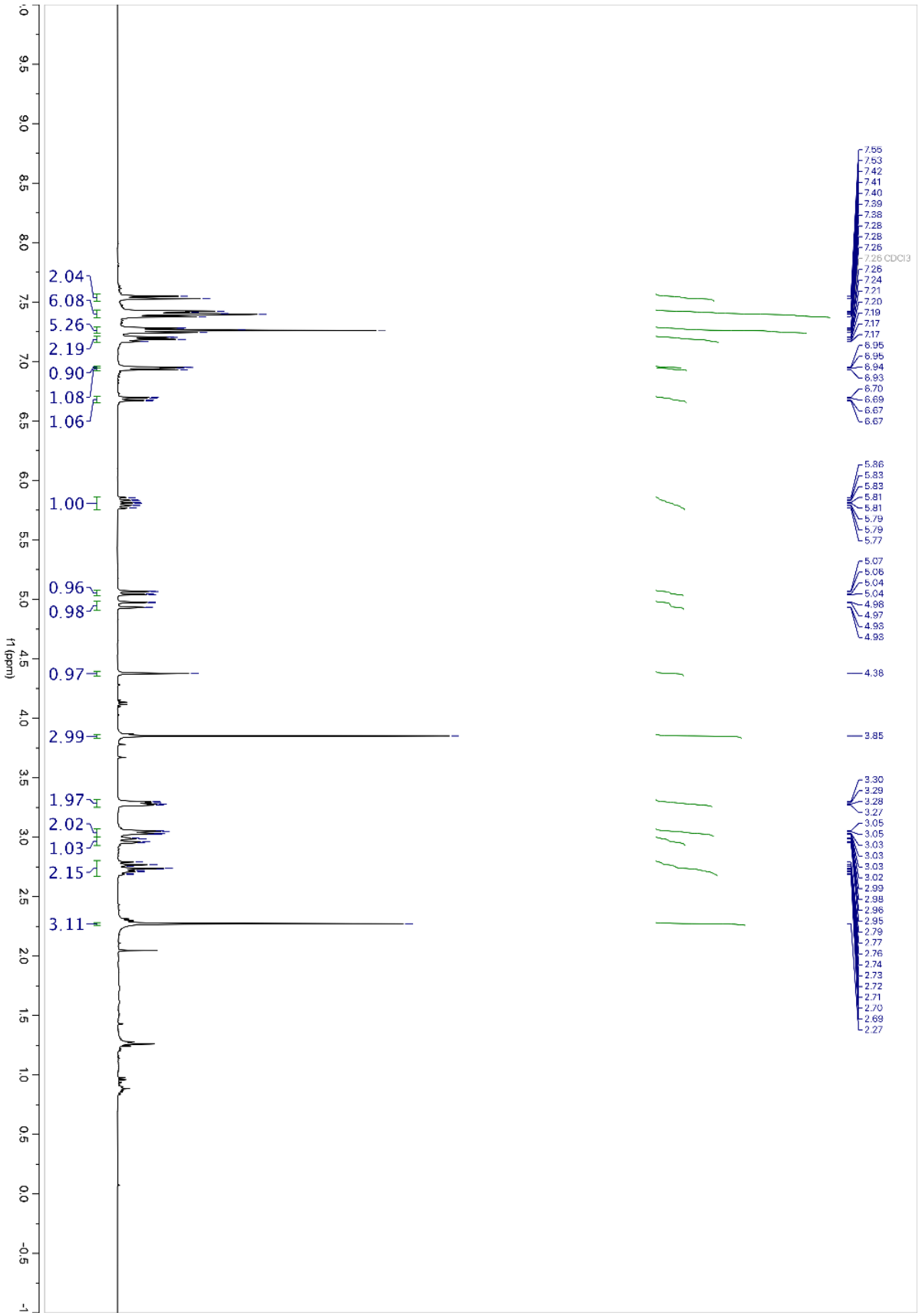
TLC (SiO_2): R_f = 0.68 (hexanes: ethyl acetate = 1:1).

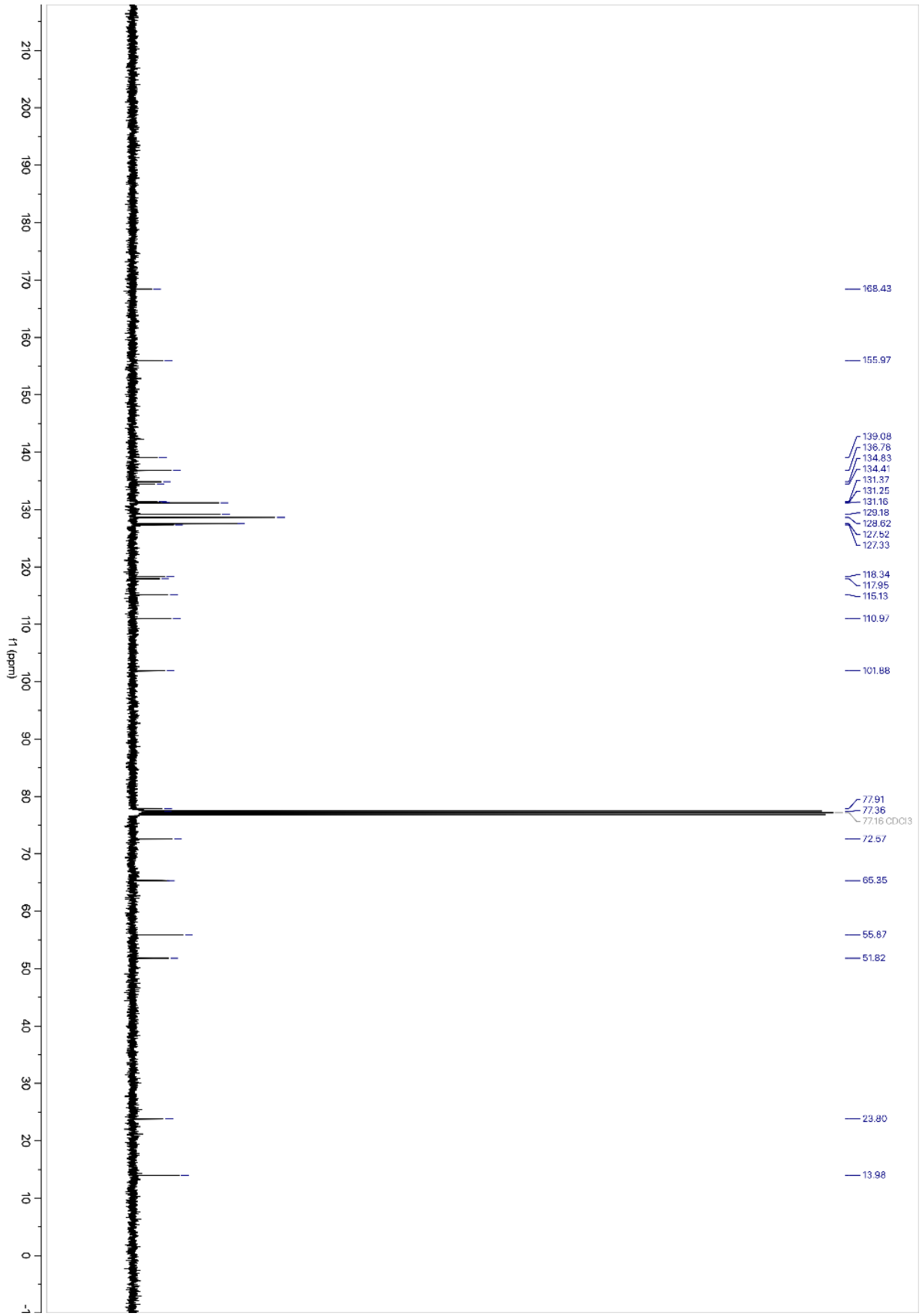
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.46 – 7.34 (m, 6H), 7.29 – 7.23 (m, 5H), 7.21 – 7.16 (m, 2H), 6.95 (d, *J* = 1.6 Hz, 1H), 6.94 (d, *J* = 5.0 Hz, 1H), 6.68 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.81 (ddd, *J* = 17.1, 10.1, 8.5 Hz, 1H), 5.05 (dd, *J* = 10.3, 1.8 Hz, 1H), 4.95 (dd, *J* = 17.2, 1.8 Hz, 1H), 4.38 (s, 1H), 3.85 (s, 3H), 3.28 (dd, *J* = 8.4, 3.8 Hz, 2H), 3.04 (dd, *J* = 8.0, 2.5 Hz, 2H), 3.00 – 2.92 (m, 1H), 2.81 – 2.64 (m, 2H), 2.27 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 168.4, 156.0, 139.1, 136.8, 134.8, 134.4, 131.4, 131.2, 131.2, 129.2, 128.6, 127.5, 127.3, 118.3, 118.0, 115.1, 111.0, 101.9, 77.9, 77.4, 72.6, 65.3, 55.9, 51.8, 23.8, 14.0.
HRMS (APCI): Calculated for $C_{37}H_{35}ClN_2O_3$ [M+H$^+$] = 591.2409, found 591.2411

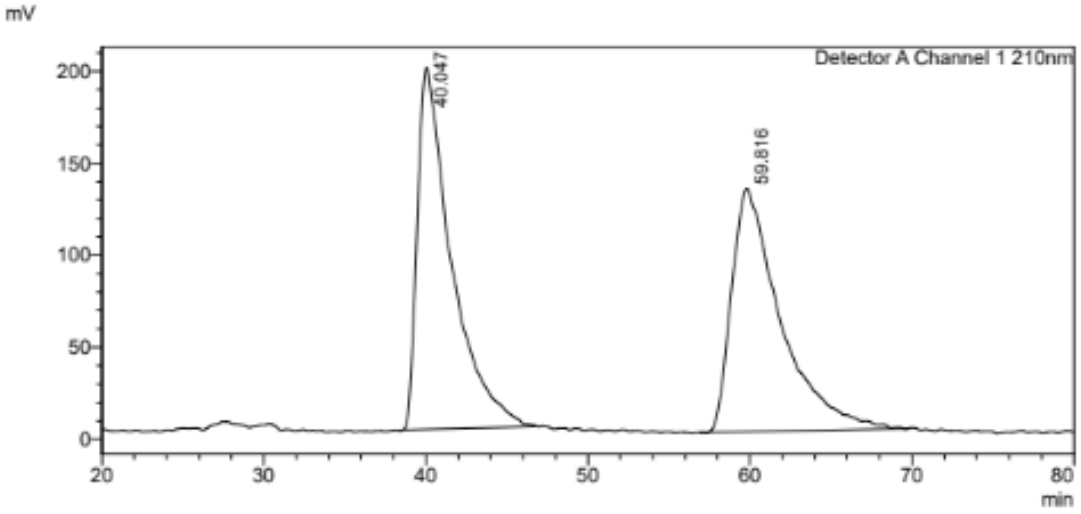
FTIR (neat): 3425, 3061, 2931, 2359, 1968, 1804, 1731, 1597, 1489, 1452, 1371, 1309, 1241, 1216, 1309, 1241, 1216, 1174, 1070, 1027, 927, 831, 799, 746, 703 cm^{-1}

$[\alpha]_D^{28}$ = -7.5 (*c* 0.20, $CHCl_3$)

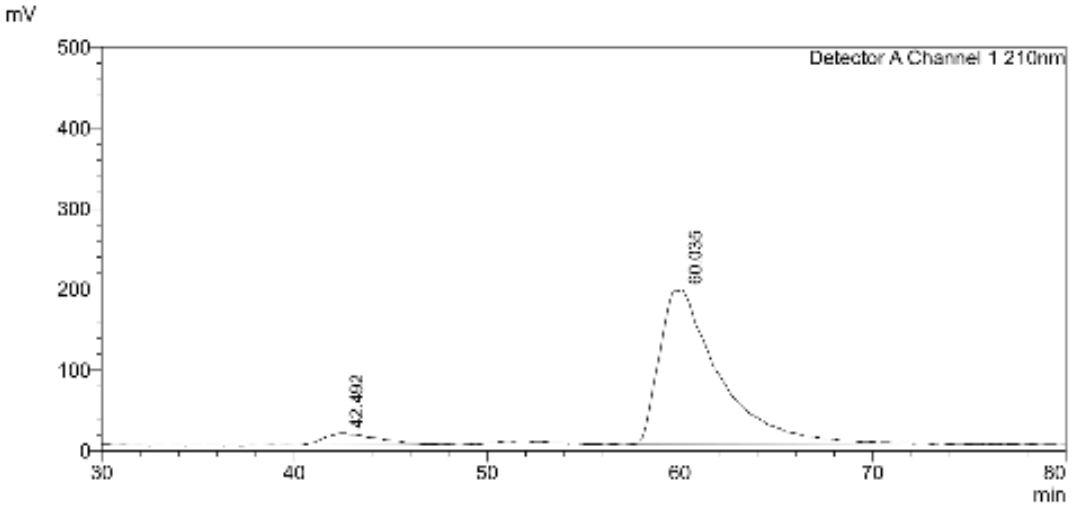
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 90:10, 1.00 mL/min, 210 nm): *ee* = 88%


f1 (ppm)
2.04
6.08
5.26
2.19
0.90
1.08
1.06
1.00
0.96
0.98
0.97
2.99
1.97
2.02
1.03
2.15
3.11
7.55
7.53
7.42
7.41
7.40
7.39
7.38
7.28
7.28
7.26
7.26 CDCl3
7.26
7.24
7.21
7.20
7.19
7.17
7.17
6.95
6.95
6.94
6.93
6.70
6.69
6.67
6.67
5.86
5.83
5.83
5.81
5.81
5.79
5.79
5.77
5.07
5.06
5.04
5.04
4.98
4.97
4.93
4.93
4.38
3.85
3.30
3.29
3.28
3.27
3.05
3.05
3.03
3.03
3.03
3.02
2.99
2.98
2.96
2.95
2.79
2.77
2.76
2.74
2.73
2.72
2.71
2.70
2.69
2.27


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
168.43
155.97
139.08
136.78
134.83
134.41
131.37
131.25
131.16
129.18
128.62
127.52
127.33
118.34
117.95
115.13
110.97
101.88
77.91
77.36
77.16 CDCl3
72.57
65.35
55.87
51.82
23.80
13.98

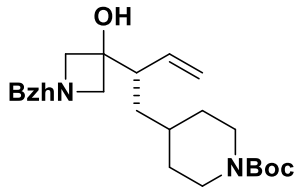


Peak#	Ret. Time	Area	Area%
1	40.047	28710225	50.966
2	59.816	27622051	49.034
Total		56332275	100.000



Peak#	Ret. Time	Area	Conc.	Area%
1	42.492	2889877	6.602	6.602
2	60.035	40881306	93.398	93.398
Total		43771183		100.000

(4o) tert-butyl (S)-4-(2-(1-benzhydryl-3-hydroxyazetidin-3-yl)but-3-en-1-yl)piperidine-1-carboxylate



Procedure

Allyl acetate **2o** (89.2 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 ^{o}C, 36 hr). The title compound was obtained in 68% yield (64.8 mg, 0.136 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–3:1).

TLC (SiO_2): R_f = 0.55 (hexanes: ethyl acetate = 1:1).

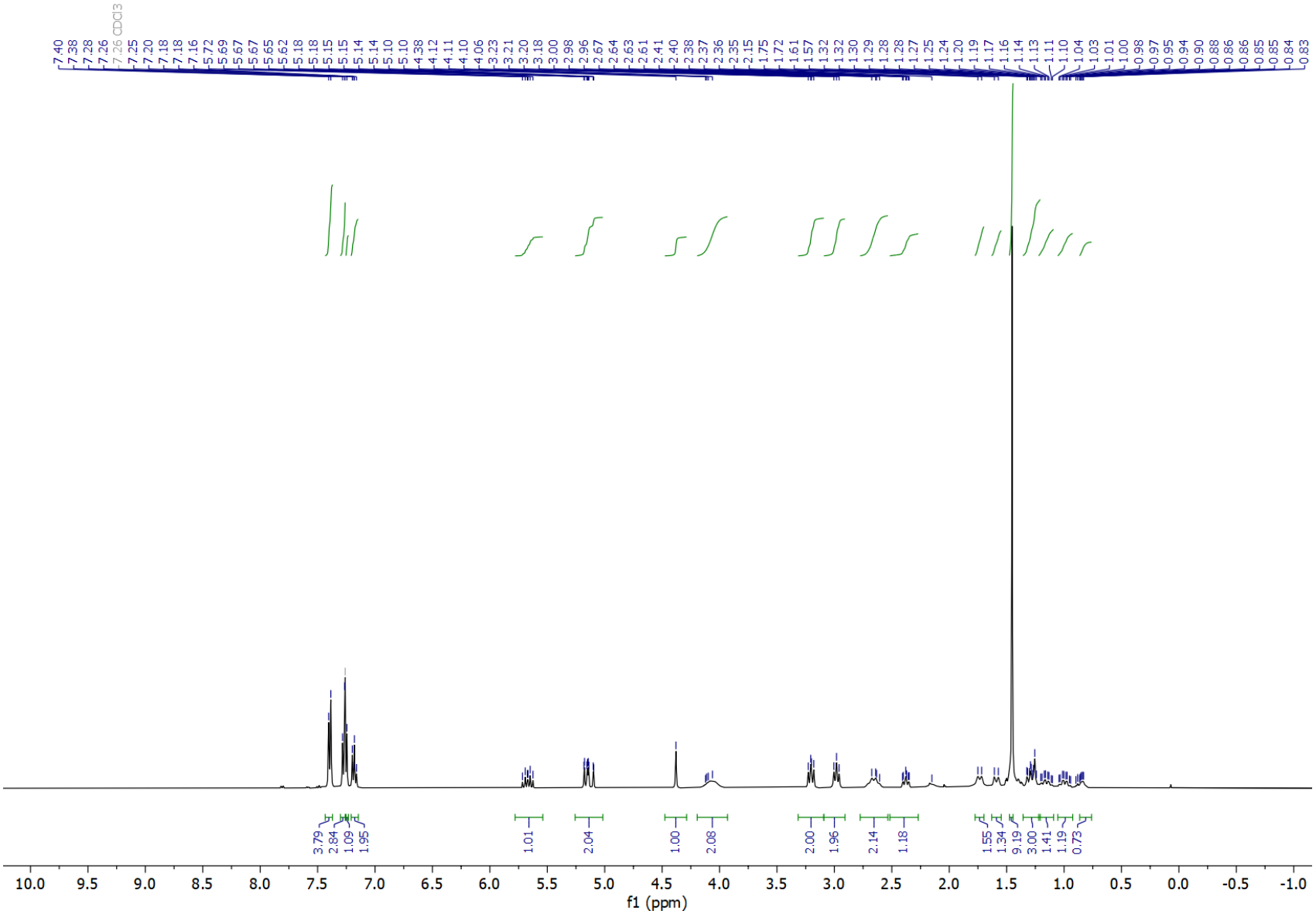
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, J = 7.5 Hz, 4H), 7.27 (d, J = 7.2 Hz, 3H), 7.25 (s, 1H), 7.18 (t, J = 7.3 Hz, 2H), 5.67 (dt, J = 17.1, 9.8 Hz, 1H), 5.17 (dd, J = 10.4, 2.0 Hz, 1H), 5.12 (dd, J = 17.2, 1.9 Hz, 1H), 4.38 (s, 1H), 4.15 – 3.97 (m, 2H), 3.20 (dd, J = 11.0, 8.3 Hz, 2H), 2.98 (t, J = 9.1 Hz, 2H), 2.74 – 2.57 (m, 2H), 2.38 (td, J = 10.2, 9.0, 2.8 Hz, 1H), 2.15 (s, 1H), 1.73 (d, J = 13.2 Hz, 2H), 1.59 (d, J = 13.7 Hz, 1H), 1.36 – 1.23 (m, 2H), 1.15 (qd, J = 12.1, 4.1 Hz, 1H), 0.99 (qd, J = 12.4, 4.1 Hz, 1H), 0.91 – 0.75 (m, 1H).

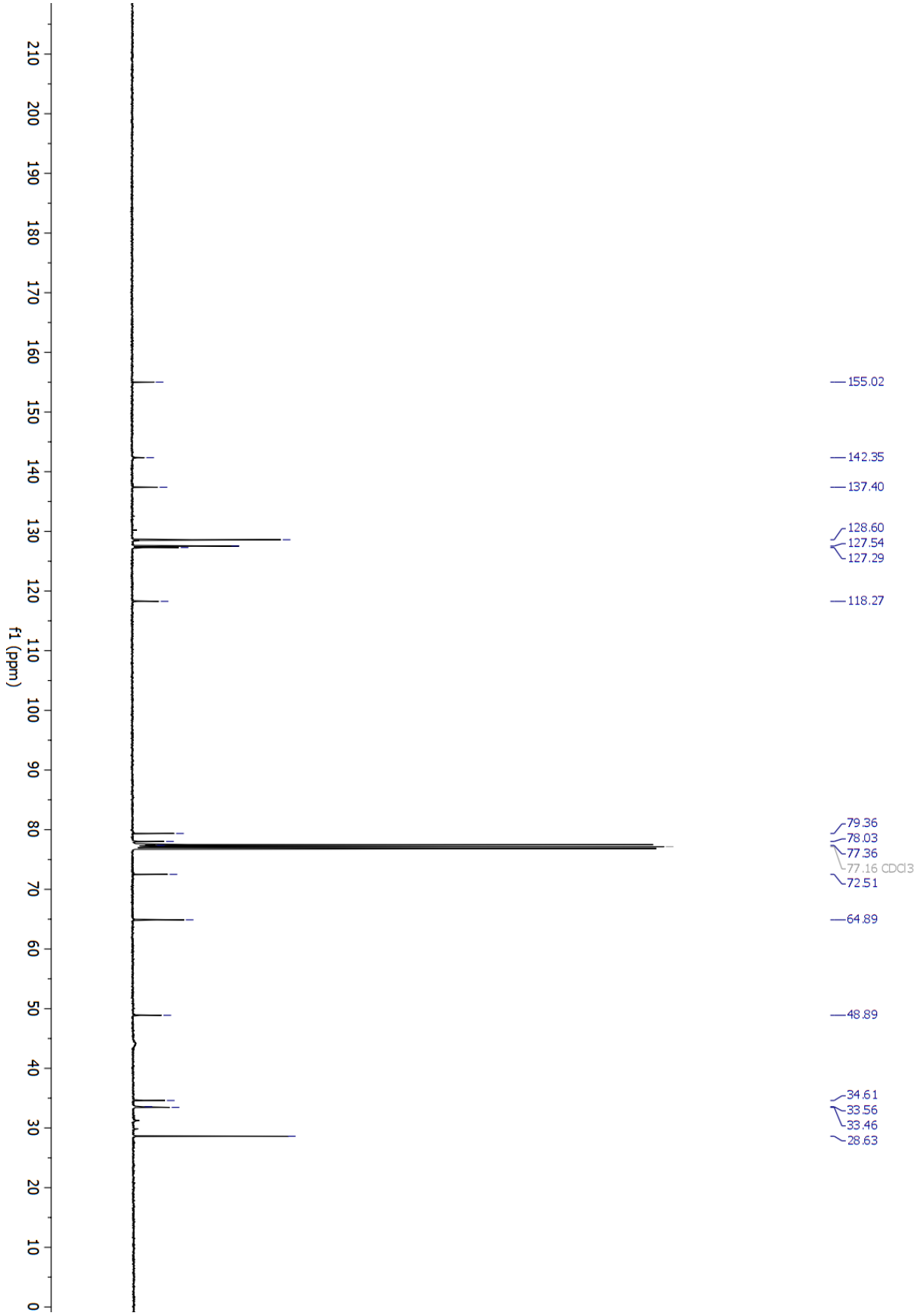
^{13}C NMR (101 MHz, $CDCl_3$): δ 155.02, 142.35, 137.40, 128.60, 127.54, 127.29, 118.27, 79.36, 78.03, 77.36, 72.51, 64.89, 48.89, 34.61, 33.56, 33.46, 28.63.
HRMS (ESI): Calculated for $C_{30}H_{40}N_2O_3$ [M+H+]= 476.3039, found= 476.3043

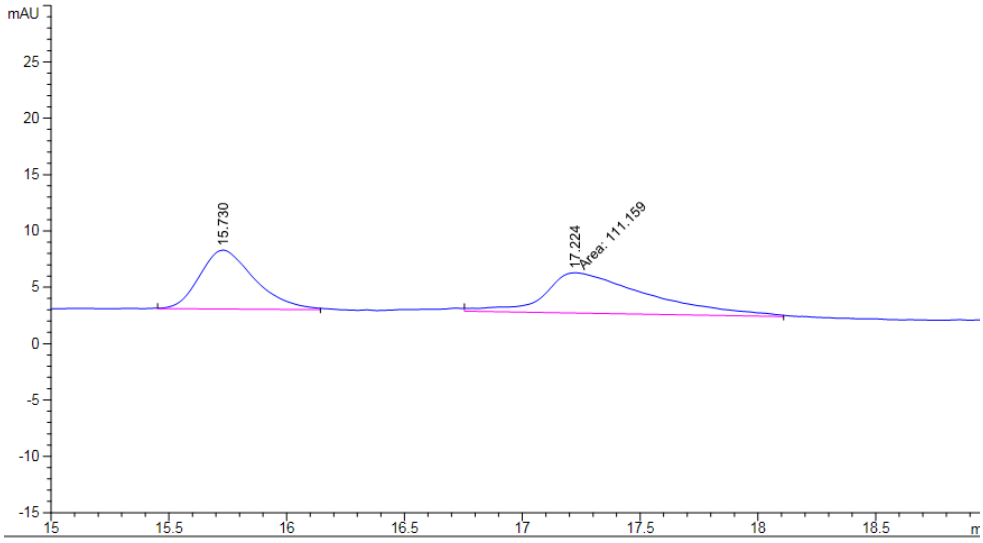
FTIR (neat): 3456, 3001, 2970, 2929, 2849, 1689, 1665, 1425, 1365, 1278, 1228, 1216, 703 cm^{-1}

$[\alpha]_D^{28}$= -86.5 (*c* 0.10, $CHCl_3$)

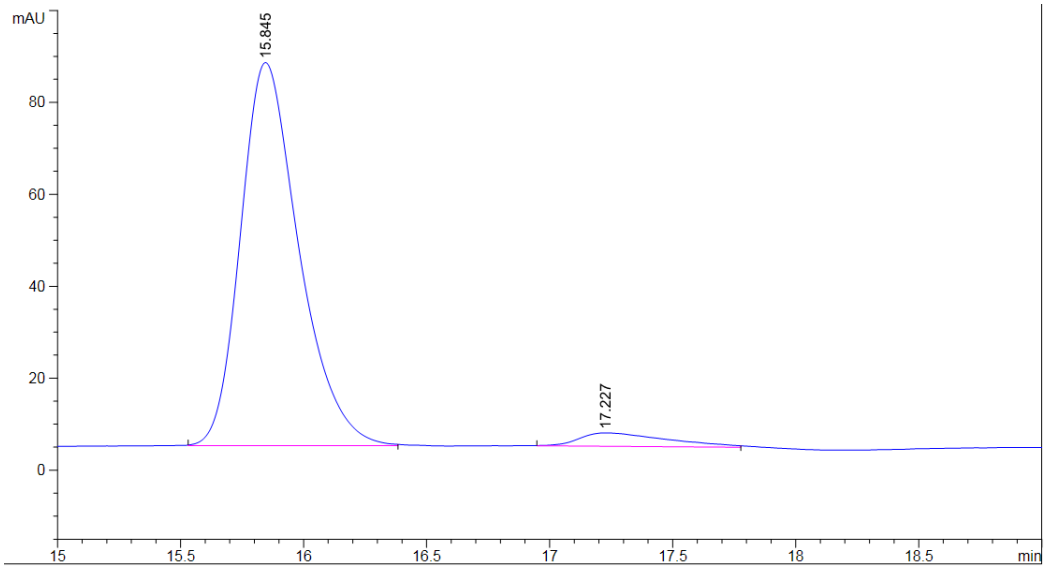
HPLC (Phenomenex Amylose column in series with a Phenomenex Cellulose column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm): *ee* = 90%


7.40 7.38 7.28 7.26 7.26 CDCl3 7.25 7.20 7.18 7.18 7.16 5.72 5.69 5.67 5.67 5.65 5.62 5.18 5.18 5.15 5.15 5.14 5.14 5.10 5.10 4.38 4.12 4.11 4.10 4.06 3.23 3.21 3.20 3.18 3.00 2.98 2.96 2.67 2.64 2.63 2.61 2.41 2.40 2.38 2.37 2.36 2.35 2.15 1.75 1.72 1.61 1.57 1.32 1.30 1.29 1.28 1.28 1.27 1.25 1.24 1.20 1.19 1.17 1.16 1.14 1.13 1.11 1.10 1.04 1.03 1.01 1.00 0.98 0.97 0.95 0.94 0.90 0.88 0.86 0.86 0.85 0.84 0.83
3.79 2.84 1.09 1.95 1.01 2.04 1.00 2.08 2.00 1.96 2.14 1.18 1.55 1.34 9.19 3.00 1.41 1.19 0.73
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


f1 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
155.02
142.35
137.40
128.60
127.54
127.29
118.27
79.36
78.03
77.36
77.16 CDCl3
72.51
64.89
48.89
34.61
33.56
33.46
28.63

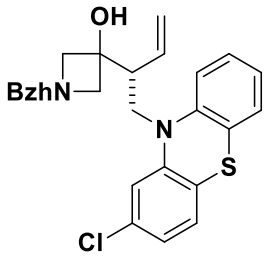


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.730	BB	0.2491	84.83456	5.23298	43.2845
2	17.224	MM	0.5164	111.15856	3.58768	56.7155



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.845	BB	0.2505	1375.41406	83.35380	94.9328
2	17.227	BB	0.3472	73.41555	2.92133	5.0672

(4p) (R)-1-benzhydryl-3-(1-(2-chloro-10H-phenothiazin-10-yl)but-3-en-2-yl)azetidin-3-ol



Procedure

Allyl acetate **2p** (93.3 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 36 hr). The title compound was obtained in 89% yield (93.2 mg, 0.178 mmol) as a white solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–4:1).

TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 7.41 (t, *J* = 8.5 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.27 (s, 1H), 7.23 (dd, *J* = 11.7, 6.6 Hz, 4H), 7.17 (dd, *J* = 10.7, 7.8 Hz, 4H), 7.06 (d, *J* = 8.1 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.88 (m, 3H), 5.82 (dq, *J* = 17.1, 10.8, 9.7 Hz, 1H), 5.22 (d, *J* = 10.3 Hz, 1H), 5.16 (d, *J* = 17.3 Hz, 1H), 4.31 (s, 1H), 4.26 (dd, *J* = 13.8, 6.6 Hz, 1H), 3.85 (dd, *J* = 13.8, 6.3 Hz, 1H), 3.41 (d, *J* = 8.4 Hz, 1H), 3.30 (d, *J* = 8.4 Hz, 1H), 3.05 (d, *J* = 8.4 Hz, 1H), 2.95 (dt, *J* = 14.6, 8.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 146.9, 144.8, 134.7, 133.5, 128.6, 128.5, 128.3, 128.0, 127.5, 127.5, 127.3, 126.0, 124.7, 123.4, 122.8, 119.4, 116.5, 116.3, 71.6, 65.5, 65.0, 64.9, 48.0, 46.8.

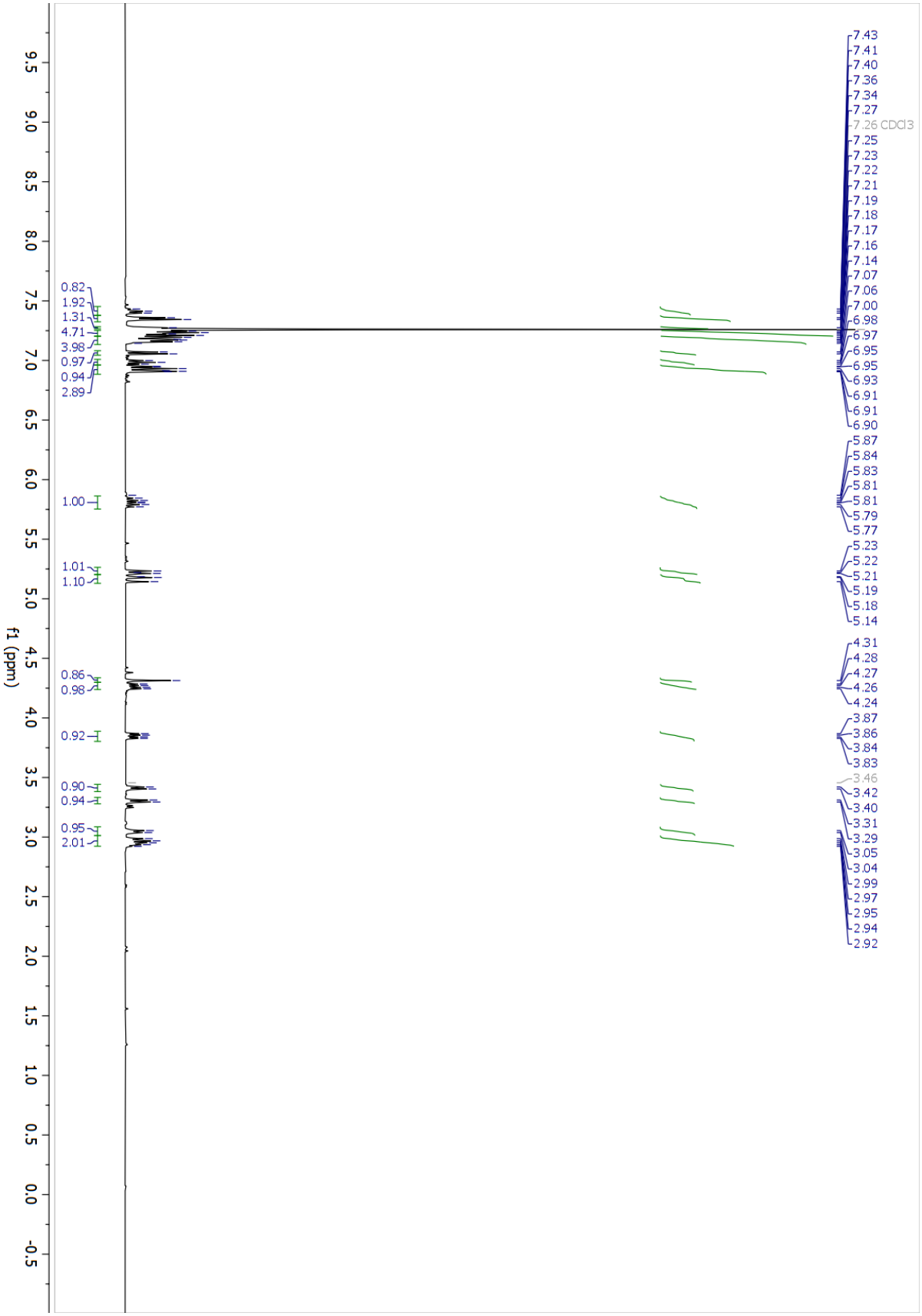
HRMS (ESI): Calculated for $C_{32}H_{29}ClN_2OS$ $[M+H^+]$ =525.1762, found 525.1770

FTIR (neat): 1566, 1454, 1225, 746, 702 cm^{-1}

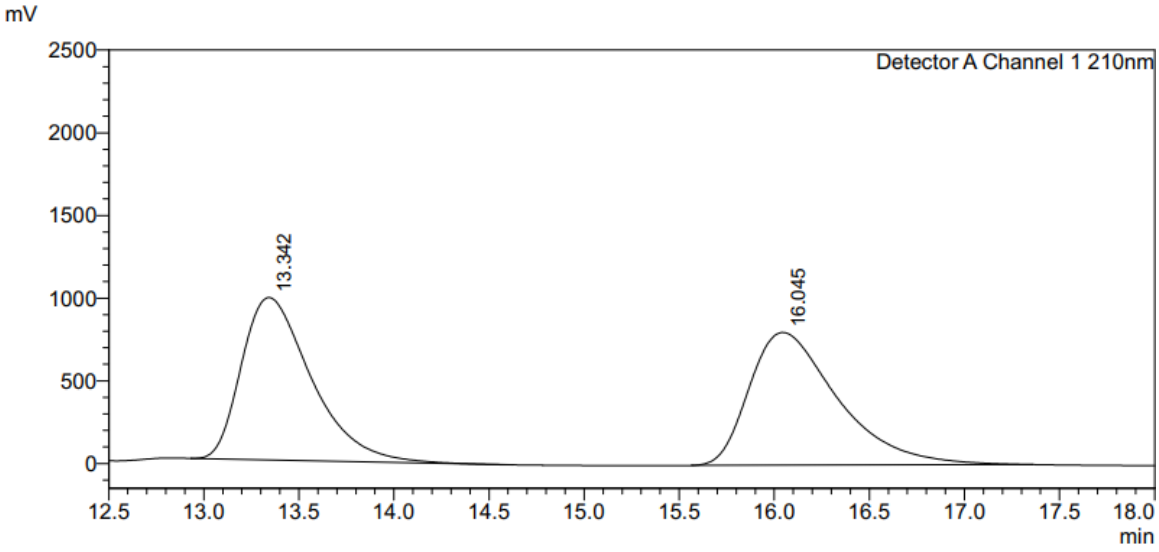
$[\alpha]_D^{28}$= -38.7^0 (c = 0.98, $CHCl_3$)

MP: 79-87 ^{0}C

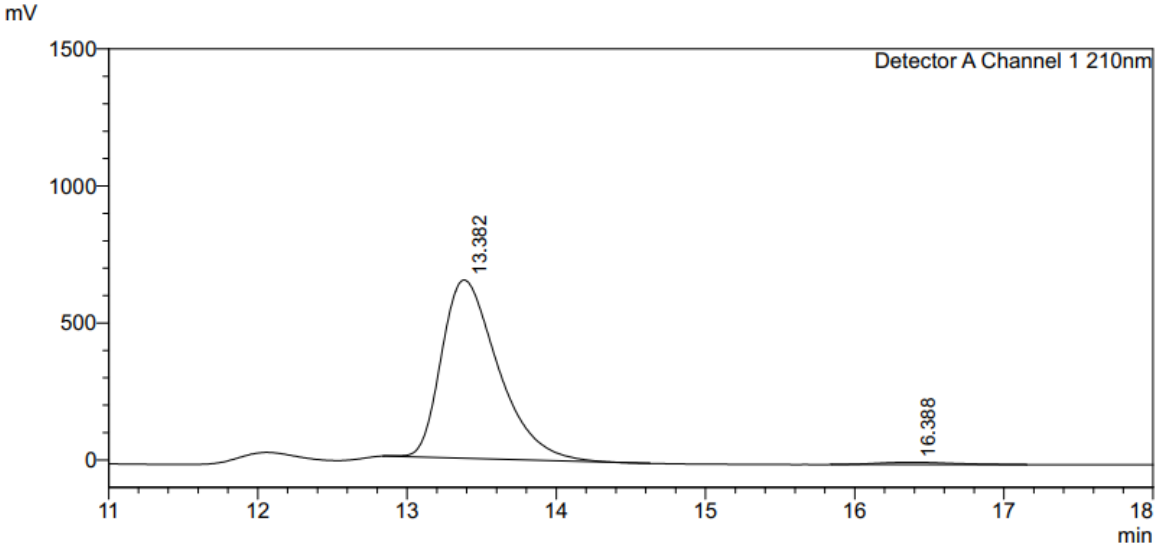
HPLC (Chiralcel column OD-H in series with chiralcel column AD-H, hexane:*i*-PrOH = 90:10, 1 mL/min, 210 nm): *ee*= 97%


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0.82
1.92
1.31
4.71
3.98
0.97
0.94
2.89
1.00
1.01
1.10
0.86
0.98
0.92
0.90
0.94
0.95
2.01
7.43
7.41
7.40
7.36
7.34
7.27
7.26 CDCl3
7.25
7.23
7.22
7.21
7.19
7.18
7.17
7.16
7.14
7.07
7.06
7.00
6.98
6.97
6.95
6.95
6.93
6.91
6.91
6.90
5.87
5.84
5.83
5.81
5.81
5.79
5.77
5.23
5.22
5.21
5.19
5.18
5.14
4.31
4.28
4.27
4.26
4.24
3.87
3.86
3.84
3.83
3.46
3.42
3.40
3.31
3.29
3.05
3.04
2.99
2.97
2.95
2.94
2.92

f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
146.86
144.79
134.68
133.46
128.61
128.54
128.31
127.95
127.55
127.47
127.25
126.00
124.74
123.36
122.76
119.39
116.48
116.32
77.16 CDCl3
71.57
65.52
65.01
64.88
48.01
46.76

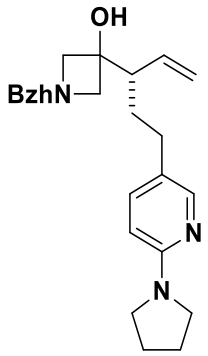


Peak#	Ret. Time	Area	Height	Area%
1	13.342	25141860	982244	49.112
2	16.045	26050896	802658	50.888
Total		51192756	1784902	100.000



Peak#	Ret. Time	Area	Height	Area%
1	13.382	17220052	650510	98.341
2	16.388	290482	8403	1.659
Total		17510533	658914	100.000

(4q) (S)-1-benzhydryl-3-(5-(6-(pyrrolidin-1-yl)pyridin-3-yl)pent-1-en-3-yl)azetidin-3-ol



Procedure

Allyl acetate **2q** (82.3 mg, 0.300 mmol, 150 mol%) was subjected to a modified version of general procedure D using (S)-Ir-SEGPHOS (11.8 mg, 0.01 mmol, 5 mol%, 100 ^{o}C, 48 hr). The title compound was obtained in 65% yield (58.9 mg, 0.130 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, dichloromethane: ethyl acetate = 1:1).

