Development of New Strategies Towards Accessing Chiral Nitrogen Heterocycles

by

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To my family and friends

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LIST OF ABBREVIATIONS

°C	degrees Celsius
δ	chemical shift in parts per million
Abs	absorbance
AIBA	aminoisobutyric acid
Ala	alanine
allyl-TMS	allyltrimethylsilane
aq.	Aqueous
Ar	aryl
atm	atmosphere
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
Cbz	carboxybenzyl
CH_3CN	acetonitrile
^{Cl}Ts	4-chlorobenzenesulfonyl
Cy	cyclohexyl
DCC	*N*,*N*'-dicyclohexycarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublet
DFT	density functional theory
DMF	dimethylformamide
DMSO	dimethylsulfoxide
ee	enantiomeric excess
equiv	molar equivalents
Et	ethyl
EtOAc	ethyl acetate
^{F}Ts	4-(trifluoromethyl)benzenesulfonyl
g	grams
Gly	glycine
h	hour
HCl	hydrochloric acid
HCV	hepatitis C virus
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
^{H}Ts	benzenesulfonyl
Hz	Hertz
INT	intermediate

iPr	isopropyl
K_2CO_3	potassium carbonate
L	liter
M	molarity (mol/L)
*m*CPBA	*meta*-chloroperoxybenzoic acid
Me	methyl
MeOH	methanol
Mes	mesylate
mg	milligrams
$MgSO_4$	magnesium sulfate
MHz	megahertz
min	minutes
mL	milliliters
mmol	millimoles
mol	moles
$NaHCO_3$	sodium bicarbonate
Na_2SO_4	sodium sulfate
NHC	*N*-heterocyclic carbene
NMM	*N*-methylmorpholine
NMR	nuclear magnetic resonance
Nos	*o*-nitrobenzenesulfonyl
^{OMe}Ts	4-methoxylbenzenesulfonyl
PDT	carbonyl-olefin metathesis product
PG	protecting group
Ph	phenyl
ppm	parts per million
q	quartet
RCM	ring-closing metathesis
rt	room temperature
s	singlet
S	substrate for a given metathesis reaction (following the number scheme in the main text)
SFC	supercritical fluid chromatography
t	triplet
T	temperature
TBDMS	*tert*-butyldimethylsilyl
*t*BuOH	*tert*-butanol
THF	tetrahydrofuran
TLC	thin layer chromatography
Ts	tosyl
TS	transition state
Val	valine
W	watts
WA	Weinreb amide intermediate

ABSTRACT

The olefin-olefin metathesis reaction is a revolutionary industrial process that utilizes precious metal complexes to enable direct carbon-carbon bond formation from simple olefin starting materials. This powerful tool has been utilized in a wide range of applications including natural product synthesis, materials and polymers, medicines, and fine chemical synthesis. While this approach has been employed for the construction of new carbon-carbon bonds in a wide range of systems through the use of metal alkylidene catalysts, recent advances have led to the development of the direct metathesis between carbonyls and olefins that relies on Lewis acids catalysts. This method is not only marked by the use of inexpensive sustainable catalysts, but it also eliminates the need for the prerequisite synthesis of the olefin substrates.

The Schindler lab recently identified an inexpensive iron catalyst capable of promoting exclusively carbonyl-olefin metathesis reactions with catalyst loadings as low as 1 mol percent. This design principle fundamentally differs from stoichiometric carbonyl-olefin metathesis protocols proceeding via intermediate oxametallacycles. It is instead based on the *in situ* formation of oxetanes as reactive intermediates via initial cycloaddition of a carbonyl and an olefin. While this method has been successfully applied to a wide range of carbocyclic systems, we envisioned that this could be a valuable method towards the synthesis of nitrogen heterocycles, which are ubiquitous in both

natural products and pharmaceuticals. This thesis details the application of the carbonyl-olefin metathesis reaction towards the synthesis of chiral nitrogen heterocycles. While nitrogen containing systems have previously represented challenging substrates for metathesis reactions due to their ability to coordinate to the active catalyst, Chapter 2 describes the development and application of electron-deficient protecting groups enable the successful progression of the reaction as well as a general synthetic strategy from chiral amino acids that provides access to a diverse array of chiral substrates that can be utilized to access both chiral 3-pyrrolines. Chapter 3 further describes the application of both the synthetic strategy and carbonyl-olefin metathesis towards the preparation of tetrahydropyridines and other diverse nitrogen heterocycles in a unified approach.

In order to gain insight into the principals governing this reaction, conducted a series of experimental and computational studies to model that provided a variety of mechanistic insights into the reaction pathway of both 3-pyrrolines and tetrahydropyridines. These studies have not only provided further insights into the electronics of the sulfonamide and its role as a competitive binding sight, but they have also provided key insights into substrate design. The details of these efforts are provided in Chapter 4.

Chapter 1

Developments in the Synthesis of Nitrogen Heterocycles via Olefin Metathesis*

1.1 Introduction

Nitrogen heterocycles are among the most prevalent structural motifs that can be found in a variety of biologically active compounds, natural products, therapeutics, and valuable materials (Figure 1.1). The simplest example comes from the fact that they are present in both amino acids and nucleobases, which are ubiquitous in all life. In addition to these biologically essential components, nitrogen heterocycles have played a huge role in the advancements of pharmaceuticals. Once such example came from the discovery of haloperidol by P.A. Janssen.[1-3] This antipsychotic is considered one of the greatest advances of 20th century psychiatry and is included in the World Health Organization's list of essential medicines for its contributions to both palliative care and the treatment of mental and behavioral disorders.[4] Further studies of the piperidine scaffold led to the development of new medicines for the treatment of debilitating and chronic pain including the introduction of analgesics such as fentanyl that could be used as an alternative to opioid-based anesthesias (also derived from nitrogen heterocycles) with fewer side-effects.[5] Nitrogen heterocycles continue to be among the most prevalent scaffold found in pharmaceuticals, and they can be found in over 59% of the U.S. FDA approved drugs.[6]

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* Groso, E.J.; Schindler, C.S. *Synthesis*. **2019**, *Accepted.* Submitted as an invited contribution to the "Golden Synthesis Anniversary Special Issue.

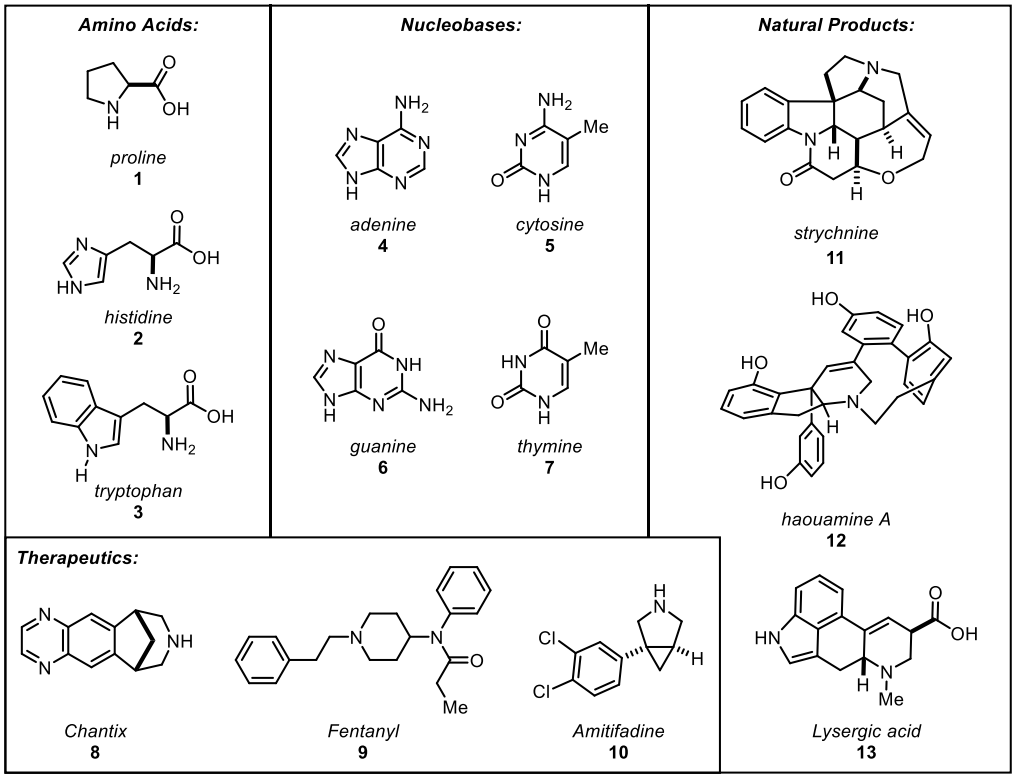

Figure 1.1 Selected examples of nitrogen heterocycles found in amino acids, nucleobases, therapeutics, and natural products.

In this introduction, the synthetic strategies towards accessing 5- and 6-membered nitrogen heterocycles are first presented. The discussion will focus on pyrrolidine and piperidine scaffolds. It is then expanded to include recent strategies towards the application of ring-closing metathesis towards the synthesis of these privileged motifs including the development of new catalysts and enantioselective systems. Finally, the method of ring-closing carbonyl-olefin metathesis, which was the basis of this work, is introduced and its application towards carbocyclic systems is examined.

1.2 Strategies Towards the Synthesis of Nitrogen Heterocycles

For the purposes of this review, we will focus on the unsaturated five- and six-membered nitrogen heterocycles – specifically 3-pyrrolines and tetrahydropyridines (Figure 1.2). Such compounds serve as useful synthetic building blocks as the resulting

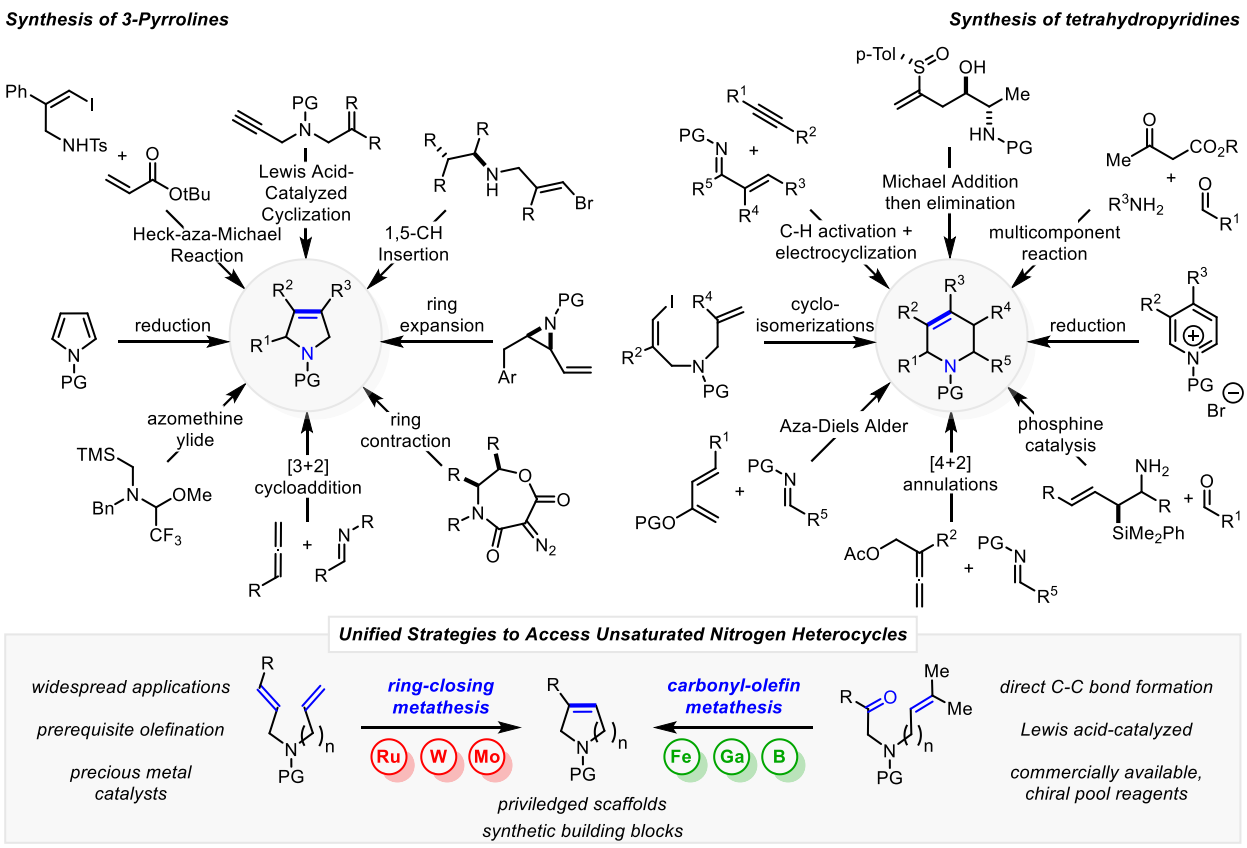

Figure 1.2 Current strategies towards accessing 3-pyrrolines and tetrahydropyridines.

olefin provides a functional handle for further diversification.[9] There are a variety of strategies to directly access these aza-cycles.[7,8] Several cyclization strategies have been developed to access 3-pyrrolines, including the cyclization of α-amino allenes mediated by transition metals[10] and potassium carbonate.[11] Other cyclization strategies include Heck-aza-Michael reactions,[12] in situ formation of alkylidene carbenes from vinyl bromides resulting in 1,5-C–H insertion,[13] the use of azomethine ylides,[14] and Lewis acid-mediated cyclizations.[15] Another interesting approach includes the ring-expansion of aziridines[16] to the corresponding pyrroline, or alternatively the ring contraction of diazo-oxazepanes.[17] Tetrahydropyridines present a greater challenge, however many versatile methods have been developed including 6π-cyclization strategies[18] such as the aza-Diels-Alder reaction[19] (Figure 1.2). Alternative strategies take advantage of traditional

amine reactivity including nucleophilic additions to substituted olefins[20] and phosphine catalysis[21] to promote the cyclization to generate the desired tetrahydropyridines. Finally, similar mechanistic strategies for accessing 3-pyrrolines and tetrahydropyridines have been reported, including allene annulation[22] and the reduction of the aromatic pyrroles and pyridines.[23]

One strategy that has been proven effective for the synthesis of unsaturated nitrogen heterocycles is ring-closing olefin metathesis. Metal alkylidenes have been implemented in ring-closing metathesis reactions to access both aliphatic and heterocyclic rings,[24] however electron-rich amines have proven to be challenging substrates under metathesis conditions. The synthesis of aza-cycles via olefin-olefin metathesis was initially reported by Grubbs,[25] who found that subjecting allylamines to a metal alkylidene such as Grubb's first-generation catalyst **G-I** or Schrock's catalyst provided the ring-closing metathesis product in good to excellent yields. As this approach was expanded to more complex amine-containing systems, it was revealed that the ring-closing metathesis worked well for substituted or electron-deficient amines. However, systems in which the amines maintained high electron densities shut down due to decomposition of the catalyst caused by coordination between the amines and the metal alkylidene complex.[26]

While the presence of Lewis basic amines in metathesis substrates has created a dogma that amines will disrupt the desired reaction, several strategies have emerged that have successfully led to favorable outcomes including utilizing steric affects, attenuating amine basicity, and controlling the nature of the catalyst itself. There have been several excellent reviews on this topic covering substrate design strategies that have led to the application of ring-closing metathesis to access increasingly complex nitrogen

heterocycles.[27] This review will instead focus on recent developments in both reaction and catalyst design that have further advanced the field.

1.3 Application of Olefin Metathesis

Since its discovery in the late 1950s, olefin-olefin metathesis emerged as a highly successful synthetic tool that has been applied towards the synthesis high value materials including polymers, natural products, and therapeutics. While this method has been a significant development, one key application of this method was towards the synthesis of heterocycles via the ring closing metathesis reaction. This strategy has been valuable for the synthesis of nitrogen-containing compounds including pyrrolidines and piperidines which constitute ubiquitous scaffolds in natural products and bioactive compounds.

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While the presence of Lewis basic amines has created this dogma that amines will shut down the desired metathesis, several strategies have emerged that have successfully led to favorable outcomes including utilizing steric affects, attenuating amine basicity, and controlling the nature of the catalyst itself. There have been several excellent reviews on this topic,[27] but this chapter will focus on developments in both reaction and catalyst design since 2010.

1.3.1 Previous Challenges

As previously mentioned, amines representing a challenging functional group that can coordinate to metal alkylidenes resulting in catalyst decomposition and inhibition of olefin metathesis reactions.[26] A variety of strategies have been employed to overcome this inherent shortcoming, including deactivation of the amine by introducing steric bulk to the substrates or by reducing electron density around the nitrogen atom. With these solutions available, ring-closing metathesis has been successfully applied to increasing complex nitrogen heterocycles with lower catalyst loadings and shorter reaction times.

Since olefin metathesis was first applied towards the synthesis of heterocyclic amines, ruthenium catalysts and the understanding of the reaction mechanism have enabled the ring-closing metathesis reaction of unencumbered bis-allylamine

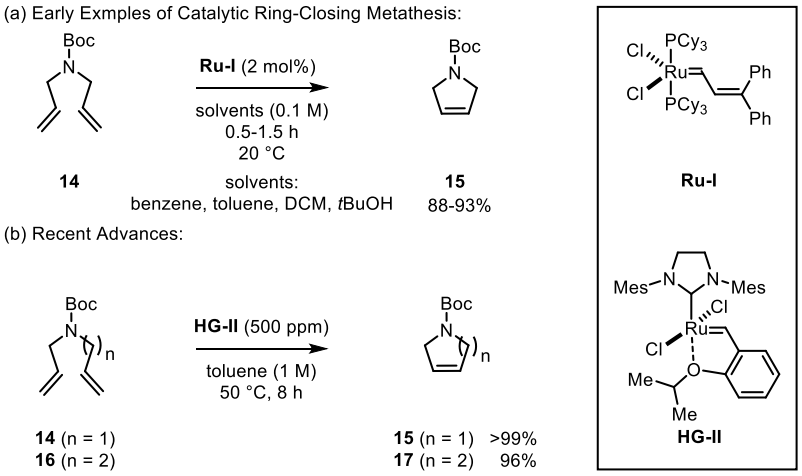
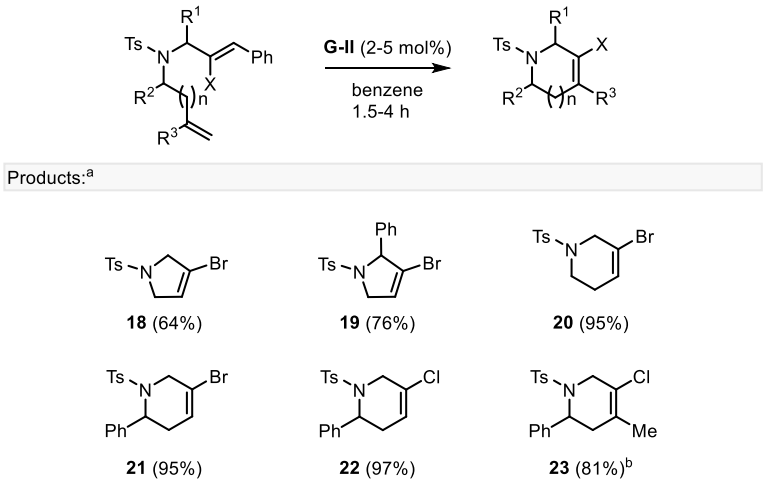


Figure 1.3 Recent advances in the application of catalytic ring-closing metathesis towards the synthesis of nitrogen heterocycles.

14 in good yields with low catalyst loadings. Yields continue to rise as the phosphine ligands were replaced with *N*-heterocyclic carbenes as in **HG-II**.[28] However, while these homogeneous catalysts have been employed in a variety of systems, one challenge – particularly on an industrial scale – is the high catalyst coast and the removal of residual ruthenium. As such there has been a continued effort to lower catalyst loadings.[29,30] Kuhn, et al.[30] recently employed high throughput robotic techniques using Symyx technology in order to identify the optimum reaction conditions for accessing five-, six-, and seven-membered nitrogen heterocycles. They found that by extending the reaction times to 8 h, the catalyst loading could be lowered to as little as 500 ppm and generate the cyclic amines in as high as 99% yield (Figure 1.3). The approach also works well for di-, tri-, and tetra-substituted olefins.

Another hurdle that has been surpassed in recent years was the application of ring closing metathesis to access cyclic alkenyl halides which are valuable synthons. The first reported examples of utilizing ring-closing metathesis for the synthesis of vinyl halides came from Weinreb and co-workers[31] who were able to access cyclic chloroalkenes in good yields; however the method did not work for the synthesis of the more synthetically useful vinyl-bromides.[32] Dorta and co-

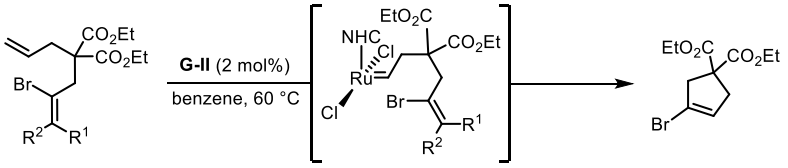


Conditions: a) Reactions were performed using 0.16 mmol of substrate in 0.1 M benzene and 2 mol% of **G-II**. Reactions were run for 1.5-2 h. b) Reaction was run for 4 h with 5 mol% of **G-II** in DCM.

Table 1.1 Catalytic ring-closing metathesis towards the synthesis of cyclic alkenyl halides.

workers[33] recently reported the first example of the synthesis of cyclic alkenyl bromides by replacing the unsubstituted olefins with the styrene derivatives in order to avoid undesired reactivity between the olefin and the active ruthenium species. This method has also been applied to towards tosyl-protected amines to access pyrroles and tetrahydropyridines (Table 1.1). The reaction worked well for both unsubstituted substrates **18** and **20**. Yields were further increased up to 97% by adding a phenyl substituent adjacent to the amine (**19**, **21**, and **22**). The method was also surprisingly facile and led to the synthesis of tetra-substituted cyclic chloro-alkenes **22** and **23** (Table 1.1). Norta proposes that the terminal olefins **24** undergo initiation with **G-II** to generate intermediates **25**. The bromoalkenes **25** can then react with the Ru-center leading to undesired catalyst decomposition (Table 1.2). During examination of the bromoalkenes, Dorta[33] found that while the unsubstituted **24a** and (*E*)-styrene **24b** both led to complete decomposition of the catalyst, the (*Z*)-styrene provided the desired product in just 30 minutes with greater than 98% yield (Table 1.2, entry 3).

Table 1.2 Investigation into the olefin subunit for the synthesis of alkenyl halides.



24 **25** **26**

entry	*substrate*	R^1	R^2	*time*	*%yield*
1	**24a**	H	H	24 h	0
2	**24b**	Ph	H	24 h	0
3	**24c**	H	Ph	30 min	>98

Conditions: All reactions were performed in benzene with 0.1 M substrate concentration. Yields are based on NMR analysis.

While this strategy focused on substrate modification, many approaches have targeted ways to reduce the electron-density around the amine without the introduction of additional functional groups or steps. One such approach involves the *in situ* protection of amines via the formation of amine salts in order to prevent catalyst decomposition

(Figure 1.4). Similar deactivation strategies have been employed performing the in situ deactivation of amines via the addition of Brønsted[34] or Lewis acids.[35] Recently, this approach was successfully utilized by Woodward, *et al*.[36] to generate both cyclic and acyclic aminoalkenes.

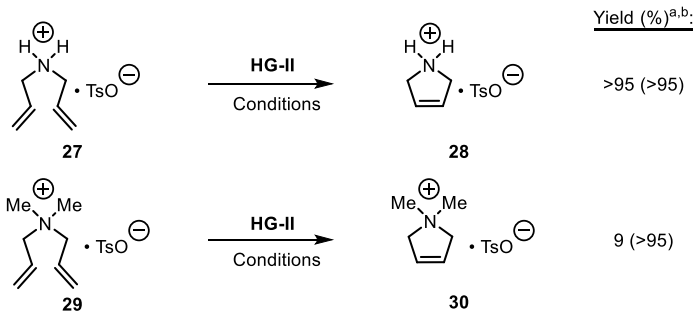


Figure 1.4 Application of olefin-metathesis towards ammonium salts. (a) Conventional Method: **HG-II** (5 mol%), 0.1 M DCM, 40 °C, 24 h. (b) Microwave Conditions (yield in parentheses): **HG-II** (5 mol%), 0.1 M DCM, 2 h, 100 W, under nitrogen. All yields determined by 1H NMR spectroscopy in *d4*-MeOH.

Initially, the approach was hindered by the solubility of the amine salts in organic solvents. After examining a variety of amine salts including halide, triflate, and tetrafluoroborate salts, the amine tosylate salts **27** and **29** were identified as superior substrates due to their solubility in dichloromethane at elevated temperatures. The amine tosylate salts were subject to ring closing metathesis under both conventional and microwave heating conditions. While the ammonium salt **27** gave excellent yields under both conditions, the quaternary amine **29** gave low conversion (9%) under conventional methods. However, when subjected to microwave irradiation the reaction proceeded to generate pyrroline **30** in excellent yield. Furthermore, this approach is desirable that the resulting product **28** could be readily deprotected via subjection to a base without further chemical transformations required.

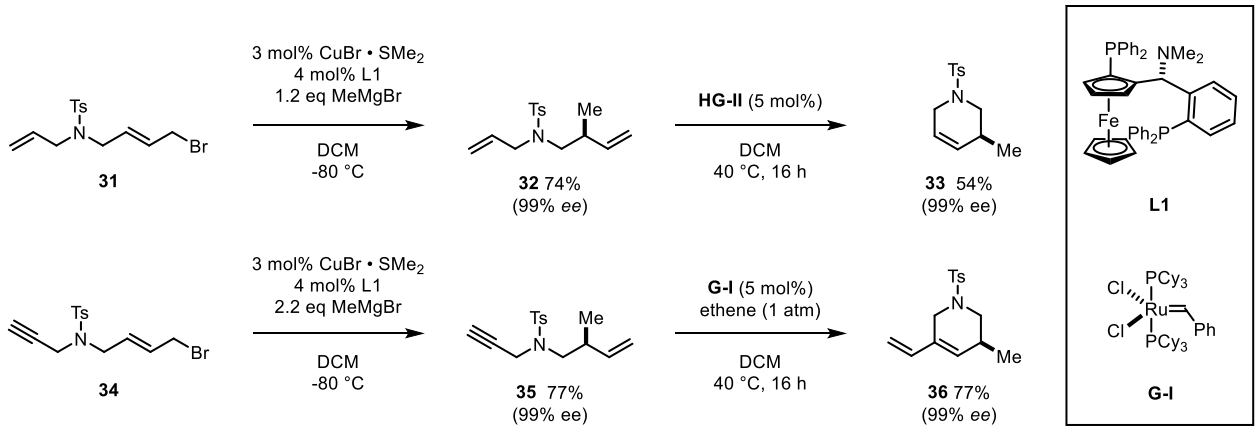
Other advances in the metathesis-mediated formation of nitrogen heterocycles is the strategic implementation of the synthetic tool to access highly desired chiral nitrogen heterocycles.37 One such example came from Feringa and coworkers,38 who developed a copper-catalyzed method for the asymmetric substitution of allylic bromides with

Grignard reagents through the use of chiral ferrocene-based bisphosphine ligands L1. heterocycles.[37] One such example came from Feringa and coworkers,[38] who developed a copper-catalyzed method for the asymmetric substitution of allylic bromides with Grignard reagents through the use of chiral ferrocene-based bisphosphine ligands L1. Recognizing that this method produced terminal olefins, Feringa utilized this method to access chiral products **32** and **35** from the allylic bromides **31** and **34** (Figure 1.5). The allylic bromides could then be subjected to either olefin metathesis or ene-yne metathesis to provide chiral tetrahydropyridines **33** and **36** in good yields and complete stereoretention (Figure 1.5). This method could also be applied to seven- and eight-membered rings.

1.3.2 Advances in Catalyst Design

While the previous discussion focused on modifications in the reaction design and conditions to promote the desired ring-closing metathesis, another key strategy employs changes in catalyst design. Significant advances in metathesis reactions have been realized as the result of the development of more robust and highly reactive ruthenium catalysts that promote ring-closing metathesis without unfavorable side reactions.

Figure 1.5 Asymmetric allylic alkylation and subsequent RCM for the preparation of chiral tetrahydropyridines.



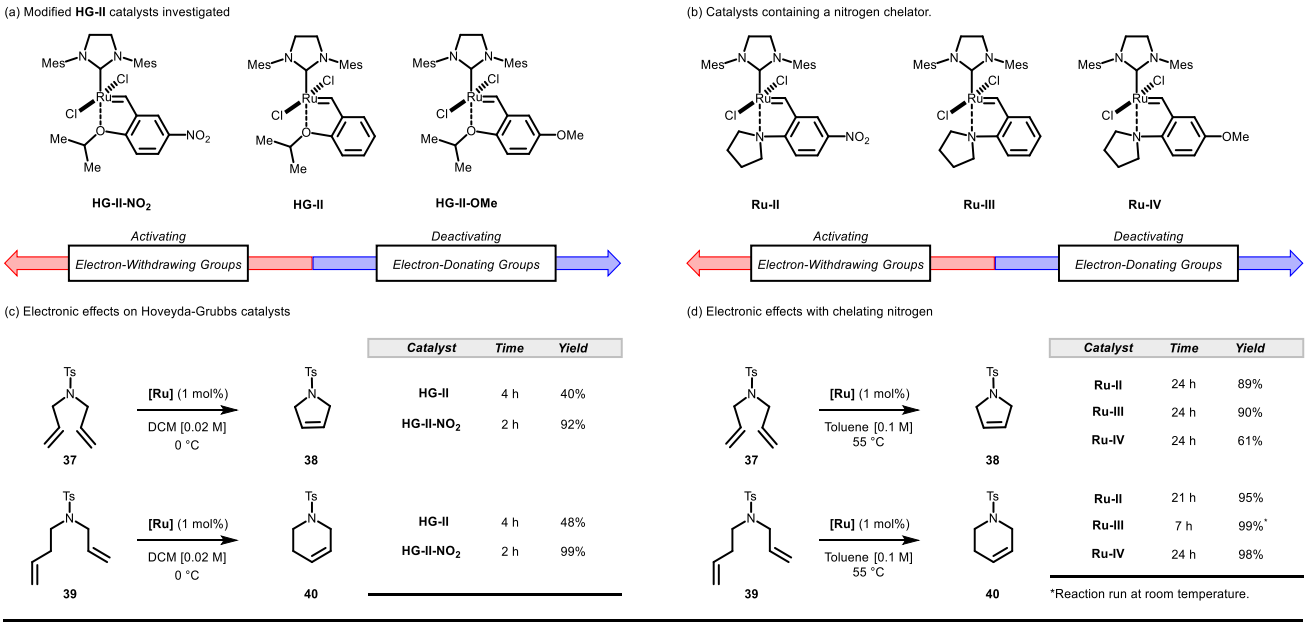


Figure 1.6 Role of electronics on benzylidene catalyst design.

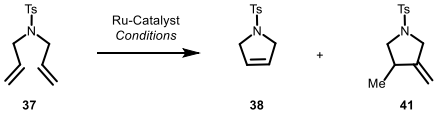
Specifically, modifications on the benzylidene ligands have resulted in significant changes in steric strain, chelate ring size, and electron density of the aromatic ring. Two such examples of major modifications in ligand design have been the replacement of the tricyclohexyl phosphine ligand from **G-I** with a more active *N*-heterocyclic carbene (**G-II**)[28] and the incorporation of benzylidene ligands (**HG-II**).[39]

Continued studies of ligand development and design reveal that the electronic substitution of the ligand also plays a critical role in catalyst reactivity and stability (Figure 1.6).[40] For instance, the reactivity of **HG-II** can be significantly enhanced by the addition of an electron-withdrawing substituent such as the nitro group in **HG-II-NO$_2$** which diminishes the donor activity of the oxygen chelate (Figure 1.6c). Grela and Lemcoff[41] recently undertook a variety of studies exploring electronic effects in ruthenium catalysts containing oxygen, nitrogen, and sulfur-chelated ligands. Changing the chelating heteroatom had a significant impact on the reactivity of the catalyst and its ability to undergo initiation. The electron-rich nitrogen (**Ru-II**, **Ru-III**, and **Ru-IV**) and sulfur

derivatives required elevated temperatures and longer reaction times to give yields comparable to those obtained with **HG-II** and **HG-II-NO$_2$** (Figure 1.6d). However, while these catalysts were relatively slow to initiate, addition of the nitro group greatly affected the overall stability of the catalyst and its ability to mediate the ring-closing metathesis of allyl amines **37**and **39**. The reaction temperature could be lowered from 55 °C to room temperature and provided good yields of the product, albeit in longer reaction times. When the ligand was altered to contain an electron-rich benzylidene ring as in **Ru-IV**, the yield decreased to 61% (Figure 1.6c). A similar trend was observed in the synthesis of tetrahydropyridine **40**. Use of electron-rich catalyst **Ru-IV** required elevated temperature and longer reaction times whereas the electron-deficient catalyst **Ru-III** gave similar yields at room temperature in only 7 hours.

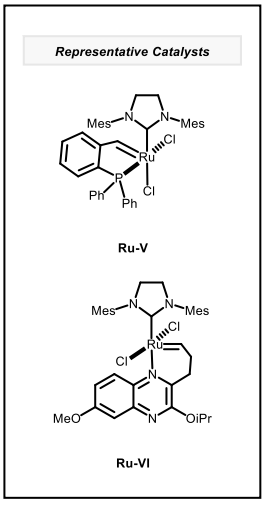
The chelating heteroatom can also play a significant role in the catalyst stability. While most metal alkylidene catalysts perform well at room temperature or slightly elevated temperatures, some selected applications require that the catalyst have high thermal stability. For examples, the latent catalyst is activated, the methylidene species

Table 1.3 Role of chelating ligands, solvents and additives in ring closing metathesis.



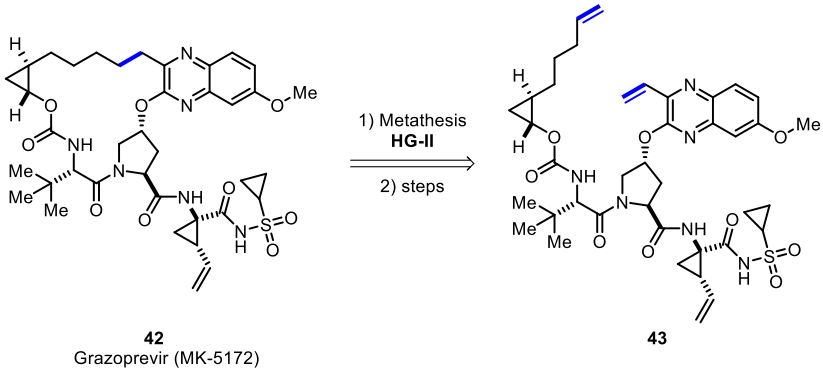
37 **38** **41**

entry	*catalyst*	*additive*	*T (°C)*	*t (h)*	*solvent*	**37** *(%)*	**38** *(%)*	**41** *(%)*
1	**Ru-V**	--	110	72	toluene	--	>97	traces
2	**Ru-V**	--	50	48	toluene	47	52	--
3	**Ru-V**	--	50	72	toluene	52	48	--
4	**Ru-V**	--	50	72	acetone	42	51	7
5	**Ru-V**	--	50	72	$CHCl_3$	--	89	11
6	**Ru-V**	benzoquinone	50	72	$CHCl_3$	18	82	--
7	**Ru-VI**	--	30	6	DCM	--	99.8	--
8	**Ru-VI**	--	30	6	toluene	--	94.5	--
9	**Ru-VI**	$AlCl_3$•THF	30	0.5	DCM	--	98.6	--
10	**Ru-VI**	$AlCl_3$•THF	30	0.5	toluene	--	98.7	--



can rapidly form in solution. At higher temperatures, decomposition of the metal alkylidene is proven to lead to the formation of ruthenium hydride species that can result in the isomerization of olefinic bonds and the formation of byproducts such as **42** (Table 1.3).[42] Ligands with a strongly coordinating heteroatom chelator such as oxygen,[43] nitrogen,[44] sulfur,[45] and selenium[46] provide greater thermal stability. For instance, Slugovc *et al*.[47] began exploring the use of ruthenium alkylidene catalysts bearing a chelating phosphine ligand **Ru-V** for both ring-opening metathesis polymerization and ring-closing metathesis. When this catalyst was used for the synthesis of pyrroline **33**, it provided the desired product in >97% yield with reaction temperatures as high as 110 ˚C. Slugovc also found that the catalyst **Ru-V** could provide good yields of the product at lower temperatures when the solvent was switched to chloroform. At both elevated and lower temperatures, some traces of the isomerized product **41** were observed, but this could further be avoided by the introduction of a hydride scavenger such as benzoquinone (Table 1.3, entry 6).

While the phosphine chelator provides increased stability of the active methylidene species at elevated temperatures, another continued goal is accessing a tunable, shelf-stable catalyst. Such a catalyst was serendipitously discovered during the synthesis of the macrocyclic backbone of the HCV therapeutic agent grazoprevir **42** (MK-5172, Figure 1.7).[48]



42
Grazoprevir (MK-5172)

43

Figure 1.7 Retrosynthetic strategy towards the synthesis of grazoprevir via an olefin ring-closing metathesis and subsequent reduction.

The first quinoxaline **Ru-VI** was isolated as a byproduct of the metathesis reaction to obtain the desired macrocycle from **43**. Quinoxaline **Ru-VI** was found to be stable in deuterated dichloromethane for up to 30 days, while the neat catalyst demonstrated shelf stability of up to 6 months. This stability is likely due the steric repulsion between the quinoxaline and the mesitylene rings preventing the rearrangement to the inactive *cis* isomer of the catalyst.[49]

The effectiveness of the catalyst **Ru-VI** was tested against allyl amine **37** to access pyrroline **38**. Catalyst **Ru-VI** gave complete conversion of sulfonamide **32** in 6 hours and 99% yield (Table 1.3, entry 7). Considering that electron-deficient catalysts are more active in ring-closing metathesis reactions, McLaughlin proposed[49] that the reaction rate could be increased through the protonation of the quinoxaline ligand with an acid catalyst. After examining both Brønsted and Lewis acids, $AlCl_3$ was found to give complete conversion and excellent yields of **37** in only 30 minutes (Table 1.3, entries 9 and 10).

As previously discussed, the decomposition of the active methylidene species in solution to ruthenium hydrides results in undesired isomerization of the olefins.[42] While hydride

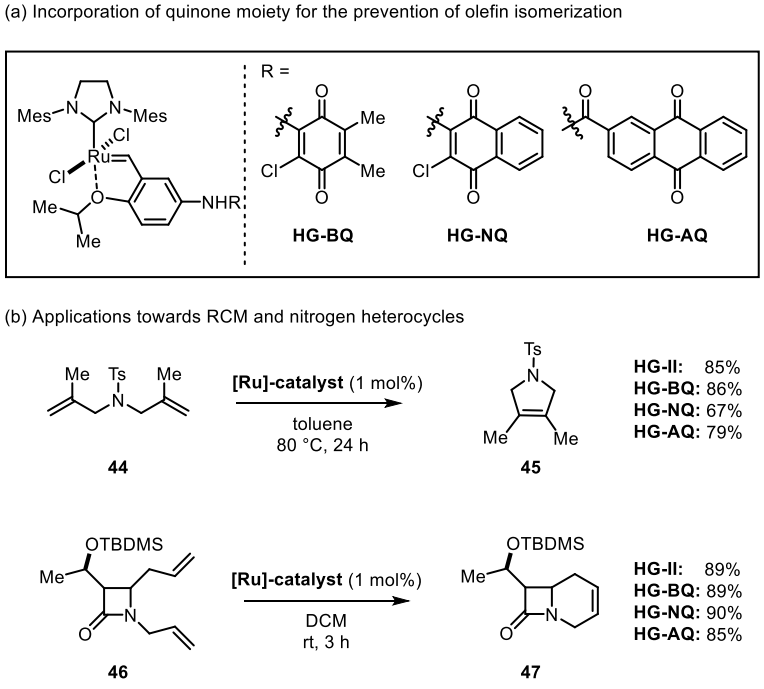


Figure 1.8 Study of ruthenium catalysts containing quinone ligands. (a) Application of quinone moiety as part of ligand design to function as a Ru-hydride scavenger; (b) Comparison of catalysts containing quinone motifs towards the synthesis of nitrogen heterocycles.

scavengers such as quinones, acids, and chlorocatecholborane have proven effective in the prevention of undesired pathways, they do not necessarily prevent catalyst decomposition. Wozniak and coworkers[50] envisioned incorporating the quinone moiety into the catalyst structure, and synthesized the Hoveyda-Grubbs derivatives with benzoquinone **HG-BQ**, napthoquinone **HG-NQ**, and anthraquinone moieties **HG-AQ**. These catalysts were tested and compared to **HG-II** for the metathesis of tosylamide **44** and lactam **46** (Figure 1.8). The benzoquinone catalyst gave comparable yields to **HG-II** demonstrating that there is no loss in reactivity of the catalyst. These catalysts were also tested for their ability to prevent olefin isomerization by gauging their ability to selectively perform the homodimerisation of dodec-1-ene. While **HG-II** could perform the metathesis reaction in 69% conversion, it only had a selectivity of 70%. However, **HG-BQ** and **HG-NQ** were able to complete the reaction in 89% and 94% conversion, respectively. And not only did these catalysts outperform **HG-II**, but they both formed the desired product in 95% selectivity.

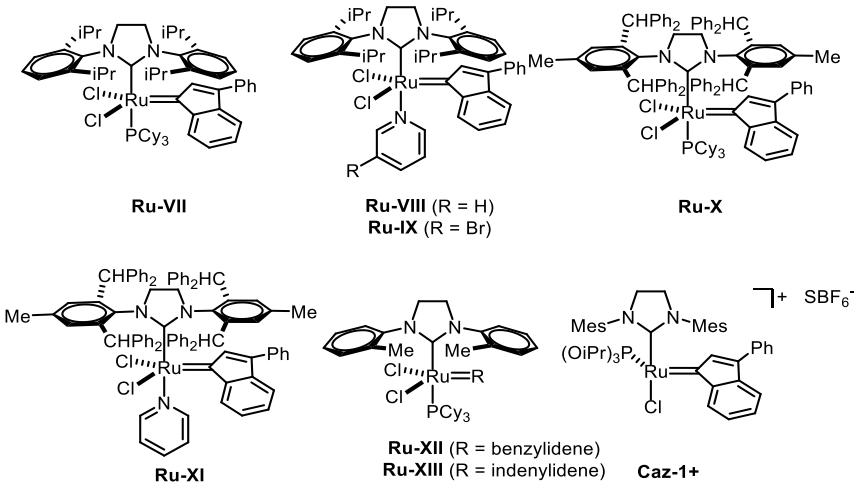
1.3.3 Indenylidene Complexes

One class of ruthenium catalysts that has become increasingly popular are ruthenium-pyridine adducts which have been referred to as the “third generation” of olefin metathesis catalysts.[51] Such complexes are straightforward to access via ligand substitution by stirring in excess pyridine.[52] One advantage of the pyridine ligands is that they are only weakly coordinating to the metal center, and initiation of the catalyst is much faster. Unfortunately, this means the catalysts show decreased stability overtime and are often outperformed by their tricyclohexylphosphine-containing analogues.[53] In an effort to increase the overall stability of these ruthenium-pyridine catalysts, indenylidene catalyst

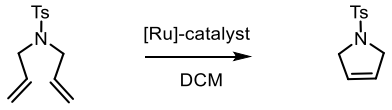
have been developed. This new class of catalyst is accessible from commercially available ruthenium precursors. These complexes exhibit enhanced stability in harsh reaction conditions, higher functional group tolerance, and greater stability on the bench.[53c,54,55]

Nolan and coworkers[55] recently reported a series of indenylidene catalysts (Figure 1.9) to explore their reactivity and effects of sterics in ring-closing, enyne, and cross metathesis reactions. When tested against the diallylamine **37**, the pyridine ligands outperformed the phosphine derivatives by up to 30% with catalyst loadings as low as 100 ppm (Figure 1.9b, entries 1, 2, and 3). The reaction also worked exceedingly well with the more substituted prenyl amine, however, higher catalyst loadings of 250 ppm were required due to the increase in steric bulk around the olefin.

(a) Development of Ruthenium Indenylidene Catalysts



(b) Analysis of the role of sterics on the synthesis of 1-tosyl-2,5-dihydro-1H-pyrrole.



entry	catalyst	loading	T (°C)	t (h)	concentration (M)	conversion (%)
1	**Ru-VII**	100 ppm	30	1	0.5	50
2	**Ru-VIII**	100 ppm	30	1	0.5	76
3	**Ru-IX**	100 ppm	30	1	0.5	88
4	**Ru-VII**	1 mol%	rt	0.5	0.1	>99
5	**Ru-VIII**	1 mol%	rt	0.25	0.1	>99
6	**Ru-X**	1 mol%	rt	3	0.1	>99
7	**Ru-XI**	1 mol%	rt	3	0.1	96

Figure 1.9 Studies into indenylidene catalysts: (a) catalyst design and synthesis; (b) analysis of new catalysts towards the synthesis of 3-pyrroline; (b) applications of indenylidene catalysts towards the synthesis of substituted pyrrolines and tetrahydropyridines.

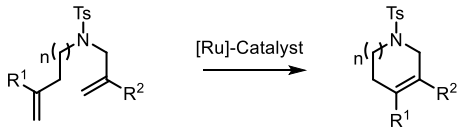
Nolan, et al.56 expanded studies on the indenylidene catalysts and synthesized catalysts Ru-XI, Ru-XII, and Ru-XIII. For the unsubstituted diallylamine 37, all the catalysts were able to provide the metathesis product 38 in excellent yields, however, a significant difference in reactivity between the more substituted catalysts was observed. The NHC ligands bearing increased steric bulk required longer reaction times of 3 hours (Figure 1.9, entries 6 and 7). Comparing catalyst Ru-VII and Ru-VIII, the catalyst containing the pyridine ligand was more reactive than the phosphane. The reaction went to completion in 30 min with Ru-VII, while the reaction with Ru-VIII was completed in 15 min (Figure 1.9b, entries 4 and 5, respectively).

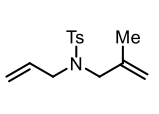
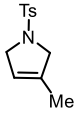
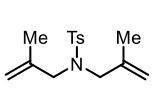
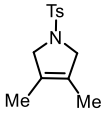
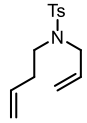
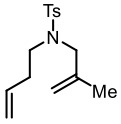
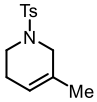
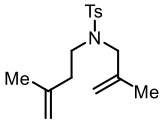
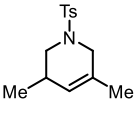
When the amine bearing the substituted olefin **48** was subjected to metathesis conditions with catalyst **Ru-X**, the reaction required 3 hours and only resulted in 76% conversion of the starting material. This may be due to unfavorable steric interactions of the catalyst that slows down the reaction, but when the phosphane was replaced with the pyridine analogue **Ru-XI**, the reaction proceeded in >99% conversion in just 1 hour. The reaction also resulted in excellent yields of the pyrroline **49**, while the more reactive analogue did give a slightly diminished yield.

Because less sterically encumbered NHC ligands such as **Ru-VIII** tend to be more reactive, albeit less stable overall, there have been significant efforts made to improve their general stability to make them more productive for catalysis. One factor that contributes to the decomposition of the less substituted (and more reactive) indenylidene catalysts is due to increased rotation around the aryl C–N bond.[57] In an effort to prevent this rotation, one strategy to increase stability is to add alkyl substituents to the backbone as illustrated in **Ru-XI**,[58] however, bulky substituents are also known to lead to reaction

inhibition. A viable alternative is to replace the benzylidene with the more stable indenylidene **Ru-XIII**.[59] When this catalyst was used to promote the ring-closing metathesis of substituted olefin **45** (Table 1.4), it out performed its benzylidene counterpart resulting in 98% of the desired product. The catalyst could also be applied towards the synthesis of substituted tetrahydropyridines **33** and **51**, albeit with longer reaction times and in diminished yields.

Table 1.4 Application of Indenylidenes towards the synthesis of nitrogen heterocycles.



entry	substrate	product	catalyst	loading (mol%)	t (h)	Yield (%)
1[a]			**Ru-X**	1	3	76
2[a]			**Ru-XI**	1	1	>99
	48	**49**				
3[b]			**Ru-XII**	0.5	1	69
4[b]			**Ru-XIII**	0.5	1	98
5[c]	**44**	**45**	**Caz-1+**	0.1	0.25	90
6[c]			**Caz-1+**	0.1	0.25	97
	39	**40**				
7[b]			**Ru-XIII**	0.5	18	74
	32	**33**				
8[b]			**Ru-XIII**	0.5	1	55
9[c]			**Caz-1+**	0.1	0.25	85
	50	**51**				

Conditions: (a) rt, DCM [0.1 M], (b) 60 °C, toluene [0.1 M], (c) 140 °C, xylene [0.25M].

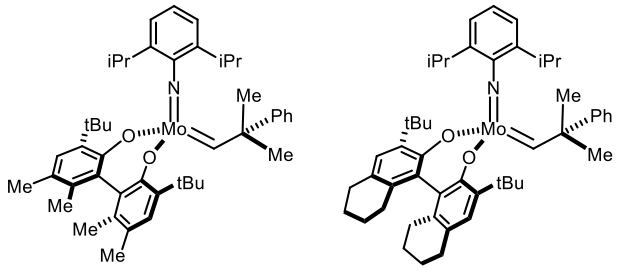
Another new and exciting field is the conversion of the neutral NHC catalysts to their corresponding cationic derivatives. Only a handful of groups have developed systems that utilize cationic catalysts in ring-closing metathesis, but the catalysts can be a powerful tool for accessing challenging metathesis products.[60] A recent example comes from Cazin, *et al*.[61] with the synthesis of cationic catalyst **Caz-1$^+$** with a phosphite ligand. Interestingly, similarly reported cationic ruthenium species which are 14 electron complexes tend to dimerize to the more stable 16 electron species. In the case of cationic

species **Caz-1⁺**, no dimerization is observed due to the formation of an unusual sawhorse geometry. This makes the catalyst especially stable in solution. While studying ability of the catalyst **Caz-1⁺** to convert tosylamine **44** to the pyrroline **45** compared to **G-II** and **HG-II** at 140 °C, **G-II** and **HG-II** both displayed rapid decomposition and only 40% conversion of the tosylamine. Interestingly, **Caz-1⁺** displayed higher thermal stability and reached 90% conversion after only 10 min. This catalyst was used to access other challenging substrates including tetrahydropyridines **40** and **51** in 97% and 85% yield, respectively.

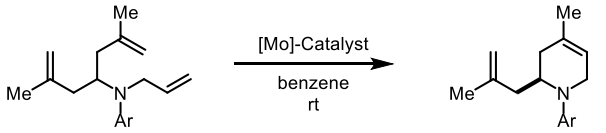
1.3.4 Unsymmetrical NHC Ligands

While NHC ligands have led to a new generation of metal alkylidene catalysts that enable access to new, more complex structures, an ongoing challenge in ring-closing metathesis reactions is performing them asymmetrically to access enantioenriched products.[62] While asymmetric olefin metathesis reactions have been successfully employed in ring-opening cross metathesis, controlling the olefin geometry continues to be a challenge in asymmetric ring closing metathesis. Key strategies for applying ring-closing metathesis are through the kinetic resolution of dienes or the

(a) Chiral molybdenum catalysts of interest.



(b) Application of Mo-I and Mo-II towards tetrahydropyridines.

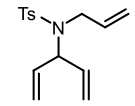
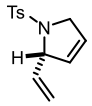
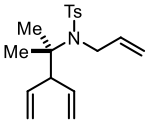
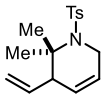


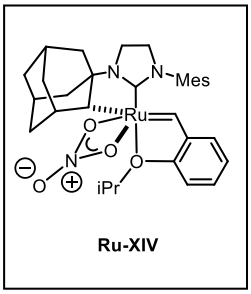
entry	Ar		catalyst	time (h)	conversion (%)	*ee* (%)
1	Ph	**52**	**Mo-I**	0.3	95	98
2	Ph	**52**	**Mo-II**	1	95	94
3	*p*-OMePh	**53**	**Mo-I**	0.35	97	97
4	*p*-BrPh	**54**	**Mo-I**	0.35	>98	98

Figure 1.10 Molybdenum catalysts in asymmetric ring-closing olefin metathesis. (a) Development of chiral molybdenum catalysts and (b) applications of chiral alkylidenes towards the synthesis of enantioenriched tetrahydropyridines.

desymmetrization of meso- trienes, particularly when the unique olefin is less bulky than the enantiotopic olefins.[62] Asymmetric ring closing metathesis has been successfully applied to a variety of systems using molybdenum alkylidene catalysts (Figure 1.10).[63] Specifically Hoveyda and coworkers were able to utilize molybdenum catalyst **Mo-I** to access both cyclic six-, seven-, and eight-membered rings and bicyclic amines in good yields with up to 98% *ee*.[64]

Grubbs and coworkers[65] postulated that for prochiral trienes to proceed in an enantioselective metathesis reaction, the pathway can either consist of an irreversible alkylidene formation of one to the enantiotopic olefins, or the alkylidene can from the unique olefin which can then cyclize with one of the other enantiotopic olefins. Cavallow[66] performed computational studies on the origin of stereoselectivity and found that the non-reacting olefin is oriented in pseudo-equitorial and pseudo-axial positions in the respective diastereomeric transition states for cyclization. With larger substituents, higher selectivities are expected due to the large energy difference between the two configurations. Grubbs hypothesized that utilizing adamantyl catalyst **Ru-XIV** would promote the alkylidene form cation with the unique olefin (Table 1.5). The utility of this catalyst was first probed against tosylamine **55**, and the reaction gave good yields of the pyrroline **56** with modest enantioselectivity. The reaction

substrate	product	%yield (%*ee*)
 **55**	 **56**	95 (54)
 **57**	 **58**	90 (57)



Ru-XIV

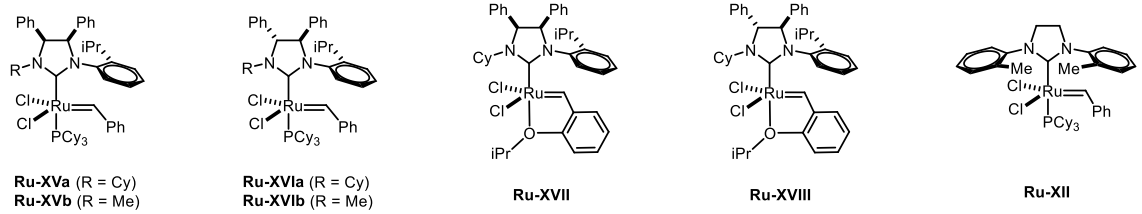
Conditions: 5 mol% **Ru-XII**, THF [0.5 M], 23 °C, 24 h.

Table 1.5 Application of adamantyl-containing ruthenium catalyst towards the synthesis of chiral pyrrolines and tetrahydropyridines.

also works well in the synthesis of tetrahydropyridine **58** providing the product with similar yield and slightly higher *ee*. It is proposed that the stereoinduction is due to the possible transition state in which the vinyl groups are in the pseudo-equitorial position.

Unsymmetrical NHC catalysts are also of interest for addressing the challenge of achieving high selectivity in certain metathesis reactions. Such complexes, as demonstrated in the previous examples can significantly alter the stability of key intermediates thus introducing the ability to control the reaction outcome. In order to expand this class of catalyst, Grisi and Grela[67] set out to identify new ways to enhance the stability of the unsymmetrical NHC catalysts by introducing substituents to the ligand backbone. In particular, syn- and anti-complexes Ru-XV and Ru-XVI were synthesized, as well as catalysts containing the *N*-neopentyl backbone (Figure 1.11). After 1 week, the *syn* complexes **Ru-XVa** and **Ru-XVb** were almost completely decomposed, however, the *anti-*

(a) Recent developments in unsymmetrical N-heterocyclic carbenes as catalysts in ring-closing metathesis.



Ru-XVa (R = Cy)
Ru-XVb (R = Me)

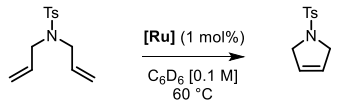
Ru-XVIa (R = Cy)
Ru-XVIb (R = Me)

Ru-XVII

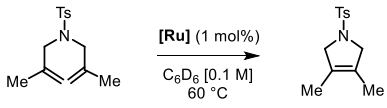
Ru-XVIII

Ru-XII

(b) Key results form kinetic profiles comparing unsymmetrical N-heterocyclic carbenes in the synthesis of **38** and **46**.



37 **38**



45 46

entry	catalyst	time (min)	%yield
1	**Ru-XVa**	32	60
2	**Ru-XVb**	65	60
3	**Ru-XVIa**	94	35
4	**Ru-XVIb**	94	35
5	**Ru-XVII**	60	94
6	**Ru-XVIII**	3	99
7	**Ru-XII**	>99	27
8	**HG-II**	4	>99

entry	catalyst	time (min)	%yield
9	**Ru-XVa**	60	33
10	**Ru-XVb**	60	29
11	**Ru-XVIa**	60	64
12	**Ru-XVIb**	60	31
13	**Ru-XVII**	60	77
14	**Ru-XVIII**	60	97
15	**Ru-XII**	60	92
16	**HG-II**	60	72

Figure 1.11 Development of unsymmetrical catalysts.

complexes **Ru-XVIa** and **Ru-XVIb** proved more resistant to decomposition and were stable for up to 10 days. Furthermore, bulkier *N*-alkyl groups tended to help stabilize the catalyst.

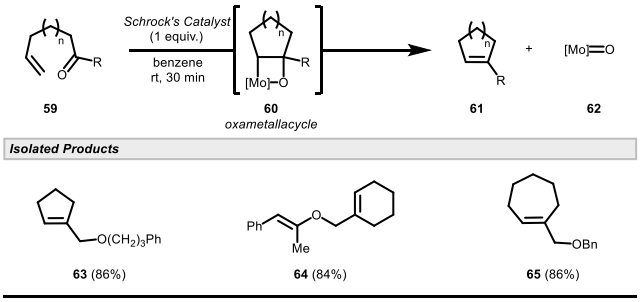
In terms of overall reactivity, the *N*-alkyl substituent did not play a major role in the catalyst reactivity (Figure 1.11b). When less substituted olefin **32** was subjected to a variety of catalysts with varying *N*-alkyl substituents, no significant difference in yield was observed, however, the bulkier catalysts required slightly longer reaction times. The backbone substituents played a more significant role in reactivity, as the *anti*-complexes **Ru-XVIa** and **Ru-XVIb** gave higher yields than their *syn*-counterparts. In the presence of bulkier olefins, a slight decrease in reactivity was observed which is attributed to unfavorable steric interactions.[68]

1.4 The Development of the Carbonyl-Olefin Metathesis Reaction

Metal-catalyzed metathesis reactions have revolutionized today's industrial processes and led to more advanced technologies, medicines, and materials. One of the biggest challenges facing our generation is identifying sustainable alternatives to precious metals that are often required for these processes. Precious metals such as gold, platinum, palladium and ruthenium are characterized by their limited geochemical abundance. The olefin-olefin metathesis reaction is a revolutionary industrial process that utilizes precious metal complexes to enable direct carbon-carbon bond formation from simple olefin starting materials.[69] Its importance was recognized in 2005 when Grubbs, Schrock, and Chauvin received the Nobel Prize for their contribution to its development. In this transformation, parts of the olefin substrates are exchanged upon reaction with a ruthenium catalyst and recombined to form a new olefin product. Current limitations in

metathesis reactions include the need for precious metals, high catalyst loadings, and the required synthesis of olefin substrates.[70] Prerequisite synthesis of substrates, prepared from carbonyl compounds via olefination reactions, use stoichiometric reagents. This is problematic in that one equivalent of reagent is required per substrate and inevitably results in the formation of an undesired waste product in equal amounts. Consequently, the direct conversion of a carbonyl and olefin substrate in a carbonyl-olefin metathesis reaction would obviate this limitation.

Table 1.6 Early examples of carbonyl-olefin metathesis applied towards the synthesis of cycloalkenes.



While traditional olefin-olefin metathesis has been a powerful tool in a wide range of applications including natural product synthesis, materials and polymers, medicines, and fine chemical synthesis, a continued challenge is finding inexpensive, sustainable catalysts. An intriguing alternative that has emerged in recent years is the application of carbonyl-olefin metathesis. In 1993 Grubbs and Fu reported the synthesis of five-, six-, and seven-membered cycloalkenes (Table 1.6) by subjecting various olefinic ketones **59** to Schrock's catalyst to perform the carbonyl-olefin metathesis sequence via the formation and fragmentation of intermediate oxametallacycles **60**.[71] However, stoichiometric quantities of Schrock's catalyst were required due to the formation of a metal-oxo species **62**, which is difficult to reduce back to the active metal alkylidene.

The first reported example of carbonyl-olefin metathesis in the presence of amines came from Zhou and Rainier.70 Their strategy focused on the formation of titanium alkylidenes. This method was used to synthesize five-, six-, and seven-membered rings through a carbonyl-olefin metathesis pathway (Figure 1.12). Mechanistic insights for this synthesis came when tosylamine 71 was subjected to the metathesis conditions resulting in a mixture of tetrahydropyridine **73A** and acyclic enamide **73B**. When the acyclic enamide was resubjected to the reaction conditions, none of the cyclic product was formed. This supports the hypothesis that the cyclic product proceeds via a carbonyl-olefin pathway as opposed to an olefin-olefin metathesis mechanism (Figure 1.12a).

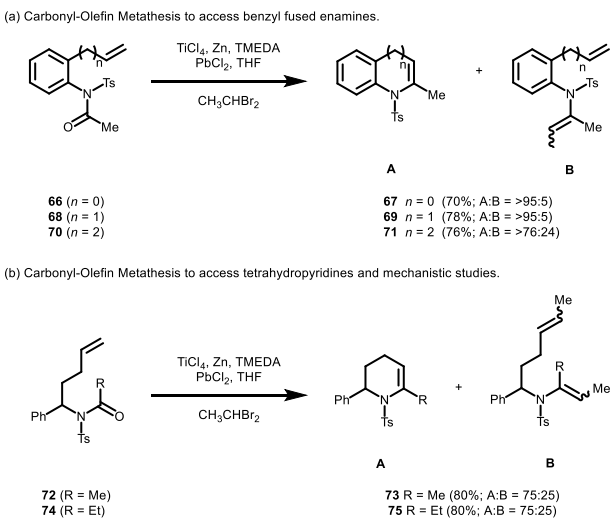


Figure 1.12 Titanium-mediated carbonyl-olefin metathesis for the synthesis of unsaturated nitrogen heterocycles (a) quinolines and (b) tetrahydropyridines.

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Chapter 2

Application of Carbonyl-Olefin Metathesis Towards the Synthesis of Chiral 3-Pyrrolines**

2.1 Introduction

Chiral pyrrolidine and pyrrole derivatives represent ubiquitous structural motifs in biologically active natural products[1] and serve as important templates in drug discovery.[2] Moreover, chiral pyrrolidines function as ligands in asymmetric catalysis[3] and are crucial

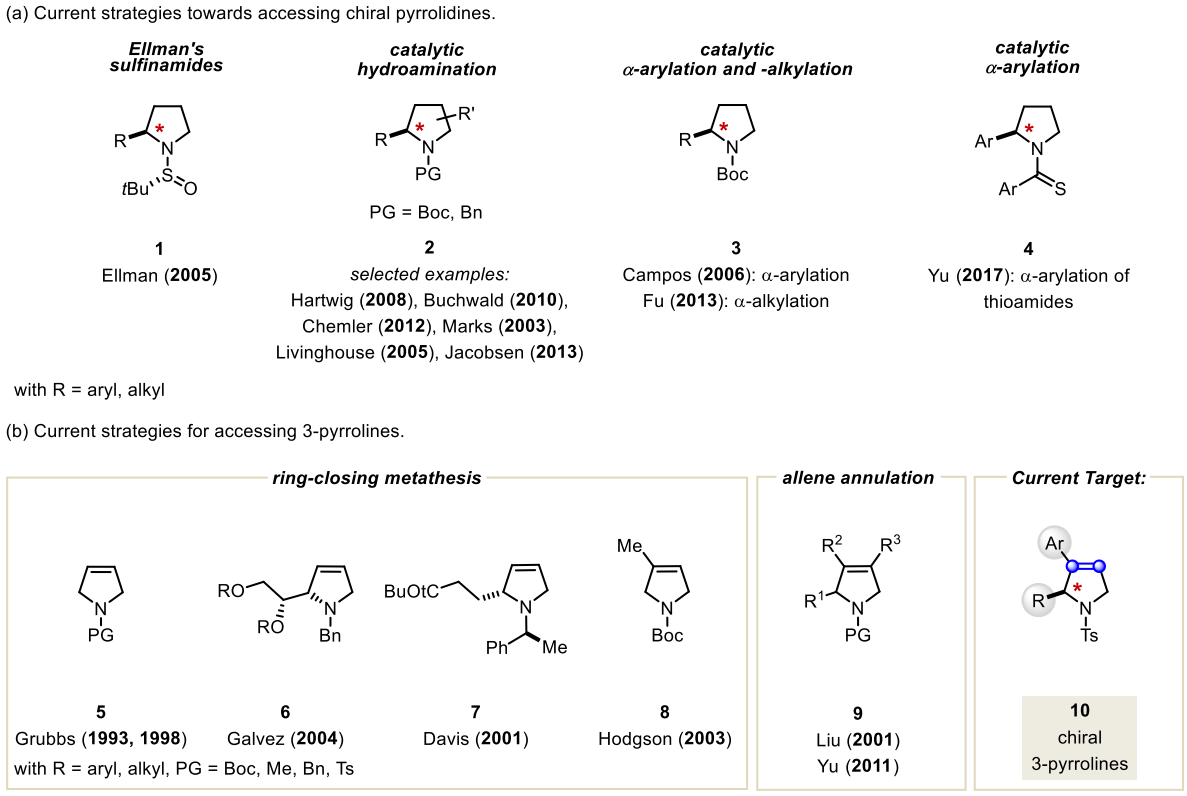


Figure 2.1 Strategies towards accessing chiral nitrogen heterocycles.

** Groso, E.J.; Golonka, A.N.; Harding, R.A.; Alexander, B.W.; Sodano, T.M.; Schindler, C.S. *ACS Catal.* **2018**, *8*, 2006-2011.

components of hydrogen-bond donor catalysts.[4] As a result of these wide-ranging implications, the development of synthetic strategies to chiral nitrogen-containing heterocycles constitutes an active area of research. Among the currently available synthetic strategies are the reductive cyclization of *N*-tert-butanesulfinyl ketimines[5,6] to access chiral pyrrolidines **1** (Figure 2.1a). An alternative approach relies on enantioselective olefin hydroamination strategies[7-10] as a synthetic approach to α-substituted pyrrolidines **2**. Additionally, transition-metal catalyzed asymmetric α-arylation and -alkylation strategies[11-14] give rise to protected pyrrolidines **3** and **4**. However, xamples of direct cyclization strategies towards accessing chiral 3-pyrrolines are somewhat limited (Figure 2.1b). The most common strategy for accessing this motif is via ring closing metathesis (**5-8**, Figure 2.1b), however, recent reports have employed allene annulation to access substituted 3-pyrrolines **9**. Despite these efforts, imparting stereochemistry still presents a challenge (Figure 2.1b). Furthermore, precursors can be challenging to access and these approaches often require expensive precious metal catalysts.

With the recent development of carbonyl-olefin metathesis, we envisioned a strategy that would enable us to access chiral 3-pyrrolines **10** by utilizing chiral pool reagents. This

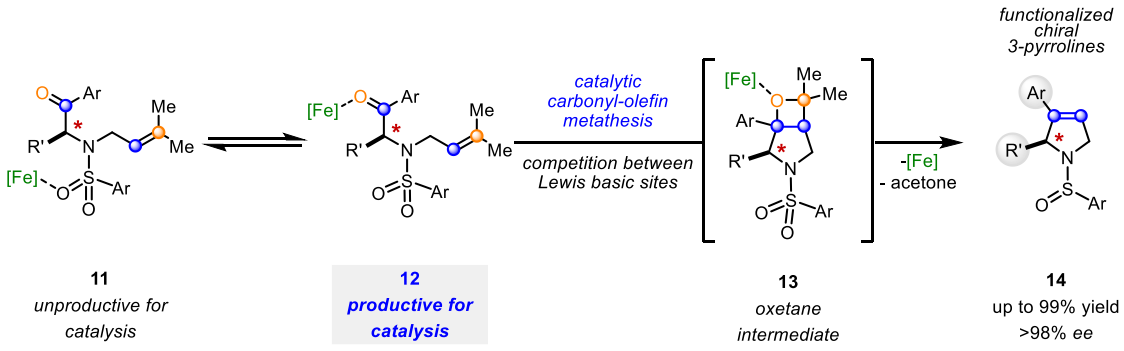


Figure 2.2 Strategies towards accessing chiral 3-pyrrolines.

chapter describes the development of a synthetic strategy towards access chiral α-amino ketones and the application of the Lewis-acid catalyzed carbonyl-olefin metathesis reaction. Our strategy relies on an iron(III)-catalyzed carbonyl-olefin ring-closing metathesis reaction which enables the direct coupling of carbonyl and olefin functional groups **12** to form intermediate oxetanes **13** which then fragment generating the desired metathesis products **14**.[15,16] Substrates containing nitrogen atoms were previously shown to be problematic in carbonyl-olefin ring-closing metathesis reactions.[16a,17] In this report, we identify the sulfonamide as a competitive binding site of the FeCl3 catalyst which prevents the desired metathesis (**11**, Figure 2.2b). Based on these insights, we show that attenuating the Lewis basicity of the sulfonamide moiety is a viable strategy to overcome this limitation due to iron sequestration to ultimately promote the desired carbonyl-olefin metathesis. This approach enables efficient turnover of the iron catalyst and results in the desired, chiral pyrrolines in high yields.

2.2 Results and Discussion

At the outset of our investigations, we developed a concise and modular synthetic strategy to access metathesis substrates from commercially available amino acids which enables distinct variations of the α-amino and aryl ketone substituents (Figure 2.3).[18] Starting with the protected amino acids **15**, we first performed a peptide coupling reaction

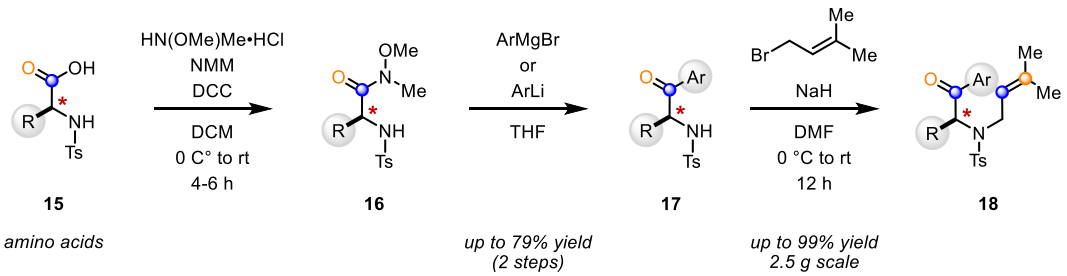


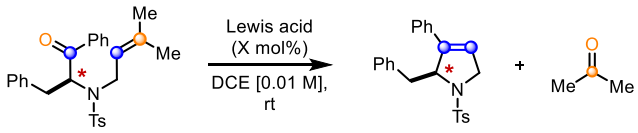
Figure 2.3 Flexible 3-step strategy for accessing substrates from commercially available, chiral amino acids.

using DCC to access the Weinreb amides **16**. Upon subjecting the Weinreb amide to either the aryl Grignard or aryl lithium reagents, we were able to access the aryl ketones **17** in up to 79% yield over two steps. Alkylation of the secondary amine with prenyl bromide provides the desired substrates **18** in up to 99% yield. Some key highlights of 3this synthetic sequence are that it is a concise, 3-step reaction sequence that is scalable and lends itself well to accessing a diverse array of chiral substrates.

With a substrate synthesis in hand, we first accessed the chiral phenylalanine derivative **19** and tested it against a variety of Lewis and Brønsted acids. When the *N*-tosyl amine **19** was reacted with 20 mol% of weak Lewis acids (e.g. $ZnCl_2$, $FeCl_2$) no formation of the desired metathesis product **20** was observed. Similarly, catalytic amounts of the strong Lewis acid $AlCl_3$ resulted in exclusive re-isolation of unreacted starting material. Notably, the use of $SnCl_4$ and $GaCl_3$ under otherwise identical reaction conditions resulted in the formation of desired metathesis product **20**, albeit in low yields while significant amounts of dealkylated starting material were observed (entries 1 and 2, Table 2.1).

Subsequent experiments identified $FeCl_3$ as a superior Lewis acid which formed **20** in 19% yield while no competing substrate dealkylation was observed (entry 3, Table 1). These results are consistent with our previous studies of catalytic carbonyl-olefin metathesis reactions which

Table 2.1 Evaluation of carbonyl-olefin metathesis conditions.



19
98% *ee*

20
98% *ee*

entry	Lewis acid	mol%	yield (%)	conversion (%)
1	$SnCl_4$	20	3	26
2	$GaCl_3$	20	8	59
3	$FeCl_3$	20	19	19
4	$FeCl_3$	30	24	24
5	$FeCl_3$	40	53	91
6	$FeCl_3$	50	72	100
7	*p*TsOH	20	0	0
8	HCl (in DCE)	20	0	0

Conditions: all reactions were performed using 0.06 mmol of the substrate in DCE (0.01M) for 24 h. Yields are reported as NMR yields with naphthalene as internal standard.

illustrated that a fine-tuned combination of Lewis acidity and oxophilicity was essential for an efficient Lewis acid catalyst.[16b,19]

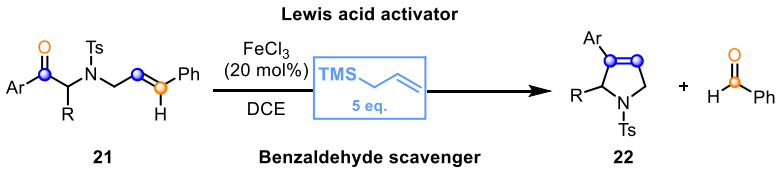


Figure 2.4 Preparation of 3-pyrrolines using allyltrimethylsilane as a superstoichiometric additive.

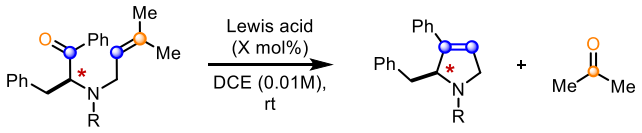
Longer reaction times did not improve the yield, however, higher catalyst loadings of up to 50 mol% resulted in increased yields of metathesis product 12a in 72% (entries 4-6, Table 2.1). Importantly, no erosion in enantioselectivity was observed in the carbonyl-olefin metathesis of **19**, resulting in the formation of the desired product in 98% *ee*. Brønsted acids such as pTsOH and anhydrous HCl did not promote the desired carbonyl-olefin metathesis reaction (entries 7 and 8, Table 2.1). During our initial investigations into the synthesis of highly valuable heterocyclic compounds using carbonyl-olefin metathesis, we observed the need for super stoichiometric amounts of $FeCl_3$ or additional nucleophilic reagents and hypothesized that competitive Lewis acid binding to the tosyl protecting group was hampering effective catalysis. Li and coworkers reported a procedure that utilized styrenyl olefins **21** in place of the prenyl fragment, however, this strategy relied on the use of super stoichiometric allyltrimethylsilane (5.0 equiv.) as additive. Li proposed product inhibition was due to the formation of the benzaldehyde byproduct and that the allyltrimethylsilane could play a dual role by acting as both a benzaldehyde scavenger as well as activating the $FeCl_3$ for catalysis.[17]

This strategy was proven to be quite effective, but we postulated that the presence of Lewis basic sites other than the carbonyl oxygen in **19** was leading to sequestration of the catalyst, so higher catalyst loadings were required. Subsequent efforts focused on the evaluation of electronically distinct nitrogen-protecting groups (e.g. Boc, Cbz, Ns) in the

carbonyl-olefin metathesis of phenylalanine-based substrates which resulted in increased substrate dealkylation and provided diminished yields of the desired metathesis products. We hypothesized that attenuating the electronic properties of the sulfonamide functionality by adding electron-withdrawing substituents to the aromatic ring would disfavor sequestering of FeCl3 and prevent stalling of the carbonyl-olefin metathesis reaction. When the tosyl group was replaced with *N*-4-chlorobenzene-sulfonamide **23** and subjected to carbonyl-olefin metathesis, the desired product was obtained in up to 96% yield (entry 2, Table 2.2). These yields were increased to 99% yield when the protecting group was replaced with the *N*-(4-trifluoromethyl)-benzenesulfonyl group (entry 3, Table 2.2), supporting our initial hypothesis. Importantly, the desired carbonyl-olefin metathesis product **26** is now obtainable in up to 80% yield with as low as 5 mol% $FeCl_3$ (entry 6, Table 2.2). In comparison.

Subsequent competitive binding studies supported our initial hypothesis that an

Table 2.2 Evaluation of nitrogen protecting groups and their effect on carbonyl-olefin metathesis.



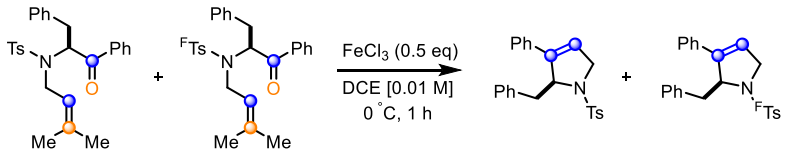
19: R = Ts (98% *ee*)
23: R = ^{Cl}Ts
25: R = ^{F}Ts

20: R = Ts (98% *ee*)
24: R = ^{Cl}Ts
26: R = ^{F}Ts

entry	Lewis acid	mol%	R	yield (%)	conversion (%)
1	$FeCl_3$	50	Ts	72	100
2	$FeCl_3$	50	^{Cl}Ts	96	100
3	$FeCl_3$	50	^{F}Ts	99	100
4	$FeCl_3$	30	^{F}Ts	96	100
5	$FeCl_3$	20	^{F}Ts	90	100
6	$FeCl_3$	5	^{F}Ts	80	100

Conditions: all reactions were performed using 0.06 mmol of the substrate in DCE (0.01M) for 24 h. Yields are reported as NMR yields with naphthalene as internal standard.

Table 2.3 Competitive binding studies with different sulfonamides.



19 **25** **20** **26**

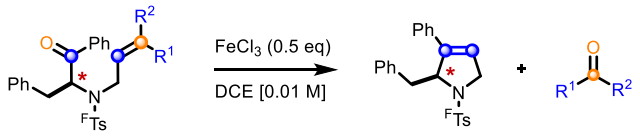
entry	**19** (eq.)	**25** (eq.)	$FeCl_3$ (eq. **19**+**25**)	**20** (%)	**26** (%)
1	0	1	0.5	-	83
2	0.3	1	0.5	49	76
3	1	1	0.5	56	53
4	1	0	0.5	66	-

Conditions: reactions were performed using 0.033 mmol of substrates (**19** + **25**) with 0.017 mmol of $FeCl_3$ (50 mol%) in DCE (0.01M). Reactions were stirred for 1 h at 0 °C.

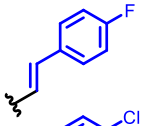
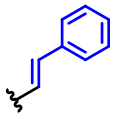
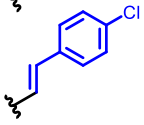
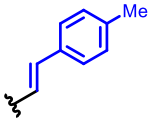
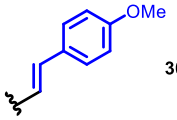
electron-deficient sulfonamide moiety enables better turnover of the Lewis acid catalyst (Table 2.3). When **25** was subjected to attenuated reaction conditions, metathesis product **26** was formed in 83% yield (entry 1, Table 2.3). However, when the reaction of **25** was conducted in the presence of 0.3 equiv. of *N*-tosyl amine **19**, **26** was formed in decreased yields of 76% (entry 2, Table 2.3). The yield is further reduced to 53% of **26** when equimolar amounts of both amines **19** and **25** are converted under the carbonyl-olefin metathesis conditions (Table 2.3, entry 3).

We next evaluated the effect of varying olefin substitution on the iron(III)-catalyzed carbonyl-olefin metathesis reaction (Table 2.4). Prenylated moieties proved to be superior and led to efficient formation of the desired metathesis products in up to 99% yield (entry 1, Table 2.4). Styrene derivatives **28-34** resulted in overall decreased yields of 3-pyrroline **26** (entries 2-6, Table 2.4). Importantly, *para*-methoxystyrene **30** failed to undergo carbonyl-olefin metathesis and resulted in complete dealkylation of the starting material.[19] While prenyl-derived alkenes undergo the desired transformation in an asynchronous, concerted fashion, the corresponding styrenyl-derivatives proceed via a distinct reaction pathway.[21] For these

Table 2.4 Evaluation of olefin substituents on the carbonyl-olefin reaction.



26 **27**

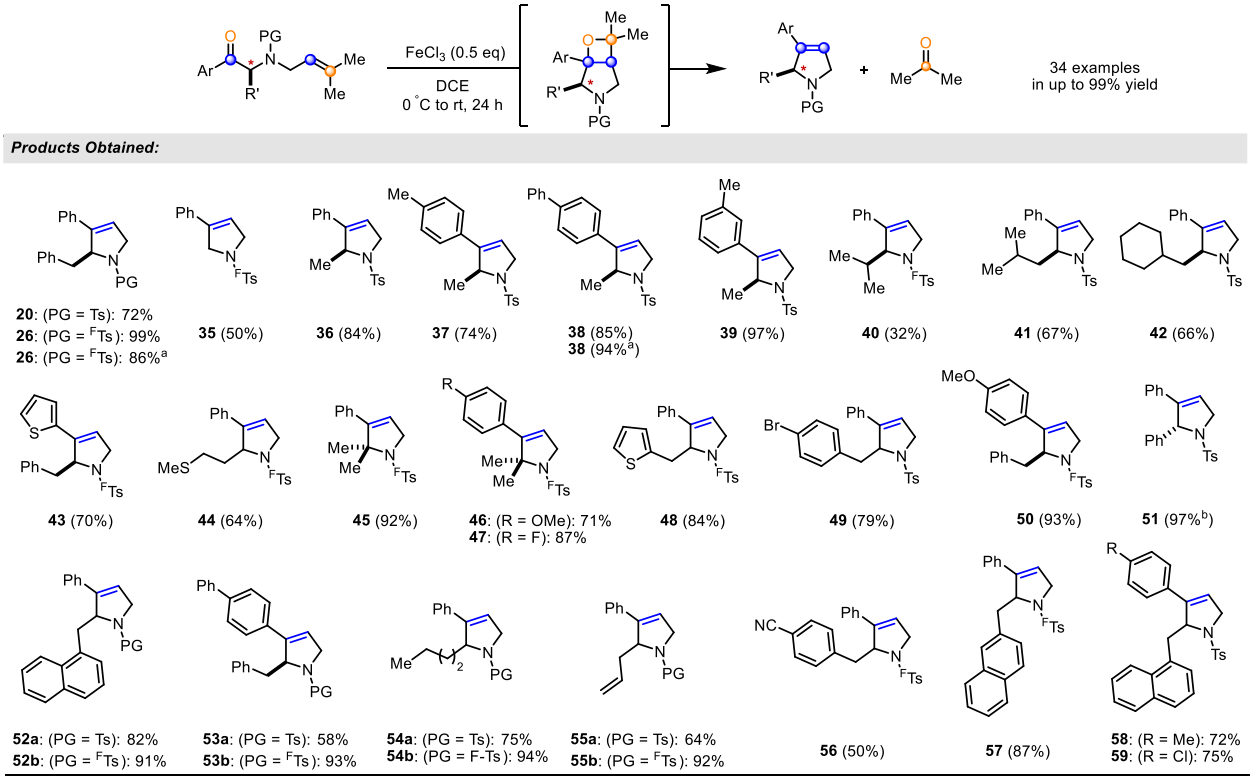
entry	substrate		yield (%)	entry	substrate		yield (%)
1		**19** **25**	72 95	5		**31**	49
2		**28**	39	6		**32**	34
3		**29**	58	7		**33**	0
4		**30**	0	8		**34**	0

Conditions: all reactions were performed using 0.1 mmol of substrate and $FeCl_3$ (50 mol%) in DCE [0.01 M]. The reactions were stirred at rt for 24 h.

substrates, oxetane fragmentation has been found to occur in a stepwise fashion via intermediate carbocations. This does explain the lower yields obtained for these substrates as a result of competing reaction paths (entries 2-6, Table 2.4). In comparison, no formation of the desired metathesis products was observed when crotyl alkene **33** or terminal alkene **34** were subjected to the optimized reaction conditions, which is consistent with previous reports.[16,19] These results support our previous findings which establish prenyl-derived alkenes as superior substrates for catalytic carbonyl-olefin metathesis.[21]

The optimized reaction conditions developed for the iron(III)-catalyzed carbonyl-olefin metathesis reaction proved efficient to access a wide range of commercially available, natural and unnatural amino acid-derived 3-pyrrolines (Table 2.5). Importantly, toluene

Table 2.5 Evaluation of substrate scope.

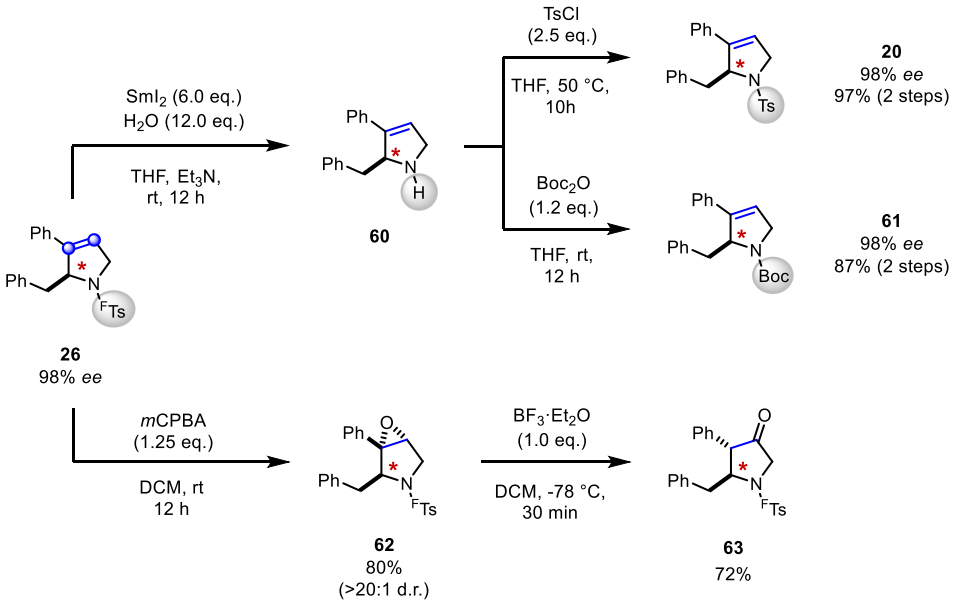


Conditions: reactions were performed using 0.20 mmol of substrate and $FeCl_3$ (0.5 eq) in DCE [0.01 M]. The reactions were stirred at 0 °C for 1 h and then warmed to rt.
[a]Reactions were run in toluene [0.0 1M] under otherwise identical conditions.[b]Reaction was run using 5.0 equiv of allylTMS as an additive.

was established as a viable alternative solvent (**26** and **38**, Table 2.5) resulting in up to 94% yield of the desired metathesis product. Substrates stemming from alanine resulted in the desired metathesis products in good to excellent yields (**36**-**39**, Table 3). Similarly, phenylalanine-derived starting materials proved efficient in the carbonyl-olefin metathesis reaction and resulted in the corresponding 3-pyrrolines in excellent yields (**20**, **26**, **50**, and **53**, Table 2.5).

Substrates incorporating heteroatoms were also compatible with the optimal reaction conditions for carbonyl-olefin metathesis. Methionine-derived 3-pyrroline **44** is obtained in 64% yield while the metathesis product **48** stemming from thienyl-alanine is obtained in 84% yield. This method is amendable to heteroaromatic ketones as well - the thienyl derivative **43** provided 70% of the desired product. Additional unnatural amino acid analogs of phenylalanine bearing naphthyl substituents provided the desired metathesis products in good to excellent yields of up to 91% (**52**, **57**, **58** and **59**, Table 2.5). It is interesting to note that glycine-derived 3-pyrroline **35** was formed in diminished yield of 50% while lower yields are also observed for the valine-derived substrate **40**. In comparison, the leucine-derived 3-pyrroline **41** is obtained in good yields of 67%. We suspect that a methylene-substituent in α-position to the nitrogen-heteroatom is beneficial for the formation of an intermediate oxetane whereas additional steric bulk at the β-positions leads to more sterically constrained oxetane intermediates and thus diminished yields of the desired products. Notably, aryl substitution in the α-position is well tolerated resulting in 97% yield (**51**) with addition of allytrimethylsilane. Furthermore, 2-amino isobutyric acid-derived 3-pyrrolines bearing a gem-dimethyl substituent in the α-position

Figure 2.5 Secondary modifications to chiral 3-pyrrolines.



are formed in excellent yields of up to 92% (**45**-**47**, Table 2.5). Further evaluation revealed that the carbonyl-olefin metathesis reaction is well tolerated by both electron deficient and electron-rich aryl ketone substrates (**37**-**39**, **46**-**47**, **49**, **50**, **56**, and **59**, Table 2.5). Additionally, the substrates bearing the electron-deficient sulfonamide protecting groups unanimously resulted in higher yields than their corresponding *N*-tosylated analogs, providing further support for our design principle for iron-catalyzed carbonyl-olefin metathesis reactions (**26**, **52**-**55** Table 2.5).

Finally, the resulting chiral 3-pyrroline building blocks can undergo facile subsequent modifications to result in valuable chiral building blocks (Figure 2.5). Cleavage of the protecting group is facile with SmI2 to generate the free amines **60** which could then be reprotected with TsCl to access **20** or the Boc-protected 3-pyrroline **61**.[22] Importantly, the reaction sequence proceeds with complete stereoretention (98% *ee*) and generates the desired products in up to 97% yield (over two steps). Furthermore, these

building blocks can be used to access epoxides **62** bearing three contiguous stereocenters, as well as pyrrolidin-3-ones **63** (Figure 2.5).

2.3 Conclusions

The development of a new strategy for the synthesis of chiral 3-pyrrolines is reported relying on the design principle of an iron(III)-catalyzed carbonyl-olefin metathesis reaction. Importantly, the carbonyl-olefin metathesis reaction described herein is operationally facile, relies on commercially available chiral pool reagents and proceeds under mild reaction conditions with complete stereoretention to result in the desired 3-pyrrolines in up to 98% *ee*. We expect that our strategy of attenuating the Lewis basicity of the sulfonamide to enable the desired mode of Lewis acid-activation for carbonyl-olefin metathesis can serve as a general strategy for other reactions in which sequestering of the active Lewis acid catalyst is observed.

2.4 Experimental Procedures

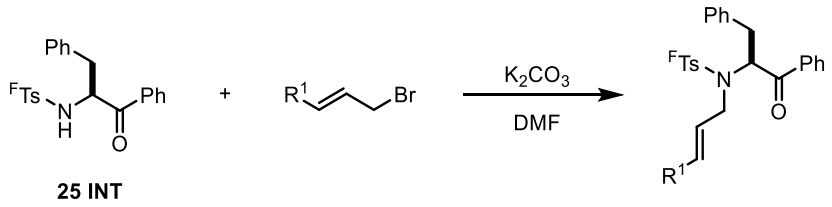
2.4.1 General Considerations

General Laboratory Procedures. All moisture-sensitive reactions were performed under an atmosphere of nitrogen in flame-dried round bottom flasks or glass vials fitted with rubber septa and/or septa equipped screw caps. Stainless steel syringes were used to transfer air or moisture sensitive liquids. Flash chromatography was performed using silica gel Silia Flash® 40-63 micron (230-400 mesh) from Silicycle.

Materials and Instrumentation. All chemicals were purchased from Sigma-Aldrich, VWR, Oakwood or Acros and were used as received unless otherwise stated. Tetrahydrofuran was dried by being passed through columns of activated alumina and distilled over sodium hydride and benzophenone. Triethylamine was distilled over calcium

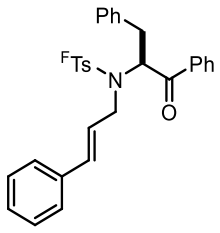
hydride, and water was degassed following the freeze-pump-thaw approach. Proton Nuclear Magnetic Resonance NMR (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Unity Plus 400, Varian MR400, Varian vnmrs 500, Varian Inova 500, Varian Mercury 500, and Varian vnmrs 700 spectrometers. Chemical shifts for protons are reported in parts per million and are references to the NMR solvent peak ($CDCl_3$: δ 7.26, C_6D_6: δ 7.16, DMSO-*d*$_6$: δ 2.50, or CD_2Cl_2: δ 5.32). Chemical shifts for carbons are reported in parts per million and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ77.16, C_6D_6: δ 128.06, DMSO-*d*$_6$: δ 39.52, or CD_2Cl_2: δ 53.84). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants in Hertz (Hz). Mass spectroscopic (MS) data was recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan in Ann Arbor, MI on an Agilent Q-TOF HPLC-MS with ESI high resolution mass spectrometer. Infrared (IR) spectra were obtained using either an Avatar 360 FT-IR or Perkin Elmer Spectrum BX FT-IR spectrometer. IR data are represented as frequency of absorption (cm^{-1}). High-performance liquid chromatography (HPLC) was performed on an Agilent 1260 series instrument with a binary pump and a variable wavelength detector with Chiralpak AD-H and Chiralpak IB columns (4.6 x 250 mm).

2.4.2 General Alkylation Procedure for the Synthesis of Styrenyl Olefin Substrates



25 INT

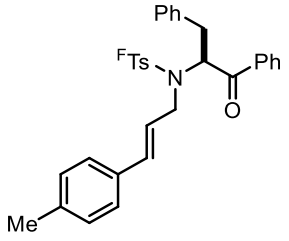
A round bottom flask equipped with a magnetic stir bar was charged with the secondary amine and sealed under a nitrogen atmosphere. Dry DMF (0.1 M) was added via syringe, and the reaction mixture was cooled to 0 ^{o}C. Potassium carbonate (2 eq) was added in one portion, and the reaction was allowed to stir at 0 ^{o}C for 30 minutes. The respective alkyl bromide (2 eq) was then added via one portion. The mixture was allowed to warm to room temperature over 16 hours, or until judged complete by TLC analysis. The reaction was quenched with deionized water, diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with deionized water (2x), brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate in 16-57% yield.



28

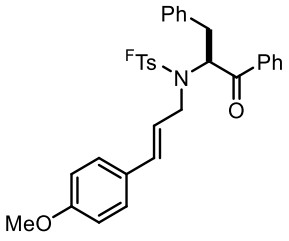
(*S*)-*N*-cinnamyl-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (28): Purification by flash column chromatography provided **28** as a white foam. **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 7.87 (d, *J* = 7.9 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.58 (t, *J* = 6.8 Hz, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.28 (dd, *J* = 14.7, 6.8 Hz, 8H), 7.16 (d, *J* = 7.2 Hz, 2H), 6.44 (d, *J* = 15.9 Hz, 1H), 5.92 – 5.77 (m, 2H), 4.27 – 4.12 (m, 2H), 3.48 (dd, *J* =

13.9, 8.1 Hz, 1H), 2.91 (dd, *J* = 14.0, 6.4 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.1, 144.0, 136.6, 136.1, 135.9, 134.72 – 133.90 (m), 133.9, 133.8, 129.5, 128.9, 128.7, 128.6, 128.1, 128.1, 127.1, 126.5, 126.13 – 126.03 (m), 125.1, 123.22 (q, *J* = 272.9 Hz), 60.9, 47.6, 35.7; **IR** (neat) 3122, 1686, 1596, 1580, 1496, 1448, 1404, 1320, 1233, 1160, 1131, 1108, 1095, 1061, 1014 cm^{-1}; **HRMS** calcd for $C_{31}H_{26}F_3NO_3S^{+NH4}$: 567.1924, found: 567.1917.



29

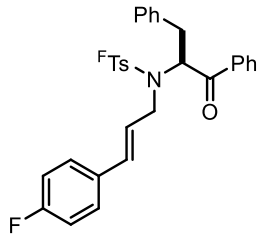
(*S*,*E*)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-*N*-(3-(p-tolyl)allyl)-4-(trifluoromethyl)benzenesulfonamide (29): Purification by flash column chromatography provided **29** as a colorless solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.53 (dd, *J* = 14.3, 7.9 Hz, 3H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.18 (m, 5H), 7.04 (dd, *J* = 25.9, 8.1 Hz, 4H), 6.38 (d, *J* = 15.9 Hz, 1H), 5.88 (dd, *J* = 8.3, 6.2 Hz, 1H), 5.72 (dt, *J* = 15.8, 6.8 Hz, 1H), 4.16 (qd, *J* = 17.1, 7.3 Hz, 2H), 3.47 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.91 (dd, *J* = 13.9, 6.1 Hz, 1H), 2.33 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.0, 144.0, 137.9, 136.7, 135.9, 134.1 (dd, *J* = 66.1, 33.1 Hz), 133.8, 133.7, 133.3, 129.5, 129.2, 128.80, 128.79, 128.7, 128.1, 126.4, 126.0 (q, *J* = 3.6 Hz), 124.3 (q, *J* = 272.8 Hz), 123.9, 61.0, 47.6, 35.6, 21.3; **IR** (neat) 2920, 2852, 1683, 1596, 1512, 1496, 1448, 1404, 1321, 1262, 1236, 1162, 1128, 1108, 1096, 1061, 1014 cm^{-1}; **HRMS** calcd for $C_{32}H_{28}F_3NO_3S^{+Na}$: 586.1634, found: 586.1625.



30

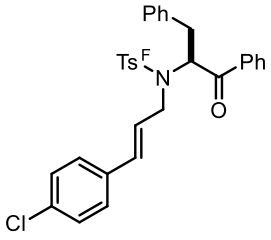
(*S*,*E*)-*N*-(3-(4-methoxyphenyl)allyl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (30): Purification by flash column chromatography provided **30** as a colorless solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 – 7.82 (m, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.55 (dd, *J* = 12.4, 7.9 Hz, 3H), 7.38 (dd, *J* = 17.5, 9.9 Hz, 2H), 7.30 – 7.17 (m, 5H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.37 (d, *J* = 15.9 Hz, 1H), 5.90 (dd, *J* = 8.2, 6.2 Hz, 1H), 5.64 (dt, *J* = 15.8, 6.7 Hz, 1H), 4.16 (qd, *J* = 16.0, 6.7 Hz, 2H), 3.83 (s, 3H), 3.50 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.93 (dd, *J* = 13.9, 6.1 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.1, 159.6, 144.1, 136.8, 136.0, 134.2 (q, *J* = 33.0 Hz), 133.7,

133.6, 129.5, 128.94, 128.87, 128.86, 128.8, 128.1, 127.8, 127.1, 126.1 (q, *J* = 3.4 Hz), 123.3 (q, *J* = 273.0 Hz), 122.6, 114.0, 61.0, 55.4, 47.8, 35.7; **IR** (neat) 2931, 1734, 1683, 1606, 1579, 1511, 1448, 1404, 1347, 1321, 1247, 1160, 1130, 1107, 1094, 1061, 1032, 1014 cm^{-1}; **HRMS** calcd for $C_{32}H_{28}F_3NO_4S^{+NH4}$: 597.2029, found: 597.2020.



31

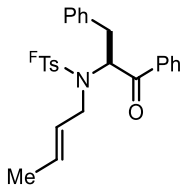
(*S*,*E*)-*N*-(3-(4-fluorophenyl)allyl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoro-methyl)benzenesulfonamide (31): Purification by flash column chromatography provided **31** as a colorless solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 3H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.30 – 7.22 (m, 5H), 7.10 (dd, *J* = 7.8, 5.7 Hz, 2H), 6.98 (t, *J* = 8.4 Hz, 2H), 6.39 (d, *J* = 15.9 Hz, 1H), 5.97 – 5.92 (m, 1H), 5.79 – 5.71 (m, 1H), 4.27 – 4.10 (m, 2H), 3.50 (dd, *J* = 13.9, 8.4 Hz, 1H), 2.91 (dt, *J* = 18.6, 9.3 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.0, 162.6 (d, *J* = 247.5 Hz), 143.9, 136.6, 135.8, 134.3 (t, *J* = 49.6 Hz), 133.8, 132.6, 132.3 (d, *J* = 3.3 Hz), 129.4, 128.9, 128.7, 128.08, 128.07, 128.02, 127.1, 126.1 (q, *J* = 3.5 Hz), 124.8 (d, *J* = 2.1 Hz), 123.2 (q, *J* = 273.0 Hz), 115.6 (d, *J* = 21.7 Hz), 60.8, 47.4, 35.6; **IR** (neat) 2924, 1682, 1602, 1546, 1508, 1446, 1404, 1320, 1282, 1231, 1181, 1155, 1120, 1109, 1091, 1060, 1013 cm^{-1}; **HRMS** calcd for $C_{31}H_{25}F_4NO_3S^{+NH4}$: 585.1830, found: 585.1824.



32

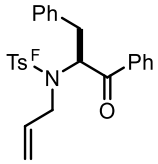
(*S*,*E*)-*N*-(3-(4-chlorophenyl)allyl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoro-methyl)benzenesulfon-amide (32): Purification by flash column chromatography provided **31** as a yellow oil. **^{1}H NMR** (500 MHz, CD_2Cl_2) δ 7.85 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.19 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.37 (d, *J* = 15.9 Hz, 1H), 5.87 (t, *J* = 7.3 Hz, 1H), 5.81 (dt, *J* = 15.7, 6.5 Hz, 1H), 4.17 (qd, *J* = 16.4, 6.5 Hz, 1H), 3.44 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.86 (dd, *J* = 14.1, 6.6 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.9, 143.8, 136.5, 135.7, 134.6, 134.2 (q, *J* = 33.1 Hz), 133.8, 133.6, 132.4, 128.9, 128.8, 128.73, 128.66, 126.1 (q, *J* = 3.5 Hz), 125.9, 123.2 (q, *J* = 273.0 Hz), 60.7, 47.3, 35.5; **IR** (neat) 3060.8, 1686.2, 1595.9, 1581.3,

1490.6, 1447.9, 1403.8, 1344.6, 1320.8, 1263.5, 1233.0, 1161.8, 1132.1, 1091.9, 1107.5, 11061.7, 1013.3 cm^{-1}; **HRMS** calcd for $C_{31}H_{25}ClF_3NO_3S^{+NH4}$: 601.1534, found: 601.1532.



33

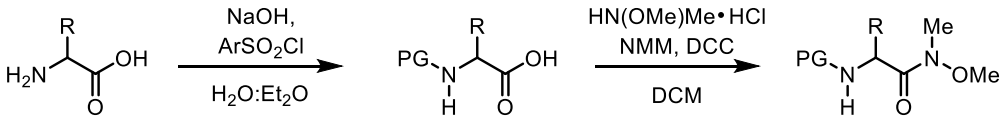
(*S*,*E*)-*N*-(but-2-en-1-yl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (33): Purification by flash column chromatography provided **33** as a colorless solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 – 7.81 (m, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.55 (dd, *J* = 11.8, 4.3 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.15 (m, 5H), 5.79 (dd, *J* = 8.7, 5.6 Hz, 1H), 5.55 (dq, *J* = 13.1, 6.5 Hz, 1H), 5.17 (dtd, *J* = 15.2, 6.6, 1.6 Hz, 1H), 3.92 (qd, *J* = 16.0, 6.7 Hz, 2H), 3.44 (ddd, *J* = 13.9, 8.7, 5.3 Hz, 1H), 2.84 (dd, *J* = 13.8, 5.5 Hz, 1H), 1.53 (dd, *J* = 6.5, 1.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.8, 144.0, 136.9, 136.0, 134.2 (q, *J* = 33.0 Hz), 133.7, 130.6, 129.4, 128.80, 128.78, 128.7, 128.1, 127.0, 126.6, 126.0 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 272.9 Hz), 60.9, 47.5, 35.5, 17.7; **IR** (neat) 3064, 2936, 2922, 2856, 1687, 1597, 1582, 1496, 1448, 1404, 1345, 1320, 1233, 1161, 1129, 1107, 1091, 1061, 1014; **HRMS** calcd for $C_{26}H_{24}F_3NO_3S^+$: 488.1502, found: 488.1497.



34

(*S*)-*N*-allyl-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (34): Purification by flash column chromatography provided **21b** as a colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.8 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.25 – 7.17 (m, 5H), 5.80 (dd, *J* = 8.7, 5.8 Hz, 1H), 5.64 (ddt, *J* = 16.6, 10.2, 6.3 Hz, 1H), 5.17 (d, *J* = 17.2 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 4.03 (qd, *J* = 16.4, 6.3 Hz, 2H), 3.42 (dd, *J* = 13.8, 8.8 Hz, 1H), 2.86 (dd, *J* = 13.8, 5.7 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.9, 143.7, 136.6, 136.0, 134.4 (q, *J* = 33.1 Hz), 134.4, 133.8 , 129.4, 128.87, 128.87, 128.7, 128.1, 127.1, 126.1 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 273.1 Hz), 118.6, 60.8, 48.0, 35.7; **IR** (neat) 3065, 3029, 1687, 1597, 1582, 1496, 1448, 1404, 1349, 1320, 1233, 1162, 1129, 1107, 1091, 1061, 1030, 1014; **HRMS** calcd for $C_{25}H_{22}F_3NO_3S^+$: 488.1502, found: 488.1497.

2.4.3 General Weinreb Amidation Procedure for *N*-protected Amino Acids[23, 24]

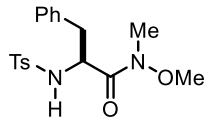


WA

A round bottom flask equipped with a magnetic stir bar was charged with the appropriate amino acid. Deionized water (0.4 M) was then added, followed by NaOH (2.5 eq), and the mixture was stirred until all solid was fully dissolved. To the resulting mixture was added a solution of the aryl sulfonyl chloride (1.2 eq) in diethyl ether (0.4 M). The reaction was allowed to stir for 12 hours, or until judged complete by TLC analysis. Aqueous hydrochloric acid (1 M) was added until the the reaction mixture had a pH = 1, and the layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The combined organic layers were washed with brine (1x), dried over anyhydrous Na_2SO_4, and concentrated under reduced pressure to give the desired protected amino acid, which was carried forward without purification.

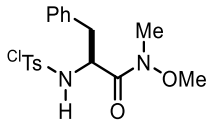
A round bottom flask equipped with a magnetic stir bar was charged with the protected amino acid and *N,O*-dimethylhydroxylamine hydrochloride (1.1 eq). The flask was sealed under a nitrogen atmosphere, and dry DCM (0.3 M) and NMM (1.4 eq) were subsequently added via syringe. The stirring mixture was cooled to 0 ^{o}C, and DCC (1.1 eq) was added in one portion. The reaction was allowed to warm to room temperature over 12 hours, or until judged complete by TLC analysis. The reaction was then filtered over a pad of celite, eluted with multiple DCM washes, and the combined organic eluent was washed with saturated aqueous $NaHCO_3$ (2x). The organic layer was washed with

brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography eluting with EtOAc/hexanes (1:1) provided the desired Weinreb amide in 45-76% yield.



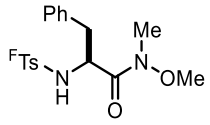
19 WA

(*S*)-*N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (19 WA): Purifi-cation by flash column chromatography provided **19 WA** as a faint white oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.20 (dd, *J* = 12.1, 7.4 Hz, 5H), 7.11 – 7.06 (m, 2H), 5.40 (d, *J* = 9.8 Hz, 1H), 4.53 (dd, *J* = 16.1, 6.9 Hz, 1H), 3.43 (s, 3H), 3.00 – 2.91 (m, 4H), 2.83 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.38 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.1, 143.2, 136.9, 135.8, 129.5, 129.4, 128.4, 127.2, 126.9, 61.2, 54.1, 39.7, 32.0, 21.5.



23 WA

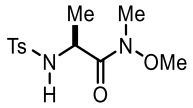
(*S*)-2-((4-chlorophenyl)sulfonamido)-*N*-methoxy-*N*-methyl-3-phenylpropanamide (23 WA): Purification by flash column chromatography provided **23 WA** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, 2H), 7.32 – 7.29 (m, 2H), 7.20 – 7.18 (m, 3H), 7.09 – 7.05 (m, 2H), 5.88 (d, *J* = 19.6 Hz, 1H), 4.53 (dd, *J* = 14.8, 8.4 Hz, 1H), 3.38 (s, 3H), 3.01 (s, 3H), 2.98 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.80 (dd, *J* = 13.5, 8.0); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.1, 138.8, 138.6, 135.9, 129.5, 129.0, 128.5, 128.4, 126.9, 61.4, 54.4, 39.4, 32.0, 14.2.



25 WA

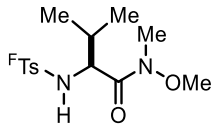
(*S*)-*N*-methoxy-*N*-methyl-3-phenyl-2-((4-(trifluoromethyl)phenyl)sulfonamido)pro-penamide (25 WA): Purification by flash column chromatography provided **25 WA** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.21 – 7.15 (m, 3H), 7.09 – 7.02 (m, 2H), 5.51 (d, *J* = 10.0 Hz, 1H), 4.55 (dd, *J* = 14.5, 8.7 Hz, 1H), 3.53 (s, 3H), 3.06 – 2.96 (m, 4H), 2.78 (dd, *J* = 13.6, 8.3 Hz, 1H); **^{13}C**

NMR (176 MHz, $CDCl_3$) δ 171.1, 143.6, 135.9, 134.1 (q, *J* = 32.7 Hz), 129.6, 128.6, 127.7, 127.3, 126.0 (q, *J* = 3.6 Hz), 123.4 (q, *J* = 272.7 Hz), 61.6, 54.8, 39.6, 32.2.



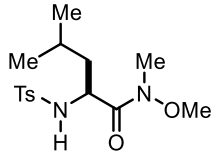
36 WA

(*S*)-*N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)propenamide (36 WA): Purification by flash column chromatography provided **36 WA** as a clear oil that slowly solidified to give a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.2 Hz, 2H), 5.50 (d, J = 9.1 Hz, 1H), 4.41 – 4.23 (m, 1H), 3.55 (s, 3H), 2.98 (s, 3H), 2.40 (s, 3H), 1.28 (d, J = 13.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.3, 143.4, 137.1, 129.5, 127.2, 61.4, 48.8, 32.1, 21.5, 19.9.



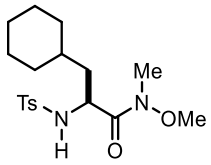
40 WA

(*S*)-*N*-methoxy-*N*-3-dimethyl-2-((4-(trifluoromethyl)phenyl)sulfonamido)butan-amide (40 WA): Purifi-cation by flash column chromatography provided **40 WA** as a clear oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 6.05 (d, *J* = 10.1 Hz, 1H), 4.09 (dd, *J* = 10.3, 5.1 Hz, 1H), 3.48 (s, 3H), 2.86 (s, 3H), 1.94 – 1.83 (m, 1H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.2, 143.8, 134.1 (q, *J* = 33.0 Hz), 128.0, 125.9 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.8 Hz), 61.2, 57.9, 31.8, 31.2, 19.5, 16.8.



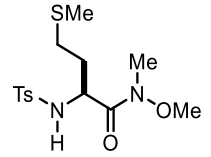
41 WA

(*S*)-*N*-methoxy-*N*,4-dimethyl-2-((4-methylphenyl)sulfonamido)pentanamide (41 WA): Purification by flash column chromatography provided **41 WA** as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.4 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 5.42 (d, *J* = 10.1 Hz, 1H), 4.25 (td, *J* = 10.5, 3.1 Hz, 1H), 3.54 (s, 3H), 2.90 (s, 3H), 2.38 (s, 3H), 1.40 (td, *J* = 12.0, 10.4, 3.7 Hz, 1H), 1.33 – 1.22 (m, 2H), 0.88 (d, *J* = 3.9 Hz, 3H), 0.87 (d, *J* = 3.6 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 172.6, 143.5, 136.9, 129.5, 127.5, 61.4, 51.6, 42.5, 32.2, 24.2, 23.4, 21.6, 21.0.



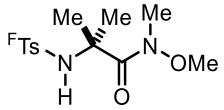
42 WA

(*S*)-3-cyclohexyl-*N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)propenamide (42 WA): Purification by flash column chromatography provided **42 WA** as a white foam. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.52 (d, *J* = 10.1 Hz, 1H), 4.25 (td, *J* = 10.2, 3.6 Hz, 1H), 3.52 (s, 3H), 2.88 (s, 3H), 2.34 (s, 3H), 1.69 (d, *J* = 12.7 Hz, 1H), 1.63 – 1.41 (m, 5H), 1.29 (ddq, *J* = 19.4, 10.0, 5.4, 4.7 Hz, 2H), 1.18 – 0.98 (m, 3H), 0.84 (qd, *J* = 12.5, 3.4 Hz, 1H), 0.76 – 0.67 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.9, 143.5, 137.0, 129.5, 127.6, 61.4, 50.8, 41.1, 34.1, 33.4, 32.3, 31.8, 26.6, 26.3, 26.0, 21.6.



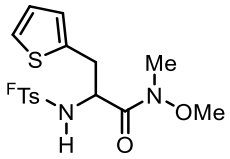
44 WA

***N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)-4-(methylthio)butanamide (44 WA):** Purification by flash column chromatography provided **44 WA** as a white foam. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 6.7 Hz, 2H), 5.52 (d, *J* = 9.4 Hz, 1H), 4.39 (t, *J* = 8.3 Hz, 1H), 3.54 (s, 3H), 2.98 (s, 3H), 2.64 (ddd, *J* = 12.7, 7.3, 5.0 Hz, 1H), 2.60 – 2.53 (m, 1H), 2.41 (s, 3H), 2.06 (s, 3H), 1.91 – 1.83 (m, 1H), 1.77 – 1.67 (m, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.6, 143.7, 136.8, 129.6, 127.6, 61.6, 52.1, 32.7, 32.4, 30.1, 21.7, 15.4.



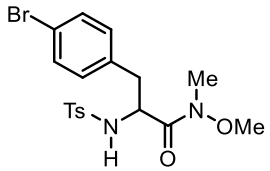
45 WA

***N*-methoxy-*N*,2-dimethyl-2-((4-(trifluoromethyl)phenyl)sulfonamido)propenamide (45 WA):** Purification by flash column chromatography provided **45 WA** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 6.05 (s, 1H), 3.74 (s, 3H), 3.13 (s, 3H), 1.50 (s, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 173.0, 146.4, 134.1 (q, *J* = 33.1 Hz), 127.7, 126.2 (q, *J* = 3.6 Hz), 123.4 (q, *J* = 272.9 Hz), 61.2, 60.3, 33.9, 25.3.



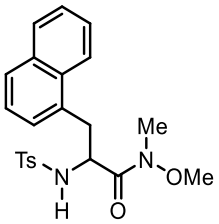
48 WA

***N*-methoxy-*N*-methyl-3-(thiophen-2-yl)-2-((4-(trifluoromethyl)phenyl)sulfonamido)-propenamide (48 WA):** Purification by flash column chromatography provided **48 WA** as a pale yellow foam. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.09 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.83 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.75 (d, *J* = 3.4 Hz, 1H), 5.88 (d, *J* = 9.8 Hz, 1H), 4.55 (ddd, *J* = 9.9, 7.6, 5.0 Hz, 1H), 3.57 (s, 3H), 3.20 (dd, *J* = 14.8, 5.1 Hz, 1H), 3.08 (dd, *J* = 14.8, 7.6 Hz, 1H), 3.02 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.5, 143.9, 137.6, 134. 1 (q, *J* = 33.0 Hz), 127.7, 127.10, 127.08, 126.0 (q, *J* = 3.9 Hz), 125.0, 123.3 (q, *J* = 273.6 Hz), 61.63, 54.81, 33.42, 32.17.



49 WA

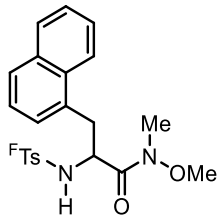
3-(4-bromophenyl)-*N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)propen-amide (49 WA): Purification by flash column chromatography provided **49 WA** as a white foam. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 5.43 (d, *J* = 9.3 Hz, 1H), 4.44 (dq, *J* = 8.9, 5.2 Hz, 1H), 3.56 (s, 3H), 3.03 (s, 3H), 2.91 (dd, *J* = 13.7, 5.2 Hz, 1H), 2.72 (dd, *J* = 13.8, 8.1 Hz, 1H), 2.41 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.9, 143.5, 136.7, 134.9, 131.4, 131.2, 129.4, 127.1, 121.0, 61.4, 54.1, 38.9, 32.1, 21.6.



52a WA

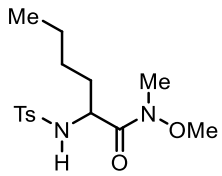
***N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)-3-(naphthalen-1-yl)propen-amide (52a WA):** Purification by flash column chromatography provided **52a WA** as a white foam. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 9.2 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.44 (p, *J* = 6.9 Hz, 2H), 7.31 (dd, *J* = 17.5, 8.1 Hz, 3H), 7.22 (d, *J* = 6.9 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 2H), 5.48 (d, *J* = 9.9 Hz, 1H), 4.71 – 4.62 (m, 1H), 3.42 (dd, *J* = 13.9, 6.0 Hz, 1H), 3.34 (s, 3H), 3.21 (dd, *J* = 13.8, 8.4 Hz, 1H), 3.01 (s, 3H), 2.29 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.3, 143.0, 136.8, 133.6, 133.3, 132.4,

129.1, 128.2, 127.9, 127.6, 127.52, 127.49, 126.9, 125.9, 125.6, 61.5, 54.4, 39.5, 32.1, 21.4.



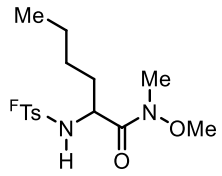
52b WA

***N*-methoxy-*N*-methyl-3-(naphthalen-1-yl)-2-((4-(trifluoromethyl)phenyl)sulfonamido)propenamide (52b WA):** Purification by flash column chromatography provided **52b WA** as a white foam. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.46 (dt, *J* = 18.8, 7.1 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.29 – 7.17 (m, 4H), 6.03 (d, *J* = 10.0 Hz, 1H), 4.75 (td, *J* = 10.0, 4.7 Hz, 1H), 3.62 (s, 3H), 3.51 (dd, *J* = 14.2, 4.8 Hz, 1H), 3.18 (s, 3H), 3.13 (dd, *J* = 14.1, 10.0 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.5, 143.1, 133.7, 133.5 (q, *J* = 37.2 Hz), 132.0, 131.7, 129.1, 128.7, 128.1, 126.9, 126.3, 125.7, 125.5 (q, *J* = 3.5 Hz), 125.4, 123.4 (q, *J* = 272.8 Hz), 122.9, 61.7, 54.0, 36.5, 32.3.



54a WA

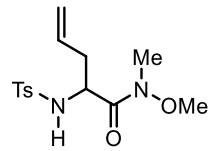
***N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)hexanamide (54a WA):** Purification by flash column chromatography provided **54a WA** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.52 (d, *J* = 9.8 Hz, 1H), 4.19 (td, *J* = 9.3, 4.0 Hz, 1H), 3.51 (s, 3H), 2.93 (s, 3H), 2.37 (s, 3H), 1.62 – 1.41 (m, 2H), 1.41 – 1.15 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.1, 143.4, 137.0, 129.4, 127.4, 61.3, 52.9, 33.1, 32.1, 27.2, 22.1, 21.5, 13.8.



54b WA

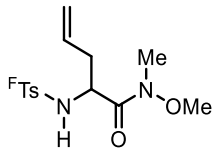
***N*-methoxy-*N*-methyl-2-((4-(trifluoromethyl)phenyl)sulfonamido)hexanamide (54b WA):** Purification by flash column chromatography provided **54b WA** as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H), 5.61 (d, *J* =

9.0 Hz, 1H), 4.27 (td, *J* = 9.3, 3.8 Hz, 1H), 3.57 (s, 3H), 2.92 (s, 3H), 1.65 – 1.58 (m, 1H), 1.53 – 1.46 (m, 1H), 1.44 – 1.36 (m, 1H), 1.36 – 1.27 (m, 2H), 1.27 – 1.20 (m, 1H), 0.85 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.9, 143.8, 134.3 (q, *J* = 33.0 Hz), 127.9, 126.0 (dd, *J* = 6.9, 3.3 Hz), 123.3 (q, *J* = 272.8 Hz), 61.5, 53.1, 33.0, 32.1, 27.3, 22.0, 13.8.



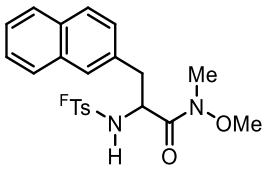
55a WA

***N*-methoxy-*N*-methyl-2-((4-methylphenyl)sulfonamido)pent-4-enamide (55a WA):** Purification by flash column chromatography provided **55a WA** as a white foam. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 5.70 (ddd, *J* = 23.6, 10.7, 7.2 Hz, 1H), 5.42 (d, *J* = 9.4 Hz, 1H), 5.10 (s, 1H), 5.06 (d, *J* = 8.0 Hz, 1H), 4.40 – 4.29 (m, 1H), 3.56 (s, 3H), 2.98 (s, 3H), 2.41 (s, 3H), 2.38 – 2.27 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.0, 143.4, 137.0, 132.1, 129.5, 127.3, 118.9, 61.4, 52.6, 37.8, 32.1, 21.5.



55b WA

***N*-methoxy-*N*-methyl-2-((4-(trifluoromethyl)phenyl)sulfonamido)pent-4-enamide (55b WA):** Purification by flash column chromatography **55b WA** as a pale yellow foam. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 5.68 (ddd, *J* = 24.2, 10.7, 7.2 Hz, 1H), 5.54 (d, *J* = 9.7 Hz, 1H), 5.14 – 5.05 (m, 2H), 4.41 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.60 (s, 3H), 2.96 (s, 3H), 2.46 – 2.30 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.7, 143.7, 134.3 (q, *J* = 33.0 Hz), 131.8, 127.8, 126.0 (q, *J* = 3.6 Hz), 123.2 (q, *J* = 272.9 Hz), 119.2, 61.5, 52.7, 37.6, 32.0.



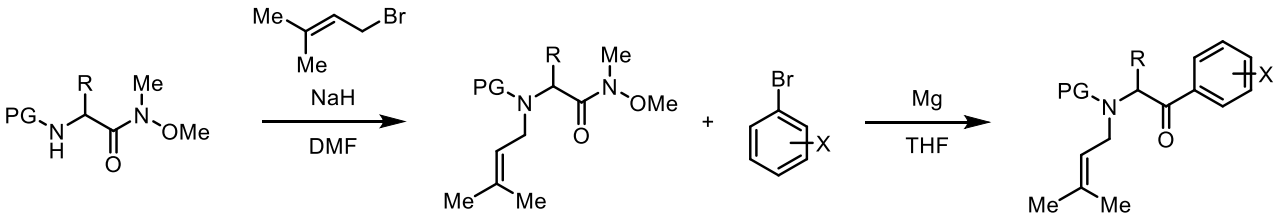
57 WA

***N*-methoxy-*N*-methyl-3-(naphthalen-2-yl)-2-((4-(trifluoromethyl)phenyl)sulfonamido)propenamide (57 WA):** Purification by flash column chromatography provided **57 WA** as a white foam. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 6.1, 3.4 Hz, 1H), 7.68 (dd, *J* = 6.2, 3.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.50 (s, 1H),

7.45 (dd, *J* = 6.3, 3.2 Hz, 2H), 7.25 (d, *J* = 5.0 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 1H), 5.94 (d, *J* = 9.9 Hz, 1H), 4.65 (td, *J* = 9.4, 4.8 Hz, 1H), 3.62 (s, 3H), 3.16 (dd, *J* = 13.6, 4.8 Hz, 1H), 3.09 (s, 3H), 2.90 (dd, *J* = 13.7, 9.0 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.3, 143.6, 133.7 (q, *J* = 32.8 Hz), 133.5, 133.4, 132.5, 128.5, 128.3, 127.7, 127.5, 127.4, 127.2, 126.4, 126.0, 125.5 (q, *J* = 3.8 Hz), 123.1 (q, *J* = 273.4 Hz), 61.7, 55.0, 39.6, 32.3.

2.4.4 General Procedures for the Synthesis of Metathesis Substrates

(a) General Procedure A: *N*-Alkylation of Weinreb Amide followed by Grignard Reaction[24]

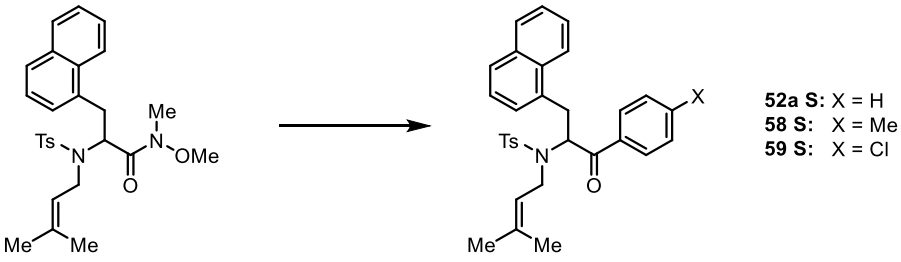


WA **INT** **S**

A round bottom flask equipped with a magnetic stir bar was charged with Weinreb amide **WA** and sealed under a nitrogen atmosphere. Dry DMF (0.1 M) was added via syringe, and the reaction mixture was cooled to 0 °C. Sodium hydride (2 eq, 60% dispersion in mineral oil) was added in one portion, and the reaction was allowed to stir at 0 °C for 30 minutes before prenyl bromide (1.2 eq) was added via syringe. The mixture was allowed to warm to room temperature over 3 hours, or until judged complete by TLC analysis. The reaction was quenched with deionized water, diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with an aqueous 5% LiCl solution (3x), brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **INT** in 63-99% yield.

A round bottom flask equipped with a magnetic stir bar was charged with acid-washed magnesium turnings (3 eq) and sealed under a nitrogen atmosphere. Dry THF

(0.2 M) was added via syringe, followed by the desired aryl bromide (3 eq). The solution was allowed to stir (heating as necessary) until all magnesium turnings had dissolved, and was then cooled to 0 °C. To the mixture was added intermediate **INT** suspended in dry THF (0.2 M) dropwise via cannula. The reaction was allowed to warm to room temperature over 12 hours, or until judged complete by TLC analysis, at which point it was quenched with a saturated ammonium chloride solution. The reaction mixture was diluted with EtOAc, the layers were partitioned, and the organic layer was collected. The aqueous phase was extracted with EtOAc (3x), and the combined organic layers were washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired substrate **S** in 71-86% yield.



52a INT

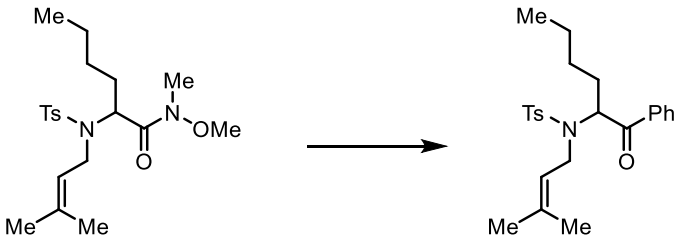
***N*-methoxy-*N*-methyl-2-((4-methyl-*N*-(3-methylbut-2-en-1-yl)phenyl)sulfonamido)-3-(naphthalen-1-yl)propenamide (52a INT):** Purification by flash column chromatography provided **52a INT** as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.71 (dd, *J* = 6.7, 2.8 Hz, 1H), 7.60 (d, *J* = 7.9 Hz, 2H), 7.56 – 7.51 (m, 1H), 7.50 – 7.45 (m, 1H), 7.36 – 7.31 (m, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 5.55 (dd, *J* = 10.3, 5.4 Hz, 1H), 5.20 (t, *J* = 6.4 Hz, 1H), 4.52 (dd, *J* = 16.8, 7.6 Hz, 1H), 4.14 (dd, *J* = 16.6, 7.8 Hz, 1H), 3.58 (dd, *J* = 13.6, 10.1 Hz, 1H), 3.50 (dd, *J* = 13.6, 5.3 Hz, 1H), 2.85 (s, 6H), 2.37 (s, 3H), 1.72 (s, 3H), 1.60 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.0, 143.0, 137.9, 133.8, 132.6, 132.2, 129.3, 128.8, 128.0, 127.7, 127.45, 127.45, 126.4, 125.7, 125.4, 123.7, 123.0, 61.0, 54.0, 43.1, 34.9, 31.7, 25.8, 21.6, 18.0.

(*S*)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(3-(naphthalen-1-yl)-1-oxo-1-phenylpropan-2-yl)benzene-sulfonamide (52a S): Bromobenzene was employed to synthesize substrate **52a S**. Purification by flash column chromatography provided **42a S** as a pale

yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.65 (dd, *J* = 8.0, 1.9 Hz, 3H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.34 (d, *J* = 7.0 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.01 (dd, *J* = 9.8, 4.5 Hz, 1H), 4.94 (t, *J* = 6.9 Hz, 1H), 4.14 (dd, *J* = 16.4, 7.1 Hz, 1H), 3.99 (dd, *J* = 16.3, 6.4 Hz, 1H), 3.84 (dd, *J* = 14.0, 9.9 Hz, 1H), 3.47 (dd, *J* = 14.0, 4.5 Hz, 1H), 2.33 (s, 3H), 1.61 (s, 3H), 1.51 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.4, 143.4, 137.4, 136.4, 135.3, 133.9, 133.1, 132.8, 132.0, 129.5, 129.0, 128.5, 128.4, 128.1, 127.6, 127.6, 126.4, 125.7, 125.4, 123.6, 121.5, 58.6, 43.2, 32.8, 25.7, 21.5, 17.9; **IR** (neat) 2918, 1686, 1596, 1448, 1339, 1233, 1155, 1091, 1013, 942, 904, 799, 778, 758, 694, 660 cm^{-1}; **HRMS** calcd for $C_{31}H_{31}NO_3S^+$: 498.2097, found: 498.2091.

4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(3-(naphthalen-1-yl)-1-oxo-1-(p-tolyl)propan-2-yl)benzene-sulfonamide (58 S): 4-bromotoluene was employed to synthesize substrate **58 S**. Purification by flash column chromatography provided **46 S** as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.61 – 7.46 (m, 6H), 7.34 (d, *J* = 6.7 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.07 (dd, *J* = 15.9, 8.0 Hz, 4H), 6.00 (dd, *J* = 9.8, 4.6 Hz, 1H), 4.99 – 4.92 (m, 1H), 4.16 (dd, *J* = 16.4, 7.1 Hz, 1H), 4.00 (dd, *J* = 16.4, 6.3 Hz, 1H), 3.82 (dd, *J* = 14.0, 9.8 Hz, 1H), 3.45 (dd, *J* = 14.0, 4.6 Hz, 1H), 2.34 (s, 3H), 2.32 (s, 3H), 1.62 (s, 3H), 1.51 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.9, 144.1, 143.4, 137.4, 135.1, 133.9, 133.8, 132.9, 132.0, 129.5, 129.2, 129.0, 128.7, 128.0, 127.6, 127.5, 126.4, 125.7, 125.5, 123.7, 121.7, 58.3, 43.1, 32.8, 25.7, 21.7, 21.6, 17.9; **IR** (neat) 2925, 1679, 1605, 1442, 1408, 1378, 1335, 1234, 1206, 1184, 1153, 1090, 1018, 940, 907, 793, 774, 730, 672, 657 cm^{-1}; **HRMS** calcd for $C_{32}H_{33}NO_3S^+$: 512.2254, found: 512.2246

***N*-(1-(4-chlorophenyl)-3-(naphthalen-1-yl)-1-oxopropan-2-yl)-4-methyl-*N*-(3-methyl-but-2-en-1-yl)benzenesulfonamide (59 S):** 4-chlorobromobenzene was employed to synthesize substrate **59 S**. Purification by flash column chromatography provided **59 S** as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.61 – 7.47 (m, 6H), 7.31 – 7.24 (m, 2H), 7.21 – 7.18 (m, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 5.91 (dd, *J* = 10.1, 4.3 Hz, 1H), 4.99 – 4.92 (m, 1H), 4.14 (dd, *J* = 16.3, 7.0 Hz, 1H), 4.00 (dd, *J* = 16.3, 6.7 Hz, 1H), 3.82 (dd, *J* = 13.9, 10.1 Hz, 1H), 3.43 (dd, *J* = 13.9, 4.3 Hz, 1H), 2.35 (s, 3H), 1.62 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.3, 143.7, 139.6, 137.3, 135.7, 134.7, 134.0, 132.7, 132.0, 129.9, 129.6, 129.1, 128.7, 128.1, 127.7, 127.6, 126.5, 125.8, 125.5, 123.6, 121.4, 58.6, 43.2, 32.6, 25.8, 21.6, 17.9; **IR** (neat) 2922, 1688, 1588, 1441, 1400, 1339, 1231, 1156, 1091, 1013, 940, 910, 796, 777, 729, 661 cm^{-1}; **HRMS** calcd for $C_{31}H_{30}ClNO_3S^+$: 532.1708, found: 532.1709.

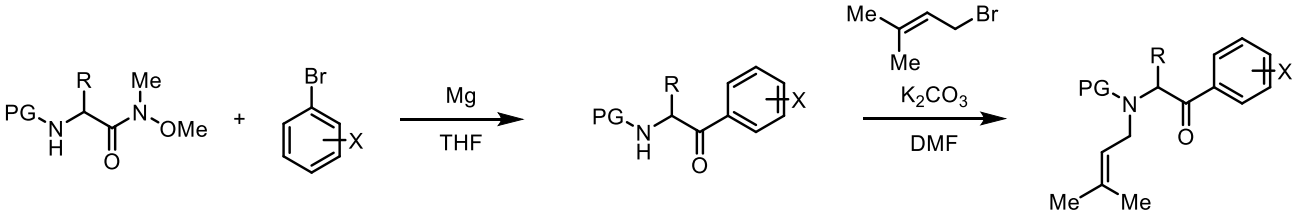


52a INT **52a S**

***N*-methoxy-*N*-methyl-2-((4-methyl-*N*-(3-methylbut-2-en-1-yl)phenyl)sulfonamido)-hexanamide (52a INT):** Purification by flash column chromatography provided **52a INT** as a clear oil. **^{1}H NMR** (401 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 5.20 (t, *J* = 6.7 Hz, 1H), 4.96 (s, 1H), 4.26 (dd, *J* = 16.8, 7.8 Hz, 1H), 3.95 (dd, *J* = 16.8, 5.6 Hz, 1H), 3.76 (s, 3H), 3.07 (s, 3H), 2.40 (s, 3H), 1.77 – 1.67 (m, 1H), 1.64 (s, 3H), 1.63 (s, 3H), 1.40 – 1.19 (m, 5H), 0.86 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.50, 143.03, 137.82, 133.38, 129.34, 127.40, 122.84, 61.68, 55.17, 43.09, 32.04, 29.83, 28.39, 25.74, 22.32, 21.58, 17.89, 13.94.

4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-phenylhexan-2-yl)benzenesulfonamide (52a S): Purification by flash column chromatography provided **42a S** as a yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 3H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.42 (t, *J* = 6.7 Hz, 1H), 4.99 – 4.93 (m, 1H), 3.98 (dd, *J* = 16.2, 7.1 Hz, 1H), 3.76 (dd, *J* = 16.2, 6.6 Hz, 1H), 2.36 (s, 3H), 1.98 – 1.91 (m, 1H), 1.57 – 1.50 (m, 6H), 1.42 – 1.20 (m, 5H), 0.85 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 198.0, 143.4, 137.4, 136.2, 135.1, 133.3, 129.5, 128.73, 128.68, 127.5, 121.5, 60.0, 43.1, 29.0, 28.5, 25.7, 22.6, 21.6, 17.8, 14.0; **IR** (neat) 2928, 2860, 1687, 1597, 1494, 1448, 1340, 1304, 1232, 1202, 1156, 1090, 1045, 1016, 937, 908, 850, 814, 754, 722, 694, 674 cm^{-1}; **HRMS** calcd for $C_{24}H_{31}NO_3S^{+NH4}$: 485.2080, found: 485.2081.

(b) General Procedure B: Grignard Addition to Weinreb Amide followed by *N*-Alkylation

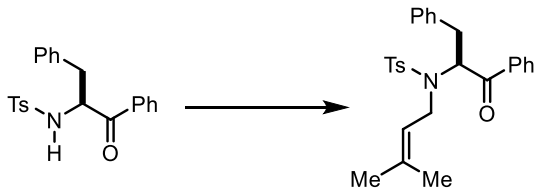


WA **INT** **S**

A round bottom flask equipped with a magnetic stir bar was charged with acid-washed magnesium turnings (3 eq) and sealed under a nitrogen atmosphere. Dry THF (0.2 M) was added via syringe, followed by the desired aryl bromide (3 eq). The solution was allowed to stir (heating as necessary) until all magnesium turnings had dissolved,

and was then cooled to 0 ^{o}C. To the mixture was added Weinreb amide **WA** suspended in dry THF (0.2 M) dropwise via cannula. The reaction was allowed to warm to room temperature over 12 hours, or until judged complete by TLC analysis, at which point it was quenched with a saturated ammonium chloride solution. The reaction mixture was diluted with EtOAc, the layers were partitioned, and the organic layer was collected. The aqueous phase was extracted with EtOAc (3x), and the combined organic layers were washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **INT** in 51-90% yield.

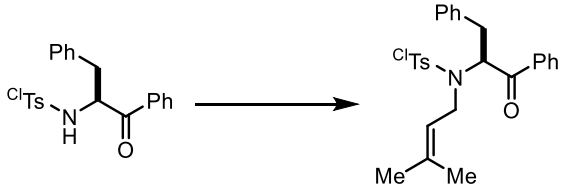
A round bottom flask equipped with a magnetic stir bar was charged with intermediate **INT** and sealed under a nitrogen atmosphere. Dry DMF (0.1 M) was added via syringe, and the reaction mixture was cooled to 0 ^{o}C. Potassium carbonate (2 eq) was added in one portion, and the reaction was allowed to stir at 0 ^{o}C for 30 minutes before prenyl bromide (1.2 eq) was added via syringe. The mixture was allowed to warm to room temperature over 3 hours, or until judged complete by TLC analysis. The reaction was quenched with deionized water, diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with an aqueous 5% LiCl solution (3x), brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired substrate **S** in 73-99% yield.



20 INT **20**

(*S*)-4-methyl-*N*-(1-oxo-1,3-diphenylpropan-2-yl)benzenesulfonamide (20 INT): Purification by flash column chromatography provided **20 INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 3H), 7.17 (s, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 6.99 (s, 2H), 5.66 (d, *J* = 8.7 Hz, 1H), 5.15 (dd, *J* = 14.4, 5.9 Hz, 1H), 3.14 (dd, *J* = 14.0, 5.7 Hz, 1H), 2.96 (dd, *J* = 14.0, 5.9 Hz, 1H), 2.28 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.3, 143.4, 136.8, 134.9, 134.2, 134.0, 129.62, 129.57, 128.8, 128.4, 127.1, 127.0, 58.2, 40.2, 21.4.

(*S*)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)benzenesulfonamide (20): Purification by flash column chromatography provided **20** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 4.4 Hz, 4H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.18 – 7.13 (m, 1H), 5.75 (dd, *J* = 9.9, 4.0 Hz, 1H), 4.82 (t, *J* = 6.8 Hz, 1H), 3.94 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.78 (dd, *J* = 15.9, 7.3 Hz, 1H), 3.44 (dd, *J* = 13.5, 9.9 Hz, 1H), 2.67 (dd, *J* = 13.5, 4.0 Hz, 1H), 2.39 (s, 3H), 1.56 (s, 3H), 1.50 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.3, 143.5, 137.5, 137.4, 136.0, 135.8, 133.1, 129.6, 129.4, 128.7, 128.5, 128.4, 127.5, 126.5, 120.7, 60.8, 43.1, 34.4, 25.5, 21.5, 17.7; **IR** (neat): 3063, 3030, 2925, 1683, 1597, 1580, 1495, 1449, 1341, 1261, 1228, 1157, 1091, 978, 947, 914, 813 cm^{-1}; **HRMS** calcd for $C_{27}H_{29}NO_3S^+$: 448.1941, found: 418.1943.

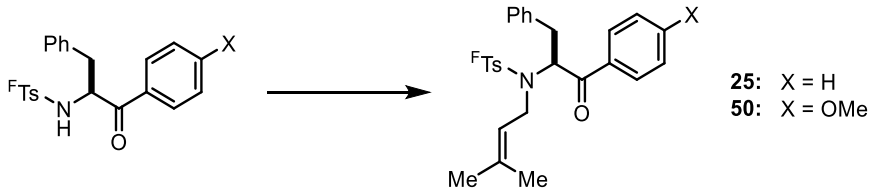


23 INT **23**

(*S*)-4-chloro-*N*-(1-oxo-1,3-diphenylpropan-2-yl)benzenesulfonamide (23 INT): Purification by flash column chromatography provided **23 INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.9 Hz, 2H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.24 – 7.21 (m, 2H), 7.05 – 7.01 (m, 2H), 5.71 (dd, *J* = 8.6, 3.0 Hz, 1H), 5.19 (dt, *J* = 8.9, 6.0 Hz, 1H), 3.19 (dd, *J* = 14.0, 5.4 Hz, 1H), 2.97 (dd, *J* = 14.0, 6.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.1, 138.4, 134.8, 134.2, 134.0, 129.5, 129.2, 129.0, 128.4, 128.1, 127.2, 126.9, 125.8, 58.4, 40.1.

(S)-4-chloro-N-(3-methylbut-2-en-1-yl)-N-(1-oxo-1,3-diphenylpropan-2-yl)benzenesulfonamide (23): Purification by flash column chromatography provided **23** as a yellow solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.3 Hz, 2H), 7.55 – 7.53 (m, 3H), 7.41 (t,

J = 7.8 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.25 (s, 1H), 7.23 (t, *J* = 6.3 Hz, 3H), 7.18 (t, *J* = 7.0 Hz, 1H), 5.77 (dd, *J* = 9.1, 5.0 Hz, 1H), 4.81 (t, *J* = 6.8 Hz, 1H), 3.96 (dd, *J* = 16.0, 6.6 Hz, 1H), 3.84 (dd, *J* = 16.0, 7.0 Hz, 1H), 3.44 (dd, *J* = 13.7, 9.2 Hz, 1H), 2.77 (dd, *J* = 13.7, 5.0 Hz, 1H), 1.58 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.5, 139.1, 138.9, 137.1, 136.1, 135.9, 133.4, 129.3, 129.1, 128.9, 128.6, 128.5, 126.7, 125.8, 120.5, 60.7, 43.2, 34.9, 25.6, 17.7; **IR** (neat): 3063, 3028, 2828, 1688, 1597, 1583, 1495, 1448, 1344, 1278, 1233, 1206, 11160, 1092, 1012, 944, 901, 829, 765 cm^{-1}; **HRMS** calcd for $C_{26}H_{26}ClNO_3S^{+NH4}$: 485.1660, found: 485.1661.



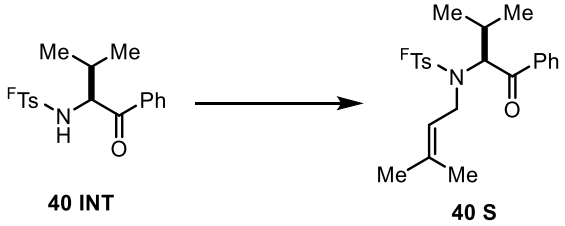
(*S*)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (25 INT): Purification by flash column chromatography provided **25 INT** as a white crystalline solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.9 Hz, 4H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.20 – 7.13 (m, 3H), 7.02 – 6.95 (m, 2H), 5.67 (d, *J* = 9.0 Hz, 1H), 5.18 (ddd, *J* = 9.0, 6.9, 5.4 Hz, 1H), 3.16 (dd, *J* = 14.1, 5.3 Hz, 1H), 2.92 (dd, *J* = 14.1, 6.9 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.1, 143.6, 134.9, 134.5, 134.3 (q, *J* = 33.0 Hz), 134.0, 129.6, 129.2, 128.7, 128.6, 127.6, 127.5, 126.2 (q, *J* = 3.6 Hz), 123.2 (q, *J* = 273.0 Hz), 58.7, 40.3.

(*S*)-*N*-(1-(4-methoxyphenyl)-1-oxo-3-phenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (50 INT): Purification by flash column chromatography provided **50 INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.9 Hz, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.19 – 7.15 (m, 3H), 7.00 (dd, *J* = 6.5, 2.7 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 5.70 (d, *J* = 9.0 Hz, 1H), 5.10 (ddd, *J* = 9.0, 6.7, 5.5 Hz, 1H), 3.88 (s, 3H), 3.14 (dd, *J* = 14.0, 5.3 Hz, 1H), 2.92 (dd, *J* = 14.0, 6.9 Hz, 1H); **^{13}C NMR (**126 MHz, $CDCl_3$) δ 195.1, 164.4, 143.5, 135.0, 134.0 (q, *J* = 33.0 Hz), 130.8, 129.5, 128.5, 127.5, 127.2, 126.7, 126.0 (q, *J* = 3.5 Hz), 123.3 (q, *J* = 272.8 Hz), 114.2, 58.2, 55.6, 40.5.

(*S*)-*N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfon-amide (25): Purification by flash column chromatography provided **25** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.29 – 7.17 (m, 5H), 5.81 (dd, *J* = 8.7, 5.5 Hz, 1H), 4.82 (t, *J* = 6.8 Hz, 1H), 3.96 (ddd, *J* = 51.8, 16.1, 6.8 Hz, 2H), 3.44 (dd, *J* = 13.8, 8.8 Hz, 1H), 2.83 (dd, *J* = 13.8, 5.5 Hz, 1H), 1.60 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.7, 144.1, 137.1, 136.4, 136.0, 134.2 (q, *J* = 33.0 Hz), 133.6, 129.5, 128.80, 128.78, 128.7, 128.0, 127.0, 126.0 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 273.0 Hz), 120.6, 60.9, 43.5, 35.3, 25.7, 17.9; **IR** (neat) 3069, 3024, 2973, 2951, 2925, 2852, 1692, 1607, 1597, 1581, 1495, 1448, 1435, 1403, 1378, 1345, 1322,

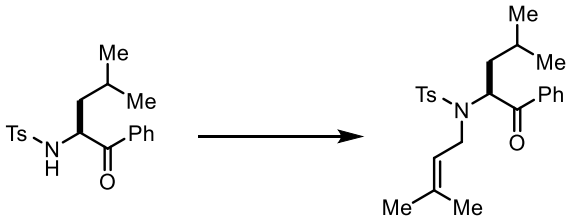
1275, 1234, 1207, 1187, 1156, 1132, 1104, 1061, 1013; **HRMS** calcd for $C_{27}H_{26}F_3NO_3S^{+NH4}$: 519.1924, found: 519.1923.

(*S*)-*N*-(1-(4-methoxyphenyl)-1-oxo-3-phenylpropan-2-yl)-*N*-(3-methylbut-2-en-1-yl)-4-(trifluorometh-yl)benzenesulfonamide (50 S): Purification by flash column chromatography provided **50 S** as a pale yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.8 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 7.4 Hz, 2H), 7.23 – 7.18 (m, 3H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.79 (dd, *J* = 8.8, 5.6 Hz, 1H), 4.84 (t, *J* = 6.5 Hz, 1H), 4.04 (dd, *J* = 16.1, 6.7 Hz, 1H), 3.96 – 3.89 (m, 1H), 3.85 (s, 3H), 3.40 (dd, *J* = 13.8, 8.9 Hz, 1H), 2.80 (dd, *J* = 13.8, 5.5 Hz, 1H), 1.61 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 194.9, 164.0, 144.3, 137.1, 136.0, 134.2 (q, *J* = 32.9 Hz), 131.2, 129.5, 128.80, 128.77, 128.0, 126.9, 126.0 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 272.8 Hz), 120.9, 114.0, 60.3, 55.6, 43.4, 35.5, 25.7, 17.9; **IR** (neat): 2936.18, 1678, 1512, 1322, 1264, 1241, 1180, 1132, 1107, 1093, 1062, 1105, 841 cm^{-1}; **HRMS** calcd for $C_{28}H_{28}F_3NO_4S^+$: 532.1764, found: 532.1759.



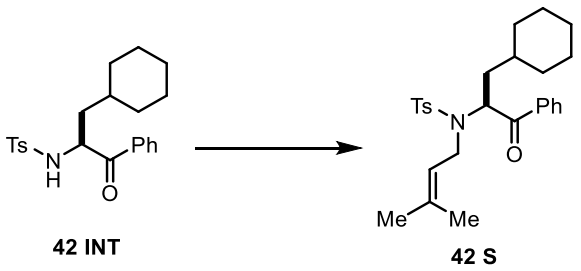
(*S*)-*N*-(3-methyl-1-oxo-1-phenylbutan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (40 INT): Purification by flash column chromatography provided **40 INT** as a pale yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.59 – 7.51 (m, 3H), 7.41 (t, *J* = 7.8 Hz, 2H), 5.92 (d, *J* = 9.6 Hz, 1H), 4.77 (dd, *J* = 9.6, 3.9 Hz, 1H), 2.15 – 2.05 (m, 1H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.9, 143.4, 134.30, 134.30 (q, *J* = 33.0 Hz), 129.0, 128.3, 128.2, 127.8, 126.1 (q, *J* = 3.7 Hz), 123.1 (q, *J* = 272.7 Hz), 62.5, 31.7, 20.1, 16.2.

(*S*)-*N*-(3-methyl-1-oxo-1-phenylbutan-2-yl)-*N*-(3-methylbut-2-en-1-yl)-4-(trifluoro-methyl)benzenesulfonamide (40 S): Purification by flash column chromatography provided **40 S** as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.3 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 5.25 (d, *J* = 10.6 Hz, 1H), 4.90 – 4.81 (m, 1H), 4.24 (dd, *J* = 16.1, 8.7 Hz, 1H), 3.85 (dd, *J* = 15.7, 3.9 Hz, 1H), 2.44 – 2.32 (m, 1H), 1.63 (s, 3H), 1.50 (s, 3H), 1.14 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 198.7, 144.6, 137.6, 135.5, 133.9, 133.8 (q, *J* = 32.9 Hz), 129.1, 128.6, 127.8, 125.5 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.7 Hz), 120.8, 63.4, 42.7, 27.8, 25.8, 25.7, 19.9, 19.8, 17.8; **IR** (neat) 2967, 1683, 1596, 1448, 1404, 1321, 1293, 1220, 1161, 1131, 1107, 1091, 1062, 1042, 1012, 944, 906, 842, 805, 785, 754, 712, 694, 668 cm^{-1}; **HRMS** calcd for $C_{23}H_{26}F_3NO_3S^{+Na}$: 476.1478, found: 476.1474.



(*S*)-4-methyl-*N*-(4-methyl-1-oxo-1-phenylpentan-2-yl)benzenesulfonamide (41 INT): Purification by flash column chromatography provided **41 INT** as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.68 (d, *J* = 6.9 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 5.62 (d, *J* = 9.5 Hz, 1H), 4.87 (td, *J* = 9.9, 3.6 Hz, 1H), 2.24 (s, 3H), 2.01 (dddd, *J* = 13.4, 10.7, 6.7, 4.0 Hz, 1H), 1.39 (qdd, *J* = 14.3, 9.8, 3.8 Hz, 2H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 198.6, 143.6, 136.7, 134.0, 133.9, 129.6, 128.9, 128.3, 127.3, 56.1, 43.1, 24.7, 23.4, 21.5, 21.2.

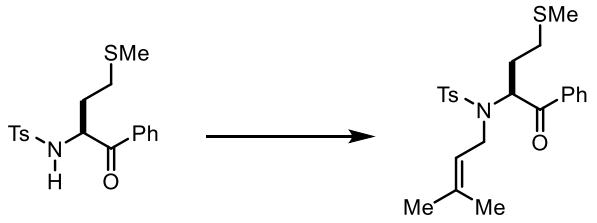
(*S*)-4-methyl-*N*-(4-methyl-1-oxo-1-phenylpentan-2-yl)-*N*-(3-methylbut-2-en-1-yl)-benzenesulfonamide (41 S): Purification by flash column chromatography provided **41 S** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 2H), 7.59 – 7.54 (m, 3H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 5.58 (dd, *J* = 7.6, 5.7 Hz, 1H), 5.08 – 5.00 (m, 1H), 4.03 (dd, *J* = 16.4, 7.4 Hz, 1H), 3.83 (dd, *J* = 16.5, 6.1 Hz, 1H), 2.35 (s, 3H), 1.77 – 1.69 (m, 2H), 1.57 (s, 3H), 1.56 (s, 3H), 1.40 – 1.30 (m, 1H), 0.99 (d, *J* = 5.9 Hz, 3H), 0.87 (d, *J* = 6.1 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 198.2, 143.3, 137.4, 136.0, 134.5, 133.3, 129.5, 128.8, 128.6, 127.5, 122.0, 58.2, 43.2, 37.7, 25.7, 25.3, 22.7, 22.2, 21.6, 17.8; **IR** (neat) 2954, 1685, 1652, 1597, 1448, 1339, 1245, 1206, 1156, 1122, 1089, 1042, 1002, 909, 813, 740, 694, 676, 653 cm^{-1}; **HRMS** calcd for $C_{24}H_{31}NO_3S^+$: 414.2097, found: 414.2092.



(*S*)-*N*-(3-cyclohexyl-1-oxo-1-phenylpropan-2-yl)-4-methylbenzenesulfonamide (42 INT): Purification by flash column chromatography provided **42 INT** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.5 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 5.66 (d, *J* = 9.5 Hz, 1H), 4.90 (td, *J* = 10.2, 2.9 Hz, 1H), 2.25 (s, 3H), 1.98 (d, *J* = 11.9 Hz, 1H), 1.74 – 1.58 (m, 4H), 1.58 – 1.39 (m, 2H), 1.30 (ddd, *J* = 14.3, 10.7, 3.6 Hz, 1H), 1.21 (dddd, *J* = 15.7, 12.5, 7.8, 3.4 Hz, 2H), 1.14 – 1.04 (m, 1H), 0.86 (ttd, *J* = 12.4, 9.1, 8.6, 4.4 Hz, 2H); **^{13}C NMR** (101 MHz,

$CDCl_3$) δ 198.7, 143.5, 136.7, 134.0, 133.8, 129.6, 128.8, 128.3, 127.3, 55.6, 41.6, 34.0, 33.7, 32.0, 26.5, 26.2, 26.0, 21.5.

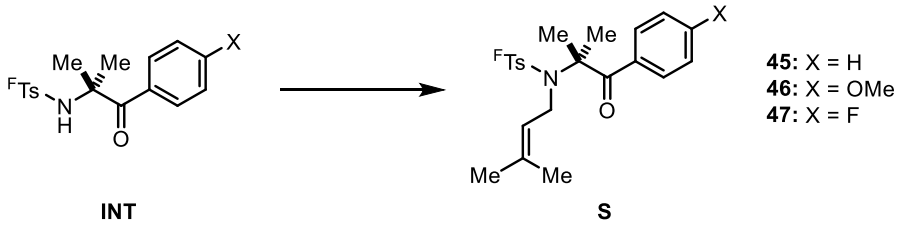
(*S*)-*N*-(3-cyclohexyl-1-oxo-1-phenylpropan-2-yl)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-benzenesulfonamide (42 S): Purification by flash column chromatography provided **42 S** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 2H), 7.61 – 7.53 (m, 3H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.60 (t, *J* = 6.9 Hz, 1H), 5.04 (t, *J* = 7.0 Hz, 1H), 4.02 (dd, *J* = 16.4, 7.4 Hz, 1H), 3.85 (dd, *J* = 16.4, 6.2 Hz, 1H), 2.36 (s, 3H), 1.91 (dt, *J* = 12.6, 3.0 Hz, 1H), 1.75 (dt, *J* = 14.0, 7.1 Hz, 1H), 1.72 – 1.60 (m, 3H), 1.57 (s, 3H), 1.56 (s, 3H), 1.43 – 1.28 (m, 2H), 1.28 – 1.05 (m, 4H), 0.87 (qt, *J* = 12.4, 3.5 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 198.3, 143.3, 137.4, 135.9, 134.4, 133.3, 129.5, 128.8, 128.6, 127.5, 122.1, 57.6, 43.2, 36.3, 34.6, 33.5, 32.9, 26.5, 26.3, 26.2, 25.7, 21.6, 17.8; **IR** (neat) 2922, 2852, 1688, 1597, 1447, 1339, 1230, 1207, 1160, 1092, 814, 740, 697, 676, 653 cm^{-1}; **HRMS** calcd for $C_{27}H_{35}NO_3S^+$: 454.2410, found 454.2402.



44 INT **44 S**

(*S*)-4-methyl-*N*-(4-(methylthio)-1-oxo-1-phenylbutan-2-yl)benzenesulfonamide (44 INT): Purification by flash column chromatography provided **44 INT** as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 7.0 Hz, 2H), 7.58 (dd, *J* = 10.6, 4.3 Hz, 1H), 7.44 (t, *J* = 7.1 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 5.76 (d, *J* = 8.8 Hz, 1H), 5.06 (td, *J* = 9.0, 1.7 Hz, 1H), 2.72 (dt, *J* = 15.2, 7.8 Hz, 1H), 2.67 – 2.59 (m, 1H), 2.28 (s, 3H), 2.05 (s, 3H), 2.01 – 1.92 (m, 1H), 1.72 (ddt, *J* = 10.1, 7.6, 5.2 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.7, 143.8, 136.5, 134.3, 133.6, 129.8, 129.0, 128.6, 127.3, 56.4, 33.6, 30.4, 21.6, 15.7.

(*S*)-4-methyl-N-(3-methylbut-2-en-1-yl)-*N*-(4-(methylthio)-1-oxo-1-phenylbutan-2-yl)benzenesulfonamide (44 S): Purification by flash column chromatography provided **44 S** as a yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.9 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 5.66 (t, *J* = 6.8 Hz, 1H), 4.94 (t, *J* = 6.5 Hz, 1H), 3.95 (dd, *J* = 16.0, 7.0 Hz, 1H), 3.78 (dd, *J* = 16.0, 6.6 Hz, 1H), 2.60 (dt, *J* = 13.8, 7.0 Hz, 1H), 2.48 (dt, *J* = 13.6, 6.9 Hz, 1H), 2.38 (s, 3H), 2.28 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.07 (s, 3H), 1.69 (td, *J* = 13.8, 6.9 Hz, 1H), 1.54 (s, *J* = 9.4 Hz, 6H); **^{13}C NMR** (176 MHz, CD_2Cl_2) δ 197.7, 144.1, 137.7, 136.4, 136.0, 133.6, 129.9, 129.0, 129.0, 127.8, 121.5, 59.3, 43.7, 31.6, 28.3, 25.7, 21.6, 17.8, 15.7; **IR** (neat) 2969, 2917, 2856, 1685, 1597, 1580, 194, 1447, 1377, 1339, 1305, 1237, 1208, 1183, 1154, 1090, 1043, 1018, 1001 cm^{-1}; **HRMS** calcd for $C_{23}H_{29}NO_3S_2^+$: 432.1662, found: 432.1664.



***N*-(2-methyl-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (45 INT):** Purification by flash column chromatography provided **45 INT** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.2 Hz, 2H), 7.81 – 7.76 (m, 2H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 7.9 Hz, 2H), 5.88 (s, 1H) 1.67 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 201.2, 146.3, 135.0, 134.3 (q, *J* = 33.5 Hz), 132.6, 129.1, 128.6, 127.5, 126.3 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.8 Hz), 64.6, 27.0.

***N*-(1-(4-methoxyphenyl)-2-methyl-1-oxopropan-2-yl)-4-(trifluoromethyl)benzene-sulfonamide (46 INT):** Purification by flash column chromatography provided **46 INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 20.7, 8.5 Hz, 4H), 7.70 (d, *J* = 8.2 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 6.08 (s, 1H), 3.85 (s, 3H), 1.87 – 1.67 (m, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 198.3, 163.4, 146.5, 134.1 (q, *J* = 33.0 Hz), 132.1, 127.4, 126.4, 126.2 (q, *J* = 3.6 Hz), 123.4 (q, *J* = 272.8 Hz), 113.8, 64.4, 55.6, 27.3.

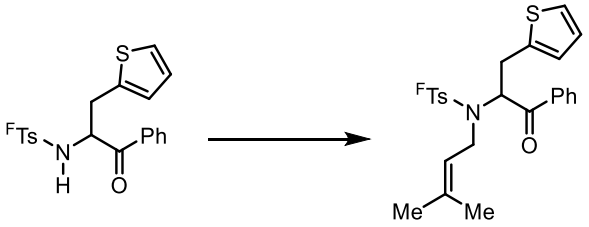
***N*-(1-(4-fluorophenyl)-2-methyl-1-oxopropan-2-yl)-4-(trifluoromethyl)benzenesulf-onamide (47 INT):** Purification by flash column chromatography provided **47 INT** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 9.9, 4.6 Hz, 4H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.08 (t, *J* = 8.6 Hz, 2H), 5.73 (s, 1H), 1.65 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 199.1, 165.3 (d, *J* = 255.4 Hz), 146.2, 134.4 (q, *J* = 33.1 Hz), 132.1 (d, *J* = 9.1 Hz), 130.9 (d, *J* = 3.3 Hz), 127.5, 126.3 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 272.7 Hz), 115.7 (d, *J* = 21.8 Hz), 64.4, 27.1.

***N*-(2-methyl-1-oxo-1-phenylpropan-2-yl)-*N*-(3-methylbut-2-en-1-yl)-4-(trifluoro-methyl)benzenesulfonamide (45 S):** Purification by flash column chromatography provided **45 S** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 – 7.95 (m, 2H), 7.62 (m, 4H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 5.21 (t, *J* = 6.9 Hz, 1H), 3.99 (d, *J* = 6.4 Hz, 2H), 1.68 (s, 6H), 1.66 (s, 3H), 1.62 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 200.3, 143.7, 136.1, 135.3, 134.3 (q, *J* = 33.0 Hz), 132.1, 129.6, 128.9, 128.3, 125.8 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 272.9 Hz), 121.1, 68.9, 44.3, 26.5, 25.9, 18.0; **IR** (neat) 2918, 1684, 1596, 1479, 1446, 1401, 1361, 1320, 1265, 1208, 1183, 1169, 1144, 1121, 1110, 1088, 1061, 1042, 1008 cm^{-1}; **HRMS** calcd for $C_{22}H_{24}F_3NO_3S^+$: 440.1502, found: 440.1502.

***N*-(1-(4-methoxyphenyl)-2-methyl-1-oxopropan-2-yl)-*N*-(3-methylbut-2-en-1-yl)-4-(trifluoromethyl)-benzenesulfonamide (46 S):** Purification by flash column chromatography provided **46 S** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.20 (t, *J* = 5.8 Hz, 1H), 4.02 (d, *J* = 6.3 Hz, 2H), 3.86 (s, 3H), 1.65 (s, 3H), 1.64 (s, 6H),

1.62 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.9, 162.8, 144.1, 135.4, 134.2 (q, *J* = 33.0 Hz), 132.1, 128.7, 128.0, 125.8 (dd, *J* = 7.2, 3.5 Hz), 123.3 (dd, *J* = 545.8, 272.9 Hz), 121.1, 113.4, 68.8, 55.5, 44.6, 26.5, 25.9, 18.0; **IR** (neat) 2984, 2946, 1674, 1600, 1504, 1457, 1444, 1419, 1404, 1382, 1363, 1330, 1254, 1207, 1190, 1163, 1145, 1125, 1088, 1062, 1053, 1035, 1010 cm^{-1}; **HRMS** calcd for $C_{23}H_{26}F_3NO_4S^{+NH4}$: 487.1873, found: 487.1871.

***N*-(1-(4-fluorophenyl)-2-methyl-1-oxopropan-2-yl)-*N*-(3-methylbut-2-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (47 S):** Purification by flash column chromatography provided **47 S** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.9, 5.5 Hz, 2H), 7.69 (dd, *J* = 22.9, 8.4 Hz, 4H), 7.07 (t, *J* = 8.7 Hz, 2H), 5.14 (s, 1H), 4.00 (d, *J* = 6.3 Hz, 2H), 1.63 (s, 3H), 1.62 (s, 6H), 1.60 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 198.2, 165.0 (d, *J* = 254.2 Hz), 143.8, 135.6, 134.5 (q, *J* = 33.1 Hz), 132.3 (d, *J* = 8.9 Hz), 132.0 (d, *J* = 3.0 Hz), 128.8, 126.0 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 273.0 Hz), 120.7, 115.3 (d, *J* = 21.5 Hz), 68.7, 44.4, 26.3, 25.8, 17.9; **IR** (neat) 2920, 1682, 1596, 1505, 1480, 1436, 1402, 1362, 1322, 1297, 1265, 1246, 1208, 1138, 1110, 1088, 1063, 1042, 1009; **HRMS** calcd for $C_{22}H_{23}F_4NO_3S^{+Na}$: 480.1227, found: 480.1225.

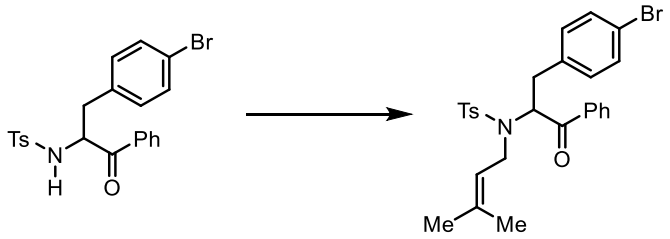


48 INT **48 S**

***N*-(1-oxo-1-phenyl-3-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (48 INT):** Purification by flash column chromatography provided **48 INT** as a pale yellow foam. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 7.7 Hz, 2H), 7.64 – 7.57 (m, 3H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.09 (d, *J* = 5.1 Hz, 1H), 6.81 (s, 1H), 6.64 (d, *J* = 3.4 Hz, 1H), 5.97 (d, *J* = 8.6 Hz, 1H), 5.19 (q, *J* = 6.1 Hz, 1H), 3.38 (dd, *J* = 15.2, 5.0 Hz, 1H), 3.20 (dd, *J* = 15.2, 6.3 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.5, 143.6, 136.1, 134.5, 134.4 (q, *J* = 33.1 Hz), 133.8, 129.2, 128.6, 127.6, 127.4, 127.1, 126.3 (q, *J* = 3.5 Hz), 125.3, 123.2 (q, *J* = 272.7 Hz), 58.5, 34.5.

