New Pd and Cu-Based Catalysts for Carbon-Heteroatom Bond Formation

By

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B.Sc. Biochemistry
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Submitted to the Department of Chemistry in Partial Fulfillment of the Requirement for the Degree of

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New Pd and Cu-Based Catalysts for Carbon-Heteroatom Bond Formation

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ABSTRACT

The research presented in this dissertation is aimed at the development of novel methodologies for carbon-heteroatom cross-coupling reactions catalyzed by late-transition metals. Both palladium and copper are central to the field of transition metal-catalysis and are integral to the catalyst systems developed as part of our continual advancement in cross-coupling reactions. The first part of this thesis focuses on the use of palladium catalysts to form carbon-sulfur bonds directed towards aryl sulfonamide synthesis. The second part of the thesis describes the recent development in the copper(I) hydride mediated formation of carbon-nitrogen bonds via hydroamination of olefins.

Part I.

Chapter 1. Palladium-Catalyzed Chlorosulfonylation of Arylboronic Acids

Using a biaryl phosphine ligand platform, the first palladium-catalyzed cross-coupling reaction of phenyl chlorosulfate with arylboronic acids was achieved. In this context, the arylsulfonyl chloride products serve as useful precursors to a variety of sulfonyl functional groups, such as aryl sulfonamides, aryl sulfones, and arenesulfonate esters. In particular, this method allows for the preparation of a number of arylsulfonyl chlorides that are not accessible via electrophilic aromatic substitution pathways and under mild reaction conditions. Additionally, this methodology points to an unprecedented selectivity for the phenylchlorosulfate electrophiles used in the cross-coupling reactions.

Part II.

Chapter 2. Enantio- and Regioselective Copper-Catalyzed Hydroamination of Styrenes and the Extension of the Methodology towards Anti-Markovnikov Hydroamination of Terminal Aliphatic Alkenes

The development of a copper-mediated strategy towards the hydroamination of styrene derivatives is reported. In this system, the reaction proceeds regioselectively and enantioselectively to generate α-branched amines. The system can transform a wide variety of substituted styrenes, including *trans-*, *cis-*, and β-disubstituted styrenes. In addition, our

extension to copper-catalyzed hydroamination reactions of unactivated aliphatic olefins is reported. Using terminal aliphatic alkenes, the copper-catalyzed hydroamination reactions proceed with anti-Markovnikov regioselectivity. Preliminary results point to the application of this methodology towards β-chiral amine synthesis via the hydroamination of 1,1-disubstituted alkenes.

Chapter 3. α-Aminosilane Synthesis via Copper-Catalyzed Hydroamination of Vinylsilanes

The copper-catalyzed hydroamination of vinylsilanes is described. This regioselective reaction generates α-chiral aminosilanes in high yields and enantioselectivities. The method is compatible with differentially substituted vinylsilanes and allows access to many valuable chiral organosilicon compounds.

Chapter 4. Synthesis of γ-Chiral Amines via Copper-Catalyzed Hydroamination of 3,3-Disubstituted Allylic Alcohols and 3,3-Disubstituted Allylic Benzoates

An investigation into the copper-catalyzed hydroamination of allylic alcohols and allylic benzoates is reported. The reaction proceeds via a β-alkoxy elimination, setting a stereogenic center at the 3-postion to generate γ-chiral amine products. The reaction is more efficient using allylic benzoates. This method is completely regioselective and is applicable to aliphatic allylic benzoates as well as aromatic allylic benzoates. Additionally, we demonstrated that this strategy is applicable towards an allylic epoxide substrate to generate δ-chiral amine.

Thesis Supervisor: Stephen L. Buchwald
Title: Camille Dreyfus Professor of Chemistry

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Graduate school is the part of my life that allows me to grow not just professionally but personally. Coming into graduate school, I was excited to learn new chemistries and expose myself to areas of research I knew nothing about. My advisor, Prof. Stephen L. Buchwald, had provided me with such an opportunity, and had convinced me to go for something that is far outside my comfort zone, in order for me to have acquired the most from the graduate experience. With that I will forever be grateful to him for continuously believing in my ability, and for constantly pushing me to work as hard and to learn as much. I also would like to thank my thesis committee members, Prof. Tim Jamison and Prof. Tim Swager, for the extra guidance and support, and for helping me throughout my oral exam to my thesis defense.

Being is Steve's lab has many advantages, which contribute to the speed of doing research. This includes not only the available resources in terms equipment we have access to, but also the human resources. I have been very fortunate in being trained by, working with, and alongside extremely talented graduate students and post-docs. I would like to first acknowledge Dr. Robb DeBergh and Dr. Shaolin Zhu, who I have had the opportunity to work with on the same projects, and whom I consider to be great mentors. They both are incredible chemists, and I am very proud to have been a part of their teams in contributing to the development of groundbreaking research.

To go back to the beginning, I have to thank Brett Fors for training me on all the basic skills needed to be an accomplished experimentalist. Brett Fors, Sophie Rousseaux, and Luca Salvi were the first people who welcomed me into the lab, and were always there whenever a first year like me needed guidance. They gave me the best introduction to graduate school and to the Buchwald lab anyone could have asked for, and I cherish the friendship that I have developed with them throughout the years.

I also had the opportunity to work alongside Nate Jui, Alex Spokoyny, Andrew DeAngelis, Andrew Parsons, Tom Maimone, Ye Zhu, Tim Noel, and Kashif Khan, all of whom are not just great friends, but amazing mentors. I feel very fortunate to have had the opportunity to learn from them. You all have taught me a great deal and also helped me to be as accomplished as I am in my graduate career. I am very thankful for your eagerness to help me develop professionally, and for your time in being great friends to me.

Apart from the incredible post-docs we have in the lab, I am very thankful for all the talented graduate students that I have worked alongside. Special thanks to Phill Milner, Mingjuan Su, Nathan Park, and Nick Bruno, who were always there for me for chemistry and non-chemistry related problems; Todd Senecal and Georgiy Teverovskiy for their eagerness to help younger graduate students; Yang Yang who I have learned a great deal from and really enjoyed talking chemistry with; and Spencer Shinabery, for all the time he sacrificed to make sure our lab is a very safe and organized working environment. Also special thank to Katrin Niederman, Katya Vinogradova, and Christine Nguyen for showing me that graduate school is not just about doing research, but also about creating balance. To Rong Zhu, Paula Ruiz-Castillo, James Colombe, Yuxuan Ye, and Pedro Arrechea, my graduate school experience would not have been complete without you guys.

I would also like to acknowledge the recent post-docs whom despite the short amount of time working together, have still taught me a great deal. Aaron Sather, Daniel Cohen, Yiming Wang, Dawen Nui, Mike Pirnot, Jeff Bandar, Sandra King, John Nguyen, Esben Olsen, Kurt Amburst and Shiliang Shi. I really enjoyed working with all of you, and am very thankful for the knowledge and wisdom that you have shared with me.

Last but not least, I have to thank my family for their continual support throughout my graduate studies—to my parents, for making graduate school life very easy for me; to my little sister, Nink, who visited me every year; and to Matt Haley, who was always there to support, guide, and continuously lift my spirit. I know that graduate school was as challenging for me as it was for all of you, and I thank and love all of you for being with me until the end.

PREFACE

Parts of this thesis have been adapted from the following published articles co-written by the author.

"Synthesis of Aryl Sulfonamides via Palladium-Catalyzed Chlorosulfonylation of Arylboronic Acids" DeBergh, J. R.; Niljianskul, N.; Buchwald, S. L. *J. Am. Chem. Soc.*, **2013**, *135*, 10638.

"Enantio- and Regioselective CuH-Catalyzed Hydroamination of Alkenes" Zhu, S.; Niljianskul, N.; Buchwald, S. L. *J. Am. Chem. Soc.*, **2013**, *135*, 15746.

"Enantioselective Synthesis of α-Aminosilanes by Copper-Catalyzed Hydroamination of Vinylsilanes" Niljianskul, N.; Zhu, S.; Buchwald, S. L. *Angew. Chem. Int. Ed.*, **2015**, *54*, 1638.

RESPECTIVE CONTRIBUTIONS

This thesis is the result of collaborative effort of the author and other colleagues at MIT. The specific contributions of the author are detailed below.

The work disclosed in **Chapter 1** resulted from collaboration between Dr. J. Robb DeBergh and the author. Dr. DeBergh performed the initial experiments for this project. The author contributed in the areas of ligand design and synthesis, and reaction optimization. Dr. DeBergh and the author collaborated on the examination of the scope of chlorosulfonylation as well as the one-pot arylsulfonamide synthesis. The author conducted the application of the reaction towards arenesulfonate ester synthesis and diarylsulfone synthesis.

The work disclosed in **Chapter 2** resulted from collaboration between Dr. Shaolin Zhu and the author. Dr. Zhu is credited with discovering the initial reaction and the optimization. Dr. Zhu and the author collaborated on the exploration of the scope of this method.

The work disclosed in **Chapter 3** resulted from collaboration between Dr. Shaolin Zhu and the author. Dr. Zhu and the author collaborated on the investigation of the initial hydroamination conditions towards vinylsilanes. The author is responsible for all optimization and synthetic work presented in this chapter. Dr. Zhu assisted the author in the mechanistic studies as presented in Scheme 4.

The work disclosed in **Chapter 4** was a collaborative effort between Dr. Shaolin Zhu and the author. Dr. Zhu discovered the initial reaction. Dr. Zhu and the author collaborated on reaction optimization (Table 1 and 2), as well as exploration of the substrate scope. The author carried out the experiments in Scheme 7. Dr. Zhu carried out the experiments in Schemes 9, 12, and 13. Both the author and Dr. Zhu collaborated on the experiments and the substrate synthesis for Schemes 3, 4, 8, and 10–11.

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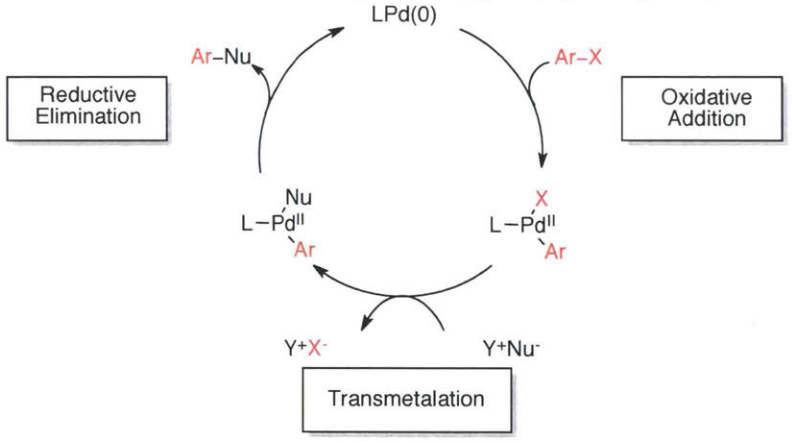
Chapter 4. Synthesis of γ-Chiral Amines via Copper-Catalyzed Hydroamination of 3,3-Disubstituted Allylic Alcohols and 3,3-Disubstituted Allylic Benzoates.

INTRODUCTION

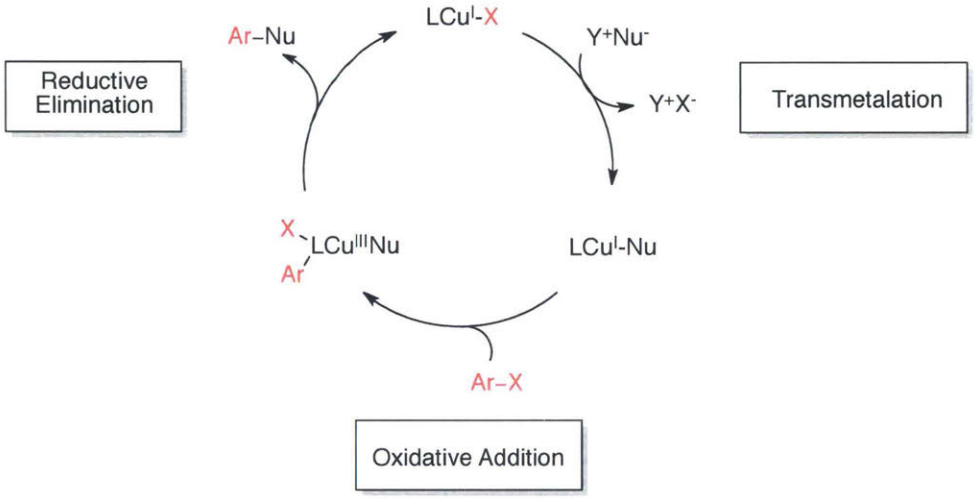
Transition metal-catalyzed transformations play a pivotal role in synthetic organic chemistry as chemists seek to improve the yield, selectivity, scalability, and safety of known reactions, as well as to develop fundamentally new chemical transformations. Recent advances in homogenous catalysis have positively impacted the fields of natural product synthesis,[1] medicinal chemistry,[2] and material science.[3,4] Although many late-transition metal-catalyzed methodologies have been developed, there is still room for advancement of other desirable, efficient, and selective transformations. The design and implementation of new cross-coupling methodologies can provide alternate methods that overcome current limitations.

Over the past decades, much advancement has been made in the fields of palladium and copper catalysis. Both of these transition metals have been used in numerous carbon-carbon bond-forming reactions as well as more recently in carbon-heteroatom bond-forming reactions. Fundamental to the activities of these late transition metals are their distinct modes of catalysis. For generic palladium-catalyzed cross-coupling reactions, the catalytic cycle begins with a Pd(0) species, which then undergoes oxidative addition with an electrophile to afford a Pd(II) species, followed by transmetalation with a nucleophile, and reductive elimination to yield the cross-coupled product and regenerate the Pd(0) species (Scheme 1). The copper catalytic cycle begins with a Cu(I) species, which undergoes transmetalation with a nucleophile, followed by oxidative addition with an electrophile to a Cu(III) species, and reductive elimination to deliver the cross-coupled product and regenerate the Cu(I) species (Scheme 2).

Scheme 1. *Fundamental steps of Pd(0)/Pd(II) catalytic cycle.*



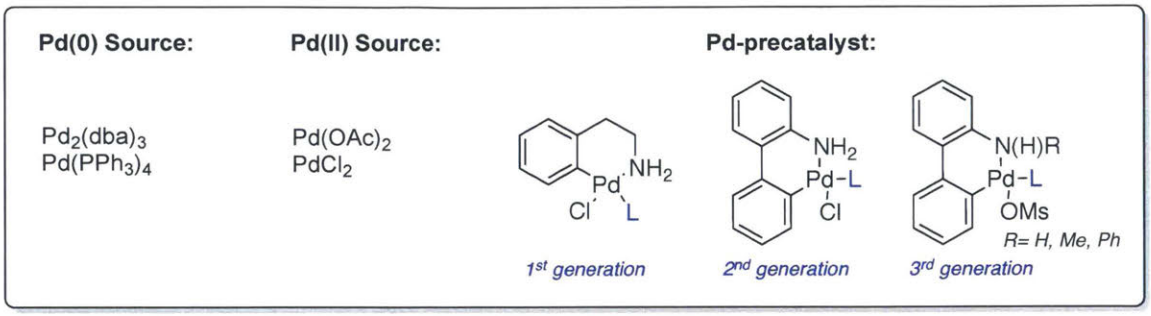
Scheme 2. *Fundamental steps of Cu(I)/Cu(III) catalytic cycle.*



Despite the apparent simplicity of their catalytic cycles, there are many elements that must align to overcome the formation of undesired byproducts and achieve successful bond formation. These issues are present at every step including the initial active catalyst generation. Often some palladium and copper precursors require a change in oxidation state; the palladium cycle may require the generation of active Pd(0) species from Pd(II) precursors and copper cycle may require the generation of active Cu(I) species from Cu(II) precursors. Additionally, these metals needed to bind to the right supporting ligands in order to enable catalysis of the desired transformations.

There have been many developments in active catalyst generations for palladium-catalyzed cross-coupling reactions.[5] These range from the simple pre-stirring of a Pd(0) source with a phosphine ligand to the in situ reduction of Pd(II) to active $L_1Pd(0)$ species using excess amounts of ligand or water activation.[5a] These methods have drawbacks in that the Pd(0) source often has ligands that can interfere with the reaction, such as in the case of $Pd_2(dba)_3$ to Pd(0).[6] Additionally, reduction of Pd(II) is not always an efficient process and can consume precious ligand. Recently, our laboratory has developed Pd-precatalysts to overcome the problems associated with catalyst pre-activation (Figure 1).[5b-d] These Pd-precatalysts (categorized as 1st to 3rd generation precatalysts) are pre-monoligated Pd(II) species that are readily converted to $L_1Pd(0)$ under ambient conditions with weak base.

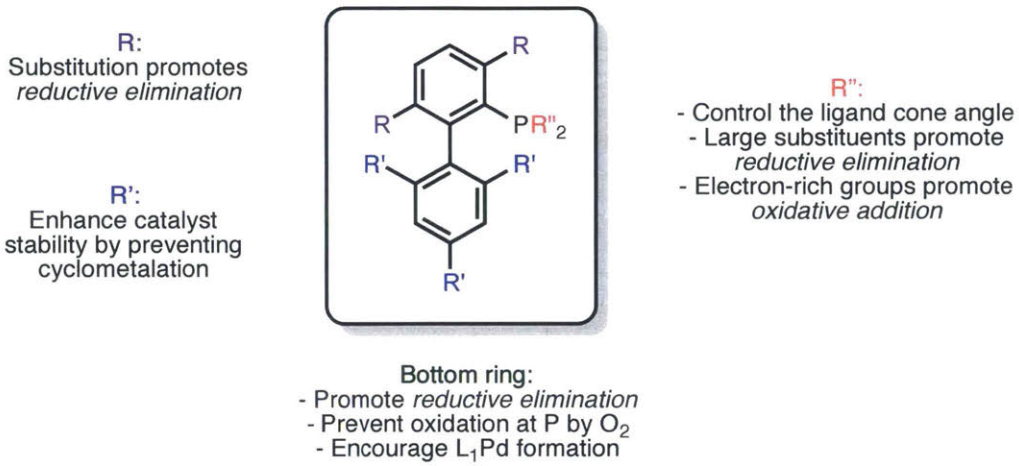
Figure 1. *Common Precursors to Active Monoligated-Palladium(0) Catalyst*



As the experience of reagent's reactivity and compatibility for cross-coupling reactions increase, understanding around these factors help us fine-tune these systems to limit the formation of by-products (e.g. from homocoupling and reduction) and improve the reaction efficiency (e.g. milder conditions and lower catalyst loadings). Although there are many factors which are key to the success of both palladium and copper catalyzed reactions, advances in transition metal-catalyzed cross-coupling reactions can be credited largely to the development of new supporting ligands. The supporting ligand can play a significant role on each step of the catalytic cycle in addition to contributing to the overall stability of the catalyst.

Phosphine ligands play a crucial role in the success of both Pd-catalyzed and Cu-catalyzed bond forming reactions. In this context, our laboratory has invested tremendous efforts to develop biaryl phosphine ligands that can be tailored to a variety of Pd-catalyzed cross-coupling reactions.[7] These ligands play a significant role in catalyst activity as well as stability. First, the presence of the bottom aryl ring (Figure 2) provides a secondary interaction to Pd via the "*ipso*" interaction, which enables the formation of reactive monoligated $L_1Pd(0)$ complexes, thereby promoting oxidative addition of electrophiles.[8] Second, biaryl phosphine ligands can help facilitate transmetalation.[9] Furthermore, the ability of the bottom aryl ring to provide a secondary interaction with Pd and the choice of the substituent on the phosphine can further assist reductive elimination.[8a,c,10] As will be demonstrated in the following chapters, the structure of supporting ligands is crucial to the success of transition metal-catalyzed transformations.

Figure 2. *Structural Element of Biarylphosphine Ligands and Their Contribution to the Elementary Steps in the Catalytic Cycle*



The amount of knowledge regarding palladium and copper catalytic cycles has enabled significant contributions to the applications of these catalysts. The results reported herein focus on the development of palladium and copper catalysts to carry out novel carbon-heteroatom bond-forming reactions through functionalization of arenes and alkenes. The body of work presented in this thesis will fall into two distinct parts. The first is the development of palladium-catalyzed cross-coupling reactions between arylchlorosulfate electrophiles with organometallic reagents to generate arylsulfonyl chlorides and the applications thereof. The second part details a copper-catalyzed formal hydroamination reaction which utilizes a copper(I) hydride species to effect C–N bond formation and the application of this methodology towards the synthesis of various classes of chiral amines.

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Part I.

Chapter 1.
Palladium-Catalyzed Chlorosulfonylation of Arylboronic Acids

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Synthesis of Aryl Sulfonamides via Palladium-Catalyzed Chlorosulfonylation of Arylboronic Acids

J. Robb DeBergh, Nootaree Niljianskul, and Stephen L. Buchwald

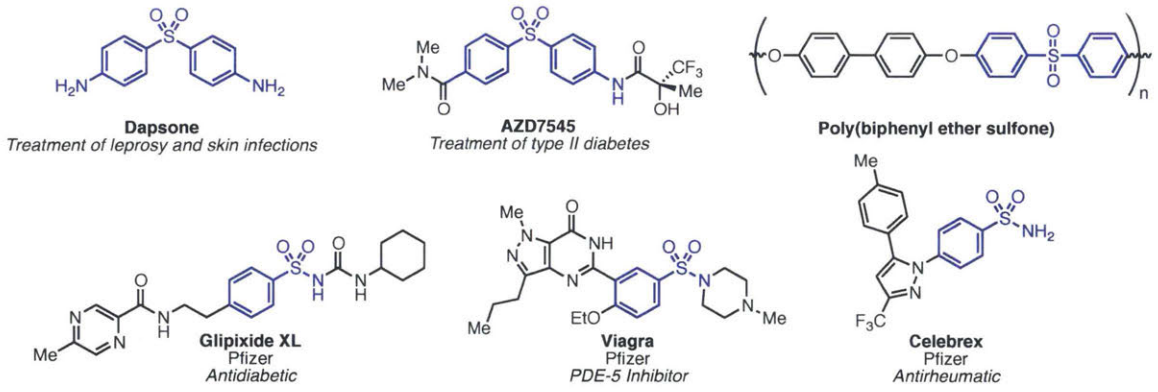
Journal of the American Chemical Society, **2013,** *135* (29), 10638–10641

DOI: 10.1021/ja405949a

1.1 Introduction

Sulfonyl subunits (-SO_2-) are important due to their presence in many molecular building blocks and biologically active compounds. For instance, aryl sulfonamides are contained in several important pharmaceuticals currently on the market. Diaryl sulfone structural units can be found in biologically active molecules as well as polymer materials (Figure 1).[1] Thus, a general method to install these sulfonyl groups would serve as a powerful tool to many industries.

Figure 1. *Important Molecules Containing the Sulfonyl Subunit*



Aryl sulfonamides in medicinal chemistry can be traced back to the 1930's, with the discovery and development of the first commercially available antibiotics, sulfanilamide (Figure 2).[2] Today, the presence of sulfonamides in medicinal agents is widespread; close to ten percent of the top 100 pharmaceuticals prescribed in 2011 either bear a sulfonamide subunit or are co-administered with a sulfonamide-containing drug.[3] In general, aryl sulfonamides can be prepared by the straightforward reaction of a sulfonyl chloride with an amine.[4] However, the difficulties associated with sulfonamide synthesis stem not from the amination reaction, but from the preparation of sulfonyl chlorides.

Figure 2. *Structure of Prontosil, the Prodrug to the First Sulfonamide Antibiotics*

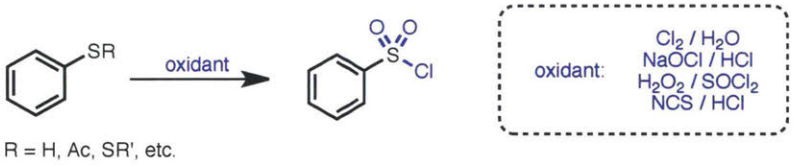
The following two processes represent the state of the art methods in arylsulfonyl chloride synthesis: (1) electrophilic aromatic substitution (EAS) with chlorosulfonic acid[5] (Scheme 1, Eq. 1) and (2) oxidative chlorination of organosulfur compounds (Eq. 2).[6-10] Both approaches suffer from significant limitations. In particular, the acidic conditions required for the EAS processes (and most oxidative chlorination methods) impose severe restrictions on substrate scope. Furthermore, desired substitution patterns may be inaccessible via EAS as the regioselectivity is dictated by the intrinsic properties of the parent arene. Traditionally, oxidative chlorination involves the use of hazardous reagents (e.g., aqueous chlorine)[7] or strong chlorinating agents (e.g., $SOCl_2$[8] and SO_2Cl_2).[9] Although milder conditions have been reported,[10] oxidative chlorination of thiophenol derivatives ultimately require prior formation of a carbon–sulfur bond.

Scheme 1. *Preparation of Arylsulfonyl Chlorides*

1) Electrophilic Aromatic Substitution:

(Eq. 1)

2) Oxidative Chlorination:

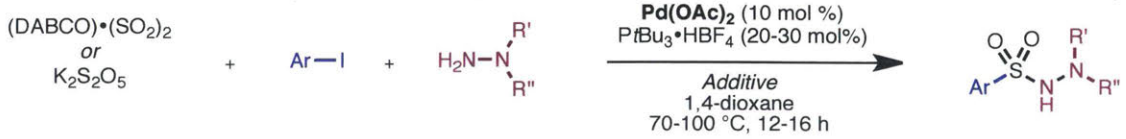


(Eq. 2)

R = H, Ac, SR', etc.

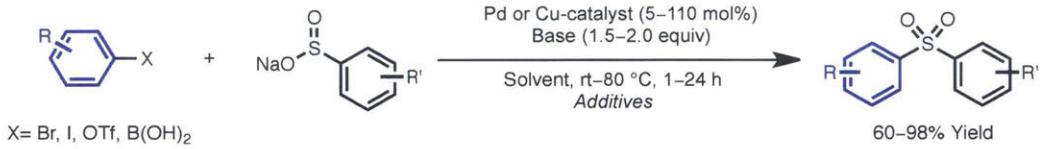
In principle, a transition metal catalyst could obviate the need for such reagents and permit the convergent synthesis of aryl sulfonamide analogs (as well as diaryl sulfones), allowing variation of both sulfonyl ($-SO_2-$) substituents. Unfortunately, the success of Pd-catalyzed arylsulfonamide synthesis is limited to a single aminosulfonylation process, initially reported by Willis in 2010, to prepare *N*-amino-sulfonamides from aryl iodides and hydrazines (Scheme 2).[11] While this example represents an important achievement in sulfonylation chemistry, amine nucleophiles remain incompatible with these types of couplings.[11,12]

Scheme 2. *Synthesis of N-aminosulfonamides via Pd-catalysis*



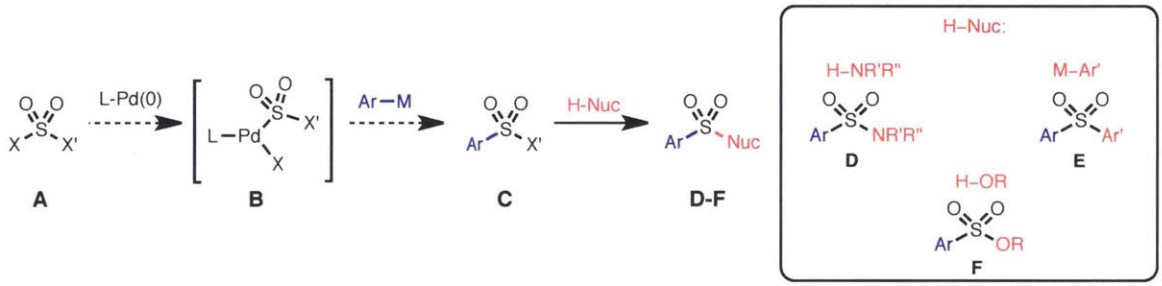
On the other hand, diaryl sulfones are traditionally synthesized by the oxidation of the corresponding sulfide or by the Friedel–Crafts reaction of arenes with arenesulfonyl halides.[13] The sulfide precursors to sulfones are typically prepared via an Ullmann coupling of thiophenol derivatives with aryl halides.[13a] Current strategies to synthesize aryl sulfones through transition metal-catalysis are less common and often employ aryl sulfinate nucleophiles (Scheme 3).[14] These methods are either limited by the availability of aromatic sulfinates and thio-arenes, or require multiple synthetic operations to access the desired sulfone.

Scheme 3. *Synthesis of Diarylsulfones via Pd-catalysis*



To address these limitations in arylsulfonamide and diarylsulfone synthesis, we devised an alternative strategy (Figure 3). This strategy involves oxidative addition of LPd(0) to an electrophile of the type X–SO_2–X' (**A**), where X and X' represent leaving groups of different reactivity, to generate an oxidative addition complex **B**. Subsequent coupling with an organometallic nucleophile would afford electrophilic species **C**, which in turn, would serve as useful precursors to a variety of sulfonyl functional groups, such as aryl sulfonamides (**D**), aryl sulfones (**E**), and arenesulfonate esters (**F**).

Figure 3. *Palladium-Catalyzed Sulfonylation of Activated Arenes*

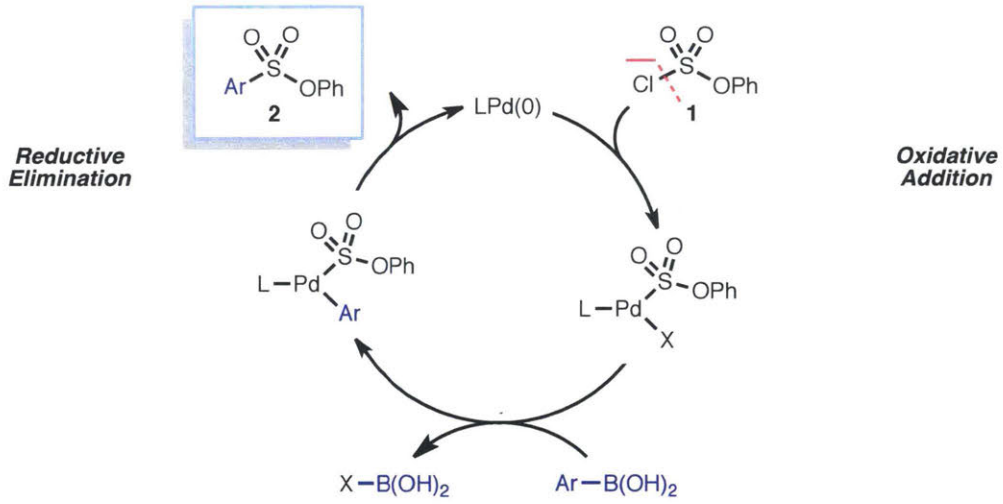


We envisioned that when using a readily prepared aryl chlorosulfate (**1**) as our electrophile (Figure 4), Pd(0) would insert into the SO_2–Cl bond (pathway (i)), and the cross-coupling with a weak nucleophile such as an arylboronic acid would then generate the arenesulfonate ester (**2**). The resultant intermediate could subsequently react with a carbon- or heteroatom-based nucleophile to afford the desired sulfonyl products (**D-F**, see Figure 3). An

alternative pathway (ii) involving Pd(0) insertion into the SO_2–OAr bond of **1** to generate the arenesulfonyl chloride (**3**) after coupling with the boronic acid is also possible. The catalytic cycle corresponding to pathway (i) is illustrated in Figure 5.

Figure 4. *Palladium-Catalyzed Sulfonylation of Activated Arenes*

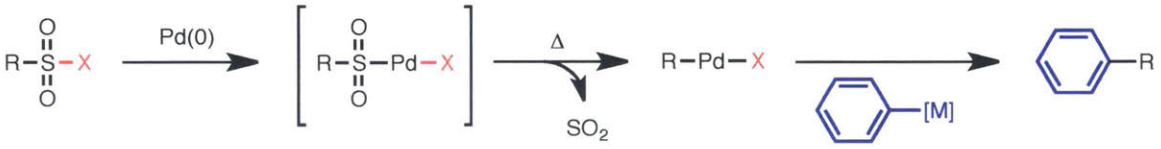
Figure 5. *Proposed Mechanistic Cycle*



Other similar electrophiles, such as sulfonyl chlorides (RSO_2Cl, R = aryl, alkenyl, benzyl, 2-methallyl) have been employed as the electrophilic reagents in metal-catalyzed desulfitative cross-coupling reactions to construct carbon–carbon bonds.[15] The insertion of Pd(0) into the S–Cl bond of arenesulfonyl chlorides is generally followed by the loss of SO_2 from the resulting Cl-Pd-SO_2R complexes to generate the Cl-Pd-R species (Scheme 4).[16] However, this desulfonylation process can be suppressed by carrying out reactions at low temperatures (< 25 °C), as has been previously used to generate sulfones.[17] In addition, electron-rich phosphine ligands have been shown to improve the stability of Cl-Pd-SO_2R complexes.[18] Thus, we

expected to overcome the undesired pathway through ligand design and reaction optimization. Based on the known stability of phosphine-ligated Pd-SO_2 complexes, we hypothesized that electron-rich biarylphosphines would serve as ideal ligands to help stabilize Pd-SO_2 complexes.[18]

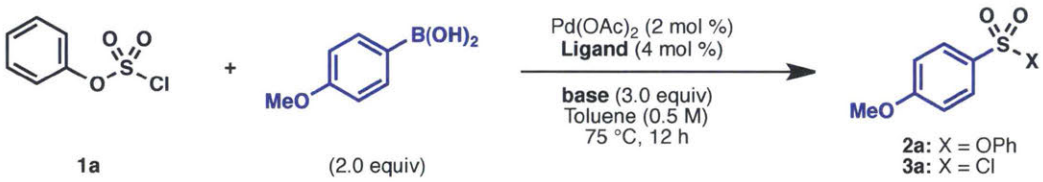
Scheme 4. *Palladium-Catalyzed Desulfitative Cross-coupling*



1.2 Results and Discussion

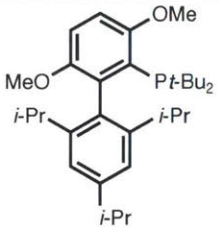
We began our study by examining the reaction of phenyl chlorosulfate (**1a**) and coupling partner arylboronic acid using $Pd(OAc)_2$ as the palladium source in conjunction with an electron-rich ligand and an inorganic base. We chose phenyl chlorosulfate (**1a**) because of its simplicity, ease of preparation, and it is an easy to handle liquid.[19] We selected arylboronic acids as coupling partners because of their compatibility with other functional groups as well as ready availability and ease of handling.

Table 1. *Preliminary Investigation of Reaction Conditions*[a]

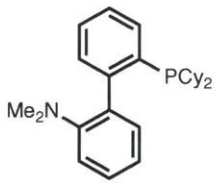


1a (2.0 equiv)

Entry	Ligand	Base	**2a** (%)[b]	**3a** (%)[b]
1	*t*-BuBrettPhos	K_3PO_4	31	4
2	*t*-BuBrettPhos	K_2CO_3	15	22
3	*t*-BuBrettPhos	Na_2CO_3	4	36
4	*t*-BuBrettPhos	none	0	59
5	DavePhos	none	0	87
6	none[c]	none	0	0



t-BuBrettPhos



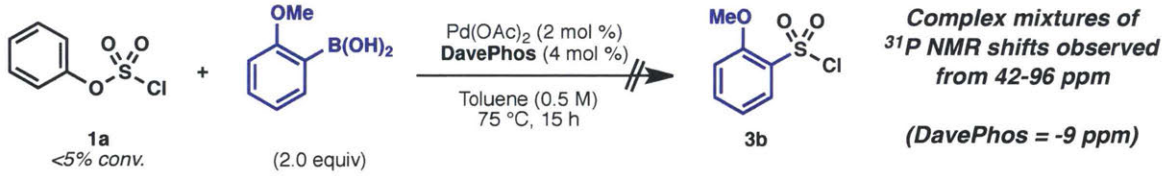
DavePhos

[a]Performed on a 0.5 mmol scale with respect to **1a**. [b]GC yields. [c]Performed without palladium catalyst for 24 h.

Results from a preliminary survey of bases are outlined in Table 1, utilizing 4-methoxyphenylboronic acid in combination with a catalyst derived from $Pd(OAc)_2$ and *tert*-ButylBrettPhos or DavePhos. Unexpectedly, we observed mixtures of **2a** and the corresponding sulfonyl chloride (**3a**) when excess base was used (Table 1, entries 1–3). However, we discovered that **3a** could be formed exclusively in the absence of base (entries 4 and 5). Without the use of base, we proposed that we could inhibit the hydrolysis of our electrophiles. Further, control experiments showed that neither product is formed in the absence of palladium or phosphine ligand (entry 6).[20]

In light of these results, we tested the system on other arylboronic acids, with the attempt to generate arylsulfonyl chlorides. However, these newly identified conditions proved ineffective for *ortho*-substituted arylboronic acids. For example, subjecting 2-methoxyphenylboronic acid to these conditions resulted in near complete recovery of phenyl chlorosulfate (**1a**) (Scheme 5). Additionally, upon the examination of the ^{31}P NMR signals at the end of the reaction, we observed multiple peaks, which corresponded to oxidized phosphine. This leads us to speculate that the ligand may be oxidized under the reaction conditions with the phenylchlorosulfate electrophile acting as a strong oxidizing reagent.

Scheme 5. *Reactions with Ortho-Substituted Arylboronic Acids*

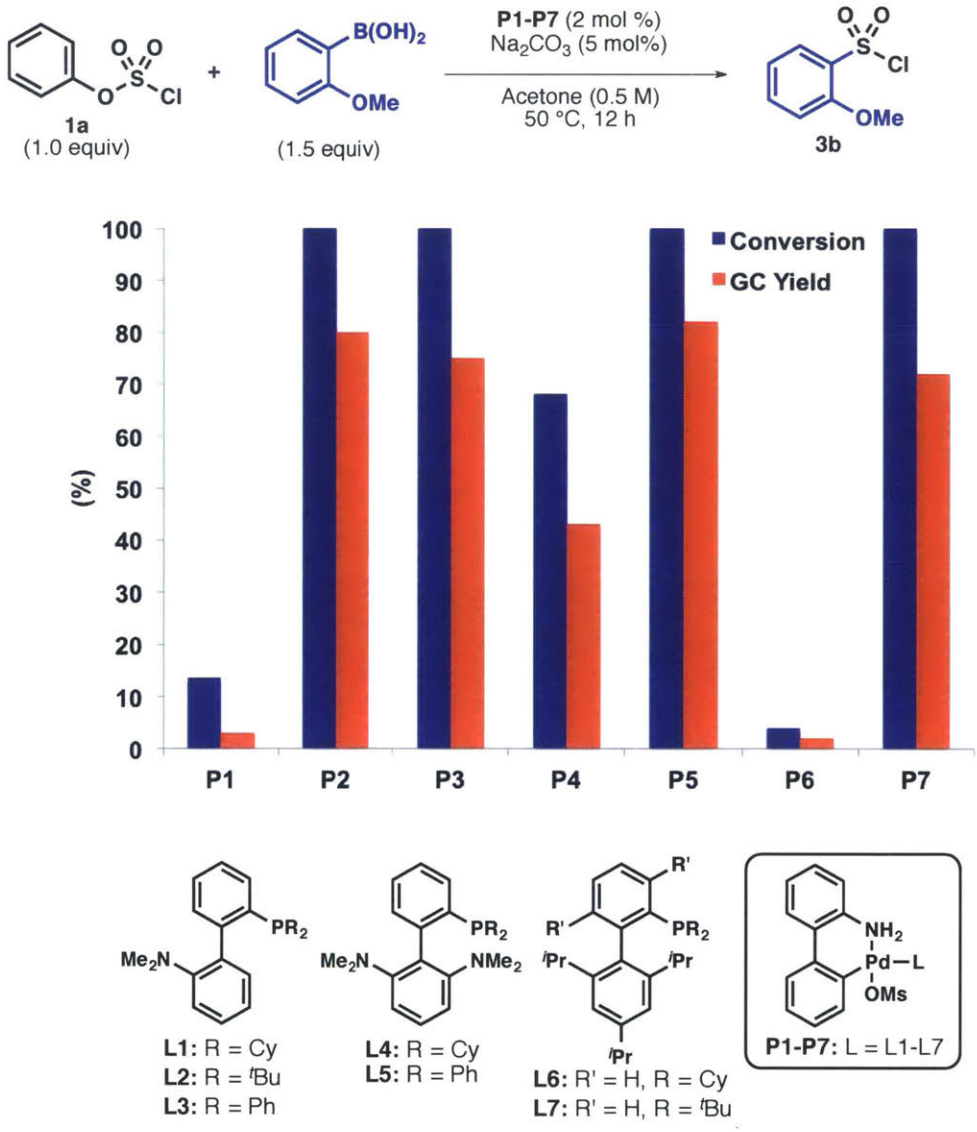


We proposed that we could minimize the oxidation of the ligand by employing a preligated Pd complex. Additionally, we hypothesized that phosphine ligand with more electron-deficient substituents at the phosphine would be slower to oxidize. To this end we investigated the pre-ligated Pd complexes in conjunction with 2-methoxyphenylboronic.

Figure 6 shows the ligands examined when pre-ligated palladium complexes were used. The use of palladacyclic precatalysts[25] (**P1–P7**) allowed for these experiments to be conducted at lower temperatures presumably due to the milder conditions needed for the generation of LPd(0) complex. In this case, a catalytic amount of base (5 mol% Na_2CO_3) was needed for precatalyst activation. Solvent investigations showed the reaction to be optimal using anhydrous acetone.

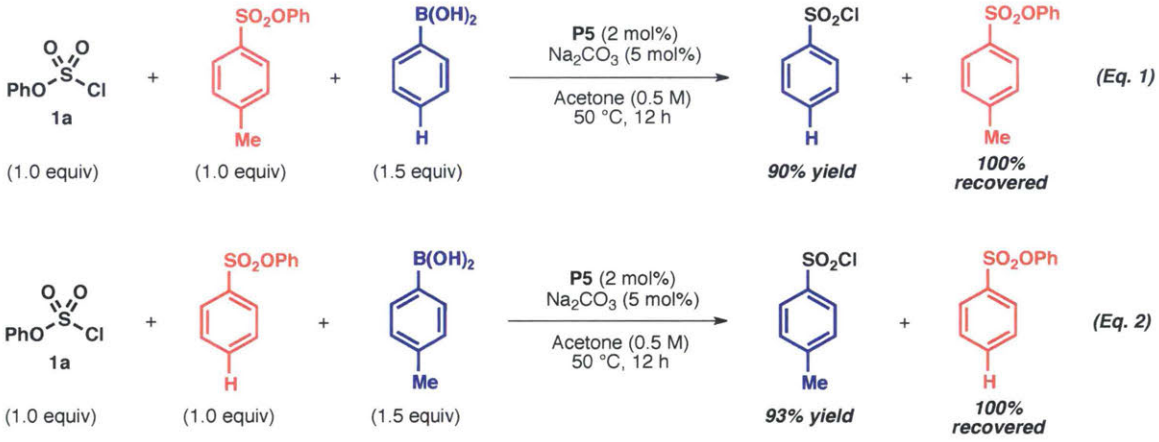
As shown in the coupling of **1a** with 2-methoxyphenylboronic acid (Figure 6), precatalysts based on diphenyl- (**L3** and **L5**) and di-*tert*-butylbiaryl phosphine ligands (**L2** and **L7**) proved to be the most effective. In particular, the PhCPhos precatalyst (**P5**) afforded **3b** in the highest yield (82%), albeit with only a slight improvement over that derived from *tert*-BuDavePhos, **L2** (80%).[26] In contrast, the use of XPhos (**L6**),[27] previously reported to be an excellent ligand for Suzuki–Miyaura reactions, provided little product.

Figure 6. *Ligand Effects*

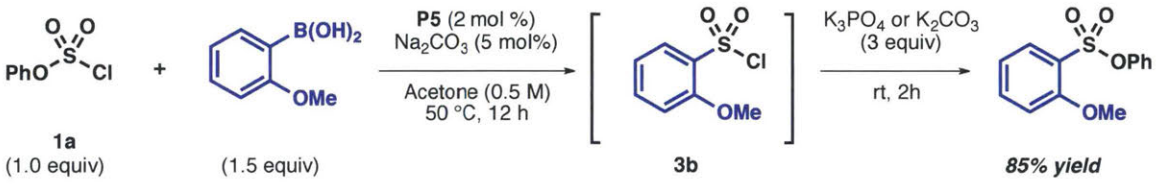


We verified that aryl sulfonate esters (**2**) are not converted to the corresponding sulfonyl chlorides (**3**) under the reaction conditions (Scheme 6).[21] However, we noted that the ester **2a** is generated when crude reaction mixtures of **3a** were treated with excess K_3PO_4 or K_2CO_3 (following complete consumption of **1a** in the absence of base, Scheme 7). This supports that the arylsulfonyl chloride is the cross-coupling product.

Scheme 6*. Control Experiment: To confirm that sulfonate esters are not converted to sulfonyl chlorides*

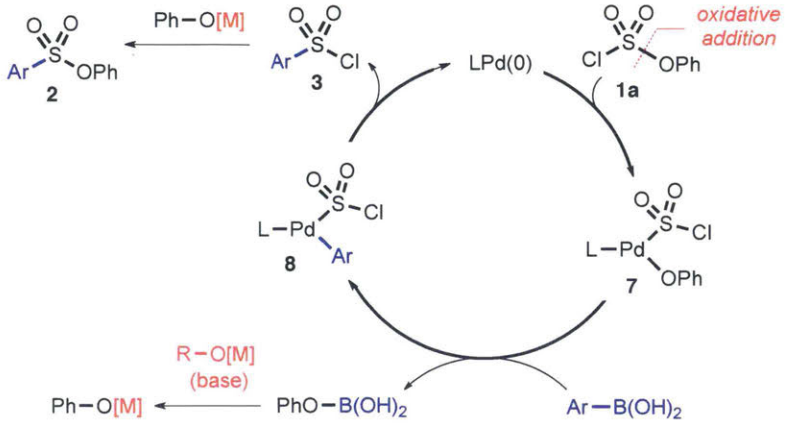


Scheme 7*. Control Experiment: To confirm that Sulfonate Esters are generated in situ from Sulfonyl Chlorides*



The above results suggested a catalytic cycle in which Pd(0) inserted into the SO_2–OPh bond of phenyl chlorosulfate (**1a**, Figure 7).[22] The phenoxy substituent of the resulting Pd-sulfinate complex (**6**) would be expected to facilitate transmetalation without the aid of a base;[23] subsequent reductive elimination from intermediate **8** would yield sulfonyl chloride **3** and regenerate the active Pd(0) catalyst. Base likely promotes the generation of phenoxide, which in turn would react with the sulfonyl chloride to provide sulfonate ester **2**. To the best of our knowledge, such a reactivity pattern with a Pd(0)/Pd(II) system has never been reported.

Figure 7. *Proposed Catalytic Cycle*



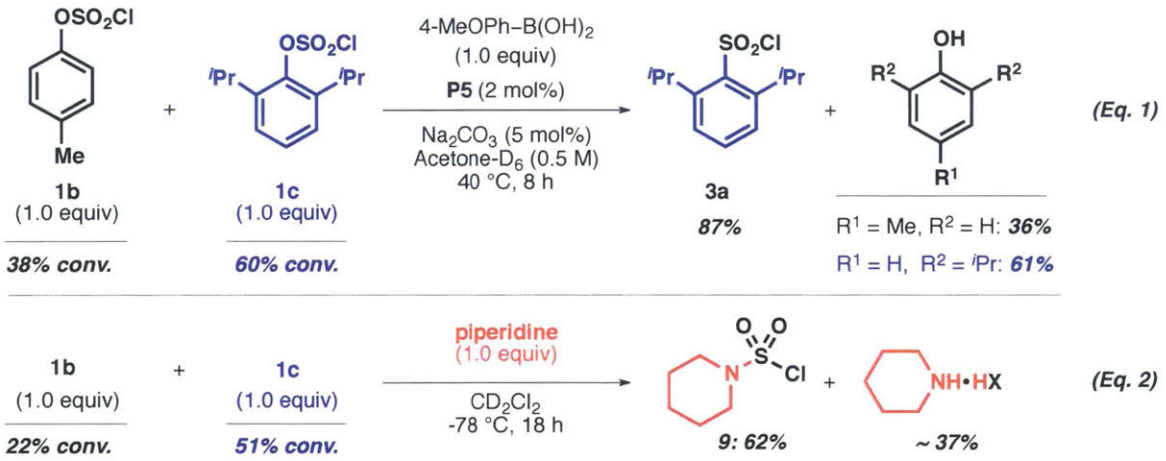
However, Buncel and co-workers have previously observed the displacement of aryloxide from aryl chlorosulfate derivatives (**1**) in the context of direct nucleophilic additions (Scheme 8).[24] They rationalized the preferred displacement as attributed by relief in the internal steric strain, and that the partial rupture of the S–O bond in the bipyramidal transition state is accompanied by a gain in vibrational and rotational degrees of freedom which combined to yield a more positive change in the transition state entropy. This precedent demonstrates the lability of the SO_2–OPh bond, as we have observed for the transfer of $-SO_2Cl$ in the analogous Pd-catalyzed process.

Scheme 8. *S-O Bond Scission for Reaction with Piperidine*

Regarding the oxidative addition step, we surmised that the sp^3 oxygen atom of **1a** might direct the insertion of Pd(0) into the proximal PhO–SO_2 bond. However, results from a competition experiment between **1b** and the bulkier **1c** (Scheme 9, Eq. 1) revealed that **1c** is slightly more reactive than **1b** (ratio of recovered **1b**/**1c** = 1.7:1).[37] Moreover, this trend in reactivity is not specific to Pd-catalysis. For example, reacting a 1:1 mixture of **1b** and **1c** with piperidine (Scheme 9, Eq. 2) resulted in a comparable ratio of recovered **1b**/**1c** (1.6:1) along

with formation of the sulfamoyl chloride (**9**) derived from piperidine. This is consistent with Buncel's rationale in which elongation of the S–O bond relieves considerable strain in the bipyramidal transition state, which according to the authors, such relieve of strain would not accompany partial rupture of the S–Cl bond.[24] In this regard, increasing the size of the aryloxy substituent of **2** may intensify this stereoelectronic effect and further weakens the S–O bond.

Scheme 9. Competition Experiment of Aryl Chlorosulfate Electrophiles

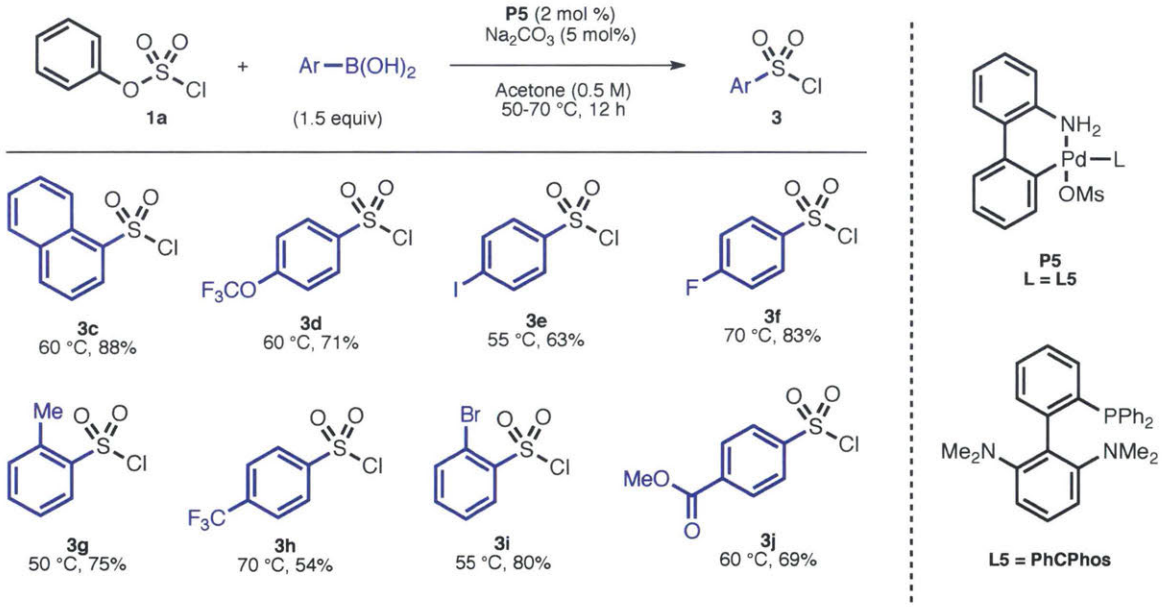


We note that while others have demonstrated that arylsulfonyl chlorides are efficient cross-coupling partners for various Pd-catalyzed processes,[33-35] these intermediates are essentially unreactive under our mild chlorosulfonylation conditions. For instance, palladium typically catalyzes the desulfonylation of arylsulfonyl chlorides; and these substrates (**3**) are often used as aryl halide equivalents for carbon–carbon bond-forming processes.[35] In contrast, we found that using our palladium precatalyst in conjunction with biarylbiphenyl CPhos ligand, the other undesired pathways were suppressed, allowing us to obtain the arylsulfonyl chloride products.[36]

With the improved protocol, utilizing 2 mol % **P5** and 5 mol % of Na_2CO_3 in acetone, we next prepared a number of arylsulfonyl chlorides (Scheme 12). In general, electron-rich, electron-neutral, and electron-deficient arylboronic acid reagents were all compatible substrates. Couplings with electron-rich substrates can be conducted at 50 °C, while reactions with electron-deficient substrates are typically slower and require higher temperatures.[28,29] The cross-

coupling reaction is tolerant of iodo-, bromo-, and chloro-substituted phenylboronic acids as well as those bearing ester and acetyl groups (Table 2). Furthermore, substitution patterns that cannot be accessed by an EAS processes can now be achieved (**3h–3j**). We noted that while most of the sulfonyl chlorides are stable to chromatography, electron-deficient compounds, such as **3h** and **3j**, were found to decompose to varying degrees upon attempted purification, resulting in lower isolated yields in these cases.[30]

Table 2. *Palladium-Catalyzed Chlorosulfonylation of Arylboronic Acids*[a]

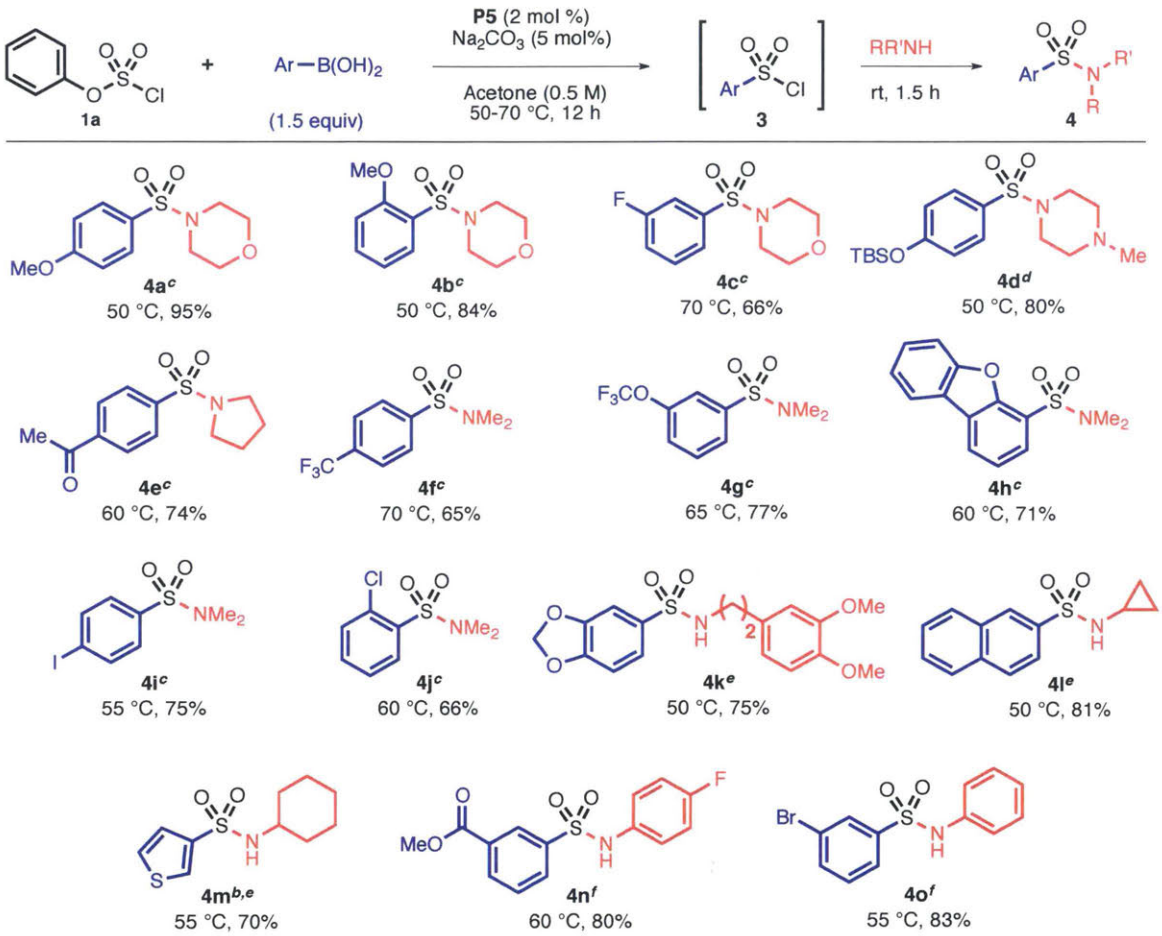


[a]Yields represent isolated yields (average of two runs): **1a** (1 mmol), $ArB(OH)_2$ (1.5 mmol), Na_2CO_3 (5 mol %), **P5** (2 mol %), degassed, anhydrous acetone (2 mL), 50-70 °C, 12 h.

To demonstrate the synthetic utility of this method we attempted to prepare a range of arenesulfonyl compounds by reacting the sulfonyl chloride intermediates with a variety of nucleophiles. Nitrogen-based nucleophiles were first examined in efforts to synthesize aryl sulfonamides in a one-pot process. We found that various sulfonamides can be generated in good yields from primary (**4k–4o**) and secondary amines (**4a–4j**) (Table 3). Even weakly nucleophilic aniline derivatives can be incorporated into the sulfonamide moiety with the use of pyridine to facilitate the amination step (**4n, 4o**). The chlorosulfonylation reaction also tolerates chlorosubstituted arylboronic acids (**4j**) as well as substrates containing TBS-ethers (**4d**), esters (**4n**), and acetyl functional groups (**4e**). Heteroaryl substrates, such as 3-thiophene (**4m**) and 2-

dibenzofuran boronic acid were also suitable coupling partners (**4m, 4k**).[32] Additionally, for electron-deficient sulfonyl chlorides such as **3h** and **3j**, instability to chromatography is obviated by this one-pot process.[31]

Table 3. *One-pot Preparation of Sulfonamides via Arylsulfonyl Chlorides*[a]



[a]Isolated yields (average of two runs). **Step 1:** See conditions in Table 2. [b]**P4** (2 mol %) was used. **Step 2:** [c] R_2NH (2.2 mmol), rt, 1.5 h. [d]1-methylpiperazine (1.2 equiv) and DIPEA (2.0 equiv) were used. [e]RNH_2 (3.0 equiv), rt, 1.5 h. [f]$ArNH_2$ (1.2 equiv), pyridine (3.0 equiv), rt, 5 h.

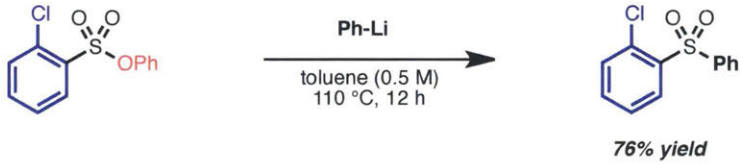
Since diaryl sulfones are also important motifs useful in medicinal chemistry and material science,[1] we next explored the applications of our Pd-catalyzed chlorosulfonylation product towards their syntheses. The organozinc reagents were tested as nucleophiles for the synthesis of sulfones. Our first attempt used the readily prepared benzo[*b*]thiophen-2-ylzinc chloride (**10**), which was added directly to the crude reaction mixture (Scheme 10). However, this one-pot

protocol was unsuccessful as the major product of the reaction was the phenyl arenesulfonate ester **2b**. It appears that the phenol generated from the initial oxidative insertion reacted with the arylzinc reagent to form phenoxide, which further reacted with the arylsulfonyl chloride to generate sulfonate ester **2b**. We noted that using pure arenesulfonyl chlorides **3**, the reaction with arylzinc chloride **10** proceeded cleanly to generate the corresponding sulfones (**11**, Scheme 11). Product **2b** was not reactive towards substitution by organozinc, -magnesium, and -lithium reagents at ambient condition, however, it does react with phenyl lithium upon refluxing in toluene (Scheme 12).

Scheme 10. *Attempted One-Pot Synthesis of Unsymmetrical Diaryl Sulfones via Arylsulfonyl Chlorides*

Scheme 11. *Synthesis of Arylsulfones from Purified Arylsulfonyl Chlorides*[a]

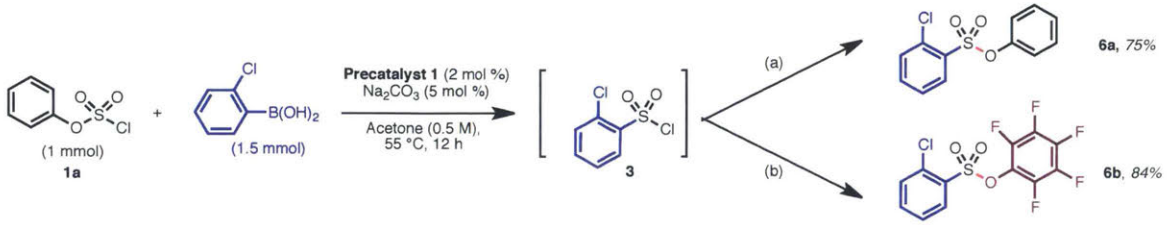
Scheme 12. *Reaction of Aryl Sulfonate Ester with Aryl Lithium Reagent*



As harsh conditions were required for conversion of phenyl arenesulfonate esters to diaryl sulfones, we felt that they were not optimal intermediates for this process. Thus, we sought to transform the arylsulfonyl chloride products into an arene sulfonate that would be more reactive and could be done in a one-pot sequence. By exploiting the higher acidity of the perfluorophenol when compared to the phenol, we proposed conversion of the arylsulfonyl chloride to its corresponding perfluorophenyl arenesulfonate. Indeed, treating the crude reaction mixture with perfluorophenol and diisopropylethylamine, we were able to generate the

corresponding perfluorophenyl arenesulfonate (**6b**, Scheme 13).

Scheme 13. *Synthesis of Arenesulfonate Esters from Sulfonyl Chlorides*[a]



[a]Reaction conditions: (a) Diisopropylethylamine (2 mmol, 2 equiv), 0 °C to rt, 2 h. (b) Pentafluorophenol (2 mmol, 2 equiv), diisopropylethylamine (1.5 mmol, 1.5 equiv), 0 °C to rt, 2 h. Isolated yields.

With the more electron-withdrawing perfluorophenyl ester (**6b**), nucleophilic substitution using phenyl lithium proceeded at room temperature to generate the diaryl sulfone (Scheme 14). Additionally, these perfluorophenyl arenesulfonates are desirable products themselves as they are significantly more stable than the corresponding chlorides.[43] We have demonstrated the one-pot synthesis of a range of perfluorophenyl arenesulfonate derivatives (Table 4). In particular, we have synthesized analogues of arylsulfonyl chlorides that are unstable (**6d**), as well as other perfluoroarene sulfonates with an aryl halide moiety (**6b, 6e**).

Scheme 14. *Synthesis of Arylsulfone from Perfluorophenyl Arenesulfonate*

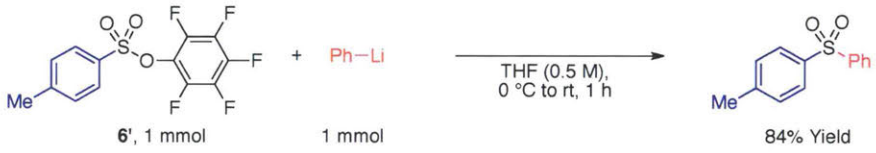
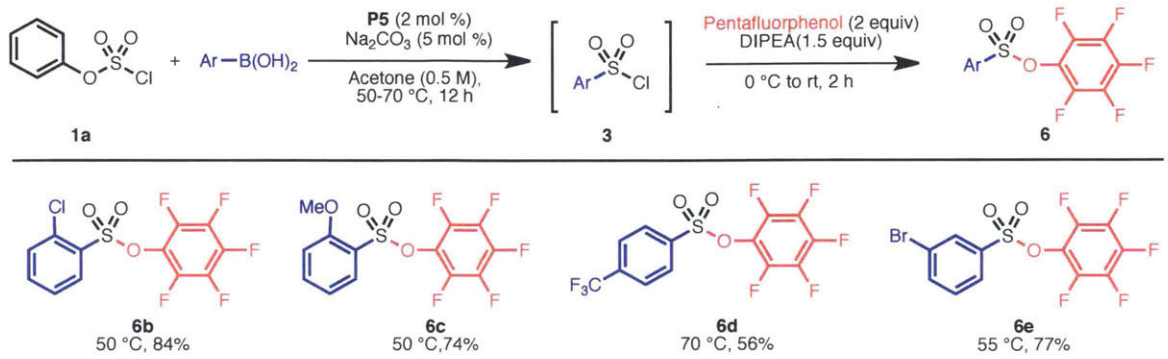


Table 4. *One-pot Preparation of Perfluorophenyl Arenesulfonates via Arylsulfonyl Chlorides*[a]



[a]Reaction conditions: Precatalyst 1 (2 mol %), **1a** (1.0 mmol, 1.0 equiv), $ArB(OH)_2$ (1.5 mmol, 1.5 equiv), Na_2CO_3 (0.05 mmol), Acetone (2 mL); isolated yields.

1.3 Conclusions

In conclusion, the first Pd(0)/Pd(II)-catalyzed chlorosulfonylation reaction of arylboronic acids has been developed. We have demonstrated that phenyl chlorosulfate (**1a**) represents an excellent $[SO_2Cl]^+$ synthon in the context of Pd-catalyzed Suzuki-Miyaura cross-coupling. The chlorosulfonylation reaction exhibits considerable functional group tolerance and the transformation is inherently regioselective; the substitution patterns of many of the products shown (such as **3h–3j**) cannot be accessed by EAS processes. Several additional features of this chemistry are also noteworthy. First, Pd(0) reacts with phenyl chlorosulfate (**1a**) in preference to aryl iodide groups bearing electron-withdrawing sulfonyl groups *para* to the iodo-substituents (e.g. **3e** and **4i**). Second, while others have demonstrated that arylsulfonyl chlorides are efficient cross-coupling partners for various Pd-catalyzed processes,[33-35] these intermediates are essentially unreactive under the chlorosulfonylation conditions. As such, this reaction represents a useful alternative to known methods of installing SO_2-Cl functional groups. Furthermore, the sulfonyl chlorides can be derivatized and isolated as the corresponding sulfonamides, sulfones, and sulfonate esters. Investigations aimed at broadening the scope of this transformation are currently in progress.

1.4 Experimental

I. General Information

General Reagent Information

Unless otherwise stated, all reactions were set-up on the bench top and carried out under an argon atmosphere. Anhydrous acetone was purchased from Acros Organics. All other solvents were purified and dried by passage through successive alumina and Q5 reactant-packed columns on a solvent purification system. Sulfuryl chloride, phenol, pyridine, and *N,N*-diisopropylethylamine were purchased from Aldrich Chemical Co. and used as received. Anhydrous Na_2CO_3 was received from VWR. The arylboronic acid substrates were purchased from Frontier Scientific, Combi-Blocks, and Aldrich and used as received without further purification. Ligand PhDavePhos (**L3**) was purchased from Strem, and *tert*-BuDavePhos (**L2**) was obtained from Aldrich. CPhos (**L4**)[38] and precatalysts of **P1**, **P2**, **P6**, and **P7** were synthesized according to literature procedures.[25] Compounds were purified by flash chromatography using Silicycle SiliaFlashP60 (230-400 mesh) silica gel.

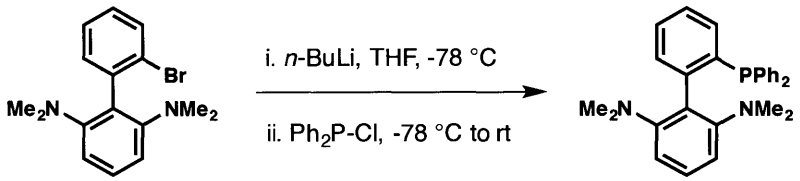
General Analytical Information

All compounds (starting materials and products) were characterized by ^1H NMR, ^{13}C NMR, ^{31}P NMR (when applicable), ^{19}F NMR (when applicable), IR spectroscopy, melting point (when applicable), and elemental analysis or mass spectrometry. The ^1H, ^{13}C, ^{31}P, and ^{19}F NMR spectra can be found in Section 1.6. ^1H, ^{13}C, ^{31}P, and ^{19}F NMR spectra were recorded on Varian 300 MHz, Varian 500 MHz or Bruker 400 MHz spectrometers. The spectra were calibrated according to residual solvent peaks ($CDCl_3$: 7.26 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR; CD_2Cl_2: 5.32 ppm for ^1H NMR and 53.84 ppm for ^{13}C NMR), an external reference (H_3PO_4: 0 ppm for ^{31}P), or an internal reference (CF_3Ph: -63.7 ppm for ^{19}F). The ^{13}C, and ^{31}P NMR spectra were obtained with ^1H decoupling, and the ^{19}F NMR spectra were obtained without ^1H decoupling. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m= multiplet, br = broad, app = apparent. IR spectra were obtained on a Thermo Scientific iD5 ATR Nicolet iS5 FT-IR spectrometer. Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, GA. ESI-MS spectra were recorded on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). Melting points (m.p.) were obtained on a Mel-Temp capillary

melting point apparatus. Gas chromatographic (GC) analyses were performed on an Agilent 7890A instrument (FID detector) using a J&W DB-1 column (10m, 0.1 mm I.D.). Reactions were monitored by GC and thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) or Fluka aluminum oxide/TLC-cards using UV light as a visualizing agent.

II. Experimental Procedures and Characterization Data

A) Synthesis of PhCPhos (L5):

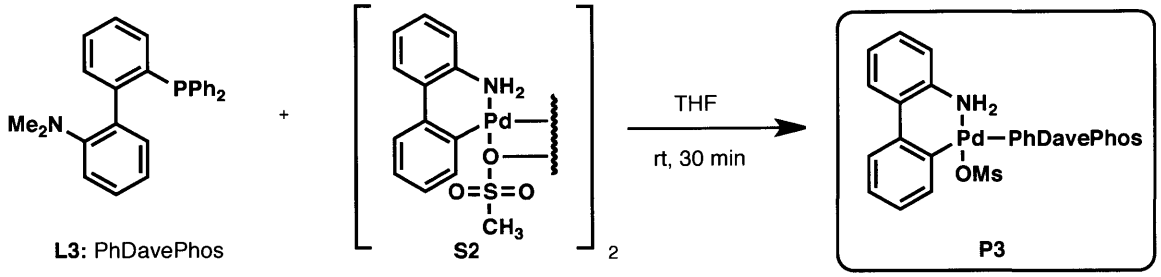


S1 **L5:** PhCPhos

2'-(Diphenylphosphino)-6-methoxy-*N*,*N*-dimethylbiphenyl-2-amine (L5): The starting material, 2'-bromo-6-methoxy-*N*,*N*-dimethylbiphenyl-2-amine (**S1**), was synthesized according to a procedure reported by Han and Buchwald.[38] An oven-dried 250 mL round-bottom flask, which was equipped with a magnetic stir bar and fitted with a Teflon septum, was charged with **S1** (4.58 g, 14.35 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times). THF (58.0 mL) was added via syringe and the solution was cooled to -78 °C. n-Butyllithium (2.5 M solution in hexanes, 6.06 mL, 15.1 mmol, 1.05 equiv) was added dropwise via syringe over 15 min and the resulting mixture was stirred at -78 °C for 45 min. Chlorodicyclohexylphosphine (2.85 mL, 15.1 mmol, 1.05) was then added dropwise via syringe over 15 min. The reaction mixture was stirred at -78 °C for 2 h and then allowed to slowly warm to room temperature overnight (~ 12 h). The reaction was quenched by addition of methanol (~1.0 mL), filtered through a pad of SiO_2 topped with a layer of Celite, and eluted with ethyl acetate (300 mL). The filtrate was concentrated *in vacuo* to afford a yellow solid. Recrystallization from dichloromethane and methanol provided the title compound as a white solid (5.13 g, 84% yield); mp = 134-136 °C.

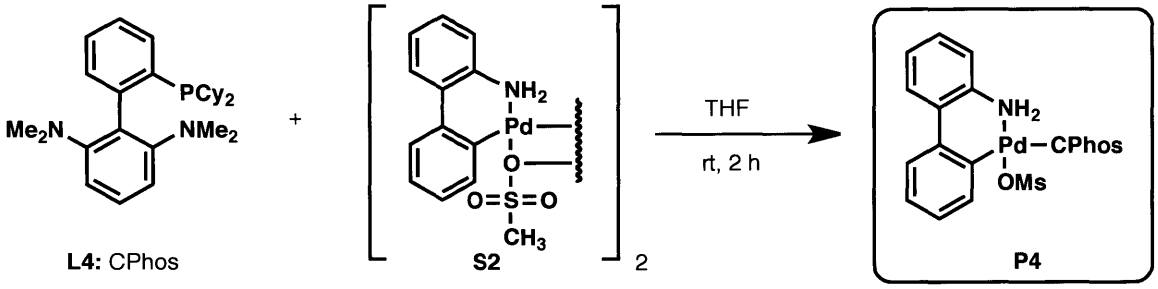
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 – 7.38 (m, 3H), 7.35 (d, J = 8.1 Hz, 1H), 7.32 – 7.21 (m, 11H), 6.88 (d, J = 8.0 Hz, 2H), 2.22 (s, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.0, 145.8, 145.3, 140.3, 140.1, 136.5, 136.4, 136.3, 136.2, 133.1, 132.9, 132.4, 132.3, 129.9, 129.8, 128.9, 128.6, 127.9, 127.8, 127.4, 126.3, 113.3, 43.4 (Observed complexity due to C—P splitting). **^{31}P NMR** (121 MHz, $CDCl_3$) δ -13.8. **IR** (neat, cm^{-1}): 2934, 2824, 2778, 1573, 1462, 1432, 1293, 1163, 1088, 1043, 1005, 935, 808, 768, 742, 694, 570. **Anal.** Calculated for $C_{16}H_{19}BrN_2$: C, 79.22; H, 6.89. Found C, 79.34; H, 6.94.

B) Synthesis of Pd-Precatalysts P3–P5:



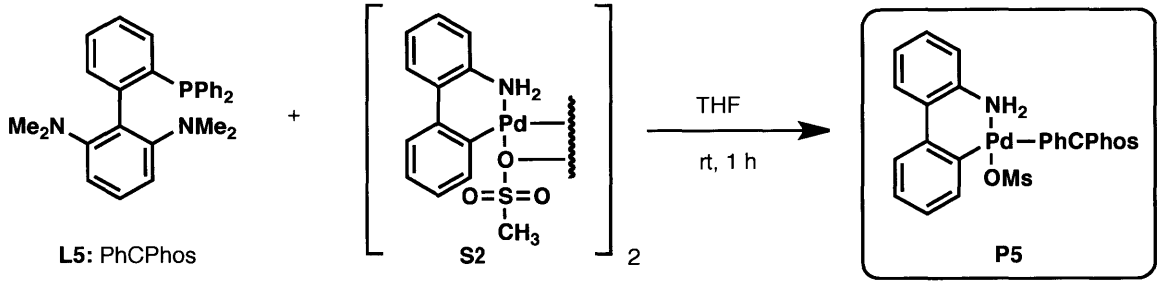
PhDavePhos (L3) Palladacyclic Precatalyst, P3: An oven-dried flask equipped with a magnetic stir bar was charged with μ-mesylate dimer **S2** (370 mg, 0.5 mmol, 0.50 equiv) and PhDavePhos (389 mg, 1.0 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous THF (4 mL) was then added via syringe. After the mixture was allowed to stir for 30 min at room temperature, the stir bar was removed and ~90% of solvent was removed under vacuum at room temperature. The residue was then triturated with pentane, and the resulting yellow crystals were isolated via filtration and further dried under vacuum. Precatalyst **P3** was obtained as an inseparable mixture of two phosphorous-containing compounds (0.71g total, 94% yield).

^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.00 (ddt, J = 11.7, 6.1, 1.7 Hz, 2H), 7.86 – 7.49 (m, 4H), 7.50 – 6.76 (m, 18H), 6.63 (td, J = 7.4, 6.7, 1.3 Hz, 1H), 6.18 – 5.93 (m, 1H), 3.49 (d, J = 11.1 Hz, 1H), 3.07 (s, 1H), 2.57 (s, 6H), 2.39 (s, 3H). **^{13}C NMR** (75 MHz, CD_2Cl_2) δ 154.2, 148.3, 147.9, 147.6, 139.6, 137.5, 137.3, 137.3, 136.6, 136.5, 135.1, 134.9, 134.3, 133.5, 133.4, 133.1, 132.4, 132.2, 131.6, 130.9, 130.8, 130.6, 130.0, 129.9, 129.09, 128.4, 128.3, 128.1, 128.0, 127.9, 127.5, 127.3, 127.2, 126.4, 125.6, 121.3, 120.7, 117.3, 43.7, 39.5, 34.3. (Observed complexity due to C—P splitting). **^{31}P NMR** (121 MHz, CD_2Cl_2) δ 40.5, 35.5. **IR** (neat, cm^{-1}): 3050, 1575, 1493, 1434, 1421, 1191, 1157, 1096, 1035, 1020, 1001, 946, 737, 693, 616, 569, 557.



CPhos (L4) Palladacyclic Precatalyst, P4: An oven-dried flask equipped with a magnetic stir bar was charged with μ-mesylate dimer **S2** (1.85 g, 5.0 mmol, 0.50 equiv) and CPhos (2.19 mg, 1.0 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous THF (20 mL) was then added via syringe. After the mixture was allowed to stir for 2 h min at room temperature, the stir bar was removed from the vessel and the reaction mixture was transferred to a scintillation vial. The majority of solvent was removed under vacuum at room temperature until ~10% of the initial volume remained. The residue was then triturated with pentane. The resulting yellow solid was isolated via filtration and further dried under vacuum to afford 4.03 g of **P4** (98% yield). This compound is light sensitive, and so it was stored in a scintillation vial wrapped with aluminum foil.

^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.81 (t, J = 8.1 Hz, 1H), 7.67 (t, J = 7.7, 1H), 7.56 – 7.29 (m, 4H), 7.29 – 6.94 (m, 9H), 5.44 (d, J = 9.7 Hz, 1H), 2.78 – 2.58 (m, 1H), 2.57-2.19 (m, 2H), 2.51 (s, 6H), 2.39 (s, 3H), 2.30 (s, 6H), 2.10 – 1.59 (m, 6H), 1.58 – 1.16 (m, 9H), 1.07-0.79 (m, 4H), 0.45 – 0.11 (m, 1H). **^{13}C NMR** (126 MHz, CD_2Cl_2) δ 159.4, 154.9, 146.2, 146.1, 142.7, 140.4, 139.3, 137.4, 137.3, 135.0, 134.6, 134.2, 133.8, 132.1, 128.3, 127.7, 127.0, 126.9, 125.6, 120.9, 113.2, 113.0, 111.7, 68.1, 44.9, 43.8, 39.6, 37.38, 37.2, 37.0, 36.9, 31.1, 30.3, 30.2, 29.9, 29.6, 28.4, 27.6, 27.2, 26.3, 26.3, 26.0, 26.0 (Observed complexity due to C—P splitting). **^{31}P NMR** (121 MHz, CD_2Cl_2) δ 40.8. **IR** (neat, cm^{-1}): 2928, 2852, 1569, 1491, 1421, 1211, 1191, 1164, 1131, 1034, 1018, 1002, 780, 758, 737, 555.

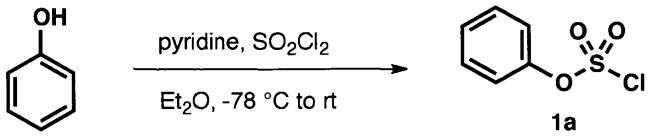


PhCPhos (L5) Palladacyclic Precatalyst, P5: An oven-dried flask equipped with a magnetic stir bar was charged with μ-mesylate dimer **S2** (591 mg, 0.80 mmol, 0.50 equiv) and PhCPhos (678 mg, 1.6 mmol, 1.0 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous THF (6.5 mL) was then added via syringe. After the mixture was allowed to stir for 1 h at room temperature, the stir bar was removed from the vessel and the reaction mixture was transferred to a scintillation vial. The majority of solvent was removed under vacuum at room temperature until ~10% of the initial volume remained. The residue was then triturated with pentane. The resulting yellow solid was isolated via filtration and further dried under vacuum to afford 1.27 g of **P5** (quantitative yield).

^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.86 (t, J = 8.1 Hz, 1H), 7.65 – 7.48 (m, 4H), 7.47 – 7.03 (m, 16H), 7.00 (t, J = 7.3 Hz, 1H), 6.89 (dd, J = 8.1, 0.9 Hz, 1H), 6.67 (dddd, J = 8.0, 7.2, 1.7, 0.9 Hz, 1H), 6.37 (ddd, J = 7.6, 6.3, 1.1 Hz, 1H), 6.03 (dd, J = 10.7, 4.9 Hz, 1H), 2.73-2.61 (m, 1H), 2.69 (s, 6H), 2.31 (s, 3H), 1.88 (s, 6H). **^{13}C NMR** (75 MHz, CD_2Cl_2) δ 156.9, 155.2, 146.0, 145.7, 145.1, 140.1, 138.8, 137.9, 137.8, 136.7, 136.0, 135.8, 135.2, 134.7, 134.3, 134.2, 134.0, 132.8, 132.4, 132.2, 131.5, 131.3, 130.2, 129.5, 128.9, 128.8, 128.7, 128.5, 128.4, 128.2, 128.1, 127.9, 127.6, 127.0, 126.7, 125.7, 121.2, 113.8, 113.2, 112.1, 44.7, 43.2, 39.5 (Observed complexity due to C—P splitting). **^{31}P NMR** (121 MHz, CD_2Cl_2) δ 40.2. **IR** (neat, cm^{-1}): 3286, 2942, 1571, 1492, 1434, 1424, 1226, 1175, 1160, 1091, 1035, 1019, 1001, 793, 771, 748, 697, 614, 572.

C) Preparation of Aryl Chlorosulfates (1a–1c):

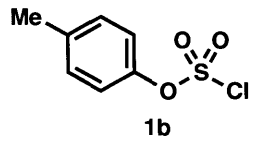
Representative Procedure:



1a

Phenyl chlorosulfate (1a): An oven-dried 500 mL round-bottom flask equipped with a large stir bar was charged with phenol (9.5 g, 100 mmol, 1.0 equiv). The vessel was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times). Anhydrous Et_2O (125 mL) and pyridine (8.09 mL, 100 mmol, 1.0 equiv) were then added via syringe and the solution was cooled to -78 °C. A separate oven-dried 200 mL round-bottom flask was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times). Anhydrous Et_2O (125 mL) was added to the 200 mL flask via syringe, and the flask was placed in a separate dry ice/acetone bath and allowed to cool to -78 °C. Neat sulfuryl chloride (8.36 mL, 100 mmol, 1.0 equiv) was then added via syringe to the 200 mL flask at -78 °C (the addition of neat SO_2Cl_2 to anhydrous Et_2O is exothermic and will cause the Et_2O to evaporate if not performed at lower temperatures). The cooled solution of SO_2Cl_2 in Et_2O was transferred slowly (over 20 min) via canula to the vigorously stirred solution of phenol and pyridine at -78 °C. (**Note:** Stirring becomes difficult as the pyridinium salt is formed, and so periodic swirling of the reaction flask by hand may be required. We observed no problems with stirring when an IKA RCT Basic stir plate was used, however). After stirring for 2 h at -78 °C, no additional dry ice was added to the cooling bath and the reaction mixture was allowed to slowly warm to room temperature overnight. The crude reaction mixture was filtered through a pad of celite, and the reaction flask was washed with additional Et_2O (100-200 mL). The filtrate was then concentrated and the resulting residue was purified immediately via SiO_2 flash chromatography (0-3% EtOAc in hexanes) to afford **2a** as a colorless oil (16.19 g, 84 % yield).

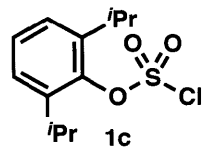
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.37 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.0, 130.2, 128.8, 121.6. **IR** (neat, cm^{-1}): 1586, 1485, 1410, 1197, 1172, 1131, 1023, 913, 875, 774, 657, 685, 611, 584. **EI-MS** (*m/z*): 192 $[M]^+$.



1b

4-Methylphenyl chlorosulfate (1b): Following the representative procedure for the preparation of **2a**, the title compound was prepared using *p*-cresol (5.34 g, 50 mmol, 1.0 equiv), pyridine (4.1 mL, 50 mmol, 1.0 equiv), and sulfuryl chloride (4.18 mL, 50 mmol, 1.0 equiv). The crude product was purified by flash column chromatography (0-1% EtOAc in hexanes) to afford **2b** as a clear, colorless oil (9.5 g, 92% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (s, 4H), 2.40 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.0, 139.0, 130.7, 121.4, 21.0. **IR** (neat, cm^{-1}): 1500, 1411, 1199, 1175, 1132, 1018, 880, 823, 802, 720, 692, 639, 591, 576. **EI-MS** (*m/z*): 206 $[M]^+$.



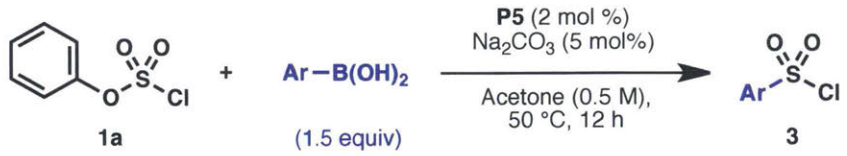
1c

2,6-Diisopropylphenyl chlorosulfate (1c): Following the representative procedure for the preparation of **2a**, the title compound was prepared using 2,6-diisopropylphenol (9.55 mL, 50 mmol, 1.0 equiv), pyridine (4.1 mL, 50 mmol, 1.0 equiv), and sulfuryl chloride (4.18 mL, 50 mmol, 1.0 equiv). The crude product was purified by flash column chromatography (0-1% EtOAc in hexanes) to afford **2c** as a clear, colorless oil (10.1 g, 73% yield).

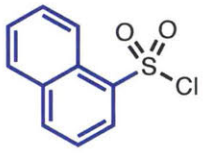
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, J = 8.2, 7.1 Hz, 1H), 7.24 (d, J = 7.6 Hz, 2H), 3.43 (m, 2H), 1.27 (d, J = 6.8 Hz, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.0, 141.8, 128.9, 125.2, 27.76, 23.6. **IR** (neat, cm^{-1}): 1406, 1387, 1192, 1129, 1071, 1045, 889, 864, 799, 767, 744, 618, 571. **EI-MS** (*m/z*): 276 $[M]^+$.

D) Preparation of Arylsulfonyl Chlorides (3c–j)

Generation Procedure A:



An oven-dried test tube equipped with a magnetic stir bar was charged with **P5** (0.02 mmol, 2 mol%), Na_2CO_3 (5.3 mg, 0.05 mmol, 5 mol%), and the arylboronic acid (1.5 mmol, 1.5 equiv) and the tube was sealed with a Teflon screw-cap septum. The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous acetone (2.0 mL) was then added via syringe. After the mixture was allowed to stir for ~3 min at room temperature, neat phenyl chlorosulfate (133 μL, 1.0 mmol, 1.0 equiv) was added. The vessel was then placed in a preheated oil bath and the reaction mixture was allowed to stir at the desired temperature for 12 h. After the reaction mixture was allowed to cool to room temperature, it was diluted with EtOAc and filtered through a pad of silica gel topped with a layer of celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonyl chloride.

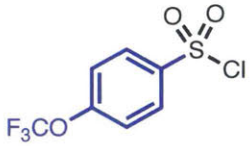


3c

Naphthalene-1-sulfonyl chloride (3c): Following *General Procedure A*, the title compound was prepared using 1-napthaleneboronic acid (258 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 60 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-5% EtOAc in hexanes) to afford **3c** as a white solid (200 mg, 88% yield); mp = 60-62 °C (lit.[39] 64-67 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, J = 8.6 Hz, 1H), 8.37 (dd, J = 7.5, 1.3 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 8.01 (d, J = 8.3, 1H), 7.81 (ddd, J = 8.6, 6.9, 1.4 Hz, 1H), 7.70 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 7.60 (dd, J = 7.9 Hz, J = 7.9 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 139.3, 137.0, 134.3, 129.4, 129.3, 129.2, 127.6, 127.2, 123.9, 123.8. **IR** (neat, cm^{-1}): 1592, 1504, 1365,

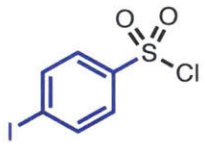
1346, 1169, 1136, 966, 830, 800, 760, 736, 673, 619, 572, 559. **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ Calcd. for $C_{10}H_7ClO_2S$, 244.0194; found, 244.0196.



3d

4-(Trifluoromethoxy)benzenesulfonyl chloride (3d): Following *General Procedure A*, the title compound was prepared using 4-trifluoromethoxyphenylboronic acid (309 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 60 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-3% EtOAc in hexanes) to afford **3d** as a colorless oil (173 mg, 66% yield).

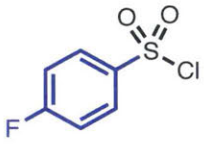
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 – 8.05 (m, 2H), 7.44 (d, J = 7.8 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 154.1 (q, J = 1.9), 142.2, 129.7, 120.4 (q, J = 260.8), 121.3. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -57.8. **IR** (neat, cm^{-1}): 1589, 1493, 1381, 1254, 1207, 1156, 1082, 1015, 840, 808, 688, 667, 583, 559. **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ Calcd. for $C_7H_4ClF_3O_3S$, 277.9860; found, 277.9868.



3e

4-Iodobenzenesulfonyl chloride (3e): Following *General Procedure A*, the title compound was prepared using 4-iodophenylboronic acid (372 mg, 1.5 mmol). (**Note:** Stirring was difficult during the first 1-2 h of this reaction, and so an IKA RCT Basic stir plate was used to facilitate stirring). The reaction was judged as complete by TLC and GC after 12 h at 55 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, (0-7% EtOAc in hexanes) to afford **3e** as a white solid (183 mg, 64%); mp = 83-86 °C (lit.[39] 80-82 °C).

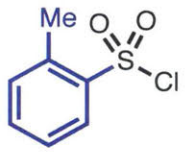
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 8.8 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.0, 139.3, 128.3, 104.0. **IR** (neat, cm^{-1}): 1560, 1369, 1176, 1157, 1076, 1051, 1005, 834, 813, 729, 694, 581, 551. **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ Calcd. for $C_6H_4ClIO_2S$, 319.9004; found, 319.9020.



3f

4-Fluorobenzenesulfonyl chloride (3f): Following *General Procedure A*, the title compound was prepared using 4-fluorophenylboronic acid (210 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 70 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-4% EtOAc in hexanes) to afford **3f** as a yellow solid (165 mg, 85% yield); mp = 33-36 °C (lit.[39] 29-31 °C; lit.[40] 34 °C).

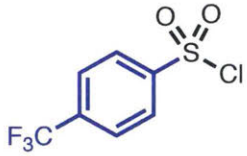
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 – 8.02 (m, 2H), 7.38 – 7.21 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.6 (d, J = 259.8), 140.5 (d, J = 3.2 Hz), 130.4 (d, J = 10.1 Hz), 117.4 (d, J = 23.2 Hz). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -99.6. **IR** (neat, cm^{-1}): 1587, 1491, 1409, 1377, 1294, 1242, 1178, 1156, 1081, 838, 816, 706, 658, 561. **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ Calcd. for $C_6H_4ClFO_2S$, 211.9943; found, 211.9946.



3g

2-Methylbenzenesulfonyl chloride (3g): Following *General Procedure A*, the title compound was prepared using 2-methylphenylboronic acid (204 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 50 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, chromatography (Biotage, 25g SNAP column, 0-6% EtOAc in hexanes) to afford **3g** as a colorless oil (143 mg, 75% yield). Note: The chemical shifts in the ^{1}H NMR spectrum of **3g** were consistent with those in the ^{1}H NMR spectrum of an authentic sample obtained from Sigma-Aldrich.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (dd, J = 8.4, 1.4 Hz, 1H), 7.76 – 7.52 (m, 1H), 7.48 – 7.31 (m, 2H), 2.79 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 143.2, 138.3, 135.5, 133.6, 129.0, 127.0, 20.5. **IR** (neat, cm^{-1}): 1471, 1365, 1280, 1173, 1131, 1057, 1036, 806, 757, 700, 686, 577, 558. **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ Calcd. for $C_7H_7ClO_2S$, 208.0194; found, 208.0198.



3h

4-Trifluoromethylbenzenesulfonyl chloride (3h): Following *General Procedure A*, the title compound was prepared using 4-trifluorophenylboronic acid (285 mg, 1.5 mmol) and Na_2CO_3 (10.6 mg, 0.1 mmol, 10 mol%). The reaction was judged as complete by TLC and

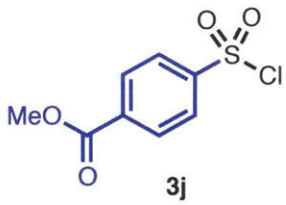
GC after 12 h at 70 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 0-4% EtOAc in hexanes) to afford **4h** as a off-white solid (131 mg, 54% yield); mp = 30-32 °C (lit.[41] oil). Note: Compound **4h** undergoes significant decomposition upon purification with SiO_2 gel. The chemical shifts in the ^{1}H NMR spectrum of **4h** were consistent with those obtained from an authentic sample from Sigma-Aldrich.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 8.2 Hz, 2H), 7.92 (d, J = 8.3 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.1 (app d, J = 1.4 Hz), 136.7 (q, J = 33.6 Hz), 127.6, 127.0 (q, J = 3.7 Hz), 122.7 (q, J = 273.4 Hz). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.5. **IR** (neat, cm^{-1}): 1407, 1382, 1319, 1174, 1135, 1109, 1061, 1016, 842, 711, 600, 578, 557. **EI-MS** (*m/z*): 244 $[M]^+$.

3i

2-Bromobenzenesulfonyl chloride (3i): Following *General Procedure A*, the title compound was prepared using 2-bromophenylboronic acid (301 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 55 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 3-10% EtOAc in hexanes) to afford **3i** as a yellow solid (202 mg, 79% yield); mp = 50-52 °C (lit.[39] 49-52 °C; lit.[42]45-48 °C).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 – 8.12 (m, 1H), 7.91 – 7.79 (m, 1H), 7.64 – 7.49 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 143.2, 136.7, 136.2, 131.0, 128.3, 120.9. **IR** (neat, cm^{-1}): 1567, 1445, 1429, 1369, 1252, 1179, 1098, 1021, 759, 735, 694, 646, 573, 551. **HRMS-ESI** (*m/z*) $[M + H]^+$ Calcd. for $C_6H_4BrClO_2S$, 254.8877; found, 254.8890.

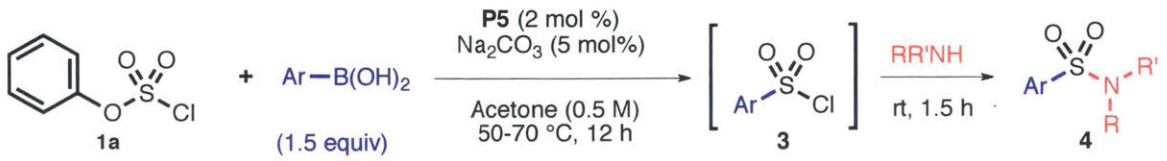


3j

4-(Methoxycarbonyl)benzenesulfonyl chloride (3j): Following *General Procedure A*, the title compound was prepared using 4-methoxycarbonylphenylboronic acid (270 mg, 1.5 mmol). The reaction was judged as complete by TLC and GC after 12 h at 60 °C. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 2-7% EtOAc in hexanes) to afford **3j** as a slightly pink solid (152 mg, 65% yield); mp = 73-76 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 8.9 Hz, 2H), 8.12 (d, J = 8.9 Hz, 2H), 3.99 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.1, 147.6, 136.3, 131.1, 127.3, 53.2. **IR** (neat, cm^{-1}): 1725, 1435, 1400, 1377, 1280, 1188, 1168, 1106, 1011, 966, 866, 832, 758, 733, 684, 582, 560. **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ Calcd. for $C_8H_7ClO_4S$, 252.0092; found, 252.0101.

E) Preparation of Aryl Sulfonamides (4a–4o)



Generation Procedure B: Preparation of Sulfonamides Derived from Secondary Amines.

Following *General Procedure A*, a mixture of **P5** (15.9 mg, 0.02 mmol, 2 mol%), Na_2CO_3 (5.3 mg, 0.05 mmol, 5 mol%), arylboronic acid (1.5 mmol, 1.5 equiv), and phenyl chlorosulfate (133 µL, 1.0 mmol, 1.0 equiv) in anhydrous acetone (2.0 mL) was stirred at the desired temperature for 12 h. After the reaction mixture was allowed to cool to room temperature, it was placed under a positive atmosphere of argon and anhydrous THF (1.0 mL) was added via syringe (additional THF was not added to reactions in which a commercially available 2.0 M solution of Me_2NH in THF was used). The reaction mixture was cooled to 0 °C and the desired secondary amine (2.2 mmol, 2.2 equiv) was then added to the vigorously stirred solution of crude sulfonyl chloride. After stirring for 5 min at 0 °C, the reaction vessel was removed from the ice bath, allowed to warm to room temperature, and stirred for 1.5 h. The reaction mixture was then diluted with EtOAc and filtered through a pad of silica gel topped with a layer of celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonamide.

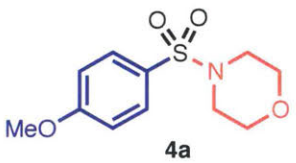
Generation Procedure C: Preparation of Sulfonamides Derived from Primary Amines.

Following *General Procedure A*, a mixture of **P5** (15.9 mg, 0.02 mmol, 2 mol%), Na_2CO_3 (5.3 mg, 0.05 mmol, 5 mol%), arylboronic acid (1.5 mmol, 1.5 equiv), and phenyl chlorosulfate (133 µL, 1.0 mmol, 1.0 equiv) in anhydrous acetone (2.0 mL) was stirred at the desired temperature for 12 h. After the mixture was allowed to cool to room temperature, the reaction mixture was placed under a positive atmosphere of argon and anhydrous THF (1.0 mL) was added via syringe. The reaction was cooled to 0 °C and the desired primary amine (3.0 mmol, 3.0 equiv or 2.2 mmol, 2.0 equiv) was then added to the vigorously stirred solution of crude sulfonyl chloride. After stirring for 5 min at 0 °C, the reaction vessel was removed from the ice bath,

allowed to warm to room temperature, and stirred for 1.5 h at this temperature. The reaction mixture was then diluted with EtOAc and filtered through a pad of silica gel topped with a layer of celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonamide.

Generation Procedure D: Preparation of Sulfonamides Derived from Anilines.

Following *General Procedure A*, a mixture of **P5** (15.9 mg, 0.02 mmol, 2 mol%), Na_2CO_3 (5.3 mg, 0.05 mmol, 5 mol%), arylboronic acid (1.5 mmol, 1.5 equiv), and phenyl chlorosulfate (133 µL, 1.0 mmol, 1.0 equiv) in anhydrous acetone (2.0 mL) was stirred at the desired temperature for 12 h. The reaction mixture was allowed to cool to room temperature, placed under a positive atmosphere of argon, and then cooled to 0 °C. The desired aniline (1.2 mmol, 1.2 equiv.) and pyridine (0.245 mL, 3.0 mmol, 3.0 equiv) were then added successively to the vigorously stirred solution of the crude sulfonyl chloride at 0 °C. After stirring for 30 min at 0 °C, the reaction vessel was removed from the ice bath, allowed to warm to room temperature, and stirred for 5 h at this temperature. The reaction mixture was then diluted with EtOAc and filtered through a pad of silica gel topped with a layer of celite, which was washed with additional EtOAc. The filtrate was concentrated and the resulting residue was purified by flash chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired sulfonamide.

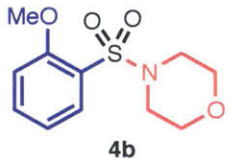


4a

4-Methoxybenzenesulfonylmorpholide (4a): Following *General Procedure B*, the title compound was prepared using 4-methoxyphenylboronic acid (228 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 50 °C for 12 h. Morpholine (192 µL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-50% EtOAc in hexanes) to afford **4a** as a white solid (246 mg, 96% yield); mp = 110-111 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72-7.61 (m, 2H), 7.04-6.99 (m, 2H), 3.88 (s, 3H), 3.76-3.72

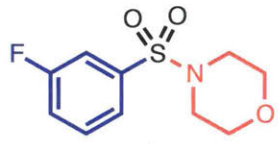
(m, 4H), 2.99-2.96 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.0, 129.8, 126.3, 114.1, 65.8, 55.5, 45.8. **IR** (neat, cm^{-1}): 3103, 2928, 2847, 1598, 1578, 1499, 1439. **Anal.** Calcd. for $C_{11}H_{15}NO_4S$: C, 51.35; H, 5.88; N, 5.44. Found C, 51.38; H, 5.96.



4b

2-Methoxybenzenesulfonylmorpholide (4b): Following *General Procedure B*, the title compound was prepared using 2-methoxyphenylboronic acid (228 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 50 °C for 12 h. Morpholine (192 μL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-45% EtOAc in hexanes) to afford **4b** as a white solid (216 mg, 84% yield); mp = 86.0-86.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 8.0, 1.8 Hz, 1H), 7.49 (ddd, J = 8.3, 7.4, 1.8 Hz, 1H), 7.07 – 6.88 (m, 2H), 3.88 (s, 3H), 3.74 – 3.56 (m, 4H), 3.22 – 3.08 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.0, 134.8, 131.8, 125.7, 120.4, 112.4, 66.7, 56.0, 46.0. **IR** (neat, cm^{-1}): 2968, 2921, 2863, 1592, 1579, 1480, 1465, 1447, 1433, 1342, 1331, 1325, 1279, 1262, 1155, 1141, 1114, 1078, 1062, 1044, 1016, 944, 924, 858, 768, 758, 735, 614, 588, 573, 567, 565. **Anal.** Calcd. for $C_{11}H_{15}NO_4S$: C, 51.35; H, 5.88Found C, 51.54; H, 5.80.

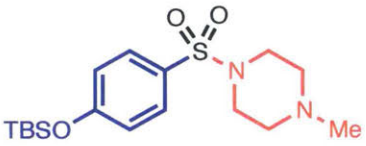


4c

3-Fluorobenzenesulfonylmorpholide (4c): Following *General Procedure B*, the title compound was prepared using 3-fluorophenylboronic acid (210 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 70 °C for 12 h. Morpholine (192 μL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-30% EtOAc in hexanes) to afford **4c** as a white solid (161 mg, 66% yield); mp = 112.2-113.2 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59-7.51 (m, 2H), 7.49-7.44 (m, 1H), 7.39-7.30 (m, 1H), 3.77-3.73 (m, 4H), 3.04-3.00 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4 (d, J = 252.0 Hz), 137.2

(d, J = 6.5 Hz), 130.9 (d, J = 7.8 Hz), 123.5 (d, J = 3.4 Hz), 120.2 (d, J = 21.2 Hz), 115.0 (d, J = 24.2 Hz), 65.9, 45.9. **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ -109.4 (s, 1F). **IR** (neat, cm^{-1}): 2917, 2863, 1589, 1475, 1392, 1346, 1329, 1294, 1272, 1261, 1220, 1155, 1112, 1088. **Anal.** Calculated for $C_{10}H_{10}FNO_3S$: C, 48.97; H, 4.93. Found C, 48.98; H, 4.82.



4d

1-Methylpiperazine-4-(4-(*tert*-butyldimethylsilyloxy) benzenesulfonamide (5d): Following a modification of *General Procedure B*, the title compound was prepared using 4-(*tert*-butyldimethylsilyloxy)phenyl boronic acid (378 mg, 1.5 mmol) and **P5**. The cross-coupling reaction was carried out at 50 °C for 12 h. Following complete chlorosulfonylation, the reaction was cooled to 0 °C, and DIPEA (0.348 mL, 2 mmol, 2.0 equiv) and 1-Methylpiperazine (0.135 mL, 1.2 mmol, 1.0 equiv) were added successively. After 5 min, the reaction vessel was removed from the ice bath and stirred for 1.5 h at rt. The mixture was then diluted with EtOAc and filtered through a plug of SiO_2, using 30% MeOH in EtOAc as the eluent. The product was purified by flash column chromatography (Biotage, 25g SNAP column, 50-100% EtOAc in hexanes, followed by 15% MeOH in EtOAc) to afford **4d** as a yellow solid (296 mg, 80% yield); mp = 70-73 °C. **Note:** Compound **4d** was characterized immediately following purification because it undergoes rapid desilylation to form the corresponding free phenol.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J = 9.0 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 3.02 (br s, 4H), 2.55 – 2.40 (m, 4H), 2.27 (s, 3H), 0.98 (s, 9H), 0.23 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.7, 129.8, 127.4, 120.1, 53.9, 45.8, 45.6, 25.4, 18.1, -4.50. **IR** (neat, cm^{-1}): 2934, 2856, 2794, 2765, 1590, 1490, 1472, 1405, 1384, 1371, 1342, 1329, 1285, 1252, 1167, 1152, 1144, 1098, 1065, 890, 854, 825, 783, 758, 666, 631, 610, 581, 575, 563, 557. **Anal.** Calcd. for $C_{17}H_{30}N_2O_3SSi$: C, 55.10; H, 8.16. Found C, 55.07; H, 8.09.

4e

Pyrrolidine-4-Acetylbenzenesulfonamide (4e): Following *General Procedure B*, the title compound was prepared using 4-acetylphenylboronic acid (246 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 60 °C for 12 h. Pyrrolidine (181 μL, 2.2 mmol) was used as the secondary amine to form the desired

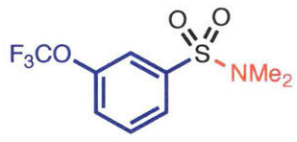
sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 10-50% EtOAc in hexanes) to afford **4e** as a white solid (187 mg, 74% yield); mp = 143.5-144.5 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 8.8 Hz, 2H), 7.93 (d, J = 8.8 Hz, 2H), 3.53 – 3.03 (m, 4H), 2.66 (s, 3H), 1.84 – 1.72 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.8, 140.7, 139.8, 128.7, 127.5, 47.8, 26.7, 25.1. **IR** (neat, cm^{-1}): 3096, 2968, 2873, 1692, 1595, 1396, 1292, 1006, 774, 1066, 958, 852, 774, 748, 725, 634. **Anal.** Calcd. for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97. Found C, 56.86; H, 5.81.

4f

***N,N*-dimethyl-4-(trifluoromethyl)benzenesulfonamide (4f):** Following *General Procedure B*, the title compound was prepared using 4-trifluorophenylboronic acid (285 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 70 °C for 12 h. Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 3-15% EtOAc in hexanes) to afford **4f** as a yellow solid (165 mg, 65% yield); mp = 80.5-81.5 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 2H), 7.82 (d, J = 8.2 Hz, 2H), 2.75 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.4, 134.3 (q, J = 33.0 Hz), 128.1, 126.2 (q, J = 3.7 Hz), 123.3 (q, J = 272.9 Hz), 37.8. **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ -63.2. **IR** (neat, cm-1): 1458, 1407, 1337, 1325, 1314, 1296, 1148, 1110, 1092, 1015, 947, 840, 788, 742, 692, 596, 582, 574, 566. **Anal.** Calcd. for $C_9H_{10}F_3NO_2S$: C, 42.69; H, 3.98. Found C, 42.87; H, 3.94.



4g

***N,N*-dimethyl-3-(trifluoromethoxy)benzenesulfonamide (4g):** Following *General Procedure B*, the title compound was prepared using 3-trifluoromethoxyphenylboronic acid (309 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 65 °C for 12 h. Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 2-15% EtOAc in hexanes) to afford **4g** as a white solid (207 mg, 77% yield); mp = 46.0-48.0 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (dd, J = 7.8, 1.7 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.50 – 7.42 (m, 1H), 2.73 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.2 (q, J = 2.0 Hz), 137.5, 130.7, 125.3, 125.0 (q, J = 1.0 Hz), 120.21 (q, J = 258.8 Hz), 120.16 (q, J = 1.1 Hz), 37.8. **^{19}F NMR** (376.5 MHz, $CDCl_3$) δ -58.1 (s, 3F). IR (neat, cm^{-1}): 1473, 1458, 1437, 1337, 1307, 1280, 1256, 1221, 1204, 1179, 1143, 1094, 1082, 1050, 1000, 950, 919, 682. **Anal.** Calcd. for $C_9H_{10}F_3NO_3S$: C, 40.15; H, 3.74. Found C, 40.26; H, 3.66.

4h

***N,N*-dimethyl-4-dibenzofuransulfonamide (4h):** Following *General Procedure B*, the title compound was prepared using dibenzofuran-4-boronic acid (318 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 60 °C for 12 h and **P1** as the catalyst. (**Note:** Stirring was difficult during the first 1-2 h of the chlorosulfonylation reaction, and so an IKA RCT Basic stir plate was used to facilitate stirring). Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 3-18% EtOAc in hexanes) to afford **4h** as a white solid (195 g, 71% yield); mp = 146.5-147.5 °C.

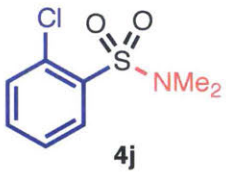
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (dd, J = 7.7, 1.3 Hz, 1H), 8.00 (ddd, J = 7.7, 1.4, 0.7 Hz, 1H), 7.91 (dd, J = 7.8, 1.3 Hz, 1H), 7.72 – 7.63 (m, 1H), 7.59 – 7.38 (m, 3H), 2.90 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.3, 151.6, 128.3, 128.0, 126.5, 125.5, 123.7, 122.8, 122.7, 121.1, 120.9, 112.2, 37.8. **IR** (neat, cm^{-1}): 1469, 1441, 1418, 1354, 1339, 1188, 1161, 1154, 1111, 1059, 960, 637, 582, 577. **Anal.** Calcd. for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76. Found C, 60.81; H, 4.79.

4i

***N,N*-dimethyl-4-iodobenzenesulfonamide (4i):** Following *General Procedure B*, the title compound was prepared using 4-iodophenylboronic acid (372 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 55 °C for 12 h. (**Note:** Stirring was difficult during the first 1-2 h of the chlorosulfonylation reaction, and so an IKA RCT Basic stir plate was used to facilitate stirring). Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product

was purified by flash column chromatography (Biotage, 25g SNAP column, 3-10% EtOAc in hexanes) to afford **4i** as a white solid (233 g, 75% yield); mp = 134-135 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 8.7 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 2.71 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.3, 135.3, 129.1, 100.2, 37.9. IR (neat, cm^{-1}): 3079, 1567, 1466, 1450, 1387, 1341, 1328, 1271, 1257, 1180, 1163, 1088. Anal. Calcd. for $C_8H_{10}INO_2S$: C, 30.88; H, 3.24. Found C, 31.15; H, 3.08. HRMS-ESI (*m/z*) $[M + H]^+$ Calcd. for $C_8H_{10}IO_2S$, 311.9550; found, 311.9548.



4j

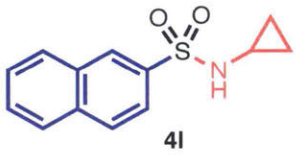
***N,N*-dimethyl-2-chlorobenzenesulfonamide (4j):** Following *General Procedure B*, the title compound was prepared using 2-chlorophenylboronic acid (235 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 60 °C for 12 h. Dimethylamine (0.5 M in THF, 1.1 mL, 2.2 mmol) was used as the secondary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (3-15% EtOAc in hexanes) to afford **4j** as a white solid (145 g, 66% yield); mp = 40.0-41.8 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.9, 1.6 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.39 (ddd, J = 7.9, 7.1, 1.6 Hz, 1H), 2.88 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.9, 133.5, 132.1, 132.0, 126.9, 37.3. (**Note:** only 6 carbon signals for **4j** resolve in the ^{13}C spectrum). **IR** (neat, cm^{-1}): 3090, 2872, 1569, 1450, 1346, 1256, 1160, 1106, 1041, 954, 754, 713, 690, 654, 578. **Anal.** Calcd. for $C_8H_{10}ClNO_2S$: C, 43.74; H, 4.54. Found C, 43.99; H, 4.68.

4k

***N*-[2-(3,4-dimethoxyphenyl)ethyl]-1,3-benzodioxole-5-sulfonam-ide (4k):** Following *General Procedure C*, the title compound was prepared using 3,4-methylenedioxyphenylboronic acid (249 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 50 °C for 12 h. 3,4-Dimethoxyphenethylamine (373 µL, 2.2 mmol) was used as the primary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 20% EtOAc in hexanes) to afford **4k** as a white solid (274 mg, 75% yield); mp = 118-120 °C.

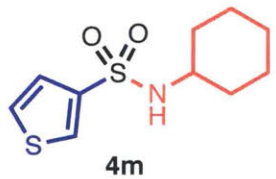
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, J = 8.2, 1.9 Hz, 1H), 7.15 (d, J = 1.9 Hz, 1H), 6.84 (d, J = 8.2 Hz, 1H), 6.77 (d, J = 8.1 Hz, 1H), 6.63 (dd, J = 8.1, 2.0 Hz, 1H), 6.57 (d, J = 2.0 Hz, 1H), 6.07 (s, 2H), 4.55 – 4.25 (m, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.19 (app q, J = 6.6 Hz, 2H), 2.71 (t, J = 6.8 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.1, 148.9, 148.1, 147.7, 132.9, 130.1, 122.6, 120.6, 111.6, 111.1, 107.9, 107.1, 102.2, 55.8, 55.7, 44.3, 35.2. **IR** (neat, cm^{-1}): 3231, 2931, 1594, 1512, 1501, 1483, 1471, 1356, 1328, 1255, 1231, 1174, 1147, 1137, 1111, 1069, 1022, 936, 909, 858, 846, 830, 764, 727, 709, 667, 634, 618, 602, 573, 561, 558, 551. **Anal.** Calcd. for $C_{17}H_{19}NO_6S$: C, 55.88; H, 5.24. Found C, 55.59; H, 5.31.



4l

***N*-cyclopropylnaphthalene-2-sulfonamide (4l):** Following *General Procedure C*, the title compound was prepared using 2-naphthaleneboronic acid (258 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction reaction was carried out at 50 °C for 12 h. Cyclopropylamine (208 μL, 3.0 mmol) was used as the primary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-30% EtOAc in hexanes) to afford **4l** as a white solid (200 g, 81% yield); mp = 99.5-101.0 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.08 – 7.76 (m, 4H), 7.75 – 7.52 (m, 2H), 5.04 (br s, 1H), 2.31–2.23 (m, 1H), 0.66-0.53 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 136.4, 134.7, 132.0, 129.3, 129.1, 128.7, 128.7, 127.8, 127.4, 122.4, 24.2, 5.99. **IR** (neat, cm^{-1}): 3279, 1591, 1502, 1455, 1406, 1366, 1306, 1226, 1160, 967, 884, 751, 694, 640, 567. **Anal.** Calcd. for $C_{13}H_{13}NO_2S$: C, 63.13; H, 5.30. Found C, 63.05; H, 5.33.

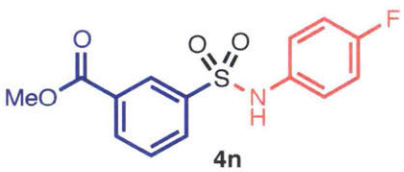


4m

***N*-cyclohexylthiophene-3-sulfonamide (4m)**: Following of the *General Procedure C*, the title compound was prepared using 3-thiopheneboronic acid (192 mg, 1.5 mmol) and **P4** (16.1 mg, 0.02 mmol, 2 mol%). The chlorosulfonylation reaction reaction was carried out at 55 °C for 12 h. Cyclohexylamine (343 μL, 3.0 mmol) was used as the primary amine to form the desired sulfonamide. The crude product was purified by flash column chromatography

(Biotage, 25g SNAP column, 5-25% EtOAc in hexanes) to afford **4m** as a white solid (171 mg, 70% yield); mp = 94.0-95.0 °C.

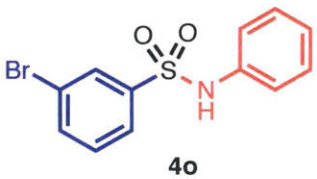
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (dd, J = 3.1, 1.3 Hz, 1H), 7.41 (dd, J = 5.1, 3.1 Hz, 1H), 7.35 (dd, J = 5.1, 1.3 Hz, 1H), 4.49 (d, J = 7.8 Hz, 1H), 3.33 – 3.02 (m, 1H), 1.90 – 1.39 (m, 5H), 1.37 – 1.03 (m, 5H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.5, 129.9, 127.9, 125.5, 52.8, 33.8, 25.1, 24.6. **IR** (neat, cm^{-1}): 3264, 3106, 2932, 2854, 1448, 1312, 1297, 1209, 927, 998, 927, 891, 881, 815, 800, 729, 698, 641, 629, 597. **Anal.** Calcd. for $C_{10}H_{15}NO_2S_2$: C, 48.95; H, 6.16. Found C, 49.08; H, 6.20.



4n

Methyl 3-(*N*-(4-fluorophenyl)sulfamoyl)benzoate (4n): Following *General Procedure D*, the title compound was prepared using 3-methoxycarbonylphenylboronic acid (270 mg, 1.5 mmol) and **P5**. The chlorosulfonylation reaction was carried out at 60 °C for 12 h. 4-Fluoroaniline (114 μL, 1.2 mmol) was used as the aniline to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-25% EtOAc in hexanes) to afford **4n** as an off-white solid (247 mg, 80% yield); mp = 104.8-105.8 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 – 8.38 (m, 1H), 8.20 (ddd, J = 7.8, 1.7, 1.2 Hz, 1H), 7.89 (ddd, J = 7.9, 1.9, 1.2 Hz, 1H), 7.58 – 7.46 (m, 1H), 7.31 (s, 1H), 7.11 – 7.02 (m, 2H), 6.97 – 6.87 (m, 2H), 3.91 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.5, 160.7 (d, J = 246 Hz), 139.3, 133.8, 131.9 (d, J = 2.96), 131.3, 131.2, 129.3, 128.3, 124.7 (d, J = 9.0 Hz), 116.2 (d, J = 22.8 Hz), 52.7. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -115.8. **IR** (neat, cm^{-1}): 3239, 1728, 1505, 1437, 1336, 1309, 1292, 1259, 1232, 1204, 1191, 1170, 1156, 1124, 1098, 1085, 1076, 1014, 965, 856, 831, 814, 751, 678, 639, 589, 575. **Anal.** Calcd. for $C_{14}H_{12}FNO_4S$: C, 54.36; H, 3.91. Found C, 54.49; H, 3.91.



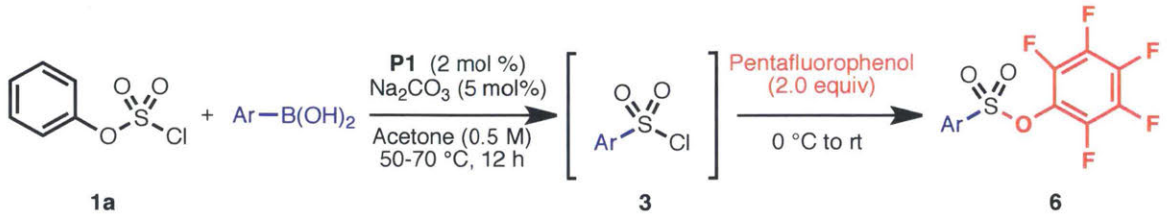
4o

3-Bromo-*N*-phenylbenzenesulfonamide (4o): Following *General Procedure D*, the title compound was prepared using 3-bromophenylboronic acid (301 mg, 1.5 mmol) and **P5**. The cross-coupling reaction was carried out at 55 °C for 12 h. Aniline (109 μL,

1.2 mmol) was used as the aniline to form the desired sulfonamide. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, 5-25% EtOAc in hexanes) to afford **4o** as a yellow solid (259 g; 83% yield); mp = 104.5-105.5 °C.

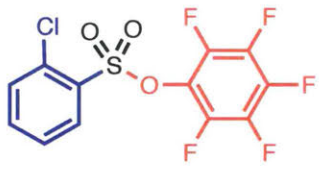
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.66 (d, J = 8 Hz, 2H), 7.33-7.24 (m, 3H), 7.19-7.13 (m, 1H), 7.09-7.05 (m, 2H), 6.68 (br s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.6, 136.0, 135.8, 130.5, 130.0, 129.4, 125.7, 125.7, 122.9, 121.8. **IR** (neat, cm^{-1}): 3259, 1600, 1571, 1481, 1463, 1339, 1298, 1154, 1096, 1086, 920, 902, 785, 767, 752, 619, 580, 573, 558. **Anal.** Calcd. for $C_{12}H_{10}BrNO_2S$: C, 46.17; H, 3.23. Found C, 46.32; H, 3.22.

F) Preparation of Perfluorophenyl Arenesulfonates (6b-6e)



Generation Procedure D: Preparation of Perfluorophenyl Arenesulfonates

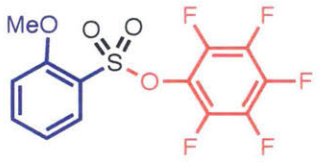
Following *General Procedure A*, a mixture of **P5** (15.9 mg, 0.02 mmol, 2 mol%), Na_2CO_3 (5.3 mg, 0.05 mmol, 5 mol%), arylboronic acid (1.5 mmol, 1.5 equiv), and phenyl chlorosulfate (133 µL, 1.0 mmol, 1.0 equiv) in anhydrous acetone (2.0 mL) was stirred at the desired temperature for 12 h. After the reaction mixture was allowed to cool to room temperature, it was placed under a positive atmosphere of argon and anhydrous THF (1.0 mL) was added via syringe (additional THF was not added to reactions in which a commercially available 2.0 M solution of Me_2NH in THF was used). The reaction mixture was cooled to 0 °C. Pentafluorophenol (214 µL, 2.0 mmol, 2.0 equiv) was then added via a syringe, followed by the addition of anhydrous diisopropylethylamine (261 uL, 1.5 mmol, 1.5 equiv) via a syringe. The reaction was then removed from the cooling bath and stirred at rt for 2 h, after which the crude product was concentrated and load directly onto Biotage SNAP 25 g cartridge and purified by flash column chromatography (using a Biotage Isolera Four system with a SNAP 25 g cartridge) to afford the desired pentafluorophenyl arenesulfonates.



6b

Perfluorophenyl 2-chlorobenzenesulfonate (6b): Following *General Procedure D*, the title compound was prepared using 2-chlorophenylboronic acid (235 mg, 1.5 mmol) as the arylboronic acid. The cross-coupling reaction was carried out at 55 °C for 12 h, after which the crude reaction mixture was carried forward to the desired perfluorophenyl arenesulfonate. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, EtOAc/hexane gradient: 0% EtOAc for 5 CV, 0-10% for 10 CV, 10% for 10 CV) to afford the product as an off-white solid (302 mg, 84% yield); mp 92.0-92.7 °C.

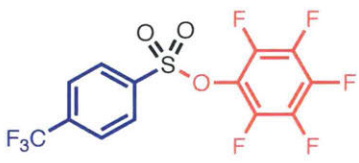
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.98 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.71-7.66 (m, 2H), 7.50-7.45 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.5 (m, 1C), 141.7 (m, 1C), 140.8 (m, 1C), 139.3-139.0 (m, 2C), 136.6 (m, 1C), 136.0 (s, 1C), 133.9 (s, 1C), 133.4 (s, 1C), 132.5 (s, 1C), 131.7 (s, 1C), 127.2 (s, 1C). **^{19}F NMR (376.5 MHz, $CDCl_3$)** δ -150.7 (m, 2F), -155.1 (t, 1F), -161.1 (m, 2F). IR (neat, cm^{-1}): 1514, 1457, 1437, 1389, 1376, 1195, 1022, 989, 966, 770, 761, 718, 668, 605, 578, 564, 553. **Anal.** Calculated for $C_{12}H_4ClF_5O_3S$: C, 40.18; H, 1.12; Cl, 9.88; F, 26.48; O, 13.38; S, 8.94. Found C, 40.40, H, 1.08.



6c

Perfluorophenyl 2-methoxybenzenesulfonate (6c): Following *General Procedure D*, the title compound was prepared using 2-methoxyphenylboronic acid (228 mg, 1.5 mmol) as the arylboronic acid. The cross-coupling reaction was carried out at 50 °C for 12 h, after which the crude reaction mixture was carried forward to the desired perfluorophenyl arenesulfonate. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, EtOAc/hexane gradient: 0% EtOAc for 5 CV, 0-10% for 10 CV, 10% for 10 CV) to afford the product as a brown solid (262 mg, 74% yield); mp 123-126 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.72-7.67 (ddd, *J* = 8.3, 7.9, 1.7 Hz, 1H), 7.14-7.11 (dd, J = 8.3, 1.0 Hz, 1H), 7.10-7.08 (td, *J* = 7.9, 1.0 Hz, 1H), 3.99 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ158.3 (s, 1C), 143.6 (m, 1C), 141.0 (m, 1C), 140.9 (m, 1C), 138.9 (m, 1C), 137.3 (s, 1c), 136.6 (m, 1C), 131.5 (s, 1c), 124.6 (m, 1C), 122.8 (s, 1C), 120.3 (S, 1C), 112.7 (s, 1C), 56.3 (s, 1C). **^{19}F NMR (376.5 MHz, $CDCl_3$)** δ -150.72 (m, 2F), -156.2 (t, 1F), -161.8 (m, 2F). IR (neat, cm^{-1}): 1594, 1578, 517, 1482, 1469, 1434, 1380, 1287, 1255, 1188, 1166, 1149, 1135, 1068, 990, 809, 786, 763, 746, 723, 696, 601, 588, 567. **Anal.** Calculated for $C_{13}H_7F_5O_4S_2$: C, 44.08; H, 1.99; F, 26.82; O, 18.07; S, 9.05. Found C, 44.12; H, 2.15.

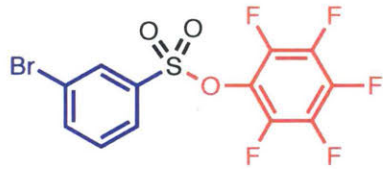


6d

Perfluorophenyl 4-(trifluoromethyl)benzenesulfonate (6d) Following *General Procedure D*, the title compound was prepared using 4-trifluorophenylboronic acid (285 mg, 1.5

mmol) as the arylboronic acid. The cross-coupling reaction was carried out at 70 °C for 12 h, after which the crude reaction mixture was carried forward to the desired perfluorophenyl arenesulfonate. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, EtOAc/hexane gradient: 0% EtOAc for 5 CV, 0-10% for 10 CV, 10% for 10 CV) to afford the product as a white solid (220 mg,56% yield); mp 70-72 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.13 (d, J = 8.3 Hz, 2H), 7.92-7.90 (d, J = 8.3 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.5 (m, 2C), 141.8 (m, 1C), 140.9 (m, 2C), 139.2 (m, 1C), 138.5 (s, 1C), 137.3-136.3 (q, J = 33.6 Hz, 1C), 129.1 (s, 2C), 126.8-126.7 (q, J = 3.7 Hz, 2C), 126.0-118.7 (q, J = 273 Hz, 1C). **^{19}F NMR (376.5 MHz, $CDCl_3$)** δ -63.5 (s, 3F), -150.7 (m, 2F), -154.6 (t, 1F), -160.6 (m, 2F). IR (neat, cm^{-1}): 1514, 1397, 1380, 1198, 1188, 1169, 1148, 1110, 1027, 1016, 990, 849, 790, 756, 722, 710, 615, 598. **Anal.** Calculated for $C_{13}H_4F_8O_3S$: C, 39.81; H, 1.03; F, 38.75; O, 12.24; S, 8.18. Found C, 40.14, H, 1.00.

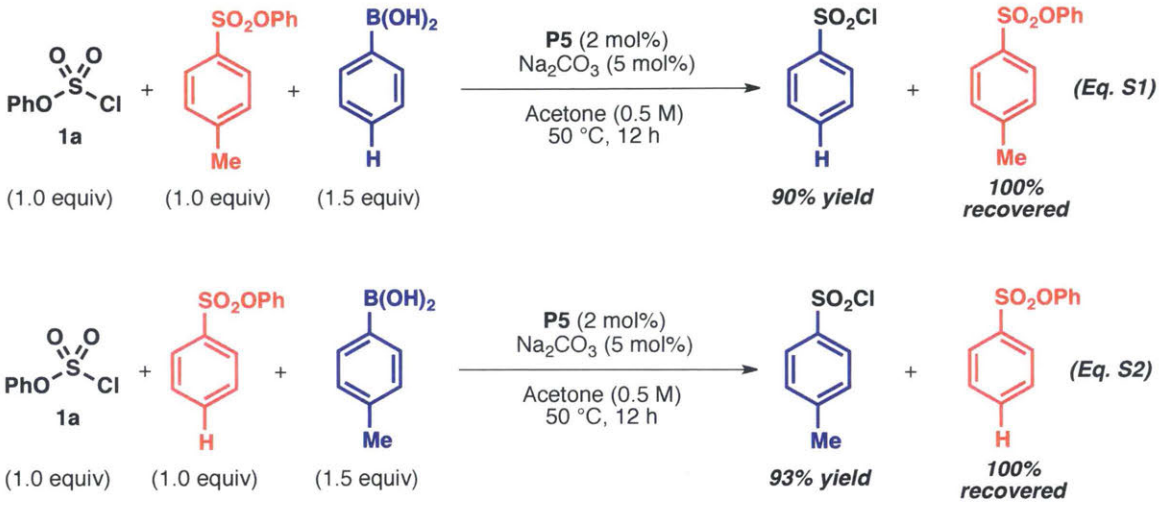


6e

Perfluorophenyl 3-bromobenzenesulfonate (6e): Following *General Procedure D*, the title compound was prepared using 3-bromophenylboronic acid (301 mg, 1.5 mmol) as the arylboronic acid. The cross-coupling reaction was carried out at 55 °C for 12 h, after which the crude reaction mixture was carried forward to the desired perfluorophenyl arenesulfonate. The crude product was purified by flash column chromatography (Biotage, 25g SNAP column, EtOAc/hexane gradient: 0% EtOAc for 5 CV, 0-2% for 5 CV, 2% for 2 CV then 5% for 10 CV) to afford the product as yellow oil (308.4 mg, 77% yield).

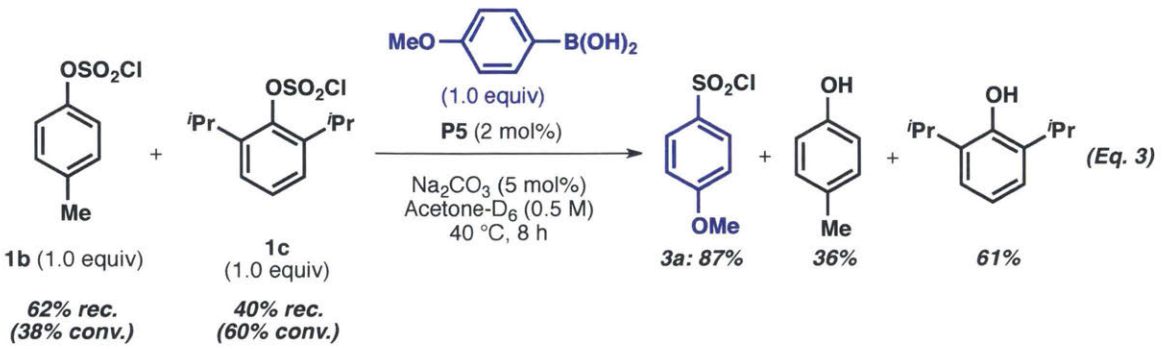
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13-8.12 (t, J = 1.8 Hz 2H), 7.93-7.88 (m, 2H), 7.54-7.49 (t, J = 8.0 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 143.5 (m, 1C), 141.7 (m, 1C), 140.8 (m, 1C), 139.3-139.0 (m, 2C), 138.3 (s, 1C), 136.6 (m, 1C), 136.5 (s, 1C), 131.2 (s, 1C), 131.0 (s, 1C), 127.0 (s, 1C), 123.4 (s, 1C). **^{19}F NMR (376.5 MHz, $CDCl_3$)** δ -150.7 (m, 2F), -155.1 (t, 1F), -160.9 (m, 2F). IR (neat, cm^{-1}): 1514, 1466, 1394, 1194, 1021, 989, 782, 743, 715, 673, 656, 604, 591, 581, 570. **Anal.** Calculated for $C_{12}H_4BrF_5O_3S$: C, 35.75; H, 1.00; Br, 19.82; F, 23.56; O, 11.91; S, 7.95. Found C, 36.03, H, 0.95.

G) Control Experiments: To confirm that sulfonate esters are not converted to sulfonyl chlorides:



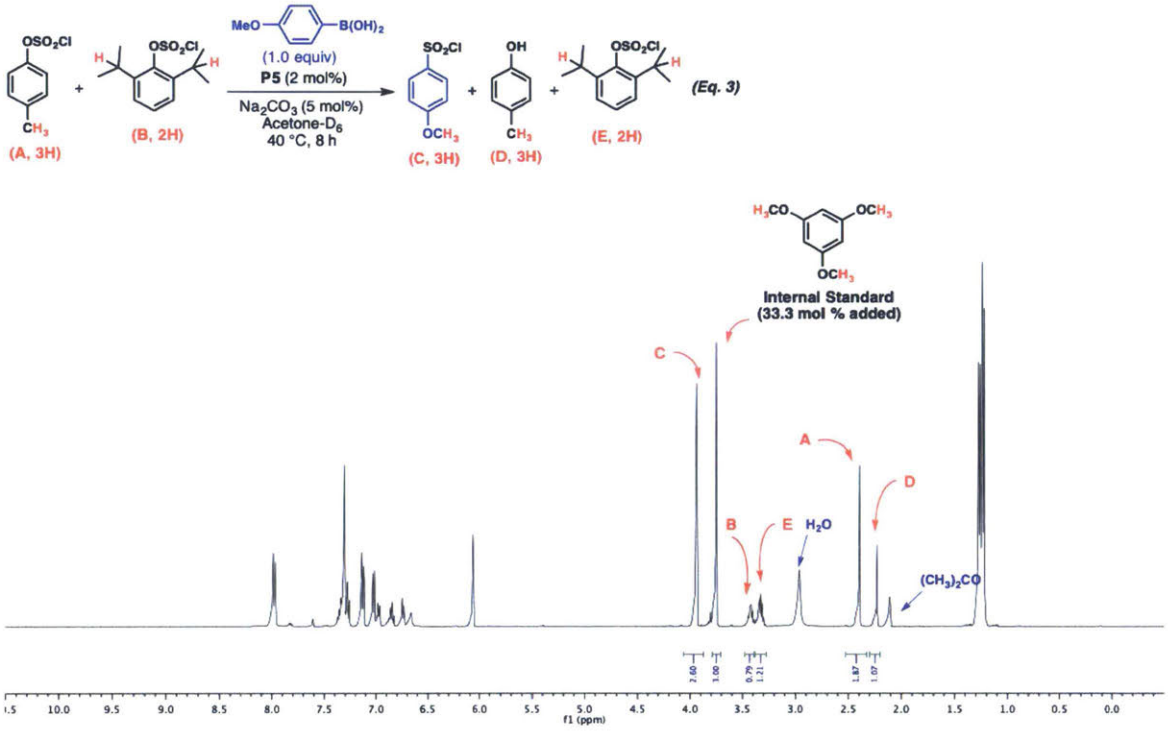
Two separate oven-dried test tubes, each equipped with a magnetic stir bar, were charged with **P5** (7.94 mg, 0.01 mmol, 2 mol%), Na_2CO_3 (2.65 mg, 0.025 mmol, 5 mol%), either phenylboronic acid (for Eq. S1, 93 mg, 0.75 mmol, 1.5 equiv) or 4-methylphenylboronic acid (for Eq. S2, 104 mg, 0.75 mmol, 1.5 equiv), and either phenyl tosylate (for Eq. S1, 124 mg, 0.5 mmol, 1.0 equiv) or phenyl benzenesulfonate (for Eq. S2, 117 mg, 0.5 mmol, 1.0 equiv). The tubes were sealed with a Teflon screw-cap septum. The vessels were evacuated and backfilled with argon (this process was repeated a total of 3 times), and anhydrous acetone (1.0 mL) was then added via syringe. After the mixtures were allowed to stir for ~3 min at room temperature, neat phenyl chlorosulfate (66 μL, 0.5 mmol, 1.0 equiv) was added. The vessels were then placed in a preheated oil bath at 50 °C and the reaction mixtures were allowed to stir for 12 h. After the reaction mixtures were allowed to cool to room temperature, an internal standard was added (tetradecane) and the mixtures were diluted with EtOAc and filtered through a short plug of silica gel. The crude reaction mixtures were analyzed by GC and the results are shown in Equations S1 and S2. In each case, 100% of the phenyl sulfonate ester was recovered while the sulfonyl chloride derived from the arylboronic acid was formed in near quantitative yield, thus demonstrating that the sulfonate esters are not converted to the corresponding sulfonyl chlorides under these conditions.

H) Competition Experiments Between 1b and 1c:



An oven-dried test tube equipped with a magnetic stir bar was charged with **P5** (0.01 mmol, 2 mol%), Na_2CO_3 (2.65 mg, 0.025 mmol, 5 mol%), and the 4-methoxyphenylboronic acid (76 mg, 0.5 mmol, 1.0 equiv), and the tube was sealed with a Teflon screw-cap septum. The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times), and deuterated acetone-D_6 (1.0 mL) was then added via syringe. After the mixture was allowed to stir for ~3 min at room temperature, neat **1b** (75.4 μL, 0.5 mmol, 1.0 equiv) and **1c** (116 μL, 0.5 mmol, 1.0 equiv) were added sequentially. The vessel was then placed in a preheated oil bath at 40 °C and the reaction mixture was allowed to stir for 8 h. After the reaction mixture was allowed to cool to room temperature, an internal standard (1,3,5-trimethoxybenzene, 28.03 mg) was added. A small aliquot (~0.2 mL) of the crude reaction mixture was filtered through a short plug of SiO_2 (~1.5 cm in a pipette with a cotton filter), which was further washed with CD_3Cl (~0.6 mL). The resulting yellow solution was then analyzed by ^1H NMR. Because both **1b** and **1c** are converted to the same sulfonyl chloride product (**3a**, 87% NMR yield), the amounts of recovered **1b** (40%) and **1c** (62%) were quantified along with the corresponding phenol byproducts. The NMR data show that **1c** undergoes higher conversion to **3a**, which suggests that the more sterically hindered substrate (**1c**) is slightly more reactive than **1b** (Figure 8).

Figure 8. *^{1}H NMR Analysis of Crude Reaction Mixture of Equation 3.*



Note: The integrals of the benzylic protons of **1c** and 2,6-diisopropylphenol were used to calculate the NMR yields of these compounds, but these signals overlap to a small degree in the ^{1}H NMR spectrum above. The benzylic protons signals completely resolve from one another if the crude reaction mixture is first filtered through a short plug of SiO_2, concentrated and then dissolved in CD_3Cl. However, **1b** is volatile, and a significant amount of this compound is removed upon concentrating the sample; therefore, this workup procedure was not used to prepare the NMR sample used to analyze the substrate and product distributions of Eq. S3. To show an example of a spectrum in which the signals of **1c** and 2,6-diisopropylphenol are completely differentiated from one another, we included the ^{1}H NMR spectrum of the crude reaction mixture of Eq. S3 below (Figure 9). In order to promote full conversion of the arylboronic acid to **1a**, the reaction depicted in Eq. S3 was conducted at 50 °C for 10 h, but under otherwise identical conditions to those depicted in Eq. 3.

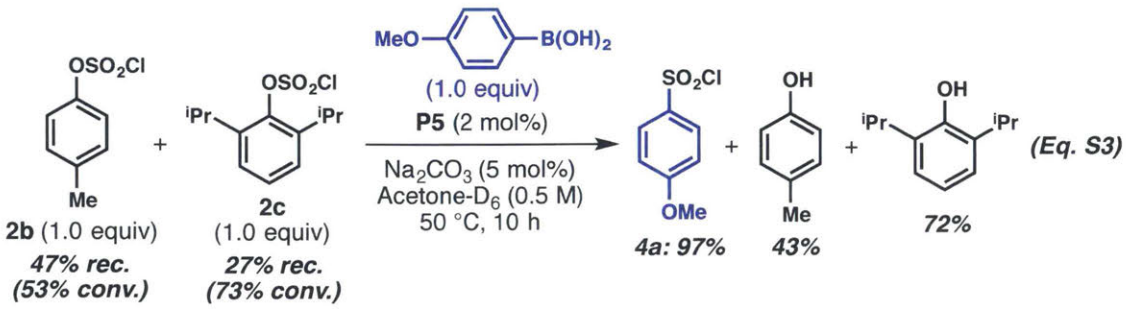
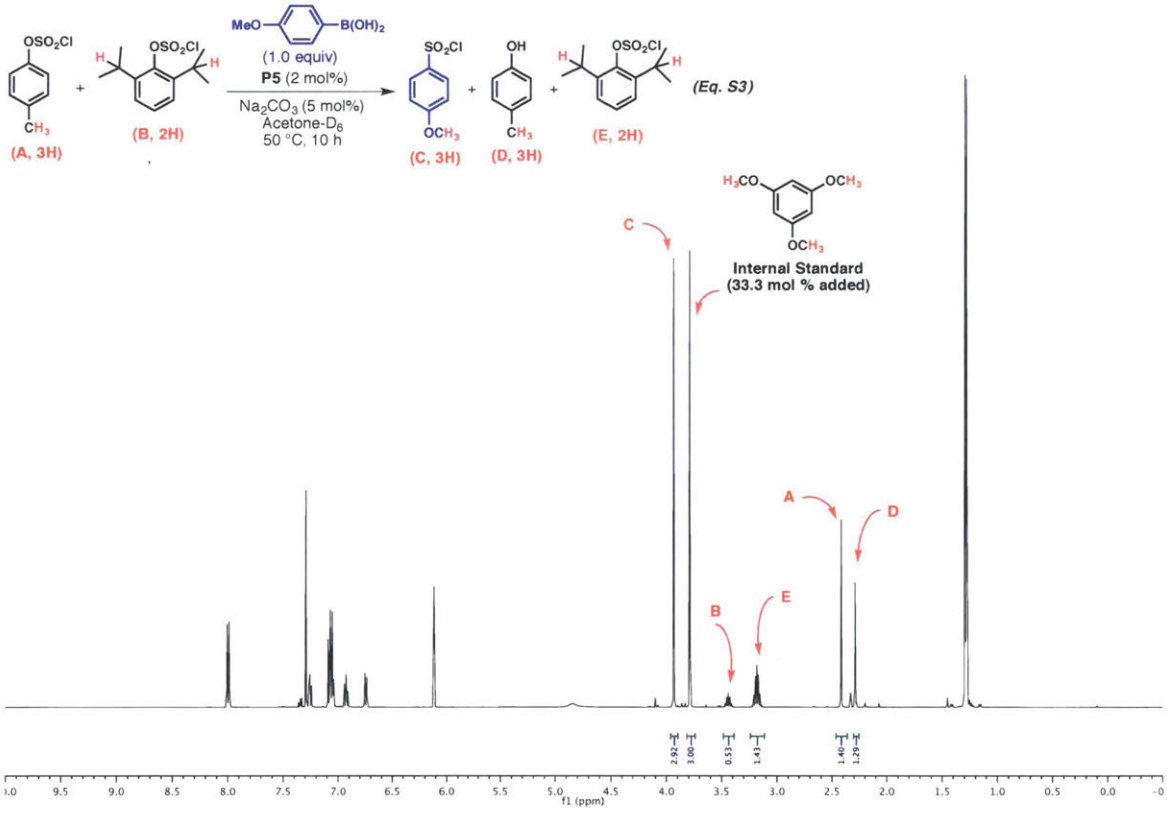
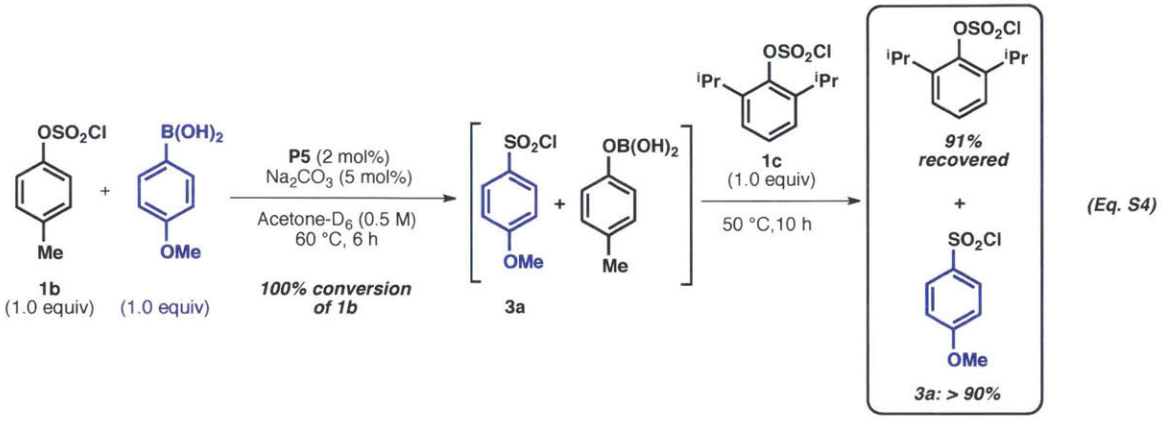


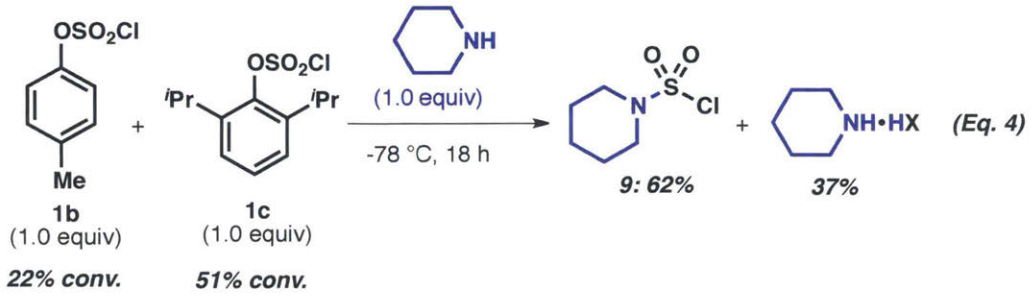
Figure 9. *^{1}H NMR Analysis of Crude Reaction Mixture of Equation S3 (Crude Reaction Mixture Filtered through SiO_2, Concentrated, and Dissolved in $CDCl_3$)*





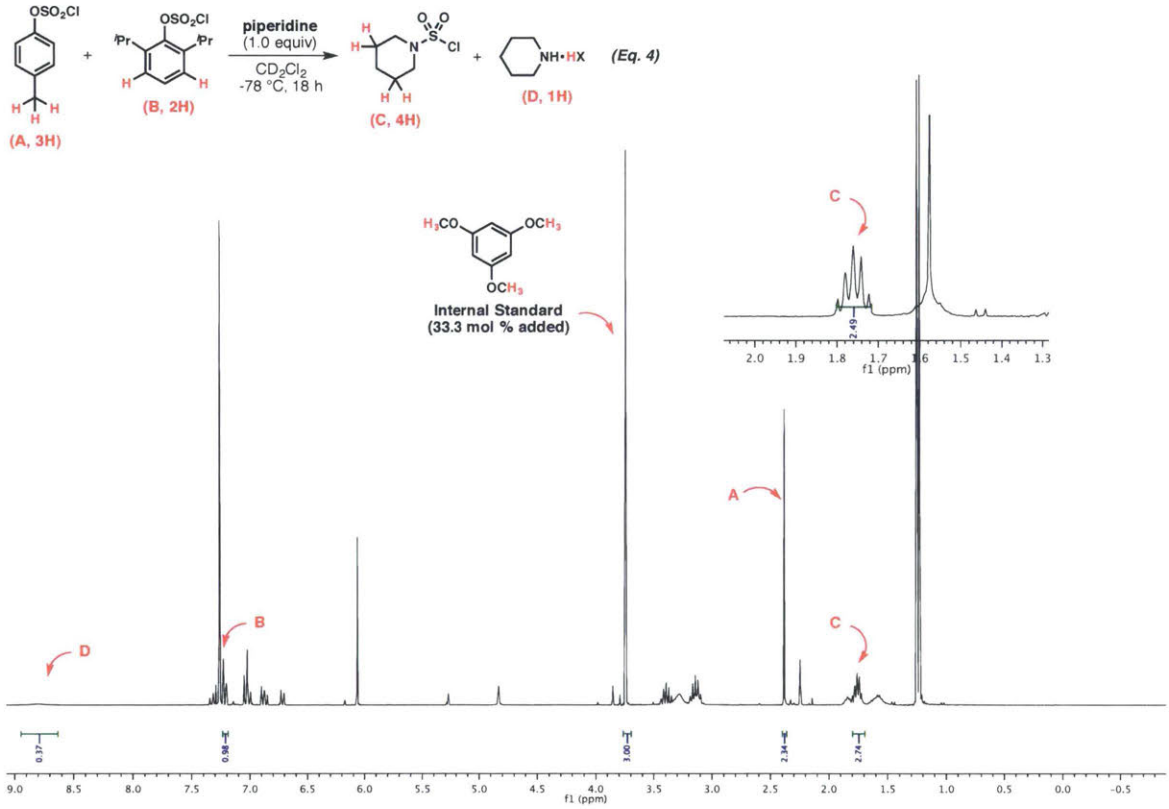
Additionally, the control experiment (Eq. S4) was performed to show that **1c** is not converted to **1b** during the competition experiments (Eq. 3 and Eq. S3). First, substrate **1b** was subjected to the chlorosulfonylation conditions in the absence of **1c**. Following complete conversion of **1b** to the sulfonyl chloride (**3a**), substrate **1c** was then added and the reaction mixture was allowed to stir at 50 °C for 10 h. Analysis by ^{1}H NMR showed 91% recovery of **1c**, 0% recovery of **1b**, and > 90% NMR yield of **3a**.

I) Competition Experiment with Piperidine:



An oven-dried test tube equipped with a magnetic stir bar was sealed with a Teflon screw-cap septum. The vessel was evacuated and backfilled with N_2 (this process was repeated a total of 3 times), and neat **1b** (75.4 μL, 0.5 mmol, 1.0 equiv), neat **1c** (116 μL, 0.5 mmol, 1.0 equiv), and CD_2Cl_2 (2.0 mL) were added under a N_2 atmosphere. The vessel was allowed to cool to -78 °C in a dry ice/acetone bath, and a solution of piperidine (50 μL, 0.5 mmol, 1.0 equiv) in CD_2Cl_2 (0.5 mL) was added slowly via syringe (over 2 min) along the inner wall of the vessel. The reaction mixture was stirred for 18 h at -78 °C. Immediately after the reaction mixture was allowed to warm to room temperature, an internal standard (1,3,5-trimethoxybenzene, 28.03 mg) was added, and a small aliquot (~0.2 mL) of the crude reaction mixture was diluted with CD_3Cl (~0.6 mL) and analyzed by ^1H NMR. **Note:** The signals of the sulfamoyl chloride (**8**) and the piperidinium salt overlap in the ^1H NMR spectrum. Therefore, a separate aliquot (~0.2 mL) of the crude reaction mixture was filtered through a short plug of SiO_2 (~1.5 cm in a pipette with a cotton filter) to remove the piperidinium salt. The filter was further washed with CD_3Cl (~0.6 mL) and the combined filtrate was analyzed by ^1H NMR (see expanded region on Figure 10). Because both **1b** and **1c** are converted to the same sulfamoyl chloride product (**9**), the amounts of recovered **1b** and **1c** were quantified. The NMR data show that a larger amount of the sterically hindered substrate (**1c**) is consumed than **1b**. In addition, **1b** and **1c** react with piperidine to form the corresponding sulfamoyl chloride (**9**), demonstrating that S-O bond cleavage is also favored in the absence of a palladium catalyst.

Figure 10. *^{1}H NMR Analysis of Crude Reaction Mixture of Eq. 4 (Expanded signal C taken from Spectrum Recorded After Piperidinium Salt Removed via SiO_2 Filtration)*



1.5 References and Notes

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19) Phenyl chlorosulfate is prepared by reacting phenol SO_2Cl_2 and pyridine at –78 °C. Compound 2a is stable in neat form for at least one year when stored at 4 °C.

20) No reaction was observed when solutions of 4-methoxyphenylboronic acid (1.5 equiv) and **1a** (1.0 equiv) in toluene or 1,4- dioxane were stirred at 110 °C for 24 h.

21) See the experimental section for details.

22) An alternative mechanism might involve reversible oxidative addition to **1a**, with transmetalation occurring at the –OPh group of **8** in preference to the –Cl group of the related Pd–Cl species. Oxidative addition is typically considered an irreversible process, although examples of reductive elimination of aryl halides have been reported. See: (a) Roy, A. H.;

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23) Alkoxo- and (phenoxo)Pd(II) complexes are known to undergo efficient transmetalation without the aid of base. For reviews and discussions, see: (a) Miyaura, N. *J. Organomet. Chem.* **2002**, *653*, 54. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

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26) The diarylphosphine moiety is essential for most substrates because more electron-rich dialkylphosphine ligands were oxidized under the reaction conditions (as indicated by the ^{31}P NMR spectra of the crude reaction mixtures).

27) For examples of cross-couplings using XPhos precatalysts, see: (a) Kinzel, T.; Zhang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 14073. (b) Oberli, M. A.; Buchwald, S. L. *Org. Lett.* **2012**, *14*, 4606. Similarly, little to no product was observed using SPhos or RuPhos ligands. For a review of Suzuki–Miyaura reactions employing dialkylbiaryl phosphine ligands, see: (c) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461.

28) Both Pd(0) and phosphine ligands can potentially react with **3**; thus, to limit product decomposition and promote complete conversion of **1a**, we chose to increase the reaction temperatures accordingly rather than adjust the respective catalyst loadings.

29) Electron-poor arylboronic acids typically undergo transmetalation at a slower rate than electron-neutral and electron-rich arylboronic acids.

30) The volatility of **3d–3i** may also contribute to lower yields.

31) The stoichiometry of the amine can be reduced to 1.2 equiv if DIPEA is used as a sacrificial base. See conditions for product **4d** (Table 3).

32) Currently, boronic acids derived from nitrogen heterocycles do not couple in useful yields. This inefficiency is due to deboronation of the starting material and/or the instability of the corresponding sulfonyl chlorides. See: Caldwell, W. T.; Kornfeld, E. C. *J. Am. Chem. Soc.* **1950**, *72*, 4890.

33) The order of reactivity of electrophiles for Suzuki–Miyaura cross-coupling is ArI > $ArSO_2Cl$ > ArBr ≫ ArCl (see ref 16a).

34) Aryl sulfonyl chlorides have been used as precursors to diaryl sulfones. See: Bandgar, B. P.; Bettigeri, S. V.; Phopase, *J. Org. Lett.* **2004**, *6*, 2105.

35) For examples of desulfonylative cross-couplings of sulfonyl chlorides to form C—C bonds, see: (a) Miura, M.; Itoh, K. *Chem. Lett.* **1989**, *18*, 77. (b) Dubbaka; S.R.; Vogel; P. *J. Am. Chem. Soc.* **2003**, *125*, 15292. (c) Dubbaka; S.R.; Vogel; P. *Org. Lett.* **2004**, *6*, 95. (d) Dubbaka; S.R.; Vogel; P. *Tetrahedron Lett.* **2006**, *47*, 3345.

36) We observe homocoupling (< 15% biaryl) of certain electron-deficient and *ortho*-substituted arylboronic acids (e.g. corresponding to **5f** and **5j**). This side reaction may occur at the expense of **2a** via an oxidative addition/desulfonylation pathway.

37) A control experiment in which **2c** is introduced after complete conversion of **2b** verified that **2c** is not converted to **2b**. See Supporting Information for details.

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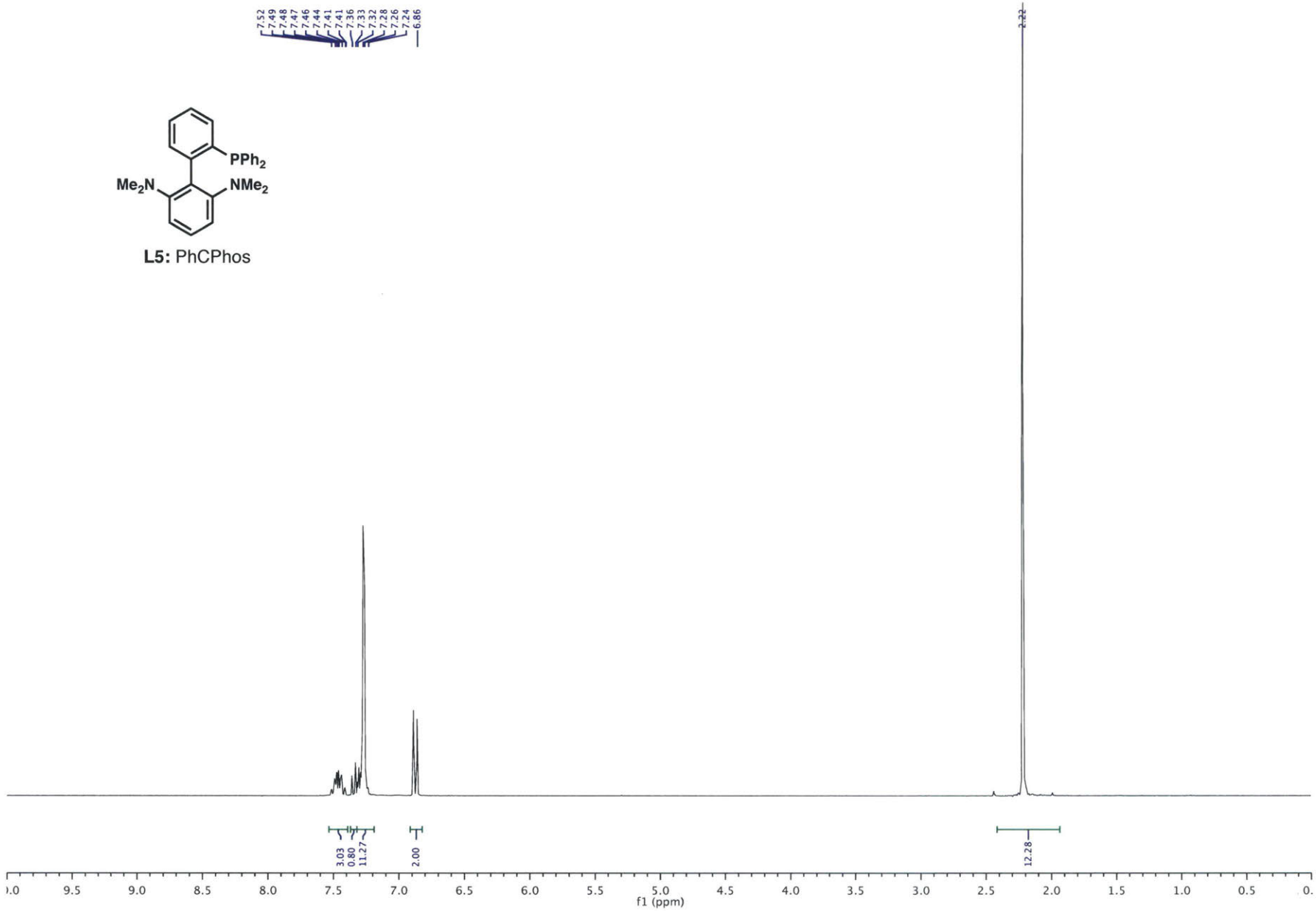
43) ^{1}H NMR of perfluorophenyl arenesulfonates stored under ambient conditions after 3 years showed no decomposition of the materials.

1.5 ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR Spectra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7.24
6.86
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L5: PhCPhos
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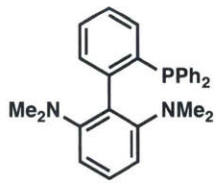
f1 (ppm)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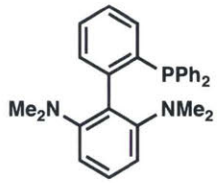
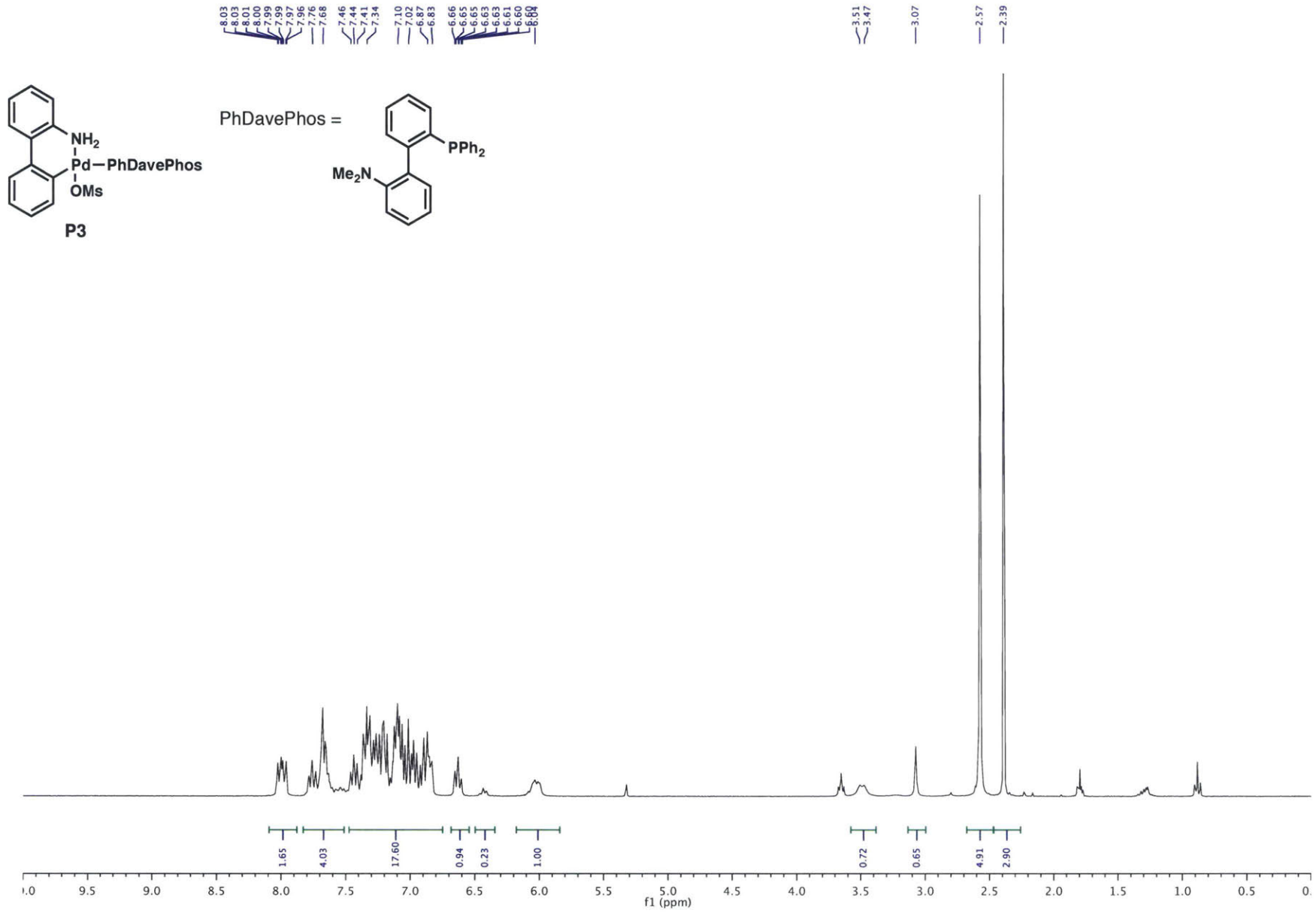
f1 (ppm)



L5: PhCPhos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7.10
7.02
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6.83
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6.63
6.63
6.61
6.60
6.60
6.04
3.51
3.47
3.07
2.57
2.39
NH2
Pd—PhDavePhos
OMs
P3
PhDavePhos =
PPh2
Me2N
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4.03
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1.00
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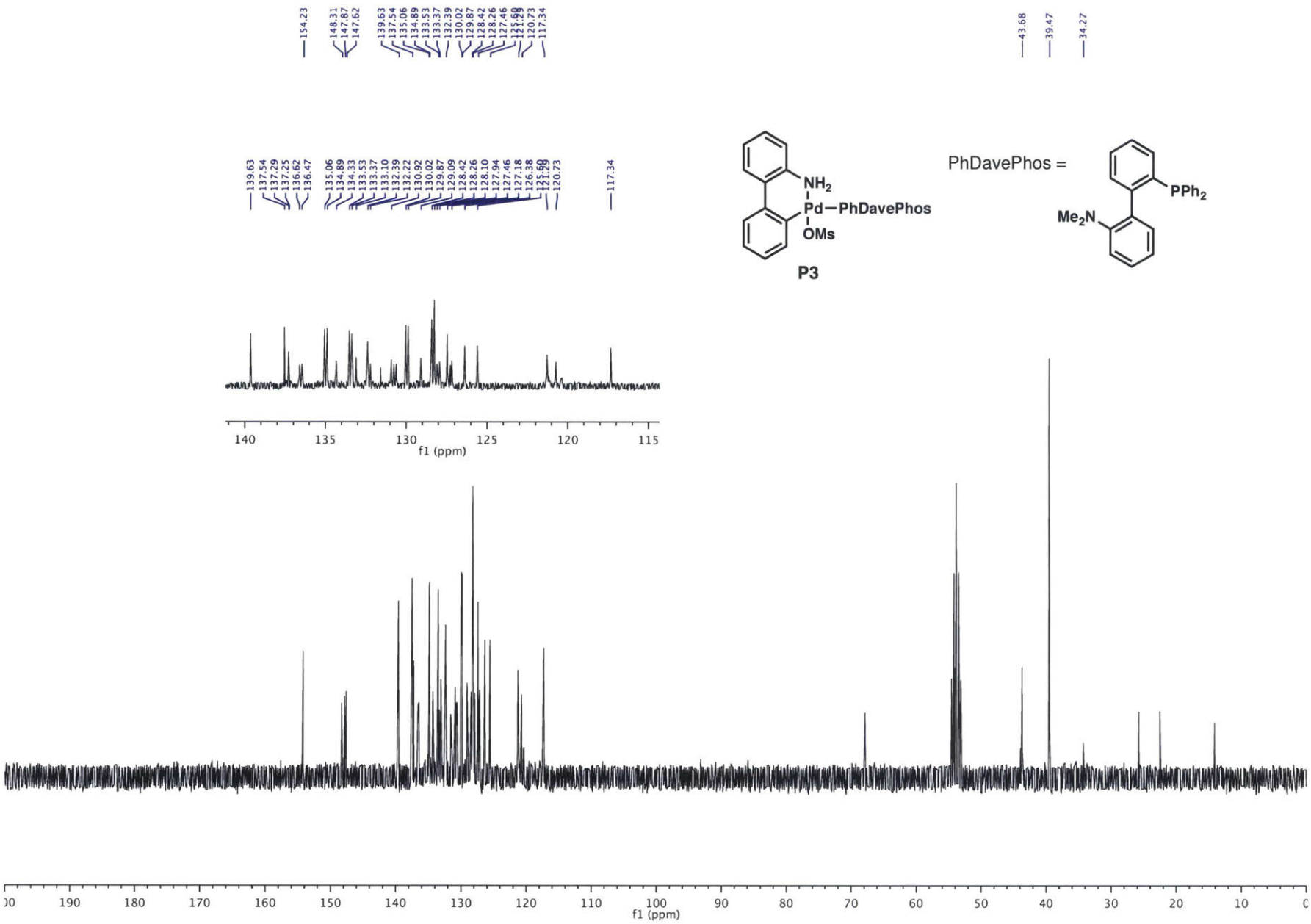
0.65
4.91
2.90
f1 (ppm)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128.26
127.46
121.73
120.73
117.34
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OMs
P3
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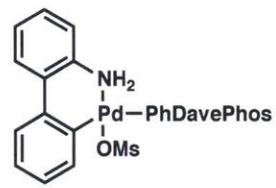
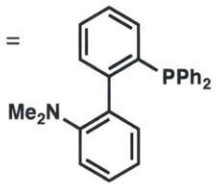
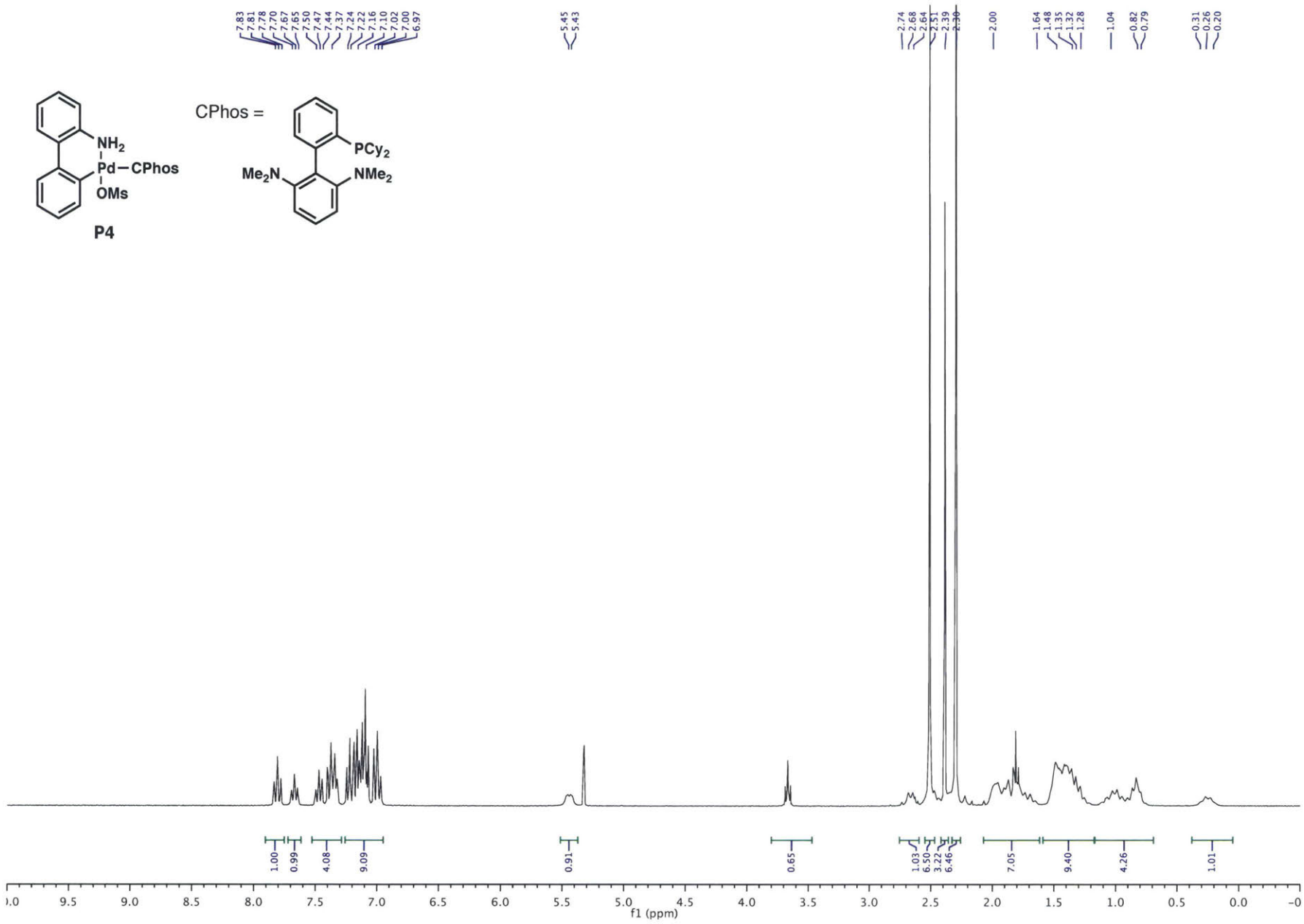
PPh2
Me2N
f1 (ppm)



P3

PhDavePhos =

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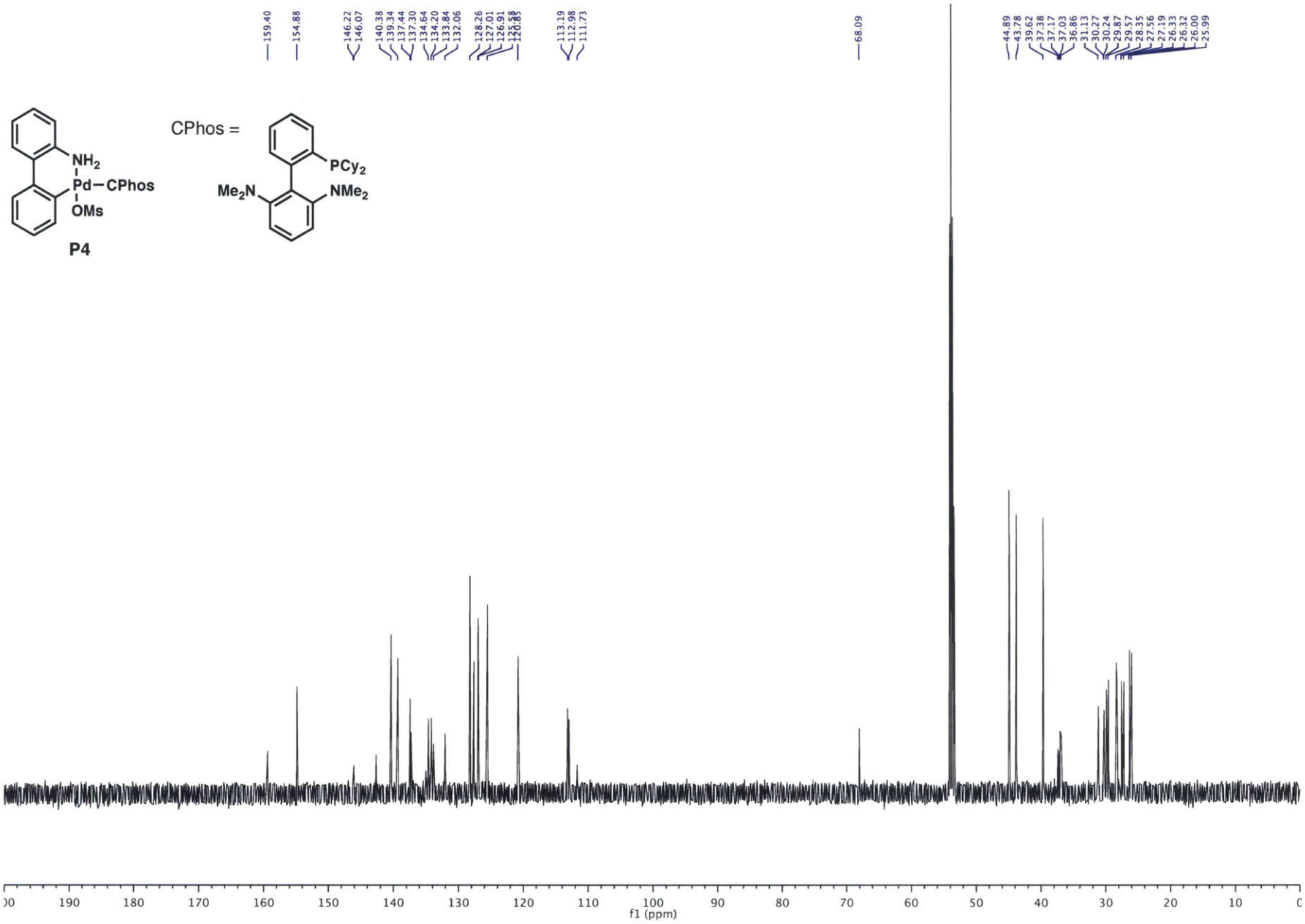
Pd—CPhos
OMs
P4
CPhos =
PCy2
Me2N
NMe2
f1 (ppm)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43.78
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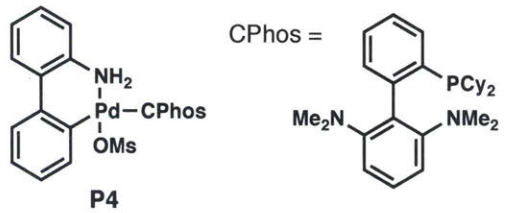
28.35
27.56
27.19
26.33
26.32
26.00
25.99
NH2
Pd—CPhos
OMs
P4
CPhos =
PCy2
Me2N
NMe2
f1 (ppm)

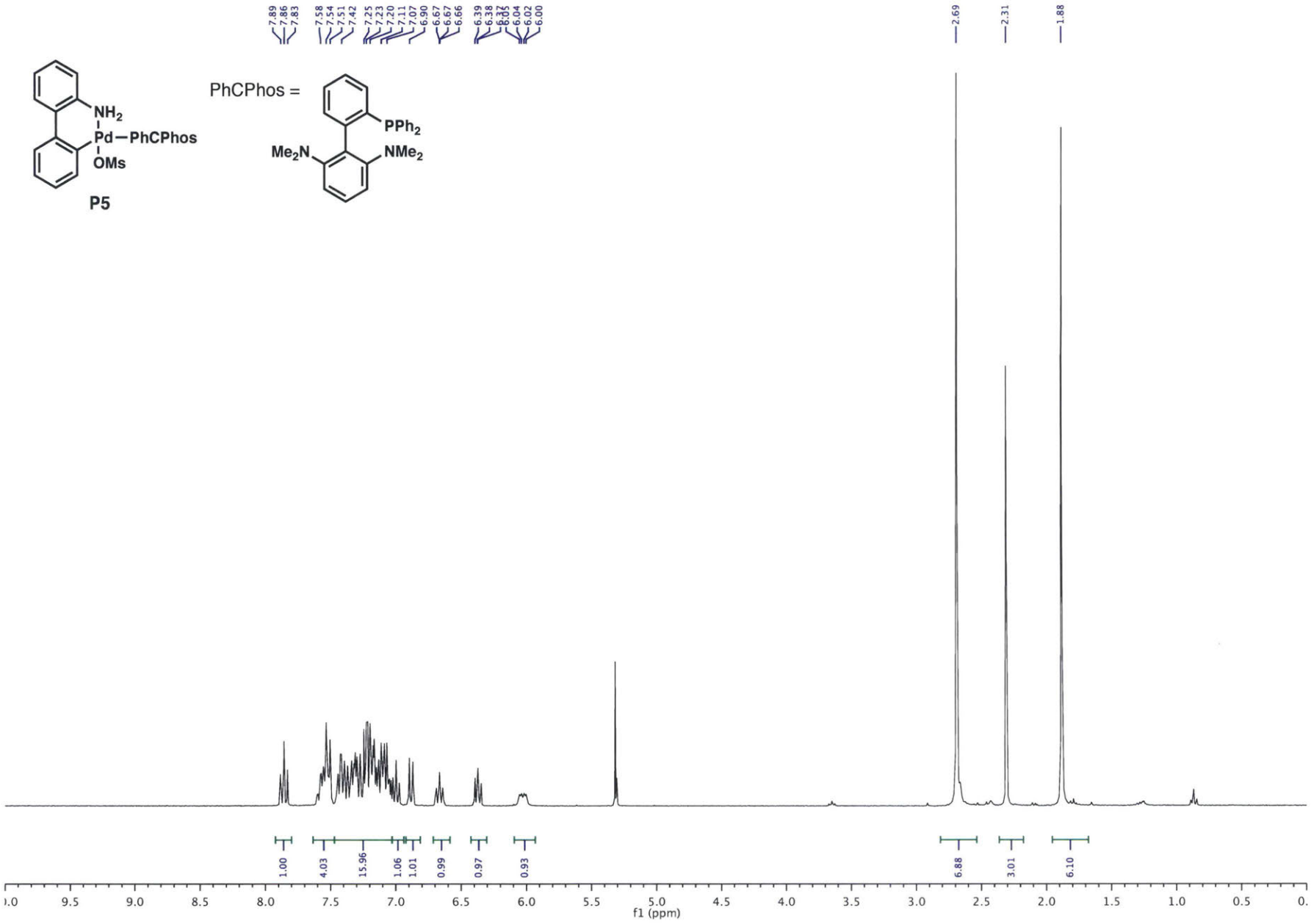

NH2
Pd—CPhos
OMs

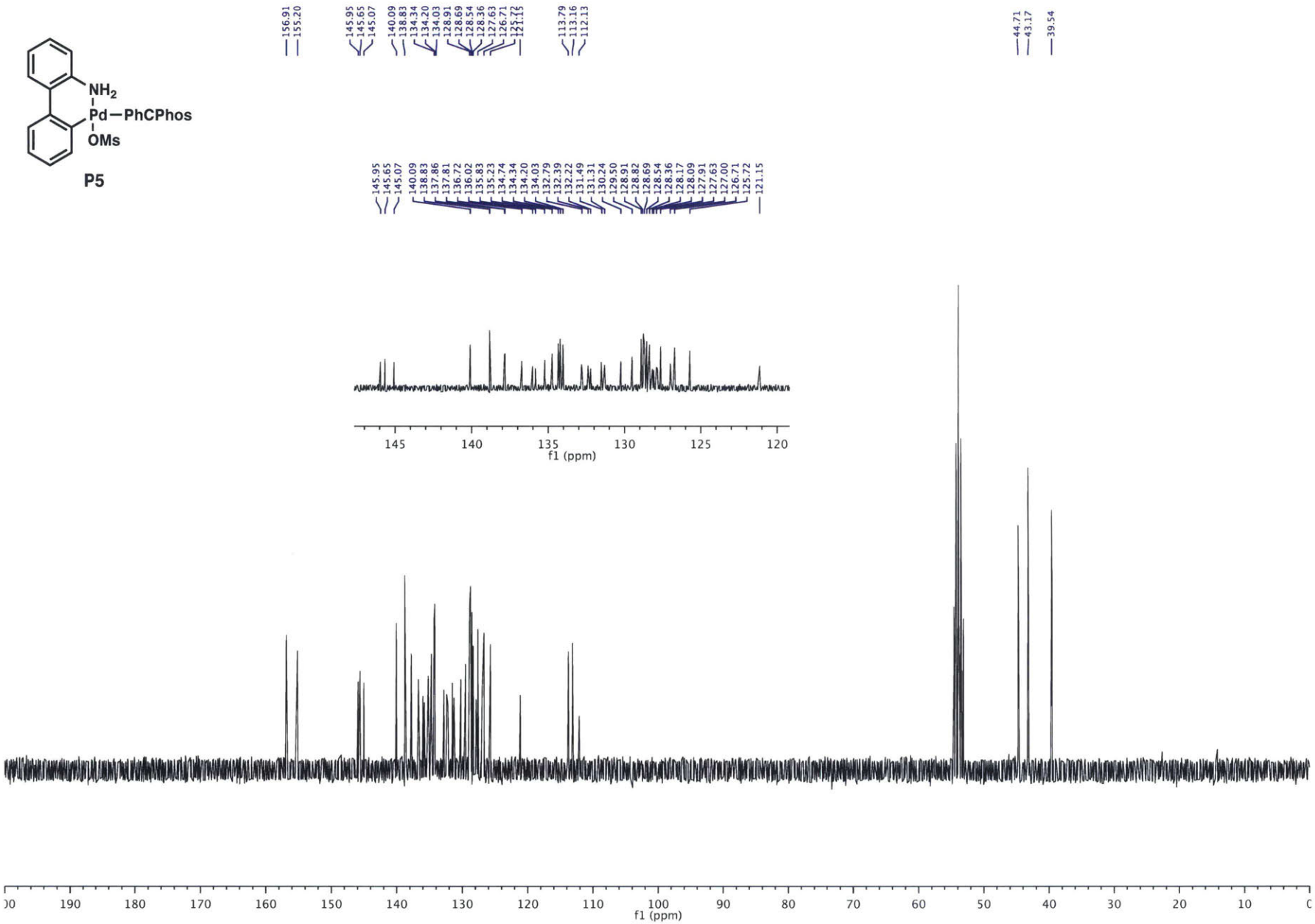
P4

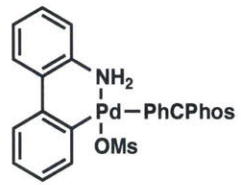
CPhos =

PCy2
Me2N
NMe2

40.78
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
f1 (ppm)

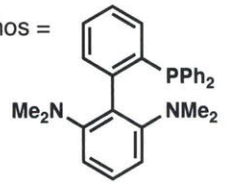

NH2
Pd—PhCPhos
OMs
P5
PhCPhos =
PPh2
Me2N
NMe2
7.89
7.86
7.83
7.58
7.54
7.51
7.42
7.25
7.23
7.20
7.11
7.07
6.90
6.67
6.67
6.66
6.39
6.38
6.04
6.02
6.00
2.69
2.31
1.88
1.00
4.03
15.96
1.06
1.01
0.99
0.97
0.93
6.88
3.01
6.10
f1 (ppm)


NH2
Pd—PhCPhos
OMs
P5
156.91
155.20
145.95
145.65
145.07
140.09
138.83
134.34
134.20
134.03
128.91
128.69
128.54
128.36
127.63
126.71
125.72
121.15
113.79
113.16
112.13
44.71
43.17
39.54
f1 (ppm)


NH2
Pd—PhCPhos
OMs

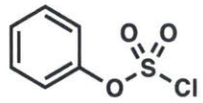
P5

PhCPhos =

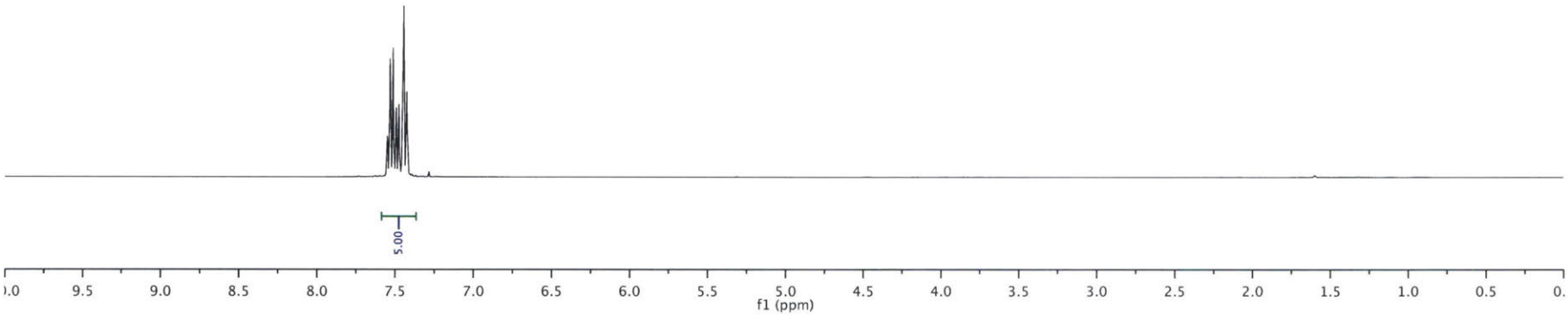

PPh2
Me2N
NMe2

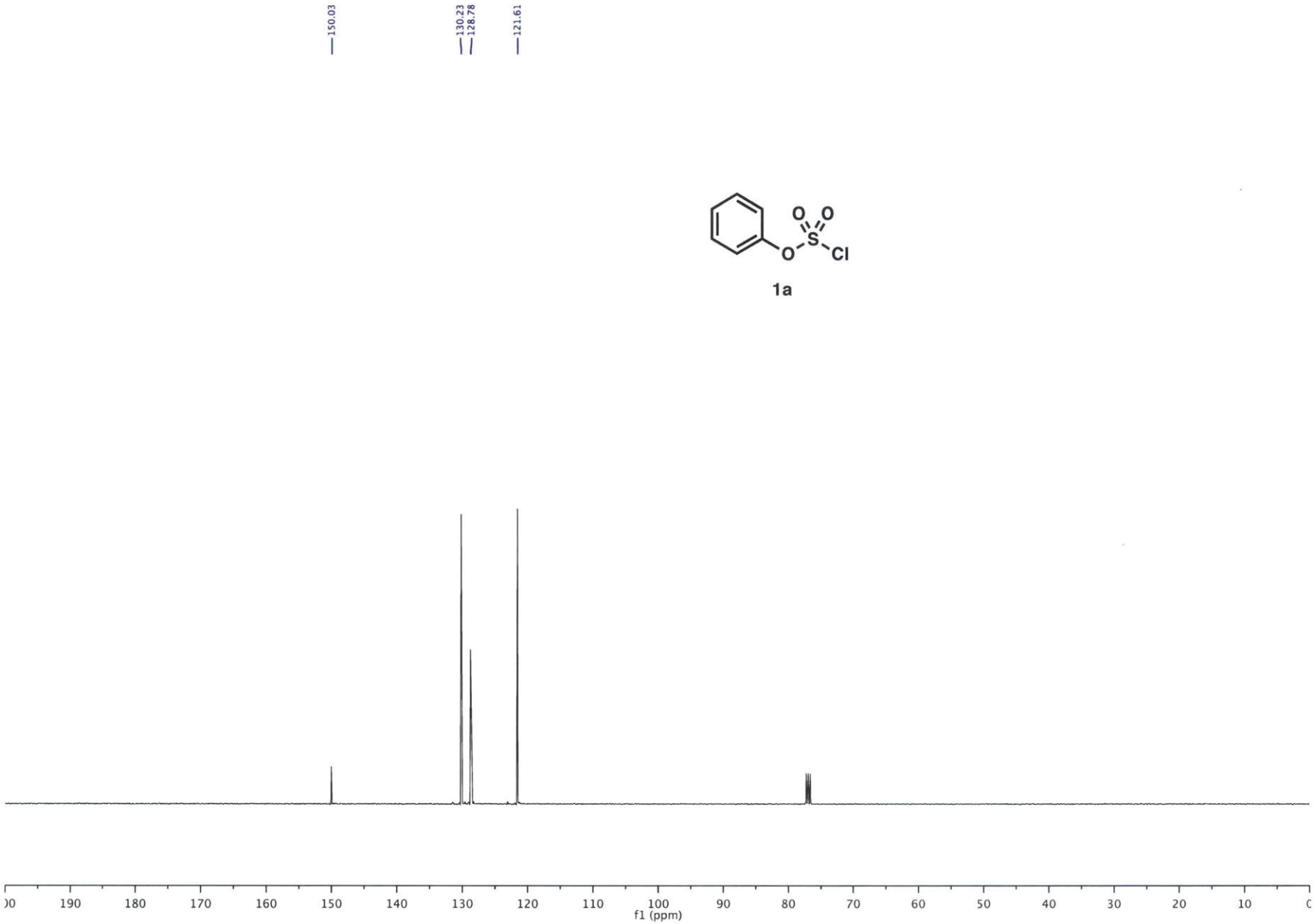
40.24
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
f1 (ppm)

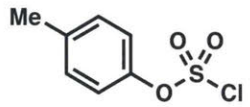

7.55
7.55
7.53
7.51
7.44
7.42
7.42


O
O
S
O
Cl

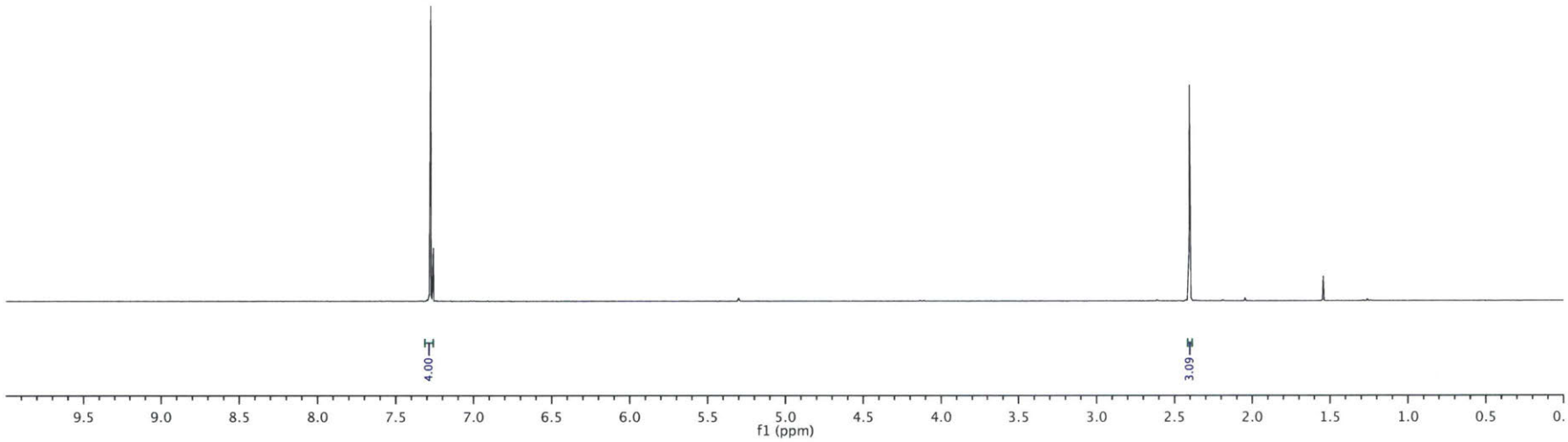
1a

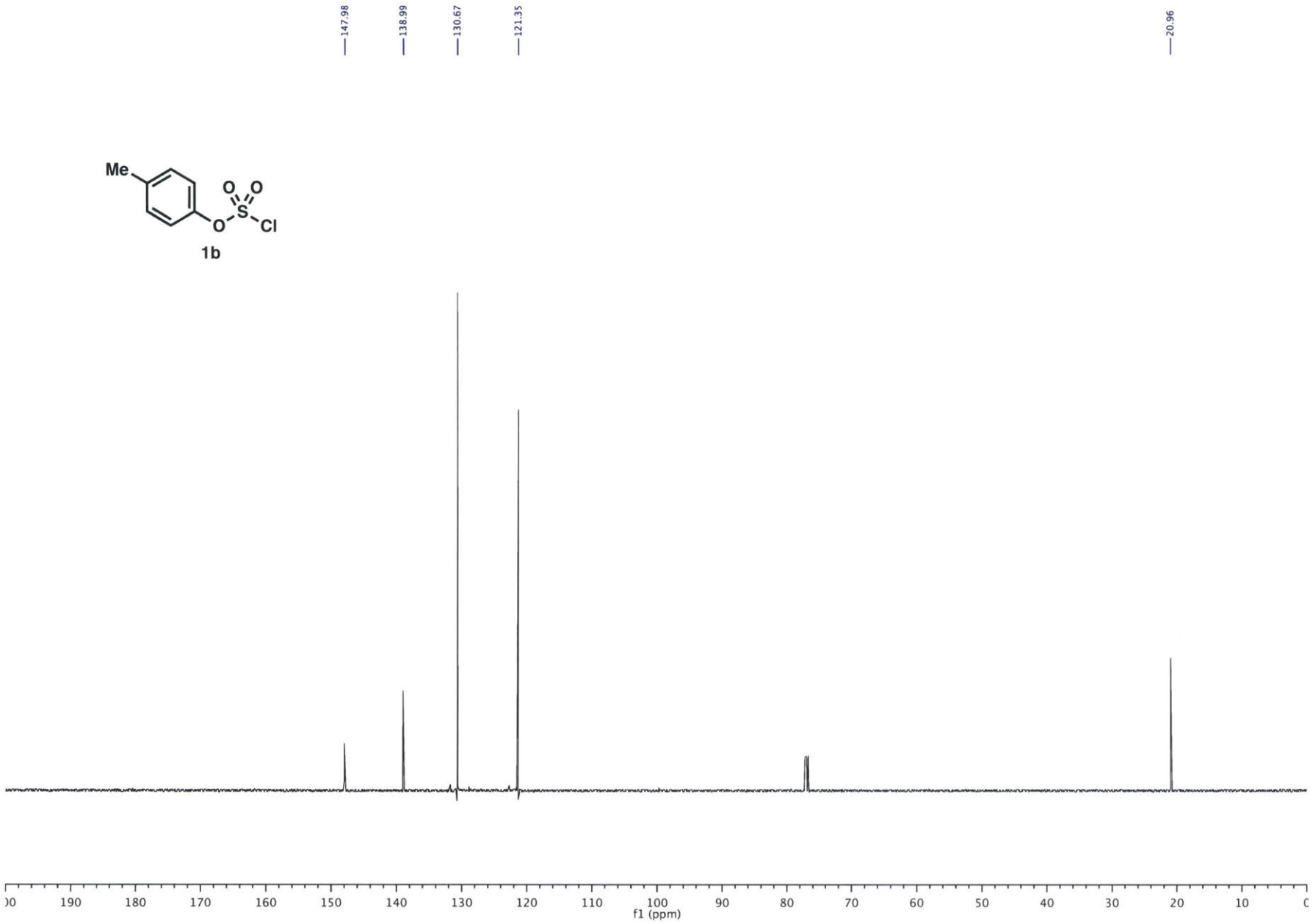

5.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

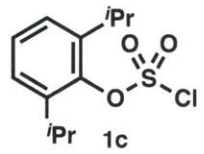

150.03
130.23
128.78
121.61
O
O
S
O
Cl
1a
190
180
170
160
150
140
130
120
110
100
f1 (ppm)
90
80
70
60
50
40
30
20
10


Me
O
O
S
O
Cl

1b

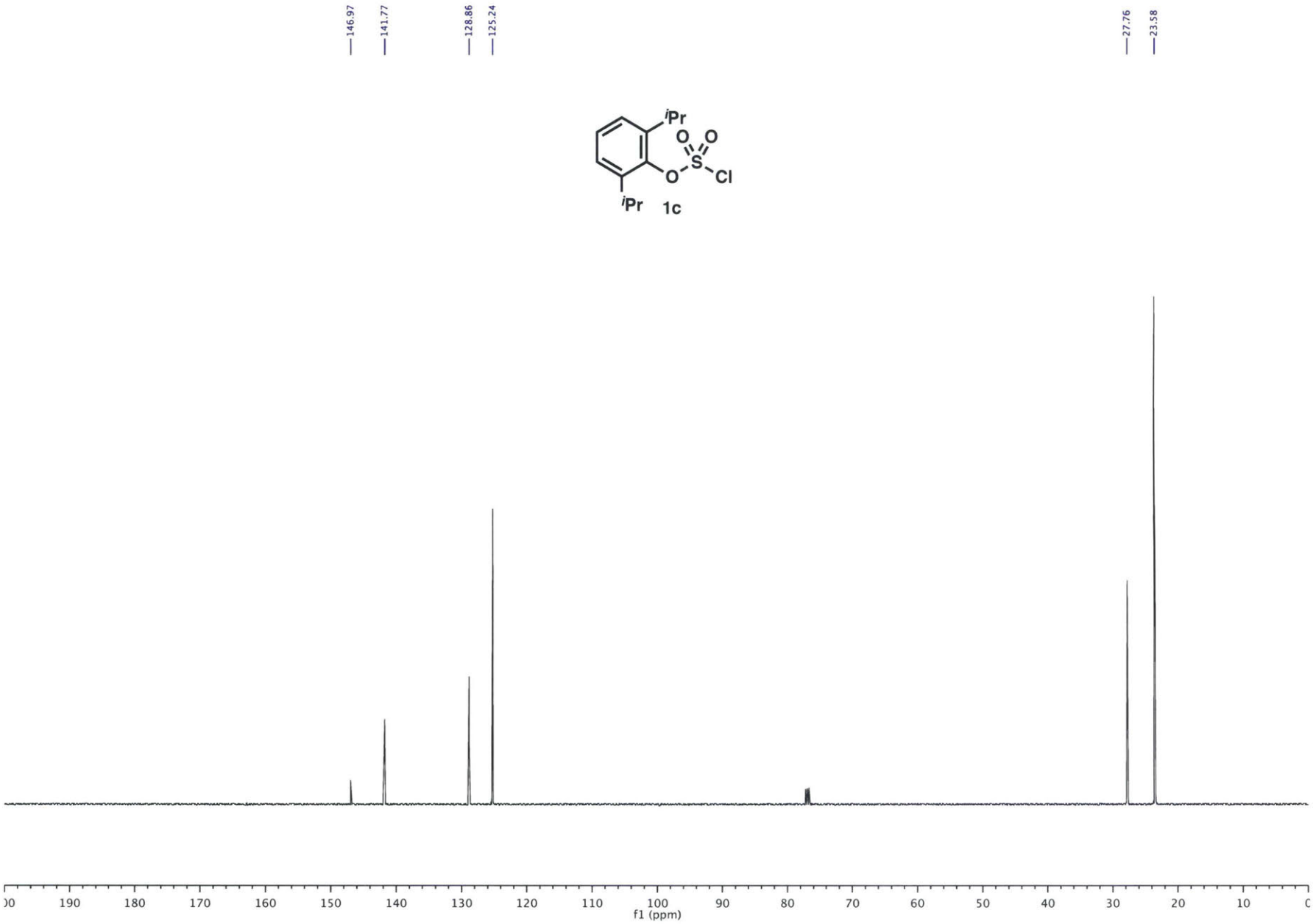

4.00
3.09
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


147.98
138.99
130.67
121.35
20.96
Me
O
O
S
O
Cl
1b
f1 (ppm)

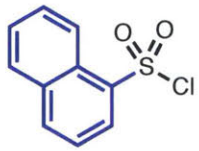

iPr
O
O
S
O
Cl
iPr

1c

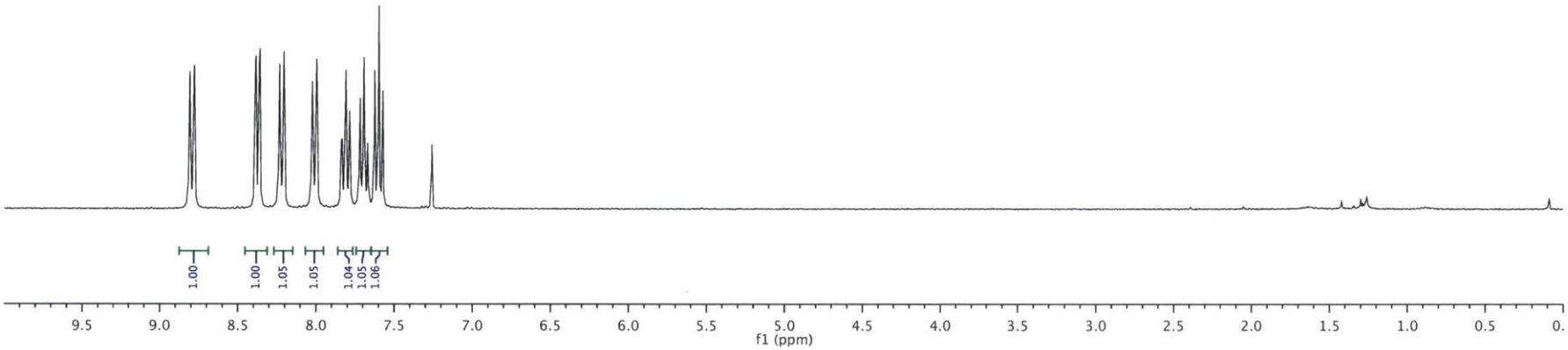
0.97
2.01
1.92
13.70
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

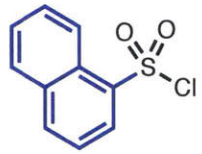

146.97
141.77
128.86
125.24
27.76
23.58
iPr
O
O
S
O
Cl
iPr
1c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.81
8.81
8.78
8.78
8.39
8.38
8.36
8.36
8.02
8.00
7.84
7.83
7.82
7.81
7.80
7.79
7.78
7.72
7.72
7.70
7.70
7.69
7.67
7.67
7.63
7.60
7.57


O
O
S
Cl

3c

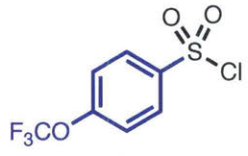

1.00
1.00
1.05
1.05
1.04
1.05
1.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


O
O
S
Cl

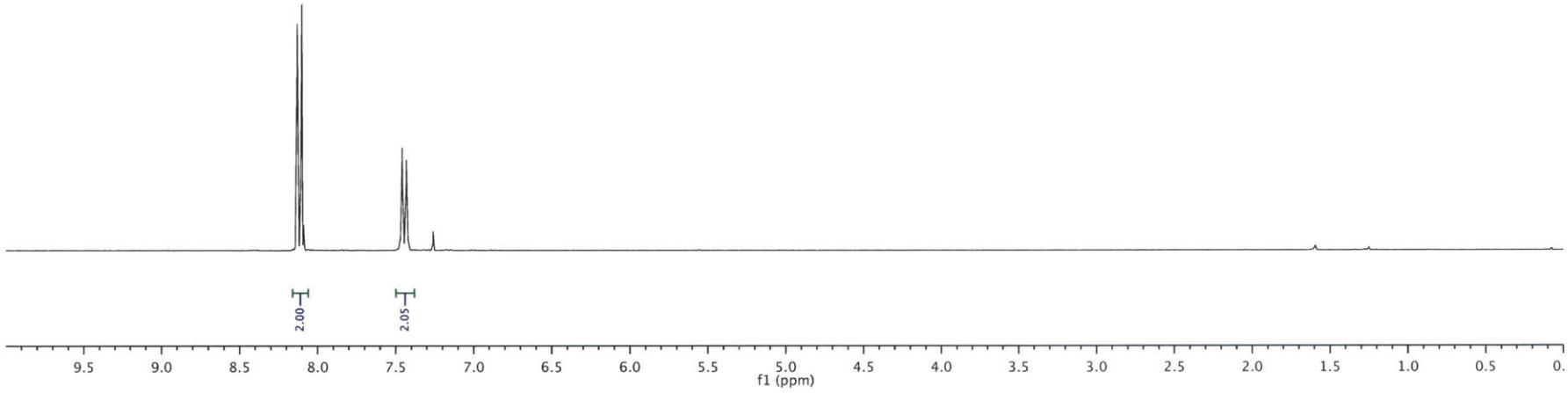
3c

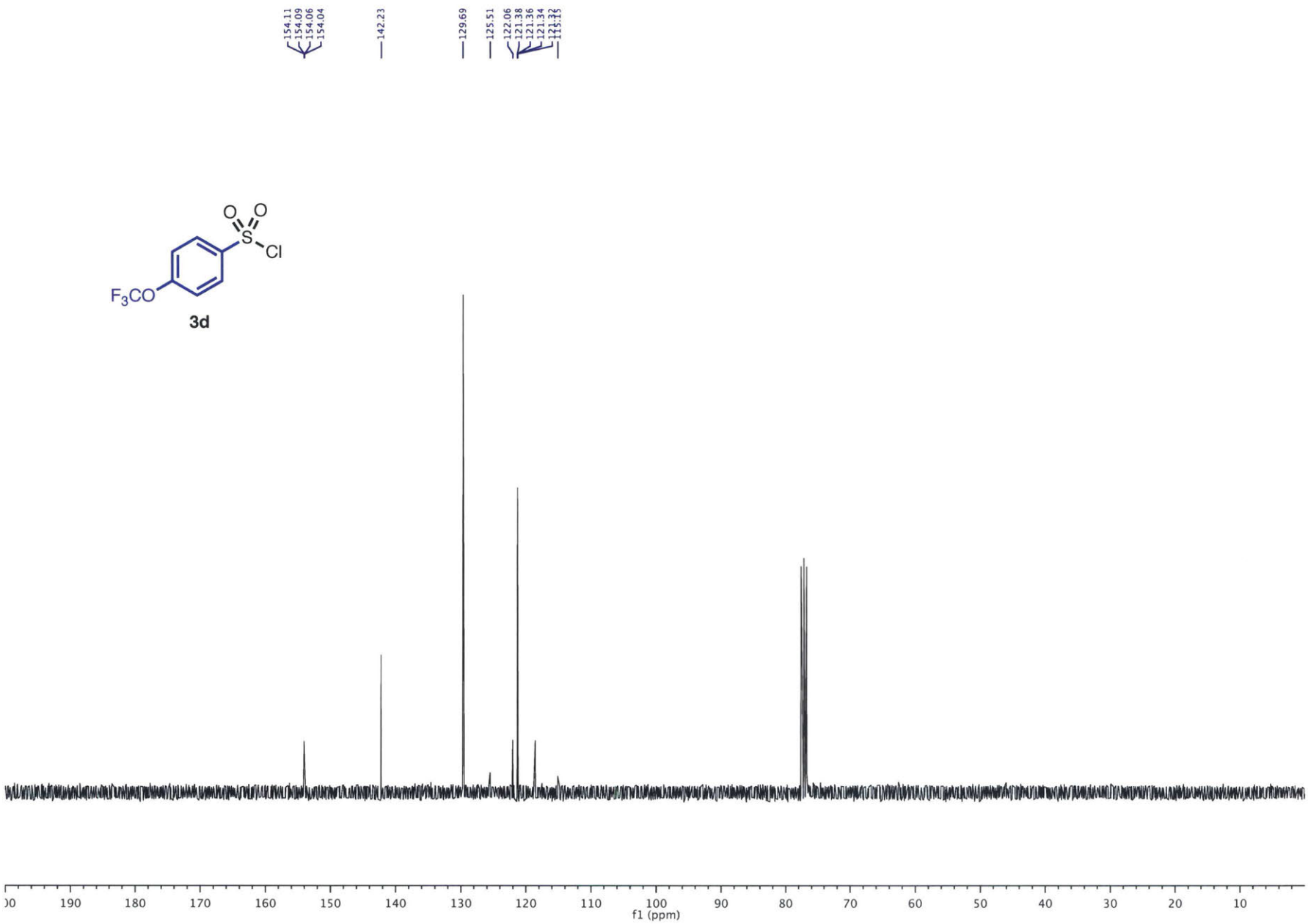
139.27
136.96
134.26
129.38
129.26
129.17
127.63
127.20
123.91
123.79
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

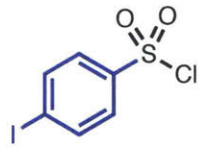

8.14
8.13
8.12
8.11
8.10
8.09
7.46
7.43


O
O
S
Cl
F3CO

3d

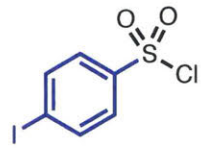

2.00
2.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


154.11
154.09
154.06
154.04
142.23
129.69
125.51
122.06
121.38
121.36
121.34
O
O
S
Cl
F3CO
3d
f1 (ppm)


O
O
S
Cl
I

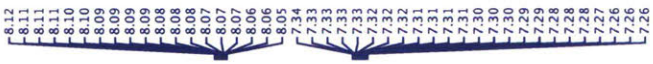
3e

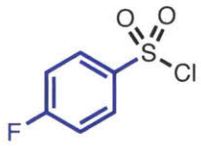
8.01
7.98
7.76
7.73
2.00
1.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


O
O
S
Cl
I

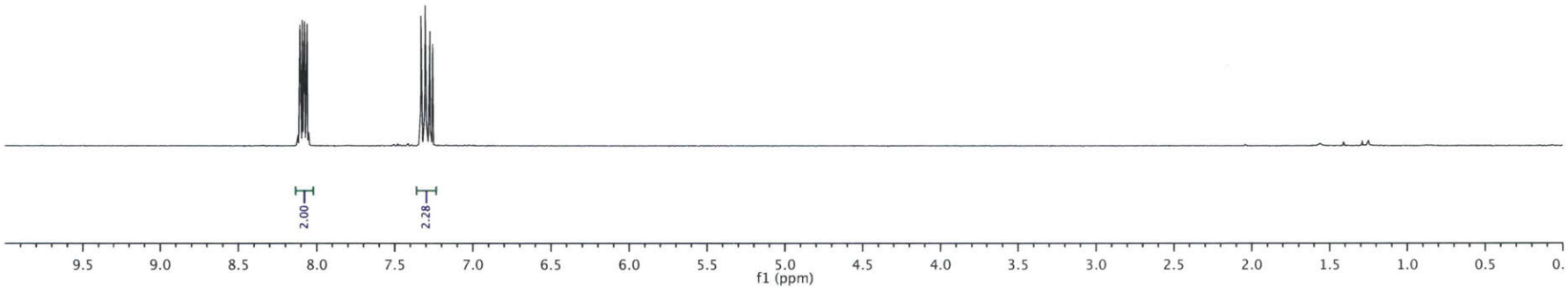
3e

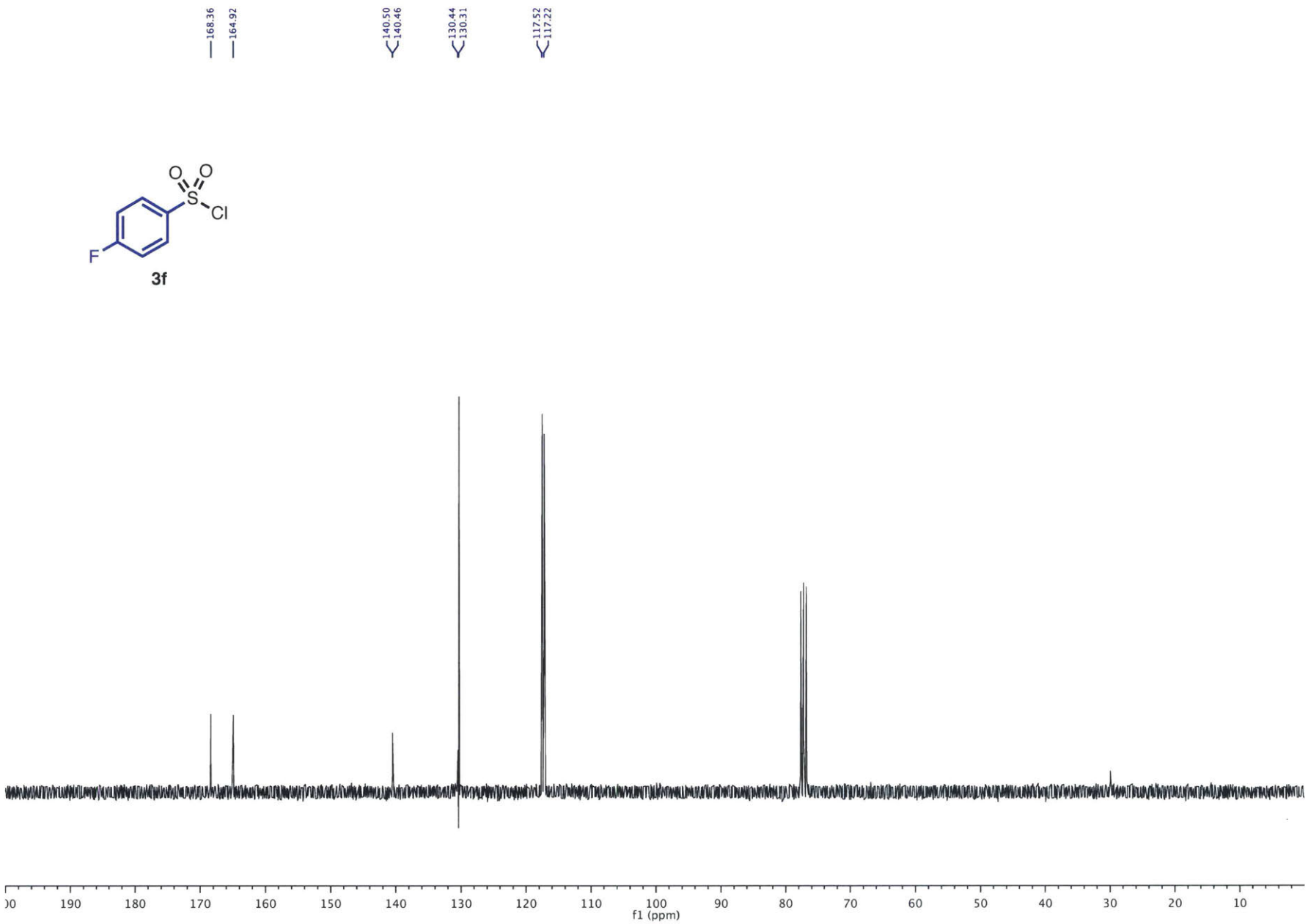
144.03
139.26
128.32
104.00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

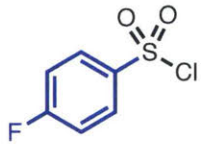

8.12
8.11
8.11
8.11
8.10
8.10
8.09
8.09
8.09
8.09
8.08
8.08
8.08
8.08
8.07
8.07
8.07
8.06
8.06
8.05
7.34
7.33
7.33
7.33
7.33
7.32
7.32
7.32
7.31
7.31
7.31
7.31
7.30
7.30
7.30
7.29
7.29
7.28
7.28
7.28
7.27
7.26
7.26
7.26


O
O
S
Cl
F

3f


2.00
2.28
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.
f1 (ppm)


168.36
164.92
140.50
140.46
130.44
130.31
117.52
117.22
O
O
S
Cl
F
3f
f1 (ppm)


O
O
S
Cl
F

3f

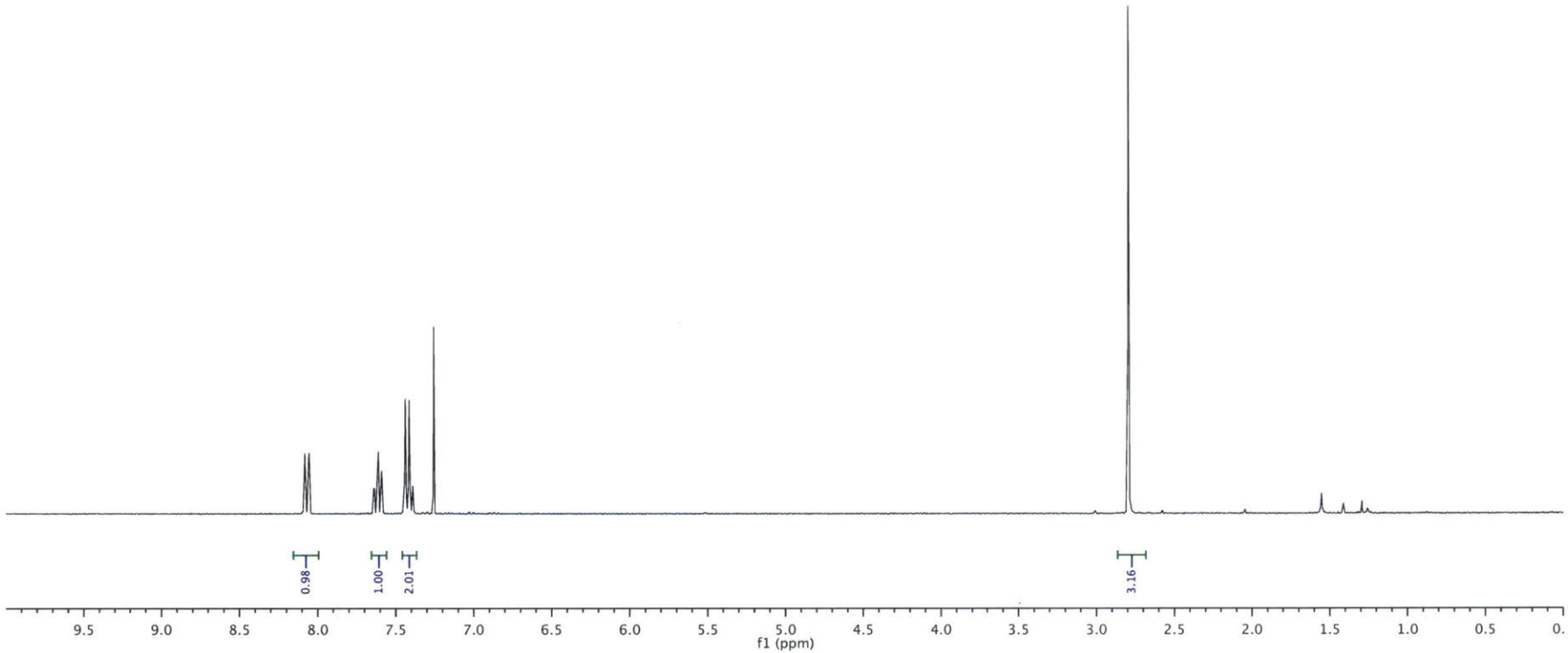
63.76
-99.61
-5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145
f1 (ppm)


8.09
8.08
8.06
8.06
7.64
7.64
7.62
7.62
7.61
7.61
7.61
7.61
7.59
7.59
7.44
7.44
7.44
7.44
7.44
7.43
7.43
7.42
7.42
7.42
7.41
7.41
7.41
7.39
7.39
7.39
7.39

2.79


Me
O
O
S
Cl

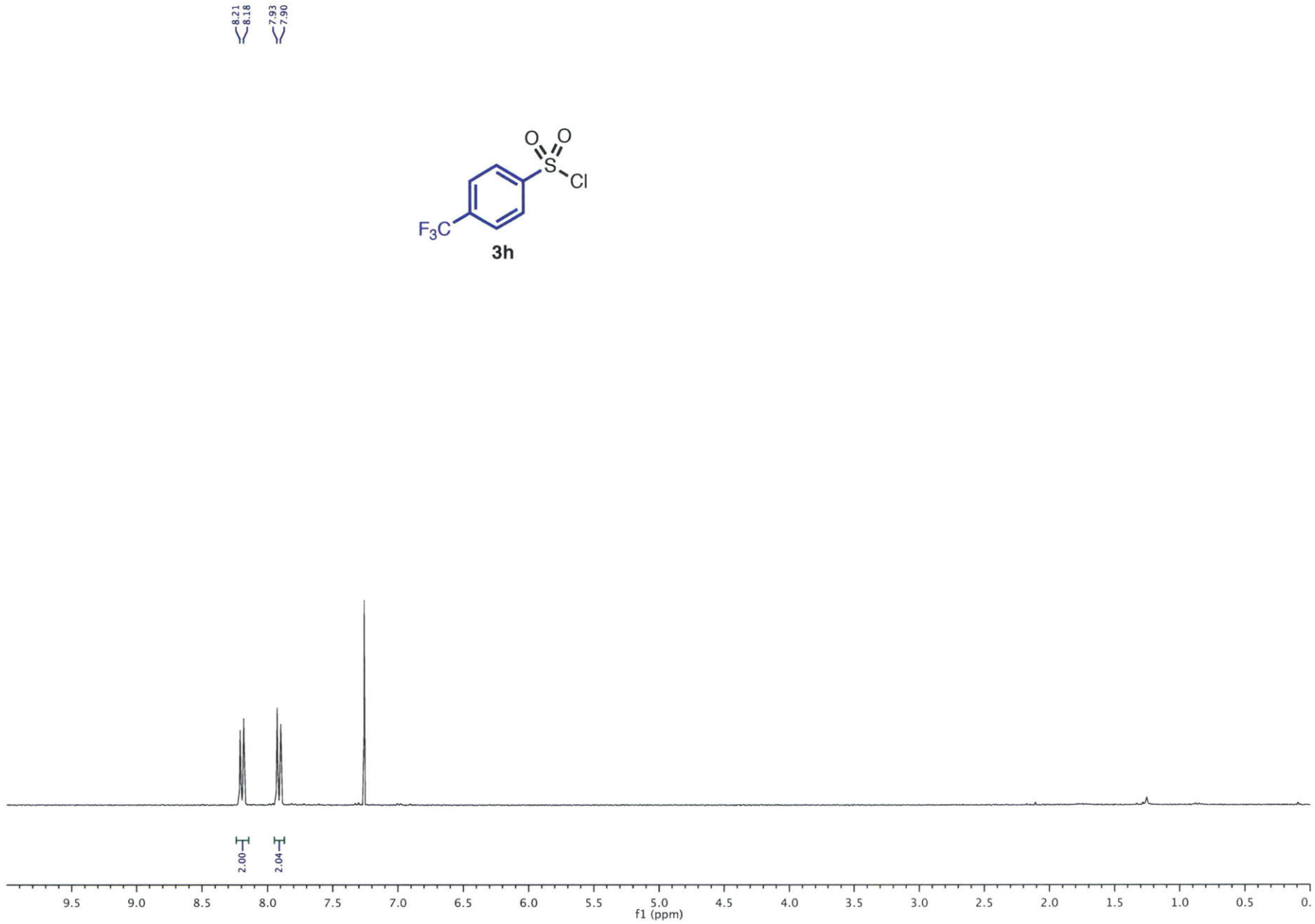
3g

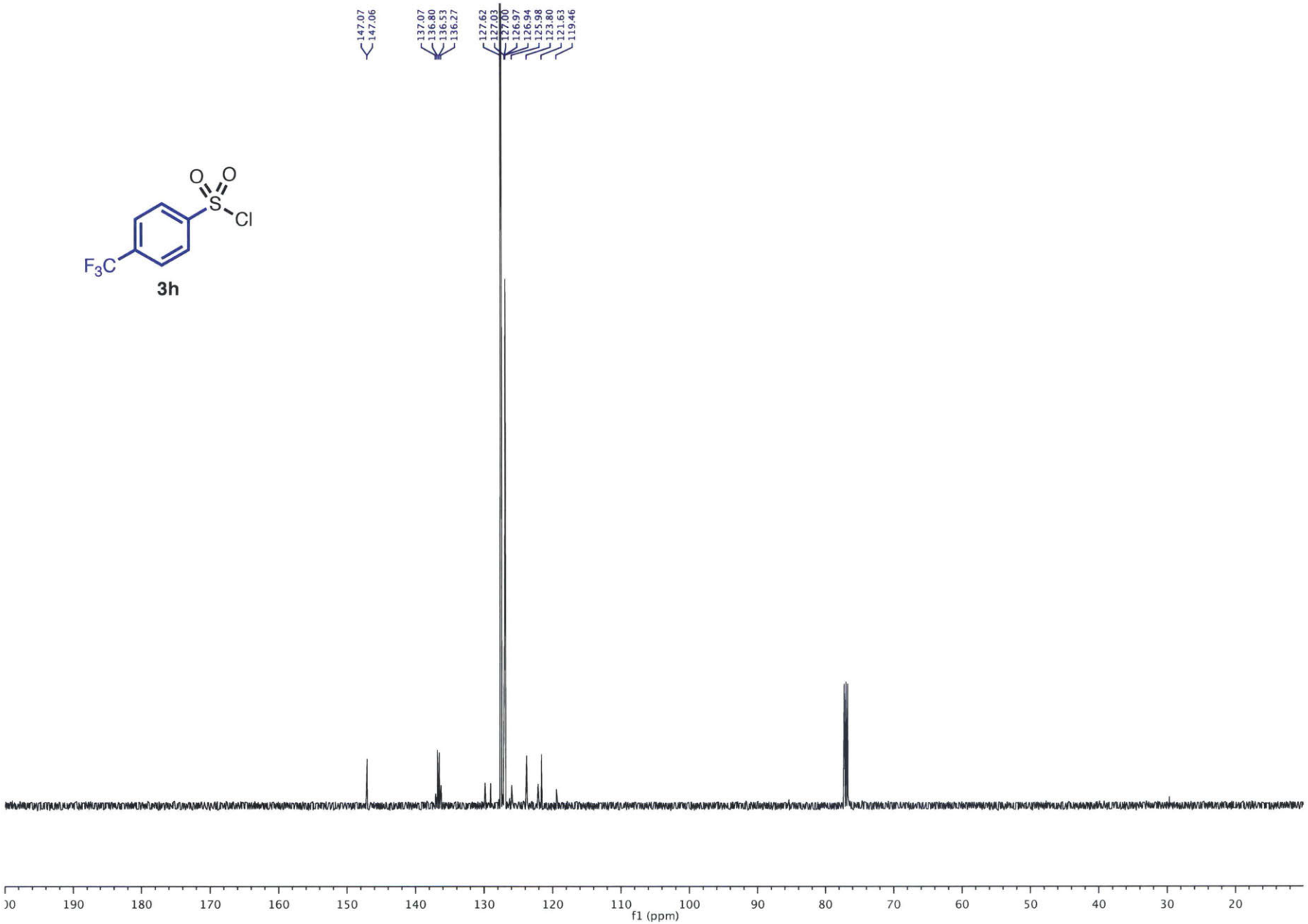

0.98
1.00
2.01
3.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


Me
O
O
S
Cl

3g

143.15
138.34
135.52
133.63
128.95
127.02
20.54
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

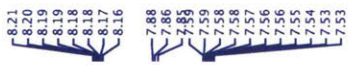

8.21
8.18
7.93
7.90
O
O
S
Cl
F3C
3h
2.00
2.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


147.07
147.06
137.07
136.80
136.53
136.27
127.62
127.03
127.00
126.97
126.94
125.98
123.80
121.63
119.46
O
O
S
Cl
F3C
3h
f1 (ppm)


O
O
S
Cl
F3C

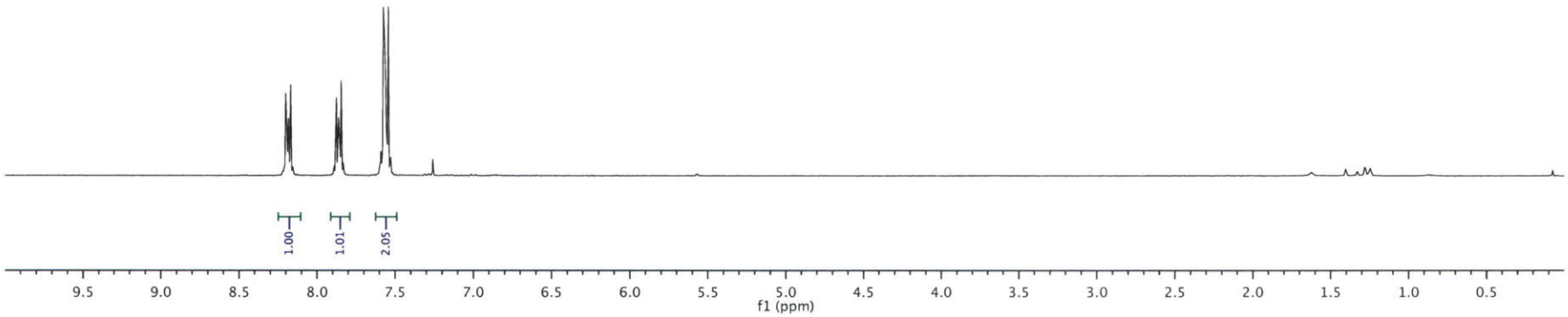
3h

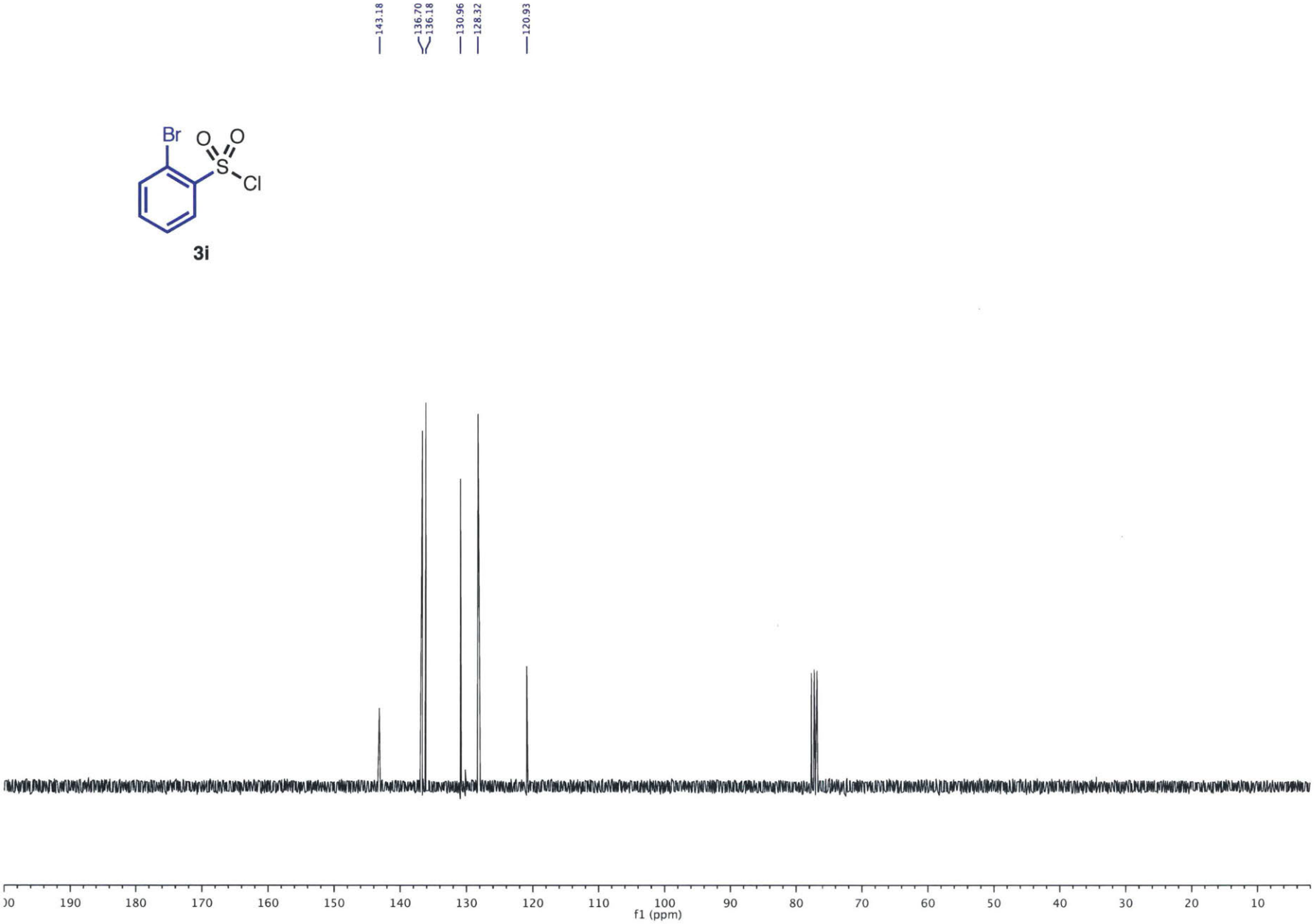
-63.48
-63.70 CF3Ph
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

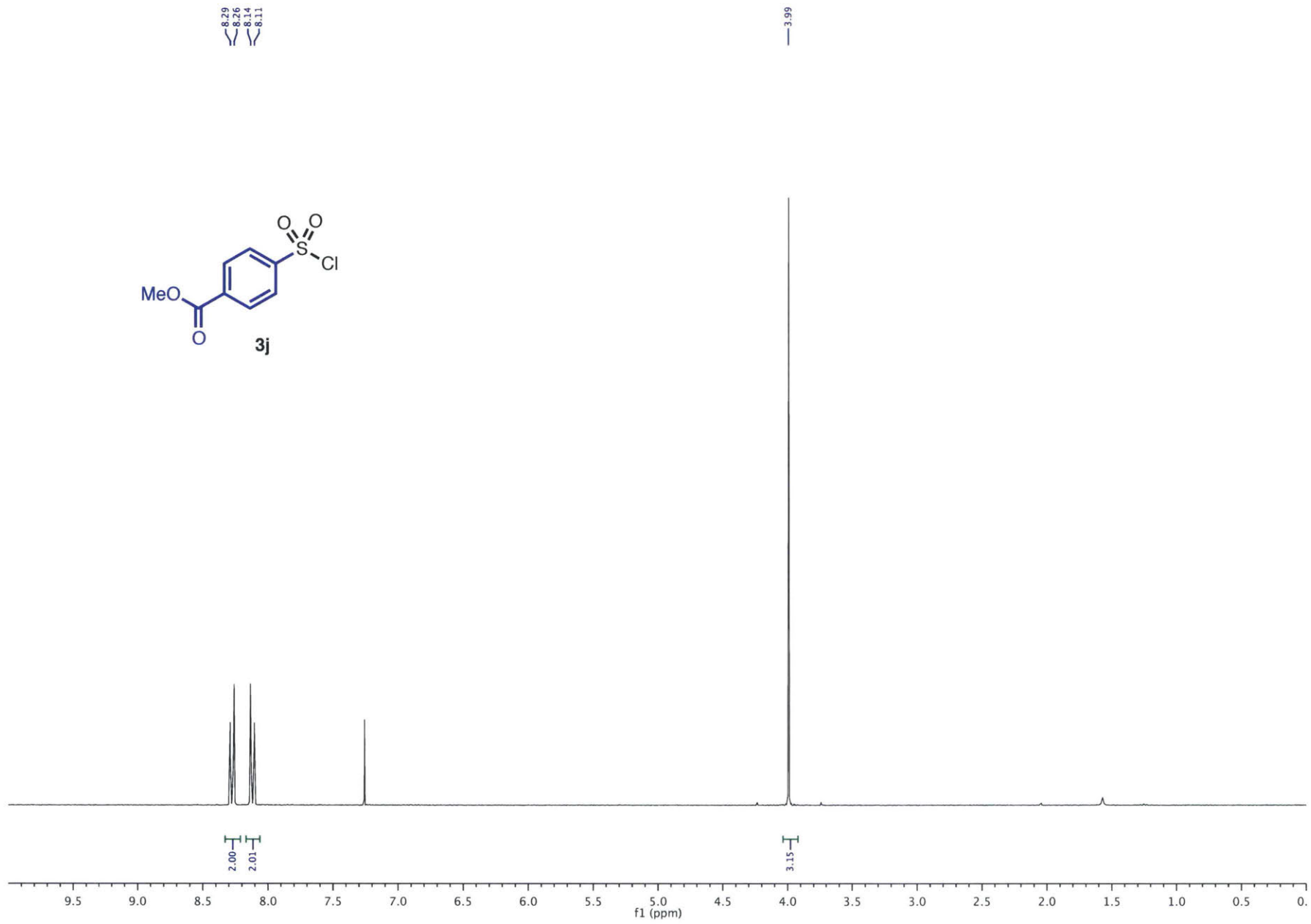

8.21
8.20
8.19
8.19
8.18
8.18
8.17
8.16
7.88
7.86
7.59
7.59
7.58
7.58
7.57
7.56
7.56
7.55
7.54
7.53
7.53

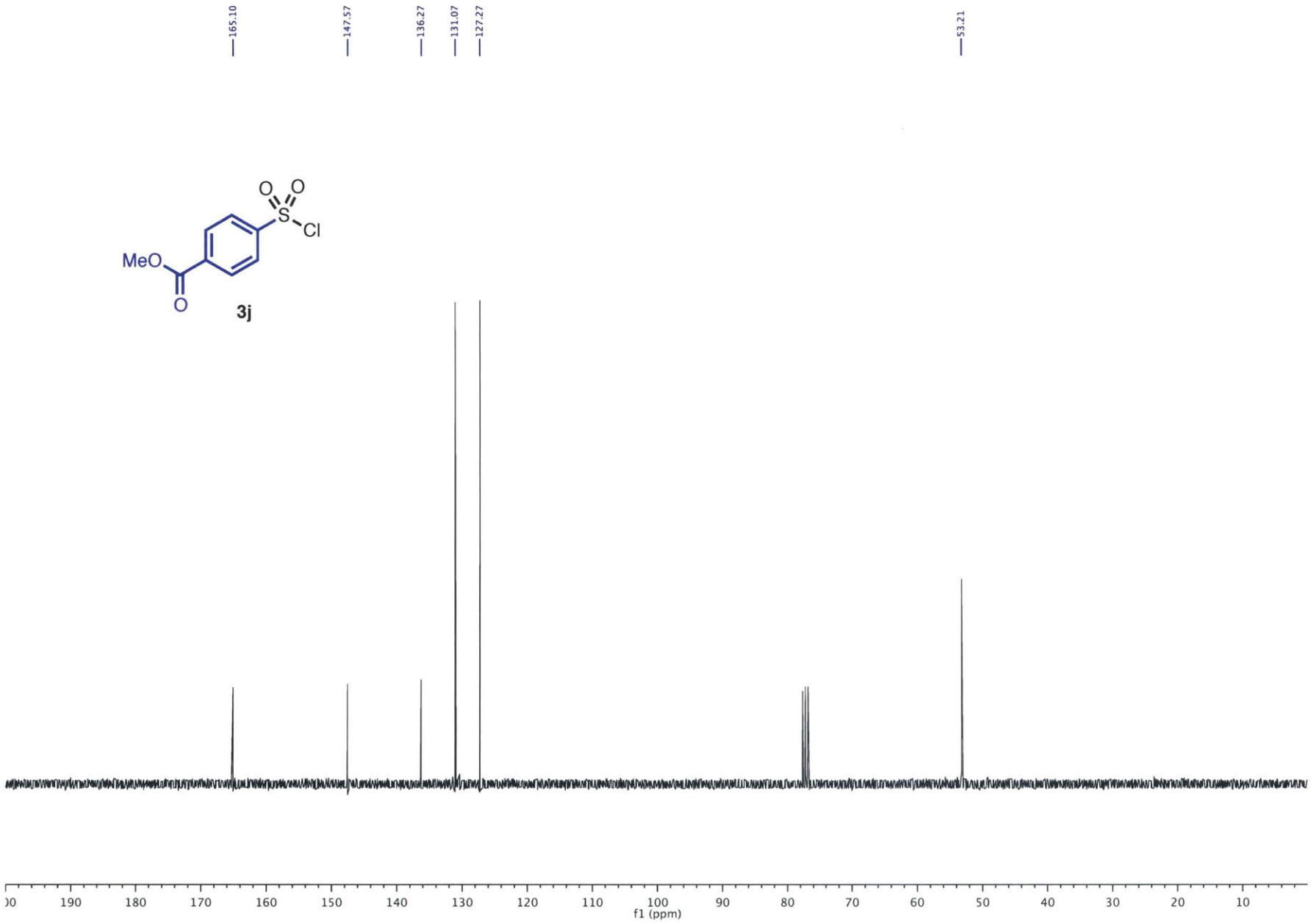

Br
O
O
S
Cl

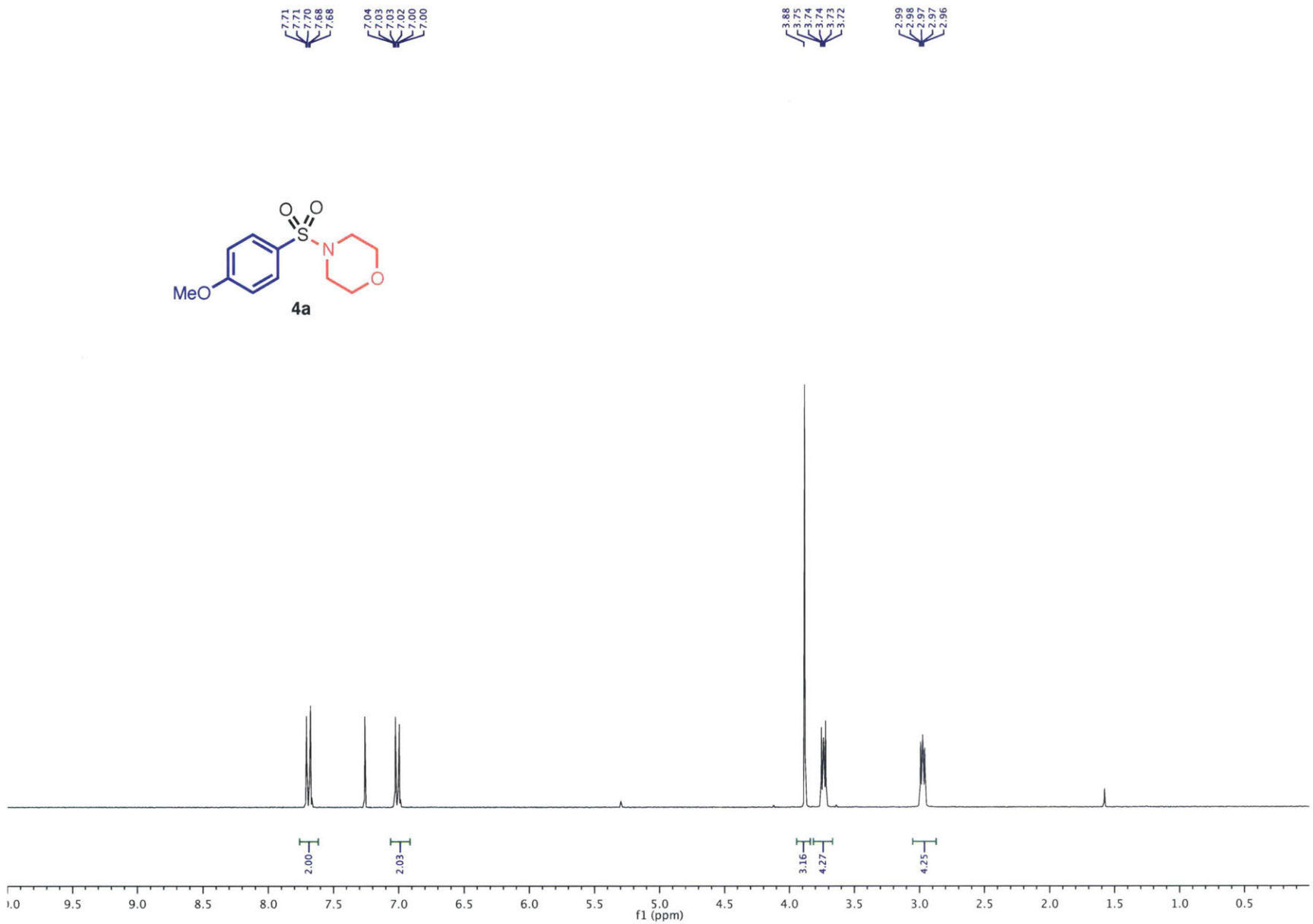
3i

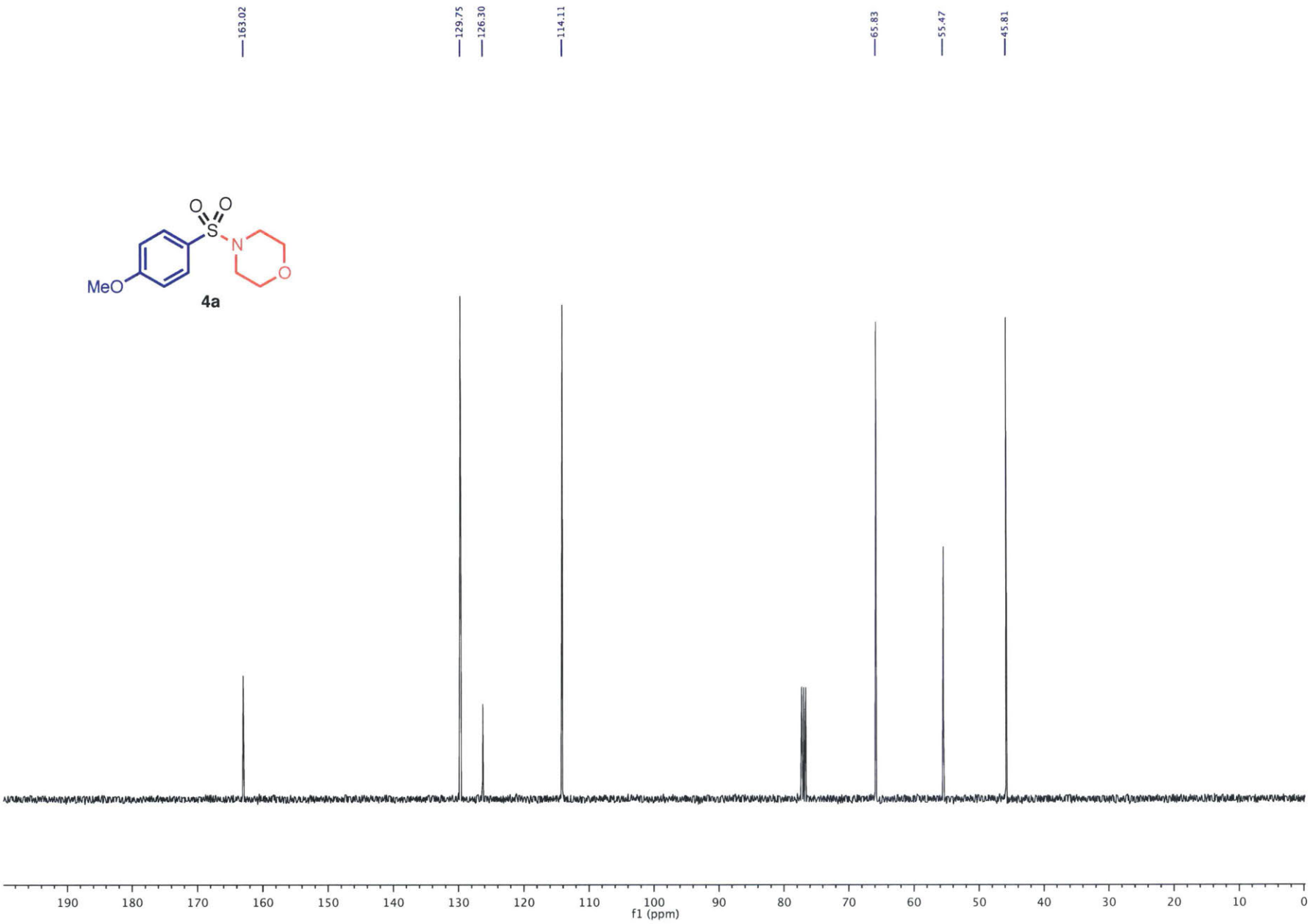

1.00
1.01
2.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

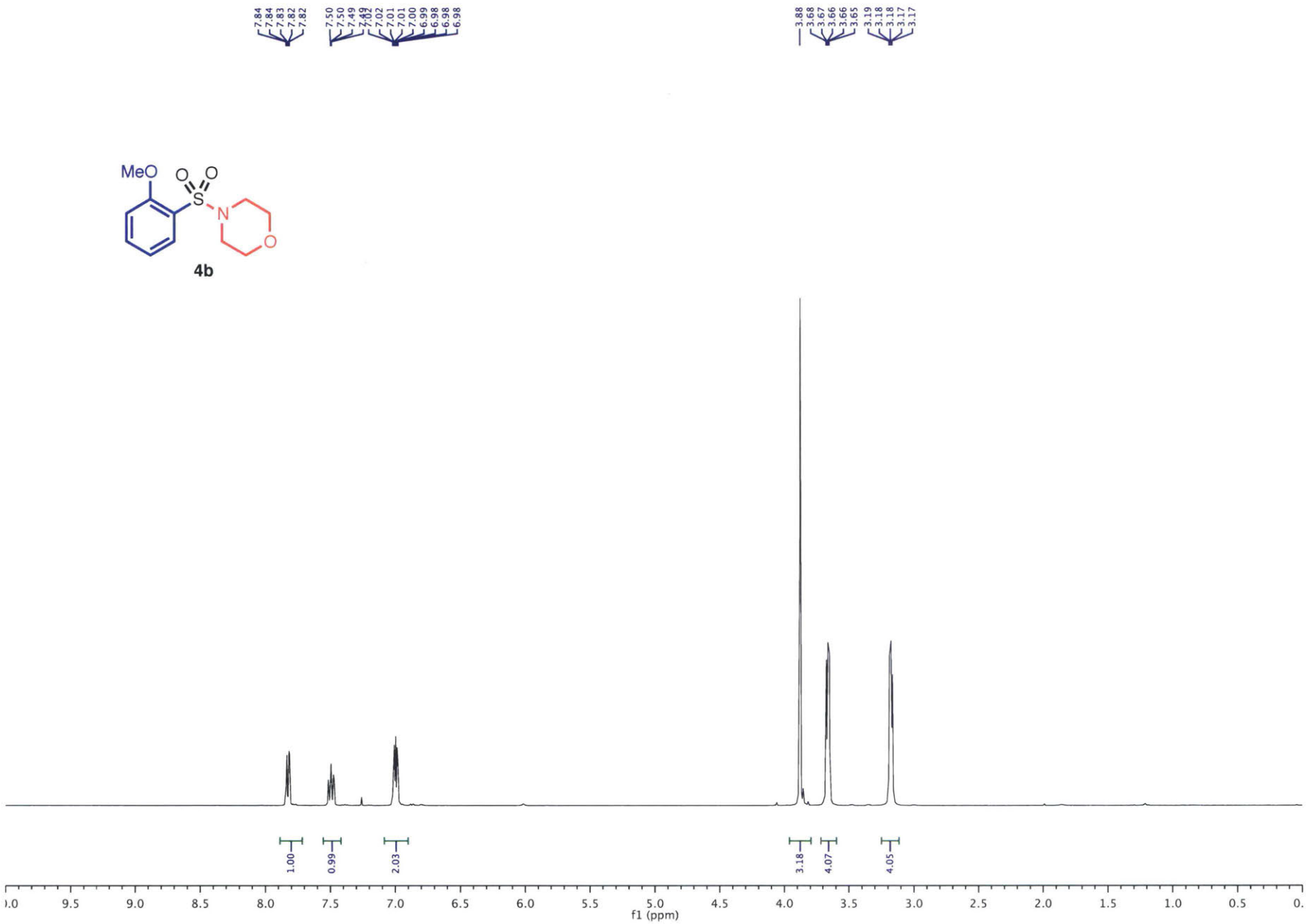

143.18
136.70
136.18
130.96
128.32
120.93
Br
O
O
S
Cl
3i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