TLC (SiO_2): R_f = 0.10 (dichloromethane: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 7.97 (d, *J* = 2.3 Hz, 1H), 7.38 (dd, *J* = 7.7, 3.5 Hz, 5H), 7.27 (d, *J* = 2.7 Hz, 2H), 7.26 – 7.21 (m, 2H), 7.21 – 7.14 (m, 2H), 6.32 (d, *J* = 8.5 Hz, 1H), 5.71 (dt, *J* = 17.0, 9.7 Hz, 1H), 5.23 (dd, *J* = 10.4, 1.9 Hz, 1H), 5.16 (dd, *J* = 17.3, 1.9 Hz, 1H), 4.36 (s, 1H), 3.45 (m, 4H), 3.19 (t, *J* = 7.0 Hz, 2H), 2.98 (t, *J* = 9.2 Hz, 2H), 2.59 (ddd, *J* = 14.0, 9.0, 4.7 Hz, 1H), 2.35 (dt, *J* = 13.9, 8.4 Hz, 1H), 2.25 (td, *J* = 11.3, 5.5 Hz, 1H), 2.06 – 1.95 (m, 4H), 1.79 (qd, *J* = 10.7, 8.6, 5.9 Hz, 1H), 1.74 – 1.60 (m, 1H).

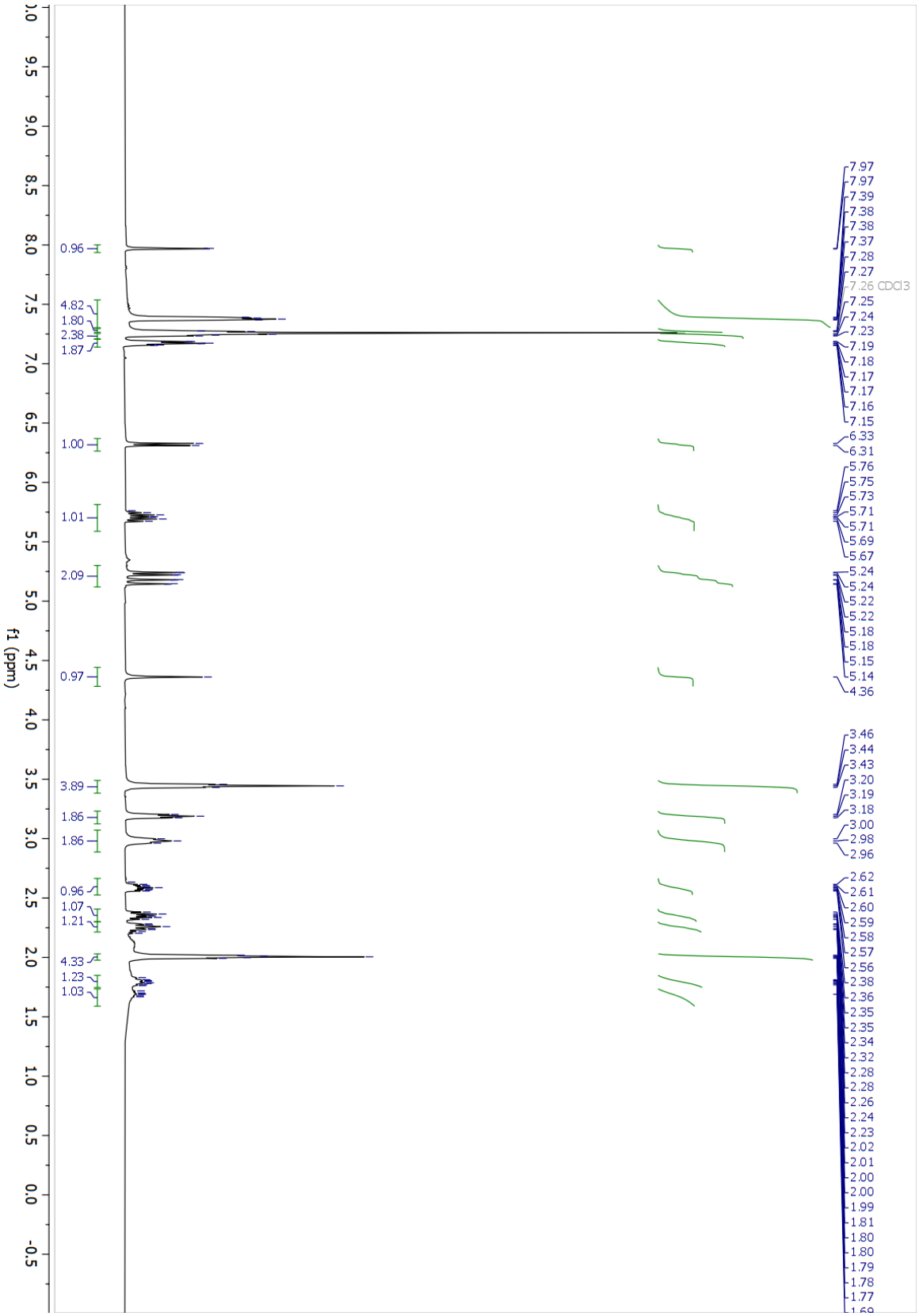
^{13}C NMR (126 MHz, $CDCl_3$): δ156.0, 147.5, 137.2, 136.9, 128.3, 128.3, 127.3, 127.0, 123.9, 118.6, 106.3, 77.7, 72.1, 64.6, 64.5, 50.9, 46.7, 29.6, 29.5, 25.5.

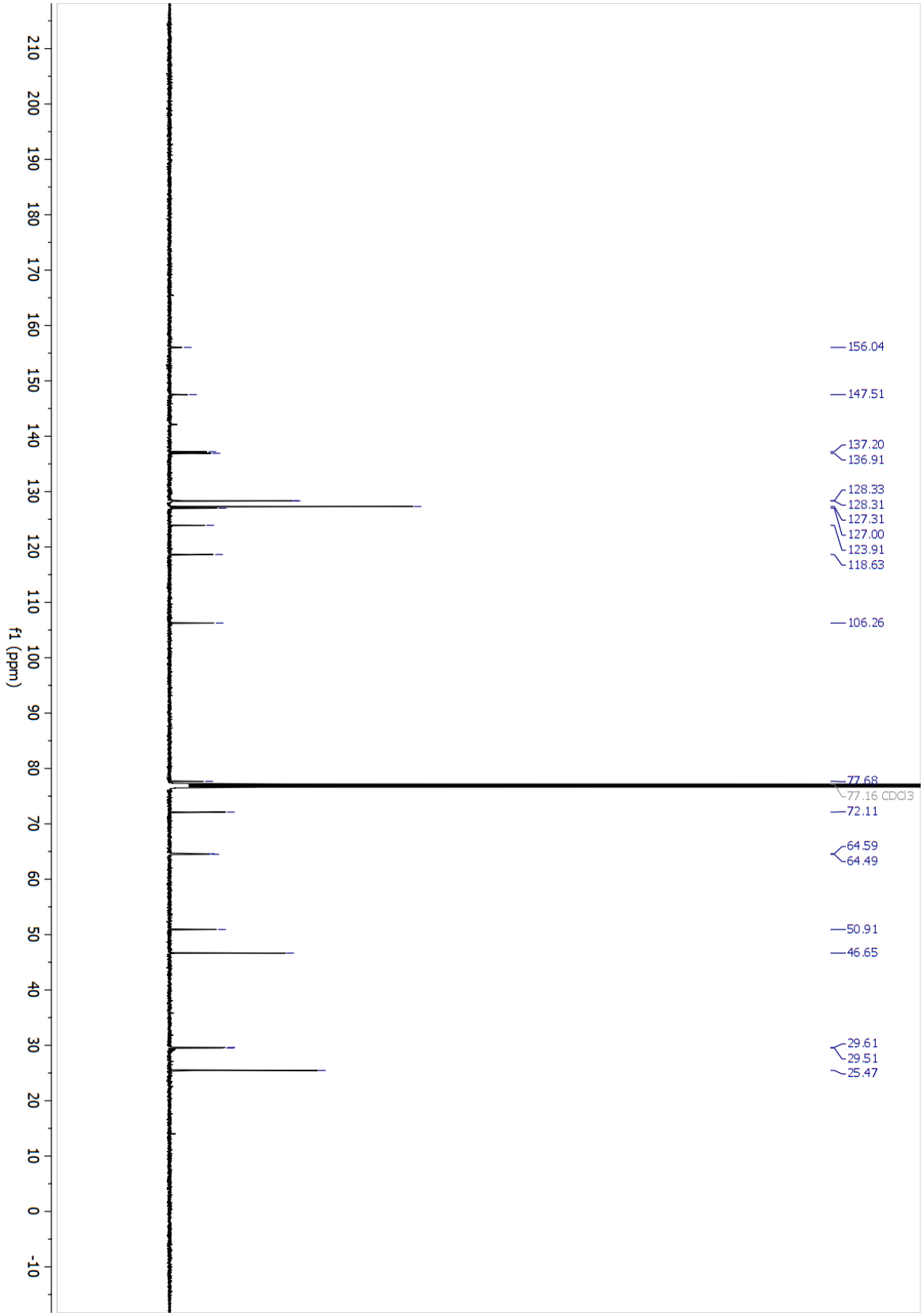
HRMS (ESI): Calculated for $C_{30}H_{35}N_3O$ $[M+H^+]$ =454.2853, found 454.2856

FTIR (neat): 2939, 1611, 1507, 1416, 810, 702 cm^{-1}

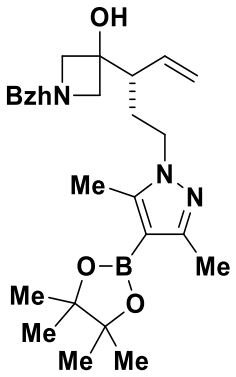
$[\alpha]_D^{28}$ = -5.71^0 (c = 0.35, $CHCl_3$)

Enantiomeric excess determined by derivative **6q**.


f1 (ppm)
0.96
4.82
1.80
2.38
1.87
1.00
1.01
2.09
0.97
3.89
1.86
1.86
0.96
1.07
1.21
4.33
1.23
1.03
7.97
7.97
7.39
7.38
7.38
7.37
7.28
7.27
7.26 CDCl3
7.25
7.24
7.23
7.19
7.18
7.17
7.17
7.16
7.15
6.33
6.31
5.76
5.75
5.73
5.71
5.71
5.69
5.67
5.24
5.24
5.22
5.22
5.18
5.18
5.15
5.14
4.36
3.46
3.44
3.43
3.20
3.19
3.18
3.00
2.98
2.96
2.62
2.61
2.60
2.59
2.58
2.57
2.56
2.38
2.36
2.35
2.35
2.34
2.32
2.28
2.28
2.26
2.24
2.23
2.02
2.01
2.00
2.00
1.99
1.81
1.80
1.80
1.79
1.78
1.77


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
156.04
147.51
137.20
136.91
128.33
128.31
127.31
127.00
123.91
118.63
106.26
77.68
77.16 CDCl3
72.11
64.59
64.49
50.91
46.65
29.61
29.51
25.47

(4r) (S)-1-benzhydryl-3-(5-(3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)pent-1-en-3-yl)azetidin-3-ol



Procedure

Allyl acetate **2r** (104.5 mg, 0.300 mmol, 150 mol%) was subjected to a modified version of general procedure C using (S)-Ir-SEGPHOS (11.8 mg, 0.01 mmol, 5 mol%, 100 ^{o}C, 48 hr).The title compound was obtained in 77% yield (84 mg, 0.154 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, dichloromethane: ethyl acetate = 1:1).

TLC (SiO_2) R_f = 0.20 (dichloromethane: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 7.42 – 7.34 (m, 4H), 7.27 (s, 1H), 7.24 (d, *J* = 7.3 Hz, 3H), 7.22 – 7.13 (m, 2H), 5.80 (dt, *J* = 17.0, 9.5 Hz, 1H), 5.23 (dd, *J* = 10.3, 1.8 Hz, 1H), 5.17 (dd, *J* = 17.2, 1.9 Hz, 1H), 4.35 (s, 1H), 3.99 (ddd, *J* = 13.6, 8.5, 4.9 Hz, 1H), 3.88 (dt, *J* = 13.7, 7.9 Hz, 1H), 3.23 (t, *J* = 8.0 Hz, 2H), 2.93 (dd, *J* = 8.4, 4.2 Hz, 2H), 2.62 (s, 1H), 2.35 (s, 3H), 2.33 (s, 3H), 2.32 – 2.26 (m, 1H), 2.23 – 2.11 (m, 1H), 1.81 (tdd, *J* = 13.4, 9.2, 4.8 Hz, 1H), 1.29 (s, 12H).

^{13}C NMR (126 MHz, $CDCl_3$): δ:154.7, 147.0, 136.9, 128.5, 127.6, 127.5, 127.2, 127.2, 118.7, 82.6, 78.0, 72.1, 64.9, 64.5, 49.2, 46.5, 28.7, 25.1, 14.1, 11.3.

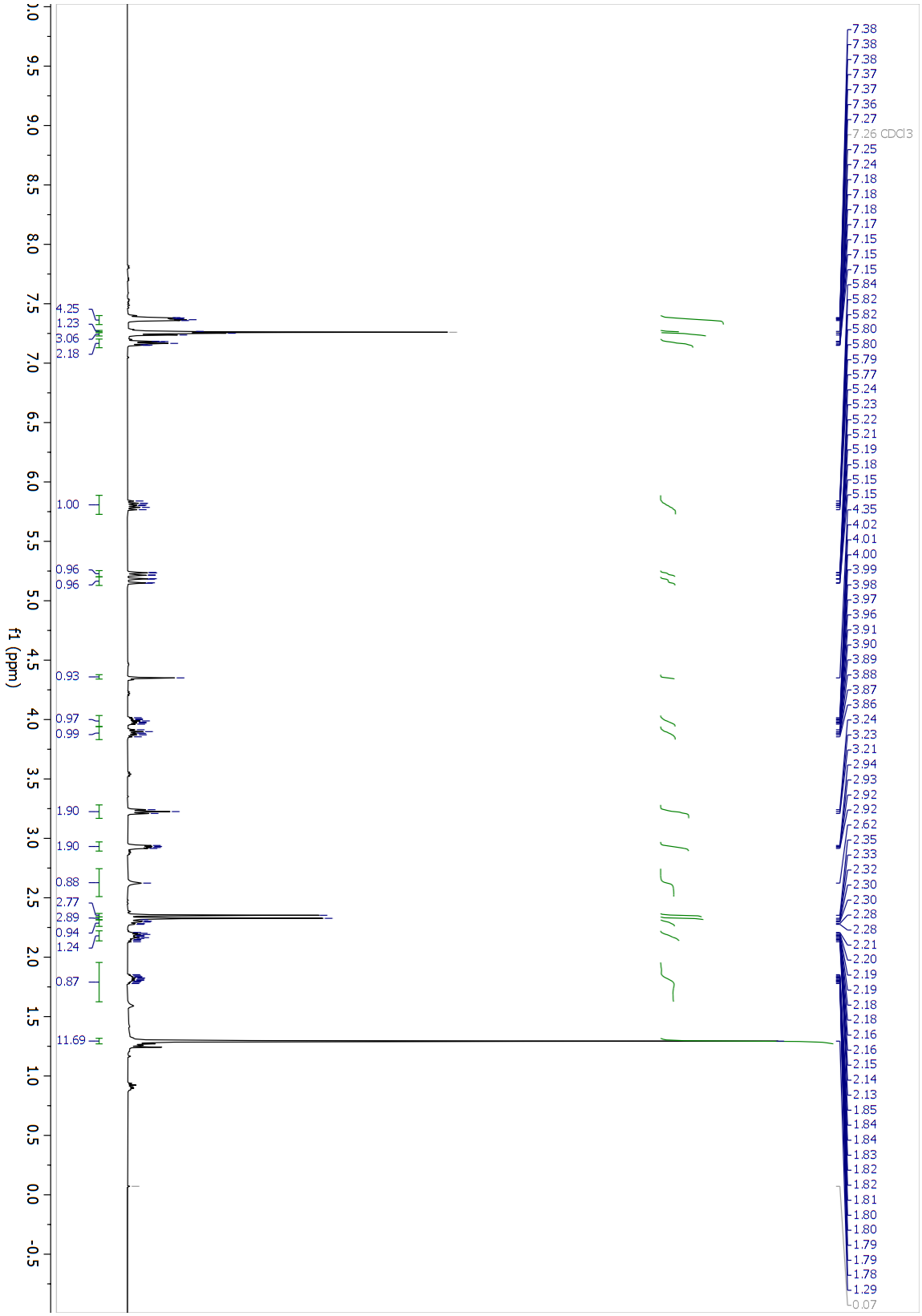
HRMS (ESI): Calculated for $C_{32}H_{42}BN_3O_3$ $[M+H^+]$ =527.3428, found 527.3434

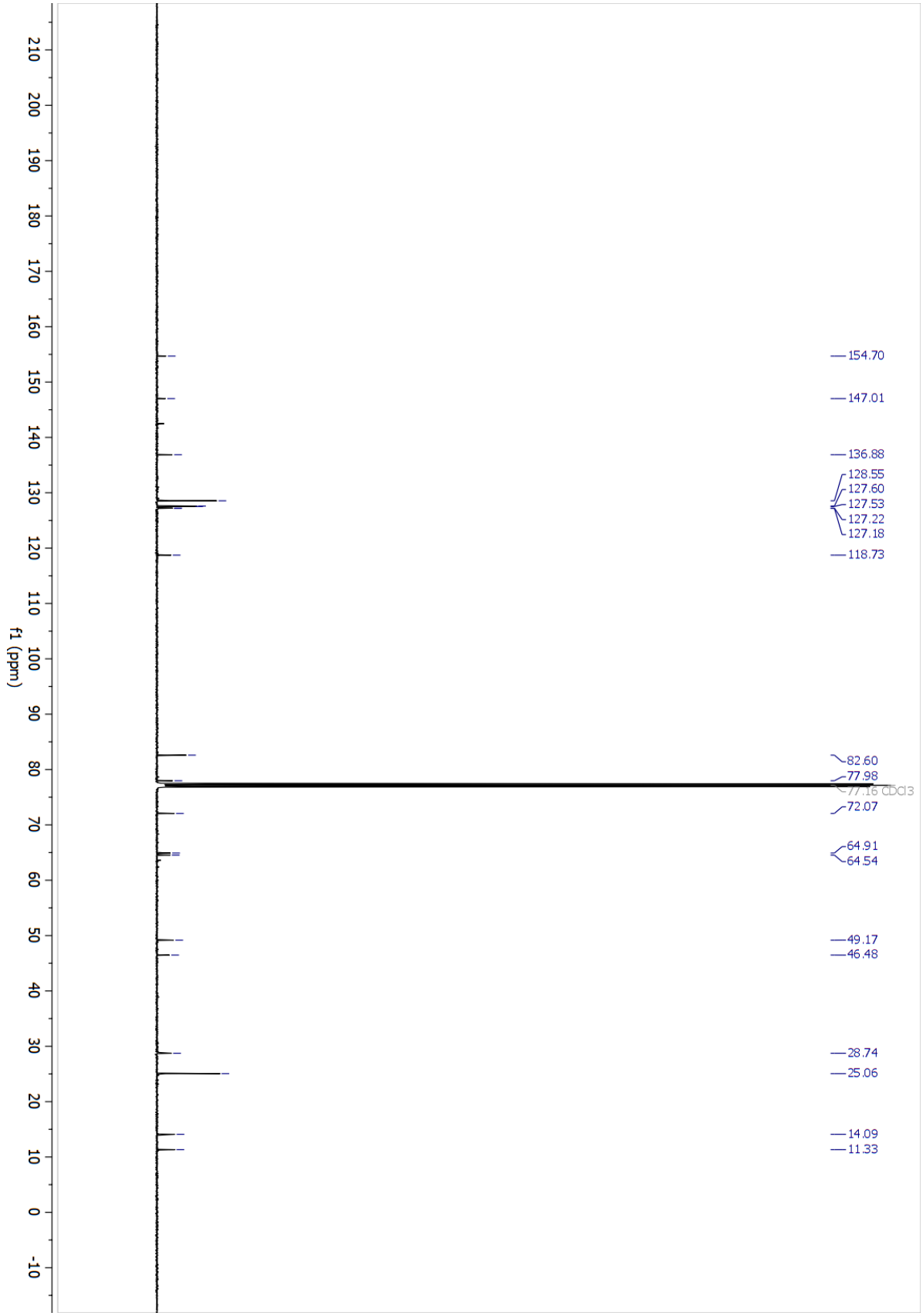
FTIR (neat): 2977, 2928, 1545, 1145, 1077, 745, 703 cm^{-1}

$[\alpha]_D^{28}$ = -4.28^0 (c = 0.70, $CHCl_3$)

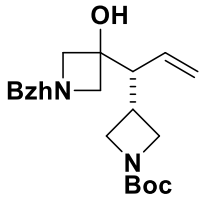
MP: 70-75 ^{0}C

Enantiomeric excess determined by derivative **5r**.


f1 (ppm)
4.25
1.23
3.06
2.18
1.00
0.96
0.96
0.93
0.97
0.99
1.90
1.90
0.88
2.77
2.89
0.94
1.24
0.87
11.69
7.38
7.26 CDCl3
7.25
7.24
5.84
5.82
5.80
5.79
5.77
5.24
5.23
5.22
5.21
5.19
5.18
5.15
4.35
4.02
4.01
4.00
3.99
3.98
3.97
3.96
3.91
3.90
3.89
3.88
3.87
3.86
3.24
3.23
3.21
2.94
2.93
2.92
2.62
2.35
2.33
2.32
2.30
2.28
2.21
2.20
2.19
2.18
2.16
2.15
2.14
2.13
1.85
1.84
1.83
1.82
1.81
1.80
1.79
1.78
1.29
0.07


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
154.70
147.01
136.88
128.55
127.60
127.53
127.22
127.18
118.73
82.60
77.98
77.16 CDCl3
72.07
64.91
64.54
49.17
46.48
28.74
25.06
14.09
11.33

(4s) tert-butyl (R)-3-(1-(1-benzhydryl-3-hydroxyazetidin-3-yl)allyl)azetidine-1-carboxylate



Procedure

Allyl acetate **2s** (76.6 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 36 hr). The title compound was obtained in 72% yield (62.6 mg, 0.144 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

TLC (SiO_2): R_f = 0.44 (hexanes: ethyl acetate = 2:1).

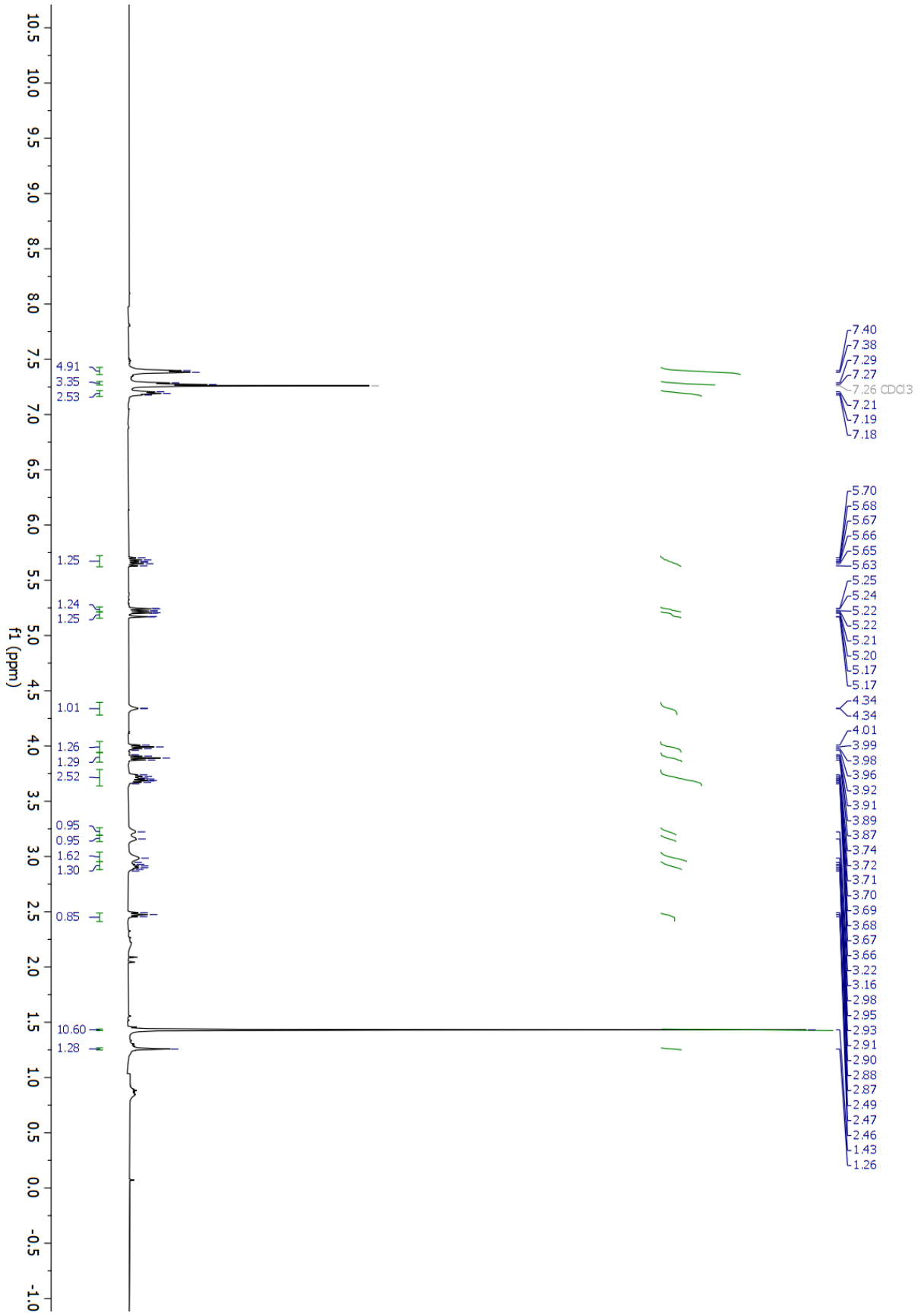
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, J = 7.6 Hz, 5H), 7.28 (d, J = 7.6 Hz, 3H), 7.19 (t, J = 7.4 Hz, 2H), 5.67 (dt, J = 17.1, 9.8 Hz, 1H), 5.23 (dd, J = 10.4, 1.8 Hz, 1H), 5.19 (dd, J = 17.2, 1.8 Hz, 1H), 4.36 – 4.32 (m, 1H), 3.99 (t, J = 8.4 Hz, 1H), 3.89 (t, J = 8.7 Hz, 1H), 3.76 – 3.64 (m, 2H), 3.22 (s, 1H), 3.16 (s, 1H), 2.98 (s, 2H), 2.90 (p, J = 7.8 Hz, 1H), 2.47 (t, J = 9.1 Hz, 1H), 1.43 (s, 9H), 1.26 (s, 1H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 156.5, 134.0, 130.0, 128.7, 128.4, 127.5, 119.9, 79.4, 78.1, 72.2, 65.2, 54.7, 29.9, 28.6, 28.5.

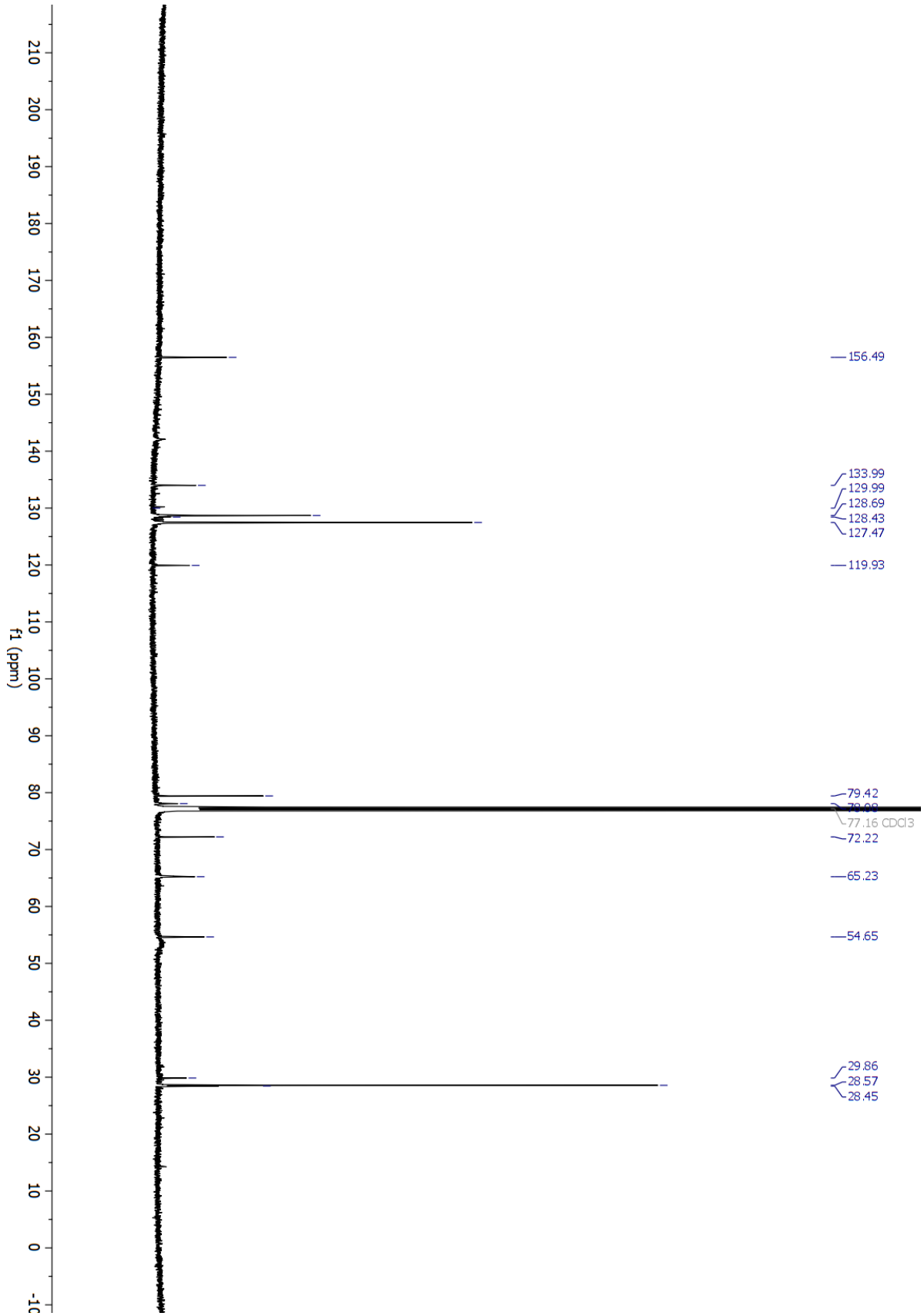
HRMS (ESI): Calculated for $C_{27}H_{34}N_2O_3$ [M+Na^+]= 435.2642 , found= 435.2649

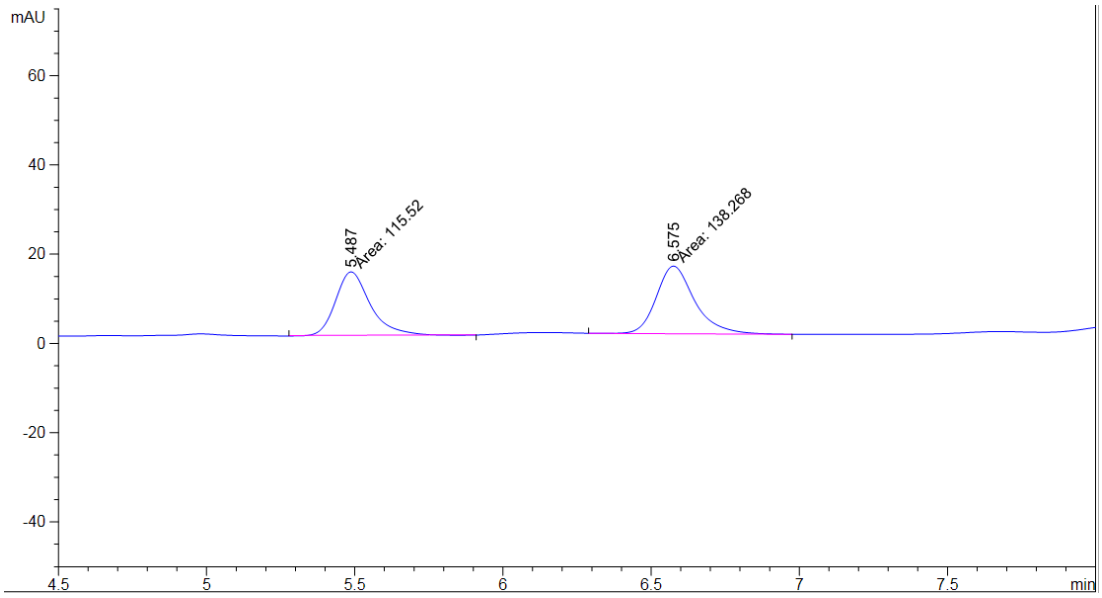
FTIR (neat): 3307, 3010, 2962, 2851, 1654, 1477, 1450, 1420, 1365, 1203, 1136, 984, 923cm^{-1}

$[\alpha]_D^{28}$= -35.0 (*c* 0.10, $CHCl_3$)

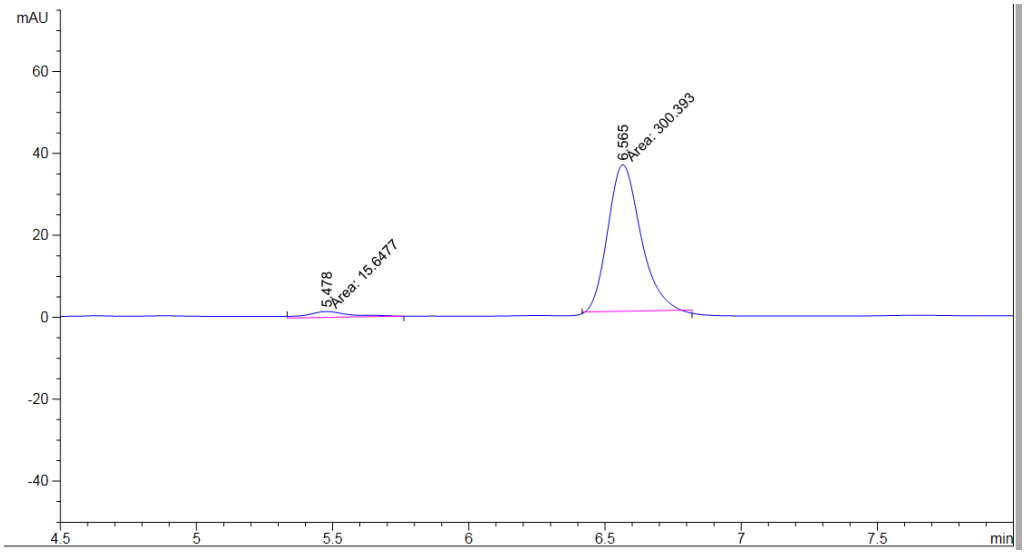
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 230 nm): *ee* = 90%


f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
4.91
3.35
2.53
1.25
1.24
1.25
1.01
1.26
1.29
2.52
0.95
0.95
1.62
1.30
0.85
10.60
1.28
7.40
7.38
7.29
7.27
7.26 CDCl3
7.21
7.19
7.18
5.70
5.68
5.67
5.66
5.65
5.63
5.25
5.24
5.22
5.22
5.21
5.20
5.17
5.17
4.34
4.34
4.01
3.99
3.98
3.96
3.92
3.91
3.89
3.87
3.74
3.72
3.71
3.70
3.69
3.68
3.67
3.66
3.22
3.16
2.98
2.95
2.93
2.91
2.90
2.88
2.87
2.49
2.47
2.46
1.43
1.26


156.49
133.99
129.99
128.69
128.43
127.47
119.93
79.42
77.16 CDCl3
72.22
65.23
54.65
29.86
28.57
28.45
f1 (ppm)

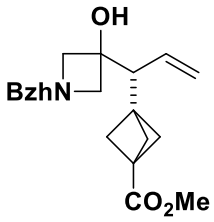


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.487	MM	0.1351	115.51977	14.25017	45.5183
2	6.575	MM	0.1514	138.26750	15.21686	54.4817



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.478	MM	0.1790	15.64768	1.45721	4.9512
2	6.565	MM	0.1396	300.39255	35.87188	95.0488

(4t) methyl (R)-3-(1-(1-benzhydryl-3-hydroxyazetidin-3-yl)allyl)bicyclo[1.1.1]pentane-1-carboxylate



Procedure

Allyl acetate **2t** (67.3mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 ^{o}C, 36 hr). The title compound was obtained in 71% yield (57.2mg, 0.142 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2): R_f = 0.21 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.35 (m, 4H), 7.28 (d, J = 1.3 Hz, 3H), 7.25 (s, 1H), 7.22 – 7.14 (m, 3H), 5.70 (dt, J = 17.1, 9.9 Hz, 1H), 5.15 (dd, J = 10.3, 1.9 Hz, 1H), 5.10 (dd, J = 17.1, 1.9 Hz, 1H), 4.38 (s, 1H), 3.64 (s, 3H), 3.24 (dd, J = 27.0, 8.5 Hz, 1H), 3.02 (dd, J = 36.6, 8.5 Hz, 1H), 2.46 (d, J = 9.5 Hz, 1H), 2.00 (s, 6H).