***N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-phenyl-3-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (48 S):** Purification by flash column chromatography provided **48 S** as a pale yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.96 (d, *J* = 6.9 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.13 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.88 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.83 (d, *J* = 2.9 Hz, 1H), 5.73 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.84 (tt, *J* = 6.9, 1.6 Hz, 1H), 3.98 (dd, *J* = 15.9, 6.6 Hz, 1H), 3.85 (dd, *J* = 16.0, 7.2 Hz, 1H), 3.70 (dd, *J* = 14.7, 8.9 Hz, 1H), 2.89 (dd, *J* = 14.7, 4.8 Hz, 1H), 1.59 (s, 3H), 1.53 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.1, 144.1, 139.2, 136.8, 135.8, 134.4 (q, *J* = 33.0 Hz), 133.7, 128.8, 128.8, 128.1, 127.2, 126.7, 126.2 (q, *J* = 3.7 Hz), 124.6, 123.3 (q, *J* = 273.4 Hz), 120.3, 61.4, 43.6, 29.3, 25.7,

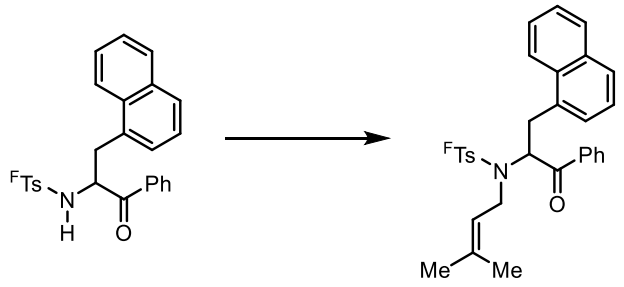
17.9; **IR** (neat) 2925, 1689, 1597, 1448, 1404, 1321, 1228, 1162, 1132, 1107, 1092, 1062, 1014, 908, 844, 743, 712 cm^{-1}; **HRMS** calcd for $C_{25}H_{24}F_3NO_3S_2^+$: 508.1228, found: 508.1226.



49 INT **49 S**

***N*-(3-(4-bromophenyl)-1-oxo-1-phenylpropan-2-yl)-4-methylbenzenesulfonamide (49 INT):** Purification by flash column chromatography provided **49 INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.7 Hz, 2H), 7.60 (t, J = 7.8 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 6.84 (d, *J* = 7.9 Hz, 2H), 5.63 (d, *J* = 8.6 Hz, 1H), 5.10 (dd, *J* = 14.1, 5.9 Hz, 1H), 3.10 (dd, *J* = 14.0, 5.2 Hz, 1H), 2.86 (dd, *J* = 14.0, 6.3 Hz, 1H), 2.31 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.9, 143.6, 136.7, 134.2, 134.0, 133.9, 131.4, 131.3, 129.6, 129.0, 128.4, 127.0, 121.2, 58.0, 39.5, 21.5.

***N*-(3-(4-bromophenyl)-1-oxo-1-phenylpropan-2-yl)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-benzenesulfonamide (49 S):** Purification by flash column chromatography provided **49 S** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.9 Hz, 2H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.53 (dd, *J* = 13.9, 7.1 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 5.68 (dd, *J* = 9.7, 4.0 Hz, 1H), 4.78 (t, *J* = 6.4 Hz, 1H), 3.91 (dd, *J* = 15.8, 6.2 Hz, 1H), 3.74 (dd, *J* = 15.9, 7.3 Hz, 1H), 3.41 (dd, *J* = 13.5, 9.8 Hz, 1H), 2.64 (dd, *J* = 13.5, 3.9 Hz, 1H), 2.40 (s, 3H), 1.54 (s, 3H), 1.49 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.2, 143.8, 137.4, 136.7, 136.3, 136.0, 133.5, 131.7, 131.3, 129.8, 128.9, 128.7, 127.7, 126.6, 120.7, 60.8, 43.2, 34.0, 25.7, 21.7, 17.8; **IR** (neat): 2360, 2339, 1716, 1697, 1683, 1652, 1558, 1540, 1521, 1506, 1489, 1456, 1339, 158, 902, 756 cm^{-1}; **HRMS** calcd for $C_{27}H_{28}BrNO_3S^+$: 526.1046, found: 526.1033.

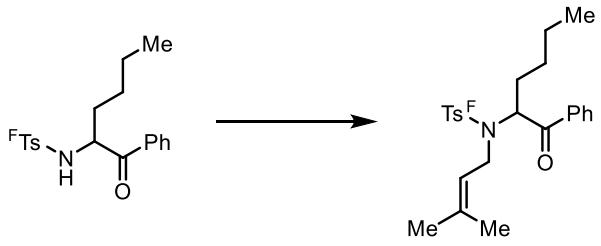


52b INT **52b S**

(*S*)-*N*-(3-(naphthalen-1-yl)-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)benzene-sulfonamide (52b INT): Purification by flash column chromatography provided **52b INT** as a white foam. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 8.4

Hz, 1H), 7.67 (d, *J* = 7.9 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.51 (ddt, *J* = 21.9, 13.5, 7.1 Hz, 5H), 7.41 – 7.29 (m, 4H), 7.16 (dt, *J* = 15.5, 7.1 Hz, 2H), 5.95 (d, *J* = 9.3 Hz, 1H), 5.34 (td, *J* = 8.7, 6.2 Hz, 1H), 3.46 (dd, *J* = 14.3, 6.1 Hz, 1H), 3.37 (dd, *J* = 14.2, 8.2 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 198.5, 143.2, 134.4, 134.4, 133.9 (q, *J* = 33.0 Hz), 133.9, 131.8, 131.5, 129.2, 129.0, 128.4, 128.4, 128.3, 127.1, 126.6, 125.9, 125.8 (q, *J* = 3.7 Hz), 125.3, 123.2 (q, *J* = 273.2 Hz), 123.1, 57.9, 37.4.

(*S*)-*N*-(3-methylbut-2-en-1-yl)-*N*-(3-(naphthalen-1-yl)-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (52b S): Purification by flash column chromatography provided **52b S** as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.63 – 7.48 (m, 6H), 7.47 – 7.41 (m, 3H), 7.32 – 7.21 (m, 4H), 6.02 (dd, *J* = 9.0, 5.6 Hz, 1H), 4.95 (tt, *J* = 6.2, 1.7 Hz, 1H), 4.23 (dd, *J* = 16.3, 7.4 Hz, 1H), 4.08 (dd, *J* = 16.3, 6.3 Hz, 1H), 3.80 (dd, *J* = 14.1, 9.0 Hz, 1H), 3.56 (dd, *J* = 14.1, 5.6 Hz, 1H), 1.65 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.6, 144.0, 136.4, 136.0, 134.0, 133.9 (q, *J* = 33.0 Hz), 133.5, 132.4, 131.9, 129.2, 128.6, 128.3, 128.2, 127.9, 127.8, 126.7, 125.9, 125.7 (q, *J* = 3.7 Hz), 125.5, 123.4, 123.1 (q, *J* = 273.4 Hz), 121.2, 58.8, 43.5, 33.3, 25.7, 18.0; **IR** (neat) 2913, 2364, 1685, 1597, 1559, 1448, 1404, 1322, 1230, 1162, 1132, 1107, 1093, 1062, 1014, 942, 906, 844, 797, 778, 710 cm^{-1}; **HRMS** calcd for $C_{31}H_{28}F_3NO_3S^+$: 552.1815, found: 552.1839.

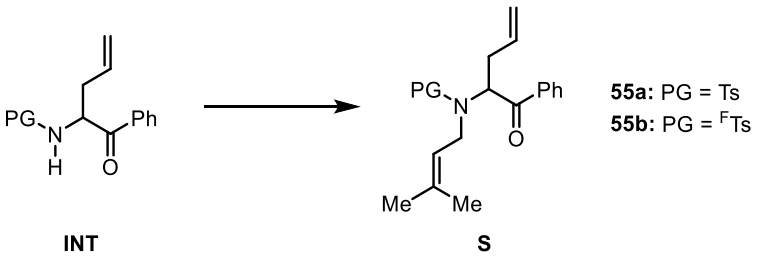


54b INT **54b S**

***N*-(1-oxo-1-phenylhexan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (54b INT):** Purification by flash column chromatography provided **54b INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 7.9 Hz, 2H), 7.60 (t, *J* = 8.5 Hz, 3H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.78 (d, *J* = 8.9 Hz, 1H), 4.88 (td, *J* = 8.5, 4.0 Hz, 1H), 1.80 (ddd, *J* = 14.5, 10.0, 4.9 Hz, 1H), 1.57 – 1.50 (m, 1H), 1.44 – 1.17 (m, 4H), 0.82 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.7, 143.6, 134.47, 134.46 (q, *J* = 33.1 Hz), 133.7, 129.1, 128.3, 127.8, 126.2 (q, *J* = 3.6 Hz), 123.2 (q, *J* = 273.0 Hz), 57.8, 33.9, 27.1, 22.3, 13.9.

***N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-phenylhexan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (54b S):** Purification by flash column chromatography provided **54b S** as a pale yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.8 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.60 (t, *J* = 8.1 Hz, 3H), 7.48 (t, *J* = 7.6 Hz, 2H), 5.48 (t, *J* = 7.0 Hz, 1H), 5.01 (t, *J* = 6.5 Hz, 1H), 4.06 (dd, *J* = 16.2, 7.5 Hz, 1H), 3.88 (dd, *J* = 16.2, 6.0 Hz, 1H), 1.95 (dt, *J* = 15.0, 6.3 Hz, 1H), 1.59 (s, 3H), 1.57 (s, 3H), 1.50 (td, *J* = 13.9, 8.8 Hz, 1H), 1.43 – 1.33 (m, 3H), 1.28 (dd, *J* = 13.8, 6.9 Hz, 1H), 0.88 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176

MHz, $CDCl_3$) δ 197.9, 144.1, 135.9, 135.5, 134.2 (q, *J* = 33.0 Hz), 133.7, 129.0, 128.5, 127.9, 126.0 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 272.9 Hz), 121.3, 60.3, 43.5, 29.1, 28.9, 25.7, 22.5, 17.9, 14.0; **IR** (neat) 2960, 2932, 2874, 1689, 1597, 1581, 1448, 1404, 1345, 1321, 1233, 1162, 1131, 1092, 1107, 1062, 1014 cm^{-1}; **HRMS** calcd for $C_{24}H_{28}F_3NO_3S^{+NH4}$: 485.2080, found: 485.2081.



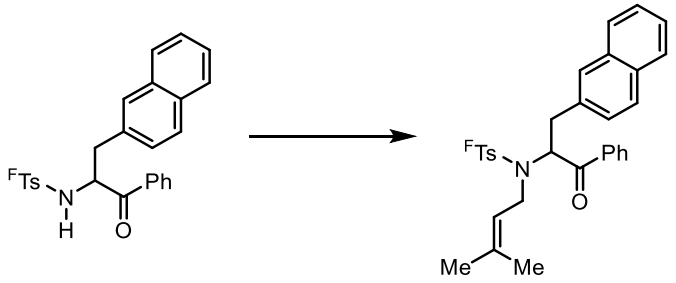
4-methyl-*N*-(1-oxo-1-phenylpent-4-en-2-yl)benzenesulfonamide (55a INT): Purification by flash column chromatography provided **55a INT** as a white solid. **^{1}H NMR** (401 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.3 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 5.69 (d, *J* = 8.6 Hz, 1H), 5.62 (ddd, *J* = 17.2, 8.6, 5.7 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H), 4.99 – 4.91 (m, 2H), 2.62 – 2.53 (m, 1H), 2.42 – 2.32 (m, 1H), 2.30 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.1, 143.5, 139.4, 136.8, 134.0, 133.9, 131.1, 129.6, 128.8, 128.3, 119.5, 57.0, 38.3, 21.4.

***N*-(1-oxo-1-phenylpent-4-en-2-yl)-4-(trifluoromethyl)benzenesulfonamide (55b INT):** Purification by flash column chromatography provided **55b INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.93 (t, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 7.9 Hz, 2H), 7.63 – 7.56 (m, 3H), 7.46 – 7.41 (m, 2H), 5.99 (d, *J* = 8.7 Hz, 1H), 5.67 – 5.58 (m, 1H), 5.08 – 5.01 (m, 2H), 4.98 (dd, *J* = 17.1, 7.0 Hz, 1H), 2.63 – 2.57 (m, 1H), 2.44 – 2.38 (m, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.78 (s), 143.7, 134.34, 134.29 (q, *J* = 33.1 Hz), 133.7, 130.9, 129.0, 128.3, 127.6, 126.1 (q, *J* = 3.6 Hz), 123.1 (q, *J* = 273.0 Hz), 119.8, 57.2, 38.2.

4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-phenylpent-4-en-2-yl)benzenesulfonamide (55a S): Purification by flash column chromatography provided **55a S** as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.4 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.73 (ddd, *J* = 23.9, 10.1, 6.9 Hz, 1H), 5.48 (dd, *J* = 8.8, 5.1 Hz, 1H), 5.10 – 5.00 (m, 2H), 4.85 (t, *J* = 6.8 Hz, 1H), 3.92 (dd, *J* = 15.8, 6.4 Hz, 1H), 3.69 (dd, *J* = 15.9, 7.2 Hz, 1H), 2.80 (dt, *J* = 14.9, 7.6 Hz, 1H), 2.40 (s, 3H), 2.09 (dt, *J* = 13.5, 6.2 Hz, 1H), 1.51 (s, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.9, 143.6, 137.5, 136.1, 136.0, 134.1, 133.4, 129.7, 128.9, 128.7, 127.7, 120.9, 118.2, 59.8, 43.2, 32.6, 25.7, 21.7, 17.8. **IR** (neat): 2925, 16686, 1597, 1448, 1340, 1239, 1178, 1089, 1000, 911, 814 cm^{-1}; **HRMS** calcd for $C_{27}H_{28}NaNO_3S^{+Na}$: 420.1604, found: 420.1603.

***N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-phenylpent-4-en-2-yl)-4-(trifluoromethyl)-benzenesulfonamide (55b S):** Purification by flash column chromatography provided **55b S** as a pale yellow oil. **^{1}H NMR** (401 MHz, $CDCl_3$) δ 7.99 – 7.92 (m, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.67 – 7.56 (m, 3H), 7.47 (t, *J* = 7.7 Hz, 2H), 5.76 (ddt, *J* = 16.9, 10.2, 6.9

Hz, 1H), 5.58 – 5.51 (m, 1H), 5.14 – 5.04 (m, 2H), 4.89 (t, *J* = 6.8 Hz, 1H), 3.99 (dd, *J* = 16.0, 7.0 Hz, 1H), 3.82 (dd, *J* = 16.1, 6.8 Hz, 1H), 2.80 (dt, *J* = 14.3, 7.2 Hz, 1H), 2.25 (dt, *J* = 13.9, 6.7 Hz, 1H), 1.57 (s, 3H), 1.53 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.8, 144.2, 136.3, 135.9, 134.3 (q, *J* = 33.1 Hz), 133.6, 133.5, 128.8, 128.7, 128.1, 126.0 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 272.9 Hz), 120.6, 118.6, 59.9, 43.5, 33.3, 25.6, 17.8; **IR** (neat) 3075, 2931, 2859, 1688, 1642, 1597, 1581, 1448, 1404, 1346, 1320, 1240, 1207, 1161, 1130, 1107, 1092, 1061, 1014, 1001 cm^{-1}; **HRMS** calcd for $C_{23}H_{24}F_3NO_3S^+$: 452.1502, found: 452.1495.

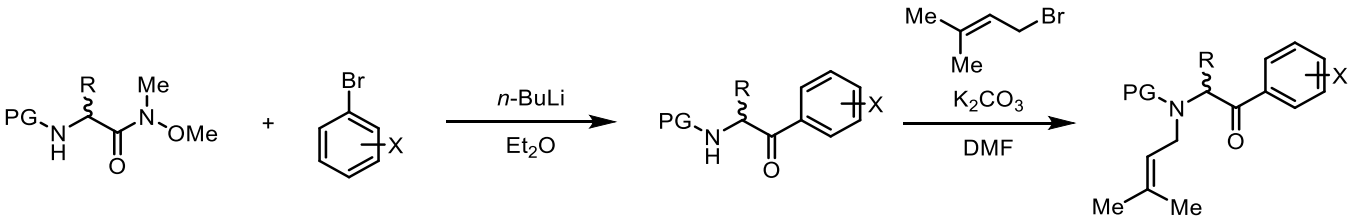


57 INT **57 S**

(*R*)-*N*-(3-(naphthalen-2-yl)-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)benzene-sulfonamide (57 INT): Purification by flash column chromatography provided **57 INT** as a white foam. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.4 Hz, 2H), 7.76 (dd, *J* = 6.1, 3.4 Hz, 1H), 7.64 (ddt, *J* = 13.3, 7.5, 4.5 Hz, 5H), 7.53 – 7.40 (m, 5H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.11 (dd, *J* = 8.3, 1.8 Hz, 1H), 5.78 (d, *J* = 9.0 Hz, 1H), 5.29 (ddd, *J* = 9.1, 7.7, 4.8 Hz, 1H), 3.33 (dd, *J* = 14.1, 4.8 Hz, 1H), 3.01 (dd, *J* = 14.1, 7.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.1, 143.5, 134.5, 134.1 (q, *J* = 32.8 Hz), 134.0, 133.4, 132.6, 132.5, 129.3, 128.7, 128.6, 128.4, 127.8, 127.6, 127.4, 127.3, 126.5, 126.1, 125.9 (q, *J* = 3.8 Hz), 123.0 (q, *J* = 278.5 Hz), 58.9, 40.4.

(*R*)-*N*-(3-methylbut-2-en-1-yl)-*N*-(3-(naphthalen-2-yl)-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)-benzenesulfonamide (57 S): Purification by flash column chromatography provided **57 S** as a pale yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.4 Hz, 2H), 7.83 – 7.79 (m, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.62 (s, 1H), 7.55 (dd, *J* = 22.4, 7.8 Hz, 3H), 7.48 – 7.44 (m, 2H), 7.43 – 7.36 (m, 5H), 5.95 (dd, *J* = 8.1, 6.2 Hz, 1H), 4.87 – 4.79 (m, 1H), 4.02 (dd, *J* = 16.1, 6.6 Hz, 1H), 3.96 (dd, *J* = 16.1, 7.1 Hz, 1H), 3.59 (dd, *J* = 14.0, 8.1 Hz, 1H), 3.03 (dd, *J* = 14.0, 6.2 Hz, 1H), 1.63 (s, 3H), 1.54 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.8, 144.0, 136.4, 135.9, 134.6, 133.9 (q, *J* = 33.0 Hz), 133.7, 133.6, 132.4, 128.8, 128.7, 128.5, 128.4, 128.0, 127.73, 127.66, 127.4, 126.4, 126.0, 125.7 (q, *J* = 3.7 Hz), 123.1 (q, *J* = 273 Hz), 120.6, 61.1, 43.4, 35.4, 25.8, 17.9; **IR** (neat) 2920, 1687, 1597, 1448, 1404, 1321, 1161, 1131, 1107, 1062, 1015, 909, 843, 816, 742, 709, 691 cm^{-1}; **HRMS** calcd for $C_{31}H_{28}F_3NO_3S^+$: 552.1815, found: 552.1812.

(c) General Procedure C: Aryl Lithium[3] Addition to Weinreb Amide followed by *N*-Alkylation

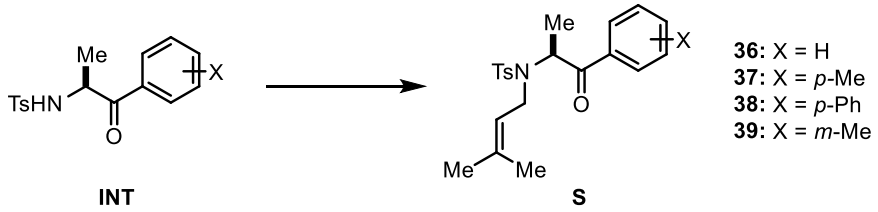


WA **INT** **S**

A round bottom flask charged with a stir bar was sealed under a nitrogen atmosphere and cooled to 0 ^oC. Dry Et_2O (1.33 M) was added via syringe, followed by *n*-butyllithium (4 equiv., 2.5 M in hexanes) and the desired aryl bromide (4.1 equiv.), respectively. The solution was allowed to stir at 0 ^oC for 30 minutes, and then transferred to a -78 ^oC solution of Weinreb amide **WA** in Et_2O (0.05 M) via cannula. The resulting mixture was allowed to warm to 0 ^oC over 2 hours, or until judged complete by TLC analysis. The reaction was quenched with deionized water, diluted with Et_2O, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with Et_2O (3x). The combined organic layers were then washed with brine (1x), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **INT** in 68-95% yield.

A round bottom flask equipped with a magnetic stir bar was charged with intermediate **INT** and sealed under a nitrogen atmosphere. Dry DMF (0.1 M) was added via syringe, and the reaction mixture was cooled to 0 ^oC. Potassium carbonate (2 eq) was added in one portion, and the reaction was allowed to stir at 0 ^oC for 30 minutes before prenyl bromide (1.2 eq) was added via syringe. The mixture was allowed to warm to room temperature over 3 hours, or until judged complete by TLC analysis. The reaction was

quenched with deionized water, diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with an aqueous 5% LiCl solution (3x), brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **S** in 71-86% yield.



(*S*)-4-methyl-*N*-(1-oxo-1-phenylpropan-2-yl)benzenesulfonamide (36 INT): Purification by flash column chromatography provided **36 INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.2 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.78 (m, *J* = 7.6 Hz, 1H), 5.00 – 4.83 (m, 1H), 2.31 (s, 3H), 1.40 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 198.2, 143.6, 137.1, 134.2, 133.4, 129.7, 128.9, 128.6, 127.1, 53.4, 21.5, 21.2.

(*S*)-4-methyl-*N*-(1-oxo-1-(p-tolyl)propan-2-yl)benzenesulfonamide (37 INT): Purification by flash column chromatography provided **37 INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.81 (d, *J* = 7.9 Hz, 1H), 4.89 (q, *J* = 7.2 Hz, 1H), 2.40 (s, 3H), 2.31 (s, 3H), 1.38 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.6, 145.2, 143.4, 137.1, 130.8, 129.6, 129.5, 128.6, 127.0, 53.2, 21.7, 21.4, 21.3.

(*S*)-4-methyl-*N*-(1-oxo-1-(p-*tert*-butyl)propan-2-yl)benzenesulfonamide (38 INT): Purification by flash column chromatography provided **38 INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 2H), 5.79 (d, *J* = 7.9 Hz, 1H), 5.00 – 4.92 (m, 1H), 2.32 (s, 3H), 1.44 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.6, 146.8, 143.5, 139.3, 137.1, 131.9, 129.7, 129.1, 129.0, 128.6, 127.4, 127.2, 127.0, 53.3, 21.5, 21.3.

(*S*)-4-methyl-*N*-(1-oxo-1-(m-tolyl)propan-2-yl)benzenesulfonamide (39 INT): Purification by flash column chromatography provided **39 INT** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.78 (d, *J* = 10.4 Hz, 1H), 4.91 (p, *J* = 7.3 Hz, 1H), 2.39 (s, 3H), 2.32 (s, 3H), 1.39 (d, *J* = 7.2 Hz, 3H); **^{13}C NMR** (176 MHz,

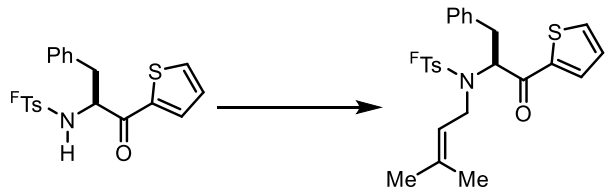
$CDCl_3$) δ 198.4, 143.6, 139.0, 137.2, 135.0, 133.5, 129.8, 129.1, 128.8, 127.2, 125.8, 53.5, 21.6, 21.5, 21.4.

(*S*)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-phenylpropan-2-yl)benzenesulfonamide (36 S): Purification by flash column chromatography provided **36 S** as a white solid. **^{1}H NMR** (700 MHz, C_6D_6) δ 8.32 (d, *J* = 7.8 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.14 – 7.11 (m, 3H), 6.73 (d, *J* = 7.9 Hz, 2H), 5.57 (q, *J* = 6.8 Hz, 1H), 4.97 (t, *J* = 7.0 Hz, 1H), 3.96 (dd, *J* = 15.3, 5.8 Hz, 1H), 3.55 (dd, *J* = 15.3, 8.0 Hz, 1H), 1.86 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H), 1.08 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 198.2, 143.7, 137.3, 136.9, 136.0, 133.1, 129.8, 129.0, 128.6, 127.7, 120.5, 77.2, 56.1, 42.7, 25.7, 21.7, 17.8, 13.3; **IR** (neat): 2924, 1687, 1597, 1448, 1378, 1340, 1229, 1159, 1090, 992, 954, 890, 816 cm^{-1}; **HRMS** calcd for $C_{21}H_{25}NO_3S^+$: 372.1628, found: 372.1623.

(*S*)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-(p-tolyl)propan-2-yl)benzenesulfonamide (37 S): Purification by flash column chromatography provided **37 S** as a white solid. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 5.48 (q, *J* = 6.8 Hz, 1H), 4.72 (t, *J* = 6.3 Hz, 1H), 3.77 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.58 (dd, *J* = 15.6, 7.8 Hz, 1H), 2.39 (s, 6H), 1.46 (s, 3H), 1.43 (s, 3H), 1.07 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 197.2, 143.4, 143.3, 137.0, 135.5, 133.0, 129.7, 128.9, 128.6, 127.2, 120.6, 55.9, 42.3, 25.4, 21.2, 21.0, 17.4, 13.0; **IR** (neat): 2925.0, 1597, 1513, 450, 1334, 1158, 094, 1048, 1016, 799 cm^{-1}; **HRMS** calcd for $C_{22}H_{27}NO_3S^+$: 386.1784, found 386.1789.

(*S*)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-N-(1-oxo-1-(p-*tert*-butyl)propan-2-yl)benzenesulfonamide (38 S): Purification by flash column chromatography provided **38 S** as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.4 Hz, 2H), 7.73 – 7.63 (m, 6H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 2H), 5.57 (q, *J* = 6.8 Hz, 1H), 4.82 (t, *J* = 7.5 Hz, 1H), 3.89 (dd, *J* = 15.4, 6.0 Hz, 1H), 3.62 (dd, *J* = 15.5, 7.8 Hz, 1H), 2.41 (s, 3H), 1.49 (s, 3H), 1.47 (s, 3H), 1.25 (t, *J* = 8.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.5, 145.4, 143.4, 139.8, 137.0, 136.7, 134.4, 129.5, 129.3, 128.9, 128.1, 127.5, 127.1, 126.9, 120.3, 55.9, 42.5, 25.4, 21.4, 17.5, 13.0; **IR** (neat): 2925, 1684, 1603, 1487, 1446, 1340, 1231, 1161, 1119, 1090, 993, 951, 892 cm^{-1}; **HRMS** calcd for $C_{27}H_{29,}NO_3S^+$: 448.1941, found 448.1934.

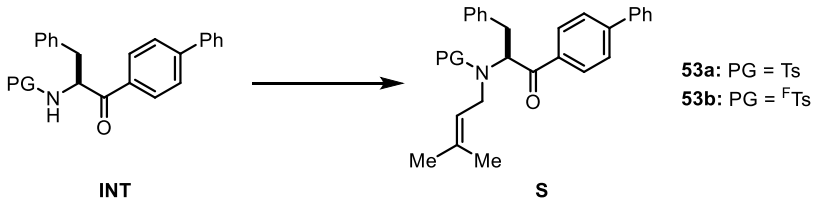
(*S*)-4-methyl-*N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-(m-tolyl)propan-2-yl)benzenesulfonamide (39 S): Purification by flash column chromatography provided **39 S** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.8 Hz, 2H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.25 (s, 1H), 5.54 (q, *J* = 6.8 Hz, 1H), 4.78 (t, *J* = 6.5 Hz, 1H), 3.86 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.60 (dd, *J* = 15.4, 7.7 Hz, 1H), 2.41 (s, 3H), 1.47 (s, 3H), 1.45 (s, 3H), 1.23 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 198.2, 143.7, 137.2, 136.9, 135.9, 133.1, 129.8, 128.9, 128.6, 127.7, 120.5, 56.1, 42.7, 25.7, 21.69, 21.67, 17.7, 13.3; **IR** (neat): 2964, 1684, 1604, 1444, 1378, 1339, 1233, 1160, 1090, 952, 892, 846 cm^{-1}**; HRMS** calcd for $C_{25}H_{30}NO_3S^+$: 386.1784; found: 386.1794.



43 INT **43 S**

(*S*)-N-(1-oxo-3-phenyl-1-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)benzene-sulfonamide (43 INT): Purification by flash column chromatography provided **43 INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 5.8 Hz, 1H), 7.69 (d, *J* = 5.8 Hz, 2H), 7.58 (d, *J* = 3.8 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.19 – 7.15 (m, 3H), 7.11 – 7.08 (m, 1H), 7.03 (m, 2H), 5.74 (d, *J* = 9.3 Hz, 1H), 4.95 – 4.91 (m, 1H), 3.16 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.98 (dd, *J* = 14.0, 7.3 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 189.8, 143.4, 140.9, 135.9, 135.1, 134.4 (q, *J* = 33.2 Hz), 133.4, 129.6, 128.7, 128.6, 127.4, 126.1 (q, *J* = 3.6 Hz), 60.0, 40.9.

(*S*)-N-(3-methylbut-2-en-1-yl)-N-(1-oxo-3-phenyl-1-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (43 S): Purification by flash column chromatography provided **43 S** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.91 (d, *J* = 3.8 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.65 (d, *J* = 5.6 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 2H), 7.19 (dd, *J* = 12.7, 7.1 Hz, 3H), 7.09 – 7.06 (m, 1H), 5.66 (dd, *J* = 8.9, 5.6 Hz, 1H), 4.90 (t, *J* = 6.8 Hz, 1H), 4.10 (dd, *J* = 16.1, 6.6 Hz, 1H), 3.95 (dd, *J* = 16.0, 7.1 Hz, 1H), 3.38 (dd, *J* = 13.8, 9.0 Hz, 1H), 2.78 (dd, *J* = 13.8, 5.6 Hz, 1H), 1.63 (s, 3H), 1.54 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.5, 139.1, 138.9, 137.1, 136.1, 135.9, 133.4, 129.3, 129.1, 128.9, 128.6, 128.5, 126.7, 125.8, 120.5, 60.7, 43.2, 34.9, 25.6, 17.7; **IR** (neat): 3060, 2829, 1665, 1643, 1607, 1500, 1460, 1413, 1403, 1322, 1247, 1162, 1132, 1093, 1062, 1014, 917, 886 cm^{-1}; **HRMS** calcd for $C_{25}H_{24}F_3NO_3S_2^{+Na}$: 530.1042, found: 530.1042.



INT **S**

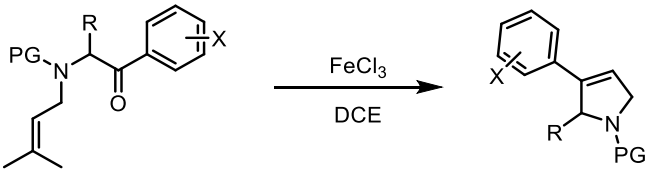
(*S*)-*N*-(1-([1,1'-biphenyl]-4-yl)-1-oxo-3-phenylpropan-2-yl)-4-methylbenzenesulfon-amide (53a INT): Purification by flash column chromatography provided **53a INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.67 – 7.58 (m, 6H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.23 – 7.15 (m, 3H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.02 (dd, *J* = 6.4, 2.9 Hz, 2H), 5.63 (d, *J* = 8.8 Hz, 1H), 5.17 (dt, *J* = 8.8, 5.8 Hz, 1H), 3.18 (dd, *J* = 13.9, 5.8 Hz, 1H), 3.01 (dd, *J* = 13.9, 5.9 Hz, 1H), 2.29 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.91, 146.77, 143.59, 139.50, 136.98, 135.07, 132.93, 129.79, 129.72, 129.19, 129.15, 128.72, 128.55, 127.50, 127.37, 127.26, 127.19, 58.33, 40.45, 21.58.

(*S*)-*N*-(1-([1,1'-biphenyl]-4-yl)-1-oxo-3-phenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (53b INT): Purification by flash column chromatography provided **53b INT** as a white solid. **^{1}H NMR** (401 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 7.0 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.02 (dd, *J* = 6.5, 2.9 Hz, 2H), 5.70 (d, *J* = 9.1 Hz, 1H), 5.20 (ddd, *J* = 9.0, 6.7, 5.4 Hz, 1H), 3.20 (dd, *J* = 14.0, 5.3 Hz, 1H), 2.96 (dd, *J* = 14.0, 6.9 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.4, 147.0, 143.4, 139.2, 134.8, 134.1 (q, *J* = 33.2 Hz), 132.4, 129.5, 129.04, 128.99, 128.6, 128.5, 127.6, 127.4, 127.3, 127.23, 126.02 (q, *J* = 3.6 Hz), 123.0 (q, *J* = 272.8 Hz), 58.6, 40.2.

(*S*)-*N*-(1-([1,1'-biphenyl]-4-yl)-1-oxo-3-phenylpropan-2-yl)-4-methyl-*N*-(3-methylbut-2-en-1-yl)benzenesulfonamide (53a S): Purification by flash column chromatography provided **53a S** as a clear, colorless oil. **^{1}H NMR** (400 MHz, $cdcl_3$) δ 8.05 (d, *J* = 8.4 Hz, 2H), 7.68 – 7.59 (m, 5H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.24 (dd, *J* = 11.4, 6.5 Hz, 6H), 7.18 (t, *J* = 10.7 Hz, 1H), 5.79 (dd, *J* = 9.9, 3.9 Hz, 1H), 4.87 (t, *J* = 6.7 Hz, 1H), 3.98 (dd, *J* = 16.0, 6.3 Hz, 1H), 3.81 (dd, *J* = 16.0, 7.3 Hz, 1H), 3.47 (dd, *J* = 13.4, 10.0 Hz, 1H), 2.68 (dd, *J* = 13.4, 3.9 Hz, 1H), 2.38 (s, 3H), 1.58 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (100 MHz, $cdcl_3$) δ 195.91, 145.91, 143.68, 139.96, 137.62, 137.54, 135.96, 134.81, 129.74, 129.58, 129.51, 129.09, 128.65, 128.38, 127.68, 127.37, 127.20, 126.68, 120.97, 60.95, 43.25, 34.49, 25.74, 21.65, 17.89; **IR** (neat): 2926, 1685, 1603, 1494, 1449, 1341, 1289, 1235, 1184, 1158, 1091, 945, 902, 845, 815 cm^{-1}; **HRMS** calcd for $C_{33}H_{33}NO_3S^{+}$: 524.2254, found: 524.2245.

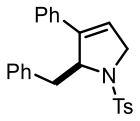
(*S*)-*N*-(1-([1,1'-biphenyl]-4-yl)-1-oxo-3-phenylpropan-2-yl)-*N*-(3-methylbut-2-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (53b S): Purification by flash column chromatography provided **53b S** as a clear, colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.55 – 7.48 (m, 6H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.19 – 7.07 (m, 5H), 5.75 (dd, *J* = 8.7, 5.5 Hz, 1H), 4.75 (t, *J* = 6.2 Hz, 1H), 3.94 (dd, *J* = 16.1, 6.5 Hz, 1H), 3.84 (dd, *J* = 16.0, 6.9 Hz, 1H), 3.35 (dd, *J* = 13.8, 8.8 Hz, 1H), 2.72 (dd, *J* = 13.8, 5.4 Hz, 1H), 1.51 (s, 3H), 1.43 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.2, 146.3, 144.2, 139.7, 137.1, 136.3, 134.6, 134.3 (q, *J* = 33.1 Hz), 129.5, 129.4, 129.1, 128.8, 128.54, 128.48, 128.1, 127.4, 127.0, 126.1 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 272.9 Hz), 120.7, 60.9, 43.5, 35.4, 25.8, 17.9; **IR** (neat): 2931, 1684, 1603, 1496, 1404, 1321, 1236, 1162, 1132, 1093, 1062, 1014, 975, 906, 843 cm^{-1}; **HRMS** calcd for $C_{30}H_{33}F_3NO_3S^{+Na}$: 600.1791, found: 600.1791.

2.4.5 General Procedure for the Carbonyl-Olefin Metathesis Reaction



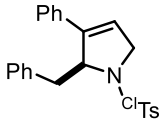
S

A round bottom flask equipped with a magnetic stir bar was charged with substrate **S** (0.25 mmol) and sealed under a nitrogen atmosphere. Dry DCE (0.01 M) was added via syringe, and the solution was cooled to 0 °C. To the stirring solution was added $FeCl_3$ (0.5 eq) in one portion. The reaction was allowed to warm to room temperature over 3 hours, or until judged complete by TLC analysis. The reaction mixture was filtered over a silica plug, eluting thoroughly with DCM, and the resulting eluent was concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired metathesis product.



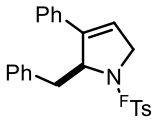
20

(*S*)-2-benzyl-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (20): Purification by flash column chromatography provided **20** as a white foam in 72% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.35 (dd, *J* = 14.5, 6.9 Hz, 3H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.1 Hz, 2H), 7.17 – 7.13 (m, 3H), 7.01 (dd, *J* = 6.4, 2.9 Hz, 2H), 5.62 (s, 1H), 5.30 (s, 1H), 4.05 (d, *J* = 15.8 Hz, 1H), 3.56 (dd, *J* = 15.8, 3.6 Hz, 1H), 3.36 (dd, *J* = 13.7, 4.7 Hz, 1H), 3.02 (dd, *J* = 13.7, 2.5 Hz, 1H), 2.39 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.6, 140.7, 136.3, 135.2, 133.4, 130.8, 129.9, 129.0, 128.4, 127.7, 127.3, 126.6, 126.4, 121.3, 67.4, 55.7, 39.8, 21.7; **IR** (neat): 2962, 1724, 1598, 1495, 1453, 1333, 1161, 1094, 910, 841 cm^{-1}; **HRMS** calcd for $C_{24}H_{23}NO_2S^+$: 389.1450, found 389.1452.



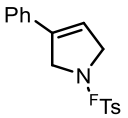
24

(*S*)-2-benzyl-1-((4-chlorophenyl)sulfonyl)-3-phenyl-2,5-dihydro-1H-pyrrole (24): Purification by flash column chromatography provided **24** as a clear, colorless oil in 96% yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 7.3 Hz, 3H), 7.27 (d, *J* = 3.8 Hz, 2H), 7.20 – 7.16 (m, 3H), 7.02 (d, *J* = 3.9 Hz, 2H), 5.66 (s, 1H), 5.29 (s, 1H), 4.03 (d, *J* = 15.7 Hz, 1H), 3.57 (dd, *J* = 15.7, 4.8 Hz, 1H), 3.36 (dd, *J* = 13.7, 4.7 Hz, 1H), 3.03 (d, *J* = 12.2 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.6, 139.2, 136.5, 135.9, 132.9, 130.6, 129.5, 128.9, 128.5, 128.4, 127.6, 126.4, 120.9, 67.4, 55.5, 39.6; **IR** (neat) 3061, 3028, 2928, 2853, 1585, 1495, 1476, 1454, 1476, 1447, 1394, 1335, 1162, 1098, 1088, 1012, 910 cm^{-1}; **HRMS** calcd for $C_{23}H_{20}ClNO_2S^+$: 410.0976, found: 410.0977.



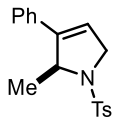
26

(*S*)-2-benzyl-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (26): Purification by flash column chromatography provided **26** as a white foam in 99% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.35 (dq, *J* = 14.2, 7.1 Hz, 3H), 7.27 (d, *J* = 4.6 Hz, 2H), 7.21 – 7.13 (m, 3H), 7.02 – 6.97 (m, 2H), 5.67 (s, 1H), 5.32 (s, 1H), 4.04 (d, *J* = 15.2 Hz, 1H), 3.57 (dd, *J* = 15.5, 3.8 Hz, 1H), 3.37 (dd, *J* = 13.7, 4.7 Hz, 1H), 3.03 (dd, *J* = 13.7, 2.4 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.8, 140.7, 135.9, 134.5 (q, *J* = 33.1 Hz), 132.9, 130.7, 129.1, 128.6, 127.8, 127.7, 126.6, 126.5, 126.5 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 272.9 Hz), 120.9, 67.6, 55.7, 39.7; **IR** (neat) 3060, 2917, 1495, 1454, 1402, 1320, 1248, 1163, 1130, 1105, 1061, 1014 cm^{-1}; **HRMS** calcd for $C_{24}H_{20}F_3NO_2S^+$: 444.1240, found: 444.1243.



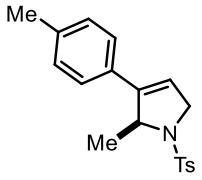
35

3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (35): Purification by flash column chromatography provided **35** as a white solid in 50% yield. **^{1}H NMR** (401 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.32 (m, 5H), 6.06 – 5.99 (m, 1H), 4.52 (dd, *J* = 5.7, 2.9 Hz, 2H), 4.34 (dd, *J* = 6.3, 4.4 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 141.0, 137.5, 134.6 (q, *J* = 33.1 Hz), 132.3, 128.9, 128.8, 128.0, 126.6 (q, *J* = 3.6 Hz), 125.5, 123.4 (q, *J* = 273.0 Hz), 118.7, 55.9, 55.1; **IR** (neat) 2860, 1608, 1498, 1473, 1448, 1402, 1343, 1322, 1187, 1154, 1108, 1081, 1060, 1008 cm^{-1}; **HRMS** calcd for $C_{17}H_{14}F_3NO_2S^+$: 354.0770, found: 354.0771.



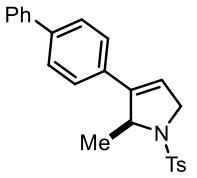
36

(*S*)-2-methyl-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (36): Purification by flash column chromatography provided **36** as a white solid in 84% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.35 – 7.24 (m, 7H), 5.82 (q, *J* = 2.0 Hz, 1H), 5.04 – 4.97 (m, 1H), 4.33 – 4.23 (m, 2H), 2.40 (s, 3H), 1.47 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 143.56, 143.48, 135.2, 133.1, 129.9, 128.8, 128.3, 127.4, 126.5, 118.9, 63.0, 54.9, 22.2, 21.7; **IR** (neat): 2923, 2360, 1598, 1496, 1448, 1339, 1161, 1095, 815, 755 cm^{-1}; **HRMS** calcd for $C_{18}H_{19}NO_2S^+$: 13.1136, found: 13.1138.



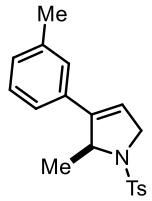
37

(*S*)-2-methyl-3-(p-tolyl)-1-tosyl-2,5-dihydro-1H-pyrrole (37): Purification by flash column chromatography provided **37** as a white solid in 74% yield. **^{1}H NMR** (700 MHz, DMSO-d_6) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 5.97 (s, 1H), 5.03 – 4.96 (m, 1H), 4.20 (dd, *J* = 16.0, 3.4 Hz, 1H), 4.14 (d, *J* = 15.9 Hz, 1H), 2.35 (s, 3H), 2.27 (s, 3H), 1.34 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR** (176 MHz, DMSO-d_6) δ 143.3, 142.0, 137.5, 134.1, 129.8, 129.6, 129.2, 127.2, 126.2, 118.5, 62.1, 54.9, 22.1, 20.9, 20.7; **IR** (neat): 2864, 1597, 1514, 1450, 1335, 1158, 1094, 812 cm^{-1}; **HRMS** calcd for $C_{19}H_{21}NO_2S^+$: 328.1366, found: 328.1367.



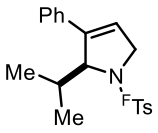
38

(*S*)-3-([1,1'-biphenyl]-4-yl)-2-methyl-1-tosyl-2,5-dihydro-1H-pyrrole (38): Purification by flash column chromatography provided **38** as a yellow oil in 67% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.57 (t, *J* = 9.1 Hz, 4H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.88 (s, 1H), 5.07 – 5.02 (m, 1H), 4.35 – 4.27 (m, 2H), 2.40 (s, 3H), 1.52 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 143.6, 143.1, 141.1, 140.4, 135.2, 132.0, 129.9, 129.0, 127.7, 127.5, 127.4, 127.1, 126.9, 119.0, 63.0, 54.9, 22.3, 21.7; **IR** (neat): 2928, 1598, 1489, 1448, 1336, 1161, 1095, 1050, 910, 815 cm^{-1}; **HRMS** calcd for $C_{24}H_{23}NO_2S^+$: 390.1521, found 390.1521.



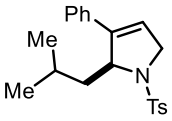
39

(*S*)-2-methyl-3-(m-tolyl)-1-tosyl-2,5-dihydro-1H-pyrrole (39): Purification by flash column chrom-atography provided **39** as a clear yellow oil in 97% yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.07 (dd, *J* = 15.9, 9.5 Hz, 3H), 5.80 (s, 1H), 5.04 – 4.94 (m, 1H), 4.27 (m, 2H), 2.40 (s, 3H), 2.34 (s, 3H), 1.47 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.5, 143.4, 138.3, 135.1, 132.9, 129.7, 128.9, 128.5, 127.2, 127.0, 123.4, 118.5, 62.9, 54.7, 22.1, 21.5, 21.4; **IR** (neat): 2923, 598, 1493, 1451, 1340, 1161, 1095 1051, 1016, 815 cm^{-1}; **HRMS** calcd for $C_{19}H_{21}NO_2S^+$: 328.1366, found: 328.1369.



40

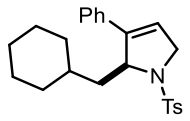
(*S*)-2-isopropyl-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (40): Purification by flash column chromatography provided **40** as a colorless oil in 32% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.35 – 7.27 (m, 3H), 7.25 – 7.20 (m, 2H), 5.79 (s, 1H), 5.02 (s, 1H), 4.32 – 4.12 (m, 2H), 2.15 – 2.00 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.6, 141.8, 134.5 (q, *J* = 33.3 Hz), 133.7, 128.9, 128.5, 128.0, 126.7, 126.3 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 273.1 Hz), 120.7, 73.0, 56.6, 32.8, 19.7, 16.9; **IR** (neat) 3062, 3029, 2966, 2929, 2874, 1608, 1577, 1496, 1463, 1447, 1402, 1389, 1351, 1320, 1164, 1129, 1107, 1061, 1014 cm^{-1}; **HRMS** calcd for $C_{20}H_{20}F_3NO_2S^+$: 396.1240, found: 396.1237.



41

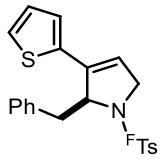
***(S)*-2-isobutyl-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (41):** Purification by flash column chromatography provided **41** as a pale yellow oil in 67% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.29 – 7.21 (m, 5H), 5.77 (s, 1H), 5.09 – 5.02 (m, 1H), 4.31 (d, *J* = 16.5 Hz, 1H), 4.24 (d, *J* = 16.5 Hz, 1H), 2.35 (s, 3H), 2.04 (dt, *J* = 13.3, 6.5 Hz, 1H), 1.56 (t, *J* = 6.0 Hz, 2H), 1.06 (d, *J* = 6.1 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.49, 143.45, 134.9, 133.2, 129.7, 128.7, 128.2, 127.4, 126.3, 119.5, 65.9, 55.0, 43.2, 24.3, 24.0, 22.4, 21.6; **IR** (neat) 2953,

1598, 1494, 1446, 1336, 1160, 1093, 1043, 911, 813, 752, 729, 678, 662 cm^{-1}; **HRMS** calcd for $C_{21}H_{25}NO_2S^+$: 356.1679, found: 356.1684.



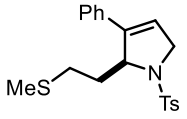
42

(*S*)-2-(cyclohexylmethyl)-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (42): Purification by flash column chromatography provided **42** as a pale yellow oil in 66% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.18 (m, 7H), 5.75 (s, 1H), 5.07 (dt, *J* = 7.6, 3.6 Hz, 1H), 4.26 (ddd, *J* = 12.8, 3.3, 1.6 Hz, 2H), 2.35 (s, 3H), 2.12 – 2.03 (m, 1H), 1.75 – 1.43 (m, 7H), 1.37 – 1.01 (m, 3H), 0.86 (dqd, *J* = 27.6, 12.4, 3.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.6, 143.5, 135.0, 133.3, 129.7, 128.8, 128.2, 127.4, 126.4, 119.5, 65.4, 55.0, 41.9, 34.5, 33.5, 33.2, 26.7, 26.5, 26.3, 21.6; **IR** (neat) 2921, 2853, 1713, 1599, 1494, 1340, 1156, 1089, 1038, 814, 736, 684, 662 cm^{-1}; **HRMS** calcd for $C_{24}H_{29}NO_2S^+$: 396.1992, found: 396.1987.



43

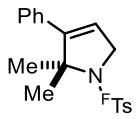
(*S*)-2-benzyl-3-(thiophen-2-yl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (43): Purification by flash column chromatography provided **43** as a pale yellow oil in 66% yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 2H), 7.75 (d, *J* = 7.2 Hz, 2H), 7.25 (s, 1H), 7.18 (s, 3H), 7.06 (s, 2H), 7.02 (s, 1H), 6.98 (s, 1H), 5.57 (s, 1H), 5.18 (s, 1H), 3.97 (d, *J* = 15.9 Hz, 1H), 3.49 (d, *J* = 14.4 Hz, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.17 (d, *J* = 13.8 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.7, 136.2, 135.5, 134.5, 134.4 (q, *J* = 33.2 Hz), 130.6, 127.8, 127.7, 127.5, 126.3 (q, *J* = 3.4 Hz), 125.8, 125.1, 120.3, 68.2, 55.2, 40.0; **IR** (neat) 3030, 2930, 2865, 1608, 1495, 1454, 1404, 1321, 1164, 1131, 1107, 1062, 1032, 1014, 909, 873 cm^{-1}; **HRMS** calcd for $C_{22}H_{18}F_3NO_2S_2^+$: 450.0804, found: 450.0802.



44

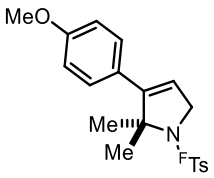
2-(2-(methylthio)ethyl)-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (44): Purification by flash column chromatography provided **44** as a colorless oil in 64% yield. **^{1}H NMR** (700 MHz, CD_2Cl_2) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.32 (t, *J* = 8.4 Hz, 4H), 7.27 (dd, *J* = 7.6, 6.5

Hz, 3H), 5.85 (s, 1H), 5.12 – 5.09 (m, 1H), 4.32 – 4.21 (m, 2H), 2.66 – 2.60 (m, 1H), 2.41 – 2.35 (m, 4H), 2.20 – 2.12 (m, 1H), 1.96 (s, 3H), 1.94 – 1.87 (m, 1H); **^{13}C NMR** (176 MHz, CD_2Cl_2) δ 144.2, 141.6, 134.9, 133.1, 130.2, 129.1, 128.7, 127.6, 126.7, 120.8, 66.4, 56.0, 33.7, 29.1, 21.6, 15.5; **IR** (neat) 3060, 3028, 2916, 2861, 1597, 1494, 1446, 1400, 1333, 1306, 1291, 1260, 1191, 1157, 1092, 1059, 1017 cm^{-1}; **HRMS** calcd for $C_{20}H_{23}NO_2S_2^+$: 374.1243, found: 374.1245.



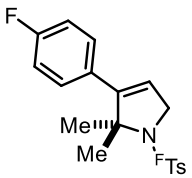
45

2,2-dimethyl-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (45): Purification by flash column chromatography provided **45** as a white solid in 92% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.31 (m, 3H), 7.21 – 7.17 (m, 2H), 5.61 (t, *J* = 2.1 Hz, 1H), 4.21 (d, *J* = 2.1 Hz, 2H), 1.61 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.5, 144.8, 134.6, 134.1 (q, *J* = 33.0 Hz), 128.7, 128.4, 128.2, 127.9, 126.2 (q, *J* = 3.6 Hz), 123.5 (q, *J* = 272.8 Hz), 119.7, 73.7, 53.7, 27.2; **IR** (neat) 2961, 2932, 2862, 1608, 1494, 1462, 1442, 1402, 1336, 1320, 1217, 1159, 1128, 1106, 1097, 1061, 1014 cm^{-1}, **HRMS** calcd for $C_{19}H_{18}F_3NO_2S^+$: 382.1083, found: 382.1081.



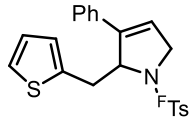
46

3-(4-methoxyphenyl)-2,2-dimethyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (46): Purification by flash column chromatography provided **46** as a white solid in 71% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.3 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.55 (t, *J* = 2.0 Hz, 1H), 4.17 (d, *J* = 2.1 Hz, 2H), 3.79 (s, 3H), 1.58 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.5, 148.0, 144.7, 134.0 (q, *J* = 32.9 Hz), 129.7, 127.8, 126.8, 126.2 (dd, *J* = 7.1, 3.5 Hz), 123.4 (q, *J* = 272.9 Hz), 119.1, 113.8, 73.6, 55.4, 53.5, 27.1; **IR** (neat) 2932, 2839, 1734, 1607, 1572, 1511, 1462, 1337, 1320, 1295, 1259, 1246, 1217, 1160, 1127, 1106, 1098, 1061, 1034, 1015 cm^{-1}; **HRMS** calcd for $C_{20}H_{20}F_3NO_3S^+$: 412.1189, found: 412.1191.



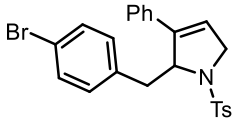
47

3-(4-fluorophenyl)-2,2-dimethyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (47): Purification by flash column chromatography provided **47** as a white solid in 87% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.16 (dd, *J* = 8.3, 5.6 Hz, 2H), 7.02 (t, *J* = 8.6 Hz, 2H), 5.60 (s, 1H), 4.20 (d, *J* = 1.4 Hz, 2H), 1.59 (s, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 162.7 (d, *J* = 247.6 Hz), 147.5, 144.6, 134.1 (q, *J* = 33.0 Hz), 130.5 (d, *J* = 3.4 Hz), 130.40, 130.36, 126.2 (q, *J* = 3.6 Hz), 123.4 (q, *J* = 272.8 Hz), 120.2, 115.4 (d, *J* = 21.4 Hz), 73.5, 53.6, 27.1; **IR** (neat) 2932, 2866, 2356, 2334, 1599, 1500, 1461, 1402, 1338, 1322, 1305, 1299, 1213, 1156, 1125, 1097, 1064, 1016 cm^{-1}; **HRMS** calcd for $C_{19}H_{17}F_4NO_2S^+$: 400.0989, found: 400.0985.



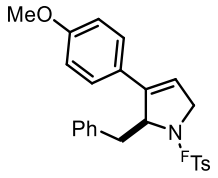
48

3-phenyl-2-(thiophen-2-ylmethyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (48): Purification by flash column chromatography provided **48** as a pale yellow oil in 84% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.22 (m, 5H), 7.11 (dd, *J* = 5.2, 1.1 Hz, 1H), 6.83 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.54 (d, *J* = 3.4 Hz, 1H), 5.74 (q, *J* = 2.0 Hz, 1H), 5.30 (td, *J* = 4.6, 2.1 Hz, 1H), 4.15 (dt, *J* = 15.4, 2.2 Hz, 1H), 3.90 (ddd, *J* = 15.4, 5.4, 1.9 Hz, 1H), 3.59 (dd, *J* = 15.0, 4.4 Hz, 1H), 3.27 (dd, *J* = 15.0, 2.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.9, 140.5, 137.0, 134.6 (q, *J* = 33.3 Hz), 132.8, 129.0, 128.7, 127.8, 127.5, 126.6, 126.5 (q, *J* = 3.8 Hz), 126.4, 124.8, 123.3 (q, *J* = 273.4 Hz), 121.3, 67.3, 56.0, 34.1; **IR** (neat) 2922, 1598, 1496, 1403, 1321, 1166, 1131, 1106, 1062, 1014, 842, 800, 755, 737, 713, 693, 669 cm^{-1}; **HRMS** calcd for $C_{22}H_{18}F_3NO_2S_2^+$: 450.0804, found: 450.0803.



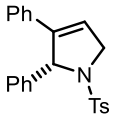
49

(*S*)-2-(4-bromobenzyl)-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (49): Purification by flash column chromatography provided **49** as a white solid in 79% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 8.2 Hz, 2H), 5.64 (s, 1H), 5.26 (s, 1H), 4.04 (d, *J* = 15.7 Hz, 1H), 3.58 (dd, *J* = 15.7, 5.0 Hz, 1H), 3.32 (dd, *J* = 13.8, 4.7 Hz, 1H), 2.96 (dd, *J* = 13.7, 2.2 Hz, 1H), 2.39 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.8, 140.3, 135.3, 134.9, 133.1, 132.5, 130.8, 130.0, 129.0, 128.5, 127.3, 126.5, 121.4, 120.6, 67.1, 55.7, 39.1, 21.7; **IR** (neat): 2922, 1598, 1487, 1447, 1404, 323, 1162, 1134, 1105, 1062, 1012, 911, 816 cm^{-1}; **HRMS** calcd for $C_{24}H_{22}BrNO_2S^+$: 468.0627, found: 468.0629.



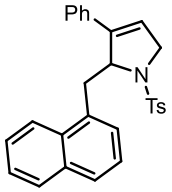
50

(*S*)-2-benzyl-3-(4-methoxyphenyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (50): Purification by flash column chromatography provided **50** as a white solid in 93% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 6.5 Hz, 3H), 7.03 – 6.99 (m, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.54 (s, 1H), 5.28 (s, 1H), 4.01 (d, *J* = 15.4 Hz, 1H), 3.84 (s, 3H), 3.55 (dd, *J* = 15.4, 5.0 Hz, 1H), 3.35 (dd, *J* = 13.7, 4.5 Hz, 1H), 3.03 (d, *J* = 13.6 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 159.8, 141.9, 140.2, 136.0, 134.5 (q, *J* = 33.2 Hz), 130.8, 127.84, 127.78, 127.7, 126.6, 126.5 (q, *J* = 3.5 Hz), 125.6, 123.3 (q, *J* = 272.9 Hz), 118.9, 114.4, 67.7, 55.6, 55.5, 39.7; **IR** (neat): 2935, 1608, 1513, 1454, 1403, 1322, 1259, 1165, 1132, 1107, 1062, 1033, 1015, 910, 840 cm^{-1}; **HRMS** calcd for $C_{25}H_{22}F_3NO_3S^+$: 474.1345, found: 474.1346.



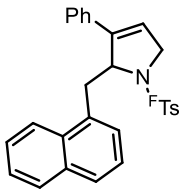
51

(*R*)-2,3-diphenyl-1-tosyl-2,5-dihydro-1H-pyrrole (51): Purification by flash column chromatography provided **51** as a clear oil in 97% yield. Characterization matches previously reported product.[4]



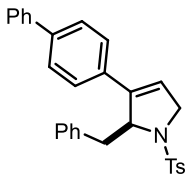
52a

(*S*)-2-(naphthalen-1-ylmethyl)-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (52a): Purification by flash column chromatography provided **52a** as a pale yellow solid in 82% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 – 8.10 (m, 1H), 7.75 (dd, *J* = 9.7, 6.9 Hz, 3H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.21 – 7.10 (m, 4H), 7.04 – 6.97 (m, 3H), 5.59 (s, 1H), 5.50 (d, *J* = 4.6 Hz, 1H), 4.05 (dd, *J* = 16.1, 2.0 Hz, 1H), 3.75 – 3.51 (m, 3H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.6, 142.1, 135.0, 133.74, 133.68, 133.1, 132.9, 129.9, 129.2, 128.6, 128.3, 128.1, 127.3, 127.2, 126.4, 125.7, 125.4, 125.0, 124.9, 121.4, 67.4, 55.2, 38.1, 21.6; **IR** (neat) 2930, 1653, 1340, 1204, 1176, 1155, 1096, 760, 679, 660 cm^{-1}; **HRMS** calcd for $C_{28}H_{25}NO_2S^+$: 440.1679, found: 440.1679.



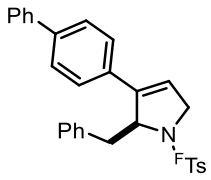
52b

(*S*)-2-(naphthalen-1-ylmethyl)-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (52b): Purification by flash column chromatography provided **52b** as a white foam in 91% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.9 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.44 (p, *J* = 6.7 Hz, 2H), 7.23 (q, *J* = 7.1, 6.2 Hz, 3H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 8.0 Hz, 3H), 5.66 (s, 1H), 5.55 (q, *J* = 4.9 Hz, 1H), 4.08 (dd, *J* = 16.0, 2.7 Hz, 1H), 3.73 (dd, *J* = 14.2, 6.2 Hz, 1H), 3.63 (ddd, *J* = 20.4, 15.0, 4.2 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 142.2, 141.7, 134.4 (q, *J* = 33.2 Hz), 133.7, 133.2, 132.8, 132.7, 129.1, 128.8, 128.5, 128.4, 127.6, 127.4, 126.4 (q, *J* = 3.5 Hz), 126.3, 125.8, 125.5, 125.0, 124.7, 123.3 (q, *J* = 274.6 Hz), 121.0, 67.6, 55.1, 37.8; **IR** (neat) 3054, 1608, 1496, 1447, 1402, 1321, 1164, 1129, 1106, 1062, 1014, 842, 796, 777, 754, 736, 712, 693, 671 cm^{-1}; **HRMS** calcd for $C_{28}H_{22}F_3NO_2S^+$: 494.1396, found: 494.1394.



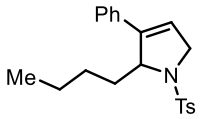
53a

(*S*)-3-([1,1'-biphenyl]-4-yl)-2-benzyl-1-tosyl-2,5-dihydro-1H-pyrrole (53a): Purification by flash column chromatography provided **53a** as a clear, colorless oil in 53% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 4H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.31 (dd, *J* = 10.8, 8.3 Hz, 4H), 7.20 – 7.15 (m, 3H), 7.05 (dd, *J* = 6.3, 2.8 Hz, 2H), 5.67 (s, 1H), 5.33 (s, 1H), 4.06 (d, *J* = 15.8 Hz, 1H), 3.57 (dd, *J* = 15.8, 5.1 Hz, 1H), 3.38 (dd, *J* = 13.7, 4.8 Hz, 1H), 3.07 (dd, *J* = 13.7, 2.4 Hz, 1H), 2.39 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.65, 141.10, 140.38, 140.32, 136.31, 135.18, 132.27, 130.85, 129.96, 129.03, 127.77, 127.72, 127.59, 127.28, 127.09, 126.98, 126.43, 121.34, 67.45, 55.70, 39.89, 21.67; **IR** (neat): 2922, 1599, 1488, 1452, 1334, 1161, 1095, 847, 814 cm^{-1}; **HRMS** calcd for $C_{30}H_{27}NO_2S^+$: 466.1835, found: 466.187.



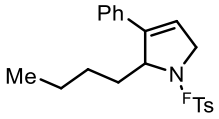
53b

(*S*)-3-([1,1'-biphenyl]-4-yl)-2-benzyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (53b): Purification by flash column chromatography provided **53b** as a clear, colorless oil in 93% yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 7.9 Hz, 4H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.22 – 7.16 (m, 3H), 7.05 (dd, *J* = 6.3, 2.9 Hz, 2H), 5.73 (s, 1H), 5.37 (s, 1H), 4.07 (d, *J* = 15.7 Hz, 1H), 3.60 (ddd, *J* = 15.6, 5.0, 1.4 Hz, 1H), 3.40 (dd, *J* = 13.8, 4.8 Hz, 1H), 3.10 (dd, *J* = 13.8, 2.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.9, 141.4, 140.4, 140.3, 135.9, 134.6 (q, *J* = 33.0 Hz), 131.8, 130.8, 129.1, 127.8, 127.70, 127.69, 127.1, 127.0, 126.6, 126.5 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 272.9 Hz), 121.0, 67.7, 55.7, 39.8; **IR** (neat): 2926, 1603, 1488, 1403, 1321, 1165,1132, 1106, 1062, 1014, 909, 883, 844 cm^{-1}; **HRMS** calcd for $C_{30}H_{24}F_3NO_2S^+$: 520.1553, found: 520.1551.



54a

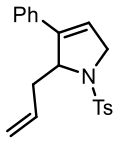
2-butyl-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (54a): Purification by flash column chromatography provided **54a** as a pale yellow oil in 75% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.36 – 7.21 (m,7H), 5.81 (s, 1H), 5.07 (s, 1H), 4.35 – 4.18 (m, 2H), 2.38 (s, 3H), 1.95 (ddd, *J* = 18.2, 9.8, 4.3 Hz, 1H), 1.73 – 1.58 (m, 1H), 1.40 – 1.07 (m, 4H), 0.78 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 143.5, 141.9, 135.2, 133.3, 129.8, 128.8, 128.3, 127.3, 126.4, 119.9, 67.1, 55.7, 33.5, 25.5, 22.7, 21.6, 14.2; **IR** (neat) 2956, 2927, 2856, 1598, 1494, 1446, 1340, 1333, 1188, 1160, 1134, 1123, 1097, 1074, 1058, 1019 cm^{-1}; **HRMS** calcd for $C_{21}H_{25}NO_2S^+$: 356.1679, found: 356.1670.



54b

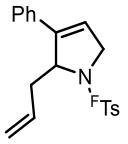
2-butyl-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (54b): Purification by flash column chromatography provided **54b** as a pale yellow oil in 94% yield. **^{1}H NMR** (700 MHz, C_6D_6) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 7.02 (t, *J* = 7.5 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.94 (d, *J* = 7.3 Hz, 2H), 5.18 – 5.12 (m, 2H), 4.04 (d, *J* = 15.8 Hz, 1H), 3.90 (dd, *J* = 15.8, 3.6 Hz, 1H), 2.06 (ddt, *J* = 15.9, 11.8, 4.3 Hz, 1H), 1.62 (ddt, *J* = 16.1, 11.7, 4.4 Hz, 1H), 1.34 – 1.26 (m, 1H), 1.20 – 1.12 (m, 1H), 1.12 – 1.06 (m, 1H), 1.06 – 0.97 (m, 1H), 0.71 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (126

MHz, $CDCl_3$) δ 142.1, 141.9, 134.5 (q, *J* = 33.0 Hz), 132.9, 128.9, 128.6, 127.8, 126.40, 126.40 (q, *J* = 3.3 Hz), 123.4 (q, *J* = 273.2 Hz), 119.6, 67.4, 55.8, 33.3, 25.4, 22.7, 14.1; **IR** (neat) 2958, 2934, 2861, 1608, 1496, 1466, 1448, 1403, 1349, 1340, 1321, 1165, 1130, 1106, 1061, 1014 cm^{-1}; **HRMS** calcd for $C_{21}H_{22}F_3NO_2S^+$: 410.1396, found: 410.1397.



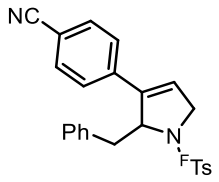
55a

2-allyl-3-phenyl-1-tosyl-2,5-dihydro-1H-pyrrole (55a): Purification by flash column chromatography provided **55a** as a pale yellow oil in 64% yield. **^{1}H NMR** (700 MHz, DMSO-d_6) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 4H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.3 Hz, 1H), 6.06 (s, 1H), 5.66 (td, *J* = 17.2, 7.1 Hz, 1H), 5.17 (d, *J* = 4.1 Hz, 1H), 4.96 (d, *J* = 10.0 Hz, 1H), 4.84 (d, *J* = 17.0 Hz, 1H), 4.16 (d, *J* = 16.1 Hz, 1H), 4.09 (dd, *J* = 16.1, 3.6 Hz, 1H), 2.60 (ddd, *J* = 14.6, 6.9, 4.3 Hz, 1H), 2.41 (ddd, *J* = 14.5, 7.1, 3.8 Hz, 1H), 2.34 (s, 3H); **^{13}C NMR** (176 MHz, DMSO-d_6) δ 143.4, 140.1, 134.2, 132.7, 132.5, 129.8, 128.6, 128.1, 127.3, 126.3, 121.0, 118.2, 65.7, 55.4, 37.9, 20.9; **IR** (neat): 2922, 1598, 1495, 1446, 1349, 1331, 1160, 1094, 1059, 996, 916, 816 cm^{-1}; **HRMS** calcd for $C_{20}H_{21}NO_2S^+$: 340.1366, found: 340.1371.



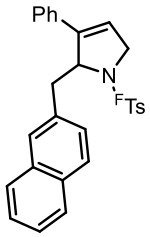
55b

2-allyl-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (55b): Purification by flash column chromatography provided **55b** as a colorless oil in 92% yield. **^{1}H NMR** (400 MHz, C_6D_6) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 7.06 – 6.98 (m, 3H), 6.89 (dd, *J* = 7.6, 1.8 Hz, 2H), 5.69 (ddt, *J* = 17.3, 10.2, 7.2 Hz, 1H), 5.18 (s, 1H), 5.12 (d, *J* = 3.2 Hz, 1H), 4.99 – 4.81 (m, 2H), 4.03 – 3.95 (m, 1H), 3.86 (ddd, *J* = 15.6, 5.1, 1.8 Hz, 1H), 2.92 – 2.82 (m, 1H), 2.35 (ddd, *J* = 14.4, 7.0, 3.3 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.1, 141.3, 134.5 (q, *J* = 33.1 Hz), 132.8, 132.0, 128.9, 128.6, 127.8, 126.5, 126.4 (q, *J* = 3.7 Hz), 123.3 (q, *J* = 272.9 Hz), 120.1, 119.1, 67.0, 55.8, 37.9; **IR** (neat) 3079, 2981, 2921, 2866, 1642, 1609, 1577, 1497, 1467, 1447, 1403, 1351, 1320, 1164, 1129, 1105, 1061, 1014 cm^{-1}; **HRMS** calcd for $C_{20}H_{18}F_3NO_2S^+$: 394.1083, found: 394.1085.



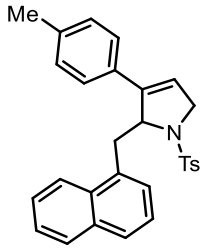
56

(*S*)-4-(2-methyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrol-3-yl)benzonitrile (56): Purification by flash column chromatography provided **56** as a yellow oil in 50% yield. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.41 – 7.35 (m, 3H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 5.69 (s, 1H), 5.31 (s, 1H), 4.04 (d, *J* = 15.7 Hz, 1H), 3.60 (ddd, *J* = 15.7, 5.2, 1.4 Hz, 1H), 3.47 (dd, *J* = 13.6, 4.9 Hz, 1H), 3.11 (dd, *J* = 13.6, 2.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.8, 141.2, 140.3, 134.9 (q, *J* = 33.2 Hz), 132.5, 131.6, 131.5, 129.3, 129.0, 127.8, 126.7 (q, *J* = 3.6 Hz), 126.5, 123.3 (q, *J* = 273.0), 121.2, 119.1, 110.7, 67.3, 55.8, 39.8; **IR** (neat): 2923, 2228 1608, 1496, 1447, 1403, 1321, 1166, 1132, 1107, 1062 1014, 911, 833 cm^{-1}; **HRMS** calcd for $C_{25}H_{19}F_3N_2O_2S^+$: 469.1192, found: 469.1191.



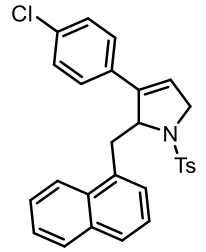
57

(*R*)-2-(naphthalen-2-ylmethyl)-3-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-2,5-dihydro-1H-pyrrole (57): Purification by flash column chromatography provided **57** as a white foam in 87% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.78 (dd, *J* = 9.1, 2.9 Hz, 3H), 7.65 (t, *J* = 8.4 Hz, 2H), 7.46 – 7.33 (m, 5H), 7.33 (s, 1H), 7.32 – 7.24 (m, 2H), 7.21 (dd, *J* = 8.4, 1.7 Hz, 1H), 5.60 (t, *J* = 1.9 Hz, 1H), 5.41 (dq, *J* = 3.3, 1.6 Hz, 1H), 4.03 (ddd, *J* = 15.7, 2.7, 1.4 Hz, 1H), 3.58 – 3.48 (m, 2H), 3.20 (dd, *J* = 13.8, 2.7 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.9, 140.8, 134.5 (q, *J* = 33.2 Hz), 133.6, 133.2, 133.0, 132.4, 129.3, 129.1, 129.1, 128.7, 127.8, 127.7, 127.6, 127.2, 126.6, 126.5 (q, *J* = 3.7 Hz), 125.8, 125.5, 123.3 (q, *J* = 274.7), 121.0, 67.8, 55.7, 39.8; **IR** (neat) 2928, 1600, 1403, 1322, 1166, 1132, 1107, 1062, 1015, 844, 820, 754, 715, 672 cm^{-1}; **HRMS** calcd for $C_{28}H_{22}F_3NO_2S^+$: 494.1396, found: 494.1396.



58

(*S*)-2-(naphthalen-1-ylmethyl)-3-(p-tolyl)-1-tosyl-2,5-dihydro-1H-pyrrole (58): Purification by flash column chromatography provided **58** as a pale yellow solid in 72% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 – 8.14 (m, 1H), 7.80 – 7.70 (m, 3H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.07 – 6.99 (m, 3H), 6.95 (d, *J* = 7.9 Hz, 2H), 5.53 (s, 1H), 5.49 (d, *J* = 4.8 Hz, 1H), 4.02 (dd, *J* = 16.1, 2.8 Hz, 1H), 3.74 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.60 (dd, *J* = 14.0, 3.5 Hz, 1H), 3.50 (dd, *J* = 16.0, 3.7 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.5, 141.8, 138.0, 135.1, 133.7, 133.2, 133.0, 130.8, 129.8, 129.3, 129.2, 128.3, 127.2, 127.1, 126.3, 125.7, 125.4, 125.1, 124.9, 120.4, 67.5, 55.1, 37.7, 21.6, 21.3; **IR** (neat) 2923, 1596, 1558, 1457, 1335, 1184, 1158, 1100, 1055, 798, 778, 735, 709, 667 cm^{-1}; **HRMS** calcd for $C_{29}H_{27}NO_2S^+$: 454.1835, found: 454.1837.

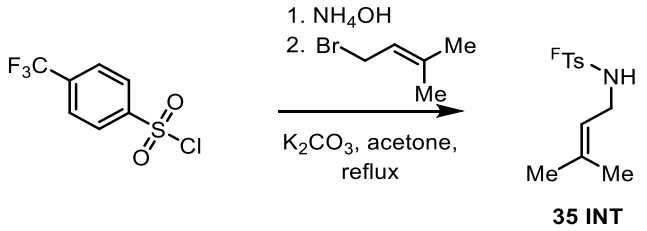


59

(*S*)-3-(4-chlorophenyl)-2-(naphthalen-1-ylmethyl)-1-tosyl-2,5-dihydro-1H-pyrrole (59): Purification by flash column chromatography provided **59** as a yellow solid in 75% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 – 8.12 (m, 1H), 7.80 – 7.71 (m, 3H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.14 – 7.09 (m, 1H), 7.06 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 7.0 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 5.60 (s, 1H), 5.47 – 5.39 (m, 1H), 4.09 (dd, *J* = 16.3, 1.9 Hz, 1H), 3.76 – 3.62 (m, 2H), 3.61 (dd, *J* = 14.0, 6.9 Hz, 1H), 2.36 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.7, 141.4, 135.0, 133.8, 133.7, 133.0, 132.7, 132.3, 129.9, 129.0, 128.6, 128.5, 127.6, 127.3, 127.3, 125.9, 125.5, 125.0, 124.7, 122.0, 67.3, 55.1, 38.7, 21.7; **IR** (neat) 2927, 1596, 1492, 1345, 1160, 1092, 1013, 802, 778, 738, 709, 666 cm^{-1}; **HRMS** calcd for $C_{28}H_{24}ClNO_2S^+$: 474.1289, found: 474.1284.

2.4.6 Miscellaneous Procedures

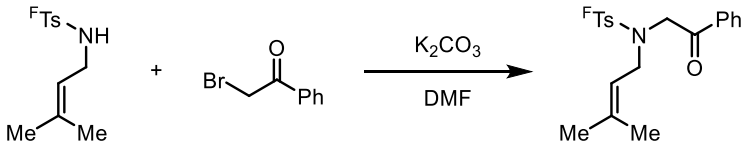
Glycine Substrate Synthesis



35 INT

***N*-(3-methylbut-2-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (35 INT):** A round bottom flask equipped with a magnetic stir bar was charged with 4-(trifluoromethyl)benzenesulfonyl chloride. The solid was suspended in a 30% ammonium hydroxide solution (0.1 M) and allowed to stir at room temperature for 16 hours. The reaction mixture was diluted with EtOAc, and aqueous hydrochloric acid (1 M) was added until the pH was less than 9, then the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. A magnetic stir bar and K_2CO_3 (2 eq) were added to the flask containing the crude sulfonamide, which was subsequently sealed under nitrogen. The crude mixture was suspended in acetone (0.1 M) and allowed to stir for 30 minutes, at which point prenyl bromide (0.67 eq) was added via syringe. The flask was fitted with a reflux condenser and allowed to stir at reflux for 14 hours. Deionized water and EtOAc were added to the reaction mixture, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **35 INT** (65%

over two steps) as yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 5.04 (t, *J* = 5.7 Hz, 1H), 4.99 (t, *J* = 7.4 Hz, 1H), 3.58 (t, *J* = 6.6 Hz, 2H), 1.57 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.0, 138.0, 134.3 (q, *J* = 33.0 Hz), 127.8, 126.2 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.8 Hz), 118.6, 41.2, 25.5, 17.8.

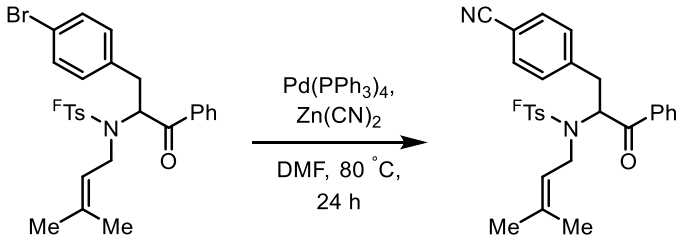


35 INT **35 S**

***N*-(3-methylbut-2-en-1-yl)-*N*-(2-oxo-2-phenylethyl)-4-(trifluoromethyl)benzenesulfonamide (35 S):** A round bottom flask equipped with a magnetic stir bar was charged with starting material **35 INT** and potassium carbonate (2 eq) The flask was sealed under nitrogen, and dry DMF (0.5 M) was added via syringe. To the stirring solution was added 2-bromoacetophenone (1.1 eq) suspended in dry DMF (0.5 M) via syringe. The reaction was allowed to stir for 3 hours, at which point it was quenched with deionized water and diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with an aqueous 5% LiCl solution (3x), washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **35 S** as a pale yellow oil in 85% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.88 (d, *J* = 7.2 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 5.07 (tt, *J* = 7.5, 1.4 Hz, 1H), 4.76 (s, 2H), 3.95 (d, *J* = 7.5 Hz, 2H), 1.63 (s, 3H), 1.46 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.1, 143.9, 139.8, 134.9, 134.1 (q, *J* = 32.9 Hz), 134.0, 129.0, 128.1, 128.0, 126.1 (q, *J* = 3.8 Hz), 123.5 (q,

J = 273.0 Hz), 118.0, 51.7, 45.6, 25.8, 17.7; **IR** (neat) 2920, 1699, 1598, 1582, 1449, 1404, 1320, 1226, 1159, 1128, 1108, 1093, 1061, 1016, 989, 929, 908, 842, 810, 787, 748, 731, 706, 689, 662 cm^{-1}; **HRMS** calcd for $C_{20}H_{20}F_3NO_3S^+$: 412.1189, found: 412.1190.

Synthesis of *p*-Cyanophenylalanine Substrate[25]



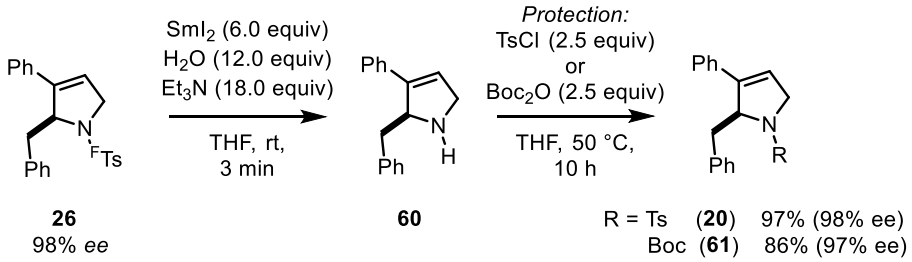
49 S **56 S**

A round-bottom flask equipped with a magnetic stir bar was charged with starting material **49 S** and sealed under nitrogen. Dry, degassed DMF (0.3 M) was added via syringe, followed by addition of zinc cyanide (0.6 eq) and the palladium catalyst (0.05 M) in one portion. The reaction was heated to 80 °C and allowed to stir under nitrogen for 12 hours, or until the reaction was judged complete by TLC analysis. The reaction was then cooled to room temperature and quenched by the addition of a saturated aqueous $NaHCO_3$ solution. EtOAc was added to the reaction mixture, and the resulting layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with an aqueous 5% LiCl solution (3x), brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **56 S** as a pale yellow oil in 15% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.8 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H),

7.12 (d, *J* = 8.0 Hz, 2H), 5.73 (dd, *J* = 8.7, 5.3 Hz, 1H), 4.79 (t, *J* = 6.2 Hz, 1H), 3.98 (dd, *J* = 16.0, 6.7 Hz, 1H), 3.86 (dd, *J* = 16.0, 6.7 Hz, 1H), 3.42 (dd, *J* = 13.7, 9.0 Hz, 1H), 2.79 (dd, *J* = 13.8, 5.1 Hz, 1H), 1.58 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.3, 144.0, 136.7, 136.1, 135.9, 134.4 (q, *J* = 33.2 Hz), 133.8, 131.9, 131.8, 131.3, 128.9, 128.7, 128.0, 126.1 (q, *J* = 3.8 Hz), 123.3 (q, *J* = 272.5 Hz), 120.9, 120.4, 60.8, 43.5, 34.8, 25.7, 17.9; **IR** (neat): 2929, 1688, 1608, 1448, 1325, 1233, 1163, 1134, 1062, 1014, 845 cm^{-1}; **HRMS** calcd for $C_{28}H_{25}F_3NO_2S^+$: 527.1611, found: 527.1607.

Deprotection with SmI_2

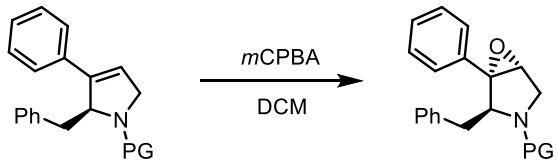
A 0.13 M solution of SmI_2 is prepared with samarium metal a diiodoethane according to previously reported procedures.[5] The carbonyl-olefin metathesis product **26** (0.1 mmol) is added to a round-bottom flask equipped with a stir and placed under a nitrogen atmosphere. The SmI_2 solution (6.0 equiv) is then added to the flask while stirring. Next a degassed solution of water (12.0 equiv) is added to the reaction mixture, which immediately turns red. Triethylamine (18.0 equiv) is then added. After 3 minutes, the reaction mixture is filtered under nitrogen over a celite plug. The crude product **60** is collected into a flask and subjected to protection conditions to give **20** (TsCl, 2.5 equiv) and **62** (Boc_2O, 2.5 equiv).



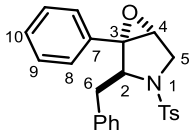
***tert*-butyl-(*S*)-2-benzyl-3-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate (61):** Purification by flash column chromatography provided **61** as a clear oil and a mixture of rotamers. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 8H), 7.34 – 7.31 (m, 2H), 7.15 – 7.12 (m, 6H), 6.86 – 6.83 (m, 4H), 5.85 (s, 1H), 5.79 (s, 1H), 5.40 (s, 1H), 5.30 (s, 1H),

4.18 (d, *J* = 16.0 Hz, 1H), 4.04 (d, *J* = 15.9 Hz, 1H), 3.52 (dd, *J* = 13.6, 5.3 Hz, 1H), 3.42 (ddd, *J* = 16.1, 5.1, 1.5 Hz, 1H), 3.30 (dd, *J* = 13.7, 4.9 Hz, 1H), 3.28 – 3.23 (m, 1H), 2.85 (t, *J* = 13.2 Hz, 2H), 1.61 (s, 9H), 1.55 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.00, 140.85, 140.78, 137.18, 136.94, 134.07, 134.03, 130.41, 130.23, 128.95, 128.89, 128.05, 128.02, 127.80, 127.54, 126.58, 126.29, 126.12, 121.72, 121.54, 79.95, 79.44, 77.34, 77.16, 76.98, 64.42, 64.17, 53.87, 53.60, 37.31, 35.71, 28.86, 28.75.; **IR** (neat) 2974, 2361, 2338, 17501, 1734, 1695, 1684, 1559, 1464, 1399, 1363, 1254, 1170, 1115, 1077, 968 cm^{-1}; **HRMS** calcd for $C_{22}H_{25}NO_2^{+Na}$: 358.1778, found: 358.1779.

Epoxidation of Metathesis Products



A round bottom flask equipped with a magnetic stir bar was charged with *m*CPBA (1.25 eq, 77% purity) and sealed under nitrogen. Dry DCM (0.2 M) was added via syringe, and the mixture was cooled to 0 °C before the 3-pyrroline was added portion-wise over 5 minutes. The resultant mixture was allowed to warm to room temperature over 16 hours, or until judged complete by TLC analysis. The reaction was quenched with saturated aqueous $NaHCO_3$, diluted with DCM, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with DCM (3x). The organic layers were combined, washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired epoxide.

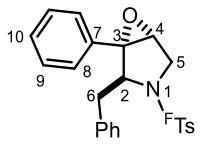


62a

(1*S*,2*S*,5*R*)-2-benzyl-1-phenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane (62a): Purification by flash column chromatography provided **62** as a white foam in 86% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.41 – 7.36 (m, 3H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.27 – 7.24 (m, 2H), 7.21 – 7.15 (m, 3H), 6.98 (dd, *J* = 6.3, 2.8 Hz, 2H), 4.62 (dd,

J = 5.7, 3.6 Hz, 1H), 3.75 (s, 1H), 3.60 (d, *J* = 12.9 Hz, 1H), 3.15 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.00 (d, *J* = 12.8 Hz, 1H), 2.89 (dd, *J* = 14.0, 3.5 Hz, 1H), 2.41 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 143.5, 136.3, 135.7, 132.3, 130.5, 129.6, 129.5, 129.2, 128.9, 128.1, 127.7, 126.6, 68.9, 63.0, 59.3, 49.0, 38.4, 21.7; **IR** (neat) 2923, 1453, 1338, 1160, 1121, 1091, 1007, 815, 759, 720, 698, 678, 667 cm^{-1}; **HRMS** calcd for $C_{24}H_{23}NO_3S^+$: 406.1471, found: 406.1476.

Position	δ_C	δ_H	m (*J* (Hz))	NOE
C6	38.4	3.15, 2.89	dd (14.0, 6.0), dd (14.0, 3.5)	H8
C8	130.5	6.98	dd (6.3, 2.8)	H6

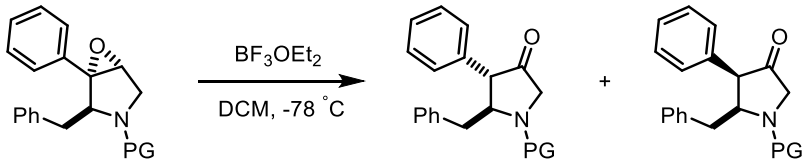


62b

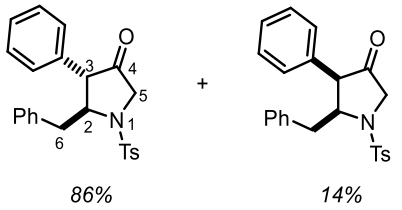
(1*S*,2*S*,5*R*)-2-benzyl-1-phenyl-3-((4-(trifluoromethyl)phenyl)sulfonyl)-6-oxa-3-aza-bicyclo[3.1.0]hexane (62b): Purification by flash column chromatography provided **51b** as a white foam in 80% yield. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.44 – 7.38 (m, 3H), 7.29 (d, *J* = 6.2 Hz, 2H), 7.22 – 7.16 (m, 3H), 7.01 – 6.96 (m, 2H), 4.66 (t, *J* = 4.9 Hz, 1H), 3.80 (s, 1H), 3.65 (d, *J* = 13.0 Hz, 1H), 3.12 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.05 (d, *J* = 13.0 Hz, 1H), 2.86 (dd, *J* = 14.0, 4.2 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 142.3, 136.0, 134.2 (q, *J* = 33.0 Hz), 131.9, 130.3, 129.7, 129.1, 129.0, 128.3, 128.1, 126.9, 126.1 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.8 Hz), 68.8, 63.5, 59.0, 49.0, 38.2; **IR** (neat) 2931, 1496, 1455, 1404, 1322, 1165, 1129, 1108, 1062, 1016, 842, 760, 712, 698, 674 cm^{-1}; **HRMS** calcd for $C_{24}H_{20}F_3NO_3S^+$: 460.1189, found: 460.1190.

Position	δ_C	δ_H	m (*J* (Hz))	NOE
C6	38.2	3.12, 2.86	dd (14.0, 5.6), dd (14.0, 4.2)	H8
C8	130.3	7.01-6.96	m	H6

Rearrangement of Pyrrolidine Epoxides to 3-oxo pyrrolidines



A round bottom flask equipped with a magnetic stir bar was charged with the epoxide substrate and sealed under nitrogen. The substrate was suspended in dry DCM (0.1 M), and the mixture was cooled to -78 ^{o}C before BF_3OEt_2 (1 eq) was added slowly via syringe. The reaction was allowed to stir for 30 minutes and then quenched with the addition of water. The mixture was then diluted with DCM, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with DCM (3x). The organic layers were combined, washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired ketone as an intractable mixture of diastereomers.

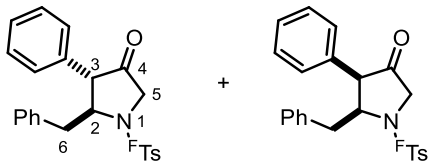


63a

(4*S*/*R*,5*S*)-5-benzyl-4-phenyl-1-tosylpyrrolidin-3-one (63a): Purification by flash column chromatography provided **63a** as a white solid in 74% yield and 86:14 *d.r*. Data reported as a mixture of diastereomers, NOE data reported for major diastereomer. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.9 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 0.32H), 7.35 – 7.27 (m, 4H), 7.25 (d, *J* = 7.4 Hz, 3H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.06 (t, *J* = 7.7 Hz, 2H), 6.92 – 6.87 (m, 0.32H), 6.53 (d, *J* = 7.8 Hz, 2H), 4.85 (dd, *J* = 14.1, 9.1 Hz, 0.16H), 4.49 – 4.42 (m, 1H), 4.16 (d, *J* = 19.0 Hz, 0.16H), 3.84 (d, *J* = 18.3 Hz, 1H), 3.78 (d, *J* = 8.3 Hz, 0.16H), 3.70 (d, *J* = 18.3 Hz, 1H), 3.48 (d, *J* = 3.6 Hz, 1H), 3.25 – 3.10 (m, 2H), 2.45 (s, 3H), 2.39 (s, 0.48H); **^{13}C NMR** (126 MHz, $CDCl_3$, minor diastereomer carbons marked

with *) δ 208.2, 144.4, 136.4, 135.9, 135.3*, 134.9, 130.3, 130.2, 130.0*, 129.9*, 129.4*, 129.1, 128.9, 128.4, 127.6, 127.5, 127.4, 124.9*, 66.2, 63.8*, 57.9, 53.8, 41.4, 37.1*, 21.7; **IR** (neat) 2928, 1761, 1598, 1495, 1453, 1347, 1155, 1091, 1038, 911, 815, 735, 699, 664 cm^{-1}; **HRMS** calcd for $C_{24}H_{23}NO_3S^-$: 404.1326, found: 404.1321.

Position	δ_C	δ_H	m (*J* (Hz))	NOE
C3	53.8	3.48	d (3.6)	H6
C6	41.4	3.25-3.10	m	H3



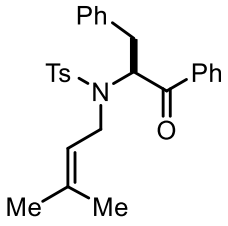
88% *12%*

63b

(4*S*/*R*,5*S*)-5-benzyl-4-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-3-one (63b): Purification by flash column chromatography provided **63b** as a white solid in 72% yield and 88:12 *d.r*. Data reported as a mixture of diastereomers, NOE data reported for major diastereomer. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 0.24H), 7.45 (d, *J* = 8.2 Hz, 0.24H), 7.37 (t, *J* = 7.6 Hz, 0.12H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.28 (d, *J* = 7.1 Hz, 1H), 7.24 (d, *J* = 6.8 Hz, 2H), 7.12 (d, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 7.4 Hz, 0.24H), 7.03 (t, *J* = 7.6 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 0.24H), 6.49 (d, *J* = 7.7 Hz, 2H), 5.03 – 4.97 (m, 0.12H), 4.54 (dt, *J* = 7.6, 3.0 Hz, 1H), 4.40 (d, *J* = 18.5 Hz, 0.12H), 4.14 (d, *J* = 8.1 Hz, 0.12H), 3.86 (d, *J* = 18.3 Hz, 1H), 3.71 (d, *J* = 18.3 Hz, 1H), 3.66 (d, *J* = 18.6 Hz, 0.12H), 3.54 (s, 1H), 3.24 (dd, *J* = 13.6, 3.8 Hz, 1H), 3.08 (dd, *J* = 13.6, 8.5 Hz, 1H), 2.50 (dd, *J* = 14.4, 4.1 Hz, 0.12H), 2.32 (dd, *J* = 14.2, 11.6 Hz, 0.12H); **^{13}C NMR** (176 MHz, $CDCl_3$, minor diastereomer carbons marked with *) δ 207.8, 141.8, 136.3, 135.6, 134.9 (q, *J* = 33.2 Hz), 130.1, 129.9*, 129.22, 129.19*, 129.12, 129.07*, 128.6*, 127.8, 127.7, 127.6, 127.0*, 126.9, 126.6 (q, *J* = 3.6 Hz), 123.2 (q, *J* = 273.0), 67.1, 64.4*, 59.2*, 57.7, 53.4, 51.7*, 42.1, 37.1*; **IR** (neat) 2928, 1762, 1607, 1496, 1454, 1404, 1355, 1321, 1248, 1161, 1131, 1108, 1093, 1061, 1013, 910, 843, 787, 741, 711, 698, 668; **HRMS** calcd for $C_{24}H_{20}F_3NO_3S^-$: 458.1043, found: 458.1036.

Position	δ_C	δ_H	m (*J* (Hz))	NOE
C3	53.4	3.54	s	H6
C6	42.1	3.24, 3.08	dd (13.6, 3.8), dd (13.6, 8.5)	H3

2.5 ^{1}H and ^{13}C NMR Spectra



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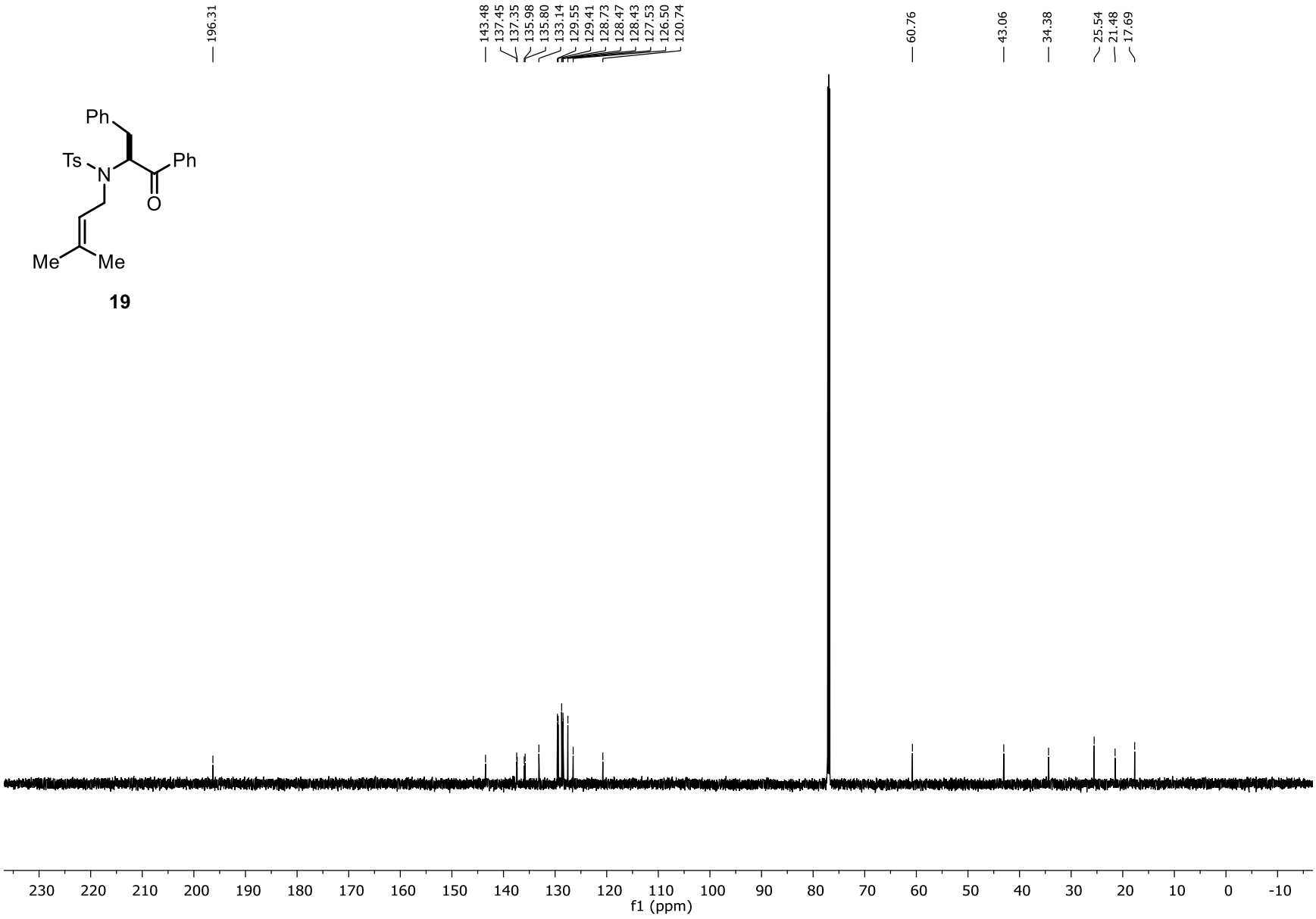
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127.53
126.50
120.74
60.76
43.06
34.38
25.54
21.48
17.69
Ph
Ts
N
Ph
O
Me
Me
19
230
220
210
200
190
180
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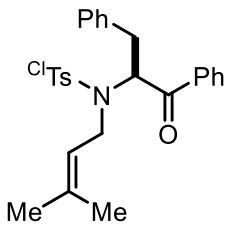
f1 (ppm)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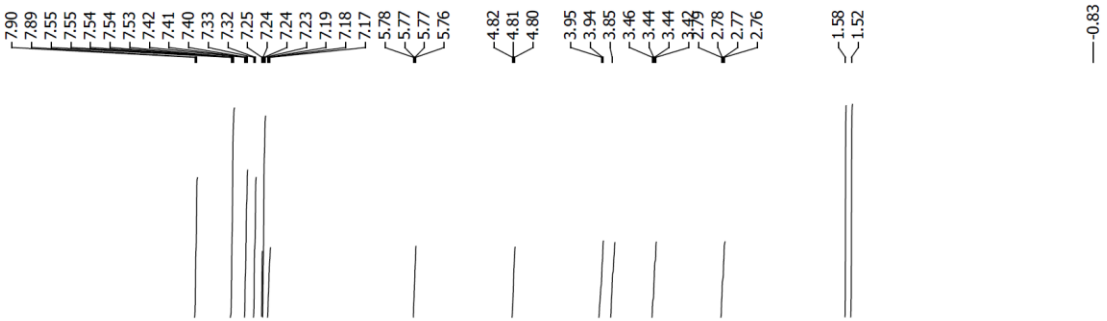
N
Ph
O
Me
Me

23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7.24
7.24
7.23
7.19
7.18
7.17
5.78
5.77
5.77
5.76
4.82
4.81
4.80
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3.94
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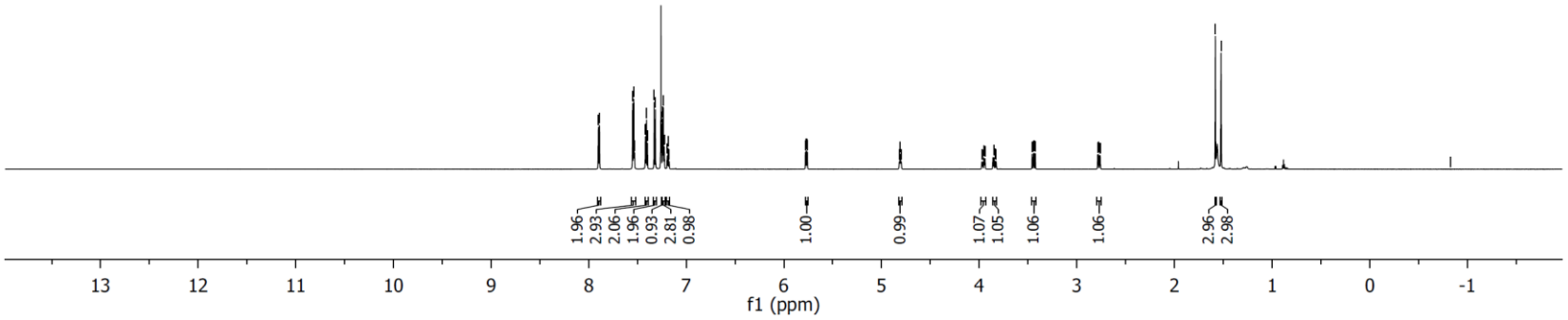
1.52
0.83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2.06
1.96
0.93
2.81
0.98
1.00
0.99
1.07
1.05
1.06
1.06
2.96
2.98
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12
11
10
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8
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4
3
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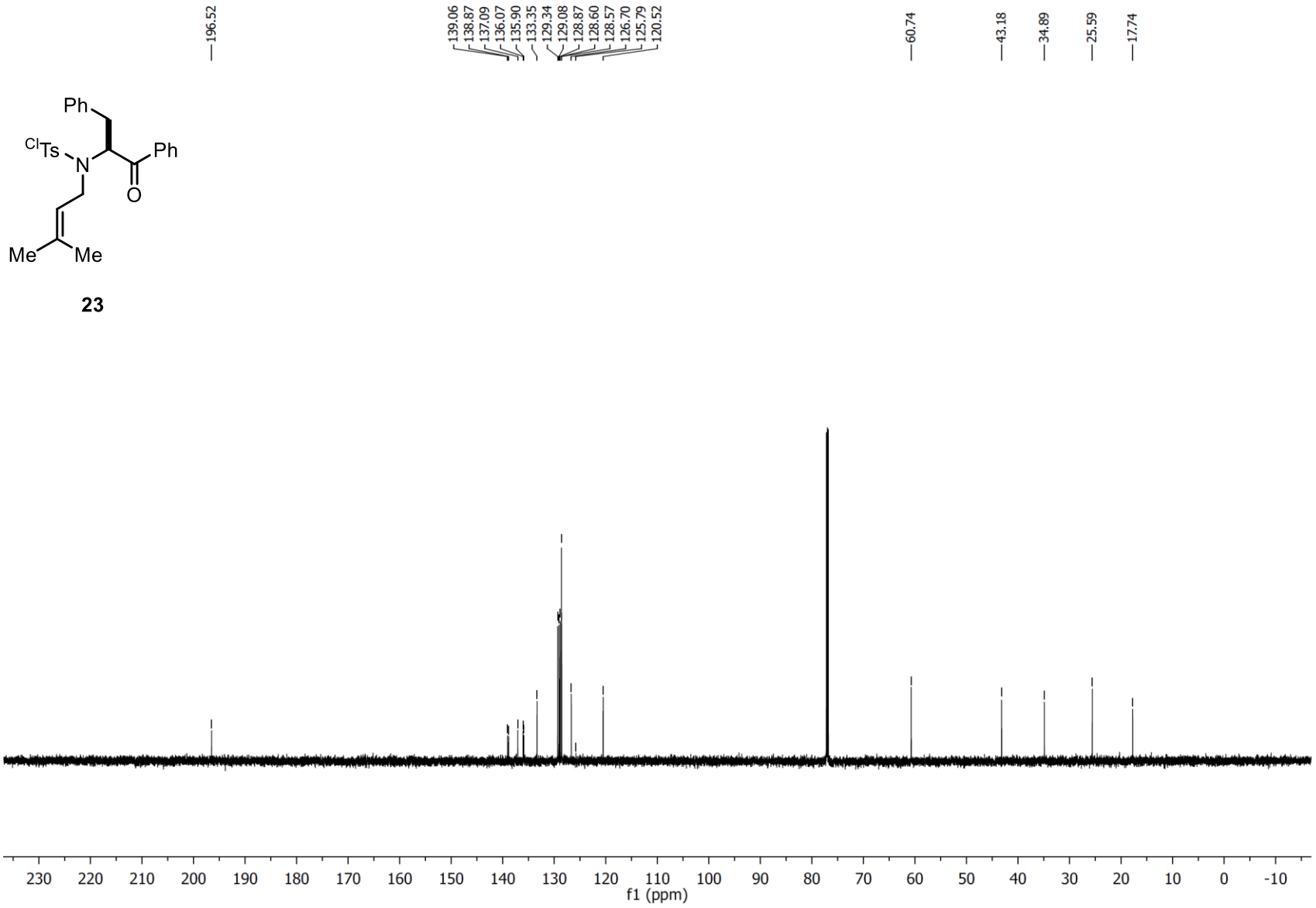
-1
f1 (ppm)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129.34
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126.70
125.79
120.52
60.74
43.18
34.89
25.59
17.74
Ph
Cl
Ts
N
Ph
O
Me
Me
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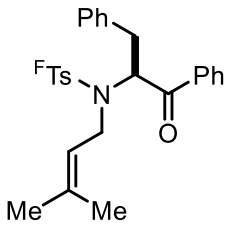
f1 (ppm)

23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N
Ph
O
Me
Me

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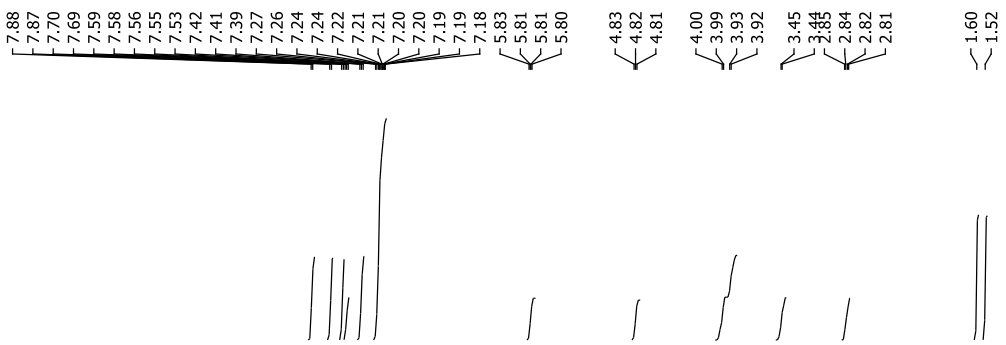
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7.26
7.24
7.24
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.18
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5.81
5.81
5.80
4.83
4.82
4.81
4.00
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2.81
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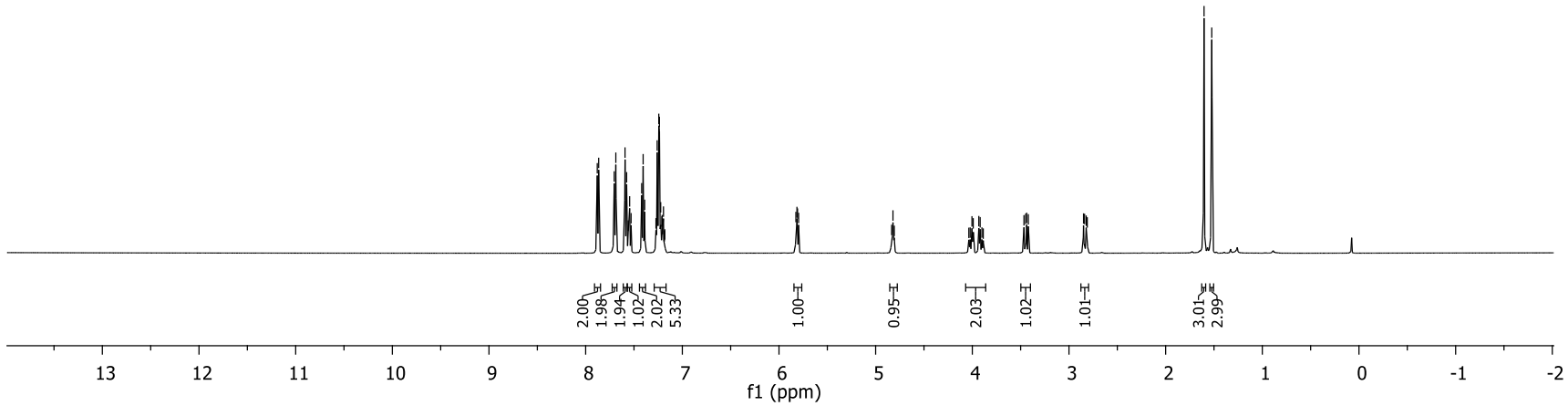
1.52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1.02
1.01
3.01
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7
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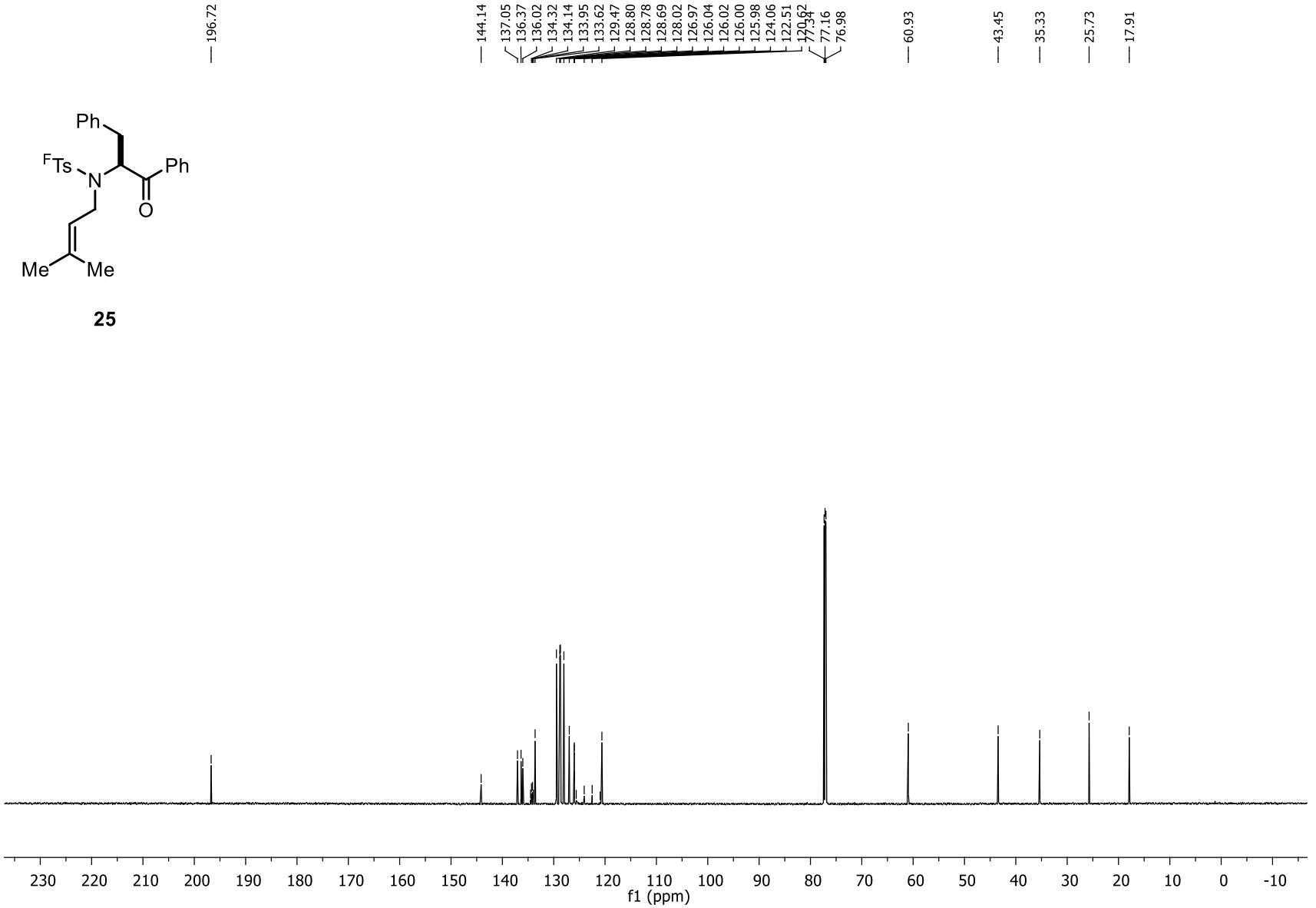
-2
f1 (ppm)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128.02
126.97
126.04
126.02
126.00
125.98
124.06
122.51
120.62
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76.98
60.93
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25.73
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Ph
FTs
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Ph
O
Me
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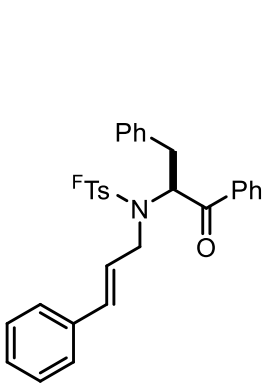
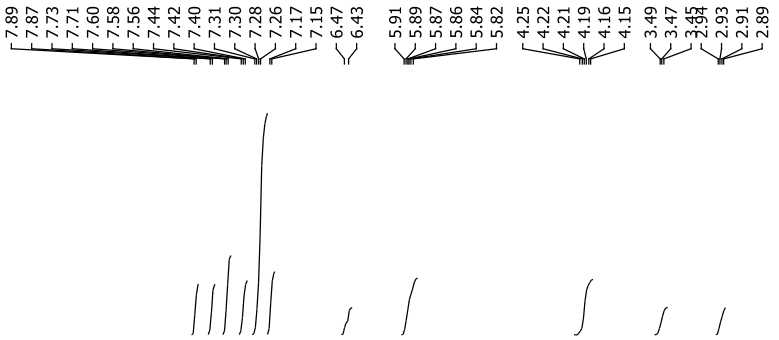
f1 (ppm)

25


Ph
FTs
N
Ph
O

28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7.17
7.15
6.47
6.43
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5.87
5.86
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3.45
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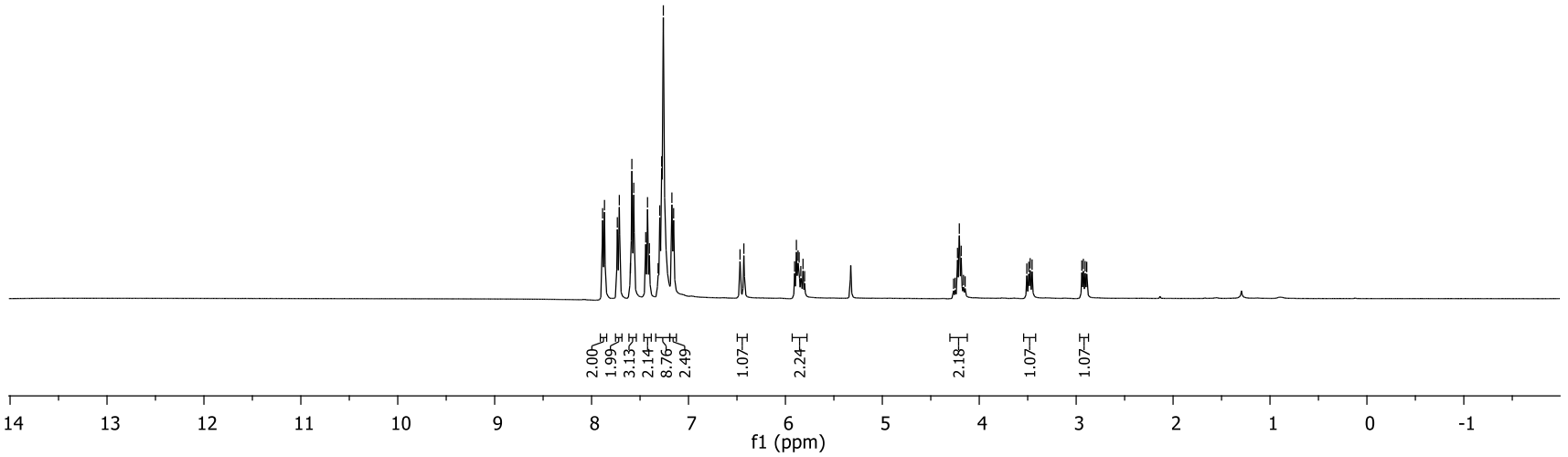
2.89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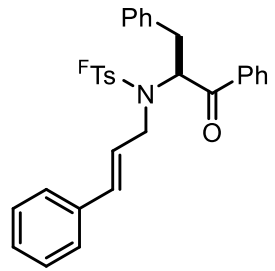
f1 (ppm)


Ph
FTs
N
Ph
O

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128.09
128.06
127.07
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126.10
126.07
126.04
126.01
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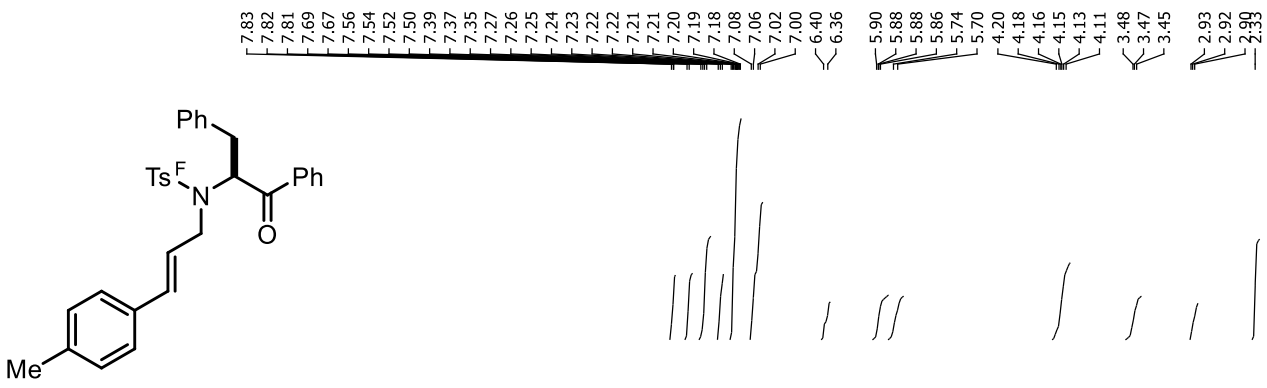
f1 (ppm)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7.20
7.19
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5.88
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4.11
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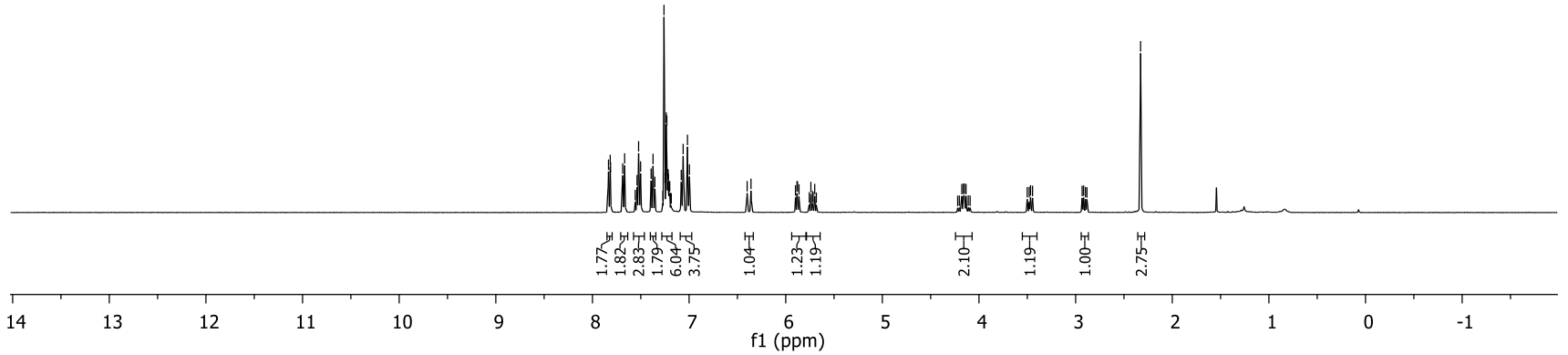
Ph
Ts
F
N
Ph
O
Me

29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2.10
1.19
1.00
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3
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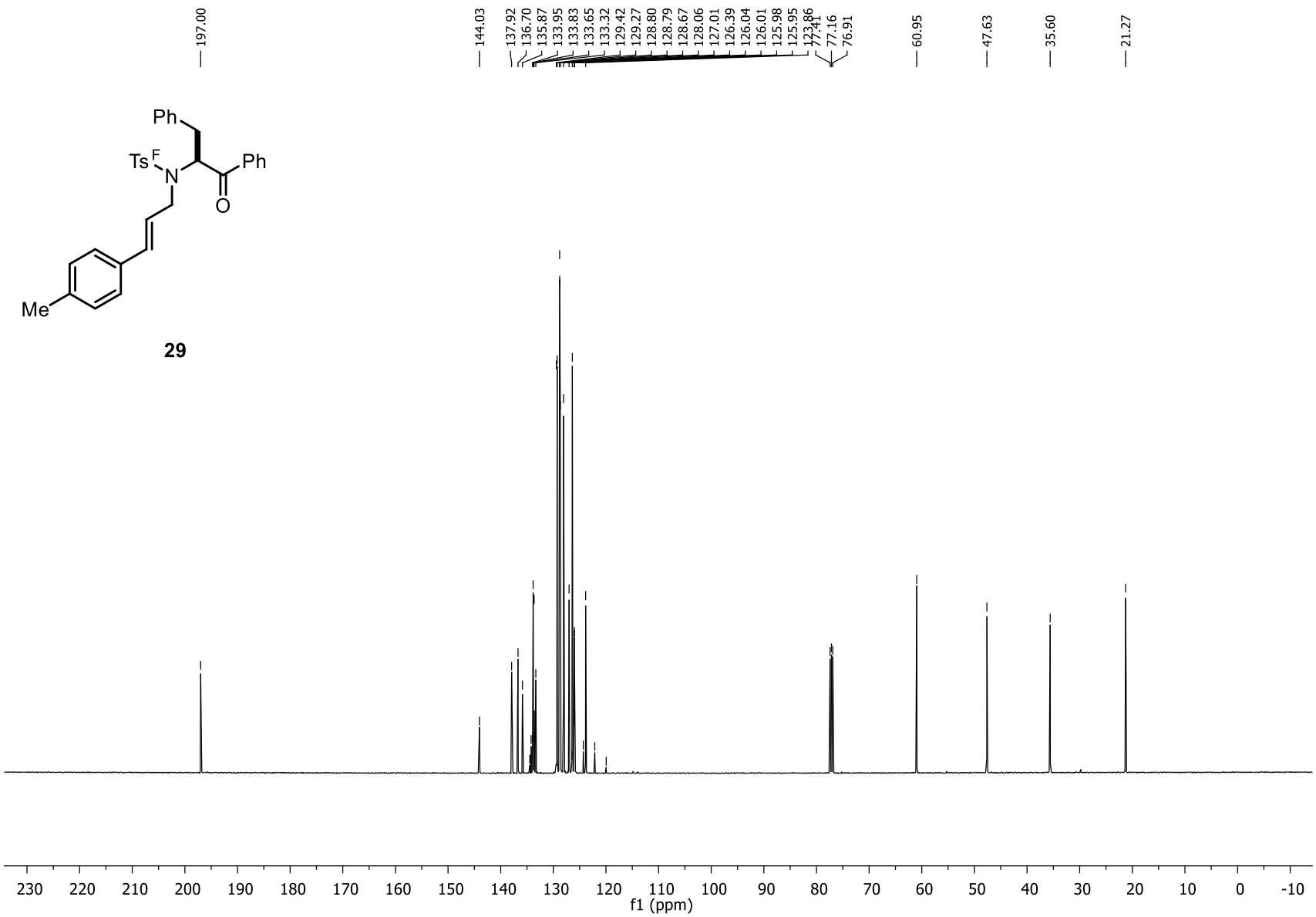
f1 (ppm)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125.95
123.86
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77.16
76.91
60.95
47.63
35.60
21.27
Ph
Ts
F
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Ph
O
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200
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180
170
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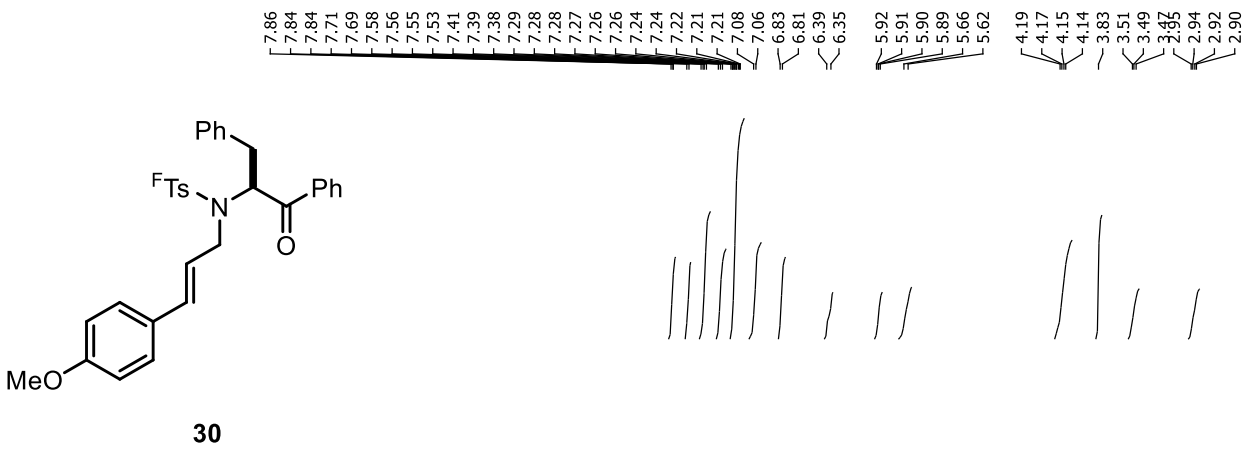

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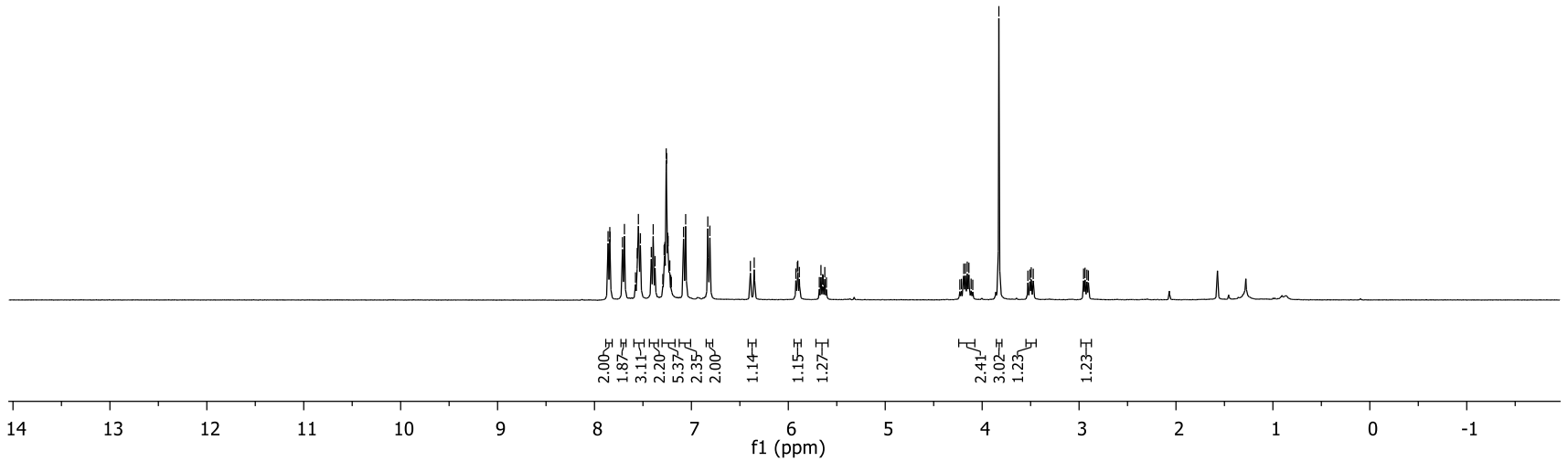

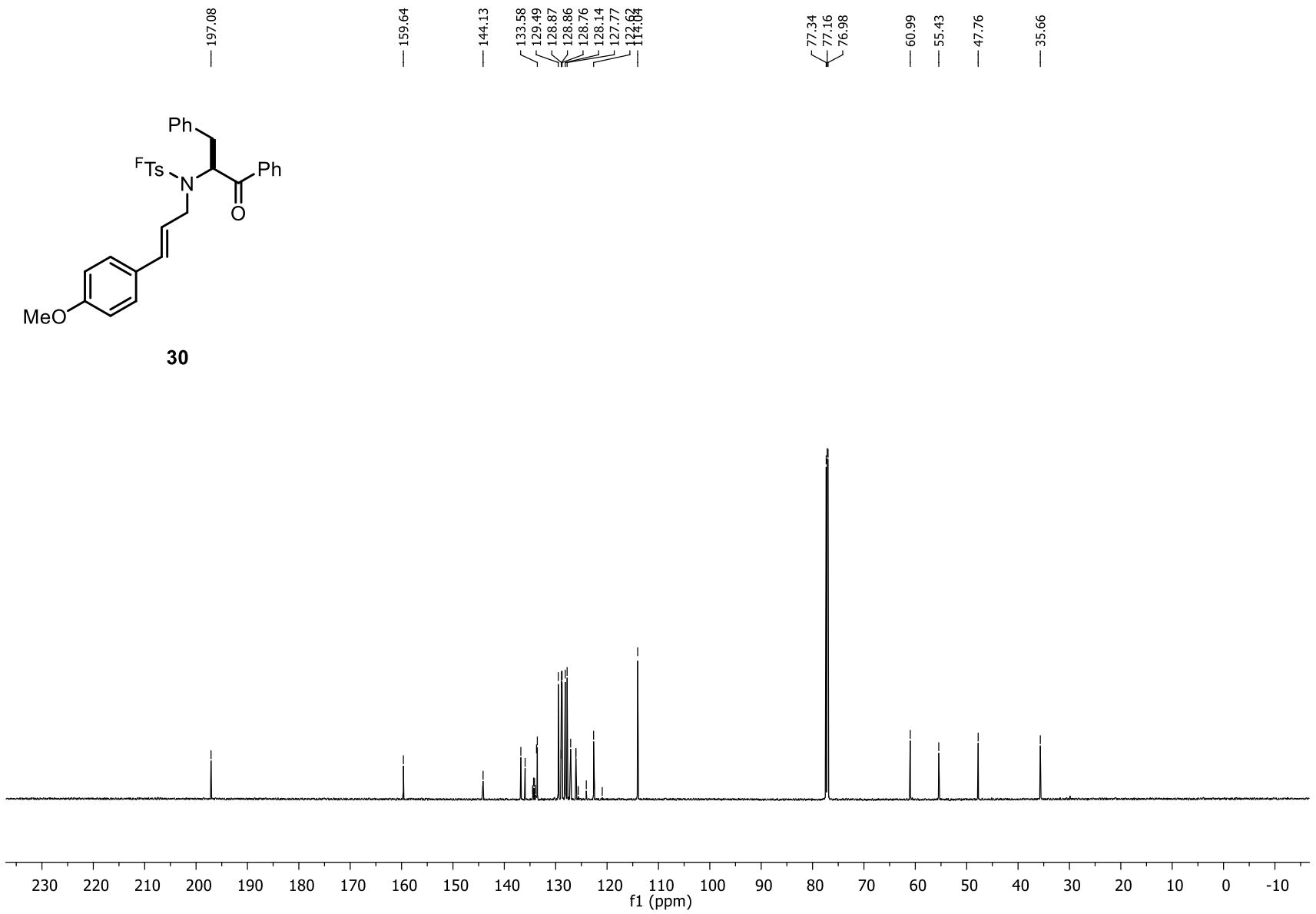
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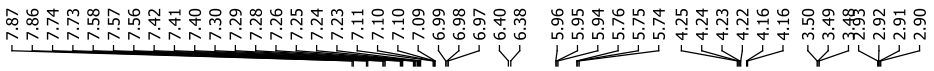
f1 (ppm)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5.94
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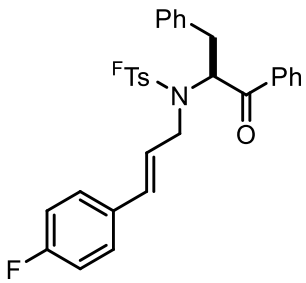
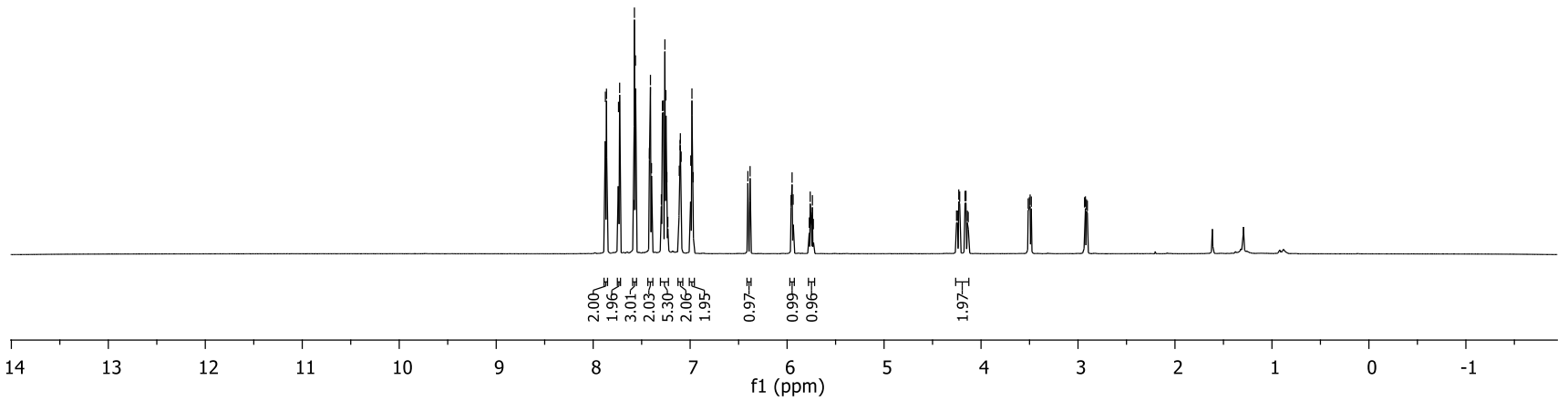
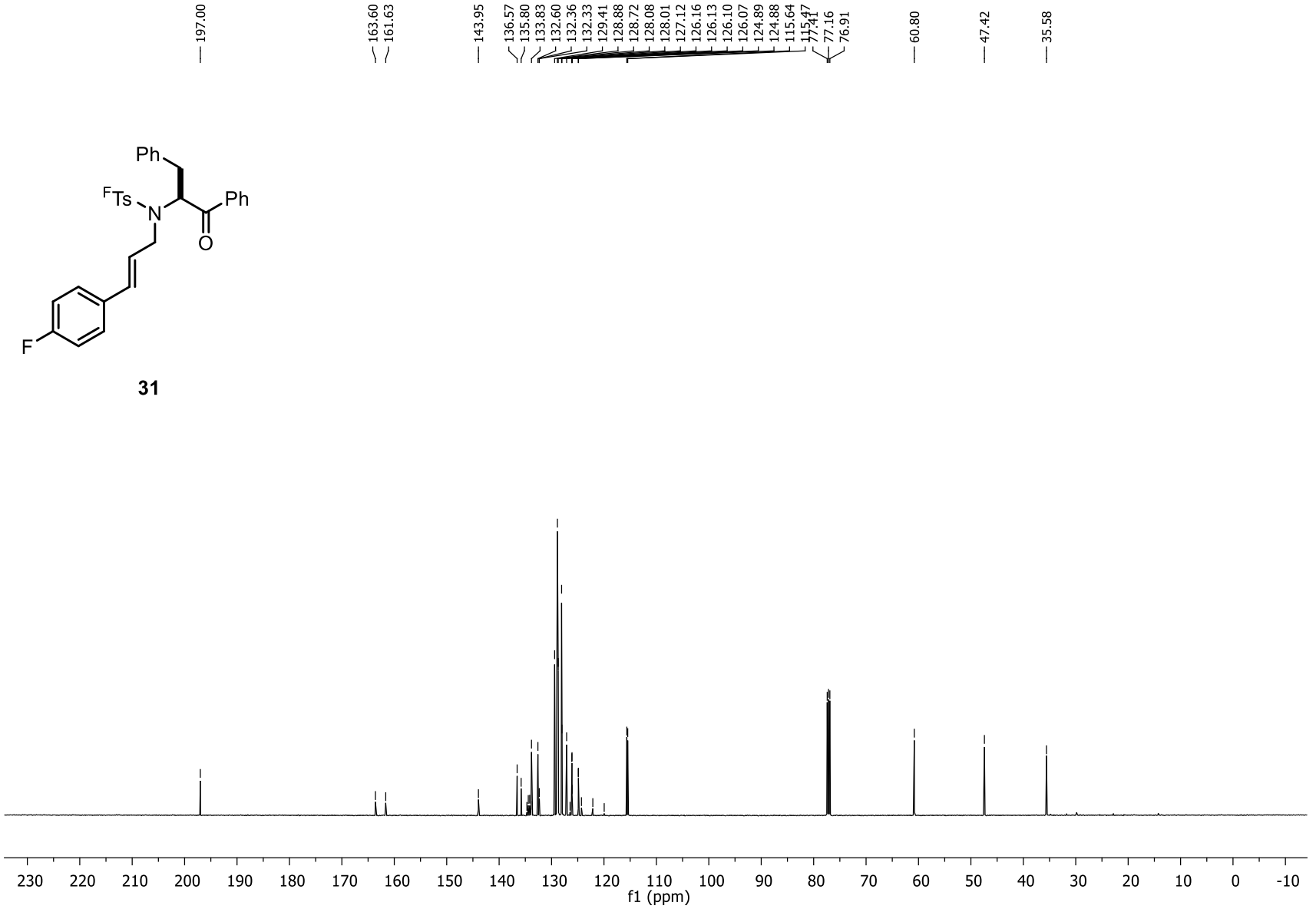
5.75
5.74
4.25
4.24
4.23
4.22
4.16
4.16
3.50
3.49
3.48
2.93
2.92
2.91
2.90


Ph
FTs
N
Ph
O
F

31


2.00
1.96
3.01
2.03
5.30
2.06
1.95
0.97
0.99
0.96
1.97
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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163.60
161.63
143.95
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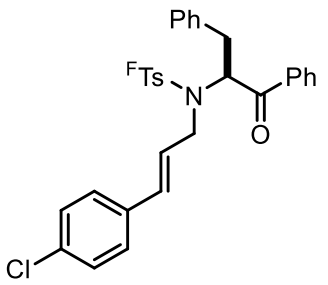
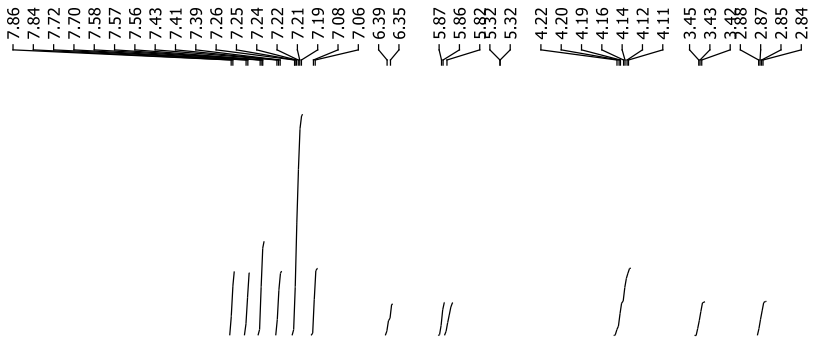
135.80
133.83
132.60
132.36
132.33
129.41
128.88
128.72
128.08
128.01
127.12
126.16
126.13
126.10
126.07
124.89
124.88
115.64
115.47
77.41
77.16
76.91
60.80
47.42
35.58
Ph
FTs
N
Ph
O
F
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

31


Ph
FTs
N
Ph
O
Cl

32


7.86
7.84
7.72
7.70
7.58
7.57
7.56
7.43
7.41
7.39
7.26
7.25
7.24
7.22
7.21
7.19
7.08
7.06
6.39
6.35
5.87
5.86
5.82
5.32
4.22
4.20
4.19
4.16
4.14
4.12
4.11
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3.43
3.42
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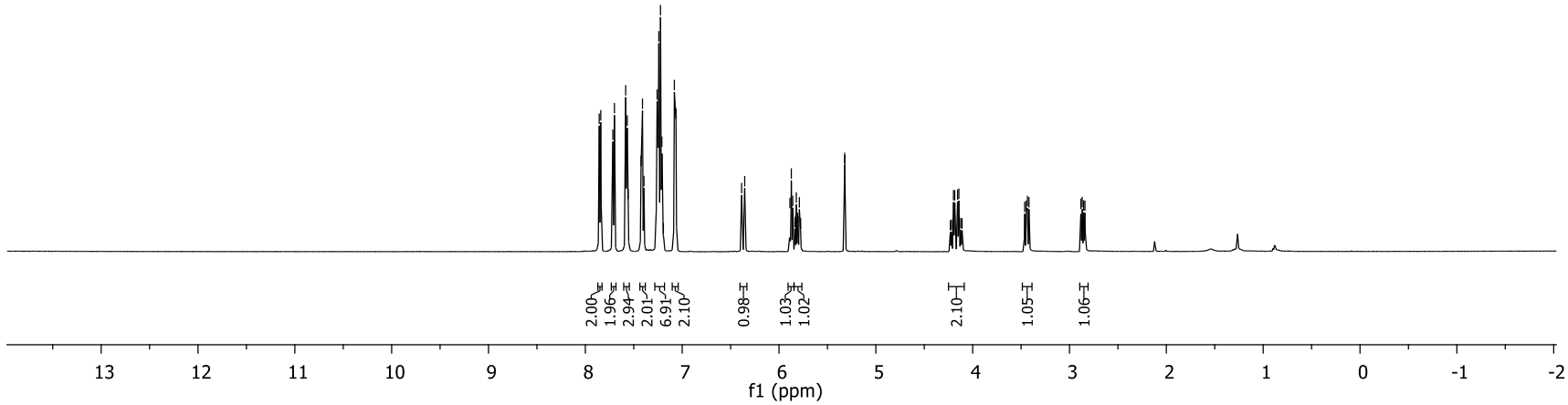
2.87
2.85
2.84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1.96
2.94
2.01
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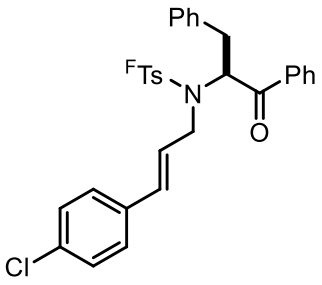
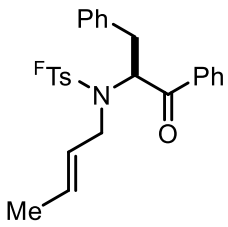
2.10
0.98
1.03
1.02
2.10
1.05
1.06
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

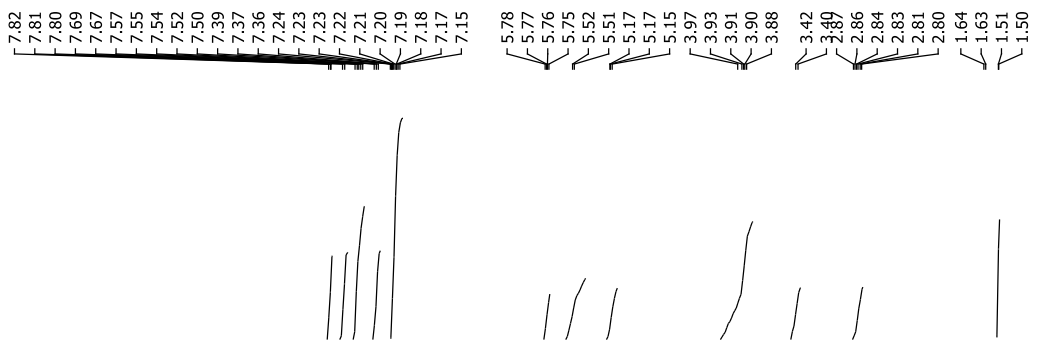

Ph
FTs
N
Ph
O
Cl

32

196.93
143.80
136.46
135.69
134.63
134.33
134.15
133.81
133.63
132.36
129.34
128.85
128.84
128.73
128.66
126.12
126.10
126.08
126.06
125.89
123.94
77.34
77.16
76.98
60.73
47.30
35.48
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
FTs
N
Ph
O
Me

33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7.81
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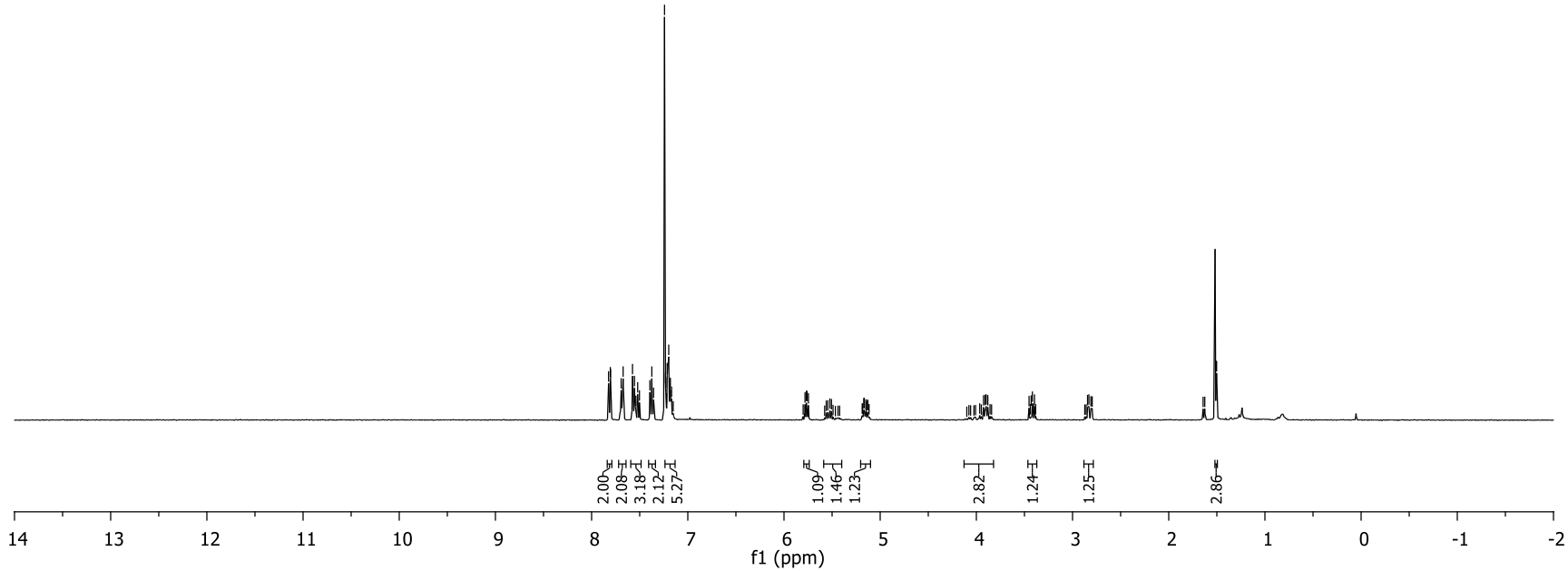
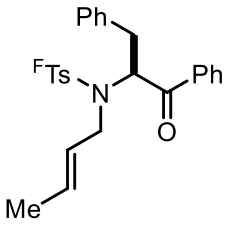
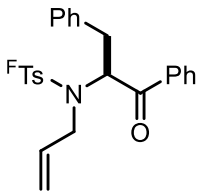
7.55
7.54
7.52
7.50
7.39
7.37
7.36
7.24
7.23
7.23
7.22
7.21
7.20
7.19
7.18
7.17
7.15
5.78
5.77
5.76
5.75
5.52
5.51
5.17
5.17
5.15
3.97
3.93
3.91
3.90
3.88
3.42
2.86
2.84
2.83
2.81
2.80
1.64
1.63
1.51
1.50


2.00
2.08
3.18
2.12
5.27
1.09
1.46
1.23
2.82
1.24
1.25
2.86
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

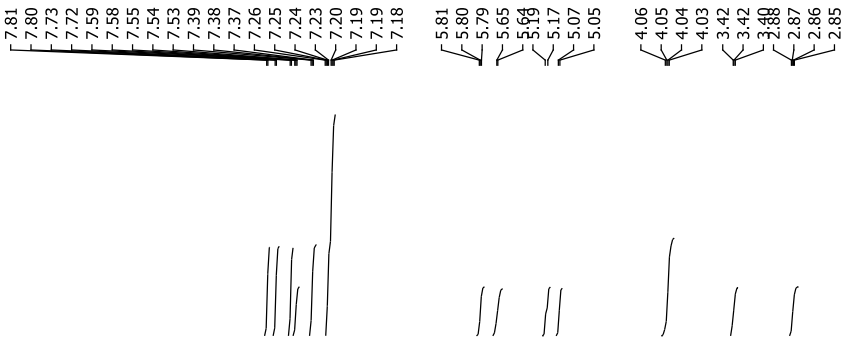

Ph
FTs
N
Ph
O
Me

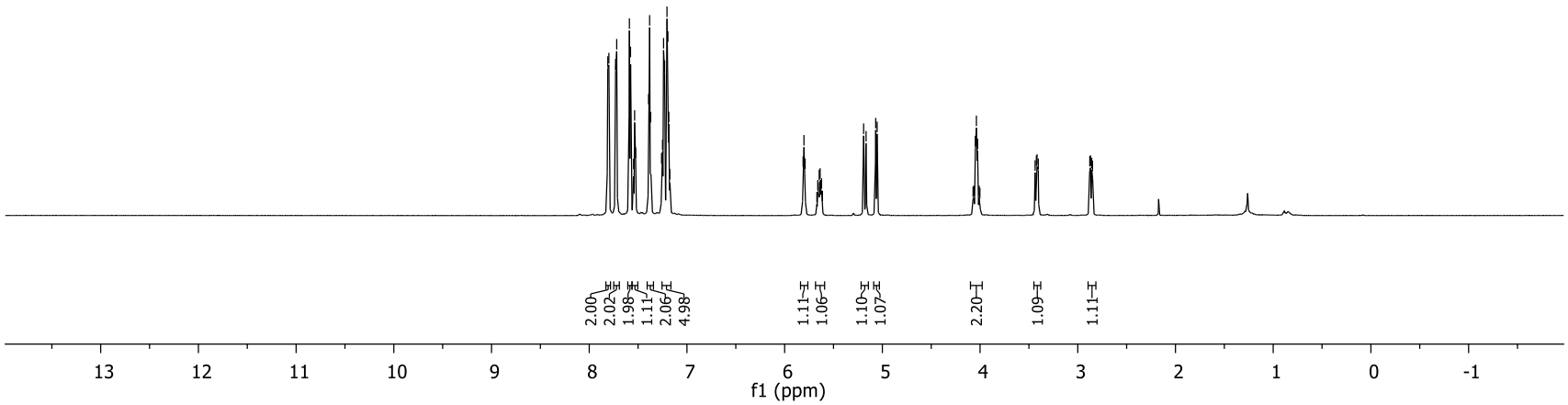
33

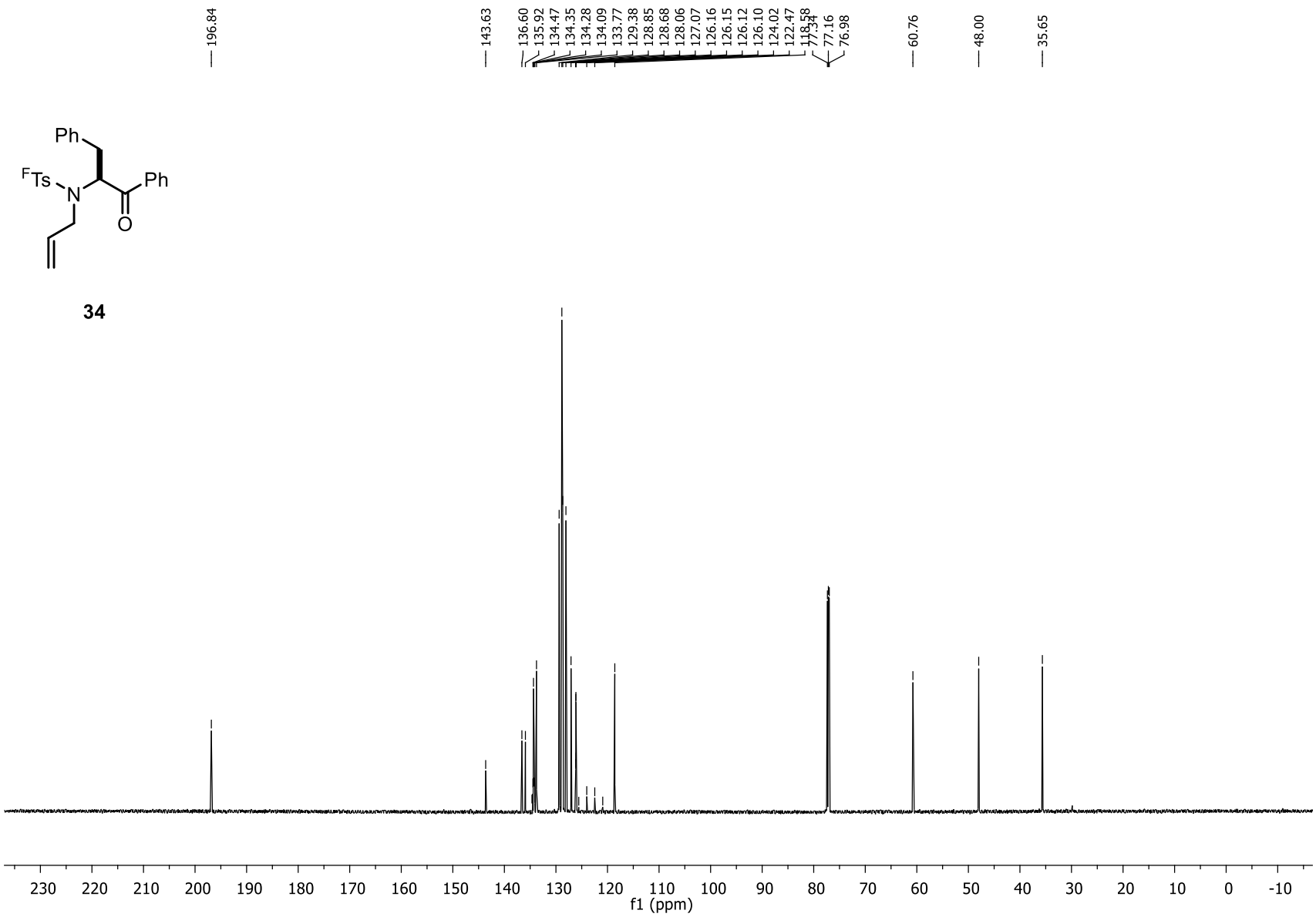
196.80
196.78
143.98
143.86
136.91
136.02
133.70
130.57
129.43
129.40
128.82
128.80
128.78
128.69
128.08
128.00
127.01
126.99
126.64
126.06
126.04
126.02
126.00
125.94
77.16
76.98
60.89
60.83
47.45
42.17
35.53
35.46
17.68
13.04
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
FTs
N
Ph
O

34


7.81
7.80
7.73
7.72
7.59
7.58
7.55
7.54
7.53
7.39
7.38
7.37
7.26
7.25
7.24
7.23
7.20
7.19
7.19
7.18
5.81
5.80
5.79
5.65
5.64
5.19
5.17
5.07
5.05
4.06
4.05
4.04
4.03
3.42
3.42
2.88
2.87
2.86
2.85


2.00
2.02
1.98
1.11
2.06
4.98
1.11
1.06
1.10
1.07
2.20
1.09
1.11
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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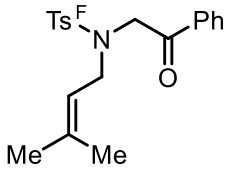
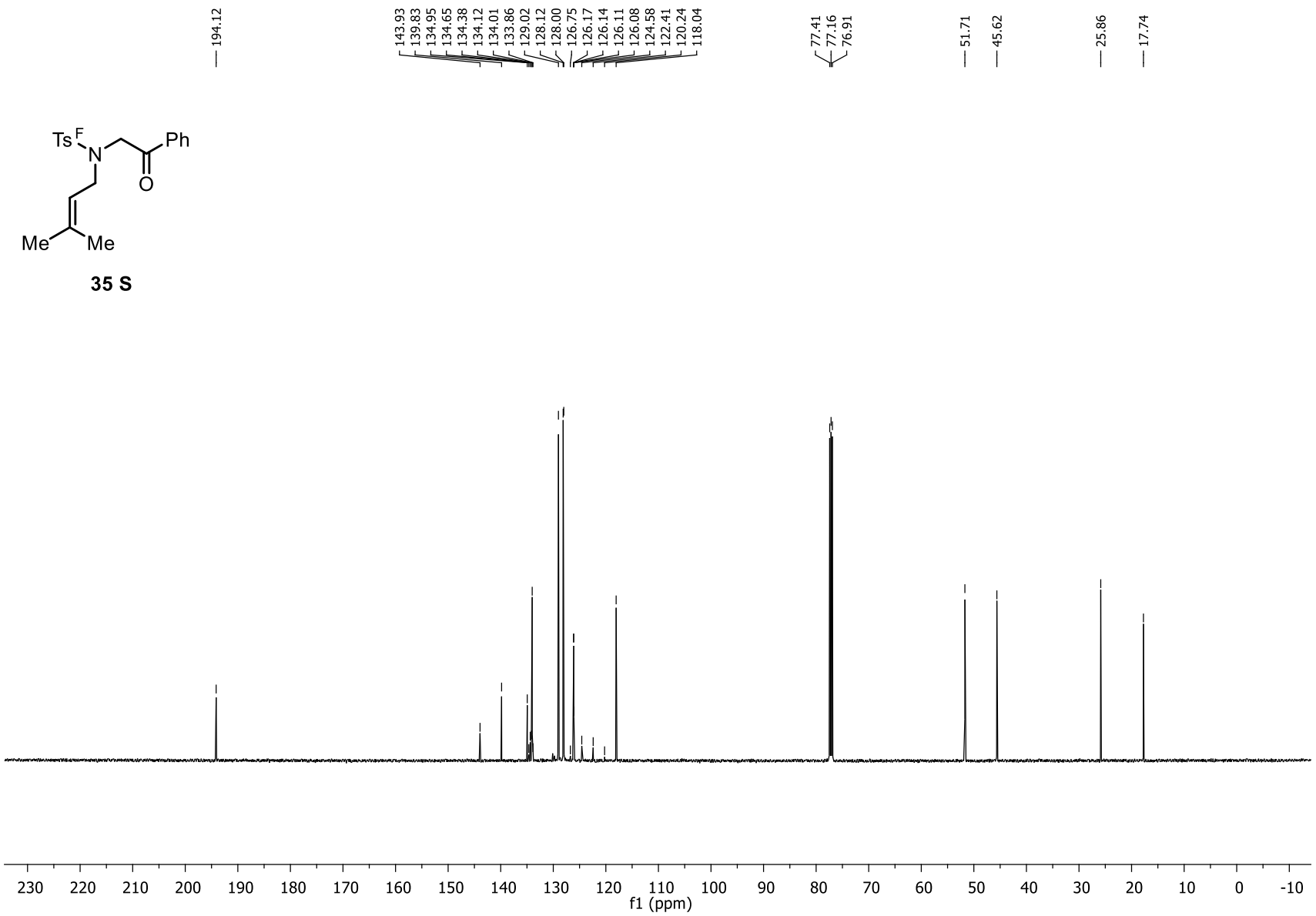
143.63
136.60
135.92
134.47
134.35
134.28
134.09
133.77
129.38
128.85
128.68
128.06
127.07
126.16
126.15
126.12
126.10
124.02
122.47
118.58
77.34
77.16
76.98
60.76
48.00
35.65
Ph
FTs
N
Ph
O
34
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Ts
F
N
Ph
O
Me
Me