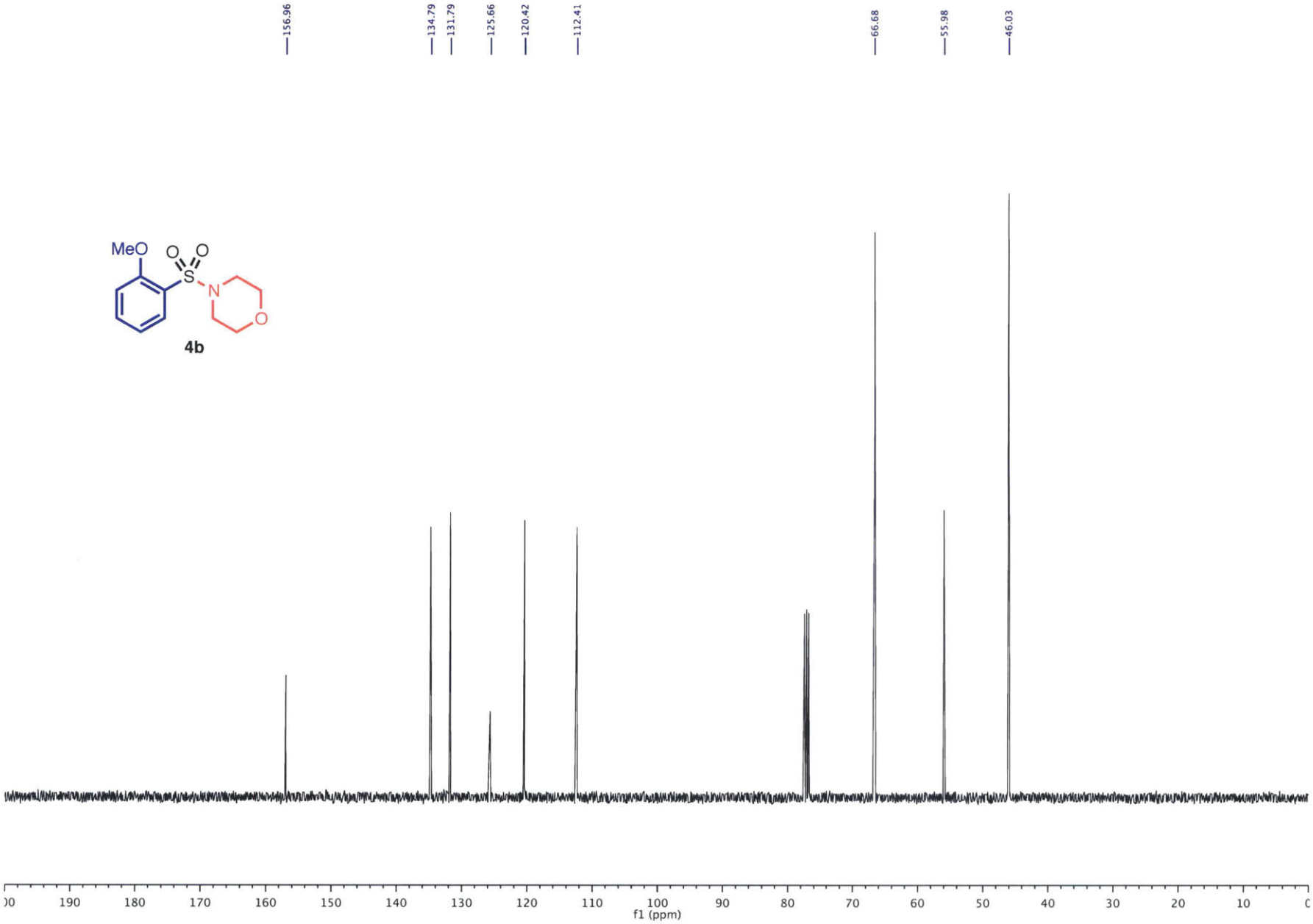

8.29
8.26
8.14
8.11
3.99
MeO
O
O
S
Cl
O
3j
2.00
2.01
3.15
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


165.10
147.57
136.27
131.07
127.27
53.21
MeO
O
O
S
O
Cl
3j
f1 (ppm)


7.71
7.71
7.70
7.68
7.68
7.04
7.03
7.03
7.02
7.00
7.00
3.88
3.75
3.74
3.74
3.73
3.72
2.99
2.98
2.97
2.97
2.96
O
O
S
N
O
MeO
4a
2.00
2.03
3.16
4.27
4.25
f1 (ppm)


163.02
129.75
126.30
114.11
65.83
55.47
45.81
MeO
4a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.84
7.84
7.83
7.82
7.82
7.50
7.50
7.49
7.49
7.02
7.01
7.01
7.00
6.99
6.98
6.98
6.98
3.88
3.68
3.67
3.66
3.66
3.65
3.19
3.18
3.18
3.17
3.17
MeO
O
O
S
N
O
4b
1.00
0.99
2.03
3.18
4.07
4.05
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
f1 (ppm)

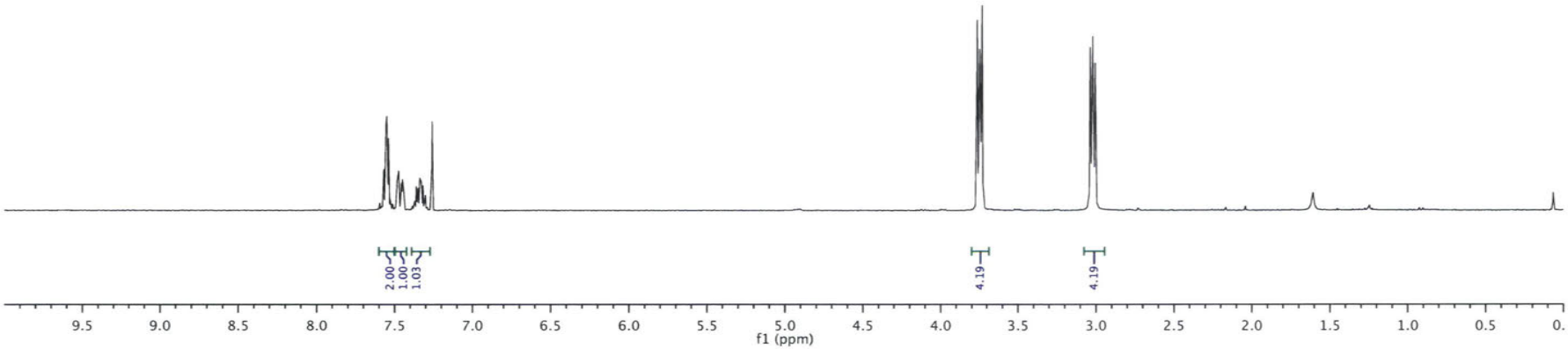

156.96
134.79
131.79
125.66
120.42
112.41
66.68
55.98
46.03
MeO
O
O
S
N
O
4b
f1 (ppm)

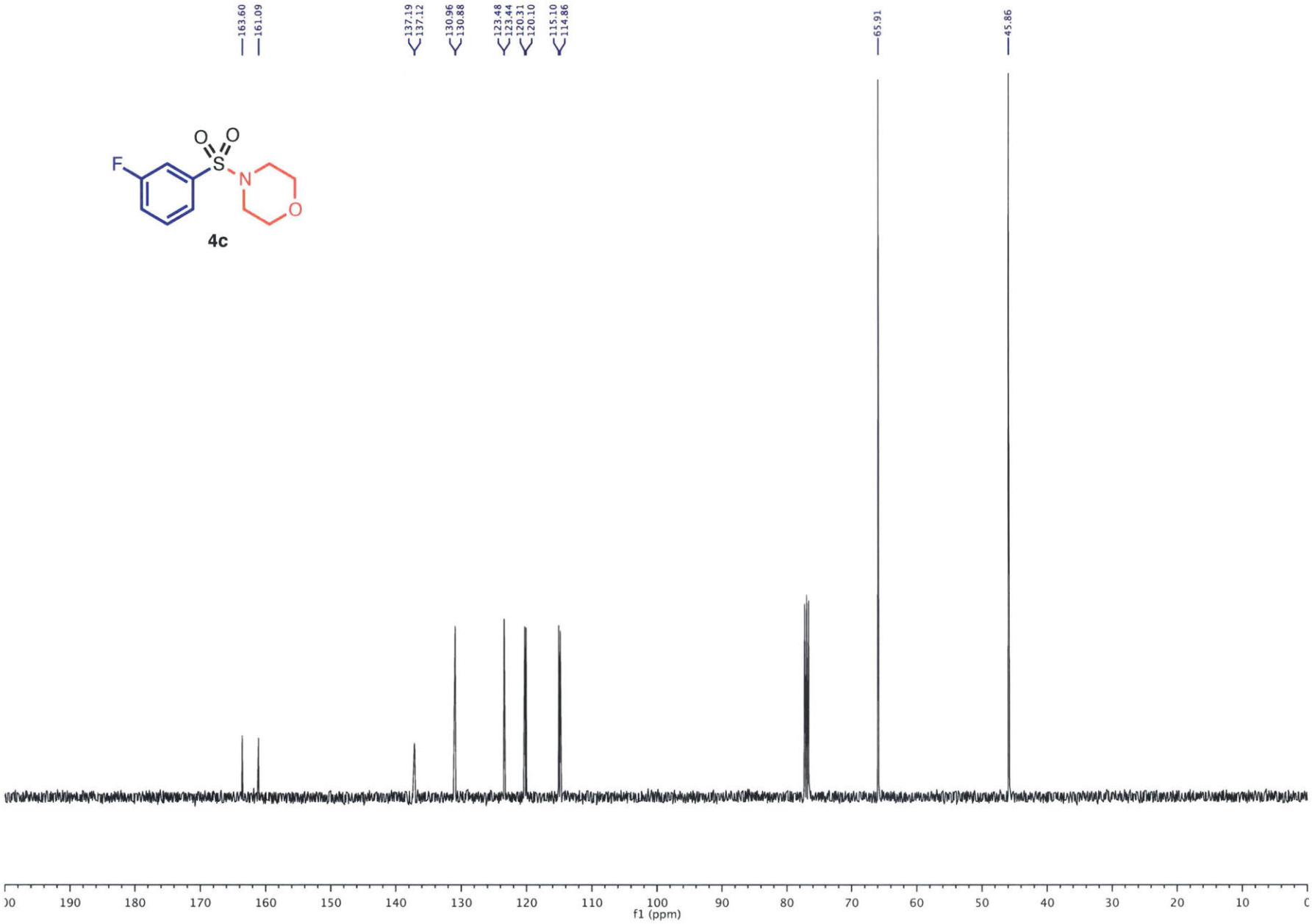

7.57
7.57
7.56
7.56
7.56
7.55
7.55
7.55
7.54
7.54
7.54
7.49
7.48
7.48
7.48
7.47
7.47
7.46
7.46
7.45
7.45
7.45
7.45
7.44
7.37
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.30


3.77
3.76
3.75
3.74
3.73
3.04
3.03
3.02
3.01
3.00


O
O
S
F
N
O

4c

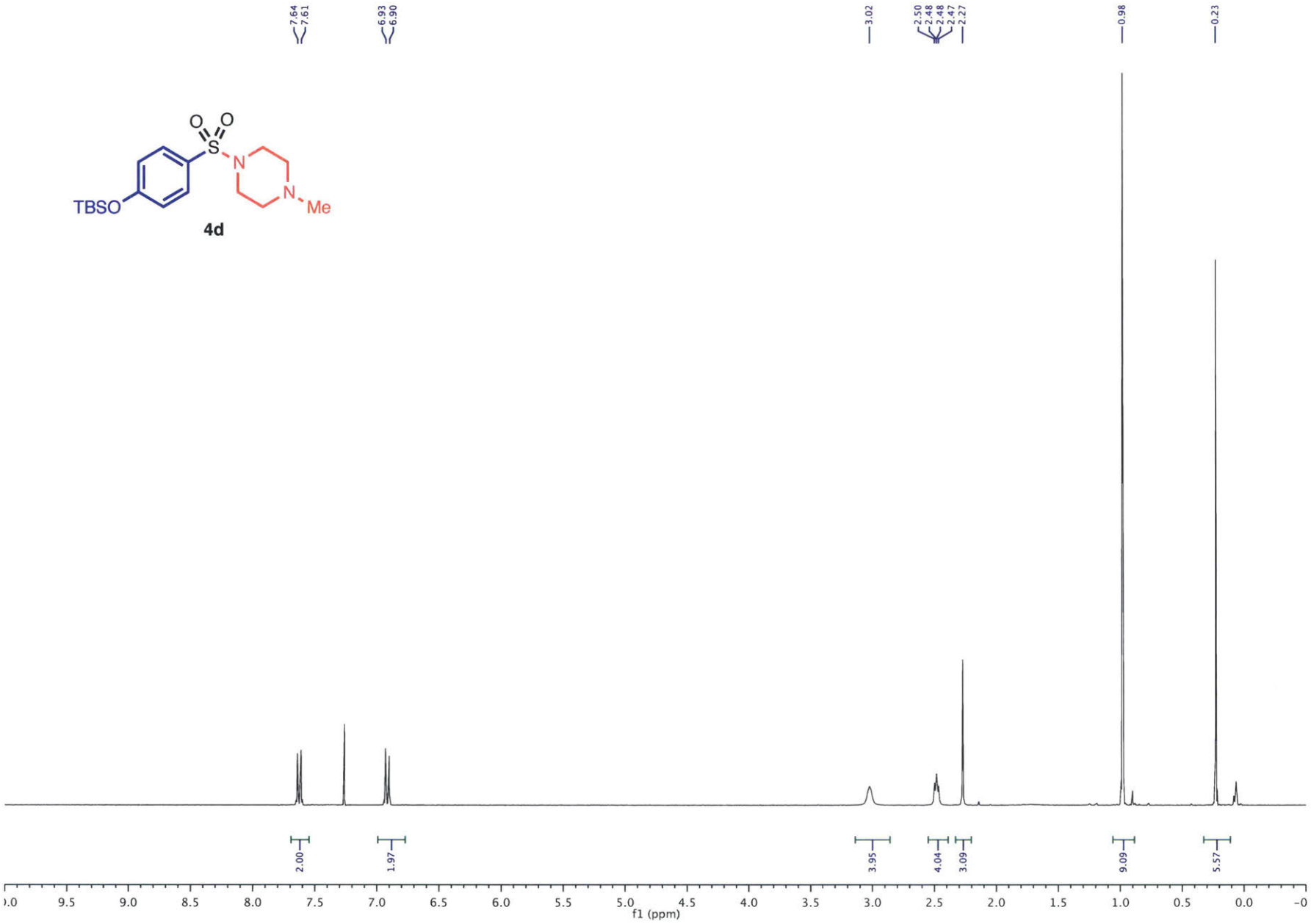

2.00
1.00
1.03
4.19
4.19
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

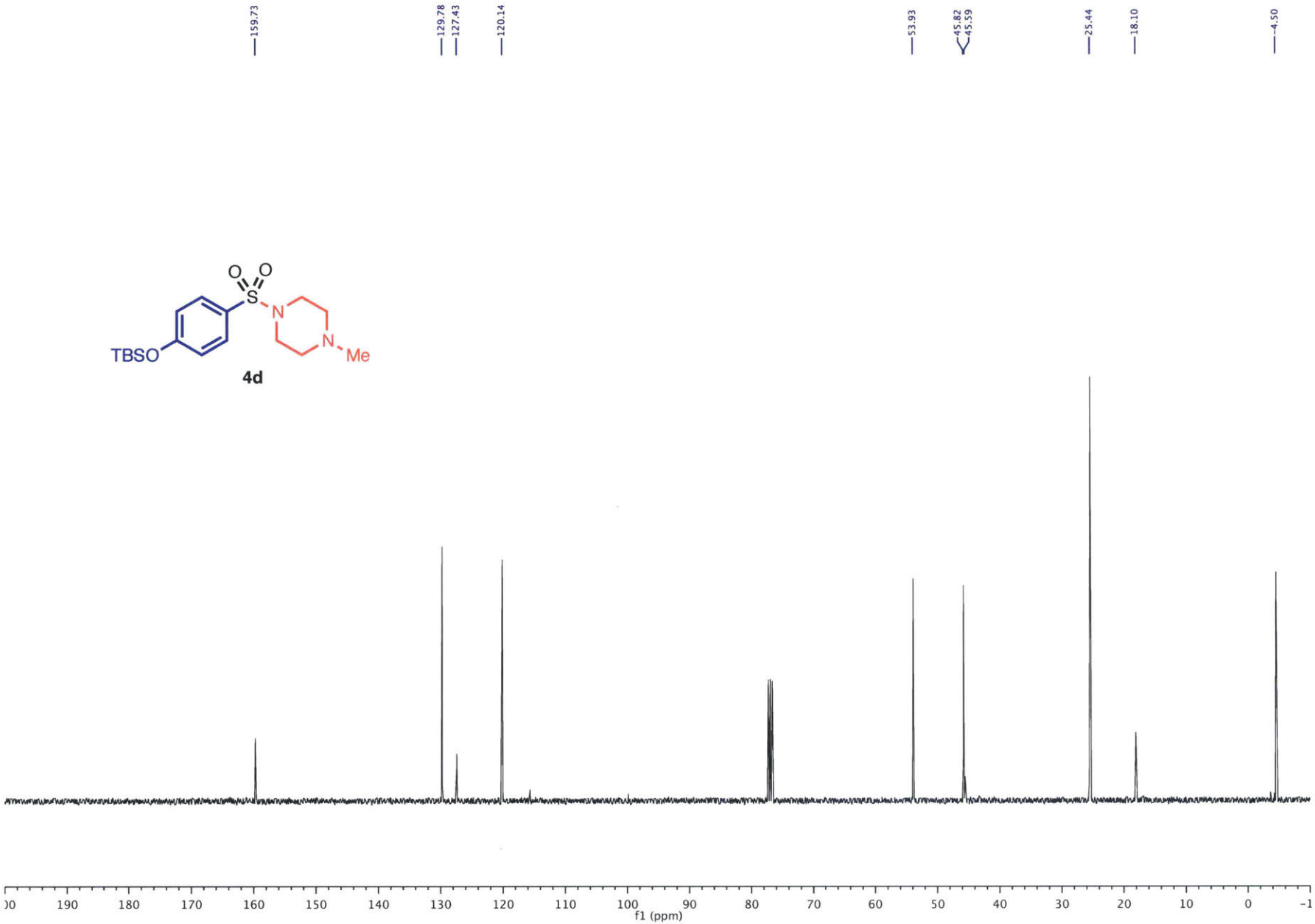

163.60
161.09
137.19
137.12
130.96
130.88
123.48
123.44
120.31
120.10
115.10
114.86
65.91
45.86
F
S
O
O
N
O
4c
f1 (ppm)

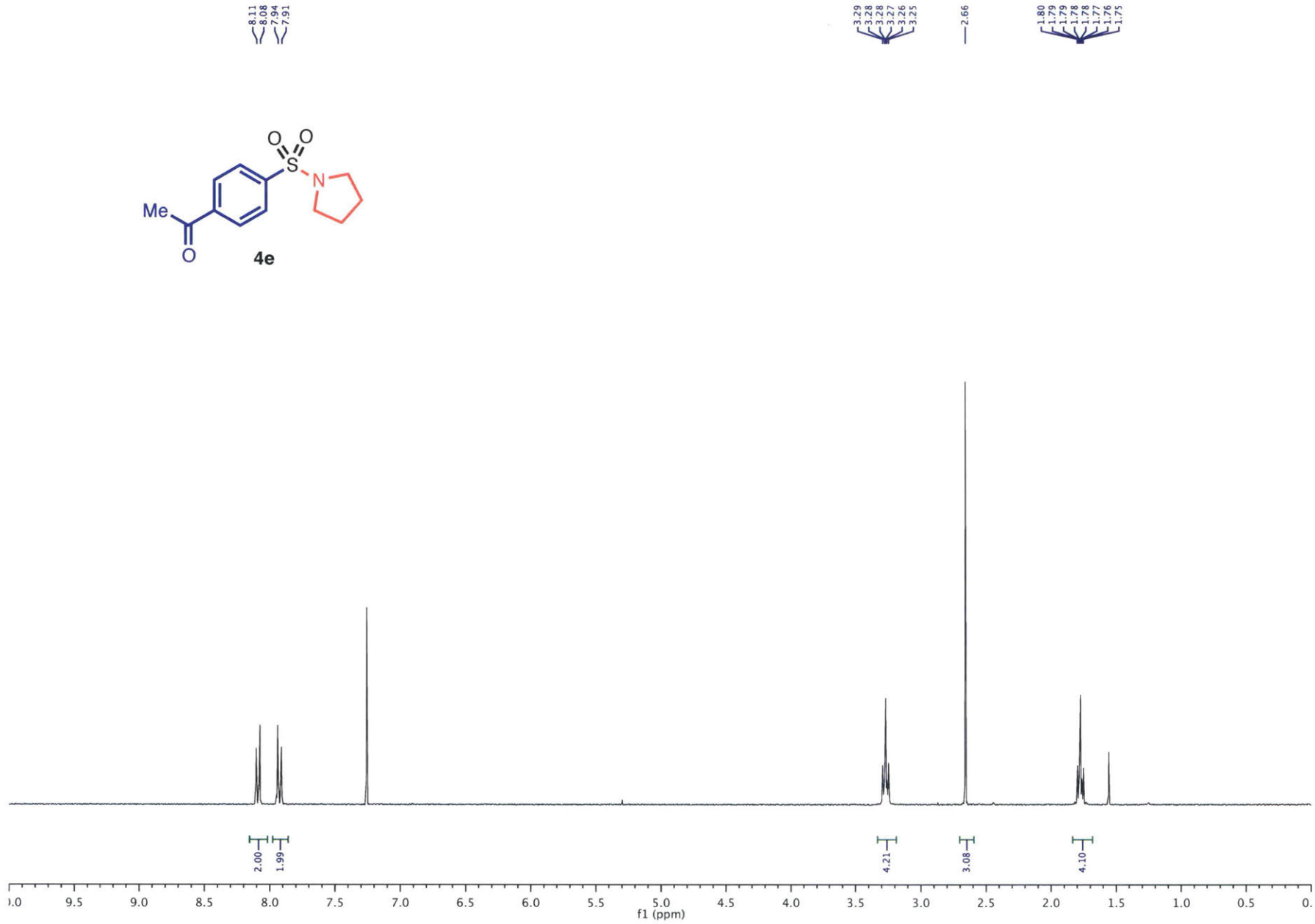

O
O
S
F
N
O

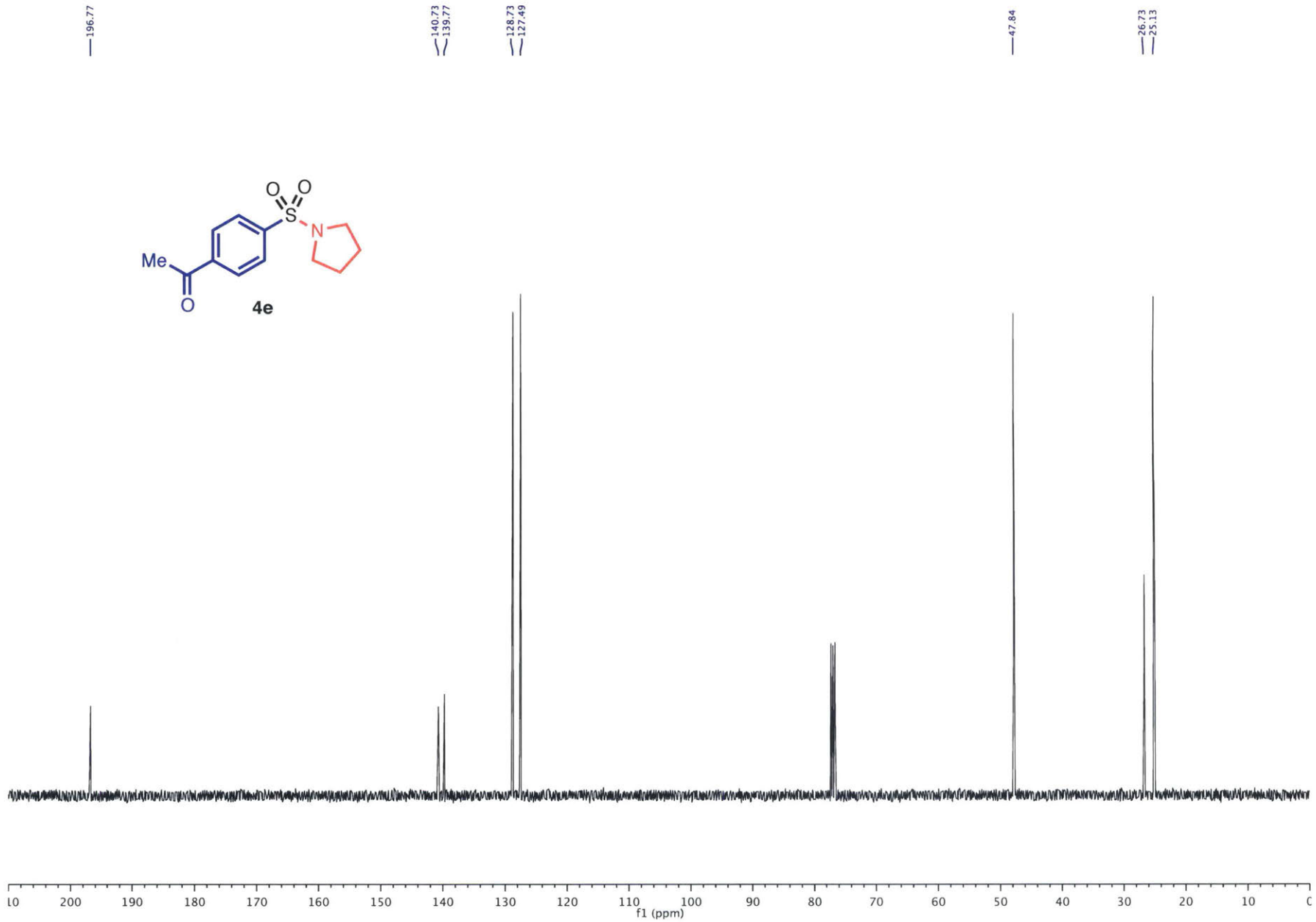
4c

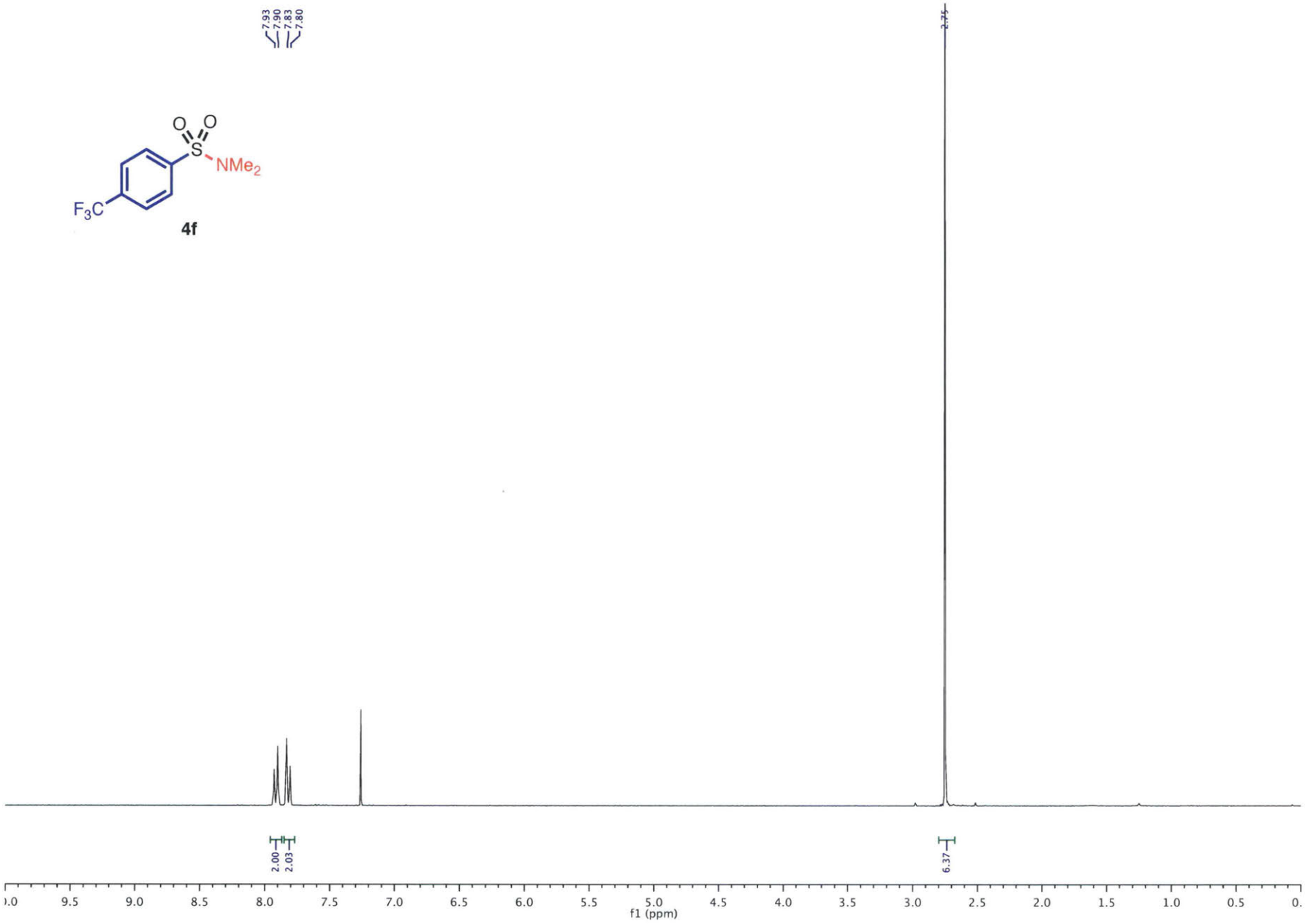
63.70 CF3Ph
-109.39
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

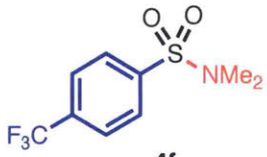

7.64
7.61
6.93
6.90
3.02
2.50
2.48
2.48
2.47
2.27
0.98
0.23
TBSO
N
N
Me
4d
2.00
1.97
3.95
4.04
3.09
9.09
5.57
f1 (ppm)


159.73
129.78
127.43
120.14
53.93
45.82
45.59
25.44
18.10
-4.50
TBSO
N
N
Me
O
O
S
4d
f1 (ppm)


8.11
8.08
7.94
7.91
3.29
3.28
3.28
3.27
3.26
3.25
2.66
1.80
1.79
1.79
1.78
1.78
1.77
1.76
1.75
Me
O
O
S
N
O
4e
2.00
1.99
4.21
3.08
4.10
f1 (ppm)

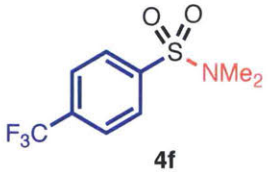

196.77
140.73
139.77
128.73
127.49
47.84
26.73
25.13
Me
O
O
O
S
N
4e
f1 (ppm)


7.93
7.90
7.83
7.80
O
O
S
NMe2
F3C
4f
2.00
2.03
6.37
f1 (ppm)


O
O
S
NMe2
F3C

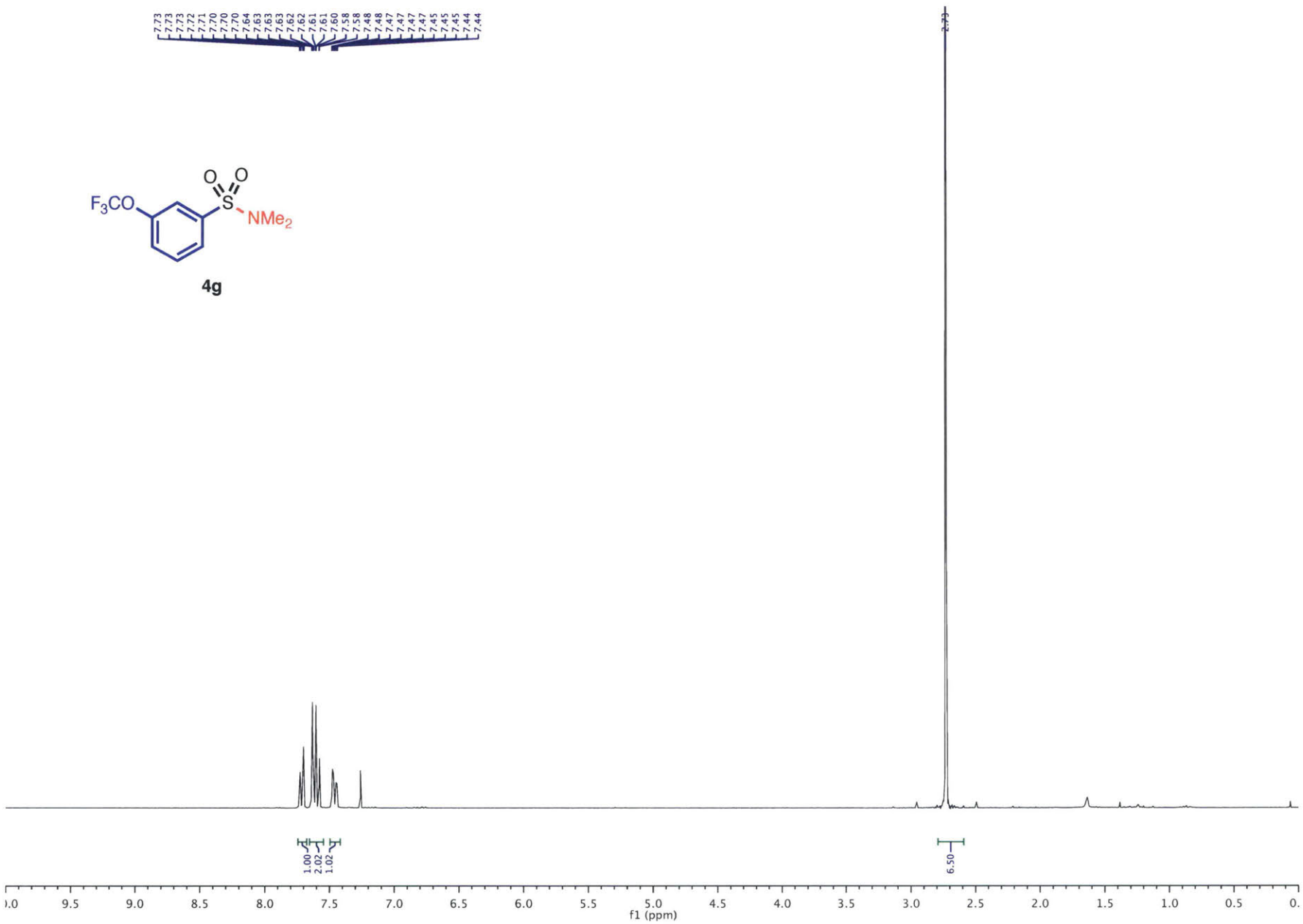
4f

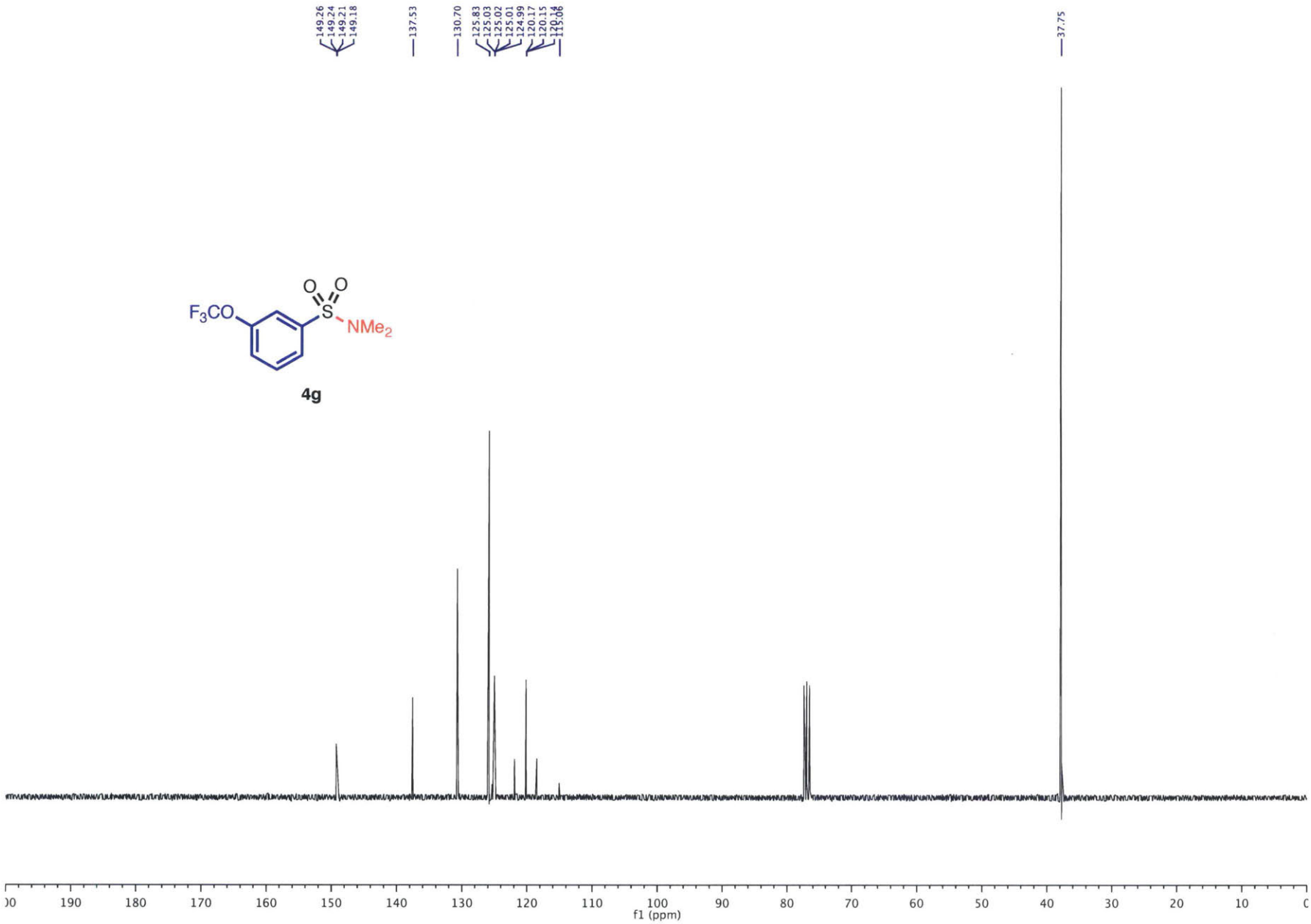
139.37
134.83
134.50
134.17
133.84
128.14
127.32
126.25
126.21
126.17
126.14
124.61
121.90
119.18
37.78
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O
O
S
NMe2
F3C

4f

-63.21
-63.70 CF3Ph
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

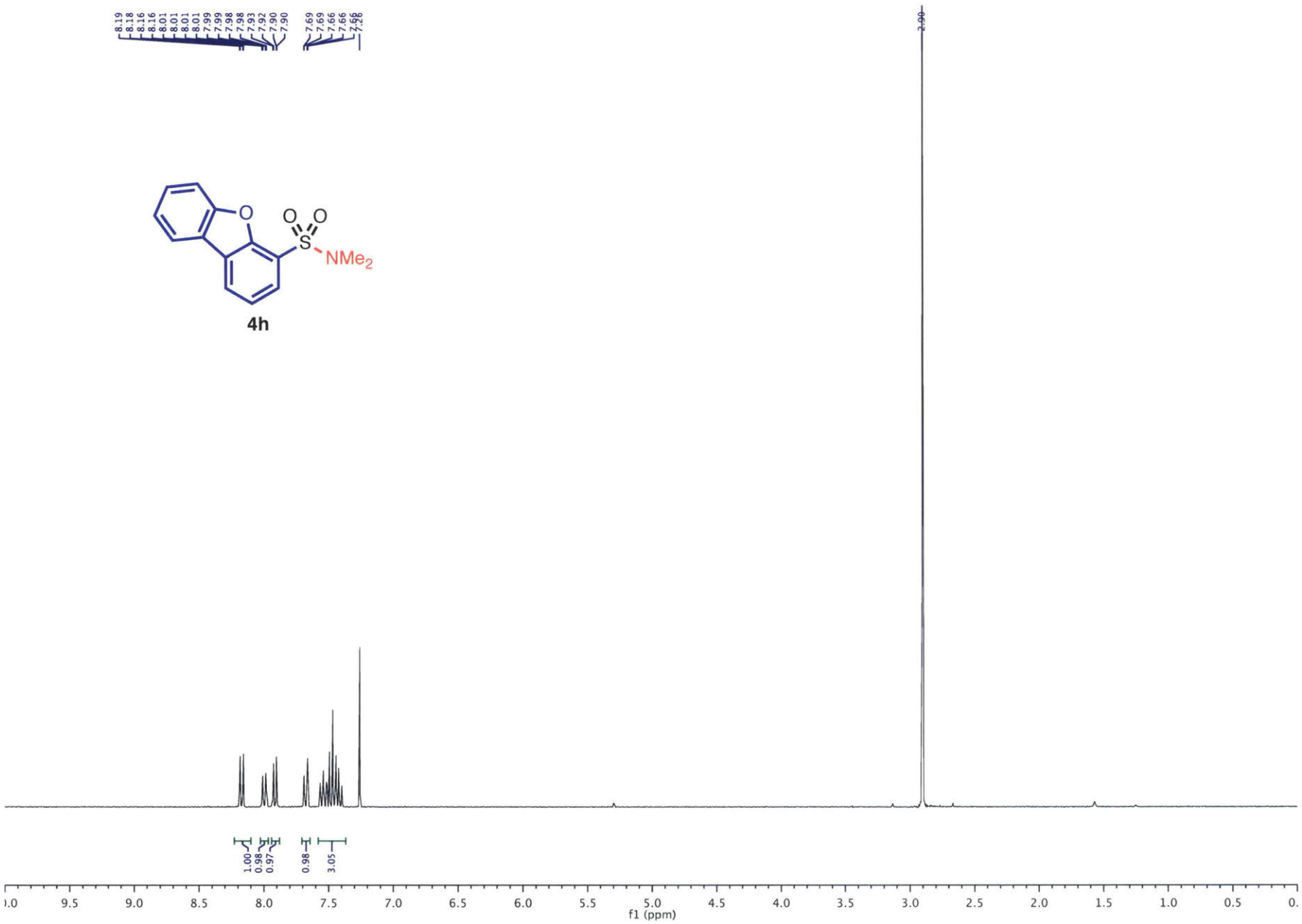

7.73
7.73
7.73
7.72
7.71
7.70
7.70
7.70
7.64
7.63
7.63
7.63
7.62
7.62
7.61
7.61
7.60
7.58
7.48
7.48
7.47
7.47
7.47
7.47
7.45
7.45
7.45
7.44
7.44
2.73
O
O
S
F3CO
NMe2
4g
1.00
2.02
1.02
6.50
f1 (ppm)


149.26
149.24
149.21
149.18
137.53
130.70
125.83
125.03
125.02
125.01
124.99
120.17
120.15
37.75
O
O
S
F3CO
NMe2
4g
f1 (ppm)

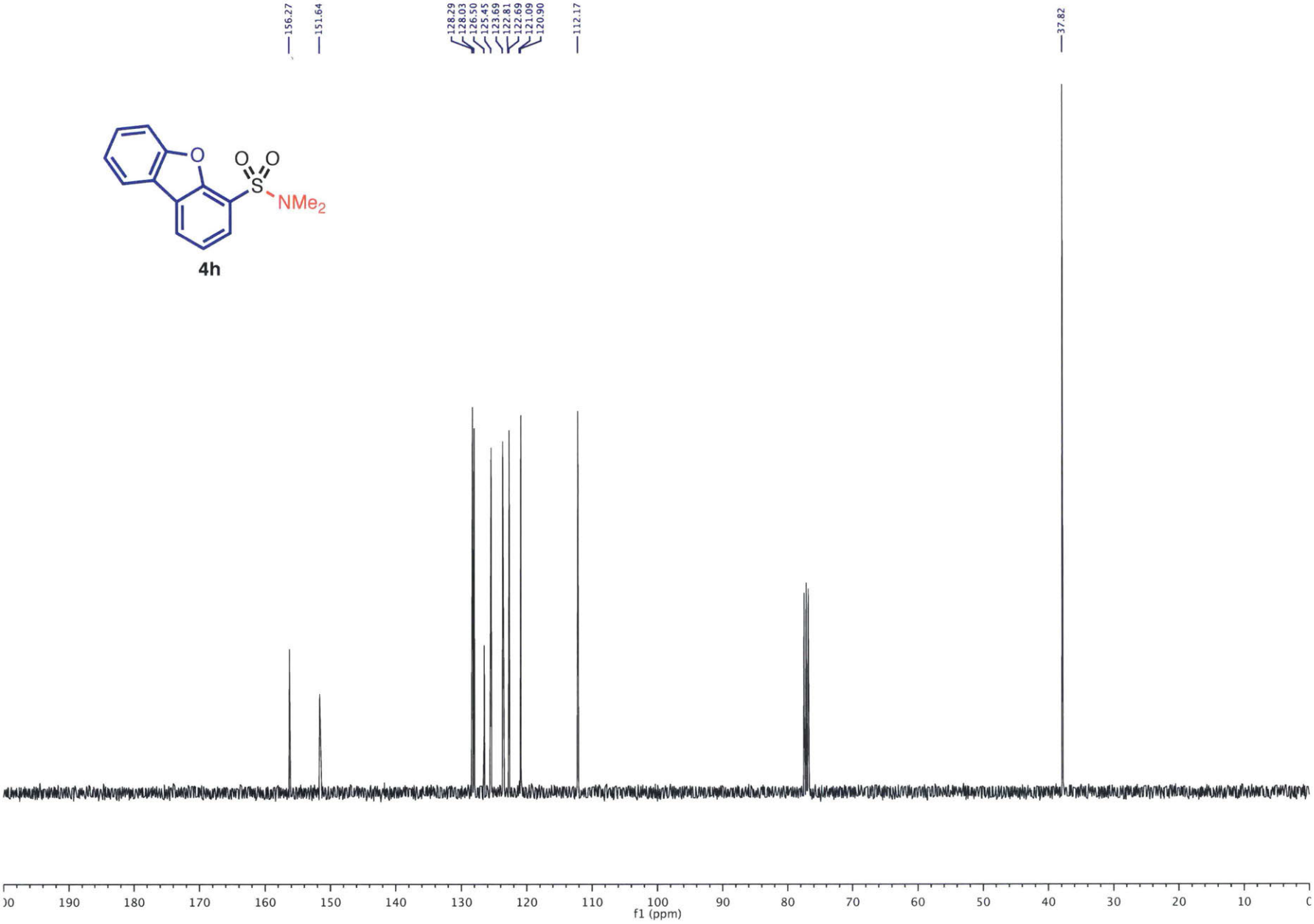

O
O
S
F3CO
NMe2

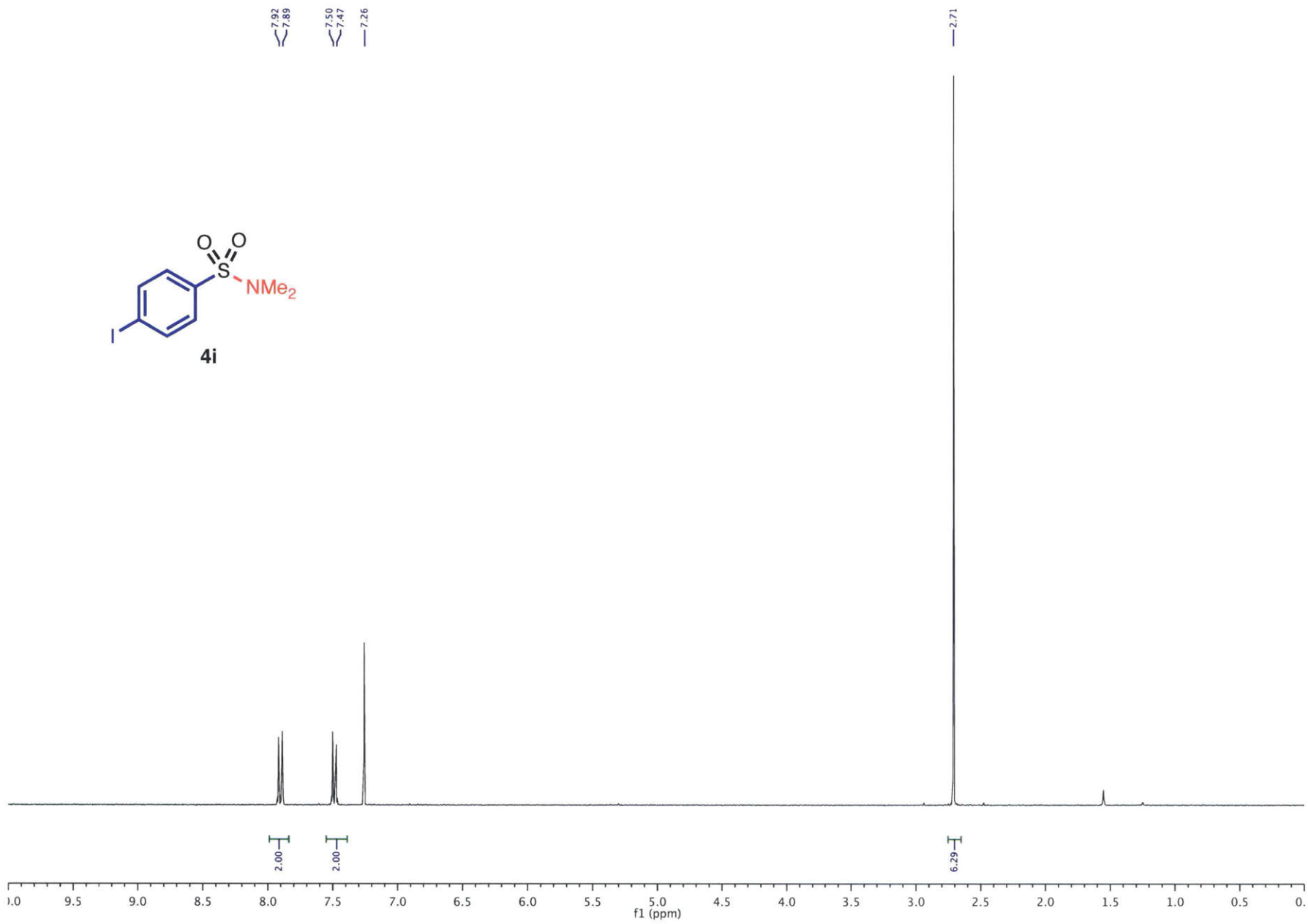
4g

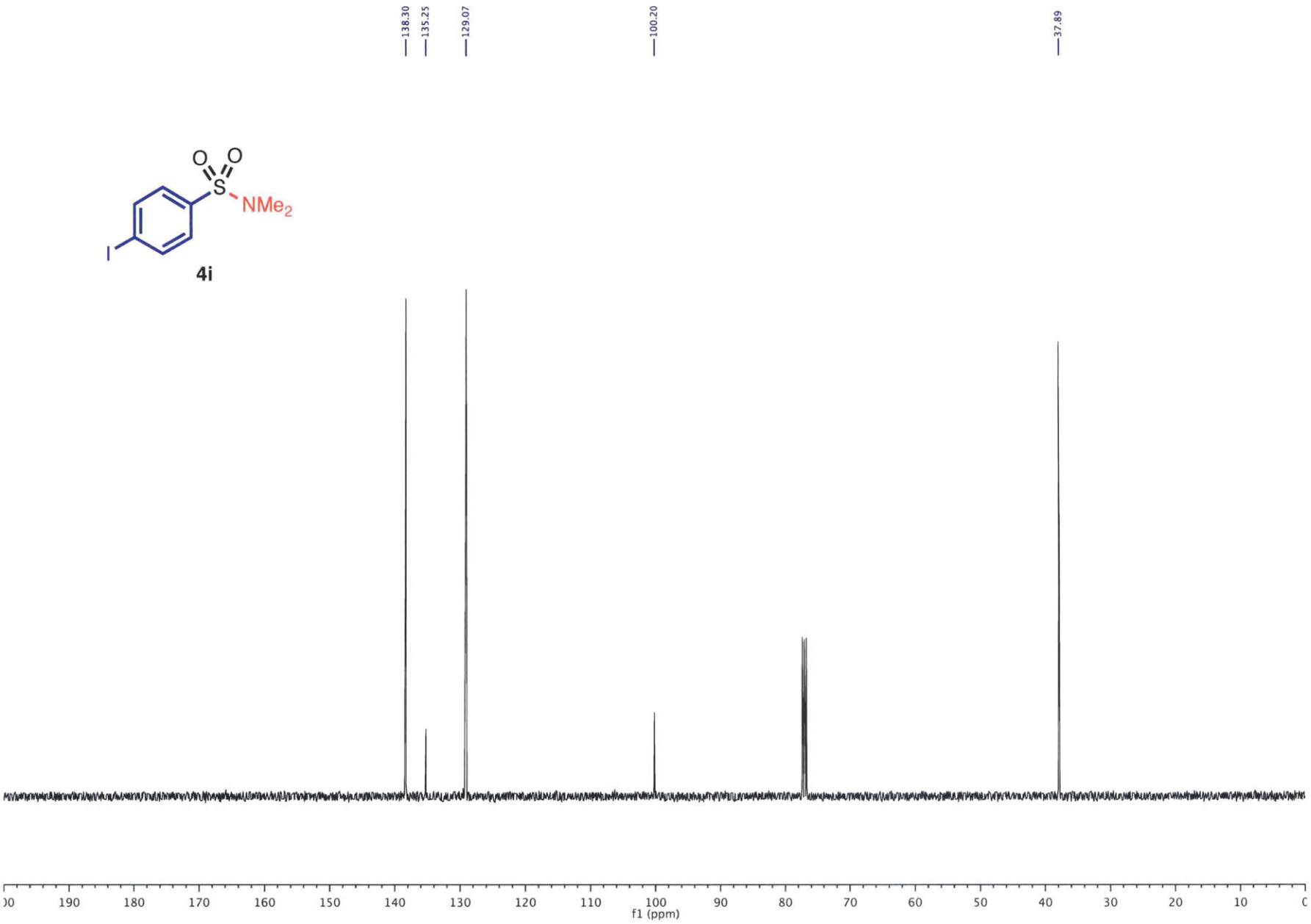
-58.13
-63.70 CF3Ph
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

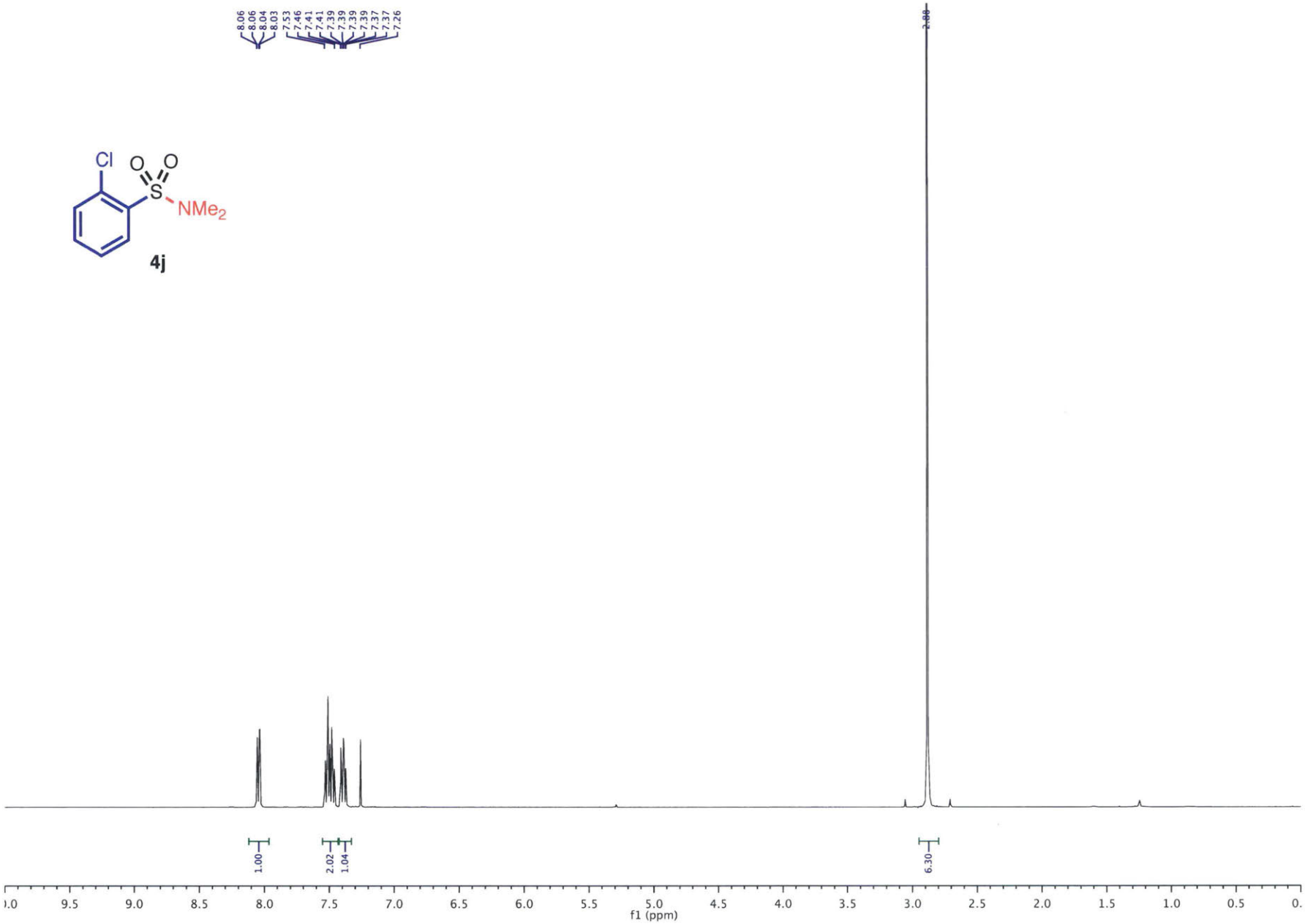

8.19
8.18
8.16
8.16
8.01
8.01
8.01
7.99
7.99
7.98
7.98
7.93
7.92
7.90
7.90
7.69
7.69
7.66
7.66
7.66
7.66
2.90
O
O
O
S
NMe2
1.00
0.98
0.97
0.98
3.05
f1 (ppm)

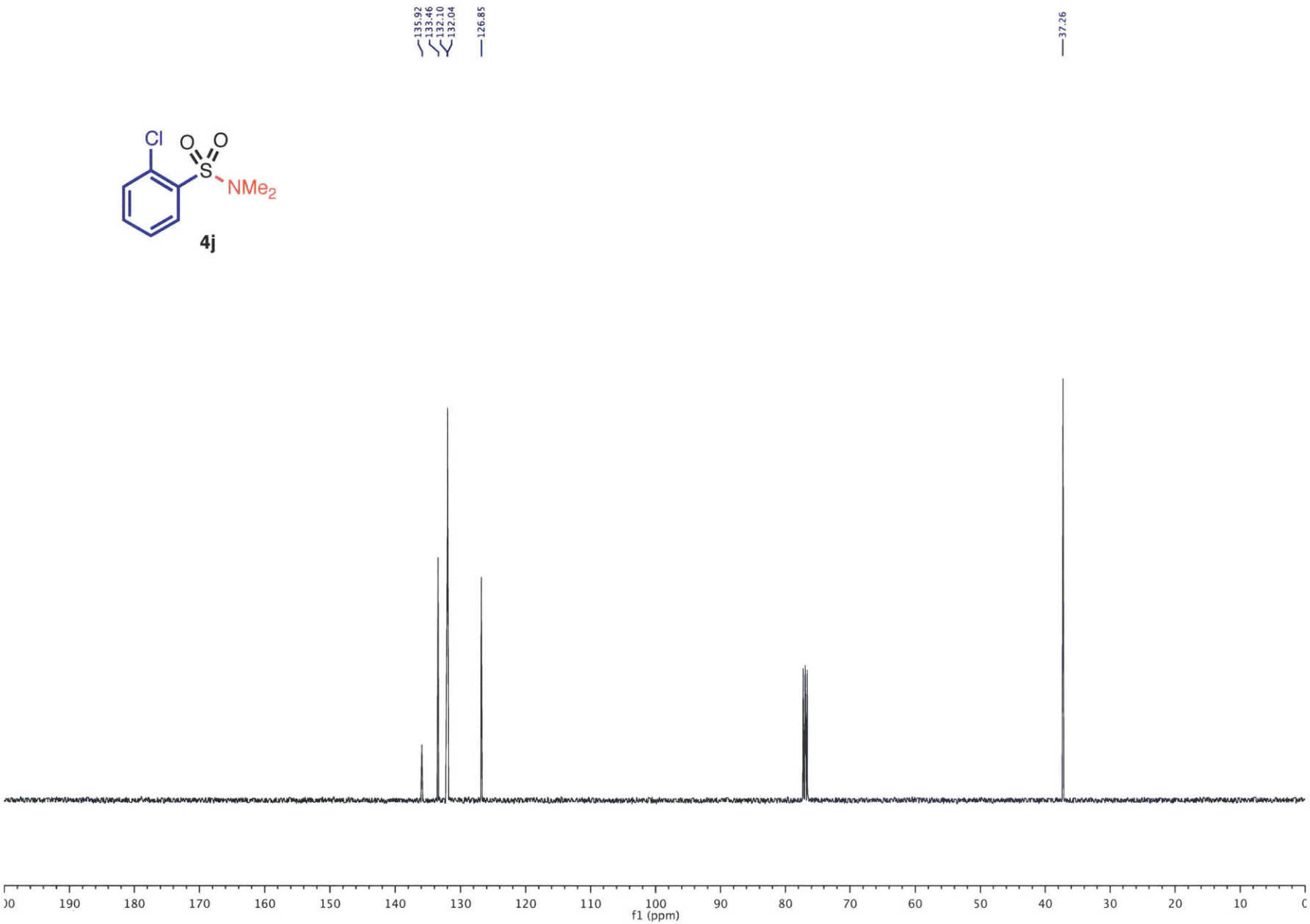
4h

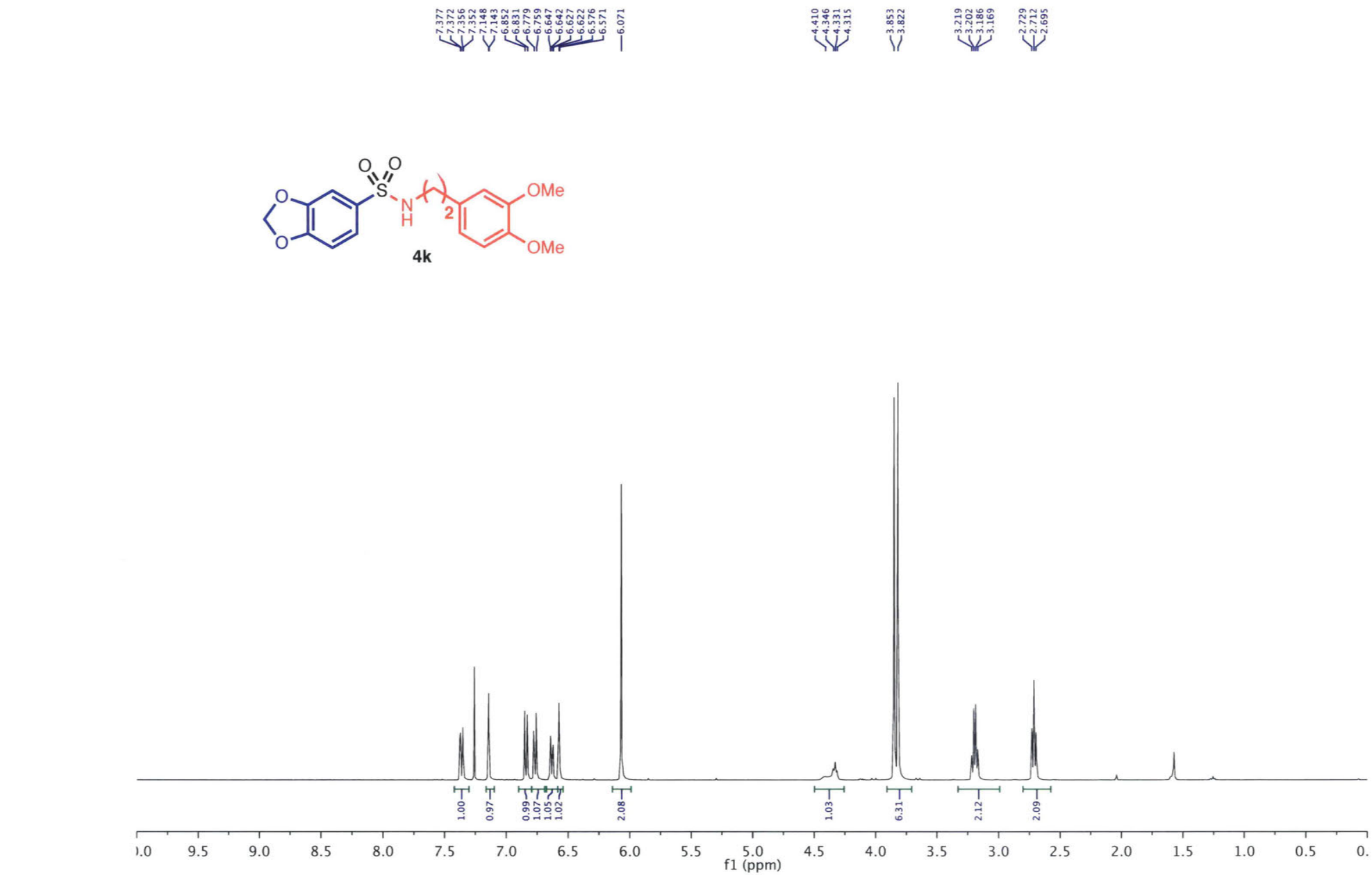

156.27
151.64
128.29
128.03
126.50
125.45
123.69
122.81
122.69
121.09
120.90
112.17
37.82
O
O
O
S
NMe2
4h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

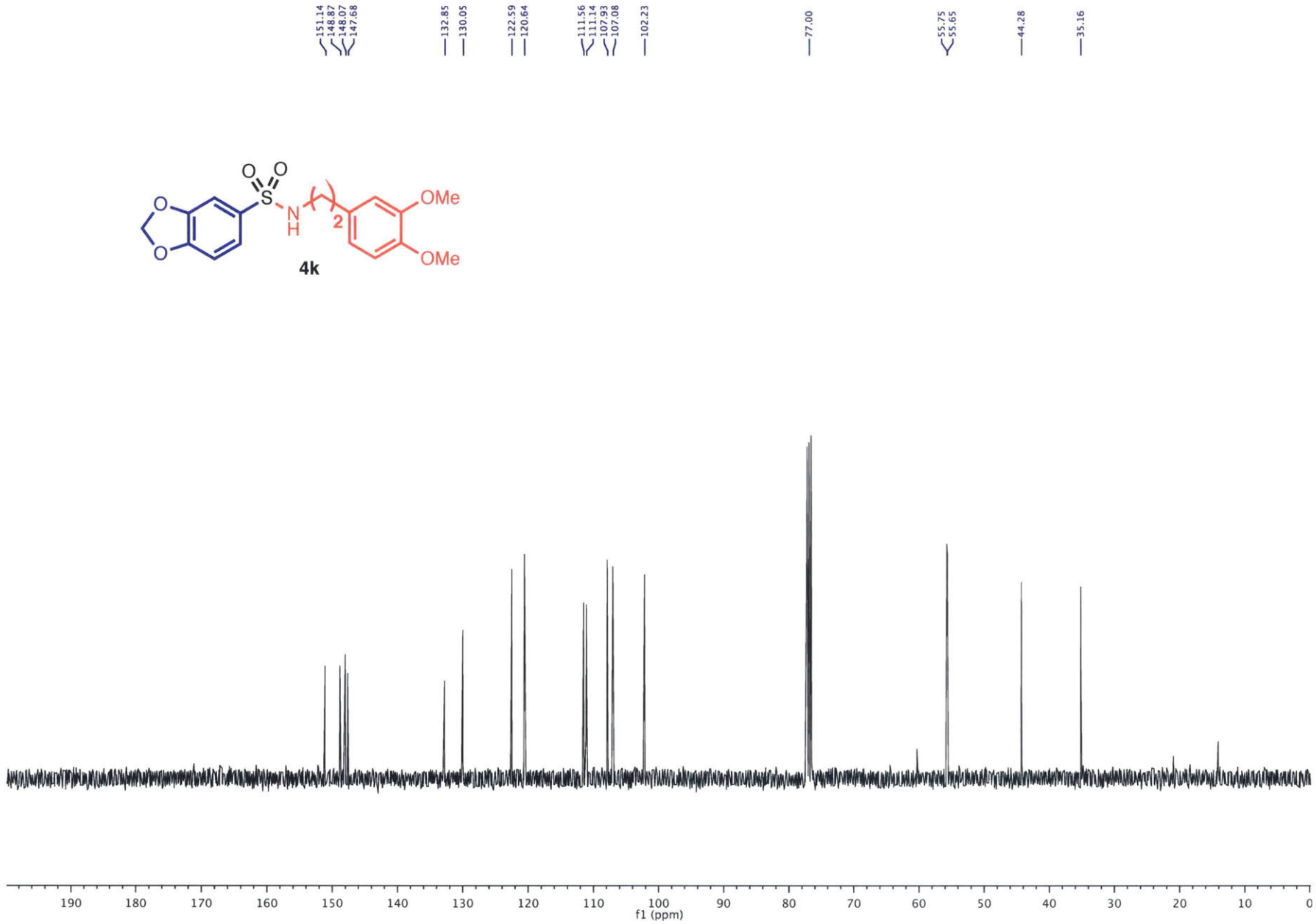

7.92
7.89
7.50
7.47
7.26
2.71
O
O
S
NMe2
I
4i
2.00
2.00
6.29
f1 (ppm)

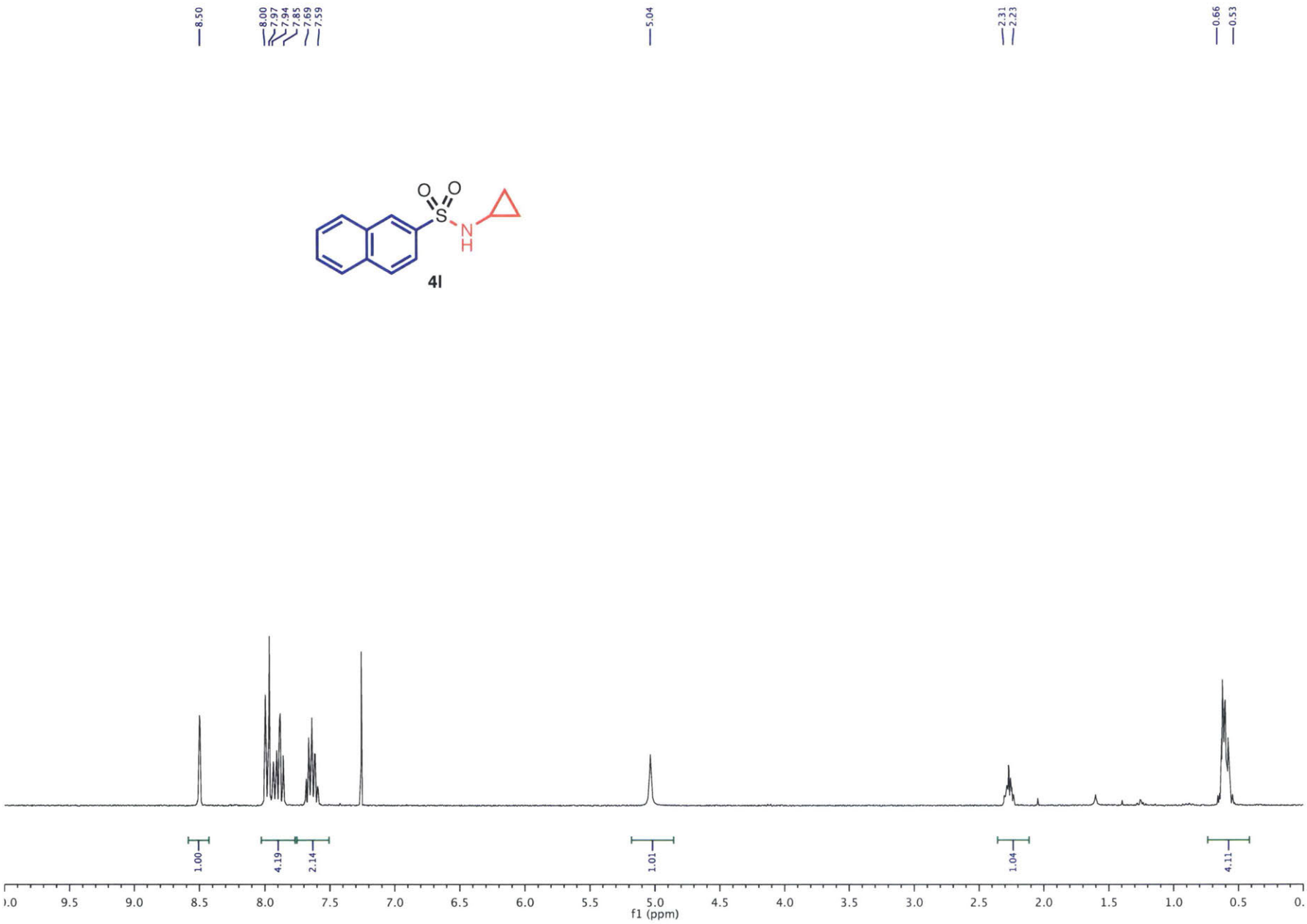

138.30
135.25
129.07
100.20
37.89
O
O
S
NMe2
I
4i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

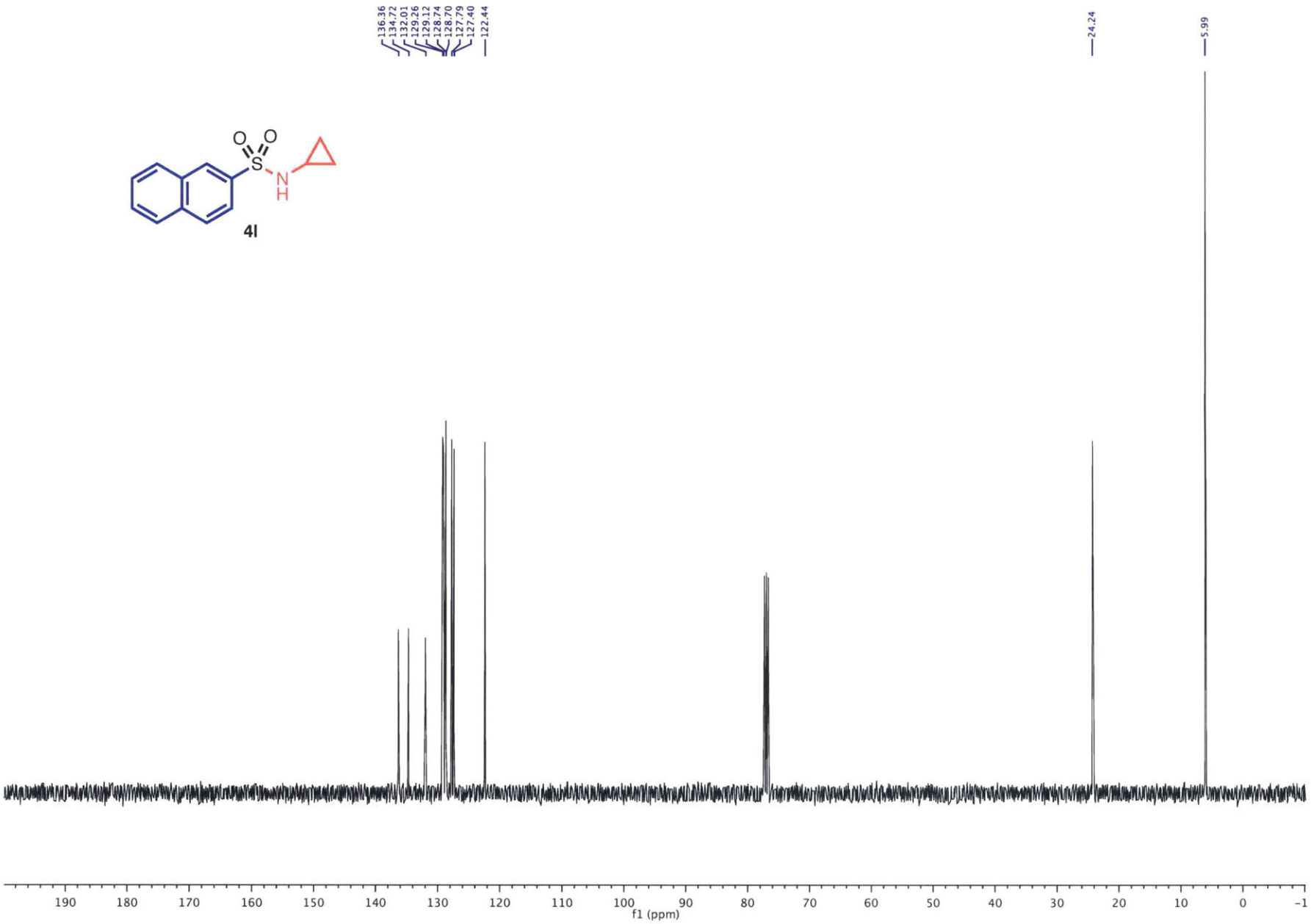

8.06
8.06
8.04
8.03
7.53
7.46
7.41
7.41
7.39
7.39
7.39
7.39
7.37
7.37
7.26
2.88
Cl
O
O
S
NMe2
4j
1.00
2.02
1.04
6.30
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

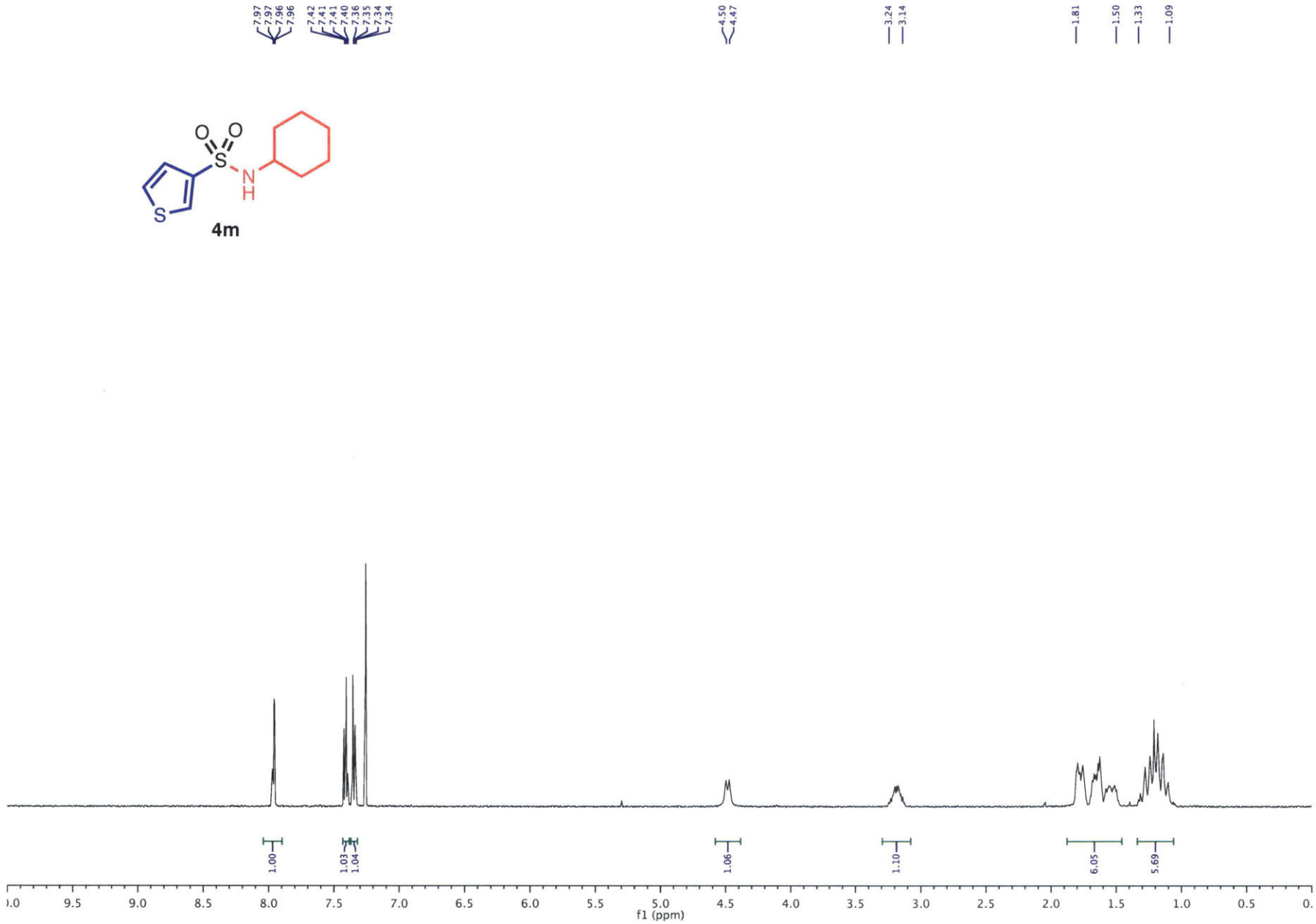

135.92
133.46
132.10
132.04
126.85
37.26
Cl
O
O
S
NMe2
4j
f1 (ppm)

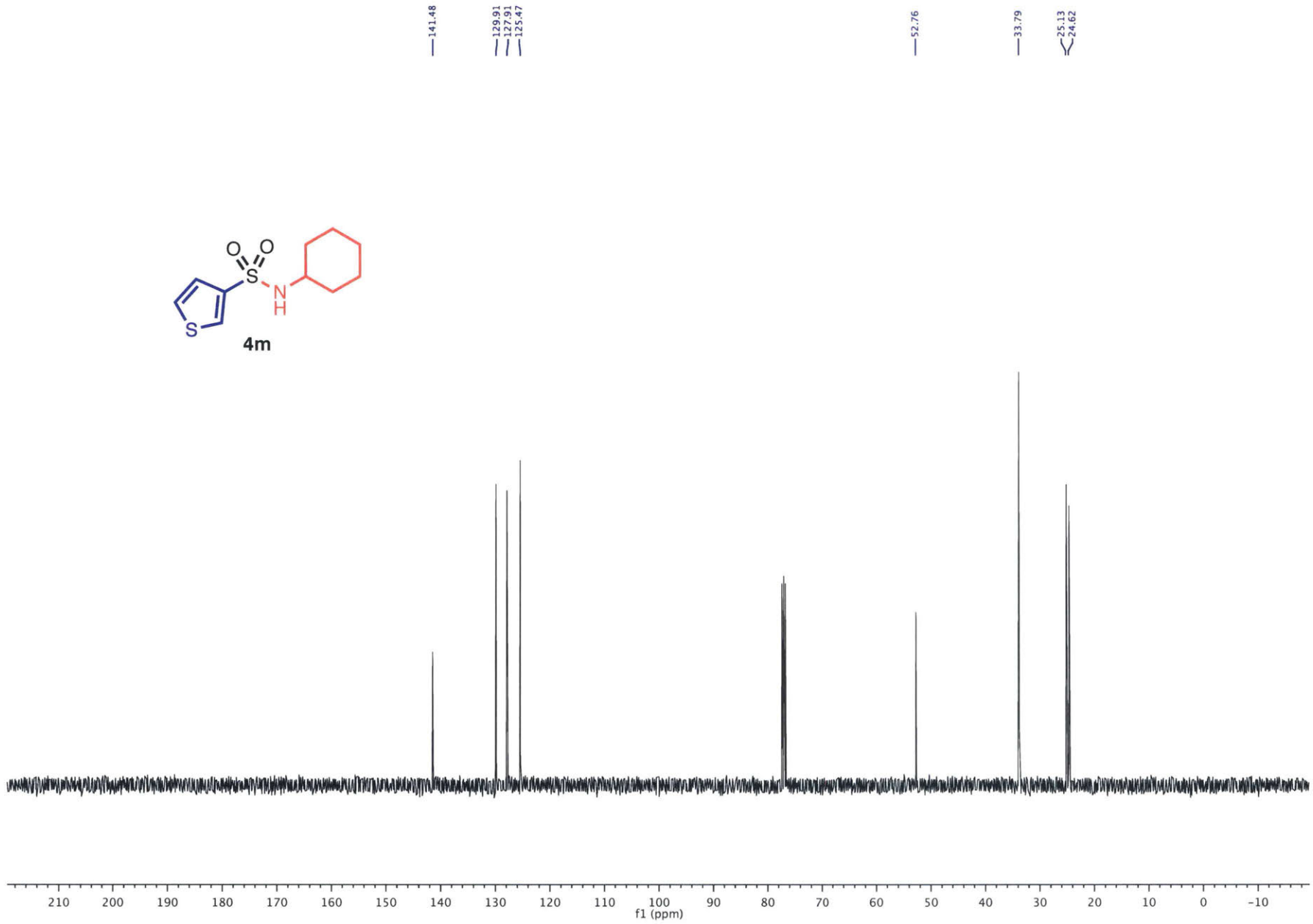

7.377
7.372
7.356
7.352
7.148
7.143
6.852
6.831
6.779
6.759
6.647
6.642
6.627
6.622
6.576
6.571
6.071
4.410
4.346
4.331
4.315
3.853
3.822
3.219
3.202
3.186
3.169
2.729
2.712
2.695
O
O
S
N
H
2
OMe
OMe
O
O
4k
1.00
0.97
0.99
1.07
1.05
1.02
2.08
1.03
6.31
2.12
2.09
f1 (ppm)

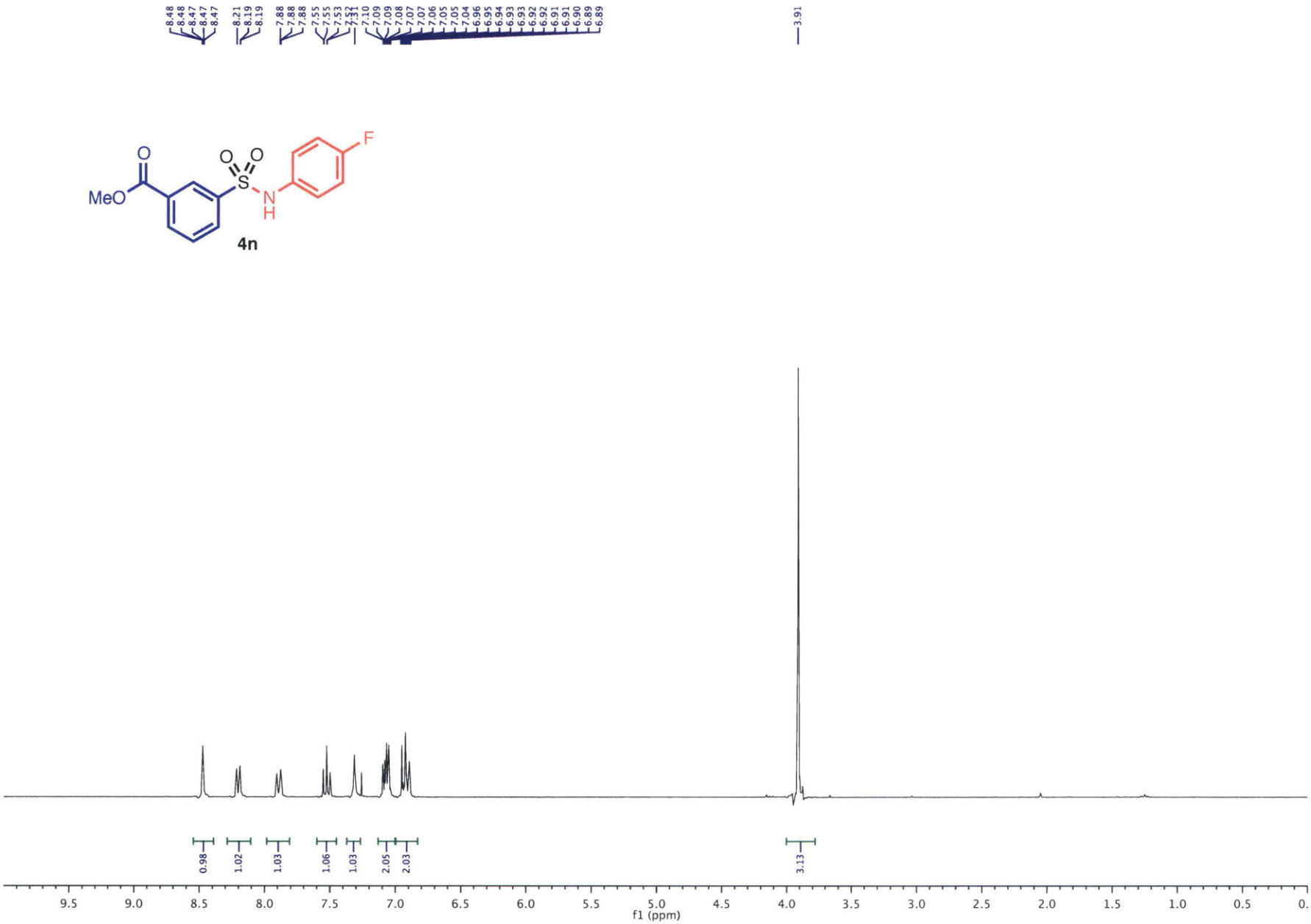

151.14
148.87
148.07
147.68
132.85
130.05
122.59
120.64
111.56
111.14
107.93
107.08
102.23
77.00
55.75
55.65
44.28
35.16
O
O
S
N
H
2
OMe
OMe
4k
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

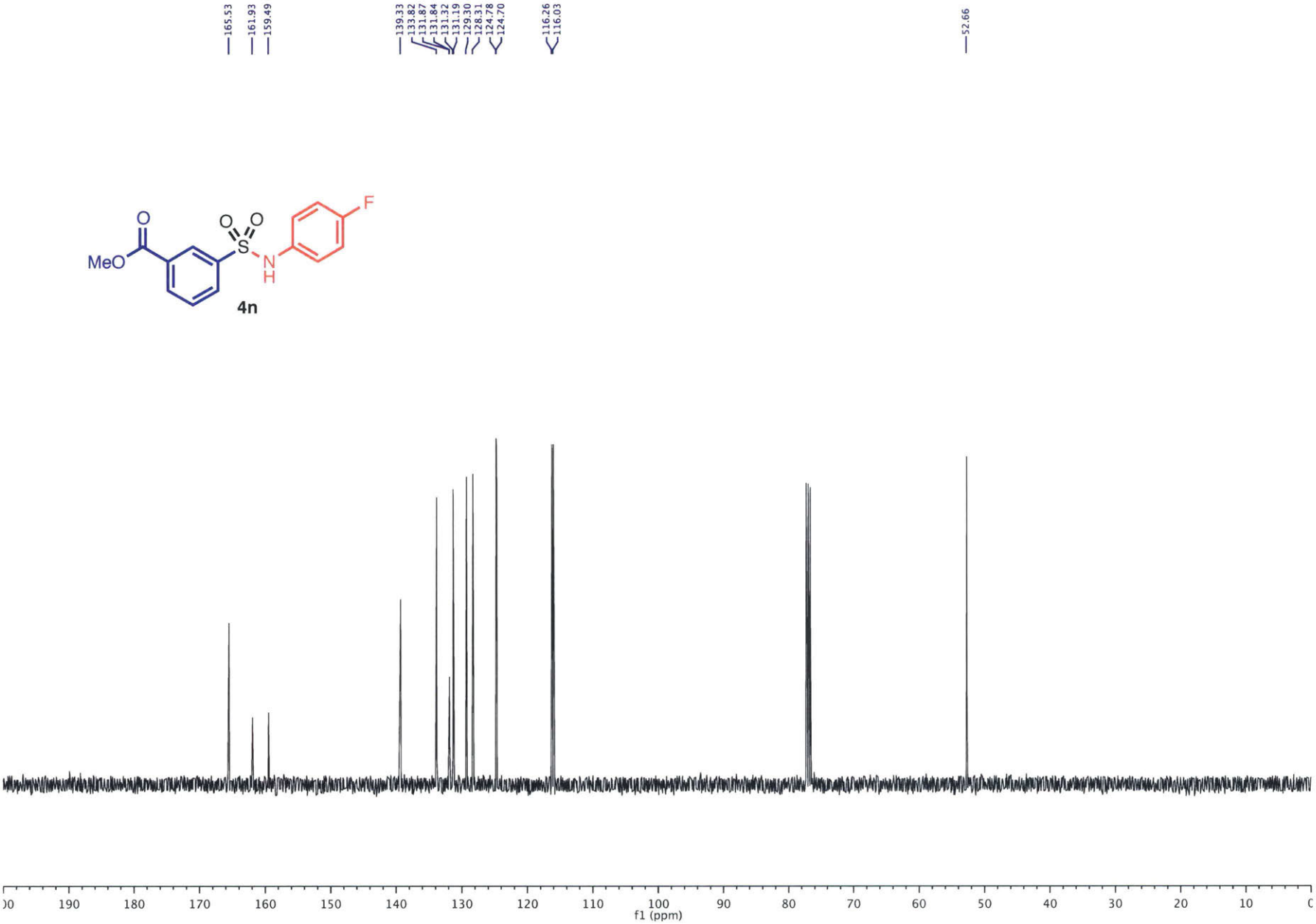

8.50
8.00
7.97
7.94
7.85
7.69
7.59
5.04
2.31
2.23
0.66
0.53
O
O
S
N
H
4l
1.00
4.19
2.14
1.01
1.04
4.11
f1 (ppm)

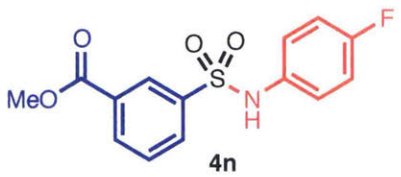

136.36
134.72
132.01
129.26
129.12
128.74
128.70
127.79
127.40
122.44
24.24
5.99
O
O
S
N
H
4l
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.97
7.97
7.96
7.96
7.42
7.41
7.41
7.40
7.36
7.35
7.34
7.34
4.50
4.47
3.24
3.14
1.81
1.50
1.33
1.09
O
O
S
N
H
S
4m
1.00
1.03
1.04
1.06
1.10
6.05
5.69
f1 (ppm)


141.48
129.91
127.91
125.47
52.76
33.79
25.13
24.62
O
O
S
N
H
S
4m
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

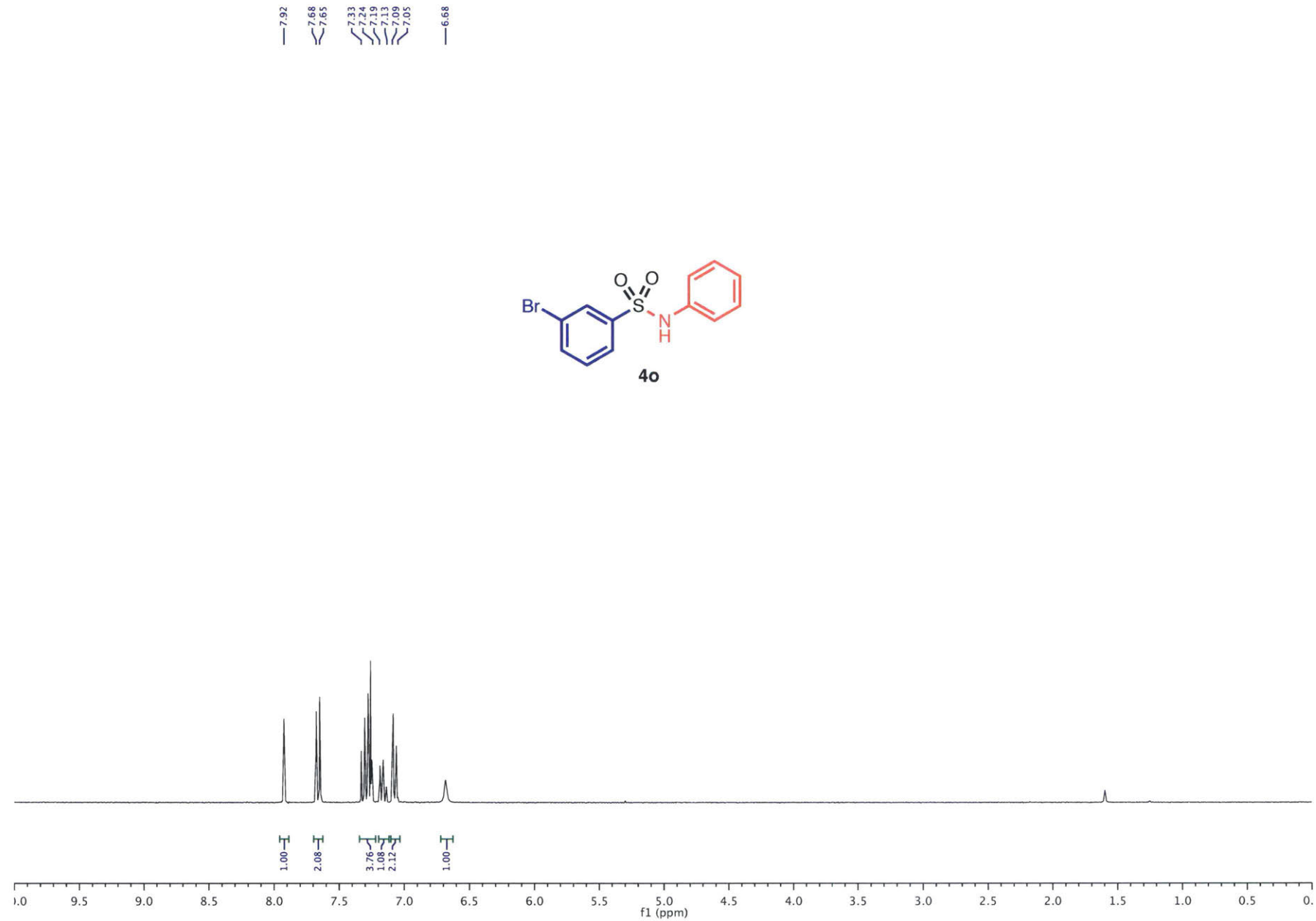

8.48
8.48
8.47
8.47
8.47
8.21
8.19
8.19
7.88
7.88
7.88
7.55
7.55
7.53
7.53
7.31
7.10
7.09
7.09
7.08
7.07
7.07
7.06
7.05
7.05
7.04
6.96
6.95
6.94
6.93
6.93
6.92
6.92
6.91
6.91
6.90
6.89
6.89
3.91
O
O
O
S
N
H
MeO
F
4n
0.98
1.02
1.03
1.06
1.03
2.05
2.03
3.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

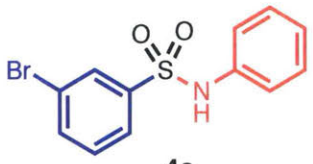

165.53
161.93
159.49
139.33
133.82
131.87
131.84
131.32
131.19
129.30
128.31
124.78
124.70
116.26
116.03
52.66
MeO
O
O
O
S
N
H
F
4n
f1 (ppm)


O
MeO
O
O
S
N
H
F

4n

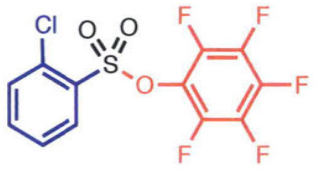
63.70 CF3Ph
-115.83
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)


7.92
7.68
7.65
7.33
7.24
7.19
7.13
7.09
7.05
6.68
Br
O
O
S
N
H
4o
1.00
2.08
3.76
1.08
2.12
1.00
f1 (ppm)


Br
O
O
S
N
H

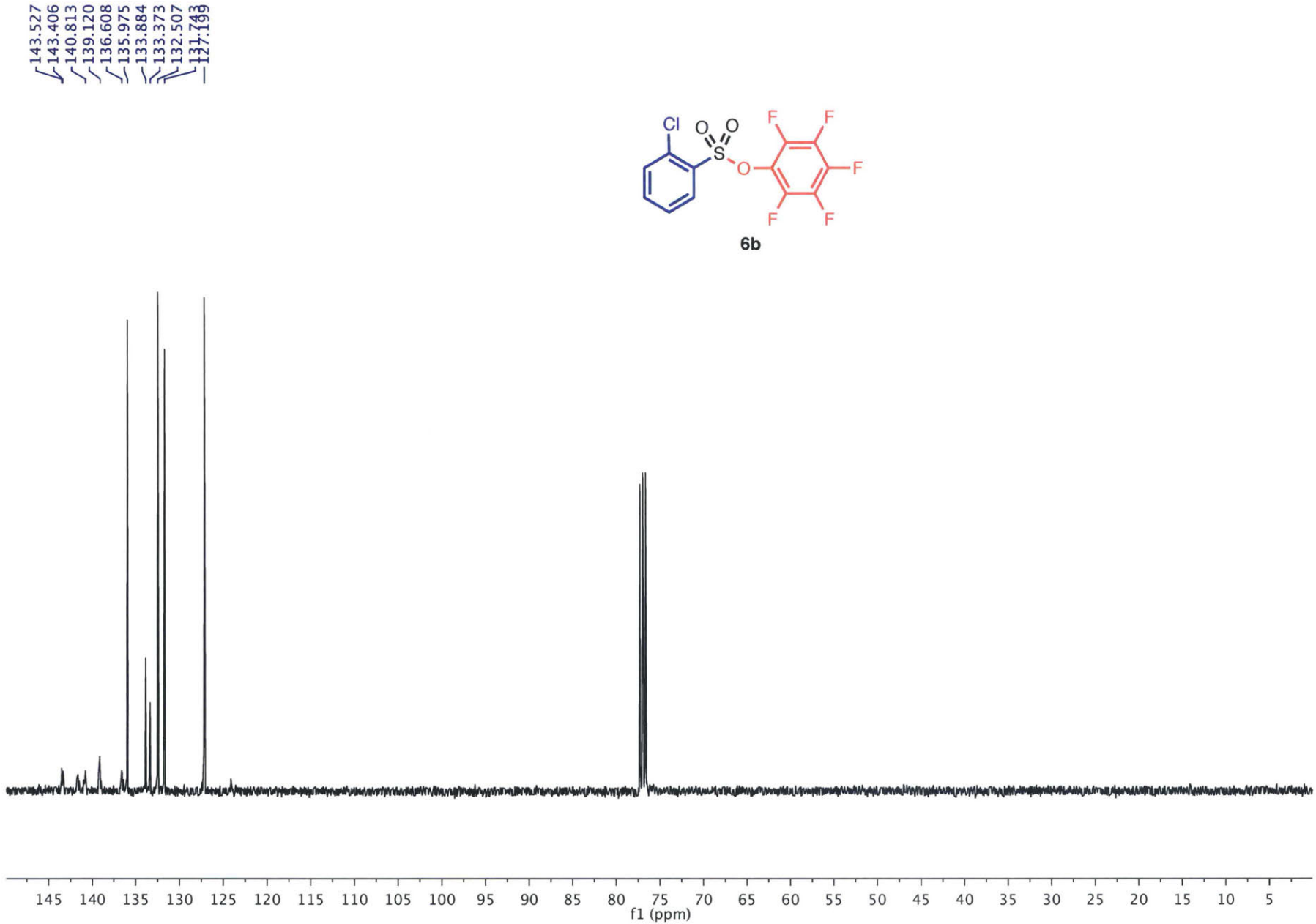
4o

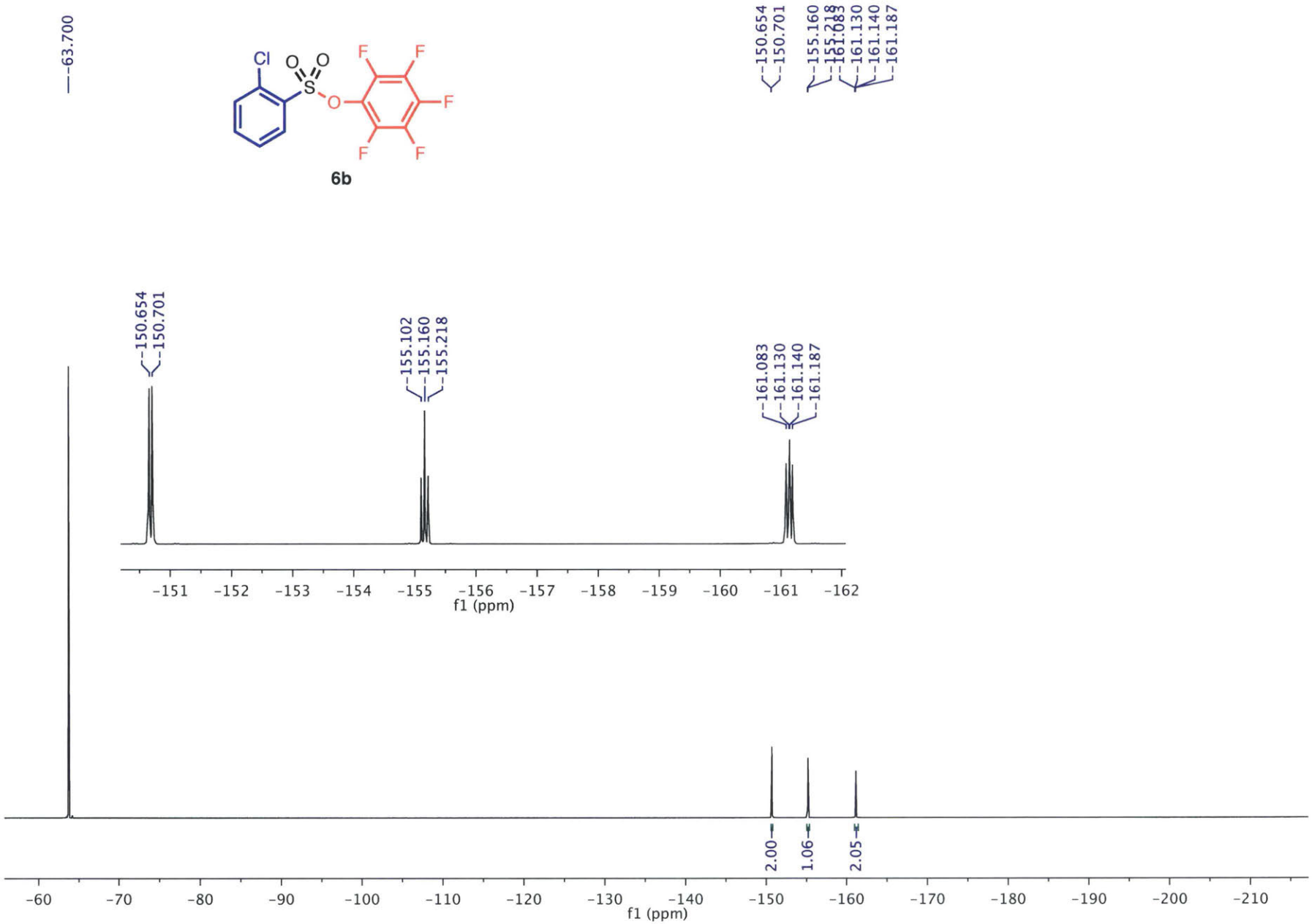
140.57
136.01
135.84
130.48
130.02
129.36
125.71
125.69
122.91
121.78
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

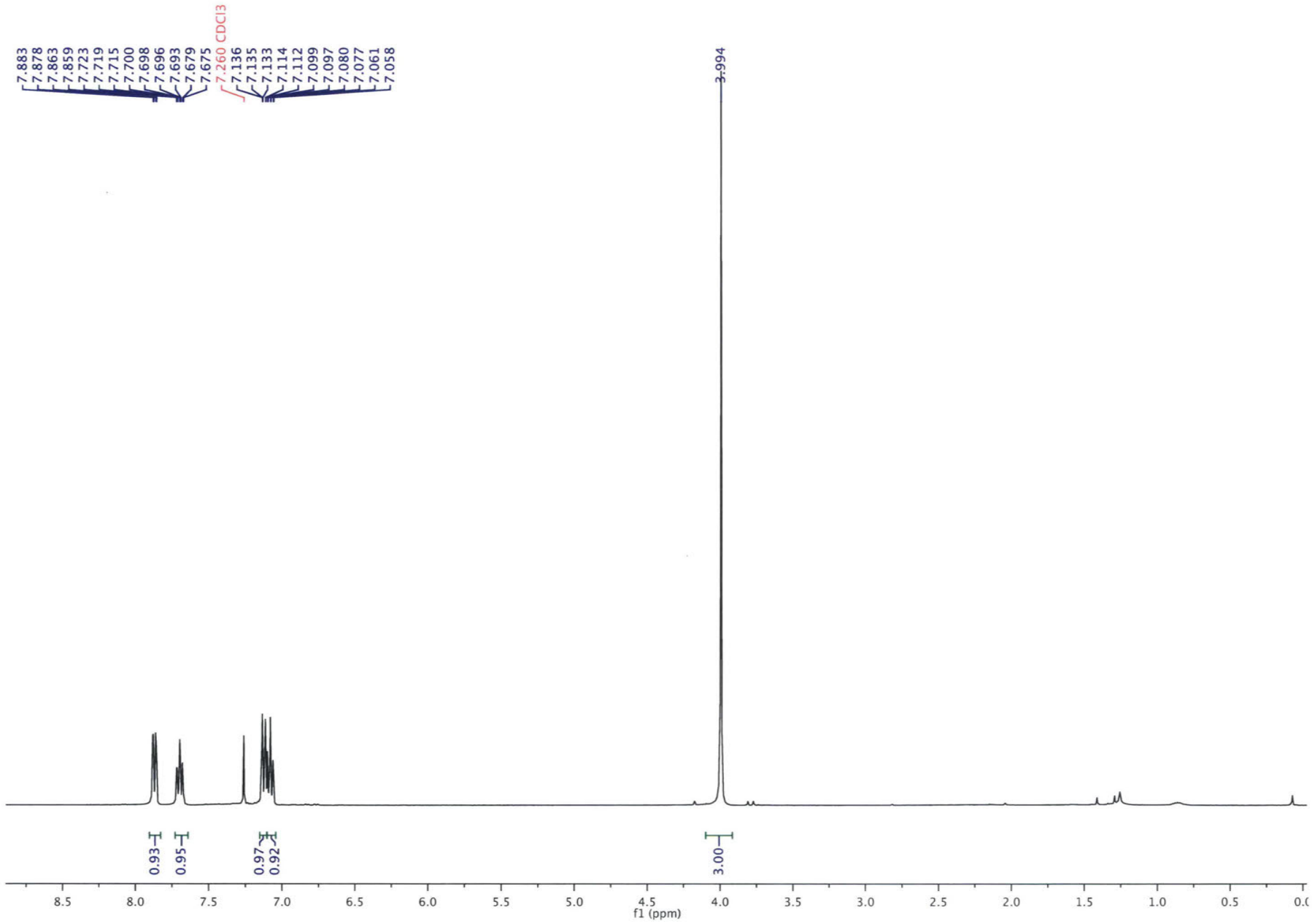

Cl
O
O
S
O
F
F
F
F
F

6b

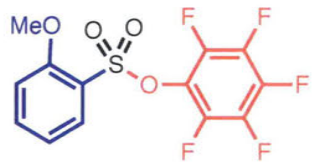
8.012
8.009
7.993
7.991
7.988
7.708
7.704
7.700
7.696
7.688
7.684
7.680
7.673
7.671
7.660
7.650
7.518
7.501
7.489
7.481
7.475
7.469
7.467
7.460
7.456
7.447
7.435
7.260 CDCl3
1.00
2.06
1.08
8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
8.5 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
f1 (ppm)


143.527
143.406
140.813
139.120
136.608
135.975
133.884
133.373
132.507
Cl
O
O
S
O
F
F
F
F
F
6b
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5
f1 (ppm)

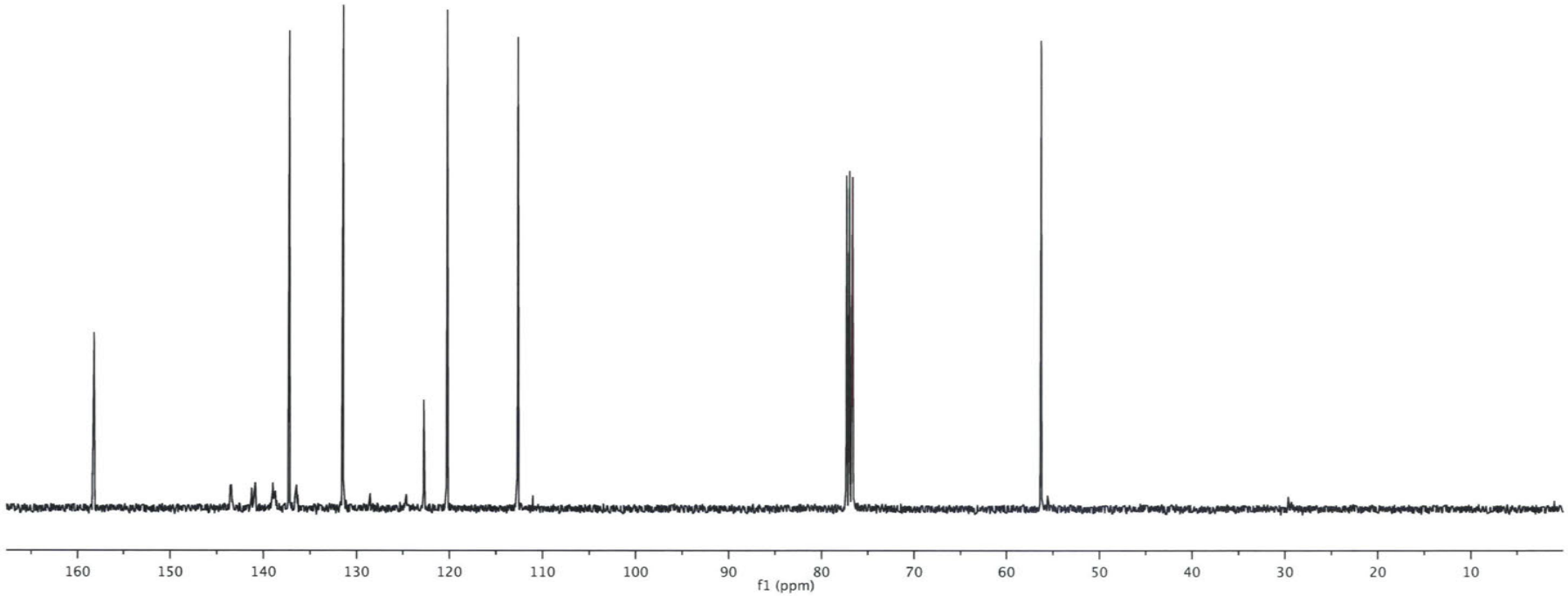

-63.700
Cl
O
O
S
O
F
F
F
F
F
6b
-150.654
-150.701
-155.160
-155.218
-161.083
-161.130
-161.140
-161.187
-150.654
-150.701
-155.102
-155.160
-155.218
-161.083
-161.130
-161.140
-161.187
-151 -152 -153 -154 -155 -156 -157 -158 -159 -160 -161 -162
f1 (ppm)
2.00
1.06
2.05
-60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

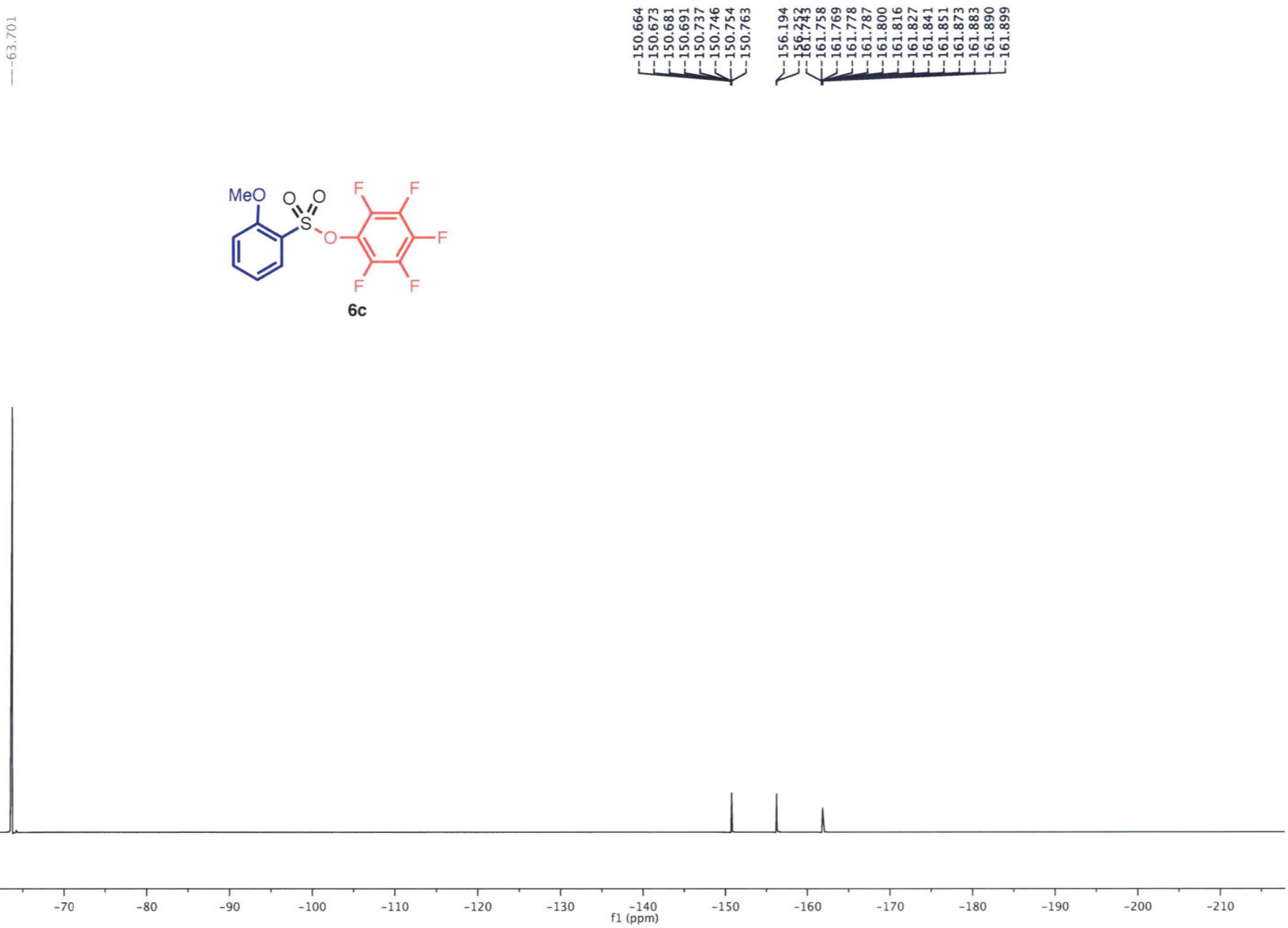

7.883
7.878
7.863
7.859
7.723
7.719
7.715
7.700
7.698
7.696
7.693
7.679
7.675
7.260 CDCl3
7.136
7.135
7.133
7.114
7.112
7.099
7.097
7.080
7.077
7.061
7.058
3.994
0.93
0.95
0.97
0.92
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

158.247
143.551
143.425
141.264
141.018
140.973
140.937
140.895
140.852
138.997
137.258
136.521
136.458
131.380
124.645
122.760
120.271
112.682
56.278

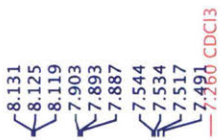


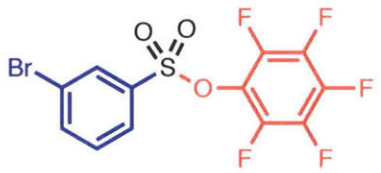
6c



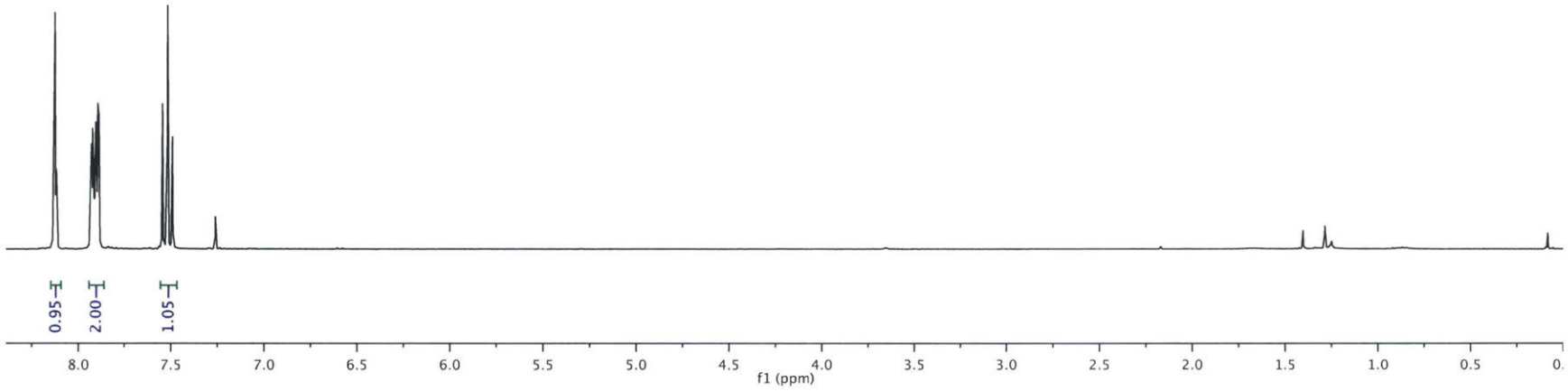

-63.701
150.664
150.673
150.681
150.691
150.737
150.746
150.754
150.763
156.194
156.252
161.743
161.758
161.769
161.778
161.787
161.800
161.816
161.827
161.841
161.851
161.873
161.883
161.890
161.899
MeO
O
O
S
O
F
F
F
F
F
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

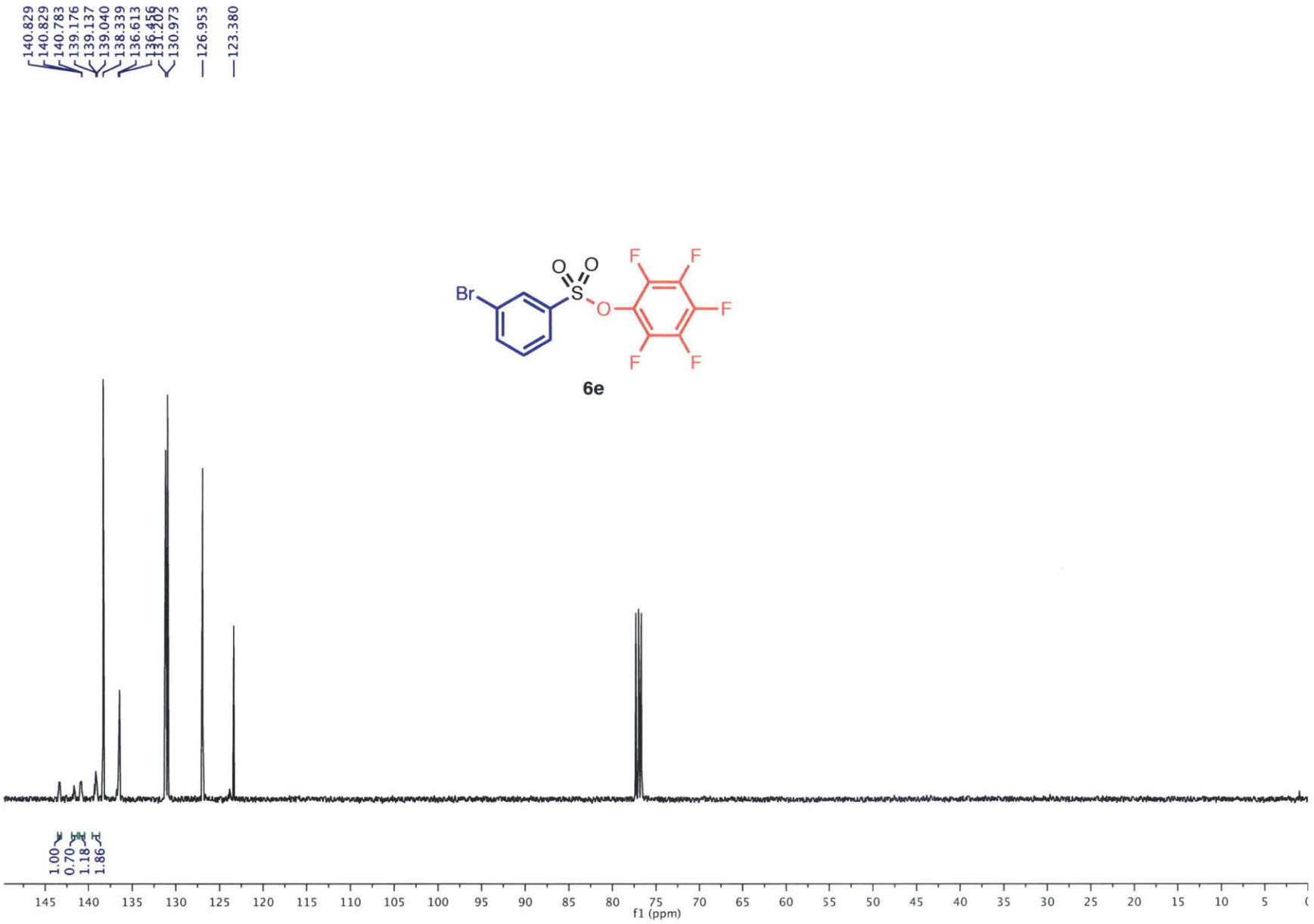
6c

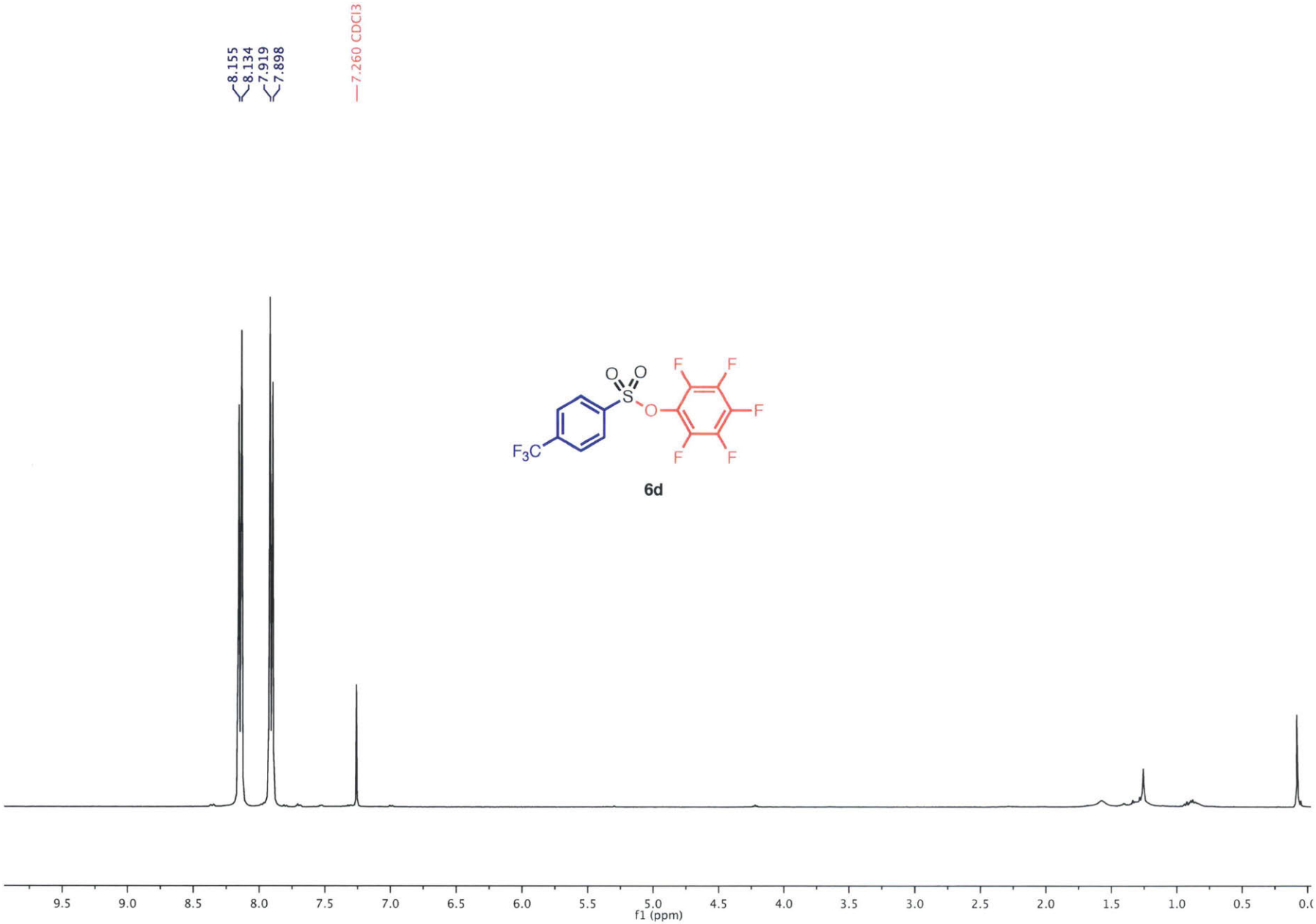

8.131
8.125
8.119
7.903
7.893
7.887
7.544
7.534
7.517
7.491
7.260 CDCl3


Br
O
O
S
O
F
F
F
F
F

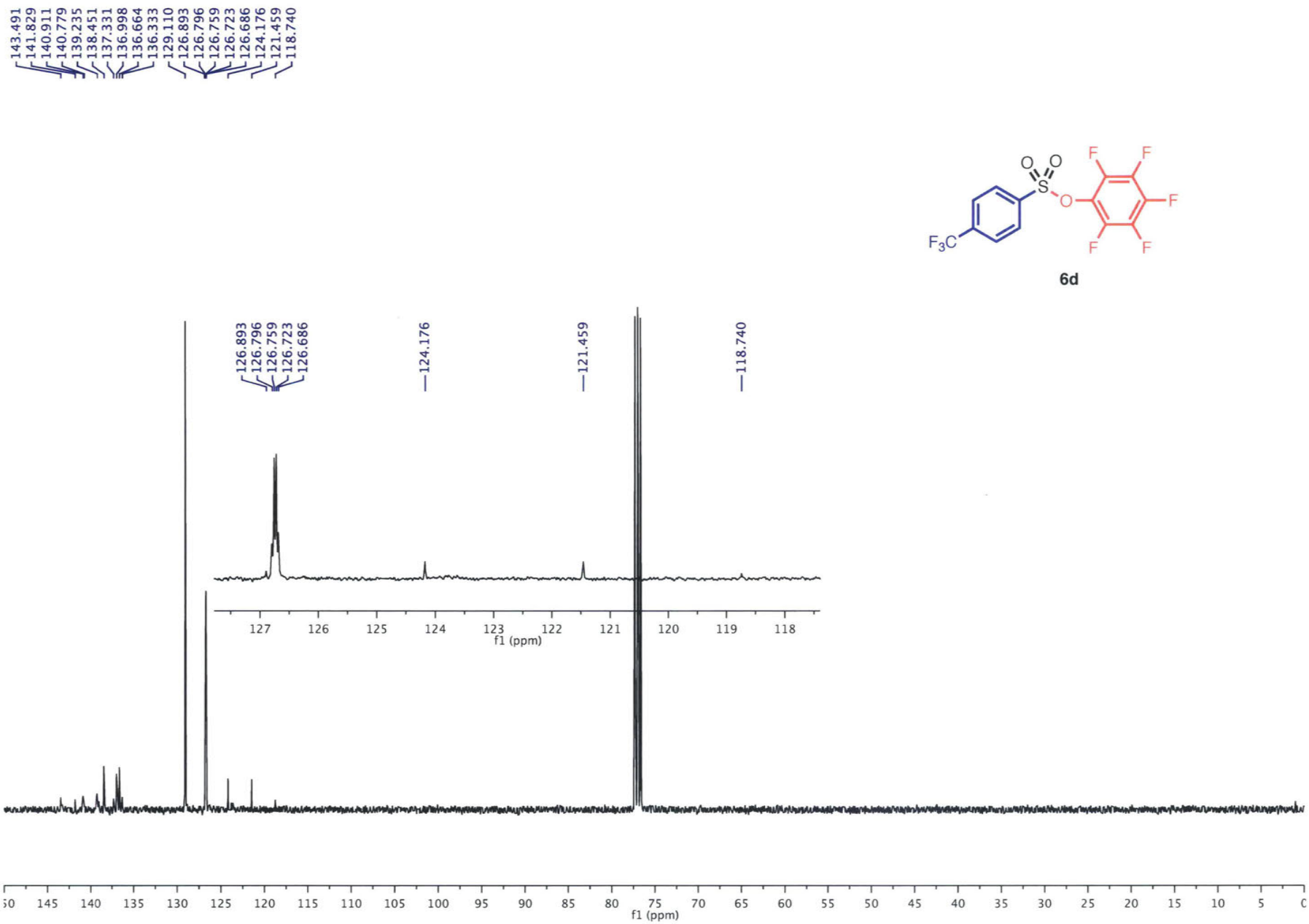
6e

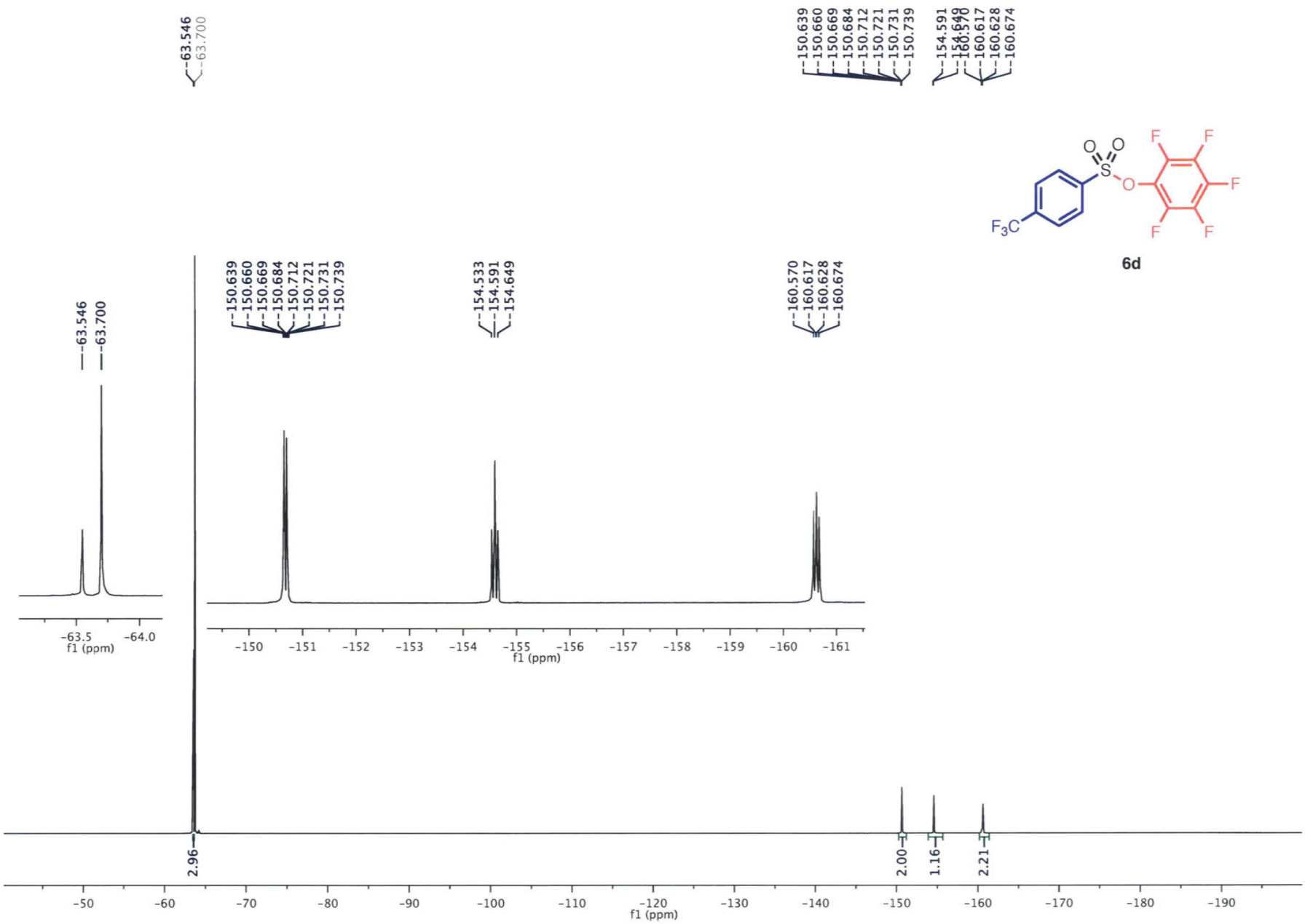

0.95
2.00
1.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


140.829
140.829
140.783
139.176
139.137
139.040
138.339
136.613
136.456
131.202
130.973
126.953
123.380
Br
O
O
S
O
F
F
F
F
F
6e
1.00
0.70
1.18
1.86
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
f1 (ppm)


8.155
8.134
7.919
7.898
7.260 CDCl3
F3C
O
S
O
O
F
F
F
F
F
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
f1 (ppm)

6d


143.491
141.829
140.911
140.779
139.235
138.451
137.331
136.998
136.664
136.333
129.110
126.893
126.796
126.759
126.723
126.686
124.176
121.459
118.740
F
F
F
F
F
O
O
S
O
F3C
6d
f1 (ppm)
f1 (ppm)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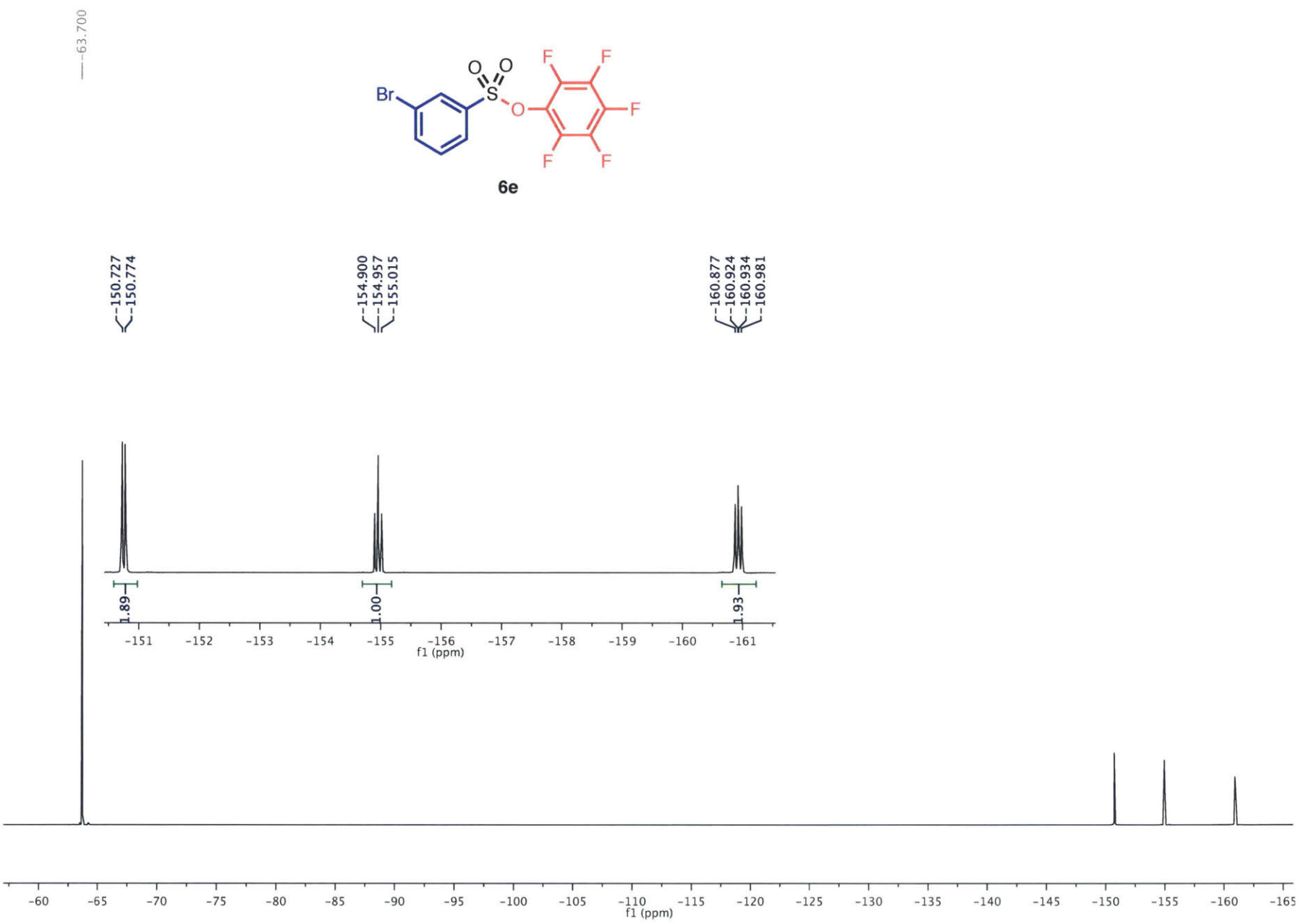
-63.700
150.639
150.660
150.669
150.684
150.712
150.721
150.731
150.739
154.591
154.649
160.570
160.617
160.628
160.674
F
F
F
F
F
O
O
S
O
F3C
6d
-63.546
-63.700
-63.5
-64.0
f1 (ppm)
150.639
150.660
150.669
150.684
150.712
150.721
150.731
150.739
154.533
154.591
154.649
160.570
160.617
160.628
160.674
-150
-151
-152
-153
-154
-155
-156
-157
-158
-159
-160
-161
f1 (ppm)
2.96
2.00
1.16
2.21
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


-63.700
Br
O
O
S
O
F
F
F
F
F
6e
-150.727
-150.774
-154.900
-154.957
-155.015
-160.877
-160.924
-160.934
-160.981
1.89
1.00
1.93
-151
-152
-153
-154
-155
-156
-157
-158
-159
-160
-161
f1 (ppm)
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
f1 (ppm)

Part II.

Chapter 2.

Enantio- and Regioselective Copper-Catalyzed Hydroamination of Styrenes and the Extension of the Methodology towards Anti-Markovnikov Hydroamination of Terminal Aliphatic Alkenes

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Enantio- and Regioselective CuH-Catalyzed Hydroamination of Alkenes

Shaolin Zhu, Nootaree Niljianskul, and Stephen L. Buchwald

Journal of the American Chemical Society, **2013,** *135* (42), 15746–15749

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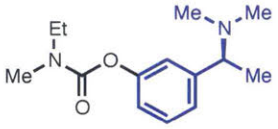
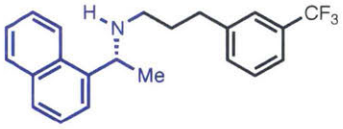
2.1 Introduction

Chiral amines are an important class of compounds ubiquitous in the pharmaceutical industry and natural products (Figure 1).[1a] Because chiral amines are valuable synthons and synthetic targets, many approaches towards their synthesis have been developed.[1b] Some examples include nucleophilic addition to imines, radical addition to imino compounds, chiral Brønsted acid-catalyzed transformation, asymmetric reduction, and asymmetric reductive amination.[1b]

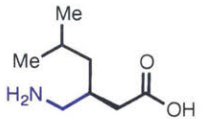
Figure 1. *Pharmaceutical Drugs Containing Chiral Amine Motifs*



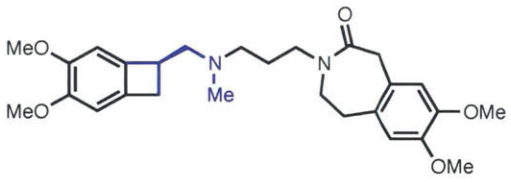
Exelon
Novartis
Anti-alzheimer



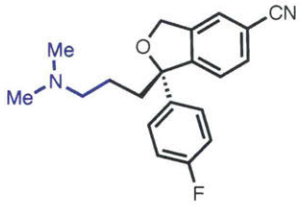
Sensipar
Amgen
Parathyroid hormone regulator



Lyrica
Pfizer
Antiepileptics



Procoralan
Servier
Heart rate reduction



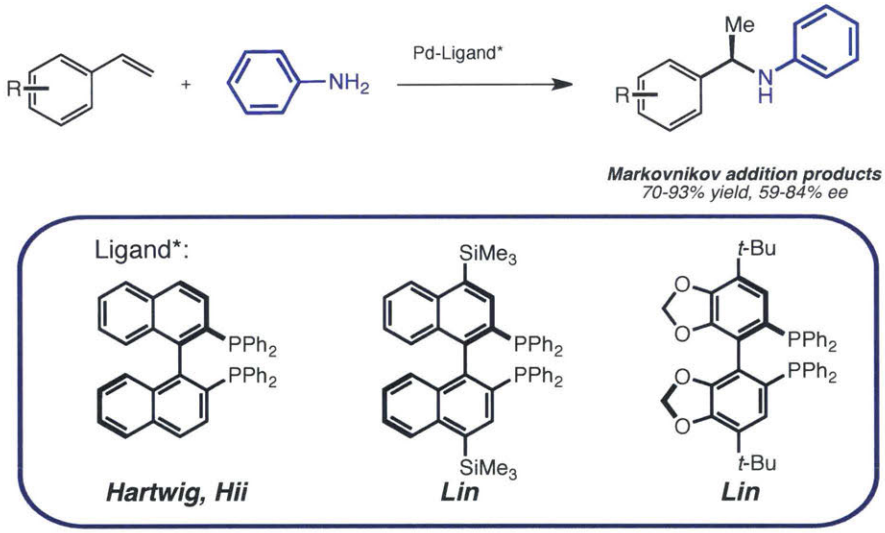
Lexapro
Forest Lab, Inc.
Antidepressant

Hydroamination, the formation of a C-N bond by the formal addition of an amine to an olefin, is one of the most direct methods to access amine derivatives. Additionally, this method has the potential to gain access to amine products from readily available feedstocks such as alkenes and alkynes. Indeed, over the past six decades, many hydroamination reactions have been developed.[1b]

Despite the significant progress that has been made in the field of late transition metal-catalyzed hydroamination,[2,3] several challenges still exist. For example, the intermolecular system requires activated alkenes such as vinyl arenes or acrylic acid derivatives.[2] For the asymmetric variants, the state of art systems are the palladium-catalyzed approaches as reported

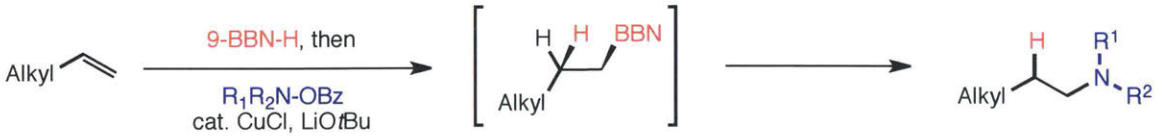
by Hartwig, Hii, and Lin (Scheme 1).[2j-l] Although this represents a significant advancement in the field of late transition metal-catalyzed hydroamination reactions, the systems are limited to the addition of aryl amines to simple β-unsubstituted styrene derivatives and achieve only moderate levels of enantiomeric excess (Scheme 1).

Scheme 1. *Enantioselective Hydroamination Reactions Catalyzed by Late Transition Metals*



Furthermore, the hydroamination of unactivated alkenes using metal catalysis is still quite limited. Currently, there is no precedent for late-transition metal catalyzed anti-Markovnikov intermolecular hydroamination of unactivated olefins. However, Lalic has recently reported a strategy to achieve intermolecular anti-Markovnikov hydroamination products from aliphatic alkenes by intermediate hydroboration of the olefin, followed by a copper-catalyzed amination (Scheme 2).[4]

Scheme 2. *Anti-Markovnikov Hydroamination of Aliphatic Alkenes*[4]

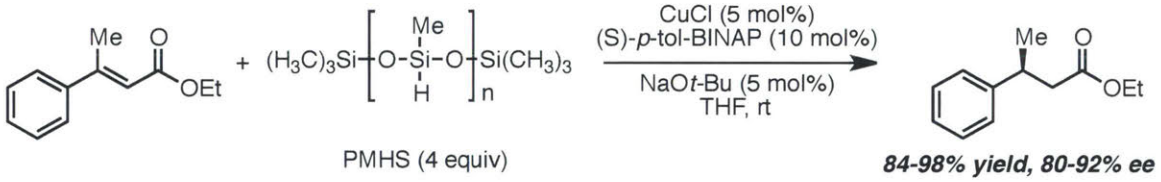


Thus, there remains a need to develop asymmetric hydroamination reaction conditions

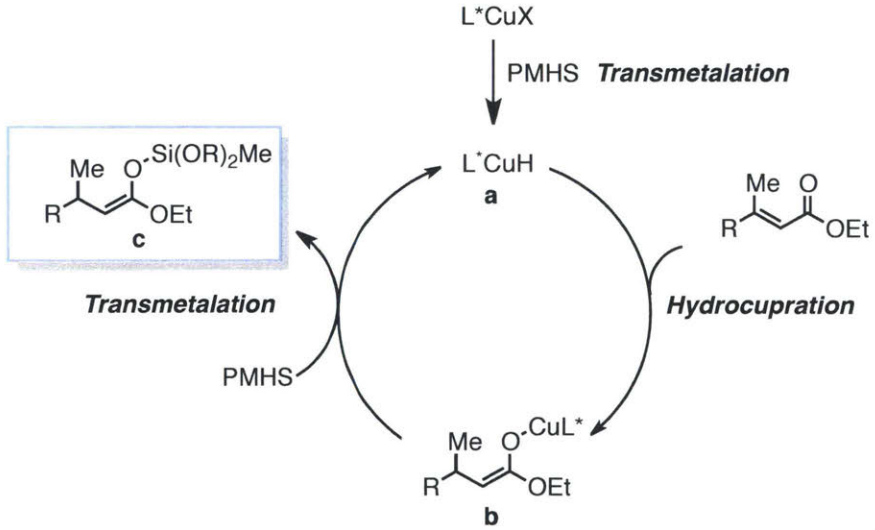
that tolerate a wide variety of substitution patterns on both the alkene and the amine components, which possess high regio- and enantioselectivity. We are, therefore, interested in pursuing a mild and general approach to synthesize a broad range of chiral amines. Challenges that we specifically wanted to address included incompatibilities with alkyl amine substrates and β-substituted substrates.

Over the last decade our group has explored and developed successful asymmetric reduction methods, one of which is the asymmetric copper hydride-mediated (CuH) transformation shown in Scheme 3.[5a-e] This asymmetric reduction strategy exploits a copper hydride species, formed in situ, to promote a conjugate reduction of α,β-unsaturated compounds (Scheme 4).[5a-c] It was proposed that this reaction occurs via CuH (**a**) addition to the olefin, a "hydrocupration process," which generates a copper-enolate species (**b**). Transmetalation of the cuprate with a silane reagent affords a sily enol ether (**c**) while regenerating the CuH species (**a**).

Scheme 3. *Previously Reported CuH-Catalyzed Asymmetric Reduction*[5a-e]

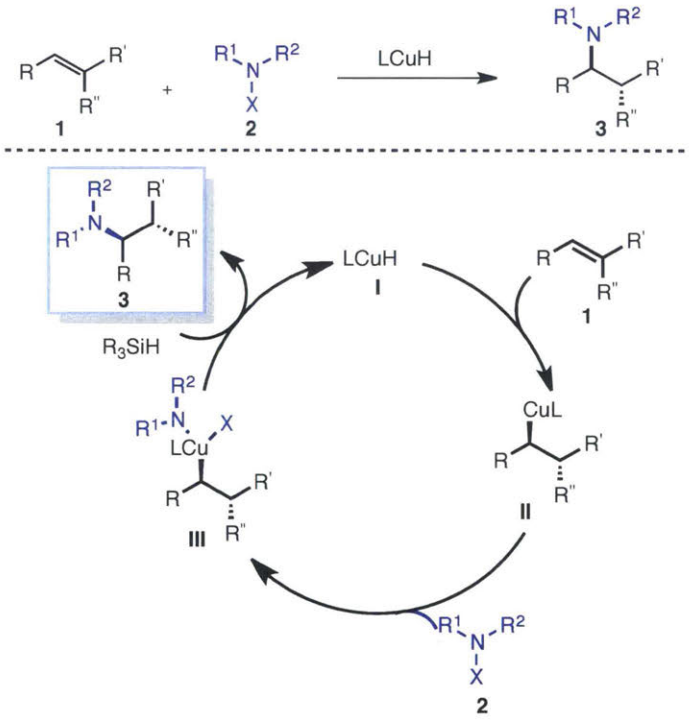


Scheme 4. *Proposed Catalytic Cycle for CuH-Catalyzed Asymmetric Reduction*[5a-e]



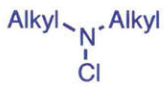
As shown in Scheme 5, we envisioned an approach for asymmetric intermolecular hydroamination that would include a hydrocupration process to generate an alkyl-copper complex (**II**).[9] An electrophilic amine synthon (**3**) could then intercept this alkyl-copper complex via an oxidative addition to provide Cu(III) intermediate (**III**). Reductive elimination and transmetalation would follow to regenerate CuH (**I**) while providing chiral amine product **3**.[5a,10]

Scheme 5. *Our Strategy Towards CuH-Catalyzed Asymmetric Hydroamination*

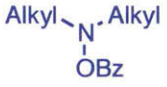


Two classes of electrophilic alkylamine reagents, *N,N*-disubstituted-*N*-chloroamines (**A**) and *N,N*-disubstituted-*O*-benzoylhydroxylamines (**B**), were attractive to us due to the versatility of substitution on the amines (Figure 2).[6-8] *O*-benzoylhydroxylamine electrophiles (**B**) were previously observed to undergo purported oxidative addition with copper,[6] where as *N*-chloroamines (**A**) have only been shown to undergo oxidative addition with nickel.[8] Additionally, it is known that more basic Cu-carboxylate species, generated from the use of the benzyloxyamines (**B**), undergo facile transmetalation with silane reagents,[9] whereas copper(I) chloride species, generated from a chloroamine reagent (**B**), would require transformation to a more basic species before transmetalation with a silane could occur.

Figure 2. *Alkyl,Alkyl-Substituted Electrophilic Amine Reagents*



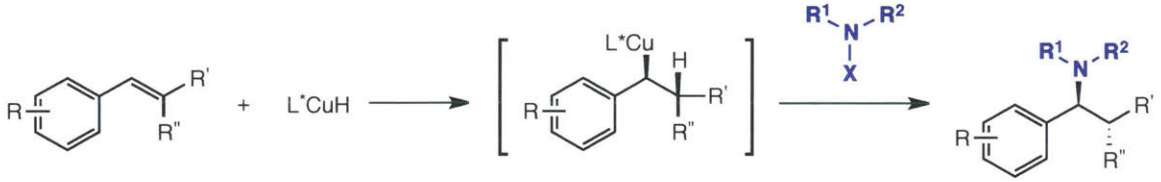
A



B

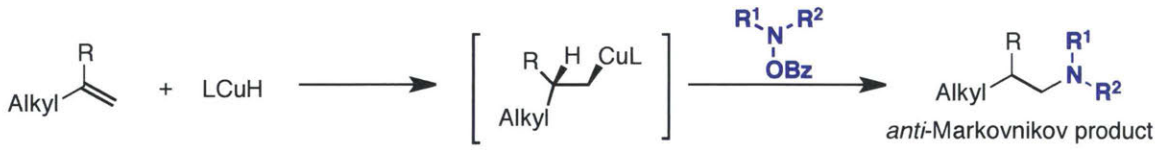
We envisioned applying these strategies towards activated olefins such as styrenes. It was postulated that the intermolecular hydroamination of styrenes would proceed regioselectively to afford Markovnikov products as there is an electronic advantage for the copper to form a benzylic-Cu intermediate (Scheme 6). We note that Marder has previously reported calculations on the regiochemistry of insertion reactions of styrenes in an analogous borylcupration process, which supports the formation of a benzylic-Cu intermediate.[13]

Scheme 6. *Proposed Regioselectivity for CuH-Catalyzed Hydroamination of Styrene Derivatives*



For terminal aliphatic alkenes, we proposed that the reaction would proceed to give the anti-Markovnikov regioselectivity. This is because the hydride migration from the copper catalyst should proceed to form the less sterically crowded terminal copper intermediate (Scheme 7) since there is no electronic advantage. Thus, we expected the steric property of the substrate to control the regioselectivity of hydrocupration.

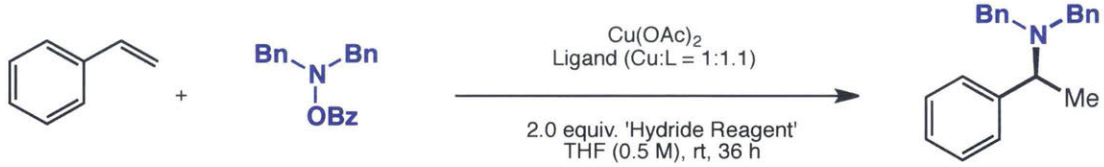
Scheme 7. *Proposed Regioselectivity for Copper-Catalyzed Hydroamination of Terminal Aliphatic Alkene*



2.2 Results and Discussion

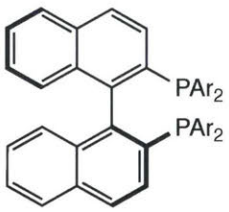
We began our investigation by attempting the hydroamination of styrene (**1a**) using readily available $Cu(OAc)_2$ (Table 1). As previously discussed, *O*-benzoylhydroxylamine electrophiles were previously shown to be efficient for copper-catalysis.[6] We chose to employ electrophilic amine reagent **2a** for our initial screening. We investigated common hydride reagents using BINAP (**L1**), a ligand previously shown to be effective toward our Cu-catalyzed asymmetric reduction chemistry (entry 1-3).[5a-c]

Table 1. *Reaction Optimization*

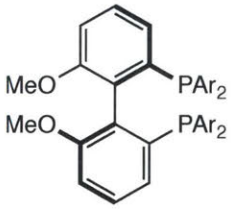


1a (1.0 equiv) + **2a** (1.2 equiv) → **3a**

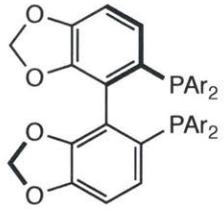
Entry	$Cu(OAc)_2$	Hydride Reagent	L	Yield 4a[a]	ee
1	10 mol%	HBpin	L1	2%	nd[b]
2	10 mol%	PMHS	L1	40%	-74%
3	10 mol%	DEMS	L1	64%	-73%
4	10 mol%	DEMS	L2	83%	-65%
5	10 mol%	DEMS	L3	99%	-95%
6	10 mol%	DEMS	L4	99%	79%
7	10 mol%	DEMS	L5	99%	97%
8[c]	2 mol%	DEMS	L5	97%	97%



Ar = Ph
(*S*)-BINAP (**L1**)
Ar = *p*-Tol
(*S*)-p-Tol-BINAP (**L2**)



Ar = 3,5-*t*-Bu-C_6H_4
(*S*)-3,5-*t*-Bu-MeO-BIPHEP (**L3**)



Ar = Ph
(*R*)-SEGPHOS (**L4**)
Ar = 3,5-*t*-Bu-4-MeOC_6H_2
(*R*)-DTBM-SEGPHOS (**L5**)

[a]GC yields with dodecane as the internal standard. [b]Not determined. [c]Reaction was carried out at 40 °C.

This study of hydride reagents showed silyl hydrides to be proficient for CuH generation, while borohydrides yielded only trace amounts of product (entry 1–3). We found that using polymethylhydosiloxane (PMHS), the hydride reagent shown to be superior for our copper-catalyzed asymmetric conjugate reduction chemistry,[5a-c] in combination with *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**), we were able to generate the desired Markovnikov addition product in good level of enantioselectivity, albeit in moderate yield after 36 hours (entry 2). We proposed that a more reactive hydride reagent could enhance the rate of transmetalation to regenerate the copper hydride species and consequently leads to an increase in reaction rate as well as allows for a decrease in catalyst and hydride reagent loading. Indeed, diethoxymethylsilane (DEMS) proved to be more reactive than its polymeric counterpart (PMHS) (entry 3). We were discouraged from examining more reactive hydride reagents such as trialkoxysilanes due to their tendency to disproportionate to the pyrophoric silane gas SiH_4.[17]

Next, we studied the effect of the ligands on the reaction efficiency as well as the enantioselectivities. When BINAP (**L1**) was used as the supporting ligand, the reaction generated the desired product in 64% yield (entry 3). The yield was increased to 83% when *p*-Tol-BINAP (**L2**) was employed. We found that near quantitative yields were achieved using BIPHEP-type ligand **L3** and SEGPHOS-type ligands **L4** and **L5**. The enantiomeric excess of the product increased as the steric bulk of the supporting ligand was increased to the bulkier 3,5-*t*-Bu-MeOBIPHEP (**L3**) (entry 5). The enantiomeric excess was also improved by switching from SEGPHOS (**L4**) to a bulkier DTBM-SEPHOS ligand (**L5,** entry 6 versus 7). Although the level of enantiomeric excess was similar for 3,5-*t*-Bu-MeOBIPHEP (**L3**, entry 5) when compared to DTBM-SEGPHOS (**L5,** entry 7), we pursued **L5** due to its lower cost. We believe that the larger ligand cone angle as a result of the *ortho* substituents on the phosphine provide a more restrictive chiral pocket, which was necessary for high levels of enantioselectivity.

Further optimization revealed that the reaction proceeded with low catalyst loading (2 mol%) at 40 °C (entry 8) without diminishing the yield or enantioselectivity. Regioselectivity was excellent as the reaction exclusively generated α-branched amines, consistent with our proposal that the hydride migration from the copper catalyst to the alkene would generate the more stable benzylic Cu species.[12,13]

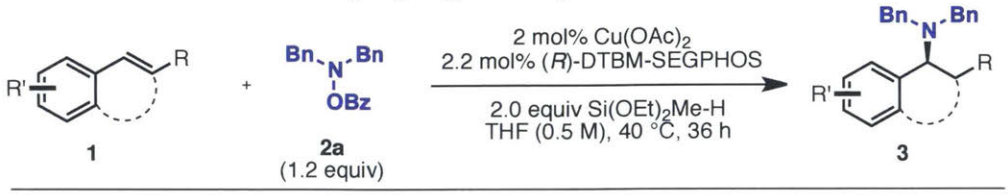
With the optimized protocol in hand, we then explored the substrate scope with respect to the styrene component (Table 2). The hydroamination reaction tolerates a variety of electron

withdrawing substituents on styrene, including fluorides (**3b**), chlorides (**3c**), and trifluoromethyl groups (**3d**) as well as electron-donating groups (**3f**). The reaction also tolerates *ortho*-substituents (**3c** and **3e**) and vinyl naphthalene (**3g**), albeit at a slightly diminished level of enantioselectivity.

As previously mentioned, a persisting challenge for late transition-metal catalyzed hydroamination is incompatibility with β-substitution.[2j-l] Thus, we pursued the hydroamination of β-substituted styrenes. We found that the reaction works efficiently with both *trans*- and *cis*-β-substituted styrenes (**3h–3o**). However, *trans*-β-substituted styrenes afforded the desired products at higher levels of enantioselectivity than their *cis* counterparts Additionally, we found that our system is compatible with hindered β-disubstituted styrenes with the desired product generated in high yield and *ee* (**3p–3q**). Notably, the hydroamination of β-disubstituted styrene **1q** gave the product **3q** as a single diastereomer.

We believed that under our Cu-catalyzed hydroamination strategy, β-substituents are tolerated as the reaction proceeds via a benzylic-Cu intermediate (Scheme 6). For the palladium-catalyzed approach as reported by Hartwig, Hii, and Lin (Scheme 1), a Wacker-type mechanism is proposed.[2j-l] With this mechanism, an intermediate where palladium is bounded at the β-position is generated (Scheme 8). With the reaction going through β-Pd-bound intermediate **i**, it is expected that β-substituents could significantly impede the reaction of these substrates.

Table 2. *Scope of Different Styrene Derivatives* [a]



■ Substrate Scope: Styrenes

3a
91% yield, 96% *ee*

3b
86% yield, 97% *ee*

3c[b]
86% yield, 92% *ee*

3d[b]
88% yield, 95% *ee*

3e
80% yield, 91% *ee*

3f
89% yield, >99% *ee*

3g
86% yield, 95% *ee*

■ Substrate Scope: β–Substituted Styrene

Trans:

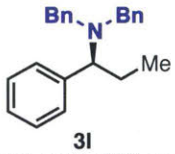
3h
98% yield, 99% *ee*

3i
93% yield, 99% *ee*

3j
92% yield, 99% *ee*

3k
95% yield, 98% *ee*

Cis:



3l
88% yield, 97% *ee*

3m
94% yield, 88% *ee*

3n
84% yield, 97% *ee*

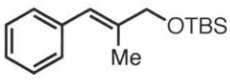
3o
87% yield, 86% *ee*

■ Substrate Scope: β–Disubstituted Styrene

3p[c]
77% yield, >99% *ee*

3q[c]
83% yield, >99% *ee*
(single diastereomer)

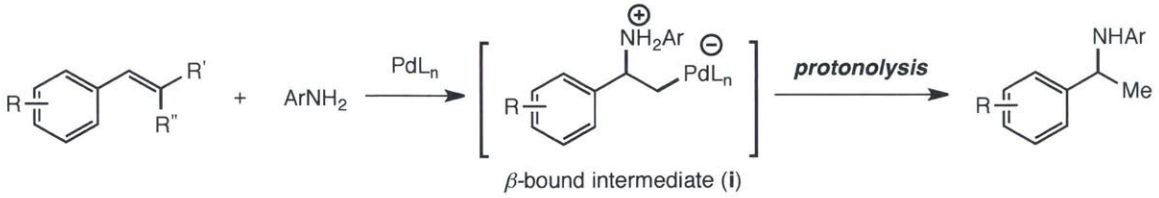
3q from:



1q

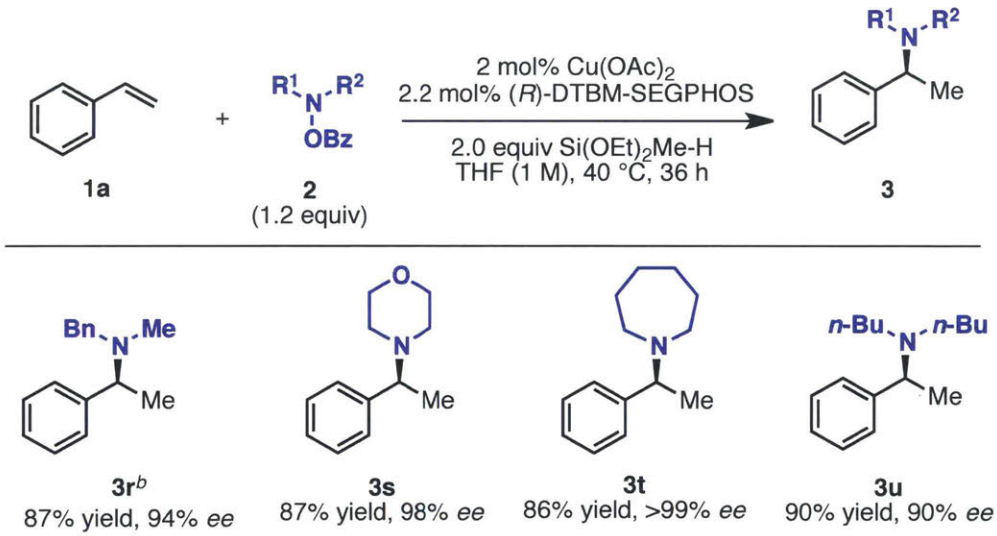
[a]Isolated yields (average of two runs). **2** (1 mmol), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (1.2 mmol), $Cu(OAc)_2$ (2 mol %), (*R*)-DTBM-SEGPHOS (2.2 mol %), diethoxymethylsilane (2 mmol), THF (0.5 M), 40 °C, up to 36 h. [b]$Cu(OAc)_2$ (4 mol %), (*R*)-DTBM-SEGPHOS (4.4 mol %). [c]THF (1 M).

Scheme 8. *Proposed Intermediate for Palladium-Catalyzed Approach*



We next explored the use of other electrophilic amine reagents. It was observed that these conditions are amenable to several alkyl- and dialkyl-*N*-OBz amines (Table 3). *N*-(OBz)azepane (**3t**) and other heterocyclic-*N*-OBz (**3s**) amines also furnished the respective hydroamination products in high yields and enantioselectivities.

Table 3. *Scope of Amine Electrophiles with Styrene*[a]

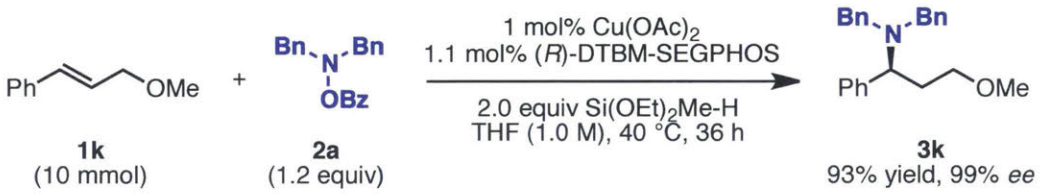


[a]Isolated yields (average of two runs). **2** (1 mmol), *O*-benzoylhydroxylamine (1.2 mmol), $Cu(OAc)_2$ (2 mol %), (*R*)-DTBM-SEGPHOS (2.2 mol %), diethoxymethylsilane (2 mmol), THF (1 M), 40 °C, up to 36 h. [b]THF (0.5 M).

As a demonstration of the robustness and practicality of this method, the hydroamination reaction was carried out at a 10-mmol scale (Scheme 9). We ran the reaction using ((*E*)-(3-

methoxyprop-1-en-1-yl)benzene) (**1k**) because β-substituted styrenes are known to be difficult substrates in asymmetric hydroamination reactions.[2] We were able to lower the catalyst loading to 1 mol% with no decrease in yield or enantioselectivity of the desired product dibenzylamine **3k**.

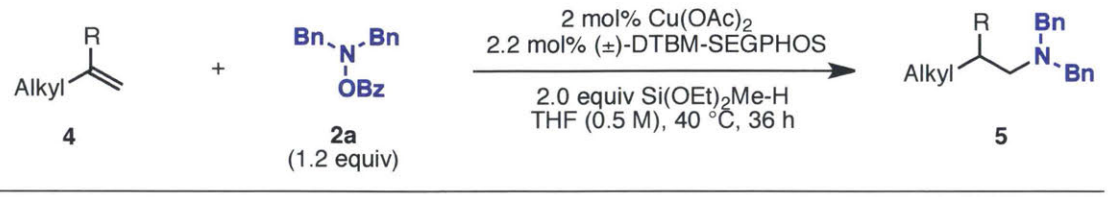
Scheme 9. *Large-scale Hydroamination Reaction of β–substituted Styrene*

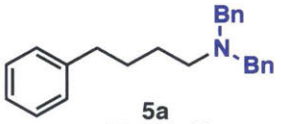


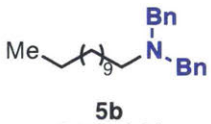
Since the hydroamination of unactivated alkenes remained a challenge, we next investigated the developed protocol with aliphatic alkenes. This began with the use of mono-substituted terminal aliphatic alkenes. These transformations were carried out under the conditions initially developed for the copper-catalyzed hydroamination of styrenes. Using readily available $Cu(OAc)_2$ and *O*-benzoylhydroxylamine **2a**, we found that terminal aliphatic alkenes effectively underwent hydroamination reaction to afford alkyl amines (**5**) (Table 4).

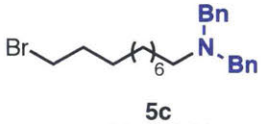
As Table 4 illustrates, the reactions proceed to generate the anti-Markovnikov addition products exclusively. This protocol tolerated alkenes containing primary alkyl bromides (**5c**), epoxides (**5g**), sulfonamides (**5d**), amides (**5e**), pyridines (**5f**), and *tert*-butyldimethylsilyl ethers (**5i**). Additionally, we found that the reaction is compatible with geminally disubstituted aliphatic alkenes (**5h** and **5i**). The compatibility of this methodology with 1,1-disubstituted alkenes was of paramount significance as this implied that this method could potentially be applied towards the synthesis of β-chiral amines.[16]

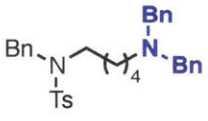
Table 4. *Hydroamination of Terminal Aliphatic Alkenes*[a]

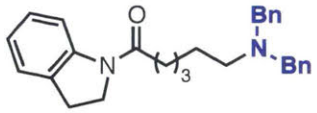


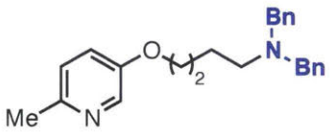

5a
89% yield

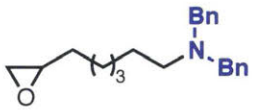

5b
94% yield

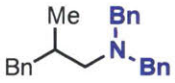

5c
90% yield

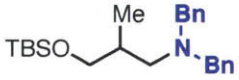

5d
95% yield


5e
88% yield


5f
92% yield


5g
90% yield

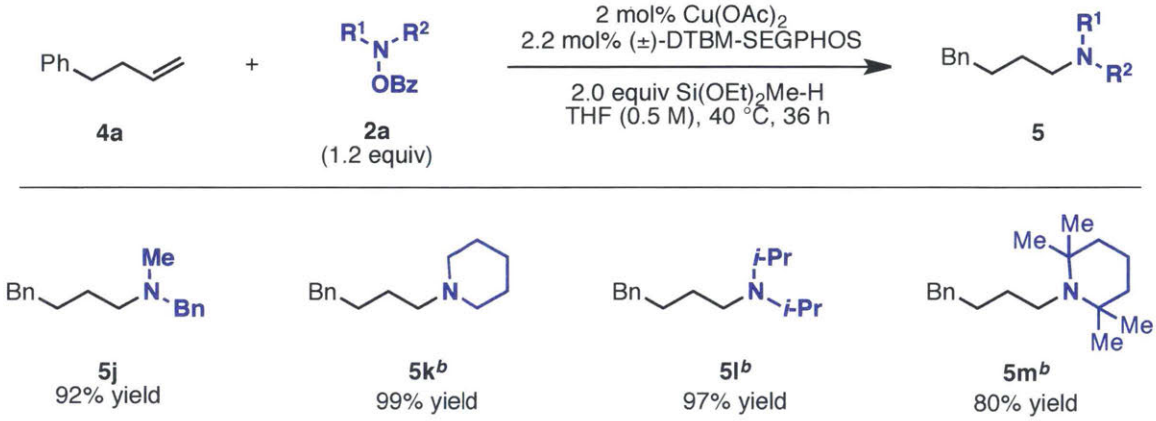

5h[b]
89% yield


5i[b]
87% yield

[a]Isolated yields (average of two runs). **4** (1 mmol), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (1.2 mmol), $Cu(OAc)_2$ (2 mol %), (±)-DTBM-SEGPHOS (2.2 mol %), diethoxymethylsilane (2 mmol), THF (0.5 M), 40 °C, up to 36 h. [b]THF (1 M).

We next explored the use of other amine electrophiles and found this reaction to tolerate several alkyl- and dialkyl-*N*-OBz amines (Table 5). Cyclic *O*-benzoylhydroxyamine (**5k**), as well as sterically hindered diisopropyl *O*-benzoylhydroxyamine (**5l**), and tetramethylpiperidine *O*-benzoylhydroxyamine (**5m**) furnished their respective anti-Markovnikov hydroamination products in high yield.

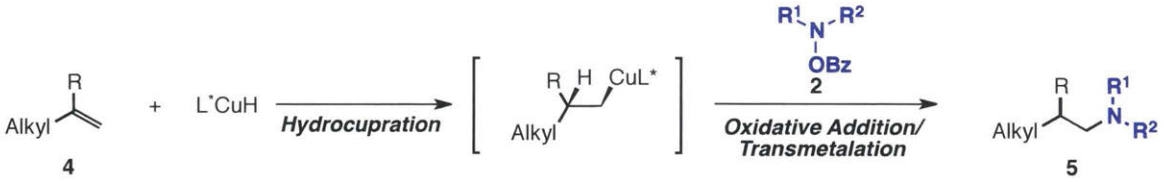
Table 5. *Scope of Amine Electrophiles with 4-Phenyl-1-butene*[a]



[a]Isolated yields (average of two runs). **2** (1 mmol), *O*-benzoylhydroxylamine (1.2 mmol), $Cu(OAc)_2$ (2 mol %), (±)-DTBM-SEGPHOS (2.2 mol %), DEMS (2 mmol), THF (1 M), 40 °C, up to 36 h. [b]THF (0.5 M).

Counter to the styrenes, our hypothesis for the observed anti-Markovnikov selectivity is that the hydride migration from the copper catalyst proceeds to form the less sterically crowded terminal copper intermediate as there is no electronic advantage to form the secondary alkyl-Cu intermediate (Scheme 6). Oxidative addition of the *O*-benzoylhydroxylamine (**2**) and subsequent reductive elimination of this terminal organocuprate would generate the unbranched tertiary amine (**5**).

Scheme 6. *Anti-Markovnikov Hydroamination of Aliphatic Alkenes*



2.3 Conclusion

In summary, a copper-catalyzed hydroamination strategy applicable towards activated and unactivated olefins has been developed. We have reported a mild method for synthesizing chiral tertiary amines by employing an asymmetric copper-catalyzed hydroamination of styrenes. Substitution occurs in a regioselective manner to generate a C–N bond at the α-position of styrene derivatives. This method has been shown to be compatible with various substituents on the aryl ring as well as styrenes with β–substitution. Additionally, we have reported the first anti-Markovnikov hydroamination of unactivated olefins via a copper-catalyzed hydroamination strategy. This method tolerates a wide range of functional groups on the alkene and was compatible with heterocyclic as well as sterically hindered electrophilic amine reagents. Investigations into expanding the scope of this transformation towards the synthesis of β-chiral amines has been carried out in our lab.[16] The optimization and development of this transformations towards additional classes of alkenes will be described in the following chapters.

2.4 Experimental

I. General Information

General Reagent Information

Unless otherwise stated, all reactions were set-up on the bench top and carried out under an argon atmosphere. All solvents were purified and dried by passage through successive alumina and Q5 reactant-packed columns on a solvent purification system. Diethoxymethylsilane was purchased from TCI America and stored under nitrogen at 4 °C in a Schlenk flask (diethoxymethylsilane is moisture sensitive, and proper Schlenk technique was used for handling this reagent. *O*-benzoyl-*N,N*-dialkylhydroxylamines were synthesized according to a published procedure.[5b] Styrene reagents, amines, benzoyl peroxide, and copper(II)acetate were purchased from Frontier Scientific, Combi-Blocks, GFS chemicals, Ark Pharm, Alfa Aesar, Sigma-Aldrich, or Strem Chemicals, and were used as received. DTBM-SEGPHOS (L5) was purchased from Takasago. Ligands L1 – L4 were purchased from Strem Chemicals. Compounds were purified using Silicycle SiliaFlashP60 (230-400 mesh) silica gel on a Biotage SP4 instrument.

General Analytical Information

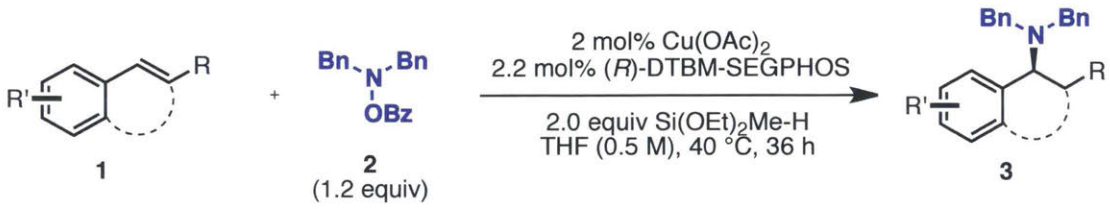
All compounds (starting materials and products) were characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR (when applicable), IR spectroscopy, melting point (when applicable), and elemental analysis or mass spectrometry. The ^{1}H, ^{13}C, and ^{19}F NMR spectra can be found in Section III of the supporting information. ^{1}H, ^{13}C, ^{31}P, and ^{19}F NMR spectra were recorded on Varian 300 MHz, Varian 500 MHz or Bruker 400 MHz spectrometers. The spectra were calibrated according to residual solvent peaks ($CDCl_3$: 7.26 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR; CD_2Cl_2: 5.32 ppm for ^{1}H NMR and 53.84 ppm for ^{13}C NMR), or an internal reference (CF_3Ph: -63.7 ppm for ^{19}F). The ^{13}C, and ^{31}P NMR spectra were obtained with ^{1}H decoupling, and the ^{19}F NMR spectra were obtained without ^{1}H decoupling. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m= multiplet, br = broad, app = apparent. IR spectra were obtained on a Thermo Scientific iD5 ATR Nicolet iS5 FT-IR spectrometer. Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, GA. ESI-MS spectra were recorded on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. Gas

chromatographic (GC) analyses were performed on an Agilent 7890A instrument (FID detector) using a J&W DB-1 column (10m, 0.1 mm I.D.). Reactions were monitored by GC and thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) or Fluka aluminum oxide/TLC-cards using UV light, I_2, or by treatment with a solution of phosphomolybdic acid in ethanol followed by heating to assist in visualization. High pressure liquid chromatography (HPLC) was performed on Hewlett-Packard 1100 Series chromatographs using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL. For *N*-(1-phenylethyl)amine (**3r**, **u**), the enantiomeric excesses were determined by ^{1}H NMR analysis using our previously published procedure.[12]

II. Experimental Procedures and Characterization Data

A) Cu-Catalyzed Hydroamination of Alkenes

General Procedure for Cu-Catalyzed Hydroamination of Styrenes.



$Cu(OAc)_2$ (3.6 mg, 2 mol%) and (*R*)-DTBM-SEGPHOS (25.9 mg, 2.2 mol%) were added to a screw-cap test tube. The tube was then sealed evacuated and backfilled with Argon. The process was repeated for a total of three times. Anhydrous THF (2.0 mL, 0.5 M) was added. The mixture was stirred for 15 min, then diethoxymethylsilane (270 mg, 320 μL, 2.0 equiv.) was added dropwise and the stirring was continued for another 10 min at rt before being added by a syringe to another screw-cap test tube containing styrene (104 mg, 1.0 mmol, 1.0 equiv.) and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv.). The reaction tube was stirred at 40°C for 36 h. Dodecane (100 μL) was added as the internal standard for GC analysis. The reaction mixture was diluted with EtOAc, quenched with saturated aqueous Na_2CO_3 solution, extracted with EtOAC, dried over Na_2SO_4, filtered through a pad of silica, concentrated, and purified by column chromatography on silica gel.

3a

(*S*)-*N*,*N*-dibenzyl-1-phenylethan-1-amine (Table 2, entry **3a**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, styrene (104 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a liquid in 95% and 86% yield. IR (thin film) 3028, 2820, 1493, 1452, 1123, 1027, 742, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.46 – 7.18 (m, 15H), 3.94 (q, J = 6.9 Hz, 1H), 3.63 (d, J = 14.0 Hz, 2H), 3.48 (d, J = 13.6

Hz, 2H), 1.46 (d, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.86, 140.56, 128.77, 128.31, 128.15, 128.08, 126.85, 126.83, 56.30, 53.71, 13.91. HRMS (DART-TOF) calculated for $C_{22}H_{23}N$ $[M+H]^+$ m/z 302.1903, found 302.1901. Anal. Calcd. for $C_{22}H_{23}N$: C, 87.66; H, 7.69. Found: C, 87.64; H, 7.79. $[\alpha]_D^{25}$ = –97.1 (c = 1.29, $CHCl_3$); HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 4.8 minutes, t_R (minor) = 5.4 minutes.

3b

(*S*)-*N*,*N*-dibenzyl-1-(4-fluorophenyl)ethan-1-amine (Table 2, entry **3b).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, 4-fluorostyrene (122.1 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a liquid in 86% and 85% yield. IR (thin film) 1602, 1506, 1453, 1221, 807, 740, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44 – 7.37 (m, 6H), 7.36 – 7.30 (m, 4H), 7.28 – 7.21 (m, 2H), 7.05 (t, J = 8.7 Hz, 2H), 3.93 (q, J = 6.9 Hz, 1H), 3.60 (d, J = 13.8 Hz, 2H), 3.49 (d, J = 13.8 Hz, 2H), 1.45 (d, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 161.84 (d, J = 244.6 Hz), 140.37, 138.72 (d, J = 3.0 Hz), 129.54 (d, J = 7.8 Hz), 128.75, 128.36, 126.95, 114.80 (d, J = 20.9 Hz), 55.53, 53.60, 13.49; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -116.43; HRMS (ESI-TOF) calculated for $C_{22}H_{22}FN$ $[M+H]^+$ m/z 320.1809, found 320.1807. Anal. Calcd. for $C_{26}H_{25}N$: C, 82.72; H, 6.94. Found: C, 82.54; H, 6.82. $[\alpha]_D^{25}$ = –79.6 (c = 1.10, $CHCl_3$); HPLC analysis (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 4.8 minutes, t_R (minor) = 5.5 minutes.

3c

(*S*)-*N*,*N*-dibenzyl-1-(2-chlorophenyl)ethan-1-amine (Table 2, entry **3c).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, 2-chlorostyrene (138.6 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a white solid in 79 % and 92%

yield. m.p. 67-68°C. IR (thin film, $CHCl_3$) 3025, 2802, 1493, 1453, 1367, 1035, 746, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.78 (dd, J = 7.8, 1.7 Hz, 1H), 7.48 – 7.41 (m, 5H), 7.41 – 7.33 (m, 5H), 7.33 – 7.27 (m, 2H), 7.27 – 7.21 (m, 1H), 4.51 (q, J = 6.8 Hz, 1H), 3.84 (d, J = 14.1 Hz, 2H), 3.69 (d, J = 14.2 Hz, 2H), 1.45 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.12, 140.30, 134.17, 129.84, 128.85, 128.14, 127.95, 126.77, 126.76, 56.79, 54.96, 18.15; HRMS (DART-TOF) calculated for $C_{22}H_{22}ClN$ $[M+H]^+$ m/z 336.1514, found 336.1513. Anal. Calcd. for $C_{22}H_{22}ClN$: C, 78.67; H, 6.60. Found: C, 78.64; H, 6.71. $[\alpha]_D^{25}$ = +53.0 (c = 1.13, $CHCl_3$); HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (major) = 5.2 minutes, t_R (minor) = 5.8 minutes.

3d

(*S*)-*N*,*N*-dibenzyl-1-(4-(trifluoromethyl)phenyl)ethan-1-amine (Table 2, entry **3d).** Prepared following the general procedure using 4 mol% $Cu(OAc)_2$, 4.4% (*R*)-DTBM-SEGPHOS, 4-(trifluoromethyl)styrene (172.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a liquid in 92% and 84% yield. IR (thin film) 3028, 2973, 2804, 1323, 1162, 1120, 1069, 1016, 737, 696 1453, 1367, 1035, 843, 746, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.72 – 7.64 (m, 2H), 7.64 – 7.58 (m, 2H), 7.50 – 7.43 (m, 4H), 7.42 – 7.35 (m, 4H), 7.35 – 7.29 (m, 2H), 4.05 (q, J = 6.8 Hz, 1H), 3.68 (d, J = 13.8 Hz, 2H), 3.58 (d, J = 13.8 Hz, 2H), 1.53 (d, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 147.45 (q, J = 1.3 Hz), 140.08, 129.07 (q, J = 32.2 Hz), 128.76, 128.45, 128.33, 127.09, 125.05 (q, J = 3.8 Hz), 124.52 (q, J = 272.7 Hz), 56.02, 53.76, 13.16; ^{19}F NMR (376 MHz, $CDCl_3$) δ: -62.11; HRMS (ESI-TOF) calculated for $C_{23}H_{22}F_3N$ $[M+H]^+$ m/z 370.1777, found 370.1775. Anal. Calcd. for $C_{23}H_{22}F_3N$: C, 74.78; H, 6.00. Found: C, 74.81; H, 6.14. $[\alpha]_D^{25}$ = –93.8 (c = 1.12, $CHCl_3$); HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 95% ee: t_R (major) = 4.8 minutes, t_R (minor) = 6.5 minutes.

3e

(*S*)-*N*,*N*-dibenzyl-1-(*o*-tolyl)ethan-1-amine (Table 2, entry **3e**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, 2-methylstyrene (118.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a white solid in 85% and 74% yield. m.p.: 83.5-84.0 °C. IR (thin film, $CHCl_3$) 3026, 2970, 2801, 1739, 1494, 1453, 1377, 741, 677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.54 (d, J = 7.5 Hz, 1H), 7.33 – 7.29 (m, 8H), 7.28 – 7.18 (m, 3H), 7.18 – 7.15 (m, 2H), 4.14 (q, J = 6.8 Hz, 1H), 3.68 (d, J = 13.6 Hz, 2H), 3.63 (d, J = 13.7 Hz, 2H), 2.19 (s, 3H), 1.44 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.22, 140.38, 137.27, 130.69, 129.15, 128.11, 127.19, 126.79, 126.68, 125.60, 54.95, 54.50, 19.55, 14.44; HRMS (ESI-TOF) calculated for $C_{23}H_{25}N$ $[M+H]^+$ m/z 316.2060, found 316.2057. Anal. Calcd. for $C_{23}H_{25}N$: C, 87.57; H, 7.99. Found: C, 87.68; H, 7.96. $[\alpha]_D^{25}$ = +34.8 (c = 0.92, $CHCl_3$); HPLC analysis (OJ, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (major) = 6.2 minutes, t_R (minor) = 8.7 minutes.

3f

(*S*)-*N*,*N*-dibenzyl-1-(4-methoxyphenyl)ethan-1-amine (Table 2, entry **3f**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, 4-vinylanisole (134.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 5-10% EtOAc in hexane to provide the title compound as a liquid in 89% and 88% yield. IR (thin film) 3025, 2960, 2833, 1510, 1244, 1176, 1028, 832, 739, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.47 – 7.39 (m, 4H), 7.39 – 7.30 (m, 6H), 7.28 – 7.20 (m, 2H), 6.93 (d, J = 8.7 Hz, 2H), 3.92 (q, J = 6.9 Hz, 1H), 3.85 (s, 3H), 3.63 (d, J = 13.8 Hz, 2H), 3.49 (d, J = 13.9 Hz, 2H), 1.45 (d, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.46, 140.64, 134.84, 129.14, 128.74, 128.28, 126.81, 113.39, 55.55, 55.28, 53.58, 13.96; HRMS (DART-TOF) calculated for $C_{23}H_{25}NO$ $[M+H]^+$ m/z 332.2009, found 332.2006. Anal. Calcd. for $C_{23}H_{25}NO$: C, 83.34; H, 7.60. Found: C, 83.28; H, 7.60. $[\alpha]_D^{25}$ = –117.3 (c = 0.93, $CHCl_3$); HPLC analysis (OJ, 10% IPA/hexane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R

(major) = 9.0 minutes, t_R (minor) = 17.9 minutes.

3g

(*S*)-*N*,*N*-dibenzyl-1-(naphthalen-2-yl)ethanamine (Table 3, entry **3g).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, 2-vinylnapthalene (154 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a colorless crystal in 83% and 89% yield. m. p. 123~124 °C. IR (thin film) 3057, 3024, 2968, 1500, 1453, 1379, 1124, 857, 819, 582, 579, 560, 557 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.90 (dd, J = 7.6, 3.3 Hz, 3H), 7.85 – 7.80 (m, 1H), 7.72 (dd, J = 8.5, 1.7 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.48 (m, 4H), 7.38 (m, 4H), 7.32 – 7.26 (m, 2H), 4.16 (q, J = 6.8 Hz, 1H), 3.70 (d, J = 13.6 Hz, 2H), 3.63 (d, J = 13.6 Hz, 2H), 1.61 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.83, 140.52, 133.28, 132.71, 128.86, 128.34, 128.02, 127.67, 127.31, 126.91, 126.10, 125.94, 125.64, 56.35, 53.76, 13.24. HRMS (DART-TOF) calculated for $C_{26}H_{25}N$ $[M+H]^+$ m/z 352.2060, found 352.2059. Anal. Calcd. for $C_{26}H_{25}N$: C, 87.57; H, 7.99. Found: C, 87.45; H, 8.16. $[\alpha]_D^{25}$ = – 149.63 (c = 1.00, $CHCl_3$); HPLC analysis (OJ, 10% IPA/hexane, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 10.9 minutes, t_R (minor) = 36.2 minutes.

3h, 3l

(*S*)-*N*,*N*-dibenzyl-1-phenylpropan-1-amine (Table 2, entry **3h & 3l).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, *trans*-β-methylstyrene or *cis*-β–methylstyrene (118.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a liquid. 97% and 98% yields from *trans*-β-methylstyrene; 89% and 87% from *cis*-β-methylstyrene. IR (thin film) 3025, 2960, 2930, 2800, 1493, 1452, 1027, 739, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.47 – 7.39 (m, 6H), 7.35 (t, J = 7.5 Hz, 5H), 7.30 – 7.23 (m, 4H), 3.87 (d, J = 13.8 Hz, 2H), 3.64 (t, J = 7.5 Hz, 1H), 3.20 (d, J = 13.9 Hz, 2H), 2.12 (dt, J = 13.7, 7.3 Hz, 1H), 1.96 – 1.75 (m, 1H), 0.97 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ:

140.56, 139.08, 129.07, 128.80, 128.25, 127.95, 126.98, 126.75, 63.83, 53.74, 24.31, 11.81; HRMS (DART-TOF) calculated for $C_{23}H_{25}N$ $[M+H]^+$ m/z 316.2060, found 316.2053. Anal. Calcd. for $C_{23}H_{25}N$: C, 87.57; H, 7.99. Found: C, 87.45; H, 8.16. $[\alpha]_D^{25}$ = –112.9 (c = 1.19, $CHCl_3$); HPLC analysis (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee (from *trans*-), 96% ee (from *cis*-): t_R (major) = 4.8 minutes, t_R (minor) = 5.6 minutes.

3i, 3m

(*S*)-*N*,*N*-dibenzyl-1,2-diphenylethan-1-amine (Table 2, entry **3i & 3m).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, *trans*-stilbene or *cis*-stilbene (180.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a white solid. 95% and 94% yields from *trans*-stilbene; 93% and 93% from *cis*-stilbene. m. p. 73.5-74.0 °C. IR (thin film, $CHCl_3$) 3025, 1493, 1452, 1028, 740, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.43 (t, *J* = 7.7 Hz, 2H), 7.38 – 7.21 (m, 16H), 7.14 (d, *J* = 7.7 Hz, 2H), 4.11 (t, *J* = 7.7 Hz, 1H), 3.94 (d, *J* = 13.9 Hz, 2H), 3.44 (dd, *J* = 14.0, 8.4 Hz, 1H), 3.25 (d, *J* = 14.0 Hz, 2H), 3.13 (dd, *J* = 14.0, 6.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.10, 139.96, 138.57, 129.69, 129.17, 128.76, 128.28, 128.13, 128.07, 127.26, 126.83, 126.04, 63.32, 53.69, 37.75; HRMS (DART-TOF) calculated for $C_{28}H_{27}N$ $[M+H]^+$ m/z 378.2216, found 378.2203. Anal. Calcd. for $C_{28}H_{27}N$: C, 89.08; H, 7.21. Found: C, 89.13; H, 7.29. $[\alpha]_D^{25}$ = –55.7 (c = 0.97, $CHCl_3$); HPLC analysis (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee (from trans-), 88% ee (from cis): t_R (major) = 5.2 minutes, t_R (minor) = 6.5 minutes.

3j

(*S*)-*N*,*N*-dibenzyl-1-(4-methoxyphenyl)propan-1-amine (Table 2, entry **3j).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, trans-anethole (148.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a

colorless liquid in 91% and 92% yield. IR (thin film) 2932, 2832, 1510, 1453, 1247, 1178, 1037, 826, 741, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.56 – 7.46 (m, 4H), 7.45 – 7.35 (m, 4H), 7.35 – 7.27 (m, 2H), 7.27 – 7.20 (m, 2H), 7.04 – 6.95 (m, 2H), 3.91 (d, J = 13.9 Hz, 2H), 3.91 (s, 3H), 3.66 (t, J = 7.5 Hz, 1H), 3.25 (d, J = 13.9 Hz, 2H), 2.16 (dt, J = 13.7, 7.3 Hz, 1H), 1.95 – 1.78 (m, 1H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 158.60, 140.70, 131.22, 130.09, 128.84, 128.29, 126.78, 113.34, 63.17, 55.29, 53.75, 24.55, 11.91; HRMS (DART-TOF) calculated for $C_{24}H_{27}NO$ $[M+H]^+$ m/z 346.2165, found 346.2171. Anal. Calcd. for $C_{24}H_{27}NO$: C, 83.44; H, 7.88. Found: C, 83.58; H, 7.82. $[\alpha]_D^{25}$ = –137.0 (c = 1.95, $CHCl_3$); HPLC analysis (OJ, 10% EtOH/hexane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (major) = 8.3 minutes, t_R (minor) = 23.6 minutes.

3k

(*S*)-*N*,*N*-dibenzyl-3-methoxy-1-phenylpropan-1-amine (Table 2, entry **3k).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, (E)-(3-methoxyprop-1-en-1-yl)benzene (148.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a colorless liquid in 94% and 95% yield. IR (thin film) 2932, 2832, 1493, 1452, 1113, 739, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.50 – 7.42 (m, 6H), 7.42 – 7.35 (m, 5H), 7.34 – 7.26 (m, 4H), 4.00 – 3.85 (m, 3H), 3.56 – 3.47 (m, 2H), 3.33 (d, J = 0.9 Hz, 3H), 3.23 (d, J = 13.8 Hz, 2H), 2.45 (ddd, J = 13.9, 7.6, 6.4 Hz, 1H), 2.21 – 1.96 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.32, 138.49, 129.05, 128.85, 128.33, 128.10, 127.26, 126.90, 70.58, 58.94, 58.59, 53.82, 31.61; HRMS (DART-TOF) calculated for $C_{24}H_{27}NO$ $[M+H]^+$ m/z 346.2165, found 346.2162. Anal. Calcd. for $C_{24}H_{27}NO$: C, 83.44; H, 7.88. Found: C, 83.17; H, 8.02. $[\alpha]_D^{25}$ = –89.9 (c = 0.91, $CHCl_3$); HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 98% ee (for 1 mmol scale), 99% ee (for 10 mmol scale): t_R (major) = 6.0 minutes, t_R (minor) = 6.7 minutes.

3n

(*S*)-*N*,*N*-dibenzyl-2,3-dihydro-1*H*-inden-1-amine (Table 2, entry **3n).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-

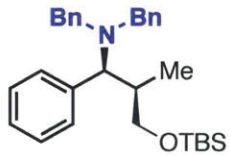
DTBM-SEGPHOS, s indene (116.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF 2 mL for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a white solid in 95% and 73% yield. m. p. 89-90 °C. IR (thin film) 3024, 2934, 2798, 1493, 1452, 1372, 1117, 1027, 742, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.71 – 7.59 (m, 1H), 7.56 (m, 4H), 7.40 (m, 4H), 7.33 – 7.19 (m, 5H), 4.57 (t, *J* = 7.8 Hz, 1H), 3.67 (d, *J*= 13.6 Hz, 2H), 3.50 (d, *J*= 13.6 Hz, 2H), 3.03 (dt, *J* = 16.1, 6.4 Hz, 1H), 2.86 (dt, *J* = 16.3, 8.5 Hz, 1H), 2.21 (tdd, *J* = 8.3, 6.4, 1.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 144.51, 143.69, 140.47, 128.66, 128.33, 127.39, 126.88, 126.48, 124.72, 124.62, 64.65, 54.31, 30.61, 23.46; HRMS (DART-TOF) calculated for $C_{23}H_{23}N$ $[M+H]^+$ m/z 314.1903, found 314.1902. Anal. Calcd. for $C_{23}H_{23}N$: C, 88.13; H, 7.40. Found: C, 87.84; H, 7.31. $[\alpha]_D^{25}$ = –99.4 (c = 1.35, $CHCl_3$); HPLC analysis (OJ, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 5.9 minutes, t_R (minor) = 7.6 minutes.

3o

(*S*)-*N*,*N*-dibenzyl-1,2,3,4-tetrahydronaphthalen-1-amine (Table 2, entry **3o**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, 1,2-dihydronaphthalene (130.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a colorless liquid in 92% and 82% yield. IR (thin film) 2928, 1493, 1452, 1366, 1121, 1027, 973, 740, 696cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.07 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.53 (d, *J* = 7.3 Hz, 4H), 7.38 (dd, *J* = 8.2, 6.9 Hz, 4H), 7.32 – 7.22 (m, 3H), 7.17 (tt, *J* = 7.3, 1.1 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 4.00 (dd, *J* = 10.2, 5.7 Hz, 1H), 3.87 (d, *J* = 13.6 Hz, 2H), 3.54 (d, *J* = 13.6 Hz, 2H), 2.91 – 2.66 (m, 2H), 2.32 – 2.14 (m, 1H), 2.06 (dtt, *J* = 13.7, 5.6, 3.1 Hz, 1H), 1.85 (tdd, *J* = 12.5, 10.1, 2.8 Hz, 1H), 1.76 – 1.58 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.51, 139.20, 138.84, 128.76, 128.69, 128.34, 128.10, 126.88, 126.22, 126.02, 56.45, 53.77, 30.27, 22.37, 20.67; HRMS (DART-TOF) calculated for $C_{24}H_{25}N$ $[M+H]^+$ m/z 328.2060, found 328.2068. Anal. Calcd. for $C_{24}H_{25}N$: C, 88.03; H, 7.70. Found: C, 87.77; H, 7.74. $[\alpha]_D^{25}$ = –77.0 (c = 1.09, $CHCl_3$); HPLC analysis (OJ, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 86% ee: t_R (major) = 5.8 minutes, t_R (minor) = 7.7 minutes.

3p

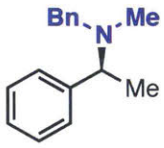
(*S*)-*N*,*N*-dibenzyl-2-methyl-1-phenylpropan-1-amine (Table 2, entry **3p**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, 2-methyl-1-phenylpropene (132.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a colorless liquid in 77% and 76% yield. IR (thin film) 3025, 2955, 1493, 1452, 1092, 1069, 1121, 1028, 761, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.47 (d, J = 7.6 Hz, 4H), 7.42 (t, J = 7.3 Hz, 2H), 7.35 (t, J = 7.5 Hz, 5H), 7.29 – 7.22 (m, 2H), 7.15 (d, J = 6.9 Hz, 2H), 3.93 (d, J = 13.8 Hz, 2H), 3.22 (d, J = 10.9 Hz, 1H), 3.00 (d, J = 13.9 Hz, 2H), 2.54 – 2.35 (m, 1H), 1.31 (d, J = 6.5 Hz, 3H), 0.63 (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.45, 137.03, 129.68, 128.89, 128.37, 127.91, 126.97, 126.82, 69.37, 53.68, 28.68, 21.29, 20.92; HRMS (DART-TOF) calculated for $C_{24}H_{27}N$ $[M+H]^+$ m/z 330.2216, found 330.2216. Anal. Calcd. for $C_{24}H_{25}N$: C, 87.49; H, 8.26. Found: C, 87.29; H, 8.43. $[\alpha]_D^{25} = -114.5$ (c = 1.14, $CHCl_3$); HPLC analysis (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee, single isomer: t_R (major) = 4.7 minutes, t_R (minor) = 6.1 minutes.



3q

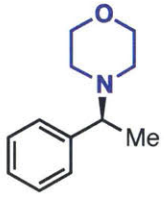
(1*S*,2*R*)-*N*,*N*-dibenzyl-3-((*tert*-butyldimethylsilyl)oxy)-2-methyl-1-phenylpropan-1-amine (Table 2, entry **3q**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, (*E*)-*tert*-butyldimethyl((2-methyl-3-phenylallyl)oxy)silane (262.5 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a colorless solid in 84% and 82% yield. m. p. 93~94 °C. IR (thin film) 2955, 2927, 2855, 1494, 1453, 1257, 1084, 834, 763, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45 – 7.37 (m, 6H), 7.37 – 7.30 (m, 5H), 7.29 – 7.21 (m, 2H), 7.20 – 7.13 (m, 2H), 4.49 (dd, J = 9.8, 3.9 Hz, 1H), 3.93 (d, J = 13.9 Hz, 2H), 3.54 – 3.33 (m, 2H), 3.01 (d, J = 13.9 Hz, 2H), 2.60 – 2.44 (m, 1H), 0.97 (s, 9H), 0.66 (d, J = 6.5 Hz, 3H), 0.12 (d, J = 5.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.05, 135.91, 129.73, 128.72, 128.29, 127.87, 127.04, 126.80, 66.74, 65.63, 53.70, 36.07, 26.14, 18.55, 15.68, -5.13, -5.17.

HRMS (DART-TOF) calculated for $C_{30}H_{41}NOSi$ $[M+H]^+$ m/z 460.3030, found 460.3026. Anal. Calcd. for $C_{30}H_{41}NOSi$: C, 78.38; H, 8.99. Found: C, 78.54; H, 9.01. $[\alpha]_D^{25} = -73.5$ (c = 0.86, $CHCl_3$); HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee, single isomer: t_R (major) = 4.3 minutes, t_R (minor) = 4.9 minutes.



3r

(*S*)-*N*-benzyl-*N*-methyl-1-phenylethanamine (Table 3, entry **3r**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (R)-DTBM-SEGPHOS, styrene (104 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*-benzyl-*N*-methylhydroxylamine (290 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a colorless liquid crystal in 90% and 84% yield. IR (thin film) 2971, 2784, 1494, 1451, 1074, 1028, 761, 735, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.44 (m, 2H) 7.42 – 7.22 (m, 8H), 3.69 – 3.64 (q, *J* = 6.7 Hz, 1H), 3.63 – 3.59 (d, *J* = 13.3 Hz, 1H), 3.35 – 3.32 (d, *J* = 13.3 Hz, 1H), 2.16 (s, 3H), 1.46 – 1.44 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 128.89, 128.31, 128.3, 127.8, 126.9, 126.9, 63.4, 59.0, 38.5, 18.5; HRMS (DART-TOF) calculated for $C_{16}H_{19}N$ $[M+H]^+$ m/z 226.1590, found 226.1582. Anal. Calcd. for $C_{16}H_{19}N$: C, 82.70; H, 11.28. Found: C, 82.64; H, 11.28. $[\alpha]_D^{25} = -15.3$ (c = 1.02, $CHCl_3$); ^1H NMR analysis of the amine and (*R*) and (*S*)-O-acetylmandelic acid indicated 94% ee.



3s

(*S*)-4-(1-phenylethyl)morpholine (Table 3, entry **3s**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (R)-DTBM-SEGPHOS, styrene (104 mg, 1.0 mmol, 1.0 equiv), morpholino benzoate (207.23 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a liquid in 88% and 85% yield. IR (thin film) 2957, 2851, 2803, 1450, 1116, 946, 865, 759, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39 – 7.31 (m, 4H), 7.29 – 7.23 (m, 1H), 3.72 (dd, *J* = 5.3, 4.1 Hz, 4H), 3.33 (q, *J* = 6.7 Hz, 1H), 2.62 – 2.45 (m, 2H), 2.45 – 2.30 (m, 2H), 1.38 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 144.05, 128.33, 127.61, 127.00, 67.22, 65.40, 51.37, 19.96; HRMS (DART-TOF) calculated for $C_{12}H_{17}NO$ $[M+H]^+$ m/z 192.1383, found 192.1381. Anal. Calcd. for $C_{12}H_{17}NO$: C, 75.35; H, 8.96. Found:

C, 75.09; H, 8.81. $[a]_D^{24}$ = –36.5 (c = 0.98, $CHCl_3$); $[a]_D^{25}$ = –41.0 (c = 1.10, EtOH); Literature $[a]_D^{25}$ = –41.6 (c = 1.10, EtOH)[13]. ee: 98%. GC condition: Varian CP7502 column (25 m×0.25 mm×0.25 μm, chiralsil-DEX CB), H2 2.7 mL/min, programmed from 100 °C to 125 °C at 0.5 °C /min; t_R (minor) = 28.41 min, and t_R (major) = 29.24 min.

3t

(*S*)-1-(1-phenylethyl)azepane (Table 3, entry **3t**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, styrene (104 mg, 1.0 mmol, 1.0 equiv), azepan-1-yl benzoate (219 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 20-50% EtOAc in hexane to provide the title compound as a liquid in 86% yield for both runs. IR (thin film) 2922, 1492, 1451, 1128, 909, 762, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.43 – 7.37 (m, 2H), 7.37 – 7.30 (m, 2H), 7.28 – 7.21 (m, 1H), 3.80 (q, *J* = 6.7 Hz, 1H), 2.66 (s, 4H), 1.62 (s, 8H), 1.39 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 144.94, 127.95, 127.60, 126.46, 63.21, 52.06, 28.96, 27.07, 18.26; HRMS (DART-TOF) calculated for $C_{14}H_{21}N$ $[M+H]^+$ m/z 204.1747, found 204.1745. Anal. Calcd. for $C_{14}H_{21}N$: C, 82.70; H, 10.41. Found: C, 82.58; H, 10.47. $[a]_D^{25}$ = +6.5 (c = 1.10, $CHCl_3$); ee>99%. GC condition: Varian CP7502 column (25 m×0.25 mm×0.25 μm, chiralsil-DEX CB), H_2 2.7 mL/min, programmed from 100 °C to 125 °C at 0.5 °C /min; *t*R =35.2 min (minor) and *t*R=35.8 min (major).

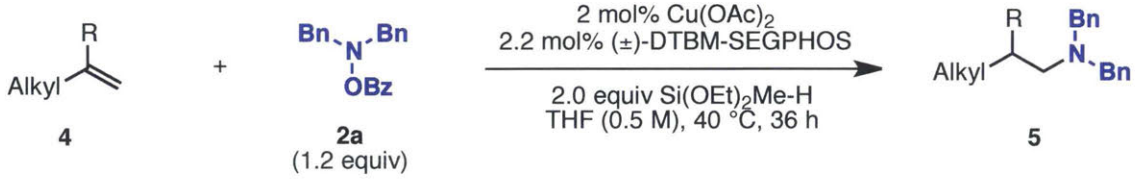
3u

(*S*)-*N*-butyl-*N*-(1-phenylethyl)butan-1-amine (Table 3, entry **3u**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (*R*)-DTBM-SEGPHOS, styrene (104 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*,*N*-dibutylhydroxylamine (249 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was quenched with Na_2CO_3 solution, and the crude product extracted with ethyl acetate (x3) (NB: This step is necessary to remove N-OBz compounds). The reaction was then purified by an acid-base treatment, where the amine was first protonated with dilute HCl solution and the aqueous layer washed with ethyl acetate (x1), then treated with 1 M NaOH to deprotonate the amine. The aqueous layer was then extracted with EtOAc (x3), and the organic combined and concentrated to give the pure product as a yellow liquid in 90% yields (for both runs). IR (thin film) 2955, 2929, 2871, 1452, 1367, 1081, 776, 759, 697, 553

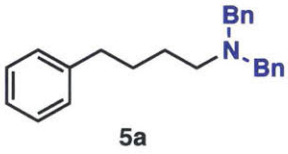
cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.42 (m, 2H), 7.39 – 7.31 (m, 2H), 7.30 – 7.22 (m, 1H), 3.90 (q, J = 6.8 Hz, 1H), 2.58 – 2.47 (m, 2H), 2.42 (m, 2H), 1.54 – 1.41 (m, 4H), 1.38 (m, 3H), 1.36 – 1.18 (m, 4H), 0.92 (t, J = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 145.00, 127.89, 127.76, 126.39, 58.96, 49.65, 30.0, 20.62, 16.49, 14.14; HRMS (DART-TOF) calculated for $C_{24}H_{27}N$ $[M+H]^+$ m/z 234.2216, found 234.2209. Anal. Calcd. for $C_{16}H_{27}N$: C, 83.76; H, 11.10. Found: C, 83.63; H, 11.28. $[\alpha]_D^{25}$ = +2.9 (c = 0.57, $CHCl_3$); ^1H NMR analysis of the amine and (*R*) and (*S*)-O-acetylmandelic acid indicated 90% ee.

B) Cu-Catalyzed Hydroamination of Alkenes

General Procedure for Cu-Catalyzed Hydroamination of Aliphatic Alkenes.



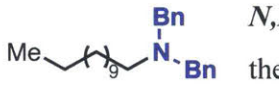
$Cu(OAc)_2$ (3.6 mg, 2 mol%) and (±)-DTBM-SEGPHOS (25.9 mg, 2.2 mol%) were added to a screw-cap test tube. The tube was then sealed evacuated and backfilled with Argon. The process was repeated for a total of three times. Anhydrous THF (2.0 mL, 0.5 M) was added. The mixture was stirred for 15 min, then diethoxymethylsilane (270 mg, 320 μL, 2.0 equiv) was added dropwise and the stirring was continued for another 10 min at rt before being added by a syringe to another screw-cap test tube containing styrene (104 mg, 1.0 mmol, 1.0 equiv) and *O*-benzoyl-*N*, *N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv). The reaction tube was stirred at 40°C for 36 h. Dodecane (100 μL) was added as the internal standard for GC analysis. The reaction mixture was diluted with EtOAc, quenched with saturated aqueous Na_2CO_3 solution, extracted with EtOAC, dried over Na_2SO_4, filtered through a pad of silica, concentrated, and purified by column chromatography on silica gel.



5a

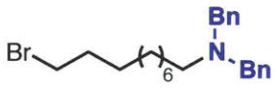
***N,N*-dibenzyl-4-phenylbutan-1-amine** (Table 4, entry **5a**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, but-3-en-1-ylbenzene (132.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% Ether in hexane to provide the title compound as a colorless liquid in 90% and 87% yield. IR (thin film) 2933, 2792, 1494, 1451, 1125, 1027, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.51 – 7.09 (m, 15H), 3.61 (s, 4H), 2.58 (t, J = 7.4 Hz, 2H), 2.51 (t, J = 6.8 Hz, 2H), 1.74 – 1.58 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.74, 140.10, 128.91, 128.52, 128.34, 128.27, 126.87, 125.71, 58.47, 53.20, 35.73, 29.00, 26.65; HRMS

(DART-TOF) calculated for $C_{24}H_{27}N$ $[M+H]^+$ m/z 330.2216, found 330.2215. Anal. Calcd. for $C_{24}H_{27}N$: C, 87.49; H, 8.26. Found: C, 87.48; H, 8.27.



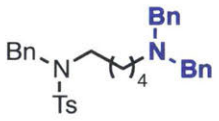
5b

***N,N*-dibenzyldodecan-1-amine** (Table 4, entry **5b**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, dodec-1-ene (168.3 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound as a colorless liquid in 94% and 95% yield. IR (thin film) 2922, 2852, 1494, 1452, 1028, 734, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.60 – 7.09 (m, 10H), 3.58 (s, 4H), 2.43 (t, J = 7.2 Hz, 2H), 1.67 – 1.42 (m, 2H), 1.41 – 1.09 (m, 18H), 0.92 (t, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.11, 128.79, 128.13, 126.71, 58.29, 53.43, 31.97, 29.71, 29.68(3C), 29.54, 29.40, 27.29, 27.00, 22.74, 14.17; HRMS (Dart-TOF) calculated for $C_{26}H_{39}N$ $[M+H]^+$ m/z 366.3155, found 366.3147. Anal. Calcd. for $C_{26}H_{39}N$: C, 85.42; H, 10.75. Found: C, 85.40; H, 10.78.



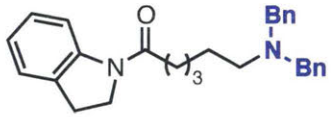
5c

***N,N*-dibenzyl-10-bromodecan-1-amine** (Table 4, entry **5c**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, 10-bromo-1-decene (219.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 5-10% Ethyl acetate in hexane to provide the title compound as a colorless liquid in 89% and 90% yield. IR (thin film) 2925, 2853, 1494, 1452, 742, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.44 – 7.38 (m, 4H), 7.34 (t, J = 7.4 Hz, 4H), 7.28 (s, 2H), 3.58 (s, 4H), 3.44 (t, J = 6.8 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 1.84 – 1.90 (m, 2H), 1.59 – 1.48 (m, 2H), 1.48 – 1.37 (m, 2H), 1.37 – 1.17 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.10, 128.81, 128.18, 126.76, 58.38, 53.42, 34.06, 32.91, 29.58, 29.50, 29.48, 28.83, 28.25, 27.28, 27.06; HRMS (DART-TOF) calculated for $C_{24}H_{34}NBr$ $[M+H]^+$ m/z 416.1947, found 416.1943. Anal. Calcd. for $C_{24}H_{34}NBr$: C, 69.22; H, 8.23. Found: C, 69.51; H, 8.13.



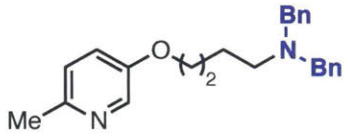
5d

***N*-benzyl-*N*-(5-(dibenzylamino)pentyl)-4-methylbenzenesulfonamide** (Table 4, entry **5d).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, *N*-benzyl-4-methyl-*N*-(pent-4-en-1-yl)benzenesulfonamide (329.5 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 10-15% EtOAc in hexane (contain 0.5% TEA) to provide the title compound as a colorless liquid in 95% and 95% yield. IR (thin film) 2932, 1494, 1338, 1155, 1090, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.73 (m, 2H), 7.46 – 7.14 (m, 17H), 4.29 (s, 2H), 3.50 (s, 4H), 3.16 – 2.95 (t, *J* = 7.6 Hz, 2H), 2.45 (s, 3H), 2.29 (t, *J* = 7.2 Hz, 2H), 1.42 – 1.19 (m, 4H), 1.17 – 0.96 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 143.13, 139.93, 137.17, 136.66, 129.69, 128.74, 128.52, 128.25, 128.17, 127.70, 127.19, 126.78, 58.27, 53.18, 51.92, 48.11, 27.87, 26.53, 24.31, 21.55; HRMS (DART-TOF) calculated for $C_{33}H_{38}N_2O_2S$ $[M+H]^+$ m/z 527.2727, found 527.2738.



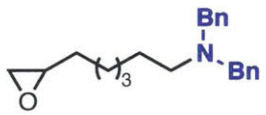
5e

6-(dibenzylamino)-1-(indolin-1-yl)hexan-1-one (Table 4, entry **5e).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, 1-(indolin-1-yl)hex-5-en-1-one (215.3 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 15-20% EtOAc in hexane (contain 0.5% TEA) to provide the title compound as a colorless liquid in 85% and 91% yield. IR (thin film) 2932, 1658, 1598, 1481, 1404, 1262, 747, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.29 (d, *J* = 8.1 Hz, 1H), 7.41 (d, *J* = 7.3 Hz, 4H), 7.34 (t, *J* = 7.5 Hz, 4H), 7.30 – 7.17 (m, 4H), 7.09 – 6.99 (m, 1H), 4.01 (t, *J* = 8.5 Hz, 1.78 H) & 4.17 (m, 0.22 H) due to rotamer, 3.61 (s, 4H), 3.20 (t, *J* = 8.5 Hz, 1.78 H) & 3.07 (m, 0.22H) due to rotamer, 2.49 (t, *J* = 7.2 Hz, 2H), 2.38 (t, *J* = 7.5 Hz, 1.78H) & 2.65 (m, 0.22H) due to rotamer, 1.79 – 1.66 (m, 2H), 1.66 – 1.53 (m, 2H), 1.47 – 1.35 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 171.40, 143.20, 140.02, 131.09, 128.87, 128.23, 127.60, 126.84, 124.55, 123.51, 117.06, 58.44, 53.43, 48.03, 35.97, 28.10, 27.12, 27.04, 24.55; HRMS (DART-TOF) calculated for $C_{28}H_{32}N_2O$ $[M+H]^+$ m/z 413.2587, found 413.2595. Anal. Calcd. for $C_{28}H_{32}N_2O$: C, 81.28; H, 7.83. Found: C, 81.28; H, 7.83.



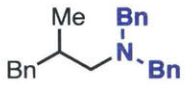
5f

***N,N*-dibenzyl-4-((6-methylpyridin-3-yl)oxy)butan-1-amine** (Table 4, entry **5f**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, 5-(but-3-en-1-yloxy)-2-methylpyridine (163.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 20-50% EtOAc in hexane (contain 0.5% TEA) to provide the title compound as a colorless liquid in 92% yield for both runs. IR (thin film) 2942, 2793, 1494, 1262, 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.15 (dd, J = 2.6, 1.0 Hz, 1H), 7.42 – 7.35 (m, 4H), 7.35 – 7.29 (m, 4H), 7.28 – 7.22 (m, 2H), 7.08 – 6.99 (m, 2H), 3.85 (t, J = 6.3 Hz, 2H), 3.59 (s, 4H), 2.51 (s, 3H), 2.50 (t, J = 6.9 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.73 – 1.66 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 153.20, 150.10, 139.85, 136.79, 128.86, 128.45, 128.22, 126.88, 123.24, 121.96, 67.99, 58.43, 52.56, 26.73, 23.42, 23.36; HRMS (DART-TOF) calculated for $C_{24}H_{28}N_2O$ $[M+H]^+$ m/z 361.2274, found 361.2270. Anal. Calcd. for $C_{24}H_{28}N_2O$: C, 79.96; H, 7.83. Found: C, 79.83; H, 7.75.



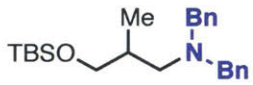
5g

***N,N*-dibenzyl-6-(oxiran-2-yl)hexan-1-amine** (Table 4, entry **5g**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, 1,2-epoxy-7-octene (126.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 5-10% EtOAc in hexane (contain 0.5% TEA) to provide the title compound as a colorless liquid in 90% and 91% yield. IR (thin film) 2928, 2855, 2790, 1494, 1128, 1028, 743, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.40 (d, J = 6.7 Hz, 4H), 7.34 (t, J = 7.4 Hz, 4H), 7.26 (t, J = 7.2 Hz, 2H), 3.58 (s, 4H), 2.96 – 2.87 (m, 1H), 2.77 (dd, J = 5.0, 4.0 Hz, 1H), 2.48 (dd, J = 5.0, 2.7 Hz, 1H), 2.44 (t, J = 7.2 Hz, 2H), 1.62 – 1.37 (m, 6H), 1.37 – 1.22 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.03, 128.77, 128.14, 126.74, 58.36, 53.25, 52.31, 47.07, 32.47, 29.24, 27.12, 26.91, 25.96; HRMS (DART-TOF) calculated for $C_{22}H_{29}NO$ $[M+H]^+$ m/z 324.2322, found 324.2314.



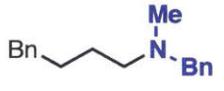
5h

***N,N*-dibenzyl-2-methyl-3-phenylpropan-1-amine** (Table 4, entry **5h).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, (2-methylallyl)benzene (132.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (1 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 5-10% EtOAc in hexane to provide the title compound as a colorless liquid in 87% and 90% yields. IR (thin film) 3025, 2795, 1494, 1452, 1066, 1028, 735, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.46 – 7.40 (m, 4H), 7.36 (t, J = 7.4 Hz, 4H), 7.28 (s, 4H), 7.22 (d, J = 7.3 Hz, 1H), 7.15 – 7.08 (m, 2H), 3.62 (d, J = 13.6 Hz, 2H), 3.58 (d, J = 13.6 Hz, 2H), 2.97 (dd, J = 13.1, 4.6 Hz, 1H), 2.38 (dd, J = 12.5, 7.3 Hz, 1H), 2.29 (dd, J = 12.4, 6.9 Hz, 1H), 2.15 (dd, J = 13.1, 9.1 Hz, 1H), 2.11 – 1.99 (m, 1H), 0.86 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 141.64, 139.96, 129.26, 129.04, 128.28, 128.22, 126.91, 125.70, 60.72, 59.08, 41.50, 33.68, 18.09; HRMS (DART-TOF) calculated for $C_{24}H_{27}N$ $[M+H]^+$ m/z 330.2216, found 330.2203. Anal. Calcd. for $C_{24}H_{27}N$: C, 87.49; H, 8.26 Found: C, 87.59; H, 8.24.



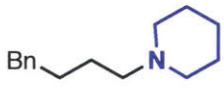
5i

***N,N*-dibenzyl-3-((tert-butyldimethylsilyl)oxy)-2-methylpropan-1-amine** (Table 4, entry **5i).** Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, *tert*-butyldimethyl((2-methylallyl)oxy)silane (132.2 mg, 1.0 mmol, 1.0 equiv), *O*-benzoyl-*N,N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), THF (1 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 5-10% EtOAc in hexane to provide the title compound as a colorless liquid in 88% an 87% yield. IR (thin film) 2927, 1452, 1250, 1086, 834, 773, 743, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39 – 7.27 (m, 8H), 7.25 – 7.19 (m, 2H), 3.63 – 3.54 (m, 3H), 3.47 (d, J = 13.6 Hz, 2H), 3.28 (dd, J = 9.8, 6.7 Hz, 1H), 2.37 (dd, J = 12.6, 6.7 Hz, 1H), 2.18 (dd, J = 12.5, 7.6 Hz, 1H), 1.99 – 1.85 (m, 1H), 0.87 (m, 3H), 0.87 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.01, 128.99, 128.23, 126.86, 67.12, 58.99, 57.51, 34.43, 26.12, 18.49, 15.80, -5.19; HRMS (DART-TOF) calculated for $C_{24}H_{37}NOSi$ $[M+H]^+$ m/z 384.2717, found 384.2718.



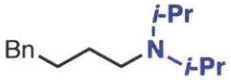
5j

***N*-benzyl-*N*-methyl-4-phenylbutan-1-amine** (Table 5, entry **5j**). Prepared following the general procedure using 2 mol% $Cu(OAc)_2$, 2.2% (±)-DTBM-SEGPHOS, *but-3-en-1-ylbenzene* (132.2 mg, 1.0 mmol, 1.0 equiv), O-benzoyl-N-benzyl-N-methylhydroxylamine (290 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 20-50% EtOAc in hexane (contain 0.5% TEA) to provide the title compound as a colorless liquid in 91% and 92% yield. IR (thin film) 2937, 2785, 1495, 1452, 1027, 736, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.37 – 7.25 (m, 7H), 7.24 – 7.17 (m, 3H), 3.51 (s, 2H), 2.64 (t, J = 7.6 Hz, 2H), 2.42 (t, J = 7.6 Hz, 2H), 2.21 (s, 3H), 1.74 – 1.64 (m, 2H), 1.64 – 1.54 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.67, 139.32, 129.14, 128.50, 128.34, 128.27, 126.97, 125.73, 62.50, 57.35, 42.34, 35.90, 29.30, 27.10; HRMS (DART-TOF) calculated for $C_{18}H_{23}N$ $[M+H]^+$ m/z 254.1903, found 254.1897. Anal. Calcd. for $C_{18}H_{23}N$: C, 85.32; H, 9.15 Found: C, 85.06; H, 9.14.



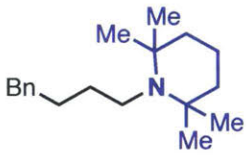
5k

1-(4-phenylbutyl)piperidine (Table 5, entry **5k**). Prepared following the general procedure using 4 mol% $Cu(OAc)_2$, 4.4% (±)-DTBM-SEGPHOS, but-3-en-1-ylbenzene (132.2 mg, 1.0 mmol, 1.0 equiv), piperidin-1-yl benzoate (246.3 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 10-20% EtOAc in hexane (contain 1% TEA) to provide the title compound as a colorless liquid in 99% yield for both runs. IR (thin film) 2931, 1738, 1453, 1350, 1122, 1039, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.35 – 7.25 (m, 2H), 7.25 – 7.15 (m, 3H), 2.65 (t, J = 7.5 Hz, 2H), 2.40 – 2.33 (m, 4H), 2.33 (t, J = 7.5 Hz, 2H), 1.73 – 1.51 (m, 8H), 1.51 – 1.39 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.52, 128.39, 128.23, 125.63, 59.44, 54.68, 35.91, 29.63, 26.67, 26.02, 24.53; HRMS (DART-TOF) calculated for $C_{15}H_{23}N$ $[M+H]^+$ m/z 218.1903, found 218.1895. Anal. Calcd. for $C_{15}H_{23}N$: C, 82.89; H, 10.67 Found: C, 82.76; H, 10.69.



5l

***N,N*-diisopropyl-4-phenylbutan-1-amine** (Table 5, entry **5l**). Prepared following the general procedure using 4 mol% $Cu(OAc)_2$, 4.4% (±)-DTBM-SEGPHOS, *but-3-en-1-ylbenzene* (132.2 mg, 1.0 mmol, 1.0 equiv.), *O*-benzoyl-*N,N*-diisopropylhydroxylamine (246.3 mg, 1.2 mmol, 1.2 equiv), THF (1 mL) for 36 h at 40 °C. The reaction mixture was purified by flash chromatography on silica gel using 20-50% EtOAc in hexane (contain 1% TEA) to provide the title compound as a colorless liquid in 97% yield for both runs. IR (thin film) 2961, 2933, 1453, 1384, 1360, 1206, 1158, 742, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.33 – 7.26 (m, 2H), 7.24 – 7.16 (m, 3H), 3.13 – 2.89 (m, 2H), 2.64 (t, J = 7.6 Hz, 2H), 2.43 (t, J = 7.6 Hz, 2H), 1.69 –1.57 (m, 2H), 1.55 – 1.40 (m, 2H), 1.02 (d, J = 6.6 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.91, 128.40, 128.23, 125.57, 48.40, 45.10, 35.99, 31.13, 29.33, 20.71; HRMS (DART-TOF) calculated for $C_{16}H_{27}N$ $[M+H]^+$ m/z 234.2216, found 234.2213. Anal. Calcd. for $C_{16}H_{27}N$: C, 82.34; H, 11.66 Found: C, 82.086; H, 11.66.

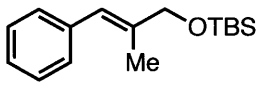


5m

2,2,6,6-Tetramethyl-1-(4-phenylbutyl)piperidine (Table 5, entry **5m**). Prepared following the general procedure using 4 mol% $Cu(OAc)_2$, 4.4% (±)-DTBM-SEGPHOS, but-3-en-1-ylbenzene (132.2 mg, 1.0 mmol, 1.0 equiv), 2,2,6,6-tetramethylpiperidin-1-yl benzoate (314 mg, 1.2 mmol, 1.2 equiv), THF (2 mL) for 36 h at 40 °C. The reaction mixture was quenched with Na_2CO_3 solution, and the crude product extracted with EtOAc (x3) (NB: This step is necessary to remove N-OBz compounds). The reaction was then purified by an acid-base treatment, where the amine was first protonated with dilute HCl solution and the aqueous layer washed with EtOAc (x1), then treated with 1 M NaOH to deprotonate the amine. The aqueous layer was then extracted with EtOAc (x3), and the organic combined and concentrated to give the pure product as a yellow liquid in 83% and 76% yields. IR (thin film) 2963, 2925, 2868, 1453, 1377, 1359, 1350, 1261, 1175, 1129, 1108, 1025, 746, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.38 – 7.26 (m, 2H), 7.24 – 7.18 (m, 3H), 2.65 (t, J = 7.5 Hz, 2H), 2.47 – 2.35 (m, 2H), 1.60 – 1.50 (m, 6H), 1.47 – 1.39 (m, 4H), 1.05 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 143.05, 128.44, 128.33, 125.67, 54.58, 45.12, 41.28, 36.12, 35.87, 29.55, 27.63, 17.92; HRMS (DART-TOF) calculated for $C_{19}H_{31}N$ $[M+H]^+$ m/z 274.2529, found 274.2519.

C. Substrate Preparation

Synthesis of substrates 1q:



1q

(*E*)-*tert*-butyldimethyl((2-methyl-3-phenylallyl)oxy)silane (Table 2, 1q) To a 50 mL round-bottom flask containing trans-2-Methyl-3-phenyl-2-propen-1-ol (2.964 g, 20 mmol, 1.00 equiv), imidazole (26 mmol, 1.3 equiv) was added DMF (20 mL). Then TBSCl (3.62 g, 24 mmol, 1.2 equiv) was added in one portion. The mixture was allowed to stir overnight. It was then diluted with ethyl acetate and washed with water, extracted 2 times with ethyl acetate and the combined organic layers were washed with brine and dried over Na_2SO_4. The mixture was purified by flash chromatography on silica gel using 0-5% EtOAc in hexane to provide the title compound in 90% yield as a colorless oil. IR (thin film) 2957, 2928, 2855, 1257, 1110, 1076, 835, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.40 – 7.29 (m, 4H), 7.23 (t, J = 7.1 Hz, 1H), 6.56 (s, 1H), 4.26 – 4.14 (m, 2H), 1.86 (d, J = 1.3 Hz, 3H), 0.98 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.17, 137.62, 129.03, 128.19, 126.25, 123.83, 68.64, 26.12, 18.61, 15.15, -5.09; HRMS (DART-TOF) calculated for $C_{16}H_{26}OSi$ $[M+H]^+$ m/z 263.1826, found 263.1889.