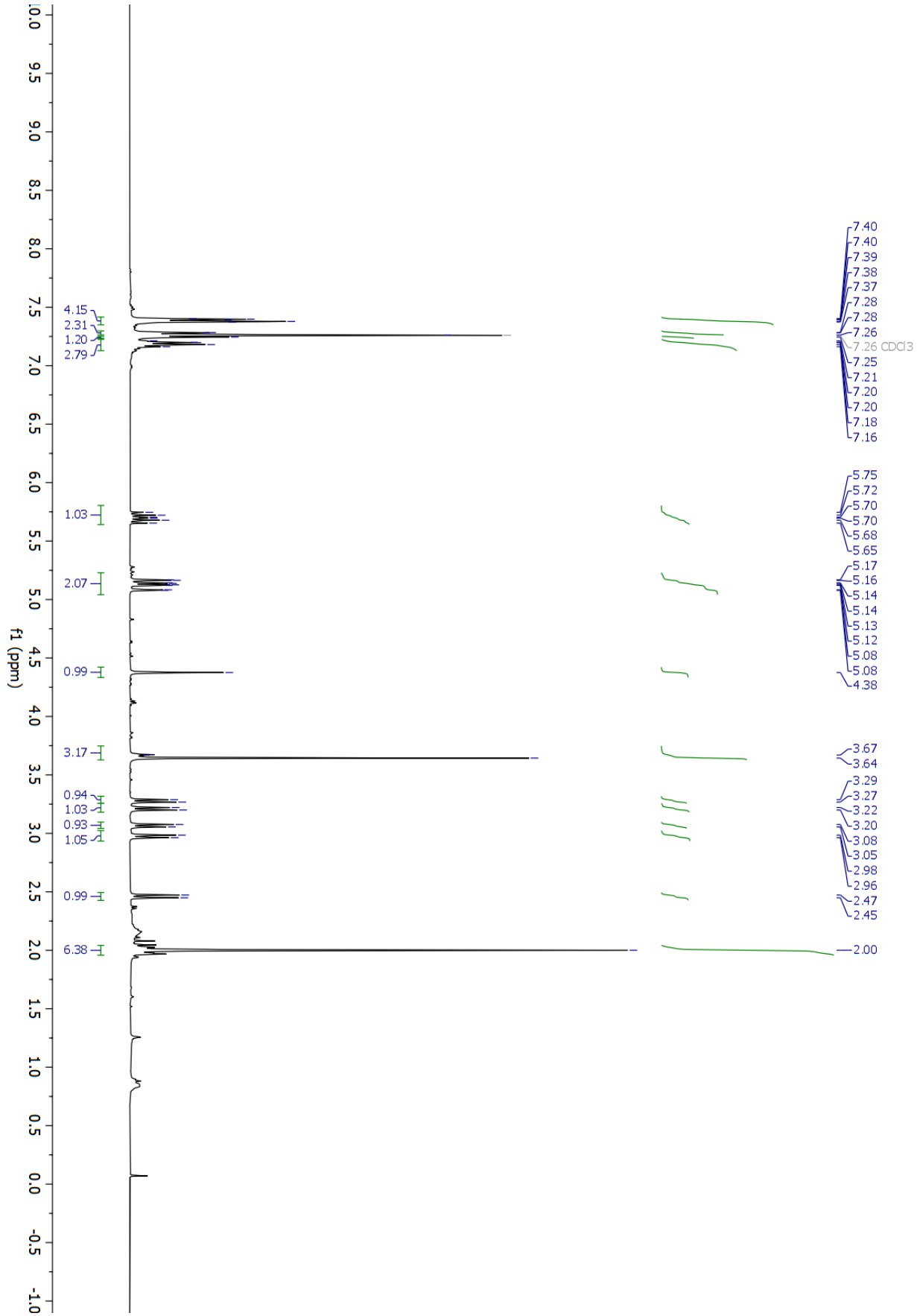
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 142.2, 134.2, 128.6, 127.5, 127.3, 118.7, 78.1, 77.4, 72.7, 65.8, 52.3, 52.2, 51.7, 39.9, 39.1

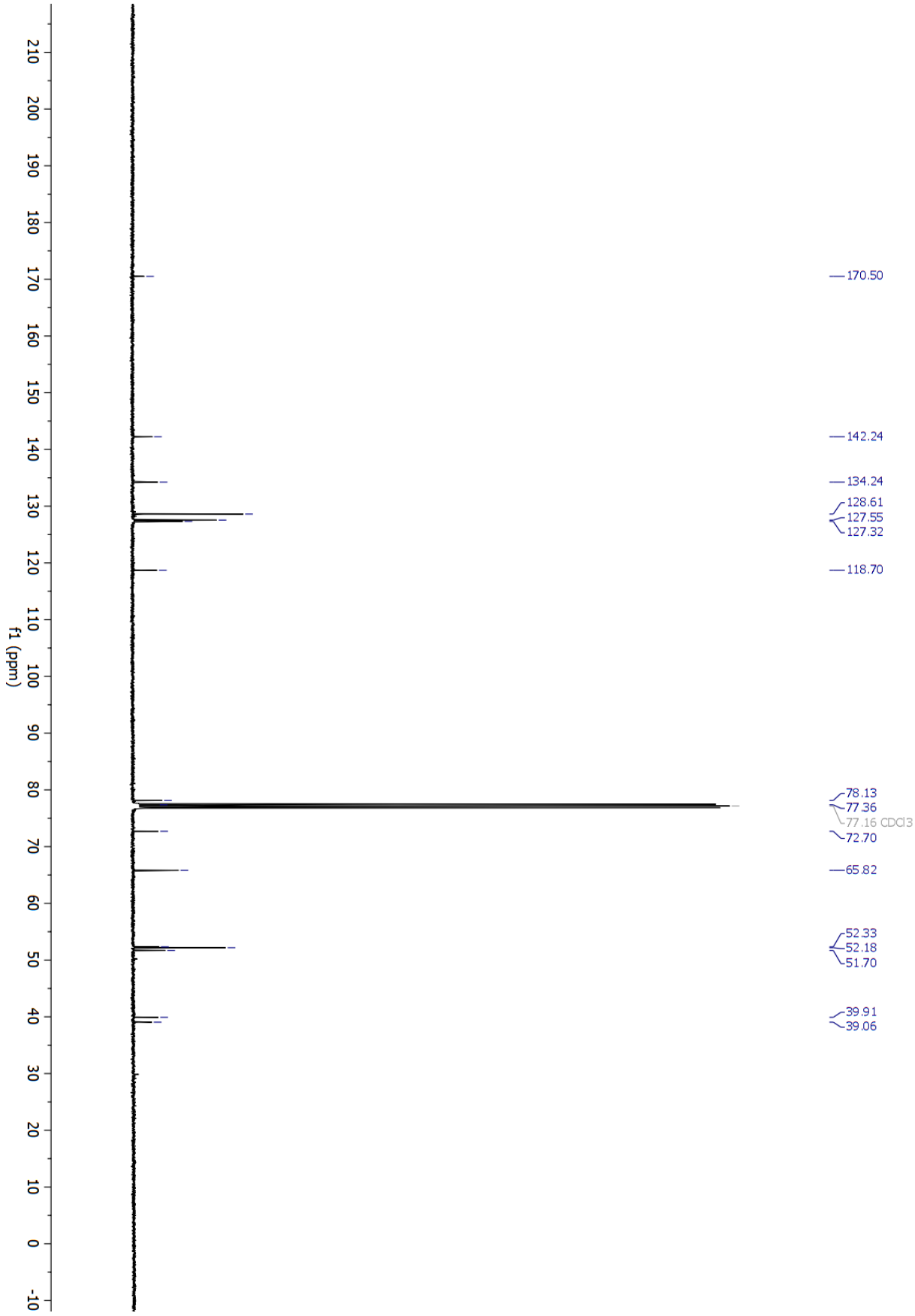
HRMS (ESI): Calculated for $C_{26}H_{29}NO_3$ $[M+H^+]$= 404.2220, found= 404.2228

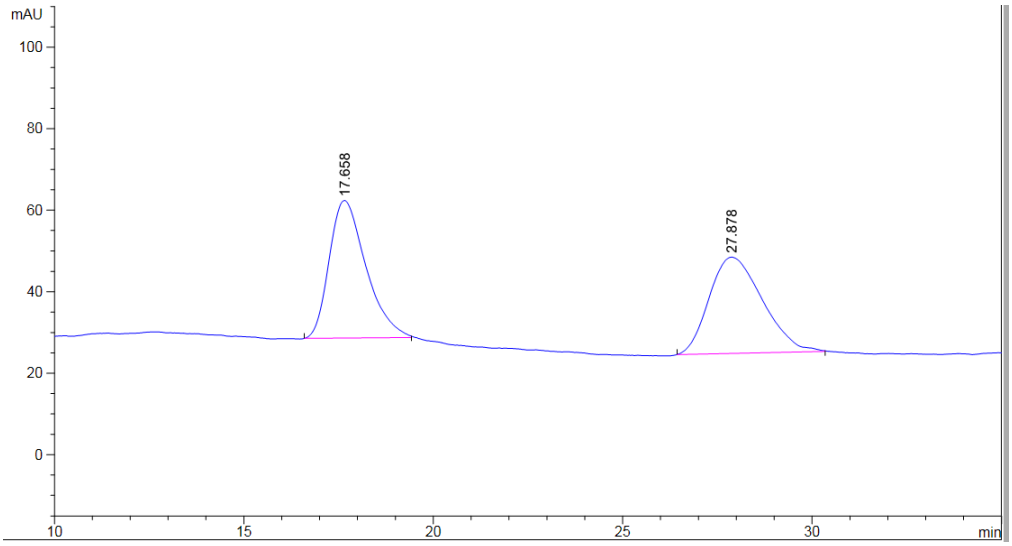
FTIR (neat): 3420, 3012, 2916, 2886, 1654, 1606, 1525, 1312, 1221, 1137, 1120, 1080, 656 cm^{-1}

$[\alpha]_D^{28}$= -22.3 (*c* 0.10, $CHCl_3$)

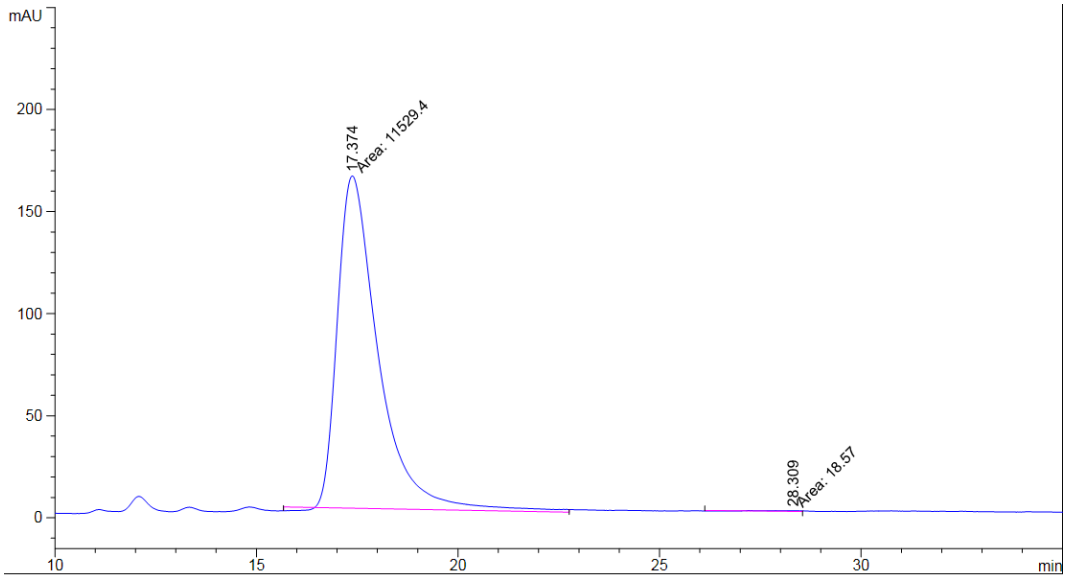
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm): *ee* = 99%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
4.15
2.31
1.20
2.79
1.03
2.07
0.99
3.17
0.94
1.03
0.93
1.05
0.99
6.38
7.40
7.40
7.39
7.38
7.37
7.28
7.28
7.26
7.26 CDCl3
7.25
7.21
7.20
7.20
7.18
7.16
5.75
5.72
5.70
5.70
5.68
5.65
5.17
5.16
5.14
5.14
5.13
5.12
5.08
5.08
4.38
3.67
3.64
3.29
3.27
3.22
3.20
3.08
3.05
2.98
2.96
2.47
2.45
2.00


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
170.50
142.24
134.24
128.61
127.55
127.32
118.70
78.13
77.36
77.16 CDCl3
72.70
65.82
52.33
52.18
51.70
39.91
39.06

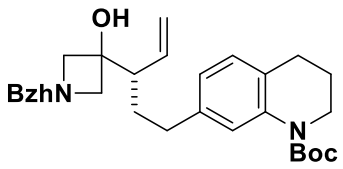


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.658	BB	0.8892	2280.67603	33.80150	49.6953
2	27.878	BB	1.1527	2308.64355	23.65434	50.3047



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.374	MM	1.1801	1.15294e4	162.82782	99.8392
2	28.309	MM	0.8875	18.56996	3.48729e-1	0.1608

(4u) tert-butyl (S)-6-(3-(1-benzhydryl-3-hydroxyazetidin-3-yl)pent-4-en-1-yl)-3,4-dihydroquinoline-1(2H)-carboxylate



Procedure

Allyl acetate **2u** (107.8 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 °C, 36 hr). The title compound was obtained in 67% yield (72.2 mg, 0.134 mmol) as a pale-yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–1:1).

TLC (SiO_2): R_f = 0.30 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, J = 8.4 Hz, 1H), 7.38 (dd, J = 7.5, 2.5 Hz, 4H), 7.24 (dd, J = 5.2, 2.6 Hz, 4H), 7.17 (dd, J = 7.2, 1.6 Hz, 2H), 6.92 (dd, J = 8.5, 2.1 Hz, 1H), 6.85 (d, J = 2.1 Hz, 1H), 5.71 (dt, J = 17.0, 9.7 Hz, 1H), 5.35 – 5.06 (m, 2H), 4.39 (s, 1H), 4.11 (q, J = 7.1 Hz, 1H), 3.68 (td, J = 5.6, 1.6 Hz, 2H), 3.22 (d, J = 8.4 Hz, 2H), 3.08 – 2.94 (m, 2H), 2.70 (t, J = 6.6 Hz, 2H), 2.63 (ddd, J = 14.4, 10.0, 4.7 Hz, 1H), 2.39 (ddd, J = 13.9, 9.8, 7.2 Hz, 1H), 2.30 – 2.22 (m, 1H), 2.03 (s, 1H), 1.94 – 1.82 (m, 2H), 1.82 (dt, J = 9.7, 3.0 Hz, 1H), 1.67 (dtd, J = 18.5, 9.4, 8.5, 4.2 Hz, 1H), 1.51 (s, 9H).

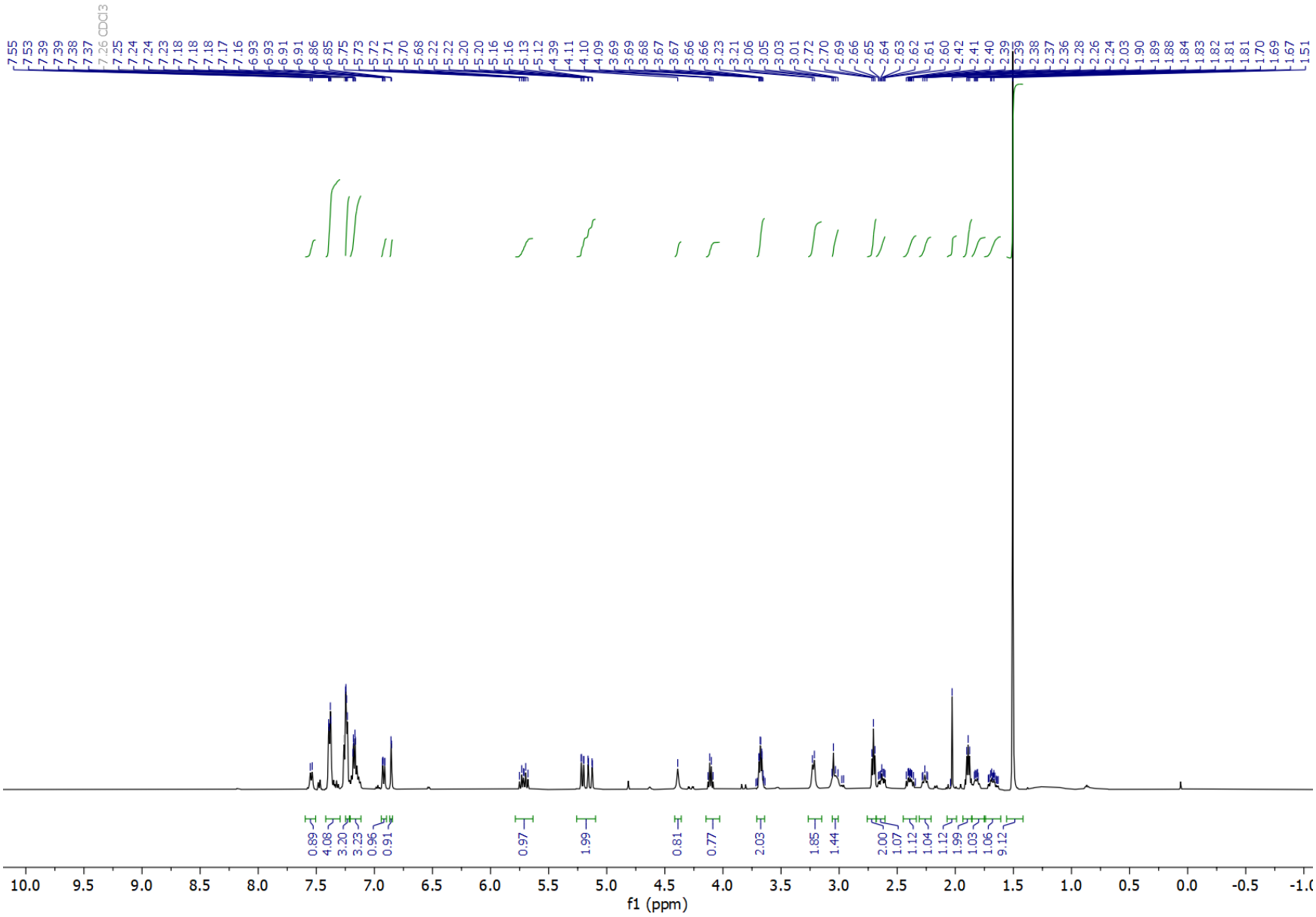
^{13}C NMR (126 MHz, $CDCl_3$): δ 154.4, 137.4, 136.8, 130.0, 128.9, 128.7, 127.8, 127.6, 126.2, 124.4, 118.9, 78.1, 72.6, 65.2, 65.1, 60.8, 51.9, 45.0, 33.3, 30.1, 30.0, 28.8, 27.9, 24.0.

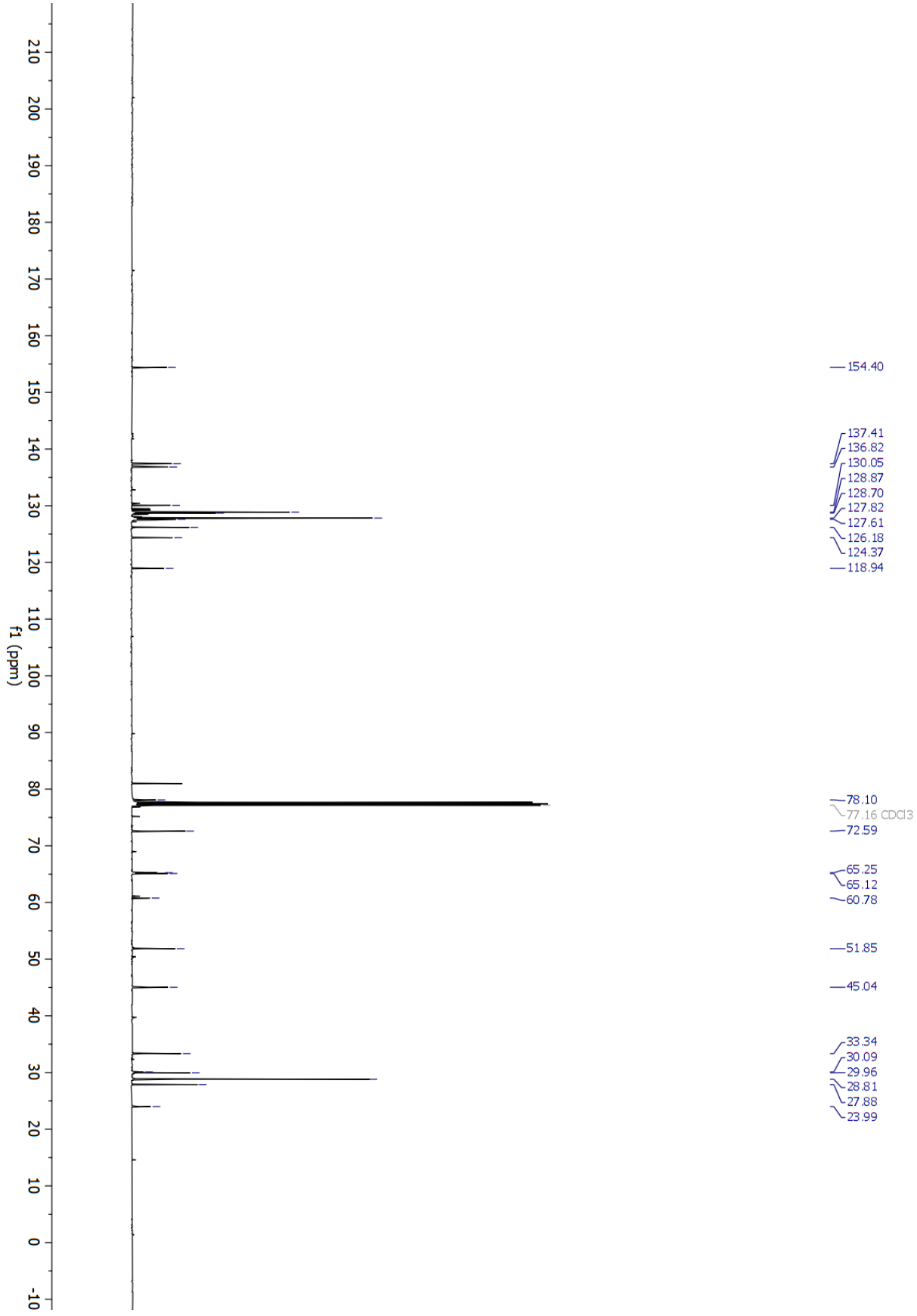
HRMS (ESI): Calculated for $C_{35}H_{42}N_2O_3$ $[M+H^+]$= 539.3268, found= 539.3257

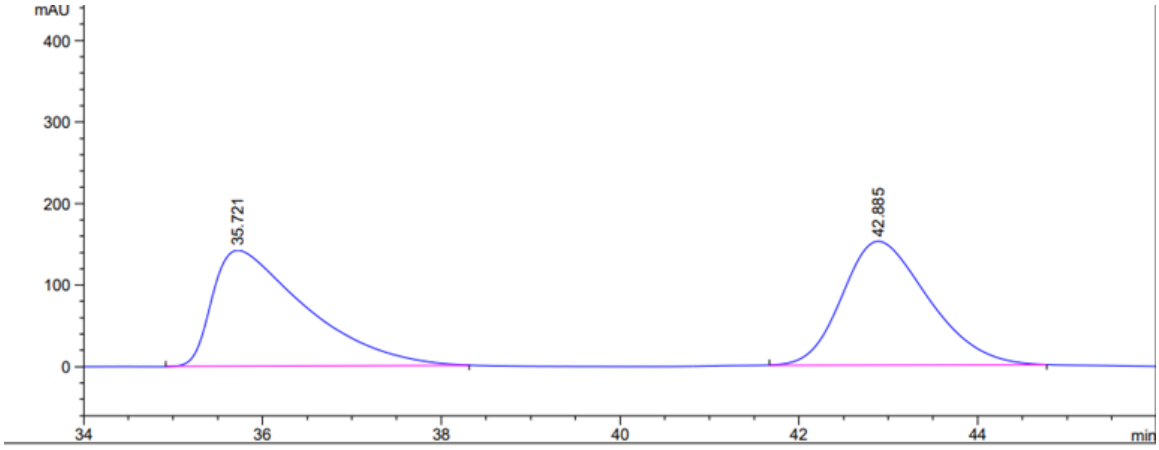
FTIR (neat): 3456, 3024, 2970, 2939, 1654, 1499, 1451, 1366, 1228, 1216, 1160, 1136, 1074, 702 cm^{-1}

$[\alpha]_D^{28}$= -85.0 (*c* 0.10, $CHCl_3$)

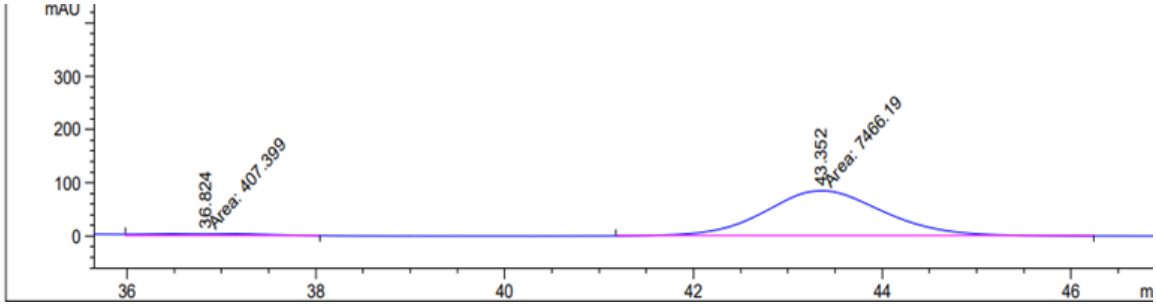
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 230 nm): *ee* = 90%


7.55 7.53 7.39 7.39 7.38 7.37 7.26 CDCl3 7.25 7.24 7.24 7.23 7.18 7.18 7.18 7.17 7.16 6.93 6.93 6.91 6.91 6.86 6.85 5.75 5.73 5.72 5.71 5.70 5.68 5.22 5.22 5.20 5.20 5.16 5.16 5.13 5.12 4.39 4.11 4.10 4.09 3.69 3.69 3.68 3.67 3.67 3.66 3.66 3.23 3.21 3.06 3.05 3.03 3.01 2.72 2.70 2.69 2.66 2.65 2.64 2.63 2.62 2.61 2.60 2.42 2.41 2.40 2.39 2.39 2.38 2.37 2.36 2.28 2.26 2.24 2.03 1.90 1.89 1.88 1.84 1.83 1.82 1.81 1.81 1.70 1.69 1.67 1.51
0.89 4.08 3.20 3.23 0.96 0.91 0.97 1.99 0.81 0.77 2.03 1.85 1.44 2.00 1.07 1.12 1.04 1.12 1.99 1.03 1.06 9.12
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
154.40
137.41
136.82
130.05
128.87
128.70
127.82
127.61
126.18
124.37
118.94
78.10
77.16 CDCl3
72.59
65.25
65.12
60.78
51.85
45.04
33.34
30.09
29.96
28.81
27.88
23.99

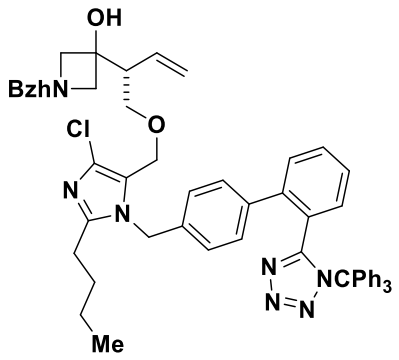


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.721	BB	1.0024	1.03449e4	142.25600	50.2116
2	42.885	BB	1.0031	1.02577e4	152.04002	49.7884



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.824	MF	1.4279	407.39920	4.75518	5.1742
2	43.352	MM	1.4685	7466.19434	84.73927	94.8258

(4v) (R)-1-benzhydryl-3-(1-((2-butyl-4-chloro-1-((2'-(1-trityl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1H-imidazol-5-yl)methoxy)but-3-en-2-yl)azetidin-3-ol



Procedure

Allyl acetate **2v** (233.1 mg, 0.300 mmol, 150 mol%) was subjected to modified version of general procedure C using 7.5 mol% (S)-Ir-tol-BINAP (100 °C, 48hr). The title compound was obtained in 68% yield (129.9 mg, 0.136 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1–1:1).

TLC (SiO_2): Rf = 0.25 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.85 (m, 1H), 7.41 (qt, J = 7.5, 3.7 Hz, 2H), 7.29 – 7.13 (m, 11H), 7.07 (dd, J = 27.5, 7.6 Hz, 3H), 6.93 – 6.76 (m, 7H), 6.62 (d, J = 7.8 Hz, 2H), 5.79 (ddd, J = 17.1, 10.4, 8.5 Hz, 1H), 5.17 – 5.02 (m, 2H), 4.91 (s, 2H), 4.32 (s, 1H), 4.07 (s, 2H), 3.20 (t, J = 7.4 Hz, 2H), 2.92 (dd, J = 11.8, 8.2 Hz, 2H), 2.55 (dt, J = 9.8, 5.3 Hz, 1H), 2.41 (t, J = 7.8 Hz, 2H), 1.57 (p, J = 7.7 Hz, 2H), 1.21 (q, J = 6.2 Hz, 2H), 0.86 – 0.66 (m, 3H).

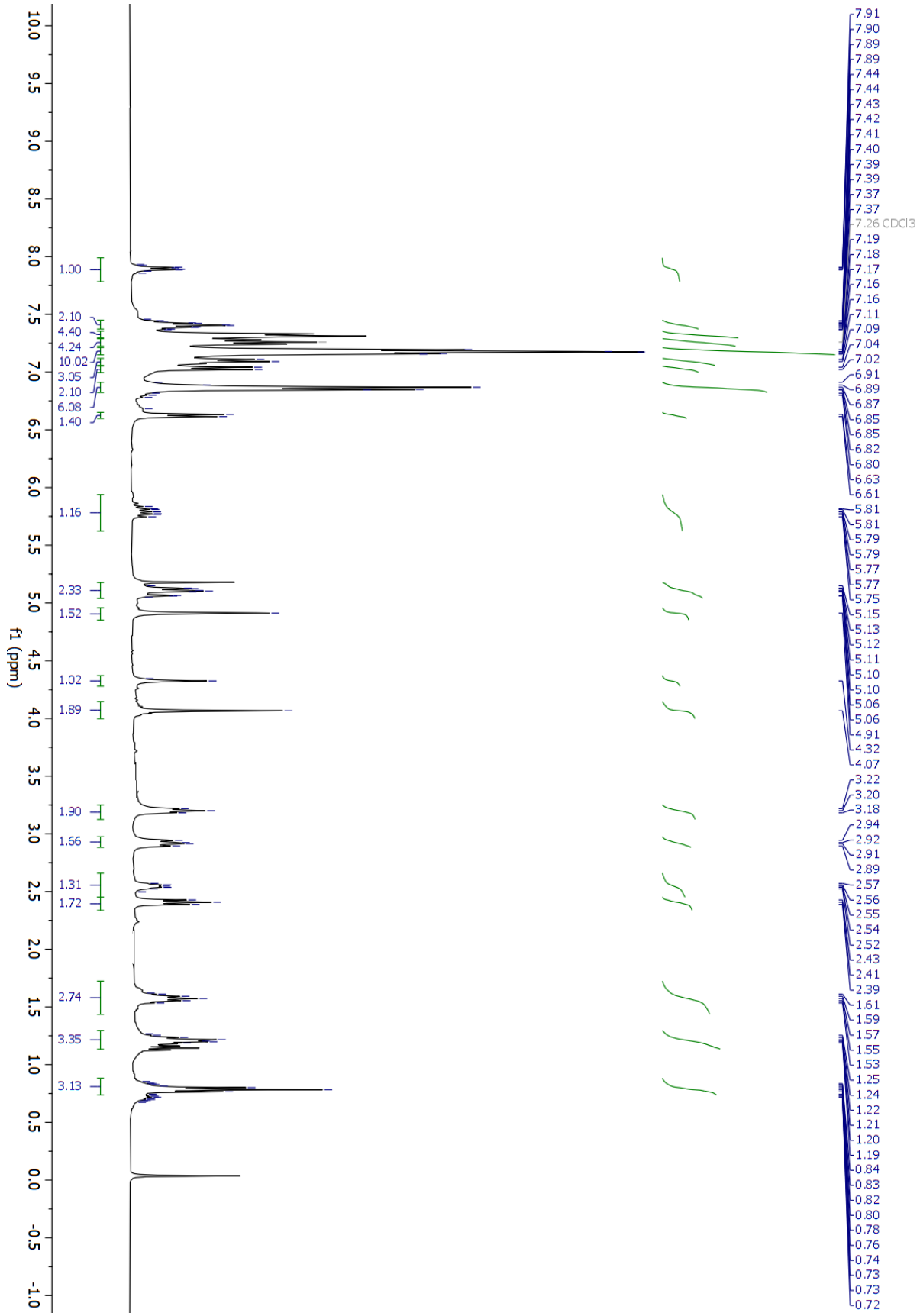
^{13}C NMR (101 MHz, $CDCl_3$): δ 163.9, 148.9, 142.2, 141.3, 141.0, 134.7, 134.3, 130.8, 130.2, 129.9, 129.92, 129.5, 128.4, 128.4, 128.4, 127.7, 127.4, 127.1, 126.2, 125.1, 121.4, 118.4, 82.9, 77.8, 71.7, 70.0, 65.9, 65.1, 64.2, 61.0, 53.5, 50.1, 47.0, 29.7, 26.7, 22.4, 15.3.

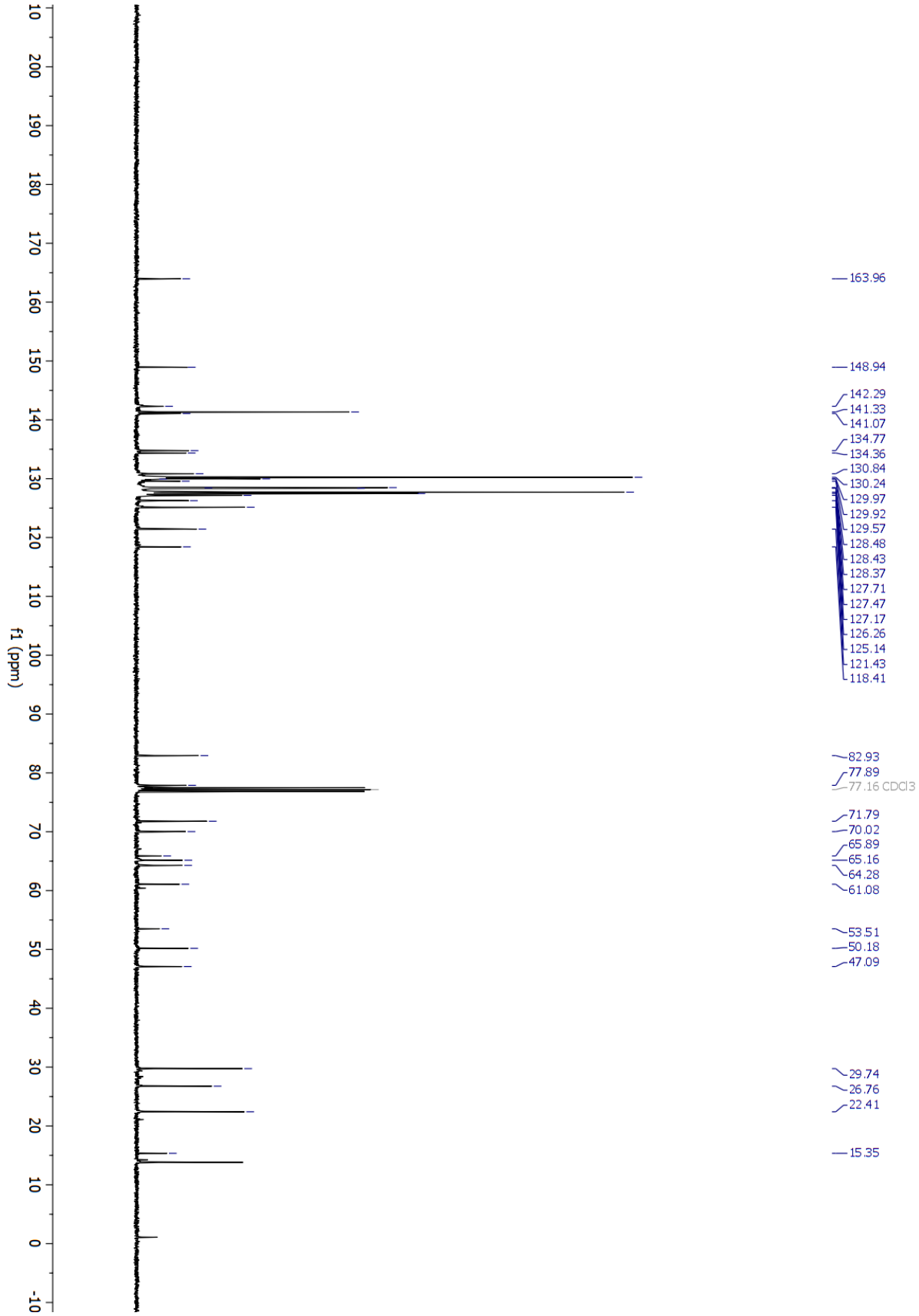
FTIR (neat): 3386, 3073, 2977, 2922, 2871, 2356, 1740, 1430, 1410, 1356,1159, 798, 784, 758, 748 cm^{-1}

$[\alpha]_D^{28}$= -85.0 (c 0.10, $CHCl_3$)

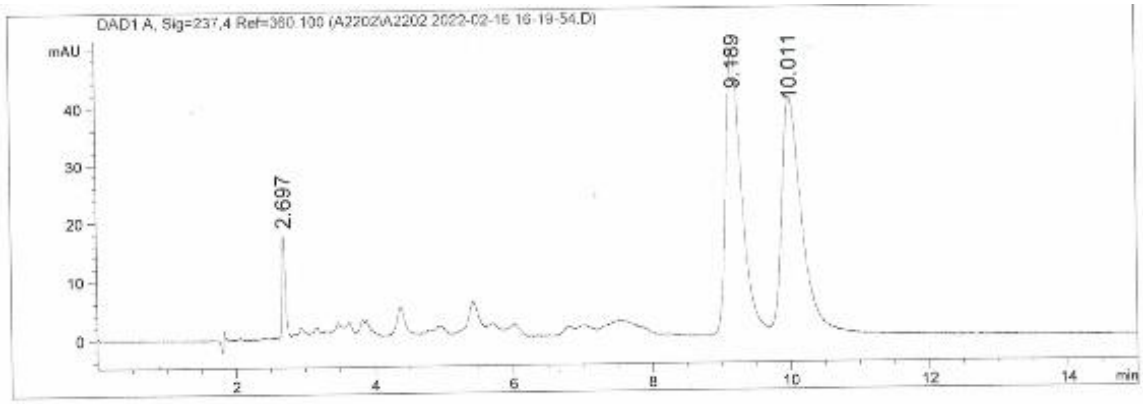
HRMS (ESI): Calculated for $C_{61}H_{58}ClN_7O_2$ $[M+H^+]$= 956.4413, found= 956.4414

HPLC (AZYP NicoShell column, MeOH/EtOH/Hexanes = 10:10:80, 0.3 mL/min, 360 nm): *ee* = 86%

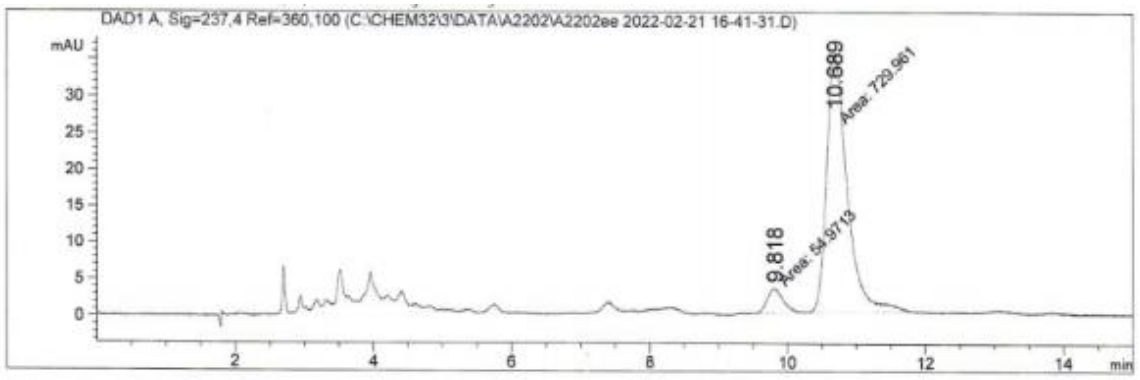

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.00
2.10
4.40
4.24
10.02
3.05
2.10
6.08
1.40
1.16
2.33
1.52
1.02
1.89
1.90
1.66
1.31
1.72
2.74
3.35
3.13
7.91
7.90
7.89
7.89
7.44
7.44
7.43
7.42
7.41
7.40
7.39
7.39
7.37
7.37
7.26 CDCl3
7.19
7.18
7.17
7.16
7.16
7.11
7.09
7.04
7.02
6.91
6.89
6.87
6.85
6.85
6.82
6.80
6.63
6.61
5.81
5.81
5.79
5.79
5.77
5.77
5.75
5.15
5.13
5.12
5.11
5.10
5.10
5.06
5.06
4.91
4.32
4.07
3.22
3.20
3.18
2.94
2.92
2.91
2.89
2.57
2.56
2.55
2.54
2.52
2.43
2.41
2.39
1.61
1.59
1.57
1.55
1.53
1.25
1.24
1.22
1.21
1.20
1.19
0.84
0.83
0.82
0.80
0.78
0.76
0.74
0.73
0.73
0.72


f1 (ppm)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
163.96
148.94
142.29
141.33
141.07
134.77
134.36
130.84
130.24
129.97
129.92
129.57
128.48
128.43
128.37
127.71
127.47
127.17
126.26
125.14
121.43
118.41
82.93
77.89
77.16 CDCl3
71.79
70.02
65.89
65.16
64.28
61.08
53.51
50.18
47.09
29.74
26.76
22.41
15.35

\



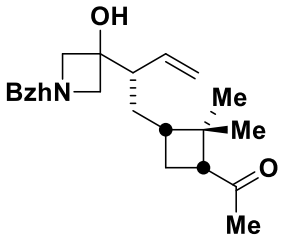
RetTime [min]	k'	Area [mAU*s]	Height [mAU]	Symm.	Width [min]	Plates	Resolution	Selectivity
2.697	-	52.52391	17.47417	0.84	0.0450	19904	-	-
9.189	-	752.25867	48.68874	0.75	0.2350	8472	27.24	3.41
10.011	-	724.10107	39.81644	0.68	0.2783	7168	1.88	1.09



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.818	MM	0.2754	54.97131	3.32680	7.0033
2	10.689	MM	0.3455	729.96057	35.20898	92.9967

NOTE: Separation of the enantiomers of compound **4v** via chiral stationary phase HPLC was exceptionally challenging. After much unsuccessful effort, this compound was sent to Professor Daniel Armstrong of UT Arlington who achieved separation of the enantiomers on a NicoShell chiral stationary phase HPLC column developed in his laboratory [67-70]

(4w) 1-((1*R*,3*S*)-3-((*S*)-2-(1-benzhydryl-3-hydroxyazetidin-3-yl)but-3-en-1-yl)-2,2-dimethylcyclobutyl)ethan-1-one



Procedure

Allyl acetate **2w** (71.5 mg, 0.300 mmol, 150 mol%) was subjected to a modified version of general procedure D using 5 mol% (S)-Ir-Cl, OMe-BIPHEP (10.1 mg, 0.010 mmol, 5 mol%, 100 ^{o}C, 36 hr). The title compound was obtained in 97% yield (81.2 mg, 0.194 mmol, 5.5:1 dr) as an orange oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1—3:1).