35 S

8.02
8.00
7.89
7.87
7.87
7.79
7.77
7.63
7.61
7.59
7.50
7.48
7.46
7.26
5.09
5.07
5.07
5.07
5.05
4.76
3.96
3.94
1.64
1.46
2.00
2.08
2.04
1.13
2.17
1.11
2.10
2.10
3.13
3.07
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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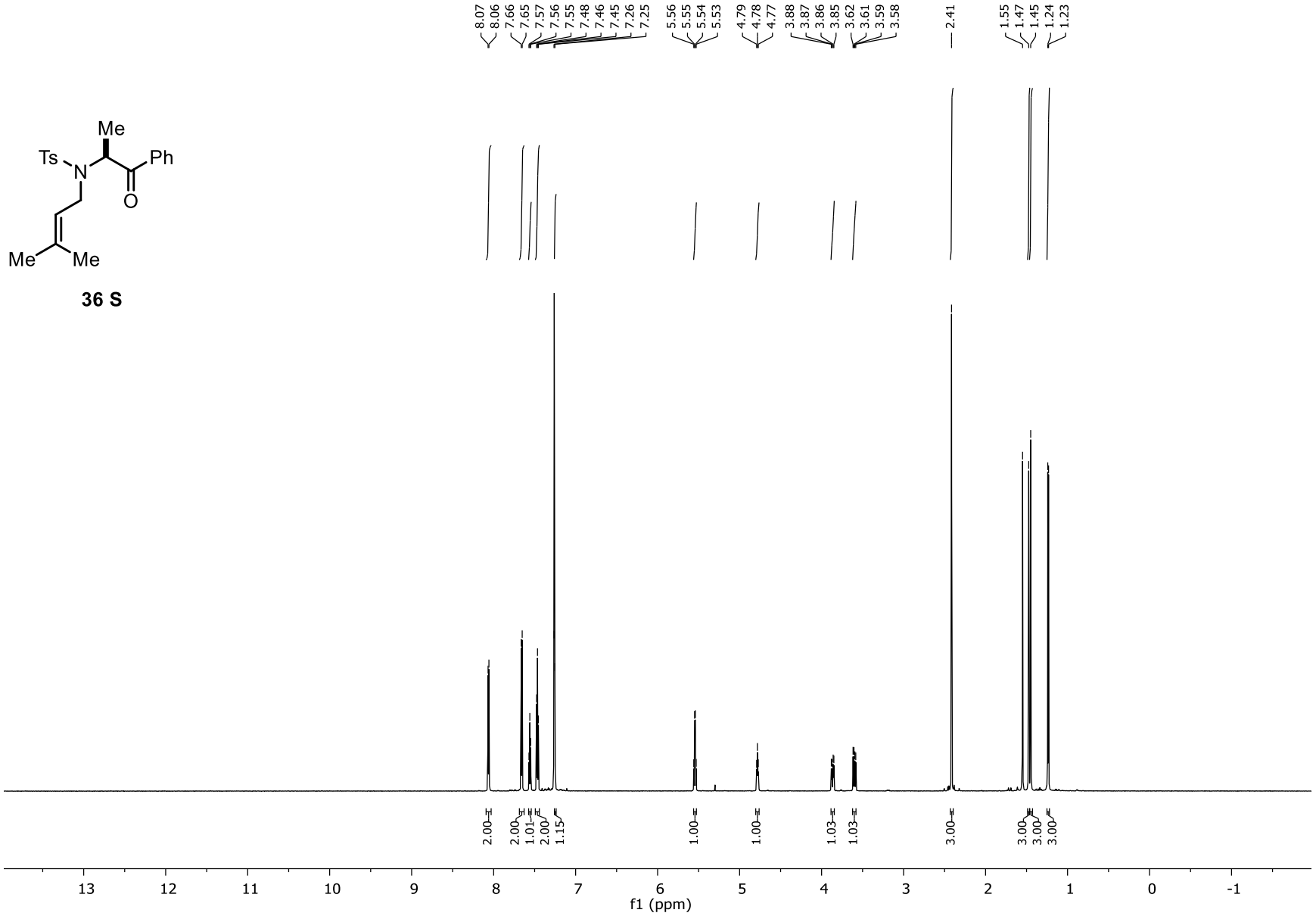
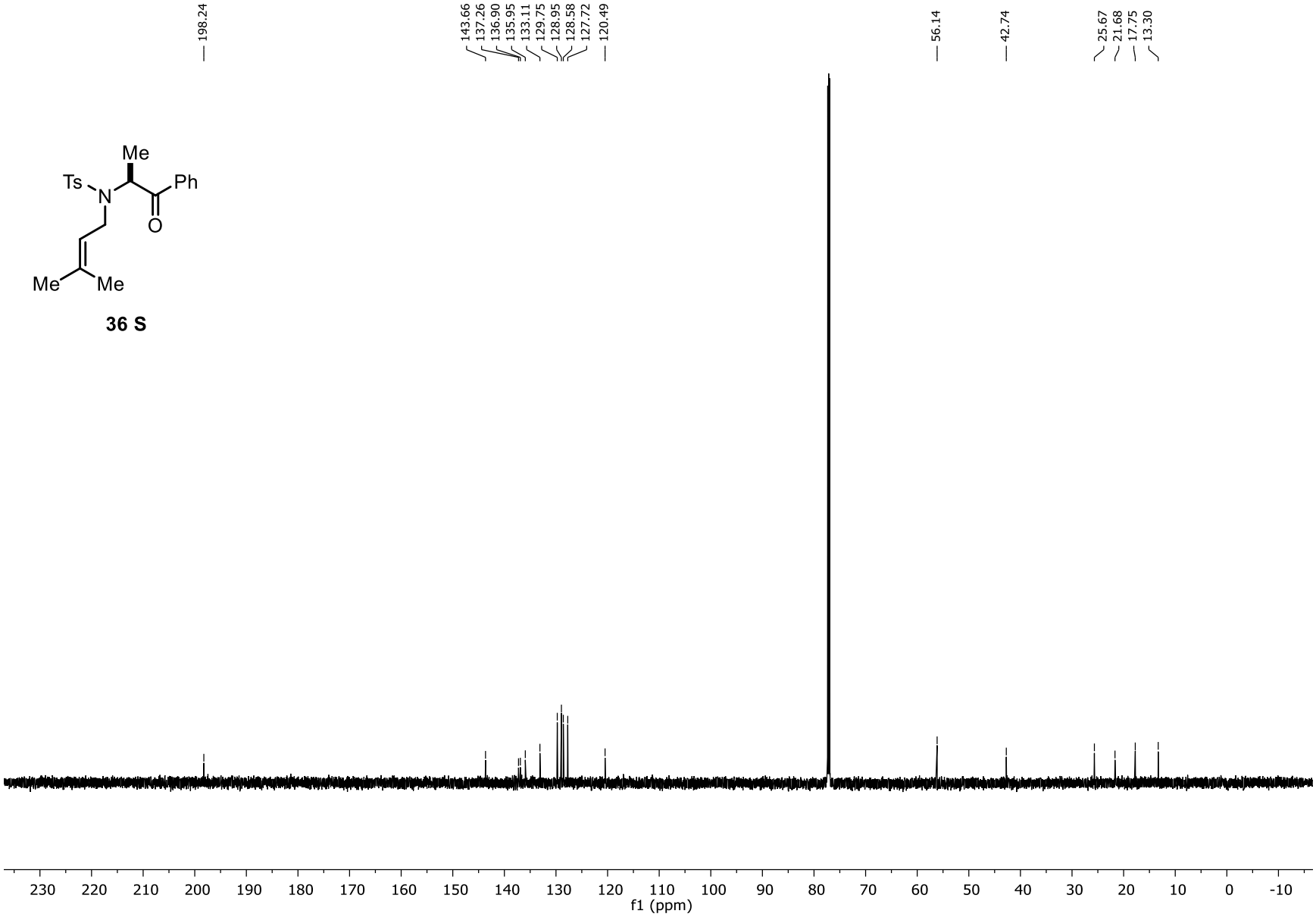
134.01
133.86
129.02
128.12
128.00
126.75
126.17
126.14
126.11
126.08
124.58
122.41
120.24
118.04
77.41
77.16
76.91
51.71
45.62
25.86
17.74
Ts
F
N
Ph
O
Me
Me
35 S
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
Ts
N
Ph
O
Me
Me
36 S
8.07
8.06
7.66
7.65
7.57
7.56
7.55
7.48
7.46
7.45
7.26
7.25
5.56
5.55
5.54
5.53
4.79
4.78
4.77
3.88
3.87
3.86
3.85
3.62
3.61
3.59
3.58
2.41
1.55
1.47
1.45
1.24
1.23
2.00
2.00
1.01
2.00
1.15
1.00
1.00
1.03
1.03
3.00
3.00
3.00
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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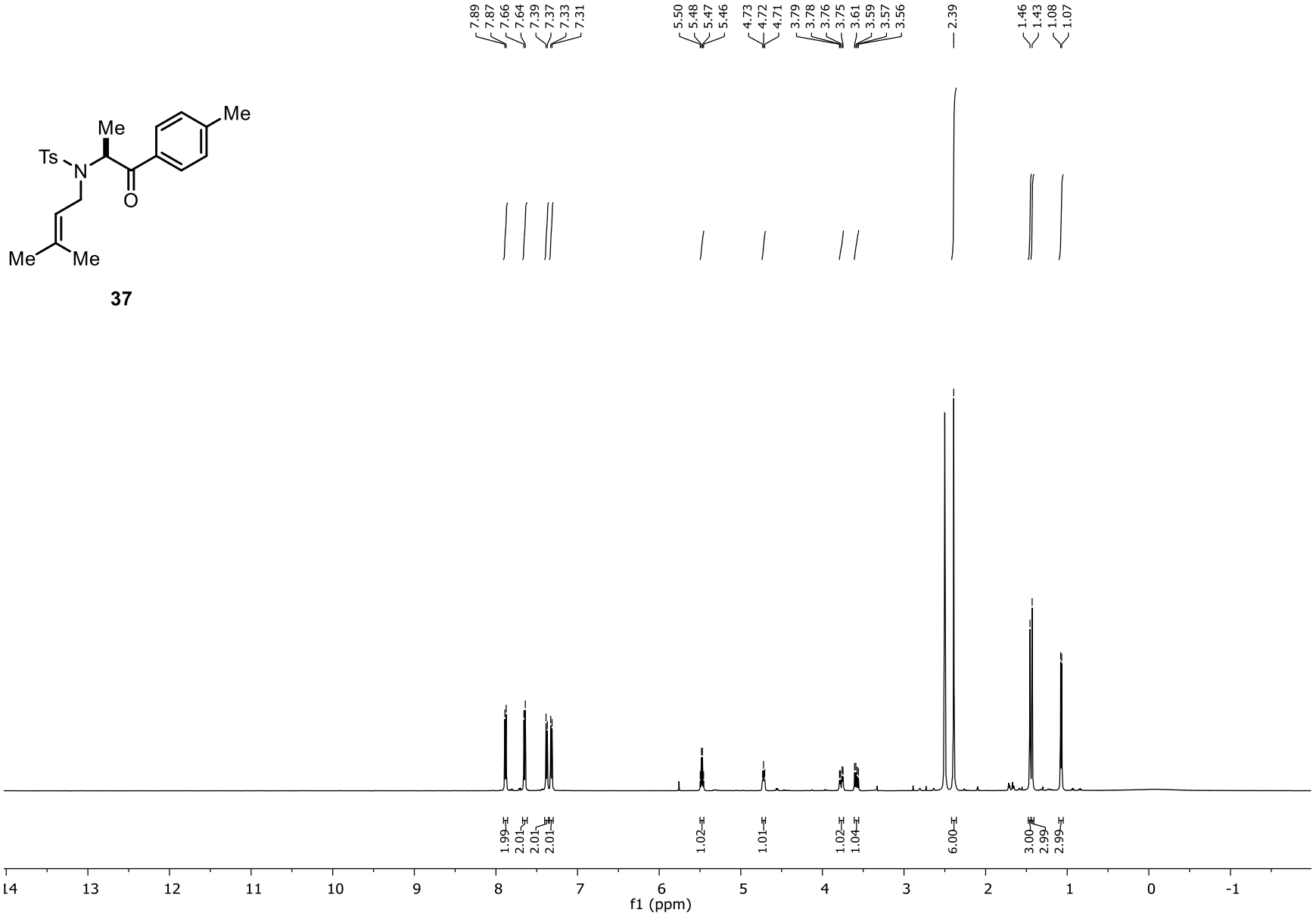
133.11
129.75
128.95
128.58
127.72
120.49
56.14
42.74
25.67
21.68
17.75
13.30
Me
Ts
N
Ph
O
Me
Me
36 S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.37
7.33
7.31
5.50
5.48
5.47
5.46
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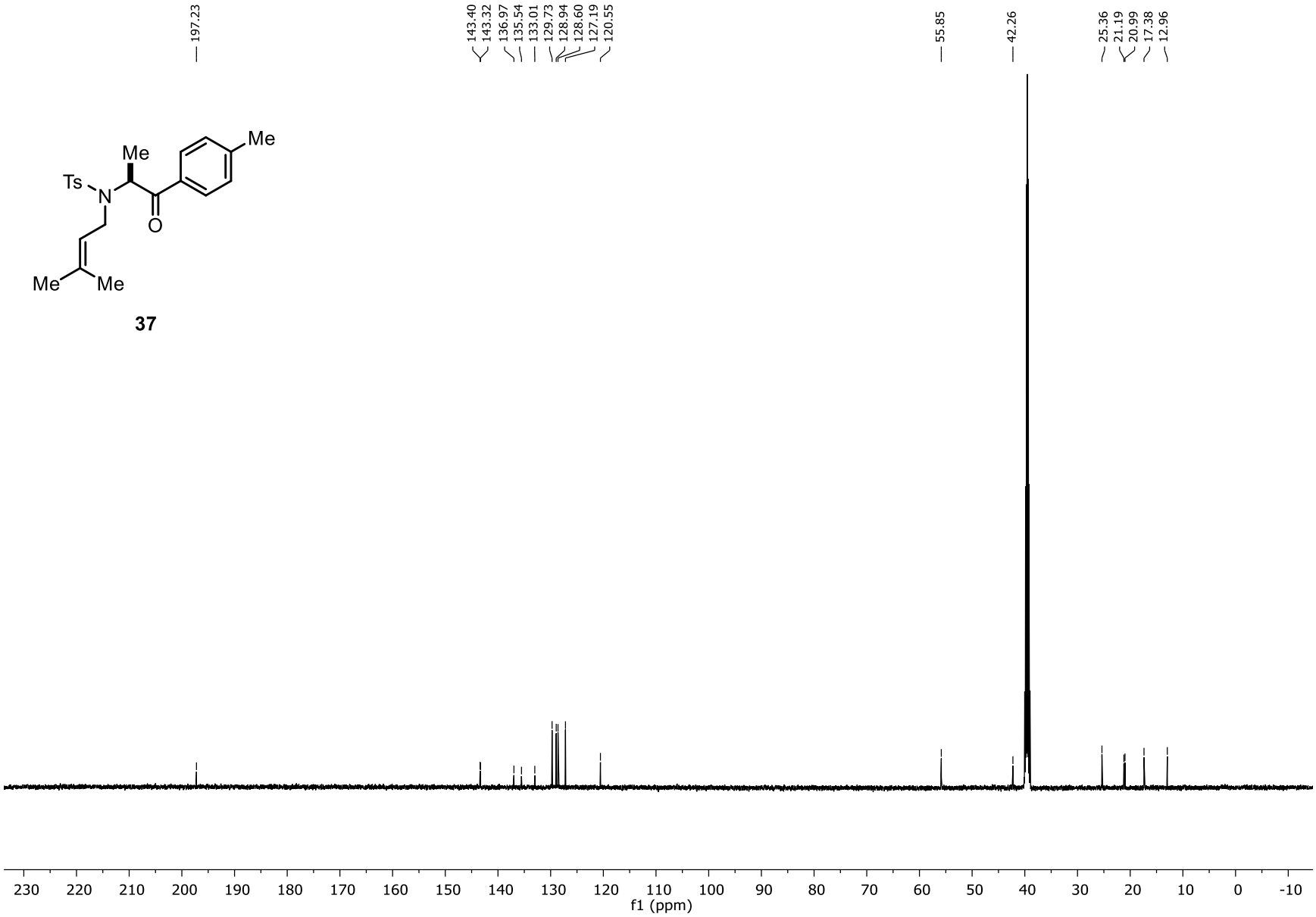
4.72
4.71
3.79
3.78
3.76
3.75
3.61
3.59
3.57
3.56
2.39
1.46
1.43
1.08
1.07
Me
Me
Ts
N
O
Me
Me
1.99
2.01
2.01
2.01
1.02
1.01
1.02
1.04
6.00
3.00
2.99
2.99
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

37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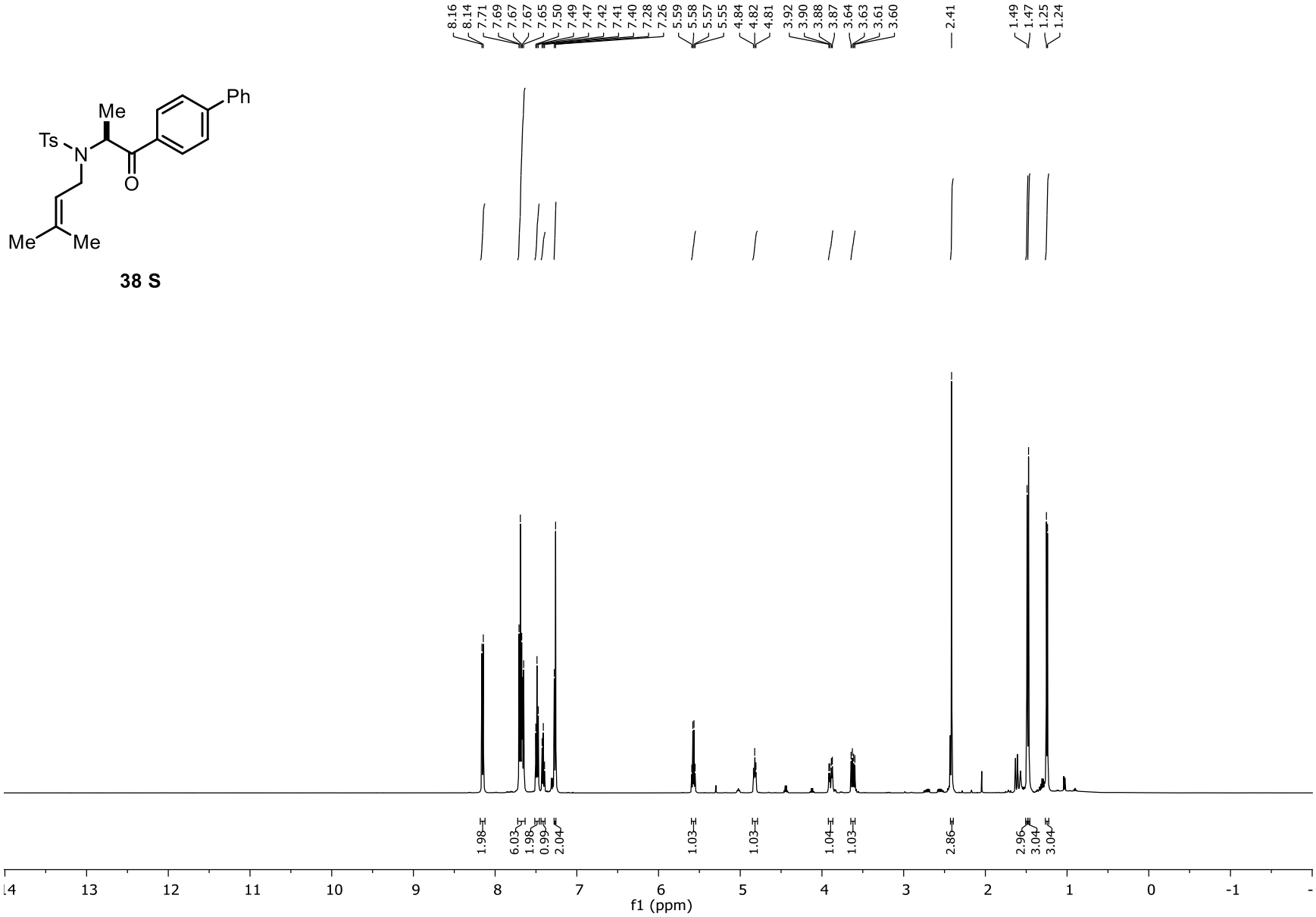
133.01
129.73
128.94
128.60
127.19
120.55
55.85
42.26
25.36
21.19
20.99
17.38
12.96
Me
Me
Ts
N
O
Me
Me
37
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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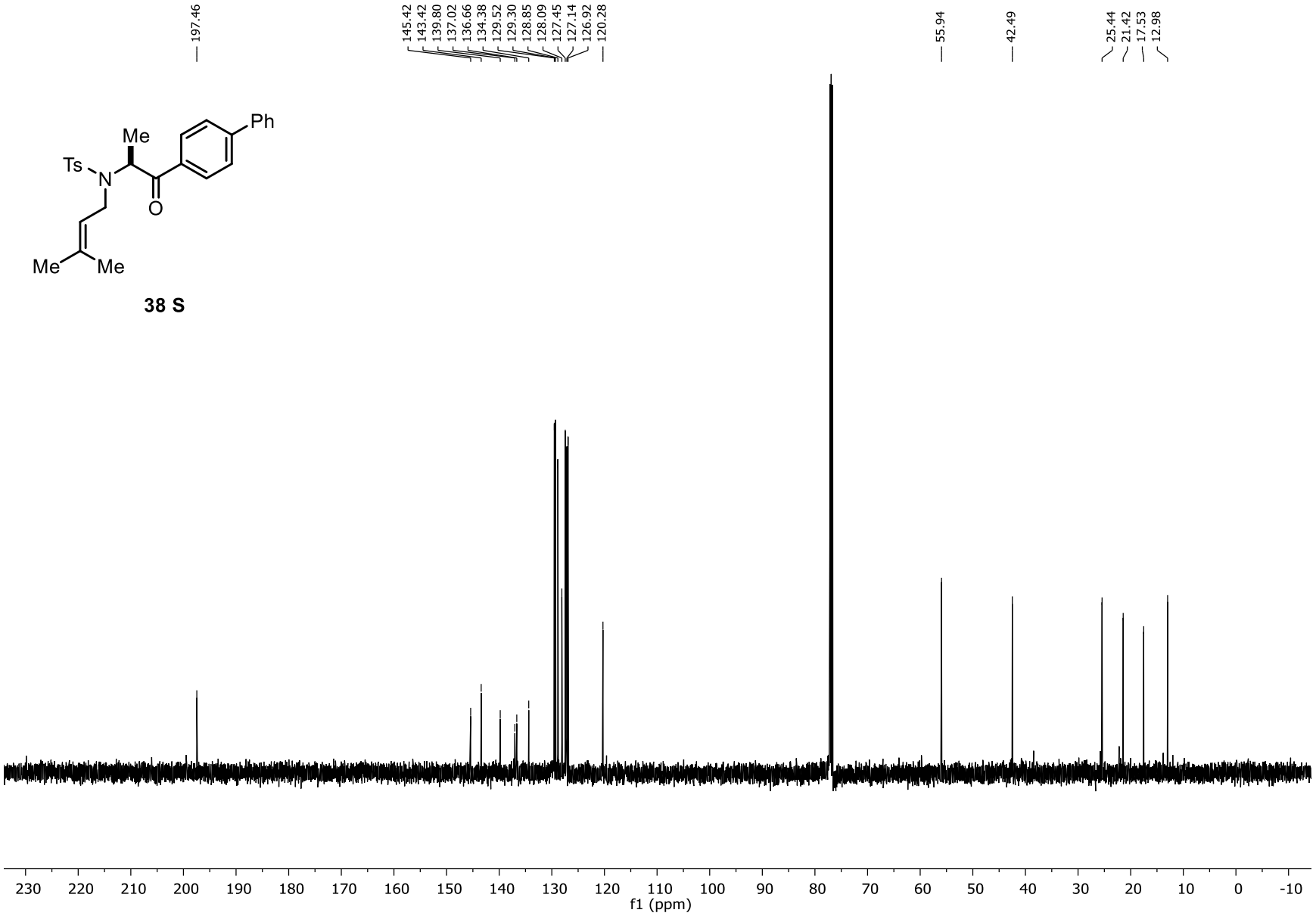
7.50
7.49
7.47
7.42
7.41
7.40
7.28
7.26
5.59
5.58
5.57
5.55
4.84
4.82
4.81
3.92
3.90
3.88
3.87
3.64
3.63
3.61
3.60
2.41
1.49
1.47
1.25
1.24
Ph
Me
Ts
N
O
Me
Me
1.98
6.03
1.98
0.99
2.04
1.03
1.03
1.04
1.03
2.86
2.96
3.04
3.04
f1 (ppm)

38 S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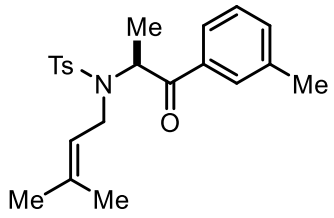
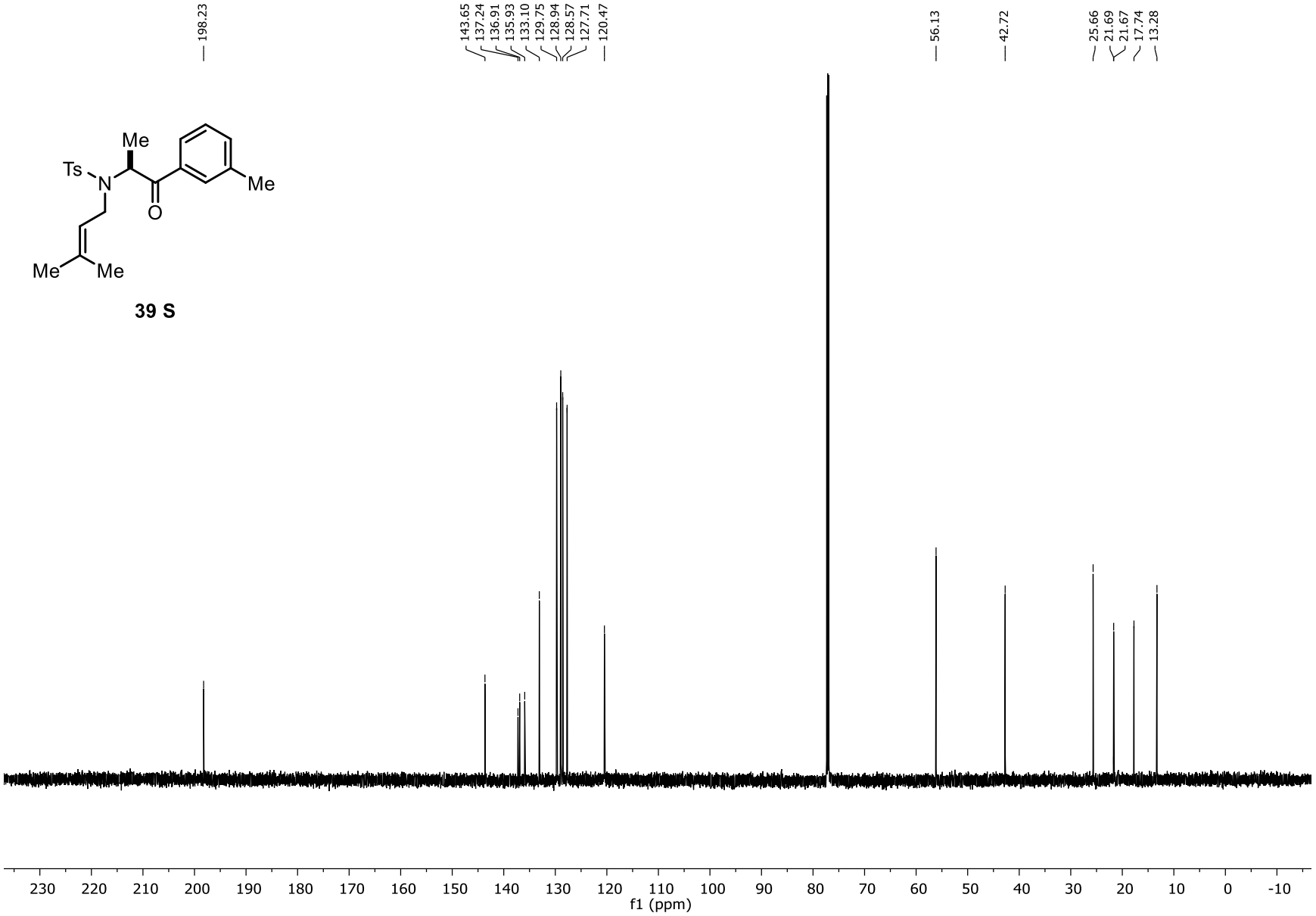
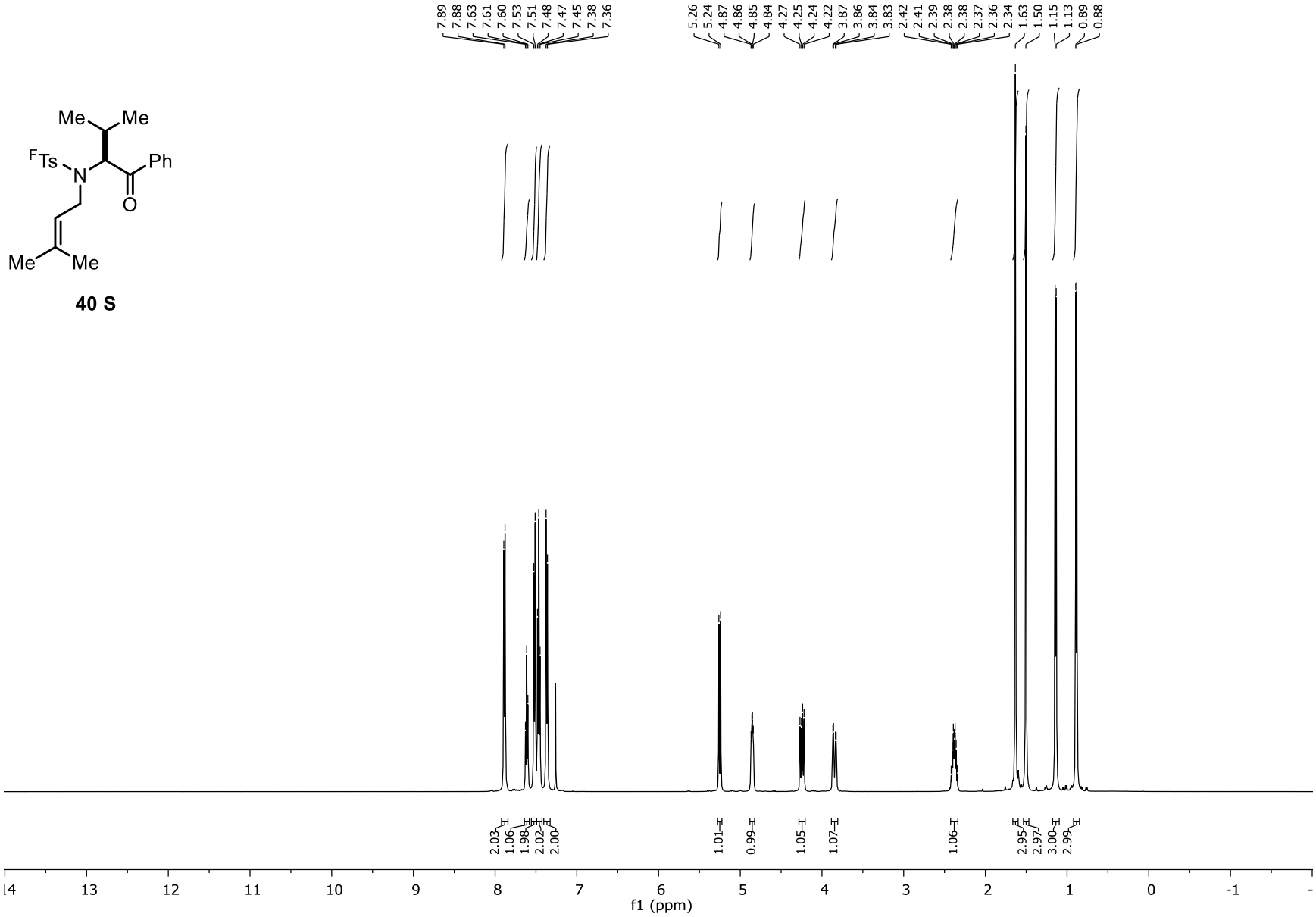
134.38
129.52
129.30
128.85
128.09
127.45
127.14
126.92
120.28
55.94
42.49
25.44
21.42
17.53
12.98
Ph
Me
Ts
N
O
Me
Me
38 S
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

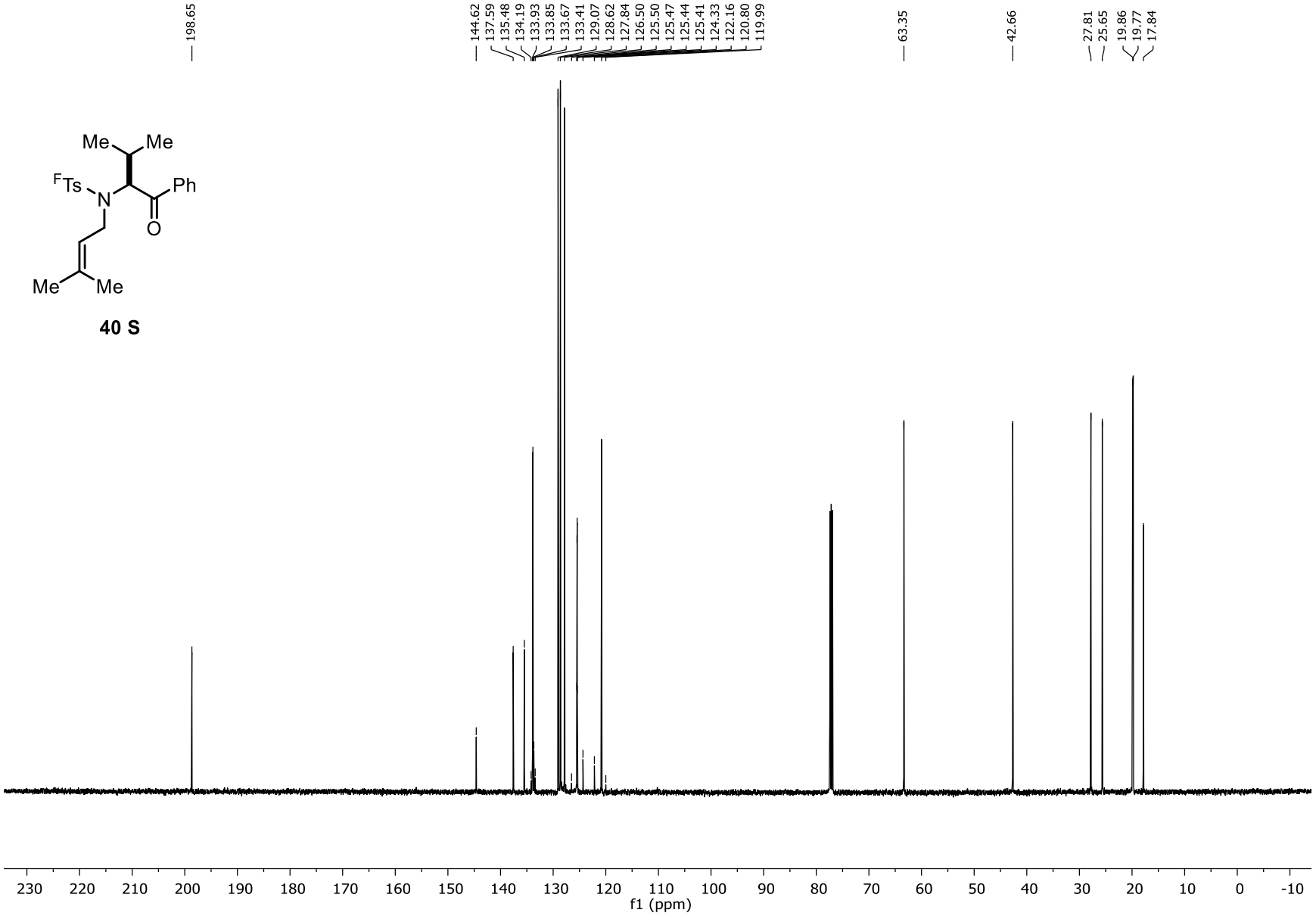

Me
Ts
N
O
Me
Me
Me

39 S

8.07
8.06
7.66
7.65
7.57
7.56
7.55
7.47
7.46
7.45
7.26
7.25
5.56
5.55
5.54
5.53
4.79
4.78
4.77
3.88
3.87
3.86
3.85
3.61
3.60
3.59
3.58
2.41
1.47
1.45
1.24
1.23
1.97
1.96
1.03
2.01
1.02
1.01
1.00
1.00
1.01
3.02
3.01
3.00
3.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


198.23
143.65
137.24
136.91
135.93
133.10
129.75
128.94
128.57
127.71
120.47
56.13
42.72
25.66
21.69
21.67
17.74
13.28
Me
Ts
N
O
Me
Me
Me
39 S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
Me
FTs
N
Ph
O
Me
Me
40 S
7.89
7.88
7.63
7.61
7.60
7.53
7.51
7.48
7.47
7.45
7.38
7.36
5.26
5.24
4.87
4.86
4.85
4.84
4.27
4.25
4.24
4.22
3.87
3.86
3.84
3.83
2.42
2.41
2.39
2.38
2.37
2.36
2.34
1.63
1.50
1.15
1.13
0.89
0.88
2.03
1.06
1.98
2.02
2.00
1.01
0.99
1.05
1.07
1.06
2.95
2.97
3.00
2.99
f1 (ppm)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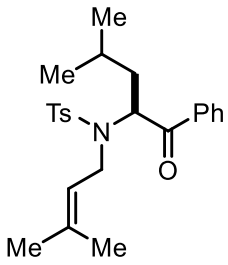
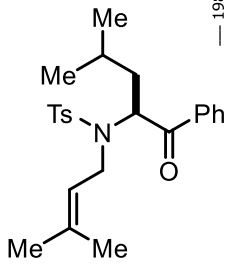
144.62
137.59
135.48
134.19
133.93
133.85
133.67
133.41
129.07
128.62
127.84
126.50
125.50
125.47
125.44
125.41
124.33
122.16
120.80
119.99
63.35
42.66
27.81
25.65
19.86
19.77
17.84
Me
Me
FTs
N
Ph
O
Me
Me
40 S
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
Me
Ts
N
Ph
O
Me
Me

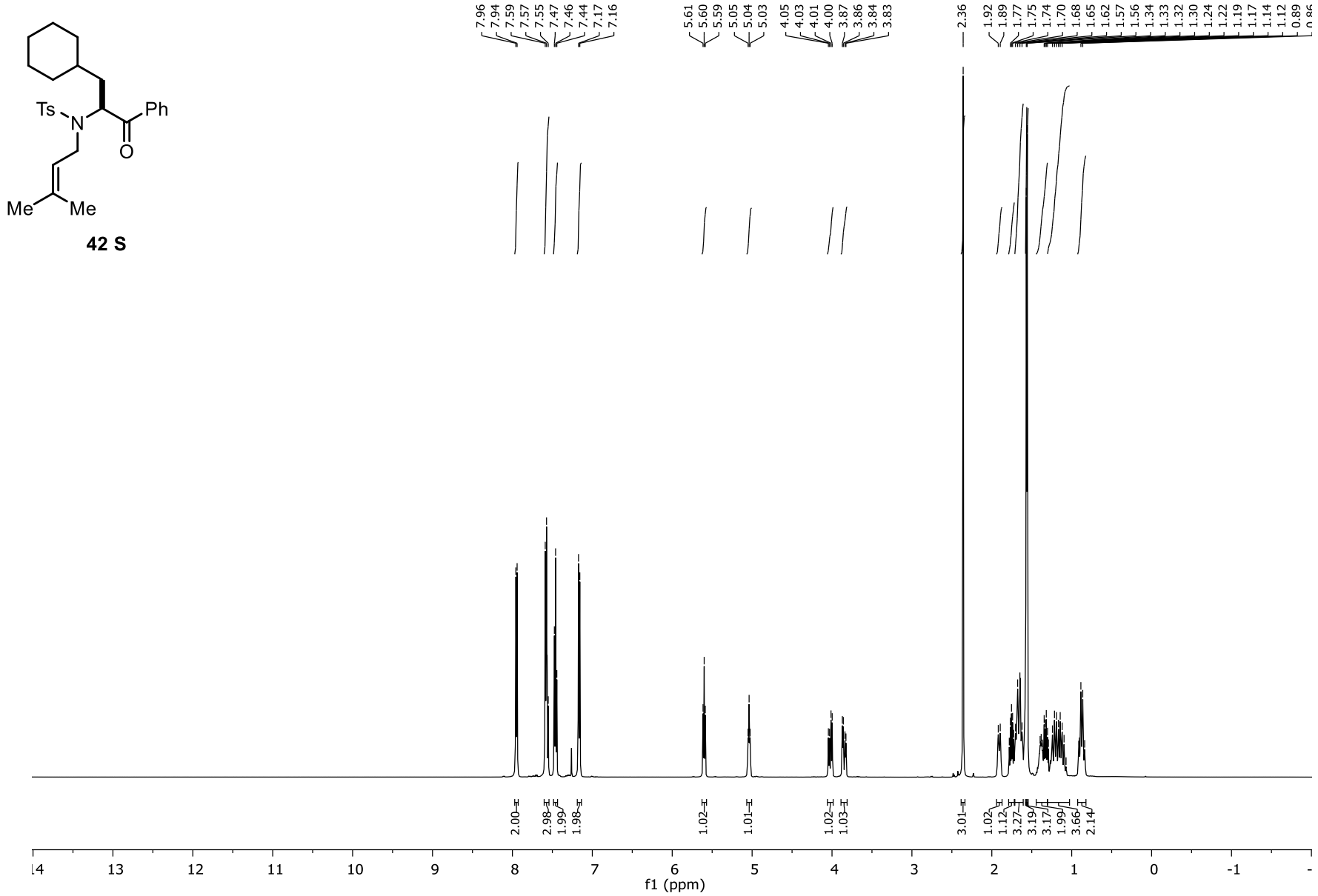
41 S

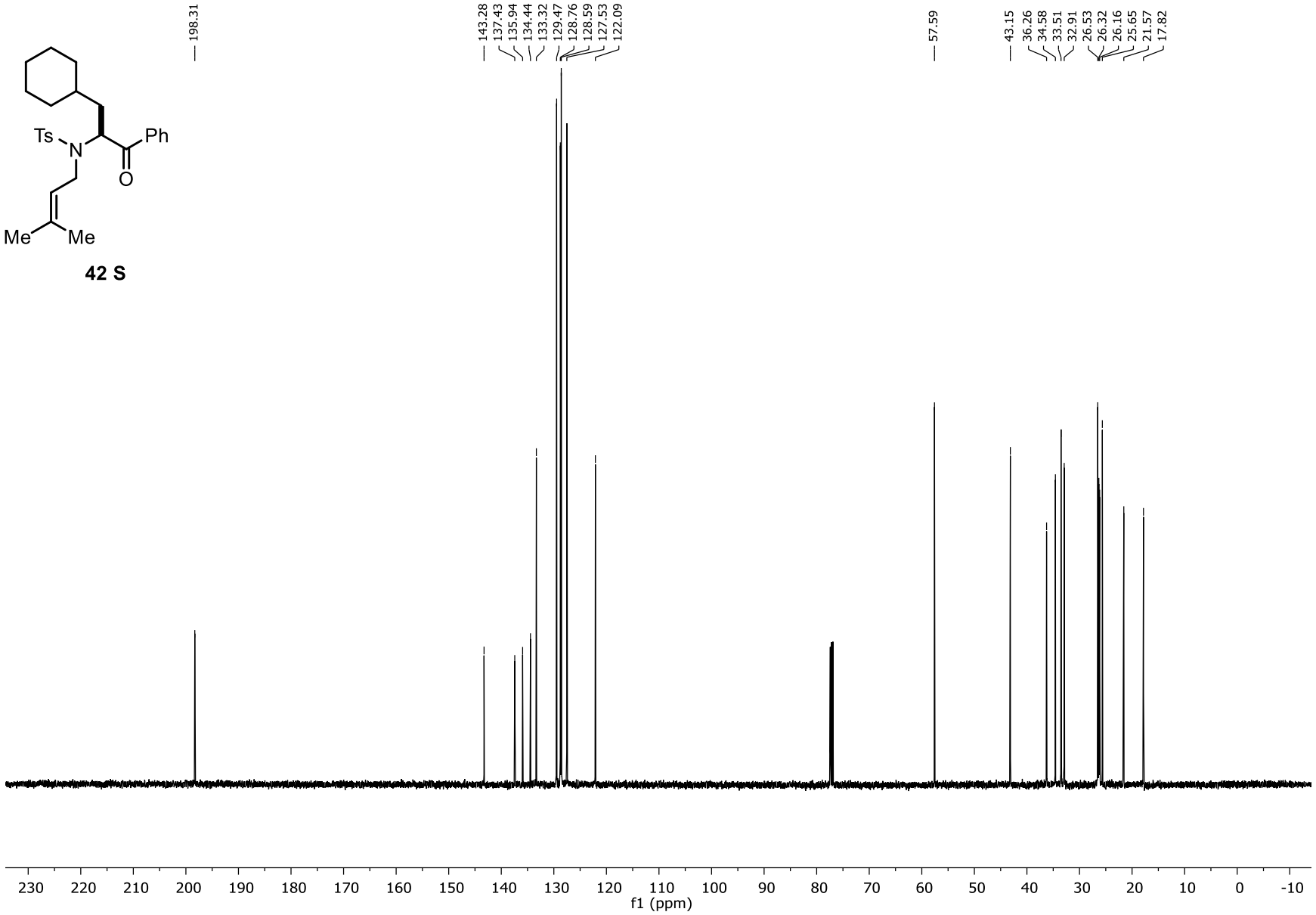
7.96
7.94
7.58
7.56
7.55
7.47
7.46
7.44
7.16
7.14
5.60
5.58
5.57
5.06
5.04
5.03
4.06
4.04
4.02
4.01
3.85
3.84
3.82
3.80
2.35
1.77
1.75
1.74
1.73
1.72
1.70
1.57
1.56
1.39
1.37
1.35
1.34
1.32
1.00
0.99
0.87
0.86
2.00
2.95
2.04
1.99
1.07
1.08
1.13
1.12
3.01
1.97
2.80
3.07
1.01
3.07
3.09
f1 (ppm)


Me
Me
Ts
N
Ph
O
Me
Me

41 S

198.24
143.28
137.35
135.98
134.46
133.34
129.45
128.77
128.55
127.51
122.03
58.23
43.18
37.67
25.68
25.27
22.67
22.19
21.55
17.80
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ts
N
Ph
O
Me
Me
42 S
7.96
7.94
7.59
7.57
7.55
7.47
7.46
7.44
7.17
7.16
5.61
5.60
5.59
5.05
5.04
5.03
4.05
4.03
4.01
4.00
3.87
3.86
3.84
3.83
2.36
1.92
1.89
1.77
1.75
1.74
1.70
1.68
1.65
1.62
1.57
1.56
1.34
1.33
1.32
1.30
1.24
1.22
1.19
1.17
1.14
1.12
0.89
2.00
2.98
1.99
1.98
1.02
1.01
1.02
1.03
3.01
1.02
1.12
3.27
3.19
3.17
1.99
3.66
2.14
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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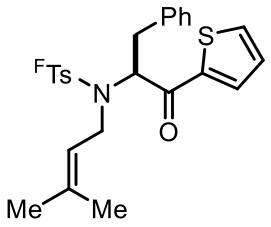
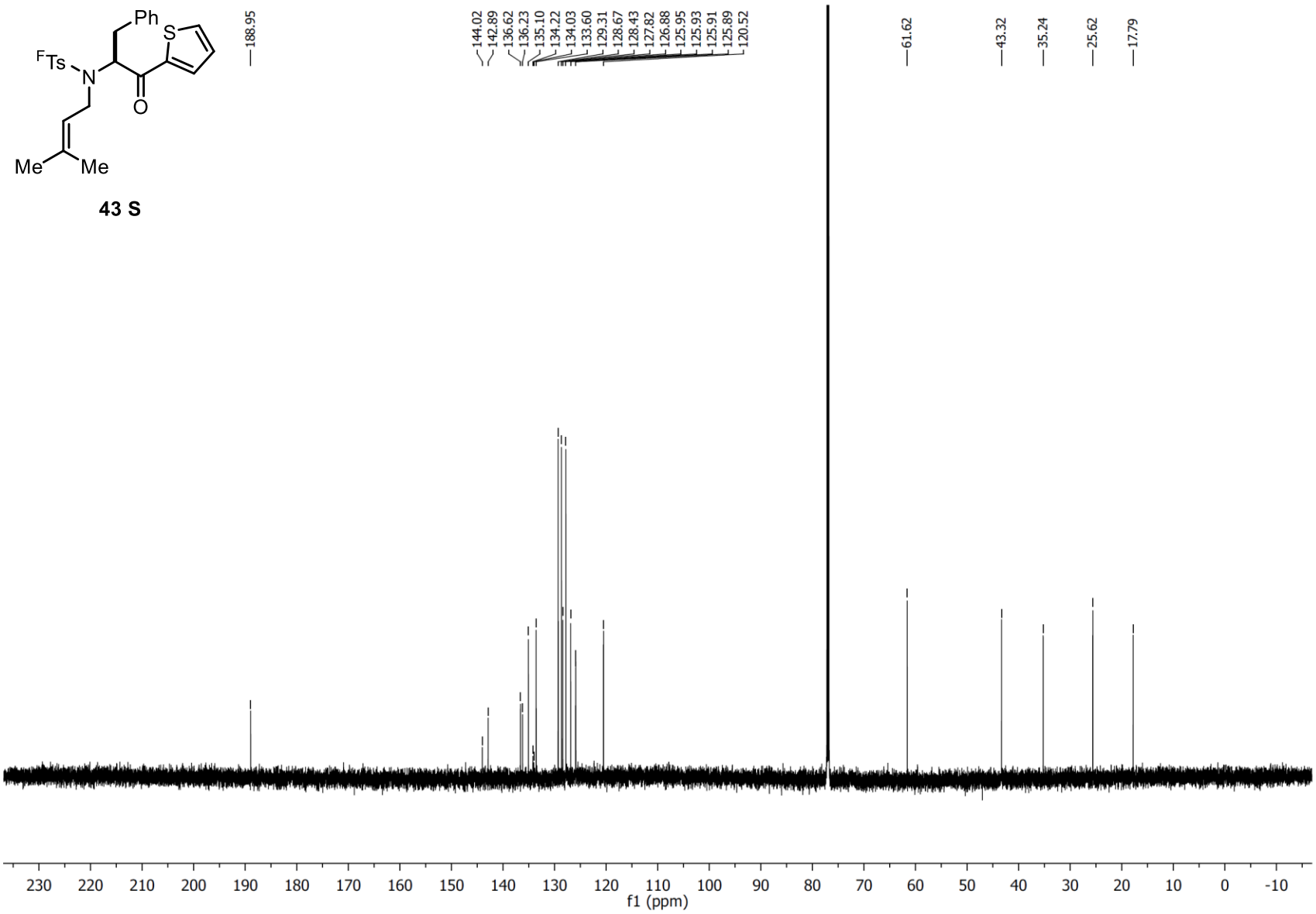
135.94
134.44
133.32
129.47
128.76
128.59
127.53
122.09
57.59
43.15
36.26
34.58
33.51
32.91
26.53
26.32
26.16
25.65
21.57
17.82
Ts
N
Ph
O
Me
Me
42 S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

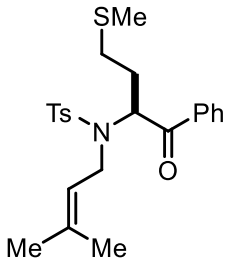

Ph
S
FTs
N
O
Me
Me

43 S

7.91
7.91
7.73
7.72
7.65
7.64
7.63
7.62
7.25
7.24
7.23
7.21
7.20
7.19
7.18
7.09
7.08
7.08
5.67
5.66
5.66
5.65
4.91
4.90
4.89
4.09
4.08
3.97
3.96
3.38
3.37
3.36
2.79
2.78
2.77
2.76
0.90
1.82
0.88
1.85
1.91
2.86
0.92
1.00
0.98
1.12
1.12
1.09
1.05
2.75
2.90
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

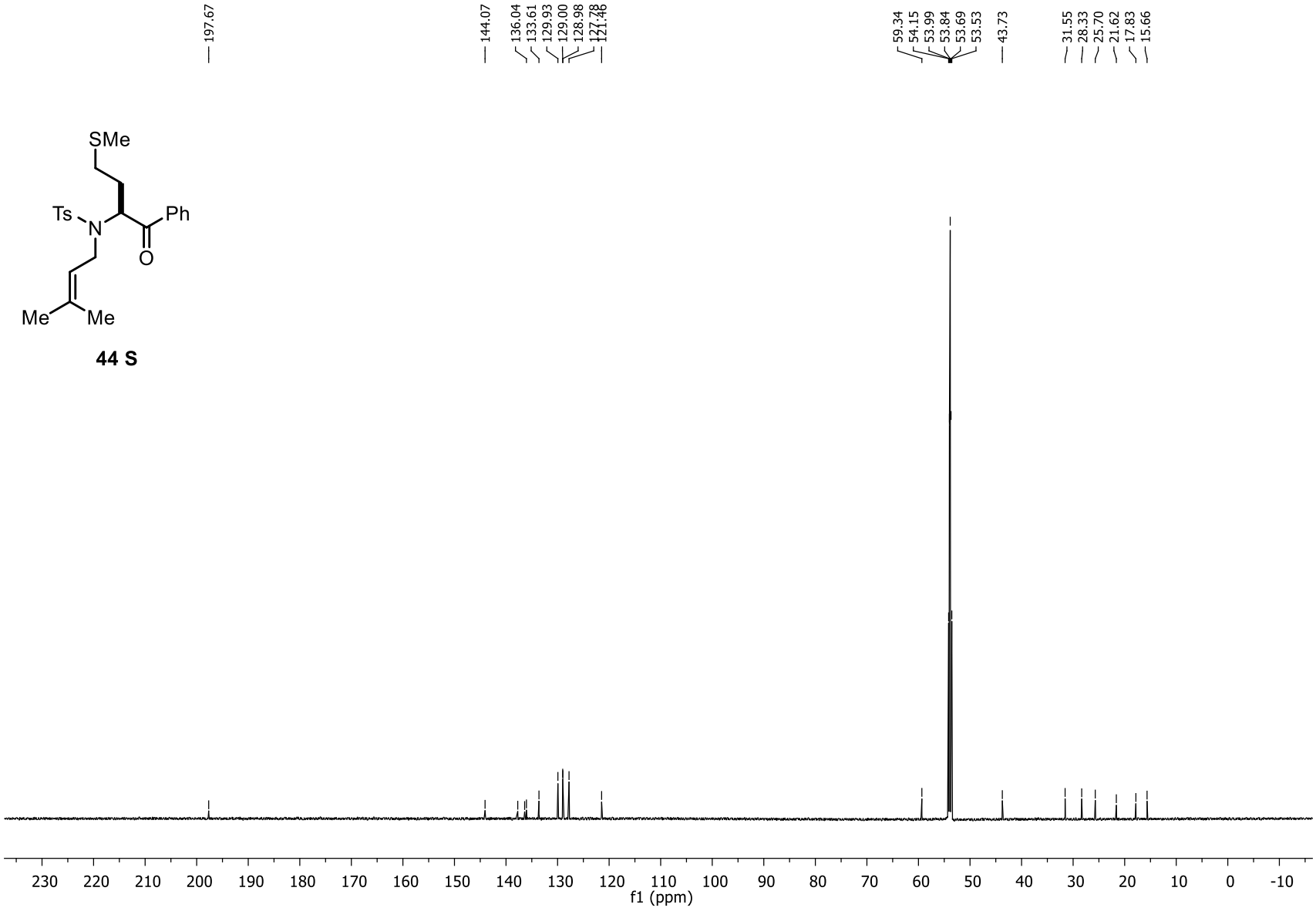

Ph
S
FTs
N
O
Me
Me
188.95
144.02
142.89
136.62
136.23
135.10
134.22
134.03
133.60
129.31
128.67
128.43
127.82
126.88
125.95
125.93
125.91
125.89
120.52
61.62
43.32
35.24
25.62
17.79
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

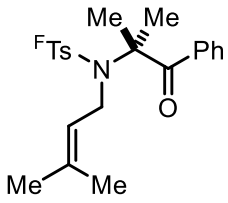
43 S


SMe
Ts
N
Ph
O
Me
Me

44 S

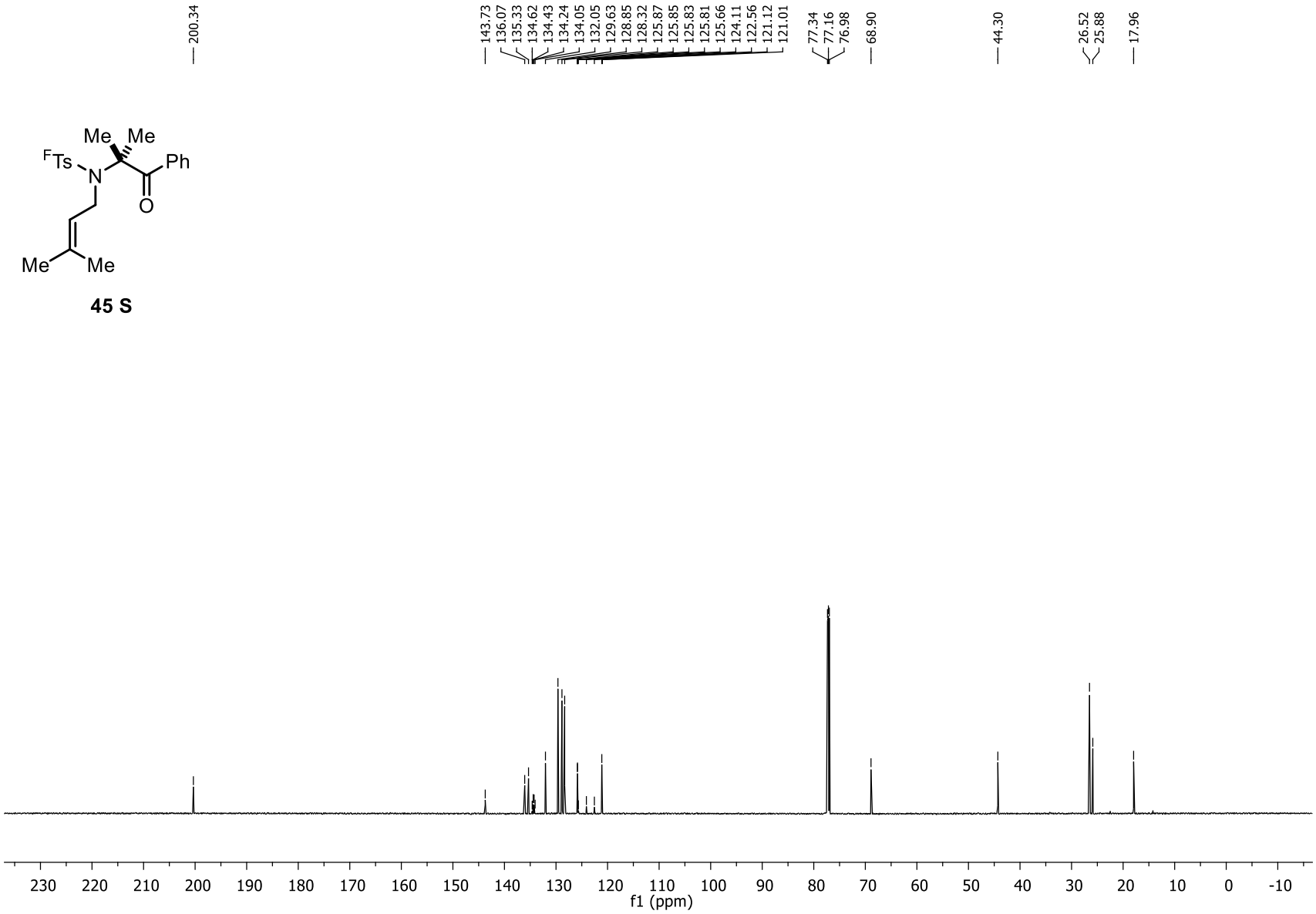
8.01
8.00
7.61
7.60
7.58
7.47
7.46
7.45
7.26
7.20
5.67
5.66
5.65
4.94
4.94
4.93
3.97
3.96
3.95
3.94
3.79
3.78
3.77
2.62
2.61
2.60
2.59
2.58
2.50
2.49
2.48
2.48
2.47
2.38
2.30
2.29
2.28
2.27
2.26
2.25
2.07
1.71
1.70
1.69
1.68
1.67
1.66
1.55
1.53
2.00
1.93
1.20
2.15
2.01
1.07
1.09
1.13
1.10
1.26
1.14
3.08
1.16
3.04
1.24
3.11
3.13
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

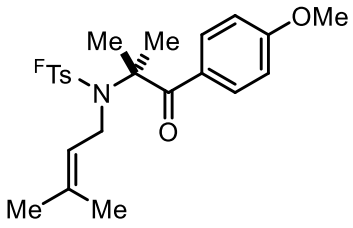

197.67
144.07
136.04
133.61
129.93
129.00
128.98
127.78
121.46
59.34
54.15
53.99
53.84
53.69
53.53
43.73
31.55
28.33
25.70
21.62
17.83
15.66
SMe
Ts
N
Ph
O
Me
Me
44 S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
Me
FTs
N
Ph
O
Me
Me

45 S

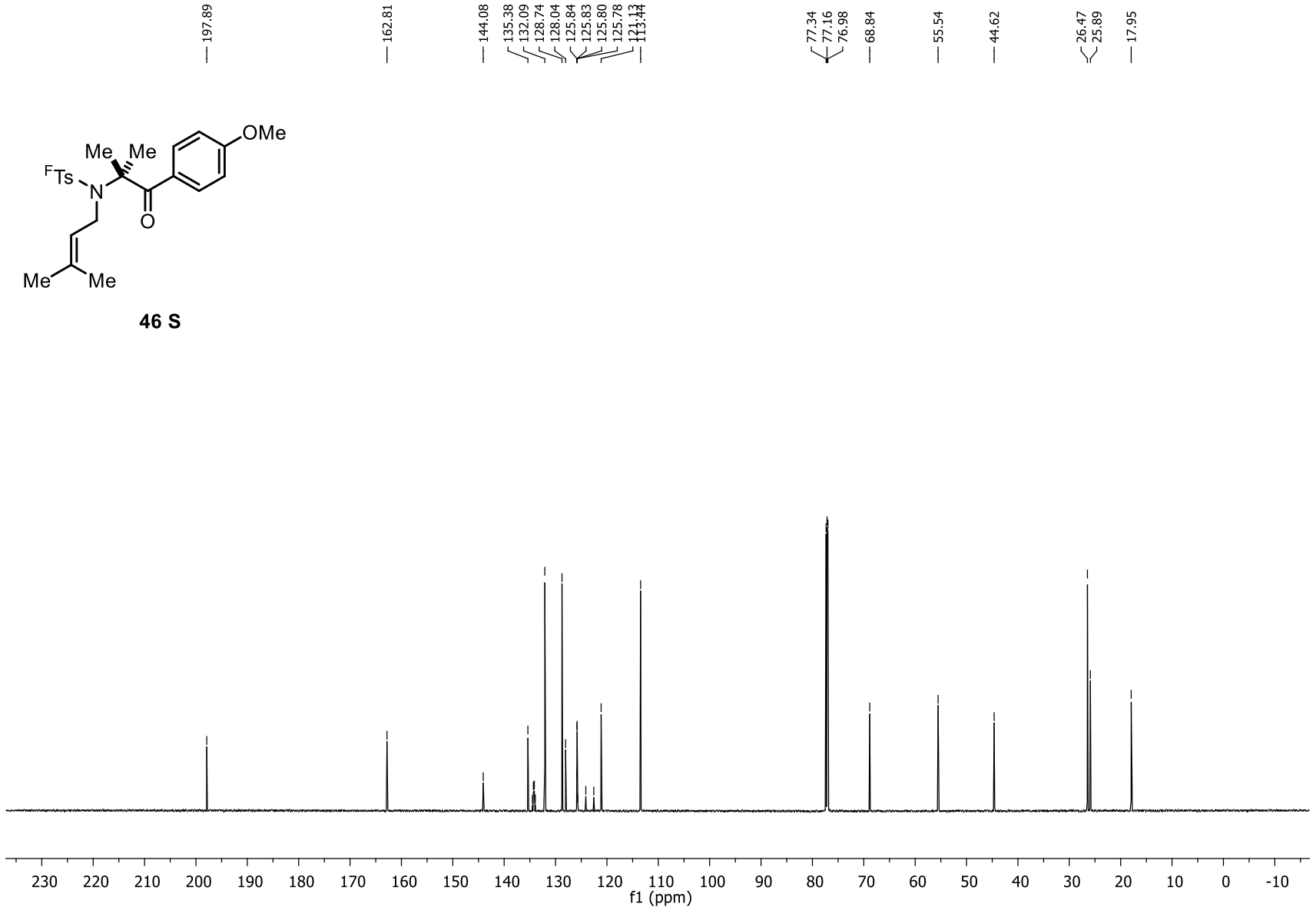
7.99
7.97
7.62
7.55
7.53
7.51
7.42
7.40
7.38
7.26
5.22
5.21
5.19
4.00
3.98
1.68
1.66
1.62
2.12
4.00
1.22
2.21
1.21
2.23
6.23
3.39
3.31
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

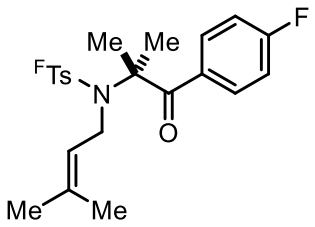

200.34
143.73
136.07
135.33
134.62
134.43
134.24
134.05
132.05
129.63
128.85
128.32
125.87
125.85
125.83
125.81
125.66
124.11
122.56
121.12
121.01
77.34
77.16
76.98
68.90
44.30
26.52
25.88
17.96
Me
Me
FTs
N
Ph
O
Me
Me
45 S
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OMe
Me
Me
FTs
N
O
Me
Me

46 S

8.02
8.01
7.69
7.68
7.64
7.63
7.26
6.86
6.85
5.21
5.20
5.19
4.02
4.01
3.86
1.65
1.64
1.62
2.00
1.91
1.97
1.01
0.96
2.01
3.05
3.28
5.92
3.20
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


197.89
162.81
144.08
135.38
132.09
128.74
128.04
125.84
125.83
125.80
125.78
121.13
113.44
77.34
77.16
76.98
68.84
55.54
44.62
26.47
25.89
17.95
OMe
Me
Me
FTs
N
O
Me
Me
46 S
230
220
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)


Me
Me
F
Ts
N
O
Me
Me

47 S

8.09
8.08
8.07
8.06
7.75
7.73
7.69
7.67
7.26
7.11
7.09
7.06
5.16
4.03
4.01
1.65
1.63
1.62
2.00
4.22
2.23
1.21
1.89
2.84
5.42
3.23
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

198.24
165.72
164.27
143.83
135.61
134.57
134.38
134.19
132.33
132.28
131.98
131.96
128.78
125.98
125.96
125.94
125.92
124.05
122.50
120.95
120.86
115.39
115.26
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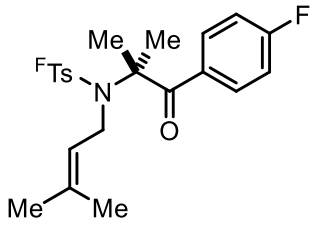
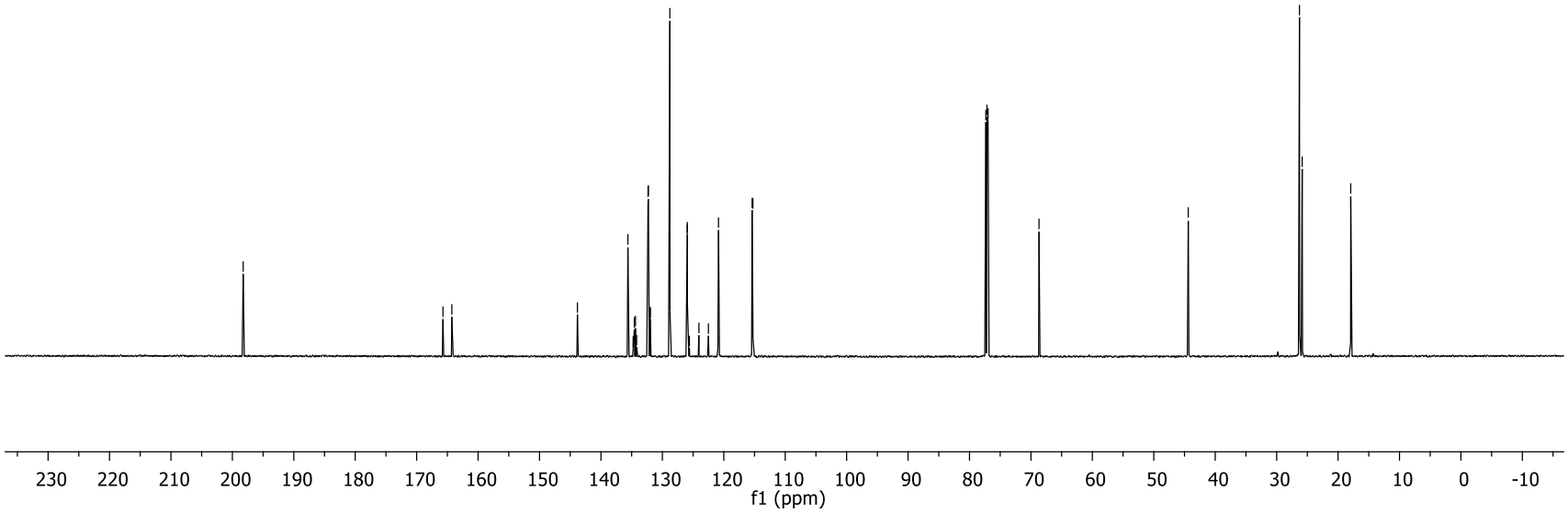
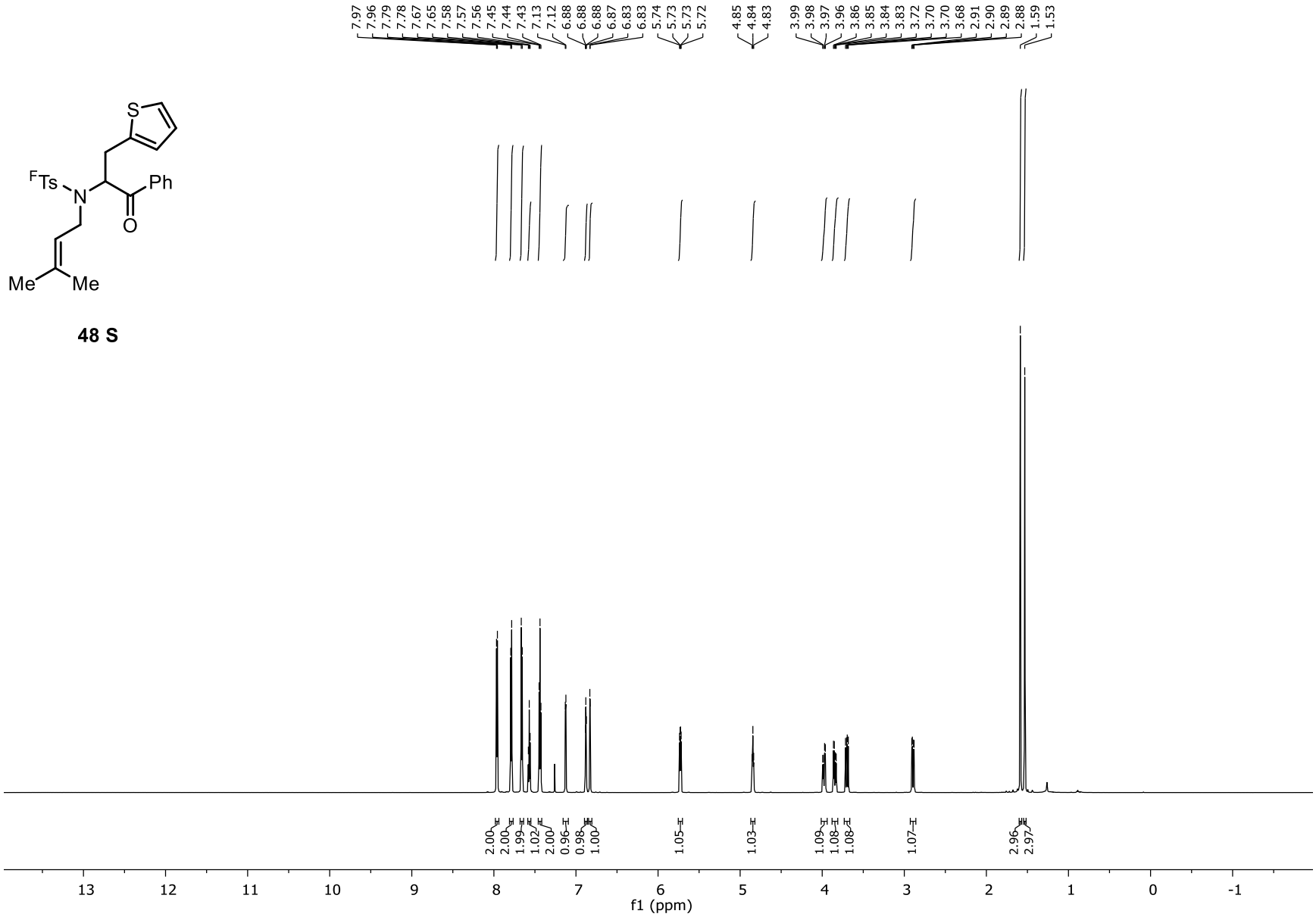
76.98
68.69
44.39
26.29
25.84
17.94

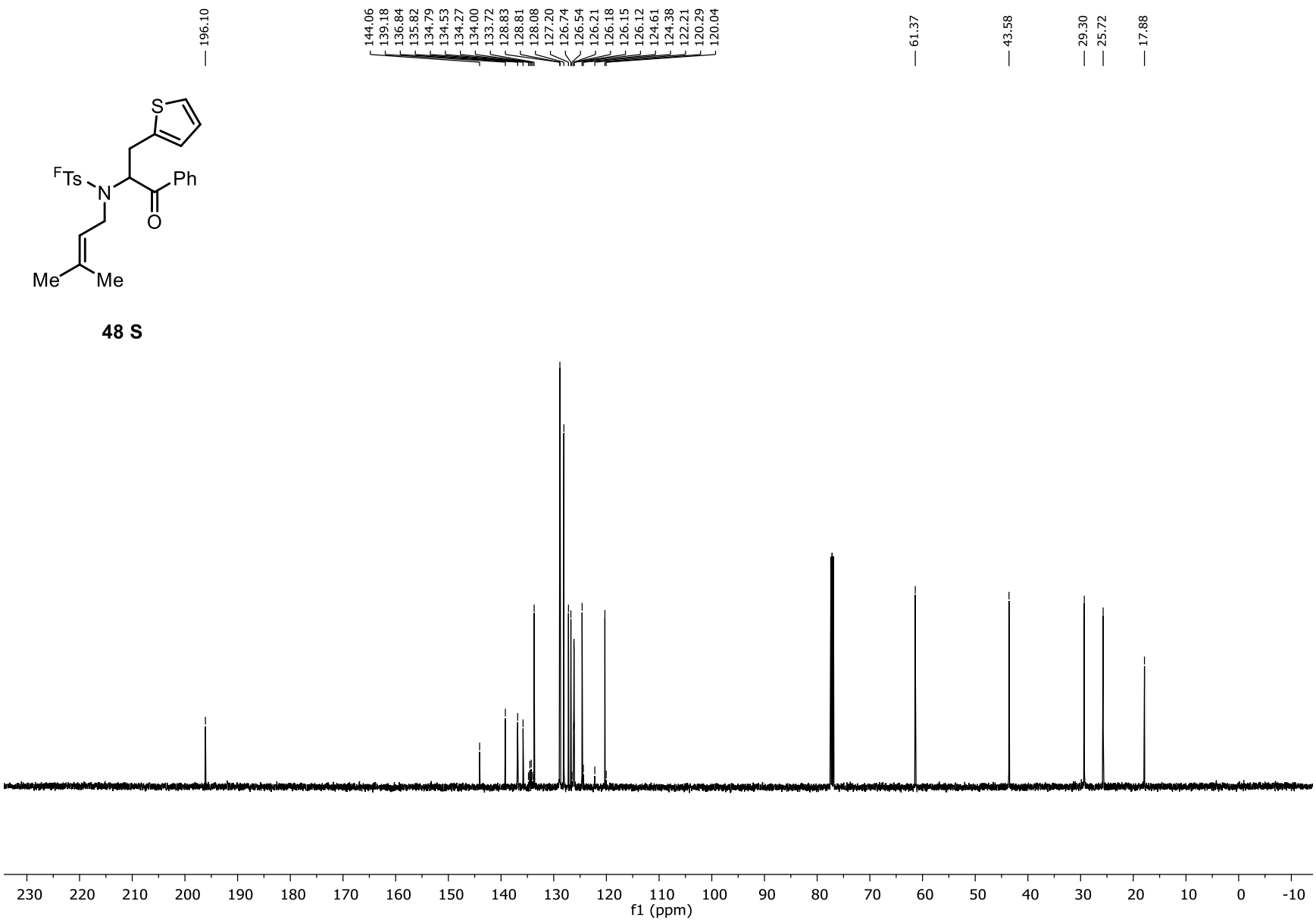


47 S

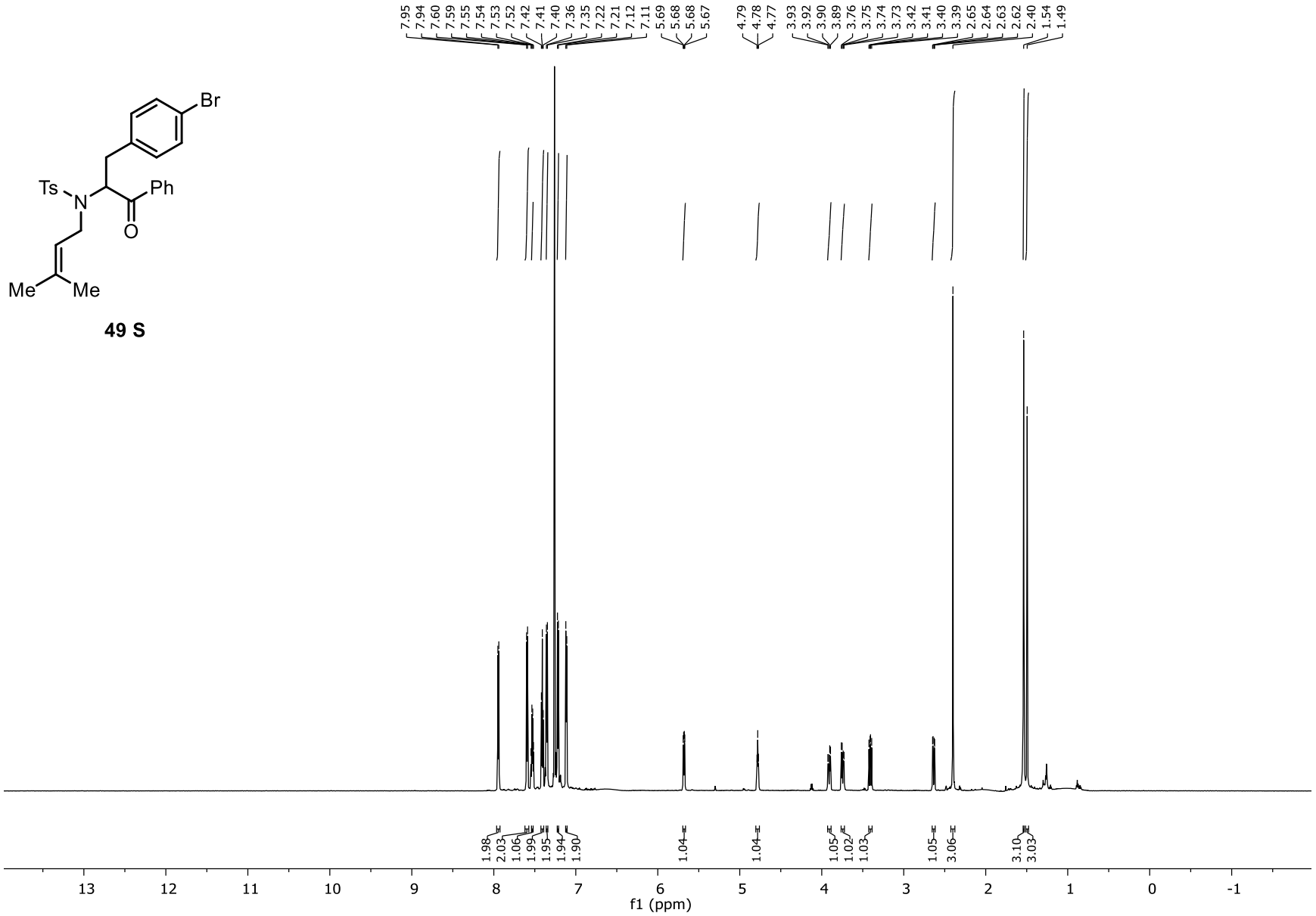



7.97
7.96
7.79
7.78
7.67
7.65
7.58
7.57
7.56
7.45
7.44
7.43
7.13
7.12
6.88
6.88
6.88
6.87
6.83
6.83
5.74
5.73
5.73
5.72
4.85
4.84
4.83
3.99
3.98
3.97
3.96
3.86
3.85
3.84
3.83
3.72
3.70
3.70
3.68
2.91
2.90
2.89
2.88
1.59
1.53
S
FTs
N
Ph
O
Me
Me
2.00
2.00
1.99
1.02
2.00
0.96
0.98
1.00
1.05
1.03
1.09
1.08
1.08
1.07
2.96
2.97
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

48 S


196.10
144.06
139.18
136.84
135.82
134.79
134.53
134.27
134.00
133.72
128.83
128.81
128.08
127.20
126.74
126.54
126.21
126.18
126.15
126.12
124.61
124.38
122.21
120.29
120.04
61.37
43.58
29.30
25.72
17.88
S
FTs
N
Ph
O
Me
Me
230
220
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)

48 S


Br
Ts
N
Ph
O
Me
Me
49 S
7.95
7.94
7.60
7.59
7.55
7.54
7.53
7.52
7.42
7.41
7.40
7.36
7.35
7.22
7.21
7.12
7.11
5.69
5.68
5.68
5.67
4.79
4.78
4.77
3.93
3.92
3.90
3.89
3.76
3.75
3.74
3.73
3.42
3.41
3.40
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2.65
2.64
2.63
2.62
2.40
1.54
1.49
1.98
2.03
1.06
1.99
1.95
1.94
1.90
1.04
1.04
1.05
1.02
1.03
1.05
3.06
3.10
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12
11
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4
3
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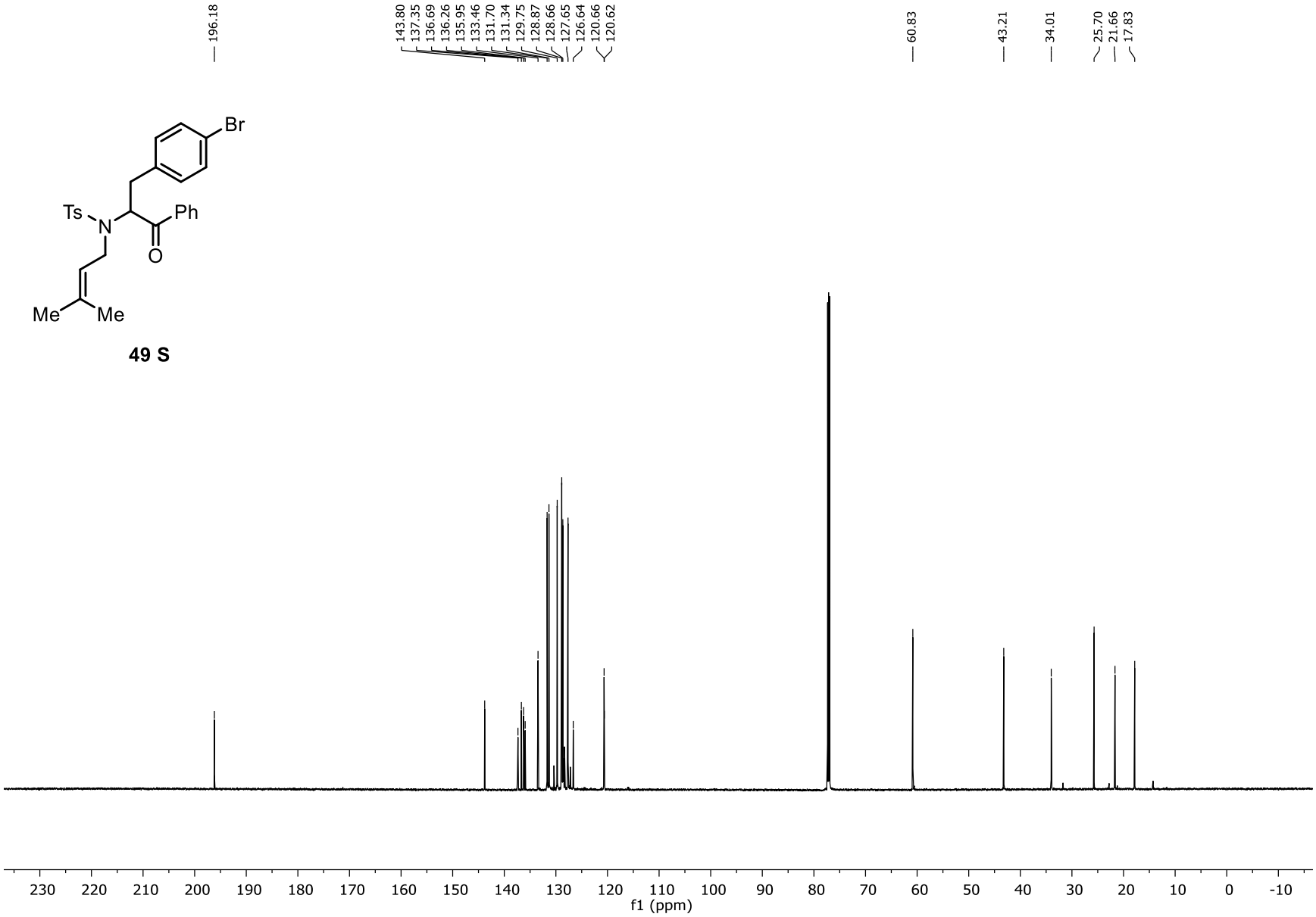
-1
f1 (ppm)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127.65
126.64
120.66
120.62
60.83
43.21
34.01
25.70
21.66
17.83
Br
Ts
N
Ph
O
Me
Me
49 S
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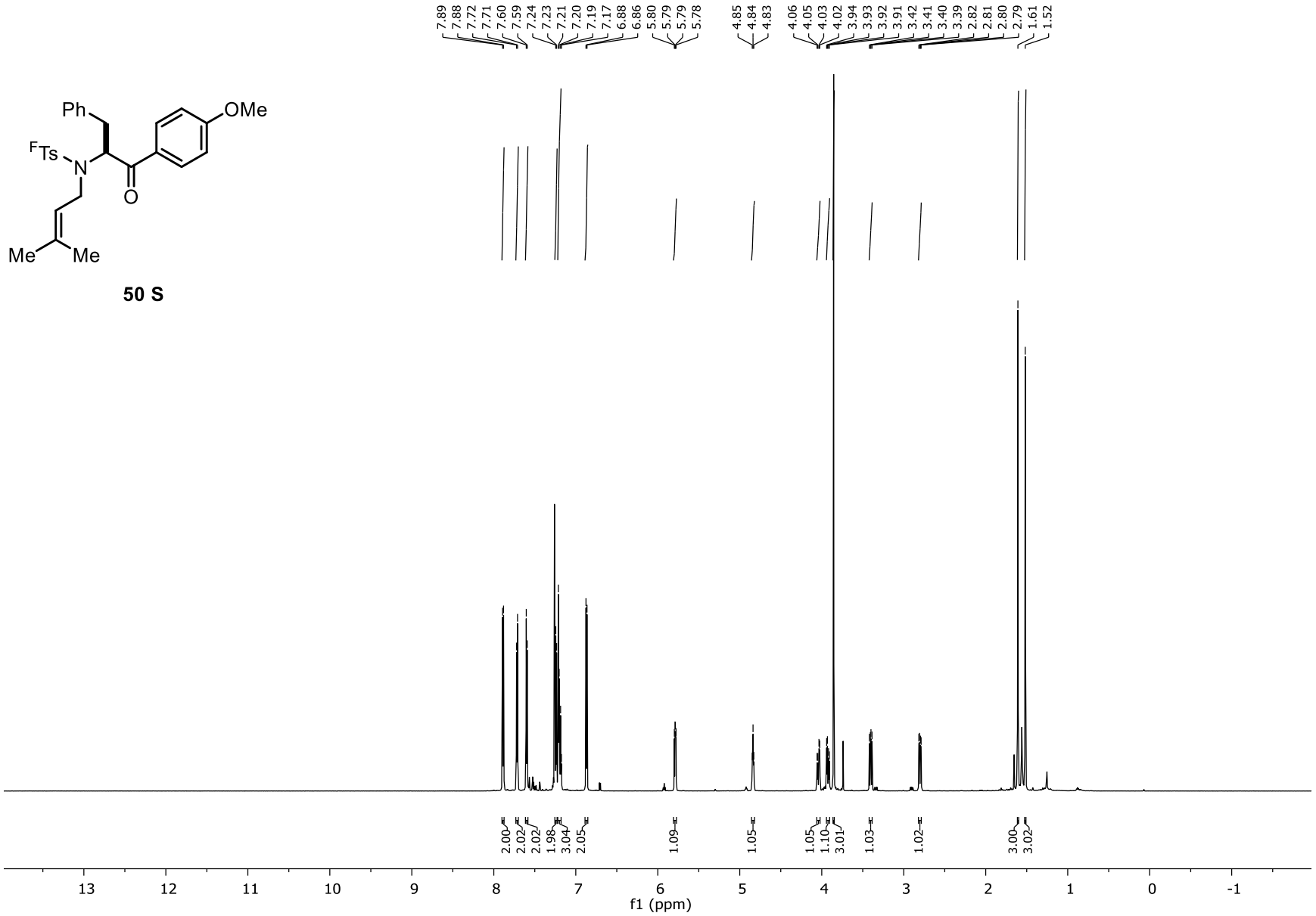
f1 (ppm)


Ph
OMe
FTs
N
O
Me
Me
50 S
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7.72
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7.23
7.21
7.20
7.19
7.17
6.88
6.86
5.80
5.79
5.79
5.78
4.85
4.84
4.83
4.06
4.05
4.03
4.02
3.94
3.93
3.92
3.91
3.42
3.41
3.40
3.39
2.82
2.81
2.80
2.79
1.61
1.52
2.00
2.02
2.02
1.98
3.04
2.05
1.09
1.05
1.05
1.10
3.01
1.03
1.02
3.00
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10
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8
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3
2
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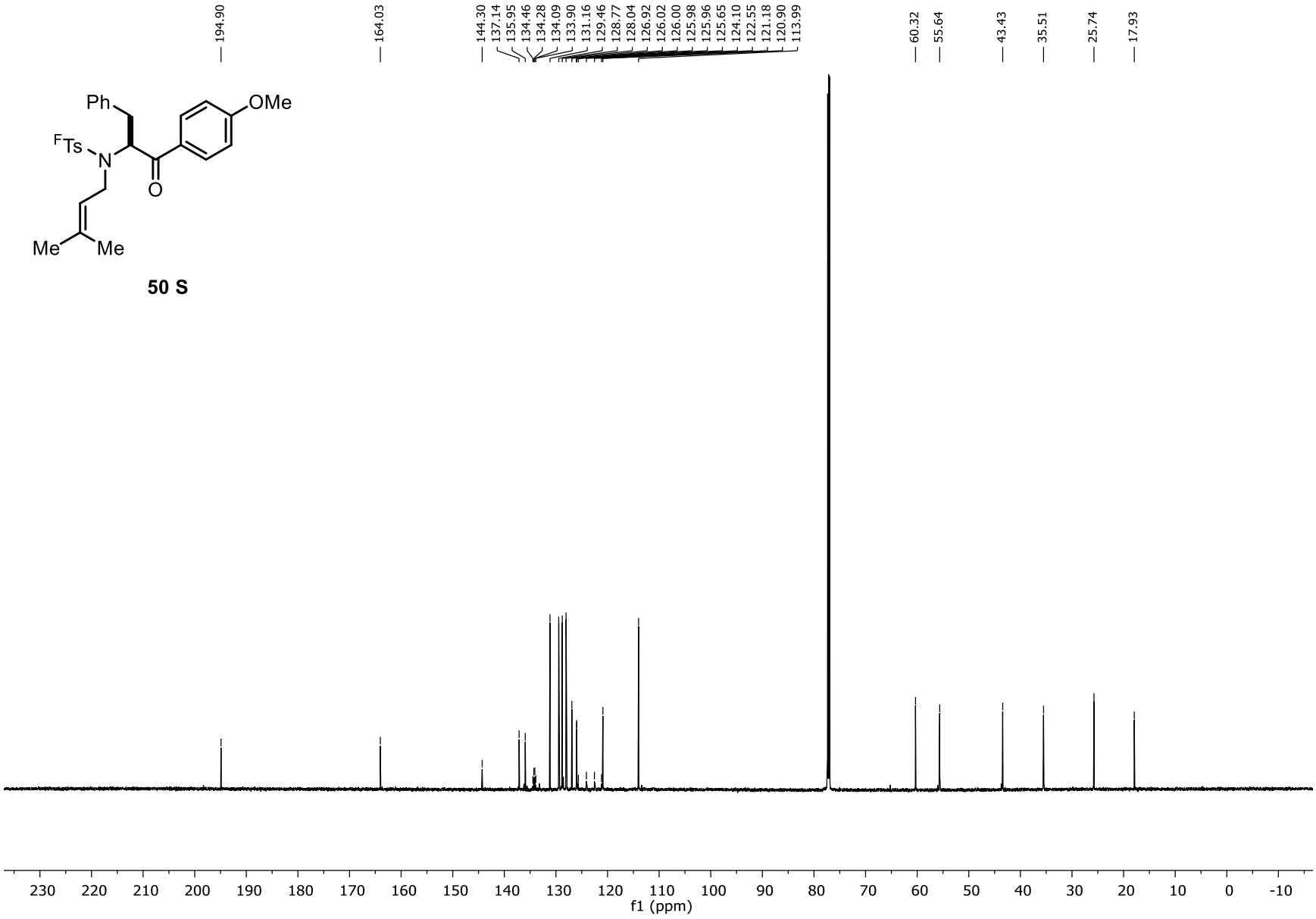
f1 (ppm)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128.04
126.92
126.02
126.00
125.98
125.96
125.65
124.10
122.55
121.18
120.90
113.99
60.32
55.64
43.43
35.51
25.74
17.93
Ph
OMe
FTs
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O
Me
Me
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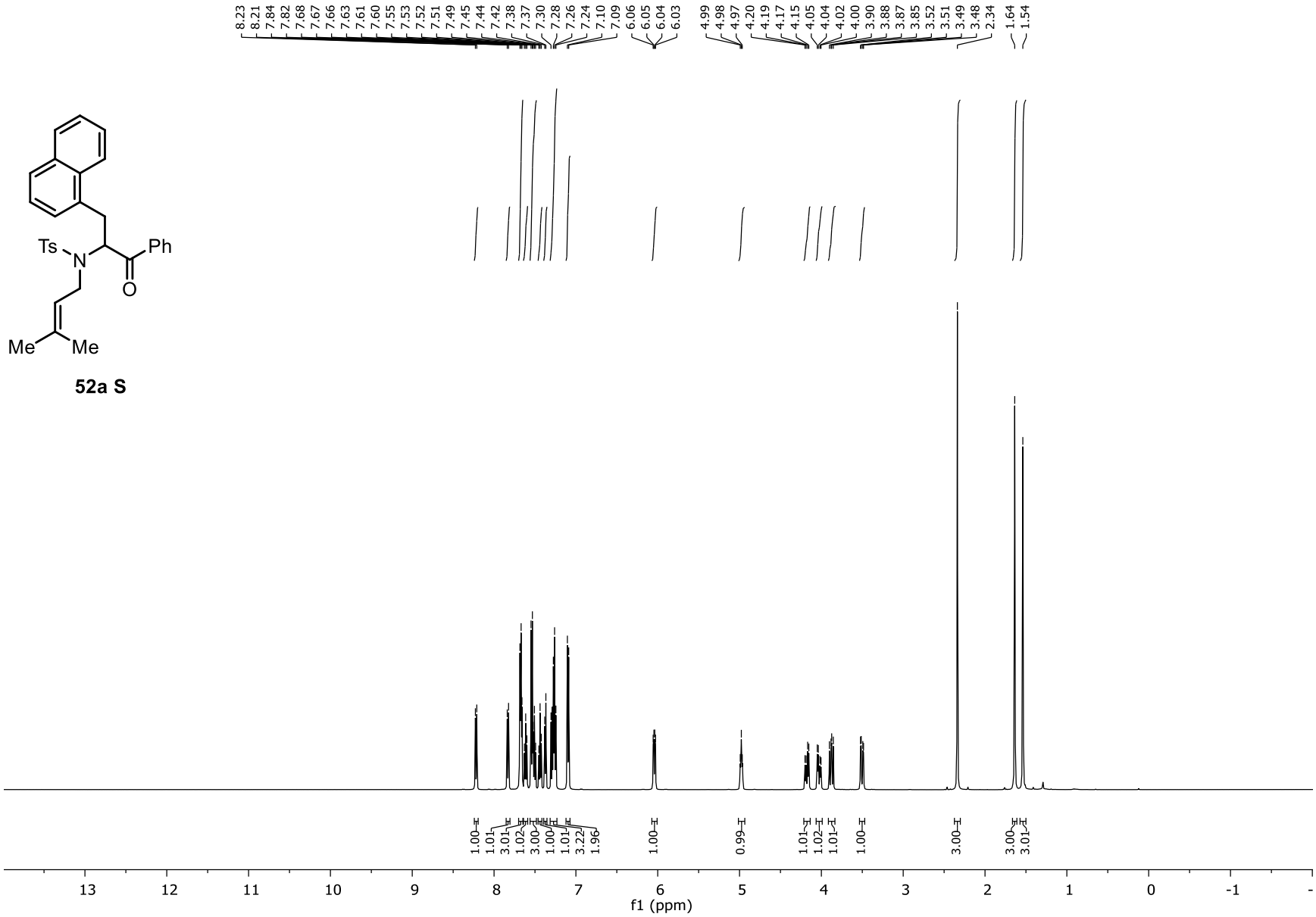
f1 (ppm)

50 S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7.60
7.55
7.53
7.52
7.51
7.49
7.45
7.44
7.42
7.38
7.37
7.30
7.28
7.26
7.24
7.10
7.09
6.06
6.05
6.04
6.03
4.99
4.98
4.97
4.20
4.19
4.17
4.15
4.05
4.04
4.02
4.00
3.90
3.88
3.87
3.85
3.52
3.51
3.49
3.48
2.34
1.64
1.54
Ts
N
Ph
O
Me
Me
52a S
1.00
1.01
3.01
1.02
3.00
1.00
1.01
3.22
1.96
1.00
0.99
1.01
1.02
1.01
1.00
3.00
3.00
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12
11
10
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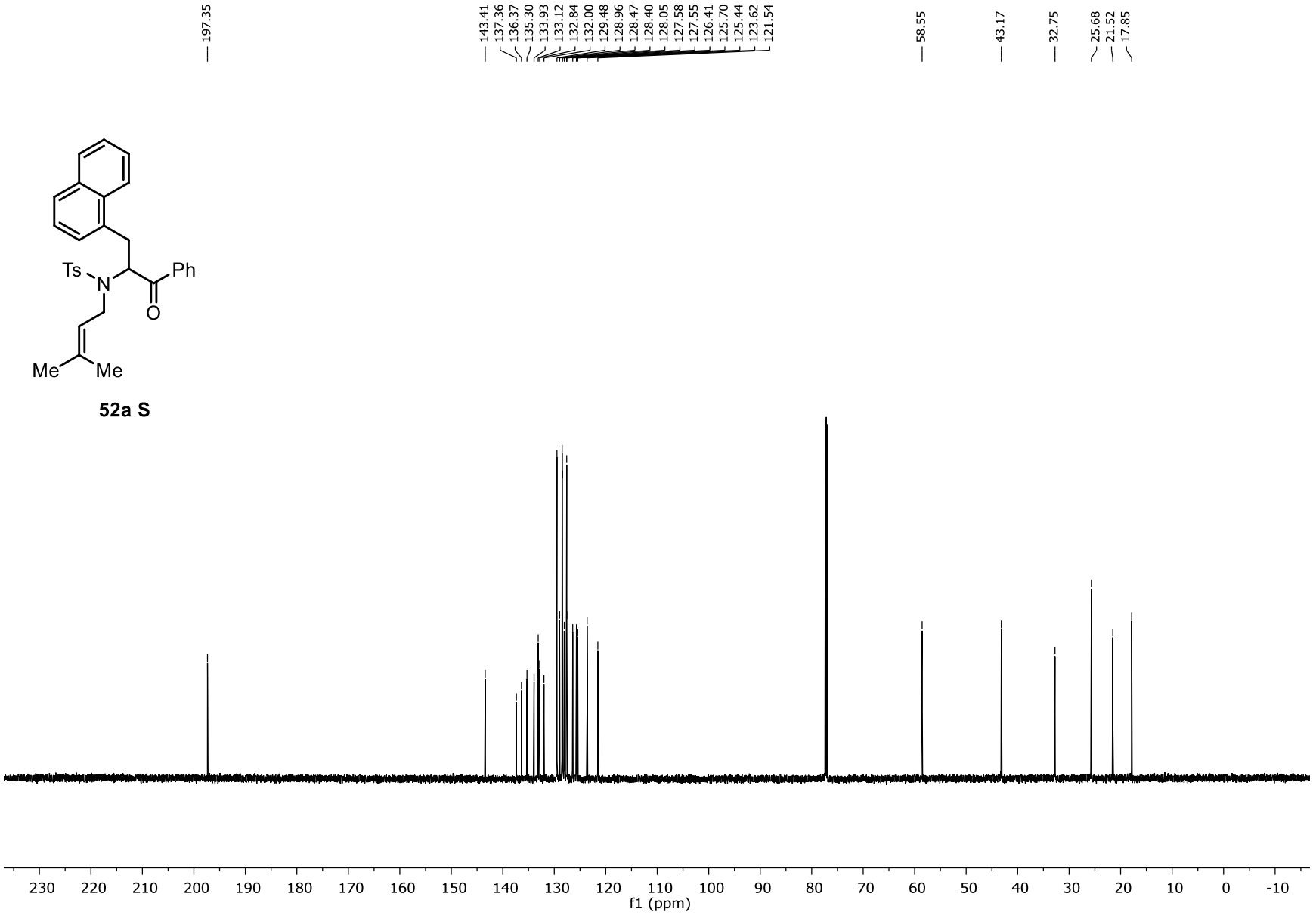
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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128.40
128.05
127.58
127.55
126.41
125.70
125.44
123.62
121.54
58.55
43.17
32.75
25.68
21.52
17.85
Ts
N
Ph
O
Me
Me
52a S
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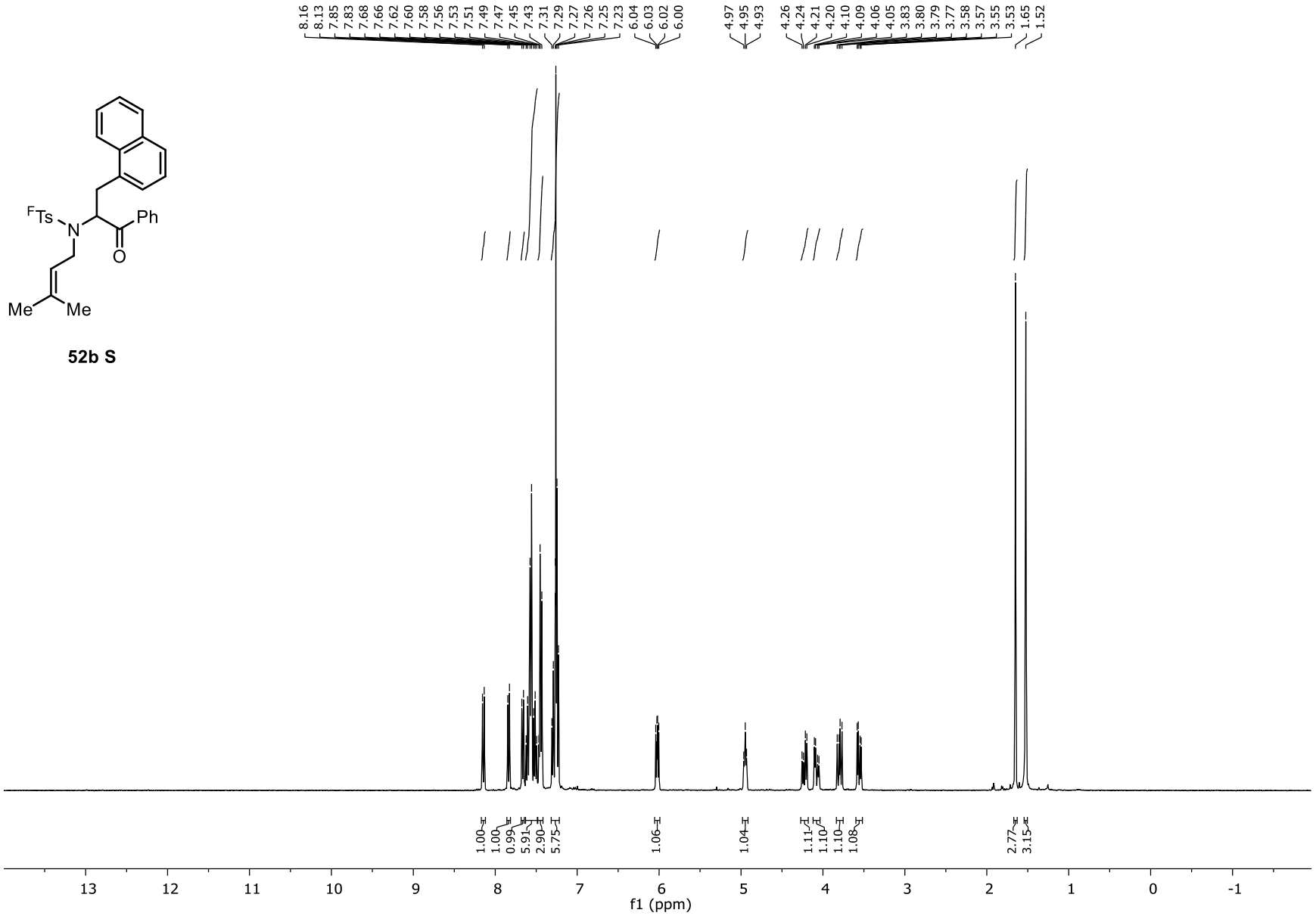
f1 (ppm)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7.66
7.62
7.60
7.58
7.56
7.53
7.51
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7.47
7.45
7.43
7.31
7.29
7.27
7.26
7.25
7.23
6.04
6.03
6.02
6.00
4.97
4.95
4.93
4.26
4.24
4.21
4.20
4.10
4.09
4.06
4.05
3.83
3.80
3.79
3.77
3.58
3.57
3.55
3.53
1.65
1.52
FTs
N
Ph
O
Me
Me
52b S
1.00
1.00
0.99
5.91
2.90
5.75
1.06
1.04
1.11
1.10
1.10
1.08
2.77
3.15
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12
11
10
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8
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4
3
2
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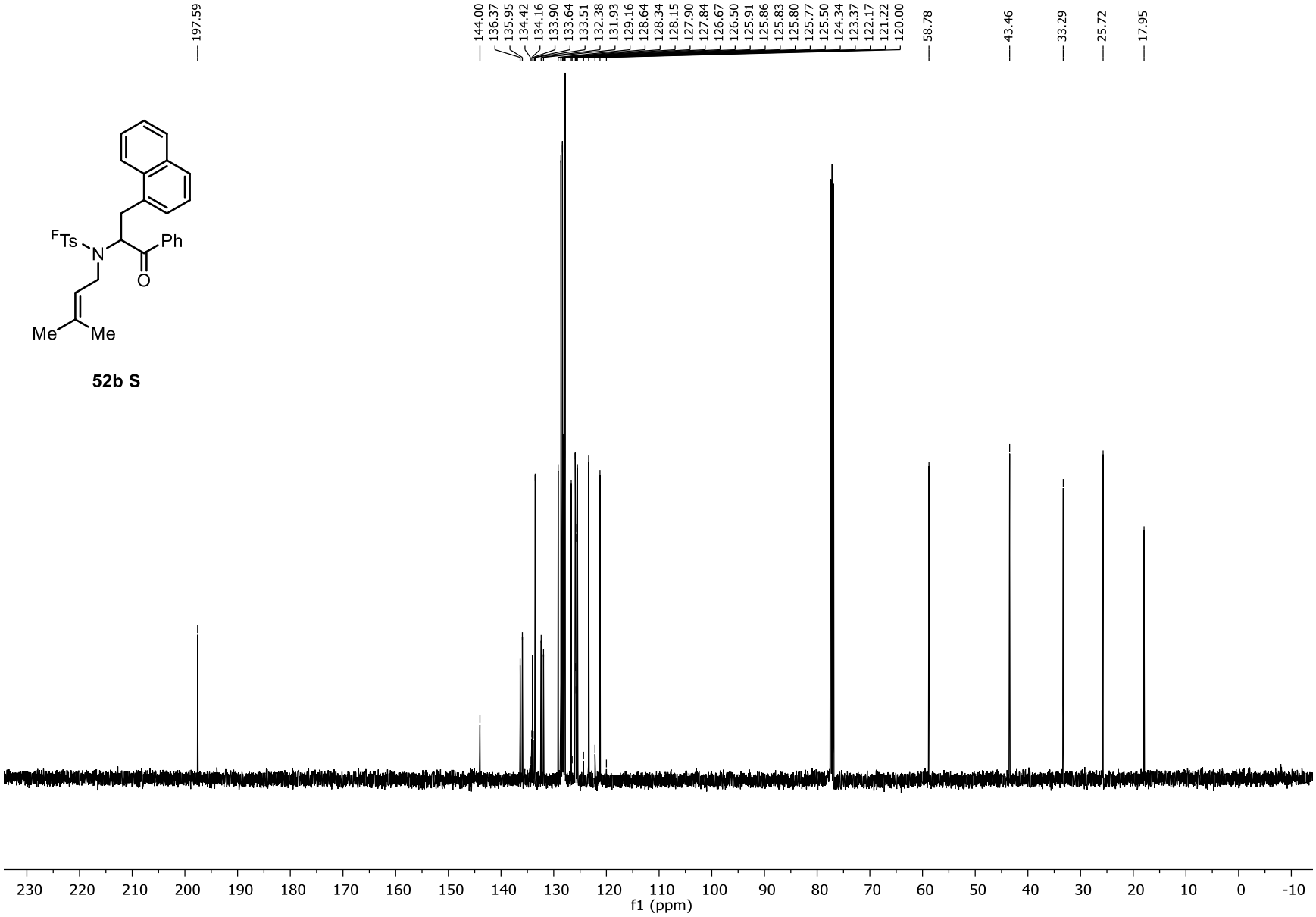
-1
f1 (ppm)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133.64
133.51
132.38
131.93
129.16
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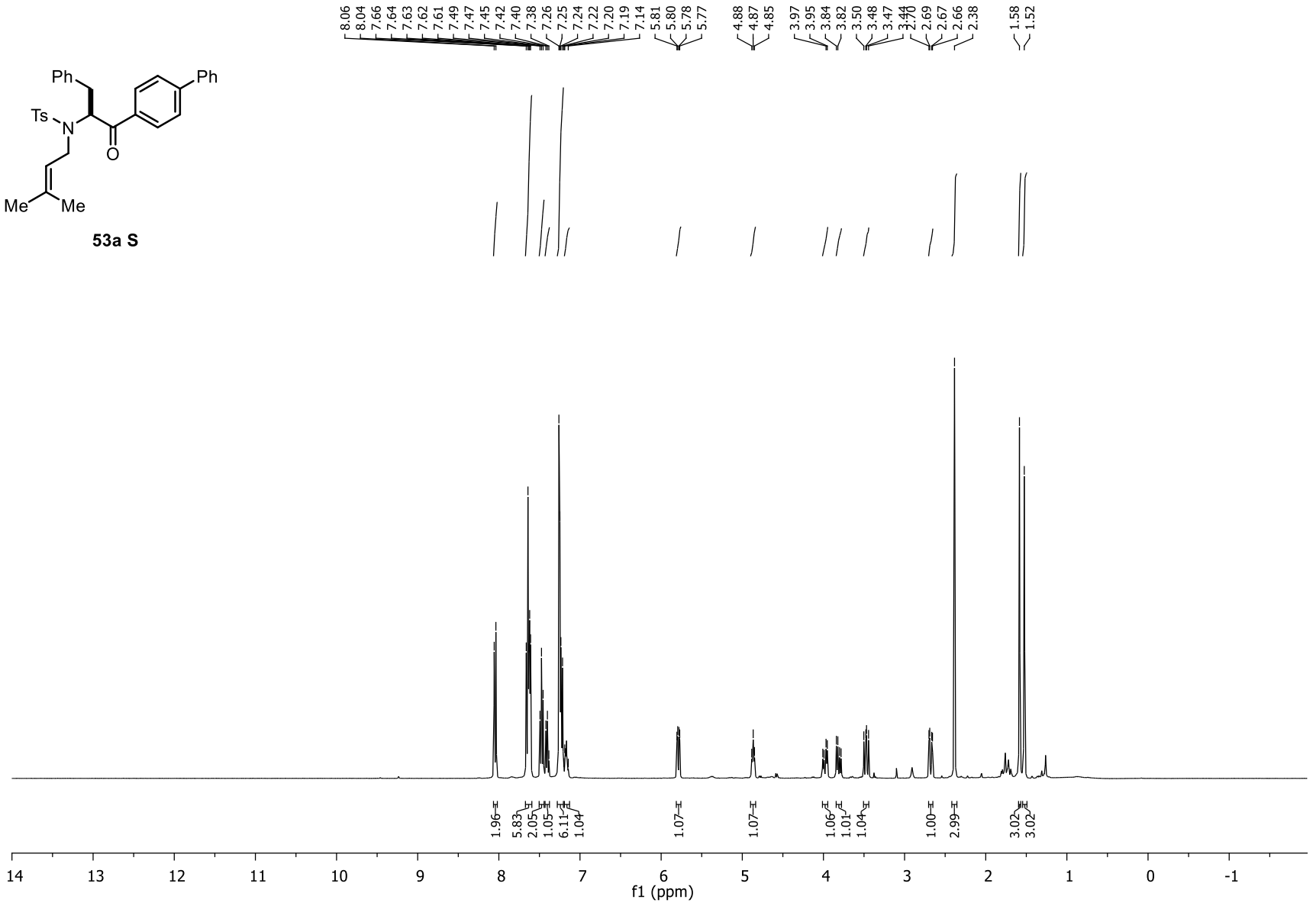
128.34
128.15
127.90
127.84
126.67
126.50
125.91
125.86
125.83
125.80
125.77
125.50
124.34
123.37
122.17
121.22
120.00
58.78
43.46
33.29
25.72
17.95
FTs
N
Ph
O
Me
Me
52b S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Ph
Ts
N
O
Me
Me
53a S
8.06
8.04
7.66
7.64
7.63
7.62
7.61
7.49
7.47
7.45
7.42
7.40
7.38
7.26
7.25
7.24
7.22
7.20
7.19
7.14
5.81
5.80
5.78
5.77
4.88
4.87
4.85
3.97
3.95
3.84
3.82
3.50
3.48
3.47
3.44
2.70
2.69
2.67
2.66
2.38
1.58
1.52
1.96
5.83
2.05
1.05
6.11
1.04
1.07
1.07
1.06
1.01
1.04
1.00
2.99
3.02
3.02
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11
10
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8
7
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5
4
3
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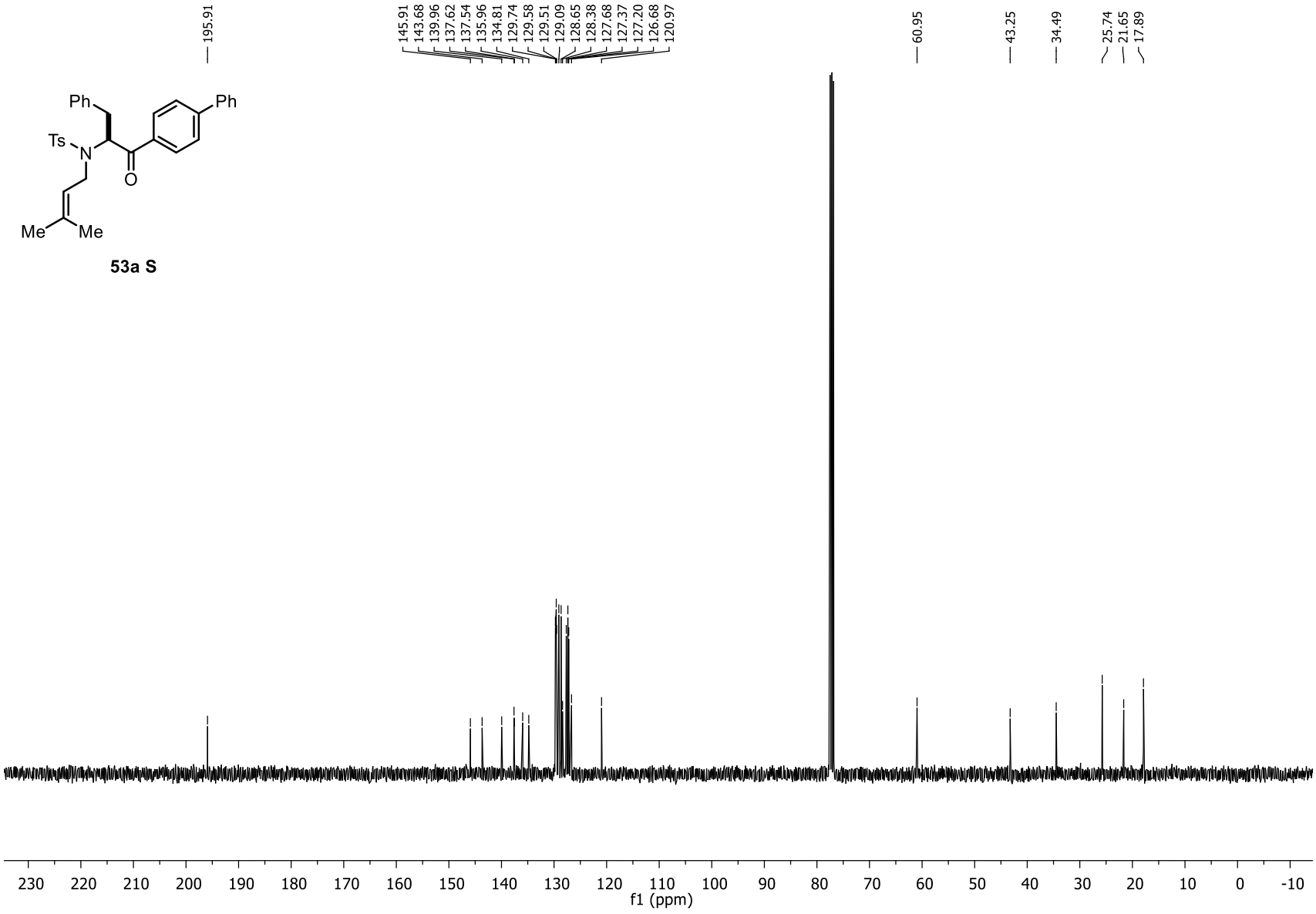
0
-1
f1 (ppm)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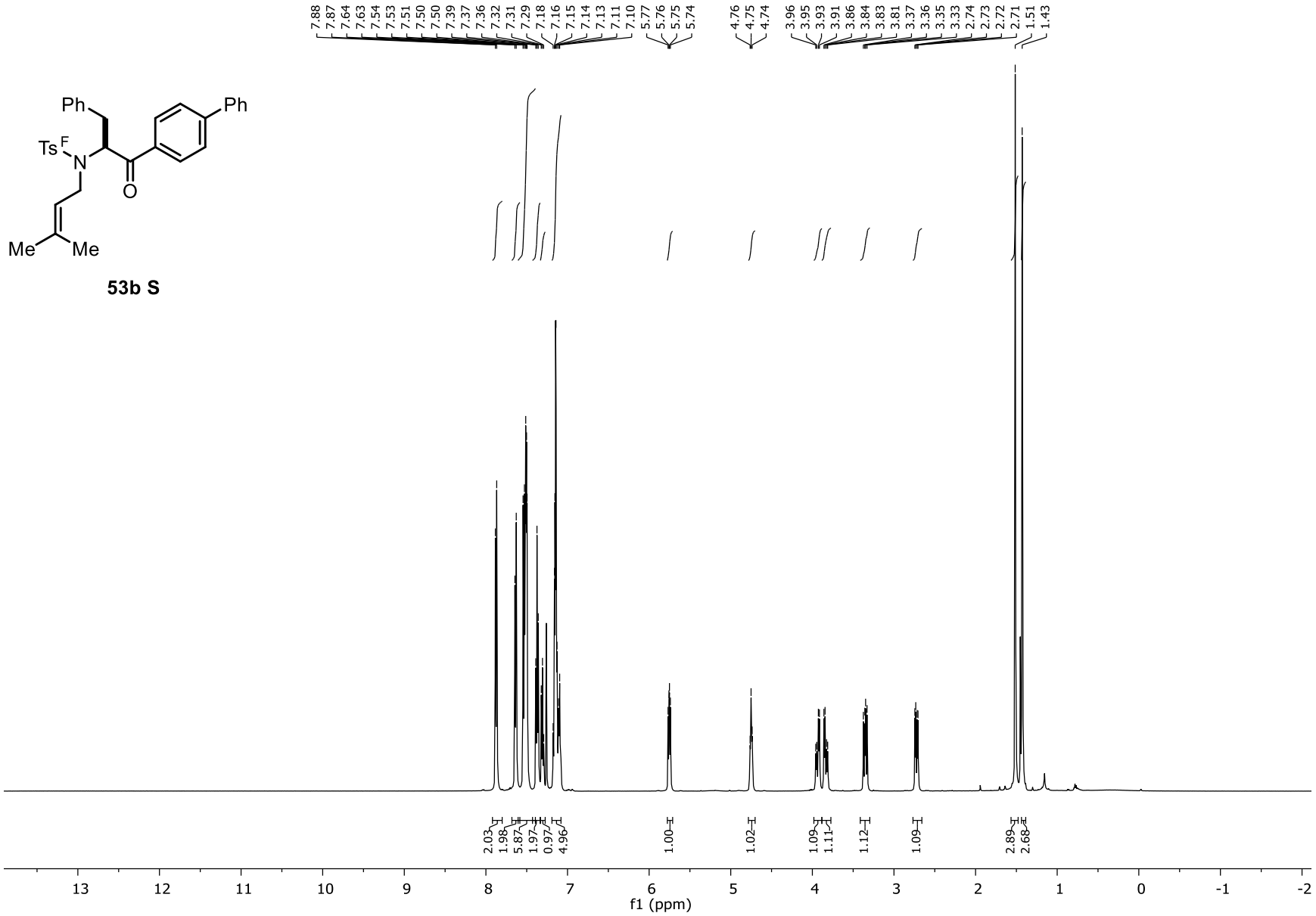
145.91
143.68
139.96
137.62
137.54
135.96
134.81
129.74
129.58
129.51
129.09
128.65
128.38
127.68
127.37
127.20
126.68
120.97
60.95
43.25
34.49
25.74
21.65
17.89
Ph
Ph
Ts
N
O
Me
Me
53a S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Ts F
N
O
Ph
Me
Me
53b S
7.88
7.87
7.64
7.63
7.54
7.53
7.51
7.50
7.50
7.39
7.37
7.36
7.32
7.31
7.29
7.18
7.16
7.15
7.14
7.13
7.11
7.10
5.77
5.76
5.75
5.74
4.76
4.75
4.74
3.96
3.95
3.93
3.91
3.86
3.84
3.83
3.81
3.37
3.36
3.35
3.33
2.74
2.73
2.72
2.71
1.51
1.43
2.03
1.98
5.87
1.97
0.97
4.96
1.00
1.02
1.09
1.11
1.12
1.09
2.89
2.68
13
12
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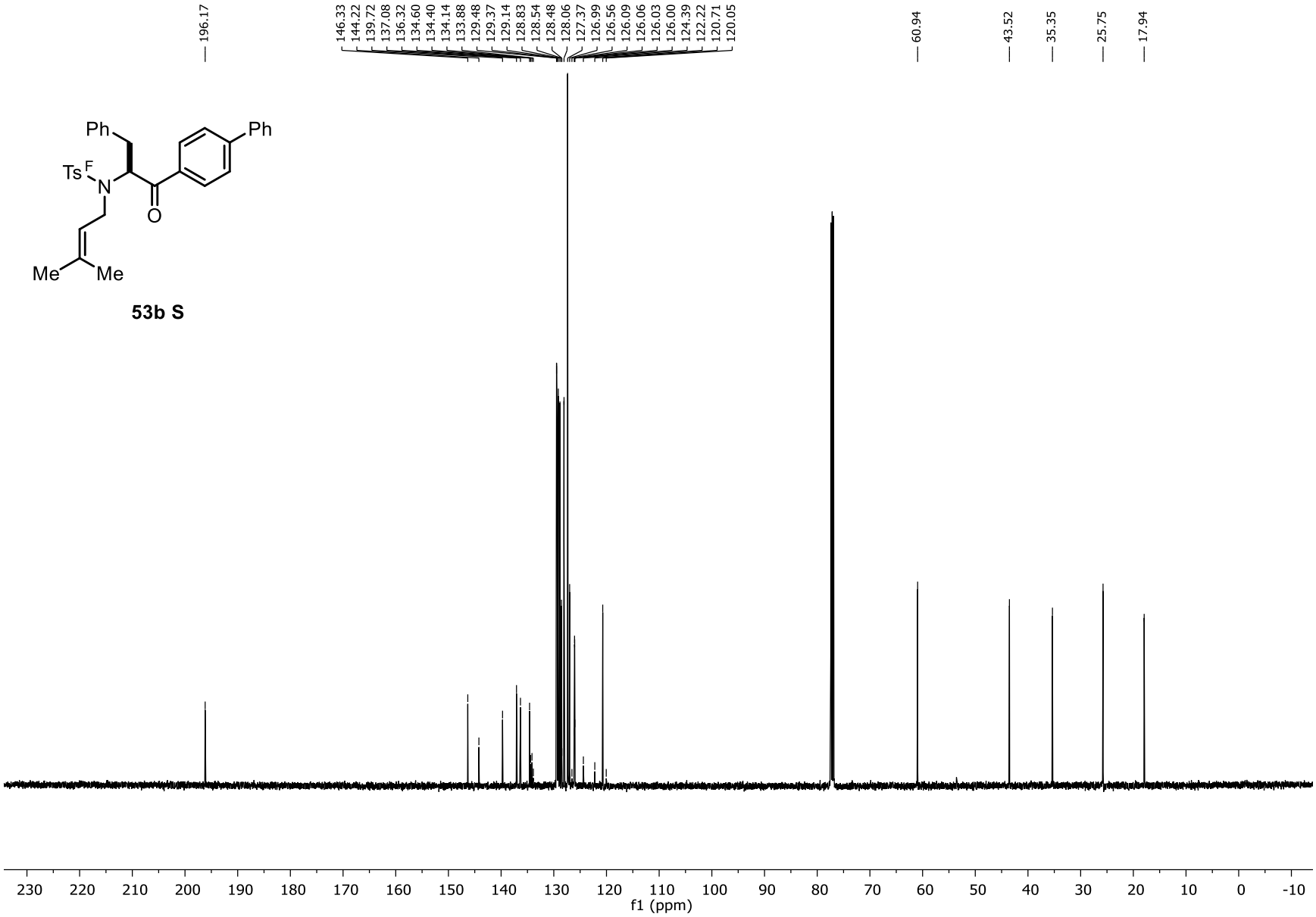
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)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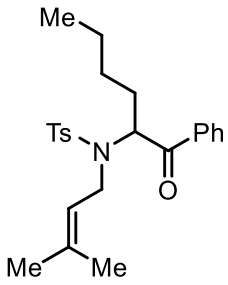
136.32
134.60
134.40
134.14
133.88
129.48
129.37
129.14
128.83
128.54
128.48
128.06
127.37
126.99
126.56
126.09
126.06
126.03
126.00
124.39
122.22
120.71
120.05
60.94
43.52
35.35
25.75
17.94
Ph
Ph
Ts
F
N
O
Me
Me
53b S
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
Ts
N
Ph
O
Me
Me

54a S

7.99
7.97
7.59
7.57
7.57
7.56
7.49
7.47
7.45
7.26
7.18
5.43
5.41
4.98
4.96
4.95
4.01
3.99
3.97
3.95
3.79
3.78
3.75
3.74
2.37
1.54
1.36
1.35
1.34
1.33
0.86
0.84
2.17
3.37
2.24
2.26
1.13
1.04
1.02
1.08
3.64
0.72
6.06
6.84
3.50
14
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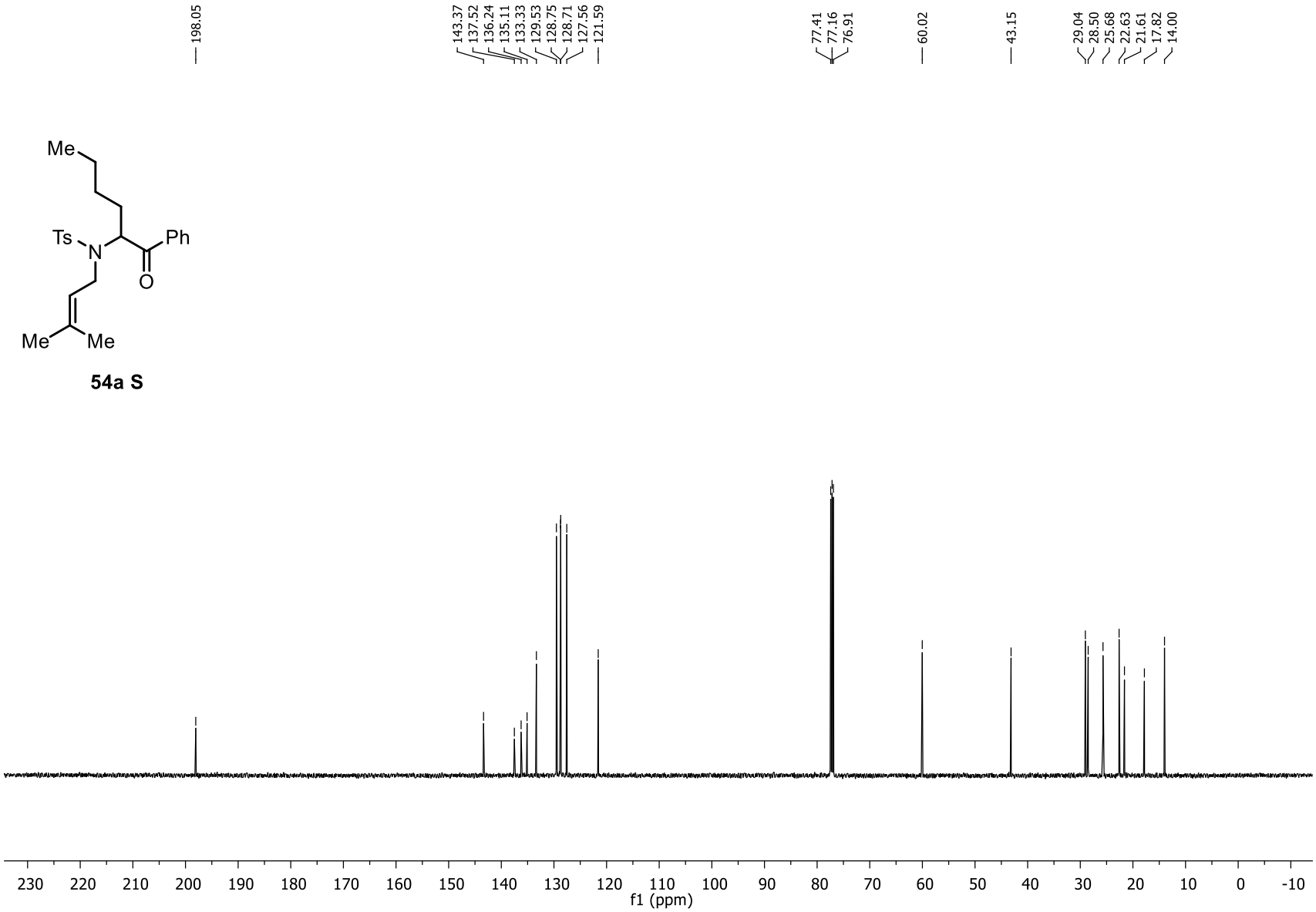
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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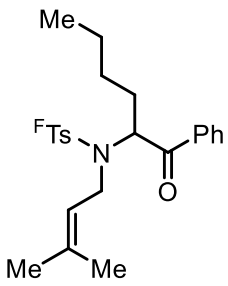
129.53
128.75
128.71
127.56
121.59
77.41
77.16
76.91
60.02
43.15
29.04
28.50
25.68
22.63
21.61
17.82
14.00
Me
Ts
N
Ph
O
Me
Me
54a S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
FTs
N
Ph
O
Me
Me

54b S

7.91
7.90
7.78
7.77
7.61
7.60
7.59
7.49
7.48
7.47
7.26
5.49
5.48
5.47
5.02
5.01
5.00
4.08
4.07
4.05
4.04
3.89
3.88
3.87
3.86
1.96
1.95
1.94
1.93
1.59
1.57
1.52
1.51
1.50
1.49
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.30
1.29
1.28
1.27
1.26
0.89
0.88
0.87
1.81
1.86
2.78
1.93
1.13
0.97
1.10
1.09
1.06
2.67
2.84
1.23
3.14
1.18
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12
11
10
9
8
7
6
5
4
3
2
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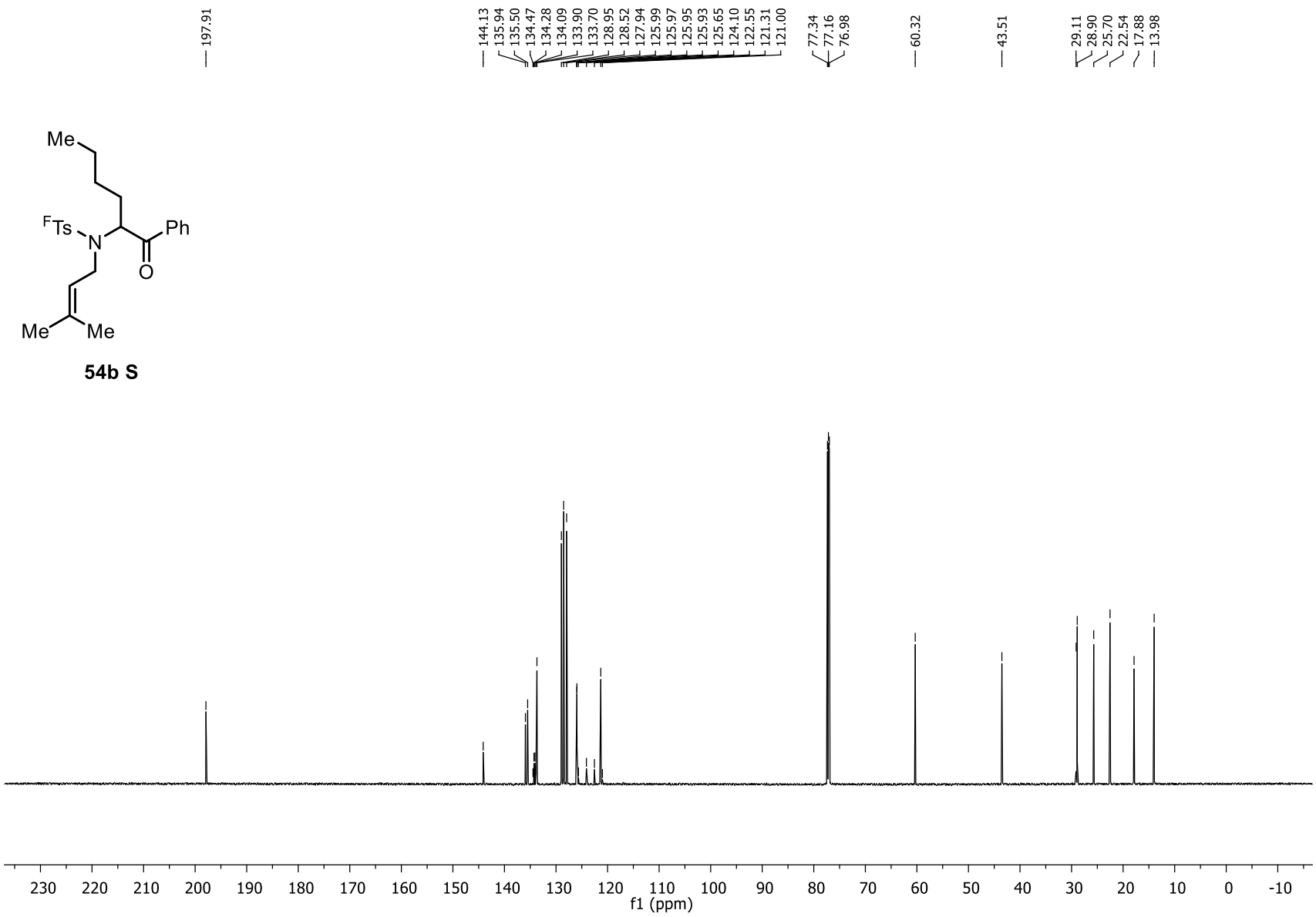
0
-1
f1 (ppm)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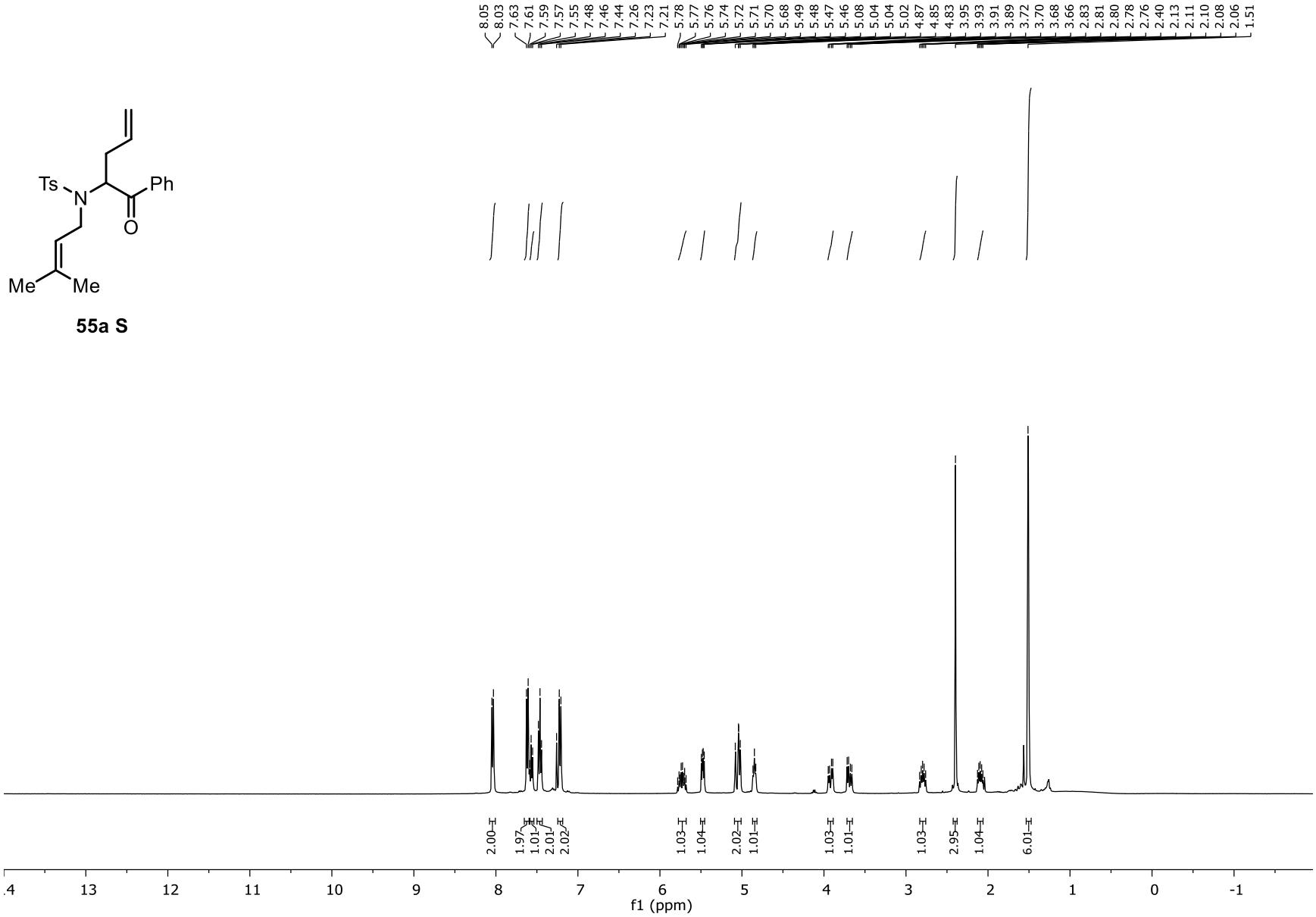
135.94
135.50
134.47
134.28
134.09
133.90
133.70
128.95
128.52
127.94
125.99
125.97
125.95
125.93
125.65
124.10
122.55
121.31
121.00
77.34
77.16
76.98
60.32
43.51
29.11
28.90
25.70
22.54
17.88
13.98
Me
FTs
N
Ph
O
Me
Me
f1 (ppm)

54b S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8.03
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7.44
7.26
7.23
7.21
5.78
5.77
5.76
5.74
5.72
5.71
5.70
5.68
5.49
5.48
5.47
5.46
5.08
5.04
5.04
5.02
4.87
4.85
4.83
3.95
3.93
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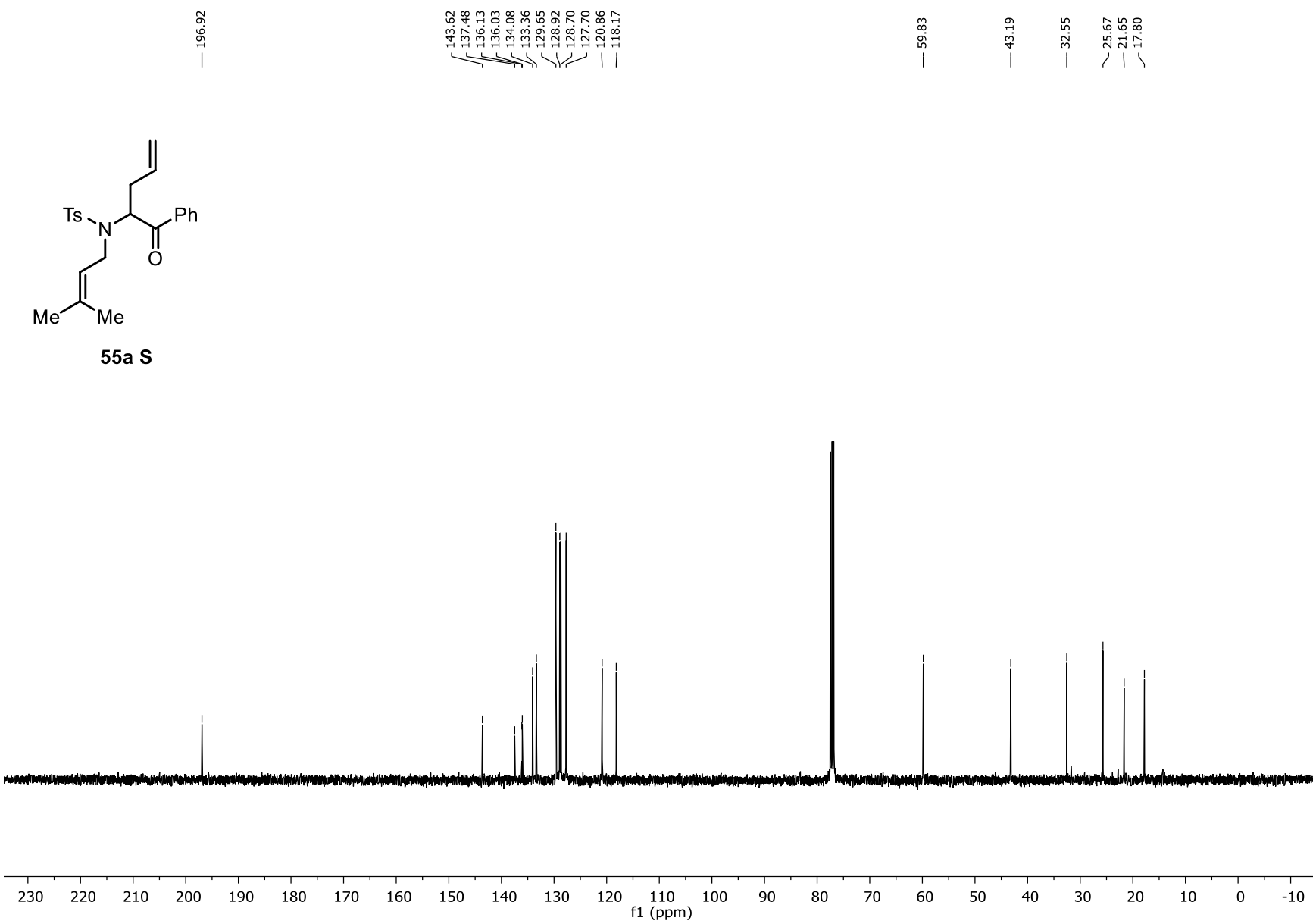
3.72
3.70
3.68
3.66
2.83
2.81
2.80
2.78
2.76
2.40
2.13
2.11
2.10
2.08
2.06
1.51
Ts
N
Ph
O
Me
Me
55a S
2.00
1.97
1.01
2.01
2.02
1.03
1.04
2.02
1.01
1.03
1.01
1.03
2.95
1.04
6.01
f1 (ppm)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129.65
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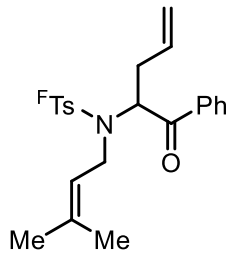
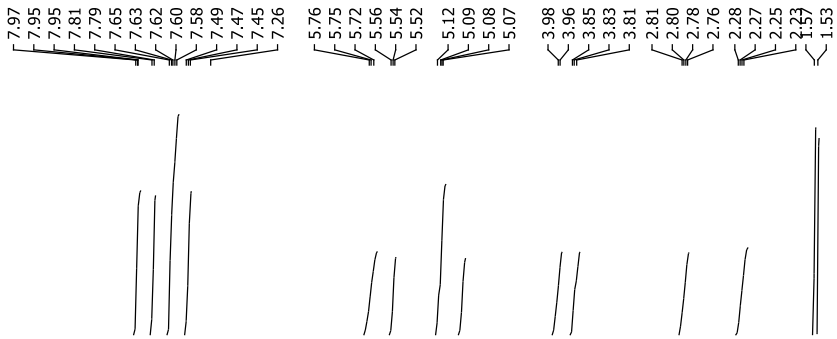
128.70
127.70
120.86
118.17
59.83
43.19
32.55
25.67
21.65
17.80
Ts
N
O
Ph
Me
Me
55a S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


FTs
N
Ph
O
Me
Me

55b S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7.62
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7.58
7.49
7.47
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7.26
5.76
5.75
5.72
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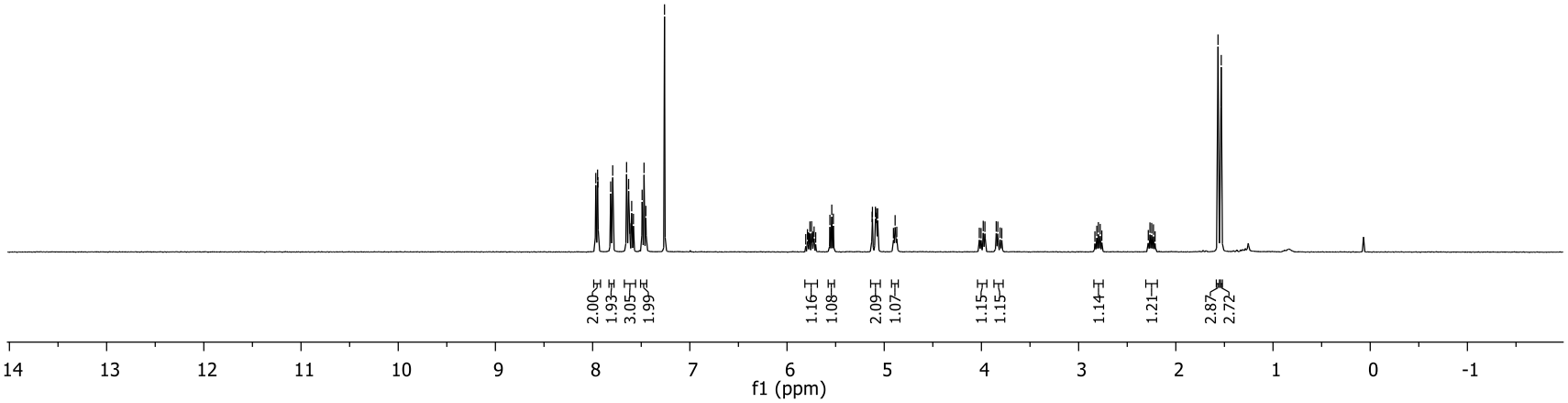
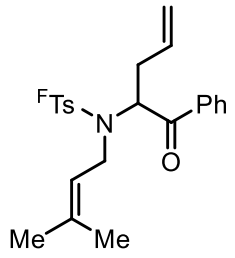
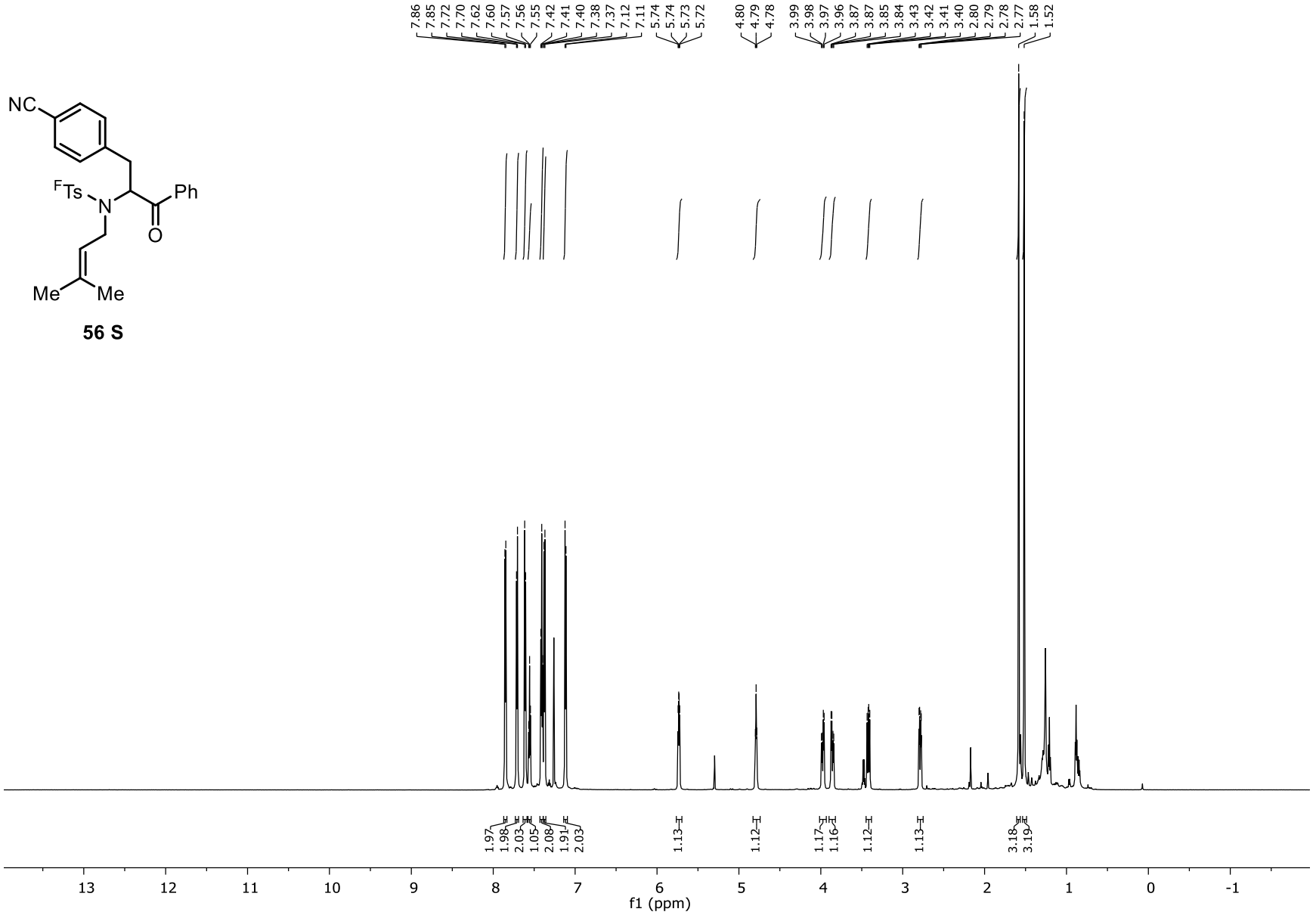
5.54
5.52
5.12
5.09
5.08
5.07
3.98
3.96
3.85
3.83
3.81
2.81
2.80
2.78
2.76
2.28
2.27
2.25
1.57
1.53


2.00
1.93
3.05
1.99
1.16
1.08
2.09
1.07
1.15
1.15
1.14
1.21
2.87
2.72
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


FTs
N
Ph
O
Me
Me

55b S

196.78
144.17
136.26
135.92
134.77
134.44
134.11
133.78
133.64
133.48
128.84
128.67
128.05
127.36
126.03
125.99
125.96
125.92
124.64
121.93
120.62
118.57
77.48
77.16
76.84
59.85
43.47
33.26
25.62
17.79
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


NC
FTs
N
Ph
O
Me
Me
56 S
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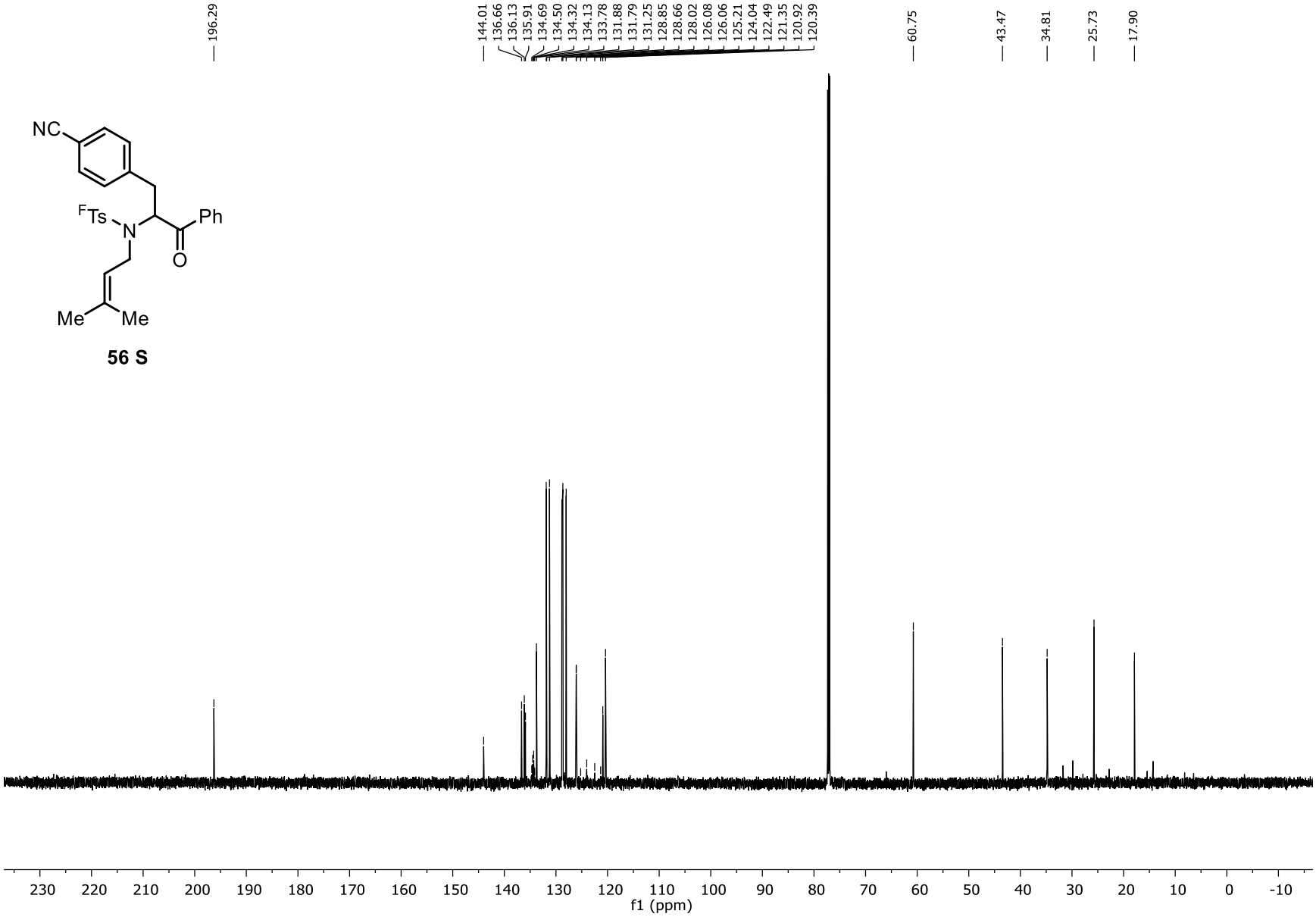
7.56
7.55
7.42
7.41
7.40
7.38
7.37
7.12
7.11
5.74
5.74
5.73
5.72
4.80
4.79
4.78
3.99
3.98
3.97
3.96
3.87
3.87
3.85
3.84
3.43
3.42
3.41
3.40
2.80
2.79
2.78
2.77
1.58
1.52
1.97
1.98
2.03
1.05
2.08
1.91
2.03
1.13
1.12
1.17
1.16
1.12
1.13
3.18
3.19
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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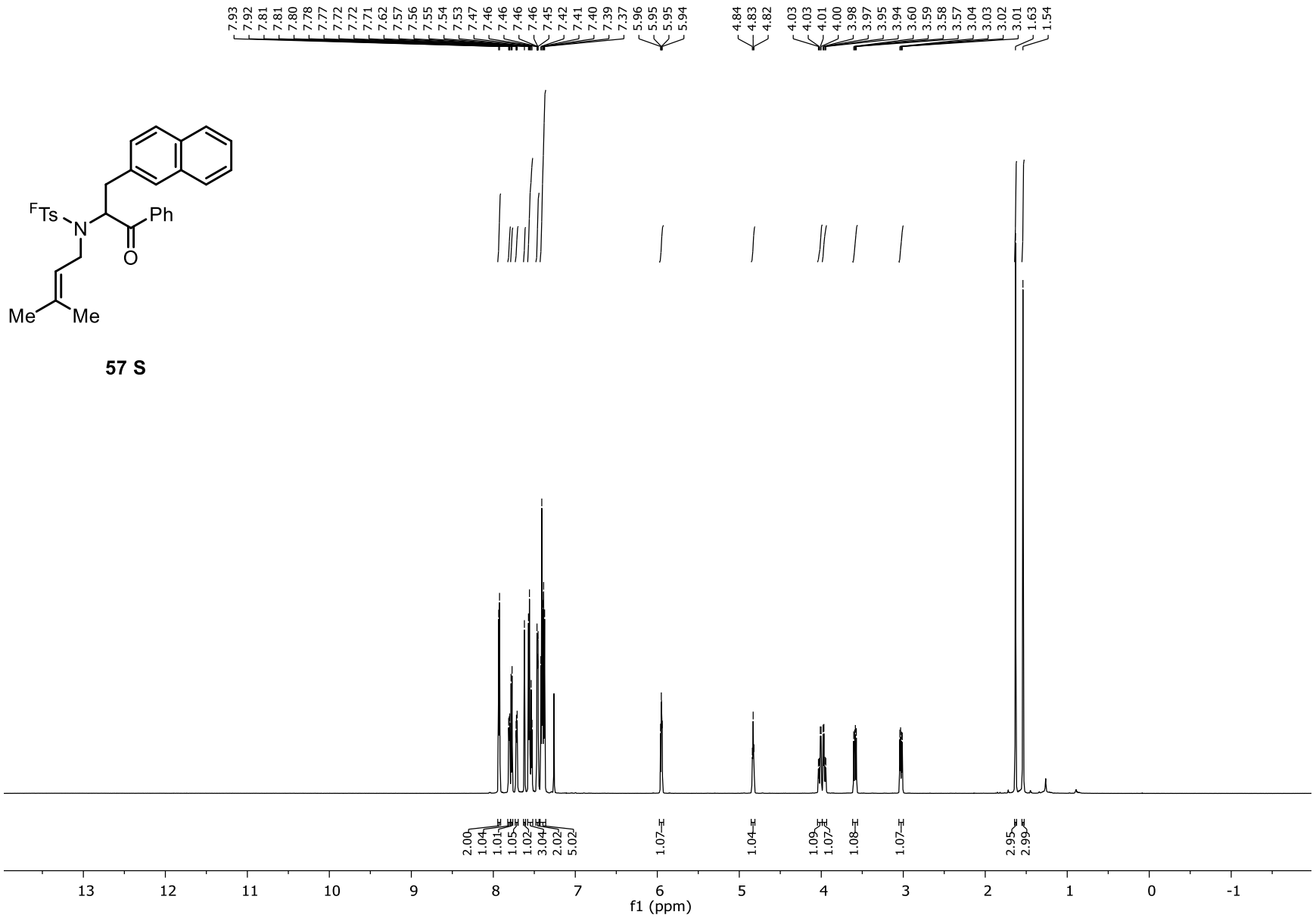
144.01
136.66
136.13
135.91
134.69
134.50
134.32
134.13
133.78
131.88
131.79
131.25
128.85
128.66
128.02
126.08
126.06
125.21
124.04
122.49
121.35
120.92
120.39
60.75
43.47
34.81
25.73
17.90
NC
FTs
N
Ph
O
Me
Me
56 S
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.92
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7.81
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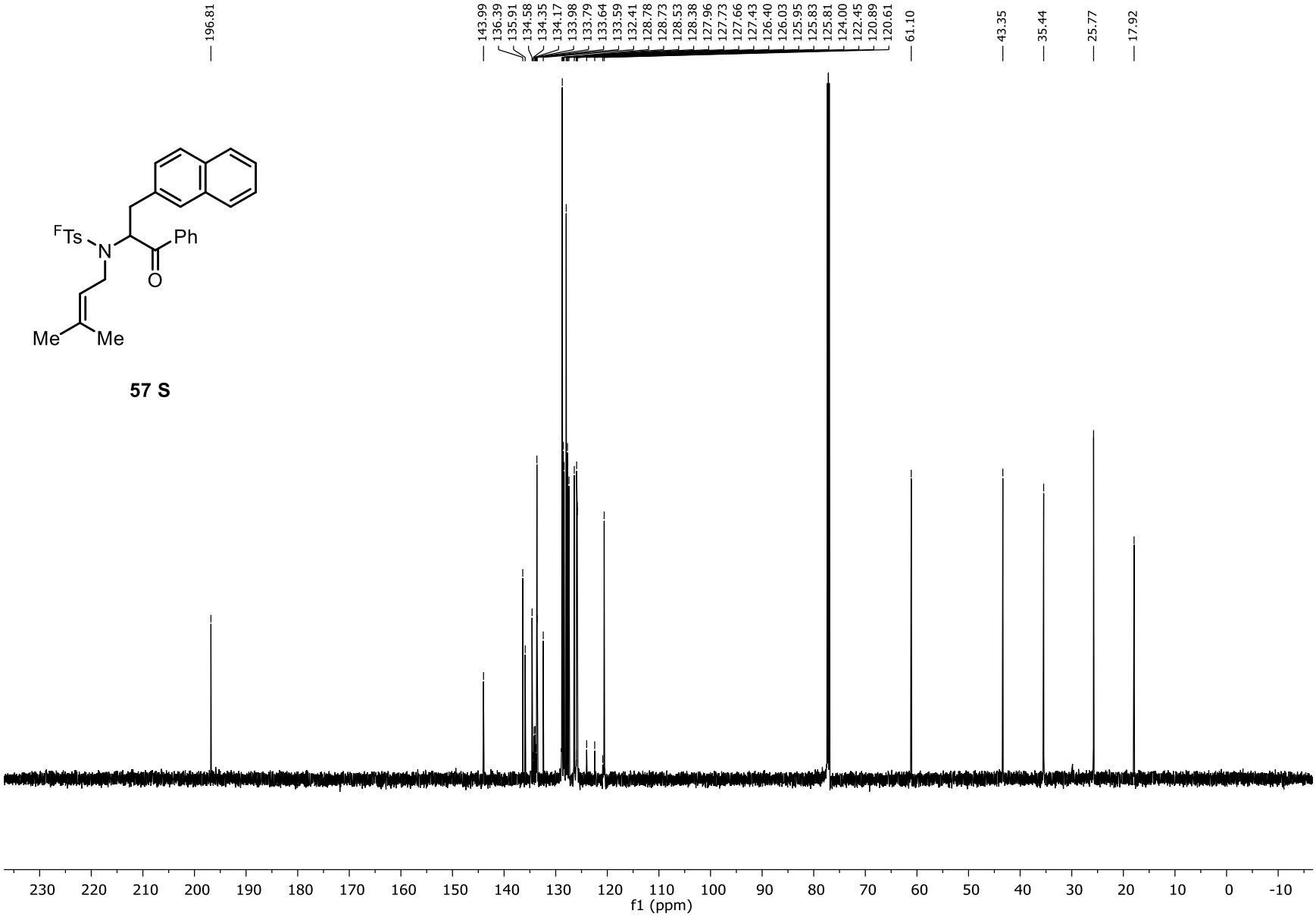
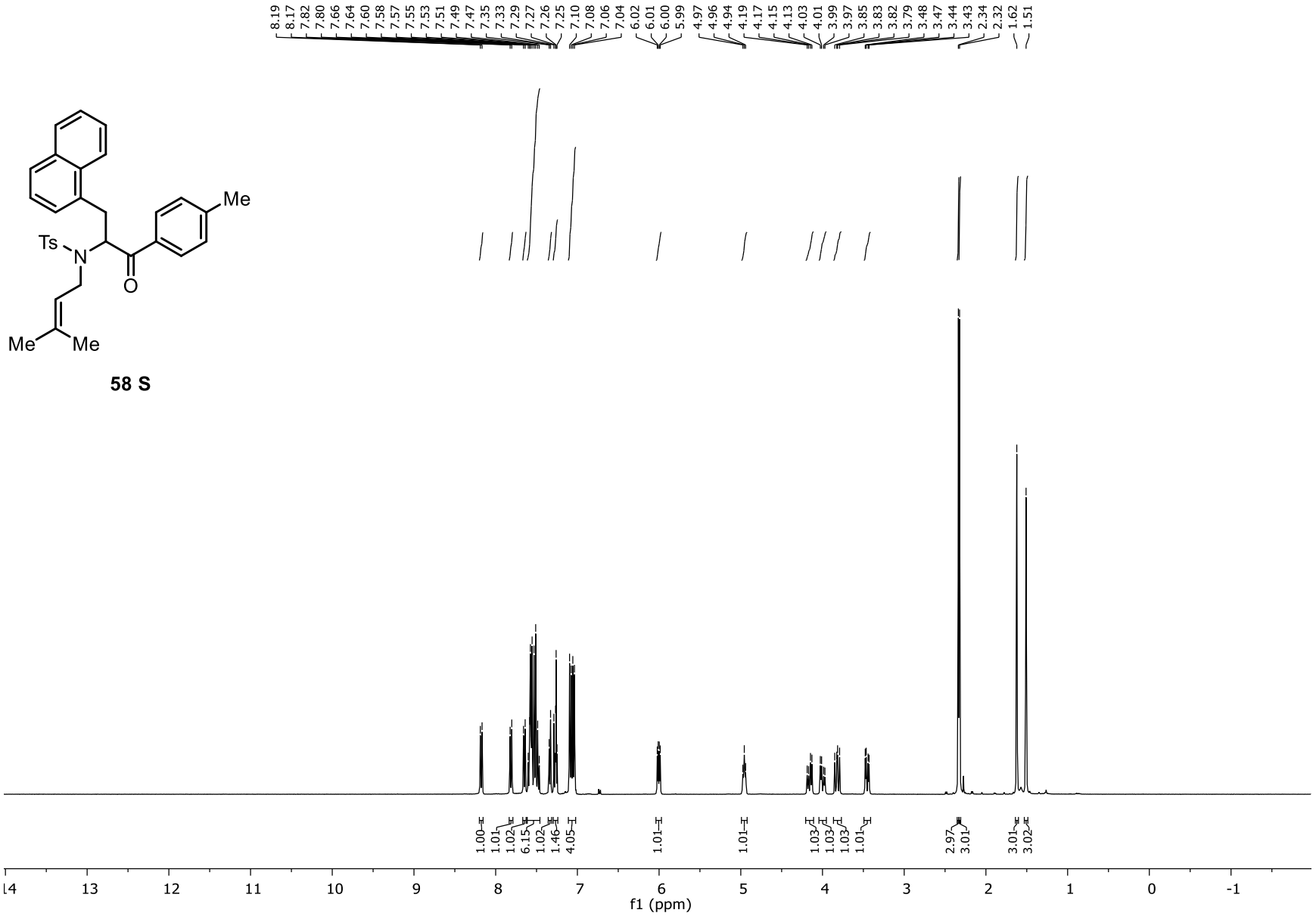
7.77
7.72
7.72
7.71
7.62
7.57
7.56
7.55
7.54
7.53
7.47
7.46
7.46
7.46
7.46
7.45
7.42
7.41
7.40
7.39
7.37
5.96
5.95
5.95
5.94
4.84
4.83
4.82
4.03
4.03
4.01
4.00
3.98
3.97
3.95
3.94
3.60
3.59
3.58
3.57
3.04
3.03
3.02
3.01
1.63
1.54
FTs
N
Ph
O
Me
Me
2.00
1.04
1.01
1.05
1.02
3.04
2.02
5.02
1.07
1.04
1.09
1.07
1.08
1.07
2.95
2.99
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

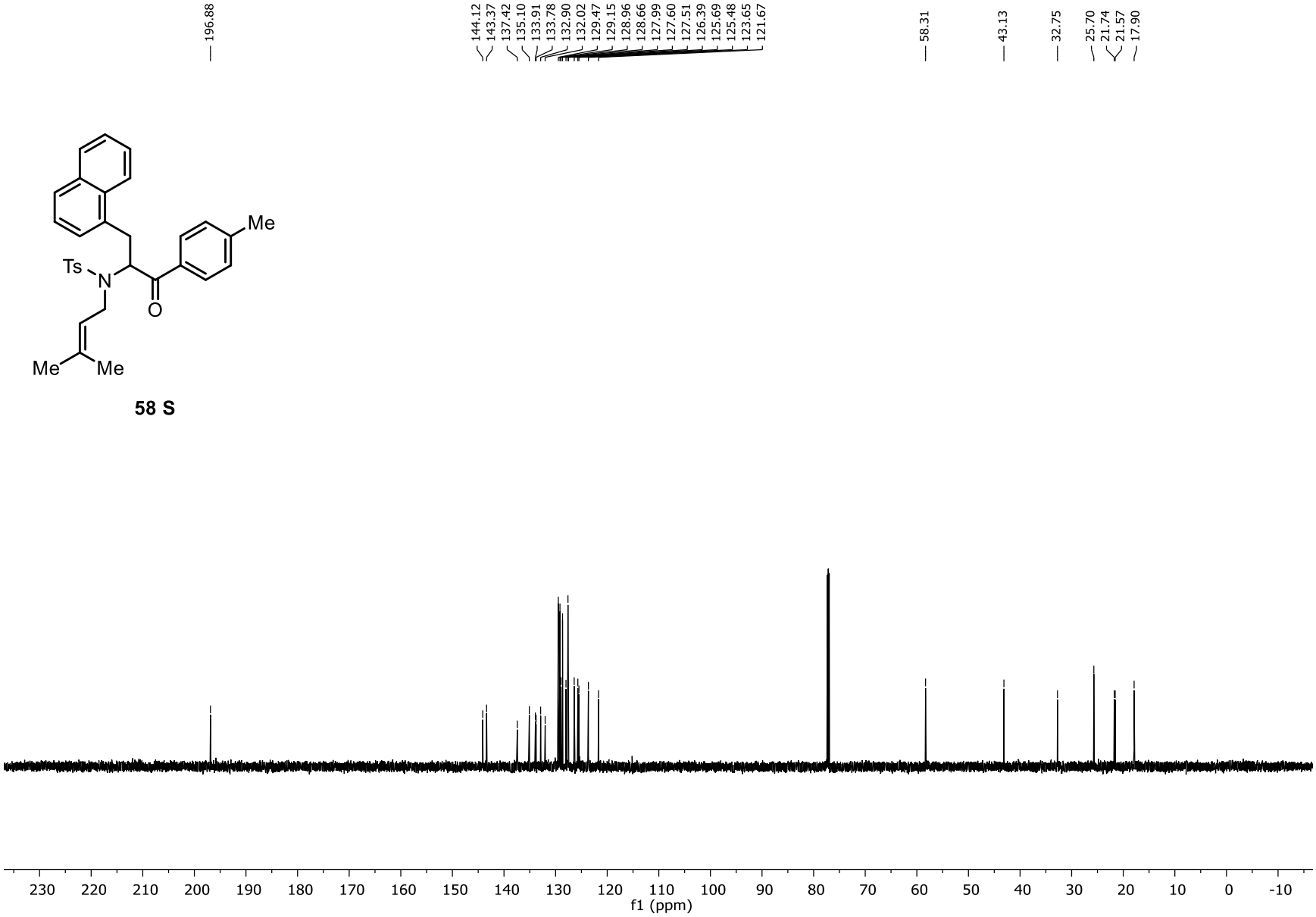
57 S


196.81
143.99
136.39
135.91
134.58
134.35
134.17
133.98
133.79
133.64
133.59
132.41
128.78
128.73
128.53
128.38
127.96
127.73
127.66
127.43
126.40
126.03
125.95
125.83
125.81
124.00
122.45
120.89
120.61
61.10
43.35
35.44
25.77
17.92
FTs
N
Ph
O
Me
Me
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