2.5 References and Notes

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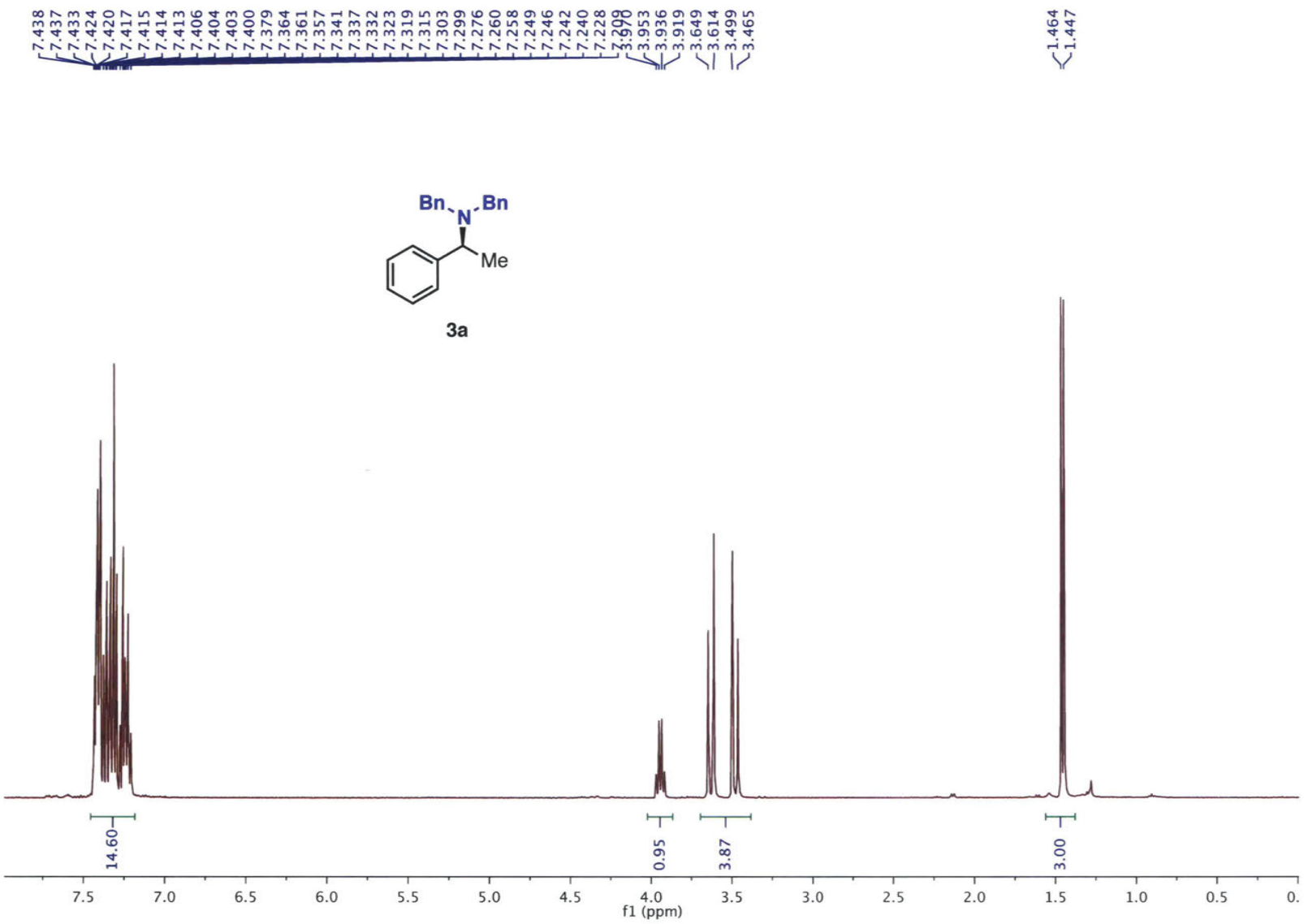
2.6 ^{1}H, ^{13}C, and ^{19}F NMR Spectra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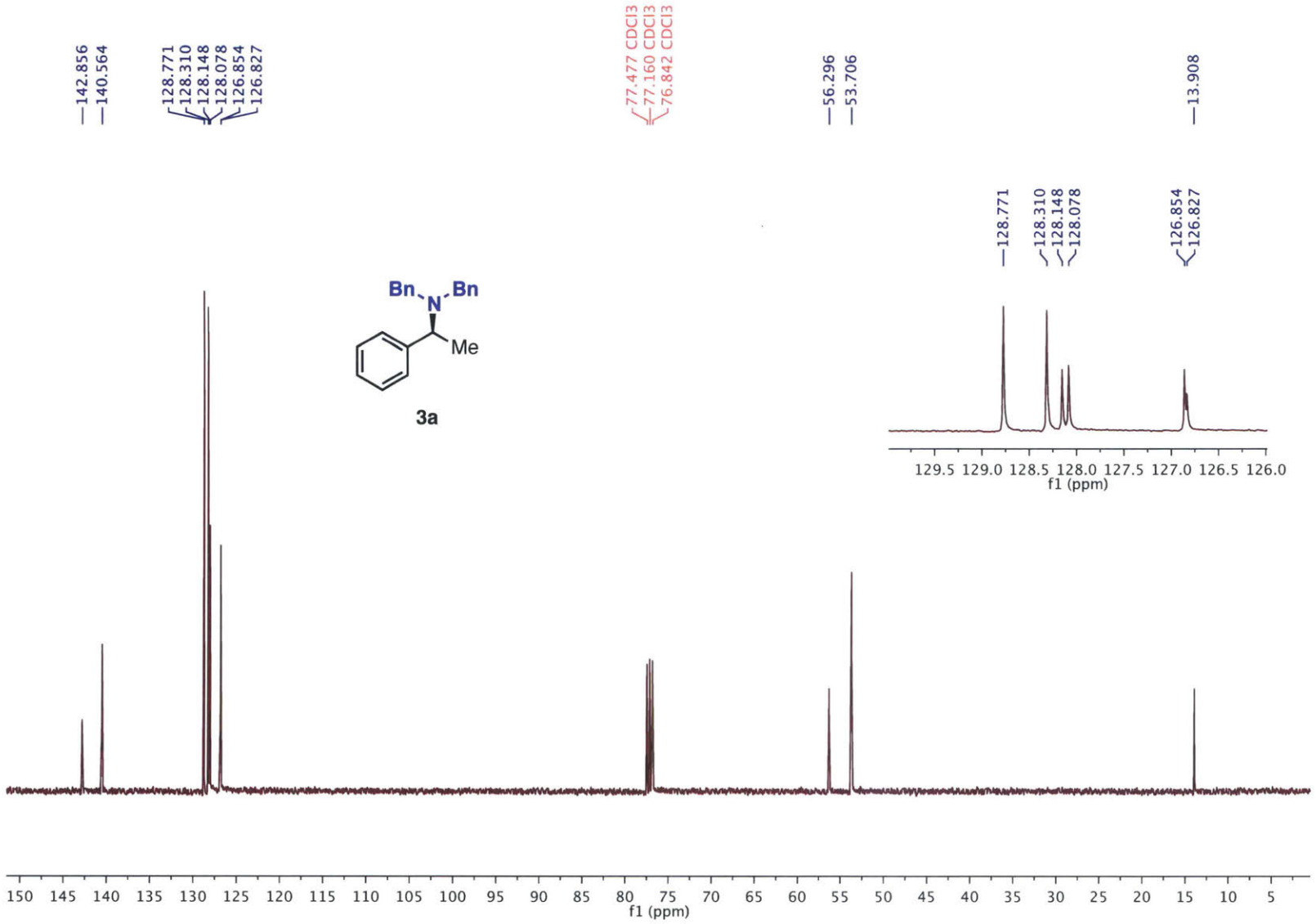
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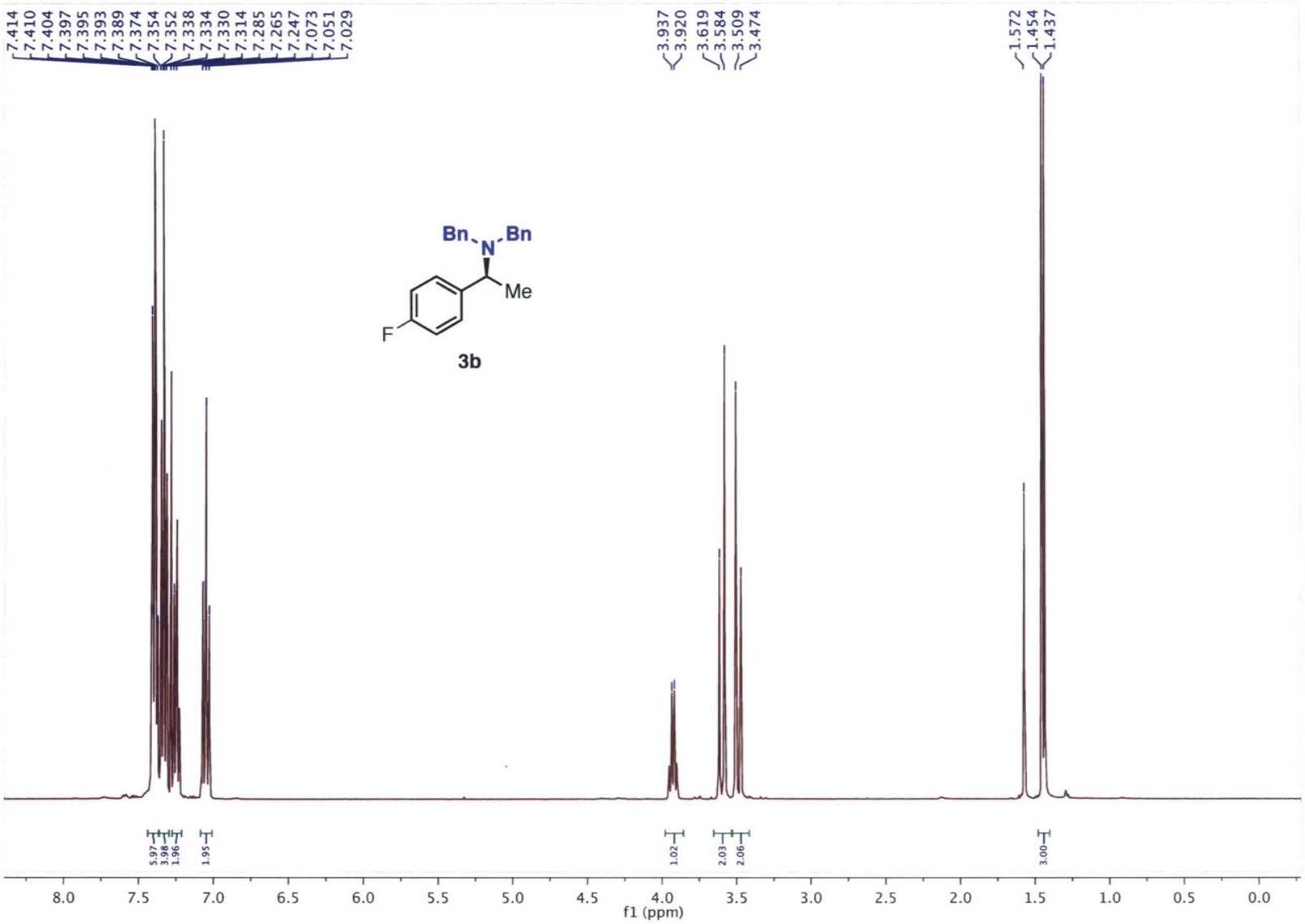
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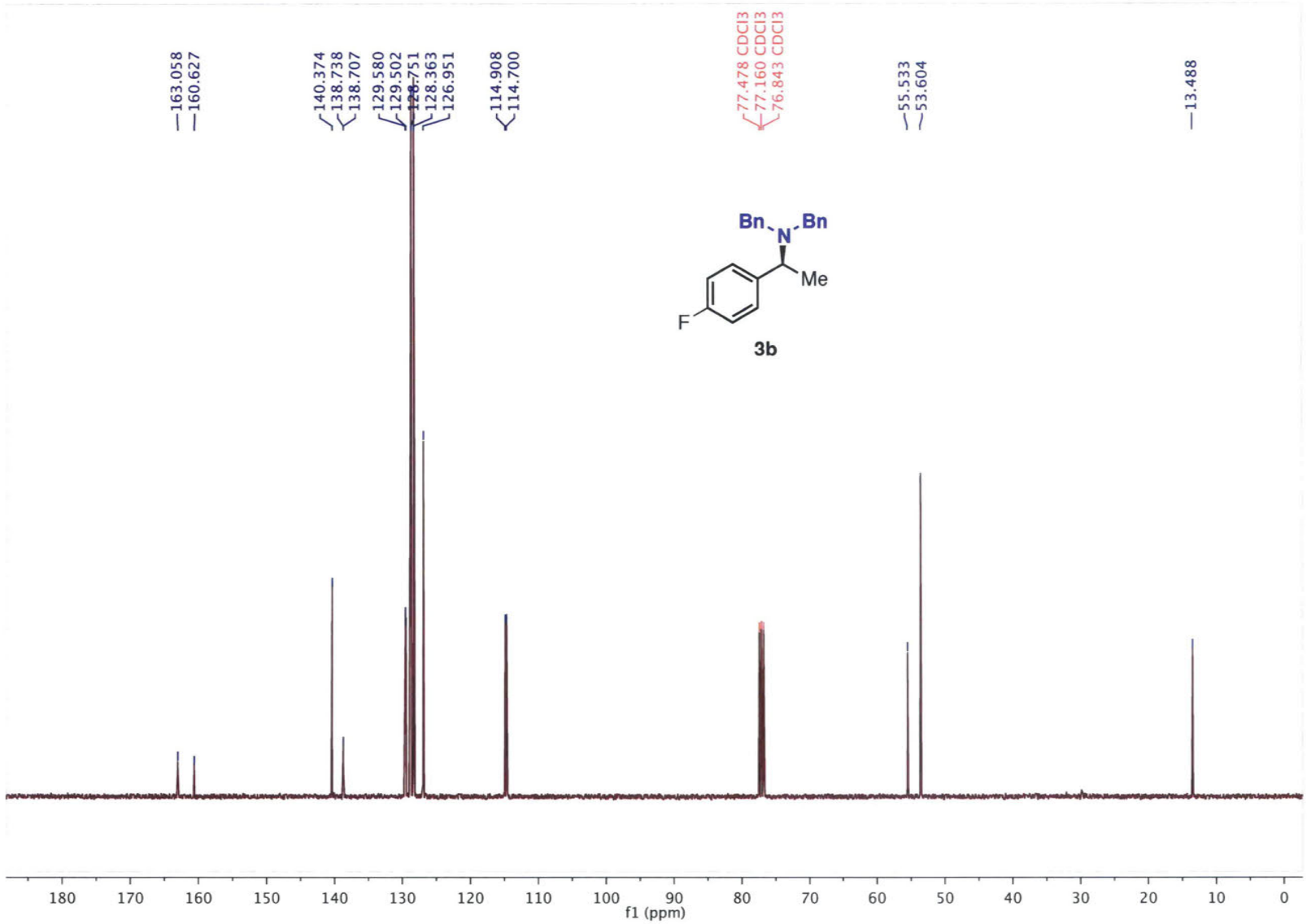
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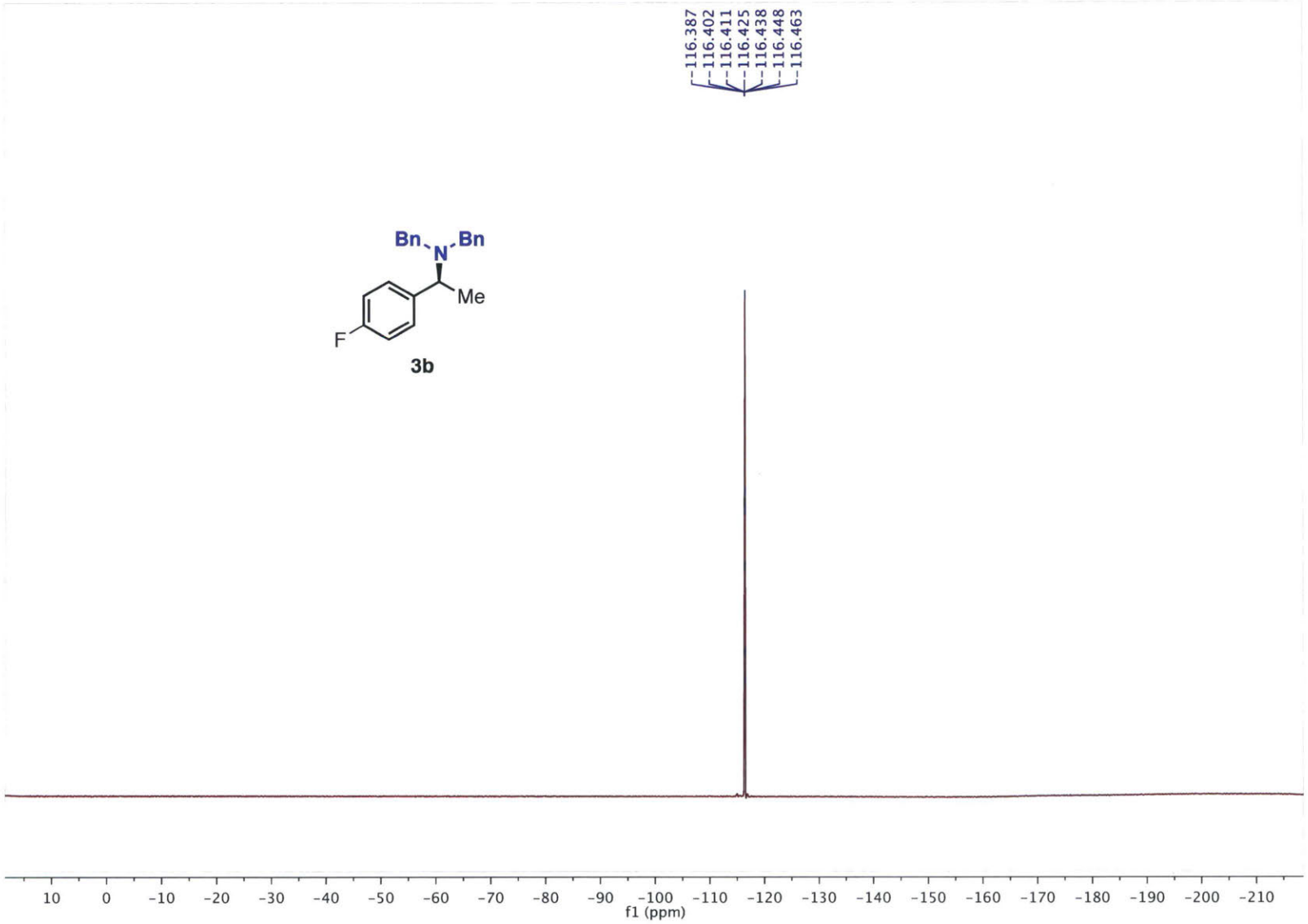
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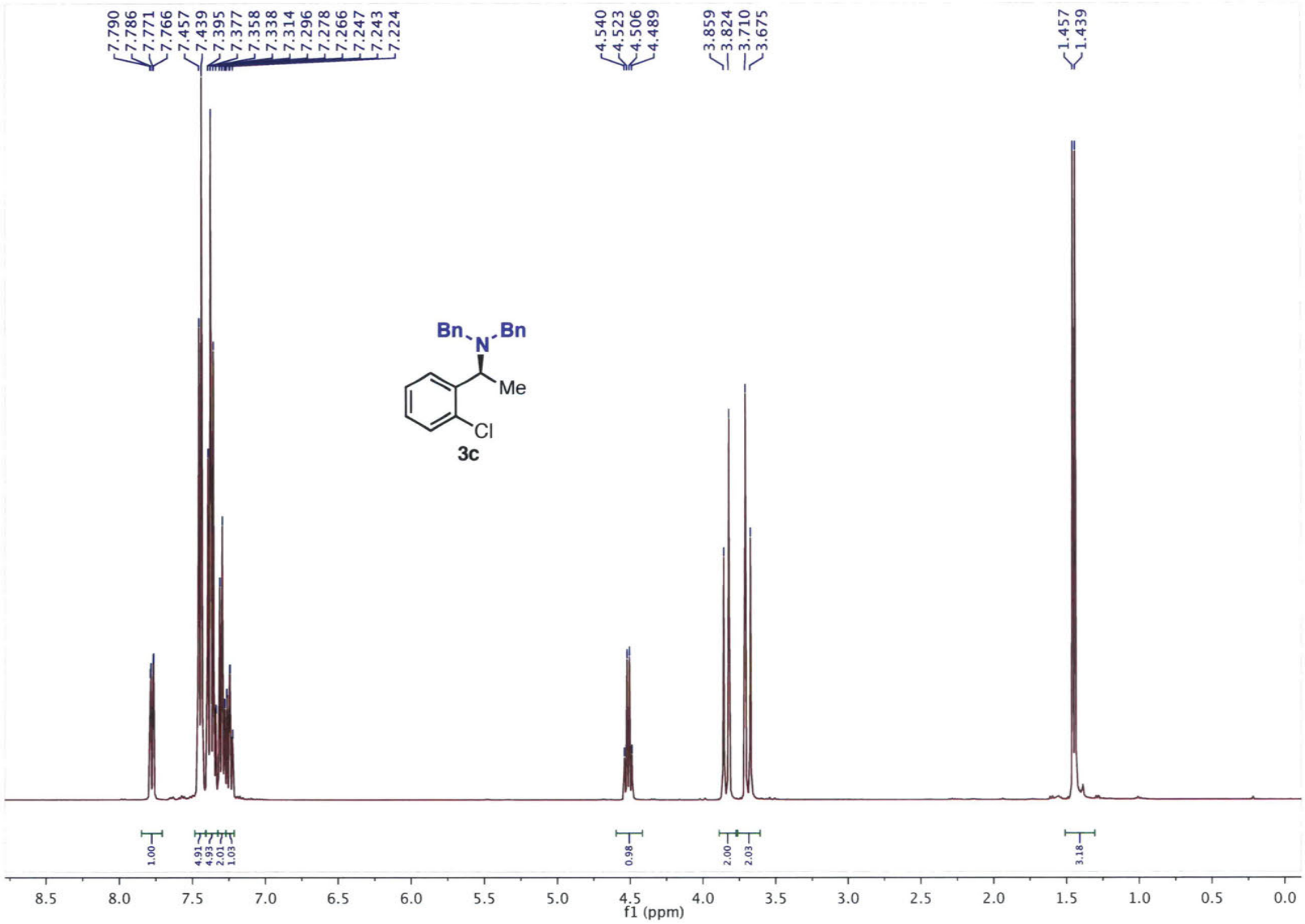
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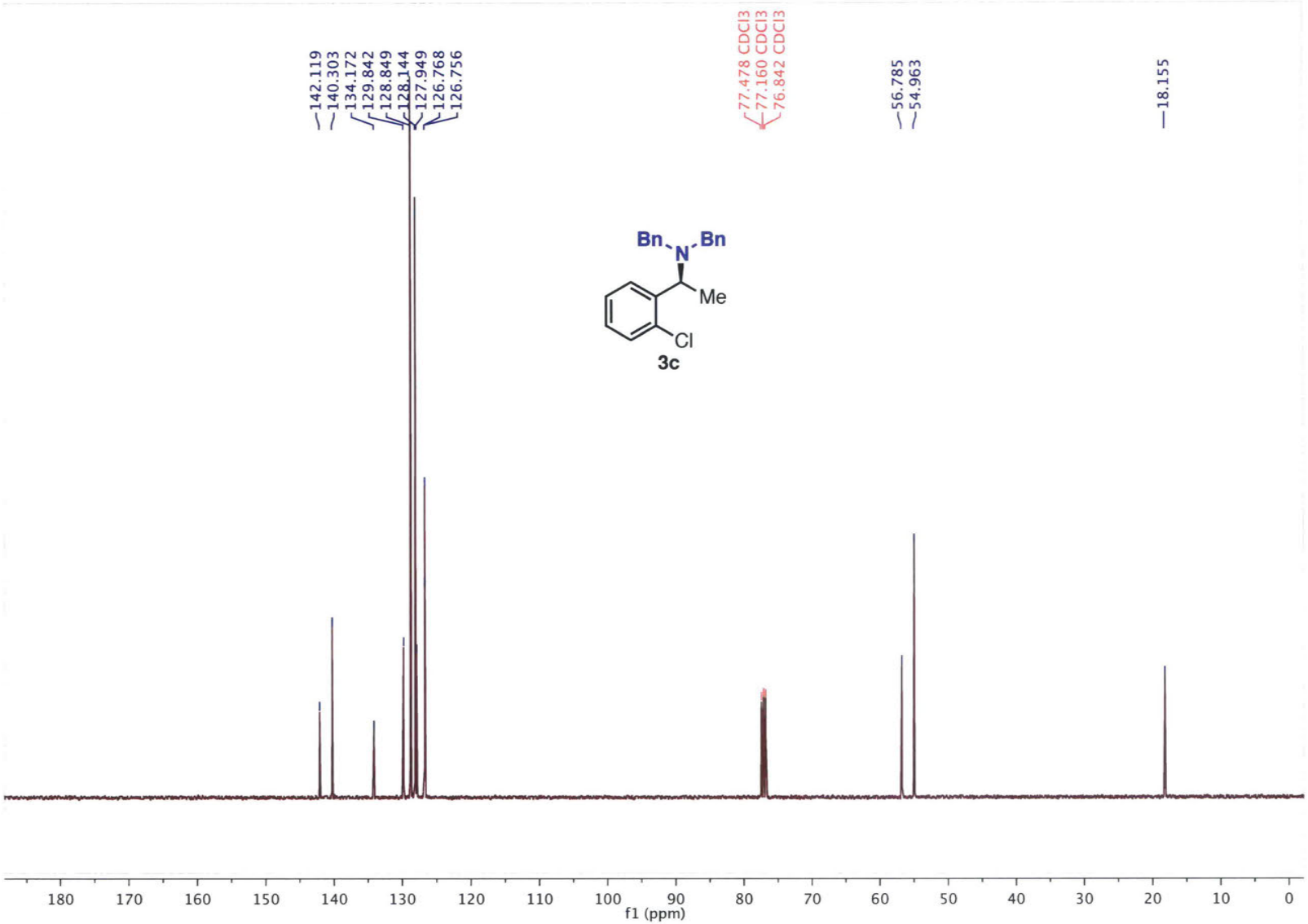
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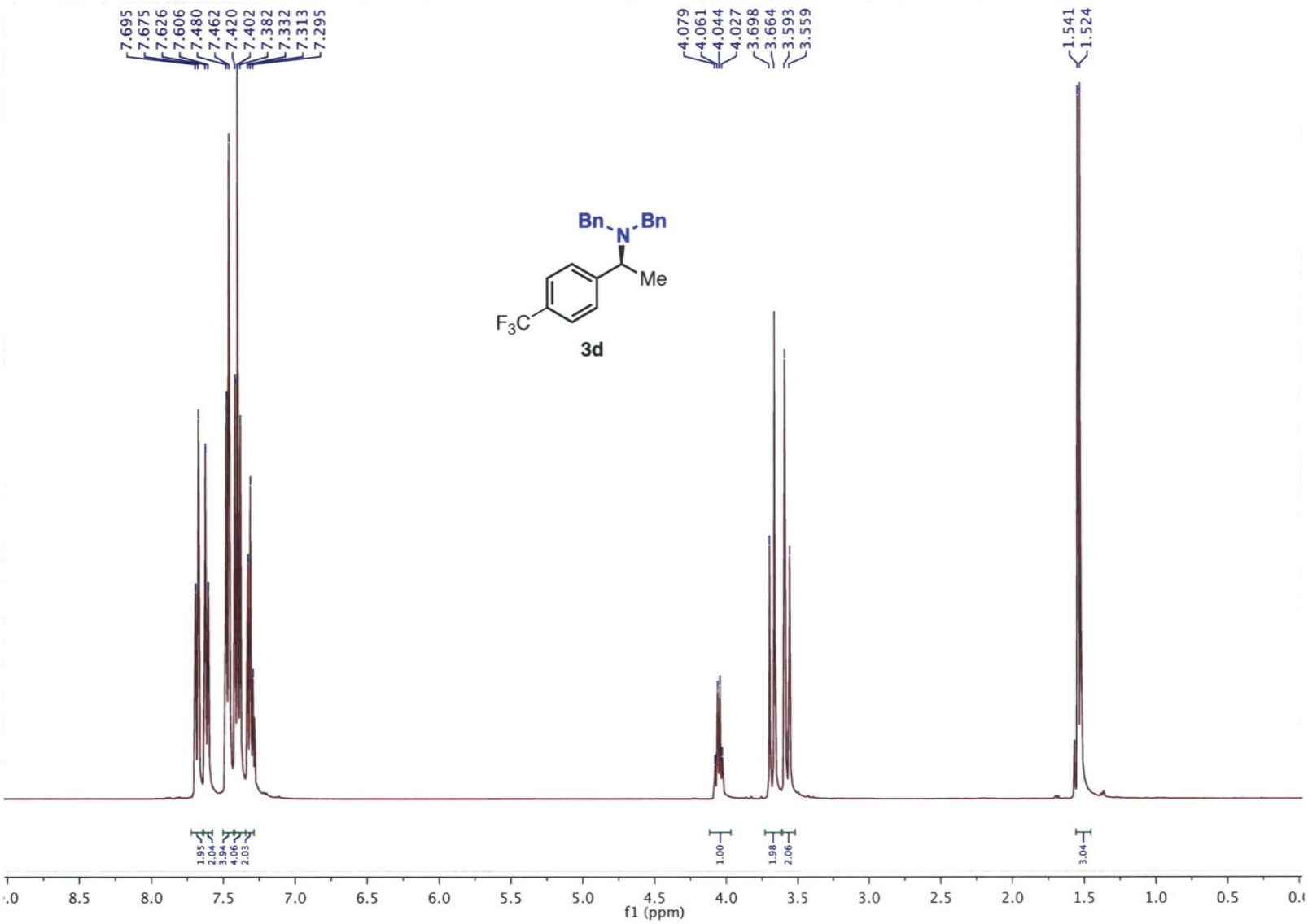
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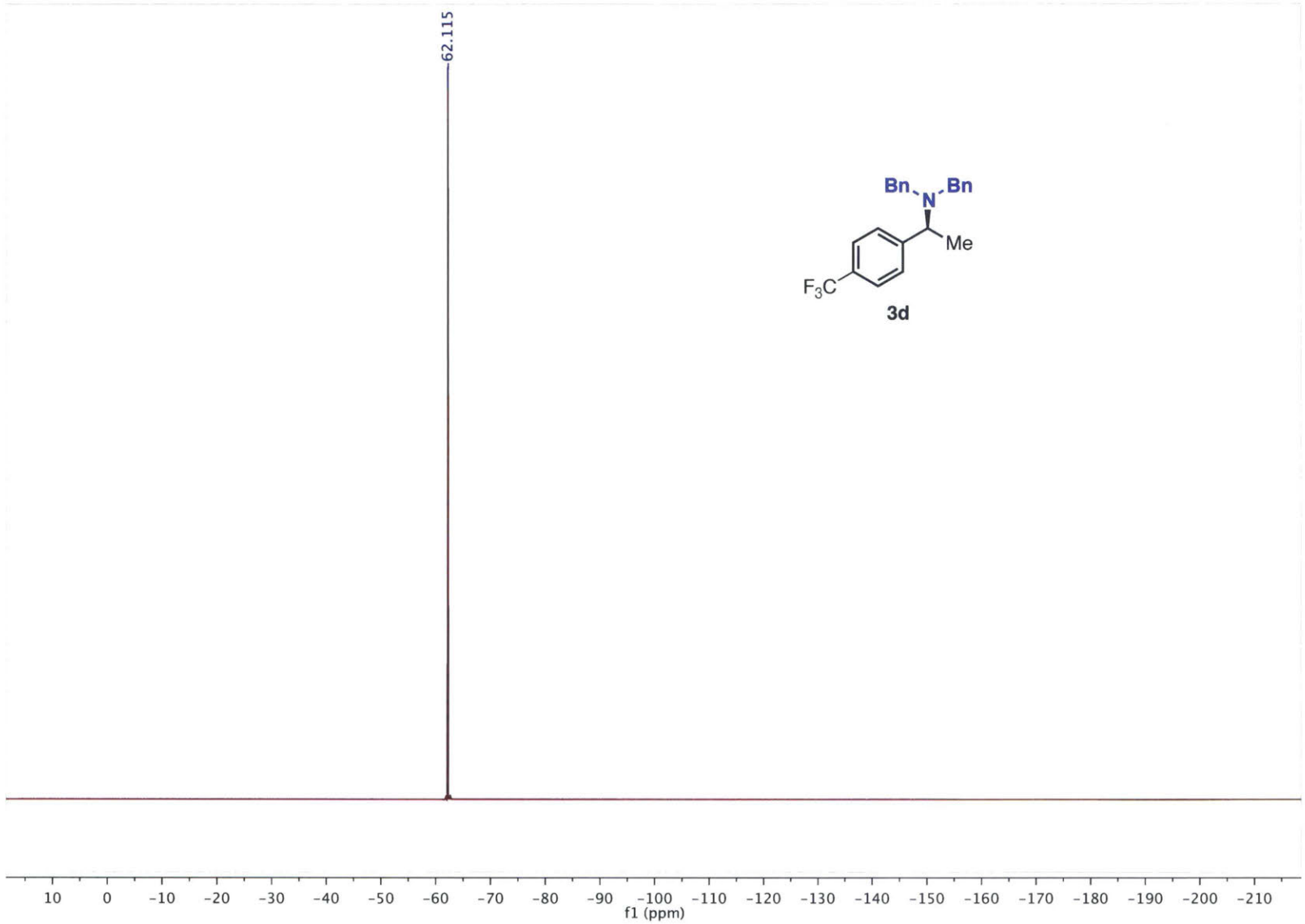
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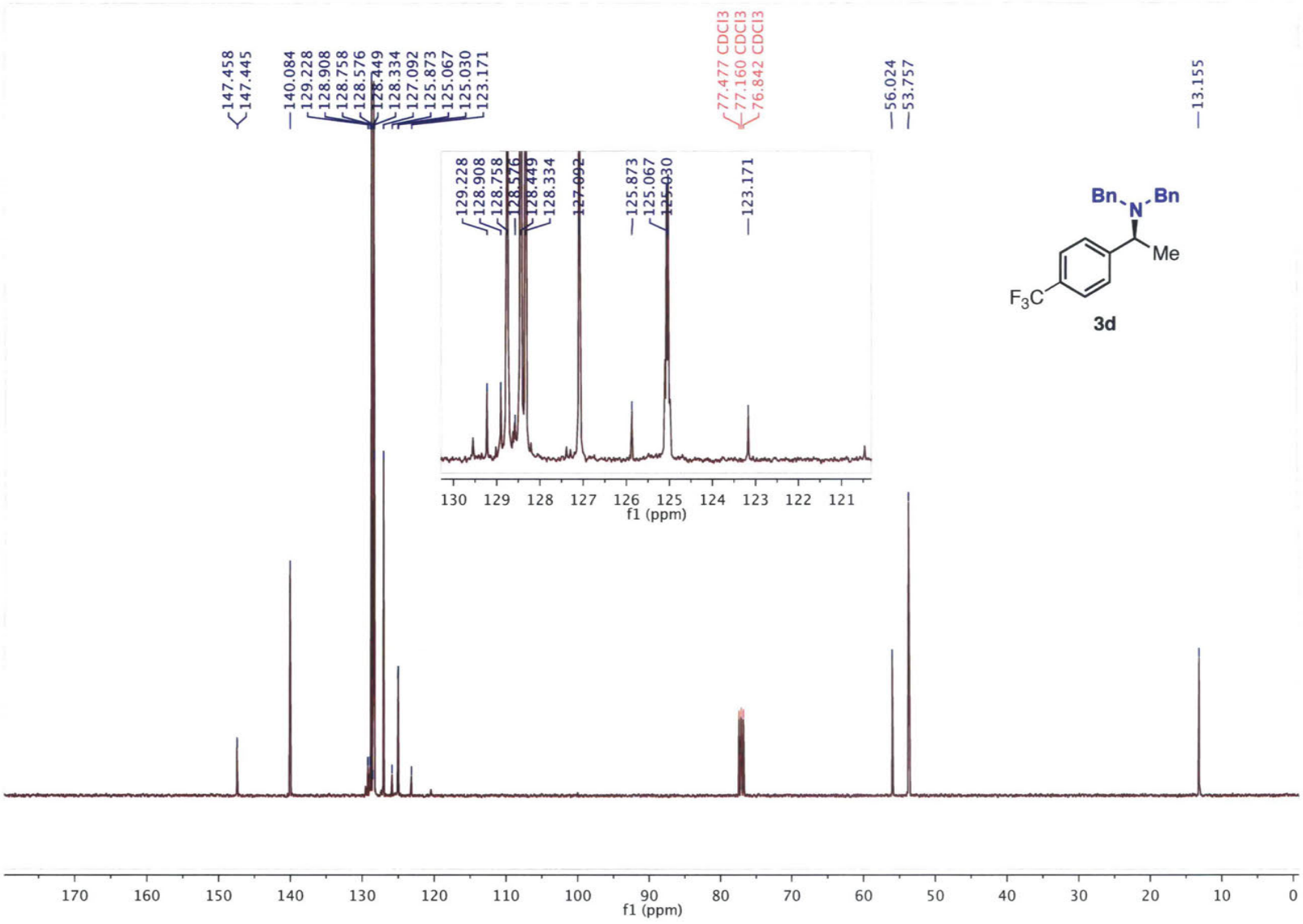
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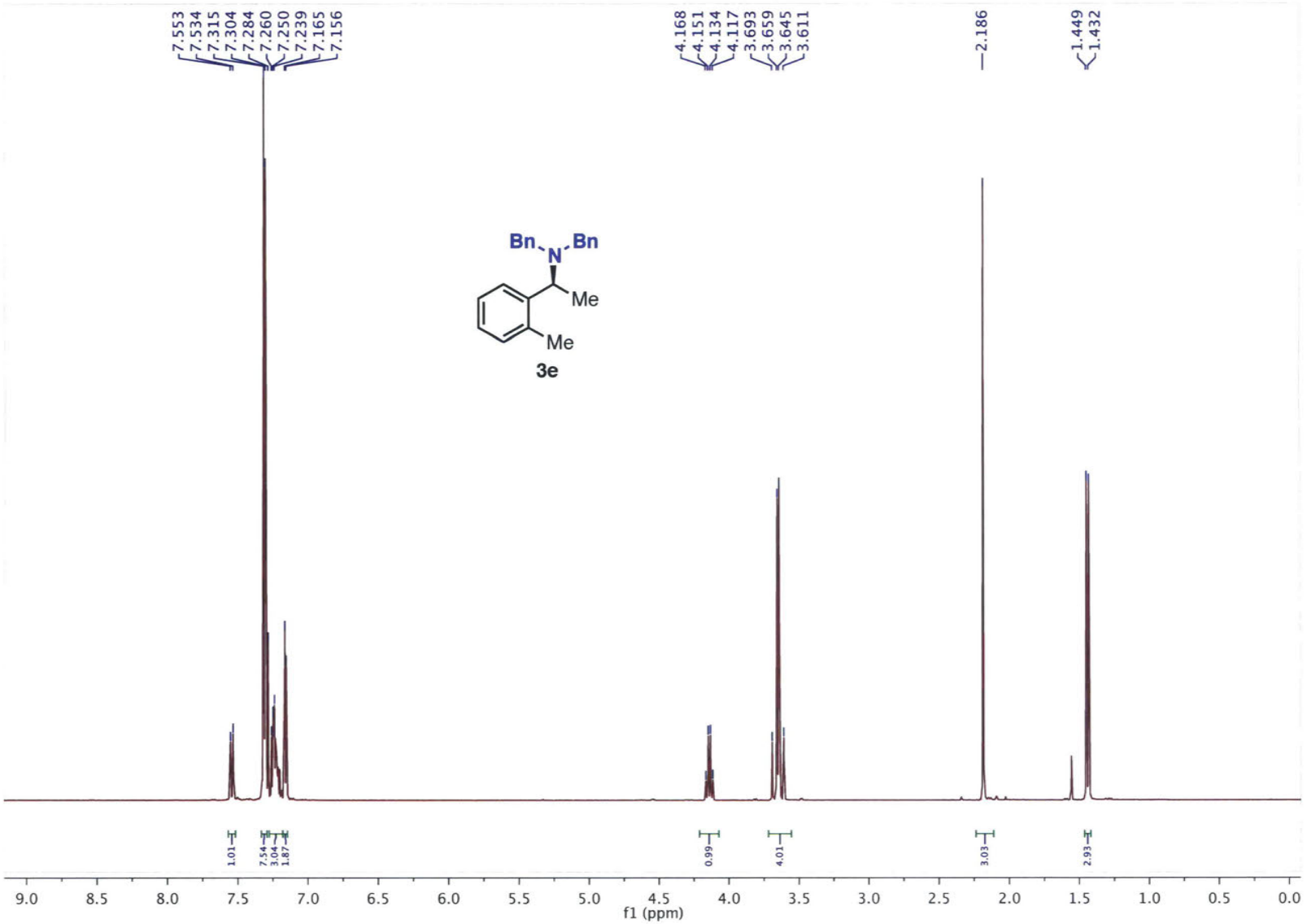
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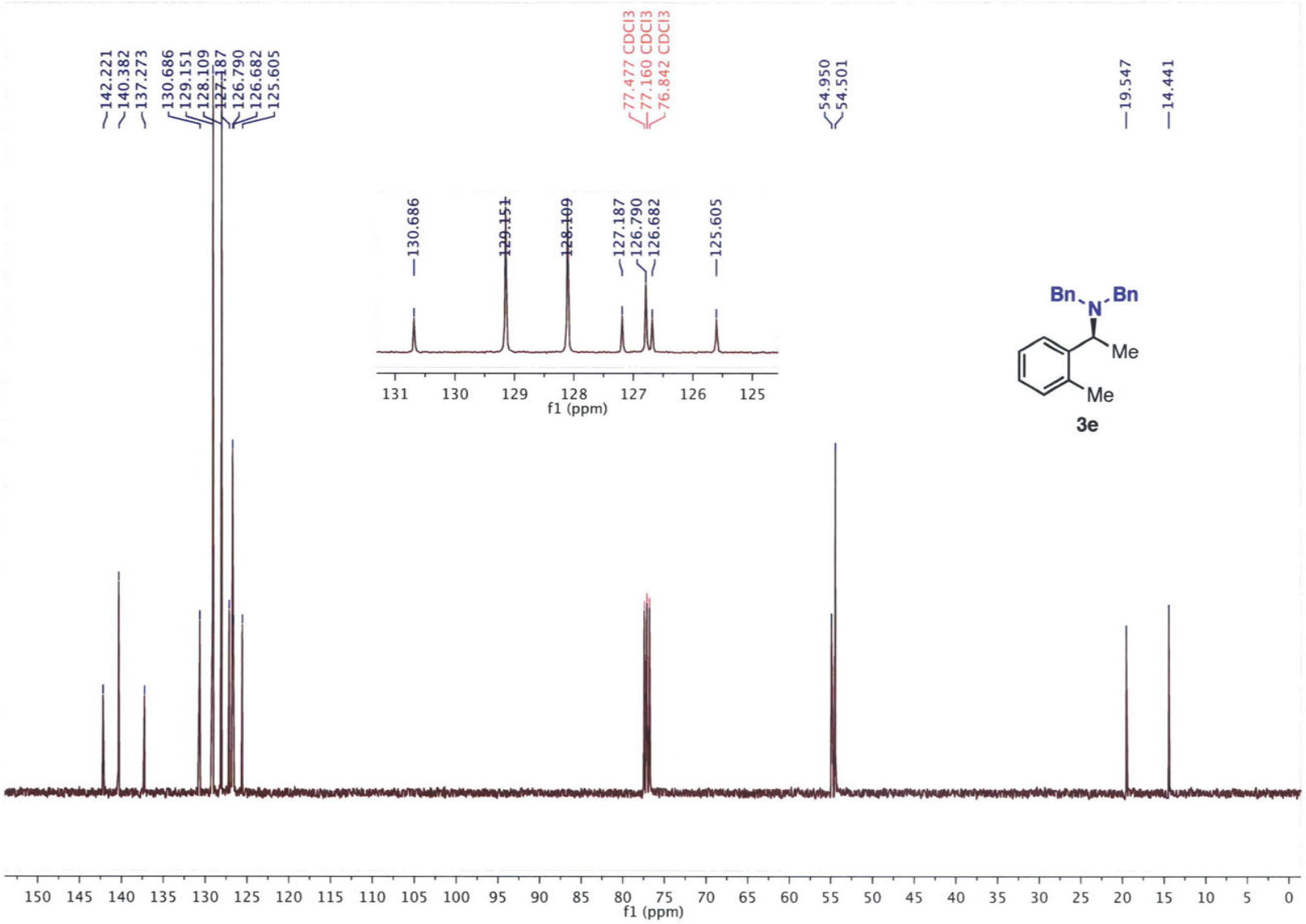
7.156
4.168
4.151
4.134
4.117
3.693
3.659
3.645
3.611
2.186
1.449
1.432
Bn
N
Bn
Me
Me
3e
1.01
7.54
3.04
1.87
0.99
4.01
3.03
2.93
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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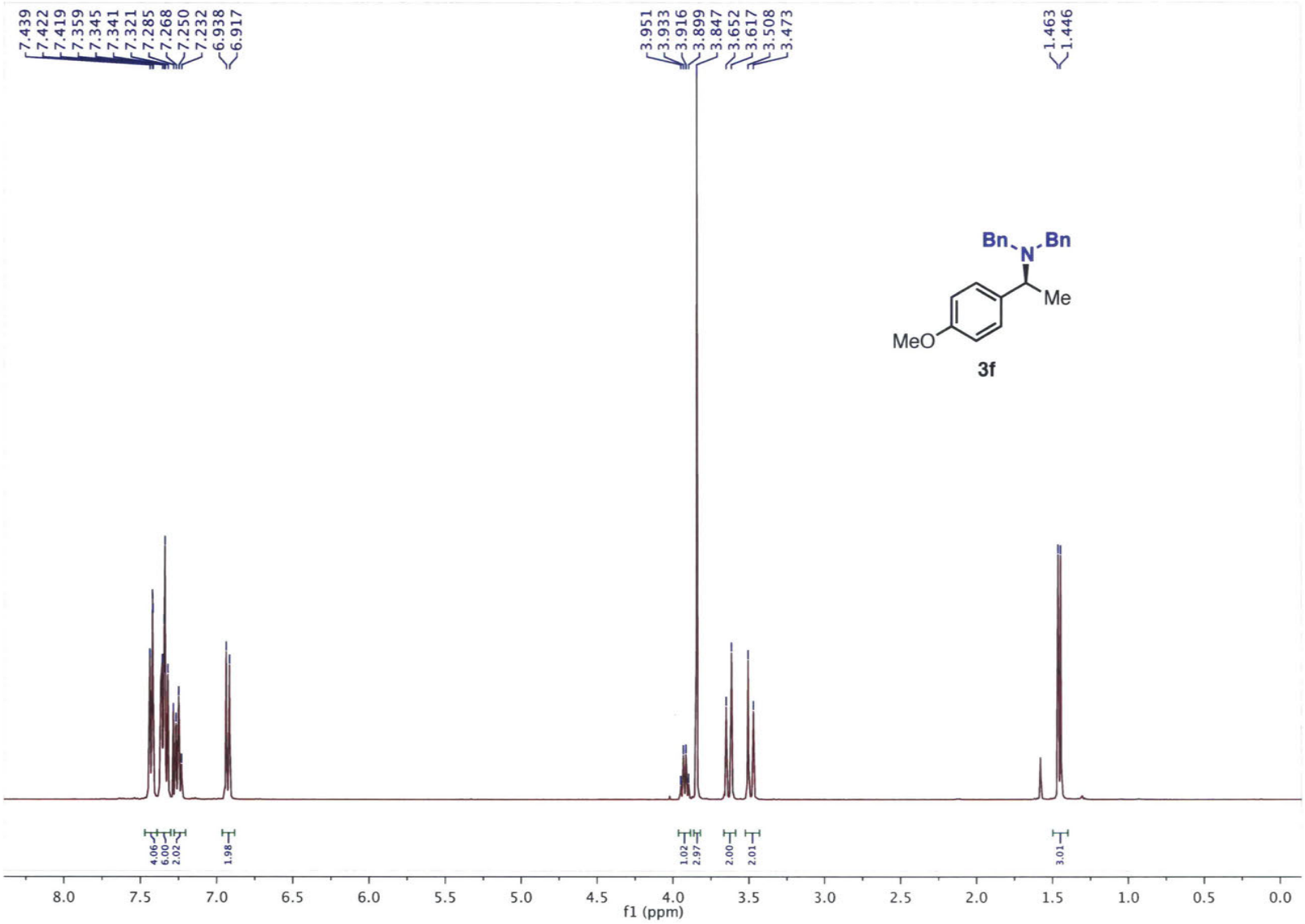
140.382
137.273
130.686
129.151
128.109
127.187
126.790
126.682
125.605
77.477 CDCl3
77.160 CDCl3
76.842 CDCl3
54.950
54.501
19.547
14.441
130.686
129.151
128.109
127.187
126.790
126.682
125.605
131 130 129 128 127 126 125
f1 (ppm)
Bn
N
Bn
Me
Me
3e
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)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7.422
7.419
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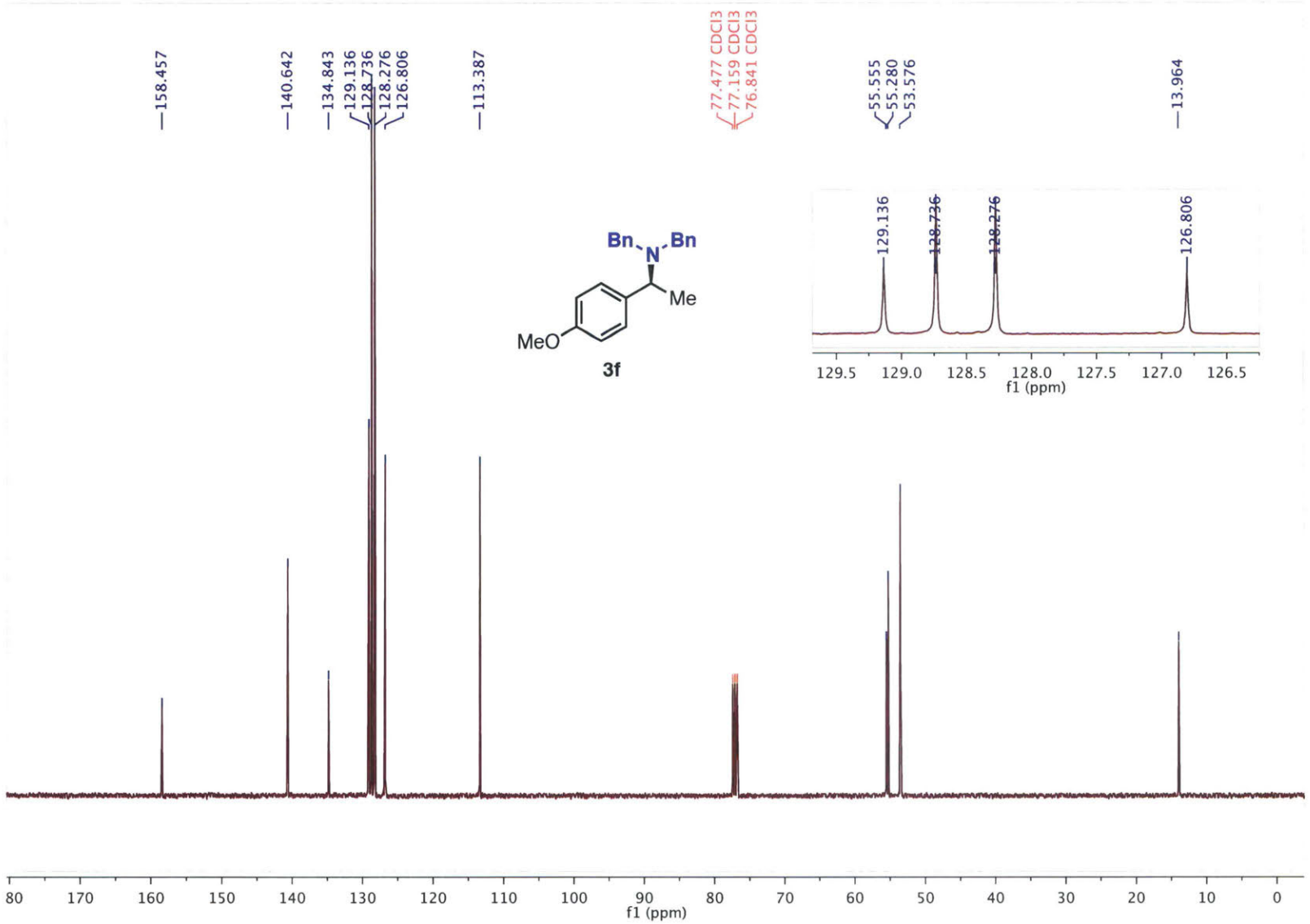
7.341
7.321
7.285
7.268
7.250
7.232
6.938
6.917
3.951
3.933
3.916
3.899
3.847
3.652
3.617
3.508
3.473
1.463
1.446
Bn
N
Bn
Me
MeO
3f
4.06
6.00
2.02
1.98
1.02
2.97
2.00
2.01
3.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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140.642
134.843
129.136
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128.276
126.806
113.387
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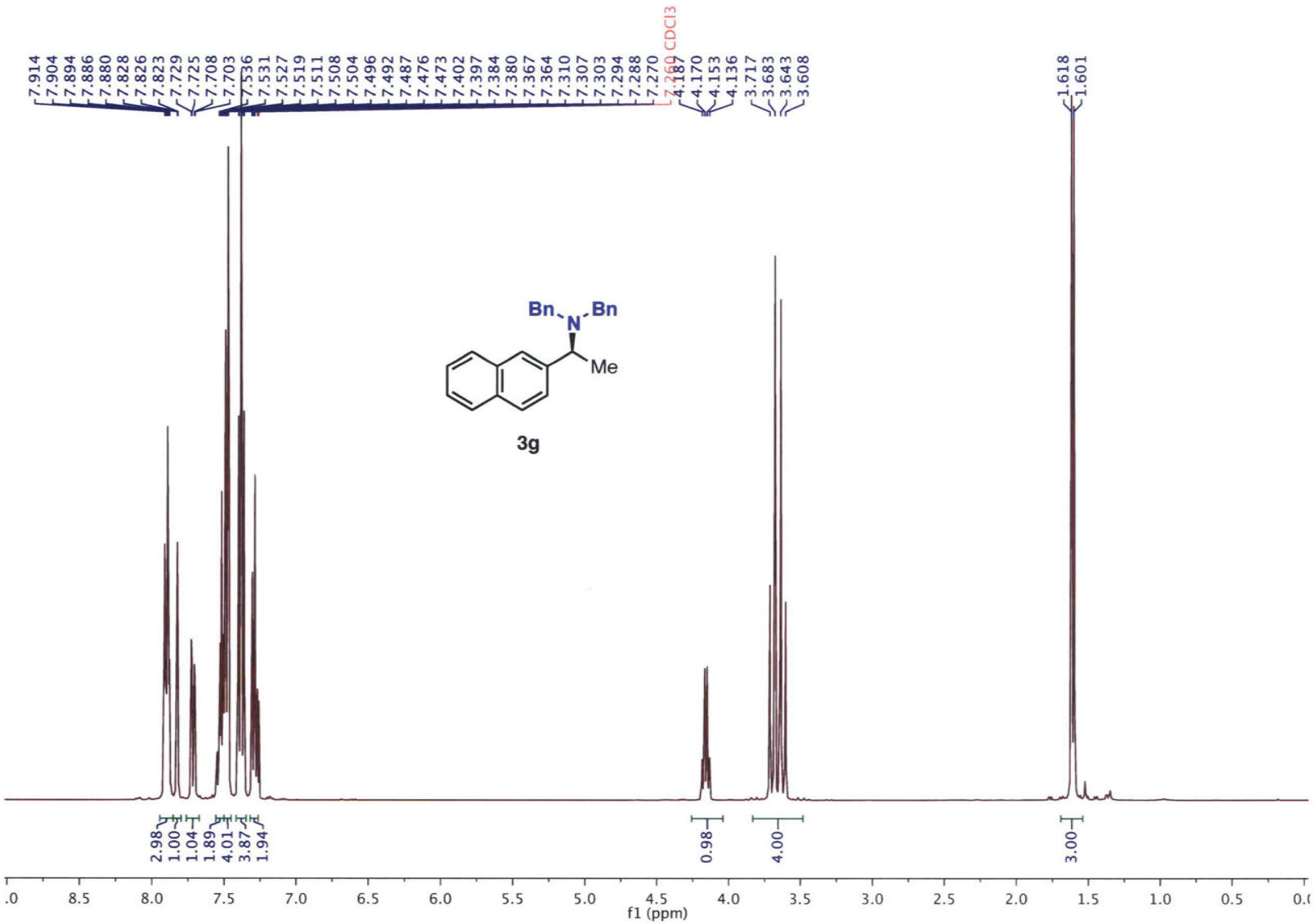
77.159 CDCl3
76.841 CDCl3
55.555
55.280
53.576
13.964
Bn
N
Bn
Me
MeO
3f
129.136
128.736
128.276
126.806
129.5
129.0
128.5
128.0
127.5
127.0
126.5
f1 (ppm)
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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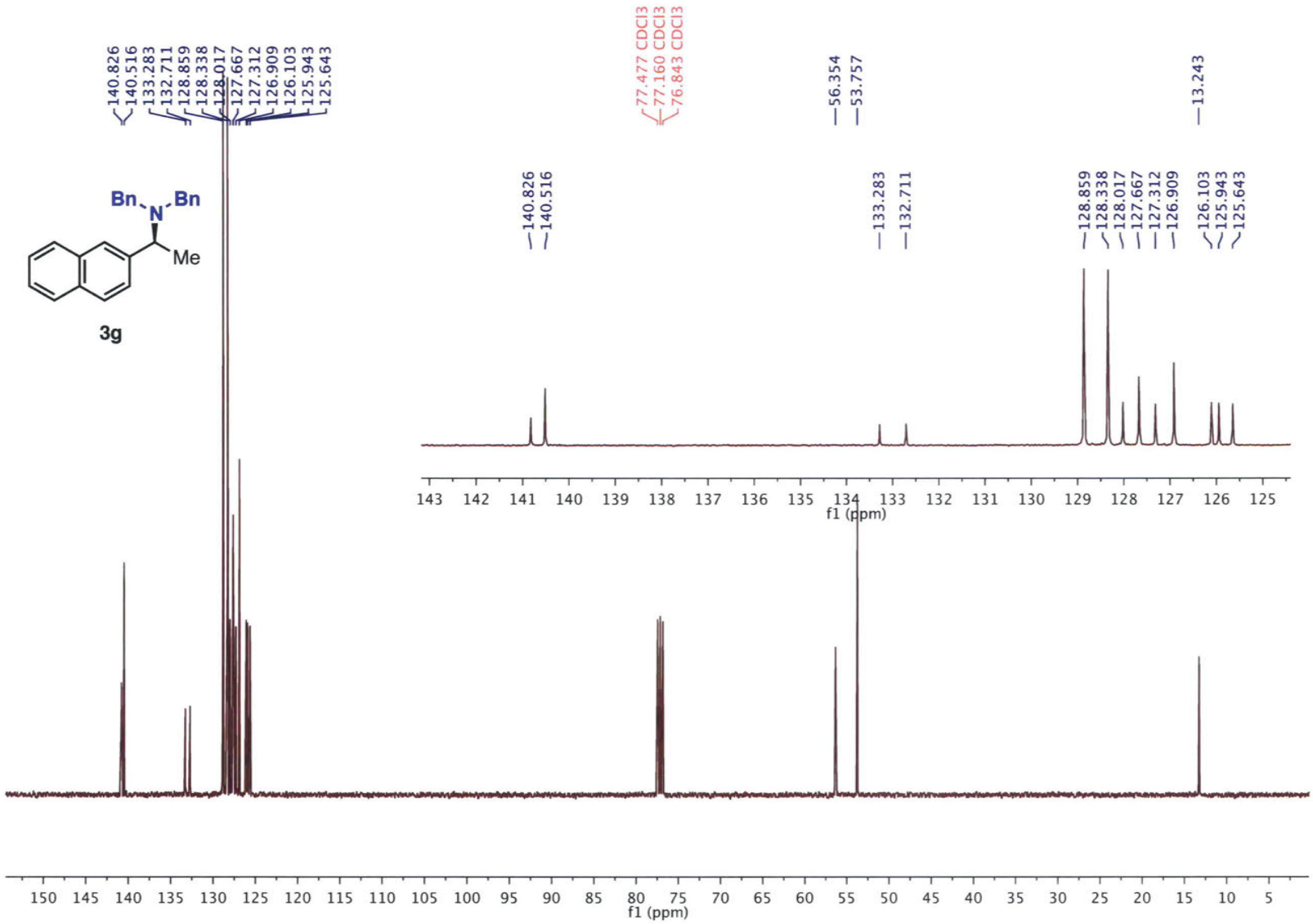
7.904
7.894
7.886
7.880
7.828
7.826
7.823
7.729
7.725
7.708
7.703
7.536
7.531
7.527
7.519
7.511
7.508
7.504
7.496
7.492
7.487
7.476
7.473
7.402
7.397
7.384
7.380
7.367
7.364
7.310
7.307
7.303
7.294
7.288
7.270
7.260 CDCl3
4.187
4.170
4.153
4.136
3.717
3.683
3.643
3.608
1.618
1.601
Bn
N
Bn
Me
3g
2.98
1.00
1.04
1.89
4.01
3.87
1.94
0.98
4.00
3.00
f1 (ppm)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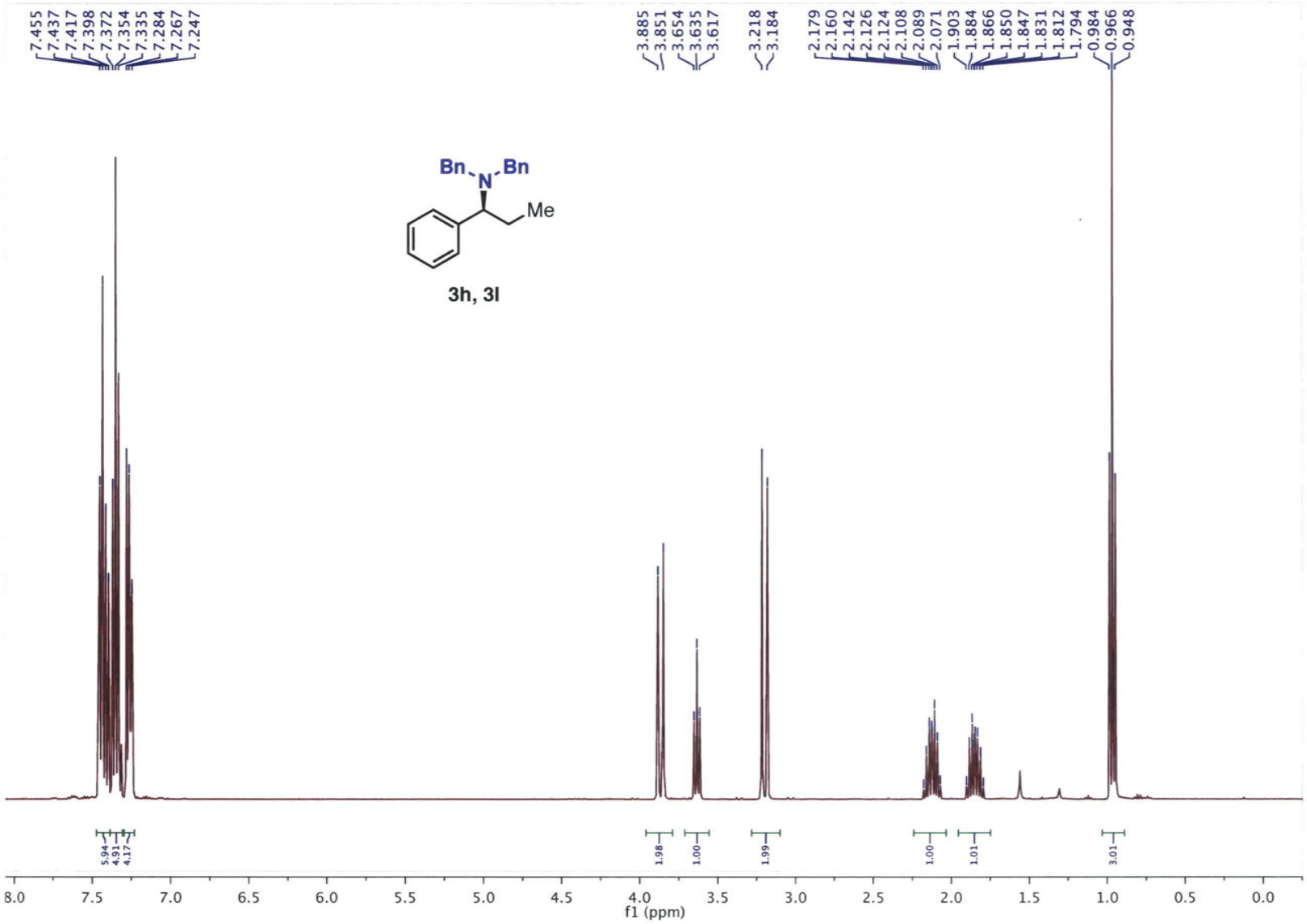
133.283
132.711
128.859
128.338
128.017
127.667
127.312
126.909
126.103
125.943
125.643
77.477 CDCl3
77.160 CDCl3
76.843 CDCl3
56.354
53.757
13.243
Bn
N
Bn
Me
3g
f1 (ppm)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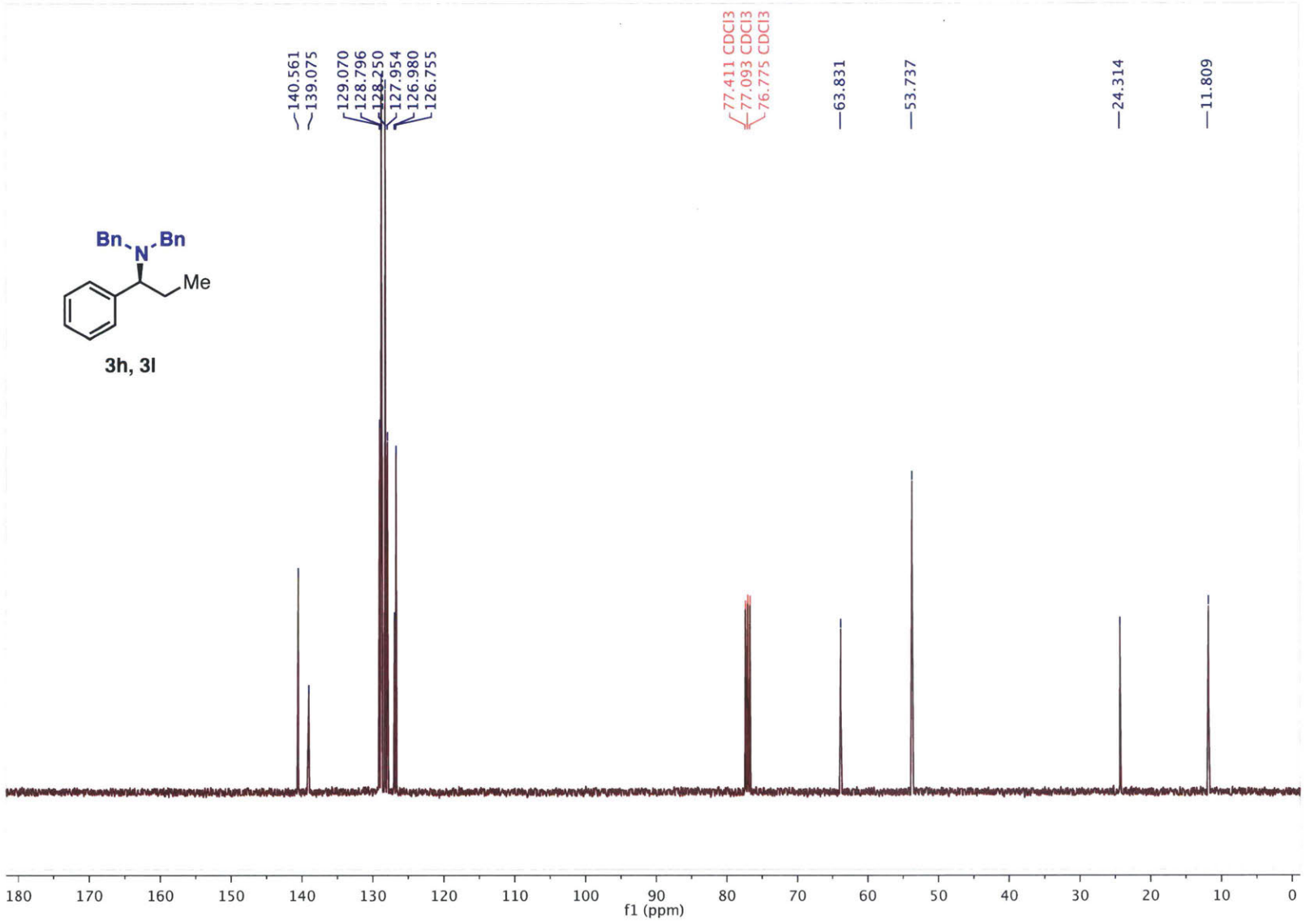
7.417
7.398
7.372
7.354
7.335
7.284
7.267
7.247
3.885
3.851
3.654
3.635
3.617
3.218
3.184
2.179
2.160
2.142
2.126
2.124
2.108
2.089
2.071
1.903
1.884
1.866
1.850
1.847
1.831
1.812
1.794
0.984
0.966
0.948
Bn
N
Bn
Me
3h, 3l
5.94
4.91
4.17
1.98
1.00
1.99
1.00
1.01
3.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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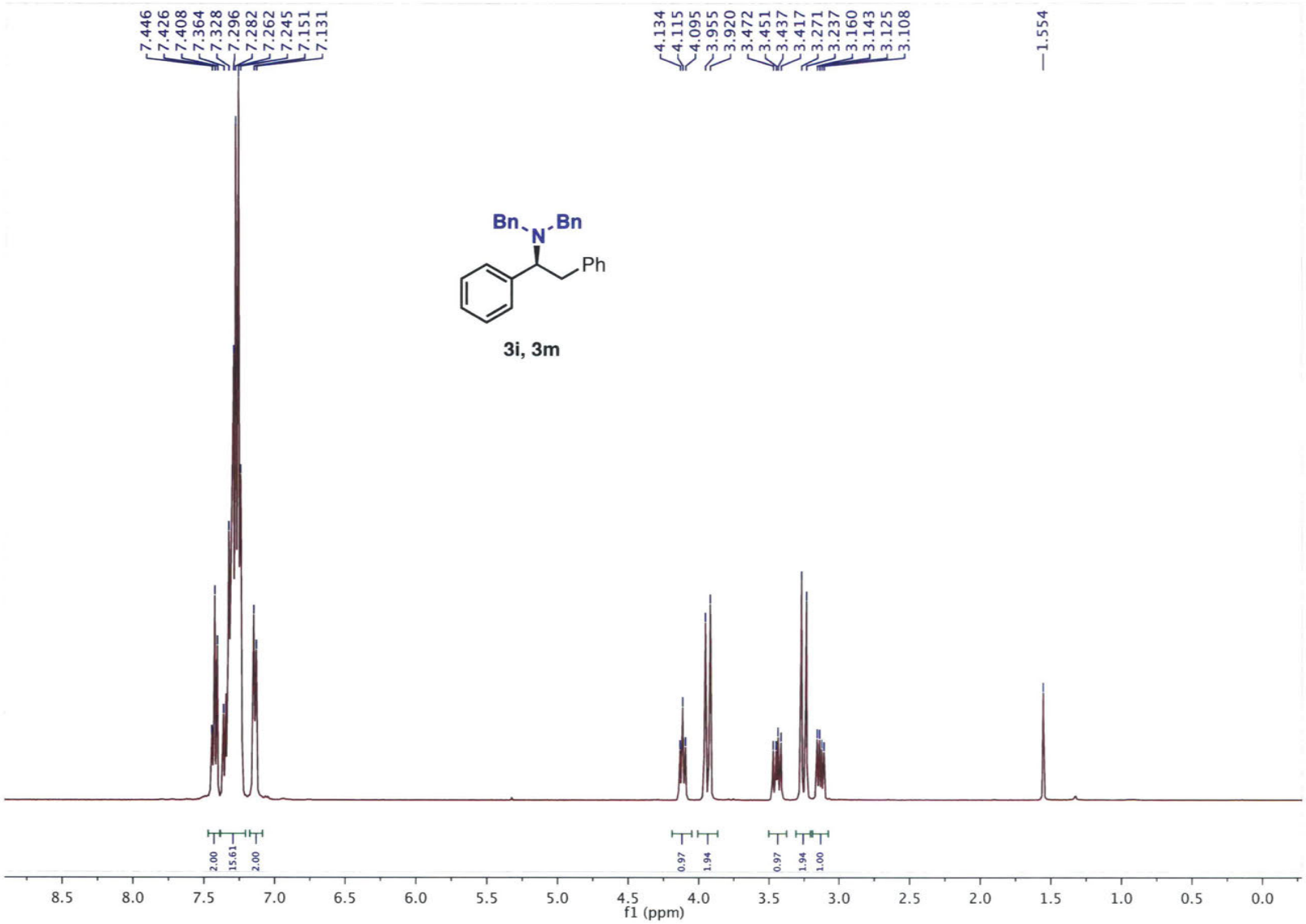
139.075
129.070
128.796
128.250
127.954
126.980
126.755
77.411 CDCl3
77.093 CDCl3
76.775 CDCl3
63.831
53.737
24.314
11.809
Bn
N
Bn
Me
3h, 3l
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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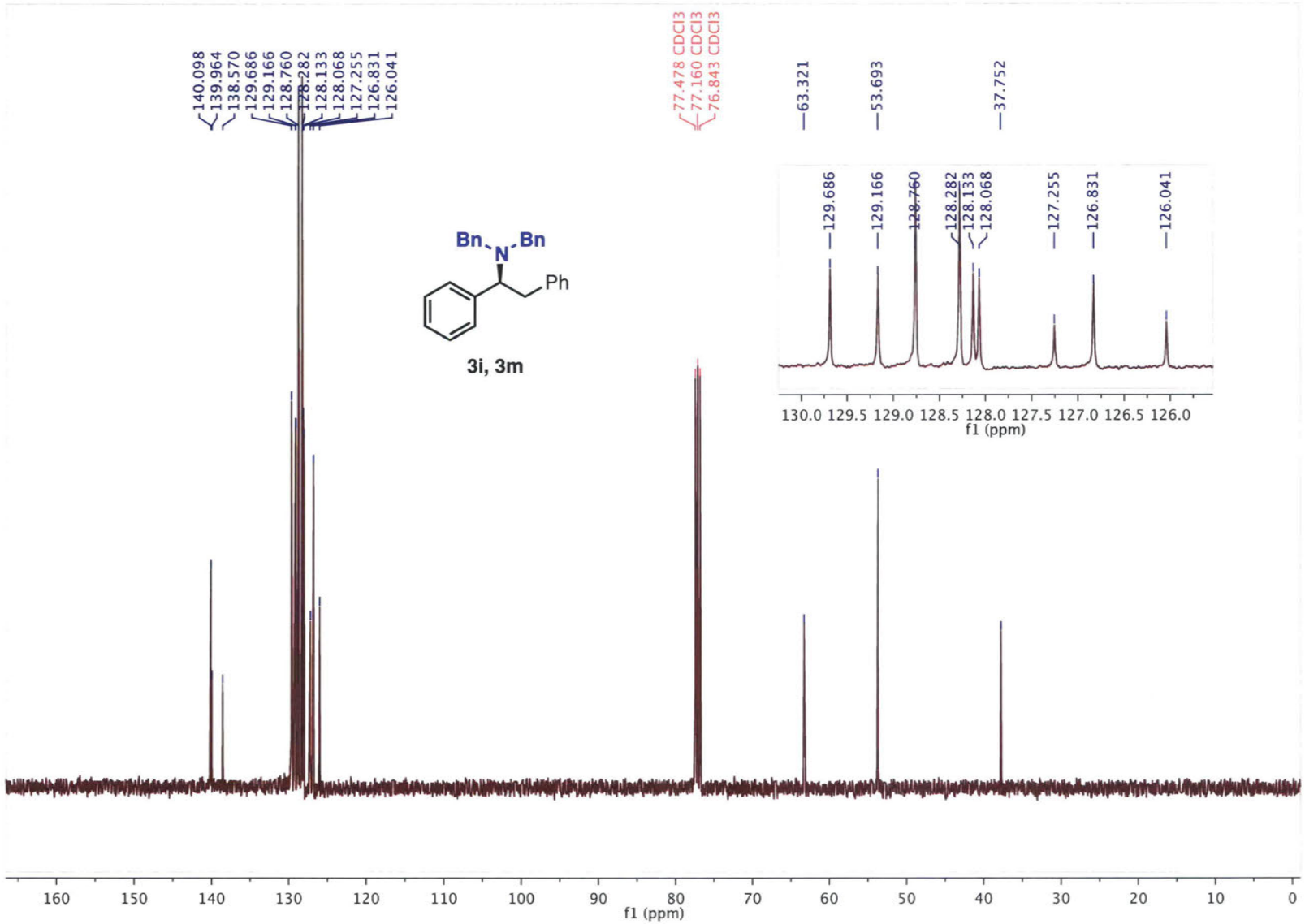
7.426
7.408
7.364
7.328
7.296
7.282
7.262
7.245
7.151
7.131
4.134
4.115
4.095
3.955
3.920
3.472
3.451
3.437
3.417
3.271
3.237
3.160
3.143
3.125
3.108
1.554
Bn
N
Bn
Ph
3i, 3m
2.00
15.61
2.00
0.97
1.94
0.97
1.94
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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139.964
138.570
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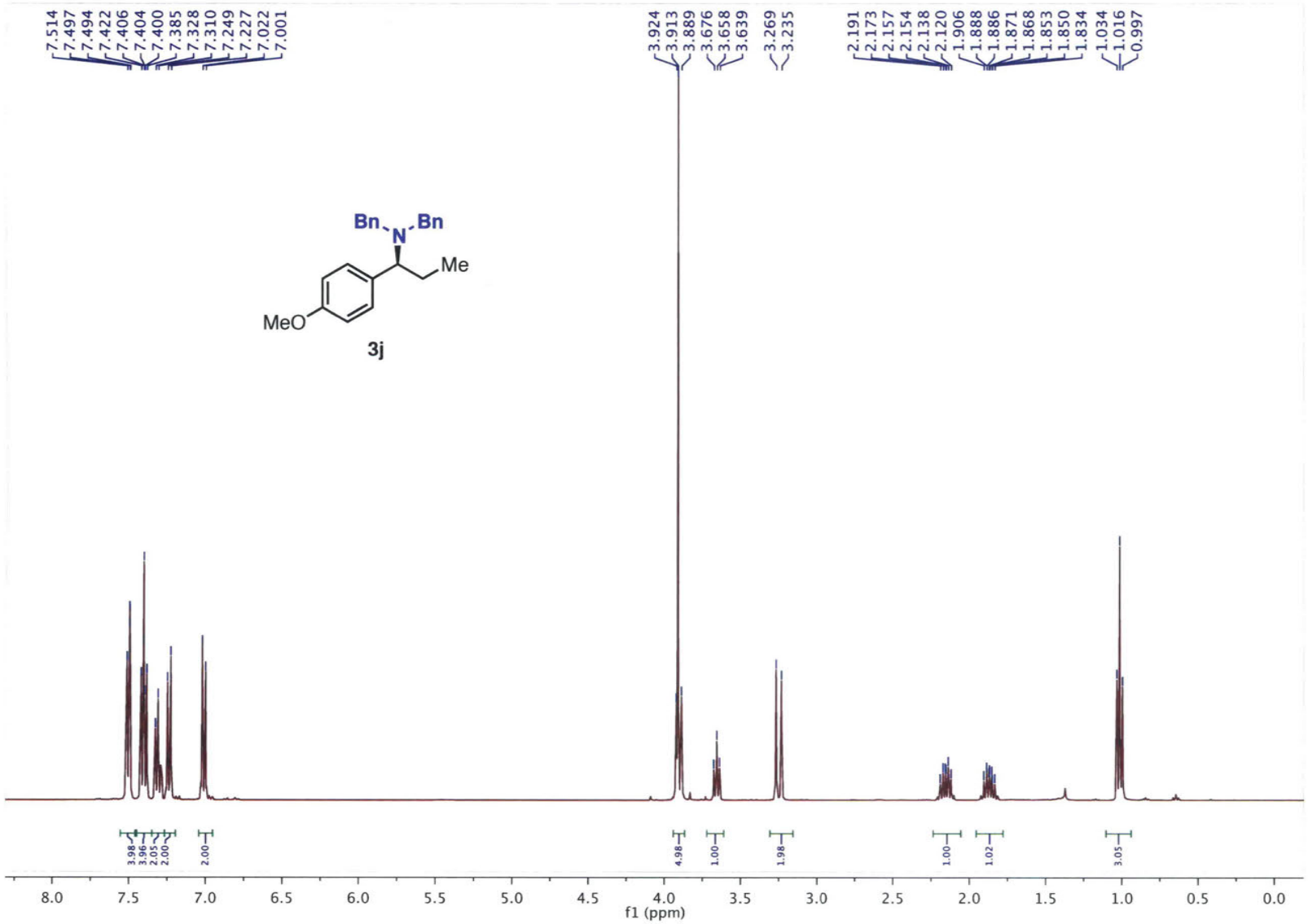
128.760
128.282
128.133
128.068
127.255
126.831
126.041
77.478 CDCl3
77.160 CDCl3
76.843 CDCl3
63.321
53.693
37.752
Bn
N
Bn
Ph
3i, 3m
129.686
129.166
128.760
128.282
128.133
128.068
127.255
126.831
126.041
130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5 126.0
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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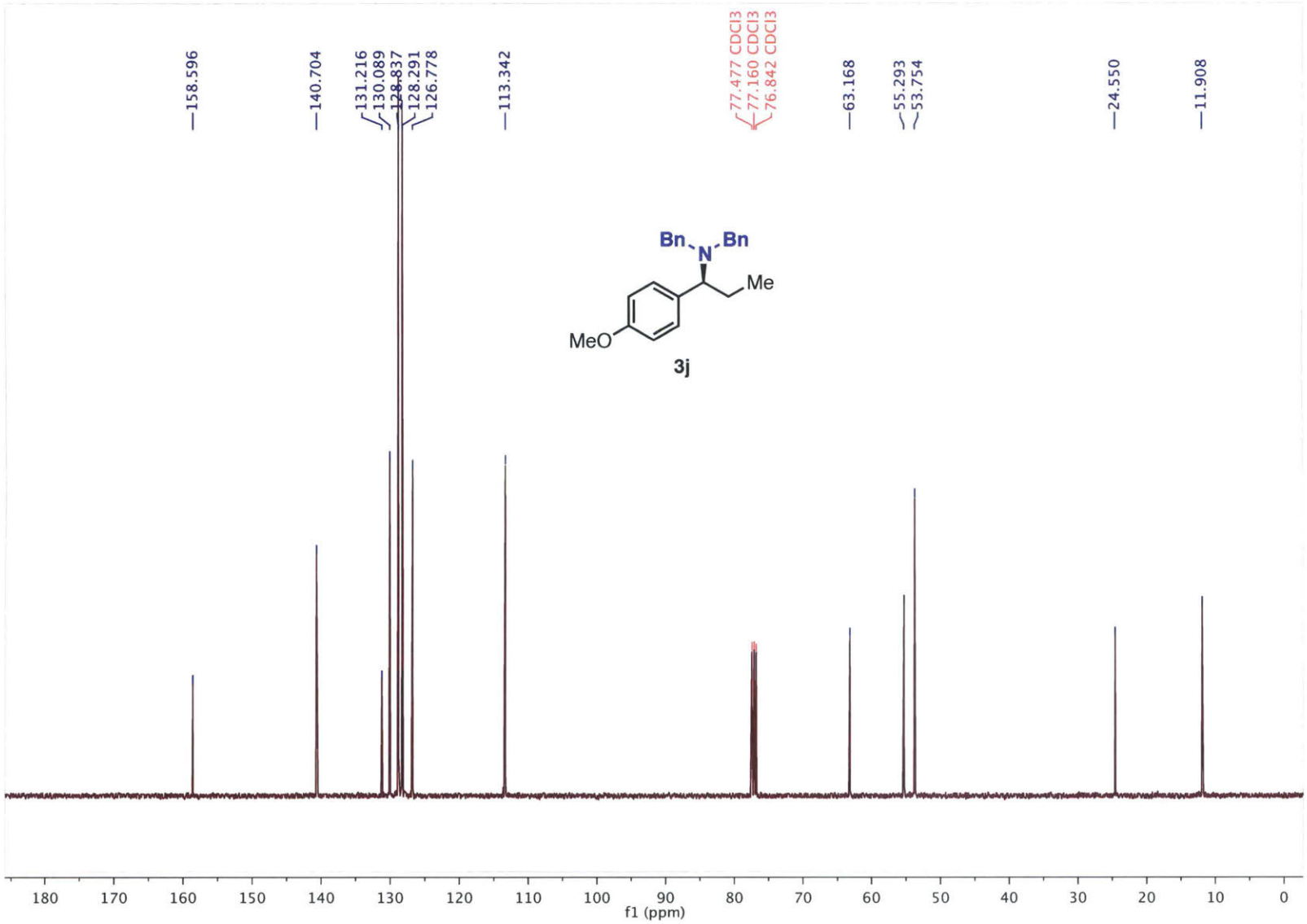
7.497
7.494
7.422
7.406
7.404
7.400
7.385
7.328
7.310
7.249
7.227
7.022
7.001
3.924
3.913
3.889
3.676
3.658
3.639
3.269
3.235
2.191
2.173
2.157
2.154
2.138
2.120
1.906
1.888
1.886
1.871
1.868
1.853
1.850
1.834
1.034
1.016
0.997
Bn
N
Bn
Me
MeO
3j
3.98
3.96
2.05
2.00
2.00
4.98
1.00
1.98
1.00
1.02
3.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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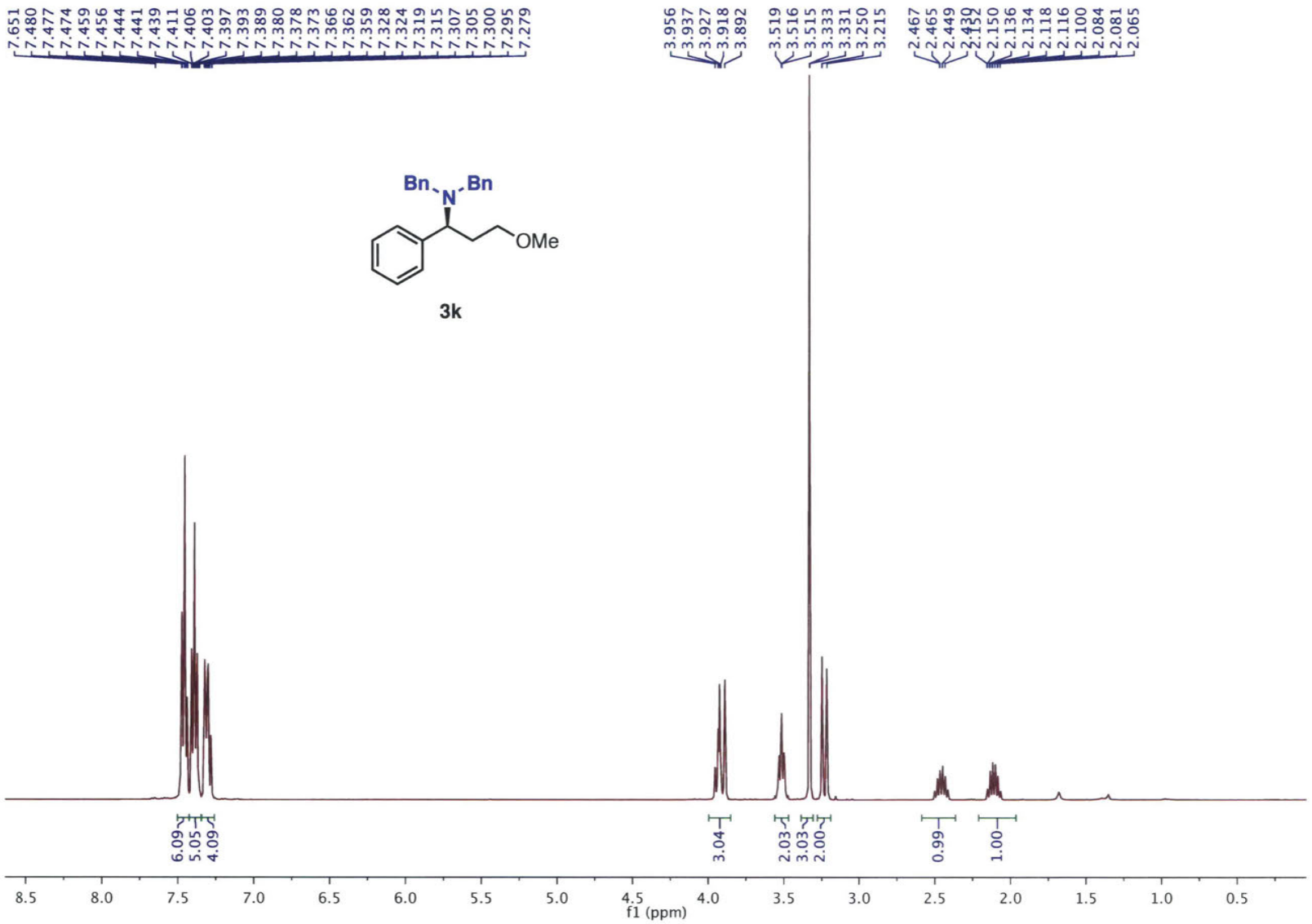
140.704
131.216
130.089
128.837
128.291
126.778
113.342
77.477 CDCl3
77.160 CDCl3
76.842 CDCl3
63.168
55.293
53.754
24.550
11.908
Bn
N
Bn
Me
MeO
3j
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.406
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7.397
7.393
7.389
7.380
7.378
7.373
7.366
7.362
7.359
7.328
7.324
7.319
7.315
7.307
7.305
7.300
7.295
7.279
3.956
3.937
3.927
3.918
3.892
3.519
3.516
3.515
3.333
3.331
3.250
3.215
2.467
2.465
2.449
2.150
2.136
2.134
2.118
2.116
2.100
2.084
2.081
2.065
Bn
N
Bn
OMe
3k
6.09
5.05
4.09
3.04
2.03
3.03
2.00
0.99
1.00
8.5
8.0
7.5
7.0
6.5
6.0
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4.0
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3.0
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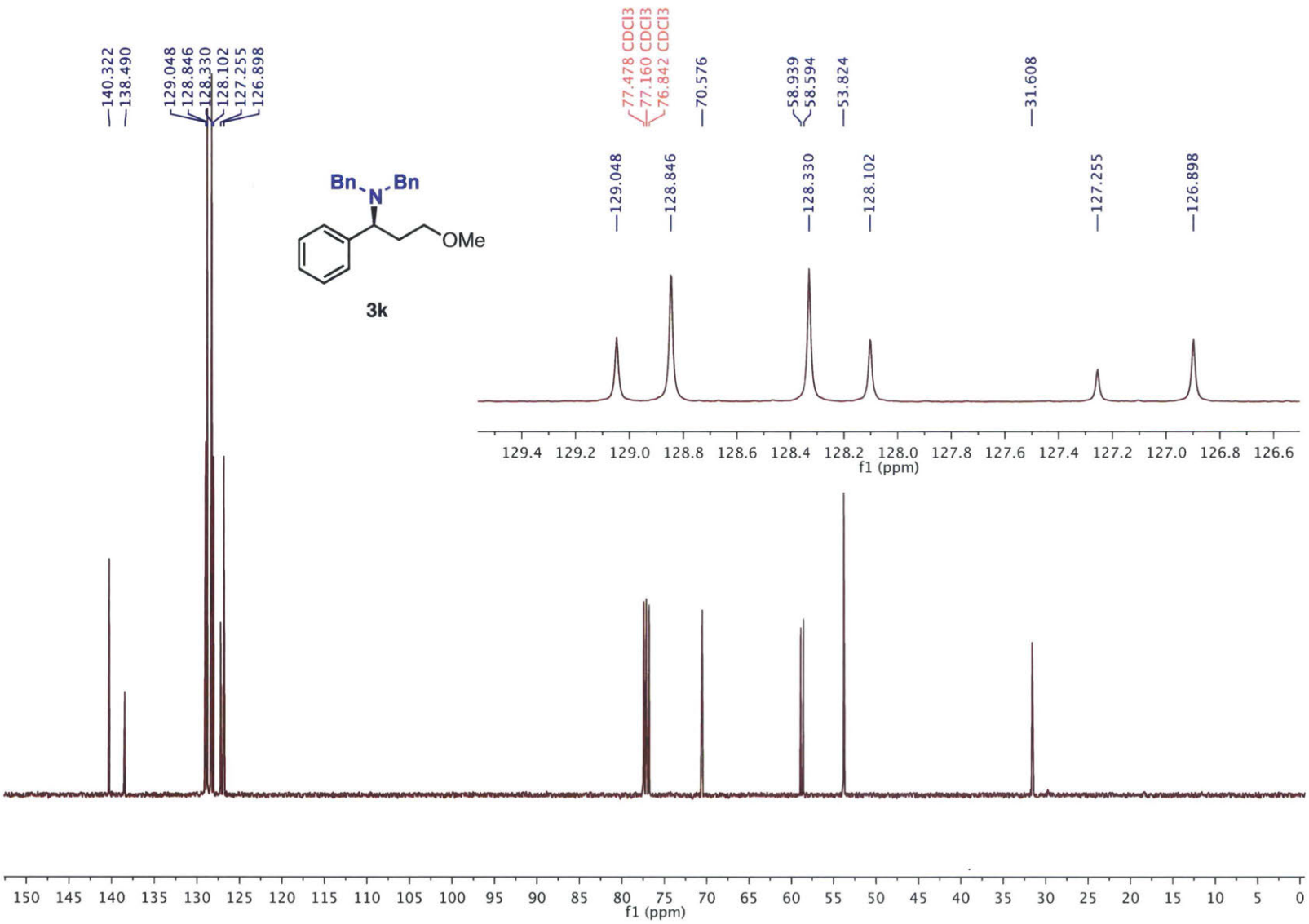
1.5
1.0
0.5
f1 (ppm)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77.160 CDCl3
76.842 CDCl3
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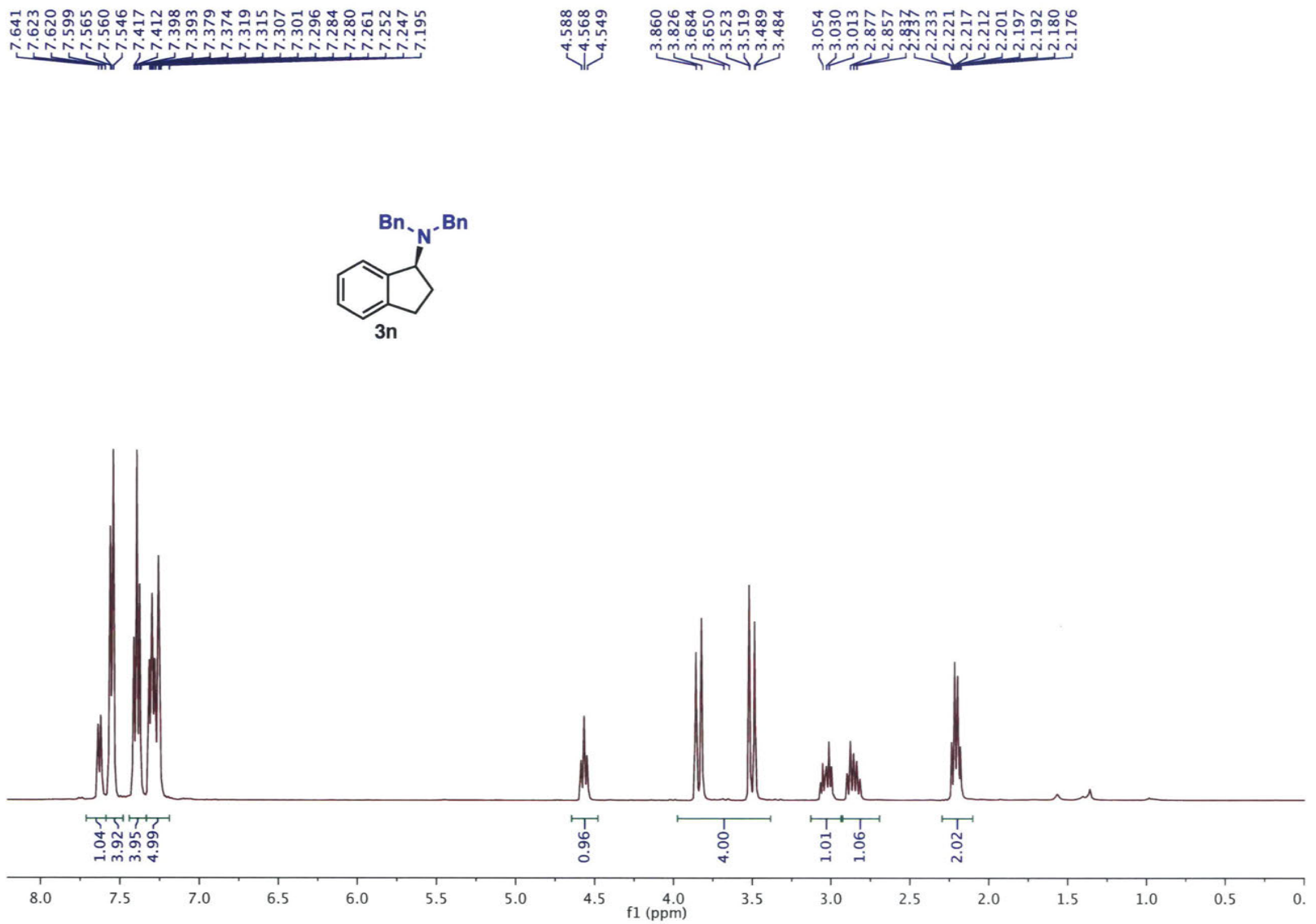
58.594
53.824
31.608
Bn
N
Bn
OMe
3k
f1 (ppm)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7.374
7.319
7.315
7.307
7.301
7.296
7.284
7.280
7.261
7.252
7.247
7.195
4.588
4.568
4.549
3.860
3.826
3.684
3.650
3.523
3.519
3.489
3.484
3.054
3.030
3.013
2.877
2.857
2.233
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2.217
2.212
2.201
2.197
2.192
2.180
2.176
Bn
N
Bn
3n
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3.92
3.95
4.99
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4.00
1.01
1.06
2.02
8.0
7.5
7.0
6.5
6.0
5.5
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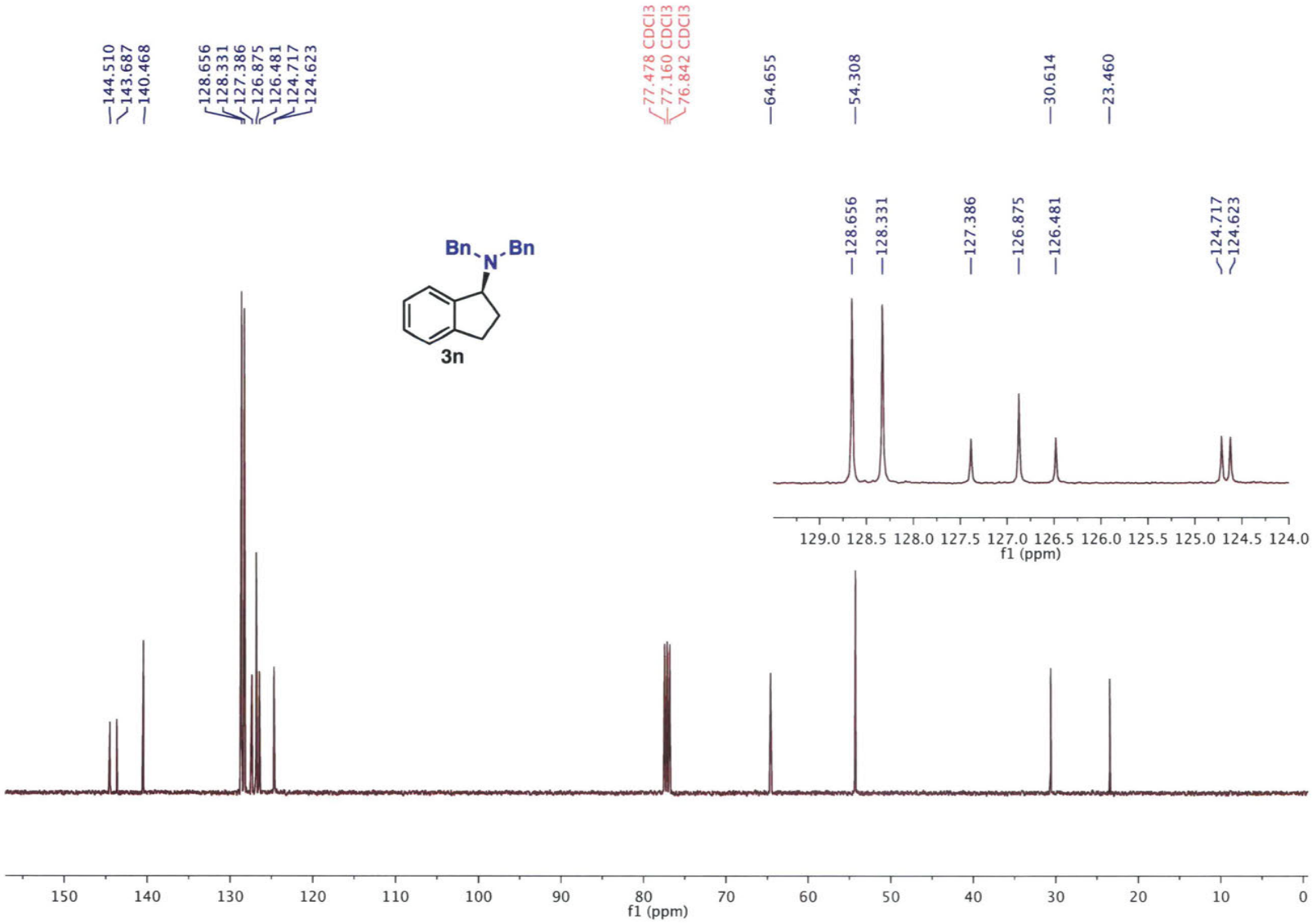
1.0
0.5
0.
f1 (ppm)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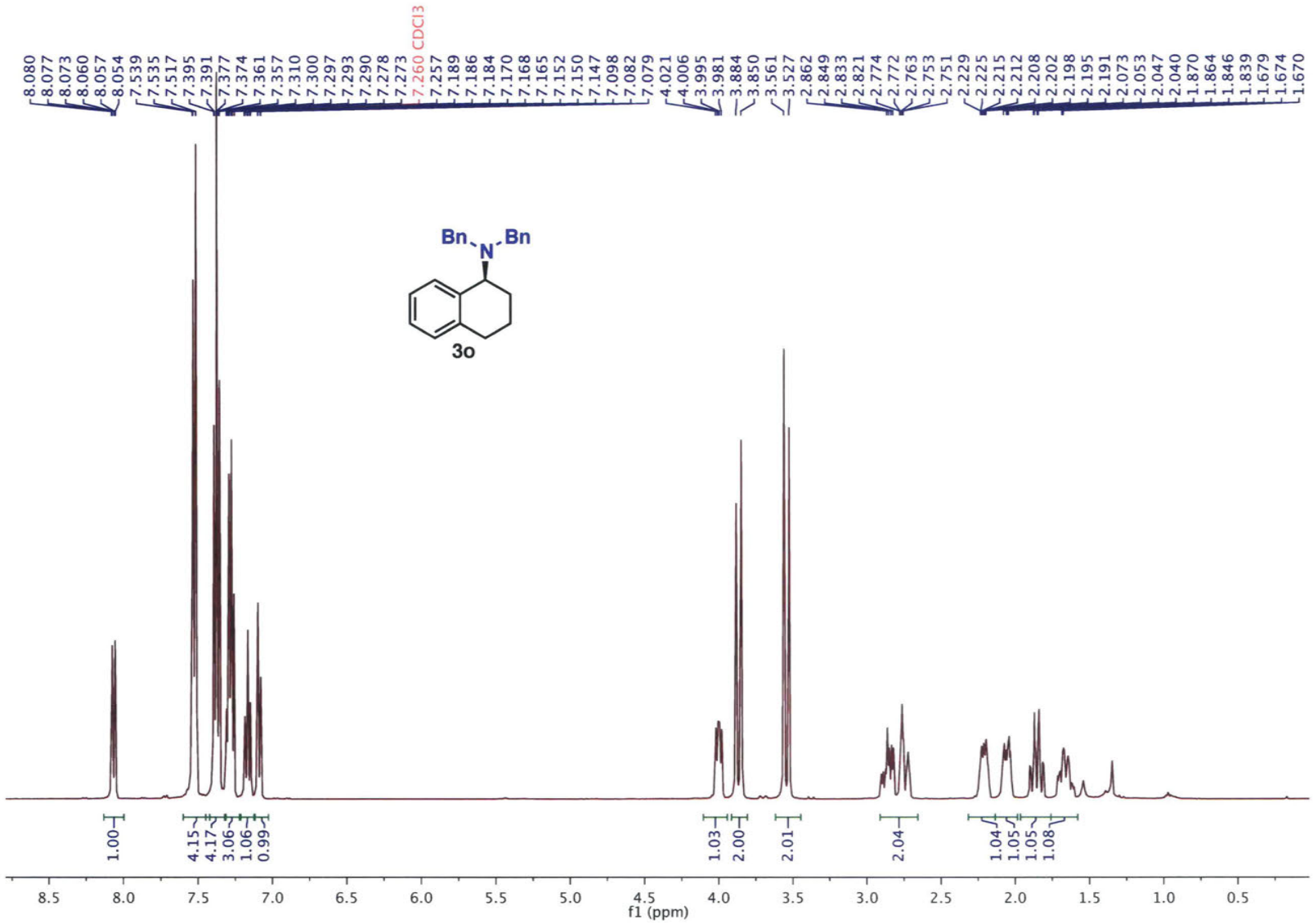
126.481
124.717
124.623
77.478 CDCl3
77.160 CDCl3
76.842 CDCl3
64.655
54.308
30.614
23.460
Bn
N
Bn
3n
f1 (ppm)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7.361
7.357
7.310
7.300
7.297
7.293
7.290
7.278
7.273
7.260 CDCl3
7.257
7.189
7.186
7.184
7.170
7.168
7.165
7.152
7.150
7.147
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7.082
7.079
4.021
4.006
3.995
3.981
3.884
3.850
3.561
3.527
2.862
2.849
2.833
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2.774
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2.763
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2.751
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2.208
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2.198
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2.191
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2.047
2.040
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1.864
1.846
1.839
1.679
1.674
1.670
Bn
N
Bn
3o
1.00
4.15
4.17
3.06
1.06
0.99
1.03
2.00
2.01
2.04
1.04
1.05
1.05
1.08
8.5
8.0
7.5
7.0
6.5
6.0
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3.0
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1.5
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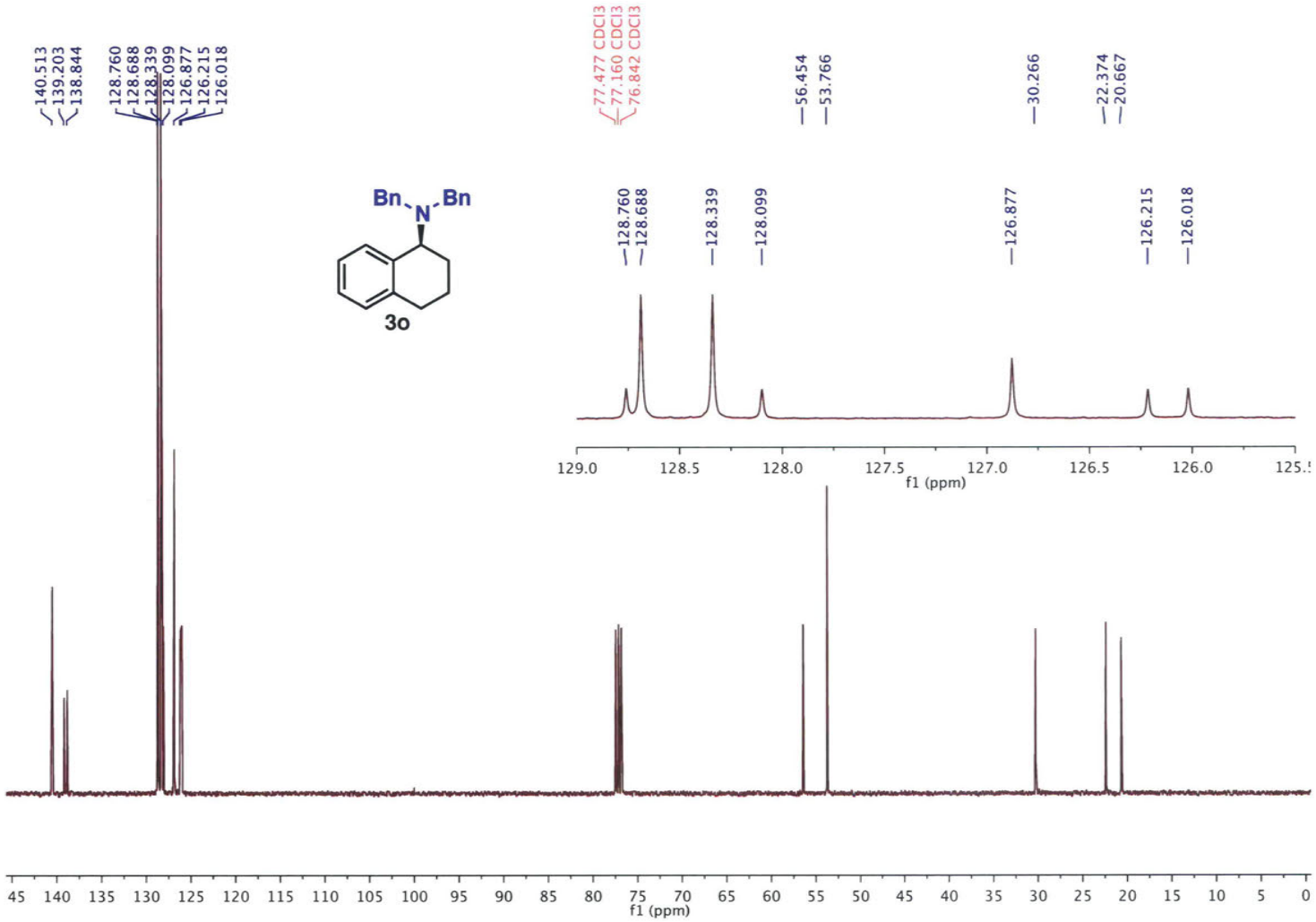
f1 (ppm)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126.877
126.215
126.018
77.477 CDCl3
77.160 CDCl3
76.842 CDCl3
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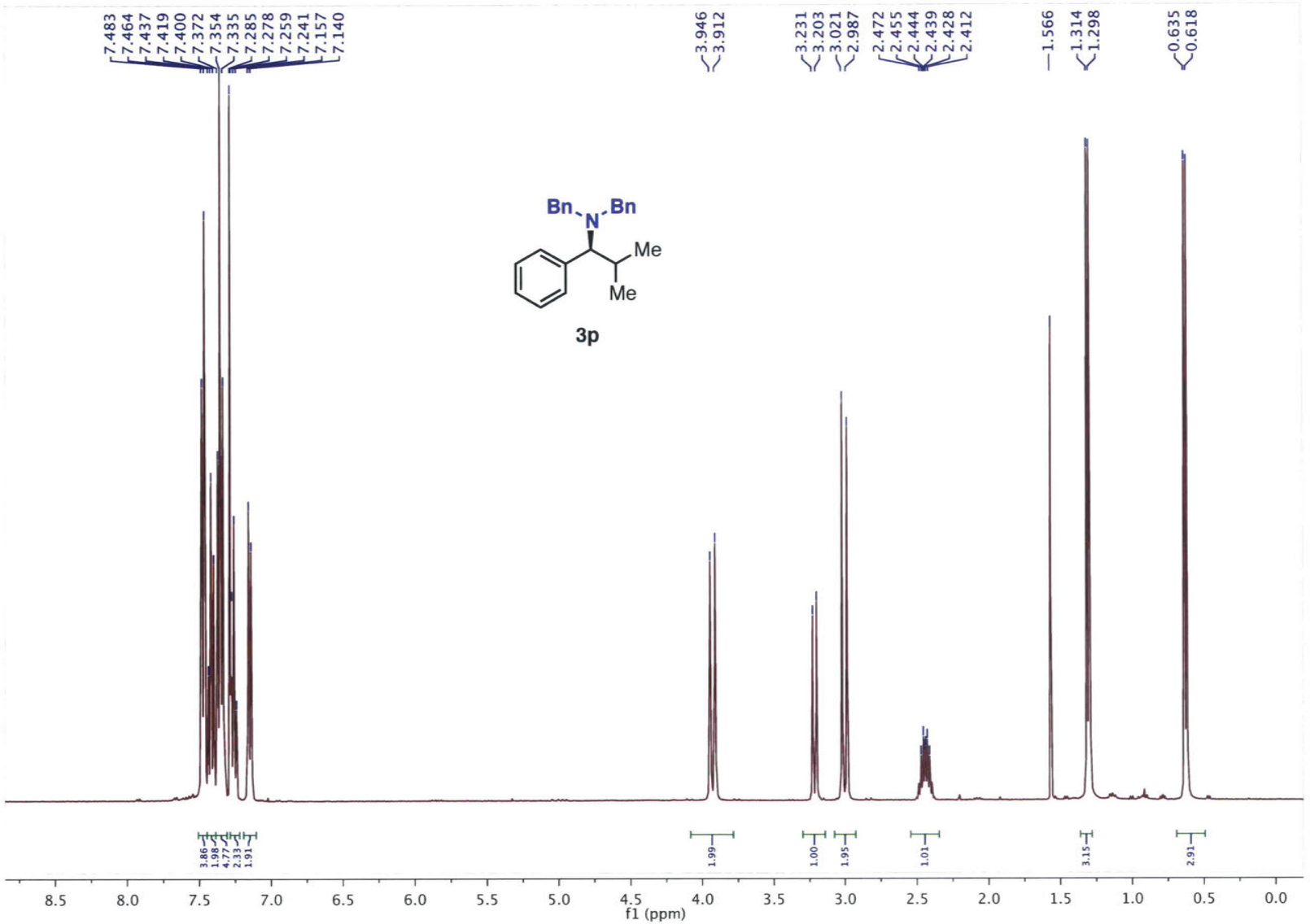
53.766
30.266
22.374
20.667
Bn
N
Bn
3o
f1 (ppm)
f1 (ppm)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7.464
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7.419
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7.354
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7.157
7.140
3.946
3.912
3.231
3.203
3.021
2.987
2.472
2.455
2.444
2.439
2.428
2.412
1.566
1.314
1.298
0.635
0.618
Bn
N
Bn
Me
Me
3p
3.86
1.98
4.77
2.33
1.91
1.99
1.00
1.95
1.01
3.15
2.91
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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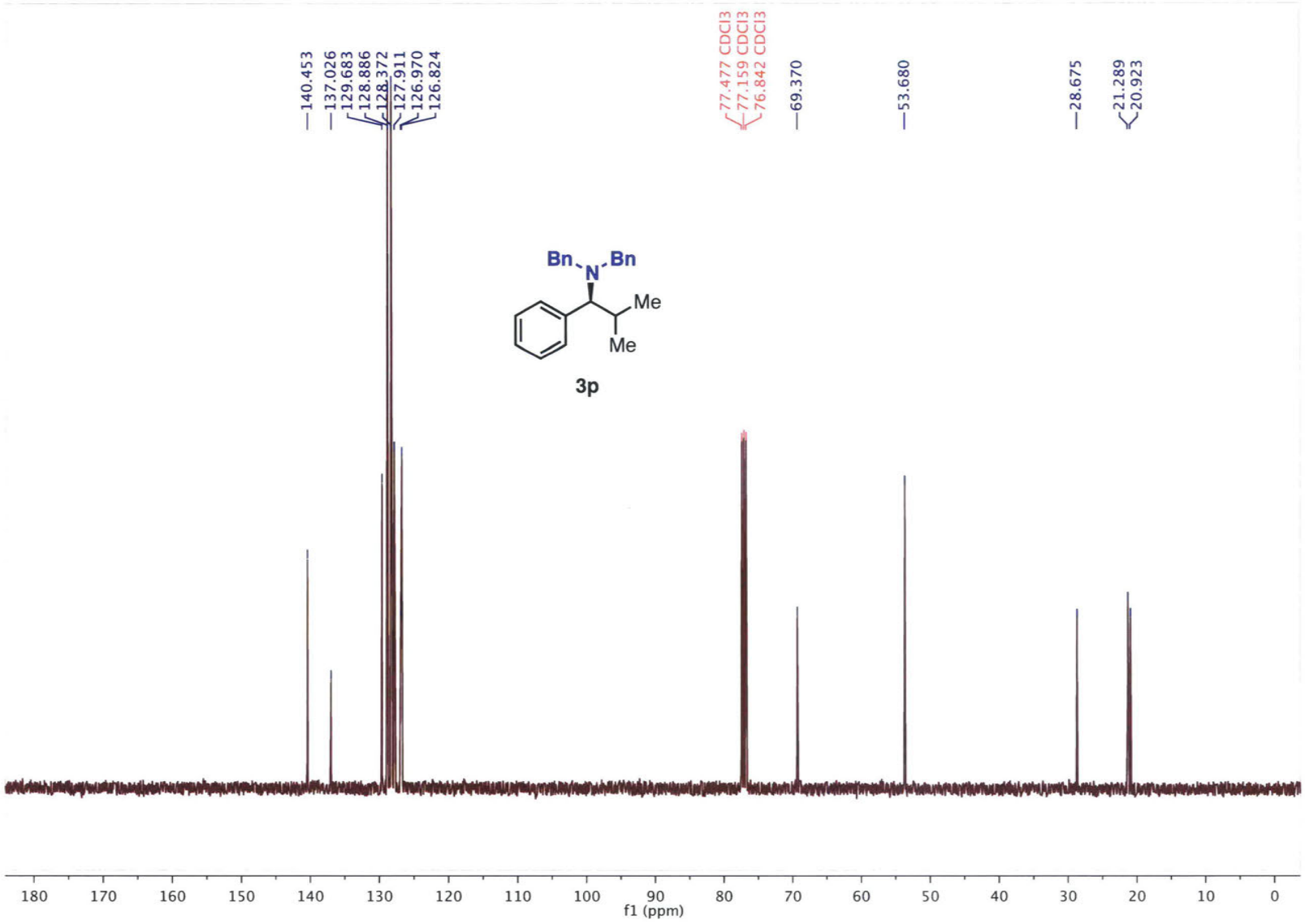
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


140.453
137.026
129.683
128.886
128.372
127.911
126.970
126.824
77.477 CDCl3
77.159 CDCl3
76.842 CDCl3
69.370
53.680
28.675
21.289
20.923
Bn
N
Bn
Me
Me
3p
180
170
160
150
140
130
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110
100
90
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70
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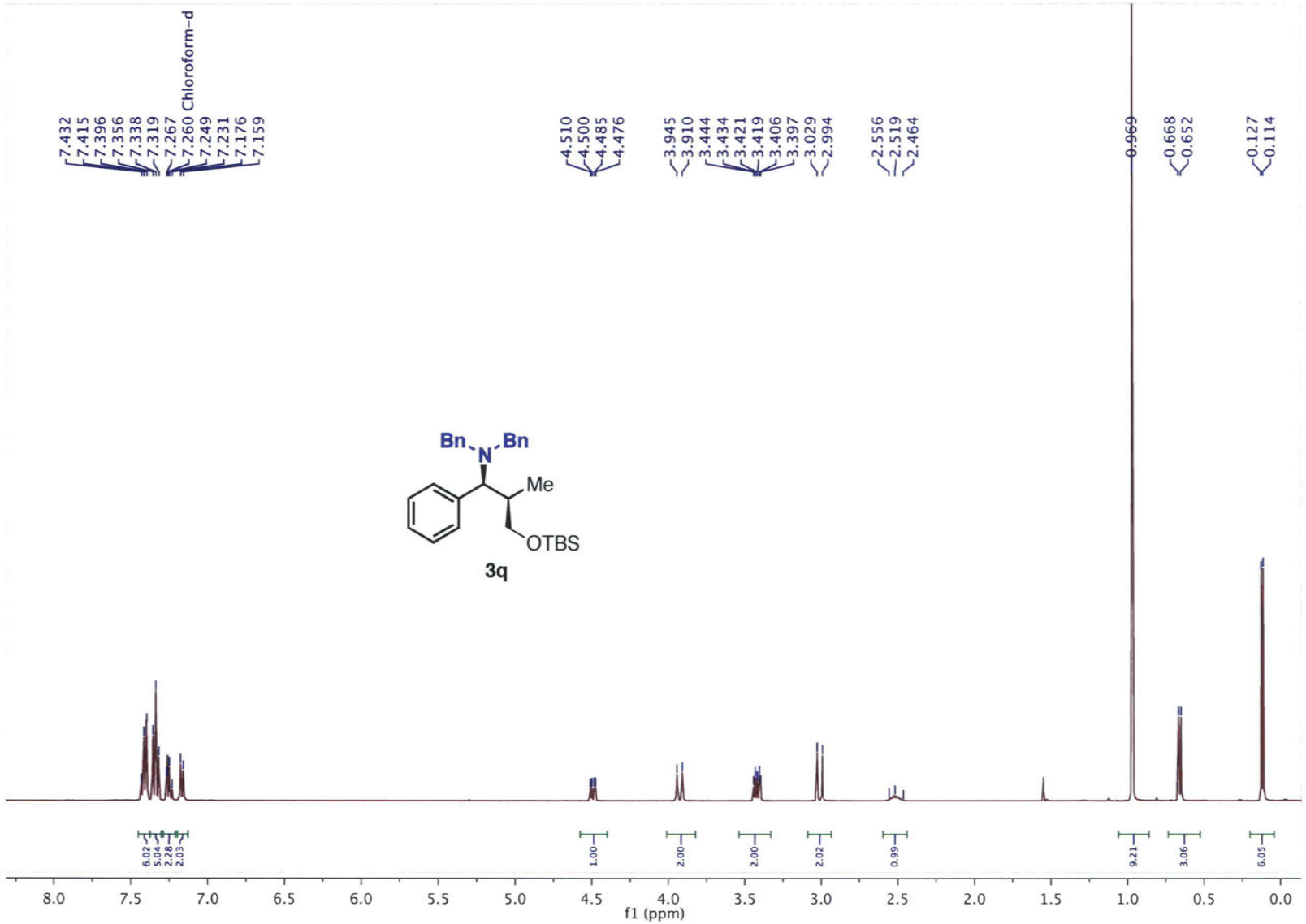
50
40
30
20
10
0
f1 (ppm)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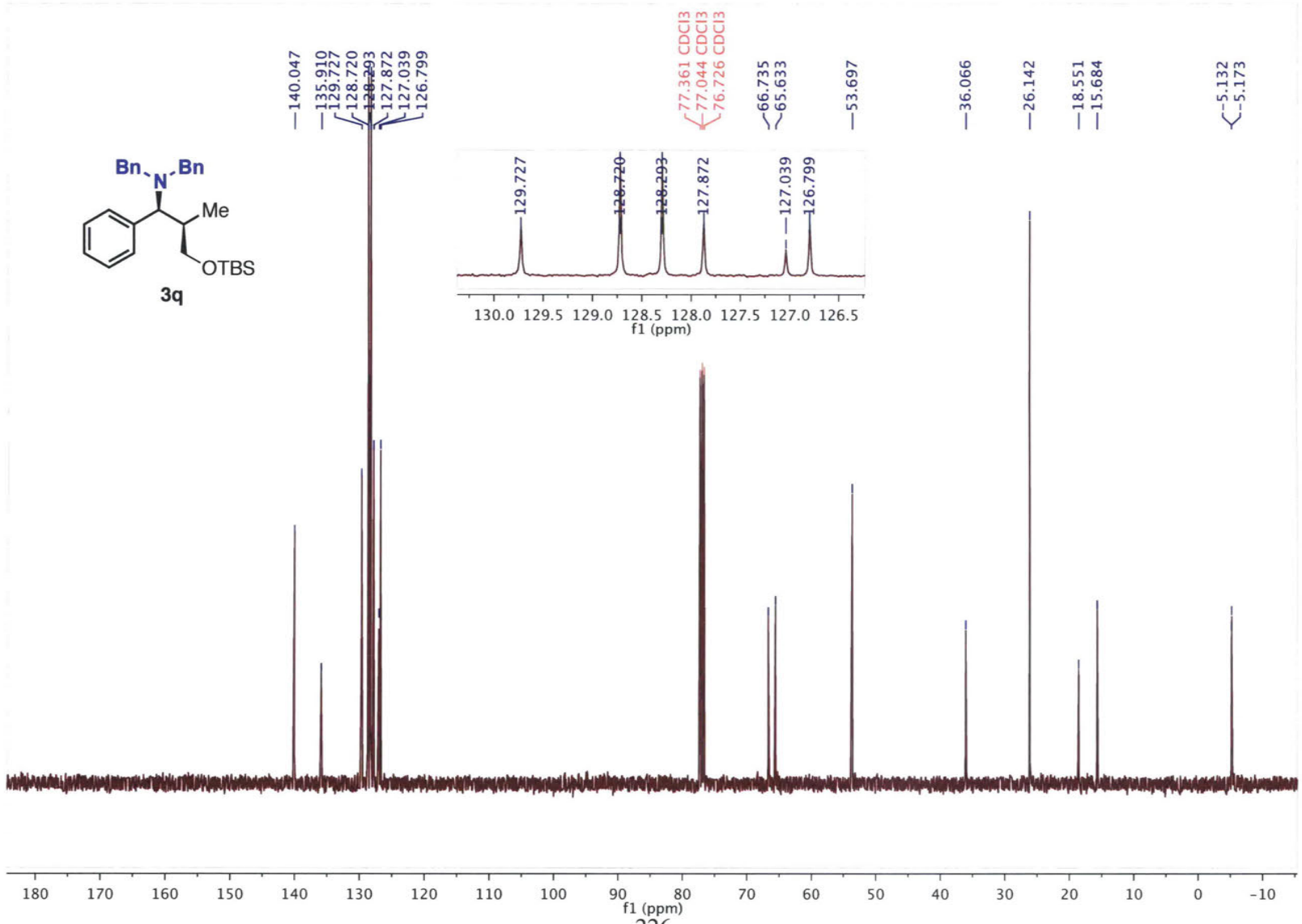
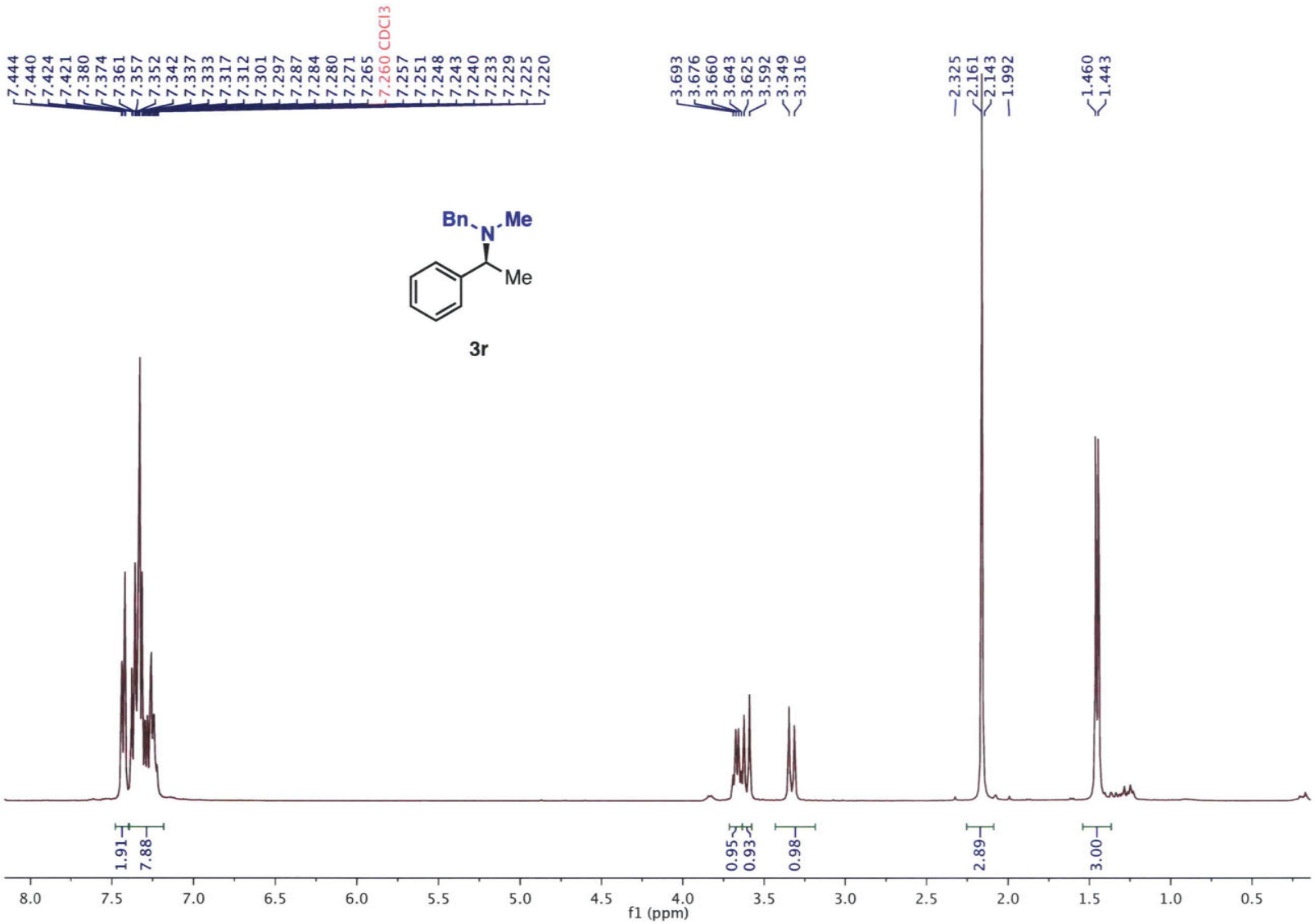
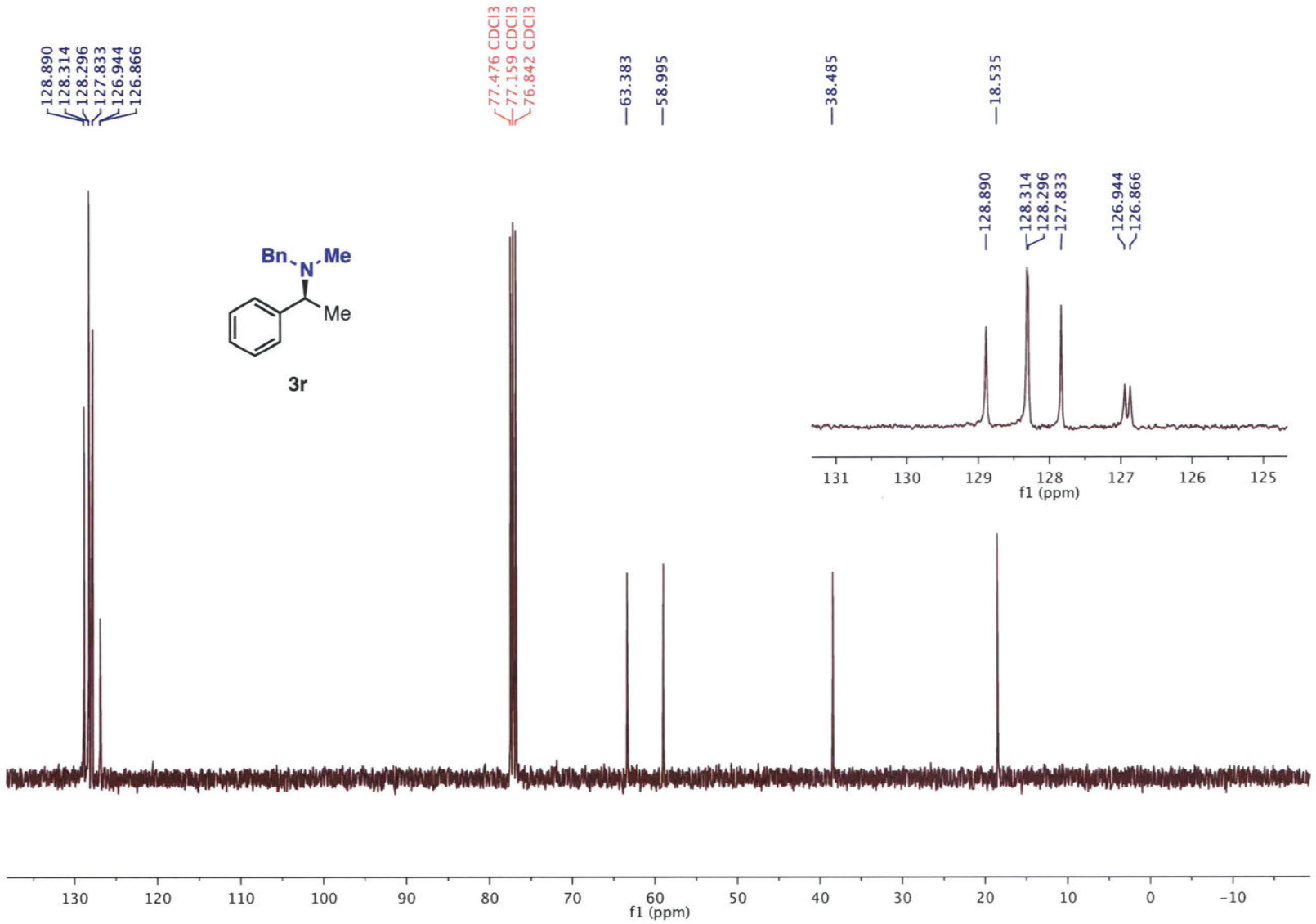
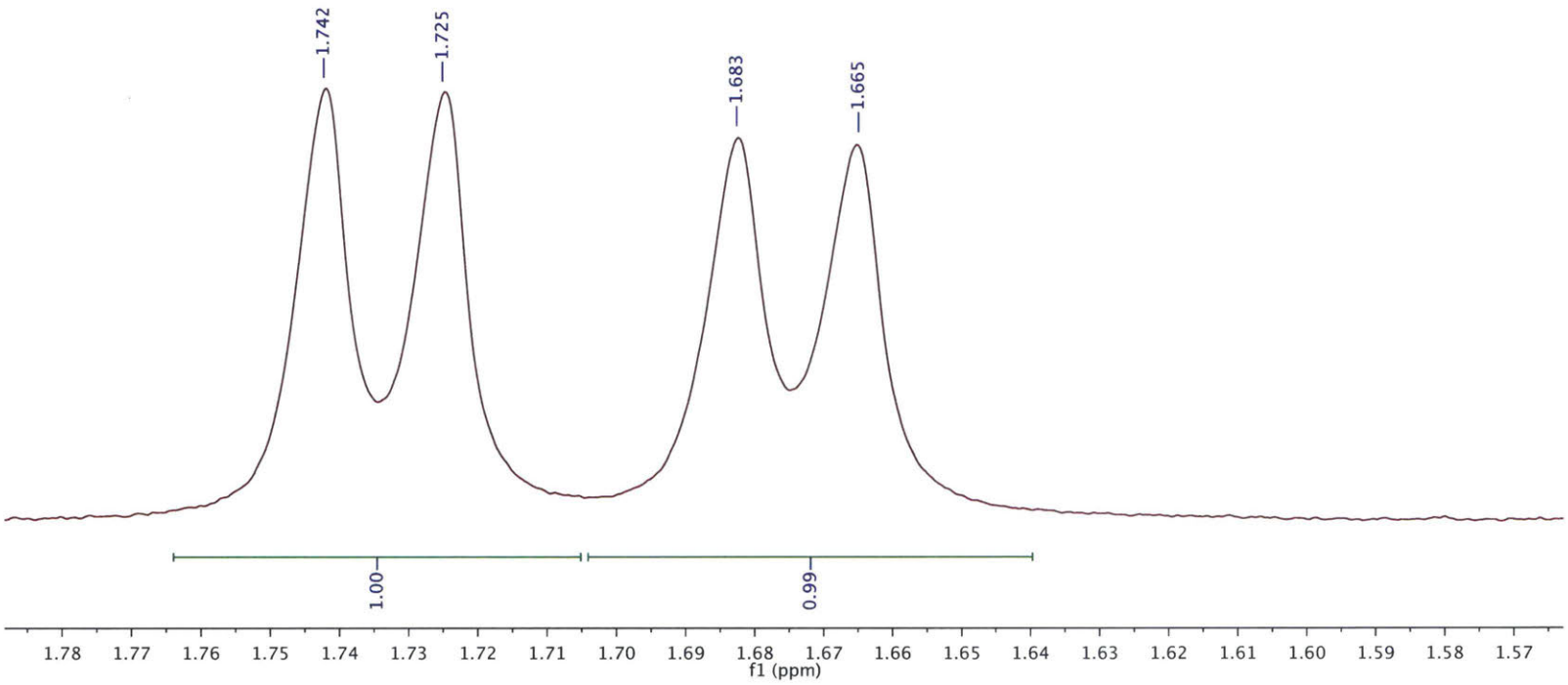
7.319
7.267
7.260 Chloroform-d
7.249
7.231
7.176
7.159
4.510
4.500
4.485
4.476
3.945
3.910
3.444
3.434
3.421
3.419
3.406
3.397
3.029
2.994
2.556
2.519
2.464
0.969
0.668
0.652
0.127
0.114
Bn
N
Bn
Me
OTBS
3q
6.02
5.04
2.28
2.03
1.00
2.00
2.00
2.02
0.99
9.21
3.06
6.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Bn
N
Bn
Me
OTBS
3q
140.047
135.910
129.727
128.720
128.293
127.872
127.039
126.799
77.361 CDCl3
77.044 CDCl3
76.726 CDCl3
66.735
65.633
53.697
36.066
26.142
18.551
15.684
-5.132
-5.173
130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5
f1 (ppm)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

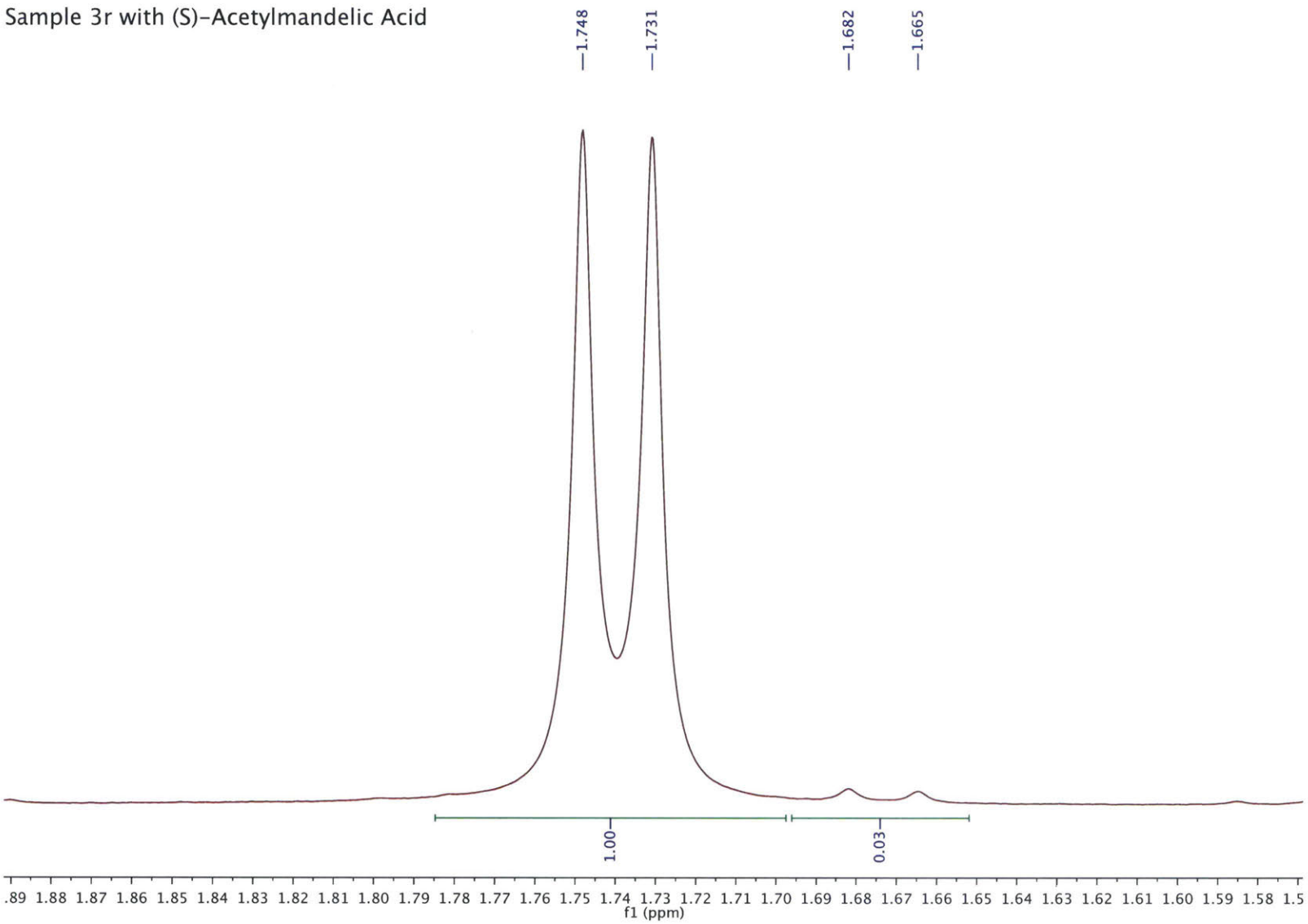

7.444
7.440
7.424
7.421
7.380
7.374
7.361
7.357
7.352
7.342
7.337
7.333
7.317
7.312
7.301
7.297
7.287
7.284
7.280
7.271
7.265
7.260 CDCl3
7.257
7.251
7.248
7.243
7.240
7.233
7.229
7.225
7.220
3.693
3.676
3.660
3.643
3.625
3.592
3.349
3.316
2.325
2.161
2.143
1.992
1.460
1.443
Bn
N
Me
Me
3r
1.91
7.88
0.95
0.93
0.98
2.89
3.00
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
f1 (ppm)

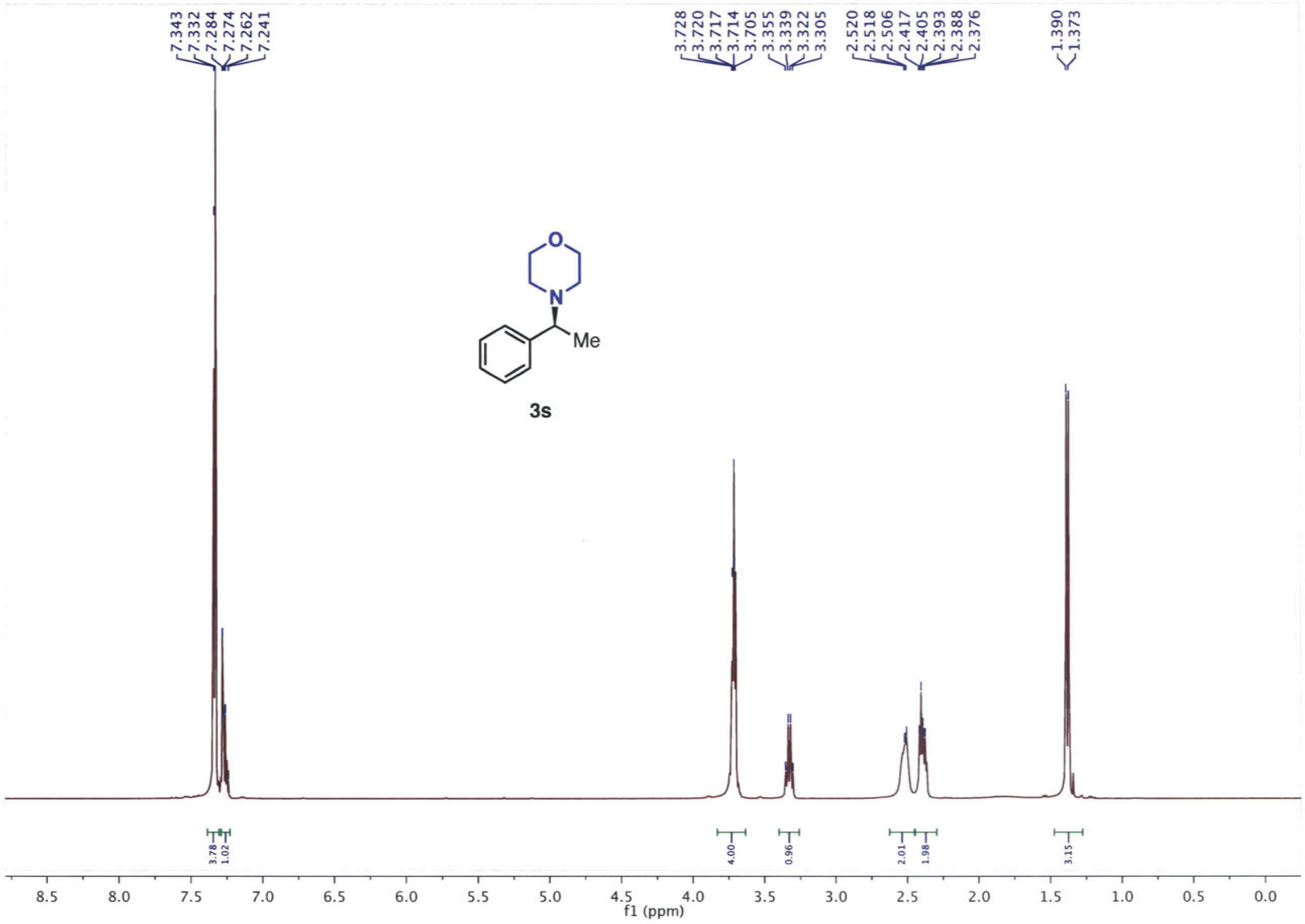

128.890
128.314
128.296
127.833
126.944
126.866
77.476 CDCl3
77.159 CDCl3
76.842 CDCl3
63.383
58.995
38.485
18.535
Bn
N
Me
Me
3r
f1 (ppm)
f1 (ppm)

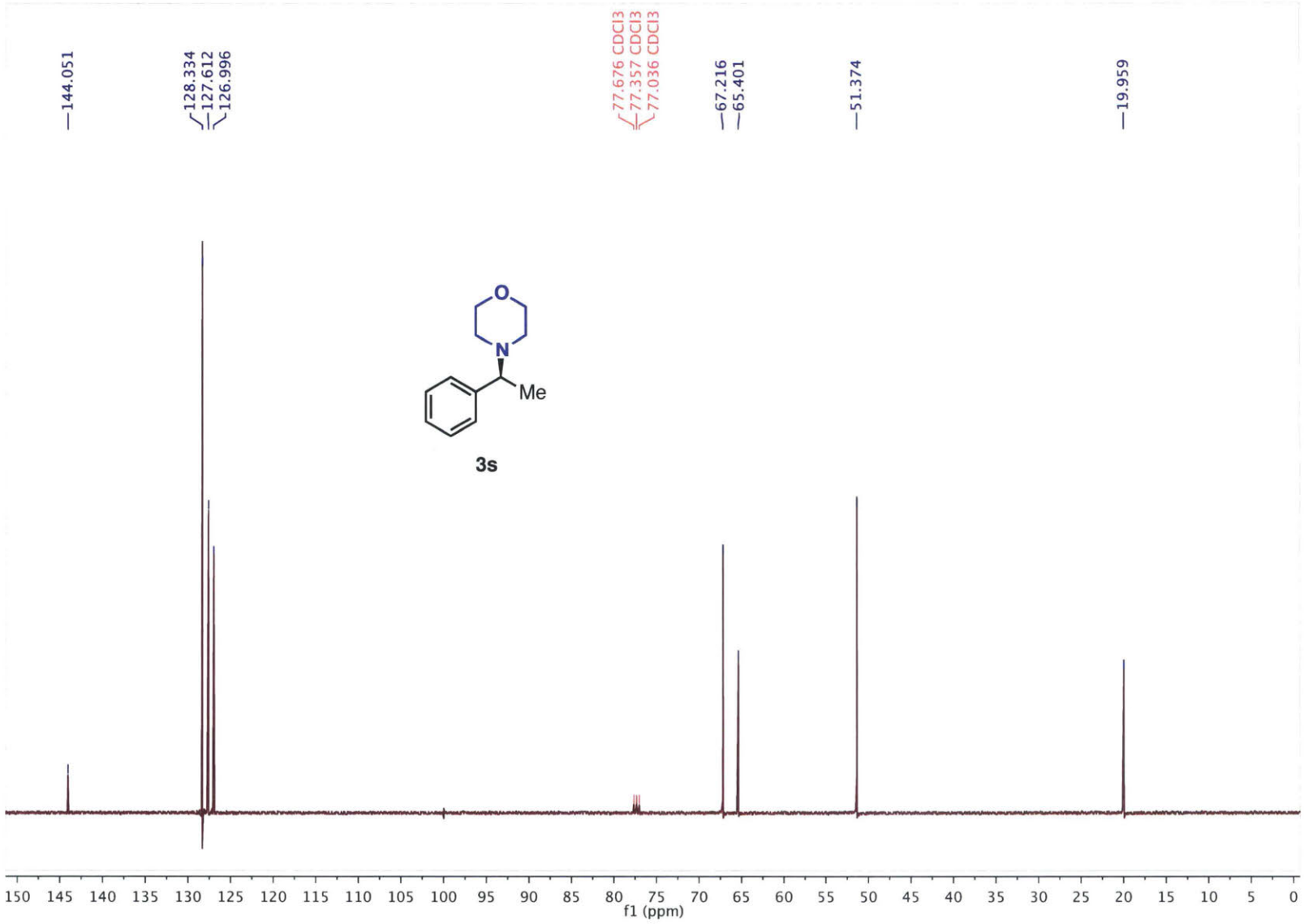
Racemic 3r with (R)-Acetylmandelic Acid

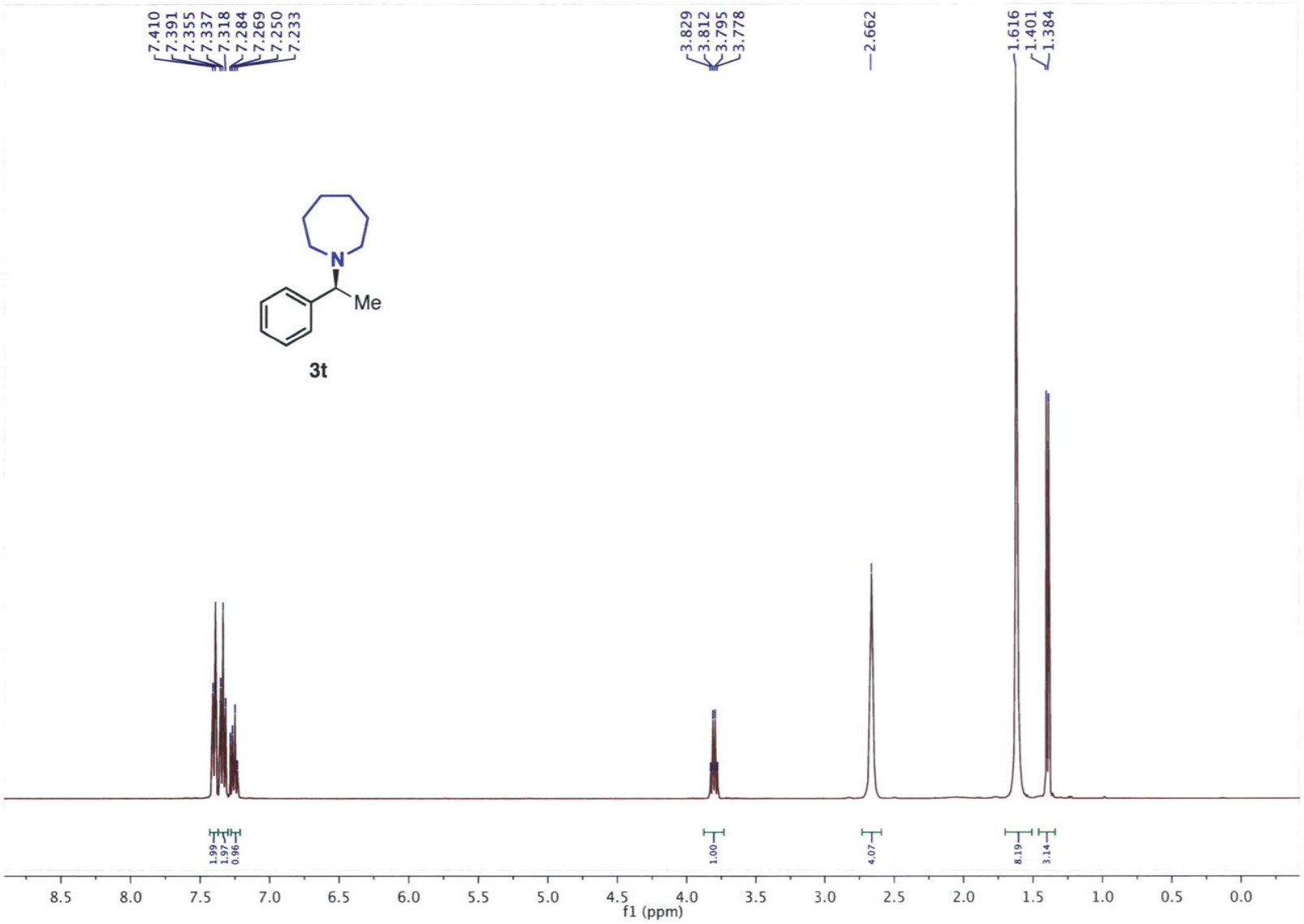


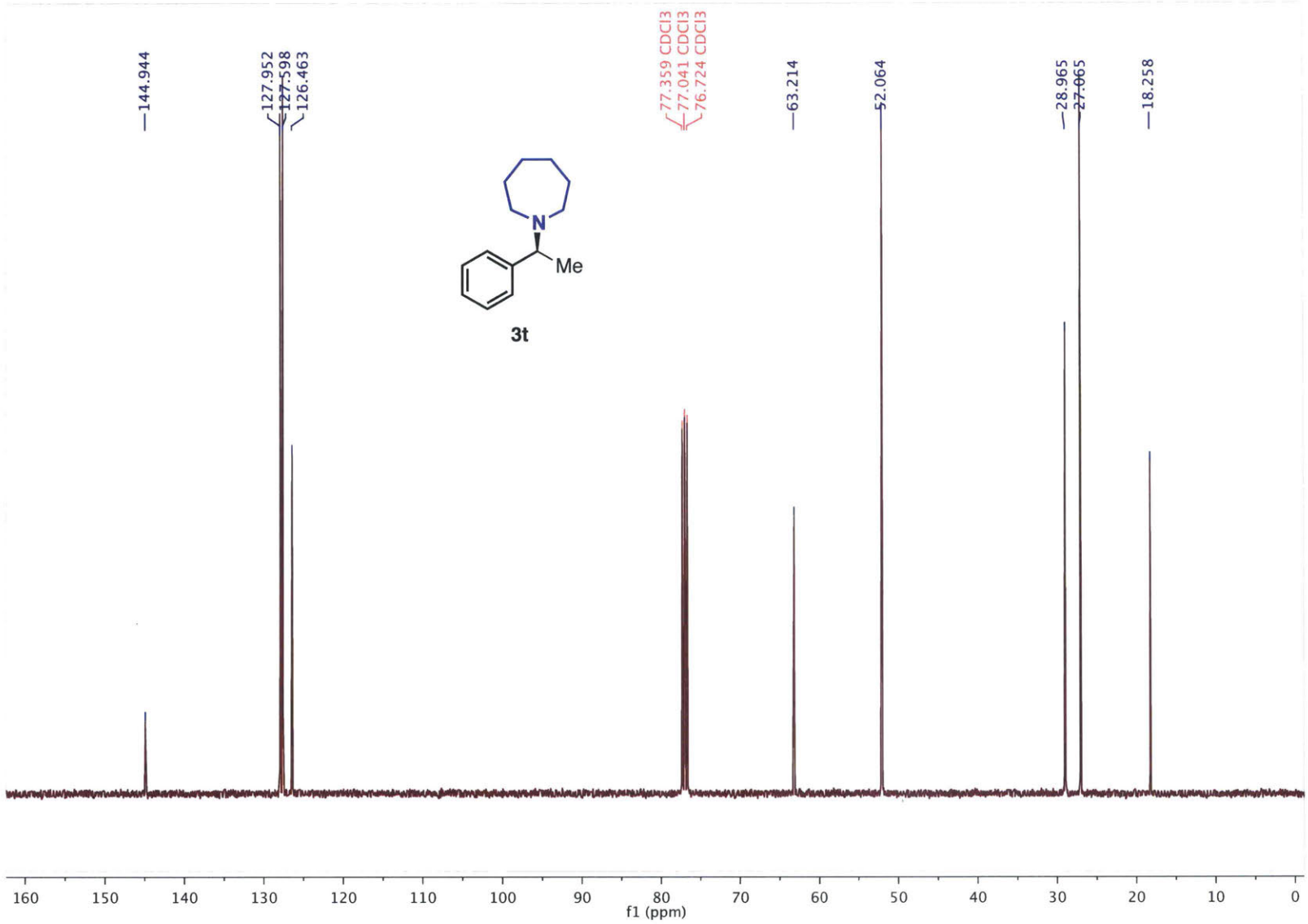
Sample 3r with (S)-Acetylmandelic Acid

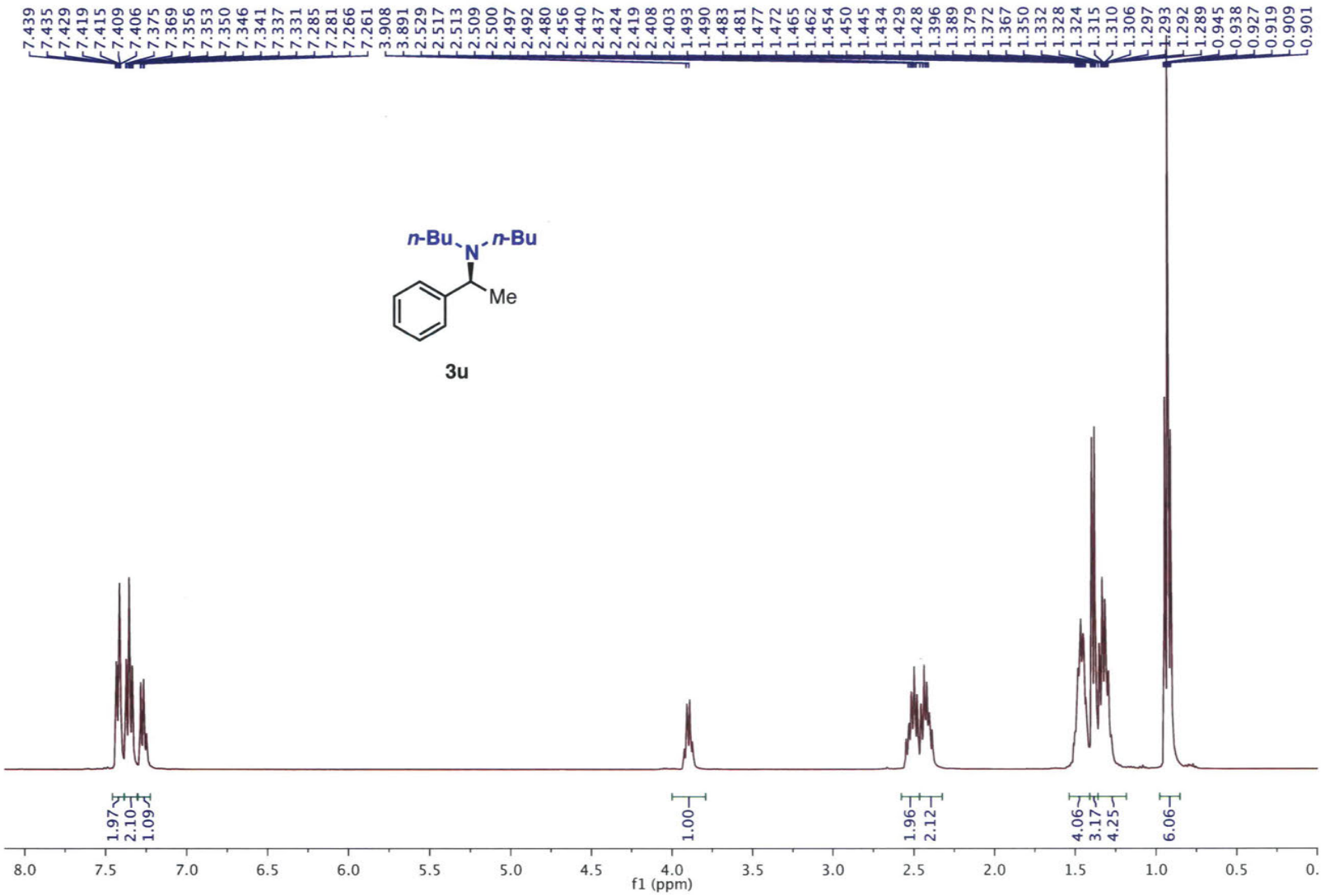


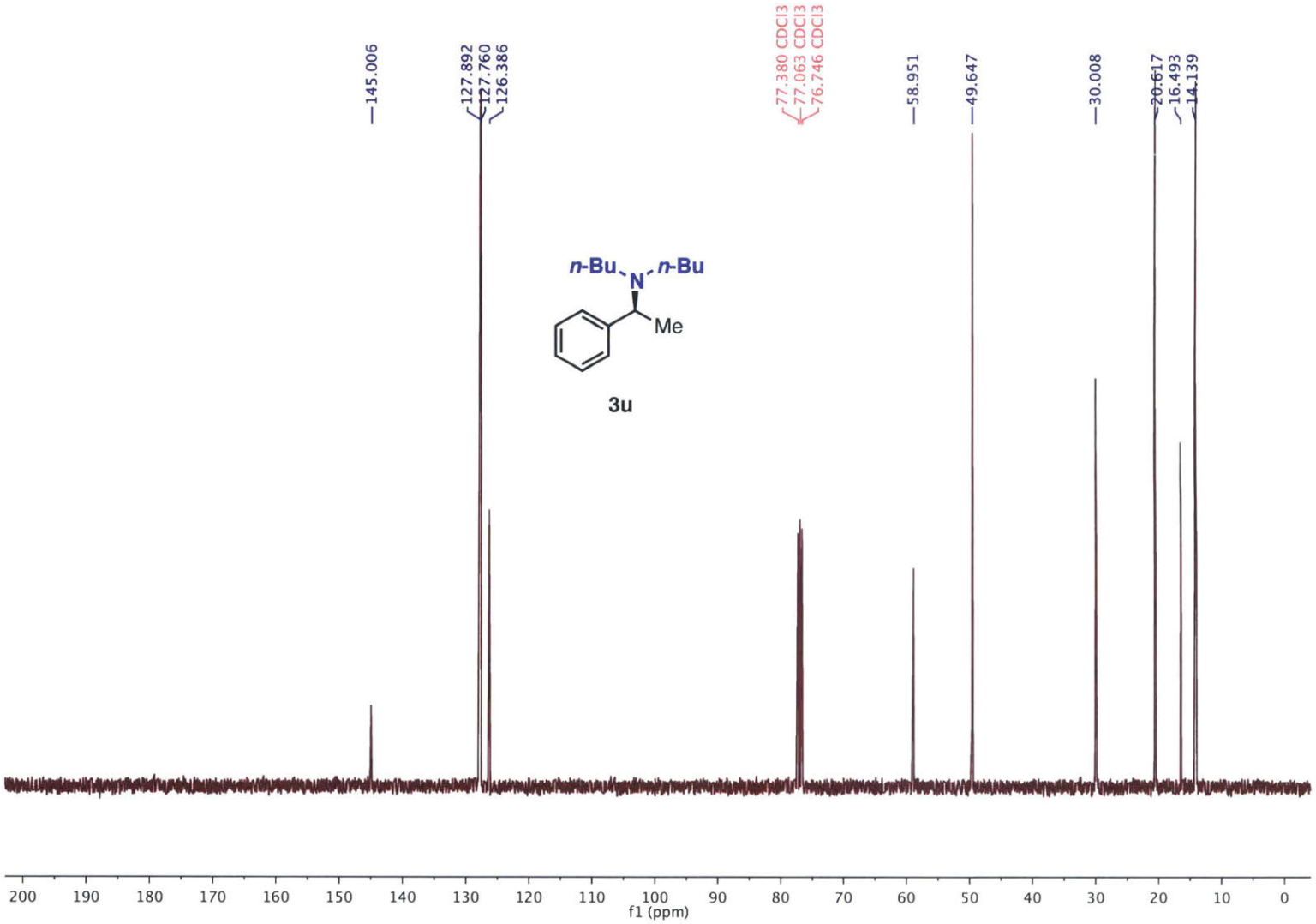

7.343
7.332
7.284
7.274
7.262
7.241
3.728
3.720
3.717
3.714
3.705
3.355
3.339
3.322
3.305
2.520
2.518
2.506
2.417
2.405
2.393
2.388
2.376
1.390
1.373
O
N
Me
3s
3.78
1.02
4.00
0.96
2.01
1.98
3.15
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


144.051
128.334
127.612
126.996
77.676 CDCl3
77.357 CDCl3
77.036 CDCl3
67.216
65.401
51.374
19.959
O
N
Me
3s
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

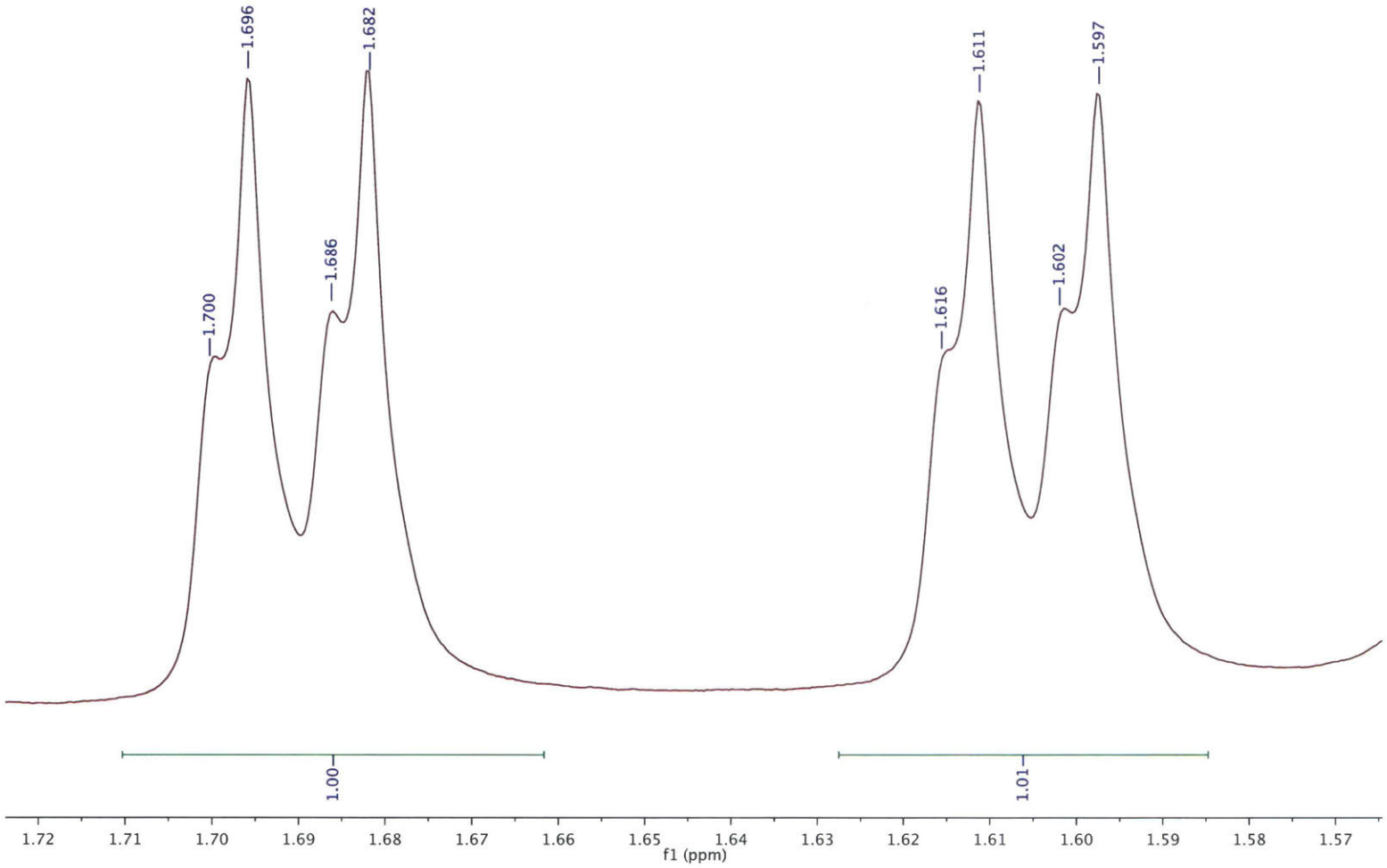

7.410
7.391
7.355
7.337
7.318
7.284
7.269
7.250
7.233
3.829
3.812
3.795
3.778
2.662
1.616
1.401
1.384
N
Me
3t
1.99
1.97
0.96
1.00
4.07
8.19
3.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


144.944
127.952
127.598
126.463
77.359 CDCl3
77.041 CDCl3
76.724 CDCl3
63.214
52.064
28.965
27.065
18.258
N
Me
3t
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

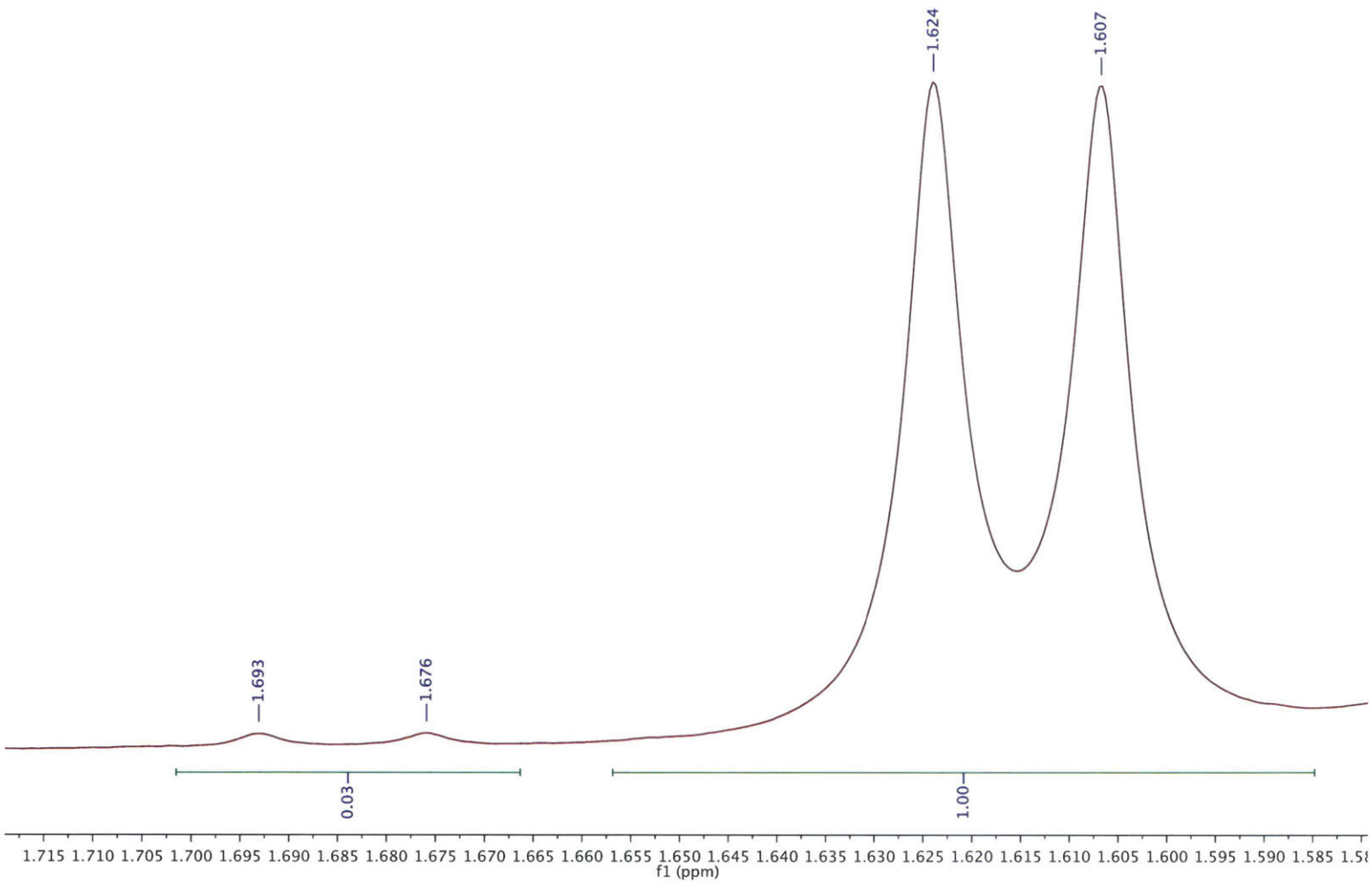

7.439
7.435
7.429
7.419
7.415
7.409
7.406
7.375
7.369
7.356
7.353
7.350
7.346
7.341
7.337
7.331
7.285
7.281
7.266
7.261
3.908
3.891
2.529
2.517
2.513
2.509
2.500
2.497
2.492
2.480
2.456
2.440
2.437
2.424
2.419
2.408
2.403
1.493
1.490
1.483
1.481
1.477
1.472
1.465
1.462
1.454
1.450
1.445
1.434
1.429
1.428
1.396
1.389
1.379
1.372
1.367
1.350
1.332
1.328
1.324
1.315
1.310
1.306
1.297
1.293
1.292
1.289
0.945
0.938
0.927
0.919
0.909
0.901
n-Bu
N
n-Bu
Me
3u
1.97
2.10
1.09
1.00
1.96
2.12
4.06
3.17
4.25
6.06
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.
f1 (ppm)

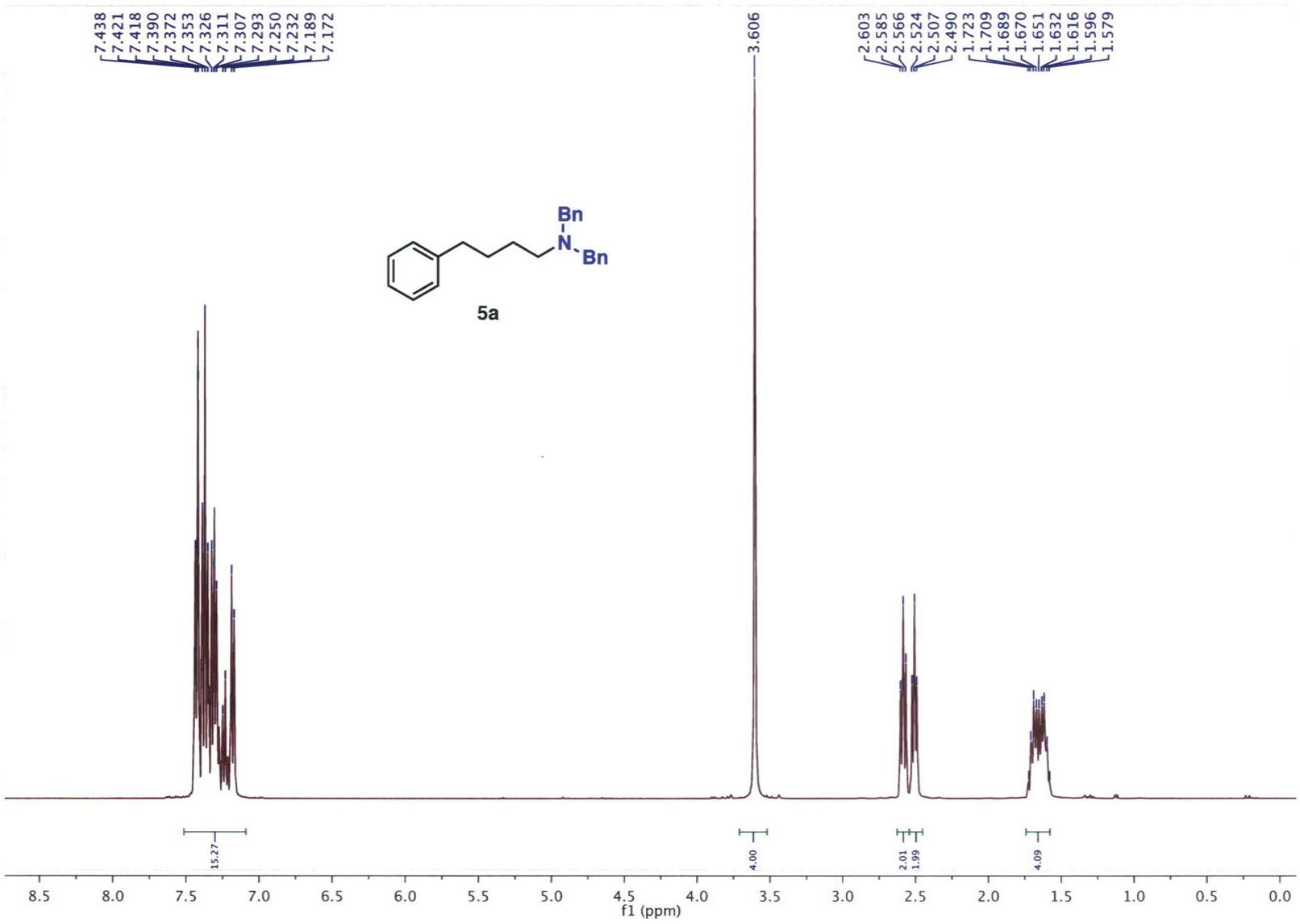

145.006
127.892
127.760
126.386
77.380 CDCl3
77.063 CDCl3
76.746 CDCl3
58.951
49.647
30.008
20.617
16.493
14.139
n-Bu
N
n-Bu
Me
3u
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

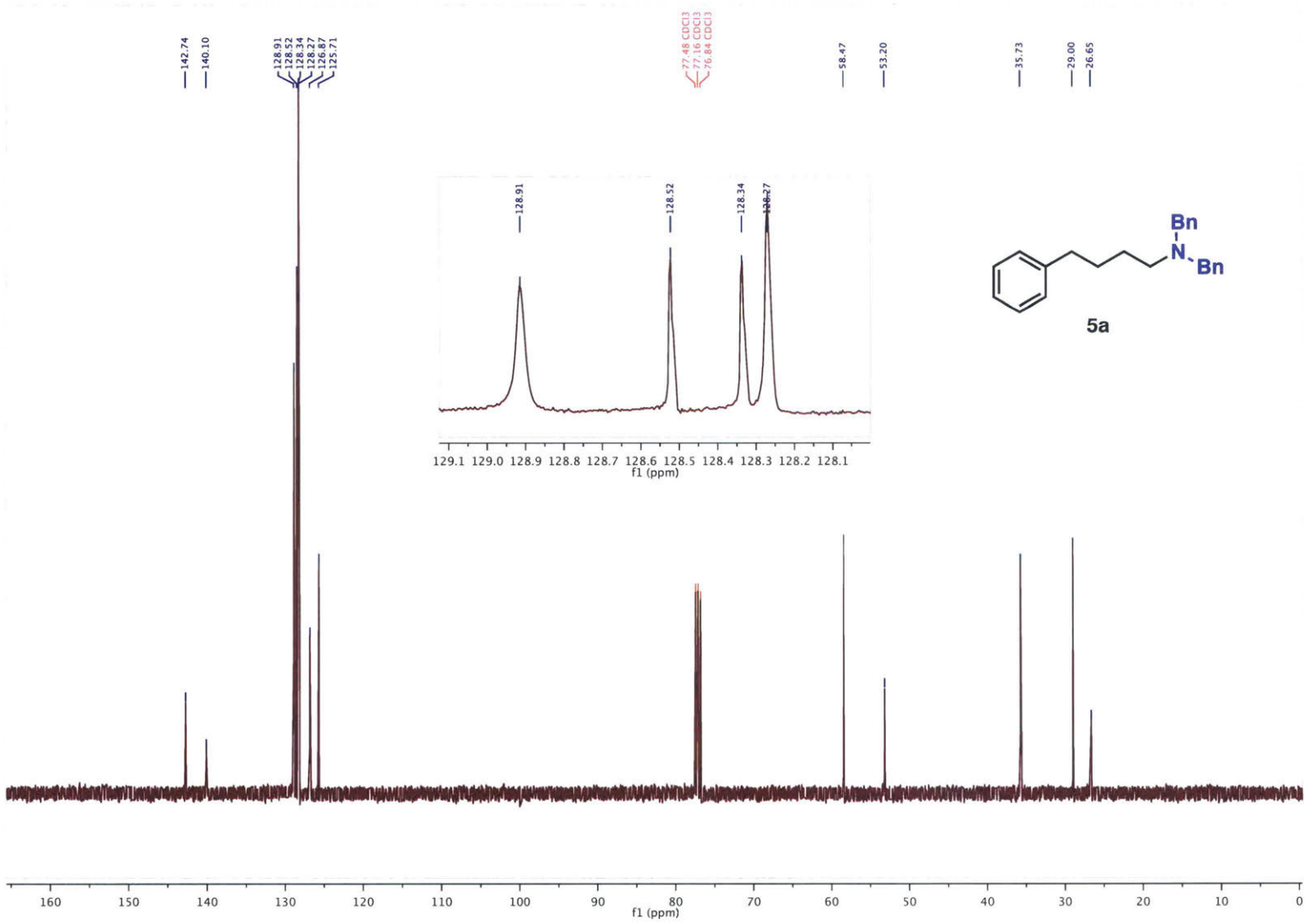
Racemic 3u with (R)-Acetylmandelic Acid

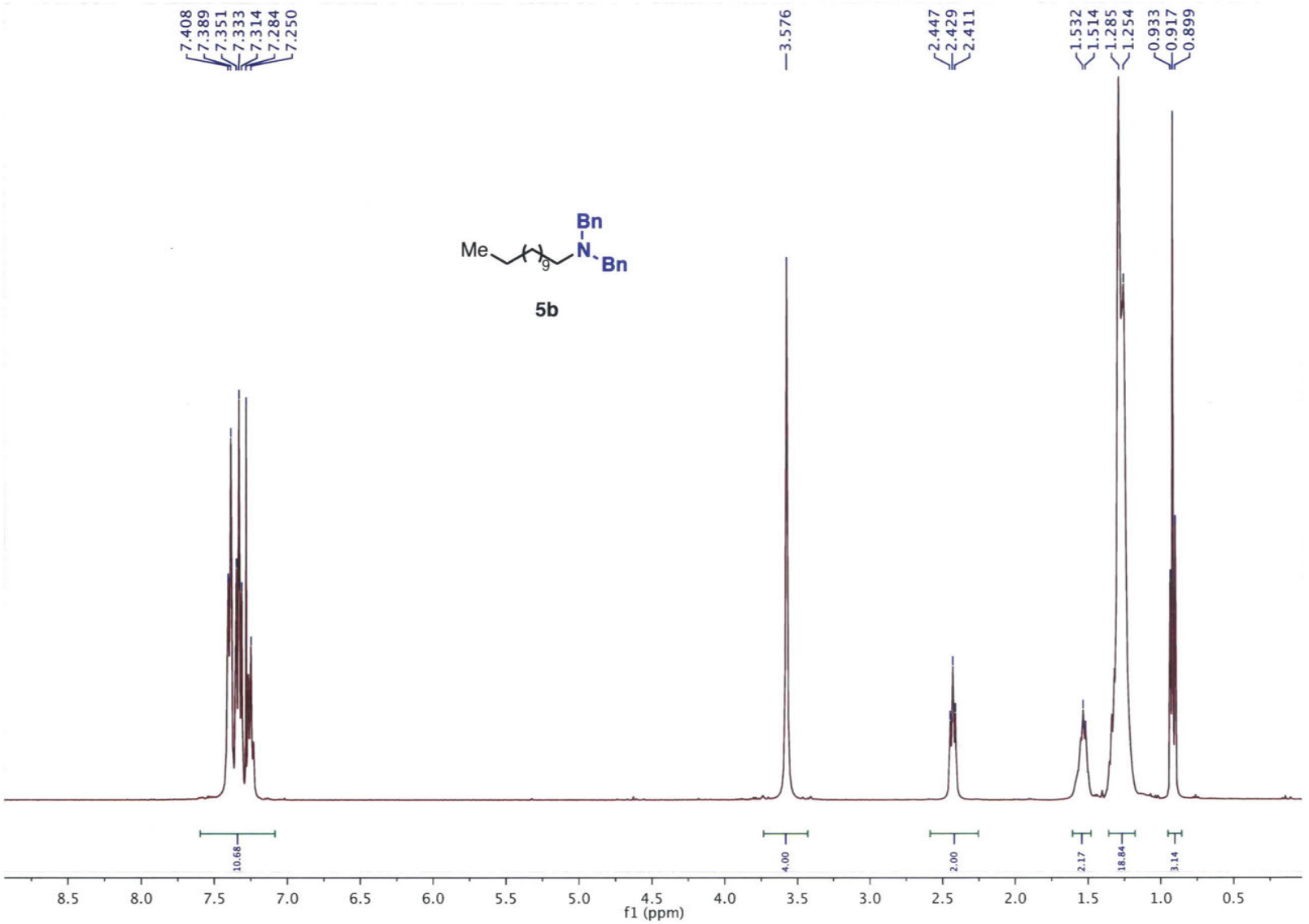


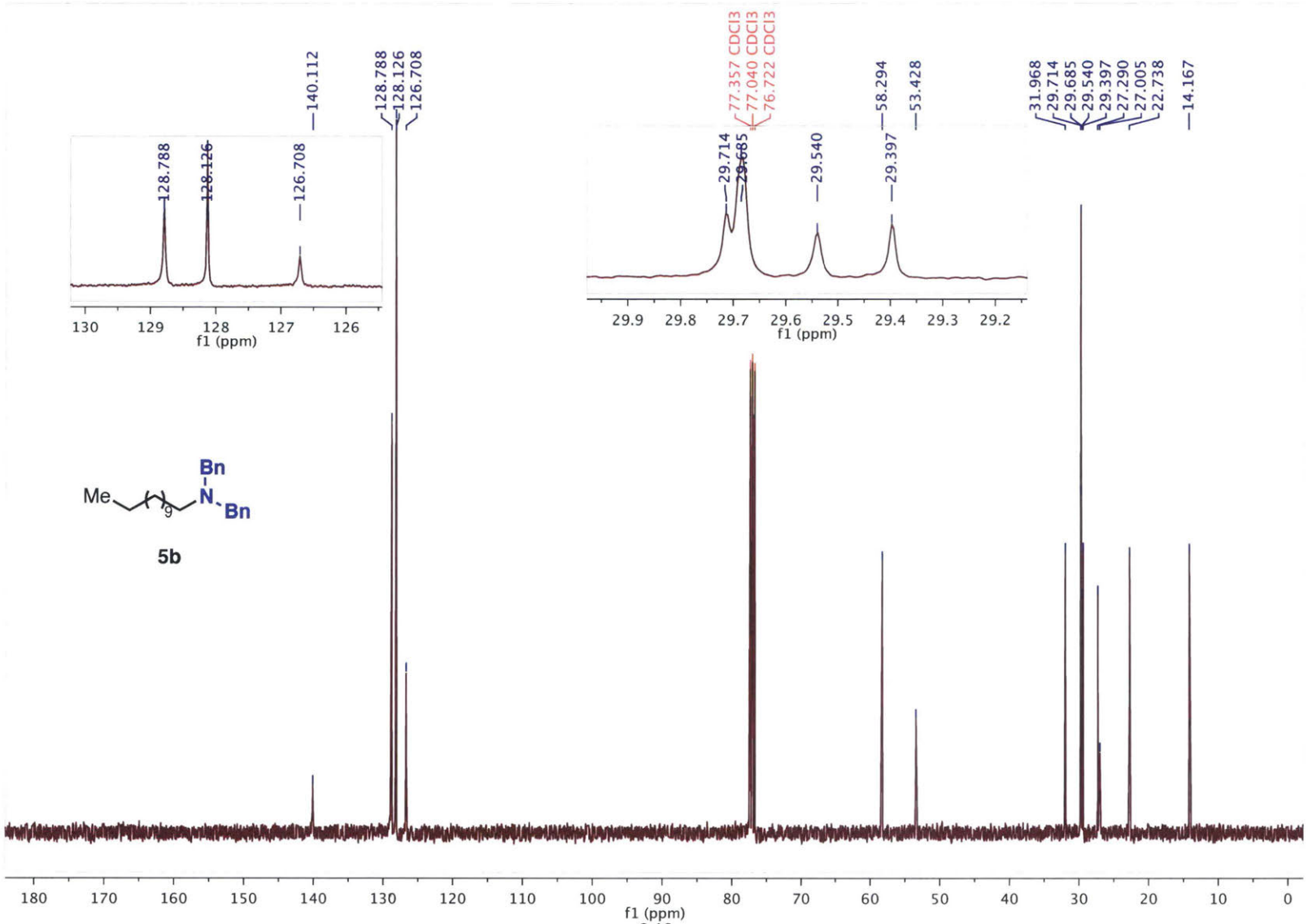
Sample of 3u with (R)-Acetylmandelic Acid

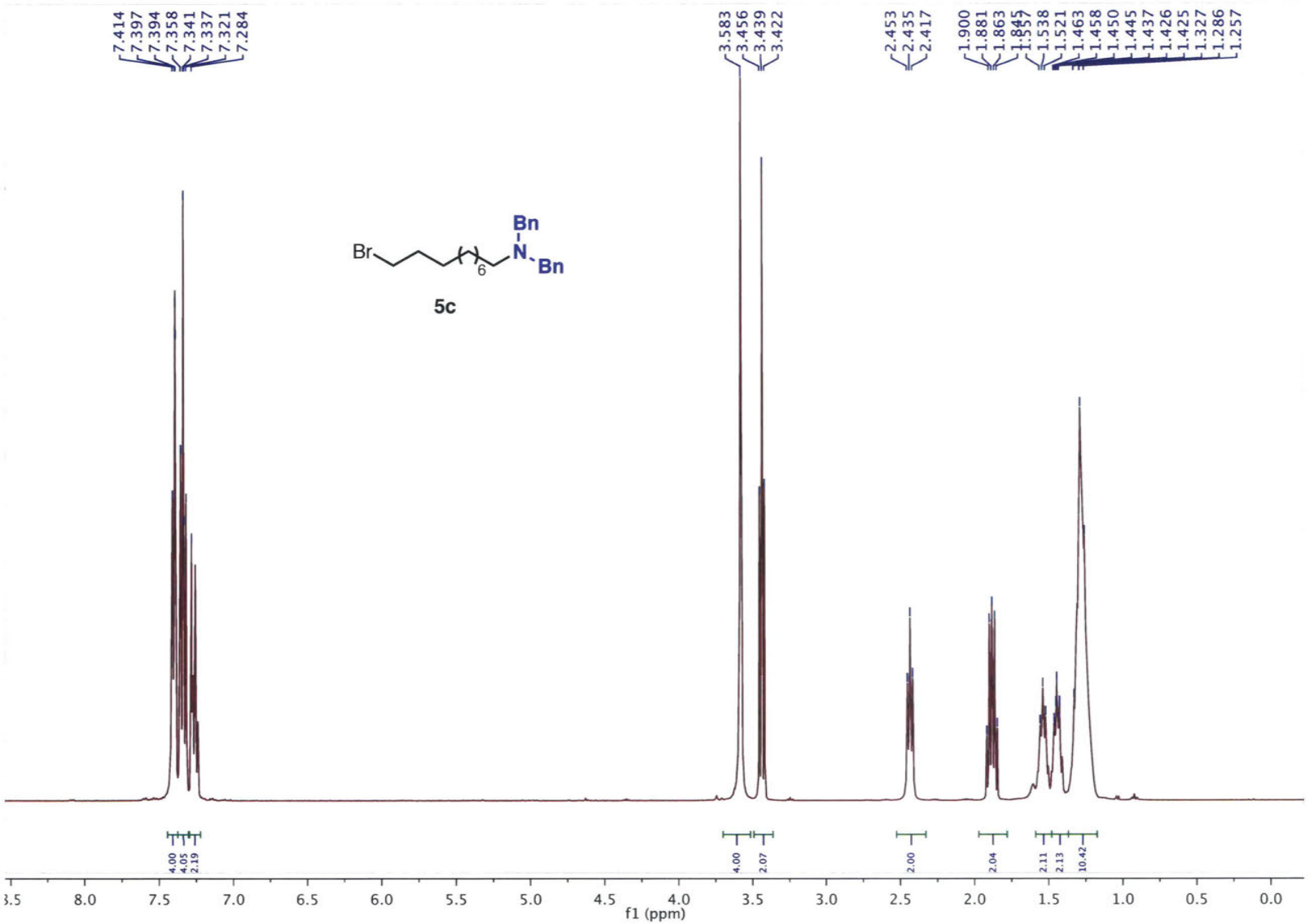


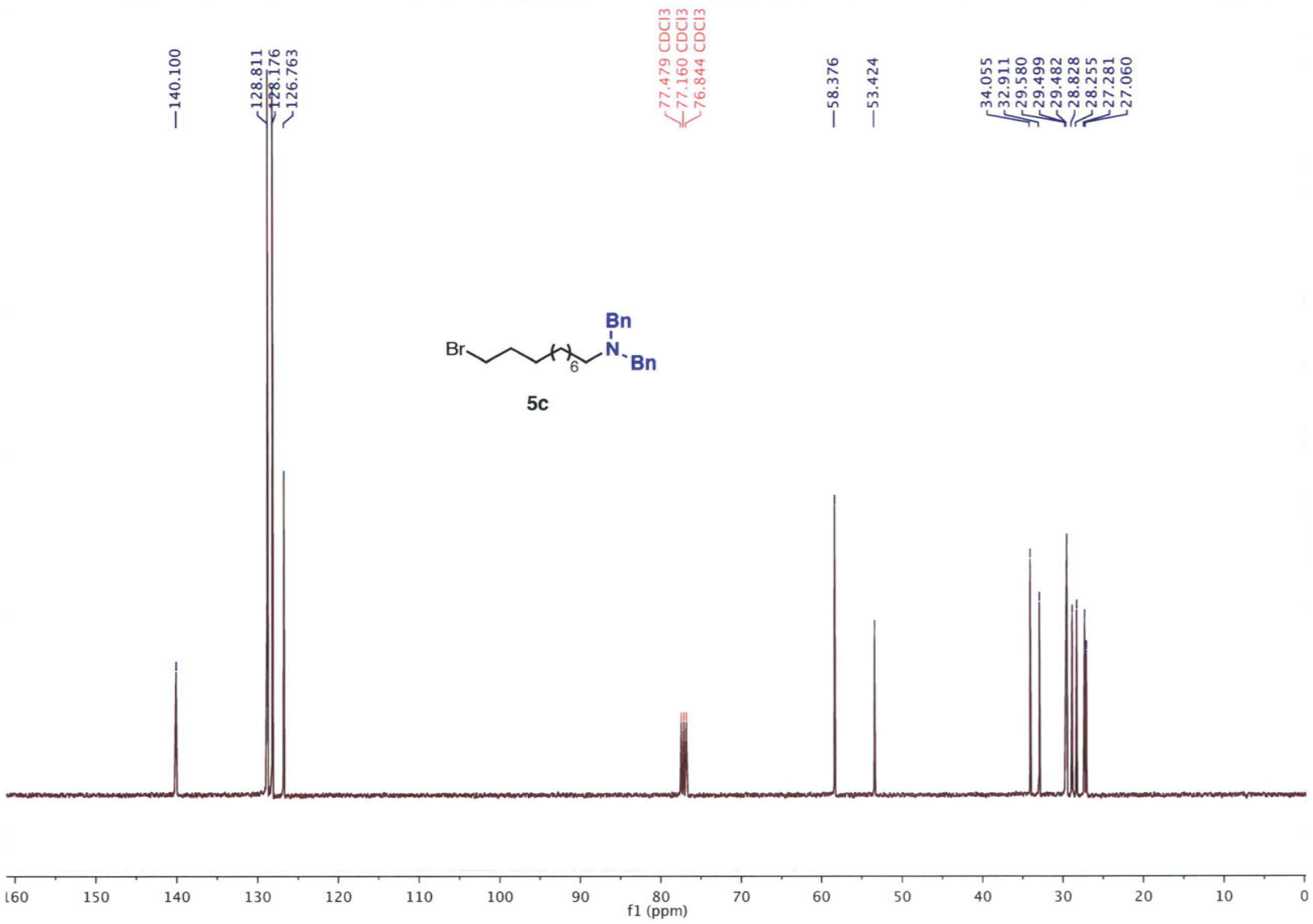

7.438
7.421
7.418
7.390
7.372
7.353
7.326
7.311
7.307
7.293
7.250
7.232
7.189
7.172
3.606
2.603
2.585
2.566
2.524
2.507
2.490
1.723
1.709
1.689
1.670
1.651
1.632
1.616
1.596
1.579
Bn
N
Bn
5a
15.27
4.00
2.01
1.99
4.09
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

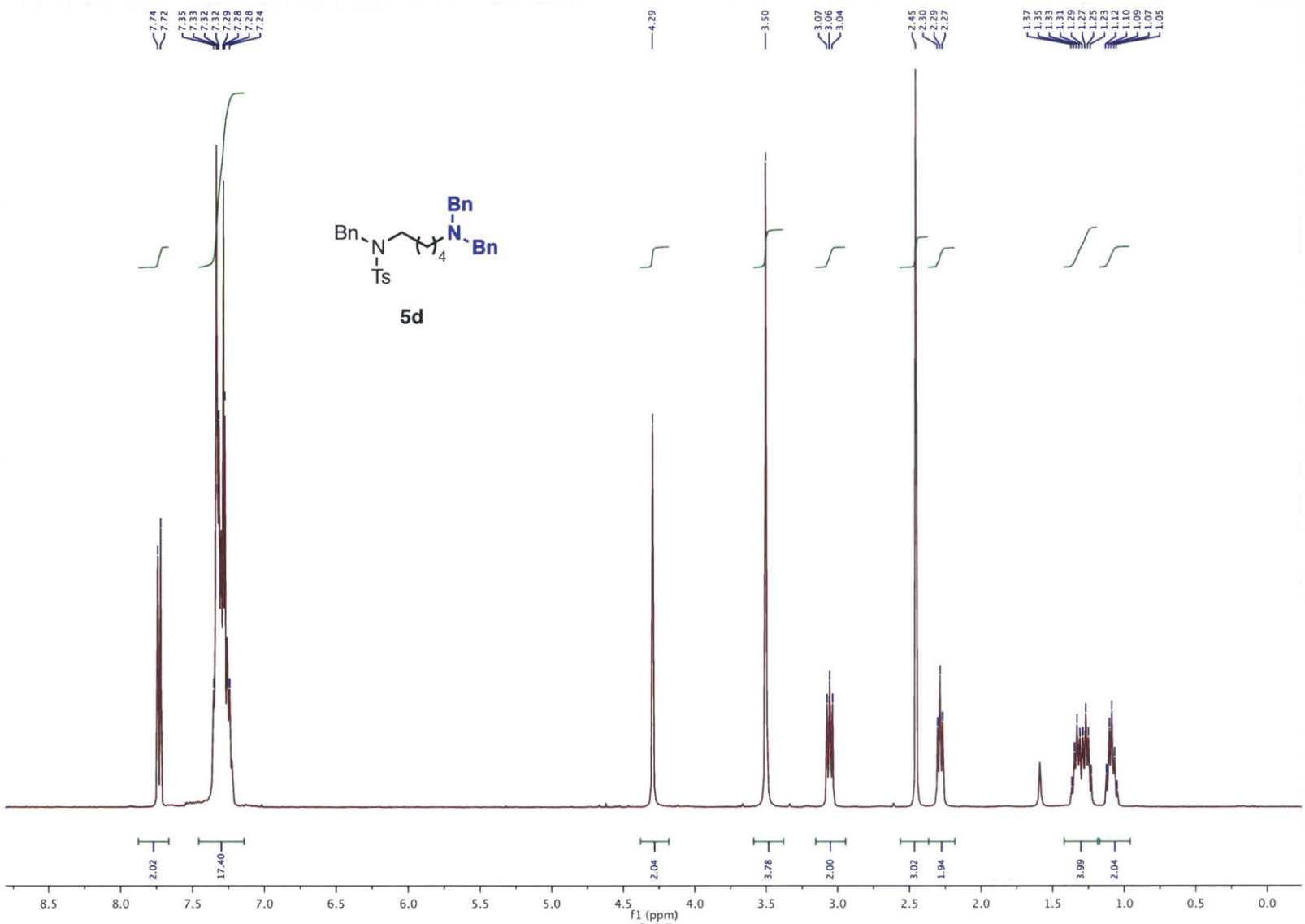

142.74
140.10
128.91
128.52
128.34
128.27
126.87
125.71
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
58.47
53.20
35.73
29.00
26.65
128.91
128.52
128.34
128.27
129.1 129.0 128.9 128.8 128.7 128.6 128.5 128.4 128.3 128.2 128.1
f1 (ppm)
Bn
N
Bn
5a
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

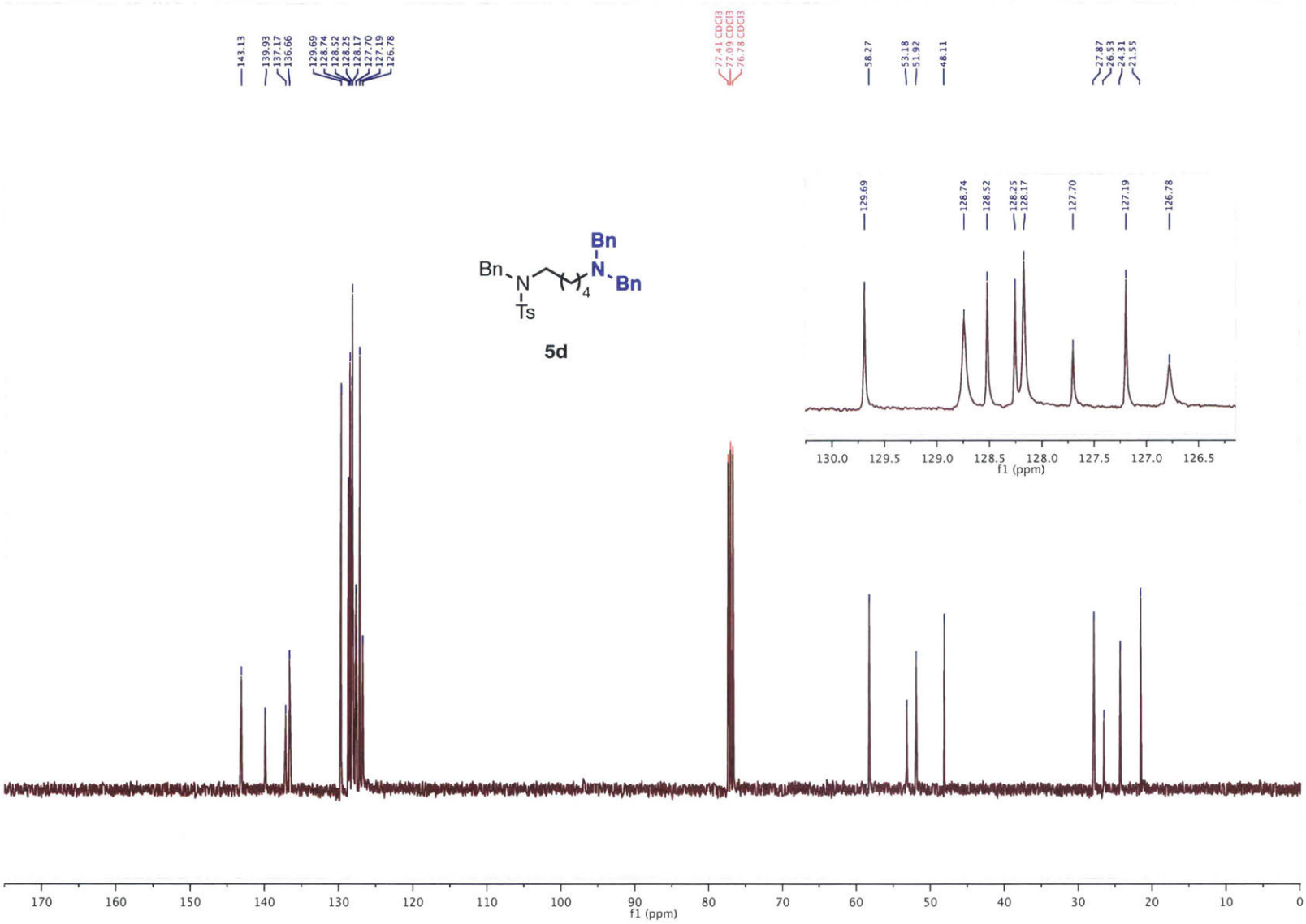

7.408
7.389
7.351
7.333
7.314
7.284
7.250
3.576
2.447
2.429
2.411
1.532
1.514
1.285
1.254
0.933
0.917
0.899
Bn
N
Bn
Me
g
5b
10.68
4.00
2.00
2.17
18.84
3.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

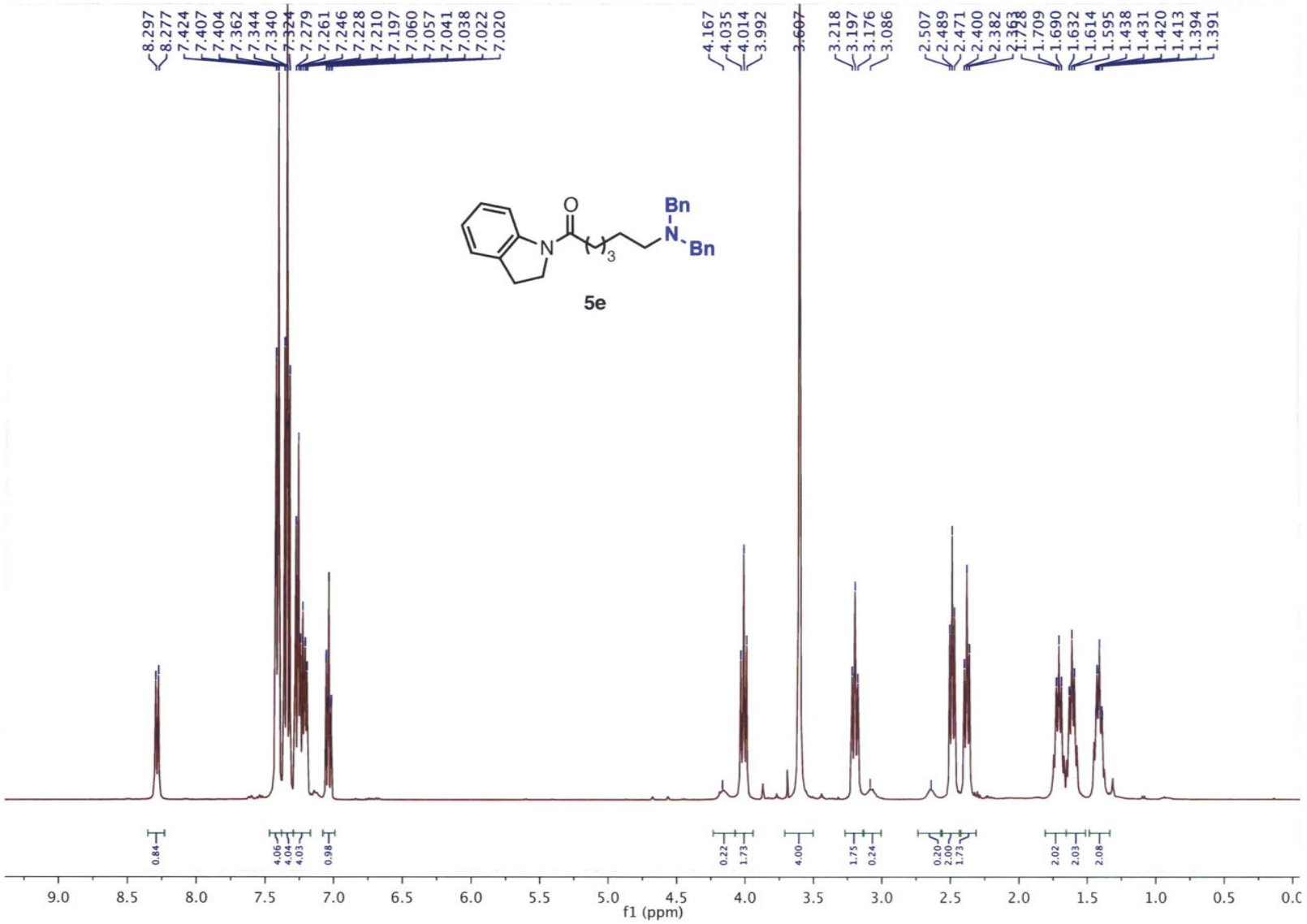

140.112
128.788
128.126
126.708
77.357 CDCl3
77.040 CDCl3
76.722 CDCl3
58.294
53.428
31.968
29.714
29.685
29.540
29.397
27.290
27.005
22.738
14.167
Bn
N
Bn
Me
9
5b
f1 (ppm)

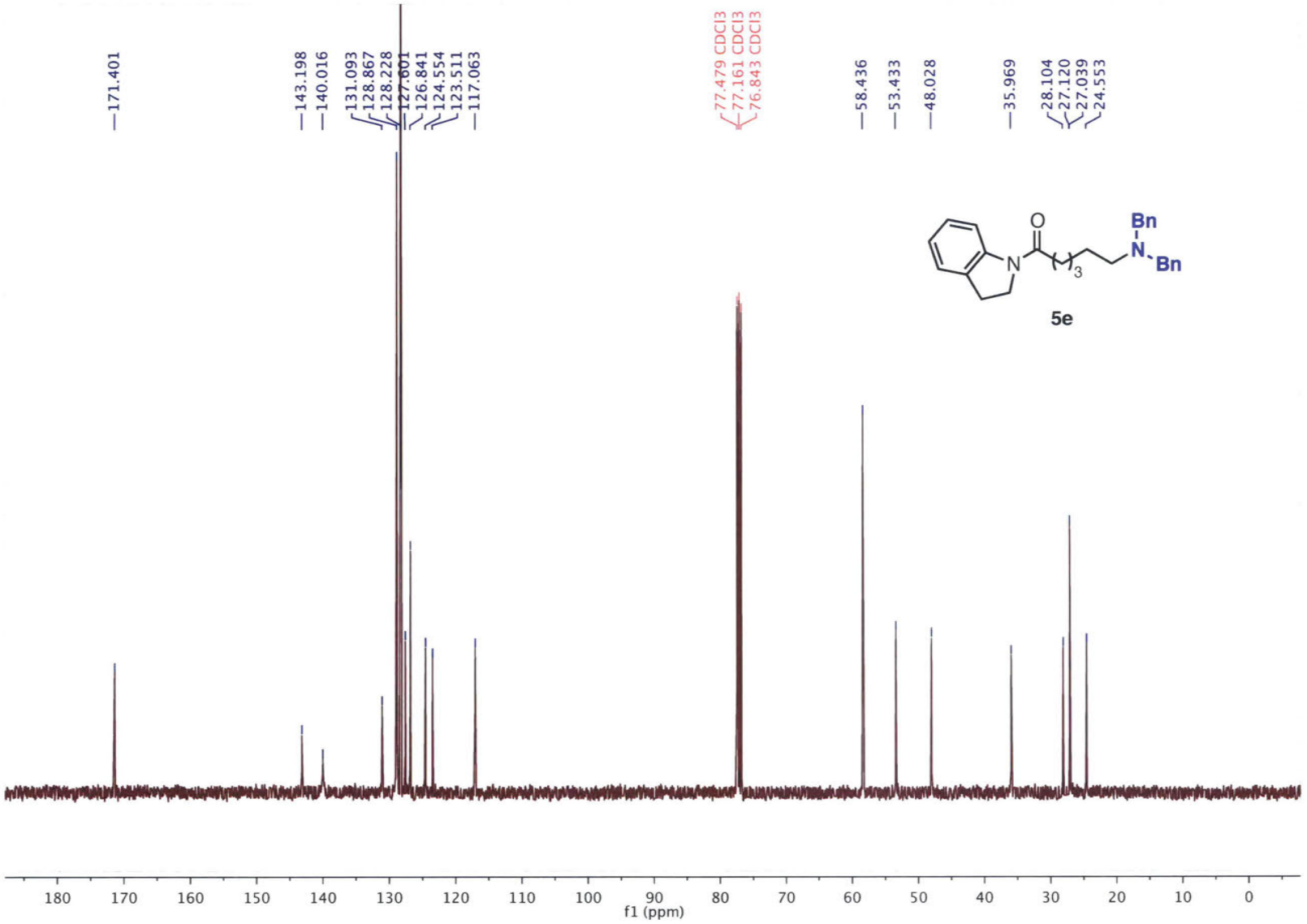

7.414
7.397
7.394
7.358
7.341
7.337
7.321
7.284
3.583
3.456
3.439
3.422
2.453
2.435
2.417
1.900
1.881
1.863
1.557
1.538
1.521
1.463
1.458
1.450
1.445
1.437
1.426
1.425
1.327
1.286
1.257
Br
6
N
Bn
Bn
5c
4.00
4.05
2.19
4.00
2.07
2.00
2.04
2.11
2.13
10.42
f1 (ppm)

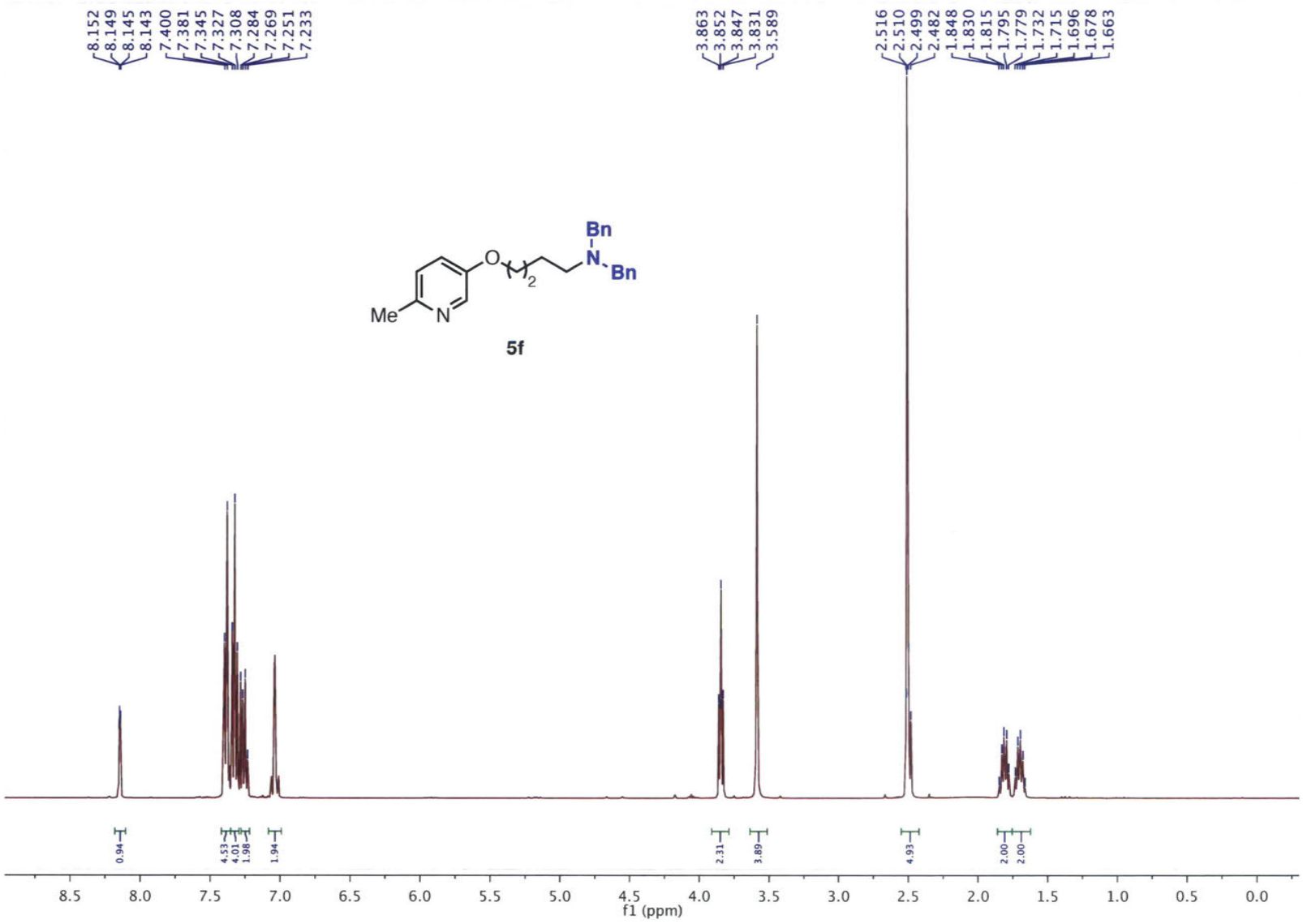

140.100
128.811
128.176
126.763
77.479 CDCl3
77.160 CDCl3
76.844 CDCl3
58.376
53.424
34.055
32.911
29.580
29.499
29.482
28.828
28.255
27.281
27.060
Br
Bn
N
Bn
6
5c
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

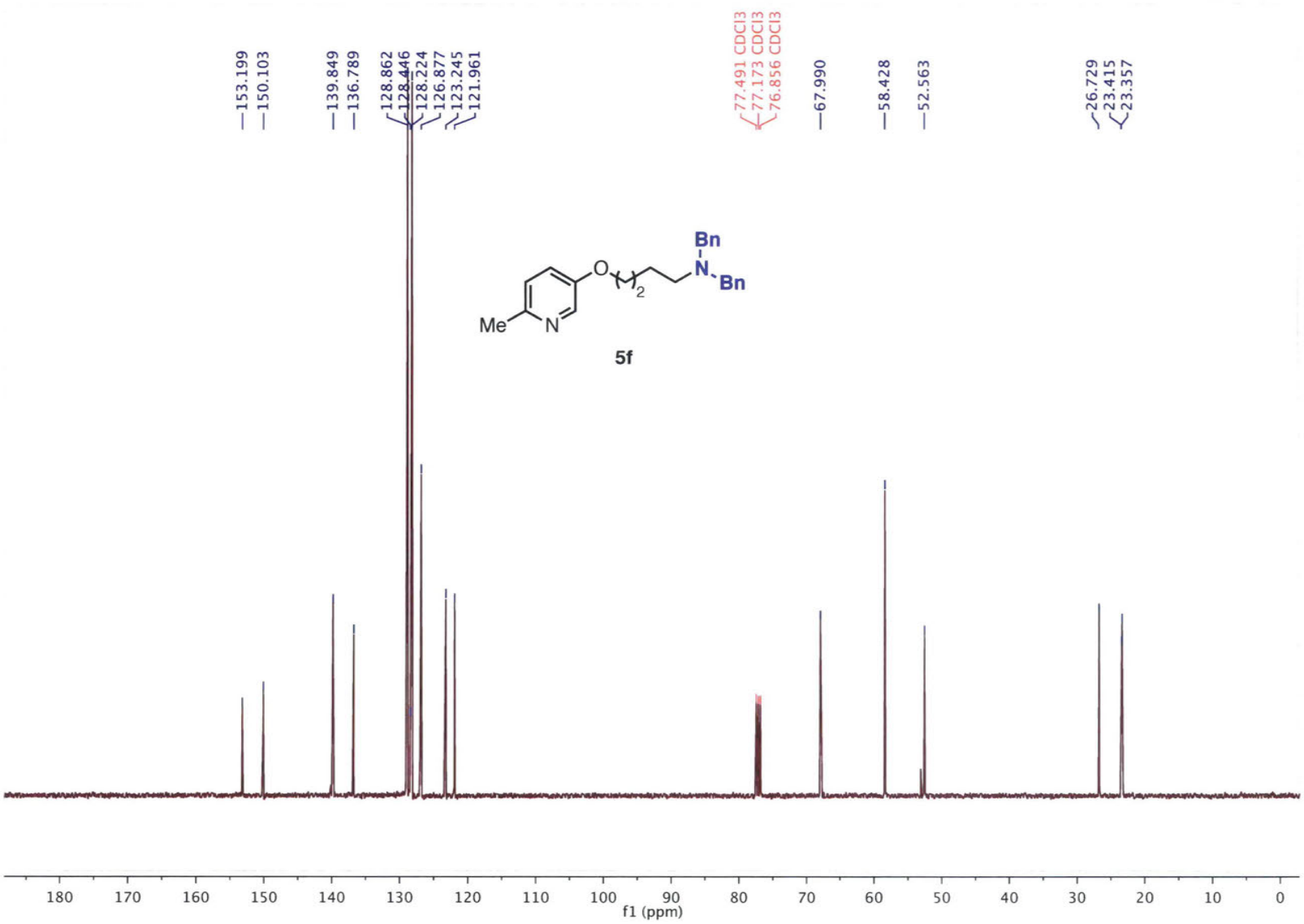

7.74
7.72
7.35
7.33
7.32
7.32
7.29
7.28
7.28
7.24
4.29
3.50
3.07
3.06
3.04
2.45
2.30
2.29
2.27
1.37
1.35
1.33
1.31
1.29
1.27
1.25
1.23
1.12
1.10
1.09
1.07
1.05
Bn
N
Ts
4
N
Bn
Bn
5d
2.02
17.40
2.04
3.78
2.00
3.02
1.94
3.99
2.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

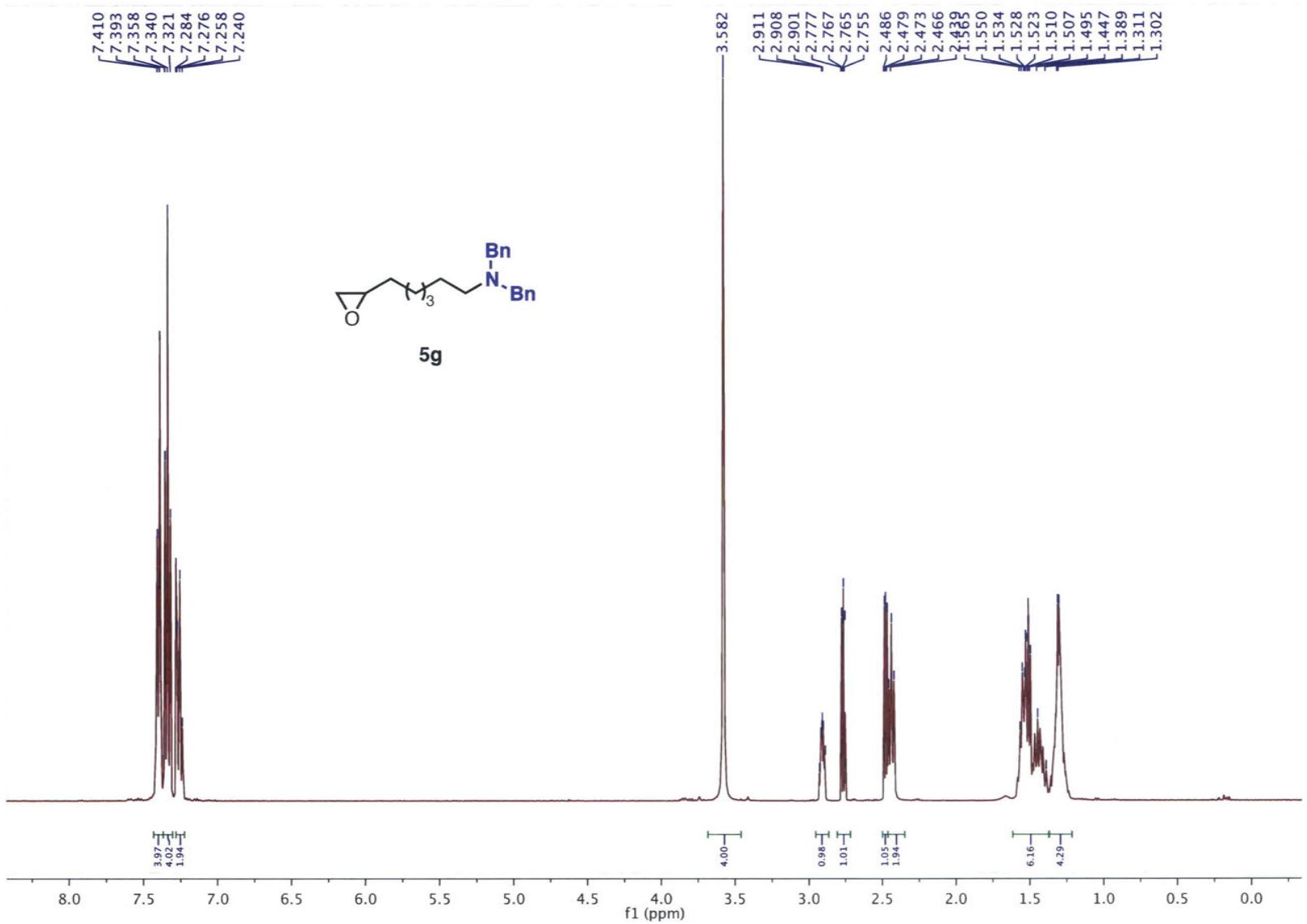

143.13
139.93
137.17
136.66
129.69
128.74
128.52
128.25
128.17
127.70
127.19
126.78
77.41 CDCl3
77.09 CDCl3
76.78 CDCl3
58.27
53.18
51.92
48.11
27.87
26.53
24.31
21.55
Bn
N
Ts
Bn
N
Bn
4
5d
f1 (ppm)

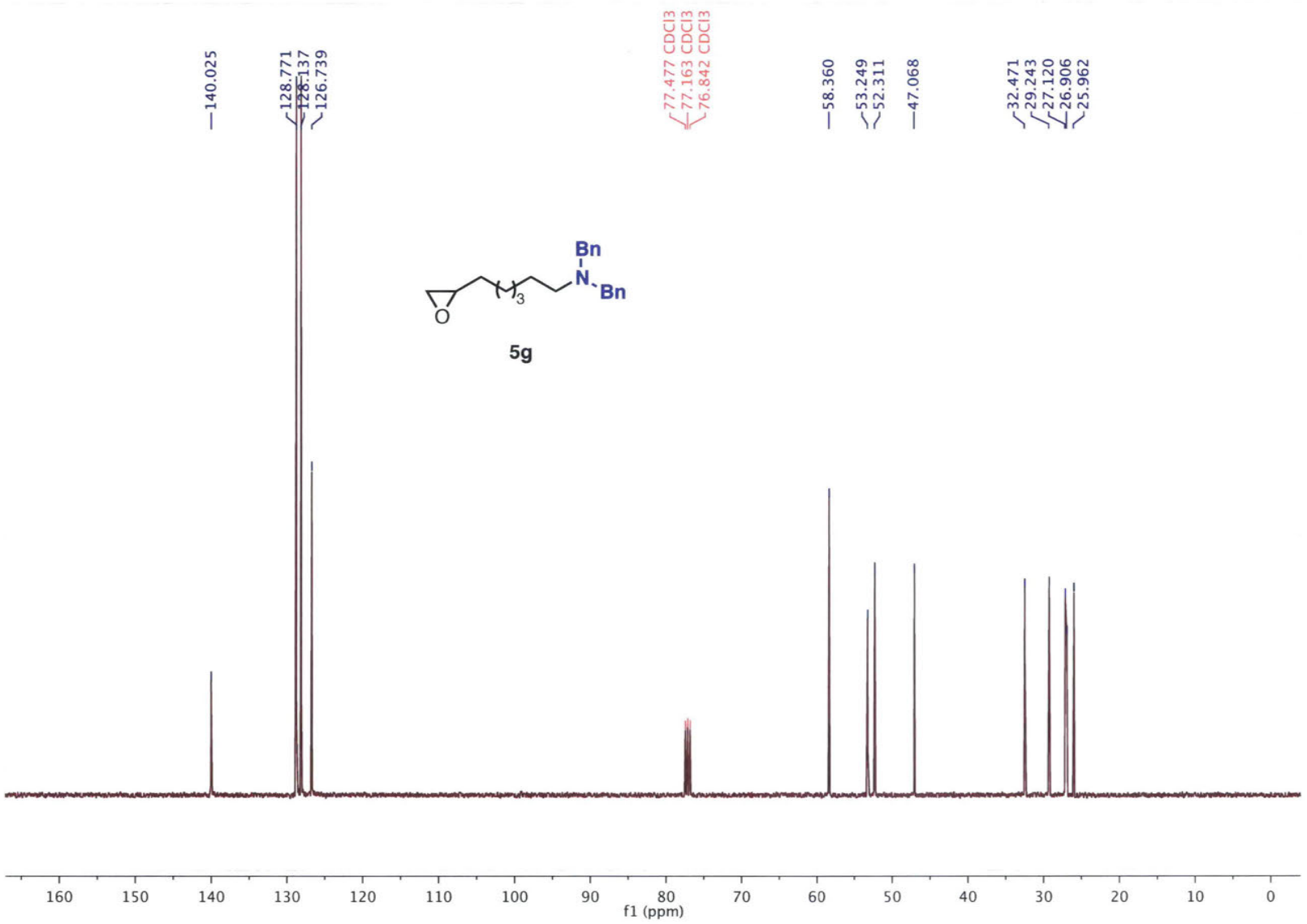

8.297
8.277
7.424
7.407
7.404
7.362
7.344
7.340
7.324
7.279
7.261
7.246
7.228
7.210
7.197
7.060
7.057
7.041
7.038
7.022
7.020
4.167
4.035
4.014
3.992
3.607
3.218
3.197
3.176
3.086
2.507
2.489
2.471
2.400
2.382
1.728
1.709
1.690
1.632
1.614
1.595
1.438
1.431
1.420
1.413
1.394
1.391
O
N
Bn
N
Bn
3
5e
0.84
4.06
4.04
4.03
0.98
0.22
1.73
4.00
1.75
0.24
0.20
2.00
1.73
2.02
2.03
2.08
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
f1 (ppm)

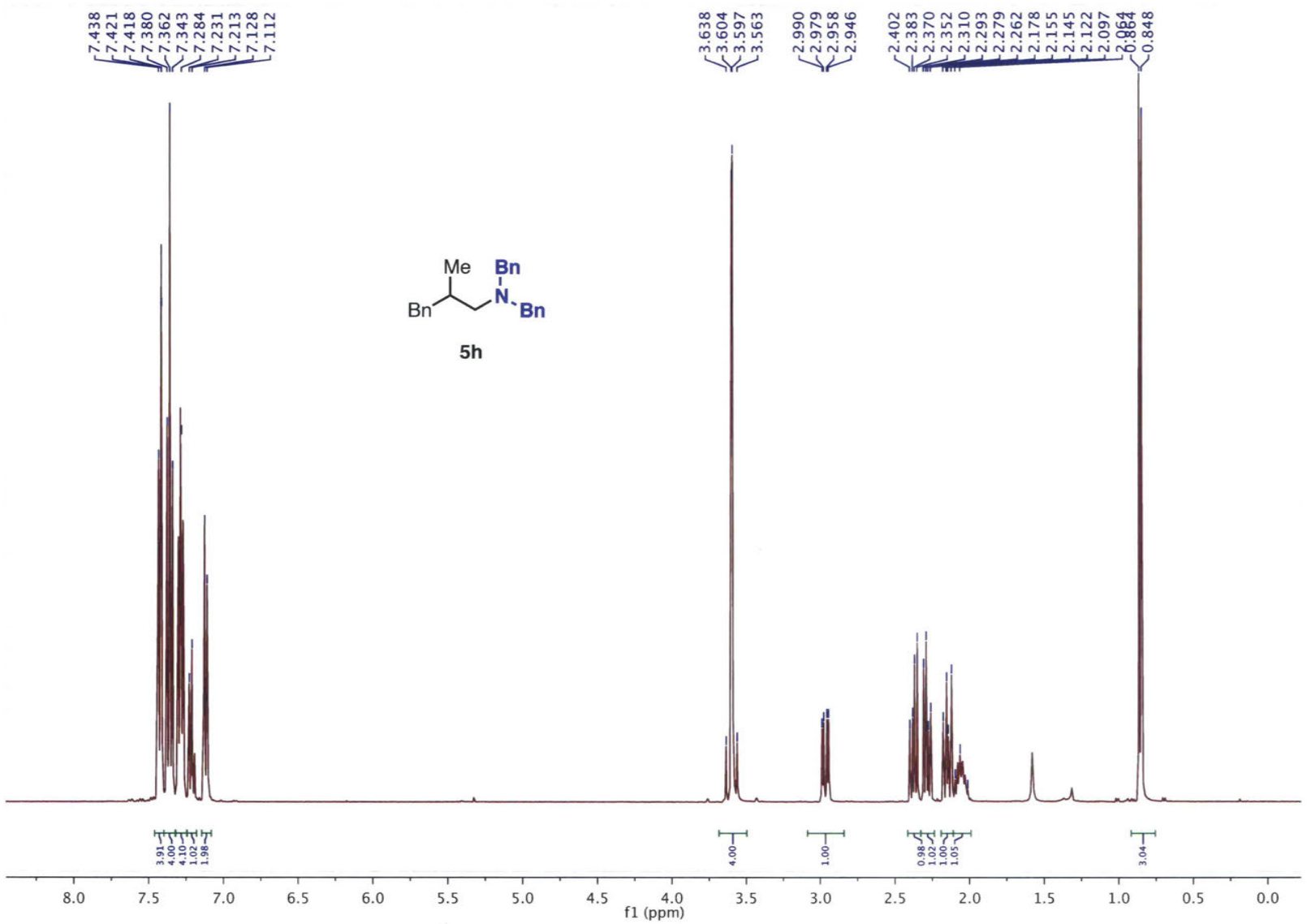

171.401
143.198
140.016
131.093
128.867
128.228
127.601
126.841
124.554
123.511
117.063
77.479 CDCl3
77.161 CDCl3
76.843 CDCl3
58.436
53.433
48.028
35.969
28.104
27.120
27.039
24.553
O
N
3
Bn
N
Bn
5e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.152
8.149
8.145
8.143
7.400
7.381
7.345
7.327
7.308
7.284
7.269
7.251
7.233
3.863
3.852
3.847
3.831
3.589
2.516
2.510
2.499
2.482
1.848
1.830
1.815
1.795
1.779
1.732
1.715
1.696
1.678
1.663
Bn
N
Bn
O
2
Me
N
5f
0.94
4.53
4.01
1.98
1.94
2.31
3.89
4.93
2.00
2.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


153.199
150.103
139.849
136.789
128.862
128.446
128.224
126.877
123.245
121.961
77.491 CDCl3
77.173 CDCl3
76.856 CDCl3
67.990
58.428
52.563
26.729
23.415
23.357
Bn
N
Bn
O
2
Me
N
5f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.410
7.393
7.358
7.340
7.321
7.284
7.276
7.258
7.240
3.582
2.911
2.908
2.901
2.777
2.767
2.765
2.755
2.486
2.479
2.473
2.466
1.550
1.534
1.528
1.523
1.510
1.507
1.495
1.447
1.389
1.311
1.302
Bn
N
Bn
3
O
5g
3.97
4.02
1.94
4.00
0.98
1.01
1.05
1.94
6.16
4.29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


140.025
128.771
128.137
126.739
77.477 CDCl3
77.163 CDCl3
76.842 CDCl3
58.360
53.249
52.311
47.068
32.471
29.243
27.120
26.906
25.962
Bn
N
Bn
3
O
5g
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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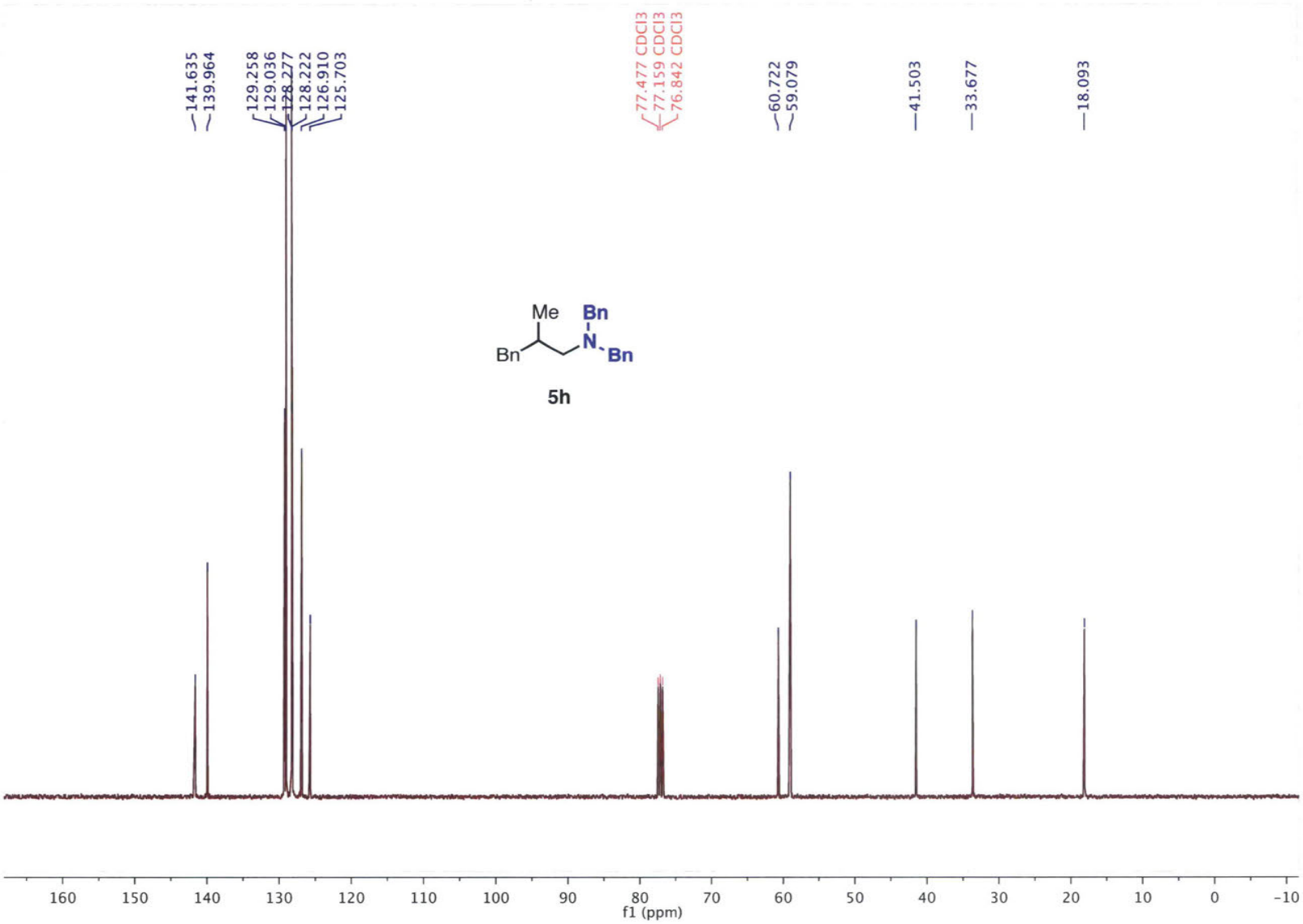
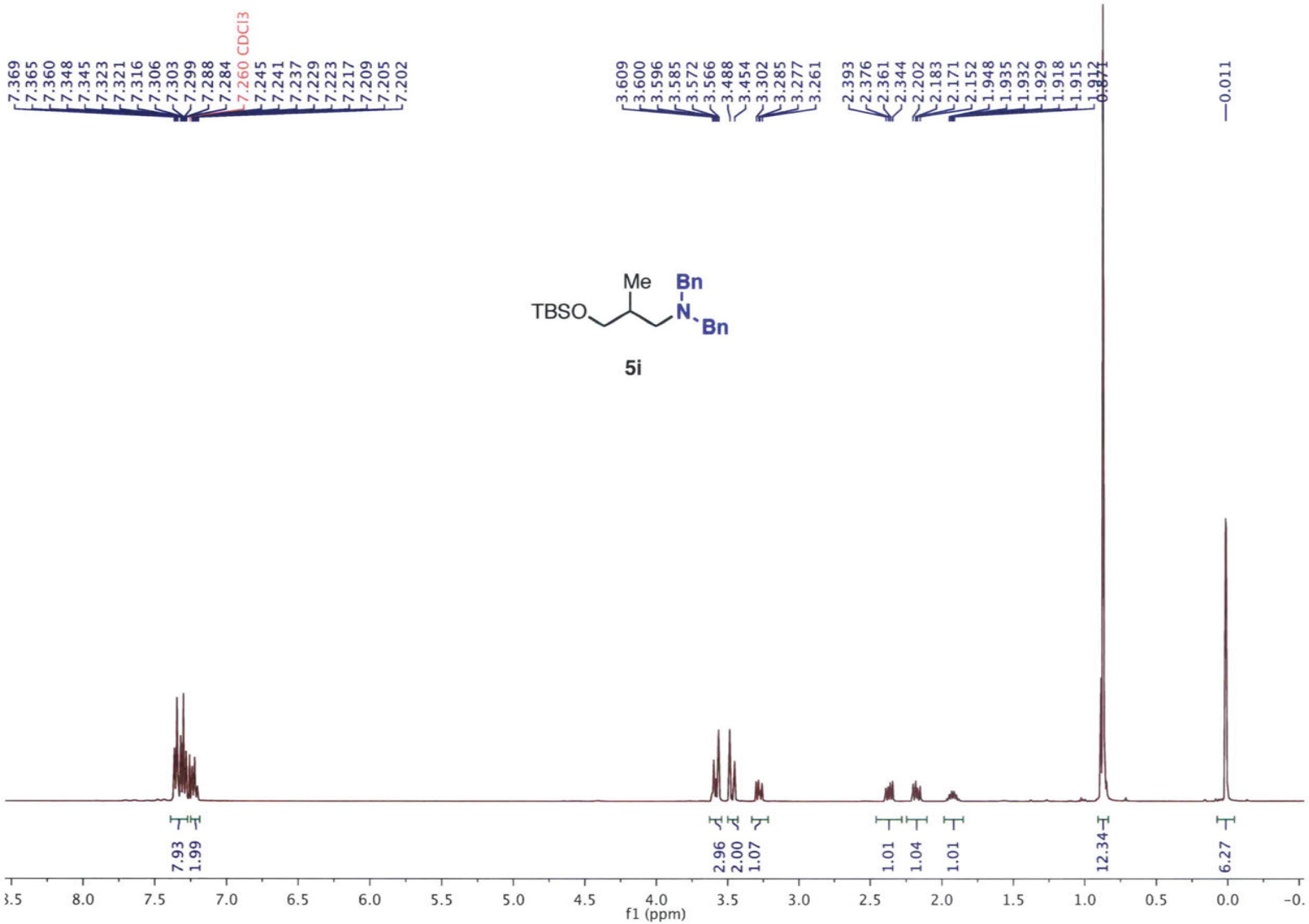
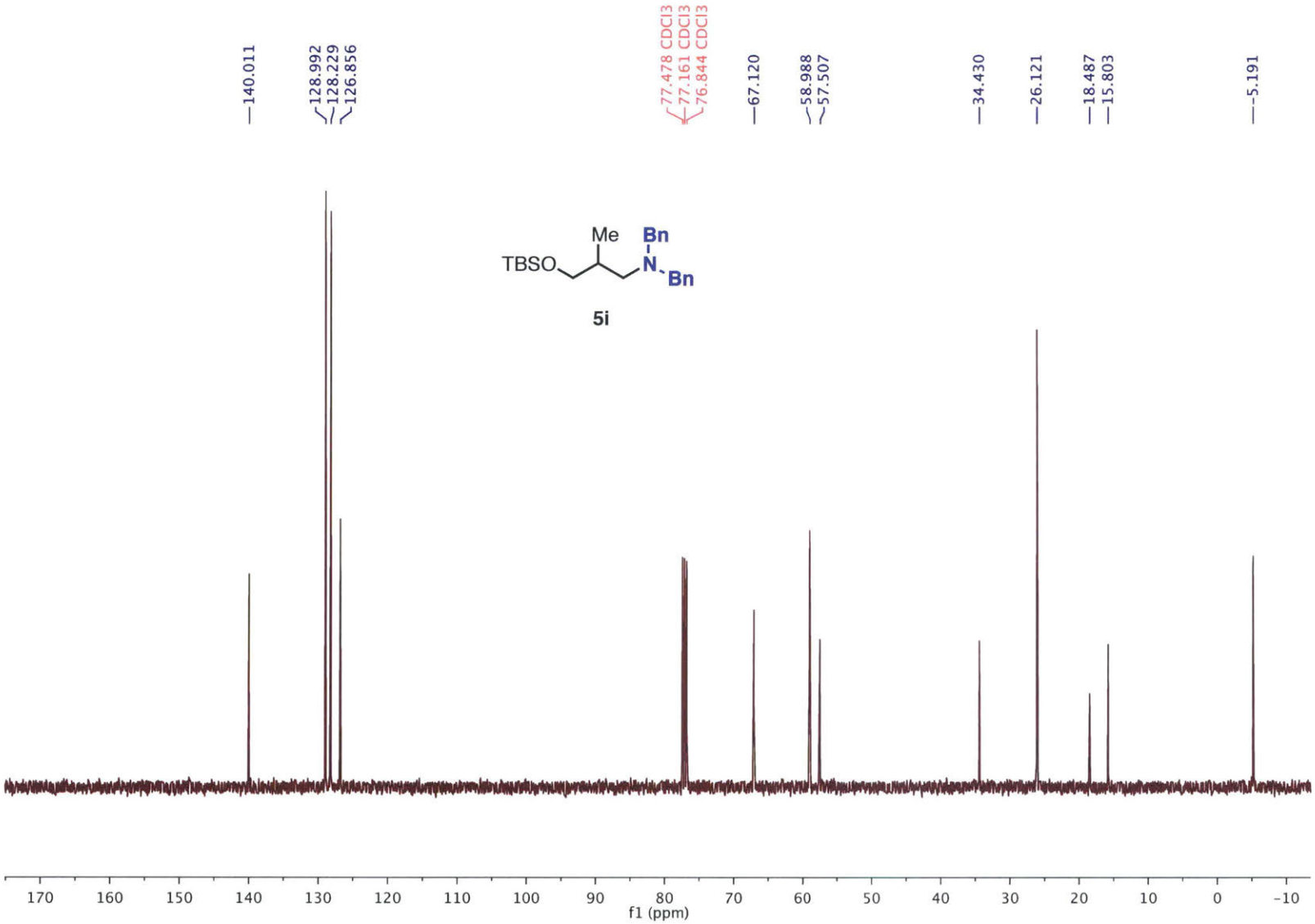
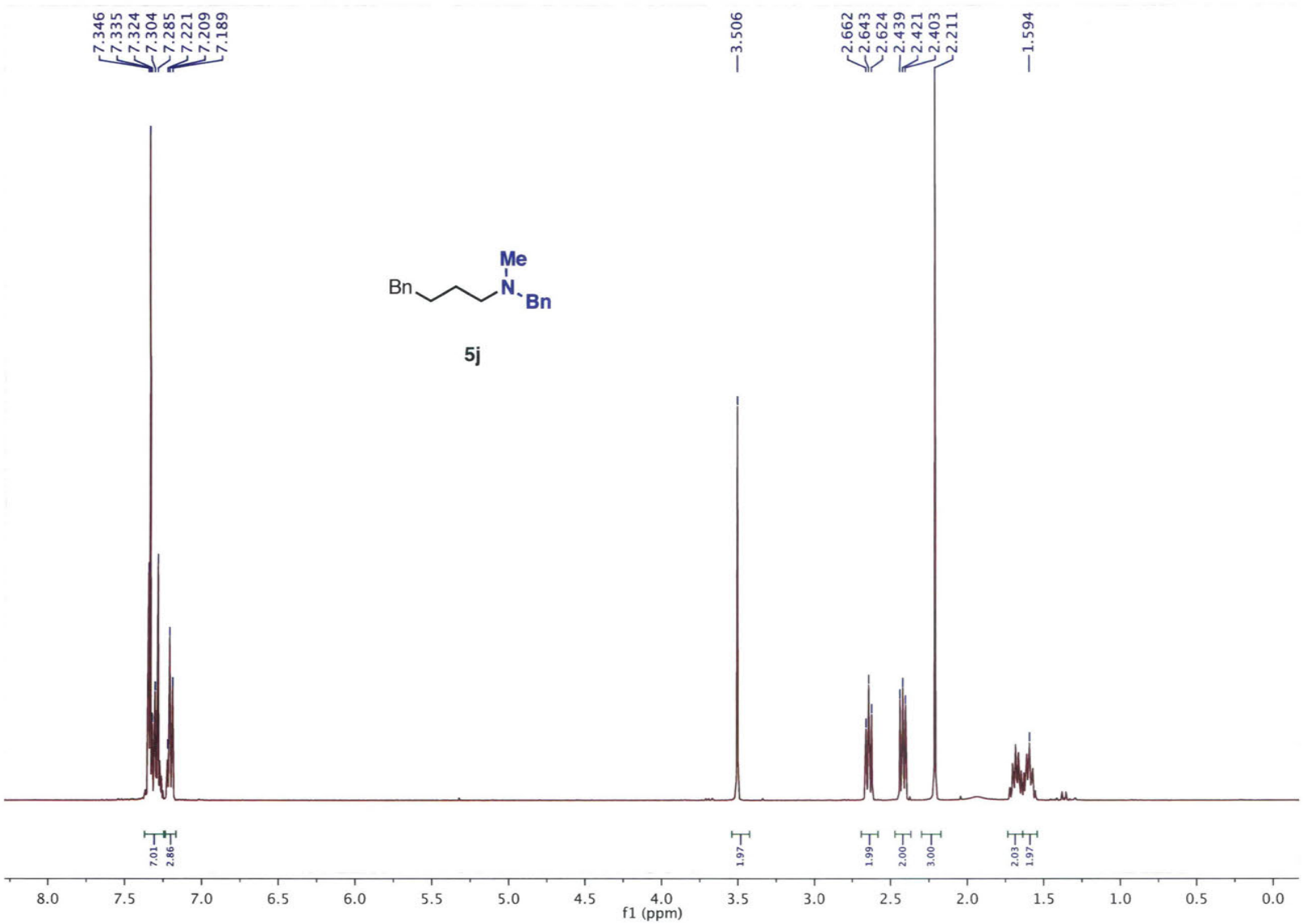
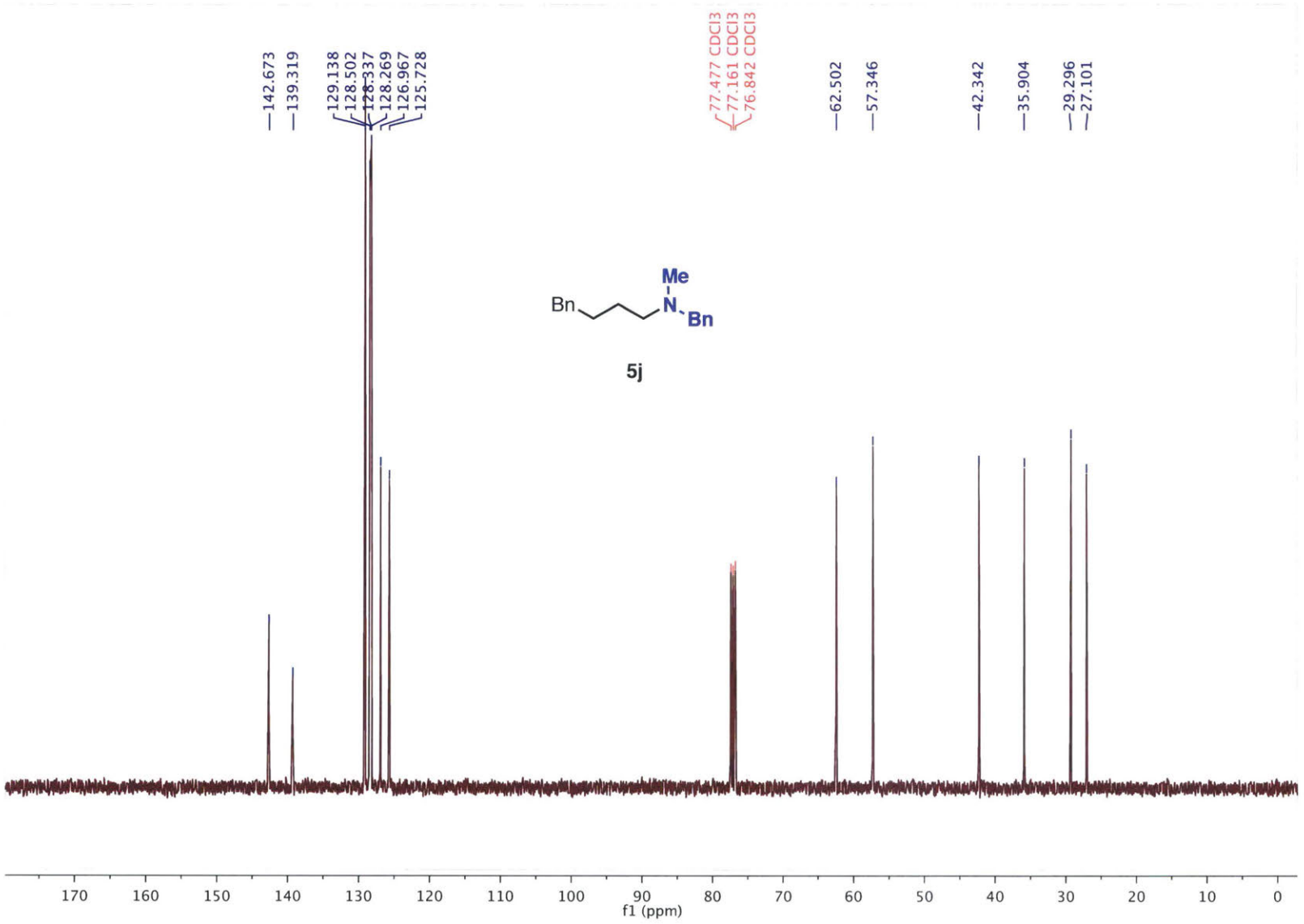
7.421
7.418
7.380
7.362
7.343
7.284
7.231
7.213
7.128
7.112
3.638
3.604
3.597
3.563
2.990
2.979
2.958
2.946
2.402
2.383
2.370
2.352
2.310
2.293
2.279
2.262
2.178
2.155
2.145
2.122
2.097
0.864
0.848
Me
Bn
Bn
N
Bn
5h
3.91
4.00
4.10
1.02
1.98
4.00
1.00
0.98
1.02
1.00
1.05
3.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

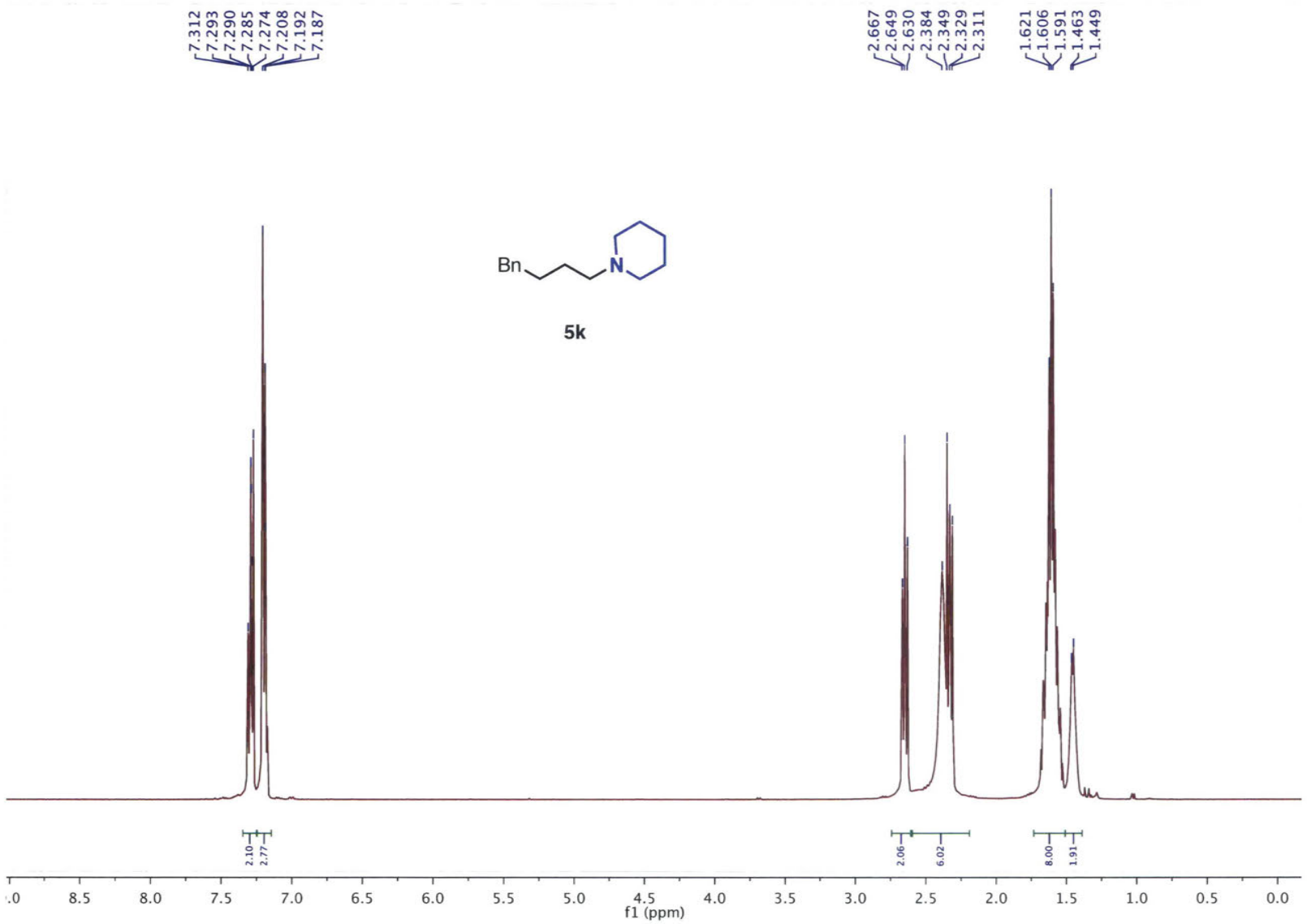

141.635
139.964
129.258
129.036
128.277
128.222
126.910
125.703
77.477 CDCl3
77.159 CDCl3
76.842 CDCl3
60.722
59.079
41.503
33.677
18.093
Me
Bn
N
Bn
Bn
5h
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

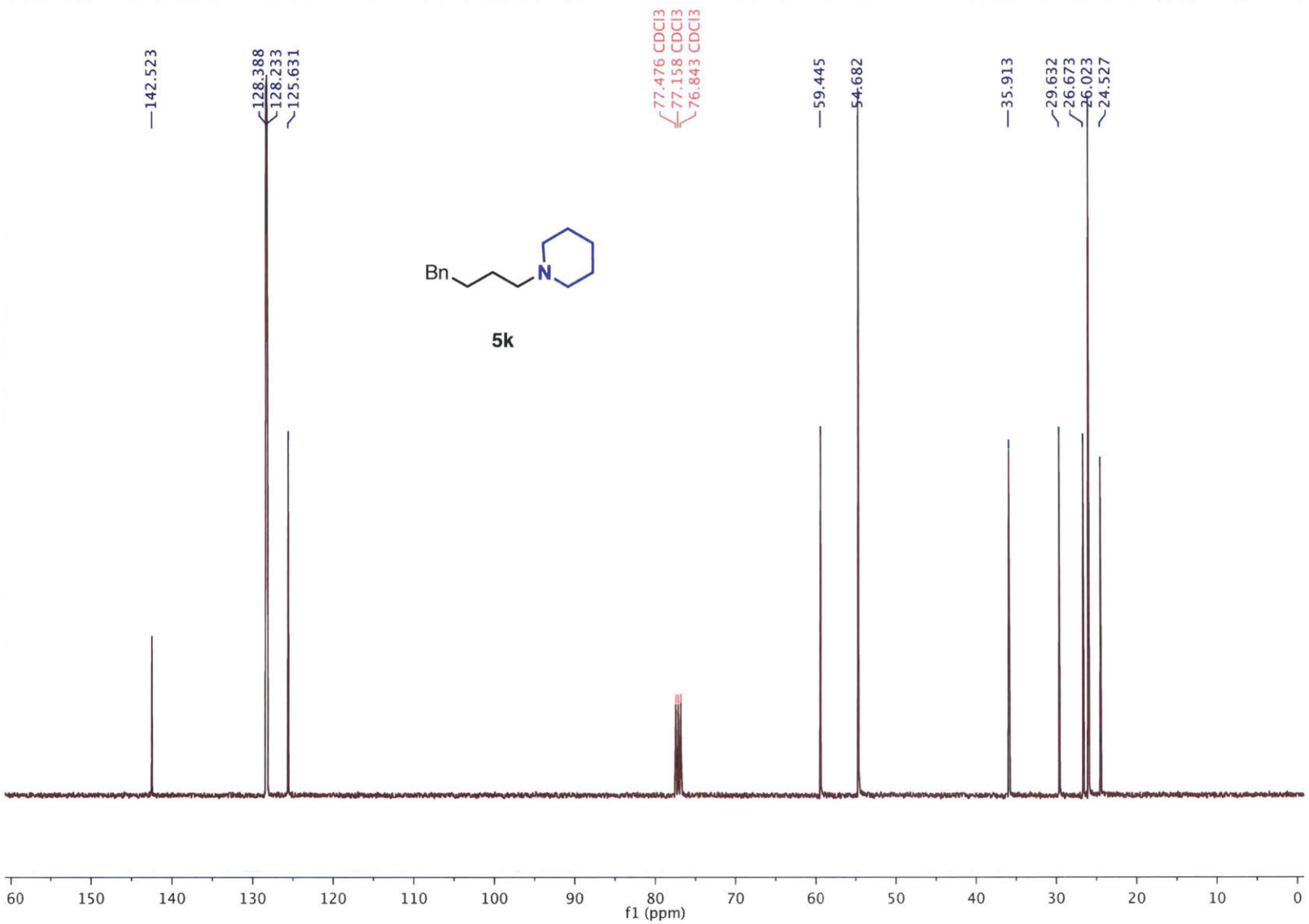

7.369
7.365
7.360
7.348
7.345
7.323
7.321
7.316
7.306
7.303
7.299
7.288
7.284
7.260 CDCl3
7.245
7.241
7.237
7.229
7.223
7.217
7.209
7.205
7.202
3.609
3.600
3.596
3.585
3.572
3.566
3.488
3.454
3.302
3.285
3.277
3.261
2.393
2.376
2.361
2.344
2.202
2.183
2.171
2.152
1.948
1.935
1.932
1.929
1.918
1.915
1.912
0.877
0.011
Me
Bn
TBSO
N
Bn
5i
7.93
1.99
2.96
2.00
1.07
1.01
1.04
1.01
12.34
6.27
f1 (ppm)

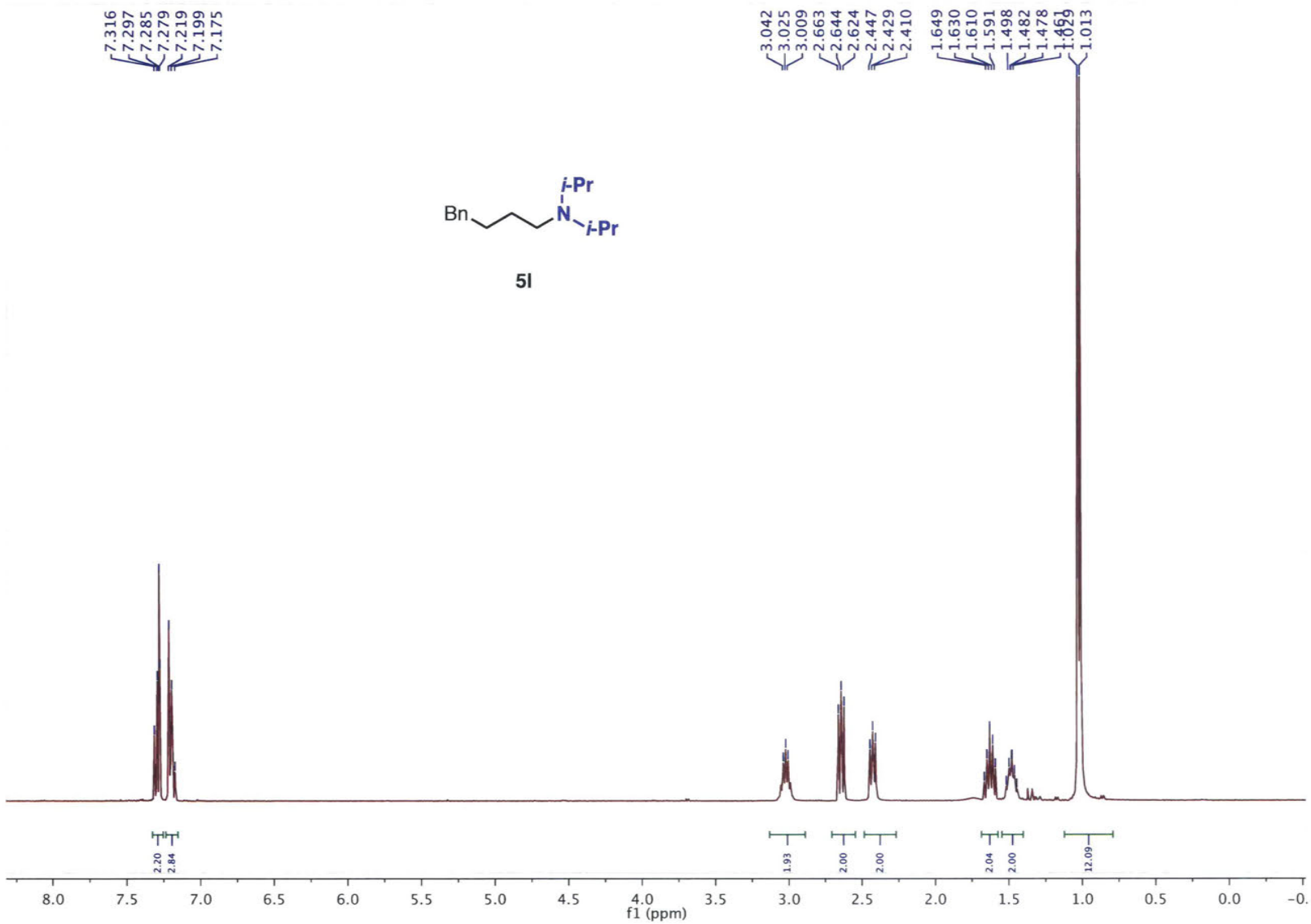

140.011
128.992
128.229
126.856
77.478 CDCl3
77.161 CDCl3
76.844 CDCl3
67.120
58.988
57.507
34.430
26.121
18.487
15.803
5.191
Me
Bn
TBSO
N
Bn
5i
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

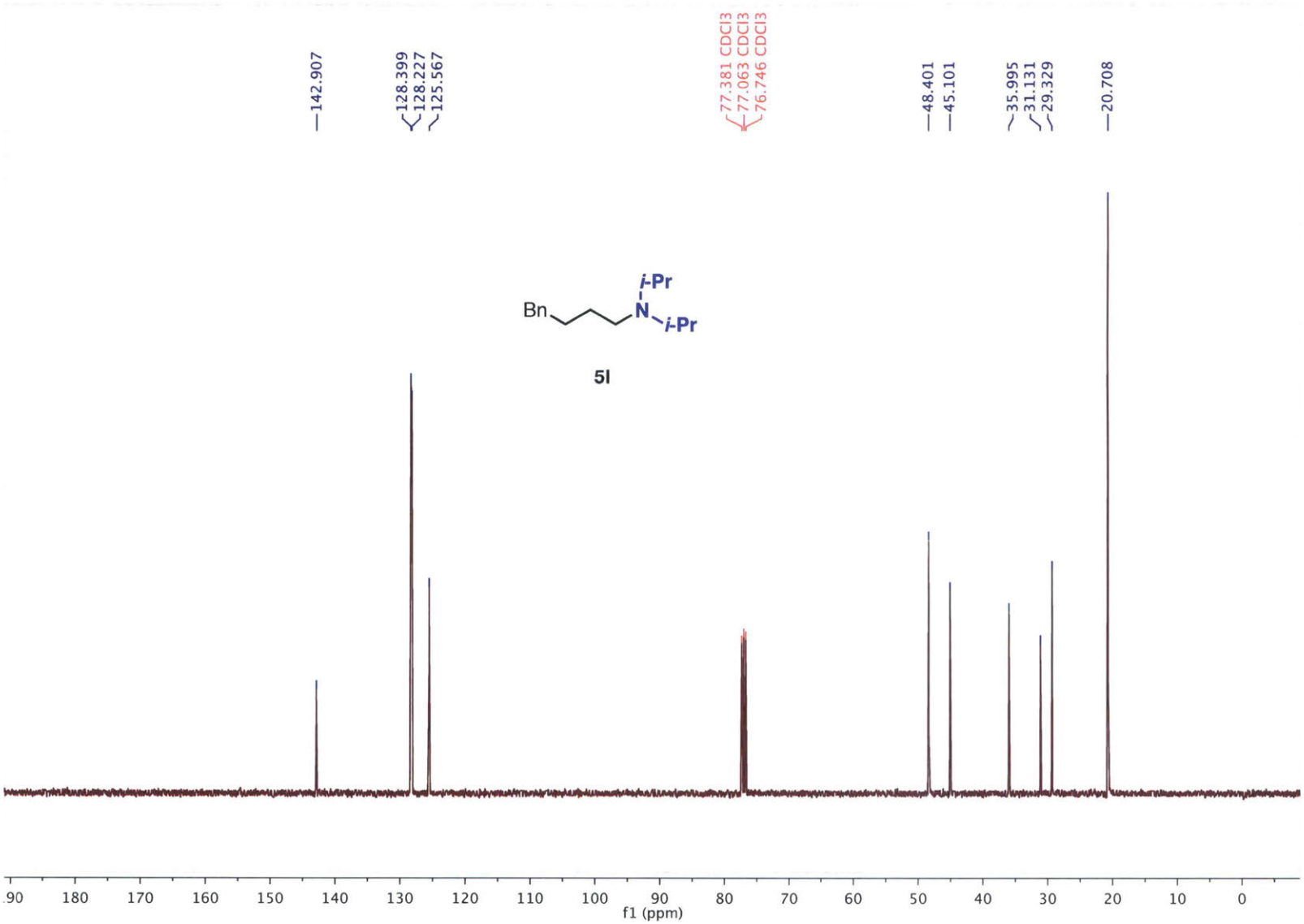

7.346
7.335
7.324
7.304
7.285
7.221
7.209
7.189
3.506
2.662
2.643
2.624
2.439
2.421
2.403
2.211
1.594
Me
Bn
N
Bn
5j
7.01
2.86
1.97
1.99
2.00
3.00
2.03
1.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

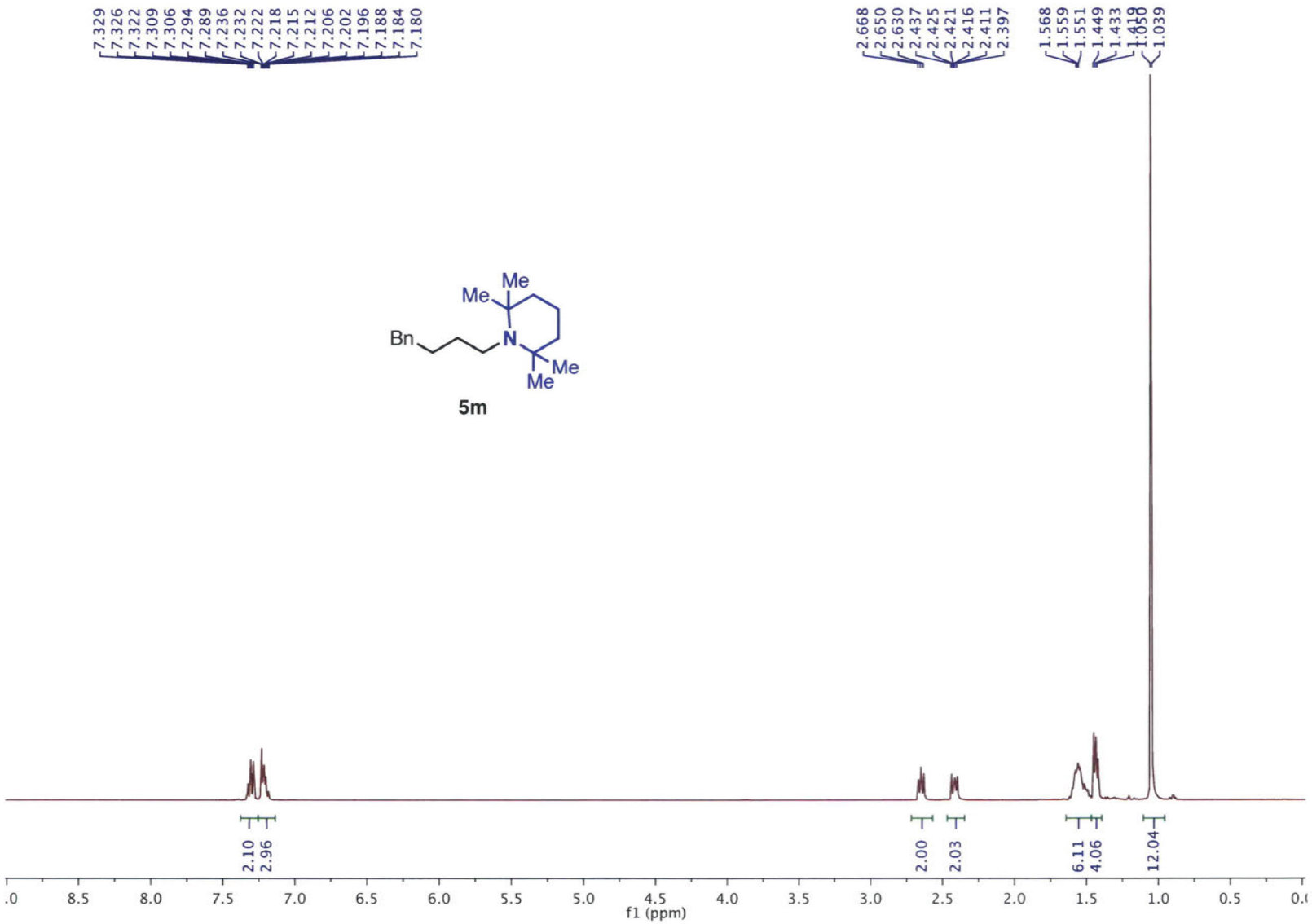

142.673
139.319
129.138
128.502
128.337
128.269
126.967
125.728
77.477 CDCl3
77.161 CDCl3
76.842 CDCl3
62.502
57.346
42.342
35.904
29.296
27.101
Me
N
Bn
Bn
5j
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

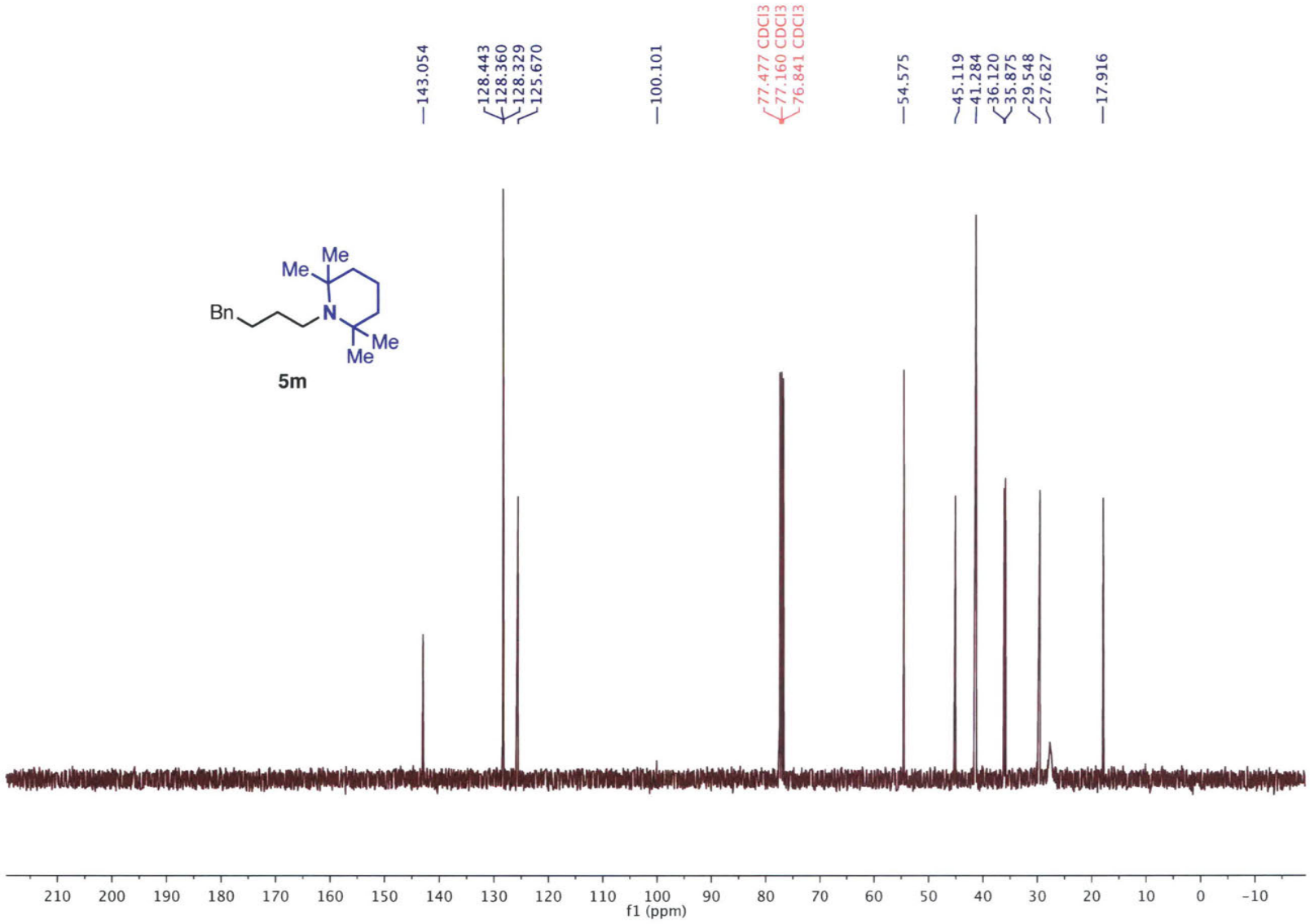

7.312
7.293
7.290
7.285
7.274
7.208
7.192
7.187
2.667
2.649
2.630
2.384
2.349
2.329
2.311
1.621
1.606
1.591
1.463
1.449
Bn
N
5k
2.10
2.77
2.06
6.02
8.00
1.91
f1 (ppm)


142.523
128.388
128.233
125.631
77.476 CDCl3
77.158 CDCl3
76.843 CDCl3
59.445
54.682
35.913
29.632
26.673
26.023
24.527
Bn
N
5k
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.316
7.297
7.285
7.279
7.219
7.199
7.175
3.042
3.025
3.009
2.663
2.644
2.624
2.447
2.429
2.410
1.649
1.630
1.610
1.591
1.498
1.482
1.478
1.029
1.013
Bn
i-Pr
N
i-Pr
5l
2.20
2.84
1.93
2.00
2.00
2.04
2.00
12.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


142.907
128.399
128.227
125.567
77.381 CDCl3
77.063 CDCl3
76.746 CDCl3
48.401
45.101
35.995
31.131
29.329
20.708
i-Pr
Bn
N
i-Pr
5l
f1 (ppm)


7.329
7.326
7.322
7.309
7.306
7.294
7.289
7.236
7.232
7.222
7.218
7.215
7.212
7.206
7.202
7.196
7.188
7.184
7.180
2.668
2.650
2.630
2.437
2.425
2.421
2.416
2.411
2.397
1.568
1.559
1.551
1.449
1.433
1.039
Me
Me
Bn
N
Me
Me
5m
2.10
2.96
2.00
2.03
6.11
4.06
12.04
f1 (ppm)

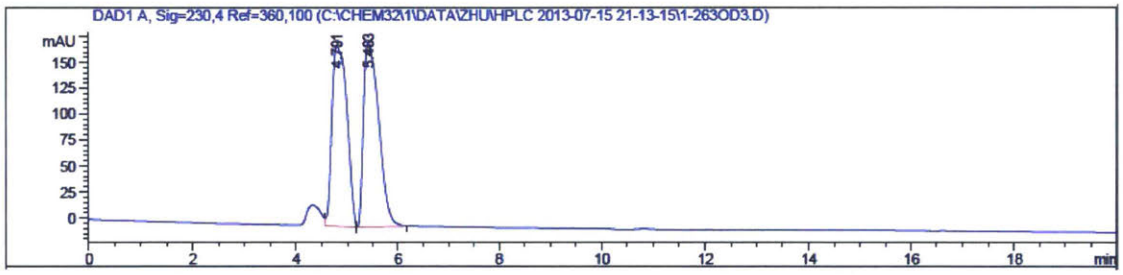

143.054
128.443
128.360
128.329
125.670
100.101
77.477 CDCl3
77.160 CDCl3
76.841 CDCl3
54.575
45.119
41.284
36.120
35.875
29.548
27.627
17.916
Me
Me
Bn
N
Me
Me
5m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

2.7 Chiral HPLC and Chiral GC Spectra

3a

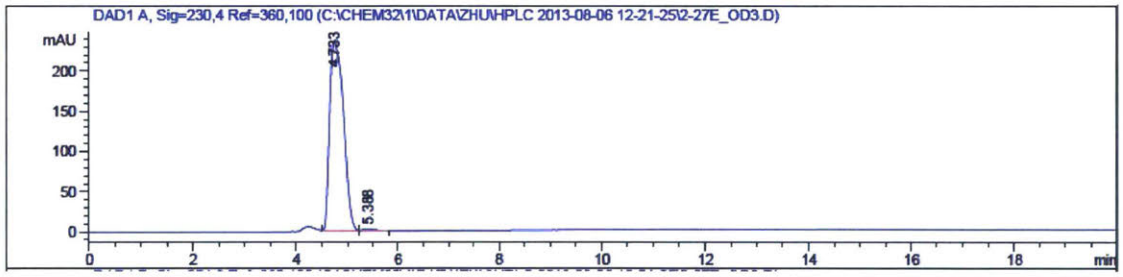
(*S*)-*N*,*N*-dibenzyl-1-phenylethan-1-amine (Table 2, entry **3a**): HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 4.8 minutes, t_R (minor) = 5.4 minutes.