TLC (SiO_2): R_f = 0.59 (hexanes: ethyl acetate = 1:1).

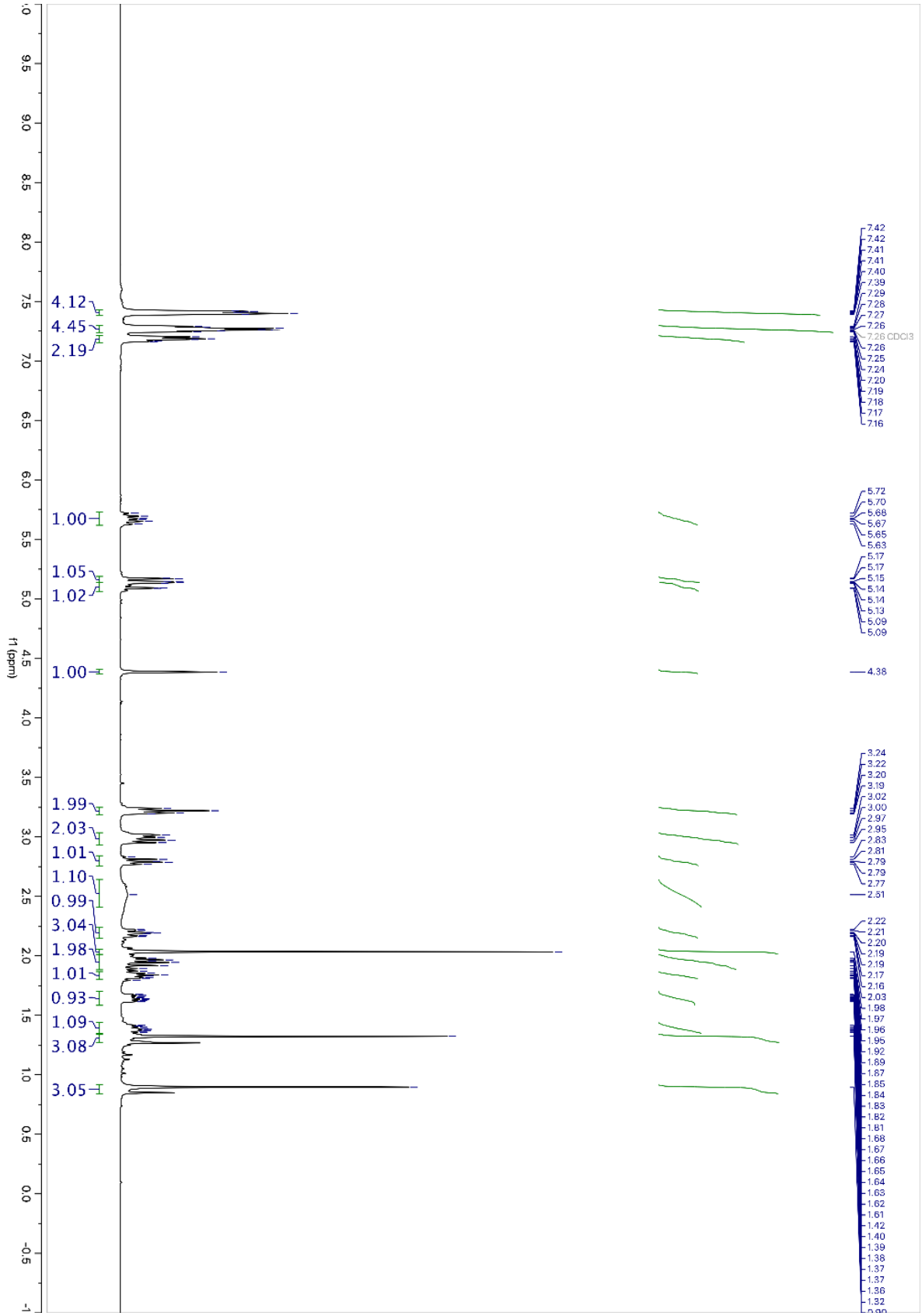
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.38 (m, 4H), 7.30 – 7.23 (m, 4H), 7.18 (dd, *J* = 8.3, 5.8 Hz, 2H), 5.67 (dt, *J* = 17.1, 9.7 Hz, 1H), 5.16 (dd, *J* = 10.4, 2.2 Hz, 1H), 5.14 – 5.07 (m, 1H), 4.38 (s, 1H), 3.22 (t, *J* = 7.6 Hz, 2H), 2.98 (dd, *J* = 17.8, 8.2 Hz, 2H), 2.79 (dd, *J* = 9.6, 7.3 Hz, 1H), 2.51 (s, 1H), 2.19 (ddd, *J* = 11.6, 9.4, 2.9 Hz, 1H), 2.03 (s, 3H), 2.00 – 1.89 (m, 2H), 1.88 – 1.77 (m, 1H), 1.65 (ddd, *J* = 14.0, 7.3, 3.1 Hz, 1H), 1.38 (ddd, *J* = 14.1, 11.4, 6.5 Hz, 1H), 1.32 (s, 3H), 0.90 (s, 3H).

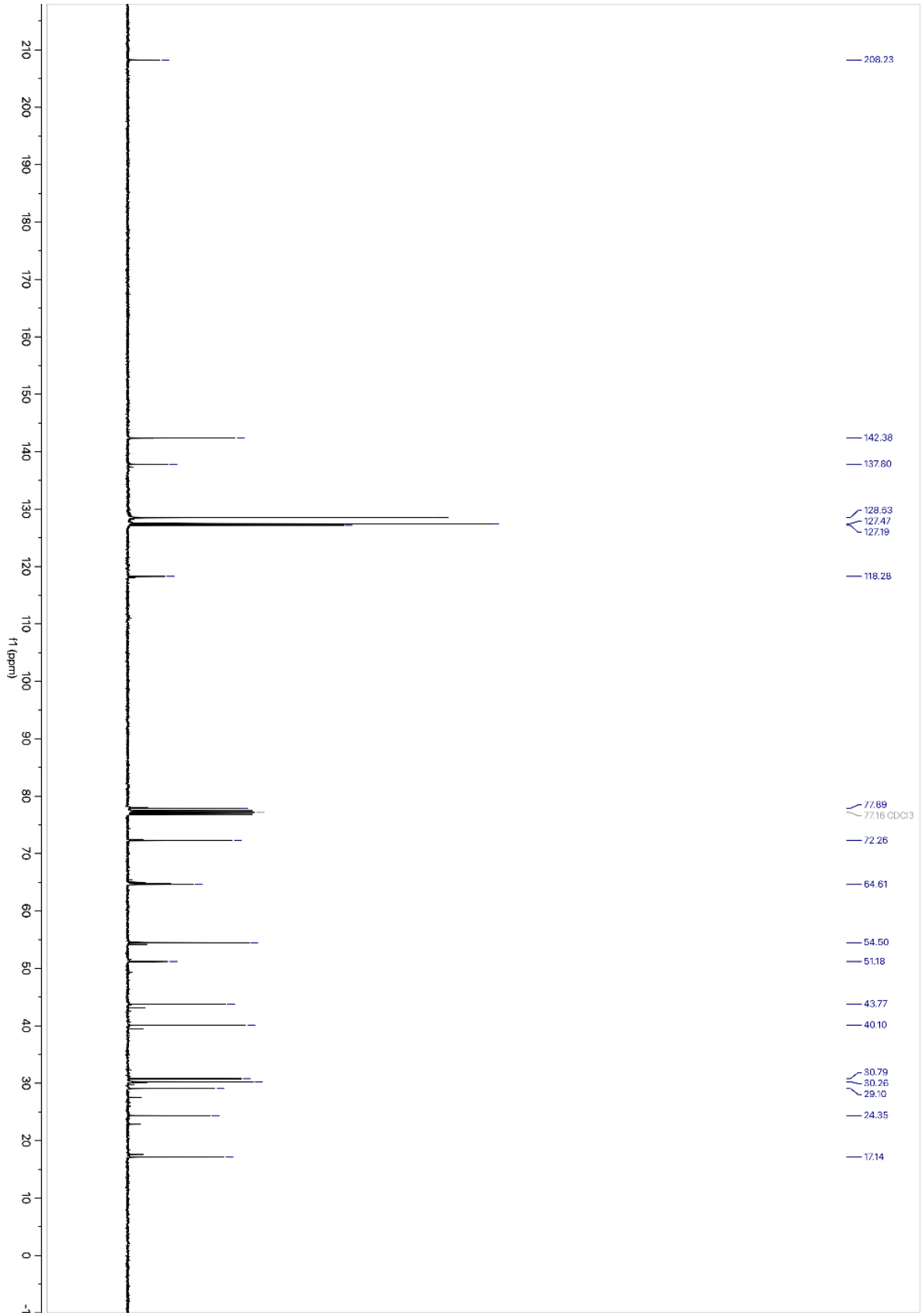
^{13}C NMR (101 MHz, $CDCl_3$): δ 208.2, 142.4, 137.8, 128.5, 127.5, 127.2, 118.3, 77.9, 72.3, 64.6, 54.5, 51.2, 43.8, 40.1, 30.8, 30.3, 29.1, 24.3, 17.1.

HRMS (APCI): Calculated for $C_{28}H_{35}NO_2$ [M+H$^+$] = 418.2741, found 418.2748

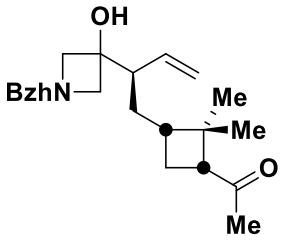
FTIR (neat): 3435, 3061, 2950, 2359, 1808, 1696, 1637, 1599, 1385, 1356, 1309, 821, 732, 703 cm^{-1}

$[\alpha]_D^{28}$ = -15.5 (*c* 0.15, $CHCl_3$)


f1 (ppm)
4.12
4.45
2.19
1.00
1.05
1.02
1.00
1.99
2.03
1.01
1.10
0.99
3.04
1.98
1.01
0.93
1.09
3.08
3.05
7.42
7.42
7.41
7.41
7.40
7.39
7.29
7.28
7.27
7.26
7.26 CDCl3
7.26
7.25
7.24
7.20
7.19
7.18
7.17
7.16
5.72
5.70
5.68
5.67
5.65
5.63
5.17
5.17
5.15
5.14
5.14
5.13
5.09
5.09
4.38
3.24
3.22
3.20
3.19
3.02
3.00
2.97
2.95
2.83
2.81
2.79
2.79
2.77
2.51
2.22
2.21
2.20
2.19
2.19
2.17
2.16
2.03
1.98
1.97
1.96
1.95
1.92
1.89
1.87
1.85
1.84
1.83
1.82
1.81
1.68
1.67
1.66
1.65
1.64
1.63
1.62
1.61
1.42
1.40
1.39
1.38
1.37
1.37
1.36
1.32


208.23
142.38
137.80
128.53
127.47
127.19
118.28
77.89
77.16 CDCl3
72.26
64.61
54.50
51.18
43.77
40.10
30.79
30.26
29.10
24.35
17.14
f1 (ppm)

(*iso*-4w)1-((1*R*,3*S*)-3-((*R*)-2-(1-benzhydryl-3-hydroxyazetidin-3-yl)but-3-en-1-yl)-2,2-dimethylcyclobutyl)ethan-1-one



Procedure

Allyl acetate **2w** (71.5 mg, 0.300 mmol, 150 mol%) was subjected to a modified version of general procedure C using 5 mol% (R)-Ir-Cl, OMe-BIPHEP (10.1 mg, 0.010 mmol, 5 mol%, 100 °C, 36 hr). The title compound was obtained in 96% yield (79.8 mg, 0.191 mmol, 6:1 dr) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1—3:1).

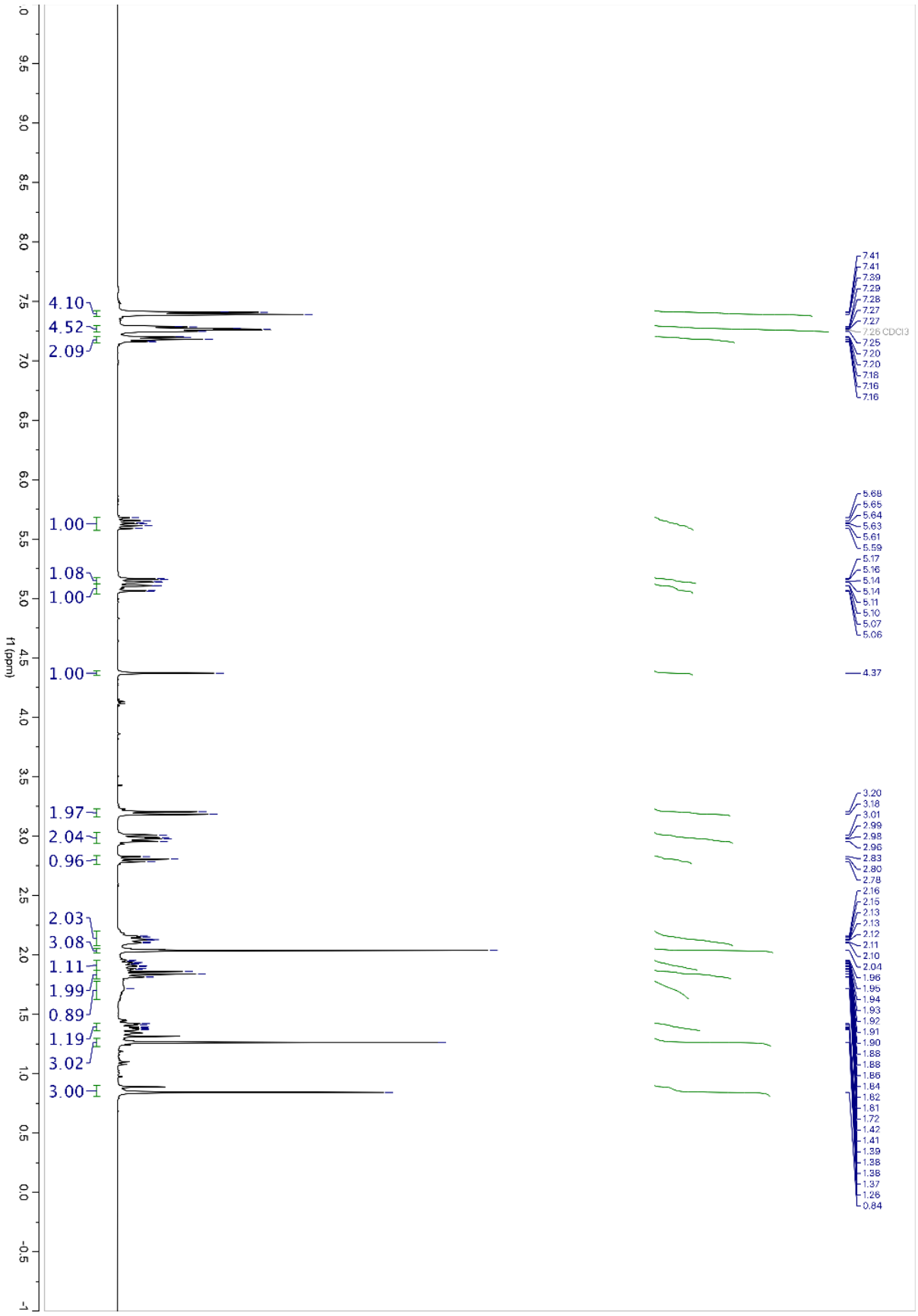
TLC (SiO_2): R_f = 0.59 (hexanes: ethyl acetate = 1:1).

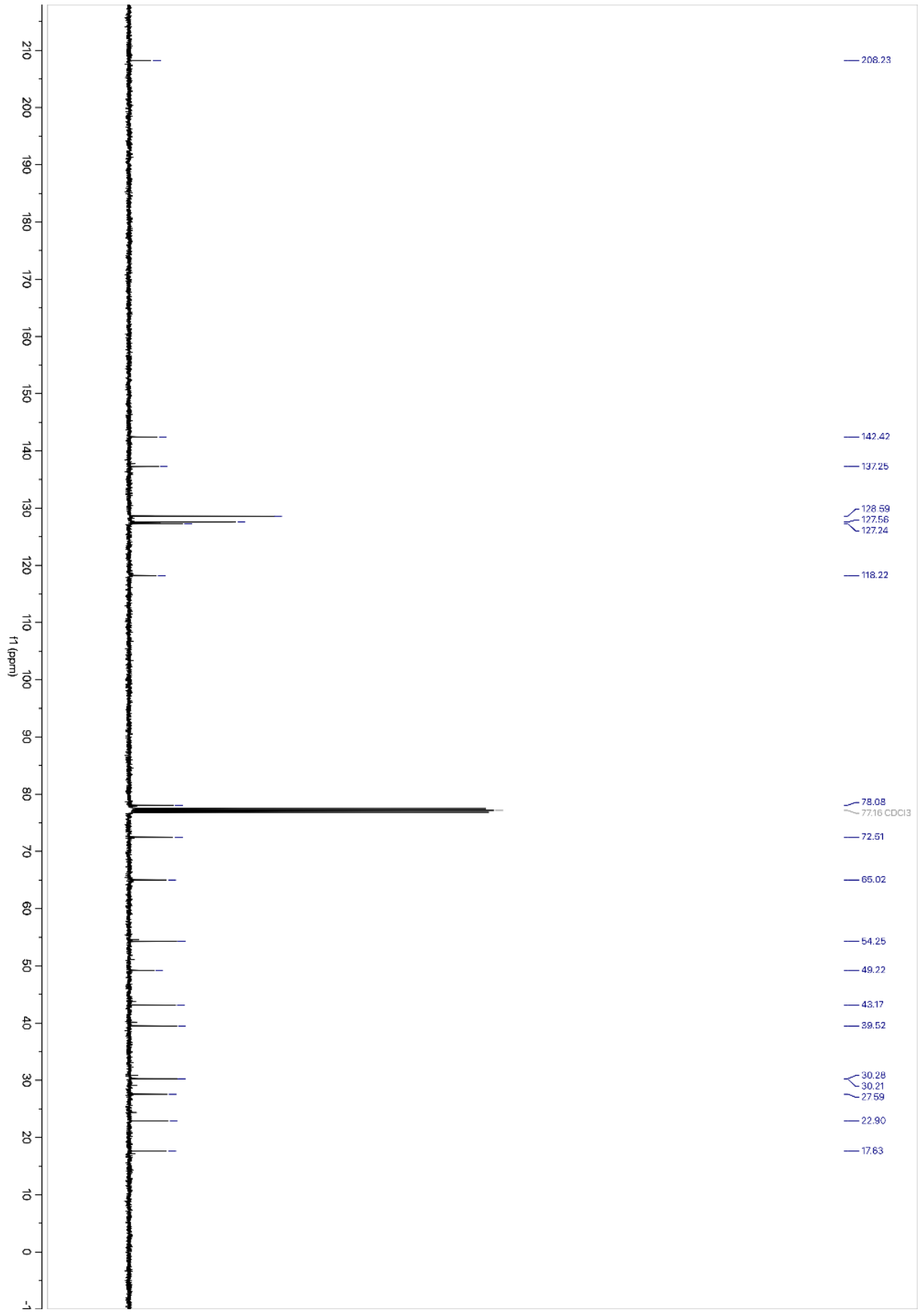
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.3 Hz, 4H), 7.31 – 7.21 (m, 4H), 7.24 – 7.12 (m, 2H), 5.63 (dt, *J* = 17.0, 9.8 Hz, 1H), 5.15 (dd, *J* = 10.3, 2.0 Hz, 1H), 5.08 (dd, *J* = 17.1, 2.0 Hz, 1H), 4.37 (s, 1H), 3.19 (d, *J* = 8.6 Hz, 2H), 2.98 (dd, *J* = 12.8, 8.5 Hz, 2H), 2.80 (t, *J* = 8.5 Hz, 1H), 2.17 – 2.09 (m, 2H), 2.04 (s, 3H), 1.97 – 1.87 (m, 1H), 1.84 (t, *J* = 9.3 Hz, 2H), 1.72 (s, 1H), 1.43 – 1.36 (m, 1H), 1.26 (s, 3H), 0.84 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 208.2, 142.4, 137.2, 128.6, 127.6, 127.2, 118.2, 78.1, 72.5, 65.0, 54.2, 49.2, 43.2, 39.5, 30.3, 30.2, 27.6, 22.9, 17.6.

HRMS (ESI): Calculated for $C_{28}H_{35}NO_2$ [M+H$^+$] = 418.2741, found 418.2741

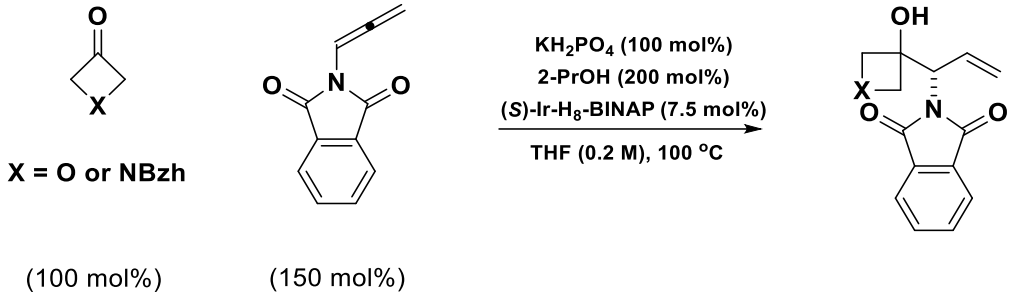
FTIR (neat): 3435, 3026 2950, 2359, 1808, 1696, 1637, 1599, 1385, 1356, 1209, 1074, 732, 703 cm^{-1}

$[\alpha]_D^{28}$= +21.2 (*c* 0.20, $CHCl_3$)


f1 (ppm)
4.10
4.52
2.09
1.00
1.08
1.00
1.00
1.97
2.04
0.96
2.03
3.08
1.11
1.99
0.89
1.19
3.02
3.00
7.41
7.41
7.39
7.29
7.28
7.27
7.27
7.26 CDCl3
7.25
7.20
7.20
7.18
7.16
7.16
5.68
5.65
5.64
5.63
5.61
5.59
5.17
5.16
5.14
5.14
5.11
5.10
5.07
5.06
4.37
3.20
3.18
3.01
2.99
2.98
2.96
2.83
2.80
2.78
2.16
2.15
2.13
2.13
2.12
2.11
2.10
2.04
1.96
1.95
1.94
1.93
1.92
1.91
1.90
1.88
1.88
1.86
1.84
1.82
1.81
1.72
1.42
1.41
1.39
1.38
1.38
1.37
1.26
0.84


f1 (ppm)
208.23
142.42
137.25
128.59
127.56
127.24
118.22
78.08
77.16 CDCl3
72.51
65.02
54.25
49.22
43.17
39.52
30.28
30.21
27.59
22.90
17.63

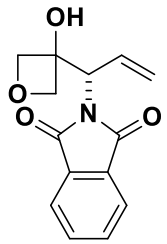
General Procedure E



(100 mol%) (150 mol%)

An oven-dried pressure tube equipped with a magnetic stir bar was charged phthalimido-allene (55.0 mg, 0.30 mmol, 150 mol%), (*S*)-Ir-H_8-BINAP (16.4 mg, 0.015 mmol, 7.5 mol%), and potassium dihydrogen phosphate (27.2 mg, 0.200 mmol, 100 mol%) and ketone. The tube was purged with argon and 2-propanol (30 µL, 0.40 mmol, 200 mol%) was added by syringe, followed by THF (1.00 mL, 0.2 M). The septum was removed, and the tube was sealed with a polytetrafluoroethylene-lined screwcap. The tube was placed in an oil bath at 100 °C and stirred for 48 hours. The vessel was allowed to cool to ambient temperature. Upon cooling the reaction mixture was concentrated onto silica gel and purified by flash chromatography.

(3y) (S)-2-(1-(3-hydroxyoxetan-3-yl)allyl)isoindoline-1,3-dione



Procedure

phthalimido-allene (56.1 mg, 0.300 mmol, 150 mol%) was subjected to general procedure D (100 ^{o}C, 48 hr). The title compound was obtained in 93% yield (48.7 mg, 0.186 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 2:1).

TLC (SiO_2): R_f = 0.16 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (dt, *J* = 7.3, 3.7 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.17 (ddd, *J* = 17.3, 10.4, 8.0 Hz, 1H), 5.39 – 5.31 (m, 3H), 5.08 (s, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.61 (d, *J* = 6.9 Hz, 1H), 4.57 (d, *J* = 6.6 Hz, 1H), 4.37 (d, *J* = 6.6 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ:169.3, 134.8, 131.6, 129.6, 124.0, 120.7, 81.8, 81.3, 75.4, 59.8.

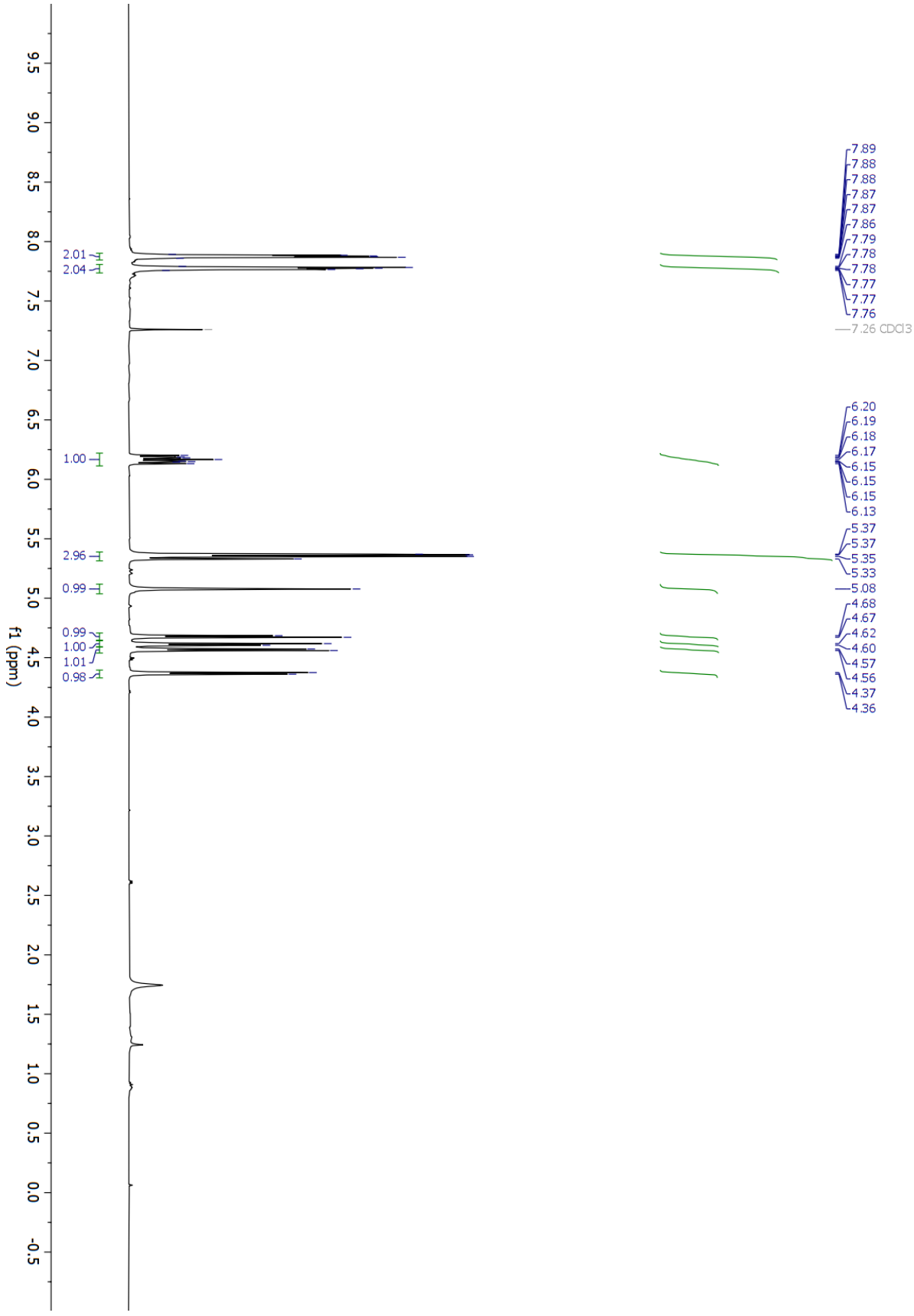
HRMS (ESI): Calculated for $C_{14}H_{13}NO_4$ [M+H^+] =260.0917, found 260.0916

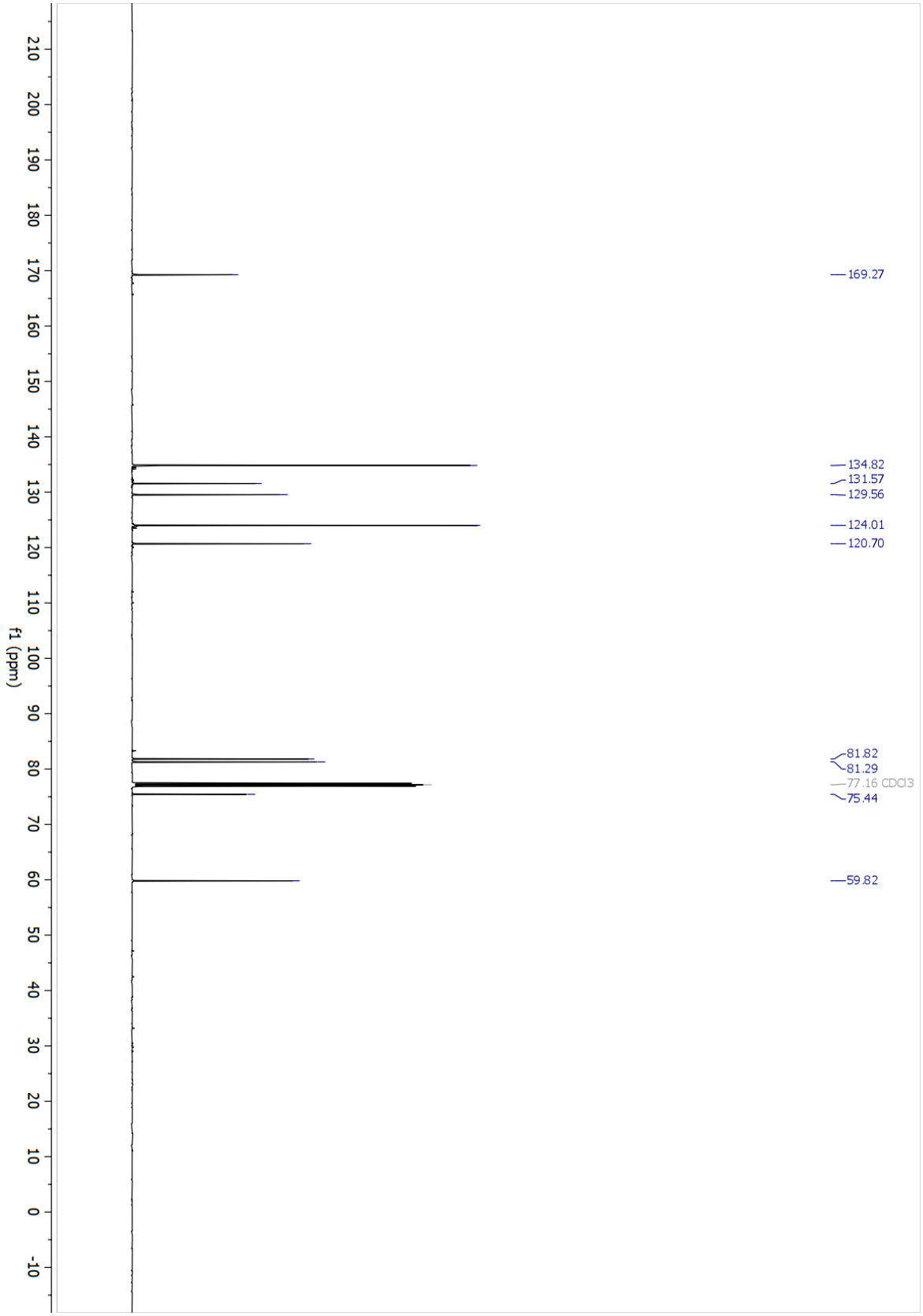
FTIR (neat): 3375, 1701, 1384, 914, 875, 717 cm^{-1}

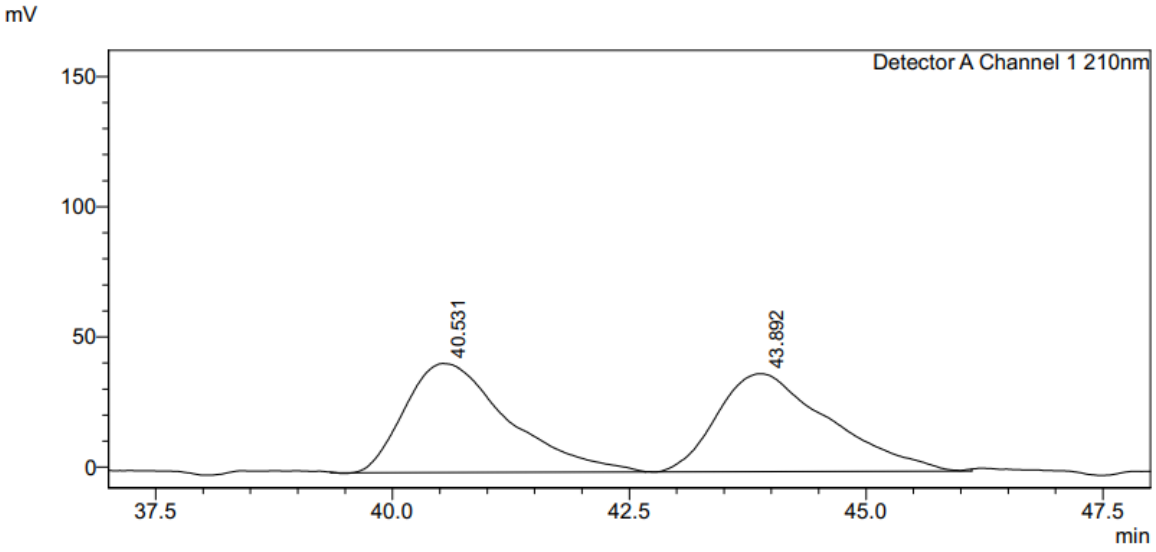
$[\alpha]_D^{28}$= -103^{0} (c = 0.83, CDCl3)

MP: 140-147 ^{0}C

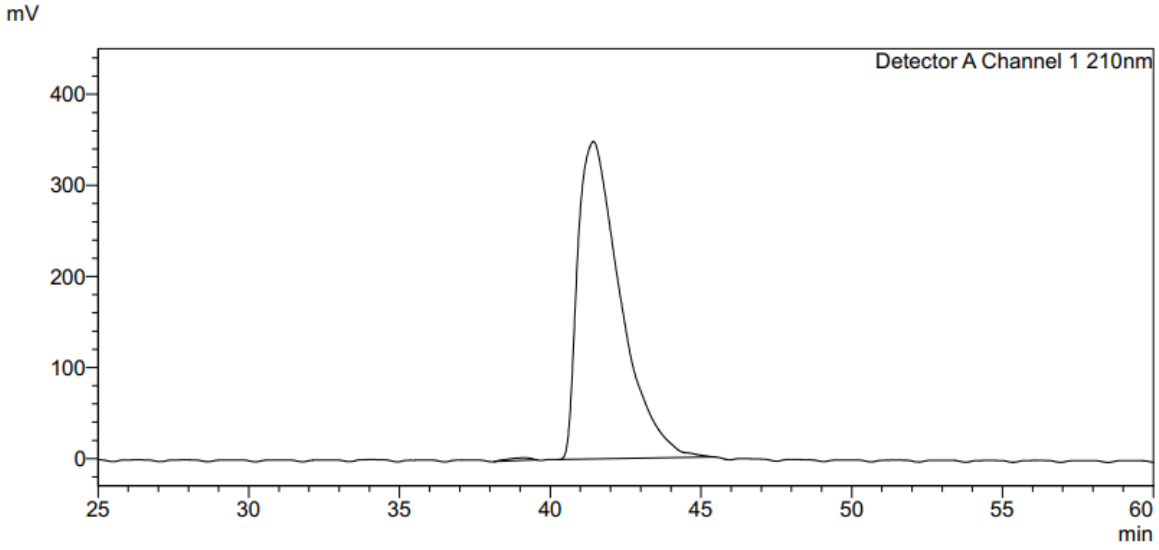
HPLC (Chiralcel column OD-H, hexane:*i*-PrOH = 97:3, 1 mL/min, 210 nm): *ee*= 99%


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.01
2.04
1.00
2.96
0.99
0.99
1.00
1.01
0.98
7.89
7.88
7.88
7.87
7.87
7.86
7.79
7.78
7.78
7.78
7.77
7.77
7.76
7.26 CDCl3
6.20
6.19
6.18
6.17
6.15
6.15
6.15
6.13
5.37
5.37
5.35
5.33
5.08
4.68
4.67
4.62
4.60
4.57
4.56
4.37
4.36


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
169.27
134.82
131.57
129.56
124.01
120.70
81.82
81.29
77.16 CDCl3
75.44
59.82

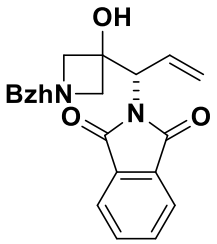


Peak#	Ret. Time	Area	Height	Area%
1	40.531	3165251	41804	50.491
2	43.892	3103746	37550	49.509
Total		6268997	79354	100.000



Peak#	Ret. Time	Area	Height	Area%
1	39.128	165811	2935	0.481
2	41.431	34316867	348854	99.519
Total		34482678		100.000

(4y) (S)-2-(1-(1-benzhydryl-3-hydroxyazetidin-3-yl)allyl)isoindoline-1,3-dione



Procedure

phthalimido-allene (56.1 mg, 0.30 mmol, 150 mol%) was subjected to general procedure D (100 ^{o}C, 72 hr). The title compound was obtained in 75% yield (63.9 mg, 0.15 mmol) as a pale-yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1).

TLC (SiO_2): R_f = 0.20 (hexanes: ethyl acetate = 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.46 – 7.31 (m, 4H), 7.28 (s, 1H), 7.25 (d, *J* = 3.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.18 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.39 (d, *J* = 6.8 Hz, 1H), 5.33 – 5.24 (m, 2H), 5.10 (s, 1H), 4.42 (s, 1H), 3.41 (dd, *J* = 7.9, 2.4 Hz, 1H), 3.16 (dd, *J* = 7.8, 2.3 Hz, 1H), 3.07 (d, *J* = 8.0 Hz, 1H), 2.91 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.7 142.6, 142.5, 135.0, 131.9, 130.7, 128.8, 128.8, 127.9, 127.8, 127.5, 127.4, 124.2, 119.8, 78.0, 71.4, 64.4, 63.8, 61.2.