57 S


8.19
8.17
7.82
7.80
7.66
7.64
7.60
7.58
7.57
7.55
7.53
7.51
7.49
7.47
7.35
7.33
7.29
7.27
7.26
7.25
7.10
7.08
7.06
7.04
6.02
6.01
6.00
5.99
4.97
4.96
4.94
4.19
4.17
4.15
4.13
4.03
4.01
3.99
3.97
3.85
3.83
3.82
3.79
3.48
3.47
3.44
3.43
2.34
2.32
1.62
1.51
Me
Ts
N
O
Me
Me
1.00
1.01
1.02
6.15
1.02
1.46
4.05
1.01
1.01
1.03
1.03
1.03
1.01
2.97
3.01
3.01
3.02
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

58 S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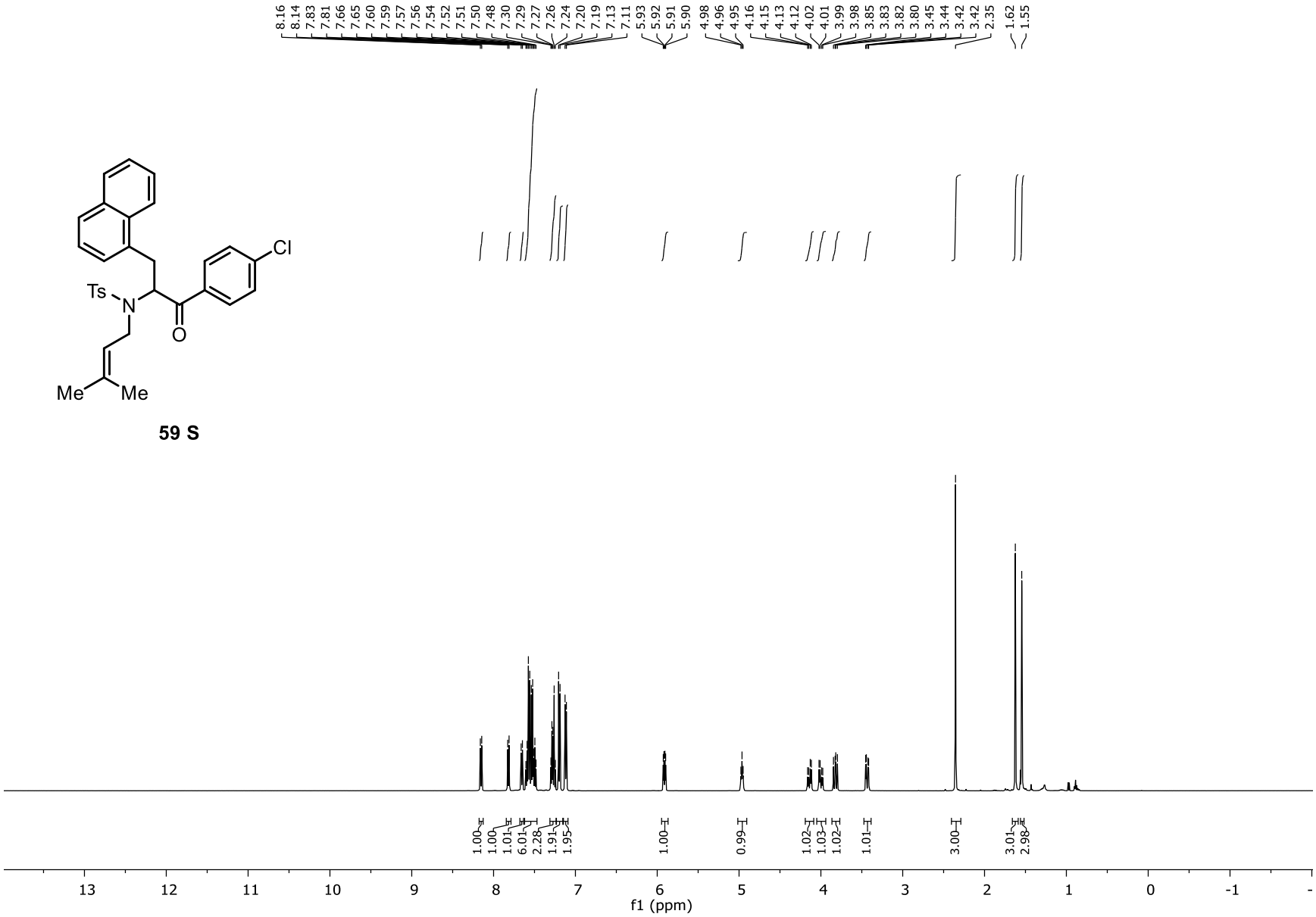
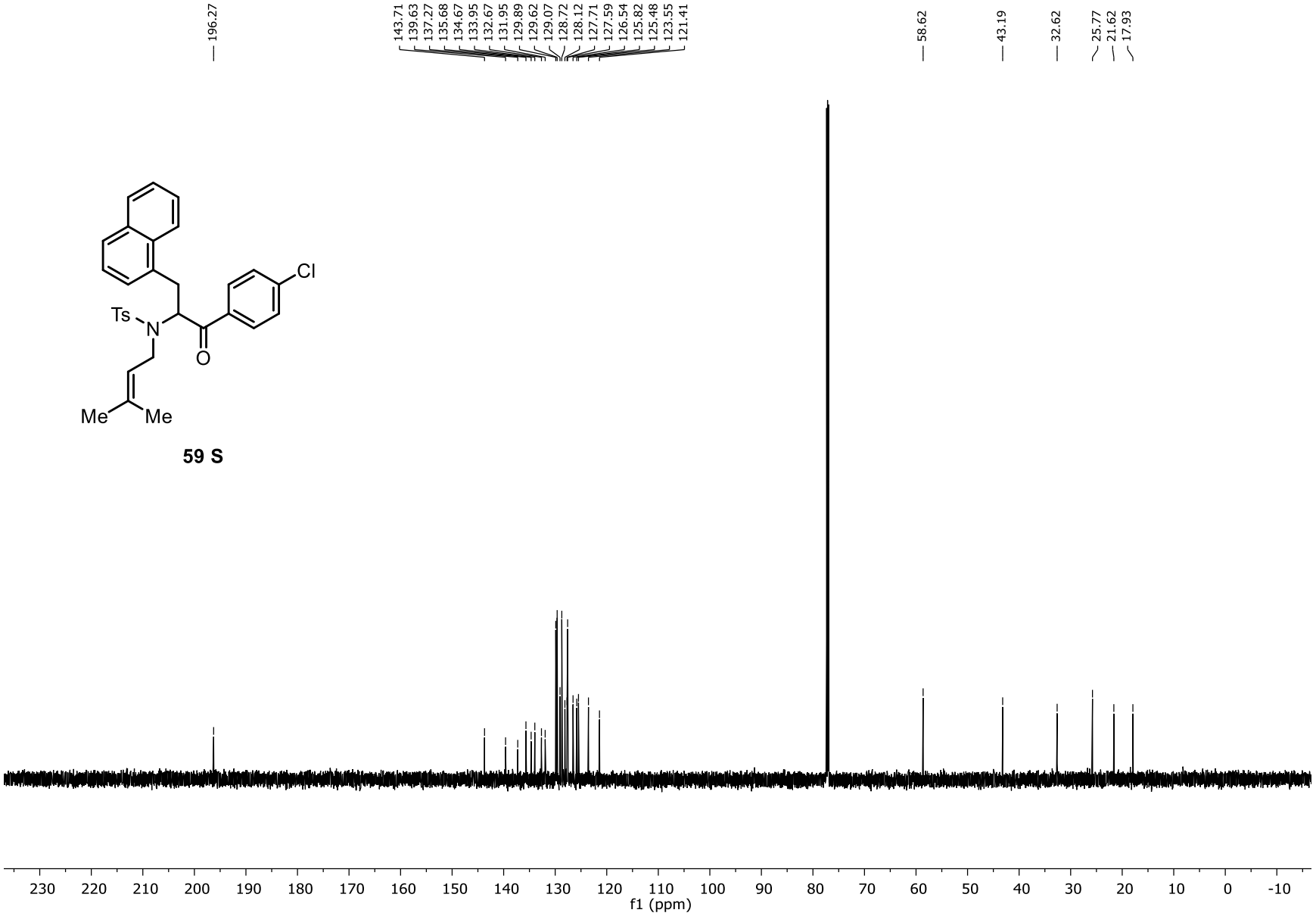
143.37
137.42
135.10
133.91
133.78
132.90
132.02
129.47
129.15
128.96
128.66
127.99
127.60
127.51
126.39
125.69
125.48
123.65
121.67
58.31
43.13
32.75
25.70
21.74
21.57
17.90
Me
Ts
N
O
Me
Me
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

58 S


8.16
8.14
7.83
7.81
7.66
7.65
7.60
7.59
7.57
7.56
7.54
7.52
7.51
7.50
7.48
7.30
7.29
7.27
7.26
7.24
7.20
7.19
7.13
7.11
5.93
5.92
5.91
5.90
4.98
4.96
4.95
4.16
4.15
4.13
4.12
4.02
4.01
3.99
3.98
3.85
3.83
3.82
3.80
3.45
3.44
3.42
3.42
2.35
1.62
1.55
Cl
Ts
N
O
Me
Me
1.00
1.00
1.01
6.01
2.28
1.91
1.95
1.00
0.99
1.02
1.03
1.02
1.01
3.00
3.01
2.98
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

59 S


196.27
143.71
139.63
137.27
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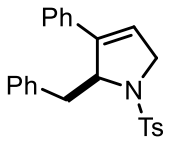
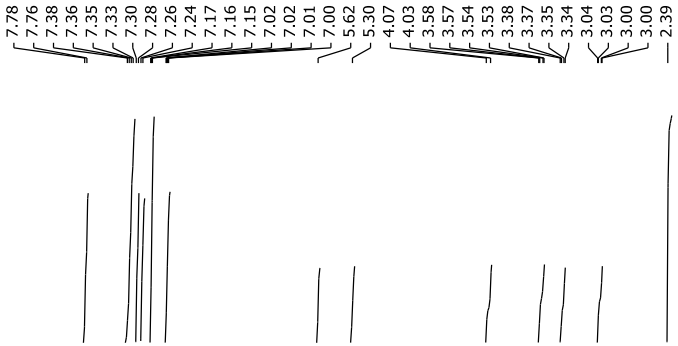
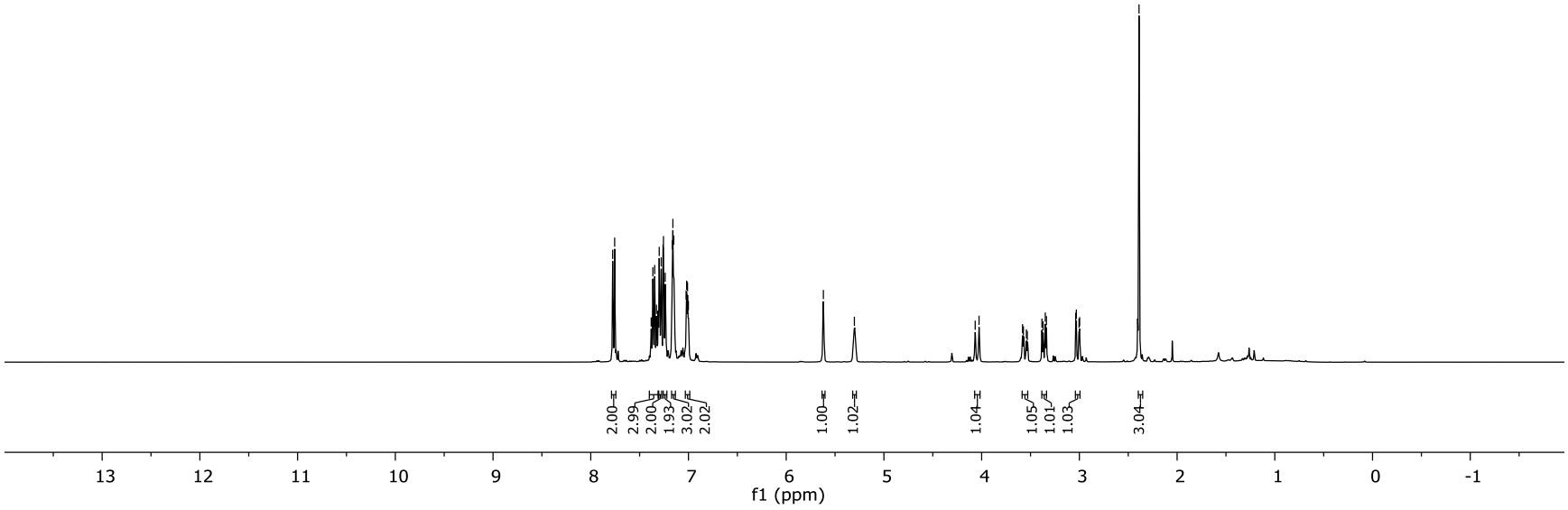
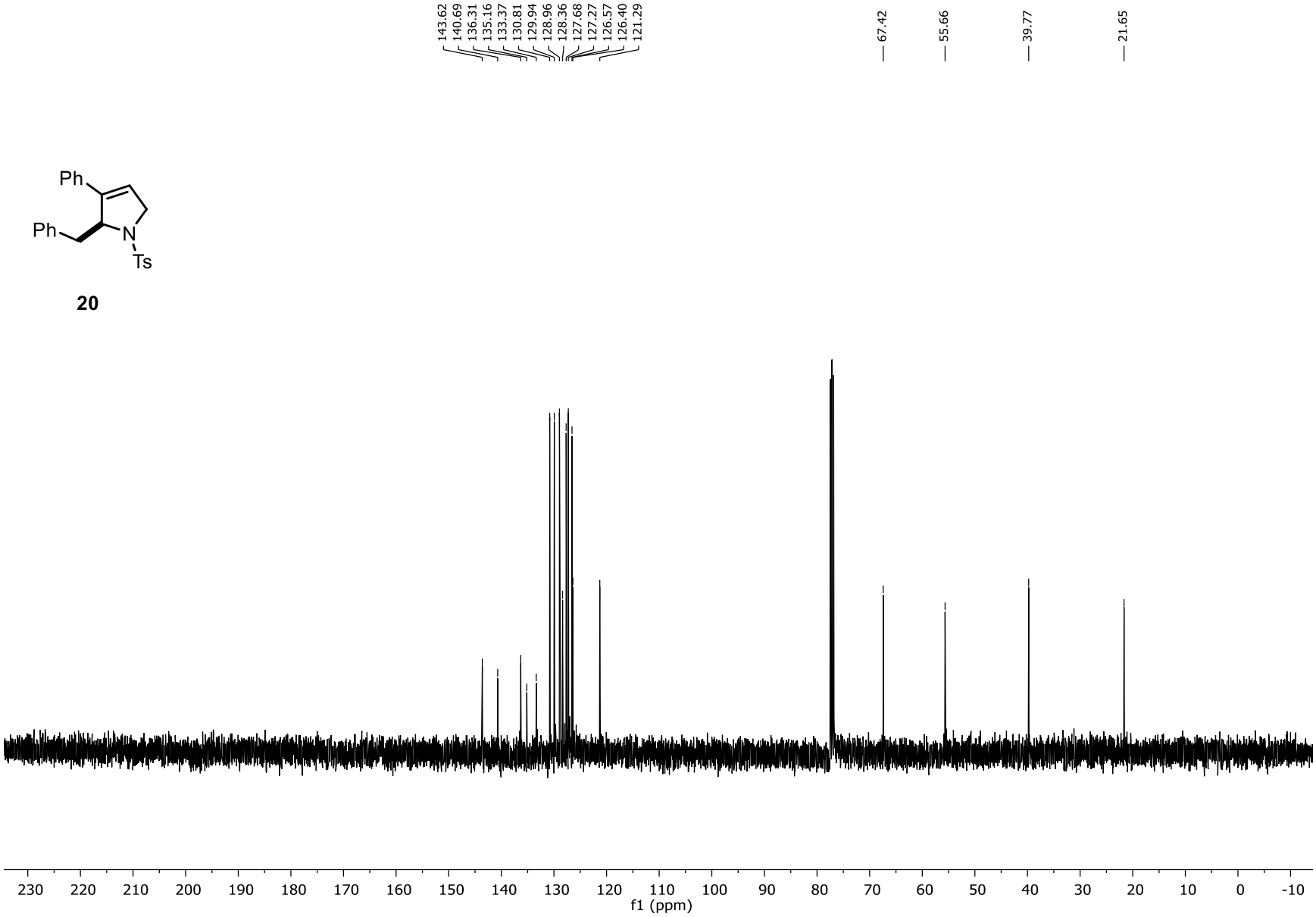
134.67
133.95
132.67
131.95
129.89
129.62
129.07
128.72
128.12
127.71
127.59
126.54
125.82
125.48
123.55
121.41
58.62
43.19
32.62
25.77
21.62
17.93
Cl
Ts
N
O
Me
Me
59 S
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Ph
Ph
N
Ts

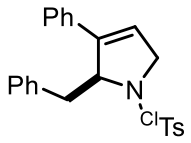
20


7.78
7.76
7.38
7.36
7.35
7.33
7.30
7.28
7.26
7.24
7.17
7.16
7.15
7.02
7.02
7.01
7.00
5.62
5.30
4.07
4.03
3.58
3.57
3.54
3.53
3.38
3.37
3.35
3.34
3.04
3.03
3.00
3.00
2.39

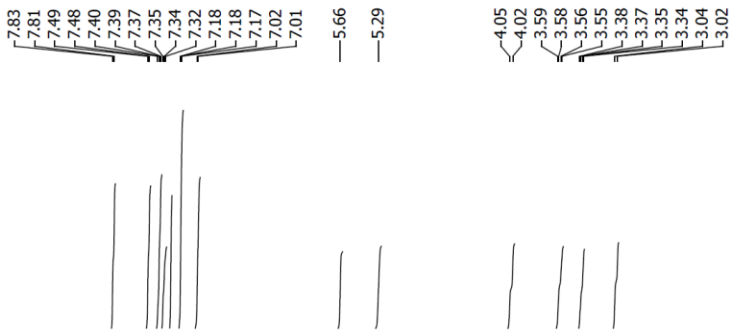

2.00
2.99
2.00
1.93
3.02
2.02
1.00
1.02
1.04
1.05
1.01
1.03
3.04
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


143.62
140.69
136.31
135.16
133.37
130.81
129.94
128.96
128.36
127.68
127.27
126.57
126.40
121.29
67.42
55.66
39.77
21.65
Ph
Ph
N
Ts
230
220
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)

20


Ph
Ph
N
Cl
Ts

24


7.83
7.81
7.49
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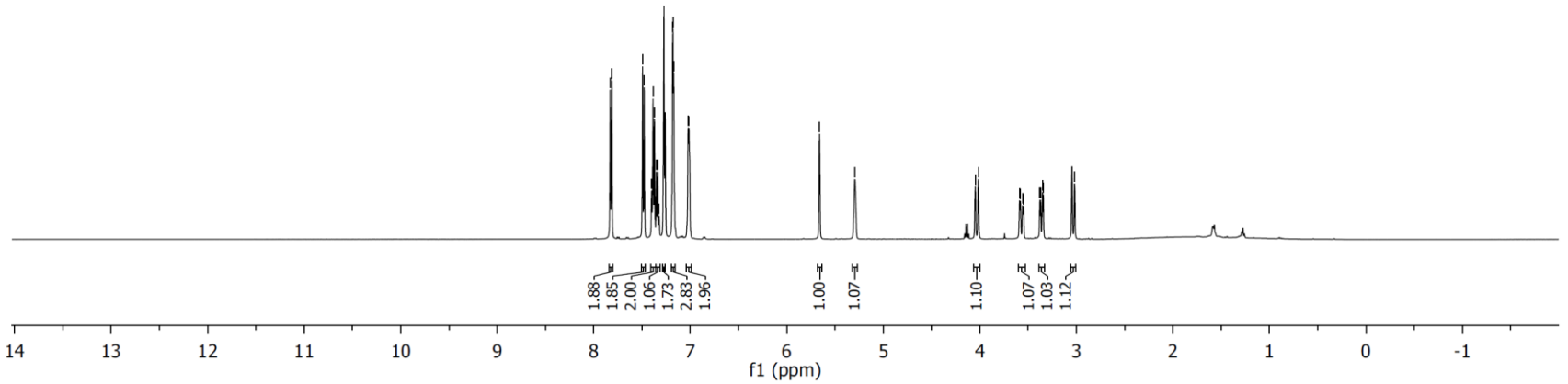
7.37
7.35
7.34
7.32
7.18
7.18
7.17
7.02
7.01
5.66
5.29
4.05
4.02
3.59
3.58
3.56
3.55
3.38
3.37
3.35
3.34
3.04
3.02


1.88
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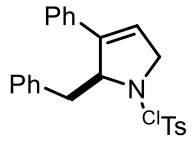
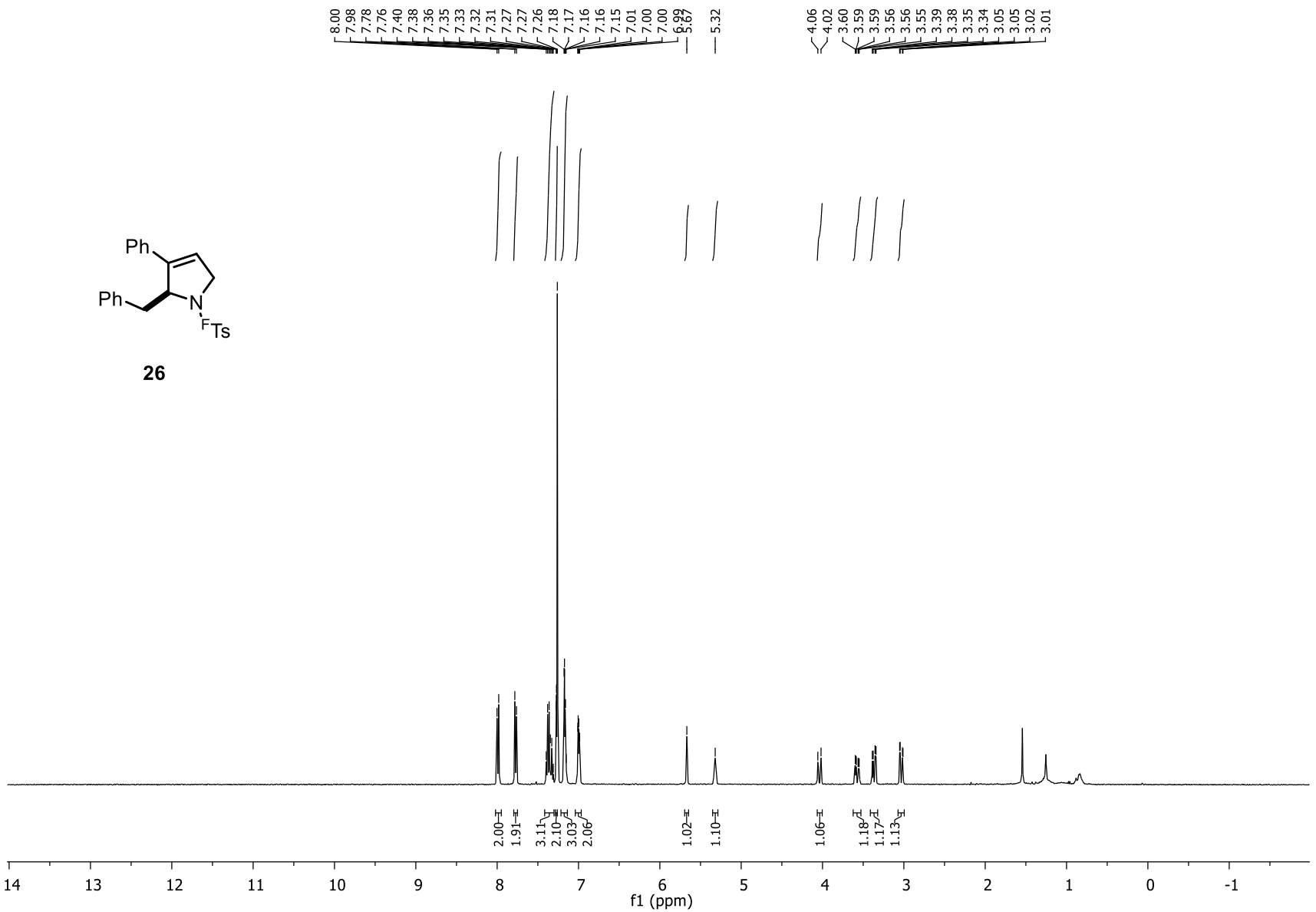
1.06
1.73
2.83
1.96
1.00
1.07
1.10
1.07
1.03
1.12
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


Ph
Ph
N
Cl
Ts

24

140.61
139.23
136.54
135.90
132.93
130.61
129.49
128.89
128.48
128.39
127.60
126.40
126.37
120.92
67.39
55.52
39.58
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.36
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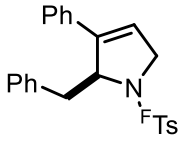
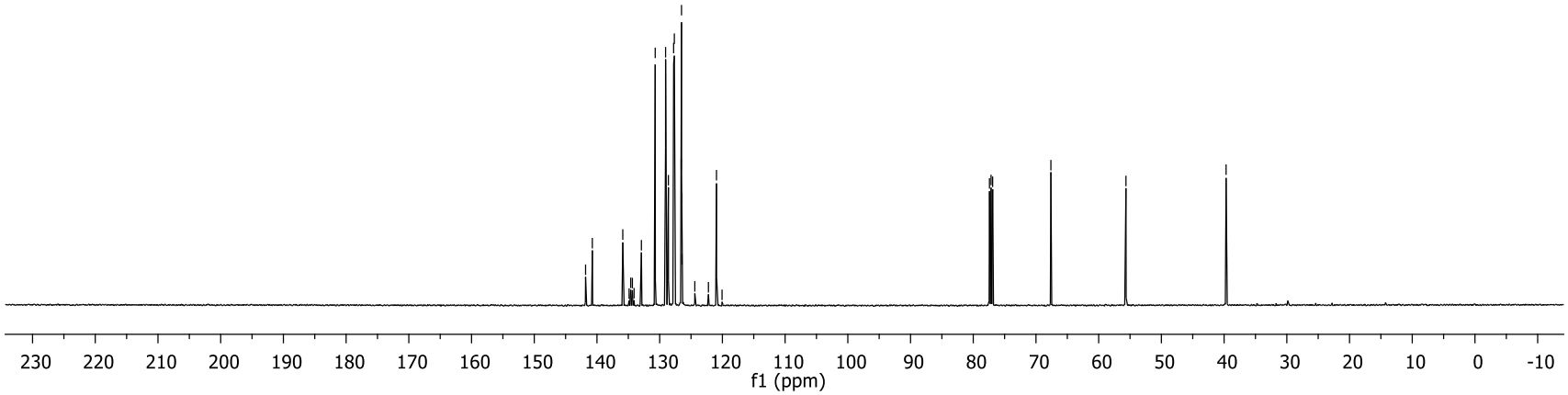
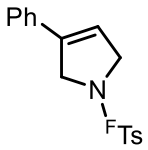
7.32
7.31
7.27
7.27
7.26
7.18
7.17
7.16
7.16
7.15
7.01
7.00
7.00
6.99
6.97
5.32
4.06
4.02
3.60
3.59
3.59
3.56
3.56
3.55
3.39
3.38
3.35
3.34
3.05
3.05
3.02
3.01
Ph
Ph
N
FTs
26
2.00
1.91
3.11
2.10
3.03
2.06
1.02
1.10
1.06
1.18
1.17
1.13
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


141.82
140.74
135.88
134.88
134.61
134.35
134.09
132.92
130.71
129.06
128.61
127.78
127.66
126.58
126.52
126.48
126.45
124.40
122.23
120.94
120.05
77.41
77.16
76.91
67.62
55.65
39.68


Ph
Ph
N
F
Ts

26


230
220
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)


Ph
N
F
Ts

35

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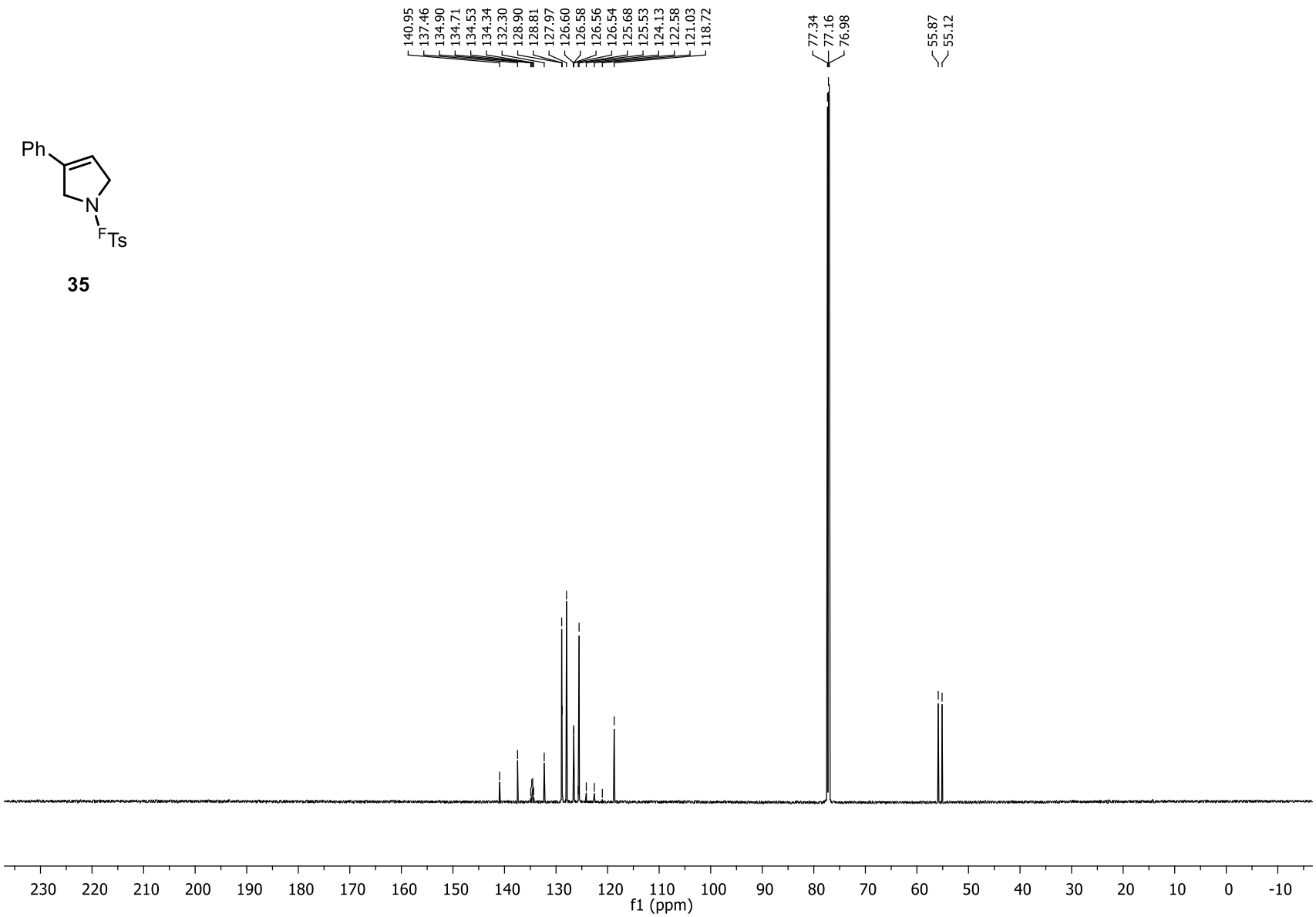
8.01
7.81
7.80
7.35
7.34
7.33
7.31
7.29
7.28
7.26
6.03
4.52
4.52
4.34
1.90
1.91
2.00
2.93
2.13
2.13
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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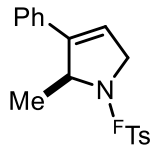
134.34
132.30
128.90
128.81
127.97
126.60
126.58
126.56
126.54
125.68
125.53
124.13
122.58
121.03
118.72
77.34
77.16
76.98
55.87
55.12
Ph
N
F
Ts
35
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
N
F
Ts

36

7.76
7.75
7.33
7.32
7.31
7.30
7.29
7.27
7.26
7.25
5.82
5.82
5.82
5.81
5.02
5.01
5.01
5.01
5.00
5.00
4.99
4.32
4.31
4.31
4.31
4.29
4.29
4.29
4.29
4.27
4.27
4.27
4.25
4.25
4.24
2.40
1.48
1.47
2.00
8.77
1.07
1.12
2.32
3.21
3.28
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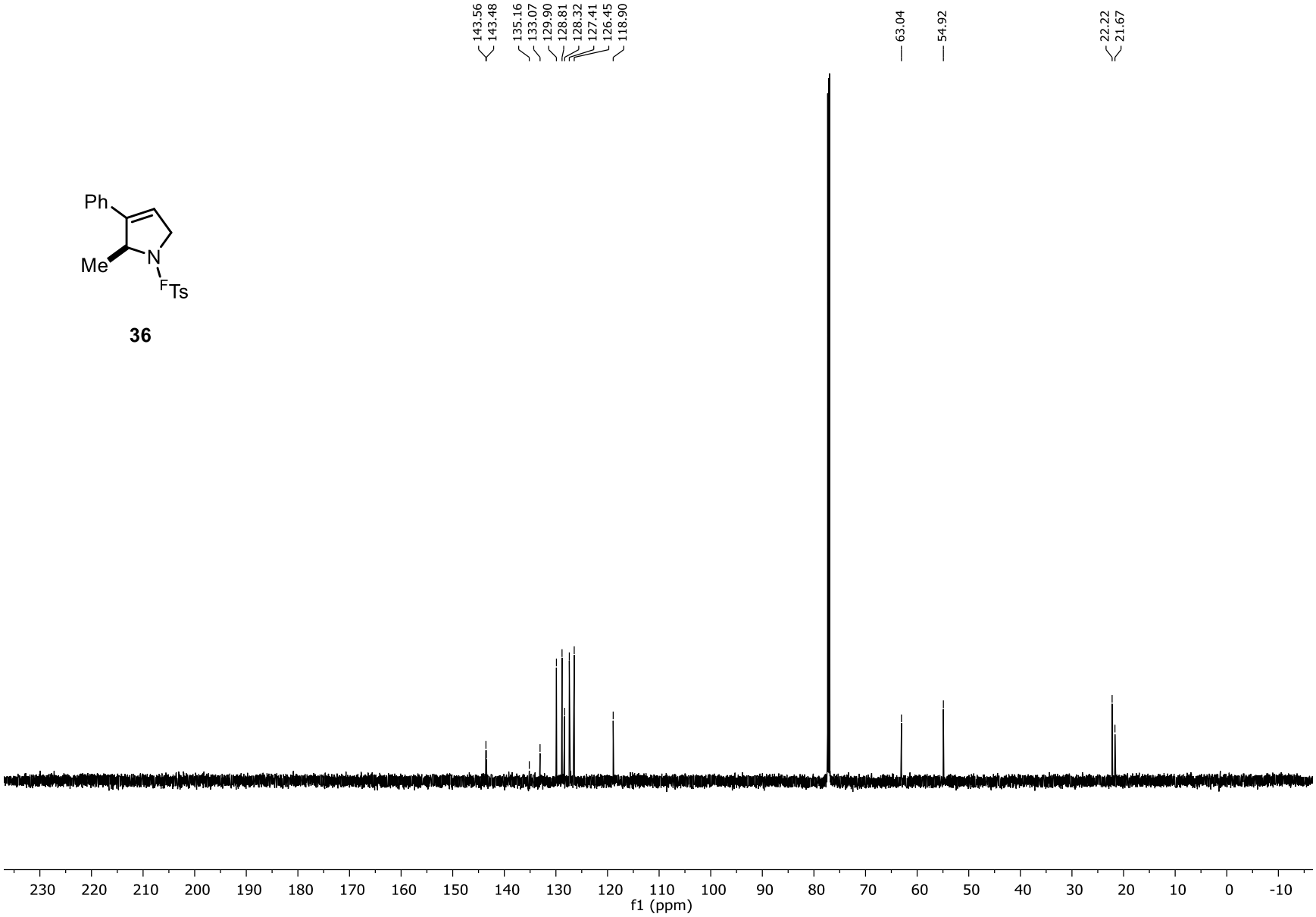
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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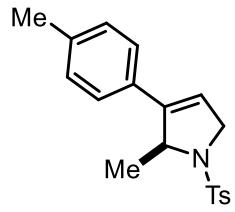
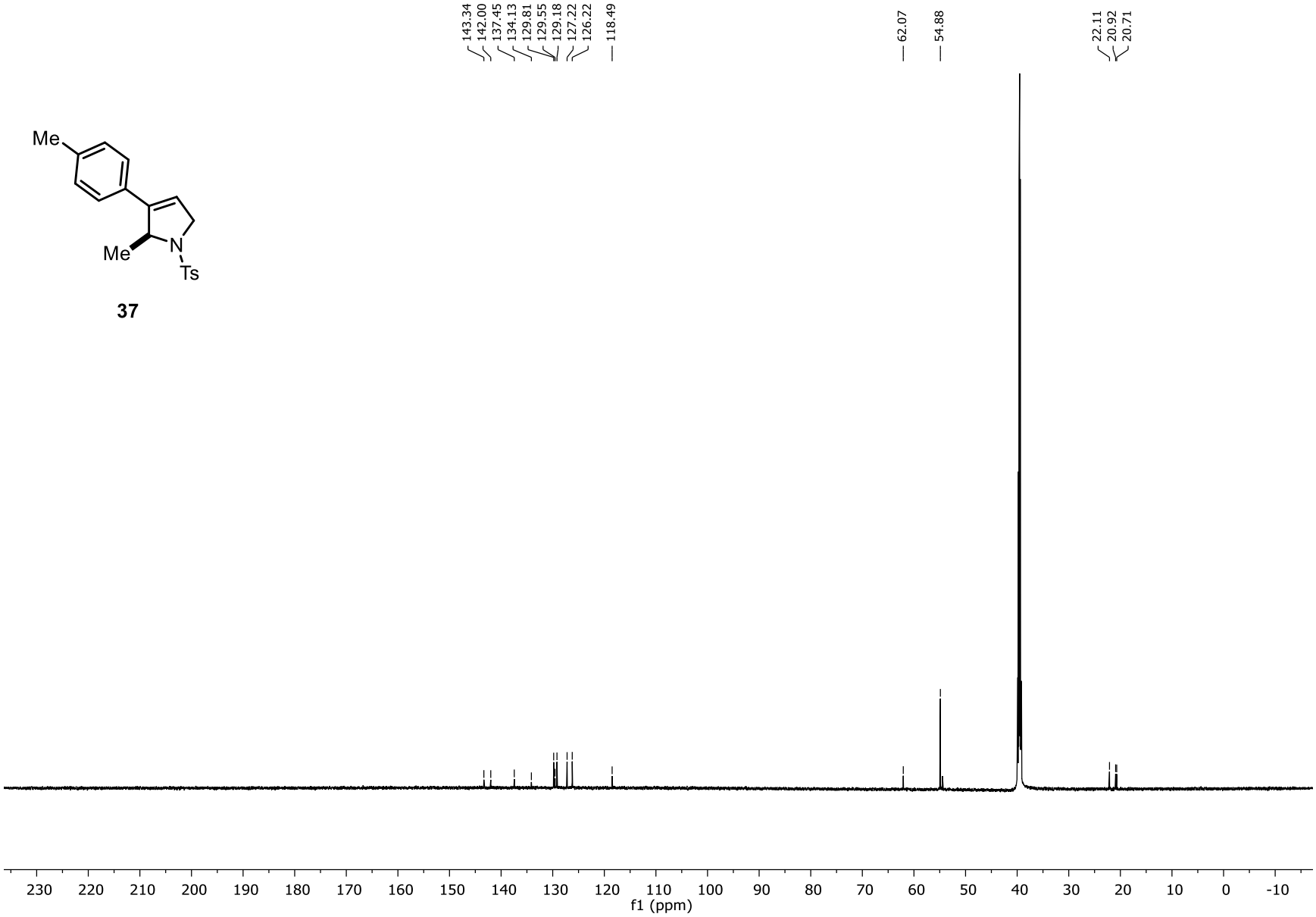
135.16
133.07
129.90
128.81
128.32
127.41
126.45
118.90
63.04
54.92
22.22
21.67
Ph
Me
N
FTs
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

36


Me
Me
N
Ts

37

7.79
7.78
7.39
7.38
7.29
7.28
7.14
7.13
5.97
5.01
5.00
4.99
4.22
4.21
4.20
4.19
4.15
4.13
2.35
2.27
1.34
1.33
1.96
2.03
2.00
2.02
1.02
1.04
1.01
1.02
3.00
3.03
2.99
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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134.13
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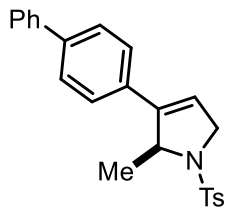
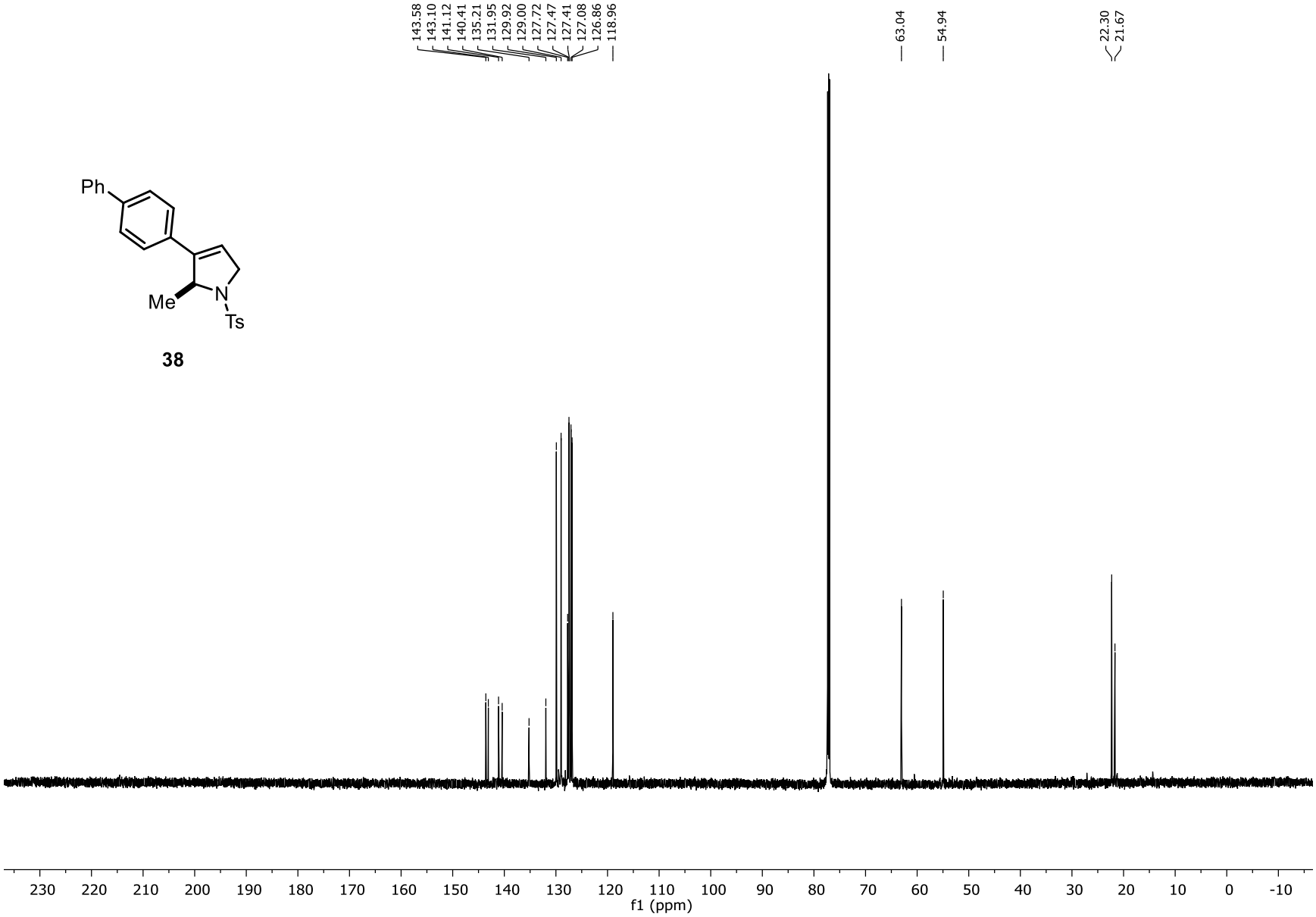
129.55
129.18
127.22
126.22
118.49
62.07
54.88
22.11
20.92
20.71
Me
Me
N
Ts
37
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
N
Ts

38

7.78
7.77
7.58
7.56
7.55
7.45
7.44
7.43
7.37
7.36
7.35
7.34
7.31
7.30
5.88
5.05
5.05
5.04
4.34
4.34
4.34
4.33
4.32
4.32
4.31
4.30
4.27
2.40
1.52
1.51
1.99
4.03
2.04
1.04
2.07
2.02
1.00
1.08
2.24
3.00
3.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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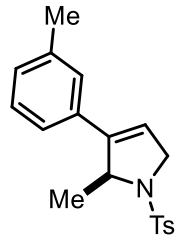
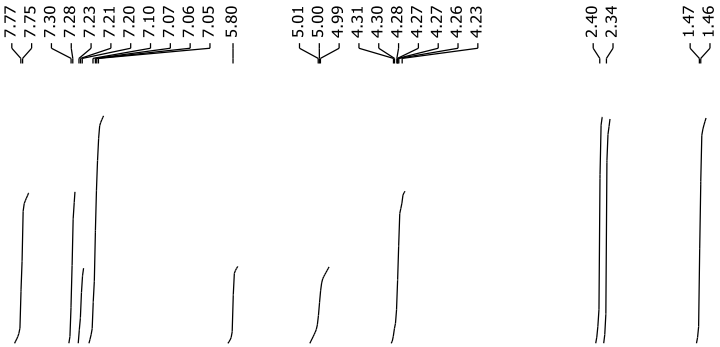
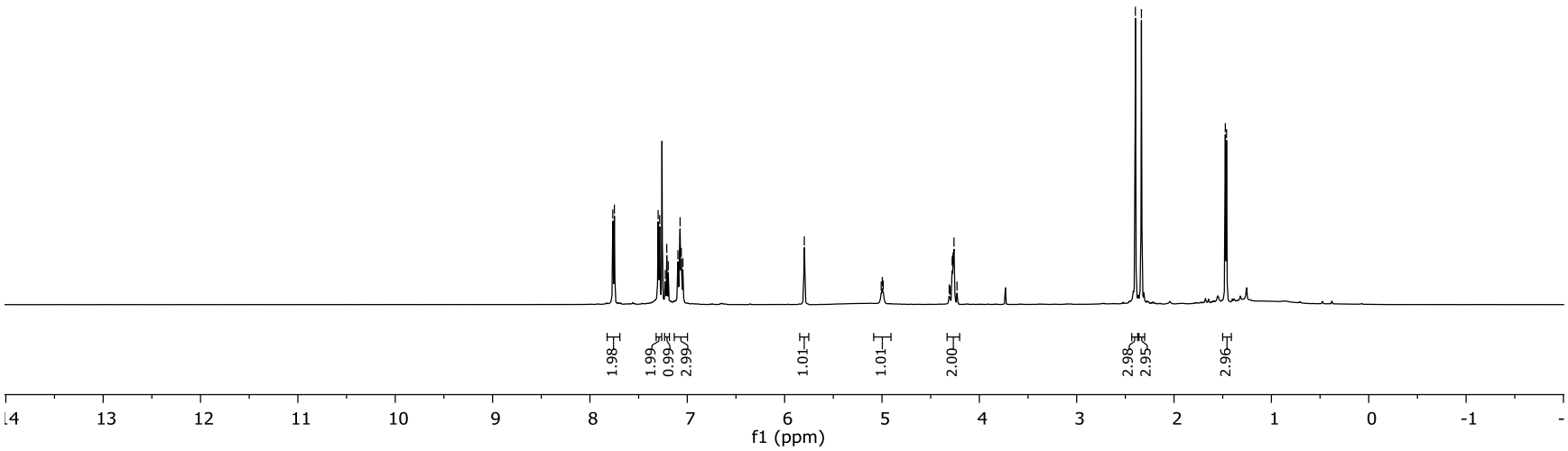
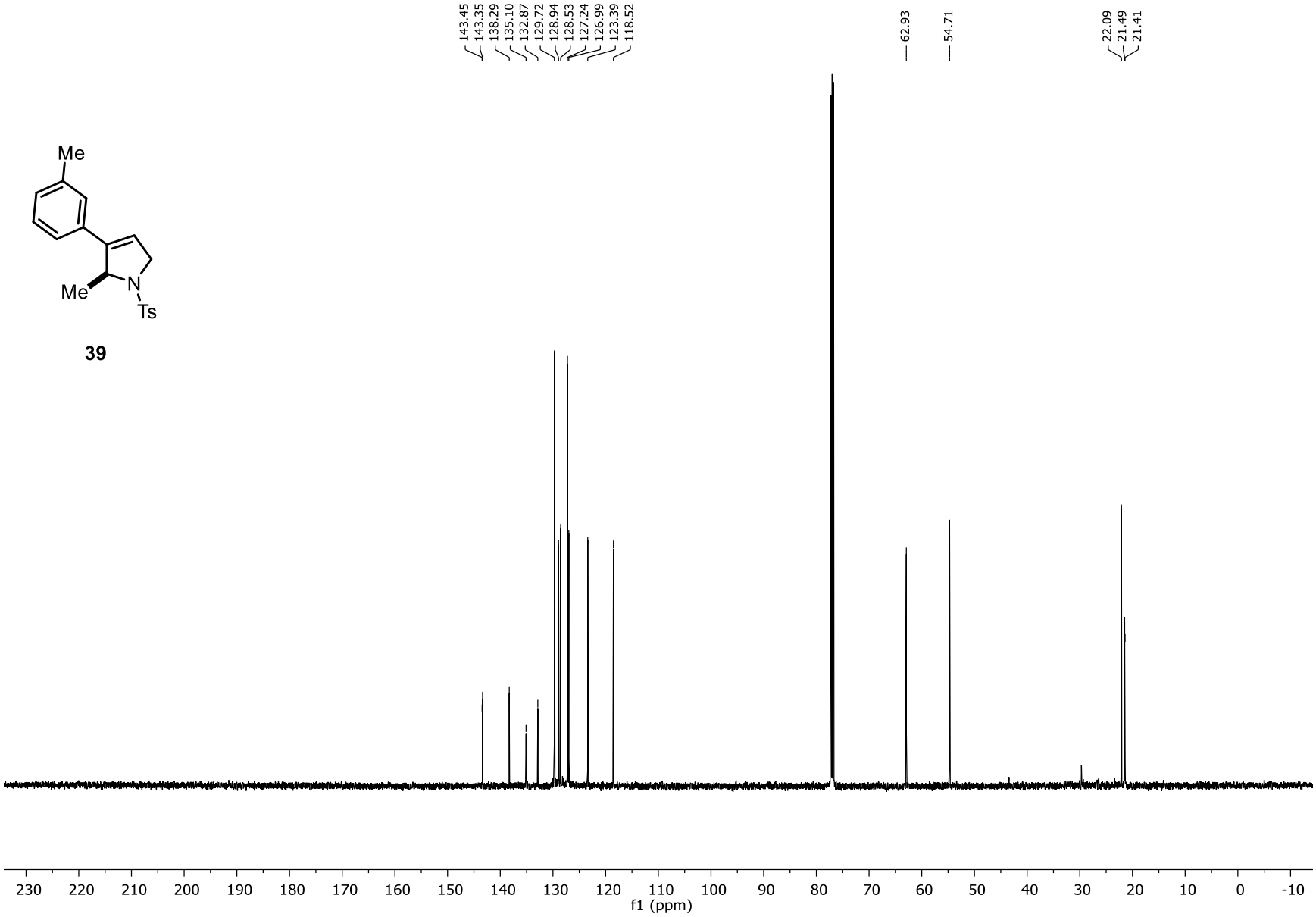
143.10
141.12
140.41
135.21
131.95
129.92
129.00
127.72
127.47
127.41
127.08
126.86
118.96
63.04
54.94
22.30
21.67
Ph
Me
N
Ts
38
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

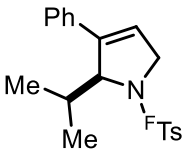

Me
Me
N
Ts

39

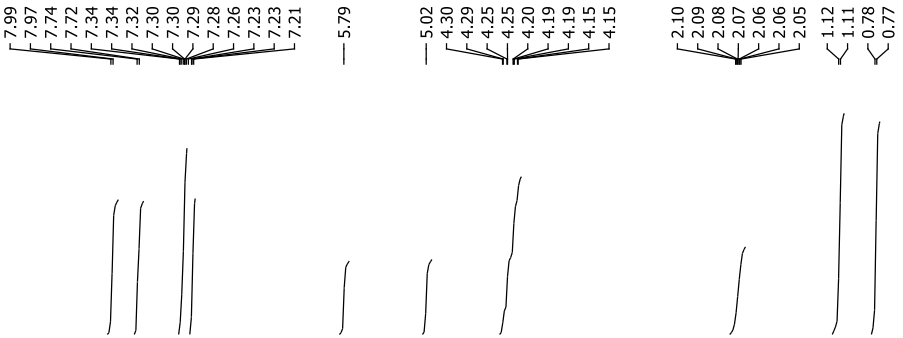

7.77
7.75
7.30
7.28
7.23
7.21
7.20
7.10
7.07
7.06
7.05
5.80
5.01
5.00
4.99
4.31
4.30
4.28
4.27
4.27
4.26
4.23
2.40
2.34
1.47
1.46

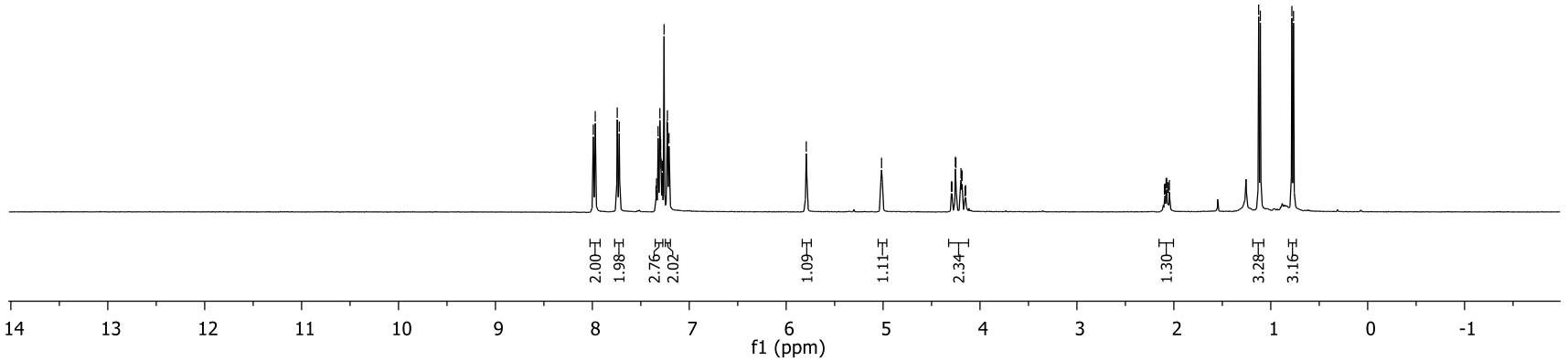

1.98
1.99
0.99
2.99
1.01
1.01
2.00
2.98
2.95
2.96
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

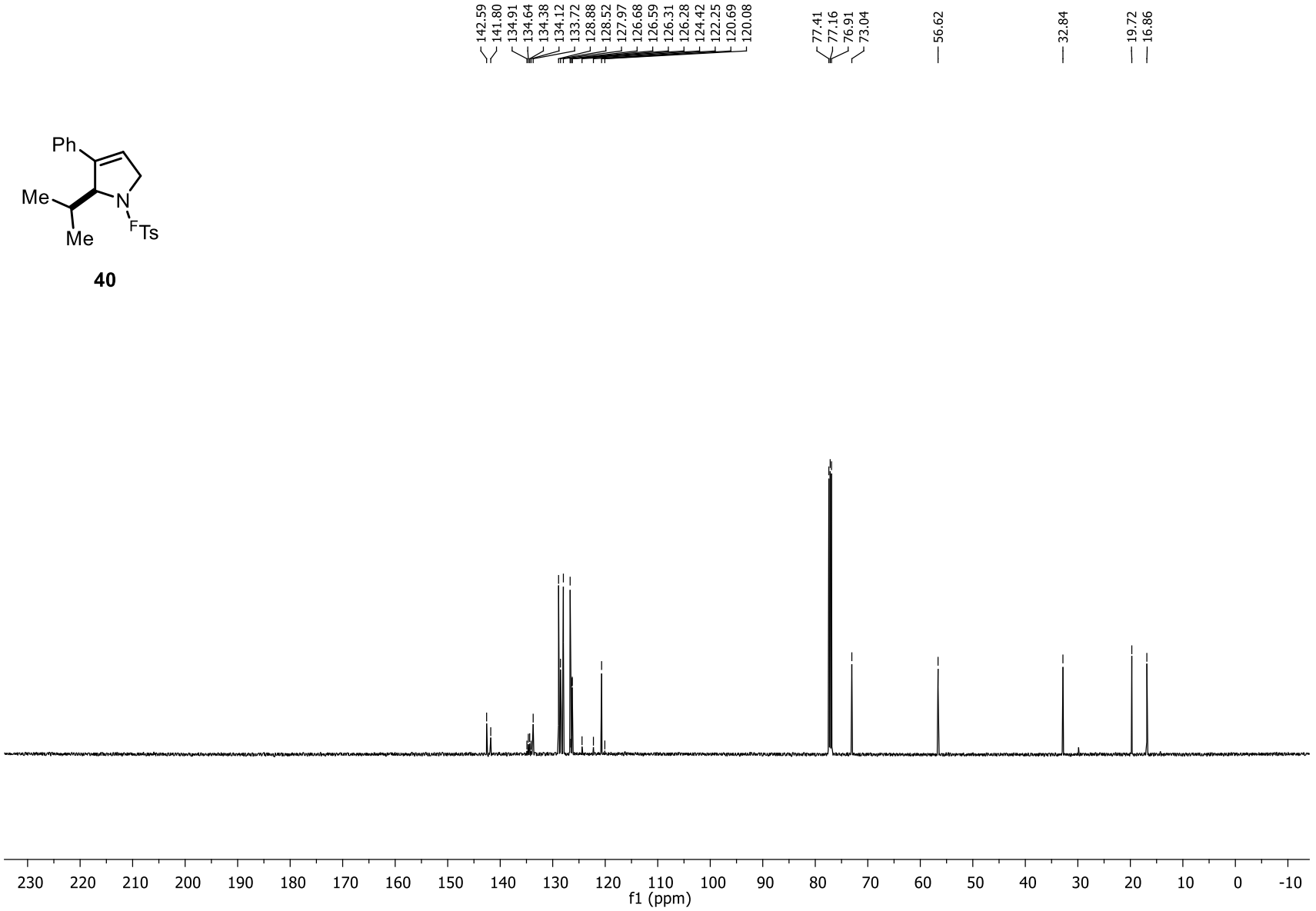

143.45
143.35
138.29
135.10
132.87
129.72
128.94
128.53
127.24
126.99
123.39
118.52
62.93
54.71
22.09
21.49
21.41
Me
Me
N
Ts
39
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
N
Me
FTs

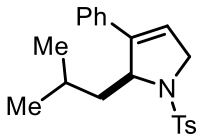
40


7.99
7.97
7.74
7.72
7.34
7.34
7.32
7.30
7.30
7.29
7.28
7.26
7.23
7.23
7.21
5.79
5.02
4.30
4.29
4.25
4.25
4.20
4.19
4.19
4.15
4.15
2.10
2.09
2.08
2.07
2.06
2.06
2.05
1.12
1.11
0.78
0.77


2.00
1.98
2.76
2.02
1.09
1.11
2.34
1.30
3.28
3.16
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

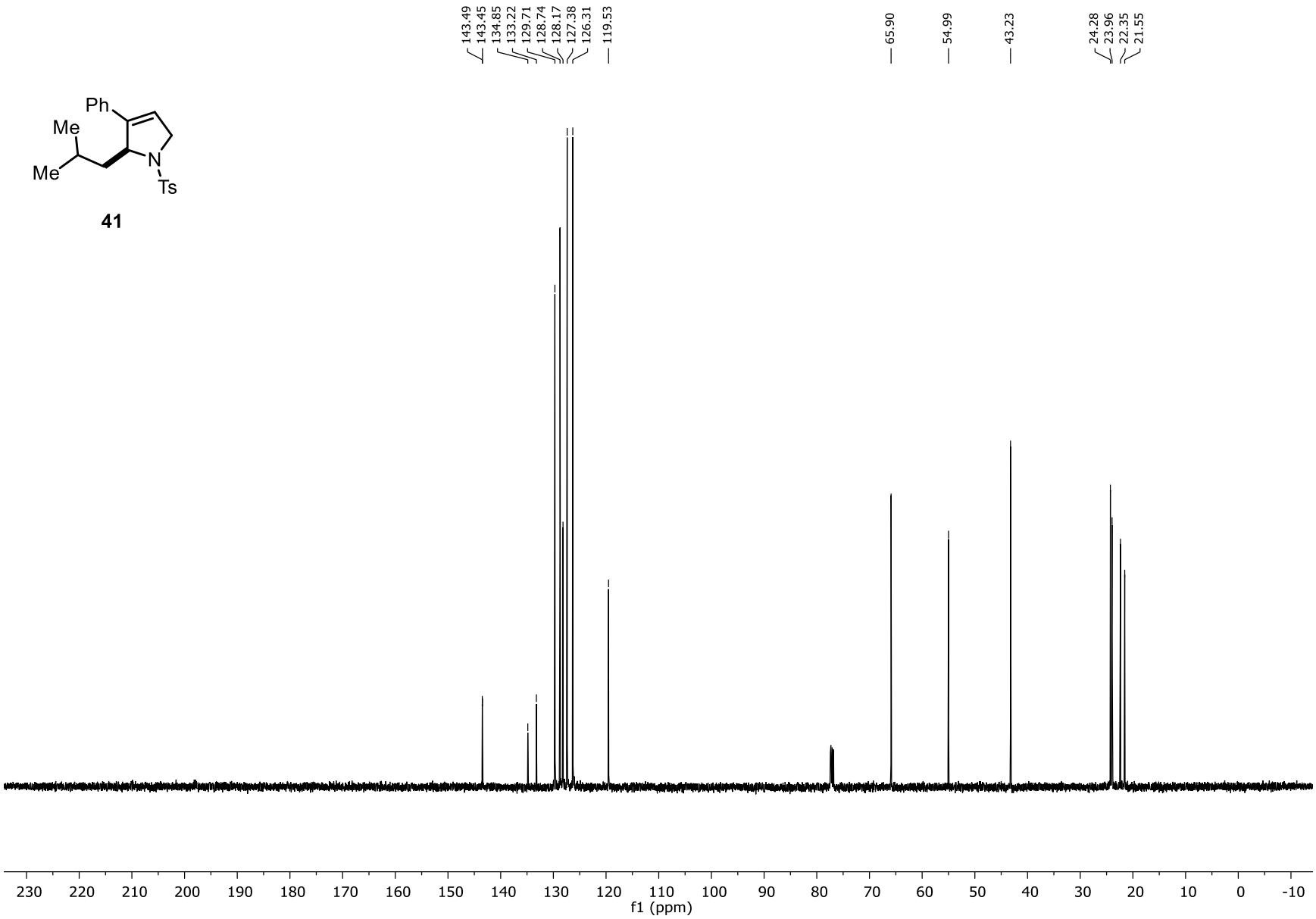

142.59
141.80
134.91
134.64
134.38
134.12
133.72
128.88
128.52
127.97
126.68
126.59
126.31
126.28
124.42
122.25
120.69
120.08
77.41
77.16
76.91
73.04
56.62
32.84
19.72
16.86
Ph
Me
Me
N
F
Ts
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

40


Ph
Me
Me
N
Ts

41

7.74
7.73
7.33
7.32
7.31
7.28
7.27
7.26
7.25
7.24
7.23
5.77
5.06
5.05
4.32
4.29
4.25
4.23
2.35
2.06
2.05
2.04
2.03
2.02
1.57
1.56
1.55
1.07
1.06
0.84
0.83
1.96
2.04
1.06
3.99
0.99
1.02
1.03
1.02
3.02
1.04
2.05
3.09
3.09
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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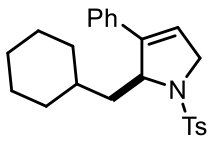
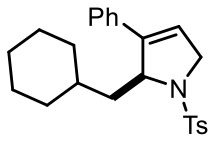
143.45
134.85
133.22
129.71
128.74
128.17
127.38
126.31
119.53
65.90
54.99
43.23
24.28
23.96
22.35
21.55
Ph
Me
Me
N
Ts
41
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
N
Ts

42

7.73
7.71
7.33
7.31
7.29
7.28
7.26
7.24
7.22
7.21
5.75
5.08
5.07
5.06
4.32
4.28
4.24
4.24
4.21
4.20
2.35
2.09
2.06
1.72
1.69
1.64
1.61
1.60
1.58
1.55
1.51
1.49
1.44
1.32
1.30
1.26
1.24
1.20
1.15
1.11
1.08
0.94
0.91
0.89
0.86
0.84
0.81
0.77
2.00
7.61
0.98
1.02
2.10
3.01
1.05
7.37
3.25
2.28
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


Ph
N
Ts

42

143.58
143.50
134.95
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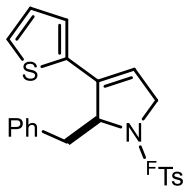
129.74
128.77
128.19
127.42
126.37
119.50
65.38
55.02
41.85
34.51
33.51
33.17
26.70
26.46
26.30
21.62
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


S
Ph
N
FTs

43

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7.76
7.75
7.25
7.18
7.06
7.02
6.98
5.57
5.18
3.98
3.95
3.51
3.48
3.40
3.37
3.19
3.16
2.08
2.10
0.87
3.33
3.15
1.24
1.00
1.14
1.17
1.23
1.20
1.14
14
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10
9
8
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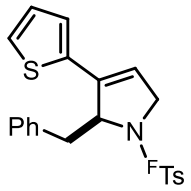
6
5
4
3
2
1
0
-1
-2
f1 (ppm)


S
Ph
N
FTs

43

141.68
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134.54
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134.28
134.02
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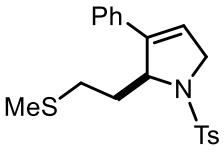
127.75
127.67
127.51
126.57
126.41
126.39
126.36
126.33
125.75
125.10
120.29
68.24
55.18
40.02
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
MeS
N
Ts

44

7.74
7.73
7.33
7.32
7.31
7.28
7.28
7.27
7.26
5.85
5.32
5.11
5.11
5.10
4.30
4.30
4.28
4.24
4.24
4.24
4.22
2.65
2.64
2.63
2.63
2.62
2.62
2.61
2.40
2.40
2.38
2.36
2.18
2.17
2.17
2.16
2.16
2.15
2.15
2.14
2.14
2.13
1.93
1.92
1.91
1.91
1.90
1.89
1.89
2.00
4.00
3.13
1.05
1.13
2.47
1.23
4.41
1.31
3.04
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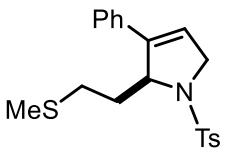
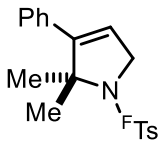
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


Ph
MeS
N
Ts

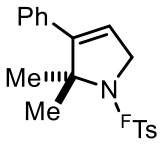
44

144.22
141.57
134.92
133.13
130.16
129.08
128.67
127.64
126.69
120.75
66.36
55.98
54.15
53.99
53.84
53.69
53.53
33.71
29.09
21.62
15.45
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
Me
N
F
Ts

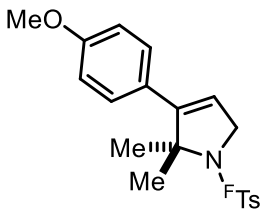
45

8.06
8.04
7.79
7.78
7.33
7.32
7.32
7.26
7.20
7.19
7.19
7.18
5.61
5.61
4.22
4.21
1.61
1.96
2.03
2.88
1.99
0.93
2.02
6.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


Ph
Me
Me
N
Ts
F

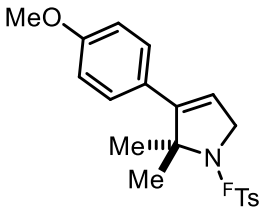
45

148.52
144.76
134.61
134.46
134.20
133.94
133.68
128.66
128.36
128.19
127.88
126.72
126.24
126.21
126.18
126.15
124.55
122.38
120.22
119.73
77.41
77.16
76.91
73.70
53.67
27.18
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeO
Me
Me
N
F
Ts

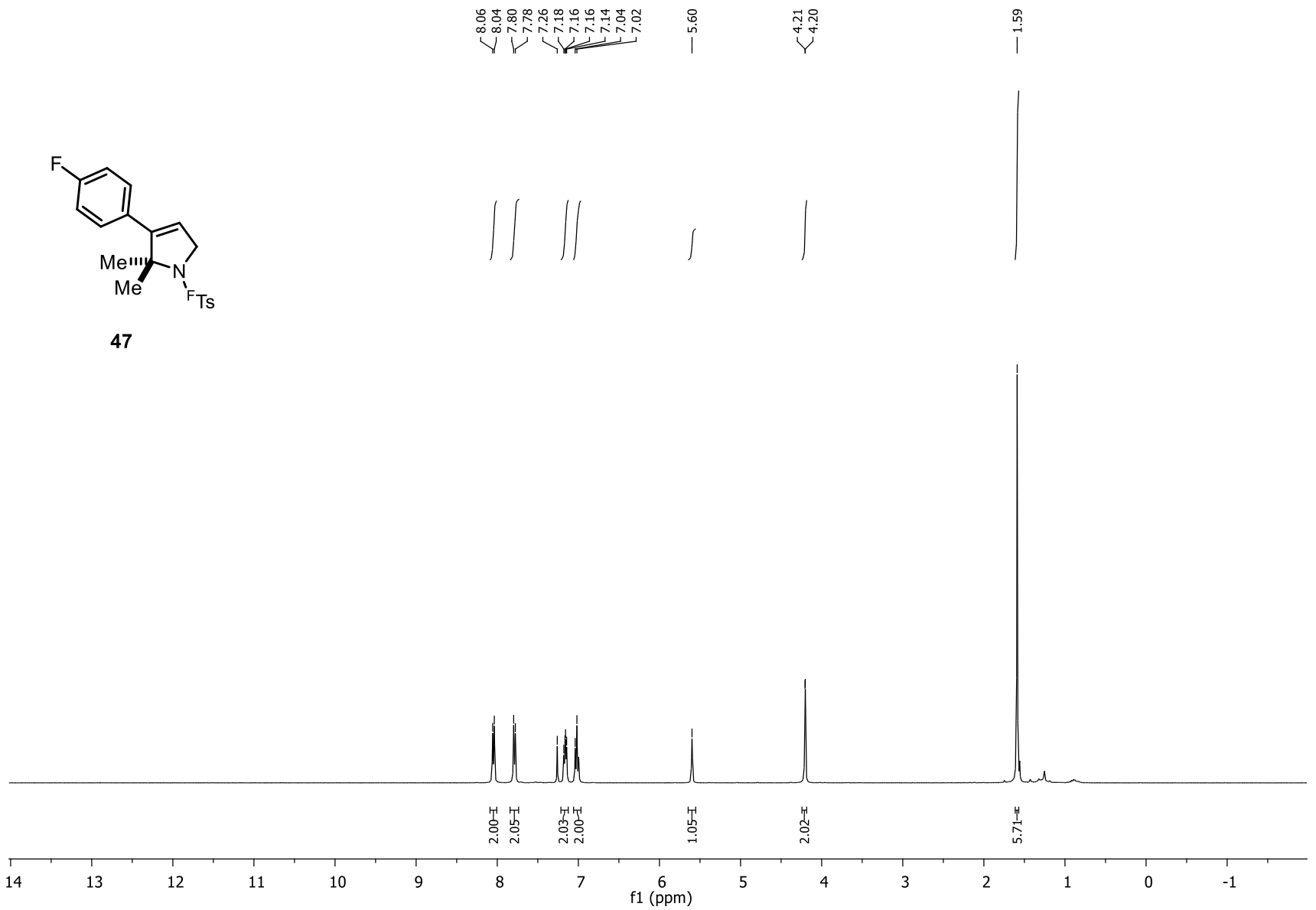
46

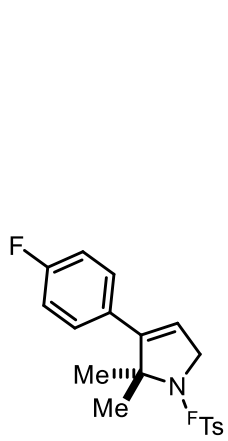
8.06
8.03
7.79
7.77
7.26
7.14
7.12
6.86
6.84
5.58
5.57
5.57
4.20
4.19
3.81
1.60
2.00
2.08
2.01
2.27
1.01
1.96
3.06
6.03
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


MeO
Me
Me
N
F
Ts

46

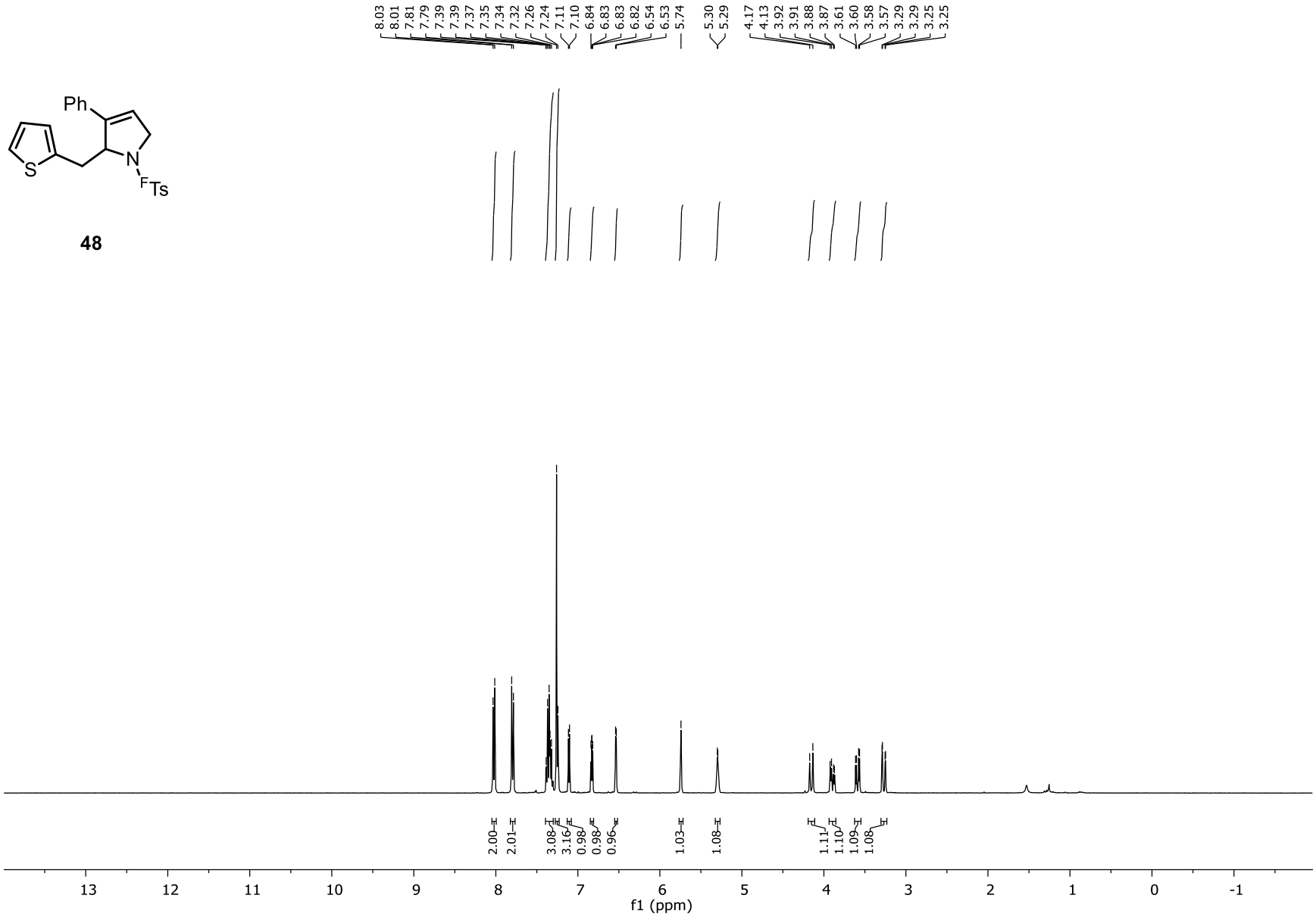
159.52
147.99
144.74
134.35
134.09
133.83
133.57
129.70
127.84
126.77
126.70
126.19
126.16
126.13
126.10
124.53
122.36
120.19
119.11
113.76
77.41
77.16
76.91
73.57
55.35
53.54
27.13
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8.06
8.04
7.80
7.78
7.26
7.18
7.16
7.16
7.14
7.04
7.02
5.60
4.21
4.20
1.59
F
Me
Me
N
F
Ts
47
2.00
2.05
2.03
2.00
1.05
2.02
5.71
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

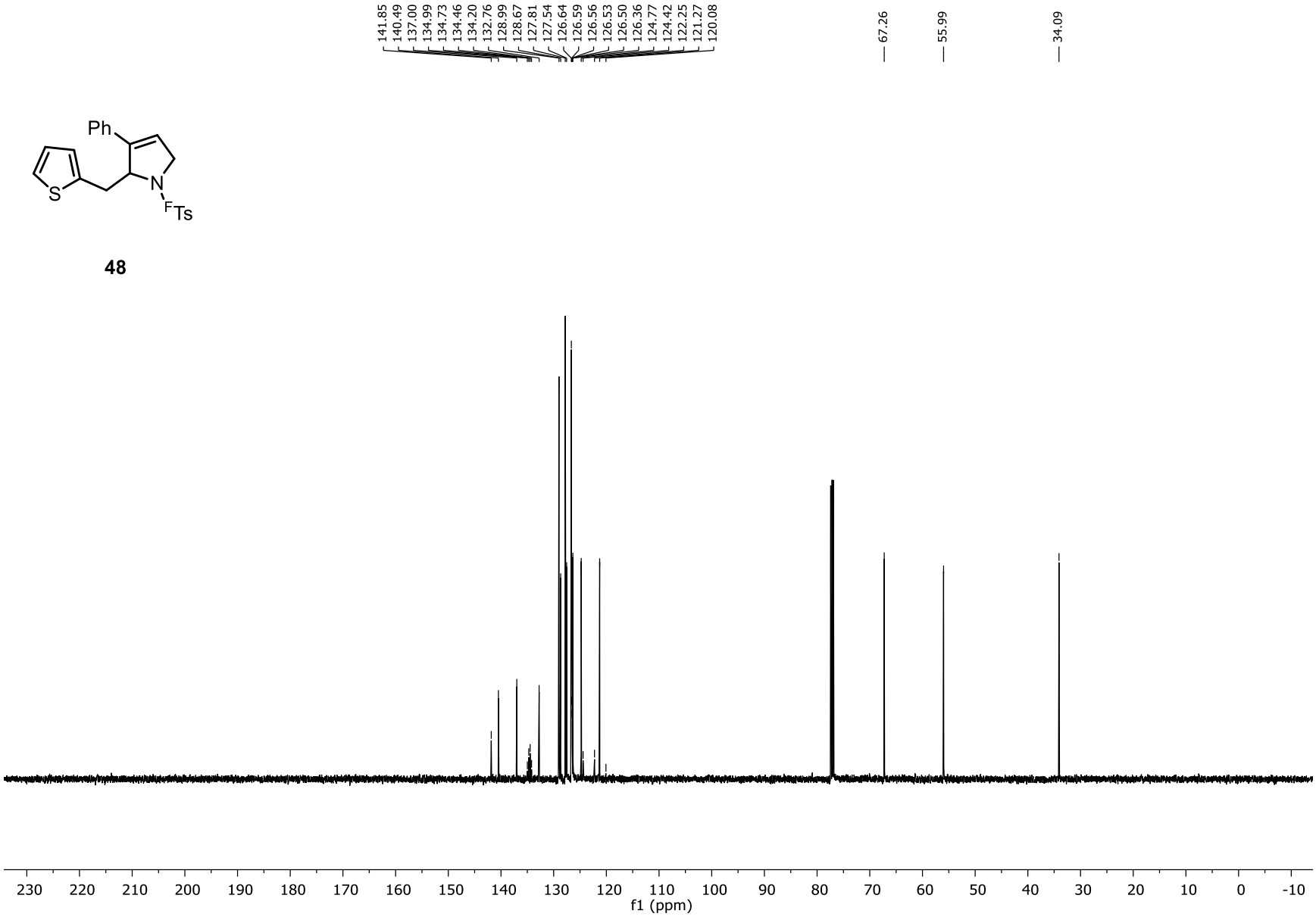

F
Me
Me
N
F
Ts

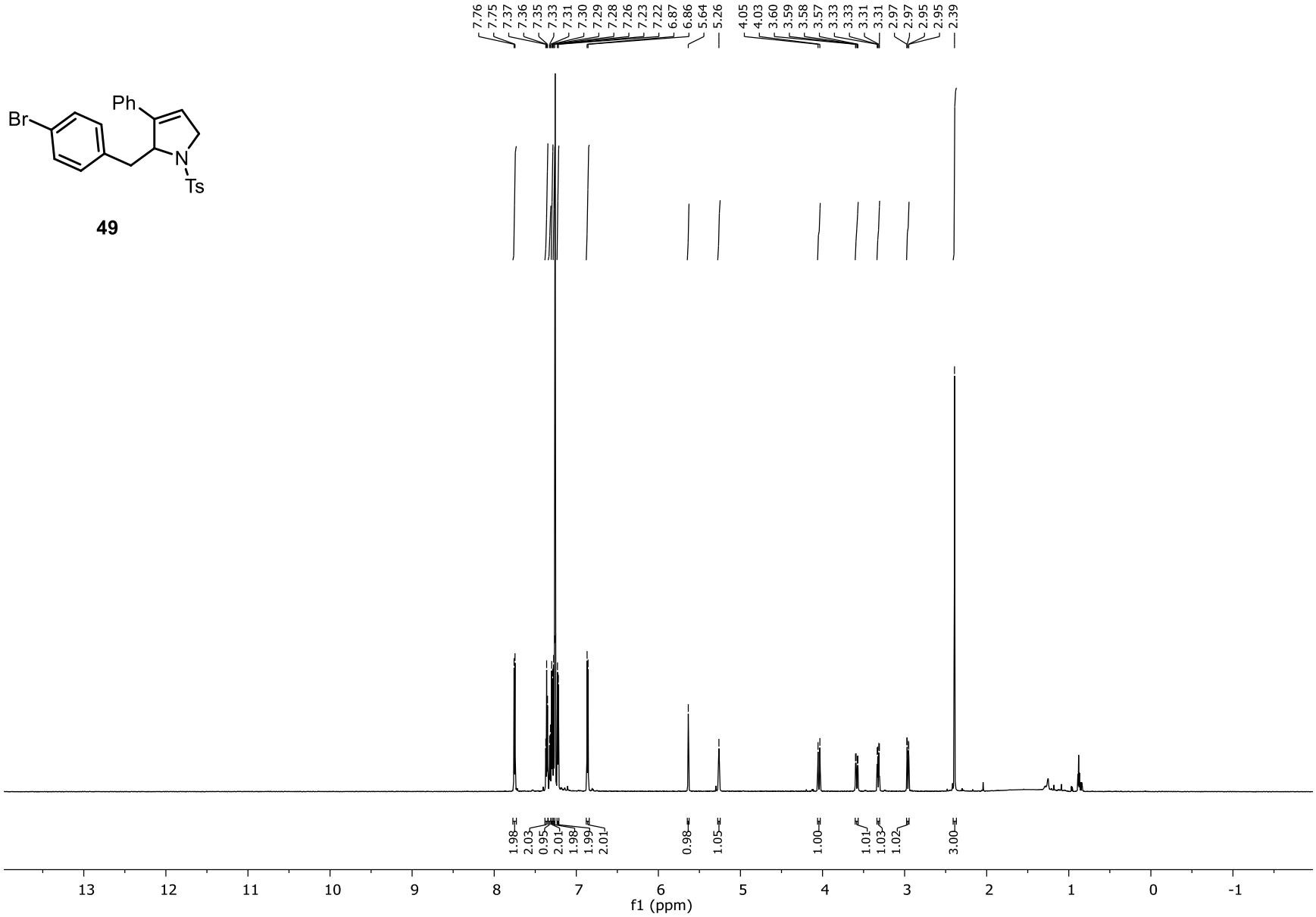
47

163.40
161.99
147.48
144.61
134.34
134.16
133.97
133.78
130.52
130.51
130.40
130.36
127.86
126.23
126.21
126.19
126.17
125.75
124.20
122.65
121.10
120.21
115.42
115.30
77.34
77.16
76.98
73.50
53.58
27.07
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

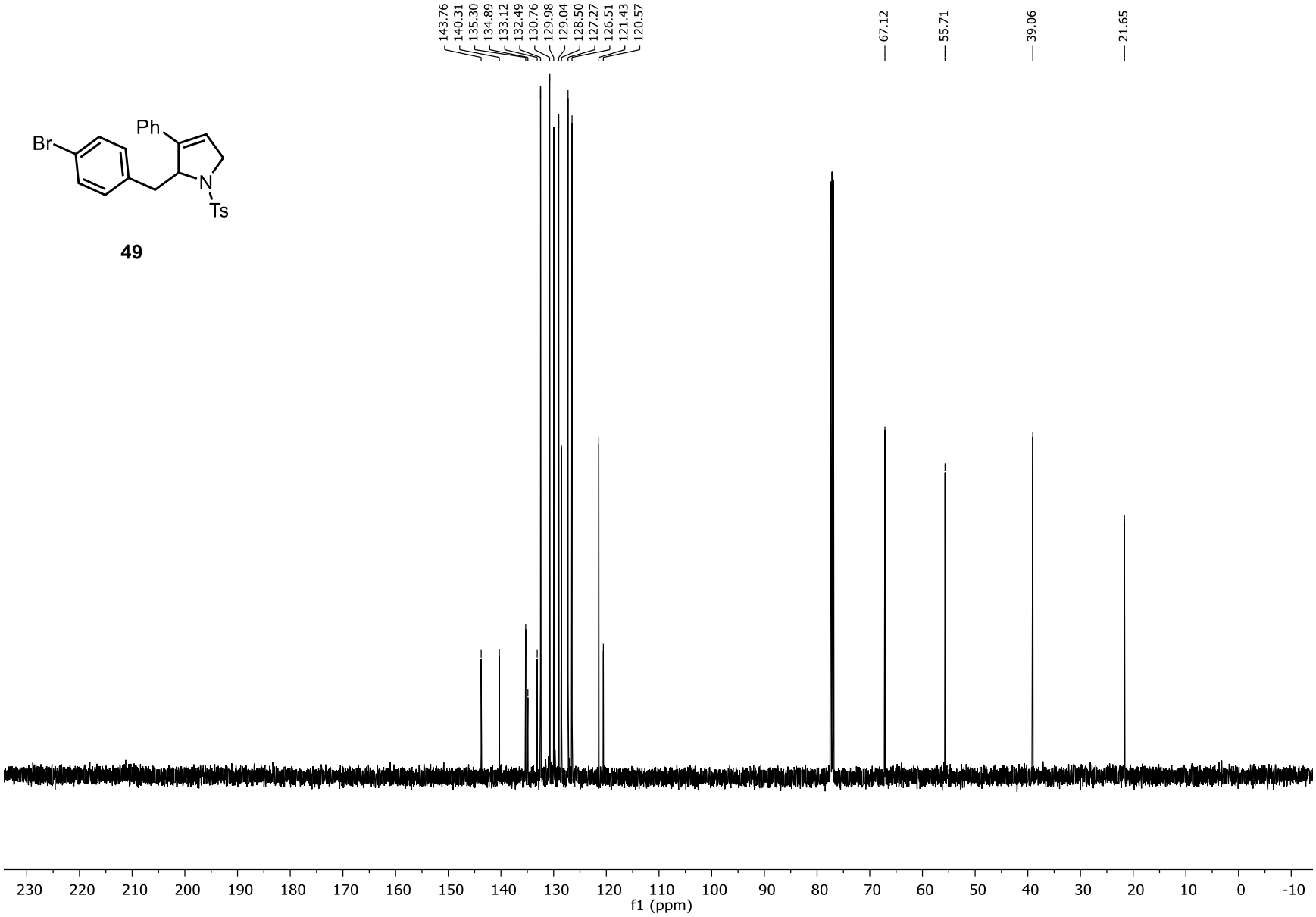

8.03
8.01
7.81
7.79
7.39
7.39
7.37
7.35
7.34
7.32
7.26
7.24
7.11
7.10
6.84
6.83
6.83
6.82
6.54
6.53
5.74
5.30
5.29
4.17
4.13
3.92
3.91
3.88
3.87
3.61
3.60
3.58
3.57
3.29
3.29
3.25
3.25
Ph
S
N
FTs
2.00
2.01
3.08
3.16
0.98
0.98
0.96
1.03
1.08
1.11
1.10
1.09
1.08
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

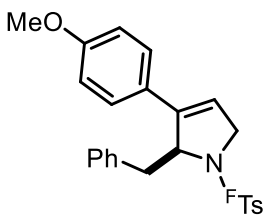
48


141.85
140.49
137.00
134.99
134.73
134.46
134.20
132.76
128.99
128.67
127.81
127.54
126.64
126.59
126.56
126.53
126.50
126.36
124.77
124.42
122.25
121.27
120.08
67.26
55.99
34.09
Ph
S
N
FTs
48
230
220
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)

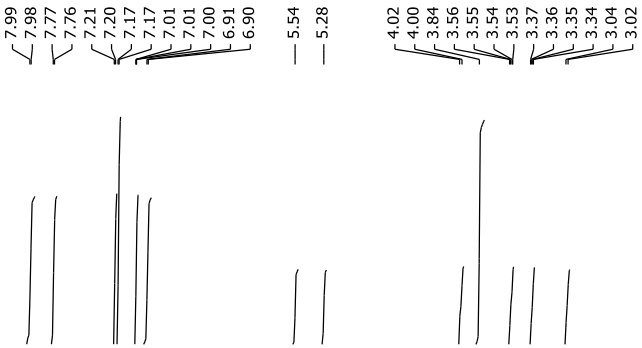

Br
Ph
N
Ts
7.76
7.75
7.37
7.36
7.35
7.33
7.31
7.30
7.29
7.28
7.26
7.23
7.22
6.87
6.86
5.64
5.26
4.05
4.03
3.60
3.59
3.58
3.57
3.33
3.33
3.31
2.97
2.97
2.95
2.95
2.39
1.98
2.03
0.95
2.01
1.98
1.99
2.01
0.98
1.05
1.00
1.01
1.03
1.02
3.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

49


143.76
140.31
135.30
134.89
133.12
132.49
130.76
129.98
129.04
128.50
127.27
126.51
121.43
120.57
67.12
55.71
39.06
21.65
Br
Ph
N
Ts
49
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeO
Ph
N
Ts
F

50


7.99
7.98
7.77
7.76
7.21
7.20
7.17
7.17
7.01
7.01
7.00
6.91
6.90
5.54
5.28
4.02
4.00
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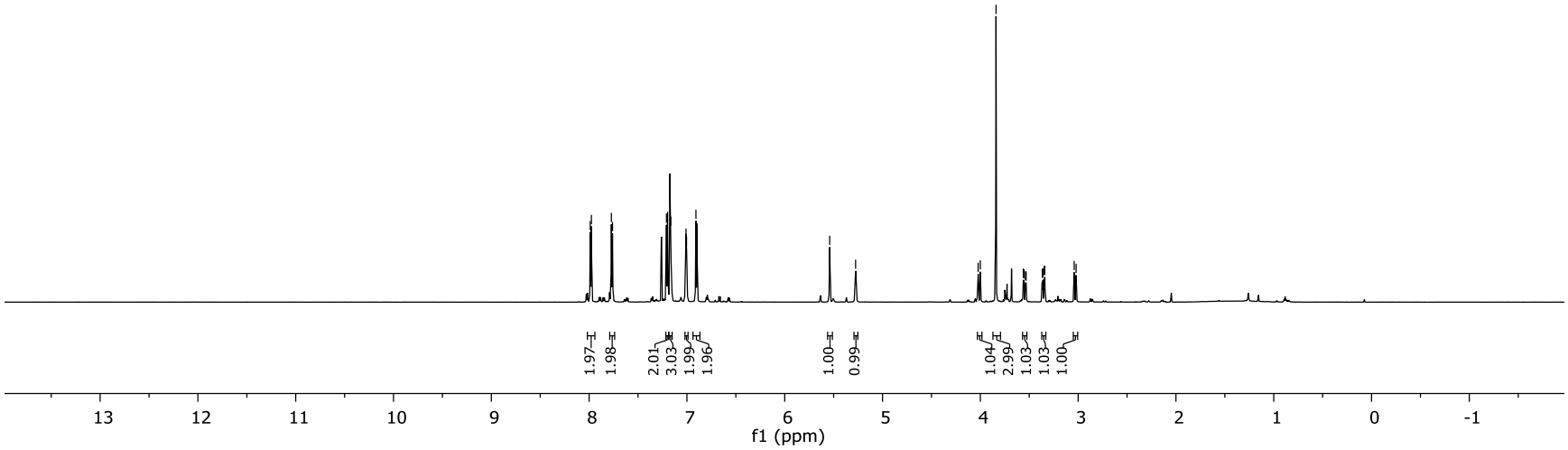
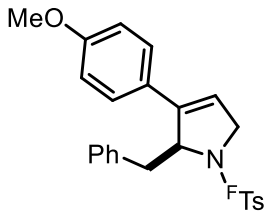
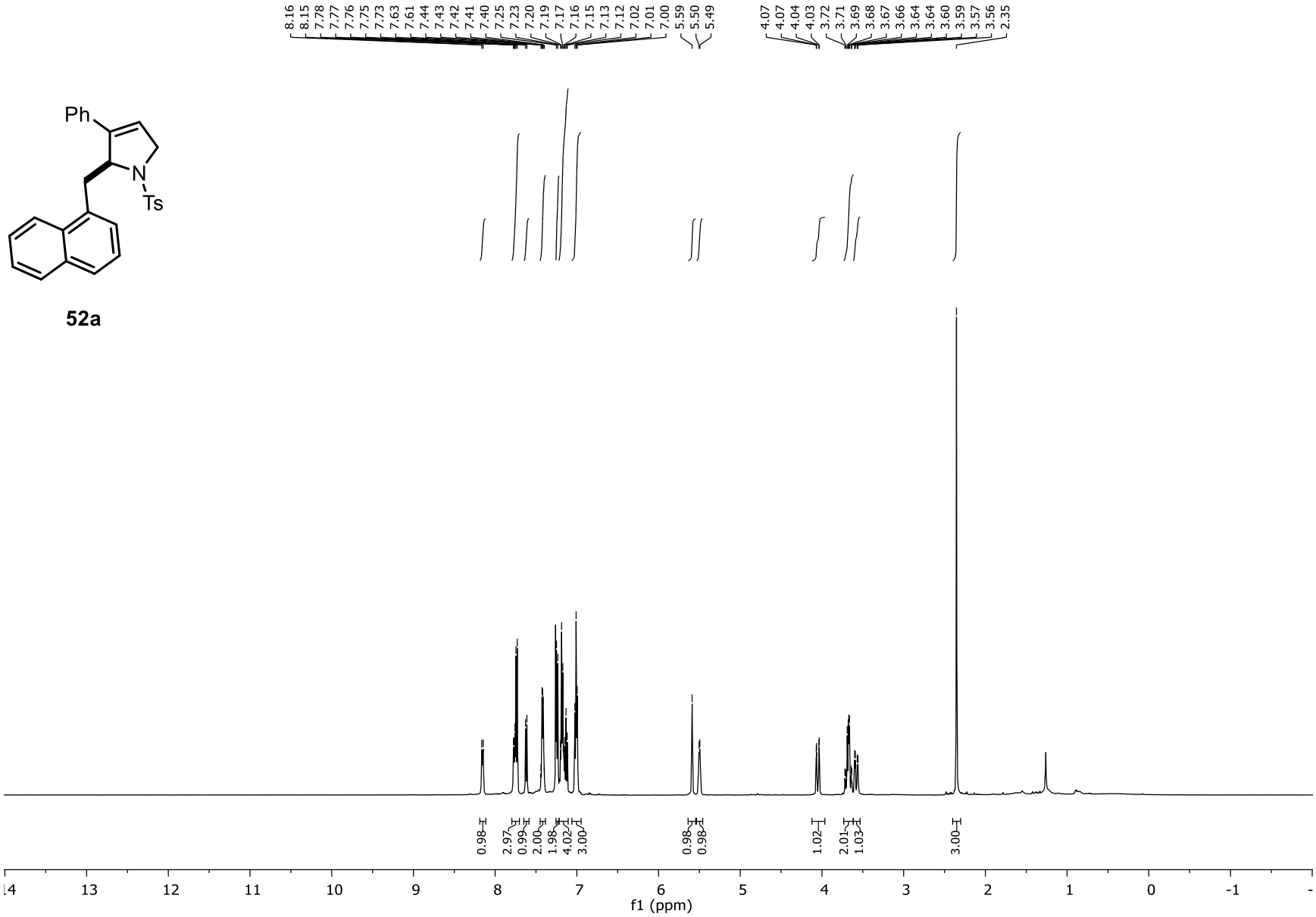
3.55
3.54
3.53
3.37
3.36
3.35
3.34
3.04
3.02

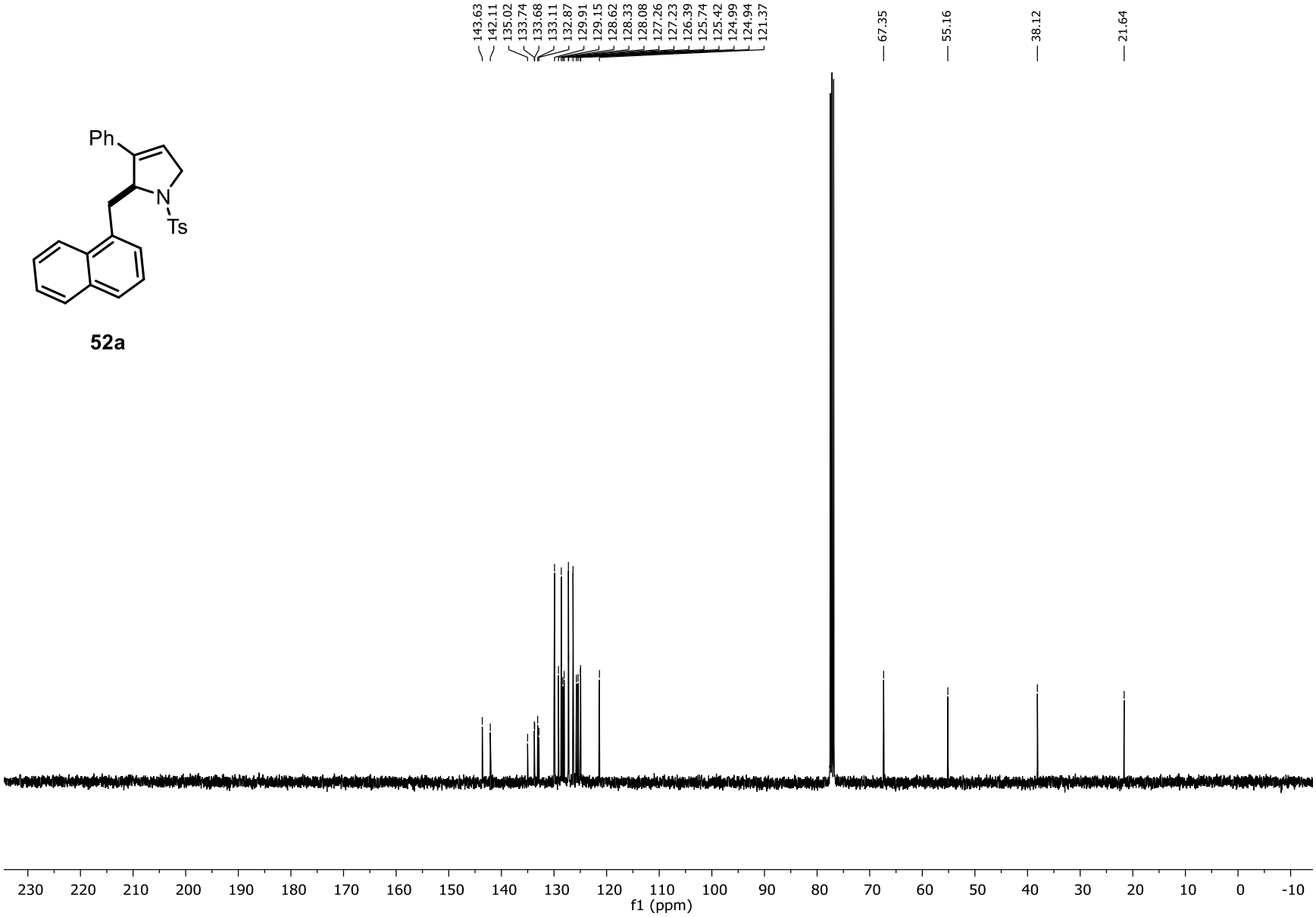

1.97
1.98
2.01
3.03
1.99
1.96
1.00
0.99
1.04
2.99
1.03
1.03
1.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

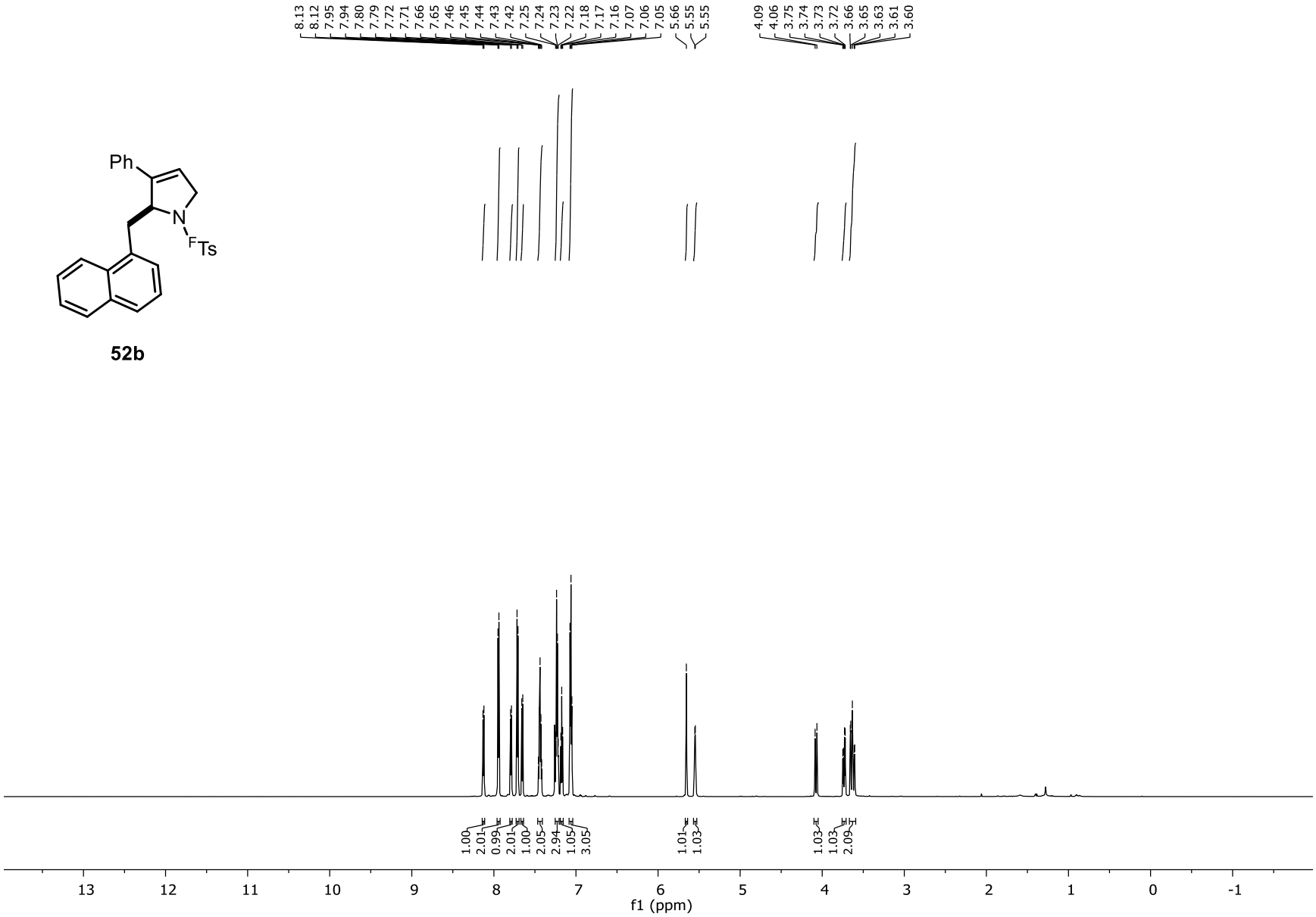

MeO
Ph
N
F
Ts

50

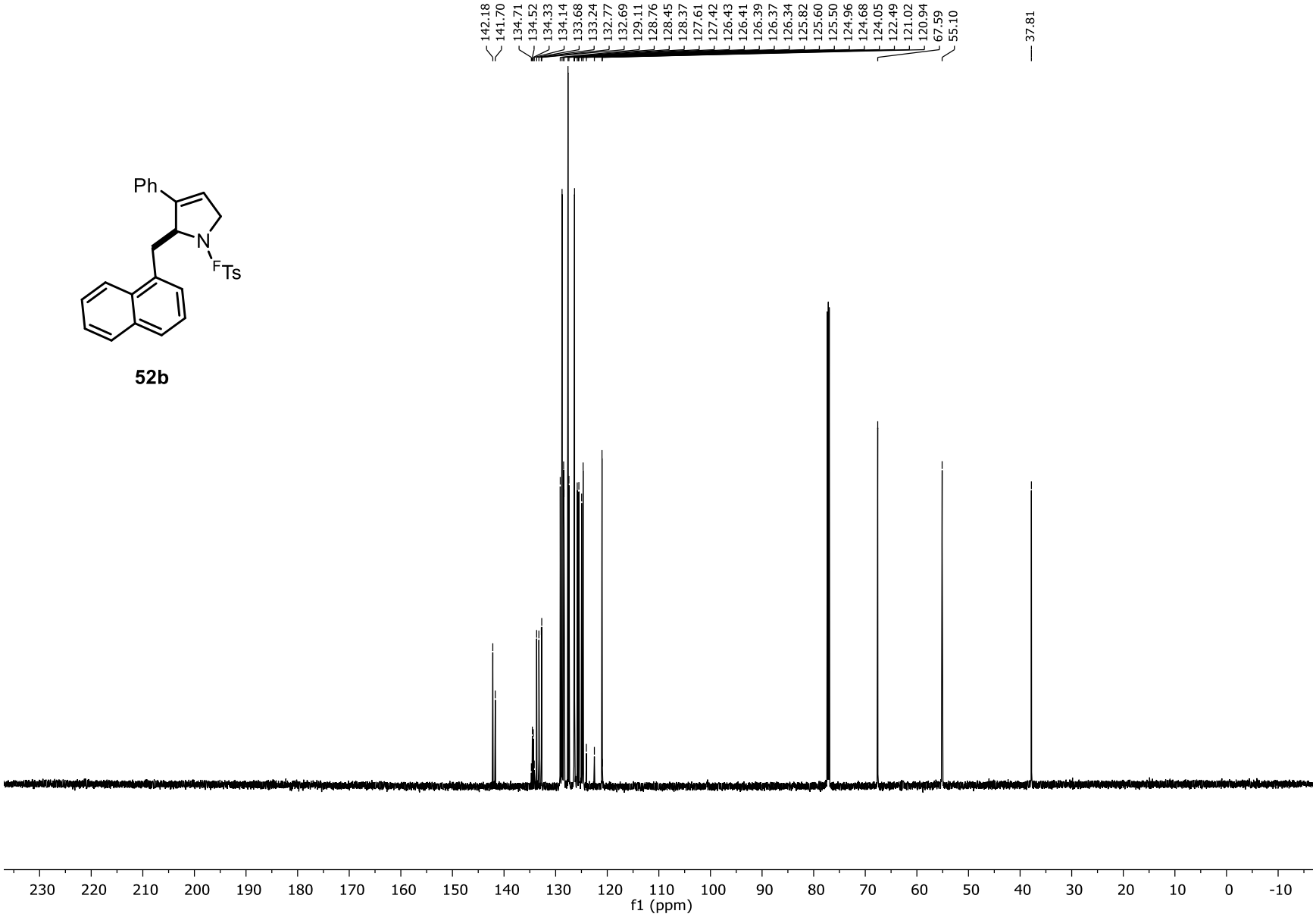
159.82
141.91
140.15
135.97
134.77
134.58
134.39
134.20
130.75
127.84
127.78
127.66
126.57
126.52
126.51
126.48
126.46
125.67
125.56
124.12
122.57
121.07
118.94
114.44
67.71
55.64
55.49
39.72
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

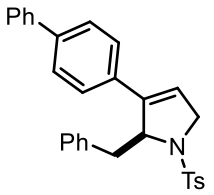

8.16
8.15
7.78
7.77
7.76
7.75
7.73
7.63
7.61
7.44
7.43
7.42
7.41
7.40
7.25
7.23
7.20
7.19
7.17
7.16
7.15
7.13
7.12
7.02
7.01
7.00
5.59
5.50
5.49
4.07
4.07
4.04
4.03
3.72
3.71
3.69
3.68
3.67
3.66
3.64
3.64
3.60
3.59
3.57
3.56
2.35
Ph
N
Ts
52a
0.98
2.97
0.99
2.00
1.98
4.02
3.00
0.98
0.98
1.02
2.01
1.03
3.00
f1 (ppm)


143.63
142.11
135.02
133.74
133.68
133.11
132.87
129.91
129.15
128.62
128.33
128.08
127.26
127.23
126.39
125.74
125.42
124.99
124.94
121.37
67.35
55.16
38.12
21.64
Ph
N
Ts
52a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

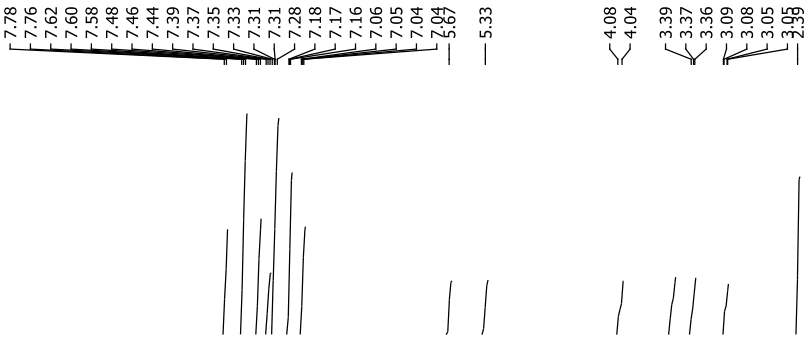

8.13
8.12
7.95
7.94
7.80
7.79
7.72
7.71
7.66
7.65
7.46
7.45
7.44
7.43
7.42
7.25
7.24
7.23
7.22
7.18
7.17
7.16
7.07
7.06
7.05
5.66
5.55
5.55
4.09
4.06
3.75
3.74
3.73
3.72
3.66
3.65
3.63
3.61
3.60
Ph
N
FTs
1.00
2.01
0.99
2.01
1.00
2.05
2.94
1.05
3.05
1.01
1.03
1.03
1.03
2.09
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

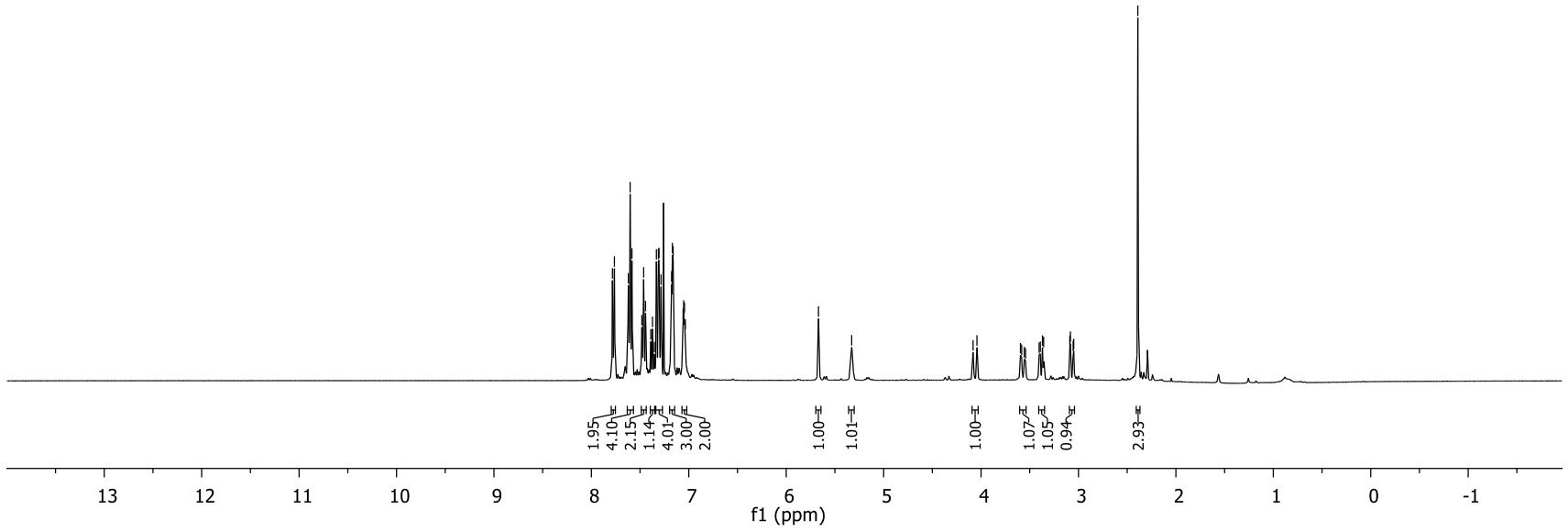
52b

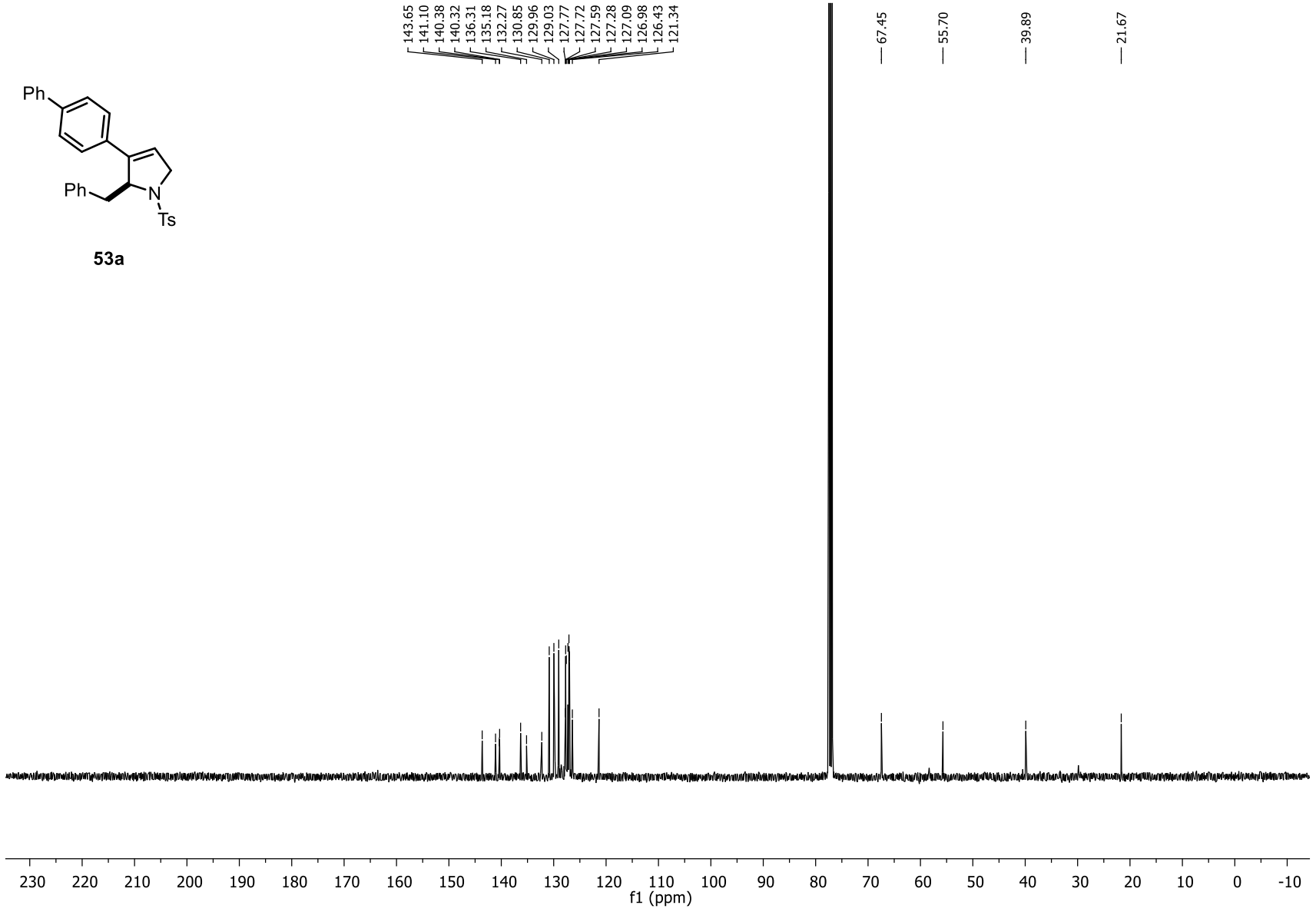

142.18
141.70
134.71
134.52
134.33
134.14
133.68
133.24
132.77
132.69
129.11
128.76
128.45
128.37
127.61
127.42
126.43
126.41
126.39
126.37
126.34
125.82
125.60
125.50
124.96
124.68
124.05
122.49
121.02
120.94
67.59
55.10
37.81
Ph
N
F
Ts
52b
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Ph
Ph
N
Ts

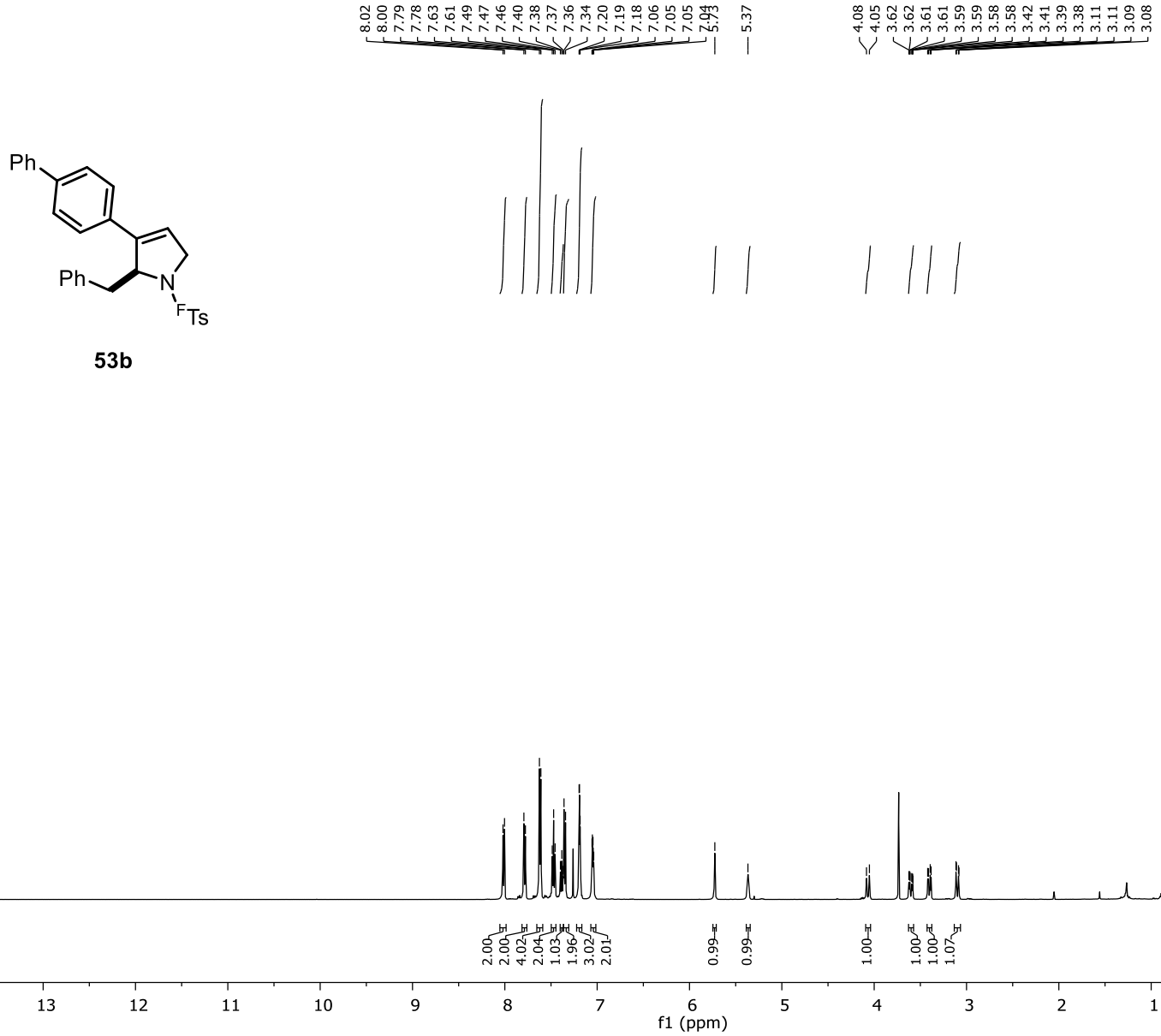
53a


7.78
7.76
7.62
7.60
7.58
7.48
7.46
7.44
7.39
7.37
7.35
7.33
7.31
7.31
7.28
7.18
7.17
7.16
7.06
7.05
7.04
7.04
5.67
5.33
4.08
4.04
3.39
3.37
3.36
3.09
3.08
3.05
2.39

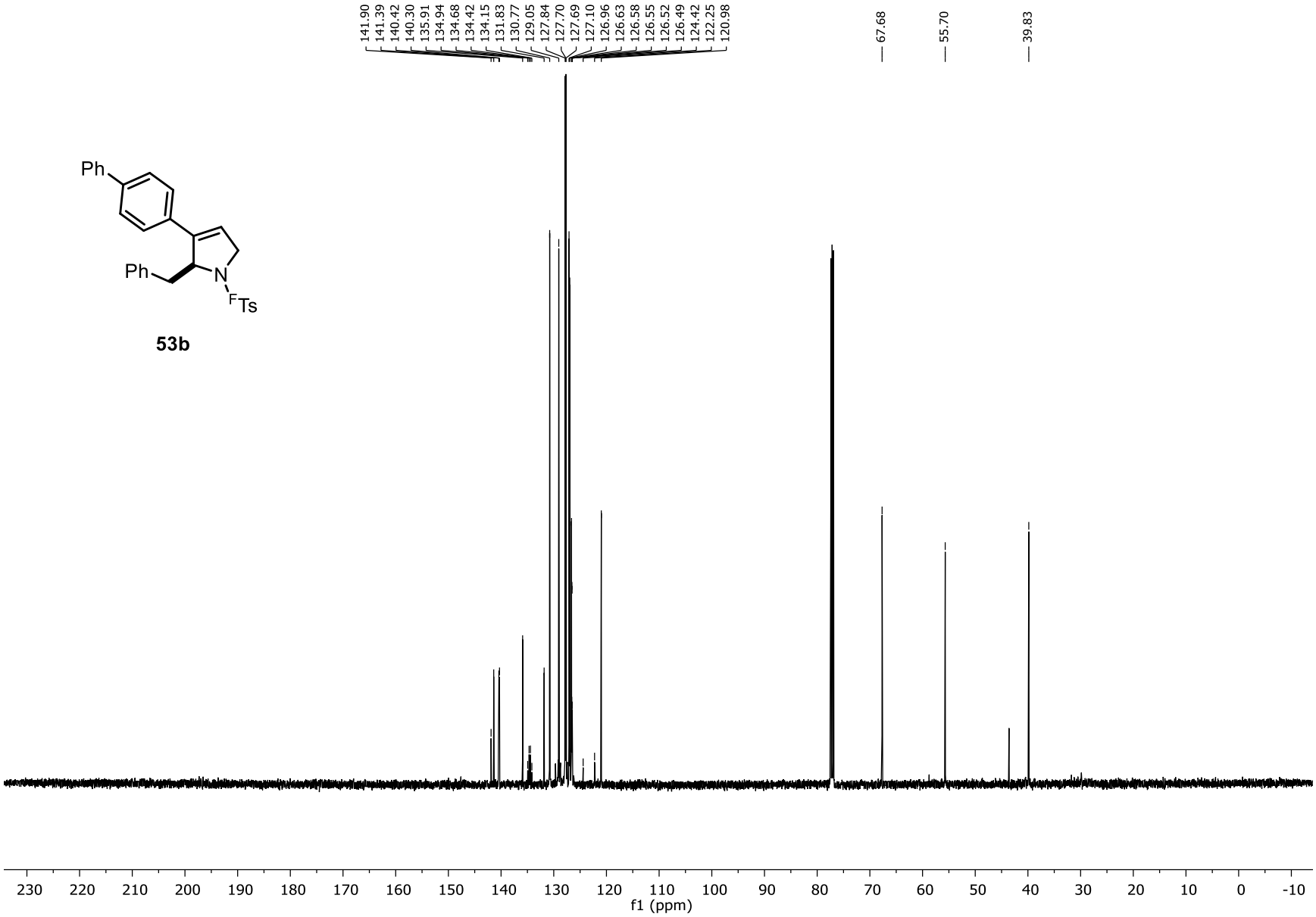

1.95
4.10
2.15
1.14
4.01
3.00
2.00
1.00
1.01
1.00
1.07
1.05
0.94
2.93
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

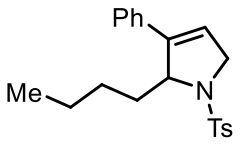

Ph
Ph
N
Ts
143.65
141.10
140.38
140.32
136.31
135.18
132.27
130.85
129.96
129.03
127.77
127.72
127.59
127.28
127.09
126.98
126.43
121.34
67.45
55.70
39.89
21.67
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

53a

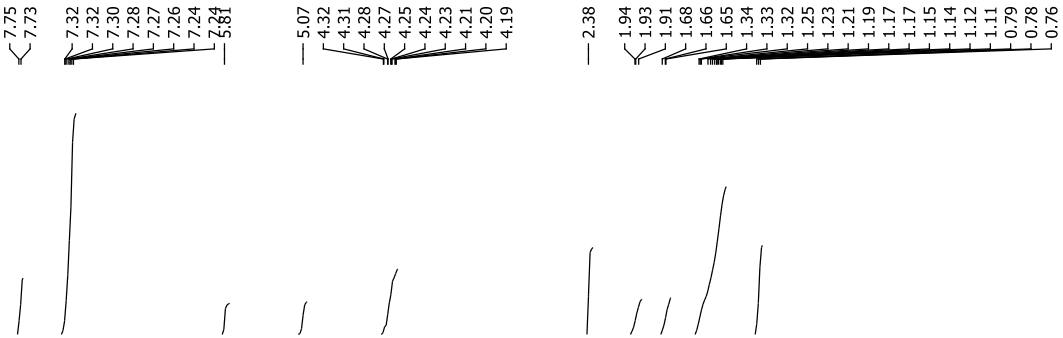

8.02
8.00
7.79
7.78
7.63
7.61
7.49
7.47
7.46
7.40
7.38
7.37
7.36
7.34
7.20
7.19
7.18
7.06
7.05
7.05
7.04
5.73
5.37
4.08
4.05
3.62
3.62
3.61
3.61
3.59
3.59
3.58
3.58
3.42
3.41
3.39
3.38
3.11
3.11
3.09
3.08
Ph
Ph
N
FTs
2.00
2.00
4.02
2.04
1.03
1.96
3.02
2.01
0.99
0.99
1.00
1.00
1.00
1.07
f1 (ppm)

53b


141.90
141.39
140.42
140.30
135.91
134.94
134.68
134.42
134.15
131.83
130.77
129.05
127.84
127.70
127.69
127.10
126.96
126.63
126.58
126.55
126.52
126.49
124.42
122.25
120.98
67.68
55.70
39.83
Ph
Ph
N
FTs
53b
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
N
Ts

54a


7.75
7.73
7.32
7.32
7.30
7.28
7.27
7.26
7.24
5.81
5.07
4.32
4.31
4.28
4.27
4.25
4.24
4.23
4.21
4.20
4.19
2.38
1.94
1.93
1.91
1.68
1.66
1.65
1.34
1.33
1.32
1.25
1.23
1.21
1.19
1.17
1.17
1.15
1.14
1.12
1.11
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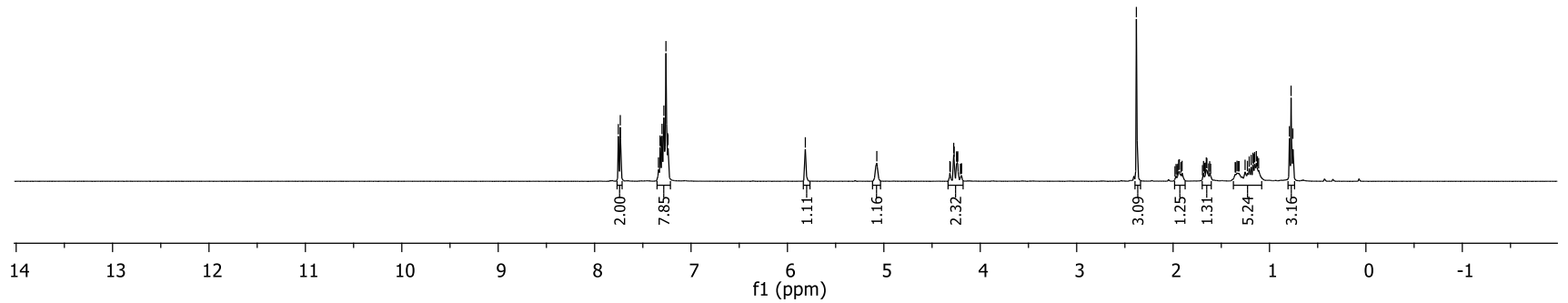
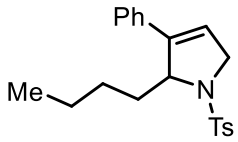
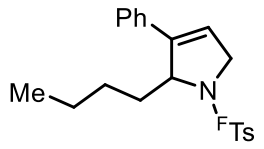
0.78
0.76


2.00
7.85
1.11
1.16
2.32
3.09
1.25
1.31
5.24
3.16
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


Ph
Me
N
Ts

54a

143.48
141.91
133.31
129.81
128.78
128.27
127.35
126.41
119.90
77.34
77.16
76.98
67.07
55.72
33.50
25.49
22.79
22.72
21.61
14.26
14.16
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
N
FTs

54b

8.00
7.98
7.77
7.76
7.34
7.33
7.32
7.30
7.29
7.28
7.26
7.25
5.86
5.12
5.12
4.33
4.30
4.28
4.28
4.28
4.26
4.25
1.96
1.95
1.95
1.94
1.93
1.93
1.69
1.68
1.67
1.66
1.27
1.26
1.26
1.25
1.25
1.19
1.18
1.17
1.17
1.16
1.14
1.14
1.13
1.12
1.11
0.77
0.76
0.75
2.00
1.98
2.03
1.10
0.99
1.01
1.07
2.24
1.15
1.15
1.42
3.48
3.14
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12
11
10
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8
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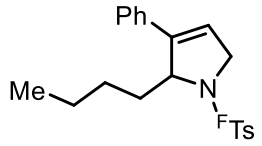
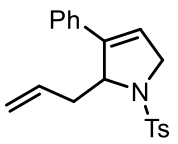
6
5
4
3
2
1
0
-1
f1 (ppm)


Ph
Me
N
F
Ts

54b

142.06
141.92
134.84
134.58
134.32
134.05
132.91
128.90
128.56
127.76
126.60
126.44
126.40
126.35
124.43
122.26
120.09
77.41
77.16
76.91
67.35
55.77
33.34
25.37
22.66
14.12
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
N
Ts

55a

7.81
7.80
7.40
7.39
7.38
7.34
7.33
7.32
7.28
7.27
7.26
6.06
5.69
5.68
5.66
5.65
5.64
5.63
5.17
5.17
4.97
4.95
4.85
4.82
4.17
4.14
4.10
4.10
4.08
4.07
2.62
2.61
2.61
2.60
2.60
2.59
2.59
2.58
2.42
2.42
2.41
2.41
2.40
2.40
2.39
2.39
2.34
2.00
3.98
2.05
1.07
1.04
1.11
1.07
1.07
1.11
1.10
1.14
1.20
1.22
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11
10
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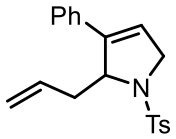
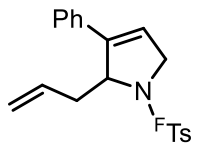
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

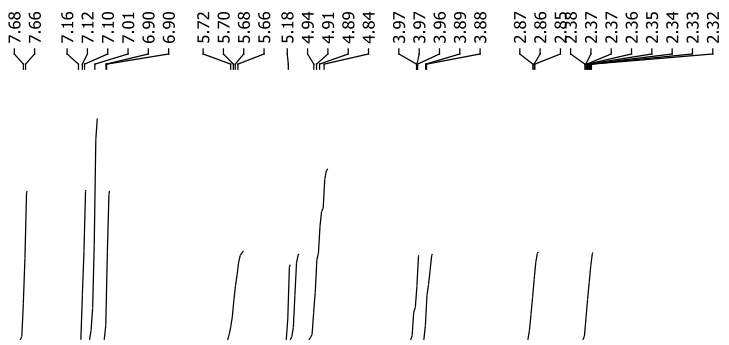

Ph
N
Ts

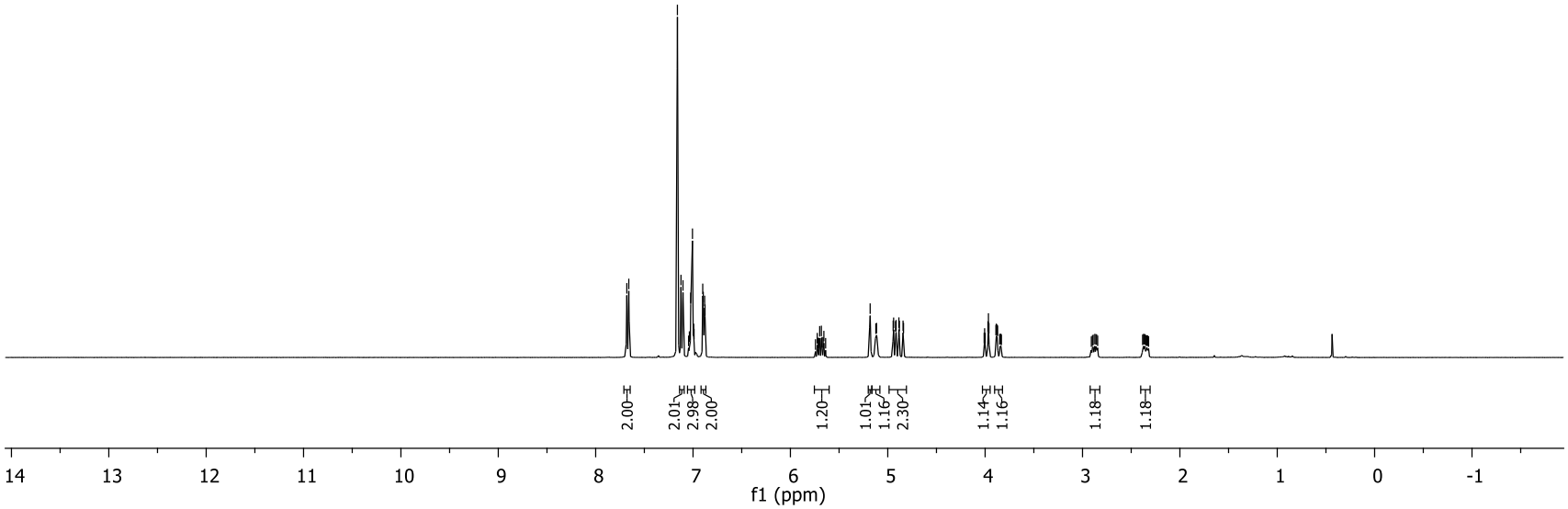
55a

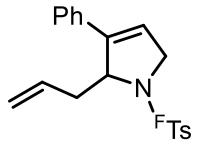
143.41
140.06
134.19
132.72
132.49
129.82
128.62
128.08
127.25
126.34
120.96
118.18
65.66
55.39
37.89
20.93
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
N
F
Ts

55b

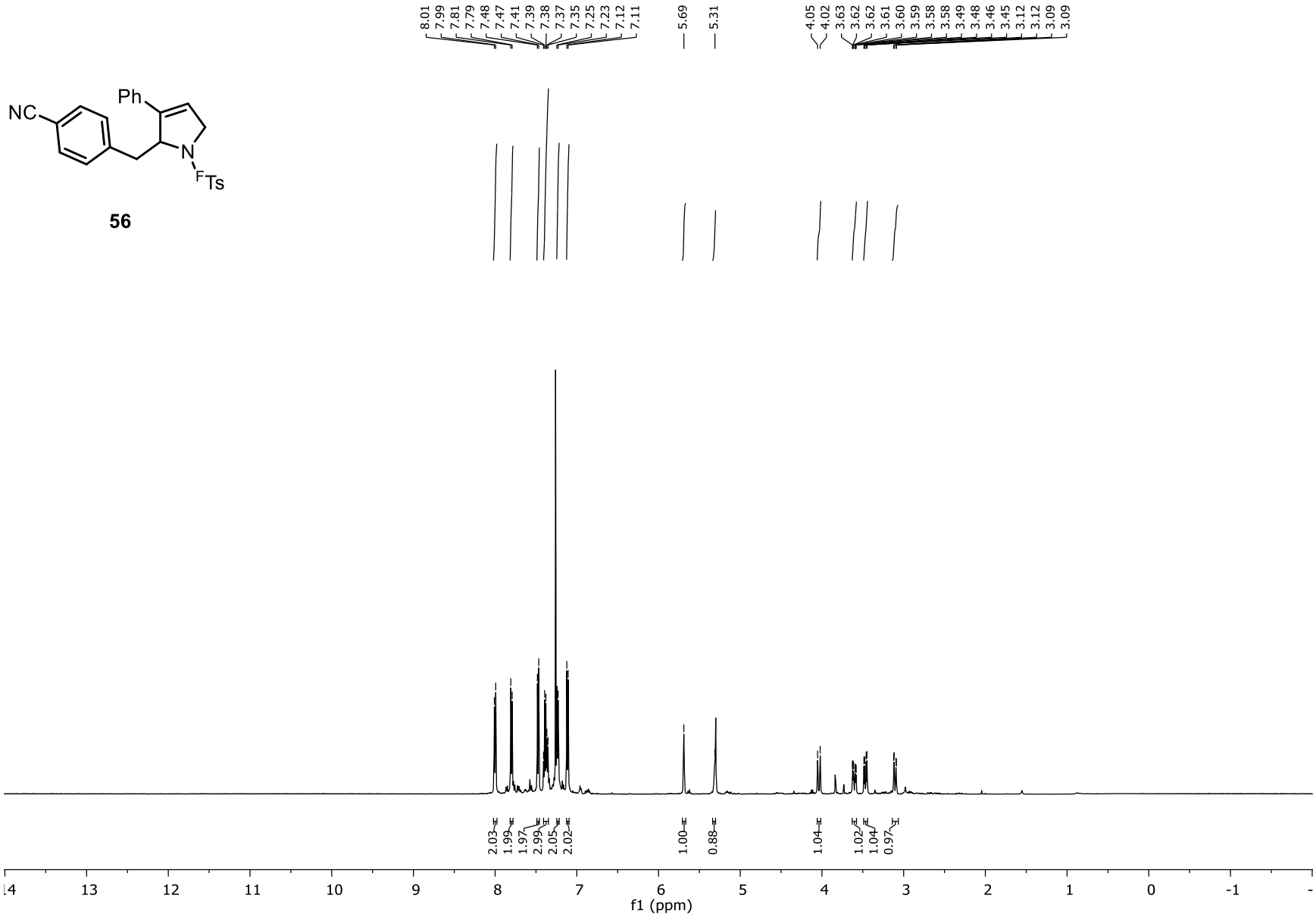

7.68
7.66
7.16
7.12
7.10
7.01
6.90
6.90
5.72
5.70
5.68
5.66
5.18
4.94
4.91
4.89
4.84
3.97
3.97
3.96
3.89
3.88
2.87
2.86
2.37
2.37
2.36
2.35
2.34
2.33
2.32

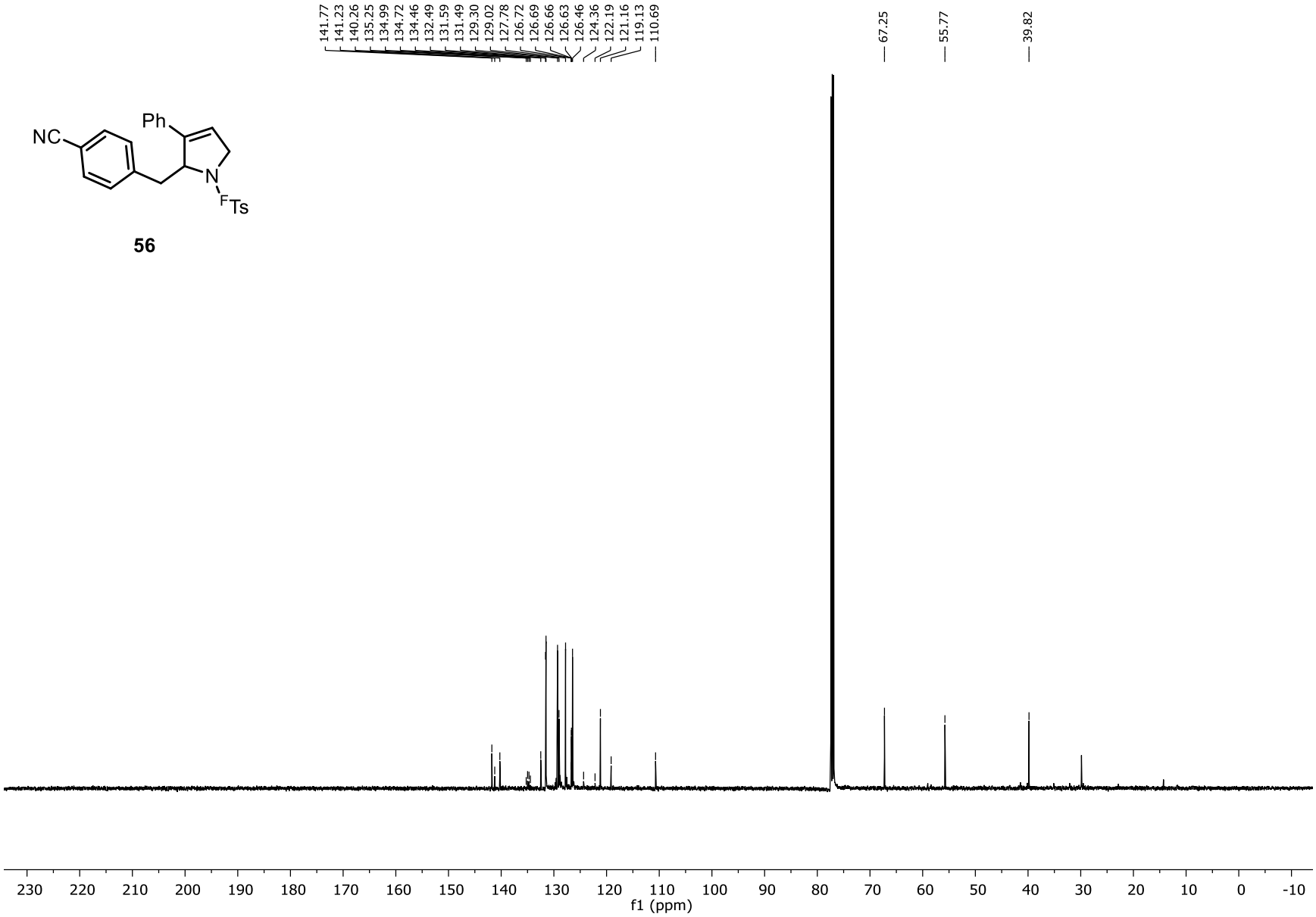

2.00
2.01
2.98
2.00
1.20
1.01
1.16
2.30
1.14
1.16
1.18
1.18
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

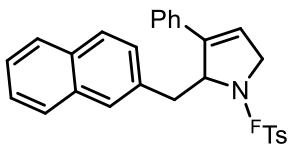

Ph
N
F
Ts

55b

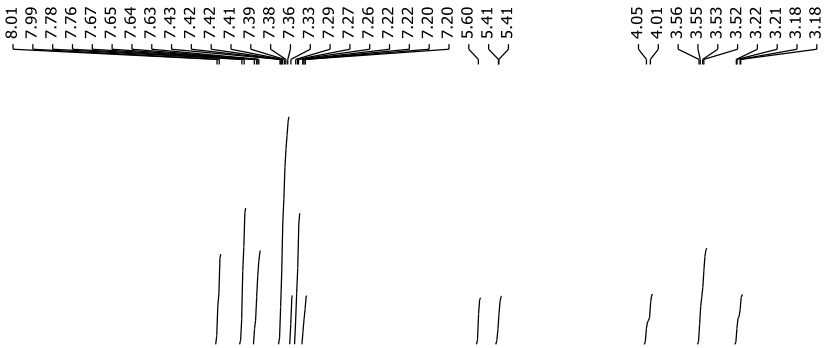
142.06
141.26
134.96
134.63
134.31
133.98
132.76
131.97
128.91
128.60
127.39
126.50
126.46
126.42
126.38
124.68
121.97
120.11
119.27
119.10
77.48
77.16
76.84
66.95
55.82
37.95
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

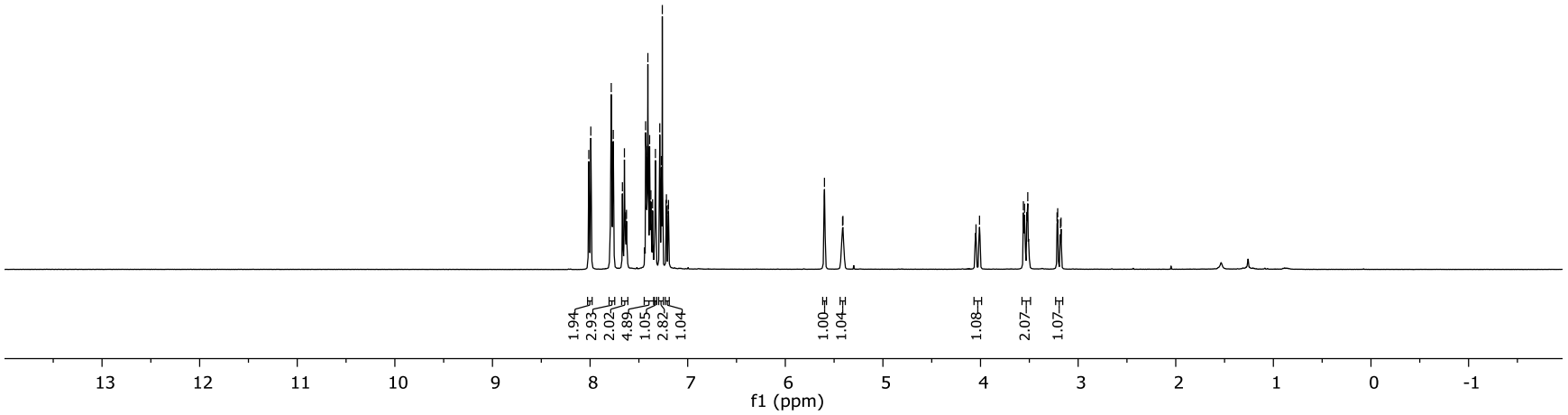

8.01
7.99
7.81
7.79
7.48
7.47
7.41
7.39
7.38
7.37
7.35
7.25
7.23
7.12
7.11
5.69
5.31
4.05
4.02
3.63
3.62
3.62
3.61
3.60
3.59
3.58
3.58
3.49
3.48
3.46
3.45
3.12
3.12
3.09
3.09
Ph
NC
N
FTs
56
2.03
1.99
1.97
2.99
2.05
2.02
1.00
0.88
1.04
1.02
1.04
0.97
f1 (ppm)

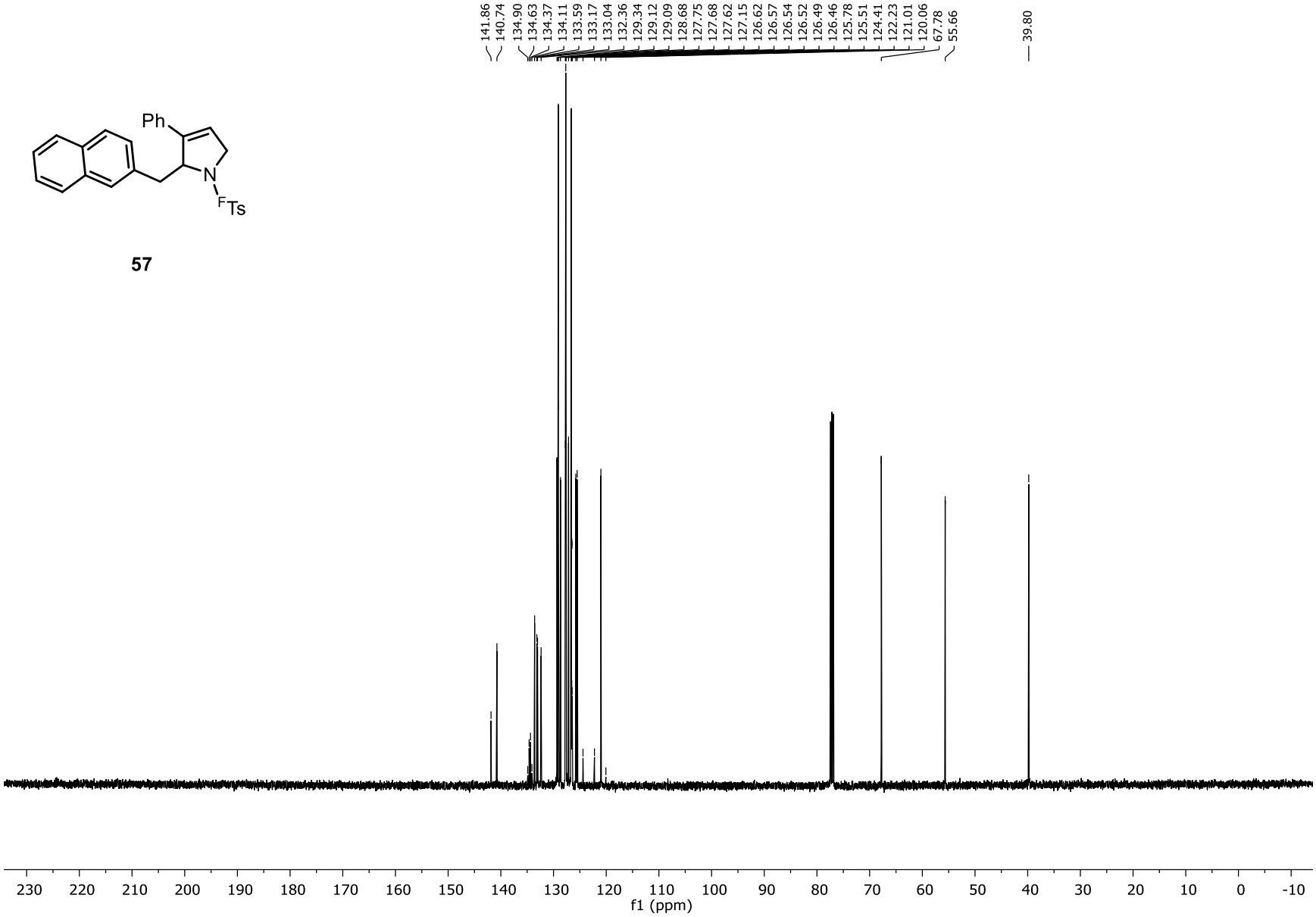

141.77
141.23
140.26
135.25
134.99
134.72
134.46
132.49
131.59
131.49
129.30
129.02
127.78
126.72
126.69
126.66
126.63
126.46
124.36
122.19
121.16
119.13
110.69
67.25
55.77
39.82
Ph
NC
N
FTs
56
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Ph
N
FTs

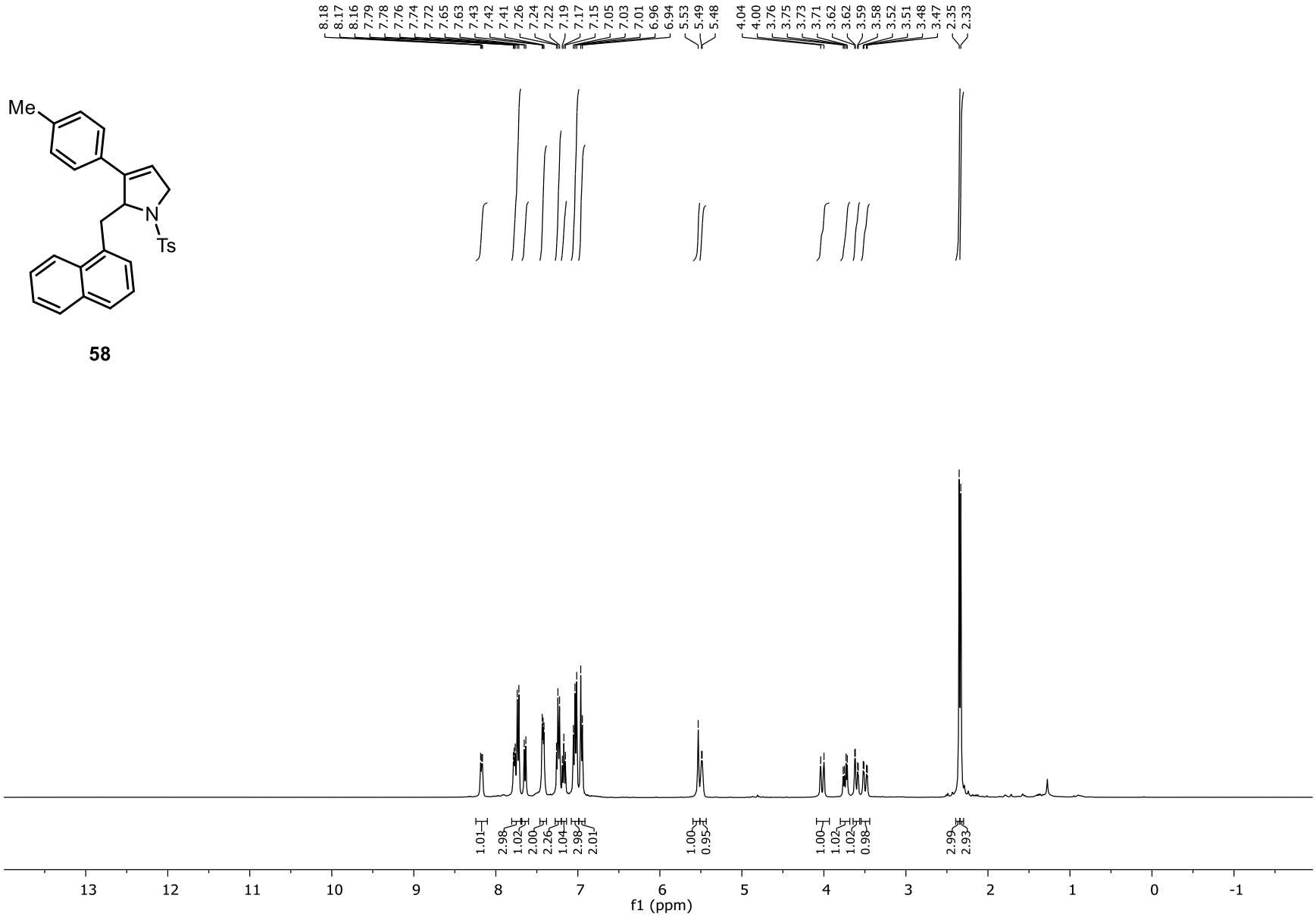
57


8.01
7.99
7.78
7.76
7.67
7.65
7.64
7.63
7.43
7.42
7.42
7.41
7.39
7.38
7.36
7.33
7.29
7.27
7.26
7.22
7.22
7.20
7.20
5.60
5.41
5.41
4.05
4.01
3.56
3.55
3.53
3.52
3.22
3.21
3.18
3.18


1.94
2.93
2.02
4.89
1.05
2.82
1.04
1.00
1.04
1.08
2.07
1.07
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


141.86
140.74
134.90
134.63
134.37
134.11
133.59
133.17
133.04
132.36
129.34
129.12
129.09
128.68
127.75
127.68
127.62
127.15
126.62
126.57
126.54
126.52
126.49
126.46
125.78
125.51
124.41
122.23
121.01
120.06
67.78
55.66
39.80
Ph
N
F
Ts
230
220
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)

57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8.17
8.16
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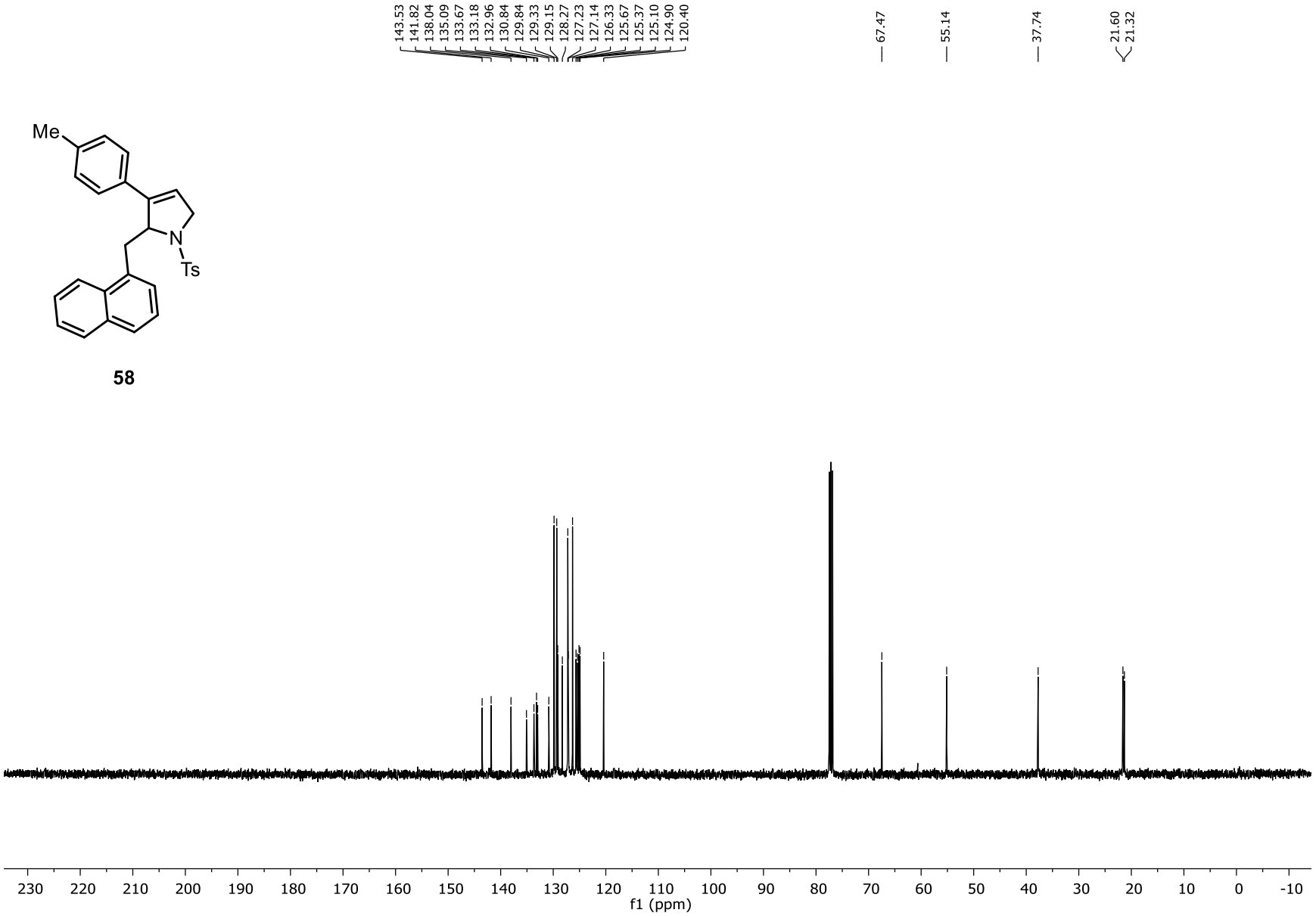
7.78
7.76
7.74
7.72
7.65
7.63
7.43
7.42
7.41
7.26
7.24
7.22
7.19
7.17
7.15
7.05
7.03
7.01
6.96
6.94
5.53
5.49
5.48
4.04
4.00
3.76
3.75
3.73
3.71
3.62
3.62
3.59
3.58
3.52
3.51
3.48
3.47
2.35
2.33
Me
N
Ts
1.01
2.98
1.02
2.00
2.26
1.04
2.98
2.01
1.00
0.95
1.00
1.02
1.02
0.98
2.99
2.93
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