Rac-**3a**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.791	VV	0.2825	3560.30688	174.18317	48.9500
2	5.403	VB	0.3406	3713.04492	178.58705	51.0500
Totals :				7273.35181	352.77022	

(S)-**3a** from **styrene** (**1a**): 97% *ee*

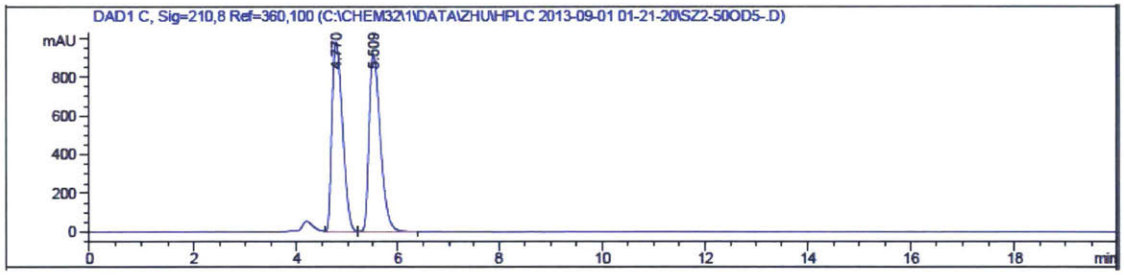


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.733	VV	0.2684	4479.54980	237.15596	98.8905
2	5.388	VB	0.2378	50.25723	2.61964	1.1095
Totals :				4529.80703	239.77560	

3b

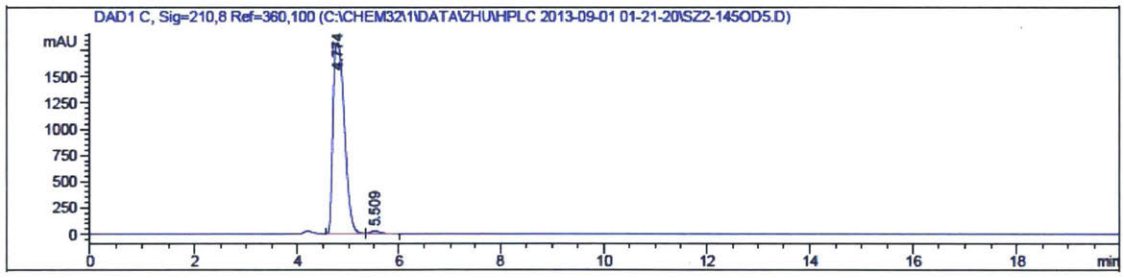
(*S*)-*N*,*N*-dibenzyl-1-(4-fluorophenyl)ethan-1-amine (Table 2, entry **3b**): HPLC analysis (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 4.8 minutes, t_R (minor) = 5.5 minutes.

Rac-**3b**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.770	VV	0.2313	1.42485e4	982.05505	49.8634
2	5.509	VB	0.2444	1.43265e4	916.38263	50.1366
Totals :				2.85750e4	1898.43768	

(S)-**3b** from **1-Fluoro-4-vinylbenzene (1b)**: 97% ee

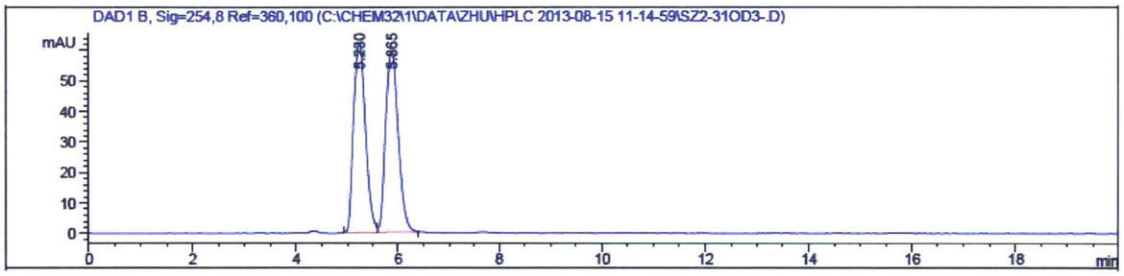


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.774	VV	0.2520	2.84310e4	1822.87952	98.3950
2	5.509	VB	0.2429	463.77542	28.63951	1.6050
Totals :				2.88948e4	1851.51903	

3c

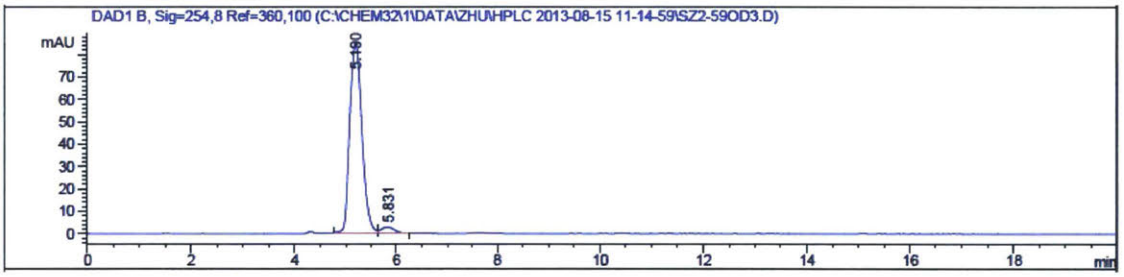
(*S*)-*N*,*N*-dibenzyl-1-(2-chlorophenyl)ethan-1-amine (Table 2, entry **3c**): HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (major) = 5.2 minutes, t_R (minor) = 5.8 minutes.

Rac-**3c**

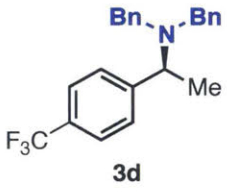


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.230	BV	0.2645	1018.62762	62.36912	49.7150
2	5.865	VB	0.2753	1030.30859	59.71028	50.2850
Totals :				2048.93622	122.07940	

(S)-**3c** from **1-Chloro-2-vinylbenzene** (**1c**): 92% ee



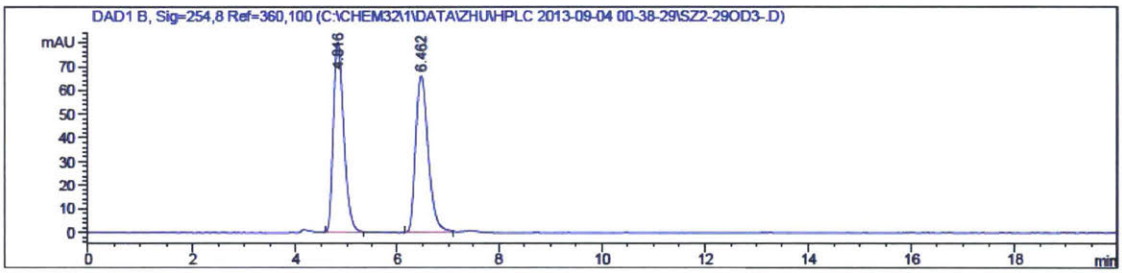
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.190	BV	0.2671	1423.92590	85.15365	96.6429
2	5.831	VB	0.2743	49.46318	2.74400	3.3571
Totals :				1473.38908	87.89765	



3d

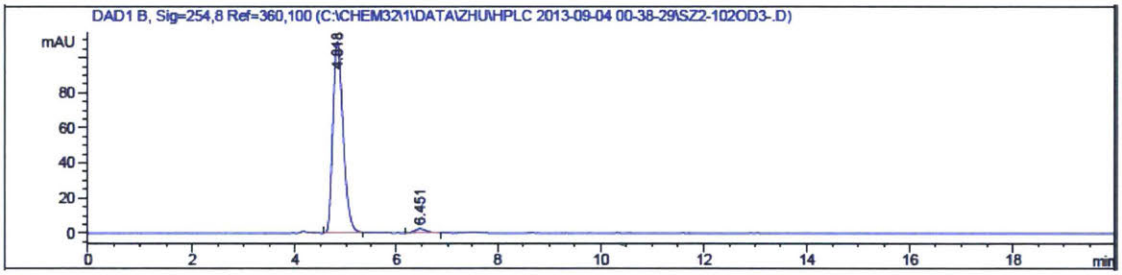
(*S*)-*N*,*N*-dibenzyl-1-(4-(trifluoromethyl)phenyl)ethan-1-amine (Table 2, entry **3d**): **HPLC analysis (OD-H,** 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 95% ee: t_R (major) = 4.8 minutes, t_R (minor) = 6.5 minutes.

Rac-**3d**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.816	BB	0.2241	1150.32434	79.83385	50.4896
2	6.462	BB	0.2659	1128.01599	65.84871	49.5104
Totals :				2278.34033	145.68256	

(S)-**3d** from **1-(trifluoromethyl)-4-vinylbenzene** (**1d**): 95% ee

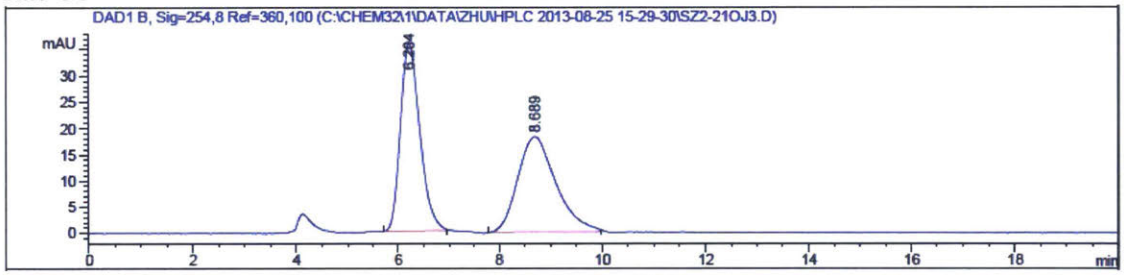


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.818	BB	0.2209	1535.72363	108.66138	97.5437
2	6.451	BB	0.2230	38.67113	2.36222	2.4563
Totals :				1574.39477	111.02360	

3e

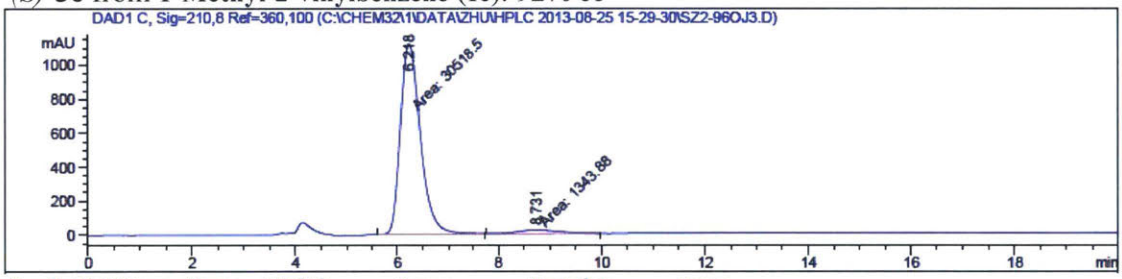
(*S*)-*N,N*-dibenzyl-1-(***o*-tolyl)ethan-1-amine** (Table 2, entry **3e**): HPLC analysis (OJ, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (major) = 6.2 minutes, t_R (minor) = 8.7 minutes.

Rac-**3e**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.204	BB	0.4134	950.30396	35.83410	50.2459
2	8.689	BB	0.6719	941.00232	18.23969	49.7541
Totals :				1891.30627	54.07379	

(*S*)-**3e** from **1-Methyl-2-vinylbenzene** (**1e**): 92% ee

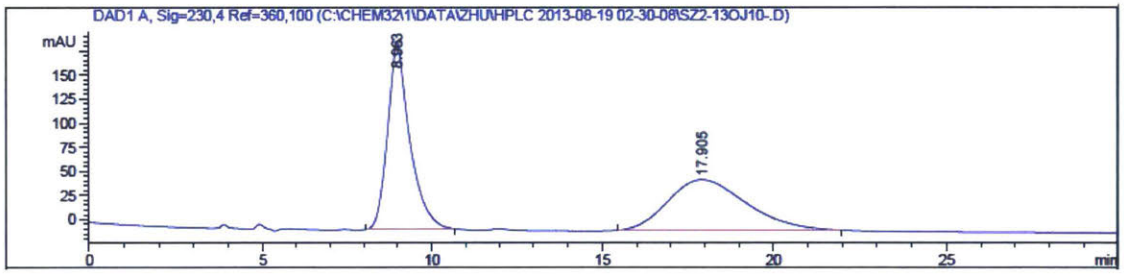


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.220	BB	0.4081	1076.14355	41.01268	93.8658
2	8.739	MM	1.0644	70.32650	1.10121	6.1342
Totals :				1146.47005	42.11388	

3f

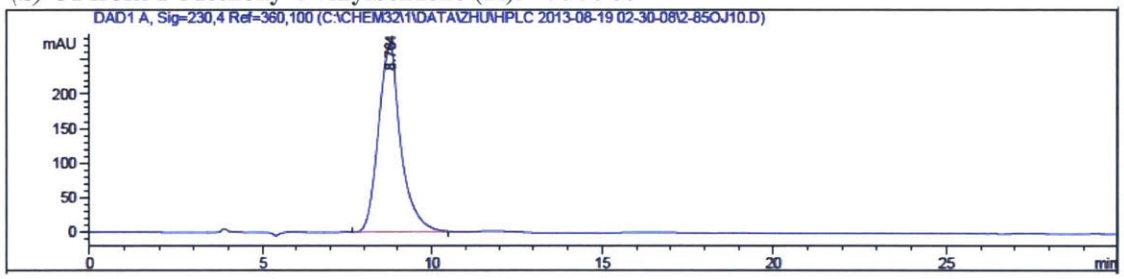
(*S*)-*N*,*N*-dibenzyl-1-(4-methoxyphenyl)ethan-1-amine (Table 2, entry **3f**): HPLC analysis (OJ, 10% IPA/hexane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (major) = 9.0 minutes, t_R (minor) = 17.9 minutes.

Rac-**3f**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.963	BB	0.6455	8854.01953	195.07523	51.3217
2	17.905	BB	1.8692	8397.97656	52.52849	48.6783
Totals :				1.72520e4	247.60371	

(S)-**3f** from **1-Methoxy-4-vinylbenzene** (**1f**): >99% ee

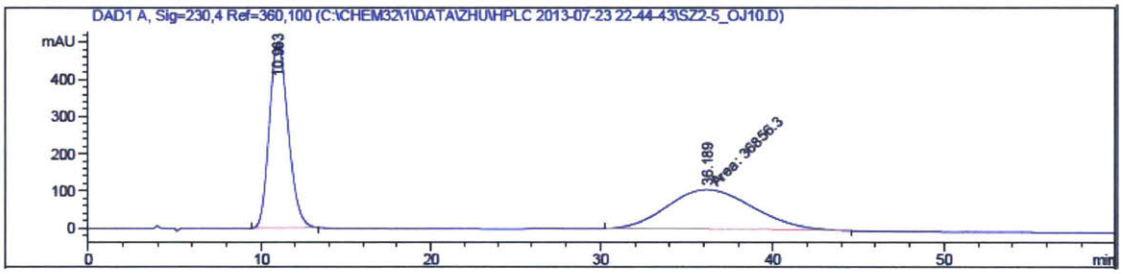


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.764	VB	0.6829	1.24944e4	272.52264	100.0000
Totals :				1.24944e4	272.52264	

3g

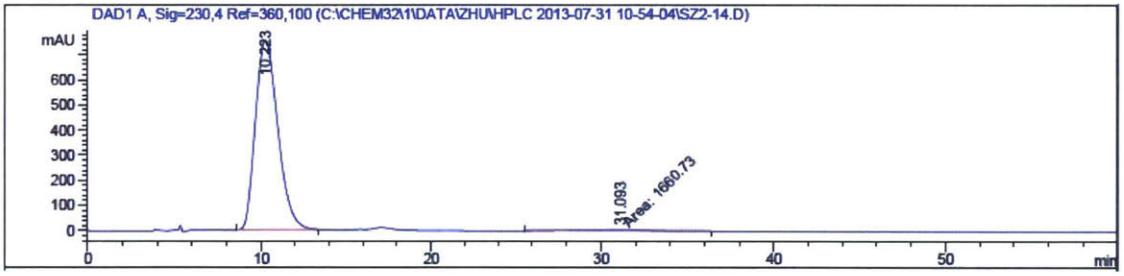
(*S*)-*N*,*N*-dibenzyl-1-(naphthalen-2-yl)ethanamine (Table 3, entry **3g**): HPLC analysis (OJ, 10% IPA/hexane, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 10.9 minutes, t_R (minor) = 36.2 minutes.

Rac-**3g**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.963	BB	1.1386	3.83449e4	501.21277	50.9897
2	36.189	MM	5.7725	3.68563e4	106.41365	49.0103
Totals :				7.52013e4	607.62642	

(*S*)-**3g** from **1-Fluoro-4-vinylbenzene** (**1g**): 97% ee

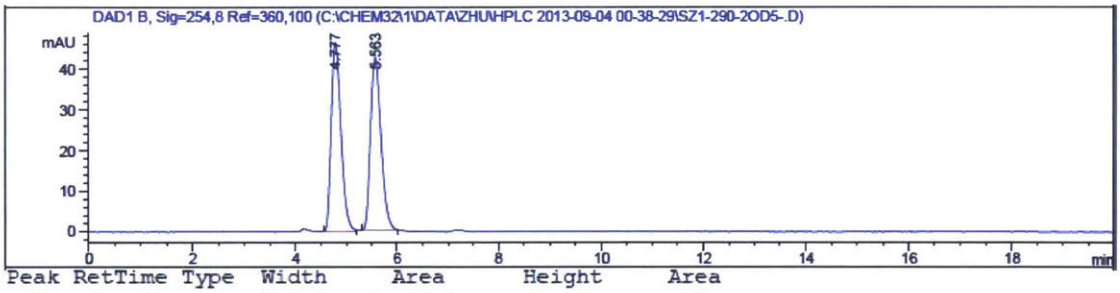


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.223	BB	1.3532	6.86279e4	754.51062	97.6373
2	31.093	MM	4.7568	1660.73291	5.81875	2.3627
Totals :				7.02886e4	760.32937	

3h, 3l

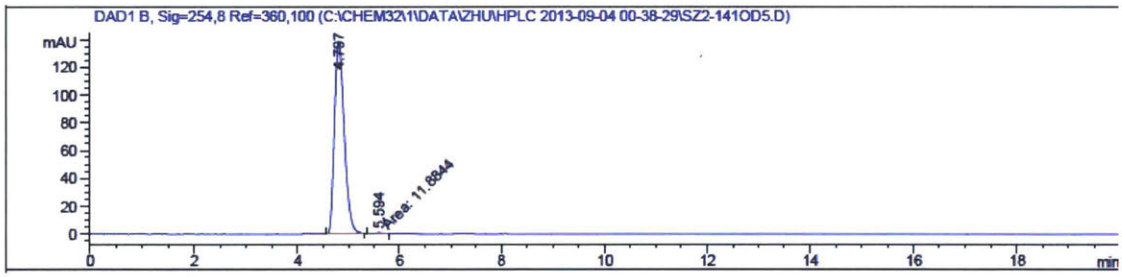
(*S*)-*N*,*N*-dibenzyl-1-phenylpropan-1-amine (Table 2, entry 3h & 3l): **HPLC analysis** (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee (from *trans*-), 96% ee (from *cis*-): t_R (major) = 4.8 minutes, t_R (minor) = 5.6 minutes.

Rac-**3h, l**



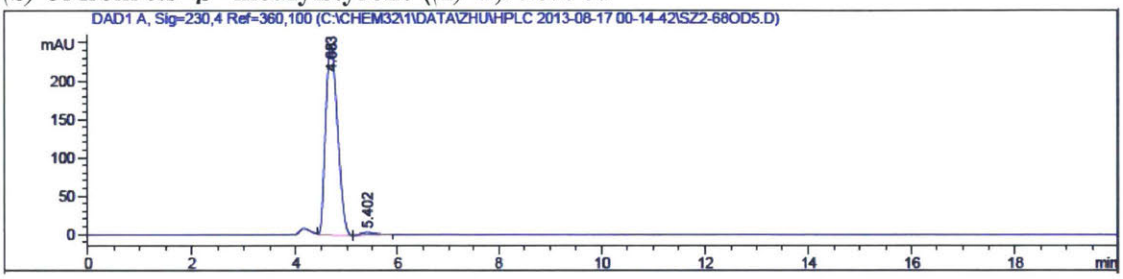
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.777	BV	0.2114	1649.06104	122.22649	49.8602
2	5.563	VB	0.2281	1658.30701	112.40995	50.1398
Totals :				3307.36804	234.63644	

(*S*)-**3h** from ***trans*-β-methylstyrene** ((*E*)-**1h**): >99% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.797	BB	0.2115	4882.22217	361.74579	99.5765
2	5.590	BB	0.1914	20.76602	1.53891	0.4235
Totals :				4902.98819	363.28470	

(S)-**3l** from ***cis*- β -methylstyrene** (*(Z)*-**1l**): 96% ee

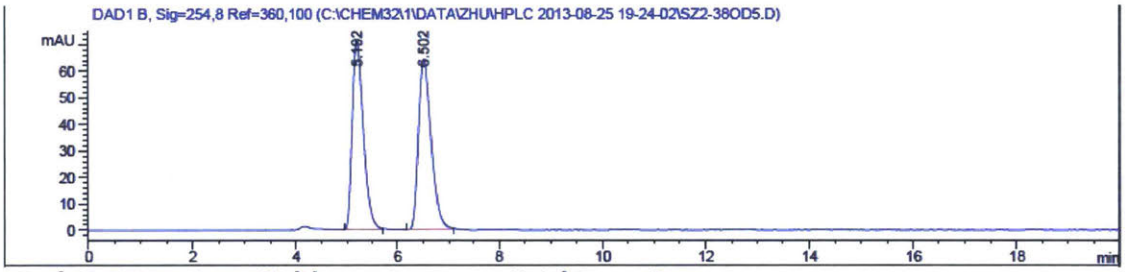


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.683	VV	0.2669	4066.69287	248.51657	98.1083
2	5.402	VB	0.2858	78.41167	3.54871	1.8917
Totals :				4145.10455	252.06528	

3i, 3m

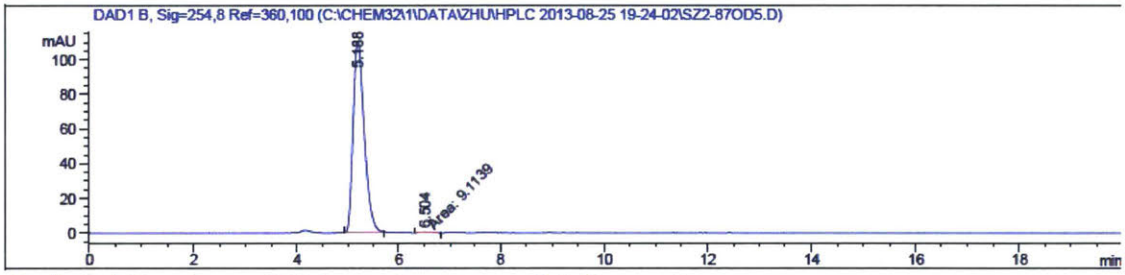
(*S*)-*N*,*N*-dibenzyl-1,2-diphenylethan-1-amine (Table 2, entry **3i & 3m**): HPLC analysis (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee (from trans-), 88% ee (from cis): t_R (major) = 5.2 minutes, t_R (minor) = 6.5 minutes.

Rac-**3i, m**



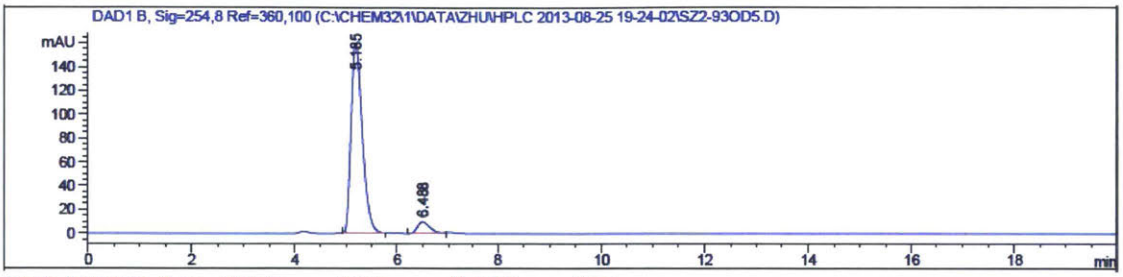
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.193	BB	0.2362	3069.68823	200.92946	49.8528
2	6.503	BB	0.2670	3087.81689	177.44810	50.1472
Totals :				6157.50513	378.37756	

(S)-**3i**from ***trans*-stillbene** ((*E*)-**1i**): >99% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.189	BB	0.2353	4730.73340	311.31937	99.5199
2	6.517	BV	0.2048	22.82083	1.35311	0.4801
Totals :				4753.55423	312.67248	

(S)-**3i**from ***cis*-stillbene** ((Z)-**1m**): 88% ee

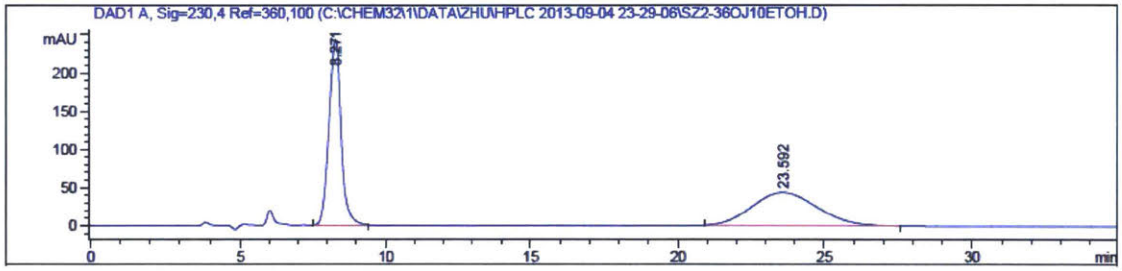


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.185	BB	0.2352	6844.63623	450.68427	93.7745
2	6.487	BB	0.2555	454.40448	27.69054	6.2255
Totals :				7299.04071	478.37481	

3j

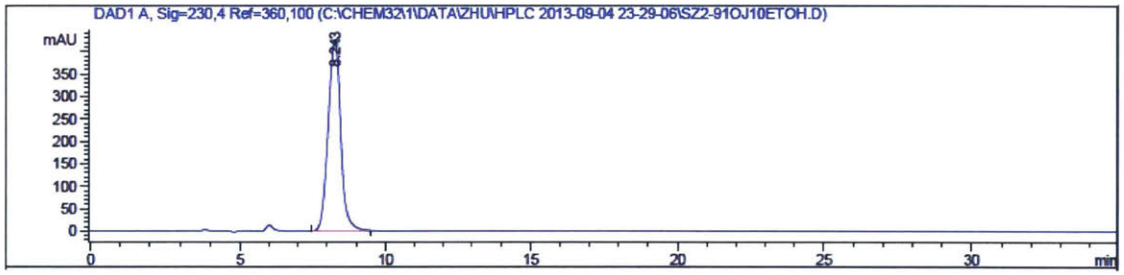
(*S*)-*N*,*N*-dibenzyl-1-(4-methoxyphenyl)ethan-1-amine (Table 2, entry **3j**): HPLC analysis (OJ, 10% EtOH/hexane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (major) = 8.3 minutes, t_R (minor) = 23.6 minutes.

Rac-**3j**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.271	VB	0.4486	1.41796e4	485.75226	50.0589
2	23.571	BB	1.8556	1.41463e4	89.23178	49.9411
Totals :				2.83259e4	574.98404	

(S)-**3j** from **(*E*)-1-methoxy-4-(prop-1-en-1-yl)benzene** (**1j**): >99% ee

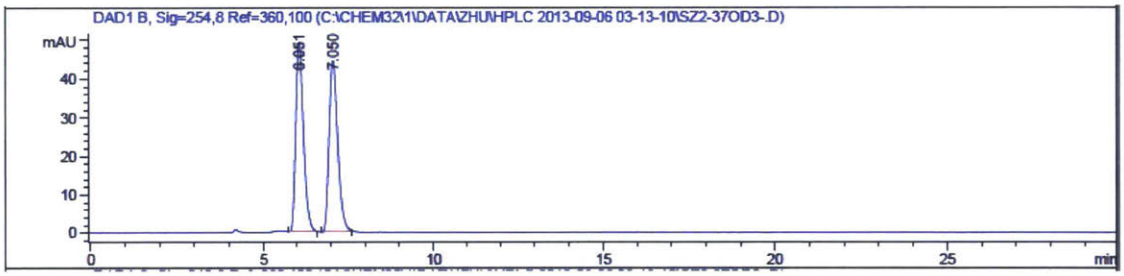


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.243	BB	0.4600	1517.36401	50.87385	100.0000
Totals :				1517.36401	50.87385	

3k

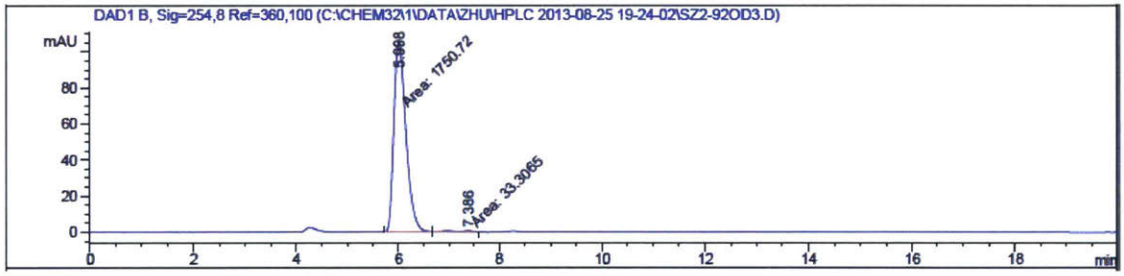
(*S*)-*N*,*N*-dibenzyl-3-methoxy-1-phenylpropan-1-amine (Table 2, entry **3k**)**:** HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (major) = 6.0 minutes, t_R (minor) = 6.7 minutes.

Rac-**3k**



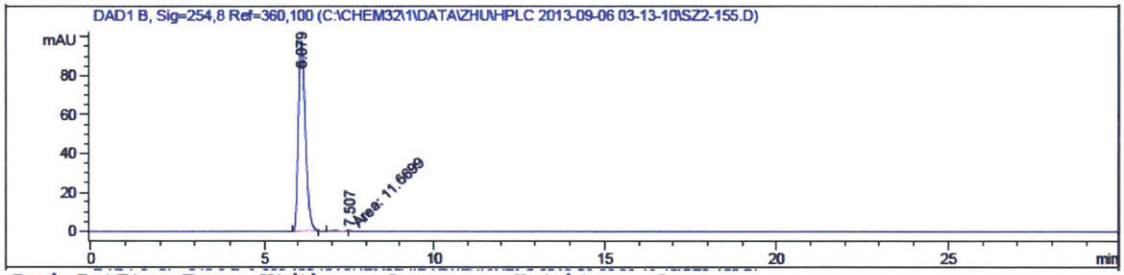
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.051	VV	0.2538	1.41525e4	851.76758	50.4456
2	7.049	VB	0.2805	1.39025e4	770.35675	49.5544
Totals :				2.80549e4	1622.12433	

(S)-**3k** from **(*E*)-(3-methoxyprop-1-en-1-yl)benzene** (**1k**):
1 mmol scale: 98% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.000	MF	0.2921	2.81014e4	1603.61926	99.1340
2	6.966	FM	0.3587	245.47841	11.40637	0.8660
Totals :				2.83469e4	1615.02564	

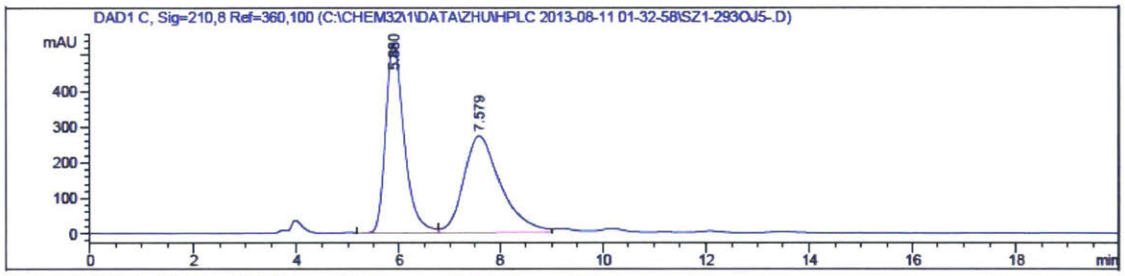
10 mmol scale: 99% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.079	BB	0.2239	3916.92163	268.90894	99.5534
2	7.069	BB	0.2091	17.57214	1.05054	0.4466
Totals :				3934.49377	269.95948	

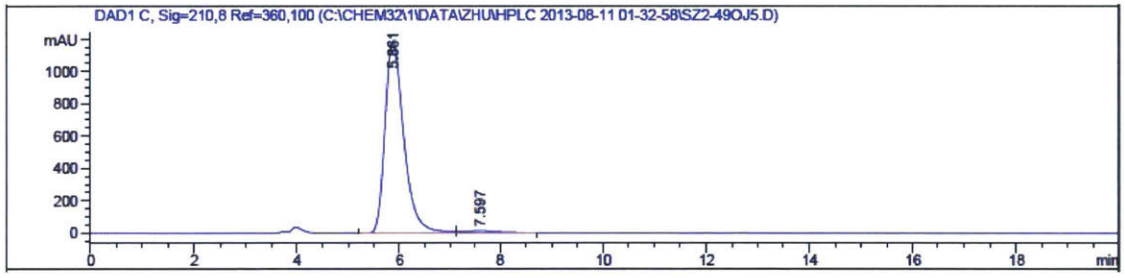
(*S*)-*N*,*N*-dibenzyl-2,3-dihydro-1*H*-inden-1-amine (Table 2, entry **3n**): HPLC analysis (OJ, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated 95% ee: t_R (major) = 5.9 minutes, t_R (minor) = 7.6 minutes.

Rac-**3n**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.880	VV	0.3834	1.34774e4	532.35504	48.8098
2	7.579	VB	0.7611	1.41346e4	272.51981	51.1902
Totals :				2.76120e4	804.87485	

(S)-**3n** from **1*H*-indene** (**1n**): 95% ee

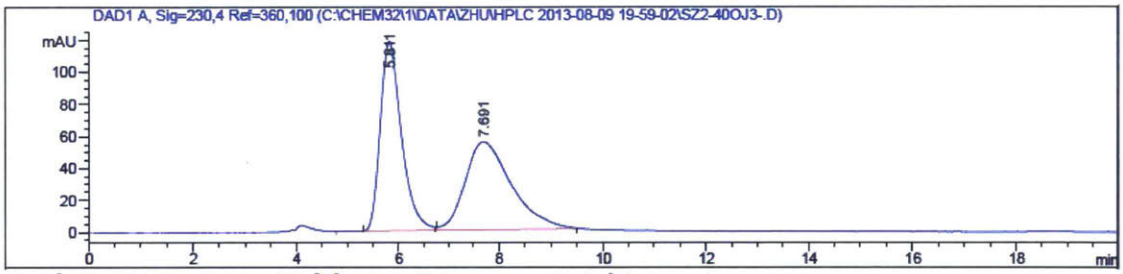


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.866	BB	0.3726	3289.06836	133.86964	99.1659
2	7.641	BB	0.2301	27.66391	1.48003	0.8341
Totals :				3316.73227	135.34968	

3o

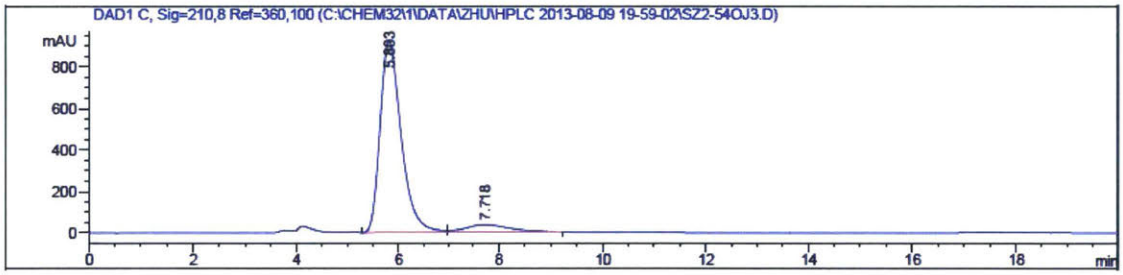
(*S*)-*N*,*N*-dibenzyl-1,2,3,4-tetrahydronaphthalen-1-amine (Table 2, entry **3o**): HPLC analysis (OJ, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated 86% ee: t_R (major) = 5.8 minutes, t_R (minor) = 7.7 minutes.

Rac-**3o**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.811	BB	0.4354	3422.00732	118.33289	49.2643
2	7.691	BB	0.8790	3524.22021	55.34014	50.7357
Totals :				6946.22754	173.67303	

(S)-**3o** from **(*E*)-(3-methoxyprop-1-en-1-yl)benzene** (**1o**): 86% ee

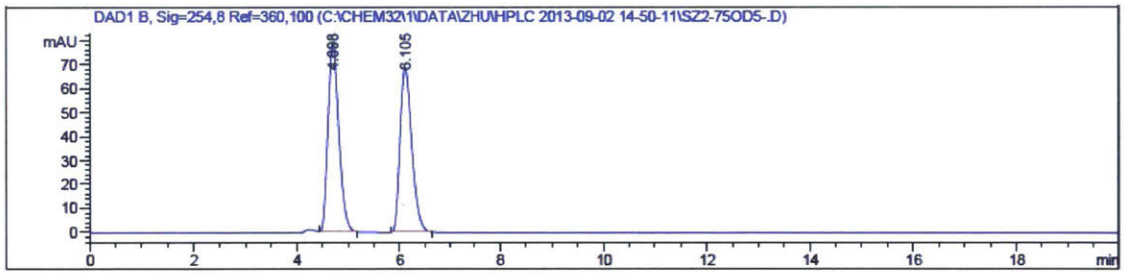


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.806	BB	0.4247	800.18469	28.75187	93.2555
2	7.700	MM	0.9159	57.87141	1.05308	6.7445
Totals :				858.05611	29.80495	

3p

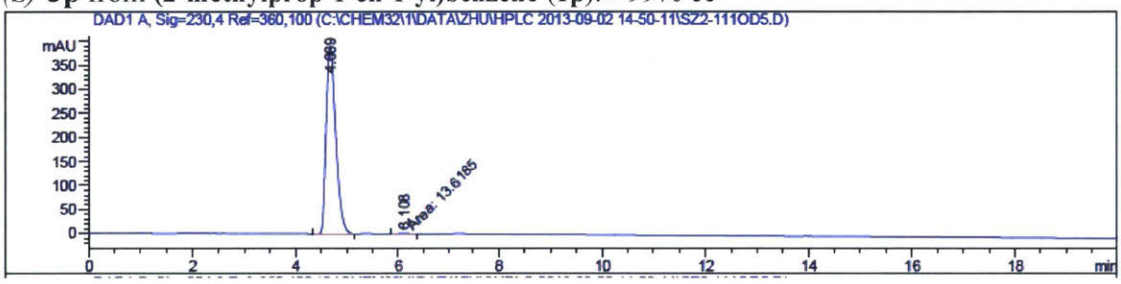
(*S*)-*N*,*N*-dibenzyl-2-methyl-1-phenylpropan-1-amine (Table 2, entry **3p**): HPLC analysis (OD-H, 5% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee, single isomer: t_R (major) = 4.7 minutes, t_R (minor) = 6.1 minutes.

Rac-**3p**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.697	VV	0.2393	2973.19531	193.43083	51.5631
2	6.105	FM	0.2809	2792.93506	165.68793	48.4369
Totals :				5766.13037	359.11876	

(S)-**3p** from **(2-methylprop-1-en-1-yl)benzene** (**1p**): >99% ee

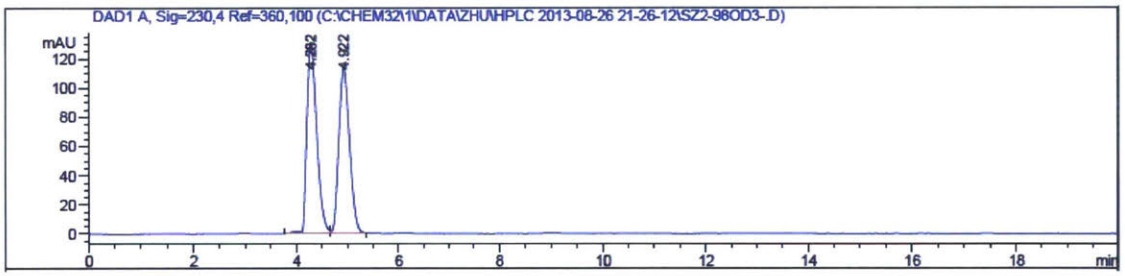


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.669	VV	0.2041	5094.11279	390.70959	99.7334
2	6.108	MM	0.2387	13.61854	9.51028e-1	0.2666
Totals :				5107.73134	391.66062	

3q

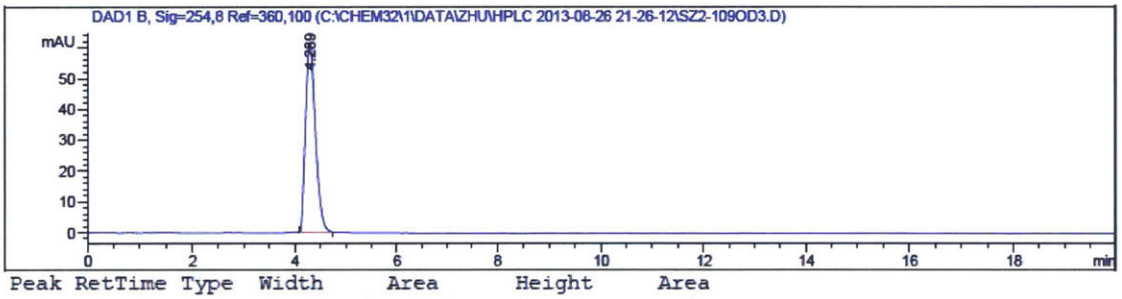
(1*S*,2*R*)-*N*,*N*-dibenzyl-3-((*tert*-butyldimethylsilyl)oxy)-2-methyl-1-phenylpropan-1-amine (Table 2, entry **3q**)**:** HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee, single isomer: t_R (major) = 4.3 minutes, t_R (minor) = 4.9 minutes.

Rac-**3q**

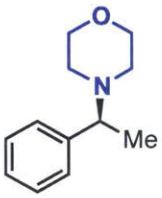


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.281	BV	0.2121	722.25366	54.69595	50.0921
2	4.922	VB	0.2314	719.59875	48.42576	49.9079
Totals :				1441.85242	103.12171	

(S)-**3q** from **(*E*)-*tert*-butyldimethyl((2-methyl-3-phenylallyl)oxy)silane** (**1q**): >99% ee



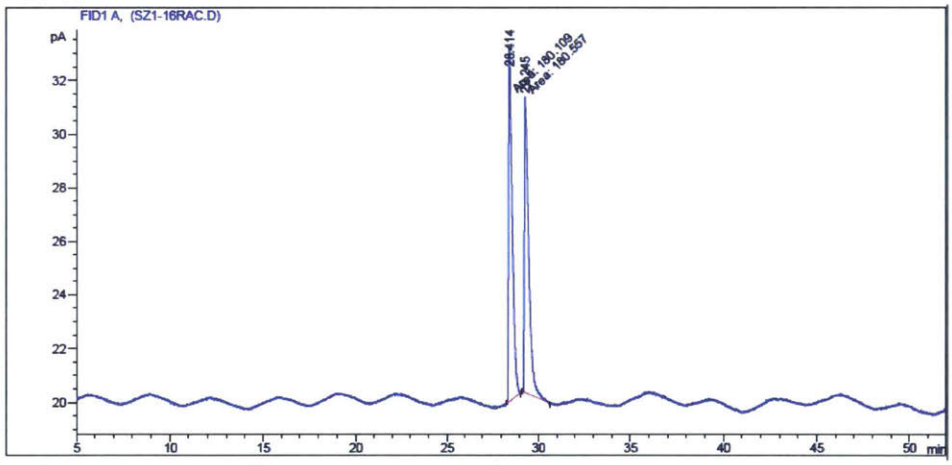
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.289	BB	0.2107	2030.43677	149.31010	100.0000
Totals :				2030.43677	149.31010	



3s

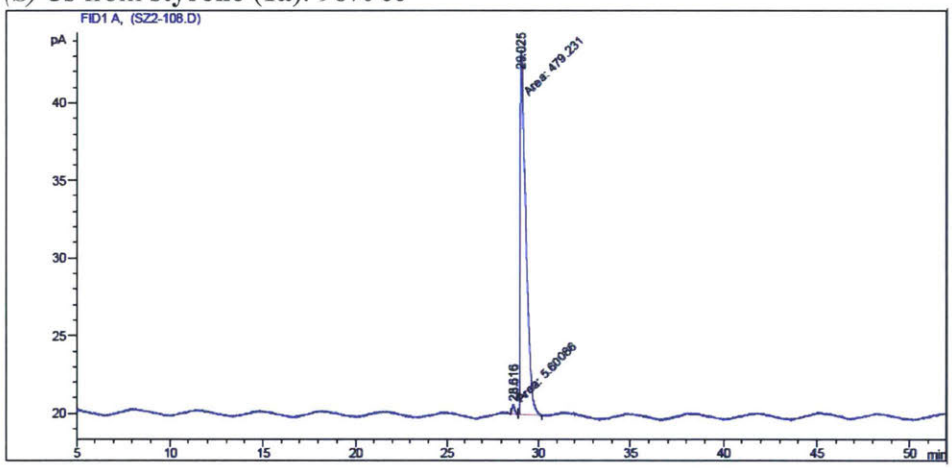
(*S*)-4-(1-phenylethyl)morpholine (Table 3, entry **3s**): GC condition: Varian CP7502 column (25 m×0.25 mm×0.25 μm, chiralsil-DEX CB), H2 2.7 mL/min, programmed from 100 °C to 125 °C at 0.5 °C /min; t_R (minor) = 28.41 min, and t_R (major) = 29.24 min.

Rac-**3s**

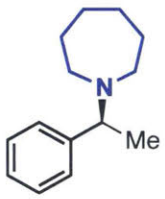


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.414	MM	0.2280	180.10864	13.16769	49.93779
2	29.245	MM	0.2727	180.55737	11.03511	50.06221

(S)-**3s** from **styrene** (**1a**): 98% ee



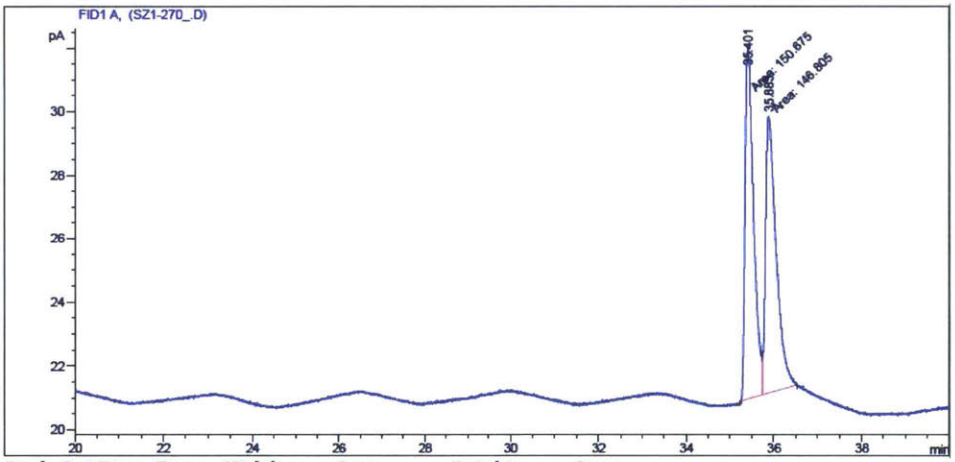
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.616	MM	0.1567	5.60086	5.95790e-1	1.15522
2	29.025	MM	0.3406	479.23148	23.44999	98.84478



3t

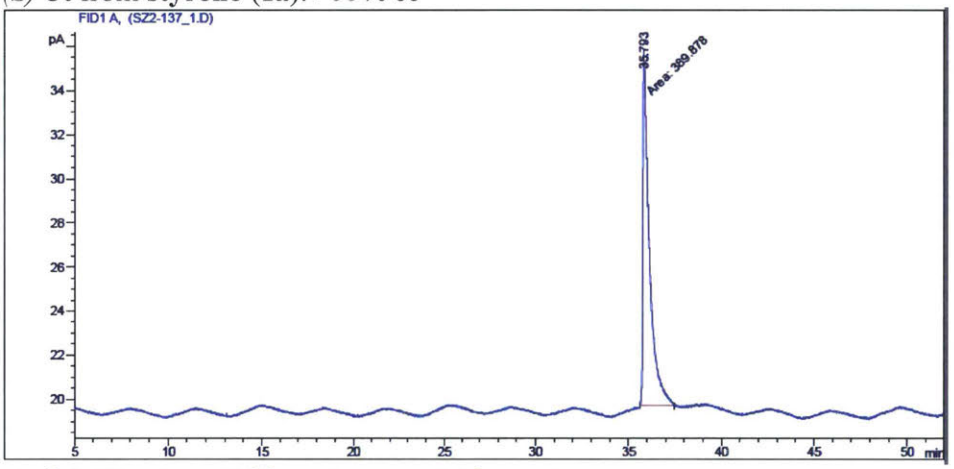
(*S*)-*N*,*N*-dibenzyl-3-methoxy-1-phenylpropan-1-amine (Table 2, entry **3t**)**:** HPLC analysis (OD-H, 3% IPA/hexane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (major) = 6.0 minutes, t_R (minor) = 6.7 minutes.

Rac-**3t**



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.401	MF	0.2269	150.67537	11.06964	50.65056
2	35.883	FM	0.2805	146.80479	8.72269	49.34944

(S)-**3t** from **styrene** (**1a**): >99% ee



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.793	MM	0.4050	389.87814	16.04535	1.000e2

Chapter 3.

α-Aminosilanes Synthesis via Copper-Catalyzed Hydroamination of Vinylsilanes

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Enantioselective Synthesis of α-Aminosilanes by Copper-Catalyzed Hydroamination of Vinylsilanes

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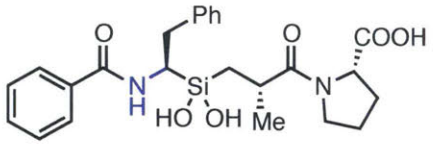
3.1 Introduction

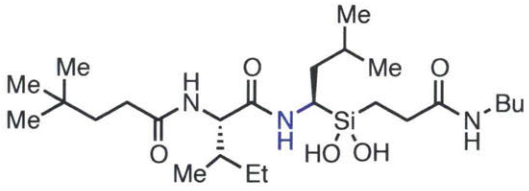
Organosilicon compounds have recently gained prominence within the field of medicinal chemistry. Silicon is often used as an isostere for carbon due to its similar valency and tetrahedral bonding pattern.[1] In addition, because of its larger covalent radius, electropositive/lipophilic nature, and low intrinsic toxicity, silicon is complementary to carbon and is valuable in medicinal chemistry.[2] Among the many subclasses of organosilicon compounds, chiral α-aminosilanes in particular have demonstrated significant bioactivities.[2,3] Several potent inhibitors of proteolytic enzymes possess the α-aminosilane motif, and α-aminosilanes have been incorporated into peptide isosteres (Figure 1).[2-4] Thus, the development of robust methods for the construction of chiral α-aminosilanes is an important area of research.

Figure 1. *Examples of Silicon-Containing Peptidomimetics and Amino Acids*

■ Silanediol protease inhibitors:

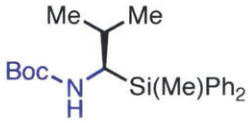


angiotensin-converting enzyme (ACE) inhibitor



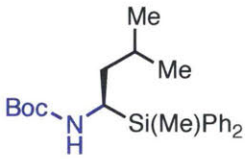
serine protease human neutrophil elastase (HNE) inhibitor

■ Chiral diarylsilylamino acid analogues:

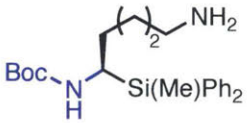


valine mimic

methionine mimic



leucine mimic



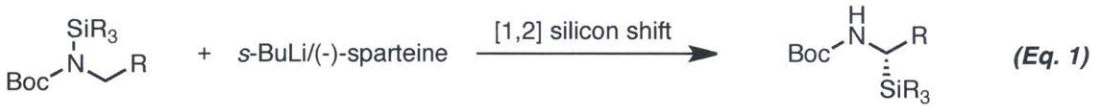
lysine mimic

Although there has been progress in the synthesis of racemic α-aminosilanes,[5,6] enantioselective approaches remain limited. Previous methods include asymmetric deprotonation followed by reverse aza-Brook rearrangement (Scheme 1, eq. 1).[7] Other approaches have utilized Davis' or Ellman's chiral auxiliary-protected aldimines in conjunction

with silyllithium reagents (eq. 2).[3,8] Recently, Oestreich reported an elegant process catalyzed by a chiral N-heterocyclic carbene-Cu complex using Suginome's $Ph(Me)_2SiBpin$ reagent (eq. 3).[8f] However, these methods have limitations with respect to the scope of the amine, and, with the exception of Oesterich's report, require the use of a stoichiometric chiral auxiliary or reagent.

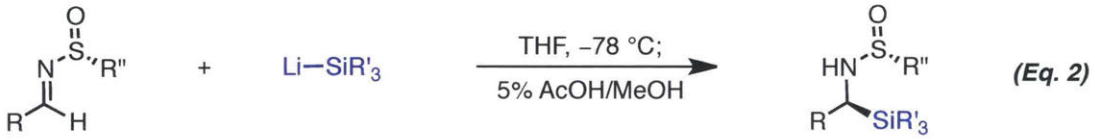
Scheme 1. Previous Approaches Towards the Synthesis of Chiral α-Aminosilanes

Reverse aza-Brook Rearrangement Approach: *Voyer, Sieburth*



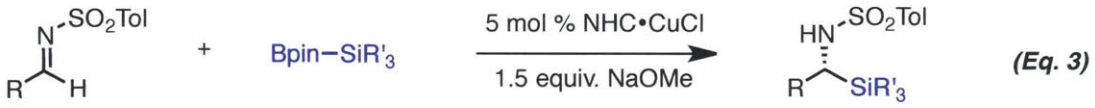
(Eq. 1)

Chiral Auxiliary Approach: *Scheidt, Skrydstrup, Sieburth*



(Eq. 2)

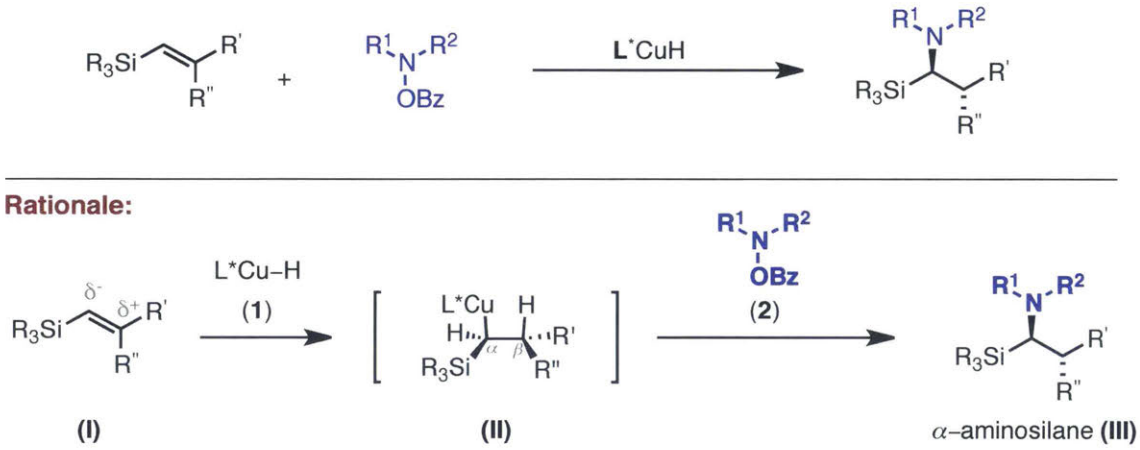
Cu-catalyzed Approach: *Oestreich*



(Eq. 3)

Recently, we developed the copper-catalyzed asymmetric Markovnikov hydroamination of styrenes.[9] We felt that this methodology applied to vinylsilanes substrates would allow for the generation of a broad range of chiral α-aminosilanes (Scheme 2). As vinylsilanes are readily prepared and bench stable, they are attractive as starting materials for the synthesis of α-aminosilanes.[10] We proposed that the intermolecular hydroamination of vinylsilanes would proceed regioselectively to give chiral α-aminosilanes (**III**) via the α-silyl alkylcopper intermediate **II** (Scheme 2) based on literature precedent.[11] Subsequent reaction with *O*-benzoyl hydroxylamine electrophile **2** would provide the desired α-aminosilane (**III**).[9]

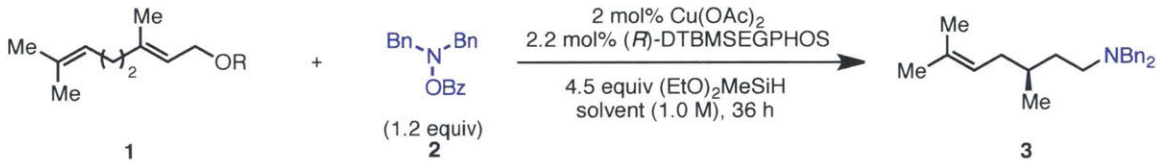
Scheme 2. Our Strategy Towards the Synthesis of Chiral α-Aminosilanes and the Regioselectivity Rationale



3.2 Results and Discussion

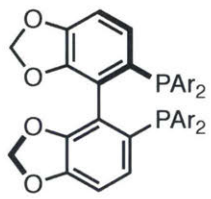
We began our investigation by examining the hydroamination of (*E*)-triethylsilylvinylsilane **1a** using conditions previously developed for the hydroamination of styrene (Table 1).[9] The reaction regioselectively furnished α-aminosilane **3a** in quantitative yield with >99% ee after 8 h (entry 1). Switching the solvent to cyclohexane, diethyl ether, or toluene (entries 2–4) had no effect, but no conversion was seen in dichloromethane (entry 5). We also examined other chiral ligands that were previously shown to be effective in reactions mediated by a copper(I)hydride complex (entries 6–8).[17] However, the use of (*R*)-DTBM-SEGPHOS was found to give the highest reactivity and selectivity.

Table 1. *Reaction Optimization*[a]

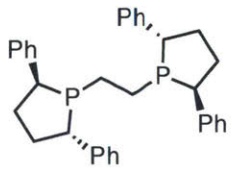


1 2 3

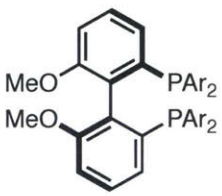
Entry	Solvent	L	Yield 3a [%][b]	ee [%][c]
1	THF	L1	>99	>99
2	cyclohexane	L1	>99	>99
3	Et_2O	L1	>99	>99
4	toluene	L1	>99	>99
5	CH_2Cl_2	L1	0[e,f,g]	-
6	THF	L2	37[f]	95
7	THF	L3	92[d]	98
8[c]	THF	L4	0[e,f,h]	-



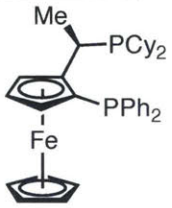
Ar = 3,5-*t*-Bu-4-MeOC_6H_2
(*R*)-DTBM-SEGPHOS (**L1**)



(*S,S*)-Ph-BPE
(**L2**)



Ar = 3,5-*t*-Bu-C_6H_4
(*S*)-3,5-*t*-Bu-MeO-BIPHEP (**L3**)

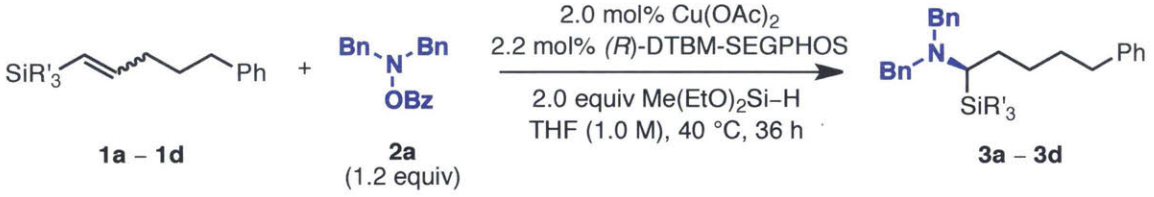


(*R,S*)-Josiphos
(**L4**)

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), $Cu(OAc)_2$ (0.02 mmol), Ligand (0.022 mmol), solvent (1 mL). [b]Isolated yields. [c]Determined by chiral HPLC analysis. [d]16 h. [e]Yield determined by GC (dodecane as an internal standard). [f]36 h. [g]77% of **1a** remained. [h]96% of **1a** remained.

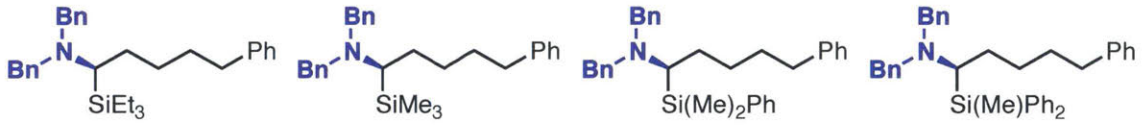
We next investigated the influence of the nature of the silyl group and olefin geometry on reactivity and enantioselectivity (Table 2). The reaction was compatible with vinylsilanes containing triethylsilyl (**3a**), trimethylsilyl (**3b**), dimethylphenylsilyl (**3c**), and methyldiphenylsilyl groups (**3d**).[18] In all cases, the reactions proceeded regioselectively to give α-aminosilane products. Interestingly, we found: 1) both *(E)* and (*Z*)-isomers provided the same enantiomeric product, and 2) (*E*) substrates invariably reacted faster and with a higher level of enantioselectivity than the corresponding (*Z*) substrates.

Table 2. *Influence of the Silyl Group and Olefin Geometry on Yield and Enantioselectivity*[a]



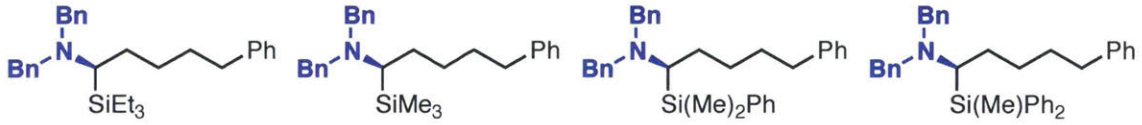
1a – 1d | **2a** (1.2 equiv) | **3a – 3d**

■ *(Z)*-Vinylsilanes



3a[b] 80% yield, 93% *ee* | **3b** 99% yield, 92% *ee* | **3c** 80% yield, 93% *ee* | **3d**[d] 84% yield, 84% *ee*

■ *(E)*-Vinylsilanes



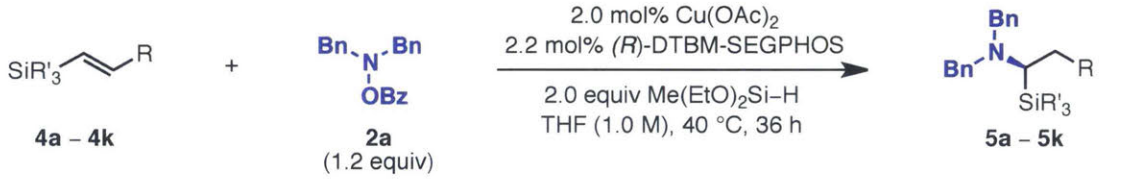
3a[c] 99% yield, >99% *ee* | **3b**[c] 90% yield, 99% *ee* | **3c** 92% yield, 99% *ee* | **3d** 86% yield, 99% *ee*

[a]Reaction conditions: **1a – 1d** (1 mmol), **2a** (1.2 mmol), $Cu(OAc)_2$ (0.02 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs). [b]$Cu(OAc)_2$ (0.04 mmol), (*R*)-DTBM-SEGPHOS (0.044 mmol). [c]8 h. [d]$Cu(OAc)_2$ (0.04 mmol), (*R*)-DTBM-SEGPHOS (0.044 mmol), THF (0.5 mL, 2 M).

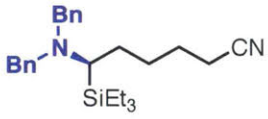
Thus, we chose to examine the scope of the hydroamination of *E*-vinylsilanes. This method accommodates a broad range of functional groups (Table 3). Vinylsilanes containing a nitrile

(**5a**), an alkyl chloride (**5b**), an ester (**5c**), a sulfonamide (**5d**), a *t*-butyldimethylsilyl ether (**5e**), and an allylic ether moiety (**5f**) were readily handled. Minor competitive elimination of alkoxide was observed with ether **5f.**[19] Additionally, we applied our method to the synthesis of α-amino acid mimics by hydroamination of 2° benzylamine **5i**, β-disubstituted vinylsilane **5j**, and β-isopropyl-substituted vinylsilane **5k**, to provide mimics of lysine, valine, and leucine, respectively.

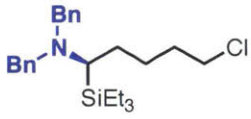
Table 3. *Hydroamination of (E)-Vinylsilanes*[a]



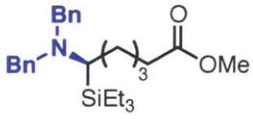
■ Vinyl Triethylsilanes



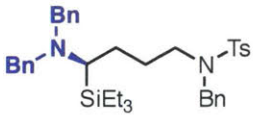
5a[b]
73% yield, 99% *ee*



5b
96% yield, >99% *ee*

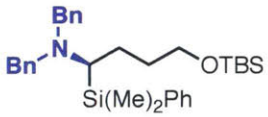


5c
80% yield, 99% *ee*



5d[c]
98% yield, 99% *ee*

■ Vinyl Dimethylphenylsilanes



5e
96% yield, 96% *ee*

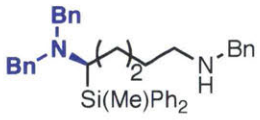
5f[c]
90% yield, 99% *ee*

5g
99% yield, 98% *ee*
98% yield, 89% *ee*[d]

5h[c]
90% yield, 92% *ee*

■ Vinyl Diphenylmethylsilanes

Chiral amino acid analogues:



5i[c]
92% yield, 93% *ee*
lysine mimic

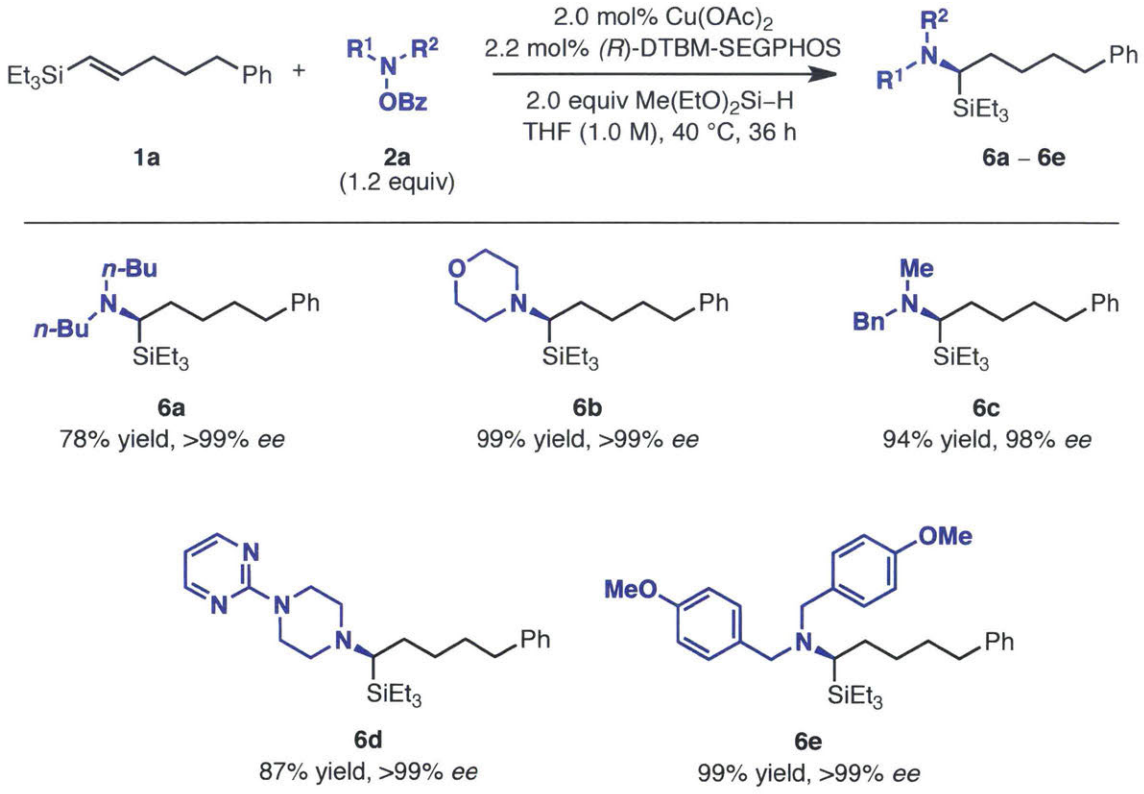
5j[c]
74% yield, 99% *ee*
valine mimic

5k
99% yield, 94% *ee*
leucine mimic

[a]Reaction conditions: **4a – 4k** (1 mmol), **2a** (1.2 mmol), $Cu(OAc)_2$ (0.02 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs). [b]16h reaction time. [c]$Cu(OAc)_2$ (0.04 mmol), (*R*)-DTBM-SEGPHOS (0.044 mmol), THF (1 mL, 1 M). [d]From (*Z*)-**4g**.

The compatibility of this reaction with a variety of *O*-benzoyl hydroxylamine electrophiles was then examined (Table 4). Acyclic dialkyl (**6a**), cyclic dialkyl (**6b**), and alkylbenzylamine-based electrophiles (**6c**) were all suitable partners, delivering the hydroaminated products with high yields and enantioselectivities. In addition, a heterocycle-containing electrophile was also tolerated (**6d**). Hydroamination to install a bis(*p*-methoxybenzyl)amino group was also successful (**6e**).

Table 4. *Scope of O-Benzoyl Hydroxylamine Electrophiles*[a]

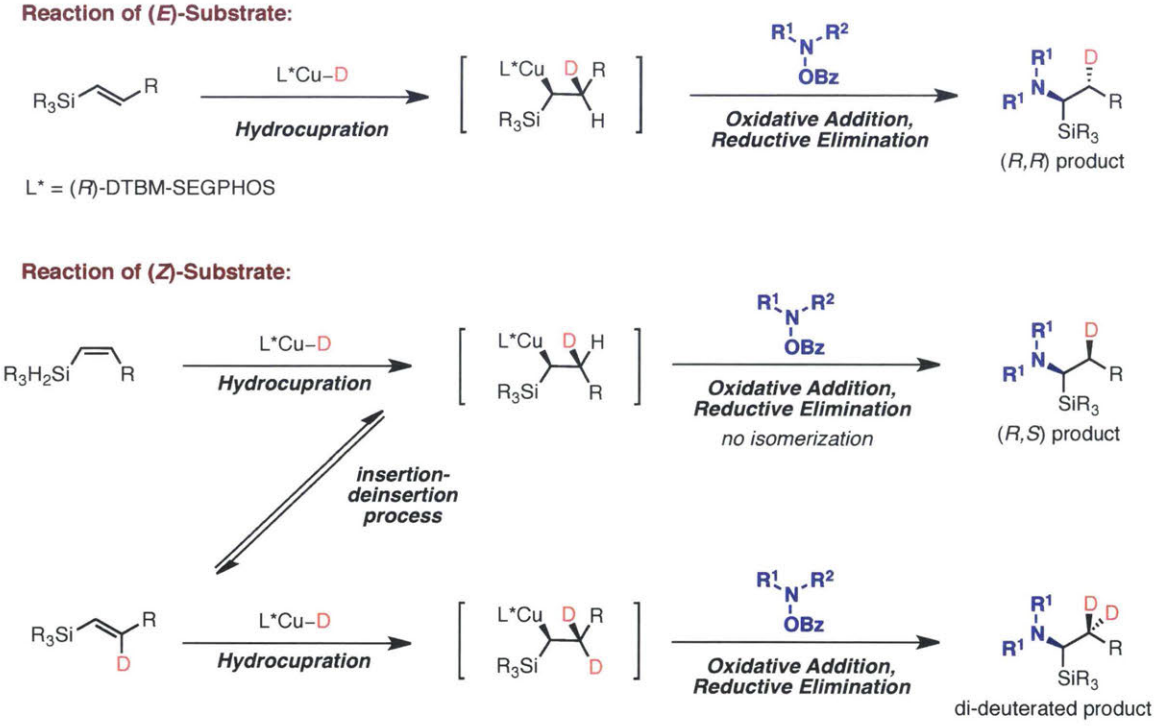


[a]Reaction conditions: **1a** (1 mmol), **2a** (1.2 mmol), $Cu(OAc)_2$ (0.02 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs).

As previously mentioned (Table 2), both (*E*) and (*Z*) substrates provide product that is the same enantiomer. However, (*E*) substrates react faster and afford a higher level of enantioselectivity than the corresponding (*Z*) substrates. We thus wondered whether, in the case of (*Z*)-alkenes, most of the hydroamination product was formed by isomerization of the slower

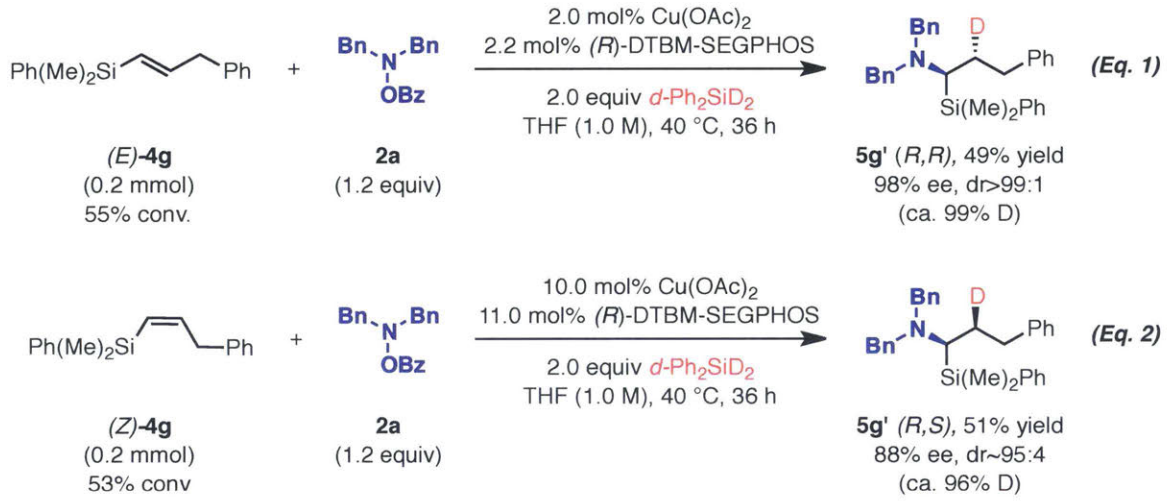
reacting (*Z*)-isomer, followed by transformation of the nascent *(E)*-isomer. We investigated this possibility through the use of a deuterated silane reagent. In this case, L*Cu–D would form and the olefin would insert into it via a *syn*-addition process (Scheme 3). For the more reactive (*E*)-substrate, subsequent reaction with the *O*-benzoyl hydroxylamine would generate the (*R*,*R*) product. For the (*Z*)-substrate, if no isomerization occurs, the reaction should generate the (*R*,*S*) product. However, if the (*Z*)-substrate undergoes Cu-catalyzed isomerization to the (*E*)- alkene prior to hydroamination, the major product would contain approximately 2 deuteria.

Scheme 3. *Possible Reaction Pathways*



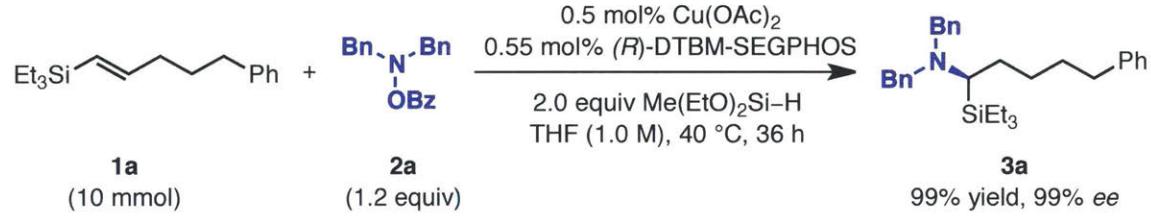
Deuterium-labelling experiments (Scheme 4) revealed that the hydroamination of (*E*)-**4g** was completely diastereoselective with ca. 99% deuterium incorporation[20] to give the mono-deuterated *(R,R)*-isomer **5g'** (eq. 1). For the (*Z*)-**4g**, the reaction was also diastereoselective to give the mono-deuterated *(R,S)*-isomer **5g'** with ca. 96% deuterium incorporation (eq. 2).[20] The stereochemical result and the presence of the mono-deuterated product from the (*Z*)-substrate indicates that most of the product does not formed via isomerization of the substrate to the (*E*)-isomer.

Scheme 4. *Deuterium-labeling Experiments*



Lastly, to demonstrate the scalability of this transformation, we carried out the hydroamination of **1a** with *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**) on a 10 mmol scale (Scheme 5). Full conversion of the vinylsilane was achieved with a catalyst loading of only 0.5 mol%. The yield and the enantioselectivity was the same as for the 1 mmol scale reaction (Table 1).

Scheme 4. *Large-Scale Hydroamination Reaction of (E)-Triethylsilylvinylsilane*



3.3Conclusion

In summary, we have developed an enantioselective Cu-catalyzed hydroamination of vinylsilanes. The reaction proceeds in a regioselective manner to provide enantioenriched α-aminosilanes in high yield with outstanding levels of enantioselectivity. The method is applicable to a variety of substrates, and provides rapid access to a family of valuable chiral organosilicon building blocks and bioactive molecules.

3.4 Experimental

I. General Information

General Reagent Information

Unless otherwise stated, all reactions were set up on the bench top and carried out under an argon atmosphere. Anhydrous cyclohexane was purchased from Sigma-Aldrich in Sure-Seal bottles and used as received. All other solvents were purified and dried by passage through successive alumina and Q5 reactant-packed columns on a solvent purification system. Diethoxymethylsilane was purchased from TCI America and stored under nitrogen at 4 °C in a Schlenk flask (diethoxymethylsilane is moisture sensitive, and proper Schlenk technique was used for handling this reagent). Diphenyl(silane-d_2) was purchased from Sigma-Aldrich and was stored and used in the nitrogen-filled glovebox. Other silane reagents, alkynes, benzoyl peroxide, amines, platinum dichloride, copper(II)acetate, and bases (MeLi and Na_2CO_3) were purchased from Frontier Scientific, Combi-Blocks, GFS chemicals, Ark Pharm, Alfa Aesar, Sigma-Aldrich, or Strem Chemicals, and were used as received. DTBM-SEGPHOS (**L1**) was purchased from Takasago. Ligands **L2 – L4** were purchased from Strem Chemicals. Compounds were purified using Silicycle SiliaFlashP60 (230-400 mesh) silica gel on a Biotage SP4 instrument.

General Analytical Information

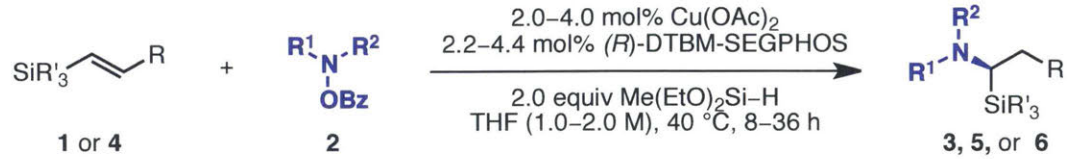
All compounds (starting materials and products) were characterized by ^{1}H NMR, ^{13}C NMR, IR spectroscopy, melting point (where applicable), and elemental analysis or high-resolution mass spectrometry. ^{1}H and ^{13}C NMR spectra were recorded on Varian 300 MHz or Bruker 400 MHz spectrometers. The spectra were calibrated according to residual solvent peaks ($CDCl_3$: δ 7.26 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR). The ^{13}C NMR spectra were obtained with ^{1}H decoupling. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, and m= multiplet. IR spectra were obtained on a Thermo Scientific iD5 ATR Nicolet iS5 FT-IR spectrometer. Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, GA. ESI-MS spectra were recorded on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic (GC) analyses were performed

on an Agilent 7890A instrument (FID detector) using a J&W DB-1 column (10m, 0.1 mm I.D.). Reactions were monitored by GC analysis and thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) or Fluka aluminum oxide/TLC-cards using UV light as a visualizing agent. High pressure liquid chromatography (HPLC) was performed on Hewlett-Packard 1100 Series using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL. The yields reported for the CuH-catalyzed hydroamination of vinylsilanes are of isolated compounds and are the average of at least two experiments.

II. Experimental Procedures and Characterization Data

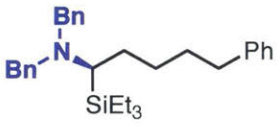
A) Cu-Catalyzed Hydroamination of Vinylsilanes

General Procedure for Cu-Catalyzed Hydroamination of Vinylsilanes:



1 or **4** **2** **3, 5,** or **6**

To an oven-dried test tube equipped with a magnetic stir bar was added $Cu(OAc)_2$ (2.0–4.0 mol%) and (*R*)-DTBM-SEGPHOS (2.2–4.4 mol%). The tube was sealed with a teflon-lined screw cap and evacuated and backfilled with argon (this process was repeated a total of 3 times). Anhydrous THF (1.0–2.0 mL) was added, and the mixture was stirred for 10 min, at which time diethoxymethylsilane (320 μL, 2.0 mmol, 2.0 equiv) was added and the stirring was continued for another 15 min at rt. Into a separate oven-dried test tube was added vinylsilane (1.0 mmol, 1.0 equiv) and *O*-benzoyl hydroxylamine (1.2 mmol, 2 equiv). The tube was sealed with a teflon-line screw cap and evacuated and backfilled with argon (this process was repeated a total of 3 times). The catalyst solution was then transferred via syringe to the reaction tube containing the substrates, and the reaction mixture was stirred at 40 °C for up to 36 h. Dodecane (100 μL) was added as the internal standard for GC analysis. The reaction mixture was quenched with saturated aqueous Na_2CO_3 solution, extracted with EtOAc, dried over Na_2SO_4, filtered through a pad of silica, concentrated, and purified by column chromatography on silica gel.



3a

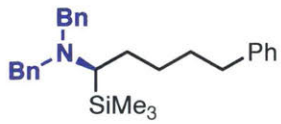
(*R*)-*N*,*N*-dibenzyl-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 2, entry **3a**)**:** From **(*Z*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*Z*)-**1a**) (261 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (7.3 mg, 0.04 mmol, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 0.044 mmol, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **3a** as a clear colorless oil (run 1: 375 mg (82%); run 2: 358 mg (78%);

average yield: 80%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 93% ee: t_R (minor) = 6.4 min, t_R (major) = 6.9 min.

From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (261 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 8 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **3a** as a clear colorless oil (run 1: 456 mg (99%); 452 mg (99%); average yield: 99%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (minor) = 6.4 min, t_R (major) = 6.9 min. $[\alpha]_D^{24} = -0.1$ (c = 1.0, $CHCl_3$).

From Scheme 3, 10 mmol scale: From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (2.60 g, 10.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (9.1 mg, 0.005 mmol, 0.5 mol%), (*R*)-DTBM-SEGPHOS (65 mg, 0.0055 mmol, 0.55 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (3.81 g, 12.0 mmol). The reaction mixture was stirred in THF (10 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **3a** as a clear colorless oil (4.57 g, 99% yield). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (minor) = 6.4 min, t_R (major) = 6.9 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 10H), 7.23 – 7.16 (m, 5H), 3.62 (s, 4H), 2.60 – 2.57 (t, *J* = 7.2 Hz, 2H), 2.33 – 2.30 (t, *J* = 5.2 Hz, 1H), 1.84 – 1.77 (m, 1H), 1.56 – 1.23 (m, 5H) 0.91 – 0.87 (t, *J* = 8.0 Hz, 9H), 0.91 – 0.87 (t, *J* = 8.0 Hz, 9H), 0.71 – 0.54 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.7, 140.7, 129.0, 128.4, 128.2, 128.3, 126.6, 125.6, 56.6, 47.3, 35.9, 31.7, 28.9, 26.1, 7.8, 3.9. **IR** (neat, cm^{-1}): 3025, 2933, 2873, 1739, 1494, 1453, 136. Anal. Calcd. for $C_{31}H_{43}NSi$: C, 81.34; H, 9.47 Found: C, 81.10; H, 9.71.



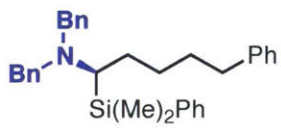
3b

(*R*)-*N*,*N*-dibenzyl-5-phenyl-1-(trimethylsilyl)pentan-1-amine (Table 2, entry **3b**)**:** From **(*Z*)-trimethyl(5-phenylpent-1-en-1-**

yl)silane ((Z)-**1b**) (218 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–3% EtOAc in hexanes) to afford **3b** as a clear colorless oil (run 1: 411 mg (99%); run 2: 411 mg (99%); average yield: 99%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (minor) = 5.4 min, t_R (major) = 6.5 min.

From **(*E*)-trimethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1b**) (207 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 8 h. The crude product was purified by flash column chromatography (0–3% EtOAc in hexanes) to afford **3b** as a clear colorless oil (run 1: 369 mg (89%); run 2: 373 mg (90%); average run: 90%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 5.4 min, t_R (major) = 6.5 min. $[\alpha]_D^{24} = -4.2$ (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.47 (dd, *J* = 6.8, 10.2 Hz, 4H), 7.44 – 7.92 (m, 2H), 7.67 – 7.40 (m, 6H), 7.36 – 7.28 (m, 5H), 3.79 (s, 1H), 2.73 – 2.70 (t, *J* = 8.0 Hz, 2H), 2.32 – 2.28 (t, *J* = 6.0 Hz, 1H), 1.94 – 1.90 (m, 2H), 1.67 – 1.42 (m, 5H), 0.22 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.7, 140.8, 128.8, 128.4, 128.2, 128.1, 126.6, 125.6, 56.4, 49.7, 35.9, 31.6, 28.6, 26.0, -0.4. **IR** (neat, cm^{-1}): 3084, 3062, 3025, 2928, 2854, 1737, 1602, 1494, 1453, 1361, 1260, 1247, 832, 743, 696. Anal. Calcd. for $C_{28}H_{37}NSi$: C, 80.90; H, 8.97 Found: C, 80.80; H, 9.06.



3c

(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-5-phenylpentan-1-amine (Table 2, entry **3c**)**:** From **(*Z*)-dimethyl(phenyl)(5-phenylpent-1-en-1-yl)silane** ((*Z*)-**1c**) (280 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-

N,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **3c** as a clear colorless oil (run 1: 354 mg (78%); run 2: 380 mg (82%); average yield: 80%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 93% ee: t_R (minor) = 8.0 min, t_R (major) = 9.0 min.

From **(*E*)-dimethyl(phenyl)(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1c**) (280 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **3c** as a clear colorless oil (run 1: 422 mg (88%); 453 mg (95%); average yield 92%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 8.0 min, t_R (major) = 9.0 min. $[\alpha]_D^{24} = -13.0$ (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.5 – 7.42 (m, 2H), 7.33 – 7.19 (m, 16H), 7.11 – 7.09 (dd, *J* = 7.6, 1.6 Hz, 2H), 3.60 (s, 4H), 2.49 – 2.45 (t, *J* = 8.4 Hz, 2H), 2.43 – 2.40 (t, *J* = 5.2 Hz, 1H), 1.78 – 1.76 (m, 1H), 1.46 – 1.36 (m, 4H), 1.19 – 1.17 (m, 1H), 0.38 (d, *J* = 2.8 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.7, 140.6, 134.0, 128.9, 128.8, 128.4, 128.2, 128.0, 127.7, 126.7, 125.5, 56.3, 49.5, 35.8, 31.4, 28.4, 26.0, -1.6, -2.7. **IR** (neat, cm^{-1}): 3062, 3024, 2928, 2854, 1739, 1602, 1494, 1453, 1427, 1365, 1246, 1229, 1217, 1108, 830, 806, 732, 695. Anal. Calcd. for $C_{33}H_{39}NSi$: C, 82.96; H, 8.23 Found: C, 82.77; H, 8.19.

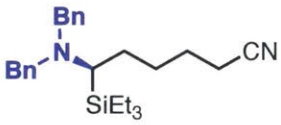
3d

(*R*)-*N*,*N*-dibenzyl-1-(methyldiphenylsilyl)-5-phenylpentan-1-amine (Table 2, entry **3d**)**:** From **(*Z*)-methyldiphenyl(5-phenylpent-1-en-1-yl)silane** ((Z)-**1d**) (342 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (7.3 mg, 0.04 mmol, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 0.044 mmol, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (0.5 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5%

EtOAc in hexanes) to afford **3d** as a clear colorless oil (run 1: 448 mg (83%); 453 mg (84%); average yield: 84%). HPLC analysis (OT-(+), 1% IPA/hexanes, 0.8 mL/min, 220 nm) indicated 84% ee: t_R (minor) = 8 min, t_R (major) = 10 min.

From **(*E*)-methyldiphenyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1d**) (342 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **3d** as a clear colorless oil (run 1: 456 mg (84%); run 2: 472 mg (87%); average yield: 86%). HPLC analysis (OT-(+), 1% IPA/hexanes, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 8 min, t_R (major) = 10 min. $[\alpha]_D^{23}$ = +6.5 (c = 2.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.53 (dt, *J* = 6.0, 1.6 Hz, 2H), 7.50 –7.48 (dt, *J* = 6.4, 1.6 Hz, 2H), 7.42 – 7.23 (m, 19H), 7.15 – 7.12 (dd, *J* = 8.0, 0.8 Hz, 2H), 3.65 (s, 4H), 3.02 – 2.98 (t, *J* = 7.2 Hz, 1H), 2.53 – 2.47 (td, *J* = 7.4, 2.8 Hz, 2H), 1.96 – 1.91 (m, 1H), 1.61 – 1.59 (m, 1H), 1.50 – 1.40 (m, 3H), 1.28 – 1.21 (m, 1H), 0.78 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.6, 140.4, 137.7, 136.8, 134.9, 134.8, 129.1, 129.0, 128.4, 128.1, 128.0, 127.8, 127.7, 126.7, 125.5, 56.3, 48.2, 35.7, 31.3, 28.4, 26.2, -3.2. **IR** (neat, cm^{-1}): 3024, 2927, 2854, 1739, 1494, 1453, 1427, 1365, 1229, 1217, 1104, 1027, 785, 734, 695. Anal. Calcd. for $C_{15}H_{16}NO_2$: C, 84.55; H, 7.66 Found: C, 84.78; H, 7.43.

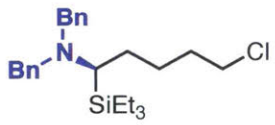


5a

(*R*)-6-(dibenzylamino)-6-(triethylsilyl)hexanenitrile (Table 3, entry **5a**)**:** From **(*E*)-6-(triethylsilyl)hex-5-enenitrile** (209 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (25.9 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 16 h. The crude product was purified by flash column chromatography (5% EtOAc in hexanes) to afford **5a** as a clear colorless oil (run 1: 312 mg (77%); run 2: 282 mg (69%); average yield: 73%). HPLC analysis

(OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 16.0 min, t_R (major) = 18.3 min. $[\alpha]_D^{24} = -28.8$ (c = 2.0, $CHCl_3$).

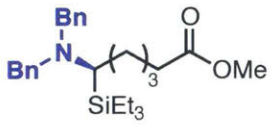
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 8H), 7.25 – 7.20 (m, 2H), 3.69 – 3.58 (d, *J* = 13.2, 14.8 Hz, 4H), 2.33 – 2.30 (dd, *J* = 4.8, 4.0 Hz, 1H), 2.22 – 2.18 (t, *J* = 6.8 Hz, 2H), 1.78 – 1.76 (m, 1H), 1.55 – 1.28 (m, 5H), 0.96 – 0.92 (t, *J* = 8.0 Hz, 9H), 0.91 – 0.87 (t, *J* = 8.0 Hz, 9H), 0.77 – 0.61 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.5, 129.0, 128.1, 126.8, 119.7, 56.7, 46.6, 27.7, 26.3, 25.2, 17.1, 7.8, 4.1. **IR** (neat, cm^{-1}): 2949, 2873, 1493, 1453, 1418, 1360, 1239, 1109, 1004, 722, 697. Anal. Calcd. for $C_{26}H_{38}N_2Si$: C, 76.79; H, 9.42 Found: C, 77.18; H, 9.06.



5b

(*R*)-*N*,*N*-dibenzyl-5-chloro-1-(triethylsilyl)pentan-1-amine (Table 3, entry **5b**)**:** From **(*E*)-(5-chloropent-1-en-1-yl)triethylsilane** (209 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5b** as a clear colorless oil (run 1: 391 mg (94%); run 2: 410 mg (98%); average yield 96%). SFC analysis[21] (Chiralpak IC(4.6x150 mm, 3μm), isocratic 3% EtOH) indicated >99% ee: t_R (minor) = 1.15 minute, t_R (major) = 1.28 min. $[\alpha]_D^{24} = -18.5$ (c = 1.0, $CHCl_3$).

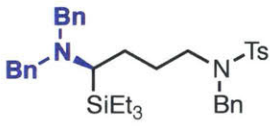
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.42 (dd, *J* = 6.4, 1.6 Hz, 4H), 7.39 – 7.35 (tt, *J* = 7.2, 1.6 Hz, 4H), 7.31 – 7.26 (tt, *J* = 7.2, 1.6 Hz, 2H), 3.71 (s, 4H), 3.54 – 3.51 (t, *J* = 5.6 Hz, 2H), 2.41 – 2.38 (dd, *J* = 8.0, 5.6 Hz, 1H), 1.90 – 1.82 (m, 1H), 1.72 – 1.56 (m, 3H), 1.49 – 1.37 (m, 2H), 1.01 – 0.97 (t, *J* = 8.0 Hz, 9H), 0.84 – 0.65 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.6, 129.0, 128.1, 126.7, 56.6, 47.0, 45.0, 32.6, 26.2, 25.8, 7.8, 4.0. **IR** (neat, cm^{-1}): 2952, 2873, 1494, 1453, 1359, 1104, 1027. 1003, 725, 653. Anal. Calcd. for $C_{25}H_{38}ClNSi$: C, 72.16; H, 9.20 Found: C, 72.13; H, 9.21.



5c

(*R*)-*N*,*N*-dibenzyl-5-chloro-1-(triethylsilyl)pentan-1-amine (Table 3, entry **5c**): From **(*E*)-methyl 6-(triethylsilyl)hex-5-enoate** (242 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5c** as a clear colorless oil (run 1: 343 mg (78%); run 2: 360 mg (82%); average yield: 80%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 7.4 min, t_R (major) = 7.9 min. $[\alpha]_D^{24} = -9.3$ (c = 2.0, $CHCl_3$).

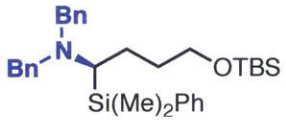
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.34 (m, 8H), 7.24 – 7.20 (tt, *J* = 7.2, 1.6 Hz, 2H), 3.69 (s, 3H), 3.63 (s, 4H), 2.33 – 2.26 (m, 3H), 1.81 – 1.76 (m, 1H), 1.60 – 1.21 (m, 5H), 0.93 – 0.89 (t, *J* = 8.0 Hz, 9H), 0.74 – 0.57 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.2, 140.6, 129.0, 128.0, 126.7, 56.6, 51.4, 47.2, 34.1, 28.7, 26.0, 25.2, 7.8, 3.9. **IR** (neat, cm^{-1}): 2950, 2874, 1739, 1494, 1453, 1360, 1168, 1075, 966, 827, 726, 697. HRMS (DART-TOF) calculated for $C_{27}H_{41}NO_2Si$ $[M+H]^+$ m/z 440.2979, found 440.2992.



5d

(*R*)-*N*-benzyl-*N*-(4-(dibenzylamino)-4-(triethylsilyl)butyl)-4-methylbenzenesulfonamide (Table 3, entry **5d**)**:** From **(*E*)-*N*-benzyl-4-methyl-*N*-(4-(triethylsilyl)but-3-en-1-yl)benzene sulfonamide** ((*E*)-**1h**) (430 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (7.3 mg, 0.04 mmol, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 0.044 mmol, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5d** as a clear colorless oil (run 1: 606 mg (97%); run 2: 624 mg (99%); average yield: 98%). HPLC analysis (OD-H, 5% IPA/pentane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 15.7 min, t_R (major) = 18.0 min. $[\alpha]_D^{24} = -7.2$ (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.72 (dt, *J* = 10.8, 3.2 Hz, 2H), 7.40 – 7.18 (m, 16H), 4.30 (s, 2H), 3.57 – 3.40 (dd, *J* = 30.4, 18.0 Hz, 2H), 3.11 – 2.96 (m, 2H), 2.43 (s, 3H), 2.14 – 2.10 (t, *J* = 8.0 Hz, 1H), 1.55 – 1.39 (m, 2H), 0.85 – 0.80 (t, *J* = 10.4 Hz, 9H), 0.63 – 0.43 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.1, 140.4, 137.2, 136.6, 129.7, 128.9, 128.5, 128.2, 128.0, 127.7, 127.1, 126.7, 56.4, 51.9, 48.6, 47.3, 28.0, 23.4, 21.5, 7.7, 3.7. **IR** (neat, cm^{-1}): 3026, 2949, 2873, 1599, 1494, 1453, 1340, 1158, 1092, 1027, 1010, 814, 726, 696, 656. Anal. Calcd. for $C_{38}H_{50}N_2O_2SSi$: C, 72.80; H, 8.04 Found: C, 72.77; H, 7.90.



5e

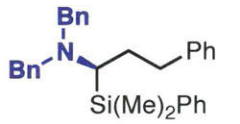
(*R*)-*N*,*N*-dibenzyl-4-((*tert*-butyldimethylsilyl)oxy)-1-(dimethyl (phenyl)silyl)butan-1-amine (Table 3, entry **5e**): From **(*E*)-*tert*-butyl((4-(dimethyl(phenyl)silyl)but-3-en-1-yl)oxy)dimethylsilane** (321 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5e** as a clear colorless oil (run 1: 503 mg (97%); run 2: 487 mg (94%); average yield: 96%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 96% ee: t_R (minor) = 5.0 min, t_R (major) = 5.5 min. $[\alpha]_D^{24} = -24.5$ (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.42 – 7.32 (m, 11H), 7.30 – 7.25 (m, 2H), 3.69 (s, 4H), 3.57 – 3.47 (m, 2H), 2.52 – 2.47 (td, *J* = 7.0, 2.0 Hz, 1H), 1.92 – 1.84 (m, 1H), 1.69 – 1.56 (m, 2H), 1.47 – 1.37 (m, 1H), 0.97 (s, 9H), 0.48 (s, 6H), 0.09 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.5, 139.3, 134.0, 128.9, 128.8, 128.0, 127.7, 126.7, 63.0, 56.3, 49.4, 32.3, 26.0, 22.3, 18.3, -1.6, -2.5, -5.6. **IR** (neat, cm^{-1}): 2927, 2855, 1494. 1453, 1248, 1096, 1027, 807, 227. 732, 696. Anal. Calcd. for $C_{32}H_{47}NOSi_2$: C, 74.21; H, 9.15 Found: C, 73.94; H, 9.25.

5f

(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-3-methoxypropan-1-amine (Table 3, entry **5f**): From **(*E*)-(3-methoxyprop-1-en-1-yl)dimethyl(phenyl)silane** (206 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (7.3 mg, 0.04 mmol, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 0.044 mmol, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (0.5 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (5–10% EtOAc in hexanes) to afford **5f** as a clear colorless oil (run 1: 366 mg (91%); run 2: 354 mg (88%); average yield: 90%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 6.2 min, t_R (major) = 7.5 min. $[\alpha]_D^{24}$ = –40.4 (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.48 (m, 2H), 7.39 – 7.22 (m, 13H), 3.63 (s, 4H), 3.43 – 3.80 (m, 1H), 3.20 (s, 3H), 3.20 – 3.15 (m, 1H), 2.58 – 2.54 (dd, *J* = 8.4, 5.6 Hz, 1H), 2.11 – 2.02 (m, 5H) 1.77 – 1.68 (m, 1H), 0.43 – 0.42 (d, *J* = 3.6 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.4, 138.9, 134.0, 128.9, 128.9, 128.0, 127.7, 126.7, 72.2, 58.3, 56.4, 46.6, 26.6, -1.9, -2.8. **IR** (neat, cm^{-1}): 2923, 1494, 1453, 1248, 1109, 807, 732, 696. HRMS (DART-TOF) calculated for $C_{26}H_{33}NOSi$ $[M+H]^+$ m/z 404.2404, found 404.2419.



5g

(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-amine (Table 3, entry **5g**): From **(*E*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane** (252 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5g** as a clear colorless oil (run 1: 444 mg (99%); run 2: 443 mg (99%); average yield: 99%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 6.1 min, t_R (major) = 8.9 min. $[\alpha]_D^{24}$ = +7.4 (c = 1.0, $CHCl_3$).

From **(*Z*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane** (252 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5g** as a clear colorless oil (run 1: 443 mg (98%); run 2: 436 mg (97%); average yield: 98%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 89% ee: t_R (minor) = 6.7 min, t_R (major) = 9.7 min. $[\alpha]_D^{24}$ = +5.4 (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H), 7.44 – 7.37 (m, 11H), 7.36 – 7.30 (m, 4H), 7.28 – 7.23 (m, 1H), 7.08 – 7.06 (dd, *J* = 8.0, 1.6 Hz, 2H), 3.75 (s, 4H), 2.80 – 2.72 (m, 1H), 2.63 – 2.60 (dd, *J* = 6.4, 1.2 Hz, 1H), 2.45 – 2.37 (m, 1H), 2.20 – 2.11 (m, 1H), 1.90 – 1.80 (m, 1H), 0.53 – 0.52 (d, *J* = 2.4 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.9, 140.5, 139.2, 134.0, 129.0, 128.9, 128.3, 128.3, 128.1, 127.8, 127.7, 126.7, 125.6, 56.4, 49.6, 35.3, 28.9, -1.6, -2.7. **IR** (neat, cm^{-1}): 3024, 1601, 1494, 1453, 1427, 1247, 1108, 1067, 1027, 806, 731, 694. HRMS (DART-TOF) calculated for $C_{31}H_{35}NSi$ $[M+H]^+$ m/z 450.2612, found 450.2631.

5h

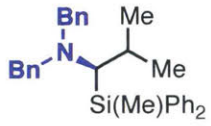
(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-2-(1-methoxycyclohexyl)ethanamine (Table 3, entry **5h**): From **(*E*)-(2-(1-methoxycyclohexyl)vinyl)dimethyl(phenyl)silane** (274 mg, 1.0 mmol,), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (7.2 mg, 0.04 mmol, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (0.5 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–20% EtOAc in hexanes) to afford **5h** as white solid (run 1: 415 mg (88%); run 2: 401 mg (85%); average yield: 86%); m.p. = 110–112 °C. HPLC analysis (OD-H, 90:5:0.1 Hexanes: IPA: Diethylamine, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (minor) = 7.4 min, t_R (major) = 7.9 min. $[\alpha]_D^{24}$ = –35.2 (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 2H), 7.39 – 7.32 (m, 11H), 7.30 – 7.44 (m, 2H), 3.81 – 3.60 (dd, J = 72.6, 13.2 Hz, 4H), 2.98 (s, 3H), 2.75 – 2.72 (dd, J = 7.8, 3.2 Hz, 1H), 1.99 – 1.93 (dd, J = 14.8, 7.62 Hz, 1H), 1.59 – 1.36 (m, 5H), 1.32 – 1.25 (m, 3H) 1.20 – 1.13 (td, J = 12.2, 3.6 Hz, 1H), 0.98 – 0.83 (m, 2H), 0.53 – 0.51 (d, J = 9.2 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.3, 139.7, 134.1, 129.3, 128.7, 128.0, 127.7, 126.7, 76.0, 56.7, 47.6, 45.8, 34.3, 33.5, 32.5, 25.3, 22.0, 21.9, -0.4, -2.2. **IR** (neat, cm^{-1}): 2945, 2856, 1491, 1453, 1244, 1070, 806, 796, 745, 732, 697. HRMS (DART-TOF) calculated for $C_{31}H_{41}NOSi$ $[M+H]^+$ m/z 472.3030, found 472.3024.

5i

(*R*)-N^1,N^1,N^5-tribenzyl-1-(methyldiphenylsilyl)pentane-1,5-diamine (Table 3, entry **5i**): From **(*E*)-*N*-benzyl-5-(methyldiphenylsilyl)pent-4-en-1-amine** (372 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (7.2 mg, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (0.5 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–20% EtOAc in hexanes) to afford **5i** as a yellow oil (run 1: 542 mg (95%); run 2: 507 mg (89%); average yield: 92%). HPLC analysis (OD-H, 90:5:0.1 Hexanes: IPA: Diethylamine, 0.8 mL/min, 220 nm) indicated 93% ee: t_R (major) = 12.3 min, t_R (minor) = 13.5 min. $[\alpha]_D^{24}$ = +0.2 (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 2H), 7.37 – 7.34 (m, 2H), 7.36 – 7.34 (m, 21H), 3.63 (s, 2H), 3.51 (s, 4H), 2.87 – 2.84 (dd, J = 7.4, 6.0 Hz, 1H), 2.37 – 2.33 (t, J = 6.4 Hz, 2H), 1.82 – 1.74 (m, 1H), 1.50 – 1.40 (m, 1H), 1.25 – 1.05 (m, 4H), 0.66 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.4, 137.6, 136.8, 134.9, 134.8, 129.18, 129.0, 128.3, 128.1, 128. 0, 127.8, 127.7, 126.8, 126.7, 56.3, 54.0, 49.2, 48.1, 29.9, 26.4, 26.3, -3.2. **IR** (neat, cm^{-1}): 3024, 2923, 1601, 1493, 1455, 1427, 1106, 784, 733. Anal. Calcd. for $C_{39}H_{44}N_2Si$: C, 82.34; H, 7.80 Found: C, 82.08; H, 7.74.



5j

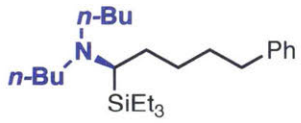
(*R*)-*N*,*N*-dibenzyl-2-methyl-1-(methyldiphenylsilyl)propan-1-amine (Table 3, entry **5j**): From **methyl(2-methylprop-1-en-1-yl)diphenylsilane** (274 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (7.2 mg, 0.04 mmol, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 0.044 mmol, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (0.5 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–3% EtOAc in hexanes) to afford **5j** as a clear colorless oil (run 1: 322 mg (72%); run 2: 339 mg (75%); average yield: 74%). HPLC analysis (OT(+), 1% IPA/Hexanes, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 6.7 min, t_R (major) = 9.3 min. $[\alpha]_D^{24} = -27.2$ (c = 1. 0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.57 (m, 4H), 7.42 – 7.26 (m, 16H), 3.86 – 3.75 (dd, *J* = 17.6, 13.6 Hz, 4H), 0.84 – 0.82 (d, *J* = 6.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.4, 138.8, 138.1, 135.2, 134.7, 129.3, 128.9, 128.8, 128.0, 127.76, 127.7, 126.7, 56.9, 55.1, 29.2, 23.4, 23.1, -1.8. **IR** (neat, cm^{-1}): 3024, 29545, 1601, 1493, 1453, 1427, 1254, 1103, 1068, 786, 728, 696, 2856, 1491, 1453, 1244, 1070, 806, 796, 745, 732, 697. HRMS (DART-TOF) calculated for $C_{31}H_{35}NSi$ $[M+H]^+$ m/z 450.2612, found 450.2592.

5k

(*R*)-*N*,*N*-dibenzyl-3-methyl-1-(methyldiphenylsilyl)butan-1-amine (Table 3, entry **5k**): From **(*E*)-methyl(3-methylbut-1-en-1-yl)diphenylsilane** (266 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–3% EtOAc in hexanes) to afford **5k** as colorless crystals (run 1: 462 mg (99%); run 2: 462 mg (99%); average yield: 99%); m.p. = 82–85 °C. HPLC analysis (OD-H, 97% Hexanes/ 3% of '97 Hexanes: 3 EtOH: 0.2 TFA: 0.1 DEA', 0.8 mL/min, 220 nm) indicated 94% *ee*: t_R (minor) = 5.4 min, t_R (major) = 5.9 min. $[\alpha]_D^{24} = -22.9$ (c = 1.0, $CHCl_3$).

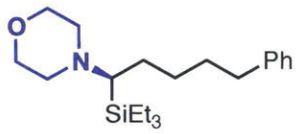
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.57 (dt, J = 5.6, 1.6 Hz, 2H), 7.55 – 7.52 (dt, J = 6.0, 1.6 Hz, 2H), 7.44 – 7.26 (m, 16H), 3.71 – 3.62(dd, J = 13.6, 6.4 Hz, 4H), 3.14 – 3.10 (dd, J = 6.0, 1.6 Hz, 1H), 1.82 – 1.66 (m, 2H), 1.40 – 1.34 (m, 1H), 0.84 (s, 3H), 0.81 – 0.80 (d, J = 6.8 Hz, 3H) 0.59 – 0.58 (d, J = 6.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.6, 137.9, 136.8, 134.9, 134.9, 129.1, 129.0, 129.0, 128.0, 127.8, 127.7, 126.7, 56.2, 45.9, 36.2, 25.3, 23.0, 22.1, -3.0. **IR** (neat, cm^{-1}): 3025, 2952, 1601, 1494, 1427, 1104, 1027, 784, 734, 724, 696. Anal. Calcd. for $C_{32}H_{37}NSi$: C, 82.88; H, 8.04 Found: C, 82.60; H, 8.11.



6a

(*R*)-*N*,*N*-dibutyl-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 4, entry **6a**)**:** From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (260 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibutylhydroxylamine (299 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **6a** as a clear colorless oil (run 1: 305 mg (78%); run 2: 303 mg (78%); average yield: 78%). HPLC analysis (3 connected OD-H columns, 97% Hexanes/ 3% of '92 Hexanes: 8 EtOH: 0.2 TFA: 0.1 DEA', 0.55 mL/min, 220 nm) indicated >99% ee: t_R (major) = 51 min, t_R (minor) = 54 min. $[\alpha]_D^{24}$ = –4.0 (c = 1.0, $CHCl_3$).

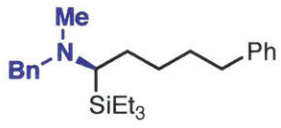
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.19 – 7.15 (m, 3H), 2.63 – 2.60 (t, J = 7.6 Hz, 2H), 2.46 – 2.35 (m, 4H), 2.25 – 2.22 (t, J = 5.2 Hz, 1H), 1.66 – 1.53 (m, 3H), 1.51– 1.46 (m, 1H), 1.39 – 1.23 (m, 10H), 0.98 – 0.94 (t, J = 8.0 Hz, 9H), 0.92 – 0.88 (t, J = 7.2 Hz, 6H), 0.66 – 0.53 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 128.48, 128.2, 125.5, 53.5, 36.0, 32.1, 31.9, 29.2, 27.1, 20.6, 14.2, 7.9, 4.0. **IR** (neat, cm^{-1}): 2953, 2928, 2872, 1496, 1453, 1076, 1010, 721, 697. HRMS (DART-TOF) calculated for $C_{25}H_{47}NSi$ $[M+H]^+$ m/z 390.3551, found 390.3534.



6b

(*R*)-4-(5-phenyl-1-(triethylsilyl)pentyl)morpholine (Table 4, entry **6b**)**:** From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (260 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and morpholino benzoate (249 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **6b** as a clear colorless oil (run 1: 347 mg (99%); run 2: 345 mg (99%); average yield: 99%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (minor) = 8.0 min, t_R (major) = 10.4 min. $[\alpha]_D^{24} = -7.4$ (c = 2.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.20 – 7.16 (m, 3H), 3.64 – 3.62 (t, *J* = 4.4 Hz, 4H), 2.68 – 2.53 (m, 4H), 2.59 – 2.53 (m, 2H), 2.10 – 2.07, (m, *J* = 8.8, 4.8 Hz, 1H), 1.74 – 1.57 (m, 2H), 1.55 – 1.45 (m, 1H), 1.42– 1.32 (m, 2H), 0.99 – 0.95 (t, *J* = 8.0 Hz, 9H), 0.64 – 0.56 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.7, 128.4, 128.2, 125.6, 67.8, 55.0, 52.2, 35.9, 31.7, 29.7, 26.4, 7.8, 3.9. **IR** (neat, cm^{-1}): 2950, 2873, 2850, 1496, 1453, 1415, 1117, 1001, 878, 715, 697. HRMS (DART-TOF) calculated for $C_{21}H_{37}NOSi$ $[M+H]^+$ m/z 348.2717, found 348.2727.

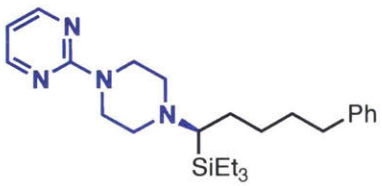


6c

(*R*)-*N*-benzyl-*N*-methyl-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 4, entry **6c**)**:** From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (260 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*-benzyl-*N*-methylhydroxylamine (290 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **6c** as a clear colorless oil in (run 1: 359 mg (94%); run 2: 359 mg (94%); average yield: 94%. $[\alpha]_D^{24} = -12.5$ (c = 2.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 6H), 7.26 – 7.18 (m, 4H), 3.69 – 3.68 (d, J = 4.0 Hz, 2H), 2.68 – 2.64 (t, J = 8.0 Hz, 2H), 2.33 – 2.30 (dd, J = 8.4, 5.2 Hz, 1H), 2.23 (s, 3H), 1.86 –1.76 (m, 1H), 1.68 –1.63 (m, 2H), 1.57 –1.54 (m, 1H), 1.47 –1.37 (m, 2H), 1.01 – 0.99 (t, J = 7.6 Hz, 9H), 0.73 – 0.58 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.8, 141.0, 128.5, 128.4, 128.2, 128.0, 126.5, 125.6, 61.6, 53.7, 40.1, 36.0, 31.9, 29.5, 26.4, 7.9, 4.0. **IR** (neat, cm^{-1}): 3026, 2932, 2873, 2784, 1739, 1494, 1453, 1365, 1229, 1217, 1119, 1006, 725, 696. Anal. Calcd. for $C_{25}H_{39}NSi$: C, 78.67; H, 10.30 Found: C, 78.54; H, 10.27.

This product was transformed into **(*R*)-*N*-methyl-*N*-(5-phenyl-1-(triethylsilyl)pentyl)acetamide** for chiral HPLC analysis using the following procedure. **6c** (76 mg, 0.2 mmol), $Pd(OH)_2$ on carbon (20 wt%, 76 mg), and acetic anhydride (1 mL) were added to a round bottom flask equipped with a stir bar. The flask was evacuated and backfilled with hydrogen (this process was repeated a total of 3 times) and stirred at rt overnight (~12 h) under a H_2 atmosphere (1 atm). The reaction mixture was filtered through a pad of Celite, then quenched with saturated aqueous Na_2CO_3 solution, extracted with EtOAc, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by preparative TLC (50% EtOAc in hexanes) to afford the title compound as a yellow oil (run 1: 50 mg (75%); run 2: 60 mg (90%); average yield: 82%). HPLC analysis (OD-H, 1% IPA/hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 13 min, t_R (major) = 15 min.

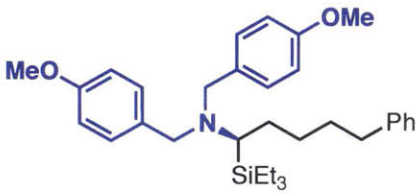


6d

(*R*)-2-(4-(5-phenyl-1-(triethylsilyl)pentyl)piperazin-1-yl)pyrimidine (Table 4, entry **6d**)**:** From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (260 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and 4-(pyrimidin-2-yl)piperazin-1-yl benzoate (**2b**) (341 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–10% EtOAc in hexanes) to afford **6d** as a clear colorless oil (run 1: 360 mg (85%); run 2: 375 mg (88%);

average yield: 87%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (minor) = 10.6 min, t_R (major) = 11.5 min. $[\alpha]_D^{24} = -1.5$ (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.29 (d, *J* = 4.8 Hz, 2H), 7.29 – 7.24 (m, 2H), 7.18 – 7.14 (m, 3H), 6.46 – 6.43 (t, *J* = 4.4 Hz, 1H), 3.75 – 3.73 (t, *J* = 4.8 Hz, 4H), 2.73 – 2.66 (m, 2H), 2.64 – 2.56 (m, 4H), 2.20 – 2.17 (dd, *J* = 8.8, 4.8 Hz, 1H), 1.74 – 1.68 (m, 1H), 1.66 – 1.57 (m, 1H), 1.51 – 1.44 (m, 1H), 1.42 – 1.31 (m, 2H), 0.99 – 0.95 (t, *J* = 8.0 Hz, 9H), 0.64 – 0.58 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.7, 157.6, 142.7, 128.3, 128.3, 125.6, 109.4, 54.9, 51.7, 44.6, 35.9, 31.7, 29.8, 26.5, 7.8, 3.9. **IR** (neat, cm^{-1}): 3024, 2932, 2872, 1738, 1584, 1545, 1495, 1445, 1355, 1259, 1217. Anal. Calcd. for $C_{25}H_{40}N_4Si$: C, 70.70; H, 9.47 Found: C, 70.40; H, 9.53.



6e

(*R*)-*N*,*N*-bis(4-methoxybenzyl)-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 4, entry **6e**)**:** From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (260 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*-benzyl-*N*-methylhydroxylamine (**2c**) (290 mg, 1.2 mmol). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **6e** as a clear colorless oil (run 1: 517 mg (99%); run 2: 515 mg (99%); average yield: 99%). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (minor) = 9.8 min, t_R (major) = 11.8 min. $[\alpha]_D^{24} = -6.7$ (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (tt, *J* = 8.0, 0.8 Hz, 2H), 7.25 – 7.17 (m, 7H), 6.86 – 6.82 (td, *J* = 8.8, 2.8 Hz, 5H), 3.80 (s, 6H), 3.54 (s, 4H), 2.61 – 2.57 (t, *J* = 8.4 Hz, 2H), 2.33 – 2.30 (dd, *J* = 5.6, 2.0 Hz, 2H), 1.82 – 1.74 (m, 1H), 1.56 – 1.22 (m, 5H), 0.93 – 0.87 (t, *J* = 8.0 Hz, 9H), 0.71 – 0.55 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.4, 142.8, 132.9, 130.0, 128.4, 128.2, 125.5, 113.4, 55.7, 55.2, 46.9, 35.9, 31.6, 28.8, 26.2, 7.8, 4.0. **IR** (neat, cm^{-1}): 2933, 2873, 1611, 1585, 1509, 1453, 1440, 1300, 1246, 1169, 1099, 1036, 1011, 822, 723, 698. HRMS (DART-TOF) calculated for $C_{33}H_{47}NO_2Si$ $[M+H]^+$ m/z 518.3449, found 518.3436.

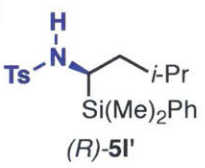
B) Determination of Absolute Configuration

The absolute configuration was determined by comparison of the optical rotation of compound **5l′** with that of a known compound.[8f] The absolute configurations of all the other aminosilanes were tentatively assigned by analogy.

5l'

$[\alpha]_D^{24}$ = –37.4° (c = 1.0, $CHCl_3$, >99% ee)

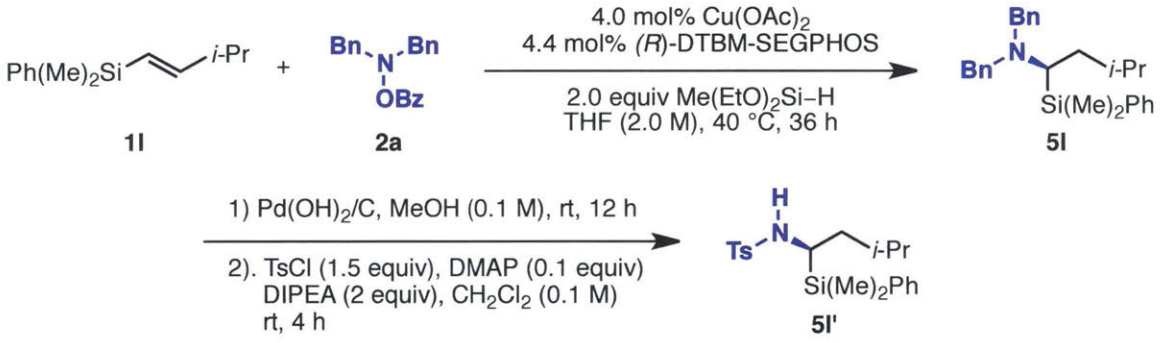
c.f.[8f]



(R)-**5l'**

$[\alpha]_D^{20}$ = –34.7° (c = 0.12, $CHCl_3$, 89% ee)

Compound **5l′** was synthesized according to the following procedure:



1l **2a** **5l** **5l'**

***(R)*-*N*,*N*-dibenzyl-3-methyl-1-(dimethyl(phenyl)silyl)butan-1-amine (5l)**: From (*E*)-dimethyl(3-methylbut-1-en-1-yl)(phenyl)silane (204 mg, 1.0 mmol), the title compound was prepared following the general procedure for CuH-catalyzed hydroamination of vinylsilanes (see section A) using $Cu(OAc)_2$ (7.2 mg, 0.04 mmol, 4 mol%), (*R*)-DTBM-SEGPHOS (52 mg, 0.044 mmol, 4.4 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol). The reaction was stirred in THF (0.5 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–3% EtOAc in hexanes) to afford **5l** as a clear colorless oil (381 mg, 95% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 2H), 7.36 – 7.16 (m, 2H), 7.44 – 7.26 (m, 13H), 3.59 – 3.58 (d, *J* = 3.3 Hz, 4H), 2.52 – 2.48 (t, *J* = 6.3 Hz, 1H), 1.66 – 1.54 (m, 2H), 1.25 – 1.12

(m, 1H), 0.73 – 0.71 (d, J = 6.3 Hz, 3H), 0.50 – 0.48 (d, J = 6.3 Hz, 3H), 0.40 – 0.38 (d, J = 4.8 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 140.7, 139.4, 134.0, 128.9, 128.7, 128.0, 127.7, 126.6, 56.3, 47.1, 35.8, 25.5, 23.0, 22.2, -1.44, -2.62. **IR** (neat, cm^{-1}): 3025, 2952, 1601, 1494, 1453, 1427, 1366, 1247, 1108, 1067, 1027, 965, 830, 808, 768, 731. HRMS (DART-TOF) calculated for $C_{27}H_{35}NSi$ $[M+H]^+$ m/z 402.2612, found 402.2628.

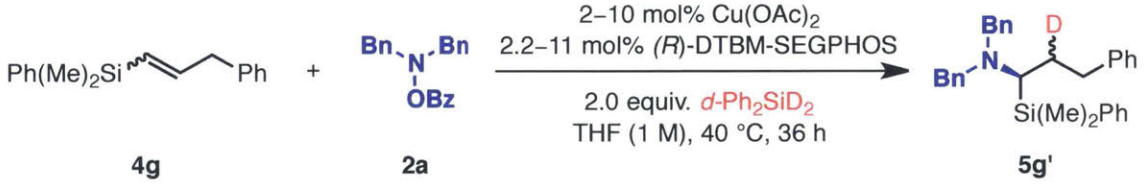
This product **5l** was transformed into **(*R*)-*N*-(1-(dimethyl(phenyl)silyl)-3-methylbutyl)-4-methylbenzenesulfonamide (5l′)** for measurement of optical rotation using the following procedure: A round bottom flask, equipped with a stir bar was charged with **5l** (161 mg, 0.4 mmol), $Pd(OH)_2$ on carbon (20 wt%, 50 mg), and MeOH (4 mL). The flask was evacuated and backfilled with hydrogen (this process was repeated a total of 3 times) and stirred at rt overnight (~12 h) under a H_2 atmosphere (1 atm). The reaction mixture was filtered thorough were added to a round bottom flask equipped with a stir bar. The flask was then capped with a 3-neck joint, with the 2nd neck attached to a H_2 balloon, and the 3rd neck attached to a vacuum pump. The reaction flask was then evacuated and backfilled with H_2 (g) (this process was repeated a total of 3 times). The reaction was stirred at rt overnight (~12 h) under H_2 atmosphere (1 atm). The reaction mixture was filtered through a pad of Celite and the solvent was removed under reduced pressure. TsCl (114 mg, 0.6 mmol), DMAP (5 mg, 0.4 mmol), and CH_2Cl_2 (4 mL) were then added to the flask containing the crude primary amine. The reaction mixture was cooled to 0 °C and DIPEA (2.0 equiv) was added. The reaction mixture was stirred at rt for 4 h. The crude product was purified by by flash column chromatography (7–11% EtOAc in hexanes) to provide **5l′** as a yellow oil (135 mg, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.67 (dd, J = 6.6, 1.2 Hz, 2H), 7.45 – 7.42 (dt, J = 8.6, 2.0 Hz, 2H), 7.41 – 7.30 (m, 1H), 7.25 – 7.23 (d, J = 6.6, 1.2 Hz, 2H), 4.20 (s, 1H), 3.07 – 3.01 (q, J = 7.2 Hz, 1H), 2.41 (s, 3H), 1.43 – 1.34 (sept, J = 6.8, 1H), 1.21 – 1.18 (t, J = 7.2 Hz, 2H), 0.70 – 0.65 (dd, J = 6.4, 4.4 Hz, 6H), 0.28 – 0.25 (d, J = 11.6 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.8, 138.5, 135.4, 134.0, 129.5, 129.3, 128.0, 127.0, 41.9, 41.9, 24.9, 22.9, 21.7, 21.4, -4.4, -5.3. **IR** (neat, cm^{-1}): 3200, 2955, 1597, 1427, 1323, 1248, 1155, 1094, 998, 836, 812, 775, 732, 700, 659. . HRMS (DART-TOF) calculated for $C_{20}H_{29}NO_2SSi$ $[M+NH_4]^+$ m/z 393.2027, found 393.2049.

C) Deuterium-labelling Experiments:

i. Reaction set-up

Compound **5g′** was synthesized according to the following procedure:



4g **2a** **5g'**

In a nitrogen-filled glovebox, $Cu(OAc)_2$ (2.0–10.0 mol%), (*R*)-DTBM-SEGPHOS (2.2–11.0 mol%), and THF (0.2 mL) were added to an oven-dried test tube equipped with a magnetic stir bar. The mixture was stirred for 10 min, at which time diphenyl(silane-d_2) (97 atom % D, 74 μL, 0.4 mmol, 2.0 equiv) was added and the stirring was continued for another 15 min at rt. Into a separate oven-dried test tube was added vinylsilane (0.2 mmol, 1.0 equiv) and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (76 mgm 0.24 mmol, 2 equiv). The catalyst solution was then transferred via syringe to the reaction tube containing the substrates, and the reaction tube was capped, removed from the glovebox, and placed in a pre-heated oil bath at 40 °C for up to 36 h. Dodecane (20 μL) was added as the internal standard for GC analysis. The reaction mixture was quenched with saturated aqueous Na_2CO_3 solution, extracted with EtOAc, dried over Na_2SO_4, filtered through a pad of silica, concentrated, and purified by column chromatography on silica gel.

NB: ***Diphenyl(silane-d_2) is less reactive than diethoxymethylsilane, and was used only for the deuterium-labeling study.***

From **(*E*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane ((*E*)-4g)**: **(*R*,*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-amine (5g'** (*R*,*R*), Scheme 4, eq. 1): The title compound was prepared following the above procedure using $Cu(OAc)_2$ (0.7 mg, 0.004 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (5 mg, 0.0044 mmol, 2.2 mol%). The reaction mixture was stirred in THF (0.2 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5g′** (*R*,*R*) as a clear colorless oil (yield: 44

mg (49%)). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 6.1 min, t_R (major) = 8.9 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H), 7.44 – 7.24 (m, 16H), 7.09 – 7.06 (m, 2H), 3.75 (s, 4H), 2.79 – 2.73 (dt, *J*= 11.8, 2.0 Hz, 1H), 2.62 – 2.60 (dd, *J* = 8.0, 2.0 Hz, 1H), 2.44 – 2.39 (dd, *J* = 13.8, 3.6 Hz, 1H), 1.86 – 1.80 (m, 1H), 0.54 – 0.52 (d, *J* = 2.0 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.9, 140.5, 139.2, 134.0, 129.0, 128.9, 128.3, 128.3, 128.1, 127.8, 126.7, 125.6, 56.4, 49.5, 35.2, 28.7 – 28.3 (t, *J* = 18.7 Hz, 1C), -1.6, -2.7. HRMS (DART-TOF) calculated for $C_{31}H_{34}DNSi$ $[M+H]^+$ m/z 451.2674, found 451.2664.

From **(*Z*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane ((*E*)-4g)**: **(*R,S*)-*N,N*-dibenzyl-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-amine** (**5g'** (*R,R*), Scheme 4, eq. 2): The title compound was prepared following the above procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 10 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 11 mol%). The reaction mixture was stirred in THF (0.2 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford **5g'** (*R,S*) as a clear colorless oil (yield: 45 mg (51%)). HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm) indicated 88% ee: t_R (minor) = 6.1 min, t_R (major) = 8.9 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H), 7.45 – 7.26 (m, 16H), 7.09 – 7.06 (dd, *J* = 8.0, 1.6 Hz, 2H), 3.75 (s, 4H), 2.79 – 2.73 (m, 1H), 2.62 – 2.60 (dt, *J* = 7.6, 2.4 Hz, 1H), 2.45 – 2.37 (m, 1H), 2.17 – 2.11 (m, 1H), 0.53 – 0.52 (d, *J* = 2.4 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.8, 140.5, 139.2, 134.0, 129.0, 128.9, 128.3, 128.3, 128.1, 127.8, 126.7, 125.6, 56.4, 49.5, 35.2, 28.6 – 28.3 (t, *J* = 18.7 Hz, 1C), -1.5, -2.7. HRMS (DART-TOF) calculated for $C_{31}H_{34}DNSi$ $[M+H]^+$ m/z 451.2674, found 451.2663.

ii. Determination of deuterium incorporation by NMR spectroscopy and mass spectrometry

Incorporation of deuterium was analyzed by ^{1}H NMR (Figure 1) and ^{2}H NMR (Figure 2). The relevant region is enlarged and aligned for comparison. For ^{1}H NMR, the diastereotopic protons H_A (δ 1.88 – 1.78 ppm) and H_B (δ 2.17 – 2.10 ppm) have distinct chemical shifts. The disappearance of the corresponding signal indicates deuterium incorporation, and percent deuterium incorporation was derived from the integration value of this signal.

Note: We have tentatively assigned the relative configuration of β-diastereotopic protons H_A and H_B by the absence of ^{1}H NMR signal in the deuterated product, based on syn-addition of Cu-D to the alkene.

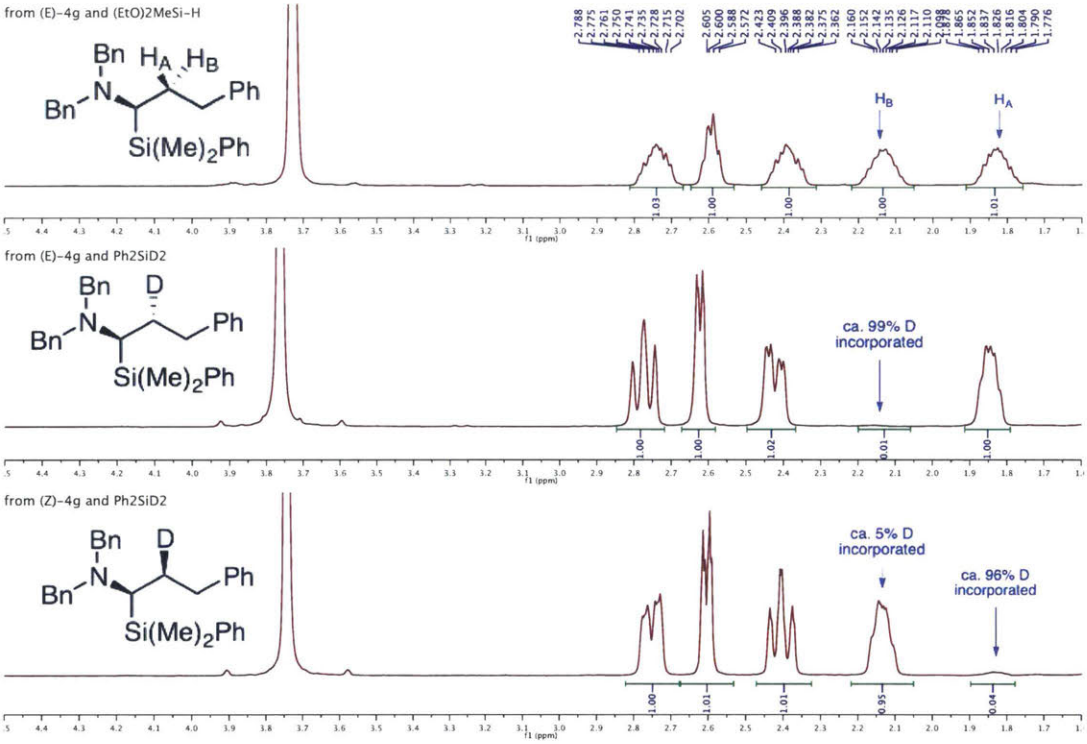


Figure 1. ^{1}H NMR Spectroscopy (Bruker 400 MHz)

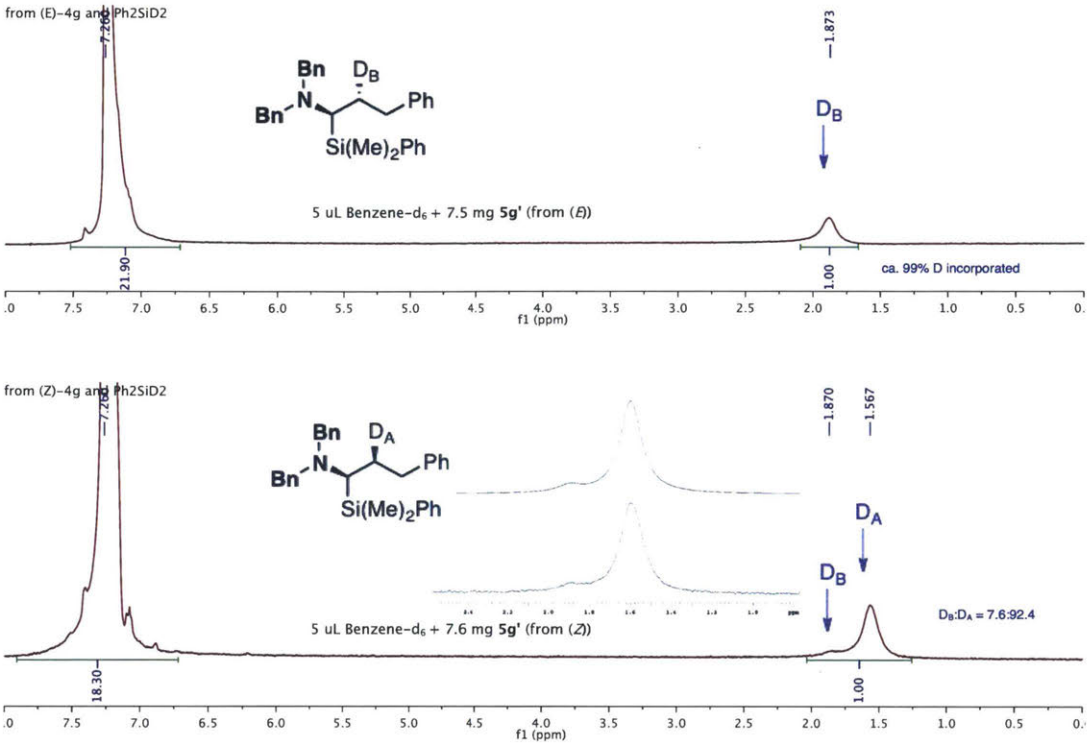


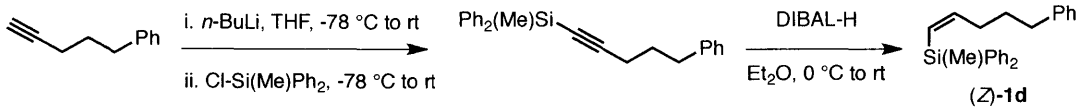
Figure 2. ^{2}H NMR Spectroscopy (Varian 500 MHz)

^{1}H and ^{2}H NMR spectroscopy reveals that ***(E)*-4g** gives the exclusive mono-deuterated product, and the result was confirmed by GC/MS. For **(*Z*)-4g,** ^{1}H NMR shows that there is a high level of deuterium incorporation (ca. 96%) at H_A and a small amount of deuterium incorporation at H_B (ca. 5%), which this was also confirmed by ^{2}H NMR (Figure 2).[22] Additionally, GC/MS shows that there is di-deuterio (H_A, H_B = D) incorporation (ca. 1%) into the product from **(*Z*)-4g**.[23]

From the ^{1}H NMR, ^{2}H NMR, and GC-MS data, we can conclude that ca. 99% of the product from the reaction of **(*Z*)-4g** did not form via isomerization of the substrate to the (*E*)-isomer. Additionally, we can conclude that the hydroamination of ***(E)*-4g** is completely diastereoselective (dr>99:1). The hydroamination of **(*Z*)-4g** is also diastereoselective with dr = 95:4, and 1% dideuterated product.

D) Synthesis of *(Z)*-Vinylsilanes:

Representative Procedure:



(Z)-methyldiphenyl(5-phenylpent-1-en-1-yl)silane ((*Z*)-**1d**)**:** An oven-dried round bottom flask equipped with a stir bar and sealed with a rubber septum was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times). The flask was charged with 5-phenyl-1-pentyne (1.57 mL, 10 mmol) and anhydrous THF (30 mL, 0.33 M). The solution was cooled to −78 °C for 10 min before dropwise addition of *n*-Butyllithium (2.5 M in hexanes, 4.2 mL, 10.5 mmol, 1.05 equiv) via syringe. The reaction mixture was stirred at rt for 30 min. The flask was again cooled to −78 °C for 10 min and chloromethyldiphenylsilane (2.31 mL, 11 mmol) was added. The reaction mixture was allowed to warm to rt and stirred overnight (~12 h). The crude reaction mixture was quenched with saturated aqueous NH_4Cl solution, extracted with EtOAc, and the combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (0-5% EtOAc in hexanes) afforded methyldiphenyl(5-phenylpent-1-en-1yl)silane in quantitative yield. The purified compound was transferred to an oven-dried round bottom flask equipped with a stir bar, and the vessel was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times). Anhydrous Et_2O (10 mL, 1 M) was added, and the solution was cooled to 0 °C for 10 min. DIBAL-H (1 M in hexanes, 16 mL, 16 mmol) was then added slowly to the reaction mixture, which was allowed to stir at rt overnight. The reaction mixture was then cooled to 0 °C, and quenched with saturated NH_4Cl solution. The biphasic mixture was filtered through Celite, extracted with EtOAc, dried over Na_2SO_4, concentrated, and purified by flash chromatography (0–5% EtOAc in hexane). (*Z*)-**1d** was obtained as a clear colorless oil (2.31 g, 68 % yield).

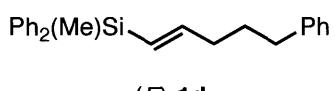
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.55 (dd, J = 7.6, 2.8 Hz, 4H), 7.41 – 7.34 (m, 6H), 7.26 – 7.22 (td, J = 8.0, 0.8 Hz, 2H) 7.18 – 7.14 (tt, J = 7.2, 1.6 Hz, 1H), 7.06 – 7.03 (dd, J = 7.2, 1.6 Hz, 2H), 6.64 – 6.57 (dt, J = 13.6, 7.6 Hz, 1H), 5.88 – 5.84 (d, J = 13.6 Hz, 1H), 2.39 – 2.35 (t, J = 8 Hz, 2H), 2.05 – 2.01 (dt, J = 7.6, 5.6 Hz, 2H), 1.57 – 1.51 (tt, J = 8, 5.6 Hz, 2H), 0.63 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.9, 142.3, 137. 6, 134.6, 129.1, 128.3, 128.2, 127.8,

125.6, 125.2, 35.5, 33.7, 31.1, -2.0. **IR** (neat, cm^{-1}): 3066, 3033, 2924, 2855, 1601, 1495, 1486, 1453, 1427, 1250, 1110, 789, 726. HRMS (DART-TOF) calculated for $C_{24}H_{26}Si$ $[M+NH_4]^+$ m/z 360.2142, found 360.2151.

(Z)-trimethyl(5-phenylpent-1-en-1-yl)silane *((Z)-**1b**),* ***(Z)-triethyl(5-phenylpent-1-en-1-yl)silane*** *((Z)-**1a**),* ***(Z)-dimethyl(phenyl)(5-phenylpent-1-en-1-yl)silane*** *((Z)-**1c**),* ***(Z)-trimethyl(styryl)silane*** *(**7a**), and* ***(Z)-triiisopropyl(styryl)silane*** *(**7b**) are known compounds and were synthesized according to the above procedure.*

E) Synthesis of *(E)*-Vinylsilanes:

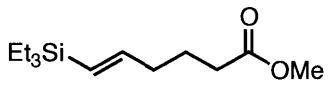
***(E)*-Vinylsilanes** ((*E*)-**1a** to (*E*)-**1d**, and **4a** to **4k**)) were synthesized according to the literature procedure[24] unless otherwise noted. All of the *(E)*-vinylsilanes used are known compounds except for the those listed below.



(*E*)-**1d**

(*E*)-Methyldiphenyl(5-phenylpent-1-en-1-yl)silane ((*E*)-1d): Following the reported procedure for hydrosilylation of alkynes[24], the title compound was prepared from 5-phenyl-1-pentyne (1.57 mL, 10 mmol, 1.0 equiv) and methyldiphenylsilane (3.0 mL, 15 mmol, 1.5 equiv). The crude product was purified by flash column chromatography (5% CH_2Cl_2 in hexanes) to afford (*E*)-**1d** as a clear, colorless oil (3.1 g, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.70 (m, 4H), 7.54 – 7.51 (m, 6H), 7.46 – 7.42 (m, 2H), 7.36 – 7.31 (m, 3H), 7.06 – 7.03 (dd, *J* = 7.2, 1.6 Hz, 2H), 6.41 – 6.33 (dt, *J* = 18.4, 6.4 Hz, 1H), 6.21 – 6.15 (d, *J* = 18.4 Hz, 1H), 2.83 – 2.79 (t, *J* = 7.6 Hz, 2H), 2.46 – 2.39 (td, *J* = 7.2, 6.4 Hz, 2H), 1.98 – 1.91 (tt, *J* = 7.6, 7.2 Hz, 2H), 0.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.8, 142.1, 136.9, 134.7, 129.1, 128.4, 128.2, 127.7, 125.8, 125.7, 36.3, 35.3, 30.2, -3.6. **IR** (neat, cm^{-1}): 3066, 3023, 2930, 1614, 1427, 1111, 788, 731. HRMS (DART-TOF) calculated for $C_{24}H_{26}Si$ $[M+NH_4]^+$ m/z 360.2142, found 360.2151.

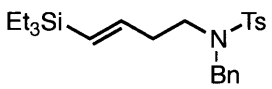


4c

(*E*)-Methyl 6-(triethylsilyl)hex-5-enoate (4c): Following the reported procedure for hydrosilylation of alkynes[24], the title compound was prepared from methyl 5-hexynoate (1.3 mL, 10 mmol, 1.0 equiv) and triethylsilane (2.4 mL, 15 mmol, 1.5 equiv). The crude product was purified by flash column chromatography (2–5% acetone in hexanes) to afford **4c** as a clear, colorless oil (2.2 g, 91% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 – 5.93 (dt, *J* = 18.8, 7.6 Hz, 1H), 5.58 – 5.53 (d, *J* = 18.8 Hz, 1H), 3.64 (s, 3H), 2.30 – 2.27 (t, *J* = 7.6 Hz, 2H), 2.17 – 2.11 (td, *J* = 7.6, 6.8 Hz, 2H), 1.76 – 1.68 (tt, *J* = 7.6, 6.8 Hz, 2H), 0.92 – 0.88 (t, *J* = 8.0 Hz, 9H), 0.55 – 0.49 (q, *J* = 8.0 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.0, 146.9, 127.1, 51.4, 51.4, 36.2, 33.3, 23.9, 7.3, 3.4. **IR**

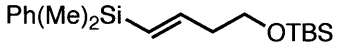
(neat, cm^{-1}): 2951, 2911, 2874, 1740, 1616, 1436, 1417, 1365, 1205, 1170, 1010, 776, 700. HRMS (DART-TOF) calculated for $C_{13}H_{26}O_2$ $[M+H]^+$ m/z 243.1775, found 243.1787.



4d

(*E*)-*N*-benzyl-4-methyl-*N*-(4-(triethylsilyl)but-3-en-1-yl)benzene sulfonamide (4d): Following the reported procedure for hydrosilylation of alkynes[24], the title compound was prepared from *N*-benzyl-*N*-(but-3-yn-1-yl)-4-methylbenzenesulfonamide (3.1 g mL, 10 mmol, 1.0 equiv) and triethylsilane (2.4 mL, 15 mmol, 1.5 equiv). The crude product was purified by flash column chromatography (5% EtOAc in hexanes) to afford **4d** as a clear, colorless oil (4.2 g, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.73 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.34 – 7.25 (m, 7H), 5.81 – 5.73 (dt, *J* = 18.8, 6.4 Hz, 1H), 5.46 – 5.40 (dt, *J* = 18.8, 1.2 Hz, 1H), 4.34 (s, 2H), 3.20 – 3.16 (t, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 2.18 – 2.12 (dt, *J* = 7.6, 6.4 Hz, 2H), 0.90 – 0.86 (t, *J* = 8.0 Hz, 9H), 0.52 – 0.46 (q, *J* = 8.0 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ. 143.7, 143.2, 137.3, 136.5, 129.7, 129.2, 128.5, 128.2, 127.7, 127.1, 51.9, 47.3, 35.7, 21.5, 7.3, 3.3.**IR** (neat, cm^{-1}): 2950, 2873, 1616, 1455, 1340, 1156, 1095, 993, 814, 784, 762, 771, 654, 600. HRMS (DART-TOF) calculated for $C_{24}H_{35}NO_2SSi$ $[M+H]^+$ m/z 430.2231, found 430.2232.

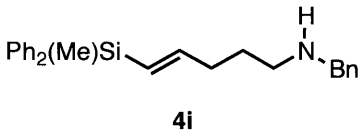


4e

(*E*)-*tert*-butyl((4-(dimethyl(phenyl)silyl)but-3-en-1-yl)oxy) dimethysilane (4e): Following the reported procedure for hydrosilylation of alkynes[24], the title compound was prepared from (but-3-yn-1-yloxy)(*tert*-butyl)dimethylsilane (1.84 g, 10 mmol, 1.0 equiv) and dimethylphenylsilane (2.3 mL, 15 mmol, 1.5 equiv). The crude product was purified by flash column chromatography (0–10% EtOAc in hexanes) to afford **4e** as a clear, colorless oil (2.8 g, 87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.569 – 7.53 (m, 2H), 7.38 – 7.37 (m, 3H), 6.19 – 6.10 (dt, *J* = 18.4, 6.4 Hz, 1H), 5.88 – 5.84 (d, *J* = 18.4 Hz, 1H), 3.73 – 3.70 (t, *J* = 6.8 Hz, 2H), 2.43 – 2.38 (dt, *J* = 6.8, 6.4 Hz, 2H), 0.918 (s, 9H), 0.35 (s, 6H), 0.07 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.7, 139.1, 133.8, 129.8, 128.8, 127.7, 62.5, 40.3, 36.4, 25.9, 18.4, -2.5, -5.3. **IR** (neat, cm^{-}

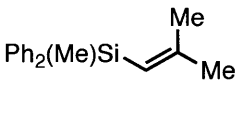
^{1}): 2954, 2927, 2857, 1739, 1616, 1247, 1101, 986, 820, 773, 728, 697. HRMS (DART-TOF) calculated for $C_{18}H_{32}OSi_2$ $[M+H]^+$ m/z 321.2064, found 321.2080.



4i

(*E*)-*N*-benzyl-5-(methyldiphenylsilyl)pent-4-en-1-amine (4i): Following the reported procedure for hydrosilylation of alkynes[24], the title compound was from prepared *N*-benzylpent-4-yn-1-amine (1.87 g, 10 mmol, 1.0 equiv) and methyldiphenylsilane (3.0 mL, 15 mmol, 1.5 equiv). The crude product was purified by flash column chromatography (0–20% EtOAc in 1:99 triethylamine:hexanes mixture) to afford **4i** as a clear, colorless oil (3.4 g, 92% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.57 (m, 4H), 7.44 – 7.28 (m, 11H), 6.27 – 6.20 (dt, J = 18.4, 6.0 Hz, 1H), 6.07 – 6.02 (d, J = 18.4 Hz, 1H), 3.84 (s, 2H), 2.73 – 2.70 (t, J = 7.2 Hz, 2H), 2.34 – 2.29 (dt, J = 7.6, 6.0 Hz, 2H), 1.76 – 1.69 (tt, J = 7.2, 7.6 Hz, 2H), 0.68 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.7, 140.48, 136.9, 134.7, 129.1, 128.3, 128.0, 127.7, 126.8, 125.7, 53.9, 49.0, 48.8, 34.5, 28.8, -3.7. **IR** (neat, cm^{-1}): 3066, 2929, 1739, 1614, 1427, 1111, 790, 690. HRMS (DART-TOF) calculated for $C_{25}H_{29}NSSi$ $[M+H]^+$ m/z 372.2142, found 372.2141.

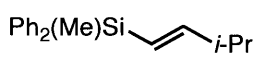


4j

Methyl(2-methylprop-1-en-1-yl)diphenylsilane (4j): An oven-dried flask equipped with a stir bar was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times). Chloromethyldiphenylsilane (2.1 mL, 10 mmol, 1 equiv) and anhydrous THF (10 mL) were added via syringe, and the solution was cooled to 0 °C. 2-Methyl-1-propenylmagnesium bromide (1.84 g, 10 mmol, 1.0 equiv) was added dropwise, and the reaction was removed from the ice bath and stirred at rt for 6 h. The crude reaction mixture was quenched with saturated aqueous NH_4Cl solution, extracted with EtOAc, and the combined organic layers were dried over Na_2SO_4 and concentrated. Purification by column chromatography (0–5% EtOAc in hexanes) afforded **4j** as a clear, colorless oil (1.7 g, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 4H), 7.44 – 7.40 (m, 6H), 5.63 (s, 1H), 2.02 (s, 3H), 1.75 (s, 3H), 0.72 (s, 3H. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.5, 138.0, 134.6, 128.9,

127.8, 120.0, 29.6, 24.0, -2.0. **IR** (neat, cm^{-1}): 3067, 3049, 1739, 1618, 1439, 1427, 1370, 1249, 1110, 851, 804, 790, 779, 728, 710, 696. HRMS (DART-TOF) calculated for $C_{17}H_{20}Si$ $[M+H]^+$ m/z 253.1407, found 253.1382.



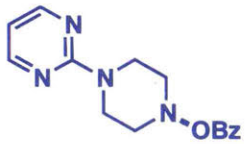
4k

(*E*)-Methyl(3-methylbut-1-en-1-yl)diphenylsilane (4k): Following the reported procedure for hydrosilylation of alkynes[24], the title compound was prepared from 3-methylbut-1-yne (1.02 g, 10 mmol, 1.0 equiv) and diphenylmethylsilane (3.0 mL, 15 mmol, 1.5 equiv). The crude product was purified by distillation to afford **4k** as a clear, colorless oil (2.2 g, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.59 (dd, *J* = 5.2, 1.2 Hz, 4H), 7.45 – 7.39 (m, 6H), 6.28 – 6.21 (dt, *J* = 18.8, 6.8 Hz, 1H), 6.00 – 5.95 (d, *J* = 18.8 Hz, 1H), 2.50 – 2.40 (tt, *J* = 8.0, 6.8 Hz, 1H), 1.11 – 1.09 (d *J* = 8.0 Hz, 6H), 0.68 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.0, 137.2, 134.8, 129.1, 127.7, 121.2, 34.5, 21.7, -3.6. **IR** (neat, cm^{-1}): 2957, 1738, 1613, 1427, 1380, 1249, 1108, 998, 815, 794, 732, 700, 696. HRMS (DART-TOF) calculated for $C_{18}H_{22}Si$ $[M+H]^+$ m/z 267.1564, found 267.1582.

F) Synthesis of *O*-Benzoyl Hydroxylamines:

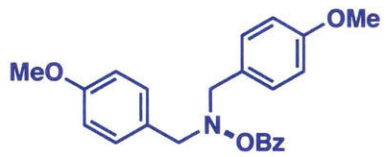
***O*-Benzoyl hydroxylamines** were synthesized according to the literature procedure[25] unless otherwise noted. All of the *O*-benzoyl hydroxylamines used are known compounds except for those listed below.



2d

4-(pyrimidin-2-yl)piperazin-1-yl benzoate (2d): Following the reported procedure,[25] the title compound was prepared from 2-(piperazin-1-yl)pyrimidine (8.21 g, 50 mmol, 1.0 equiv), benzoyl peroxide (24.2 g, 100 mmol, 2 equiv), and dipotassium hydrogen phosphate (17.4 g, 100 mmol, 2 equiv). The crude product was purified by flash column chromatography (25–33% EtOAc in hexanes) to afford **2d** as a white solid (12.8 g, 90% yield); m.p. = 83.0–83.7 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 – 8.26 (m, 2H), 8.10 – 7.92 (m, 2H), 7.67 – 7.52 (m, 1H), 7.52 – 7.38 (m, 2H), 6.56 (t, J = 4.8 Hz, 1H), 4.66 (d, J = 13.5 Hz, 2H), 3.57 (s, 4H), 3.20 – 2.83 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.8, 161.6, 157.9, 133.3, 129.6, 129.3, 128. 6, 110.5, 56.0, 42.3. **IR** (neat, cm^{-1}): 2852, 1736, 1582, 1547, 1492, 1449, 1355, 1242, 1084, 1021, 983, 796, 707. Anal. Calcd. for $C_{15}H_{16}N_4O_2$: C, 63.37; H, 5.67 Found: C, 63.52; H, 5.71.



2e

***O*-benzoyl-*N*,*N*-bis(4-methoxybenzyl)hydroxylamine (2c):** Following the reported procedure,[25] the title compound was prepared from bis(4-methoxybenzyl)amine (5.0 g, 19.4 mmol, 1.05 equiv), benzoyl peroxide (4.5 g, 18.5 mmol, 1.0 equiv), and dipotassium hydrogen phosphate (4.8 g, 27.8 mmol, 1.5 equiv). The crude product was purified by flash recrystallization (EtOAc in hexanes) to afford **2c** as a white solid (5.2 g, 71% yield); m.p. = 93.7–96.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.86 (dd, J = 8.2, 1.2 Hz, 4H), 7.53 – 7.48 (td, J = 7.2, 1.6 Hz, 1H), 7.39 – 7.33 (m, 6H), 6.85 – 6.82 (m, 4H), 4.12 (s, 4H), 3.77 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.9, 159.1, 132.8, 130.7, 129.4, 129.3, 128.3, 128.0, 113.7, 77.4, 77.1, 76.7, 61.3, 55.2. **IR** (neat, cm^{-1}): 1723, 1612, 1585, 1509, 1302, 1239, 1169, 1089, 1068, 1025, 987, 816, 807, 700. HRMS (DART-TOF) calculated for $C_{23}H_{23}NO_4$ $[M+H]^+$ m/z 378.1700, found 378.1708.

3.5 References and Notes

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Skrydstrup, T. *J. Org. Chem.* **2010**, *75*, 3283. (c) Hernandez, D.; Nielsen, L.; Lindsay, K. B.; Lopez-Garcia, M. A.; Bjerglund, K.; Skrydstrup, T. *Org. Lett.* **2010**, *12*, 3528. (d) Hernandez, D.; Mose, R.; Skrydstrup, T. *Org. Lett.* **2010**, *13*, 732. (e) Bo, Y.; Singh, S.; Duong, H. Q.; Cao, C.; Sieburth, S. M. *Org. Lett.* **2011**, *13*, 1787. (f) Hensel, A.; Nagura, K.; Delvos, L. B.; Oestreich, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 4964.

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11) For vinylsilanes, the partial positive charge is more pronounced at the β-position (to the silicon) due to the β-silicon effect (see ref. 12 and 13). The partial negative charge that develops at the α-position is stabilized by the silyl group (see ref. 14 and 15). Furthermore, intermediate **II** (Scheme 2) is thermodynamically stabilized by hyperconjugation of the *s* orbital of the Cu-alkyl bond with a s^* orbital on the silicon-carbon bond (see ref 16).

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18). The hydroamination reaction is slow for vinylsilanes with large silyl groups such as TIPS and TBDPS. After 36 h, no conversion was observed for (*Z*)-triisopropyl(5-phenylpent-1-en-1-yl)silane and only 16% conversion was observed for (*Z*)-*tert*-butyldiphenyl(5-phenylpent-1-en-1-yl)silane.

19). Competitive elimination of an allylic leaving group was previously observed in related Cu-catalyzed processes: (a) Kacprzynski, M.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004,** *124,* 10676. (b) Nakatani, A.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2012,** *14*, 2586. (c) Harada, A.; Makida, Y.; Sato, T.; Ohmiya, H.; Sawamura, M. *J. Am. Chem. Soc.* **2014,** *136*, 13932. (d) Hojoh, K.; Shido, Y.; Ohmiya, H.; Sawamura, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 4954. (e) Makida, Y.; Takayama, Y.; Ohmiya, H.; Sawamura, M. *Angew. Chem. Int. Et.* **2013**, *52*, 5350. (f) Shido, Y.; Yoshida, M.; Tanabe, M.; Ohmiya, H.; Iwai, T.; Sawamura, M. *Adv. Synth. Catal.* **2012**, *354*, 3440. (h) Nagao, K.; Yokobori, U.; Makida, Y.; Ohmiya, H.; Sawamura, M. *J. Am. Chem. Soc.* **2012**, *134,* 8982. (i) Nagao, K.; Ohmiya, H. Sawamura, M. *Synthesis*, **2012**, *44*, 1535.

20). Experimental section II, part C for a detailed analysis.

21). We thank Dr. Erik L. Regalado (Merck, Rahway, NJ) for assistance with this chiral separation.

22). Due to overlap of the two peaks, we were unable to reliably determine the relative percentage of deuterium incorporation for D_A and D_B from **(*Z*)-4g**. Using the NMR deconvolution function, we approximate the ratio of D_B and D_A to be 7.6:92.4. (We thank Dr. Jeffrey H. Simpson (MIT, DCIF facility, jsimpson@mit.edu) for assistance with ^2H NMR spectroscopy, and for carrying out deconvolution of the overlapping peaks to obtain the relative ratio of D_A and D_B.)

23). GC/MS calculation was performed by assuming the $(M-1)^+$ peak derived from the di-deuterated product have negligible contribution.

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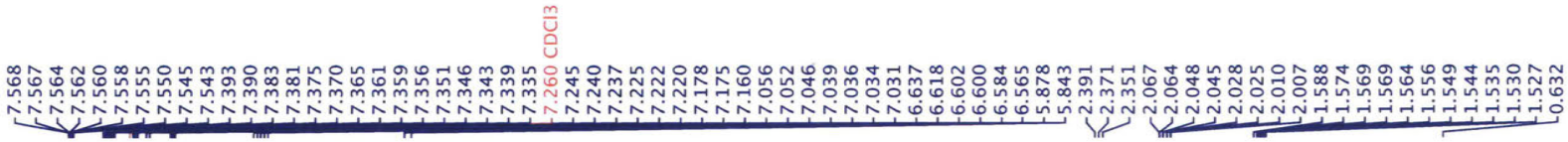
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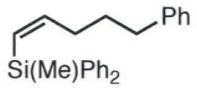
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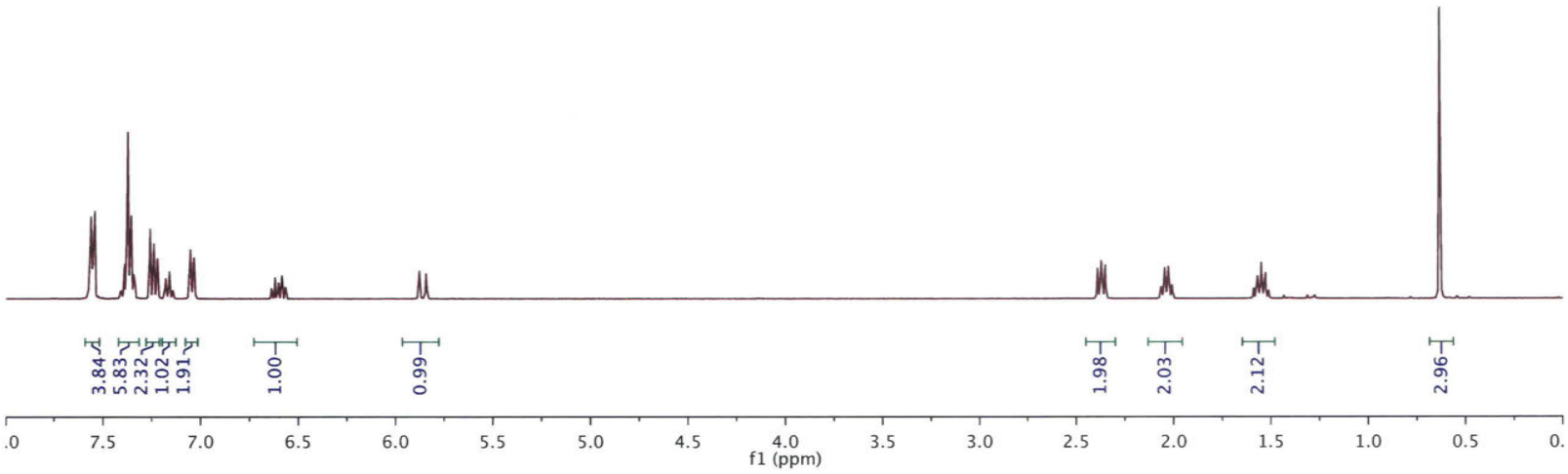
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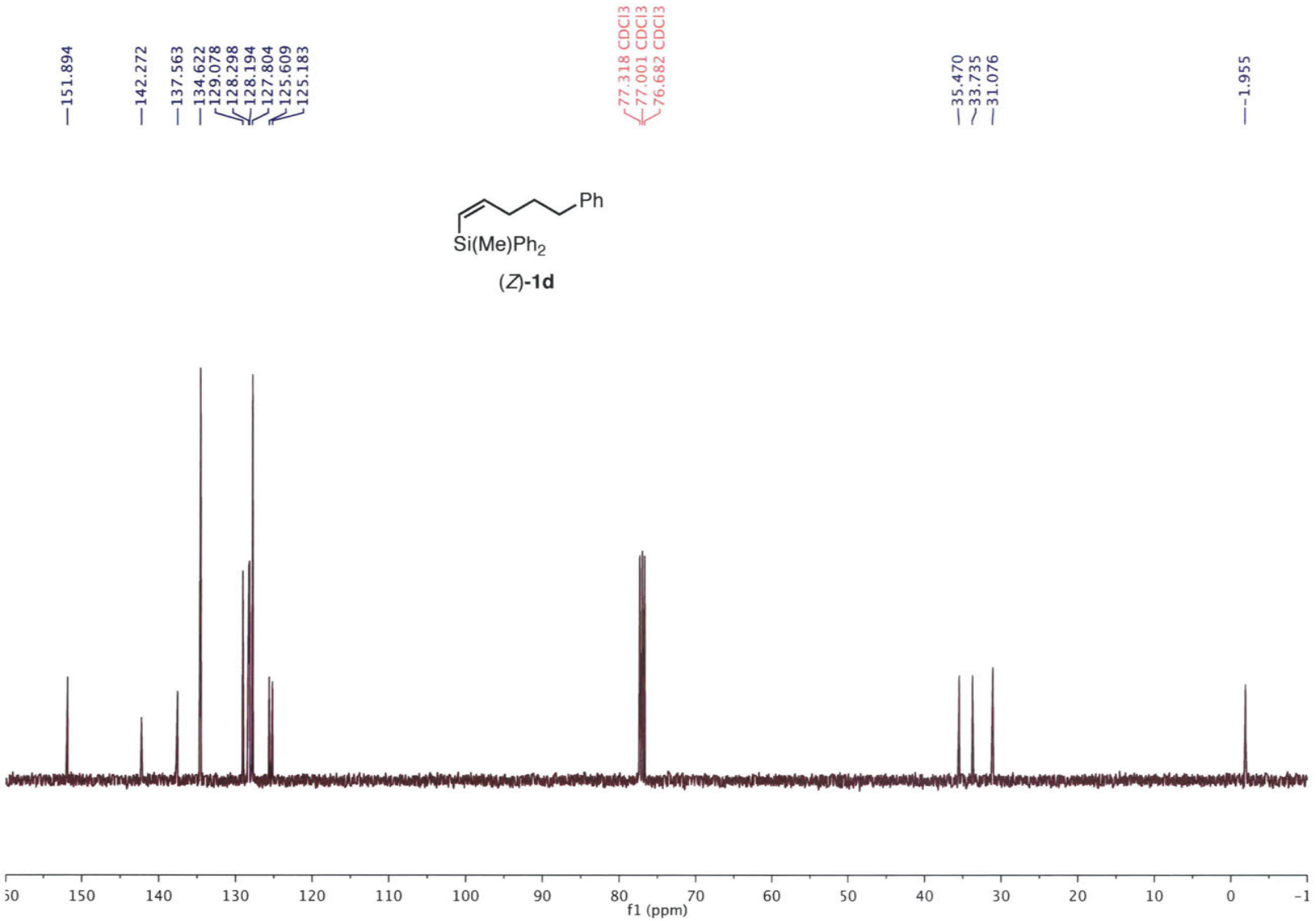
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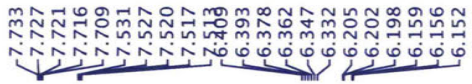
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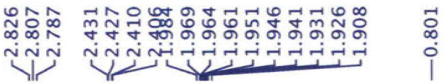
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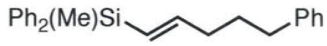
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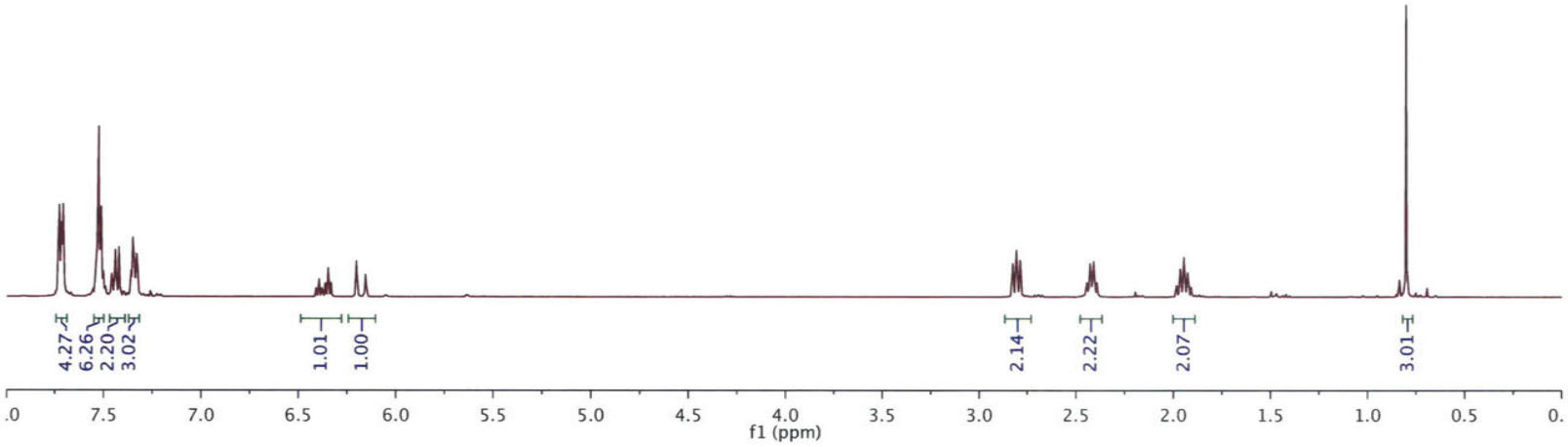
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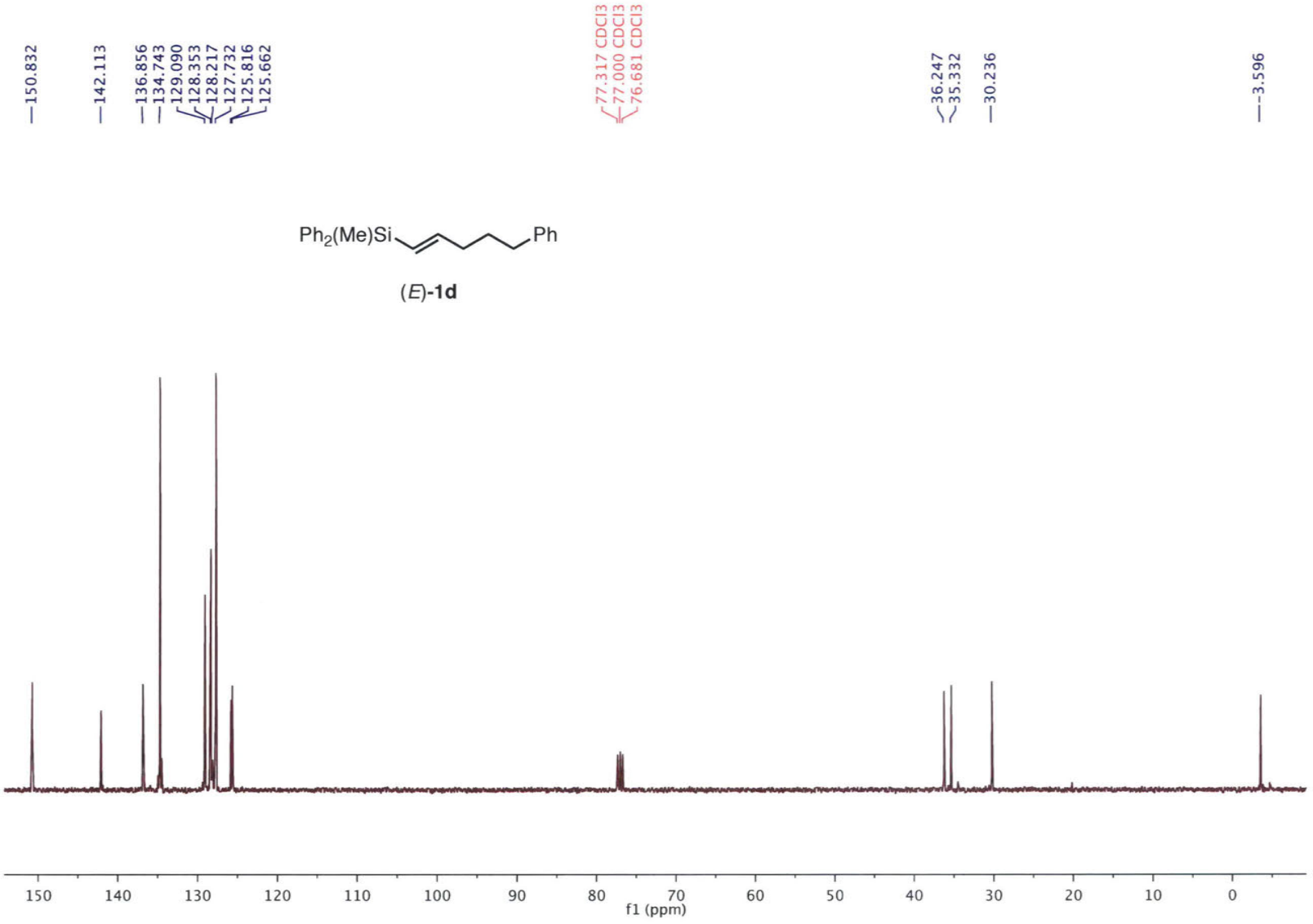
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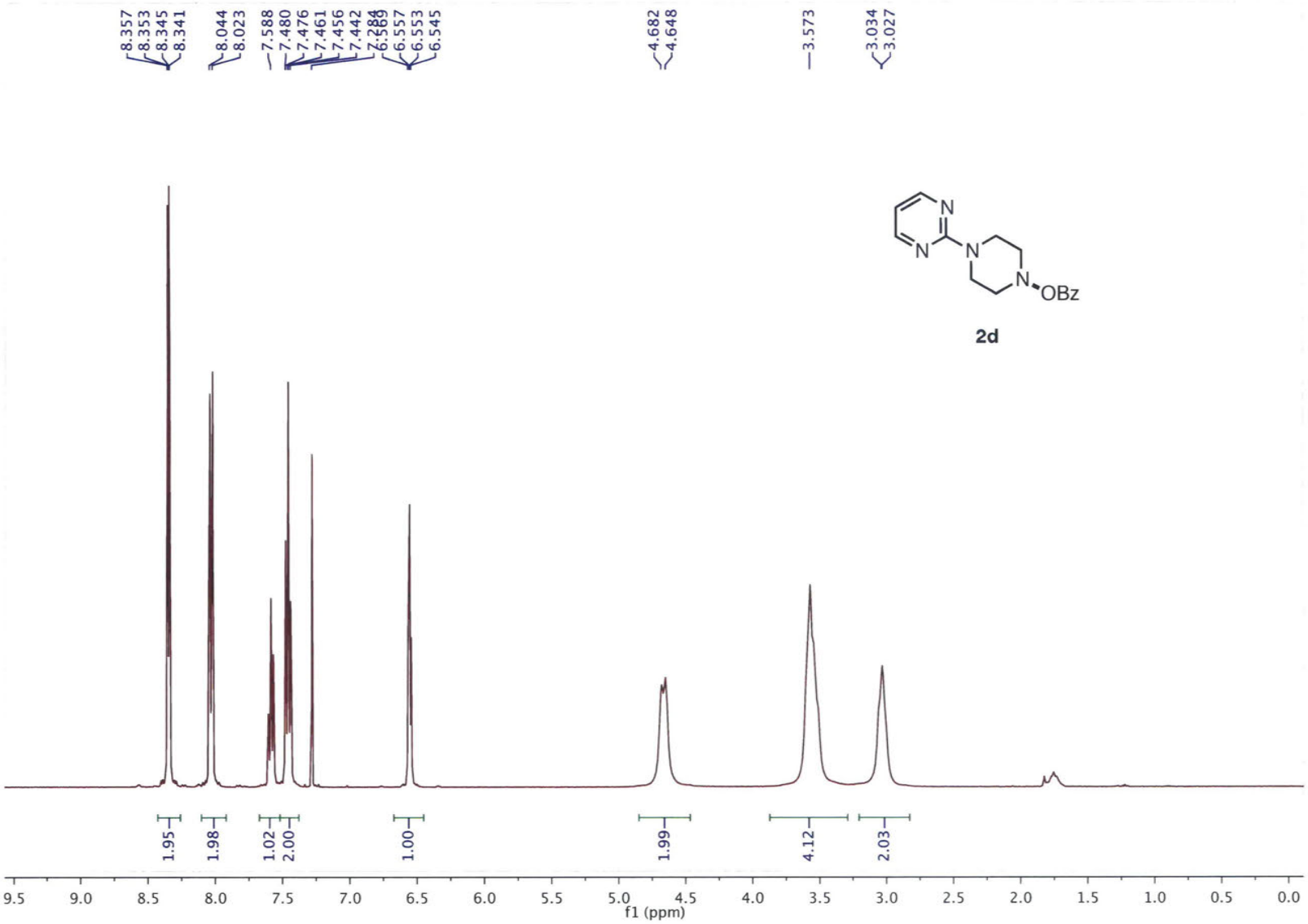
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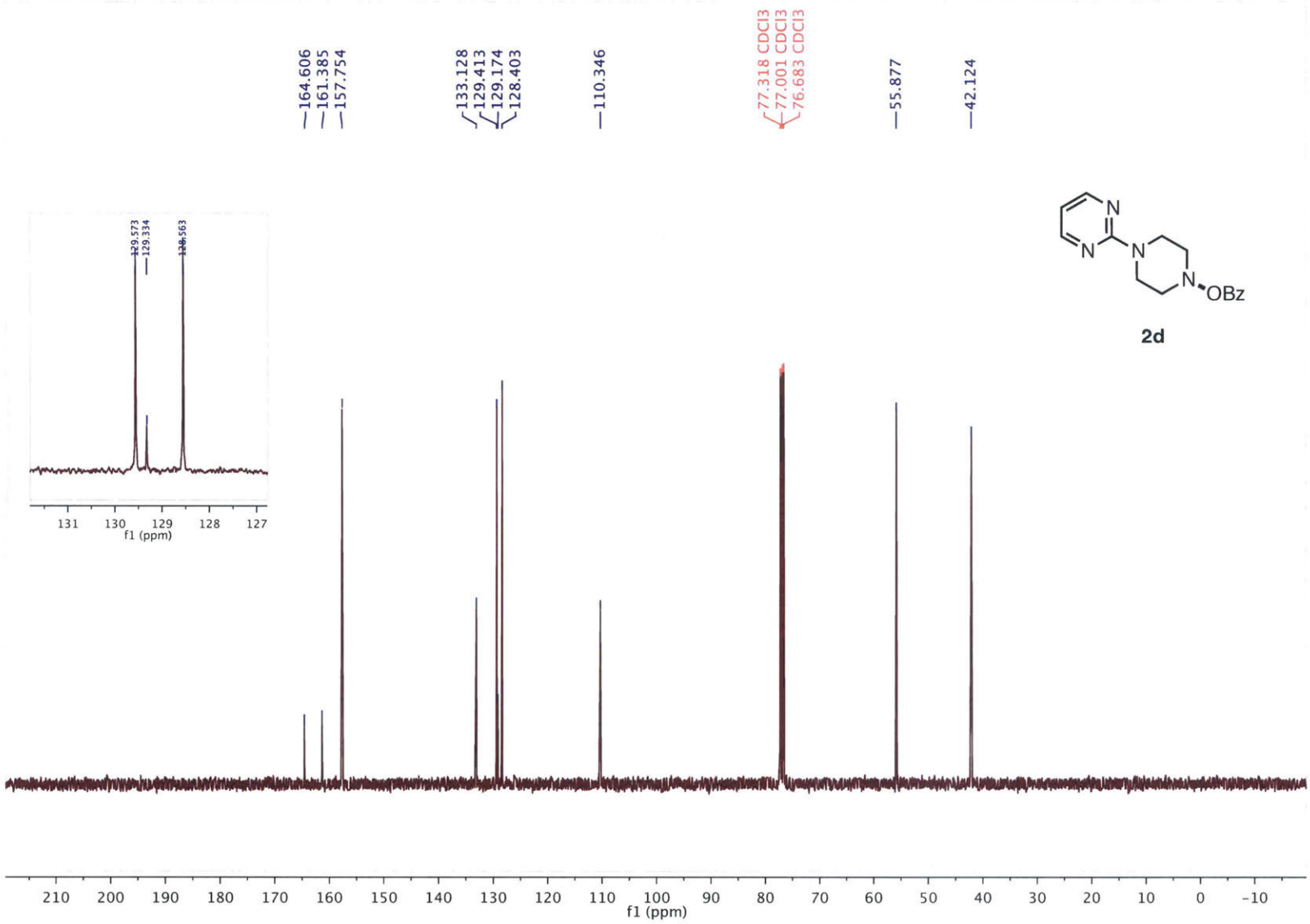
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N
N
OBz
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180
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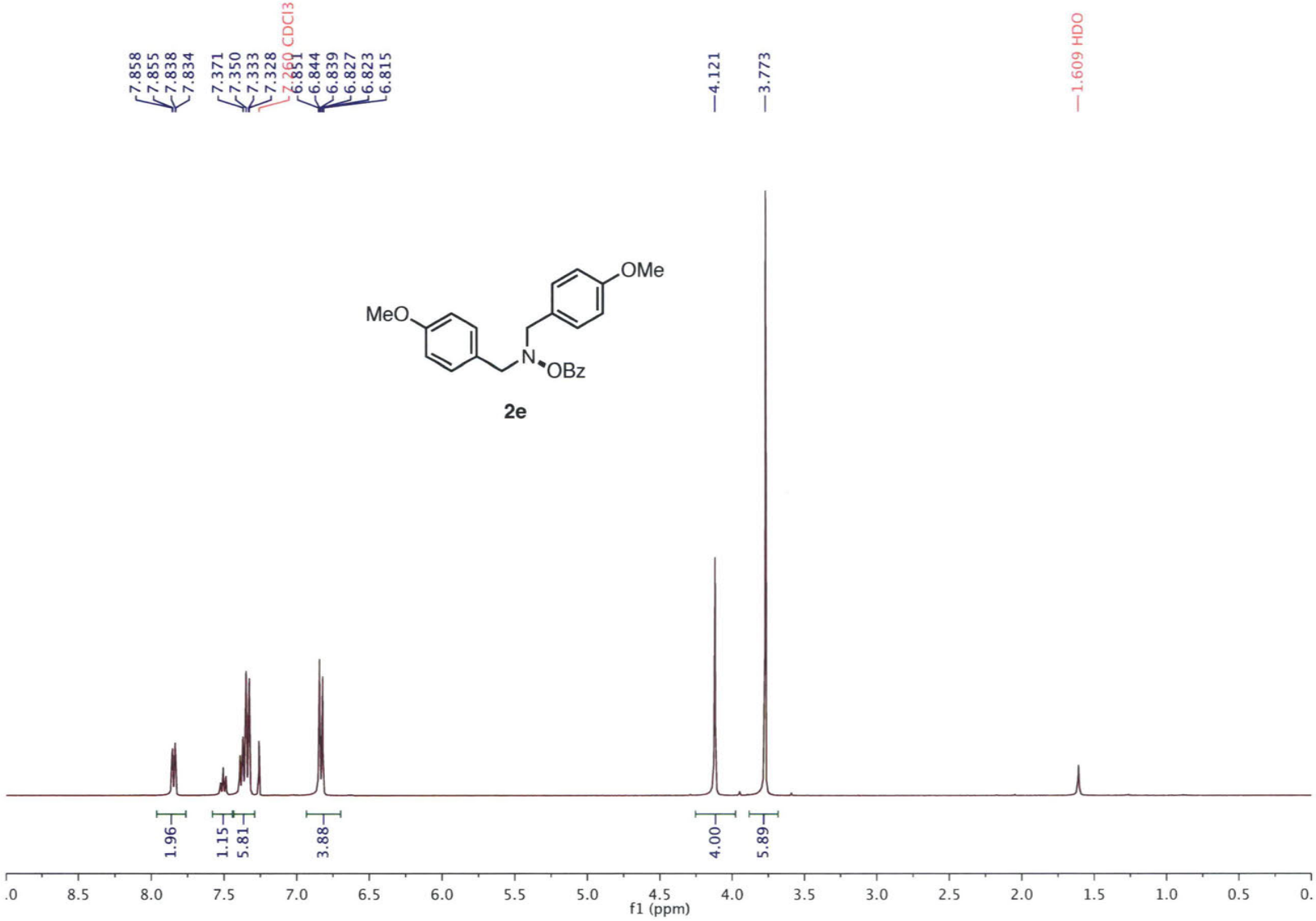
f1 (ppm)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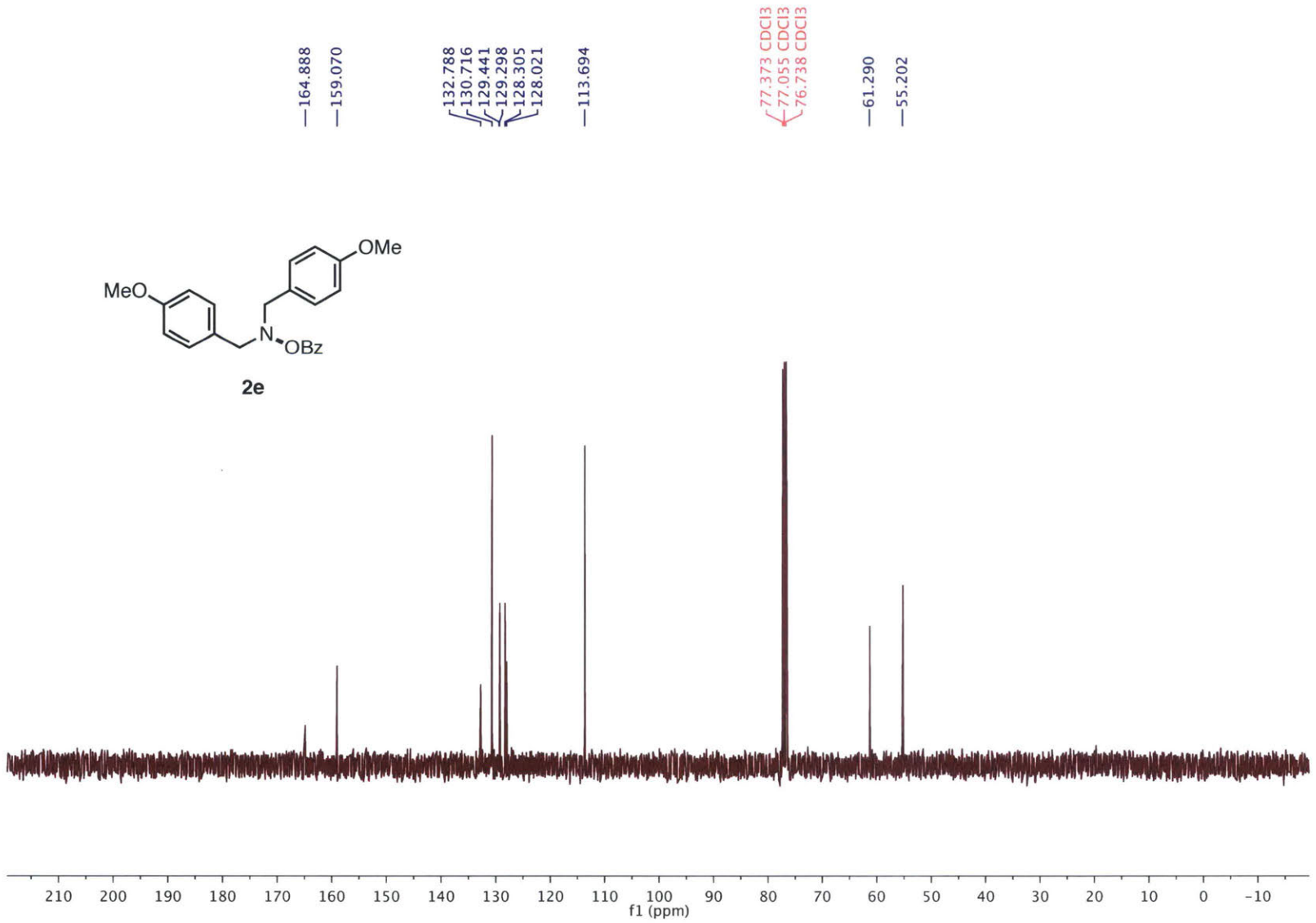
5.89
f1 (ppm)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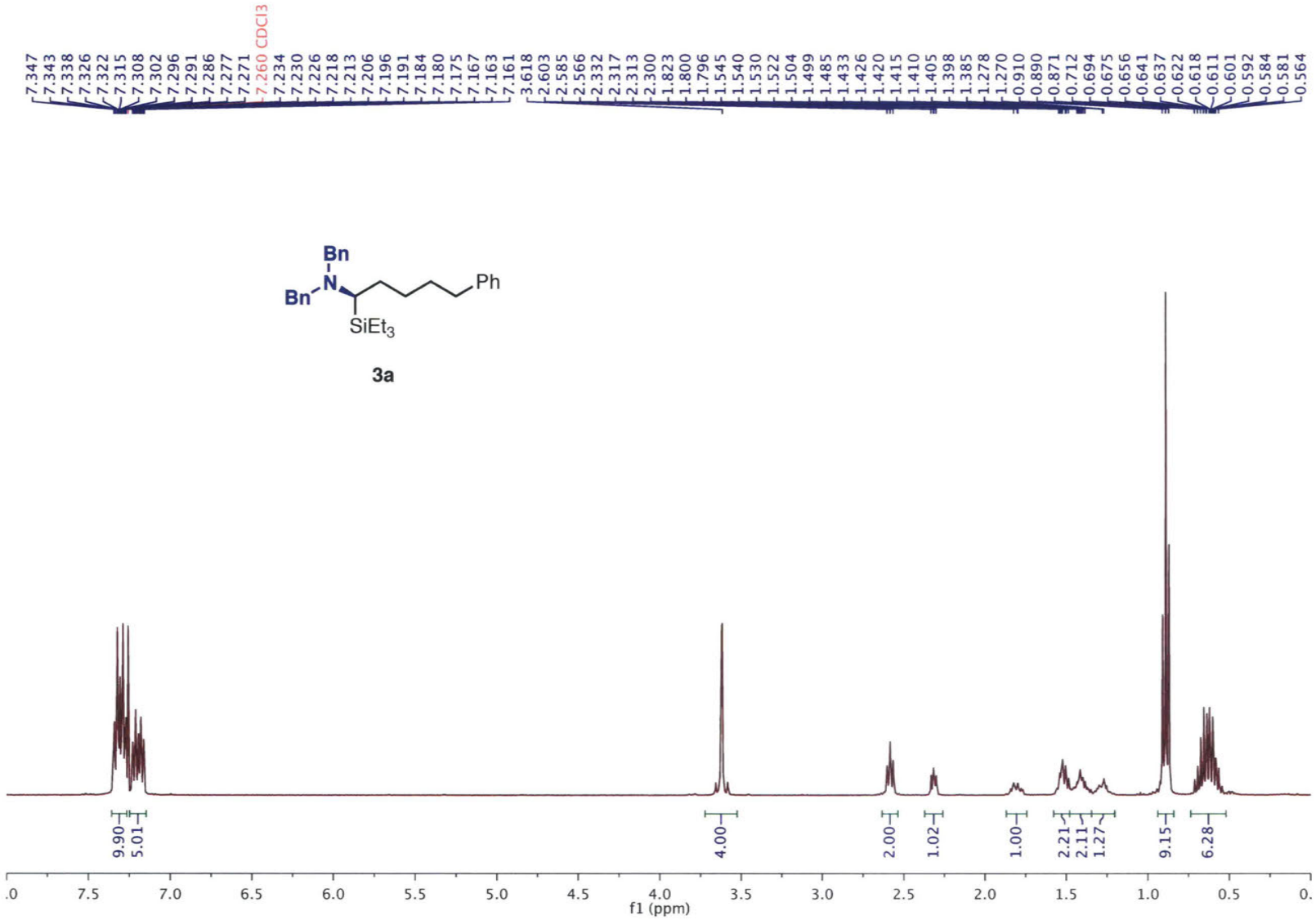
159.070
132.788
130.716
129.441
129.298
128.305
128.021
113.694
77.373 CDCl3
77.055 CDCl3
76.738 CDCl3
61.290
55.202
OMe
MeO
N
OBz
2e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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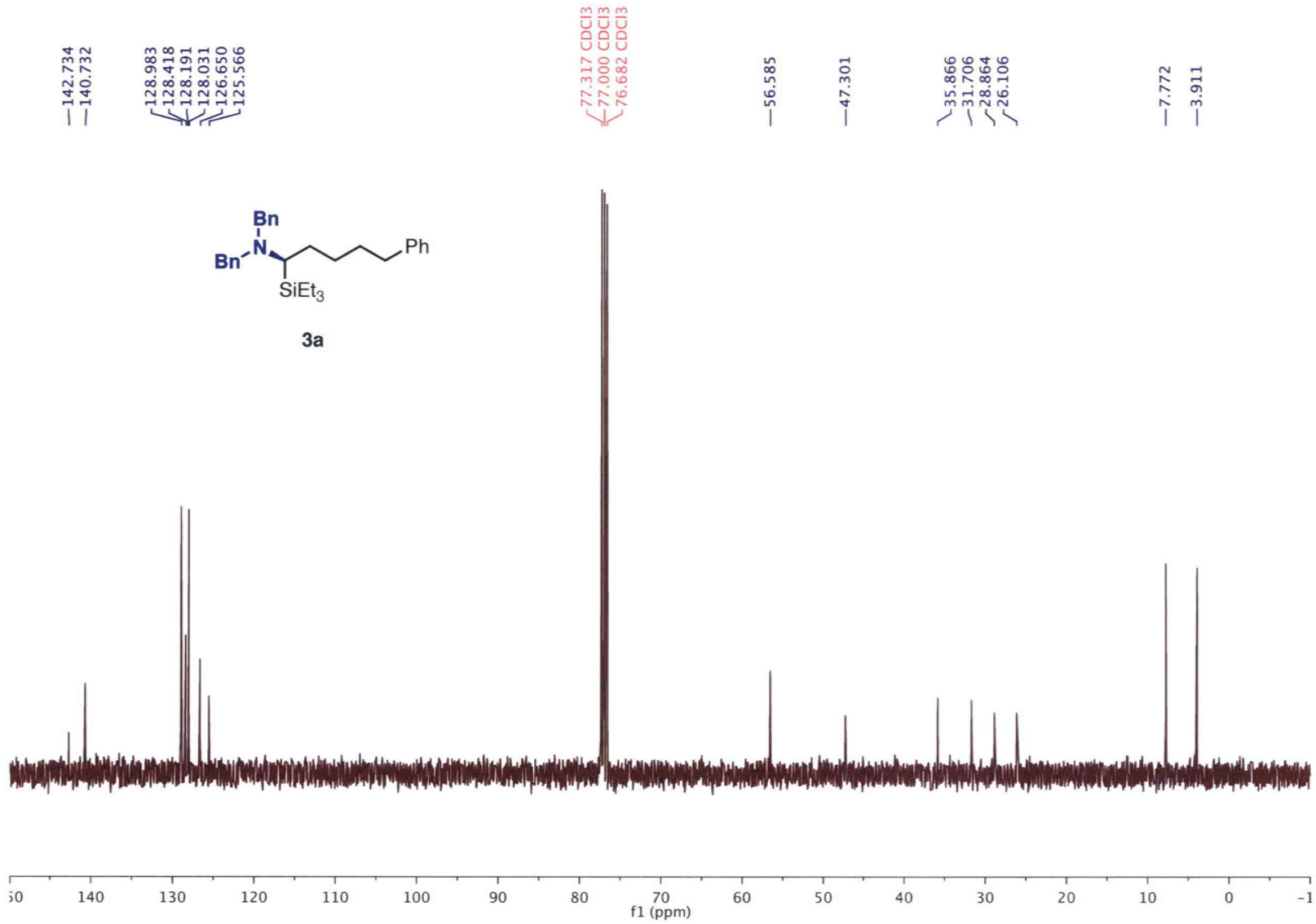
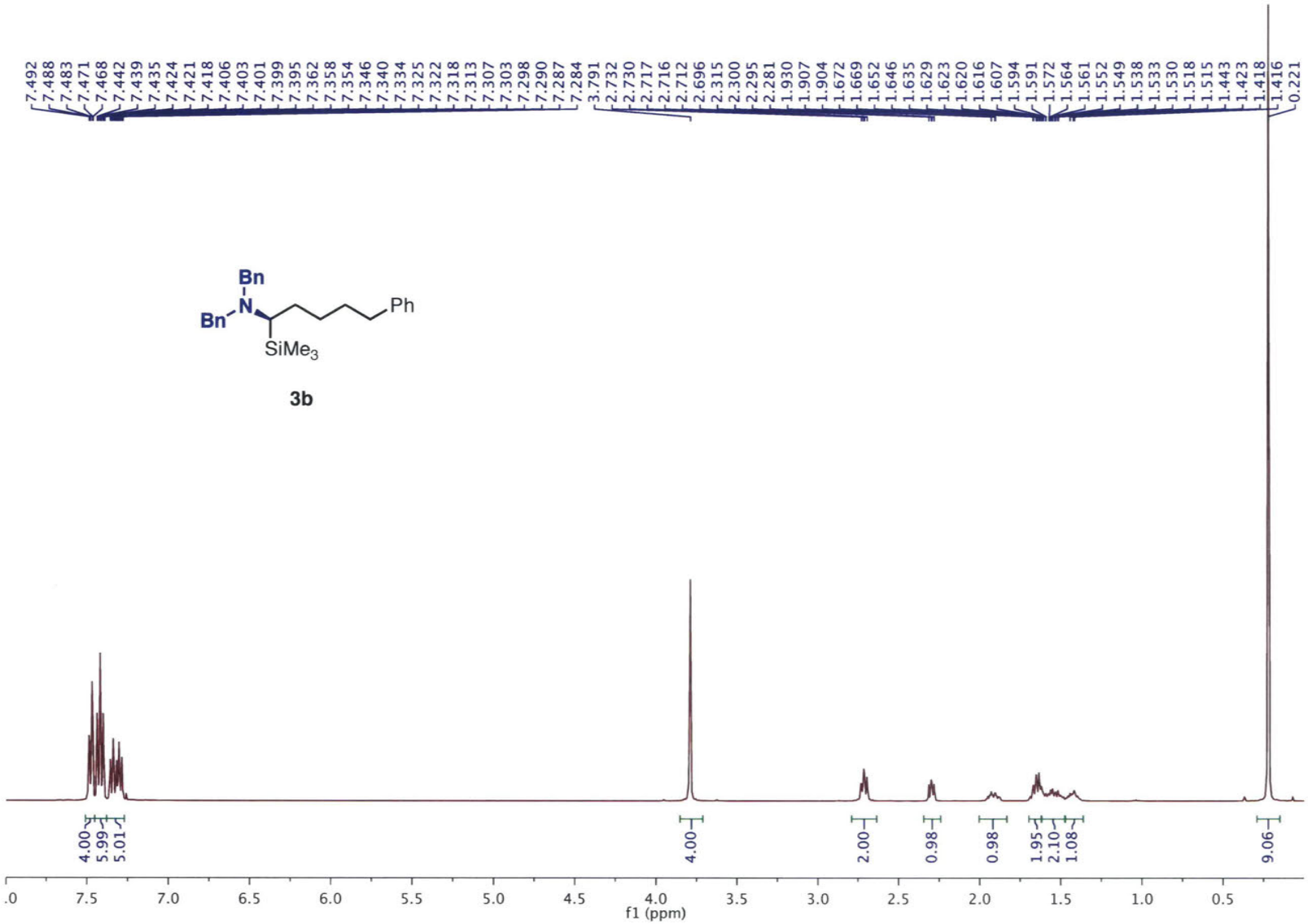
7.343
7.338
7.326
7.322
7.315
7.308
7.302
7.296
7.291
7.286
7.277
7.271
7.260 CDCl3
7.234
7.230
7.226
7.218
7.213
7.206
7.196
7.191
7.184
7.180
7.175
7.167
7.163
7.161
3.618
2.603
2.585
2.566
2.332
2.317
2.313
2.300
1.823
1.800
1.796
1.545
1.540
1.530
1.522
1.504
1.499
1.485
1.433
1.426
1.420
1.415
1.410
1.405
1.398
1.385
1.278
1.270
0.910
0.890
0.871
0.712
0.694
0.675
0.656
0.641
0.637
0.622
0.618
0.611
0.601
0.592
0.584
0.581
0.564
Bn
N
Bn
Ph
SiEt3
3a
9.90
5.01
4.00
2.00
1.02
1.00
2.21
2.11
1.27
9.15
6.28
f1 (ppm)


142.734
140.732
128.983
128.418
128.191
128.031
126.650
125.566
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
56.585
47.301
35.866
31.706
28.864
26.106
7.772
3.911
Bn
N
Bn
Ph
SiEt3
3a
f1 (ppm)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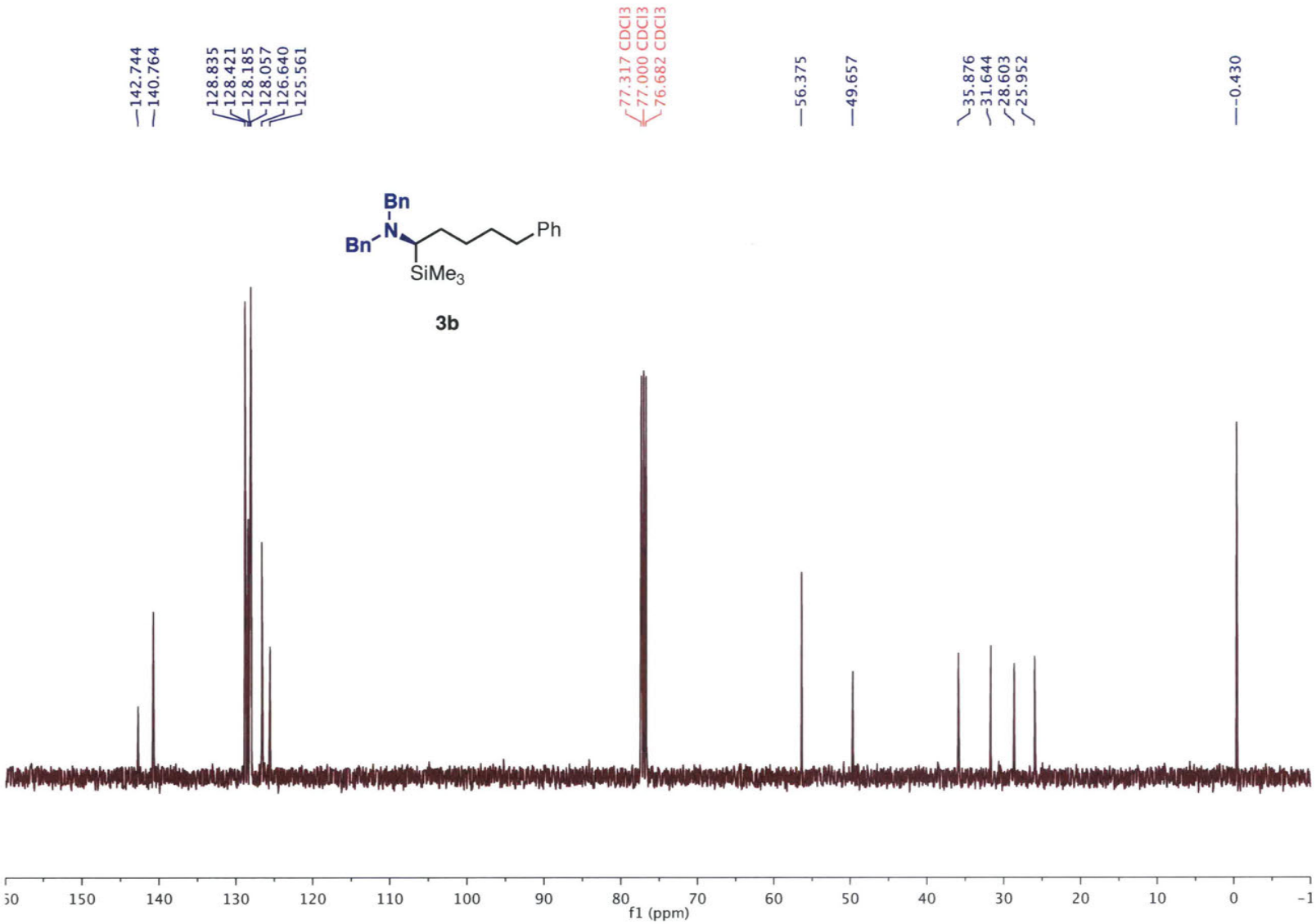
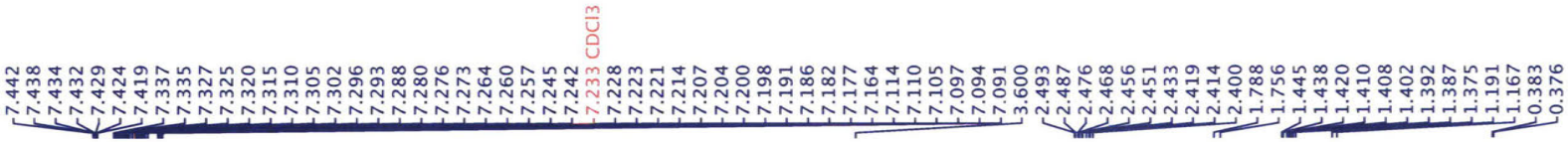
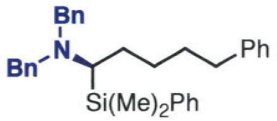
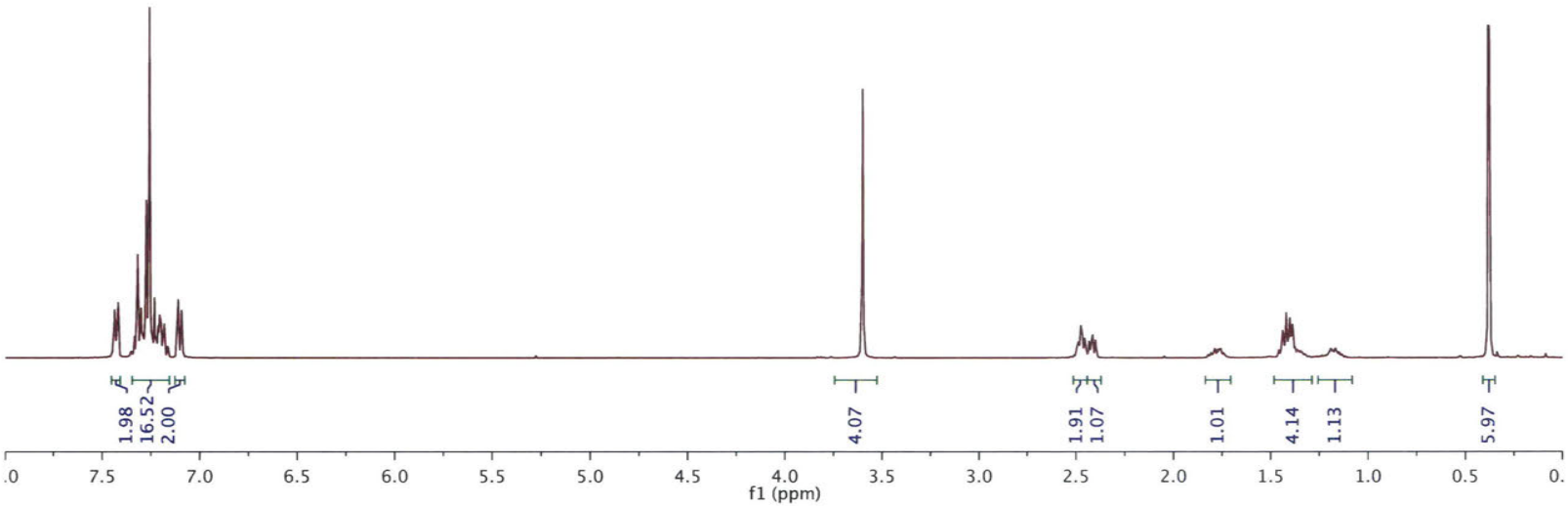
7.488
7.483
7.471
7.468
7.442
7.439
7.435
7.424
7.421
7.418
7.406
7.403
7.401
7.399
7.395
7.362
7.358
7.354
7.346
7.340
7.334
7.325
7.322
7.318
7.313
7.307
7.303
7.298
7.290
7.287
7.284
3.791
2.732
2.730
2.717
2.716
2.712
2.696
2.315
2.300
2.295
2.281
1.930
1.907
1.904
1.672
1.669
1.652
1.646
1.635
1.629
1.623
1.620
1.616
1.607
1.594
1.591
1.572
1.564
1.561
1.552
1.549
1.538
1.533
1.530
1.518
1.515
1.443
1.423
1.418
1.416
0.221
Bn
N
Bn
Ph
SiMe3
3b
4.00
5.99
5.01
4.00
2.00
0.98
0.98
1.95
2.10
1.08
9.06
.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
f1 (ppm)

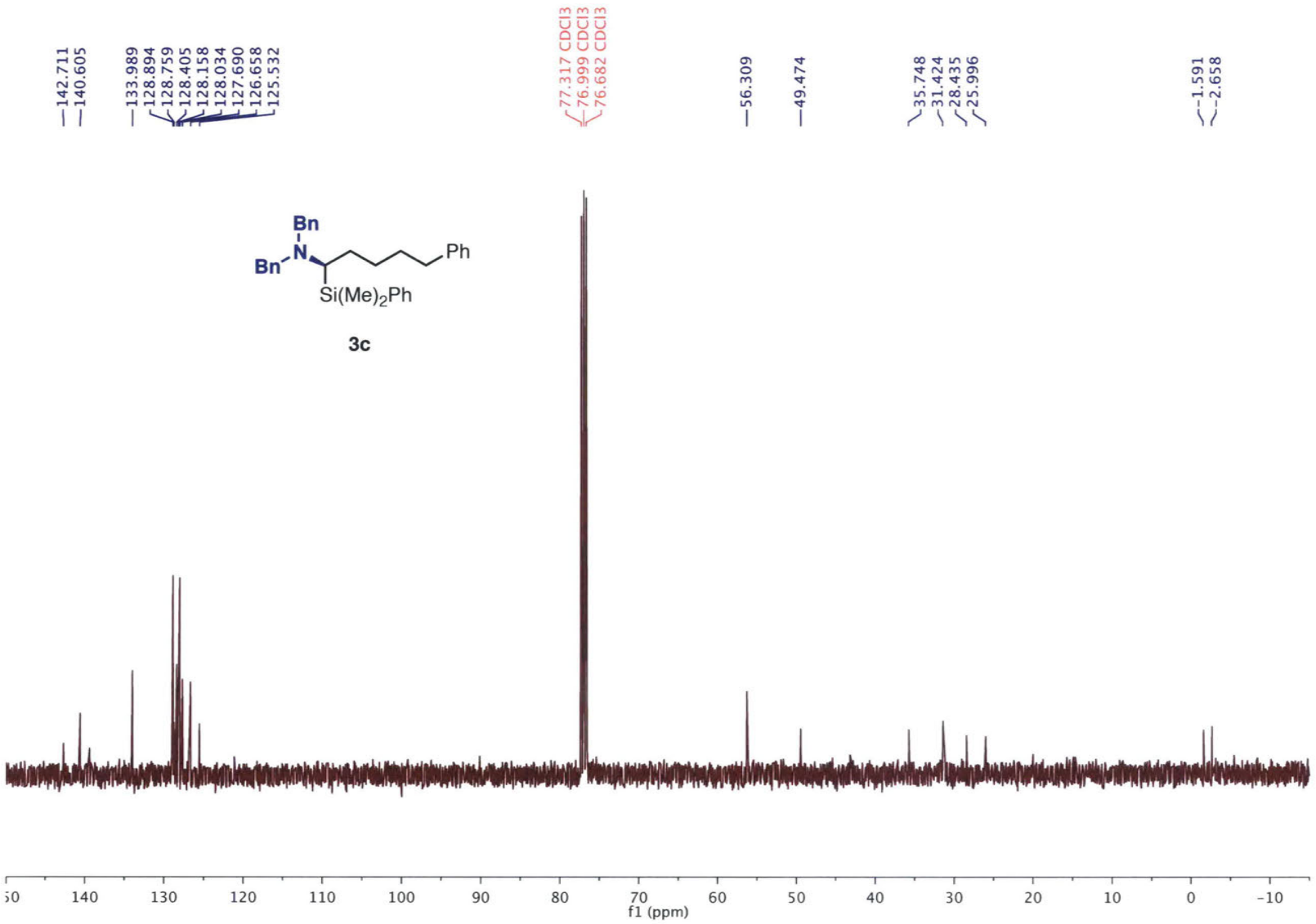

142.744
140.764
128.835
128.421
128.185
128.057
126.640
125.561
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
56.375
49.657
35.876
31.644
28.603
25.952
0.430
Bn
N
Bn
Ph
SiMe3
3b
f1 (ppm)

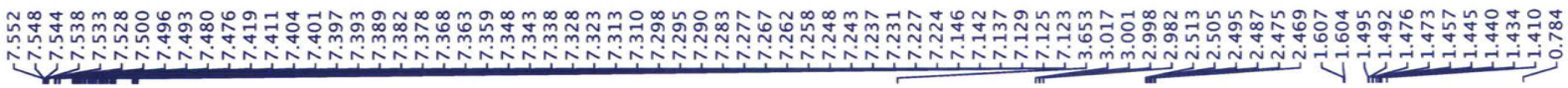

7.442
7.438
7.434
7.432
7.429
7.424
7.419
7.337
7.335
7.327
7.325
7.320
7.315
7.310
7.305
7.302
7.296
7.293
7.288
7.280
7.276
7.273
7.264
7.260
7.257
7.245
7.242
7.233 CDCl3
7.228
7.223
7.221
7.214
7.207
7.204
7.200
7.198
7.191
7.186
7.182
7.177
7.164
7.114
7.110
7.105
7.097
7.094
7.091
3.600
2.493
2.487
2.476
2.468
2.456
2.451
2.433
2.419
2.414
2.400
1.788
1.756
1.445
1.438
1.420
1.410
1.408
1.402
1.392
1.387
1.375
1.191
1.167
0.383
0.376

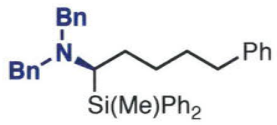

Bn
N
Bn
Ph
Si(Me)2Ph

3c

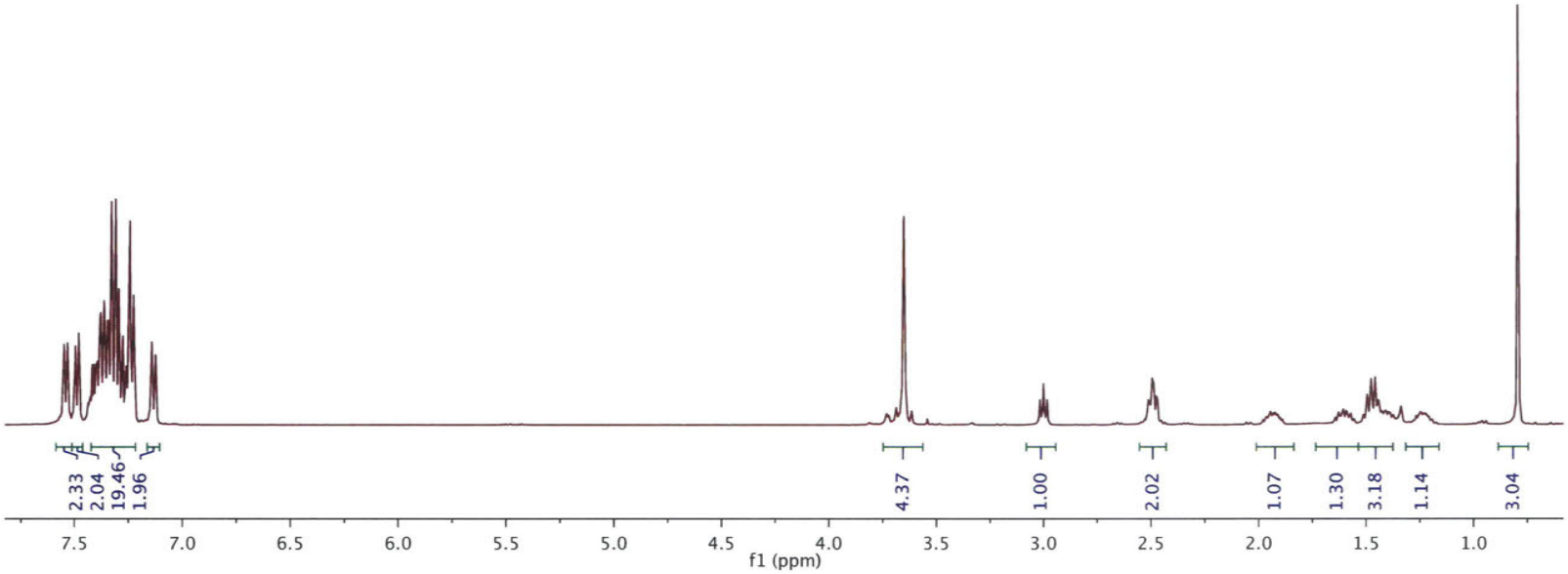

1.98
16.52
2.00
4.07
1.91
1.07
1.01
4.14
1.13
5.97
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

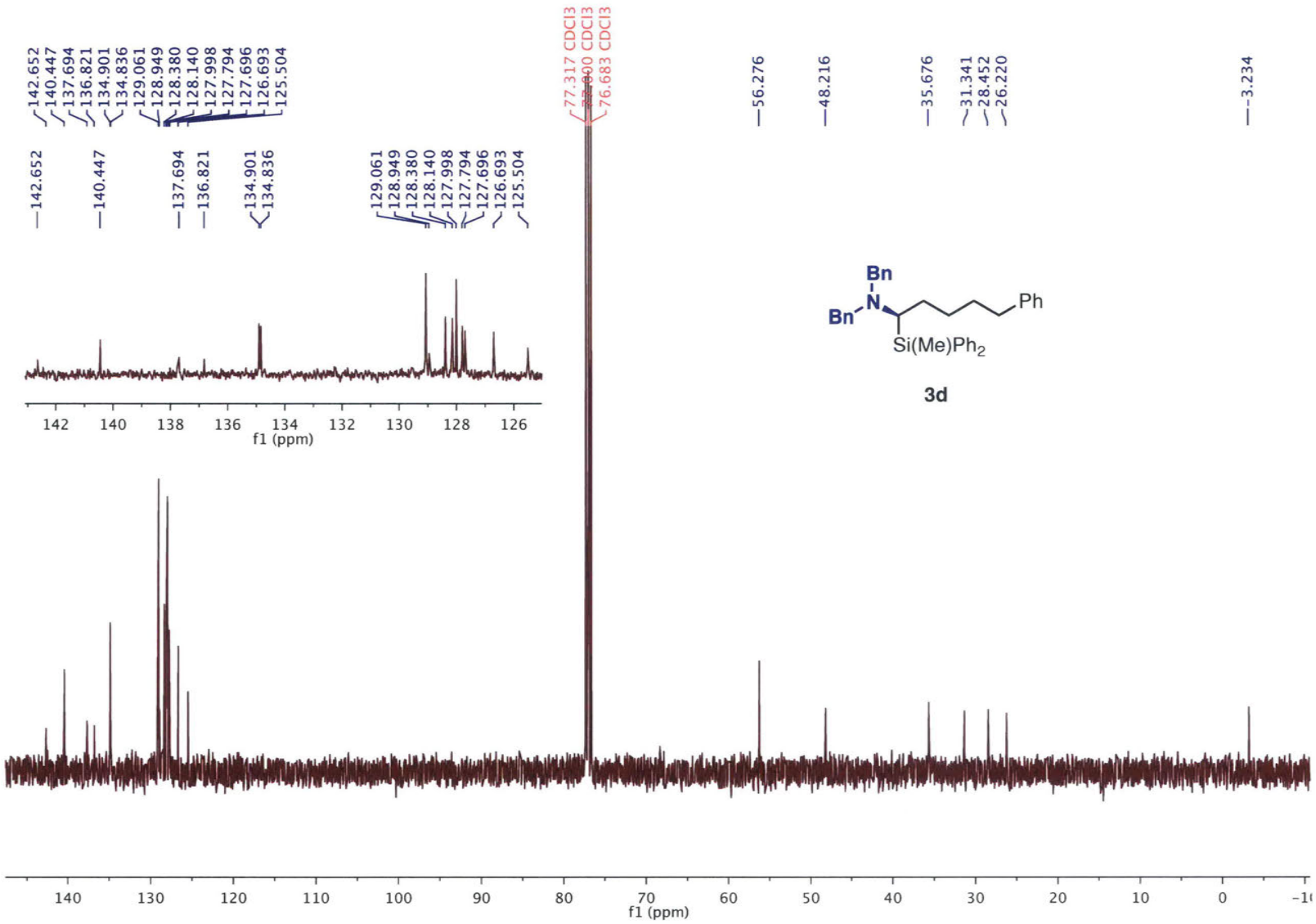

142.711
140.605
133.989
128.894
128.759
128.405
128.158
128.034
127.690
126.658
125.532
77.317 CDCl3
76.999 CDCl3
76.682 CDCl3
56.309
49.474
35.748
31.424
28.435
25.996
1.591
2.658
Bn
N
Bn
Ph
Si(Me)2Ph
3c
f1 (ppm)

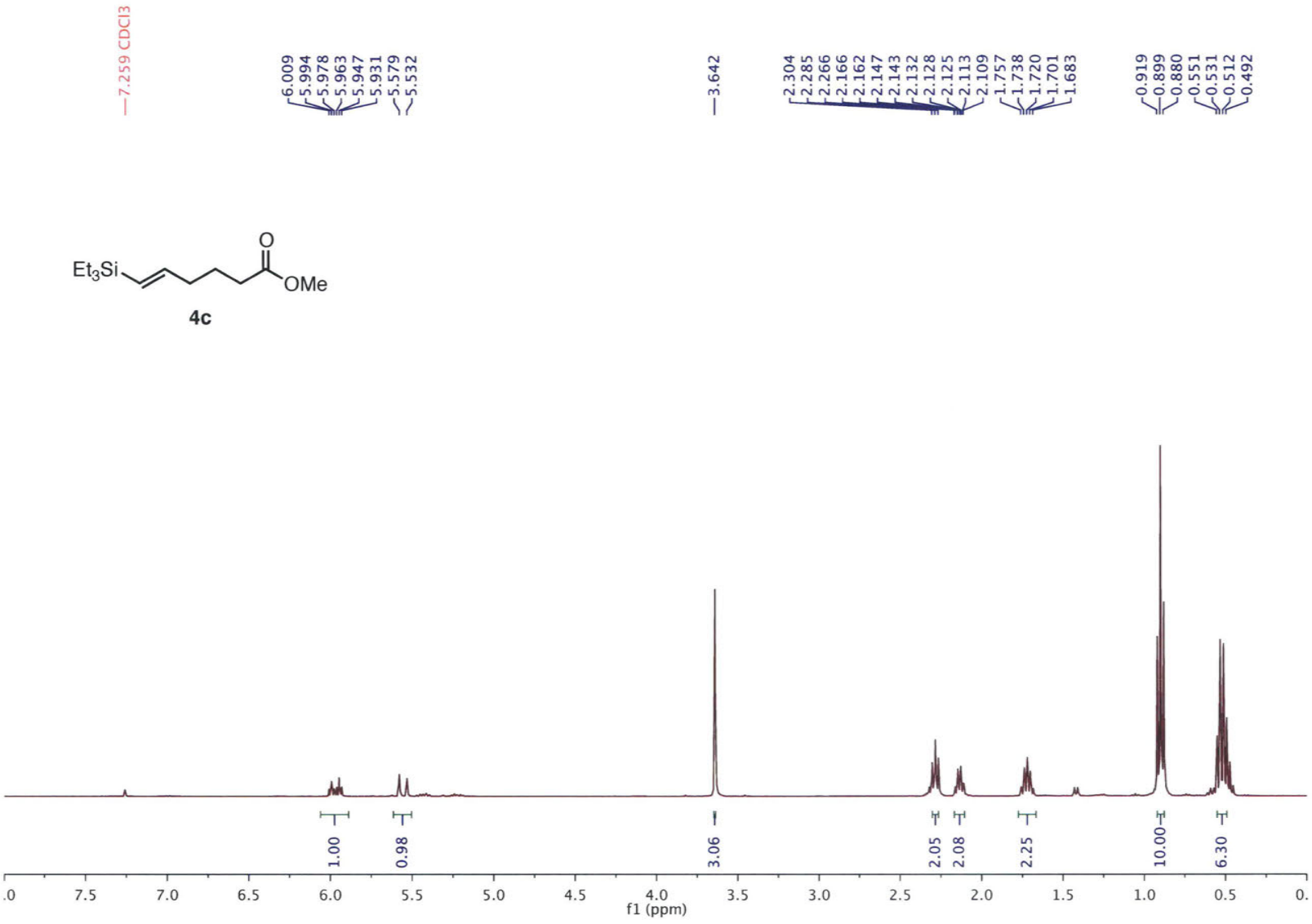

7.552
7.548
7.544
7.538
7.533
7.528
7.500
7.496
7.493
7.480
7.476
7.419
7.411
7.404
7.401
7.397
7.393
7.389
7.382
7.378
7.368
7.363
7.359
7.348
7.343
7.338
7.328
7.323
7.313
7.310
7.298
7.295
7.290
7.283
7.277
7.267
7.262
7.258
7.248
7.243
7.237
7.231
7.227
7.224
7.146
7.142
7.137
7.129
7.125
7.123
3.653
3.017
3.001
2.998
2.982
2.513
2.505
2.495
2.487
2.475
2.469
1.607
1.604
1.495
1.492
1.476
1.473
1.457
1.445
1.440
1.434
1.410
0.784