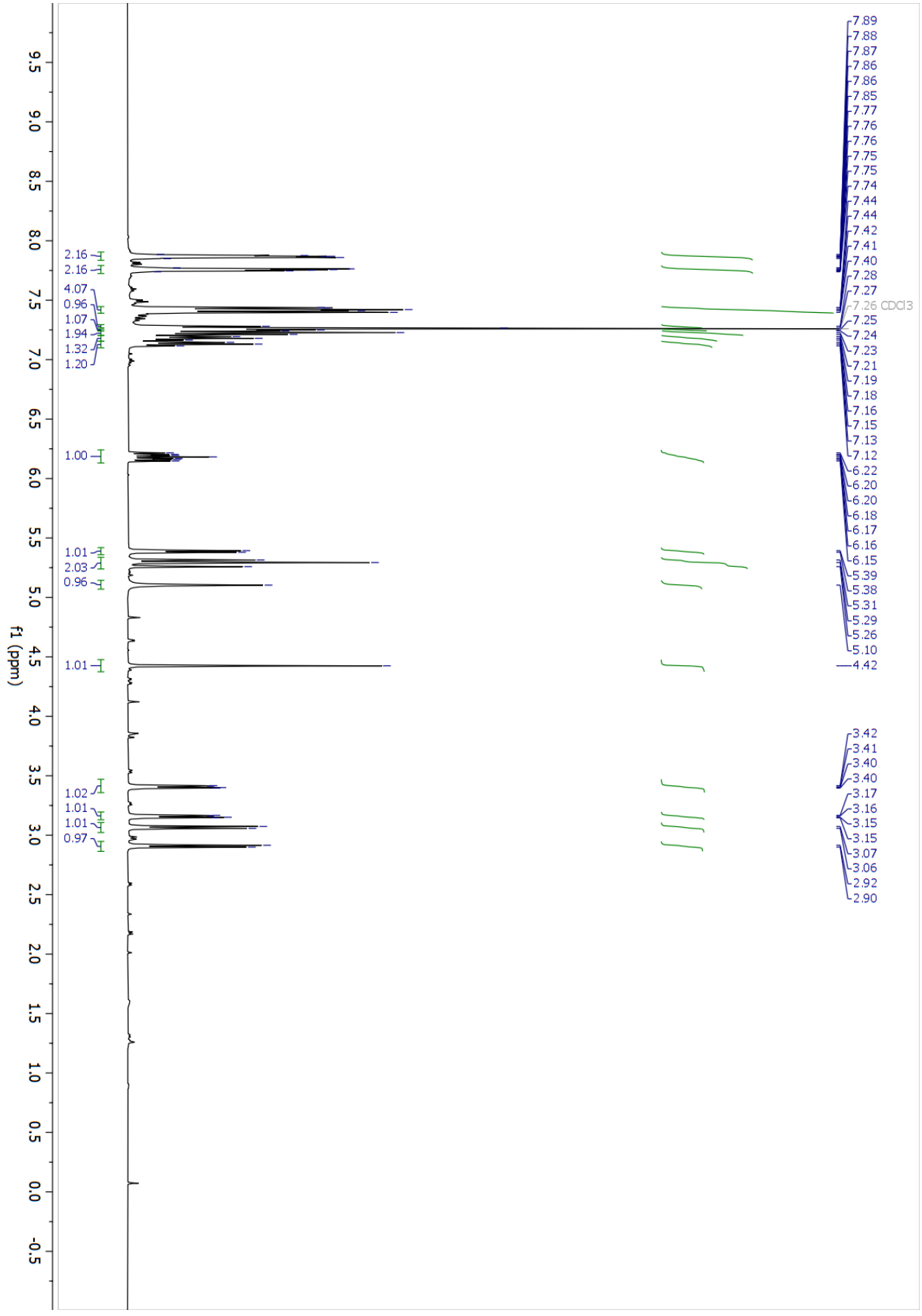
HRMS (ESI): Calculated for $C_{27}H_{24}N_2O_3$ [M+H^{+}] =425.1860, found 425.1865

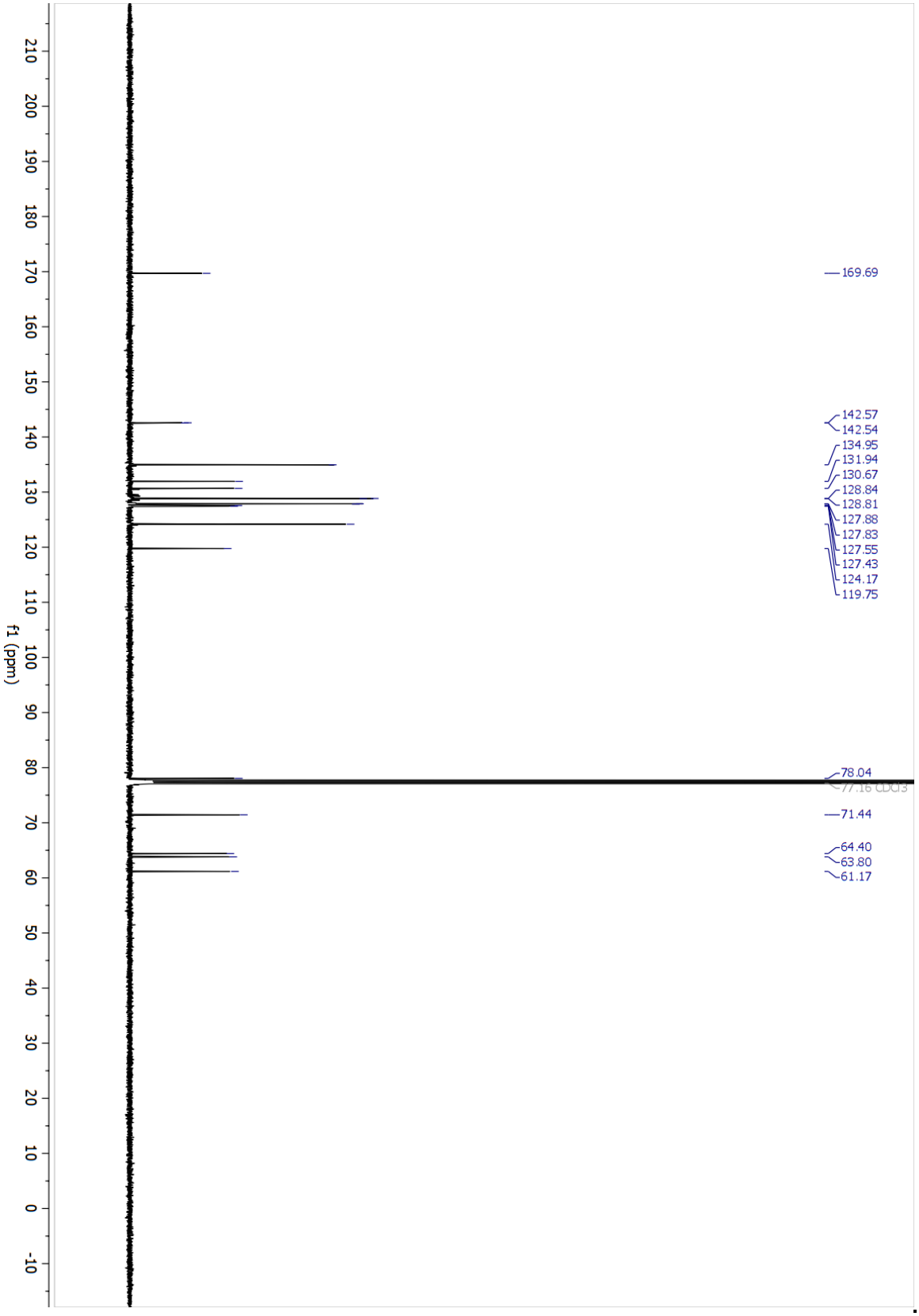
FTIR (neat): 3375, 1770, 1701, 1384, 974, 875, 717 cm^{-1}

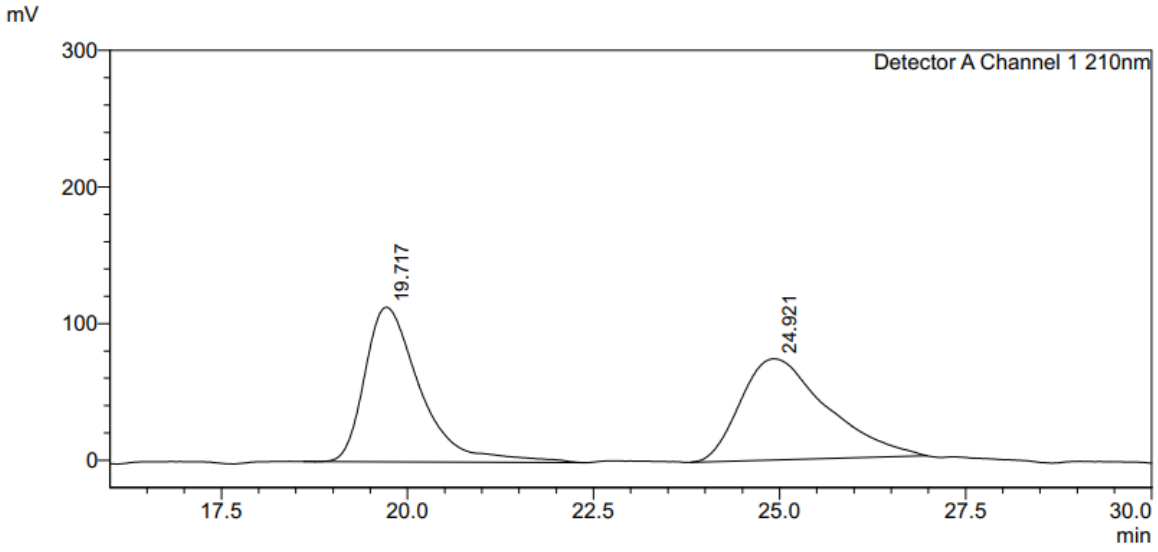
$[\alpha]_D^{28}$= -47^{0} (c = 0.68, $CHCl_3$)

MP: 74-86 ^{0}C

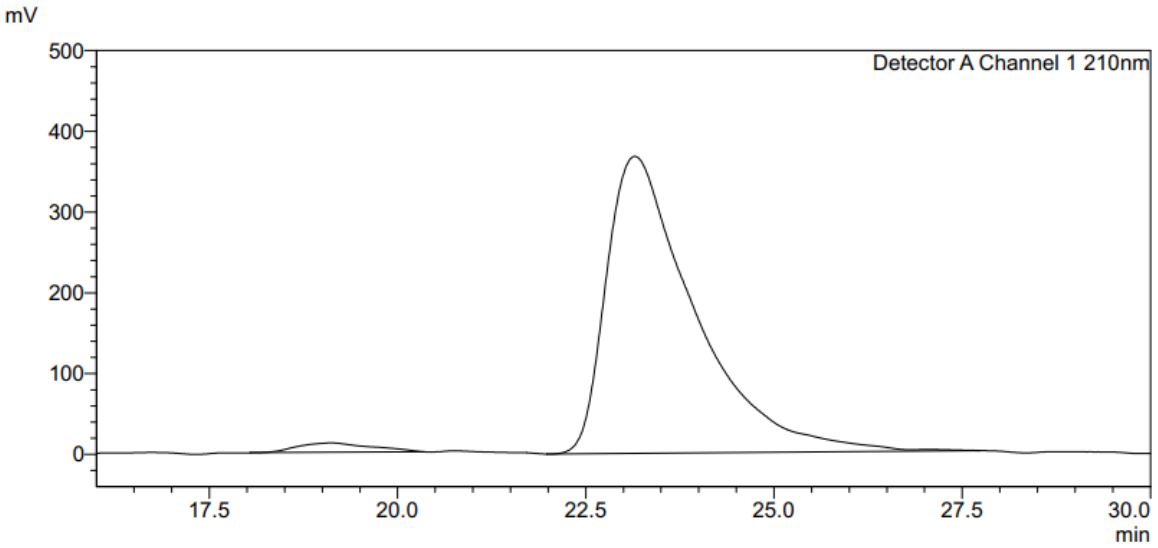
HPLC (Chiralcel column OD-H, Hexane:2-PrOH = 97:3, 1 mL/min, 210 nm): *ee*= 99%


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.16
2.16
4.07
0.96
1.07
1.94
1.32
1.20
1.00
1.01
2.03
0.96
1.01
1.02
1.01
1.01
0.97
7.89
7.88
7.87
7.86
7.86
7.85
7.77
7.76
7.76
7.75
7.75
7.74
7.44
7.44
7.42
7.41
7.40
7.28
7.27
7.26 CDCl3
7.25
7.24
7.23
7.21
7.19
7.18
7.16
7.15
7.13
7.12
6.22
6.20
6.20
6.18
6.17
6.16
6.15
5.39
5.38
5.31
5.29
5.26
5.10
4.42
3.42
3.41
3.40
3.40
3.17
3.16
3.15
3.15
3.07
3.06
2.92
2.90


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
169.69
142.57
142.54
134.95
131.94
130.67
128.84
128.81
127.88
127.83
127.55
127.43
124.17
119.75
78.04
77.16 CDCl3
71.44
64.40
63.80
61.17

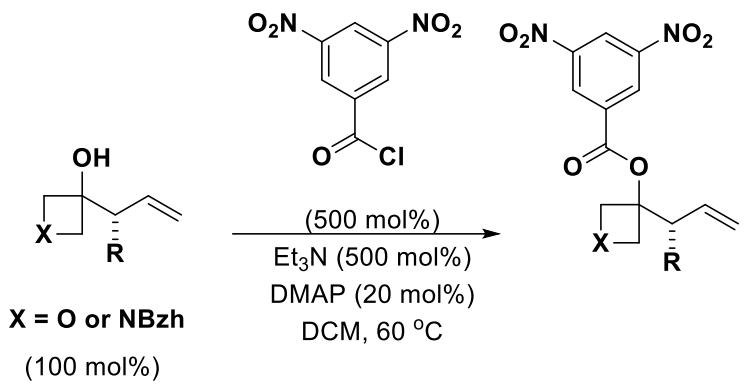


Peak#	Ret. Time	Area	Height	Area%
1	19.717	5881134	113128	49.667
2	24.921	5960099	74036	50.333
Total		11841232	187163	100.000



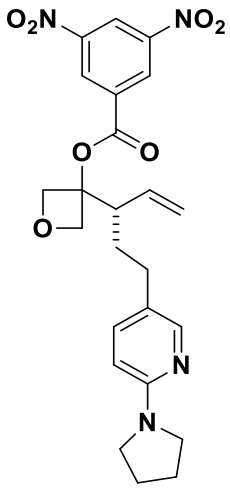
Peak#	Ret. Time	Area	Height	Area%
1	39.128	165811	2935	0.481
2	41.431	34316867	348854	99.519
Total		34482678		100.000

General Procedure F



An oven-dried pressure tube equipped with a magnetic stir bar was charged with oxetanol/azetidinol (100 mol%), triethylamine (500 mol%), 3,5-dinitro benzoyl chloride (500 mol%), 4-dimethylaminopyridine (20 mol%), and anhydrous dichloromethane (0.1 M). The reaction was refluxing at 60 ^{0}C for 16 hours. The reaction solution was diluted with dichloromethane and was washed with aqueous saturated solutions sodium bicarbonate, then distilled water, then brine. The organic layer was then separated and Na_2SO_4 (dried), filtered and concentrated *in vacuo*. The residue was directly subjected to flash column chromatography to afford the title compounds.

(5q) (S)-3-(5-(6-(pyrrolidin-1-yl)pyridin-3-yl)pent-1-en-3-yl)oxetan-3-yl 3,5-dinitrobenzoate



Procedure

oxetanol **3q** (69.4 mg, 0.143 mmol, 100 mol%) was subjected to general procedure **F.** The title compound was obtained in 55% yield (63.8 mg, 0.078 mmol) as a reddish solid after isolation by flash column chromatography (SiO_2, hexane: ethyl acetate = 2:1).

TLC (SiO_2): R_f = 0.48 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ: 9.23 (t, *J* = 2.2 Hz, 1H), 9.03 (d, *J* = 2.1 Hz, 2H), 7.86 (d, *J* = 2.4 Hz, 1H), 7.17 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.19 (d, *J* = 8.5 Hz, 1H), 5.82 (dt, *J* = 16.8, 9.8 Hz, 1H), 5.36 (dd, *J* = 10.2, 1.6 Hz, 1H), 5.28 (d, *J* = 16.9 Hz, 1H), 4.89 (dd, *J* = 7.7, 2.6 Hz, 2H), 4.79 (d, *J* = 7.8 Hz, 1H), 4.76 (d, *J* = 7.8 Hz, 1H), 3.32 (tq, *J* = 7.2, 3.3 Hz, 4H), 2.94 – 2.85 (m, 1H), 2.62 (ddd, *J* = 13.6, 8.1, 4.9 Hz, 1H), 2.33 (dt, *J* = 14.2, 8.2 Hz, 1H), 2.02 – 1.92 (m, 4H), 1.86 (dtd, *J* = 13.6, 8.4, 2.4 Hz, 1H), 1.71 (dddd, *J* = 13.1, 10.7, 7.8, 4.9 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 160.9, 156.3, 148.8, 147.9, 137.4, 135.5, 133.5, 129.4, 123.3, 122.7, 120.7, 106.3, 84.2, 78.3, 77.7, 46.9, 46.2, 30.4, 29.4, 25.6.

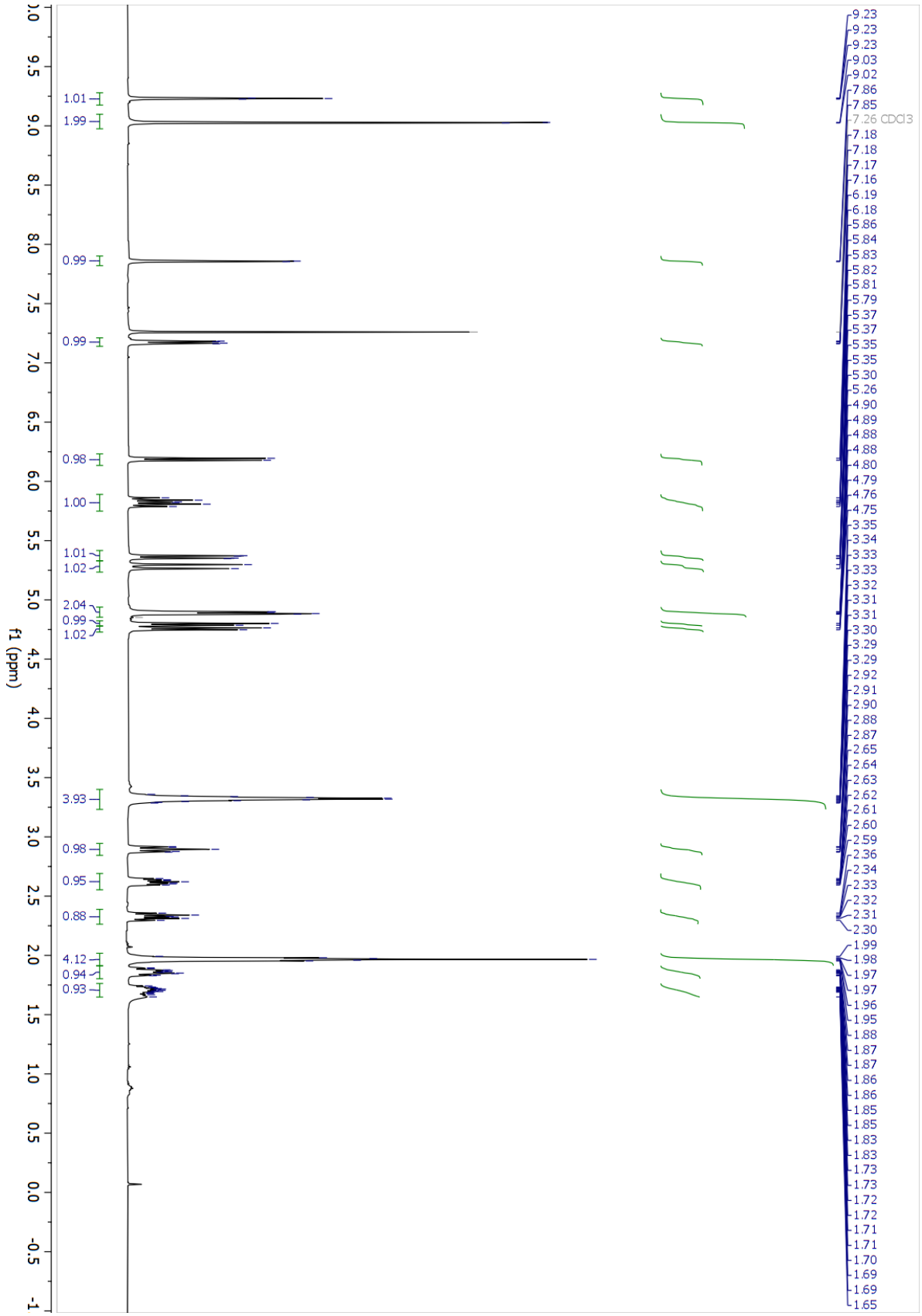
HRMS (ESI): Calculated for $C_{24}H_{26}N_4O_7$ $[M+H^+]$ =483.1874, found 483.1878

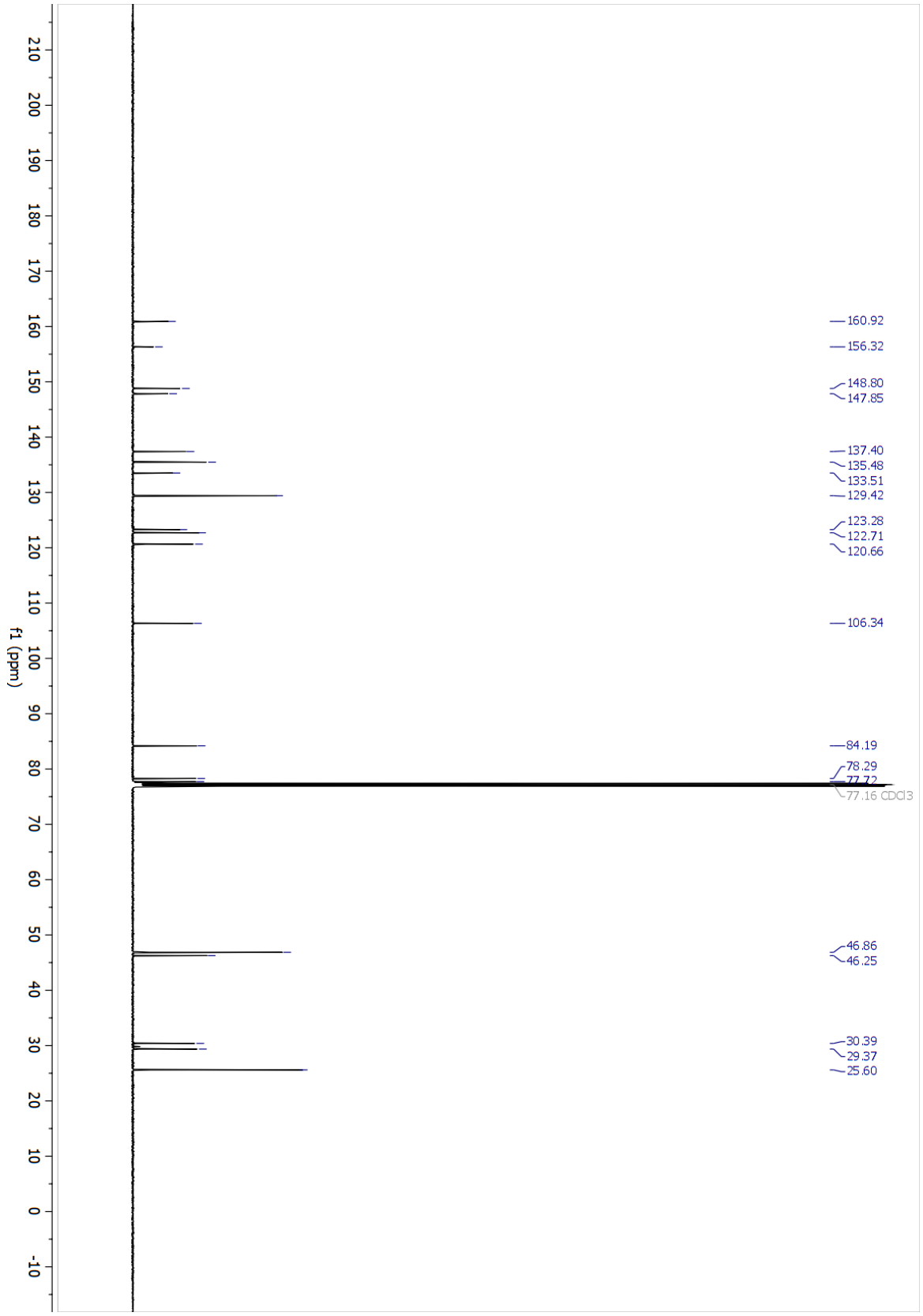
FTIR (neat): 2961, 1729, 1543, 1505, 1344, 1285, 1162, 730, 720 cm^{-1}

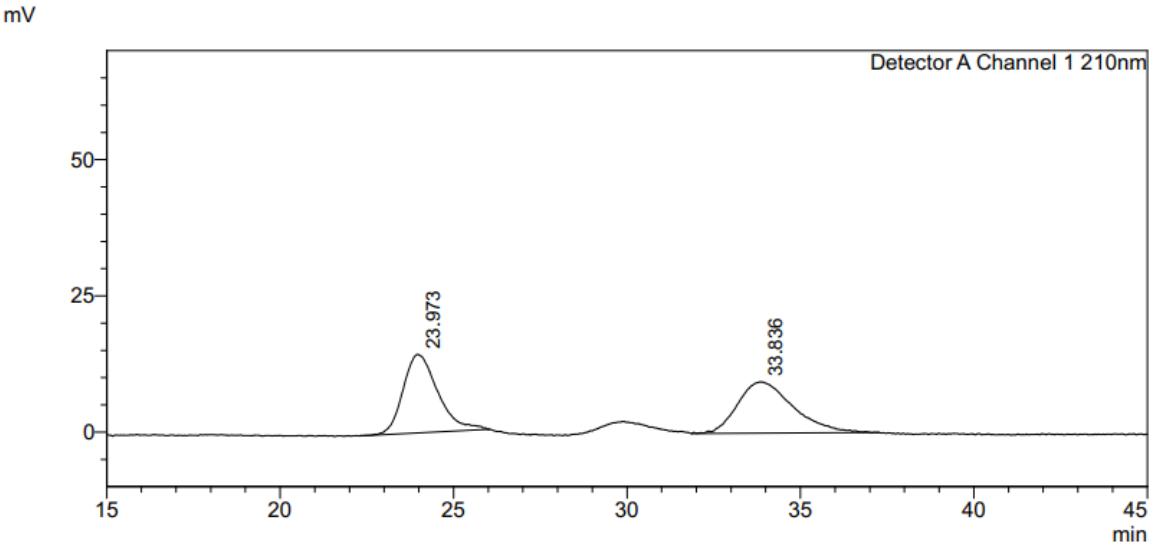
$[\alpha]_D^{28}$= -42.3^0 (c = 0.26, CDCl3)

MP: 142-150 ^{0}C

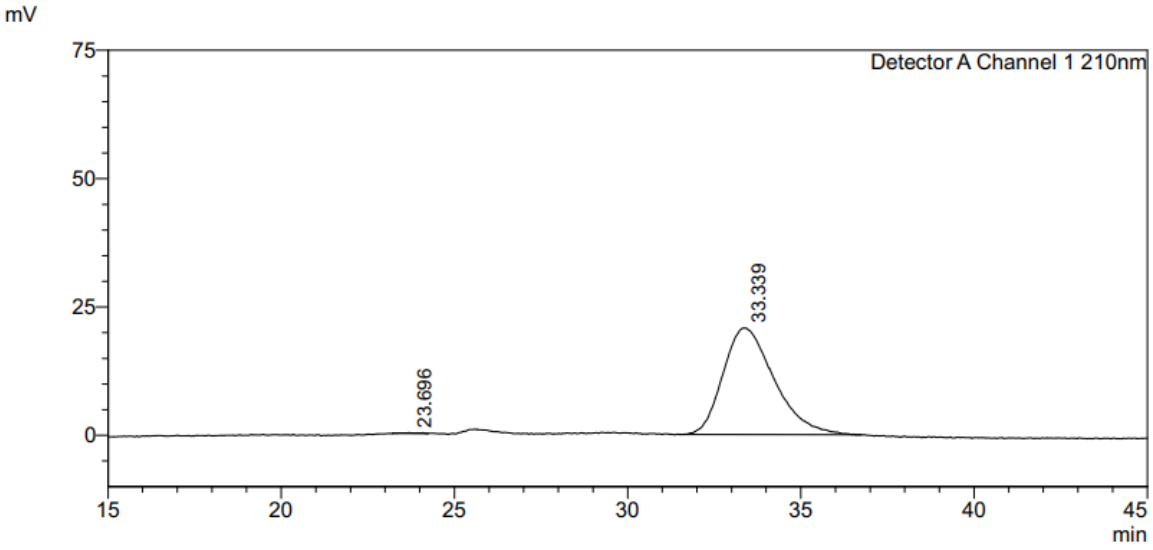
HPLC (Chiralcel column OD-H, hexane:*i*-PrOH = 85:15, 1.0 mL/min, 210 nm): *ee*= 99%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.01
1.99
0.99
0.99
0.98
1.00
1.01
1.02
2.04
0.99
1.02
3.93
0.98
0.95
0.88
4.12
0.94
0.93
9.23
9.23
9.23
9.03
9.02
7.86
7.85
7.26 CDCl3
7.18
7.18
7.17
7.16
6.19
6.18
5.86
5.84
5.83
5.82
5.81
5.79
5.37
5.37
5.35
5.35
5.30
5.26
4.90
4.89
4.88
4.88
4.80
4.79
4.76
4.75
3.35
3.34
3.33
3.33
3.32
3.31
3.31
3.30
3.29
3.29
2.92
2.91
2.90
2.88
2.87
2.65
2.64
2.63
2.62
2.61
2.60
2.59
2.36
2.34
2.33
2.32
2.31
2.30
1.99
1.98
1.97
1.97
1.96
1.95
1.88
1.87
1.87
1.86
1.86
1.85
1.85
1.83
1.83
1.73
1.73
1.72
1.72
1.71
1.71
1.70
1.69
1.69
1.65


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
160.92
156.32
148.80
147.85
137.40
135.48
133.51
129.42
123.28
122.71
120.66
106.34
84.19
78.29
77.72
77.16 CDCl3
46.86
46.25
30.39
29.37
25.60

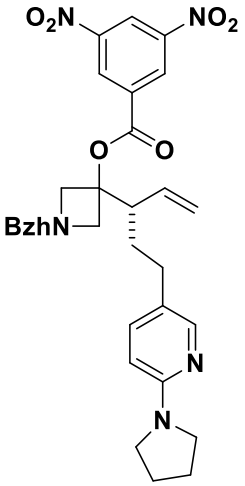


Peak#	Ret. Time	Area	Height	Area%
1	23.973	1006470	14422	49.105
2	33.836	1043154	9396	50.895
Total		2049623	23818	100.000



Peak#	Ret. Time	Area	Height	Area%
1	23.696	4576	155	0.214
2	33.339	2133225	20750	99.786
Total		2137801	20905	100.000

(6q) (S)-1-benzhydryl-3-(5-(6-(pyrrolidin-1-yl)pyridin-3-yl)pent-1-en-3-yl)azetidin-3-yl 3,5-dinitrobenzoate



Procedure

azetidinol **4q** (53.3 mg, 0.117 mmol, 100 mol%) was subjected to general procedure **F**. The title compound was obtained in 61% yield (46.4 mg, 0.071 mmol) as a reddish oil after isolation by flash column chromatography (SiO_2, hexane: ethyl acetate = 6:1).

TLC (SiO_2): R_f = 0.31 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ:9.20 (t, *J* = 2.1 Hz, 1H), 8.99 (d, *J* = 2.1 Hz, 2H), 7.90 (d, *J* = 2.3 Hz, 1H), 7.37 (t, *J* = 6.8 Hz, 4H), 7.28 (d, *J* = 7.0 Hz, 2H), 7.25 (m, 2H), 7.23 – 7.15 (m, 3H), 6.21 (d, *J* = 8.6 Hz, 1H), 5.86 (dt, *J* = 16.9, 9.8 Hz, 1H), 5.29 (dd, *J* = 10.1, 1.8 Hz, 1H), 5.19 (dd, *J* = 16.9, 1.7 Hz, 1H), 4.42 (s, 1H), 3.69 (d, *J* = 9.0 Hz, 1H), 3.63 (d, *J* = 9.0 Hz, 1H), 3.40 – 3.30 (m, *J* = 3.0 Hz, 4H), 3.26 (dd, *J* = 11.9, 9.0 Hz, 2H), 2.93 – 2.85 (m, 1H), 2.62 (ddd, *J* = 13.7, 8.5, 4.9 Hz, 1H), 2.34 (dt, *J* = 14.1, 8.2 Hz, 1H), 2.01 – 1.92 (m, 4H), 1.71 (dddd, *J* = 13.4, 10.5, 8.3, 4.9 Hz, 2H).

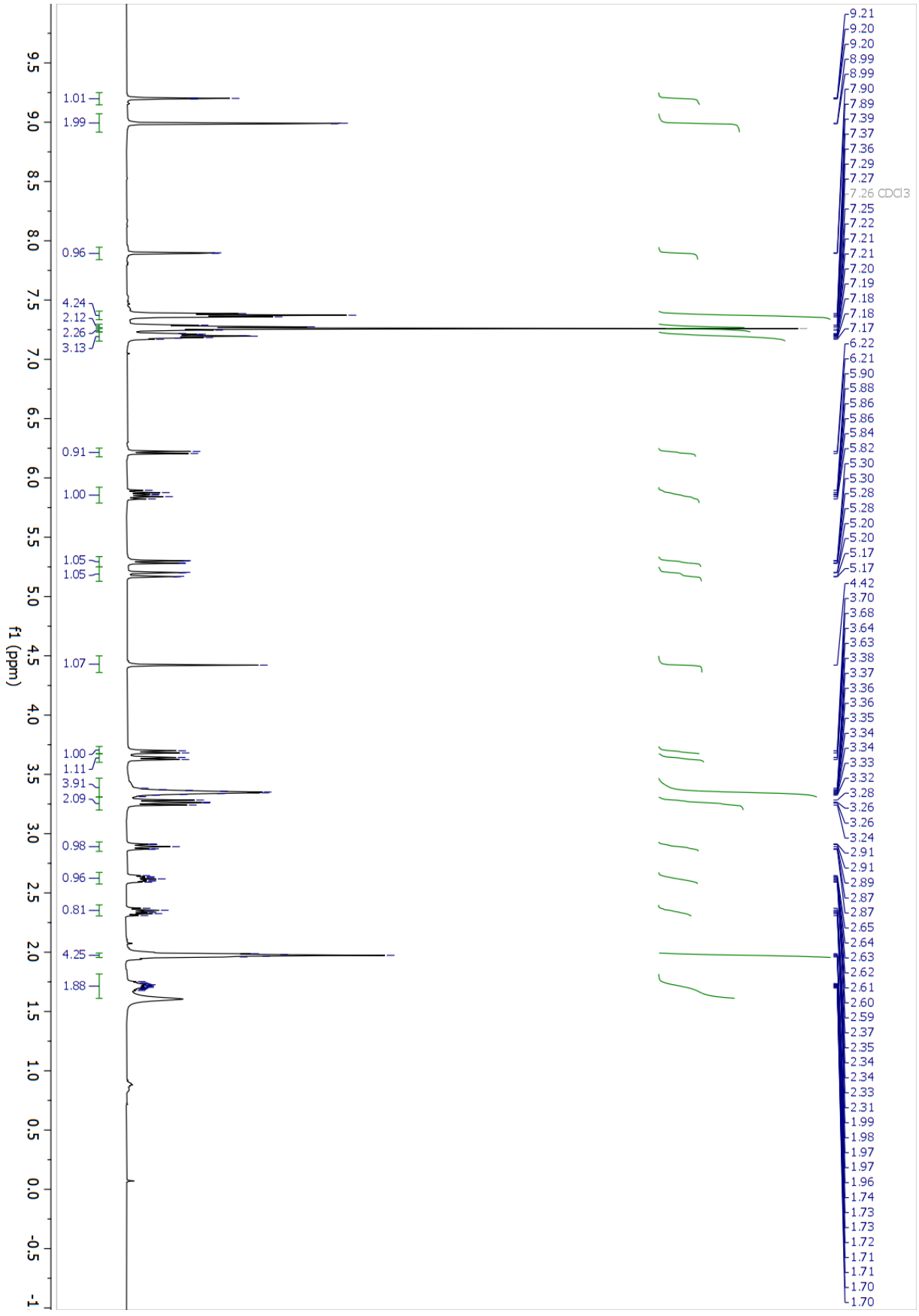
^{13}C NMR (126 MHz, $CDCl_3$): δ:160.8, 148.7, 142.0, 142.0, 137.5, 136.7, 134.2, 129.4, 128.7, 128.7, 127.5, 127.4, 123.8, 122.4, 119.1, 106.4, 80.7, 77.9, 61.3, 60.9, 47.0, 46.9, 30.6, 29.7, 25.6.