58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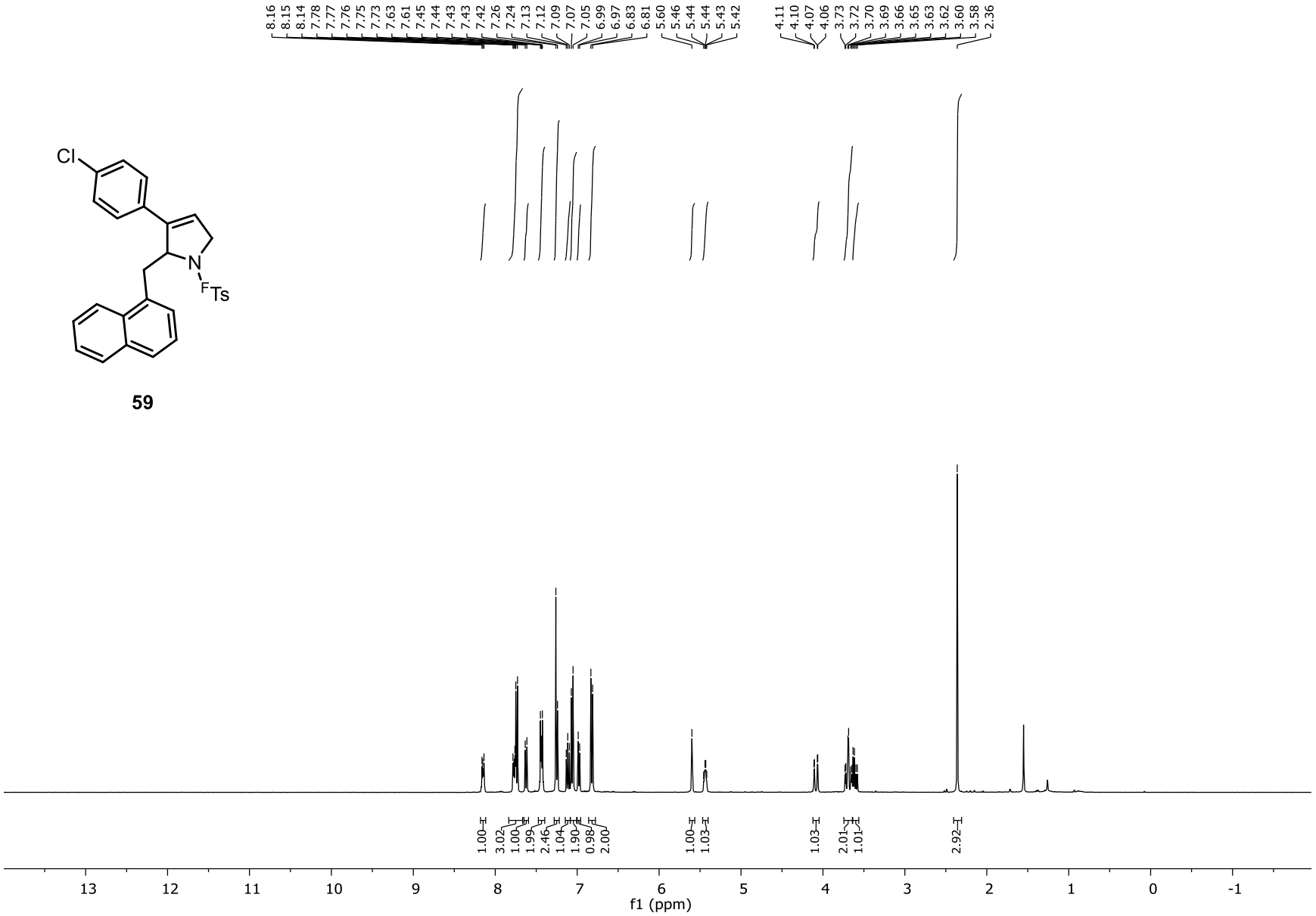
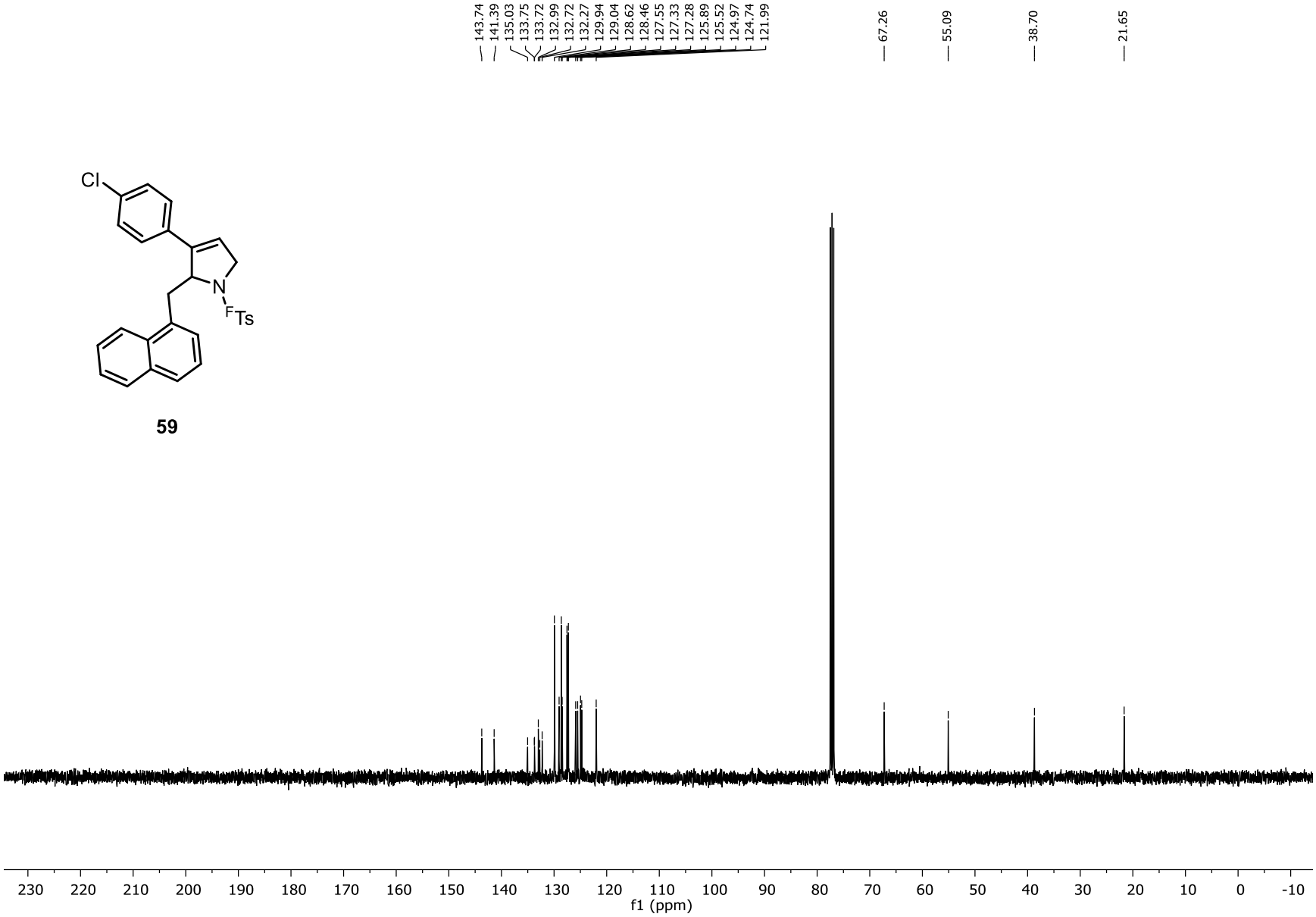
141.82
138.04
135.09
133.67
133.18
132.96
130.84
129.84
129.33
129.15
128.27
127.23
127.14
126.33
125.67
125.37
125.10
124.90
120.40
67.47
55.14
37.74
21.60
21.32
Me
N
Ts
58
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.16
8.15
8.14
7.78
7.77
7.76
7.75
7.73
7.63
7.61
7.45
7.44
7.43
7.43
7.42
7.26
7.24
7.13
7.12
7.09
7.07
7.05
6.99
6.97
6.83
6.81
5.60
5.46
5.44
5.44
5.43
5.42
4.11
4.10
4.07
4.06
3.73
3.72
3.70
3.69
3.66
3.65
3.63
3.62
3.60
3.58
2.36
Cl
N
F
Ts
1.00
3.02
1.00
1.99
2.46
1.04
1.90
0.98
2.00
1.00
1.03
1.03
2.01
1.01
2.92
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

59


143.74
141.39
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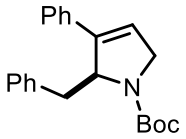
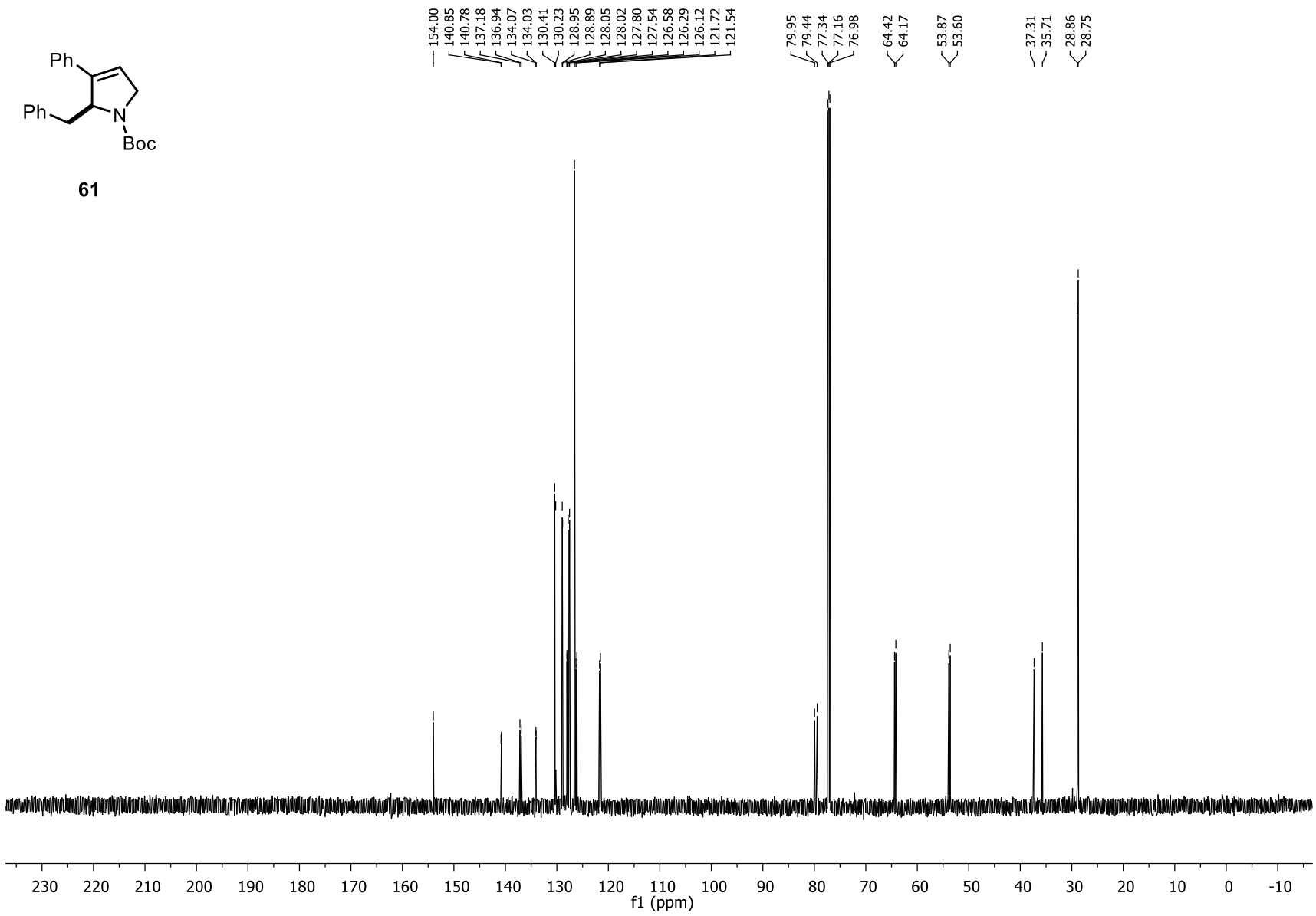
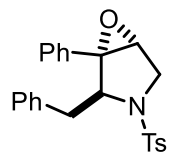
133.75
133.72
132.99
132.72
132.27
129.94
129.04
128.62
128.46
127.55
127.33
127.28
125.89
125.52
124.97
124.74
121.99
67.26
55.09
38.70
21.65
Cl
N
F
Ts
59
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Ph
Ph
N
Boc

61

7.41
7.40
7.39
7.38
7.33
7.33
7.33
7.32
7.31
7.26
7.14
7.14
7.13
6.86
6.85
6.84
6.84
5.85
5.79
5.40
5.30
4.19
4.17
4.05
4.03
3.53
3.52
3.51
3.50
3.31
3.30
3.29
2.87
2.86
1.61
1.55
8.06
2.04
5.12
4.00
0.95
0.97
1.09
1.08
1.10
1.14
1.17
1.19
1.11
1.24
2.28
9.28
9.31
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


Ph
Ph
N
Boc
61
154.00
140.85
140.78
137.18
136.94
134.07
134.03
130.41
130.23
128.95
128.89
128.05
128.02
127.80
127.54
126.58
126.29
126.12
121.72
121.54
79.95
79.44
77.34
77.16
76.98
64.42
64.17
53.87
53.60
37.31
35.71
28.86
28.75
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Ph
Ph
N
Ts

62a

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7.69
7.40
7.39
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7.26
7.26
7.25
7.18
7.18
7.18
6.98
6.98
6.98
6.97
4.63
4.63
4.62
4.62
3.75
3.61
3.59
3.16
3.15
3.14
3.13
3.01
2.99
2.90
2.90
2.88
2.88
2.41
1.95
3.01
1.99
2.18
2.99
2.00
1.05
1.02
1.08
1.06
1.08
1.06
2.97
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12
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10
9
8
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6
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4
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2
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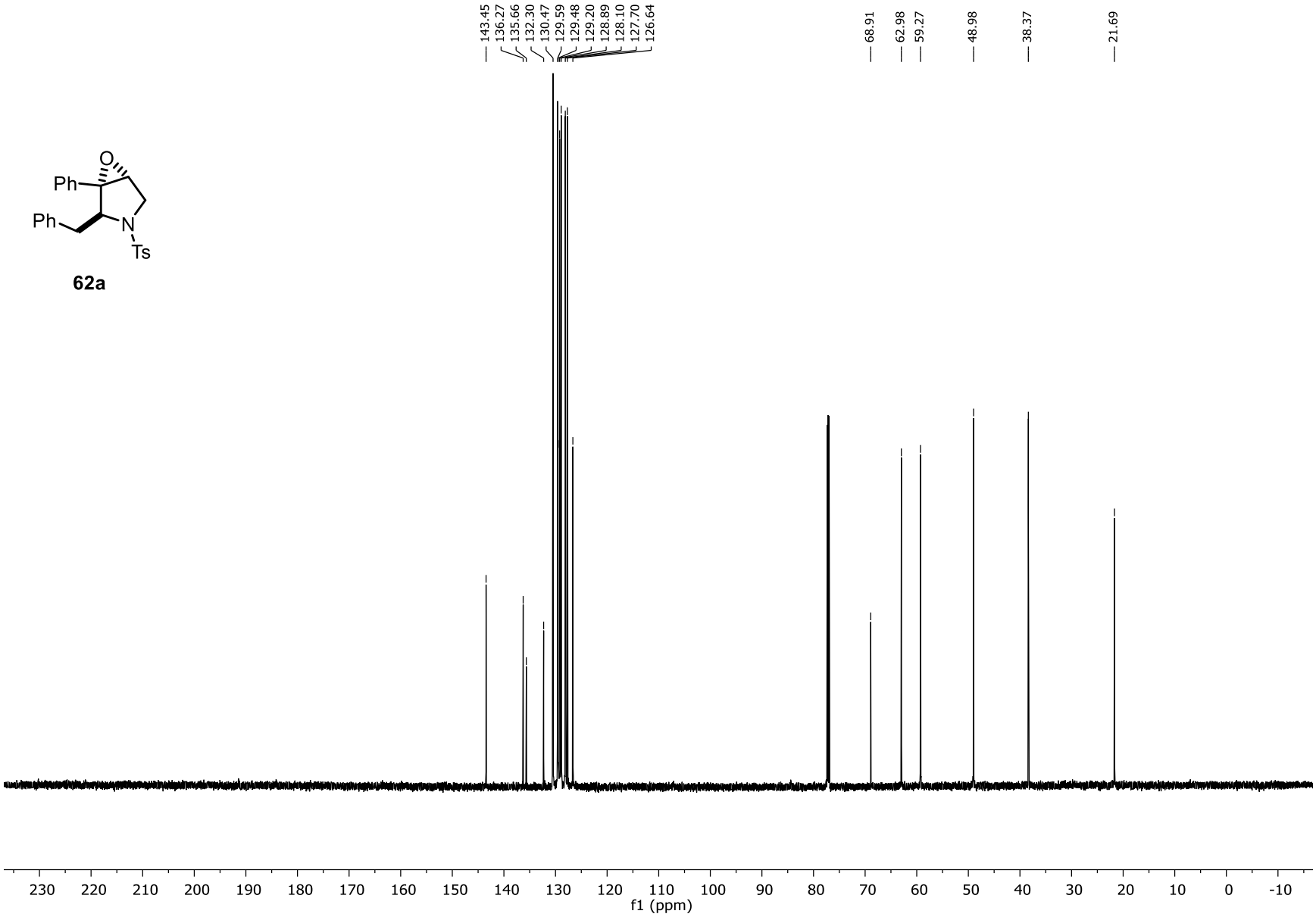
0
-1
f1 (ppm)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135.66
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130.47
129.59
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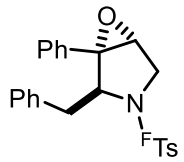
129.20
128.89
128.10
127.70
126.64
68.91
62.98
59.27
48.98
38.37
21.69
O
Ph
Ph
N
Ts
62a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Ph
Ph
N
FTs

62b

7.89
7.88
7.75
7.74
7.41
7.40
7.30
7.29
7.19
7.19
6.99
6.98
6.98
4.67
4.66
4.66
3.80
3.66
3.64
3.14
3.13
3.12
3.11
3.06
3.04
2.88
2.87
2.86
2.85
1.99
1.99
3.02
2.06
3.00
2.00
1.04
1.03
1.06
1.05
1.03
1.05
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12
11
10
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8
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6
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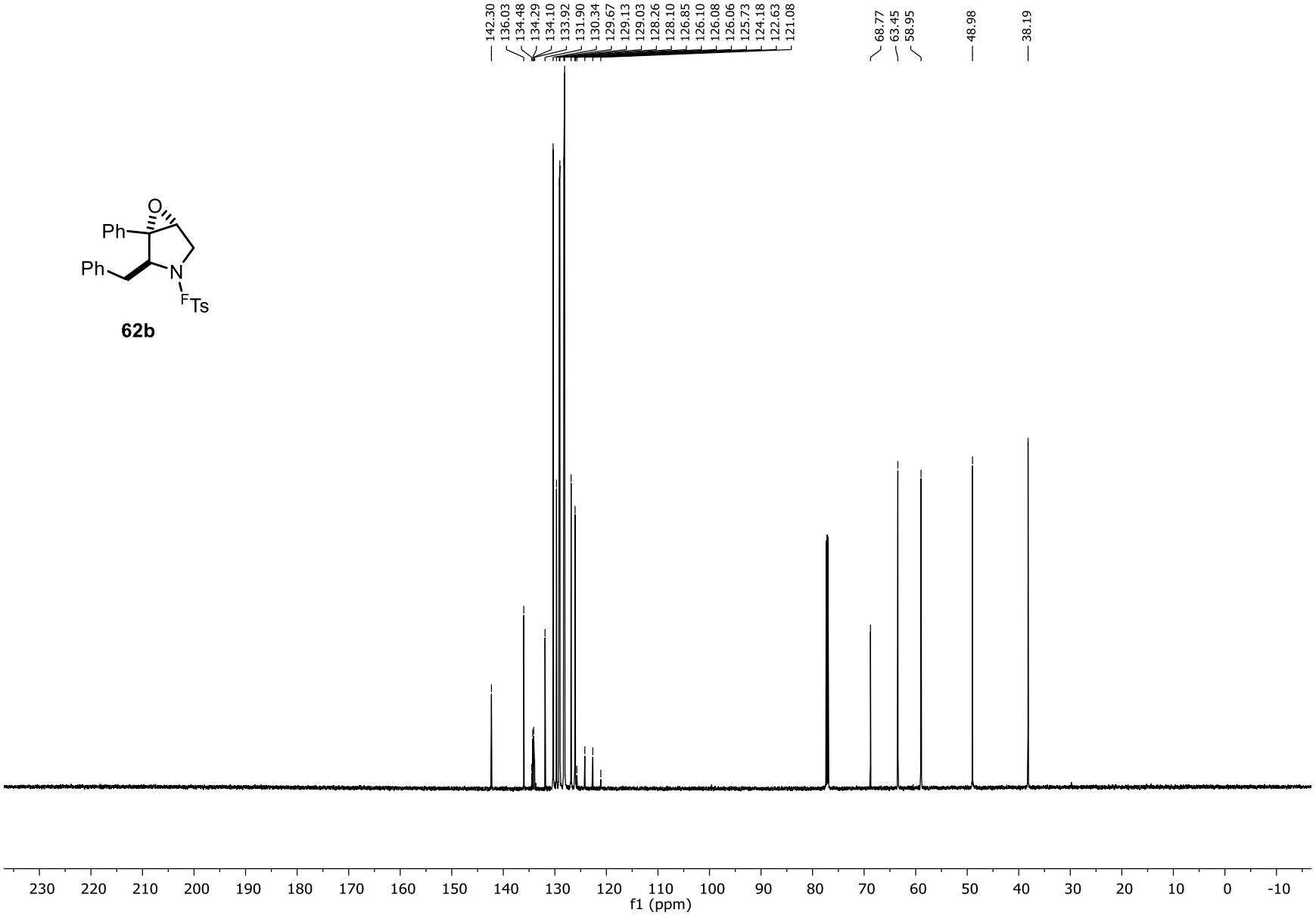
4
3
2
1
0
-1
f1 (ppm)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126.85
126.10
126.08
126.06
125.73
124.18
122.63
121.08
68.77
63.45
58.95
48.98
38.19
O
Ph
Ph
N
F
Ts
62b
230
220
210
200
190
180
170
160
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140
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120
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100
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80
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60
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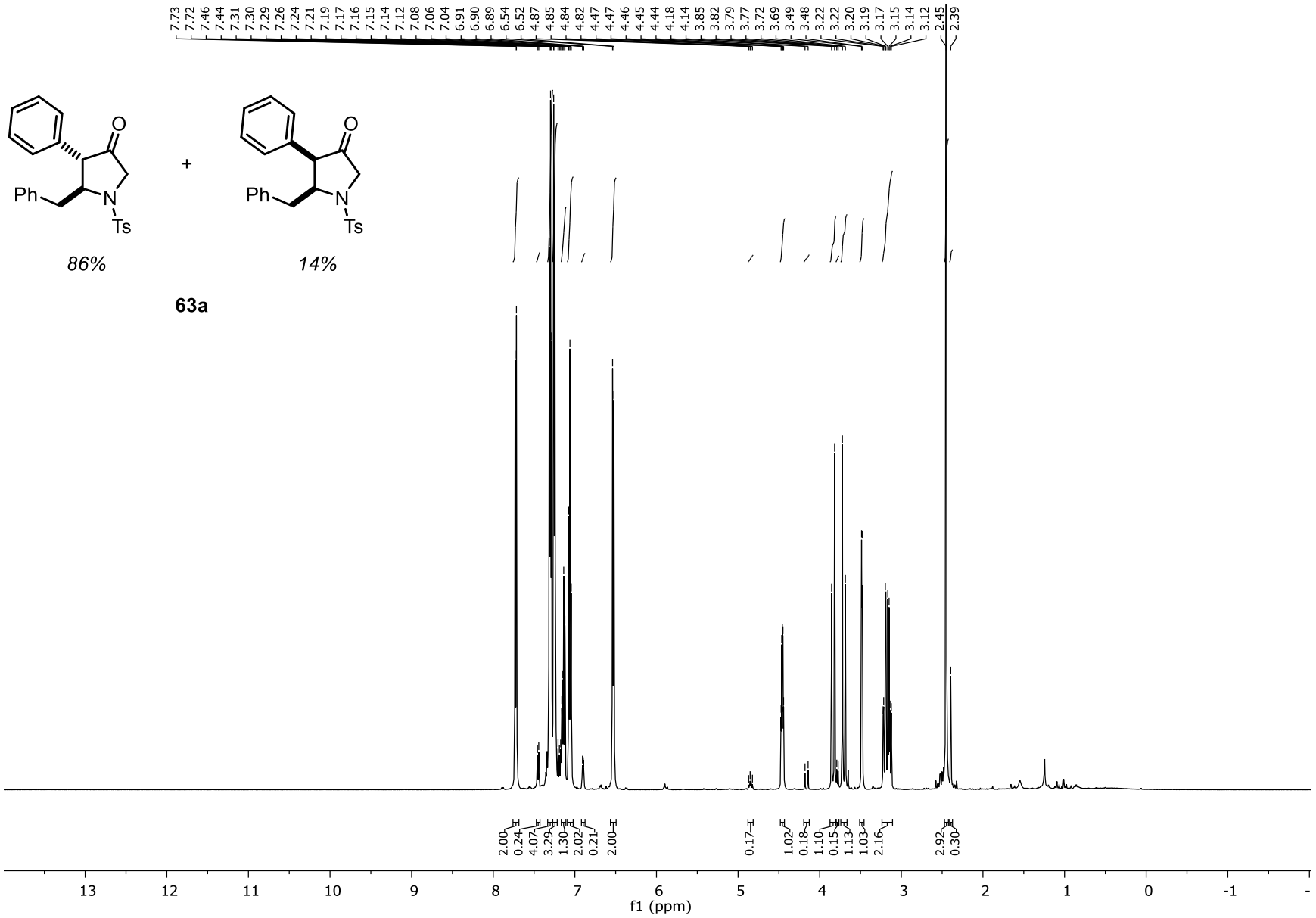
40
30
20
10
0
-10
f1 (ppm)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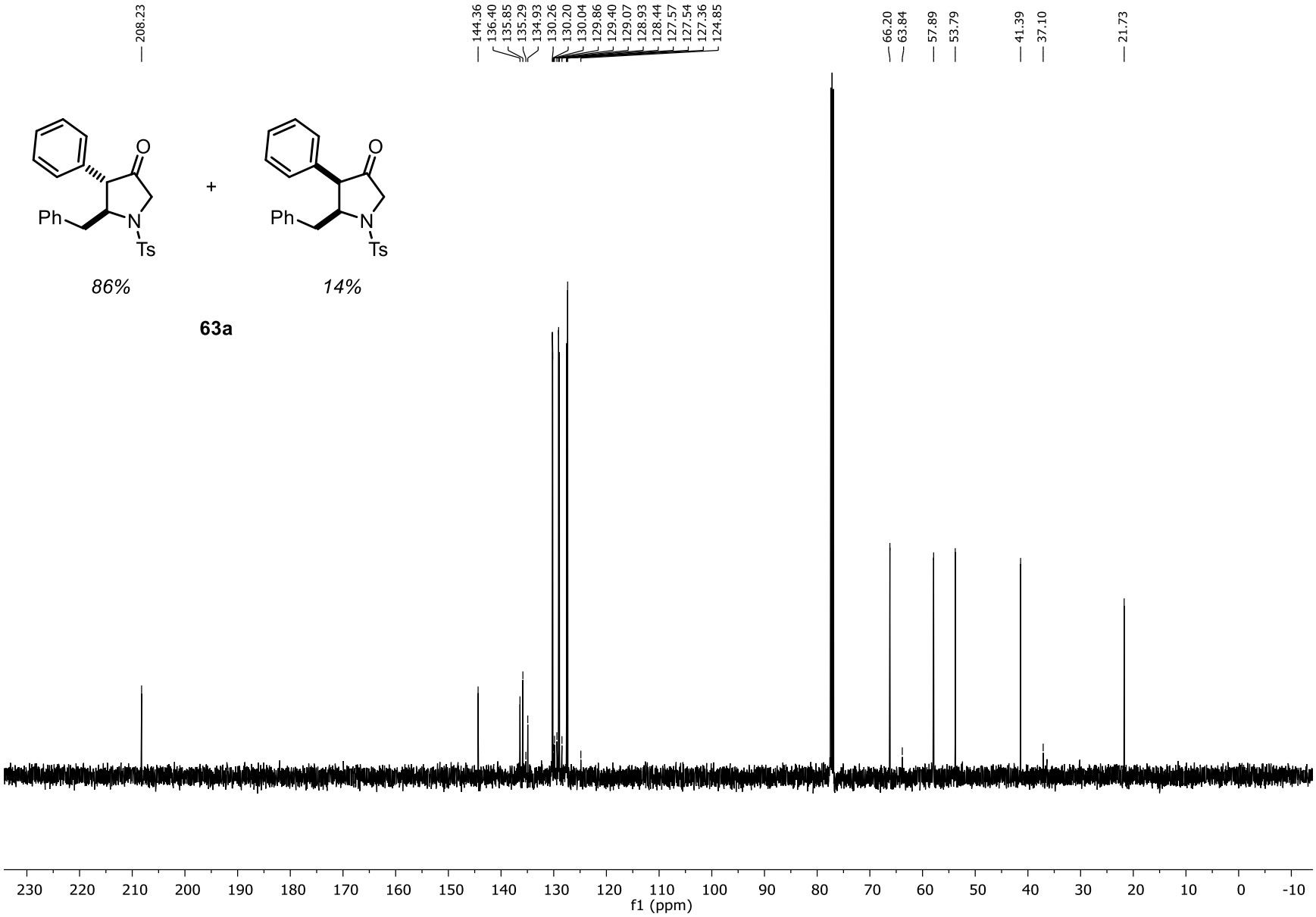
O
Ph
N
Ts
+
O
Ph
N
Ts
86%
14%
63a
2.00 0.24 4.07 3.29 1.30 2.02 0.21 2.00 0.17 1.02 0.18 1.10 0.15 1.13 1.03 2.16 2.92 0.30
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)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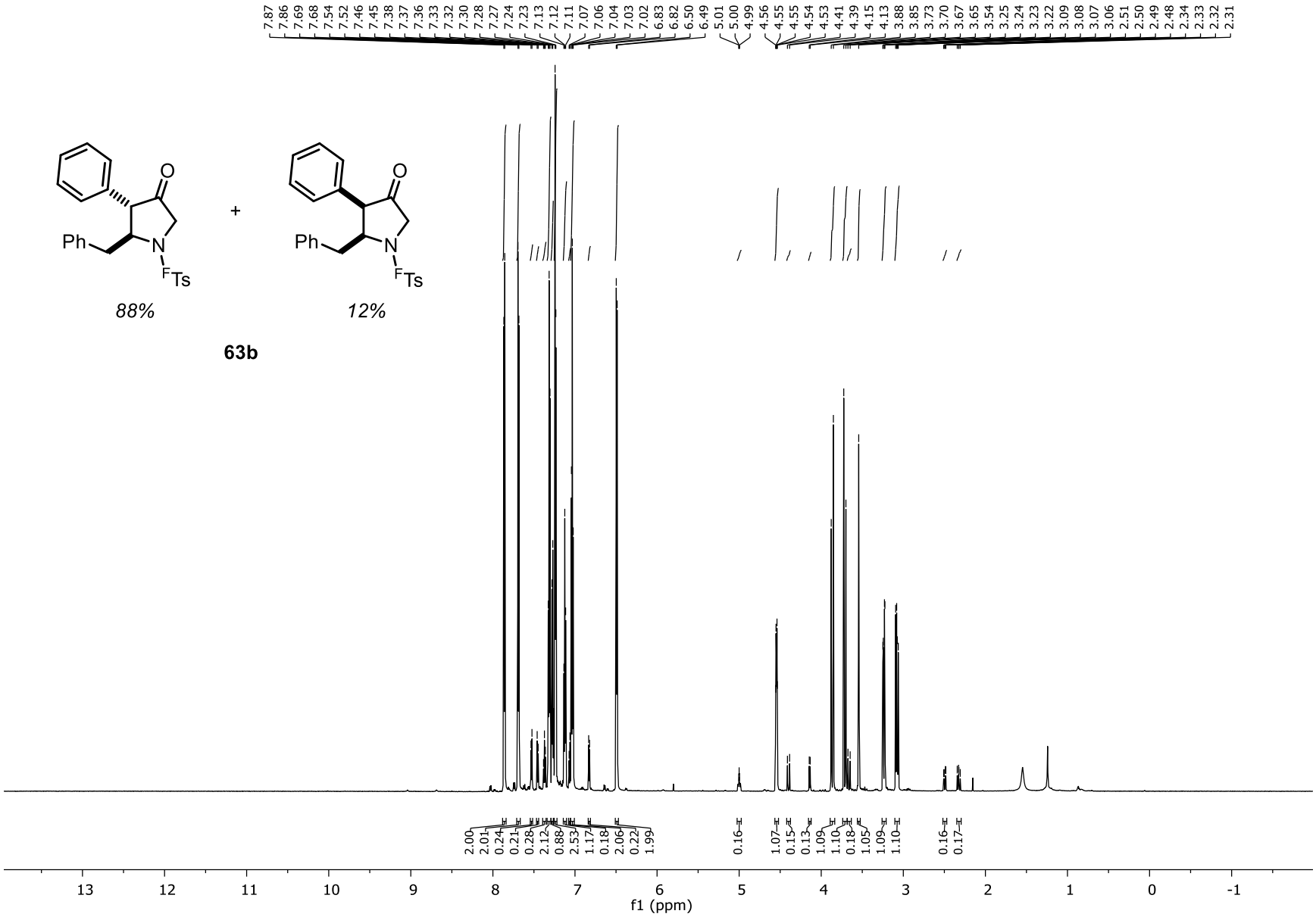
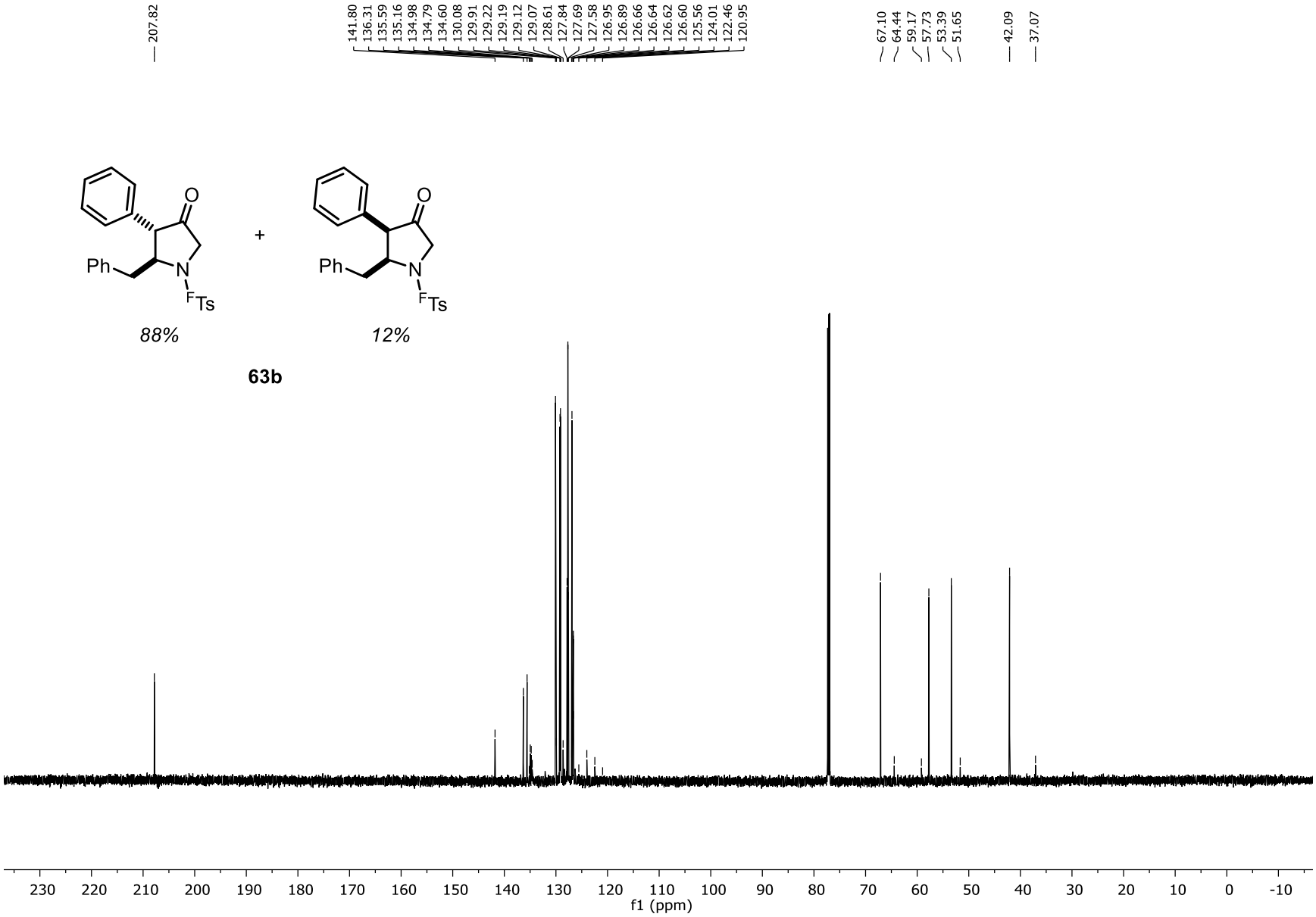
144.36
136.40
135.85
135.29
134.93
130.26
130.20
130.04
129.86
129.40
129.07
128.93
128.44
127.57
127.54
127.36
124.85
66.20
63.84
57.89
53.79
41.39
37.10
21.73
O
Ph
N
Ts
+
O
Ph
N
Ts
86%
14%
63a
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.87 7.86 7.69 7.68 7.54 7.52 7.46 7.45 7.38 7.37 7.36 7.33 7.32 7.30 7.28 7.27 7.24 7.23 7.13 7.12 7.11 7.07 7.06 7.04 7.03 7.02 6.83 6.82 6.50 6.49 5.01 5.00 4.99 4.56 4.55 4.55 4.54 4.53 4.41 4.39 4.15 4.13 3.88 3.85 3.73 3.70 3.67 3.65 3.54 3.25 3.24 3.23 3.22 3.09 3.08 3.07 3.06 2.51 2.50 2.49 2.48 2.34 2.33 2.32 2.31
Ph
N
F
Ts
O
+
88%
12%
63b
2.00 2.01 0.24 0.21 0.28 2.12 0.88 2.53 1.17 0.18 2.06 0.22 1.99 0.16 1.07 0.15 0.13 1.09 1.10 0.18 1.05 1.09 1.10 0.16 0.17
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)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135.16
134.98
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134.60
130.08
129.91
129.22
129.19
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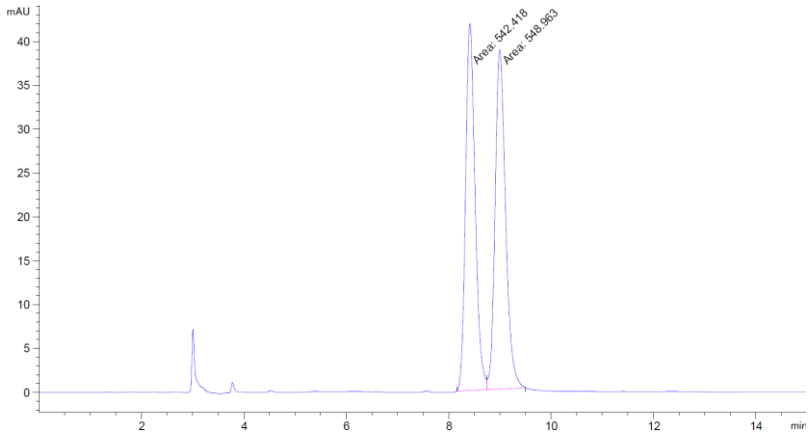
129.07
128.61
127.84
127.69
127.58
126.95
126.89
126.66
126.64
126.62
126.60
125.56
124.01
122.46
120.95
67.10
64.44
59.17
57.73
53.39
51.65
42.09
37.07
Ph
N
F
Ts
O
+
88%
12%
63b
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

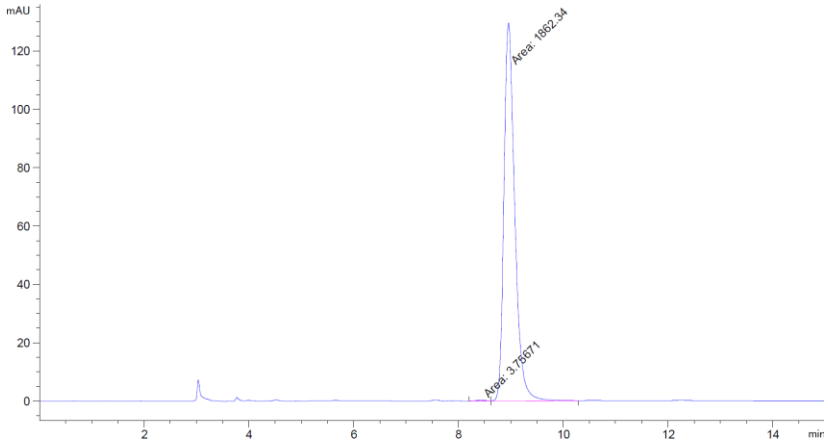
2.6 HPLC Analysis of Phenylalanine Substrate 19 and 25

Racemic phenylalanine substrate **19**: Chiralpak IB, 3% IPA in hexanes, 15 min run, 1mL/min.



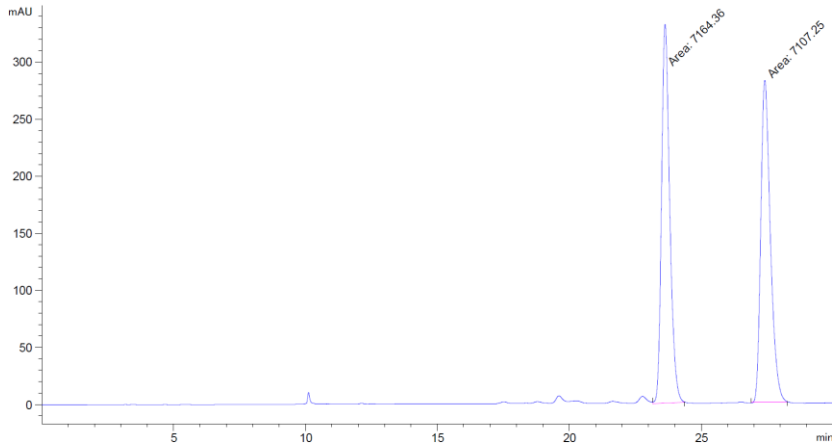
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.409	MF	0.2162	542.41815	41.82040	49.7002
2	8.992	FM	0.2366	548.96295	38.67520	50.2998

Enantioenriched phenylalanine substrate **19**: Chiralpak IB, 3% IPA in hexanes, 15 min run, 1mL/min.



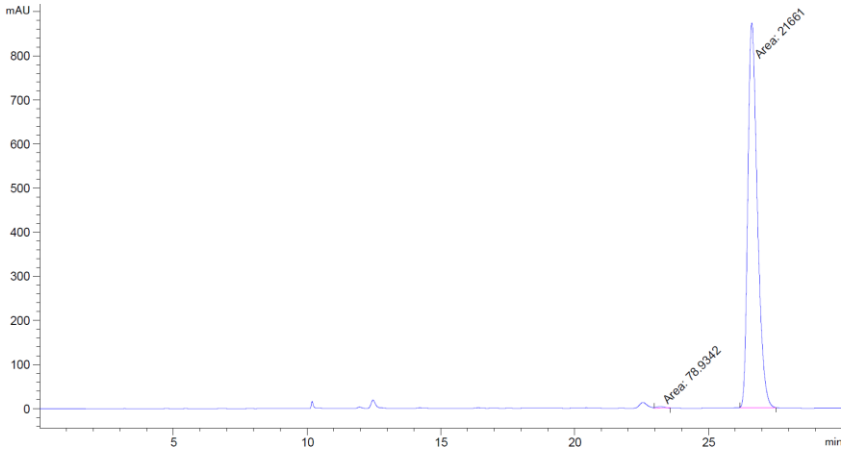
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.425	MF	0.2134	3.75671	2.93413e-1	0.2013
2	8.950	FM	0.2396	1862.33826	129.54121	99.7987

Racemic phenylalanine metathesis product **20**: Chiralpak AD-H, 10% IPA in hexanes, 30 min run, 1mL/min.



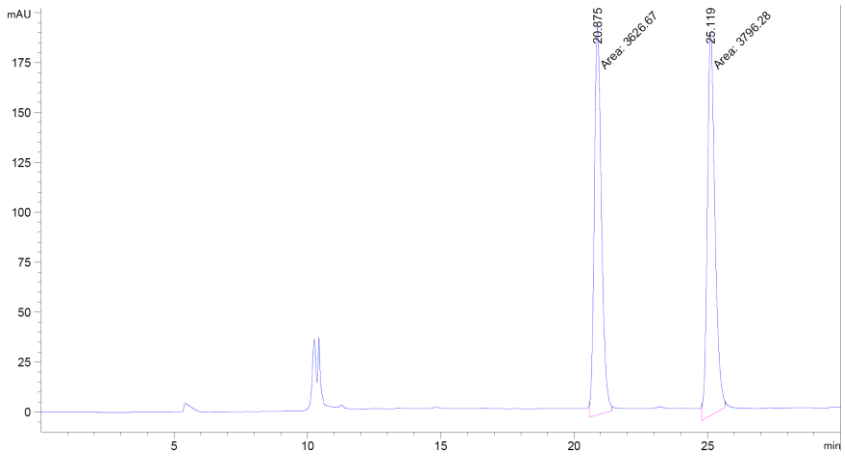
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.624	MM	0.3599	7164.35986	331.74963	50.2001
2	27.403	MM	0.4200	7107.24707	282.01395	49.7999

Enantioenriched phenylalanine metathesis product **20**: Chiralpak AD-H, 10% IPA in hexanes, 30 min run, 1mL/min.



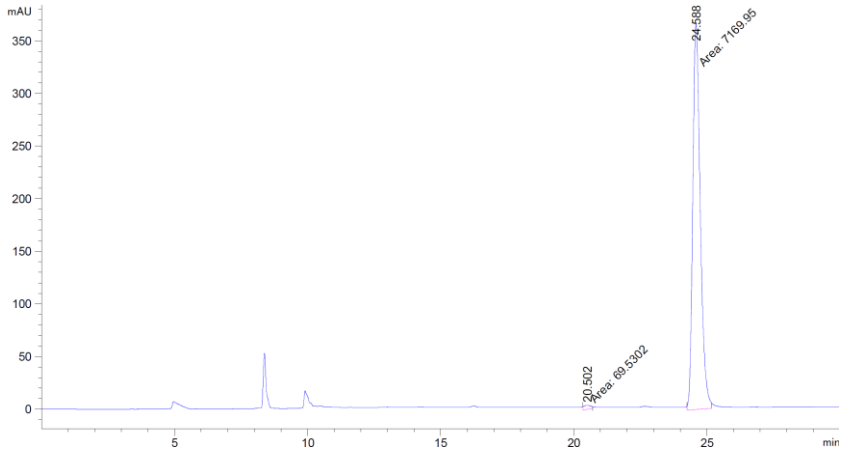
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.186	MM	0.3425	78.93417	3.84072	0.3631
2	26.613	MM	0.4141	2.16610e4	871.79901	99.6369

Racemic phenylalanine metathesis product **26**: Chiralpak AD-H, 10% IPA in hexanes, 30 min run, 1mL/min.



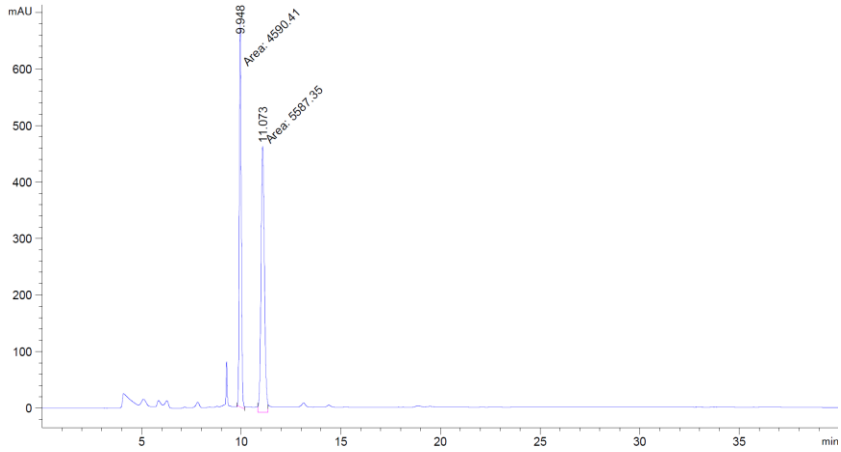
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.875	MM	0.3112	3626.67358	194.22086	48.8575
2	25.119	MM	0.3313	3796.28418	190.97502	51.1425

Enantioenriched phenylalanine metathesis product **26**: Chiralpak AD-H, 10% IPA in hexanes, 30 min run, 1mL/min.



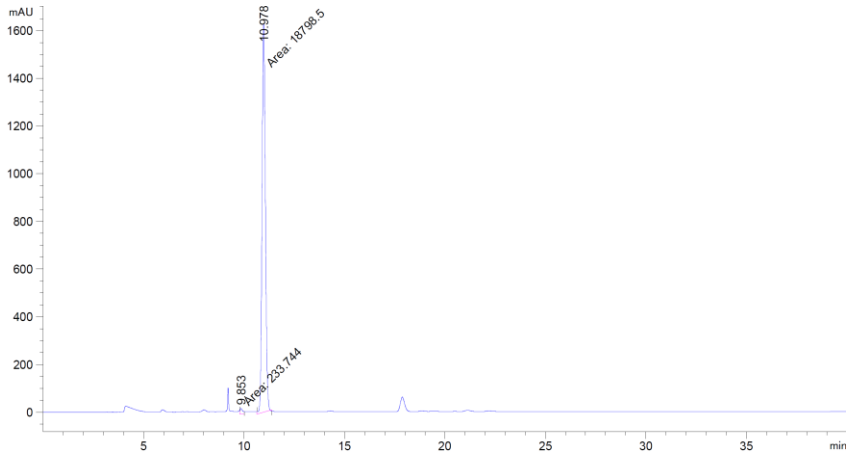
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.502	MM	0.2961	69.53020	3.91411	0.9604
2	24.588	MM	0.3264	7169.95117	366.16010	99.0396

Racemic *N*-Boc-protected phenylalanine product **61**: Chiralpak AD-H, 15% IPA in hexanes, 40 min run, 1mL/min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.948	MM	0.1128	4590.40869	678.11029	45.1023
2	11.073	MM	0.1975	5587.35352	471.61072	54.8977

Enantioenriched *N*-Boc-protected phenylalanine product **61**: Chiralpak AD-H, 15% IPA in hexanes, 40 min run, 1mL/min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.853	MM	0.1666	233.74399	23.38131	1.2281
2	10.978	MM	0.1929	1.87985e4	1623.82922	98.7719

2.7 References

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(2) For examples, see: Li, X.; Li, J. Recent Advances in the Development of MMPIs and APNIs Based on the Pyrrolidine Platforms. *Mini-Rev. Med. Chem.* **2010**, I, 794-805.

(3) For examples, see: Choi, Y.H.; Choi, J.Y.; Yang, H.Y.; Him, Y.H. Copper-catalyzed conjugate addition on macrocyclic, cyclic, and acyclic enones with a chiral phosphoramidite ligand having a C2-symmetric amine moiety. *Tetrahedron Asymmetry*. **2002**, *13* (8), 801-804.

(4) For an example, see: Reisman, S.E.; Doyle, A.G.; Jacobsen, E.N. Enantioselective Thiourea-Catalyzed Additions to Oxocarbenium Ions. *J. Am. Chem. Soc.* **2008**, *130* (23), 7198-7199.

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(7) For recent reviews on hydroamination, see: a) Chemler, S.R. The enantioselective intramolecular aminative functionalization of unactivated alkenes, dienes, allenes and alkynes for the synthesis of chiral nitrogen heterocycles. *Org. Biomol. Chem.* **2009**, *7*, 3009-3019; b) Müller, T.E.; Hultzsch, K.C.; Yus, M.; Foubelo, F.; Tada, M. Hydroamination: Direct Addition of Amines to Alkenes and Alkynes. *Chem. Rev.* **2008**, *108* (9), 3796-3892.

(8) For asymmetric intramolecular hydroamination with group 4 metals, see: (a) Knight, P.D.; Munslow, I.; O'Shaughnessy, P.N.; Scott, P. Zirconium catalysed enantioselective hydroamination/cyclisation. *Chem. Comm.* **2004**, *7*, 894-895; (b) Watson, D.A.; Chiu, M.; Bergman, R.G. Zirconium Bis(Amido) Catalysts for Asymmetric Intramolecular Alkene Hydroamination. *Organometallics* **2006**, *25* (20), 4731-4733; (c) Wood, M.C.; Leitch, D.C.; Yeung, C.S.; Kozak, J.A.; Schafer, L.L. Chiral Neutral Zirconium Amidate Complexes for the Asymmetric Hydroamination of Alkenes *Angew. Chem. Int. Ed.* **2007**, *46* (3), 354-358; (d)

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(21) ^{F}Ts sulfonamides can be cleaved under mild conditions using Mg/MeOH at ambient temperatures. For an example, see: Yu, W.Z.; Chen, F.; Cheng, Y.A.; Yeung, Y.-Y. Catalyst-Free and Metal-Free Electrophilic Bromoamidation of Unactivated Olefins Using the N-Bromosuccinimide/Sulfonamide Protocol. *J. Org. Chem.* **2015**, *80* (5), 2815-2821.

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Chapter 3

Synthesis of Tetrahydropyridines via Carbonyl-Olefin Metathesis Reaction[***]

3.1 Introduction

Chiral tetrahydropyridines and piperidines represent ubiquitous structural scaffolds found in a variety of biologically active natural products and pharmaceuticals.[1] Recent estimates report that in the past decade, over 12,000 piperidine-derived compounds were included in clinical and pre-clinical studies.[2] A variety of methods have been developed to access these nitrogen-containing heterocycles (**1**) including approaches relying on olefin-olefin metathesis,[3] asymmetric multicomponent reactions,[4] aza-Diels Alder reactions,[5] and asymmetric annulations[6] (Figure 3.1). Additional strategies include the cyclization of sulfinyl dienamines,[7] ring expansion of furan derivatives,[8] the reduction of pyridine scaffolds,[9] and transition metal-catalyzed cyclizations.[10] While these strategies provide differentially substituted tetrahydropyridines, they require precious metal catalysts, expensive chiral ligands, extended reaction times, and have a limited substrate scope.

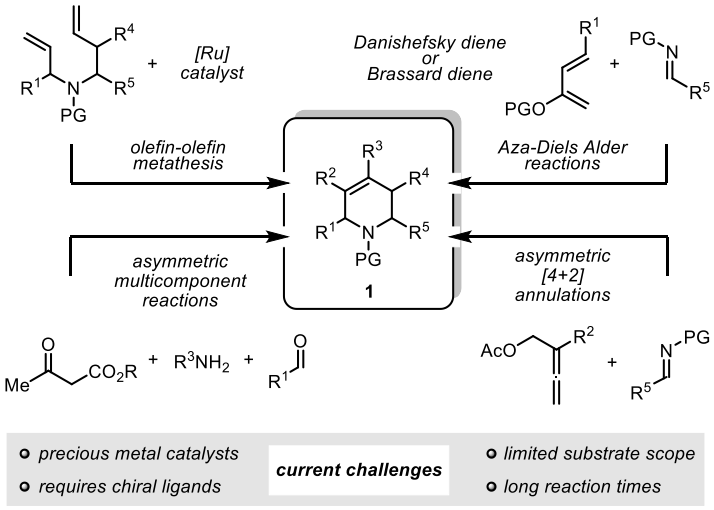


Figure 3.1 Current Strategies towards accessing tetrahydropyridines.

[***] Groso, E.J.; Schindler, C.S. *Manuscript in Revision.*

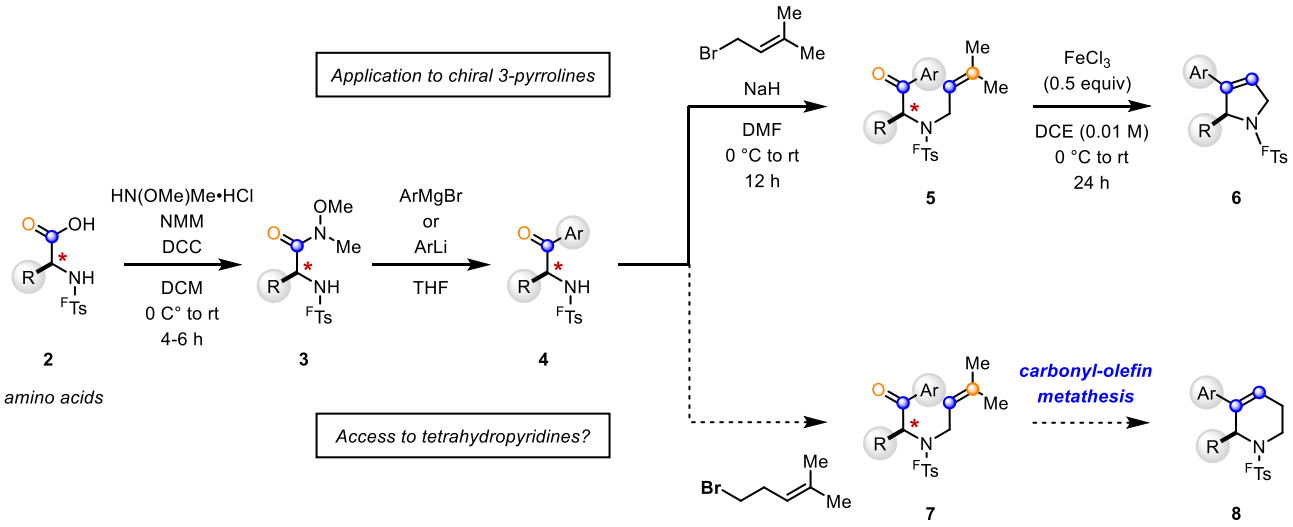


Figure 3.2 Reaction design strategy for the extension of carbonyl-olefin metathesis towards tetrahydropyridines.

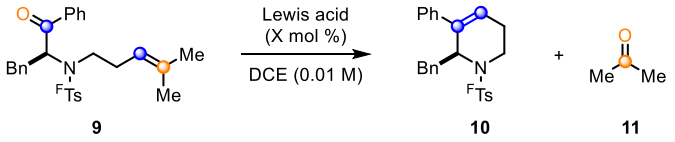
After the successful application of the carbonyl-olefin metathesis[11-12] reaction towards the synthesis of chiral 3-pyrrolines,[13] we set out to apply this strategy towards the synthesis of tetrahydropyridines. Our reaction design involved employing our previous synthetic strategy of utilizing chiral amino acids **2** to access substrates with high enantiopurity could be easily modified by alkylating the secondary amine **4** with homoprenylbromide or -iodide. With this flexible, robust synthetic strategy, we were able to rapidly access a wide range of substrates from both natural and unnatural amino acids.

This chapter is focused on the extension of the carbonyl-olefin metathesis reaction towards the synthesis of chiral tetrahydropyridines using the previously established sequence. Our approach continues to rely on readily available amino acids as chiral pool reagents and $FeCl_3$ as an inexpensive and Earth-abundant catalyst. This strategy is superior for prenyl-derived alkenes, is robust on gram-scale and results in the desired products in up to 99% yield with complete retention of enantiopurity.

3.2 Results and Discussion

With a robust substrate synthesis in hand, we turned our attention to the evaluation of distinct Lewis acids upon their ability to promote the desired carbonyl-olefin metathesis reactions (Table 3.1). While carbonyl-olefin metathesis has worked well for the synthesis of 3-pyrrolines, the application We first evaluated stronger Lewis acids for their ability to promote the desired carbonyl-olefin metathesis reaction of chiral, phenylalanine-derived substrate **9.** When aryl ketone **9** was subjected to 50 mol% of $AlCl_3$, the desired tetrahydropyridine **10** was formed in only 7% yield (entry 1, Table 3.1). Similarly, 50 mol % of $TiCl_4$ did not provide the desired heterocycle **10**, albeit complete conversion of aryl ketone **9** was observed (entry 2, Table 3.1). In comparison, the use of 50 mol % $SnCl_4$ or 50 mol % $BiCl_3$ provided the desired product **10** in 43% yield and 48% yield, respectively, with 45% conversion in both cases (entries 3 and 4, Table 3.1). Improved yields of **10** (up to 58% yield) were observed with $GaCl_3$ while a solution of $BF_3{\cdot}OEt_2$ (50 mol %) resulted in 52% yield, both with complete consumption of the starting material (entries 5 and 6, Table 3.1). Diminished yields of tetrahydropyridine **9** were obtained when $FeBr_3$ was selected as the Lewis acid

Table 3.1. Optimization of Reaction Conditions.



9 **10** **11**

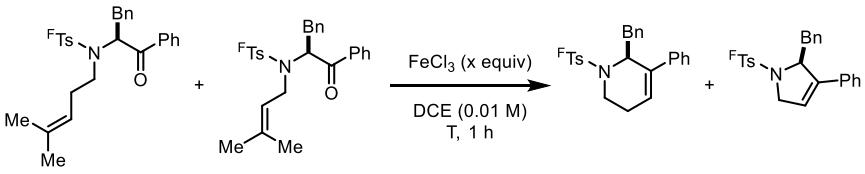
entry	Lewis acid	mol %	time (h)[a]	yield (%)[b]	conversion (%)[b]
1	$AlCl_3$	50	24	7	45
2	$TiCl_4$	50	24	0	99
3	$SnCl_4$	50	24	43	45
4	$BiCl_3$	50	24	48	49
5	$GaCl_3$	50	24	58	99
6	$BF_3{\cdot}OEt_2$	50	24	52	95
7	$FeBr_3$	50	24	40	97
8	$FeCl_3$	50	24[c]	68	99
9	$FeCl_3$	50	12	69	99
10	$FeCl_3$	50	24	88	99
11	$FeCl_3$	30	24	89	99
12	$FeCl_3$	10	24	6	10
13	$FeCl_3$	10	72	39	40
14	$Fe(OTf)_3$	50	24	30	91
15	$Sc(OTf)_3$	50	24	37	97

[a]Reactions were performed using 0.02 mmol of aryl ketone and were run at 84 °C for the indicated time. [b]Percent yield and percent conversion determined by ^{1}H-NMR using dimethyl terephthalate as an internal standard. [c]The Lewis acid was added at 0 °C and the reaction was allowed to warm to room temperature and stirred for the indicated time.

catalyst whereas $FeCl_3$ (50 mol %) proved superior and resulted in 88% yield (entries 7 and 10, Table 1). However, attempts to lower the reaction temperature to ambient conditions or shorten the reaction time to 12 hours led to diminished yields of tetrahydropyridine **6** in 68% and 69%, respectively (entries 8 and 9, Table 1). However, lower catalyst loadings of 30 mol % $FeCl_3$ were tolerated well and resulted in the formation of **6** in 89% yield with 99% conversion of starting material, which was ultimately established as the optimal set of reaction conditions (entry 11, Table 1). Interestingly, iron- and scandium-based metal triflates similarly resulted in the formation of the desired carbonyl-olefin metathesis products, albeit in diminished yields of 30% and 37%, respectively (entries 14 and 15, Table 1). Importantly, when the reaction was conducted relying on toluene as solvent under otherwise optimal reaction conditions, the desired tetrahydropyridine **6** was obtained in 75% yield.

While examining the formation of the tetrahydropyridine products, we wanted to explore the preference of five- versus six-membered ring formation. Due to the requirement of an electron-withdrawing protecting group to attenuate the Lewis basicity of the amine, we were unable to access a substrate that would accurately model a reaction preference,

Table 3.2 Evaluation of Ring Formation



9 **12** **10** **13**

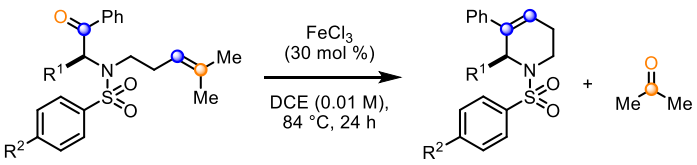
entry	**9** (equiv)	**12** (equiv)	$FeCl_3$	T	**10** (%yield)	**13** (%yield)
1	--	1	0.5	rt	--	99
2	--	1	0.5	84 °C	--	71
3	--	1	0.3	rt	--	89
4	1	1	0.3	rt	17	87
5	1	--	0.3	rt	26	--
6	1	--	0.5	rt	68	--

Conditions: Reactions were performed using a combined 0.03 mmol of substrate and 0.009 mmol (0.3 eq) of $FeCl_3$. Yields are reported as NMR yields with dimethyl terephthalate as an internal standard.

however, we did perform competition experiments between the homoallylic and allylic amino substrates **9** and **12**, respectively (Table 3.2). When selecting the conditions to best test the reactivity, attempted to find attenuated reaction conditions in order to best monitor product formation. When the prenyl amine **12** was subjected to the carbonyl-olefin metathesis conditions for only 1 hr under the otherwise optimized conditions, we still found that the reaction went to completion (entry 1, Table 3.2). When we subjected **12** to the carbonyl-olefin metathesis conditions at elevated temperatures, the desired product was obtained in 71% yield, however, the reaction went to completion (entry 2, Table 3.2). This led us to lower both the temperature and the catalyst loading which provided the desired product **13** in 89% yield (entry 3, Table 3.2). Upon subjection of substrate **9** to the attenuated reaction conditions, we observed a significant drop to on 26% yield of metathesis product **10** (entry 5). When **9** and **13** were subjected to $FeCl_3$ in the same reaction flask, there was a slight decrease in the formation of **10**, but the generation of 3-pyrroline **13** was largely unaffected. This data suggests that the carbonyl-olefin metathesis reaction favors the formation of the 5-membered ring products.

Electronically differentiated sulfonamides were then examined as nitrogen protecting groups in the catalytic carbonyl-olefin metathesis reaction towards tetrahydropyridines

Table 3.3 Evaluation of electronically differentiated protecting groups.



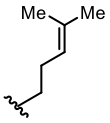
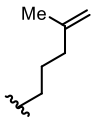
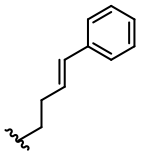
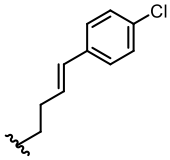
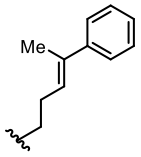
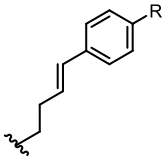
entry	substrate	R^1	R^2	σ_p	% Yield
1	**14**	H	CF_3	0.54	84
2	**15**	H	Cl	0.37	80
3	**16**	H	H	0.0	78
4	**17**	H	Me	-0.17	72
5	**18**	H	OMe	-0.27	47
6	**19**	H	OMe	-0.27	78[a]
7	**9**	Bn	CF_3	0.54	89

Conditions: all reactions were performed using 0.1 mmol of substrate and $FeCl_3$ (30 mol%) in DCE (0.01 M). The reactions were stirred for 24 h at 84 °C.
[a]Reaction was stirred for 48 h.

(Table 2). Our previous efforts focused on the development of a synthetic approach towards 3-pyrrolines revealed that the sulfonamides can function as competitive binders to $FeCl_3$, which results in sequestration of the catalyst and lower overall yields of the catalyst and lower overall yields of the desired products.[13b] By utilizing more electron-poor protecting groups,[14] the reactivity of the Lewis basic site was attenuated and the carbonyl-olefin metathesis reaction was able to proceed in excellent yields.[13b] Similar observations were made in the present study towards chiral tetrahydropyridines in which electron-deficient sulfonamides resulted in the desired metathesis products in yields up to 89% (entries 1, 2, 7, Table 2). However, more electron-rich sulfonamides also proved viable substrates and resulted in good yields of up to 78% of the desired tetrahydropyridines, albeit requiring prolonged reaction times of 48 hours (entries 4-6, Table 2). This is in stark contrast to observations made in our previous studies towards chiral 3-pyrrolines in which electron-deficient sulfonamides were essential to obtain high yields of the carbonyl-olefin metathesis product.

Next, we evaluated the effect of olefin substitution (Table 3.4). While both prenyl- or styrenyl-derived olefins were previously shown to be viable reaction partners

Table 3.4 Examination of olefin subunit.

entry	substrate		yield (%)	entry	substrate		yield (%)
1		**9**	89%	2		**20**	29%
3		**21**	0%	4		**22**	0%
5		**23**	3%	6		**24** R = Me **25** R = OMe	10% 0%

Conditions: all reactions were performed using 0.1 mmol of substrate and $FeCl_3$ (30 mol%) in DCE (0.01 M). The reactions were stirred at 84 °C for 24 h.

for catalytic carbonyl-olefin ring-closing metathesis reactions,[12] aryl ketones bearing a prenyl substituent were found to be superior in the synthesis of tetrahydropyridines resulting in up to 89% yield of the desired product (entry 1, Table 1). Importantly, the corresponding styrenyl-derivatives either failed or provided the desired tetrahydropyridines in low yields of 10% (entries 3-6, Table 3.4). The addition of superstoichiometric allyltrimethylsilane to carbonyl-olefin metathesis reactions of styrene-derivatives was previously shown to be beneficial for high yields and conversions.[15b] However, upon addition of 5.0 equivalents of allytrimethylsilane[15a] to **25** under otherwise identical reaction conditions, no formation of the desired product was observed. These results are particularly valuable to obtain further insights into the controlling features of catalytic carbonyl-olefin metathesis reaction.

Subsequent efforts focused on developing an efficient protocol for sulfonamide deprotection of the tetrahydropyridine products obtained (Figure 3.3). Reductive conditions[13b,15] relying on SmI_2 resulted in facile deprotection of **6** to the corresponding secondary amine **19** which, upon exposure to Boc_2O at 50 °C affords the corresponding carbamate **20** in 92% yield over the two-step sequence. Oxidation of the amine or aromatization to the corresponding pyridine was not observed under the optimized reaction conditions. Importantly, the sequence of deprotection and reprotection as the corresponding carbamate proceeded with complete retention of the stereocenter (98% ee) and established catalytic carbonyl-olefin metathesis reactions as a

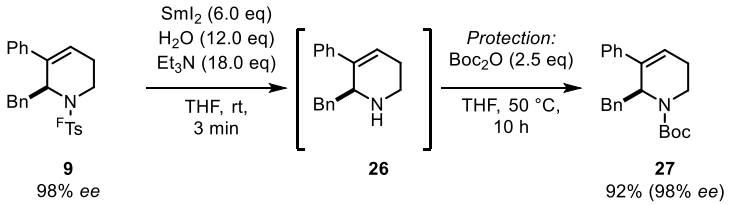
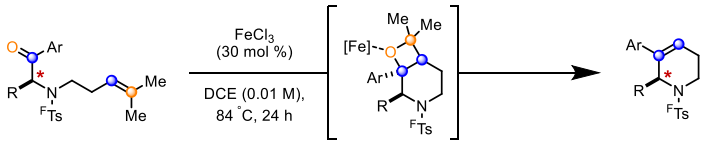


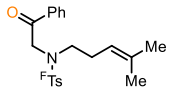
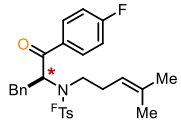
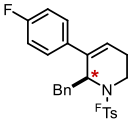
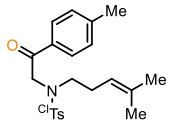
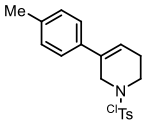
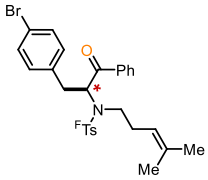
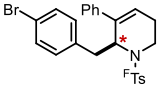
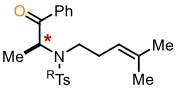
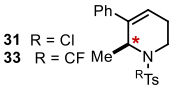
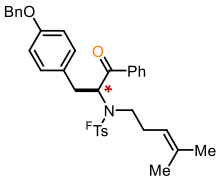
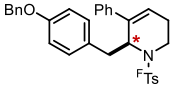
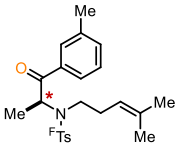
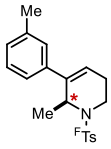
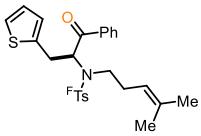
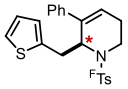
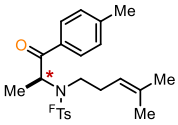
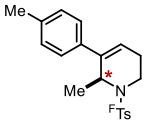
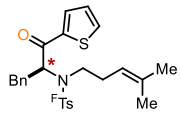
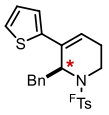
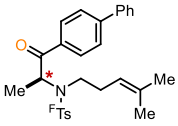
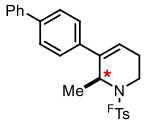
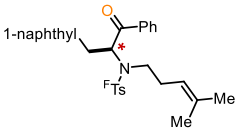
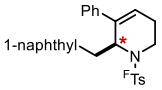
Figure 3.3 Deprotection of chiral tetrahydropyridines.

viable approach for the synthesis of chiral tetrahydropyridines from amino acids as chiral pool reagents.

With these results in hand, we investigated the scope of this transformation. Specifically, the reaction proceeds with a variety of aryl ketones derived from natural and unnatural amino acids bearing sterically and electronically distinct substitution. Previously challenging substrates such as unsubstituted glycine-derived aryl ketone **14**, provided metathesis product **28** in up to 84% yield.[13a] Furthermore, this reaction protocol was shown to be viable for substrates bearing substitution in the α–position. The reaction gave excellent yields of the alanine-derived products **32** and **34** and proceeded well for the sterically congested napthyl product **52**. Further examination of the substitution on the aromatic ring revealed that both meta- and para-substituents were also well tolerated and formed the desired alanine-derived products in up to 85% yield (**36** and **38**, Table 3.5). We next investigated the electronic effects on the aromatic ring with phenylalanine-based substrates. The reaction was tolerant of electron poor substituents **42** and **44** resulting in 76% and 77% yield, respectively. However, electron rich aryl ethers **46** formed the desired carbonyl-olefin metathesis products in slightly lower yields. It is possible that the benzyl-ether substituent acts as an additional Lewis basic site and competitively binds to the $FeCl_3$-catalyst which ultimately slows down the desired carbonyl-olefin metathesis reaction. Other electron rich systems including heteroaromatics were well tolerated, affording the desired products **48** derived from thienylalanine in 85% yield and **50** from the corresponding thienyl ketone in 84% yield. Importantly, the reaction also proceeds in good yields with other electron rich sulfonamide protecting groups such as **29** and **31**.

Table 3.5 Evaluation of Substrate Scope



entry	Substrate	Product	Yield [%]	entry	Substrate	Product	Yield [%]
1		**14**  **28**	84%	7		**41**  **42**	76%
2		**29**  **30**	53%	8		**43**  **44**	77%
3		**31** R = Cl **33** R = CF 	**32** R = Cl 93% **34** R = CF_3 99%	9		**45**  **46**	60%
4		**35**  **36**	68%	10		**47**  **48**	85%
5		**37**  **38**	85%	11		**49**  **50**	84%
6		**39**  **40**	75%	12		**51**  **52**	67%

Conditions: all reactions were performed using 0.1 mmol of substrate and $FeCl_3$ (30 mol%) in DCE (0.01 M). The reactions were stirred at 84 °C for 24 h.

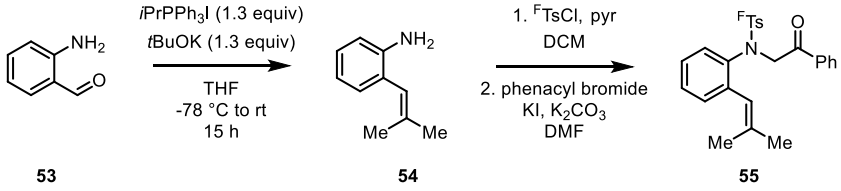
However, the 4-(trifluoromethyl)benzene-sulfonyl protecting group consistently provided the highest yield of the desired products.

Finally, we wanted to explore the application of carbonyl-olefin metathesis towards the synthesis of quinoline motifs. These fused heterocycles are important pharmacophores can be found in a variety of pharmaceuticals, specifically anti-bacterials, and they can also be found in a variety of natural products.[16] Substrates were prepared via the Wittig olefination[17] of 2-aminobenzaldehyde **53** followed by the protection and

alkylation of the amine. Once the α-amino ketone **55** was obtained, the material was subjected to the metathesis conditions (Figure 3.4). We found that while extended reaction times were required, we were able to access the desired quinoline **56** in modest yields. Unfortunately, the formation of the carbonyl-ene product **57** was found to be a competing byproduct. These preliminary results highlight the utility of this methodology and it's potential application towards an even more diverse and complex array of biologically important nitrogen heterocycles.

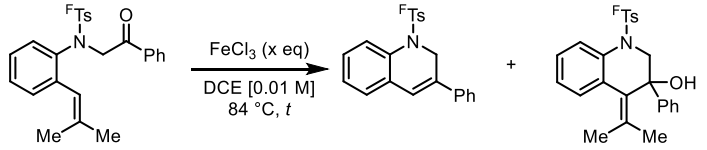
Figure 3.4 Studies towards the synthesis of quinolines.

(a) Quinoline Substrate Synthesis



53 **54** **55**

(b) Preliminary results towards the preparation of quinolines.



55 **56** **57**

entry[a]	eq. of $FeCl_3$	time (h)	%yield **56**	%yield **57**
1	0.25	48	19	15
2	0.50	48	31	22
3	1	24	29	16
4	2	24	27	16
5	1	48	41	35

Conditions: Substrate (0.03 mM) was dissolved in DCE [0.01 M] and subjected to $FeCl_3$. Reactions were stirred at 84 °C. (a) NMR yields reported with dimethyl terephthalate as an internal standard. (b) Isolated yields.

3.3 Experimental Procedures

3.3.1 General Considerations

General Laboratory Procedures. All moisture-sensitive reactions were performed under an atmosphere of nitrogen in flame-dried round bottom flasks, glass vials fitted with rubber septa and/or septa equipped screw caps, or sealed microwave vials. Stainless steel syringes were used to transfer air or moisture sensitive liquids. Flash chromatography was performed using silica gel Silia Flash® 40-63 micron (230-400 mesh) from Silicycle.

Materials and Instrumentation. All chemicals were purchased from Sigma-Aldrich, VWR, Oakwood or Acros and were used as received unless otherwise stated. Tetrahydrofuran, ether, toluene, and *N,N*-dimethylformamide were dried by being passed through columns of activated alumina. Proton Nuclear Magnetic Resonance NMR (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Unity Plus 400, Varian MR400, Varian vnmrs 500, Varian Inova 500, Varian Mercury 500, and Varian vnmrs 700 spectrometers. Chemical shifts for protons are reported in parts per million and are references to the NMR solvent peak ($CDCl_3$: δ 7.26, C_6D_6: δ 7.16, DMSO-d_6: δ 2.50, or CD_2Cl_2: δ 5.32). Chemical shifts for carbons are reported in parts per million and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ77.00, C_6D_6: δ 128.06, DMSO-d_6: δ 39.52, or CD_2Cl_2: δ 53.84). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants in Hertz (Hz). Mass spectroscopic (MS) data was recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan in Ann Arbor, MI on an Agilent Q-TOF HPLC-MS with ESI high resolution mass spectrometer. Infrared (IR) spectra were obtained using either an Avatar 360 FT-IR or Perkin Elmer Spectrum BX FT-IR spectrometer. IR data are represented as frequency of absorption (cm^{-1}) and all compounds were collected neat. Supercritical fluid chromatography (SFC) was performed on a Waters SFC instrument with a Waters Investigator SFC System with a Chiralpack AD-H column (4.6 x 250 mm).

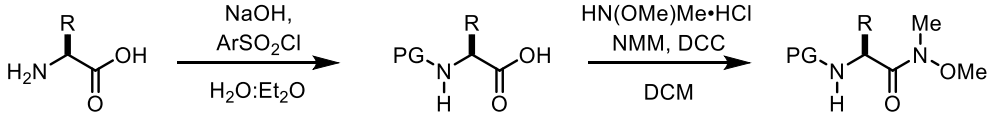
All moisture-sensitive reactions were performed under an atmosphere of nitrogen in flame-dried round bottom flasks, glass vials fitted with rubber septa and/or septa equipped

screw caps, or sealed microwave vials. Stainless steel syringes were used to transfer air or moisture sensitive liquids. Flash chromatography was performed using silica gel Silia Flash® 40-63 micron (230-400 mesh) from Silicycle.

Materials and Instrumentation. All chemicals were purchased from Sigma-Aldrich, VWR, Oakwood or Acros and were used as received unless otherwise stated. Tetrahydrofuran, ether, toluene, and N,N-dimethylformamide were dried by being passed through columns of activated alumina. Proton Nuclear Magnetic Resonance NMR (1H NMR) spectra and carbon nuclear magnetic resonance (13C NMR) spectra were recorded on a Varian Unity Plus 400, Varian MR400, Varian vnmrs 500, Varian Inova 500, Varian Mercury 500, and Varian vnmrs 700 spectrometers. Chemical shifts for protons are reported in parts per million and are references to the NMR solvent peak (CDCl3: δ 7.26, C6D6: δ 7.16, DMSO-d6: δ 2.50, or CD2Cl2: δ 5.32). Chemical shifts for carbons are reported in parts per million and are referenced to the carbon resonances of the NMR solvent (CDCl3: δ77.00, C6D6: δ 128.06, DMSO-d6: δ 39.52, or CD2Cl2: δ 53.84). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants in Hertz (Hz). Mass spectroscopic (MS) data was recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Michigan in Ann Arbor, MI on an Agilent Q-TOF HPLC-MS with ESI high resolution mass spectrometer. Infrared (IR) spectra were obtained using either an Avatar 360 FT-IR or Perkin Elmer Spectrum BX FT-IR spectrometer. IR data are represented as frequency of absorption (cm-1) and all compounds were collected neat. Supercritical fluid chromatography (SFC) was performed

on a Waters SFC instrument with a Waters Investigator SFC System with a Chiralpack AD-H column (4.6 x 250 mm).

3.3.2 General Procedure for the *N*-Protection and Weinreb Amidation of Amino Acids

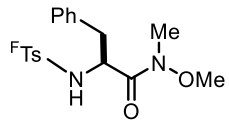


WA

A round bottom flask equipped with a magnetic stir bar was charged with the appropriate amino acid. The amino acid was dissolved in deionized water (0.4 M), and NaOH (2.5 eq) was added. The mixture was stirred until the solid was fully dissolved. To the resulting mixture was added a solution of the aryl sulfonyl chloride (1.2 eq) in diethyl ether (0.4 M). The reaction stirred for 12 hours, or until judged complete by TLC analysis. Aqueous hydrochloric acid (1 M) was added until the reaction mixture had a pH = 1, and the layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The combined organic layers were washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give the desired protected amino acid, which was carried forward without purification.[1]

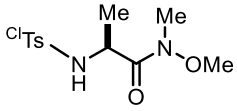
A round bottom flask equipped with a magnetic stir bar was charged with the protected amino acid and *N,O*-dimethylhydroxylamine hydrochloride (1.1 eq). The flask was sealed under a nitrogen atmosphere, and dry DCM (0.3 M) followed by NMM (1.4 eq) were subsequently added via syringe. The stirring mixture was cooled to 0 °C, and DCC (1.1 eq) was added in one portion. The reaction was allowed to warm to room temperature over 4-6 hours based on TLC analysis. The reaction was then filtered over a pad of celite, eluted with multiple DCM washes, and the combined organic eluent was washed with

saturated aqueous $NaHCO_3$ (2x). The organic layer was washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give the crude product. Purification by flash column chromatography eluting with EtOAc/hexanes (1:1) provided the desired Weinreb amide in 45-80% yield.[2]



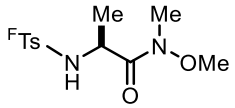
9 WA

(*S*)-*N*-methoxy-*N*-methyl-3-phenyl-2-((4-(trifluoromethyl)phenyl)sulfonamido)-propenamide (9 WA): Purification by flash column chromatography provided **9 WA** as a white solid. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.21 – 7.15 (m, 3H), 7.09 – 7.02 (m, 2H), 5.51 (d, *J* = 10.0 Hz, 1H), 4.55 (dd, *J* = 14.5, 8.7 Hz, 1H), 3.53 (s, 3H), 3.06 – 2.96 (m, 4H), 2.78 (dd, *J* = 13.6, 8.3 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.1, 143.6, 135.9, 134.1 (q, *J* = 32.7 Hz), 129.6, 128.6, 127.7, 127.3, 126.0 (q, *J* = 3.6 Hz), 123.4 (q, *J* = 272.7 Hz), 61.6, 54.8, 39.6, 32.2.



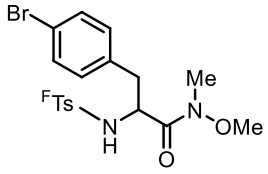
31 WA

(*S*)-2-((4-chlorophenyl)sulfonamido)-*N*-methoxy-*N*-methylpropanamide (31 WA): Purification by flash column chromatography provided **31 WA** as a clear oil that slowly solidified to give a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 5.77 – 5.55 (m, 1H), 4.52 – 4.15 (m, 1H), 3.59 (s, 3H), 3.00 (s, 3H), 1.31 (d, *J* = 7.0 Hz, 3H).; **^{13}C NMR** (176 MHz, $CDCl_3$) δ 172.09, 139.10, 138.60, 129.15, 128.70, 61.47, 49.03, 32.15, 19.99, 14.17.; **IR:** 2929.96, 2939.78, 1651.18, 1585.99, 1476.77, 1437.83, 1387.35, 1334.33, 1277.72, 1163.19, 1083.41, 1052.04, 1013.62, 1052.04, 1013.62, 985.44, 911.10, 871.97, 829.89; **HRMS:** calcd for $C_{11}H_{15}ClN_2O_4S^+$: 329.0333, found: 329.0332.



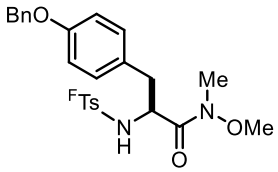
33 WA

(*S*)-*N*-methoxy-*N*-methyl-2-((4-(trifluoromethyl)phenyl)sulfonamido)propenamide (33 WA): Purifi-cation by flash column chromatography provided **33 WA** as a clear oil that solidified to give a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 5.61 (d, *J* = 7.9 Hz, 1H), 4.42 – 4.30 (m, 1H), 3.57 (s, 3H), 2.95 (s, 3H), 1.31 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.05, 143.84, 134.44 (q, *J* = 32.8 Hz), 127.93, 126.16 (q, *J* = 7.1, 3.4 Hz), 125.66 (dd, *J* = 588.3, 244.9 Hz), 61.62, 49.17, 32.21, 20.03; **IR:** 2940.40, 1721.9, 1654.85, 1404.75, 1384.61, 1320.91, 1267.74, 1167.86, 1129.60, 1107.94, 1093.36, 1061.36, 1017.35, 989.00, 911.31, 874.23, 842.57; **HRMS** calcd for $C_{12}H_{15}F_3N_2O_4S^{+H}$: 341.0777, found: 341.0780.



43 WA

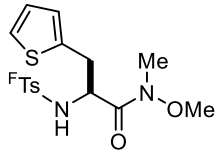
3-(4-bromophenyl)-*N*-methoxy-*N*-methyl-2-((4-(trifluoromethyl)phenyl)sulfon-amido)propanamide (43 WA): Purification by flash column chromatography provided **36 WA** as an off-white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.06 (d, *J* = 9.9 Hz, 1H), 4.50 (td, *J* = 9.1, 5.1 Hz, 1H), 3.61 (s, 3H), 3.05 (s, 3H), 2.94 (dd, *J* = 13.9, 4.9 Hz, 1H), 2.72 (dd, *J* = 13.8, 8.7 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.80, 143.50, 134.83, 134.12 (dd, *J* = 56.2, 22.9 Hz), 131.54, 131.11, 127.42, 125.88 (dd, *J* = 6.9, 3.5 Hz), 121.11, 61.53, 54.49, 38.54, 32.04; **IR:** 2944.73, 1721.98, 1647.67, 1488.46, 1436.46, 1405.00, 1324.05, 1163.40, 1126.86, 1106.64, 1096.78, 1061.75, 1011.35, 989.89, 964.88, 865.66, 843.63, 806.05; **HRMS** calcd for $C_{18}H_{18}BrF_3N_2O_4S^{+Na}$: 517.0015, found: 517.0012.



45 WA

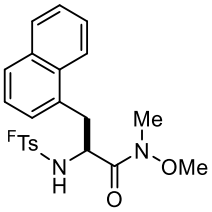
(*S*)-3-(4-(benzyloxy)phenyl)-*N*-methoxy-N-methyl-2-((4-(trifluoromethyl)phenyl)-sulfonamido)propan-amide (45 WA): Purification by flash column chromatography provided **45 WA** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 24.8, 8.6 Hz, 2H), 7.80 (d, *J* = 8.1 Hz, 4H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.38 – 7.32 (m, 1H), 7.24 (d, *J* =

2.7 Hz, 2H), 7.18 (d, *J* = 2.9 Hz, 3H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.32 – 5.25 (m, 1H), 4.85 (d, *J* = 16.0 Hz, 1H), 4.75 (d, *J* = 16.0 Hz, 1H), 3.30 (s, 3H), 3.17 (dd, *J* = 13.2, 9.6 Hz, 1H), 2.83 (s, *J* = 22.8 Hz, 3H), 2.77 (dd, *J* = 13.2, 4.9 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 169.34, 148.05, 143.90, 138.90, 136.88, 136.09, 136.05, 135.77 (dd, *J* = 66.5, 33.3 Hz), 130.69, 128.95, 128.20, 127.78, 127.43, 126.29 (dd, *J* = 7.1, 3.5 Hz), 125.73, 123.02 (q, *J* = 231.0 Hz), 122.17, 65.24, 61.31, 56.23, 48.81, 36.29, 31.65; **HRMS** calcd for $C_{25}H_{25}F_3N_2O_5S^{+NH4}$: 540.1175, found: 540.2824.



47 WA

(*S*)-*N*-methoxy-*N*-methyl-3-(thiophen-2-yl)-2-((4-(trifluoromethyl)phenyl)sulfonamido)propanamide (47 WA): Purification by flash column chromatography provided **47 WA** as a pale yellow foam. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.09 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.83 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.75 (d, *J* = 3.4 Hz, 1H), 5.88 (d, *J* = 9.8 Hz, 1H), 4.55 (ddd, *J* = 9.9, 7.6, 5.0 Hz, 1H), 3.57 (s, 3H), 3.20 (dd, *J* = 14.8, 5.1 Hz, 1H), 3.08 (dd, *J* = 14.8, 7.6 Hz, 1H), 3.02 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.5, 143.9, 137.6, 134. 1 (q, *J* = 33.0 Hz), 127.7, 127.10, 127.08, 126.0 (q, *J* = 3.9 Hz), 125.0, 123.3 (q, *J* = 273.6 Hz), 61.63, 54.81, 33.42, 32.17.

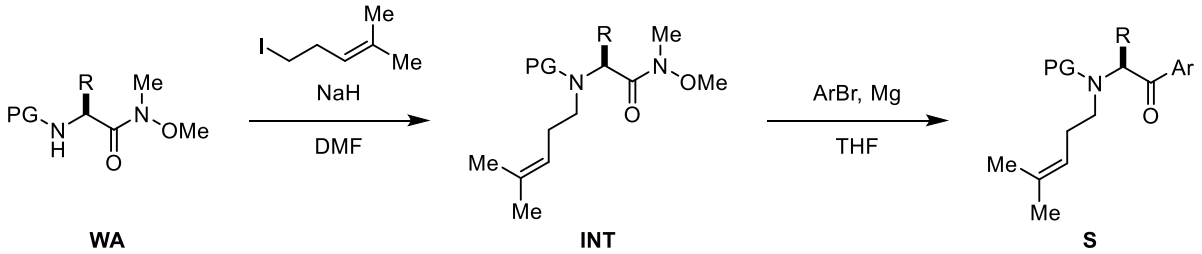


51 WA

(*S*)-*N*-methoxy-*N*-methyl-3-(naphthalen-1-yl)-2-((4-(trifluoromethyl)phenyl)sulfonamido)propenamide (44 WA): Purification by flash column chromatography provided **51 WA** as a white foam. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.46 (dt, *J* = 18.8, 7.1 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.29 – 7.17 (m, 4H), 6.03 (d, *J* = 10.0 Hz, 1H), 4.75 (td, *J* = 10.0, 4.7 Hz, 1H), 3.62 (s, 3H), 3.51 (dd, *J* = 14.2, 4.8 Hz, 1H), 3.18 (s, 3H), 3.13 (dd, *J* = 14.1, 10.0 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.5, 143.1, 133.7, 133.5 (q, *J* = 37.2 Hz), 132.0, 131.7, 129.1, 128.7, 128.1, 126.9, 126.3, 125.7, 125.5 (q, *J* = 3.5 Hz), 125.4, 123.4 (q, *J* = 272.8 Hz), 122.9, 61.7, 54.0, 36.5, 32.3.

3.3.3 General Procedures for the Synthesis of Metathesis Substrates

General Procedure A: *N*-Alkylation of Weinreb Amides followed by Grignard Reaction

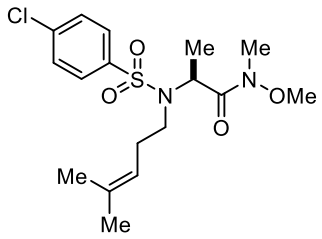


WA **INT** **S**

A round bottom flask equipped with a magnetic stir bar was charged with Weinreb amide **WA** and sealed under a nitrogen atmosphere. Dry DMF (0.1 M) was added via syringe, and the reaction mixture was cooled to 0 ^{o}C. Sodium hydride (2 eq, 60% dispersion in mineral oil) was added in one portion, and the reaction was allowed to stir at 0 ^{o}C for 30 minutes before homoprenyl iodide (1.2 eq) was added via syringe. The mixture was allowed to warm to room temperature over 3 hours, or until judged complete by TLC analysis. The reaction was quenched with deionized water, diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed brine (3x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **INT** in 55-99% yield.

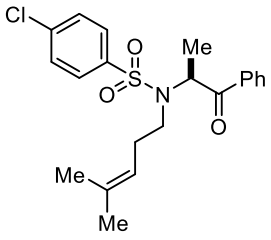
A round bottom flask equipped with a magnetic stir bar was charged with acid-washed magnesium turnings (3 eq) and a crystal of iodine then sealed under a nitrogen atmosphere. Dry THF (0.2 M) was added via syringe, followed by the desired aryl bromide (3 eq). The solution was allowed to stir (heating as necessary) until all magnesium turnings had dissolved and was then cooled to 0 °C. The mixture was then cooled to 0 °C

and added to a cooled solution (0 °C) of intermediate **INT** suspended in dry THF (0.2 M) dropwise via cannula. The reaction was allowed to warm to room temperature over 12 hours, or until judged complete by TLC analysis, at which point it was quenched with 1M HCl. The reaction mixture was diluted with EtOAc, the layers were partitioned, and the organic layer was collected. The aqueous phase was extracted with EtOAc (3x), and the combined organic layers were washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired substrate **S** in 65-95% yield.



31 INT

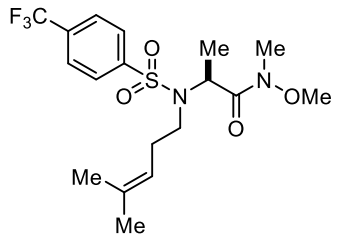
(*S*)-2-((4-chloro-N-(4-methylpent-3-en-1-yl)phenyl)sulfonamido)-*N*-methoxy-*N*-methylpropanamide (24 INT): Purification by flash column chromatography provided **31 INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.7 Hz, 2H), 7.44 (d, *J* = 7.9 Hz, 2H), 5.09 (s, 1H), 5.03 (t, *J* = 6.9 Hz, 1H), 3.76 (s, 3H), 3.36 – 3.28 (m, 1H), 3.26 – 3.18 (m, 1H), 3.07 (s, 3H), 2.44 – 2.34 (m, 1H), 2.33 – 2.25 (m, 1H), 1.67 (s, 3H), 1.62 (s, 3H), 1.28 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.90, 138.92, 138.55, 134.39, 129.08, 128.76, 120.15, 61.71, 51.09, 44.82, 30.59, 25.64, 17.80, 14.15; **HRMS** calcd for $C_{17}H_{25}ClN_2O_4S^{+Na}$: 411.1116, found: 411.1113.



31

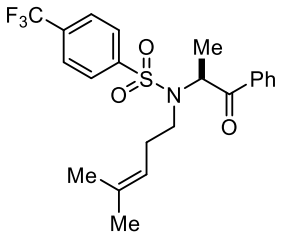
(*S*)-4-chloro-*N*-(4-methylpent-3-en-1-yl)-N-(1-oxo-1-phenylpropan-2-yl)benzene-sulfonamide (31): Purification by flash column chromatography provided **31** as a clear, colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.3 Hz, 2H), 7.71 (d, *J* = 8.6 Hz,

2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 5.60 (q, *J* = 7.0 Hz, 1H), 4.92 (t, *J* = 7.4 Hz, 1H), 3.17 – 3.11 (m, 1H), 3.08 – 3.03 (m, 1H), 2.21 – 2.10 (m, 2H), 1.60 (s, 3H), 1.54 (s, 3H), 1.27 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.64, 139.23, 138.36, 135.22, 134.68, 133.62, 129.29, 128.85, 128.82, 128.74, 119.80, 55.85, 44.84, 29.99, 25.59, 17.70, 14.42; **IR:** 2738, 1687, 1448, 1342, 1159, 1093, 738, 638; **HRMS** calcd for $C_{21}H_{24}ClNO_3S^{+NH4}$: 423.1504, found: 423.1039.



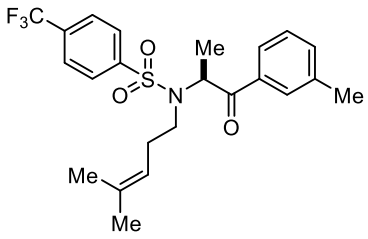
33 INT

***(S)*-*N*-methoxy-*N*-methyl-2-((*N*-(4-methylpent-3-en-1-yl)-4-(trifluoromethyl)phenyl)-sulfonamido)prop-anamide (33 INT):** Purification by flash column chromatography provided **33** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 5.12 (s, 1H), 5.04 (t, *J* = 6.6 Hz, 1H), 3.76 (s, 3H), 3.34 (d, *J* = 9.8 Hz, 1H), 3.27 (d, *J* = 10.1 Hz, 1H), 3.05 (s, 3H), 2.47 – 2.36 (m, 1H), 2.35 – 2.25 (m, 1H), 1.68 (s, 1H), 1.63 (s, 3H), 1.32 (d, *J* = 5.8 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 171.79, 143.54, 134.53, 134.12 (q, *J* = 33.2 Hz), 127.84, 125.95, 125.93 (q, *J* = 3.3 Hz), 123.24 (dd, *J* = 545.8, 272.8 Hz), 120.02, 61.70, 51.27, 45.02, 32.04, 30.64, 25.64, 17.81, 16.07; **HRMS** calcd for $C_{18}H_{25}F_3N_2O_4S^{+Na}$: 445.1379, found: 445.1377.



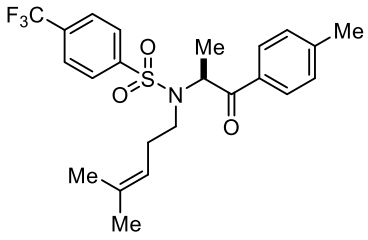
34

(*S*)-*N*-(4-methylpent-3-en-1-yl)-*N*-(1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)-benzenesulfonamide (34): Purification by flash column chromatography provided **34** as a clear, colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.7 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 5.63 (q, *J* = 7.0 Hz, 1H), 4.94 (t, *J* = 7.2 Hz, 1H), 3.22 – 3.07 (m, 2H), 2.24 – 2.15 (m, 2H), 1.61 (s, 3H), 1.55 (s, 3H), 1.31 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.49, 143.35, 135.12, 134.78, 134.32 (q, *J* = 33.1 Hz), 133.70, 128.85, 128.64, 127.91, 126.11 (q, *J* = 3.7 Hz), 126.11 (q, *J* = 3.7 Hz), 123.17 (q, *J* = 273.0 Hz), 119.68, 55.94, 45.03, 30.07, 25.58, 17.69, 14.79; **IR** (neat): 2932, 1688, 1597, 1449, 1403, 1342, 1322, 1229, 1167, 1134, 1108, 1091, 1062, 1017, 991, 963, 920, 844, 787; **HRMS** calcd for $C_{22}H_{24}F_3NO_3S^{+Na}$: 462.1321, found: 462.1323.



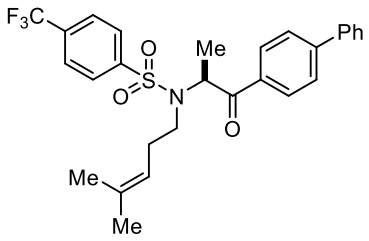
35

(*S*)-*N*-(4-methylpent-3-en-1-yl)-*N*-(1-oxo-1-(*m*-tolyl)propan-2-yl)-4-(trifluoromethyl)-benzenesulfon-amide (35): Purification by flash column chromatography provided **35** as a clear, colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.80 – 7.76 (m, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 5.62 (q, *J* = 7.1 Hz, 1H), 4.95 (t, *J* = 7.3 Hz, 1H), 3.23 – 3.11 (m, 2H), 2.41 (s, 3H), 2.22 (dd, *J* = 16.0, 7.9 Hz, 2H), 1.63 (s, 3H), 1.56 (s, 3H), 1.32 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.78, 143.40, 135.16, 134.75, 134.50, 134.27 (q, *J* = 33.0 Hz), 123.19 (q, *J* = 272.8 Hz), 129.08, 128.73, 127.85, 126.08 (q, *J* = 3.6 Hz), 125.80, 123.19 (q, *J* = 272.8 Hz), 119.75, 55.88, 45.11, 30.19, 25.60, 21.34, 17.72, 15.13; **IR:** 2760, 1688, 1403, 1323, 1253, 1167, 1135, 1108, 1062, 1018, 844 cm^{-1}; **HRMS** calcd for $C_{23}H_{26}F_3NO_3S^{+Na}$: 476.1478, found: 476.1530.



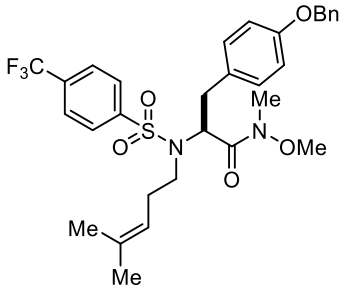
37

(*S*)-*N*-(4-methylpent-3-en-1-yl)-N-(1-oxo-1-(p-tolyl)propan-2-yl)-4-(trifluoromethyl)-benzenesulfonamide (37): Purification by flash column chromatography provided **37** as a clear colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.0 Hz, 4H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 9.1 Hz, 2H), 5.60 (q, *J* = 7.0 Hz, 1H), 4.94 (t, *J* = 7.4 Hz, 1H), 3.18 (ddd, *J* = 16.5, 10.5, 6.2 Hz, 1H), 3.15 – 3.08 (m, 1H), 2.42 (s, 3H), 2.24 – 2.14 (m, 2H), 1.62 (s, 3H), 1.56 (s, *J* = 4.9 Hz, 2H), 1.30 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 197.01, 144.72, 143.41, 134.72, 134.25 (q, *J* = 33.1 Hz), 132.55, 129.54, 128.75, 127.89, 126.08 (dd, *J* = 7.3, 3.6 Hz), 123.18 (q, *J* = 273.0 Hz), 119.73, 77.18, 77.00, 76.82, 55.75, 45.01, 30.18, 25.58, 21.69, 17.70, 14.92; **IR** (neat) 2925, 1686, 1607, 1404, 1323, 1167, 1135, 1100, 1062, 1017, 924, 843 cm^{-1}; **HRMS** calcd for $C_{23}H_{26}F_3NO_3S^{+Na}$: 476.1478, found: 476.1474.



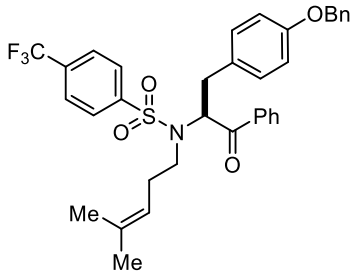
40

(*S*)-*N*-(1-([1,1'-biphenyl]-4-yl)-1-oxopropan-2-yl)-N-(4-methylpent-3-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (40): Purification by flash column chromatography provided **40** as a clear, faintly yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.3 Hz, 2H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.71 (dd, *J* = 8.2, 2.9 Hz, 4H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 5.67 (q, *J* = 7.0 Hz, 1H), 4.95 (t, *J* = 7.3 Hz, 1H), 3.20 (ddd, *J* = 16.3, 10.7, 6.0 Hz, 1H), 3.16 – 3.10 (m, 1H), 2.27 – 2.17 (m, 2H), 1.62 (s, 3H), 1.56 (s, 3H), 1.32 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.94, 146.39, 143.38, 139.58, 134.81, 134.35 (q, *J* = 33.1 Hz), 133.71, 130.92, 129.31, 129.01, 128.43, 127.94, 127.45, 127.25, 126.15 (dd, *J* = 7.2, 3.5 Hz), 123.18 (dd, *J* = 545.9, 272.8 Hz), 119.70, 55.95, 45.02, 30.12, 25.59, 17.72, 14.70; **IR** (neat): 2925, 1684, 1603, 1404, 1322, 1230, 1167, 1135, 1107, 1062, 1017, 922, 847 cm^{-1}; **HRMS** calcd for $C_{28}H_{28}F_3NO_3S^{+Na}$: 538.1634, found: 538.1631.



45 INT

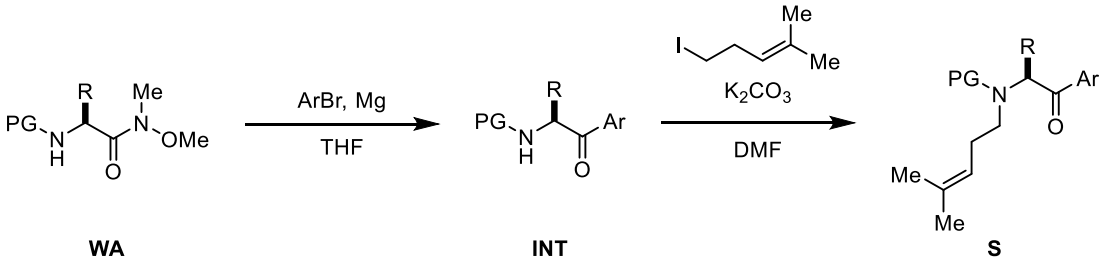
(*S*)-3-(4-(benzyloxy)phenyl)-*N*-methoxy-*N*-methyl-2-((*N*-(4-methylpent-3-en-1-yl)-4-(trifluoromethyl)phenyl)sulfonamido)propanamide (45 INT): Purification by flash column chromatography provided **45 INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 6.9 Hz, 2H), 7.23 – 7.19 (m, 3H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 5.30 (dd, *J* = 9.6, 4.4 Hz, 1H), 5.19 (t, *J* = 7.1 Hz, 1H), 4.84 (dd, *J* = 87.0, 16.0 Hz, 3H), 3.87 (t, *J* = 7.1 Hz, 2H), 3.22 (s, 3H), 3.15 (dd, *J* = 13.1, 10.3 Hz, 1H), 2.82 (s, 3H), 2.71 (dd, *J* = 13.0, 4.3 Hz, 1H), 2.45 (q, *J* = 7.0 Hz, 2H), 1.72 (s, 3H), 1.65 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 169.70, 157.95, 144.15, 137.32, 134.42, 133.87 (q, *J* = 32.9 Hz), 130.38, 128.16, 127.80, 125.64 (q, *J* = 2.7 Hz), 123.21 (d, *J* = 272.8 Hz), 119.43, 114.56, 67.64, 61.29, 56.44, 48.77, 36.36, 31.55, 28.19, 25.71, 17.81; **HRMS** calcd for $C_{31}H_{35}F_3N_2O_5S^{+Na}$: 643.1850, found: 643.2677.



45

(*S*)-*N*-(3-(4-(benzyloxy)phenyl)-1-oxo-1-phenylpropan-2-yl)-*N*-(4-methylpent-3-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (45): Purification by flash column chromatography provided **45** as a clear, colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 16.2, 8.0 Hz, 4H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.37 (q, *J* = 7.7 Hz, 6H), 7.31 (t, *J* = 6.7 Hz, 1H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 5.70 (dd, *J* = 9.4, 4.7 Hz, 1H), 4.99 (s, 2H), 4.96 (t, *J* = 7.1 Hz, 1H), 3.36 (dd, *J* = 13.5, 9.7 Hz, 1H), 3.32 – 3.15 (m, 2H), 2.65 (dd, *J* = 13.7, 4.6 Hz, 1H), 2.27 – 2.09 (m, 2H), 1.63 (s, 3H), 1.57 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.53, 157.68, 143.45, 136.86, 135.79, 134.89, δ 134.27 (q, *J* = 33.1 Hz), 133.65, 130.23, 128.73, 128.63, 128.59, 128.55, 127.95, 127.84, 127.42, 126.09 (q, *J* = 3.5 Hz), 123.12 (q, *J* = 273.0 Hz), 119.63, 115.05, 69.95, 60.42, 45.00, 34.09, 29.70, 25.62, 17.72; **IR** (neat): 2925, 1686, 1610, 1582, 1512, 1449, 1494, 1322, 1244, 1164, 1134, 1108, 1092, 1062, 1016, 942, 844, 822 cm^{-1}; **HRMS** calcd for $C_{35}H_{34}F_3NO_4S^+$: 622.2233, found: 622.2228.

General Procedure B: Grignard Addition to Weinreb Amides followed by *N*-Alkylation

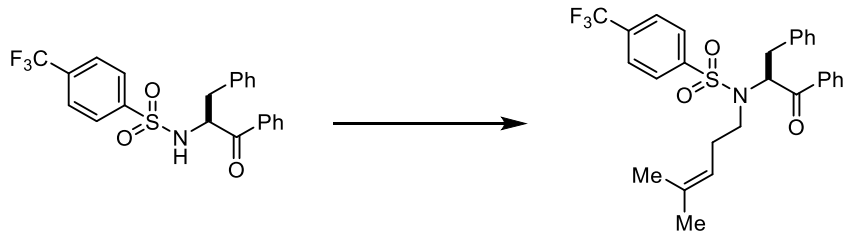


WA **INT** **S**

A round bottom flask equipped with a magnetic stir bar was charged with acid-washed magnesium turnings (3 eq) and a crystal of iodine then sealed under a nitrogen atmosphere. Dry THF (0.2 M) was added via syringe, followed by the desired aryl bromide (3 eq). The solution was allowed to stir (heating as necessary) until all magnesium turnings had dissolved, and was then cooled to 0 ^oC. To the mixture was added Weinreb amide **WA** suspended in dry THF (0.2 M) dropwise via cannula. The reaction was allowed

to warm to room temperature over 12 hours, or until judged complete by TLC analysis, at which point it was quenched with a saturated ammonium chloride solution. The reaction mixture was diluted with EtOAc, the layers were partitioned, and the organic layer was collected. The aqueous phase was extracted with EtOAc (3x), and the combined organic layers were washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **INT** in 51-90% yield.

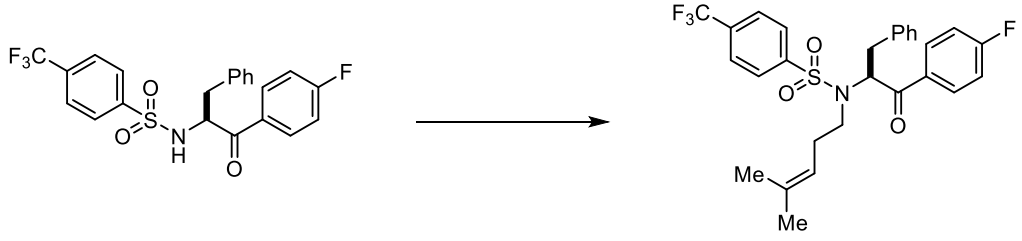
A round bottom flask equipped with a magnetic stir bar was charged with intermediate **INT** and sealed under a nitrogen atmosphere. Dry DMF (0.1 M) was added via syringe, and the reaction mixture was cooled to 0 ^oC. Potassium carbonate (2 eq) was added in one portion, and the reaction was allowed to stir at 0 ^oC for 30 minutes before prenyl bromide (1.2 eq) was added via syringe. The mixture was allowed to warm to room temperature over 3 hours, or until judged complete by TLC analysis. The reaction was quenched with deionized water, diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with an aqueous 5% LiCl solution (3x), brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography eluting with EtOAc/hexanes (1:4) afforded the desired substrate **S** in 65-99% yield.



9 INT **9**

(*S*)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (9 INT) Purification by flash column chromatography provided **9 INT** as a white solid. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.09 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.83 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.75 (d, *J* = 3.4 Hz, 1H), 5.88 (d, *J* = 9.8 Hz, 1H), 4.55 (ddd, *J* = 9.9, 7.6, 5.0 Hz, 1H), 3.57 (s, 3H), 3.20 (dd, *J* = 14.8, 5.1 Hz, 1H), 3.08 (dd, *J* = 14.8, 7.6 Hz, 1H), 3.02 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 170.5, 143.9, 137.6, 134. 1 (q, *J* = 33.0 Hz), 127.7, 127.10, 127.08, 126.0 (q, *J* = 3.9 Hz), 125.0, 123.3 (q, *J* = 273.6 Hz), 61.63, 54.81, 33.42, 32.17.

(*S*)-*N*-(4-methylpent-3-en-1-yl)-N-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (9) Purification by flash column chromatography provided **9** as a white solid. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.8 Hz, 2H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.21 (d, *J* = 7.3 Hz, 2H), 7.18 – 7.13 (m, 3H), 3.41 (dd, *J* = 13.6, 9.4 Hz, 1H), 3.31 – 3.26 (m, 1H), 3.24 – 3.19 (m, 1H), 2.72 (dd, *J* = 13.7, 4.8 Hz, 1H), 2.22 (tt, *J* = 12.4, 6.4 Hz, 1H), 2.15 (ddd, *J* = 17.6, 12.2, 5.8 Hz, 1H), 1.62 (s, 3H), 1.56 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.35, 143.38, 136.44, 135.67, 134.90, 134.27 (q, *J* = 33.1 Hz), 133.68, 129.15, 128.73, 128.69, 128.58, 127.82, 126.87, 126.10 (q, *J* = 3.6 Hz), 123.09 (q, *J* = 273.0 Hz), 119.58, 65.83, 44.99, 34.86, 29.65, 25.60, 17.69.

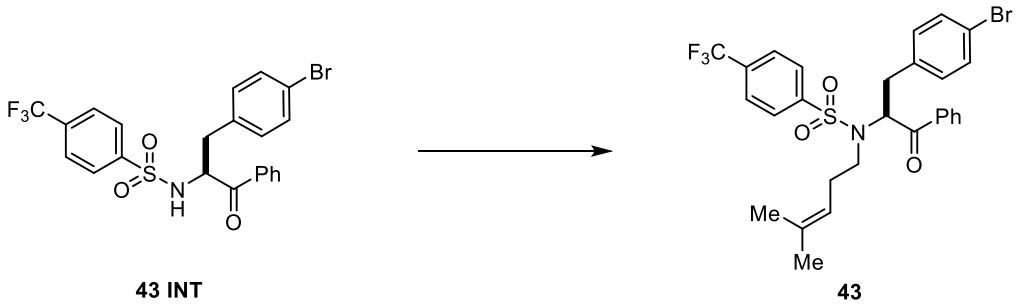


41 INT **41**

(*S*)-*N*-(1-(4-fluorophenyl)-1-oxo-3-phenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (41 INT): Purification by flash column chromatography provided **41 INT** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.83 – 7.72 (m, 4H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.19 – 7.08 (m, 5H), 6.98 (dd, *J* = 7.0, 2.3 Hz, 2H), 5.76 (d, *J* = 9.1 Hz, 1H), 5.13 (ddd, *J* = 9.1, 6.9, 5.6 Hz, 1H), 3.12 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.91 (dd, *J* = 14.0, 7.0 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ ^{13}C NMR (176 MHz, cdcl$_3$) δ 195.58, 167.03, 165.57, 143.45, 134.69, 134.20 (q, *J* = 33.1 Hz), 131.16 (d, *J* = 9.6 Hz), 130.34 (d, *J* = 2.9 Hz),

129.40, 128.58, 127.42, 127.37, 126.04 (q, *J* = 3.6 Hz), 123.05 (q, *J* = 272.9 Hz), 116.27 (d, *J* = 22.1 Hz), 58.50, 40.18; **IR:** **HRMS** calcd for $C_{22}H_{17}F_4NO_3S^{+Na}$: 474.0757, found: 474.0731.

(*S*)-*N*-(1-(4-fluorophenyl)-1-oxo-3-phenylpropan-2-yl)-*N*-(4-methylpent-3-en-1-yl)-4-(trifluoromethyl)-benzenesulfonamide (41): Purification by flash column chromatography provided **41** as a pale yellow oil. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.22 (t, *J* = 7.2 Hz, 2H), 7.17 (d, *J* = 6.9 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 2H), 7.07 (t, *J* = 8.5 Hz, 2H), 5.72 (dd, *J* = 9.6, 4.7 Hz, 1H), 4.95 (t, *J* = 7.2 Hz, 1H), 3.38 (dd, *J* = 13.5, 9.7 Hz, 1H), 3.30 – 3.14 (m, 2H), 2.62 (dd, *J* = 13.6, 4.6 Hz, 1H), 2.28 – 2.18 (m, 1H), 2.10 (ddd, *J* = 18.7, 12.9, 6.2 Hz, 1H), 1.63 (s, 3H), 1.57 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.57, 143.20, 138.32, 136.05, 135.26 – 134.11 (m), 135.16, 130.97, 129.14, 129.04, 128.82, 127.84, 127.07, 126.26 (q, *J* = 3.7 Hz), 125.77 (q, *J* = 3.5 Hz), 119.36, 60.82, 45.01, 34.43, 29.59, 25.59, 17.70; **IR** (neat) 2931, 1692, 1608, 1495, 1454, 1405, 1321, 1164, 1128, 1093, 1108, 1063, 1017, 941, 844, 788 cm^{-1}; **HRMS** calcd for $C_{28}H_{27}F_4NO_3S^{+NH4}$: 551.1986, found: 551.3545.

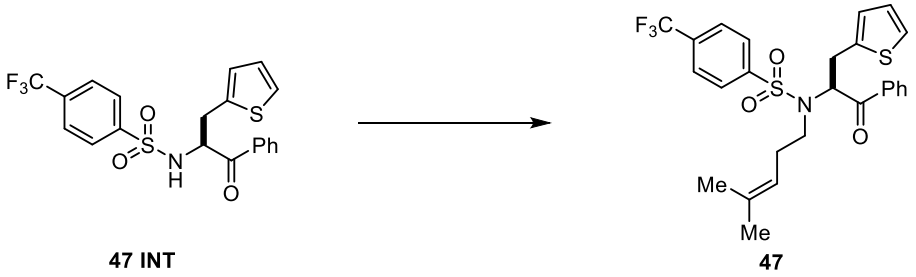


43 INT **43**

(*S*)-*N*-(3-(4-bromophenyl)-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)-benzenesulfonamide (43 INT): Purification by flash column chromatography provided **43 INT** as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ7.77 (dd, *J* = 15.5, 7.8 Hz, 4H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.3 Hz, 2H), 5.70 (d, *J* = 8.8 Hz, 1H), 5.15 (ddd, *J* = 8.8, 6.5, 5.5 Hz, 1H), 3.14 (dd, *J* = 14.1, 5.2 Hz, 1H), 2.88 (dd, *J* = 14.1, 6.7 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.48, 143.28, 134.55, δ 134.35 (dd, *J* = 67.4, 34.3 Hz), 133.66, 133.55, 131.61, 131.22, 129.14, 128.34, 127.41, 126.11 (q, *J* = 3.7 Hz), 121.43, 58.22, 39.56; **IR:** 2930.22, 1684.65, 1596.99, 1506.27, 1457.48, 1430.58, 1407.13, 1324.95, 1297.09, 1263.20, 1228.60, 1166.45, 1154.60, 1126.64, 1093.69, 1109.19, 1063.16, 1016.15, 982.86, 950.19, 915.97, 875.28, 837.52; **HRMS** calcd for $C_{22}H_{17}BrF_3NO_3S^{+Na}$: 533.9957, found: 533.9952.

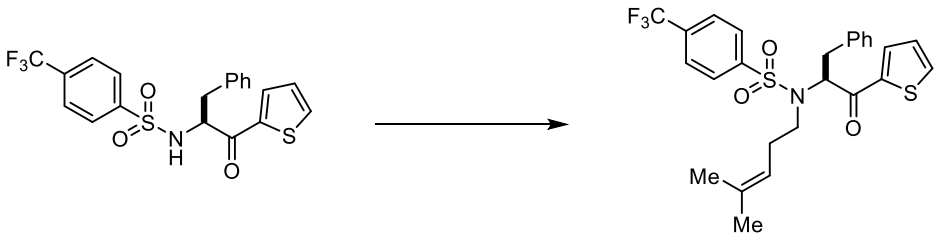
(*S*)-*N*-(3-(4-bromophenyl)-1-oxo-1-phenylpropan-2-yl)-*N*-(4-methylpent-3-en-1-yl)-4-(trifluoromethyl)-benzenesulfonamide (43): Purification by flash column chromatography provided **43** as a white solid. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 16.6, 7.9 Hz, 4H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 5.69 (dd, *J* = 9.5, 4.7 Hz, 1H), 4.93

(t, *J* = 7.2 Hz, 1H), 3.40 (dd, *J* = 13.6, 9.6 Hz, 1H), 3.29 – 3.12 (m, 2H), 2.68 (dd, *J* = 13.6, 4.7 Hz, 1H), 2.23 – 2.05 (m, *J* = 5.8 Hz, 2H), 1.62 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 195.95, 143.33, 135.56, 135.54, 135.02, 134.44 (q, J = 33.2 Hz), 133.86, 131.80, 130.94, 128.82, 128.57, 127.84, 126.16 (q, J = 3.7 Hz), 120.89 (q, J = 272.9 Hz) 120.85, 119.45, 60.15, 45.00, 34.38, 29.54, 25.59, 17.68; **IR** (neat): 2929, 1686, 1596, 1489, 1449, 1320, 1161, 1132, 1107, 1092, 1012, 932, 908, 871, 843 cm^{-1}; **HRMS** calcd for $C_{28}H_{27}BrF_3NO_3S^+$: 594.0920, found: 594.0728.



***N*-(1-oxo-1-phenyl-3-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)benzene-sulfonamide (47 INT):** Pur-ification by flash column chromatography provided **47 INT** as an off-white solid. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 7.9 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.10 (d, *J* = 4.7 Hz, 1H), 6.87 – 6.82 (m, 1H), 6.77 (s, 1H), 5.71 (dd, *J* = 9.3, 3.9 Hz, 1H), 4.93 (t, *J* = 6.4 Hz, 1H), 3.69 (dd, *J* = 14.3, 9.7 Hz, 1H), 3.27 – 3.20 (m, 1H), 3.16 – 3.09 (m, 1H), 2.73 (dd, *J* = 14.5, 3.5 Hz, 1H), 2.25 – 2.18 (m, 1H), 2.12 (dt, *J* = 12.0, 6.3 Hz, 1H), 1.61 (s, 3H), 1.56 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.5, 143.6, 136.1, 134.5, 134.4 (q, *J* = 33.1 Hz), 133.8, 129.2, 128.6, 127.6, 127.4, 127.1, 126.3 (q, *J* = 3.5 Hz), 125.3, 123.2 (q, *J* = 272.7 Hz), 58.5, 34.5.

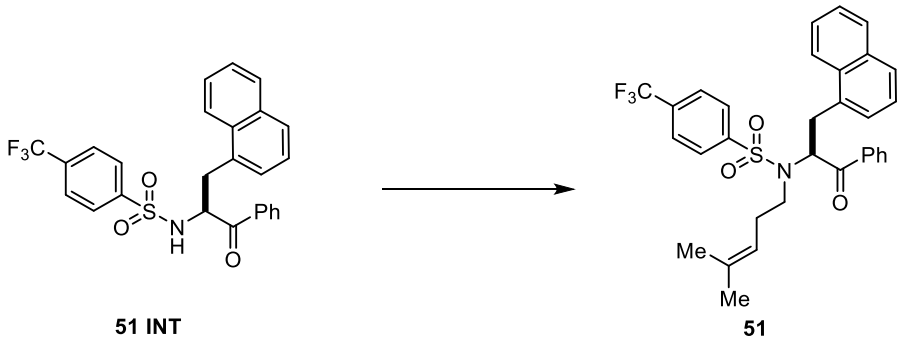
***N*-(3-methylbut-2-en-1-yl)-*N*-(1-oxo-1-phenyl-3-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (47):** Purification by flash column chromatography provided **47** as a pale yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.96 (d, *J* = 6.9 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.13 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.88 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.83 (d, *J* = 2.9 Hz, 1H), 5.73 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.84 (tt, *J* = 6.9, 1.6 Hz, 1H), 3.98 (dd, *J* = 15.9, 6.6 Hz, 1H), 3.85 (dd, *J* = 16.0, 7.2 Hz, 1H), 3.70 (dd, *J* = 14.7, 8.9 Hz, 1H), 2.89 (dd, *J* = 14.7, 4.8 Hz, 1H), 1.59 (s, 3H), 1.53 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.76, 143.32, 138.48, 135.49, 135.03, 134.48 (q, *J* = 33.1 Hz), 133.85, 128.81, 127.90, 127.10, 126.51, 126.28 (dd, *J* = 7.2, 3.5 Hz), 124.51, 122.34 (dd, *J* = 906.3, 413.1 Hz), 119.45, 60.70, 45.08, 29.65, 28.76, 25.59, 17.69; **IR** (neat) 2929, 1685, 1597, 1448, 1404, 1347, 1322, 1228, 1162, 1134, 1107, 1092, 1062, 1014, 908, 844, 743, 712 cm^{-1}; **HRMS** calcd for $C_{26}H_{26}F_3NO_3S_2^{+Na}$: 544.1198, found: 544.1199.



49 INT 49

(*S*)-N-(1-oxo-3-phenyl-1-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)benzene-sulfonamide (49 INT): Purification by flash column chromatography provided **49 INT** as a white solid. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 5.8 Hz, 1H), 7.69 (d, *J* = 5.8 Hz, 2H), 7.58 (d, *J* = 3.8 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.19 – 7.15 (m, 3H), 7.11 – 7.08 (m, 1H), 7.03 (m, 2H), 5.74 (d, *J* = 9.3 Hz, 1H), 4.95 – 4.91 (m, 1H), 3.16 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.98 (dd, *J* = 14.0, 7.3 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 189.8, 143.4, 140.9, 135.9, 135.1, 134.4 (q, *J* = 33.2 Hz), 133.4, 129.6, 128.7, 128.6, 127.4, 126.1 (q, *J* = 3.6 Hz), 60.0, 40.9.

(*S*)-N-(3-methylbut-2-en-1-yl)-N-(1-oxo-3-phenyl-1-(thiophen-2-yl)propan-2-yl)-4-(trifluoromethyl)-benzenesulfonamide (49): Purification by flash column chromatography provided **49** as a clear, faintly yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 13.7, 5.8 Hz, 3H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 4.8 Hz, 1H), 7.22 (t, *J* = 7.2 Hz, 2H), 7.18 (d, *J* = 7.0 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 2H), 7.06 (t, *J* = 4.3 Hz, 1H), 5.60 (dd, *J* = 9.5, 5.0 Hz, 1H), 5.00 (t, *J* = 7.2 Hz, 1H), 3.43 – 3.32 (m, 2H), 3.27 – 3.19 (m, 1H), 2.67 (dd, *J* = 13.6, 4.9 Hz, 1H), 2.35 – 2.17 (m, 2H), 1.66 (s, 3H), 1.60 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 188.85, 143.36, 142.80, 136.24, 135.41, 134.93, 134.33 (dd, *J* = 66.3, 33.2 Hz), 133.87, 129.17, 128.69, 128.51, 127.79, 126.92, 126.18 (q, *J* = 3.6 Hz), 123.13 (q, *J* = 272.9 Hz), 119.60, 61.44, 45.06, 34.79, 29.75, 25.61, 17.70; **IR** (neat): 2732, 1662, 1413, 1404, 1321, 1248, 1163, 1138, 1132, 1249, 1163, 1138, 1108, 1062, 1017, 847, 737 cm^{-1}; **HRMS** calcd for $C_{26}H_{26}F_3NO_3S_2^{+Na}$: 544.1198, found: 544.1187.



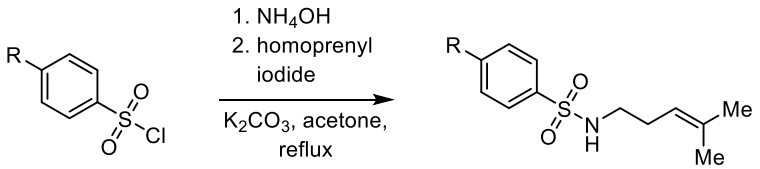
51 INT 51

(*S*)-*N*-(3-(naphthalen-1-yl)-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)benzene-sulfonamide (51 INT): Purification by flash column chromatography provided **51 INT** as a white solid. . Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 7.9 Hz,

2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.51 (ddt, *J* = 21.9, 13.5, 7.1 Hz, 5H), 7.41 – 7.29 (m, 4H), 7.16 (dt, *J* = 15.5, 7.1 Hz, 2H), 5.95 (d, *J* = 9.3 Hz, 1H), 5.34 (td, *J* = 8.7, 6.2 Hz, 1H), 3.46 (dd, *J* = 14.3, 6.1 Hz, 1H), 3.37 (dd, *J* = 14.2, 8.2 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 198.5, 143.2, 134.4, 134.4, 133.9 (q, *J* = 33.0 Hz), 133.9, 131.8, 131.5, 129.2, 129.0, 128.4, 128.4, 128.3, 127.1, 126.6, 125.9, 125.8 (q, *J* = 3.7 Hz), 125.3, 123.2 (q, *J* = 273.2 Hz), 123.1, 57.9, 37.4.

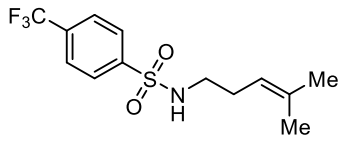
(*S*)-*N*-(3-methylbut-2-en-1-yl)-*N*-(3-(naphthalen-1-yl)-1-oxo-1-phenylpropan-2-yl)-4-(trifluoromethyl)-benzenesulfonamide (51): Purification by flash column chromatography provided **51** as a clear, colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.63 – 7.48 (m, 6H), 7.47 – 7.41 (m, 3H), 7.32 – 7.21 (m, 4H), 6.02 (dd, *J* = 9.0, 5.6 Hz, 1H), 4.95 (tt, *J* = 6.2, 1.7 Hz, 1H), 4.23 (dd, *J* = 16.3, 7.4 Hz, 1H), 4.08 (dd, *J* = 16.3, 6.3 Hz, 1H), 3.80 (dd, *J* = 14.1, 9.0 Hz, 1H), 3.56 (dd, *J* = 14.1, 5.6 Hz, 1H), 1.65 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ ^{13}C NMR (126 MHz, $cdcl_3$) δ 197.29, 143.27, 136.02, 134.92, 134.50 – 133.62 (m), 133.82, 133.50, 131.84, 131.76, 129.02, 128.55, 128.14, 127.88, 127.83, 127.66, 126.58, 125.86 (q, *J* = 3.7 Hz), 125.80, 125.36, 123.10, 123.06 (q, *J* = 272.8 Hz), 119.78, 58.26, 45.00, 33.09, 30.06, 25.66, 17.78; **IR** (neat) 2940, 1666, 1459, 1403, 1322, 1164, 1132, 1108, 1092, 1062, 1017, 996, 931, 843, 799 cm^{-1}; **HRMS** calcd for $C_{32}H_{30}F_3NO_3S^{+K}$: 604.1530, found: 604.1767.

General Procedure C: Preparation of Protected, Homoprenylated Secondary Amines



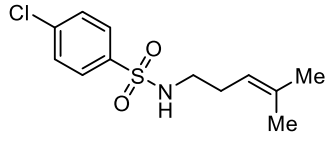
INT

A round bottom flask equipped with a magnetic stir bar was charged with the para-substituted benzenesulfonyl chloride. The solid was suspended in a 30% ammonium hydroxide solution (0.1 M) and allowed to stir at room temperature for 16 hours. The reaction mixture was diluted with EtOAc, and aqueous hydrochloric acid (1 M) was added until the pH was less than 9, then the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure



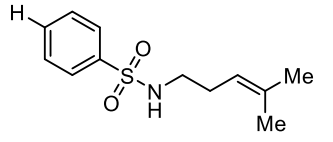
14 INT

***N*-(4-methylpent-3-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (14 INT):** Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **16 INT** as a clear faintly yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 4.91 (t, *J* = 6.9 Hz, 1H), 4.69 (t, *J* = 5.6 Hz, 1H), 2.99 (q, *J* = 6.5 Hz, 2H), 2.17 (q, *J* = 6.9 Hz, 2H), 1.65 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.66, 136.00, 134.29 (q, *J* = 33.1 Hz), 127.55, 126.23 (q, *J* = 3.6 Hz), 126.70 – 119.70 (m), 119.31, 43.01, 28.17, 25.72, 17.81; **IR:** 3268.44, 2972.65, 1430.10, 1404.92, 1326.60, 1307.93, 1296.26, 1160.20, 1131.60, 1109.32, 1094.11, 1065.57, 1015.18, 898.37, 854.48; **HRMS** calcd for $C_{13}H_{16}F_3NO_2S^{+Na}$: 330.0746, found: 330.0732.



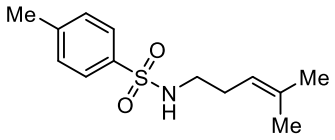
15 INT

4-chloro-*N*-(4-methylpent-3-en-1-yl)benzenesulfonamide (15 INT): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **15 INT** as a clear colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 4.91 (t, *J* = 7.0 Hz, 1H), 4.78 (t, *J* = 5.8 Hz, 1H), 2.94 (q, *J* = 6.6 Hz, 2H), 2.14 (q, *J* = 6.9 Hz, 2H), 1.64 (s, 3H), 1.54 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 143.14, 136.90, 135.18, 129.53, 127.00, 119.69, 42.87, 28.07, 25.60, 21.37, 17.69; **IR:** 2970.11, 2915.12, 1585.56, 1475.39, 1450.58, 1338.45, 1276.19, 1199.41, 1156.65, 1091.91, 1013.50, 955.40, 916.22, 872.82, 826.73; **HRMS** calcd for $C_{12}H_{16}ClNO_2S^{+Na}$: 286.0663, found: 286.0657.



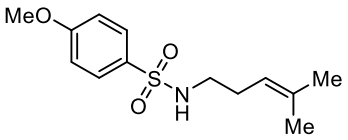
16 INT

***N*-(4-methylpent-3-en-1-yl)benzenesulfonamide (16 INT):** Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **16 INT** as a clear, colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.5 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 2H), 4.95 – 4.88 (m, 1H), 4.43 (d, *J* = 20.5 Hz, 1H), 2.97 (q, *J* = 6.7 Hz, 2H), 2.14 (q, *J* = 6.9 Hz, 2H), 1.66 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.98, 132.55, 129.06, 127.04, 119.59, 42.93, 28.47, 28.15, 25.75, 17.84; **IR:** 3346.05, 3251.80, 1553.35, 1447.05, 1331.17, 1311.05, 1180.27, 1158.50, 1091.17, 1071.24, 1025.33, 997.77, 904.69, 755.37; **HRMS** calcd for $C_{12}H_{17}NO_2S^{+H}$: 240.1053, found: 240.1050.



17 INT

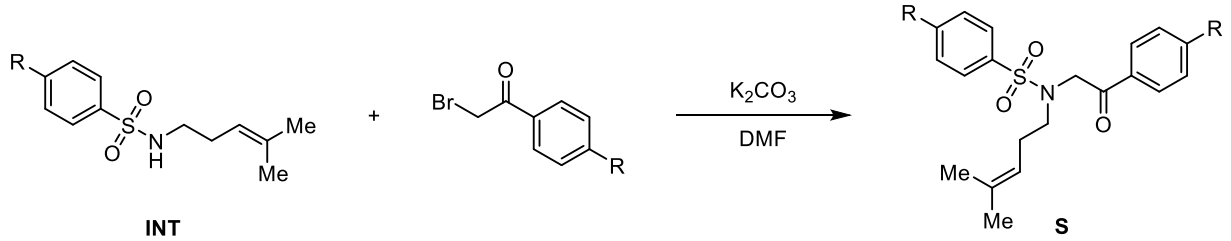
4-methyl-*N*-(4-methylpent-3-en-1-yl)benzenesulfonamide (11 INT): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **11 INT** as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 4.91 (t, *J* = 7.0 Hz, 1H), 4.84 (t, *J* = 5.6 Hz, 1H), 2.90 (q, *J* = 6.7 Hz, 2H), 2.40 (s, 3H), 2.12 (q, *J* = 6.8 Hz, 2H), 1.62 (s, 3H), 1.52 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.14, 136.90, 135.18, 129.53, 127.00, 119.69, 42.87, 28.07, 25.60, 21.37, 17.69; **IR:** 3355.91; 3259.70, 2929.72, 1598.48, 1526.91, 1446.36, 1386.86, 1299.78, 1248.50, 1156.31, 1096.08, 1018.22, 902.74, **IR** 3355.91, 3259.70, 2919.72, 1598.48, 1526.91, 1446.36, 1386.86, 1299.78, 1248.50, 1156.31, 1096.08, 1018.22, 902.74, 816.17; **HRMS** calcd for $C_{13}H_{19}NO_2S^{+Na}$: 276.1029, found: 276.1025.



18 INT

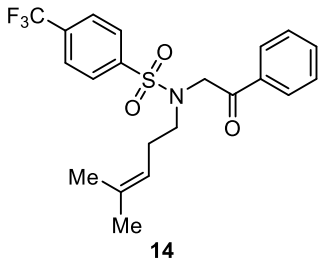
4-methoxy-*N*-(4-methylpent-3-en-1-yl)benzenesulfonamide (18 INT): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired intermediate **18 INT** as a clear colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 4.91 (t, *J* = 7.2 Hz, 1H), 4.67 (t, *J* = 5.9 Hz, 1H), 3.85 (s, 3H), 2.90 (q, *J* = 6.7 Hz, 2H), 2.12 (q, *J* = 6.9 Hz, 2H), 1.64 (s, 3H), 1.53 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.72, 135.35, 131.48, 129.14, 119.71, 114.12, 55.53, 42.86, 28.07, 25.66, 17.76.; **IR:** 3277.20, 2929.06, 1596.22, 1579.06, 1497.91, 1440.79, 1377.40, 1321.51, 1300.36, 1257.13, 1179.57, 1148.41, 1111.74, 1094.18, 1023.78, 935.22, 885.92, 832.15, 803.01; **HRMS** calcd for $C_{13}H_{19}NO_3S^{+Na}$: 292.0978, found: 292.0963.

General Procedure D: Alkylation of Secondary Amines with 2-bromoacetophenones



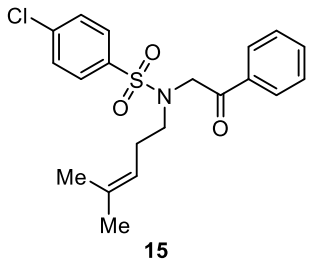
INT **S**

A round bottom flask equipped with a magnetic stir bar was charged with starting material **INT** and K_2CO_3 (2 eq). The flask was sealed under nitrogen, and dry DMF (0.5 M) was added via syringe. To the stirring solution was added 2-bromoacetophenone (1.1 eq) suspended in dry DMF (0.5 M) via syringe. The reaction was allowed to stir for 3 hours or until complete by TLC analysis, at which point it was quenched with deionized water and diluted with EtOAc, and the resultant layers were partitioned. The organic layer was collected, and the aqueous phase was extracted with EtOAc (3x). The organic layers were then combined, washed with brine (1x), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The glycine substrates were obtained in 85-99% yield.



14

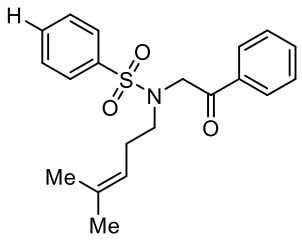
***N*-(4-methylpent-3-en-1-yl)-N-(2-oxo-2-phenylethyl)-4-(trifluoromethyl)benzene-sulfonamide (14 S):** Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **14 S** as a pale yellow oil. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 7.6 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 4.96 (t, *J* = 6.8 Hz, 1H), 4.87 (s, 2H), 3.35 – 3.21 (m, 2H), 2.24 (dd, *J* = 14.5, 7.2 Hz, 2H), 1.61 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.1, 143.9, 139.8, 134.9, 134.1 (q, *J* = 32.9 Hz), 134.0, 129.0, 128.1, 128.0, 126.1 (q, *J* = 3.8 Hz), 123.5 (q, *J* = 273.0 Hz), 118.0, 51.7, 45.6, 25.8, 17.7.



15

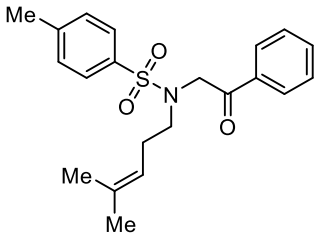
4-chloro-*N*-(4-methylpent-3-en-1-yl)-N-(2-oxo-2-phenylethyl)benzenesulfonamide (15): Purification by flash column chromatography over silica eluting with EtOAc/hexanes

(1:4) afforded the desired substrate **15** as slightly yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.1 Hz, 2H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (dd, *J* = 9.4, 7.0 Hz, 4H), 4.96 (t, *J* = 7.1 Hz, 1H), 4.83 (s, 2H), 3.30 – 3.23 (m, 2H), 2.22 (q, *J* = 7.3 Hz, 2H), 1.61 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 193.66, 138.89, 138.50, 134.69, 133.84, 129.04, 128.89, 128.82, 127.86, 119.76, 52.79, 47.88, 27.09, 25.58, 17.71; **IR** (neat) 2914, 2361, 1700, 1597, 1584, 1476, 1337, 1224, 1224, 1156, 1093, 1013, 970, 942, 912, 827 cm^{-1}; **HRMS** calcd for $C_{20}H_{22}ClNO_3S^{+Na}$: 414.0901, found: 414.0896.



16

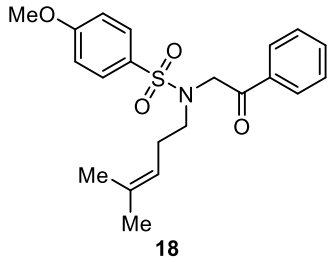
***N*-(4-methylpent-3-en-1-yl)-N-(2-oxo-2-phenylethyl)benzenesulfonamide (16):** Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **16** as a clear, colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.88 (d, *J* = 7.2 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 5.07 (tt, *J* = 7.5, 1.4 Hz, 1H), 4.76 (s, 2H), 3.95 (d, *J* = 7.5 Hz, 2H), 1.63 (s, 3H), 1.46 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.1, 143.9, 139.8, 134.9, 134.1 (q, *J* = 32.9 Hz), 134.0, 129.0, 128.1, 128.0, 126.1 (q, *J* = 3.8 Hz), 123.5 (q, *J* = 273.0 Hz), 118.0, 51.7, 45.6, 25.8, 17.7; **IR** (neat) 2929, 1702, 1598, 1450, 1405, 1322, 1226, 1161, 1132, 1094, 1108, 1062, 1016, 1001, 973, 913, 844, 788 cm^{-1}; **HRMS** calcd for $C_{20}H_{23}NO_3S^+$: 412.1189, found: 412.1190.



17

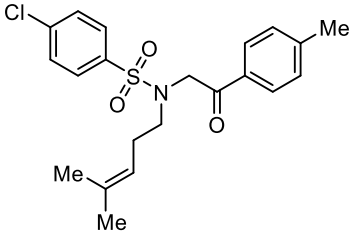
4-methyl-*N*-(4-methylpent-3-en-1-yl)-N-(2-oxo-2-phenylethyl)benzenesulfonamide (17): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **11 S** as a an off-white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.94 (t, *J* = 7.8 Hz, 1H), 4.76 (s, 2H), 3.23 (dd, *J* = 8.5, 6.9 Hz, 2H), 2.43 (s, 3H), 2.19 (dd, *J* = 14.9, 7.4 Hz, 2H), 1.59 (s, 3H), 1.53 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.02, 143.24, 136.82, 134.91, 134.46, 133.69, 129.47, 128.77, 128.00, 127.45, 119.97, 53.10, 47.95, 27.11, 25.58, 21.51, 17.69.; **IR**

(neat) 2919, 1700, 1597, 1448, 1333, 1289, 1224, 1183, 1153, 1091, 1001, 969, 942, 912, 813 cm^{-1}; **HRMS** calcd for $C_{21}H_{25}FNO_3S^+$: 412.1189, found: 412.1190.



18

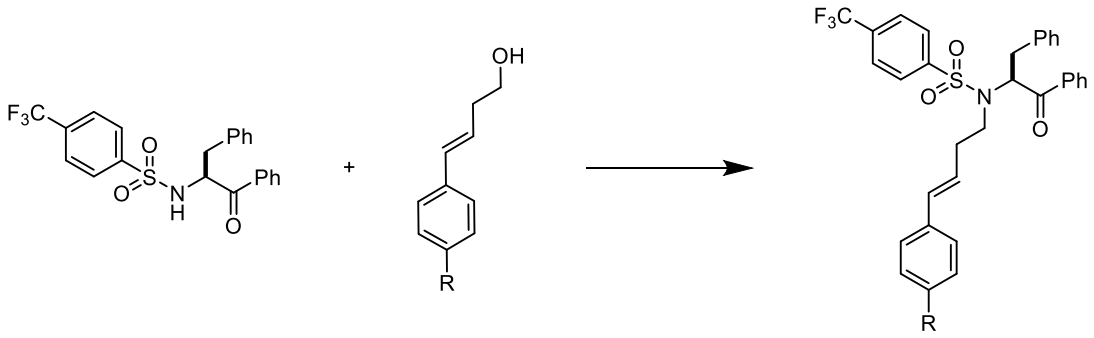
4-methoxy-*N*-(4-methylpent-3-en-1-yl)-*N*-(2-oxo-2-phenylethyl)benzenesulfonamide (18): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **18** as a clear colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 4.76 (s, 1H), 3.87 (s, 2H), 3.73 (s, 1H), 3.25 – 3.17 (m, 1H), 2.19 (dd, *J* = 14.9, 7.3 Hz, 1H), 1.60 (s, 1H), 1.53 (s, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 194.20, 162.79, 134.94, 134.49, 133.71, 131.47, 129.61, 128.79, 128.03, 120.01, 114.01, 55.54, 53.11, 47.96, 27.13, 25.61, 17.73; **IR** (neat): 2916, 1700, 1596, 1579, 1498, 1449, 1413, 1334, 1302, 1259, 1302, 1259, 1224, 1151, 1093, 1025, 971, 943, 912, 834, 805, 752 cm^{-1}; **HRMS** calcd for $C_{21}H_{25}F_3NO_4S^{+Na}$: 410.1397, found: 410.1270.



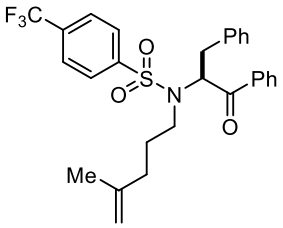
29

4-chloro-*N*-(4-methylpent-3-en-1-yl)-N-(2-oxo-2-(p-tolyl)ethyl)benzenesulfonamide (29): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **29** as white solid **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.4, 2.7 Hz, 4H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 4.95 (t, *J* = 6.4 Hz, 1H), 4.80 (s, 2H), 3.29 – 3.19 (m, 2H), 2.42 (s, 3H), 2.21 (dd, *J* = 13.9, 6.8 Hz, 2H), 1.61 (s, 3H), 1.55 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 193.29, 144.91, 138.93, 138.54, 134.75, 132.25, 129.55, 129.08, 128.95, 128.02, 119.81, 52.65, 47.88, 27.14, 25.64, 21.75, 17.77.; **IR** (neat) 2917, 2361, 2337, 1700, 1695, 1684, 1652, 1576, 1559, 1539, 1506, 1456, 1336, 1229, 1155, 1092, 1012, 924, 826, 808, 786 cm^{-1}; **HRMS** calcd for $C_{21}H_{24}ClNO_3S^{+Na}$: 428.1058, found: 428.1056.

Mitsunobu Reaction Conditions to Obtain Differentiated-Olefin Substrates



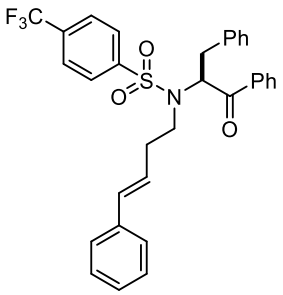
A round bottom flask equipped with a magnetic stir bar was charged with a solution of the secondary the secondary amine (1.0 mmol), alcohol (2.2 mmol, 2.2 equiv)[5] and PPh_3 (3.0 mmol). The flask was sealed under nitrogen, and dry DCM (10 mL) was added via syringe. To the stirring solution was added DEAD (3.0 mmol, 40% solution in toluene) dropwise at 0 °C. The mixure was warmed to room temperature and stirred under a nitrogen atmosphere for 24 h, at which point the reaction mixture was quenched with deionized water and diluted with EtOAc. The resultant layers were partition and the organic phase was collected. The aqueous phase was extracted with EtOac (3x). The organic layers were then combined, washed with brine (2x), and dried over Na_2SO_4. Purification by chromatography on silica gel gave the desired product in 40% to 93% yield.



20

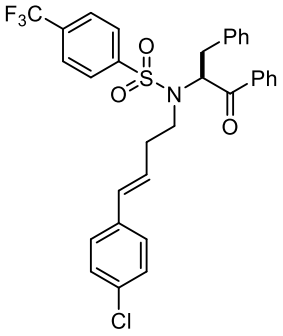
(*S*)-*N*-(4-methylpent-4-en-1-yl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoro-methyl)benzenesulfonamide (20): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **40** as a colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.4 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.25 – 7.21 (m, 2H), 7.19 – 7.15 (m, 3H), 5.77 (dd, *J* = 9.4, 5.0 Hz, 1H), 4.67 (d, *J* = 64.7 Hz, 2H), 3.42 (dd, *J* = 13.7, 9.4 Hz, 1H), 3.37 – 3.31 (m, 1H), 3.28 – 3.23 (m, 1H), 2.72 (dd, *J* = 13.7, 4.9 Hz, 1H), 1.92 (t, *J* = 7.4 Hz, 2H), 1.73 – 1.67 (m, 1H), 1.66 (s, 3H), 1.65 – 1.59 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.55, 144.25, 143.42, 136.43, 135.70, 134.31 (q, *J* = 33.1 Hz), 133.71, 129.14, 128.76, 128.72, 128.57, 127.82, 126.90, 126.12 (q, *J* = 3.6 Hz), 123.11 (q, *J* = 272.9 Hz), 110.62, 77.18, 77.00, 76.82, 60.31, 45.12, 35.02, 28.10, 22.14; **IR** (neat) 2926, 1687, 1597, 1496, 1449, 1404, 1349, 1323, 1233, 1164, 1134, 1108,

1063, 1016, 945, 890, 844, 787 cm^{-1}; **HRMS** calcd for $C_{28}H_{28}F_3NO_3S^{+Na}$: 538.1634, found: 538.1724.



21

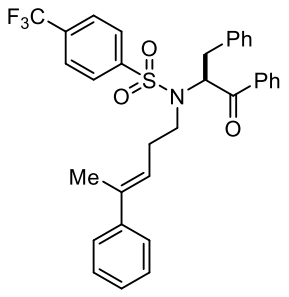
(*S*,*E*)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-*N*-(4-phenylbut-3-en-1-yl)-4-(trifluoromethyl)benzenesulfonamide (21): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **21** as a colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.84 (t, *J* = 6.8 Hz, 4H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.28 (dd, *J* = 17.3, 9.1 Hz, 4H), 7.25 – 7.20 (m, 3H), 7.18 (s, 3H), 6.32 (d, *J* = 15.8 Hz, 1H), 6.06 – 5.98 (m, 1H), 5.78 (dd, *J* = 8.2, 4.6 Hz, 1H), 3.56 – 3.38 (m, 4H), 2.76 (dd, *J* = 13.6, 4.9 Hz, 1H), 2.50 – 2.39 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 196.54, 143.28, 137.08, 136.29, 135.64, 134.38 (q, *J* = 32.7 Hz), 133.75, 132.49, 129.14, 128.76, 128.75, 128.58, 128.48, 127.88, 127.29, 126.96, 126.16 (dd, *J* = 7.1, 3.5 Hz), 126.05, 125.81, 123.07 (q, *J* = 265.8 Hz), 60.30, 45.06, 34.99, 34.34; **IR** (neat) 2934, 1685, 1597, 1582, 1495, 1448, 1404, 1347, 1320, 1233, 1162, 1130, 1107, 1090, 1062, 1015, 935, 943, 909, 842 cm^{-1}; **HRMS** calcd for $C_{32}H_{28}F_3NO_3S^+$: 564.1815, found: 564.1815.



22

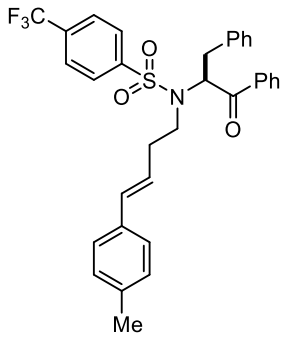
(*S*,*E*)-*N*-(4-(4-chlorophenyl)but-3-en-1-yl)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (22): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **22** as a clear colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 4H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.23 (dd, *J* = 13.7, 7.3 Hz, 4H), 7.18 – 7.14 (m, 5H), 6.26 (d, *J* = 15.9 Hz, 1H), 6.02 – 5.96 (m, 1H), 5.78 (dd, *J* = 9.2, 5.1 Hz, 1H), 3.54 – 3.48 (m, 1H), 3.44 (ddd, *J* = 22.8, 14.5, 8.3 Hz, 2H), 2.72 (dd, *J* = 13.7, 4.9 Hz, 1H), 2.45 (dd, *J* = 15.0, 9.9 Hz, 2H); **^{13}C NMR** (176 MHz,

$CDCl_3$) δ 196.49, 143.21, 136.19, 135.59, 134.46 (q, *J* = 33.1 Hz), 133.80, 132.85, 131.29, 129.10, 128.77, 128.61, 128.59, 127.87, 127.25, 126.99, 126.60, 126.20 (q, *J* = 3.8 Hz), 60.25, 44.92, 34.92, 34.31; **IR** (neat) 2729, 1685, 1596, 1491, 1449, 1322, 1234, 1164, 1133, 1091, 11008, 1062, 1013, 968, 945, 844 cm^{-1}; **HRMS** calcd for $C_{32}H_{27}ClF_3NO_3S^+$: 59.1425, found: 598.1420.



23

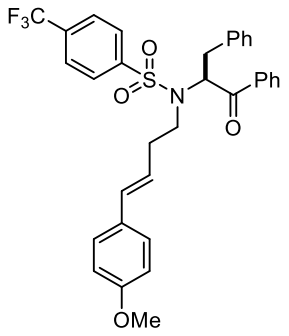
(*S*,*E*)-N-(1-oxo-1,3-diphenylpropan-2-yl)-*N*-(4-phenylpent-3-en-1-yl)-4-(trifluoro-methyl)benzenesulfon-amide (23) Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **23** as a clear, slightly yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 13.0, 7.9 Hz, 4H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.29 (q, *J* = 7.8 Hz, 4H), 7.22 (t, *J* = 6.0 Hz, 3H), 7.16 (d, *J* = 7.2 Hz, 3H), 5.78 (dd, *J* = 9.3, 5.1 Hz, 1H), 5.59 (t, *J* = 7.0 Hz, 1H), 3.49 – 3.30 (m, 3H), 2.75 (dd, *J* = 13.7, 5.0 Hz, 1H), 2.41 (ddd, *J* = 18.1, 12.5, 6.9 Hz, 2H), 1.98 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.49, 143.33, 143.28, 137.71, 136.34, 135.64, 134.36 (q, *J* = 33.0 Hz), 133.75, 129.15, 128.77, 128.74, 128.58, 128.16, 127.84, 126.94, 126.88, 126.16 (q, *J* = 3.6 Hz), 125.59, 123.01, 60.29, 44.70, 34.98, 30.36, 15.83; **IR** (neat) 2923, 1685, 1596, 1581, 1495, 1448, 1404, 1321, 1266, 1233, 1163, 1131, 1108, 1091, 1062, 1028, 1016, 944, 843, 787 cm^{-1}; **HRMS** calcd for $C_{33}H_{30}F_3NO_3S^{+Na}$: 616.5130, found: 616.1714.



24

(*S*,*E*)-*N*-(1-oxo-1,3-diphenylpropan-2-yl)-N-(4-(p-tolyl)but-3-en-1-yl)-4-(trifluoro-methyl)benzenesulfonamide (24): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **24** as a clear,

colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.86 – 7.82 (m, 3H), 7.66 – 7.59 (m, 3H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 3H), 7.20 – 7.15 (m, 5H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.29 (d, *J* = 15.8 Hz, 1H), 5.99 – 5.92 (m, 1H), 5.78 (dd, *J* = 9.1, 5.1 Hz, 1H), 3.53 – 3.41 (m, 3H), 2.77 (dd, *J* = 13.7, 5.0 Hz, 1H), 2.43 (qt, *J* = 20.9, 10.6 Hz, 2H), 2.33 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.55, 143.31, 137.06, 136.33, 135.67, 134.35 (q, *J* = 33.0 Hz), 134.30, 133.72, 132.34, 129.18, 129.14, 128.82, 128.76, 128.74, 128.58, 127.87, 126.94, 126.14 (q, *J* = 3.6 Hz), 125.95, 124.71, 123.09 (q, *J* = 273.0 Hz), 60.32, 45.14, 35.01, 34.33, 21.14; **IR** (neat) 3027, 1686, 1595, 1581, 1513, 1495, 1448, 1430, 1348, 1321, 1233, 1163, 1132, 1107, 1062, 1015, 968, 943, 842, 787 cm^{-1}; **HRMS** calcd for $C_{33}H_{30}F_3NO_3S^+$: 578.1971, found: 578.1970.

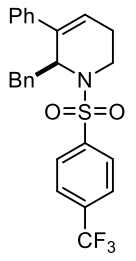


25

(*S*,*E*)-*N*-(4-(4-methoxyphenyl)but-3-en-1-yl)-N-(1-oxo-1,3-diphenylpropan-2-yl)-4-(trifluoromethyl)benzenesulfonamide (25): Purification by flash column chromatography over silica eluting with EtOAc/hexanes (1:4) afforded the desired substrate **25** as a 1.5:1 mixture of *E:Z* isomers. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.83 (t, *J* = 8.4 Hz, 4H), 7.62 (t, *J* = 8.2 Hz, 3H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.39 – 7.34 (m, 2H), 7.19 (qd, *J* = 23.0, 9.5 Hz, 9H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.26 (d, *J* = 15.8 Hz, 1H), 5.89 – 5.83 (m, 1H), 5.79 (ddd, *J* = 17.5, 9.4, 4.9 Hz, 2H), 3.52 – 3.41 (m, 3H), 2.80 – 2.73 (m, 2H), 2.41 (pd, *J* = 13.8, 6.5 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ ^{13}C NMR (176 MHz, cdcl$_3$) δ 196.53, 158.97, 143.31, 136.32, 135.94, 135.66, 134.45, 134.26, 133.72, 133.39, 131.87, 130.30, 129.92, 129.24, 129.14, 128.74, 128.60, 128.58, 128.47, 128.32, 128.14, 127.87, 127.79, 127.52, 127.17, 126.94, 126.78, 126.14 (q, *J* = 3.5 Hz), 125.84, 125.81, 125.80, 123.53, 113.90, 113.52, 60.31, 55.27, 48.69, 45.16, 34.99, 34.30; **IR** (neat) 2919, 1686, 1607, 1512, 1448, 1403, 1320, 1247, 1151, 1129, 1088, 1060, 1031, 1015, 966, 943, 842, 805, 786 cm^{-1}; **HRMS** calcd for $C_{33}H_{30}F_3NO_4S^+$: 594.1920, found: 594.1920.

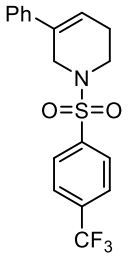
3.3.4 General Procedure for the Carbonyl-Olefin Metathesis Reaction

A microwave vial is charged with a stir bar and $FeCl_3$ (30 mol %) and placed under a nitrogen atmosphere. To the reaction vessel is added a 0.01 M solution of substrate (0.1 mmol) in anhydrous DCE via syringe. The microwave vial is then sealed, and the reaction mixture is heated to 84 °C and allowed to stir for 24 h. The reaction is then cooled to room temperature and flushed through a small silica plug with DCM. The resultant organic mixture is then concentrated under reduced pressure to give the crude product. Purification by flash column chromatography eluting with EtOAc/hexanes (1:9) provided the desired tetrahydropyridine in 47-99% yield.



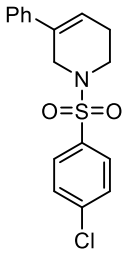
10

(*S*)-6-benzyl-5-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydro-pyridine (10): Purification by flash column chromatography provided **10** as a clear, colorless oil. Spectral data was found to be in accordance with literature data.[3] The reaction was also run on a 1 mmol scale in otherwise identical conditions to provide 88% of the desired product. Furthermore, the reaction could be run on a 0.02 mmol scale with 0.3 eq $FeCl_3$ in toluene (0.01 M) at 84 °C for 24 h and resulted in 75% yield of the metathesis product. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 4.3 Hz, 3H), 7.34 (td, *J* = 8.4, 4.0 Hz, 1H), 7.19 – 7.14 (m, 2H), 7.04 – 6.98 (m, 2H), 5.92 (d, *J* = 2.6 Hz, 1H), 5.21 (d, *J* = 8.5 Hz, 1H), 3.77 (dd, *J* = 14.6, 6.7 Hz, 1H), 3.19 – 3.11 (m, 1H), 2.88 (dd, *J* = 14.3, 3.7 Hz, 1H), 2.73 (dd, *J* = 14.3, 9.4 Hz, 1H), 2.36 – 2.24 (m, 1H), 2.09 – 2.03 (m, 1H).; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.32, 139.48, 139.24, 137.73, 133.61 (q, *J* = 35.1 Hz), 129.31, 128.85, 128.33, 128.03, 127.82, 127.32, 126.56, 126.23, 125.84 (q, *J* = 3.7 Hz), 123.92, 122.54 (q, *J* = 255.1 Hz), 56.74, 39.01, 37.66, 24.37; **IR** (neat) 3028, 2927, 1607, 1495, 1454, 1403, 1321, 1162, 1130, 1107, 1096, 1062, 1016, 973, 957, 911, 880, 845 cm^{-1}; **HRMS** calcd for $C_{25}H_{22}F_3NO_2S^+$: 458.1396, found: 458.1396.



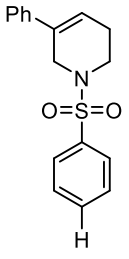
28

5-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydropyridine (28): Purification by flash column chromatography provided as **28** a clear, colorless oil. Spectral data was found to be in accordance with literature data.[3] **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.96 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 8.3 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.28 (t, J = 8.9 Hz, 3H), 6.12 – 6.05 (m, 1H), 4.00 (s, 2H), 3.31 (t, J = 5.8 Hz, 2H), 2.39 (qd, J = 6.1, 2.6 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.39, 138.40, 134.58 (q, *J* = 33.1 Hz), 133.22, 128.59, 128.04, 127.88, 126.29 (q, *J* = 3.7 Hz), 125.17, 122.16, 46.31, 42.32, 25.46; **IR** (neat) 2925, 1404, 1347, 1322, 1169, 1132, 1107, 1062, 970, 90, 845 cm^{-1}; **HRMS** calcd for $C_{18}H_{16}F_3NO_2S^{+H}$: 368.0927, found: 368.0921.



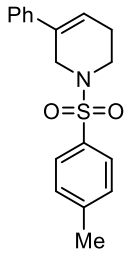
15 PDT

1-((4-chlorophenyl)sulfonyl)-5-phenyl-1,2,3,6-tetrahydropyridine (15 PDT): Purification by flash column chromatography provided **15 PDT** as a clear, slightly yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.36 – 7.30 (m, 2H), 7.28 (t, *J* = 5.6 Hz, 3H), 6.10 – 6.04 (m, 1H), 3.97 (d, *J* = 2.0 Hz, 2H), 3.28 (t, *J* = 5.8 Hz, 2H), 2.39 (d, *J* = 3.5 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.37, 138.54, 135.23, 133.33, 129.40, 128.99, 128.57, 127.81, 125.19, 122.16, 46.35, 42.31, 25.49.; **IR** (neat) 2833, 1585, 1495, 1476, 1446, 1394, 1343, 1278, 1204, 1166, 1097, 1010, 969, 900, 829, 797 cm^{-1}; **HRMS** calcd for $C_{17}H_{16}ClNO_2S^{+Na}$: 356.0482, found: 356.0469.



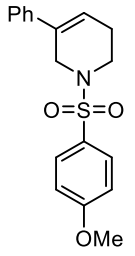
16 PDT

5-phenyl-1-(phenylsulfonyl)-1,2,3,6-tetrahydropyridine (16 PDT): Purification by flash column chromato-graphy provided **10** as a clear oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.0 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.36 – 7.27 (m, 5H), 6.07 (tt, *J* = 3.9, 1.8 Hz, 1H), 3.97 (dd, *J* = 4.5, 2.4 Hz, 2H), 3.27 (t, *J* = 5.8 Hz, 2H), 2.39 (qd, *J* = 6.1, 2.6 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.67, 136.54, 133.44, 132.77, 129.07, 128.53, 127.73, 127.62, 125.20, 122.17, 77.32, 77.00, 76.68, 46.37, 42.35, 25.59.**IR** (neat) 2921, 1495, 1446, 1342, 1169, 1098, 1011, 969, 899, 854, 744 cm^{-1}; **HRMS** calcd for $C_{17}H_{17}NO_2S^{+Na}$: 322.0872, found: 322.0859.



17 PDT

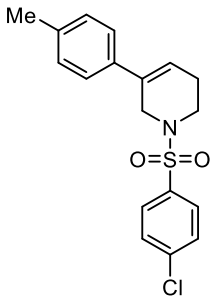
5-phenyl-1-tosyl-1,2,3,6-tetrahydropyridine (17 PDT): Purification by flash column chromatography provided **17 PDT** as a clear, colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.37 – 7.26 (m, 7H), 6.07 (tt, *J* = 3.8, 1.8 Hz, 1H), 3.94 (dd, *J* = 4.5, 2.3 Hz, 2H), 3.24 (t, *J* = 5.8 Hz, 2H), 2.43 (s, 3H), 2.39 (td, *J* = 5.8, 3.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.58, 138.72, 133.47, 133.41, 129.67, 128.50, 127.69, 125.20, 122.15, 46.39, 42.34, 25.63, 21.51; **IR** (neat) 2920, 1597, 1493, 1446, 1341, 1305, 1267, 1240, 1164, 1097, 1010, 979, 853, 816, 757 cm^{-1}; **HRMS** calcd for $C_{18}H_{19}NO_2S^{+Na}$: 336.1029, found: 336.0993.



18 PDT

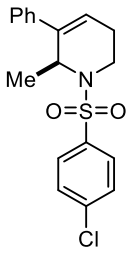
1-((4-methoxyphenyl)sulfonyl)-5-phenyl-1,2,3,6-tetrahydropyridine (18 PDT): Purification by flash column chromatography provided **18 PDT** as a clear, colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.6 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.30 – 7.24 (m, 4H), 6.99 (d, *J* = 8.5 Hz, 2H), 6.07 (d, *J* = 1.5 Hz, 1H), 3.94 (s, 2H), 3.86 (s, 3H), 3.24 (t, *J* = 5.6 Hz, 2H), 2.39 (s, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 163.00, 138.74, 133.49, 129.76, 128.50, 128.05, 127.68, 125.20, 122.16, 114.21, 55.58, 46.41, 42.34, 25.62.; **IR** (neat) 2921, 2814, 1596, 1577, 1460, 1446, 1340, 1306, 1260, 1179, 1098, 1013, 1025,

969, 900, 835, 805, 757 cm^{-1}; **HRMS** calcd for $C_{18}H_{19}NO_3S^{+Na}$: 352.0978, found: 352.0976.



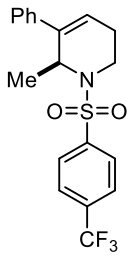
30

1-((4-chlorophenyl)sulfonyl)-5-(p-tolyl)-1,2,3,6-tetrahydropyridine (30): Purification by flash column chromatography provided **30** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.15 (dd, *J* = 20.8, 8.1 Hz, 4H), 6.03 (m, 1H), 3.95 (q, *J* = 2.0 Hz, 2H), 3.27 (t, *J* = 5.8 Hz, 2H), 2.37 (m, *J* = 3.4 Hz, 2H), 2.34 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.33, 137.65, 135.20, 133.10, 129.37, 129.23, 128.99, 125.03, 121.31, 46.36, 42.33, 25.44, 21.07; **IR** (neat) 2921, 1586, 1513, 1475, 1460, 1394, 1343, 1278, 1242, 1166, 1097, 1087, 1020, 972, 900, 812, 762 cm^{-1}; **HRMS** calcd for $C_{18}H_{18}ClNO_2S^{+Na}$: 370.0639, found: 370.0629.