Bn
N
Bn
Ph
Si(Me)Ph2

3d


2.33
2.04
19.46
1.96
4.37
1.00
2.02
1.07
1.30
3.18
1.14
3.04
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
f1 (ppm)


142.652
140.447
137.694
136.821
134.901
134.836
129.061
128.949
128.380
128.140
127.998
127.794
127.696
126.693
125.504
77.317 CDCl3
77.000 CDCl3
76.683 CDCl3
56.276
48.216
35.676
31.341
28.452
26.220
3.234
f1 (ppm)
Bn
N
Bn
Ph
Si(Me)Ph2
3d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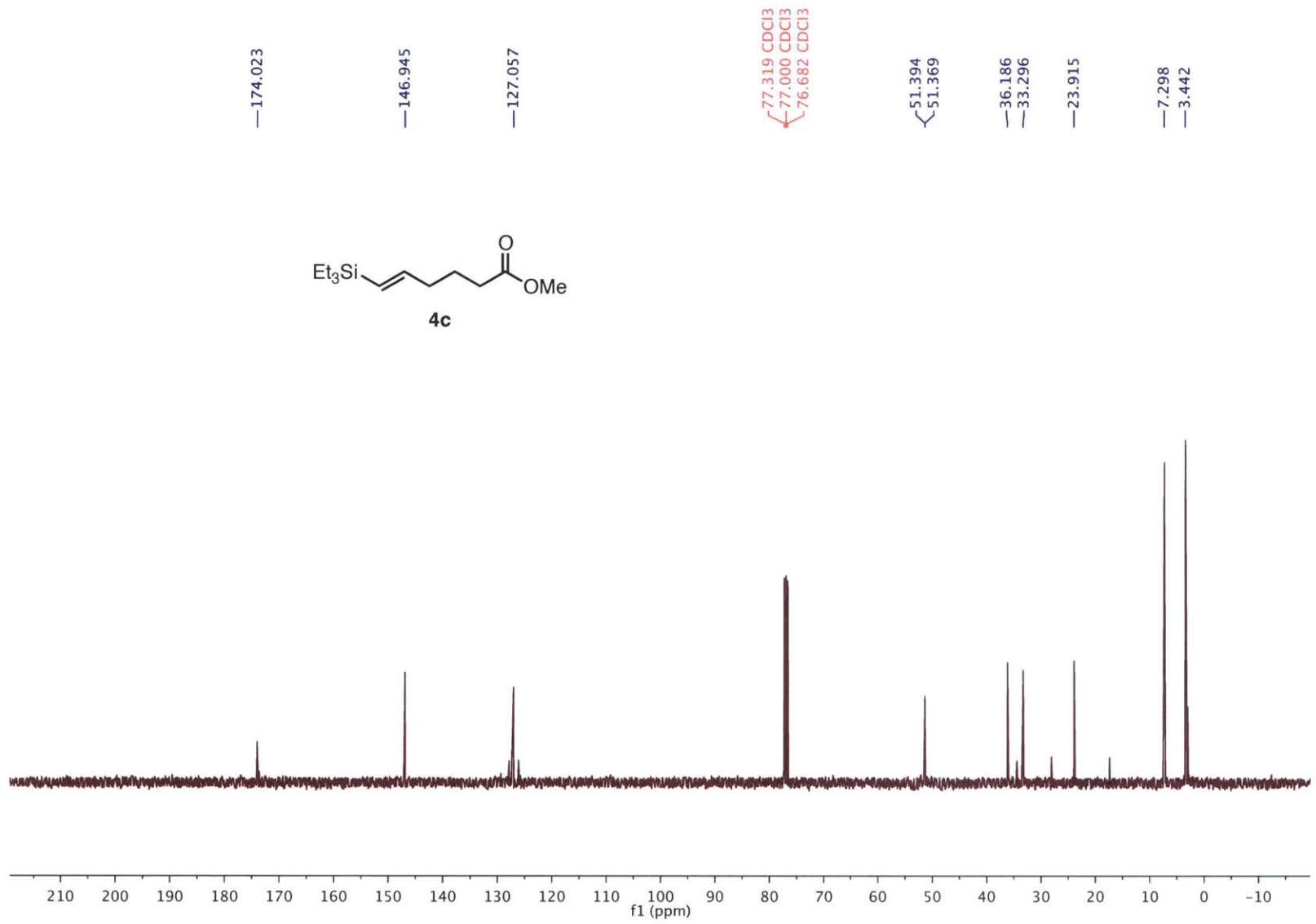
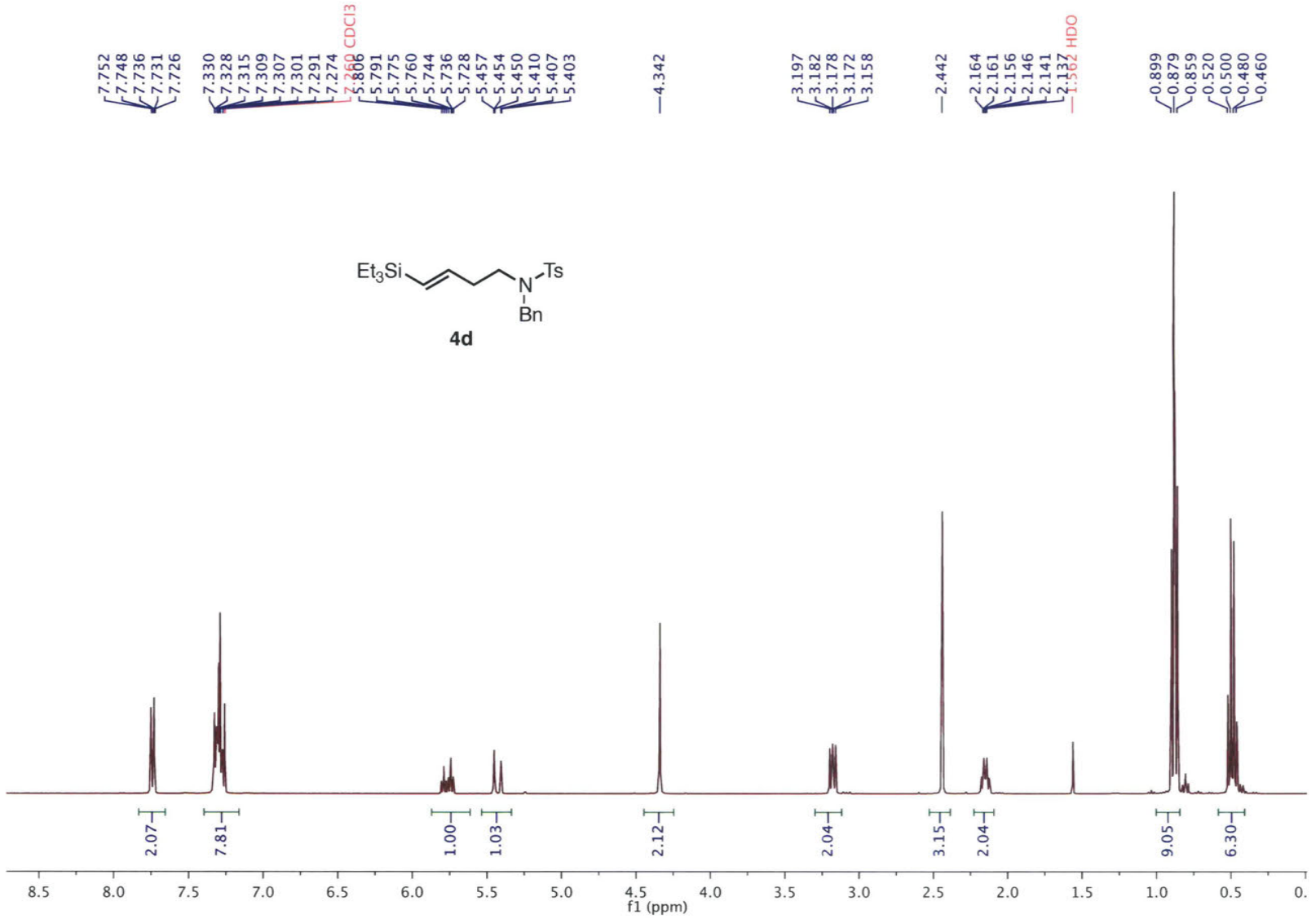
6.009
5.994
5.978
5.963
5.947
5.931
5.579
5.532
3.642
2.304
2.285
2.266
2.166
2.162
2.147
2.143
2.132
2.128
2.125
2.113
2.109
1.757
1.738
1.720
1.701
1.683
0.919
0.899
0.880
0.551
0.531
0.512
0.492
Et3Si
O
OMe
4c
1.00
0.98
3.06
2.05
2.08
2.25
10.00
6.30
f1 (ppm)


174.023
146.945
127.057
77.319 CDCl3
77.000 CDCl3
76.682 CDCl3
51.394
51.369
36.186
33.296
23.915
7.298
3.442
Et3Si
O
OMe
4c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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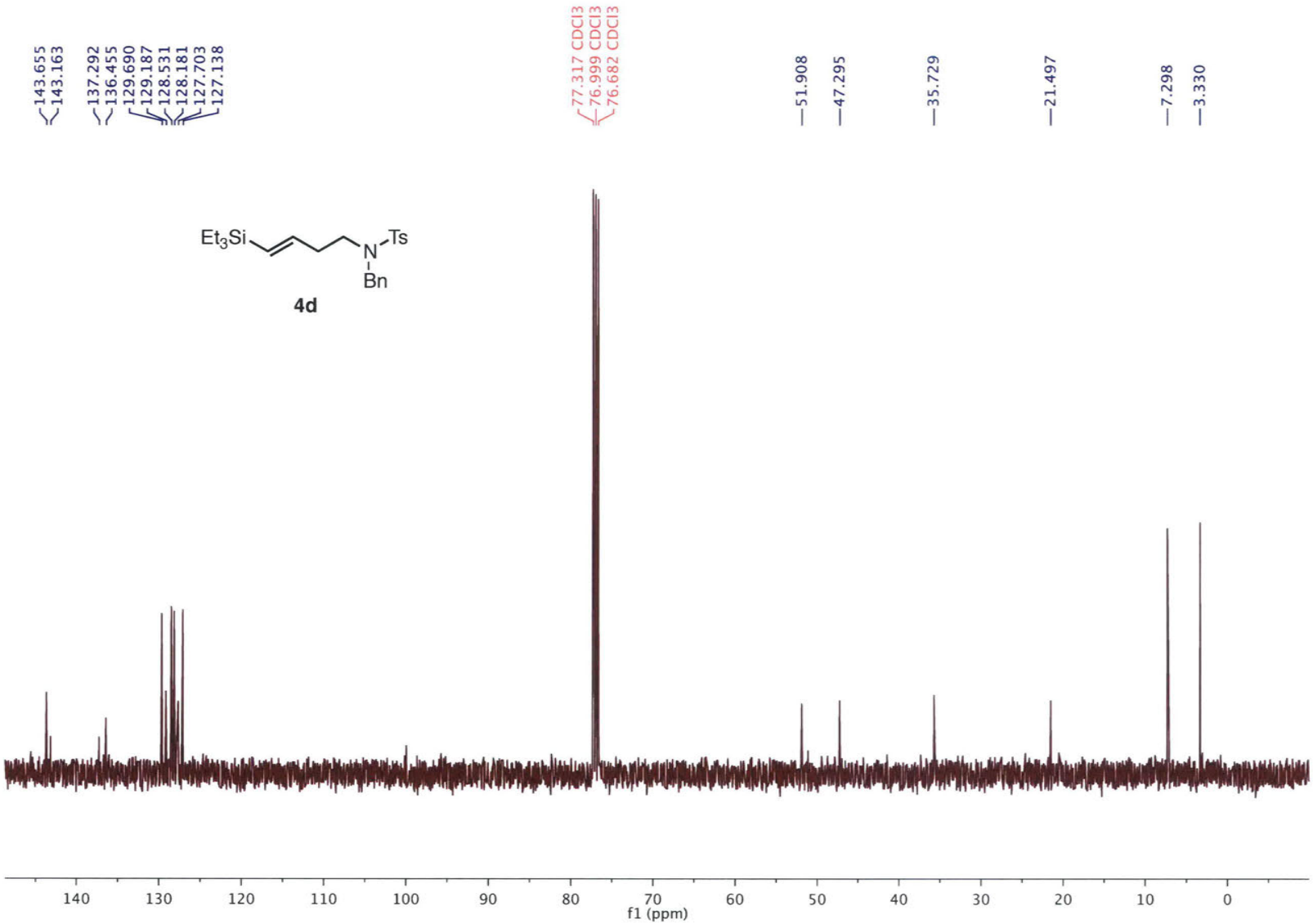
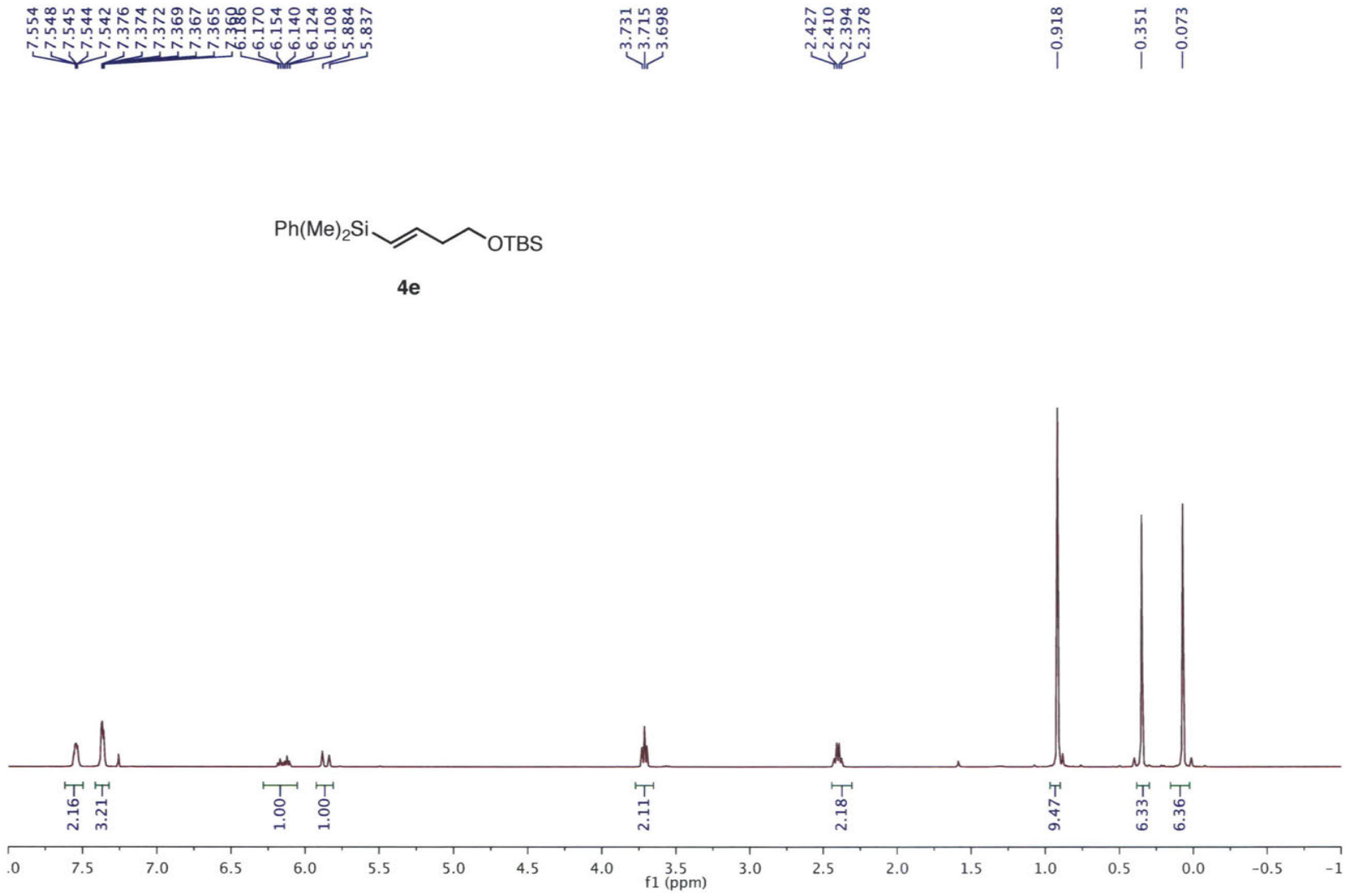
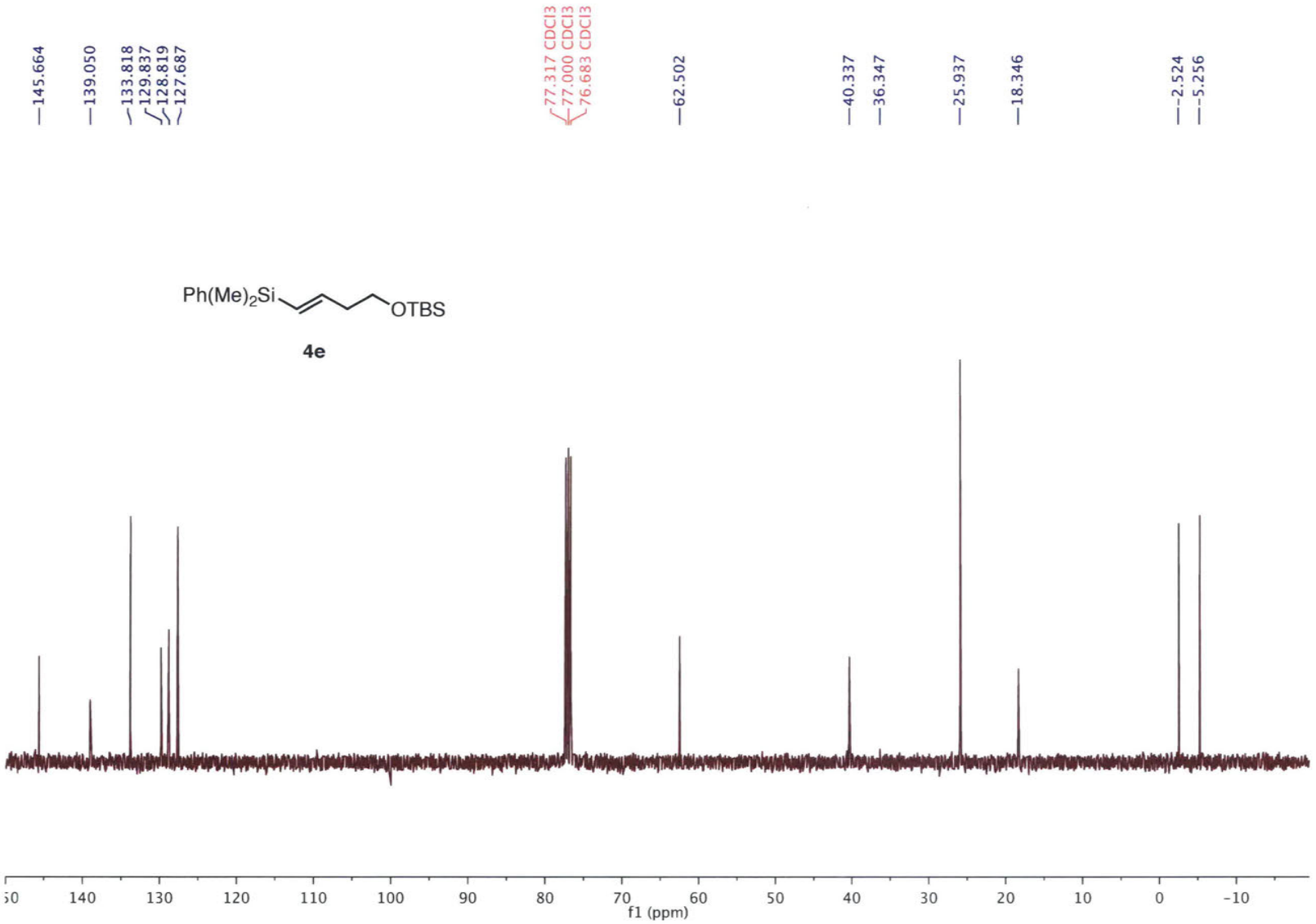
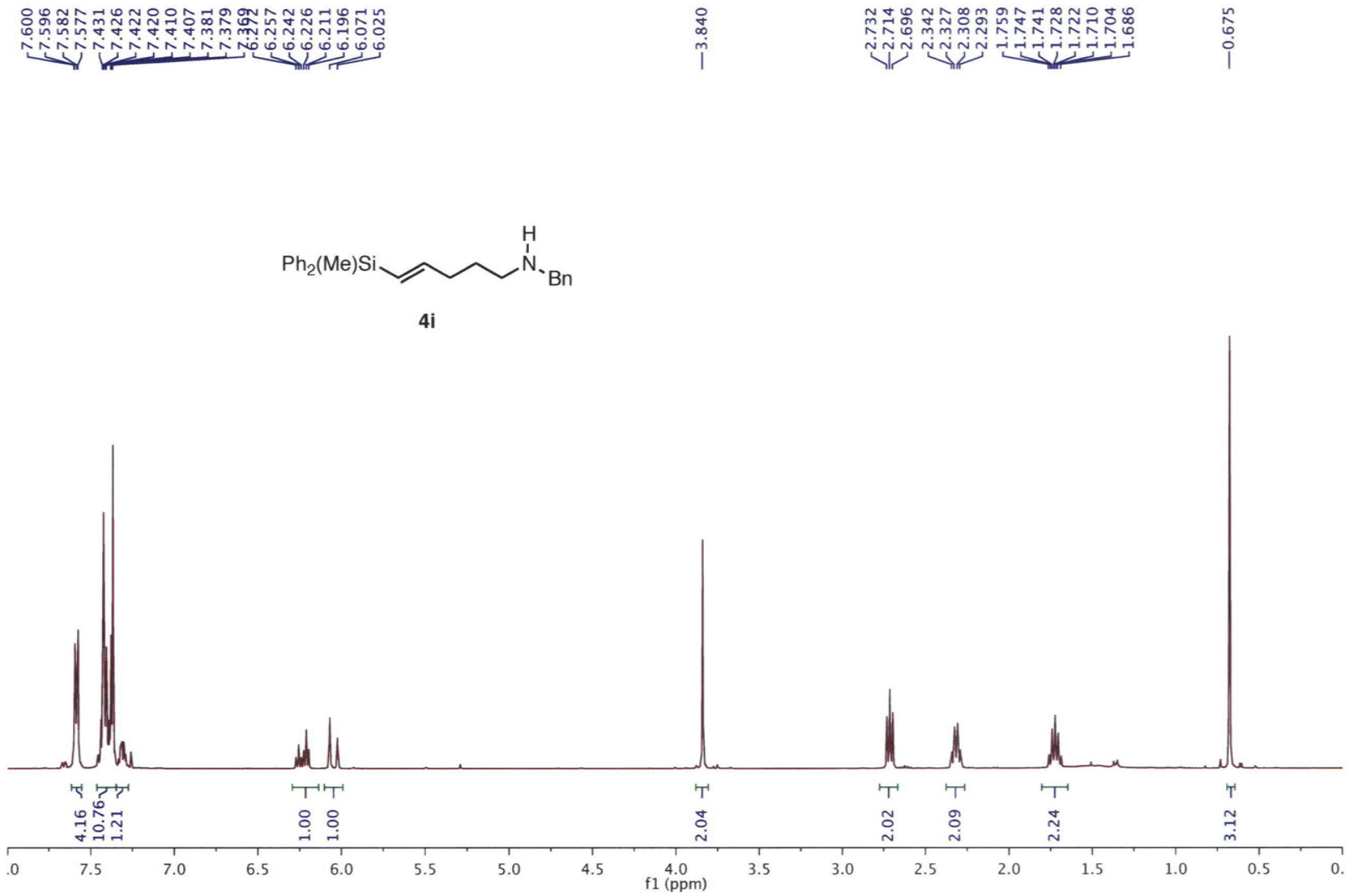
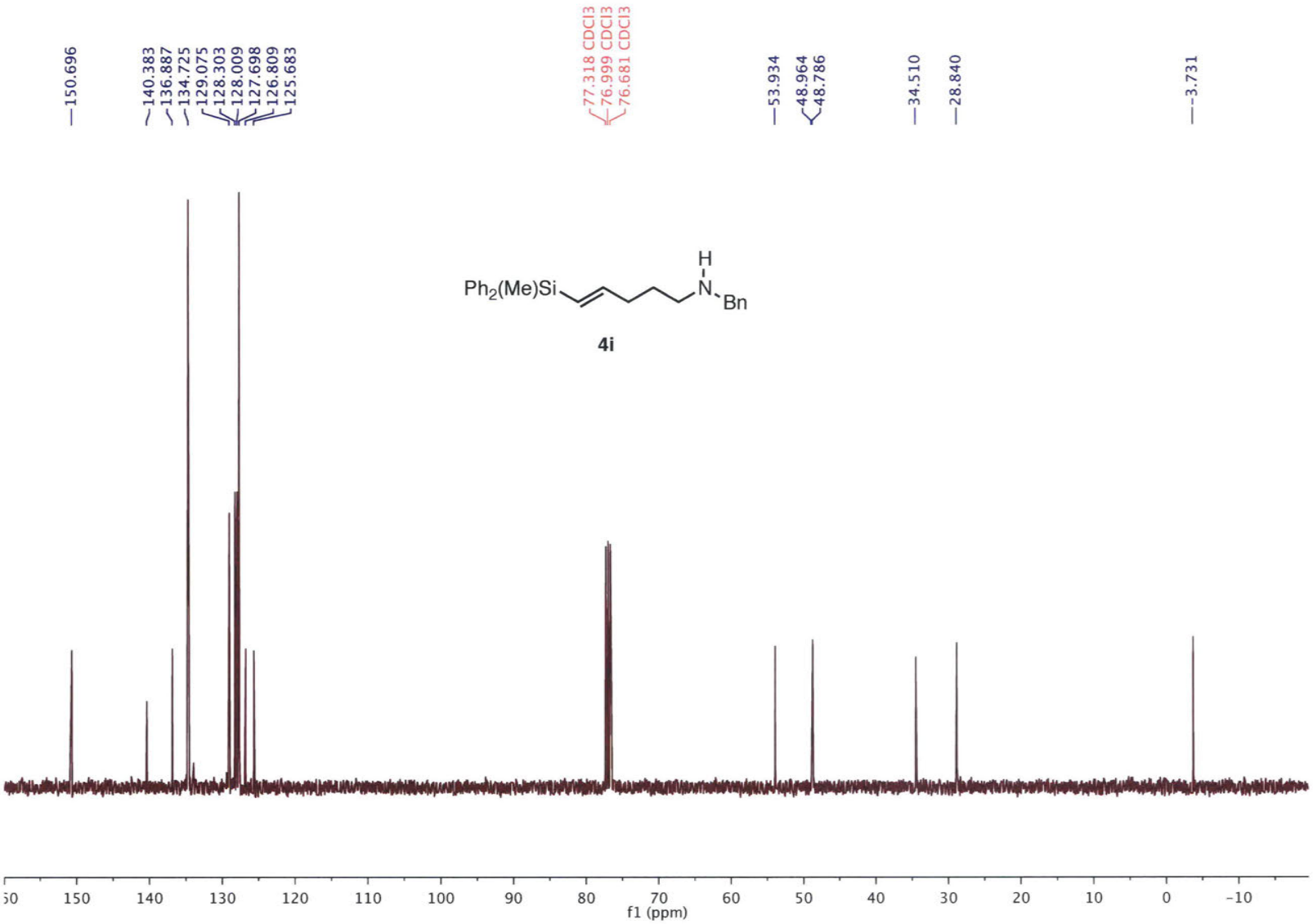
7.736
7.731
7.726
7.330
7.328
7.315
7.309
7.307
7.301
7.291
7.274
7.260 CDCl3
5.806
5.791
5.775
5.760
5.744
5.736
5.728
5.457
5.454
5.450
5.410
5.407
5.403
4.342
3.197
3.182
3.178
3.172
3.158
2.442
2.164
2.161
2.156
2.146
2.141
2.137
1.582 HDO
0.899
0.879
0.859
0.520
0.500
0.480
0.460
Et3Si
N
Ts
Bn
4d
2.07
7.81
1.00
1.03
2.12
2.04
3.15
2.04
9.05
6.30
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.
f1 (ppm)

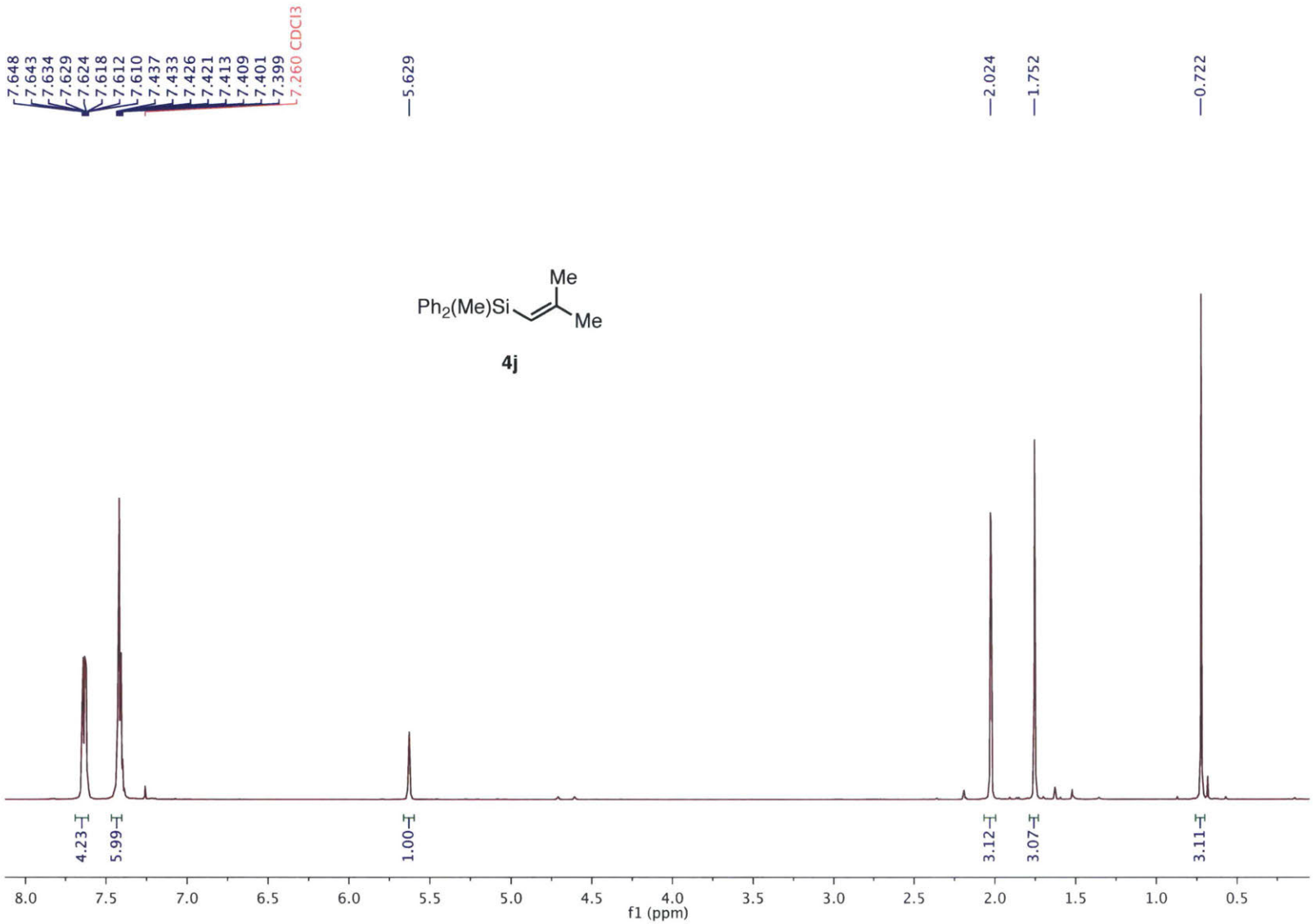

143.655
143.163
137.292
136.455
129.690
129.187
128.531
128.181
127.703
127.138
77.317 CDCl3
76.999 CDCl3
76.682 CDCl3
51.908
47.295
35.729
21.497
7.298
3.330
Et3Si
N
Ts
Bn
4d
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

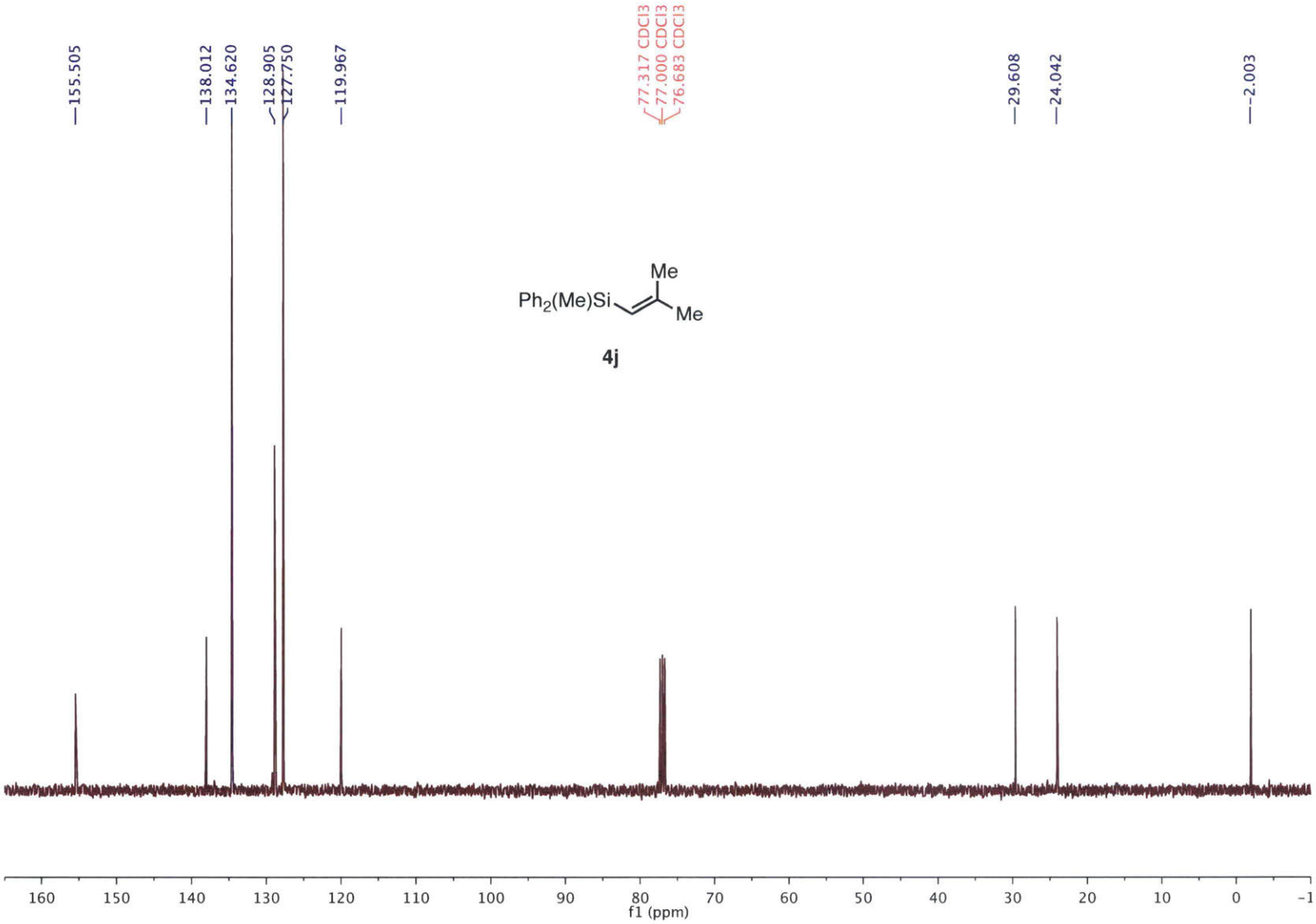

7.554
7.548
7.545
7.544
7.542
7.376
7.374
7.372
7.369
7.367
7.365
7.360
6.170
6.154
6.140
6.124
6.108
5.884
5.837
3.731
3.715
3.698
2.427
2.410
2.394
2.378
0.918
0.351
0.073
Ph(Me)2Si
OTBS
4e
2.16
3.21
1.00
1.00
2.11
2.18
9.47
6.33
6.36
f1 (ppm)

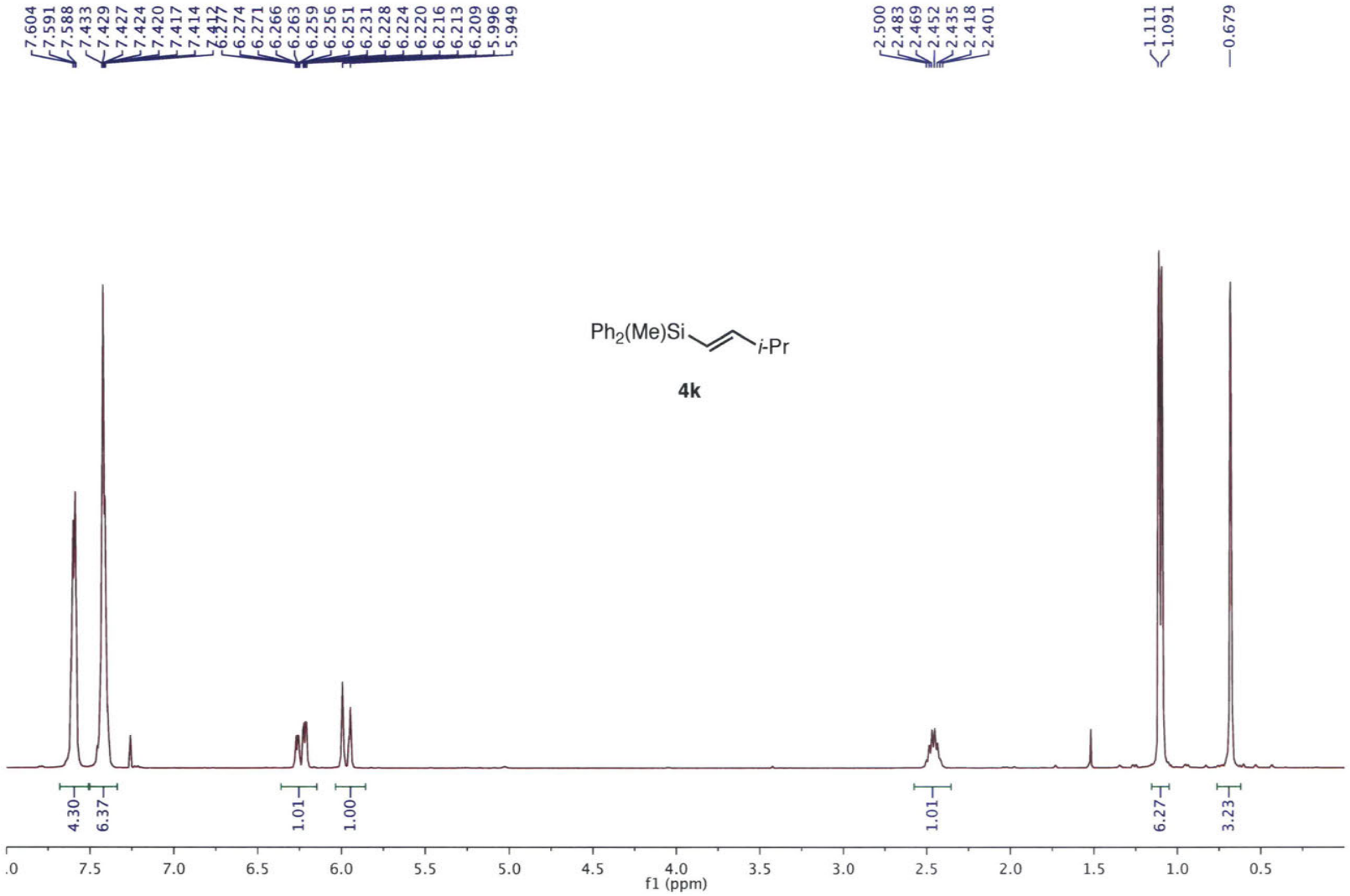

145.664
139.050
133.818
129.837
128.819
127.687
77.317 CDCl3
77.000 CDCl3
76.683 CDCl3
62.502
40.337
36.347
25.937
18.346
-2.524
-5.256
Ph(Me)2Si
OTBS
4e
f1 (ppm)


7.600
7.596
7.582
7.577
7.431
7.426
7.422
7.420
7.410
7.407
7.381
7.379
6.257
6.242
6.226
6.211
6.196
6.071
6.025
3.840
2.732
2.714
2.696
2.342
2.327
2.308
2.293
1.759
1.747
1.741
1.728
1.722
1.710
1.704
1.686
0.675
Ph2(Me)Si
H
N
Bn
4i
4.16
10.76
1.21
1.00
1.00
2.04
2.02
2.09
2.24
3.12
f1 (ppm)


150.696
140.383
136.887
134.725
129.075
128.303
128.009
127.698
126.809
125.683
77.318 CDCl3
76.999 CDCl3
76.681 CDCl3
53.934
48.964
48.786
34.510
28.840
3.731
Ph2(Me)Si
H
N
Bn
4i
f1 (ppm)


7.648
7.643
7.634
7.629
7.624
7.618
7.612
7.610
7.437
7.433
7.426
7.421
7.413
7.409
7.401
7.399
7.260 CDCl3
5.629
2.024
1.752
0.722
Me
Ph2(Me)Si
Me
4j
4.23
5.99
1.00
3.12
3.07
3.11
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
f1 (ppm)


155.505
138.012
134.620
128.905
127.750
119.967
77.317 CDCl3
77.000 CDCl3
76.683 CDCl3
29.608
24.042
2.003
Me
Ph2(Me)Si
Me
4j
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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6.266
6.263
6.259
6.256
6.251
6.231
6.228
6.224
6.220
6.216
6.213
6.209
5.996
5.949
2.500
2.483
2.469
2.452
2.435
2.418
2.401
1.111
1.091
0.679
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i-Pr
4k
4.30
6.37
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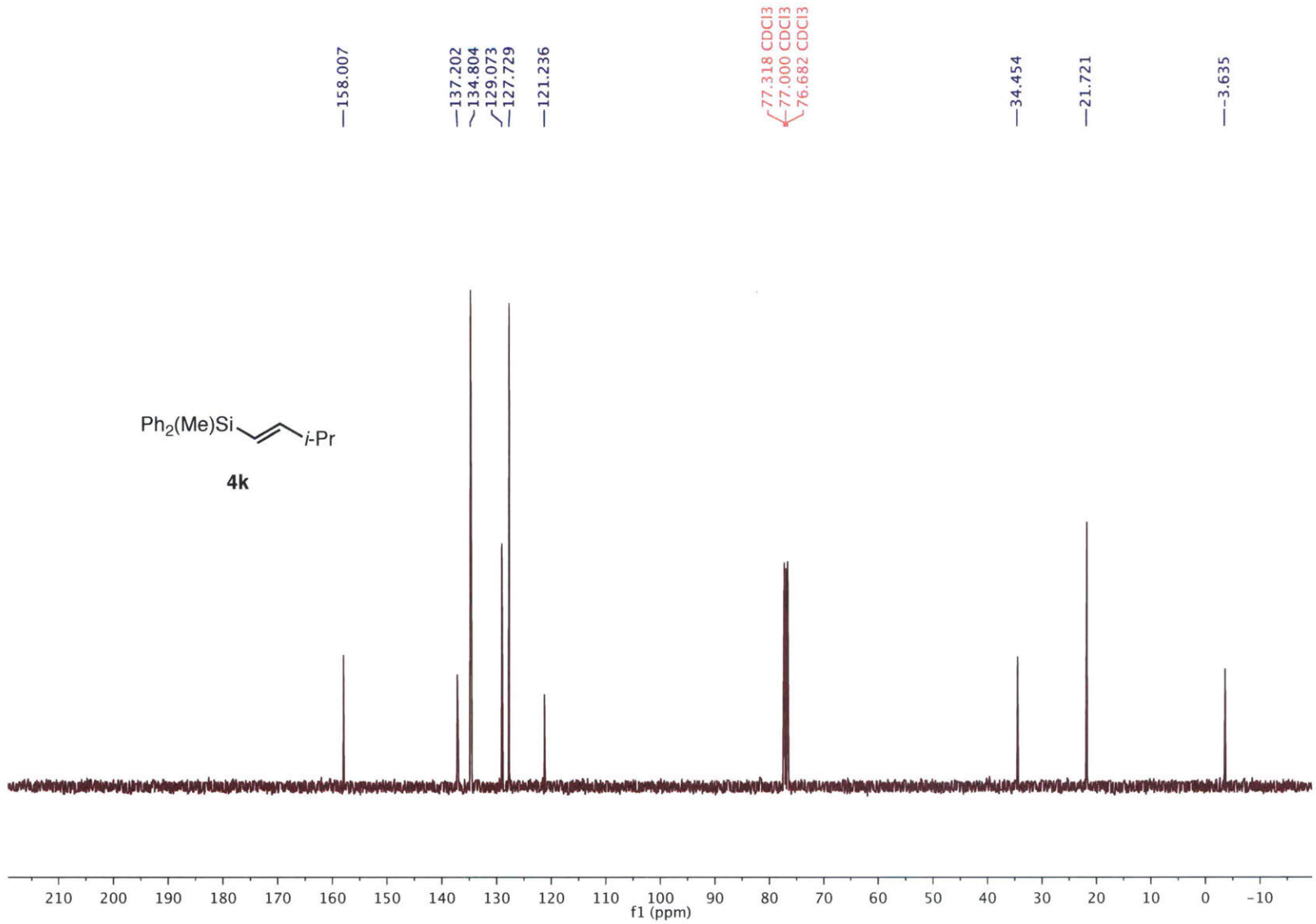
1.00
1.01
6.27
3.23
f1 (ppm)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77.000 CDCl3
76.682 CDCl3
34.454
21.721
-3.635
Ph2(Me)Si
i-Pr
4k
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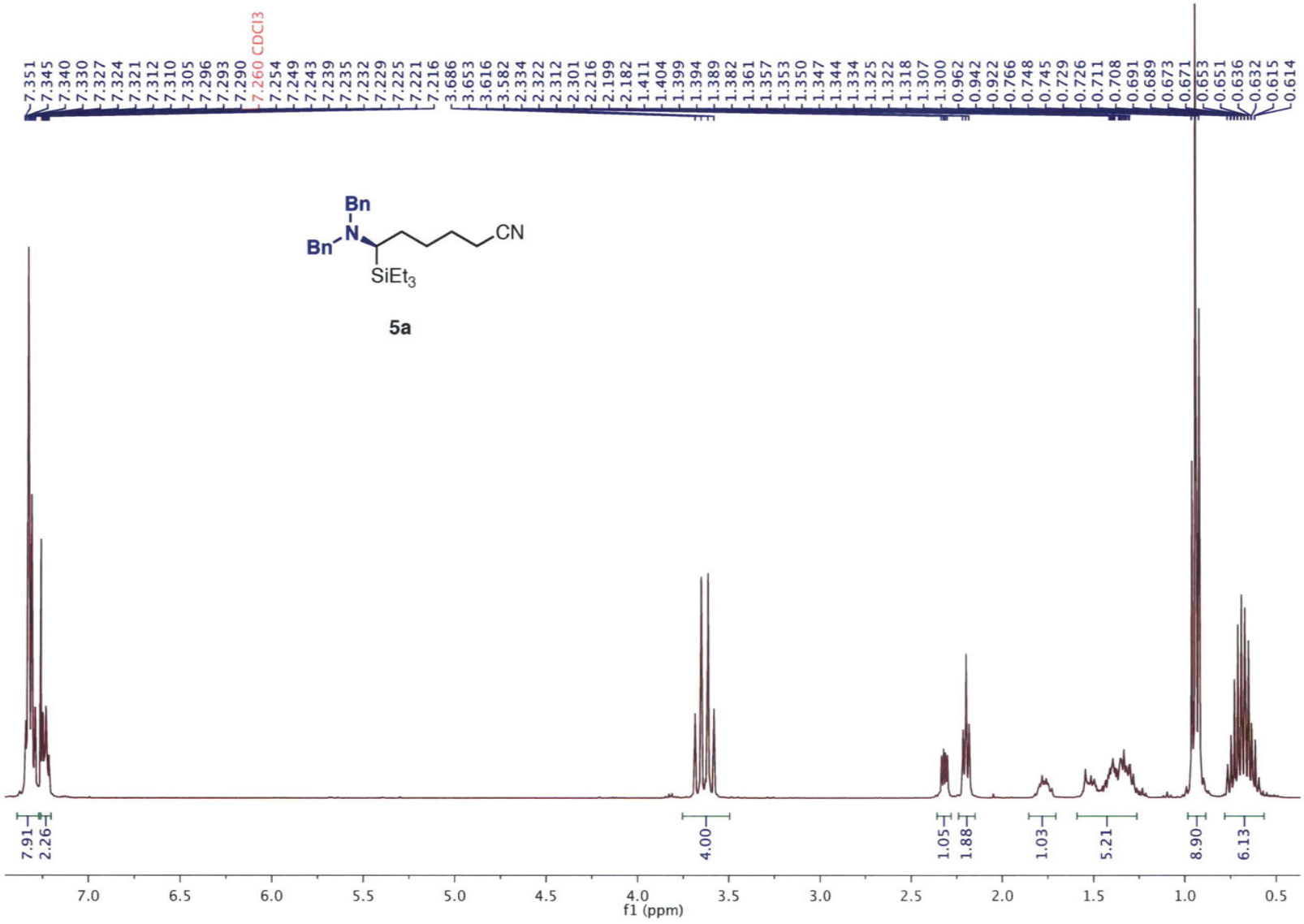
f1 (ppm)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7.260 CDCl3
7.254
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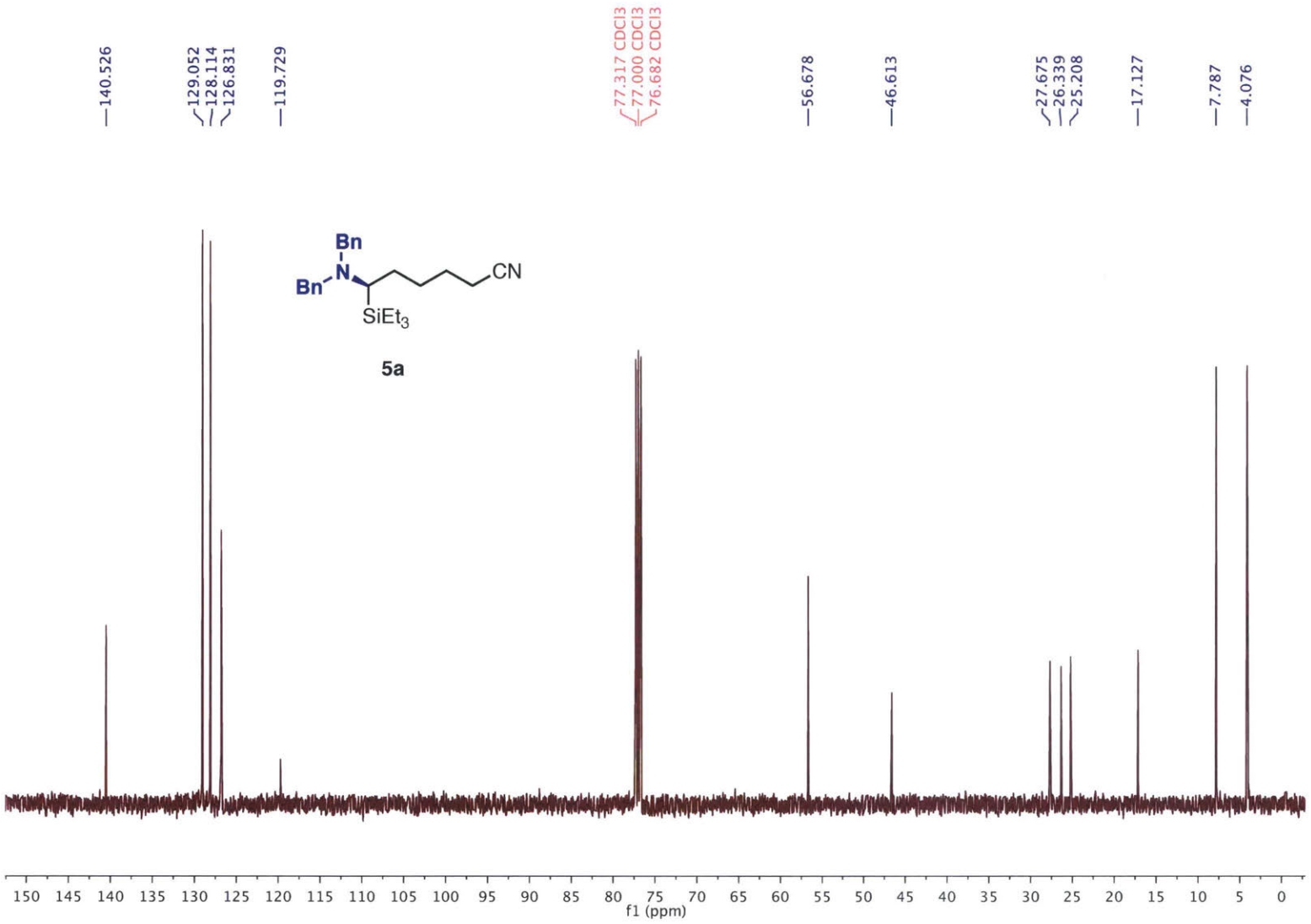
7.243
7.239
7.235
7.232
7.229
7.225
7.221
7.216
3.686
3.653
3.616
3.582
2.334
2.322
2.312
2.301
2.216
2.199
2.182
1.411
1.404
1.399
1.394
1.389
1.382
1.361
1.357
1.353
1.350
1.347
1.344
1.334
1.325
1.322
1.318
1.307
1.300
0.962
0.942
0.922
0.766
0.748
0.745
0.729
0.726
0.711
0.708
0.691
0.689
0.673
0.671
0.653
0.651
0.636
0.632
0.615
0.614
Bn
N
Bn
CN
SiEt3
5a
7.91
2.26
4.00
1.05
1.88
1.03
5.21
8.90
6.13
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
f1 (ppm)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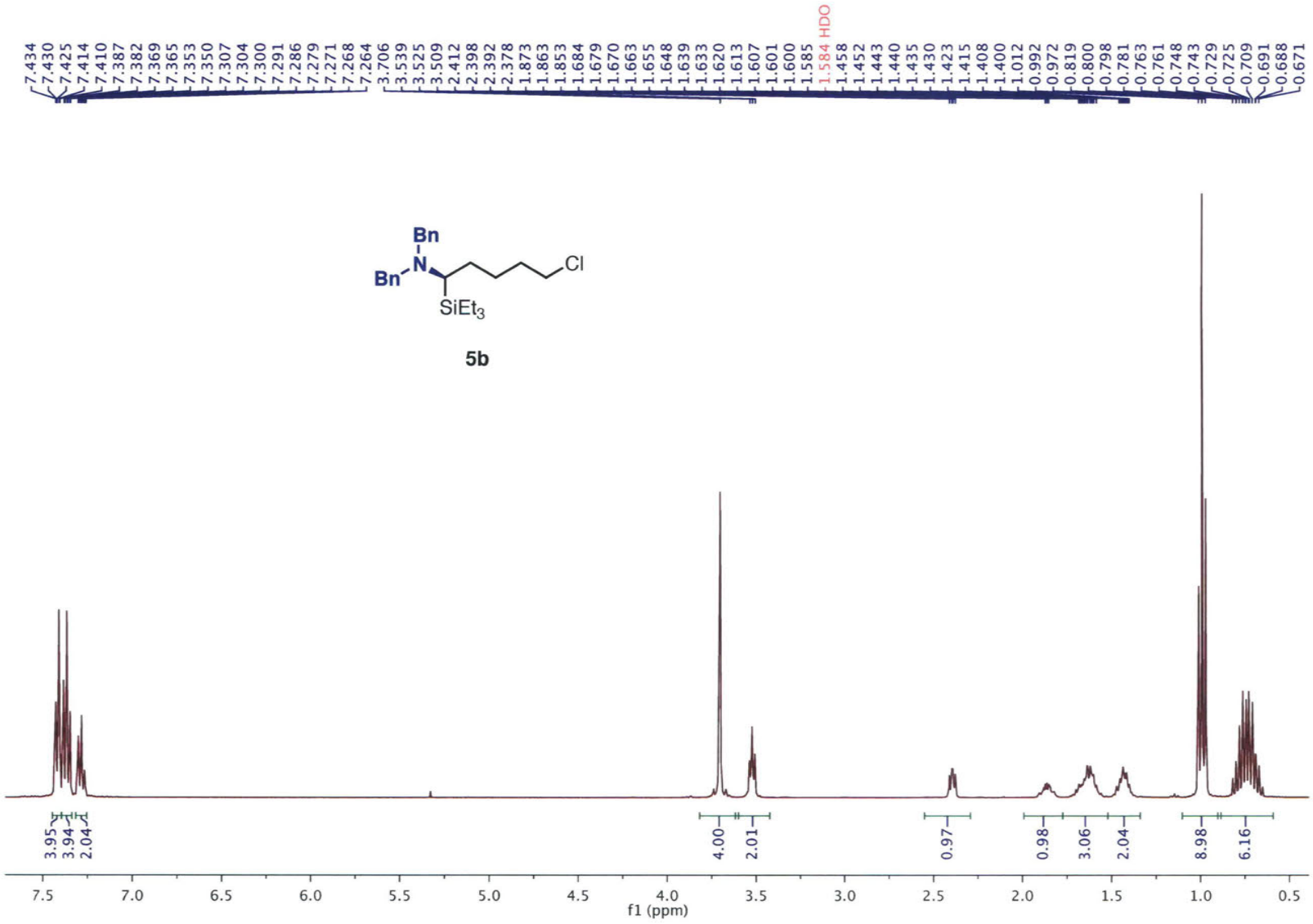
128.114
126.831
119.729
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
56.678
46.613
27.675
26.339
25.208
17.127
7.787
4.076
Bn
N
Bn
CN
SiEt3
5a
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)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7.304
7.300
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7.286
7.279
7.271
7.268
7.264
3.706
3.539
3.525
3.509
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2.392
2.378
1.873
1.863
1.853
1.684
1.679
1.670
1.663
1.655
1.648
1.639
1.633
1.620
1.613
1.607
1.601
1.600
1.585
1.584 HDO
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1.452
1.443
1.440
1.435
1.430
1.423
1.415
1.408
1.400
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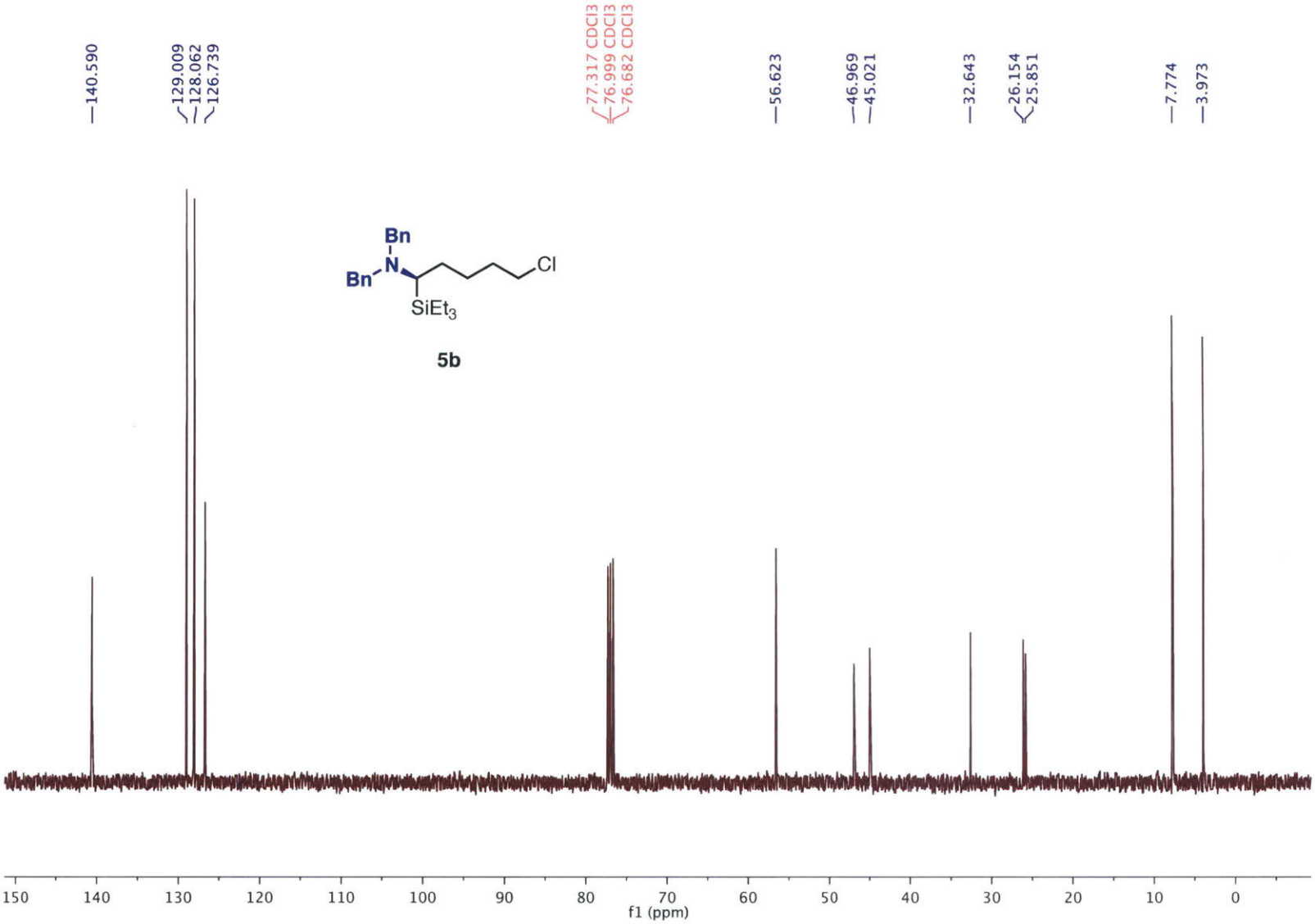
0.992
0.972
0.819
0.800
0.798
0.781
0.763
0.761
0.748
0.743
0.729
0.725
0.709
0.691
0.688
0.671
Bn
N
Bn
Cl
SiEt3
5b
3.95
3.94
2.04
4.00
2.01
0.97
0.98
3.06
2.04
8.98
6.16
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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128.062
126.739
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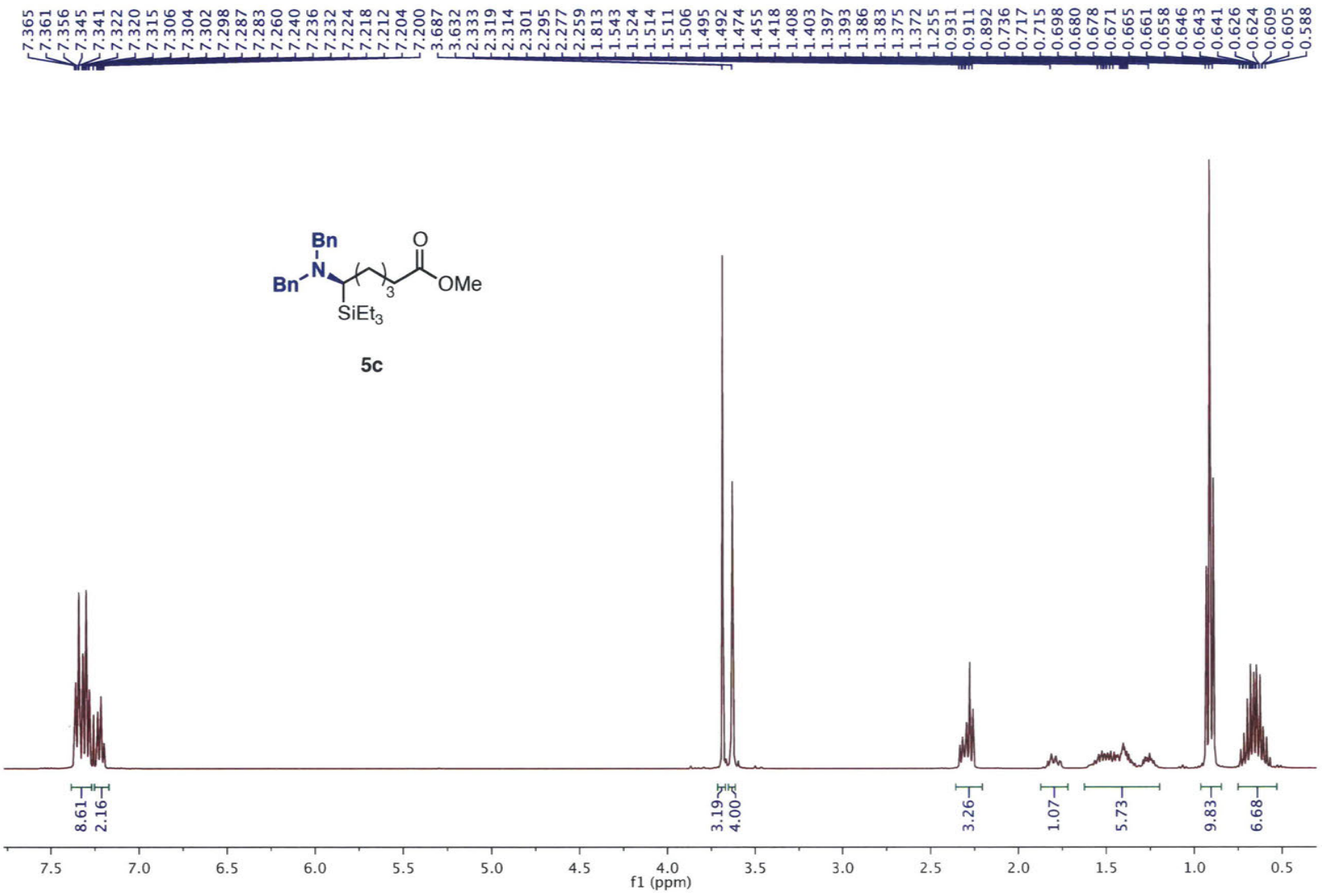
76.999 CDCl3
76.682 CDCl3
56.623
46.969
45.021
32.643
26.154
25.851
7.774
3.973
Bn
N
Bn
Cl
SiEt3
5b
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.315
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7.302
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7.287
7.283
7.260
7.240
7.236
7.232
7.224
7.218
7.212
7.204
7.200
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3.632
2.333
2.319
2.314
2.301
2.295
2.277
2.259
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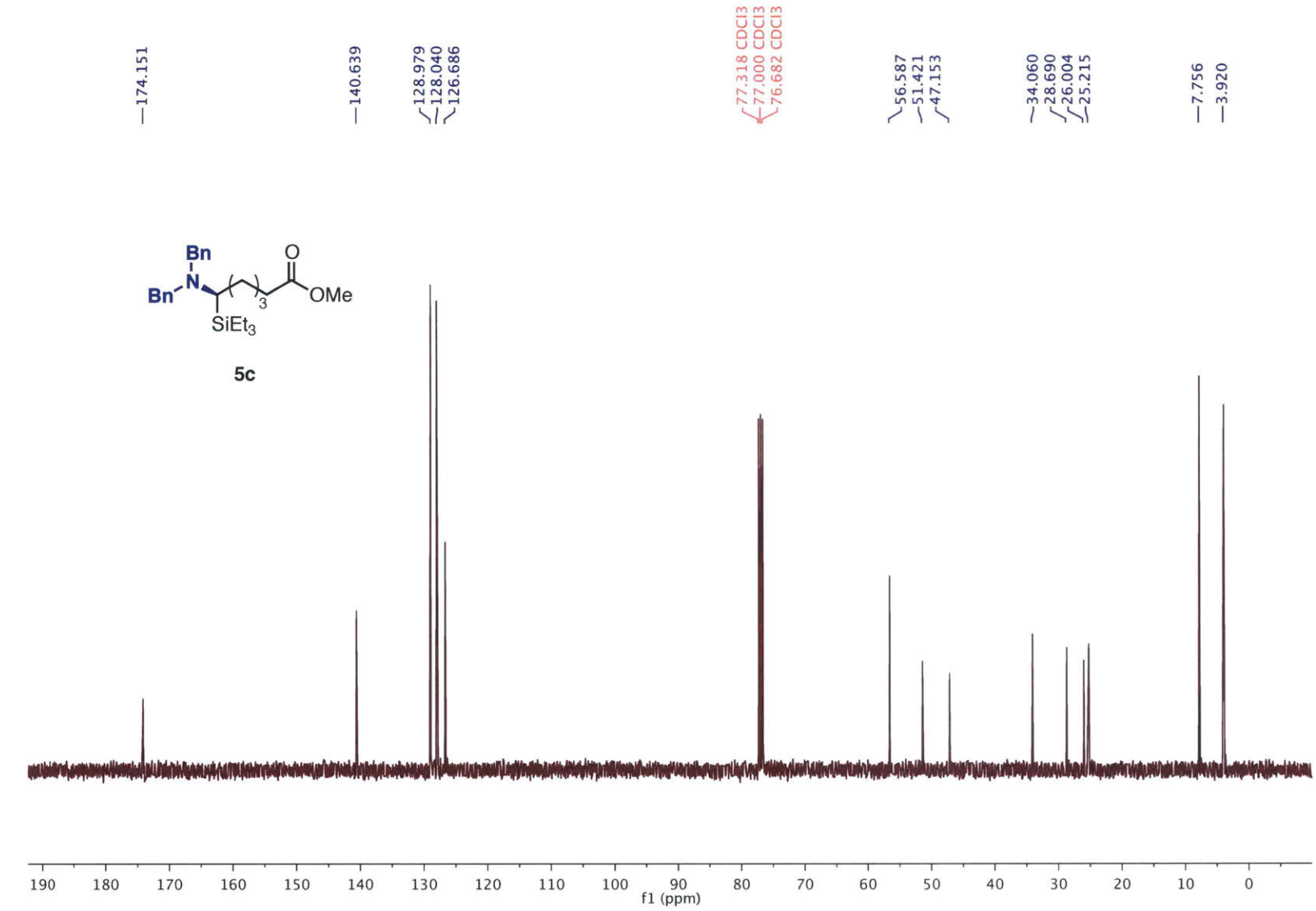
1.543
1.524
1.514
1.511
1.506
1.495
1.492
1.474
1.455
1.418
1.408
1.403
1.397
1.393
1.386
1.383
1.375
1.372
1.255
0.931
0.911
0.892
0.736
0.717
0.715
0.698
0.680
0.678
0.671
0.665
0.661
0.658
0.646
0.643
0.641
0.626
0.624
0.609
0.605
0.588
Bn
N
Bn
O
OMe
3
SiEt3
5c
8.61
2.16
3.19
4.00
3.26
1.07
5.73
9.83
6.68
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
f1 (ppm)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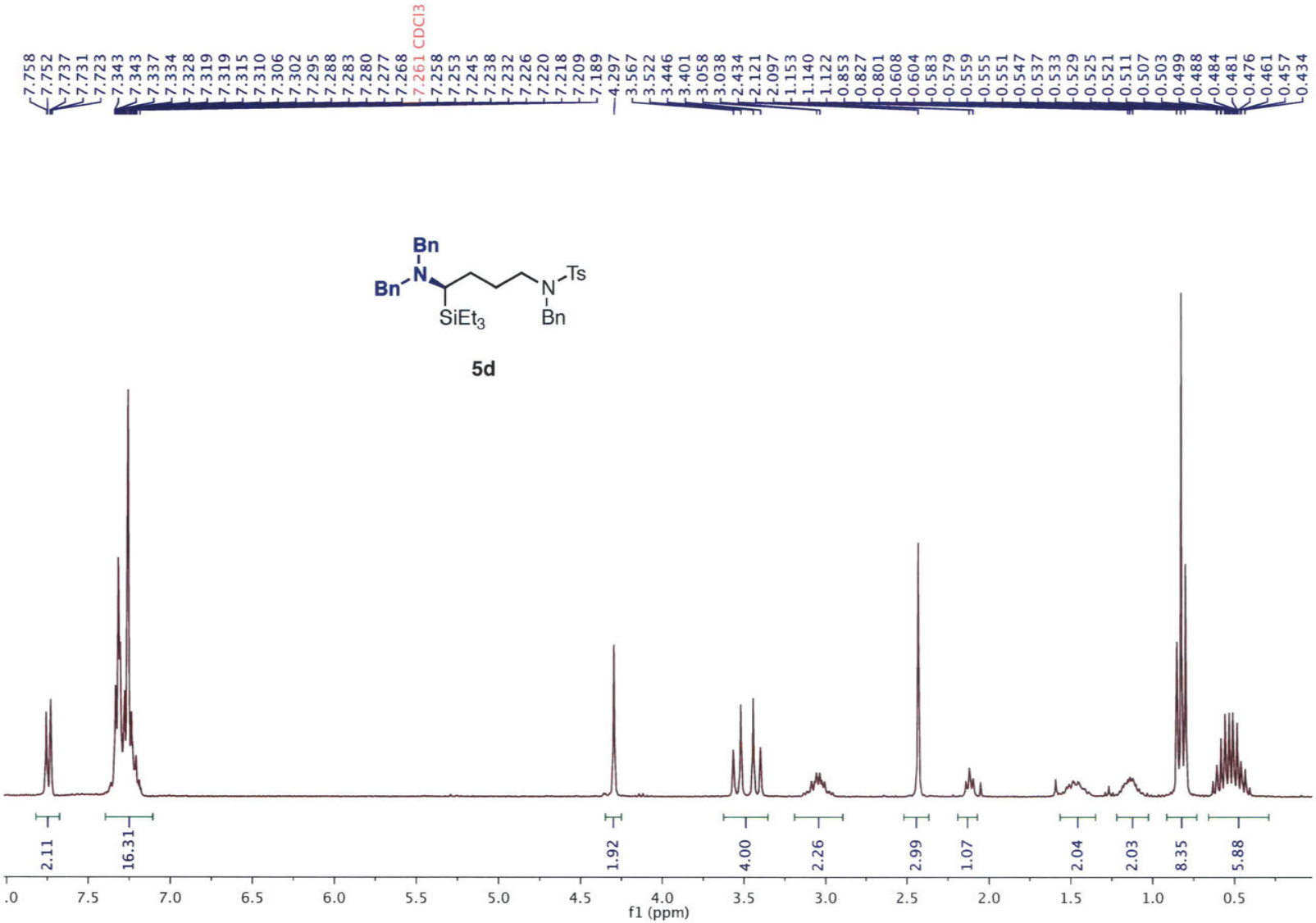
77.000 CDCl3
76.682 CDCl3
56.587
51.421
47.153
34.060
28.690
26.004
25.215
7.756
3.920
Bn
N
Bn
3
OMe
O
SiEt3
5c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.319
7.315
7.310
7.306
7.302
7.295
7.288
7.283
7.280
7.277
7.268
7.261 CDCl3
7.258
7.253
7.245
7.238
7.232
7.226
7.220
7.218
7.209
7.189
4.297
3.567
3.522
3.446
3.401
3.058
3.038
2.434
2.121
2.097
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1.140
1.122
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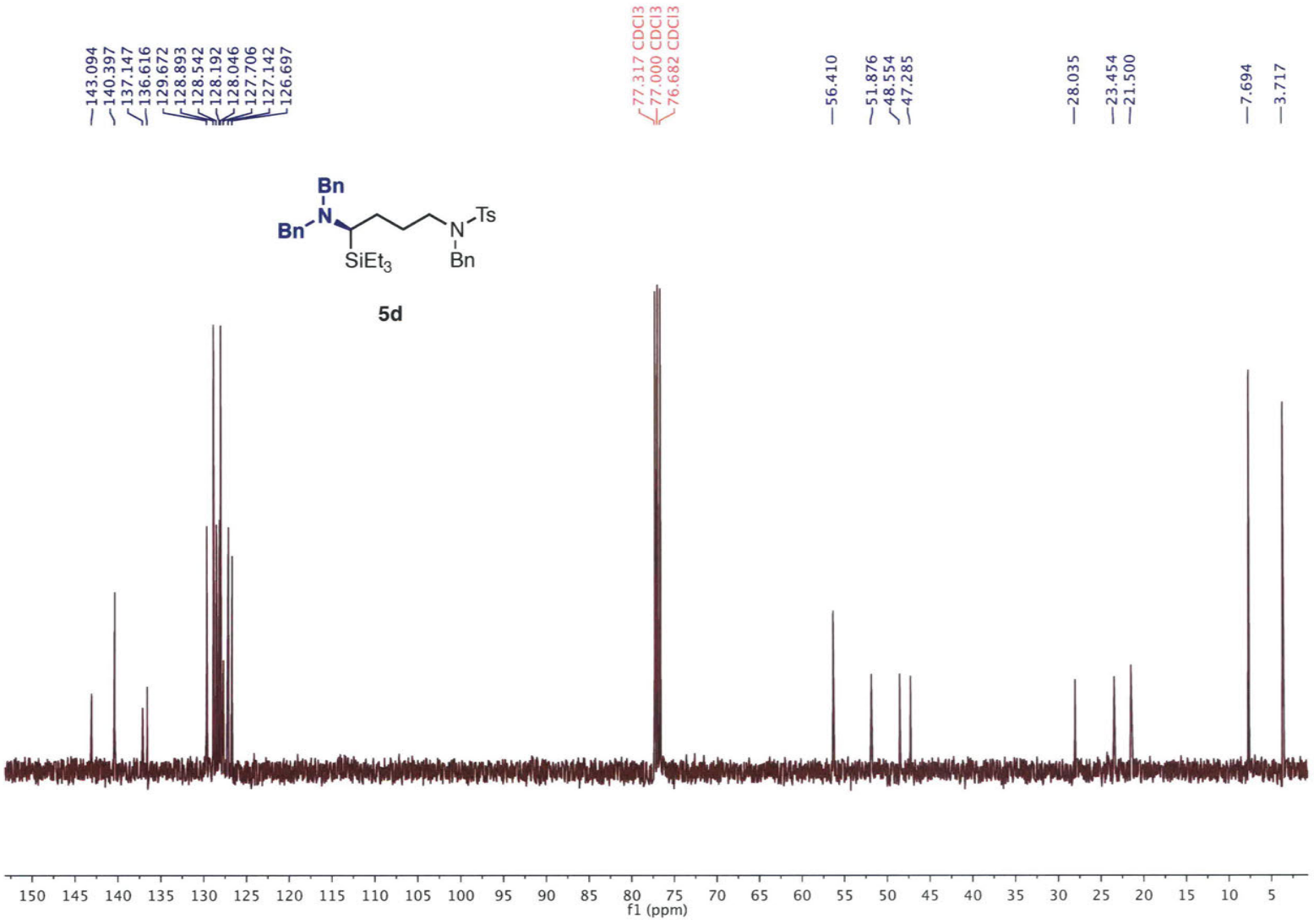
0.827
0.801
0.608
0.604
0.583
0.579
0.559
0.555
0.551
0.547
0.537
0.533
0.529
0.525
0.521
0.511
0.507
0.503
0.499
0.488
0.484
0.481
0.476
0.461
0.457
0.434
Bn
N
Bn
SiEt3
N
Ts
Bn
5d
2.11
16.31
1.92
4.00
2.26
2.99
1.07
2.04
2.03
8.35
5.88
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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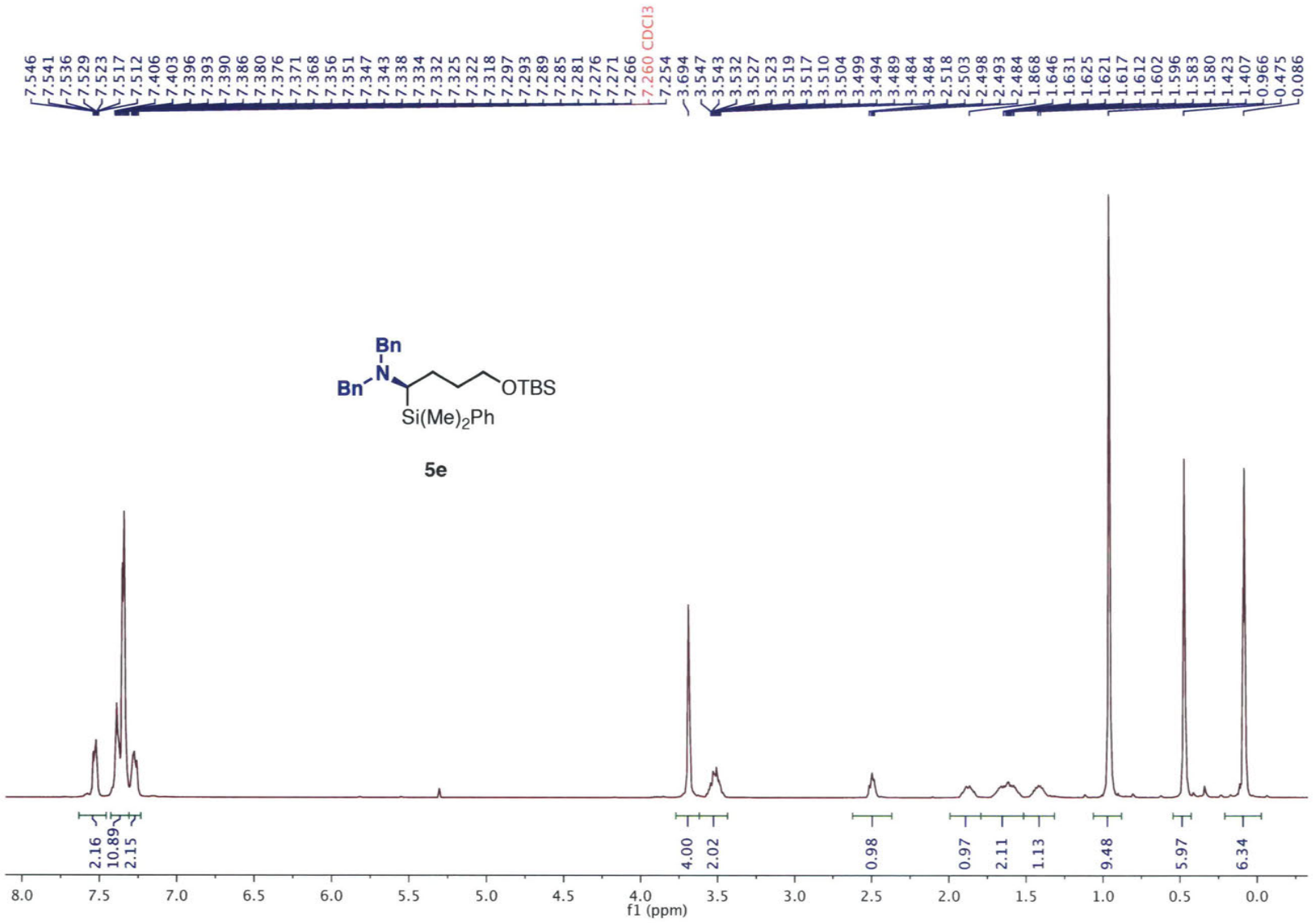
128.192
128.046
127.706
127.142
126.697
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
56.410
51.876
48.554
47.285
28.035
23.454
21.500
7.694
3.717
Bn
N
Bn
SiEt3
N
Ts
Bn
5d
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5
f1 (ppm)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7.356
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7.347
7.343
7.338
7.334
7.332
7.325
7.322
7.318
7.297
7.293
7.289
7.285
7.281
7.276
7.271
7.266
7.260 CDCl3
7.254
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3.547
3.543
3.532
3.527
3.523
3.519
3.517
3.510
3.504
3.499
3.494
3.489
3.484
3.484
2.518
2.503
2.498
2.493
2.484
1.868
1.646
1.631
1.625
1.621
1.617
1.612
1.602
1.596
1.583
1.580
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0.475
0.086
Bn
N
Bn
OTBS
Si(Me)2Ph
5e
2.16
10.89
2.15
4.00
2.02
0.98
0.97
2.11
1.13
9.48
5.97
6.34
8.0
7.5
7.0
6.5
6.0
5.5
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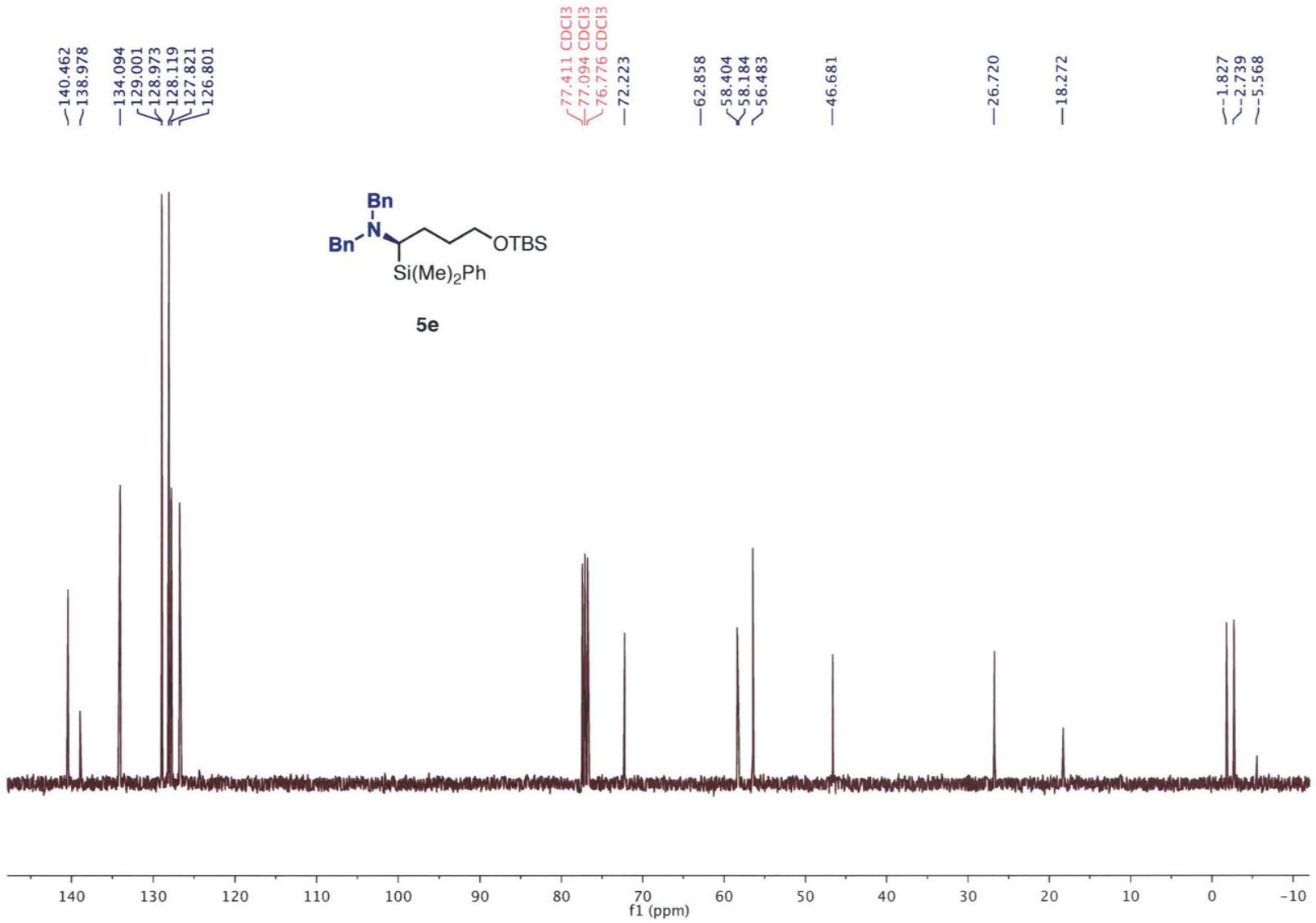
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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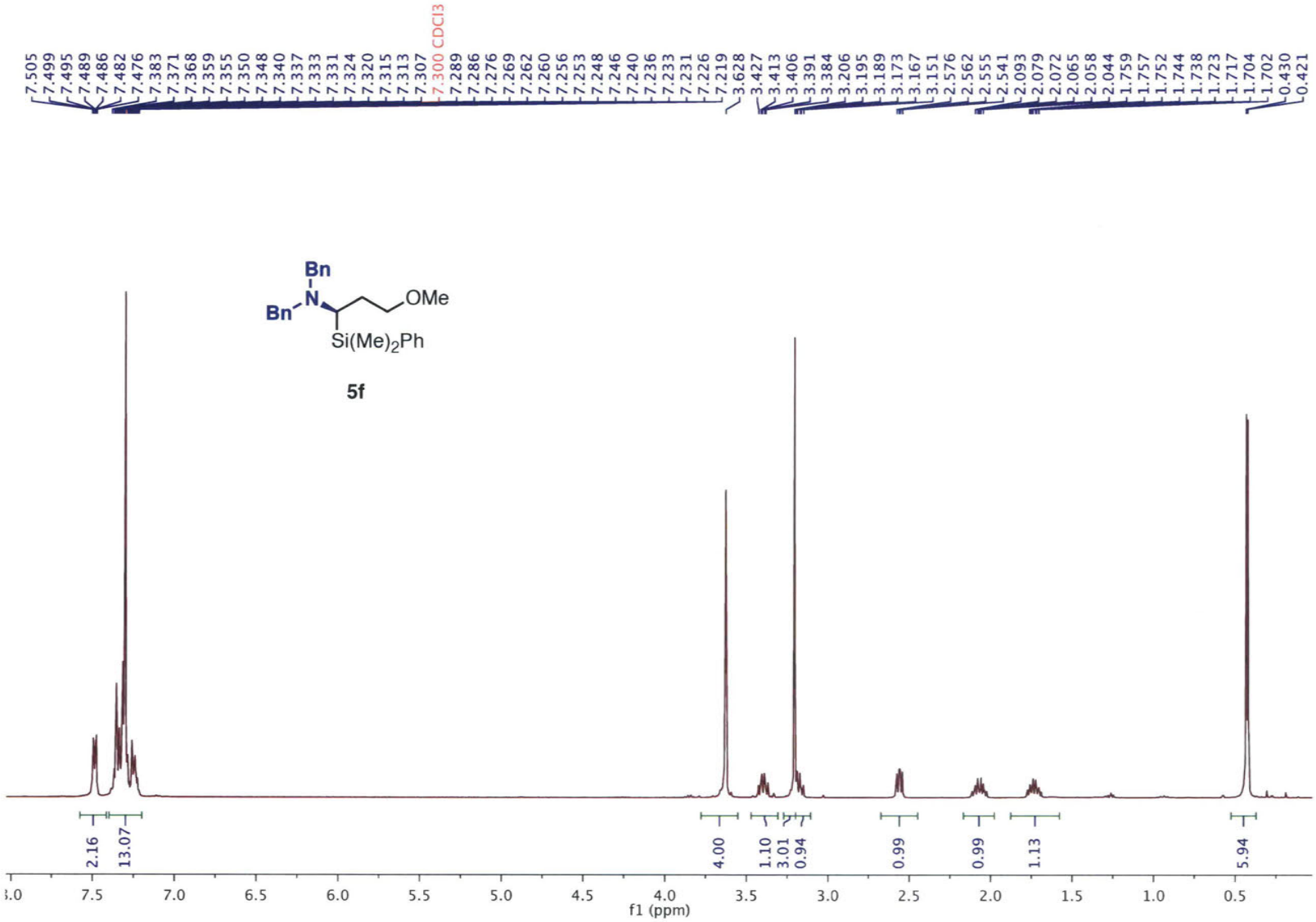
77.094 CDCl3
76.776 CDCl3
72.223
62.858
58.404
58.184
56.483
46.681
26.720
18.272
-1.827
-2.739
-5.568
Bn
N
Bn
OTBS
Si(Me)2Ph
5e
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.350
7.348
7.340
7.337
7.333
7.331
7.324
7.320
7.315
7.313
7.307
7.300 CDCl3
7.289
7.286
7.276
7.269
7.262
7.260
7.256
7.253
7.248
7.246
7.240
7.236
7.233
7.231
7.226
7.219
3.628
3.427
3.413
3.406
3.391
3.384
3.206
3.195
3.189
3.173
3.167
3.151
2.576
2.562
2.555
2.541
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2.079
2.072
2.065
2.058
2.044
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1.757
1.752
1.744
1.738
1.723
1.717
1.704
1.702
0.430
0.421
Bn
N
Bn
OMe
Si(Me)2Ph
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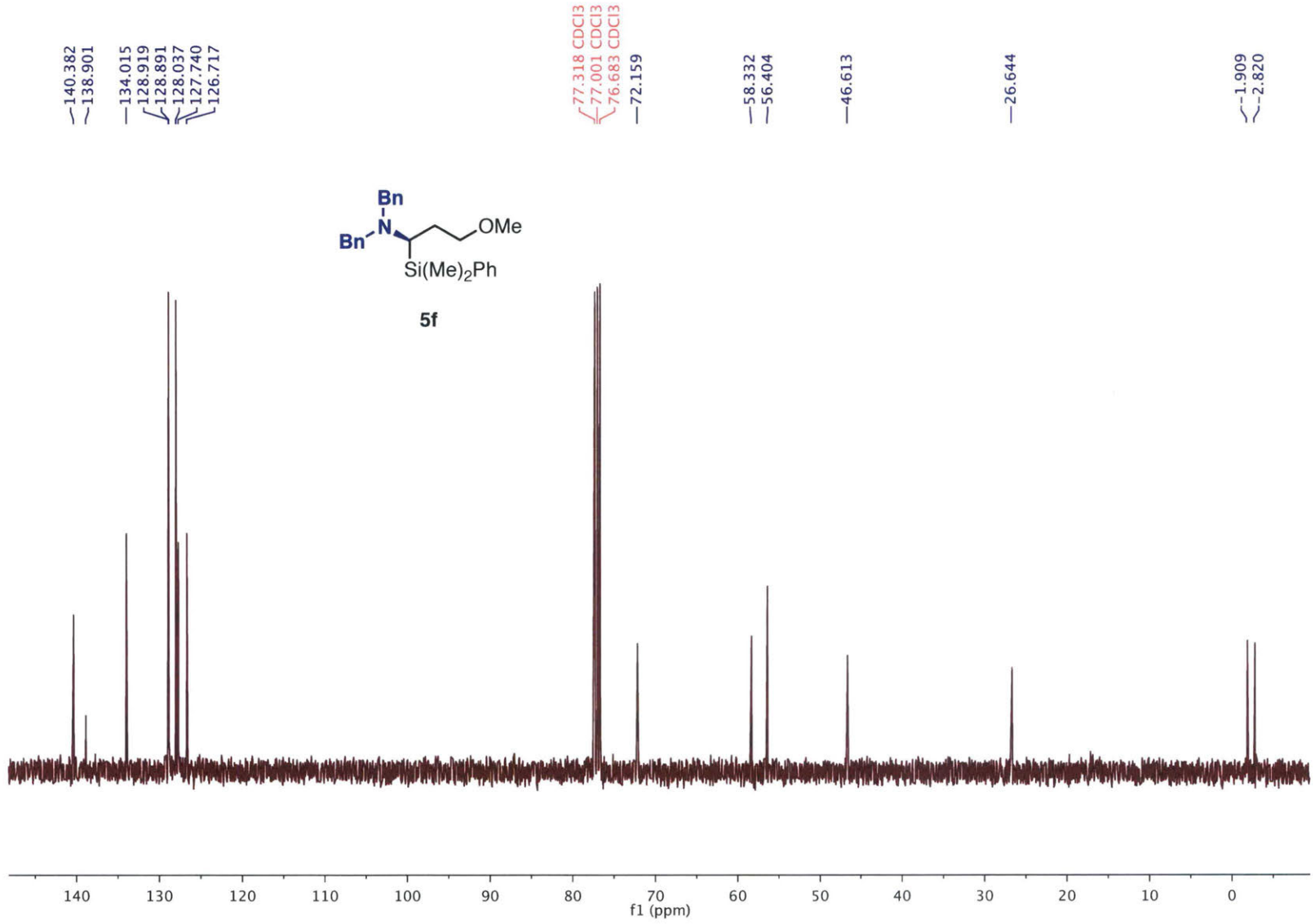
5.94
f1 (ppm)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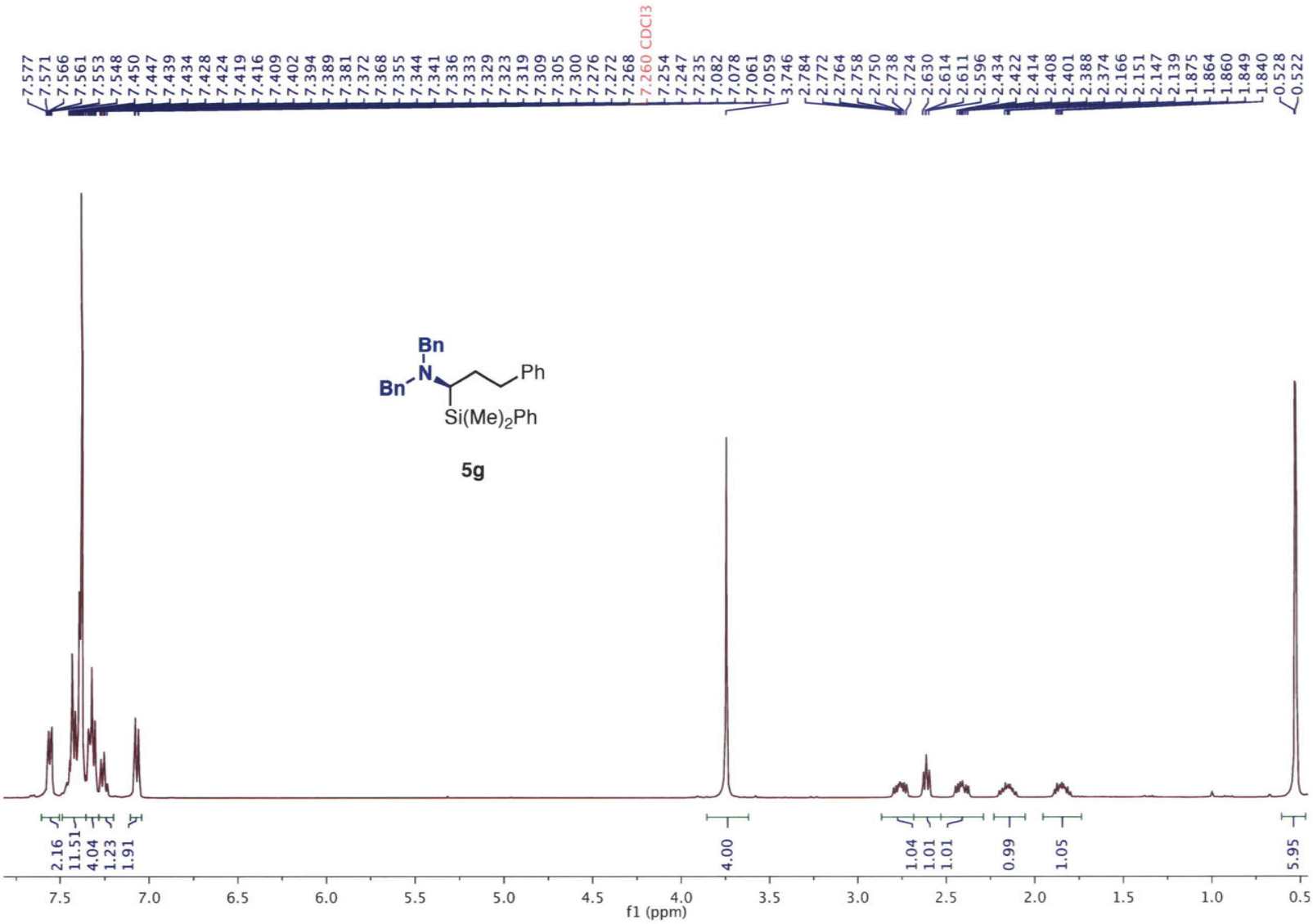
128.891
128.037
127.740
126.717
77.318 CDCl3
77.001 CDCl3
76.683 CDCl3
72.159
58.332
56.404
46.613
26.644
1.909
2.820
Bn
N
Bn
OMe
Si(Me)2Ph
5f
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.416
7.409
7.402
7.394
7.389
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7.355
7.344
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7.336
7.333
7.329
7.323
7.319
7.309
7.305
7.300
7.276
7.272
7.268
7.260 CDCl3
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7.247
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7.059
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2.414
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2.401
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1.840
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0.522
Bn
N
Bn
Ph
Si(Me)2Ph
5g
2.16
11.51
4.04
1.23
1.91
4.00
1.04
1.01
1.01
0.99
1.05
5.95
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
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1.5
1.0
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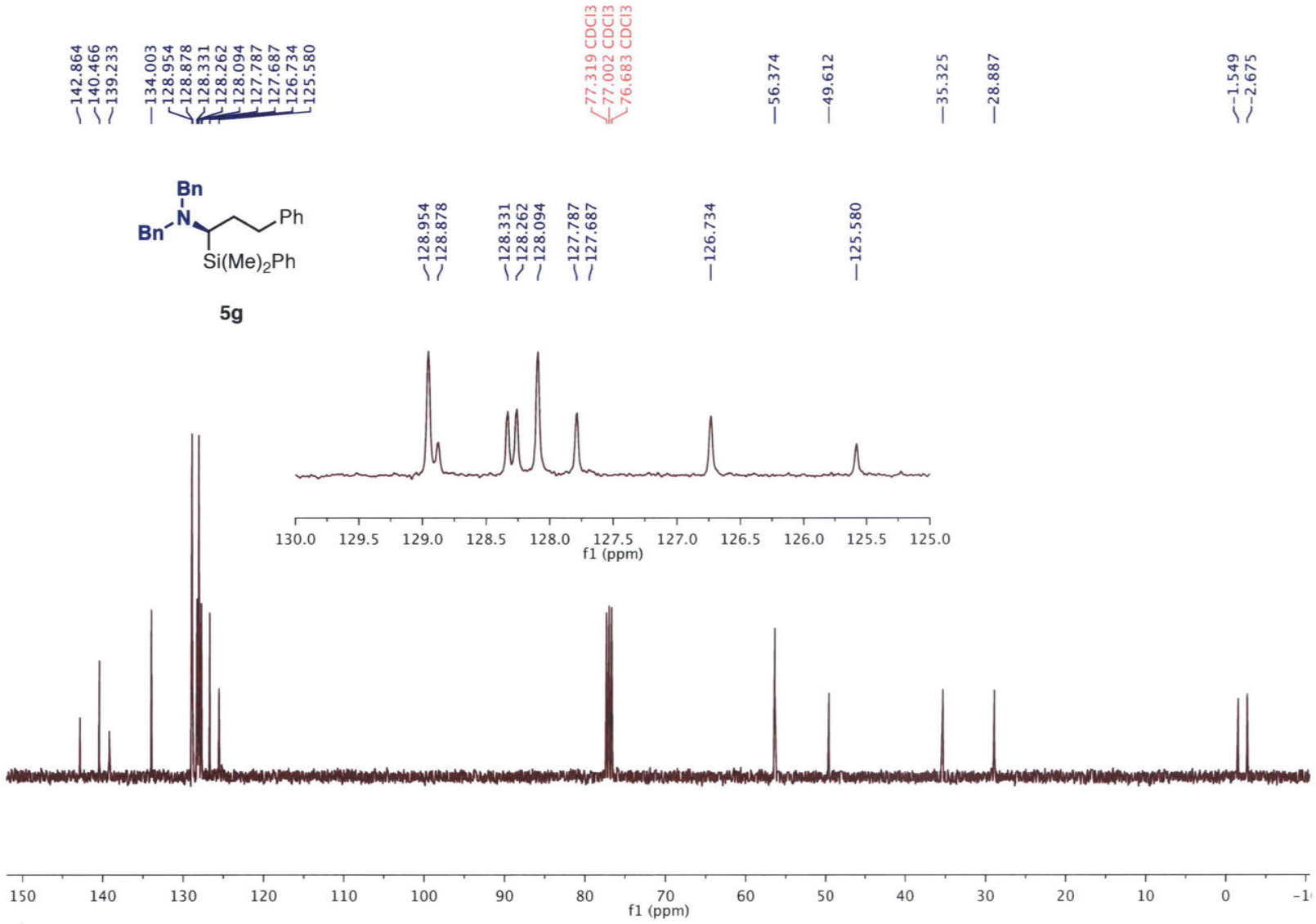
f1 (ppm)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128.262
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127.787
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126.734
125.580
77.319 CDCl3
77.002 CDCl3
76.683 CDCl3
56.374
49.612
35.325
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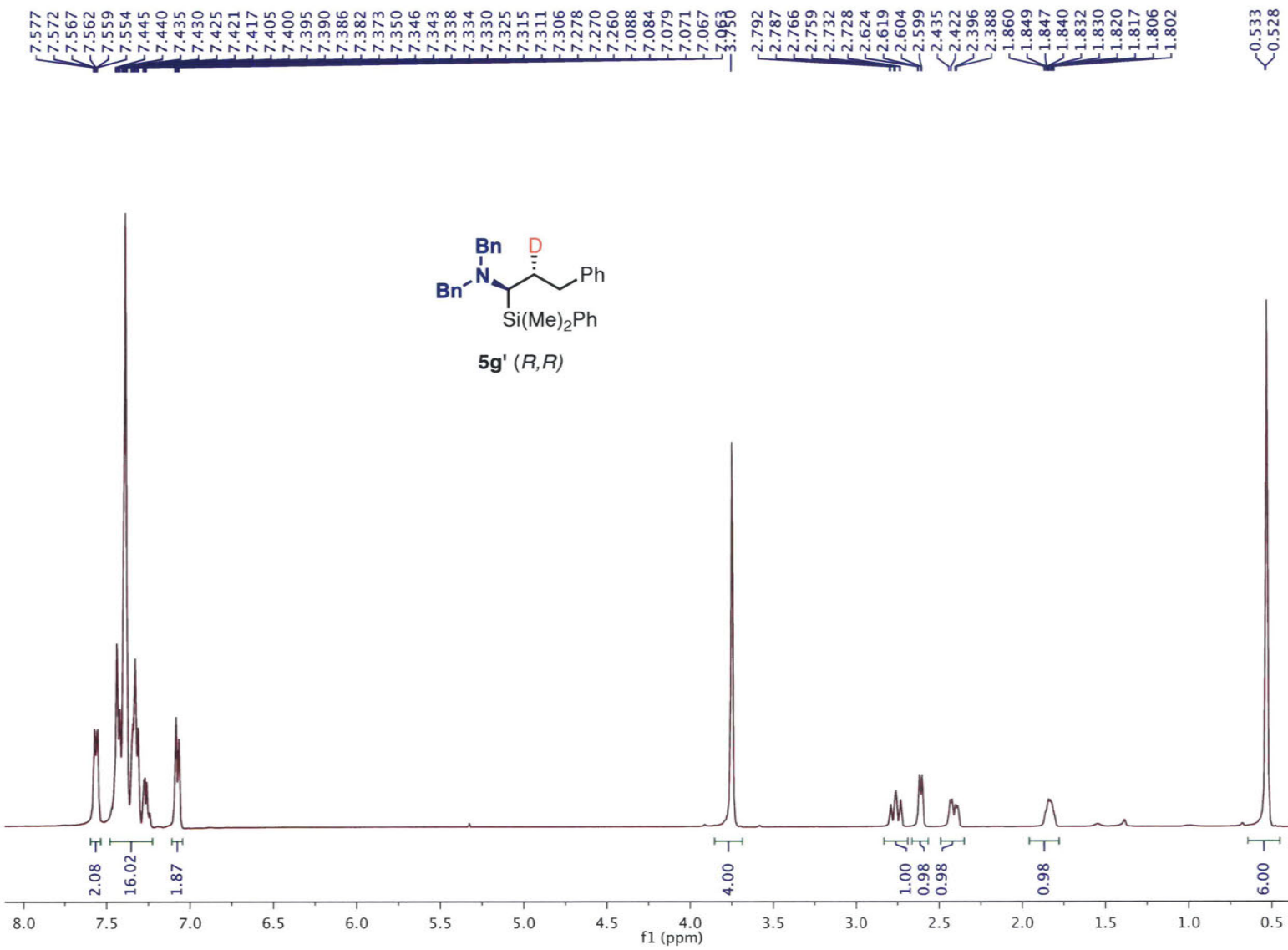
-1.549
-2.675
Bn
N
Bn
Ph
Si(Me)2Ph
5g
f1 (ppm)
f1 (ppm)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7.311
7.306
7.278
7.270
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3.950
2.792
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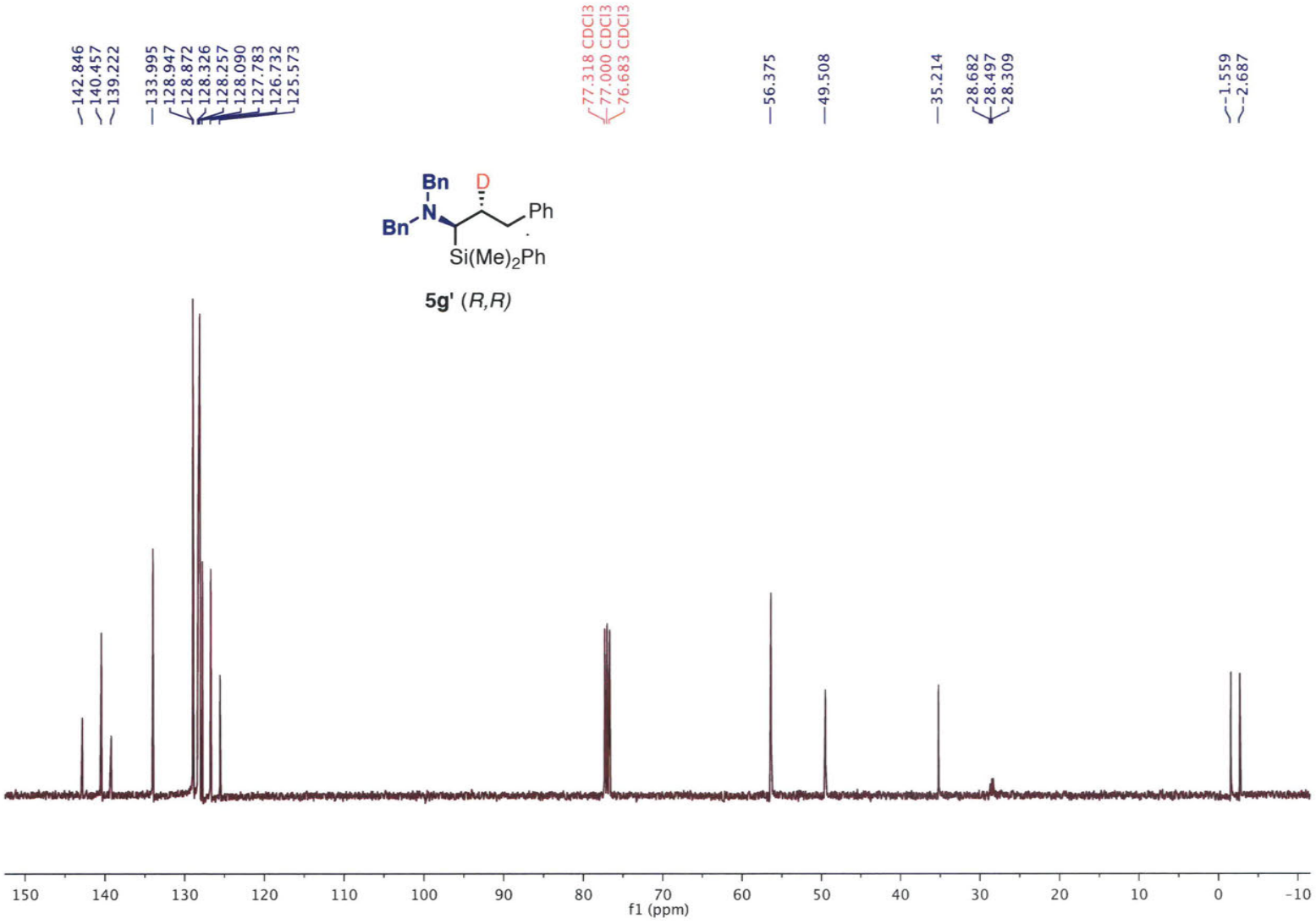
1.817
1.806
1.802
0.533
0.528
Bn
D
N
Bn
Ph
Si(Me)2Ph
5g' (R,R)
2.08
16.02
1.87
4.00
1.00
0.98
0.98
0.98
6.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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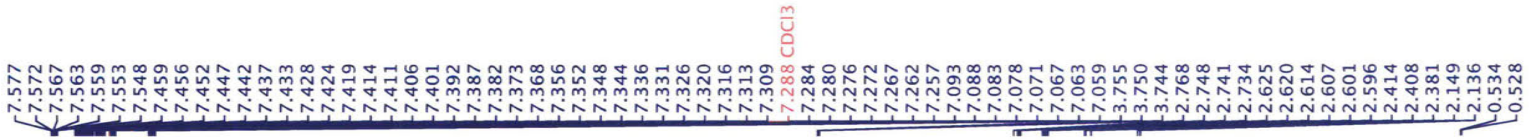
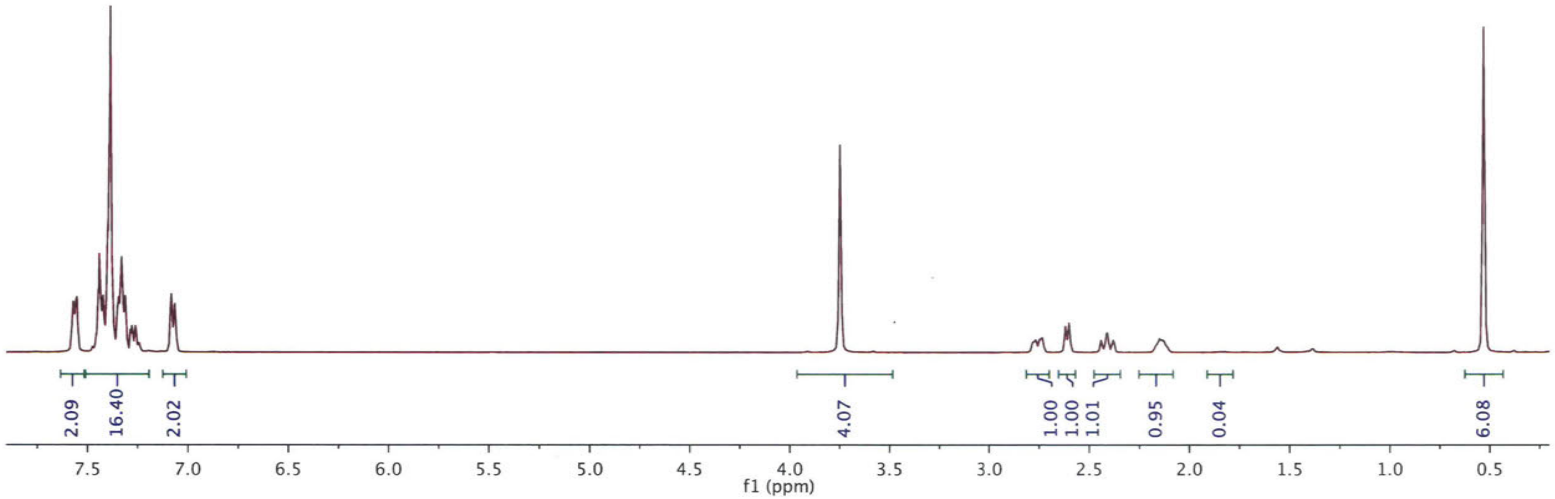
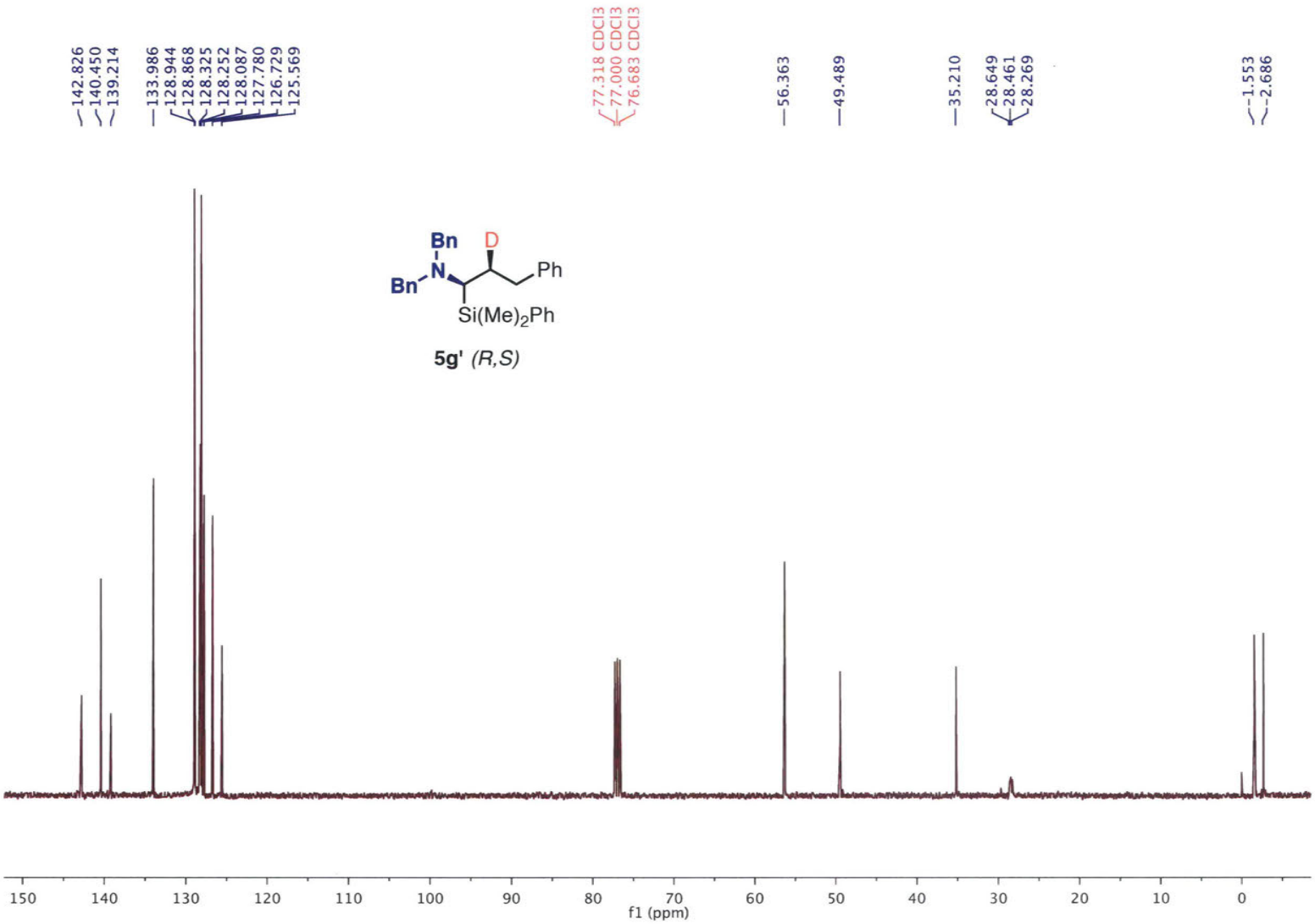
140.457
139.222
133.995
128.947
128.872
128.326
128.257
128.090
127.783
126.732
125.573
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
56.375
49.508
35.214
28.682
28.497
28.309
-1.559
-2.687
Bn
D
N
Bn
Ph
Si(Me)2Ph
5g' (R,R)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

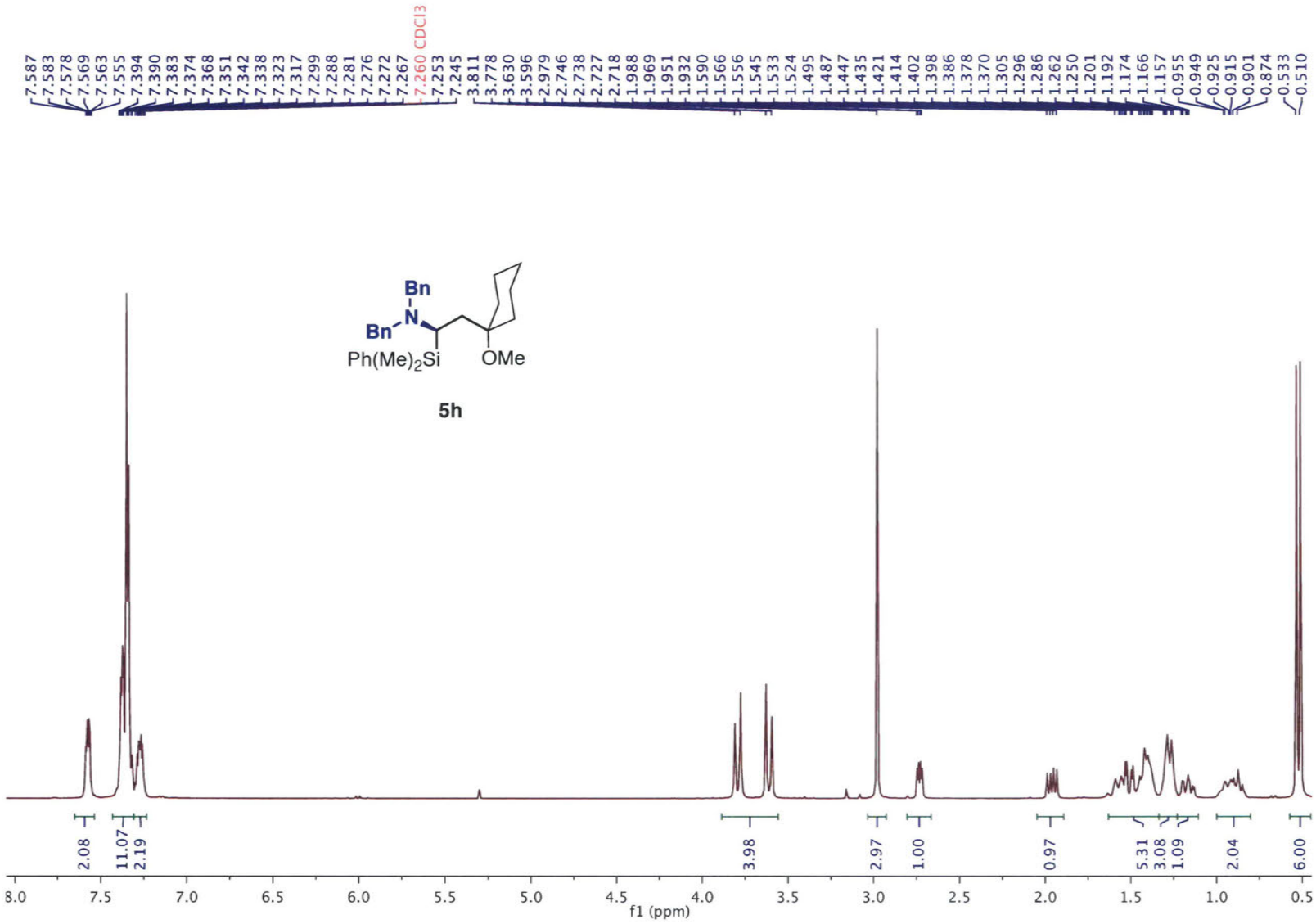

7.577
7.572
7.567
7.563
7.559
7.553
7.548
7.459
7.456
7.452
7.447
7.442
7.437
7.433
7.428
7.424
7.419
7.414
7.411
7.406
7.401
7.392
7.387
7.382
7.373
7.368
7.356
7.352
7.348
7.344
7.336
7.331
7.326
7.320
7.316
7.313
7.309
7.288 CDCl3
7.284
7.280
7.276
7.272
7.267
7.262
7.257
7.093
7.088
7.083
7.078
7.071
7.067
7.063
7.059
3.755
3.750
3.744
2.768
2.748
2.741
2.734
2.625
2.620
2.614
2.607
2.601
2.596
2.414
2.408
2.381
2.149
2.136
0.534
0.528

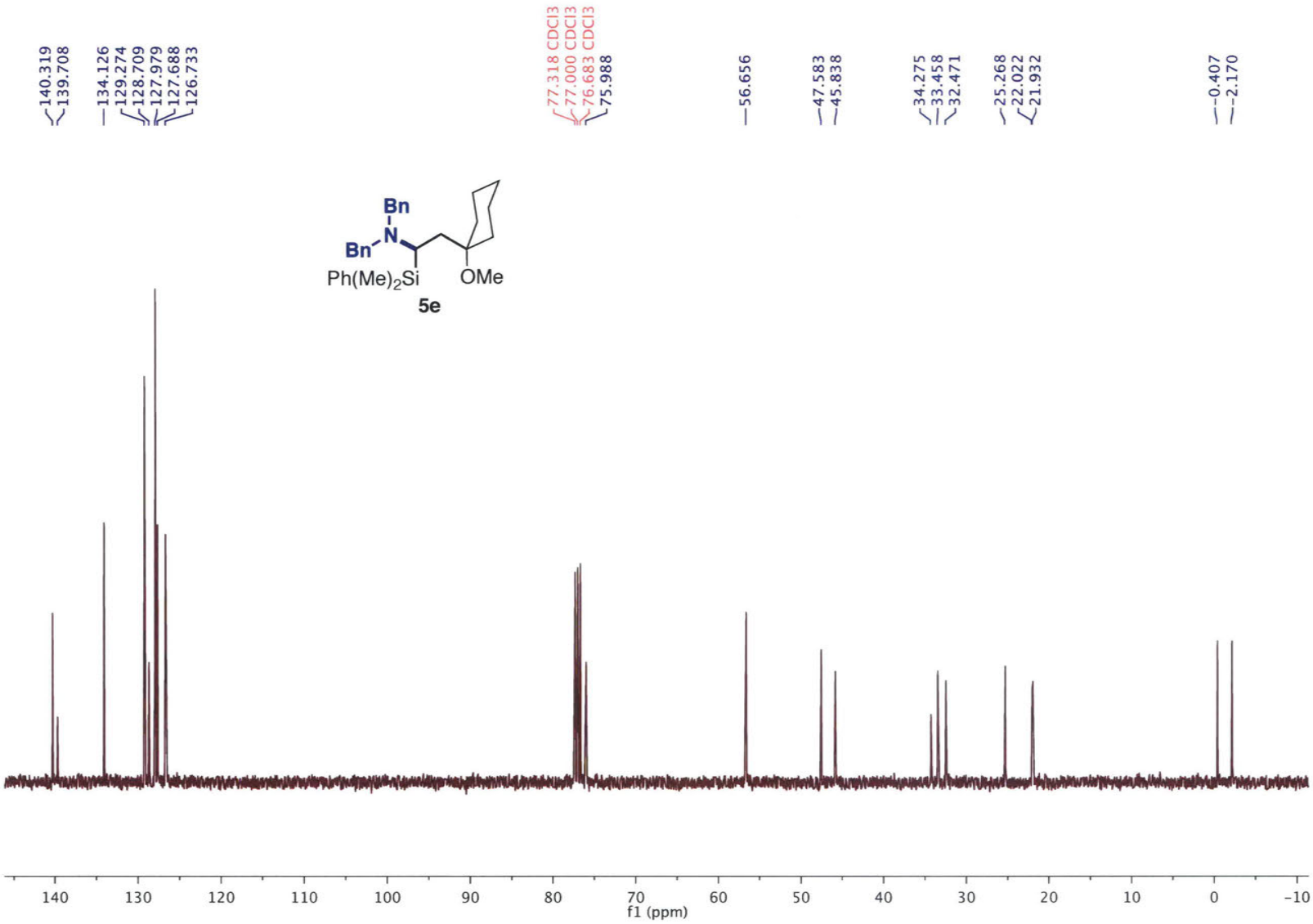

Bn
D
N
Bn
Ph
Si(Me)2Ph

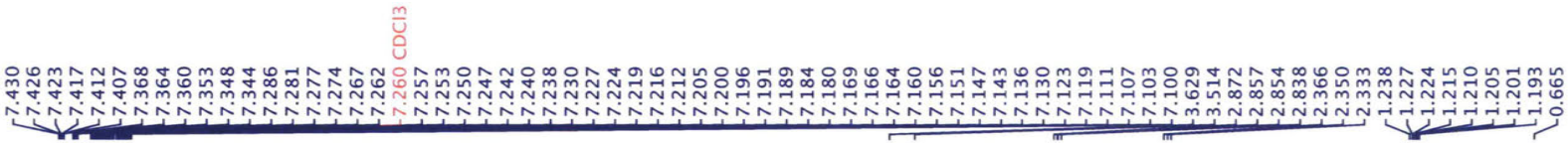
5g' *(R,S)*


2.09
16.40
2.02
4.07
1.00
1.00
1.01
0.95
0.04
6.08
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
f1 (ppm)


142.826
140.450
139.214
133.986
128.944
128.868
128.325
128.252
128.087
127.780
126.729
125.569
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
56.363
49.489
35.210
28.649
28.461
28.269
-1.553
-2.686
Bn
D
N
Bn
Ph
Si(Me)2Ph
5g' (R,S)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.587
7.583
7.578
7.569
7.563
7.555
7.394
7.390
7.383
7.374
7.368
7.351
7.342
7.338
7.323
7.317
7.299
7.288
7.281
7.276
7.272
7.267
7.260 CDCl3
7.253
7.245
3.811
3.778
3.630
3.596
2.979
2.746
2.738
2.727
2.718
1.988
1.969
1.951
1.932
1.590
1.566
1.556
1.545
1.533
1.524
1.495
1.487
1.447
1.435
1.421
1.414
1.402
1.398
1.386
1.378
1.370
1.305
1.296
1.286
1.262
1.250
1.201
1.192
1.174
1.166
1.157
0.955
0.949
0.925
0.915
0.901
0.874
0.533
0.510
Bn
N
Bn
Ph(Me)2Si
OMe
5h
2.08
11.07
2.19
3.98
2.97
1.00
0.97
5.31
3.08
1.09
2.04
6.00
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
f1 (ppm)


140.319
139.708
134.126
129.274
128.709
127.979
127.688
126.733
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
75.988
56.656
47.583
45.838
34.275
33.458
32.471
25.268
22.022
21.932
-0.407
-2.170
Bn
N
Bn
Ph(Me)2Si
OMe
5e
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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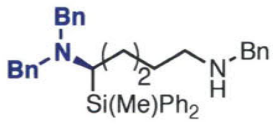
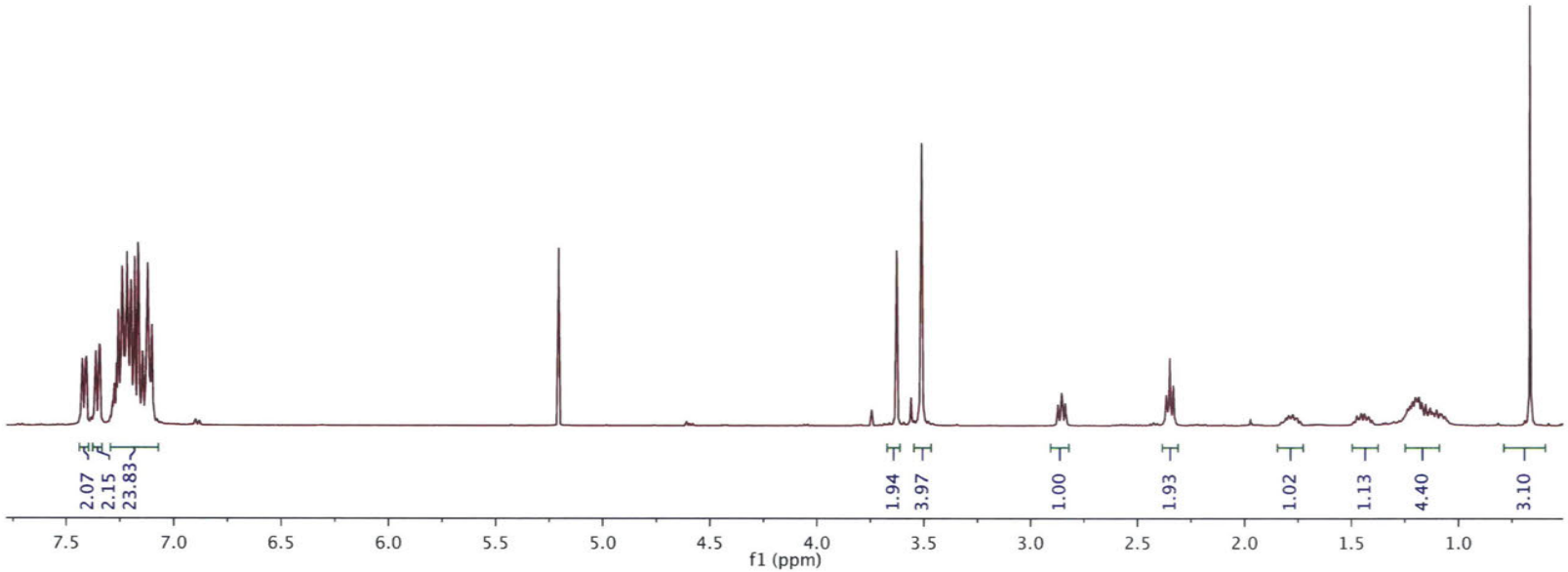
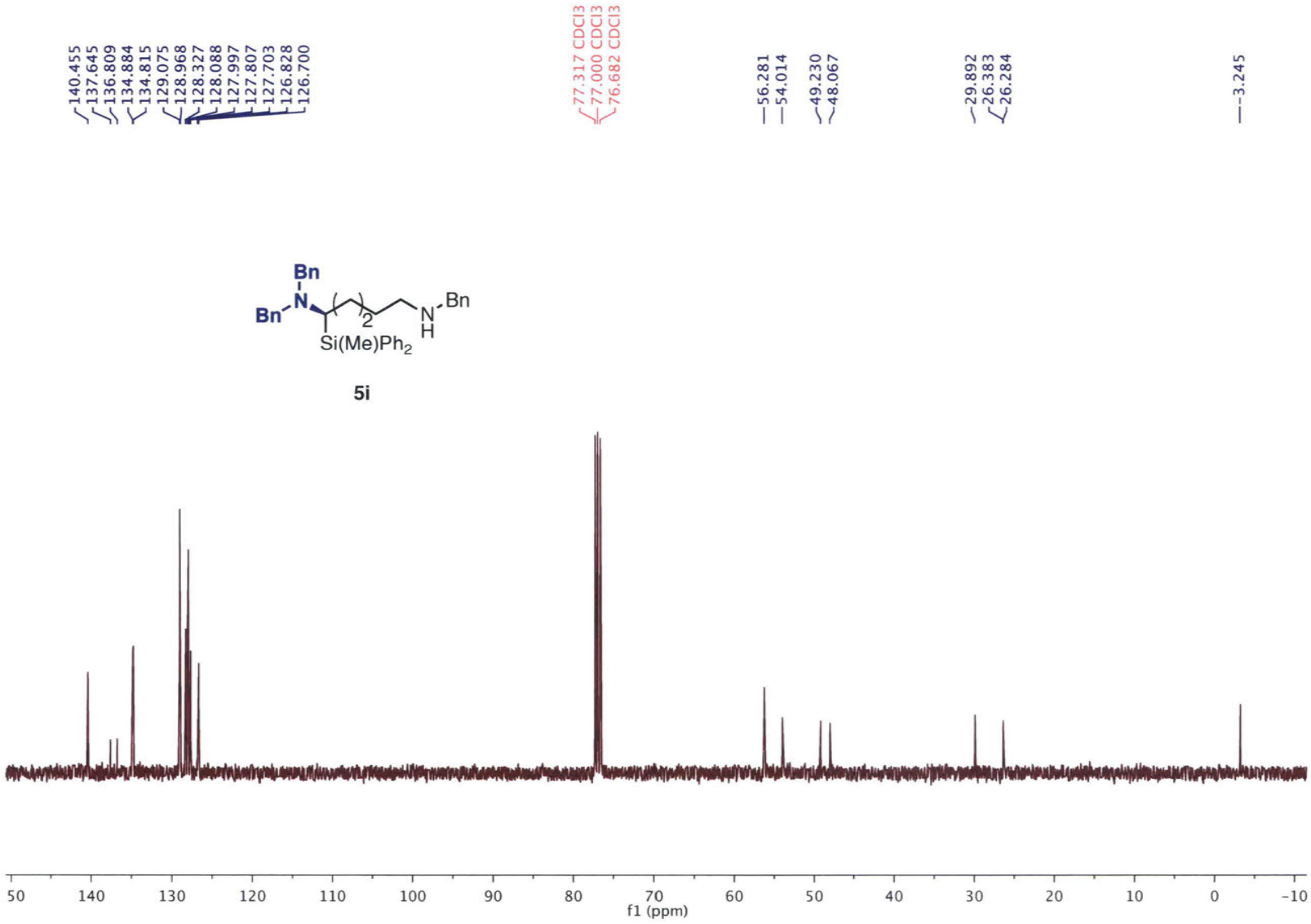
7.426
7.423
7.417
7.412
7.407
7.368
7.364
7.360
7.353
7.348
7.344
7.286
7.281
7.277
7.274
7.267
7.262
7.260 CDCl3
7.257
7.253
7.250
7.247
7.242
7.240
7.238
7.230
7.227
7.224
7.219
7.216
7.212
7.205
7.200
7.196
7.191
7.189
7.184
7.180
7.169
7.166
7.164
7.160
7.156
7.151
7.147
7.143
7.136
7.130
7.123
7.119
7.111
7.107
7.103
7.100
3.629
3.514
2.872
2.857
2.854
2.838
2.366
2.350
2.333
1.238
1.227
1.224
1.215
1.210
1.205
1.201
1.193
0.665

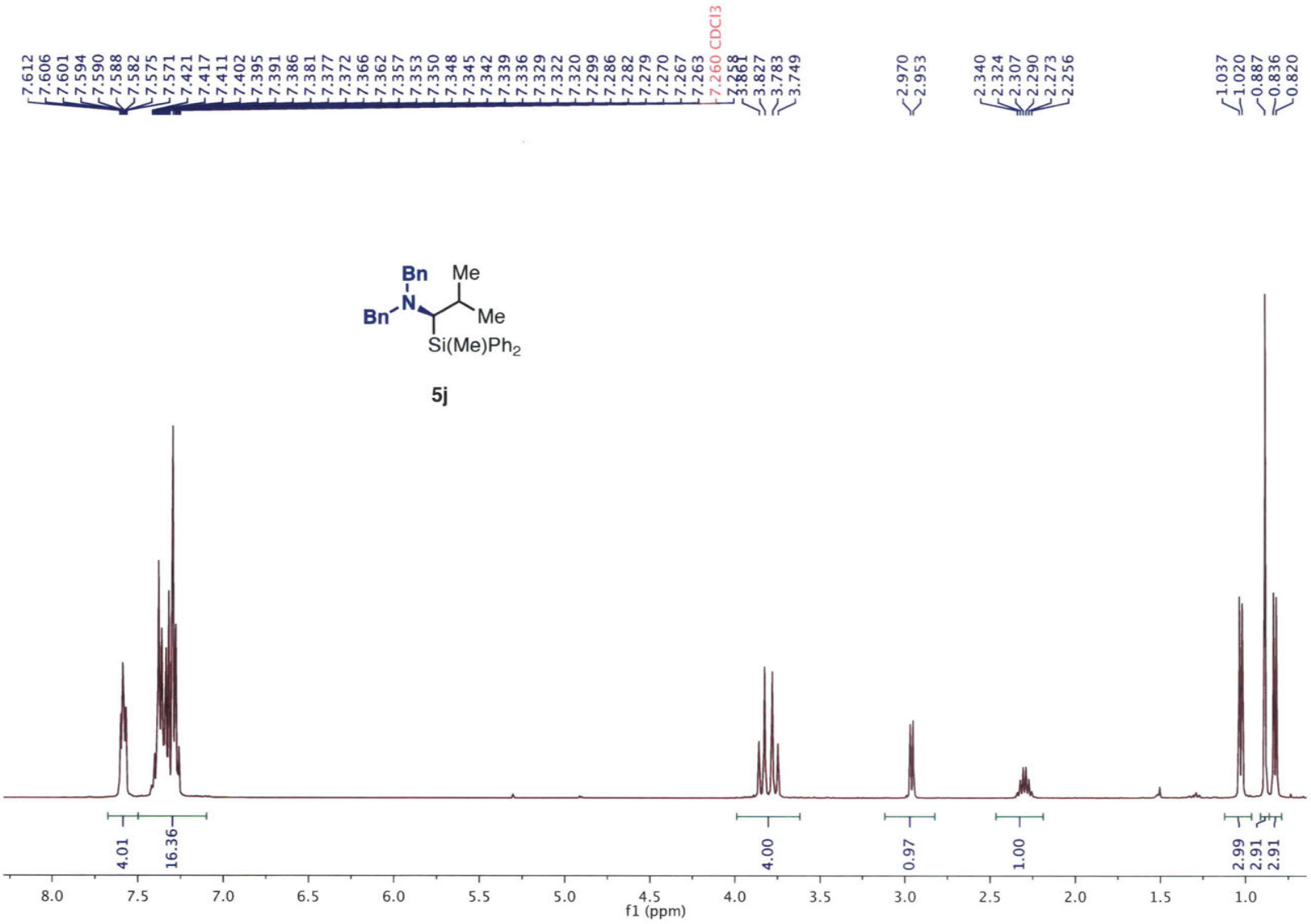

Bn
N
Bn
Bn
2
N
H
Si(Me)Ph2

5i


2.07
2.15
23.83
1.94
3.97
1.00
1.93
1.02
1.13
4.40
3.10
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
f1 (ppm)


140.455
137.645
136.809
134.884
134.815
129.075
128.968
128.327
128.088
127.997
127.807
127.703
126.828
126.700
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
56.281
54.014
49.230
48.067
29.892
26.383
26.284
-3.245
Bn
N
Bn
2
N
H
Bn
Si(Me)Ph2
f1 (ppm)

5i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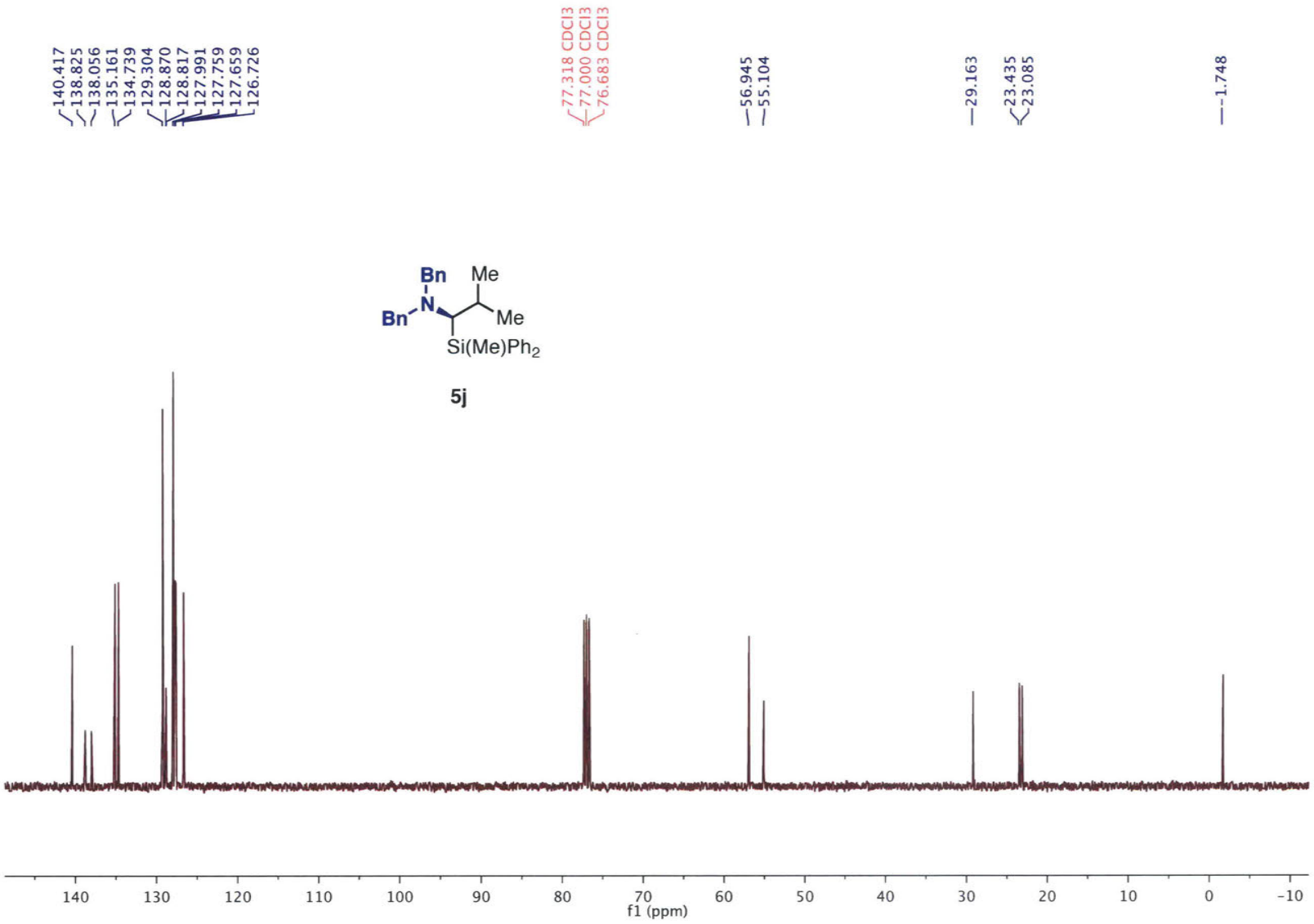
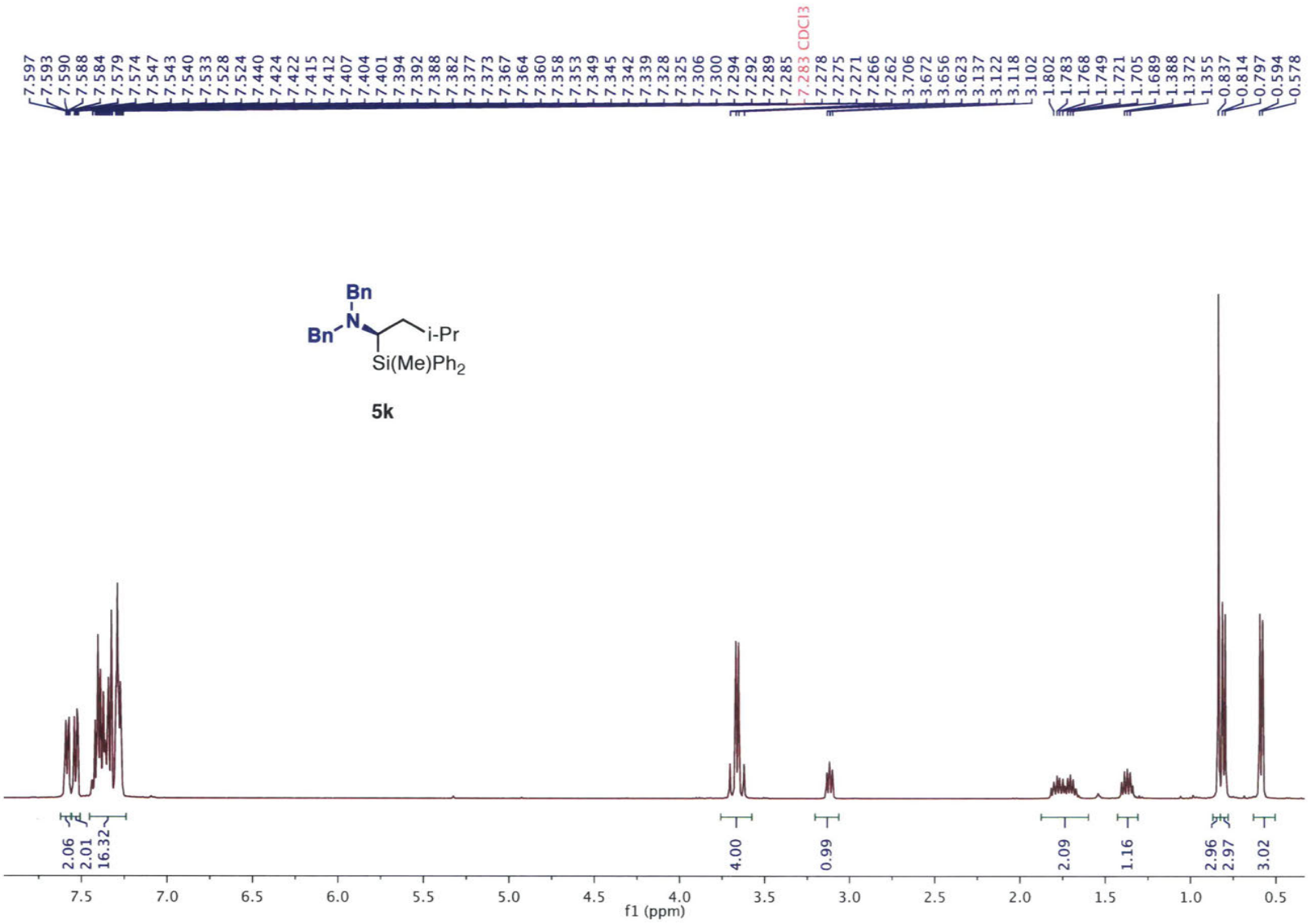
7.606
7.601
7.594
7.590
7.588
7.582
7.575
7.571
7.421
7.417
7.411
7.402
7.395
7.391
7.386
7.381
7.377
7.372
7.366
7.362
7.357
7.353
7.350
7.348
7.345
7.342
7.339
7.336
7.329
7.322
7.320
7.299
7.286
7.282
7.279
7.270
7.267
7.263
7.260 CDCl3
3.827
3.783
3.749
2.970
2.953
2.340
2.324
2.307
2.290
2.273
2.256
1.037
1.020
0.887
0.836
0.820
Bn
Me
N
Bn
Me
Si(Me)Ph2
5j
4.01
16.36
4.00
0.97
1.00
2.99
2.91
2.91
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
f1 (ppm)


140.417
138.825
138.056
135.161
134.739
129.304
128.870
128.817
127.991
127.759
127.659
126.726
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
56.945
55.104
29.163
23.435
23.085
-1.748
Bn
Me
N
Bn
Me
Si(Me)Ph2
5j
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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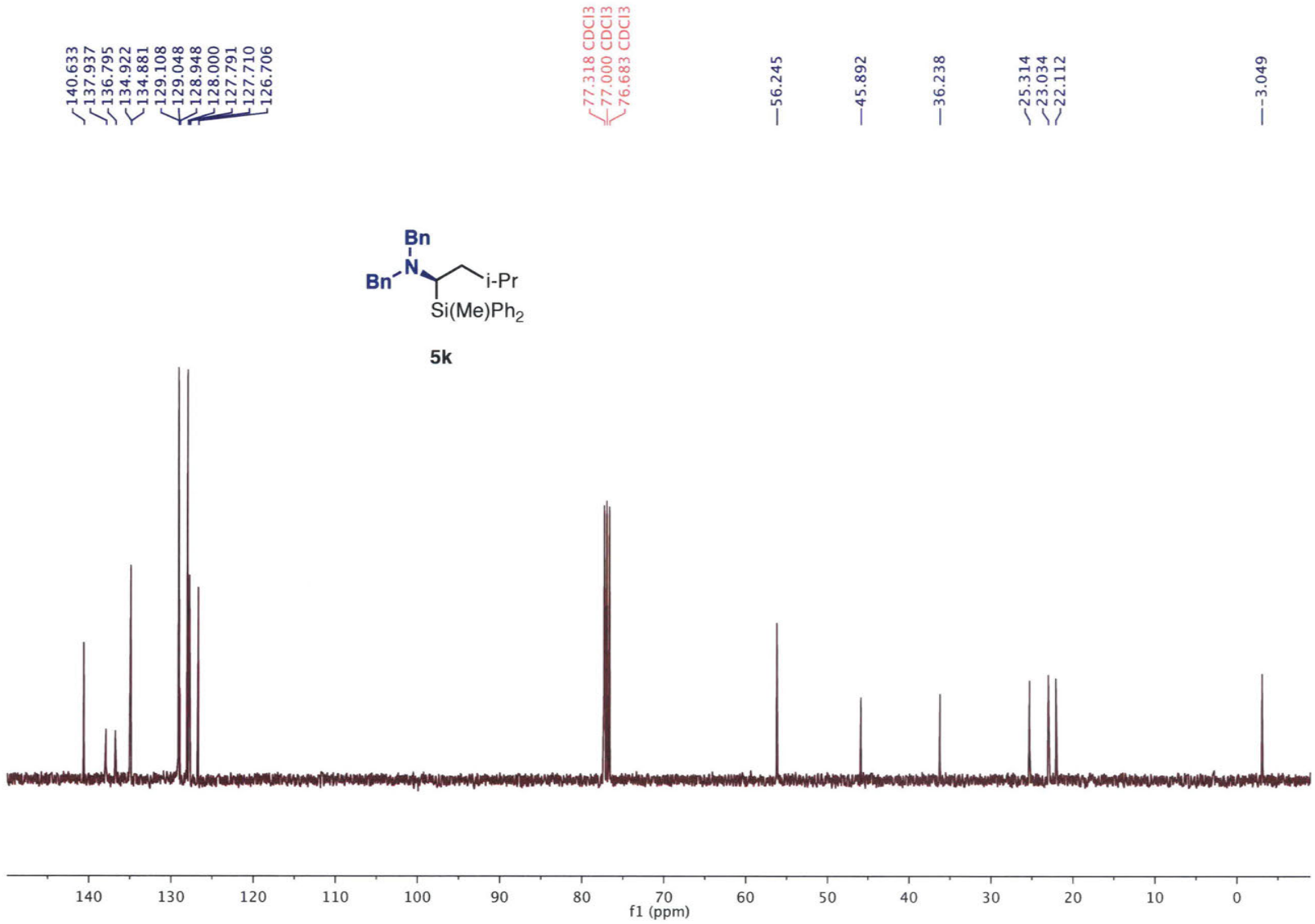
7.590
7.588
7.584
7.579
7.574
7.547
7.543
7.540
7.533
7.528
7.524
7.440
7.424
7.422
7.415
7.412
7.407
7.404
7.401
7.394
7.392
7.388
7.382
7.377
7.373
7.367
7.364
7.360
7.358
7.353
7.349
7.345
7.342
7.339
7.328
7.325
7.306
7.300
7.294
7.292
7.289
7.285
7.283 CDCl3
7.278
7.275
7.271
7.266
7.262
3.706
3.672
3.656
3.623
3.137
3.122
3.118
3.102
1.802
1.783
1.768
1.749
1.721
1.705
1.689
1.388
1.372
1.355
0.837
0.814
0.797
0.594
0.578
Bn
N
Bn
i-Pr
Si(Me)Ph2
5k
2.06
2.01
16.32
4.00
0.99
2.09
1.16
2.96
2.97
3.02
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
f1 (ppm)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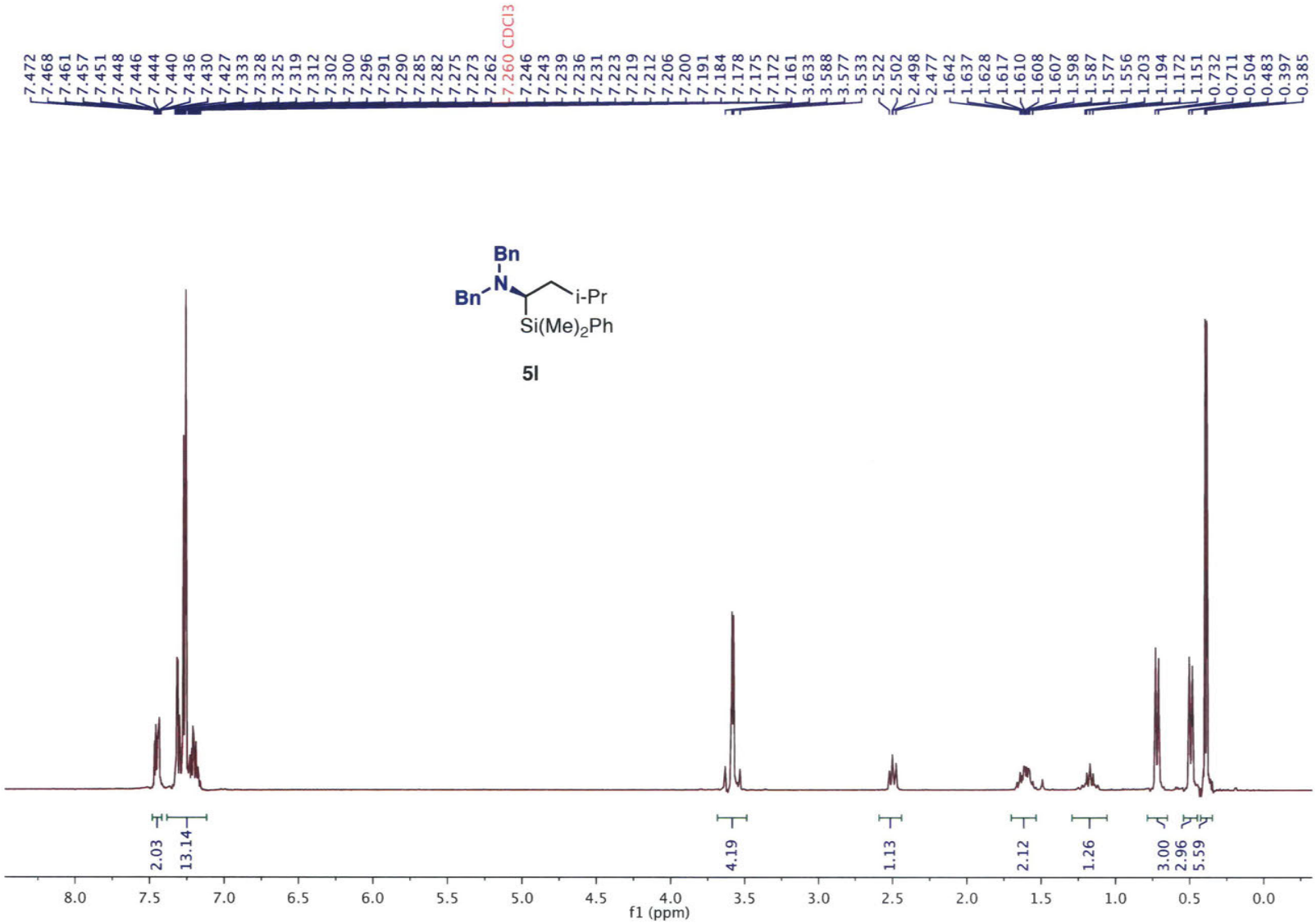
137.937
136.795
134.922
134.881
129.108
129.048
128.948
128.000
127.791
127.710
126.706
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
56.245
45.892
36.238
25.314
23.034
22.112
3.049
Bn
N
Bn
i-Pr
Si(Me)Ph2
5k
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.461
7.457
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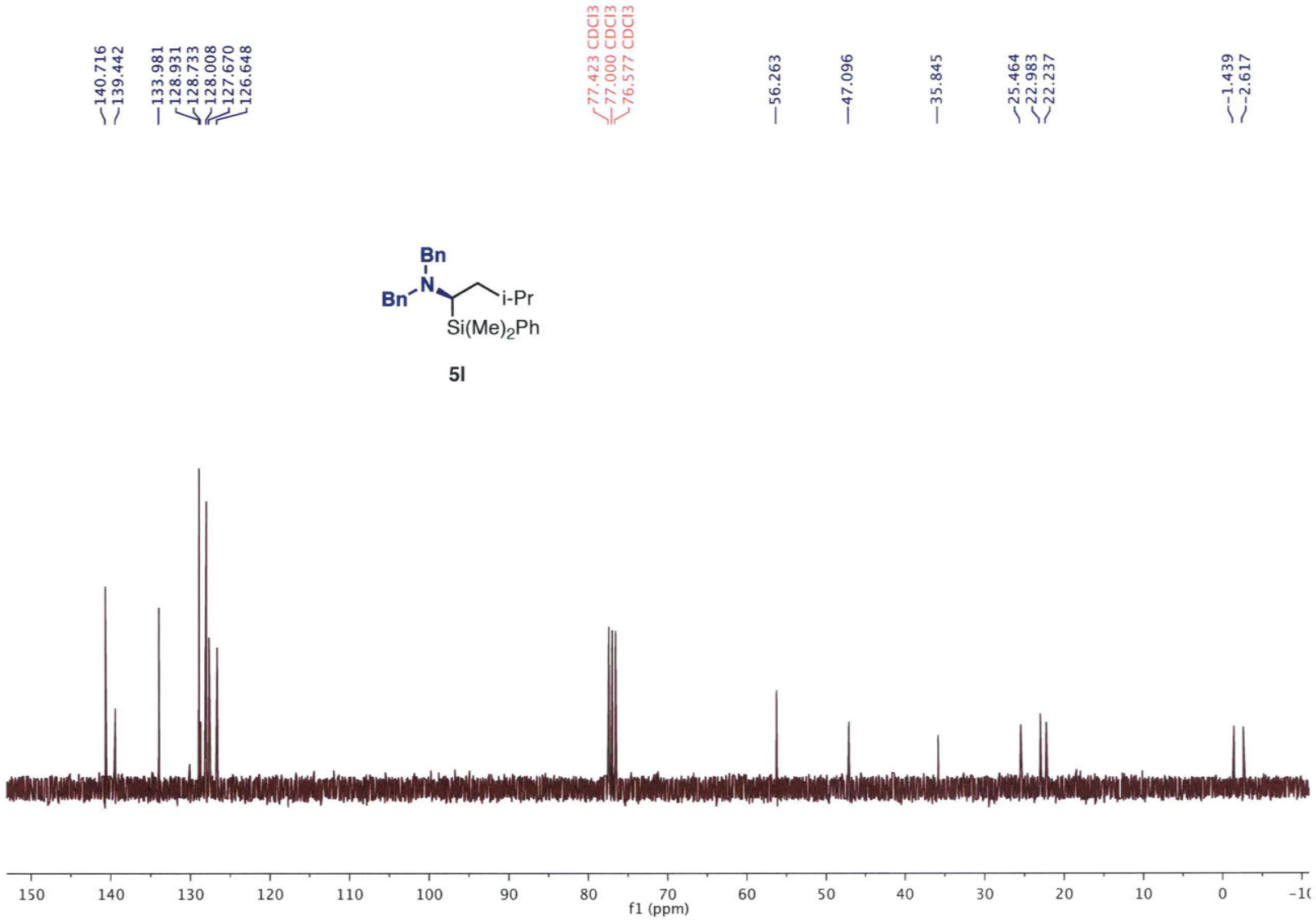
7.448
7.446
7.444
7.440
7.436
7.430
7.427
7.333
7.328
7.325
7.319
7.312
7.302
7.300
7.296
7.291
7.290
7.285
7.282
7.275
7.273
7.262
7.260 CDCl3
7.246
7.243
7.239
7.236
7.231
7.223
7.219
7.212
7.206
7.200
7.191
7.184
7.178
7.175
7.172
7.161
3.633
3.588
3.577
3.533
2.522
2.502
2.498
2.477
1.642
1.637
1.628
1.617
1.610
1.608
1.607
1.598
1.587
1.577
1.556
1.203
1.194
1.172
1.151
0.732
0.711
0.504
0.483
0.397
0.385
Bn
N
Bn
i-Pr
Si(Me)2Ph
5l
2.03
13.14
4.19
1.13
2.12
1.26
3.00
2.96
5.59
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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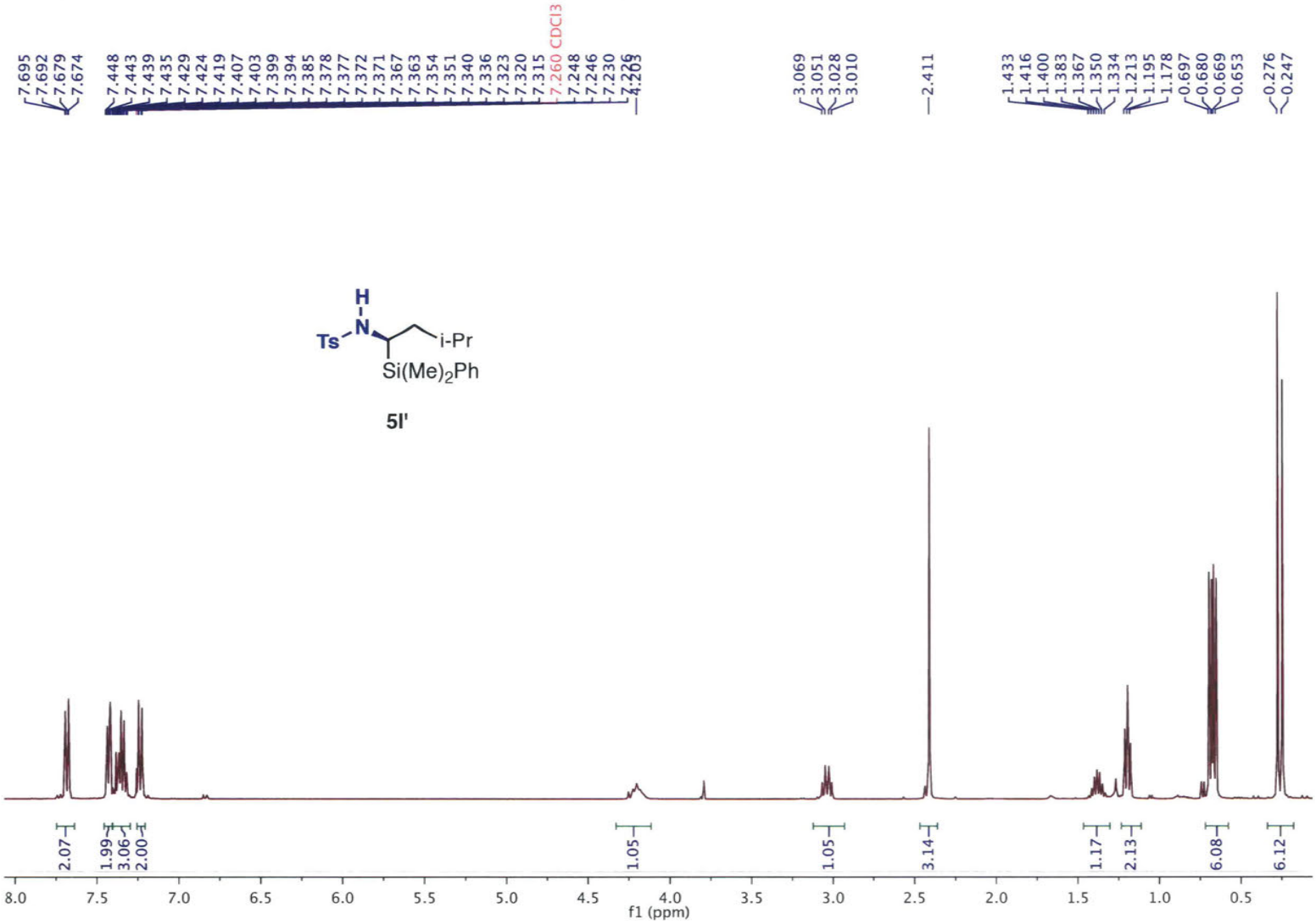
139.442
133.981
128.931
128.733
128.008
127.670
126.648
77.423 CDCl3
77.000 CDCl3
76.577 CDCl3
56.263
47.096
35.845
25.464
22.983
22.237
-1.439
-2.617
Bn
N
Bn
i-Pr
Si(Me)2Ph
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

5l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7.679
7.674
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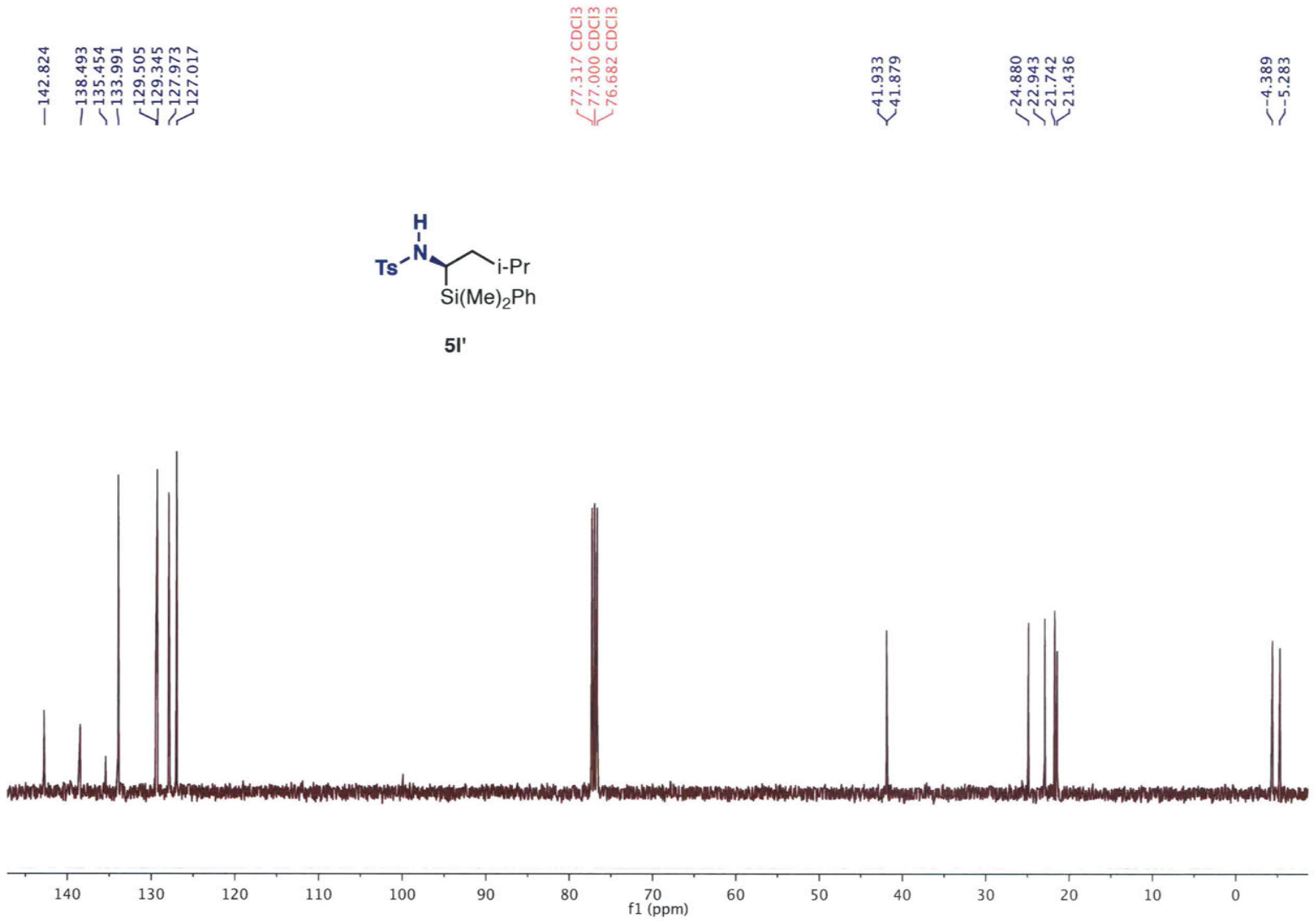
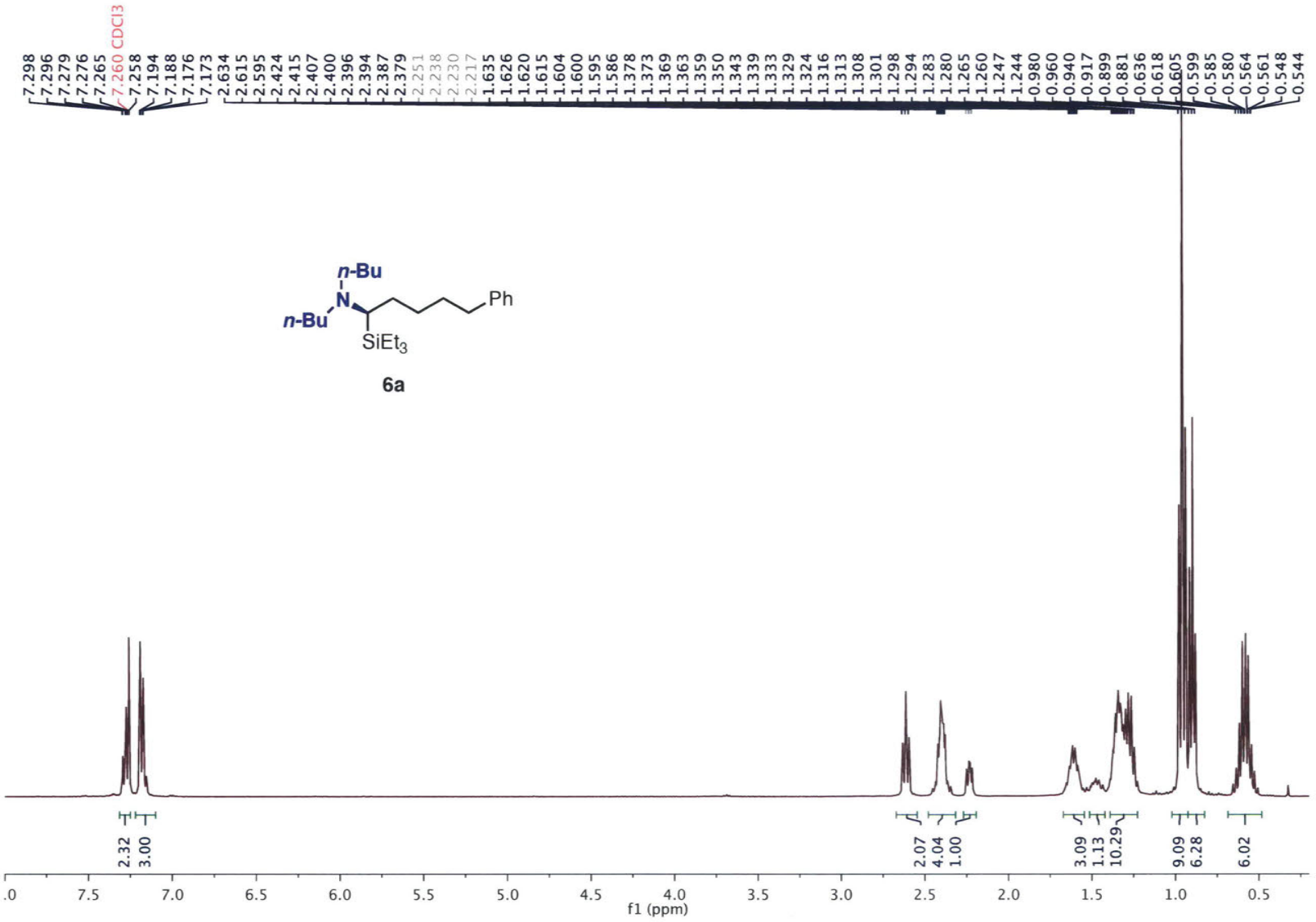
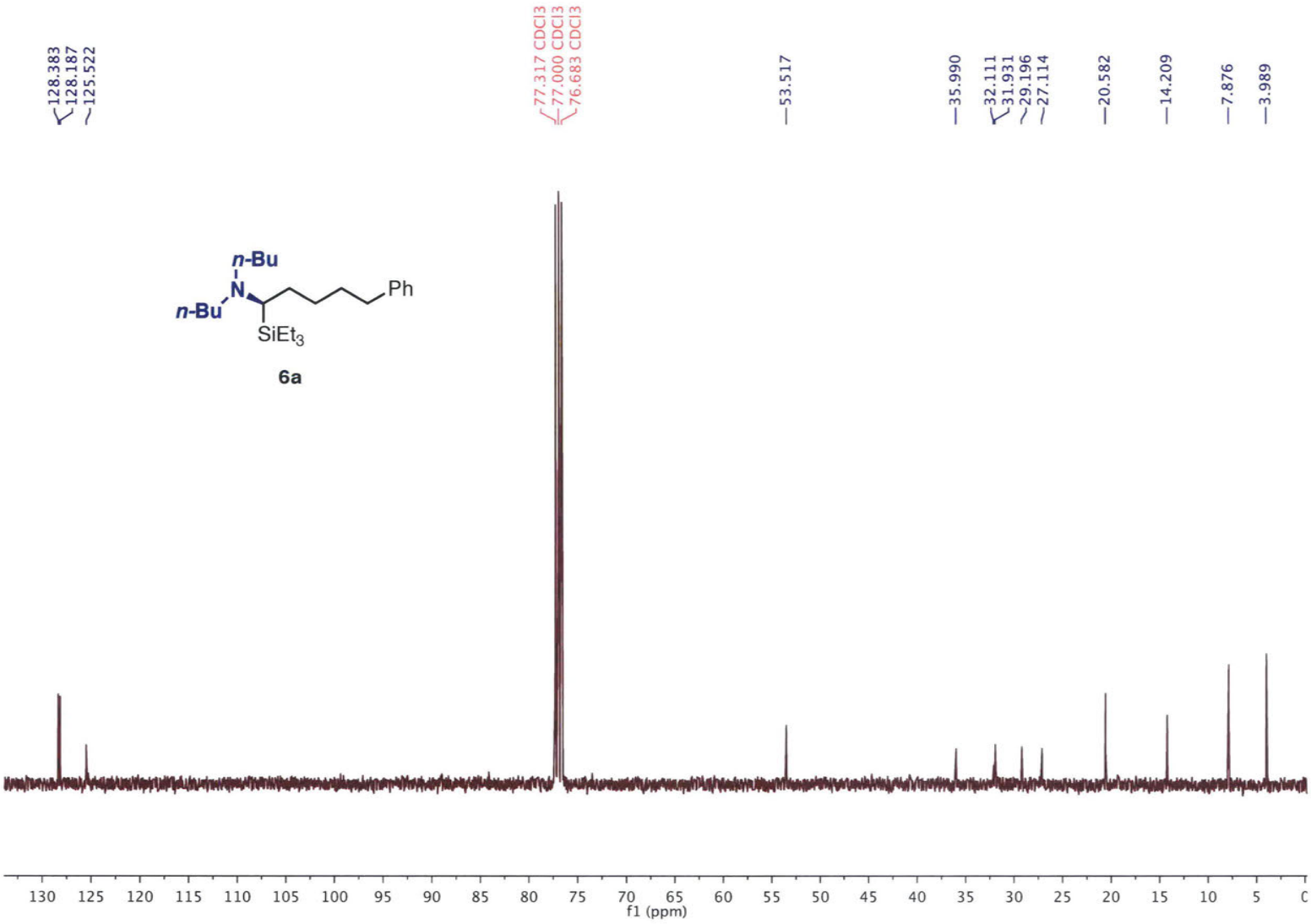
7.443
7.439
7.435
7.429
7.424
7.419
7.407
7.403
7.399
7.394
7.385
7.378
7.377
7.372
7.371
7.367
7.363
7.354
7.351
7.340
7.336
7.323
7.320
7.315
7.260 CDCl3
7.248
7.246
7.230
3.069
3.051
3.028
3.010
2.411
1.433
1.416
1.400
1.383
1.367
1.350
1.334
1.213
1.195
1.178
0.697
0.680
0.669
0.653
0.276
0.247
H
N
Ts
i-Pr
Si(Me)2Ph
5l'
2.07
1.99
3.06
2.00
1.05
1.05
3.14
1.17
2.13
6.08
6.12
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
f1 (ppm)


142.824
138.493
135.454
133.991
129.505
129.345
127.973
127.017
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
41.933
41.879
24.880
22.943
21.742
21.436
-4.389
-5.283
H
N
Ts
i-Pr
Si(Me)2Ph
5l'
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.298
7.296
7.279
7.276
7.265
7.260 CDCl3
7.258
7.194
7.188
7.176
7.173
2.634
2.615
2.595
2.424
2.415
2.407
2.400
2.396
2.394
2.387
2.379
2.251
2.238
2.230
2.217
1.635
1.626
1.620
1.615
1.604
1.600
1.595
1.586
1.378
1.373
1.369
1.363
1.359
1.350
1.343
1.339
1.333
1.329
1.324
1.316
1.313
1.308
1.301
1.298
1.294
1.283
1.280
1.265
1.260
1.247
1.244
0.980
0.960
0.940
0.917
0.899
0.881
0.636
0.618
0.605
0.599
0.585
0.580
0.564
0.561
0.548
0.544
n-Bu
N
n-Bu
Ph
SiEt3
2.32
3.00
2.07
4.04
1.00
3.09
1.13
10.29
9.09
6.28
6.02
f1 (ppm)

6a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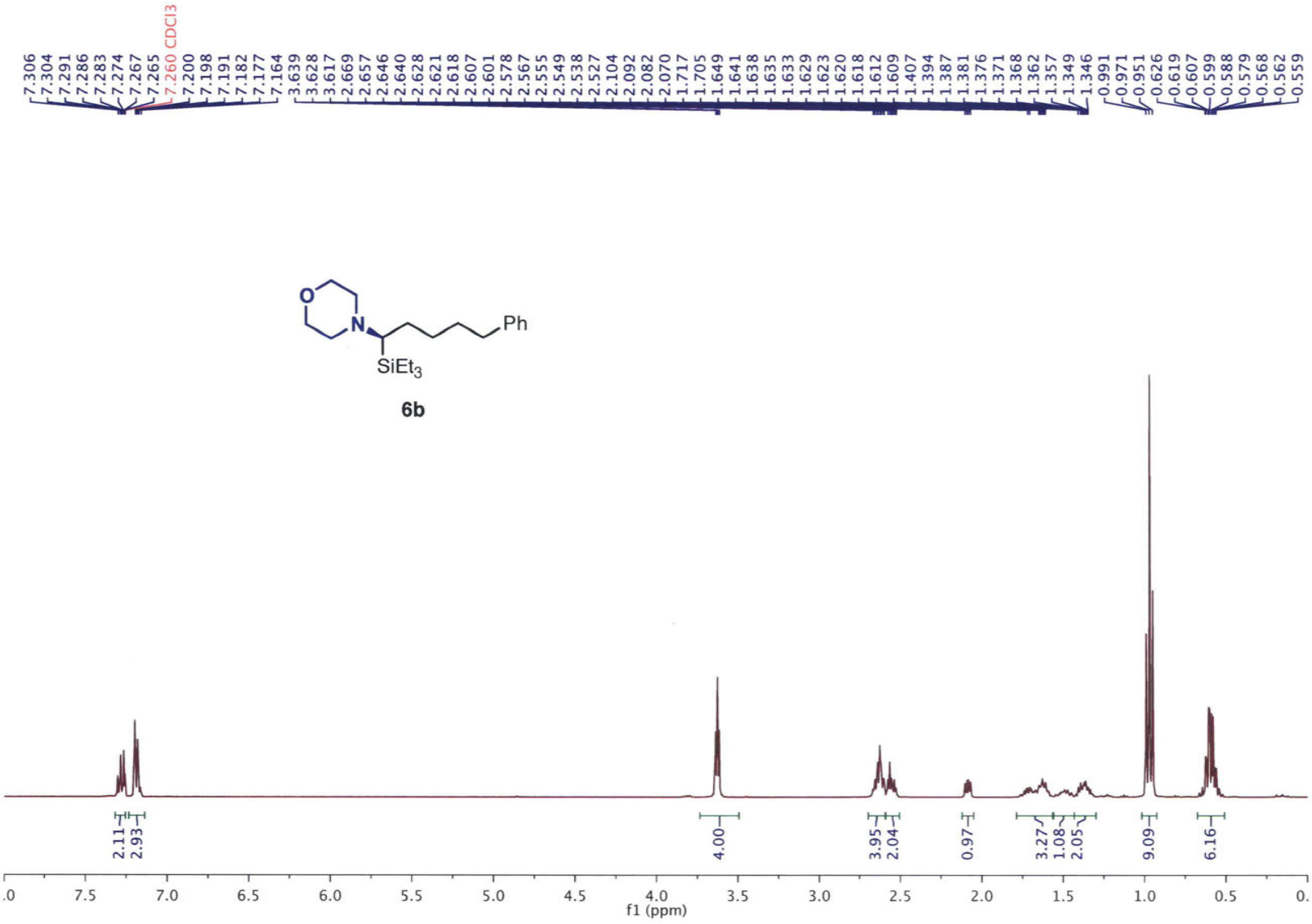
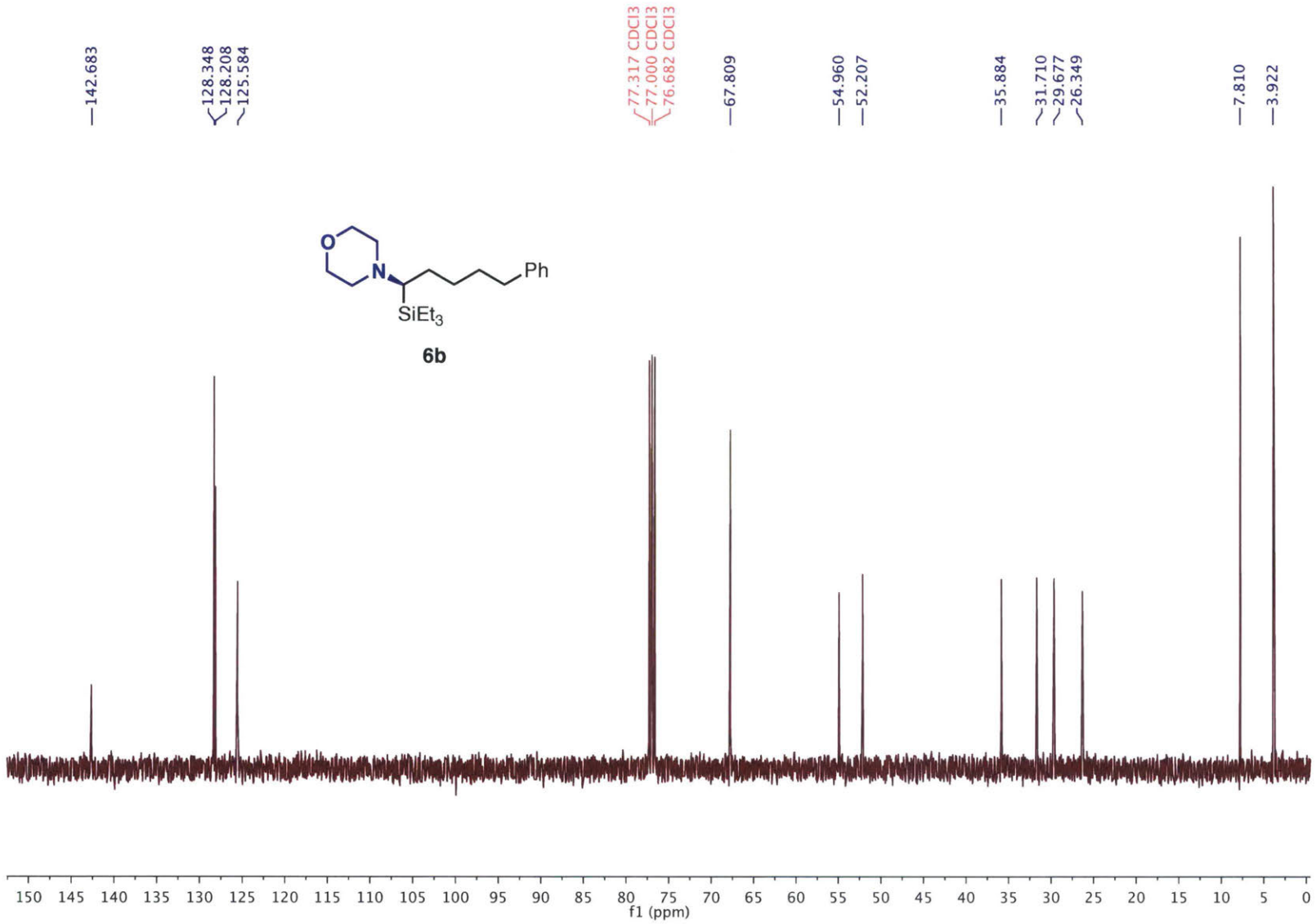
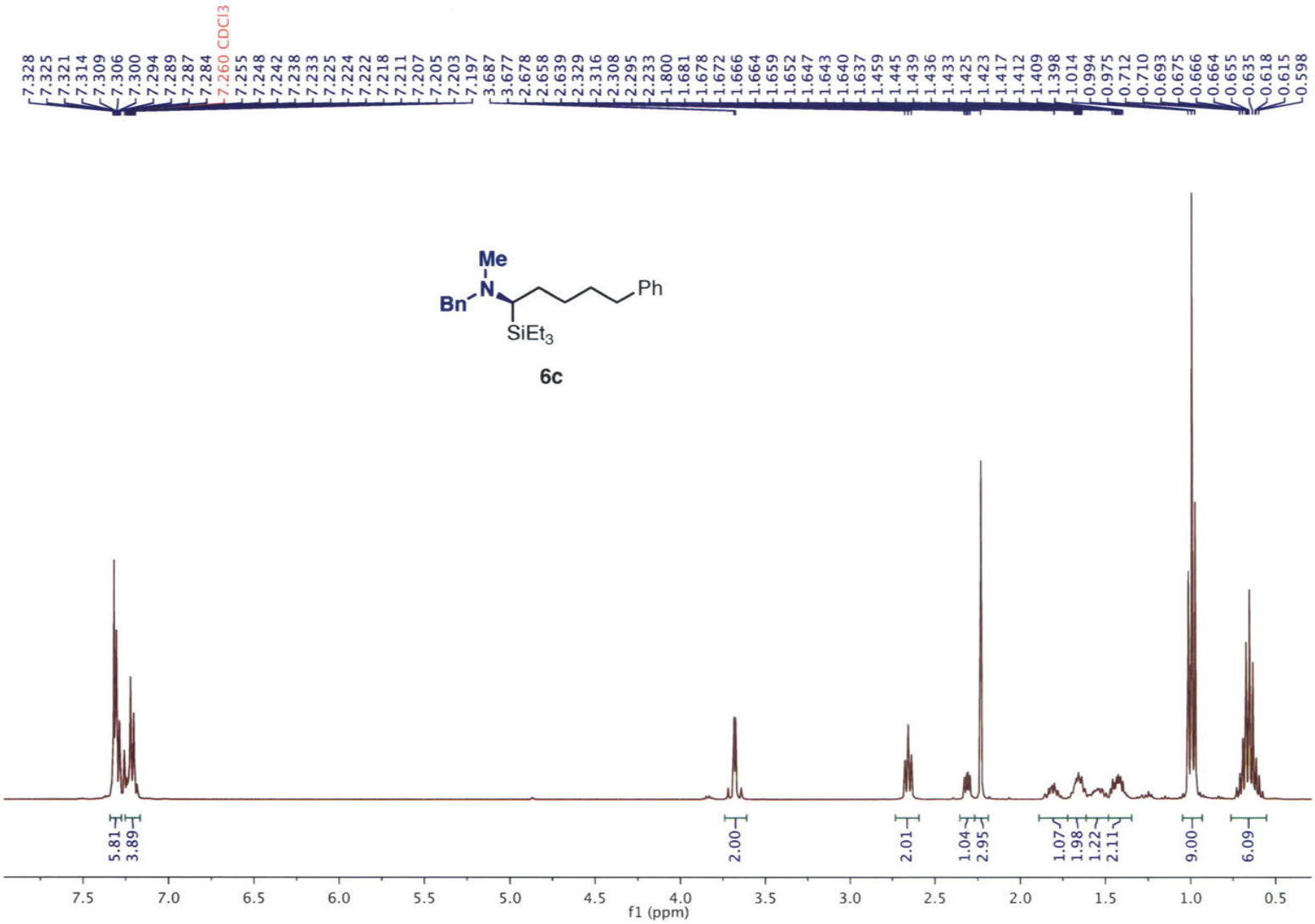
128.187
125.522
77.317 CDCl3
77.000 CDCl3
76.683 CDCl3
53.517
35.990
32.111
31.931
29.196
27.114
20.582
14.209
7.876
3.989
n-Bu
N
n-Bu
Ph
SiEt3
6a
130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)


7.306
7.304
7.291
7.286
7.283
7.274
7.267
7.265
7.260 CDCl3
7.200
7.198
7.191
7.182
7.177
7.164
3.639
3.628
3.617
2.669
2.657
2.646
2.640
2.628
2.621
2.618
2.607
2.601
2.578
2.567
2.555
2.549
2.538
2.527
2.104
2.092
2.082
2.070
1.717
1.705
1.649
1.641
1.638
1.635
1.633
1.629
1.623
1.620
1.618
1.612
1.609
1.407
1.394
1.387
1.381
1.376
1.371
1.368
1.362
1.357
1.349
1.346
0.991
0.971
0.951
0.626
0.619
0.607
0.599
0.588
0.579
0.568
0.562
0.559
O
N
Ph
SiEt3
6b
2.11
2.93
4.00
3.95
2.04
0.97
3.27
1.08
2.05
9.09
6.16
f1 (ppm)


142.683
128.348
128.208
125.584
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
67.809
54.960
52.207
35.884
31.710
29.677
26.349
7.810
3.922
O
N
Ph
SiEt3
6b
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)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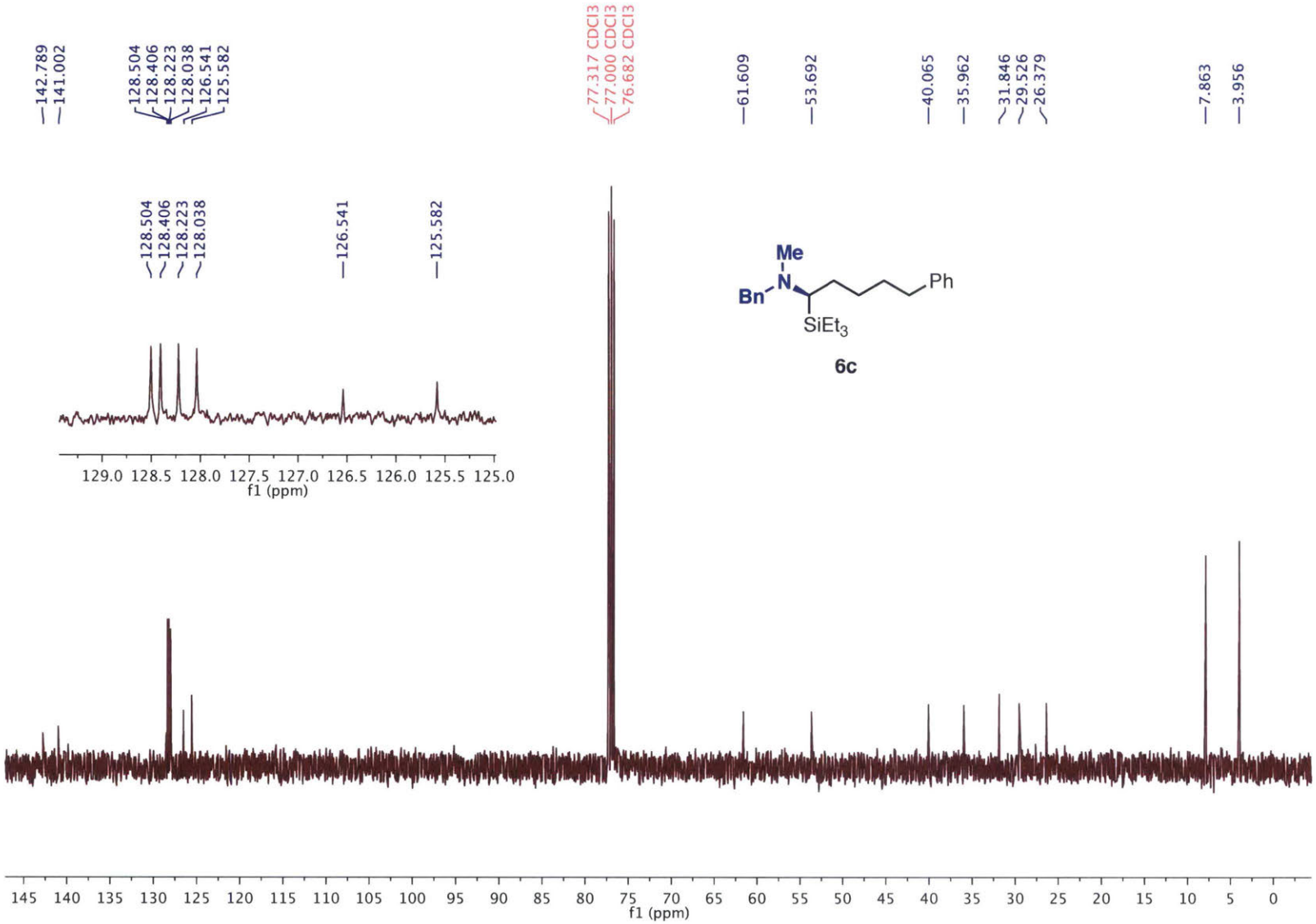
7.325
7.321
7.314
7.309
7.306
7.300
7.294
7.289
7.287
7.284
7.260 CDCl3
7.255
7.248
7.242
7.238
7.233
7.225
7.224
7.222
7.218
7.211
7.207
7.205
7.203
7.197
3.687
3.677
2.678
2.658
2.639
2.329
2.316
2.308
2.295
2.233
1.800
1.681
1.678
1.672
1.666
1.664
1.659
1.652
1.647
1.643
1.640
1.637
1.459
1.445
1.439
1.436
1.433
1.425
1.423
1.417
1.412
1.409
1.398
1.014
0.994
0.975
0.712
0.710
0.693
0.675
0.666
0.664
0.655
0.635
0.618
0.615
0.598
Me
N
Bn
Ph
SiEt3
6c
5.81
3.89
2.00
2.01
1.04
2.95
1.07
1.98
1.22
2.11
9.00
6.09
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
f1 (ppm)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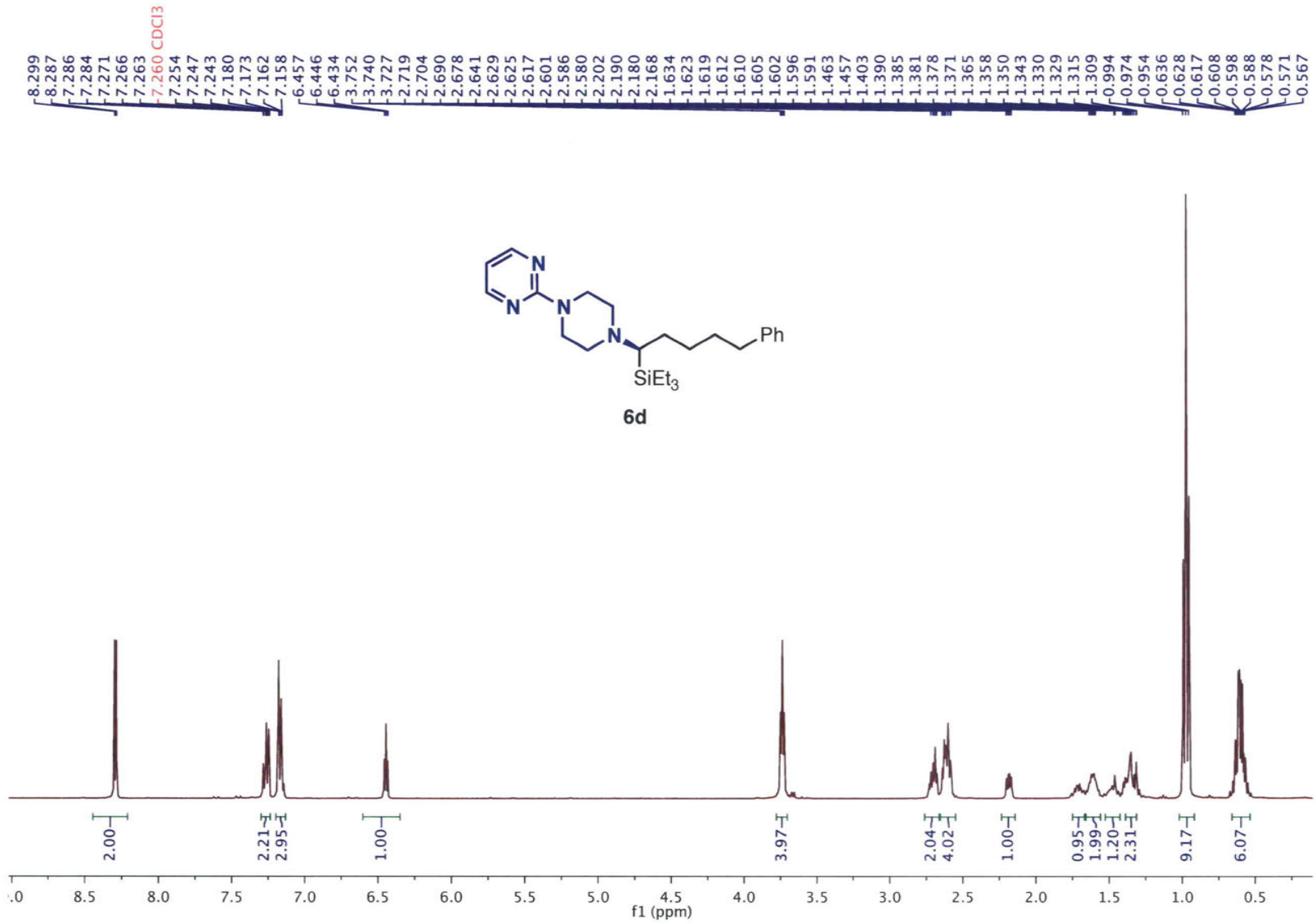
141.002
128.504
128.406
128.223
128.038
126.541
125.582
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
61.609
53.692
40.065
35.962
31.846
29.526
26.379
7.863
3.956
Me
N
Bn
Ph
SiEt3
6c
129.0 128.5 128.0 127.5 127.0 126.5 126.0 125.5 125.0
f1 (ppm)
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)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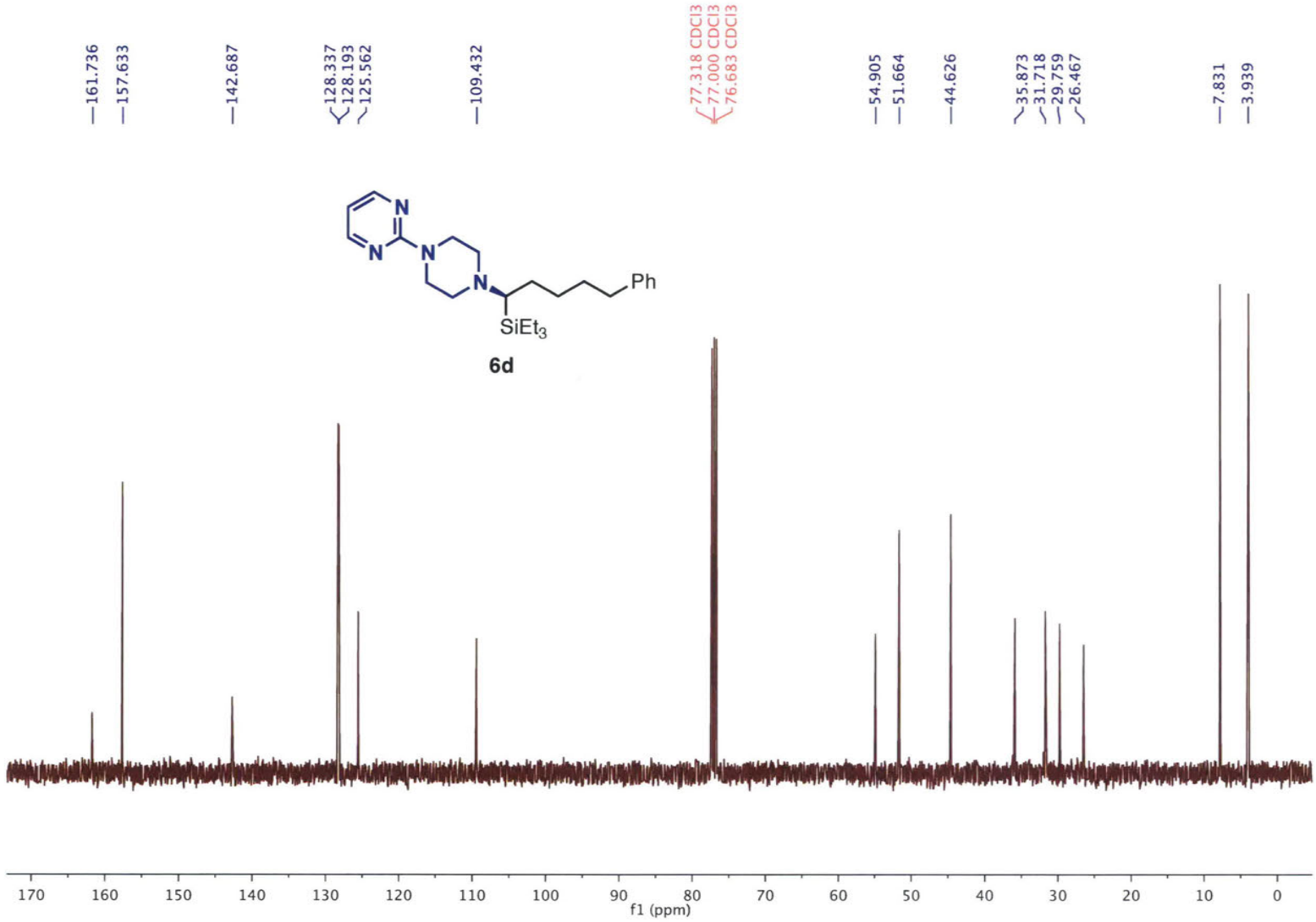
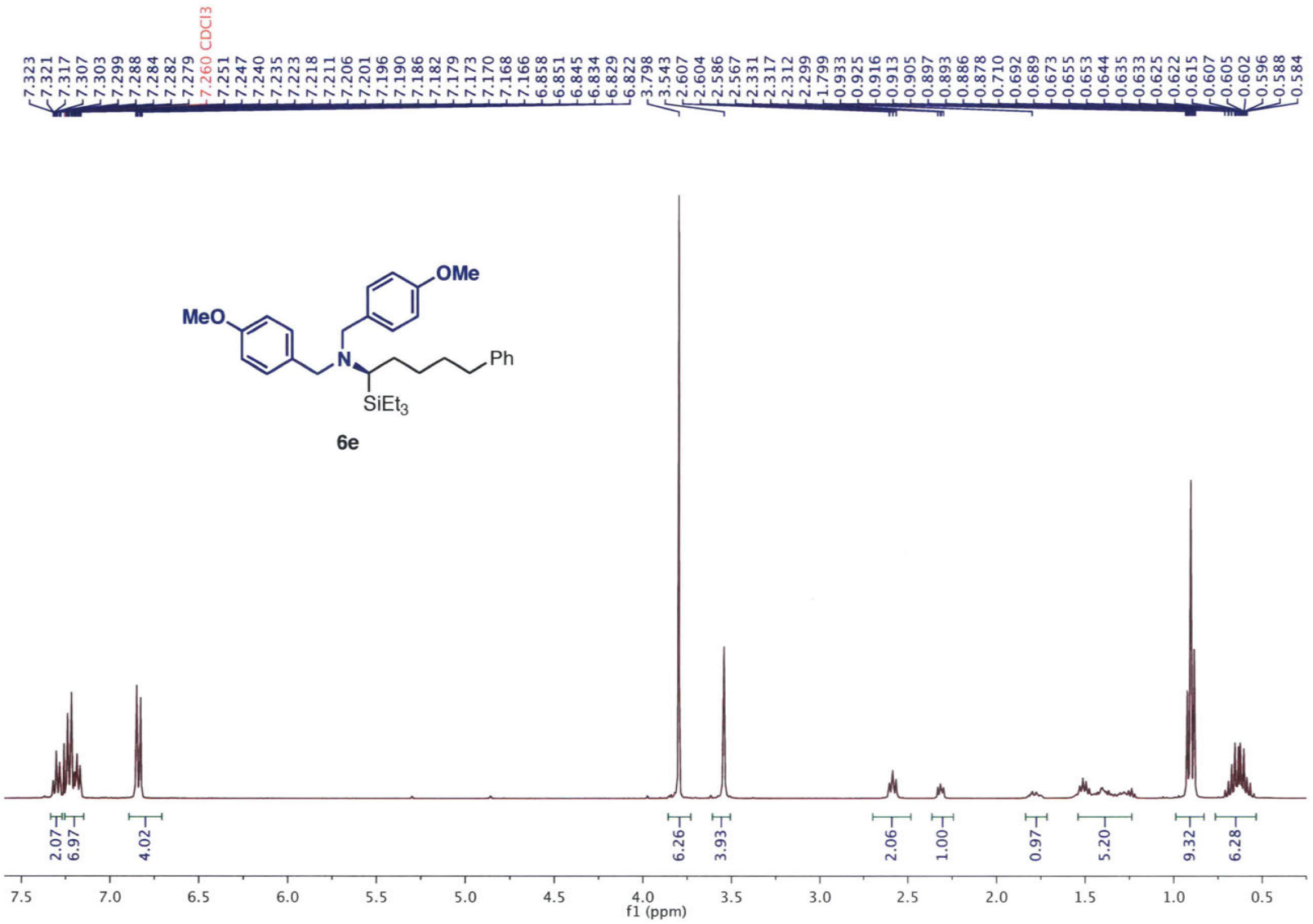
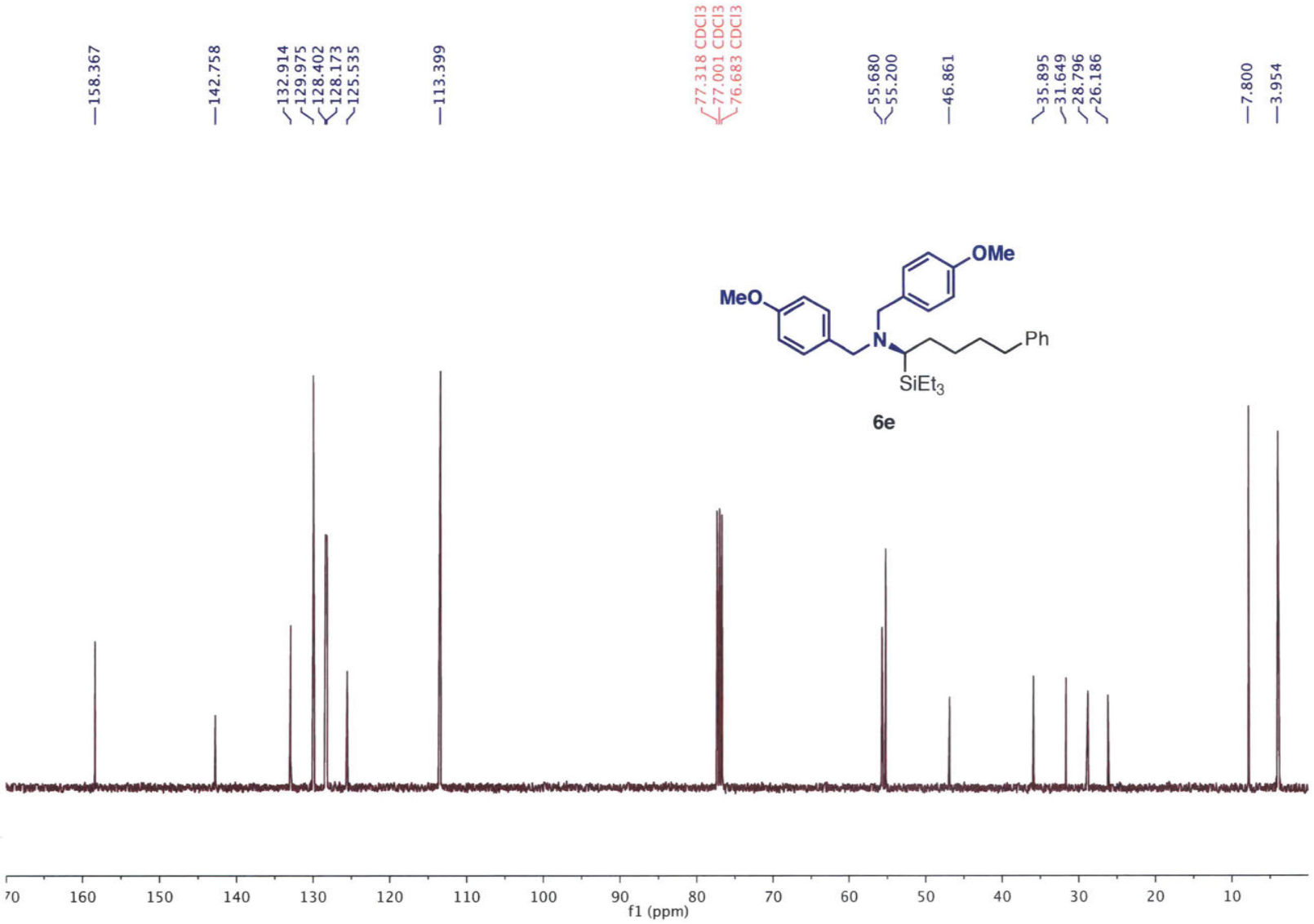
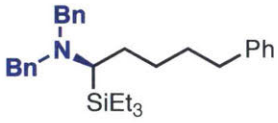
7.286
7.284
7.271
7.266
7.263
7.260 CDCl3
7.254
7.247
7.243
7.180
7.173
7.162
7.158
6.457
6.446
6.434
3.752
3.740
3.727
2.719
2.704
2.690
2.678
2.641
2.629
2.625
2.617
2.601
2.586
2.580
2.202
2.190
2.180
2.168
1.634
1.623
1.619
1.612
1.610
1.605
1.602
1.596
1.591
1.463
1.457
1.403
1.390
1.385
1.381
1.378
1.371
1.365
1.358
1.350
1.343
1.330
1.329
1.315
1.309
0.994
0.974
0.954
0.636
0.628
0.617
0.608
0.598
0.588
0.578
0.571
0.567
N
N
N
N
Ph
SiEt3
6d
2.00
2.21
2.95
1.00
3.97
2.04
4.02
1.00
0.95
1.99
1.20
2.31
9.17
6.07
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
f1 (ppm)


161.736
157.633
142.687
128.337
128.193
125.562
109.432
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
54.905
51.664
44.626
35.873
31.718
29.759
26.467
7.831
3.939
N
N
N
N
Ph
SiEt3
6d
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.323
7.321
7.317
7.307
7.303
7.299
7.288
7.284
7.282
7.279
7.260 CDCl3
7.251
7.247
7.240
7.235
7.223
7.218
7.211
7.206
7.201
7.196
7.190
7.186
7.182
7.179
7.173
7.170
7.168
7.166
6.858
6.851
6.845
6.834
6.829
6.822
3.798
3.543
2.607
2.604
2.586
2.567
2.331
2.317
2.312
2.299
1.799
0.933
0.925
0.916
0.913
0.905
0.897
0.893
0.886
0.878
0.710
0.692
0.689
0.673
0.655
0.653
0.644
0.635
0.633
0.625
0.622
0.615
0.607
0.605
0.602
0.596
0.588
0.584
MeO
OMe
N
Ph
SiEt3
6e
2.07
6.97
4.02
6.26
3.93
2.06
1.00
0.97
5.20
9.32
6.28
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
f1 (ppm)


158.367
142.758
132.914
129.975
128.402
128.173
125.535
113.399
77.318 CDCl3
77.001 CDCl3
76.683 CDCl3
55.680
55.200
46.861
35.895
31.649
28.796
26.186
7.800
3.954
OMe
MeO
N
Ph
SiEt3
6e
f1 (ppm)

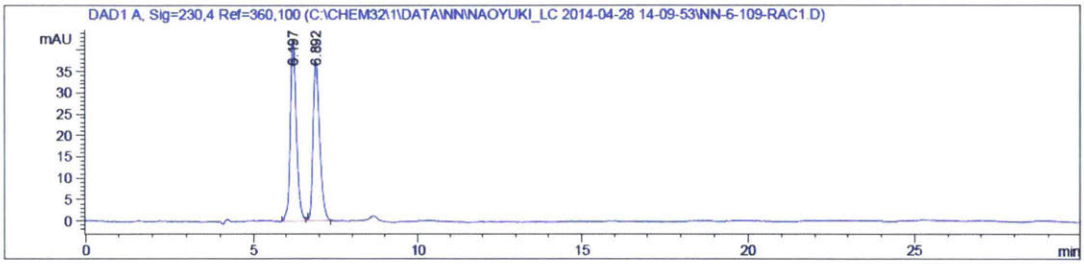
3.7 Chiral HPLC Spectra



3a

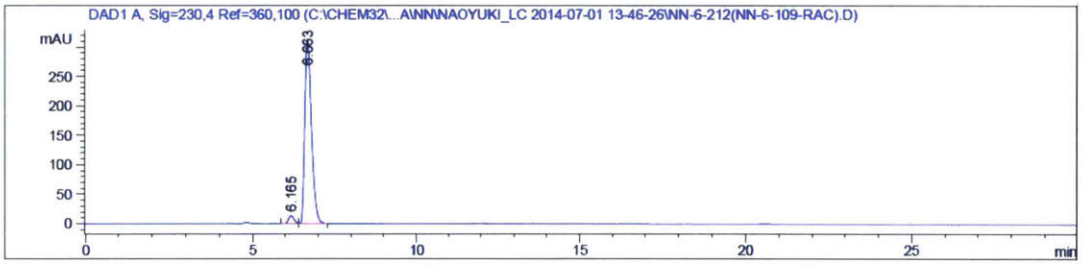
(*R*)-*N*,*N*-dibenzyl-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 2, entry **3a**)**:** HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 6.4 min, t_R (major) = 7.0 min.

Rac-**3a**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.197	BB	0.1933	545.06323	42.60482	51.0276
2	6.892	BB	0.2158	523.10999	37.25396	48.9724
Totals :				1068.17322	79.85878	

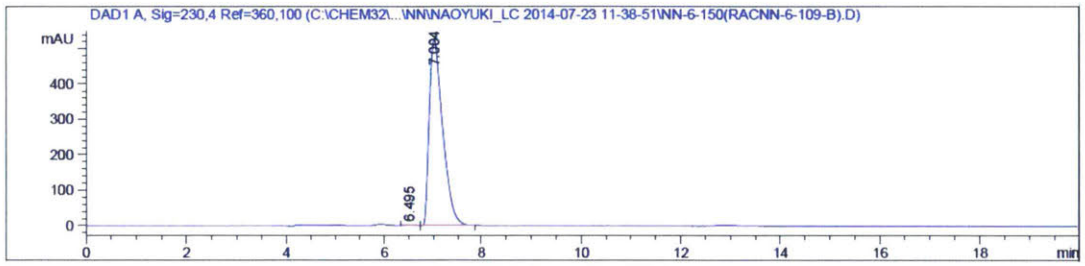
(R)-**3a** from **(*Z*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*Z*)-**1a**): **93% *ee***



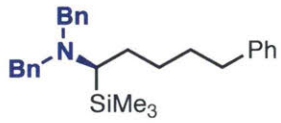
Signal 1: DAD1 A, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.165	BV	0.1833	163.27022	13.67623	3.5191
2	6.663	VB	0.2209	4476.31201	312.83578	96.4809
Totals :				4639.58223	326.51202	

(R)-**3a** from **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**): **>99% *ee***



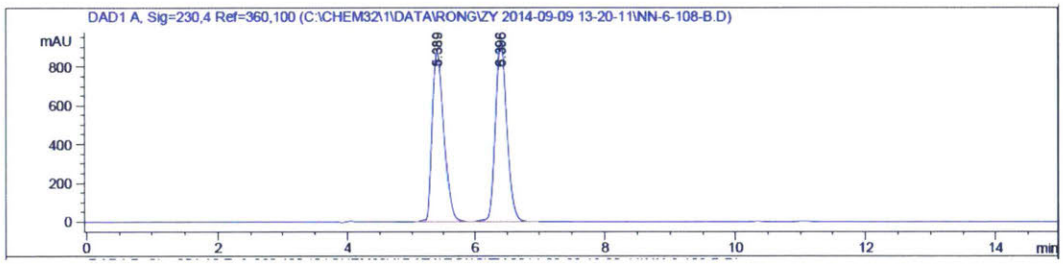
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.495	BV	0.1663	21.66092	1.82751	0.2167
2	7.004	VB	0.2919	9974.09473	524.42981	99.7833
Totals :				9995.75565	526.25732	



3b

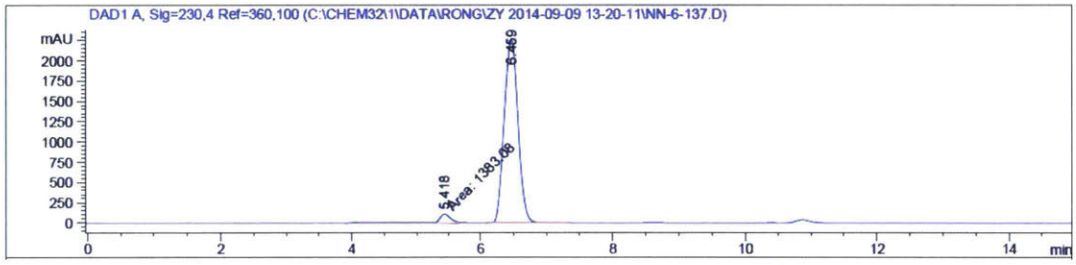
(*R*)-*N*,*N*-dibenzyl-5-phenyl-1-(trimethylsilyl)pentan-1-amine (Table 2, entry **3b**) : HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 5.4 min, t_R (major) = 6.5 min.

Rac-**3b**



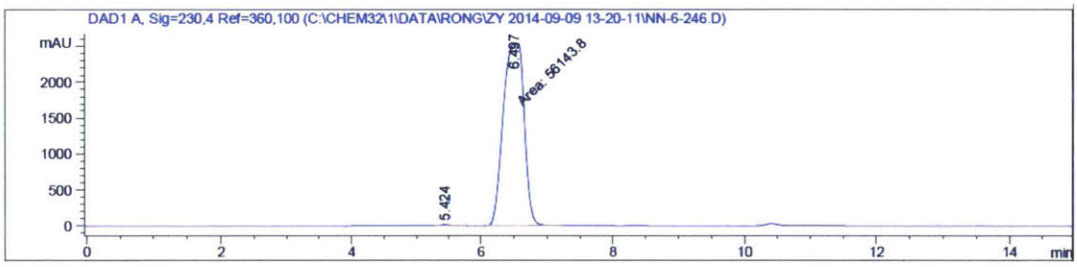
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.389	BV	0.2044	1.12807e4	875.23779	49.8289
2	6.396	VB	0.1883	1.13582e4	930.91498	50.1711
Totals :				2.26389e4	1806.15277	

(R)-**3b** from **(*Z*)-trimethyl(5-phenylpent-1-en-1-yl)silane** ((*Z*)-**1b**): **92% *ee***

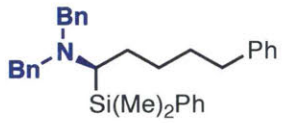


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.418	MM T	0.1947	1383.07605	118.38574	4.0208
2	6.459	BB	0.2319	3.30151e4	2267.42139	95.9792
Totals :				3.43982e4	2385.80713	

(R)-**3b** from **(*E*)-trimethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1b**): **99% *ee***



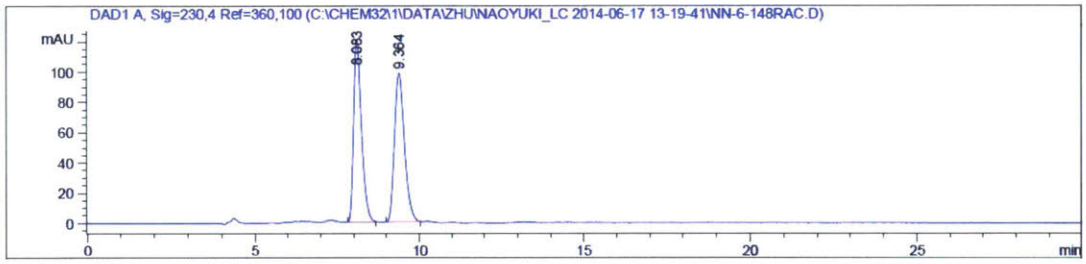
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.424	BB	0.1919	202.00739	16.37866	0.3585
2	6.497	MM T	0.3676	5.61438e4	2545.17285	99.6415
Totals :				5.63458e4	2561.55151	



3c

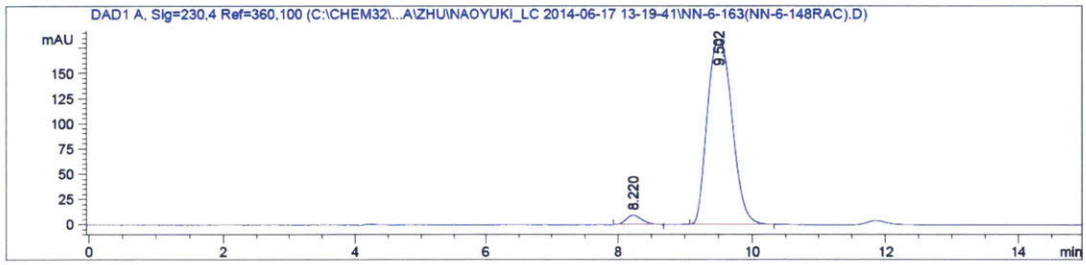
(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-5-phenylpentan-1-amine (Table 2, entry **3c**)**:** HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 8.0 min, t_R (major) = 9.0 min.

Rac-**3c**



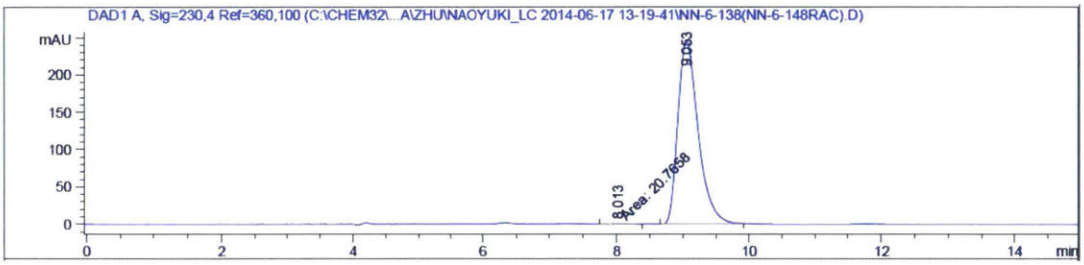
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.083	BB	0.2528	2012.46216	120.53931	49.2802
2	9.364	BB	0.3256	2071.25000	98.37413	50.7198
Totals :				4083.71216	218.91344	

(*R*)-**3c** from **(*Z*)-dimethyl(phenyl)(5-phenylpent-1-en-1-yl)silane** ((Z)-**1c**): 93% *ee*

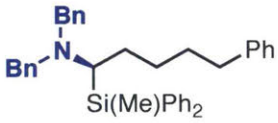


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.220	BB	0.2483	158.70294	9.43168	3.2779
2	9.502	BB	0.4204	4682.85156	183.07094	96.7221
Totals :				4841.55450	192.50262	

(R)-**3c** from **(*E*)-dimethyl(phenyl)(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1c**): 99% *ee*



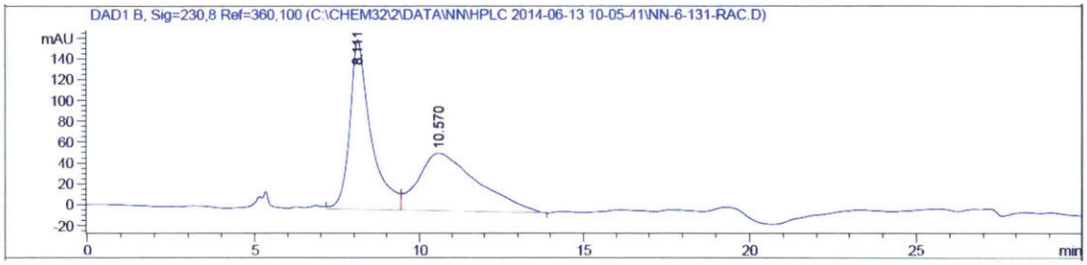
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.013	MM T	0.3359	20.76582	1.03043	0.3949
2	9.053	BB	0.3268	5237.68213	245.58714	99.6051
Totals :				5258.44795	246.61758	



3d

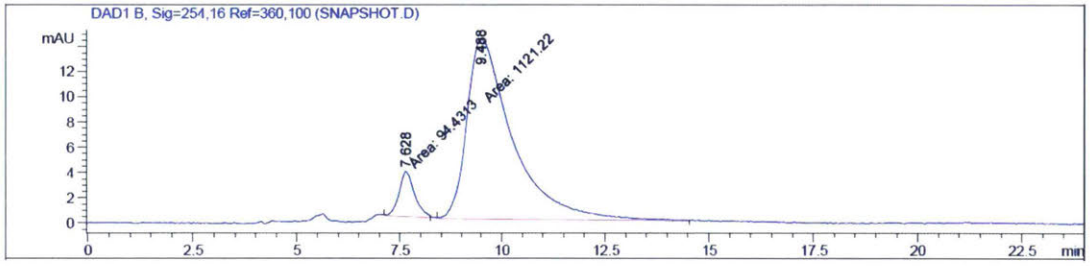
(*R*)-*N*,*N*-dibenzyl-1-(methyldiphenylsilyl)-5-phenylpentan-1-amine (Table 2, entry **3d**)**:** HPLC analysis (OT-(+), 1% IPA/hexanes, 0.8 mL/min, 220 nm): t_R (minor) = 8 min, t_R (major) = 10 min.

Rac-**3d**



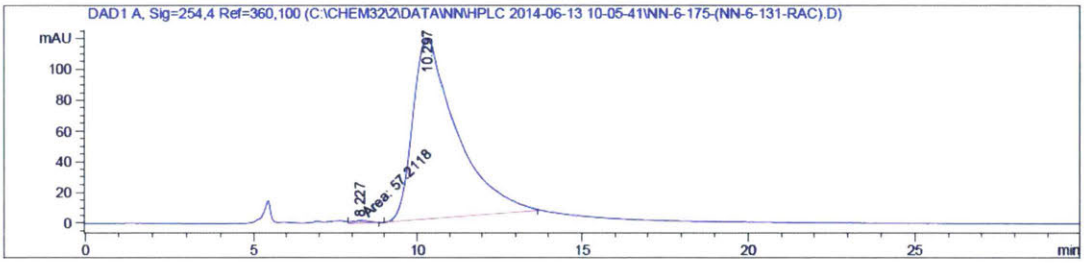
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.111	VB	0.6325	7288.47021	162.72903	50.8177
2	10.570	BV	1.6480	7053.90918	55.52910	49.1823
Totals :				1.43424e4	218.25814	

(R)-**3d** from **(*Z*)-methyldiphenyl(5-phenylpent-1-en-1-yl)silane** ((*Z*)-**1d**): 84% *ee*

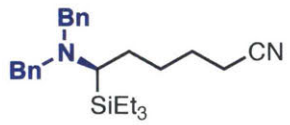


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.628	MM T	0.4381	94.43128	3.59229	7.7679
2	9.488	MM T	1.3060	1121.22412	14.30914	92.2321
Totals :				1215.65540	17.90143	

(R)-**3d** from **(*E*)-methyldiphenyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1d**): 99% *ee*



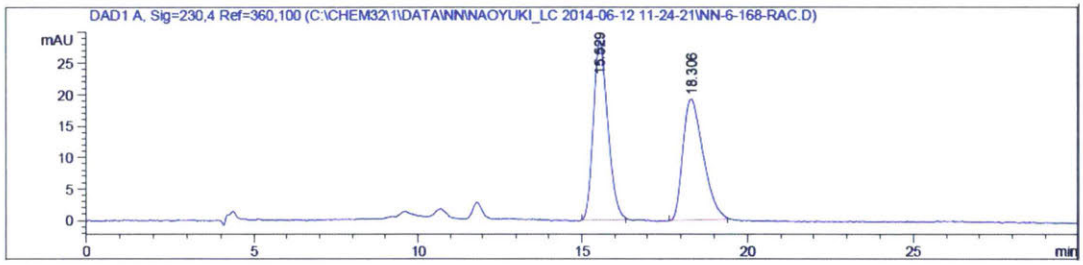
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.227	MM T	0.5136	57.21180	1.63225	0.5166
2	10.297	BB	1.3049	1.10185e4	116.97504	99.4834
Totals :				1.10757e4	118.60729	



5a

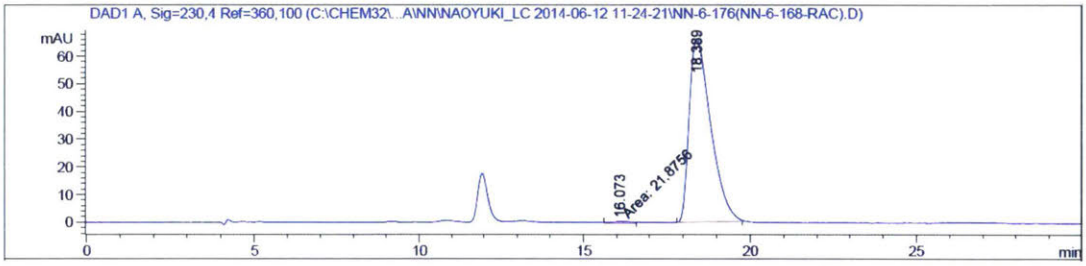
(*R*)-6-(dibenzylamino)-6-(triethylsilyl)hexanenitrile (Table 3, entry **5a**)**:** HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 16.0 min, t_R (major) = 18.3 min.

Rac-**5a**

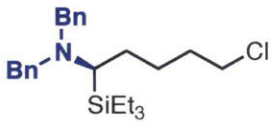


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.529	BB	0.4587	871.26416	28.49911	51.3397
2	18.306	BB	0.5159	825.79236	19.27070	48.6603
Totals :				1697.05652	47.76981	

(R)-**5a** from **(*E*)-6-(triethylsilyl)hex-5-enenitrile**: 99% *ee*



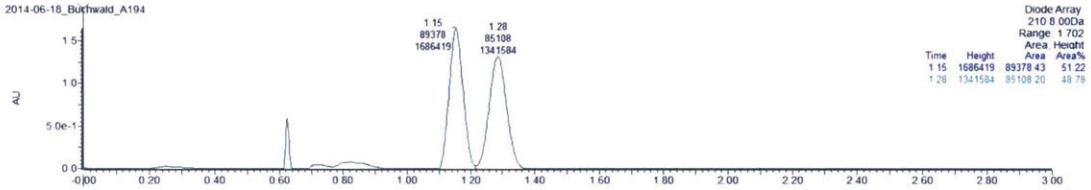
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.073	MM T	0.6182	21.87559	5.89775e-1	0.7297
2	18.389	BB	0.6406	2975.90381	66.18115	99.2703
Totals :				2997.77939	66.77093	



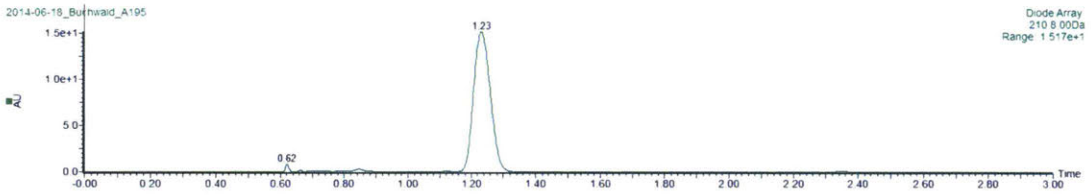
5b

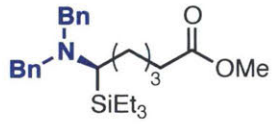
(*R*)-*N*,*N*-dibenzyl-5-chloro-1-(triethylsilyl)pentan-1-amine (Table 3, entry **5b**)**:** SFC analysis[21] (Chiralpak IC(4.6x150 mm, 3μm), isocratic 3% EtOH): t_R (minor) = 1.15 minute, t_R (major) = 1.28 min.

Rac-**5b**



(R)-**5b** from **(*E*)-(5-chloropent-1-en-1-yl)triethylsilane**: **>99%** *ee*

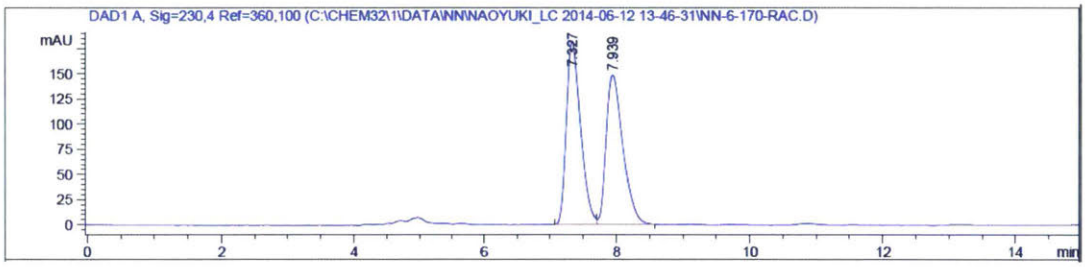




5c

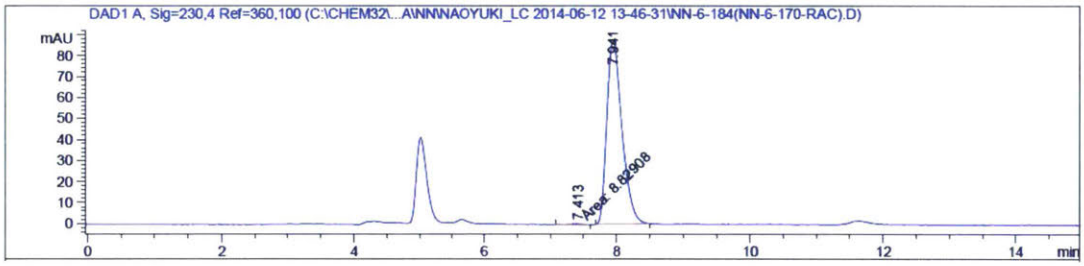
(*R*)-*N*,*N*-dibenzyl-5-chloro-1-(triethylsilyl)pentan-1-amine (Table 3, entry **5c**): HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 7.4 min, t_R (major) = 7.9 min.

Rac-**5c**

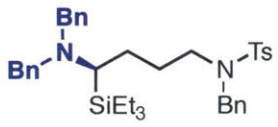


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.327	BV	0.2307	2729.22632	182.22719	50.9488
2	7.939	VB	0.2681	2627.57666	148.75972	49.0512
Totals :				5356.80298	330.98691	

(R)-**5c** from **(*E*)-methyl 6-(triethylsilyl)hex-5-enoate**: **99%** *ee*



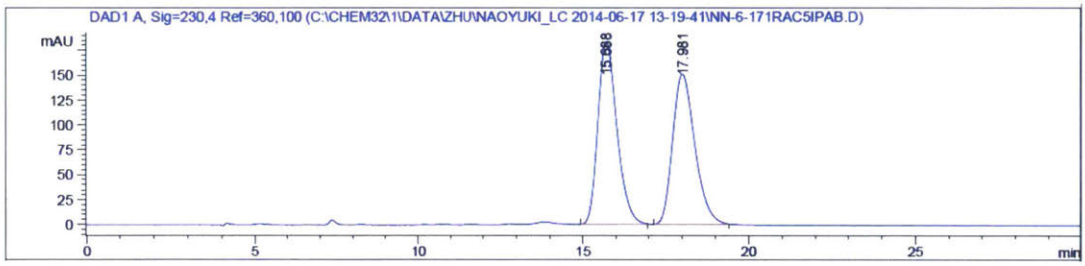
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.413	MM T	0.3181	8.82908	4.70222e-1	0.6253
2	7.941	BB	0.2458	1403.23486	88.12694	99.3747
Totals :				1412.06394	88.59716	



5d

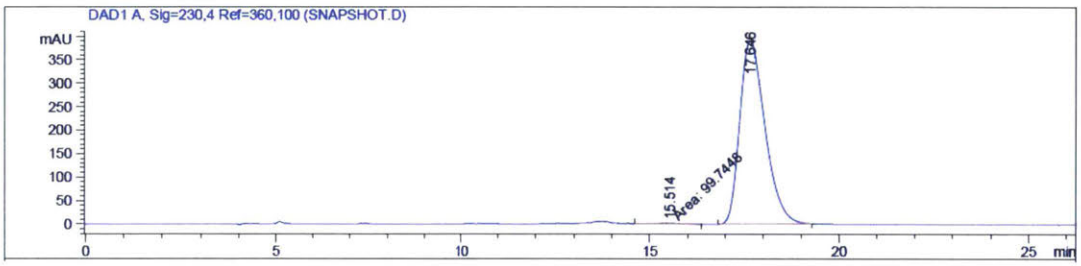
(*R*)-*N*-benzyl-*N*-(4-(dibenzylamino)-4-(triethylsilyl)butyl)-4-methylbenzenesulfonamide (Table 3, entry **5d**)**:** HPLC analysis (OD-H, 5% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 15.7 min, t_R (major) = 18.0 min.

Rac-**5d**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.688	BB	0.6135	7313.48242	183.31404	51.0250
2	17.981	BB	0.7125	7019.66016	150.95557	48.9750
Totals :				1.43331e4	334.26961	

(R)-**5d** from **(*E*)-*N*-benzyl-4-methyl-*N*-(4-(triethylsilyl)but-3-en-1-yl)benzene sulfonamide ((*E*)-1h)**: **99%** *ee*

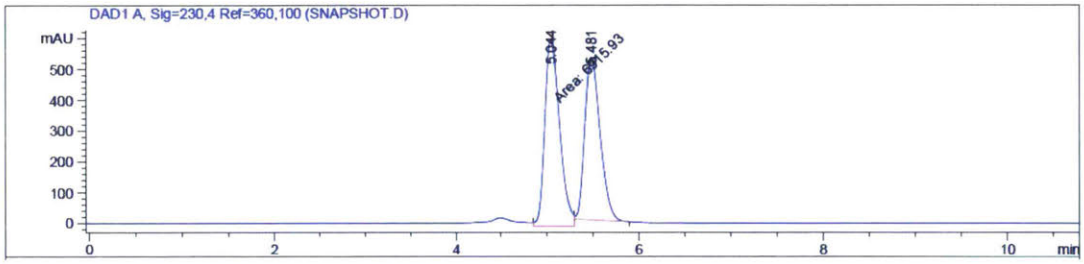


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.514	MM T	0.9468	99.74477	1.72181	0.5496
2	17.646	BB	0.7027	1.80493e4	390.91562	99.4504
Totals :				1.81491e4	392.63743	

5e

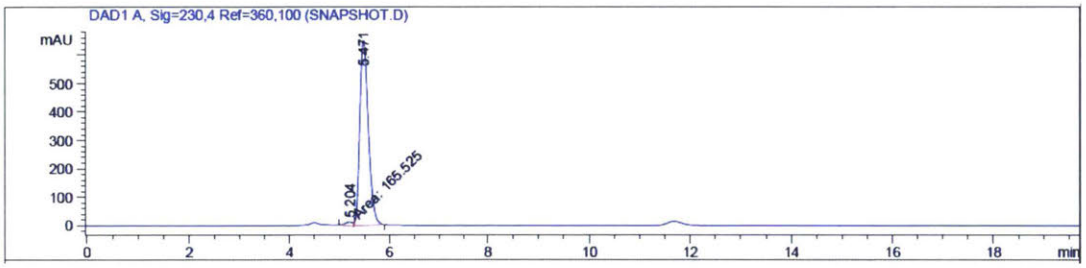
(*R*)-*N*,*N*-dibenzyl-4-((*tert*-butyldimethylsilyl)oxy)-1-(dimethyl (phenyl)silyl)butan-1-amine (Table 3, entry **5e**): HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 5.0 min, t_R (major) = 5.5 min.

Rac-**5e**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.044	MM T	0.1885	6915.92627	611.64117	53.1541
2	5.481	MM R	0.2127	6095.16309	528.28687	46.8459
Totals :				1.30111e4	1139.92804	

(R)-**5e** from **(*E*)-*tert*-butyl((4-(dimethyl(phenyl)silyl)but-3-en-1-yl)oxy)dimethylsilane**: 96% *ee*

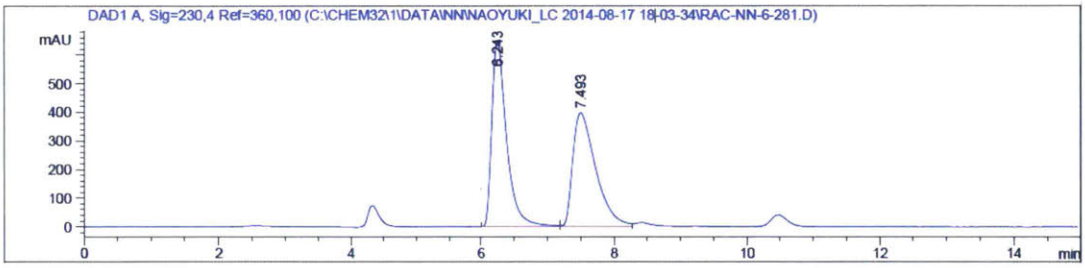


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.204	MM T	0.1885	165.52487	14.63687	2.1045
2	5.471	MM R	0.1810	7699.80469	650.49725	97.8955
Totals :				7865.32956	665.13412	

5f

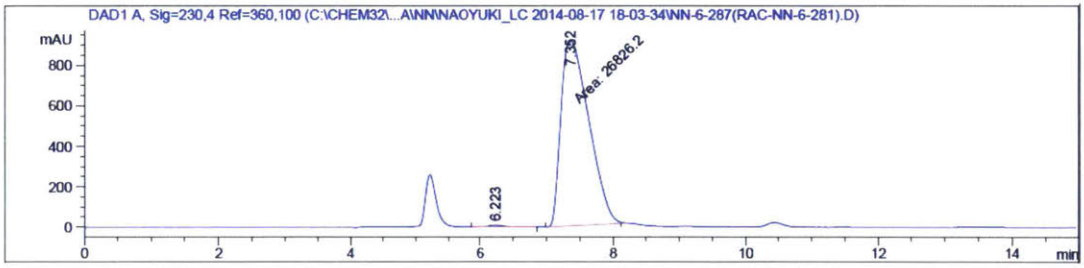
(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-3-methoxypropan-1-amine (Table 3, entry **5f**): HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 6.2 min, t_R (major) = 7.5 min.

Rac-**5f**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.243	BV	0.2309	9970.34180	650.24298	51.2264
2	7.493	VV	0.3623	9492.94727	397.97064	48.7736
Totals :				1.94633e4	1048.21362	

(R)-**5f** from **(*E*)-(3-methoxyprop-1-en-1-yl)dimethyl(phenyl)silane:** 99% *ee*

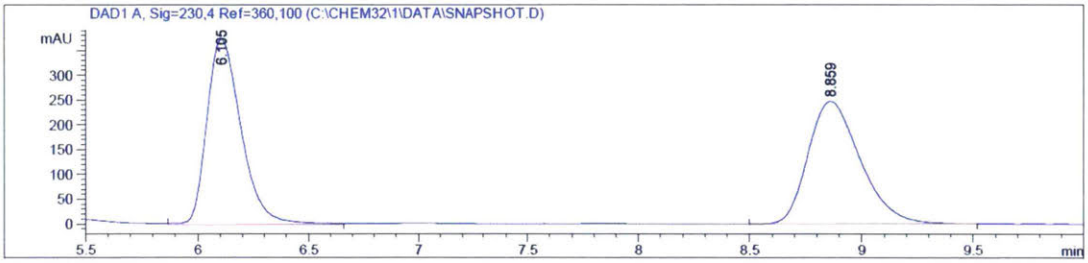


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.223	BB	0.2521	158.38020	9.23315	0.5869
2	7.352	MM T	0.5083	2.68262e4	920.57983	99.4131
Totals :				2.69846e4	929.81298	

5g

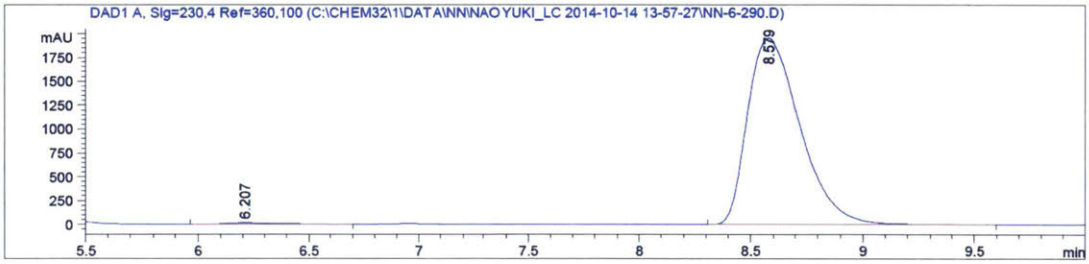
(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-amine (Table 3, entry **5g**): HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 6.1 min, t_R (major) = 8.9 min.