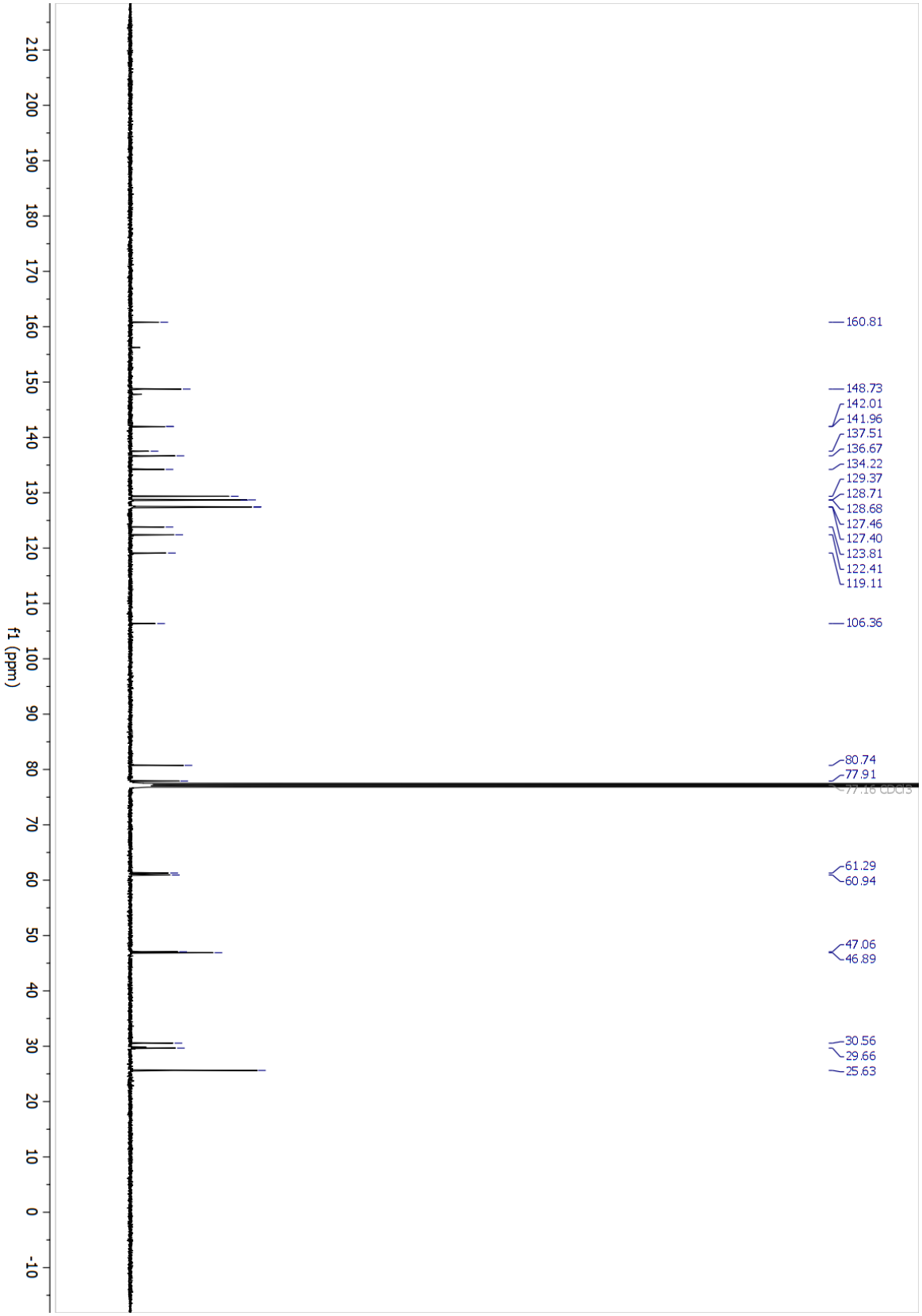
HRMS (ESI): Calculated for $C_{37}H_{37}N_5O_6$ $[M+H^+]$ =648.2817, found 648.2814

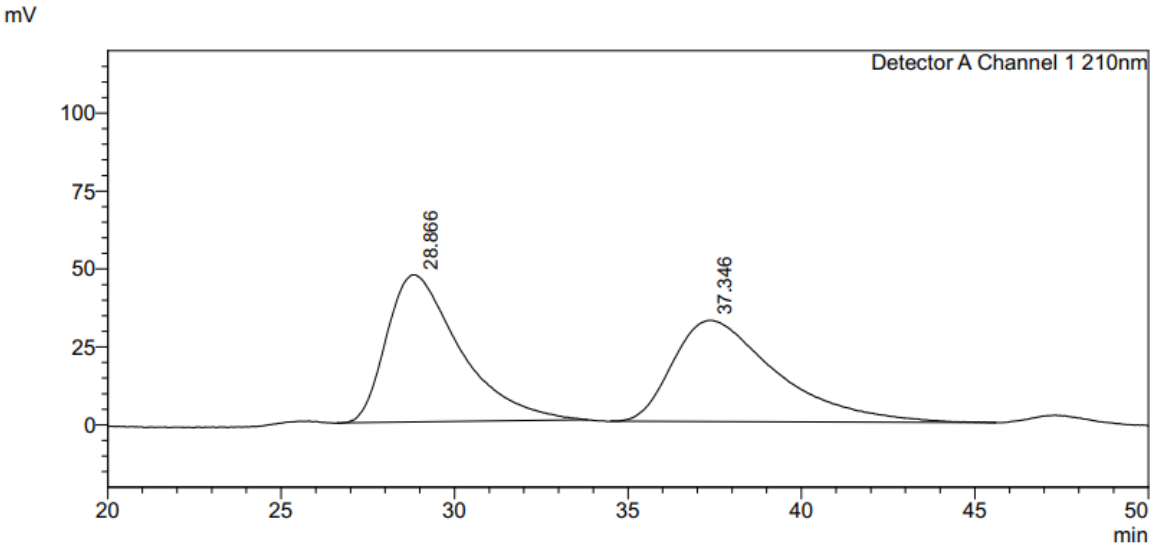
FTIR (neat): 1729, 1545, 1343, 1264, 1165, 731, 703 cm^{-1}

$[\alpha]_D^{28}$= -9.1^0 (c = 0.33, $CHCl_3$)

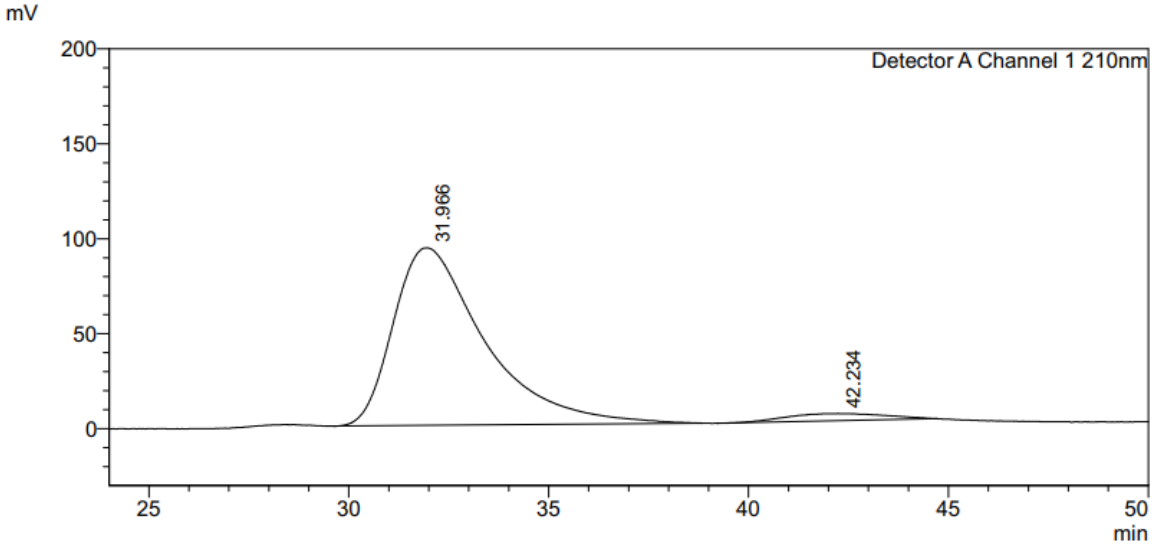
HPLC (Phenomenex Cellulose column, hexane:*i*-PrOH = 85:15, 1.0 mL/min, 210 nm): *ee*= 90%


f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.01
1.99
0.96
4.24
2.12
2.26
3.13
0.91
1.00
1.05
1.05
1.07
1.00
1.11
3.91
2.09
0.98
0.96
0.81
4.25
1.88
9.21
9.20
9.20
8.99
8.99
7.90
7.89
7.39
7.37
7.36
7.29
7.27
7.26 CDCl3
7.25
7.22
7.21
7.21
7.20
7.19
7.18
7.18
7.17
6.22
6.21
5.90
5.88
5.86
5.86
5.84
5.82
5.30
5.30
5.28
5.28
5.20
5.20
5.17
5.17
4.42
3.70
3.68
3.64
3.63
3.38
3.37
3.36
3.36
3.35
3.34
3.34
3.33
3.32
3.28
3.26
3.26
3.24
2.91
2.91
2.89
2.87
2.87
2.65
2.64
2.63
2.62
2.61
2.60
2.59
2.37
2.35
2.34
2.34
2.33
2.31
1.99
1.98
1.97
1.97
1.96
1.74
1.73
1.73
1.72
1.71
1.71
1.70
1.70


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
160.81
148.73
142.01
141.96
137.51
136.67
134.22
129.37
128.71
128.68
127.46
127.40
123.81
122.41
119.11
106.36
80.74
77.91
77.16 CDCl3
61.29
60.94
47.06
46.89
30.56
29.66
25.63

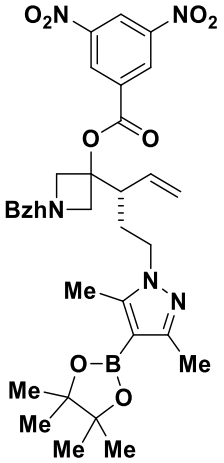


Peak#	Ret. Time	Area	Height	Area%
1	28.866	6957533	47190	50.744
2	37.346	6753634	32432	49.256
Total		13711167	79622	100.000



Peak#	Ret. Time	Area	Height	Area%
1	31.966	14861304	93428	95.728
2	42.234	663207	3809	4.272
Total		15524512	97236	100.000

(5r) (S)-1-benzhydryl-3-(5-(3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)pent-1-en-3-yl)azetidin-3-yl 3,5-dinitrobenzoate



Procedure

azetidinol **4r** (59.1mg, 0.112 mmol, 100 mol%) was subjected to general procedure **F**. The title compound was obtained in 50% yield (40 mg, 0.056 mmol) as a pale yellow oil after isolation by flash column chromatography (SiO_2, hexane: ethyl acetate = 3:1).

TLC (SiO_2) R_f = 0.73 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.15 (t, *J* = 2.2 Hz, 1H), 8.97 (d, *J* = 2.1 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 4H), 7.23 – 7.19 (m, 3H), 7.18 (m, 1H), 7.12 (td, *J* = 7.4, 4.8 Hz, 2H), 5.88 – 5.76 (m, 1H), 5.26 (dd, *J* = 10.1, 1.7 Hz, 1H), 5.16 (d, *J* = 16.9 Hz, 1H), 4.35 (s, 1H), 3.92 (ddd, *J* = 13.5, 8.8, 4.5 Hz, 1H), 3.81 (dt, *J* = 13.8, 8.0 Hz, 1H), 3.62 (d, *J* = 9.0 Hz, 1H), 3.56 (d, *J* = 9.0 Hz, 1H), 3.18 (dd, *J* = 17.7, 9.0 Hz, 2H), 2.87 – 2.79 (m, 1H), 2.38 – 2.28 (m, 1H), 2.27 (s, 3H), 2.09 (s, 3H), 1.75 (tdd, *J* = 13.0, 8.2, 4.5 Hz, 1H), 1.21 (s, 12H).

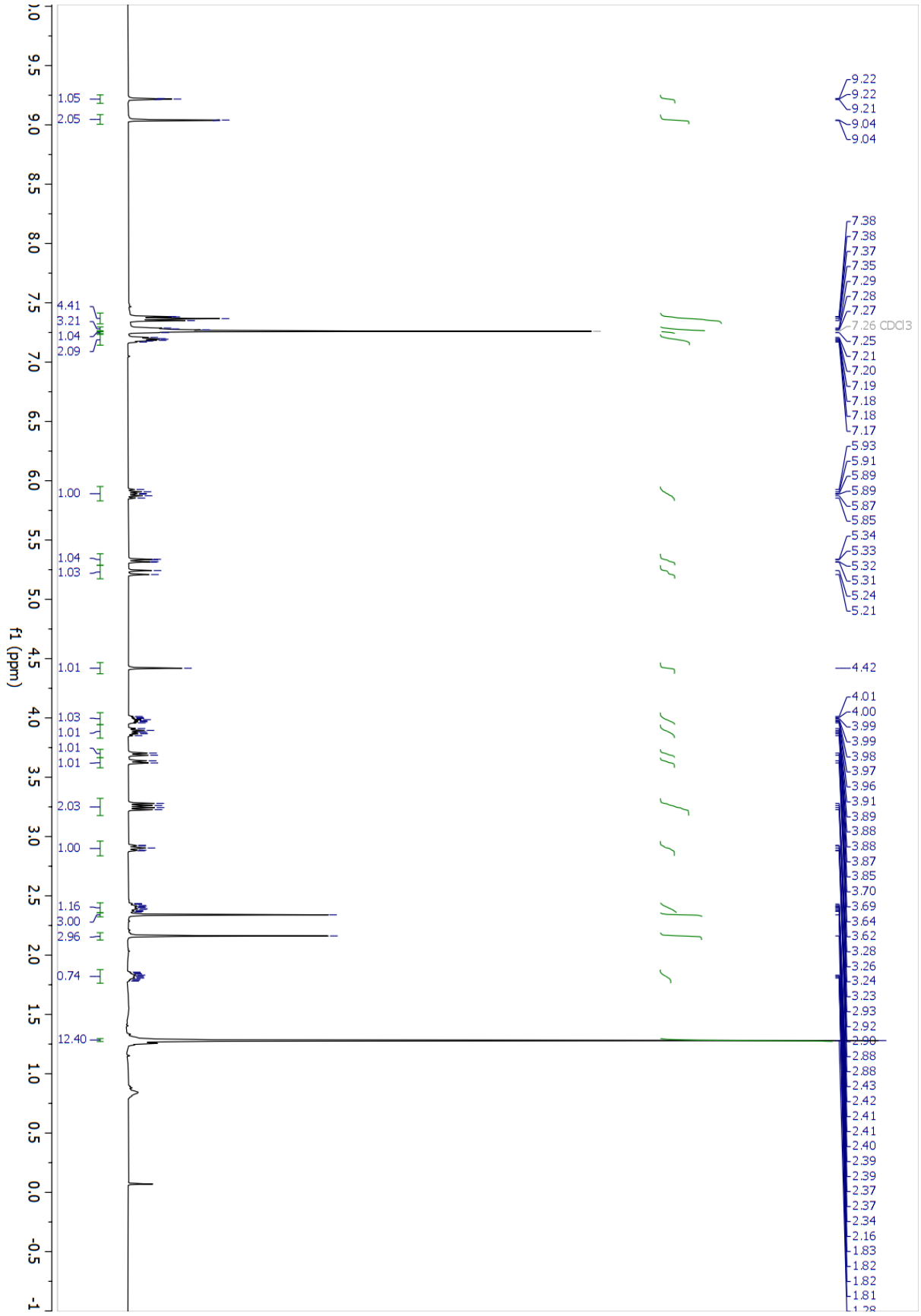
^{13}C NMR (126 MHz, $CDCl_3$): δ: 160.6, 154.5, 148.6, 146.7, 141.7, 141.6, 135.8, 134.0, 129.3, 128.5, 128.4, 127.2, 127.2, 127.2, 127.1, 122.3, 119.4, 82.4, 80.0, 77.6, 61.1, 60.5, 46.0, 45.3, 28.6, 24.8, 24.8, 13.7, 11.1.

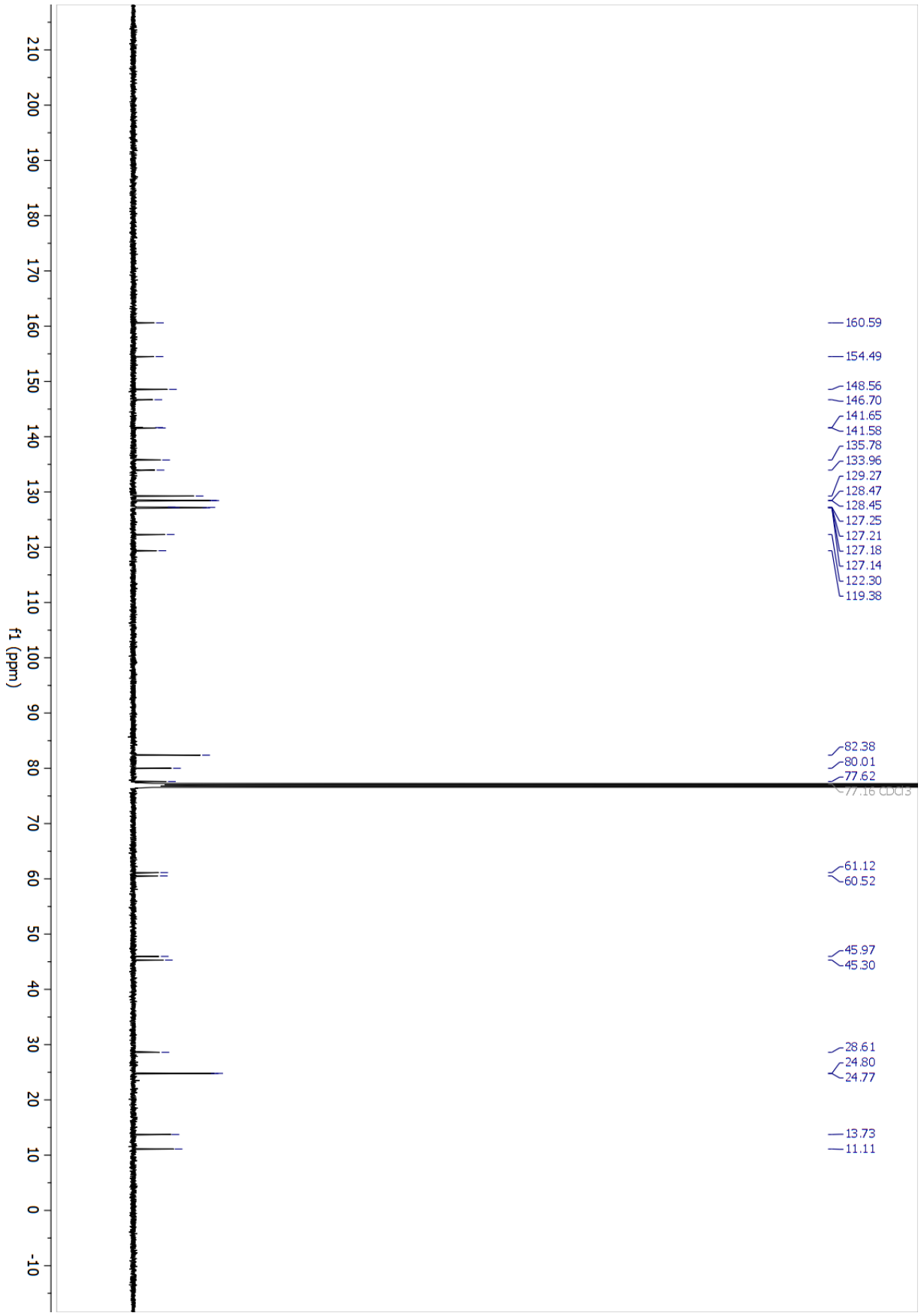
HRMS (ESI): Calculated for $C_{39}H_{44}BN_5O_8$ [M+H$^+$] =721.3392, found 721.3391

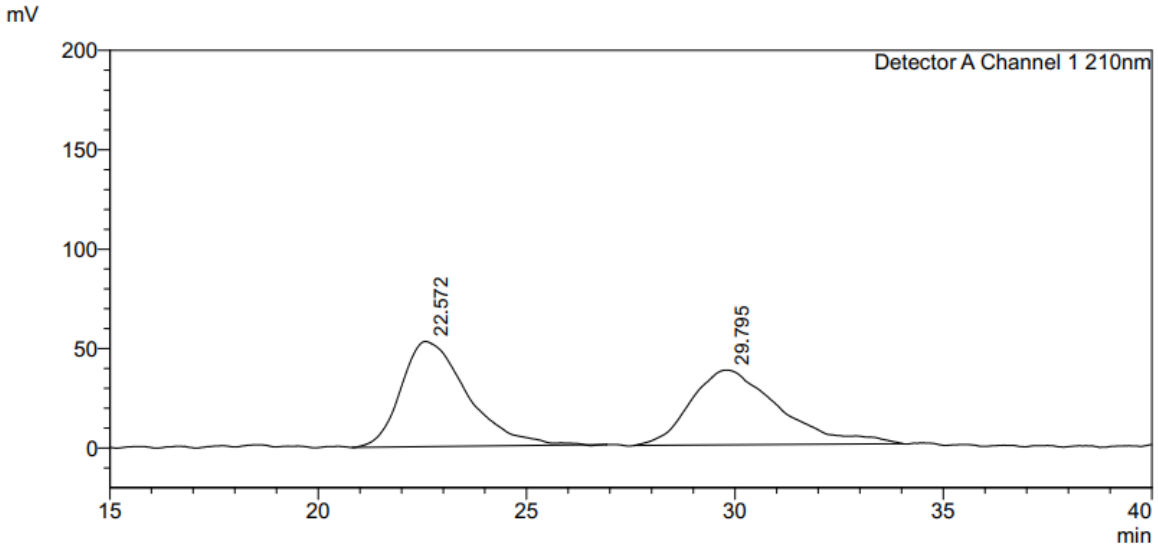
FTIR (neat): 2924, 1731, 1547, 1344, 1287, 1165, 730 cm^{-1}

$[\alpha]_D^{28}$= -14.5^0 (c = 0.69, $CHCl_3$)

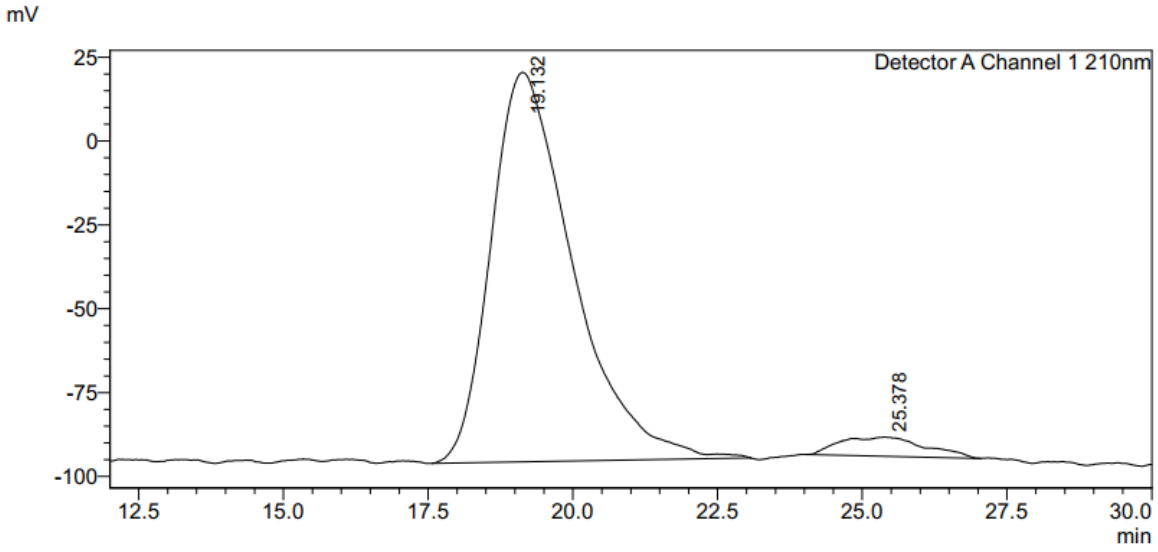
HPLC (Chiracel column OD-H, Hexane:2-PrOH = 95:05, 1 mL/min, 210 nm): *ee*= 90%


f1 (ppm)
1.05
2.05
4.41
3.21
1.04
2.09
1.00
1.04
1.03
1.01
1.03
1.01
1.01
1.01
2.03
1.00
1.16
3.00
2.96
0.74
12.40
9.22
9.22
9.21
9.04
9.04
7.38
7.38
7.37
7.35
7.29
7.28
7.27
7.26 CDCl3
7.25
7.21
7.20
7.19
7.18
7.18
7.17
5.93
5.91
5.89
5.89
5.87
5.85
5.34
5.33
5.32
5.31
5.24
5.21
4.42
4.01
4.00
3.99
3.99
3.98
3.97
3.96
3.91
3.89
3.88
3.88
3.87
3.85
3.70
3.69
3.64
3.62
3.28
3.26
3.24
3.23
2.93
2.92
2.90
2.88
2.88
2.43
2.42
2.41
2.41
2.40
2.39
2.39
2.37
2.37
2.34
2.16
1.83
1.82
1.82
1.81


160.59
154.49
148.56
146.70
141.65
141.58
135.78
133.96
129.27
128.47
128.45
127.25
127.21
127.18
127.14
122.30
119.38
82.38
80.01
77.62
77.16 CDCl3
61.12
60.52
45.97
45.30
28.61
24.80
24.77
13.73
11.11
f1 (ppm)

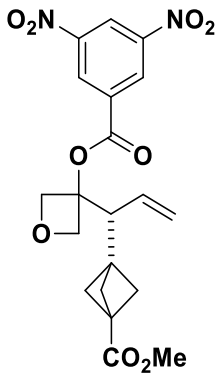


Peak#	Ret. Time	Area	Height	Area%
1	22.572	5841818	52953	51.215
2	29.795	5564643	37610	48.785
Total		11406461	90562	100.000



Peak#	Ret. Time	Area	Height	Area%
1	19.132	11437893	116093	95.163
2	25.378	581421	5669	4.837
Total		12019315	121762	100.000

(5t) methyl (R)-3-(1-(3-((3,5-dinitrobenzoyl)oxy)oxetan-3-yl)allyl)bicyclo[1.1.1]pentane-1-carboxylate



Procedure

oxetanol **3t** (22.0 mg, 0.090 mmol, 100 mol%) was subjected to general procedure **F**. The title compound was obtained in 68% yield (27.2 mg, 0.061 mmol) as a pale yellow solid after isolation by flash column chromatography (SiO_2, hexane: ethyl acetate = 3:1).

TLC (SiO_2): R_f = 0.54 (hexanes: ethyl acetate = 1:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (t, J = 2.1 Hz, 1H), 9.13 (d, J = 2.1 Hz, 2H), 5.88 (dt, J = 16.8, 10.0 Hz, 1H), 5.37 (dd, J = 10.1, 1.5 Hz, 1H), 4.95 (d, J = 7.9 Hz, 1H), 4.91 – 4.81 (m, 3H), 3.63 (s, 3H), 3.18 (d, J = 9.8 Hz, 1H), 1.99 (qd, J = 9.6, 1.7 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 160.7, 148.7, 133.1, 132.1, 129.1, 122.7, 120.9, 83.8, 78.9, 51.6, 51.5, 46.8, 38.9, 38.7.

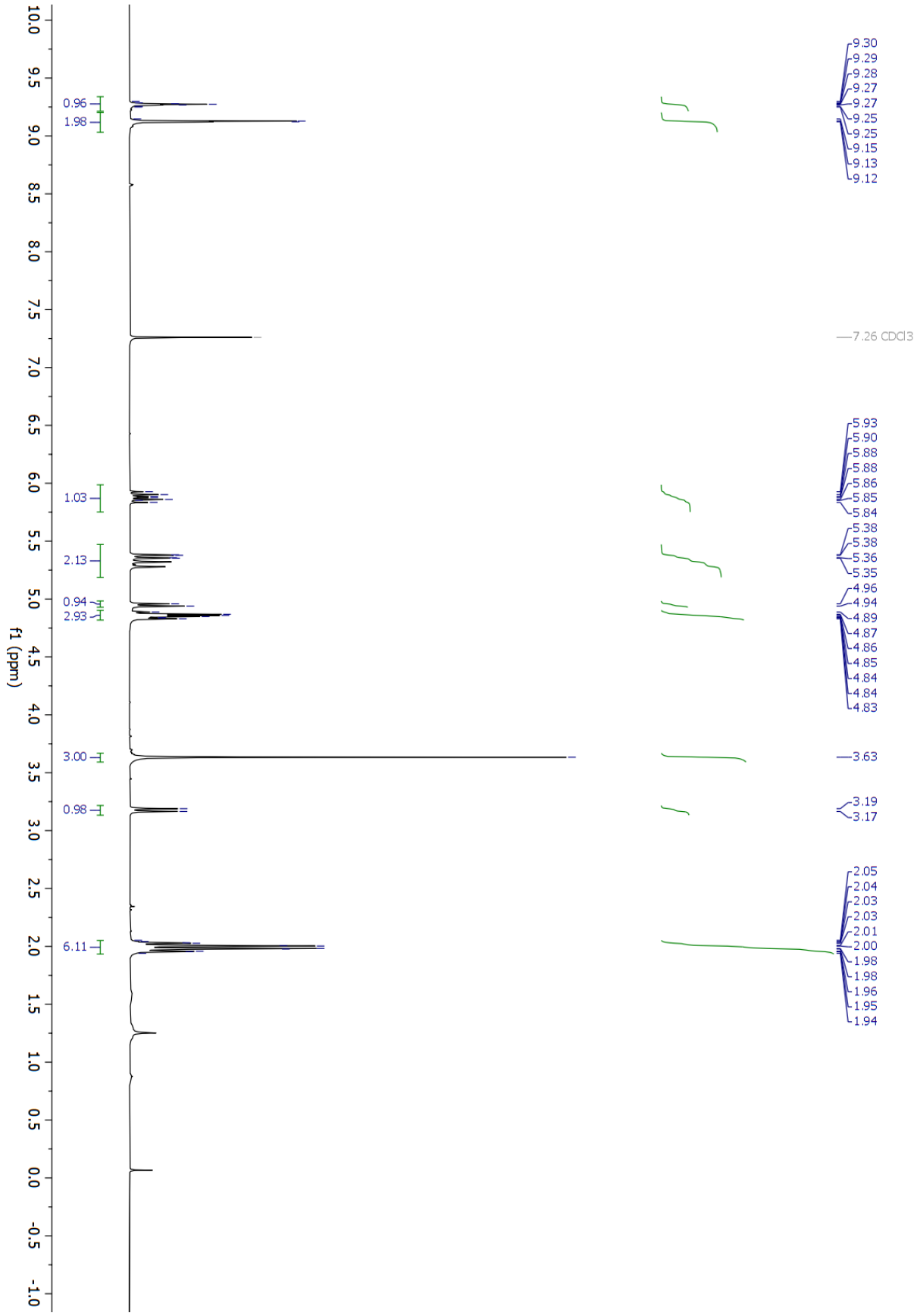
HRMS (CI): Calculated for $C_{20}H_{20}N_2O_9$ [M+H]= 433.1247, found= 433.1250

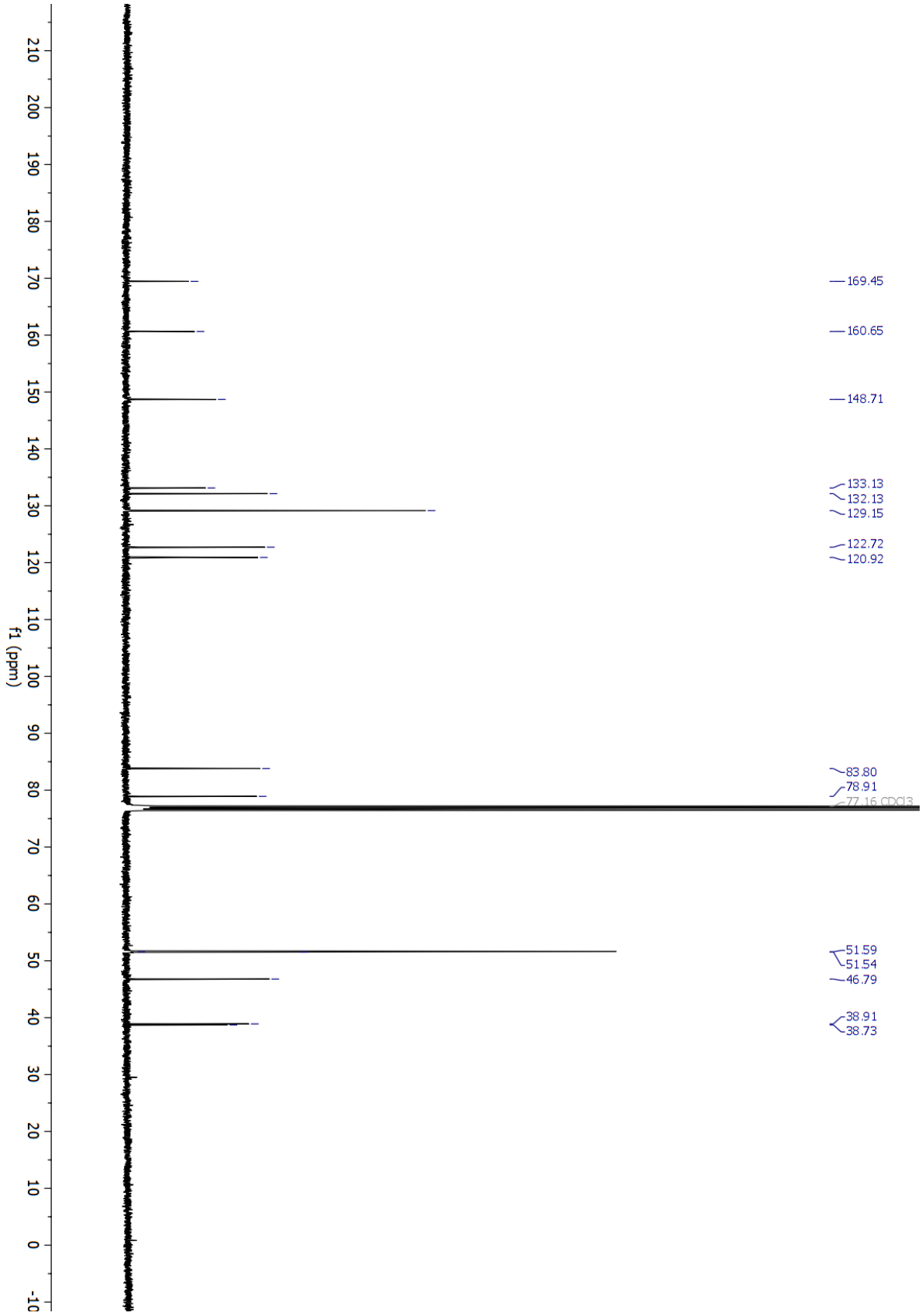
FTIR (neat): 3420, 3012, 2916, 2886, 1734, 1654, 1606, 1525, 1312, 1221, 1137, 1120, 1080, 656 cm^{-1}

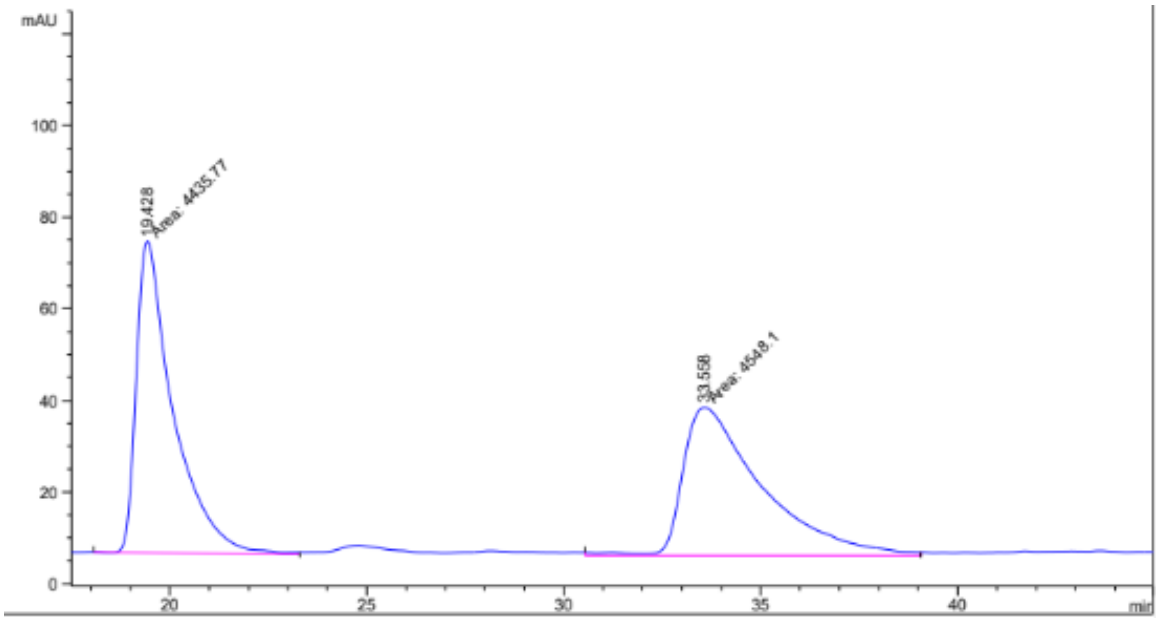
$[\alpha]_D^{28}$= -45.5^0 (c = 0.1, $CHCl_3$)

MP: 110-112 ^{0}C

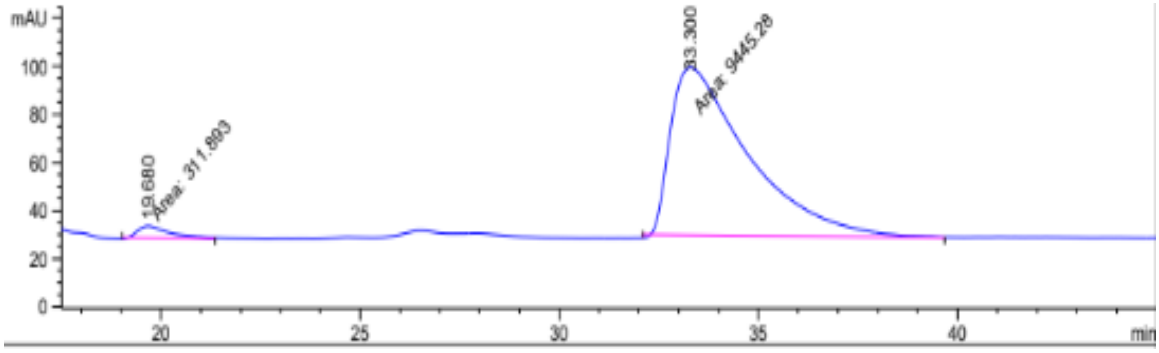
HPLC (Chiralcel column OD-H, hexane:*i*-PrOH = 95:05, 1 mL/min, 210 nm): *ee*= 93%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
0.96
1.98
1.03
2.13
0.94
2.93
3.00
0.98
6.11
9.30
9.29
9.28
9.27
9.27
9.25
9.25
9.15
9.13
9.12
7.26 CDCl3
5.93
5.90
5.88
5.88
5.86
5.85
5.84
5.38
5.38
5.36
5.35
4.96
4.94
4.89
4.87
4.86
4.85
4.84
4.84
4.83
3.63
3.19
3.17
2.05
2.04
2.03
2.03
2.01
2.00
1.98
1.98
1.96
1.95
1.94


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
169.45
160.65
148.71
133.13
132.13
129.15
122.72
120.92
83.80
78.91
77.16 CDCl3
51.59
51.54
46.79
38.91
38.73

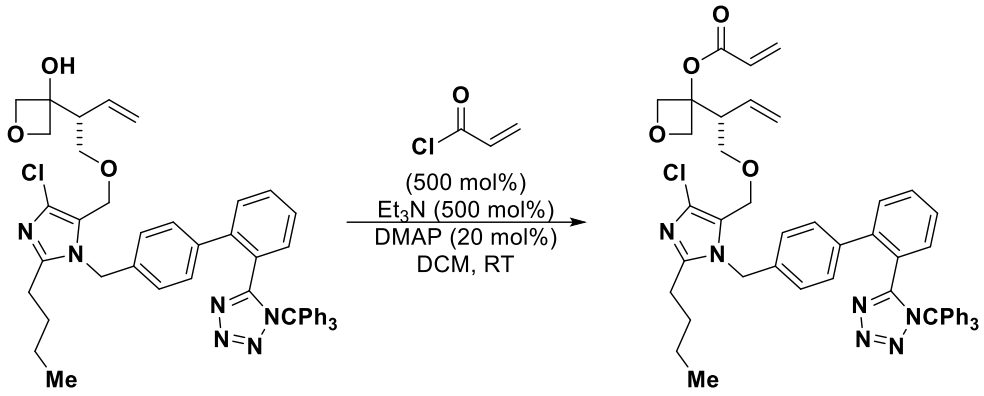


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.428	MM	1.0872	4435.77197	68.00037	49.3748
2	33.558	MM	2.3411	4548.09766	32.37852	50.6252



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.680	MM	1.0194	311.89301	5.09907	3.1965
2	33.300	MM	2.2626	9445.28418	69.57464	96.8035

(5v) (R)-3-(1-((2-butyl-4-chloro-1-((2'-(1-trityl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1H-imidazol-5-yl)methoxy)but-3-en-2-yl)oxetan-3-yl acrylate



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with oxetanol **3v** (50.0 mg, 0.063 mmol, 100 mol%) and 4-dimethylaminopyridine (1.0 mg, 0.006 mmol, 10 mol%). The flask was purged with argon and anhydrous dichloromethane (1.26mL, 0.05 M) was added. followed by triethylamine (44 µL, 0.316 mmol, 500 mol%), and acryloyl chloride (25 µL, 0.316 mmol, 500 mol%). The reaction was stirred at ambient temperature for 14 hours. The reaction solution was diluted with dichloromethane and was washed with water, then brine. The organic layer was then separated and dried over anhydrous sodium sulfate. The liquid was passed through a fritted filter into a round-bottom flask and was concentrated *in vacuo*. The residue was directly subjected to flash column chromatography (SiO_2, hexane: ethyl acetate = 5:1-2:1). **5v** was obtained in 37% yield (19.7 mg, 0.023 mmols).

TLC (SiO_2): Rf = 0.44 (hexanes: ethyl acetate = 2:1)

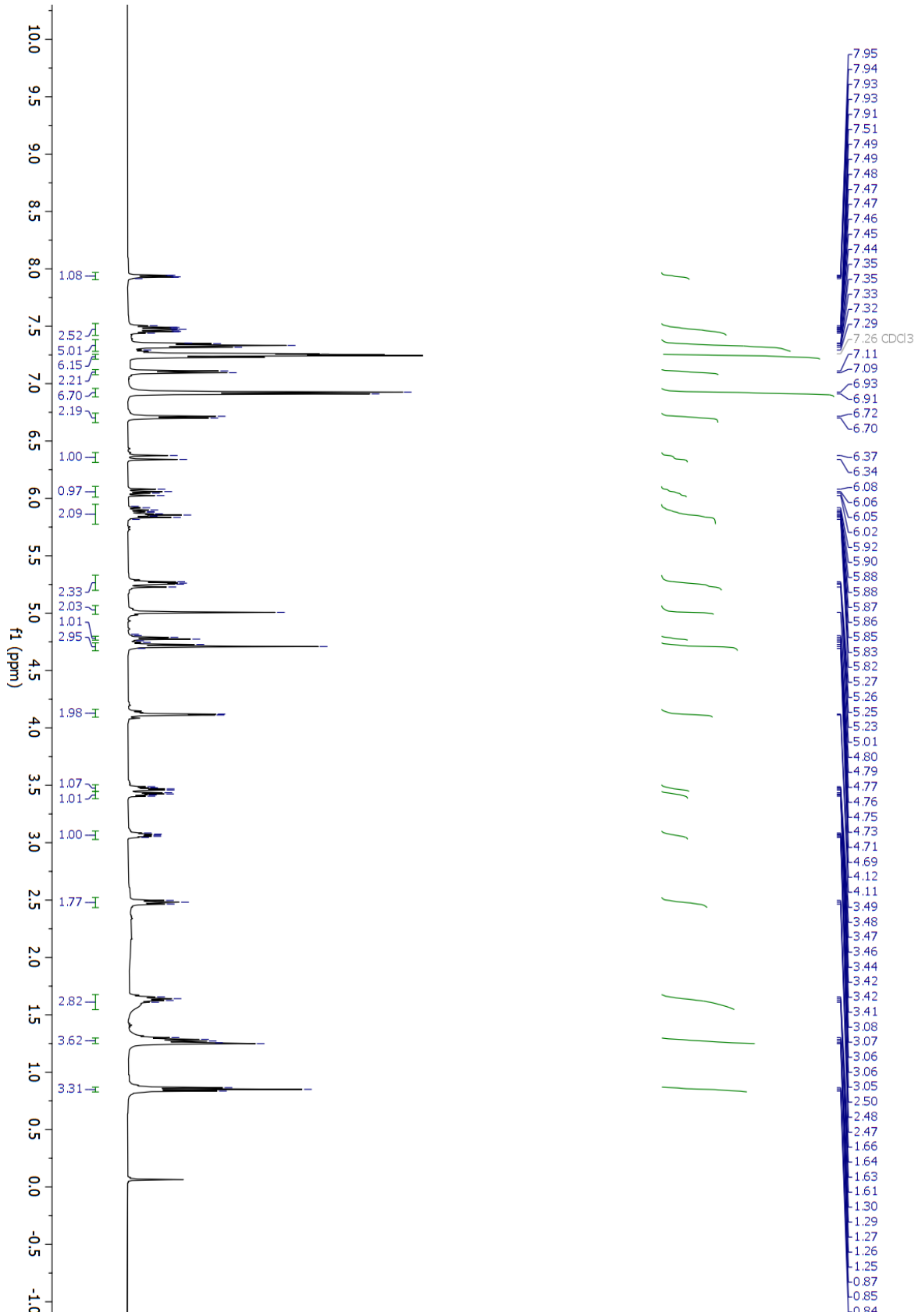
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, J = 7.3, 1.6 Hz, 1H), 7.52 – 7.43 (m, 3H), 7.33 (t, J = 7.8 Hz, 5H), 7.10 (d, J = 7.9 Hz, 3H), 6.92 (d, J = 7.8 Hz, 8H), 6.71 (d, J = 7.8 Hz, 3H), 6.36 (d, J = 17.3 Hz, 1H), 6.05 (dd, J = 17.3, 10.4 Hz, 1H), 5.94 – 5.82 (m, 2H), 5.39 – 5.13 (m, 2H), 5.01 (s, 2H), 4.78 (d, J = 7.8 Hz, 1H), 4.72 (d, J = 9.1 Hz, 3H), 4.12 (d, J = 3.9 Hz, 2H), 3.47 (dd, J = 9.7, 4.6 Hz, 1H), 3.42 (dd, J = 9.7, 5.4 Hz, 1H), 3.06 (dt, J = 9.5, 5.0 Hz, 1H), 2.48 (t, J = 7.8 Hz, 3H), 1.63 (q, J = 7.7 Hz, 3H), 1.34 – 1.17 (m, 5H), 0.85 (t, J = 7.3 Hz, 3H).