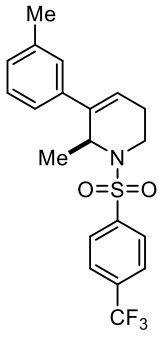
31

(*S*)-1-((4-chlorophenyl)sulfonyl)-6-methyl-5-phenyl-1,2,3,6-tetrahydropyridine (31): Purification by flash column chromatography provided **31** as a clear, yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.6 Hz, 2H), 5.77 (d, *J* = 3.9 Hz, 1H), 5.01 (q, *J* = 6.5 Hz, 1H), 3.91 (dd, *J* = 14.2, 6.5 Hz, 1H), 3.26 (ddd, *J* = 14.3, 11.9, 4.8 Hz, 1H), 2.18 – 2.08 (m, 1H), 2.03 (dt, *J* = 18.2, 5.2 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 140.35, 139.93, 139.22, 138.72, 129.22, 128.60, 128.17, 127.65, 126.11, 122.44, 50.86, 37.03, 24.44, 19.31; **IR** (neat) 2932, 1688, 1584, 1404, 1475, 1446, 1393, 1338, 1276, 1207, 1154, 1089, 1012, 1000, 953, 907, 868, 829, 755 cm^{-1}; **HRMS** calcd for $C_{18}H_{18}ClNO_2S^{+Na}$: 370.0639, found: 370.0643.



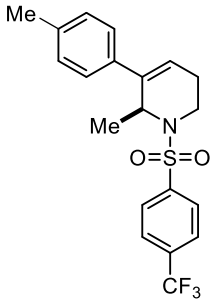
27

(*S*)-6-methyl-5-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydro-pyridine (27): Purification by flash column chromatography provided **27** as a clear, colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 14.9 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.26 (dd, *J* = 6.5, 1.6 Hz, 2H), 5.78 (d, *J* = 4.2 Hz, 1H), 5.05 (q, *J* = 6.6 Hz, 1H), 3.94 (dd, *J* = 14.2, 6.5 Hz, 1H), 3.29 (ddd, *J* = 14.0, 11.9, 4.8 Hz, 1H), 2.16 – 2.03 (m, 2H), 1.22 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 145.07, 140.40, 139.15, 134.08 (q, *J* = 33.2 Hz), 128.69, 128.94 – 123.87 (m), 127.78, 127.24, 126.17 (q, *J* = 272.9), 122.44, 51.08, 37.17, 24.59, 19.39; **IR** (neat) 3028, 2927, 1607, 1495, 1454, 1403, 1321, 1162, 1130, 1107, 1096, 1062, 1016, 973, 957, 911, 880, 845 cm^{-1}; **HRMS** calcd for $C_{19}H_{18}F_3NO_2S^{+Na}$: 404.0903, found: 404.1003.



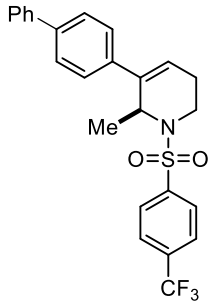
36

(*S*)-6-methyl-5-(m-tolyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydro-pyridine (36): Purification by flash column chromatography provided **36** as a clear, colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 6.7 Hz, 2H), 5.76 (d, *J* = 3.3 Hz, 1H), 5.04 (q, *J* = 6.3 Hz, 1H), 3.93 (dd, *J* = 14.0, 6.4 Hz, 1H), 3.28 (ddd, *J* = 14.2, 11.9, 4.8 Hz, 1H), 2.36 (s, 3H), 2.12 – 2.01 (m, 2H), 1.22 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) 45.10, 140.47, 139.14, 138.32, 134.07 (q, *J* = 33.2 Hz), 128.56, 128.55, 127.24, 126.89, 126.16 (dd, *J* = 7.3, 3.6 Hz), 123.26, 122.18, 121.69 (q, *J* = 296.7 Hz), 51.14, 37.19, 24.57, 21.47, 19.43.; **IR** (neat) 2933, 1607, 1403, 1322, 1165, 1134, 1107, 1062, 1016, 843, 785 cm^{-1}; **HRMS** calcd for $C_{20}H_{20}F_3NO_2S^{+}$: 396.1240, found: 396.1230.



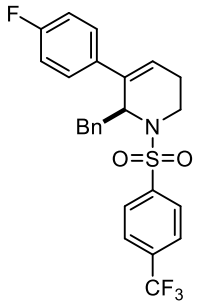
38

(*S*)-6-methyl-5-(m-tolyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetra-hydropyridine (38): Purification by flash column chromatography provided **38** as a clear, colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.16 (s, 3H), 5.74 (s, 1H), 5.04 (q, *J* = 6.4 Hz, 1H), 3.93 (dd, *J* = 14.3, 6.2 Hz, 1H), 3.32 – 3.24 (m, 1H), 2.35 (s, 3H), 2.11 – 1.99 (m, 2H), 1.22 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 145.08, 140.11, 137.62, 136.22, 134.03 (q, *J* = 33.1 Hz), 129.36, 127.22, 126.14 (q, *J* = 3.6 Hz), 125.96, 123.22 (q, *J* = 273.0), 121.65, 121.59, 51.07, 37.19, 24.52, 21.07, 19.41; **IR** (neat) 2927, 1607, 1457, 1403, 1320, 1214, 1164, 1130, 1107, 1061, 1017, 1004, 966, 880, 843, 785 cm^{-1}; **HRMS** calcd for $C_{20}H_{20}F_3NO_2S^+$: 396.1240, found: 396.1220.



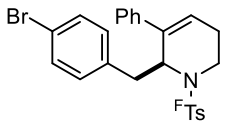
40

(S)-5-([1,1'-biphenyl]-4-yl)-6-methyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydropyridine (40): Purification by flash column chromatography provided **33** as a clear oil, colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.59 (dd, *J* = 10.7, 8.0 Hz, 3H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 8.7 Hz, 3H), 5.85 (s, 1H), 5.10 (q, *J* = 6.6 Hz, 1H), 3.95 (dd, *J* = 14.2, 6.4 Hz, 1H), 3.31 (ddd, *J* = 14.2, 11.9, 4.8 Hz, 1H), 2.16 – 2.05 (m, 2H), 1.27 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 145.06, 140.68, 140.37, 139.90, 137.92, 134.08 (q *J* = 33.1 Hz), 128.81, 127.45, 127.35, 127.24, 126.94, 126.17 (q, *J* = 3.7 Hz), 126.45, 122.43, 50.97, 37.17, 24.64, 19.46.; **IR** (neat) 2927, 1608, 1488, 1448, 1403, 1340, 1322, 1168, 1130, 1107, 1062, 1017, 1000, 956, 909, 871, 843, 827, 789 cm^{-1}; **HRMS** calcd for $C_{25}H_{22}F_3NO_2S^+$: 458.1396, found: 458.1395.



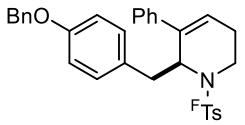
42

(*S*)-6-benzyl-5-(4-fluorophenyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydropyridine (42): Purification by flash column chromatography provided **42** as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 – 7.50 (m, 4H), 7.39 – 7.34 (m, 2H), 7.19 – 7.13 (m, 3H), 7.09 (t, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 6.9 Hz, 2H), 5.88 (d, *J* = 2.8 Hz, 1H), 5.14 (d, *J* = 8.5 Hz, 1H), 3.76 (dd, *J* = 14.5, 6.8 Hz, 1H), 3.20 – 3.12 (m, 1H), 2.85 (dd, *J* = 14.3, 3.9 Hz, 1H), 2.71 (dd, *J* = 14.3, 9.4 Hz, 1H), 2.62 (s, 1H), 2.41 – 2.28 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.43 (d, *J* = 247.1 Hz), 144.21, 138.51, 137.64, 135.68, 133.70 (q, *J* = 33.2 Hz), 133.09, 129.77, 129.26, 128.41, 127.94, 127.88, 127.34, 126.65, 125.87 (q, *J* = 3.6 Hz), 124.05, 115.76 (d, *J* = 21.5 Hz), 56.91, 39.03, 37.63, 24.46; **IR** (neat) 2927, 1685, 1602, 1508, 1454, 1403, 1322, 1262, 1232, 1160, 1131, 1107, 1062, 1017, 974, 958, 829, 786 cm^{-1}; **HRMS** calcd for $C_{25}H_{21}F_4NO_2S^{+Na}$: 498.1121, found: 498.1127.



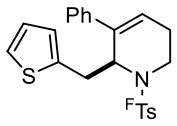
44

(*S*)-6-(4-bromobenzyl)-5-phenyl-1-(tosyl-l2-fluoraneyl)-1,2,3,6-tetrahydropyridine (44): Purification by flash column chromatography provided **44** as a clear, colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.37 – 7.31 (m, 4H), 7.29 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.1 Hz, 2H), 5.90 (d, *J* = 2.9 Hz, 1H), 5.16 (d, *J* = 8.4 Hz, 1H), 3.80 (dd, *J* = 14.5, 6.7 Hz, 1H), 3.14 – 3.07 (m, 1H), 2.83 (dd, *J* = 14.4, 3.8 Hz, 1H), 2.70 (dd, *J* = 14.4, 9.2 Hz, 1H), 2.27 – 2.19 (m, 1H), 2.06 – 1.98 (m, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 144.36, 139.34, 138.93, 136.68, 131.43, 131.08, 128.94, 127.96, 127.28, 126.23, 125.96, 124.16, 120.58, 56.56, 38.60, 37.78, 24.26; **IR** (neat) 2937, 1688, 1488, 1446, 1403, 1322, 1163, 1132, 1107, 1062, 1012, 959, 843, 809, 760 cm^{-1}; **HRMS** calcd for $C_{25}H_{21}BrF_3NO_2S^{+}$: 536.0501, found: 536.0502.



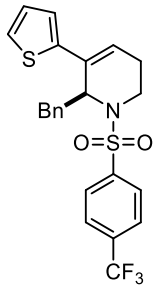
46

(*S*)-6-(4-(benzyloxy)benzyl)-5-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydro-pyridine (46): Purification by flash column chromatography provided **46** as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.35 (m, 3H), 7.33 – 7.27 (m, 6H), 7.21 (d, *J* = 7.7 Hz, 4H), 6.75 (s, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 6.54 (d, *J* = 7.9 Hz, 1H), 5.85 (s, 1H), 5.14 (s, 1H), 4.55 (s, 1H), 3.88 (d, *J* = 3.7 Hz, 2H), 3.74 (dd, *J* = 14.6, 6.8 Hz, 1H), 3.05 – 2.93 (m, 1H), 2.79 (dd, *J* = 14.4, 4.0 Hz, 1H), 2.65 (dd, *J* = 14.4, 8.6 Hz, 1H), 2.26 – 2.14 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 152.39, 144.62, 139.84, 139.53, 139.04, 131.85, 129.91, 128.83, 128.73, 128.61, 128.59, 127.77, 127.29, 126.91, 126.35, 126.26, 125.82 (q, *J* = 3.8 Hz) 124.01, 115.57, 56.70, 38.27, 37.86, 36.23, 24.37; **IR** (neat) 3029, 2925, 1685, 1609, 1511, 1495, 1453, 1403, 1322, 1262, 1163, 1133, 1107, 1062, 1016, 984, 843, 758 cm^{-1}; **HRMS** calcd for $C_{32}H_{28}F_3NO_3S^+$: 564.1815, found: 564.1813.



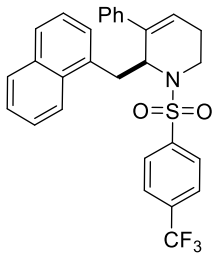
48

(*S*)-5-phenyl-6-(thiophen-2-ylmethyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydro-pyridine (48): Purification by flash column chromatography provided **48** as a clear, yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.23 – 7.14 (m, 3H), 6.96 (d, *J* = 3.4 Hz, 1H), 6.91 – 6.87 (m, 1H), 5.87 (s, 1H), 3.70 (d, *J* = 13.5 Hz, 1H), 3.25 (d, *J* = 15.3 Hz, 1H), 2.97 (dd, *J* = 26.5, 15.2 Hz, 2H), 2.10 (d, *J* = 14.5 Hz, 1H), 1.70 – 1.63 (m, 2H), 1.61 – 1.55 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) ^{13}C NMR (176 MHz, cdcl$_3$) δ 149.62, 144.56, 139.63, 138.85, 133.73 (d, *J* = 32.7 Hz), 128.31, 127.48, 127.39, 126.84, 125.96 (d, *J* = 3.7 Hz), 125.31, 124.42, 123.98, 123.60, 49.17, 48.20, 40.99, 21.49; **IR** (neat) 2919, 1403, 1322, 1163, 1130, 1107, 1062, 1015, 842, 711 cm^{-1}; **HRMS** calcd for $C_{23}H_{20}F_3NO_2S_2^+$: 464.0960, found: 464.0955.



50

(*S*)-6-benzyl-5-(thiophen-2-yl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydropyridine (50): Purification by flash column chromatography provided **50** as a clear, yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.38 (m, 4H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 5.0 Hz, 1H), 6.84 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.69 (d, *J* = 3.1 Hz, 1H), 5.93 (d, *J* = 3.8 Hz, 1H), 5.20 (d, *J* = 7.9 Hz, 1H), 3.80 (dd, *J* = 14.5, 6.7 Hz, 1H), 3.10 (dd, *J* = 15.4, 3.9 Hz, 1H), 3.03 (ddd, *J* = 14.6, 12.0, 4.8 Hz, 1H), 2.98 (dd, *J* = 15.4, 8.4 Hz, 1H), 2.25 – 2.16 (m, 1H), 2.01 (dt, *J* = 18.3, 5.0 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ ^{13}C NMR (176 MHz, cdcl$_3$) δ 144.56, 139.25, 139.14, 138.43, 133.85 (q, *J* = 33.0 Hz), 128.89, 127.95, 127.38, 126.89, 126.41, 126.31, 125.97 (q, *J* = 3.7 Hz), 124.49, 124.44, 124.02, 123.25 (q, *J* = 272.8 Hz), 122.47, 56.50, 37.89, 33.31, 24.25; **IR** (neat) 2921, 1404, 1323, 1165, 1132, 1107, 1094, 1062, 1016, 851, 764 cm^{-1}; **HRMS** calcd for $C_{23}H_{20}F_3NO_2S_2^{+Na}$: 486.0780, found: 486.0852.



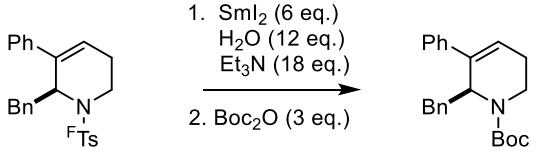
52

(*S*)-6-(naphthalen-1-ylmethyl)-5-phenyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6-tetrahydro-pyridine (52): Purification by flash column chromatography provided **52** as a clear oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.47 – 7.35 (m, 7H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 6.9 Hz, 1H), 5.96 (d, *J* = 2.7 Hz, 1H), 5.25 (d, *J* = 9.7 Hz, 1H), 4.00 (dd, *J* = 14.3, 6.7 Hz, 1H), 3.51 – 3.44 (m, 1H), 3.31 (dd, *J* = 14.8, 3.5 Hz, 1H), 3.08 (dd, *J* = 14.7, 10.5 Hz, 1H), 2.54 – 2.47 (m, 1H), 2.20 (dt, *J* = 18.2, 4.8 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 143.73, 140.27, 140.09, 133.09 (q, *J* = 32.8 Hz), 133.76, 133.60, 131.72, 128.90, 128.79, 127.92, 127.83, 127.49, 126.68, 126.62, 125.93, 125.46, 125.31 (q, *J* = 3.7 Hz), 125.09, 124.12, 123.18 (q, *J* = 272.8 Hz), 123.08, 56.55, 37.72, 35.94, 24.95.; **IR** (neat) 3057, 2937, 1597, 1511, 1444, 1403, 1320,

1157, 1129, 1095, 1081, 1061, 1017, 971, 954, 915, 884, 873, 840, 796 cm^{-1}; **HRMS** calcd for $C_{29}H_{24}F_3NO_2S^{+Na}$: 530.1372, found: 530.1380.

3.3.5 Deprotection of the Carbonyl-Olefin Metathesis Product with SmI_2

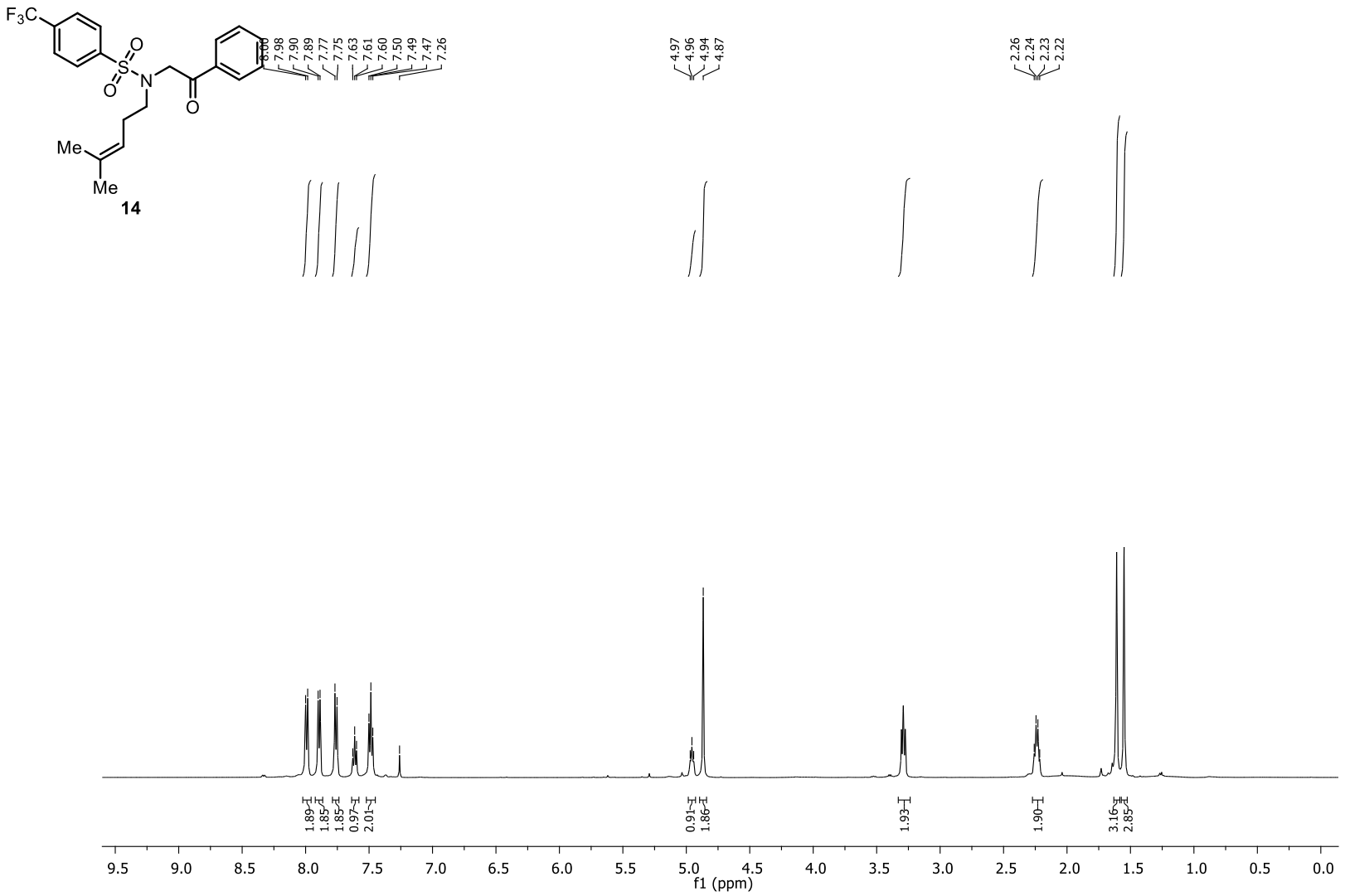
A 0.13M solution of SmI_2 is prepared with samarium metal a diiodoethane according to previously reported procedures.[6] The carbonyl-olefin metathesis product **6** (0.1 mmol) is added to a flame-dried round-bottom flask equipped with a stir bar and placed under a nitrogen atmosphere. The SmI_2 solution (6.0 equiv) is then added to the flask while stirring. Next, a degassed solution of water (12.0 equiv) is added to the reaction mixture, which immediately turns red. The reaction is allowed to stir for 3 min, at which point triethylamine (18.0 equiv) is added. After an additional 3 minutes, the reaction mixture is filtered under nitrogen over a celite plug. The crude product is collected into a flask charged with a stir bar and Boc_2O (2.5 equiv). The mixture is then heated to 50 °C and allowed to stir for 12 h. Once the reaction is complete, the mixture is concentrated under reduced pressure give the crude product. Purification by flash column chromatography eluting with EtOAc/hexanes (1:10) provided the desired carbamate **19** in 92% yield.

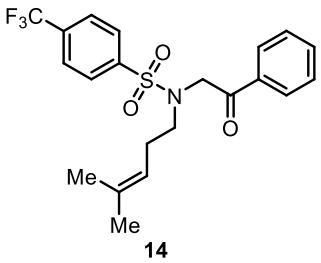


9 **27**

tert-butyl (*S*)-6-benzyl-5-phenyl-3,6-dihydropyridine-1(2H)-carboxylate (27): Purification by flash column chromatography provided **27** as a mixture of rotamers. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 13.0, 6.7 Hz, 5H), 7.37 – 7.27 (m, 3H), 7.23 (d, *J* = 7.4 Hz, 3H), 7.18 (dd, *J* = 13.7, 7.2 Hz, 3H), 7.13 (d, *J* = 7.2 Hz, 1H), 7.06 (d, *J* = 7.1 Hz, 3H), 6.04 (d, *J* = 4.3 Hz, 1H), 5.99 (d, *J* = 3.0 Hz, 1H), 5.41 (s, 1H), 5.19 (d, *J* = 9.1 Hz, 1H), 4.28 (dd, *J* = 13.3, 6.5 Hz, 1H), 3.95 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.94 (ddd, *J* = 20.2, 14.5, 4.0 Hz, 2H), 2.74 (tdd, *J* = 23.4, 16.4, 6.9 Hz, 3H), 2.48 – 2.38 (m, 1H), 2.32 (s, 1H), 2.13 (dt, *J* = 18.0, 4.6 Hz, 1H), 2.01 (d, *J* = 17.8 Hz, 1H), 1.40 – 1.32 (m, 4H), 1.19 (d, *J* = 16.3 Hz, 9H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.44, 154.39, 140.03, 139.87, 139.02, 138.46, 129.83, 129.42, 128.73, 128.59, 128.23, 127.49, 126.58, 126.34, 126.13, 124.79, 79.37, 55.34, 53.47, 38.26, 34.94, 28.56, 28.40, 28.01, 25.58; **IR** (neat) 2975, 2827, 1689, 1494, 1453, 1417, 1390, 1364, 1311, 1245, 1212, 1167, 1116, 1077, 1031, 1011, 862, 749 cm^{-1}; **HRMS** calcd for $C_{23}H_{27}NO_2^{+Na}$: 372.1934, found: 372.1933.

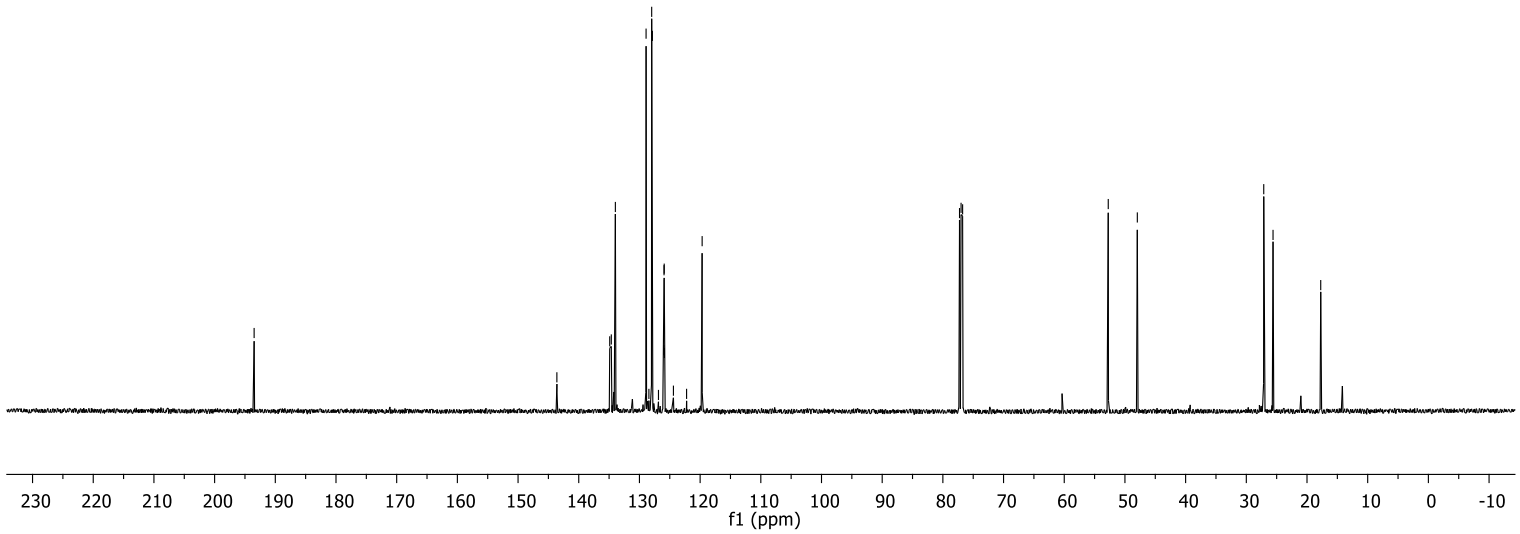
3.4 ^{1}H and ^{13}C NMR Spectra

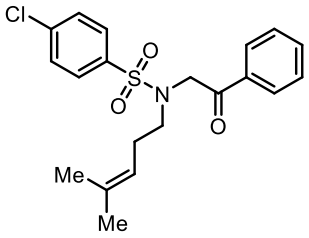




14

193.49
143.60
134.89
134.64
133.97
128.90
128.44
127.98
127.87
126.86
125.98
125.95
125.92
125.89
124.40
122.23
119.67
77.26
77.00
76.75
52.75
47.96
27.13
25.60
17.74





15

7.91
7.89
7.81
7.79
7.62
7.60
7.58
7.49
7.47
7.45
7.26
4.97
4.95
4.93
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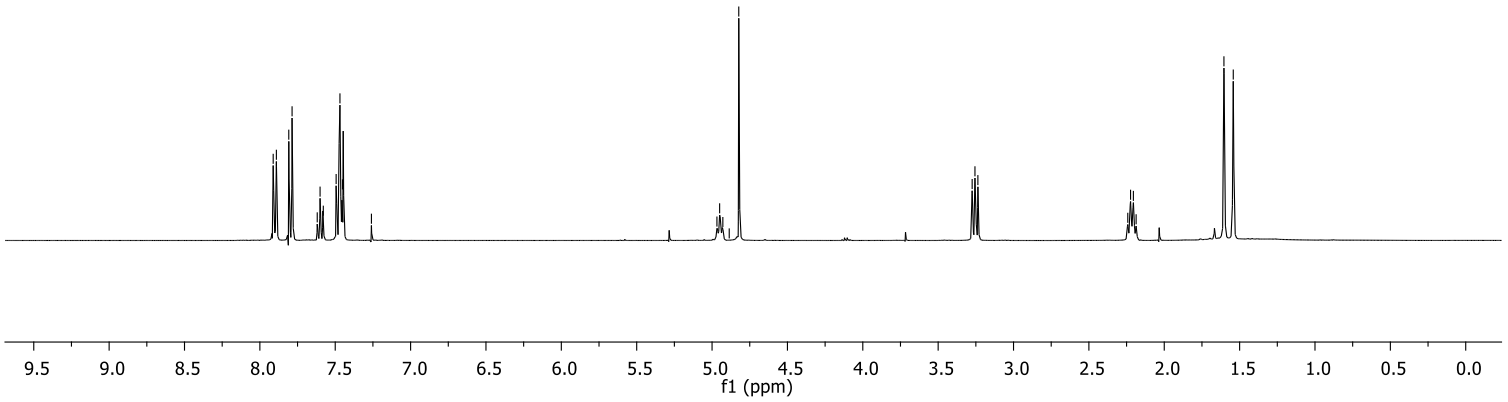
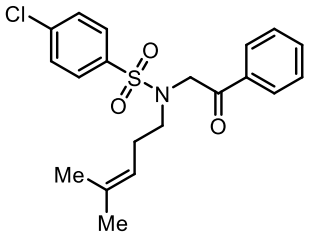
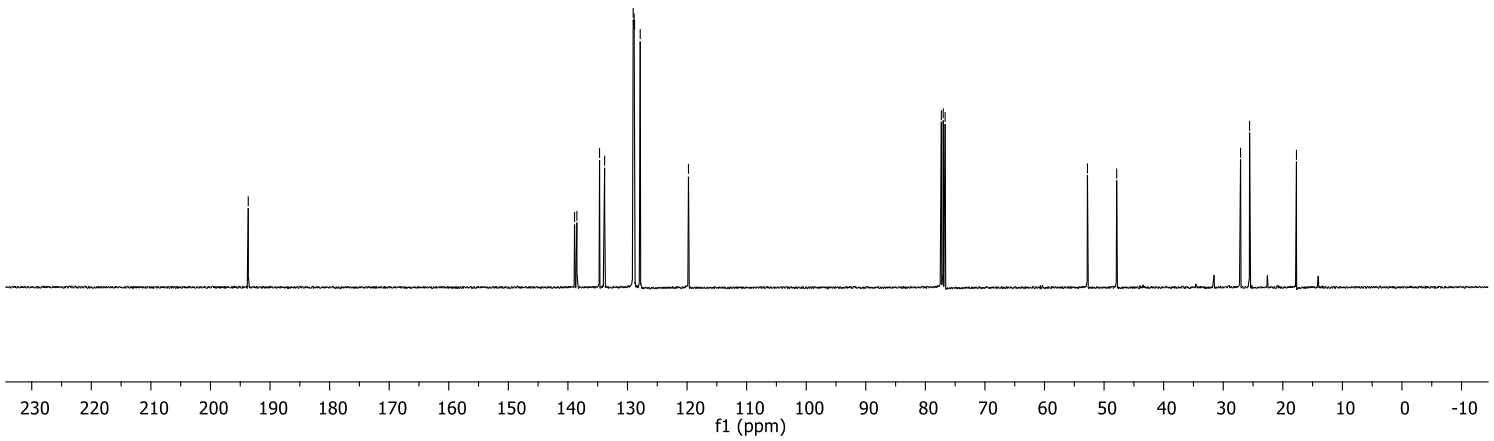
2.24
2.22
2.20
2.19
1.60
1.54

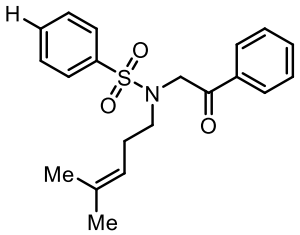




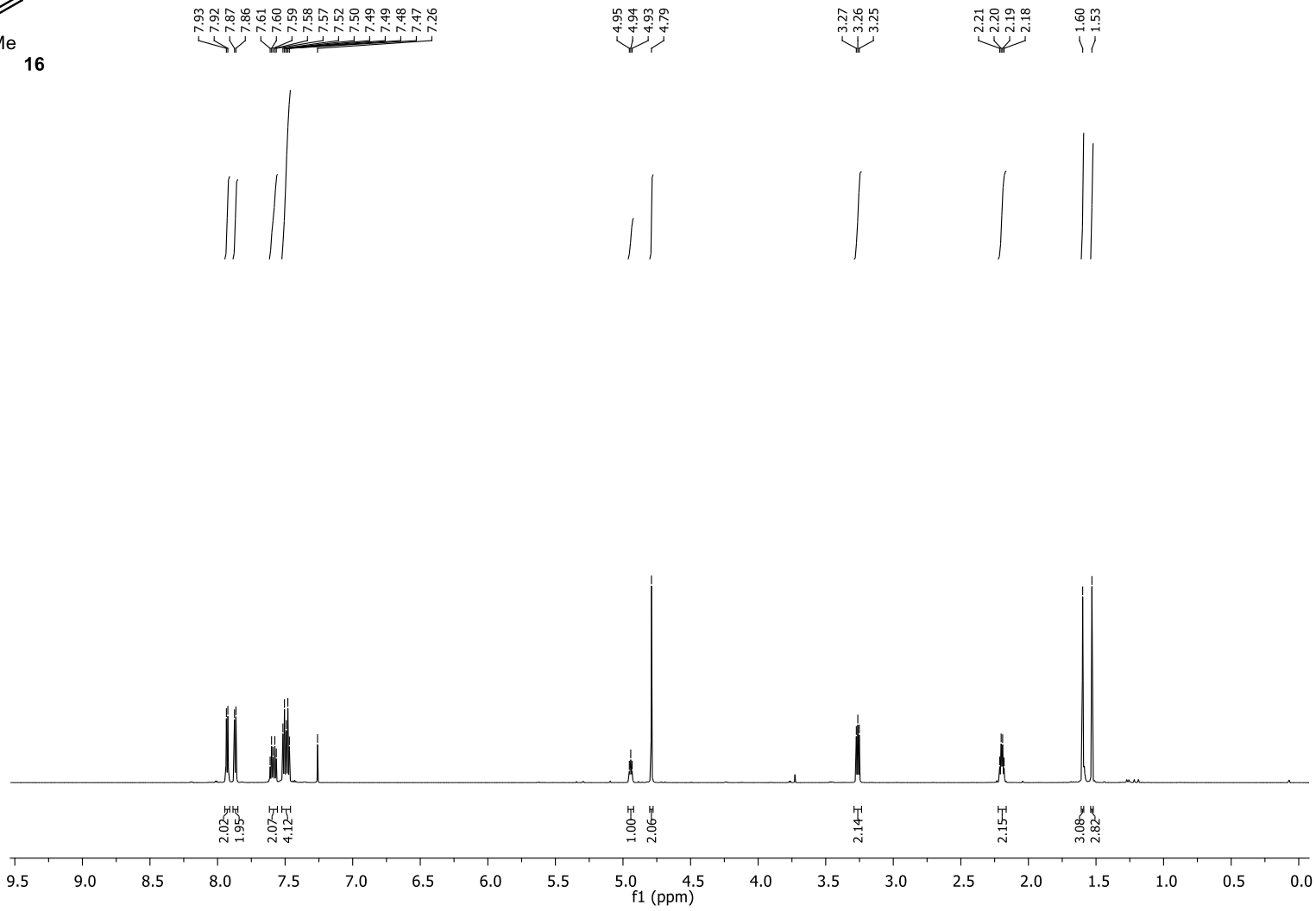
15

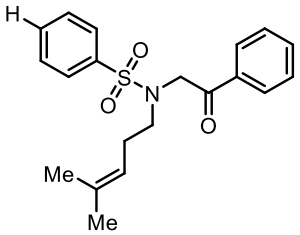
193.66
138.89
138.50
134.69
133.84
129.04
128.89
128.82
127.86
119.76
77.32
77.00
76.68
52.79
47.88
27.09
25.58
17.71




H
O
S
O
N
O
Me
Me

16


7.93
7.92
7.87
7.86
7.61
7.60
7.59
7.58
7.57
7.52
7.50
7.49
7.49
7.48
7.47
7.26
4.95
4.94
4.93
4.79
3.27
3.26
3.25
2.21
2.20
2.19
2.18
1.60
1.53
2.02
1.95
2.07
4.12
1.00
2.06
2.14
2.15
3.08
2.82
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



16

193.85
139.83
134.85
134.55
133.73
132.52
128.84
128.79
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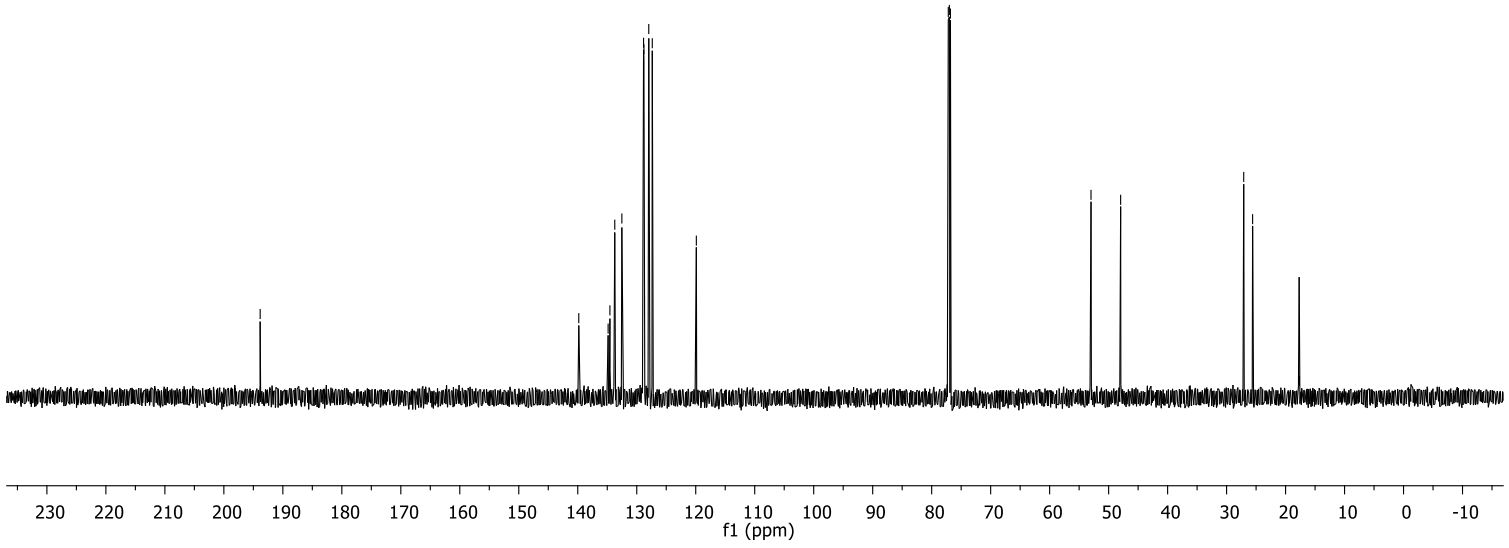
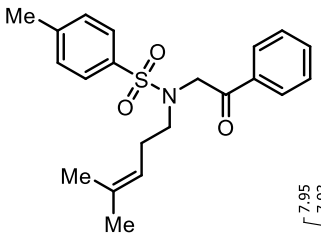
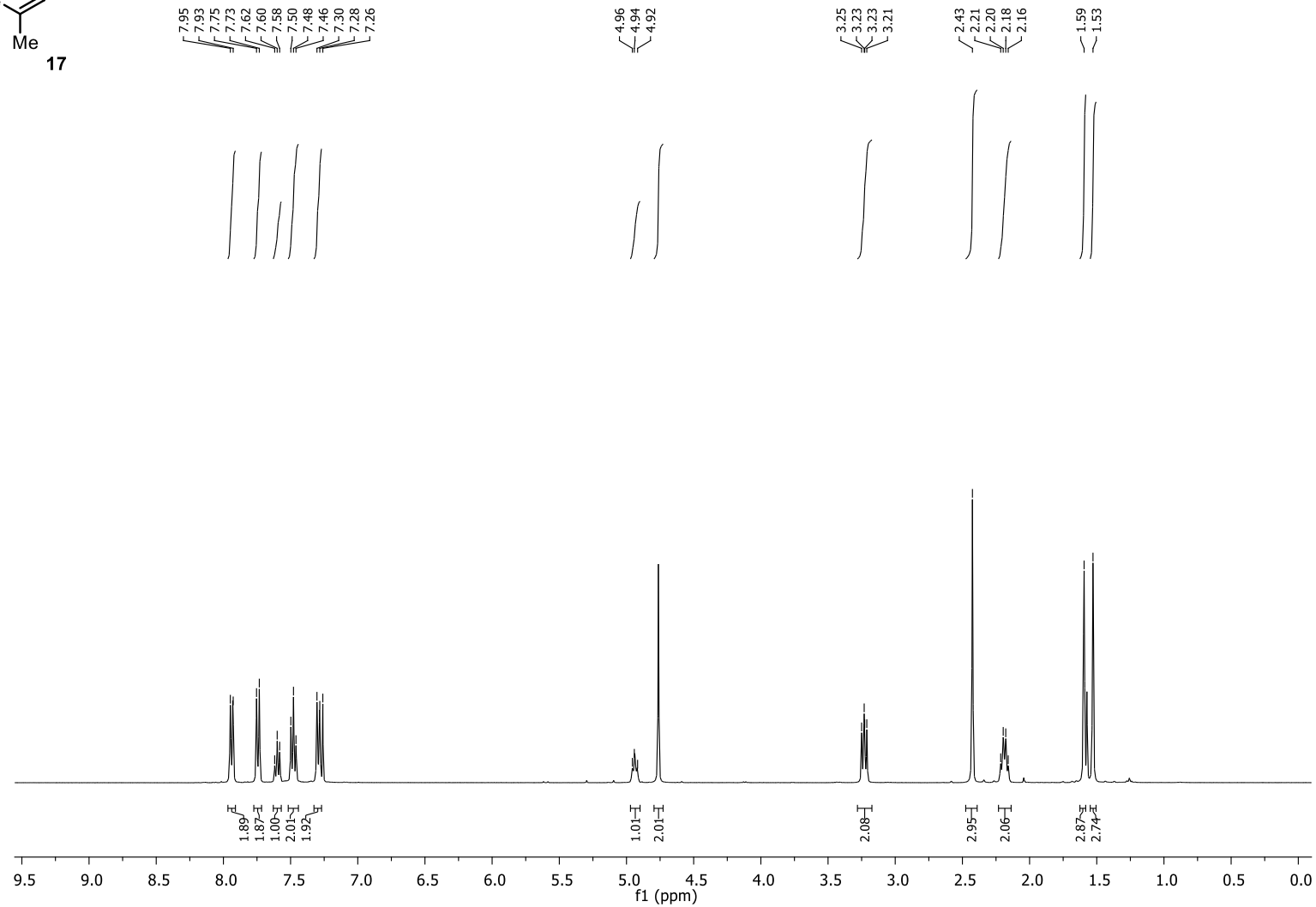
127.37
119.90
77.18
77.00
76.82
52.98
47.96
27.10
25.59
17.65




Me
O
S
O
N
O
Me
Me

17


7.95
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7.58
7.50
7.48
7.46
7.30
7.28
7.26
4.96
4.94
4.92
3.25
3.23
3.23
3.21
2.43
2.21
2.20
2.18
2.16
1.59
1.53
1.89
1.87
1.00
2.01
1.92
1.01
2.01
2.08
2.95
2.06
2.87
2.74
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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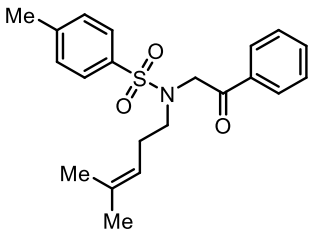
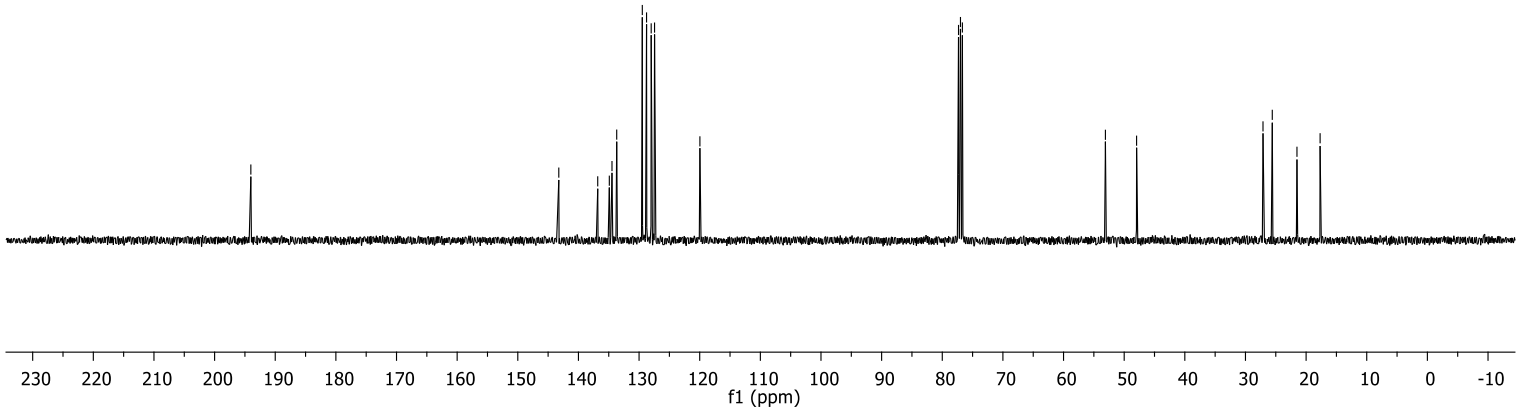
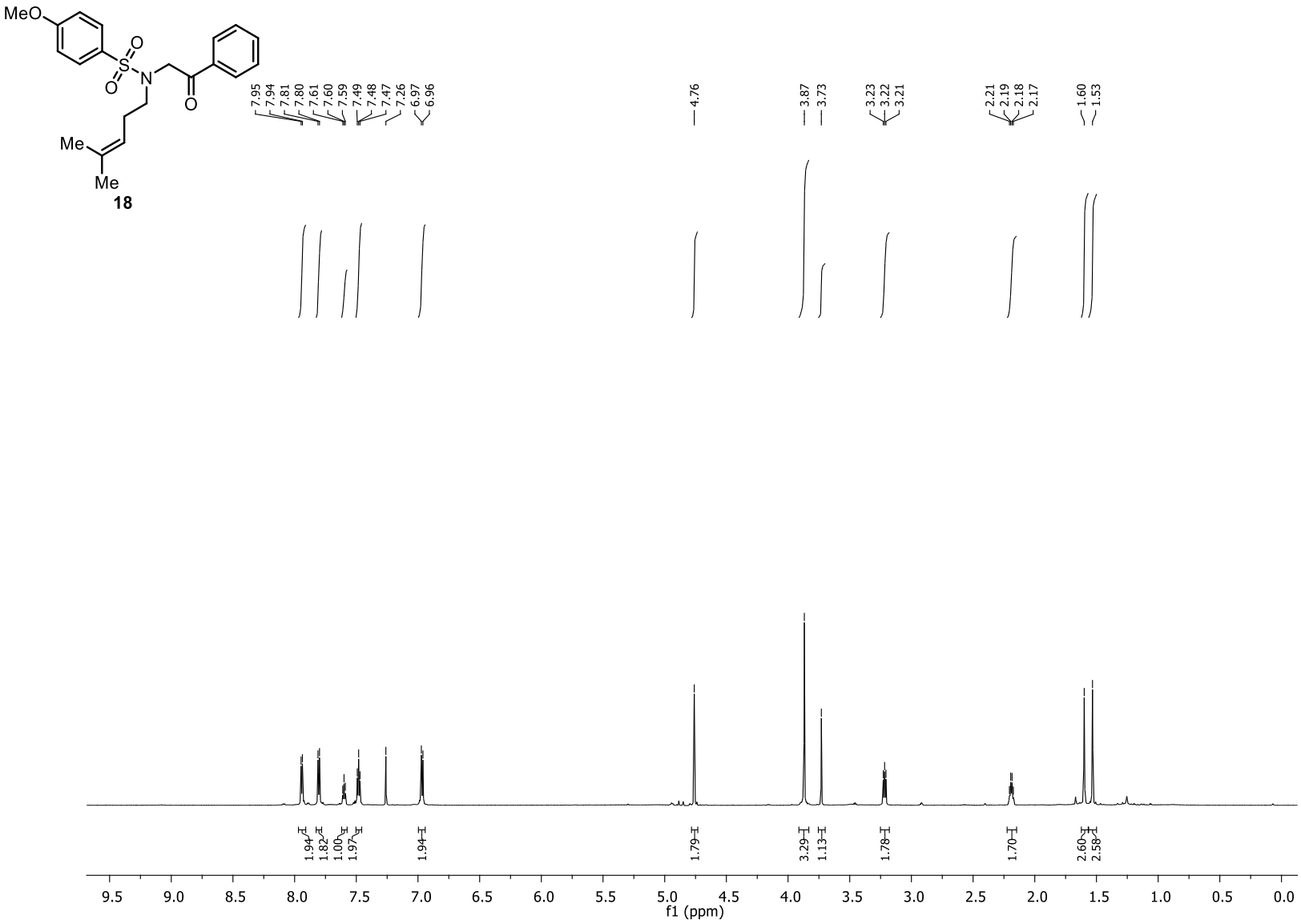
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



17

194.02
143.24
134.46
133.69
129.47
128.77
128.00
127.45
119.97
77.32
77.00
76.68
53.10
47.95
27.11
25.58
21.51
17.69




MeO
O
S
O
N
O
Me
Me
18
7.95
7.94
7.81
7.80
7.61
7.60
7.59
7.49
7.48
7.47
7.26
6.97
6.96
4.76
3.87
3.73
3.23
3.22
3.21
2.21
2.19
2.18
2.17
1.60
1.53
1.94
1.82
1.00
1.97
1.94
1.79
3.29
1.13
1.78
1.70
2.60
2.58
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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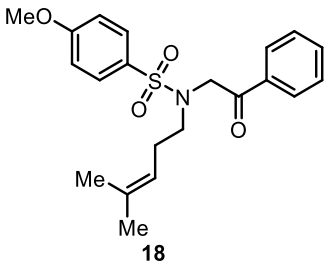
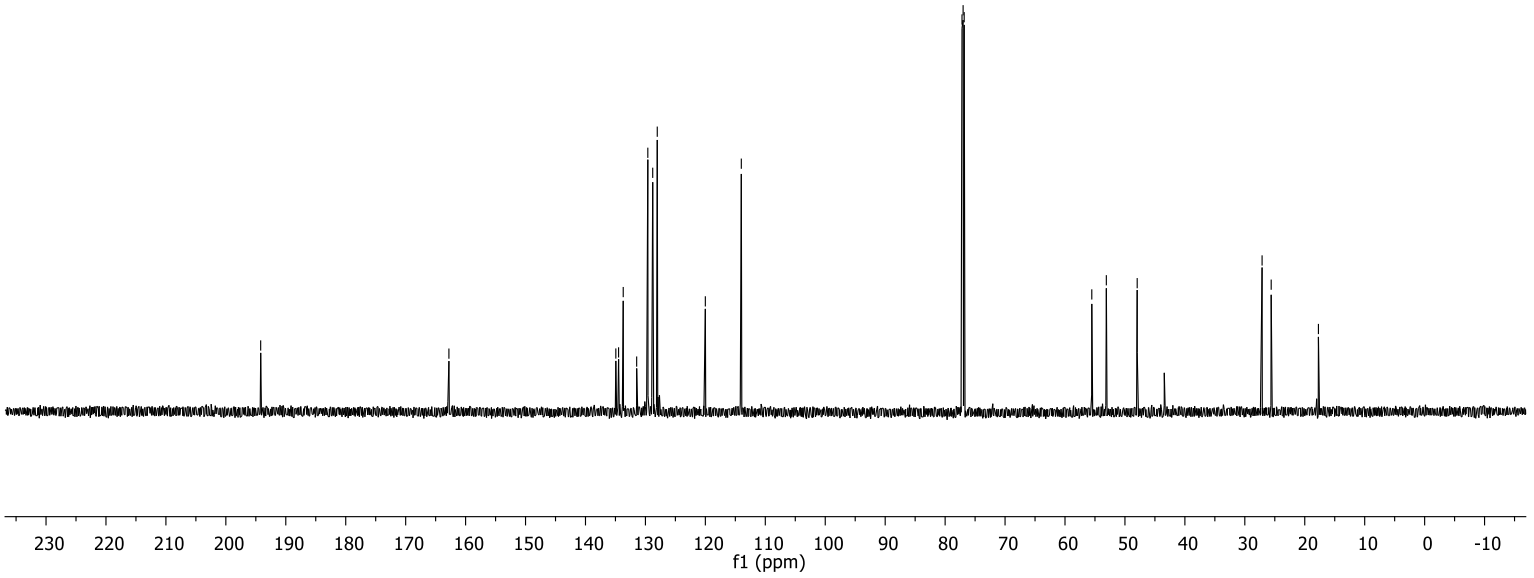
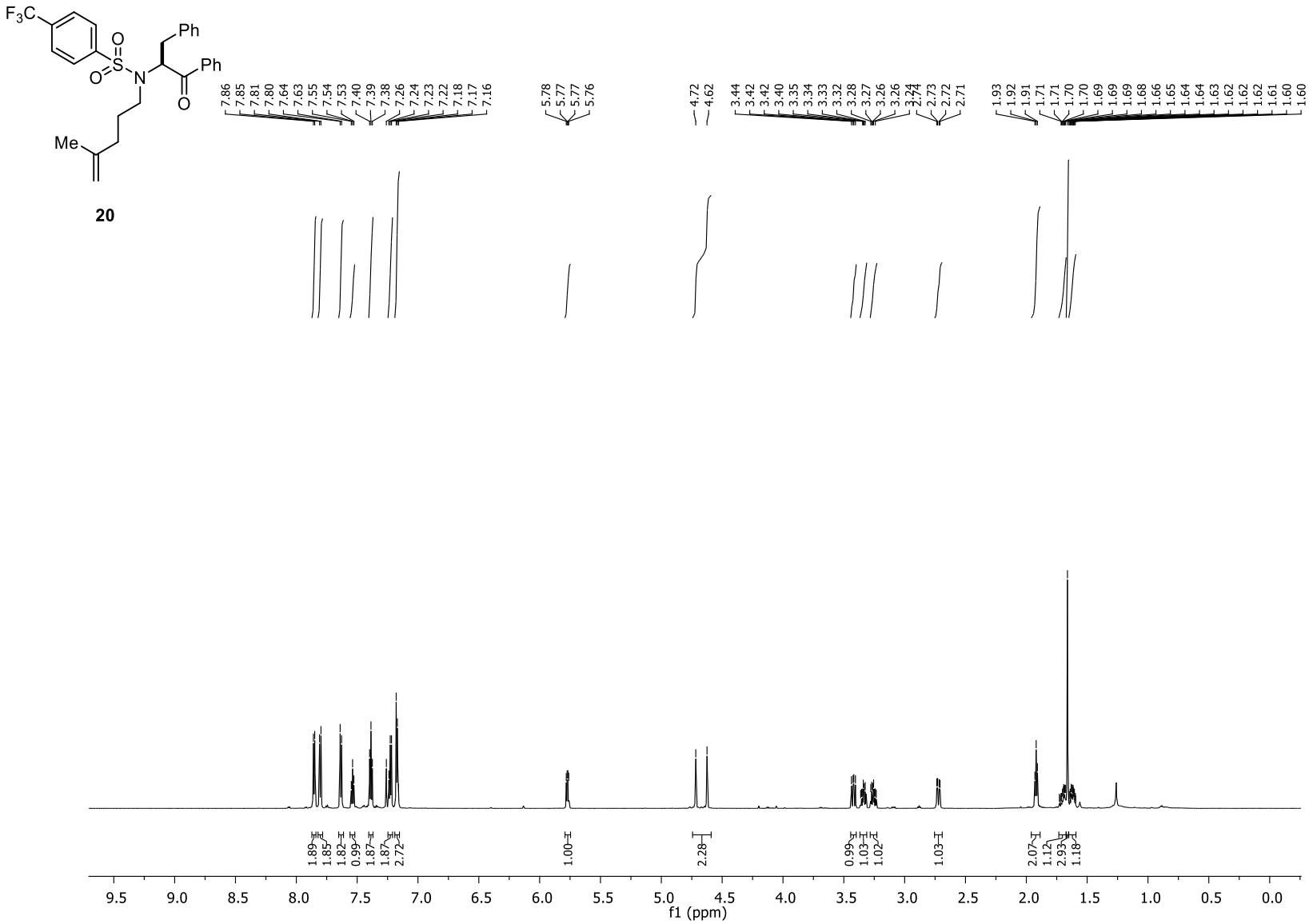
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

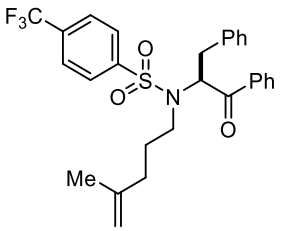


18

194.19
162.78
134.94
134.48
133.70
131.46
129.60
128.78
128.02
120.01
114.00
77.18
77.00
76.82
55.53
53.10
47.95
27.12
25.60
17.72

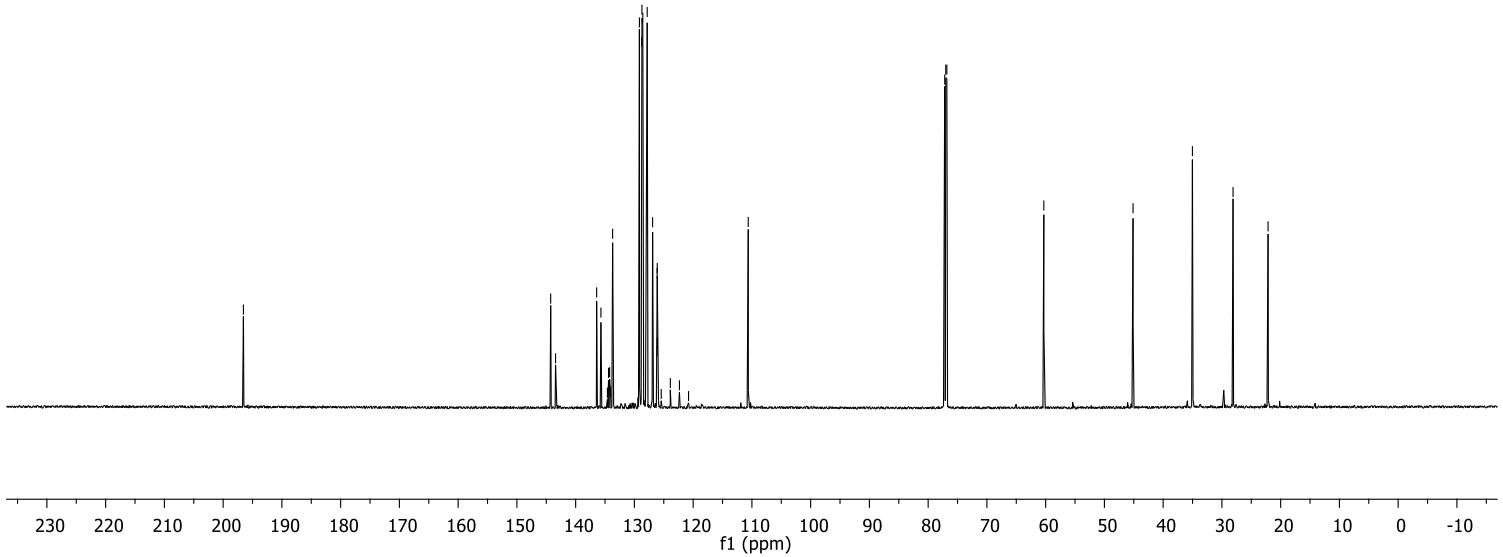


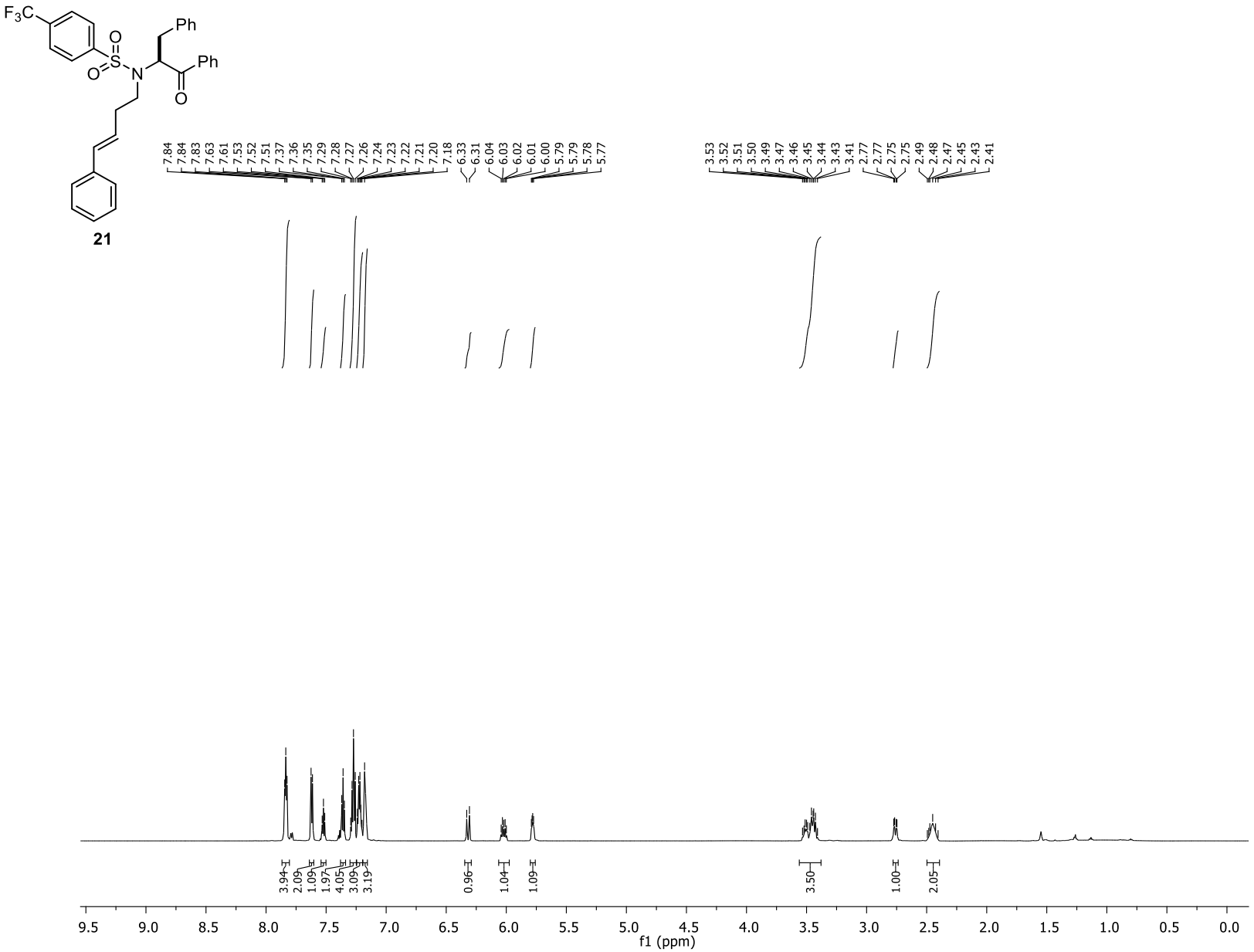

F3C
Ph
Ph
O
S
O
N
O
Me
20
7.86 7.85 7.81 7.80 7.64 7.63 7.55 7.54 7.53 7.40 7.39 7.38 7.26 7.24 7.23 7.22 7.18 7.17 7.16
5.78 5.77 5.77 5.76
4.72 4.62
3.44 3.42 3.42 3.40 3.35 3.34 3.33 3.32 3.28 3.27 3.26 3.26 3.24 2.73 2.72 2.71
1.93 1.92 1.91 1.71 1.71 1.70 1.70 1.69 1.69 1.69 1.68 1.66 1.65 1.64 1.64 1.63 1.62 1.62 1.62 1.61 1.60 1.60
1.89 1.85 1.82 0.99 1.87 1.87 2.72
1.00
2.28
0.99 1.03 1.02
1.03
2.07 1.12 2.93 1.18
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

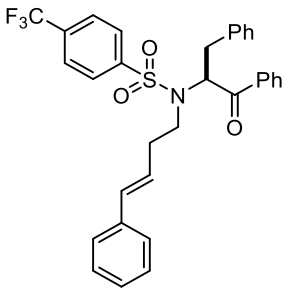


20

196.55
144.25
143.42
133.71
129.14
128.76
128.72
128.57
127.82
126.90
126.13
110.62
77.18
77.00
76.82
60.31
45.12
35.02
28.10
22.14

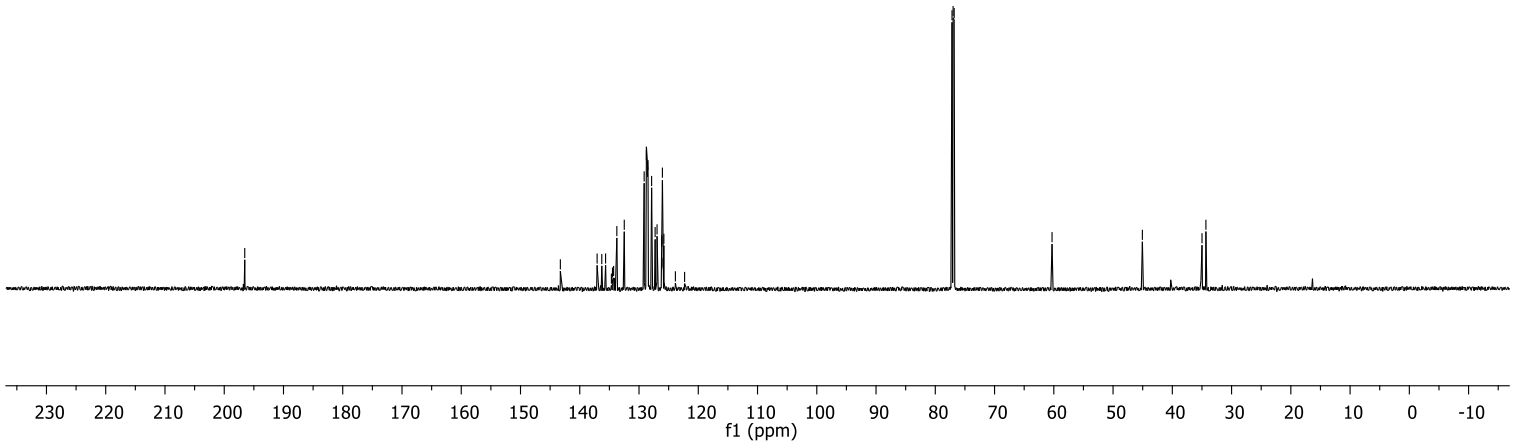


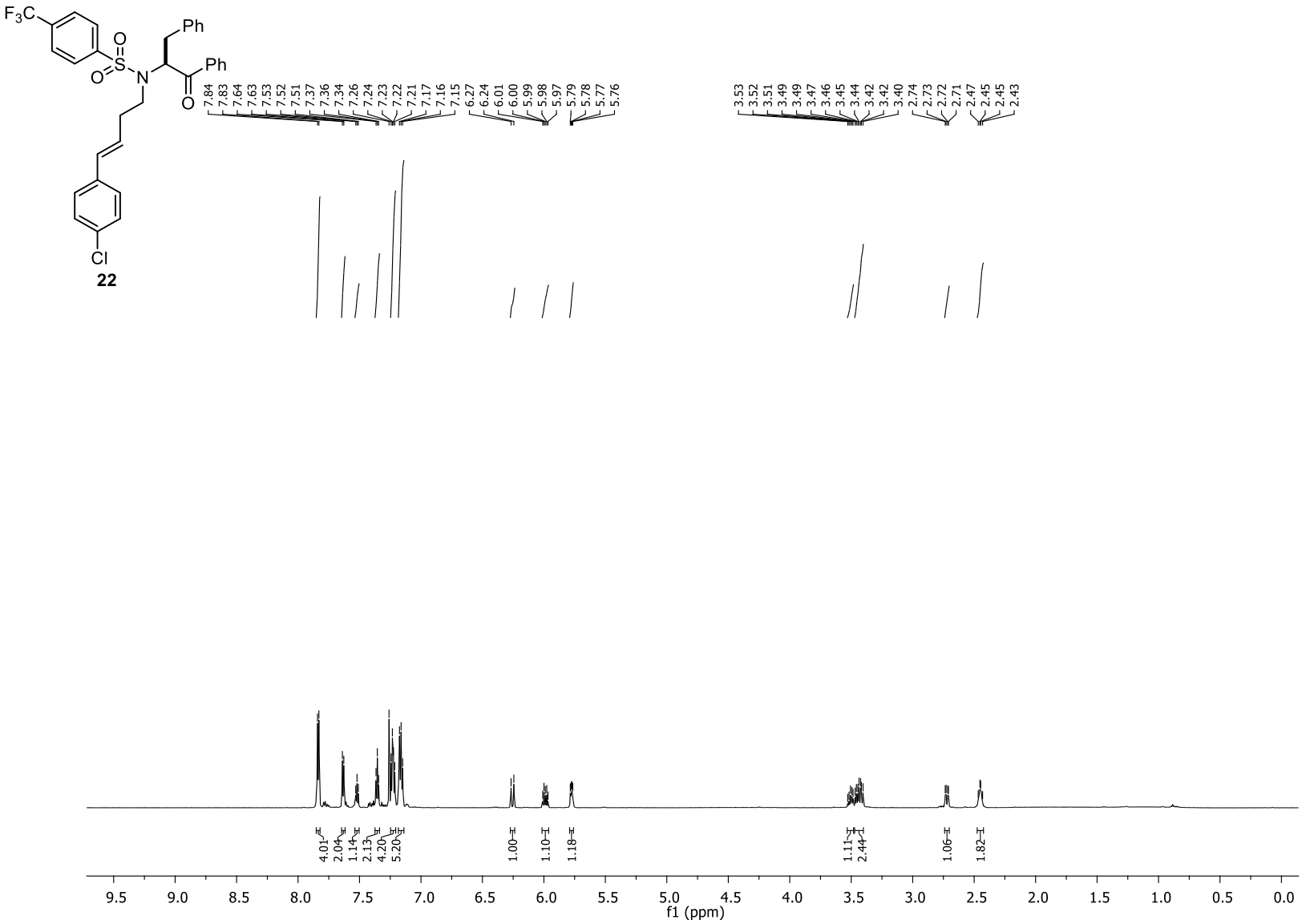

F3C
Ph
Ph
O
S
O
O
N
O
21
7.84
7.84
7.83
7.63
7.61
7.53
7.52
7.51
7.37
7.36
7.35
7.29
7.28
7.27
7.26
7.24
7.23
7.22
7.21
7.20
7.18
6.33
6.31
6.04
6.03
6.02
6.01
6.00
5.79
5.79
5.78
5.77
3.53
3.52
3.51
3.50
3.49
3.47
3.46
3.45
3.44
3.43
3.41
2.77
2.77
2.75
2.75
2.49
2.48
2.47
2.45
2.43
2.41
3.94
2.09
1.09
1.97
4.05
3.09
3.19
0.96
1.04
1.09
3.50
1.00
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
0.0
f1 (ppm)

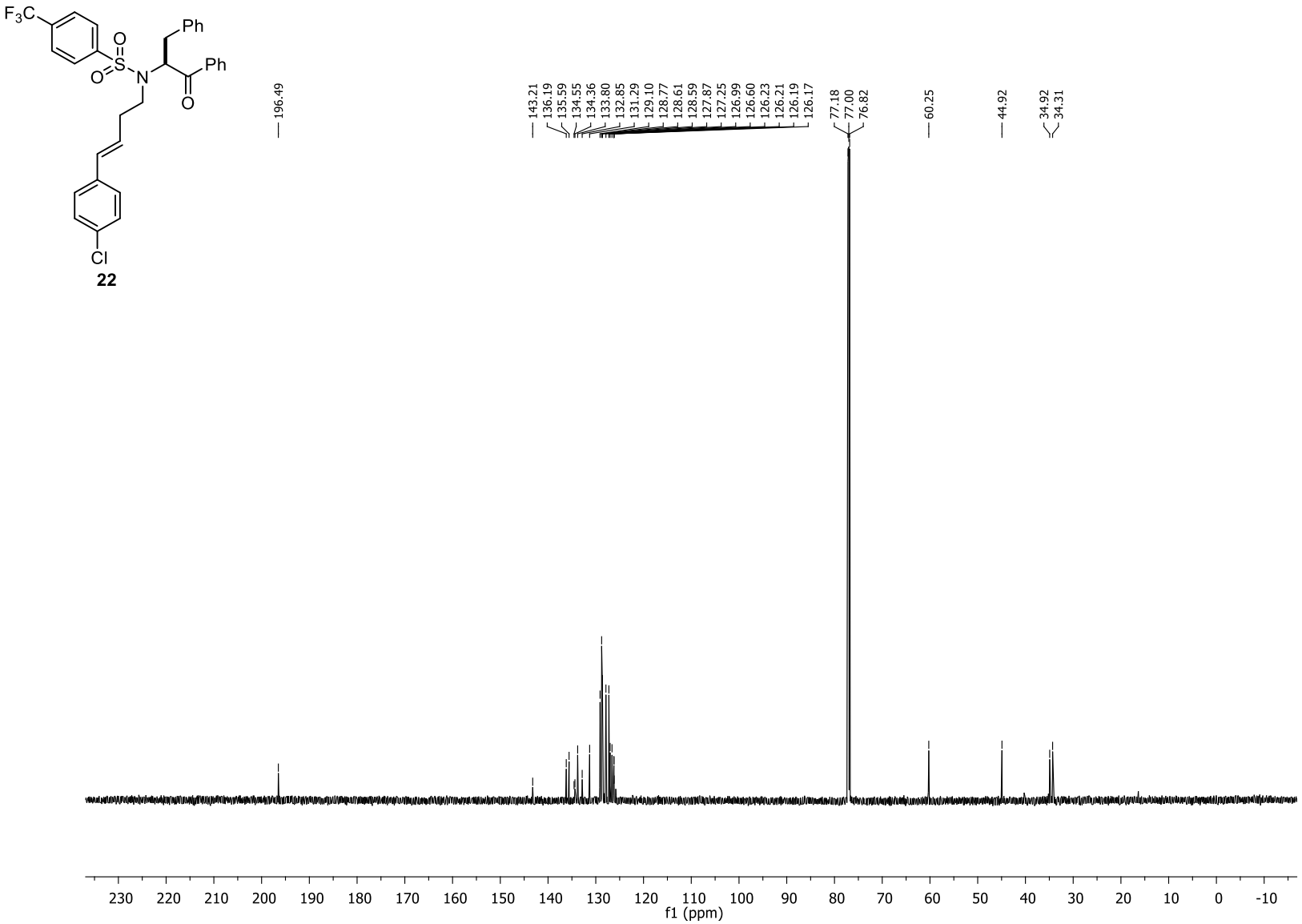


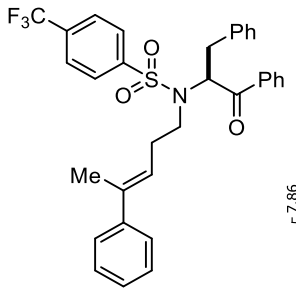
21

196.54
143.28
137.07
136.28
135.64
134.29
133.74
132.49
129.13
128.76
128.58
128.48
127.88
127.28
126.96
126.19
126.17
126.15
126.13
126.05
125.80
77.18
77.00
76.81
60.30
45.05
34.99
34.33

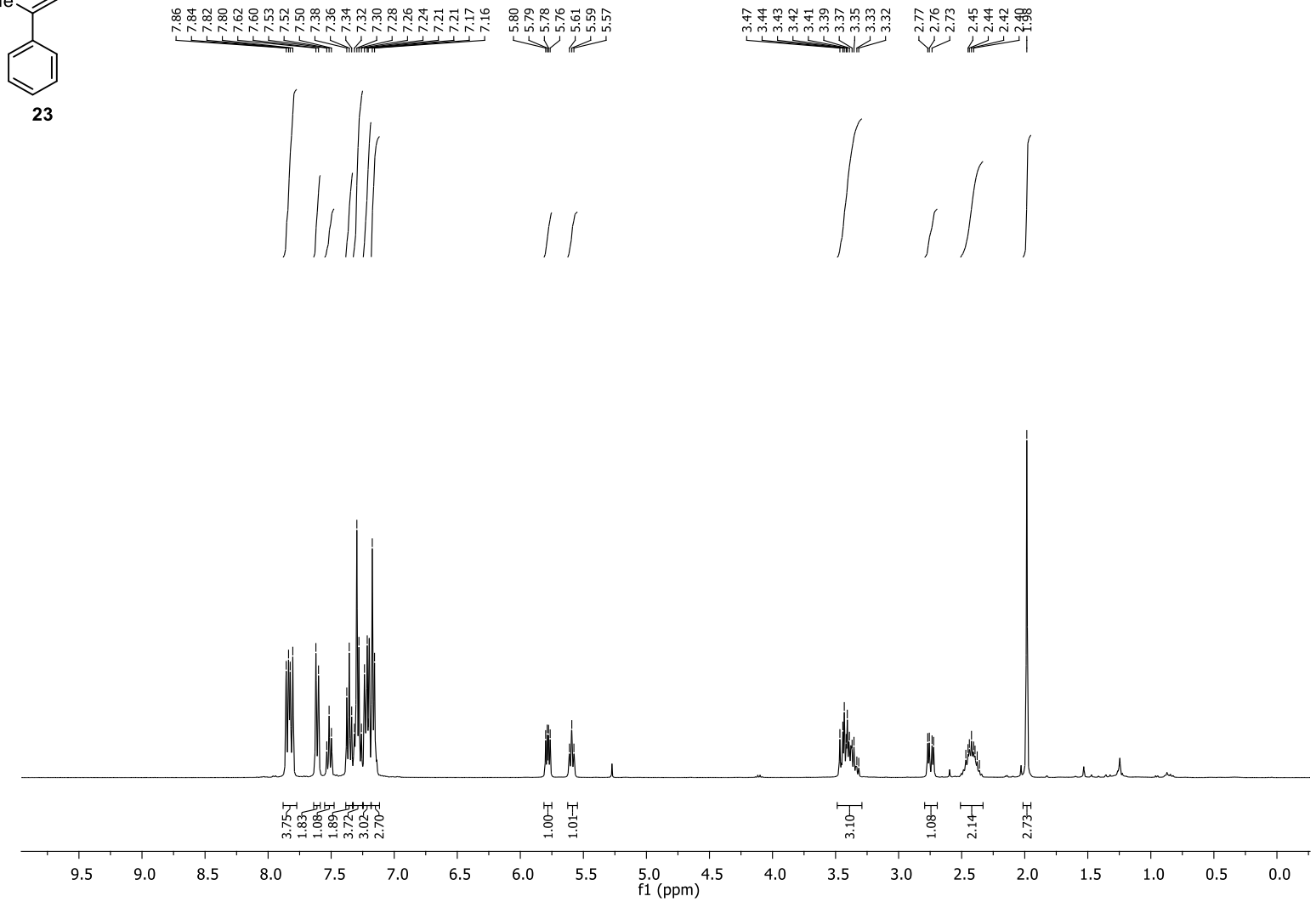



F3C
O
S
O
N
Ph
Ph
O
Cl
22
7.84
7.83
7.64
7.63
7.53
7.52
7.51
7.37
7.36
7.34
7.26
7.24
7.23
7.22
7.21
7.17
7.16
7.15
6.27
6.24
6.01
6.00
5.99
5.98
5.97
5.79
5.78
5.77
5.76
3.53
3.52
3.51
3.49
3.49
3.47
3.46
3.45
3.44
3.42
3.42
3.40
2.74
2.73
2.72
2.71
2.47
2.45
2.45
2.43
4.01
2.04
1.14
2.13
4.20
5.20
1.00
1.10
1.18
1.11
2.44
1.06
1.82
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


F3C
O
S
O
N
Ph
Ph
O
Cl
22
196.49
143.21
136.19
135.59
134.55
134.36
133.80
132.85
131.29
129.10
128.77
128.61
128.59
127.87
127.25
126.99
126.60
126.23
126.21
126.19
126.17
77.18
77.00
76.82
60.25
44.92
34.92
34.31
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F3C
O
S
O
N
Ph
Ph
O
Me

23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7.52
7.50
7.38
7.36
7.34
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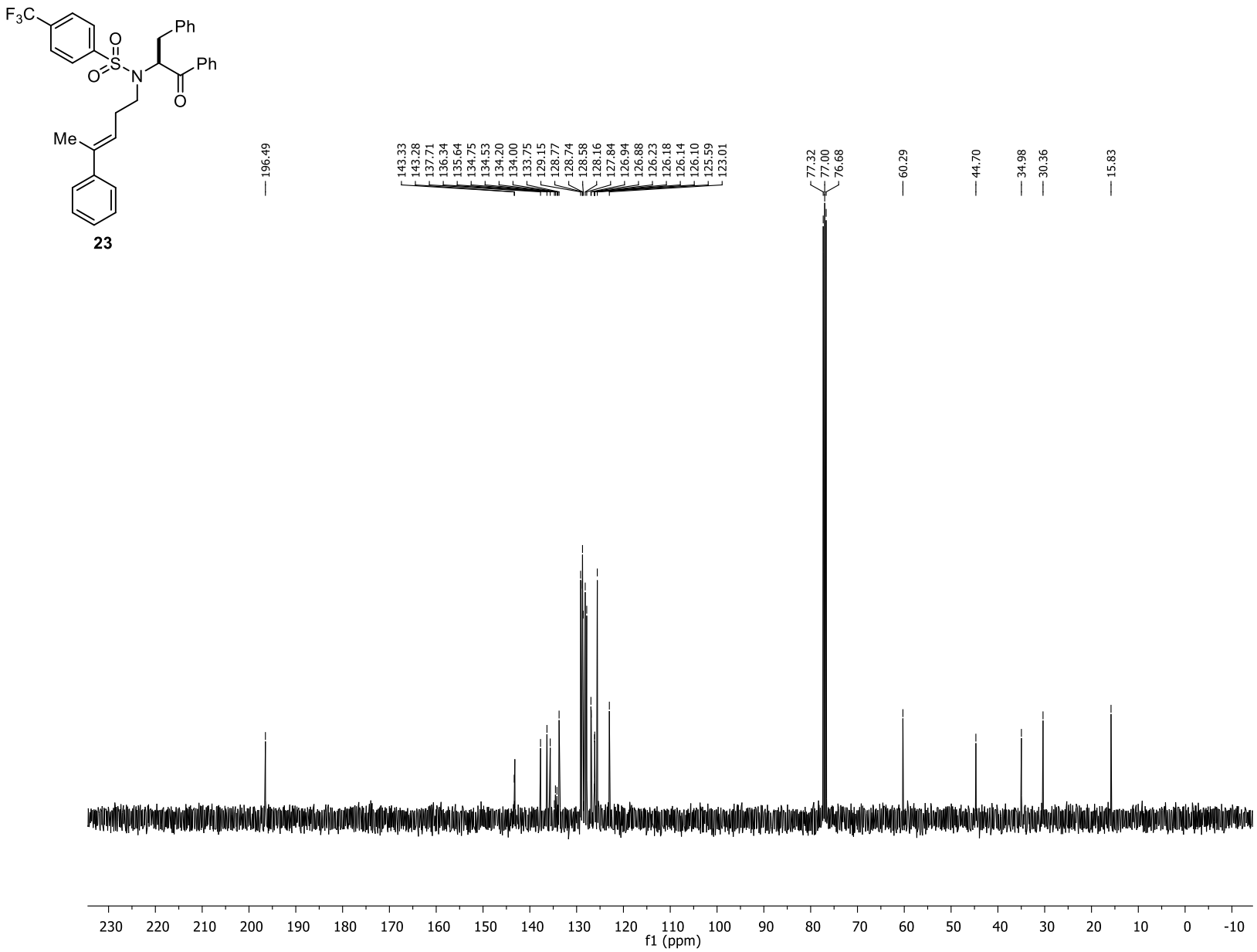
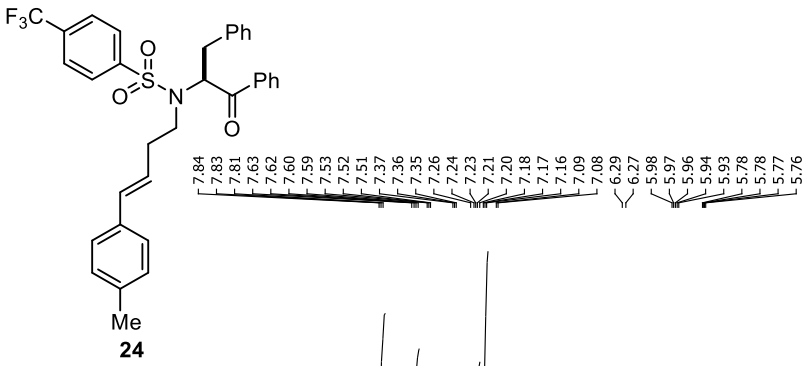
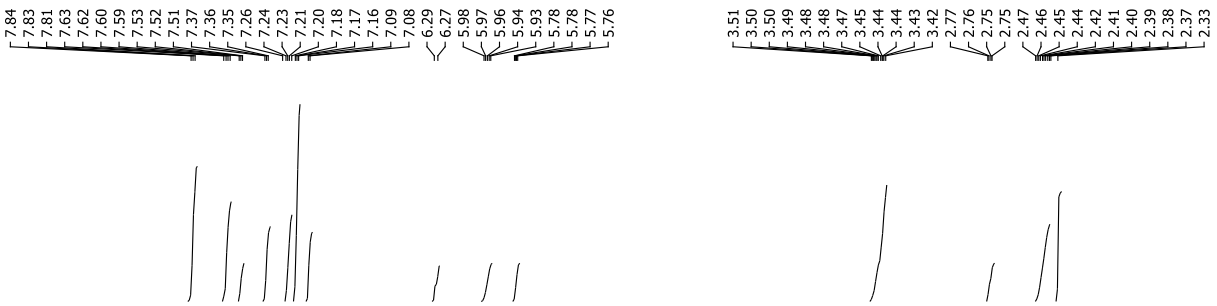
7.30
7.28
7.26
7.24
7.21
7.21
7.17
7.16
5.80
5.79
5.78
5.76
5.61
5.59
5.57
3.47
3.44
3.43
3.42
3.41
3.39
3.37
3.35
3.33
3.32
2.77
2.76
2.73
2.45
2.44
2.42
3.75
1.83
1.08
1.89
3.72
3.02
2.70
1.00
1.01
3.10
1.08
2.14
2.73
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


F3C
Ph
Ph
O
S
O
N
O
Me
23
196.49
143.33
143.28
137.71
136.34
135.64
134.75
134.53
134.20
134.00
133.75
129.15
128.77
128.74
128.58
128.16
127.84
126.94
126.88
126.23
126.18
126.14
126.10
125.59
123.01
77.32
77.00
76.68
60.29
44.70
34.98
30.36
15.83
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F3C
O
S
O
N
Ph
Ph
O
Me
24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7.63
7.62
7.60
7.59
7.53
7.52
7.51
7.37
7.36
7.35
7.26
7.24
7.23
7.21
7.20
7.18
7.17
7.16
7.09
7.08
6.29
6.27
5.98
5.97
5.96
5.94
5.93
5.78
5.78
5.77
5.76
3.51
3.50
3.50
3.49
3.48
3.48
3.47
3.45
3.44
3.44
3.43
3.42
2.77
2.76
2.75
2.75
2.47
2.46
2.45
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2.42
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2.40
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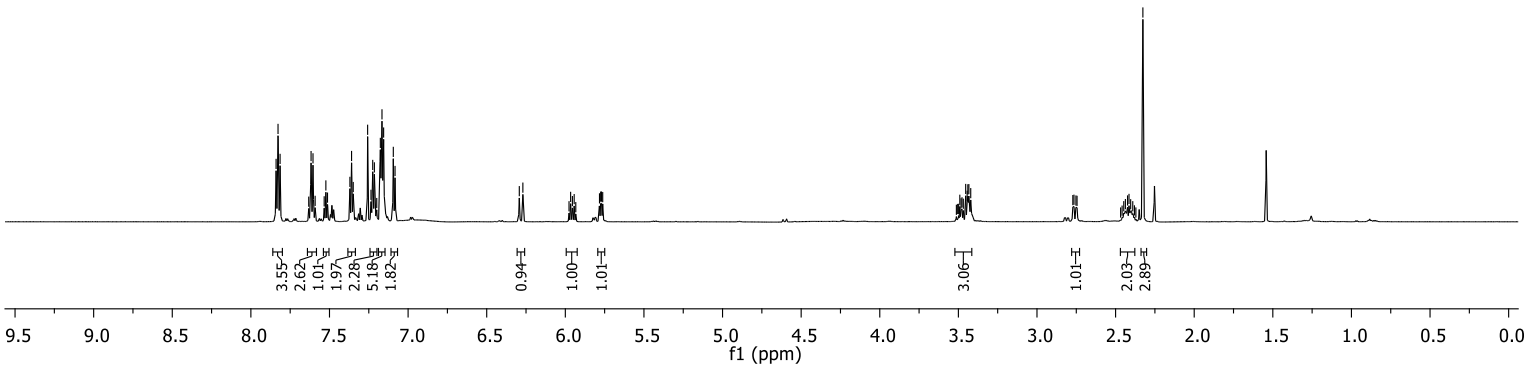
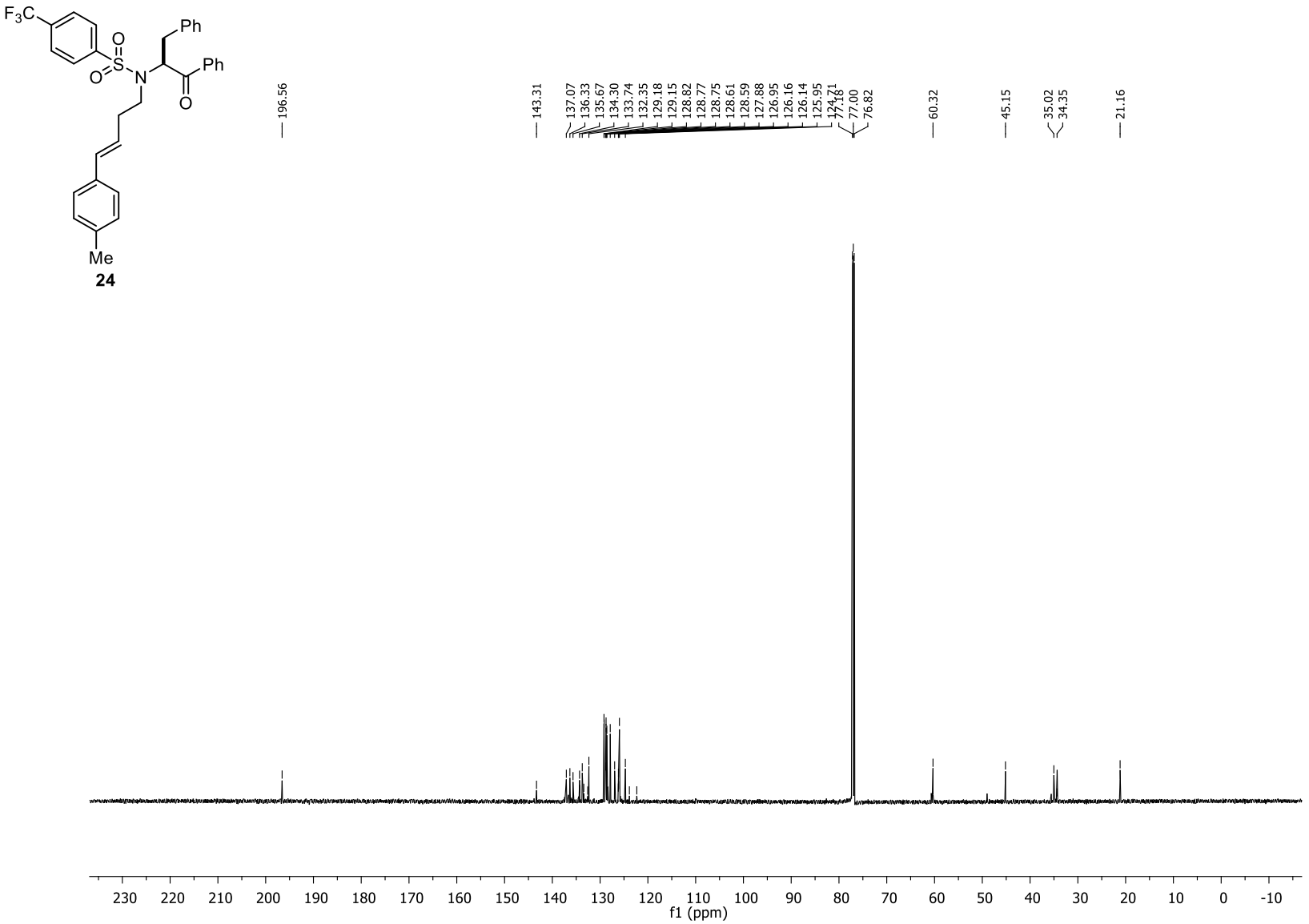
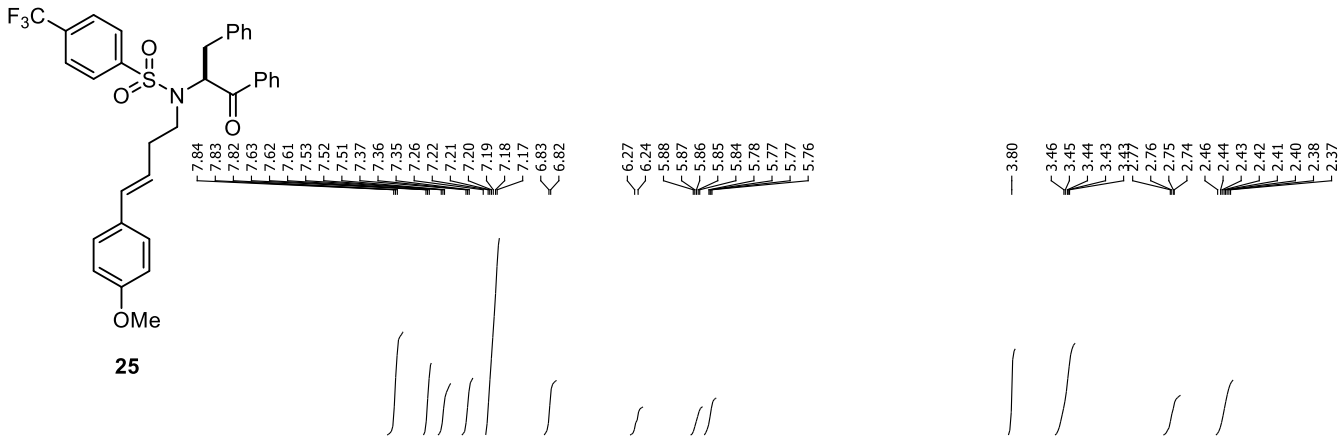
2.37
2.33


3.55
2.62
1.01
1.97
2.28
5.18
1.82
0.94
1.00
1.01
3.06
1.01
2.03
2.89
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


F3C
O
S
O
N
Ph
Ph
O
Me
24
196.56
143.31
137.07
136.33
135.67
134.30
133.74
132.35
129.18
129.15
128.82
128.77
128.75
128.61
128.59
127.88
126.95
126.16
126.14
125.95
124.71
77.18
77.00
76.82
60.32
45.15
35.02
34.35
21.16
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F3C
O
S
O
N
Ph
Ph
O
OMe
7.84
7.83
7.82
7.63
7.62
7.61
7.53
7.52
7.51
7.37
7.36
7.35
7.26
7.22
7.21
7.20
7.19
7.18
7.17
6.83
6.82
6.27
6.24
5.88
5.87
5.86
5.85
5.84
5.78
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5.77
5.76
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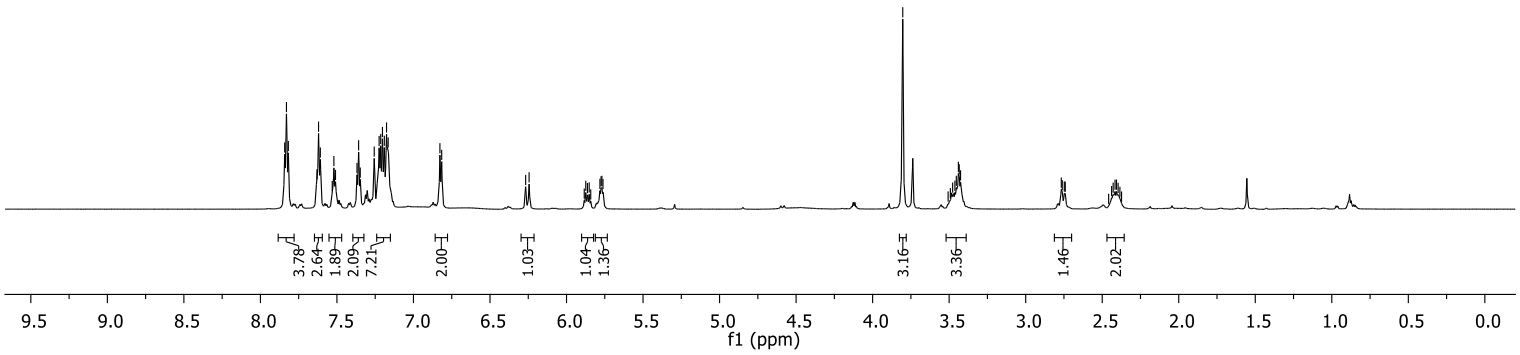
3.45
3.44
3.43
2.76
2.75
2.74
2.46
2.44
2.43
2.42
2.41
2.40
2.38
2.37

25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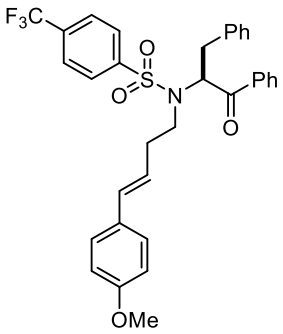
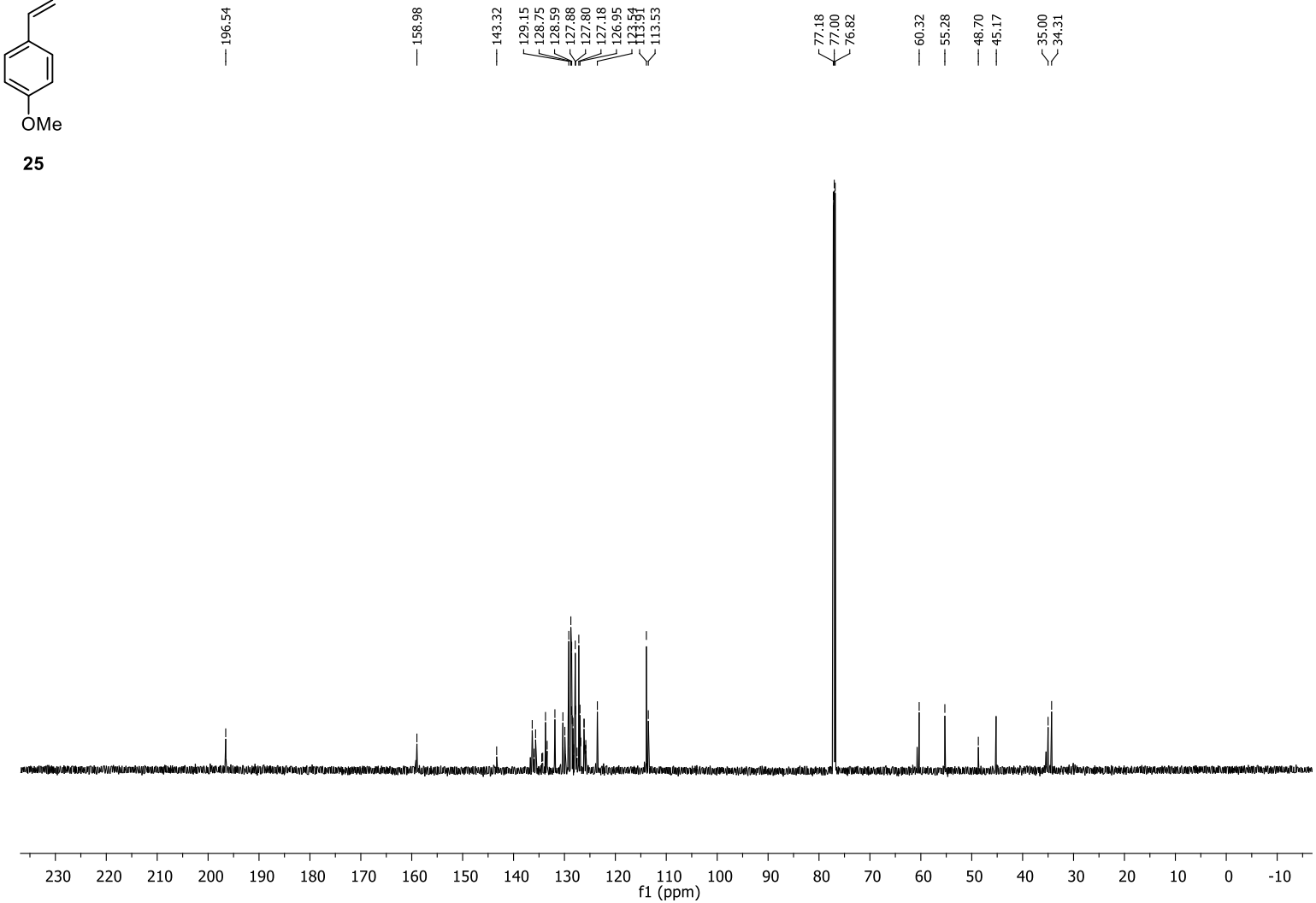
2.64
1.89
2.09
7.21
2.00
1.03
1.04
1.36
3.16
3.36
1.46
2.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


F3C
O
S
O
N
Ph
Ph
O
OMe

25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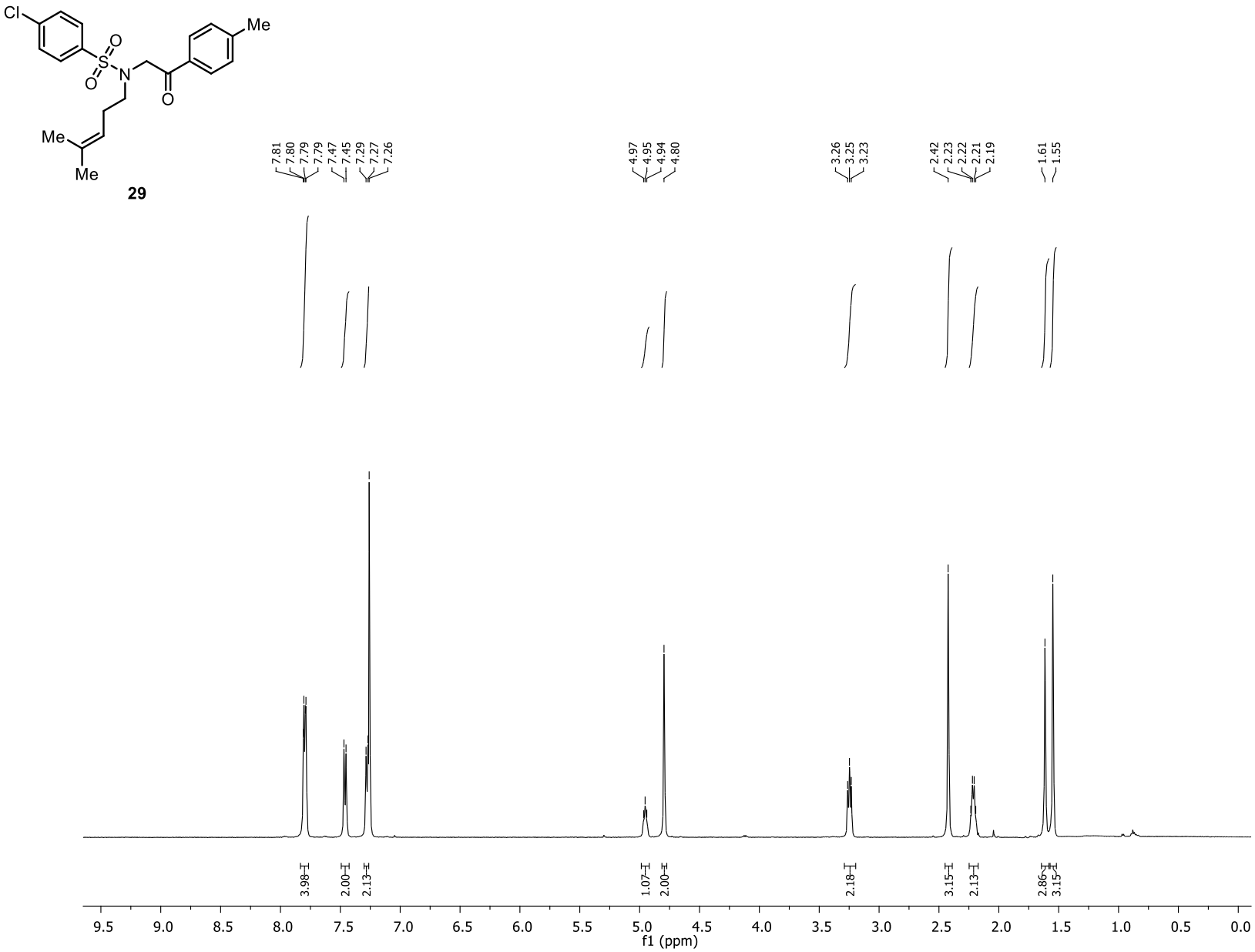
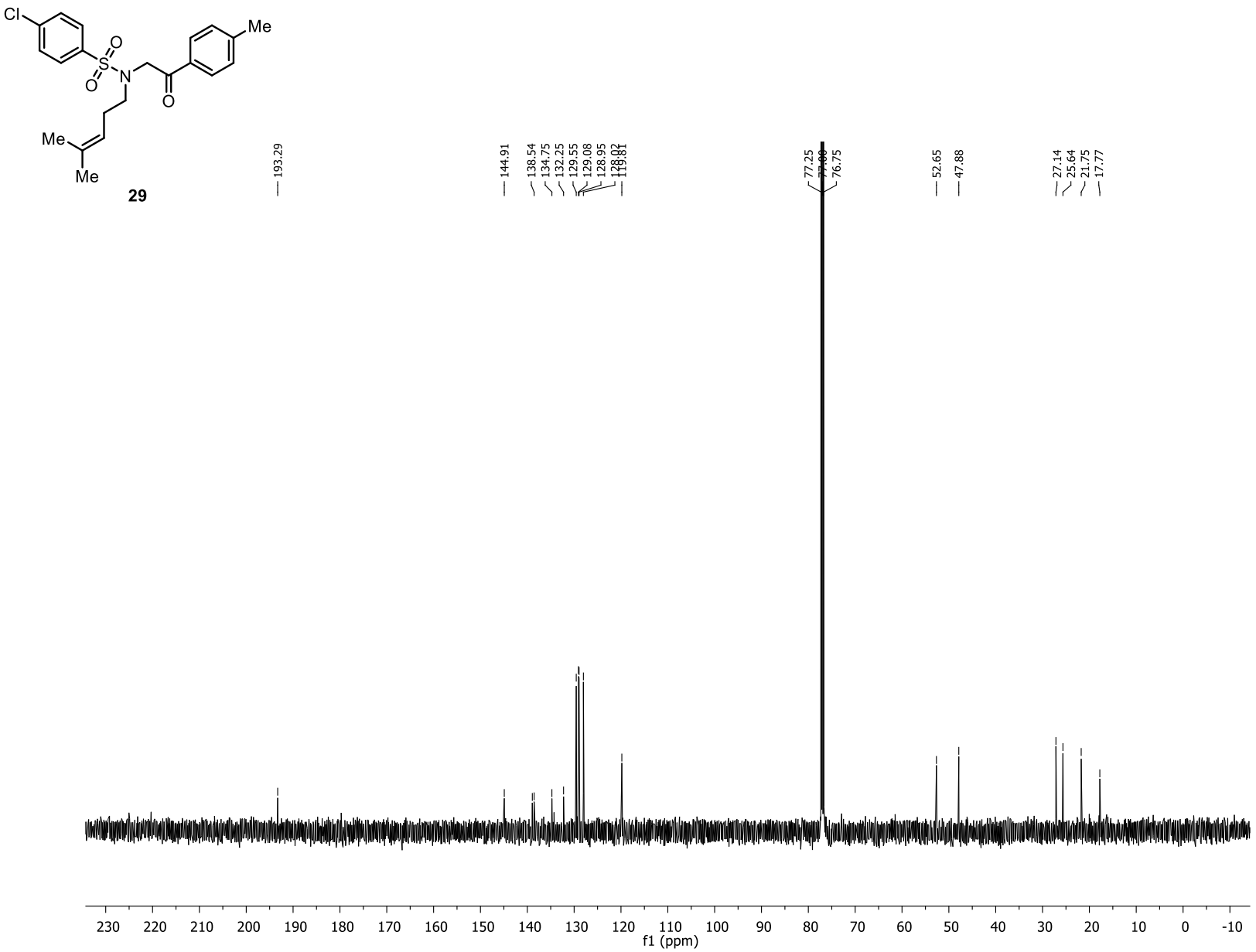
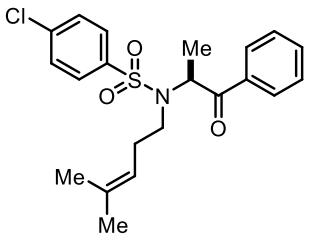
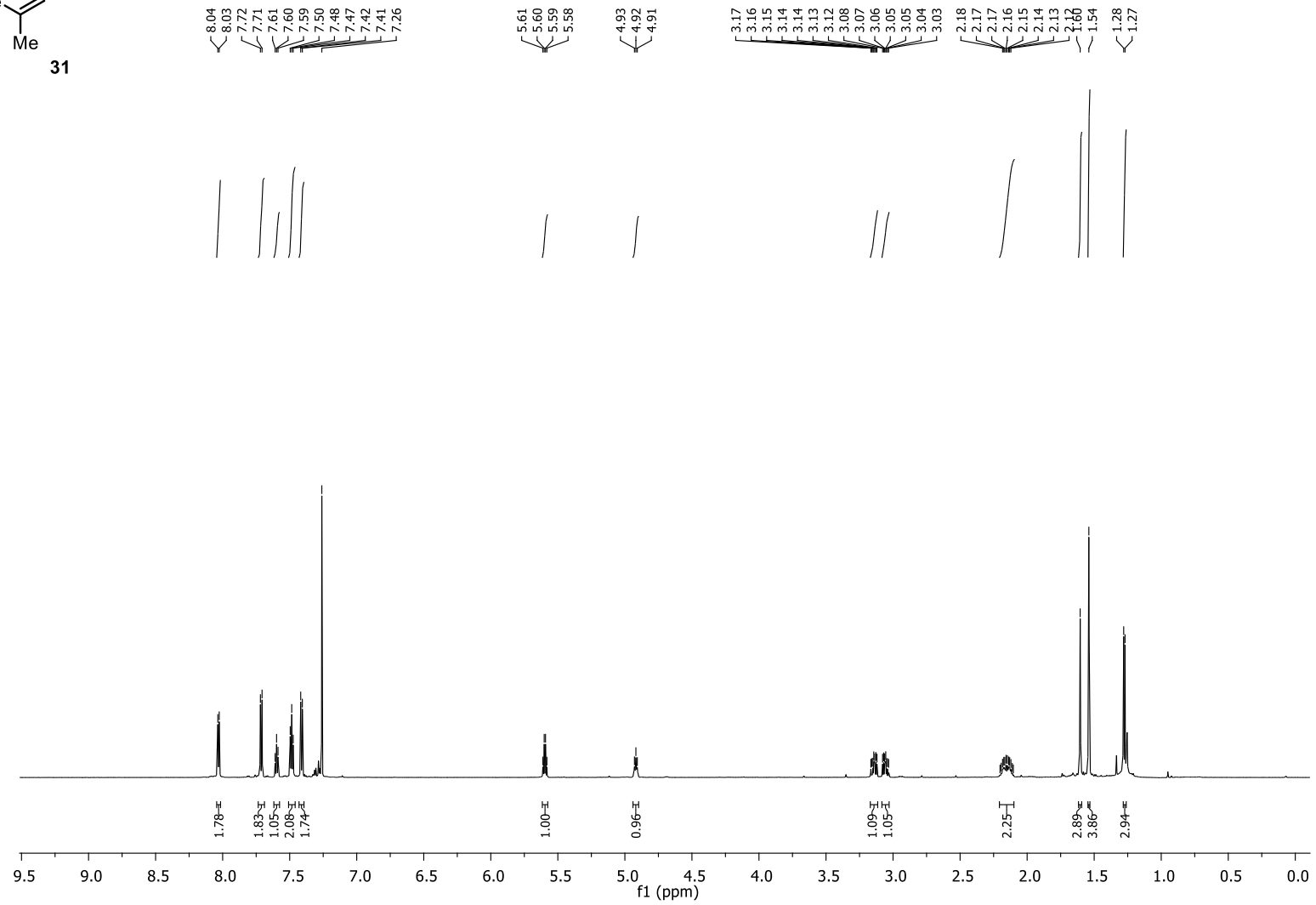
128.59
127.88
127.80
127.18
126.95
123.54
113.91
113.53
77.18
77.00
76.82
60.32
55.28
48.70
45.17
35.00
34.31
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

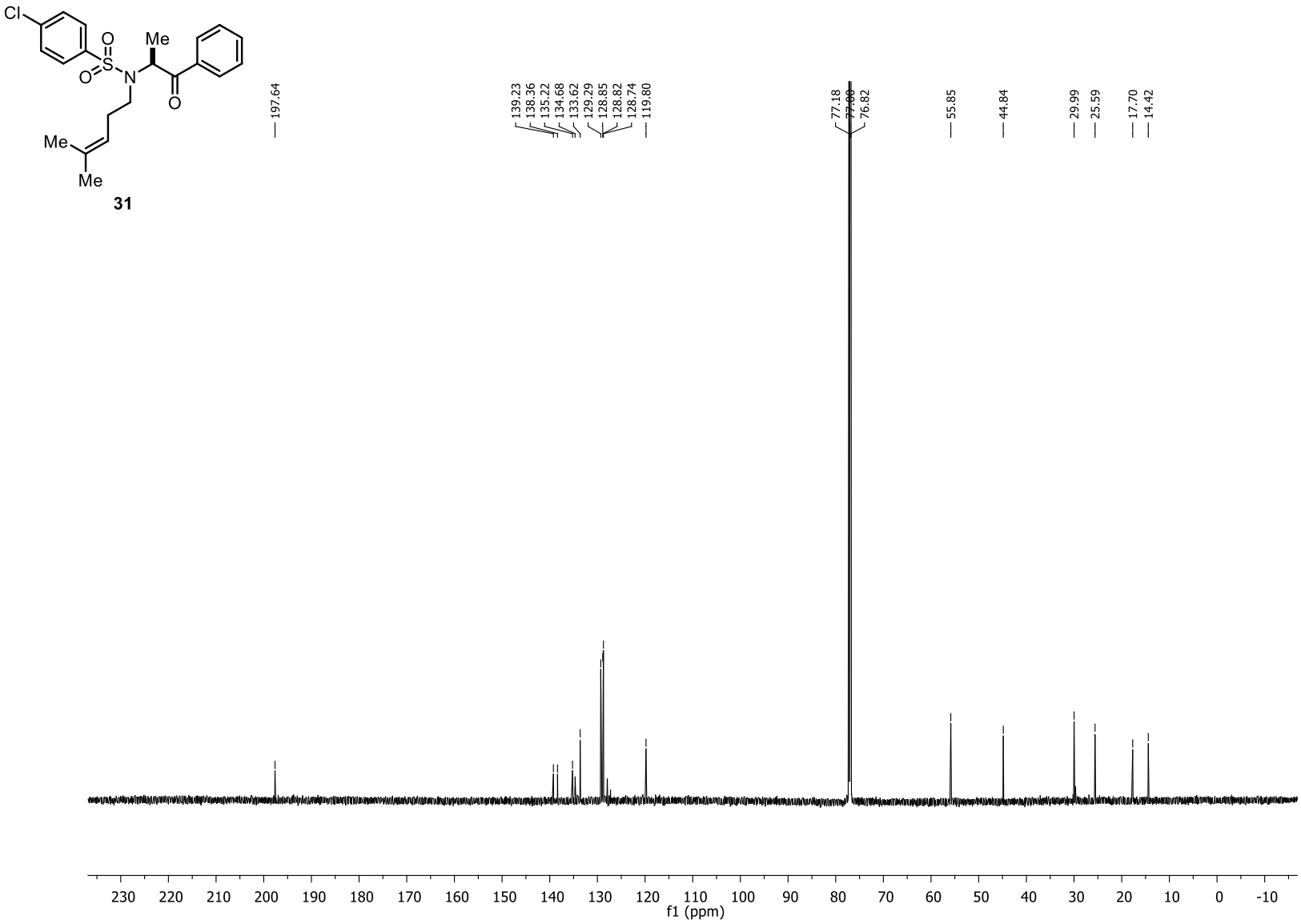

Cl
Me
Me
Me
29
7.81
7.80
7.79
7.79
7.47
7.45
7.29
7.27
7.26
4.97
4.95
4.94
4.80
3.26
3.25
3.23
2.42
2.23
2.22
2.21
2.19
1.61
1.55
3.98
2.00
2.13
1.07
2.00
2.18
3.15
2.13
2.86
3.15
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

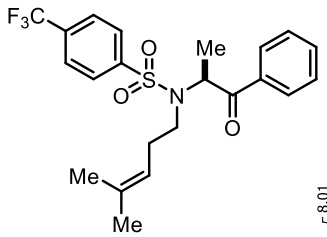

Cl
O
S
O
N
O
Me
Me
Me
29
193.29
144.91
138.54
134.75
132.25
129.55
129.08
128.95
77.25
76.75
52.65
47.88
27.14
25.64
21.75
17.77
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Cl
O
S
O
N
Me
O
Me
Me

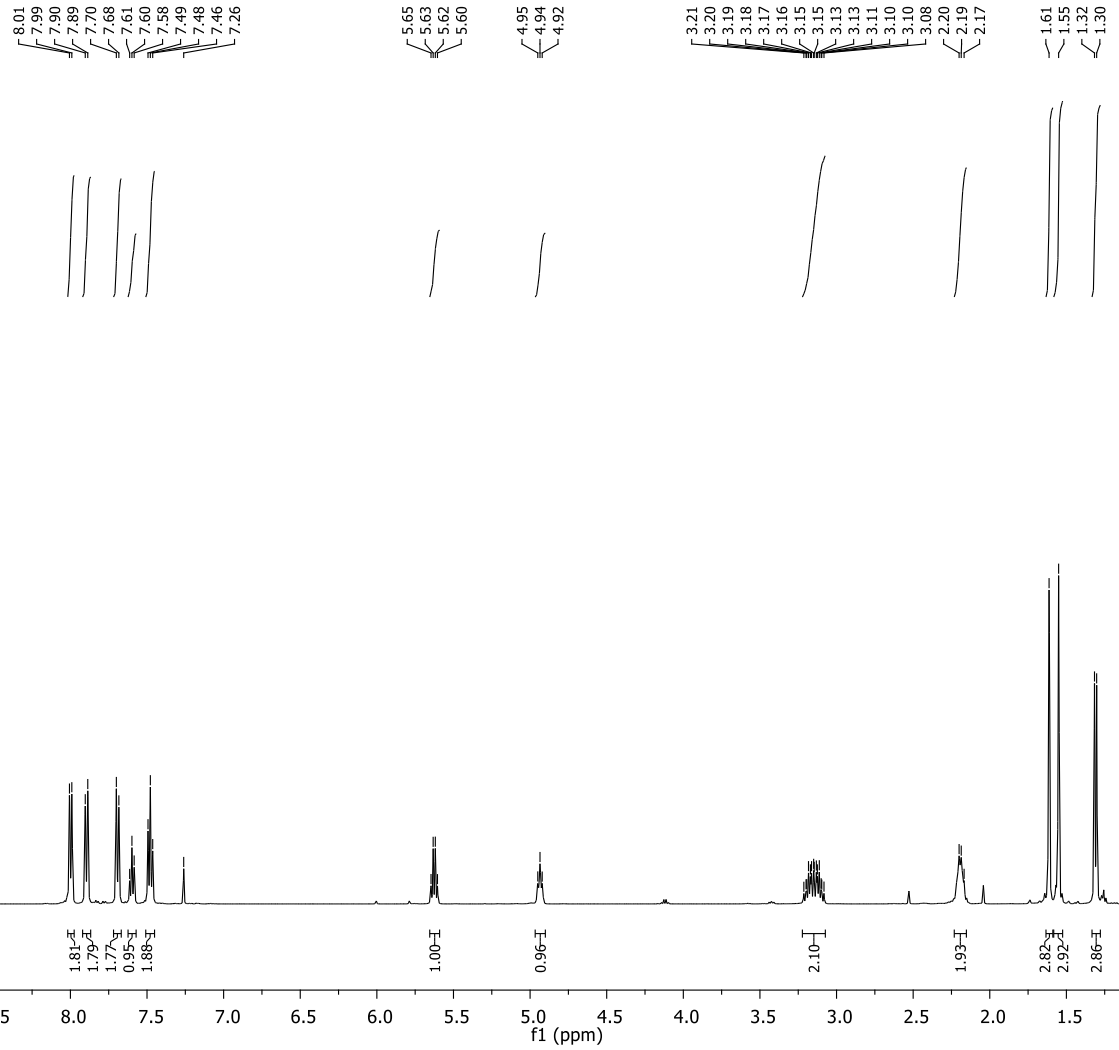
31


8.04
8.03
7.72
7.71
7.61
7.60
7.59
7.50
7.48
7.47
7.42
7.41
7.26
5.61
5.60
5.59
5.58
4.93
4.92
4.91
3.17
3.16
3.15
3.14
3.14
3.13
3.12
3.08
3.07
3.06
3.05
3.05
3.04
3.03
2.18
2.17
2.17
2.16
2.15
2.14
2.13
1.60
1.54
1.28
1.27
1.78
1.83
1.05
2.08
1.74
1.00
0.96
1.09
1.05
2.25
2.89
3.86
2.94
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Cl
O
S
O
N
Me
O
Me
Me
31
197.64
139.23
138.36
135.22
134.68
133.62
129.29
128.85
128.82
128.74
119.80
77.18
77.00
76.82
55.85
44.84
29.99
25.59
17.70
14.42
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F3C
O
S
O
N
Me
O
Me
Me

33


8.01
7.99
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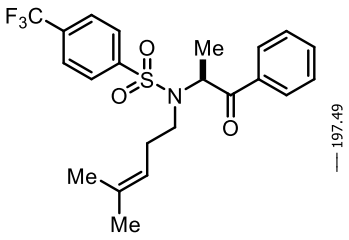
7.68
7.61
7.60
7.58
7.49
7.48
7.46
7.26
5.65
5.63
5.62
5.60
4.95
4.94
4.92
3.21
3.20
3.19
3.18
3.17
3.16
3.15
3.15
3.13
3.13
3.11
3.10
3.10
3.08
2.20
2.19
2.17
1.61
1.55
1.32
1.30
1.81
1.79
1.77
0.95
1.88
1.00
0.96
2.10
1.93
2.82
2.92
2.86
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



33

197.49

143.35
135.12
134.78
134.72
134.46
134.19
133.93
133.70
128.85
128.64
127.91
126.42
126.16
126.13
126.10
126.07
124.25
122.08
119.91
119.68

77.25
77.00
76.75

55.94

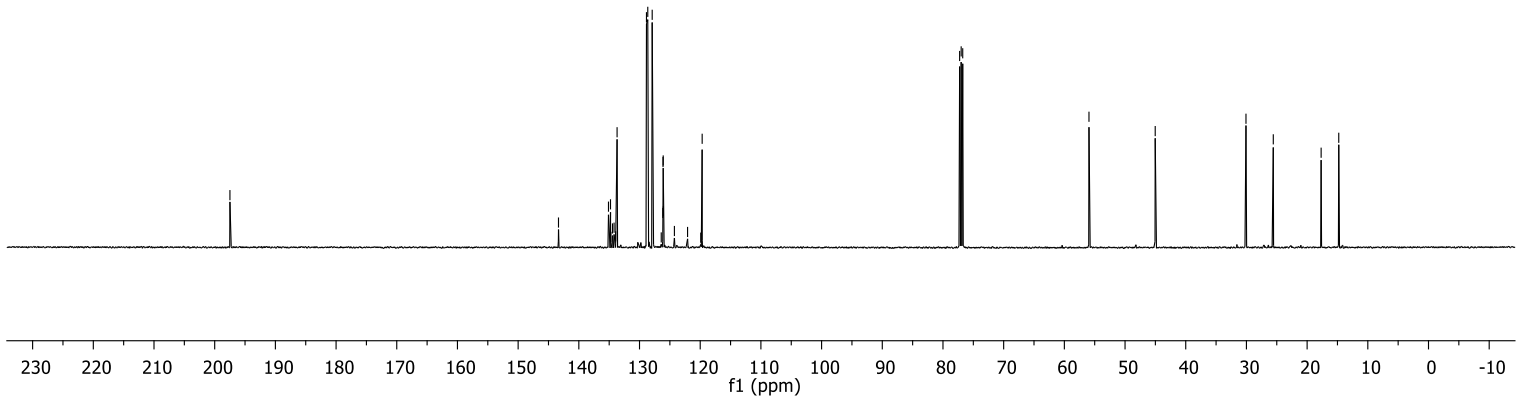
45.03

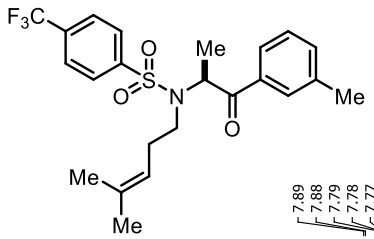
30.07

25.58

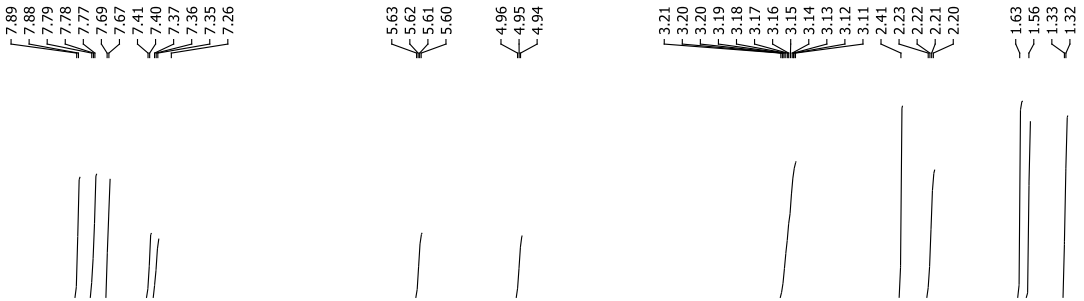
17.69

14.79




F3C
O
S
O
N
Me
O
Me
Me
Me

35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7.79
7.78
7.77
7.69
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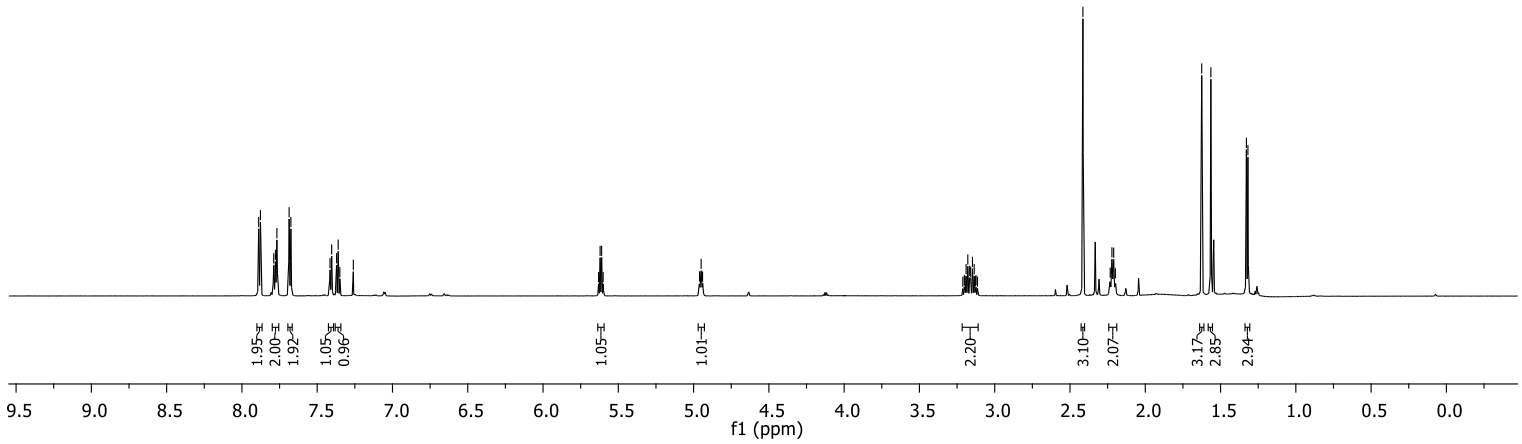
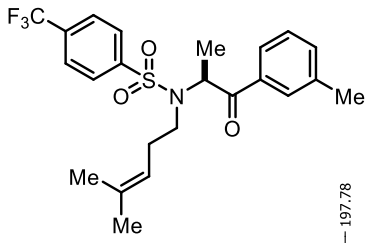
7.41
7.40
7.37
7.36
7.35
7.26
5.63
5.62
5.61
5.60
4.96
4.95
4.94
3.21
3.20
3.20
3.19
3.18
3.17
3.16
3.15
3.14
3.13
3.12
3.11
2.41
2.23
2.22
2.21
2.20
1.63
1.56
1.33
1.32


1.95
2.00
1.92
1.05
0.96
1.05
1.01
2.20
3.10
2.07
3.17
2.85
2.94
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



35

197.78

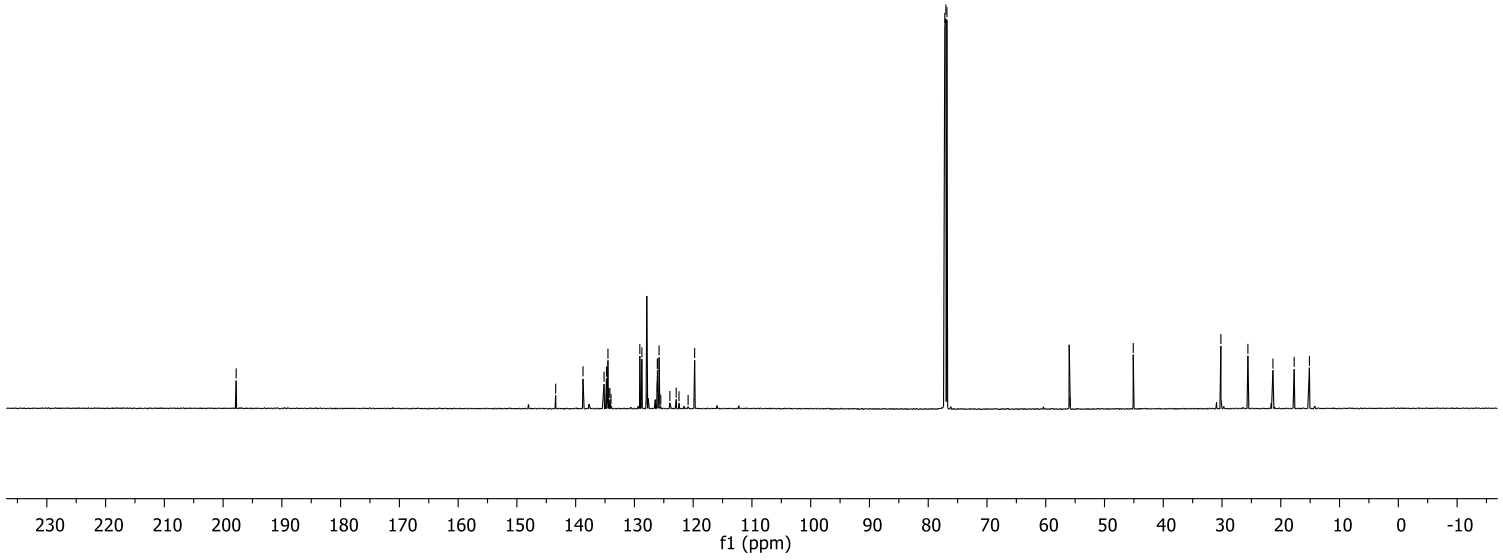
143.40
138.75
135.16
134.75
134.55
134.50
134.36
134.18
133.99
129.08
128.73
127.85
126.11
126.09
126.07
126.05
125.80
125.52
123.97
122.89
122.42
120.87
119.75

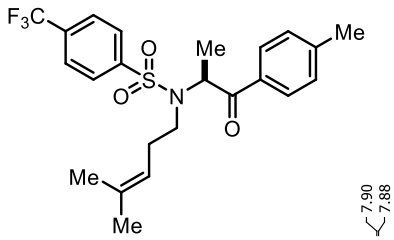
77.18
77.00
76.82

55.88

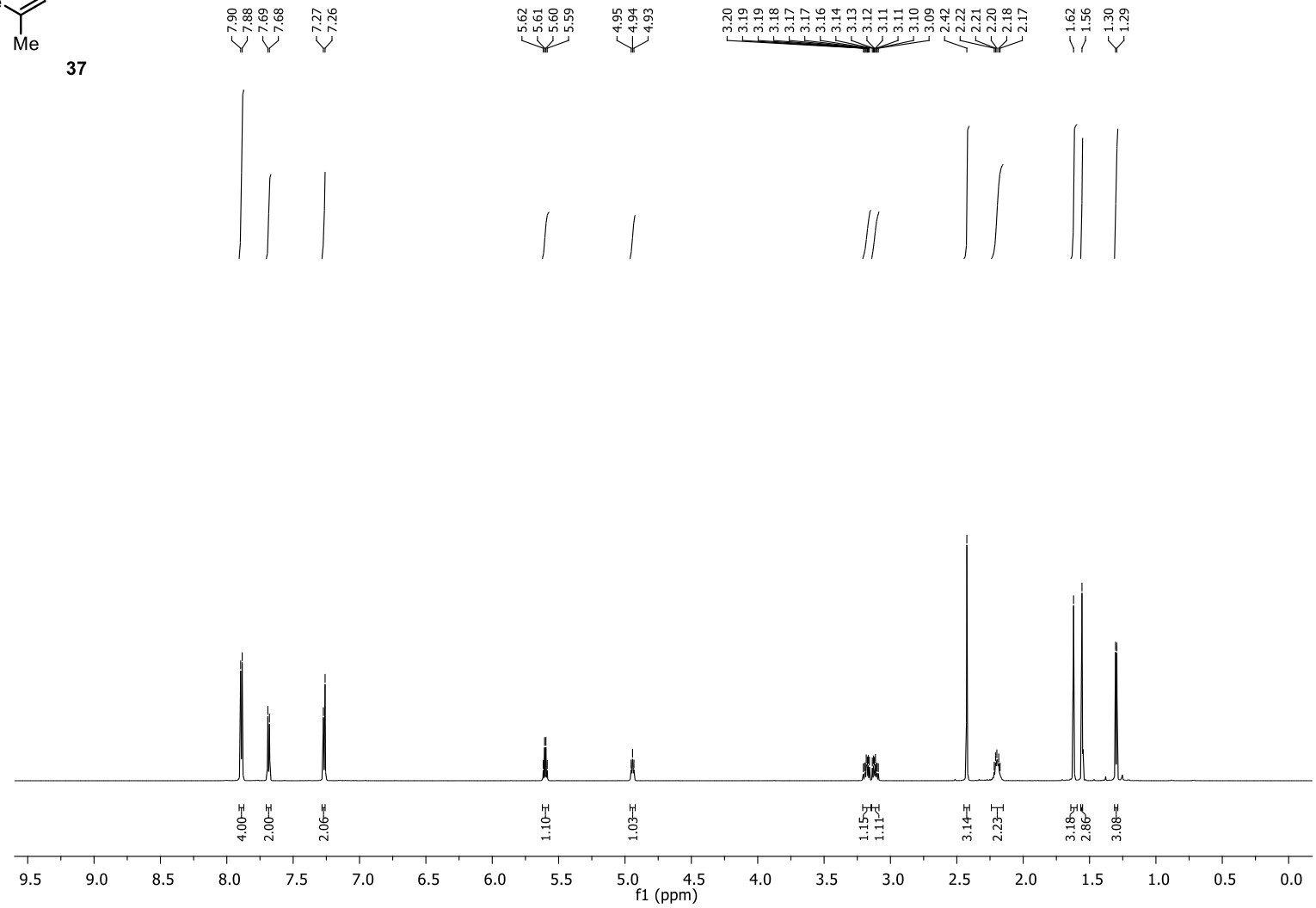
45.11

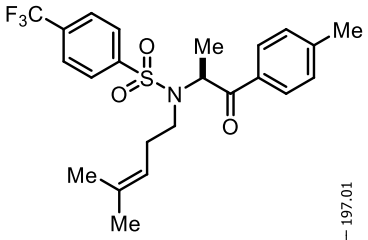
30.19
25.60
21.34
17.72
15.13




F3C
O
S
O
N
Me
O
Me
Me
Me

37


7.90
7.88
7.69
7.68
7.27
7.26
5.62
5.61
5.60
5.59
4.95
4.94
4.93
3.20
3.19
3.19
3.18
3.17
3.17
3.16
3.14
3.13
3.12
3.11
3.11
3.10
3.09
2.42
2.22
2.21
2.20
2.18
2.17
1.62
1.56
1.30
1.29
4.00
2.00
2.06
1.10
1.03
1.15
1.11
3.14
2.23
3.18
2.86
3.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



37

197.01

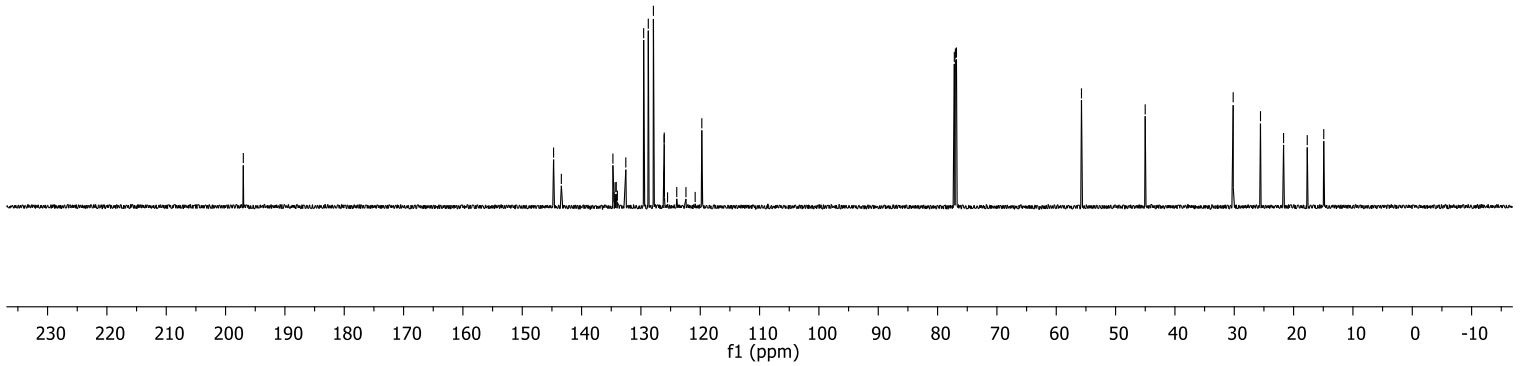
144.72
143.41
134.72
134.53
134.34
134.16
133.97
132.55
129.54
128.75
127.89
126.11
126.09
126.07
126.04
125.51
123.96
122.41
120.86
119.73

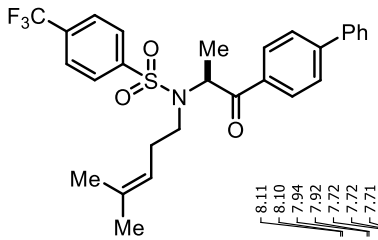
77.18
77.00
76.82

55.75

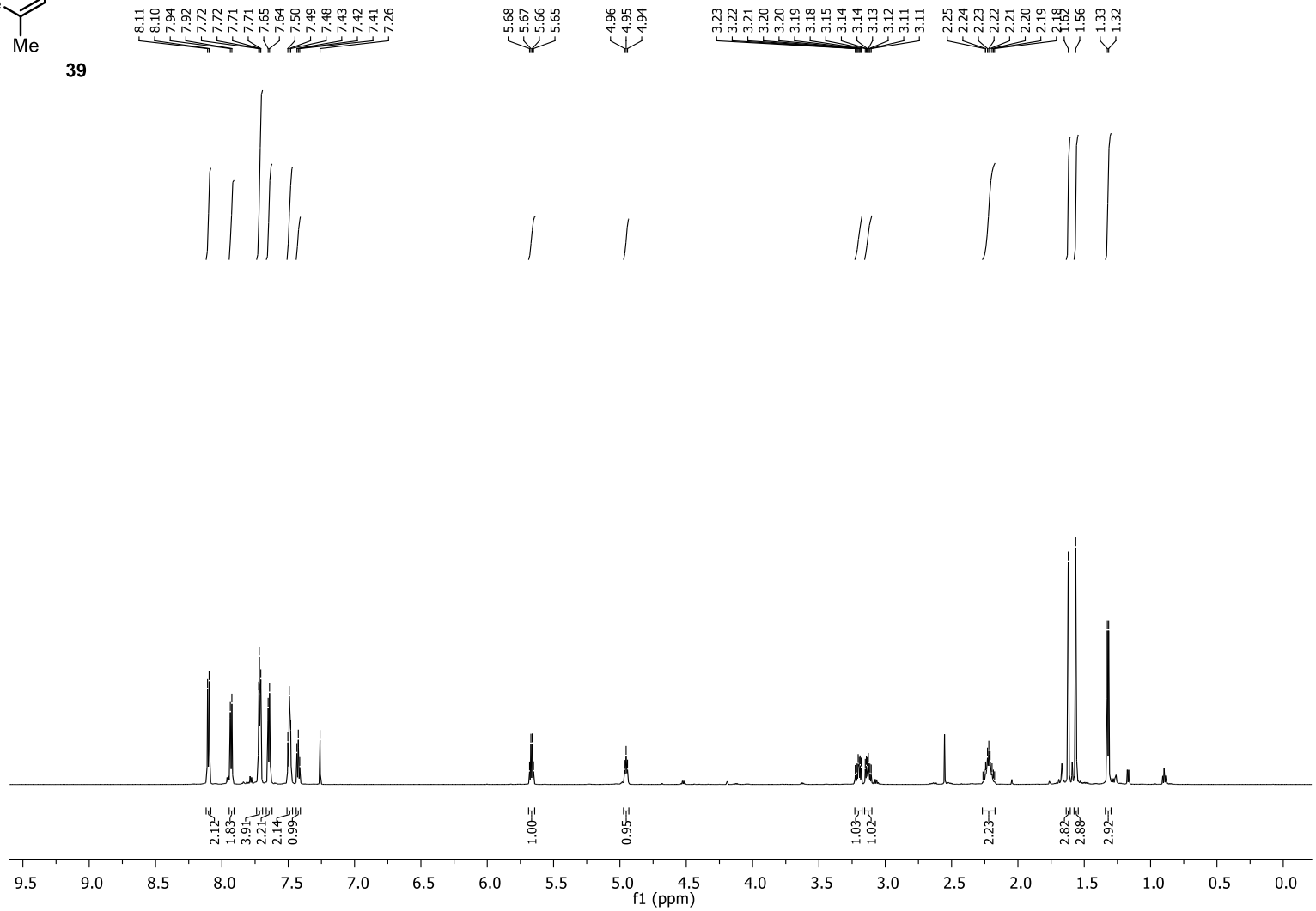
45.01

30.18
25.58
21.69
17.70
14.92




F3C
O
S
O
N
Me
O
Ph
Me
Me

39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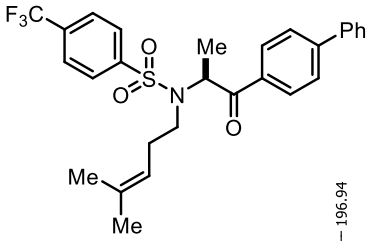
7.71
7.65
7.64
7.50
7.49
7.48
7.43
7.42
7.41
7.26
5.68
5.67
5.66
5.65
4.96
4.95
4.94
3.23
3.22
3.21
3.20
3.20
3.19
3.18
3.15
3.14
3.14
3.13
3.12
3.11
3.11
2.25
2.24
2.23
2.22
2.21
2.20
2.19
1.62
1.56
1.33
1.32
2.12
1.83
3.91
2.21
2.14
0.99
1.00
0.95
1.03
1.02
2.23
2.82
2.88
2.92
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



39

196.94

146.39
143.38
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134.81
134.64
134.45
134.26
134.07
133.71
130.92
129.31
129.01
128.43
127.94
127.45
127.25
126.18
126.16
126.14
126.12
125.50
123.95
122.40
120.84
119.70

77.18
77.00
76.82

55.95

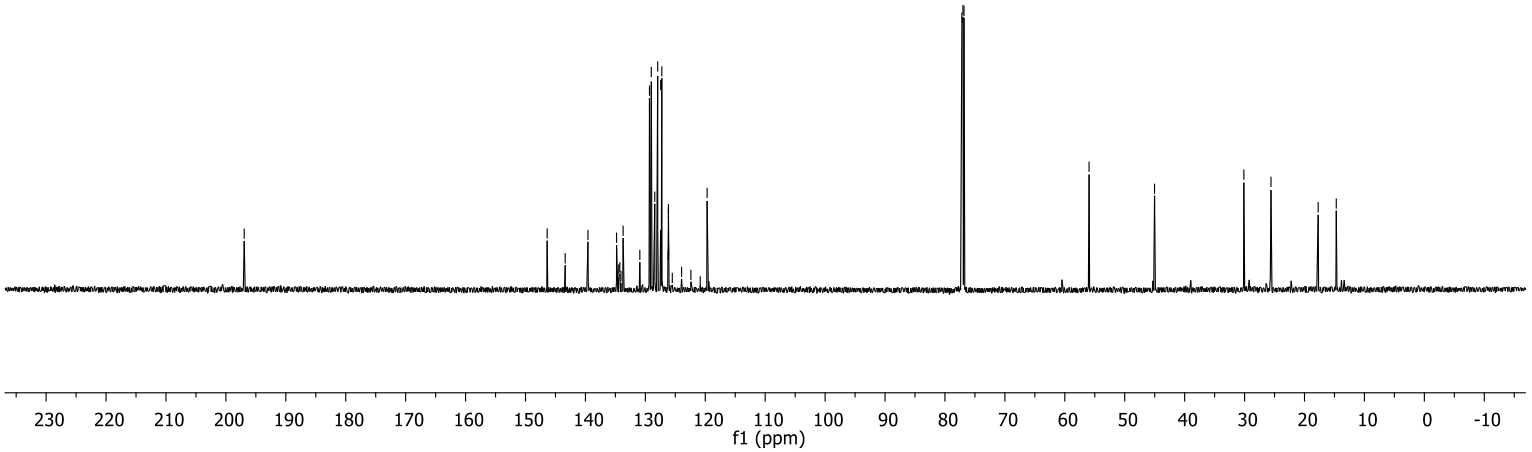
45.02

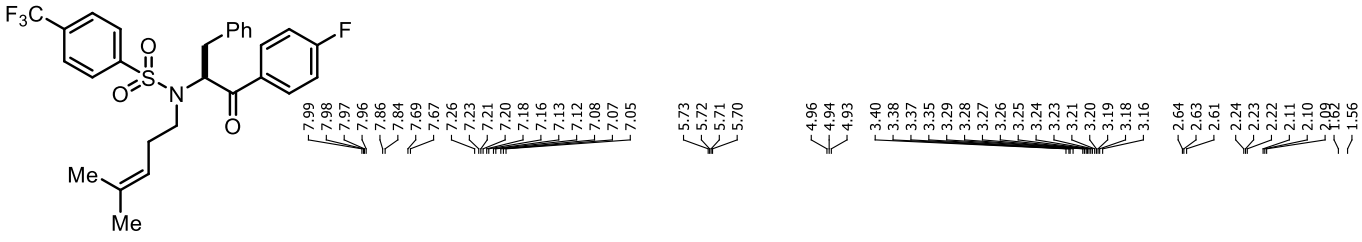
30.12

25.59

17.72

14.70




F3C
O
S
O
N
Ph
F
O
Me
Me
7.99
7.98
7.97
7.96
7.86
7.84
7.69
7.67
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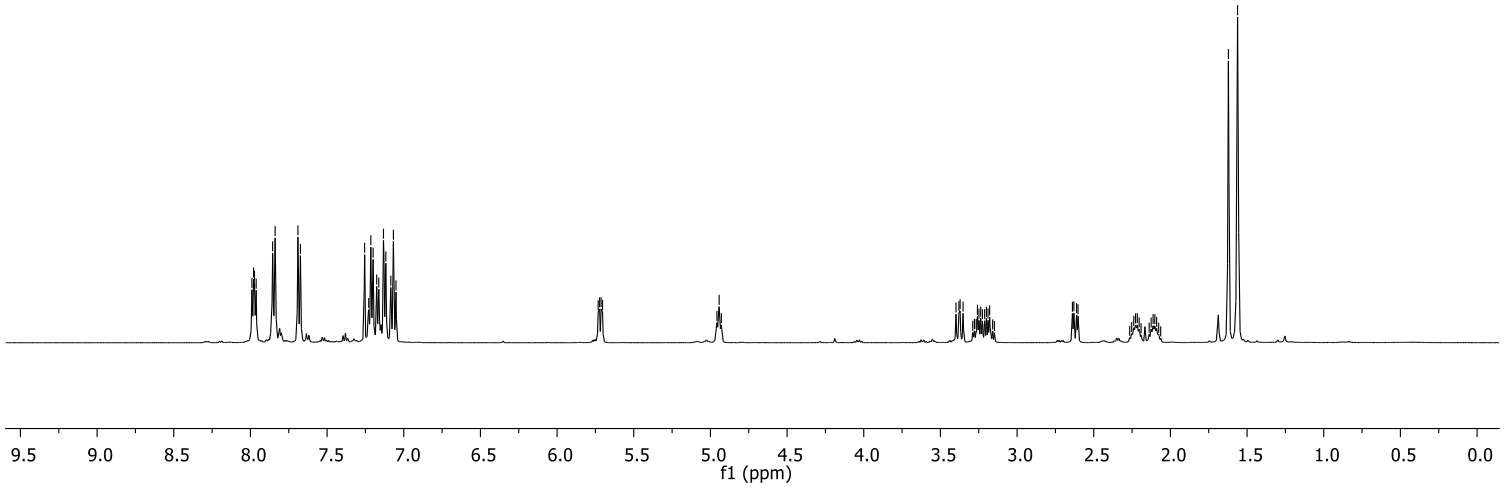
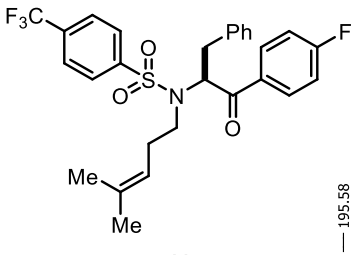
7.23
7.21
7.20
7.18
7.16
7.13
7.12
7.08
7.07
7.05
5.73
5.72
5.71
5.70
4.96
4.94
4.93
3.40
3.38
3.37
3.35
3.29
3.28
3.27
3.26
3.25
3.24
3.23
3.21
3.20
3.19
3.18
3.16
2.64
2.63
2.61
2.24
2.23
2.22
2.11
2.10
1.62
1.56

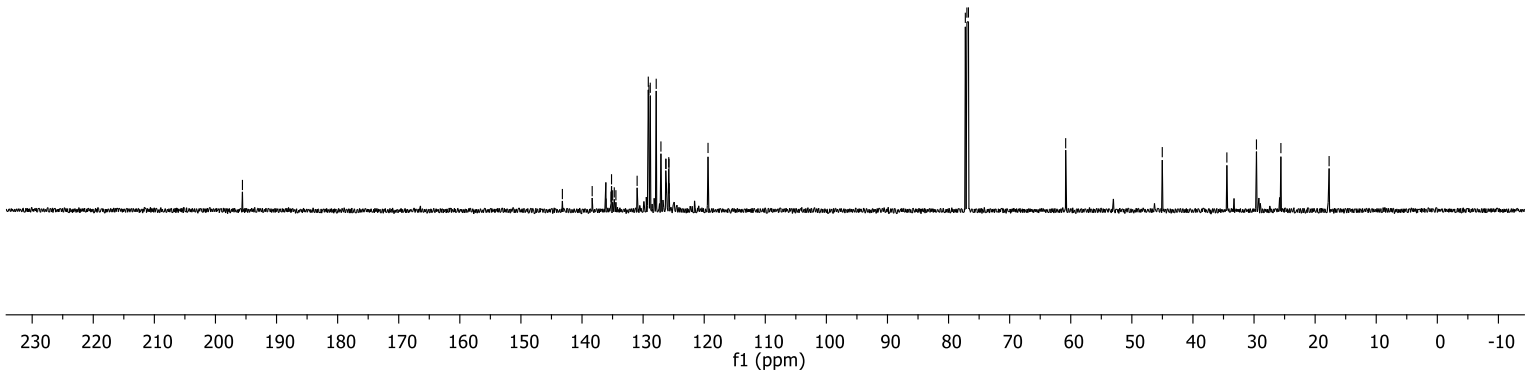
41

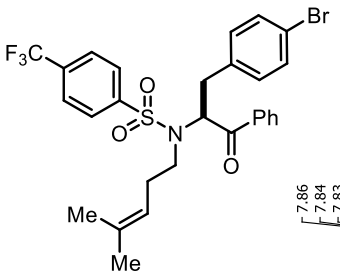

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



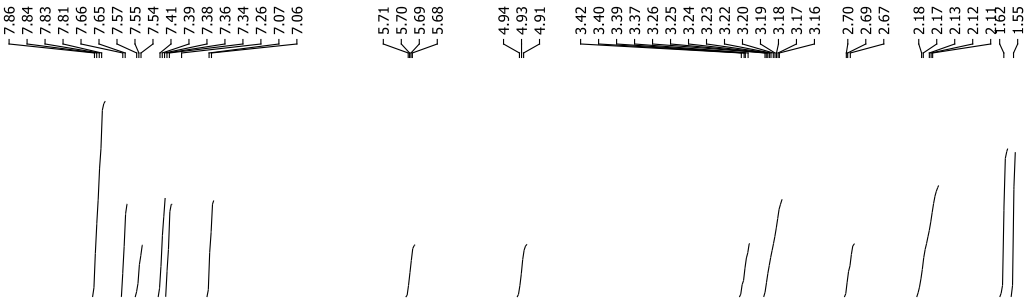
41

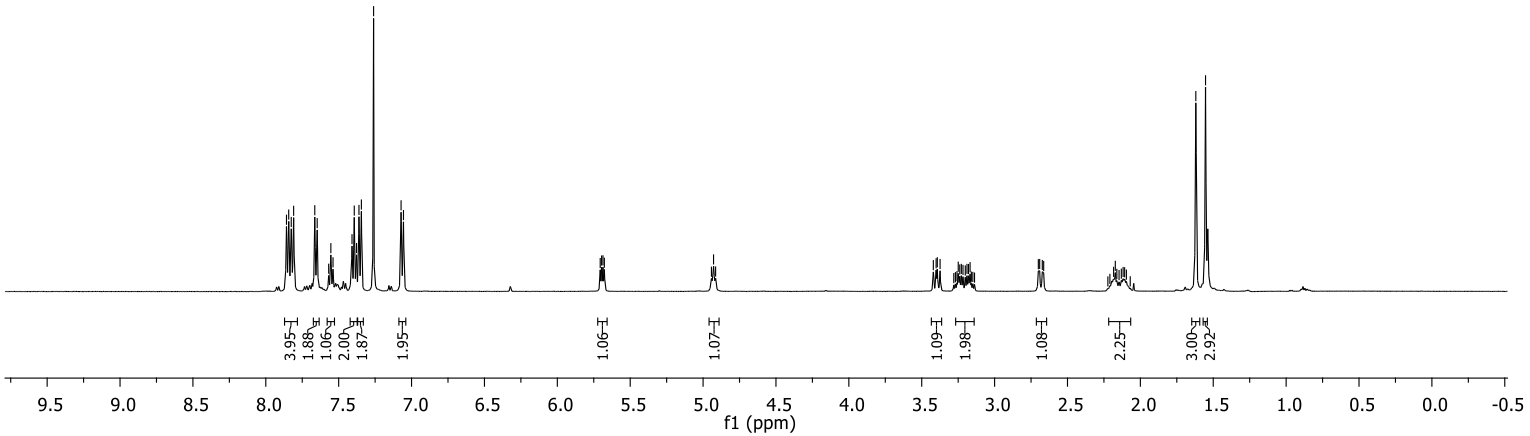
195.58
143.21
138.33
136.06
135.24
135.17
134.98
134.72
134.45
130.98
129.15
129.05
128.83
127.85
127.08
126.32
126.29
126.26
126.23
125.82
125.80
125.77
125.74
119.37
77.25
77.00
76.75
60.83
45.02
34.45
29.60
25.60
17.71

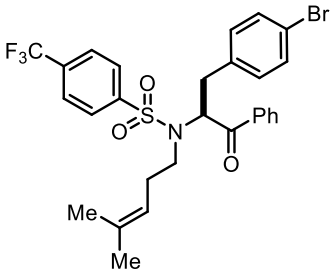



Br
F3C
O
S
O
N
Ph
O
Me
Me

43


7.86
7.84
7.83
7.81
7.66
7.65
7.57
7.55
7.54
7.41
7.39
7.38
7.36
7.34
7.26
7.07
7.06
5.71
5.70
5.69
5.68
4.94
4.93
4.91
3.42
3.40
3.39
3.37
3.26
3.25
3.24
3.23
3.22
3.20
3.19
3.18
3.17
3.16
2.70
2.69
2.67
2.18
2.17
2.13
2.12
2.11
1.62
1.55


3.95
1.88
1.06
2.00
1.87
1.95
1.06
1.07
1.09
1.98
1.08
2.25
3.00
2.92
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



43

195.96

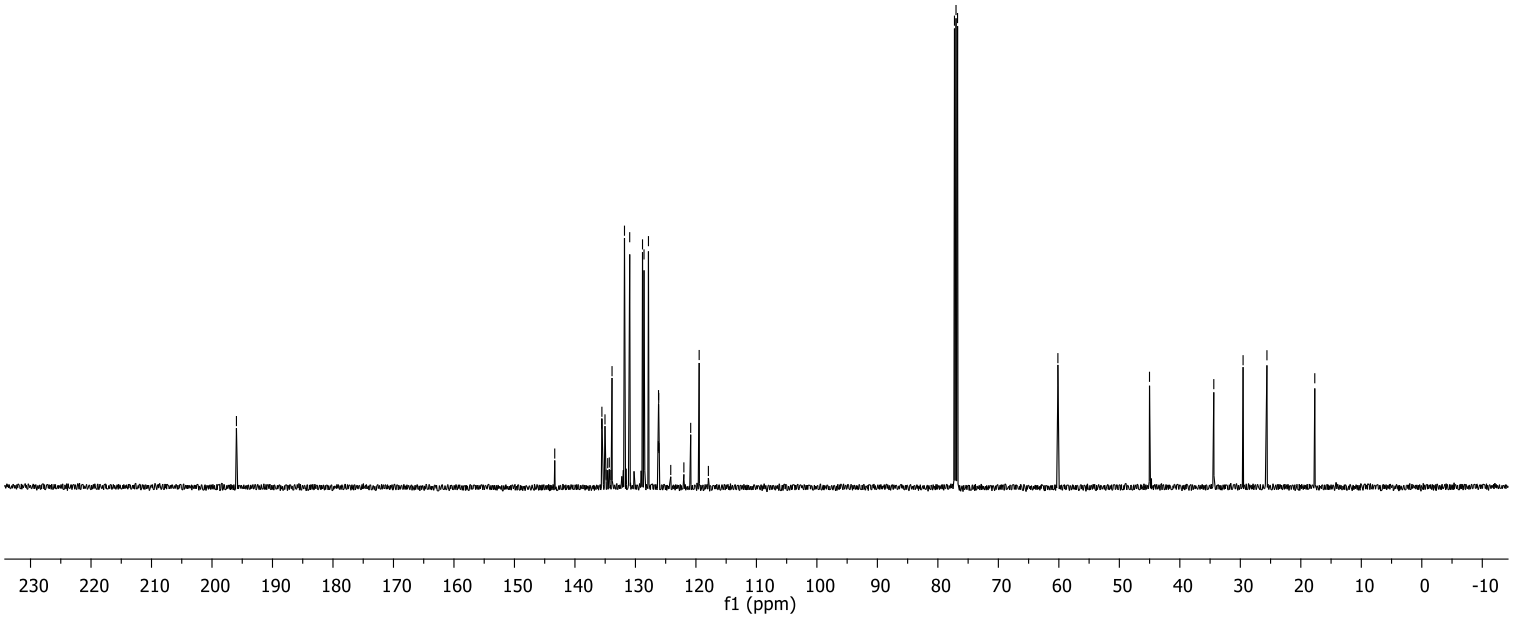
143.34
135.57
135.54
135.03
134.58
134.32
133.87
131.81
130.95
128.83
128.58
127.85
126.21
126.18
126.15
126.12
124.16
121.99
120.86
119.46
117.94
77.25
77.00
76.75

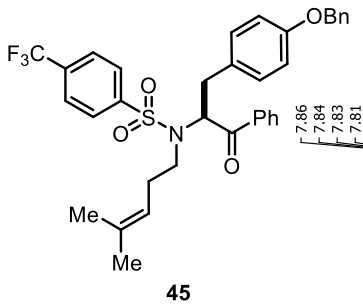
60.16

45.01

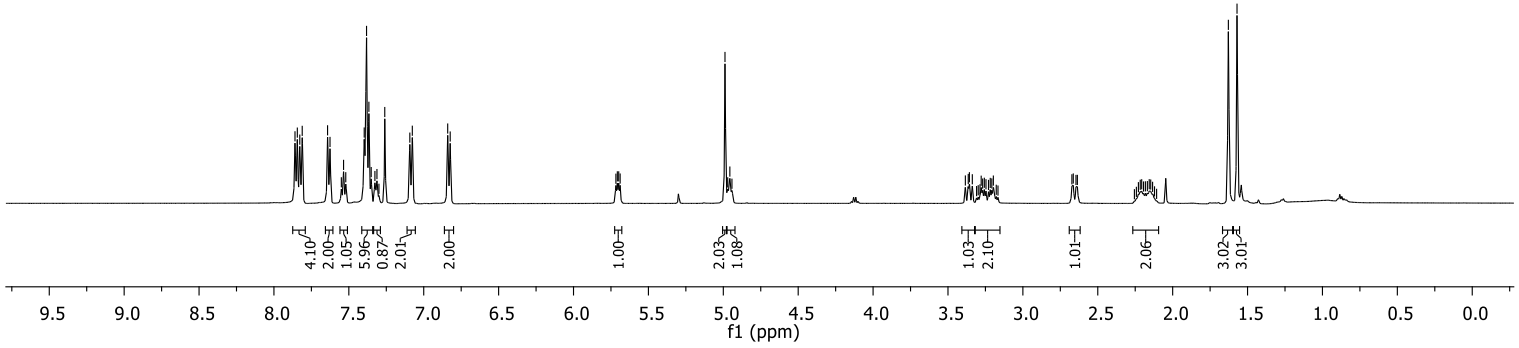
34.39
29.55
25.60

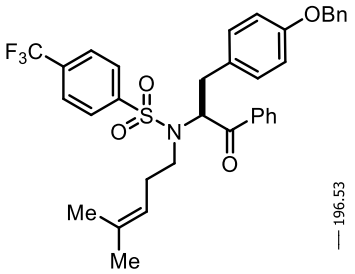
17.69




OBn
F3C
O
S
O
N
Ph
O
Me
Me

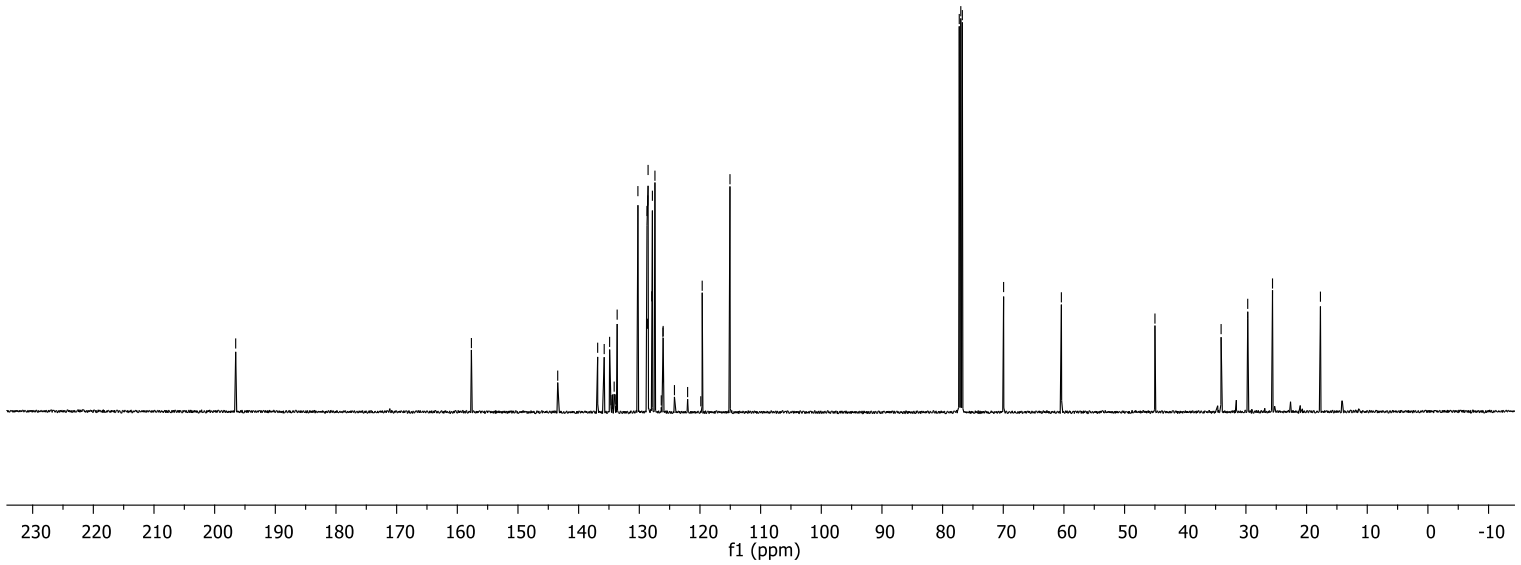
45

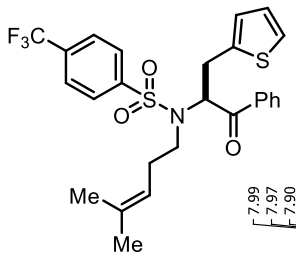

4.10
2.00
1.05
5.96
0.87
2.01
2.00
1.00
2.03
1.08
1.03
2.10
1.01
2.06
3.02
3.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