Rac-**5g**



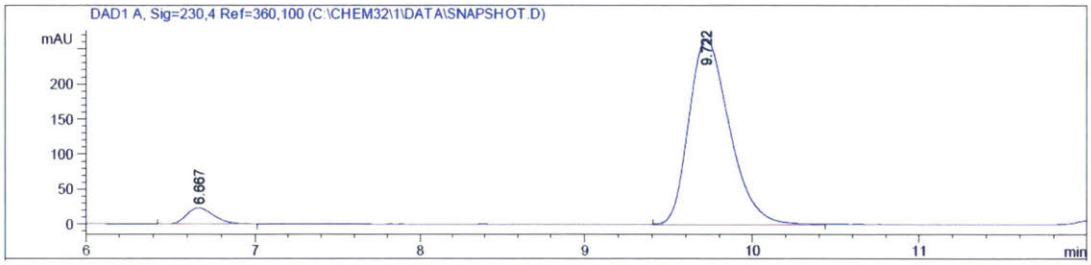
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.105	BB	0.1627	1927.91431	183.35358	50.0432
2	8.859	BB	0.2509	1924.58948	118.84383	49.9568
Totals :				3852.50378	302.19740	

(R)-**5g** from **(*E*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane:** 98% *ee*



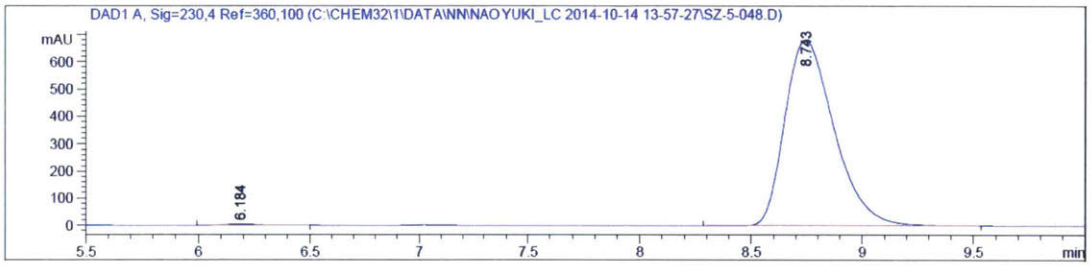
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.207	BV	0.2723	333.47437	17.34593	1.0407
2	8.579	BB	0.2558	3.17093e4	1949.43457	98.9593
Totals :				3.20427e4	1966.78050	

(R)-**5g** from **(*Z*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane:** 89% *ee*



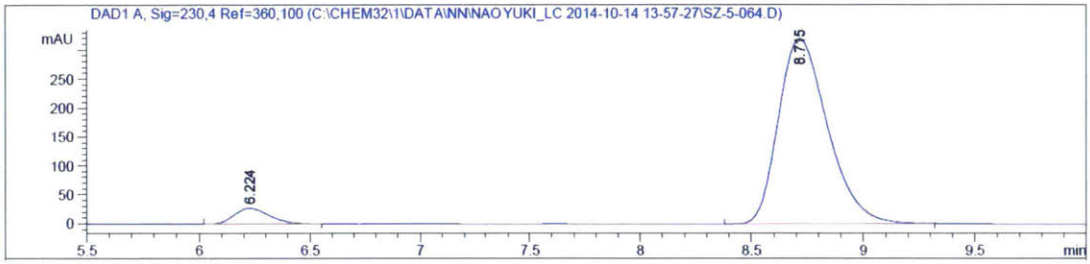
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.667	BB	0.1740	261.61649	23.12520	5.5435
2	9.722	BB	0.2608	4457.73047	264.22803	94.4565
Totals :				4719.34695	287.35323	

(R)-**5g'** from **(*E*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane** with *d*-Ph_2SiD_2**:** 98% *ee*



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.173	BV	0.1671	28.84967	2.19817	1.0612
2	8.743	VV	0.2399	2689.64868	174.41940	98.9388
Totals :				2718.49835	176.61758	

(R)-**5g'** from **(*Z*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane** with *d*-Ph_2SiD_2: 88% *ee*

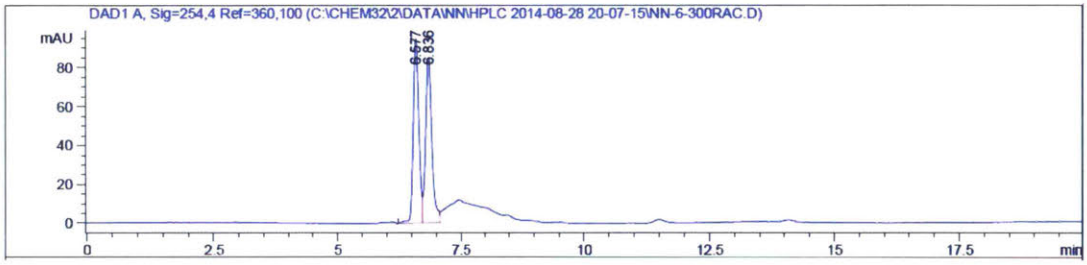


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.224	VB	0.1743	306.18033	27.42382	5.9061
2	8.715	VB	0.2365	4877.93945	318.83997	94.0939
Totals :				5184.11978	346.26379	

5h

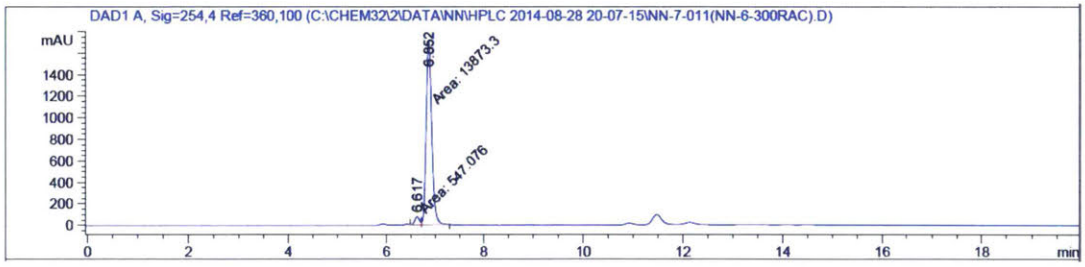
(*R*)-*N*,*N*-dibenzyl-1-(dimethyl(phenyl)silyl)-2-(1-methoxycyclohexyl)ethanamine (Table 3, entry **5h**): HPLC analysis (OD-H, 90:5:0.1 Hexanes: IPA: Diethylamine, 0.8 mL/min, 220 nm): t_R (minor) = 7.4 min, t_R (major) = 7.9 min.

Rac-**5h**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.577	VV	0.1213	759.85693	95.04185	50.4694
2	6.836	VV	0.1320	745.72137	85.33576	49.5306
Totals :				1505.57831	180.37761	

(R)-**5h** from **(*E*)-(2-(1-methoxycyclohexyl)vinyl)dimethyl(phenyl)silane**: 92% *ee*

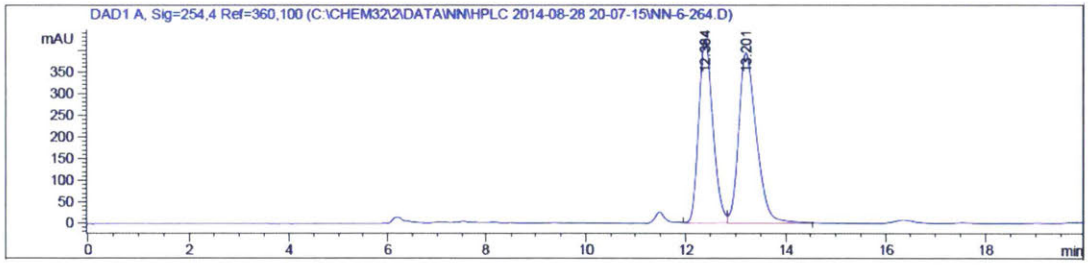


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.617	MF T	0.1326	547.07605	78.61522	3.7938
2	6.852	FM T	0.1350	1.38733e4	1712.52979	96.2062
Totals :				1.44203e4	1791.14500	

5i

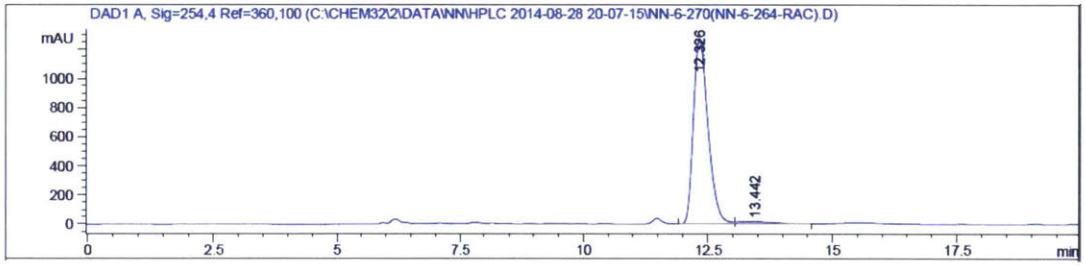
(*R*)-N^1,N^1,N^5-tribenzyl-1-(methyldiphenylsilyl)pentane-1,5-diamine (Table 3, entry **5i**): HPLC analysis (OD-H, 90:5:0.1 Hexanes: IPA: Diethylamine, 0.8 mL/min, 220 nm): t_R (major) = 12.3 min, t_R (minor) = 13.5 min.

Rac-**5i**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.384	VV	0.3088	8475.35059	424.74890	46.5247
2	13.201	VB	0.3711	9741.52637	393.12570	53.4753
Totals :				1.82169e4	817.87460	

(R)-**5i** from **(*E*)-*N*-benzyl-5-(methyldiphenylsilyl)pent-4-en-1-amine:** 93% *ee*

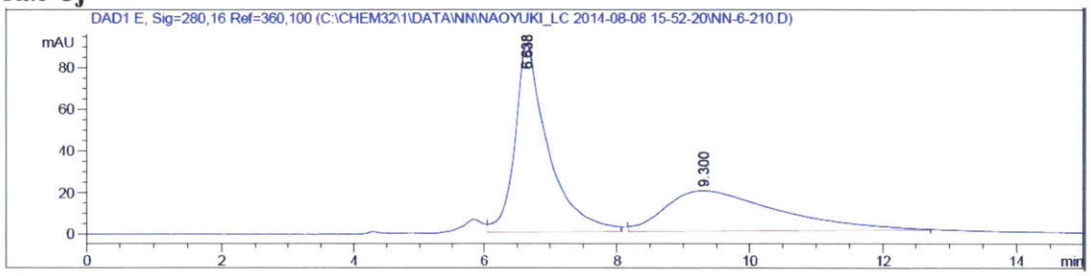


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.326	VV	0.3209	2.62779e4	1272.82495	96.3053
2	13.442	VV	0.6708	1008.12732	18.88435	3.6947
Totals :				2.72860e4	1291.70930	

5j

(*R*)-*N*,*N*-dibenzyl-2-methyl-1-(methyldiphenylsilyl)propan-1-amine (Table 3, entry **5j**): HPLC analysis (OT(+), 1% IPA/Hexanes, 0.8 mL/min, 220 nm): t_R (minor) = 6.7 min, t_R (major) = 9.3 min.

Rac-**5j**

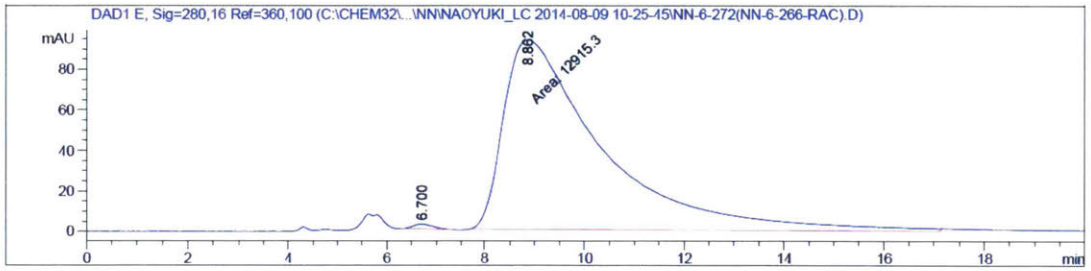



```
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.672 VV    0.6154 7.63435e4  1790.56201  48.3340
   2   9.288 VB    1.8902 8.16063e4   570.03229  51.6660

Totals :                  1.57950e5  2360.59430
```

(R)-**5j** from **methyl(2-methylprop-1-en-1-yl)diphenylsilane**: 99% *ee*



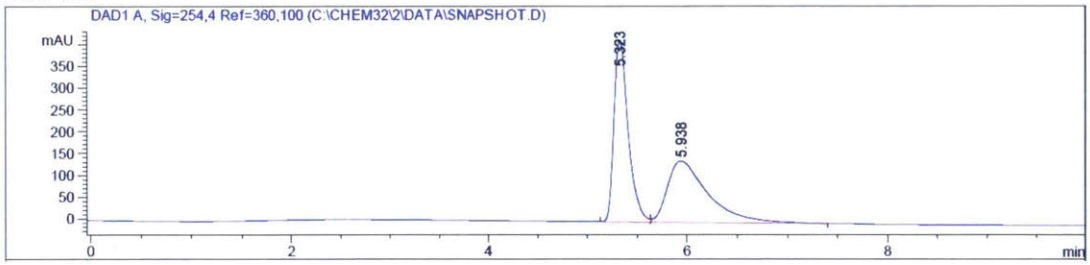

```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.700 BB    0.3616   75.41872   2.56045   0.5806
   2   8.862 MM T  2.3014 1.29153e4   93.53019  99.4194

Totals :                  1.29907e4   96.09064
```

5k

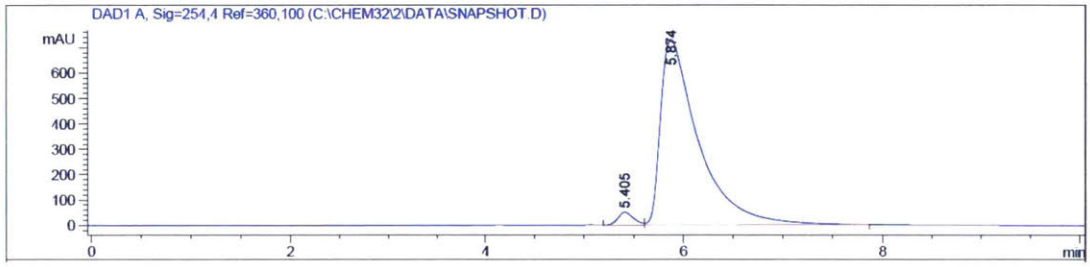
(*R*)-*N*,*N*-dibenzyl-3-methyl-1-(methyldiphenylsilyl)butan-1-amine (Table 3, entry **5k**): HPLC analysis (OD-H, 97% Hexanes/ 3% of '97 Hexanes: 3 EtOH: 0.2 TFA: 0.1 DEA', 0.8 mL/min, 220 nm): t_R (minor) = 5.4 min, t_R (major) = 5.9 min.

Rac-**5k**

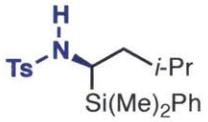


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.323	VV	0.1486	4096.53760	416.91867	50.8687
2	5.938	VB	0.4180	3956.61865	140.71378	49.1313
Totals :				8053.15625	557.63245	

(R)-**5k** from **(*Z*)-methyl(3-methylbut-1-en-1-yl)diphenylsilane**: 94% *ee*



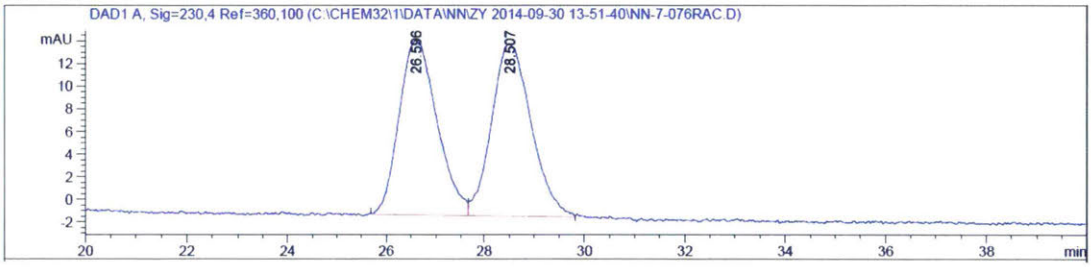
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.405	VV	0.1634	566.84027	51.89570	2.8309
2	5.874	VB	0.3861	1.94566e4	732.06128	97.1691
Totals :				2.00235e4	783.95698	



5l'

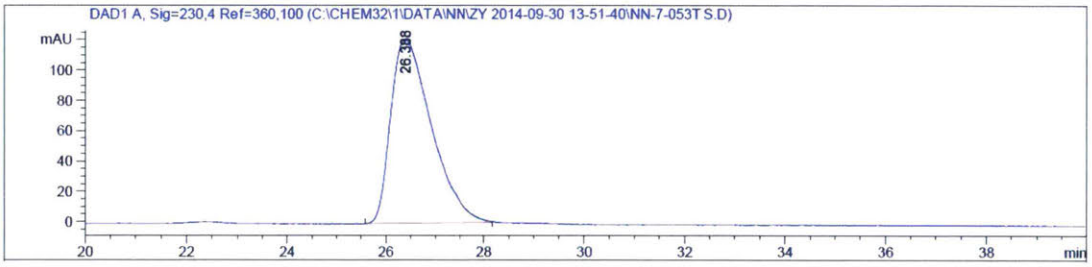
(*R*)-*N*-(1-(dimethyl(phenyl)silyl)-3-methylbutyl)-4-methylbenzenesulfonamide (5l'): HPLC analysis (OD-H, 1% IPA/Hexanes, 0.8 mL/min, 220 nm): t_R (minor) = 26.6 min, t_R (major) = 28.5 min.

Rac-**5l'**

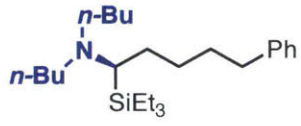


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.596	BV	0.6289	830.11871	15.54763	49.6448
2	28.507	VV	0.6549	841.99774	15.28006	50.3552
Totals :				1672.11646	30.82769	

(R)- **5l'** from **(*R*)-*N*-(1-(dimethyl(phenyl)silyl)-3-methylbutyl)-4-methylbenzenesulfonamide**: >99% *ee*



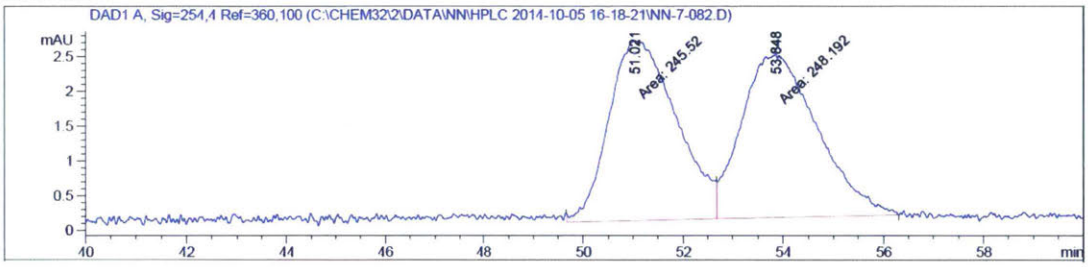
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.388	BB	0.7942	6980.40576	121.51031	100.0000
Totals :				6980.40576	121.51031	



6a

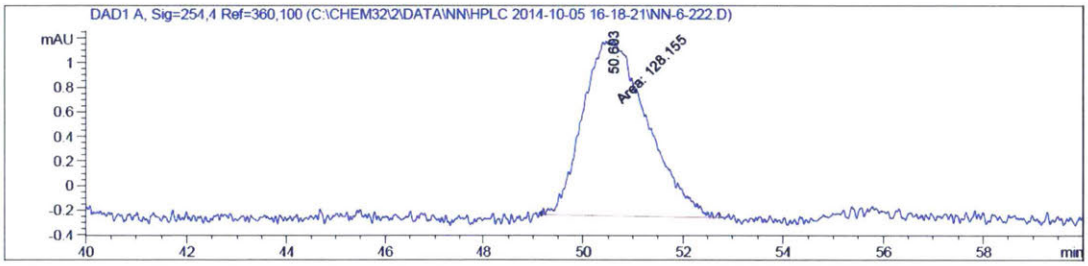
(*R*)-*N*,*N*-dibutyl-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 4, entry **6a**)**:** From **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**) (3 connected OD-H columns, 97% Hexanes/ 3% of '92 Hexanes: 8 EtOH: 0.2 TFA: 0.1 DEA', 0.55 mL/min, 220 nm): t_R (major) = 51 min, t_R (minor) = 54 min.

Rac-**6a**

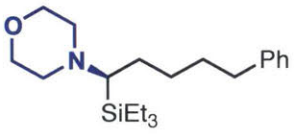


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	51.021	MF T	1.5758	245.52043	2.59674	49.7294
2	53.848	FM T	1.7471	248.19196	2.36761	50.2706
Totals :				493.71239	4.96434	

(R)-**6a** from **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**): >99% *ee*



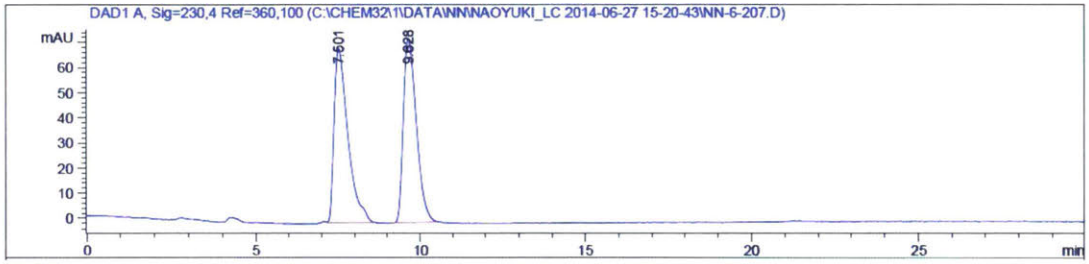
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.603	MM T	1.4914	128.15466	1.43212	100.0000
Totals :				128.15466	1.43212	



6b

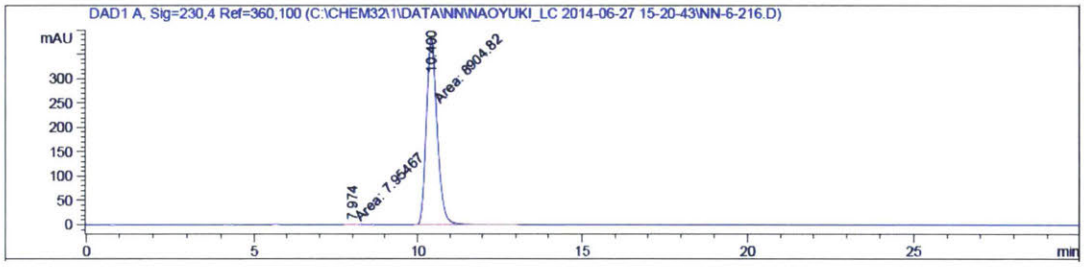
(*R*)-4-(5-phenyl-1-(triethylsilyl)pentyl)morpholine (Table 4, entry **6b**)**:** HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 8.0 min, t_R (major) = 10.4 min.

Rac-**6b**

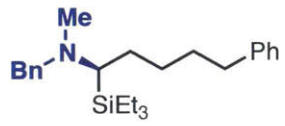


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.501	VB	0.4335	2026.45239	69.22653	50.2660
2	9.628	BB	0.4233	2005.00696	73.25804	49.7340
Totals :				4031.45935	142.48457	

(R)-**6b** from **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**): >99% *ee*



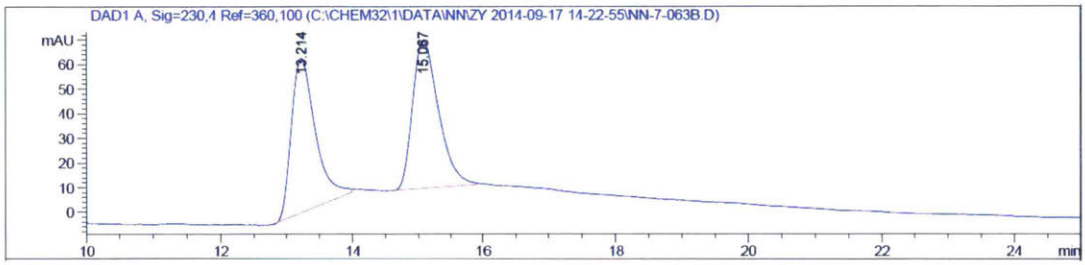
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.974	MM T	0.2593	7.95467	5.11373e-1	0.0893
2	10.400	MM T	0.4598	8904.81543	381.33731	99.9107
Totals :				8912.77010	381.84868	



6c

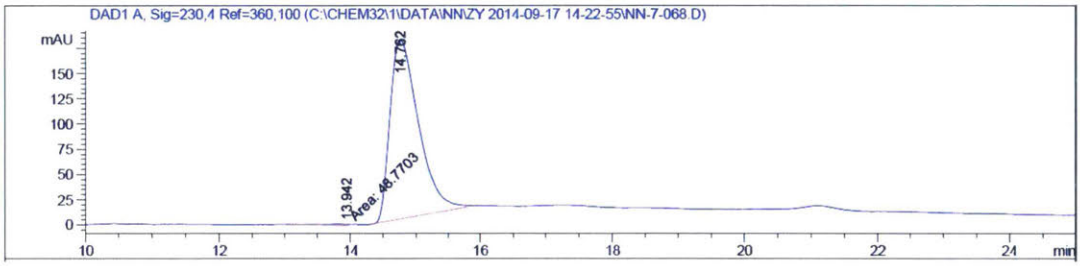
(*R*)-*N*-benzyl-*N*-methyl-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 4, entry **6c**)**:** This product was derivatized into **(*R*)-*N*-methyl-*N*-(5-phenyl-1-(triethylsilyl)pentyl)acetamide** for chiral HPLC analysis. HPLC analysis (OD-H, 1% IPA/hexanes, 0.8 mL/min, 220 nm): t_R (minor) = 13 min, t_R (major) = 15 min.

Rac-**6c**

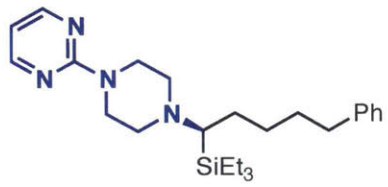


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.214	BB	0.3914	1601.63574	62.82732	49.2737
2	15.067	BB	0.4162	1648.85400	60.08541	50.7263
Totals :				3250.48975	122.91273	

(R)-**6c** from **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**): 98% *ee*



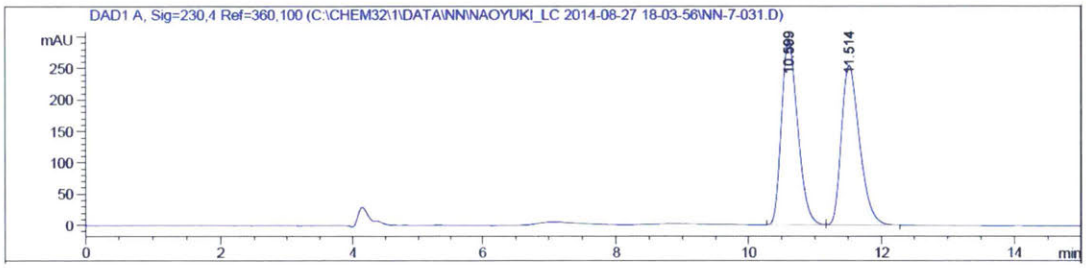
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.942	MM T	0.5525	48.77034	1.47115	0.9046
2	14.762	BB	0.4612	5342.72559	177.48306	99.0954
Totals :				5391.49593	178.95421	



6d

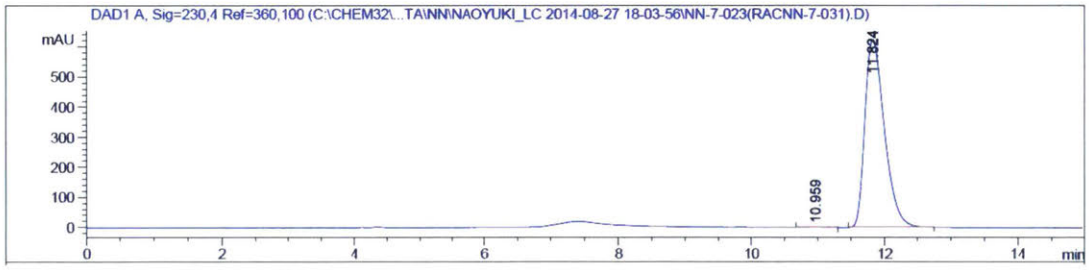
(*R*)-2-(4-(5-phenyl-1-(triethylsilyl)pentyl)piperazin-1-yl)pyrimidine (Table 4, entry **6d**)**:** HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 10.6 min, t_R (major) = 11.5 min.

Rac-**6d**

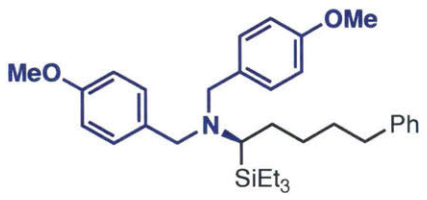


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.599	BV	0.2657	5020.25879	293.32043	50.6742
2	11.514	VB	0.2986	4886.66846	253.81593	49.3258
Totals :				9906.92725	547.13637	

(*R*)-**6d** Starting from **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**): >99% *ee*



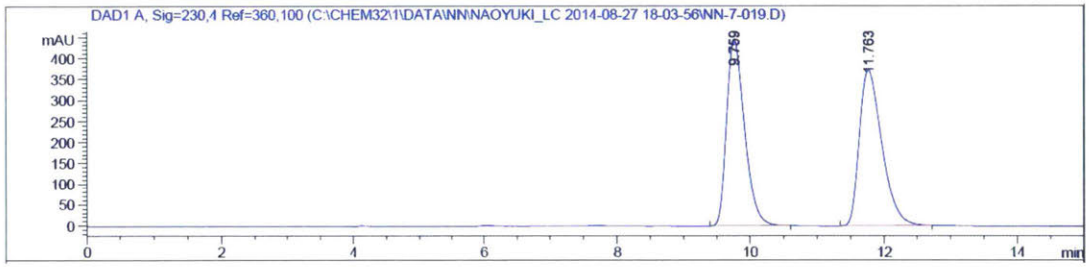
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.959	BB	0.2395	22.35949	1.14668	0.1770
2	11.824	BB	0.3122	1.26117e4	622.88629	99.8230
Totals :				1.26341e4	624.03297	



6e

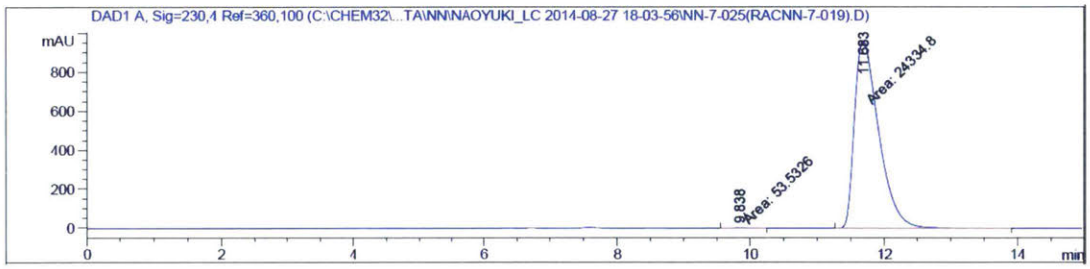
(*R*)-*N*,*N*-bis(4-methoxybenzyl)-5-phenyl-1-(triethylsilyl)pentan-1-amine (Table 4, entry **6e**)**:** HPLC analysis (OD-H, 1% IPA/pentane, 0.8 mL/min, 220 nm): t_R (minor) = 9.8 min, t_R (major) = 11.8 min.

Rac-**6e**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.759	BB	0.2880	8273.26465	442.69669	48.5564
2	11.763	BB	0.3678	8765.20703	370.71252	51.4436
Totals :				1.70385e4	813.40921	

(*R*)-**6e** from **(*E*)-triethyl(5-phenylpent-1-en-1-yl)silane** ((*E*)-**1a**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.838	MM T	0.3706	53.53262	2.40750	0.2195
2	11.683	MM T	0.4230	2.43348e4	958.88342	99.7805
Totals :				2.43883e4	961.29092	

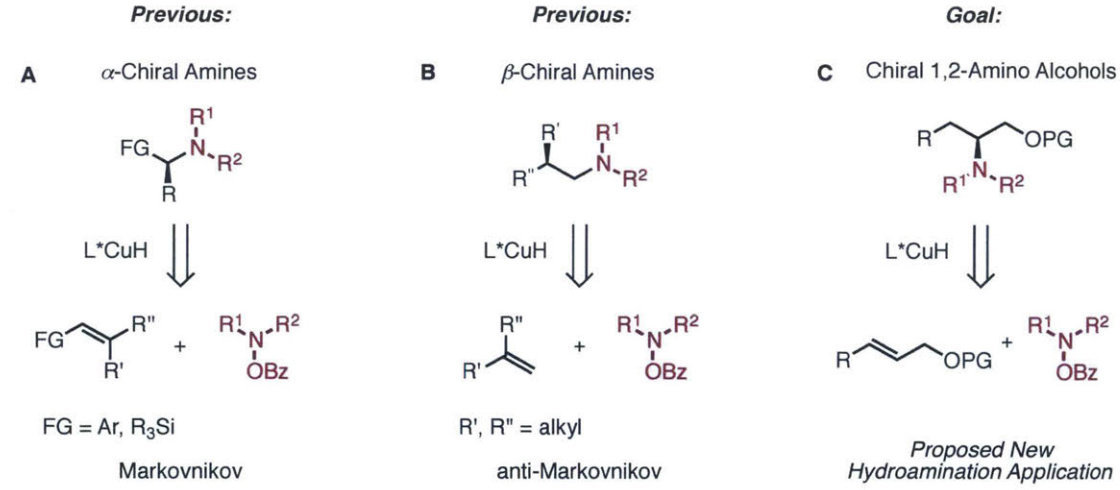
Chapter 4.

Synthesis of γ-Chiral Amines via Copper-Catalyzed Hydroamination of 3,3-Disubstituted Allylic Alcohols and 3,3-Disubstituted Allylic Benzoates

4.1 Introduction

Recently, our laboratory has reported copper-catalyzed hydroamination methodologies to access an array of chiral amines (Figure 1).[1,2] Our hydroamination strategy relies on the use of a silane, a chiral phosphine ligand (L*), and a Cu(II) salt to generate a ligated copper hydride species (L*CuH) and the use of *O*-benzoylhydroxyamine as an electrophilic amine source. With this method, α-chiral amines can be accessed from the Markovnikov hydroamination of styrenes and vinylsilanes (Figure 1, **A**),[1] and β-chiral amines can be accessed by the anti-Markovnikov hydroamination of 1,1-disubstituted aliphatic alkenes (Figure 1, **B**).[2]

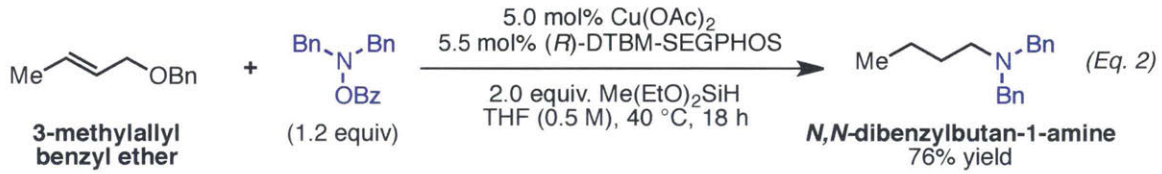
Figure 1. *Our Strategies Towards Chiral 1,2-Aminoalcohol Synthesis*



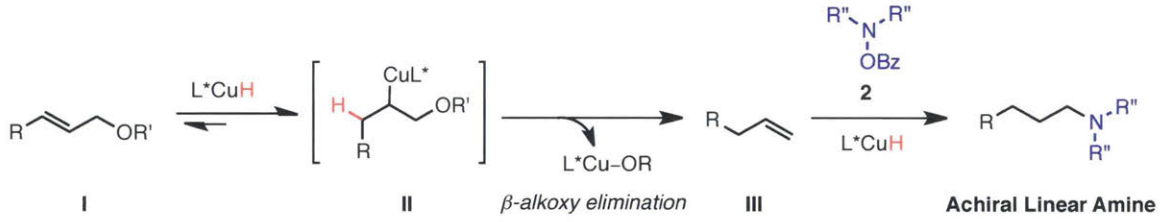
We envisioned that the extension of this methodology towards the hydroamination of 3-substituted allylic ethers (Figure 1, **C**) would allow for the generation of chiral amino alcohols, which are important structural subunits.[3] We postulated that coordination of the alkoxy group would direct copper to the 2-position (Eq. 1),[4] and subsequent reaction with electrophilic amine source would generate chiral protected 1,2-amino alcohols.

(Eq. 1)

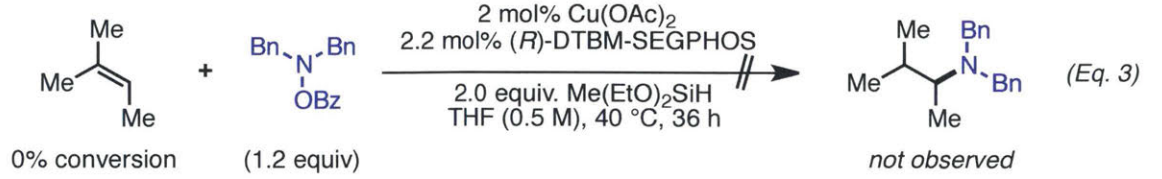
Unexpectedly, we observed that the reaction of 3-methylallyl benzyl ether generated the corresponding achiral linear amine (*N*,*N*-dibenzylbutan-1-amine) with no formation of the desired 1,2-amino alcohol product (Eq. 2). Based on this result, we proposed that following hydrocupration of **I** to produce **II**, β-alkoxy elimination[5,6] occurred to generate the terminal olefin **III**, which then underwent anti-Markovnikov hydroamination to generate the observed terminal amine (Scheme 1).[1a,2]



Scheme 1. *Plausible β-Alkoxy Elimination Pathway*



Concomitantly, we were also exploring the application of our Cu-catalyzed hydroamination methodology to tri-substituted alkenes for the synthesis of α,β-chiral amines. This is because β-disubstituted chiral amines with two contiguous stereocenters are important structural motifs found in natural products and pharmaceuticals, but methods to access this class of compounds predominantly rely on the use of chiral auxiliaries or sequential transformations.[7] However, using 2-methylbut-2-ene as a representative trisubstituted alkene gave no product formation under the standard reaction conditions (Eq. 3).



We reasoned that the copper hydride insertion is unfavorable for trialkyl-substituted olefins. Thus, we proposed integrating the use of a leaving group, as in the case of the 3-monosubstituted allylic ether **I**, to help drive the unfavorable insertion step with trisubstituted olefin substrates (Figure 2). In this way, we could convert allylic alcohols into γ-chiral amines. This is of interest as γ-chiral amines are prevalent structural subunits in both natural products and pharmaceuticals (Figure 3). Conventional strategies to access γ-chiral amines from allylic alcohols are multistep and, thus, less efficient.[8] A method that could access these chiral compounds via simultaneous installation of the chiral center and the amine would be of considerable importance.

Figure 2. *Rationale For New Proposed Substrate Class*

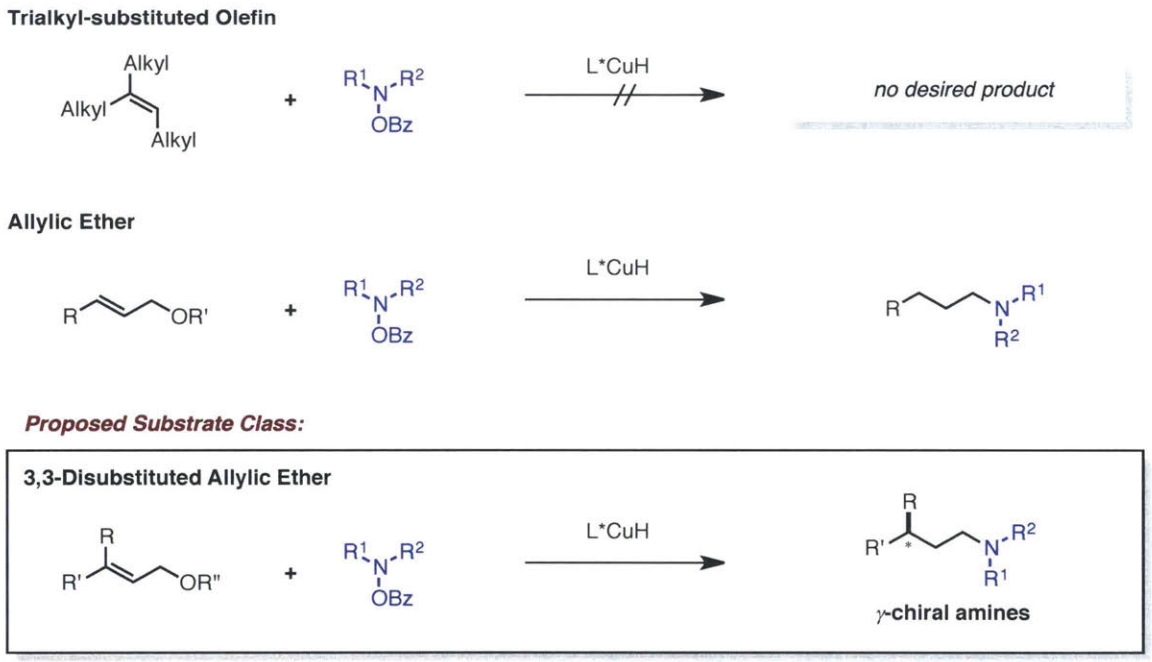
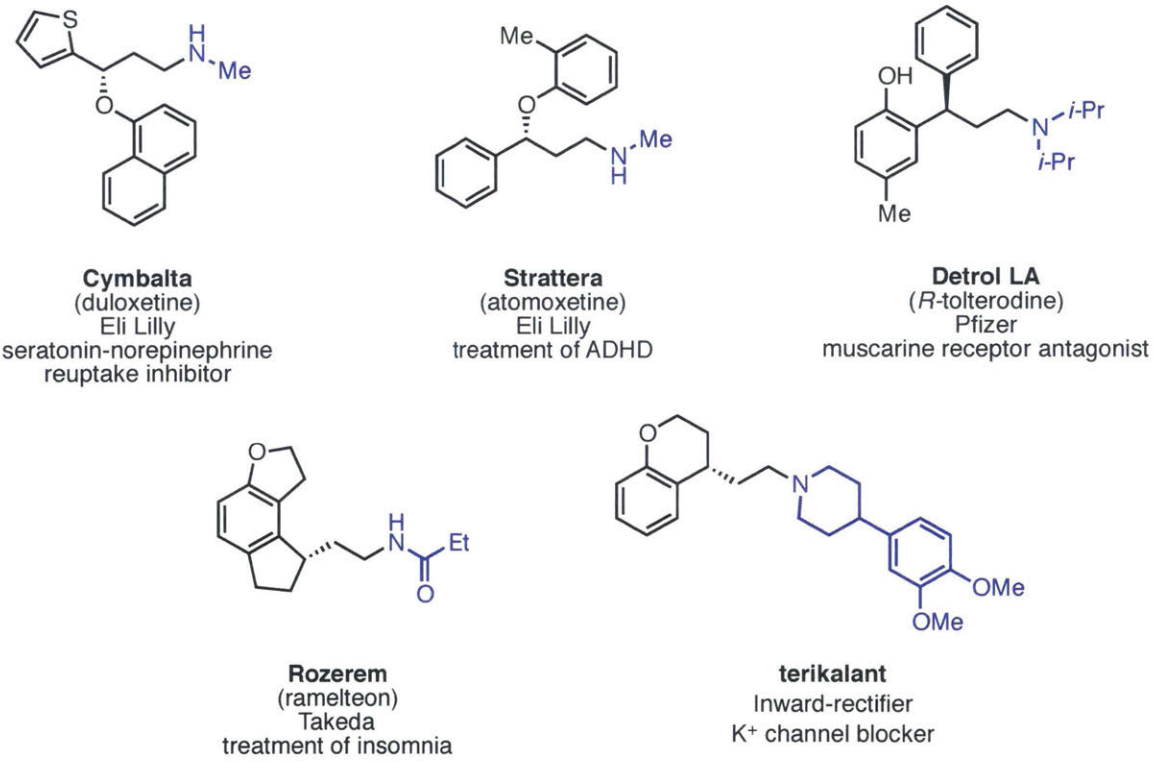


Figure 3. *Examples of Biologically Active γ-Chiral Amine Drugs*



Cymbalta
(duloxetine)
Eli Lilly
seratonin-norepinephrine
reuptake inhibitor

Strattera
(atomoxetine)
Eli Lilly
treatment of ADHD

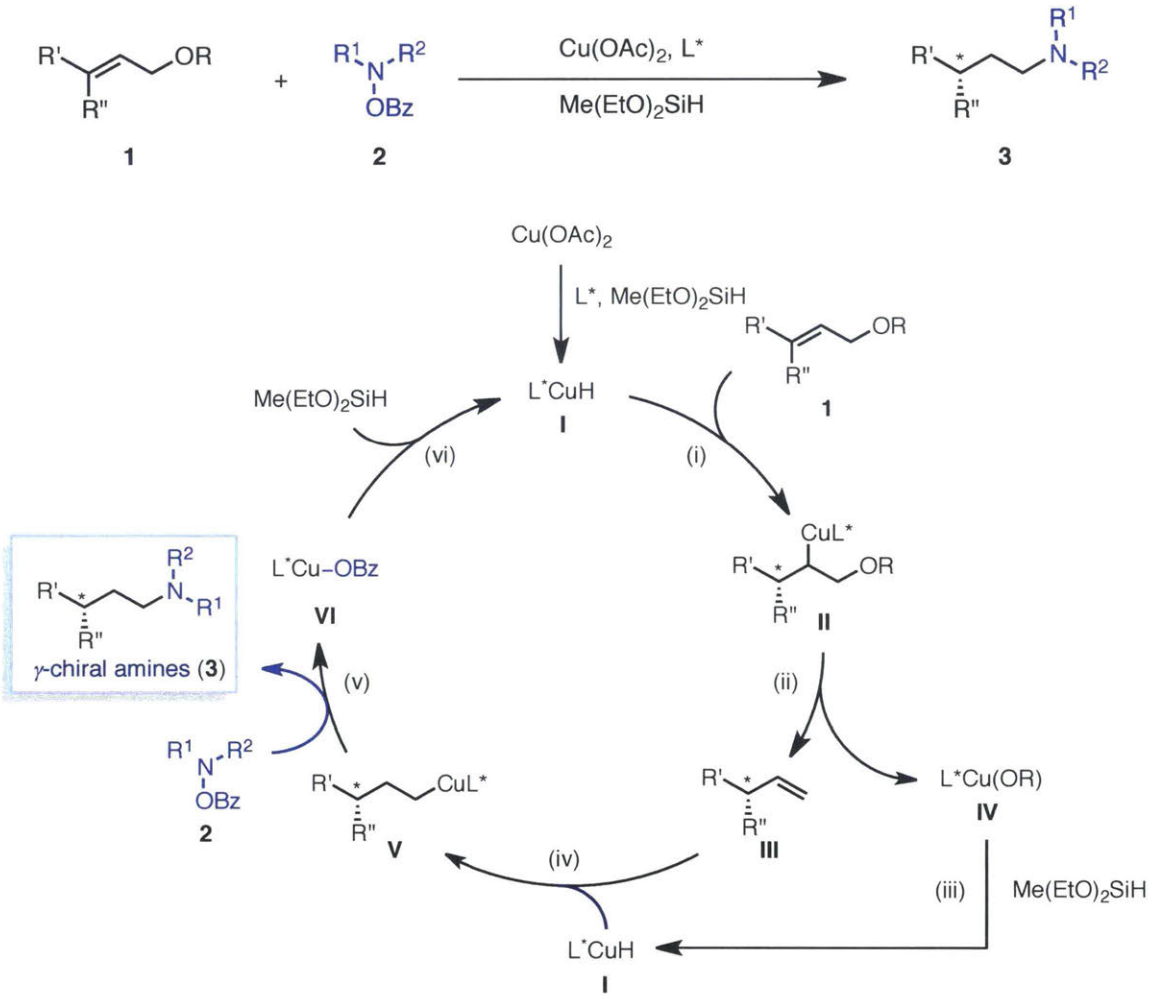
Detrol LA
(*R*-tolterodine)
Pfizer
muscarine receptor antagonist

Rozerem
(ramelteon)
Takeda
treatment of insomnia

terikalant
Inward-rectifier
K^+ channel blocker

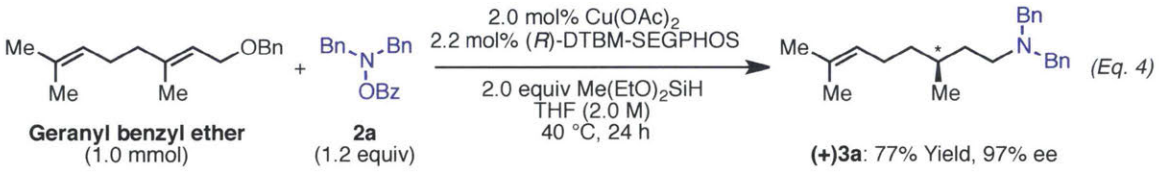
The overall catalytic cycle is shown in Scheme 2. Following the hydrocupration of 3,3-disubstituted allylic ethers (**1**) to generate the β-alkoxy copper species **II**, irreversible β-alkoxy elimination (ii) would furnish the chiral terminal alkene **III** and ligated copper alkoxide **IV**.[5,6] The ligated copper alkoxide can undergo transmetalation (iii) with diethoxymethylsilane to regenerate L*CuH (**I**). Then, terminal olefin **III** could undergo anti-Markovnikov hydrocupration (iv) followed by amine transfer (v) from *O*-benzoylhydroxylamine **2** to generate the γ-chiral amine **3**. Subsequent transmetalation (vi) would then reform **I.**

Scheme 2. *Proposed Mechanism for Copper-Catalyzed Hydroamination of 3,3-Disubstituted Allylic Ethers*



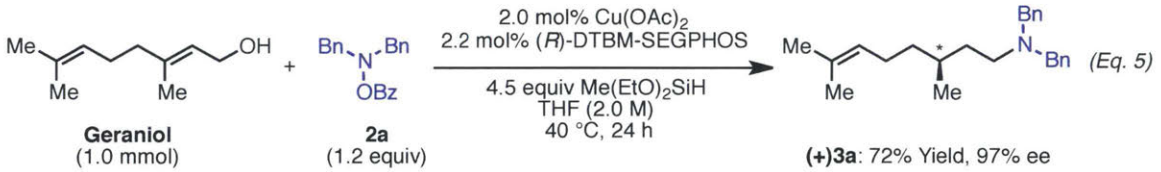
4.2 Results and Discussion

To assess the feasibility of the outlined allylic hydroamination (Scheme 2), we explored the reaction of geranyl benzyl ether using our previously reported conditions (Eq. 3).[1,2] The hydroamination of this 3,3-disubstituted allylic ether was successful in affording the γ-chiral amine **(+)3a** in high yield and enantioselectivity. Since it is well known that alcohols undergo dehydrogenative silylation in situ using a variety of metal catalysts,[9] we explored the hydroamination of geraniol using an additional equivalent of the silane reagent. Indeed reactions with geraniol first generated intermediate **VII**,[10] which then proceeded to give γ-chiral amine **(+)3a** in good yield and enantioselectivity (Eq. 4).



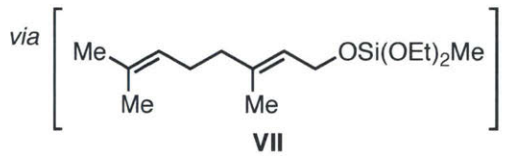
Geranyl benzyl ether (1.0 mmol) + **2a** (1.2 equiv)

(+)3a: 77% Yield, 97% ee



Geraniol (1.0 mmol) + **2a** (1.2 equiv)

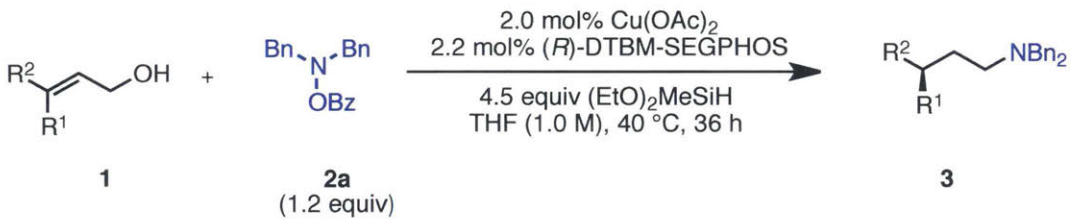
(+)3a: 72% Yield, 97% ee



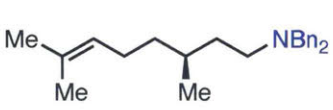
VII

We next applied the developed reaction conditions to a variety of allylic alcohols (Scheme 3) and showed that the stereochemical outcome of the reaction was dependent on the alkene geometry (*E/Z*), as geraniol generated the (*S*)-isomer of the chiral amine ((+)**3a**) and nerol generated the (*R*)-isomer of the product ((−)**3a**). For aliphatic substrates, we demonstrated that the hydroamination of simple 3,3-disubstituted allylic alcohols proceeded with excellent yields and enantioselectivities (**3b** and **3c**).

Scheme 3. *Copper-Catalyzed Hydroamination of 3,3-Disubstituted Allylic Alcohols*

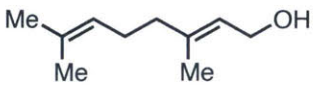


1 **2a** (1.2 equiv) **3**

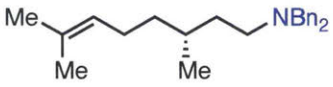


(+)3a: 75% yield, 97% ee

(+)3a from

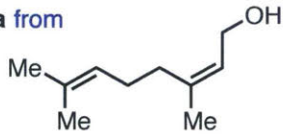


Geraniol

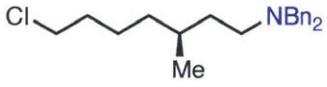


(–)3a: 71% yield, 87% ee

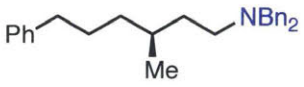
(–)3a from



Nerol



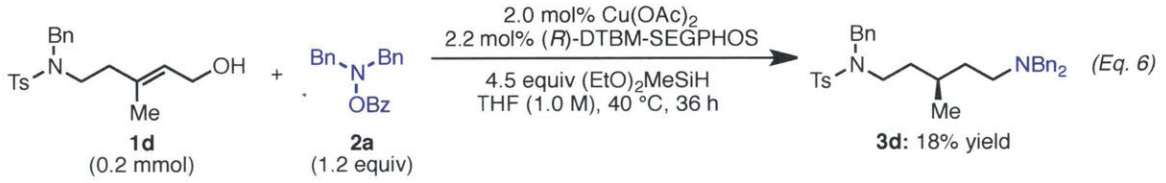
3b: 92% yield, 96% ee



3c: 82% yield, 98% ee

[a]Reaction conditions: **1** (1 mmol), **2a** (1.2 mmol), $Cu(OAc)_2$ (0.02 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), diethoxymethylsilane (4.5 equiv), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs). Enantioselectivities were determined by chiral HPLC analysis.

Attempts to expand the scope of this method to other allylic alcohols showed that the reactions sometimes proceeded with low efficiency. For example, the hydroamination of **1d** generated the γ-chiral amine **3d** in only 18% yield (Eq. 6); the remainder was the silylated starting material.

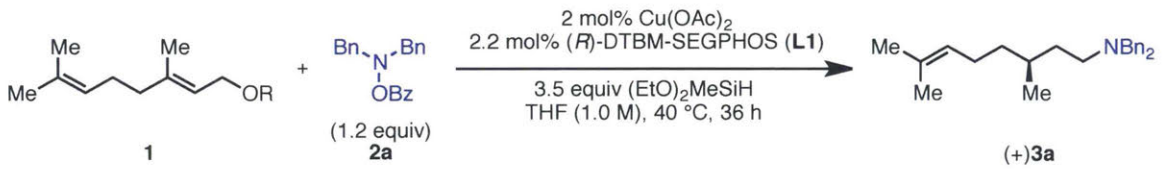


We proposed that increasing the leaving group ability of the –OR moiety should improve the overall reactivity of the trisubstituted olefin, presumably by increasing the rate of "β-alkoxide" elimination from **II** (Scheme 2). An additional benefit is that the quantity of silane reagent that was necessary would be reduced.

We examined a broad range of –OR groups. Reaction of methyl and silyl ethers showed no increase in the yield of the desired product (entries 2–4, Table 1) when compared to geraniol (entry 1). Substrates containing more stabilized alkoxy groups, such as the 3,3-disubstituted allylic acetate (entry 5) and the 3,3-disubstituted allylic methyl carbonate (entry 6), also gave similar yields to the reaction employing geraniol (entry 1). The use of a 3,3-disubstituted allylic phosphate gave a slightly improved yield of 80%.

We were also interested in exploring the reaction of 3,3-disubstituted allylic benzoates since β-alkoxy elimination (ii) would generate L*Cu-OBz species (**IV**, Scheme 2). This is the same intermediate generated following the reaction with the *O*-hydroxylamine benzoates (Scheme 4), and can be effectively converted into **I**.[1,2] We found that the reaction of geranyl benzoate generated the desired allylic hydroamination product in higher yield than that of geranyl phosphate (entry 8, Table 1). Incorporating an electron-withdrawing benzoate to increase the leaving group ability was found instead to significantly reduce the yield (entry 9). In contrast, using electron-donating substituents, such as 4-(dimethylamino)benzoate (entry 10), produced near quantitative yield of the γ–chiral amine **(+)3a**. We speculated that the faster reaction with the electron-rich benzoate is due to the faster transmetalation of the intermediate Cu-OBz with diethoxymethylsilane. We are currently examining how the structure of the benzoate affects the transmetalation step.

Table 1. *Exploration of Allylic Leaving Group on Reactivity*[a]



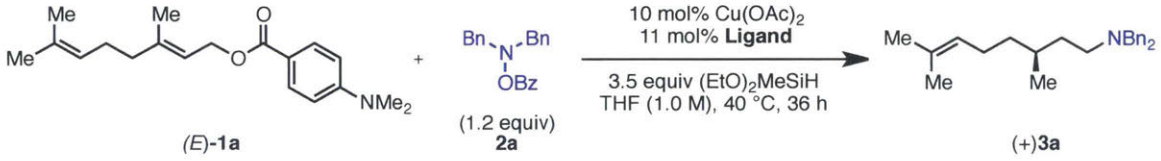
Entry	-OR	Yield (%)[b]	ee (%)[c]
1[d]	OH	70	97
2	OMe	57	96
3	OTIPS	65	97
4	OTBS	68	98
5	OAc	70	96
6	OCO(OMe)	70	98
7	$OPO(OEt)_2$	80	97
8	OBz	88	97
9	p-$CO_2MeC_6H_4CO_2$	27	97
10	p-$NMe_2C_6H_4CO_2$	92	97

[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.24 mmol), $Cu(OAc)_2$ (0.004 mmol), (*R*)-DTBM-SEGPHOS (0.0044 mmol), diethoxymethylsilane (3.5 equiv), THF (0.2 mL), 40 °C, 36 h. [b]Yields were determined by GC using dodecane or tetradecane as an internal standard. [c]Enantioselectivities were determined by chiral HPLC analysis. [d]4.5 equiv of diethoxymethylsilane was used.

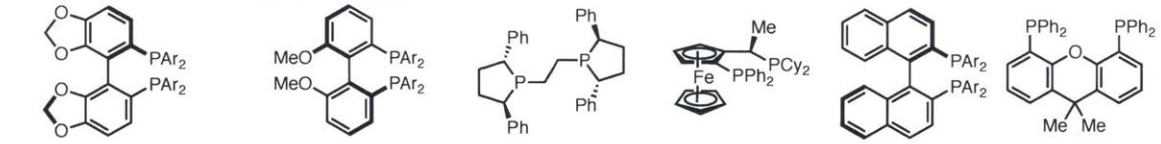
Lastly, we explored the effect of the chiral ligand on this reaction (Table 2). Ligands other than DTBM-SEGPHOS **L1**, particularly those previously shown to be effective in copper-catalyzed reactions involving ligated copper hydride species, were also investigated for impact on enantioselectivity as well as reactivity.[11] We used geranyl 4-(dimethylamino)benzoate ((*E*)-**1a**) for this ligand study and found that (*R*)-DTBM-SEGPHOS (**L1**) was superior to all the other chiral ligands in terms of both yield and enantioselectivity (entries 1–5, Table 2). When (*S*)-DTBM-MeO-BIPHEP (**L2**) was used as the supporting ligand, the reaction generated the

desired product in 74% yield and –95% ee (entry 2). Only modest yield and enantioselectivity were observed with **L3** (entry 2). Using **L5** afforded the desired product (+)-**3a** with a high level of enantioselectivity (98% ee), but in a modest 52% yield (entry 5). The desired product was not detected when using **L4** or the achiral ligand XantPhos (**L6**) (entries 4 and 6).

Table 2. *Examination of Bidentate Phosphine Ligands*[a]



Entry	Ligand	Yield (%)[b]	ee (%)[c]
1[d]	**L1**	92	97
2[d]	**L2**	74	–95
3	**L3**	12	–70
4	**L4**	0	nd[e]
5	**L5**	52	98
6	**L6**	0	nd

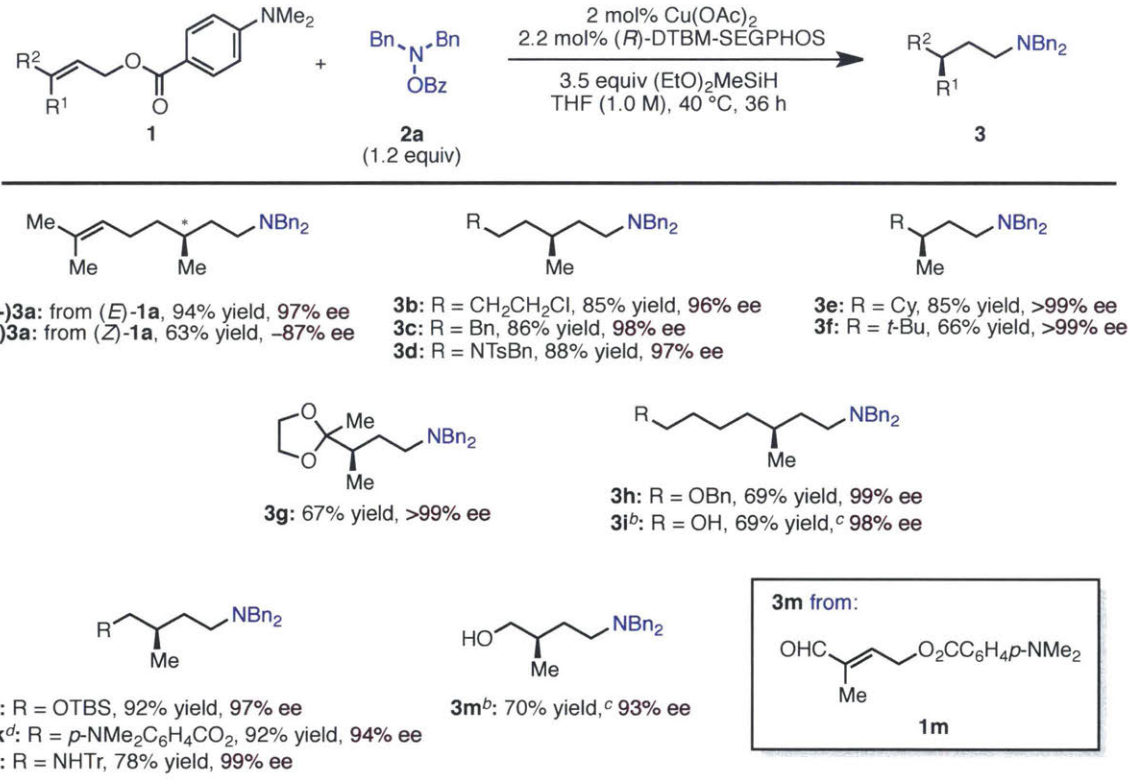


[a]Reaction conditions: (*E*)-**1a** (0.2 mmol), **2a** (0.22 mmol), $Cu(OAc)_2$ (0.020 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), diethoxymethylsilane (3.5 equiv), THF (0.2 mL), 40 °C, 36 h. [b]Yields were determined by GC using dodecane as an internal standard. [c]Enantioselectivities were determined by chiral HPLC analysis. [d]$Cu(OAc)_2$ (0.004 mmol), (*R*)-DTBM-SEGPHOS (0.0044 mmol), see Table 1 entry 10. [e]Not determined.

With the optimized protocol in hand, we next investigated the application of this reaction to various 3,3-dialkyl substituted allyl 4-(dimethylamino)benzoates (Scheme 4). As with allylic alcohols (Scheme 3), the stereochemical outcome of the reaction is dependent on the alkene geometry (**3a**). Various 3,3-disubstituted allylic 4-(dimethylamino)benzoates

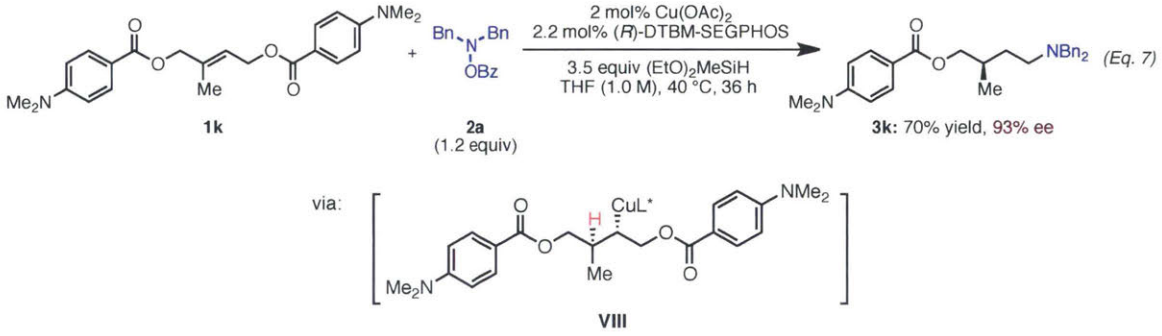
containing an alkyl chloride (**3b**), an aryl group (**3c**), a sulfonamide (**3d**), an acetal group (**3g**), a benzyl ether (**3h**), and a *tert*-butyldimethylsilyl ether (**3j**) were also compatible with the protocol (Scheme 4). The hydroamination reaction also accommodates sterically encumbered groups at the 3-position including a cyclohexyl group (**3e**) and a *tert*-butyl group (**3f**). Free alcohols (**3i**), and free N-H groups (**3l**) were also tolerated; the free hydroxyl-containing substrates were converted to diethoxymethylsilyl ethers that can be easily cleaved during work-up using tetrabutylammonium fluoride (TBAF). When aldehyde-containing substrates were employed, reduction to the alcohol was observed to produce amino alcohol product (**3m**).

Scheme 4. *Hydroamination of 3,3-Dialkyl Substituted Allyl 4-(dimethylamino)benzoates* [a]



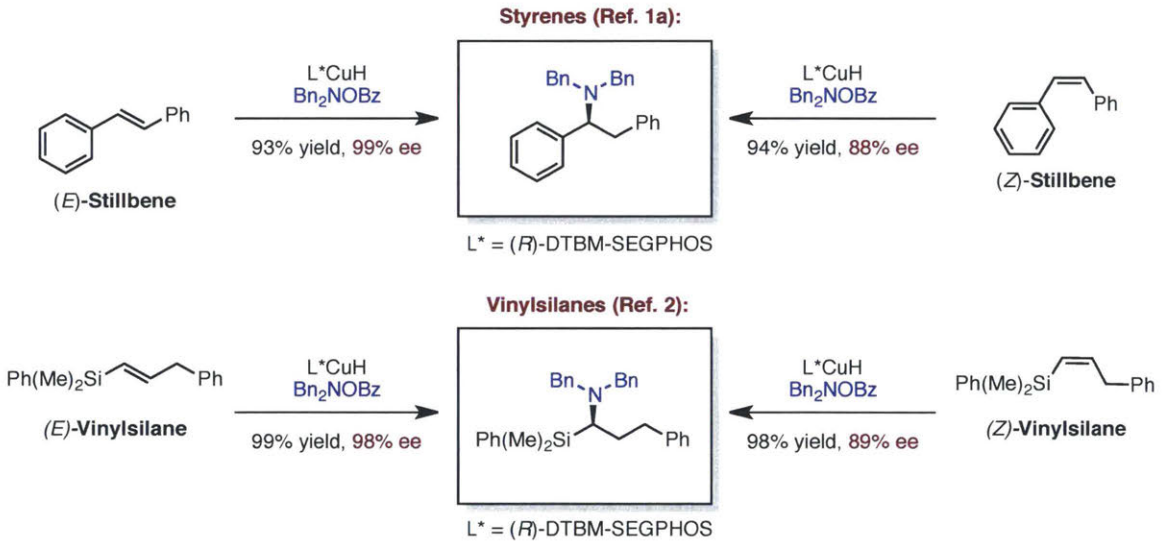
[a]Reaction conditions: **1** (1 mmol), **2a** (1.2 mmol), $Cu(OAc)_2$ (0.02 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), diethoxymethylsilane (3.5 equiv), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs). Enantioselectivities were determined by chiral HPLC analysis. [b]4.5 equiv of diethoxymethylsilane was used. [c]Yield after work-up with TBAF. [d]See Eq. 7.

Notably, hydroamination of 1,4-bisallylic 4-(dimethylamino)benzoate **1k** afforded γ-chiral amine **3k** (Scheme 4 and Eq. 7). Our hypothesis for this observed selectivity is that the olefin insertion proceeds to form the less sterically hindered copper intermediate **VIII**.



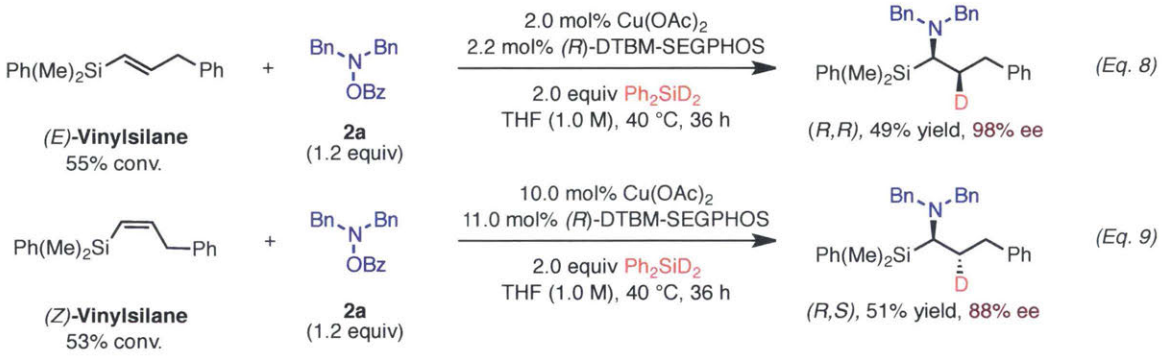
The dependence on olefin geometry for the stereochemical outcome of hydride addition in these reactions is noteworthy. As we have previously mentioned, *E*- and *Z*-trisubstituted alkenes provide different enantiomers of the product (**3a**, Schemes 3 and 4). Further, we found that use of the *E* isomer leads to formation of γ-chiral amine **3a** with a higher level of enantioselectivity than seen for the *Z*-isomer. The same trend was also observed with styrenes and vinylsilanes (Chapters 2 and 3).[1a,2] However, for disubstituted styrenes and vinylsilanes, reaction of both *Z*- and *E*-olefins gave the same absolute configuration of the product (Figure 4),[1a,2] suggesting that the facial selectivity of copper hydride addition is independent of olefin geometry.

Figure 4. *Stereoconvergence of (E)- and (Z)-Styrene and Vinylsilane Substrates*



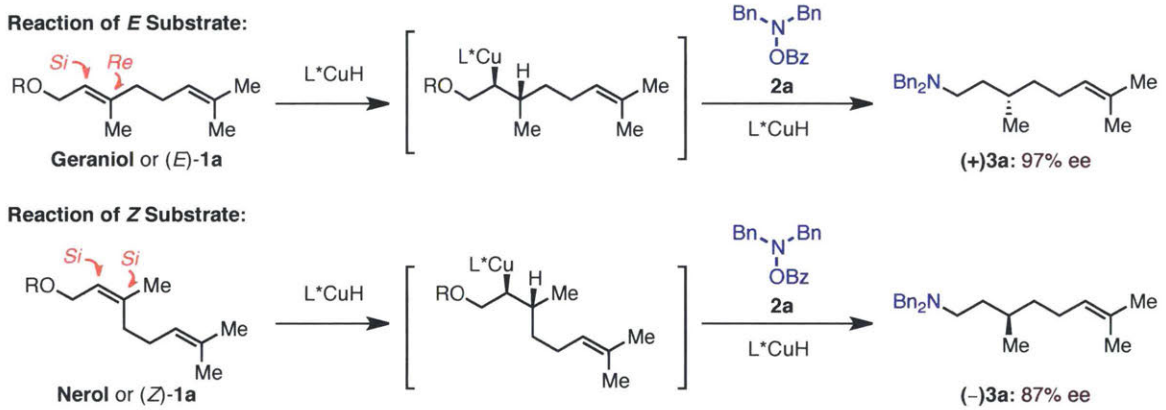
In addition to the catalyst controlled facial selectivity, we have shown through deuterium labeling experiments that subjecting *Z*- and *E*-vinylsilanes to our reaction conditions yields diastereomeric products (Chapter 3). This supports *syn*-addition of the L*CuD species to the alkene (Scheme 5, Eq. 8 and 9).[2]

Scheme 5. *Deuterium-labeling Experiments*[2]



For the allylic alcohol and benzoate substrates, the regioselectivity of L*CuH addition to the olefin is mainly determined by steric effects. It is more favorable for copper to bind to the least substituted end of the olefin. The stereochemical outcome is a result of the *syn* addition of L*CuH as depicted in Scheme 6. For geraniol or (*E*)-**1a**, the product results from *Si*,*Re* addition, while for nerol or (*Z*)-**1a**, the product results from *Si*,*Si* addition. Thus, we obtain the same stereochemistry where the copper adds to the olefin, and opposite stereochemistry where the hydride adds.

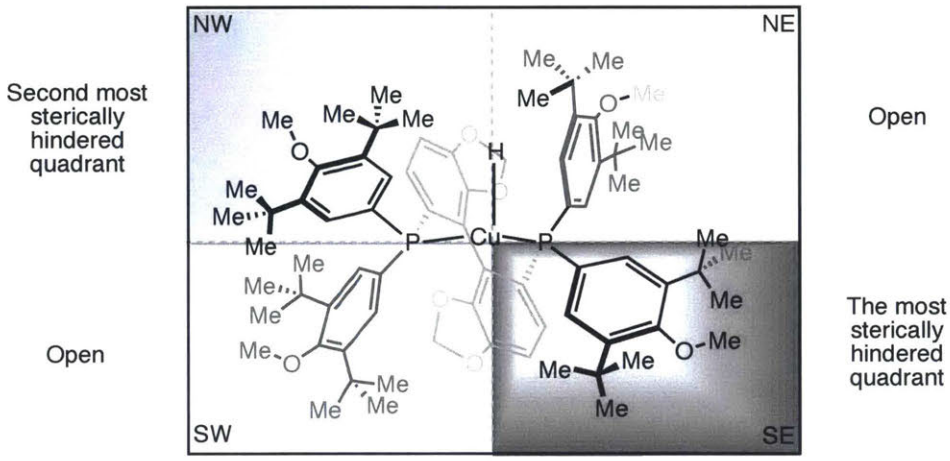
Scheme 6. *The Effect of Olefin Geometry on Stereochemical Outcome*[a]



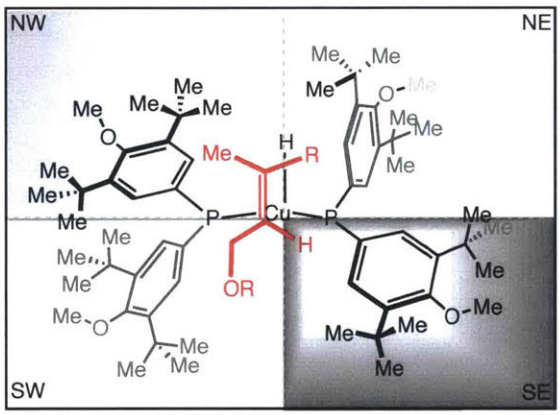
We rationalized the observed facial selectivities using quadrant diagrams and calculation performed by Mr. Yang Yang in another context (Figure 5).[12] The southeast quadrant is the most sterically hindered and therefore controls the facial selectivity. Thus, the most favored olefin orientation would be to put hydrogen, the smallest group, in the southeast quadrant and the bulky alkoxy group in the southwest quadrant. For the *E*-substrate (Figure 5a), the smaller methyl group is situated in the northwest quadrant (second least favorable position), and the larger R group in the northeast quadrant. For the *Z*- substrate (Figure 5c), the larger R group resides in the northwest quadrant (second least favorable position) and the smaller methyl group in the northeast quadrant.

To access the minor enantiomer, the *E*-substrate would have to approach L*CuH in the most energetically unfavorable orientation (Figure 5b), where both the large alkoxy group and the R group are placed in the least favorable southeast and northwest quadrants, respectively. As for the Z-substrate (Figure 5d), the minor enantiomer would result from placing the large alkoxy group in the least favorable southeast quadrant, while placing the R group in a more favorable northeast site. Since products generated from the *E*-olefin represented the lowest and the highest energy conformations, whereas products generated from the *Z*-olefin represented the two intermediate energy conformations, *E*-olefins generated products with higher ee than *Z*-olefins.

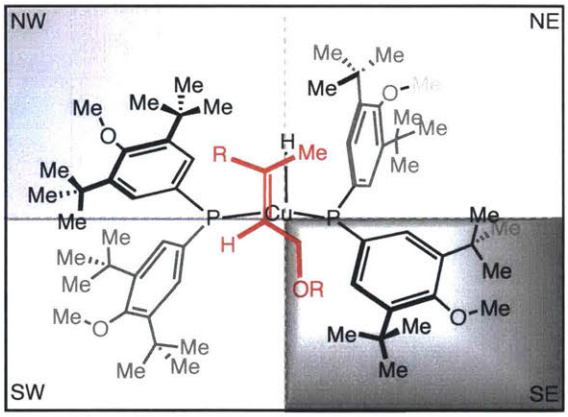
Figure 5. *Rationalization for Facial Selectivity (SEGPHOS Backbone is Omitted for Clarity)*[12]



E-Olefin with [(R)-DTBM-SEGPHOS]CuH:

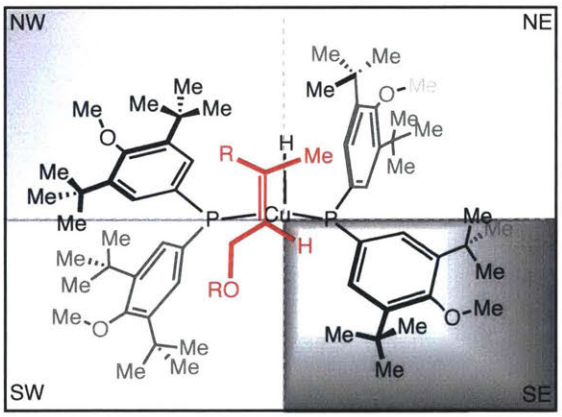


(a) Favored Si, Re addition to give (S)-product

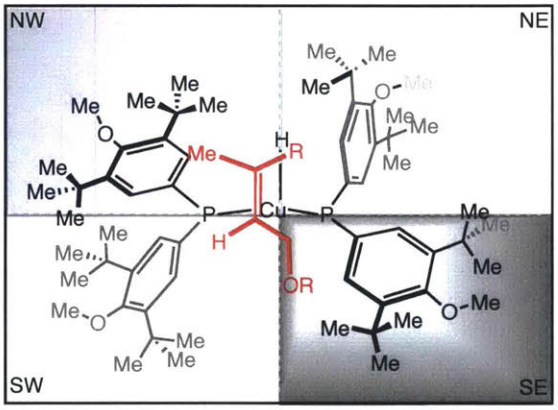


(b) Disfavored Re, Si addition to give (R)-product

Z-Olefin with [(R)-DTBM-SEGPHOS]CuH:



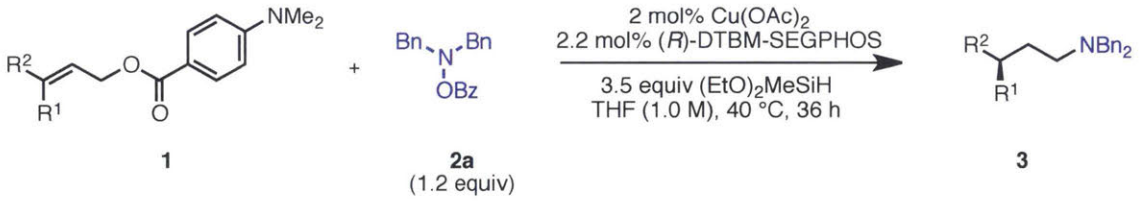
(c) Favored Si, Si addition to give (R)-product



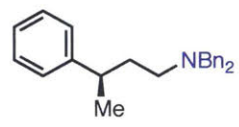
(d) Disfavored Re, Re addition to give (S)-product

We next investigated the hydroamination of 3-aryl-substituted allylic benzoates, as the aryl- and allyl benzoate functional groups have opposing electronic influence on the regioselectivity of L*CuH addition (Scheme 7).[1a] While we have shown above that aliphatic allylic alcohols exhibit anti-Markovnikov selectivity, there is an electronic preference to form a benzylic-Cu intermediate, which could compromise the general regioselectivity displayed in Scheme 4. We found, however, that the regiochemical course with aryl substituted allylic benzoates was the same as with dialkyl-substituted allylic benzoates, and γ-chiral amines were furnished in high yields and enantioselectivities in all cases (Scheme 7, **3n – 3s**).

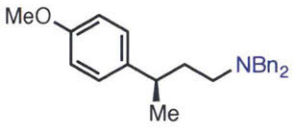
Scheme 7. *Allylic Hydroamination of 3,3-Alkyl,Aryl Substituted Allyl 4-(dimethylamino)benzoates* [a]



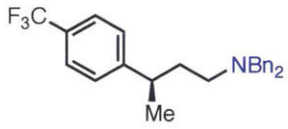
1 **2a** (1.2 equiv) **3**



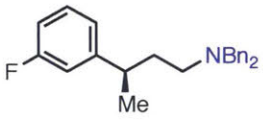
3n: 74% yield, >99% ee



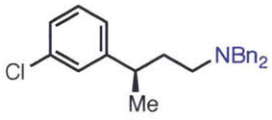
3o: 85% yield, 98% ee



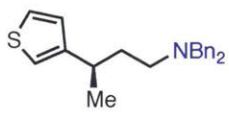
3p: 62% yield, 99% ee



3q: 77% yield, 98% ee



3r: 91% yield, 99% ee

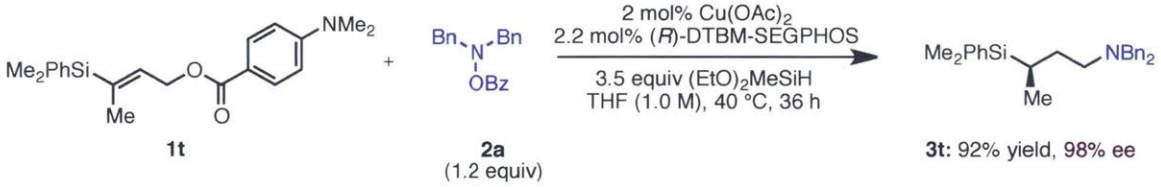


3s: 70% yield, 99% ee

[a]Reaction conditions: **1** (1 mmol), **2a** (1.2 mmol), $Cu(OAc)_2$ (0.02 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), diethoxymethylsilane (3.5 equiv), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs). Enantioselectivities were determined by chiral HPLC analysis.

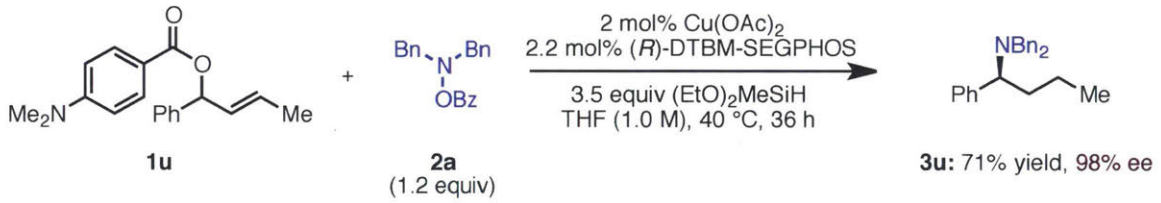
Similar to aromatic allylic benzoates, silyl allylic benzoates also have an opposing electronic influence on the regioselectivity of the L*CuH addition as there is preference for copper to form an α-silyl-Cu intermediate.[1b] Despite that, the hydroamination of the silyl allylic benzoate **1t** proceeded with the same regiochemical outcome as the aliphatic (Scheme 4) and aromatic (Scheme 7) allylic benzoate substrates to provide the γ-chiral silyl amine **3t** (Scheme 8).

Scheme 8. *Hydroamination of Silyl Substituted Allyl 4-(dimethylamino)benzoates*



In addition to a variety of 3,3-disubstituted allylic benzoates, this protocol is applicable to 1,3-substituted allylic benzoates (Scheme 9). Thus, *trans*-1-phenylbut-2-en-1-yl benzoate **1u** underwent allylic hydroamination to generate α-branched chiral amine product **3u**.

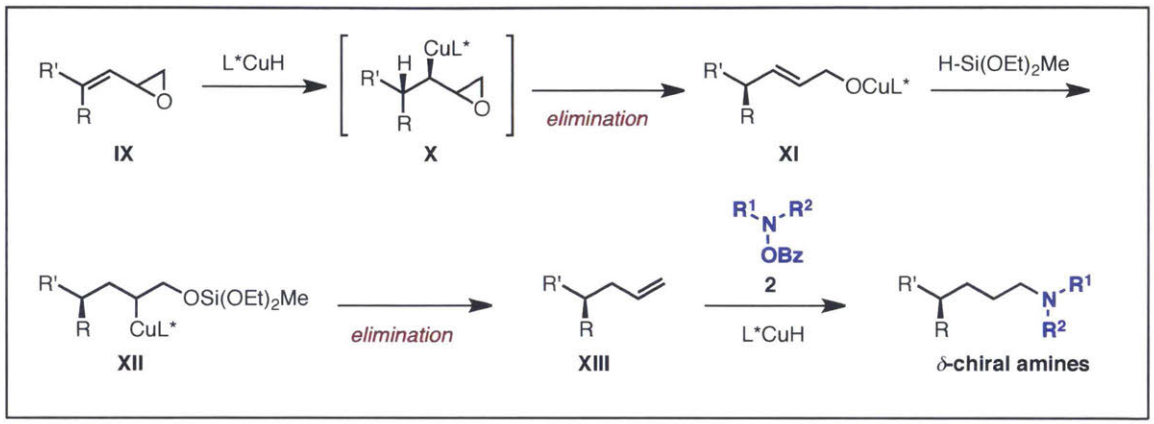
Scheme 9. *Hydroamination of 1,3 Substituted Allyl 4-(dimethylamino)benzoates*



The application of this methodology was further extended to the synthesis of an amine with a more distal chiral center via an allylic hydroamination cascade. We envisioned that hydroamination of allylic epoxide **IX** would ultimately generate the corresponding δ-chiral amine (Scheme 10). Hydrocupration of the allylic epoxide **IX** would generate copper intermediate **X**, which could then eliminate the internal epoxide C–O bond to yield allylic alcohol **XI**. This allylic alcohol is expected to undergo Cu-catalyzed dehydrogenative silylation, followed by hydrocupration and irreversible β-alkoxy elimination of intermediate

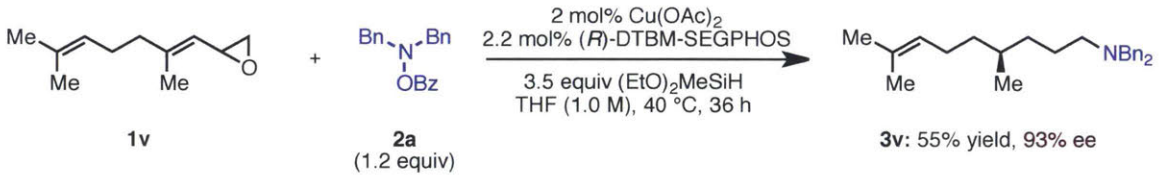
XII, furnishing the δ-chiral alkene **XIII**. Thus, anti-Markovnikov hydroamination of this olefin would provide the δ-chiral amine.

Scheme 10. *Proposed Cascade Hydroamination of Allylic Epoxides*



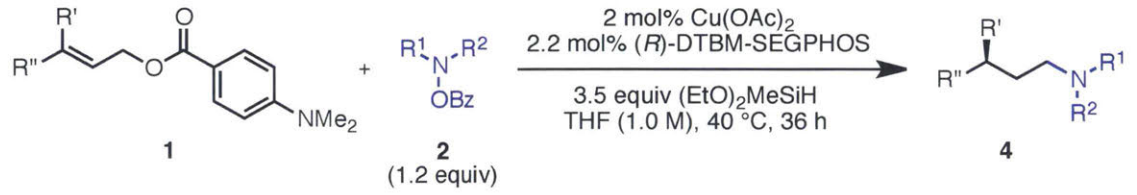
Indeed, use of the racemic allylic epoxide **1v** yielded the desired δ-chiral amine **3v**, in moderate yield (Scheme 11).

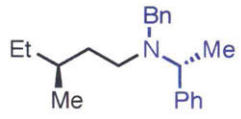
Scheme 11. *Cascade Hydroamination of an Allylic Epoxide*



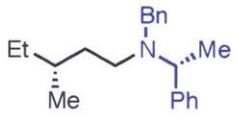
Many *O*-benzoylhydroxylamine electrophiles can be utilized with our method (Scheme 12). Of note, enantiomerically enriched hydroxylamine esters can be employed to generate diastereomeric products with a *dr* of >50:1 (**4a** and **4a'**) with complete catalyst control of the diastereomer being formed. Other *O*-benzoyl hydroxylamine electrophiles are suitable partners including the smaller alkylbenzylamine electrophiles (**4b**) and cyclic amine electrophiles, including the bulkier tetramethylpiperidine electrophiles, allowing for the generation of heterocyclic γ-chiral amines (**4c – 4f**).

Scheme 12. *Scope of O-Benzoylhydroxylamine Electrophiles*

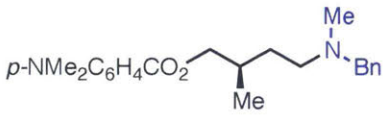




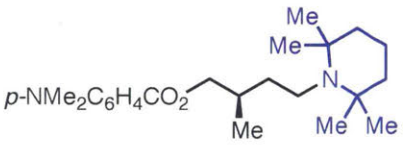
with **L1**
4a 91% yield, > 50:1 dr



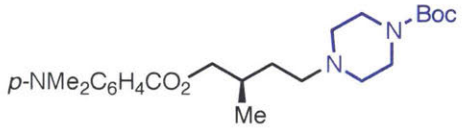
with *ent*-**L1**
4a' 90% yield, > 50:1 dr



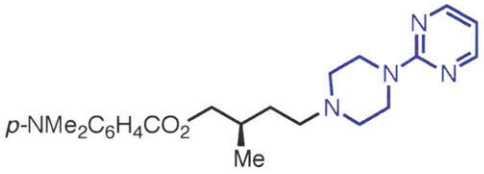
4b 92% yield, >99% ee



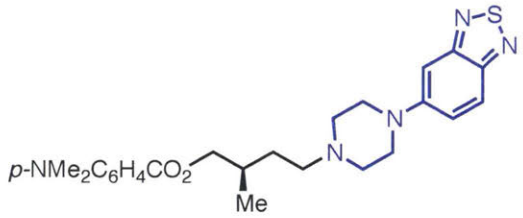
4c 89% yield, 96% ee



4d 91% yield, 96% ee



4e 87% yield, 98% ee

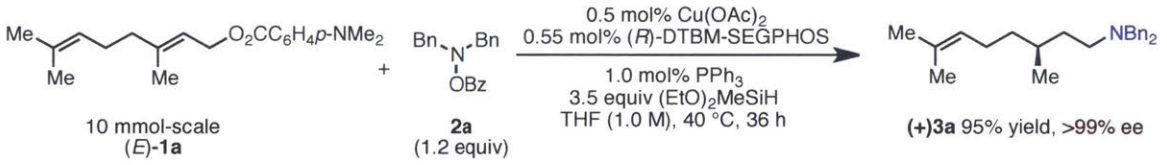


4f 78% yield, 97% ee

[a]Reaction conditions: **1** (1 mmol), **2a** (1.2 mmol), $Cu(OAc)_2$ (0.02 mmol), (*R*)-DTBM-SEGPHOS (0.022 mmol), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs). diethoxymethylsilane (3.5 equiv), THF (1 mL), 40 °C, 36 h. Yields are isolated yields (average of two runs). Enantioselectivities were determined by chiral HPLC analysis.

Lastly, to demonstrate the scalability of the developed procedure, we performed the reaction on a 10-mmol scale. As depicted in Scheme 13, in this case the allylic hydroamination can be carried out with a reduced catalyst loading of 0.5 mol % $Cu(OAc)_2$. The use of inexpensive triphenylphoshine as an additive helps to stabilize the active catalyst species at this low catalyst loading.[13]

Scheme 13. *Large Scale Cu-Catalyzed Allylic Hydroamination*



4.3 Conclusion

In summary, we have developed a new enantioselective Cu-catalyzed allylic hydroamination strategy to access γ-chiral amines from 3,3-disubstituted allylic alcohols and *N,N*-dimethylbenzoates in one step. The reactions proceed with good yields and excellent enantioselectivities and allow for the generation of a broad scope of γ-chiral amines. In addition, we have demonstrated that the methodology is applicable towards an internal allylic benzoate substrate to generate an α-chiral amine. Hydroamination of an allylic epoxide is also illustrated to further remove the chiral center from the amine moiety and generate a δ-chiral amine. Since this method promotes an unprecedented installation of the amine and the generation of a distal chiral center in a single synthetic manipulation, we anticipate it will find considerable use in natural product and pharmaceutical synthesis.

4.4 Experimental

I. General Information

General Reagent Information

Unless otherwise stated, all reactions were set up on the bench top and carried out under an argon atmosphere. Anhydrous cyclohexane was purchased from Sigma-Aldrich in Sure-Seal® bottles and used as received. All other solvents were purified and dried by passage through successive alumina and Q5 reactant-packed columns on a solvent purification system. Diethoxymethylsilane was purchased from TCI America and stored under nitrogen at 4 °C in a Schlenk flask (diethoxymethylsilane is moisture sensitive, and proper Schlenk technique was used for handling this reagent). Other commercial reagents were purchased from Aldrich Chemical, Alfa Aesar, TCI, Strem, Acros, Oakwood, Frontier Scientific, or Combi-Block and were used as received. DTBM-SEGPHOS (**L1**) was purchased from Takasago. Ligands **L2 – L4** were purchased from Strem Chemicals. Flash chromatography was either performed using glass columns with SiliaFlash® P60 (SiliCycle, 230-400 mesh), or on pre-packed Biotage® SNAP columns using a Biotage Isolera Automated Flash Chromatography System.

General Analytical Information

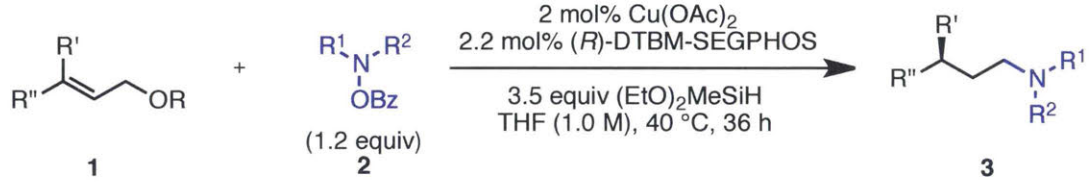
All compounds (starting materials and products) were characterized by ^{1}H NMR, ^{13}C NMR, IR spectroscopy, melting point (where applicable), and elemental analysis or high-resolution mass spectrometry. ^{1}H NMR spectra were recorded on Bruker 400 MHz or Bruker 600 MHz spectrometer and are referenced relative to residual $CDCl_3$ proton signals at δ 7.26 ppm. ^{19}F NMR spectra were recorded on a Bruker 400 MHz spectrometer and are referenced to $CFCl_3$ (δ 0.0 ppm). Data for ^{1}H and ^{19}F NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, ap = apparent), integration, and coupling constant (Hz). ^{13}C NMR spectra were recorded on a Bruker 400 MHz or Bruker 600 MHz spectrometer and are referenced to $CDCl_3$ at δ 77.16 ppm. The ^{13}C NMR spectra were obtained with ^{1}H decoupling. Data for ^{13}C NMR are reported in terms of chemical shift and multiplicity where appropriate. IR spectra were obtained on a Thermo Scientific Nicolet iS5 spectrometer (iD5 ATR, diamond) and are reported in terms of frequency of

absorption (cm^{-1}). GC analyses were performed on an Agilent 6890 gas chromatograph with an FID detector using a J & W DB-1 column (10 m, 0.1 mm I.D.). Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. High Resolution Mass spectra were obtained from on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. High-pressure liquid chromatography (HPLC) was performed on Agilent 1200 Series chromatographs using chiral columns (25 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL. Reactions were monitored by GC analysis and thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) or Fluka aluminum oxide/TLC-cards using UV light as a visualizing agent. The yields reported are the average of at least two experiments, unless otherwise indicated.

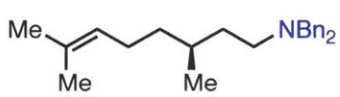
II. Experimental Procedures and Characterization Data

A) Cu-Catalyzed Hydroamination of 3,3-Disubstituted Allylic Alcohols and 3,3-Disubstituted Allylic Benzoates

General Procedure:



To an oven-dried 4 mL screw-cap vial equipped with a magnetic stir bar was charged with $Cu(OAc)_2$ (2.0-5.0 mol%) and (*R*)-DTBM-SEGPHOS (2.2-5.5 mol%). The tube was sealed with a teflon-lined screw cap, evacuated, and backfilled with argon (this process was repeated a total of 3 times). Anhydrous THF (1.0 mL) was added, and the mixture was stirred for 10 min, at which time diethoxymethylsilane (3.5-4.5 equiv) was added and the stirring was continued for another 5 min at rt. Into a separate oven-dried medium-sized screw-cap test tube was added the 3,3–disubstituted allylic alcohol (or 3,3–disubstituted allylic benzoate) (1.0 mmol, 1.0 equiv) and *O*-benzoyl-*N,N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 2 equiv). The tube was sealed with a teflon-line screw cap and evacuated and backfilled with argon (this process was repeated a total of 3 times). The catalyst solution was then transferred via syringe to the reaction tube containing the substrates, and the reaction mixture was stirred at 40 °C for up to 36 h. Dodecane (100 μL) was added as an internal standard for GC analysis or trimethoxybenzene (56 mg, 0.33 mmol, 0.33 equiv) was added as the internal standard for ^{1}H NMR analysis. After cooling to rt, the reaction mixture was quenched with saturated aqueous Na_2CO_3 solution, extracted with EtOAc, dried over Na_2SO_4, filtered through a pad of silica, concentrated, and purified by column chromatography on silica gel or by acid-base extraction as indicated for each substrate. The enantiomeric excess (% ee) was determined by HPLC analysis using chiral stationary phases.



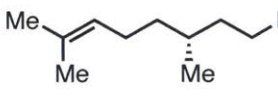
(+)**3a**

***(S)-N,N*-dibenzyl-3,7-dimethyloct-6-en-1-amine** (Scheme 3 and 4, entry (+)**3a**): From **geraniol** (154 mg, 1.0 mmol), the title

compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (720 μL, 4.5 mmol, 4.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (5–9% EtOAc in hexanes) to provide the title compound as a colorless liquid in 75% yield (251 mg).

From **(*E*)-3,7-dimethylocta-2,6-dien-1-yl 4-(dimethylamino)benzoate** ((*E*)-**1a**) (301 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (5–9% EtOAc in hexanes) to provide the title compound as a colorless liquid in 94% yield (315 mg).

IR (neat, cm^{-1}) 2916, 2793, 1494, 1452, 1375, 1028; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.52 – 7.40 (m, 4H), 7.40 – 7.33 (m, 4H), 7.33 – 7.23 (m, 2H), 5.13 (t, J = 7.5 Hz, 1H), 3.65 (d, J = 13.7 Hz, 2H), 3.57 (d, J = 13.7 Hz, 2H), 2.50 (t, J = 7.3 Hz, 2H), 2.11 – 1.91 (m, 2H), 1.74 (s, 3H), 1.65 (s, 3H), 1.63 – 1.48 (m, 2H), 1.43 – 1.26 (m, 2H), 1.22 – 1.09 (m, 1H), 0.83 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.18, 131.09, 128.93, 128.24, 126.83, 125.09, 58.44, 51.44, 37.25, 34.17, 30.52, 25.87, 25.62, 19.76, 17.79. Anal. Calcd. for $C_{24}H_{33}N$: C, 85.91; H, 9.91. Found: C, 85.71; H, 10.04. $[\alpha]_D^{24}$ = + 0.27 (c = 1.00, $CHCl_3$); HPLC analysis (OJ-H, 50% (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1)/hexanes, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 12.0 min, t_R (minor) = 14.9 min for both reactions using **geraniol** or (*E*)-**1a**.



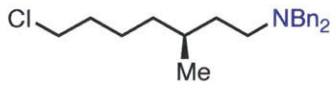
(–)**3a**

***(R)-N,N*-dibenzyl-3,7-dimethyloct-6-en-1-amine** (Scheme 3 and 4, entry (–)**3a**): From **nerol** (154 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2

mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (720 μL, 4.5 mmol, 4.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (5–9% EtOAc in hexanes) to provide the title compound as a colorless liquid in 71% yield (238 mg).

From **(Z)-3,7-dimethylocta-2,6-dien-1-yl 4-(dimethylamino)benzoate** ((*Z*)-**1a**) (301 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (5–9% EtOAc in hexanes) to provide the title compound as a colorless liquid in 63% yield (212 mg).

IR (neat, cm^{-1}) 2914, 2791, 1494, 1452, 1375, 1028; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.44 – 7.38 (m, 4H), 7.37 – 7.31 (m, 4H), 7.30 – 7.23 (m, 2H), 5.11 (t, J = 7.1 Hz, 1H), 3.63 (d, J = 13.6 Hz, 2H), 3.55 (d, J = 13.6 Hz, 2H), 2.48 (t, J = 7.3 Hz, 2H), 2.01 (dq, J = 14.6, 6.9 Hz, 1H), 1.93 (dt, J = 14.3, 7.5 Hz, 1H), 1.72 (s, 3H), 1.63 (s, 3H), 1.61 – 1.57 (m, 1H), 1.53 (dq, J = 12.8, 6.7 Hz, 1H), 1.36 (dt, J = 13.1, 7.1 Hz, 1H), 1.33 – 1.23 (m, 1H), 1.18 – 1.07 (m, 1H), 0.81 (d, J = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 140.18, 131.12, 128.92, 128.23, 126.82, 125.08, 58.42, 51.43, 37.26, 34.16, 30.51, 25.88, 25.62, 19.76, 17.80. HRMS (DART-TOF) calcd. for $C_{24}H_{33}N$ $[M+H]^+$ *m/z* 336.2586, found 336.2656. $[\alpha]_D^{24}$ = – 0.55 (*c* = 1.00, $CHCl_3$); HPLC analysis (OJ-H, 50% (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1)/hexanes, 0.8 mL/min, 220 nm) indicated 87% ee: t_R (minor) = 10.0 min, t_R (major) = 12.0 min for both reactions using nerol or (*Z*)-1a.



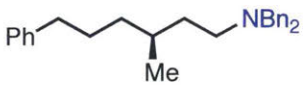
3b

(*S*)-*N*,*N*-dibenzyl-7-chloro-3-methylheptan-1-amine (Scheme 3 and 4, entry **3b**). From **(*E*)-7-chloro-3-methylhept-2-en-1-ol** (163 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS

(26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (720 μL, 4.5 mmol, 4.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–7% EtOAc in hexanes) to provide the title compound as a colorless liquid in 82% yield (317 mg).

From **(*E*)-7-chloro-3-methylhept-2-en-1-yl 4-(dimethylamino)benzoate (1b)** (310 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–7% EtOAc in hexanes) to provide the title compound as a colorless liquid in 85% yield (292 mg).

IR (neat, cm^{-1}) 2924, 1494, 1452, 1215, 746, 698, 668; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45 – 7.39 (m, 4H), 7.39 – 7.32 (m, 4H), 7.31 – 7.25 (m, 2H), 3.62 (d, J = 13.6 Hz, 2H), 3.57 (d, J = 14.4 Hz, 2H), 3.53 (t, J = 6.8 Hz, 2H), 2.55 – 2.37 (m, 2H), 1.81 – 1.66 (m, 2H), 1.62 – 1.48 (m, 2H), 1.48 – 1.29 (m, 3H), 1.29 – 1.17 (m, 1H), 1.15 – 1.01 (m, 1H), 0.81 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.14, 128.93, 128.24, 126.86, 58.52, 51.26, 45.27, 36.17, 34.16, 33.03, 30.68, 24.37, 19.81; HRMS (DART-TOF) calcd. for $C_{22}H_{30}ClN$ $[M+H]^+$ *m/z* 344.2140, found 344.2127 Anal. Calcd. for $C_{22}H_{30}ClN$: C, 76.83; H, 8.79. Found: C, 76.76; H, 8.92. $[\alpha]_D^{24}$ = – 3.1 (*c* = 1.15, $CHCl_3$); HPLC analysis (2 connected AD-H columns, 95:5:0.2:0.1 Hexanes:IPA:TFA:Diethylamine, 0.8 mL/min, 220 nm), 0.8 mL/min, 220 nm) indicated 96% ee: t_R (major) = 80.0 min, t_R (minor) = 83.8 min for both reactions using **(*E*)-7-chloro-3-methylhept-2-en-1-ol** or **1b**.



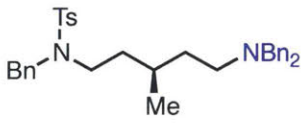
3c

(*S*)-*N*,*N*-dibenzyl-3-methyl-6-phenylhexan-1-amine (Scheme 3 and 4, entry **3c**). From **(*E*)-3-methyl-6-phenylhex-2-en-1-ol** (190 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26

mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (720 μL, 4.5 mmol, 4.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–5% EtOAc in hexanes) to provide the title compound as a colorless liquid in 82% yield (305 mg).

From **(*E*)-3-methyl-6-phenylhex-2-en-1-yl 4-(dimethylamino)benzoate (1c)** (337 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–9% EtOAc in hexanes) to provide the title compound as a colorless liquid in 86% yield (320 mg).

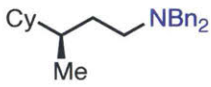
IR (neat, cm^{-1}) 2926, 2854, 2791, 1494, 1452, 1364, 1125, 744, 697; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.52 – 7.44 (m, 4H), 7.44 – 7.30 (m, 8H), 7.30 – 7.23 (m, 3H), 3.68 (d, J = 13.6 Hz, 2H), 3.62 (d, J = 13.7 Hz, 2H), 2.70 – 2.58 (m, 2H), 2.58 – 2.47 (m, 2H), 1.60 (d, J = 19.0 Hz, 4H), 1.50 – 1.29 (m, 2H), 1.27 – 1.12 (m, 1H), 0.87 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 142.96, 140.11, 128.89, 128.45, 128.31, 128.20, 126.81, 125.66, 58.43, 51.30, 36.75, 36.37, 34.14, 30.74, 29.03, 19.81. Anal. Calcd. for $C_{27}H_{33}N$: C, 87.28; H, 8.95. Found: C, 87.06; H, 9.01.). $[\alpha]_D^{24}$ = – 3.4 (c = 1.50, $CHCl_3$); HPLC analysis (OD-H, 3% IPA/hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 5.4 min, t_R (major) = 6.4 min for both reactions using **1c** or **(*E*)-3-methyl-6-phenylhex-2-en-1-ol.**



3d

(*R*)-*N*-benzyl-*N*-(5-(dibenzylamino)-3-methylpentyl)-4-methylbenzenesulfonamide (Scheme 4, entry **3d**). From **(*E*)-5-((*N*-benzyl-4-methylphenyl)sulfonamido)-3-methylpent-2-en-1-yl 4-(dimethylamino)benzoate (1d)** (507 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), , 1.0 equiv), *O*-benzoyl-*N*,*N*-

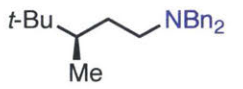
dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (15–25% EtOAc in hexanes) to provide the title compound as a colorless liquid in 88% yield (476 mg). IR (neat, cm^{-1}) 3028, 2923, 1494, 1453, 1338, 1216, 1158, 1090, 1028, 815, 750, 698; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.80 – 7.68 (m, 2H), 7.40 – 7.20 (m, 17H), 4.28 (s, 2H), 3.55 (d, J = 13.7 Hz, 2H), 3.46 (d, J = 13.7 Hz, 2H), 3.08 (t, J = 7.8 Hz, 2H), 2.46 (s, 3H), 2.31 (t, J = 7.2 Hz, 2H), 1.41 – 1.24 (m, 3H), 1.23 – 1.05 (m, 2H), 0.62 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 143.12, 139.87, 137.14, 136.61, 129.69, 128.75, 128.51, 128.32, 128.15, 127.71, 127.18, 126.78, 58.28, 58.28, 51.84, 51.05, 46.17, 34.94, 33.82, 28.56, 21.52, 19.25. HRMS (DART-TOF) calcd. for $C_{34}H_{40}N_2O_2S$ $[M+H]^+$ m/z 541.2883, found 541.2897. $[\alpha]_D^{24}$ = – 1.8 (c = 1.00, $CHCl_3$); HPLC analysis (OD-H, 5% IPA/hexanes, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (minor) = 18.2 min, t_R (major) = 20.1 min.



3e

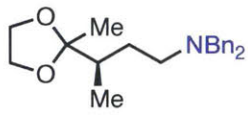
(*R*)-*N*,*N*-dibenzyl-3-cyclohexylbutan-1-amine (Scheme 4, entry **3e**). **From (*E*)-3-cyclohexylbut-2-en-1-yl 4-(dimethylamino)benzoate (1e)** (301 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 85% yield (285 mg). IR (neat, cm^{-1}) 2920, 2850, 2790, 1494, 1449, 1365, 1124, 1074, 1028, 743, 730, 697; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.51 – 7.43 (m, 4H), 7.43 – 7.36 (m, 4H), 7.35 – 7.29 (m, 2H), 3.69 (d, J = 13.6 Hz, 2H), 3.60 (d, J = 13.6 Hz, 2H), 2.59 – 2.43 (m, 2H), 1.87 – 1.76 (m, 2H), 1.76 – 1.67 (m, 2H), 1.67 – 1.57 (m, 2H), 1.52 – 1.34 (m, 2H), 1.32 – 1.14 (m, 4H), 1.14 – 0.96 (m, 2H), 0.80 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.19, 128.93, 128.22, 126.81, 58.44, 51.67, 42.64, 35.85, 31.22, 30.79, 28.68, 27.05, 27.02, 26.93, 16.27. Anal. Calcd. for $C_{24}H_{33}N$: C, 85.91; H, 9.91. Found: C, 85.61; H, 9.96. $[\alpha]_D^{24}$ = + 5.30 (c = 1.50, $CHCl_3$); HPLC

analysis (AD-H, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (major) = 9.9 min, t_R (minor) = 11.3 min.



3f

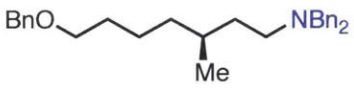
(*R*)-*N*,*N*-dibenzyl-3,4,4-trimethylpentan-1-amine (Scheme 4, entry **3f**). From **(*E*)-3,4,4-trimethylpent-2-en-1-yl 4-(dimethylamino)benzoate** (**1f**) (275 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 66% yield (182 mg). IR (neat, cm^{-1}) 2960, 1494, 1453, 1364, 1216, 1028, 745, 697; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.48 – 7.41 (m, 4H), 7.41 – 7.34 (m, 4H), 7.33 – 7.26 (m, 2H), 3.75 (d, J = 13.7 Hz, 2H), 3.51 (d, J = 13.7 Hz, 2H), 2.57 – 2.42 (m, 2H), 1.94 – 1.81 (m, 1H), 1.30 – 1.20 (m, 1H), 1.15 – 1.05 (m, 1H), 0.90 (s, 9H), 0.73 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.14, 128.95, 128.24, 126.84, 58.42, 52.74, 40.76, 33.14, 28.97, 27.46, 14.43. HRMS (DART-TOF) calcd. for $C_{22}H_{31}N$ $[M+H]^+$ *m/z* 310.2529, found 310.2515. $[\alpha]_D^{24}$ = + 5.30 (*c* = 1.50, $CHCl_3$); HPLC analysis (AD-H, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (major) = 7.9 min, t_R (minor) = 8.9 min.



3g

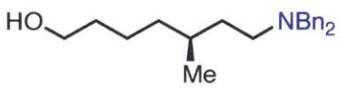
(*R*)-*N*,*N*-dibenzyl-3-(2-methyl-1,3-dioxolan-2-yl)butan-1-amine (Scheme 4, entry **3g**). From **(*E*)-3-(2-methyl-1,3-dioxolan-2-yl)but-2-en-1-yl 4-(dimethylamino)benzoate** (**1g**) (305 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (5–15% EtOAc in hexanes)

to provide the title compound as a colorless liquid in 67% yield (227 mg). IR (neat, cm^{-1}) 2937, 2876, 2794, 1494, 1453, 1379, 1219, 1149, 1062, 868, 746, 698; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.44 (s, 4H), 7.41 – 7.33 (m, 4H), 7.32 – 7.25 (m, 2H), 4.03 – 3.85 (m, 4H), 3.77 (d, J = 13.6 Hz, 2H), 3.49 (d, J = 13.6 Hz, 2H), 2.66 – 2.44 (m, 2H), 2.10 – 1.96 (m, 1H), 1.91 – 1.80 (m, 1H), 1.29 (s, 3H), 1.34 – 1.20 (m, 1H), 0.85 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.03, 128.90, 128.17, 126.78, 112.46, 64.59, 58.23, 51.49, 38.87, 28.93, 20.28, 14.58; HRMS (DART-TOF) calcd. for $C_{22}H_{29}NO_2$ $[M+H]^+$ m/z 340.2271, found 340.2249. $[\alpha]_D^{24}$ = + 16.8 (c = 1.00, $CHCl_3$); HPLC analysis (OD-H, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (minor) = 18.5 min, t_R (major) = 21.5 min.



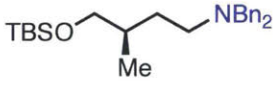
3h

(*S*)-*N*,*N*-dibenzyl-7-(benzyloxy)-3-methylheptan-1-amine (Scheme 4, entry **3h**). From **(*E*)-7-(benzyloxy)-3-methylhept-2-en-1-yl 4-(dimethylamino)benzoate** (**1h**) (382 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–7% EtOAc in hexanes) to provide the title compound as a colorless liquid in 69% yield (288 mg). IR (neat, cm^{-1}) 2930, 2855, 2791, 1494, 1452, 1363, 1219, 1101, 1028, 772, 731, 696; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.44 – 7.30 (m, 13H), 7.29 – 7.23 (m, 2H), 4.55 (s, 2H), 3.62 (d, J = 13.7 Hz, 1H), 3.56 (d, J = 13.7 Hz, 1H), 3.48 (t, J = 6.6 Hz, 2H), 2.47 (t, J = 7.6 Hz, 2H), 1.69 – 1.45 (m, 4H), 1.45 – 1.30 (m, 3H), 1.30 – 1.19 (m, 1H), 1.16 – 1.03 (m, 1H), 0.80 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.17, 138.86, 128.92, 128.47, 128.23, 127.74, 127.59, 126.83, 72.98, 70.61, 58.45, 51.37, 36.95, 34.20, 30.89, 30.19, 23.70, 19.83; Anal. Calcd. for $C_{29}H_{37}NO$: C, 83.81; H, 8.97. Found: C, 83.57; H, 9.08. $[\alpha]_D^{24}$ = – 1.0 (c = 2.00, $CHCl_3$); HPLC analysis (OJ-H, 5% IPA/hexanes, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (major) = 15.0 min, t_R (minor) = 31.9 min.



3i

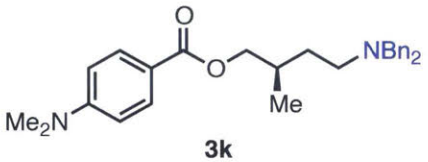
(*S*)-7-(dibenzylamino)-5-methylheptan-1-ol (Scheme 4, entry **3i**). From **(*E*)-7-hydroxy-3-methylhept-2-en-1-yl 4-(dimethylamino)benzoate** (**1i**) (291 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (720 μL, 4.5 mmol, 4.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C and quenched by adding 5 mL TBAF (1 M in THF) and stirring for an extra 1h. The crude material was purified by flash column chromatography (15–30% EtOAc in hexanes) to provide the title compound as a colorless liquid in 69% yield (225 mg). IR (neat, cm^{-1}) 2928, 2859, 2792, 1494, 1452, 1365, 1068, 1028, 745, 697; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.46 – 7.40 (m, 4H), 7.40 – 7.33 (m, 4H), 7.31 – 7.25 (m, 2H), 3.63 (d, J = 13.5 Hz, 2H), 3.63 (t, J = 6.6 Hz, 2H), 3.57 (d, J = 13.6 Hz, 2H), 2.49 (t, J = 7.3 Hz, 2H), 1.68 – 1.48 (m, 5H), 1.43 – 1.21 (m, 4H), 1.17 – 1.05 (m, 1H), 0.82 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.08, 128.90, 128.20, 126.81, 63.04, 58.43, 51.30, 36.81, 34.11, 33.15, 30.81, 23.18, 19.81; HRMS (DART-TOF) calcd. for $C_{22}H_{31}NO$ $[M+H]^+$ *m/z* 326.2478, found 326.2457. $[\alpha]_D^{24}$ = – 1.3 (*c* = 1.00, $CHCl_3$). HPLC analysis (OD-H, 5% IPA in hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 9.3 min, t_R (major) = 10.6 min.



3j

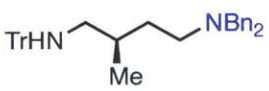
(*R*)-*N*,*N*-dibenzyl-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbutan-1-amine (Scheme 4, entry **3j**). From **(*E*)-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbut-2-en-1-yl 4-(dimethylamino)benzoate** (**1j**) (364 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 92% yield (365 mg). IR (neat, cm^{-1}) 2953, 2927, 2855, 2792, 1494, 1452, 1361, 1250, 1088, 1006, 773, 696; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.42 – 7.37 (m, 4H), 7.36 – 7.30 (m, 4H),

7.28 – 7.22 (m, 2H), 3.63 (d, J = 13.6 Hz, 2H), 3.53 (d, J = 13.6 Hz, 2H), 3.44 – 3.28 (m, 2H), 2.48 (t, J = 7.2 Hz, 2H), 1.80 – 1.62 (m, 2H), 1.34 – 1.19 (m, 1H), 0.91 (s, 9H), 0.78 (d, J = 6.6 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 140.12, 128.98, 128.24, 126.85, 68.30, 58.37, 51.26, 33.89, 30.38, 26.11, 18.48, 16.86, -5.22; Anal. Calcd. for $C_{25}H_{39}NOSi$: C, 75.51; H, 9.89. Found: C, 75.23; H, 10.00. $[\alpha]_D^{24}$ = + 2.1 (c = 1.50, $CHCl_3$). HPLC analysis (AD-H, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated 97% ee: t_R (major) = 5.4 min, t_R (minor) = 5.7 min.



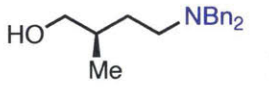
3k

(*R*)-*N*,*N*-dibenzyl-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbutan-1-amine (Scheme 4, entry **3k**). From **(*E*)-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbut-2-en-1-yl 4-(dimethylamino)benzoate** (**1k**) (364 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 92% yield (365 mg). IR (neat, cm^{-1}) 2930, 2802, 1700, 1608, 1525, 1452, 1366, 1275, 1182, 1105, 770, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ:8.02 – 7.89 (m, 2H), 7.49 – 7.40 (m, 4H), 7.40 – 7.31 (m, 4H), 7.31 – 7.23 (m, 2H), 6.71 – 6.63 (m, 2H), 4.17 – 4.01 (m, 2H), 3.68 (d, J = 13.6 Hz, 2H), 3.56 (d, J = 13.6 Hz, 2H), 3.07 (s, 6H), 2.63 – 2.49 (m, 2H), 2.14 – 1.98 (m, 1H), 1.89 – 1.77 (m, 1H), 1.52 – 1.37 (m, 1H), 0.93 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.07, 153.31, 139.89, 131.27, 128.92, 128.24, 126.87, 117.41, 110.78, 69.01, 58.40, 50.94, 40.13, 30.91, 30.85, 17.02; Anal. Calcd. for $C_{28}H_{34}N_2O_2$: C, 78.10; H, 7.96. Found: C, 77.80; H, 8.03. $[\alpha]_D^{24}$ = – 10.1 (c = 2.00, $CHCl_3$). HPLC analysis (IA, 10% EtOH in hexanes, 0.8 mL/min, 220 nm) indicated 94% ee: t_R (minor) = 8.9 min, t_R (major) = 9.6 min.



3l

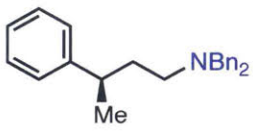
(*R*)-N^4,N^4-dibenzyl-2-methyl-N^1-tritylbutane-1,4-diamine (Scheme 4, entry **3l**). From **(*E*)-3-methyl-4-(tritylamino)but-2-en-1-yl 4-(dimethylamino)benzoate** (**1l**) (491 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 78% yield (408 mg). IR (neat, cm^{-1}) 3026, 2924, 1493, 1449, 1219, 772, 698; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.51 – 7.46 (m, 6H), 7.42 – 7.36 (m, 4H), 7.35 – 7.28 (m, 10H), 7.27 – 7.23 (m, 2H), 7.23 – 7.19 (m, 3H), 3.64 (d, J = 13.7 Hz, 2H), 3.52 (d, J = 13.7 Hz, 2H), 2.53 – 2.33 (m, 2H), 2.08 – 1.97 (m, 1H), 1.95 – 1.88 (m, 1H), 1.78 – 1.64 (m, 2H), 1.51 – 1.42 (m, 1H), 1.37 – 1.29 (m, 1H), 0.86 (d, J = 6.5 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 146.44, 140.01, 128.89, 128.78, 128.25, 127.83, 126.86, 126.21, 70.82, 58.39, 51.28, 49.71, 32.38, 32.09, 18.47; HRMS (DART-TOF) calcd. for $C_{38}H_{40}N_2$ $[M+H]^+$ *m/z* 525.3264, found 525.3264 $[\alpha]_D^{24}$ = – 11.1 (*c* = 1.00, $CHCl_3$). HPLC analysis (IA, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (major) = 9.4 min, t_R (minor) = 12.2 min.



3m

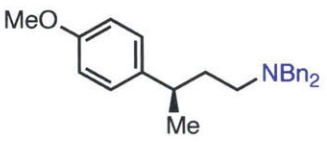
(*R*)-4-(dibenzylamino)-2-methylbutan-1-ol (Scheme 4, entry **3m**). From **(*E*)-3-methyl-4-oxobut-2-en-1-yl 4-(dimethylamino)benzoate** (**1m**) (247 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (720 μL, 4.5 mmol, 4.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C and after cooling to rt, was quenched by adding 5 mL TBAF (1 M in THF) and stirred for an additional 1h. The crude material was purified by flash column chromatography (15–30% EtOAc in hexanes) to provide the title compound as a colorless liquid in 70% yield (199 mg). IR (neat, cm^{-1}) 2921, 2798, 1494, 1452, 1366, 1028, 746, 698; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.52 – 7.33 (m, 8H), 7.33 – 7.23 (m, 2H), 4.87 (s, 1H),

3.72 (d, J = 13.3 Hz, 2H), 3.51 (d, J = 13.3 Hz, 2H), 3.46 (dd, J = 11.1, 4.3 Hz, 2H), 3.33 (dd, J = 11.0, 7.1 Hz, 1H), 2.64 – 2.44 (m, 2H), 1.78 – 1.50 (m, 3H), 0.83 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.06, 129.52, 128.40, 127.28, 68.24, 58.37, 52.06, 35.59, 32.44, 17.67; HRMS (DART-TOF) calcd. for $C_{19}H_{25}NO$ $[M+H]^+$ *m/z* 284.2009, found 284.1994. Anal. Calcd. for $C_{19}H_{25}NO$: C, 80.52; H, 8.89. Found: C, 80.22; H, 8.91. $[\alpha]_D^{24}$ = + 17.0 (c = 1.00, $CHCl_3$). HPLC analysis (AD, 5% IPA in hexanes, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (minor) = 11.7 min, t_R (major) = 12.6 min.



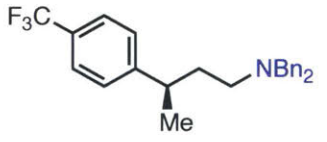
3n

(*R*)-*N*,*N*-dibenzyl-3-phenylbutan-1-amine (Scheme 7, entry **3n**). From **(*E*)-3-phenylbut-2-en-1-yl 4-(dimethylamino)benzoate** (**1n**) (295 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0–8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 74% yield (244 mg). IR (neat, cm^{-1}) 3026, 2925, 2795, 1493, 1451, 1367, 1265, 1125, 1074, 1028, 968, 968, 908, 732, 697; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.44 – 7.33 (m, 8H), 7.33 – 7.24 (m, 4H), 7.24 – 7.18 (m, 1H), 7.18 – 7.11 (m, 2H), 3.67 – 3.50 (m, 4H), 2.87 – 2.76 (m, 1H), 2.54 – 2.45 (m, 1H), 2.45 – 2.34 (m, 1H), 1.97 – 1.86 (m, 1H), 1.86 – 1.73 (m, 1H), 1.20 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 147.77, 139.98, 128.96, 128.40, 128.25, 127.03, 126.85, 125.88, 58.39, 51.64, 37.65, 35.72, 22.33; HRMS (DART-TOF) calcd. for $C_{24}H_{27}N$ $[M+H]^+$ *m/z* 330.2216, found 330.2214. $[\alpha]_D^{24}$ = – 39.0 (c = 1.00, $CHCl_3$). HPLC analysis (AD-H, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (major) = 17.1 min, t_R (minor) = 18.3 min.



3o

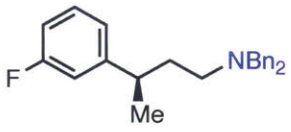
(*R*)-*N*,*N*-dibenzyl-3-(4-methoxyphenyl)butan-1-amine (Scheme 7, entry **3o**). From **(*E*)-3-(4-methoxyphenyl)but-2-en-1-yl 4-(dimethylamino)benzoate (1o)** (325 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–4% EtOAc in hexanes) to provide the title compound as clear colorless oil in 85% yield (306 mg). IR (neat, cm^{-1}): 3027, 2926, 2794, 1618, 1494, 1452, 1420, 1323, 1162, 1118, 1068, 1028, 1028, 1016, 839, 744, 732, 696, 607; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 8H), 7.25 – 7.20 (m, 2H), 7.00 – 6.98 (dt, J = 8.4, 2.0 Hz, 2H), 6.79 – 6.75 (dt, J = 8.4, 2.0 Hz, 2H), 3.78 (s, 3H), 3.56 – 3.48 (dd, J = 18.0, 13.6 Hz, 4H), 2.74 – 2.65 (m, 1H), 2.44 – 2.29 (m, 2H), 1.83 – 1.68 (m, 2H), 1.12 – 1.10 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 139.9, 139.7, 128.8, 128.1, 127.7, 126.7, 113.6, 58.3, 55.2, 51.5, 36.7, 35.8, 22.4; HRMS (DART-TOF) calculated for $C_{25}H_{29}NO$ $[M+H]^+$ m/z 360.2322, found 348.2322. $[\alpha]_D^{23.8}$ = –47.28 (c = 1.00, $CHCl_3$). HPLC analysis (OJ-H, 1% IPA/Hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 18.1 min, t_R (major) = 25.4 min.



3p

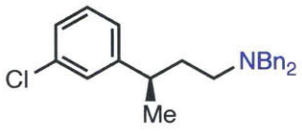
(*R*)-*N*,*N*-dibenzyl-3-(4-(trifluoromethyl)phenyl)butan-1-amine (Scheme 7, entry **3p**). From **(*E*)-3-(4-(trifluoromethyl)phenyl)but-2-en-1-yl 4-(dimethylamino)benzoate (1p)** (363 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–4% EtOAc in hexanes) to provide the title compound as a clear colorless oil in 62% yield (246 mg). IR (neat, cm^{-1}): 3027, 2926, 2794, 1618, 1494, 1452, 1323, 1162, 1118, 1068, 1028, 1016, 839, 744, 732, 696; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 –

7.45 (d, J = 8.0 Hz, 2H), 7.37 – 7.22 (m, 10H), 7.15 – 7.12 (d, J = 8.0 Hz, 2H), 3.61–3.54 (dd, J = 25.4, 13.2 Hz, 4H), 2.88 – 2.79 (m, 1H), 2.42 – 2.28 (m, 2H), 1.84 – 1.77 (m, 2H), 1.16 – 1.14 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5, 139.7, 128.8, 128.1, 127.2, 126.8, 125.2 (q, J=3.9 Hz), 58.4, 51.1, 37.4, 35.4, 22.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7. Anal. Calcd. for $C_{25}H_{26}F_3N$: C, 75.54; H, 6.59 Found: C, 75.65; H, 6.67. $[\alpha]_D^{23.7}$ = –47.33 (c = 1.82, $CHCl_3$). HPLC analysis (OJ-H, 1% IPA/Hexanes, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 19.0 min, t_R (major) = 26.0 min.



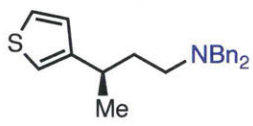
3q

(*R*)-*N*,*N*-dibenzyl-3-(3-fluorophenyl)butan-1-amine (Scheme 7, entry **3q**): From **(*E*)-3-(3-fluorophenyl)but-2-en-1-yl 4-(dimethylamino)benzoate (1q)** (313 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol), diethoxymethylsilane (560 µL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–5% EtOAc in hexanes) to afford provide the title compound as a clear colorless oil in 77% yield (268 mg). IR (neat, cm^{-1}): 3027, 2926, 2795, 1614, 1589, 1493, 1451, 1365, 1243, 1151, 1128, 1069, 1028, 967, 782, 732, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 8H), 7.27 – 7.23 (m, 2H), 7.20 – 7.14 (m, 1H), 6.87 – 6.82 (m, 2H), 6.81 – 6.78 (dt, J = 10.4, 2.0 Hz, 1H), 3.58–3.50 (dd, J = 16.8, 13.6 Hz, 4H), 2.81 – 2.73 (m, 1H), 2.45 – 2.32 (m, 2H), 1.86 – 1.72 (m, 2H), 1.14 – 1.12 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9 (d, J = 245.7 Hz), 150.3 (d, J = 6.8 Hz), 139.7, 129.6 (d, J = 6.8 Hz), 128.8, 128.1, 126.8, 122.6 (d, J = 10.4 Hz), 113.6 (d, J = 20.9 Hz), 112.5 (d, J = 21.2 Hz), 58.4, 51.3, 37.3, 35.5, 22.1;^{19}F NMR (376 MHz, $CDCl_3$) δ -114.2. HRMS (DART-TOF) calculated for $C_{24}H_{26}FN$ $[M+H]^+$ m/z 348.2122, found 348.2109. HPLC analysis (OJ-H, 3% IPA/Hexanes, 1 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 7.3 min, t_R (major) = 10.3 min. $[\alpha]_D^{23.8}$ = –48.27 (c = 1.08, $CHCl_3$).



3r

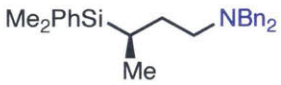
(*R*)-*N*,*N*-dibenzyl-3-(3-chlorophenyl)butan-1-amine (Scheme 7, entry **3r**). From **(*E*)-3-(3-chlorophenyl)but-2-en-1-yl 4-(dimethylamino)benzoate (1r)** (325 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), and *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–4% EtOAc in hexanes) to provide the title compound as a clear colorless oil in 91% yield (331 mg). IR (neat, cm^{-1}): 3060, 3026, 2924, 2794, 1595, 1571, 1493, 1452, 1429, 1365, 1076, 1027, 782, 744, 695; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.22 (m, 10H), 7.14 – 7.07 (m, 3H), 6.94 – 6.91 (m, 1H), 3.57 – 3.50 (dd, J = 16.4, 13.6 Hz, 4H), 2.78 – 2.63 (m, 1H), 2.41 – 2.34 (m, 2H), 1.85 – 1.69 (m, 2H), 1.12 – 1.11 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.7, 139.7, 134.0, 129.5, 128.8, 128.1, 127.0, 126.8, 125.9, 125.29, 58.4, 51.3, 37.4, 35.4, 22.1. HRMS (DART-TOF) calculated for $C_{24}H_{26}ClN$ $[M+H]^+$ m/z 364.1827, found 364.1830. $[\alpha]_D^{23.8}$ = – 53.43 (c = 1.41, $CHCl_3$). HPLC analysis (OJ-H, 3% IPA/Hexanes, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 7.5 min, t_R (major) = 9.2 min.



3s

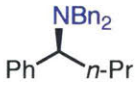
(*R*)-*N*,*N*-dibenzyl-3-(thiophen-3-yl)butan-1-amine (Scheme 7, entry **3s**): From **(*E*)-3-(thiophen-3-yl)but-2-en-1-yl 4-(dimethylamino)benzoate (1s)** (301 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol), diethyoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred in THF (1 mL) at 40 °C for 36 h. The crude product was purified by flash column chromatography (0–4% EtOAc in hexanes) to provide the title compound as a clear colorless oil (run 1: 230 mg (68%); run 2: 245 mg (73%); average yield: 70%). IR (neat, cm^{-1}): 3061, 3025, 2924, 2792, 1600, 1493, 1451, 1365, 1235, 1124, 1027, 743, 731, 694; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 8H), 7.28 – 7.24 (tt, J = 6.0, 1.6 Hz, 2H), 7.12 – 7.10 (dd, J = 5.2, 1.2 Hz, 1H), 6.89 – 6.87 (dd, J = 5.2, 3.6 Hz, 1H),

6.66 – 6.66 (dd, J = 3.6, 1.2 Hz, 1H), 3.61–3.54 (dd, J = 17.2, 13.6 Hz, 4H), 3.18 – 3.10 (m, 1H), 2.52 – 2.46 (m, 2H), 1.97 – 1.74 (m, 2H), 1.23 – 1.21 (d, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 128.9, 128.1 126.8, 126.34 122.5, 122.3, 58.3, 51.2, 36.6, 33.0, 23.0. Anal. Calcd. for $C_{22}H_{25}NS$: C, 78.76; H, 7.51 Found: C, 78.37; H, 7.46. $[\alpha]_D^{23.8}$ = –41.25 (c = 1.09, $CHCl_3$). HPLC analysis (IA, 97:5:0.2:0.1 Hexanes:EtOH:TFA:Diethylamine, 1.0 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 12.8 min, t_R (major) = 13.6 min.



3t

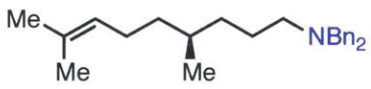
(*R*)-*N*,*N*-dibenzyl-3-(dimethyl(phenyl)silyl)butan-1-amine (Scheme 8, entry **3t**). From **(*E*)-3-phenylbut-2-en-1-yl 4-(dimethylamino)benzoate (1t)** (354 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 µL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 92% yield (358 mg). IR (neat, cm^{-1}) 2952, 1494, 1453, 1427, 1248, 1111, 832, 813, 734, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 – 7.46 (m, 2H), 7.44 – 7.31 (m, 11H), 7.30 – 7.23 (m, 2H), 3.64 (d, J = 13.6 Hz, 2H), 3.44 (d, J = 13.6 Hz, 2H), 2.47 (t, J = 7.5 Hz, 2H), 1.88 – 1.71 (m, 1H), 1.31 – 1.19 (m, 1H), 1.06 – 0.90 (m, 1H), 0.83 (d, J = 7.3 Hz, 3H), 0.25 (d, J = 0.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.10, 138.73, 134.04, 128.95, 128.86, 128.23, 127.75, 126.83, 58.42, 52.44, 28.99, 16.72, 14.15, -4.59, -4.95; HRMS (DART-TOF) calcd. for $C_{26}H_{33}NSi$ $[M+H]^+$ *m/z* 388.2455, found 388.2434. $[\alpha]_D^{24}$ = + 6.4 (*c* = 1.00, $CHCl_3$). HPLC analysis (OJ-H, 5% EtOH in hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (major) = 9.8 min, t_R (minor) = 14.4 min.



3u

(*S*)-*N*,*N*-dibenzyl-1-phenylbutan-1-amine (Scheme 9, entry **3u**). From **(*E*)-1-phenylbut-2-en-1-yl 4-(dimethylamino)benzoate (1u)** (295 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (9.1

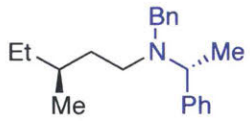
mg, 0.05 mmol, 5.0 mol%) and (*R*)-DTBM-SEGPHOS (65 mg, 0.055 mmol, 5.5 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (476 mg, 1.2 mmol, 1.5 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 71% yield (244 mg). IR (neat, cm^{-1}) 3025, 2931, 2801, 1493, 1452, 772, 744; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.80 – 7.29 (m, 15H), 3.97 (d, J = 13.8 Hz, 2H), 3.85 (t, J = 7.5 Hz, 1H), 3.30 (d, J = 13.9 Hz, 2H), 2.30 – 2.09 (m, 1H), 2.04 – 1.80 (m, 1H), 1.71 – 1.52 (m, 1H), 1.52 – 1.31 (m, 1H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.60, 139.26, 129.11, 128.87, 128.30, 128.00, 127.02, 126.82, 61.70, 53.76, 33.73, 20.29, 14.35; HRMS (DART-TOF) calcd. for $C_{24}H_{27}N$ $[M+H]^+$ *m/z* 330.2216, found 330.2209. $[\alpha]_D^{24}$ = – 98.5 (*c* = 2.00, $CHCl_3$). HPLC analysis (OD-H, 2% IPA in hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (major) = 4.9 min, t_R (minor) = 5.6 min.



3v

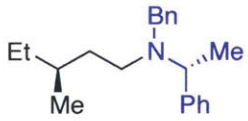
(*S*)-*N*,*N*-dibenzyl-4,8-dimethylnon-7-en-1-amine (Scheme 11, entry **3v**). From **(*E*)-2-(2,6-dimethylhepta-1,5-dien-1-yl)oxirane (1v)** (166 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2.0 mol%) and (*R*)-DTBM-SEGPHOS (23 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (381 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (640 μL, 4.0 mmol, 4.0 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-8% EtOAc in hexanes) to provide the title compound as a colorless liquid in 55% yield (192 mg). IR (neat, cm^{-1}) 2925, 2792, 1494, 1452, 1375, 1125, 1068, 1028, 978, 739, 696; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.43 (m, 4H), 7.36 (m, 4H), 7.28 (m, 2H), 5.14 (t, J = 7.0 Hz, 1H), 3.61 (m, 4H), 2.45 (t, J = 7.2 Hz, 2H), 2.00 (m, 1H), 1.94 (m, 1H), 1.74 (s, 3H), 1.65 (s, 3H), 1.63 – 1.56 (m, 1H), 1.52 (m, 1H), 1.44 – 1.28 (m, 3H), 1.21 – 1.09 (m, 2H), 0.89 (d, J = 6.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 140.20, 131.11, 128.87, 128.24, 126.81, 125.17, 58.43, 53.94, 37.25, 34.60, 32.44, 25.89, 25.72, 24.52, 19.70, 17.79; Anal. Calcd. for $C_{25}H_{35}N$: C, 85.90; H, 10.09. Found: C, 85.74; H, 10.21. $[\alpha]_D^{24}$ = + 2.9 (*c* = 1.0, $CHCl_3$). HPLC analysis (AD-H and OJ-H column in sequence, 50% (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1) in hexanes, 0.8 mL/min, 210

nm) indicated 93% ee: t_R (major) = 25.1 min, t_R (minor) = 26.4 min.



4a

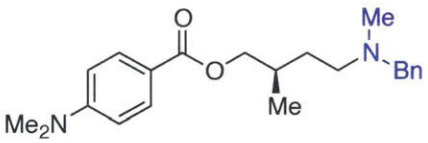
(*S*)-*N*-benzyl-3-methyl-*N*-((*R*)-1-phenylethyl)pentan-1-amine (Scheme 12, entry **4a).** From **(*E*)-3-methylpent-2-en-1-yl 4-(dimethylamino)benzoate** (**1w**) (247 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), (*R*)-*O*-benzoyl-*N*-benzyl-*N*-(1-phenylethyl)hydroxylamine (398 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-5% EtOAc in hexanes) to provide the title compound as a colorless liquid in 91% yield (269 mg). IR (neat, cm^{-1}) 2960, 2926, 2873, 1493, 1452, 748, 697; ^1H NMR (600 MHz, CD_2Cl_2) δ: 7.48 – 7.42 (m, 2H), 7.42 – 7.38 (m, 2H), 7.38 – 7.34 (m, 2H), 7.34 – 7.30 (m, 2H), 7.28 – 7.21 (m, 2H), 3.94 (q, J = 6.8 Hz, 1H), 3.61 (d, J = 14.1 Hz, 1H), 3.52 (d, J = 14.1 Hz, 1H), 2.54 (ddd, J = 14.4, 9.0, 5.6 Hz, 1H), 2.39 (ddd, J = 13.1, 9.4, 5.5 Hz, 1H), 1.55 – 1.47 (m, 1H), 1.41 (d, J = 6.8 Hz, 3H), 1.39 – 1.27 (m, 2H), 1.27 – 1.18 (m, 1H), 1.06 (dq, J = 13.7, 7.4 Hz, 1H), 0.82 (t, J = 7.4 Hz, 3H), 0.78 (d, J = 6.5 Hz, 3H); ^{13}C NMR (151 MHz, CD_2Cl_2) δ: 144.70, 141.84, 129.12, 128.60, 128.49, 128.43, 127.10, 127.08, 58.49, 54.92, 47.73, 34.64, 32.99, 29.95, 19.82, 15.83, 11.79; Anal. Calcd. for $C_{21}H_{29}N$: C, 85.37; H, 9.89. Found: C, 85.07; H, 9.94. $[\alpha]_D^{24}$ = + 34.7 (c = 1.00, $CHCl_3$). ^1H NMR analysis of the crude reaction mixture indicated >50:1 dr.



4a'

(*R*)-*N*-benzyl-3-methyl-*N*-((*R*)-1-phenylethyl)pentan-1-amine (Scheme 12, entry **4a').** From **(*E*)-3-methylpent-2-en-1-yl 4-(dimethylamino)benzoate** (**1w**) (247 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*S*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), (*R*)-*O*-benzoyl-*N*-benzyl-*N*-(1-phenylethyl)hydroxylamine (398 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture

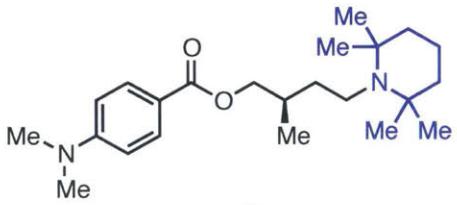
was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-5% EtOAc in hexanes) to provide the title compound as a colorless liquid in 90% yield (266 mg). IR (neat, cm^{-1}) 2960, 2924, 1493, 1452, 1372, 1219, 772, 697; ^1H NMR (600 MHz, CD_2Cl_2) δ: 7.50 – 7.44 (m, 2H), 7.42 – 7.37 (m, 2H), 7.37 – 7.34 (m, 2H), 7.34 – 7.30 (m, 2H), 7.29 – 7.21 (m, 2H), 3.95 (q, J = 6.8 Hz, 1H), 3.57 (d, J = 14.4 Hz, 1H), 3.55 (d, J = 14.4 Hz, 1H), 2.58 (ddd, J = 13.8, 9.2, 5.0 Hz, 1H), 2.37 (ddd, J = 13.0, 9.1, 6.3 Hz, 1H), 1.59 – 1.50 (m, 1H), 1.41 (d, J = 6.8 Hz, 3H), 1.35 (dt, J = 12.6, 6.2 Hz, 1H), 1.32 – 1.22 (m, 2H), 1.11 (dq, J = 13.5, 7.4 Hz, 1H), 0.84 (t, J = 7.4 Hz, 3H), 0.73 (d, J = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, CD_2Cl_2) δ: 144.84, 141.75, 129.04, 128.48, 128.36, 128.35, 126.96, 58.11, 54.71, 47.54, 34.39, 32.87, 30.14, 19.44, 15.00, 11.64; Anal. Calcd. for $C_{21}H_{29}N$: C, 85.37; H, 9.89. Found: C, 85.07; H, 10.06. $[\alpha]_D^{24}$ = + 16.4 (c = 2.00, $CHCl_3$). ^1H NMR analysis of the crude reaction mixture indicated <1:50 dr.



4b

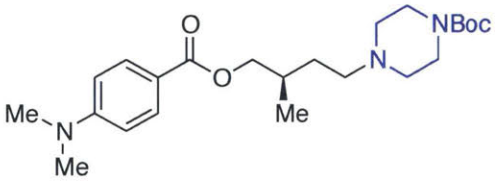
(*R*)-4-(benzyl(methyl)amino)-2-methylbutyl 4-(dimethylamino)benzoate (Scheme 12, entry **4b).** From **((*E*)-2-methylbut-2-ene-1,4-diyl bis(4-(dimethylamino)benzoate) (1k)** (396 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *O*-benzoyl-*N*-benzyl-*N*-methylhydroxylamine (290 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-40% EtOAc in hexanes, containing 1% NEt_3) to provide the title compound as a colorless liquid in 92% yield (325 mg). IR (neat, cm^{-1}) 2939, 2791, 1699, 1607, 1525, 1452, 1366, 1274, 1182, 1104, 971, 770, 698; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, J = 8.8 Hz, 2H), 7.46 – 7.17 (m, 3H), 6.66 (d, J = 8.7 Hz, 2H), 4.29 – 4.02 (m, 2H), 3.56 (d, J = 13.2 Hz, 1H), 3.50(d, J = 12.8 Hz, 1H), 3.03 (s, 6H), 2.51 (t, J = 7.4 Hz, 2H), 2.24 (s, 3H), 2.08 (dq, J = 13.0, 6.5 Hz, 1H), 1.80 (dq, J = 13.3, 7.4 Hz, 1H), 1.49 (dq, J = 14.2, 7.4 Hz, 1H), 1.05 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.91, 153.17, 139.12, 131.14, 128.95, 128.12, 126.83, 117.19, 110.64, 68.86, 62.32, 55.01, 42.10, 39.94, 31.10, 31.03, 17.11; Anal. Calcd. for

$C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53. Found: C, 74.36; H, 8.56. $[\alpha]_D^{24}$ = – 6.0 (*c* = 2.00, $CHCl_3$). HPLC analysis (IA, 10% EtOH in (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1), 0.8 mL/min, 230 nm) indicated 98% ee: t_R (minor) = 16.6 min, t_R (major) = 18.5 min.



4c

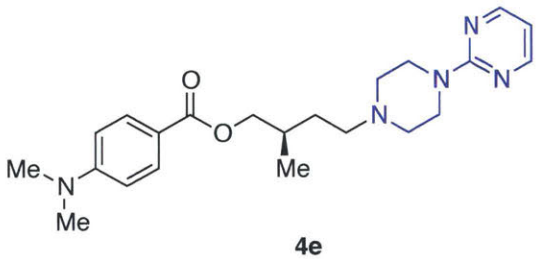
(*R*)-2-methyl-4-(2,2,6,6-tetramethylpiperidin-1-yl)butyl 4-(dimethylamino)benzoate (Scheme 12, entry **4c**). From **((*E*)-2-methylbut-2-ene-1,4-diyl bis(4-(dimethylamino)benzoate) (1k)** (396 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), 2,2,6,6-tetramethylpiperidin-1-yl benzoate (314 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 µL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-100% EtOAc in DCM, containing 1% NEt_3) to provide the title compound as a colorless liquid in 89% yield (335 mg). IR (neat, cm^{-1}) 2928, 1703, 1608, 1525, 1366, 1275, 1183, 1105, 770; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, *J* = 9.0 Hz, 2H), 6.65 (d, *J* = 8.7 Hz, 2H), 4.16 (dd, *J* = 10.7, 6.0 Hz, 1H), 4.07 (dd, *J* = 10.7, 6.7 Hz, 1H), 3.04 (s, 6H), 2.60 – 2.39 (m, 2H), 1.88 (dq, *J* = 13.1, 6.6 Hz, 1H), 1.71 – 1.59 (m, 1H), 1.59 – 1.49 (m, 2H), 1.48 – 1.34 (m, 5H), 1.04 (d, *J* = 6.7 Hz, 3H), 1.04 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 167.12, 153.30, 131.27, 117.43, 110.74, 69.07, 54.64, 42.97, 41.24, 40.13, 39.74, 32.00, 27.60, 17.85, 17.54; Anal. Calcd. for $C_{23}H_{38}N_2O_2$: C, 73.75; H, 10.23. Found: C, 73.77; H, 10.22. $[\alpha]_D^{24}$ = + 0.41 (*c* = 2.00, $CHCl_3$). HPLC analysis (AD-H, 10% EtOH in (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1), 0.8 mL/min, 280 nm) indicated 96% ee: t_R (minor) = 13.9 min, t_R (major) = 20.6 min.



4d

(*R*)-4-(4-((4-(dimethylamino)benzoyl)oxy)-3-methylbutyl)piperazine-1-carboxylate (Scheme 12, entry **4d**). From **((*E*)-2-methylbut-2-ene-1,4-diyl bis(4-(dimethylamino)benzoate) (1k)** (396

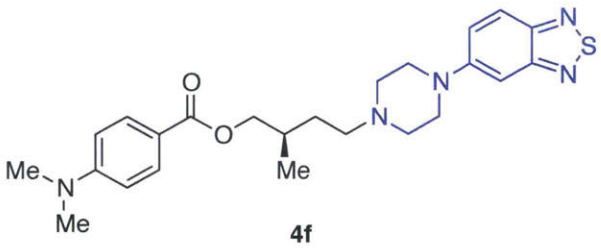
mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), *tert*-butyl 4-(benzoyloxy)piperazine-1-carboxylate (368 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 50 °C. The crude material was purified by flash column chromatography (0-100% EtOAc in hexanes, containing 1% NEt_3) to provide the title compound as a colorless liquid in 91% yield (382 mg). IR (neat, cm^{-1}) 2929, 1692, 1606, 1364, 1273, 1180, 1102, 769; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, J = 9.0 Hz, 2H), 6.67 (d, J = 9.0 Hz, 2H), 4.23 – 4.06 (m, 2H), 3.44 (t, J = 5.1 Hz, 4H), 3.06 (s, 6H), 2.51 – 2.32 (m, 6H), 2.08 – 1.91 (m, 1H), 1.80 – 1.68 (m, 1H), 1.56 – 1.36 (m, 1H), 1.48 (s, 9H), 1.05 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.98, 154.75, 153.30, 131.21, 117.17, 110.71, 79.53, 68.81, 56.38, 53.10, 43.95, 40.07, 31.36, 30.59, 28.47, 17.22; HRMS (DART-TOF) calcd. for $C_{23}H_{37}N_3O_4$ $[M+H]^+$ *m/z* 420.2857, found 420.2853. $[\alpha]_D^{24}$ = + 1.7 (c = 1.0, $CHCl_3$). HPLC analysis (AD-H, 10% EtOH in (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1), 1.0 mL/min, 280 nm) indicated 96% ee: t_R (minor) = 24.8 min, t_R (major) = 36.3 min.



4e

(*R*)-2-methyl-4-(4-(pyrimidin-2-yl)piperazin-1-yl)butyl 4-(dimethylamino)benzoate (Scheme 12, entry **4e**). From **((*E*)-2-methylbut-2-ene-1,4-diyl bis(4-(dimethylamino)benzoate) (1k)** (396 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), 4-(pyrimidin-2-yl)piperazin-1-yl benzoate (341 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-100% EtOAc in DCM, containing 1% NEt_3) to provide the title compound as a colorless liquid in 89% yield (345 mg). IR (neat, cm^{-1}) 2937, 2810, 1698, 1607, 1584, 1445, 1358, 1274, 1181, 1103, 982, 769; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.30 (d, J = 4.7 Hz, 2H), 7.91 (d, J = 9.0 Hz, 2H), 6.64 (d, J = 9.2 Hz, 2H), 6.47 (t, J = 4.7 Hz, 1H), 4.27 – 4.04 (m, 2H), 3.97 – 3.71 (m,

4H), 3.03 (s, 6H), 2.63 – 2.36 (m, 6H), 2.01 (dq, J = 13.2, 6.5 Hz, 1H), 1.77 (dq, J = 14.6, 6.3 Hz, 1H), 1.49 (dq, J = 14.0, 7.8 Hz, 1H), 1.05 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 167.04, 161.70, 157.74, 153.33, 131.26, 117.22, 110.76, 109.86, 68.86, 56.50, 53.18, 43.66, 40.12, 31.48, 30.60, 17.26; Anal. Calcd. for $C_{22}H_{31}N_5O_2$: C, 66.47; H, 7.86. Found: C, 66.29; H, 7.89. $[\alpha]_D^{24}$ = – 3.7 (c = 1.50, $CHCl_3$). HPLC analysis (IA, 10% EtOH in (hexanes:EtOH:TFA:DEA = 95:5:0.2:0.1), 0.8 mL/min, 230 nm) indicated 98% ee: t_R (minor) = 40.9 min, t_R (major) = 46.6 min.



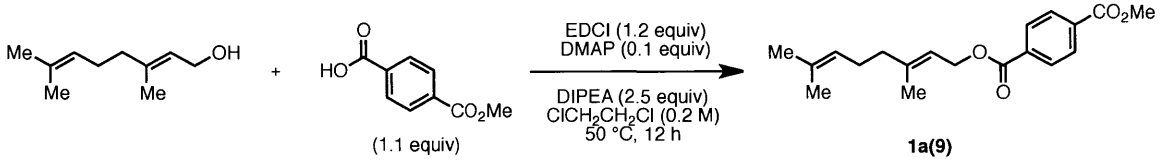
4f

(*R*)-4-(4-(benzo[*c*][1,2,5]thiadiazol-5-yl)piperazin-1-yl)-2-methylbutyl 4-(dimethylamino)benzoate (Scheme 12, entry **4f**). From **((*E*)-2-methylbut-2-ene-1,4-diyl bis(4-(dimethylamino)benzoate)** (**1k**) (396 mg, 1.0 mmol), the title compound was prepared following the general procedure using $Cu(OAc)_2$ (3.6 mg, 0.02 mmol, 2 mol%), (*R*)-DTBM-SEGPHOS (26 mg, 0.022 mmol, 2.2 mol%), 4-(benzo[*c*][1,2,5]thiadiazol-5-yl)piperazin-1-yl benzoate (407 mg, 1.2 mmol, 1.2 equiv), diethoxymethylsilane (560 μL, 3.5 mmol, 3.5 equiv), and THF (1.0 mL). The reaction mixture was stirred for 36 h at 40 °C. The crude material was purified by flash column chromatography (0-100% EtOAc in DCM, containing 1% NEt_3) to provide the title compound as a deep green solid in 78% yield (351 mg). m. p. 103-105 °C. IR (neat, cm^{-1}) 2920, 1698, 1608, 1525, 1447, 1367, 1276, 1183, 1106, 770, 753; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, J = 8.7 Hz, 2H), 7.78 (d, J = 9.6 Hz, 1H), 7.43 (d, J = 9.7 Hz, 1H), 7.08 (s, 1H), 6.65 (d, J = 8.9 Hz, 2H), 4.26 – 4.04 (m, 2H), 3.45 – 3.22 (m, 4H), 3.03 (s, 6H), 2.79 – 2.57 (m, 4H), 2.50 (t, J = 7.0 Hz, 2H), 2.13 – 1.93 (m, 1H), 1.77 (dq, J = 13.7, 6.5 Hz, 1H), 1.48 (dq, J = 14.1, 7.6 Hz, 1H), 1.06 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.98, 156.57, 153.28, 152.24, 150.76, 131.21, 124.77, 120.96, 117.12, 110.69, 101.16, 68.78, 56.23, 52.93, 48.96, 40.05, 31.36, 30.59, 17.24; HRMS (DART-TOF) calcd. for $C_{24}H_{31}N_5O_2S$ $[M+H]^+$ m/z 454.2271, found 454.2266. $[\alpha]_D^{24}$ = + 4.5 (c = 1.0, $CHCl_3$). HPLC analysis (AD-H, 30% IPA in hexanes, 0.8 mL/min, 254 nm) indicated 97% ee: t_R (minor) = 18.4 min, t_R (major) = 20.7 min.

B) Synthesis of the Substrates for Table 1

Substrates in Table 1 are known compounds synthesized according to literature procedures,[14] *except for the substrates used in entries 9 and 10.*

Preparation of substrate for Table 1, entry 9:

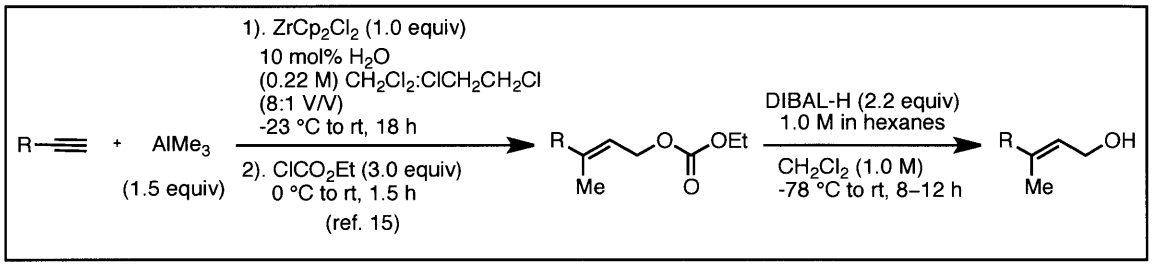


(*E*)-3,7-dimethylocta-2,6-dien-1-yl methyl terephthalate (Table 1, entry 9, **1a(9)**) To a solution of geraniol (5.30 mL, 30.0 mmol), mono-methyl terephthalate (5.96 g, 33.0 mmol, 1.1 equiv), EDCI (5.59 g, 36.0 mmol, 1.20 equiv) and DMAP (366 mg, 3.00 mmol, 0.10 equiv) in dichloroethane (150 mL, 0.2 M) was added DIPEA (12.3 mL, 75.0 mmol, 2.5 equiv). The reaction mixture was stirred in an oil bath at 50 °C overnight (12 h). The crude reaction mixture was purified by flash column chromatography (8-10% EtOAc in hexanes) to provide the title compound in 89% yield (8.45 g) as a colorless liquid. IR (neat, cm^{-1}) 2914, 1717, 1436, 1264, 1248, 1100, 1019, 928, 728; ^1H NMR (600 MHz, $CDCl_3$) δ: 8.16 – 7.96 (m, 4H), 5.47 (t, J = 7.6 Hz, 1H), 5.20 – 5.03 (m, 1H), 4.86 (d, J = 6.9 Hz, 2H), 3.95 (s, 3H), 2.21 – 1.94 (m, 4H), 1.77 (s, 3H), 1.67 (s, 3H), 1.60 (s, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ: 166.41, 165.90, 142.91, 134.41, 133.86, 131.97, 129.66, 129.59, 123.77, 118.17, 62.39, 52.51, 39.65, 26.37, 25.78, 17.81, 16.68; Anal. Calcd. for $C_{19}H_{34}O_4$: C, 72.13; H, 7.65. Found: C, 72.00; H, 7.63.

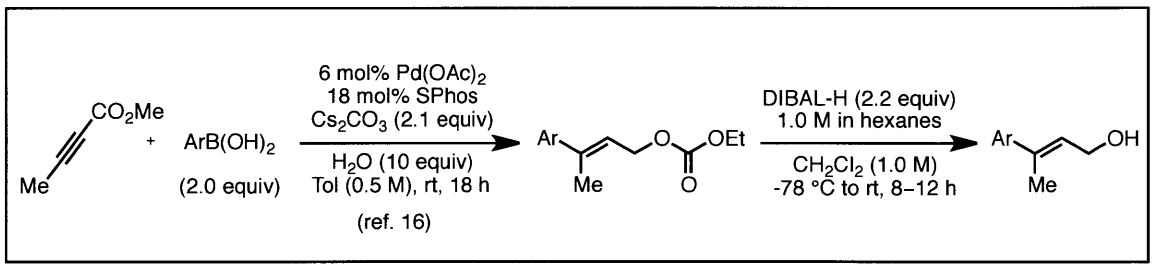
C) Synthesis of γ-Disubstituted Allylic 4-(Dimethylamino)benzoate

3,3-Disubstituted allylic benzoates were synthesized from the corresponding allylic alcohol following general procedures A or B (see below). All the 3,3-disubstituted allylic alcohols are known compounds synthesized according to literature procedures with slight modification[15,16] *The modification from literature procedures is outlined in Scheme 14 for the synthesis of 3,3-dialkyl-substituted allylic alcohols and in Scheme 15 for the synthesis of 3,3-alkyl,aryl-substituted allylic alcohols.*

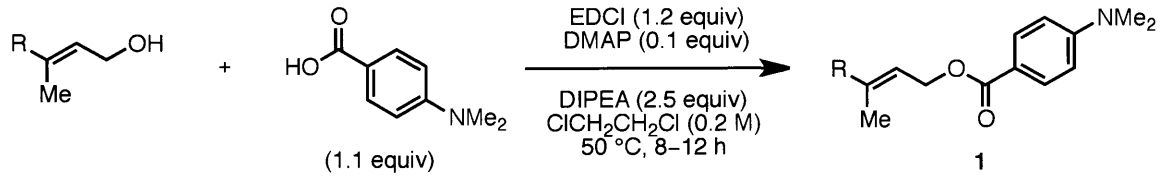
Scheme 14. *Synthesis of 3,3-Alkyl,alkyl-substituted Allylic Alcohols*



Scheme 15. *Synthesis of 3,3-Alkyl,aryl-substituted Allylic Alcohols*

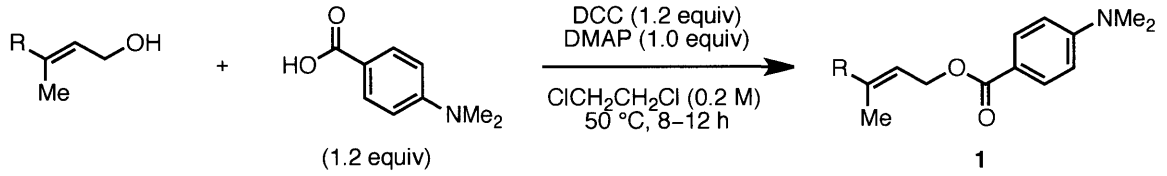


General Procedure A:

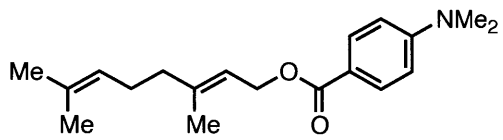


To a solution of allylic alcohol (1.0 equiv), 4-(dimethylamino)benzoic acid (1.1 equiv), EDCI (1.2 equiv), and DMAP (0.1 equiv) in dichloroethane (0.2 M) was added DIPEA (2.5 equiv). Then the reaction mixture was stirred in an oil bath at 50 °C overnight (8–12 h). The reaction mixture was allowed to cool to rt, diluted with DCM, and quenched with Na_2CO_3 (aq). The aqueous phase was extracted with DCM (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography to provide the corresponding γ-disubstituted allylic 4-(dimethylamino)benzoate.

General Procedure B:

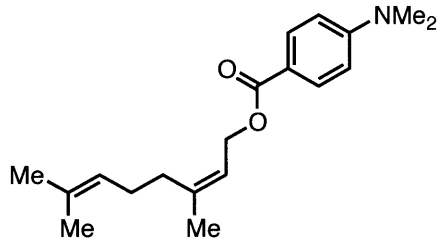


To a round bottom flask containing the allylic alcohol (1.0 equiv), 4-(dimethylamino)benzoic acid (1.2 equiv), DCC (1.2 equiv), and DMAP (1.0 equiv) was added dichloroethane (0.2 M). The reaction mixture was stirred in an oil bath at 50 °C overnight (8–12 h). The reaction mixture was allowed to cool to rt, diluted with DCM, and quenched with Na_2CO_3 (aq). The aqueous phase was extracted with DCM (2x). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography to provide the corresponding γ-disubstituted allylic 4-(dimethylamino)benzoate.



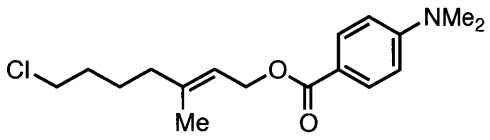
(*E*)-**1a**

(*E*)-3,7-dimethylocta-2,6-dien-1-yl 4-(dimethylamino)benzoate (Table 1 and Scheme 4, (*E*)-**1a**) Prepared following general procedure A using geraniol (2.64 mL, 15 mmol). The crude reaction mixture was purified by flash column chromatography (8-10% EtOAc in hexanes) to provide the title compound in 87% yield (3.92 g) as a white solid. m.p. 44–45 °C IR (neat, cm^{-1}) 2913, 1699, 1606, 1524, 1444, 1270, 1180, 1097, 946, 828, 769, 698; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.94 (d, J = 9.1 Hz, 2H), 6.66 (d, J = 9.1 Hz, 2H), 5.49 (td, J = 7.0, 1.2 Hz, 1H), 5.26 – 5.04 (m, 1H), 4.82 (d, J = 7.0 Hz, 2H), 3.05 (s, 6H), 2.25 – 2.02 (m, 4H), 1.78 (s, 3H), 1.71 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.14, 153.34, 141.55, 131.84, 131.37, 123.98, 119.19, 117.46, 110.77, 61.27, 40.15, 39.69, 26.48, 25.80, 17.81, 16.66, 0.11; HRMS (DART-TOF) calcd. for $C_{19}H_{27}NO_2$ $[M+H]^+$ *m/z* 302.2115, found 302.2121. Anal. Calcd. for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03. Found: C, 75.42; H, 9.13.



(*Z*)-**1a**

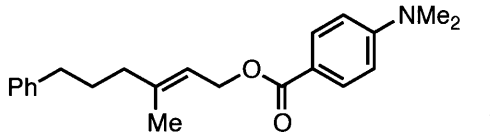
(*Z*)-3,7-dimethylocta-2,6-dien-1-yl 4-(dimethylamino)benzoate (Scheme 4, (*Z*)-**1a**) Prepared following general procedure A using nerol (3.52 mL, 20 mmol). The crude reaction mixture was purified by flash column chromatography (8-10% EtOAc in hexanes) to provide the title compound in 86% yield (5.19 g) as a white solid. m.p. 49–50 °C. IR (neat, cm^{-1}) 2913, 1698, 1606, 1524, 1444, 1365, 1270, 1180, 1098, 946, 828, 768, 698; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.94 (d, J = 9.0 Hz, 2H), 6.63 (dd, J = 9.1, 2.4 Hz, 2H), 5.51 (t, J = 7.0 Hz, 1H), 5.24 – 5.06 (m, 1H), 4.79 (d, J = 7.8 Hz, 2H), 3.02 (dd, J = 3.1, 1.2 Hz, 6H), 2.25 – 2.17 (m, 2H), 2.14 (q, J = 7.6, 7.1 Hz, 2H), 1.81 (s, 3H), 1.70 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.02, 153.23, 141.81, 132.05, 131.27, 123.75, 120.01, 117.30, 110.65, 60.87, 40.02, 32.28, 26.76, 25.73, 23.57, 17.71; HRMS (DART-TOF) calcd. for $C_{19}H_{27}NO_2$ $[M+H]^+$ *m/z* 302.2115, found 302.2124. Anal. Calcd. for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03. Found: C, 75.42; H, 9.13.



1b

(*E*)-7-chloro-3-methylhept-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1b**) Prepared following general procedure A from corresponding allylic alcohol (600 mg, 3.7 mmol). The crude reaction mixture was purified by flash column chromatography (8-10% EtOAc in hexanes) to provide the title compound in 86% yield (982 mg) as a white solid. m.p. 40–41 °C. IR (neat, cm^{-1}) 2940, 1695, 1605, 1525, 1366, 1272, 1181, 1097, 946, 830, 751; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, J = 9.1 Hz, 2H), 6.67 (d, J = 9.1 Hz, 2H), 5.49 (t, J = 7.6 Hz, 1H), 4.81 (d, J = 6.9 Hz, 2H), 3.57 (t, J = 6.6 Hz, 2H), 3.06 (s, 6H), 2.11 (t, J = 7.5 Hz, 2H), 1.85 – 1.74 (m, 2H), 1.78 (s, 3H), 1.67 – 1.59 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.12, 153.36, 140.96, 131.37, 119.71, 117.33, 110.77, 61.16, 45.07, 40.16, 38.77, 32.18, 24.84, 16.46; HRMS (DART-TOF) calcd. for $C_{17}H_{24}ClNO_2$ $[M+H]^+$ *m/z* 310.1568, found 310.1562. Anal. Calcd. for $C_{17}H_{24}ClNO_2$: C, 65.90; H, 7.81. Found: C, 65.78; H, 7.71.

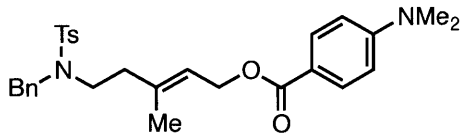
H, 7.46.



1c

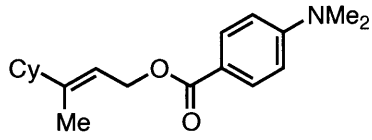
(*E*)-3-methyl-6-phenylhex-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1c**) Prepared following general procedure A from corresponding allylic alcohol (800 mg, 8.4 mmol). The crude reaction mixture was purified by flash column chromatography (8-10% EtOAc in hexanes) to provide the title compound in 82% yield (2.32 g) as a white solid. m.p. 47–48 °C. IR (neat, cm^{-1}) 2936, 1695, 1607, 1525, 1366, 1273, 1182, 1099, 750; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.03 – 7.82 (m, 2H), 7.33 – 7.19 (m, 2H), 7.19 – 7.04 (m, 3H), 6.69 – 6.45 (m, 2H), 5.57 – 5.35 (m, 1H), 4.79 (d, J = 6.9 Hz, 2H), 2.95 (s, 6H), 2.63 – 2.50 (m, 2H), 2.07 (t, J = 7.7 Hz, 2H), 1.81 – 1.64 (m, 2H), 1.73 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 166.97, 153.20, 142.32, 141.18, 131.23, 128.42, 128.25, 125.68, 119.39, 117.24, 110.64, 61.08, 39.95, 39.01, 35.40, 29.29, 16.44; HRMS (DART-TOF) calcd. for $C_{22}H_{27}NO_2$ $[M+H]^+$ *m/z* 338.2115, found 338.2121. Anal.

Calcd. for $C_{22}H_{27}NO_2$: C, 78.30; H, 8.06. Found: C, 78.16; H, 8.06.



1d

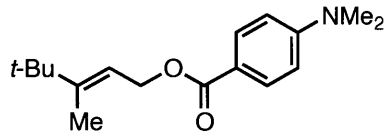
(*E*)-5-((*N*-benzyl-4-methylphenyl)sulfonamido)-3-methylpent-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1d)** Prepared following general procedure A from corresponding allylic alcohol (2.16 g, 6.0 mmol). The crude reaction mixture was purified by flash column chromatography (20-30% EtOAc in hexanes) to provide the title compound in 86% yield (2.62 g) as a white solid. m.p. 101–102 °C. IR (neat, cm^{-1}) 2921, 1695, 1605, 1525, 1365, 1336, 1273, 1181, 1156, 1098, 946, 770; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.91 (d, J = 9.1 Hz, 2H), 7.77 (d, J = 8.3 Hz, 2H), 7.41 – 7.24 (m, 7H), 6.65 (d, J = 9.1 Hz, 2H), 5.26 (t, J = 7.4 Hz, 1H), 4.69 (d, J = 6.8 Hz, 2H), 4.37 (s, 2H), 3.27 – 3.16 (m, 2H), 3.04 (s, 6H), 2.45 (s, 3H), 2.17 – 2.00 (m, 2H), 1.58 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 166.89, 153.30, 143.31, 137.74, 137.14, 136.33, 131.26, 129.77, 128.61, 128.41, 127.86, 127.19, 121.50, 117.03, 110.67, 60.77, 52.10, 46.45, 40.05, 38.25, 21.54, 16.33; HRMS (DART-TOF) calcd. for $C_{29}H_{34}N_2O_4S$ $[M+H]^+$ *m/z* 507.2312, found 507.2330. Anal. Calcd. for $C_{29}H_{34}N_2O_4S$: C, 68.75; H, 6.76. Found: C, 68.49; H, 6.82.



1e

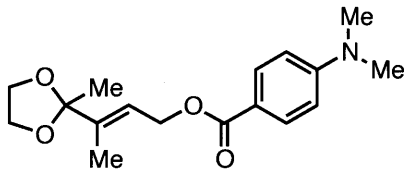
(*E*)-3-cyclohexylbut-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1e)** Prepared following general procedure A from corresponding allylic alcohol (1.90 g, 12.3 mmol). The crude reaction mixture was purified by flash column chromatography (8-10% EtOAc in hexanes) to provide the title compound in 77% yield (2.85 g) as a white solid. m.p. 63 °C. IR (neat, cm^{-1}) 2922, 2850, 1699, 1606, 1524, 1445, 1362, 1270, 1180, 1097, 946, 828, 768, 698; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.03 – 7.85 (m, 2H), 6.75 – 6.53 (m, 2H), 5.47 (tt, J = 6.7, 1.1 Hz, 1H), 4.82 (d, J = 6.8 Hz, 2H), 3.01 (s, 6H), 1.91 (t, J = 11.3 Hz, 1H), 1.84 – 1.64 (m, 8H), 1.40 – 1.11 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 166.96, 153.17, 146.25, 131.21, 117.30, 117.25, 110.60, 61.28, 47.17, 39.95, 31.66, 26.63, 26.33, 14.89; HRMS (DART-TOF) calcd. for $C_{19}H_{27}NO_2$ $[M+H]^+$ *m/z* 302.2115, found

302.2124. Anal. Calcd. for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03. Found: C, 75.63; H, 9.03.



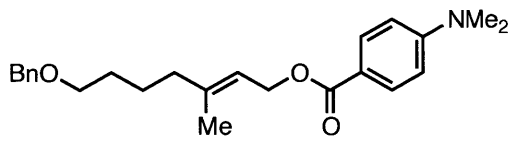
1f

(*E*)-3,4,4-trimethylpent-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1f**) Prepared following general procedure A from corresponding allylic alcohol (770 mg, 6.0 mmol). The crude reaction mixture was purified by flash column chromatography (8–10% EtOAc in hexanes) to provide the title compound in 73% yield (1.20 g) as a white solid. m.p. 45–46°C. IR (neat, cm^{-1}) 2963, 1700, 1607, 1526, 1362, 1273, 1181, 1102, 947, 770; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, J = 8.8 Hz, 2H), 6.65 (d, J = 7.4 Hz, 2H), 5.65 – 5.35 (m, 1H), 4.85 (d, J = 6.5 Hz, 2H), 3.02 (s, 6H), 1.76 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.03, 153.23, 148.48, 131.27, 117.31, 116.26, 110.66, 61.84, 40.01, 36.31, 28.85, 13.14; HRMS (DART-TOF) calcd. for $C_{17}H_{25}NO_2$ $[M+H]^+$ *m/z* 276.1958, found 276.1966.



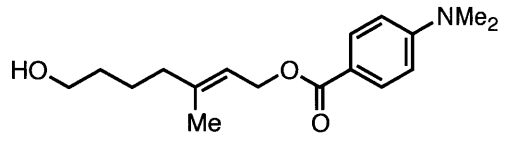
1g

(*E*)-3-(2-methyl-1,3-dioxolan-2-yl)but-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1g**) Prepared following general procedure A from corresponding allylic alcohol (3.16 g, 20 mmol). The crude reaction mixture was purified by flash column chromatography (10-20% EtOAc in hexanes) to provide the title compound in 82% yield (5.01 g) as a white solid. m.p. 92–93 °C. IR (neat, cm^{-1}) 1696, 1605, 1525, 1367, 1271, 1181, 1108, 1039, 944, 771; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, J = 9.0 Hz, 2H), 6.66 (d, J = 9.1 Hz, 2H), 6.00 – 5.85 (m, 1H), 4.85 (d, J = 6.5 Hz, 2H), 4.01 – 3.94 (m, 2H), 3.89 – 3.80 (m, 2H), 3.05 (s, 6H), 1.78 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 166.96, 153.41, 139.47, 131.40, 120.47, 117.15, 110.78, 109.46, 64.44, 61.11, 40.16, 23.91, 12.68; HRMS (DART-TOF) calcd. for $C_{17}H_{23}NO_4$ $[M+H]^+$ *m/z* 306.1700, found306.1707. Anal. Calcd. for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59. Found: C, 66.92;



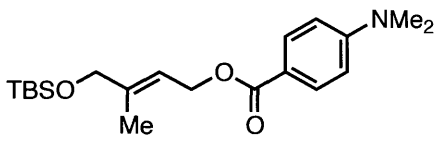
1h

(*E*)-7-(benzyloxy)-3-methylhept-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1h**) Prepared following general procedure A from corresponding allylic alcohol (2.10 g, 9.0 mmol). The crude reaction mixture was purified by flash column chromatography (8–10% EtOAc in hexanes) to provide the title compound in 84% yield (2.89 g) as a white solid. m.p. 36 °C. IR (neat, cm^{-1}) 2930, 1696, 1607, 1525, 1366, 1275, 1218, 1183, 1102, 947, 770; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.95 (d, J = 9.0 Hz, 2H), 7.37 (d, J = 4.4 Hz, 4H), 7.31 (q, J = 4.5 Hz, 1H), 6.73 – 6.60 (m, 2H), 5.49 (s, 1H), 4.82 (d, J = 6.8 Hz, 2H), 4.53 (s, 2H), 3.51 (t, J = 6.4 Hz, 2H), 3.06 (s, 6H), 2.10 (t, J = 7.4 Hz, 2H), 1.77 (s, 3H), 1.71 – 1.62 (m, 2H), 1.62 – 1.49 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 167.17, 153.34, 141.57, 138.77, 131.39, 128.47, 127.75, 127.60, 119.30, 117.41, 110.78, 72.99, 70.34, 61.28, 40.19, 39.43, 29.46, 24.31, 16.54; HRMS (DART-TOF) calcd. for $C_{24}H_{31}NO_3$ $[M+H]^+$ *m/z* 382.2377, found 382.2374. Anal. Calcd. for $C_{24}H_{31}NO_3$: C, 75.56; H, 8.19. Found: C, 75.49; H, 8.21.



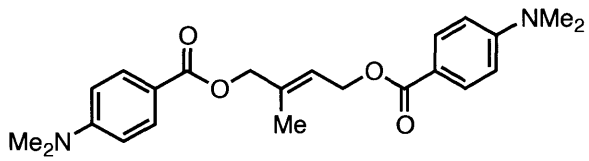
1i

(*E*)-7-hydroxy-3-methylhept-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1i**) Prepared following general procedure A from corresponding allylic alcohol (3.00 g, 7.84 mmol). The reaction was worked up with TBAF (12 mL, 1 M in THF, 1.5 equiv, remove the TBDPS group). The crude reaction mixture was purified by flash column chromatography (20–30% EtOAc in hexanes) to provide the title compound in 91% yield (1.70 g) as a colorless oil. IR (neat, cm^{-1}) 2932, 1697, 1603, 1525, 1444, 1366, 1270, 1180, 1097, 946, 828, 769, 698; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.93 (d, J = 8.9 Hz, 2H), 6.66 (d, J = 8.9 Hz, 2H), 5.49 (t, J = 6.9 Hz, 1H), 4.80 (d, J = 6.9 Hz, 2H), 3.67 (t, J = 6.1 Hz, 2H), 3.05 (s, 6H), 2.10 (t, J = 7.2 Hz, 2H), 1.77 (s, 3H), 1.67 – 1.44 (m, 5H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 167.20, 153.34, 141.45, 131.37, 119.34, 117.31, 110.76, 62.91, 61.27, 40.17, 39.32, 32.41, 23.81, 16.52; HRMS (DART-TOF) calcd. for $C_{17}H_{25}NO_3$ $[M+H]^+$ *m/z* 292.1907, found 292.1914.



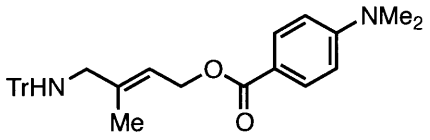
1j

(*E*)-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbut-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1j**) Prepared following general procedure A from corresponding allylic alcohol (9.95 g, 46.0 mmol). The crude reaction mixture was purified by flash column chromatography (8–10% EtOAc in hexanes) to provide the title compound in 89% yield (14.9 g) as a white solid. m.p. 118–119 °C. IR (neat, cm^{-1}) 2927, 2855, 1700, 1606, 1525, 1363, 1271, 1180, 1097, 1066, 947, 830, 769; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.94 (d, J = 9.1 Hz, 2H), 6.66 (d, J = 9.0 Hz, 2H), 5.85 – 5.70 (m, 1H), 4.86 (d, J = 6.9 Hz, 2H), 4.09 (s, 2H), 3.05 (s, 6H), 1.75 (s, 3H), 0.95 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.09, 153.36, 140.17, 131.39, 118.51, 117.36, 110.78, 67.82, 60.85, 40.17, 26.07, 18.54, 13.82, -5.18; HRMS (DART-TOF) calcd. for $C_{20}H_{33}NO_3Si$ $[M+H]^+$ *m/z* 364.2302, found 364.2305. Anal. Calcd. for $C_{20}H_{33}NO_3Si$: C, 66.07; H, 9.15. Found: C, 66.06; H, 9.13.



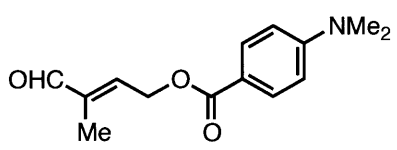
1k

(*E*)-2-methylbut-2-ene-1,4-diyl bis(4-(dimethylamino)benzoate) (Scheme 4, **1k**) Prepared following general procedure A from corresponding allylic alcohol (2.49 g, 10.0 mmol). The crude reaction mixture was purified by flash column chromatography (8–10% EtOAc in hexanes) to provide the title compound in 83% yield (3.29 g) as a white solid. m.p. 133–134 °C. IR (neat, cm^{-1}) 2885, 1692, 1605, 1523, 1364, 1269, 1179, 1095, 946, 825, 767; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.04 – 7.88 (m, 4H), 6.82 – 6.58 (m, 4H), 5.85 (t, J = 7.2 Hz, 1H), 4.89 (d, J = 6.7 Hz, 2H), 4.75 (s, 2H), 3.06 (d, J = 2.1 Hz, 12H), 1.88 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.04, 166.75, 153.51, 153.44, 136.15, 131.51, 131.47, 122.10, 117.13, 116.97, 110.85, 110.81, 68.54, 60.68, 40.20, 14.47; HRMS (DART-TOF) calcd. for $C_{23}H_{28}N_2O_4$ $[M+H]^+$ *m/z* 397.2122, found 397.2116. Anal. Calcd. for $C_{23}H_{28}N_2O_4$: C, 69.68; H, 7.12. Found: C, 69.38; H, 6.95.



1l

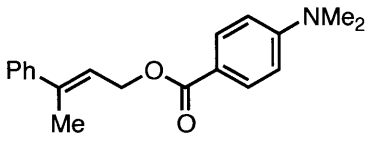
(*E*)-3-methyl-4-(tritylamino)but-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1l**) Prepared following general procedure A from corresponding allylic alcohol (3.43 g, 10.0 mmol). The crude reaction mixture was purified by flash column chromatography (8–10% EtOAc in hexanes) to provide the title compound in 84% yield (4.12 g) as a white solid. m.p. 58–59 °C. IR (neat, cm^{-1}) 1495, 1607, 1525, 1366, 1275, 1215, 1183, 1103, 947, 744; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.98 (d, J = 9.0 Hz, 2H), 7.63 – 7.51 (m, 6H), 7.40 – 7.30 (m, 6H), 7.27 – 7.19 (m, 3H), 6.74 – 6.63 (m, 2H), 5.91 (t, J = 6.3 Hz, 1H), 4.91 (d, J = 7.2 Hz, 2H), 3.07 (s, 6H), 2.74 (s, 2H), 1.85 (s, 3H), 1.69 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 167.15, 153.37, 146.17, 140.49, 131.41, 128.70, 127.95, 126.37, 119.14, 117.28, 110.78, 70.79, 61.11, 50.95, 40.18, 16.10; HRMS (DART-TOF) calcd. for $C_{33}H_{34}N_2O_2$ $[M+H]^+$ *m/z* 491.2693, found 491.2697. Anal. Calcd. for $C_{33}H_{34}N_2O_2$: C, 80.78; H, 6.99. Found: C, 80.56; H, 7.12.



1m

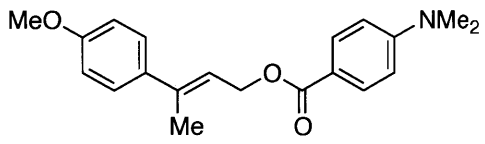
(*E*)-3-methyl-4-oxobut-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 4, **1m**) To a solution of **1j** (6.29 g, 17.3 mmol) in THF was added TBAF (15 mL, 1.5 equiv, 1.0 M in THF). After 4 h at rt, the crude reaction mixture was purified by flash column chromatography (10–30% EtOAc in hexanes) to provide **(*E*)-4-hydroxy-3-methylbut-2-en-1-yl 4-(dimethylamino)benzoate** in 83% yield (3.60 g) as a white solid. This allylic alcohol (3.60 g, 14.4 mmol) was then dissolved in CH_2Cl_2 (72 mL), and Dess-Martin periodinane (7.33 g, 17.3 mmol, 1.2 equiv) was added at rt. The resulting solution was stirred for 2 h at rt. The reaction mixture was diluted with ether and quenched with a saturated solution of Na_2SO_3 and $NaHCO_3$ (40 mL each). The reaction mixture was passed through a pad of celite. The combined organic phases were dried over anhydrous $MgSO_4$, concentrated, and purified by silica gel column chromatography to afford aldehyde **1m** (1.20 g, 34%) as a white solid. m.p. 132–133 °C. IR (neat, cm^{-1}) 1695, 1616, 1426, 1374, 1275, 1190, 1114, 1078, 769; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.50 (s, 1H), 7.95 (d, J = 9.1 Hz, 2H), 6.68 (d, J = 9.0 Hz, 2H), 6.67 – 6. 63 (m, 1H), 5.12 (dd, J = 5.8, 1.1 Hz, 1H), 3.08 (s, 6H), 1.87 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 194.41,

166.68, 153.68, 147.15, 140.28, 131.59, 116.14, 110.85, 60.82, 40.18, 9.69; HRMS (DART-TOF) calcd. for $C_{14}H_{17}NO_3$ $[M+H]^+$ *m/z* 248.1281, found 248.1283. Anal. Calcd. for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93. Found: C, 67.87; H, 6.98.



1n

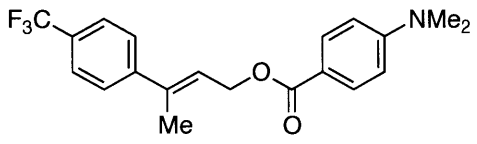
(*E*)-3-phenylbut-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 7, **1n**) Prepared following general procedure A from corresponding allylic alcohol (2.96 g, 20 mmol). The crude reaction mixture was purified by flash column chromatography (8–10% EtOAc in hexanes) to provide the title compound in 62% yield (3.69 g) as a white solid. m.p. 80–81 °C. IR (neat, cm^{-1}) 2920, 1697, 1605, 1525, 1367, 1272, 1180, 1097, 946, 757, 697; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.99 (d, *J* = 9.0 Hz, 2H), 7.57 – 7.44 (m, 2H), 7.44 – 7.35 (m, 2H), 7.35 – 7.24 (m, 1H), 6.68 (d, *J* = 9.0 Hz, 2H), 6.08 (t, *J* = 6.3 Hz, 1H), 5.03 (d, *J* = 6.7 Hz, 2H), 3.07 (s, 6H), 2.21 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 167.07, 153.39, 142.81, 139.59, 131.42, 128.35, 127.47, 125.95, 122.35, 117.11, 110.76, 61.60, 40.14, 16.37; HRMS (DART-TOF) calcd. for $C_{19}H_{21}NO_2$ $[M+H]^+$ *m/z* 296.1645, found 296.1631. Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.71. Found: C, 77.40; H, 7.11.



1o

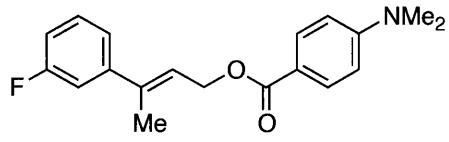
(*E*)-3-(4-methoxyphenyl)but-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 7, **1o**) Prepared following general procedure B from corresponding allylic alcohol (1.0 g, 5.7 mmol). The crude reaction mixture was purified by flash column chromatography (10–20% EtOAc in hexanes) followed by recrystallization from hexanes/EtOAc to provide the title compound in 76% yield (1.40 g) as a white solid. m.p. 91.6–92.5 °C. IR (neat, cm^{-1}) 2913, 1703, 1602, 1510, 1460, 1429, 1366, 1181, 1093, 1019, 829, 767; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.96 – 7.92 (dt, *J* = 8.8, 2.8 Hz, 2H), 7.40 – 7.37 (dt, *J* = 8.8, 3.2 Hz, 2H), 6.88 – 6.85 (dt, *J* = 12.0, 3.2 Hz, 2H), 6.68 – 6.64 (dt, *J* = 8.8, 3.2 Hz, 2H), 6.00 – 5.95 (tq, *J* = 6.8, 1.2 Hz, 1H), 4.98 – 4.96 (d, *J* = 13.2 Hz, 2H), 3.82 (s, 3H), 3.04 (m, 6H), 2.15 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 167.04, 159.11, 153.31, 139.05, 135.16, 131.36, 126.97, 120.56, 117.14, 113.63, 110.73, 61.60, 55.31, 40.08, 16.26;

HRMS (DART-TOF) calcd. for $C_{20}H_{23}NO_3$ $[M+H]^+$ *m/z* 326.1751, found 326.1760. Anal. Calcd. for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12. Found: C, 73.73; H, 7.12.



1p

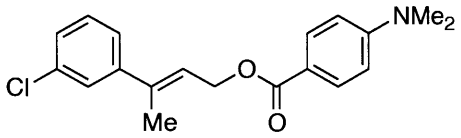
(*E*)-3-(4-(trifluoromethyl)phenyl)but-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 7, **1p**) Prepared following general procedure B from corresponding allylic alcohol (1.7 g, 7.8 mmol). The crude reaction mixture was purified by flash column chromatography (10% EtOAc in hexanes) followed by recrystallization from hexanes/EtOAc to provide the title compound in 53% yield (1.50 g) as a white solid. m.p. 102.7–103.6 °C. IR (neat, cm^{-1}) 1697, 1600, 1521, 1361, 1316, 1272, 1186, 1155, 1103, 1057, 828, 769; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.96 – 7.92 (dt, *J* = 9.2, 2.8 Hz, 2H), 7.59 – 7.57 (dt, *J* = 8.0, 0.8 Hz, 2H), 7.53 – 7.51 (dt, *J* = 8.0, 0.8 Hz, 2H), 6.69 – 6.65 (dt, *J* = 9.2, 2.8 Hz, 2H), 6.10 – 6.07 (tq, *J* = 5.8, 1.2 Hz, 1H), 3.05 (s, 6H), 2.18 – 2.18 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 170.00, 153.43, 146.35, 138.30, 131.49, 129.32 (q, *J* = 29.0 Hz), 126.3, 125.35, 124.6, 117.07 (q, *J* = 6.4 Hz), 110.90, 61.42, 40.25, 16.37; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5. HRMS (DART-TOF) calcd. for $C_{20}H_{20}F_3NO_2$ $[M+H]^+$ *m/z* 364.1519, found 364.1515. Anal. Calcd. for $C_{20}H_{20}F_3NO_2$: C, 66.11; H, 5.55. Found: C, 66.35; H, 5.50.



1q

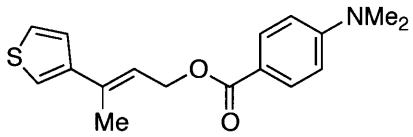
(*E*)-3-(3-fluorophenyl)but-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 7, **1q**) Prepared following general procedure B from corresponding allylic alcohol (768 mg, 4.6 mmol). The crude reaction mixture was purified by flash column chromatography (0–20% EtOAc in hexanes) followed by recrystallization from hexanes/EtOAc to provide the title compound in 91% yield (1.32 g) as a white solid. m.p. 90.0–91.0 °C. IR (neat, cm^{-1}) 2920, 1697, 1611, 1578, 1486, 1430, 1373, 1280, 1185, 1120, 1094, 947, 874, 767; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.98 – 7.96 (dt, *J* = 5.2, 1.6 Hz, 2H), 7.33 – 7.28 (m, 1H), 7.25 – 7.23 (m, 2H), 7.17 – 7.14 (m, 1H), 7.01 – 6.97 (m, 1H), 6.69 – 6.81 (d, *J* = 7.2 Hz, 2H), 6.10 – 6.08 (tq, *J* = 5.4, 1.8 Hz, 1H), 5.02 – 5.01 (d, *J* =

6.6 Hz, 2H), 3.07 (s, 6H), 2.18 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 167.02, 163.76 – 162.14 (d, J = 245 Hz), 153.41, 145.14 (d, J = 7.4 Hz), 138.37 (d, J = 2.3 Hz), 131.47, 129.80 (d, J = 8.5 Hz), 123.47, 121.61 (d, J = 2.9 Hz), 117.11, 114.30 (d, J = 21 Hz), 113.01 (d, J = 21 Hz), 110.87, 61.45, 40.22, 16.33; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.6. HRMS (DART-TOF) calcd. for $C_{19}H_{20}FNO_2$ $[M+H]^+$ *m/z* 314.1551, found 314.1552. Anal. Calcd. for $C_{19}H_{20}FNO_2$: C, 72.82; H, 6.43. Found: C, 72.99; H, 6.41.



1r

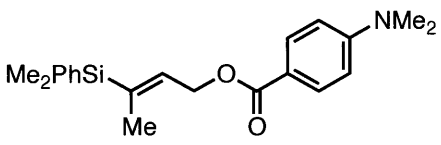
***(E)*-3-(3-chlorophenyl)but-2-en-1-yl 4-(dimethylamino)benzoate** (Scheme 7, **1r**) Prepared following general procedure B from corresponding allylic alcohol (3.6 mg, 19.6 mmol). The crude reaction mixture was purified by flash column chromatography (10–20% EtOAc in hexanes) followed by recrystallization from hexanes/EtOAc to provide the title compound in 42% yield (2.73 g) as a white solid. m.p. 56.9–57.4 °C. IR (neat, cm^{-1}) 1689, 1594, 1526, 1427, 1369, 1268, 1178, 1103, 898, 829, 768; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 – 7.93 (dt, J = 4.8, 2.0 Hz, 2H), 7.42 – 7.41 (m, 1H), 7.32 – 7.22 (m, 3H), 6.67 – 6.64 (dq, J = 9.2, 2.8 Hz, 2H), 6.06 – 6.02 (m, 1H), 4.99 – 4.97 (d, J = 6.8 Hz, 2H), 3.04 (s, 6H), 2.15 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 166.94, 153.36, 144.60, 138.19, 134.25, 131.40, 129.55, 127.40, 126.12, 124.08, 123.60, 116.95, 110.77, 61.36, 40.12, 16.26. HRMS (DART-TOF) calcd. for $C_{19}H_{20}ClNO_2$ $[M+H]^+$ *m/z* 330.1255, found 330.1253. Anal. Calcd. for $C_{19}H_{20}ClNO_2$: C, 69.19; H, 6.11. Found: C, 69.15; H, 6.09.



1s

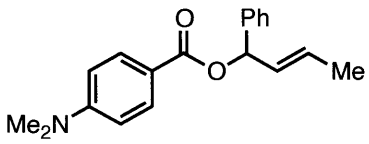
***(E)*-3-(thiophen-3-yl)but-2-en-1-yl 4-(dimethylamino)benzoate** (Scheme 7, **1s**) Prepared following general procedure B from corresponding allylic alcohol (616 mg, 4 mmol). The crude reaction mixture was purified by flash column chromatography (10–20% EtOAc in hexanes) followed by recrystallization from hexanes/EtOAc to provide the title compound in 83% yield (1.0 g) as a white solid. m.p. 88.4–89.2 °C. IR (neat, cm^{-1}) 2925, 1688, 1600, 1530, 1426, 1369, 1274, 1180, 1114, 972, 829, 768, 722, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 – 7.91 (dt, J = 8.8,

2.0 Hz, 2H), 7.09 – 7.07 (dd, J = 3.6, 1.2 Hz, 1H), 6.99 – 6.97 (dd, J = 5.2, 3.6 Hz, 1H), 6.66 – 6.63 (dq, J = 9.2, 2.8 Hz, 2H), 6.19 – 6.14 (tq, J = 6.0, 1.2 Hz, 1H), 4.97 – 4.95 (d, J = 8.0 Hz, 2H), 3.04 (s, 6H), 2.19 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 167.02, 153.39, 146.66, 133.67, 131.48, 127.45, 124.35, 123.66, 120.57, 117.18, 110.87, 61.12, 40.24, 16.31. HRMS (DART-TOF) calcd. for $C_{17}H_{19}NO_2S$ $[M+H]^+$ *m/z* 302.1209, found 302.1222. Anal. Calcd. for $C_{17}H_{19}NO_2S$: C, 67.74; H, 6.35. Found: C, 67.89; H, 6.44.



1t

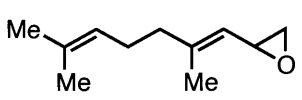
(*E*)-3-(dimethyl(phenyl)silyl)but-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 8, **1t**) Prepared following general procedure A from corresponding allylic alcohol[17] (1.45 g, 7.0 mmol). The crude reaction mixture was purified by flash column chromatography (10–15% EtOAc in hexanes) to provide the title compound in 82% yield (2.03 g) as a white solid. m.p. 61–62 °C. IR (neat, cm^{-1}) 2955, 1699, 1607, 1525, 1365, 1271, 1181, 1104, 947, 30, 815, 699; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (d, J = 9.0 Hz, 2H), 7.61 (dd, J = 6.3, 3.1 Hz, 2H), 7.50 – 7.35 (m, 3H), 6.71 (d, J = 9.1 Hz, 2H), 6.14 (ddt, J = 7.4, 5.6, 1.5 Hz, 1H), 5.02 (d, J = 5.8 Hz, 2H), 3.07 (s, 6H), 1.87 (s, 3H), 0.47 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 166.86, 153.28, 139.04, 137.72, 135.26, 133.98, 131.33, 129.05, 127.81, 117.04, 110.68, 61.32, 39.99, 15.31, -3.59; HRMS (DART-TOF) calcd. for $C_{21}H_{27}NO_2Si$ $[M+H]^+$ *m/z* 354.1884, found 354.1877. Anal. Calcd. for $C_{21}H_{27}NO_2Si$: C, 71.35; H, 7.70. Found: C, 71.07; H, 7.70.



1u

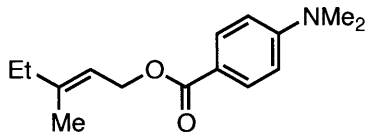
(*E*)-1-phenylbut-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 9, **1u**) Prepared following general procedure A from corresponding allylic alcohol (2.22 g, 15.0 mmol). The crude reaction mixture was purified by flash column chromatography (8–10% EtOAc in hexanes) to provide the title compound in 83% yield (3.68 g) as a white solid. m.p. 85 °C. IR (neat, cm^{-1}) 2900, 1695, 1605, 1525, 1446, 1367, 1317, 1267, 1178, 1095, 963, 828, 768, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, J = 9.0 Hz, 2H), 7.49 – 7.41 (m, 2H), 7.41 – 7.34 (m, 2H), 7.34 – 7.27 (m, 1H), 6.68 (d, J = 8.9 Hz, 2H), 6.47 (d, J = 6.2 Hz, 1H),

5.95 – 5.70 (m, 2H), 3.06 (s, 6H), 1.76 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 166.09, 153.49, 140.61, 131.55, 130.29, 129.16, 128.55, 127.77, 126.90, 117.38, 110.83, 75.91, 40.21, 17.95; HRMS (DART-TOF) calcd. for $C_{19}H_{21}NO_2$ $[M+H]^+$ *m/z* 296.1645, found 296.1638. Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17. Found: C, 77.19; H, 7.13.



1v

(*E*)-2-(2,6-dimethylhepta-1,5-dien-1-yl)oxirane (Scheme 11, **1v**) Prepared following the literature procedure.[18] The compound was characterized to ensure the (*E*)-olefin geometry is unchanged during the oxidation. IR (neat, cm^{-1}) 2968, 2913, 2855, 1445, 1377, 1251, 1106, 938, 872, 835, 772; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.08 (t, J = 6.8 Hz, 1H), 4.82 (d, J = 8.8 Hz, 1H), 3.57 (ddd, J = 8.7, 3.9, 2.9 Hz, 1H), 3.03 – 2.93 (m, 1H), 2.65 (dd, J = 5.2, 2.7 Hz, 1H), 2.16 – 2.07 (m, 2H), 2.07 – 1.99 (m, 2H), 1.82 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 144.08, 132.02, 123.81, 122.07, 49.13, 49.08, 39.78, 26.36, 25.80, 17.82, 16.86.

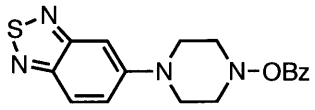


1w

(*E*)-3-methylpent-2-en-1-yl 4-(dimethylamino)benzoate (Scheme 12, **1w**) Prepared following general procedure A from corresponding allylic alcohol (1.45 g, 7.0 mmol). The crude reaction mixture was purified by flash column chromatography (10–15% EtOAc in hexanes) to provide the title compound in 82% yield (2.03 g) as a white solid. m.p. 32–33 °C. IR (neat, cm^{-1}) 2964, 1697, 1604, 1524, 1365, 1269, 1179, 1095, 946, 828, 769; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (d, J = 9.0 Hz, 2H), 6.66 (d, J = 8.8 Hz, 2H), 5.60 – 5.40 (m, 1H), 4.82 (d, J = 7.0 Hz, 2H), 3.05 (s, 6H), 2.09 (q, J = 7.5 Hz, 2H), 1.78 (s, 3H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 167.17, 153.33, 143.36, 131.35, 117.89, 117.49, 110.73, 61.35, 40.22, 32.36, 16.61, 12.37; HRMS (DART-TOF) calcd. for $C_{15}H_{21}NO_2$ $[M+H]^+$ *m/z* 248.1645, found 248.1641. Anal. Calcd. for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56. Found: C, 72.57; H, 8.58.

D) Preparation of *O*-Benzoyl Hydroxylamines

***O*-Benzoyl hydroxylamines** were synthesized according to the literature procedure.[1,2,19] All of the *O*-benzoyl hydroxylamines used are known compounds except for **2g**.



2g

4-(benzo[*c*][1,2,5]thiadiazol-5-yl)piperazin-1-yl benzoate (Scheme 8, **2g**). To a solution of benzoyl peroxide (5.33 g, 22 mmol, 1.1 equiv) and K_2HPO_4 (6.96 g, 40 mmol, 2.0 equiv) in DMF (50 mL) was added 5-(piperazin-1-yl)benzo[*c*][1,2,5]thiadiazole (4.41 g, 20 mmol, 1.0 equiv). The reaction mixture was stirred at rt overnight and then diluted with EtOAc and H_2O. The aqueous layer was extracted with EtOAc (2x), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude material was purified by flash column chromatography (10–100% EtOAc in hexanes) to provide the title compound as a white solid in 73% yield (4.97 g), m.p. 128–129 °C. IR (neat, cm^{-1}) 2825, 1733, 1609, 1450, 1242, 1083, 1022, 812, 748, 706; ^1H NMR (600 MHz, $CDCl_3$) δ: 8.02 (d, J = 7.2 Hz, 2H), 7.82 (d, J = 9.6 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.48 – 7.42 (m, 3H), 7.15 (s, 1H), 3.85 – 3.56 (m, 4H), 3.45 – 3.14 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 164.67, 156.42, 151.46, 150.94, 133.38, 129.54, 129.07, 128.58, 124.73, 121.40, 102.03, 55.58, 47.55. HRMS (DART-TOF) calcd. for $C_{10}H_{11}N_4S$ $[M–OBz]^+$ *m/z* 219.0699, found 219.0686. Anal. Calcd. for $C_{17}H_{16}N_4O_2S$: C, 59.98; H, 4.74, Found: C, 60.25; H, 4.78.