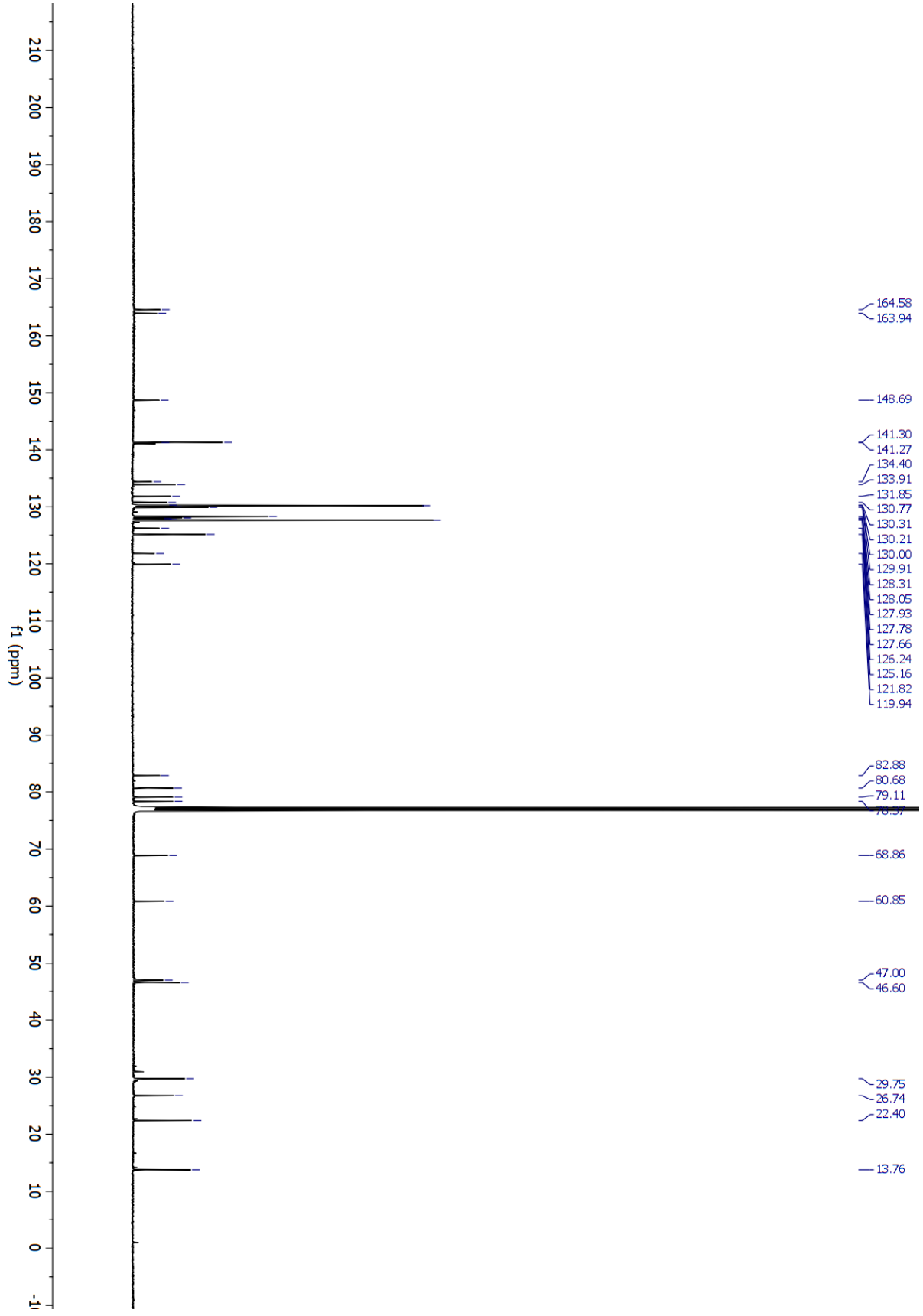
^{13}C NMR (126 MHz, $CDCl_3$): δ 164.6, 163.9, 148.7, 141.3, 141.3, 134.4, 133.9, 131.9, 130.8, 130.3, 130.2, 130.0, 129.9, 128.3, 128.1, 127.9, 127.8, 127.7, 126.2, 125.2, 121.8, 119.9, 82.9, 80.7, 79.1, 78.4, 68.9, 60.9, 47.0, 46.6, 29.8, 26.7, 22.4, 13.8.

FTIR (neat): 3384, 3071, 2966, 2924, 2870, 2356, 1740, 1720, 1430, 1410, 798, 784, 758, 748 cm^{-1}

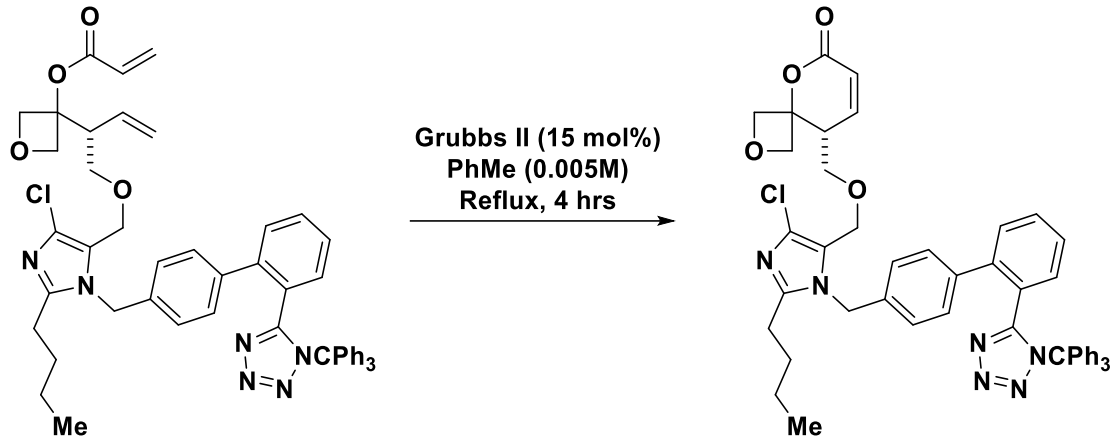
$[\alpha]_D^{28}$= -22.0(c 0.33, $CHCl_3$)

HRMS (ESI): Calculated for $C_{51}H_{49}ClN_6O_4$ [M+H+] =845.3577, found= 845.3579


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.08
2.52
5.01
6.15
2.21
6.70
2.19
1.00
0.97
2.09
2.33
2.03
1.01
2.95
1.98
1.07
1.01
1.00
1.77
2.82
3.62
3.31
7.95
7.94
7.93
7.93
7.91
7.51
7.49
7.49
7.48
7.47
7.47
7.46
7.45
7.44
7.35
7.35
7.33
7.32
7.29
7.26 CDCl3
7.11
7.09
6.93
6.91
6.72
6.70
6.37
6.34
6.08
6.06
6.05
6.02
5.92
5.90
5.88
5.88
5.87
5.86
5.85
5.83
5.82
5.27
5.26
5.25
5.23
5.01
4.80
4.79
4.77
4.76
4.75
4.73
4.71
4.69
4.12
4.11
3.49
3.48
3.47
3.46
3.44
3.42
3.42
3.41
3.08
3.07
3.06
3.06
3.05
2.50
2.48
2.47
1.66
1.64
1.63
1.61
1.30
1.29
1.27
1.26
1.25
0.87
0.85


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
164.58
163.94
148.69
141.30
141.27
134.40
133.91
131.85
130.77
130.31
130.21
130.00
129.91
128.31
128.05
127.93
127.78
127.66
126.24
125.16
121.82
119.94
82.88
80.68
79.11
68.86
60.85
47.00
46.60
29.75
26.74
22.40
13.76

(6v) (R)-9-(((2-butyl-4-chloro-1-((2'-(1-trityl-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1H-imidazol-5-yl)methoxy)methyl)-2,5-dioxaspiro[3.5]non-7-en-6-one



Procedure

An oven-dried round bottom flask equipped with a magnetic stir bar was charged with acrylate **5v** (8.0 mg, 0.009 mmol, 100 mol%). The flask was purged with argon and anhydrous toluene (0.8 mL) was added. Grubb's II (1.1 mg, 0.0013 mmol, 15 mol%) was added as a solution in toluene (0.8 ml). The reaction was heated at reflux for 4 hours. Upon completion the reaction was cooled to ambient temperature and concentrated *in vacuo*. The residue was directly subjected to flash column chromatography (SiO_2, hexane: ethyl acetate = 5:1-2:1). **6v** was obtained in 86% yield (6.3 mg, 0.0077 mmols).

TLC (SiO_2): Rf = 0.17 (hexanes: ethyl acetate = 2:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, J = 7.3, 1.7 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.34 (t, J = 7.7 Hz, 4H), 7.29 – 7.18 (m, 8H), 7.11 (d, J = 7.9 Hz, 2H), 6.93 (d, J = 7.9 Hz, 6H), 6.72 (d, J = 7.8 Hz, 2H), 6.36 (d, J = 17.2 Hz, 1H), 6.15 – 5.97 (m, 1H), 5.35 – 5.16 (m, 2H), 5.01 (s, 2H), 4.83 – 4.68 (m, 4H), 4.17 – 4.08 (m, 2H), 3.51 – 3.39 (m, 2H), 3.07 (dt, J = 9.5, 5.0 Hz, 1H), 2.52 – 2.44 (m, 2H), 1.65 (p, J = 7.8 Hz, 2H), 1.35 – 1.24 (m, 4H), 0.86 (t, J = 7.3 Hz, 3H).

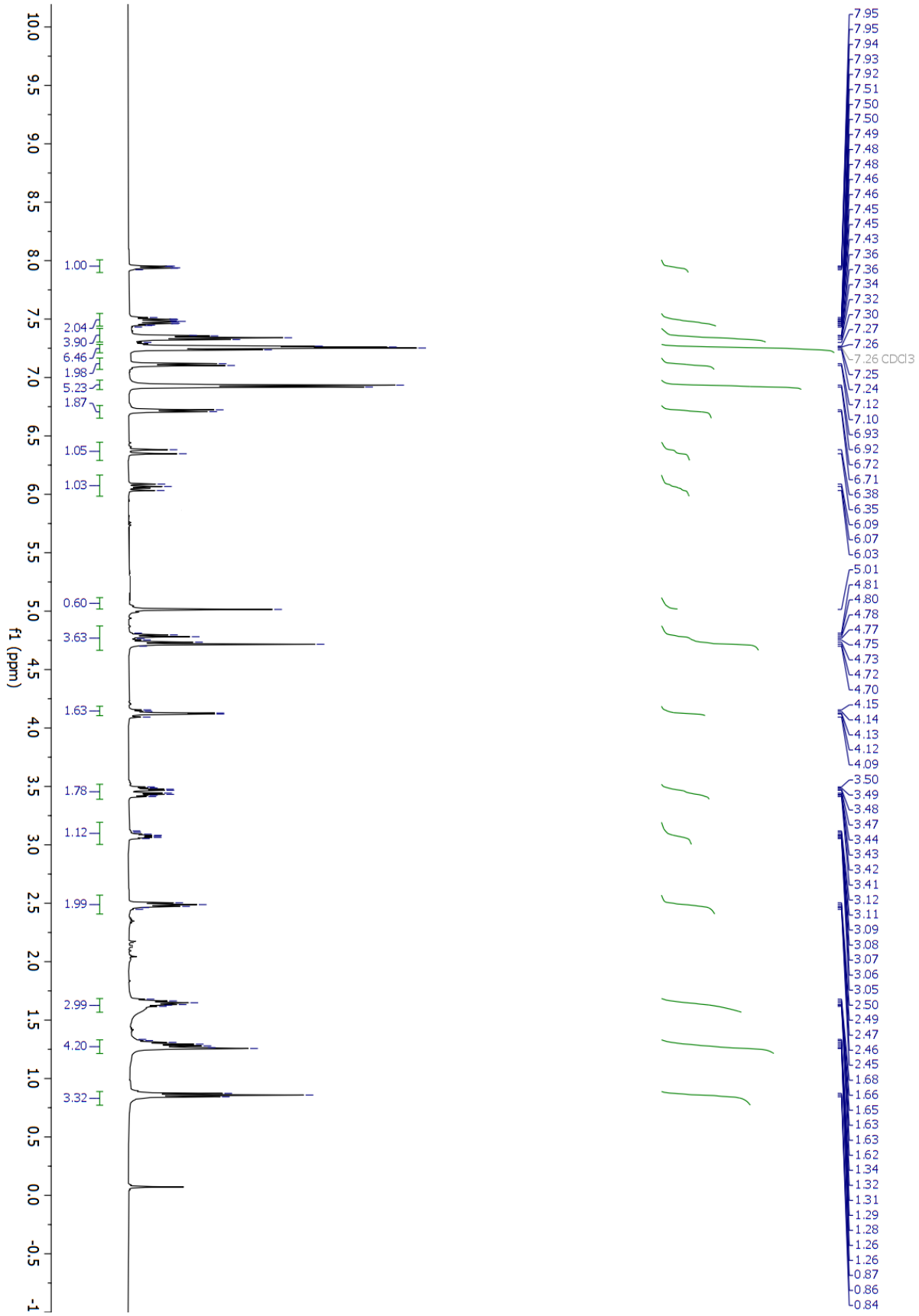
^{13}C NMR (126 MHz, $CDCl_3$): δ 163.9, 161.9, 149.1, 144.5, 141.2, 141.0, 134.2, 130.6, 130.3, 129.8, 128.2, 127.8, 127.7, 127.6, 126.1, 124.9, 122.1, 121.2, 82.8, 81.8, 81.1, 78.20, 77.5, 66.7, 60.8, 47.0, 39.8, 29.6, 22.3, 13.6.

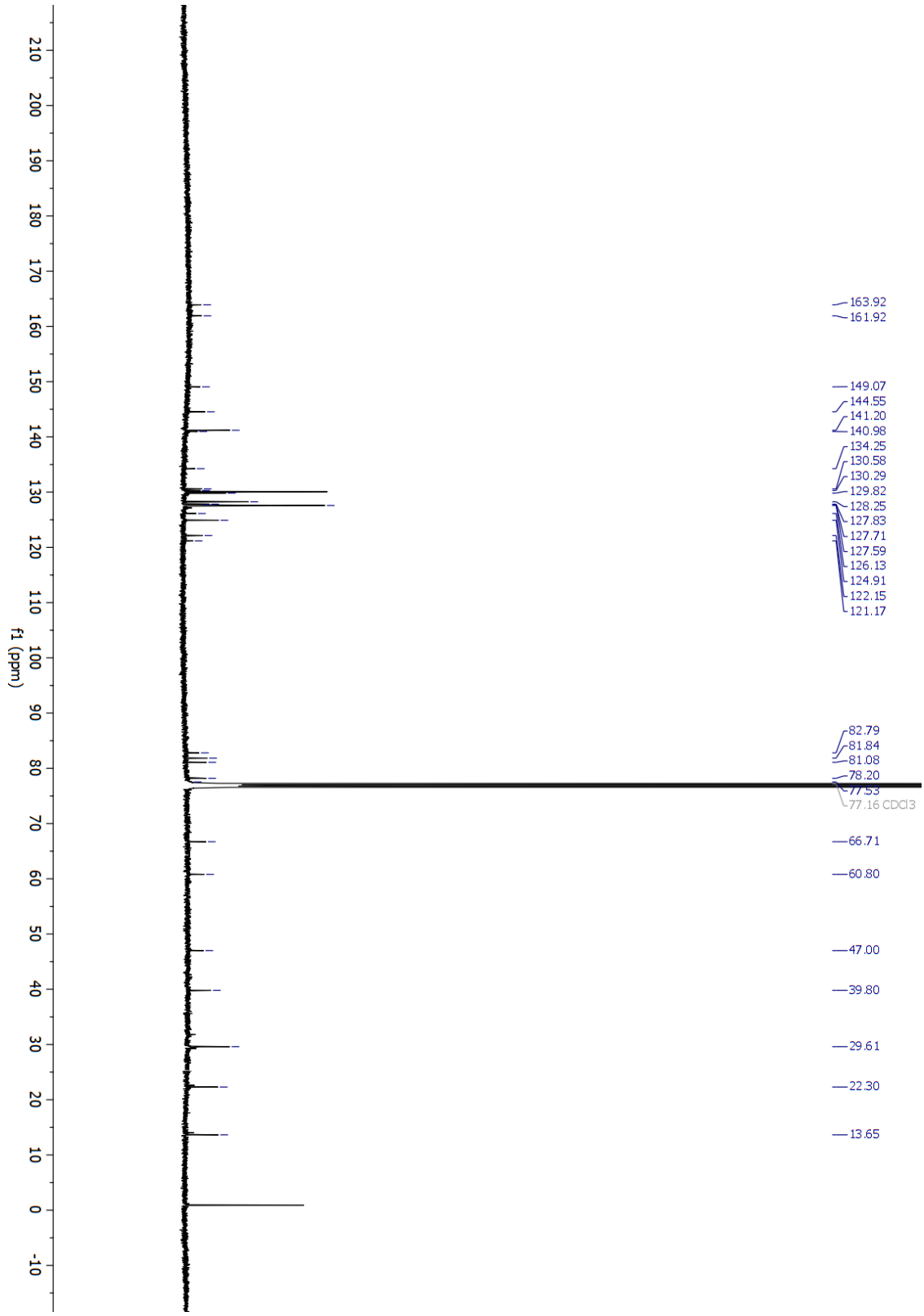
FTIR (neat): 3384, 3071, 2966, 2924, 2870, 2356, 1740, 1720, 1430, 1410, 1356,1159,784, 758, 748 cm^{-1}

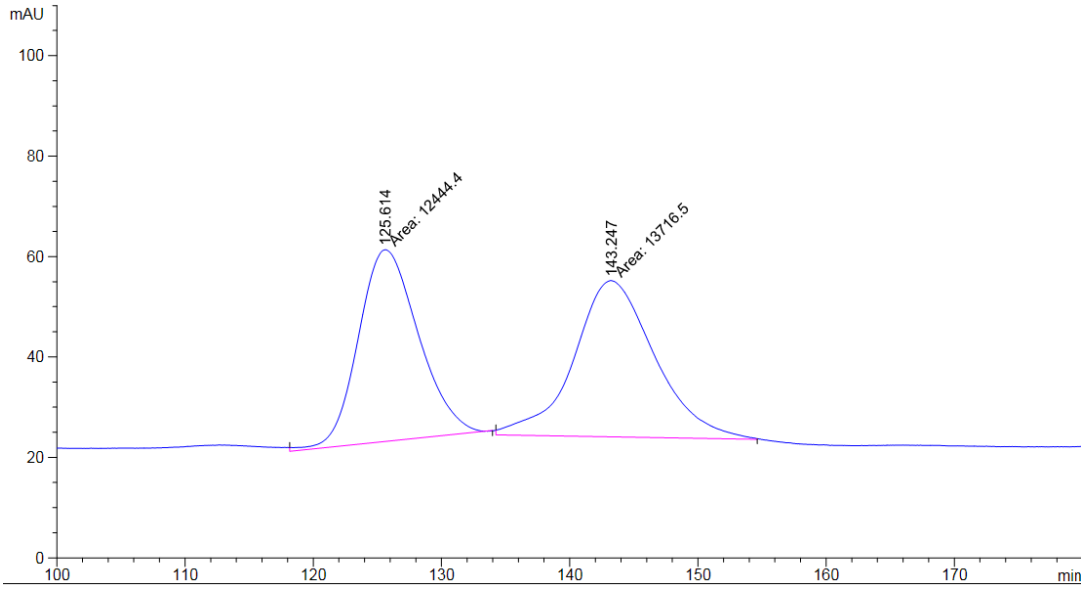
$[\alpha]_D^{28}$= -44.0(c 0.20, $CHCl_3$).

HRMS (ESI): Calculated for $C_{49}H_{45}ClN_6O_4$ $[M+H^+]$ =817.3264, found 817.3267

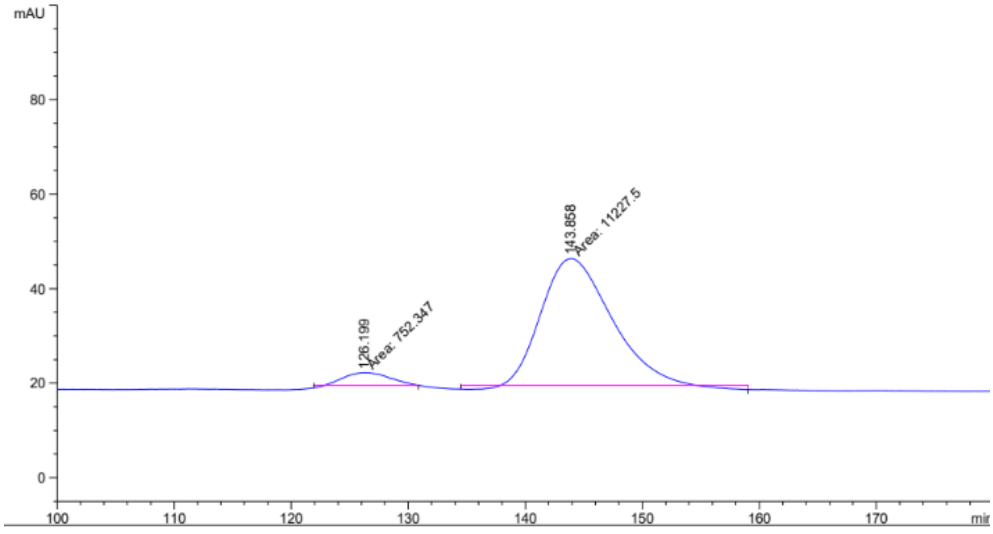
HPLC (Phenomenex Amylose column, hexane:*i*-PrOH = 67:33, 0.5 mL/min, 210 nm): *ee*= 88%


f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
1.00
2.04
3.90
6.46
1.98
5.23
1.87
1.05
1.03
0.60
3.63
1.63
1.78
1.12
1.99
2.99
4.20
3.32
7.95
7.95
7.94
7.93
7.92
7.51
7.50
7.50
7.49
7.48
7.48
7.46
7.46
7.45
7.45
7.43
7.36
7.36
7.34
7.32
7.30
7.27
7.26
7.26 CDCl3
7.25
7.24
7.12
7.10
6.93
6.92
6.72
6.71
6.38
6.35
6.09
6.07
6.03
5.01
4.81
4.80
4.78
4.77
4.75
4.73
4.72
4.70
4.15
4.14
4.13
4.12
4.09
3.50
3.49
3.48
3.47
3.44
3.43
3.42
3.41
3.12
3.11
3.09
3.08
3.07
3.06
3.05
2.50
2.49
2.47
2.46
2.45
1.68
1.66
1.65
1.63
1.63
1.62
1.34
1.32
1.31
1.29
1.28
1.26
1.26
0.87
0.86
0.84


f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
163.92
161.92
149.07
144.55
141.20
140.98
134.25
130.58
130.29
129.82
128.25
127.83
127.71
127.59
126.13
124.91
122.15
121.17
82.79
81.84
81.08
78.20
77.53
77.16 CDCl3
66.71
60.80
47.00
39.80
29.61
22.30
13.65



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	125.614	MM	5.4290	1.24444e4	38.20327	47.5686
2	143.247	MM	7.3390	1.37165e4	31.14963	52.4314



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	126.199	MM	4.5387	752.34747	2.76269	6.2801
2	143.858	MM	6.9690	1.12275e4	26.85105	93.7199

3.2f Single Crystal Diffraction Data

X-ray Experimental for **3a:** Crystals grew as clusters of colorless prisms by slow evaporation from dichloromethane. The data crystal was cut from a larger crystal and had approximate dimensions; 0.42 x 0.24 x 0.12 mm. The data were collected on a Rigaku Oxford Diffraction HyPix6000E Dual Source diffractometer using a μ-focus Cu Kα radiation source (λ = 1.5418Å) with collimating mirror monochromators. A total of 955 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 4 second per frame for frames collected with a detector offset of +/- 41.64° and 12 seconds per frame with frames collected with a detector offset of +/- 107.1°. The data were collected at 100 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table 1. Data collection, unit cell refinement and data reduction were performed using Rigaku Oxford Diffraction's CrysAlisPro V 1.171.40.71a.[57] The structure was solved by direct methods using SHELXT[8] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-2018/3.[59] Structure analysis was aided by use of the programs PLATON[60] and OLEX2.[61] Most hydrogen atoms on the carbon atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). The hydrogen atoms on the hydroxyl oxygen atom, O2, and the vinyl carbon atom, C7, were observed in a ΔF map and refined with isotropic displacement parameters. The absolute configuration was determined using the method of Flack[62] and confirmed using the Hooft y-parameter method, which resulted in a Hooft y-parameter of 0.09(4).[63]

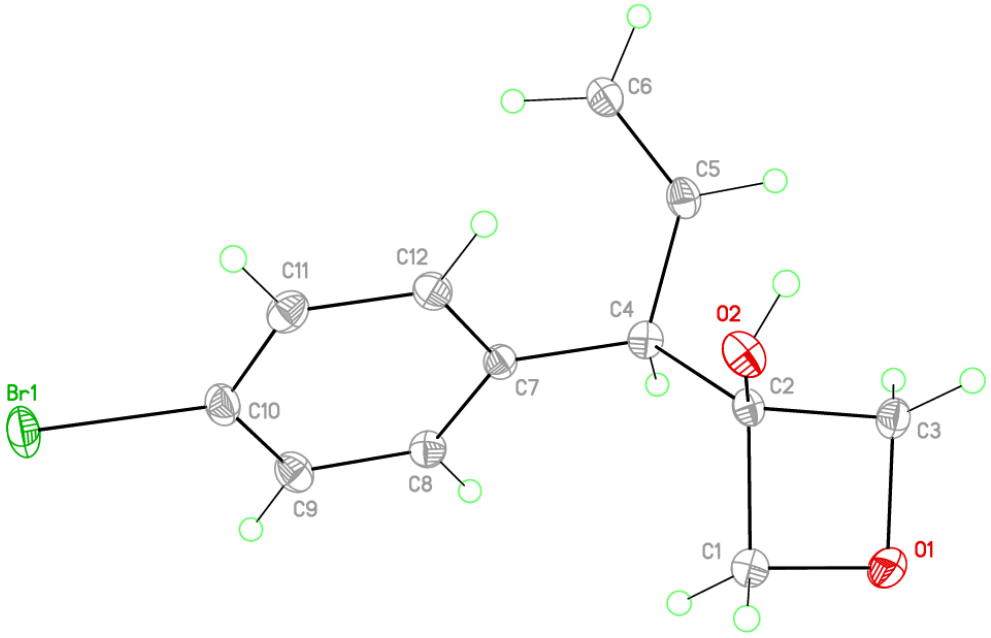
The function, $\Sigma w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.0449*P)^2 + (0.1054*P)]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.0654, with R(F) equal to

0.0251 and a goodness of fit, S, = 1.08. Definitions used for calculating R(F), $R_w(F^2)$ and the goodness of fit, S, are given below.[64] The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[65] All figures were generated using SHELXTL/PC.[66] Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found elsewhere.

Crystal data and structure refinement for **3a**

Empirical formula	C12 H13 Br O2	
Formula weight	269.13	
Temperature	100.03(11) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 5.26034(7) Å	a= 90°.
	b = 8.38912(8) Å	b= 98.1333(12)°.
	c = 12.65326(16) Å	g = 90°.
Volume	552.767(11) $Å^3$	
Z	2	
Density (calculated)	1.617 Mg/m^3	
Absorption coefficient	4.883 mm^{-1}	
F(000)	272	
Crystal size	0.288 x 0.241 x 0.088 mm^3	
Theta range for data collection	3.529 to 73.491°.	
Index ranges	-6<=h<=6, -10<=k<=10, -15<=l<=15	
Reflections collected	10369	
Independent reflections	2180 [R(int) = 0.0205]	
Completeness to theta = 67.684°	100.0 %	
Absorption correction	Gaussian and multi-scan	
Max. and min. transmission	1.000 and 0.331	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2180 / 1 / 148	
Goodness-of-fit on F^2	0.989	
Final R indices [I>2sigma(I)]	R1 = 0.0151, wR2 = 0.0378	
R indices (all data)	R1 = 0.0152, wR2 = 0.0379	
Absolute structure parameter	-0.029(8)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.214 and -0.207 $e.Å^{-3}$	

Figure 3.2. View of **3a** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



X-ray Experimental for **4a:** Crystals grew as clusters of colorless prisms by slow evaporation from dichloromethane. The data crystal was cut from a larger crystal and had approximate dimensions; 0.42 x 0.24 x 0.12 mm. The data were collected on a Rigaku Oxford Diffraction HyPix6000E Dual Source diffractometer using a μ-focus Cu Kα radiation source (λ = 1.5418Å) with collimating mirror monochromators. A total of 955 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 4 second per frame for frames collected with a detector offset of +/- 41.64° and 12 seconds per frame with frames collected with a detector offset of +/- 107.1°. The data were collected at 100 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table 1. Data collection, unit cell refinement and data reduction were performed using Rigaku Oxford Diffraction's CrysAlisPro V 1.171.40.71a.[57] The structure was solved by direct methods using SHELXT[58] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-2018/3.[59] Structure analysis was aided by use of the programs PLATON[60] and OLEX2.[61] Most hydrogen atoms on the carbon atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). The hydrogen atoms on the hydroxyl oxygen atom, O2, and the vinyl carbon atom, C7, were observed in a ΔF map and refined with isotropic displacement parameters. The absolute configuration was determined using the method of Flack[62] and confirmed using the Hooft y-parameter method, which resulted in a Hooft y-parameter of 0.09(4).[63]

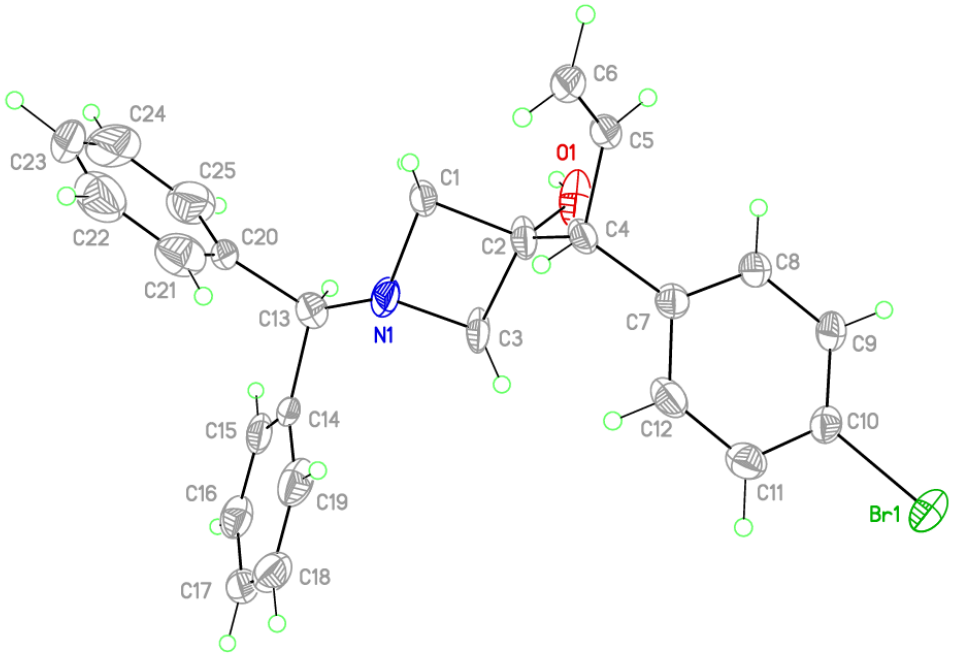
The function, $\Sigma w(|F_O|^2 - |F_C|^2)^2$, was minimized, where $w = 1/[(\sigma(F_O))^2 + (0.0449*P)^2 + (0.1054*P)]$ and $P = (|F_O|^2 + 2|F_C|^2)/3$. $R_w(F^2)$ refined to 0.0654, with R(F) equal to 0.0251 and a goodness of fit, S, = 1.08. Definitions used for calculating R(F), $R_w(F^2)$ and

the goodness of fit, S, are given below.[64] The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[65] All figures were generated using SHELXTL/PC.[66] Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found elsewhere.

Crystal data and structure refinement for **4a**.

Empirical formula	C25 H24 Br N O	
Formula weight	434.36	
Temperature	293(2) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 8.62243(12) Å	a= 90°.
	b = 5.75927(11) Å	b= 93.6461(13)°.
	c = 20.7836(3) Å	g = 90°.
Volume	1030.00(3) $Å^3$	
Z	2	
Density (calculated)	1.401 Mg/m^3	
Absorption coefficient	2.823 mm^{-1}	
F(000)	448	
Crystal size	0.45 x 0.119 x 0.09 mm^3	
Theta range for data collection	2.130 to 76.643°.	
Index ranges	-10<=h<=10, -6<=k<=7, -22<=l<=26	
Reflections collected	13324	
Independent reflections	3999 [R(int) = 0.0280]	
Completeness to theta = 67.684°	99.9 %	
Absorption correction	Gaussian and multi-scan	
Max. and min. transmission	1.000 and 0.479	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3999 / 37 / 257	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0423, wR2 = 0.1070	
R indices (all data)	R1 = 0.0424, wR2 = 0.1071	
Absolute structure parameter	0.02(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.084 and -0.570 $e.Å^{-3}$	

Figure 3.3. View of **4a** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



References

[1] Statistic refers to consumer goods produced in Germany in 2017: Schaub, T. Efficient Industrial Organic Synthesis and the Principles of Green Chemistry. Chem. Eur. J. 2021, 27, DOI: 10.1002/chem.202003544.

[2] For selected literature on ethanol production volumes and use as a C2 feedstock, see: (a) Kosaric, N.; Duvnjak, Z.; Farkas, A.; Sahm, H.; Bringer-Meyer, S.; Goebel, O.; Mayer, D. Ethanol. In Ullmann's Encyclopedia of Industrial Chemistry; Wiley-VCH Verlag GmbH & Co.: Weinheim, Germany, 2011; pp 333-403. (b) Renewable Fuels Association (RFA): http://www.ethanolrfa.org/ (accessed February 5, 2020).

[3] For selected reviews on sustainable chemical synthesis, see: (a) Petersen, G. R.; Bozell, J. J. Technology Development for the Production of Biobased Products from Biorefinery Carbohydrates – the US Department of Energy's "Top 10" Revisited. Green Chem. 2010, 12, 539-554. (b) Varma, R. S. Greener and Sustainable Trends in Synthesis of Organics and Nanomaterials. ACS Sustainable Chem. Eng. 2016, 4, 5866-5878. (c) Mika, L. T.; Cséfalvay, E.; Németh, Á. Catalytic Conversion of Carbohydrates to Initial Platform Chemicals: Chemistry and Sustainability. Chem Rev. 2018, 118, 505-613. (d) Gunukula, S.; Pendse, H. P.; DeSisto, W. J.; Wheeler, M. C. Heuristics To Guide the Development of Sustainable, Biomass-Derived, Platform Chemical Derivatives. ACS Sustainable Chem. Eng. 2018, 6, 5533-5539. (e) Gonzalez, M. A.; Takkellapati, S.; Tadele, K.; Li, T.; Varma, R. S. Framework Toward More Sustainable Chemical Synthesis Design – A Case Study of Organophophates. ACS Sustainable Chem. Eng. 2019, 7, 6744-6757.

[4] For a historical perspective on the Lebedev ethanol-to-butadiene process, see: Pomalaza, G.; Capron, M.; Ordomsky, V.; Dumeignil, F. Recent Breakthroughs in the Conversion of Ethanol to Butadiene. Catalysts 2016, 6, 203; https://doi.org/10.3390/catal6120203.

[5] For selected reviews on ethanol-to-polyethylene processes, see: (a) Collares-Queiroz, F. P.; Queiroz, A. U. B. Innovation and Industrial Trends in Bioplastics. Polym. Rev.

2009, 49, 65-78. (b) Iles, A.; Martin, A. N. Expanding Bioplastics Production: Sustainable Business Innovation in the Chemical Industry. J. Clean. Prod. 2013, 45, 38-49. (c) de Andrade Coutinho, P. L.; Morita, A. T.; Cassinelli, L. F.; Morschbacker, A.; Do Carmo, R. W. Braskem's Ethanol to Polyethylene Process Development. In Catalytic Process Development for Renewable Materials; Imhof, P., van der Waal, J. C., Eds.; Wiley-VCH Verlag GmbH & Co.: Weinheim, Germany, 2013; pp 149-166.
[6] For feedstock production volumes and synthesis from ethanol, see: (a) Eckert, M.; Fleischmann, F.; Jira, R.; Bolt, H.M.; Golka, K. Acetaldehyde. In Ullmann's Encyclopedia of Industrial Chemistry; Wiley-VCH Verlag GmbH & Co.: Weinheim, Germany, 2006; pp 191-207. (b) Zimmermann, H.; Walzl, R. Ethylene. In Ullmann's Encyclopedia of Industrial Chemistry; Wiley-VCH Verlag GmbH & Co.: Weinheim, Germany, 2009; pp 465-529. (c) Dahlmann, M.; Grub, J.; Loser, E. Butadiene. In Ullmann's Encyclopedia of Industrial Chemistry; Wiley-VCH Verlag GmbH & Co.: Weinheim, Germany, 2011; pp 1-24.

[7] For selected examples of the catalytic conversion of ethanol-to-butanol, see: (a) Dowson, G. R. M.; Haddow, M. F.; Lee, J.; Wingad, R. L.; Wass, D. F. Highly Selective Formation of n-Butanol from Ethanol through the Guerbet Process: A Tandem Catalytic Approach. Angew. Chem., Int. Ed. 2013, 52, 9005-9008. (b) Chakraborty, S.; Piszel, P. E.; Hayes, C. E.; Baker, R. T.; Jones, W. D. Catalytic Conversion of Ethanol into an Advanced Biofuel: Unprecedented Selectivity for n-Butanol. J. Am. Chem. Soc. 2015, 137, 14264-14267. (c) Xie, Y.; Ben-David, Y.; Shimon, L. J. W.; Milstein, D. Highly Efficient Process for Production of Biofuel from Ethanol Catalyzed by Ruthenium Pincer Complexes. J. Am. Chem. Soc. 2016, 138, 9077-9080.
[8] For a recent review of the catalytic conversion of ethanol-to-butanol, see: Aitchison, H.; Wingad, R. L.; Wass, D. F. Homogeneous Ethanol to Butanol Catalysis - Guerbet Renewed. ACS Catal. 2016, 6, 7125-7132.