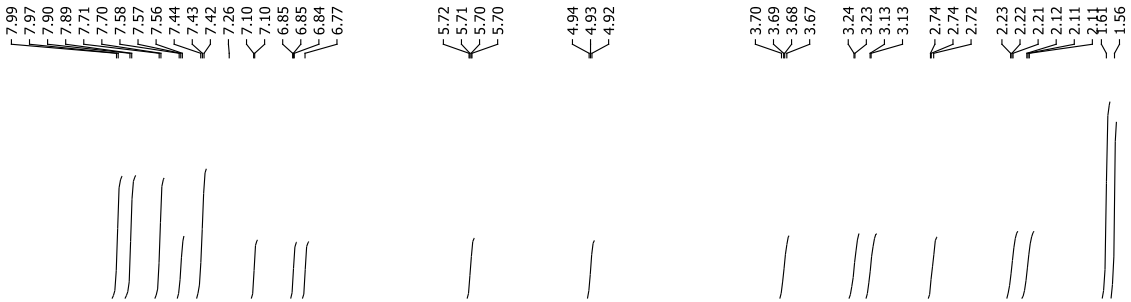
45

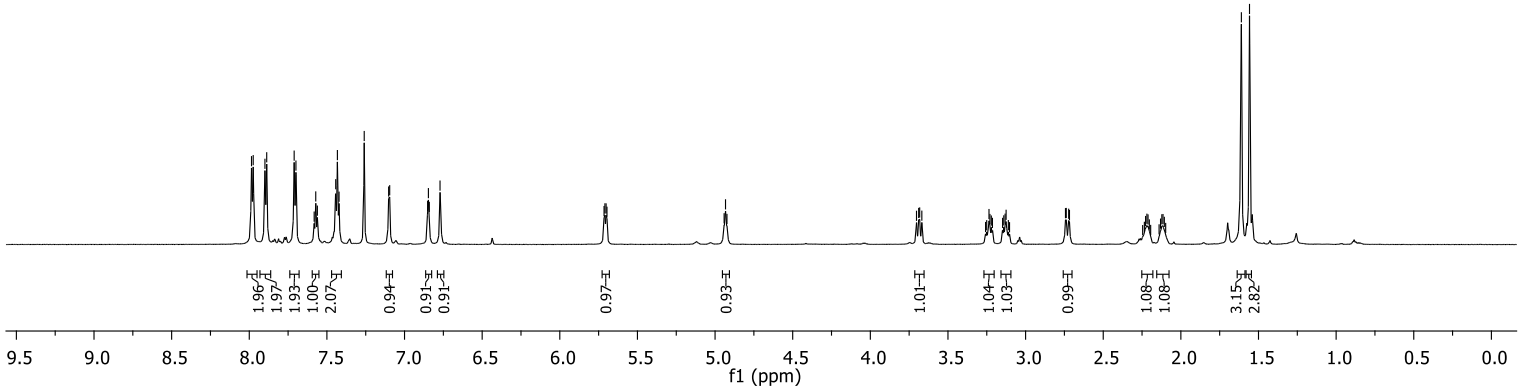
196.53
157.68
143.45
136.86
135.79
134.89
134.14
133.65
130.23
128.73
128.63
128.59
128.55
127.95
127.84
127.42
126.13
126.10
126.07
126.04
124.20
119.63
115.05
77.26
77.00
76.75
69.95
60.42
45.00
34.09
29.70
25.62
17.72

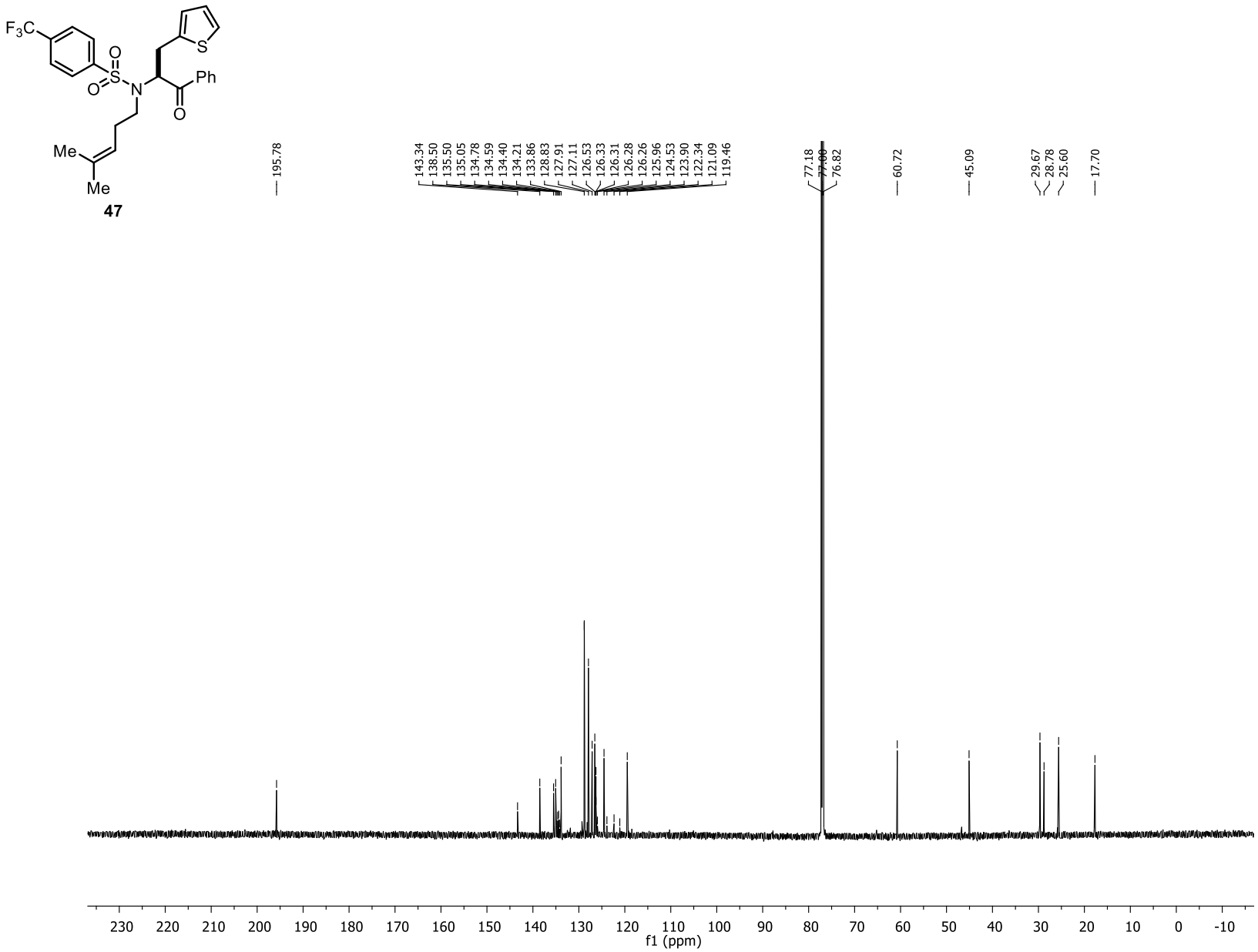


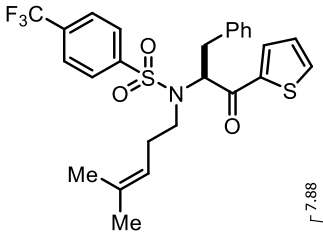

F3C
O
S
O
N
S
Ph
O
Me
Me

47

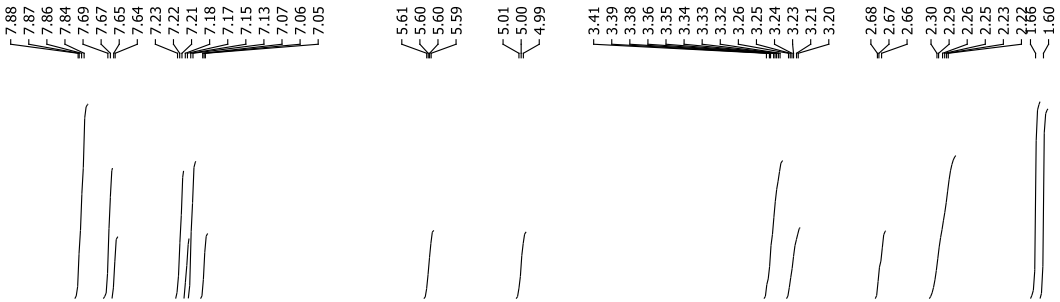

7.99
7.97
7.90
7.89
7.71
7.70
7.58
7.57
7.56
7.44
7.43
7.42
7.26
7.10
7.10
6.85
6.85
6.84
6.77
5.72
5.71
5.70
5.70
4.94
4.93
4.92
3.70
3.69
3.68
3.67
3.24
3.23
3.13
3.13
2.74
2.74
2.72
2.23
2.22
2.21
2.12
2.11
1.61
1.56

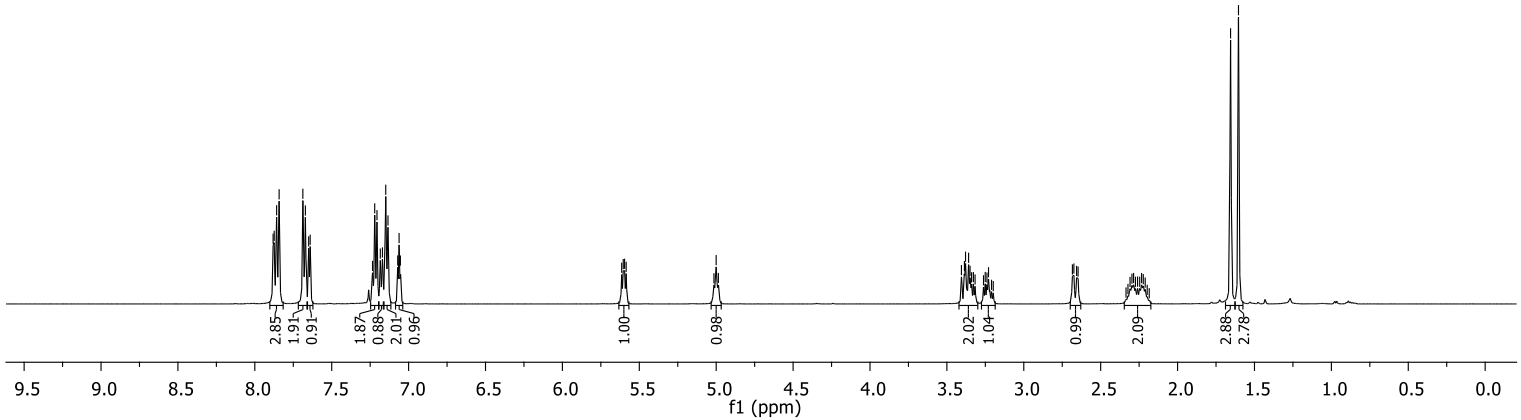

1.96
1.97
1.93
1.00
2.07
0.94
0.91
0.91
0.97
0.93
1.01
1.04
1.03
0.99
1.08
1.08
3.15
2.82
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

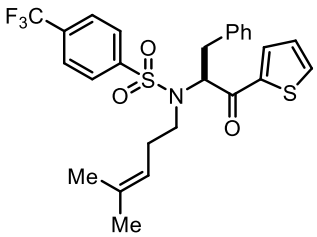

F3C
O
S
O
N
Ph
O
S
Me
Me
47
195.78
143.34
138.50
135.50
135.05
134.78
134.59
134.40
134.21
133.86
128.83
127.91
127.11
126.53
126.33
126.31
126.28
126.26
125.96
124.53
123.90
122.34
121.09
119.46
77.18
77.00
76.82
60.72
45.09
29.67
28.78
25.60
17.70
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F3C
O
S
O
N
Ph
S
O
Me
Me

49

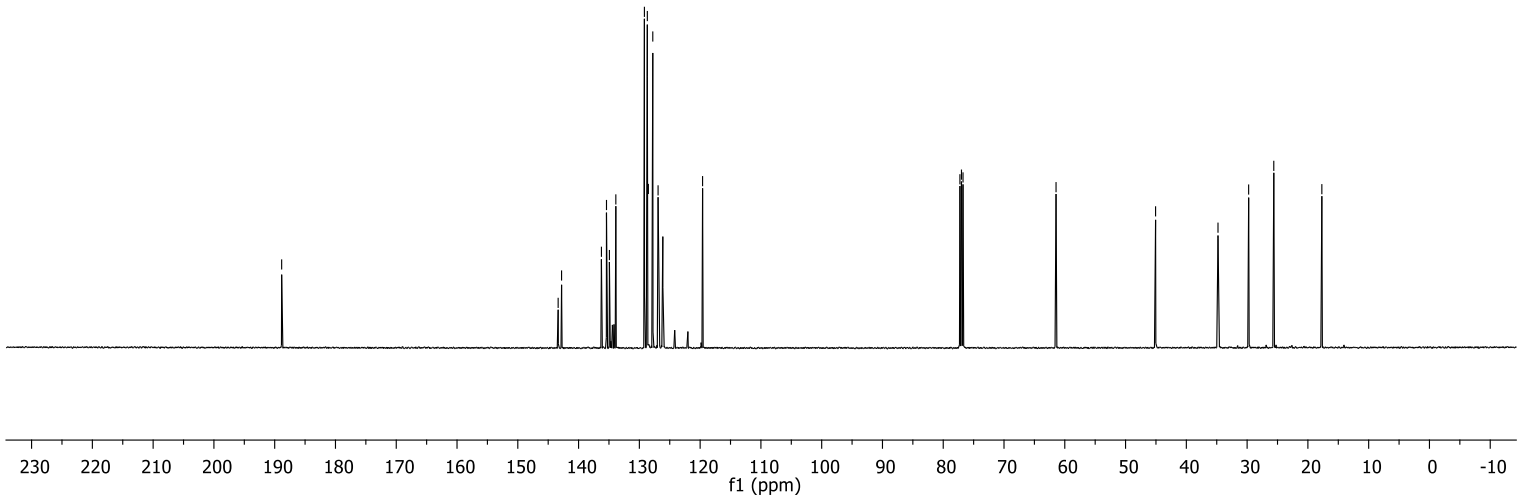

7.88
7.87
7.86
7.84
7.69
7.67
7.65
7.64
7.23
7.22
7.21
7.18
7.17
7.15
7.13
7.07
7.06
7.05
5.61
5.60
5.60
5.59
5.01
5.00
4.99
3.41
3.39
3.38
3.36
3.35
3.34
3.33
3.32
3.26
3.25
3.24
3.23
3.21
3.20
2.68
2.67
2.66
2.30
2.29
2.26
2.25
2.23
1.62
1.60

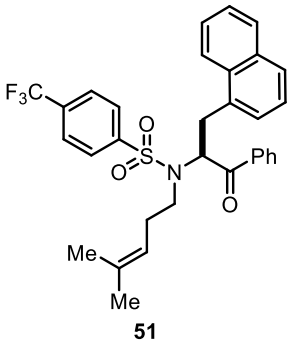

2.85
1.91
0.91
1.87
0.88
2.01
0.96
1.00
0.98
2.02
1.04
0.99
2.09
2.88
2.78
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



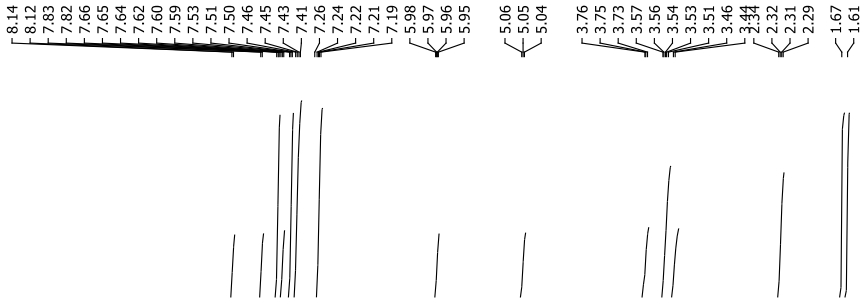
49

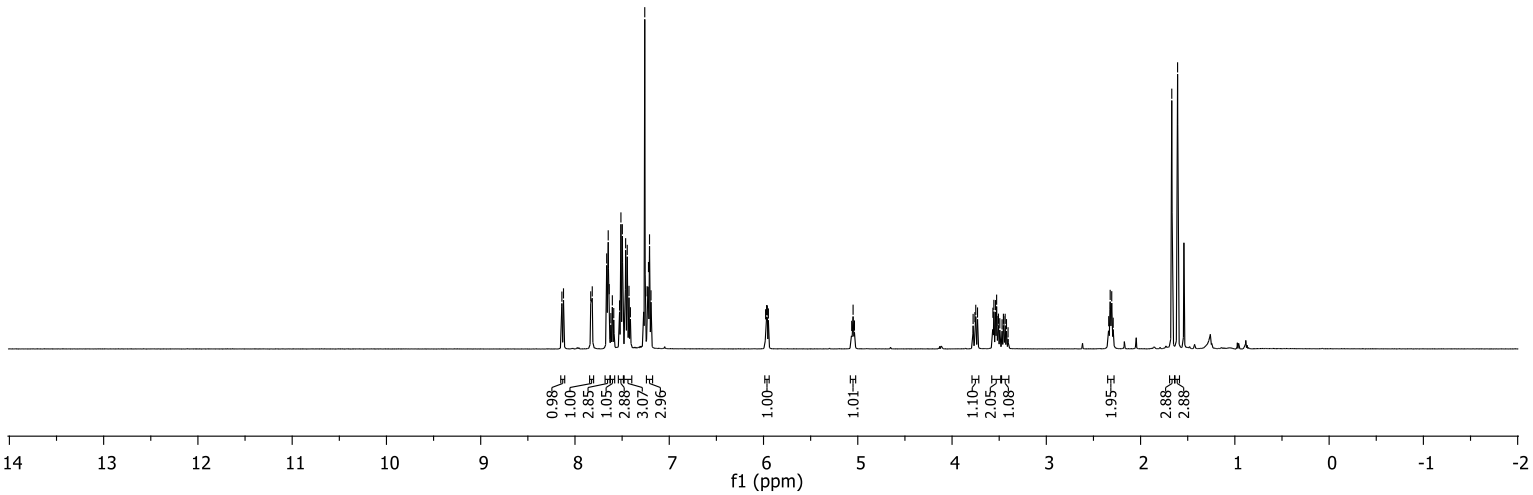
188.85
143.36
142.80
133.87
129.17
128.69
128.51
127.79
126.92
119.60
77.25
77.00
76.75
61.44
45.06
34.79
29.75
25.61
17.70

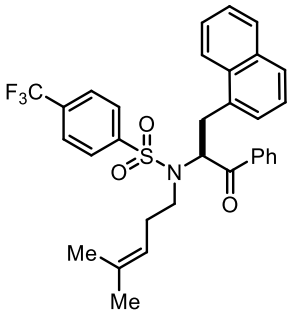



F3C
O
S
O
N
Ph
O
Me
Me

51


8.14
8.12
7.83
7.82
7.66
7.65
7.64
7.62
7.60
7.59
7.53
7.51
7.50
7.46
7.45
7.43
7.41
7.26
7.24
7.22
7.21
7.19
5.98
5.97
5.96
5.95
5.06
5.05
5.04
3.76
3.75
3.73
3.57
3.56
3.54
3.53
3.51
3.46
2.32
2.31
2.29
1.67
1.61


0.98
1.00
2.85
1.05
2.88
3.07
2.96
1.00
1.01
1.10
2.05
1.08
1.95
2.88
2.88
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)



51

197.29

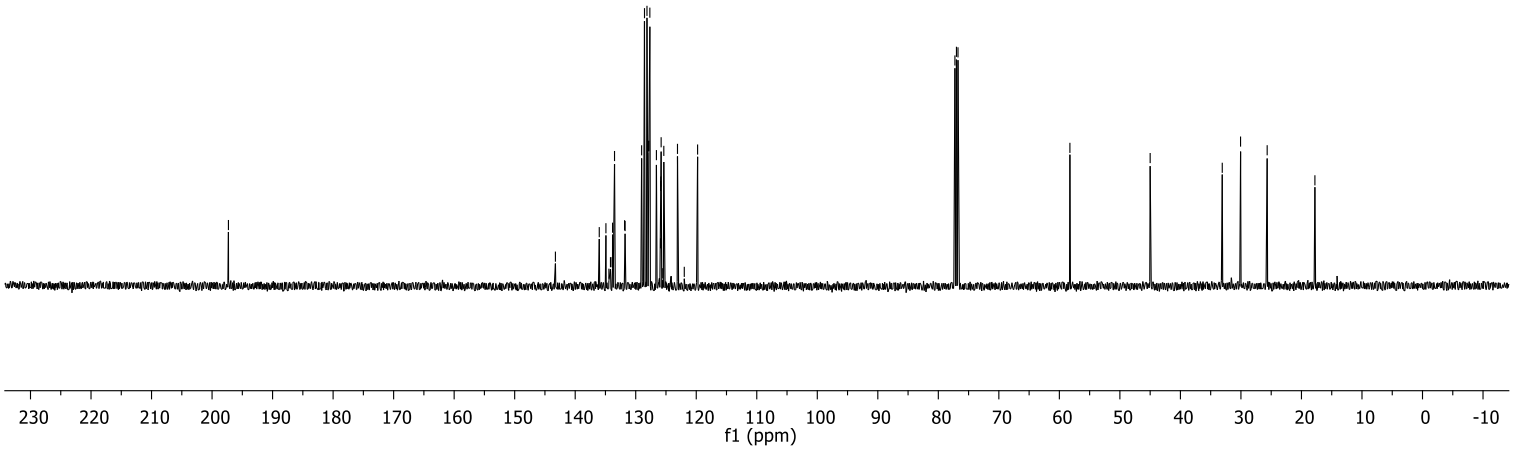
143.27
136.02
134.92
133.82
133.50
131.84
131.76
129.02
128.55
128.14
127.88
127.83
127.66
126.58
125.90
125.87
125.85
125.80
125.36
123.10
119.78
77.26
77.00
76.75

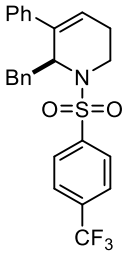
58.26

45.00

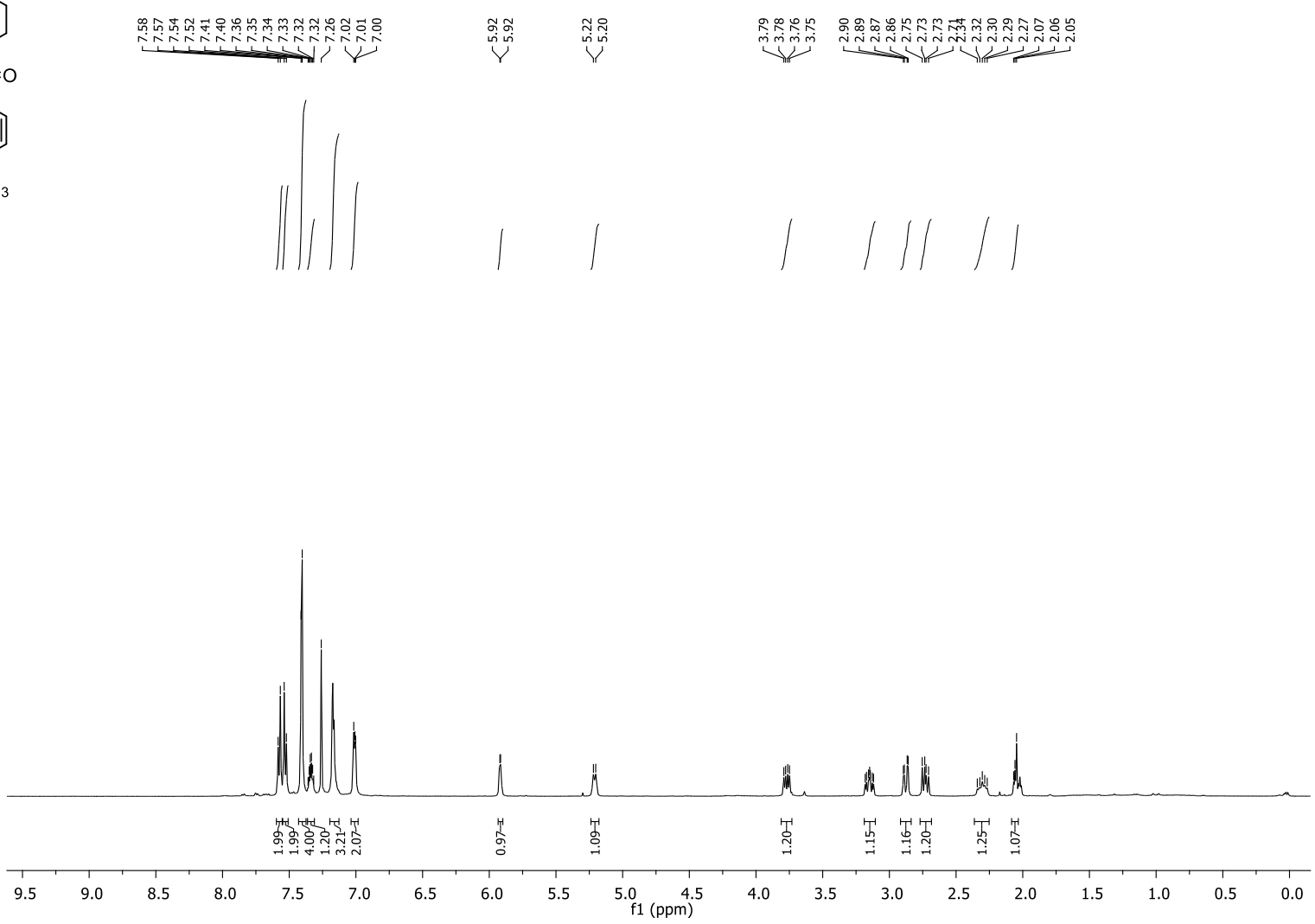
33.09
30.06
25.66

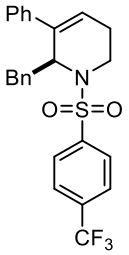
17.78



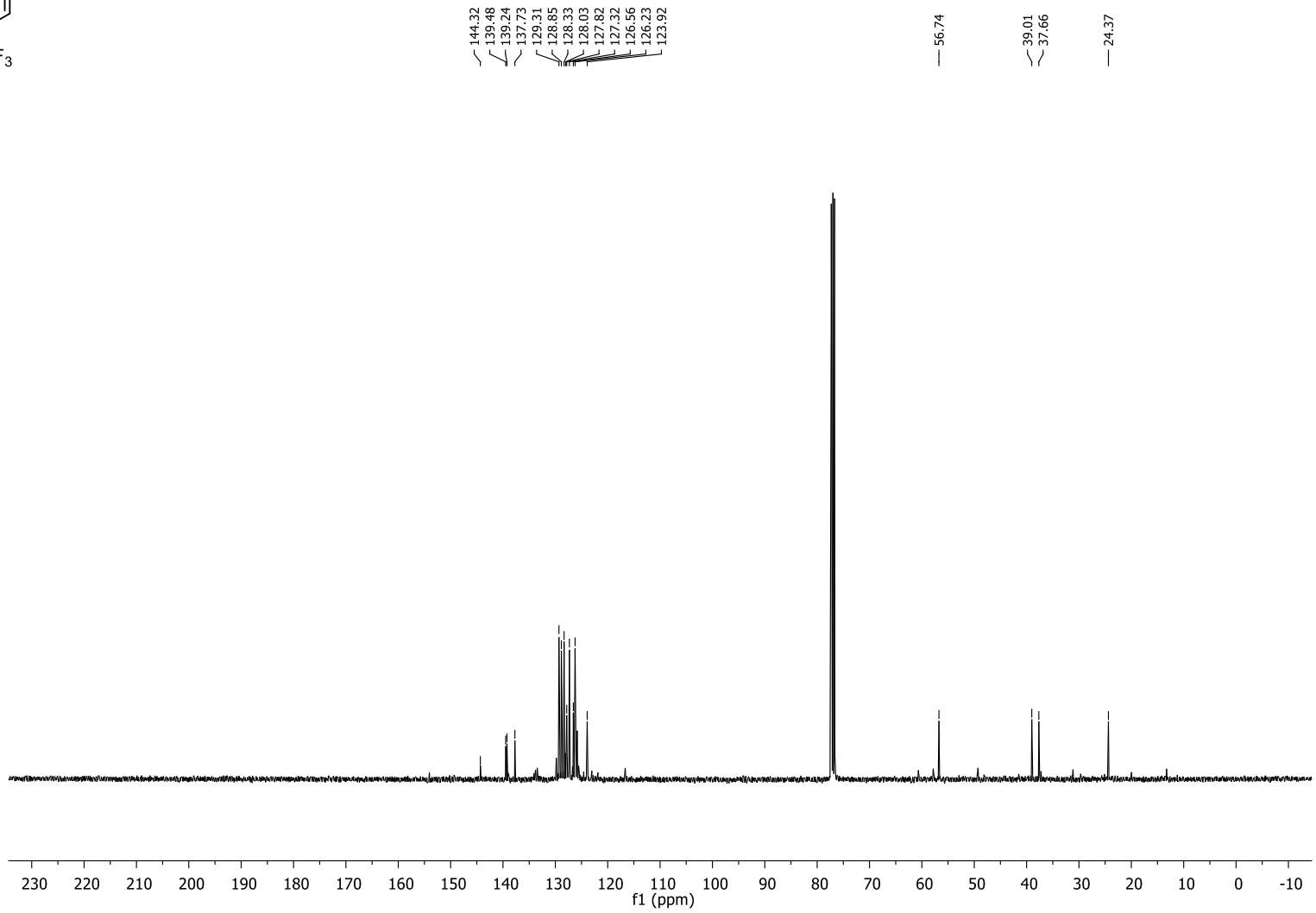

Ph
Bn
N
O=S=O
CF3

10


7.58
7.57
7.54
7.52
7.41
7.40
7.36
7.35
7.34
7.33
7.32
7.32
7.26
7.02
7.01
7.00
5.92
5.92
5.22
5.20
3.79
3.78
3.76
3.75
2.90
2.89
2.87
2.86
2.75
2.73
2.73
2.71
2.34
2.32
2.30
2.29
2.27
2.07
2.06
2.05
1.99
1.99
4.00
1.20
3.21
2.07
0.97
1.09
1.20
1.15
1.16
1.20
1.25
1.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Ph
Bn
N
O=S=O
CF3

10


144.32
139.48
139.24
137.73
129.31
128.85
128.33
128.03
127.82
127.32
126.56
126.23
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37.66
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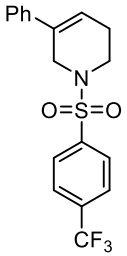
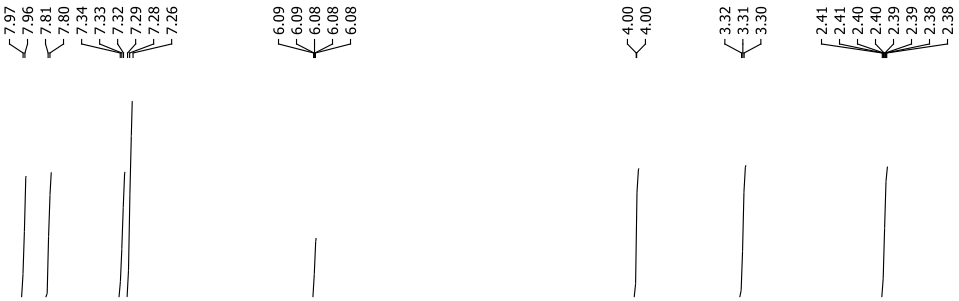
f1 (ppm)


Ph
N
O=S=O
CF3

28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6.09
6.08
6.08
6.08
4.00
4.00
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3.31
3.30
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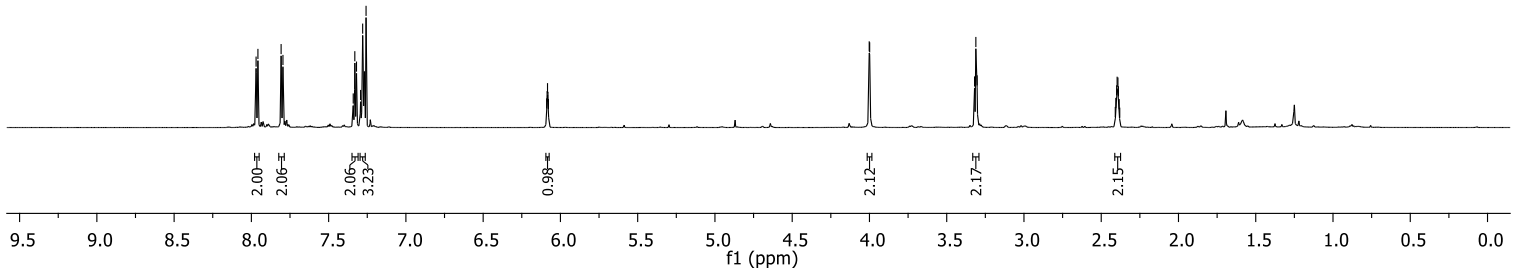
2.39
2.38
2.38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2.06
2.06
3.23
0.98
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2.17
2.15
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
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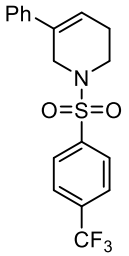
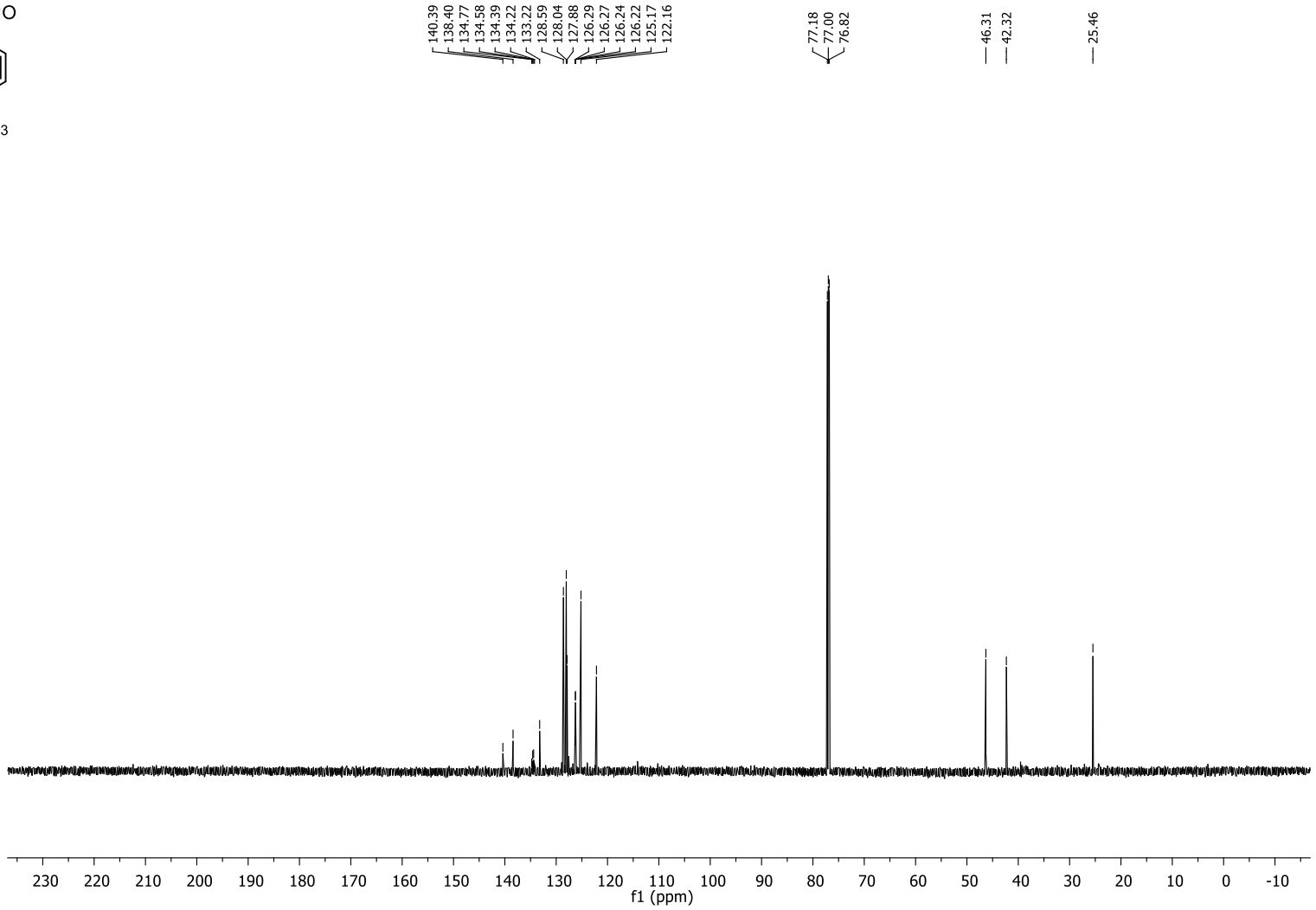
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Ph
N
O=S=O
CF3

28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126.24
126.22
125.17
122.16
77.18
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46.31
42.32
25.46
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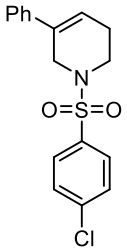
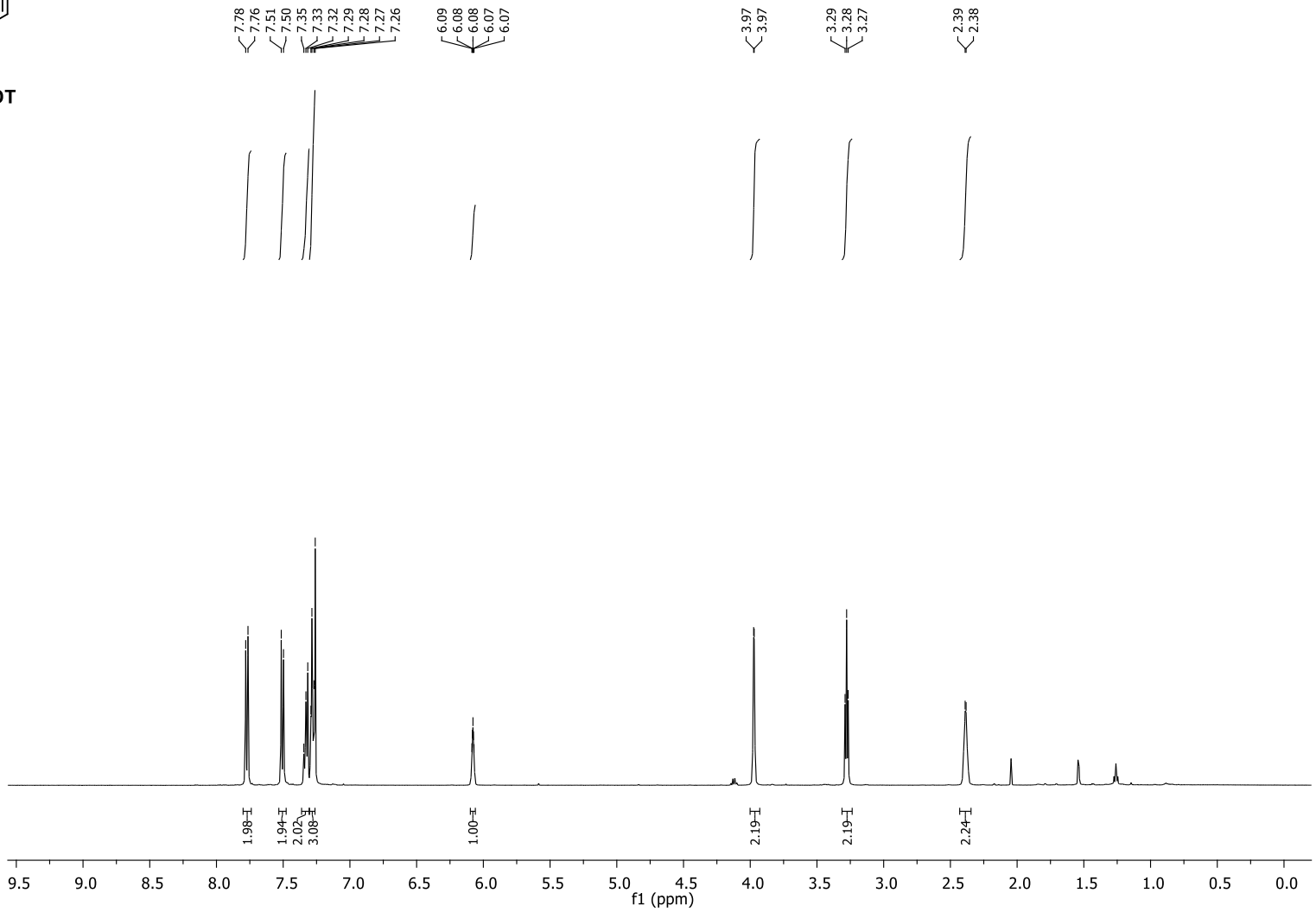
f1 (ppm)


Ph
N
O=S=O
Cl

15 PDT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7.32
7.29
7.28
7.27
7.26
6.09
6.08
6.08
6.07
6.07
3.97
3.97
3.29
3.28
3.27
2.39
2.38
1.98
1.94
2.02
3.08
1.00
2.19
2.19
2.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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2.5
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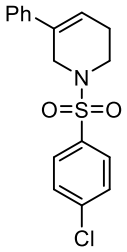
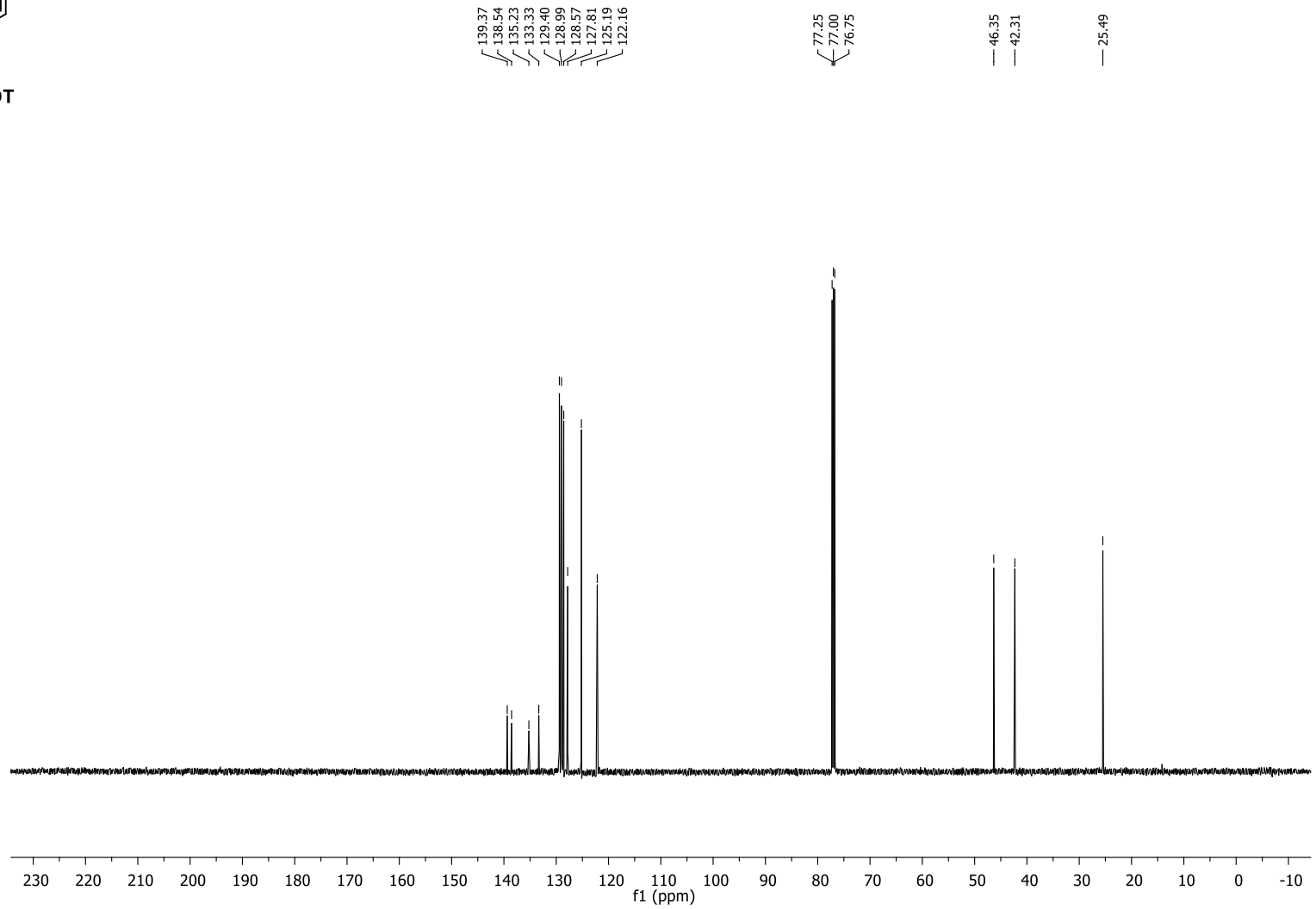
0.0
f1 (ppm)


Ph
N
O=S=O
Cl

15 PDT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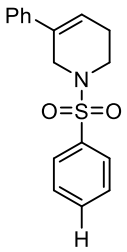
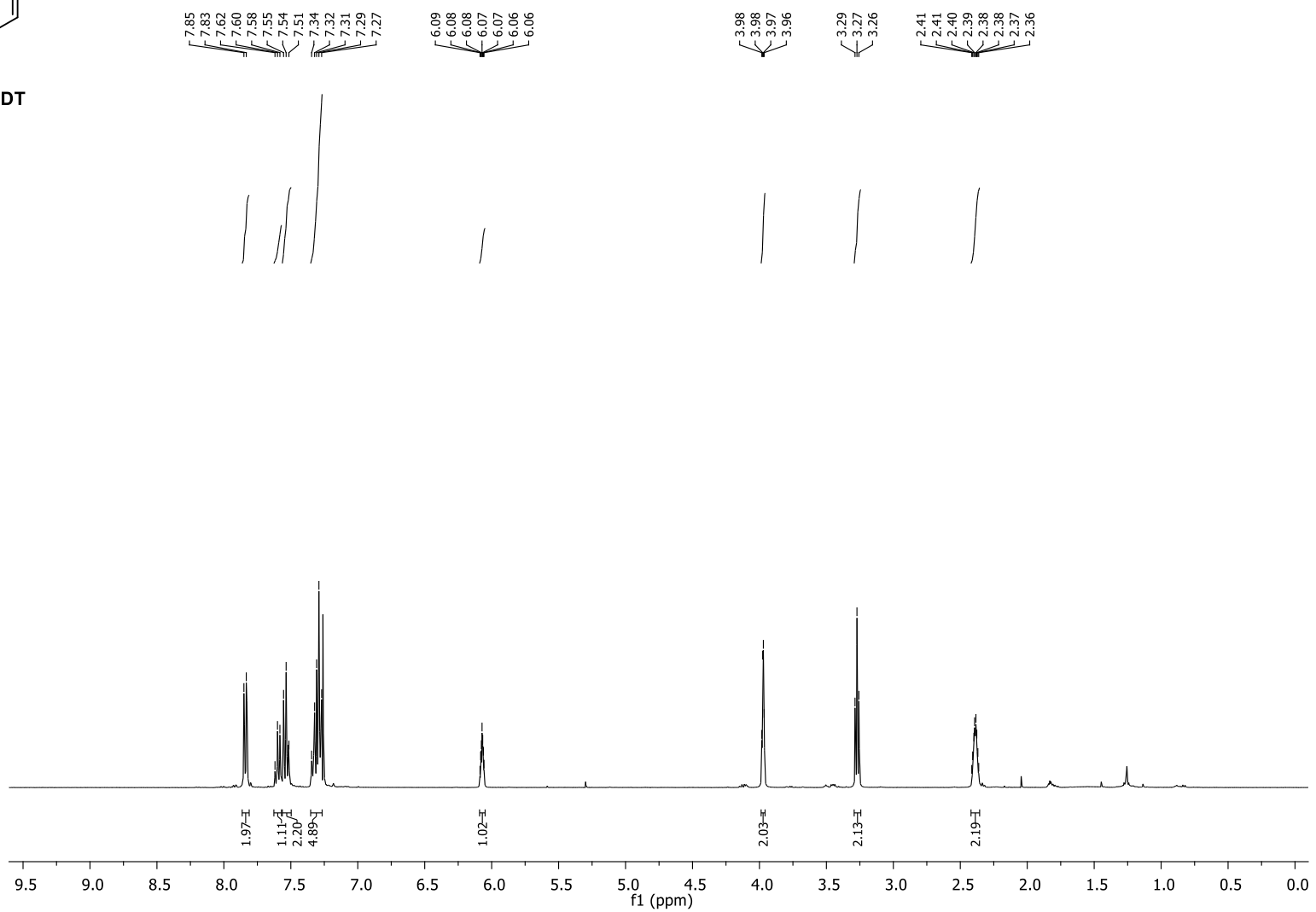
128.57
127.81
125.19
122.16
77.25
77.00
76.75
46.35
42.31
25.49
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
N
O=S=O
H

16 PDT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7.62
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7.32
7.31
7.29
7.27
6.09
6.08
6.08
6.07
6.07
6.06
6.06
3.98
3.98
3.97
3.96
3.29
3.27
3.26
2.41
2.41
2.40
2.39
2.38
2.38
2.37
2.36
1.97
1.11
2.20
4.89
1.02
2.03
2.13
2.19
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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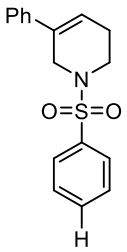
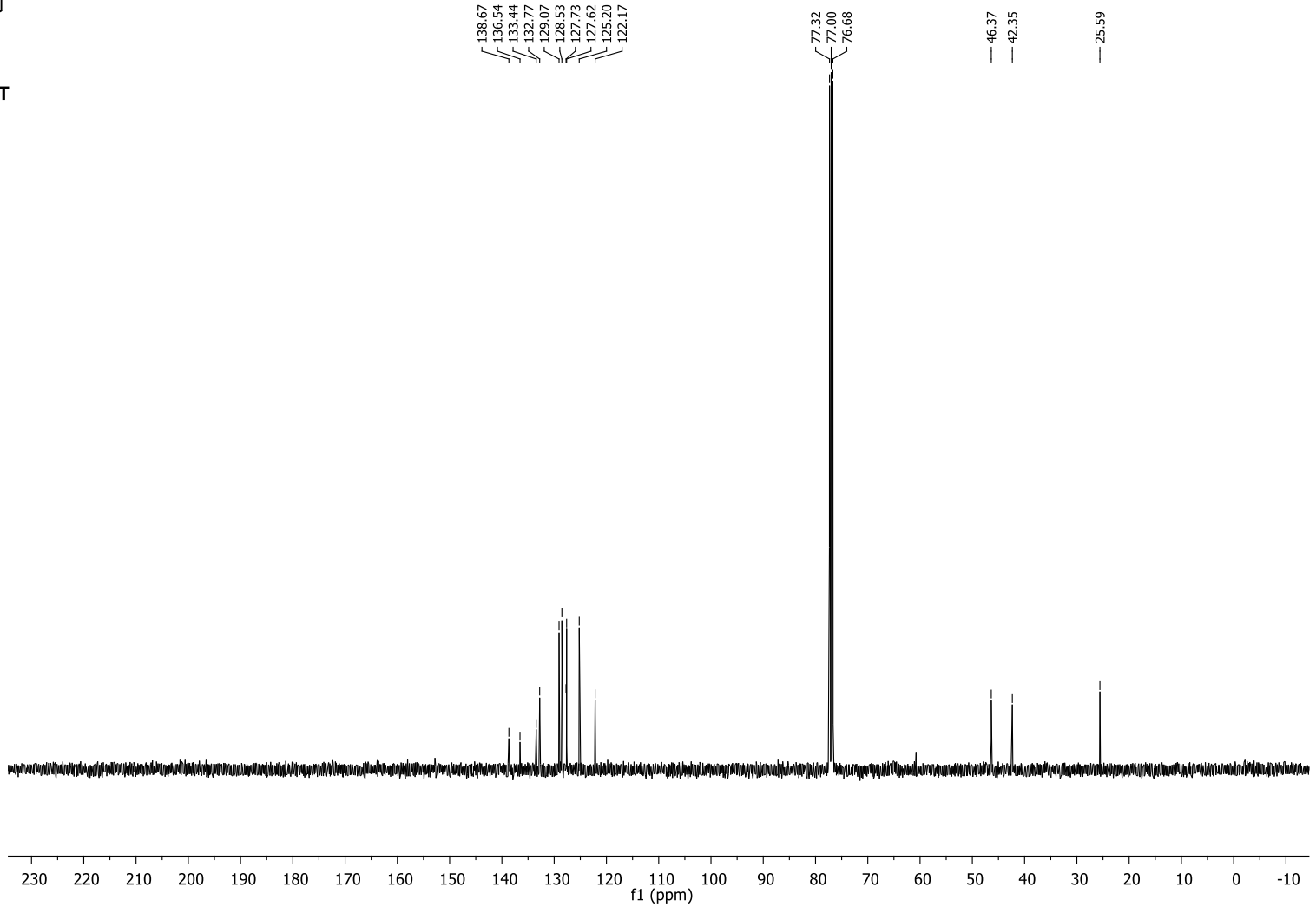
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Ph
N
O=S=O
H

16 PDT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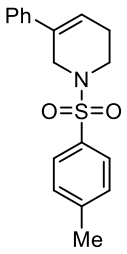
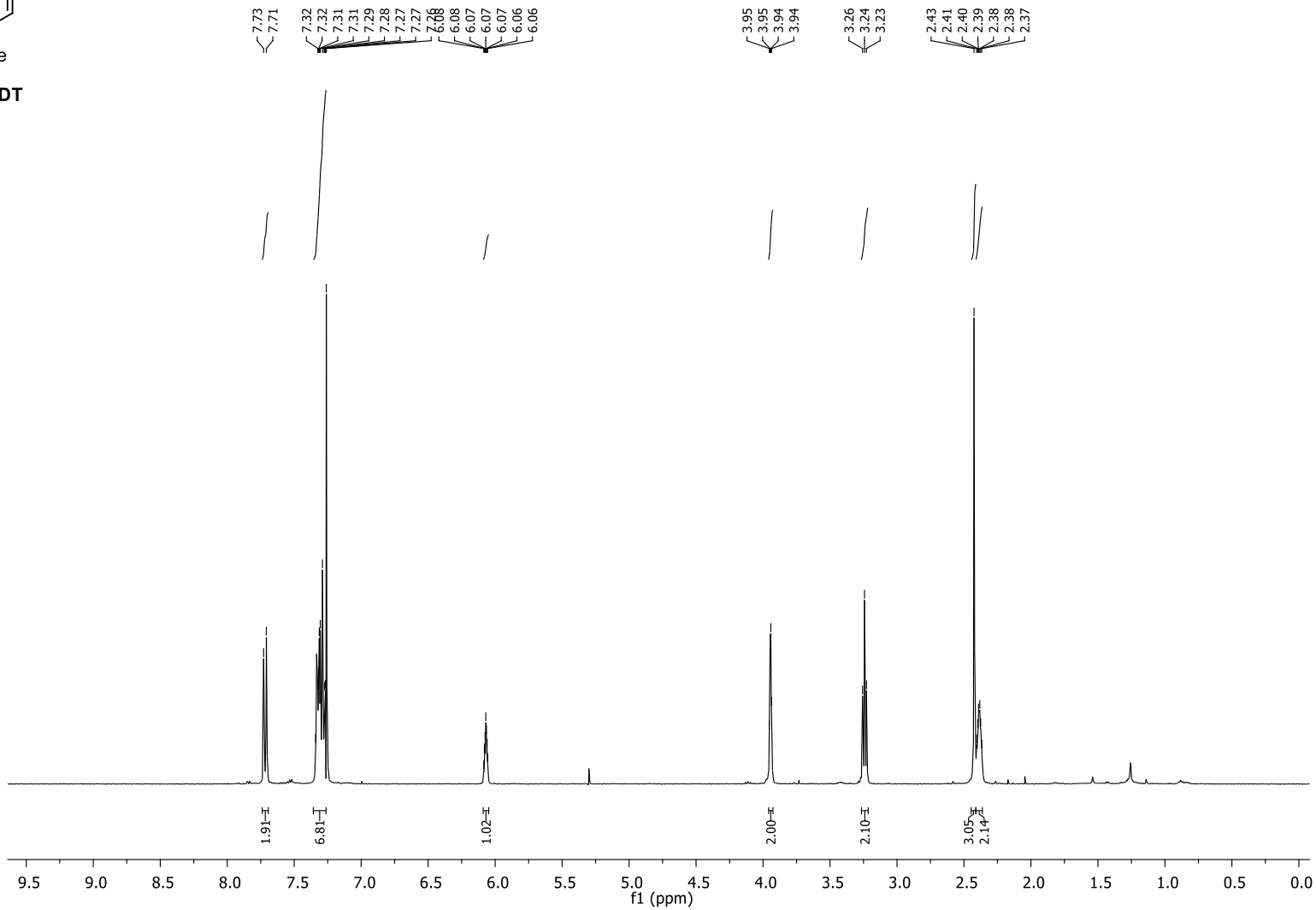
128.53
127.73
127.62
125.20
122.17
77.32
77.00
76.68
46.37
42.35
25.59
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
N
O=S=O
Me

17 PDT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7.31
7.31
7.29
7.28
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7.27
6.08
6.08
6.07
6.07
6.07
6.06
6.06
3.95
3.95
3.94
3.94
3.26
3.24
3.23
2.43
2.41
2.40
2.39
2.38
2.38
2.37
1.91
6.81
1.02
2.00
2.10
3.05
2.14
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
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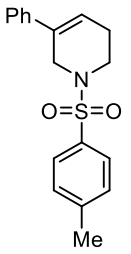
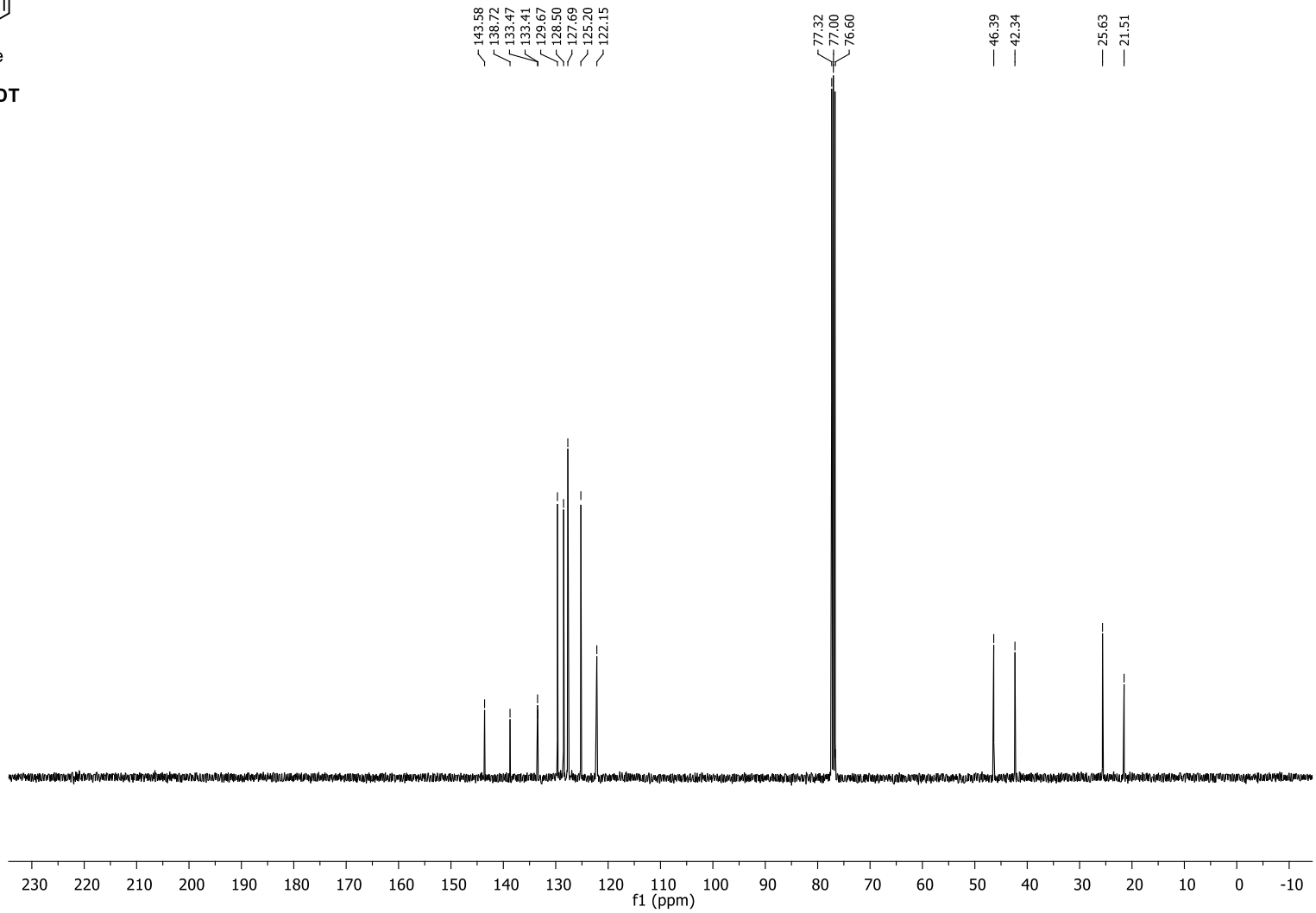
1.0
0.5
0.0
f1 (ppm)


Ph
N
O=S=O
Me

17 PDT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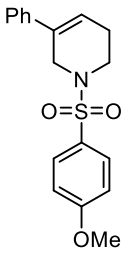
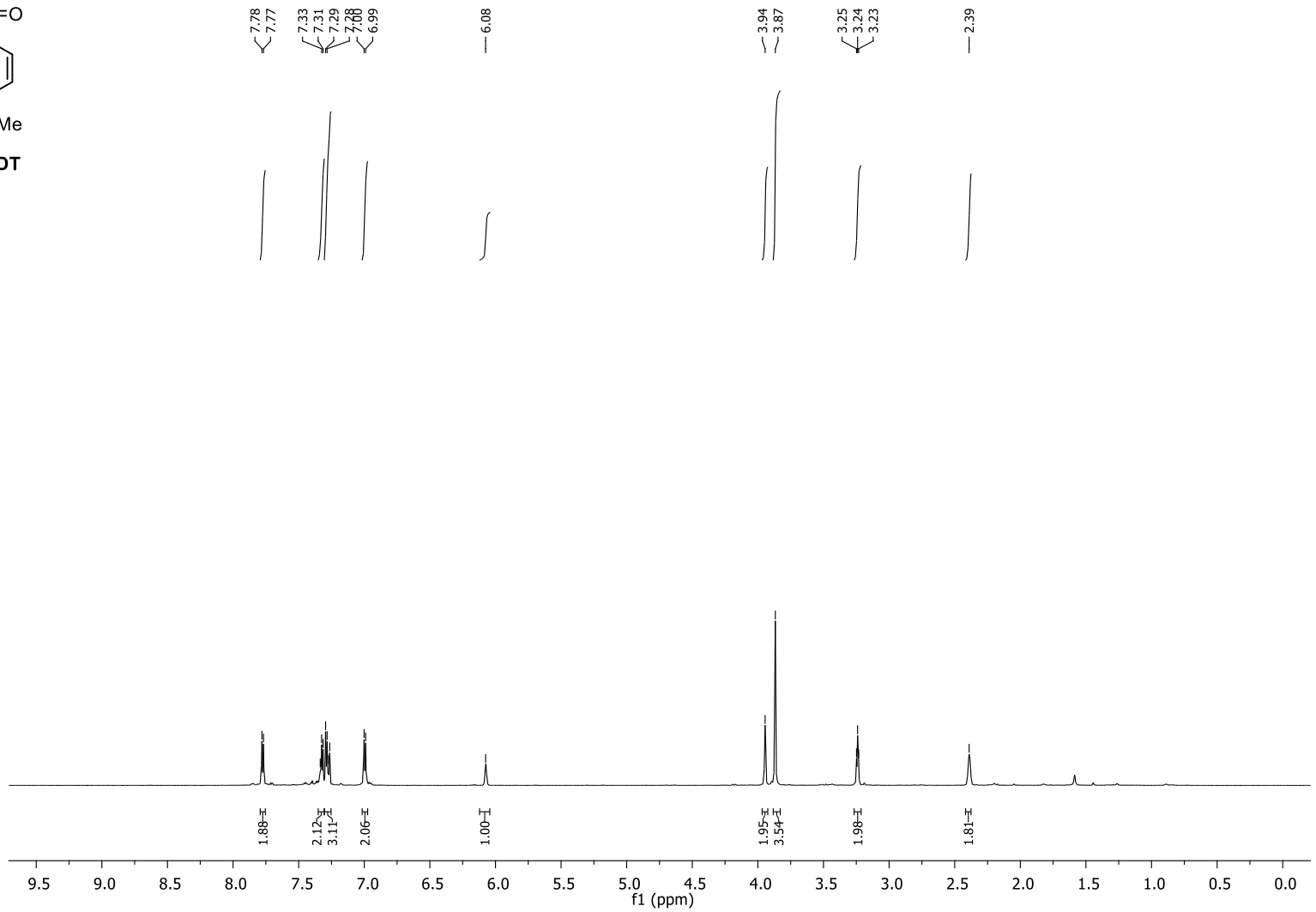
128.50
127.69
125.20
122.15
77.32
77.00
76.60
46.39
42.34
25.63
21.51
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
N
O=S=O
OMe

18 PDT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7.28
7.00
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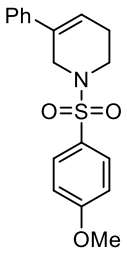
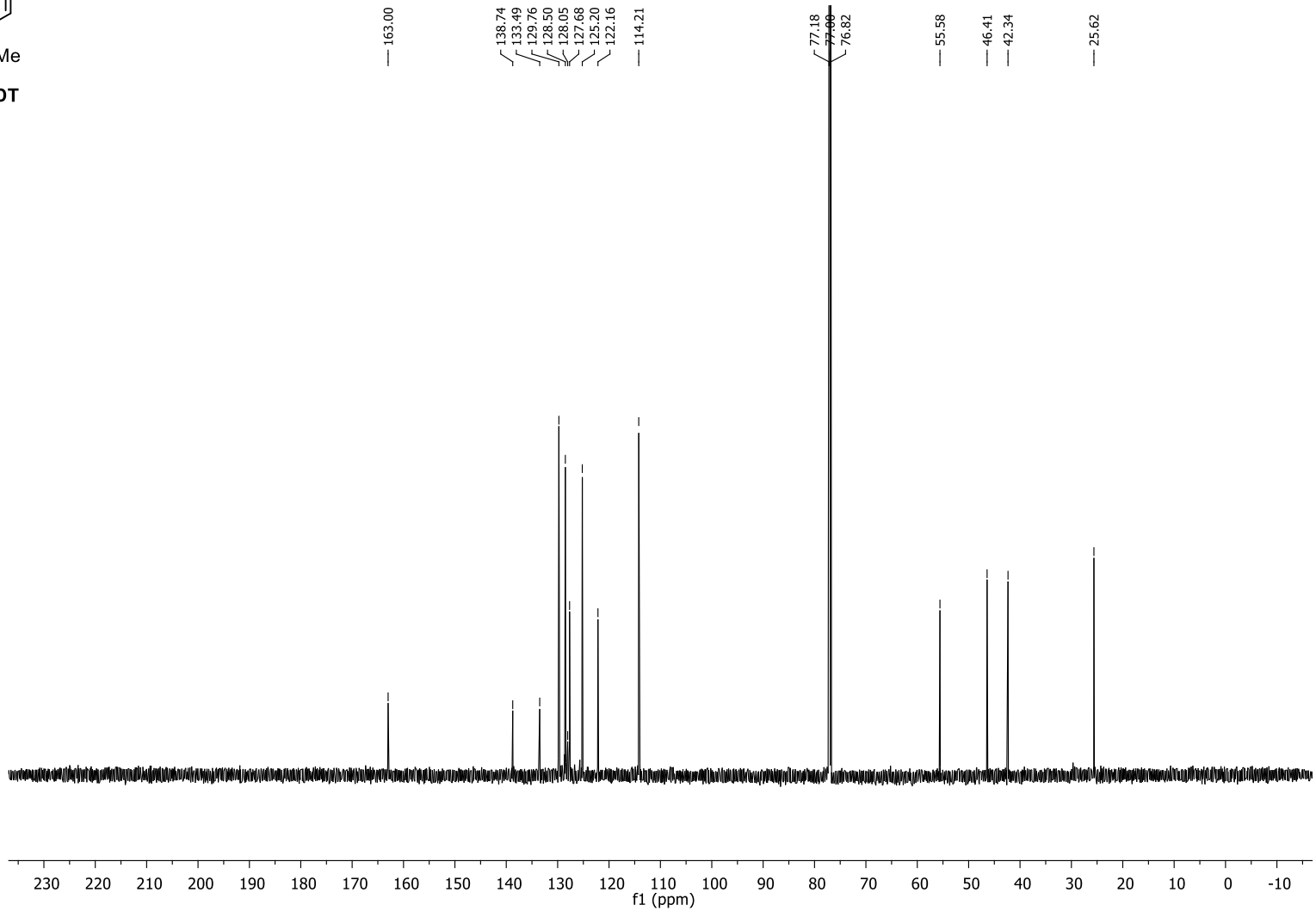
3.87
3.25
3.24
3.23
2.39
1.88
2.12
3.11
2.06
1.00
1.95
3.54
1.98
1.81
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Ph
N
O=S=O
OMe

18 PDT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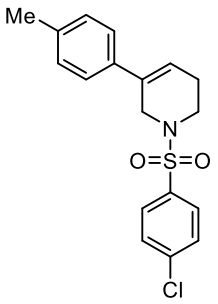
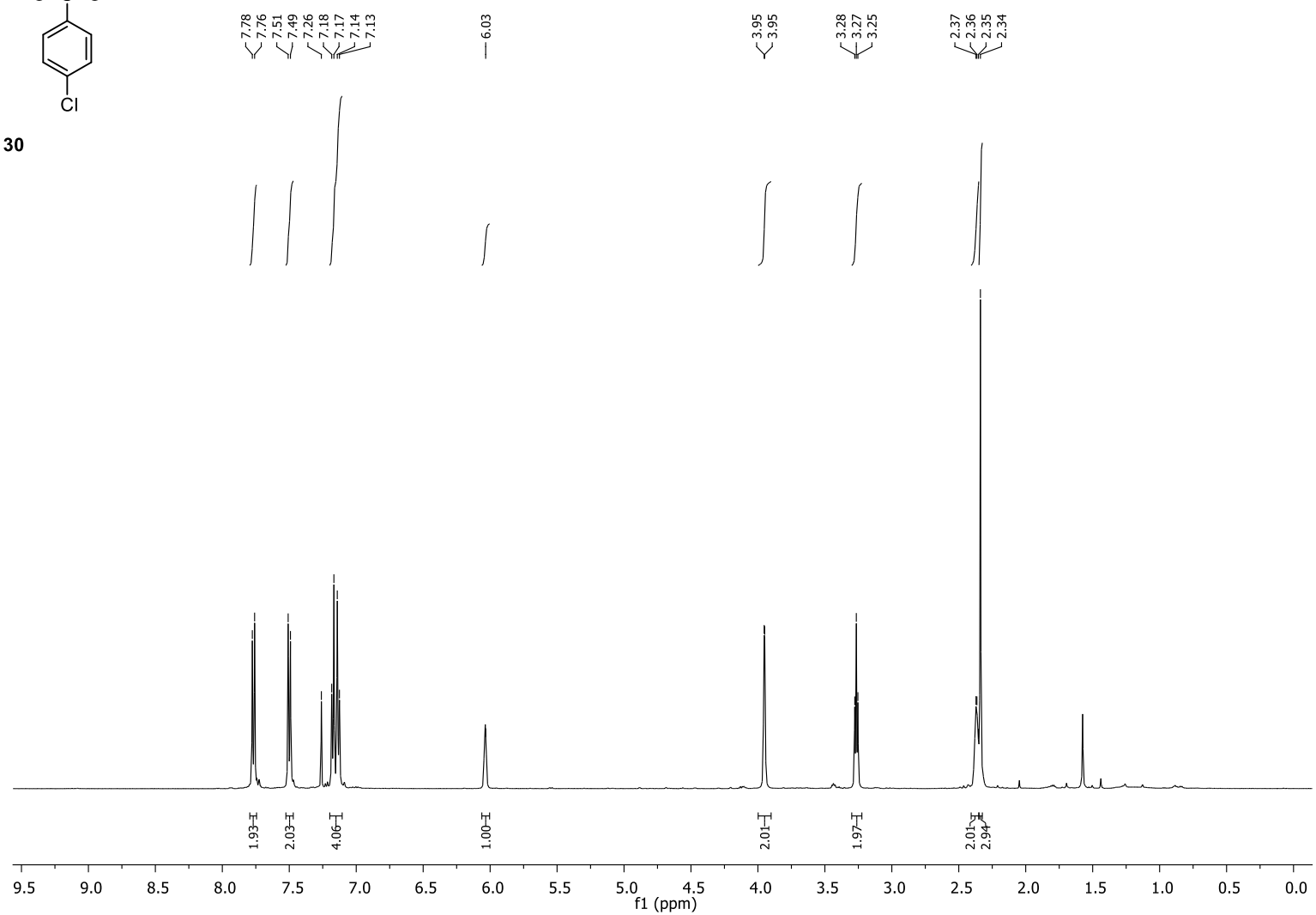
128.50
128.05
127.68
125.20
122.16
114.21
77.18
77.00
76.82
55.58
46.41
42.34
25.62
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
N
O=S=O
Cl

30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7.76
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7.26
7.18
7.17
7.14
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6.03
3.95
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3.28
3.27
3.25
2.37
2.36
2.35
2.34
1.93
2.03
4.06
1.00
2.01
1.97
2.01
2.94
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
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2.5
2.0
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1.0
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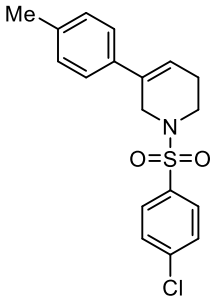
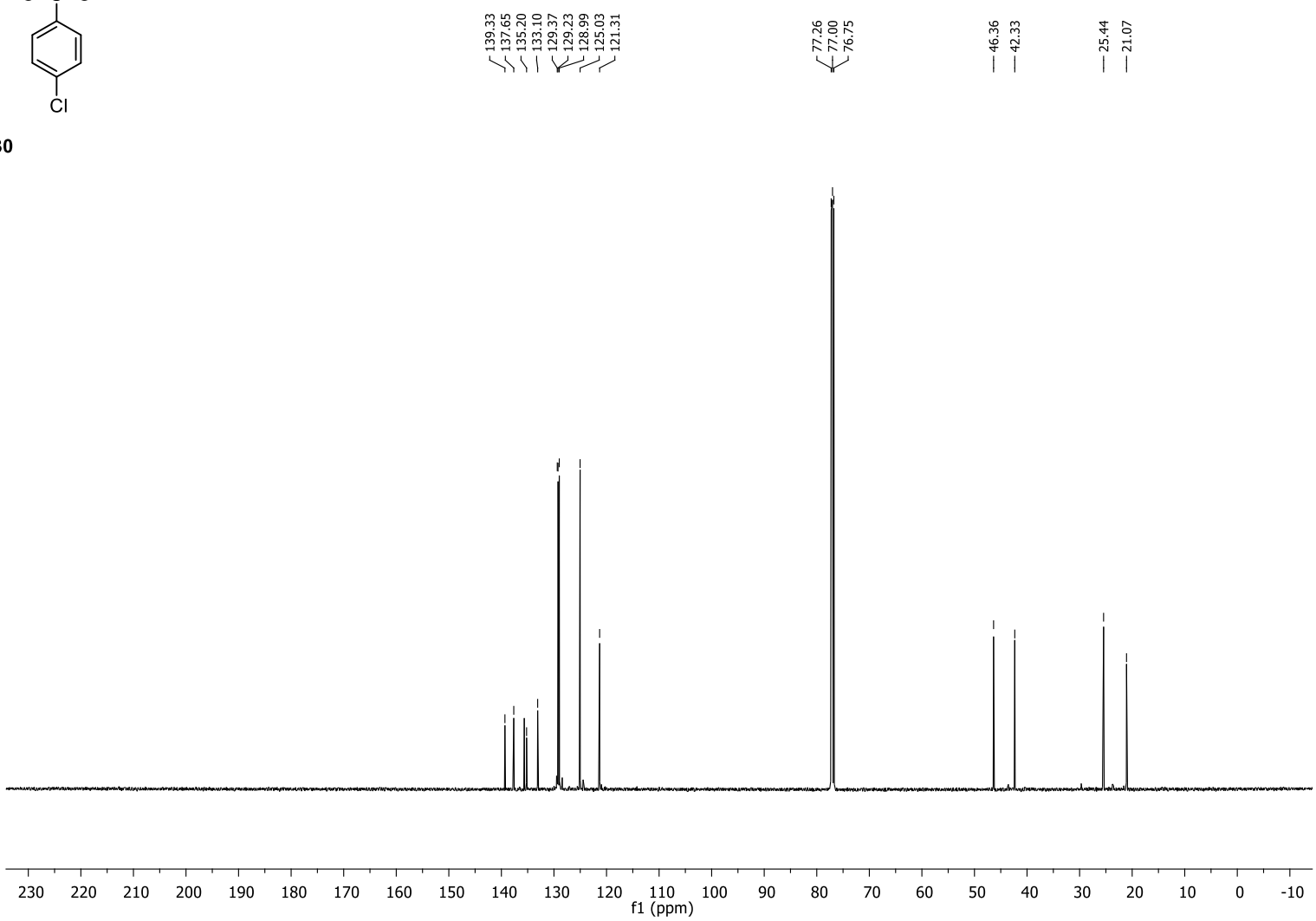
f1 (ppm)


Me
N
O=S=O
Cl

30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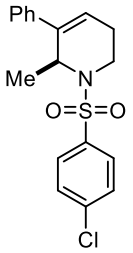
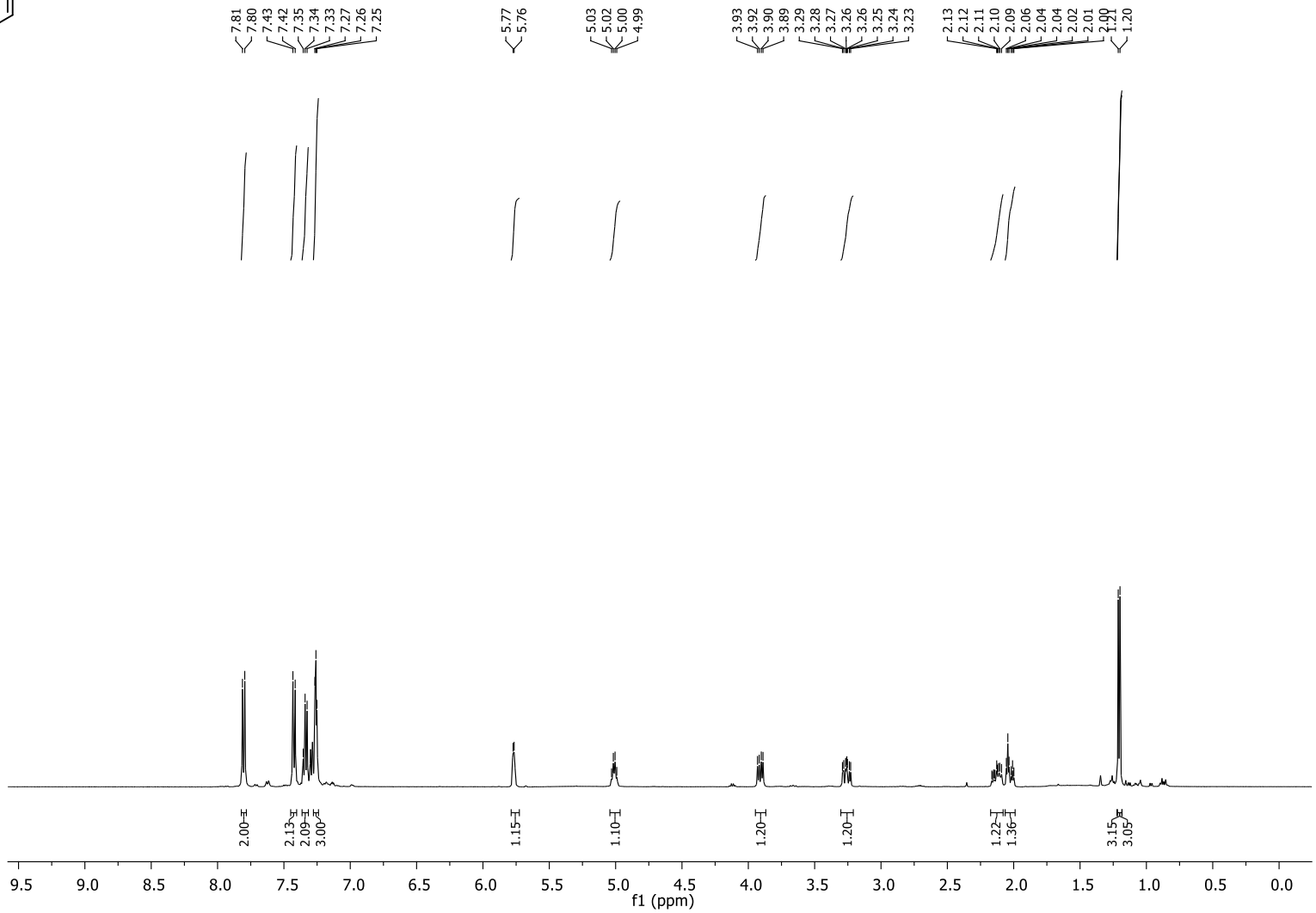
137.65
135.20
133.10
129.37
129.23
128.99
125.03
121.31
77.26
77.00
76.75
46.36
42.33
25.44
21.07
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
N
O=S=O
Cl

32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5.02
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4.99
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3.92
3.90
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3.27
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3.23
2.13
2.12
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2.06
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2.04
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1.21
1.20
2.00
2.13
2.09
3.00
1.15
1.10
1.20
1.20
1.22
1.36
3.15
3.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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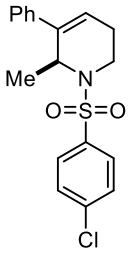
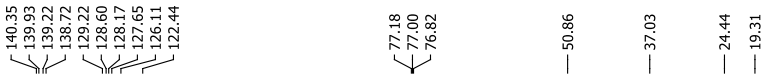
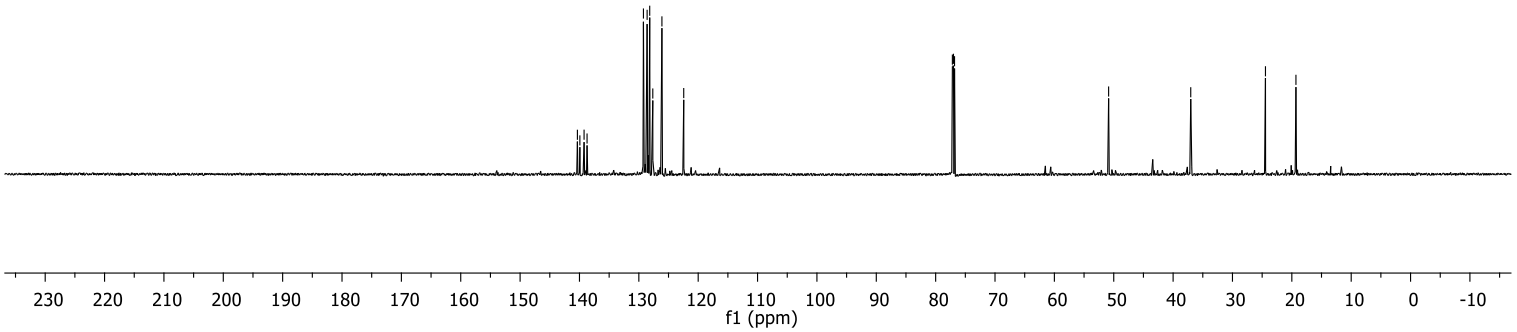
f1 (ppm)


Ph
Me
N
O=S=O
Cl

32


140.35
139.93
139.22
138.72
129.22
128.60
128.17
127.65
126.11
122.44
77.18
77.00
76.82
50.86
37.03
24.44
19.31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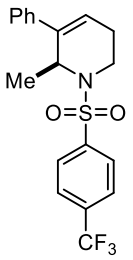
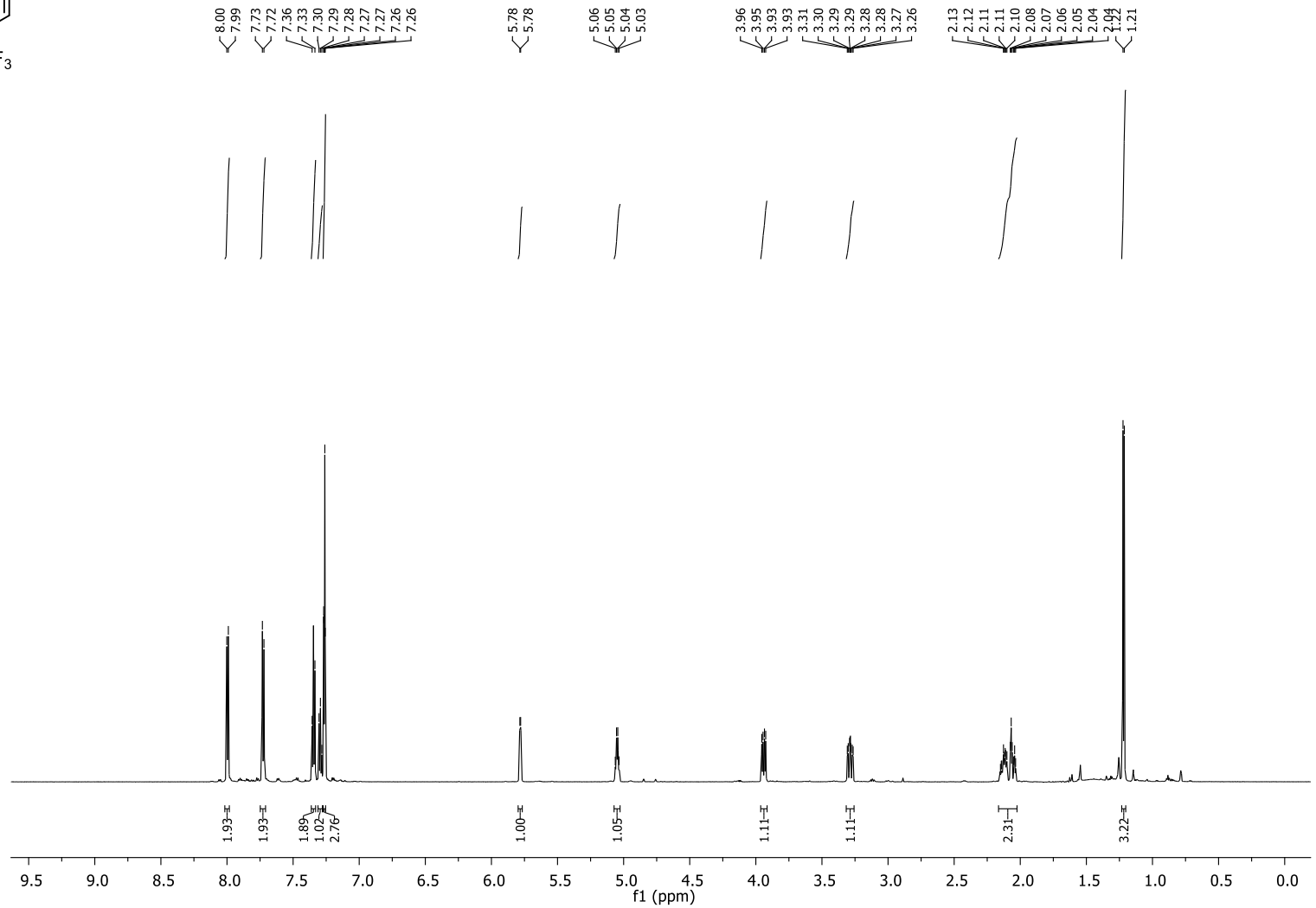
f1 (ppm)


Ph
Me
N
O=S=O
CF3

34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7.99
7.73
7.72
7.36
7.33
7.30
7.29
7.28
7.27
7.27
7.26
7.26
5.78
5.78
5.06
5.05
5.04
5.03
3.96
3.95
3.93
3.93
3.31
3.30
3.29
3.29
3.28
3.28
3.27
3.26
2.13
2.12
2.11
2.11
2.10
2.08
2.07
2.06
2.05
2.04
1.22
1.21
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1.93
1.89
1.02
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1.00
1.05
1.11
1.11
2.31
3.22
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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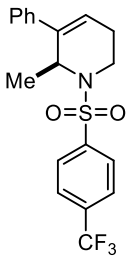
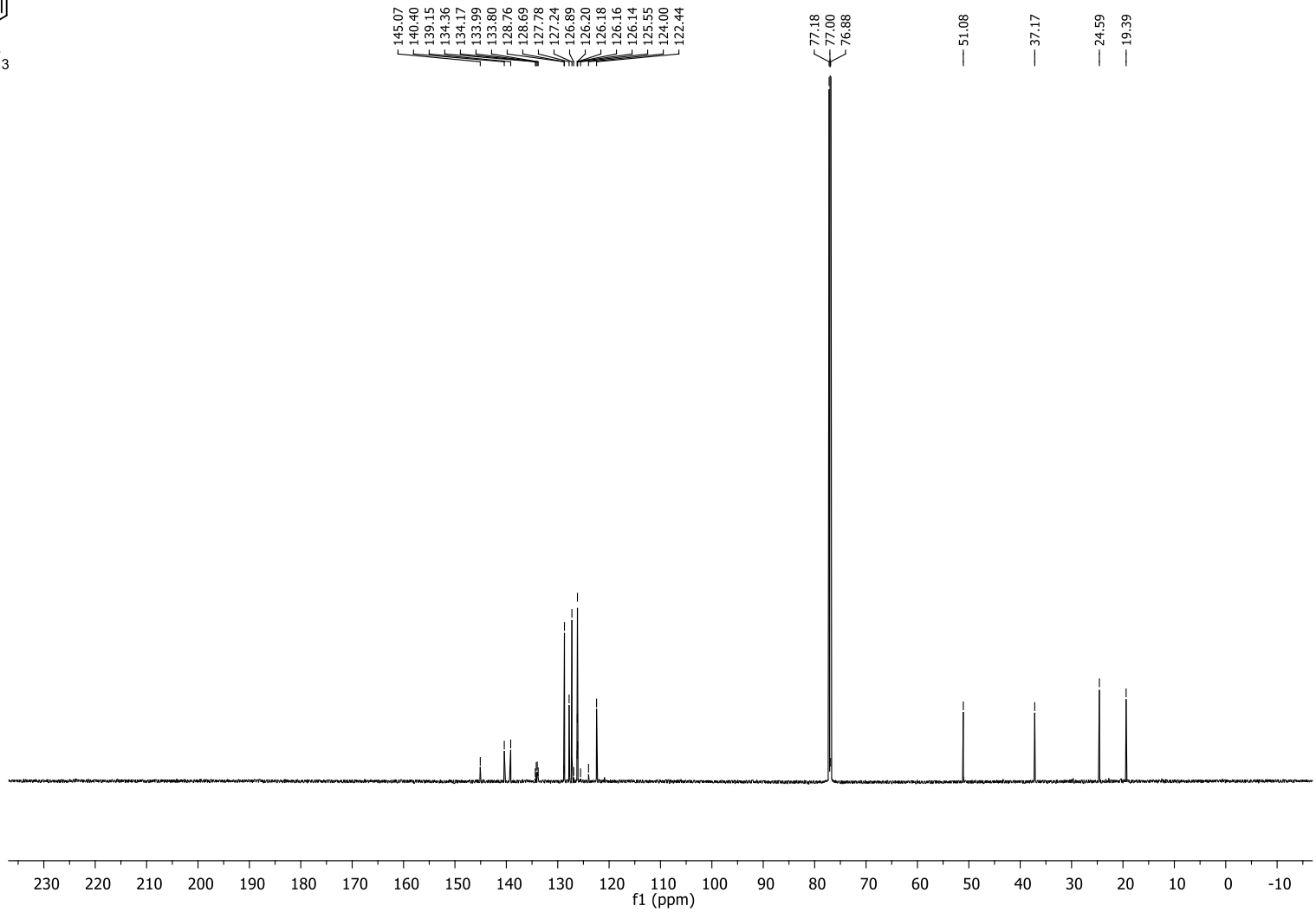
0.0
f1 (ppm)


Ph
Me
N
O=S=O
CF3

34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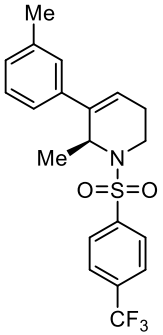
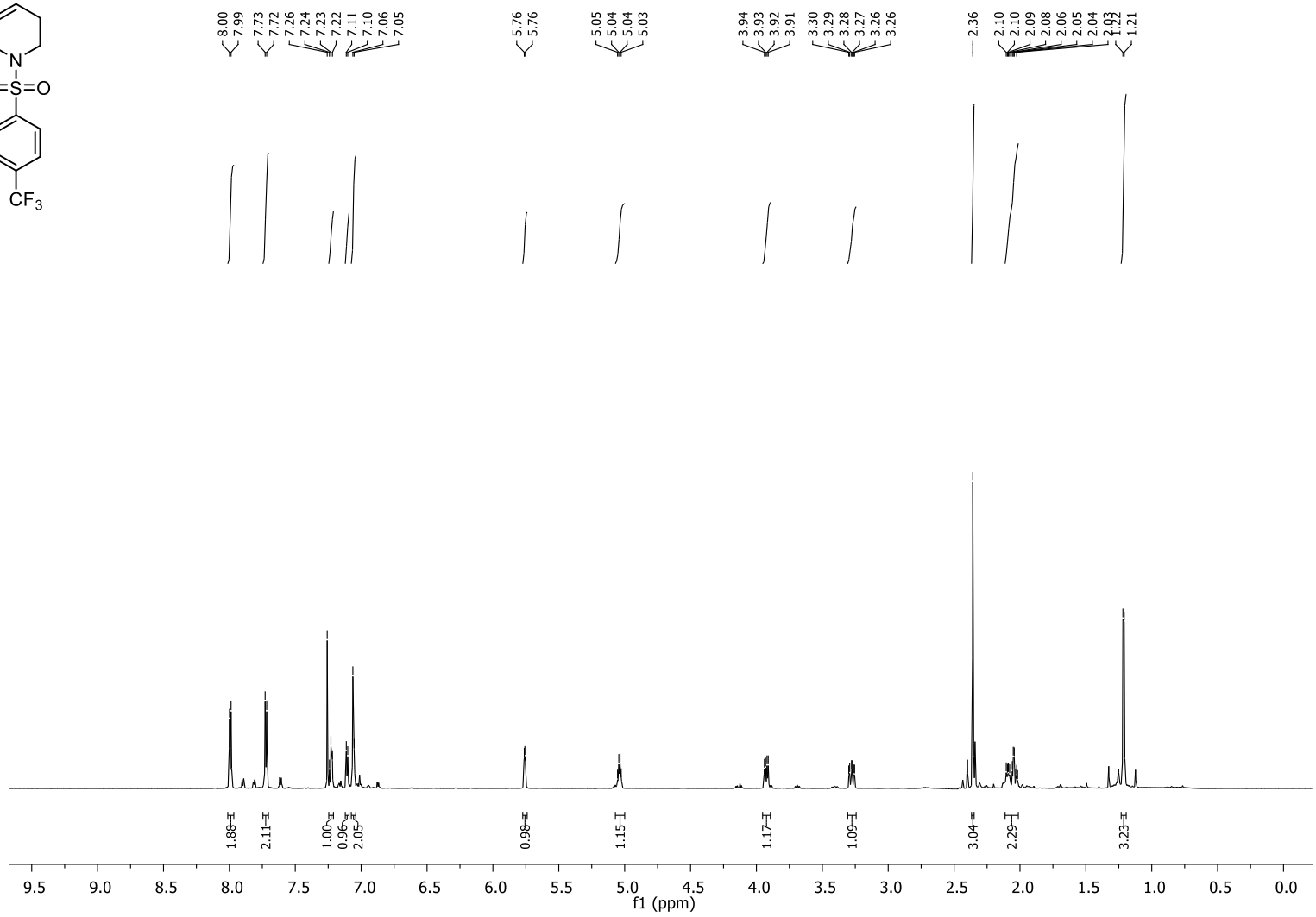
133.80
128.76
128.69
127.78
127.24
126.89
126.20
126.18
126.16
126.14
125.55
124.00
122.44
77.18
77.00
76.88
51.08
37.17
24.59
19.39
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
Me
N
O=S=O
CF3

36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7.06
7.05
5.76
5.76
5.05
5.04
5.04
5.03
3.94
3.93
3.92
3.91
3.30
3.29
3.28
3.27
3.26
3.26
2.36
2.10
2.10
2.09
2.08
2.06
2.05
2.04
1.22
1.21
1.88
2.11
1.00
0.96
2.05
0.98
1.15
1.17
1.09
3.04
2.29
3.23
9.5
9.0
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8.0
7.5
7.0
6.5
6.0
5.5
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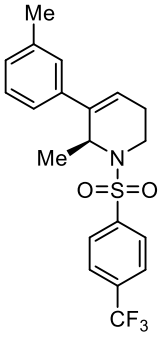
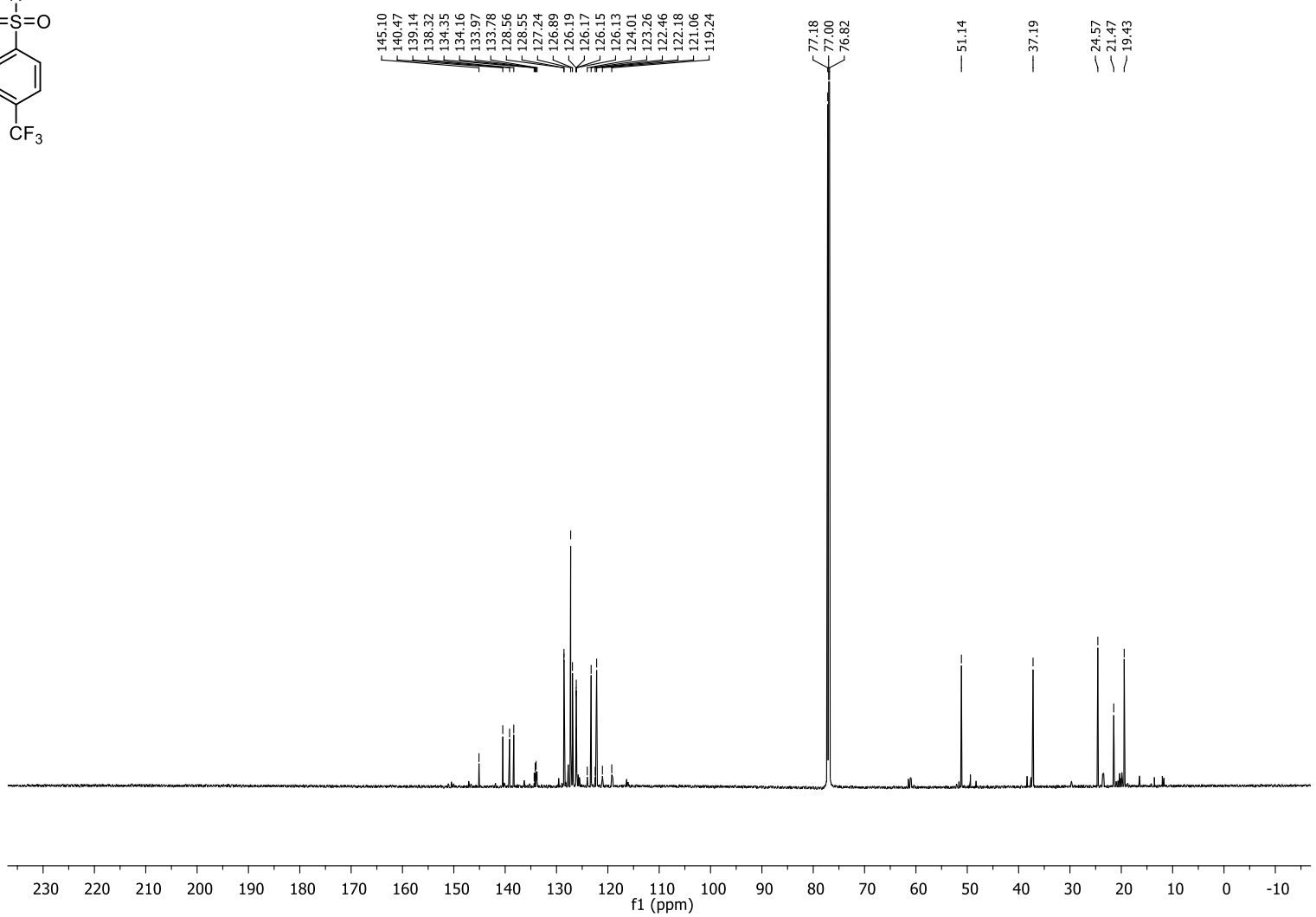
f1 (ppm)


Me
Me
N
O=S=O
CF3

36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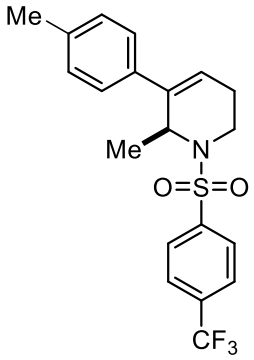
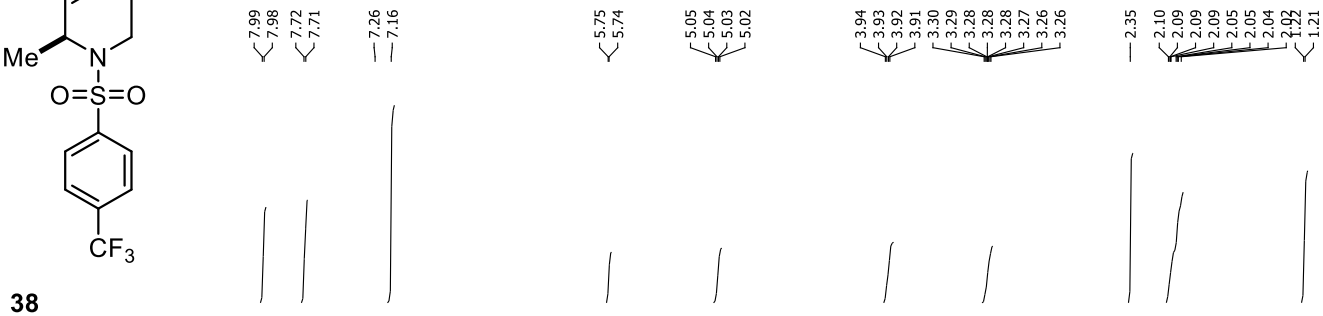
140.47
139.14
138.32
134.35
134.16
133.97
133.78
128.56
128.55
127.24
126.89
126.19
126.17
126.15
126.13
124.01
123.26
122.46
122.18
121.06
119.24
77.18
77.00
76.82
51.14
37.19
24.57
21.47
19.43
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
Me
N
O=S=O
CF3

38


7.99
7.98
7.72
7.71
7.26
7.16
5.75
5.74
5.05
5.04
5.03
5.02
3.94
3.93
3.92
3.91
3.30
3.29
3.28
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3.28
3.27
3.26
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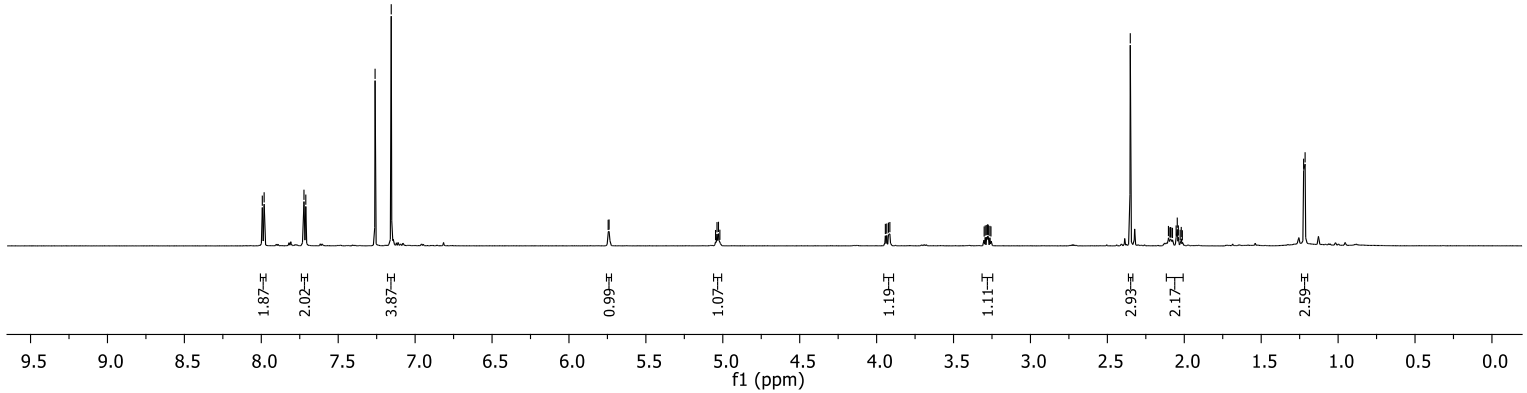
2.05
2.05
2.04
2.02
1.22
1.21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1.19
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2.93
2.17
2.59
9.5
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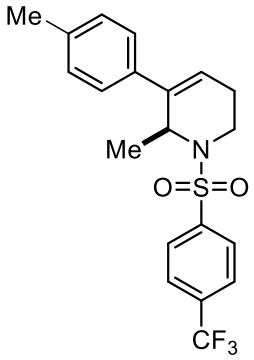
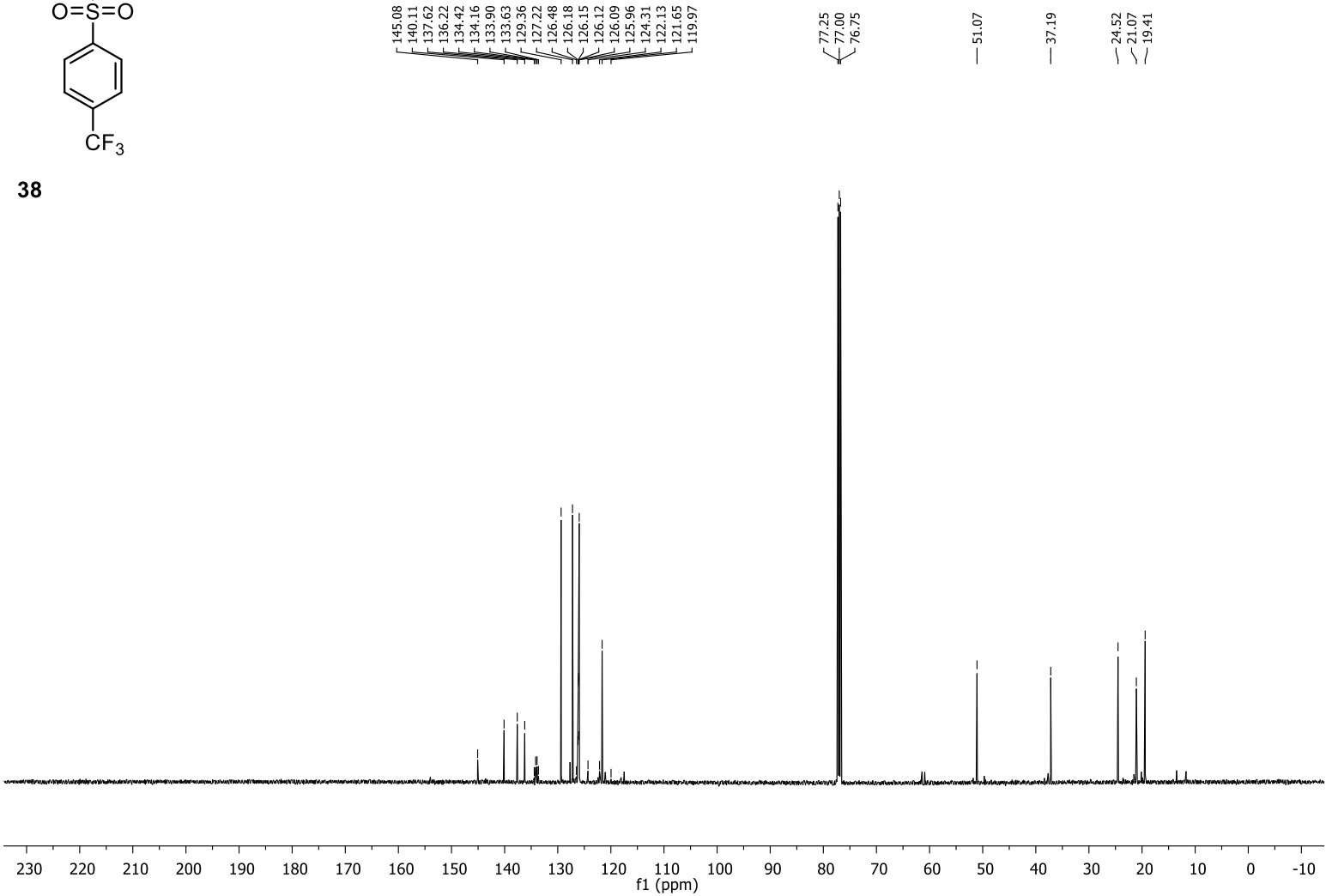
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Me
Me
N
O=S=O
CF3

38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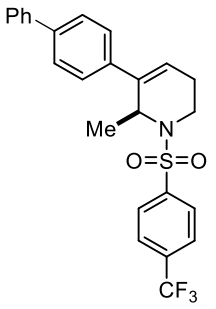
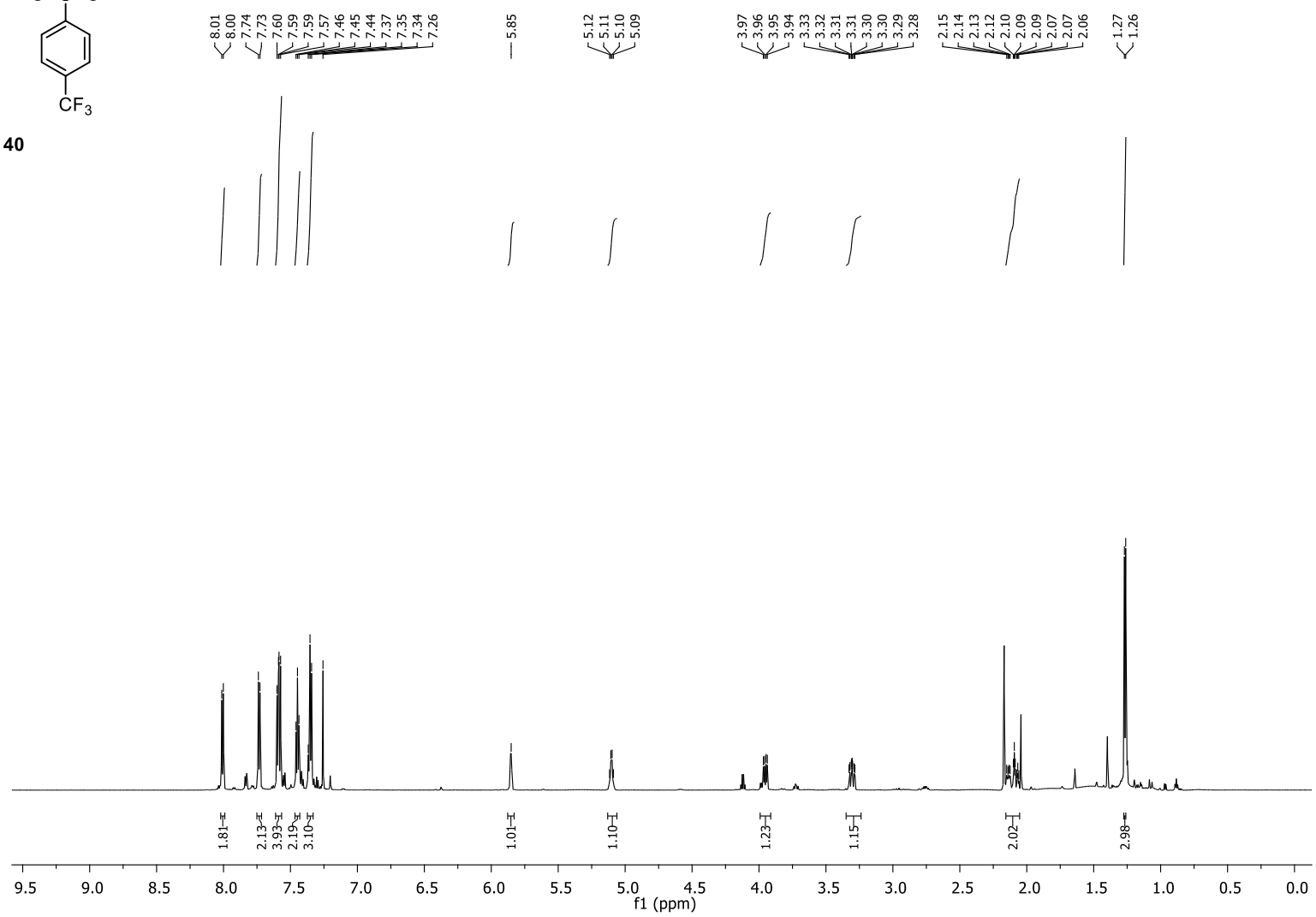
134.16
133.90
133.63
129.36
127.22
126.48
126.18
126.15
126.12
126.09
125.96
124.31
122.13
121.65
119.97
77.25
77.00
76.75
51.07
37.19
24.52
21.07
19.41
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
Me
N
O=S=O
CF3

40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7.45
7.44
7.37
7.35
7.34
7.26
5.85
5.12
5.11
5.10
5.09
3.97
3.96
3.95
3.94
3.33
3.32
3.31
3.31
3.30
3.30
3.29
3.28
2.15
2.14
2.13
2.12
2.10
2.09
2.09
2.07
2.07
2.06
1.27
1.26
1.81
2.13
3.93
2.19
3.10
1.01
1.10
1.23
1.15
2.02
2.98
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
2.5
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1.0
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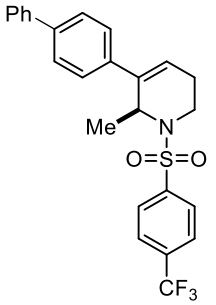
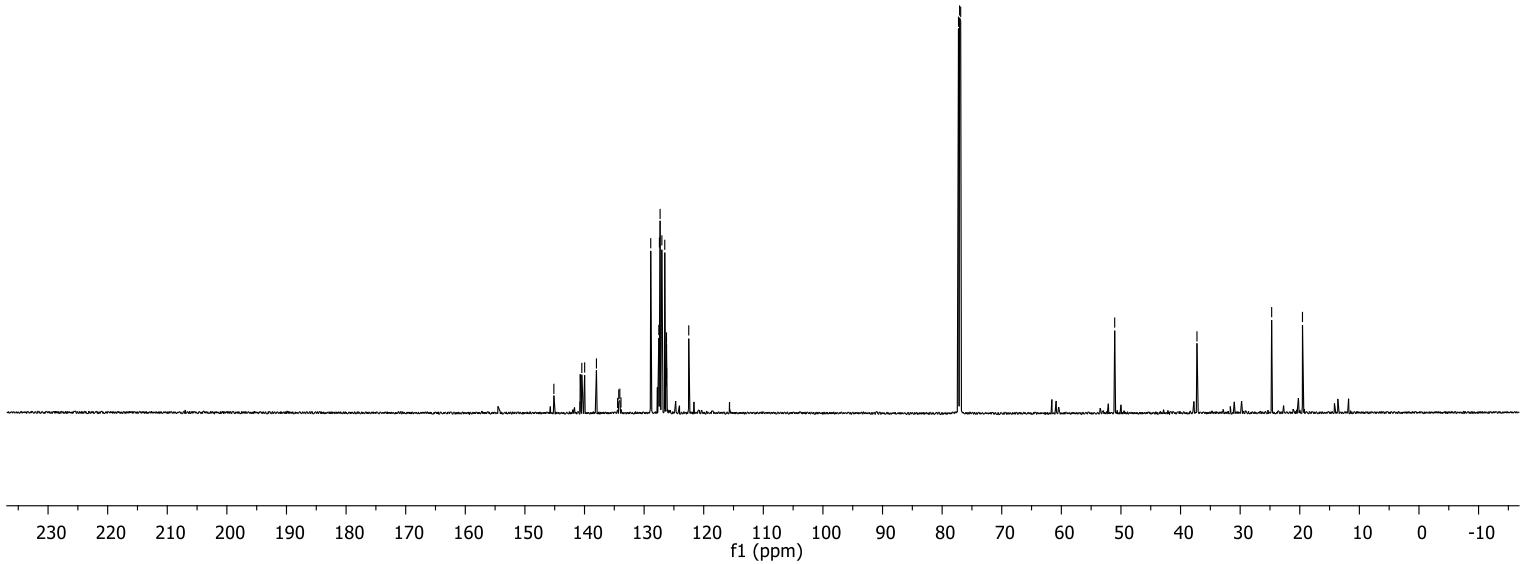
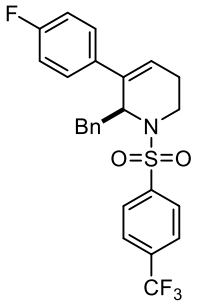
0.0
f1 (ppm)


Ph
Me
N
O=S=O
CF3

40


145.14
140.76
140.45
139.98
138.00
134.45
134.26
134.07
133.88
128.89
127.53
127.43
127.32
127.02
126.53
126.28
126.26
126.24
126.22
122.51
77.25
77.07
76.89
51.05
37.25
24.72
19.54


230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F
Bn
N
O=S=O
CF3

42


7.55
7.53
7.53
7.51
7.37
7.36
7.36
7.35
7.18
7.17
7.16
7.15
7.14
7.10
7.09
7.07
6.98
6.97
5.88
5.88
5.15
5.13
3.78
3.77
3.76
3.75
3.16
3.16
3.15
3.15
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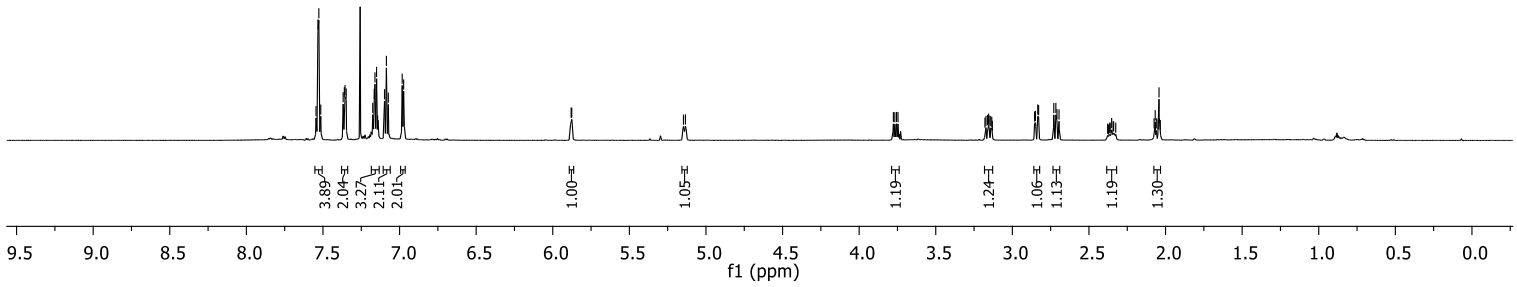
2.73
2.72
2.35
2.34
2.07
2.07
2.06
2.05
2.04
2.03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2.04
3.27
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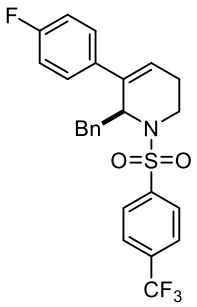
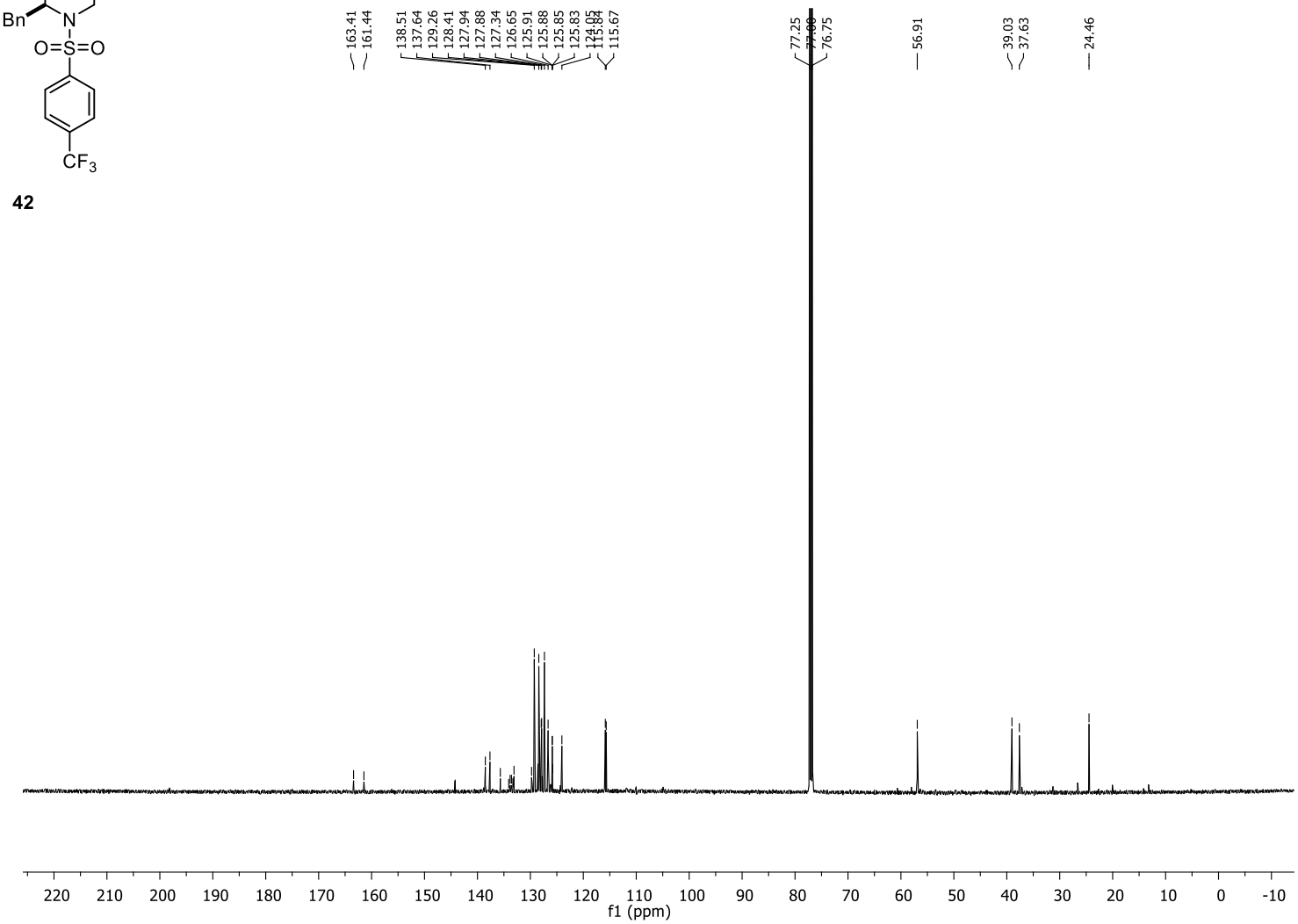
2.01
1.00
1.05
1.19
1.24
1.06
1.13
1.19
1.30
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


F
Bn
N
O=S=O
CF3

42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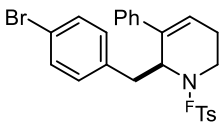
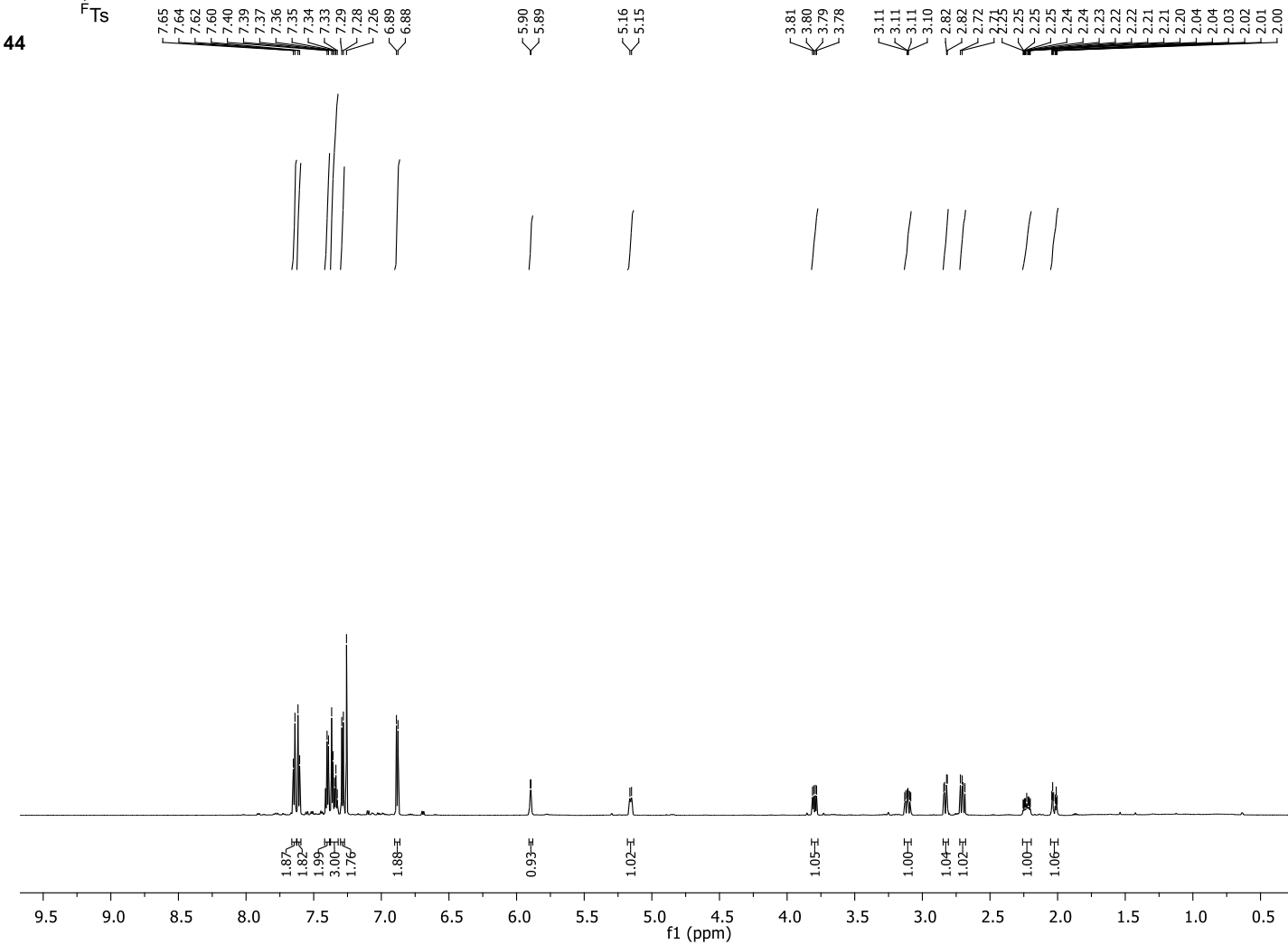
127.34
126.65
125.91
125.88
125.85
125.83
124.05
115.84
115.67
77.25
77.00
76.75
56.91
39.03
37.63
24.46
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
Ph
N
F
Ts

44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7.34
7.33
7.29
7.28
7.26
6.89
6.88
5.90
5.89
5.16
5.15
3.81
3.80
3.79
3.78
3.11
3.11
3.11
3.10
2.82
2.82
2.72
2.25
2.25
2.25
2.24
2.24
2.23
2.22
2.22
2.21
2.21
2.20
2.04
2.04
2.03
2.02
2.01
2.00
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1.82
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1.76
1.88
0.93
1.02
1.05
1.00
1.04
1.02
1.00
1.06
9.5
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8.5
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7.0
6.5
6.0
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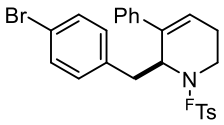
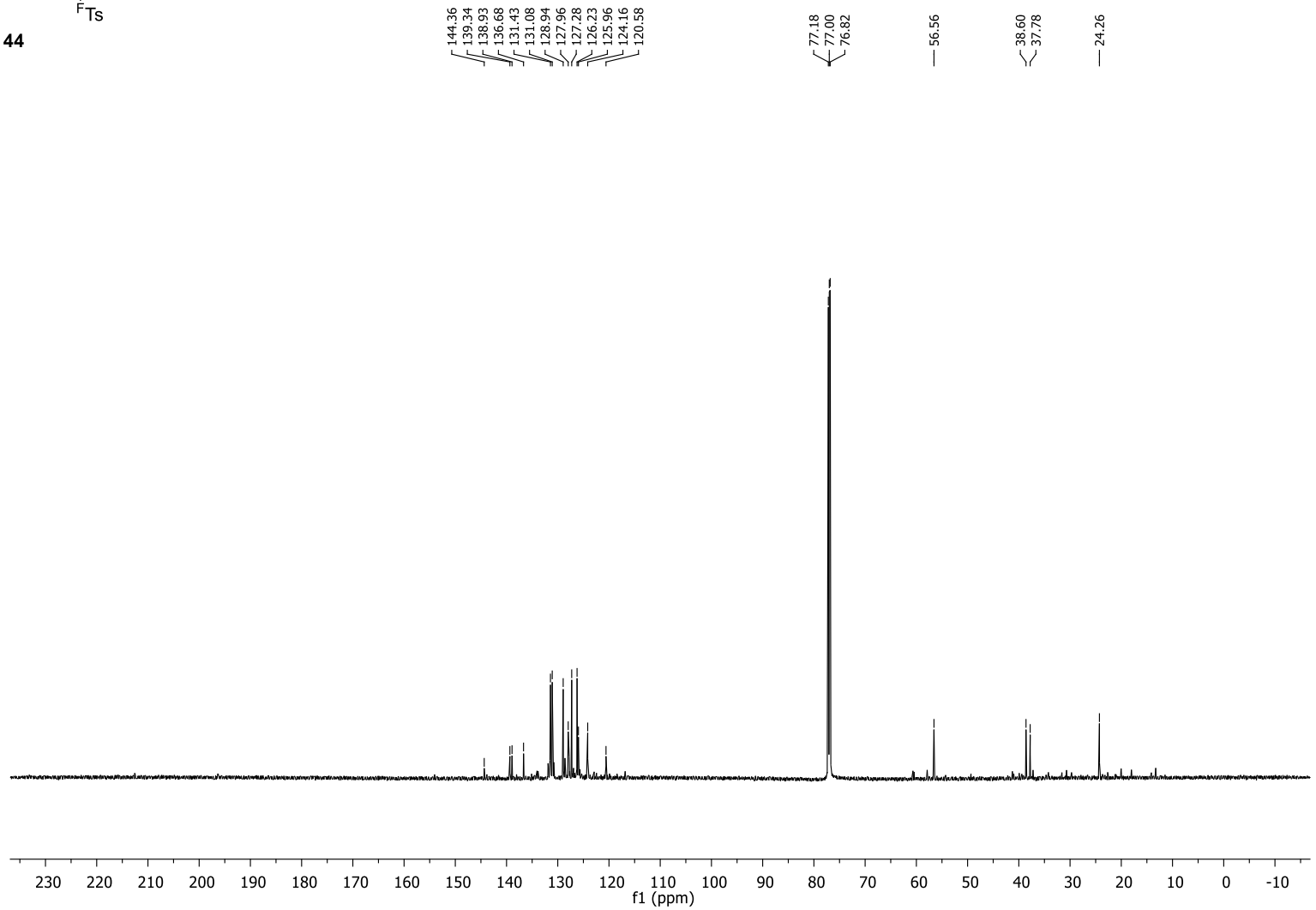
f1 (ppm)


Br
Ph
N
F
Ts

44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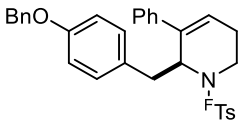
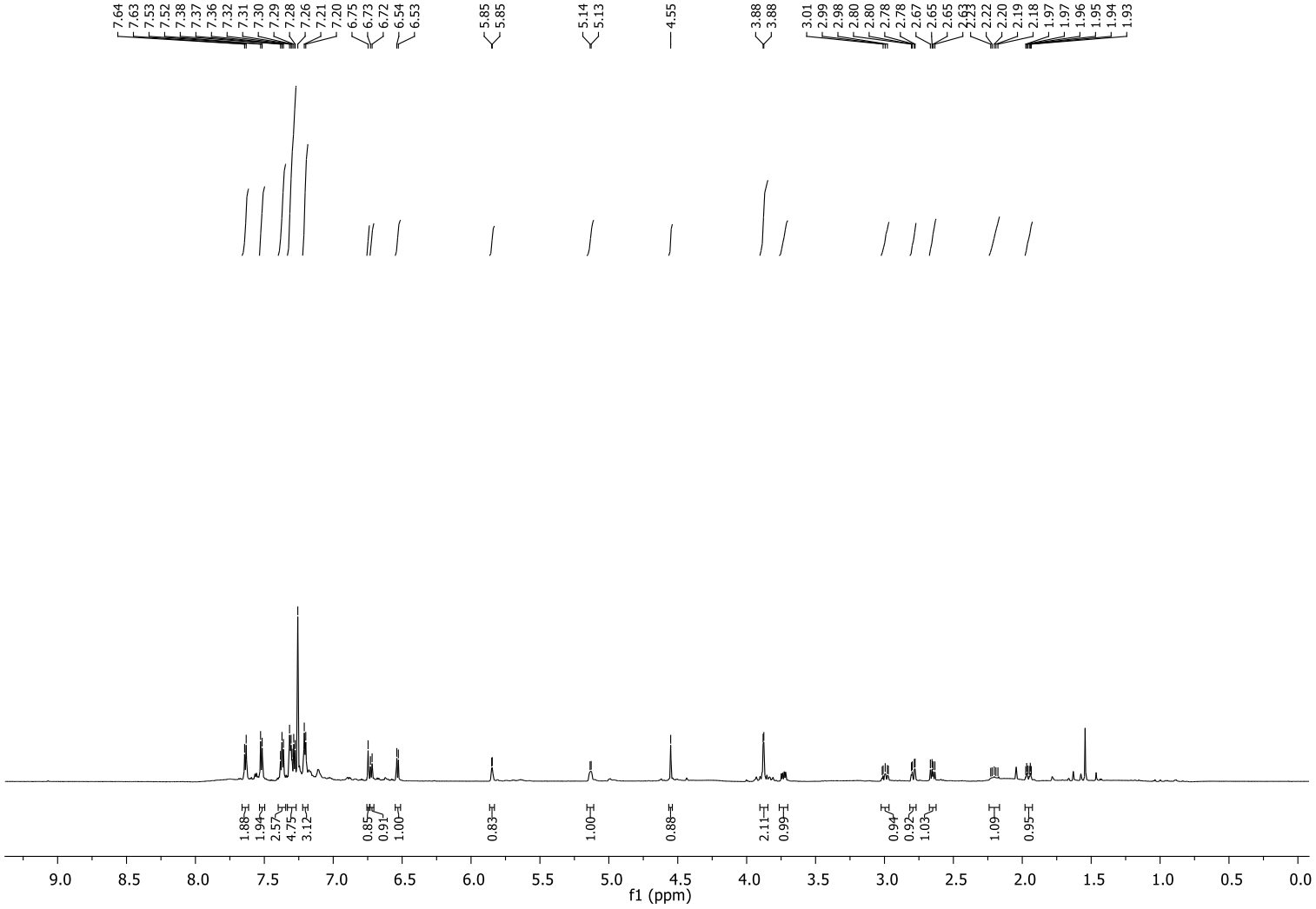
127.96
127.28
126.23
125.96
124.16
120.58
77.18
77.00
76.82
56.56
38.60
37.78
24.26
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


BnO
Ph
N
F
Ts

46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7.63
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7.52
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7.37
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7.31
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7.29
7.28
7.26
7.21
7.20
6.75
6.73
6.72
6.54
6.53
5.85
5.85
5.14
5.13
4.55
3.88
3.88
3.01
2.99
2.98
2.80
2.80
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2.78
2.67
2.65
2.65
2.63
2.23
2.22
2.20
2.19
2.18
1.97
1.97
1.96
1.95
1.94
1.93
1.88
1.94
2.57
4.75
3.12
0.85
0.91
1.00
0.83
1.00
0.88
2.11
0.99
0.94
0.92
1.03
1.09
0.95
9.0
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8.0
7.5
7.0
6.5
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1.0
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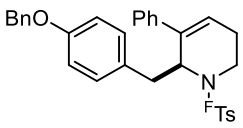
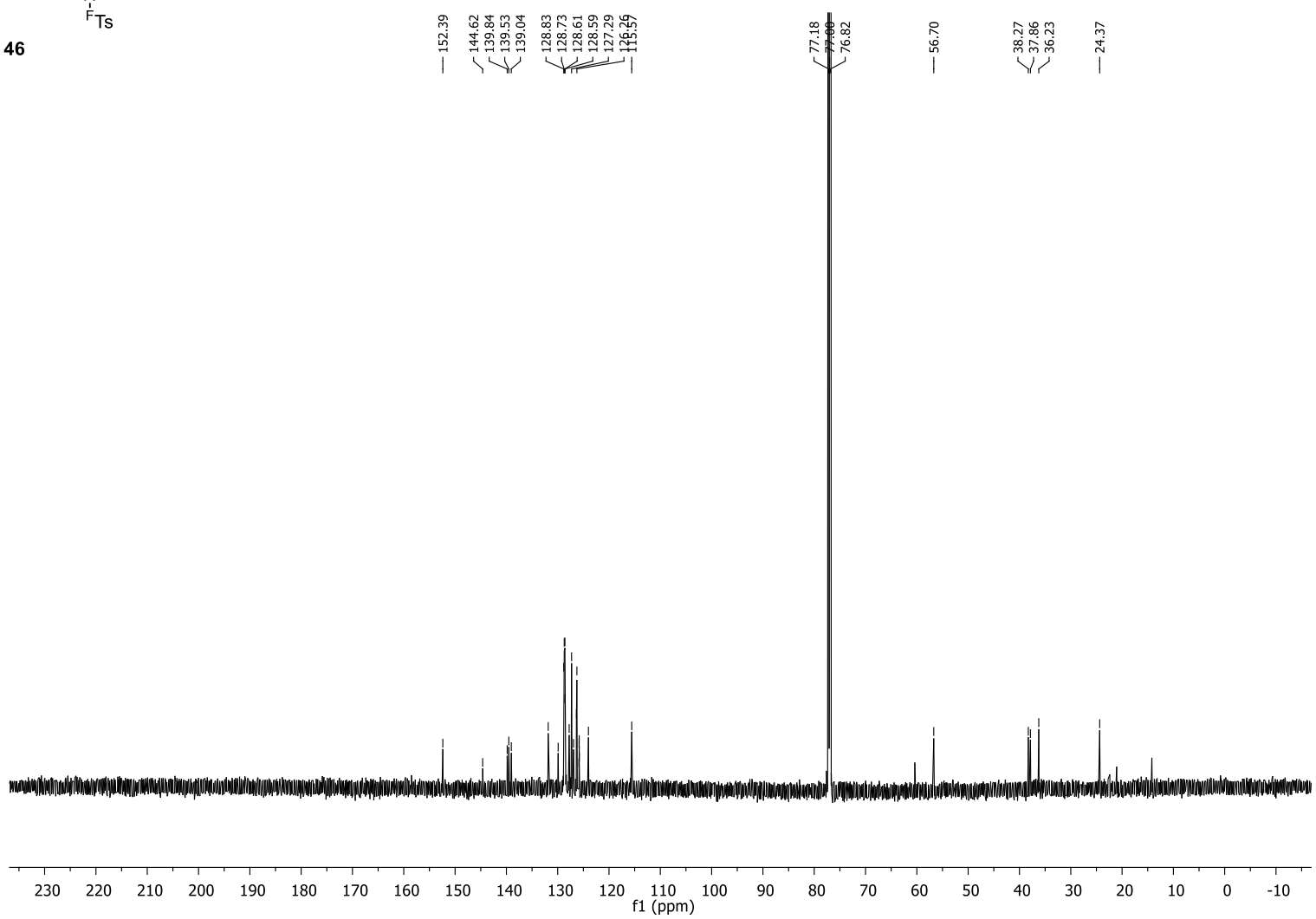
0.0
f1 (ppm)


BnO
Ph
N
F
Ts

46


152.39
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139.84
139.53
139.04
128.83
128.73
128.61
128.59
127.29
126.26
115.57
77.18
77.00
76.82
56.70
38.27
37.86
36.23
24.37
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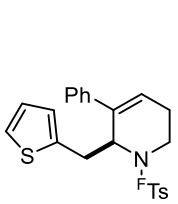
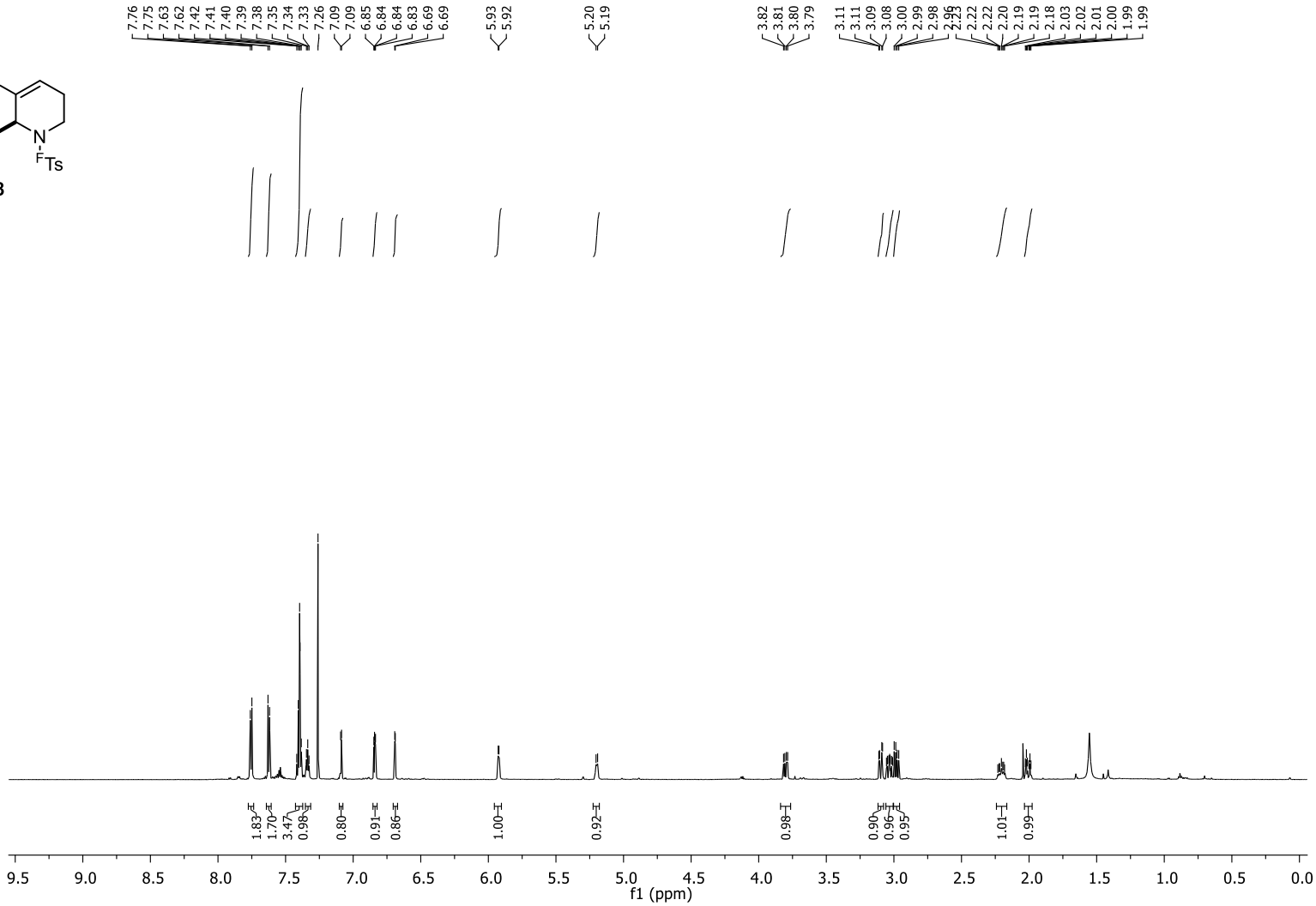
f1 (ppm)


Ph
S
N
F
Ts

48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7.09
7.09
6.85
6.84
6.84
6.83
6.69
6.69
5.93
5.92
5.20
5.19
3.82
3.81
3.80
3.79
3.11
3.11
3.09
3.08
3.00
2.99
2.98
2.96
2.23
2.22
2.22
2.20
2.19
2.19
2.18
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2.02
2.01
2.00
1.99
1.99
1.83
1.70
3.47
0.98
0.80
0.91
0.86
1.00
0.92
0.98
0.90
0.96
0.95
1.01
0.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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2.5
2.0
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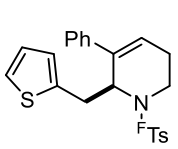
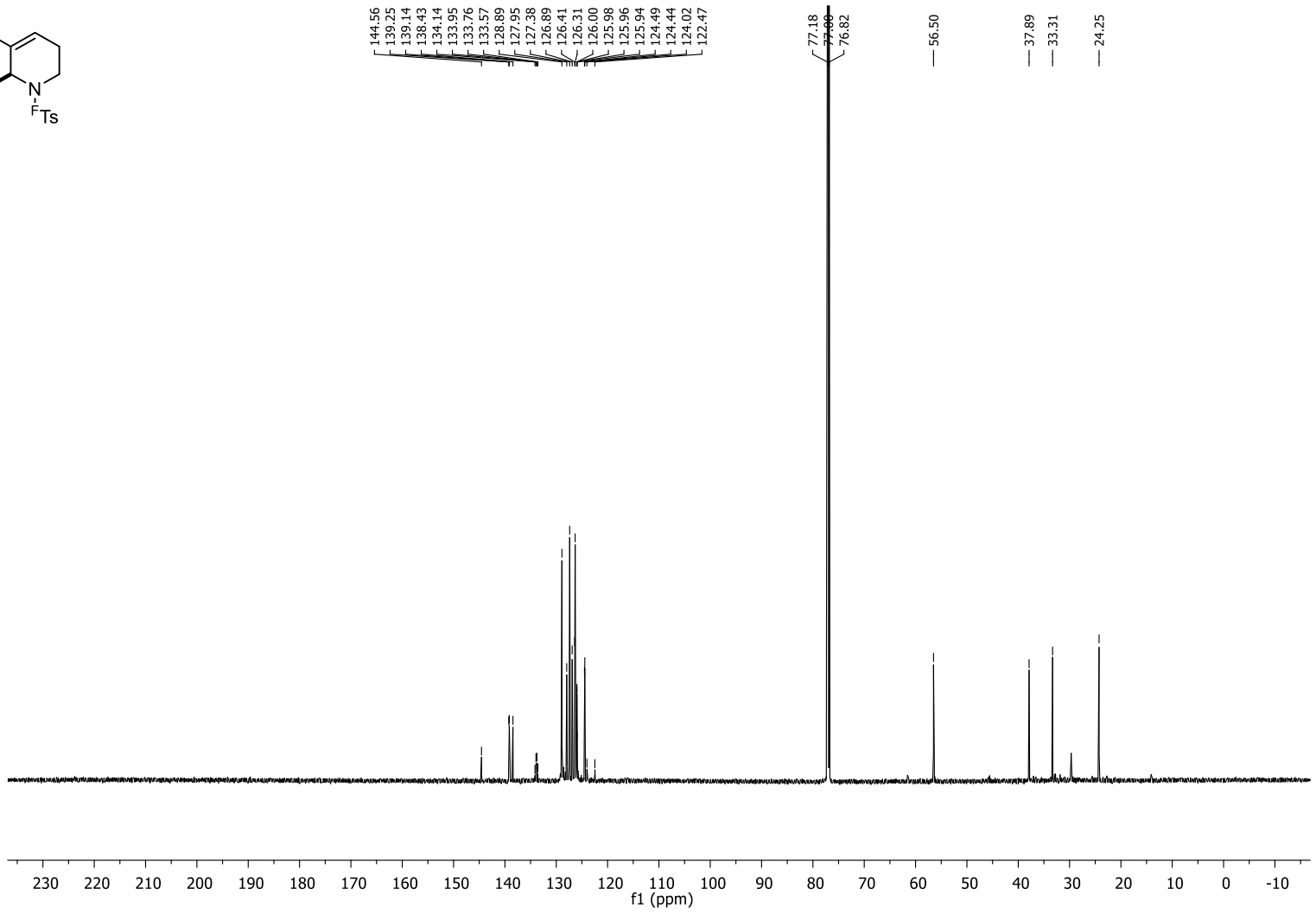
0.0
f1 (ppm)


Ph
S
N
F
Ts

48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125.96
125.94
124.49
124.44
124.02
122.47
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77.00
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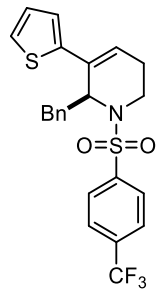
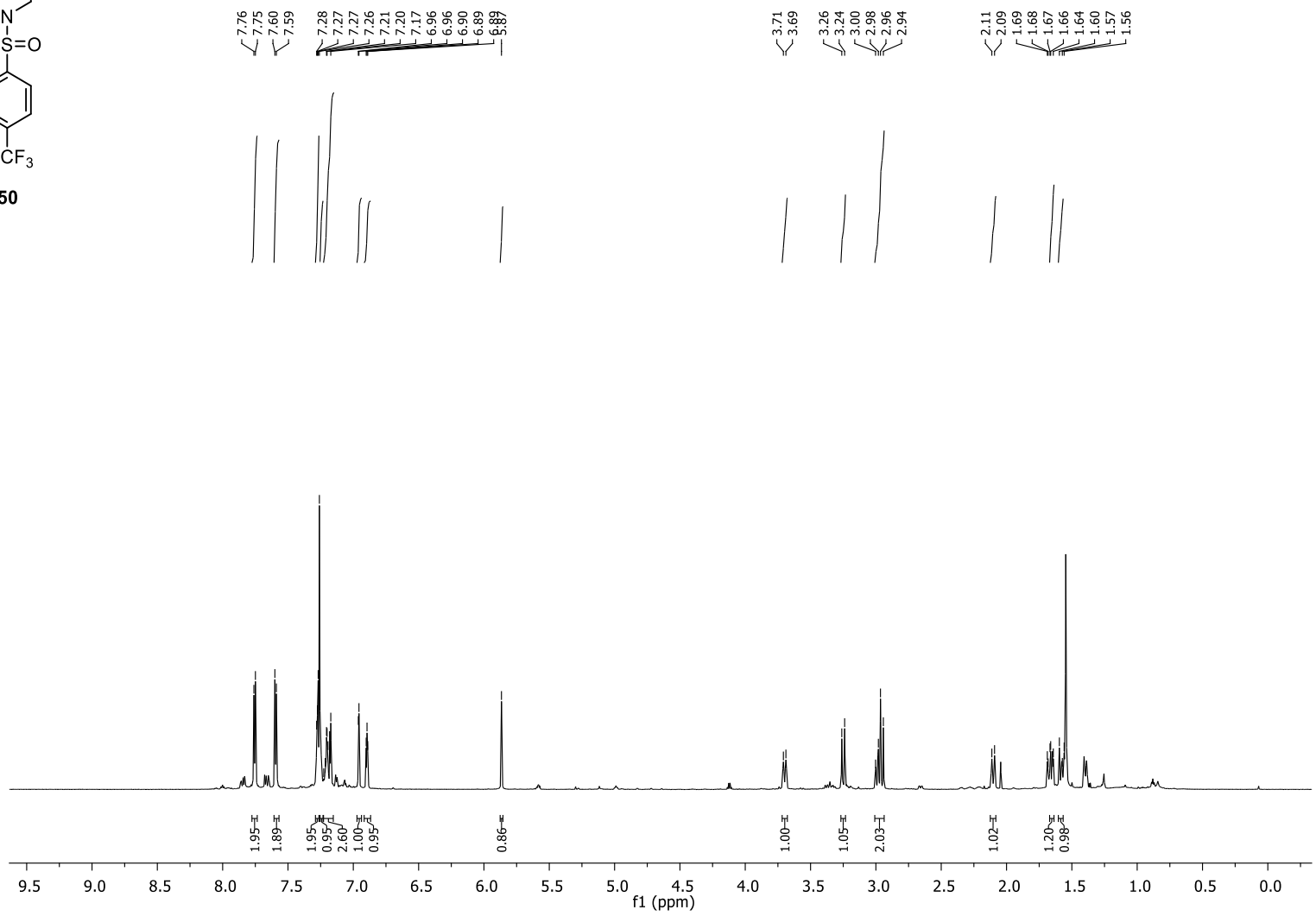
f1 (ppm)


S
Bn
N
O=S=O
CF3

50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6.90
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6.89
5.87
3.71
3.69
3.26
3.24
3.00
2.98
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2.09
1.69
1.68
1.67
1.66
1.64
1.60
1.57
1.56
1.95
1.89
1.95
0.95
2.60
1.00
0.95
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1.05
2.03
1.02
1.20
0.98
9.5
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8.0
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7.0
6.5
6.0
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2.5
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1.0
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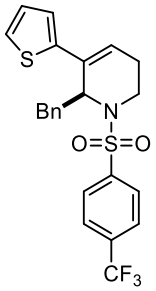
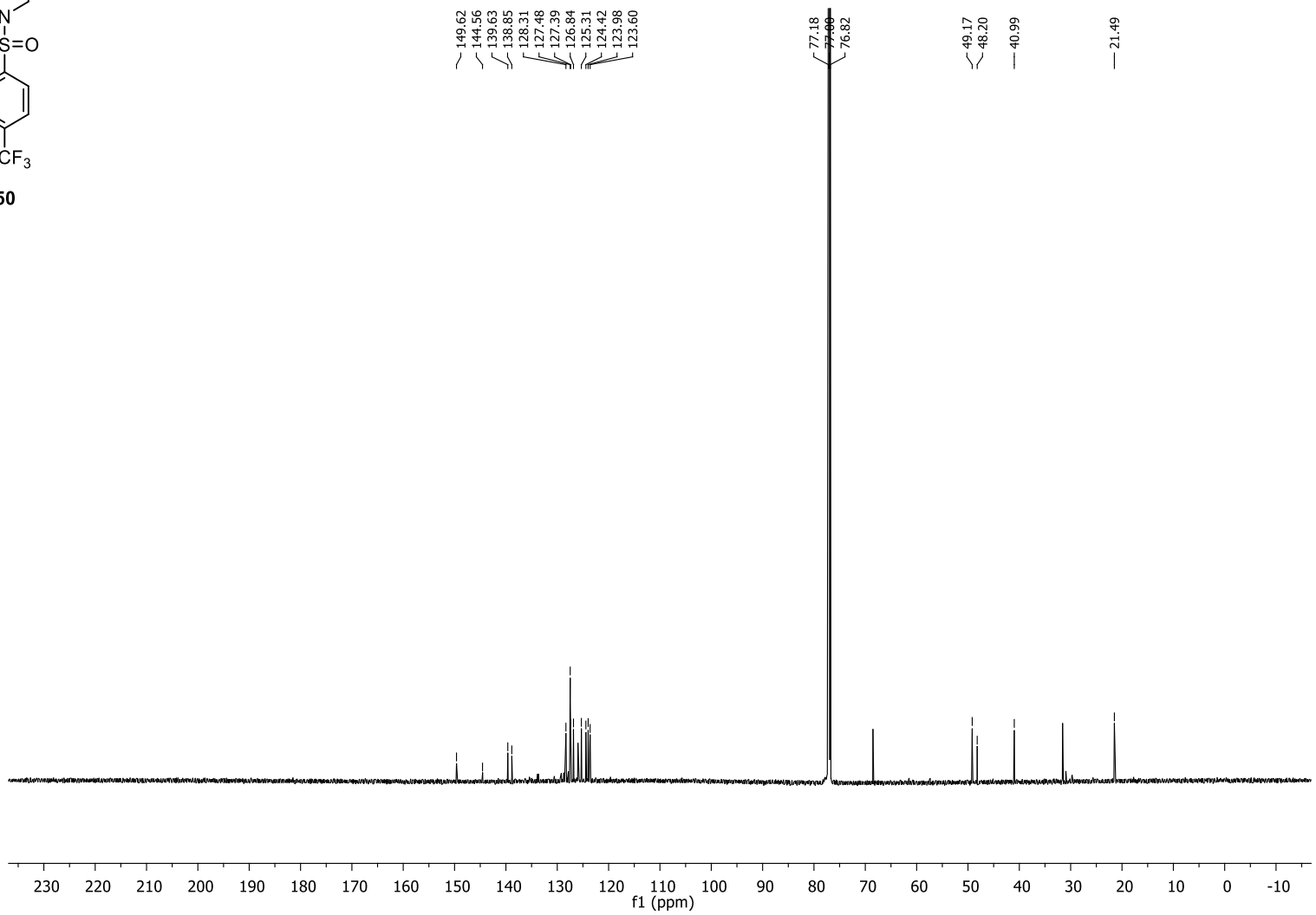
0.0
f1 (ppm)


S
Bn
N
O=S=O
CF3

50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138.85
128.31
127.48
127.39
126.84
125.31
124.42
123.98
123.60
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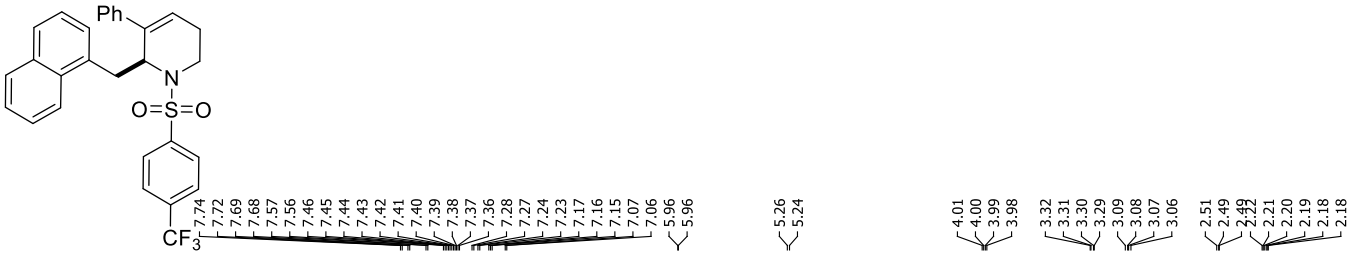
f1 (ppm)


Ph
N
O=S=O
CF3
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7.43
7.42
7.41
7.40
7.39
7.38
7.37
7.36
7.28
7.27
7.24
7.23
7.17
7.16
7.15
7.07
7.06
5.96
5.96
5.26
5.24
4.01
4.00
3.99
3.98
3.32
3.31
3.30
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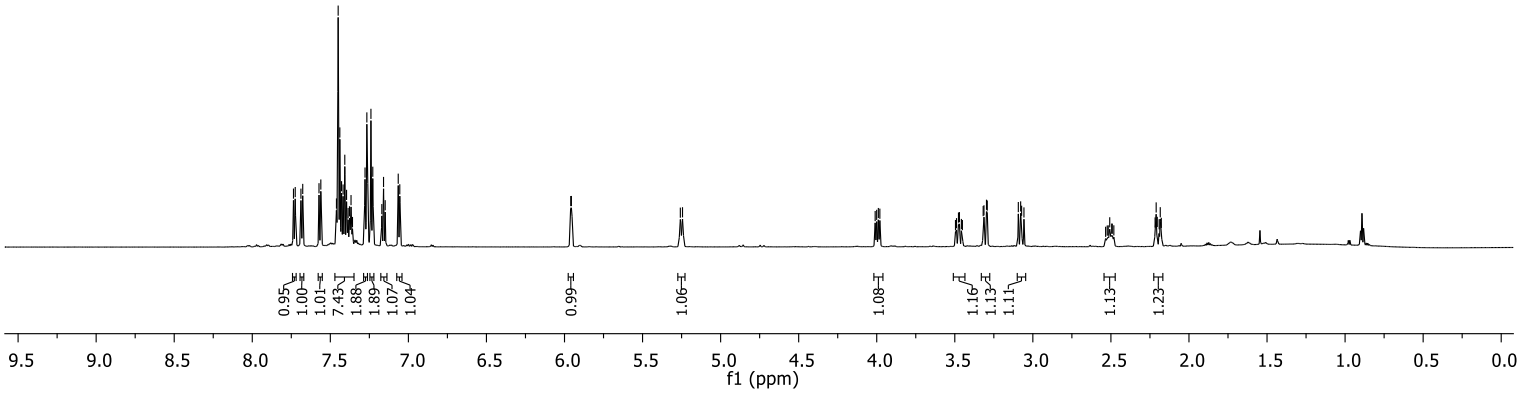
2.20
2.19
2.18
2.18

52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0.99
1.06
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1.16
1.13
1.11
1.13
1.23
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
3.0
2.5
2.0
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1.0
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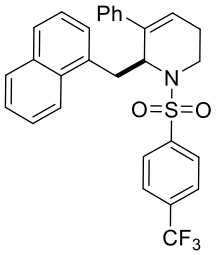
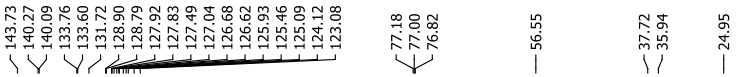
0.0
f1 (ppm)


Ph
N
O=S=O
CF3

52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128.79
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127.83
127.49
127.04
126.68
126.62
125.93
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125.09
124.12
123.08
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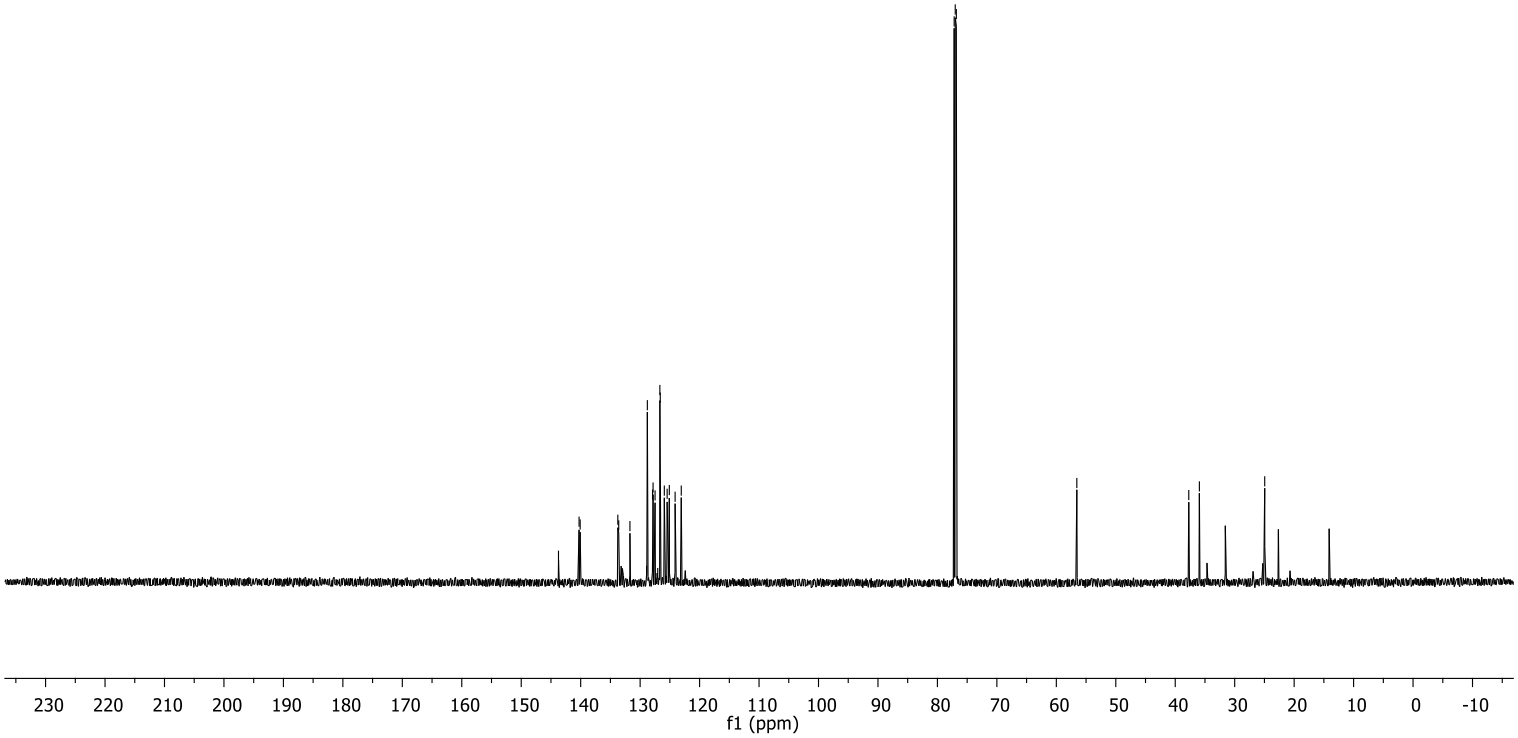
77.00
76.82
56.55
37.72
35.94
24.95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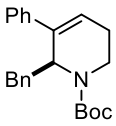
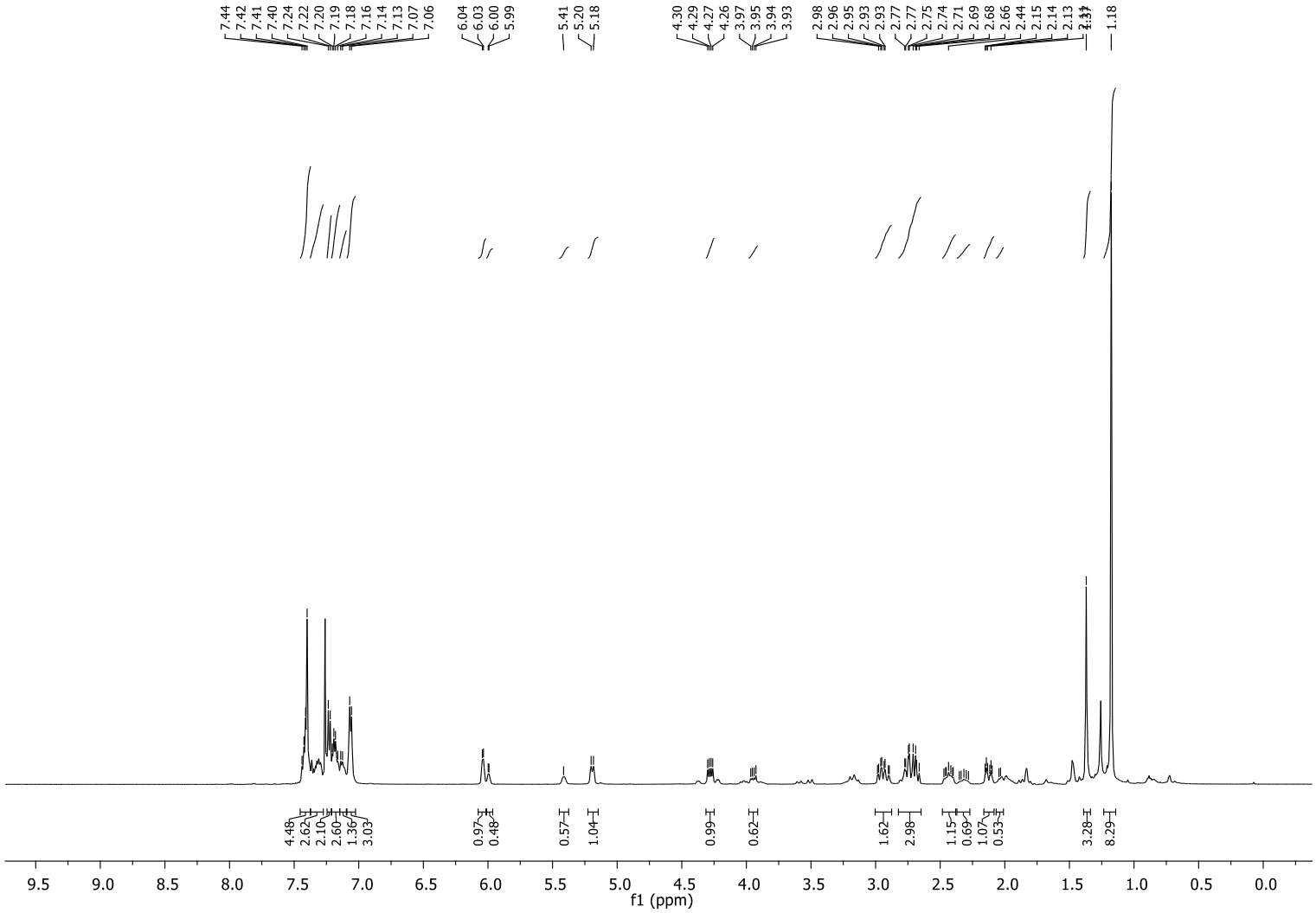
f1 (ppm)


Ph
Bn
N
Boc

27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7.14
7.13
7.07
7.06
6.04
6.03
6.00
5.99
5.41
5.20
5.18
4.30
4.29
4.27
4.26
3.97
3.95
3.94
3.93
2.98
2.96
2.95
2.93
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2.60
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1.62
2.98
1.15
0.69
1.07
0.53
3.28
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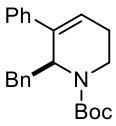
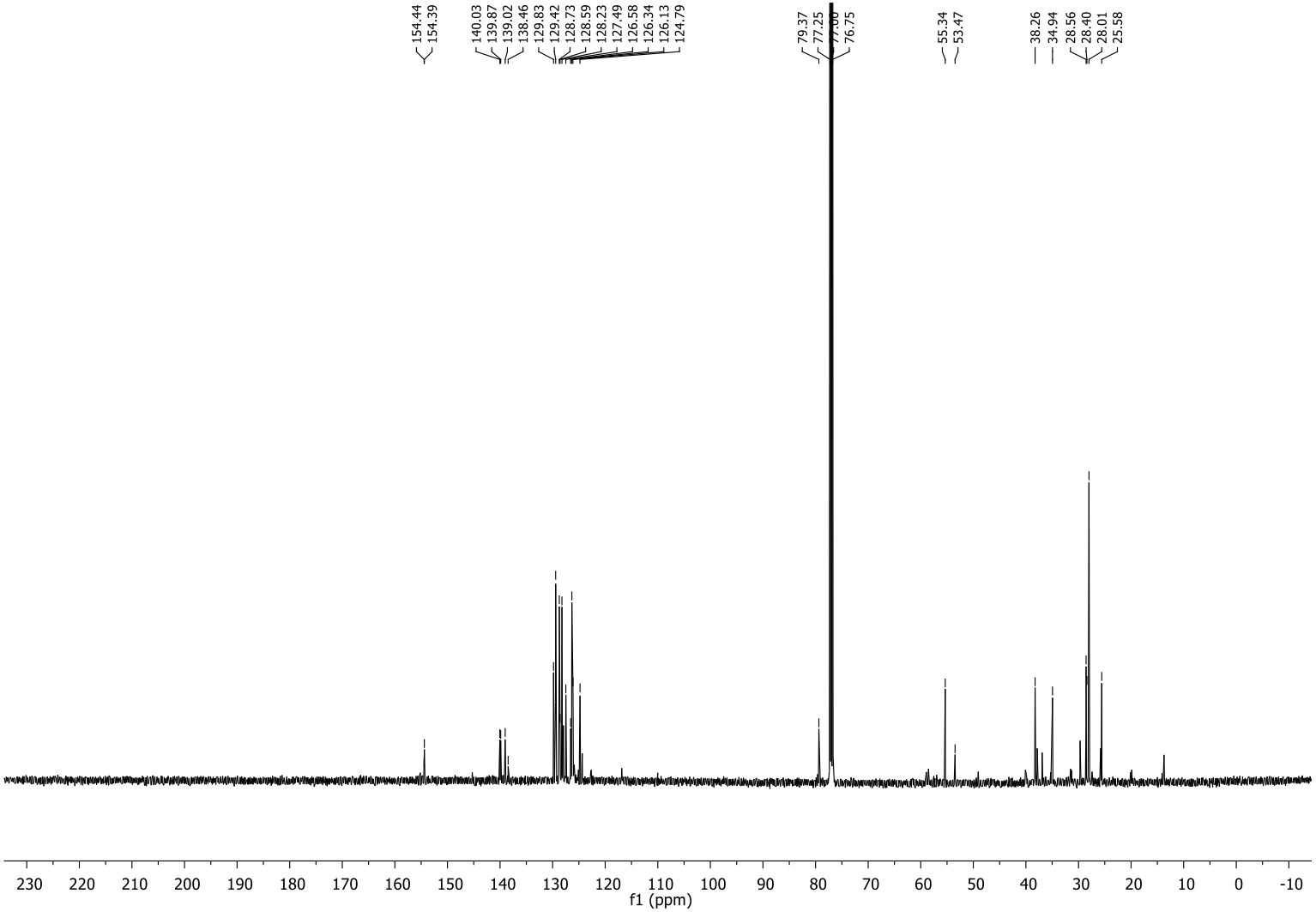
f1 (ppm)


Ph
Bn
N
Boc

27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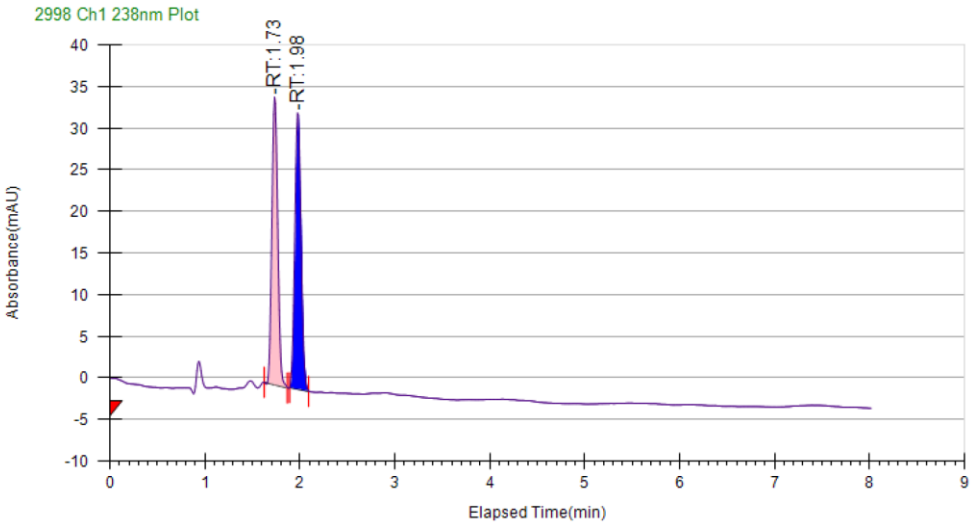
128.23
127.49
126.58
126.34
126.13
124.79
79.37
77.25
77.00
76.75
55.34
53.47
38.26
34.94
28.56
28.40
28.01
25.58
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

3.5 SFC Analysis for Compounds 10 and 27

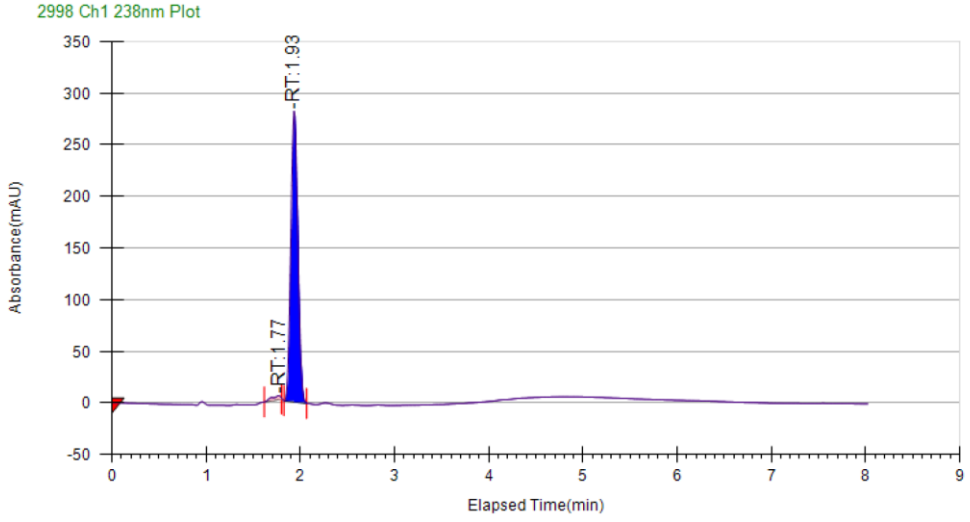
Racemic phenylalanine metathesis product **10**: Chiralpack AD-H, 30% iPrOH, 8 min run, 3.5 mL/min.



Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	49.558	143.4114	1.73 min	34.5419	1732.3333
2	50.442	145.9692	1.98 min	33.1507	1974

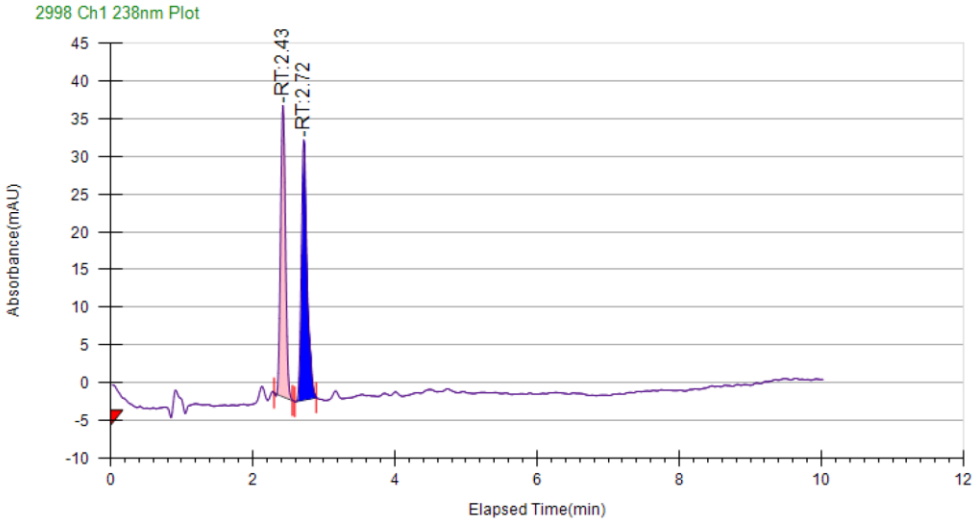
Enantioenriched phenylalanine metathesis product **10**: Chiralpack AD-H, 30% iPrOH, 8 min run, 3.5 mL/min.



Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	1.7262	24.8784	1.77 min	3.7873	1765.6667
2	98.2738	1416.3409	1.93 min	281.7983	1932.3333

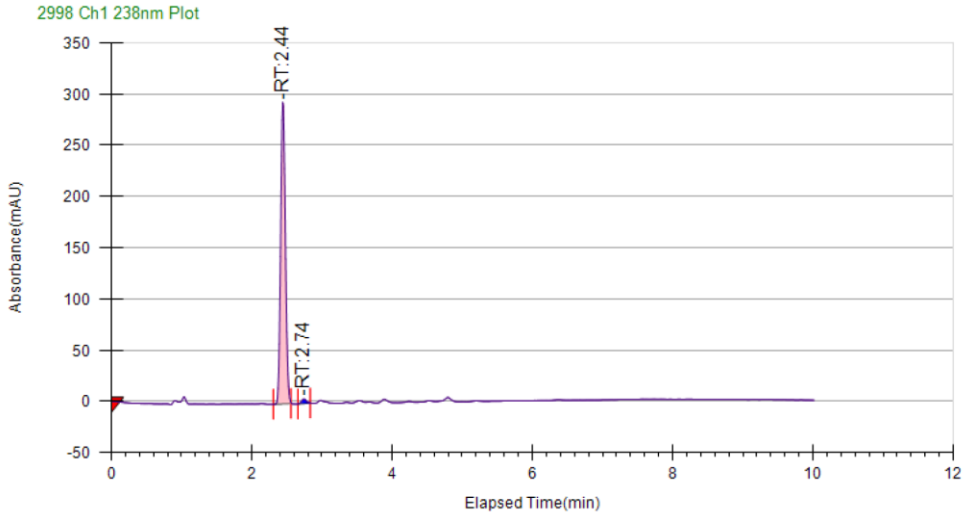
Racemic phenylalanine deprotection product **27**: Chiralpack AD-H, 10%-40% iPrOH, 10 min run, 3.5 mL/min.



Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	48.4234	178.6481	2.43 min	38.5549	2424
2	51.5766	190.2812	2.72 min	34.4533	2715.6667

Enantioenriched phenylalanine deprotection product **27**: Chiralpack AD-H, 10%-40% iPrOH, 10 min run, 3.5 mL/min.



Peak Information

Peak No	% Area	Area	Ret. Time	Height	Cap. Factor
1	98.499	1337.1297	2.44 min	294.3923	2440.6667
2	1.501	20.3756	2.74 min	4.4557	2740.6667

3.6 References

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Chapter 4

Mechanistic Investigations into the Formation of Nitrogen Heterocycles via the Carbonyl-Olefin Metathesis Reaction[****]

4.1 Introduction

So far, this work has detailed the development of a new synthetic strategy to access chiral nitrogen heterocycles from amino acid-derived substrates subjected to a Lewis acid-catalyzed carbonyl-olefin metathesis reaction. During the course of these studies, we found that the protecting group played a significant role the reaction pathway. The selection of an electron-deficient protecting group led to a significant increase in yield of the desired metathesis product.[1] We hypothesized that this reactivity was due to the presence of Lewis basic sites within the substrates. The sulfonamide moiety presented a competitive binding site that could coordinate to the $FeCl_3$, thus sequestering the iron and preventing activation of the aryl ketone. An electron-deficient protecting group, such as the 4-(trifluoromethyl)benzenesulfonyl group, is believed to attenuate this unfavourable pathway. Furthermore, we have established certain substitution patterns within the amino acid backbone play a significant role in the

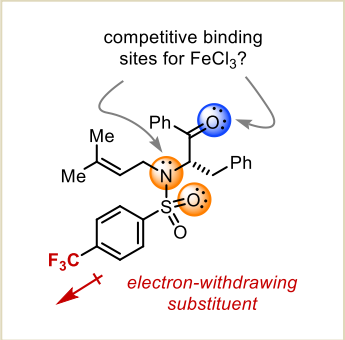


Figure 4.1 Competitive binding sites in amino acid-derived substrates.

[****] Groso, E.J.; Schindler, C.S. *Manuscript in Preparation.*

progression of the reaction. Bulkier α-substituents tend inhibit the reaction pathway, likely due to unfavourable steric interactions in the formation of intermediate oxetanes. This chapter details computational studies put forth to further probe the role of the protecting group and the steric interactions to better understand the carbonyl-olefin metathesis reaction.

4.2 Investigations into Competitive Binding Sites

To further probe the effect of the Lewis basic sites on the $FeCl_3$ catalyst, we performed a density functional theory (DFT) analysis using Q-Chem software to generate electrostatic potential diagrams of the phenylalanine-derived substrate **1** (Figure 4.2). Upon examination of the *N*-tosyl- and 4-(trifluoromethyl)benzenesulfonyl-protected derivates (**1a** and **1b**, respectively), there was not a significant difference observed

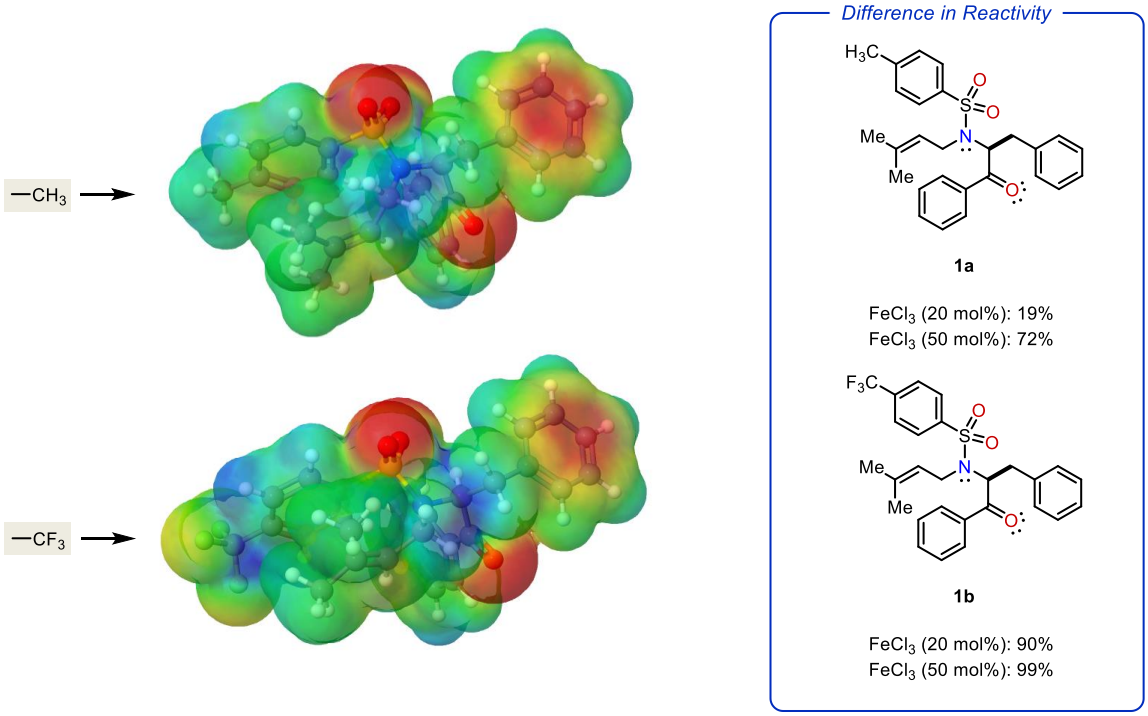


Figure 4.2 Electrostatic potential maps comparing the tosyl and 4-(trifluoromethyl)benzenesulfonyl protecting groups.

between the electronics of these two structures. Despite these initial observations, we set out probe the ability of the different binding to coordinate to the iron catalyst.

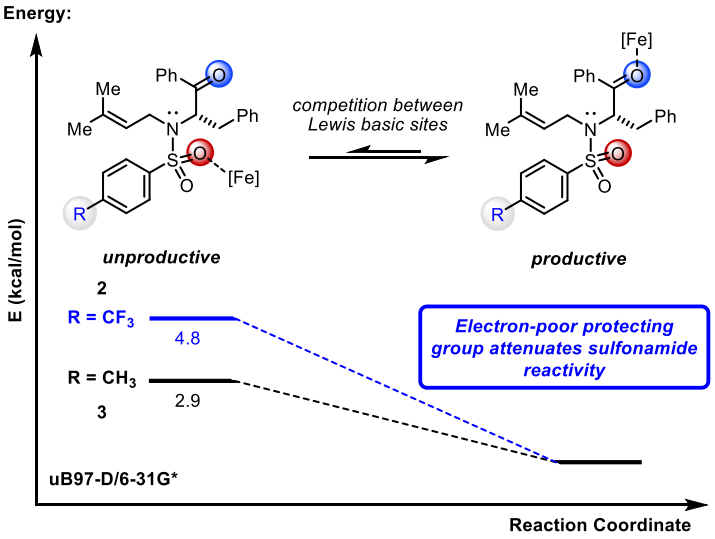


Figure 4.3 Computational studies exploring the Lewis basic binding sites and the role of the protecting.

The computational analysis (ω-UB97-D/6-31G*) revealed that unproductive binding of $FeCl_3$ to the sulfonamide oxygen in *N*-(4-trifluoromethyl)tosyl amine **2** is 1.9 kcal/mol higher in energy compared to the more electron-rich *N*-tosyl amine **3**. This difference in energy reduces the sulfonamide in from sequestering $FeCl_3$, leading to preferential binding of $FeCl_3$ to the carbonyl which is more productive for catalysis. These observations are consistent with our experimental studies.

4.3 Investigations into the Reaction Pathway and Steric Considerations

In recent years, the carbonyl-olefin metathesis reaction has emerged as a powerful tool to directly form carbon-carbon bonds from readily available precursors. This protocol has been applied towards the synthesis of five- and six-membered carbocycles with iron(iii) chloride.[2] Mechanistic and experimental studies have revealed that this reaction proceeds via the formation of an intermediate oxetane that fragments in a concerted, asynchronous pathway to generate a carbonyl by-product and a new olefin.[3] Since these initial reports and as detailed in the previous chapters, we sent out to probe the reaction pathway for the synthesis of nitrogen heterocycles. In the case of the amine-containing

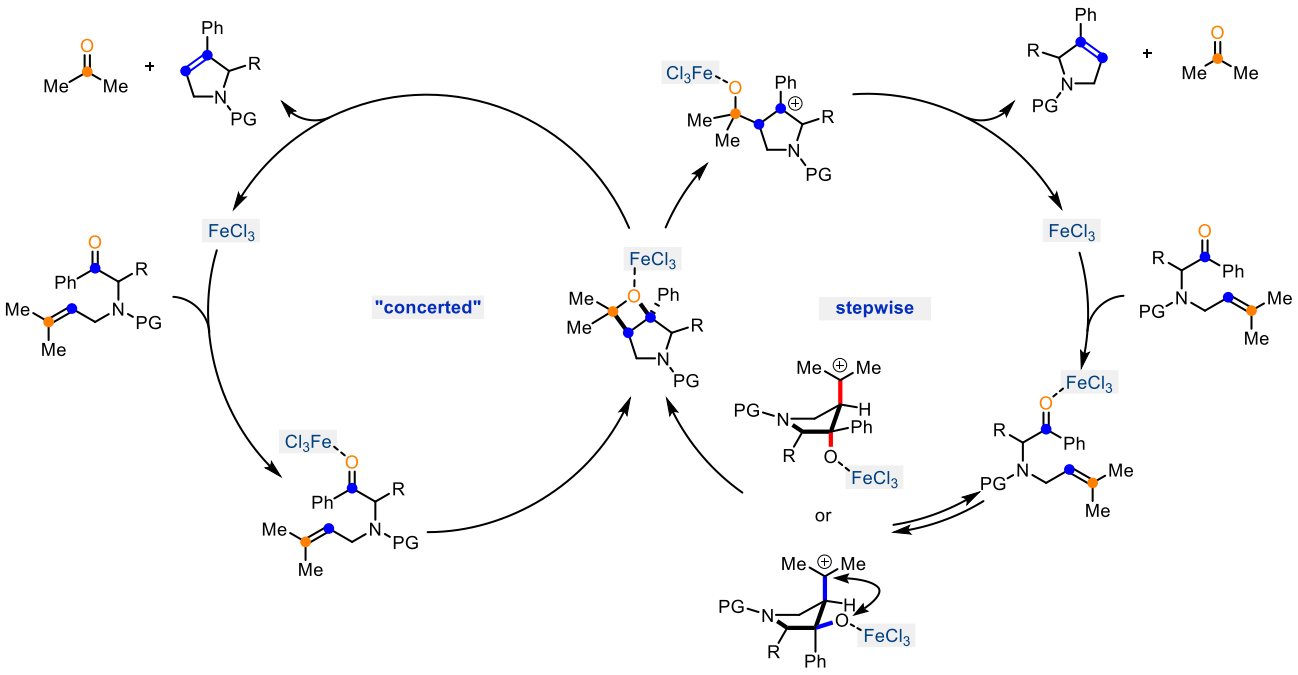


Figure 4.4 Proposed concerted and stepwise pathways for the carbonyl-olefin metathesis reaction in the presence of amines.

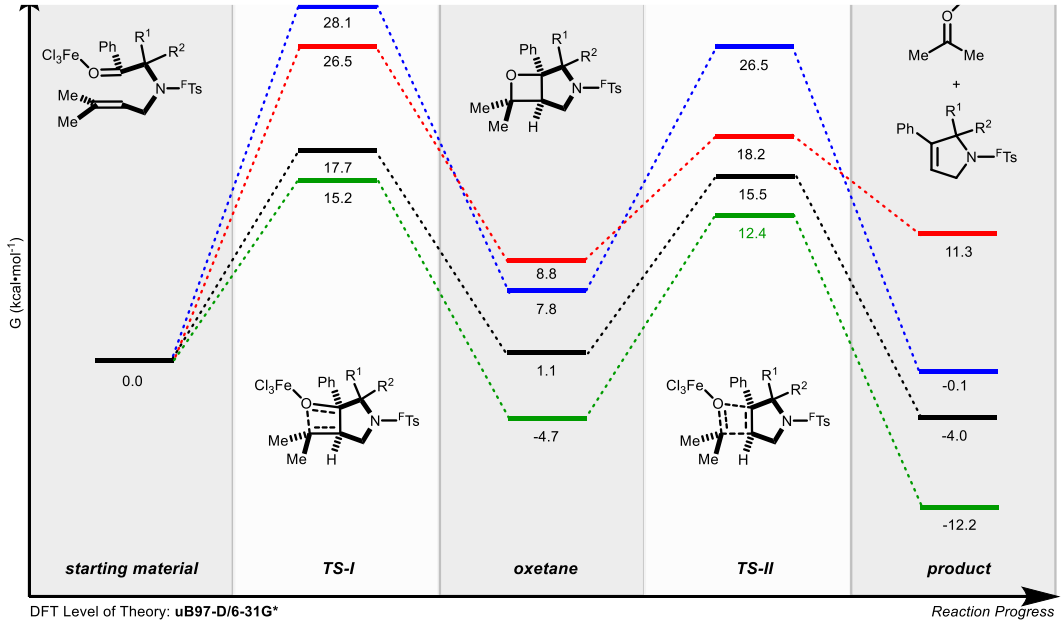
systems, we sent out to confirm that this reaction pathway still applied. In their recent report, the Li group hypothesized the substrates bearing styrenyl-olefins underwent a stepwise pathway in via intermediate carbocations.[4] We proposed that in the case of the prenyl-based olefins, the reaction instead proceeded via the concerted formation of the oxetane fragment, which could then undergo fragmentation to provide the final product (Figure 4.4). For the computational studies, we utilized reaction discovery tools developed by the Zimmerman group, specifically the Growing String Method (GSM) to identify the lowest energy reaction pathway as well as the exact transition states.

We first examined that reaction pathway of the 3-pyrrolines. From our initial report, we know that this approach worked well for a variety of substrates derived from both natural and non-natural amino acids as chiral pool reagents. However,

sterically bulky substituents led to a significant decrease in yield of the desired 3-pyrrolines. To identify the cause of this reaction inhibition, we began a series of computational studies to probe the effects of substitution on the amino acid backbone. We selected a series of substrates including the unsubstituted glycine-derived **4** and alanine-derived **5** substrates to the more sterically encumbered aminoisobutyric acid-derived **6** and valine-derived **7** substrates. These substrates had yields ranging from 32% up to 99% yield (Table 1). The results of these studies are highlighted in Figure 4.5.

The analyses first confirmed that the amine carbonyl-olefin metathesis reaction mechanism undergoes the previously reported mechanism where the starting α-amino ketones coordinate with iron and can undergo a concerted, asynchronous

Figure 4.5 Reaction profile for the carbonyl-olefin metathesis reaction of various chiral 3-pyrrolines.



(b) Comparison of Free Energy and Reported Yield

entry	*Substrate*	*Amino Acid*	R^1	R^2	E_a	ΔG_{298K} Oxetane	ΔG_{298K} PDT	%Yield[a]
1	**4**	**Gly**	H	H	28.1	7.8	-0.1	50
2	**5**	**Ala**	Me	H	17.7	1.1	-4.0	98
3	**6**	**AIB**	Me	Me	15.2	-4.7	-12.2	99
4	**7**	**Val**	iPr	H	26.5	8.8	18.2	32

Conditions: (a) ^{F}Ts-protected amino acids (0.02 mmol) were subjected to 0.5 eq of $FeCl_3$ in DCE (0.01 M) and stirred at room temperature for 24 h; (b) subtrate was the Ts-protected amino acid under otherwise identical conditions.

cyclization (Figure 4.5, **TS-I**) to generate an intermediate oxetane. No evidence of a carbocationic pathway was observed. This oxetane can then fragment via **TS-II** to generate the final 3-pyrroline product and a acetone as the carbonyl byproduct (Figure 4.5).

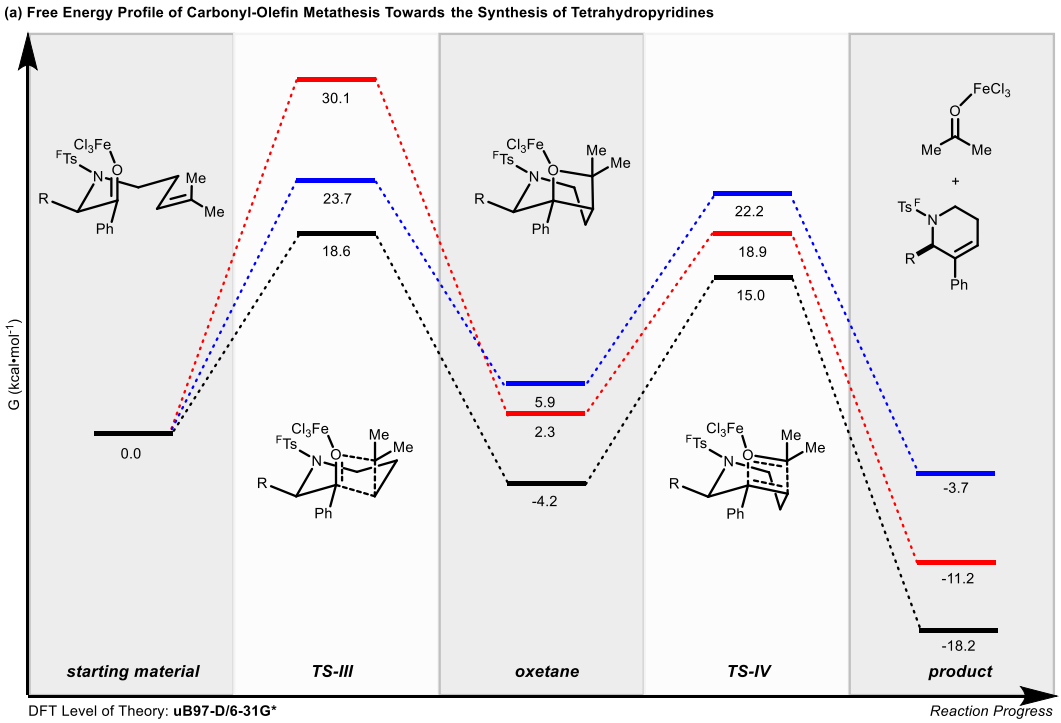
Interestingly, the results also illustrated that the product yields correlated with the activation barrier, E_a. The glycine- and valine-derived substrates **4** and **7** exhibited the highest activations barriers of 28.1 kcal·mol^{-1} and 26.5 kcal·mol^{-1}, respectively (Figure 4.5b, entries 1 and 4). These observation correlates with our previously reported experimental results, as both substrates afforded the metathesis products in diminished yields. Interestingly, the glycine-derived substrate **4** provided higher yields of the metathesis product despite having a higher activation barrier. This is likely due to the overall energetics of the reaction pathway, as the glycine product is thermodynamically favourable (ΔG_f = -12.2 kcal·mol^{-1}), whereas the valine product is significantly higher in energy overall (ΔG_f = 11.3 kcal·mol^{-1}).

Another interesting result came from the dimethyl-substituted substrate **6**. We initially expected a higher activation barrier compared to the analogous alanine-derive substrate **5**. Instead, we found the that **6** has the lowest activation barrier of all the substrates studied (15.2 kcal·mol^{-1}, Figure 4.5b, entry 3). This is likely due to the Thorpe-Ingold Effect,[5] which overcomes any increased steric bulk that could affect oxetane formation. This same effect has been reported in the analogous ring-closing olefin-olefin reaction, and has led to significant advances in the expansion of the substrate scope. The synthesis of larger ring systems can present a

significant challenge for ring-closing metathesis; however, several groups have shown that the angle compression by the *gem*-dimethyl substituents can promoted the cyclization. This strategy has been employed to access synthetically challenging 7- and 8-membered rings.[6]

Next, we set out to perform a similar computational analysis of the formation of tetrahydropyridines. Just as with the 3-pyrroline reaction pathway, we found that the mechanism of the reaction is predicted to proceed via the concerted, asynchronous (Figure 4.6, TS-III) formation of an intermediate oxetane that subsequently fragments to provide the tetrahydropyridine and acetone as a byproduct (Figure 4.6).

Figure 4.6 Reaction profile for the carbonyl-olefin metathesis reaction of tetrahydropyridines.



(b) Comparison of Free Energy and Reported Yield

entry	*Substrate*	*Amino Acid*	R^1	R^2	E_a	ΔG_{298K} Oxetane	ΔG_{298K} PDT	%Yield
1	**8**	**Gly**	H	H	23.7	5.9	-3.7	84
2	**9**	**Ala**	Me	H	18.6	-4.2	-18.2	99
3	**10**	**Val**	iPr	H	30.1	2.3	-11.2	n.r.

Conditions: ^{F}Ts-protected amino acids (0.02 mmol) were subjected to 0.5 eq of $FeCl_3$ in DCE (0.01 M) and stirred at room temperature for 24 h.

During the course of our initial reaction studies, we were surprised to find that the glycine substrate **8** afforded the desired metathesis product in significantly improved yields. We had initially expected that this substrate would give diminished yields as with the pyrroline counterpart **4**. However, the computational data revealed that the activation barrier for the formation of the intermediate oxetane was significantly lower (15.2 kcal·mol^{-1}) making the reaction kinetically favourable. Furthermore, we found that of the three substrates studied which included the unsubstituted glycine- and alanine-derived substrates (**8** and **9**, respectively) and the sterically encumbered valine-derived substrate **10**, all of the reactions were energetically favourable (Figure 4.6).

As reported above, the activation barrier to oxetane formation provided the best correlation to reaction yields. While the formation of the tetrahydropyridine rings was found to be energetically favourable in all of the substrates probed, we were unable to isolate any of the desired valine product. The reaction pathway revealed that activation barrier to access the intermediate oxetane was significantly higher valine 16 at 30.1 kcal·mol^{-1} compared to the corresponding glycine and alanine derivatives (23.7 kcal·mol^{-1} and 18.6 kcal·mol^{-1}, respectively). These results combined with the studies for the five-membered ring systems reveal that in the case of 4-(trifluoromethyl)benzenesulfonyl-protected substrates, an increase in steric bulk – particularly on the β-hydrogen will result in decreased yields of the desired metathesis products.

4.4 Computational Considerations and XYZ Files

4.4.1 Computational details

All quantum chemical calculations utilized density functional theory (DFT) as implemented in the Q-Chem 4.3 quantum chemistry package (Mol. Phys. 2015, 113, 184–215. S63). The unrestricted B97-D density functional (S. Grimme, J. Comp. Chem. 27 (2006) 1787–1799.) with singlet spin was used in combination with the 6-31G* basis set (Ditchfield, R; Hehre, W.J; Pople, J. A. (1971). J. Chem. Phys. 54 (2): 724–728.) to acquire gas phase geometries for the intermediates discussed. The reaction discovery tools developed by the Zimmerman group, specifically the Growing String Method (GSM), ((a) Zimmerman, P. M. J. Chem. Phys. 2013, 138, 184102. (b) Zimmerman, P. M. J. Chem. Theory Comput. 2013, 9, 3043−3050. (c) Zimmerman, P. M. J. Comput. Chem. 2015, 36, 601−611. (d) *J. Comput. Chem.* **2017**, *38*, 645-658.) were used to probe potential reaction paths and determine the exact transition state and minimum energy reaction path for each proposed elementary step. By optimizing the reaction path, GSM provides verification that the saddle point connects the reactant to product geometries through a single transition state. Frequency calculations were performed on all structures at the same level of theory to confirm that optimizations led to stable minima (intermediates) or transition states. Stable intermediates were characterized by all real frequencies, and transition states were identified by a single imaginary frequency. The ωB97X-D3 (Chai, J. D.; Head-Gordon, M. Phys. Chem. Chem. Phys., 2008, 10, 6615.) density functional and the triple-zeta, polarized 6-311G* basis set (ref Pople again) were used to calculate energies with the SMD solvent model (Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. J. Phys. Chem. B, 2009, 113, 6378-6396.) using 1,2-dichloroethane as the implicit solvent, in the ORCA software package (Neese, Frank (2012). "The ORCA program system". *Wiley Interdisciplinary Reviews: Computational Molecular Science*. **2** (1): 73–78.). Thermodynamic corrections were applied to the solvated energies at a temperature of 353.15 K. For these corrections, low frequencies (<50cm-1) were set to 50 cm-1. Energies reported are solvent-phase Gibbs free energies.

4.4.2 XYZ coordinates for structures

Structure 2 (uncoordinated)
61
Step 35

C	-3.81208324	2.63674031	-0.49689602
C	-2.36724056	2.20706207	-0.63648018
C	0.26255333	1.35042695	-0.88985648
C	-1.48518985	2.91060951	-1.47174400
C	-1.93533511	1.05969739	0.05740721
C	-0.61351567	0.62375058	-0.07039946
C	-0.15525713	2.48160095	-1.59963055
S	1.97781443	0.78953336	-1.08115252

N	2.40625363	0.44260231	0.54804284
O	1.95795122	-0.50728251	-1.80018524
O	2.76075583	1.92574266	-1.62406099
C	2.70991145	1.65147580	1.38589808
C	1.45243754	2.34811790	1.83039831
C	1.04738249	3.59477417	1.50819554
C	1.79411009	4.54252439	0.59559730
C	-0.25614532	4.14086632	2.05061346
C	3.29013106	-0.73707970	0.74576579
C	2.80472865	-1.34380300	2.08931524
C	4.80430810	-0.43111597	0.70937669
O	3.41920175	-1.10814696	3.13013278
C	1.52817439	-2.13301690	2.09298447
C	-0.86752627	-3.62466362	2.22878446
C	0.97364659	-2.49414457	3.34378328
C	0.86523945	-2.53462948	0.90943903
C	-0.32396814	-3.27563994	0.98073466
C	-0.21439909	-3.23115741	3.41213684
C	5.59112176	-1.72154963	0.57809184
C	6.93733576	-4.19365438	0.31617224
C	6.15687451	-2.34951421	1.70395043
C	5.70204559	-2.34850028	-0.68015345
C	6.37149043	-3.57545931	-0.81302517
C	6.82938631	-3.57664086	1.57423083
F	-4.64602022	1.81035933	-1.20517044
F	-4.03567178	3.90584120	-0.94596734
F	-4.23251931	2.59348549	0.80546966
H	-1.82549476	3.79605736	-2.00803707
H	-2.62833937	0.51958795	0.70319405
H	-0.25851804	-0.24476778	0.48216212
H	0.55142502	3.02908916	-2.22258688
H	3.24002310	1.26105281	2.26648203
H	3.40343997	2.31912390	0.85490144
H	0.80552431	1.74120555	2.47322364
H	2.16461559	5.41277250	1.16705985
H	2.63965808	4.07634043	0.07334987
H	1.10388899	4.93972013	-0.16982319
H	-0.08673097	5.07820813	2.61131989
H	-0.75807885	3.42145372	2.71601044
H	-0.94376157	4.38653294	1.22191936

H	3.07771003	-1.44084500	-0.06469350
H	4.98353063	0.21985287	-0.16103081
H	5.10077031	0.11117812	1.61797094
H	-1.79403486	-4.20112848	2.27950524
H	1.49223613	-2.18366408	4.25180349
H	1.25472828	-2.26838887	-0.07227458
H	-0.82377203	-3.58028621	0.05872885
H	-0.63243437	-3.50096007	4.38440250
H	7.45828516	-5.14878866	0.21596019
H	6.05290919	-1.87766956	2.68309639
H	5.25888932	-1.86880040	-1.55785342
H	6.45113771	-4.04732135	-1.79532028
H	7.26443033	-4.05187710	2.45682028

Structure 2 (Coordinated to FeCl3 via the Phenyl Ketone)

65

Step 29

N	-1.30532458	0.53608690	-0.16283553
C	-0.03793388	0.38374735	0.59006824
S	-2.31663642	-0.85810642	-0.22011520
O	-2.38940277	-1.36286049	1.16834433
O	-3.51870784	-0.46719121	-0.97593824
C	-1.39638697	-2.07664699	-1.18278524
C	0.36367566	-3.66644466	-2.63037886
C	-0.61352675	-3.02331213	-0.50453012
C	-1.33817514	-1.93512559	-2.57846826
C	-0.45261722	-2.74076149	-3.30362205
C	0.27205930	-3.82009268	-1.23678629
C	1.30053580	-4.56582130	-3.41354363
F	2.43613068	-4.83277992	-2.71699963
F	0.70330858	-5.75910554	-3.68687067
F	1.66448637	-4.01210408	-4.60107256
C	-1.22660386	1.37738448	-1.39197740
C	-0.99845643	2.80032871	-0.96359436
C	0.09939536	3.56131153	-1.18082701
C	1.32584735	3.13091132	-1.94526881
C	0.18994456	4.94576554	-0.58590346
C	1.14976722	-0.15384668	-0.24385104
C	0.31556267	1.69204876	1.33751021
O	1.49014164	2.12971727	1.19954044

Fe	3.16416481	2.82015498	1.94746121
C	2.22288444	-0.85035582	0.57667008
C	4.27755066	-2.14272558	2.02505436
C	3.57520718	-0.62550502	0.26421841
C	1.91255895	-1.74878618	1.61571798
C	2.93177050	-2.38774824	2.33696492
C	4.59717079	-1.26097950	0.98205672
C	-0.63443890	2.31026423	2.26800793
C	-2.39304160	3.53369180	4.08905339
C	-0.34275768	3.59300633	2.79461773
C	-1.81993274	1.64422543	2.67144590
C	-2.68584188	2.25566450	3.58150689
C	-1.21996694	4.20105993	3.69322300
Cl	4.66414822	2.65242232	0.34643972
Cl	2.99042486	4.96644301	2.44820798
Cl	3.47649115	1.57276692	3.70863654
H	-0.26686796	-0.32081817	1.40247484
H	-0.68114791	-3.10956080	0.57780820
H	-1.97458161	-1.20797904	-3.08204414
H	-0.38614927	-2.64489107	-4.38665980
H	0.91000342	-4.54008512	-0.72534065
H	-0.43999628	1.00407514	-2.06703667
H	-2.19636545	1.28452453	-1.89869357
H	-1.81338146	3.22040412	-0.36851482
H	2.19370308	3.08056475	-1.26473664
H	1.57503001	3.88197244	-2.71423156
H	1.22090345	2.15673430	-2.44079221
H	1.07216762	5.01714457	0.07518688
H	0.33197070	5.70368703	-1.37611462
H	-0.70674040	5.20424399	-0.00347970
H	1.60486720	0.67274474	-0.80262289
H	0.73984096	-0.85226576	-0.98569231
H	5.06991000	-2.62892787	2.59706851
H	3.82492532	0.06854659	-0.53880649
H	0.87222608	-1.95340550	1.87869117
H	2.67280522	-3.07009775	3.14922705
H	5.63924854	-1.05180711	0.73460799
H	-3.07641949	4.00807554	4.79610691
H	0.56619415	4.10378471	2.49101853
H	-2.05834187	0.65714139	2.28750368

H	-3.59072491	1.73366163	3.89530436
H	-0.98655826	5.19008097	4.08950429

Structure 2 (Coordinated to FeCl3 via the Sulfonamide)

65

Step 27

C	-3.56773318	2.51975707	-1.06105078
C	-2.14169462	2.01090792	-1.08426174
C	0.51288698	1.25781088	-1.01972343
C	-1.19067574	2.75709365	-1.80228142
C	-1.76614716	0.86511069	-0.36726218
C	-0.42434434	0.47381721	-0.33694274
C	0.15516148	2.38254881	-1.77562743
S	2.24705074	0.81310519	-0.94219226
N	2.48003113	0.34334445	0.65933835
O	2.43721133	-0.49135000	-1.71883718
O	3.06694382	1.95874795	-1.37467204
C	2.60328765	1.51250299	1.61232394
C	1.24929173	2.06341640	1.96103840
C	0.74012041	3.26445897	1.61897768
C	1.46246282	4.32373660	0.81947209
C	-0.67441973	3.63110382	2.01326304
C	3.37201756	-0.83026154	0.90369536
C	2.90682616	-1.40872640	2.27455242
C	4.88136372	-0.51704686	0.84610058
O	3.61325780	-1.27545550	3.27050237
C	1.54205796	-2.01439537	2.34538856
C	-1.06014454	-3.06281310	2.59908933
C	0.92458115	-2.09787147	3.61426231
C	0.84461201	-2.47987506	1.20889863
C	-0.44795298	-3.00529202	1.33655024
C	-0.37040573	-2.61051302	3.73832978
C	5.65117720	-1.80638117	0.62966706
C	6.92938294	-4.28126567	0.20089645
C	6.28568411	-2.47047078	1.69330665
C	5.65493382	-2.39598624	-0.65078304
C	6.28996086	-3.62679737	-0.86517025
C	6.92702956	-3.70083011	1.47896875
F	-4.07805157	2.61840017	-2.31573324
F	-3.60634538	3.77228503	-0.51318651

F	-4.39592099	1.73025181	-0.33289235
H	-1.50277904	3.63471135	-2.36790430
H	-2.51161010	0.28794523	0.17678754
H	-0.11279292	-0.39510275	0.23779219
H	0.91105926	2.95178378	-2.31345691
H	3.08419132	1.09046397	2.50559125
H	3.28815933	2.26770185	1.20325202
H	0.61385731	1.37252625	2.52279681
H	1.58496418	5.23955698	1.42419915
H	2.44970688	4.01126596	0.45502686
H	0.85192570	4.60521921	-0.05542435
H	-0.69123689	4.57860159	2.58021441
H	-1.14538939	2.84813416	2.62682271
H	-1.29594000	3.78580290	1.11492076
H	3.14781923	-1.56642364	0.12589540
H	5.04854658	0.17333520	0.00466934
H	5.19128571	-0.01805509	1.77500716
H	-2.07093300	-3.46410022	2.69664549
H	1.47687245	-1.74306966	4.48494995
H	1.29110844	-2.44269950	0.21674123
H	-0.96707562	-3.36064167	0.44589664
H	-0.84505291	-2.65842003	4.72022076
H	7.42358347	-5.24098706	0.03573031
H	6.25766359	-2.02615428	2.68966467
H	5.15405224	-1.88964049	-1.48038547
H	6.28232759	-4.07244019	-1.86177758
H	7.41896648	-4.20779647	2.31199385
Fe	1.49167143	-1.36918630	-3.25107636
Cl	0.85939247	0.25515336	-4.56744087
Cl	-0.18385851	-2.46329321	-2.33651155
Cl	3.03383777	-2.67919917	-4.05996650

Structure 3 (uncoordinated)
61
Step 18

C	-3.40512642	3.50496641	-1.60270053
C	-2.06648308	2.80426362	-1.71161694
C	0.39812556	1.47603313	-1.94259079
C	-1.10020230	3.23670285	-2.64144866
C	-1.76770354	1.68989137	-0.89863988

C	-0.54236401	1.02186661	-1.00616534
C	0.13429986	2.58132852	-2.76357017
S	1.96793156	0.60190002	-2.13878183
N	2.45575980	0.44543726	-0.50649128
O	1.71283757	-0.77994172	-2.61670354
O	2.87517769	1.48079100	-2.91847516
C	2.72218863	1.71911684	0.23431559
C	1.60874085	1.99790557	1.21301143
C	0.85629028	3.11338817	1.31095368
C	1.00846404	4.35286422	0.45753671
C	-0.27023819	3.19045244	2.31990031
C	3.29604857	-0.72941851	-0.18322620
C	2.94563347	-1.09300333	1.28607883
C	4.81386262	-0.53665430	-0.42220990
O	3.72622826	-0.81571891	2.19591851
C	1.60583766	-1.71200032	1.56050288
C	-0.90922841	-2.82982810	2.18967361
C	1.22989488	-1.92275844	2.90738470
C	0.70749467	-2.07727326	0.53161176
C	-0.54184896	-2.63150752	0.84756187
C	-0.01781398	-2.47603613	3.21992402
C	5.51723279	-1.87981132	-0.44671503
C	6.72538749	-4.43559459	-0.50715453
C	6.20143014	-2.37337900	0.68070917
C	5.43945682	-2.68384760	-1.60264247
C	6.03953842	-3.95252576	-1.63590342
C	6.80504767	-3.64223049	0.65021943
H	-4.15041216	3.02319847	-2.26013871
H	-3.79734953	3.46374944	-0.57420287
H	-3.32882667	4.56083741	-1.90623065
H	-1.31054463	4.10407027	-3.27246568
H	-2.49778195	1.34897682	-0.16005032
H	-0.31008387	0.18037086	-0.35458776
H	0.88876456	2.92357273	-3.47260520
H	3.67809385	1.58849995	0.76502355
H	2.87065681	2.53653525	-0.48352890
H	1.38799154	1.16801323	1.89115327
H	1.81976562	4.28689204	-0.27966986
H	0.06720618	4.55668558	-0.08268189
H	1.20477188	5.23123556	1.09905177

H	-0.32923459	2.28053454	2.93780178
H	-1.23768906	3.32135900	1.79951730
H	-0.14637619	4.06224614	2.98738516
H	2.96033452	-1.54711189	-0.83236313
H	4.92586763	-0.02892193	-1.39299993
H	5.24280781	0.10495486	0.36012876
H	-1.88324059	-3.26105706	2.43258195
H	1.93170014	-1.64247619	3.69435374
H	0.96526646	-1.92242731	-0.51504217
H	-1.22714711	-2.90629590	0.04265029
H	-0.29757799	-2.63348840	4.26404326
H	7.19404878	-5.42231627	-0.52986670
H	6.24403936	-1.76280158	1.58496431
H	4.90496612	-2.30627507	-2.47903337
H	5.97417500	-4.56122358	-2.54095965
H	7.33390767	-4.01197568	1.53216480

Structure 3 (Coordinated to FeCl3 via the Aryl Ketone)

65

Step 24

C	-3.53423785	2.62179294	0.62580616
C	-2.20369545	2.18110486	0.05503317
C	0.30668685	1.43491381	-0.95269452
C	-1.66169100	2.82355977	-1.07594289
C	-1.46648623	1.14273727	0.65709576
C	-0.21689928	0.76312259	0.15826311
C	-0.40787565	2.46148204	-1.58508403
S	1.92907798	0.98070200	-1.60314789
N	2.93236722	0.85066536	-0.22581872
O	1.85092573	-0.37986460	-2.18836064
O	2.41137805	2.11588949	-2.41475488
C	3.26975836	2.11578663	0.49838407
C	2.12988365	2.64239452	1.32508712
C	1.45903334	3.79804464	1.15219559
C	1.71796784	4.79970136	0.05106370
C	0.33147775	4.16512858	2.09122699
C	3.52436559	-0.44112931	0.14034580
C	2.89869157	-0.86502204	1.47959280
C	5.07201853	-0.46015182	0.22876158
O	3.29561826	-0.21390202	2.48678864

C	1.89743726	-1.92820968	1.57545785
C	-0.00296578	-3.99352464	1.81864018
C	1.55351255	-2.44637139	2.85102694
C	1.27234468	-2.46992789	0.41907044
C	0.32216316	-3.48513388	0.54890983
C	0.61922422	-3.47511771	2.96787509
C	5.51090389	-1.86249296	0.61017223
C	6.11300942	-4.51816133	1.34672475
C	5.79705479	-2.18474783	1.95026069
C	5.52600175	-2.88552841	-0.35699123
C	5.82963332	-4.20513795	0.00657455
C	6.09691847	-3.50513103	2.31803499
H	-4.31749531	2.63001954	-0.15003986
H	-3.46498618	3.64608457	1.03037893
H	-3.85917048	1.95852412	1.44112369
H	-2.22165441	3.62950919	-1.55641500
H	-1.86534288	0.64045310	1.54038151
H	0.35305089	-0.01773262	0.65412239
H	0.02438407	2.98015902	-2.43989358
H	4.11158501	1.86676260	1.15769386
H	3.62999176	2.84244499	-0.24149023
H	1.81864553	1.99017866	2.14331202
H	2.07519817	5.75553233	0.47466078
H	2.44317010	4.45595792	-0.69849405
H	0.77201119	5.02017573	-0.47388815
H	0.53822073	5.12819747	2.59148318
H	0.17681756	3.39615411	2.86158675
H	-0.60776532	4.29193113	1.52476685
H	3.24815093	-1.15465024	-0.63746073
H	5.45881525	-0.16391483	-0.75810531
H	5.42361093	0.26421916	0.97551224
H	-0.74001499	-4.79332249	1.91271280
H	2.03975520	-2.06150764	3.74200445
H	1.48044952	-2.06814827	-0.57018063
H	-0.16623690	-3.87908008	-0.34326845
H	0.37492409	-3.86974669	3.95464722
H	6.34584539	-5.54639267	1.63092235
H	5.77605359	-1.39978774	2.70853881
H	5.30088891	-2.64165107	-1.39880667
H	5.84525219	-4.98824950	-0.75451669

H	6.31422698	-3.73777003	3.36223502
Fe	2.95395063	0.40182986	4.32111060
Cl	3.80206196	-1.17051669	5.60324057
Cl	0.77231072	0.60690673	4.49954984
Cl	4.05402020	2.28358996	4.47668334

Structure 3 (Coordinated to FeCl3 via the Sulfonamide)
65
Step 43

C	-3.47884224	2.50791006	-1.41571071
C	-1.99553805	2.23088440	-1.31190111
C	0.73545684	1.66733101	-1.17500206
C	-1.07836950	2.93108009	-2.12315956
C	-1.50985408	1.24683615	-0.42742175
C	-0.14586225	0.95176341	-0.35303074
C	0.29151596	2.65795926	-2.06528435
S	2.47498916	1.27255505	-1.16218010
N	2.78930752	0.75946984	0.39446792
O	2.69335057	0.00359814	-1.99823104
O	3.24452582	2.45704140	-1.58126604
C	2.88021003	1.85237021	1.43448323
C	1.63607842	1.87966655	2.28084907
C	0.62013105	2.76332862	2.19973550
C	0.56940955	3.95650849	1.27609412
C	-0.61603838	2.57956207	3.05128492
C	3.54168009	-0.50462620	0.62054093
C	3.07883273	-1.01762095	2.01864939
C	5.07457348	-0.36645152	0.50693105
O	3.77909261	-0.80404509	3.00578898
C	1.73263465	-1.65668820	2.12950317
C	-0.84350927	-2.75009015	2.46068373
C	1.17567439	-1.80230999	3.42186318
C	0.98884520	-2.08899711	1.01037278
C	-0.29231497	-2.63252445	1.17566129
C	-0.10444292	-2.33802088	3.58532903
C	5.68687015	-1.74969734	0.40962222
C	6.67765169	-4.38080547	0.21638689
C	6.25803472	-2.37732602	1.53041577
C	5.60799134	-2.45410398	-0.80846519

C	6.10093645	-3.76267785	-0.90551842
C	6.75647617	-3.68566576	1.43355473
H	-3.92181299	1.90739555	-2.22903329
H	-3.67275411	3.56702919	-1.64478182
H	-4.00214497	2.24365595	-0.48416364
H	-1.44383440	3.69679467	-2.80968140
H	-2.20982660	0.69682627	0.20399393
H	0.22756285	0.19679541	0.33245260
H	1.00203416	3.19668618	-2.68988928
H	3.76389856	1.61181414	2.04137602
H	3.08159196	2.80611643	0.93172002
H	1.53815745	1.04519522	2.97943295
H	0.43284714	4.88410047	1.85974218
H	1.46530414	4.07158276	0.65255387
H	-0.30176776	3.86843099	0.60600396
H	-0.80343804	3.46797060	3.68019708
H	-0.53672407	1.69556590	3.70202263
H	-1.50159307	2.45852136	2.40087899
H	3.21507944	-1.21155171	-0.14664691
H	5.28768015	0.21326317	-0.40479239
H	5.46824686	0.18240873	1.37378455
H	-1.84457411	-3.16716330	2.58846856
H	1.76516213	-1.47699473	4.27971478
H	1.38405829	-2.00579875	0.00036593
H	-0.84944853	-2.95458439	0.29534399
H	-0.53021316	-2.43594937	4.58582107
H	7.06218812	-5.40024352	0.14187336
H	6.29294889	-1.83943844	2.47940038
H	5.15766798	-1.97439659	-1.68137204
H	6.03412308	-4.29566467	-1.85601472
H	7.20132635	-4.16268079	2.30971544
Fe	1.66711878	-0.90146722	-3.45216088
Cl	-0.05968780	-1.85695094	-2.47366682
Cl	1.08523451	0.64385559	-4.88357354
Cl	3.12234172	-2.35313799	-4.18356238

Structure 4 (Starting Material)
52

C	-2.8605731395	-0.7370887739	-3.6197229749

C	-2.6620619676	0.6081288452	-3.2721012843
C	-2.7246560385	0.9975935827	-1.9284317709
C	-2.9784292409	0.0241432466	-0.9495313952
C	-3.1978434456	-1.3222567095	-1.2867712876
C	-3.1447002750	-1.6974110152	-2.6331755790
S	-2.7482298416	0.4490971890	0.7884353142
O	-2.9337569659	1.9015034245	0.9649870313
N	-1.0377786999	0.1675681223	1.0070370175
O	-3.4393417136	-0.5427302838	1.6301476623
C	-0.2357726006	1.0048192595	0.1040026834
C	-0.6394793395	-1.2742607888	0.9543886920
C	0.7253875393	-1.4138320511	1.5656717120
C	1.2095223997	1.2380097096	0.5240812516
C	1.8681096492	-1.8125339941	0.9586084073
O	2.0792682157	1.2545705845	-0.3983850681
C	3.1648914063	-1.8273772000	1.7339209948
C	1.9967202709	-2.2398106839	-0.4808831438
C	-2.6699784554	-1.1965626953	-5.0518163323
F	-2.8152450770	-0.1828809331	-5.9434740266
F	-3.5634974793	-2.1706815002	-5.3863292645
F	-1.4261643288	-1.7207912251	-5.2201540384
C	1.6014291543	1.6095756215	1.8855263286
C	0.6309003680	1.9343403722	2.8656449036
C	1.0412744843	2.3203384652	4.1451674393
C	2.4093563077	2.3736914541	4.4638776398
C	3.3778485476	2.0605995598	3.4918105092
C	2.9801343431	1.6909550262	2.2061652294
Fe	1.8620247904	1.5538584386	-2.3738087583
Cl	3.8943334529	1.9650129363	-3.0392619867
Cl	0.4835756649	3.2713031117	-2.4233664338
Cl	0.9732888095	-0.2078906493	-3.3327921726
H	-2.4399236551	1.3459116206	-4.0410268181
H	-2.5630125014	2.0363273583	-1.6448432097
H	-3.4118452159	-2.0522026539	-0.5068654348
H	-3.3141306448	-2.7347832151	-2.9206714531
H	-0.6893078801	2.0076634229	0.0447210593
H	-0.2172137937	0.5854628275	-0.9156011393
H	-1.3808750938	-1.8219691123	1.5525816991
H	-0.6798154847	-1.6420812470	-0.0859213809
H	0.7783206838	-1.1099712273	2.6141412382

H	3.9064720197	-1.1776855416	1.2356842725
H	3.5999706749	-2.8422194932	1.7501504196
H	3.0347712889	-1.4805125006	2.7693317783
H	2.4255690329	-3.2558052468	-0.5341259065
H	1.0538751528	-2.2359936198	-1.0403850879
H	2.7029217010	-1.5757977595	-1.0082525701
H	-0.4273831570	1.8879604301	2.6197011338
H	0.2929393294	2.5800835222	4.8951361136
H	2.7225514763	2.6671987503	5.4676838553
H	4.4393704601	2.1126951843	3.7385025685
H	3.7169698113	1.4561950548	1.4388985630

Structure 4 (TS-I)
52

C	-2.2401728824	-1.2724381198	-3.3769563534
C	-2.1469979847	0.1156572460	-3.1913040769
C	-2.5085162822	0.6771854214	-1.9594398797
C	-2.9400095173	-0.1690170128	-0.9236139293
C	-3.0956229856	-1.5528505554	-1.1215987856
C	-2.7508359543	-2.1014143085	-2.3615982657
S	-2.9745434475	0.4811885926	0.7583181872
O	-3.2885247166	1.9161618716	0.7191523716
N	-1.3133403683	0.3650249813	1.1890617306
O	-3.6757907006	-0.4812445886	1.6257340265
C	-0.3651339843	1.1804816451	0.4223792549
C	-0.7849945312	-1.0043216779	1.4150169502
C	0.7357187129	-0.9122475984	1.2364077204
C	1.0537574451	0.7685190963	0.8886166332
C	1.3439638204	-1.4517332559	0.0341718136
O	1.9766563909	0.7872724212	-0.1413469199
C	2.7693018767	-1.8642176576	0.0735494143
C	0.5725219237	-1.6787191497	-1.2092353243
C	-1.6593276977	-1.9145590895	-4.6191153015
F	-1.5713832405	-1.0564018751	-5.6601797530
F	-2.3905472839	-2.9905439738	-5.0215959458
F	-0.3961905939	-2.3720557855	-4.3518430374
C	1.5496669586	1.4408934606	2.1384320540
C	0.6719521330	1.7504194051	3.2024918237
C	1.1607217968	2.3801610814	4.3514242092

C	2.5263852138	2.7019894342	4.4556220598
C	3.4024094158	2.3927073449	3.4024704026
C	2.9221471802	1.7542392820	2.2522467441
Fe	2.2308368878	1.9731194084	-1.5882677642
Cl	4.4194866557	2.0842094838	-1.8281819111
Cl	1.2408682785	3.8816030095	-1.0973725434
Cl	1.2490923204	0.9756014042	-3.3371683145
H	-1.7541914066	0.7487666020	-3.9842175205
H	-2.4291721702	1.7511697660	-1.7944845078
H	-3.4761421962	-2.1757217254	-0.3121792783
H	-2.8536847282	-3.1723095594	-2.5377378564
H	-0.5321073921	2.2476807562	0.6047843859
H	-0.4185206083	0.9995917674	-0.6651444567
H	-1.0412071072	-1.3253975533	2.4324518595
H	-1.2239655666	-1.7306419339	0.7095396747
H	1.3048173162	-1.1613445155	2.1370065437
H	3.2876514921	-1.5693665574	-0.8498191230
H	2.7877222489	-2.9723354405	0.1256090927
H	3.2892005909	-1.4639487719	0.9533165795
H	0.1294046653	-2.6927491150	-1.1334616208
H	-0.2667798040	-0.9844054292	-1.3111295311
H	1.2000784738	-1.6481431564	-2.1071901066
H	-0.3881010625	1.5088833592	3.1165050092
H	0.4761754302	2.6266960227	5.1650688291
H	2.9034899450	3.1944666180	5.3540236142
H	4.4598904623	2.6530163641	3.4729958779
H	3.5915045779	1.5287265612	1.4227212446

Structure 4 (Oxetane)
52

C	-2.1674556448	-1.1812915789	-3.4565107925
C	-2.1598618773	0.1973287468	-3.1917986716
C	-2.5862560609	0.6674734407	-1.9428138908
C	-3.0066411179	-0.2573738234	-0.9720490210
C	-3.0792862889	-1.6331905512	-1.2518995874
C	-2.6606494226	-2.0919602161	-2.5053709237
S	-3.1719801908	0.2914977227	0.7402516225
O	-3.5506470402	1.7129400130	0.7536400036
N	-1.5434758064	0.2269835337	1.2742764452

O	-3.8880388723	-0.7467576176	1.5001431814
C	-0.6140065136	1.2074163897	0.6741438153
C	-0.9229760191	-1.1246847490	1.3710273293
C	0.5887739801	-0.8455028760	1.3326700806
C	0.7771305633	0.6843071669	1.0969220814
C	1.4042783615	-1.0948390890	0.0251520150
O	1.6158234631	0.4074829713	-0.0977723028
C	2.7610416714	-1.7457660020	0.2361181226
C	0.6617658752	-1.6140931871	-1.1914978140
C	-1.5151654178	-1.7241697596	-4.7104561763
F	-1.4096194365	-0.7945661793	-5.6893298325
F	-2.1975629399	-2.7889536251	-5.2159795507
F	-0.2534225562	-2.1648187209	-4.4195487847
C	1.5012621046	1.4794657754	2.1469253163
C	0.7723475075	1.9288247125	3.2647642271
C	1.4277180211	2.6071623882	4.3004968754
C	2.8094108229	2.8487009703	4.2217639514
C	3.5332565256	2.4038420663	3.1054217594
C	2.8852059612	1.7115815880	2.0721990350
Fe	2.2530440920	1.6469808869	-1.5209712270
Cl	4.4194881629	1.3177613879	-1.5571305669
Cl	1.5700128194	3.5759089586	-0.7674827770
Cl	1.2497987310	1.0758163189	-3.3858371885
H	-1.7917306897	0.8948826160	-3.9414258433
H	-2.5789942326	1.7328839782	-1.7153920655
H	-3.4474889606	-2.3206502559	-0.4909138719
H	-2.6905257568	-3.1560035900	-2.7400891246
H	-0.8296671522	2.2108218589	1.0532368789
H	-0.6576555889	1.2207547629	-0.4295530643
H	-1.2398893024	-1.5910497671	2.3116376266
H	-1.2287631160	-1.7815153432	0.5397537552
H	1.1107716813	-1.2166507582	2.2214073078
H	3.3887089499	-1.6111264779	-0.6569536163
H	2.6199092407	-2.8242265749	0.4123199503
H	3.2713690830	-1.3042760159	1.1038887258
H	0.3794331738	-2.6646007944	-1.0187728576
H	-0.2486499274	-1.0370246038	-1.3896244864
H	1.2989772184	-1.5692393124	-2.0847736070
H	-0.3018177510	1.7398931383	3.3213127187
H	0.8573000271	2.9531797343	5.1643359960

H	3.3175805585	3.3857429764	5.0248007778
H	4.6047182864	2.5977164106	3.0312763889
H	3.4471188004	1.3775049560	1.2004876569

Structure 4 (TS-II)
52

C	-1.8992147124	-0.7508421377	-3.5333284566
C	-1.9348043070	0.5032861323	-2.9049705512
C	-2.4709295786	0.6171841834	-1.6151537541
C	-2.9376758782	-0.5382322829	-0.9665991610
C	-2.9402280468	-1.7914864748	-1.6008676387
C	-2.4285142869	-1.8887417459	-2.8981634106
S	-3.3254402126	-0.4567567666	0.7927944594
O	-3.9347033183	0.8525286312	1.0806936301
N	-1.8036541207	-0.4080932874	1.5517596246
O	-3.9221947731	-1.7409763468	1.1958691677
C	-1.0426011402	0.8390465712	1.5053926447
C	-0.9110790983	-1.5939559242	1.5941648628
C	0.5274813508	-1.0029656475	1.5747596876
C	0.3344858589	0.4519373020	1.8867790875
C	1.3548577487	-1.0218380477	0.1501984098
O	1.7038962413	0.3125256531	-0.1107980860
C	2.6376606528	-1.8548584216	0.3113824286
C	0.5084064145	-1.5770119409	-0.9991785415
C	-1.2177789614	-0.9387489917	-4.8747086397
F	-0.9674766154	0.2289242927	-5.5073488799
F	-1.9802295936	-1.7085200636	-5.7063290208
F	-0.0337319477	-1.5918824771	-4.7093230572
C	1.2952840241	1.3519552009	2.4018975451
C	1.0336628650	2.7595654952	2.3936366496
C	2.0423602926	3.6580853691	2.7249501940
C	3.3113280811	3.1796877257	3.1030476818
C	3.5776871975	1.7950420073	3.1582123722
C	2.5864936969	0.8898442514	2.8065374044
Fe	1.8966230971	1.6927014508	-1.2851028803
Cl	3.7694244898	2.7554785874	-0.7341379383
Cl	0.1113118687	3.0747417382	-0.9052313220
Cl	1.8603229415	0.9971691655	-3.3792198624
H	-1.5201446451	1.3793333702	-3.3997344008

H	-2.5051093383	1.5867896126	-1.1214607028
H	-3.3287051758	-2.6624148331	-1.0742066360
H	-2.4132076572	-2.8496623846	-3.4126180656
H	-1.4948548394	1.6075297615	2.1465415425
H	-0.9511193212	1.2899544553	0.4856692869
H	-1.0965459100	-2.1524387716	2.5244141498
H	-1.1016359679	-2.2707262299	0.7516702422
H	1.1567295304	-1.5000095142	2.3251865666
H	3.1894139131	-1.8312109683	-0.6401249007
H	2.4012161392	-2.9016019859	0.5635893243
H	3.2862814866	-1.4277197741	1.0905315349
H	0.2695019302	-2.6418889195	-0.8572546925
H	-0.4196056967	-1.0090011450	-1.1122808151
H	1.0890763572	-1.4688089218	-1.9256937487
H	0.0664188369	3.1329396722	2.0648151823
H	1.8546570212	4.7300971896	2.6715989391
H	4.1013769534	3.8894982737	3.3529553402
H	4.5651606805	1.4403768403	3.4534000583
H	2.7894194731	-0.1787799286	2.8254761459

Structure 4 (Product)
52

C	-1.8177266934	-0.8256995158	-3.4370459865
C	-2.0508705152	0.4580627409	-2.9237528710
C	-2.6333854159	0.6052285748	-1.6561607673
C	-2.9732050950	-0.5406605421	-0.9220226745
C	-2.7758834880	-1.8316081821	-1.4446099509
C	-2.1951745152	-1.9691631867	-2.7083979612
S	-3.5250923467	-0.3667090000	0.7921971926
O	-4.1054921037	0.9765032373	0.9492433355
N	-2.0883430037	-0.3685528301	1.6785812941
O	-4.2287536164	-1.6067149448	1.1639340969
C	-1.1867250010	0.8028418114	1.6082396647
C	-1.3227860245	-1.6294237057	1.8111361147
C	0.0374739906	-1.1187604293	2.1998172681
C	0.1259408423	0.2307446960	2.1194234332
C	1.8854599275	-0.5754470114	-0.3940789547
O	2.3146576475	0.5989017138	-0.4860927718
C	2.7310805923	-1.5559343069	0.3718000761

C	0.6455700885	-1.0072564399	-1.1114565059
C	-1.0907642306	-1.0309087706	-4.7490626715
F	-0.8569362010	0.1218055015	-5.4136211524
F	-1.7864277495	-1.8599580493	-5.5758321927
F	0.1216037416	-1.6336212518	-4.5225938712
C	1.2727504828	1.0823013964	2.4488087735
C	1.3122199300	2.4267634375	2.0149389534
C	2.4356276619	3.2259760092	2.2645141851
C	3.5326598150	2.7023981709	2.9646964776
C	3.4935068098	1.3767156497	3.4314629068
C	2.3745913530	0.5759939443	3.1797588063
Fe	1.9716716174	2.1533989292	-1.7019607045
Cl	3.6002726535	3.5467222646	-1.3245223421
Cl	-0.0236340220	3.0044989024	-1.3333567623
Cl	2.0630353185	1.1843079013	-3.6658643964
H	-1.7598922634	1.3377276719	-3.4939606793
H	-2.8160643707	1.5950731326	-1.2423271295
H	-3.0928381911	-2.7020476034	-0.8712187607
H	-2.0303486263	-2.9591781471	-3.1350330050
H	-1.5703524120	1.6181383828	2.2391956549
H	-1.0799853119	1.2005704015	0.5808728203
H	-1.7875864617	-2.2778223848	2.5711281702
H	-1.2930747282	-2.2050209508	0.8620282371
H	0.8295838418	-1.7866894098	2.5341558334
H	3.6421313905	-1.7490922364	-0.2218528286
H	2.2076210778	-2.5024716702	0.5512233093
H	3.0501853271	-1.0912550647	1.3163455733
H	0.2723586276	-1.9693317988	-0.7442818710
H	-0.1367089108	-0.2419382424	-1.0225645933
H	0.8789951196	-1.1005969593	-2.1867662956
H	0.4711914413	2.8450128685	1.4629694434
H	2.4565608876	4.2534243657	1.8989964937
H	4.4089740805	3.3247702172	3.1535582283
H	4.3329891298	0.9713198118	3.9998495332
H	2.3362689019	-0.4425570991	3.5714978245

Structure 5 (Starting Material)
55

N	-0.32160424	-1.15577329	3.32607955

C	1.15603194	-1.09702288	3.27542792
C	1.59352133	0.37586937	3.28019196
C	-0.18706158	-0.21909671	5.62736316
C	-0.82879443	-1.25808692	4.73515532
H	0.52731558	-0.59679072	6.36384220
H	-1.91883814	-1.11935088	4.69861729
H	-0.63034473	-2.26925166	5.12983342
O	0.97285402	1.14848592	2.50551027
C	-0.40884566	1.11548135	5.57854370
C	2.81377173	0.79119866	3.99307296
C	5.18829336	1.58867877	5.28179579
C	3.23952147	0.14254873	5.17976522
C	3.60277224	1.83951096	3.46164769
C	4.78453961	2.22739308	4.09838809
C	4.41173383	0.54738847	5.82199020
H	2.62518786	-0.63672027	5.62584605
H	3.31279588	2.31699905	2.52990552
H	5.38626772	3.02954491	3.66984706
H	4.71909014	0.05720128	6.74690712
H	6.10561300	1.90066941	5.78420807
S	-1.21559346	-2.17297764	2.23927141
O	-0.67339139	-1.98672267	0.88183502
O	-1.37963896	-3.52943217	2.81210975
C	-2.80617071	-1.31646113	2.32114905
C	-5.22491728	0.03388349	2.42333086
C	-2.88809100	-0.02981952	1.76832204
C	-3.90891704	-1.94727529	2.90884688
C	-5.13185252	-1.26189953	2.95474611
C	-4.10745637	0.64955989	1.82887964
H	-2.01509064	0.43726048	1.31689722
H	-3.80578201	-2.95157151	3.31938711
H	-6.00544613	-1.72958362	3.40690808
H	-4.18580970	1.65835985	1.42461121
C	0.35291377	2.05885127	6.47748357
H	1.01785999	1.52124191	7.17068650
H	-0.34302695	2.68496205	7.06182662
H	0.96336985	2.74878347	5.86965124
C	-1.38619073	1.76145417	4.63407925
H	-0.85470342	2.43941059	3.94795989
H	-2.09241623	2.39502370	5.19765638

H	-1.94674630	1.03860388	4.03166592
C	-6.54328341	0.78150421	2.42324937
F	-7.09408195	0.78370730	1.17777541
F	-6.37349099	2.08198935	2.78905711
F	-7.45444714	0.23269555	3.27193078
C	1.90086132	-1.73861495	2.07260828
H	1.55554045	-1.59505604	4.17079093
H	1.66372517	-2.80909092	2.01235807
H	2.98048944	-1.62498847	2.25575092
H	1.63392846	-1.25937730	1.12542531
Fe	0.77231475	2.96033844	1.75875516
Cl	2.23168812	3.02561166	0.12518982
Cl	-1.29337940	3.15971724	1.05445142
Cl	1.23741051	4.37094762	3.37696015

Structure 5 (TS-I)
55

N	-0.35286207	-0.98452995	3.24863251
C	1.11212683	-0.81604343	3.06970831
C	1.39645076	0.48935351	3.89209539
C	0.23650258	0.28442860	5.17187264
C	-0.60473022	-0.90531531	4.70133895
H	0.79642642	0.10076113	6.09318560
H	-1.68075991	-0.77153215	4.88546224
H	-0.27279007	-1.81852553	5.22594127
O	1.02832899	1.62850549	3.22463657
C	-0.34468051	1.61025814	5.12520928
C	2.78875454	0.55774159	4.47536912
C	5.40122305	0.68249710	5.52485881
C	3.29813108	-0.50280960	5.25815430
C	3.59872443	1.68475159	4.23433288
C	4.90079948	1.74067207	4.75265047
C	4.59399790	-0.44208528	5.77878033
H	2.67505259	-1.37599852	5.46654167
H	3.21510421	2.49648912	3.62075756
H	5.52289658	2.61307261	4.54601852
H	4.97641764	-1.26881546	6.38024398
H	6.41451231	0.72863388	5.92823337
S	-1.19514911	-2.31211198	2.51091611

O	-0.69016335	-2.46446697	1.13773573
O	-1.25207320	-3.46560739	3.43819353
C	-2.82389775	-1.52378476	2.47439021
C	-5.25960769	-0.19701957	2.49015539
C	-3.01378687	-0.44353907	1.60033820
C	-3.82838417	-1.96478728	3.34589196
C	-5.05786090	-1.29267866	3.34767057
C	-4.24424926	0.22340924	1.61254720
H	-2.20972074	-0.11364169	0.94424597
H	-3.64311346	-2.81185886	4.00627500
H	-5.85515864	-1.60915776	4.02008270
H	-4.40339944	1.07597517	0.95385517
C	0.30632788	2.71099095	5.86056592
H	1.17614429	2.38485768	6.44349988
H	-0.43335130	3.21800648	6.50639035
H	0.60357872	3.47208538	5.10801697
C	-1.55918504	1.90432280	4.32938113
H	-1.55247322	2.94341535	3.96990134
H	-2.42855254	1.78520072	5.00968664
H	-1.67590916	1.19798707	3.49842821
C	-6.61293309	0.48698510	2.48035031
F	-7.49711051	-0.20022000	1.70630845
F	-6.54586241	1.75455412	1.99734931
F	-7.14476310	0.55236994	3.73481921
C	1.59221714	-0.64627485	1.62671853
H	1.65126535	-1.65078744	3.55398328
H	1.61333526	-1.61598509	1.11659133
H	2.60247711	-0.21199552	1.63308526
H	0.92113413	0.02423520	1.07834678
Fe	0.94249425	2.79356199	1.80210486
Cl	2.84933683	2.84450304	0.70254231
Cl	-0.81292235	2.27523954	0.53137183
Cl	0.53097575	4.74468351	2.85782556

Structure 5 (Oxetane)

55

N	-0.39768029	-0.91082081	3.20901871
C	1.06165379	-0.65324989	2.98703747
C	1.35398881	0.47119786	4.02622436
C	0.19363883	0.42815334	5.05113999

C	-0.66050872	-0.77276387	4.66237339
H	0.47889073	0.41740129	6.10810056
H	-1.73542628	-0.61666705	4.83221089
H	-0.33579458	-1.66657510	5.22304082
O	0.85740677	1.81285798	3.51618810
C	-0.25575144	1.83014371	4.56877319
C	2.78409542	0.49676848	4.49956631
C	5.47111928	0.41465011	5.35071519
C	3.12078783	-0.05881434	5.74863700
C	3.80979441	0.99110294	3.67260840
C	5.14320997	0.95970536	4.10047739
C	4.45686582	-0.10142943	6.17124113
H	2.34439398	-0.47434143	6.39223110
H	3.57819954	1.41248466	2.69703653
H	5.92162312	1.36656518	3.45347890
H	4.70127853	-0.53299370	7.14349814
H	6.51026413	0.39196852	5.68372903
S	-1.13384159	-2.33112727	2.55072265
O	-0.64129032	-2.50741670	1.17363697
O	-1.08766922	-3.44708051	3.52185904
C	-2.82736372	-1.69033244	2.50025313
C	-5.37407161	-0.58220255	2.48172974
C	-3.13385443	-0.70134610	1.55377125
C	-3.77261624	-2.14603993	3.42713698
C	-5.05740641	-1.58536384	3.41244398
C	-4.41769842	-0.14687022	1.54642261
H	-2.37441602	-0.37064136	0.84579027
H	-3.50253068	-2.92100604	4.14418239
H	-5.80831063	-1.91784925	4.12882067
H	-4.67441184	0.62803982	0.82506696
C	0.01891226	2.92429036	5.58987461
H	1.03709408	2.83795636	5.99353361
H	-0.70275367	2.81521618	6.41596002
H	-0.11155443	3.92097207	5.14662003
C	-1.61480170	1.94627983	3.90176039
H	-1.73922614	2.94363871	3.46148170
H	-2.39170178	1.80641874	4.67084412
H	-1.73579592	1.17731587	3.12979316
C	-6.78177137	-0.01925980	2.44317053
F	-7.58645197	-0.78452272	1.65620207

F	-6.81064760	1.24569992	1.94597825
F	-7.34189565	0.01331365	3.68384675
C	1.40981283	-0.28483076	1.54650067
H	1.65718297	-1.52355828	3.32027760
H	1.22282417	-1.13299024	0.88017856
H	2.47182452	-0.01458230	1.48161172
H	0.80731482	0.57250855	1.22062191
Fe	1.68443845	3.48418106	2.75096966
Cl	2.61990117	3.04374610	0.81579918
Cl	-0.02690346	4.83164508	2.44733331
Cl	3.08482989	4.30605621	4.21564787

Structure 5 (TS-II)

55

N	-0.49940741	-0.99512391	3.21907366
C	0.93689435	-0.80032156	2.87719972
C	1.48221496	-0.08164915	4.07505671
C	0.35411534	0.32658540	4.97504568
C	-0.72573620	-0.72321492	4.65911734
H	0.65298291	0.28566055	6.02986826
H	-1.74518663	-0.34440635	4.81000631
H	-0.58610616	-1.63122425	5.27166184
O	1.13908692	2.34334336	3.96913002
C	-0.01394866	1.86276932	4.62349549
C	2.86018630	0.10650347	4.32328801
C	5.58177555	0.71296322	4.69994038
C	3.28063780	0.93430485	5.41273270
C	3.85576144	-0.43359299	3.44495164
C	5.19660199	-0.13301410	3.63630354
C	4.62586041	1.24096356	5.58687599
H	2.54072488	1.38061445	6.07056774
H	3.55838295	-1.07842238	2.61925548
H	5.94984967	-0.53672034	2.95950100
H	4.92302275	1.92085301	6.38354686
H	6.63537608	0.96504339	4.83113108
S	-1.25729699	-2.41070500	2.61451701
O	-0.69659475	-2.62225413	1.26564018
O	-1.24017542	-3.49631542	3.61953773
C	-2.94333087	-1.77192013	2.50195186
C	-5.50793488	-0.71773596	2.36761925

C	-3.20476449	-0.72877649	1.60103018
C	-3.93978769	-2.30498726	3.32951976
C	-5.23262788	-1.77013298	3.25661420
C	-4.49862188	-0.20135808	1.53549033
H	-2.40692983	-0.33253051	0.97359369
H	-3.70230380	-3.11716653	4.01602440
H	-6.02310468	-2.16131189	3.89668174
H	-4.72148653	0.61413618	0.84880078
C	-0.29858288	2.63197065	5.92364047
H	0.57215733	2.61653607	6.59442024
H	-1.16917428	2.19898185	6.44305984
H	-0.52078277	3.68127028	5.67799315
C	-1.22460862	2.00446571	3.67788586
H	-1.27279083	3.06621622	3.39500788
H	-2.16516548	1.73079425	4.18092398
H	-1.11896962	1.39541686	2.77342122
C	-6.92642062	-0.18787500	2.27248098
F	-7.68500696	-0.98411038	1.47057290
F	-6.97085679	1.06946935	1.76029577
F	-7.52644964	-0.15749400	3.49409733
C	1.11146883	0.01851079	1.56839697
H	1.45994020	-1.76664907	2.75623175
H	0.56224600	-0.50351465	0.77454495
H	2.17471007	0.08247451	1.30133741
H	0.73184540	1.03661091	1.71011418
Fe	2.09706345	3.92571082	3.95490384
Cl	3.73667258	3.56326014	2.48945786
Cl	0.68642679	5.53522382	3.37259818
Cl	2.92503631	4.28536544	6.01617870

Structure 5 (Product)
55

N	-0.37791978	-1.84643118	3.79144081
C	0.92078739	-1.38985972	3.21155450
C	1.44674828	-0.52125006	4.35836812
C	0.65064363	-0.62694618	5.44532227
C	-0.49901669	-1.57035586	5.23475483
H	0.84483511	-0.14410949	6.40216897
H	-1.48799755	-1.12980500	5.46164289

H	-0.40611801	-2.49090604	5.84026990
O	0.14462810	2.44723278	3.45992795
C	-0.63422852	2.04836283	4.35932123
C	2.73444368	0.20140433	4.32933380
C	5.22140557	1.54962123	4.38558822
C	3.59004205	0.09988840	5.45124697
C	3.14555318	1.00434110	3.24082660
C	4.37793195	1.67076564	3.27231860
C	4.82016674	0.76658728	5.47971706
H	3.28832586	-0.53356598	6.28762248
H	2.49063803	1.15057844	2.38663679
H	4.65883040	2.30627198	2.43189280
H	5.46807316	0.66936112	6.35303886
H	6.17933403	2.07194585	4.40648150
S	-1.36018426	-3.03237504	3.10591121
O	-0.69374211	-3.53530445	1.89120133
O	-1.83194182	-3.92769336	4.17965539
C	-2.75459025	-1.98120352	2.61796191
C	-4.59414282	0.03192698	2.07378413
C	-2.73535055	-1.35785221	1.36089854
C	-3.72032457	-1.65637581	3.58225255
C	-4.64158978	-0.63834062	3.30642707
C	-3.66033737	-0.34487097	1.09155720
H	-1.99259024	-1.65069152	0.62038846
H	-3.73706290	-2.18683107	4.53371154
H	-5.38623014	-0.35688871	4.05025997
H	-3.65361306	0.16400558	0.12767534
C	-0.45603002	2.49988094	5.77868992
H	0.61056486	2.59892798	6.02151970
H	-0.96811992	1.83484272	6.48493423
H	-0.90333626	3.50955550	5.85278550
C	-1.82132805	1.22015547	3.96124264
H	-2.43516214	1.79173260	3.24679379
H	-2.43408674	0.94600117	4.82696196
H	-1.48548694	0.30936272	3.44453098
C	-5.45848245	1.24970953	1.83301957
F	-5.88691277	1.32767387	0.54702324
F	-4.73777992	2.38870914	2.08567246
F	-6.55040686	1.28079440	2.63964872
C	0.75043098	-0.70726773	1.84383136

H	1.60179767	-2.25108391	3.07945986
H	0.21227563	-1.38155832	1.16719759
H	1.73782669	-0.51978243	1.40194052
H	0.20881471	0.24466821	1.92943940
Fe	1.33992120	4.08389721	3.43649457
Cl	2.25197029	4.04951437	1.45093594
Cl	-0.23790339	5.59853578	3.67272565
Cl	2.72822169	4.16693399	5.12329062

Structure 6 (Starting Material)

58

Step 15

N	-0.31602105	-1.18277643	3.24950314
C	1.17305519	-1.14708766	3.14022044
C	1.57119127	0.34347111	3.37891878
C	-0.12128506	-0.16529685	5.54241923
C	-0.82937179	-1.17165494	4.66883831
H	0.60042821	-0.57144008	6.25501654
H	-1.89885673	-0.92809330	4.60829632
H	-0.73917623	-2.17545235	5.11277890
O	0.91625864	1.17846977	2.69739876
C	-0.35693520	1.16961496	5.56550950
C	2.82307302	0.76399521	4.05111232
C	5.22758917	1.66609532	5.22269487
C	3.27787415	0.21411638	5.27352921
C	3.59703626	1.77317889	3.42958033
C	4.79416461	2.20990665	4.00409283
C	4.46229333	0.67171350	5.85692365
H	2.68167949	-0.52873357	5.79195508
H	3.28115779	2.18676935	2.47616383
H	5.38038022	2.97893068	3.49982008
H	4.78727632	0.25557189	6.81190981
H	6.15512108	2.01543001	5.67983367
S	-1.26209360	-2.29646639	2.29875482
O	-0.77317867	-2.29819347	0.90878723
O	-1.44330903	-3.57503198	3.02598999
C	-2.82742319	-1.38556526	2.32959841
C	-5.21274323	0.02870253	2.35351549
C	-2.86287820	-0.10420019	1.75814884
C	-3.96043649	-1.97872705	2.89838748
C	-5.16606031	-1.26199908	2.90304992

C	-4.06510748	0.60753919	1.78016162
H	-1.96786514	0.34143675	1.32772649
H	-3.89224927	-2.97606858	3.33263688
H	-6.06184734	-1.70013111	3.34136255
H	-4.10443497	1.61413943	1.36509466
C	0.41894498	2.08002259	6.48200659
H	1.07380247	1.52048692	7.16666715
H	-0.26558691	2.70991727	7.07545287
H	1.04145135	2.76784450	5.88337529
C	-1.35207858	1.84283972	4.66214368
H	-0.86797076	2.67594330	4.12901496
H	-2.16191352	2.29439628	5.26203070
H	-1.78607409	1.16465040	3.91935857
C	-6.51180438	0.80814274	2.31098524
F	-7.05436990	0.77263299	1.06235196
F	-6.31311098	2.11796444	2.62424309
F	-7.44199808	0.31664519	3.17411268
C	1.73665985	-1.35514897	1.69510405
C	1.84268206	-2.22477179	4.02171287
H	1.63006800	-2.40559625	1.40145324
H	2.80919450	-1.10358470	1.71080869
H	1.22349112	-0.72297786	0.96453754
Fe	0.73191271	2.92825177	1.84351709
Cl	2.11564754	2.82516194	0.14080867
Cl	-1.35075129	3.13245515	1.17816199
Cl	1.28214608	4.45233588	3.32677164
H	1.51321513	-3.20223912	3.64051658
H	1.55272451	-2.16257330	5.07691431
H	2.93780142	-2.16811841	3.95184460

Structure 6 (TS-I)
58
Step 102

N	-0.29982735	-1.12695015	3.24164635
C	1.15357425	-0.85035604	2.99131585
C	1.35061707	0.44756534	3.93065512
C	0.19360976	0.19514140	5.11385537
C	-0.53191374	-1.08278438	4.69063828
H	0.69751389	0.09760742	6.08182967
H	-1.60930346	-1.06099655	4.90568950

H	-0.10778690	-1.95215795	5.22088931
O	0.97504086	1.60117085	3.26415042
C	-0.57148039	1.45212086	5.09432744
C	2.74715798	0.58730953	4.52957966
C	5.38367657	0.82293916	5.52425735
C	3.19000230	-0.21878922	5.60023880
C	3.64560185	1.51564514	3.96786076
C	4.95524992	1.62655733	4.45843358
C	4.49373542	-0.10279538	6.09514457
H	2.51975229	-0.95372910	6.04869598
H	3.32563123	2.14205883	3.13944664
H	5.63453954	2.34944196	4.00375936
H	4.81410511	-0.73343558	6.92669840
H	6.39977417	0.91663165	5.91188078
S	-1.15374283	-2.40922239	2.46072730
O	-0.62216993	-2.54821649	1.09542135
O	-1.27171624	-3.57746904	3.36219750
C	-2.75103222	-1.55967790	2.42141025
C	-5.05829426	-0.02606217	2.55298685
C	-2.90734087	-0.49076860	1.52777073
C	-3.73461357	-1.89583247	3.36098312
C	-4.90043531	-1.11860833	3.42243546
C	-4.07170106	0.27955489	1.59709160
H	-2.11789839	-0.24111082	0.82173704
H	-3.57948030	-2.74064575	4.03206403
H	-5.67612974	-1.34874053	4.15216085
H	-4.19444593	1.13462549	0.93415692
C	-0.02039168	2.61085082	5.81635803
H	0.92291813	2.39168083	6.33056894
H	-0.77568925	3.00723472	6.51877973
H	0.13899114	3.42489386	5.07190302
C	-1.81397174	1.62681803	4.32950644
H	-1.48882722	1.82019802	3.27911038
H	-2.38987250	2.50314478	4.65489652
H	-2.43561254	0.72411256	4.26387689
C	-6.32467031	0.80581563	2.60591215
F	-7.25174743	0.34380519	1.72406234
F	-6.08200876	2.10706020	2.29435385
F	-6.89420025	0.78075261	3.84391360
C	1.44511426	-0.46175583	1.53584306

C	2.03535561	-2.05341572	3.38705328
H	1.54123275	-1.36146482	0.91716164
H	2.38683892	0.10365724	1.49763312
H	0.64093724	0.15629241	1.12308857
Fe	0.85822683	2.85936905	1.94890334
Cl	2.57928420	2.92532289	0.57730097
Cl	-1.08062121	2.45726792	0.86635919
Cl	0.61956068	4.78796806	3.08213348
H	1.79626793	-2.88637285	2.71046280
H	1.86752882	-2.38826579	4.41912295
H	3.09818068	-1.79979085	3.27620751

Structure 6 (Oxetane)
58
Step 4

N	-0.38397053	-1.00590742	3.26743359
C	1.08501134	-0.75006404	3.01205967
C	1.35097030	0.40749431	4.04833401
C	0.21142209	0.33692226	5.09690166
C	-0.63743412	-0.87144078	4.71958893
H	0.51498469	0.32651818	6.14862564
H	-1.71131555	-0.71507304	4.89624667
H	-0.31425043	-1.76416743	5.28113193
O	0.78991816	1.72824489	3.53393069
C	-0.27686830	1.73085916	4.62991054
C	2.78126115	0.53779430	4.50450635
C	5.48280124	0.66207730	5.31064290
C	3.17195008	0.06589201	5.77170126
C	3.76383553	1.05138039	3.63734475
C	5.10270755	1.12227585	4.04104690
C	4.51436739	0.12575287	6.17214695
H	2.43552247	-0.37021181	6.44718742
H	3.49466191	1.40813988	2.64617674
H	5.84408387	1.54379482	3.36083548
H	4.79910328	-0.24381920	7.15883200
H	6.52604336	0.71979282	5.62592293
S	-1.18680264	-2.37160558	2.58694197
O	-0.67410130	-2.57521316	1.21977637
O	-1.23140267	-3.49153016	3.55365142

C	-2.84431665	-1.64610336	2.49655863
C	-5.33966750	-0.43267772	2.41167270
C	-3.08477171	-0.64873190	1.53991935
C	-3.82990591	-2.05768768	3.40223930
C	-5.08854208	-1.44265859	3.35476851
C	-4.34372945	-0.04107655	1.49862738
H	-2.29426328	-0.35324424	0.85071206
H	-3.61017732	-2.84238893	4.12579276
H	-5.87115985	-1.73783609	4.05325772
H	-4.55104407	0.74100185	0.76928423
C	0.02338009	2.83174755	5.63658265
H	1.06081935	2.76461462	5.99187668
H	-0.65849763	2.71202960	6.49431855
H	-0.14491957	3.82476259	5.19726033
C	-1.66434195	1.82531868	4.02188348
H	-1.83034890	2.82474445	3.60136383
H	-2.40593257	1.65745250	4.81964734
H	-1.79778840	1.06580399	3.24356883
C	-6.72318501	0.18331211	2.33446520
F	-7.53923085	-0.56246364	1.53986497
F	-6.69394905	1.44145049	1.82087308
F	-7.30934489	0.25297556	3.56179485
C	1.33627139	-0.31050051	1.56753606
C	1.94110347	-1.98468799	3.37307291
H	1.15597874	-1.14773172	0.88463281
H	2.37981085	0.01023513	1.45420159
H	0.67787760	0.52418273	1.29812179
Fe	1.55685845	3.41514404	2.73439944
Cl	2.48924713	3.00796440	0.78881173
Cl	-0.21315931	4.68508059	2.43246517
Cl	2.93588254	4.33453014	4.16335899
H	1.67663815	-2.80706335	2.69408551
H	1.76470296	-2.31016667	4.40877298
H	3.00864437	-1.75604652	3.25775384

Structure 6 (TS-II)
58
Step 36

N	-0.39788961	-1.19501499	3.30048613
C	1.07998756	-1.04214663	3.05748781

C	1.48822534	-0.17650572	4.23612853
C	0.34646628	0.04941833	5.10901753
C	-0.66691353	-1.02644767	4.74041378
H	0.55269989	0.11969395	6.18053490
H	-1.70961782	-0.72421549	4.89919574
H	-0.47908854	-1.95260302	5.31391398
O	0.59502277	2.00409302	3.48232499
C	-0.10188025	1.67916402	4.62955004
C	2.80031548	0.32818069	4.50055349
C	5.34340427	1.39026037	5.10273518
C	3.21761079	0.50725326	5.85609258
C	3.69396234	0.71217448	3.45690750
C	4.93852108	1.25520065	3.76324517
C	4.48288730	1.00814789	6.14856062
H	2.55918289	0.19980255	6.66727096
H	3.36879893	0.69772400	2.42316996
H	5.58121023	1.60632195	2.95639377
H	4.79786177	1.11867859	7.18668033
H	6.32165815	1.81444478	5.33400475
S	-1.29286209	-2.49663169	2.60472469
O	-0.74886623	-2.76080272	1.25895614
O	-1.44887272	-3.59992833	3.57857432
C	-2.87832943	-1.64258556	2.45675976
C	-5.29583711	-0.30001150	2.23942482
C	-2.98902492	-0.58517897	1.54061625
C	-3.95194297	-2.04620252	3.26108255
C	-5.17054554	-1.36457831	3.14700647
C	-4.21053483	0.08860012	1.43412729
H	-2.13512825	-0.28897420	0.93192049
H	-3.82792754	-2.87499128	3.95737070
H	-6.02095460	-1.65211577	3.76492892
H	-4.31944147	0.91794977	0.73666231
C	0.29708490	2.55089287	5.82548371
H	1.37475776	2.47895910	6.02408627
H	-0.27439170	2.27432013	6.72562237
H	0.07443174	3.59784079	5.56509437
C	-1.60755587	1.72442459	4.36089589
H	-1.82612508	2.76024266	4.05398817
H	-2.19941876	1.48294695	5.25782045
H	-1.87692447	1.05307625	3.53558303

C	-6.64365244	0.37953712	2.08880316
F	-7.46360555	-0.35811896	1.28973410
F	-6.53808816	1.61577962	1.53772691
F	-7.26979816	0.51399566	3.29045584
C	1.32883314	-0.48938066	1.63660302
C	1.86113693	-2.38732773	3.27198481
H	0.69892549	-1.05901635	0.94503305
H	2.37086511	-0.65065329	1.33208468
H	1.08270831	0.57592213	1.58387355
Fe	1.43976547	3.56241988	2.91029141
Cl	2.35579115	3.03125821	0.94354196
Cl	-0.14136354	5.11773317	2.82930710
Cl	3.06031950	4.14101553	4.33997082
H	1.56270224	-3.07626097	2.46998452
H	1.62455273	-2.84267159	4.24479692
H	2.94188863	-2.19951815	3.20992546

Structure 6 (Product)
58
Step 66

N	-0.22277392	-2.15130062	3.65876256
C	1.09517853	-1.55031695	3.25298346
C	1.38777923	-0.69944179	4.50087694
C	0.51875515	-0.97493447	5.49437936
C	-0.51444763	-1.98972282	5.09310858
H	0.56380903	-0.54882500	6.49714009
H	-1.55161438	-1.63925865	5.25145918
H	-0.41024537	-2.94326081	5.64366827
O	-0.48421606	2.08342698	3.22861432
C	-0.72592342	1.93010785	4.45017332
C	2.56515063	0.18583558	4.64037405
C	4.77466799	1.90433943	5.04726895
C	3.43890383	-0.00716498	5.73415811
C	2.82201543	1.25385572	3.75030675
C	3.91390775	2.10887799	3.95742851
C	4.53464096	0.84268746	5.93467255
H	3.25491821	-0.84109462	6.41378945
H	2.14605375	1.44645344	2.92147500
H	4.07792132	2.93953620	3.26947091
H	5.20290794	0.67414676	6.78158149

H	5.62605030	2.56926056	5.20406807
S	-1.32067107	-2.96937753	2.69830004
O	-0.66444666	-3.30091649	1.42117869
O	-1.96643011	-3.99162819	3.54419635
C	-2.56330239	-1.67954672	2.39602675
C	-4.23334773	0.54382081	2.23399993
C	-2.30879784	-0.69416180	1.42845978
C	-3.68272262	-1.59796909	3.24048738
C	-4.52296364	-0.47927057	3.15188168
C	-3.14272093	0.42618136	1.35437424
H	-1.45741262	-0.79327907	0.75834356
H	-3.88018293	-2.39756271	3.95368525
H	-5.39012386	-0.39153946	3.80629536
H	-2.93907273	1.21501548	0.63154792
C	0.07141672	2.66109391	5.48734228
H	1.14137936	2.46022175	5.31807966
H	-0.21863083	2.37437189	6.50543723
H	-0.06588738	3.74618090	5.34295923
C	-1.89438682	1.06841829	4.81485468
H	-2.80140068	1.67857533	4.65502795
H	-1.86071191	0.73537998	5.85906610
H	-1.95959896	0.22080978	4.12454092
C	-5.03628561	1.82587415	2.27354833
F	-5.01225917	2.49220161	1.09693357
F	-4.52741924	2.67490862	3.22889437
F	-6.33671002	1.60320882	2.60607955
C	1.02830371	-0.74682214	1.94533175
C	2.16675503	-2.65863267	3.13307070
H	0.73358397	-1.40393156	1.11855410
H	2.02491063	-0.34818134	1.71700546
H	0.32520976	0.09130886	2.01430156
Fe	0.15508841	3.48488302	1.96029500
Cl	1.27736145	2.47487667	0.38064446
Cl	-1.77240209	4.26948784	1.28745962
Cl	1.36107646	4.91917003	3.09428884
H	1.91871147	-3.31502622	2.28693566
H	2.19899437	-3.25597792	4.05663893
H	3.15694023	-2.20710990	2.96526915

Structure 7 (Starting Material)

61
Step 11

N	-0.28181503	0.10935351	3.49765076
C	0.82864626	0.74289609	2.75939753
C	2.06230149	1.11398762	3.61176264
C	-0.27985297	1.74133435	5.37906255
C	-1.10252147	1.05168079	4.32794117
H	0.01129954	1.11614932	6.22695830
H	-1.57213793	1.76429756	3.63308479
H	-1.90826833	0.46739513	4.79177826
O	2.54933666	2.25378385	3.36999895
C	0.15708203	3.02217133	5.34469102
C	1.35554957	0.01035381	1.46948661
H	1.80327088	-0.94242913	1.77613908
C	2.81470151	0.12187642	4.39527775
C	4.36301121	-1.80814524	5.73254774
C	2.21602655	-0.73801217	5.34085328
C	4.20347364	0.01156781	4.13520390
C	4.96463315	-0.96113080	4.78786502
C	2.99215612	-1.68682902	6.01282557
H	1.16541125	-0.63995564	5.58356711
H	4.67067642	0.65156917	3.38881331
H	6.02839236	-1.04857676	4.56335935
H	2.51920282	-2.33285550	6.75337408
H	4.96254028	-2.55848706	6.25121256
S	-0.62659162	-1.53641444	3.70806491
O	0.34045799	-2.33784640	2.93787144
O	-0.82825866	-1.81072453	5.14857727
C	-2.28804593	-1.69181301	2.98021891
C	-4.84438500	-2.03662578	1.92853872
C	-2.81074037	-0.72504201	2.11246297
C	-3.03123962	-2.83004195	3.33789487
C	-4.31073232	-3.00146076	2.80244107
C	-4.09767562	-0.90039878	1.58491657
H	-2.22381991	0.15475577	1.85526854
H	-2.61957190	-3.55594785	4.03845742
H	-4.90529584	-3.87365428	3.07449191
H	-4.52061893	-0.15200974	0.91601704
C	1.05878959	3.54970517	6.43367983
H	1.27381601	2.78869355	7.19753288

H	0.60737498	4.43111736	6.92210041
H	2.01416044	3.89015449	6.00091851
C	-0.15069274	4.01651572	4.25218894
H	0.77231852	4.26690443	3.70451541
H	-0.51196829	4.95992631	4.69464523
H	-0.89941745	3.66943251	3.52747074
C	-6.22301209	-2.26958003	1.34410025
F	-6.18887459	-3.24735325	0.39641227
F	-6.73351079	-1.15350395	0.76048204
F	-7.10247809	-2.67258353	2.30173347
H	0.41958111	1.70578466	2.41148950
C	0.19543593	-0.25930388	0.49468721
H	0.60395120	-0.65156221	-0.44925191
H	-0.34338439	0.67606334	0.26408707
H	-0.51450875	-0.99684628	0.88120135
C	2.42738694	0.85904265	0.75052748
H	2.70076263	0.35367483	-0.18761858
H	3.34609355	0.99062011	1.33674193
H	2.03926501	1.85962280	0.50053734
Fe	4.13060738	3.38504049	3.81651290
Cl	3.35663505	5.43251945	3.67989919
Cl	4.82105917	2.91912336	5.83893314
Cl	5.59481843	2.94506722	2.23707142

Structure 7 (TS-I)

61

Step 11

N	-0.28181503	0.10935351	3.49765076
C	0.82864626	0.74289609	2.75939753
C	2.06230149	1.11398762	3.61176264
C	-0.27985297	1.74133435	5.37906255
C	-1.10252147	1.05168079	4.32794117
H	0.01129954	1.11614932	6.22695830
H	-1.57213793	1.76429756	3.63308479
H	-1.90826833	0.46739513	4.79177826
O	2.54933666	2.25378385	3.36999895
C	0.15708203	3.02217133	5.34469102
C	1.35554957	0.01035381	1.46948661
H	1.80327088	-0.94242913	1.77613908
C	2.81470151	0.12187642	4.39527775

C	4.36301121	-1.80814524	5.73254774
C	2.21602655	-0.73801217	5.34085328
C	4.20347364	0.01156781	4.13520390
C	4.96463315	-0.96113080	4.78786502
C	2.99215612	-1.68682902	6.01282557
H	1.16541125	-0.63995564	5.58356711
H	4.67067642	0.65156917	3.38881331
H	6.02839236	-1.04857676	4.56335935
H	2.51920282	-2.33285550	6.75337408
H	4.96254028	-2.55848706	6.25121256
S	-0.62659162	-1.53641444	3.70806491
O	0.34045799	-2.33784640	2.93787144
O	-0.82825866	-1.81072453	5.14857727
C	-2.28804593	-1.69181301	2.98021891
C	-4.84438500	-2.03662578	1.92853872
C	-2.81074037	-0.72504201	2.11246297
C	-3.03123962	-2.83004195	3.33789487
C	-4.31073232	-3.00146076	2.80244107
C	-4.09767562	-0.90039878	1.58491657
H	-2.22381991	0.15475577	1.85526854
H	-2.61957190	-3.55594785	4.03845742
H	-4.90529584	-3.87365428	3.07449191
H	-4.52061893	-0.15200974	0.91601704
C	1.05878959	3.54970517	6.43367983
H	1.27381601	2.78869355	7.19753288
H	0.60737498	4.43111736	6.92210041
H	2.01416044	3.89015449	6.00091851
C	-0.15069274	4.01651572	4.25218894
H	0.77231852	4.26690443	3.70451541
H	-0.51196829	4.95992631	4.69464523
H	-0.89941745	3.66943251	3.52747074
C	-6.22301209	-2.26958003	1.34410025
F	-6.18887459	-3.24735325	0.39641227
F	-6.73351079	-1.15350395	0.76048204
F	-7.10247809	-2.67258353	2.30173347
H	0.41958111	1.70578466	2.41148950
C	0.19543593	-0.25930388	0.49468721
H	0.60395120	-0.65156221	-0.44925191
H	-0.34338439	0.67606334	0.26408707
H	-0.51450875	-0.99684628	0.88120135

C	2.42738694	0.85904265	0.75052748
H	2.70076263	0.35367483	-0.18761858
H	3.34609355	0.99062011	1.33674193
H	2.03926501	1.85962280	0.50053734
Fe	4.13060738	3.38504049	3.81651290
Cl	3.35663505	5.43251945	3.67989919
Cl	4.82105917	2.91912336	5.83893314
Cl	5.59481843	2.94506722	2.23707142

Structure 7 (Oxetane)
61
Step 2

N	-0.60605880	0.35814048	3.02842718
C	0.73936369	0.88366630	2.62526101
C	1.44322374	1.11541506	4.02274075
C	0.26161855	1.60269074	4.89930075
C	-1.03032142	1.30991622	4.09628382
H	0.20722045	1.15560716	5.89569212
H	-1.42786196	2.20241868	3.59203911
H	-1.82331562	0.87825704	4.71634789
O	2.07651474	2.50685720	4.09303633
C	0.90619898	3.01518447	4.93733777
C	1.47928388	0.21418809	1.45253433
H	2.01252533	-0.67450146	1.81170927
C	2.40519782	0.07123725	4.52543923
C	4.31390586	-1.77857436	5.49053976
C	2.17302646	-0.64543648	5.71440757
C	3.60228336	-0.16908251	3.81810035
C	4.55171889	-1.07711578	4.30044767
C	3.11718344	-1.56614871	6.18845115
H	1.24263466	-0.52586468	6.26290982
H	3.81216366	0.35423064	2.89118738
H	5.47826719	-1.22616373	3.74402839
H	2.91329918	-2.11322150	7.11055839
H	5.05349558	-2.48631139	5.86934920
S	-0.76573811	-1.30486411	3.54736916
O	0.20719665	-2.12052298	2.79805358
O	-0.83931556	-1.40467952	5.02574808
C	-2.44151349	-1.63316278	2.93181729
C	-4.96713873	-2.30835473	1.98042021

C	-2.84454802	-1.16990762	1.67091204
C	-3.28262076	-2.42662189	3.72665350
C	-4.55223112	-2.76362126	3.24361969
C	-4.11580591	-1.51311180	1.19571279
H	-2.18206018	-0.53551271	1.08632539
H	-2.95020244	-2.75964713	4.70915413
H	-5.22506120	-3.37055059	3.84926021
H	-4.44871237	-1.15547871	0.22220996
C	1.35622330	3.39863528	6.33971966
H	1.93528774	2.58552981	6.79796160
H	0.44981304	3.56901420	6.94417149
H	1.95541818	4.31781800	6.34007761
C	0.23647845	4.15699028	4.19387952
H	0.93101890	5.00653039	4.13752399
H	-0.66725673	4.46870738	4.74118152
H	-0.04755260	3.86320909	3.17451709
C	-6.32493634	-2.73376070	1.45746854
F	-6.28354306	-4.00907887	0.98119728
F	-6.76018123	-1.93627466	0.44584874
F	-7.26747124	-2.70387560	2.43960042
H	0.48583296	1.89632962	2.26429759
C	0.51682871	-0.20892945	0.32459759
H	1.10583952	-0.49666527	-0.56074354
H	-0.13273247	0.63480766	0.03544090
H	-0.10367282	-1.06552280	0.61129403
C	2.47595070	1.24350309	0.86718146
H	3.18679163	0.74092331	0.19461071
H	3.05173030	1.78358178	1.62869494
H	1.92695736	1.99941961	0.27960600
Fe	4.01773197	3.05580524	4.40455452
Cl	3.79555003	5.25229450	4.49666357
Cl	4.74363407	2.22344136	6.29178374
Cl	5.38543321	2.62182783	2.74159477

Structure 7 (TS-II)
61
Step 19

N	-0.90196890	0.03413279	2.96936554
C	0.52374233	0.50391937	2.77335712
C	1.07918034	0.45407435	4.23644017

C	0.01638661	0.77361861	5.02537691
C	-1.26245598	0.79063529	4.21349396
H	0.02928225	0.88746304	6.10699009
H	-1.55399429	1.80490683	3.87842856
H	-2.11968469	0.34707240	4.73711172
O	2.71900415	3.17936606	4.04570496
C	1.74457186	3.38098261	4.80998431
C	1.31256416	0.03471557	1.52545869
H	1.90565110	-0.85644971	1.77195149
C	2.39944198	0.04561815	4.73927191
C	4.88298907	-0.79642969	5.84458942
C	2.50776969	-0.36062746	6.09895471
C	3.57162182	-0.01244721	3.94960733
C	4.79374766	-0.42466896	4.49768163
C	3.72799045	-0.76617582	6.64332881
H	1.61136946	-0.40429161	6.71730511
H	3.55078253	0.26184571	2.90357585
H	5.67987927	-0.43333802	3.86269950
H	3.77422769	-1.07356036	7.68970021
H	5.83876303	-1.10816437	6.26811704
S	-1.09812178	-1.70876426	3.29289336
O	-0.15572308	-2.44730385	2.43003956
O	-1.15577278	-2.01346705	4.74210097
C	-2.78847290	-1.88299629	2.65147172
C	-5.36052443	-2.26079514	1.66534916
C	-3.11120558	-1.39154170	1.37738545
C	-3.72796043	-2.56339765	3.43866655
C	-5.02214127	-2.75125699	2.93728594
C	-4.40694751	-1.58359761	0.88504155
H	-2.36640848	-0.85376508	0.79359251
H	-3.44801153	-2.92866109	4.42617433
H	-5.77123658	-3.27014628	3.53503601
H	-4.68073891	-1.20122413	-0.09759917
C	1.90215708	3.24722172	6.29502610
H	2.42769112	2.30573851	6.51809353
H	0.93885697	3.29397529	6.81868096
H	2.55197612	4.06722384	6.64877593
C	0.46856659	3.91364903	4.22156355
H	0.51025113	5.01526391	4.31864488
H	-0.41112909	3.56004108	4.77290239

H	0.39631485	3.67169190	3.15346943
C	-6.74616719	-2.53243563	1.11483209
F	-6.81352286	-3.78154076	0.57496740
F	-7.09623087	-1.65042679	0.14049095
F	-7.69552751	-2.46505830	2.08876368
H	0.33629862	1.57618840	2.56524001
C	0.38603851	-0.28295984	0.33043909
H	0.99416598	-0.36988325	-0.58418140
H	-0.32923285	0.54338335	0.18150156
H	-0.16503237	-1.21882700	0.46669157
C	2.23188212	1.20608981	1.07867011
H	3.01988920	0.84414899	0.40120833
H	2.71198945	1.74161283	1.90837049
H	1.62808171	1.94846652	0.52850554
Fe	4.70881541	3.39912359	4.33726806
Cl	4.70792332	5.59974328	4.38328653
Cl	5.38670438	2.61394912	6.26147378
Cl	5.69891984	2.55341893	2.58438346

Structure 7 (Product)
61
Step 19

N	-0.90196890	0.03413279	2.96936554
C	0.52374233	0.50391937	2.77335712
C	1.07918034	0.45407435	4.23644017
C	0.01638661	0.77361861	5.02537691
C	-1.26245598	0.79063529	4.21349396
H	0.02928225	0.88746304	6.10699009
H	-1.55399429	1.80490683	3.87842856
H	-2.11968469	0.34707240	4.73711172
O	2.71900415	3.17936606	4.04570496
C	1.74457186	3.38098261	4.80998431
C	1.31256416	0.03471557	1.52545869
H	1.90565110	-0.85644971	1.77195149
C	2.39944198	0.04561815	4.73927191
C	4.88298907	-0.79642969	5.84458942
C	2.50776969	-0.36062746	6.09895471
C	3.57162182	-0.01244721	3.94960733
C	4.79374766	-0.42466896	4.49768163
C	3.72799045	-0.76617582	6.64332881

H	1.61136946	-0.40429161	6.71730511
H	3.55078253	0.26184571	2.90357585
H	5.67987927	-0.43333802	3.86269950
H	3.77422769	-1.07356036	7.68970021
H	5.83876303	-1.10816437	6.26811704
S	-1.09812178	-1.70876426	3.29289336
O	-0.15572308	-2.44730385	2.43003956
O	-1.15577278	-2.01346705	4.74210097
C	-2.78847290	-1.88299629	2.65147172
C	-5.36052443	-2.26079514	1.66534916
C	-3.11120558	-1.39154170	1.37738545
C	-3.72796043	-2.56339765	3.43866655
C	-5.02214127	-2.75125699	2.93728594
C	-4.40694751	-1.58359761	0.88504155
H	-2.36640848	-0.85376508	0.79359251
H	-3.44801153	-2.92866109	4.42617433
H	-5.77123658	-3.27014628	3.53503601
H	-4.68073891	-1.20122413	-0.09759917
C	1.90215708	3.24722172	6.29502610
H	2.42769112	2.30573851	6.51809353
H	0.93885697	3.29397529	6.81868096
H	2.55197612	4.06722384	6.64877593
C	0.46856659	3.91364903	4.22156355
H	0.51025113	5.01526391	4.31864488
H	-0.41112909	3.56004108	4.77290239
H	0.39631485	3.67169190	3.15346943
C	-6.74616719	-2.53243563	1.11483209
F	-6.81352286	-3.78154076	0.57496740
F	-7.09623087	-1.65042679	0.14049095
F	-7.69552751	-2.46505830	2.08876368
H	0.33629862	1.57618840	2.56524001
C	0.38603851	-0.28295984	0.33043909
H	0.99416598	-0.36988325	-0.58418140
H	-0.32923285	0.54338335	0.18150156
H	-0.16503237	-1.21882700	0.46669157
C	2.23188212	1.20608981	1.07867011
H	3.01988920	0.84414899	0.40120833
H	2.71198945	1.74161283	1.90837049
H	1.62808171	1.94846652	0.52850554
Fe	4.70881541	3.39912359	4.33726806

Cl	4.70792332	5.59974328	4.38328653
Cl	5.38670438	2.61394912	6.26147378
Cl	5.69891984	2.55341893	2.58438346

Structure 8 (Starting Material)
55
Step 86

C	-1.63861625	0.57794199	-3.74922098
C	-1.70443058	-0.78034699	-3.39397036
C	-2.09954168	-1.14136895	-2.10335035
C	-2.43191995	-0.12942062	-1.19255107
C	-2.42880307	1.22676986	-1.54876330
C	-2.02580243	1.57885817	-2.84267723
S	-2.80886039	-0.58861147	0.51159282
O	-3.51581214	0.53984016	1.15206482
N	-1.16859032	-0.73576186	1.14441548
O	-3.36355555	-1.95546506	0.53008350
C	-0.44028317	0.54271047	1.11245220
C	-1.17892915	-1.34810634	2.51027053
C	0.30835274	0.92232791	-0.15462062
C	1.41167083	-1.48116542	2.74240415
C	0.08038238	-2.20785607	2.77127018
O	0.57632062	2.15177789	-0.29613250
C	1.86282116	-0.60568737	3.66838831
C	3.19691030	0.08599658	3.50465276
C	1.08080254	-0.21295721	4.90101949
C	-1.12961077	0.99746381	-5.11250532
F	-0.55215015	-0.03218138	-5.78969265
F	-0.18614747	1.97944829	-4.99499961
F	-2.12867940	1.49364269	-5.88646072
C	0.83047524	-0.01328280	-1.15594382
C	0.95156818	-1.40303822	-0.90714585
C	1.49869781	-2.24022288	-1.88371091
C	1.90277119	-1.71388003	-3.12350377
C	1.77070641	-0.33947049	-3.38541210
C	1.24862065	0.50839321	-2.40704826
Fe	0.27955551	3.78392491	0.81624889
Cl	-1.89251167	4.07844892	0.86361305
Cl	1.34156154	5.34496955	-0.27136722
Cl	1.13546024	3.28959171	2.78039453

H	-1.41153353	-1.54566298	-4.11011454
H	-2.13250430	-2.18588334	-1.79744201
H	-2.71326998	1.98725348	-0.82269176
H	-1.97991047	2.62832064	-3.13394233
H	-1.07910923	1.39868956	1.39449821
H	0.35082980	0.48098730	1.88247595
H	-2.05511762	-2.00564322	2.57684405
H	-1.27591977	-0.56205441	3.27743881
H	2.05397607	-1.67474648	1.87705654
H	-0.07492490	-2.67273460	3.76063055
H	0.08682185	-3.02657069	2.03451447
H	3.05602613	1.17835639	3.43090057
H	3.83964795	-0.09429103	4.38461418
H	3.72832058	-0.26176010	2.60528037
H	1.72719481	-0.25030438	5.79466033
H	0.72958804	0.83049770	4.81176472
H	0.20601526	-0.85562672	5.07865149
H	0.61164197	-1.81217200	0.03900739
H	1.60229530	-3.30751743	-1.68201282
H	2.31453283	-2.37618643	-3.88758205
H	2.05671082	0.06885151	-4.35466492
H	1.13802716	1.57223329	-2.60486129

Structure 8 (TS-I)
52
Step 20

C	-2.16745564	-1.18129158	-3.45651079
C	-2.15986188	0.19732875	-3.19179867
C	-2.58625606	0.66747344	-1.94281389
C	-3.00664112	-0.25737382	-0.97204902
C	-3.07928629	-1.63319055	-1.25189959
C	-2.66064942	-2.09196022	-2.50537092
S	-3.17198019	0.29149772	0.74025162
O	-3.55064704	1.71294001	0.75364000
N	-1.54347581	0.22698353	1.27427645
O	-3.88803887	-0.74675762	1.50014318
C	-0.61400651	1.20741639	0.67414382
C	-0.92297602	-1.12468475	1.37102733
C	0.58877398	-0.84550288	1.33267008
C	0.77713056	0.68430717	1.09692208

C	1.40427836	-1.09483909	0.02515202
O	1.61582346	0.40748297	-0.09777230
C	2.76104167	-1.74576600	0.23611812
C	0.66176588	-1.61409319	-1.19149781
C	-1.51516542	-1.72416976	-4.71045618
F	-1.40961944	-0.79456618	-5.68932983
F	-2.19756294	-2.78895363	-5.21597955
F	-0.25342256	-2.16481872	-4.41954878
C	1.50126210	1.47946578	2.14692532
C	0.77234751	1.92882471	3.26476423
C	1.42771802	2.60716239	4.30049688
C	2.80941082	2.84870097	4.22176395
C	3.53325653	2.40384207	3.10542176
C	2.88520596	1.71158159	2.07219903
Fe	2.25304409	1.64698089	-1.52097123
Cl	4.41948816	1.31776139	-1.55713057
Cl	1.57001282	3.57590896	-0.76748278
Cl	1.24979873	1.07581632	-3.38583719
H	-1.79173069	0.89488262	-3.94142584
H	-2.57899423	1.73288398	-1.71539207
H	-3.44748896	-2.32065026	-0.49091387
H	-2.69052576	-3.15600359	-2.74008912
H	-0.82966715	2.21082186	1.05323688
H	-0.65765559	1.22075476	-0.42955306
H	-1.23988930	-1.59104977	2.31163763
H	-1.22876312	-1.78151534	0.53975376
H	1.11077168	-1.21665076	2.22140731
H	3.38870895	-1.61112648	-0.65695362
H	2.61990924	-2.82422657	0.41231995
H	3.27136908	-1.30427602	1.10388873
H	0.37943317	-2.66460079	-1.01877286
H	-0.24864993	-1.03702460	-1.38962449
H	1.29897722	-1.56923931	-2.08477361
H	-0.30181775	1.73989314	3.32131272
H	0.85730003	2.95317973	5.16433600
H	3.31758056	3.38574298	5.02480078
H	4.60471829	2.59771641	3.03127639
H	3.44711880	1.37750496	1.20048766

Structure 8 (Oxetane)

55
Step 4

C	-1.72456694	-0.69070279	-3.85637175
C	-2.09599149	-1.86091302	-3.17028070
C	-2.58743619	-1.77735895	-1.86520570
C	-2.71543505	-0.51228252	-1.27241092
C	-2.39086832	0.66404984	-1.96016379
C	-1.88659063	0.56870481	-3.26308867
S	-3.20312650	-0.41627030	0.46617129
O	-3.78548988	0.91897588	0.70469253
N	-1.63743835	-0.52567223	1.17433562
O	-3.91227872	-1.65683898	0.83475304
C	-0.87224524	0.72159451	1.26921887
C	-1.42605915	-1.39163378	2.34682741
C	0.61279131	0.33945911	1.04000286
C	1.07983298	-0.89202170	1.86187886
C	0.01998922	-1.93065263	2.28601356
O	1.48274055	1.22433320	1.90177836
C	1.74152057	0.08338102	2.87645963
C	3.24490709	-0.06047445	3.05330724
C	1.01255311	0.30355710	4.19513679
C	-1.16394794	-0.82644824	-5.25495936
F	-0.19547067	-1.79242422	-5.30347707
F	-0.60340708	0.32619364	-5.70960293
F	-2.12645784	-1.19230596	-6.14284595
C	0.97727412	0.36628094	-0.42314772
C	1.00268562	-0.83586273	-1.15245340
C	1.26484949	-0.82113835	-2.52918712
C	1.51895701	0.39262905	-3.18416608
C	1.48334284	1.59531478	-2.46170481
C	1.19320015	1.58381572	-1.09117754
Fe	1.89596700	3.17117586	2.03005011
Cl	0.02309620	4.16767774	1.46048651
Cl	3.56400134	3.57691652	0.67116161
Cl	2.48405742	3.57069874	4.10319256
H	-1.97715590	-2.83144582	-3.65244861
H	-2.86501888	-2.67084023	-1.30687765
H	-2.52971069	1.63489666	-1.48669654
H	-1.60087246	1.46832627	-3.80393448
H	-1.18798480	1.44449601	0.51021625

H	-1.01296752	1.19557513	2.25552598
H	-2.13658290	-2.22529835	2.30791999
H	-1.61046228	-0.82400148	3.27726220
H	1.87843193	-1.40782080	1.31250905
H	0.29198223	-2.37631267	3.25656697
H	0.03723853	-2.74116925	1.54141364
H	3.64696786	0.80825776	3.59575055
H	3.45873450	-0.96855982	3.64030962
H	3.74196421	-0.13951316	2.07566039
H	1.08997120	-0.61956477	4.79106479
H	1.47649252	1.12156262	4.76037910
H	-0.04874078	0.53357138	4.04529254
H	0.79420394	-1.77959185	-0.64651497
H	1.25725915	-1.75264233	-3.09450503
H	1.71624149	0.39986627	-4.25653645
H	1.67325559	2.54658679	-2.96140441
H	1.14528106	2.52232204	-0.54342927

Structure 8 (TS-II)
55
Step 91

C	-1.14445728	-1.39278457	-3.22024683
C	-1.42673944	-2.36289257	-2.24039806
C	-2.18472973	-2.01755194	-1.11884637
C	-2.64548915	-0.69733406	-0.98717021
C	-2.41991334	0.25810546	-1.98691216
C	-1.66561597	-0.09578142	-3.11201533
S	-3.48956916	-0.19519368	0.53940282
O	-4.12135057	1.10314161	0.25398668
N	-2.24765923	0.13012384	1.68306076
O	-4.23345013	-1.35506802	1.06071642
C	-1.22288486	1.10580715	1.26584763
C	-1.76091570	-0.93112942	2.57930844
C	-0.06928685	0.39932575	0.57657733
C	0.46961614	-0.82042584	1.27861533
C	-0.58272309	-1.71537934	1.97771863
O	2.03946718	0.93676527	1.52073962
C	1.60437957	-0.20385872	2.23967922
C	2.76684183	-1.20090682	2.36577828
C	1.10902871	0.18364151	3.64445324

C	-0.26168360	-1.79253619	-4.38298917
F	0.89716005	-2.36427695	-3.92655777
F	0.09085569	-0.73749395	-5.16155236
F	-0.87019981	-2.71098608	-5.17575609
C	0.42983558	0.85904808	-0.67895655
C	1.19648378	0.02246038	-1.54757356
C	1.74653273	0.53026953	-2.72002343
C	1.57325136	1.88712805	-3.04830679
C	0.82673770	2.73438892	-2.20794026
C	0.24075856	2.22832826	-1.05291183
Fe	2.61770608	2.65008227	1.89364512
Cl	0.72690831	3.82642243	2.27566992
Cl	3.58472322	3.38964700	0.03523428
Cl	3.96523868	2.60768553	3.64648481
H	-1.04469756	-3.37745262	-2.35617652
H	-2.43330455	-2.75973300	-0.36142555
H	-2.82014450	1.26483868	-1.87836936
H	-1.45806843	0.64304083	-3.88359093
H	-1.70183390	1.85508987	0.63010261
H	-0.85929614	1.64129549	2.15663493
H	-2.60173952	-1.59430411	2.81118944
H	-1.46261744	-0.42394956	3.50664097
H	1.02209059	-1.44196274	0.56511338
H	-0.07957356	-2.29827185	2.76442930
H	-0.96845268	-2.43616199	1.24186668
H	3.56389281	-0.73911789	2.96795266
H	2.44174363	-2.13216556	2.85824912
H	3.17014806	-1.43743924	1.36957358
H	0.73873576	-0.69368754	4.19626217
H	1.96745878	0.60224393	4.18956477
H	0.32931474	0.95483882	3.62670333
H	1.31801210	-1.03506959	-1.32947853
H	2.30222032	-0.12820899	-3.38544519
H	2.02694521	2.28603942	-3.95707146
H	0.72843439	3.79369809	-2.44348050
H	-0.26837236	2.91202704	-0.37642367

Structure 8 (Product)
55
Step 16

C	-1.33080327	-1.80846410	-3.12885738
C	-1.88940264	-2.70872168	-2.20250499
C	-2.68725842	-2.22810793	-1.15936787
C	-2.90806259	-0.84719599	-1.05175062
C	-2.39827937	0.05127340	-1.99901827
C	-1.59932049	-0.43457038	-3.03973391
S	-3.77032863	-0.18266074	0.40172685
O	-4.36780079	1.09534868	-0.02060450
N	-2.54438762	0.22532554	1.53923121
O	-4.55959137	-1.27024455	1.01115293
C	-1.44542901	1.05418437	1.01212960
C	-2.06435170	-0.82594411	2.45339463
C	-0.29836445	0.22589144	0.41911734
C	-0.13058447	-1.05778052	0.82622184
C	-1.03951972	-1.77240857	1.79153153
O	2.62545998	1.47510556	1.72080568
C	2.38106686	0.33160330	2.17298559
C	3.01056935	-0.83455343	1.46208219
C	1.63173965	0.14970022	3.46139509
C	-0.35194663	-2.32820141	-4.15713658
F	0.88445917	-2.51954475	-3.58781976
F	-0.17949019	-1.47237632	-5.19575229
F	-0.73404508	-3.53040567	-4.66432051
C	0.55367040	0.85528864	-0.61032318
C	1.22270880	0.07404413	-1.58244407
C	2.01553715	0.67229545	-2.56714946
C	2.16537806	2.06963763	-2.59941963
C	1.50211611	2.85939761	-1.64788378
C	0.69656303	2.26027219	-0.66902377
Fe	2.50424733	3.29753072	2.54272324
Cl	0.37988970	3.69118509	2.94944838
Cl	3.38796325	4.68908306	1.12299328
Cl	3.66728562	2.98102530	4.37323951
H	-1.69763168	-3.77717580	-2.30296598
H	-3.13465452	-2.90675278	-0.43378428
H	-2.61379081	1.11509452	-1.91479801
H	-1.16500509	0.25406435	-3.76204475
H	-1.85111851	1.74916985	0.26624298
H	-1.08692134	1.67839168	1.84620014
H	-2.92823302	-1.37543467	2.84272611

H	-1.59291818	-0.28525599	3.29000262
H	0.66173883	-1.65996964	0.37871395
H	-0.45124668	-2.28811078	2.57285899
H	-1.57121419	-2.57100549	1.24364898
H	4.09424176	-0.80455865	1.67380359
H	2.60192617	-1.79494252	1.79804314
H	2.88556733	-0.70748452	0.37621299
H	1.18346919	-0.84817809	3.53551674
H	2.36401044	0.27524294	4.28128372
H	0.87533338	0.93633720	3.58638080
H	1.07073357	-1.00305113	-1.60349282
H	2.49087033	0.04389965	-3.32277745
H	2.78501770	2.53938845	-3.36536195
H	1.61696343	3.94396236	-1.65681408
H	0.19304188	2.88976786	0.06575224

Structure 9 (Starting Material)
58
Step 2

S	-1.59399894	1.07600485	0.96958200
N	-0.16077375	0.28381861	1.44655638
C	-0.44481292	-2.03034994	2.27580796
C	2.09337423	0.49187095	2.64483335
C	1.66609510	-0.50006340	3.71084514
C	0.98831129	1.16031809	1.77354890
C	0.08817161	-1.13112170	1.14562495
O	-1.75559099	2.22455103	1.87718420
O	-2.63318982	0.05013484	0.79229249
C	-1.20964089	1.75768517	-0.66722627
C	-0.50190580	2.74614890	-3.17335625
C	-1.65729148	1.09166986	-1.81903913
C	-0.43916851	2.92736585	-0.75322658
C	-0.07733835	3.41656205	-2.01538262
C	-1.30043547	1.59230905	-3.07573014
C	-0.06239120	3.21410384	-4.54543594
F	-1.07758998	3.14173539	-5.44883487
F	0.39360115	4.49453891	-4.53771969
F	0.94719422	2.42641609	-5.01735682
H	1.17675033	-1.22727543	1.10797361
C	0.18117289	-3.33454663	2.54950933

C	1.31559134	-5.85019477	3.12881993
C	-0.45349844	-4.22059203	3.45280230
C	1.39616589	-3.73534685	1.93664234
C	1.95564005	-4.98199020	2.22546345
C	0.11055278	-5.46608902	3.73943572
H	2.80688951	-0.01960996	1.97859025
H	2.66199323	1.33016368	3.08831719
C	-0.43660334	-1.69284306	-0.20499732
H	-2.28665610	0.20781362	-1.72385985
H	-0.15036911	3.45981146	0.15185823
H	0.52023687	4.32341963	-2.09898837
H	-1.64826145	1.09658451	-3.98215028
H	1.75668262	-6.82320720	3.35283437
H	-1.38607998	-3.92490546	3.92550156
H	1.91346255	-3.08008015	1.23723759
H	2.89129494	-5.27857677	1.74905669
H	-0.39380425	-6.13547183	4.43736692
O	-1.49523212	-1.67167188	2.85959995
C	0.67879930	-0.37038771	4.62717488
H	2.24572377	-1.42722404	3.73244159
C	-0.22077681	0.83706258	4.73796883
C	0.36703111	-1.50094821	5.57597069
H	1.03704112	-2.36175561	5.43187636
H	-0.67351662	-1.84061882	5.43138829
H	0.44010356	-1.16203310	6.62391635
H	-1.10693370	0.71869390	4.09257742
H	0.28394917	1.76546368	4.43519038
H	-0.58145577	0.95911216	5.77114851
Fe	-3.37654536	-1.96019267	3.35967929
Cl	-4.43610228	-0.08246107	3.65155170
Cl	-4.05599023	-3.28023156	1.74482576
Cl	-3.36384335	-3.02412887	5.31142536
H	0.57543663	2.02258158	2.30573056
H	1.46541166	1.53327668	0.84632308
H	-0.15732384	-1.00102982	-1.01173780
H	-1.52442521	-1.82155401	-0.19505035
H	0.03719517	-2.66785420	-0.38634659

Structure 9 (TS-I)
58

Step 61

S	-1.16884913	1.60094072	1.17836668
N	0.09587650	0.56303582	1.62328174
C	0.04505489	-1.69428456	2.65403681
C	1.96431106	0.17564930	3.18569925
C	0.97647349	-0.83059385	3.81338540
C	1.37919941	1.10518118	2.07860524
C	0.17881117	-0.87584781	1.31283964
O	-0.86825904	2.88697286	1.84229937
O	-2.43413154	0.88928738	1.40434831
C	-0.98941379	1.86582086	-0.60232330
C	-0.67252896	2.26438780	-3.33545147
C	-1.94448170	1.34153225	-1.48278623
C	0.11652828	2.59775684	-1.06369968
C	0.27503362	2.79198802	-2.43861325
C	-1.77925243	1.54331714	-2.86014952
C	-0.44097113	2.43742871	-4.82286371
F	-1.56857389	2.23247455	-5.55094814
F	0.01771247	3.68611578	-5.11388353
F	0.49876665	1.55507796	-5.26761459
H	1.19654028	-1.03917377	0.92165686
C	0.64364640	-3.08656867	2.48560826
C	1.74295323	-5.66374038	2.11298081
C	-0.13040050	-4.23670982	2.72692780
C	1.98279971	-3.24662413	2.06119097
C	2.52832079	-4.52178013	1.87745410
C	0.41494603	-5.51499373	2.53698128
H	2.77946115	-0.42332816	2.75742485
H	2.41511101	0.79087155	3.98021439
C	-0.79208807	-1.42637844	0.26186241
H	-2.79625794	0.78643029	-1.09129227
H	0.82605258	3.02485870	-0.35479803
H	1.12195948	3.36354262	-2.81836099
H	-2.51330868	1.14678316	-3.56062046
H	2.16747710	-6.65898195	1.96767459
H	-1.15622525	-4.13704737	3.06717945
H	2.60840856	-2.37295209	1.87205183
H	3.56426227	-4.62536301	1.54832520
H	-0.20641982	-6.39183312	2.72604773
O	-1.25288805	-1.68722375	3.09357386

C	-0.06503847	-0.33551448	4.71808996
H	1.54502357	-1.60964731	4.33768340
C	-0.69077974	0.98628751	4.63471628
C	-0.55971868	-1.23575662	5.78329924
H	-0.30067965	-2.28785071	5.61631249
H	-1.64831780	-1.11926839	5.91322268
H	-0.08996243	-0.89476394	6.72932908
H	-0.14107623	1.73623911	4.06245250
H	-0.98541665	1.35002853	5.63174061
H	-1.66403965	0.80091450	4.11655017
Fe	-3.00272033	-2.13634061	3.42101566
Cl	-3.93891798	-0.32681040	4.36536243
Cl	-4.00676328	-2.87183166	1.59880030
Cl	-2.98053237	-3.72058293	5.00974411
H	1.22591848	2.12082059	2.45656727
H	2.09625106	1.15920746	1.23605942
H	-0.64674069	-0.89812857	-0.69019809
H	-1.83441462	-1.34090528	0.57929298
H	-0.55969578	-2.48974655	0.11477886

Structure 9 (Oxetane)
58
Step 37

S	-1.08716705	1.50672907	1.17645932
N	0.36924616	0.69836712	1.51610678
C	0.36184961	-1.50963233	2.65480648
C	1.97498377	0.40150346	3.43375430
C	1.10157254	-0.79919809	3.82458711
C	1.40214861	1.35567659	2.34368607
C	0.54275446	-0.75148458	1.30842240
O	-0.96986961	2.84040992	1.80118368
O	-2.24256063	0.63403590	1.45981059
C	-1.03446658	1.73480552	-0.61796091
C	-0.93304845	2.09601107	-3.37022857
C	-2.02806023	1.15511147	-1.41646860
C	0.00307580	2.50350875	-1.16746453
C	0.05231016	2.68111338	-2.55257164
C	-1.96971278	1.33705424	-2.80526775
C	-0.81426250	2.23666217	-4.87412770
F	-1.99775685	2.03374883	-5.50878203

F	-0.36332950	3.47161459	-5.22775787
F	0.07553042	1.33062048	-5.37173741
H	1.62011078	-0.87944713	1.09527431
C	0.66078662	-2.98399273	2.50205623
C	1.34196616	-5.68372022	2.06726112
C	-0.33747325	-3.93060768	2.22223713
C	2.00702395	-3.39734452	2.54726244
C	2.34731280	-4.73909529	2.32670232
C	0.00039176	-5.27548515	2.01778096
H	2.92915827	-0.01325554	3.07226214
H	2.21451314	0.98933961	4.33355155
C	-0.20597282	-1.33782524	0.10429115
H	-2.81916436	0.56411871	-0.95664386
H	0.75335608	2.95980407	-0.52134477
H	0.84481061	3.27868020	-3.00281721
H	-2.73107720	0.89176875	-3.44452291
H	1.60370652	-6.73123619	1.90668681
H	-1.37907427	-3.62964666	2.17048068
H	2.79210114	-2.66692197	2.75647757
H	3.39422624	-5.04620048	2.36663751
H	-0.79129624	-5.99946979	1.81973237
O	-0.95631952	-1.21404216	3.30054386
C	-0.26945029	-0.61635674	4.52724518
H	1.72824722	-1.50040844	4.39027023
C	-0.75024077	0.79347338	4.83301895
C	-0.45569913	-1.55503779	5.71260862
H	-0.15554352	-2.57975875	5.45401198
H	-1.50230193	-1.56716142	6.04600913
H	0.17441706	-1.19344116	6.54197462
H	-0.77749019	1.43802491	3.95041116
H	-0.05368333	1.22989097	5.56818948
H	-1.75146564	0.77411597	5.28201897
Fe	-2.92969618	-1.69355659	3.16723053
Cl	-4.13021258	-0.14450591	4.13680175
Cl	-3.64274446	-2.30184831	1.17512732
Cl	-3.08368087	-3.49497063	4.45156765
H	0.96037006	2.24435410	2.80345096
H	2.22883890	1.69240323	1.69218814
H	0.05465791	-0.76823833	-0.79743776
H	-1.29201624	-1.32324043	0.23534512

H	0.11281023	-2.37942423	-0.03123015

Structure 9 (TS-II)
58
Step 10

S	-1.50926226	2.41968898	0.68297943
N	-0.73690840	1.30276015	1.78481579
C	0.17883966	-0.96530623	2.19653408
C	0.96059545	1.03917726	3.53579792
C	0.59337025	-0.47268435	3.54098153
C	0.62354979	1.72051377	2.20176195
C	-0.74172468	-0.12131689	1.35185756
O	-1.09406122	3.76536362	1.11144880
O	-2.92475498	2.04010837	0.57904549
C	-0.70067952	2.04067151	-0.88976020
C	0.69909486	1.23017037	-3.15484699
C	-1.27984108	1.09505702	-1.75215173
C	0.56324666	2.59339844	-1.14961965
C	1.26367662	2.18414562	-2.29138635
C	-0.57289510	0.69254300	-2.89209535
C	1.48778958	0.71122505	-4.34165032
F	0.68424434	0.45658737	-5.40766832
F	2.44563024	1.58642435	-4.74182118
F	2.11221929	-0.45890159	-4.01937821
H	-0.35334466	-0.16914761	0.31713991
C	0.59303108	-2.24298330	1.69632768
C	1.15229519	-4.88222721	0.83533652
C	1.08844252	-3.23307822	2.60596567
C	0.42154837	-2.62636531	0.32439118
C	0.70646128	-3.91881820	-0.09409618
C	1.33975638	-4.53561009	2.18268121
H	2.04119224	1.14844279	3.71285124
H	0.43646248	1.55808914	4.34663344
C	-2.15705075	-0.78501622	1.33618125
H	-2.27046493	0.69734376	-1.53481637
H	0.97699624	3.34620966	-0.47957773
H	2.24199493	2.60761404	-2.51565230
H	-1.00941421	-0.03049560	-3.58105351
H	1.35088988	-5.90239763	0.50269264
H	1.18876548	-3.01182766	3.66343202

H	0.08486991	-1.90399824	-0.41737151
H	0.57711910	-4.19083533	-1.14211565
H	1.64050865	-5.28174818	2.91660300
O	-1.19440657	-2.02247365	3.95420233
C	-0.61367956	-0.90814064	4.56938815
H	1.46607716	-1.04074113	3.87611868
C	-1.67130479	0.19894467	4.76368970
C	0.00267007	-1.27754021	5.92712546
H	0.66126435	-2.15297831	5.83234629
H	-0.81287678	-1.53658157	6.62004925
H	0.56743263	-0.43018881	6.34990516
H	-1.98603347	0.65777301	3.81999006
H	-1.30295279	0.99282931	5.43176791
H	-2.53433902	-0.28131906	5.24849880
Fe	-1.90752552	-3.65650325	4.42503746
Cl	-3.53223132	-3.28279767	5.88561761
Cl	-2.60086300	-4.52067662	2.48042850
Cl	-0.26854321	-4.91617363	5.31695344
H	0.64189098	2.80791478	2.32436178
H	1.36403398	1.43836466	1.42255987
H	-2.77114993	-0.30753332	0.56595827
H	-2.63592265	-0.67465573	2.31252720
H	-2.05555523	-1.85778322	1.13447830

Structure 9 (Product)
58
Step 46

S	-1.15063674	2.18973353	1.16371976
N	-0.04799347	1.08840350	1.94710569
C	1.04598834	-1.12313824	2.21978705
C	1.85576089	0.91523101	3.44886420
C	1.80494113	-0.56670895	3.19107507
C	1.28446939	1.66908425	2.24400427
C	0.06311039	-0.29371056	1.36754743
O	-0.74010685	3.54805042	1.57030523
O	-2.51540759	1.70458195	1.42270079
C	-0.79125347	1.99708301	-0.60200196
C	-0.11556949	1.56530953	-3.26624933
C	-1.66613182	1.27036689	-1.42049513
C	0.41040715	2.52890756	-1.09962205

C	0.74721422	2.30675641	-2.43849954
C	-1.32224818	1.05457458	-2.76211536
C	0.30803201	1.28098928	-4.69364382
F	-0.73791894	0.92039279	-5.48085969
F	0.89935113	2.36668774	-5.26300896
F	1.21818981	0.26638227	-4.73249415
H	0.49225313	-0.21043908	0.34776501
C	1.16864040	-2.57200366	1.90958875
C	1.45185146	-5.32705055	1.32347630
C	1.30676645	-3.52268204	2.94438380
C	1.17214658	-3.03153140	0.57409238
C	1.31289610	-4.39420902	0.28420887
C	1.45027209	-4.88522969	2.65536654
H	2.90049500	1.23200502	3.61063648
H	1.29576119	1.20525532	4.35755590
C	-1.30281772	-0.99896840	1.25768643
H	-2.60447662	0.89493826	-1.01445872
H	1.05424878	3.12575205	-0.45445790
H	1.67032871	2.71740733	-2.84760380
H	-1.99309320	0.49538845	-3.41308654
H	1.54607465	-6.39060681	1.09782762
H	1.27355209	-3.18667881	3.98212349
H	1.06476043	-2.31526192	-0.24252192
H	1.30946075	-4.72796644	-0.75520361
H	1.53712413	-5.60482665	3.47172897
O	-1.69879290	-2.25047550	4.46226324
C	-1.37867882	-1.15871647	4.97944117
H	2.48681251	-1.20850015	3.75371911
C	-2.09555530	0.12086452	4.68765787
C	-0.21787061	-1.13802297	5.93740639
H	0.37556922	-2.05546724	5.85063872
H	-0.63367383	-1.06826833	6.95908311
H	0.40459568	-0.24628895	5.77784049
H	-1.57976174	0.59823602	3.82932302
H	-2.03037271	0.81311138	5.53981049
H	-3.13710028	-0.05324514	4.38861473
Fe	-3.25708118	-3.16796892	3.56795823
Cl	-4.64725682	-1.69653220	2.72827554
Cl	-2.40716442	-4.50353315	2.06903155
Cl	-4.11309111	-4.18615201	5.30613002

H	1.17162966	2.73423390	2.46667842
H	1.96026044	1.54688730	1.37502471
H	-1.94338100	-0.53412700	0.50395692
H	-1.83975584	-0.95685946	2.20932269
H	-1.15729425	-2.04927956	0.98422001

Structure 10 (Starting Material)
64
Step 21

S	-0.46635003	1.42036113	1.80753369
N	0.68501857	0.13645217	1.71440692
C	-0.05272236	-2.05243621	2.68076757
C	3.23363952	-0.11571549	2.09351816
C	2.92042786	-1.14866604	3.15307863
C	2.04347549	0.52599057	1.29112522
C	0.15208614	-1.19735372	1.40174743
C	-0.79605461	1.83738696	0.07643047
C	-1.18663632	2.25230844	-2.64806670
C	-1.97517174	1.37425076	-0.52594186
C	0.17397254	2.53996238	-0.65762244
C	-0.02134775	2.73773650	-2.02825326
C	-2.16849120	1.58707148	-1.89665690
O	-1.70678306	0.84765862	2.35626337
O	0.22889140	2.56128740	2.42709056
C	-1.34208766	2.38665818	-4.14910821
F	-0.73342104	1.34462489	-4.78551267
F	-0.77399114	3.53060762	-4.61705936
F	-2.64564855	2.38675430	-4.53348595
C	0.66814919	-1.95665272	0.13685570
C	0.23738558	-1.21901629	-1.14592659
C	2.15105241	-2.37195966	0.05069970
C	-0.05623366	-3.54054392	2.61867537
C	-0.23228762	-6.33895888	2.49440532
C	-1.31975720	-4.16735315	2.55805421
C	1.11550520	-4.31898451	2.63161173
C	1.02234251	-5.71494854	2.58556458
C	-1.40067628	-5.56286739	2.47767759
H	3.92290778	-0.56261429	1.36378450
H	3.77675122	0.71538497	2.57151065
H	2.16242764	0.33307041	0.21524165

H	2.10500910	1.60894845	1.43357060
H	-0.92264294	-1.05406265	1.16771050
H	-2.72602379	0.86238711	0.07516259
H	1.05863415	2.93499689	-0.16100329
H	0.72041806	3.27840384	-2.61549010
H	-3.08004551	1.23954348	-2.38203058
H	0.09095967	-2.89394770	0.16868243
H	0.51919692	-1.81594749	-2.02732039
H	-0.85077446	-1.06003451	-1.16838600
H	0.71487280	-0.23229474	-1.23817677
H	2.54903815	-2.71050935	1.01201086
H	2.79011132	-1.55817713	-0.31741837
H	2.23613903	-3.20303476	-0.66618636
H	-0.29825783	-7.42742914	2.45210609
H	-2.22880636	-3.56575243	2.57550929
H	2.08486044	-3.83858131	2.73269613
H	1.93231601	-6.31577147	2.62764585
H	-2.38065188	-6.03934802	2.42581819
O	-0.55070422	-1.47421850	3.67046406
C	2.34861336	-0.89164481	4.35221562
H	3.30453446	-2.15659306	2.97576690
C	2.18463300	-1.97671658	5.38497985
C	1.82875762	0.46389274	4.74990193
H	2.59977992	-2.93989263	5.05163318
H	1.12121503	-2.12766909	5.62834744
H	2.67397662	-1.68522758	6.33008704
H	2.07399220	1.25228882	4.02746259
H	2.21821314	0.74432695	5.74357738
H	0.73176325	0.42989356	4.84233139
Fe	-1.65755268	-2.00737531	5.26522703
Cl	-1.00714458	-3.95668842	6.02455347
Cl	-3.68814197	-2.06279320	4.42910104
Cl	-1.33747883	-0.40401788	6.71155336

Structure 10 (TS-I)
64
Step 3

S	-0.61608172	1.24354184	1.61530428
N	0.52638226	-0.00973620	1.47730931
C	0.56213661	-2.05949757	2.86590680

C	2.85408253	-0.63759503	2.10581947
C	2.19349335	-1.45661034	3.23251530
C	1.93764344	0.33833291	1.31723833
C	0.13613088	-1.41954311	1.47151588
C	-0.80494999	1.84481719	-0.08099340
C	-1.01858171	2.62162854	-2.74409228
C	-1.96023680	1.51228706	-0.79995726
C	0.23977641	2.57766552	-0.66738607
C	0.13174095	2.96049399	-2.00800775
C	-2.06491691	1.90661880	-2.14000432
O	-1.89429306	0.64169307	2.02277408
O	0.03559889	2.32429851	2.38501860
C	-1.08026713	2.98859156	-4.21270824
F	-0.33727732	2.12039543	-4.95835016
F	-0.57793764	4.23394194	-4.43935603
F	-2.34797106	2.96176664	-4.69983853
C	0.39581194	-2.20382963	0.14744952
C	-0.31523414	-1.47259206	-1.00721181
C	1.83931734	-2.53980838	-0.26943674
C	0.53732392	-3.59022813	2.81119291
C	0.19934390	-6.39377524	2.54626090
C	-0.74688040	-4.17772864	2.86174050
C	1.64261010	-4.43527580	2.59947785
C	1.47831102	-5.82351765	2.47904084
C	-0.91425836	-5.56032995	2.72774167
H	3.29917636	-1.35614811	1.41171335
H	3.69131588	-0.06187623	2.53032111
H	2.22614871	0.33415807	0.25097533
H	2.07522496	1.35950791	1.69007731
H	-0.95565039	-1.43259013	1.58277018
H	-2.75747440	0.95400308	-0.31115616
H	1.11077895	2.86078525	-0.07719179
H	0.92854347	3.53325723	-2.48240594
H	-2.95740964	1.65930071	-2.71301057
H	-0.11556841	-3.16541167	0.30705241
H	-0.22108140	-2.05311565	-1.93843834
H	-1.38660004	-1.33113612	-0.79720844
H	0.13307591	-0.48127767	-1.17187461
H	2.38818888	-3.06588581	0.52195035
H	2.40328963	-1.64317434	-0.57039508

H	1.80402256	-3.20934386	-1.14328810
H	0.07356577	-7.47453722	2.46086065
H	-1.62642265	-3.54921801	2.99102737
H	2.65491016	-4.03729096	2.51717972
H	2.35644711	-6.45593188	2.33482493
H	-1.91979859	-5.98031008	2.78191454
O	-0.29529416	-1.55388428	3.79907128
C	2.00090481	-0.81459295	4.51527922
H	2.76359951	-2.37468074	3.40378136
C	1.95118257	-1.65176271	5.73111091
C	1.70443490	0.60981491	4.65959613
H	1.84354692	-2.72137333	5.51281679
H	1.14707805	-1.30816955	6.40434922
H	2.90154055	-1.48824286	6.27990269
H	2.04212458	1.24235938	3.83486079
H	1.98367750	1.00395028	5.64688931
H	0.58621323	0.62353198	4.64575303
Fe	-1.51153883	-1.87393835	5.15949950
Cl	-0.85726477	-3.64927812	6.33454454
Cl	-3.54454454	-2.14335650	4.32923792
Cl	-1.32473242	-0.04305797	6.44804045

Structure 10 (Oxetane)
64
Step 4

S	-0.61990984	1.27870558	1.58704095
N	0.55054965	0.05218049	1.50056245
C	0.81593142	-2.07876972	2.68620111
C	2.89928719	-0.52897672	2.15539051
C	2.21198586	-1.52614345	3.10360431
C	1.96292503	0.43204802	1.36579860
C	0.17518878	-1.36943629	1.46102087
C	-0.85334302	1.83162080	-0.11986289
C	-1.14434101	2.58825777	-2.78060131
C	-2.03339779	1.50354971	-0.79842991
C	0.17817523	2.55231764	-0.74424772
C	0.03153056	2.92363608	-2.08394227
C	-2.17694567	1.88723539	-2.13846383
O	-1.87659197	0.65643140	2.03470015
O	0.00242358	2.41301187	2.29962859

C	-1.24791770	2.94953629	-4.24808305
F	-0.51023534	2.09036146	-5.00910727
F	-0.76872917	4.20127688	-4.48956459
F	-2.52644634	2.90405237	-4.70512273
C	0.44001859	-2.10355086	0.10705804
C	-0.18722126	-1.33698774	-1.06580028
C	1.90594101	-2.46454124	-0.20556974
C	0.57350753	-3.57791613	2.71026409
C	-0.01718690	-6.34413149	2.81351826
C	-0.73104172	-4.05265943	2.45450467
C	1.57781549	-4.51766605	3.00758558
C	1.28539076	-5.88870557	3.05757698
C	-1.02633106	-5.41855312	2.51080456
H	3.49959042	-1.10784668	1.44272238
H	3.60750974	0.07026334	2.74826847
H	2.25411412	0.44874084	0.30036466
H	2.06736862	1.44890509	1.75904299
H	-0.90876707	-1.39884473	1.62831820
H	-2.82097074	0.95877528	-0.27907983
H	1.06868578	2.83470501	-0.18358945
H	0.81695102	3.48646402	-2.58821233
H	-3.08959142	1.64432660	-2.68075416
H	-0.09645481	-3.05786509	0.20875969
H	-0.06866911	-1.91597490	-1.99538880
H	-1.26167717	-1.16130322	-0.90606601
H	0.29858069	-0.36075104	-1.20806927
H	2.38668469	-2.98775743	0.63396407
H	2.50436974	-1.57717011	-0.46254203
H	1.92837234	-3.13909391	-1.07571190
H	-0.24498751	-7.41035193	2.86242572
H	-1.53099717	-3.35355976	2.22021522
H	2.60090979	-4.20161792	3.20541579
H	2.08041054	-6.59825861	3.29376999
H	-2.04830062	-5.75377273	2.32841876
O	0.21238223	-1.44602372	3.93579905
C	1.57990231	-1.01009213	4.42750441
H	2.94226048	-2.31252431	3.31868924
C	1.97607546	-1.83859013	5.64529180
C	1.60283565	0.48027079	4.71629677
H	1.89910644	-2.91459541	5.43972983

H	1.33371839	-1.59292656	6.50257474
H	3.01795866	-1.59374396	5.90961865
H	1.17197368	1.07321136	3.90360880
H	2.65125064	0.78492605	4.87158480
H	1.04198104	0.68869217	5.63706225
Fe	-1.35211509	-2.00729492	5.07491608
Cl	-0.90215492	-3.97100342	5.94397583
Cl	-3.19962957	-2.00355192	3.89521842
Cl	-1.38204919	-0.46057000	6.63157305

Structure 10 (TS-II)
64
Step 6

S	-0.80083593	1.02943187	1.42807618
N	0.48047649	-0.09699220	1.35397038
C	1.06164507	-2.28343036	2.34232514
C	2.83221044	-0.50538612	2.08904270
C	2.16128477	-1.57225191	2.96789001
C	1.85412314	0.42367118	1.33030544
C	0.19812355	-1.53272911	1.36963727
C	-0.86173826	1.75226458	-0.23438299
C	-0.94677575	2.80574786	-2.81055303
C	-1.98979654	1.52190585	-1.03302532
C	0.21337667	2.53061464	-0.69477011
C	0.17254464	3.04706095	-1.99381315
C	-2.03003553	2.05496361	-2.32782926
O	-2.04045023	0.26111058	1.62318919
O	-0.38178994	2.12124343	2.32682656
C	-0.93722944	3.32284117	-4.23451488
F	-0.16406142	2.52806227	-5.02925589
F	-0.41947492	4.57994708	-4.30611784
F	-2.18088774	3.35648518	-4.78001396
C	0.30614382	-2.24191022	-0.04465823
C	-0.57557985	-1.51549209	-1.06569722
C	1.75022239	-2.37888642	-0.56136367
C	0.76086811	-3.65794649	2.64052861
C	0.15516251	-6.33752189	3.28925397
C	-0.57889745	-4.14316733	2.56818204
C	1.78698808	-4.55927725	3.05246960
C	1.48640002	-5.88512120	3.35473455

C	-0.87370070	-5.46213811	2.90299865
H	3.46733036	-1.03718001	1.36425883
H	3.49961528	0.10242656	2.71480475
H	2.19809532	0.56473277	0.28963538
H	1.84074651	1.40618881	1.81457898
H	-0.84680391	-1.63358225	1.69458436
H	-2.81787953	0.93260339	-0.64198533
H	1.05815855	2.74643574	-0.04301661
H	0.99721064	3.65289769	-2.36947990
H	-2.90126701	1.88991758	-2.96066766
H	-0.09719611	-3.25294044	0.12128300
H	-0.66798717	-2.12619081	-1.97784893
H	-1.57893372	-1.32413425	-0.66025756
H	-0.12903401	-0.55100973	-1.34358440
H	2.39142866	-2.92474303	0.14991605
H	2.19897901	-1.39210457	-0.74948948
H	1.75042623	-2.93108250	-1.51375640
H	-0.08015731	-7.36879873	3.55728684
H	-1.39883955	-3.46489378	2.34383861
H	2.82348076	-4.22581536	3.08218010
H	2.28296932	-6.56884756	3.65069044
H	-1.91086435	-5.79624697	2.89853388
O	-0.02583767	-1.22343253	4.24055691
C	1.33038577	-1.01564906	4.41573685
H	2.93423520	-2.23428664	3.36837084
C	1.92337313	-1.88813695	5.53058413
C	1.61629315	0.46696522	4.65241682
H	1.73336293	-2.95389218	5.34776172
H	1.42381218	-1.61775339	6.47394333
H	3.00545547	-1.70761578	5.63425859
H	1.16038567	1.09491732	3.87983270
H	2.69459053	0.67230527	4.74322519
H	1.12805456	0.71734767	5.60831540
Fe	-1.38397205	-1.88855894	5.32173737
Cl	-0.83523853	-3.92830615	6.07956588
Cl	-3.15903203	-2.12365390	3.98564444
Cl	-1.61793521	-0.47579006	7.01346612

Structure 10 (Product)
64
Step 3

S	-0.13970670	1.01908923	1.33504006
N	0.78715115	-0.28985459	0.74065930
C	1.53883855	-2.24985371	2.10930025
C	3.04168593	-0.23336839	1.79486522
C	2.66464863	-1.55503928	2.41235453
C	2.21741977	0.01320356	0.52455384
C	0.46613842	-1.67498693	1.18117669
C	-0.49614914	1.90627150	-0.20160487
C	-1.01377370	3.21728970	-2.59932508
C	-1.61605319	1.52906778	-0.95856594
C	0.35440764	2.94276976	-0.61213136
C	0.09460239	3.59538996	-1.82354378
C	-1.87086191	2.19074964	-2.16491651
O	-1.40850863	0.48101011	1.85803295
O	0.70987600	1.92214024	2.15287677
C	-1.24909393	3.87951912	-3.94147014
F	-0.59305767	3.21111646	-4.93276656
F	-0.79859922	5.16359565	-3.95938580
F	-2.56687081	3.90105215	-4.27703138
C	0.15213858	-2.60063167	-0.03640468
C	-1.06457748	-2.06792044	-0.80873407
C	1.34585122	-2.82985304	-0.97789957
C	1.29448890	-3.59623127	2.68808110
C	0.85117618	-6.10713816	3.93480463
C	-0.01329191	-4.04838390	2.97512947
C	2.37461557	-4.45299848	3.00622445
C	2.15664726	-5.68828379	3.62786649
C	-0.23375228	-5.28332170	3.59933289
H	4.11831194	-0.23072234	1.54804354
H	2.87643222	0.59414446	2.50435388
H	2.56530351	-0.64561955	-0.28039868
H	2.31647235	1.04855526	0.17326921
H	-0.47007509	-1.61069371	1.75232499
H	-2.27711034	0.74277783	-0.59820174
H	1.18646439	3.25004309	0.02055766
H	0.73978023	4.40729476	-2.15806976
H	-2.73981347	1.91744110	-2.76267910

H	-0.11693634	-3.57112524	0.40807848
H	-1.31735681	-2.74361853	-1.64169401
H	-1.94375667	-1.97665520	-0.15237719
H	-0.83376075	-1.07642220	-1.22806881
H	2.25659149	-3.10449690	-0.42219638
H	1.55101616	-1.92808712	-1.57691152
H	1.11394766	-3.64477727	-1.68131611
H	0.68224684	-7.06984190	4.42086740
H	-0.87095055	-3.42297405	2.73969880
H	3.39055324	-4.15040813	2.74616746
H	3.00729503	-6.33189701	3.86248348
H	-1.25474359	-5.58240884	3.83815127
O	-0.44835872	-1.01643276	4.35556804
C	0.65509877	-1.06896437	4.94551673
H	3.36503912	-1.98228772	3.13492365
C	1.06481968	-2.26943842	5.74982929
C	1.51608677	0.16151777	4.96571635
H	0.69015003	-3.19495129	5.29815346
H	0.59405366	-2.17717809	6.74545513
H	2.15398179	-2.30377897	5.88238828
H	1.27268313	0.83334678	4.13430505
H	2.58334725	-0.09572037	4.98382730
H	1.28525129	0.68698798	5.91274623
Fe	-2.34166884	-1.60020796	4.52874487
Cl	-2.27714205	-3.29526782	5.93582189
Cl	-3.26367706	-2.22253247	2.63567272
Cl	-3.26415388	0.14359265	5.46322026

4.5 References

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Chapter 5

Conclusions and Outlook

Chiral nitrogen heterocycles are privileged scaffolds that represent ubiquitous structural motifs in biologically active natural products and serve as important templates in drug discovery. Moreover, 5- and 6-membered nitrogen heterocycles are utilized as ligands in asymmetric catalysis and as components of hydrogen-bond donor catalysis. Although many strategies towards accessing these chiral heterocyclic motifs have been developed, many of them rely on harsh reaction conditions or expensive, precious metal catalysts and are often limited in substrate scope. One such strategy that has proven effective for the synthesis of nitrogen heterocycles is the ring-closing olefin-olefin metathesis reaction. The olefin-olefin metathesis reaction is a revolutionary industrial process that utilizes precious metal complexes to enable direct carbon-carbon bond formation from simple olefin starting materials. While this strategy has been employed toward a variety of complex materials, amines often present an additional challenge due to the amine's ability to coordinate to the active catalysts which often led to catalyst decomposition. While many efforts have been made to obviate this undesired reactivity including substrate design and catalyst development, this approach still relies on expensive catalysts. In addition, access to chiral materials remains a significant challenge.

In recent years, carbonyl olefin metathesis has emerged as a powerful tool to directly form carbon-carbon bonds from readily available precursors. Our lab first reported a catalytic protocol for the synthesis five- and six-membered unsaturated carbocycles using iron(III) chloride and performed detailed mechanistic studies into the reaction pathway. With the successful application of this reaction platform towards a diverse array of cyclopentenes and cyclohexenes, we then envisioned using this synthetic tool to access nitrogen heterocycles. During the development of our synthetic strategy, we realized that we could access chiral materials through the use of amino acids as commercially available chiral pool reagents. From the protected amino acids we developed a general, 3-step substrate synthesis that allowed for a wide range of modifications and could be modified to allow for the synthesis of both 3-pyrrolines and tetrahydropyridines.

With this synthetic strategy, we were able to apply the carbonyl-olefin metathesis reaction to access a wide range of nitrogen heterocycles. Initially, we found that compared to the analogous carbocycles, the nitrogen-containing systems required higher catalyst loadings. The Lewis basic amine was subsequently identified as a competitive binding site, but we found that selection of an electron-deficient protecting group allowed for lower catalyst loadings and up to 99% yield of the desired metathesis products. This reaction was shown to be tolerant of a wide range of electronically diverse systems and both natural and unnatural amino acids. This transformation is distinguished by its operational simplicity, mild reaction conditions, and high tolerance for electronically differentiated substrates. In addition, detailed computational analyses revealed that the choice of an electron-deficient protecting group prohibits competitive binding of the iron catalyst to

Lewis basic sites and enables catalytic turnover. These studies have also provided key insights into the reaction pathway of the formation of 3-pyrrolines. Furthermore, computational studies have also provided key insights into the oxetane formation. Specifically, introduction of steric bulk on the β-position can hinder the formation of the oxetane intermediate and shut down the reaction pathway, while quaternary stereocenters in the α-position to the carbonyl can invoke the Thorpe-Ingold effect and improve the overall yield. With the knowledge of the limiting factors of this transformation, we have been able to establish a series of guidelines that can help direct the future applications of this strategy.