4.5 References and Notes

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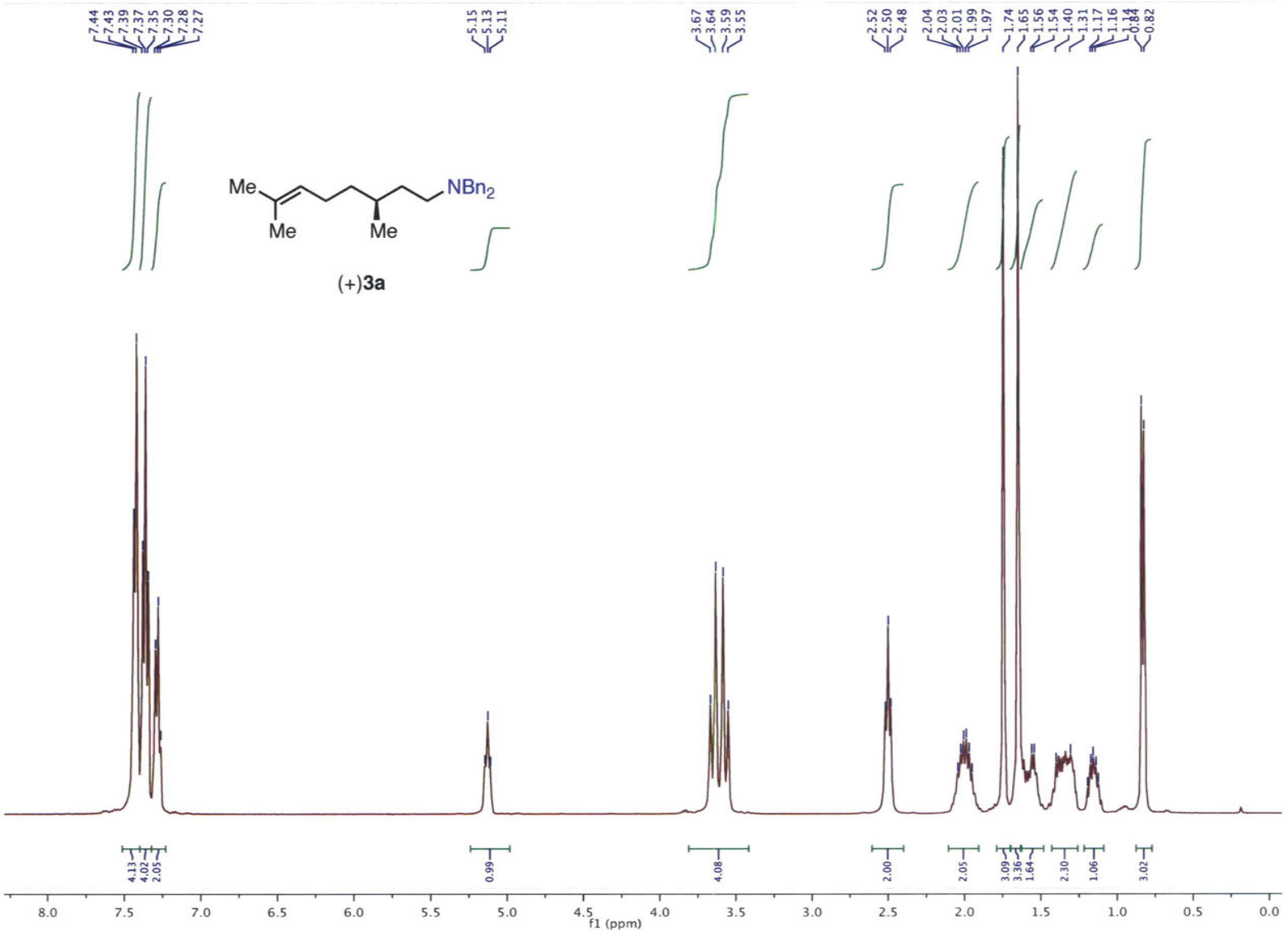
4.6 ^{1}H, ^{13}C, and ^{19}F NMR Spectra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2.01
1.99
1.97
1.74
1.65
1.56
1.54
1.40
1.31
1.17
1.16
0.84
0.82
Me
Me
Me
NBn2
(+)3a
4.13
4.02
2.05
0.99
4.08
2.00
2.05
3.09
3.36
1.64
2.30
1.06
3.02
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.5
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1.0
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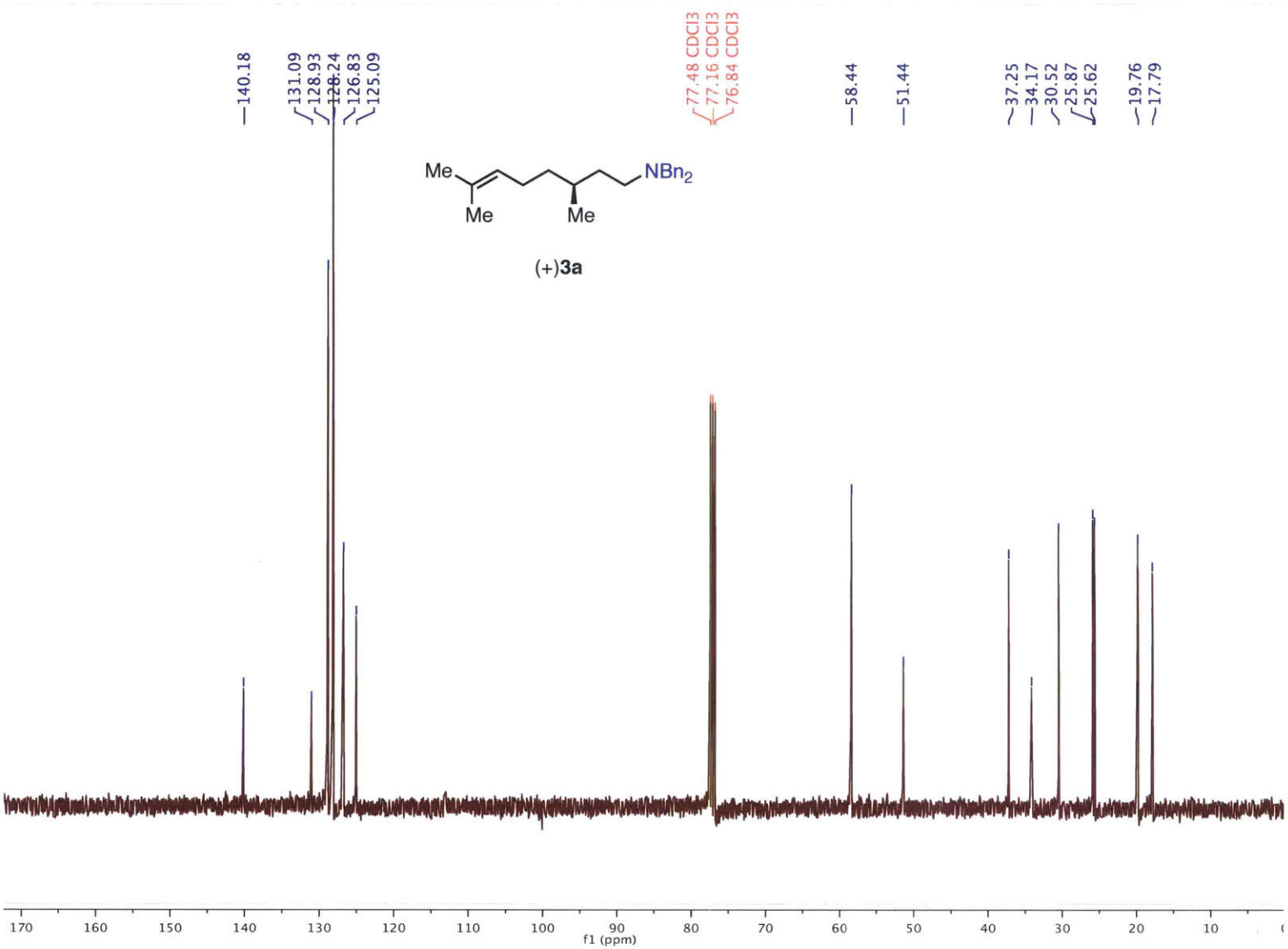
f1 (ppm)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128.24
126.83
125.09
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77.16 CDCl3
76.84 CDCl3
58.44
51.44
37.25
34.17
30.52
25.87
25.62
19.76
17.79
Me
Me
Me
NBn2
(+)3a
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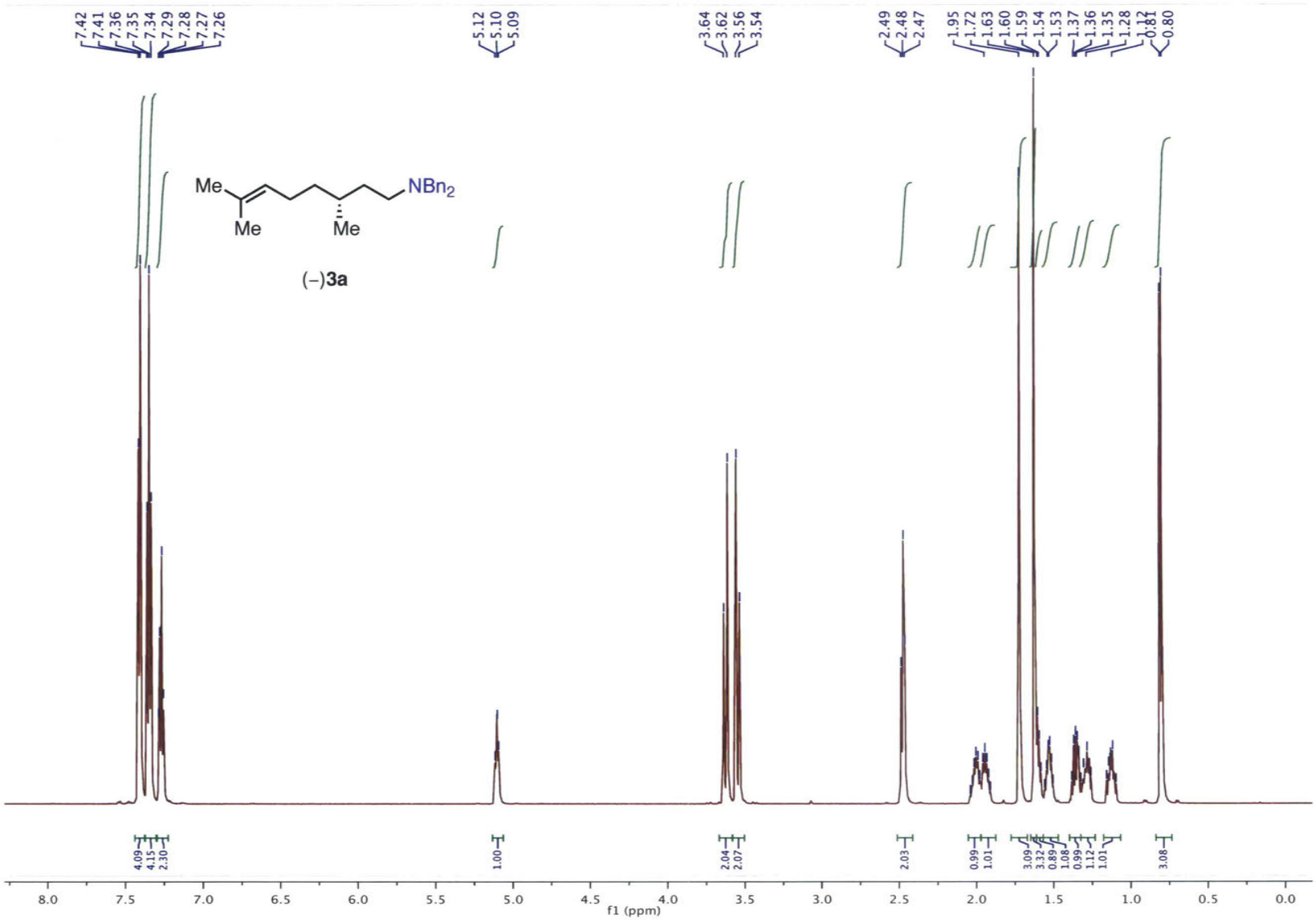
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.26
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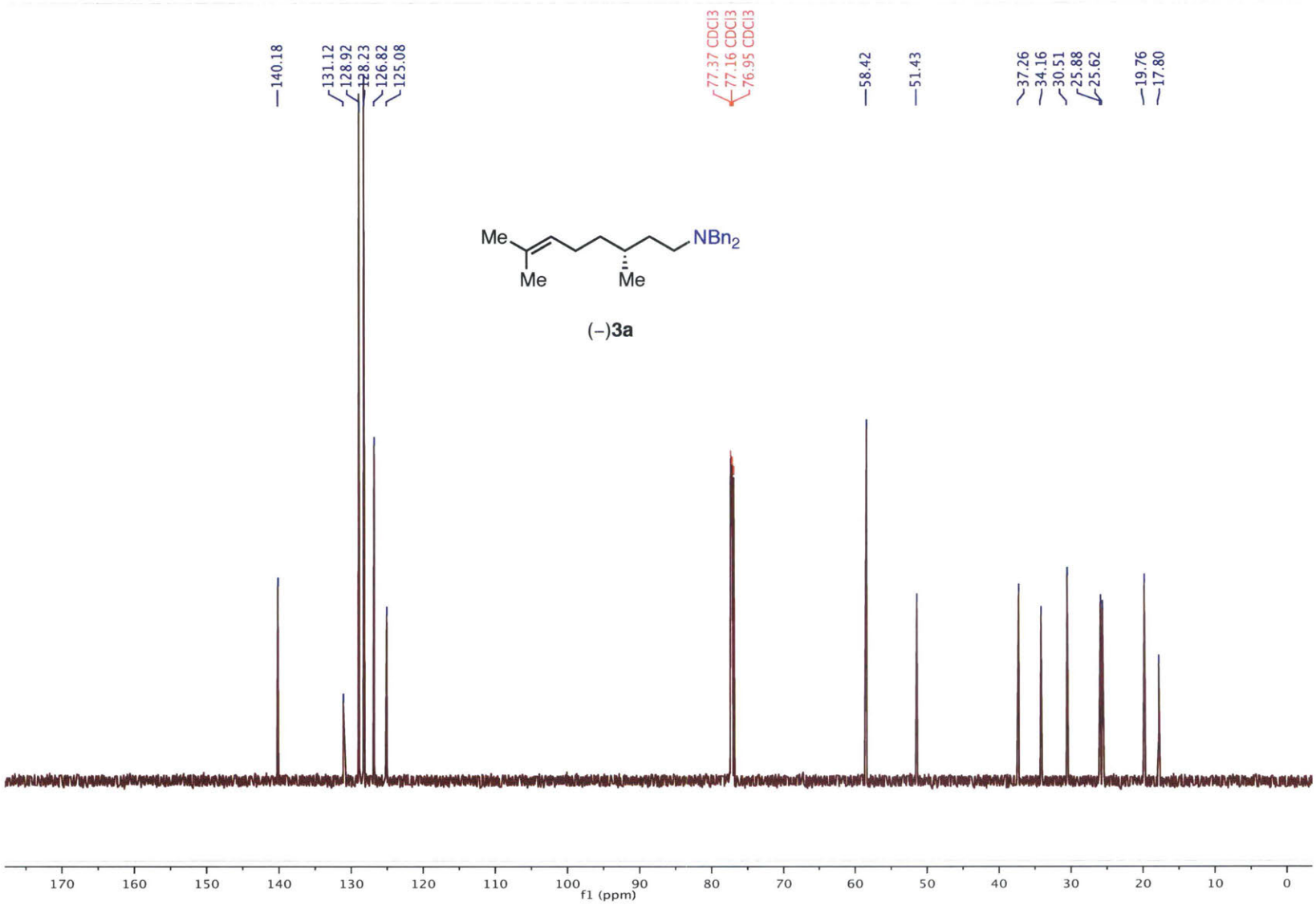
5.10
5.09
3.64
3.62
3.56
3.54
2.49
2.48
2.47
1.95
1.72
1.63
1.60
1.59
1.54
1.53
1.37
1.36
1.35
1.28
1.12
0.81
0.80
Me
Me
Me
NBn2
(–)3a
4.09
4.15
2.30
1.00
2.04
2.07
2.03
0.99
1.01
3.09
3.32
0.89
1.08
0.99
1.12
1.01
3.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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126.82
125.08
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77.16 CDCl3
76.95 CDCl3
58.42
51.43
37.26
34.16
30.51
25.88
25.62
19.76
17.80
Me
Me
Me
NBn2
(–)3a
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160
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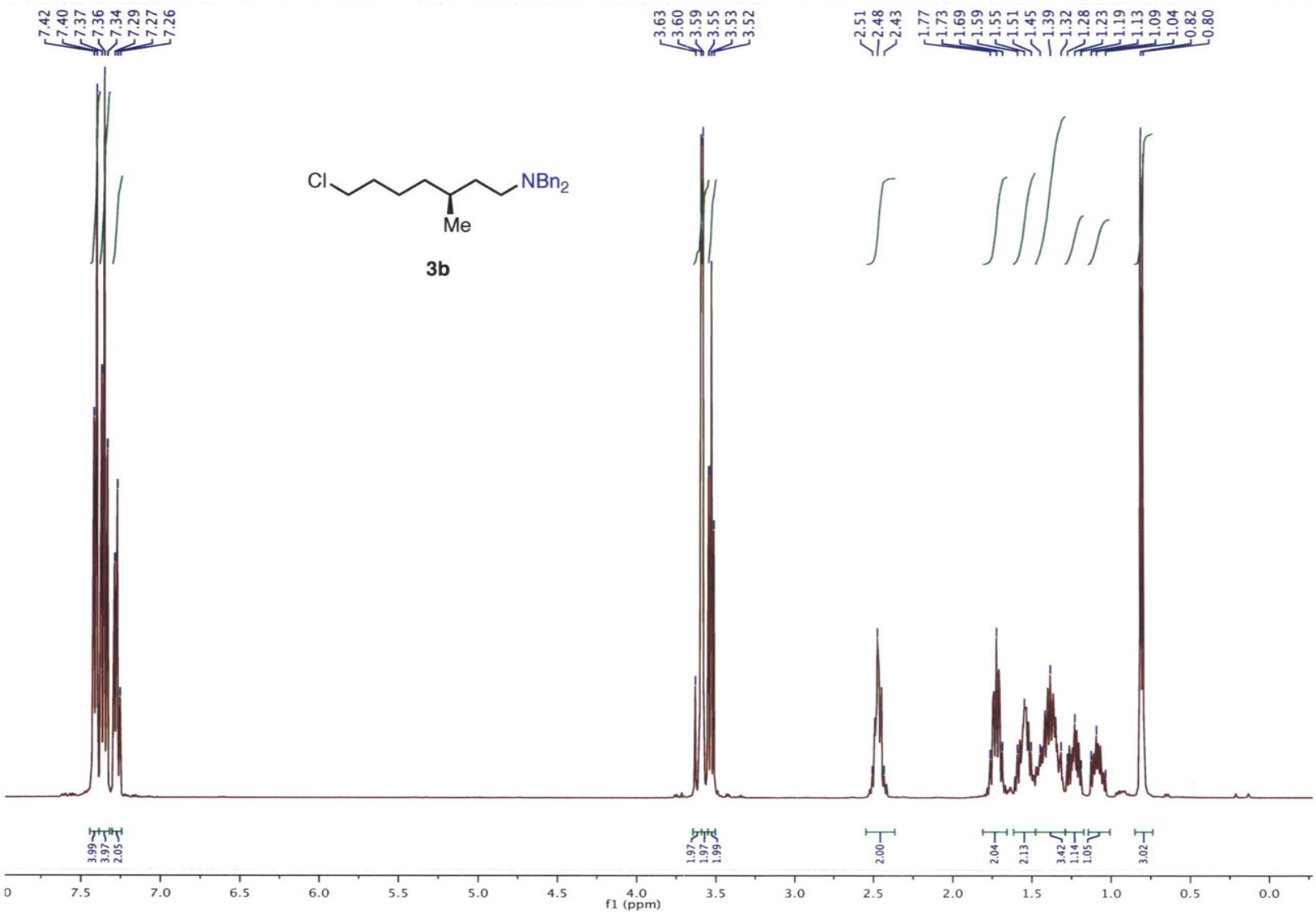
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.37
7.36
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7.29
7.27
7.26
3.63
3.60
3.59
3.55
3.53
3.52
2.51
2.48
2.43
1.77
1.73
1.69
1.59
1.55
1.51
1.45
1.39
1.32
1.28
1.23
1.19
1.13
1.09
1.04
0.82
0.80
Cl
NBn2
Me
3b
3.99
3.97
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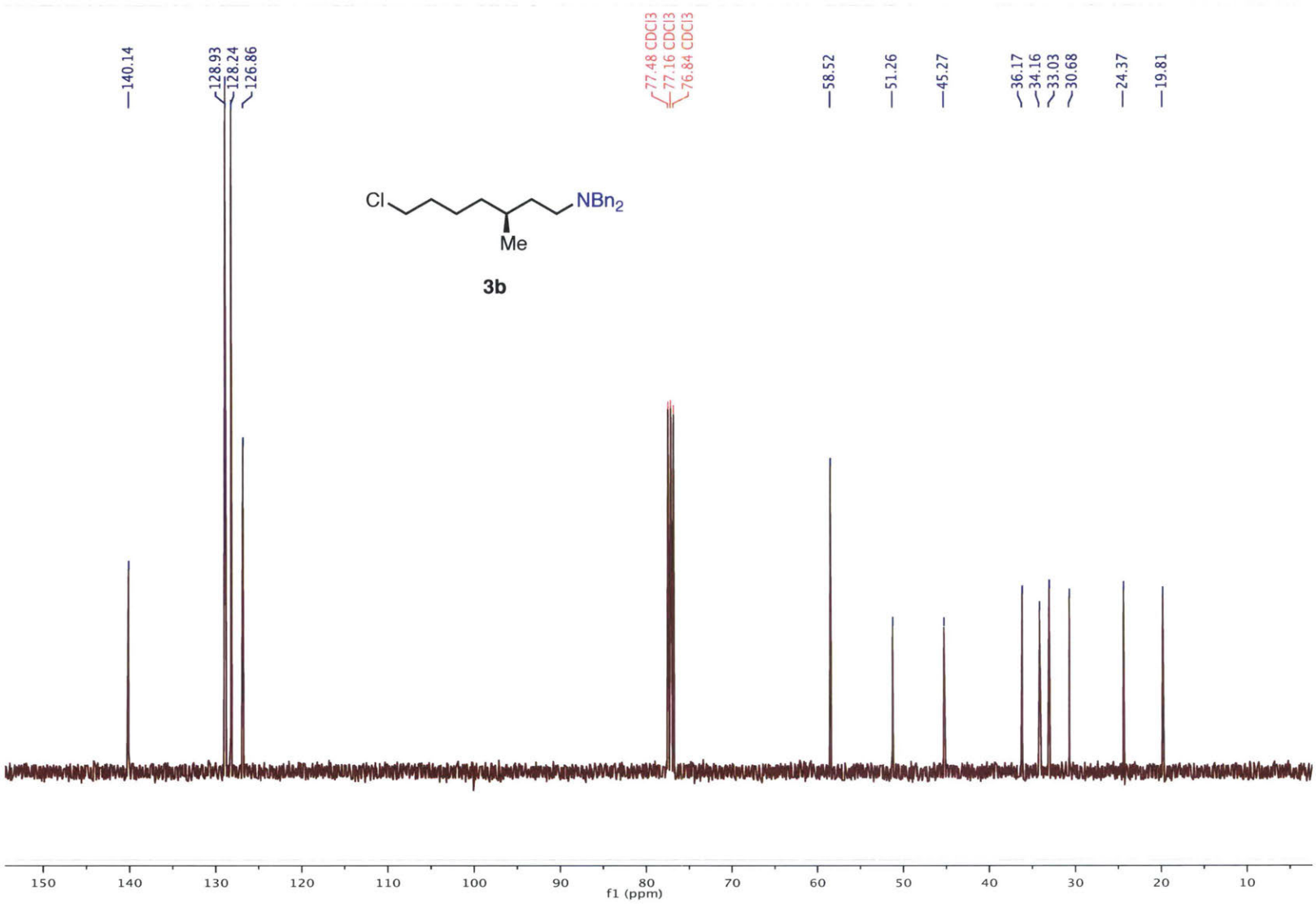
1.97
1.97
1.99
2.00
2.04
2.13
3.42
1.14
1.05
3.02
f1 (ppm)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128.93
128.24
126.86
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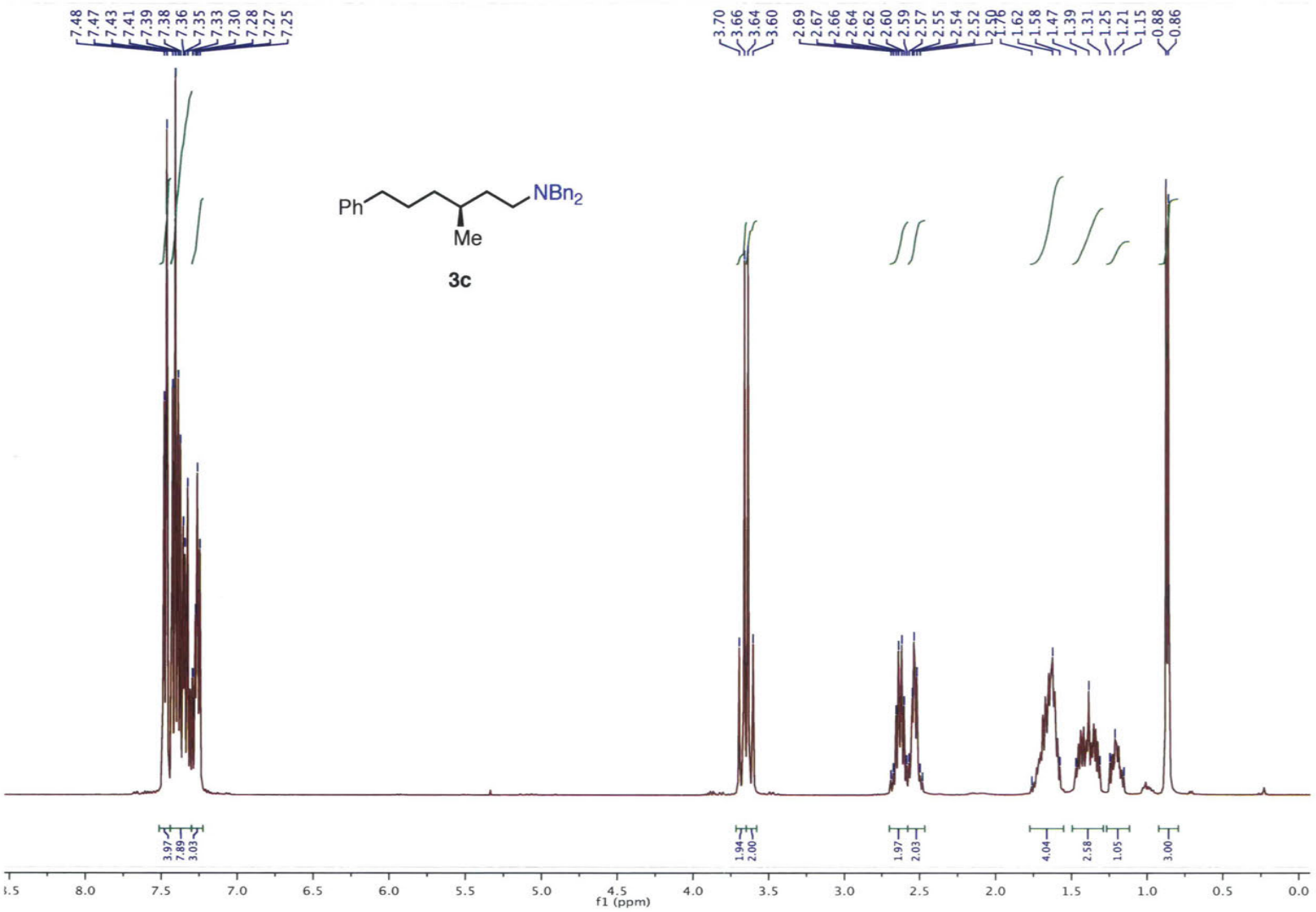
77.16 CDCl3
76.84 CDCl3
58.52
51.26
45.27
36.17
34.16
33.03
30.68
24.37
19.81
Cl
NBn2
Me
3b
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.47
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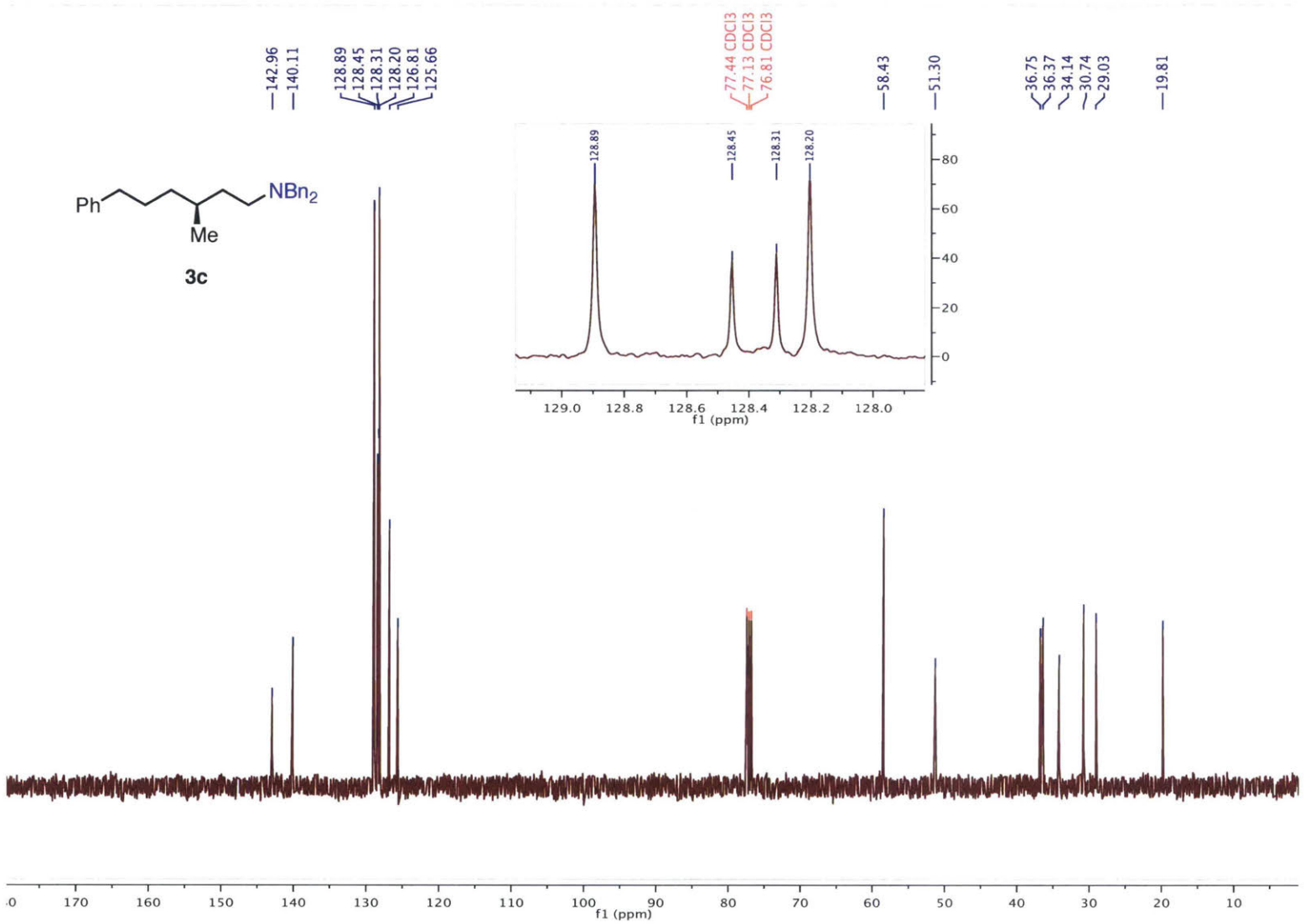
7.38
7.36
7.35
7.33
7.30
7.28
7.27
7.25
3.70
3.66
3.64
3.60
2.69
2.67
2.66
2.64
2.62
2.60
2.59
2.57
2.55
2.54
2.52
1.62
1.58
1.47
1.39
1.31
1.25
1.21
1.15
0.88
0.86
Ph
NBn2
Me
3c
3.97
7.89
3.03
1.94
2.00
1.97
2.03
4.04
2.58
1.05
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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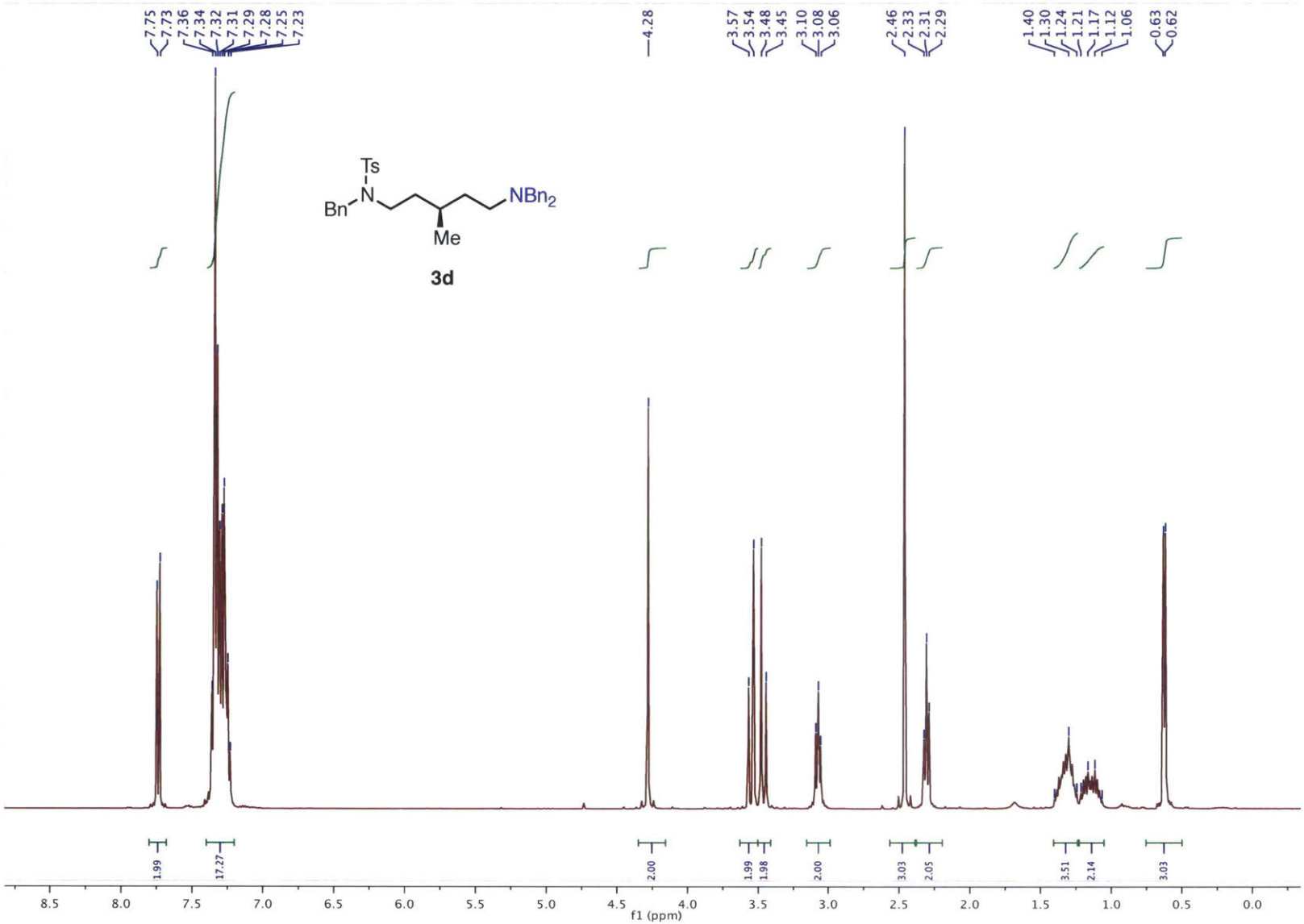
140.11
128.89
128.45
128.31
128.20
126.81
125.66
77.44 CDCl3
77.13 CDCl3
76.81 CDCl3
58.43
51.30
36.75
36.37
34.14
30.74
29.03
19.81
Ph
NBn2
Me
3c
f1 (ppm)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7.73
7.36
7.34
7.32
7.31
7.29
7.28
7.25
7.23
4.28
3.57
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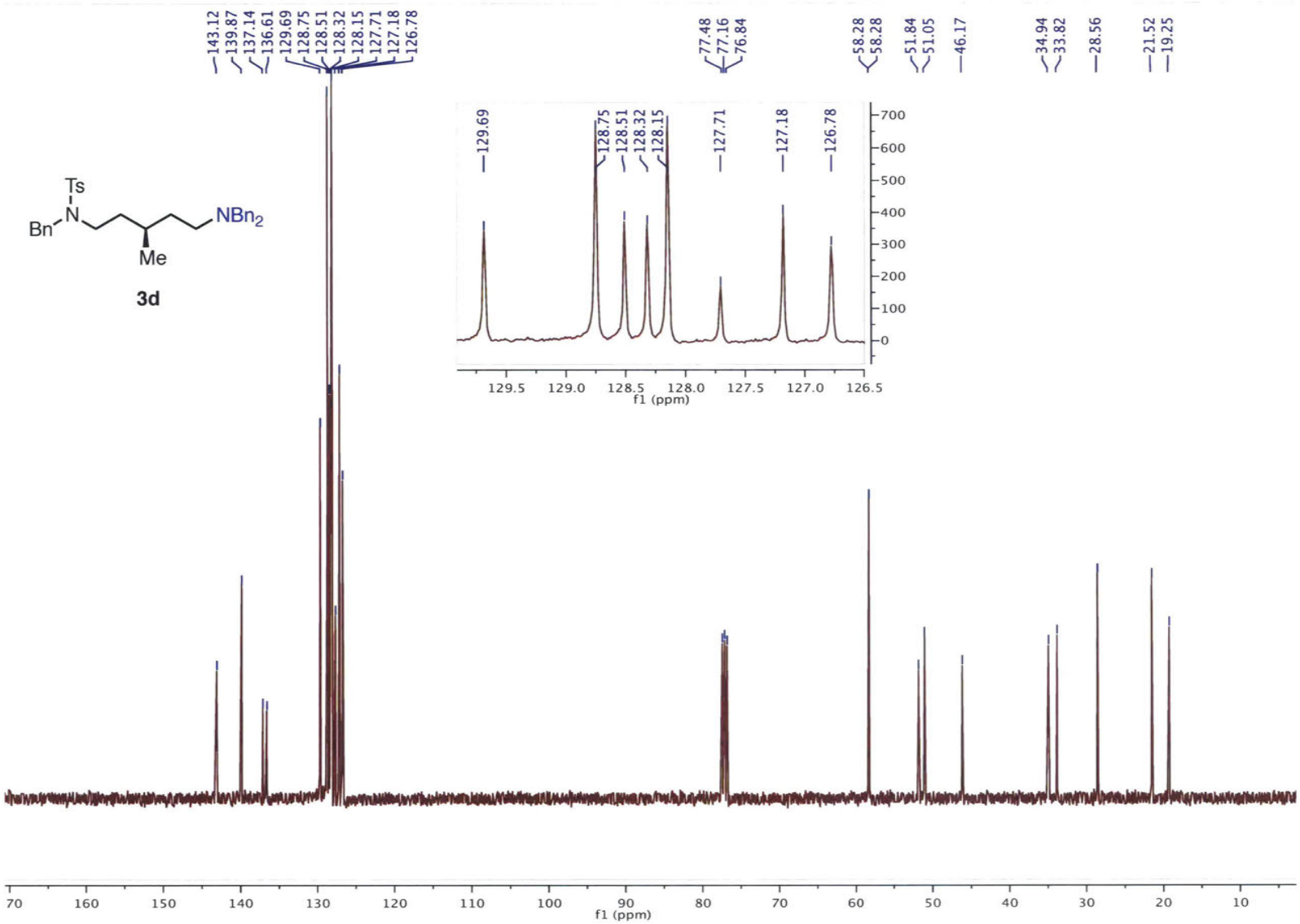
3.48
3.45
3.10
3.08
3.06
2.46
2.33
2.31
2.29
1.40
1.30
1.24
1.21
1.17
1.12
1.06
0.63
0.62
Ts
N
Bn
NBn2
Me
3d
1.99
17.27
2.00
1.99
1.98
2.00
3.03
2.05
3.51
2.14
3.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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139.87
137.14
136.61
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128.75
128.51
128.32
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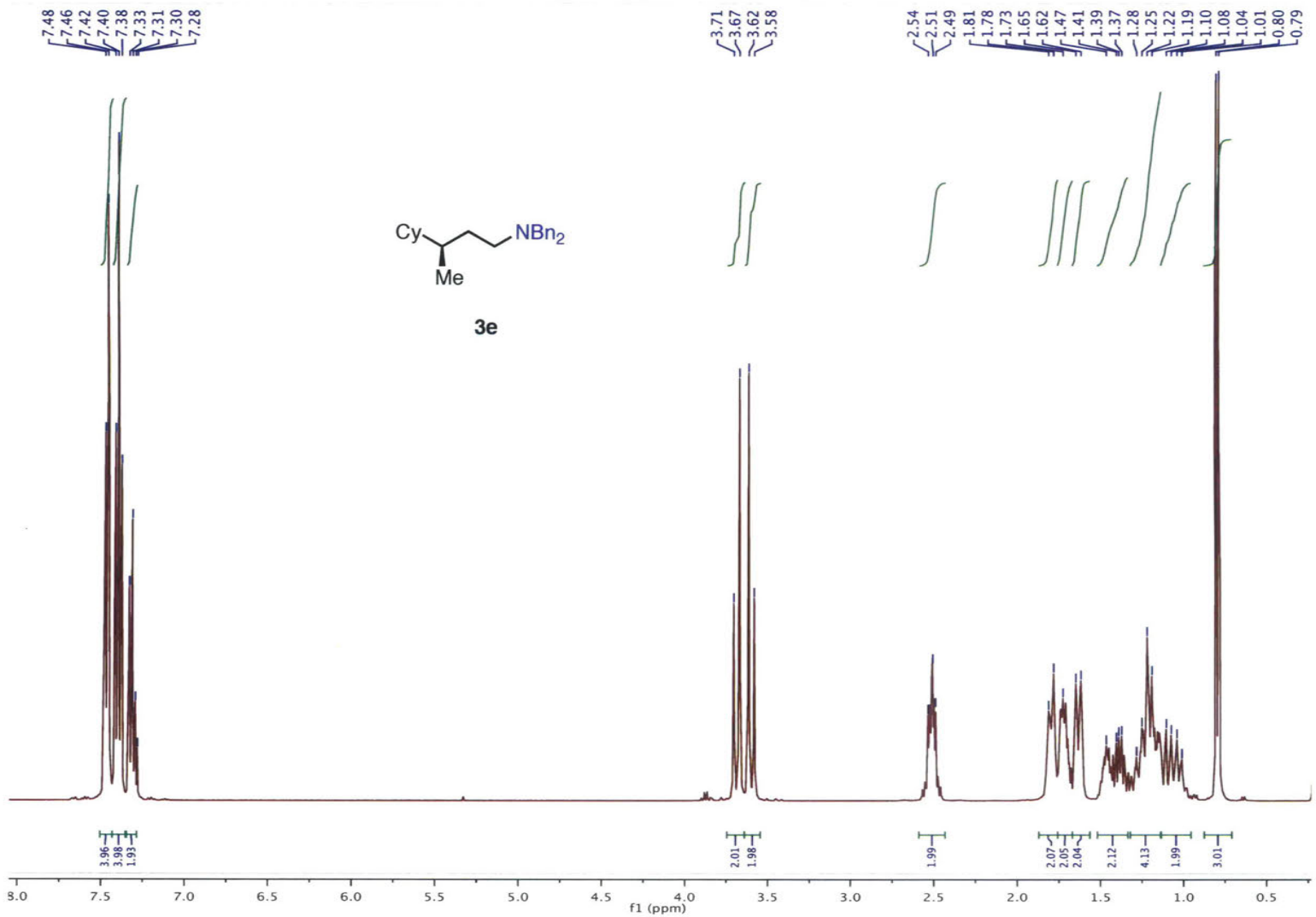
127.71
127.18
126.78
77.48
77.16
76.84
58.28
58.28
51.84
51.05
46.17
34.94
33.82
28.56
21.52
19.25
Ts
N
Bn
NBn2
Me
3d
f1 (ppm)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7.40
7.38
7.33
7.31
7.30
7.28
3.71
3.67
3.62
3.58
2.54
2.51
2.49
1.81
1.78
1.73
1.65
1.62
1.47
1.41
1.39
1.37
1.28
1.25
1.22
1.19
1.10
1.08
1.04
1.01
0.80
0.79
Cy
NBn2
Me
3e
3.96
3.98
1.93
2.01
1.98
1.99
2.07
2.05
2.04
2.12
4.13
1.99
3.01
8.0
7.5
7.0
6.5
6.0
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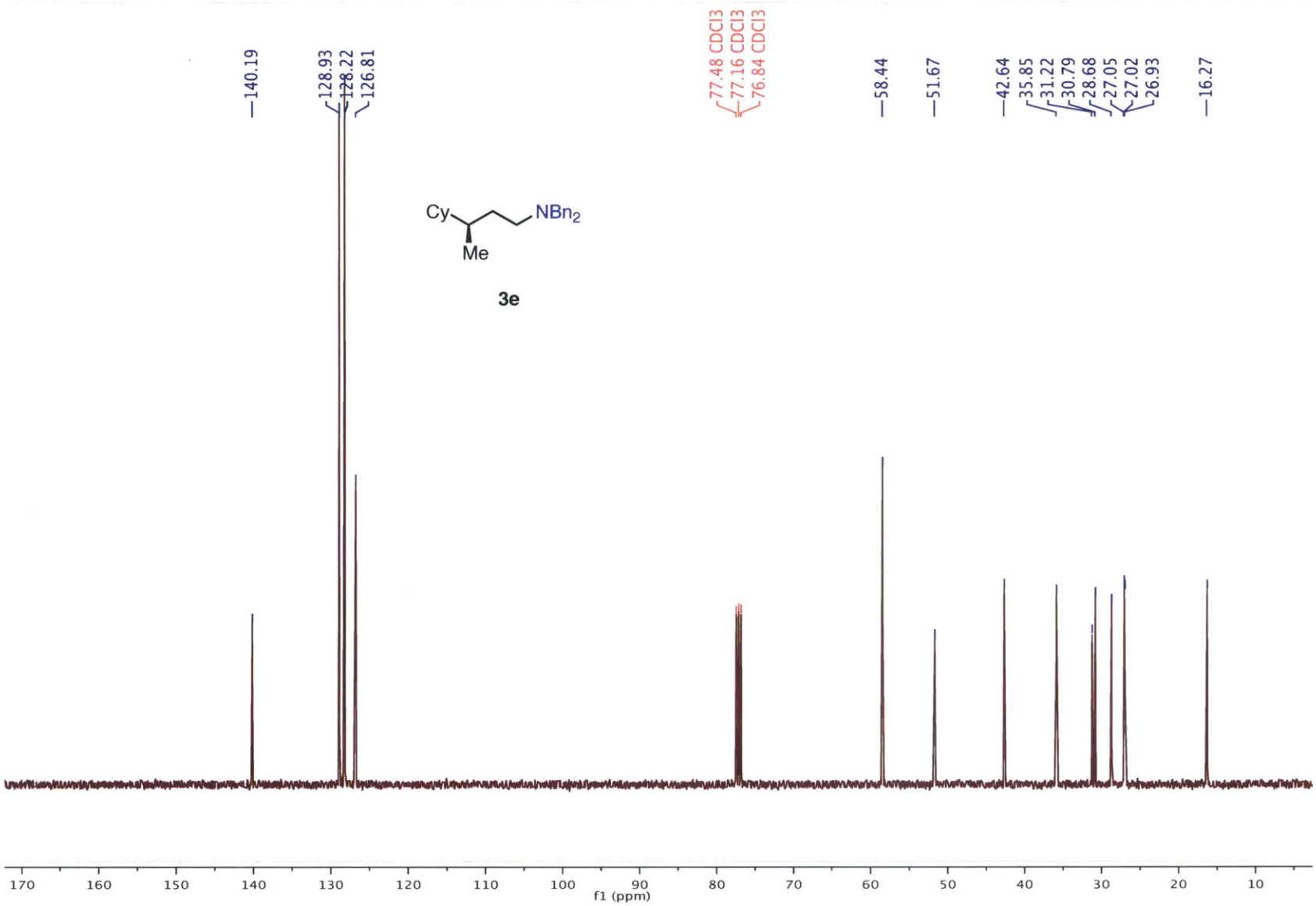
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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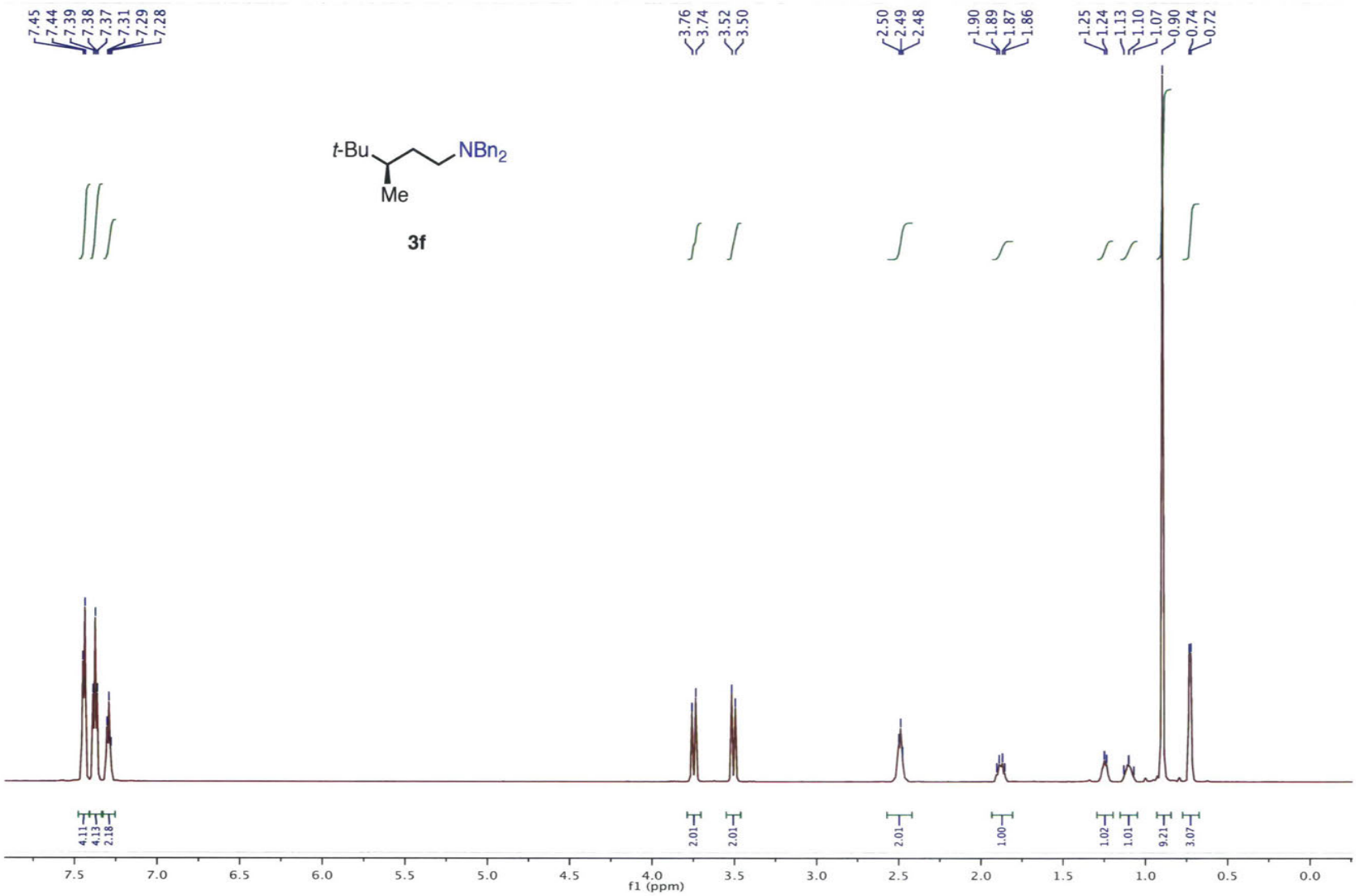
128.93
128.22
126.81
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
58.44
51.67
42.64
35.85
31.22
30.79
28.68
27.05
27.02
26.93
16.27
Cy
NBn2
Me
3e
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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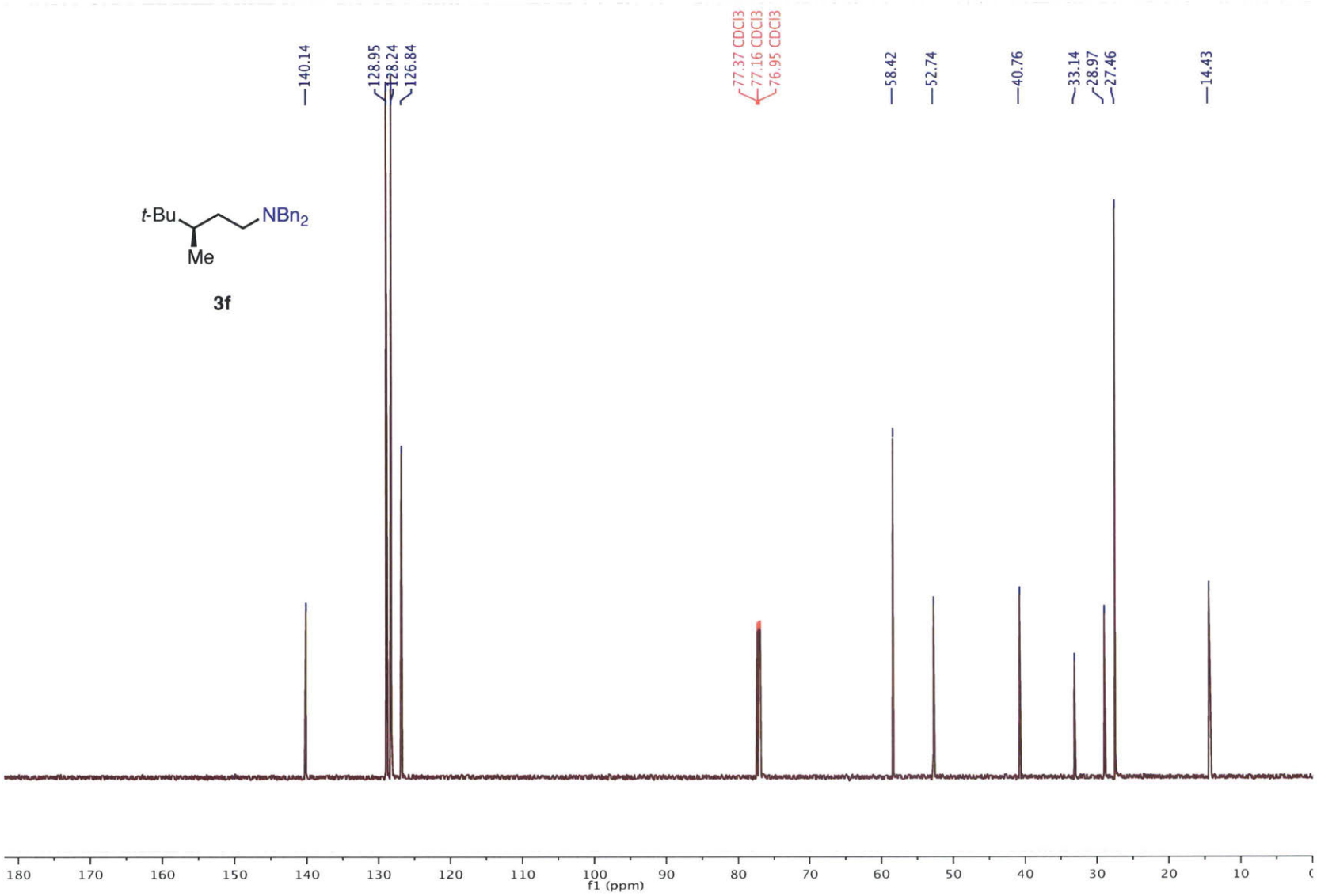
7.31
7.29
7.28
3.76
3.74
3.52
3.50
2.50
2.49
2.48
1.90
1.89
1.87
1.86
1.25
1.24
1.13
1.10
1.07
0.90
0.74
0.72
t-Bu
NBn2
Me
3f
4.11
4.13
2.18
2.01
2.01
2.01
1.00
1.02
1.01
9.21
3.07
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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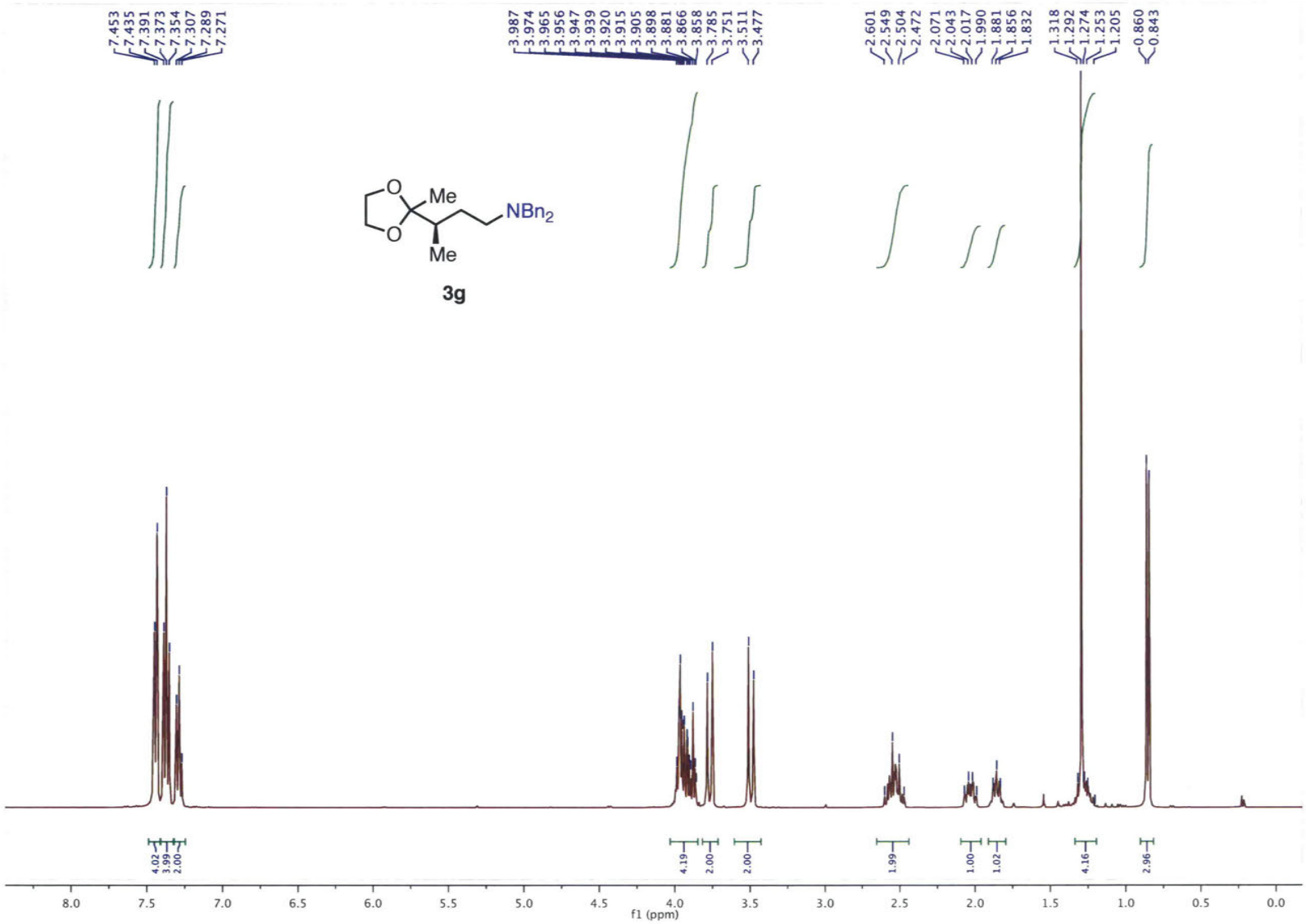
128.24
126.84
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
58.42
52.74
40.76
33.14
28.97
27.46
14.43
t-Bu
NBn2
Me
3f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.271
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3.956
3.947
3.939
3.920
3.915
3.905
3.898
3.881
3.866
3.858
3.785
3.751
3.511
3.477
2.601
2.549
2.504
2.472
2.071
2.043
2.017
1.990
1.881
1.856
1.832
1.318
1.292
1.274
1.253
1.205
0.860
0.843
Me
NBn2
Me
3g
4.02
3.99
2.00
4.19
2.00
2.00
1.99
1.00
1.02
4.16
2.96
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
2.5
2.0
1.5
1.0
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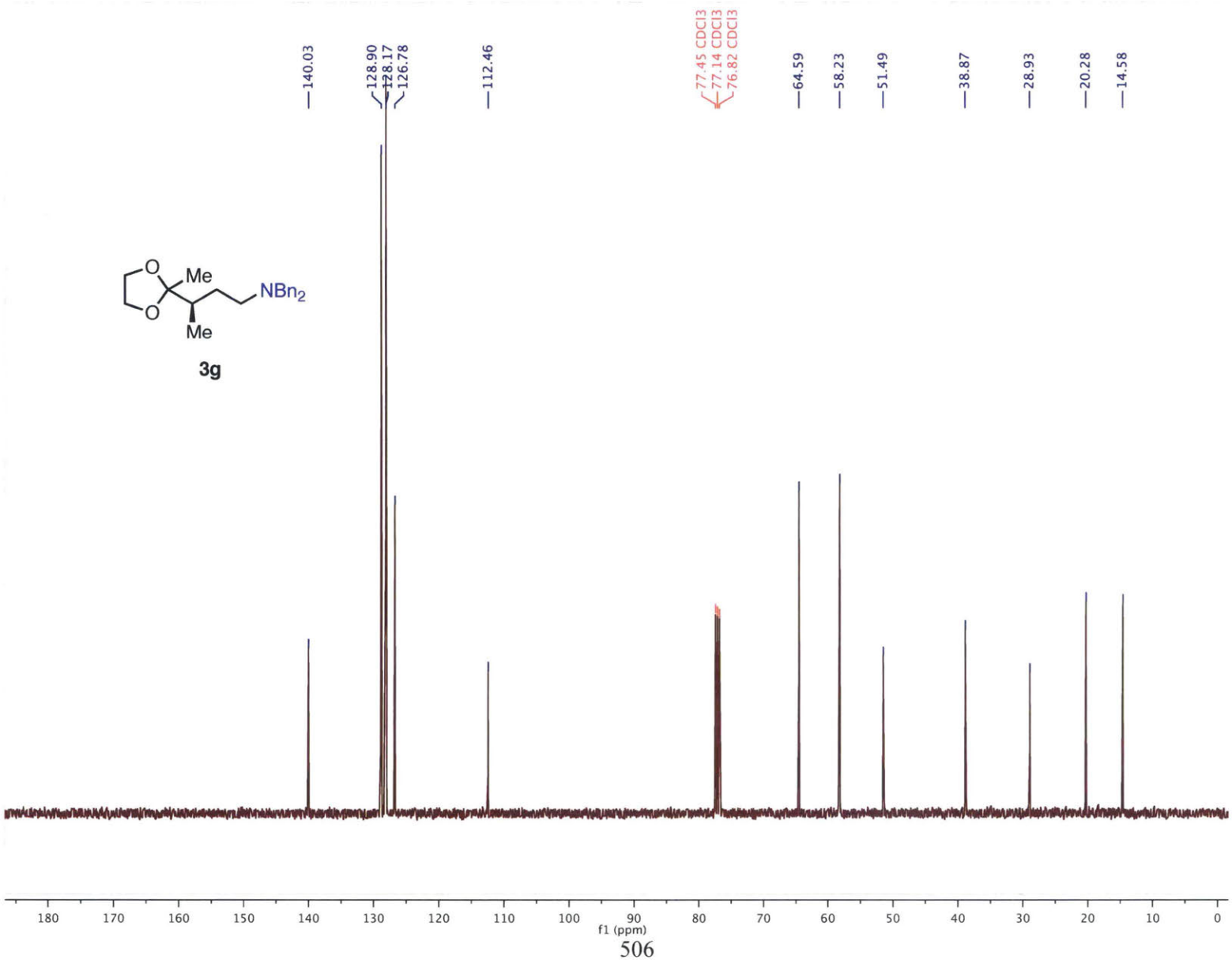
0.0
f1 (ppm)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112.46
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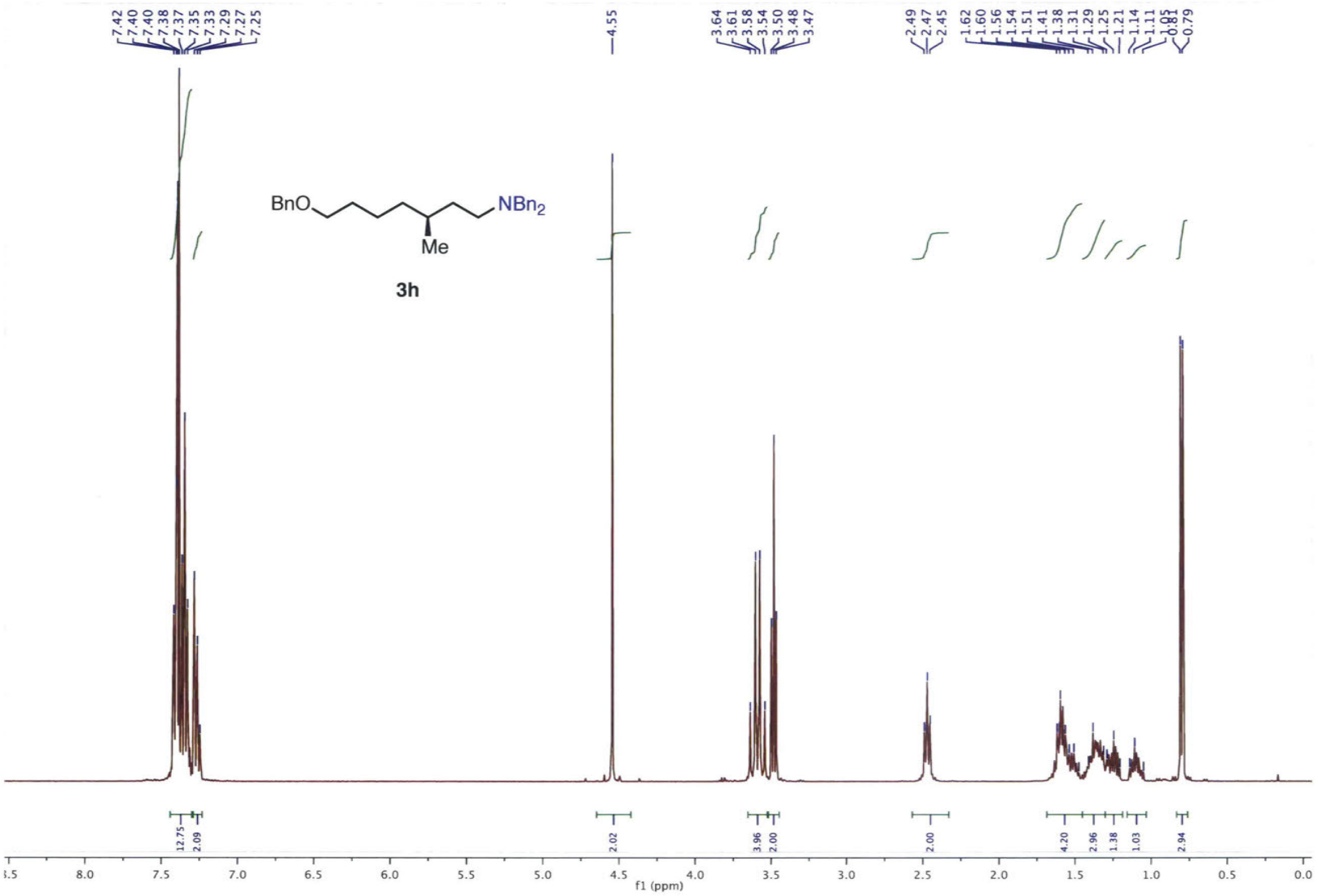
77.14 CDCl3
76.82 CDCl3
64.59
58.23
51.49
38.87
28.93
20.28
14.58
O
O
Me
Me
NBn2
3g
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.25
4.55
3.64
3.61
3.58
3.54
3.50
3.48
3.47
2.49
2.47
2.45
1.62
1.60
1.56
1.54
1.51
1.41
1.38
1.31
1.29
1.25
1.21
1.14
1.11
1.05
0.81
0.79
BnO
NBn2
Me
3h
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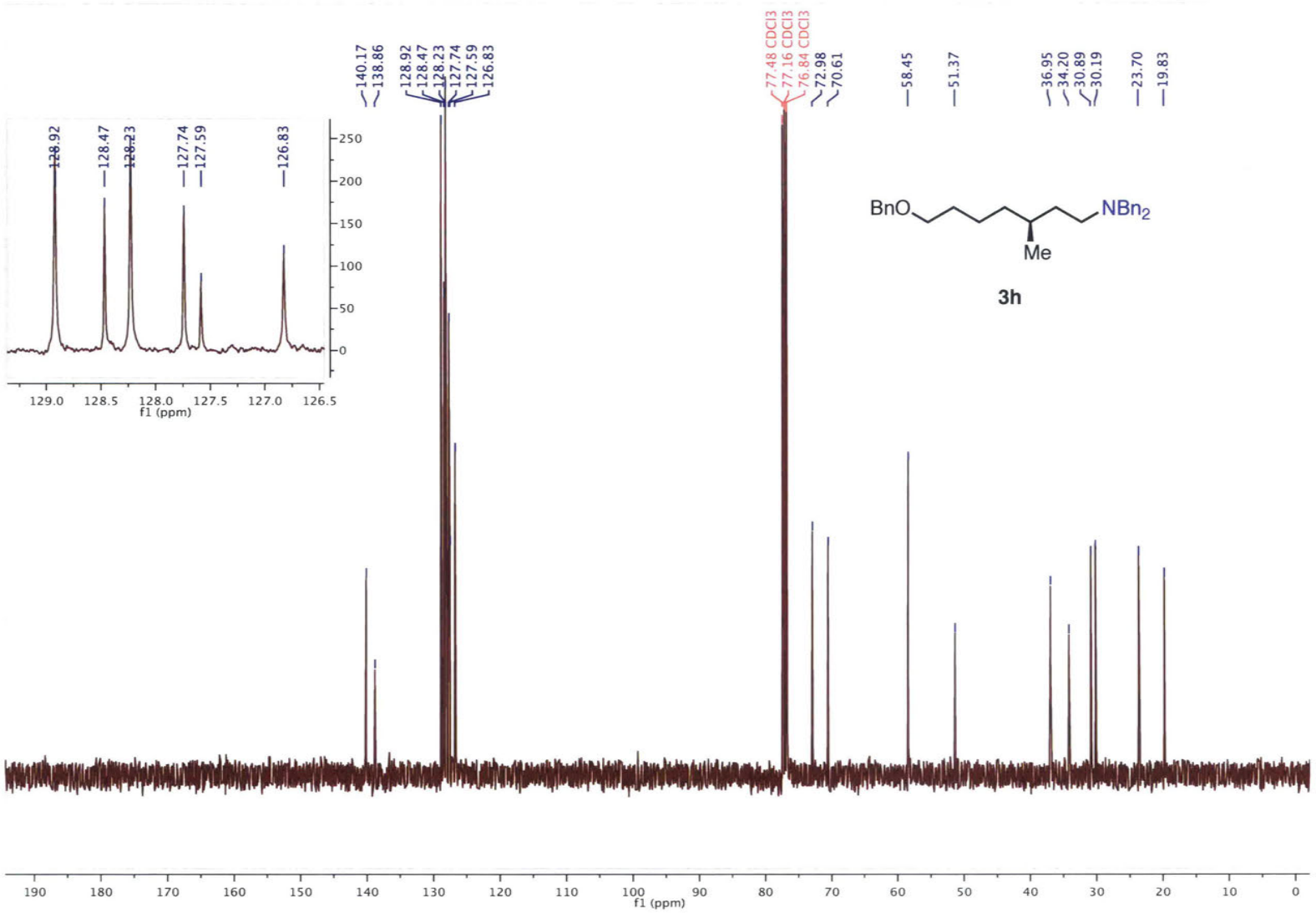
1.38
1.03
2.94
f1 (ppm)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126.83
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77.16 CDCl3
76.84 CDCl3
72.98
70.61
58.45
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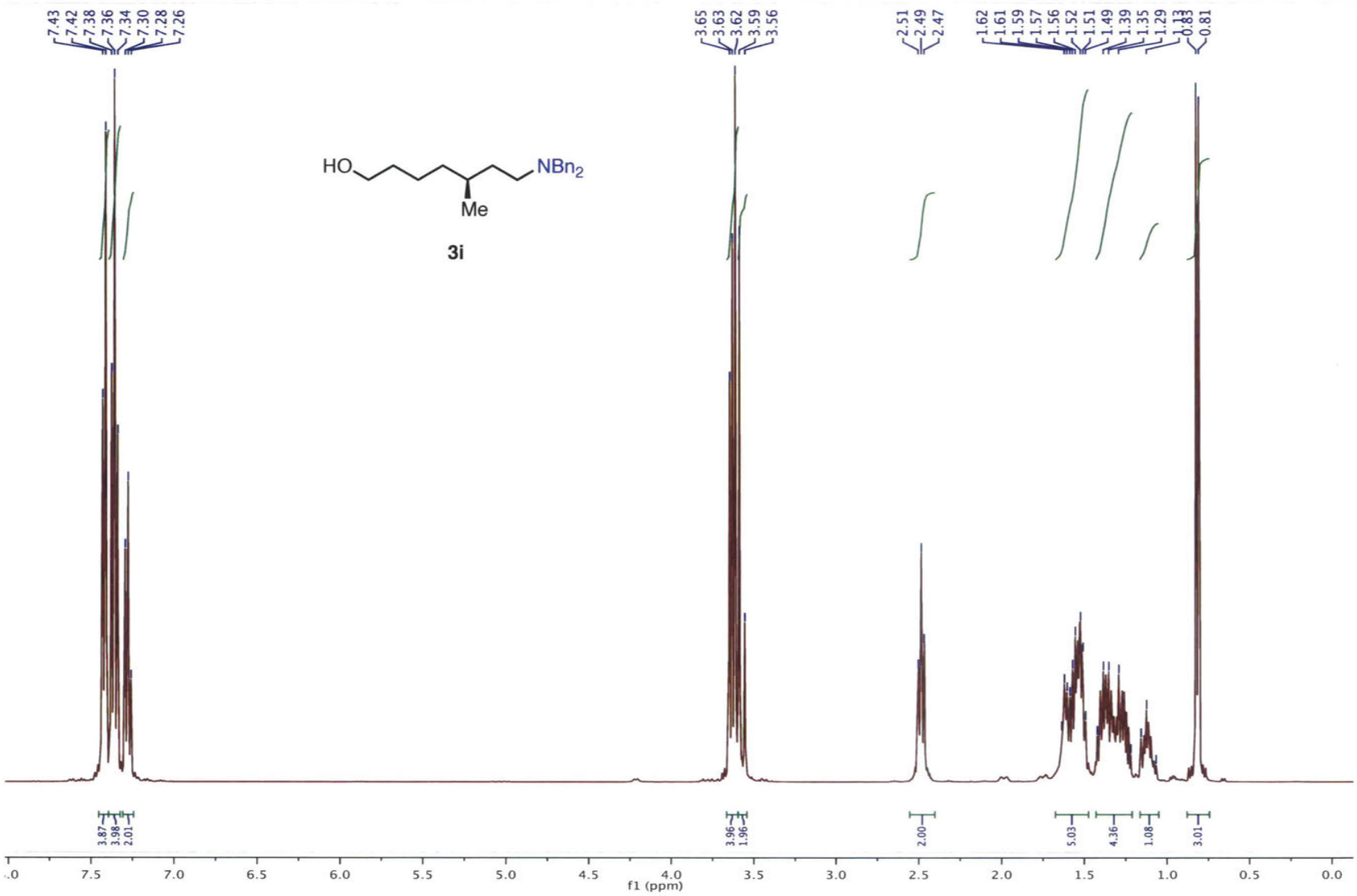
30.89
30.19
23.70
19.83
BnO
NBn2
Me
3h
f1 (ppm)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7.30
7.28
7.26
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3.63
3.62
3.59
3.56
2.51
2.49
2.47
1.62
1.61
1.59
1.57
1.56
1.52
1.51
1.49
1.39
1.35
1.29
0.83
0.81
HO
NBn2
Me
3i
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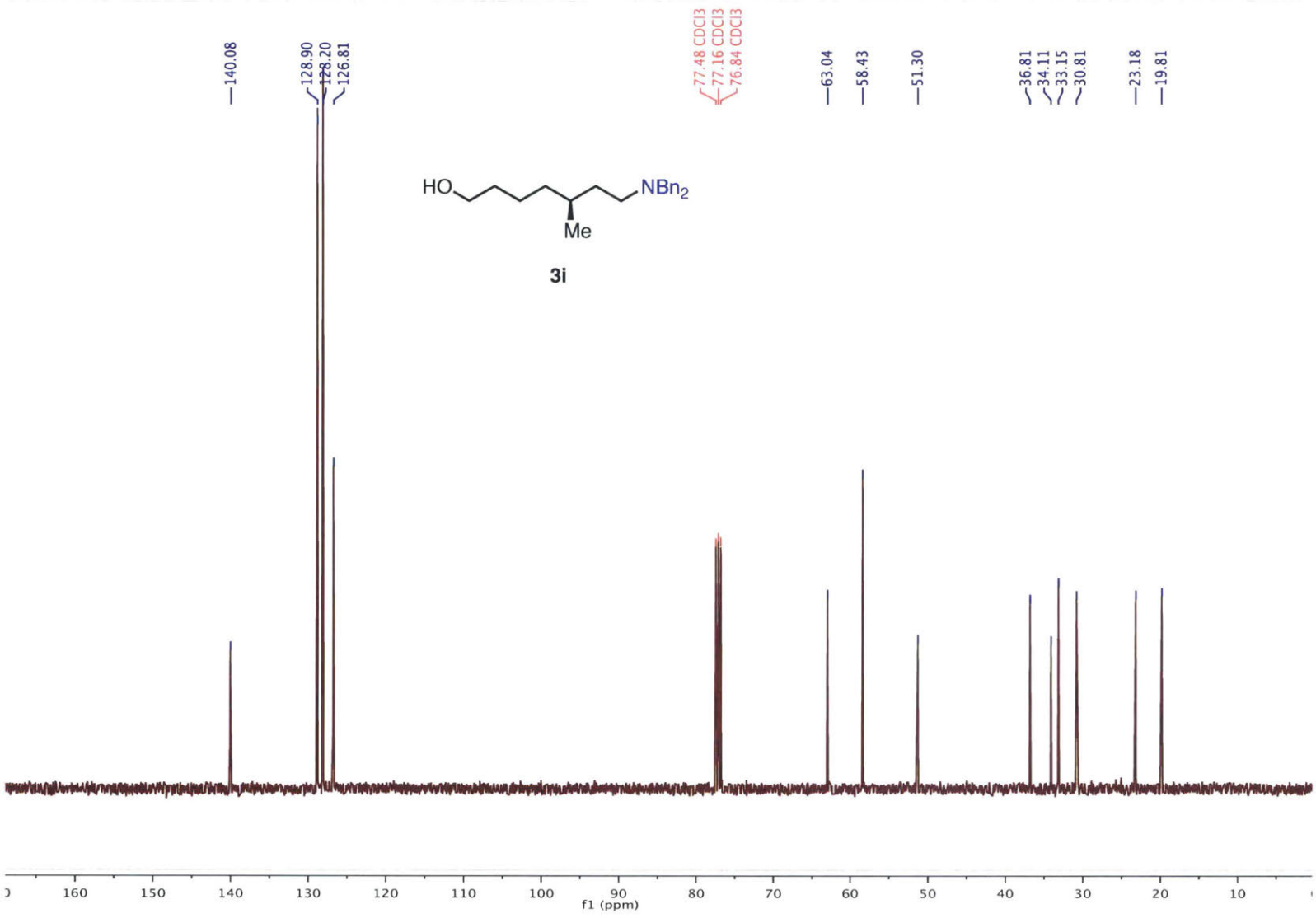
2.01
3.96
1.96
2.00
5.03
4.36
1.08
3.01
f1 (ppm)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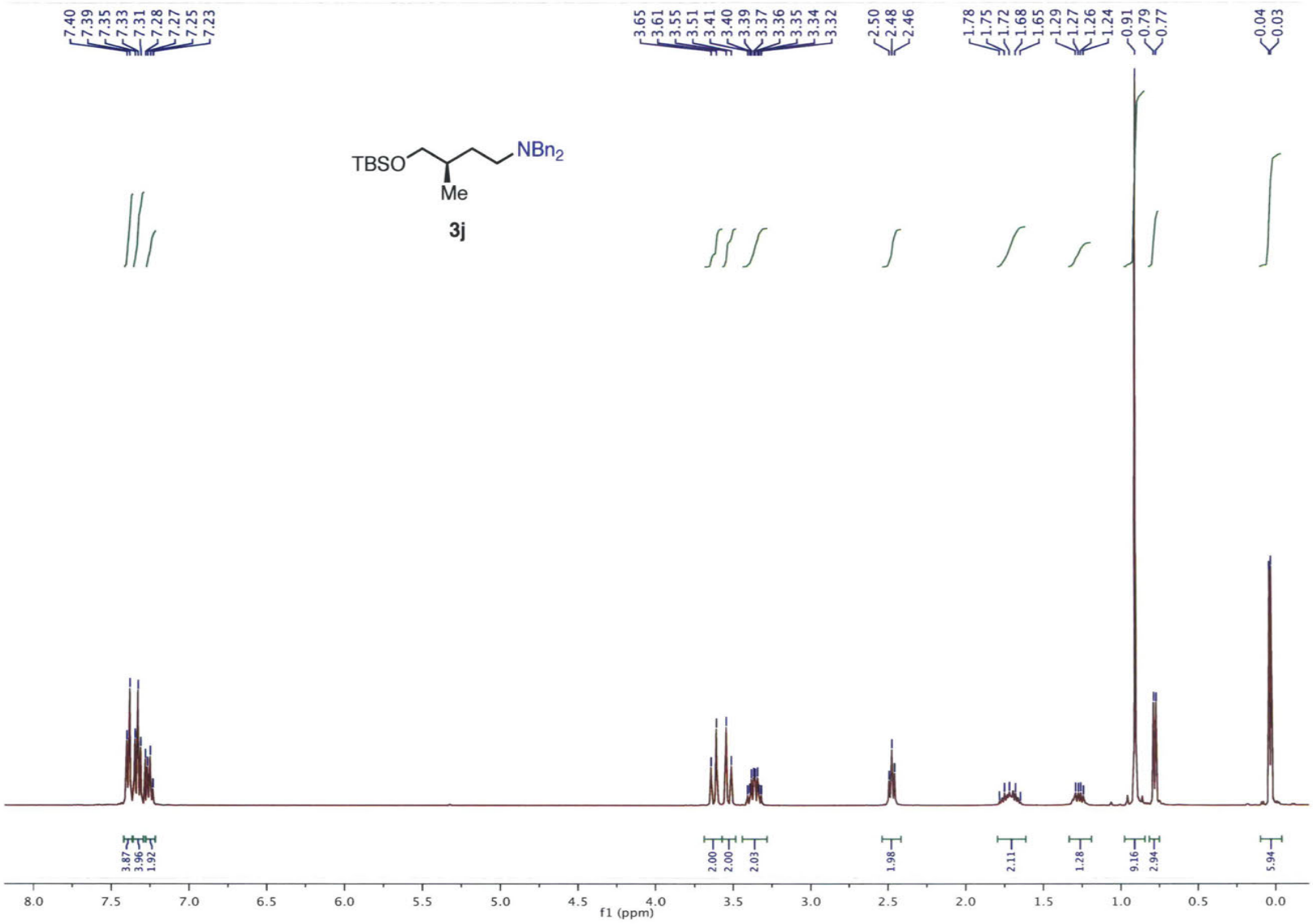
128.90
128.20
126.81
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
63.04
58.43
51.30
36.81
34.11
33.15
30.81
23.18
19.81
HO
NBn2
Me
3i
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.27
7.25
7.23
3.65
3.61
3.55
3.51
3.41
3.40
3.39
3.37
3.36
3.35
3.34
3.32
2.50
2.48
2.46
1.78
1.75
1.72
1.68
1.65
1.29
1.27
1.26
1.24
0.91
0.79
0.77
0.04
0.03
TBSO
NBn2
Me
3j
3.87
3.96
1.92
2.00
2.00
2.03
1.98
2.11
1.28
9.16
2.94
5.94
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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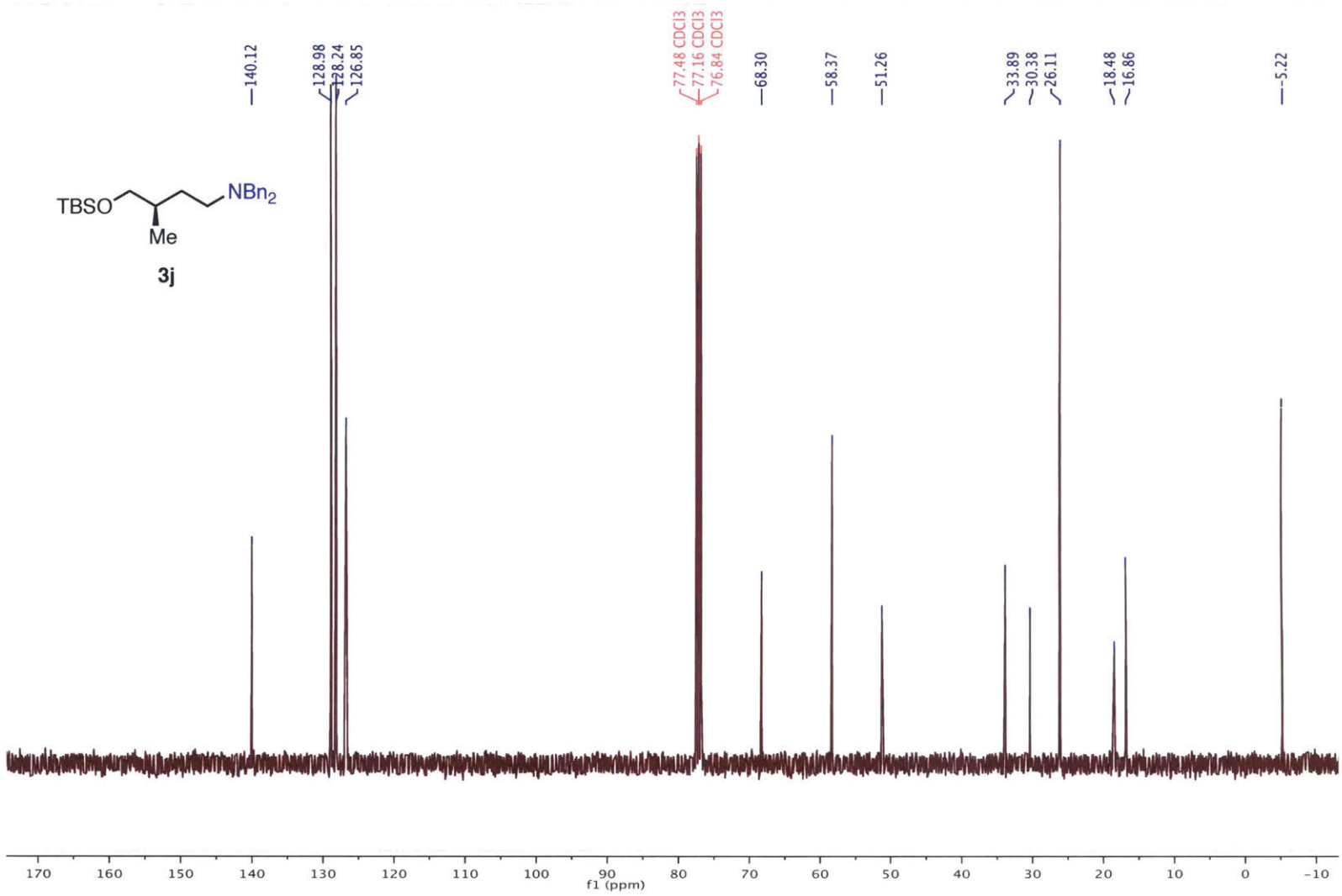
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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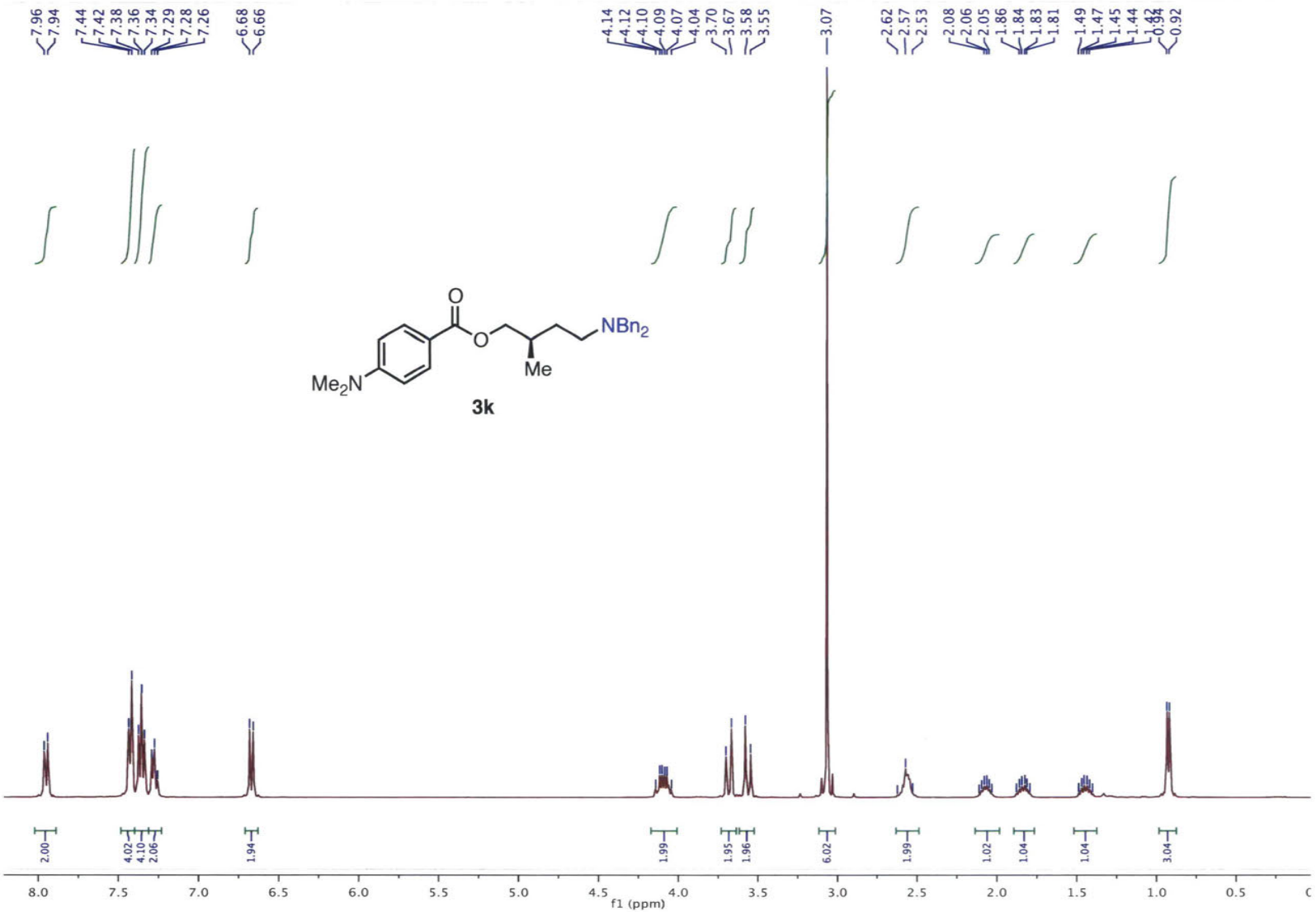
128.24
126.85
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.30
58.37
51.26
33.89
30.38
26.11
18.48
16.86
-5.22
TBSO
NBn2
Me
3j
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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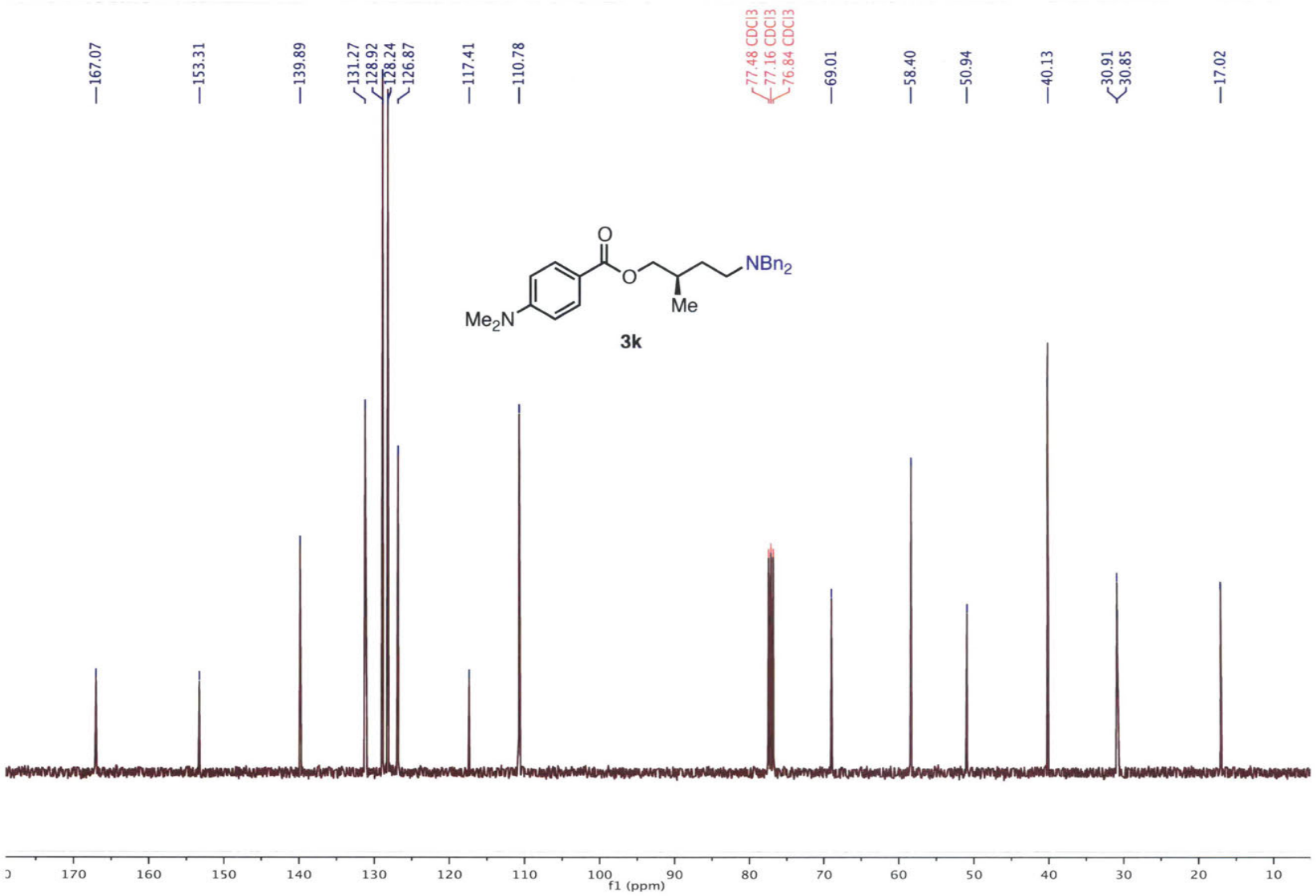
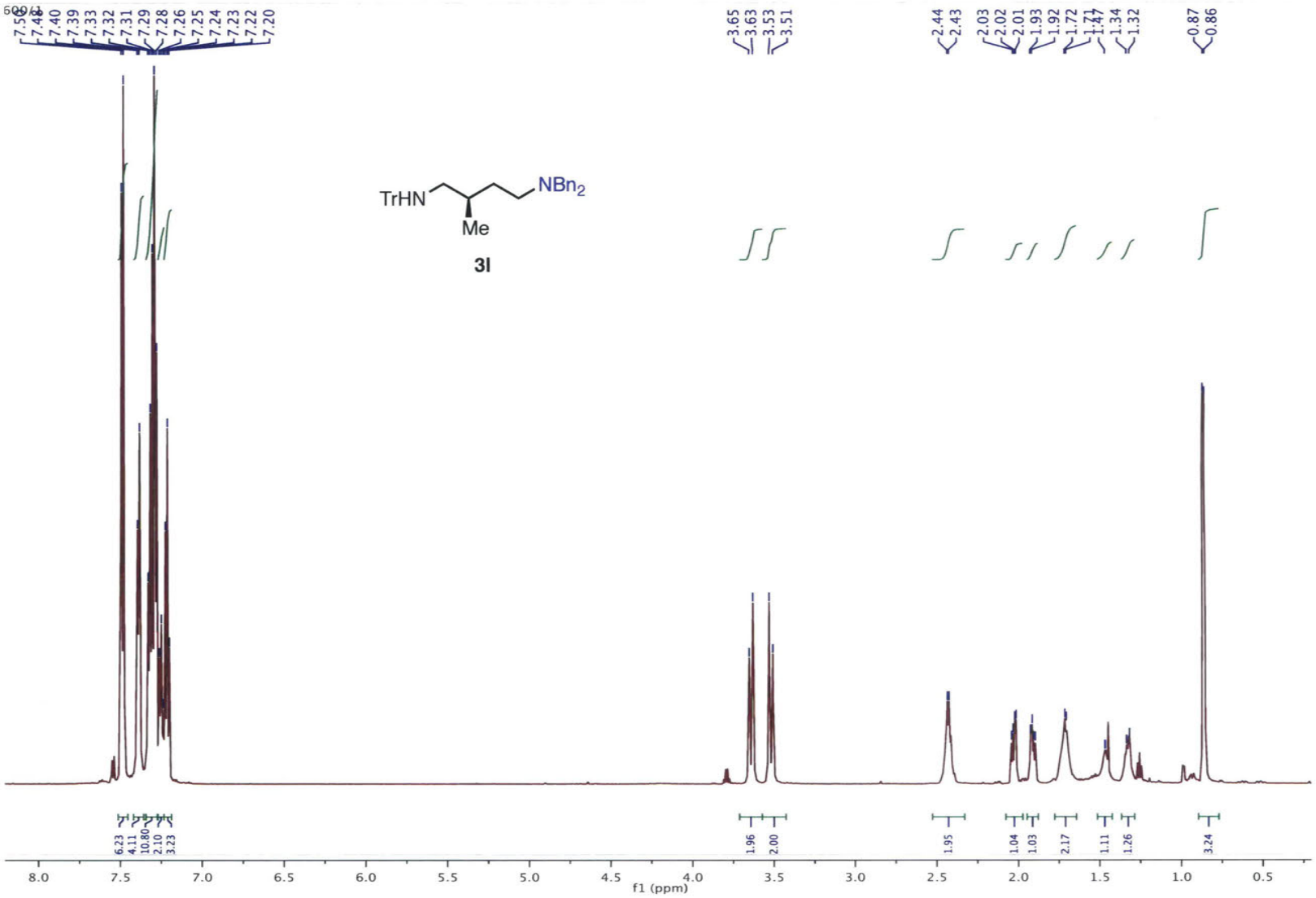
7.94
7.44
7.42
7.38
7.36
7.34
7.29
7.28
7.26
6.68
6.66
4.14
4.12
4.10
4.09
4.07
4.04
3.70
3.67
3.58
3.55
3.07
2.62
2.57
2.53
2.08
2.06
2.05
1.86
1.84
1.83
1.81
1.49
1.47
1.45
1.44
0.94
0.92
O
O
NBn2
Me
Me2N
3k
2.00
4.02
4.10
2.06
1.94
1.99
1.95
1.96
6.02
1.99
1.02
1.04
1.04
3.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


167.07
153.31
139.89
131.27
128.92
128.24
126.87
117.41
110.78
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
69.01
58.40
50.94
40.13
30.91
30.85
17.02
O
O
NBn2
Me
Me2N
3k
f1 (ppm)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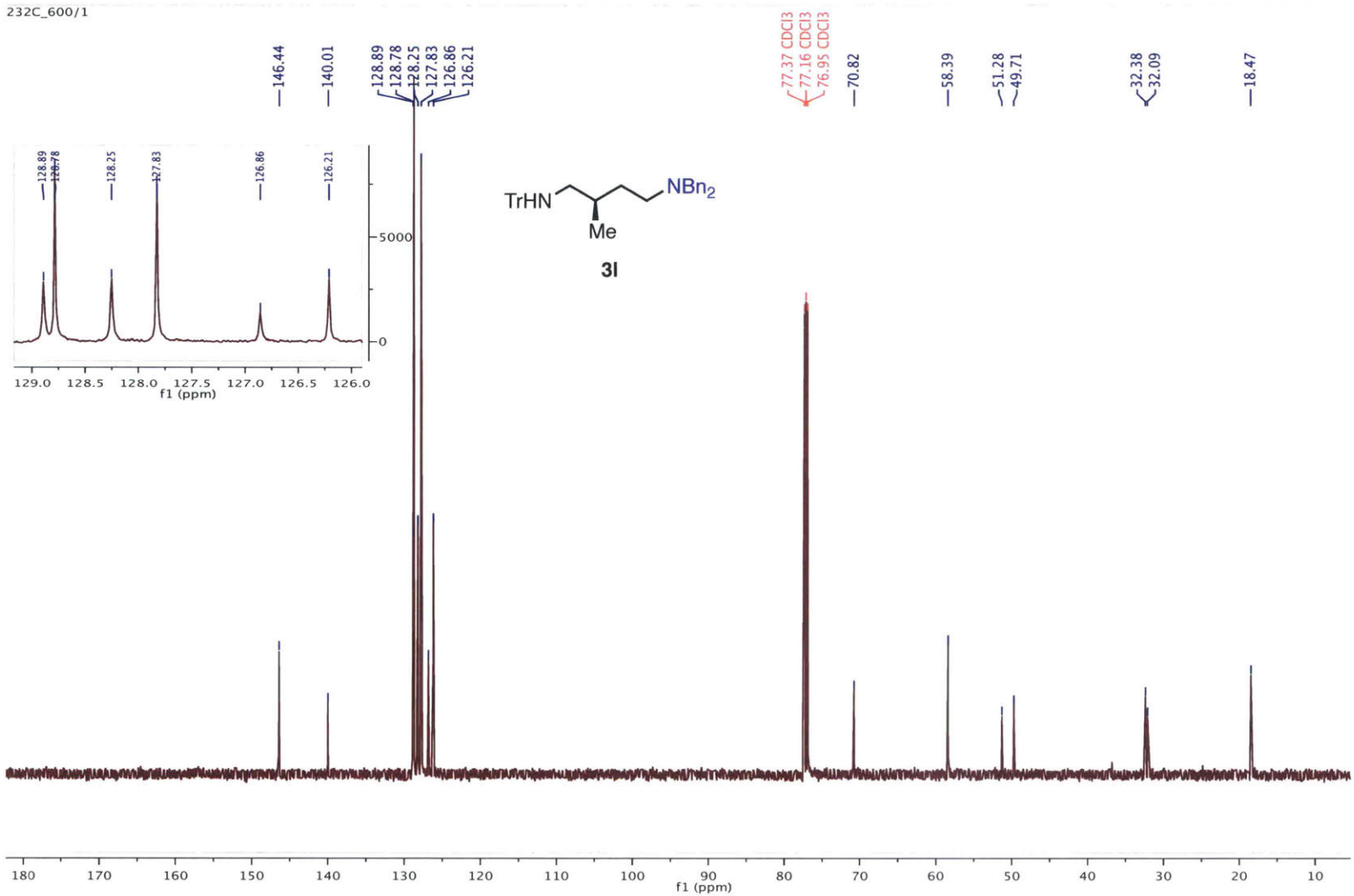
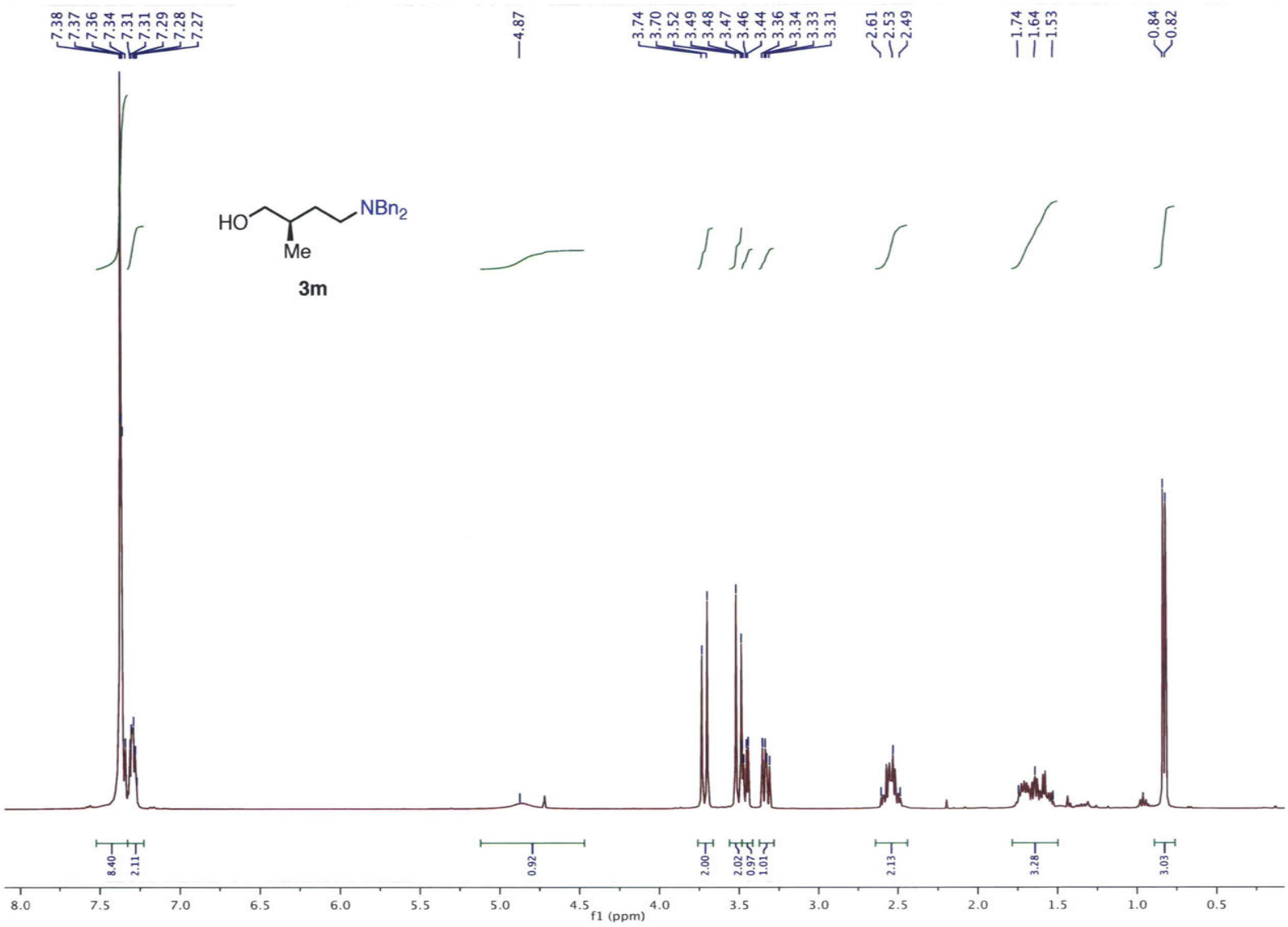
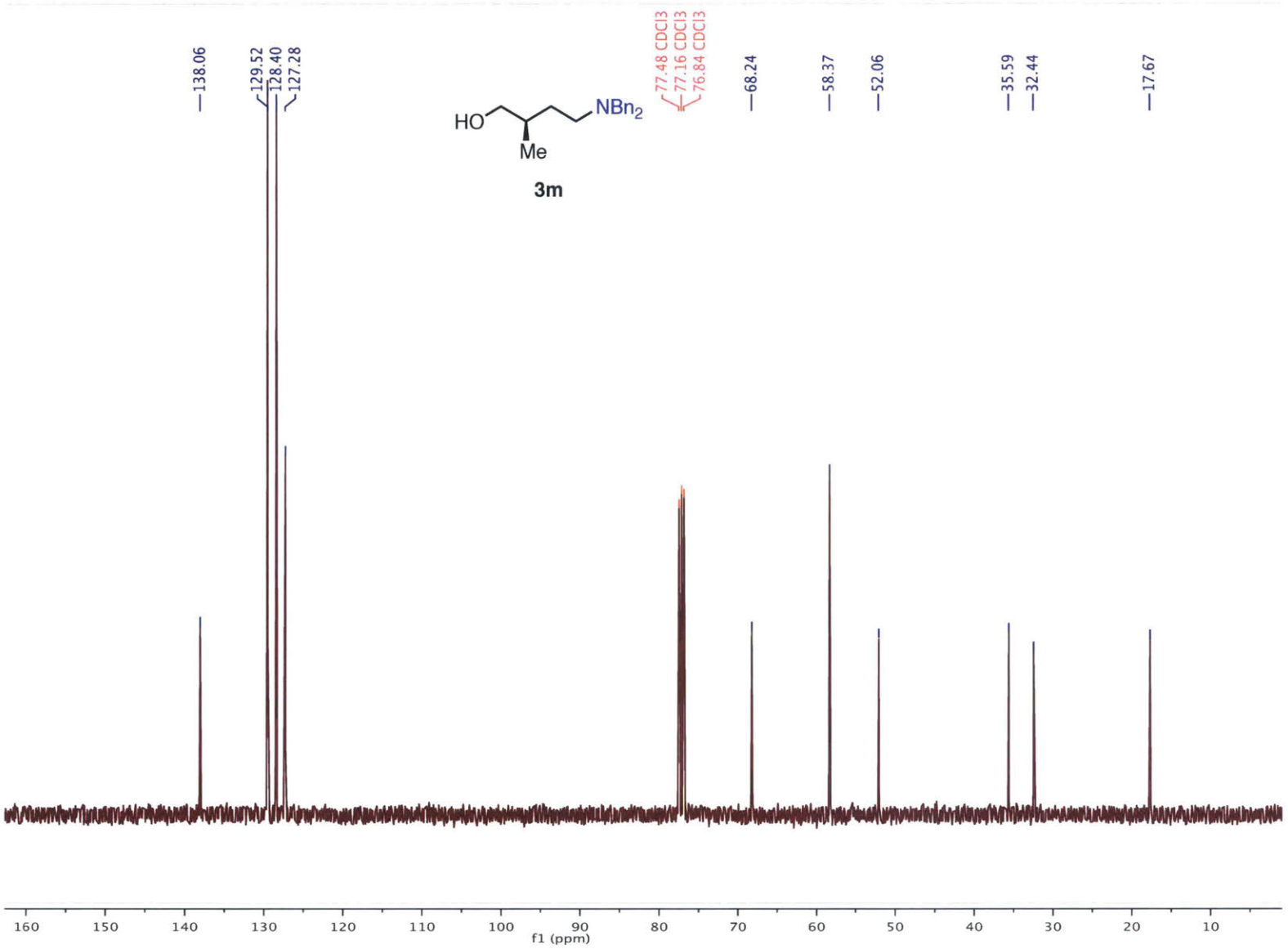
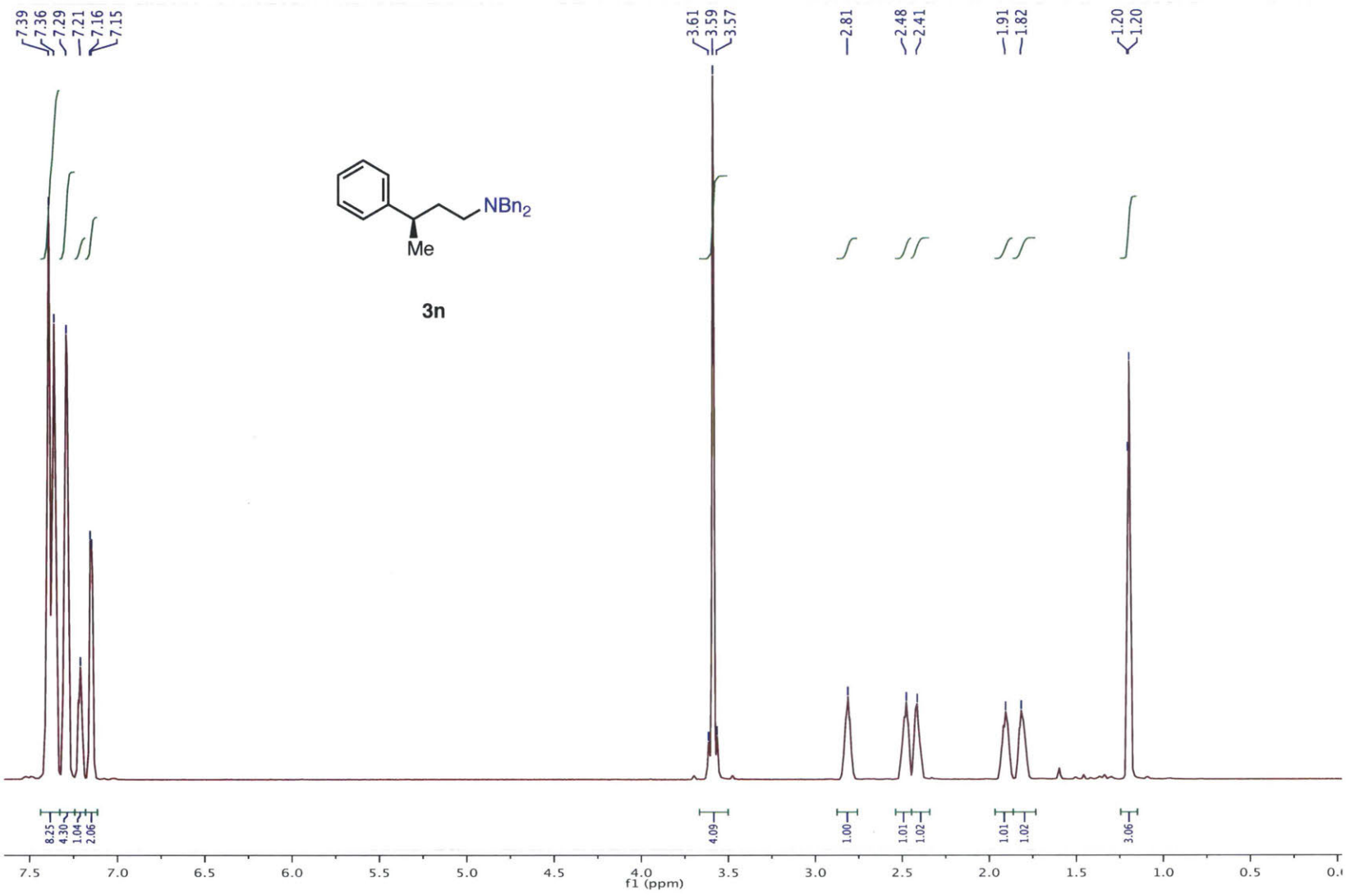
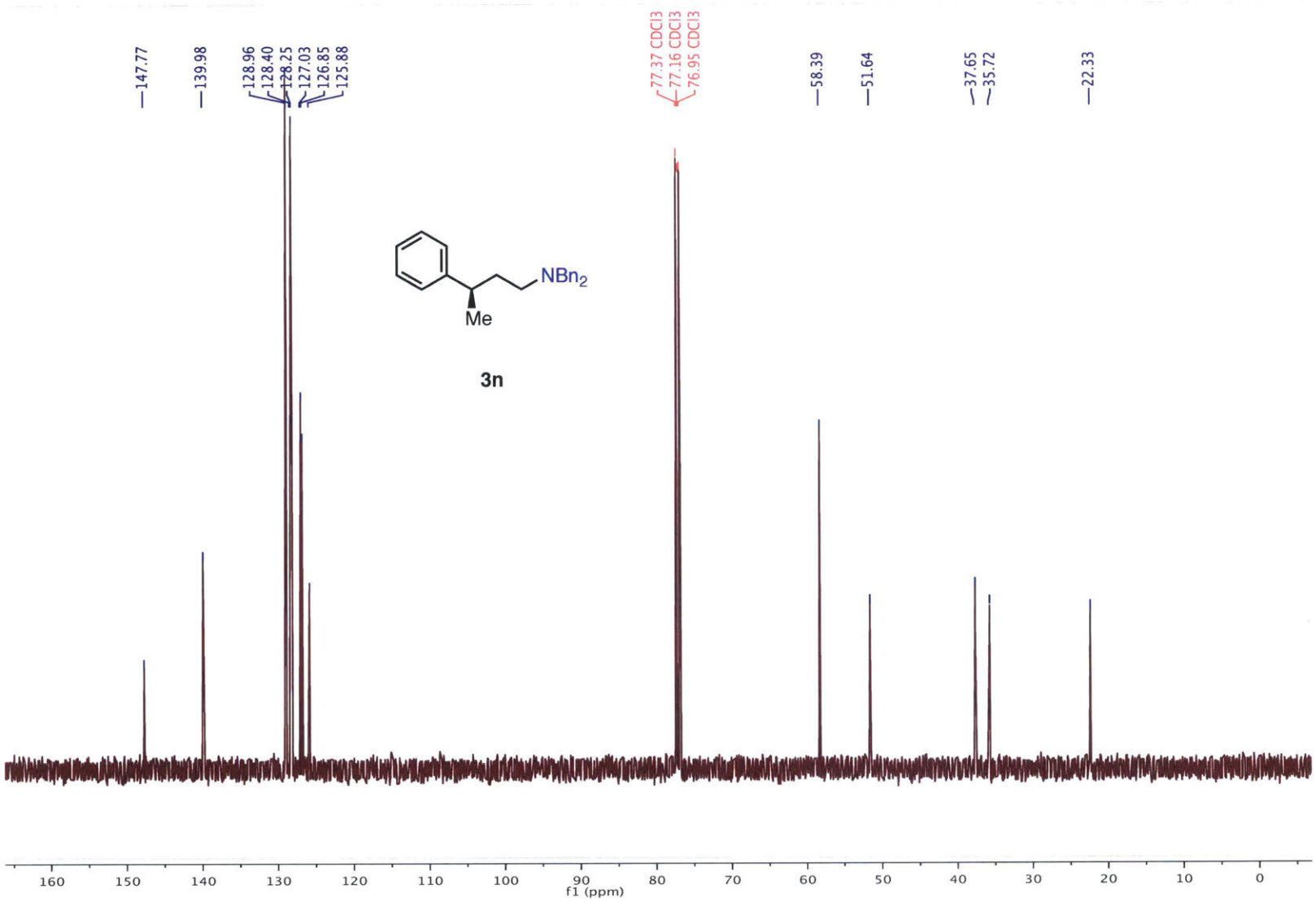
7.48
7.40
7.39
7.33
7.32
7.31
7.29
7.28
7.26
7.25
7.24
7.23
7.22
7.20
3.65
3.63
3.53
3.51
2.44
2.43
2.03
2.02
2.01
1.93
1.92
1.72
1.71
1.47
1.34
1.32
0.87
0.86
TrHN
NBn2
Me
3l
6.23
4.11
10.80
2.10
3.23
1.96
2.00
1.95
1.04
1.03
2.17
1.11
1.26
3.24
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

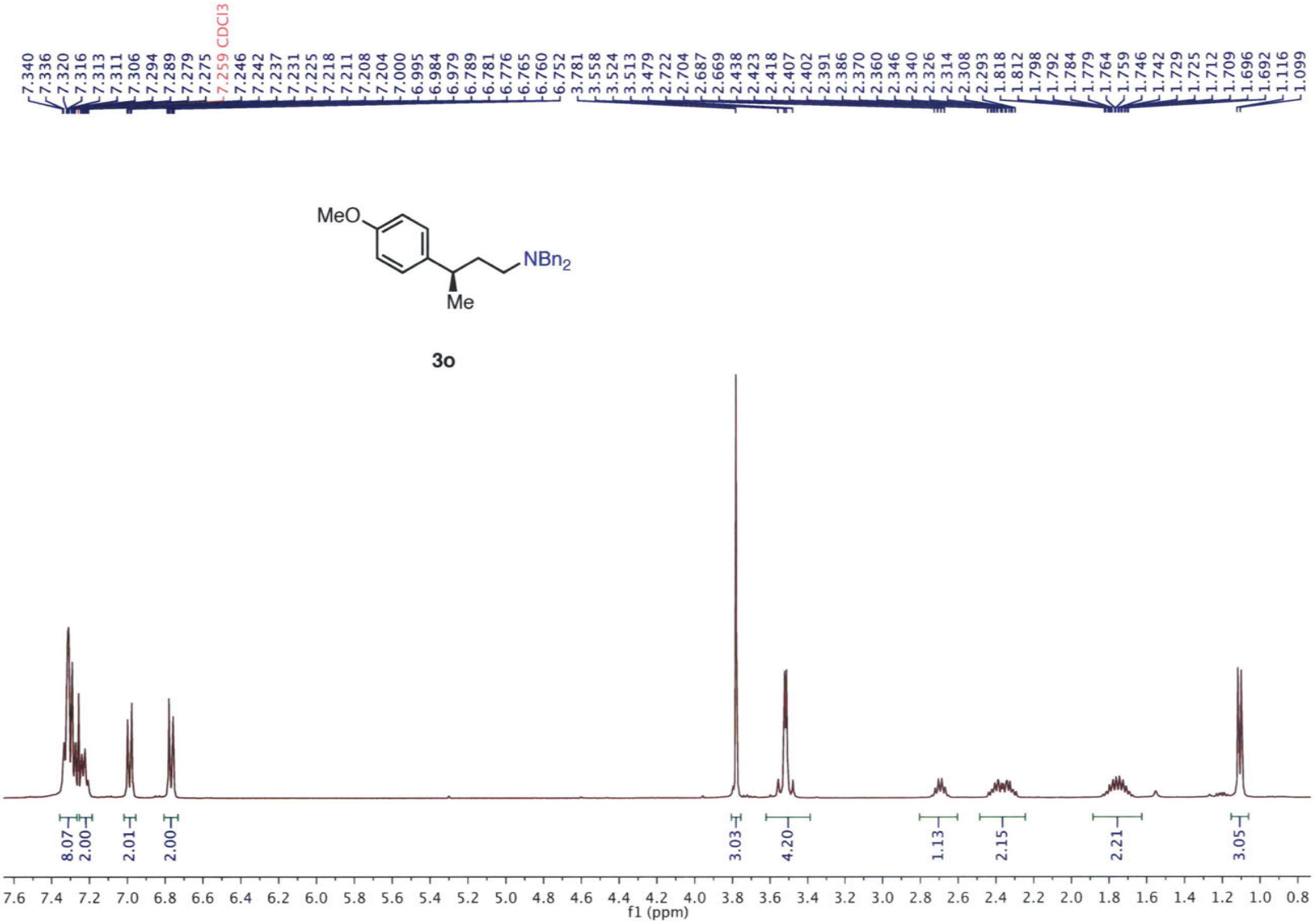

232C_600/1
146.44
140.01
128.89
128.78
128.25
127.83
126.86
126.21
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
70.82
58.39
51.28
49.71
32.38
32.09
18.47
TrHN
NBn2
Me
3l
5000
0
129.0 128.5 128.0 127.5 127.0 126.5 126.0
f1 (ppm)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

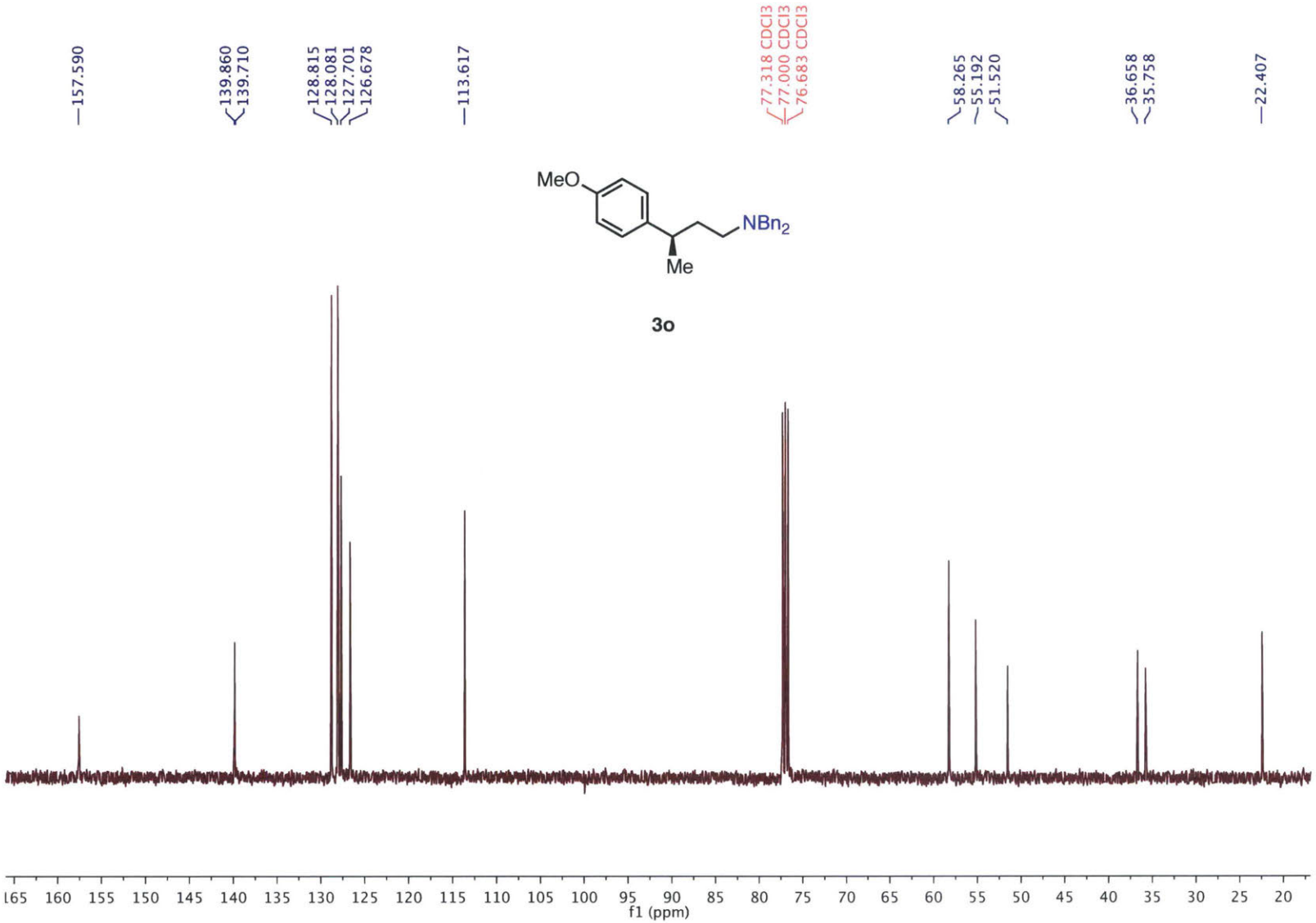

7.38
7.37
7.36
7.34
7.31
7.31
7.29
7.28
7.27
4.87
3.74
3.70
3.52
3.49
3.48
3.47
3.46
3.44
3.36
3.34
3.33
3.31
2.61
2.53
2.49
1.74
1.64
1.53
0.84
0.82
HO
NBn2
Me
3m
8.40
2.11
0.92
2.00
2.02
0.97
1.01
2.13
3.28
3.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

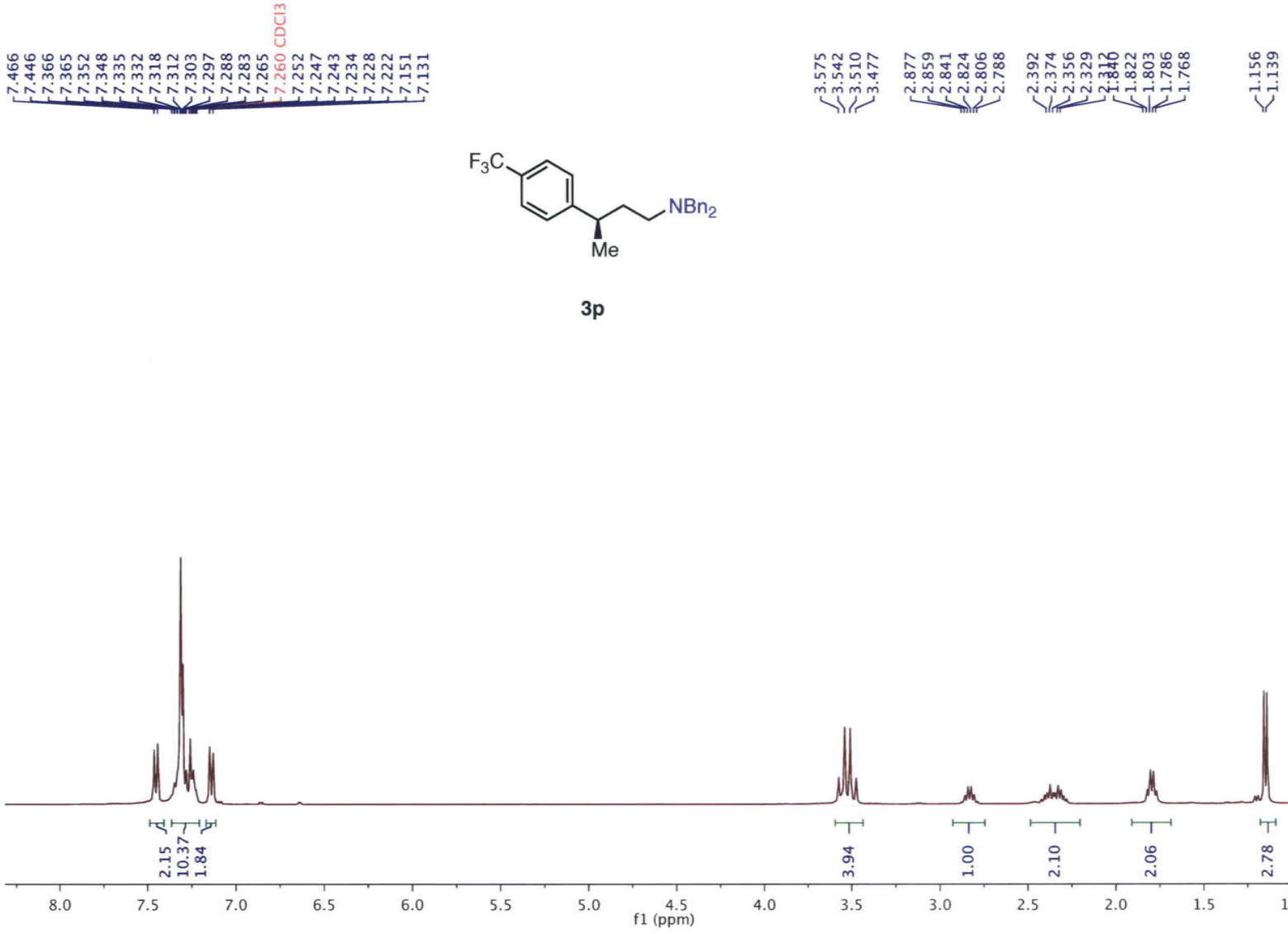

138.06
129.52
128.40
127.28
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.24
58.37
52.06
35.59
32.44
17.67
HO
NBn2
Me
3m
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.39
7.36
7.29
7.21
7.16
7.15
3.61
3.59
3.57
2.81
2.48
2.41
1.91
1.82
1.20
1.20
NBn2
Me
3n
8.25
4.30
1.04
2.06
4.09
1.00
1.01
1.02
1.01
1.02
3.06
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
f1 (ppm)

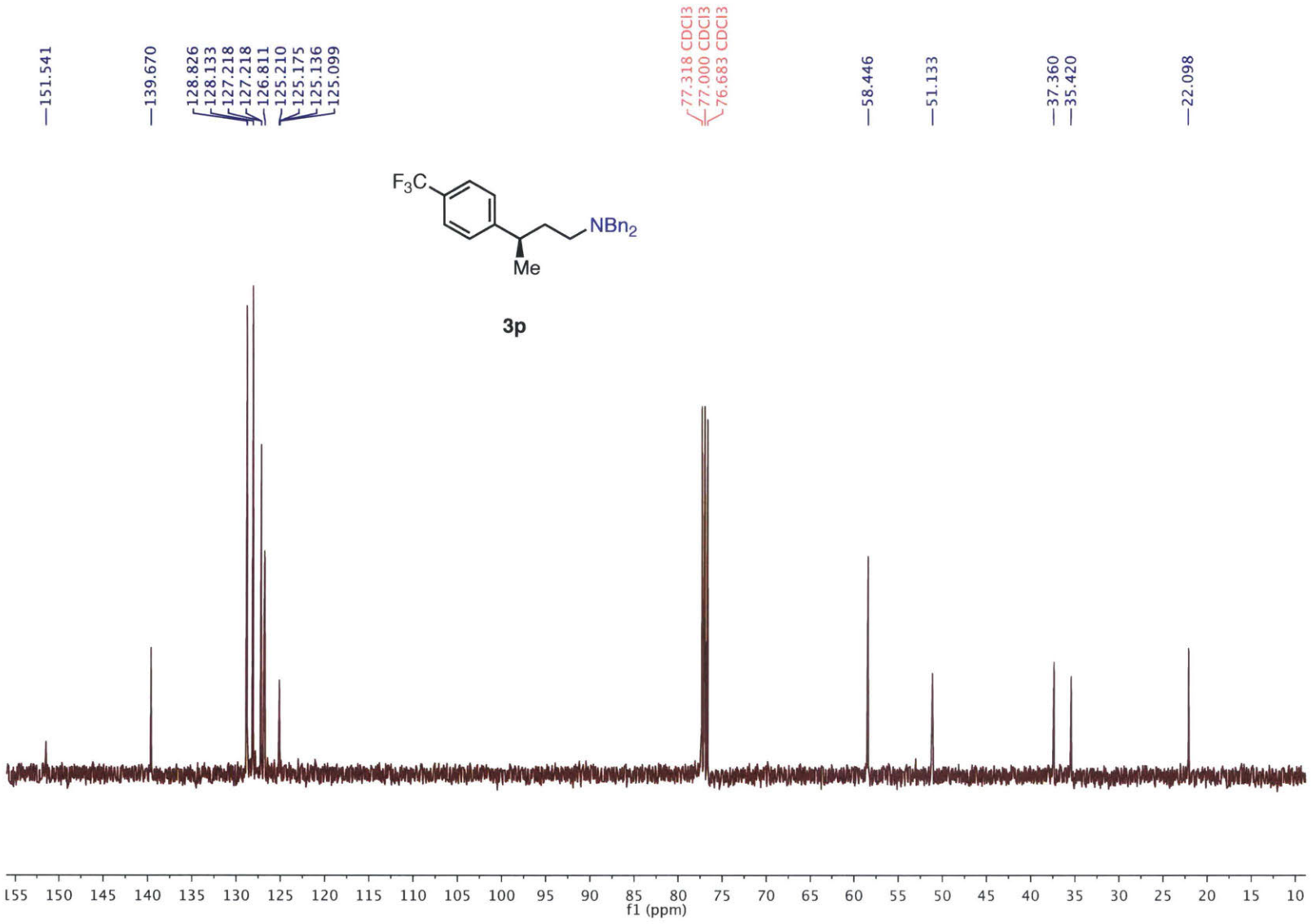

147.77
139.98
128.96
128.40
128.25
127.03
126.85
125.88
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
58.39
51.64
37.65
35.72
22.33
NBn2
Me
3n
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

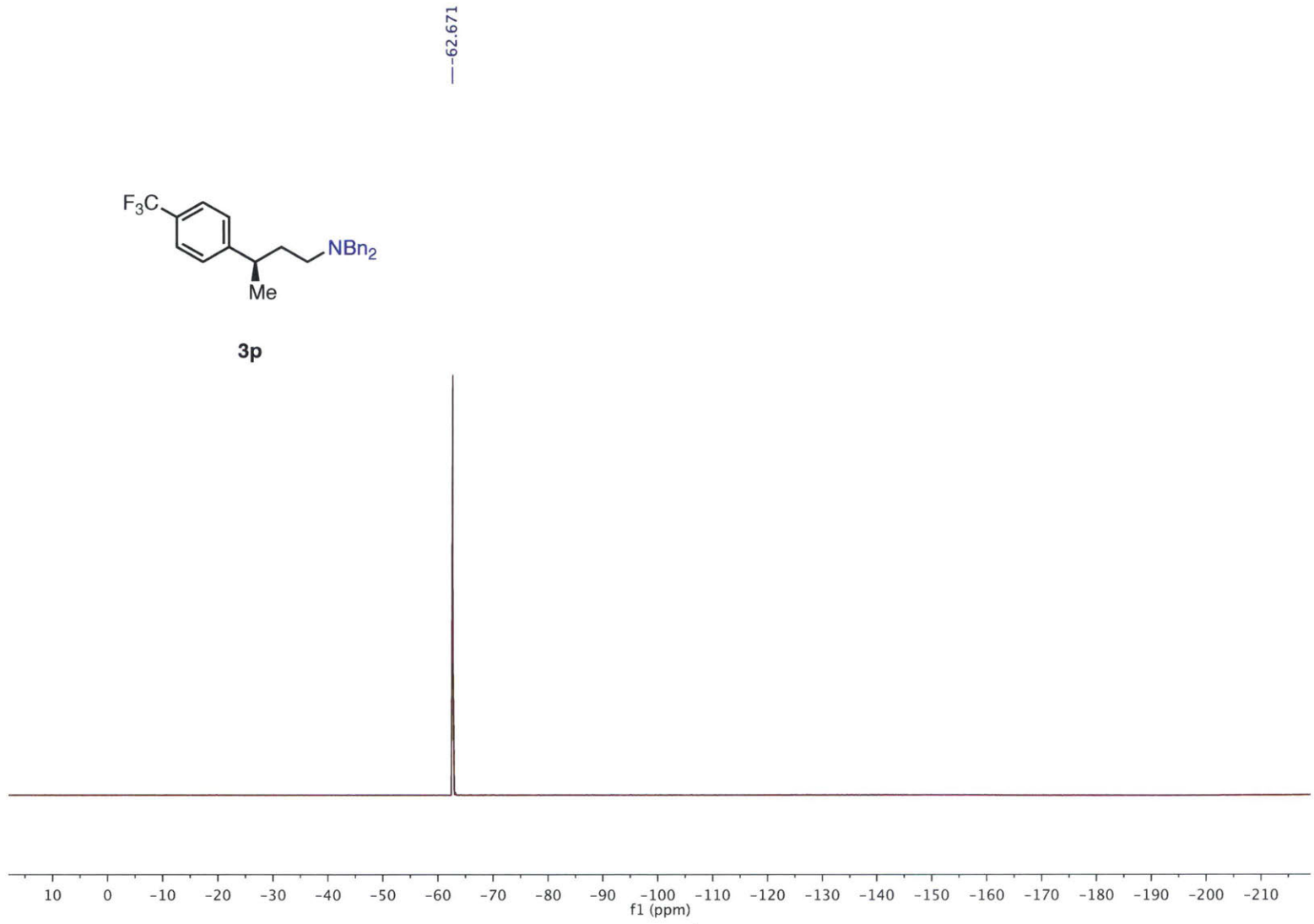

7.340
7.336
7.320
7.316
7.313
7.311
7.306
7.294
7.289
7.279
7.275
7.259 CDCl3
7.246
7.242
7.237
7.231
7.225
7.218
7.211
7.208
7.204
7.000
6.995
6.984
6.979
6.789
6.781
6.776
6.765
6.760
6.752
3.781
3.558
3.524
3.513
3.479
2.722
2.704
2.687
2.669
2.438
2.423
2.418
2.407
2.402
2.391
2.386
2.370
2.360
2.346
2.340
2.326
2.314
2.308
2.293
1.818
1.812
1.798
1.792
1.784
1.779
1.764
1.759
1.746
1.742
1.729
1.725
1.712
1.709
1.696
1.692
1.116
1.099
MeO
NBn2
Me
3o
8.07
2.00
2.01
2.00
3.03
4.20
1.13
2.15
2.21
3.05
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8
f1 (ppm)


157.590
139.860
139.710
128.815
128.081
127.701
126.678
113.617
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
58.265
55.192
51.520
36.658
35.758
22.407
MeO
NBn2
Me
3o
f1 (ppm)

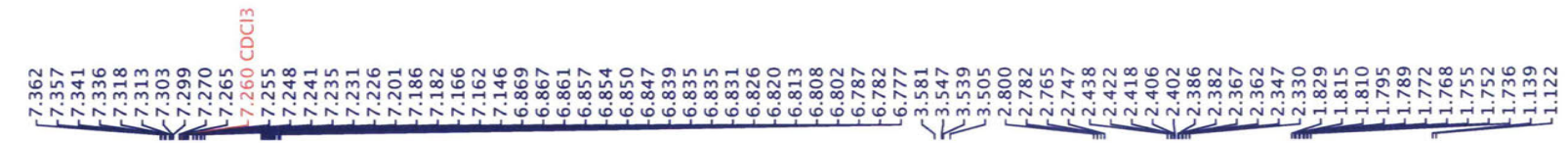

7.466
7.446
7.366
7.365
7.352
7.348
7.335
7.332
7.318
7.312
7.303
7.297
7.288
7.283
7.265
7.260 CDCl3
7.252
7.247
7.243
7.234
7.228
7.222
7.151
7.131
3.575
3.542
3.510
3.477
2.877
2.859
2.841
2.824
2.806
2.788
2.392
2.374
2.356
2.329
1.840
1.822
1.803
1.786
1.768
1.156
1.139
F3C
NBn2
Me
2.15
10.37
1.84
3.94
1.00
2.10
2.06
2.78
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
f1 (ppm)

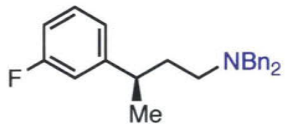
3p


151.541
139.670
128.826
128.133
127.218
127.218
126.811
125.210
125.175
125.136
125.099
77.318 CDCl3
77.000 CDCl3
76.683 CDCl3
58.446
51.133
37.360
35.420
22.098
F3C
NBn2
Me
3p
f1 (ppm)

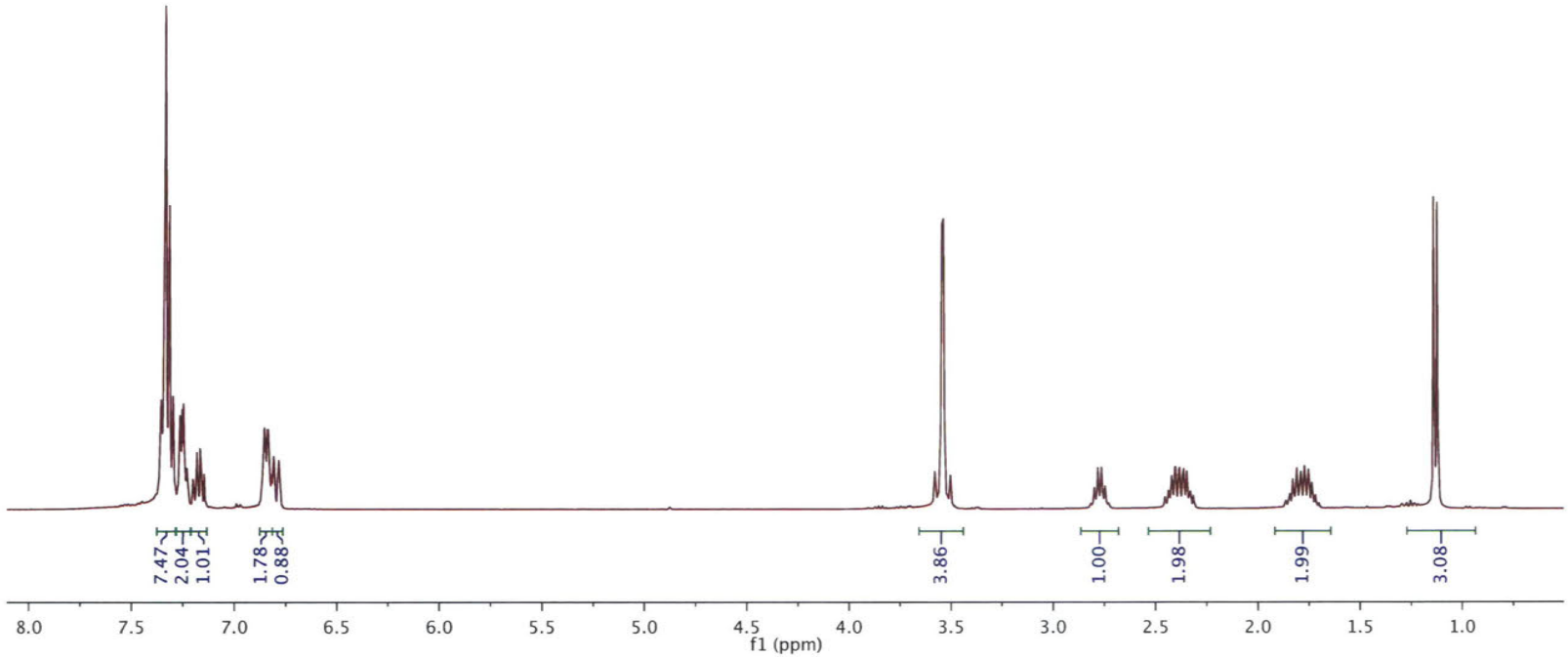

-62.671
F3C
NBn2
Me
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

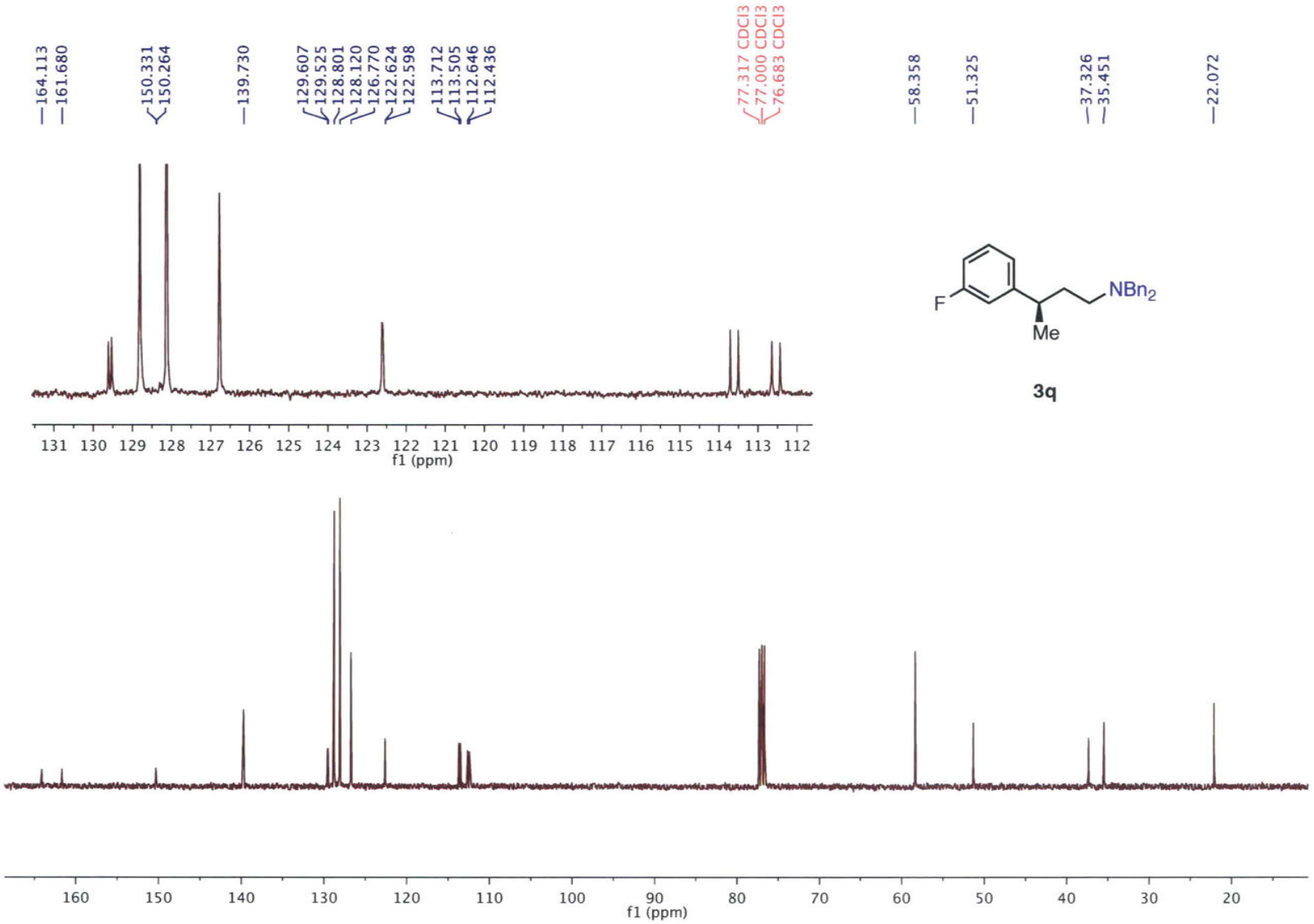
3p

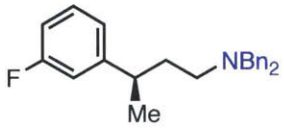

7.362
7.357
7.341
7.336
7.318
7.313
7.303
7.299
7.270
7.265
7.260 CDCl3
7.255
7.248
7.241
7.235
7.231
7.226
7.201
7.186
7.182
7.166
7.162
7.146
6.869
6.867
6.861
6.857
6.854
6.850
6.847
6.839
6.835
6.835
6.831
6.826
6.820
6.813
6.808
6.802
6.787
6.782
6.777
3.581
3.547
3.539
3.505
2.800
2.782
2.765
2.747
2.438
2.422
2.418
2.406
2.402
2.386
2.382
2.367
2.362
2.347
2.330
1.829
1.815
1.810
1.795
1.789
1.772
1.768
1.755
1.752
1.736
1.139
1.122


F
NBn2
Me

3q

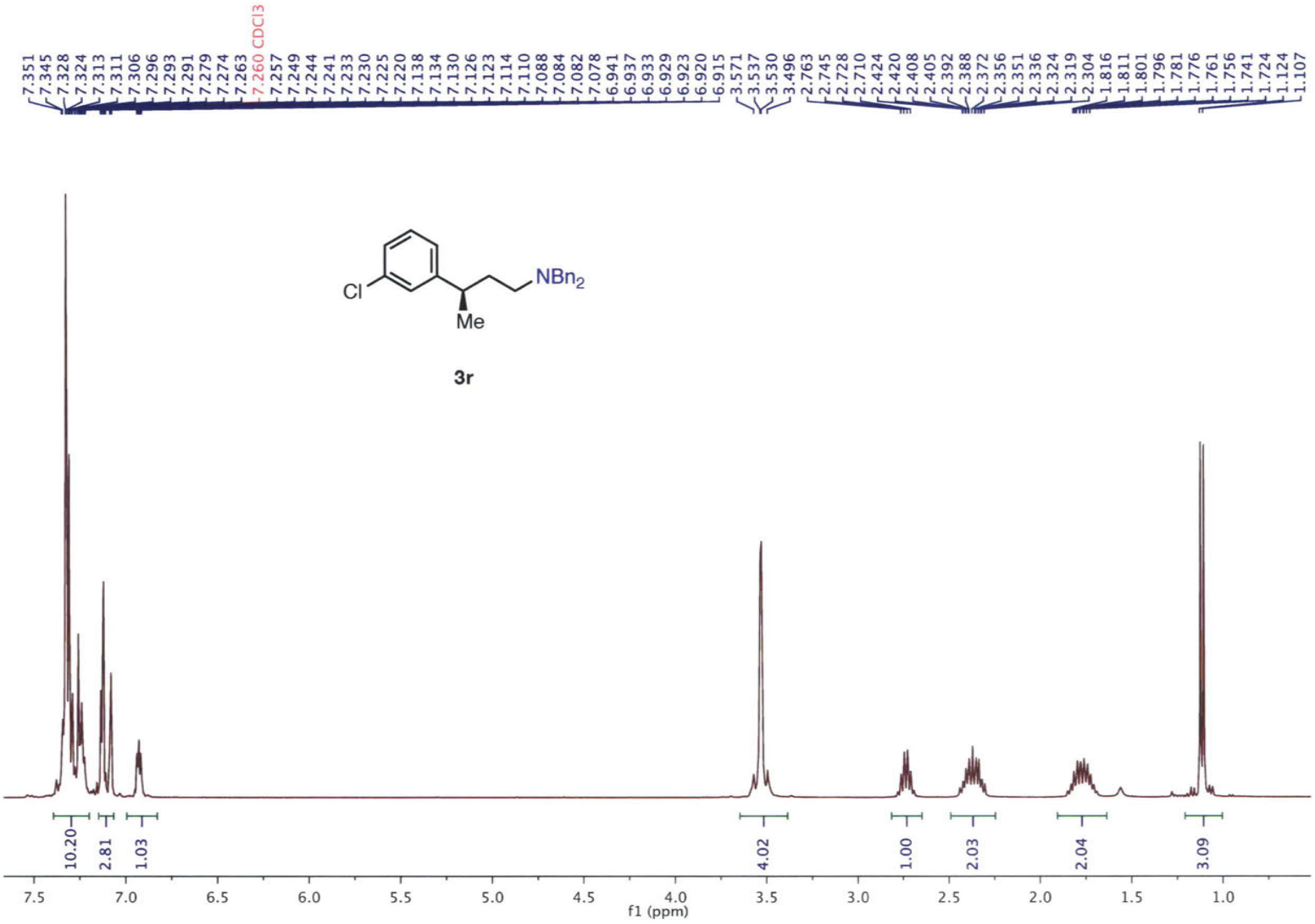

7.47
2.04
1.01
1.78
0.88
3.86
1.00
1.98
1.99
3.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

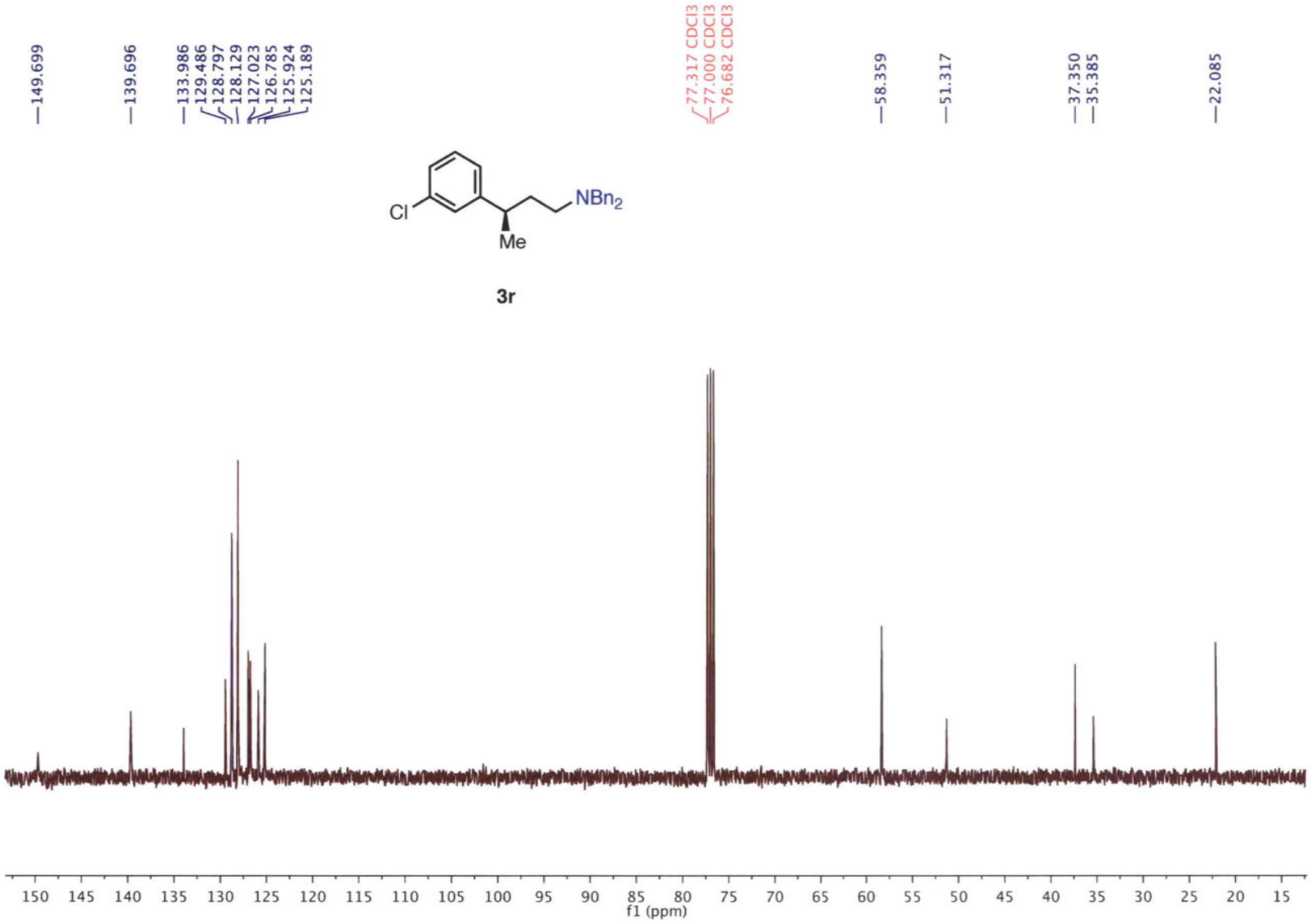

164.113
161.680
150.331
150.264
139.730
129.607
129.525
128.801
128.120
126.770
122.624
122.598
113.712
113.505
112.646
112.436
77.317 CDCl3
77.000 CDCl3
76.683 CDCl3
58.358
51.325
37.326
35.451
22.072
F
NBn2
Me
3q
131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114 113 112
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

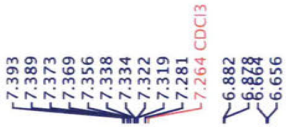

F
NBn2
Me

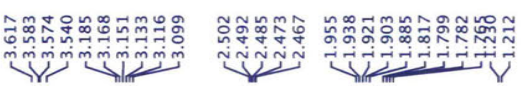
3q

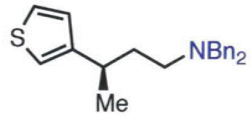
-114.162
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


7.351
7.345
7.328
7.324
7.313
7.311
7.306
7.296
7.293
7.291
7.279
7.274
7.263
7.260 CDCl3
7.257
7.249
7.244
7.241
7.233
7.230
7.225
7.220
7.138
7.134
7.130
7.126
7.123
7.114
7.110
7.088
7.084
7.082
7.078
6.941
6.937
6.933
6.929
6.923
6.920
6.915
3.571
3.537
3.530
3.496
2.763
2.745
2.728
2.710
2.424
2.420
2.408
2.405
2.392
2.388
2.372
2.356
2.351
2.336
2.324
2.319
2.304
1.816
1.811
1.801
1.796
1.781
1.776
1.761
1.756
1.741
1.724
1.124
1.107
Cl
NBn2
Me
3r
10.20
2.81
1.03
4.02
1.00
2.03
2.04
3.09
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
f1 (ppm)

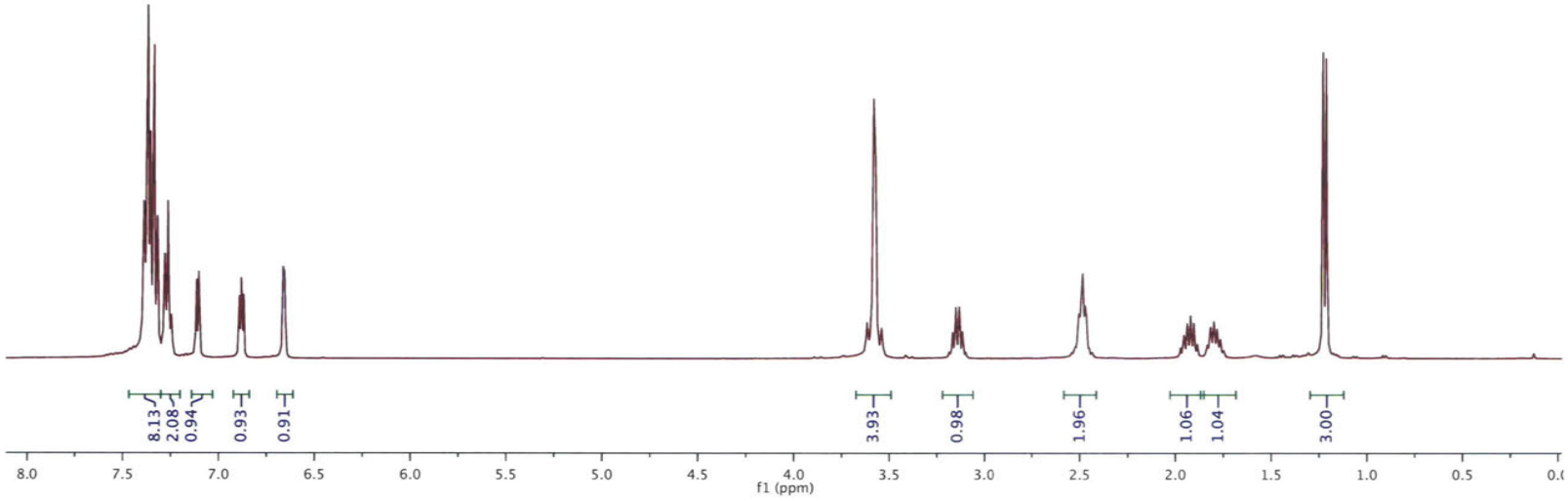

149.699
139.696
133.986
129.486
128.797
128.129
127.023
126.785
125.924
125.189
77.317 CDCl3
77.000 CDCl3
76.682 CDCl3
58.359
51.317
37.350
35.385
22.085
Cl
NBn2
Me
3r
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)

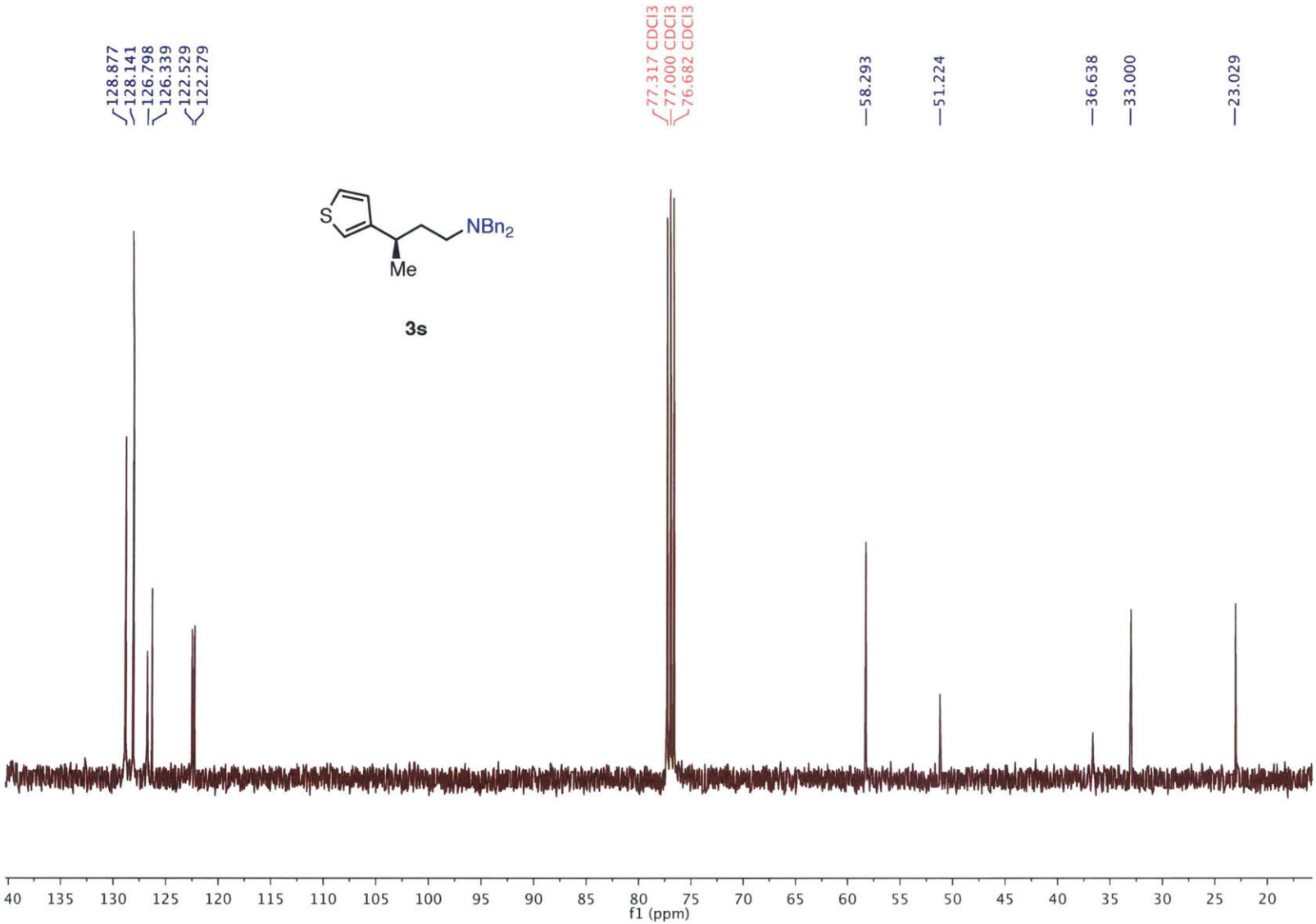

7.393
7.389
7.373
7.369
7.356
7.338
7.334
7.322
7.319
7.281
7.264 CDCl3
6.882
6.656


3.617
3.583
3.574
3.540
3.185
3.168
3.151
3.133
3.116
3.099
2.502
2.492
2.485
2.473
2.467
1.955
1.938
1.921
1.903
1.885
1.817
1.799
1.782
1.230
1.212


S
NBn2
Me

3s


8.13
2.08
0.94
0.93
0.91
3.93
0.98
1.96
1.06
1.04
3.00
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
f1 (ppm)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128.141
126.798
126.339
122.529
122.279
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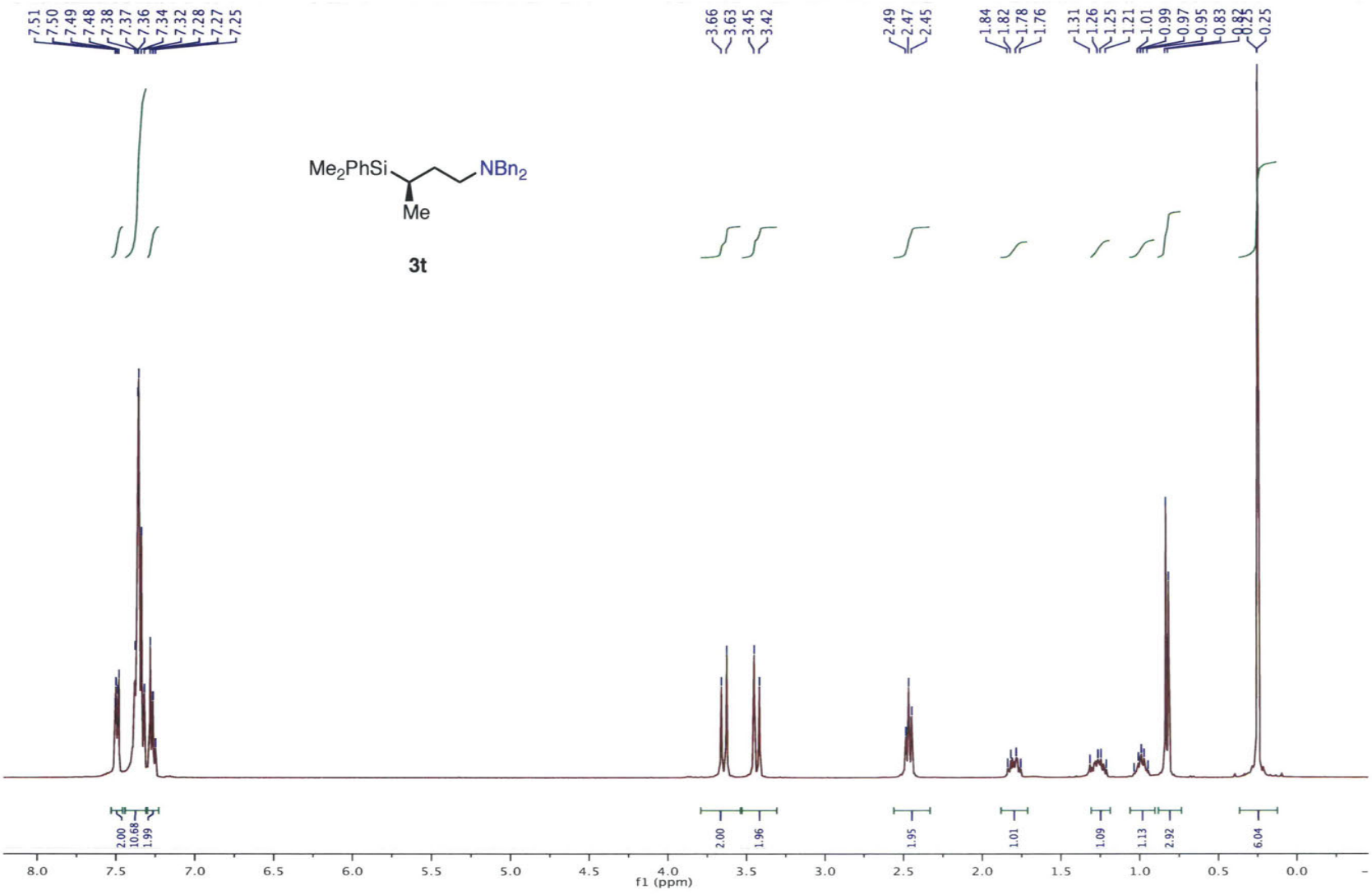
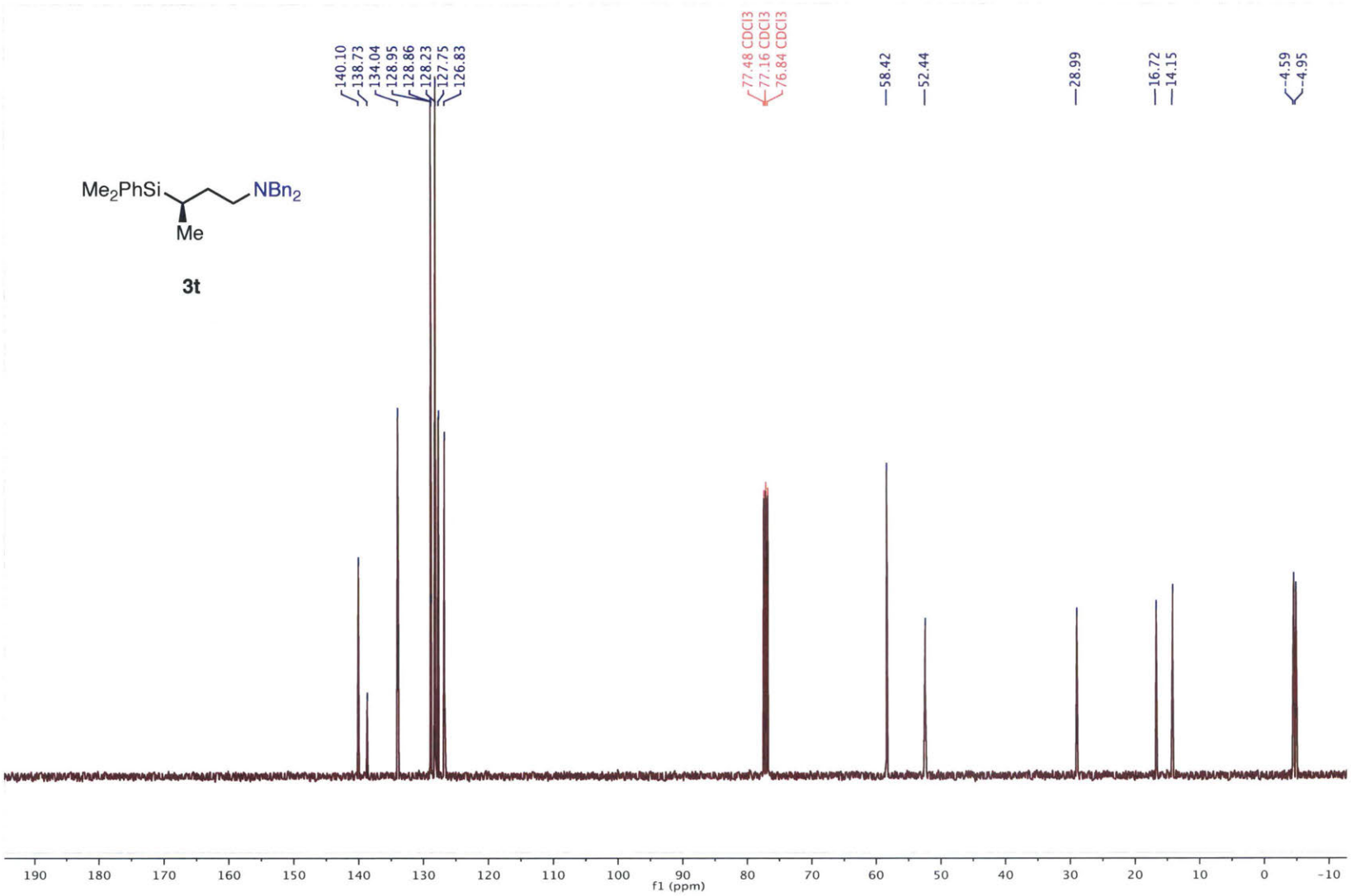
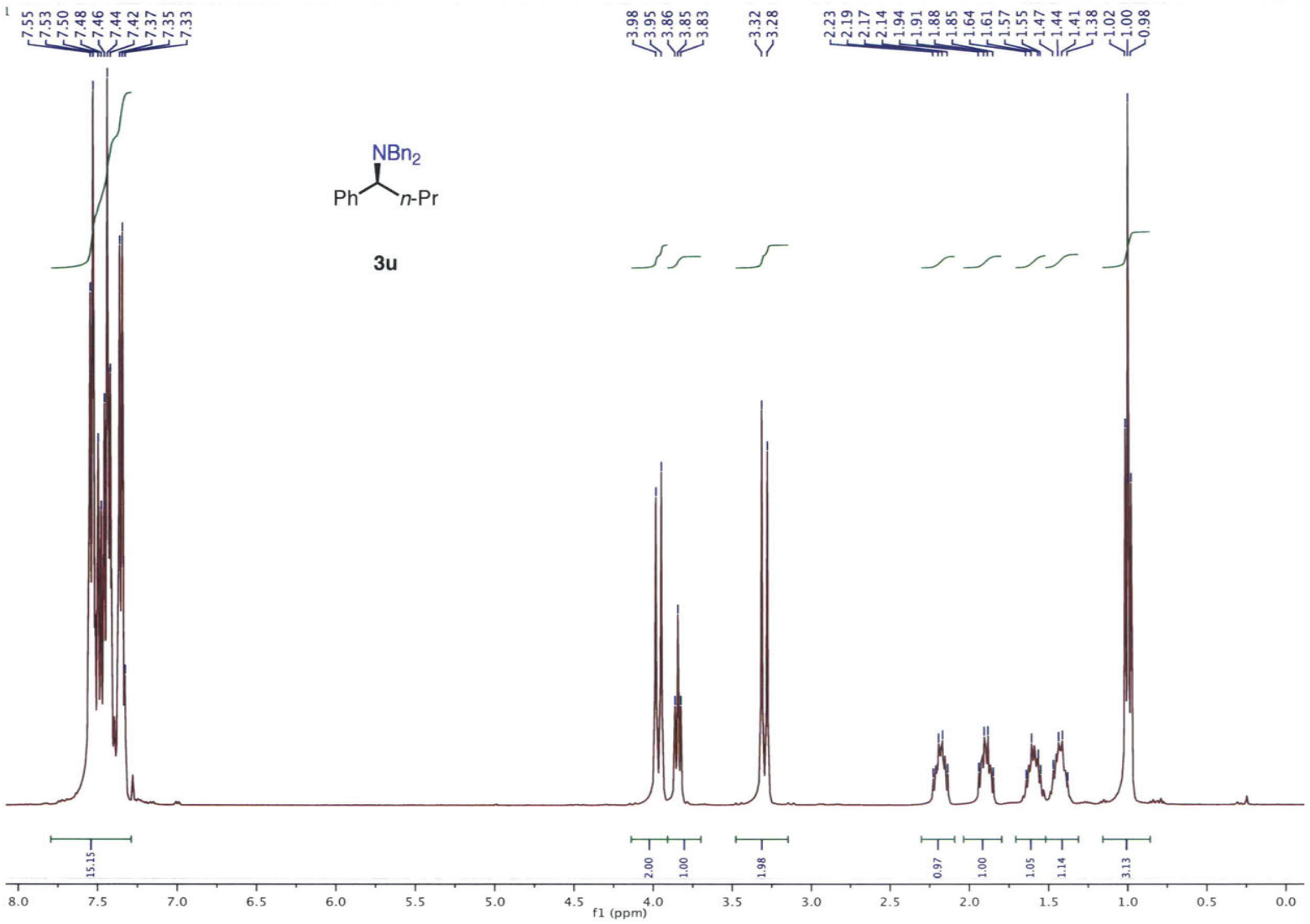
77.000 CDCl3
76.682 CDCl3
58.293
51.224
36.638
33.000
23.029
S
NBn2
Me
3s
40 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)


7.51
7.50
7.49
7.48
7.38
7.37
7.36
7.34
7.32
7.28
7.27
7.25
3.66
3.63
3.45
3.42
2.49
2.47
2.45
1.84
1.82
1.78
1.76
1.31
1.26
1.25
1.21
1.01
0.99
0.97
0.95
0.83
0.25
0.25
Me2PhSi
NBn2
Me
3t
2.00
10.68
1.99
2.00
1.96
1.95
1.01
1.09
1.13
2.92
6.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Me2PhSi
NBn2
Me
3t
140.10
138.73
134.04
128.95
128.86
128.23
127.75
126.83
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
58.42
52.44
28.99
16.72
14.15
-4.59
-4.95
f1 (ppm)


7.55
7.53
7.50
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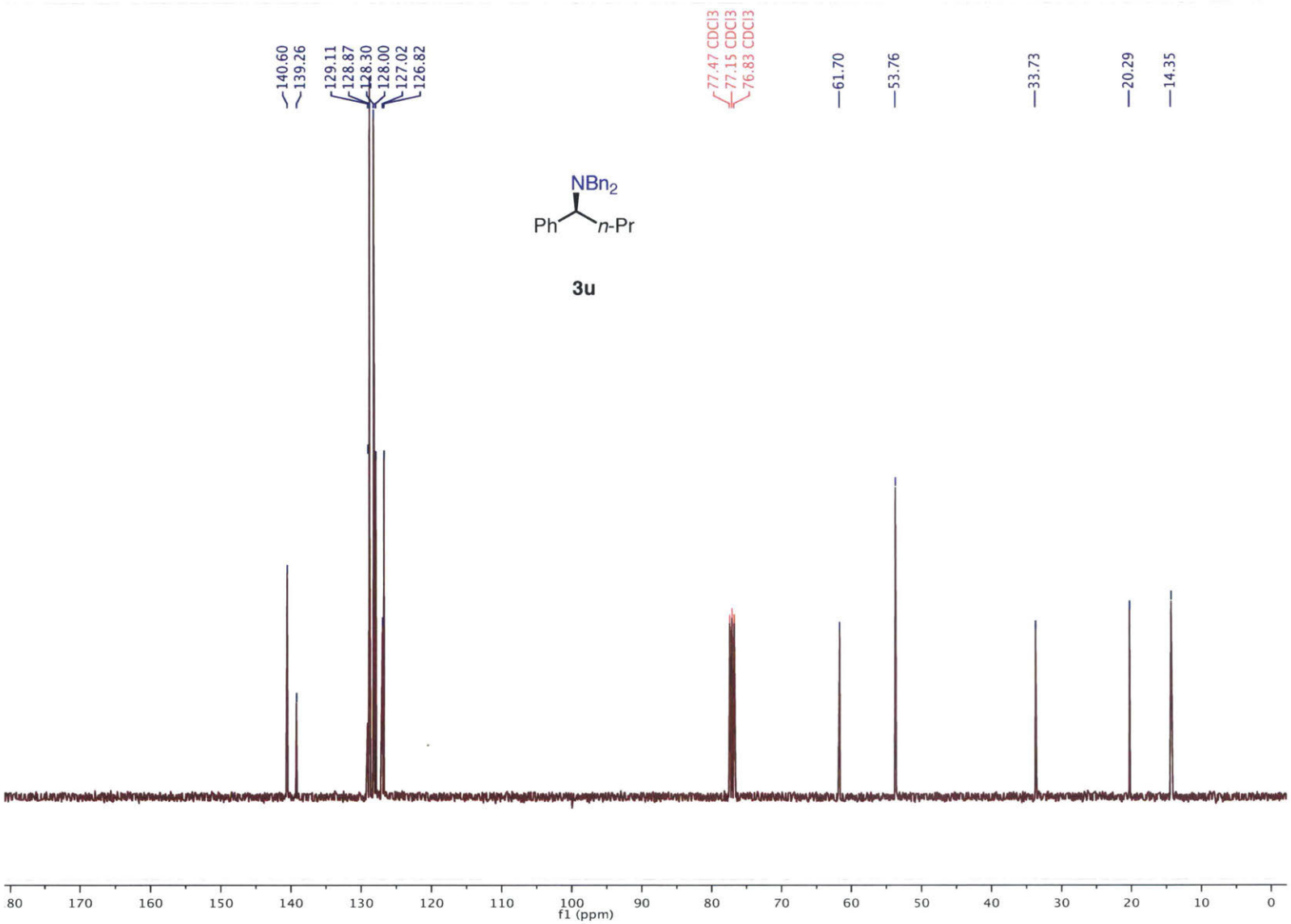
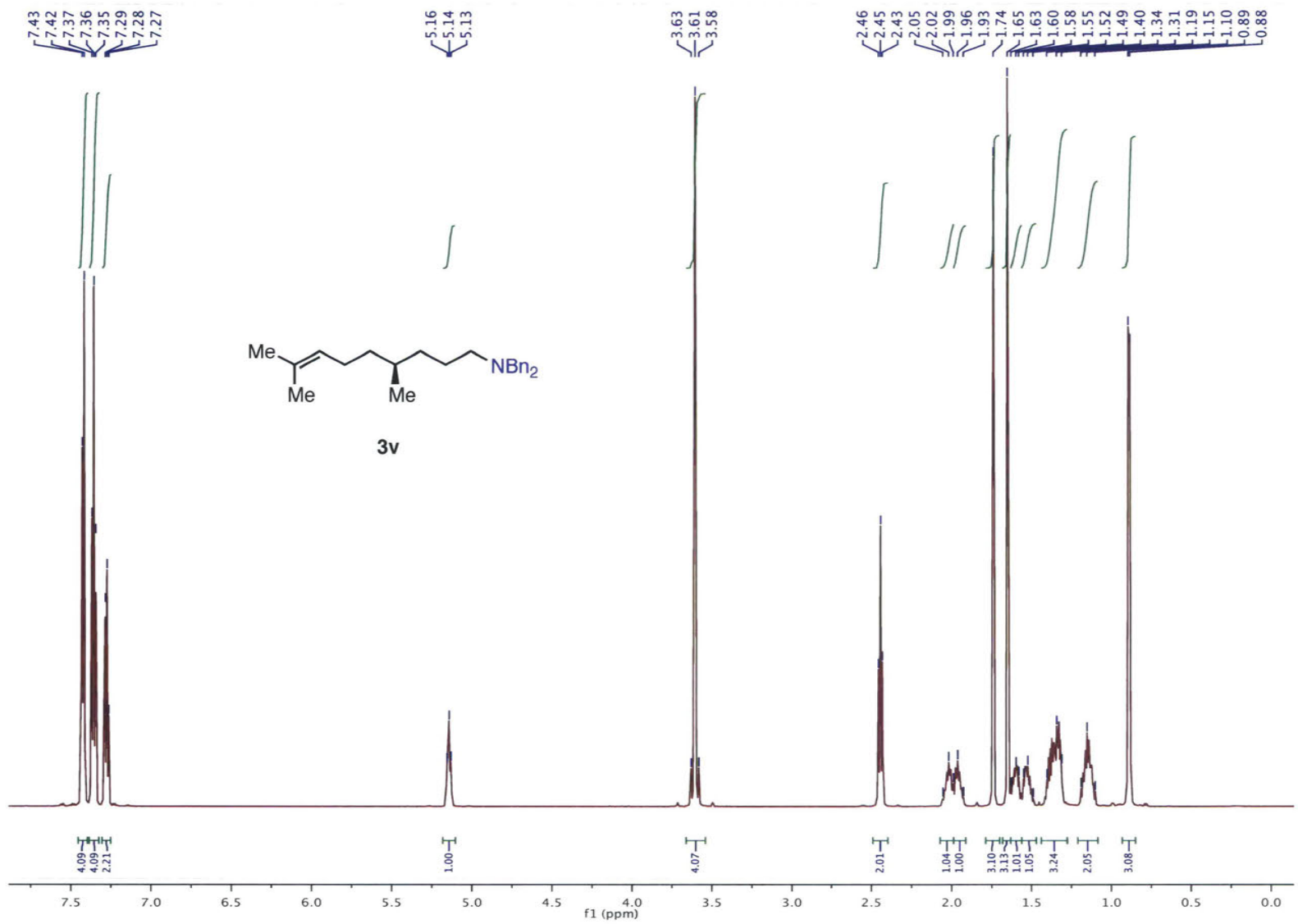
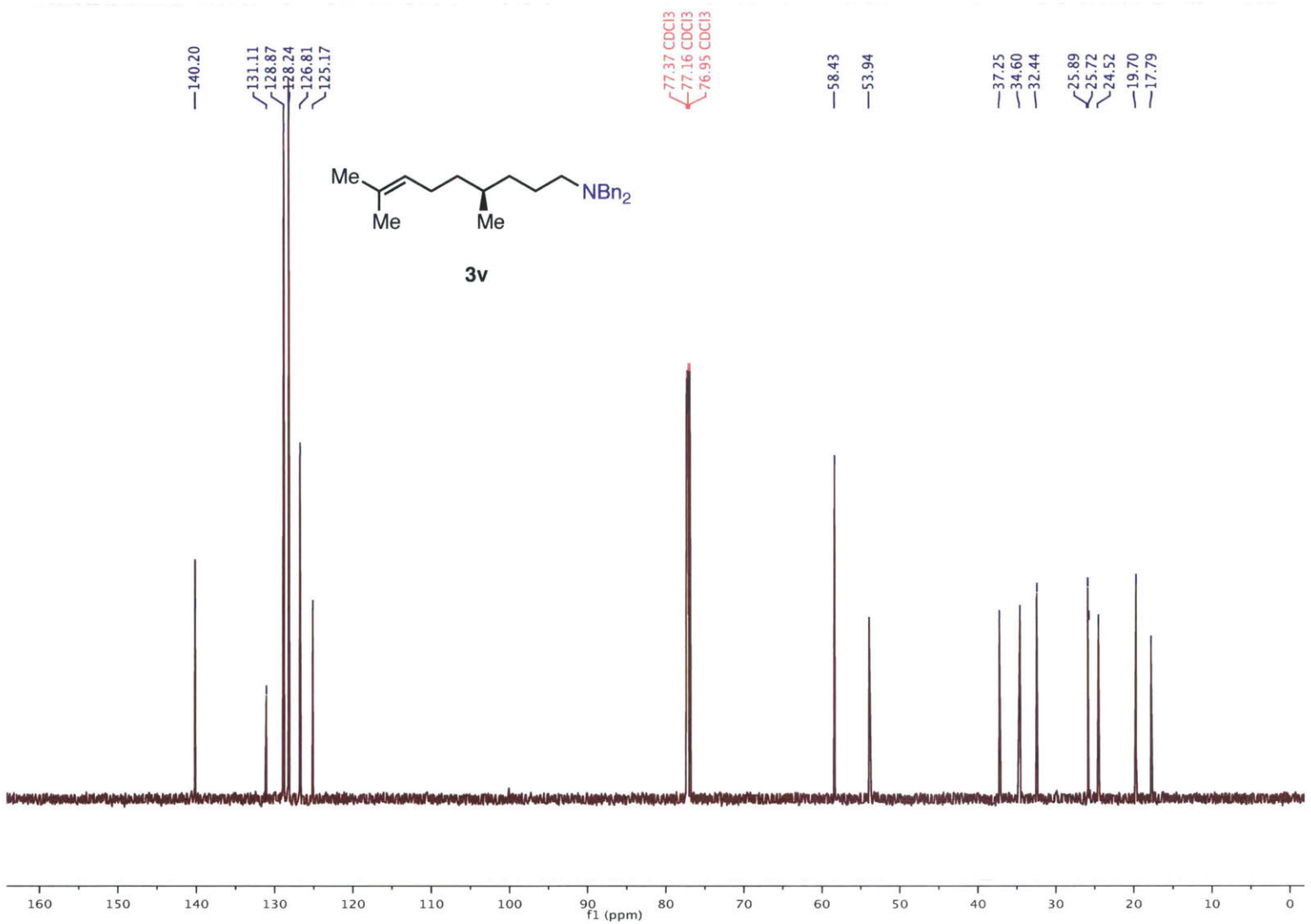
7.46
7.44
7.42
7.37
7.35
7.33
3.98
3.95
3.86
3.85
3.83
3.32
3.28
2.23
2.19
2.17
2.14
1.94
1.91
1.88
1.85
1.64
1.61
1.57
1.55
1.47
1.44
1.41
1.38
1.02
1.00
0.98
NBn2
Ph
n-Pr
3u
15.15
2.00
1.00
1.98
0.97
1.00
1.05
1.14
3.13
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


140.60
139.26
129.11
128.87
128.30
128.00
127.02
126.82
77.47 CDCl3
77.15 CDCl3
76.83 CDCl3
61.70
53.76
33.73
20.29
14.35
NBn2
Ph
n-Pr
3u
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.43
7.42
7.37
7.36
7.35
7.29
7.28
7.27
5.16
5.14
5.13
3.63
3.61
3.58
2.46
2.45
2.43
2.05
2.02
1.99
1.96
1.93
1.74
1.65
1.63
1.60
1.58
1.55
1.52
1.49
1.40
1.34
1.31
1.19
1.15
1.10
0.89
0.88
Me
Me
Me
NBn2
3v
4.09
4.09
2.21
1.00
4.07
2.01
1.04
1.00
3.10
3.13
1.01
1.05
3.24
2.05
3.08
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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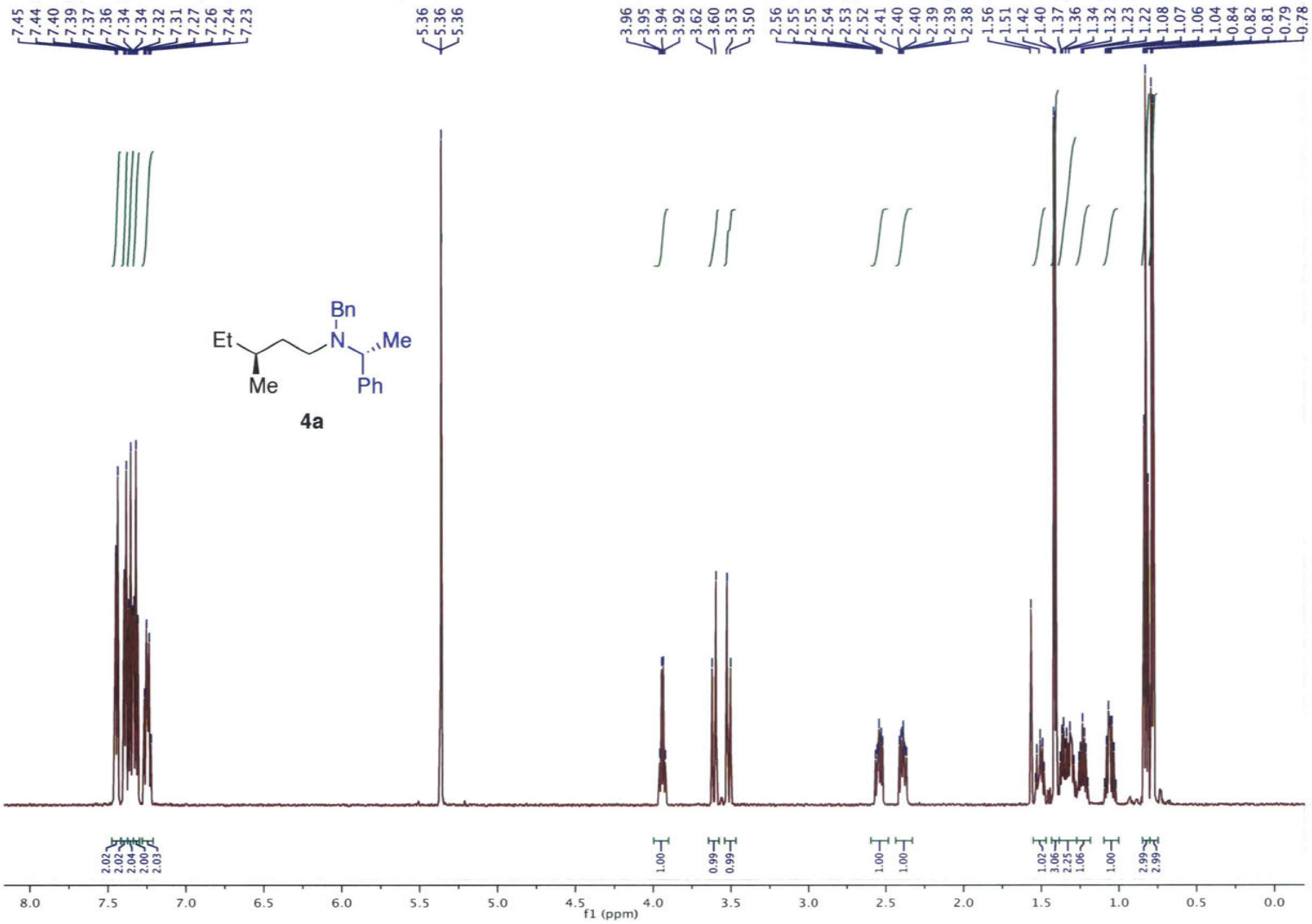
131.11
128.87
128.24
126.81
125.17
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
58.43
53.94
37.25
34.60
32.44
25.89
25.72
24.52
19.70
17.79
Me
Me
Me
NBn2
3v
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.44
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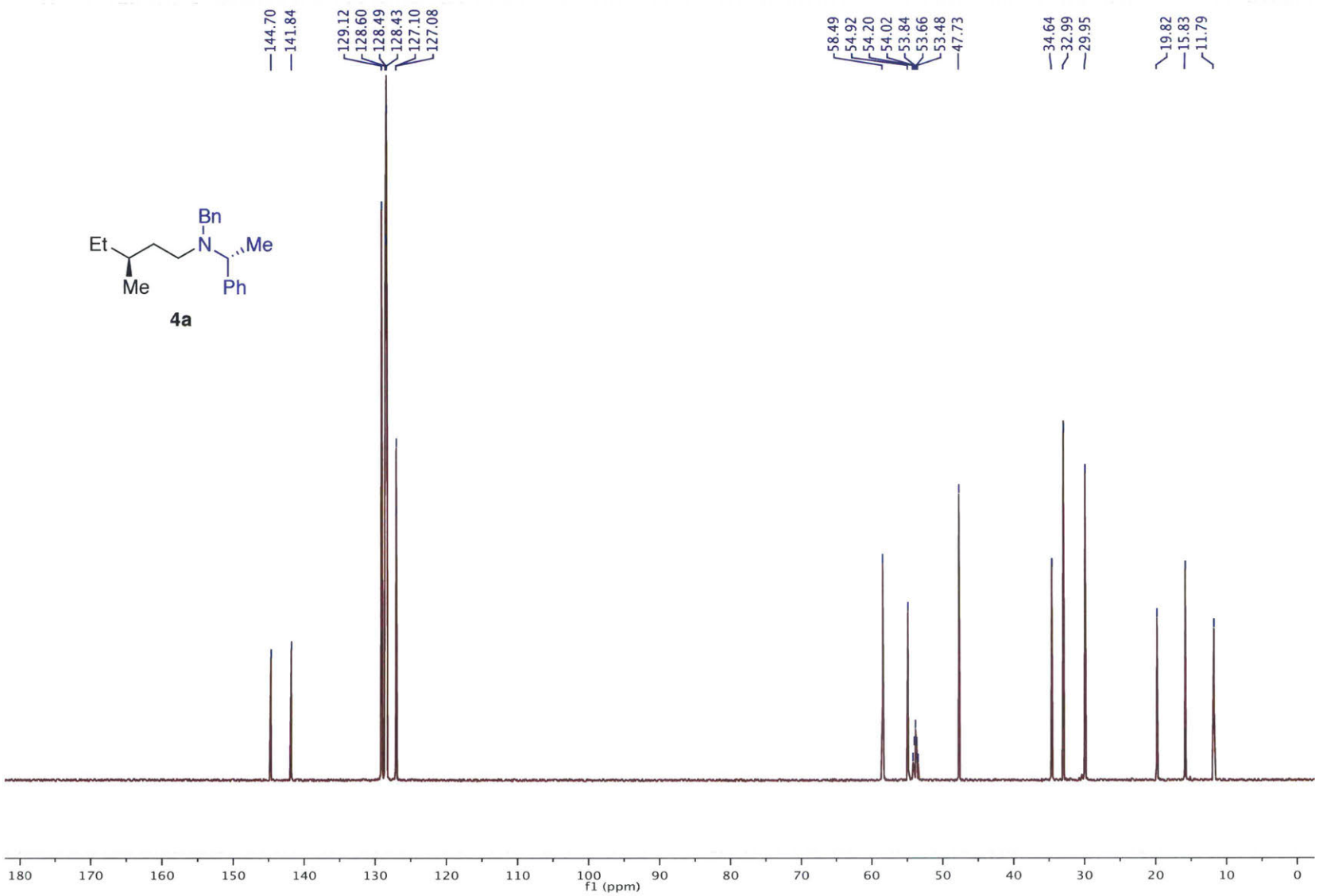
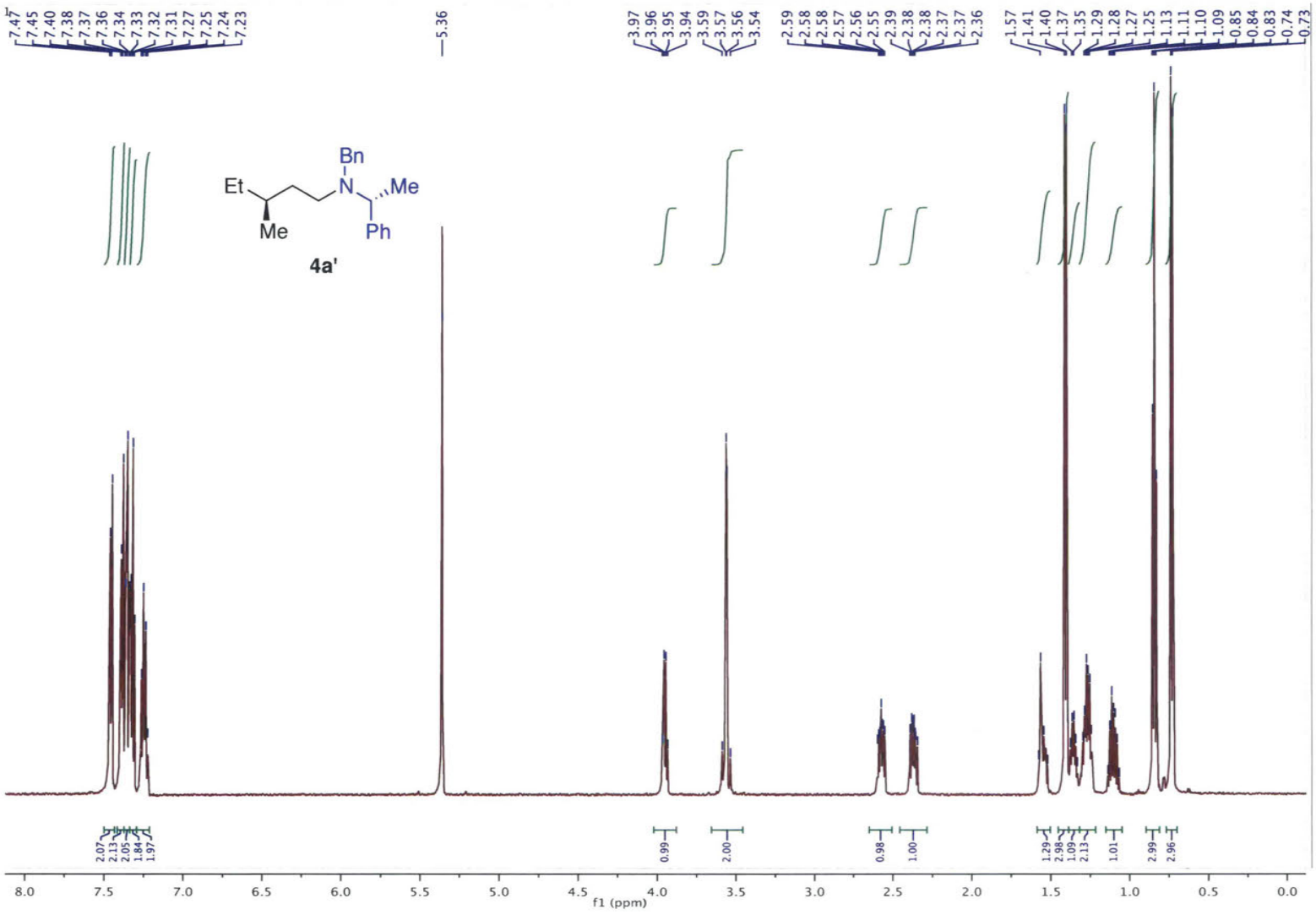
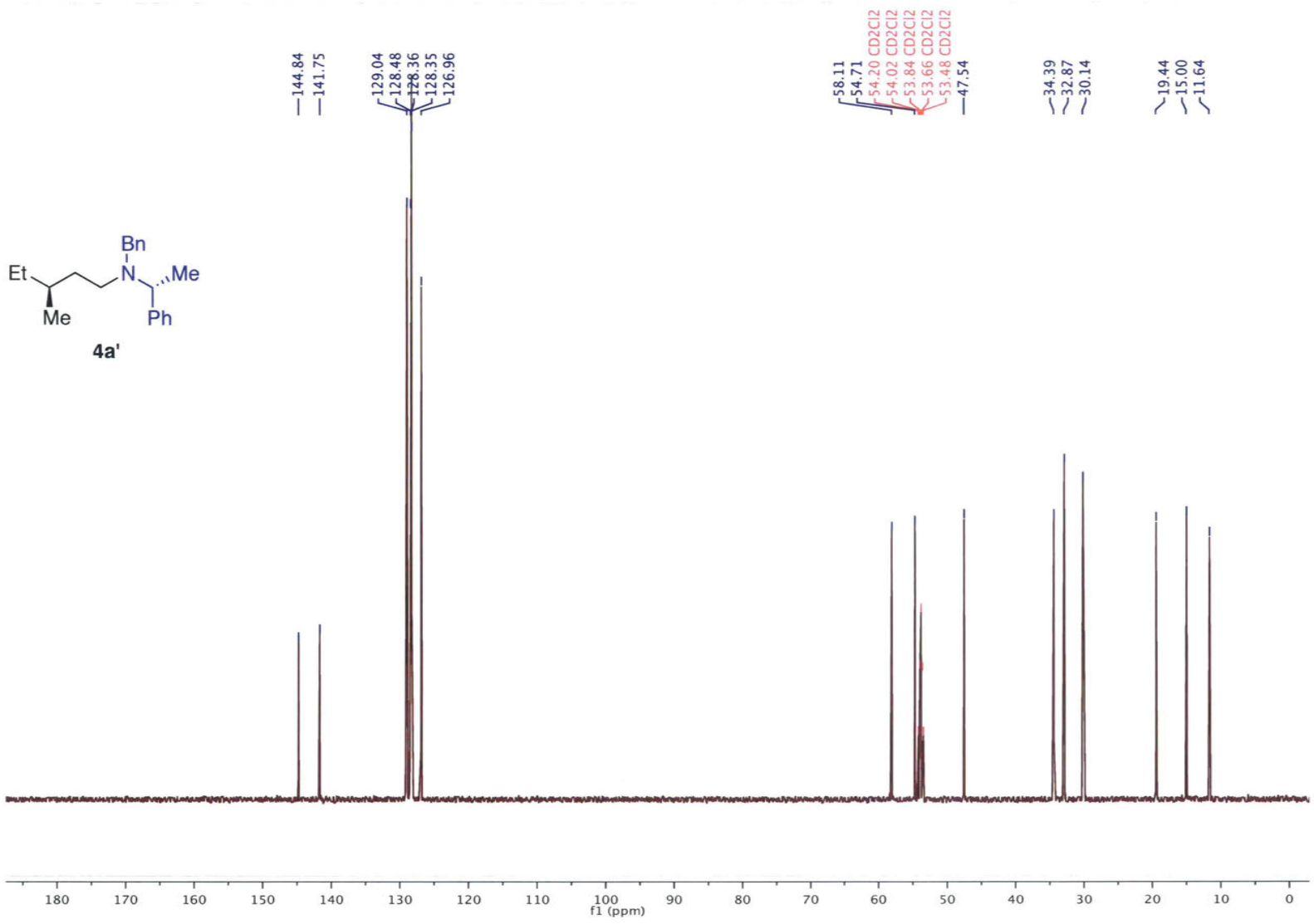
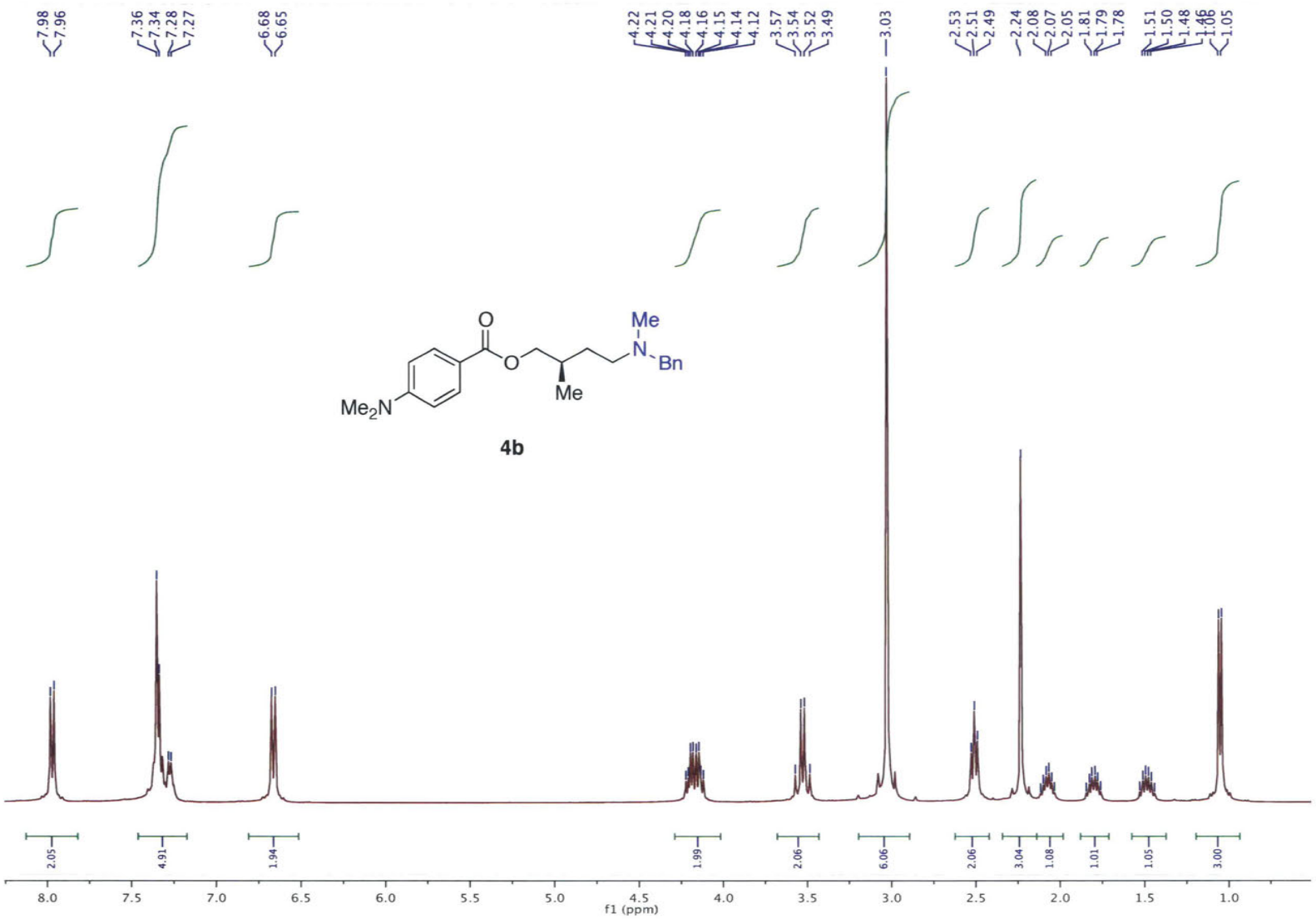
7.39
7.37
7.36
7.34
7.34
7.32
7.31
7.27
7.26
7.24
7.23
5.36
5.36
5.36
3.96
3.95
3.94
3.92
3.62
3.60
3.53
3.50
2.56
2.55
2.55
2.54
2.53
2.52
2.41
2.40
2.40
2.39
2.39
2.38
1.56
1.51
1.42
1.40
1.37
1.36
1.34
1.32
1.23
1.22
1.08
1.07
1.06
1.04
0.84
0.82
0.81
0.79
0.78
Bn
Et
N
Me
Me
Ph
4a
2.02
2.02
2.04
2.00
2.03
1.00
0.99
0.99
1.00
1.00
1.02
3.06
2.25
1.06
1.00
2.99
2.99
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

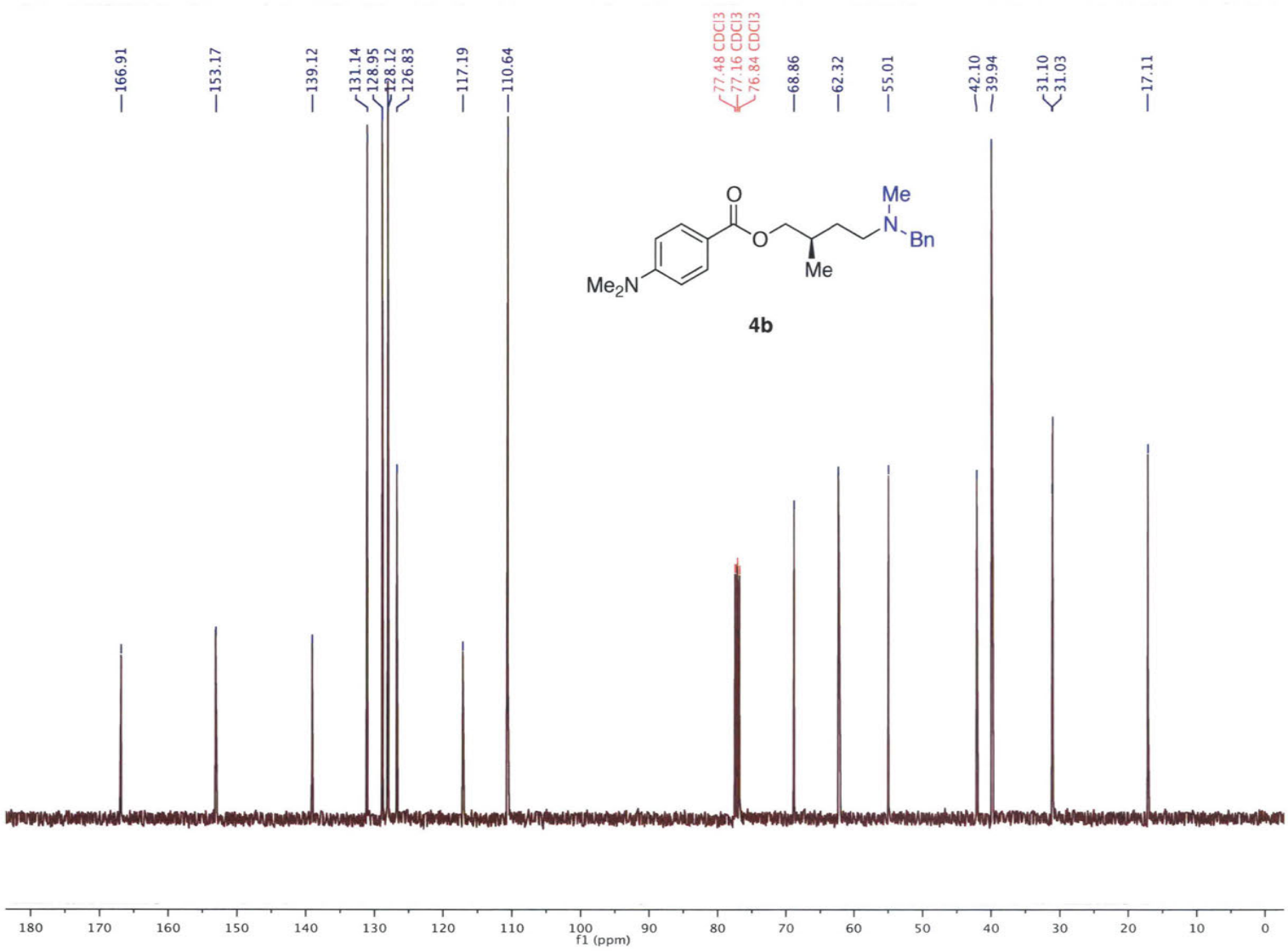

144.70
141.84
129.12
128.60
128.49
128.43
127.10
127.08
58.49
54.92
54.20
54.02
53.84
53.66
53.48
47.73
34.64
32.99
29.95
19.82
15.83
11.79
Bn
N
Et
Me
Me
Ph
4a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

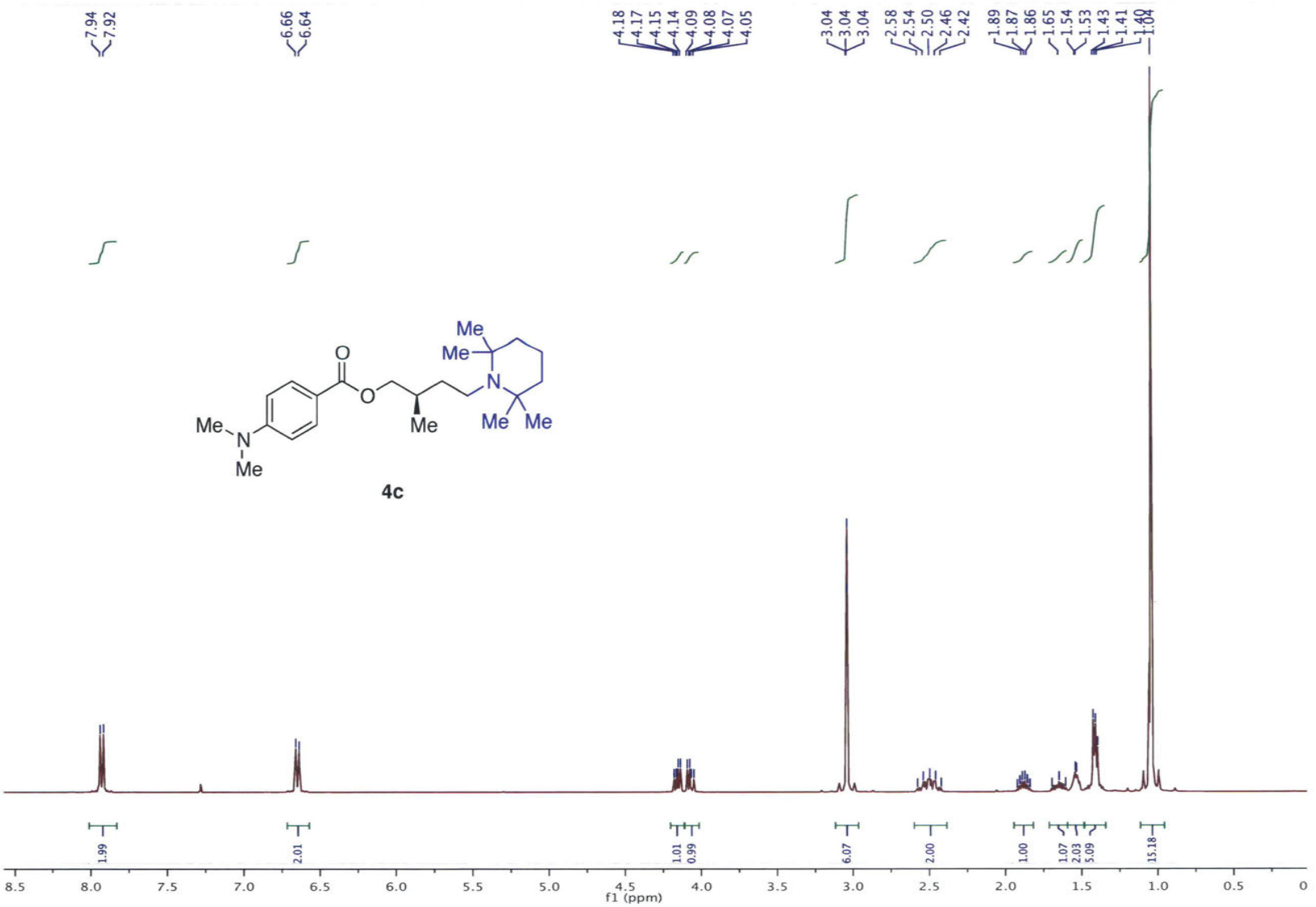

Bn
Et
N
Me
Me
Ph
4a'
f1 (ppm)


144.84
141.75
129.04
128.48
128.36
128.35
126.96
58.11
54.71
54.20 CD2Cl2
54.02 CD2Cl2
53.84 CD2Cl2
53.66 CD2Cl2
53.48 CD2Cl2
47.54
34.39
32.87
30.14
19.44
15.00
11.64
Bn
Et
N
Me
Me
Ph
4a'
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

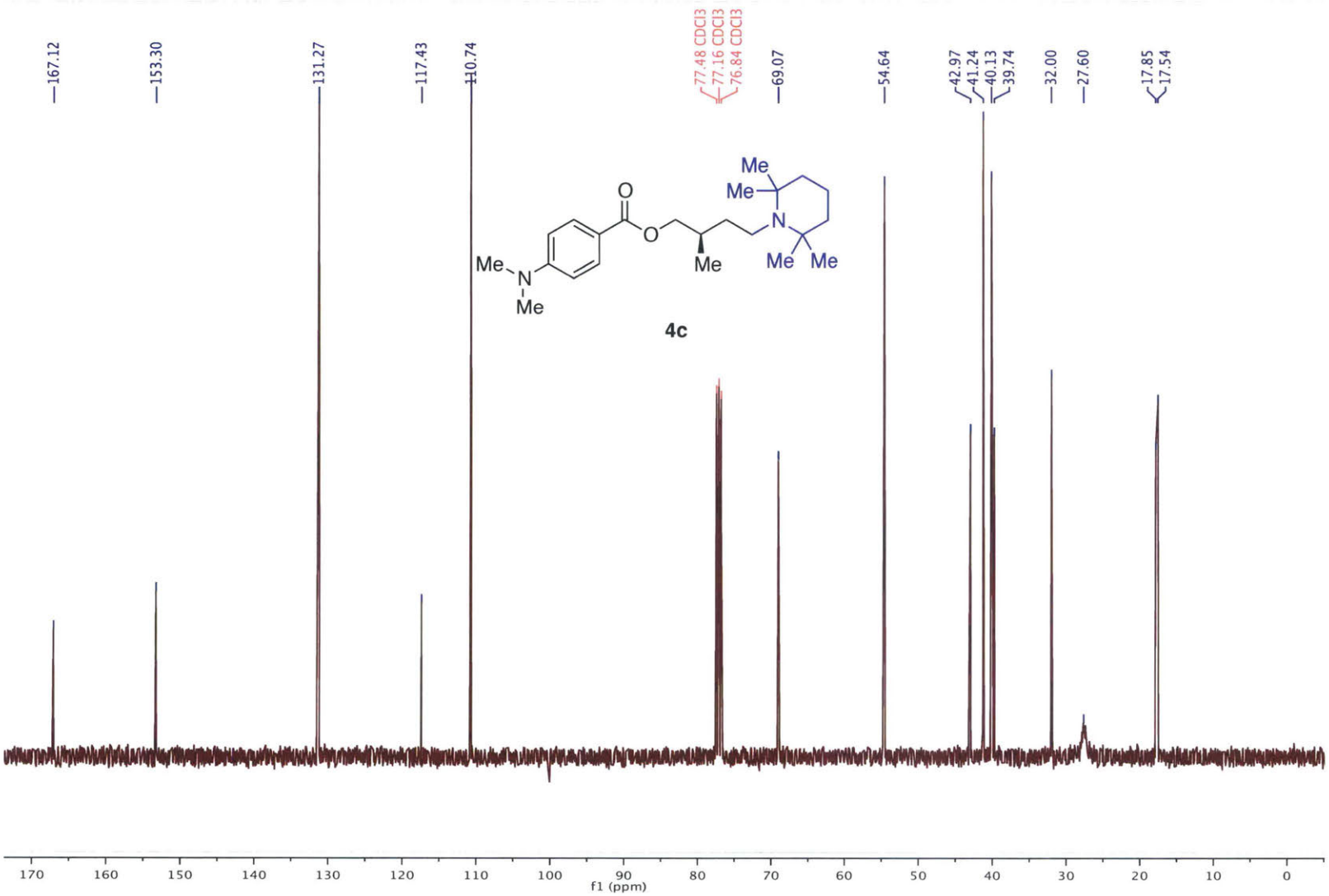

7.98
7.96
7.36
7.34
7.28
7.27
6.68
6.65
4.22
4.21
4.20
4.18
4.16
4.15
4.14
4.12
3.57
3.54
3.52
3.49
3.03
2.53
2.51
2.49
2.24
2.08
2.07
2.05
1.81
1.79
1.78
1.51
1.50
1.48
1.46
1.06
1.05
O
O
Me
N
Bn
Me
Me2N
2.05
4.91
1.94
1.99
2.06
6.06
2.06
3.04
1.08
1.01
1.05
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

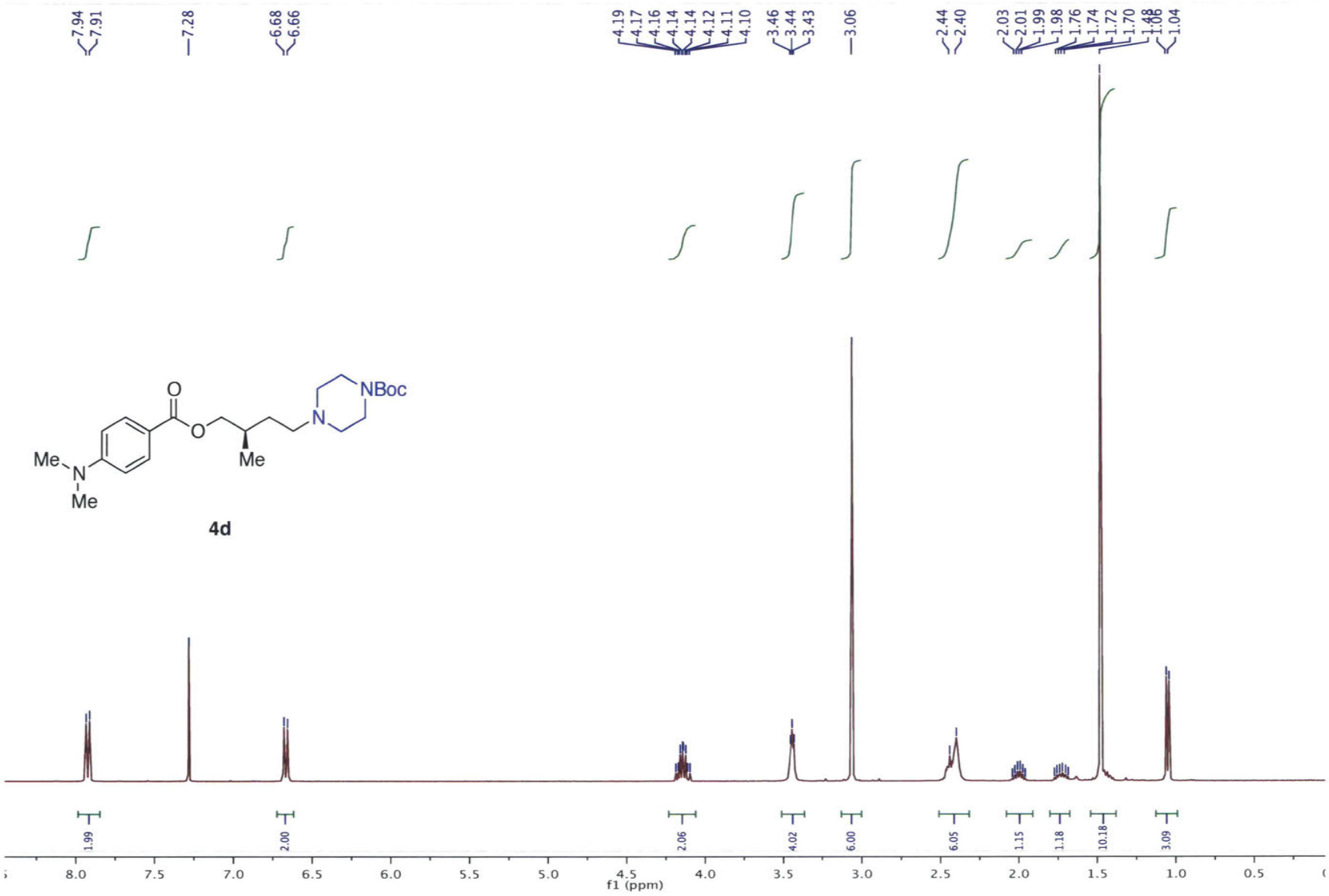
4b


166.91
153.17
139.12
131.14
128.95
128.12
126.83
117.19
110.64
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.86
62.32
55.01
42.10
39.94
31.10
31.03
17.11
O
O
Me
N
Bn
Me
Me2N
4b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

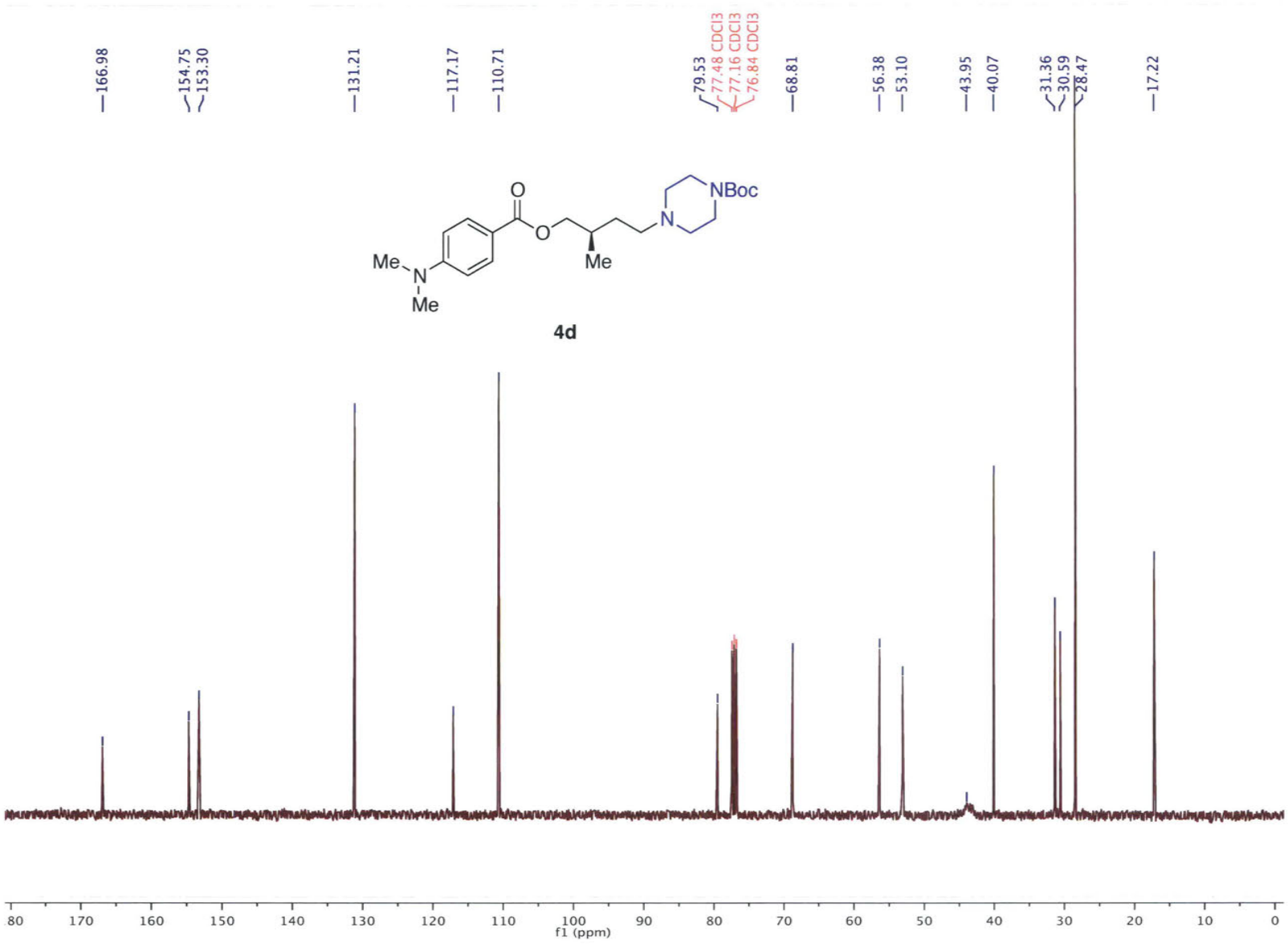

7.94
7.92
6.66
6.64
4.18
4.17
4.15
4.14
4.09
4.08
4.07
4.05
3.04
3.04
3.04
2.58
2.54
2.50
2.46
2.42
1.89
1.87
1.86
1.65
1.54
1.53
1.43
1.41
1.40
1.04
Me
Me
N
Me
Me
Me
O
O
Me
N
Me
1.99
2.01
1.01
0.99
6.07
2.00
1.00
1.07
2.03
5.09
15.18
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

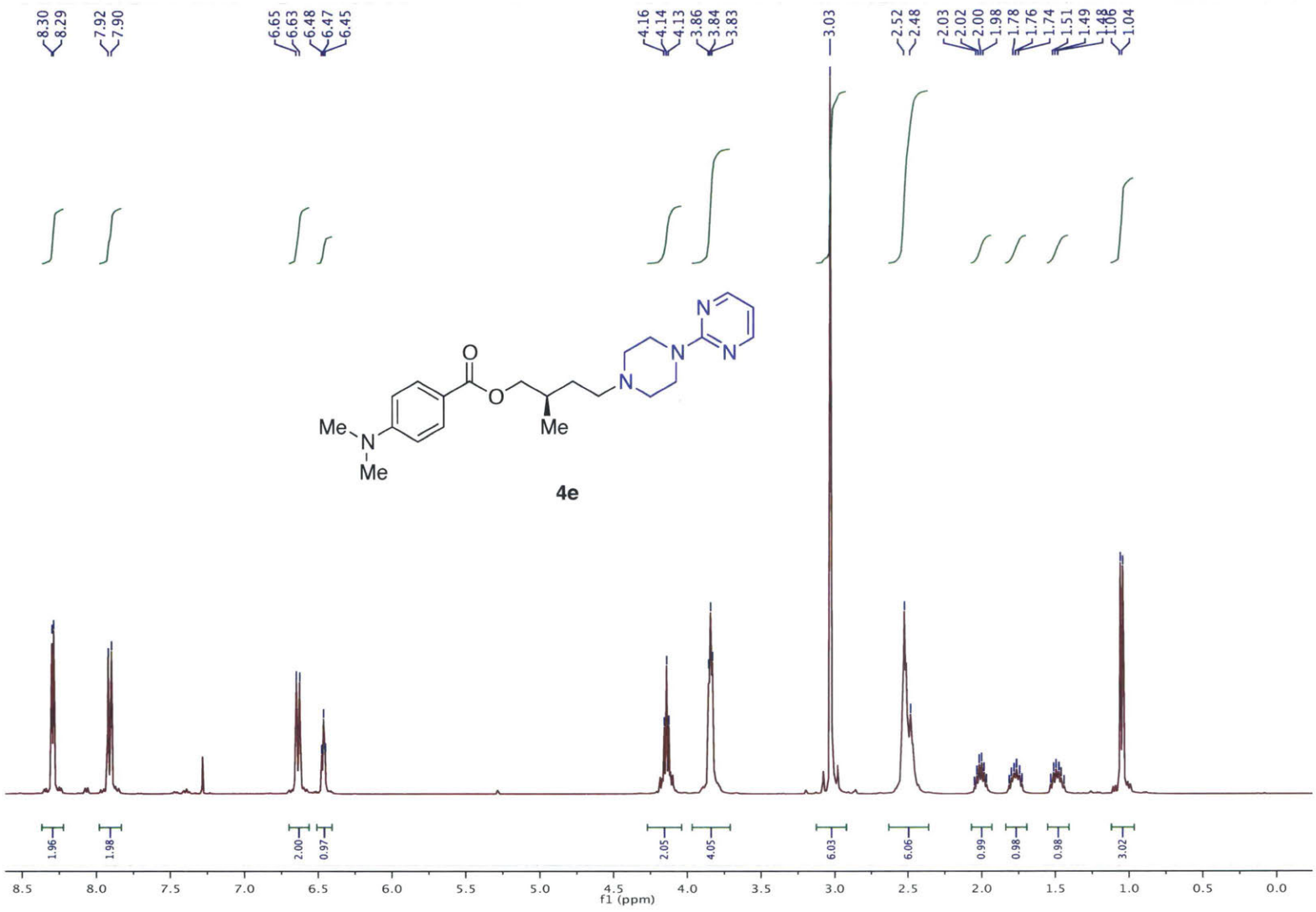
4c


167.12
153.30
131.27
117.43
110.74
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
69.07
54.64
42.97
41.24
40.13
39.74
32.00
27.60
17.85
17.54
Me
Me
N
Me
Me
Me
O
O
Me
Me
N
Me
4c
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.94
7.91
7.28
6.68
6.66
4.19
4.17
4.16
4.14
4.14
4.12
4.11
4.10
3.46
3.44
3.43
3.06
2.44
2.40
2.03
2.01
1.99
1.98
1.76
1.74
1.72
1.70
1.04
O
O
N
NBoc
Me
N
Me
Me
1.99
2.00
2.06
4.02
6.00
6.05
1.15
1.18
10.18
3.09
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
f1 (ppm)

4d


166.98
154.75
153.30
131.21
117.17
110.71
79.53
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.81
56.38
53.10
43.95
40.07
31.36
30.59
28.47
17.22
O
O
NBoc
N
Me
Me
N
Me
4d
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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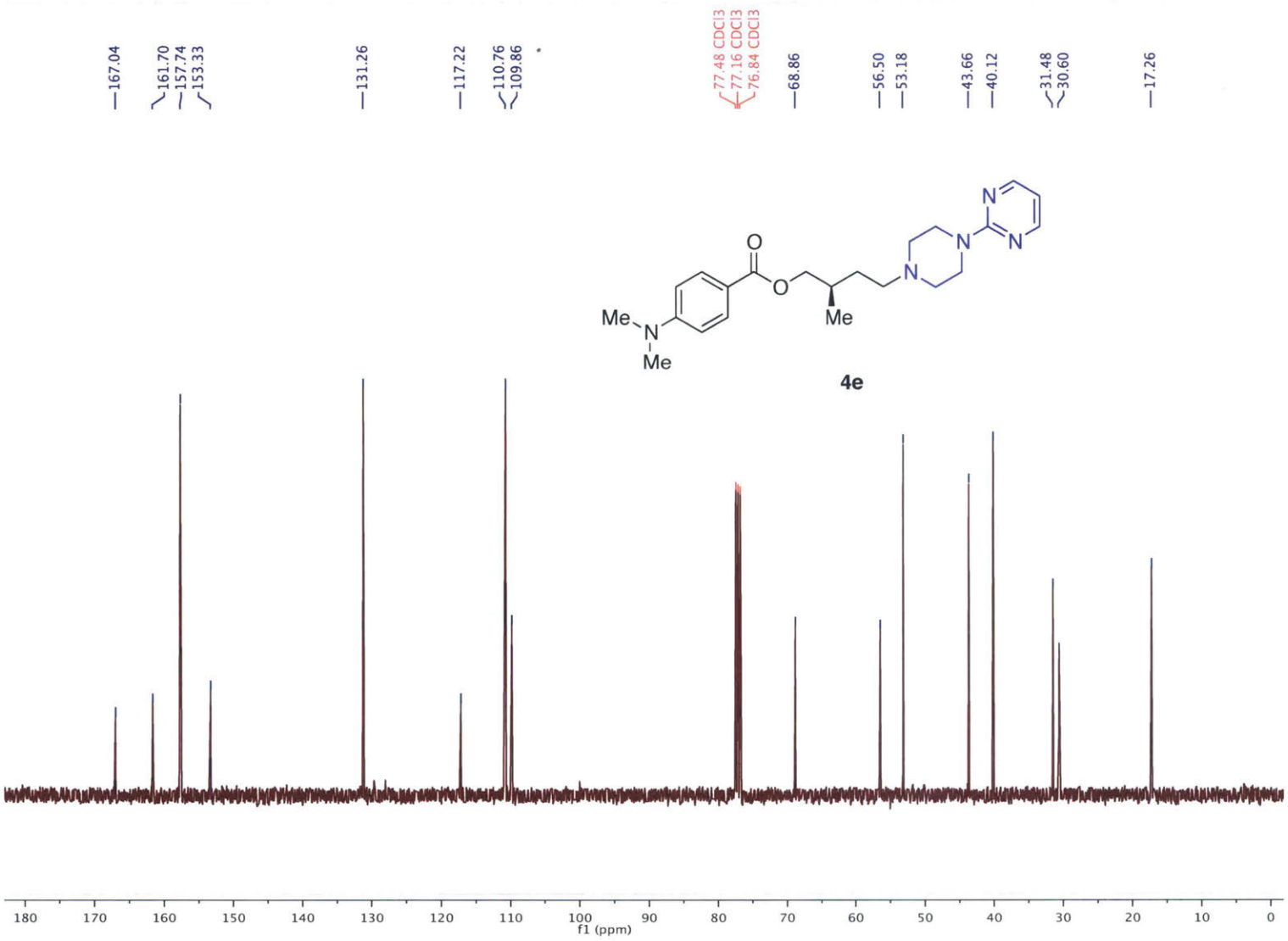
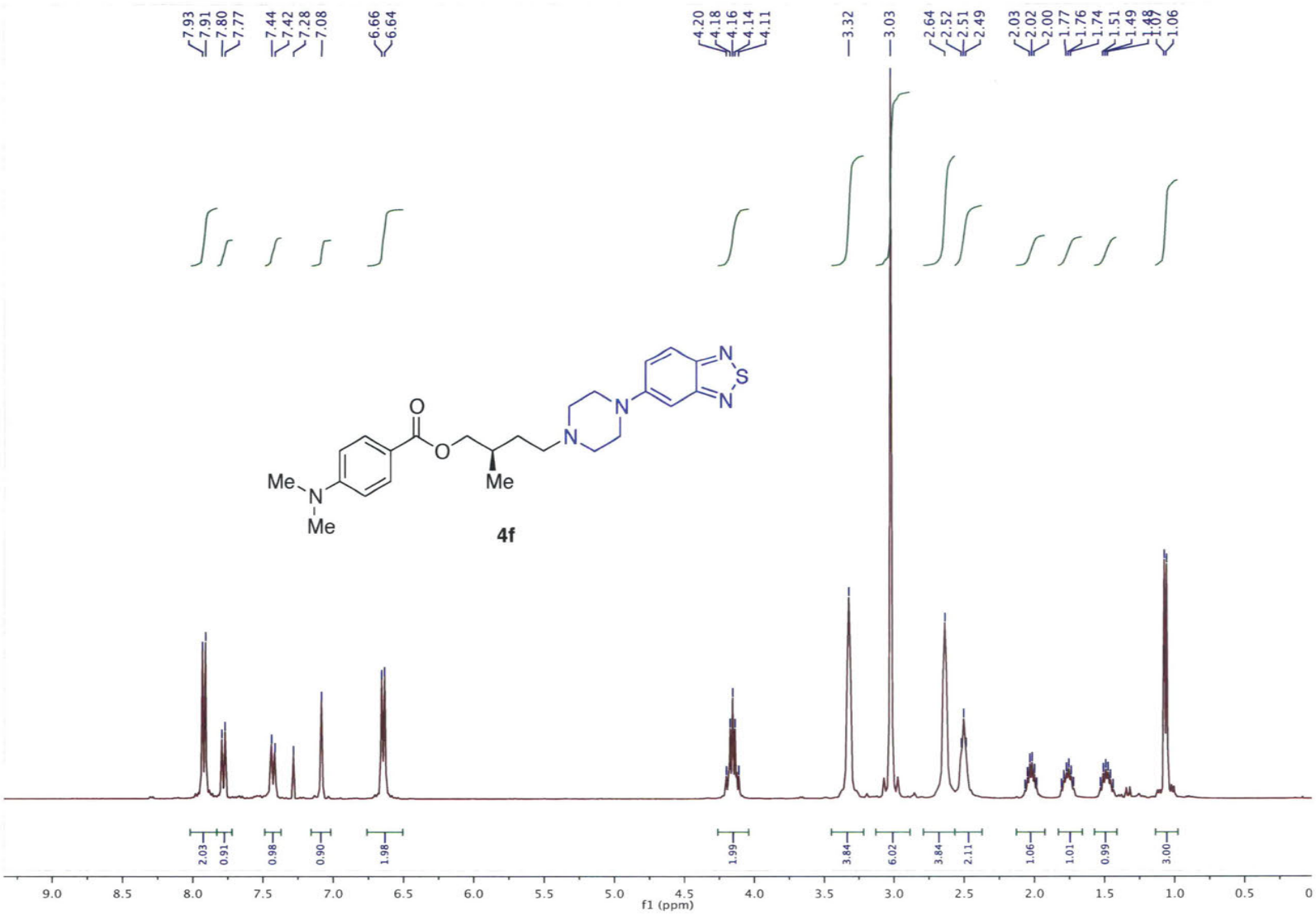
8.29
7.92
7.90
6.65
6.63
6.48
6.47
6.45
4.16
4.14
4.13
3.86
3.84
3.83
3.03
2.52
2.48
2.03
2.02
2.00
1.98
1.78
1.76
1.74
1.51
1.49
1.48
1.06
1.04
Me
N
Me
O
O
N
N
N
Me
4e
1.96
1.98
2.00
0.97
2.05
4.05
6.03
6.06
0.99
0.98
0.98
3.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.04
161.70
157.74
153.33
131.26
117.22
110.76
109.86
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.86
56.50
53.18
43.66
40.12
31.48
30.60
17.26
Me
N
Me
O
O
Me
N
N
N
4e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.93
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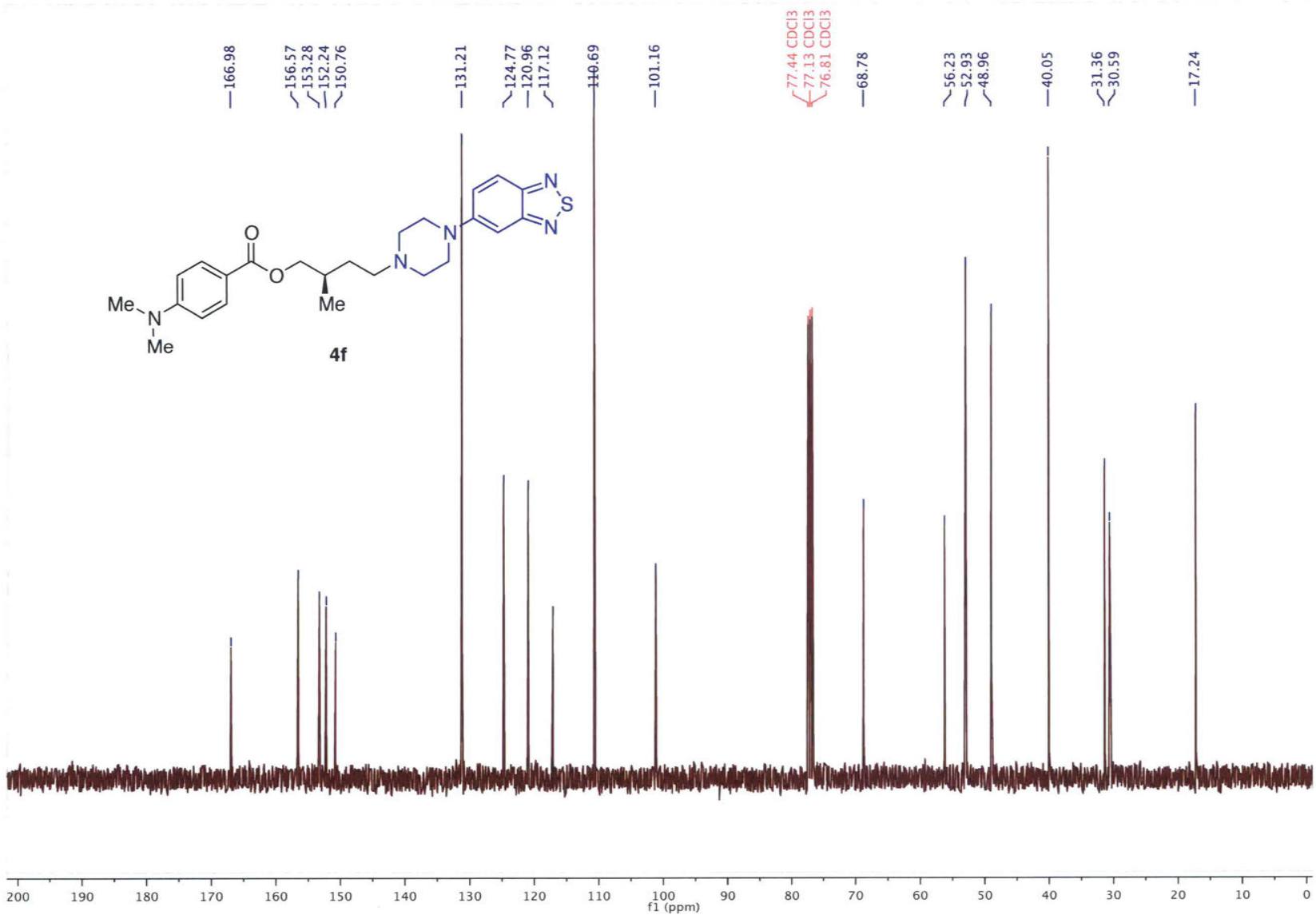
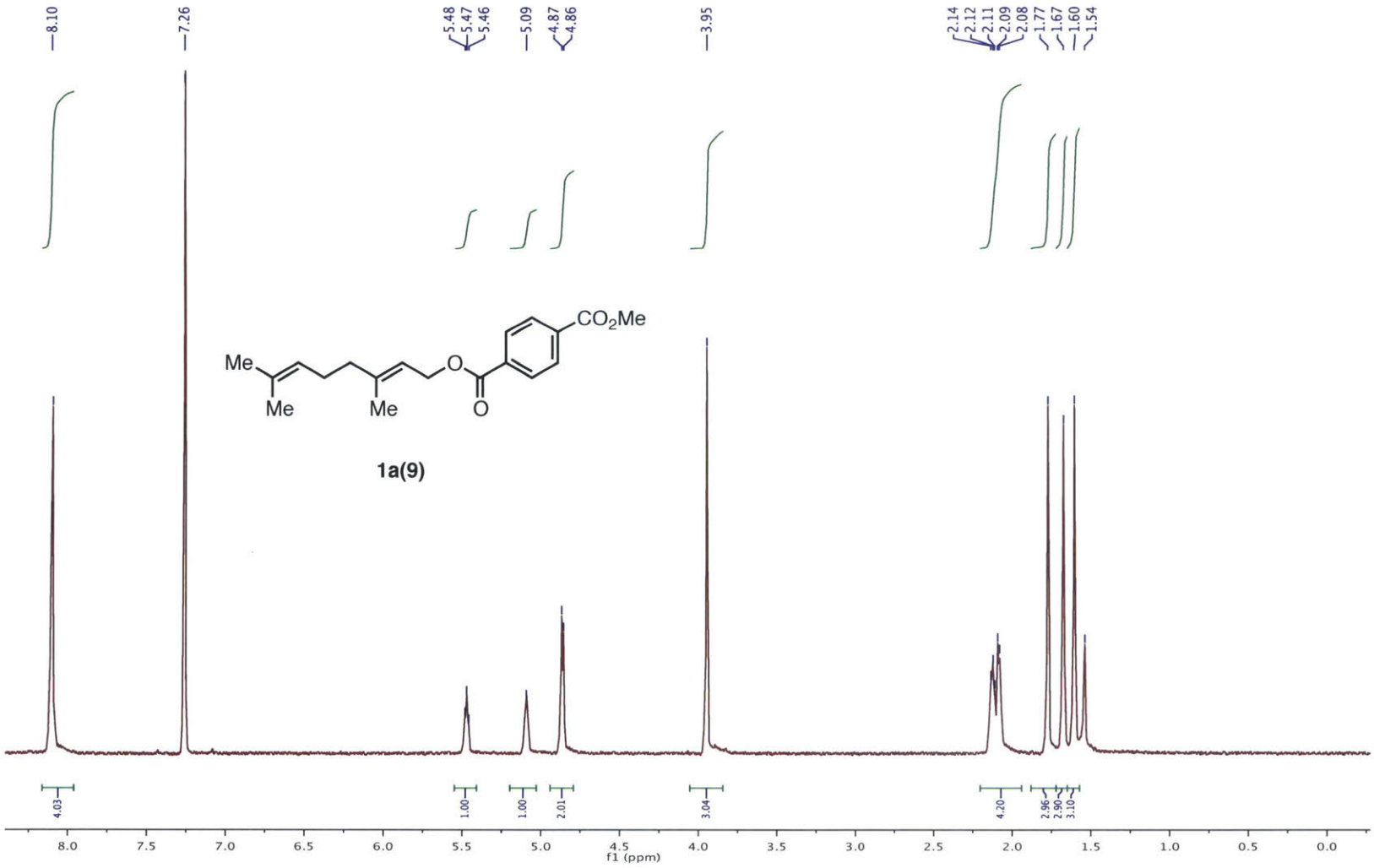
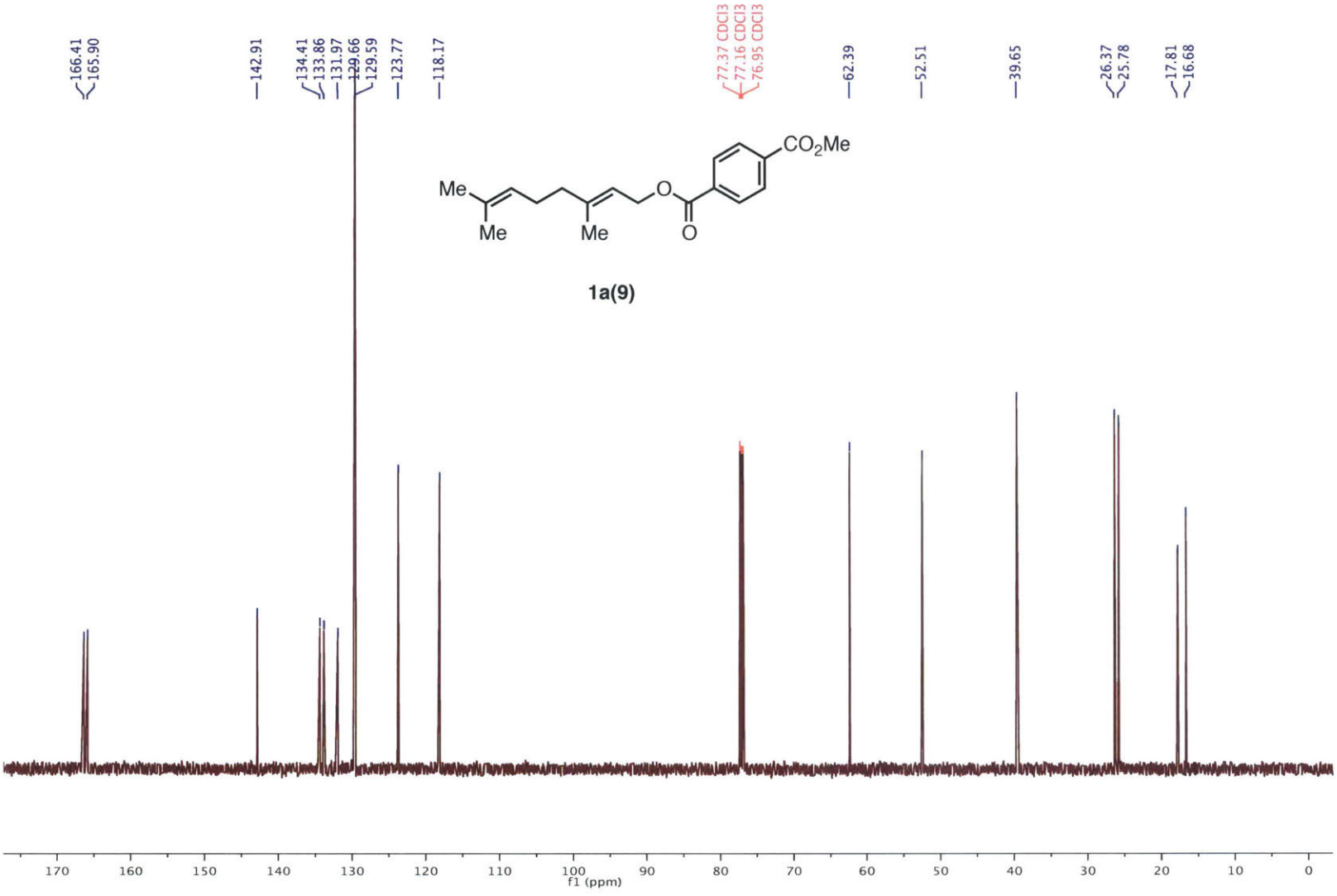
7.80
7.77
7.44
7.42
7.28
7.08
6.66
6.64
4.20
4.18
4.16
4.14
4.11
3.32
3.03
2.64
2.52
2.51
2.49
2.03
2.02
2.00
1.77
1.76
1.74
1.51
1.49
1.06
Me
N
Me
O
O
Me
N
N
N
S
N
4f
2.03
0.91
0.98
0.90
1.98
1.99
3.84
6.02
3.84
2.11
1.06
1.01
0.99
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

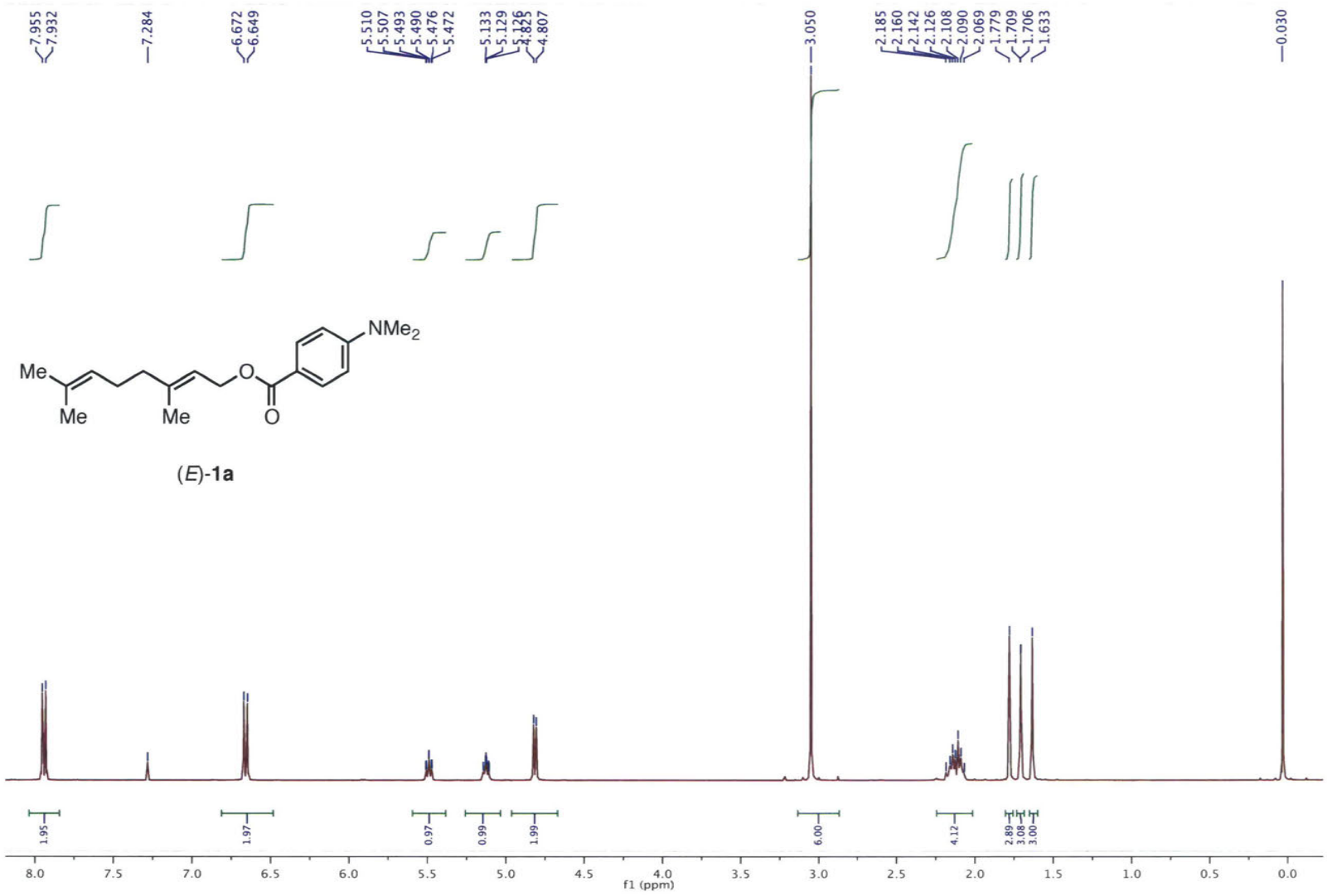

166.98
156.57
153.28
152.24
150.76
131.21
124.77
120.96
117.12
110.69
101.16
77.44 CDCl3
77.13 CDCl3
76.81 CDCl3
68.78
56.23
52.93
48.96
40.05
31.36
30.59
17.24
Me
N
Me
O
O
Me
N
N
N
S
N
4f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Characterization of Substrates:

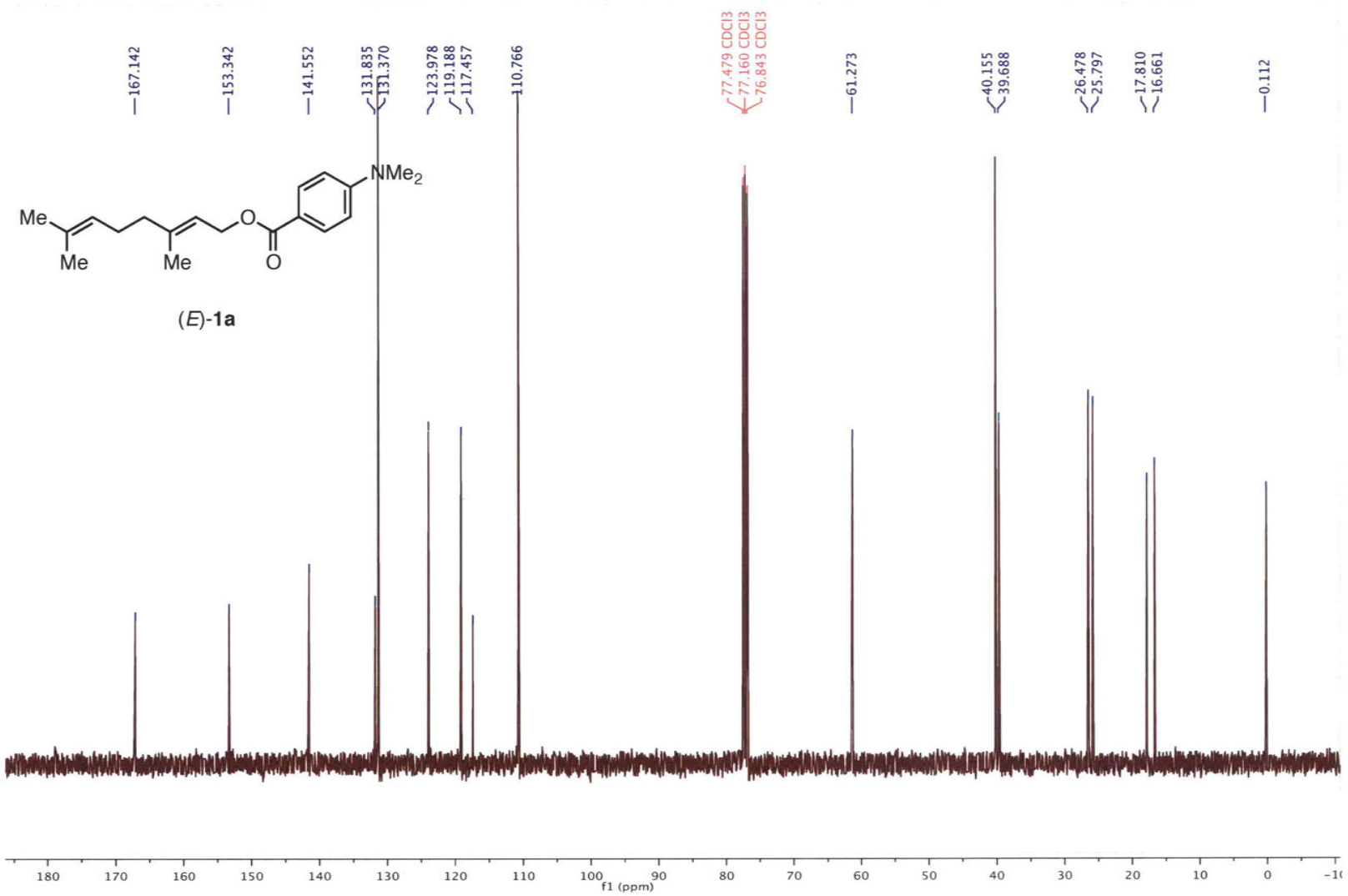


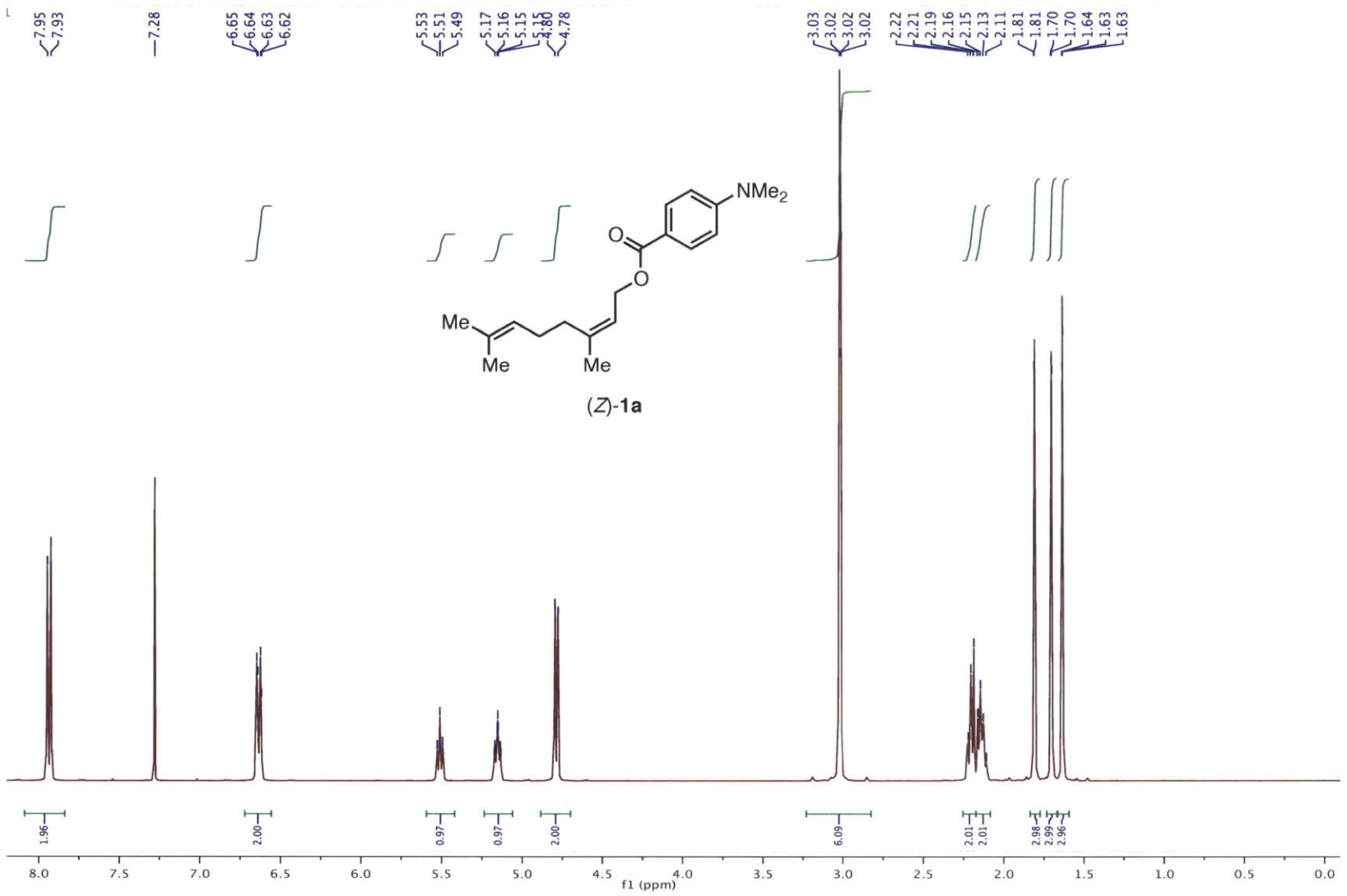
1a(9)

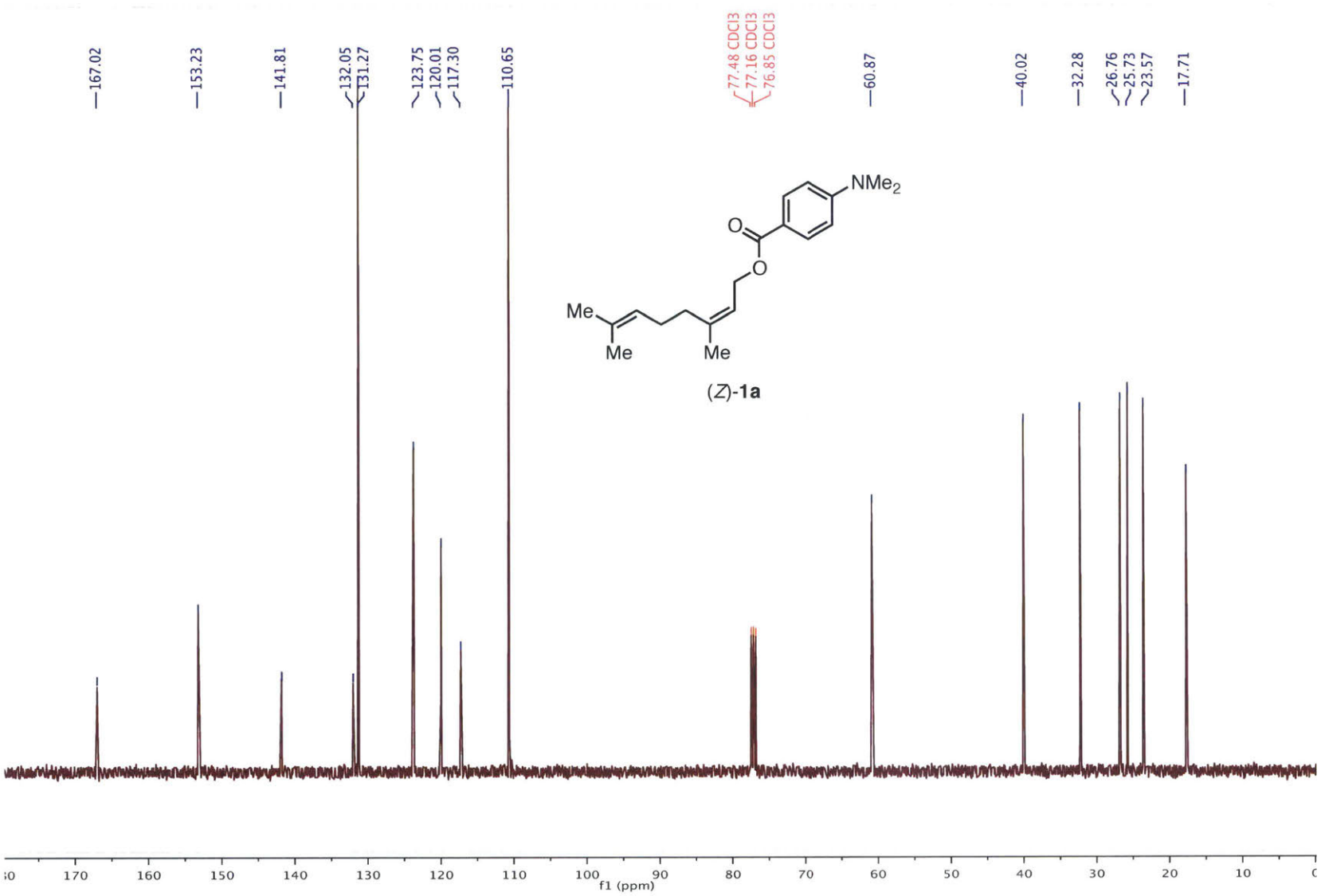

166.41
165.90
142.91
134.41
133.86
131.97
129.66
129.59
123.77
118.17
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
62.39
52.51
39.65
26.37
25.78
17.81
16.68
CO2Me
Me
Me
Me
O
O
1a(9)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

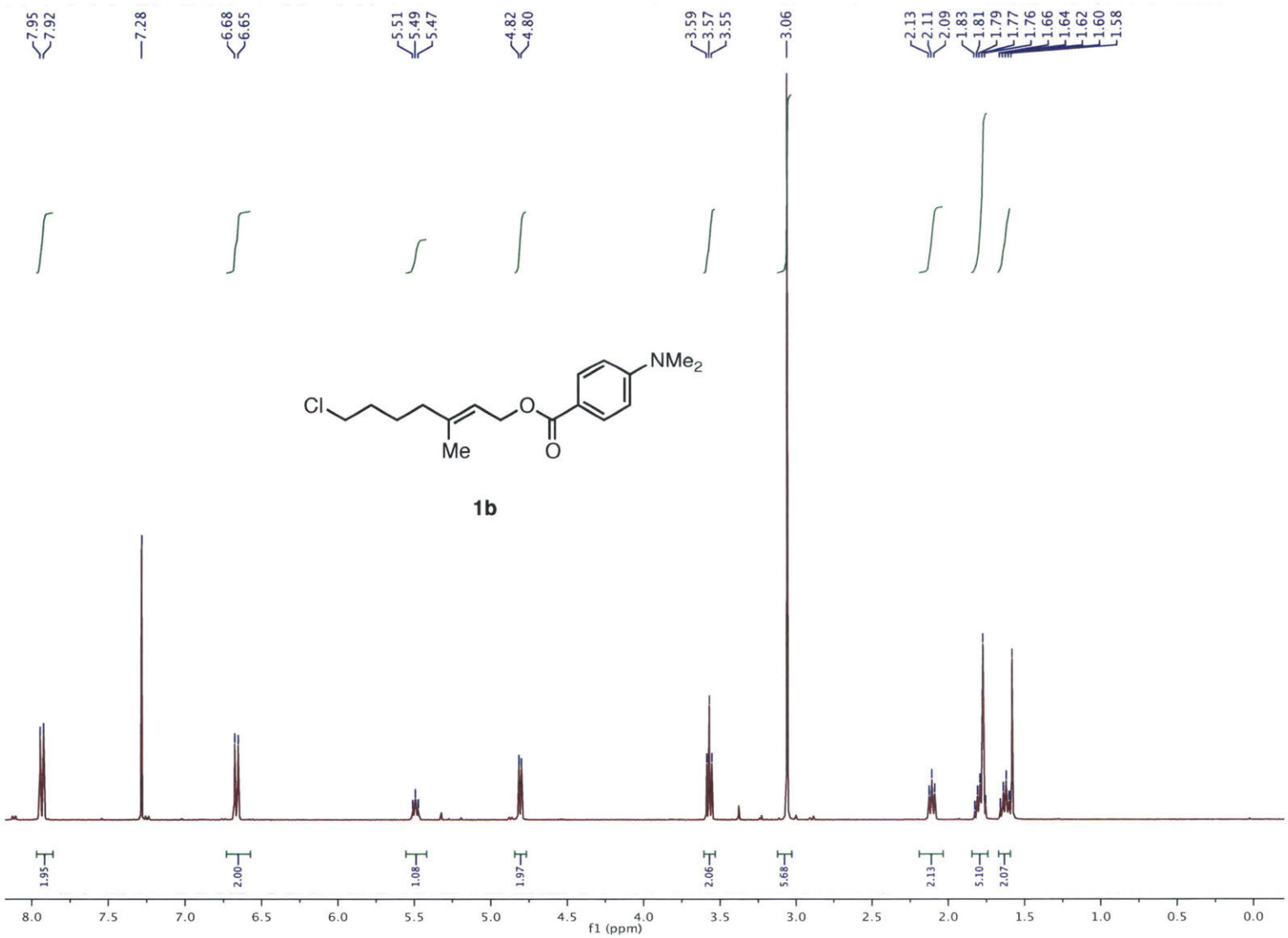

7.955
7.932
7.284
6.672
6.649
5.510
5.507
5.493
5.490
5.476
5.472
5.133
5.129
4.825
4.807
3.050
2.185
2.160
2.142
2.126
2.108
2.090
2.069
1.779
1.709
1.706
1.633
0.030
NMe2
Me
Me
Me
O
O
1.95
1.97
0.97
0.99
1.99
6.00
4.12
2.89
3.08
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

(*E*)-**1a**

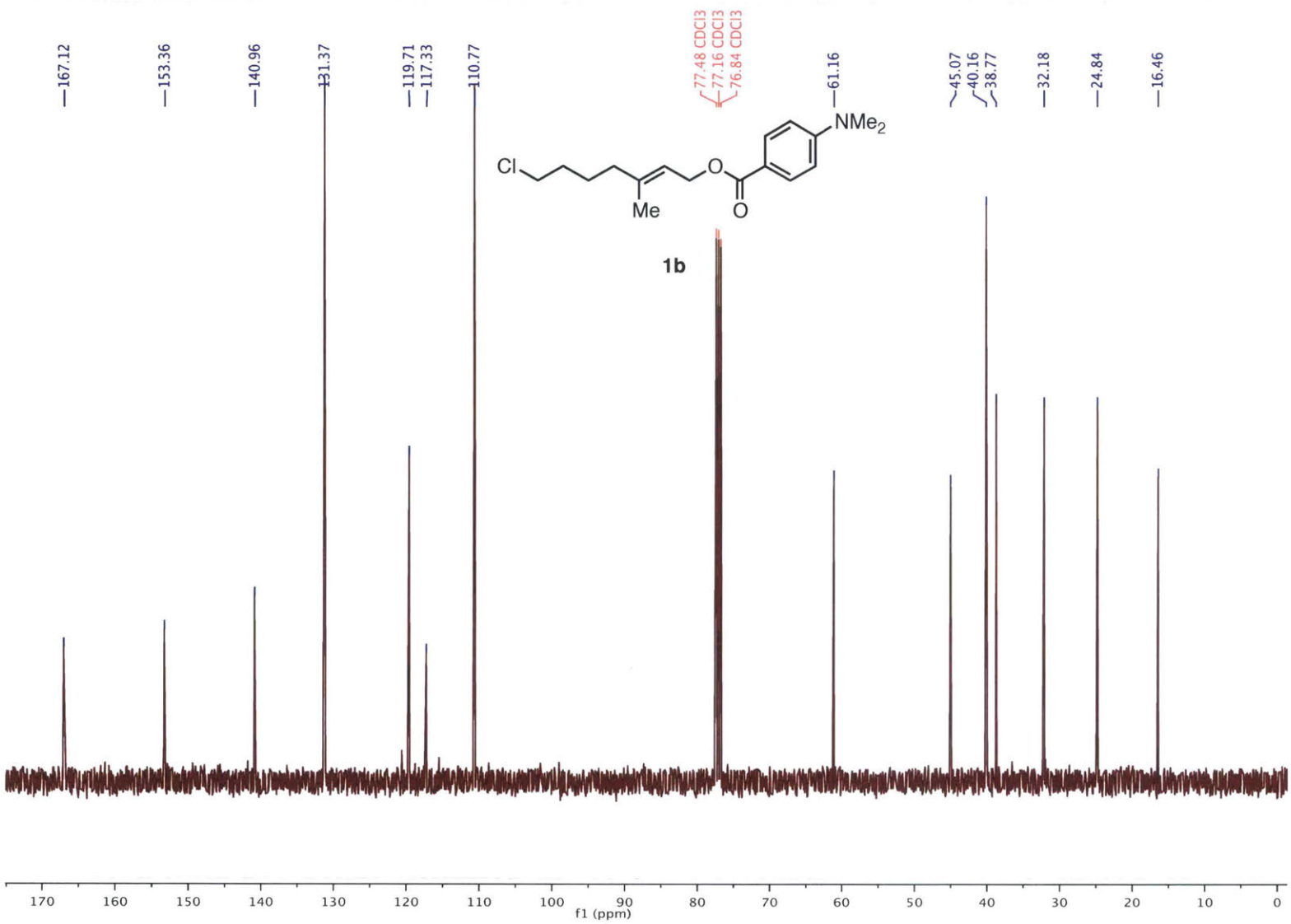

167.142
153.342
141.552
131.835
131.370
123.978
119.188
117.457
110.766
77.479 CDCl3
77.160 CDCl3
76.843 CDCl3
61.273
40.155
39.688
26.478
25.797
17.810
16.661
0.112
NMe2
Me
Me
Me
O
O
(E)-1a
f1 (ppm)

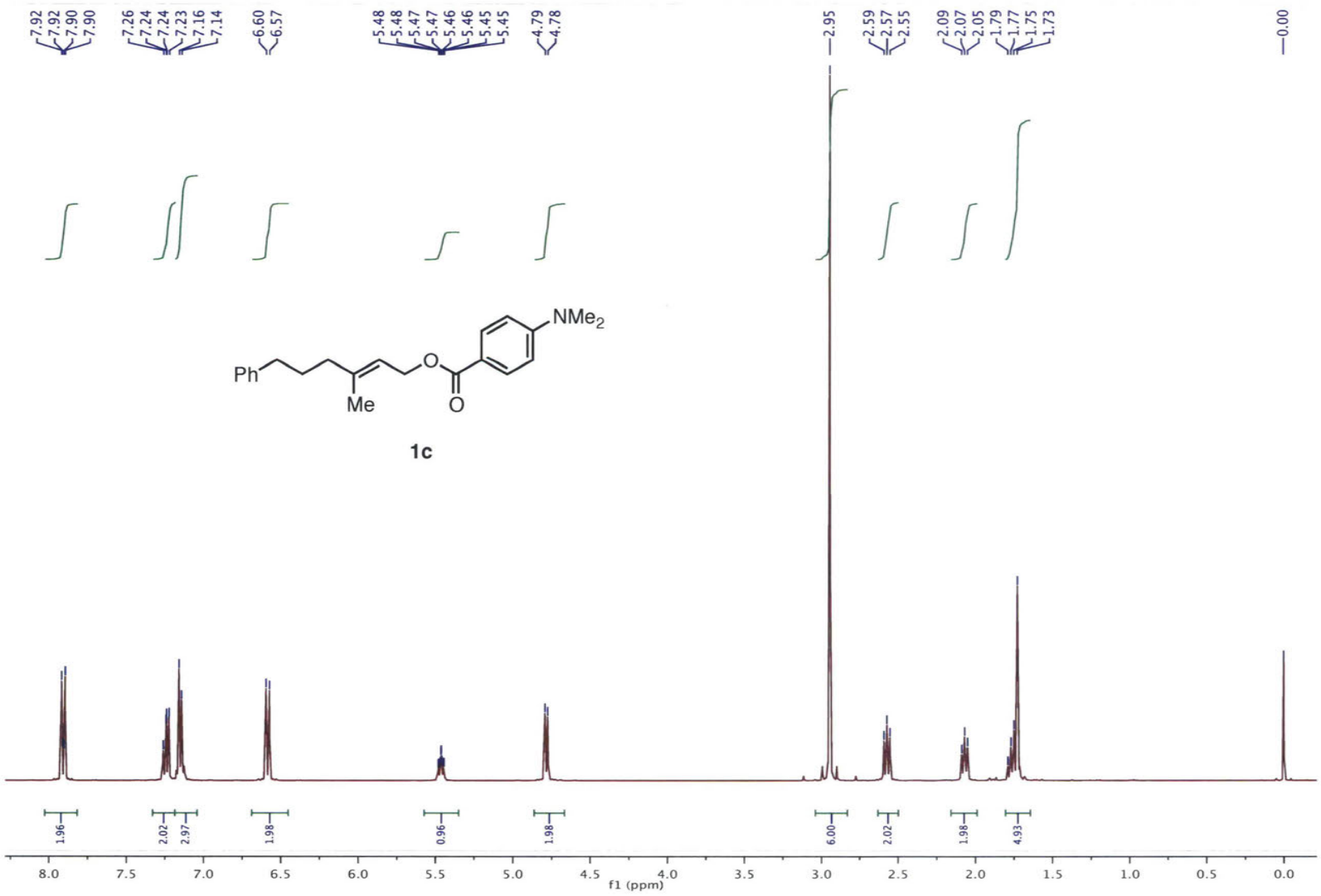

7.95
7.93
7.28
6.65
6.64
6.63
6.62
5.53
5.51
5.49
5.17
5.16
5.15
4.80
4.78
3.03
3.02
3.02
3.02
2.22
2.21
2.19
2.16
2.15
2.13
2.11
1.81
1.81
1.70
1.70
1.64
1.63
1.63
NMe2
O
O
Me
Me
Me
(Z)-1a
1.96
2.00
0.97
0.97
2.00
6.09
2.01
2.01
2.98
2.99
2.96
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

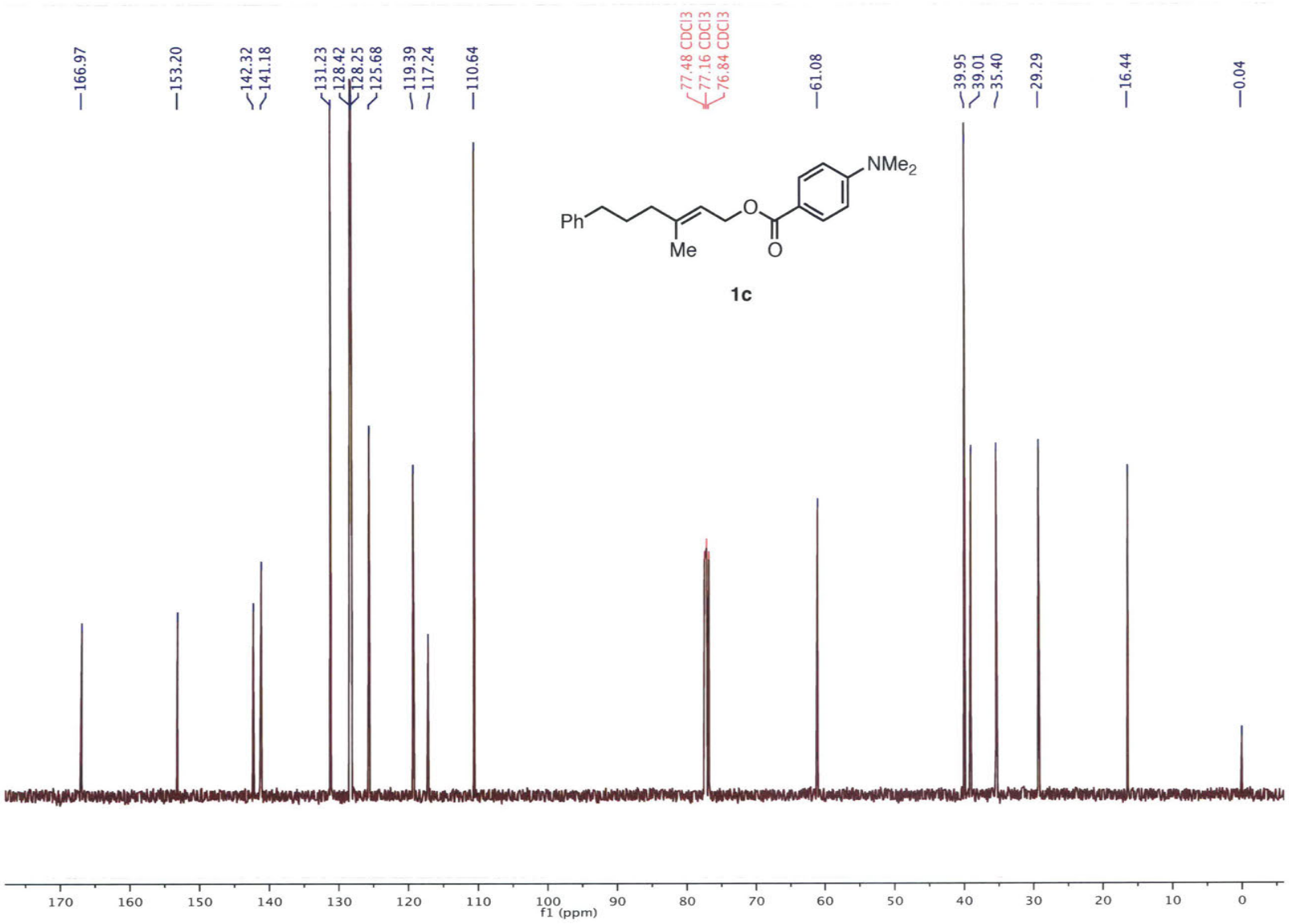

167.02
153.23
141.81
132.05
131.27
123.75
120.01
117.30
110.65
77.48 CDCl3
77.16 CDCl3
76.85 CDCl3
60.87
40.02
32.28
26.76
25.73
23.57
17.71
NMe2
O
O
Me
Me
Me
(Z)-1a
f1 (ppm)

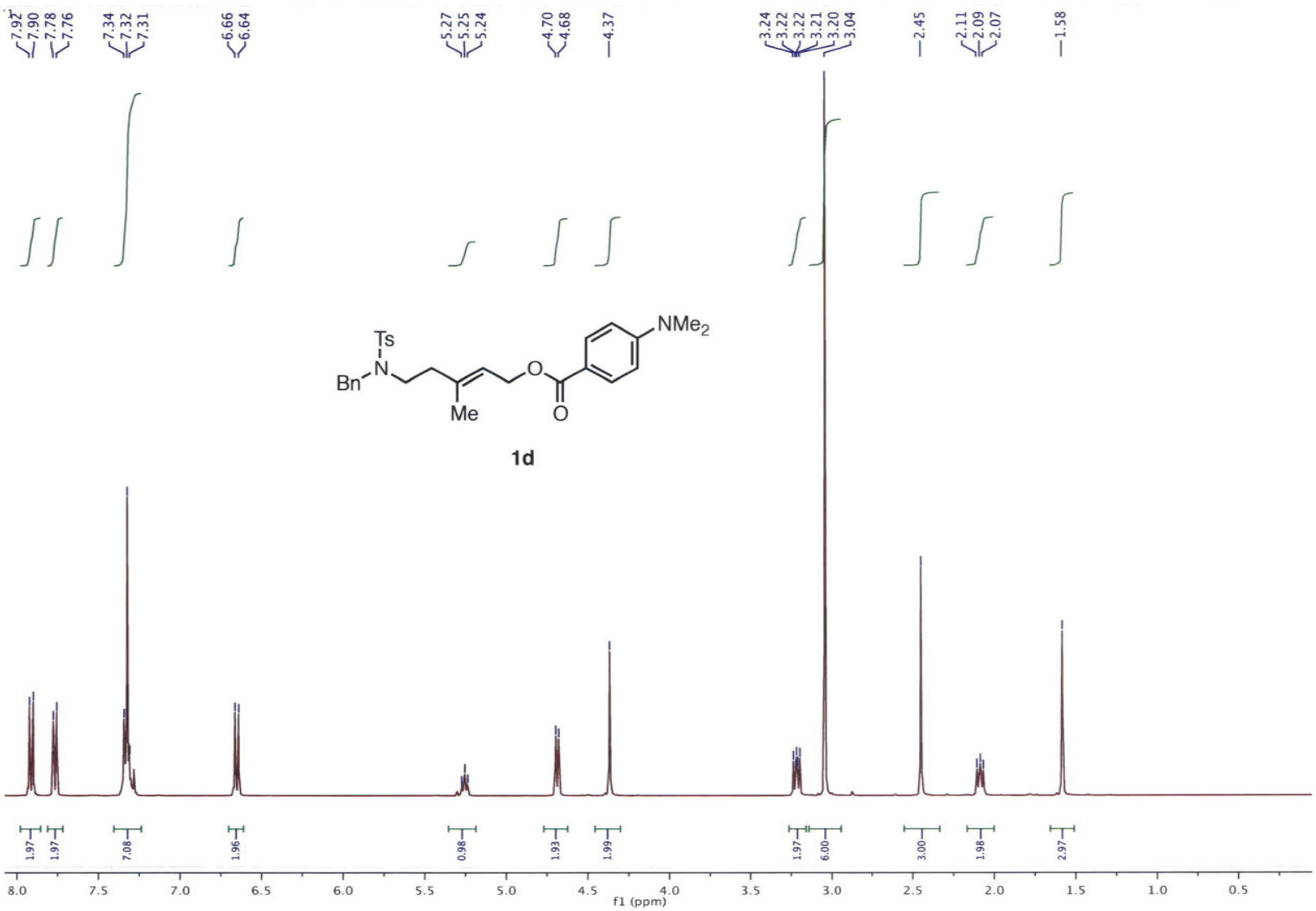

7.95
7.92
7.28
6.68
6.65
5.51
5.49
5.47
4.82
4.80
3.59
3.57
3.55
3.06
2.13
2.11
2.09
1.83
1.81
1.79
1.77
1.76
1.66
1.64
1.62
1.60
1.58
NMe2
Cl
O
Me
O
1.95
2.00
1.08
1.97
2.06
5.68
2.13
5.10
2.07
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