[9] For recent examples of the use of ethanol in Guerbet-type reactions, see: Gawali, S. S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. ACS Omega, 2019, 4, 10741-10754. (g) Kobayashi, M.; Itoh, S.; Yoshimura, K.; Tsukamoto, Y.; Obora, Y. Iridium Complex-Catalyzed C2-Extension of Primary Alcohols with Ethanol via a Hydrogen Autotransfer Reaction. J. Org. Chem. 2020, 85, 11952-11958. (c) Ng, T. W.; Liao, G.; Lau, K. K.; Pan, H.-J.; Zhao, Y. Room-Temperature Guerbet Reaction with Unprecedented Catalytic Efficiency and Enantioselectivity. Angew. Chem. Int. Ed. 2020, 59, 11384-11389.

[10] For isolated examples of the catalytic C-C couplings of ethanol to form racemic adducts beyond Guerbet-type reactions, see: (a) Shi, L.; Tu, Y.-Q.; Wang, M.; Zhang, F.-M.; Fan, C.-A.; Zhao, Y.-M. A Reaction for sp3-sp3 C-C Bond Formation via Cooperation of Lewis Acid-Promoted/Rh-Catalyzed C-H Bond Activation. J. Am. Chem. Soc. 2005, 127, 10836-10837. (b) Jiang, Y.-J.; Tu, Y.-Q.; Zhang, E.; Zhang, S.-Y.; Cao, K.; Shi, L. Palladium-Catalyzed/Lewis Acid-Promoted Alkene Dimerization and Cross-Coupling with Alcohols via C-H Bond Activation. Adv. Synth. Catal. 2008, 350, 522-556. (c) Obora, Y.; Hatanaka, S.; Ishii, Y. Iridium-Catalyzed Coupling Reactions of Primary Alcohols with 1-Aryl-1-propynes Leading to Secondary Homoallylic Alcohols. Org. Lett. 2009, 11, 3510-3513. (d) Guo, S.-r.; Yuan, Y.-q. Copper-Catalyzed Alkenylation of Alcohols with β-Nitrostyrenes via a Radical Addition-Elimination Process. Synlett 2015, 26, 1961-1968.

[11] Han, H.; Krische, M. J. Direct Ruthenium-Catalyzed C-C Coupling of Ethanol: Diene Hydro-hydroxyethylation To Form All-Carbon Quaternary Centers. Org. Lett. 2010, 12, 2844-2846.

[12] For an authoritative review on enantioselective hydrogen auto-transfer reactions, see: Kwok, T.; Hoff, O.; Armstrong, R. J.; Donohoe, T. J. Control of Absolute Stereochemistry in Transition-Metal-Catalysed Hydrogen-Borrowing Reactions. Chem. Eur. J. 2020, 26, 12912-12926.

[13] For recent reviews on alcohol-mediated carbonyl addition via metal-catalyzed hydrogen auto-transfer, see: (a) Ketcham, J. M.; Shin, I.; Montgomery, T. P.; Krische, M. J. Catalytic Enantioselective C-H Functionalization of Alcohols by Redox-Triggered Carbonyl Addition: Borrowing Hydrogen, Returning Carbon. Angew. Chem. Int. Ed. 2014, 53, 9142-9150; (b) Kim, S. W.; Zhang, W.; Krische, M. J. Catalytic Enantioselective Carbonyl Allylation and Propargylation via Alcohol-Mediated Hydrogen Transfer: Merging the Chemistry of Grignard and Sabatier. Acc. Chem. Res. 2017, 50, 2371-2380; (c) Nguyen, K. D.; Park, B. Y.; Luong, T.; Sato, H.; Garza, V. J.; Krische, M. J. Metal-catalyzed reductive coupling of olefin-derived nucleophiles: Reinventing carbonyl addition. Science 2016, 354, aah5133; (d) Holmes, M.; Schwartz, L. A.; Krische, M. J. Intermolecular Metal-Catalyzed Reductive Coupling of Dienes, Allenes, and Enynes with Carbonyl Compounds and Imines. Chem. Rev. 2018, 118, 6026-6052; (e) Doerksen, R. S.; Meyer, C. C.; Krische, M. J. Angew. Chem. Int. Ed. 2019, 58, 14055-14064.

[14] Vitaku, E.; Smith, D. T.; Njardarson, J. T. Analysis of the Structural Diversity, Substitution Patterns, and Frequency of Nitrogen Heterocycles among U.S. FDA Approved Pharmaceuticals. J. Med. Chem. 2014, 57, 10257-10274.

[15] For selected examples of the enantioselective iridium-catalyzed C-C coupling of primary alcohols with allylic acetates, see: (a) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. Enantioselective Iridium Catalyzed Carbonyl Allylation from the Alcohol or Aldehyde Oxidation Level Using Allyl Acetate as an Allyl Metal Surrogate. J. Am. Chem. Soc. 2008, 130, 6340-6341. (b) Kim, I. S.; Ngai, M.-Y.; Krische, M. J. Enantioselective Iridium Catalyzed Carbonyl Allylation from the Alcohol or Aldehyde Oxidation Level via Transfer Hydrogenative Coupling of Allyl Acetate: Departure from Chirally Modified Allyl Metal Reagents in Carbonly Addition. J. Am. Chem. Soc. 2008, 130, 14891-14899. (c) Lu, Y.; Kim, I. S.; Hassan, A.; Del Valle, D. J.; Krische, M. J. 1,n-Glycols as Dialdehyde Equivalents in Iridium Catalyzed Enantioselective Carbonyl Allylation and Iterative Two-Directional Assembly of 1,3-Polyols. Angew. Chem. Int. Ed. 2009, 48,

5018-5021. (d) Hassan, A.; Lu, Y.; Krische, M. J. Elongation of 1,3-Polyols via Iterative Catalyst-Directed Carbonyl Allylation from the Alcohol Oxidation Level. Org. Lett. 2009, 11, 3112-3115. (e) Schmitt, D. C.; Dechert-Schmitt, A.-M. R.; Krische, M. J. Iridium-Catalyzed Allylation of Chiral β-Stereogenic Alcohols: Bypassing Discrete Formation of Epimerizable Aldehydes. Org. Lett. 2012, 14, 6302-6305. (f) Dechert-Schmitt, A.-M. R.; Schmitt, D. C.; Krische, M. J. Site-Selective Primary Alcohol Dehydrogenation Enables Protecting Group-Free Diastereoselective C-C Coupling of 1,3-Glycols and Allyl Acetate. Angew. Chem. Int. Ed. 2013, 52, 3195-3198. (g) Shin, I.; Wang, G.; Krische, M. J. Catalyst-Directed Diastereo- and Site-Selectivity in Successive Nucleophilic and Electrophilic Allylations of Chiral 1,3-Diols: Protecting Group-Free Synthesis of 4-Hydroxy-2,6-cis- or trans-Pyrans. Chem. Eur. J. 2014, 20, 13382-13389. (h) Kim, S. W.; Lee, W.; Krische, M. J. Asymmetric Allylation of Glycidols Mediated by Allyl Acetate via Iridium Catalyzed Hydrogen Transfer. Org. Lett. 2017, 19, 1252-1254.

[16] For selected reviews on late-stage functionalization of complex small molecules, see: (a) Cernak, T.; Dykstra, K. D.; Tyagarajan, S.; Vachal, P.; Krska, S. W. The Medicinal Chemist's Toolbox for Late Stage Functionalization of Drug-Like Molecules. Chem. Soc. Rev. 2016, 45, 546-576. (b) Shugrue, C. R.; Miller, S. J. Applications of Nonenzymatic Catalysts to the Alteration of Natural Products. Chem. Rev. 2017, 117, 11894-11951. (c) Blakemore, D. C; Castro, L.; Churcher, I.; Churcher, I.; Rees, D. C; Thomas, A. W; Wilson, D. M; Wood, A.; Wood, A. Organic Synthesis Provides Opportunities to Transform Drug Discovery. Nat. Chem. 2018, 10, 383-394. (d) Dominguez-Huerta, A.; Dai, X.-J.; Zhou, F.; Querard, P.; Qiu, Z.; Ung, S.; Liu, W.; Li, J.; Li, C.-J. Exploration of New Reaction Tools for Late-Stage Functionalization of Complex Chemicals. Can. J. Chem. 2019, 97, 67-85.

[17] (a) Feng, J.; Garza, V. J.; Krische, M. J. Redox-Triggered C-C Coupling of Alcohols and Vinyl Epoxides: Diastereo- and Enantioselective Formation of All-Carbon Quaternary Centers via tert-(Hydroxy)-Prenylation. J. Am. Chem. Soc. 2014, 136, 8911-8914. (b) Guo, Y.-A.; Lee, W.; Krische, M. J. Diastereo- and Enantioselective Synthesis

of Oxetanes Bearing All-Carbon Quaternary Stereocenters via Iridium Catalyzed Alcohol-Vinyl Epoxide C-C Coupling. Chem. Eur. J. 2017, 23, 2557
[18] Spielmann, K.; Xiang, M.; Schwartz, L. A.; Krische, M. J. Direct Conversion of Primary Alcohols to 1,2-Amino Alcohols: Enantioselective Iridium-Catalyzed Carbonyl Reductive Coupling of Phthalimido-Allene via Hydrogen Auto-Transfer. J. Am. Chem. Soc. 2019, 141, 14136-14141.
[19] For selected reviews on phenethylamines, see: (a) Aghajanian, G. K.; Marek, G. J. Serotonin and Hallucinogens. Neuropsychopharm. 1999, 21(2s), 16S-23S. (b) Trachsel, D. Fluorine in Psychedelic Phenethylamines. Drug Test. Anal. 2012, 4, 577-590. (c) King, L. A. New Phenethylamines in Europe. Drug Test. Anal. 2013, 6, 808-818. (d) Inan, F.; Brunt, Tibor, M.; Contrucci, R. R.; Hondebrink, L.; Franssen, Eric J. F. Novel Phenethylamines and Their Potential Interactions With Prescription Drugs: A Systematic Critical Review. Ther. Drug Monit. 2020, 42, 271-281.
[20] (a) Lowe, F. C. Summary of Clinical Experiences With Tamsulosin for the Treatment of Benign Prostatic Hyperplasia. Rev. Urol. 2005, 7, S13-21. (b) Iwamoto, F. M.; Kreisl, T. N.; Kim, L.; Duic, J. P.; Butman, J. A.; Albert, P. S.; Fine, H. A. Phase II Trial of Talampanel, a Glutamate Receptor Inhibitor, for Adults with Recurrent Malignant Gliomas. Cancer 2010, 116, 1776-1782. (c) Fong, T. M.; Guan, X. M.; Marsh, D.J.; Shen, C. P.; Stribling, D. S.; Rosko, K. M.; Lao, J.; Yu, H.; Feng, Y.; Xiao, J. C. et al. Antiobesity efficacy of a novel cannabinoid-1 receptor inverse agonist, N-[(1S,2S)-3-(4-chlorophenyl)-2-(3-cyanophenyl)-1-methylpropyl]-2-methyl-2-5-(trifluoromethyl)pyridin-2-yl]oxy]propanamide (MK-0364), in rodents. J. Pharmacol. Exp. Ther. 2007, 321, 1013–1022. (d) Bouwman, S. A. M.; Zoleko-Manego, R.; Renner, K. C.; Schmitt, E. K.; Mombo-Ngoma, G.; Grobusch, M. P. The Early Preclinical and Clinical Development of Cipargamin, (KAE609), a Novel Antimalarial Compound. Travel Med. Infect. Dis. 2020, 101765, 1-8.

[21] Lal, B.; Pramanik, B. N.; Manhas, M. S.; Bose, A. K. Diphenylphosphoryl Azide: A Novel Reagent for The Stereospecific Synthesis of Azides from Alcohols. Tetrahedron Lett. 1977, 1977-1980.
[22] For a review on the Staudinger reduction, see: Gololobov, Y. G.; Zhmurova, I. N.; Kasukhin, L. F. Sixty Years of Staudinger Reaction. Tetrahedron 1981, 37, 437-472.
[23] For notable examples, see: (a) Berliner, M. A.; Dubant, S. P. A.; Makowski, T.; Ng, K.; Sitter, B.; Wager, C.; Zhang, Y. Use of an Iridium-Catalyzed Redox-Neutral Alcohol-Amine Coupling on Kilogram Scale for the Synthesis of a GlyT1 Inhibitor. Org. Process Res. Dev. 2011, 15, 1052-1062. (b) Shimizu, H.; Maeda, H.; Nara, H. Highly Productive α Alkylation of Ketones with Alcohols Mediated by an Ir-Oxalamidato/Solid Base Catalyst System. Org. Process Res. Dev. 2020, 24, 2772-2779.
[24] For selected reviews on carbonyl addition chemistry, see: (a) Noyori, R.; Kitamura, M. Enantioselective Addition of Organometallic Rea-gents to Carbonyl Compounds: Chirality Transfer, Multiplication and Amplification. Angew. Chem. Int. Ed. 1991, 30, 49–69. (b) Soai, K.; Shibata, T. Alkylation of Carbonyl Groups. In Comprehensive Asym-metric Catalysis I-III; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag Berlin Heidelberg: Germany, 1999; Vol. 2, pp 911–922. (c) Pu, L.; Yu, H.-B. Catalytic Asymmetric Organozinc Addi-tions to Carbonyl Compounds. Chem. Rev. 2001, 101, 757–824. (d) Catalytic Enantioselective Addition of Allylic Organometallic Rea-gents to Aldehydes and Ketones. Chem. Rev. 2003, 103, 2763–2793. (e) Trost, B. M.; Weiss, A. H. The Enantioselective Addition of Al-kyne Nucleophiles to Carbonyl Groups. Adv. Synth. Catal. 2009, 351, 963–983. (f) Comprehensive Organic Synthesis, 2nd ed.; Knochel, P.; Molander, G. A., Eds.; Elsevier: Oxford, 2014; Vols. 1 and 2.
[25] For selected reviews on catalytic enantioselective ketone addition, see: (a) Betancort, J. M.; Garcia, C.; Walsh, P. J. Development of the First Practical Catalyst for the Asymmetric Addition of Alkyl- and Aryl-zinc Reagents to Ketones. Synlett 2004, 5, 749–760. (b) Ramon, D. J.; Yus, M. Chiral Tertiary Alcohols Made By Catalytic Enantioselective Addition of Unreactive Zinc Reagents to Poorly Electrophilic. Angew.

Chem. Int. Ed. 2004, 43, 284–287. (c) Garcia, C.; Martin, V. S. Asymmetric Addition to Ketones: Enantioselective Formation of Ter-tiary Alcohols. Curr. Org. Chem. 2006, 10, 1849–1889. (d) Riant, O.; Hannedouche, J. Asymmetric Catalysis for The Construction of Qua-ternary Carbon Centres: Nucleophilic Addition on Ketones and Ketimines. Org. Biomol. Chem. 2007, 5, 873–888. (e) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. Enantioselective Catalytic Formation of Quaternary Stereogenic Centers. Eur. J. Org. Chem. 2007, 36, 5969–5994. (f) Hatano, M.; Ishihara, K. Recent Progress in the Catalytic Synthesis of Tertiary Alcohols from Ketones with Organometallic Re-agents. Synthesis 2008, 11, 1647–1675. (g) Shibasaki, M.; Kanai, M. Asymmetric Synthesis of Tertiary Alcohols and α-Tertiary Amines via Cu-Catalyzed C−C Bond Formation to Ketones and Ketimines. Chem. Rev. 2008, 108, 2853–2873. (h) Adachi, S.; Harada, T. Catalyt-ic Enantioselective Aldol Additions to Ketones. Eur. J. Org. Chem. 2009, 22, 3661–3671. (i) Wisniewska, H. M.; Jarvo, E. R. Enantiose-lective Propargylation and Allenylation Reactions of Ketones and Imines. J. Org. Chem. 2013, 78, 11629–11636. (j) Rong, J.; Pellegrini, T.; Harutyunyan, S. R. Synthesis of Chiral Tertiary Alcohols by CuI-Catalyzed Enantioselective Addition of Organomagnesium Reagents to Ketones. Chem. Eur. J. 2016, 22, 3558–3570. (k) Thaima, T.; Za-mani, F.; Hyland, C. J. T.; Pyne, S. G. Allenylation and Propargylation Reactions of Ketones, Aldehydes, Imines, and Iminium Ions Using Organoboronates and Related Derivatives. Synthesis 2017, 49, 1461–1480. (l) Liu, Y.-L.; Lin, X.-T. Recent Advances in Catalytic Asym-metric Synthesis of Tertiary Alcohols via Nucleophilic Addition to Ketones. Adv. Synth. Catal. 2019, 361, 876–918. [26] For examples of intermolecular catalytic enantioselective allylation of unactivated ketones using premetalated reagents, see: (a) Allylbora-tion: Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. Catalytic Enantioselective Allylboration of Ketones. J. Am. Chem. Soc. 2004, 126, 8910–8911. (b) Lou, S.; Moquist, P. N.; Schaus, S. E. Asymmet-ric Allylboration of Ketones Catalyzed by Chiral Diols. J. Am. Chem. Soc. 2006, 128, 12660–12661. (c) S., Shi-L.; Xu, L.-W.; Oisaki, K.; Kanai, M.; Shibasaki, M. Identification of Modular Chiral Bisphos-phines Effective for Cu(I)-Catalyzed

Asymmetric Allylation and Pro-pargylation of Ketones. J. Am. Chem. Soc. 2010, 132, 6638–6639. (d) Zhang, Y.; Li, N.; Qu, B.; Ma, S.; Lee, H.; Gonnella, N. C.; Gao, J.; Li, W.; Tan, Z.; Reeves, J. T.; Wang, J.; Lorenz, J. C.; Li, G.; Reeves, D. C.; Premasiri, A.; Grinberg, N.; Haddad, N.; Lu, B. Z.; Song, J. J.; Senanayake, C. H. Org. Lett. 2013, 15, 1710–1713. (e) Cu-Catalyzed Chemoselective Preparation of 2-(Pinacolato)boron-Substituted Al-lylcopper Complexes and their In Situ Site-, Diastereo-, and Enanti-oselective Additions to Aldehydes and Ketones. Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. Angew. Chem. Int. Ed. 2013, 52, 5046-5051. (f) Alam, R.; Vollgraff, T.; Eriksson, L.; Szabo, K. J. Synthesis of Adjacent Quaternary Stereocenters by Catalytic Asymmetric Al-lylboration. J. Am. Chem. Soc. 2015, 137, 11262–11265. (g) Lee, K.; Silverio, D. L.; Torker, S.; Robbins, D. W.; Haeffner, F.; van der Mei, F. W.; Hoveyda, A. H. Catalytic Enantioselective Addition of Or-ganoboron Reagents to Fluoroketones Controlled by Electrostatic In-teractions. Nature Chem. 2016, 8, 768–777. (h) Robbins, D. W.; Lee, K.; Silverio, D. L.; Volkov, A.; Torker, S.; Hoveyda, A. H. Practical and Broadly Applicable Catalytic Enantioselective Additions of Allyl-B(pin) Compounds to Ketones and α-Ketoesters. Angew. Chem. Int. Ed. 2016, 55, 9610–9614. (i) Fager, D. C.; Lee, K.; Hoveyda, A. H. Catalytic Enantioselective Addition of an Allyl Group to Ketones Containing a Tri-, a Di-, or a Monohalomethyl Moiety. Stereochemical Control Based on Distinctive Electronic and Steric Attributes of C–Cl, C–Br, and C–F Bonds. J. Am. Chem. Soc. 2019, 141, 16125–16138. (j) Zanghi, J. M.; Meek, S. J. Cu-Catalyzed Diastereo- and En-antioselective Reactions of γ,γ-Disubstituted Allyldiboron Com-pounds with Ketones. Angew. Chem. Int. Ed. 2020, 132, 8529–8533. (k) Allylsilation: Wadamoto, M.; Yamamoto, H. Silver-Catalyzed Asymmetric Sakurai-Hosomi Allylation of Ketones. J. Am. Chem. Soc. 2005, 127, 14556–14557. (l) Yamasaki, S.; Fujii, K.; Wada, R.; Kanai, M.; Shibasaki, M. A General Catalytic Allylation Using Al-lyltrimethoxysilane. J. Am. Chem. Soc. 2002, 124, 6536–6537. (m) Al-lylstannation: Casolari, S.; D'Addario, D.; Tagliavini, E. Org. Lett. 1999, 1, 1061–1063. (n) Cunningham, A.; Woodward, S. Highly En-antioselective Catalytic Ketone Allylation

with Sn(CH2CH=CH2)4/RSn(CH2CH=CH2)3 Mixtures (R = Et, Bu) Synlett 2002, 43–44. (o) Kim, J. G.; Waltz, K. M.; Kwiatkowski, D.; Walsh, P. J. J. Am. Chem. Soc. 2004, 126, 12580–12585. (p) Teo, Y.-C.; Goh, J.-D.; Loh, T.-P. Catalytic Enantioselective Allylation of Ketones via a Chiral Indium(III) Complex. Org. Lett. 2005, 7, 2743–2745. (q) Kim, Jeung Gon; Camp, Elizabeth H.; Walsh, Patrick J. Catalytic Asymmet-ric Methallylation of Ketones with an (H8-BINOLate)Ti-Based Cata-lyst Org. Lett. 2006, 8, 4413–4416. (r) Prieto, O.; Woodward, S. En-antioselective Catalytic Allylation of Aryl Methyl Ketones Using Tetraallyltin and Tin(IV) Chloride Mixtures. J. Organomet. Chem. 2006, 691, 1515–1519. (s) Zhang, X.; Chen, D.; Liu, X.; Feng, X. En-antioselective Allylation of Ketones Catalyzed by N,N'-Dioxide and Indium(III) Complex. J. Org. Chem. 2007, 72, 5227–5233.

[27] For examples of intermolecular catalytic enantioselective allylation of unactivated ketones under Nozaki-Hiyama-Kishi conditions, see: (a) Miller, J. J.; Sigman, M. S. Design and Synthesis of Modular Oxazo-line Ligands for the Enantioselective Chromium-Catalyzed Addition of Allyl Bromide to Ketones. J. Am. Chem. Soc. 2007, 129, 2752–2753. (b) Huang, X.-R.; Chen, C.; Lee, G.-H.; Peng, S.-M. A Spirocy-clic Chiral Borate for Catalytic Enantioselective Nozaki-Hiyama Al-lylation of Ketones. Adv. Synth. Catal. 2009, 351, 3089–3095.

[28] For examples of intermolecular catalytic enantioselective allylation of unactivated ketones via reductive coupling of diene and allene pronu-cleophiles, see: (a) Tsai, E. Y.; Liu, R. Y.; Yang, Y.; Buchwald, S. L. A Regio- and Enantioselective CuH-Catalyzed Ketone Allylation with Terminal Allenes. J. Am. Chem. Soc. 2018, 140, 2007–2011. (b) Liu, R. Y.; Zhou, Y.; Yang, Y.; Buchwald, S. L. Enantioselective Allyla-tion Using Allene, a Petroleum Cracking Byproduct. J. Am. Chem. Soc. 2019, 141, 2251–2256. (c) Li, C.; Liu, R. Y.; Jesikiewicz, L. T.; Yang, Y.; Liu, P.; Buchwald, S. L. CuH-Catalyzed Enantioselective Ketone Allylation with 1,3-Dienes: Scope, Mechanism, and Applica-tions. J. Am. Chem. Soc. 2019, 141, 5062–5070. (d) Feng, J.-J.; Xu, Y.; Oestreich, M. Ligand-Controlled Diastereodivergent, Enantio- and Regioselective Copper-Catalyzed

Hydroxyalkylboration of 1,3-Dienes with Ketones. Chem. Sci. 2019, 10, 9679–9683. (e) Bin, F.; Yuan, X.; Li, Y.; Wang, Y.; Zhang, Q.; Xiong, T. Copper-Catalyzed Asymmetric Reductive Allylation of Ketones with 1,3-Dienes. Org. Lett. 2019, 21, 3576–3580.
[29] For recent reviews on metal-catalyzed carbonyl reductive coupling mediated by H2, 2-PrOH, or through hydrogen auto-transfer, see: (a) Doerksen, R. S.; Meyer, C. C.; Krische, M. J. Feedstock Reagents in Metal-Catalyzed Carbonyl Reductive Coupling: Minimizing Preactiva-tion for Efficiency in Target-Oriented Synthesis. Angew. Chem. Int. Ed. 2019, 58, 14055–14064. (b) Santana, C. G.; Krische, M. J. From Hydrogenation to Transfer Hydrogenation to Hydrogen Auto-Transfer in Enantioselective Metal-Catalyzed Carbonyl Reductive Coupling: Past, Present and Future. ACS Catal. 2021, 11, 5572–5585.
[30] (a) Itoh, J.; Han, S. B.; Krische, M. J. Enantioselective Allylation, Crotylation and Reverse Prenylation of Substituted Isatins: Iridium Catalyzed C-C Bond Forming Transfer Hydrogenation. Angew. Chem. Int. Ed. 2009, 48, 6313-6316. (b) Brito, G. A.; Jung, W.-O.; Yoo, M.; Krische, M. J. Enantioselective Iridium-Catalyzed Allylation of Acetylenic Ketones via 2-Propanol-Mediated Reductive Coupling of Allyl Acetate: C14-C23 of Pladienolide D. Angew. Chem. Int. Ed. 2019, 58, 18803–18807.
[31] Gauche interactions associated with formation of vicinal tertiary-quaternary centers in ketone allylmetalations can influence the equato-rial vs axial preference of substituents in Zimmerman-Traxler transition states to invert stereoselectivity: Mejuch T.; Gilboa N.; Gayon E.; Wang H.; Houk, K. N.; Marek, I. Axial Preferences in Allylation Re-actions via The Zimmerman-Traxler Transition State. Acc. Chem. Res. 2013, 46, 1659–1669.
[32] (a) Bøgevig, A.; Kumaragurubaran, N.; Jørgensen, K. A. Direct Cata-lytic Asymmetric Aldol Reactions of Aldehydes. Chem. Commun. 2002, 620–621. (b) Oisaki, K.; Suto, Y.; Kanai, M.; Shibasaki, M. A New Method for the Catalytic Aldol Reaction of Ketones. J. Am. Chem. Soc. 2003, 125, 5644–5645. (c) Shiomi, T.; Nishiyama, H. In-termolecular Asymmetric Reductive Aldol Reactions of Ketones as Acceptors Promoted by Chiral Rh(Phebox) Catalyst. Org. Lett. 2007, 9, 1651–1654.

[33] For a recent review on the formation of enantiomerically enriched acyclic vicinal tertiary-quaternary centers, see: Pierrot, D.; Marek, I. Synthesis of Enantioenriched Vicinal Tertiary and Quaternary Carbon Stereogenic Centers within an Acyclic Chain. Angew. Chem., Int. Ed. 2020, 59, 36–49.
[34] For selected reviews on the synthesis of oxetanes and their use in chemical synthesis, see: (a) Mack, D. J.; Njardarson, J. T. Recent Ad-vances in The Metal-Catalyzed Ring Expansions of Three- and Four-Membered Rings. ACS Catal. 2013, 3, 272–286. (b) Njardarson, J. T. Catalytic Ring Expansion Adventures. Synlett 2013, 787–803. (c) D'Auria, M.; Racioppi, R. Oxetane Synthesis through the Paternò-Büchi Reaction. Molecules 2013, 18, 11384–11428. (d) Wang, Z.; Chen, Z.; Sun, J. Catalytic Asymmetric Nucleophilic Openings of 3-Substituted Oxetanes. Org. Biomol. Chem. 2014, 12, 6028–6032. (e) Carreira, E. M.; Fessard, T. C. Four-Membered Ring-Containing Spi-rocycles: Synthetic Strategies and Opportunities. Chem. Rev. 2014, 114, 8257–8322. (f) Malapit, C. A.; Howell, A. R. Recent Applica-tions of Oxetanes in the Synthesis of Heterocyclic Compounds. J. Org. Chem. 2015, 80, 8489–8495. (g) Davis, O. A.; Bull, J. A. Recent Advances in the Synthesis of 2-Substituted Oxetanes. Synlett 2015, 1283–1288.
[35] For selected reviews on the synthesis of azetidines and their use in chemical synthesis, see: (a) Couty, F.; Evano, G. Azetidines: new tools for the synthesis of nitrogen heterocycles. Synlett 2009, 3053–3064. (b) Bott, T. M.; West, F. G. Preparation and Synthetic Applications of Azetidines. Heterocycles 2012, 84, 223–264. (c) Mehra, V.; Lumb, I.; Anand, A.; Kumar, V. Recent Advances in Synthetic Facets of Im-mensely Reactive Azetidines. RSC Advances 2017, 7, 45763–45783. (d) Richardson, A. D.; Becker, M. R.; Schindler, C. S. Synthesis of Azetidines by aza Paterno-Buchi Reactions. Chem. Sci. 2020, 11, 7553–7561. (e) Milton, J. P.; Fossey, J. S. Azetidines and Their Appli-cations in Asymmetric Catalysis. Tetrahedron 2021, 77, 131767. (f) Mughal, H.; Szostak, M. Recent Advances in The Synthesis and Reac-tivity of Azetidines: Strain-

Driven Character of The Four-Membered Heterocycle. Org. Biomol. Chem. 2021, 19, 3274–3286.
[36] For selected reviews on oxetanes and azetidines in medicinal chemis-try, and crop protection, see: (a) Wuitschik, G.; Carreira, E. M.; Wag-ner, B.; Fischer, H.; Parrilla, I.; Schuler, F.; Rogers-Evans, M.; Müller, K. Oxetanes in Drug Discovery: Structural and Synthetic Insights. J. Med. Chem. 2010, 53, 3227−3246. (b) Burkhard, J. A.; Wuitschik, G.; Rogers-Evans, M.; Müller, K.; Carreira, E. M. Oxetanes as Versatile Elements in Drug Discovery and Synthesis. Angew. Chem. Int. Ed. 2010, 49, 9052–9067. (c) St. Jean, Jr., D. J.; Fotsch, C. Mitigating Heterocycle Metabolism in Drug Discovery. J. Med. Chem. 2012, 55, 6002–6020. (d) Bull, J. A.; Croft, R. A.; Davis, O. A.; Doran, R.; Morgan, K. F. Oxetanes: Recent Advances in Synthesis, Reactivity, and Medicinal Chemistry. Chem. Rev. 2016, 116, 12150–12233. (e) Delost, Michael D.; Smith, David T.; Anderson, Benton J.; Njardar-son, Jon T. Oxiranes to Oligomers: Architectures of U.S. FDA Ap-proved Pharmaceuticals Containing Oxygen Heterocycles. J. Med. Chem. 2018, 61, 10996–11020. (f) Lamberth, C. Small Ring Chemis-try in Crop Protection. Tetrahedron 2019, 75, 4365–4383. (g) Bauer, M. R.; Di Fruscia, P.; Lucas, S. C. C.; Michaelides, I. N.; Nelson, J. E.; Storer, R. I.; Whitehurst, B. C. Put a Ring on It: Application of Small Aliphatic Rings in Medicinal Chemistry. RSC Med. Chem. 2021, DOI: 10.1039/d0md00370k.
[37] For studies illustrating how oxetanes can improve the ADME proper-ties of drug candidates, see: (a) Toselli, F.; Fredenwall, M.; Svensson, P.; Li, X.-Q.; Johansson, A.; Weidolf, L.; Hayes, M. A. Hip To Be Square: Oxetanes as Design Elements To Alter Metabolic Pathways. J. Med. Chem. 2019, 62, 16, 7383–7399. (b) Dubois, M. A. J.; Croft, R. A.; Ding, Y.; Choi, C.; Owen, D. R.; Bull, J. A.; Mousseau, J. J. Inves-tigating 3,3-Diaryloxetanes as Potential Bioisosteres in Drug Discov-ery. ChemRxiv, DOI:10.26434/chemrxiv.14453187.

[38] Modelli, A.; Martin, H. Temporary Anions and Empty Level Structure in Cyclobutanediones: Through-Space and Through-Bond Interac-tions. J. Phys. Chem. A 2002, 106, 7271–7275.
[39] (a) Geden, J. V.; Beasley, B. O.; Clarkson, G. J.; Shipman, M. Asymmetric Synthesis of 2 Substituted Oxetan-3-ones via Metalated SAMP/RAMP Hydrazones. J. Org. Chem. 2013, 78, 12243–12250. (b) Dobi, Z.; Holczbauer, T.; Soos, T. Strain-Driven Direct Cross-Aldol and -Ketol Reactions of Four Membered Heterocyclic Ketones. Org. Lett. 2015, 17, 2634-2637. (c) Yufit, D. S.; Howard, J. A. K. Ac-ta Crystallogr., Sect. C: Cryst. Struct. Commun., 2011, 67, o104–o106.
[40] Vitaku, E.; Smith, D. T.; Njardarson, J. T. Analysis of the Structural Diversity, Substitution Patterns, and Frequency of Nitrogen Heterocy-cles among U.S. FDA Approved Pharmaceuticals. J. Med. Chem. 2014, 57, 10257–10274.
[41] For selected reviews on late-stage functionalization of complex small molecules, see: (a) Cernak, T.; Dykstra, K. D.; Tyagarajan, S.; Vachal, P.; Krska, S. W. The Medicinal Chemist's Toolbox for Late Stage Functionalization of Drug-Like Molecules. Chem. Soc. Rev. 2016, 45, 546–576. (b) Shugrue, C. R.; Miller, S. J. Applications of Nonenzy-matic Catalysts to the Alteration of Natural Products. Chem. Rev. 2017, 117, 11894–11951. (c) Blakemore, D. C.; Castro, L.; Churcher, I.; Rees, D. C.; Thomas, A. W.; Wilson, D. M.; Wood, A. Organic Synthesis Provides Opportunities to Transform Drug Discovery. Nat. Chem. 2018, 10, 383–394.
[42] Kim, S. W.; Meyer, C. C.; Mai, B. K.; Liu, P.; Krische, M. J. Inver-sion of Enantioselectivity in Allene Gas versus Allyl Acetate Reduc-tive Aldehyde Allylation Guided by Metal-Centered Stereogenicity: An Experimental and Computational Study. ACS Catalysis 2019, 9, 9158–9163.
[43]While it well-appreciated that saturated, stereochemically rich small molecule clinical candidates have a higher success rate, medicinal chemists appear reluctant to adopt new synthetic methods to prepare compounds of this type: (a) Lovering, F. Bikker, J.; Humblet, C. Es-cape from Flatland: Increasing Saturation as an Approach to Improv-

ing Clinical Success. J. Med. Chem. 2009, 52, 6752–6756. (b) Lover-ing, F. Escape from Flatland 2: Complexity and Promiscuity. Med. Chem. Commun. 2013, 4, 515–519. (c) Schneider, N.; Lowe, D. M.; Sayle, R. A.; Tarselli, M. A.; Landrum, G. A. Big Data from Pharma-ceutical Patents: A Computational Analysis of Medicinal Chemists' Bread and Butter. J. Med. Chem. 2016, 59, 4385−4402. (d) Brown, D. G.; Boström, J. Analysis of Past and Present Synthetic Methodologies on Medicinal Chemistry: Where Have All the New Reactions Gone? J. Med. Chem. 2016, 59, 4443–4458. (e) Boström, J.; Brown, D. G.; Young, R. J.; Keserü, G. M. Expanding the Medicinal Chemistry Syn-thetic Toolbox. Nature Rev. Drug Disc. 2018, 17, 709-727.

[44] Still, W. C.; Kahn, M.; Mitra, A. Rapid Chromatographic Technique for Preparative Separations with Moderate Resolution. J. Org. Chem. 1978, 43, 2923.

[45] Cabrera, J. M.; Tauber, J.; Zhang, W.; Xiang, M.; Krische, M. J. Selection between Diastereomeric Kinetic vs Thermodynamic Carbonyl Binding Modes Enables Enantioselective Iridium-Catalyzed anti-(α-Aryl)allylation of Aqueous Fluoral Hydrate and Difluoroacetaldehyde Ethyl Hemiacetal. J. Am. Chem. Soc. 2018, 140, 9392-9395.

[46] Spielmann, K.; Xiang, M.; Schwartz, L. A.; Krische, M. J. *J. Am. Chem. Soc.* **2019**, *141*, 14136-14141. 47 Garza, V. J.; Krische, M. J. *J. Am. Chem. Soc.* **2016**, *138*, 3655-3658.

[48] Han, M.; Yang, M.; Wu, R.; Li, Y.; Jia, T.; Gao, Y.; Ni, H.-L.; Hu, P.; Wang, B.-Q.; Cao, P. *J. Am. Chem. Soc.* **2020**, *142*, 13398-13405.

[49] Zuccarello, G.; Mayans, J. G.; Escofet, I.; Scharnagel, D.; Kirillova, M. S.; Pérez-Jimeno, A. H.; Calleja, P.; Boothe, J. R.; Echavarren, A. M. *J. Am. Chem. Soc.* **2019**, *141*, 11858-11863.

[50] Jimenez-Nunez, E.; Claverie, C. K.; Bour, C.; Cardenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2008**, *47*, 7892-7895.

[51] Lafrance, M.; Roggen, M.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2012**, *51*, 3470-3473.

[52] Ren, X.-F.; Turos, E.; Lake, C. H.; Churchill, M. R. *J. Org. Chem.* **1995**, *60*, 6468-6483.
[53] Meyer, C. C.; Stafford, N. P.; Cheng, M. J.; Krische, M. J. Ethanol: Unlocking an Abundant Renewable C2-Feedstock for Catalytic Enantioselective C−C Coupling. Angew. Chem. Int. Ed. 2021, 60, 10542-10546.
[54] Morrill, C.; Beutner, G. L.; Grubbs, R. H. Rhenium-Catalyzed 1,3-Isomerization of Allylic Alcohols: Scope and Chirality Transfer. J. Org. Chem. 2006, 71, 7813-7825.
[55] Kim, S. W.; Schempp, T. T.; Zbieg, J. R.; Stivala, C. E.; Krische, M. J. Regio- and Enantioselective Iridium-Catalyzed N-Allylation of Indoles and Related Azoles with Racemic Branched Alkyl-Substituted Allylic Acetates. Angew. Chem. Int. Ed. 2019, 58, 7762-7766
[56] Jung, W.; Mai, B. K.; Spinello, B. J.; Dubey, Z. J.; Kim, S. W.; Stivala, C. E.; Zbieg, J. R.; Liu, P.; Krische, M . J. Enantioselective Iridium-Catalyzed Allylation of Nitroalkanes: Entry to β Stereogenic α Quaternary Primary Amines. J. Am. Chem. Soc. 2021, 143. 9343-93491.
[57] CrysAlisPro. Rigaku Oxford Diffraction, HyPix6000E System, CrysAlisPro Software System, 1.171. 40.71a.
[58] SHELXT. (2015). G. M. Sheldrick. A program for crystal structure solution. Acta Cryst. A71, 3-8.
[59] Sheldrick, G. M. (2015). SHELXL-2018/3. Program for the Refinement of Crystal Structures. Acta Cryst., C71, 9-18.
[60] Spek, A. L. (2009). PLATON, A Multipurpose Crystallographic Tool. Utrecht University, The Netherlands. Acta Cryst. D65, 148-155.
[61] OLEX2. Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. and Puschmann, H. A Complete Structure Solution, Refinement and Analysis Program. J. Appl. Cryst. 42, 339-341.
[62] Flack, H. D. On enantiomorph-polarity estimation Acta Cryst 1983, A39, 876-881.

[63] Hooft, R. W. W; Straver, L. H.; Spek, A. L. Determination of absolute structure using Bayesian statistics on Bijvoet differences. J. Appl. Cryst. 2008, 41, 96-103.
[64] Rw(F2) = {Σw(|Fo|2 - |Fc|2)2/Σw(|Fo|)4}1/2 where w is the weight given each reflection.

a. R(F) = Σ (|Fo| - |Fc|)/Σ|Fo|} for reflections with Fo > 4(σ(Fo)).

b. S = [Σw(|Fo|2 - |Fc|2)2/(n - p)]1/2, where n is the number of reflections and p is the number of refined parameters.

[65] International Tables for X-ray Crystallography (1992). Vol. C, Tables 4.2.6.8 and 6.1.1.4, A. J. C. Wilson, editor, Boston: Kluwer Academic Press.
[66] Sheldrick, G. M. (1994). SHELXTL/PC (Version 5.03). Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA.
[67] CrysAlisPro. Rigaku Oxford Diffraction, HyPix6000E System, CrysAlisPro Software System, 1.171.42.25a.
[68] "Hellinghausen, G.; Diapayan, R.; Wang, Y.; Lee, J.T.; Lopez, D.; Weatherly, C.; Armstrong, D.W. A Comprehensive Methodology for the Chiral Separation of 40 Tobacco Alkaloids and their Carcinagenic E/Z-(R,S)-Tobacco-Specific Nitrosamine Metabolites. Talanta, 2018, 181, 132-141.
[69] Hellinghausen, G.; Roy, D.; Lee, J.T.; Wang, Y.; Weatherly, C.A.; Lopez, D.; Nguyen, K.; Armstrong, J.D.; Armstrong D.W. Effective Methodologies for Enantiomeric Seperation of 150 Pharmacology and Toxicology related 1°, 2°, and 3° amines with Core-Shell Chiral Stationary Phases. J. Pharm. Biomed. Anal., 2018 155, 70-81.