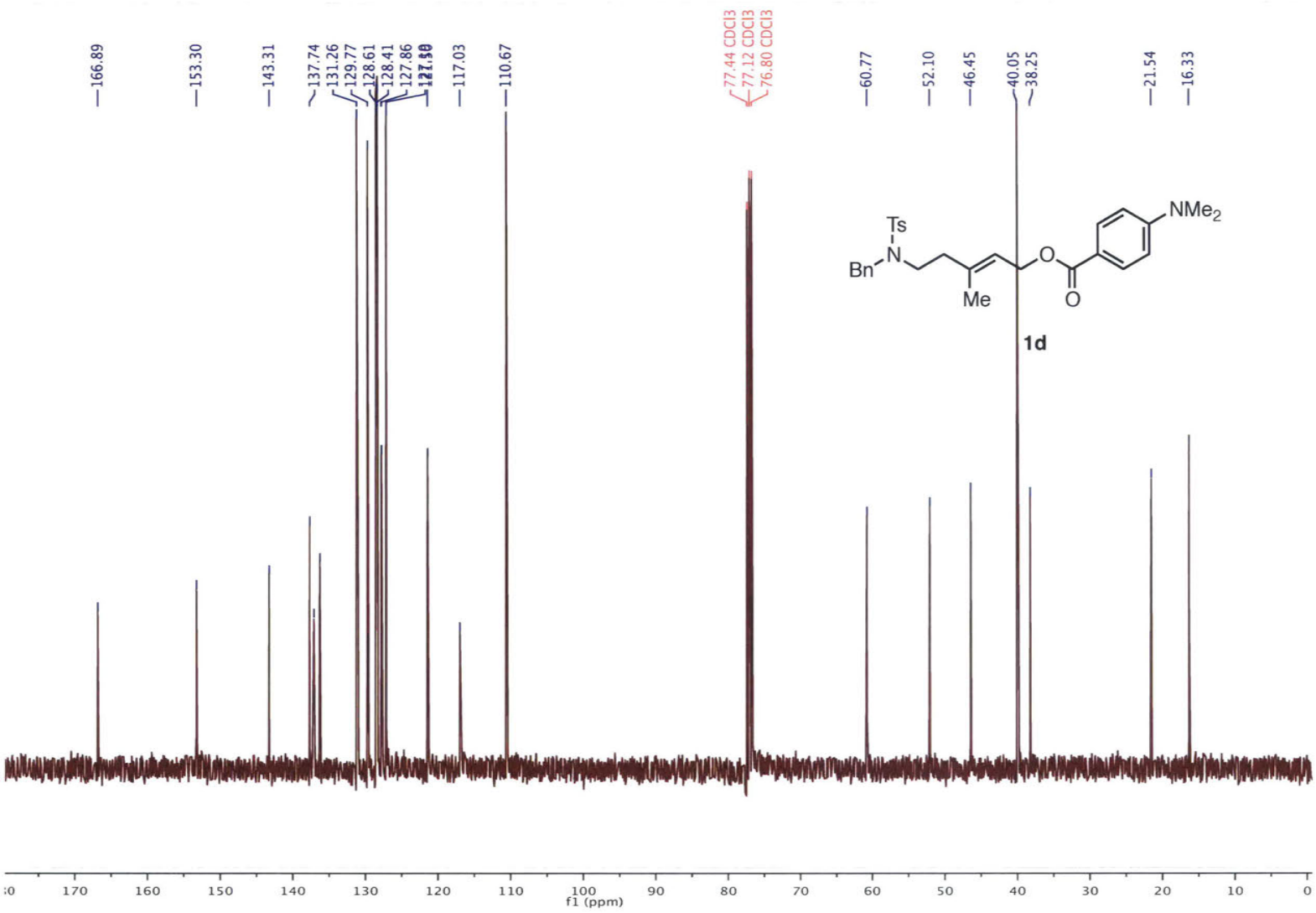
1b

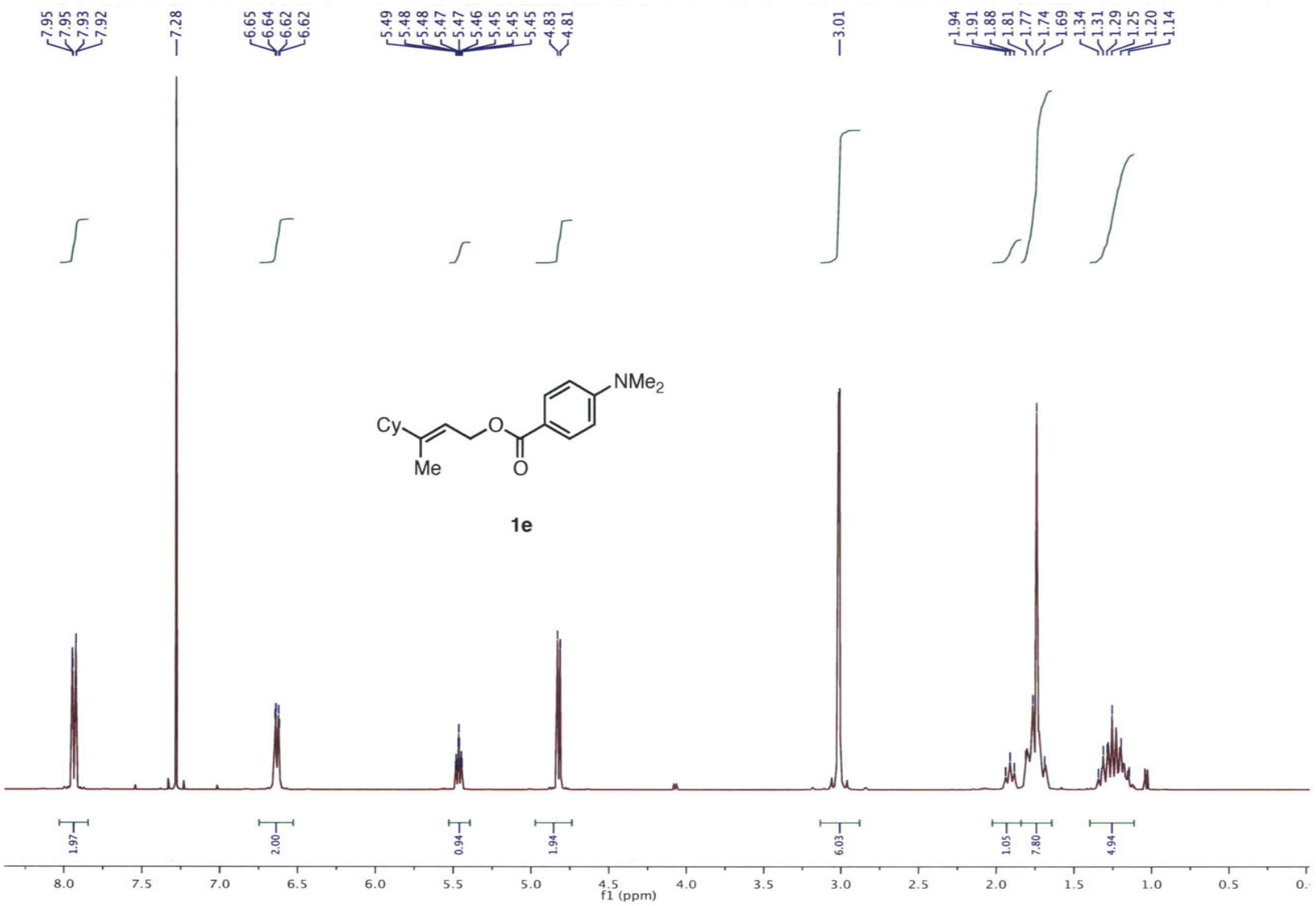

167.12
153.36
140.96
131.37
119.71
117.33
110.77
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
61.16
45.07
40.16
38.77
32.18
24.84
16.46
Cl
Me
O
O
NMe2
1b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.92
7.92
7.90
7.90
7.26
7.24
7.24
7.23
7.16
7.14
6.60
6.57
5.48
5.48
5.47
5.47
5.46
5.46
5.45
5.45
4.79
4.78
2.95
2.59
2.57
2.55
2.09
2.07
2.05
1.79
1.77
1.75
1.73
0.00
NMe2
Ph
Me
O
O
1c
1.96
2.02
2.97
1.98
0.96
1.98
6.00
2.02
1.98
4.93
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

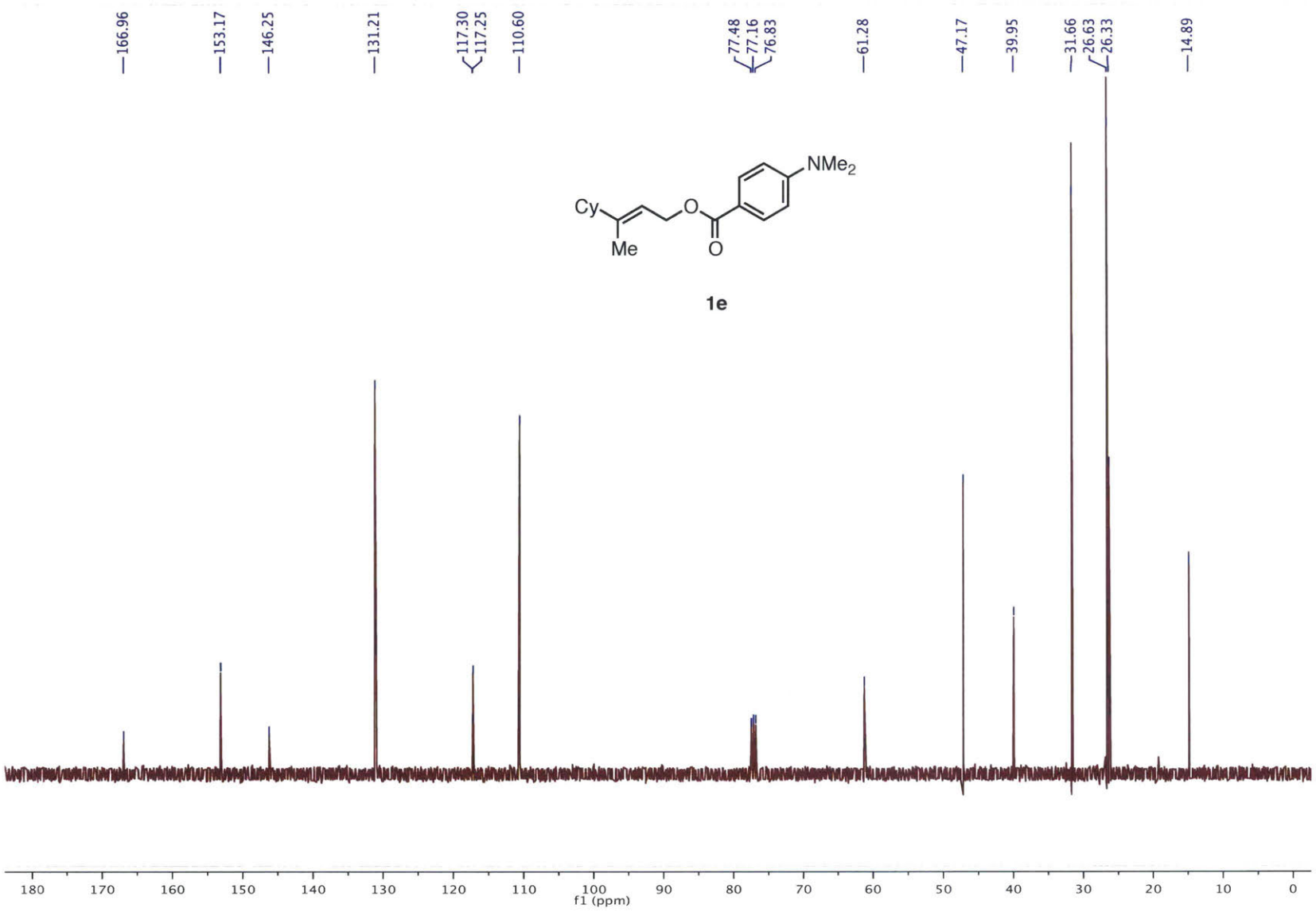

166.97
153.20
142.32
141.18
131.23
128.42
128.25
125.68
119.39
117.24
110.64
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
61.08
39.95
39.01
35.40
29.29
16.44
0.04
NMe2
Ph
Me
O
O
1c
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

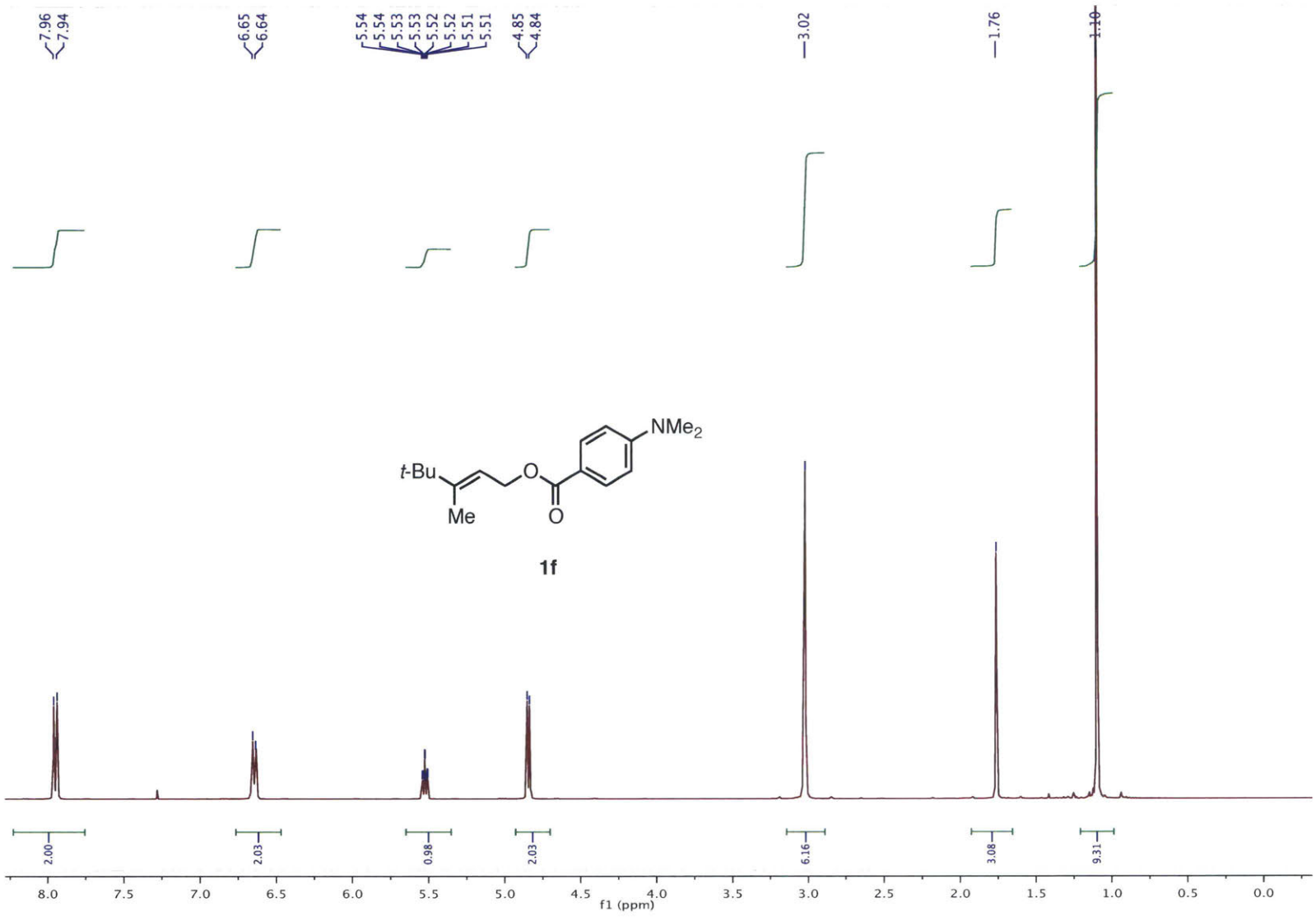

7.92
7.90
7.78
7.76
7.34
7.32
7.31
6.66
6.64
5.27
5.25
5.24
4.70
4.68
4.37
3.24
3.22
3.22
3.21
3.20
3.04
2.45
2.11
2.09
2.07
1.58
Ts
N
Bn
Me
O
O
NMe2
1d
1.97
1.97
7.08
1.96
0.98
1.93
1.99
1.97
6.00
3.00
1.98
2.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

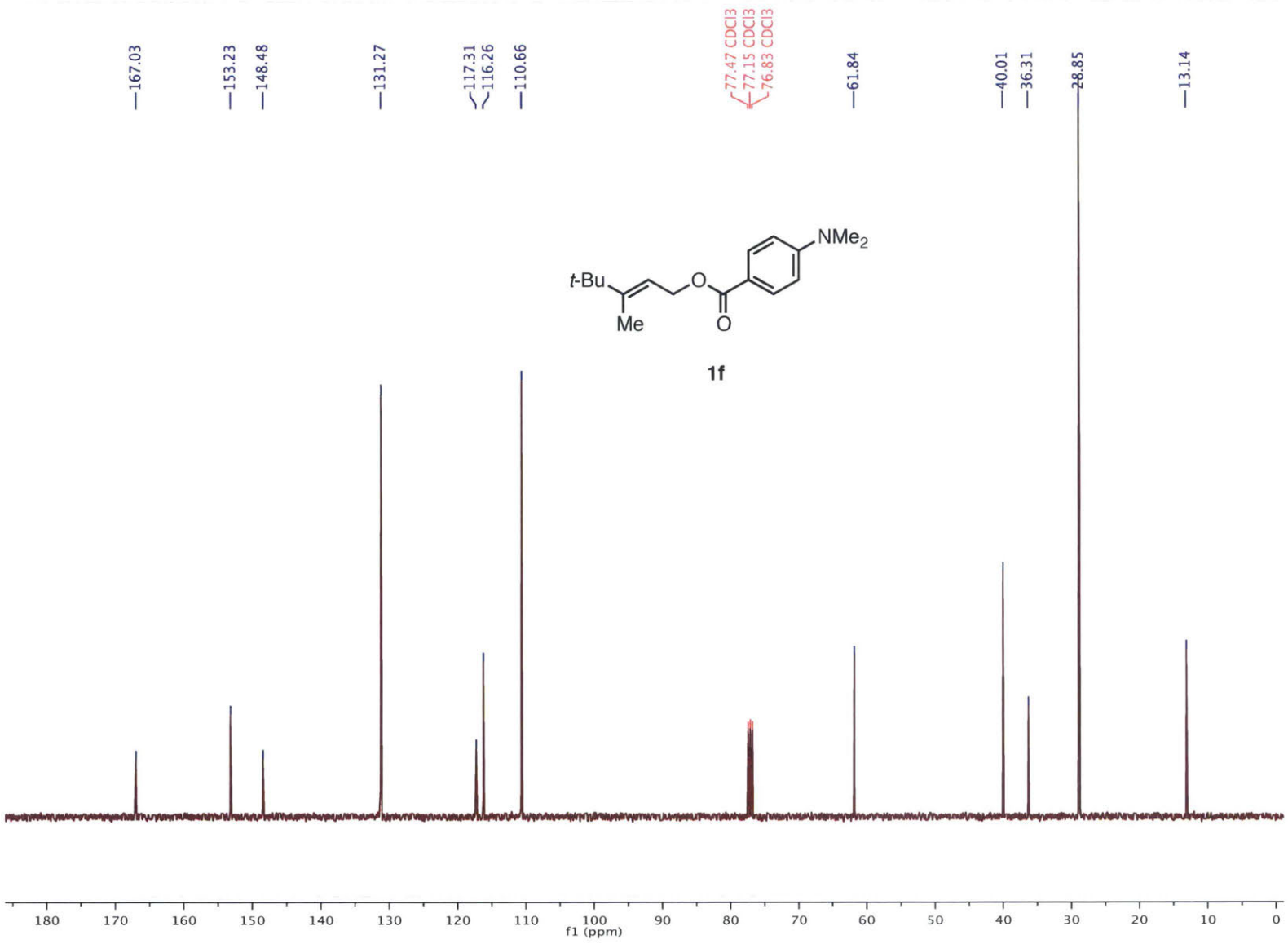

166.89
153.30
143.31
137.74
131.26
129.77
128.61
128.41
127.86
117.03
110.67
77.44 CDCl3
77.12 CDCl3
76.80 CDCl3
60.77
52.10
46.45
40.05
38.25
21.54
16.33
Ts
N
Bn
Me
O
O
NMe2
1d
f1 (ppm)

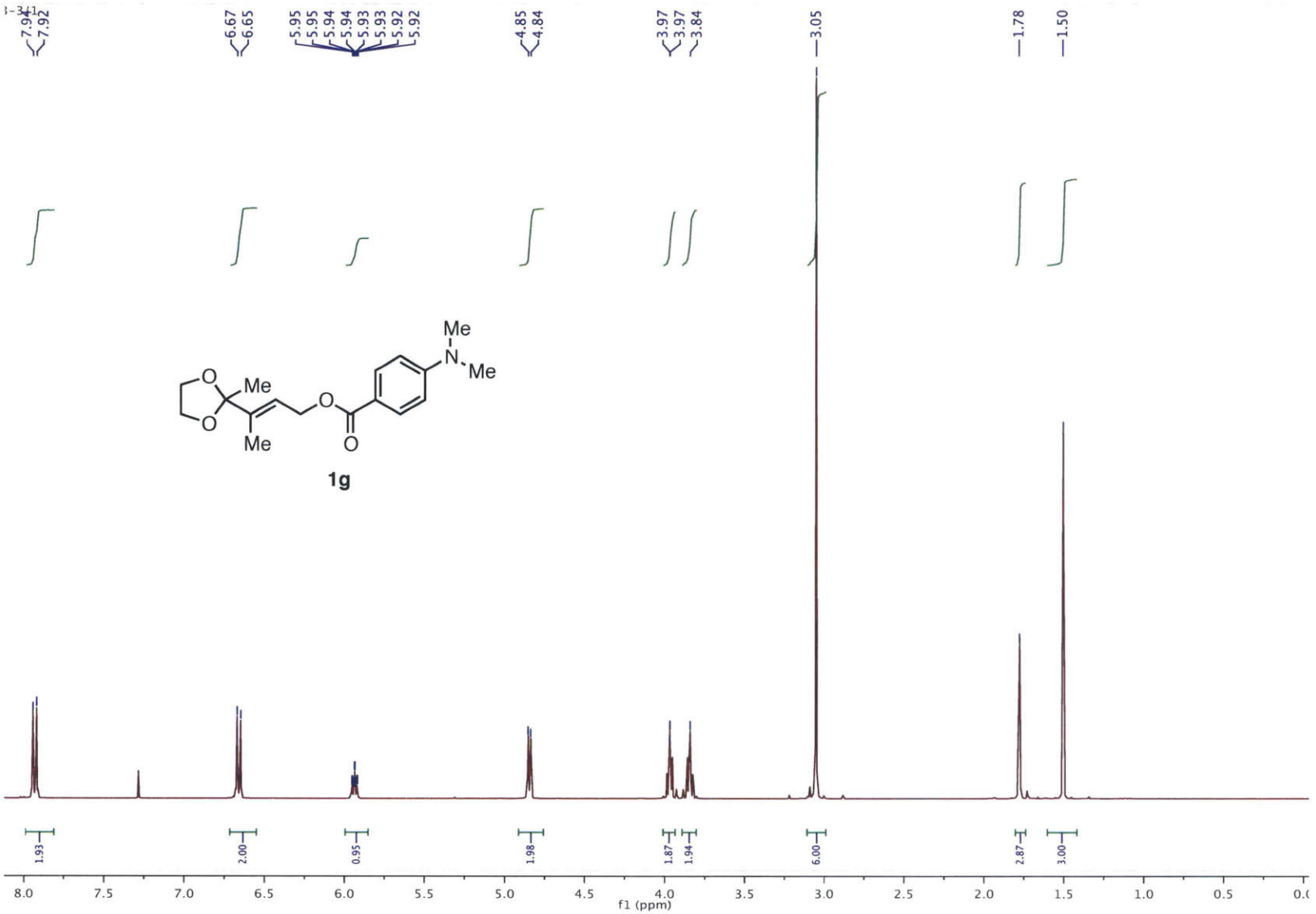

7.95
7.95
7.93
7.92
7.28
6.65
6.64
6.62
6.62
5.49
5.48
5.48
5.47
5.47
5.46
5.45
5.45
5.45
4.83
4.81
3.01
1.94
1.91
1.88
1.81
1.77
1.74
1.69
1.34
1.31
1.29
1.25
1.20
1.14
NMe2
Cy
Me
O
O
1.97
2.00
0.94
1.94
6.03
1.05
7.80
4.94
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

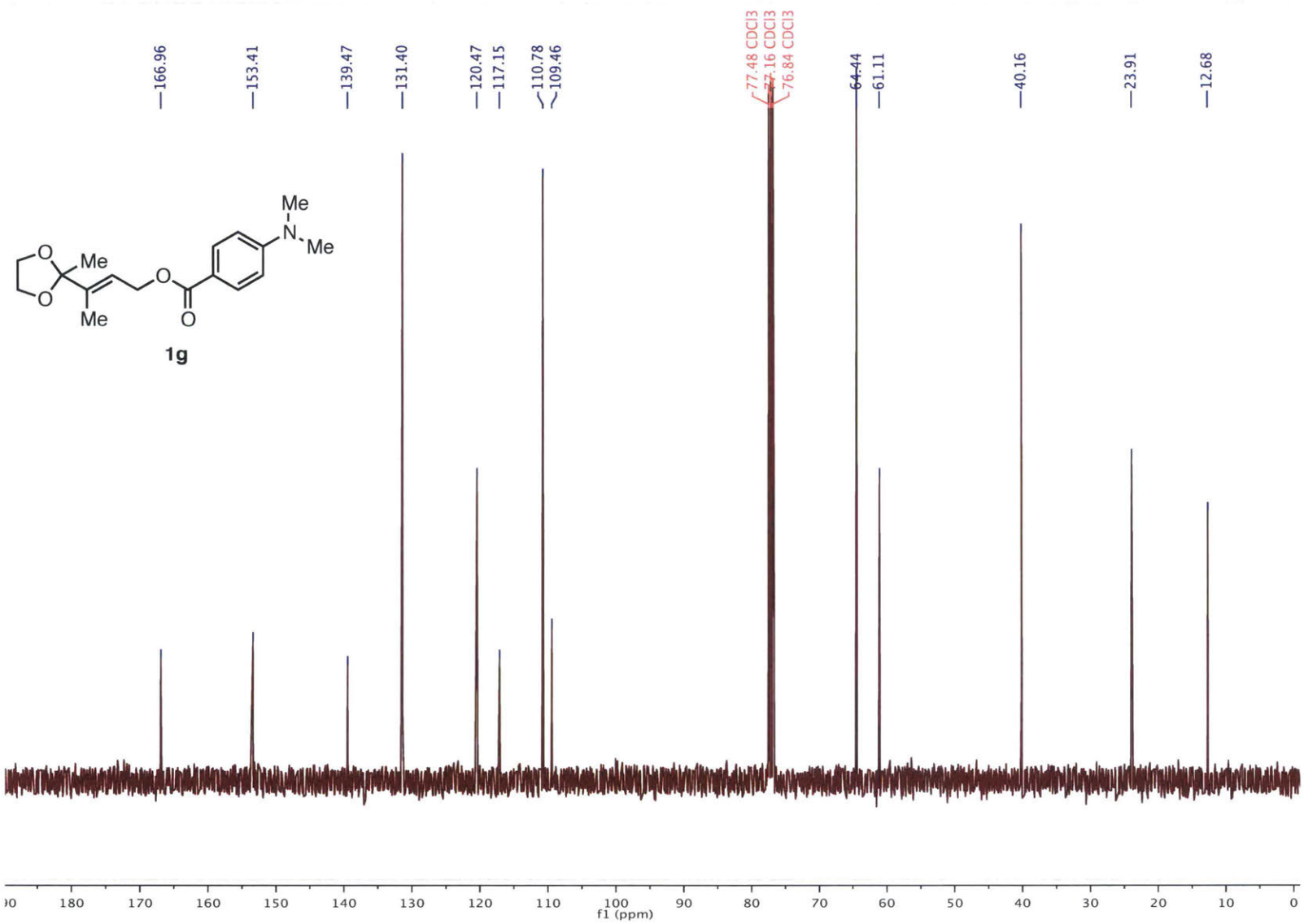
1e

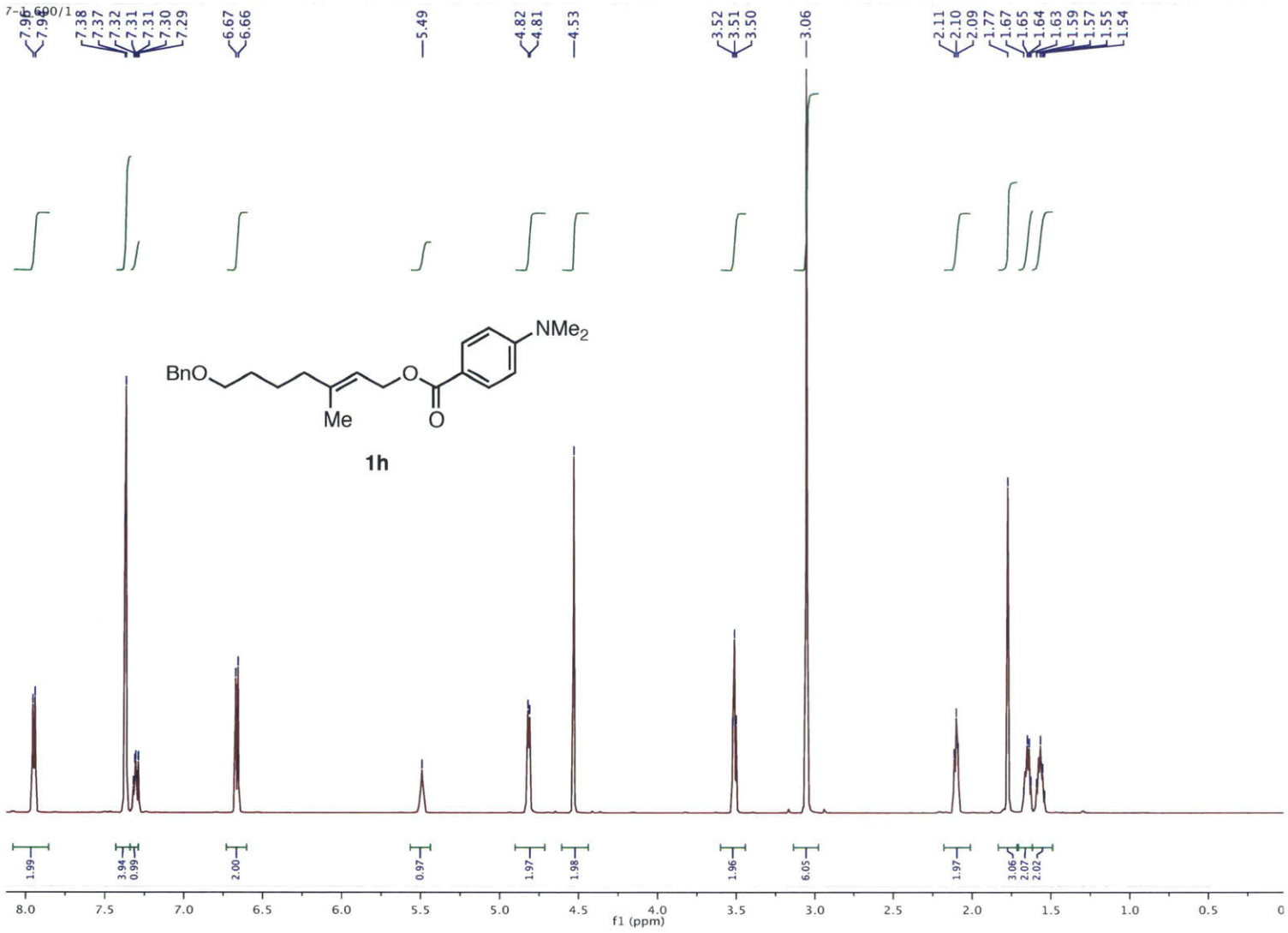

166.96
153.17
146.25
131.21
117.30
117.25
110.60
77.48
77.16
76.83
61.28
47.17
39.95
31.66
26.63
26.33
14.89
Cy
Me
O
O
NMe2
1e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

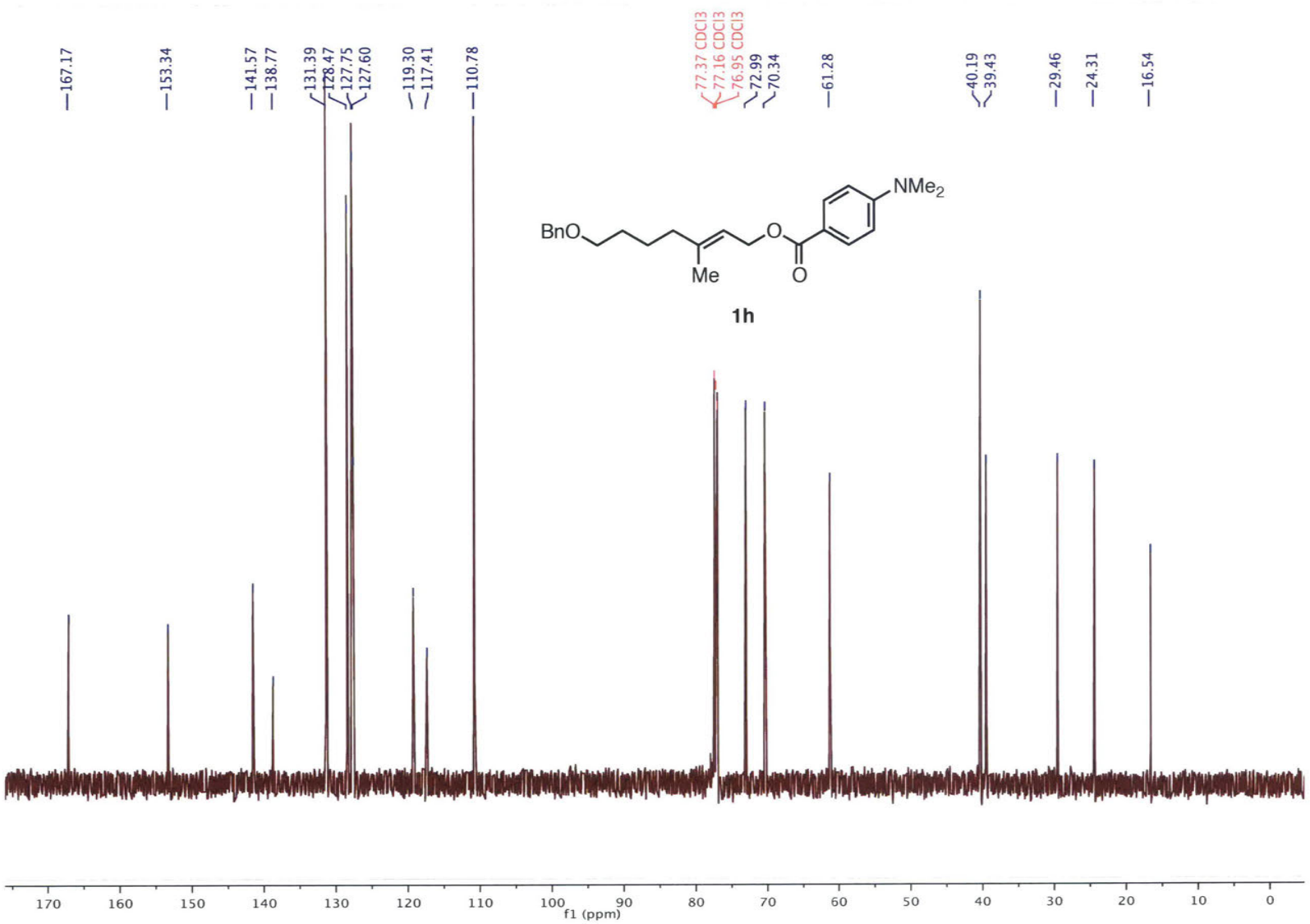

7.96
7.94
6.65
6.64
5.54
5.54
5.53
5.53
5.52
5.52
5.51
5.51
4.85
4.84
3.02
1.76
1.10
NMe2
t-Bu
O
Me
O
1f
2.00
2.03
0.98
2.03
6.16
3.08
9.31
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

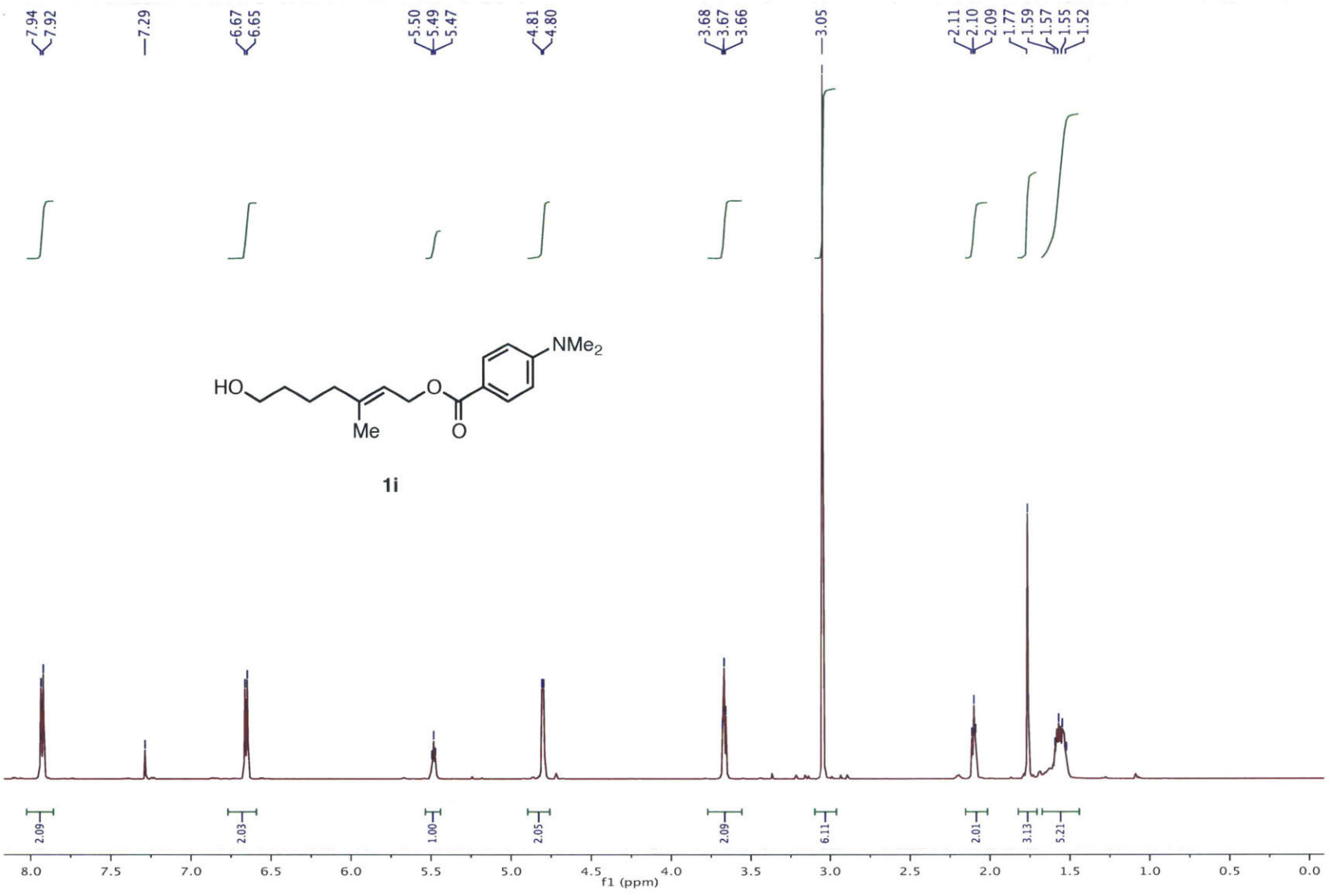

167.03
153.23
148.48
131.27
117.31
116.26
110.66
77.47 CDCl3
77.15 CDCl3
76.83 CDCl3
61.84
40.01
36.31
28.85
13.14
NMe2
t-Bu
Me
O
O
1f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.94
7.92
6.67
6.65
5.95
5.95
5.94
5.94
5.93
5.92
5.92
4.85
4.84
3.97
3.97
3.84
3.05
1.78
1.50
Me
N
Me
O
Me
O
O
Me
O
1g
1.93
2.00
0.95
1.98
1.87
1.94
6.00
2.87
3.00
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
f1 (ppm)


166.96
153.41
139.47
131.40
120.47
117.15
110.78
109.46
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
64.44
61.11
40.16
23.91
12.68
Me
N
Me
O
Me
O
O
Me
O
1g
f1 (ppm)


7.96
7.94
7.38
7.37
7.32
7.31
7.31
7.30
7.29
6.67
6.66
5.49
4.82
4.81
4.53
3.52
3.51
3.50
3.06
2.11
2.10
2.09
1.77
1.67
1.65
1.64
1.63
1.59
1.57
1.55
1.54
NMe2
BnO
O
Me
O
1h
1.99
3.94
0.99
2.00
0.97
1.97
1.98
1.96
6.05
1.97
3.06
2.07
2.02
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
f1 (ppm)


167.17
153.34
141.57
138.77
131.39
128.47
127.75
127.60
119.30
117.41
110.78
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
72.99
70.34
61.28
40.19
39.43
29.46
24.31
16.54
NMe2
BnO
O
Me
O
1h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.94
7.92
7.29
6.67
6.65
5.50
5.49
5.47
4.81
4.80
3.68
3.67
3.66
3.05
2.11
2.10
2.09
1.77
1.59
1.57
1.55
1.52
NMe2
HO
O
Me
O
1i
2.09
2.03
1.00
2.05
2.09
6.11
2.01
3.13
5.21
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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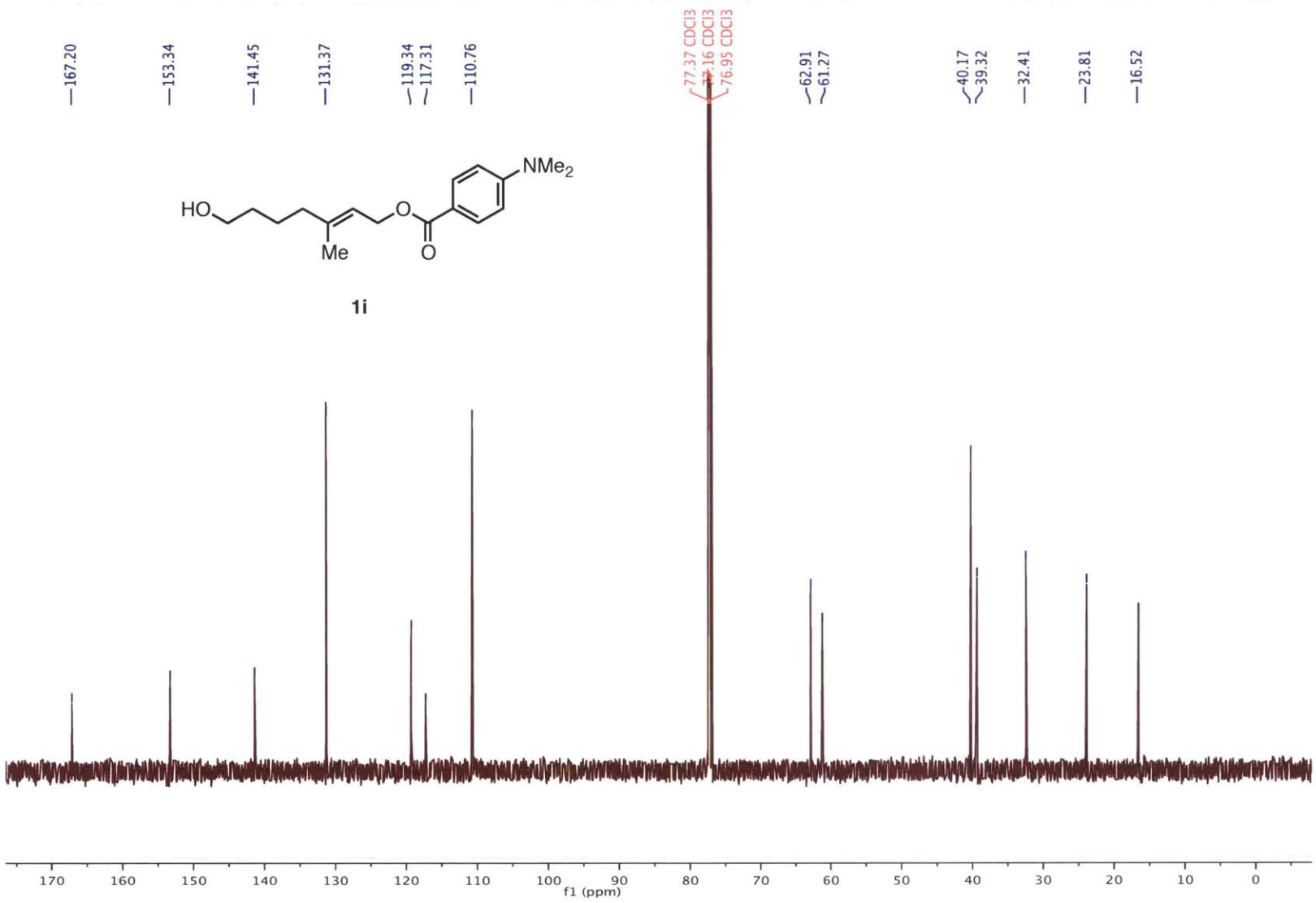
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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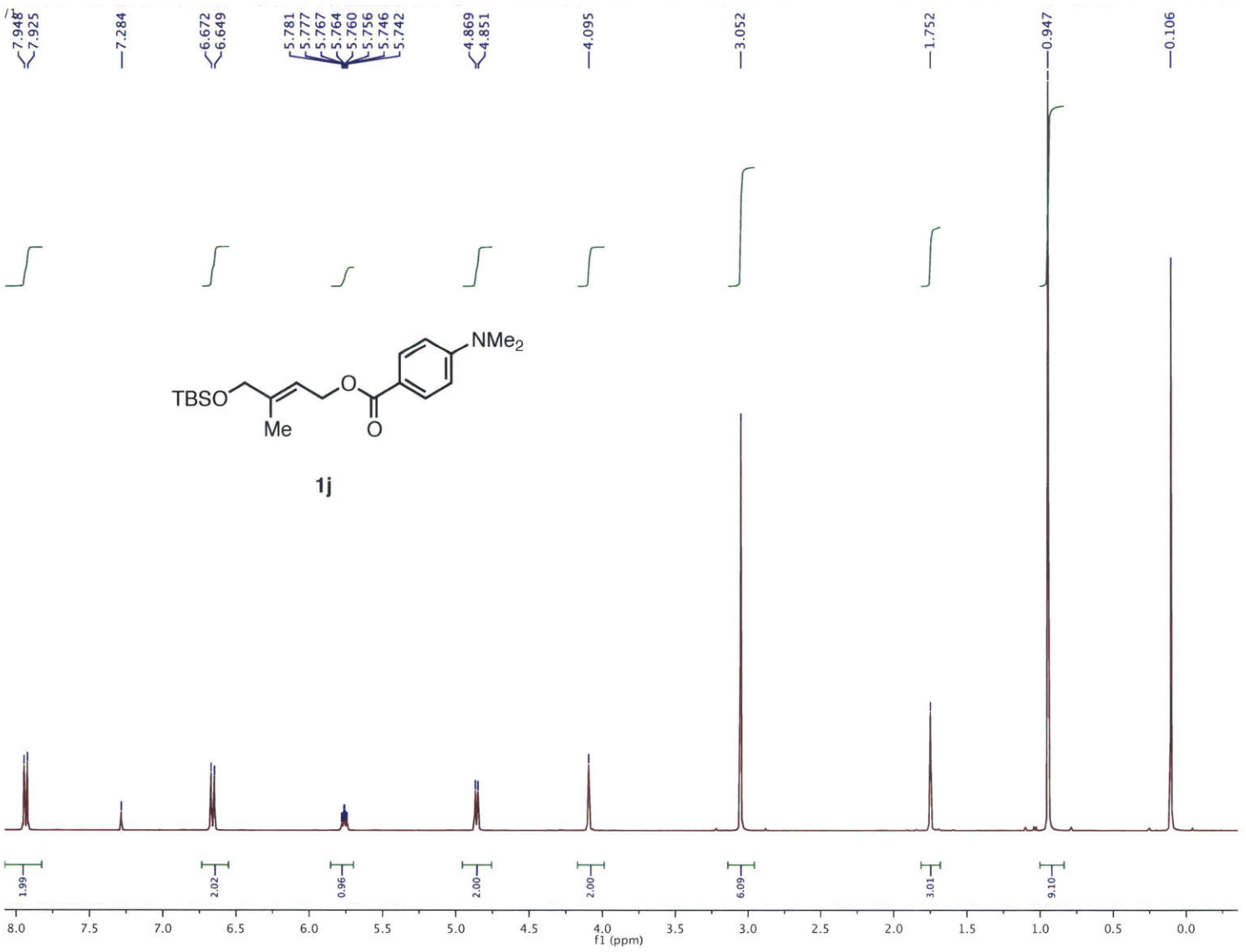
153.34
141.45
131.37
119.34
117.31
110.76
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
62.91
61.27
40.17
39.32
32.41
23.81
16.52
NMe2
HO
O
Me
O
1i
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.925
7.284
6.672
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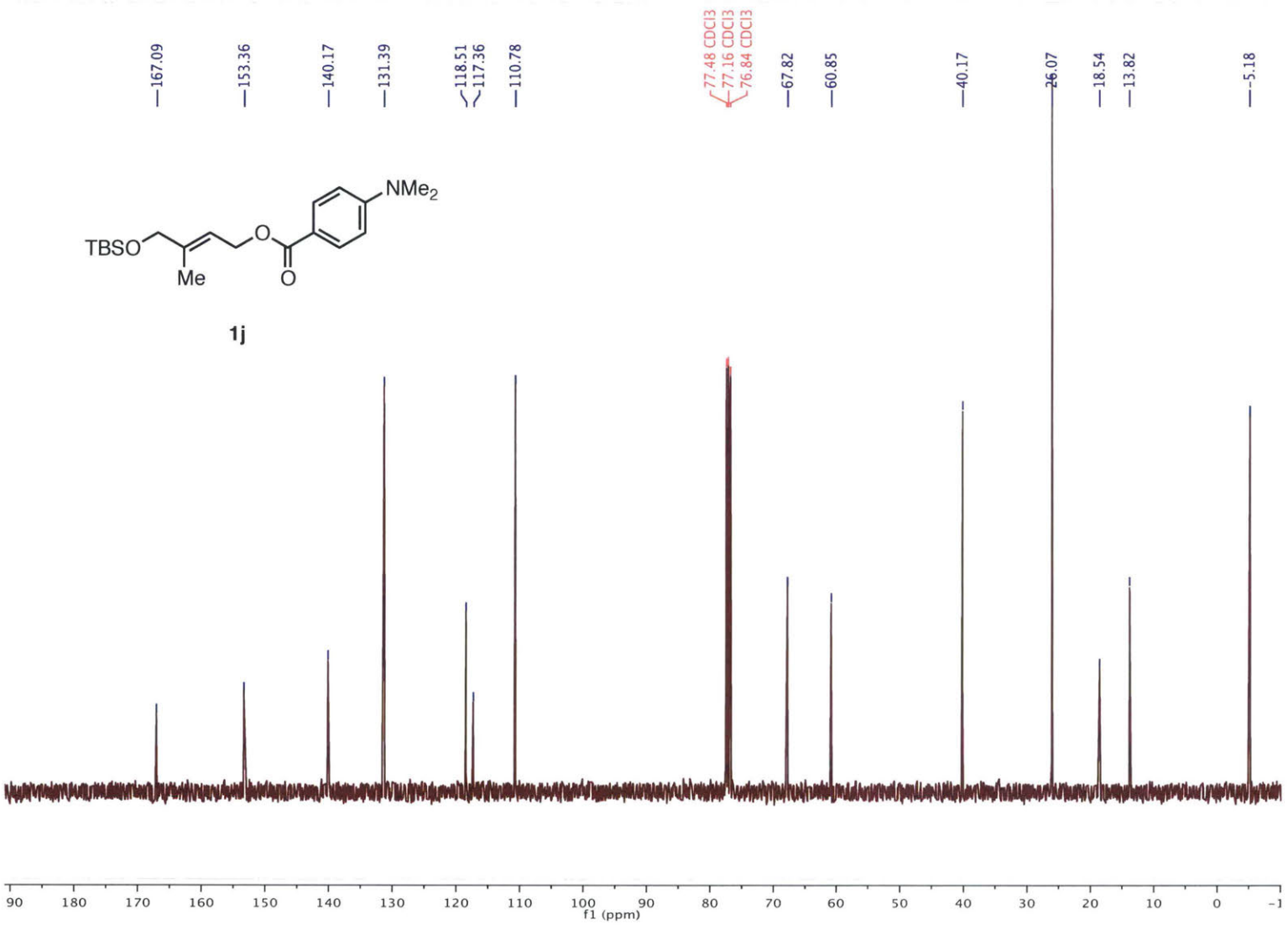
5.777
5.767
5.764
5.760
5.756
5.746
5.742
4.869
4.851
4.095
3.052
1.752
0.947
0.106
NMe2
TBSO
O
Me
O
1j
1.99
2.02
0.96
2.00
2.00
6.09
3.01
9.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.09
153.36
140.17
131.39
118.51
117.36
110.78
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
67.82
60.85
40.17
26.07
18.54
13.82
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TBSO
Me
O
O
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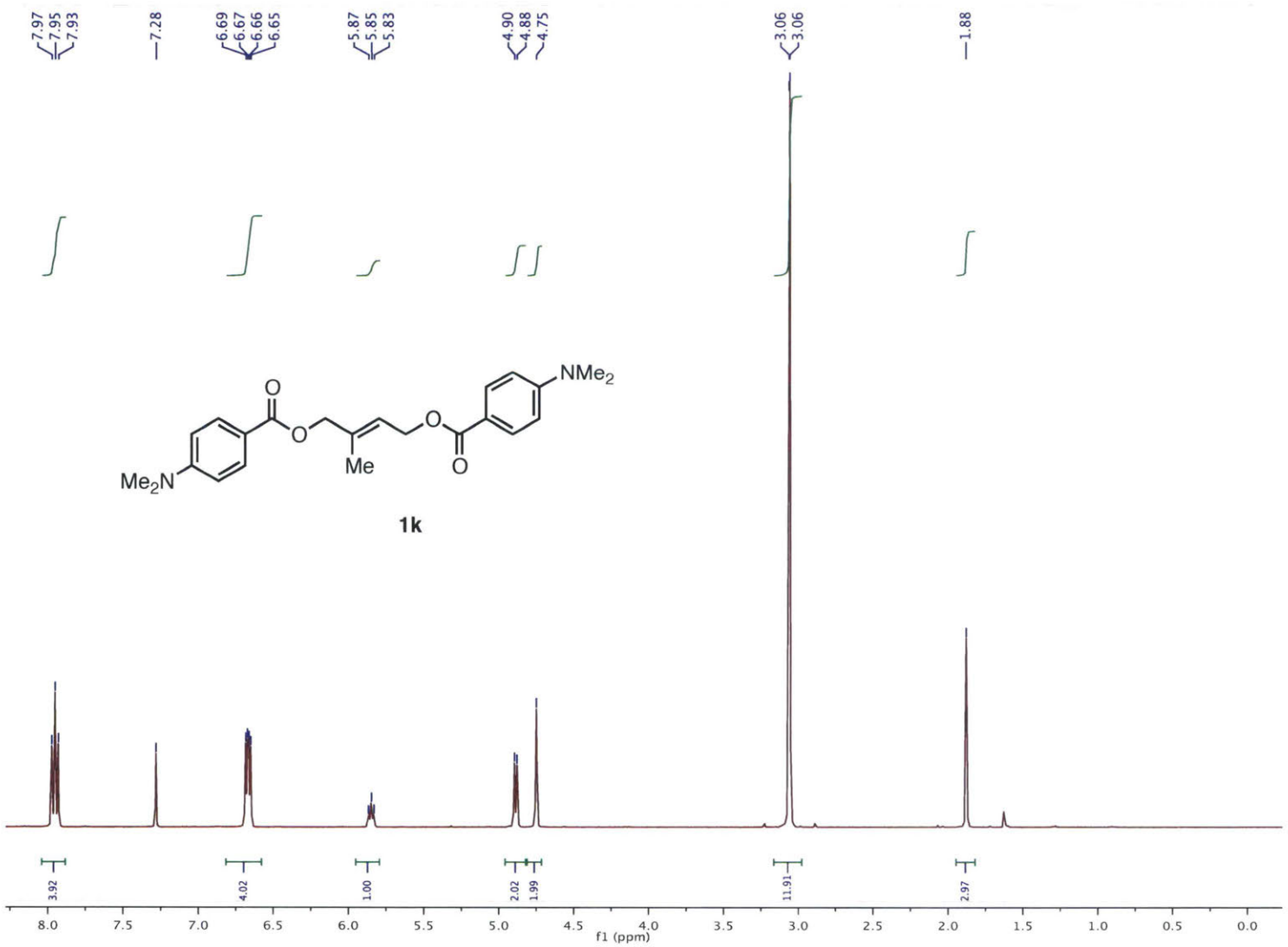
f1 (ppm)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7.95
7.93
7.28
6.69
6.67
6.66
6.65
5.87
5.85
5.83
4.90
4.88
4.75
3.06
3.06
1.88
NMe2
Me2N
O
O
O
O
Me
3.92
4.02
1.00
2.02
1.99
11.91
2.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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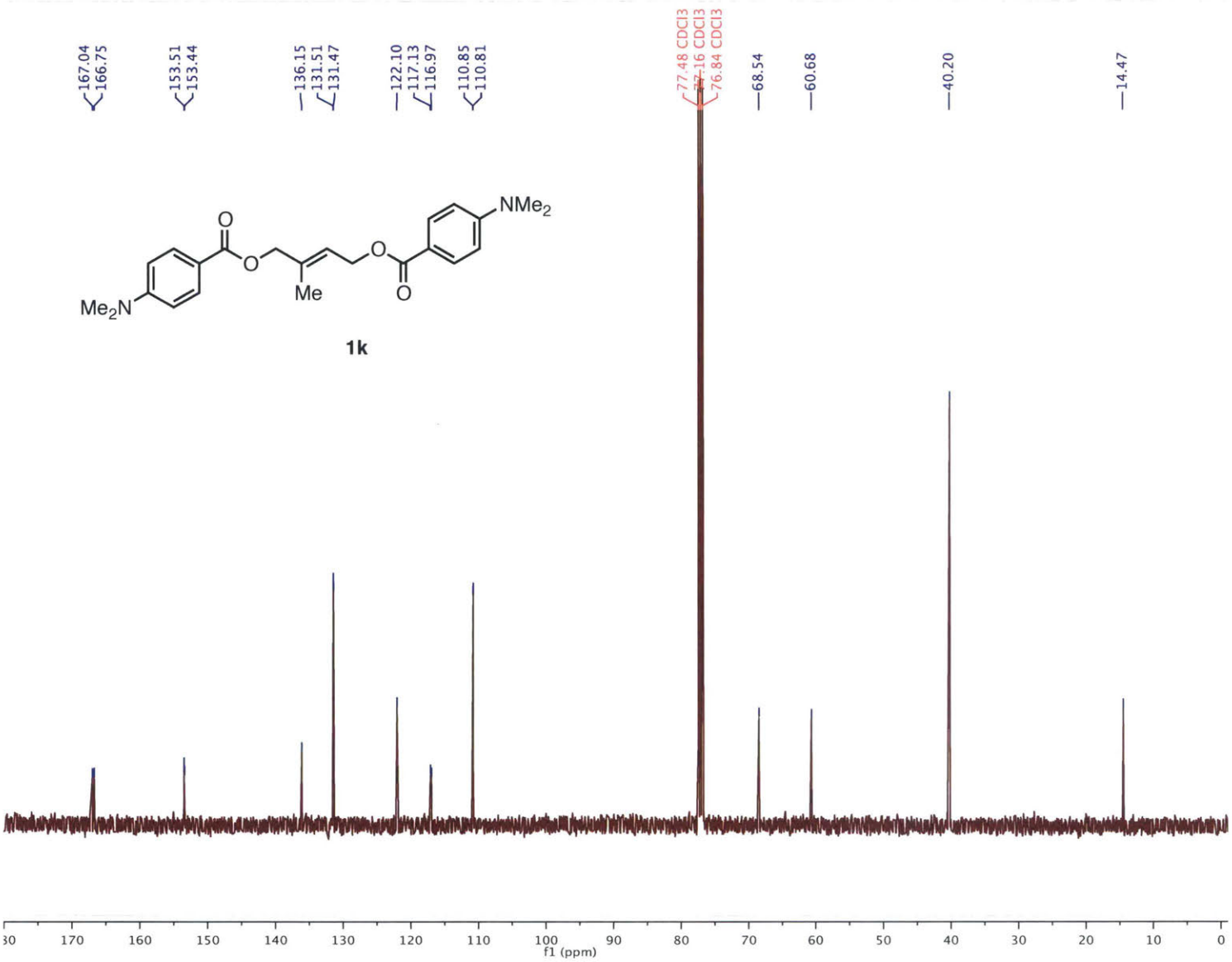
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

1k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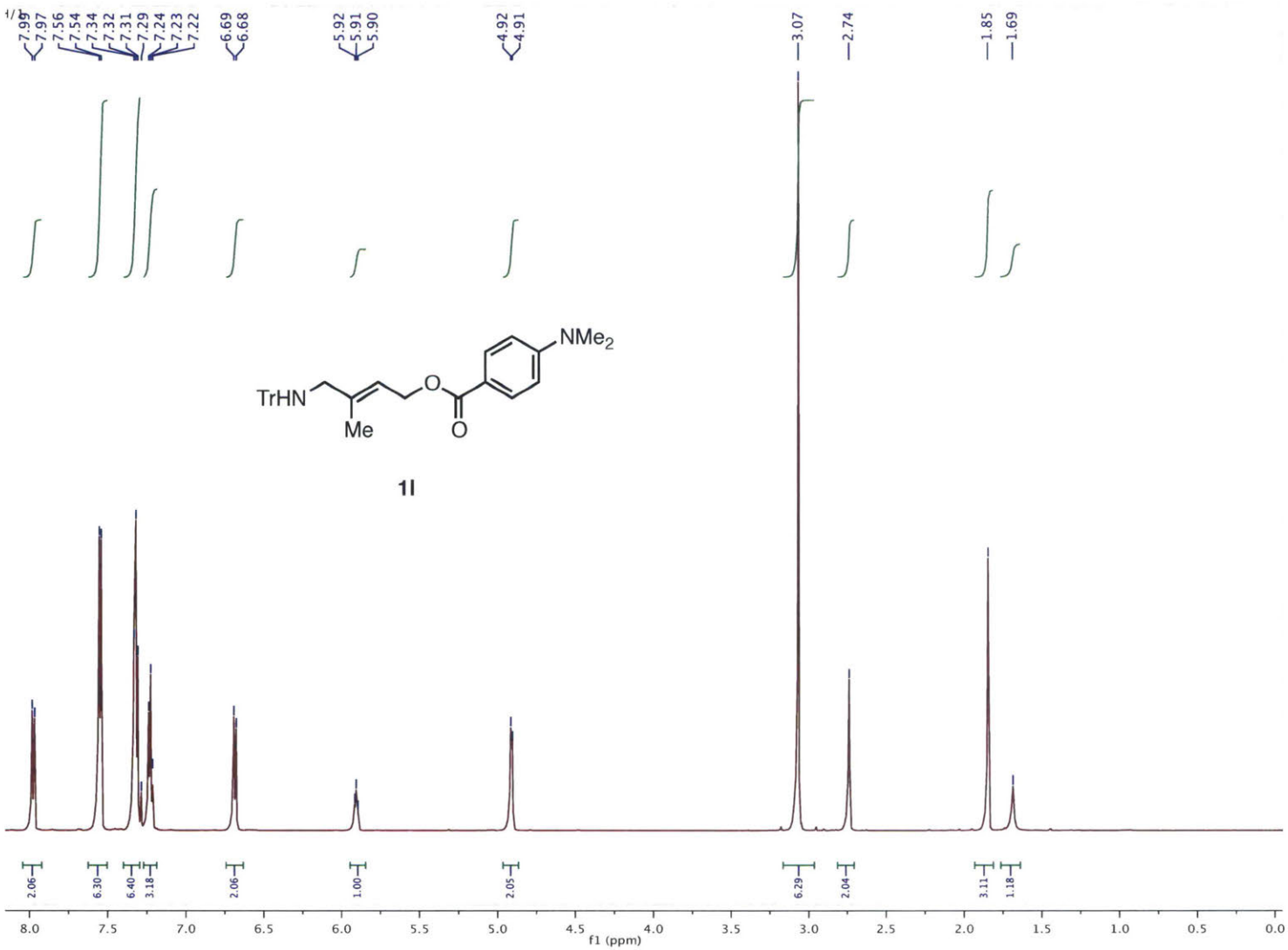
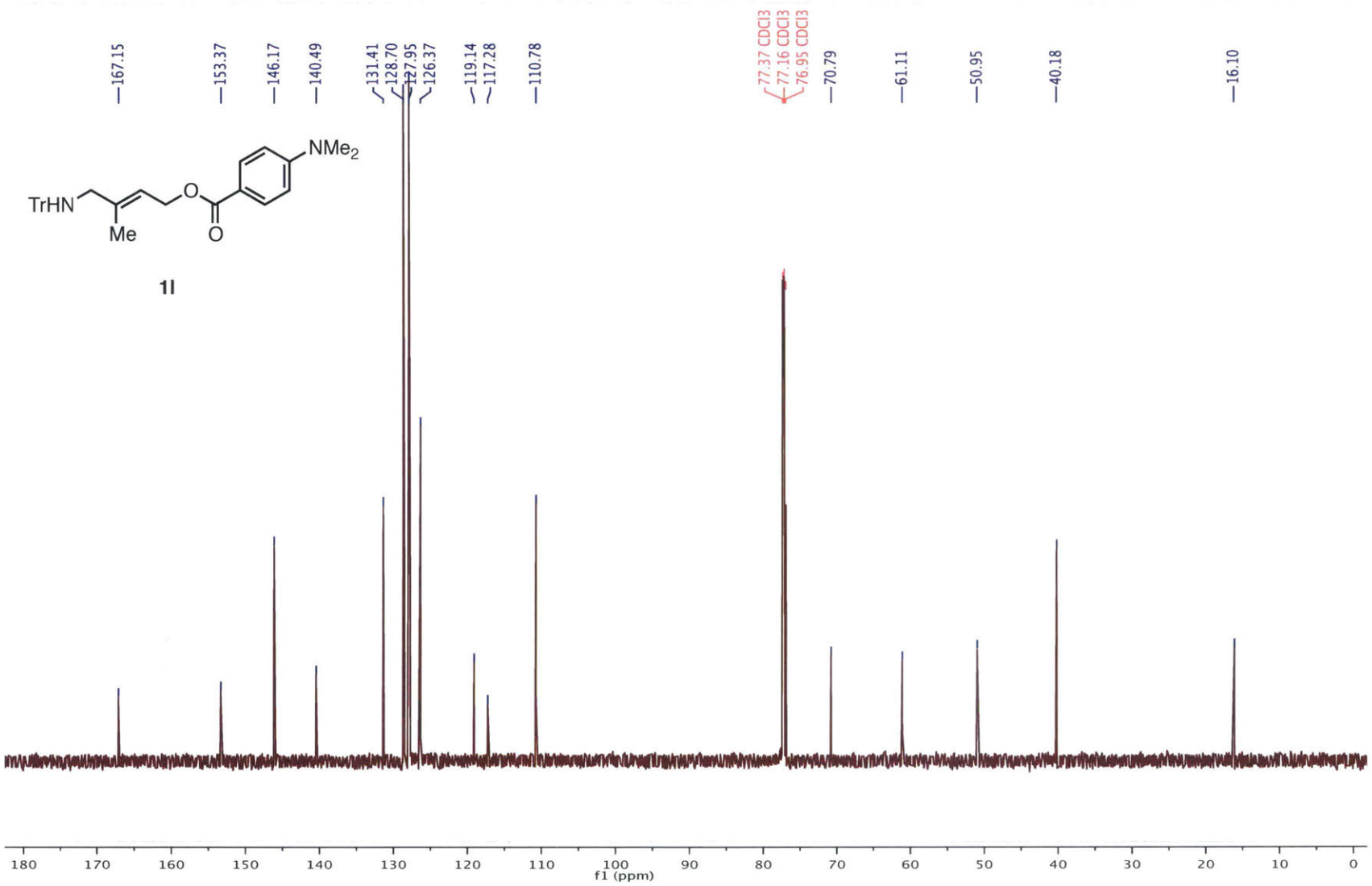
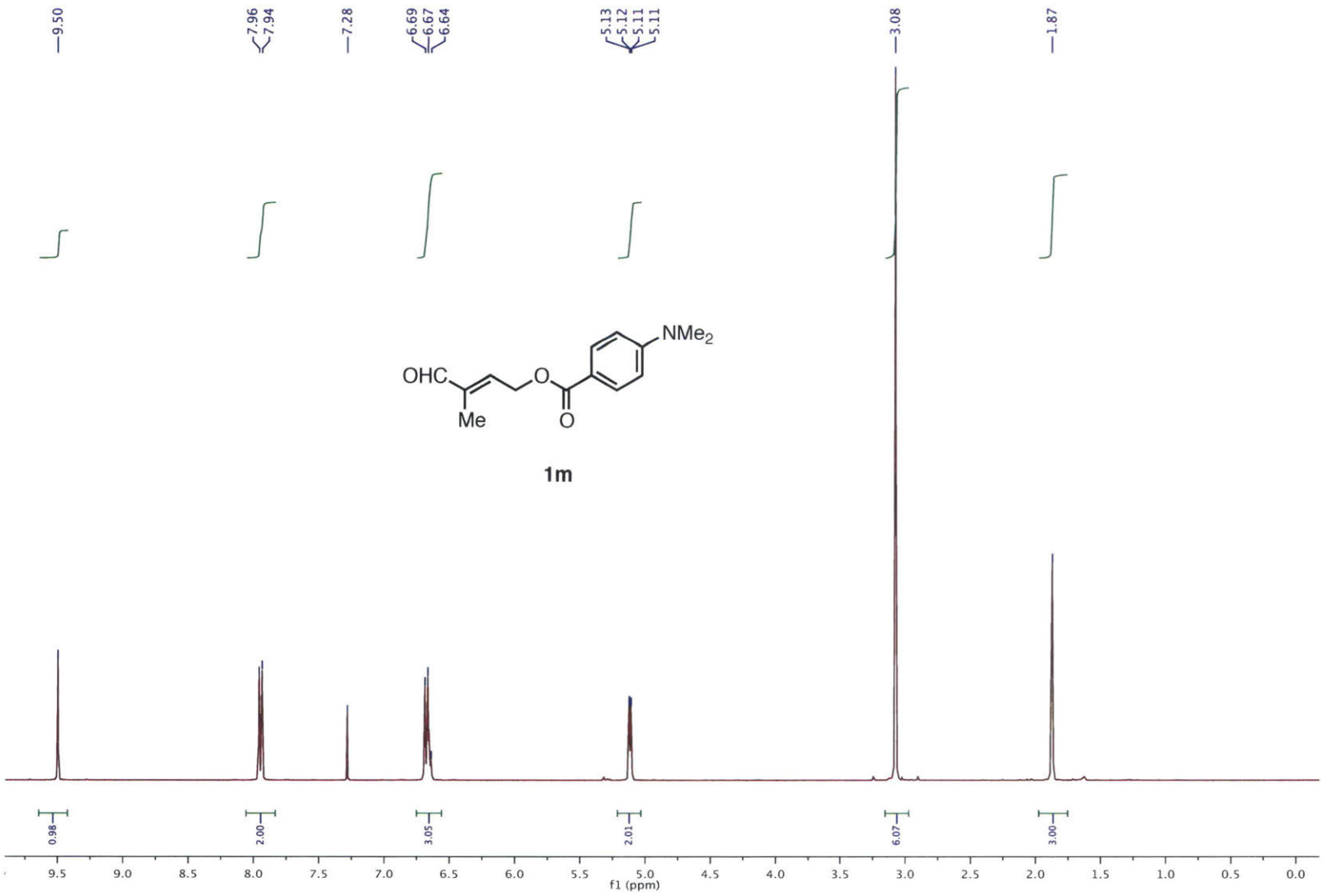
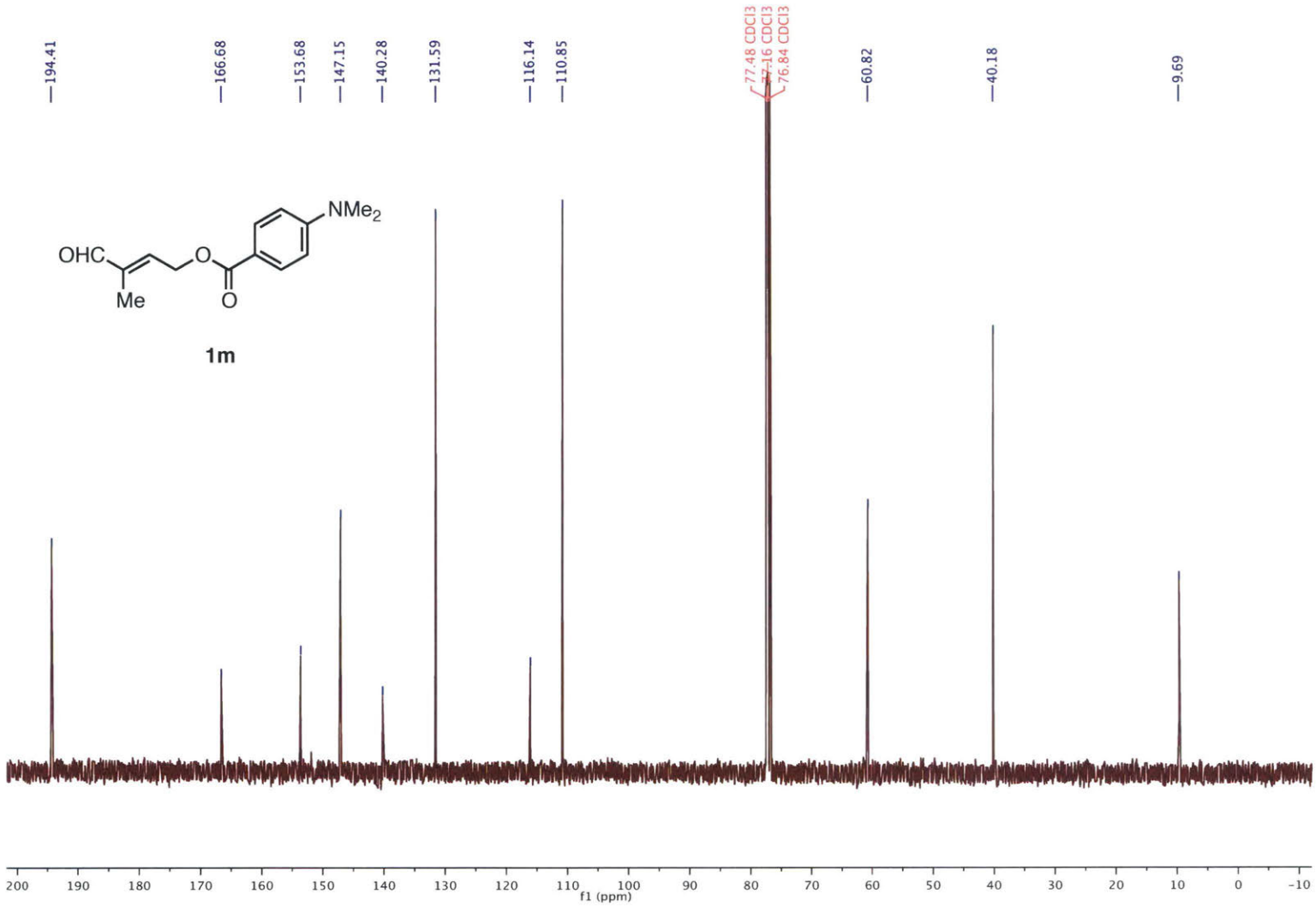
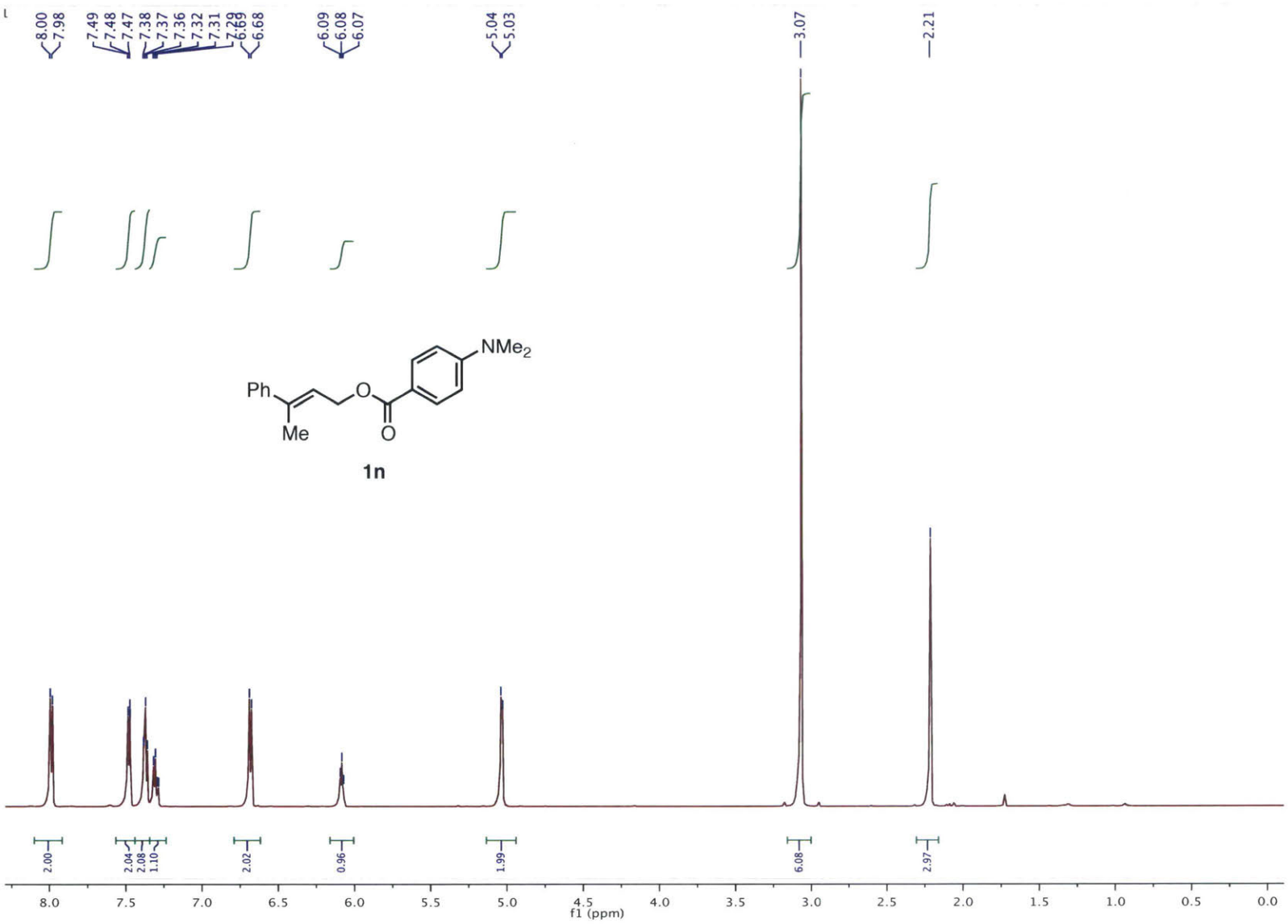
166.75
153.51
153.44
136.15
131.51
131.47
122.10
117.13
116.97
110.85
110.81
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.54
60.68
40.20
14.47
NMe2
Me2N
O
O
O
O
Me
1k
f1 (ppm)

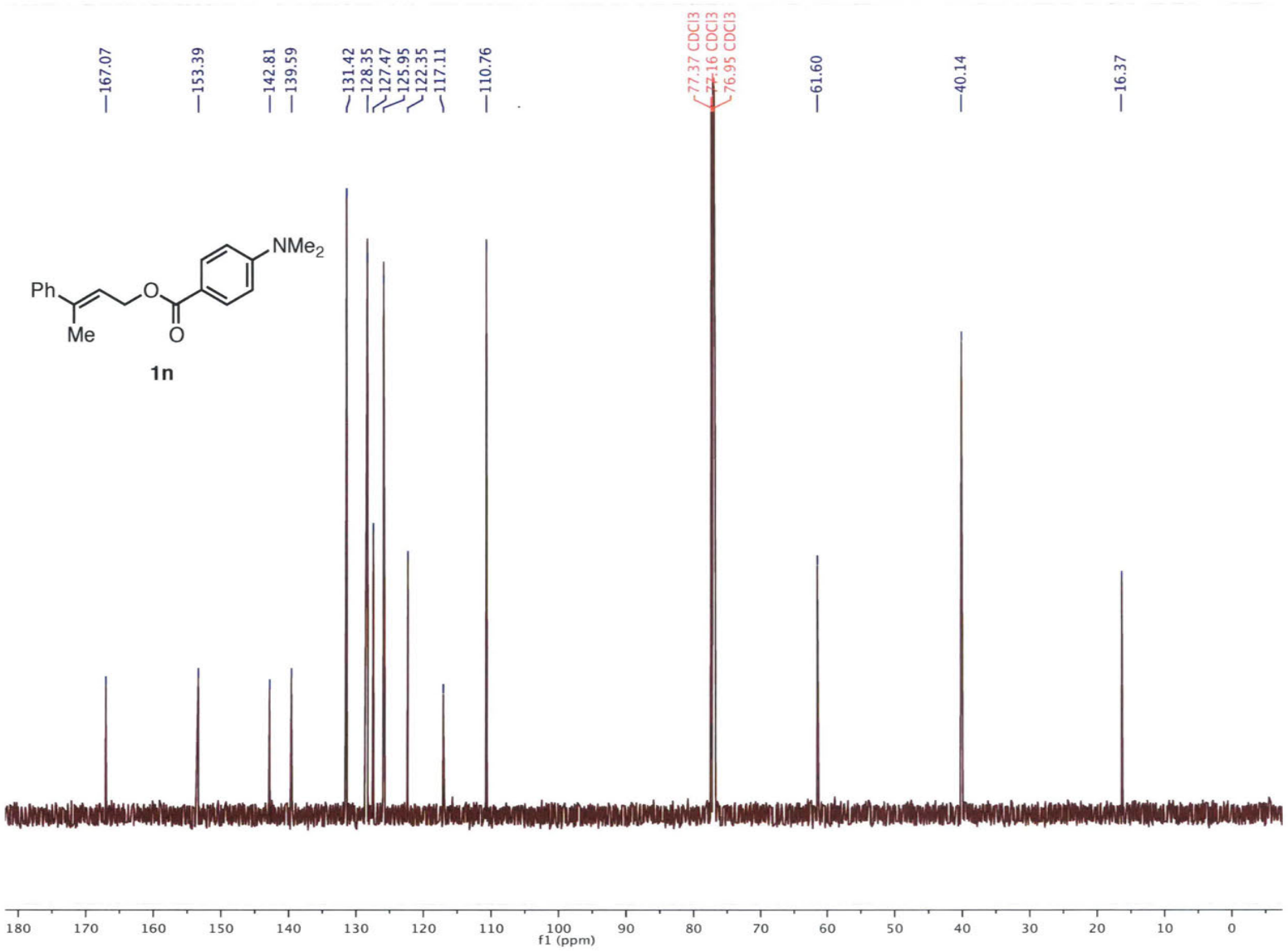

7.99
7.97
7.56
7.54
7.34
7.32
7.31
7.29
7.24
7.23
7.22
6.69
6.68
5.92
5.91
5.90
4.92
4.91
3.07
2.74
1.85
1.69
NMe2
TrHN
Me
O
O
1l
2.06
6.30
6.40
3.18
2.06
1.00
2.05
6.29
2.04
3.11
1.18
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

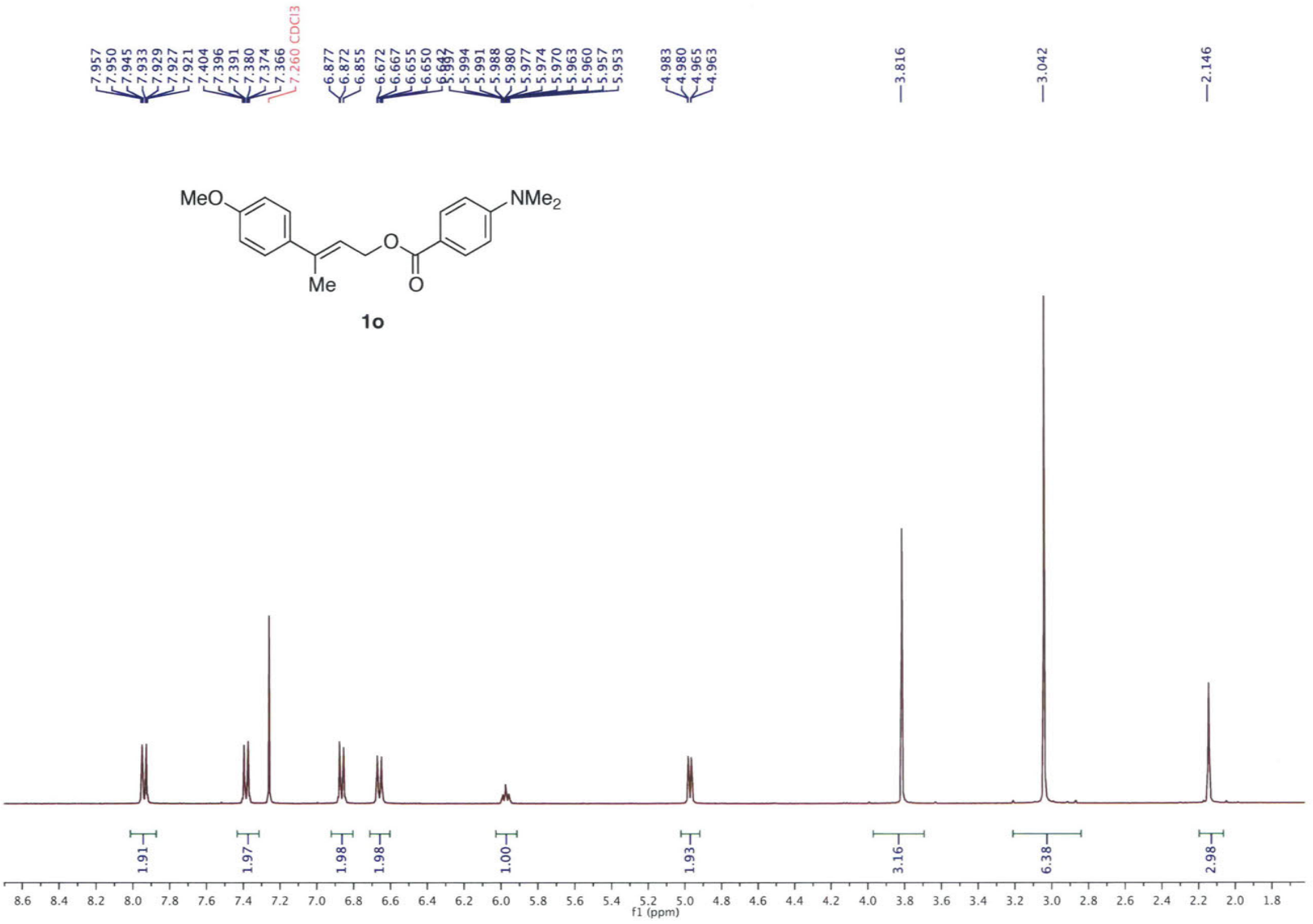

167.15
153.37
146.17
140.49
131.41
128.70
127.95
126.37
119.14
117.28
110.78
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
70.79
61.11
50.95
40.18
16.10
NMe2
TrHN
Me
O
O
1l
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

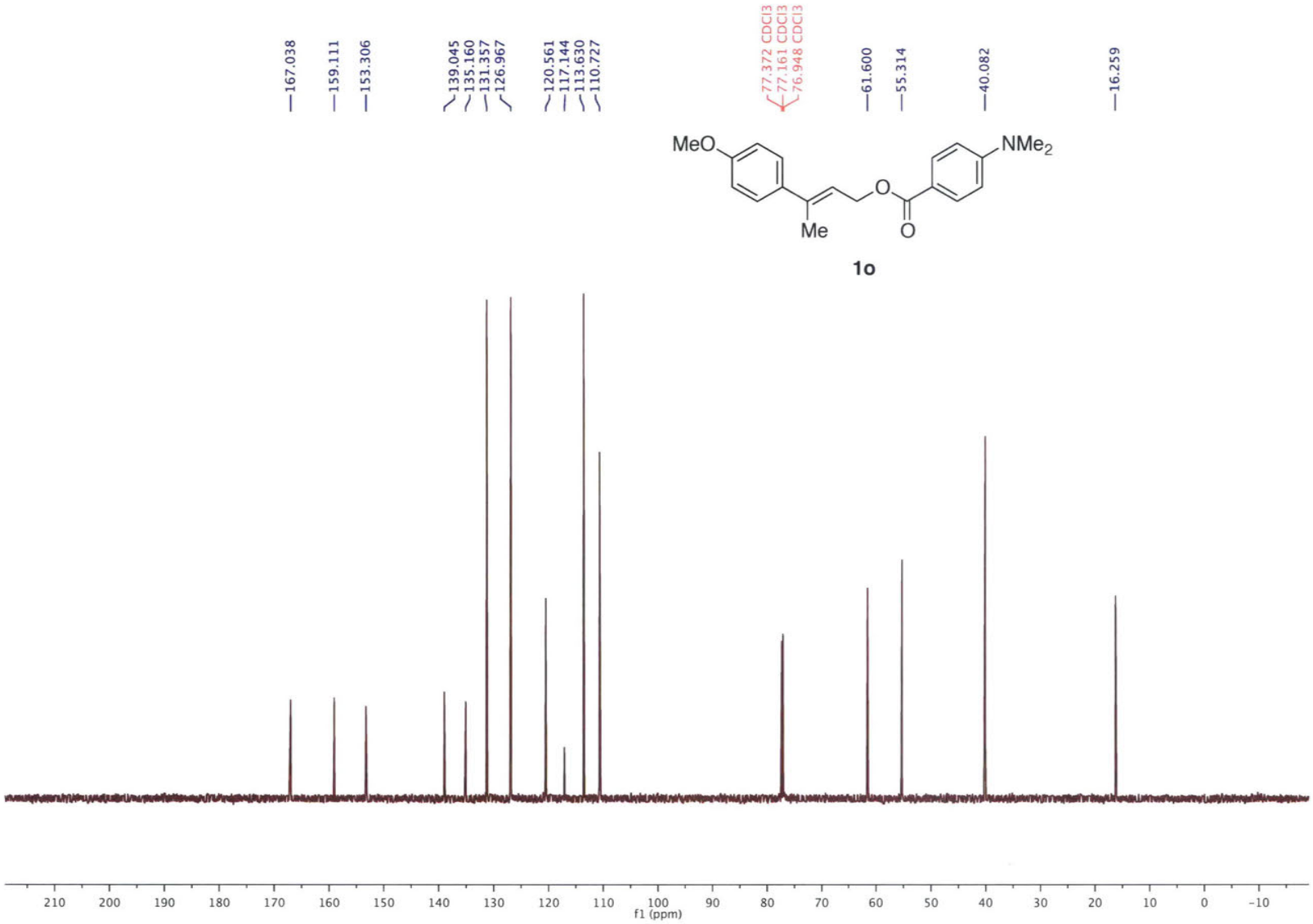

9.50
7.96
7.94
7.28
6.69
6.67
6.64
5.13
5.12
5.11
5.11
3.08
1.87
NMe2
OHC
O
Me
O
1m
0.98
2.00
3.05
2.01
6.07
3.00
f1 (ppm)

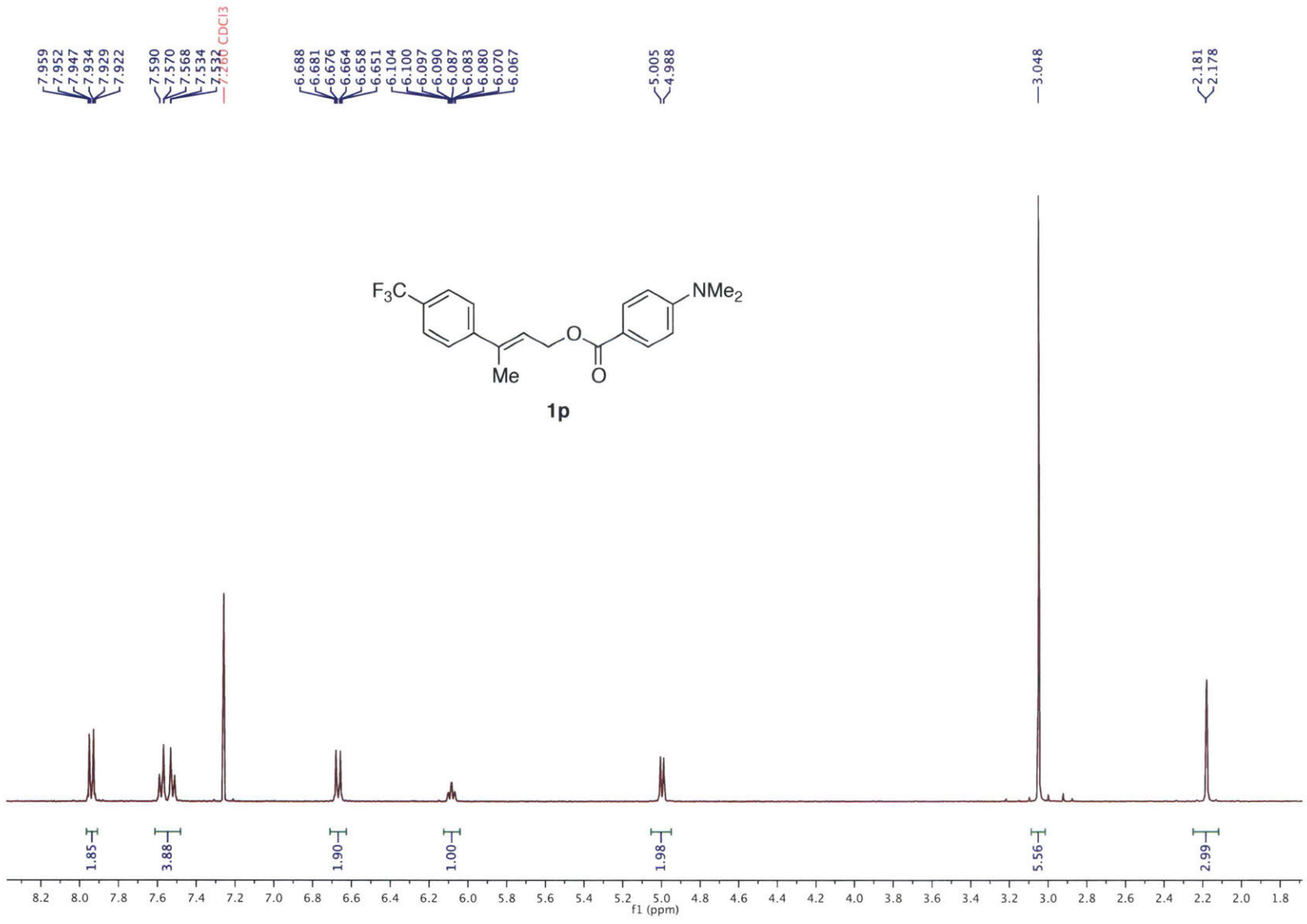

194.41
166.68
153.68
147.15
140.28
131.59
116.14
110.85
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
60.82
40.18
9.69
NMe2
OHC
O
Me
O
1m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

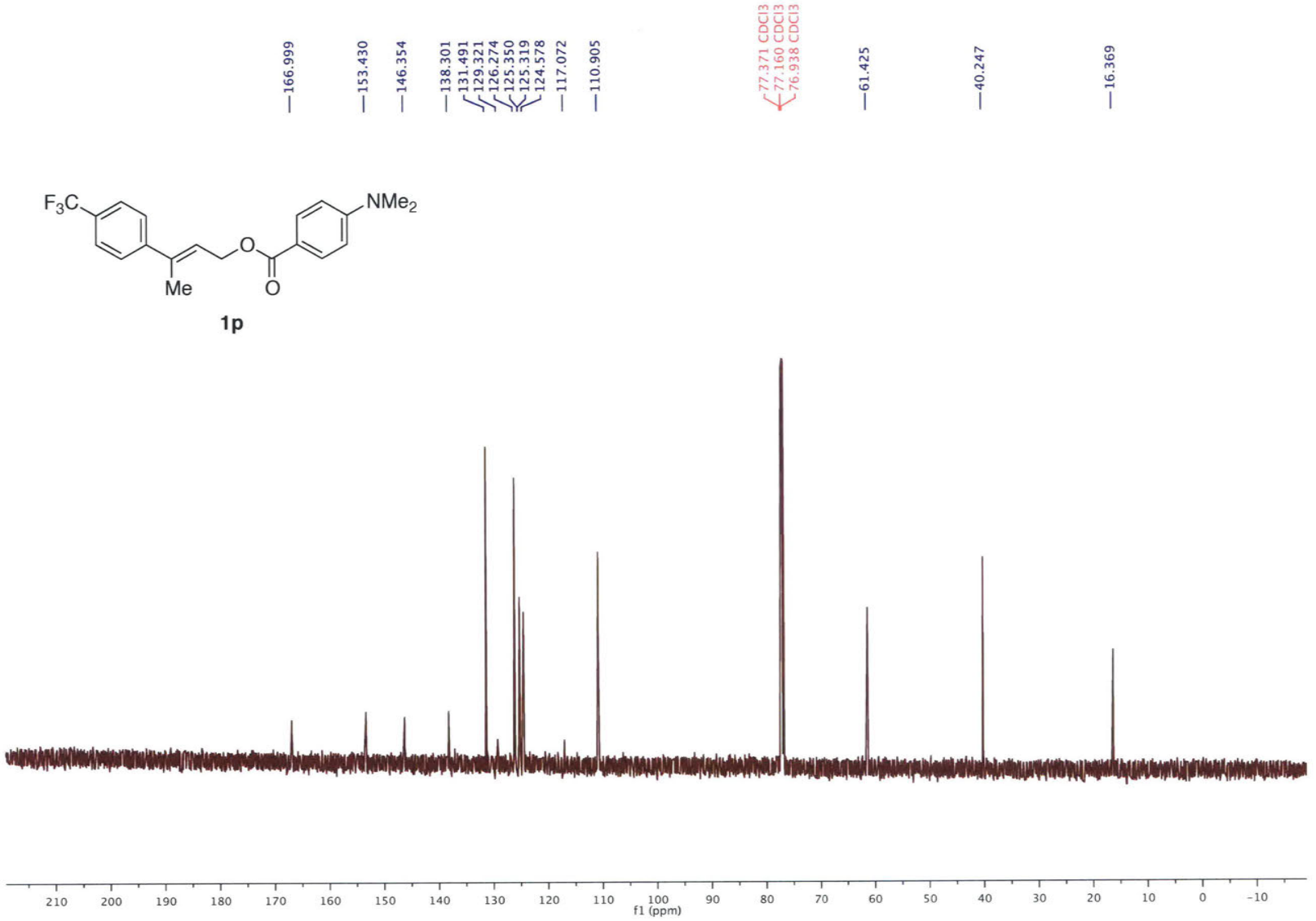

8.00
7.98
7.49
7.48
7.47
7.38
7.37
7.36
7.32
7.31
6.68
6.09
6.08
6.07
5.04
5.03
3.07
2.21
NMe2
Ph
O
Me
O
1n
2.00
2.04
2.08
1.10
2.02
0.96
1.99
6.08
2.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.07
153.39
142.81
139.59
131.42
128.35
127.47
125.95
122.35
117.11
110.76
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
61.60
40.14
16.37
NMe2
Ph
O
Me
O
1n
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.957
7.950
7.945
7.933
7.929
7.927
7.921
7.404
7.396
7.391
7.380
7.374
7.366
7.260 CDCl3
6.877
6.872
6.855
6.672
6.667
6.655
6.650
5.994
5.991
5.988
5.980
5.977
5.974
5.970
5.963
5.960
5.957
5.953
4.983
4.980
4.965
4.963
3.816
3.042
2.146
MeO
NMe2
O
O
Me
1o
1.91
1.97
1.98
1.98
1.00
1.93
3.16
6.38
2.98
f1 (ppm)


167.038
159.111
153.306
139.045
135.160
131.357
126.967
120.561
117.144
113.630
110.727
77.372 CDCl3
77.161 CDCl3
76.948 CDCl3
61.600
55.314
40.082
16.259
MeO
NMe2
O
O
Me
1o
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.959
7.952
7.947
7.934
7.929
7.922
7.590
7.570
7.568
7.534
7.532
7.260 CDCl3
6.688
6.681
6.676
6.664
6.658
6.651
6.104
6.100
6.097
6.090
6.087
6.083
6.080
6.070
6.067
5.005
4.988
3.048
2.181
2.178
F3C
NMe2
O
Me
O
1p
1.85
3.88
1.90
1.00
1.98
5.56
2.99
f1 (ppm)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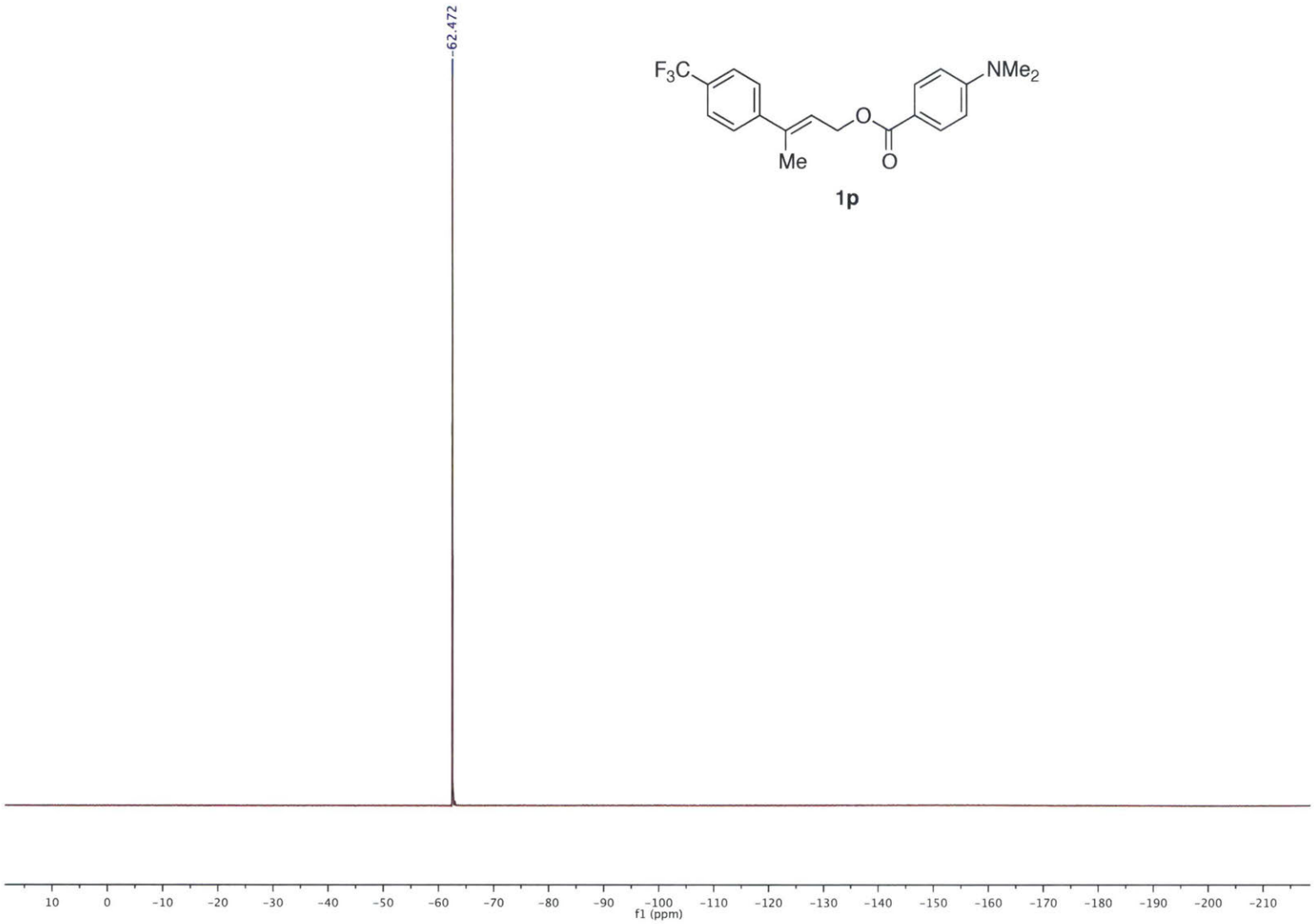
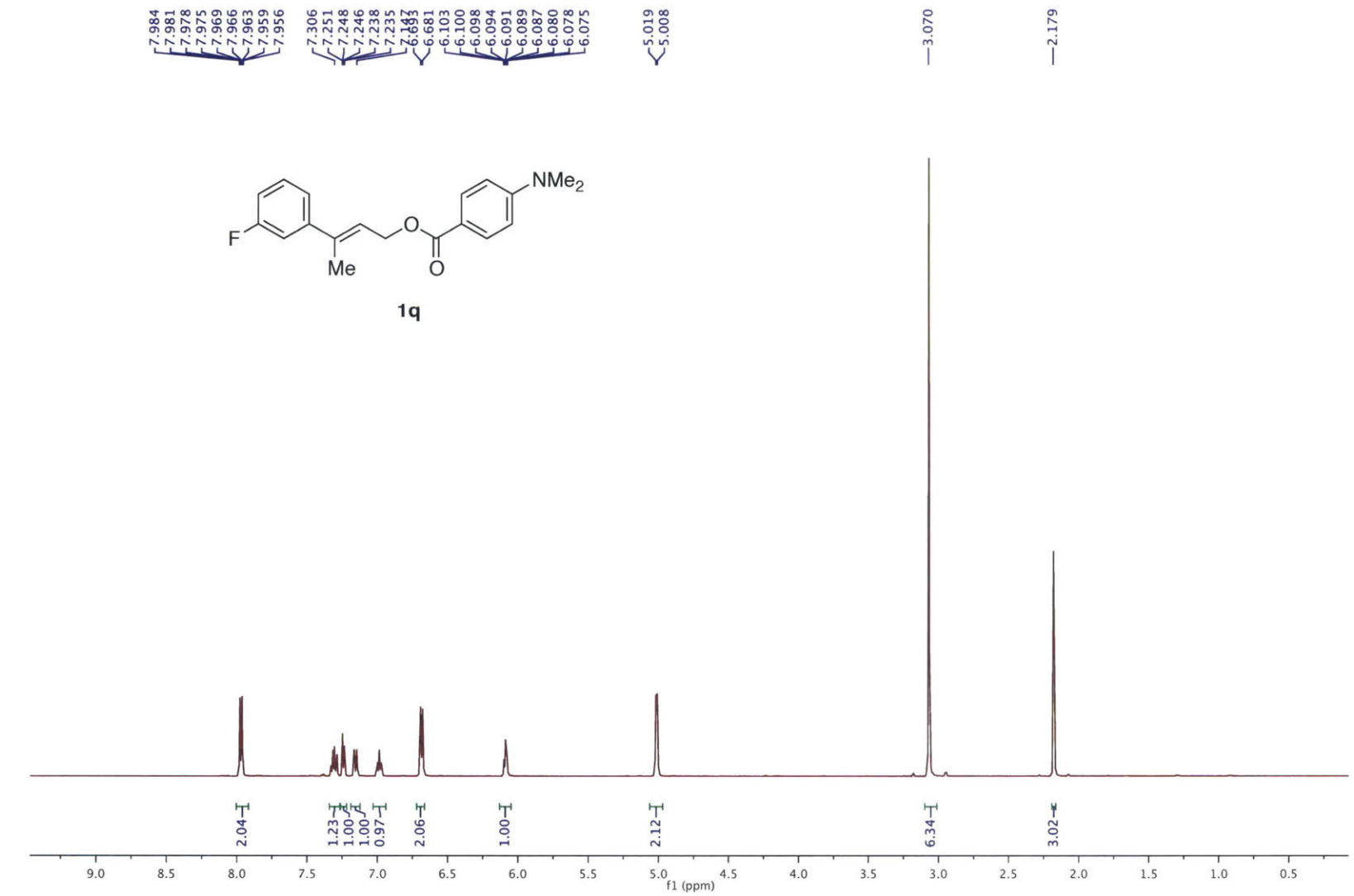
153.430
146.354
138.301
131.491
129.321
126.274
125.350
125.319
124.578
117.072
110.905
77.371 CDCl3
77.160 CDCl3
76.938 CDCl3
61.425
40.247
16.369
F3C
NMe2
O
Me
O
1p
f1 (ppm)


-62.472
F3C
NMe2
O
Me
O
1p
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)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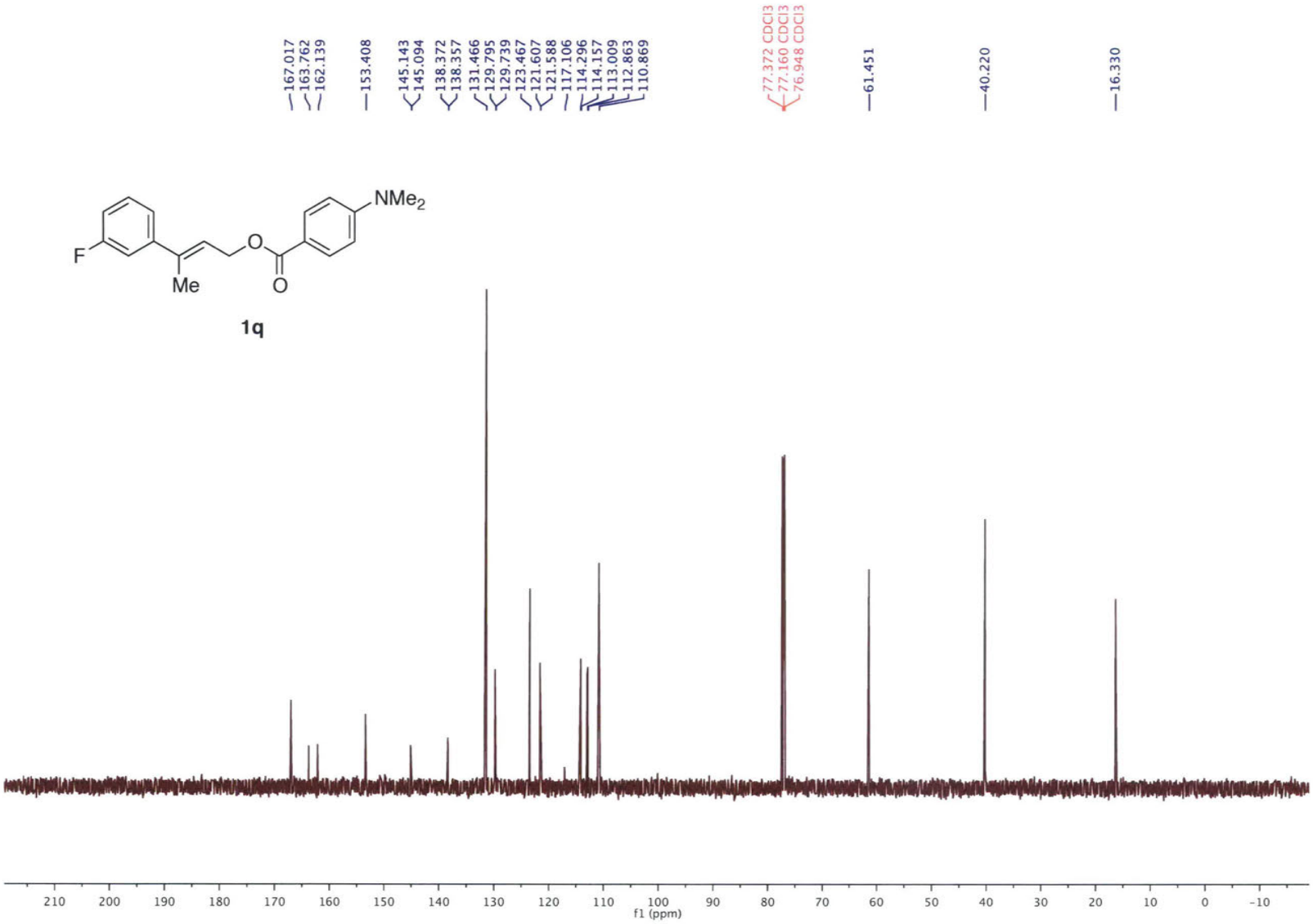
7.981
7.978
7.975
7.969
7.966
7.963
7.959
7.956
7.306
7.251
7.248
7.246
7.238
7.235
6.681
6.103
6.100
6.098
6.094
6.091
6.089
6.087
6.080
6.078
6.075
5.019
5.008
3.070
2.179
NMe2
F
O
Me
O
1q
2.04
1.23
1.00
1.00
0.97
2.06
1.00
2.12
6.34
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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162.139
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145.094
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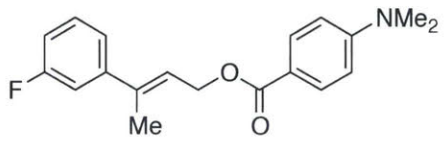
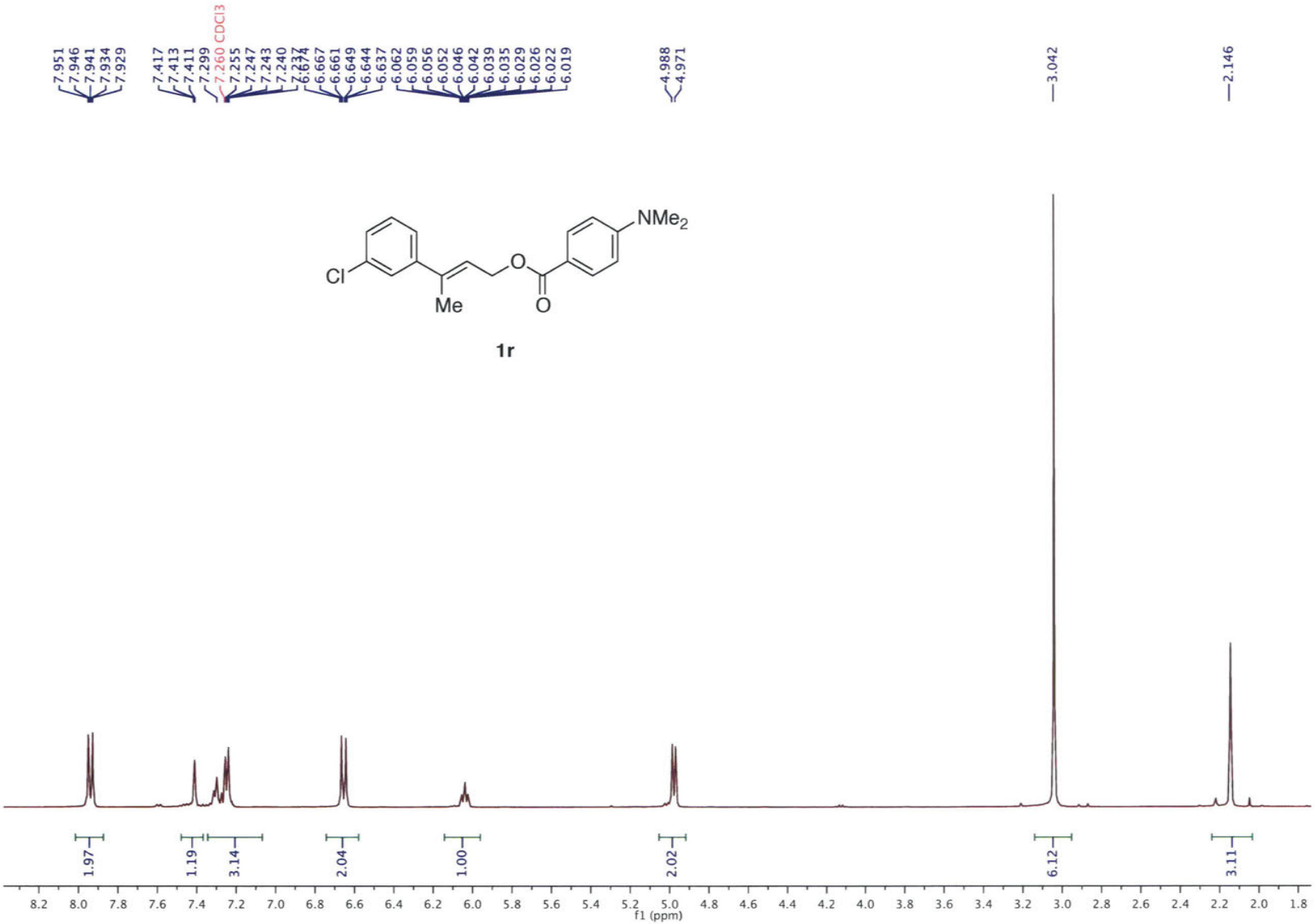
138.357
131.466
129.795
129.739
123.467
121.607
121.588
117.106
114.296
114.157
113.009
112.863
110.869
77.372 CDCl3
77.160 CDCl3
76.948 CDCl3
61.451
40.220
16.330
NMe2
F
O
O
Me
1q
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


F
Me
O
O
NMe2

1q

-113.629
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)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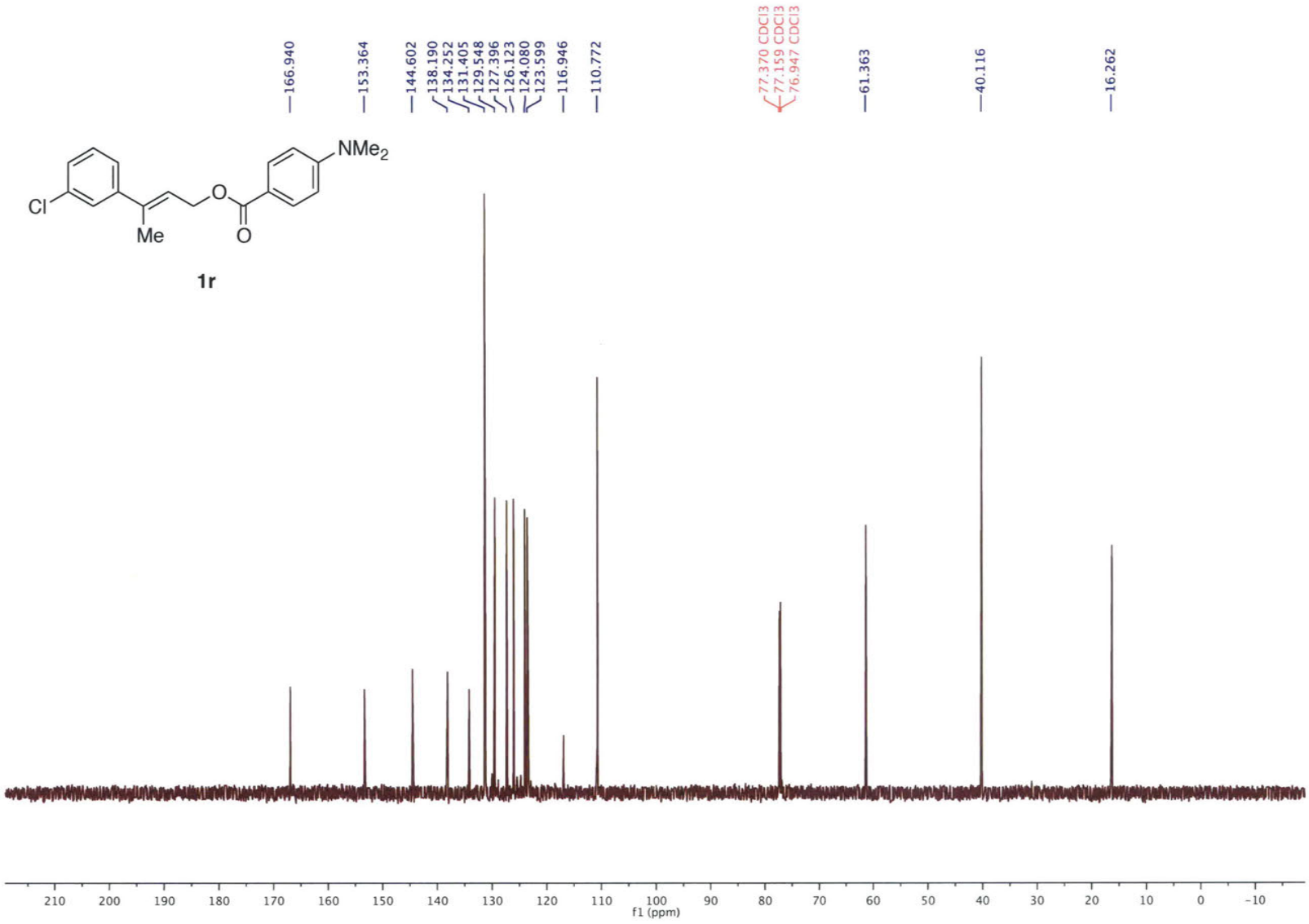
7.941
7.934
7.929
7.417
7.413
7.411
7.299
7.260 CDCl3
7.255
7.247
7.243
7.240
6.667
6.661
6.649
6.644
6.637
6.062
6.059
6.056
6.052
6.046
6.042
6.039
6.035
6.029
6.026
6.022
6.019
4.988
4.971
3.042
2.146
NMe2
Cl
O
Me
O
1r
1.97
1.19
3.14
2.04
1.00
2.02
6.12
3.11
f1 (ppm)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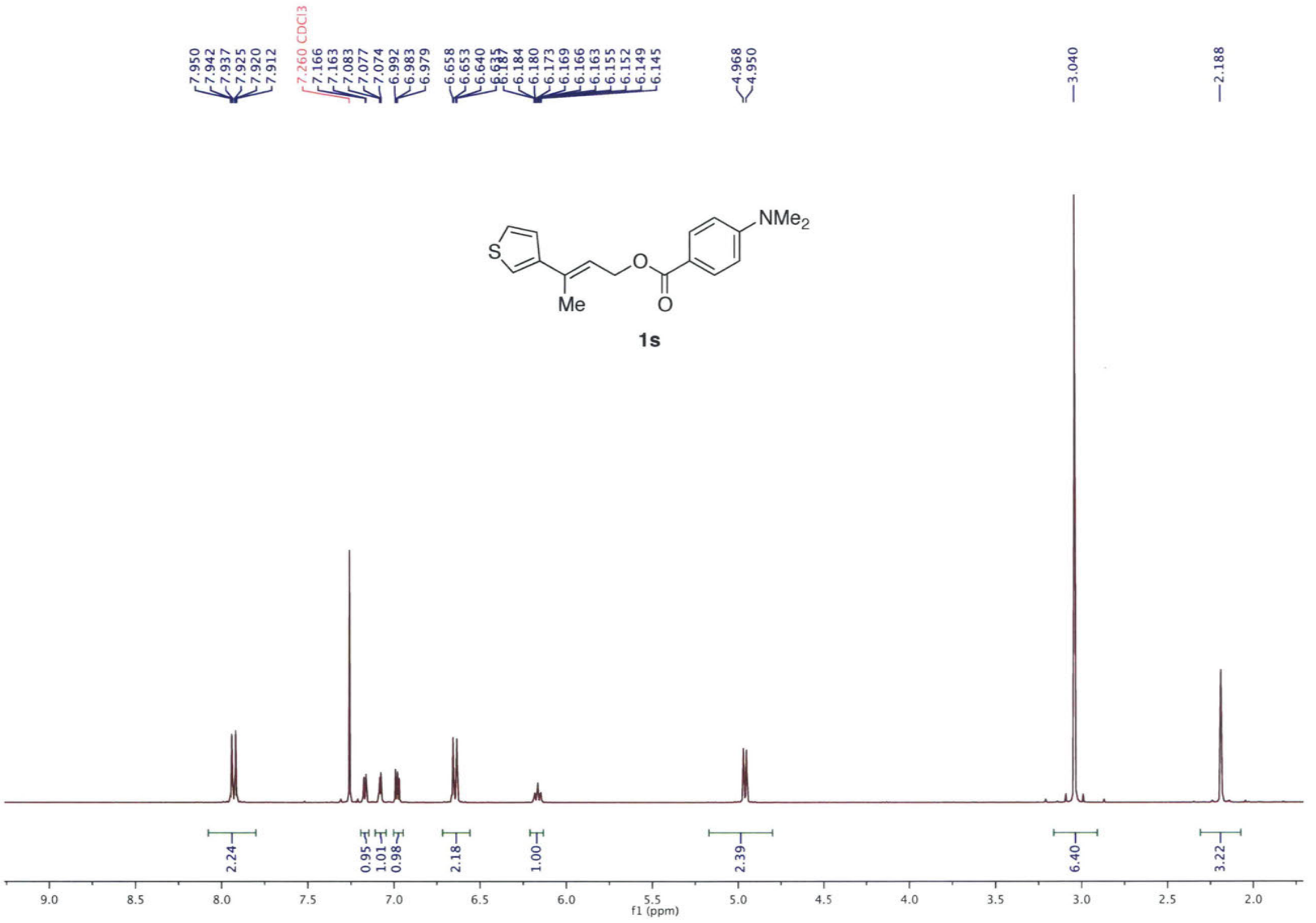
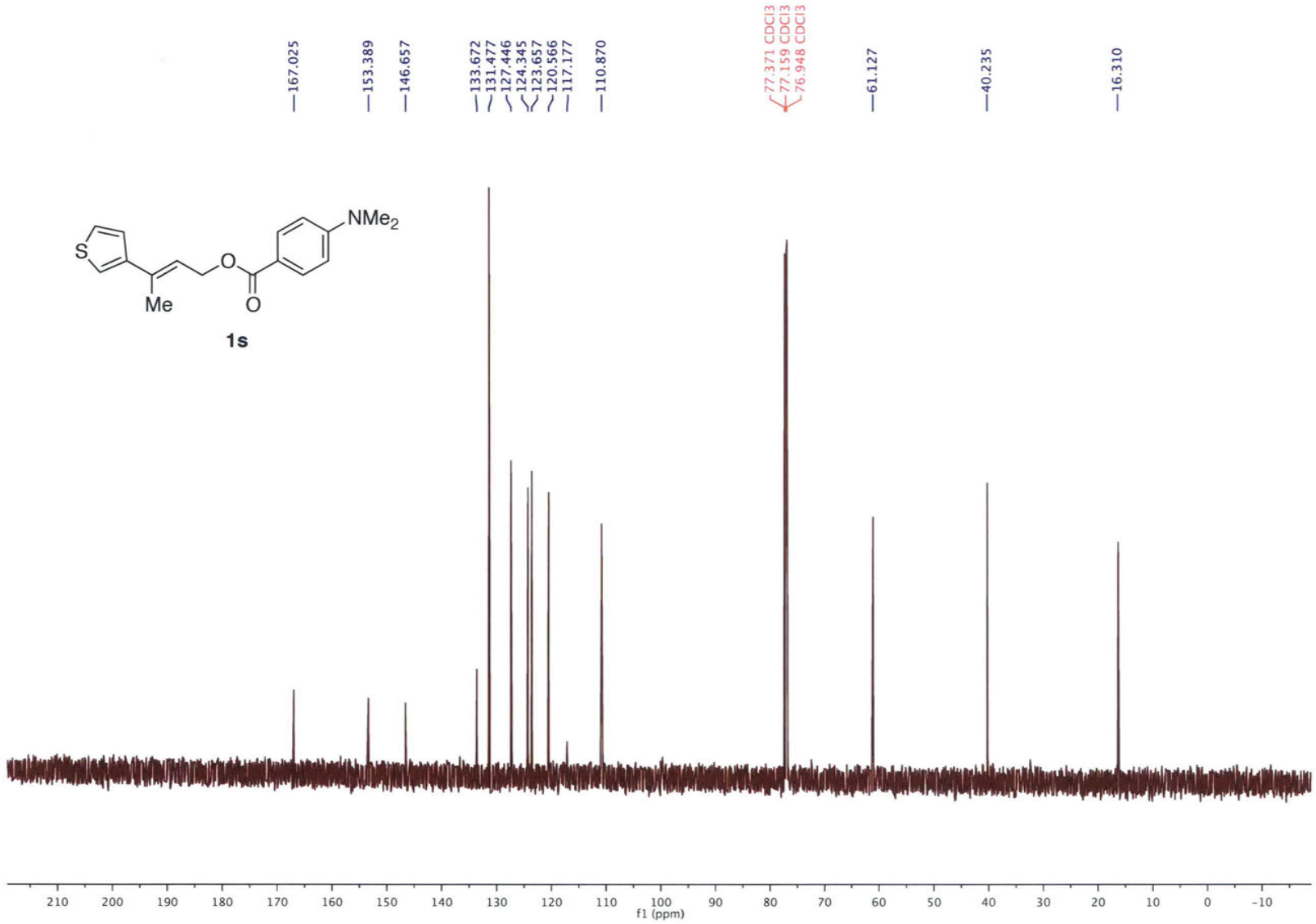
153.364
144.602
138.190
134.252
131.405
129.548
127.396
126.123
124.080
123.599
116.946
110.772
77.370 CDCl3
77.159 CDCl3
76.947 CDCl3
61.363
40.116
16.262
NMe2
Cl
O
Me
O
1r
f1 (ppm)


7.950
7.942
7.937
7.925
7.920
7.912
7.260 CDCl3
7.166
7.163
7.083
7.077
7.074
6.992
6.983
6.979
6.658
6.653
6.640
6.184
6.180
6.173
6.169
6.166
6.163
6.155
6.152
6.149
6.145
4.968
4.950
3.040
2.188
NMe2
S
O
Me
O
1s
2.24
0.95
1.01
0.98
2.18
1.00
2.39
6.40
3.22
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
f1 (ppm)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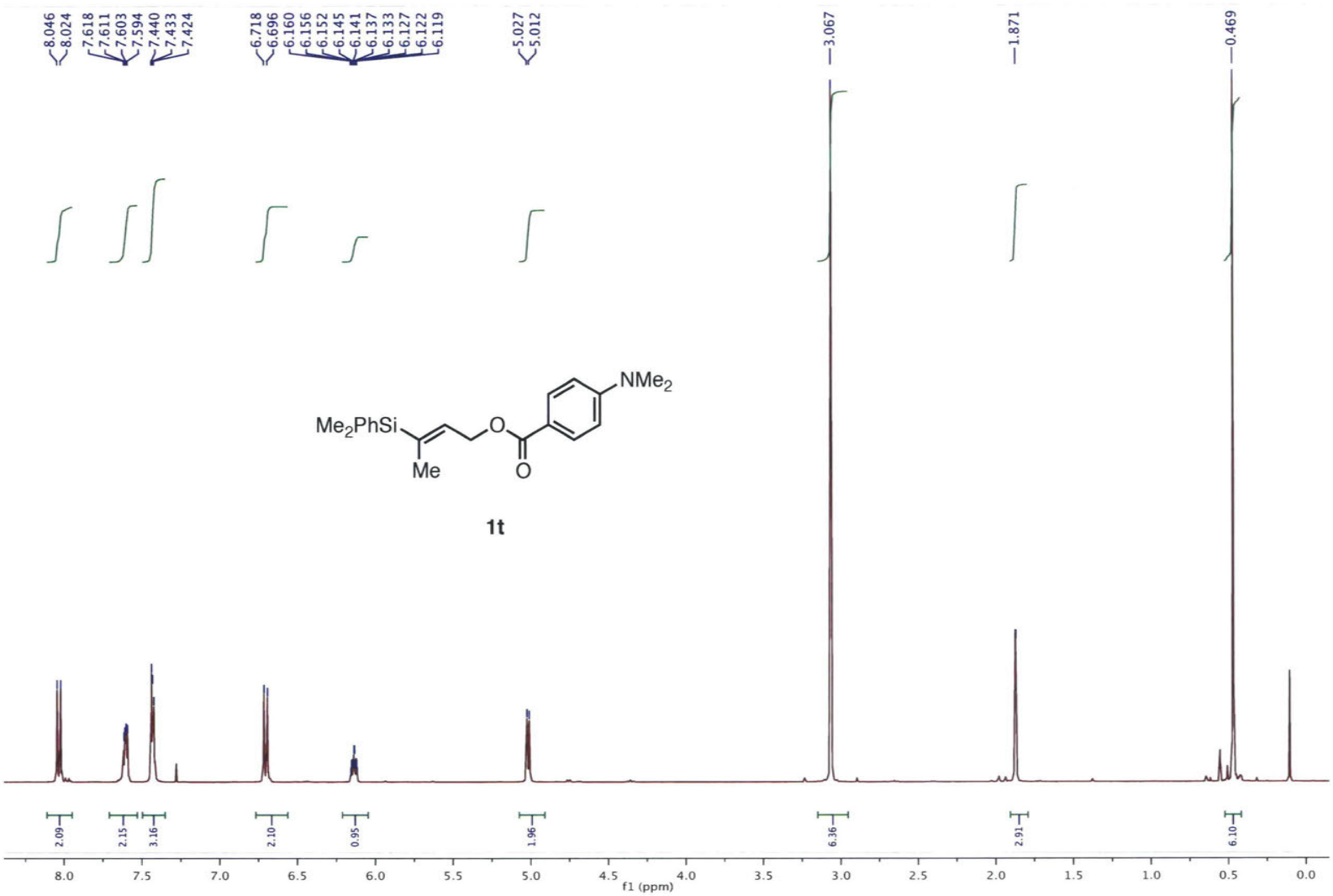
133.672
131.477
127.446
124.345
123.657
120.566
117.177
110.870
77.371 CDCl3
77.159 CDCl3
76.948 CDCl3
61.127
40.235
16.310
NMe2
S
O
Me
O
1s
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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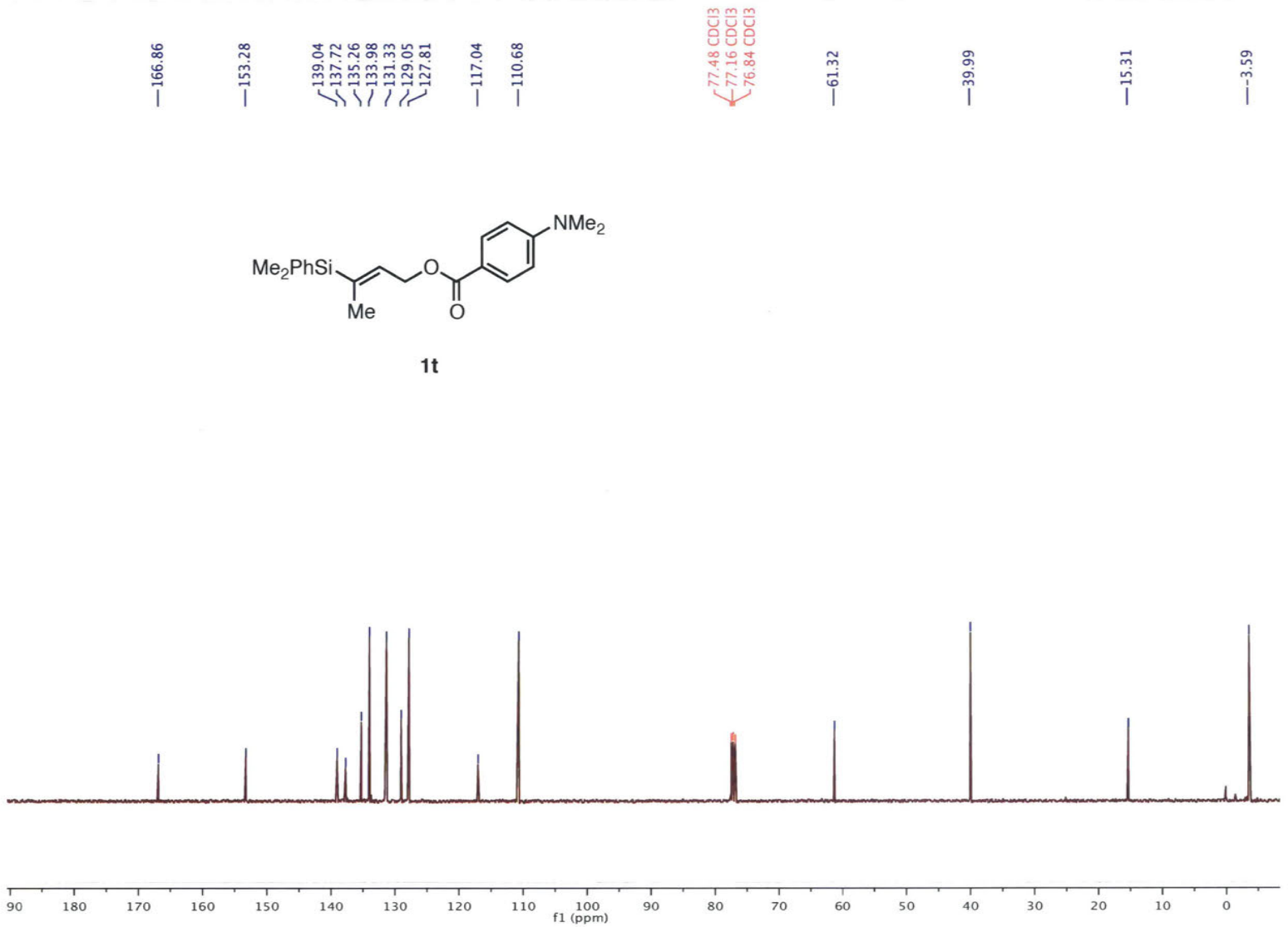
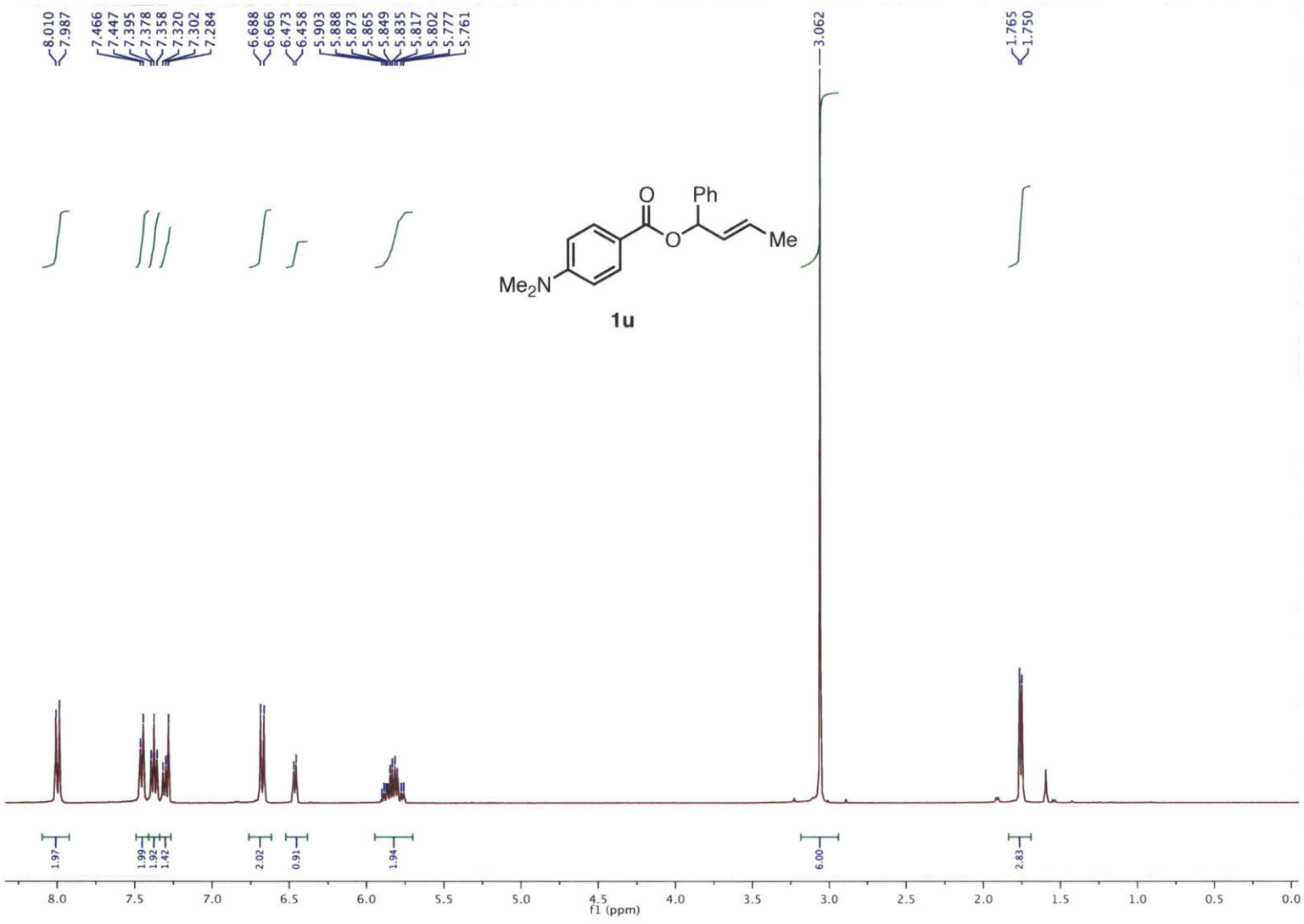
7.618
7.611
7.603
7.594
7.440
7.433
7.424
6.718
6.696
6.160
6.156
6.152
6.145
6.141
6.137
6.133
6.127
6.122
6.119
5.027
5.012
3.067
1.871
0.469
NMe2
Me2PhSi
O
Me
O
2.09
2.15
3.16
2.10
0.95
1.96
6.36
2.91
6.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

1t


166.86
153.28
139.04
137.72
135.26
133.98
131.33
129.05
127.81
117.04
110.68
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
61.32
39.99
15.31
3.59
NMe2
Me2PhSi
O
Me
O
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1t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7.395
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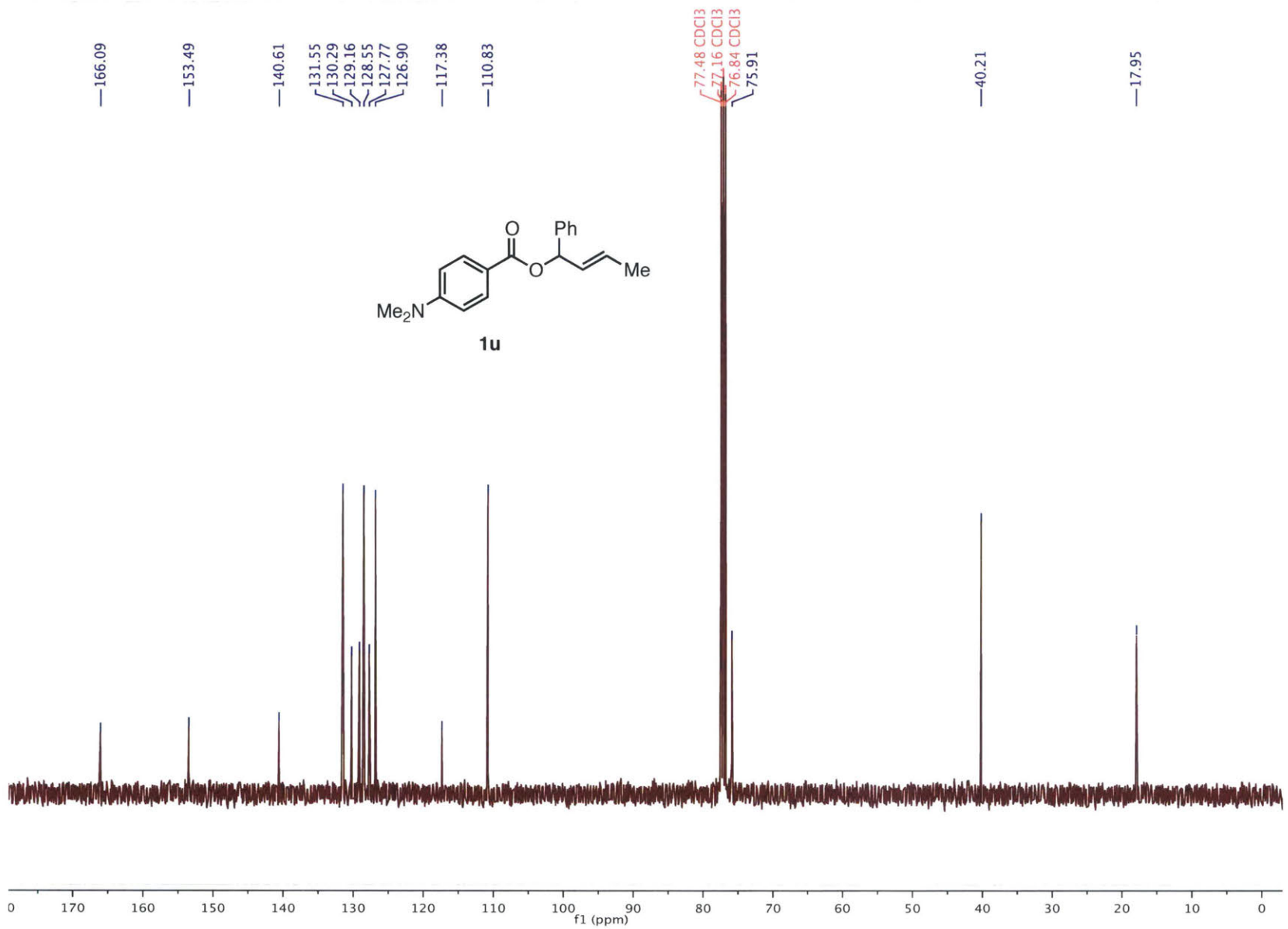
7.320
7.302
7.284
6.688
6.666
6.473
6.458
5.903
5.888
5.873
5.865
5.849
5.835
5.817
5.802
5.777
5.761
3.062
1.765
1.750
O
Ph
O
Me
Me2N
1u
1.97
1.99
1.92
1.42
2.02
0.91
1.94
6.00
2.83
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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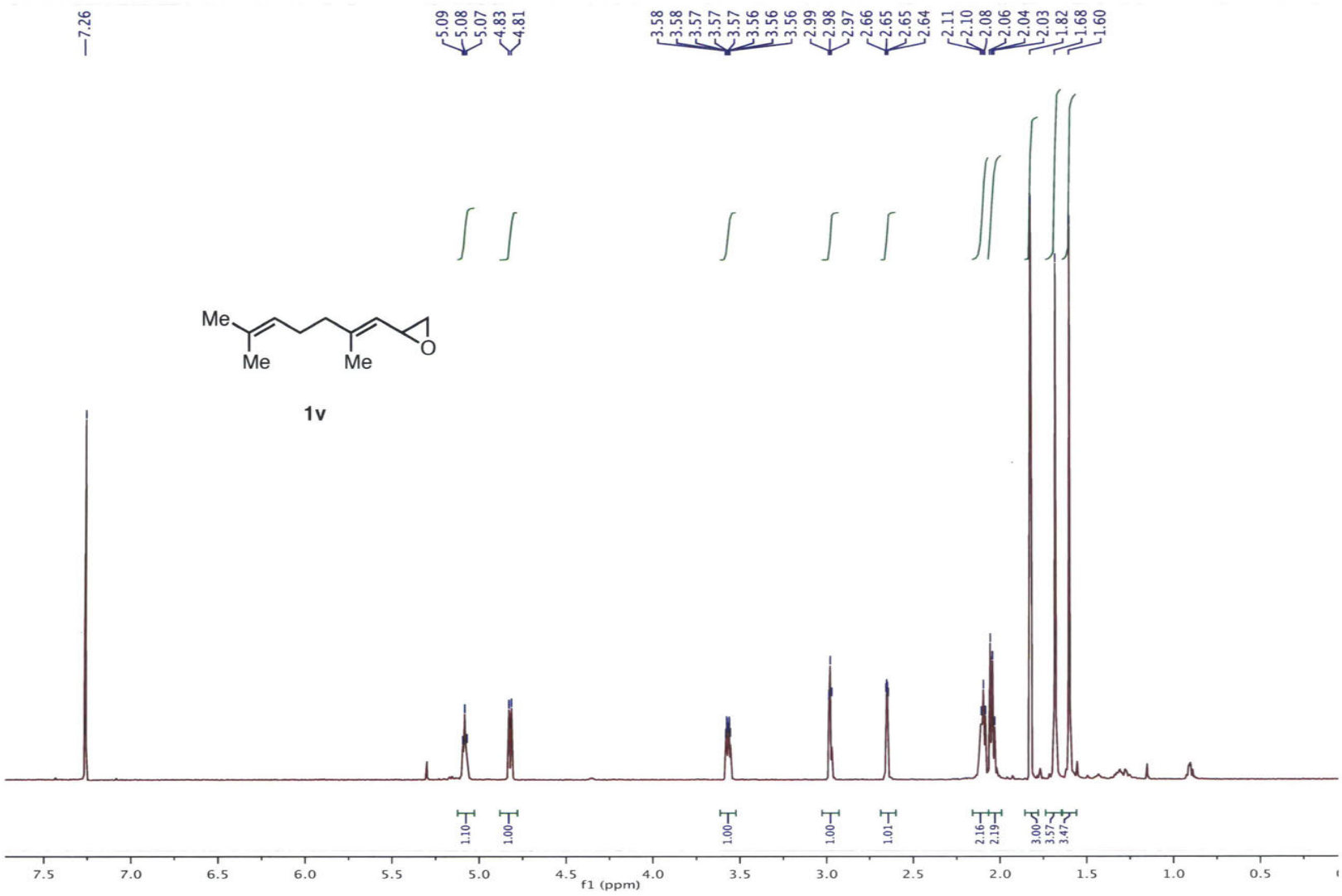
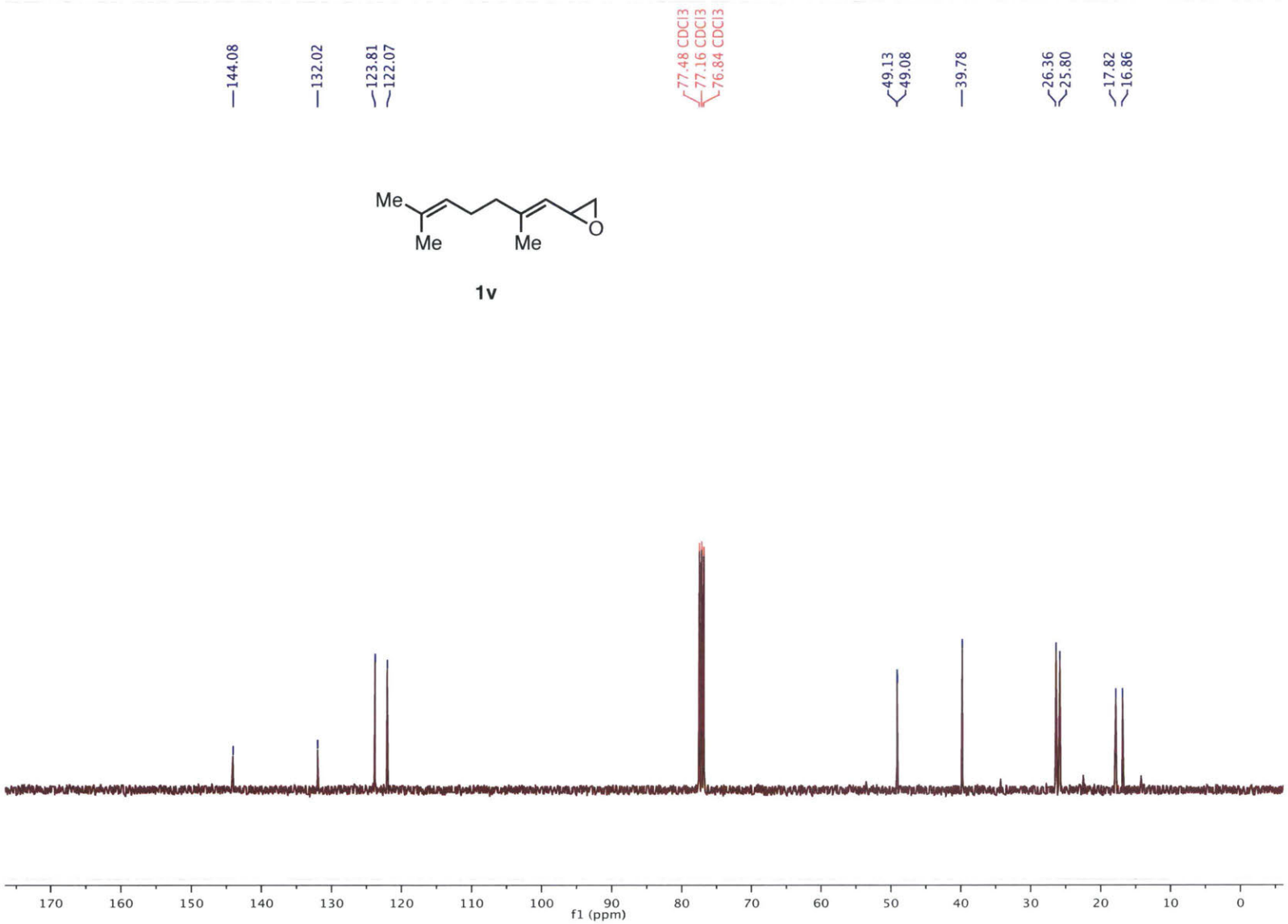
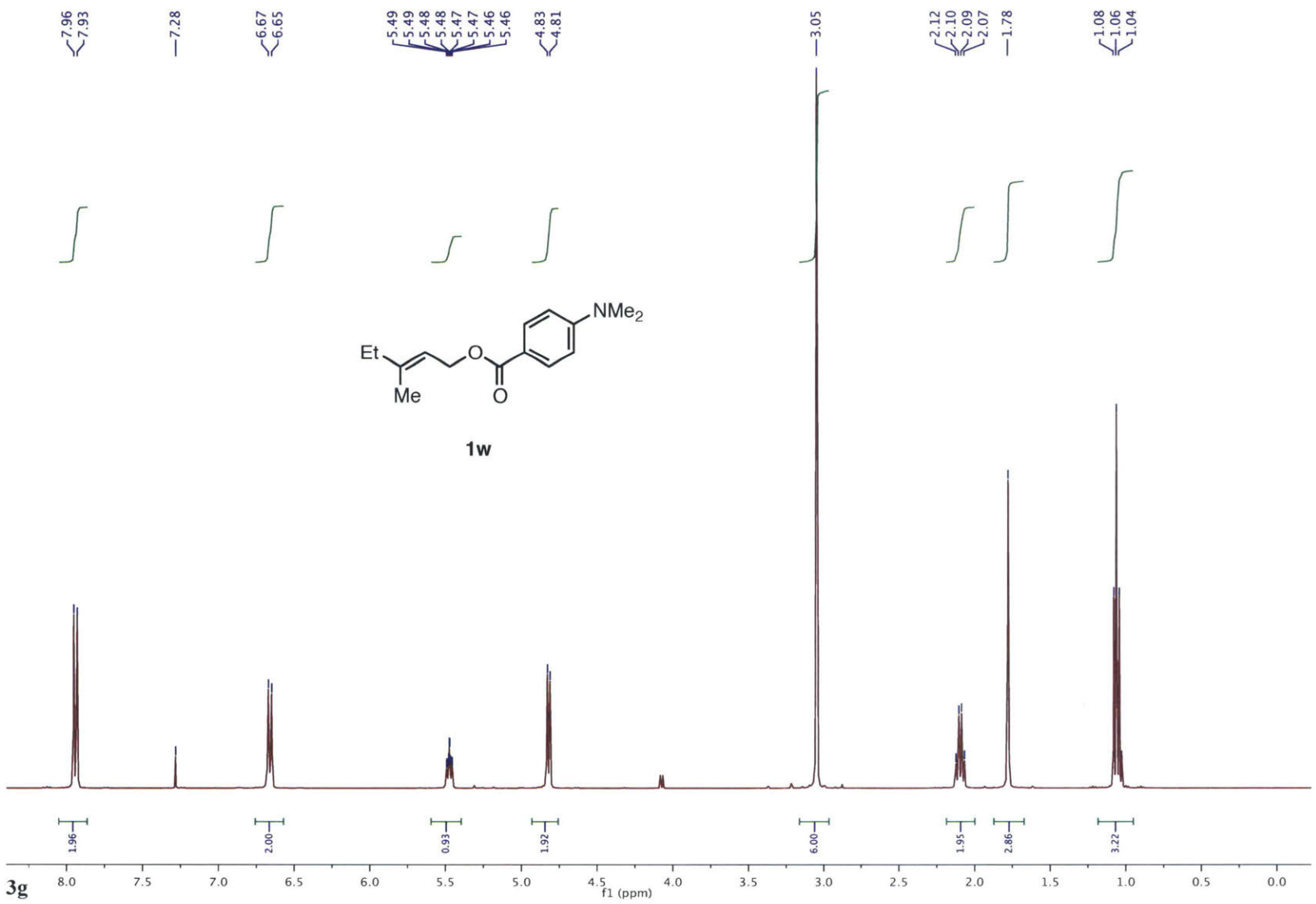
153.49
140.61
131.55
130.29
129.16
128.55
127.77
126.90
117.38
110.83
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
75.91
40.21
17.95
O
Ph
O
Me
Me2N
1u
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.26
5.09
5.08
5.07
4.83
4.81
3.58
3.58
3.57
3.57
3.57
3.56
3.56
3.56
2.99
2.98
2.97
2.66
2.65
2.65
2.64
2.11
2.10
2.08
2.06
2.04
2.03
1.82
1.68
1.60
Me
Me
Me
O
1v
1.10
1.00
1.00
1.00
1.01
2.16
2.19
3.00
3.57
3.47
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
f1 (ppm)


144.08
132.02
123.81
122.07
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
49.13
49.08
39.78
26.36
25.80
17.82
16.86
Me
Me
Me
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1v


7.96
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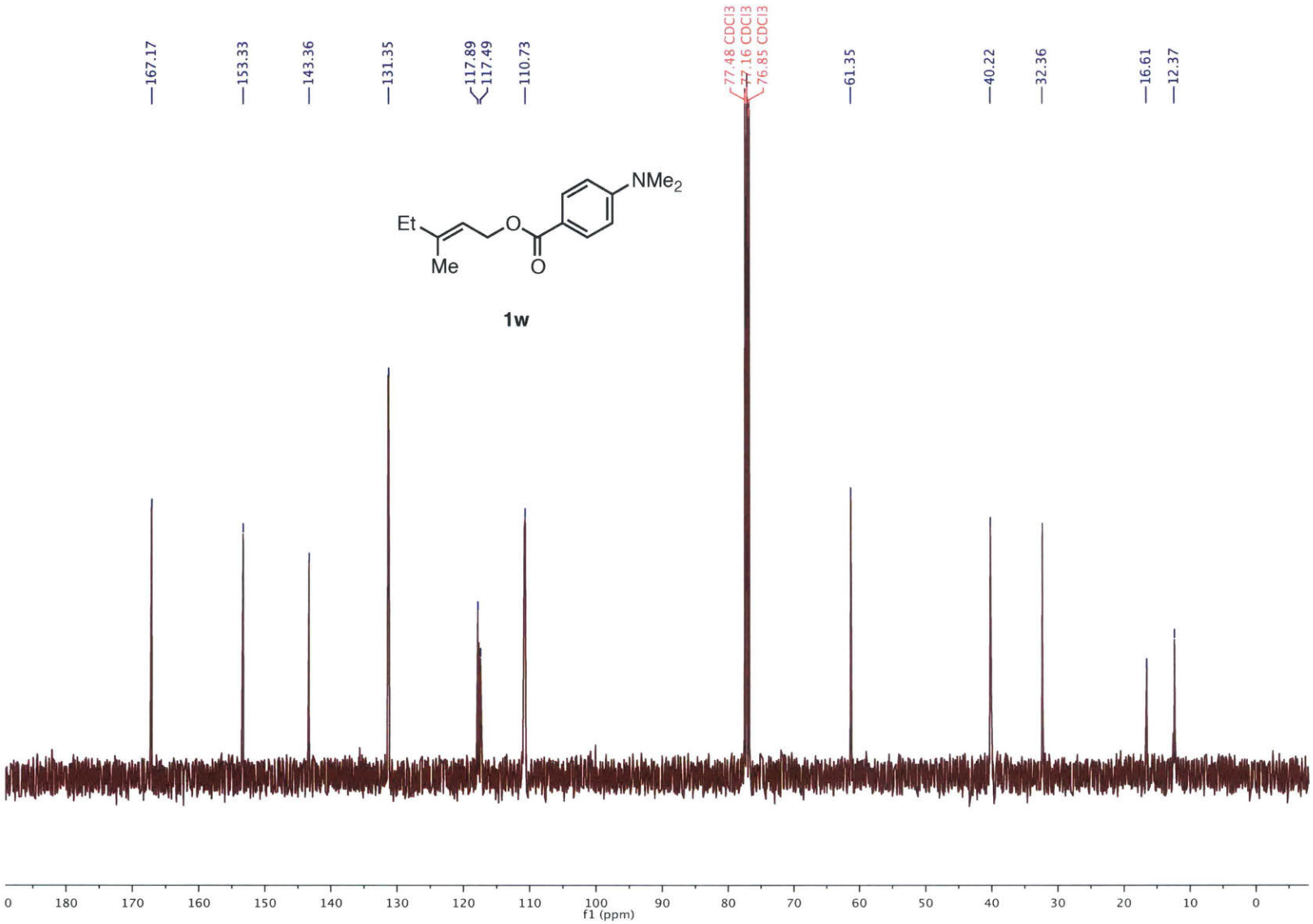
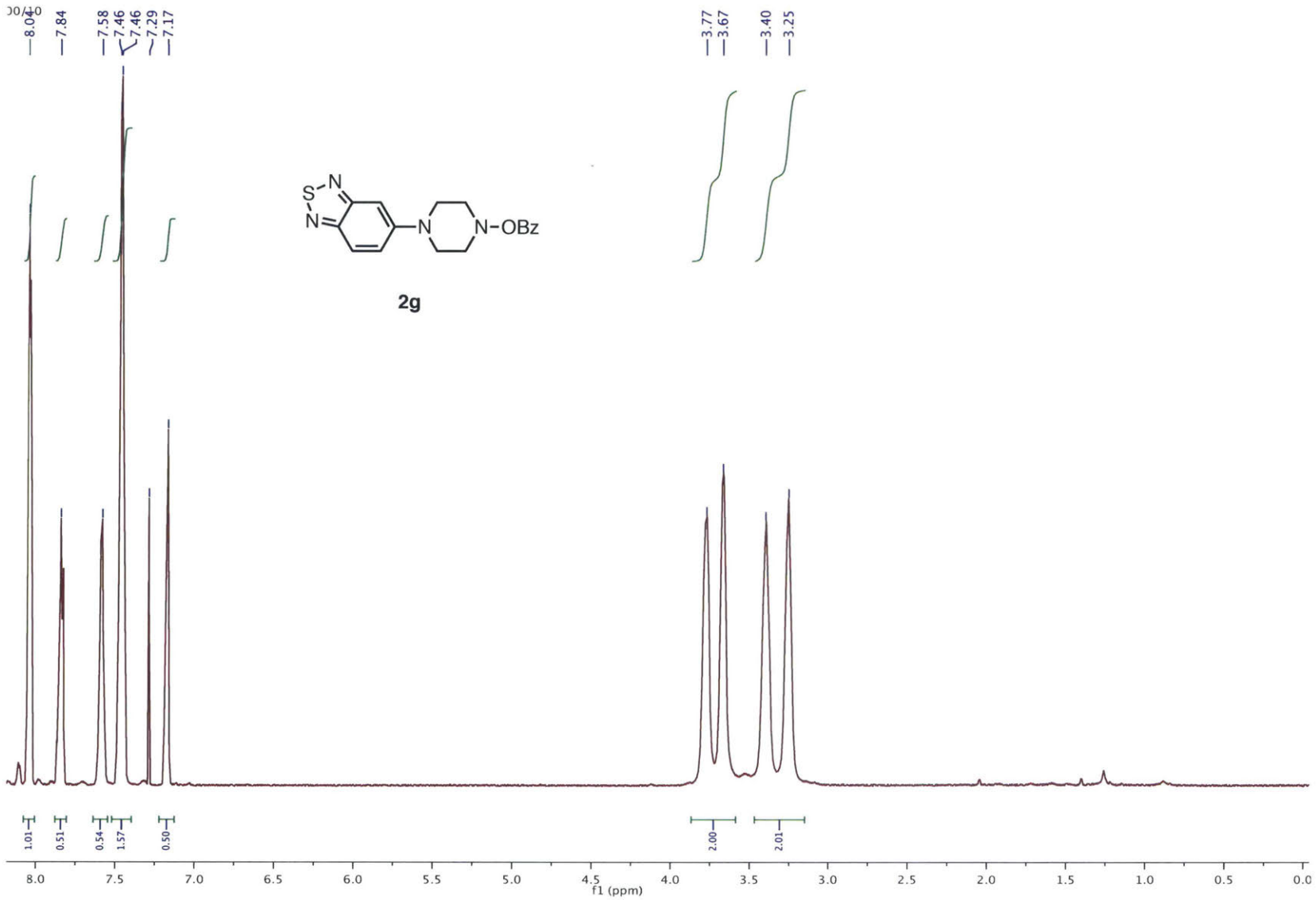
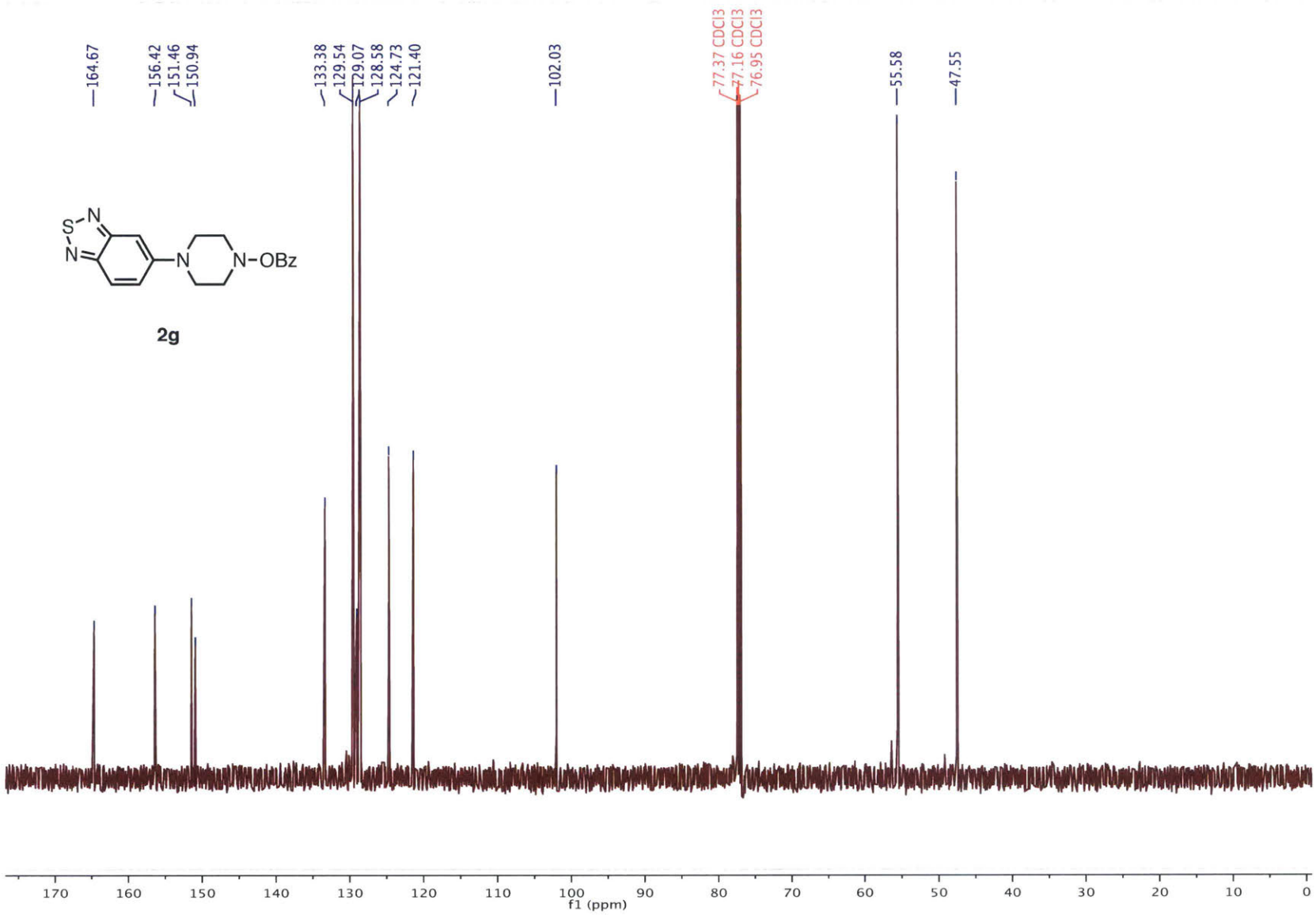
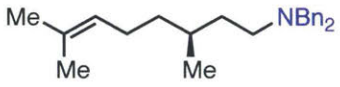
7.28
6.67
6.65
5.49
5.49
5.48
5.48
5.47
5.47
5.46
5.46
4.83
4.81
3.05
2.12
2.10
2.09
2.07
1.78
1.08
1.06
1.04
NMe2
Et
O
Me
O
1w
1.96
2.00
0.93
1.92
6.00
1.95
2.86
3.22
3g
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


167.17
153.33
143.36
131.35
117.89
117.49
110.73
77.48 CDCl3
77.16 CDCl3
76.85 CDCl3
61.35
40.22
32.36
16.61
12.37
NMe2
Et
O
Me
O
1w
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.04
7.84
7.58
7.46
7.46
7.29
7.17
3.77
3.67
3.40
3.25
N
S
N
N
N-OBz
2g
1.01
0.51
0.54
1.57
0.50
2.00
2.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.67
156.42
151.46
150.94
133.38
129.54
129.07
128.58
124.73
121.40
102.03
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
55.58
47.55
N
S
N
N
N
N-OBz
2g
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

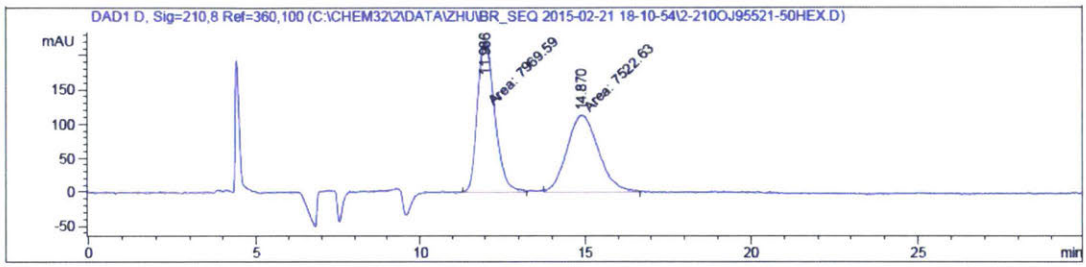
4.7 Chiral HPLC Spectra



(+)**3a**

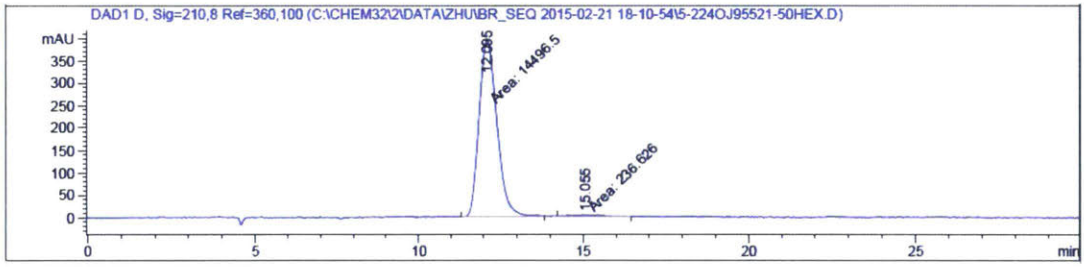
(*S*)-*N*,*N*-dibenzyl-3,7-dimethyloct-6-en-1-amine (Scheme 3 and 4, entry (+)**3a**). HPLC analysis (OJ-H, 50% (hexanes:EtOH:TFA: **Diethylamine** = 95:5:0.2:0.1)/hexanes, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (major) = 12.0 min, t_R (minor) = 14.9 min.

Rac-**3a**

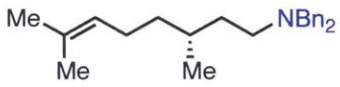


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.986	FM	0.6007	7969.59033	221.12422	51.4425
2	14.870	MF	1.1107	7522.62842	112.88332	48.5575

(+)3a: 97% *ee* (average of 2 runs)



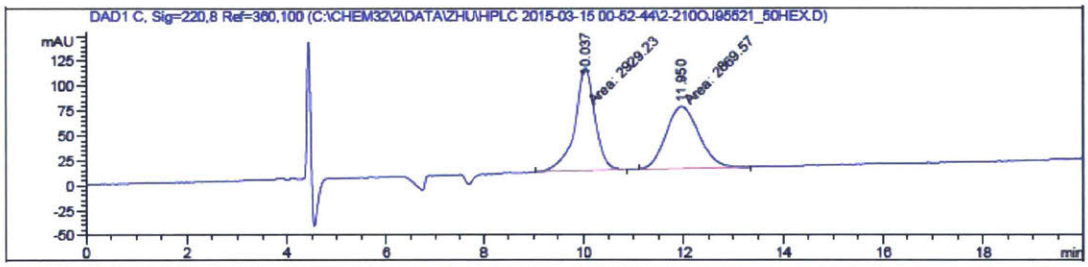
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.095	MF	0.6110	1.44965e4	395.43283	98.3939
2	15.055	FM	1.0794	236.62633	3.65359	1.6061



(–)**3a**

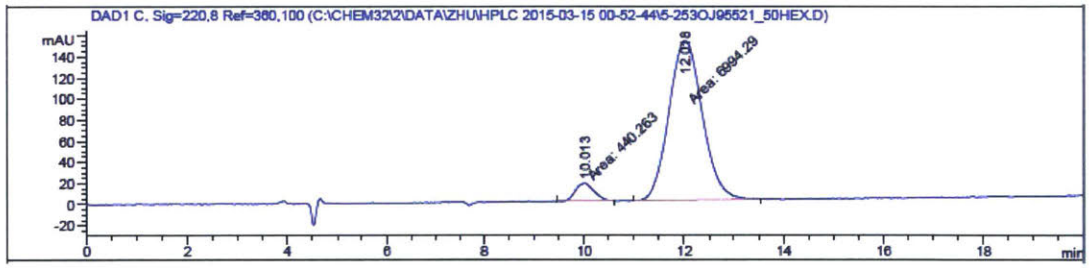
(*R*)-*N*,*N*-dibenzyl-3,7-dimethyloct-6-en-1-amine (Scheme 3 and 4, entry **3a**). HPLC analysis (OJ-H, 50% (hexanes:EtOH:TFA: **Diethylamine** = 95:5:0.2:0.1)/hexanes, 0.8 mL/min, 220 nm) indicated 87% ee: t_R (major) = 10.0 min, t_R (minor) = 12.0 min.

Rac-**3a**

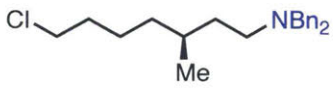


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.037	MF	0.4720	2929.22998	103.42854	50.5144
2	11.950	FM	0.7636	2869.56958	62.63537	49.4856

(–)**3a**: 87% *ee* (average of 2 runs)



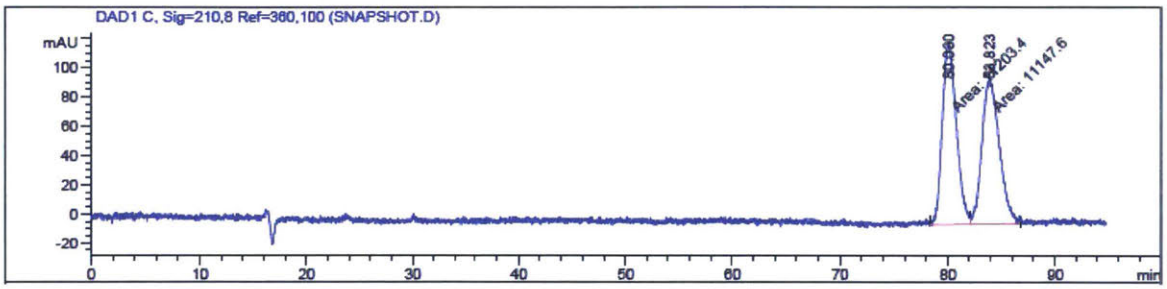
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.013	MF	0.4404	440.26276	16.66241	5.9218
2	12.018	MF	0.7709	6994.29150	151.20636	94.0782



3b

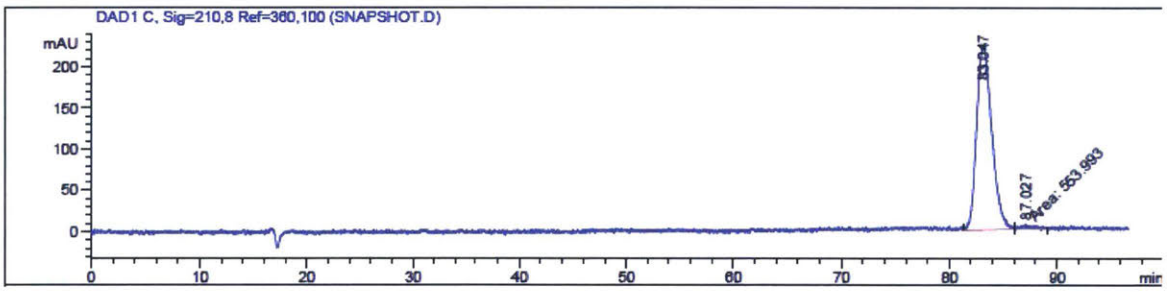
(*S*)-*N*,*N*-dibenzyl-7-chloro-3-methylheptan-1-amine (Scheme 3 and 4, entry **3b**). HPLC analysis (2 connected AD-H columns, 95:5:0.2:0.1 Hexanes: IPA: TFA: Diethylamine, 0.8 mL/min, 220 nm), 0.8 mL/min, 220 nm) indicated 96% ee: t_R (major) = 80.0 min, t_R (minor) = 83.8 min.

Rac-**3b**

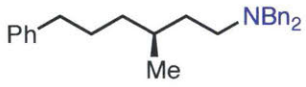


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	80.030	MF T	1.5095	1.12034e4	123.69501	50.1248
2	83.823	FM T	1.8370	1.11476e4	99.10351	49.8752

(S)-**3b**: 96% *ee* (average of 2 runs)



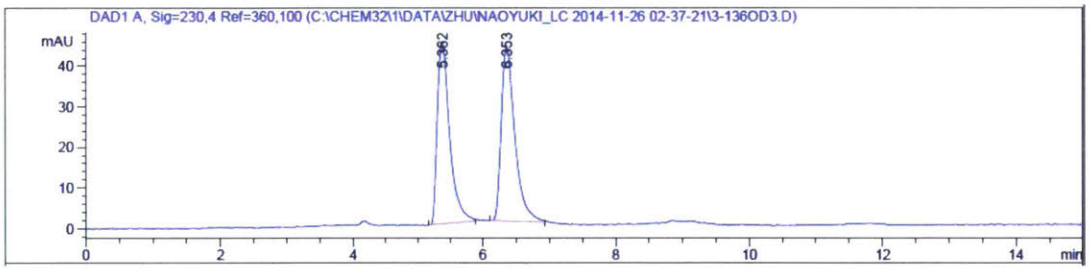
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	83.047	MM R	1.6656	2.19281e4	225.53885	97.5358
2	87.027	MM T	1.2717	553.99274	6.70303	2.4642



3c

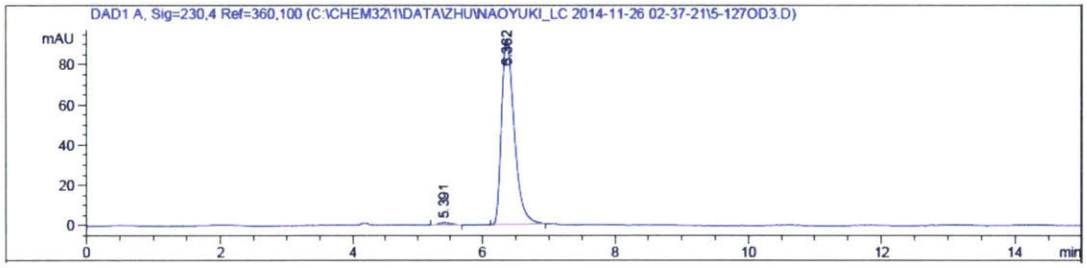
(*S*)-*N*,*N*-dibenzyl-3-methyl-6-phenylhexan-1-amine (Scheme 3 and 4, entry **3c**). HPLC analysis (OD-H, 3% IPA/hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 5.4 min, t_R (major) = 6.4 min.

Rac-**3c**

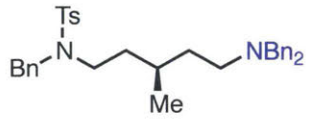


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.362	BB	0.2032	595.14020	44.72854	49.3567
2	6.353	BB	0.2188	610.65497	42.70250	50.6433

(S)-**3c**: 98% *ee* (average of 2 runs)



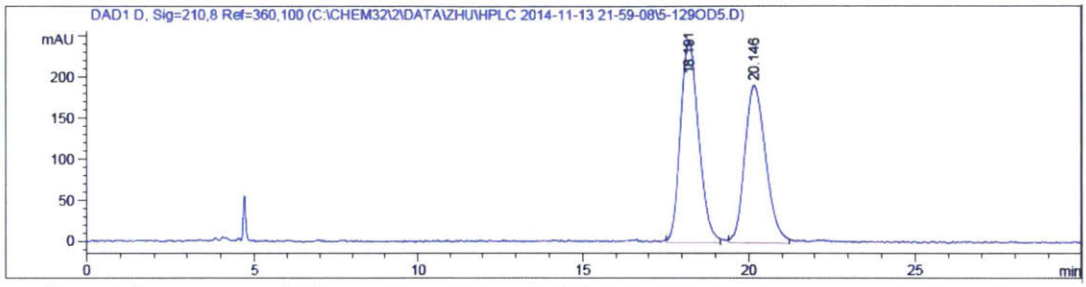
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.391	BB	0.1597	13.74097	1.10005	1.1000
2	6.362	BB	0.2065	1235.41272	92.12253	98.9000



3d

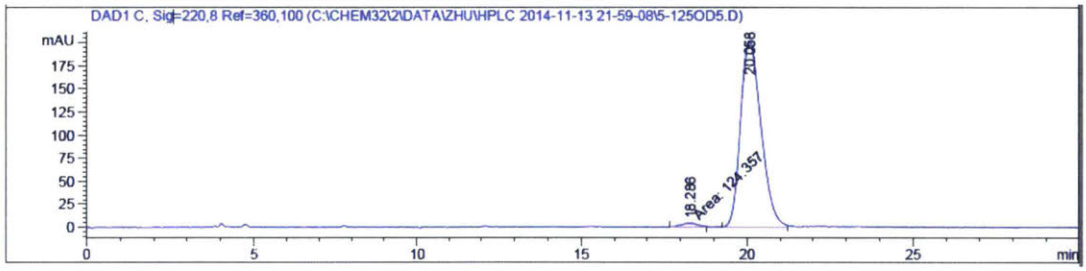
(*R*)-*N*-benzyl-*N*-(5-(dibenzylamino)-3-methylpentyl)-4-methylbenzenesulfonamide (Scheme 4, entry **3d**). HPLC analysis (OD-H, 5% IPA/hexanes, 0.8 mL/min, 220 nm) indicated 97% ee: t_R (minor) = 18.2 min, t_R (major) = 20.1 min.

Rac-**3d**

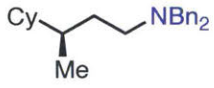


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.191	VV	0.5078	9411.24121	246.28740	52.7311
2	20.146	VV	0.5299	8436.38574	193.02434	47.2689

(R)-**3d**: 97% *ee* (average of 2 runs)



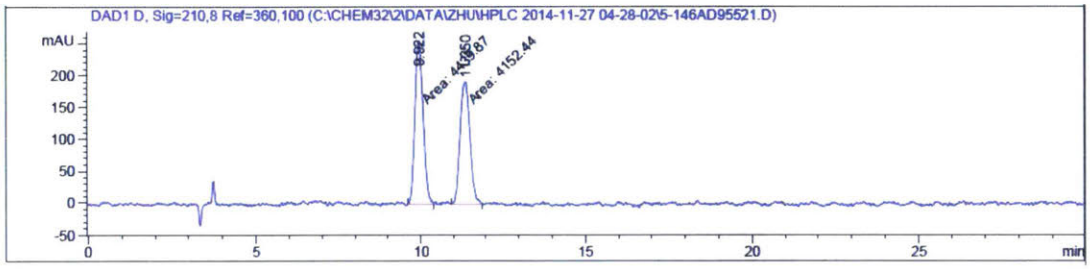
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.286	MM	0.5205	124.35655	3.98196	1.4216
2	20.058	BV	0.5553	8623.56152	201.51285	98.5784



3e

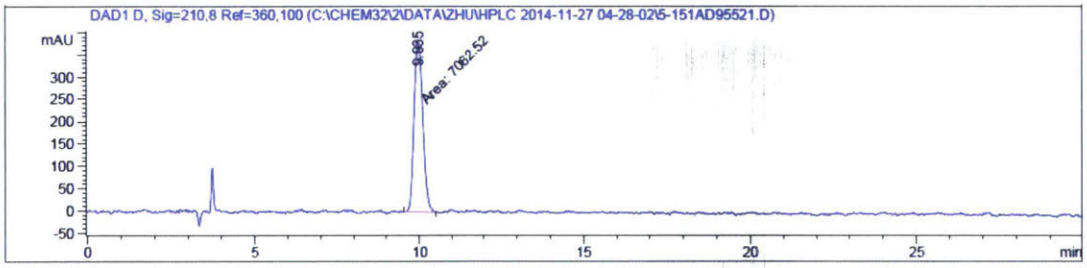
(*R*)-*N*,*N*-dibenzyl-3-cyclohexylbutan-1-amine (Scheme 4, entry **3e**). HPLC analysis (AD-H, hexanes:EtOH:TFA: Diethylamine = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (major) = 9.9 min, t_R (minor) = 11.3 min.

Rac-**3e**

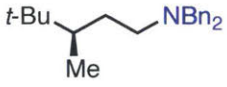


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.920	VV	0.2544	114.28241	6.65403	51.3536
2	11.311	BV	0.2619	108.25762	5.05387	48.6464

(R)-**3e**: >99% *ee* (average of 2 runs)



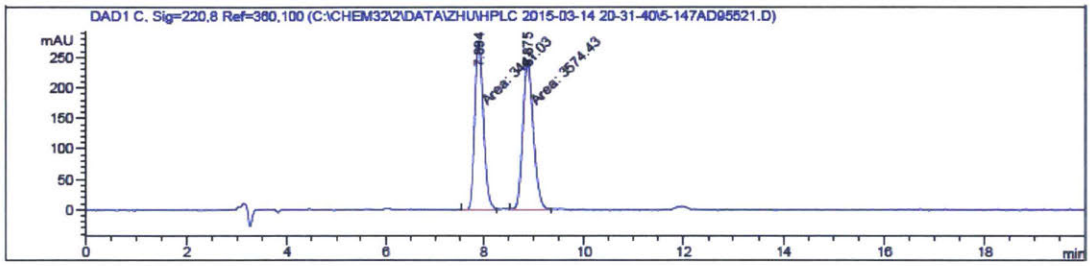
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.935	MM	0.3052	7062.52441	385.62714	100.0000



3f

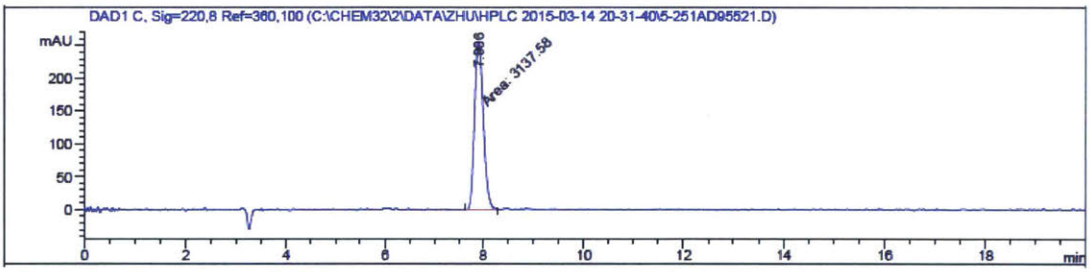
(*R*)-*N*,*N*-dibenzyl-3,4,4-trimethylpentan-1-amine (Scheme 4, entry **3f**). HPLC analysis (AD-H, hexanes:EtOH:TFA: Diethylamine = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (major) = 7.9 min, t_R (minor) = 8.9 min.

Rac-**3f**

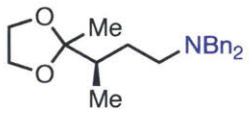


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.894	MF	0.2067	3441.03320	277.43228	49.0493
2	8.875	FM	0.2470	3574.43018	241.19066	50.9507

(R)-**3f**: >99% *ee* (average of 2 runs)



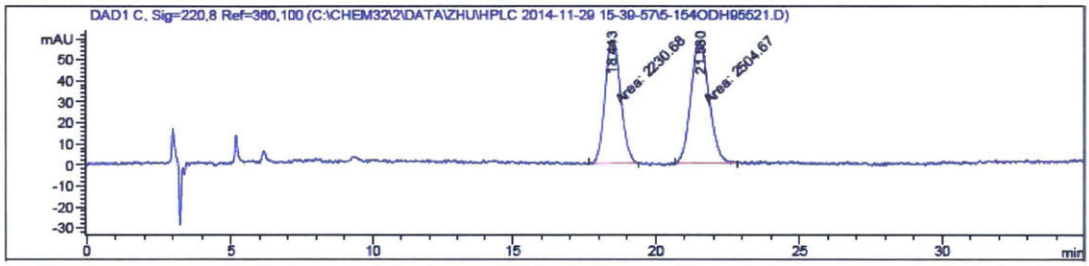
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.906	FM	0.2046	3137.57959	255.63759	100.0000



3g

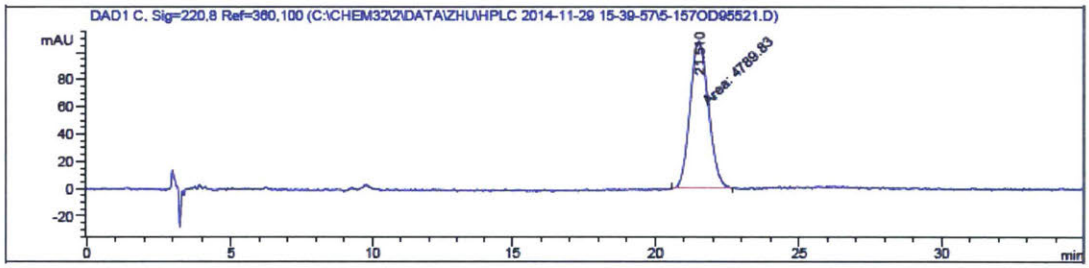
(*R*)-*N*,*N*-dibenzyl-3-(2-methyl-1,3-dioxolan-2-yl)butan-1-amine (Scheme 4, entry **3g**). HPLC analysis (OD-H, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (minor) = 18.5 min, t_R (major) = 21.5 min.

Rac-**3g**

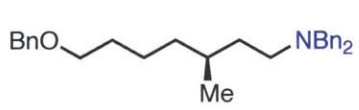


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.443	MF	0.6353	2230.67554	58.51597	47.1070
2	21.530	FM	0.7292	2504.66699	57.24741	52.8930

(R)-**3g**: >99% *ee* (average of 2 runs)



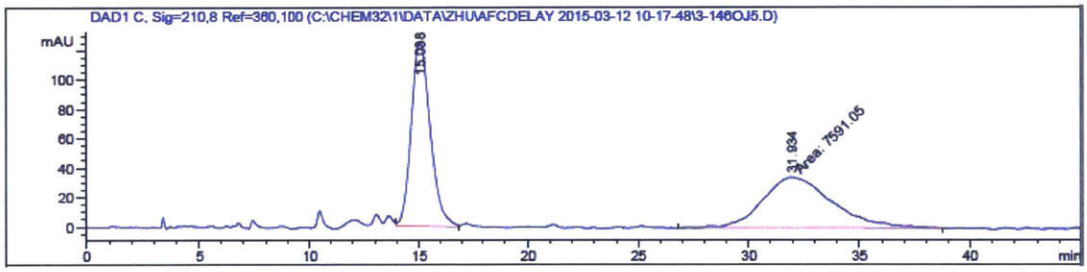
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.510	MM	0.7386	4789.82813	108.08333	100.0000



3h

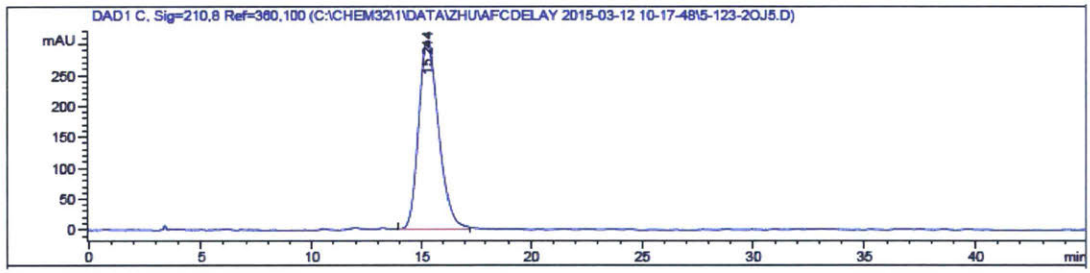
(*S*)-*N*,*N*-dibenzyl-7-(benzyloxy)-3-methylheptan-1-amine (Scheme 4, entry **3h**). HPLC analysis (OJ-H, 5% IPA/hexanes, 1.0 mL/min, 220 nm) indicated >99% ee: t_R (major) = 15.0 min, t_R (minor) = 31.9 min.

Rac-**3h**

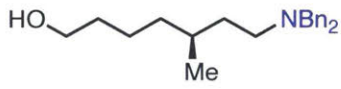


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.038	VV	0.7280	7589.89404	125.41592	49.9962
2	31.934	MM	3.6706	7591.05078	34.46750	50.0038

(R)-**3h**: >99% *ee* (average of 2 runs)



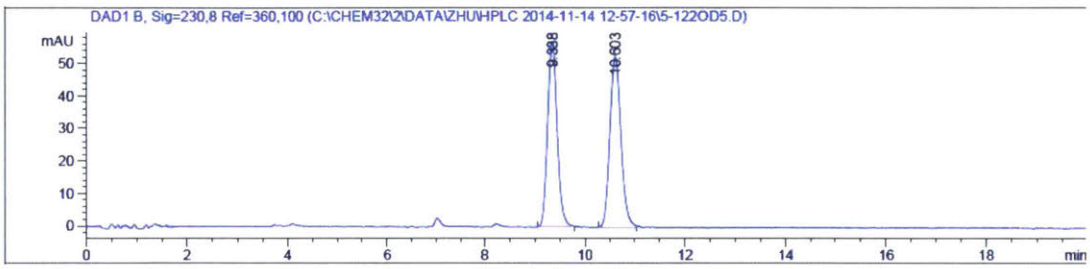
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.244	BV	0.8202	1.96079e4	304.91357	100.0000



3i

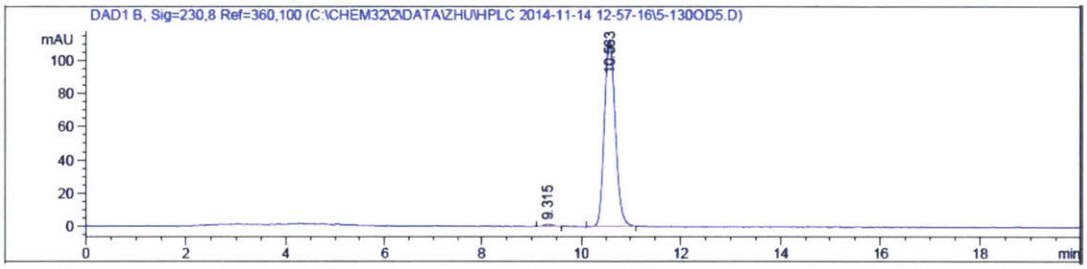
(*S*)-7-(dibenzylamino)-5-methylheptan-1-ol (Scheme 4, entry **3i**). HPLC analysis (OD-H, 5% IPA in hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 9.3 min, t_R (major) = 10.6 min.

Rac-**3i**

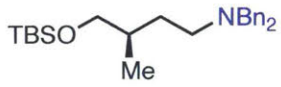


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.338	BB	0.2045	754.30957	56.96180	48.3288
2	10.603	BB	0.2378	806.47778	52.33559	51.6712

(S)-**3i**: 98% *ee* (average of 2 runs)



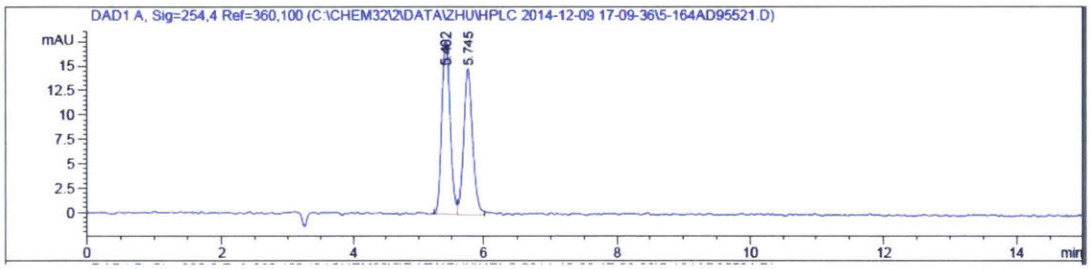
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.315	BB	0.1753	16.72666	1.32519	0.9529
2	10.563	BB	0.2380	1738.62561	112.70821	99.0471



3j

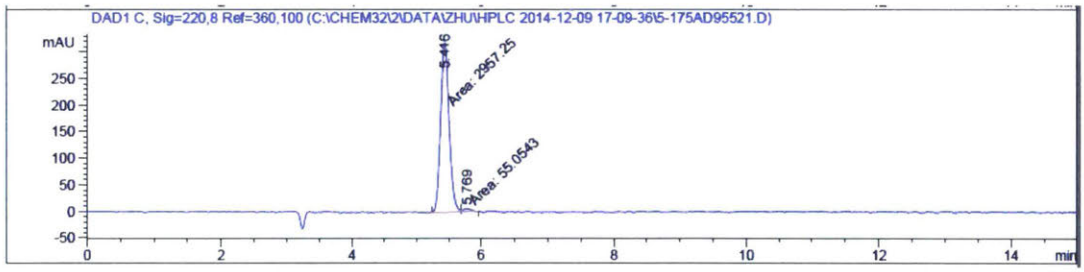
(*R*)-*N*,*N*-dibenzyl-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbutan-1-amine (Scheme 4, entry **3j**). HPLC analysis (AD-H, hexanes:EtOH:TFA:DEA = 95:5:0.2:0.1, 1.0 mL/min, 220 nm) indicated 97% ee: t_R (major) = 5.4 min, t_R (minor) = 5.7 min.

Rac-**3j**

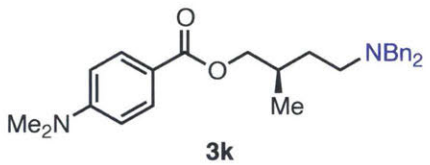


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.402	BV	0.1366	156.86540	17.84387	50.4137
2	5.745	VB	0.1565	154.29108	14.94143	49.5863

(R)-**3j**: 97% *ee* (average of 2 runs)



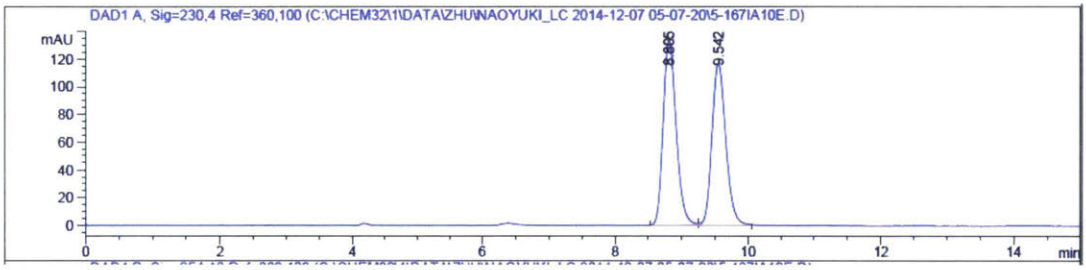
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.416	MF	0.1545	2957.24585	319.06598	98.1724
2	5.769	MF	0.1471	55.05427	6.23912	1.8276



3k

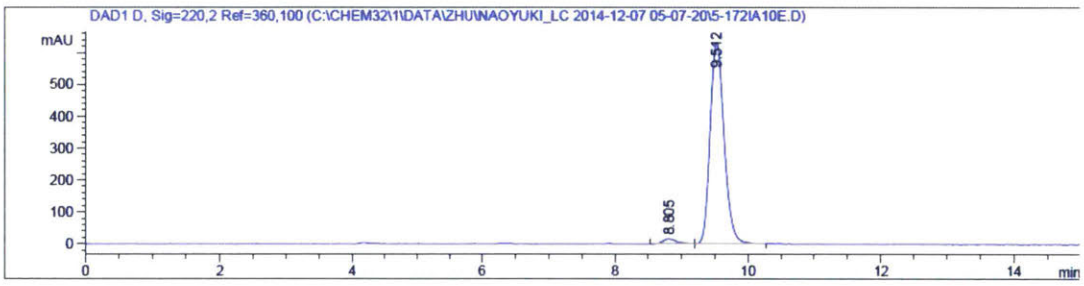
(*R*)-*N*,*N*-dibenzyl-4-((*tert*-butyldimethylsilyl)oxy)-3-methylbutan-1-amine (Scheme 4, entry **3k**). HPLC analysis (IA, 10% EtOH in hexanes, 0.8 mL/min, 220 nm) indicated 94% ee: t_R (minor) = 8.9 min, t_R (major) = 9.6 min.

Rac-**3k**

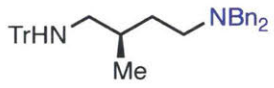


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.805	BV	0.2077	1810.62085	133.96712	51.6735
2	9.542	VB	0.2229	1693.34082	116.99877	48.3265

(R)-**3k**: 94% *ee* (average of 2 runs)



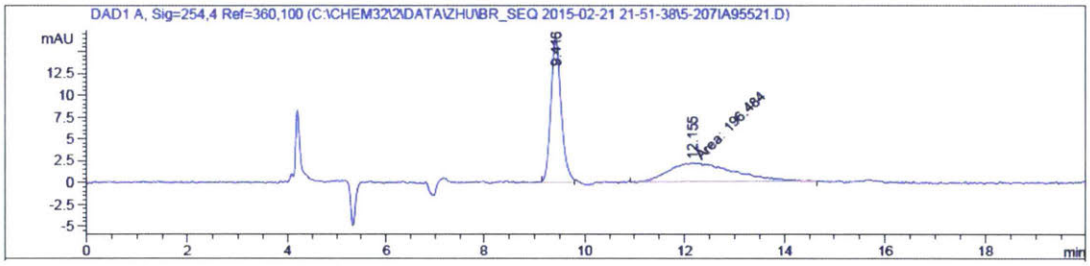
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.805	BV	0.2296	252.70154	15.88853	2.6423
2	9.512	VV	0.2296	9310.84082	632.84418	97.3577



3l

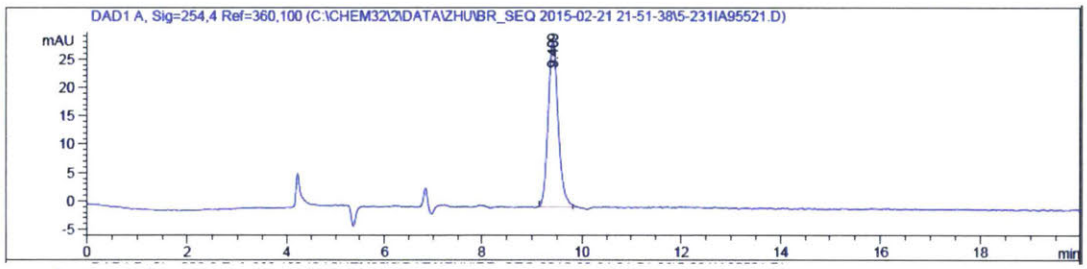
(*R*)-N^4,N^4-dibenzyl-2-methyl-N^1-tritylbutane-1,4-diamine (Scheme 4, entry **3l**). HPLC analysis (IA, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (major) = 9.4 min, t_R (minor) = 12.2 min.

Rac-**3l**

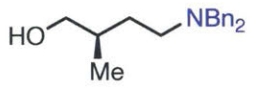


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.416	BB	0.2154	234.20042	16.31966	54.3787
2	12.155	MM	1.5031	196.48405	2.17870	45.6213

(R)-**3l**: >99% *ee* (average of 2 runs)



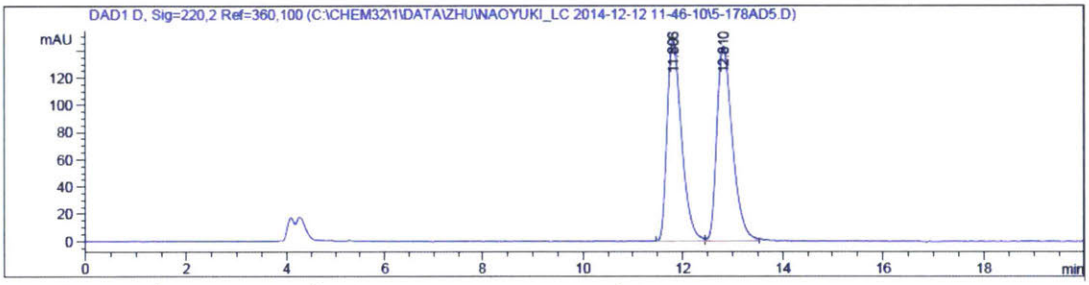
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.409	BB	0.2134	407.43216	29.09673	100.0000



3m

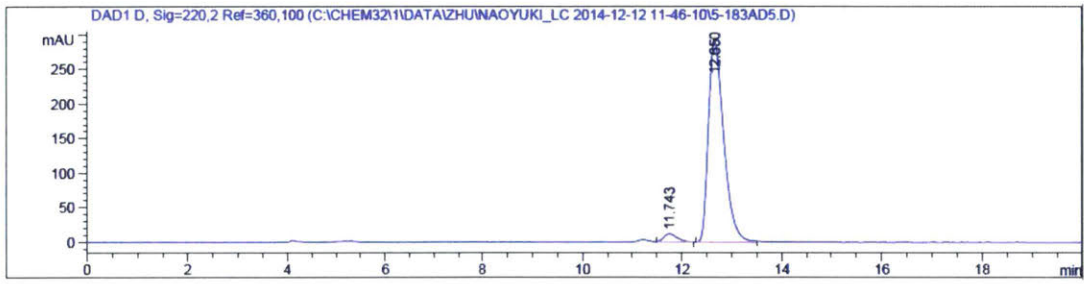
(*R*)-4-(dibenzylamino)-2-methylbutan-1-ol (Scheme 4, entry **3m**). HPLC analysis (AD, 5% IPA in hexanes, 0.8 mL/min, 220 nm) indicated 92% ee: t_R (minor) = 11.7 min, t_R (major) = 12.6 min.

Rac-**3m**

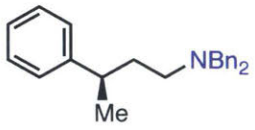


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.806	BV	0.3140	2955.79785	147.39079	48.9426
2	12.810	VV	0.3294	3083.51831	143.11217	51.0574

(R)-**3m**: 92% *ee* (average of 2 runs)



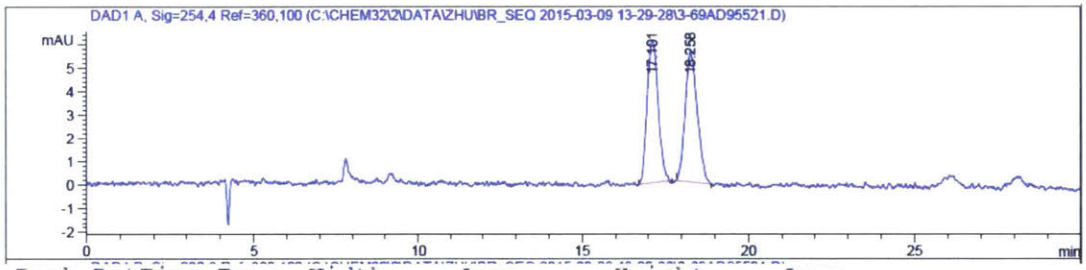
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.743	VB	0.2382	244.31319	12.27296	3.7715
2	12.650	BV	0.3240	6233.52783	290.93024	96.2285



3n

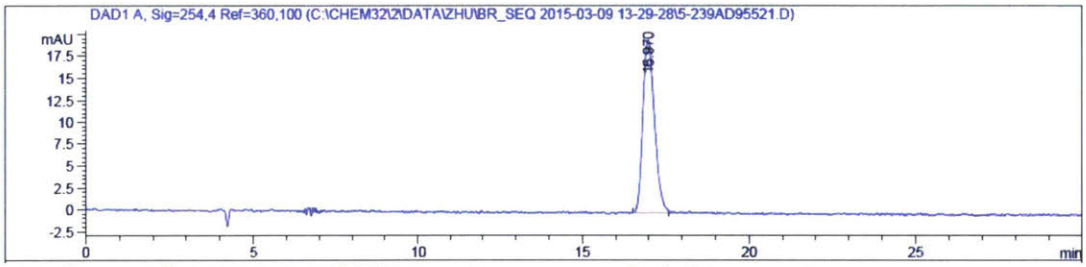
(*R*)-*N*,*N*-dibenzyl-3-phenylbutan-1-amine (Scheme 7, entry **3n**). HPLC analysis (AD-H, hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1, 0.8 mL/min, 220 nm) indicated >99% ee: t_R (major) = 17.1 min, t_R (minor) = 18.3 min.

Rac-**3n**

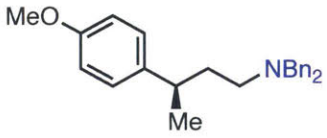


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.101	BB	0.3061	140.82396	6.03737	50.1013
2	18.258	BB	0.3037	140.25471	5.57222	49.8987

(R)-**3n**: 98% *ee* (average of 2 runs)



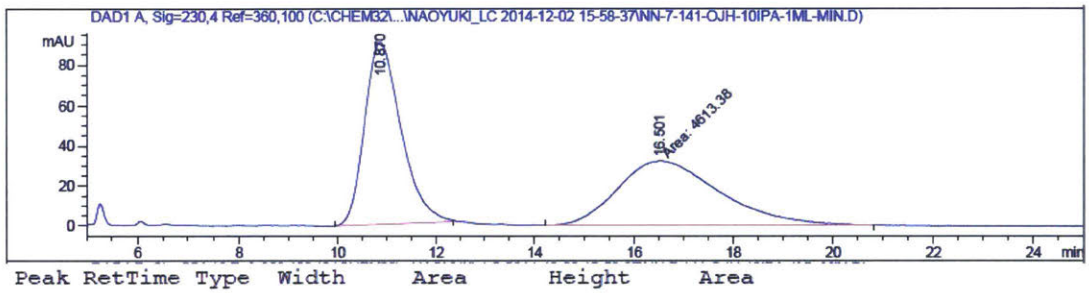
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.970	BB	0.3572	476.68036	19.63757	100.0000



3o

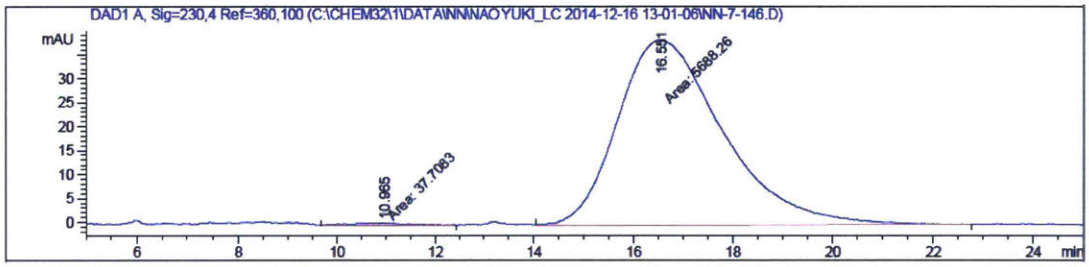
(*R*)-*N*,*N*-dibenzyl-3-(4-methoxyphenyl)butan-1-amine (Scheme 7, entry **3o**): HPLC analysis (OJ-H, 1% IPA/Hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 18.1 min, t_R (major) = 25.4 min.

Rac-**3o**

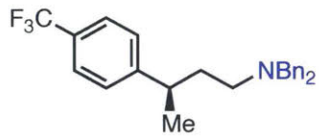


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.870	BB	0.7512	4668.04199	90.58984	50.2945
2	16.501	MM T	2.3814	4613.37988	32.28797	49.7055

(R)-**3o**: 98% *ee* (average of 2 runs)



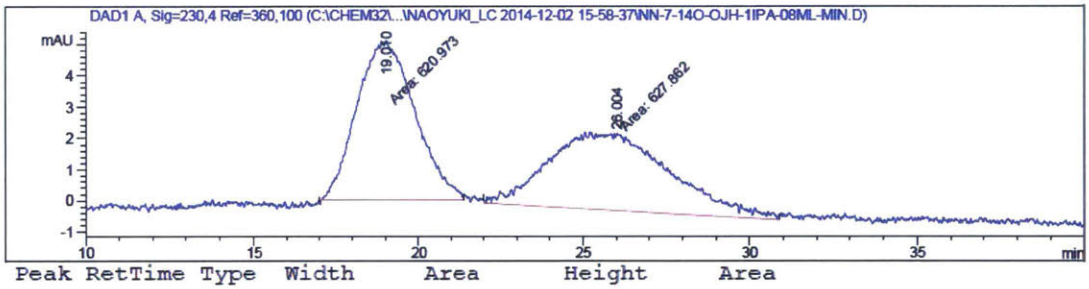
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.965	MM T	1.1673	37.70831	5.38408e-1	0.6585
2	16.551	MM T	2.4703	5688.25684	38.63075	99.3415



3p

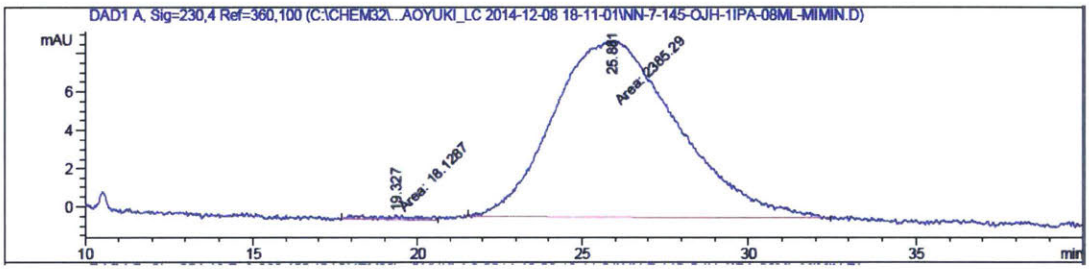
(*R*)-*N*,*N*-dibenzyl-3-(4-(trifluoromethyl)phenyl)butan-1-amine (Scheme 7, entry **3p**)**:** HPLC analysis (OJ-H, 1% IPA/Hexanes, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 19.0 min, t_R (major) = 26.0 min.

Rac-**3p**

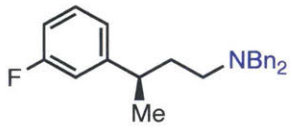


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.010	MM T	2.0508	620.97321	5.07567	49.7242
2	26.004	MM T	4.2521	627.86237	2.46100	50.2758

(R)-**3p**: 99% *ee* (average of 2 runs)



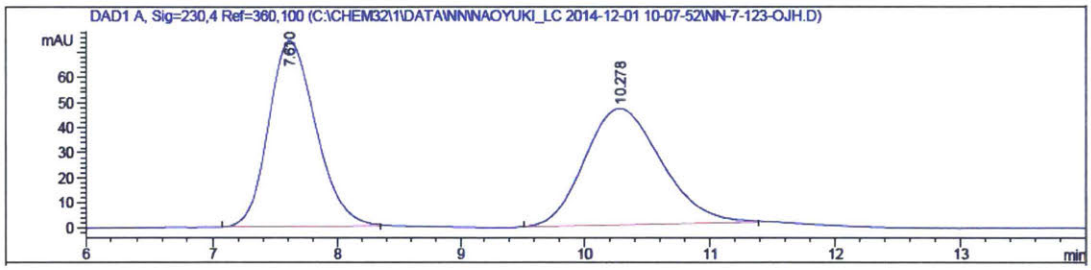
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.327	MM T	1.3004	18.12873	2.32353e-1	0.7543
2	25.881	MM T	4.3159	2385.29395	9.21125	99.2457



3q

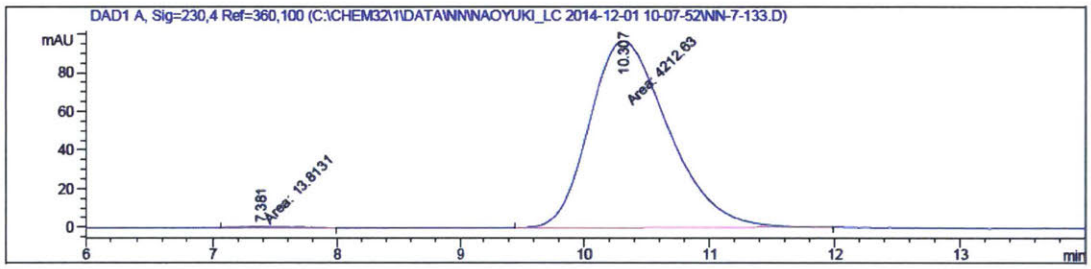
(*R*)-*N*,*N*-dibenzyl-3-(3-fluorophenyl)butan-1-amine (Scheme 7, entry **3q):** HPLC analysis (OJ-H, 3% IPA/Hexanes, 1 mL/min, 220 nm) indicated 98% ee: t_R (minor) = 7.3 min, t_R (major) = 10.3 min.

Rac-**3q**

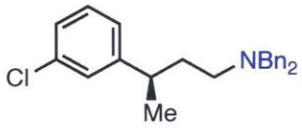


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.610	BB	0.4143	1967.04285	73.96067	49.8245
2	10.278	BB	0.6222	1980.89746	46.57705	50.1755

(R)-**3q**: 98% *ee* (average of 2 runs)



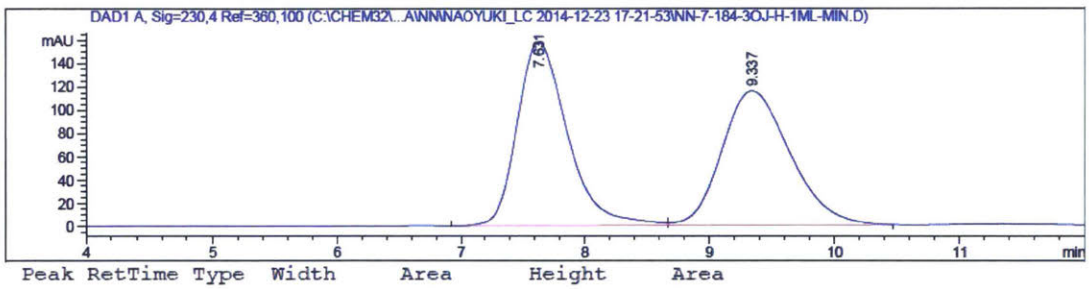
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.381	MM T	0.4429	13.81311	4.67807e-1	0.3268
2	10.307	MM T	0.7279	4212.63428	96.45867	99.6732



3r

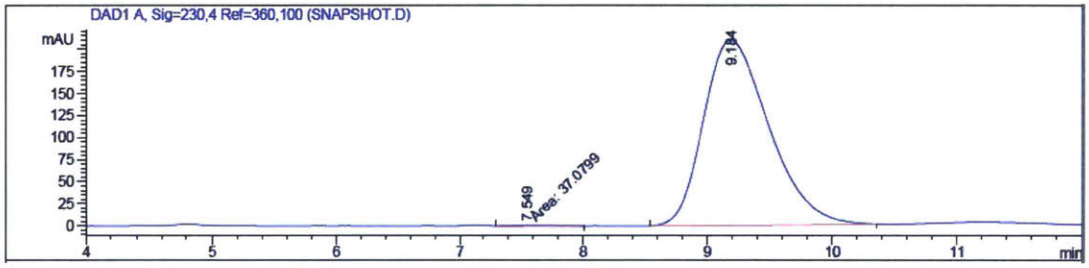
(*R*)-*N*,*N*-dibenzyl-3-(3-chlorophenyl)butan-1-amine (Scheme 7, entry **3r**): HPLC analysis (OJ-H, 3% IPA/Hexanes, 0.8 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 7.5 min, t_R (major) = 9.2 min.

Rac-**3r**

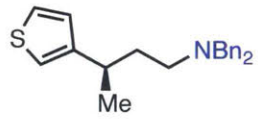


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.631	BV	0.4262	4447.40576	158.07410	50.3588
2	9.337	VB	0.5843	4384.02441	115.62588	49.6412

(R)-**3r**: 95% *ee* (average of 2 runs)



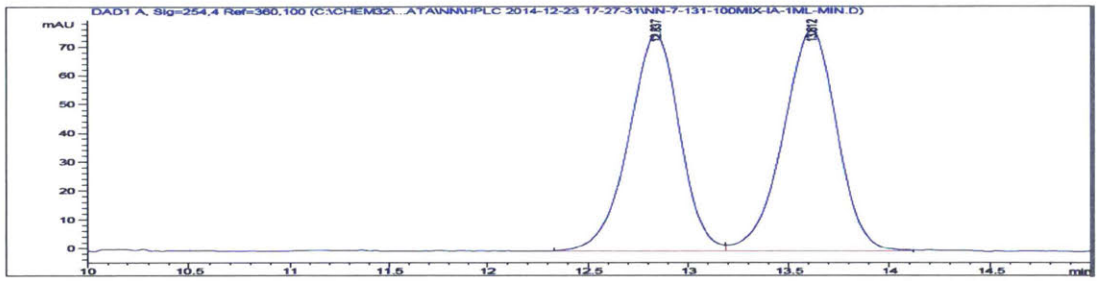
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.549	MM T	0.4367	37.07988	1.41509	0.4855
2	9.184	BB	0.5424	7600.58398	209.91634	99.5145



3s

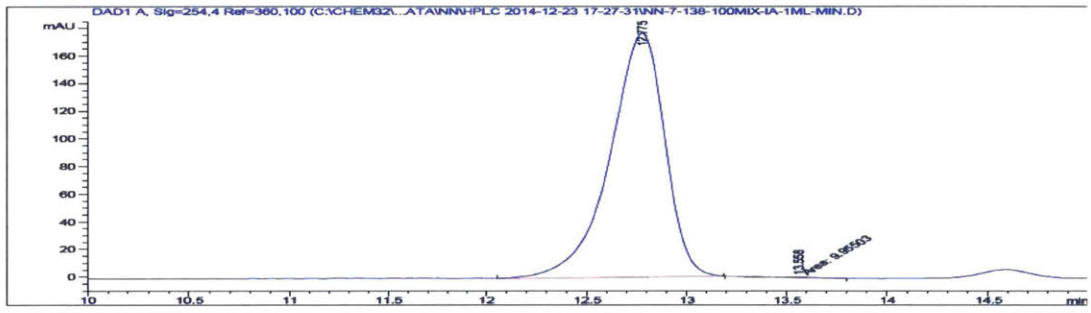
(*R*)-*N*,*N*-dibenzyl-3-(thiophen-3-yl)butan-1-amine (Scheme 7, entry **3s**): HPLC analysis (IA, 97:5:0.2:0.1 Hexanes/EtOH/TFA/Diethylamine, 1.0 mL/min, 220 nm) indicated 99% ee: t_R (minor) = 12.8 min, t_R (major) = 13.6 min.

Rac-**3s**

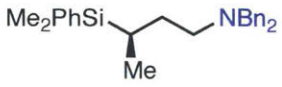


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.837	BV	0.2721	1337.37695	74.98014	48.2598
2	13.612	VB	0.2889	1433.82837	76.42850	51.7402

(R)-**3s**: 99% *ee* (average of 2 runs)



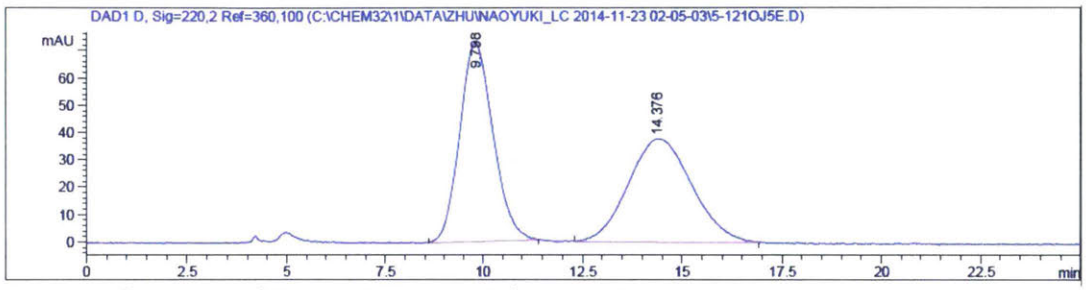
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.775	MM R	0.3195	3384.38892	176.54337	99.7067
2	13.558	MM T	0.3363	9.95503	5.34681e-1	0.2933



3t

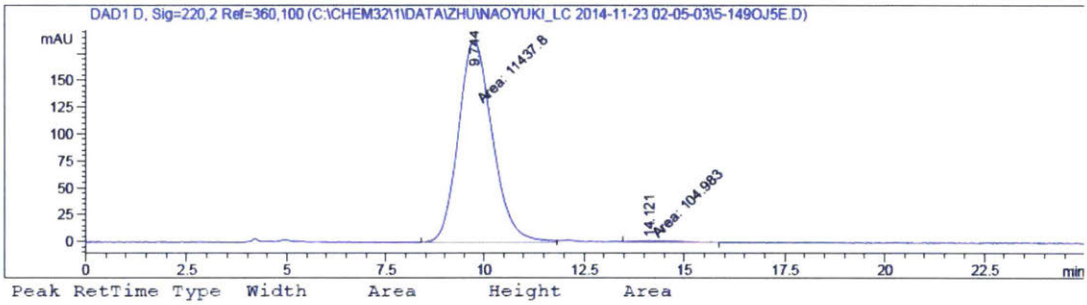
(*R*)-*N*,*N*-dibenzyl-3-(dimethyl(phenyl)silyl)butan-1-amine (Scheme 8, entry **3t**). HPLC analysis (OJ-H, 5% EtOH in hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (major) = 9.8 min, t_R (minor) = 14.4 min.

Rac-**3t**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.798	VB	0.7177	4407.80078	72.87277	51.1052
2	14.376	BV	1.3105	4217.15283	37.89015	48.8948

(R)-**3t**: **98% *ee* (average of 2 runs)**

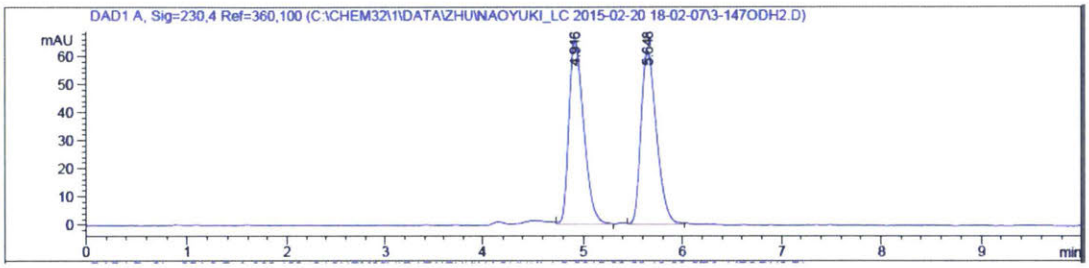


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.744	MM	1.0170	1.14378e4	187.44644	99.0905
2	14.121	MM	1.3548	104.98302	1.29149	0.9095

(*S*)-*N*,*N*-dibenzyl-1-phenylbutan-1-amine (Scheme 9, entry **3u**). HPLC analysis (OD-H, 2% IPA in hexanes, 0.8 mL/min, 220 nm) indicated 98% ee: t_R (major) = 4.9 min, t_R (minor) = 5.6 min.

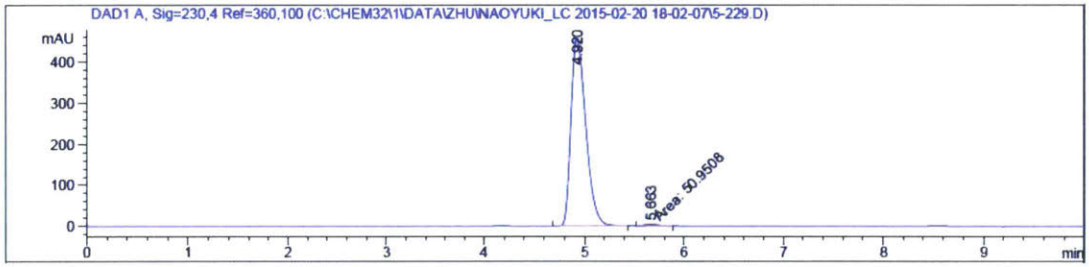
3u

Rac-**3u**

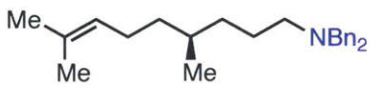


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.916	VB	0.1631	682.67163	65.77484	50.2835
2	5.648	VB	0.1697	674.97266	61.64789	49.7165

(S)-**3u**: 99% *ee* (average of 2 runs)



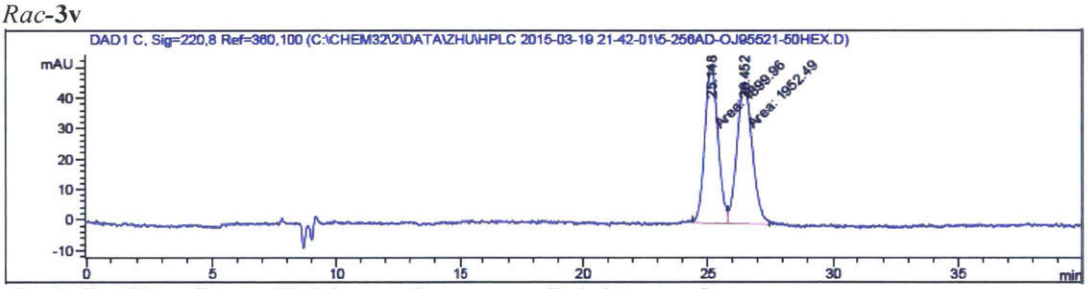
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.920	VB	0.1611	4749.11084	457.39609	98.9385
2	5.663	FM	0.1978	50.95076	4.29281	1.0615



3v

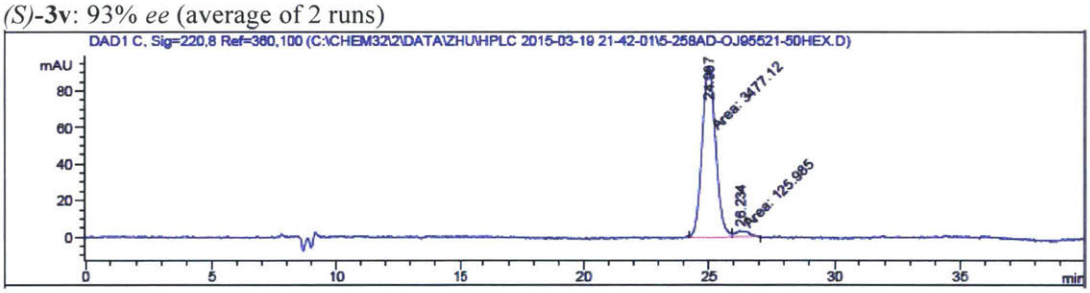
(*S*)-*N*,*N*-dibenzyl-4,8-dimethylnon-7-en-1-amine (Scheme 11, entry **3v**). HPLC analysis (AD-H and OJ-H in sequence, 50% (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1) in hexanes, 0.8 mL/min, 210 nm) indicated 93% ee: t_R (major) = 25.1 min, t_R (minor) = 26.4 min.

Rac-**3v**

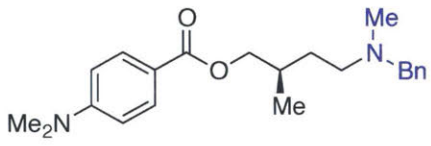


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.148	FM	0.6081	1899.96191	52.07578	49.3183
2	26.452	MF	0.6976	1952.48572	46.64882	50.6817

(S)-**3v**: 93% *ee* (average of 2 runs)



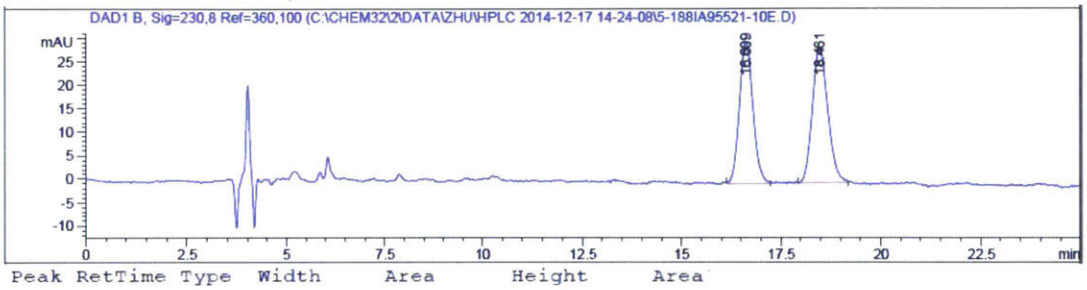
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.987	FM	0.6185	3477.12061	93.69176	96.5034
2	26.234	FM	0.6162	125.98490	3.40742	3.4966



4b

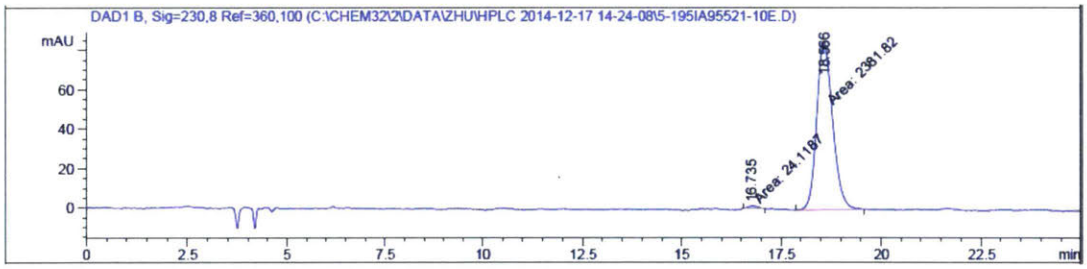
(*R*)-4-(benzyl(methyl)amino)-2-methylbutyl 4-(dimethylamino)benzoate (Scheme 12, entry **4b**). HPLC analysis (IA, 10% EtOH in (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1), 0.8 mL/min, 230 nm) indicated 98% ee: t_R (minor) = 16.6 min, t_R (major) = 18.5 min.

Rac-**4b**

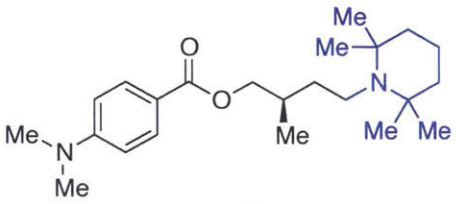


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.609	BB	0.3402	721.41504	30.25107	48.0689
2	18.461	VB	0.3619	779.37726	28.78234	51.9311

(R)-**4b**: 98% *ee* (average of 2 runs)



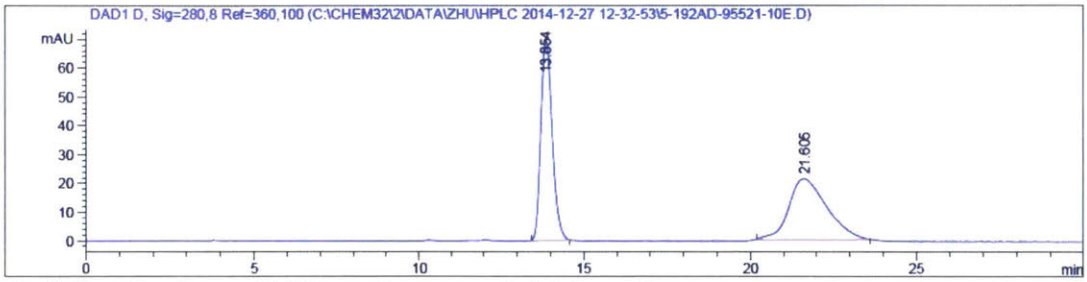
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.735	MM	0.2805	24.11870	1.43301	1.0025
2	18.566	MM	0.4631	2381.81787	85.72099	98.9975



4c

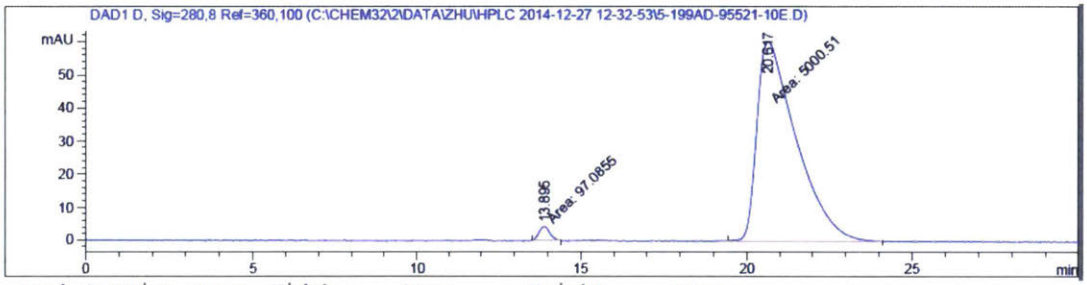
(*R*)-2-methyl-4-(2,2,6,6-tetramethylpiperidin-1-yl)butyl 4-(dimethylamino)benzoate (Scheme 12, entry **4c**). HPLC analysis (AD-H, 10% EtOH in (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1), 0.8 mL/min, 280 nm) indicated 96% ee: t_R (minor) = 13.9 min, t_R (major) = 20.6 min.

Rac-**4c**

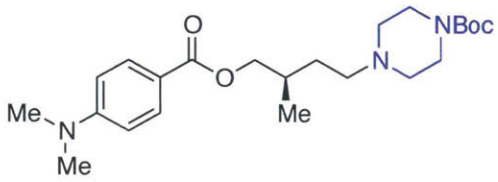


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.854	BB	0.3621	1647.07227	69.59984	48.7360
2	21.605	BB	0.9615	1732.50659	21.42357	51.2640

(R)-**4c**: 96% *ee* (average of 2 runs)



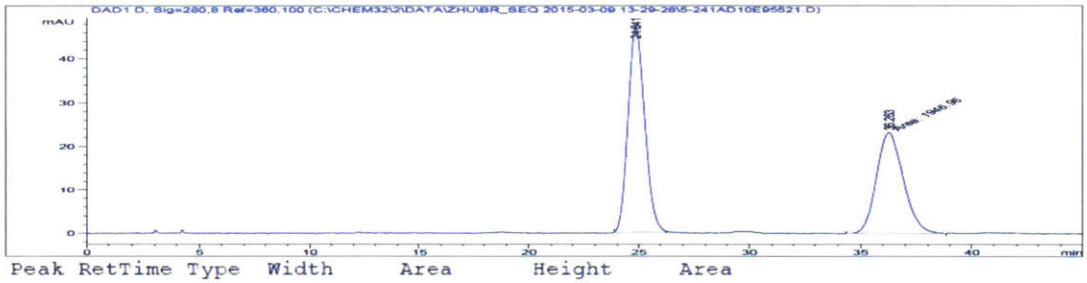
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.895	FM	0.3787	97.08546	4.27275	1.9045
2	20.617	FM	1.3794	5000.51025	60.42061	98.0955



4d

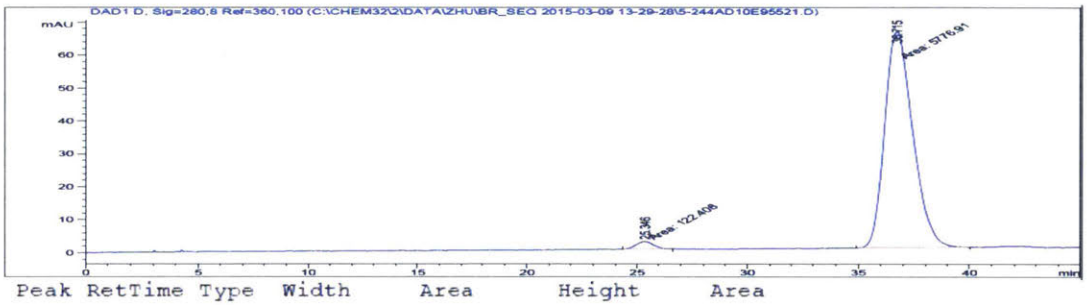
(*R*)-4-(4-((4-(dimethylamino)benzoyl)oxy)-3-methylbutyl)piperazine-1-carboxylate (Scheme 12, entry **4d**). HPLC analysis (AD-H, 10% EtOH in (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1), 1.0 mL/min, 280 nm) indicated 96% ee: t_R (minor) = 24.8 min, t_R (major) = 36.3 min.

Rac-**4d**

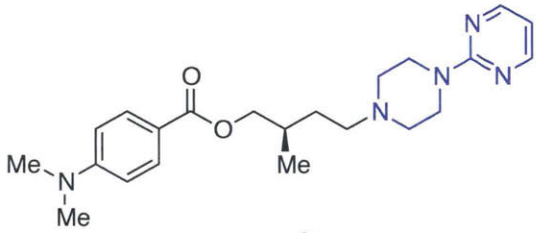


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.841	BB	0.6690	2483.16187	46.80215	56.0518
2	36.263	FM	1.4007	1946.95605	23.16616	43.9482

(R)-**4d**: 96% *ee* (average of 2 runs)



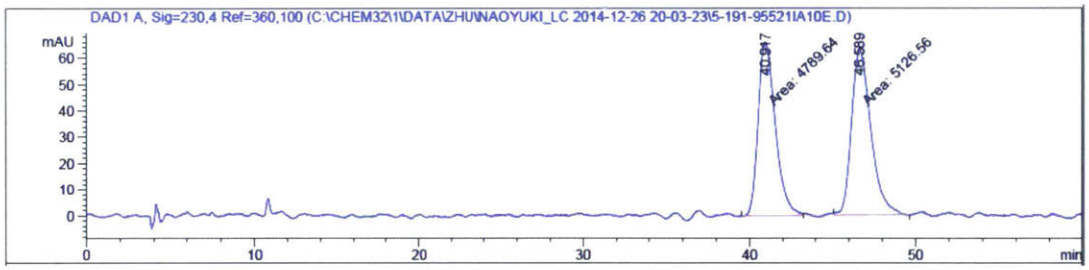
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.346	FM	0.9127	122.40763	2.23517	2.0749
2	36.715	FM	1.4698	5776.90723	65.50713	97.9251



4e

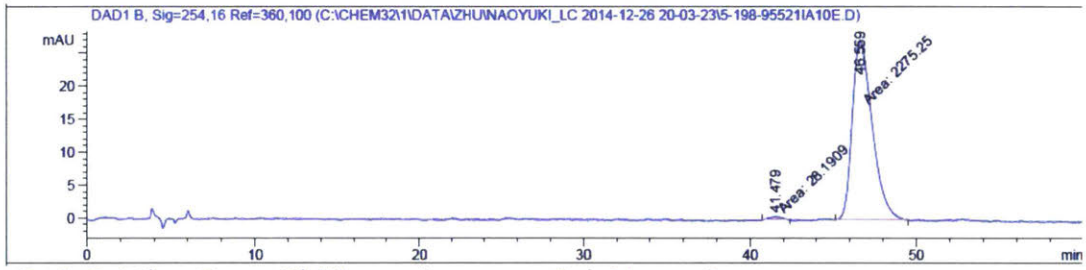
(*R*)-2-methyl-4-(4-(pyrimidin-2-yl)piperazin-1-yl)butyl 4-(dimethylamino)benzoate (Scheme 12, entry **4e**). HPLC analysis (IA, 10% EtOH in (hexanes:EtOH:TFA:Diethylamine = 95:5:0.2:0.1), 0.8 mL/min, 230 nm) indicated 98% ee: t_R (minor) = 40.9 min, t_R (major) = 46.6 min.

Rac-**4e**

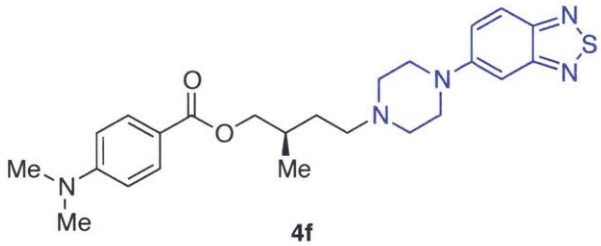


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.917	MF	1.2072	4789.63965	66.12748	48.3011
2	46.589	FM	1.3661	5126.56299	62.54295	51.6989

(R)-**4e**: 98% *ee* (average of 2 runs)



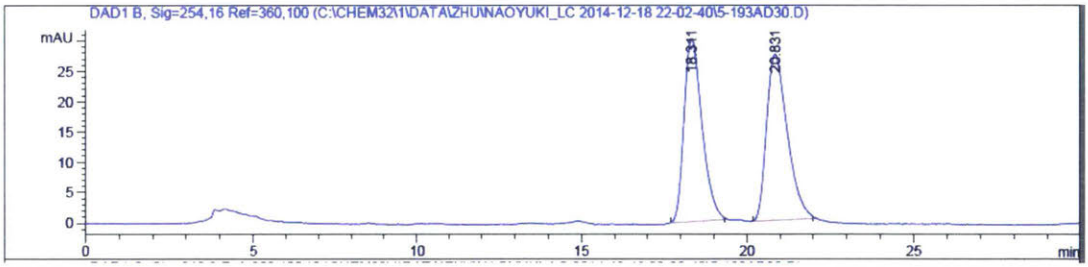
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.479	FM	0.9204	28.19092	5.10507e-1	1.2239
2	46.559	FM	1.3976	2275.24658	27.13250	98.7761



4f

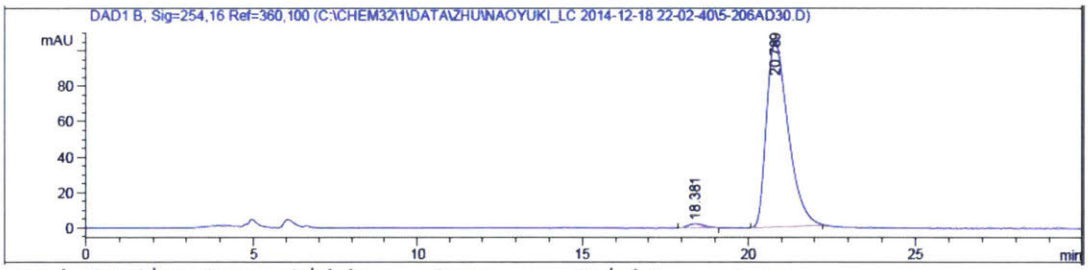
(*R*)-4-(4-(benzo[*c*][1,2,5]thiadiazol-5-yl)piperazin-1-yl)-2-methylbutyl 4-(dimethylamino)benzoate (Scheme 12, entry **4f**). HPLC analysis (AD-H, 30% IPA in hexanes, 0.8 mL/min, 254 nm) indicated 97% ee: t_R (minor) = 18.4 min, t_R (major) = 20.7 min.

Rac-**4f**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.311	BB	0.5571	1135.83215	30.17566	48.8334
2	20.831	BB	0.6094	1190.10303	27.36439	51.1666

(R)-**4f**: 97% *ee* (average of 2 runs)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.381	BB	0.4226	82.82407	2.36462	1.7028
2	20.789	BB	0.6859	4781.29590	104.88065	98.2972