Supplementary Information for

Asymmetric Synthesis of Sulfoximines, Sulfonimidoyl Fluorides, and Sulfonimidamides Enabled by an Enantiopure Bifunctional S(VI) Reagent

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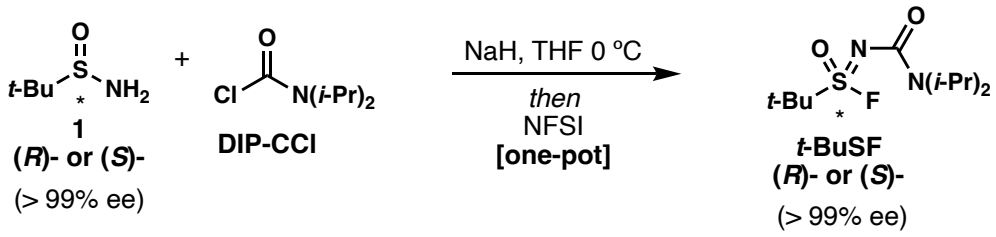
General Experimental Information

Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Anhydrous diethyl ether (Et_2O), tetrahydrofuran (THF), 2-methyl tetrahydrofuran (2-Me-THF), and toluene (PhMe) were obtained by passing the previously degassed solvent through an activated alumina column (PPT Glass Contour Solvent Purification System). Anhydrous cyclopentyl methyl ether (CPME), dimethoxyethane (DME) and methyl *tert*-butyl ether (MTBE) were purchased from Acros Organics. All glassware was flame-dried under vacuum before use. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by LC–MS or thin layer chromatography (TLC) carried out on 250 μm SiliCycle SiliaPlates (TLC Glass–Backed TLC Extra Hard Layer, 60 Å), using shortwave UV light as the visualizing agent and *p*-anisaldehyde, phosphomolybdic acid (PMA) or $KMnO_4$ with heat as developing agents. Flash column chromatography was performed with a Biotage Isolera One (ZIP or SNAP Ultra cartridges) or with traditional glass flash columns using SiliCycle SiliaFlash® P60 (particle size 40 – 63 μm). NMR spectra were recorded on a Bruker Ascend™ 500 MHz instrument or Bruker Neo600 600 MHz spectrometer and were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$: 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR; DMSO–d_6: 2.50 ppm ^{1}H NMR, 39.5 ppm ^{13}C NMR). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dddd = doublet of doublet of doublet of doublet, ddddd = doublet of doublet of doublet of doublet of doublet, tt = triplet of triplet, ddt = doublet of doublet of triplet, m = multiplet, br = broad, hept = heptet. High resolution mass spectra (HRMS) were recorded on an Agilent 6230 LC–MS TOF mass spectrometer. Enantiomeric excess (ee) was determined using a Varian Prostar HPLC with a 210 binary pump and a 335 diode array detector. Optical rotations were measured using a JASCO P-2000 polarimeter with a cell length of 1 dm. Melting points were recorded on a Chemglass DMP 100 melting point apparatus and were uncorrected.

Handling of Reagents

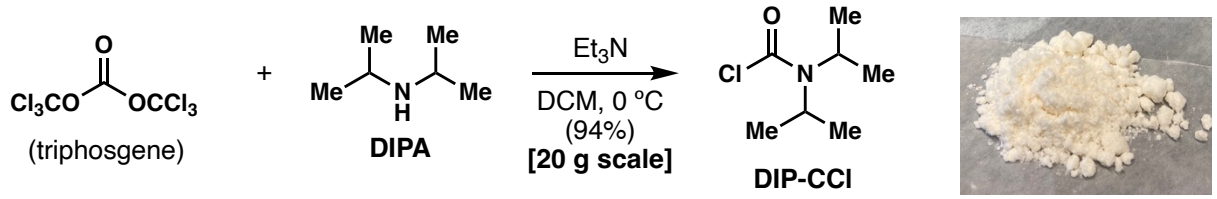
All synthesized sulfonimidoyl fluorides, sulfoximines, and sulfonimidamides were stored under ambient conditions, either room temperature or at -20 °C and appeared to be unchanged over the course of this work. All reactions were performed using dry solvents unless otherwise stated. No significant difference in reactivity and stereospecificity was observed for sulfonimidoyl fluorides used within this study. Stability analysis of the sulfonimidoyl transfer reagent ***t*-BuSF**, including bench and thermal stability, show the reagent is stable for *at least* 7-months under ambient conditions.

I. Synthesis of *N,N*-(diisopropylcarbamoyl)-2-methylpropane-2-sulfonimidoyl fluoride (*t*-BuSF).



Scheme S1: General synthesis for both enantiomers of *tert*-butyl sulfonimidoyl fluoride from commercially available chiral sources.

Ia. Synthesis of diisopropyl carbamoyl chloride (DIP-CCl).



Scheme S2: Large-scale preparation of diisopropyl carbamoyl chloride (DIP-CCl).

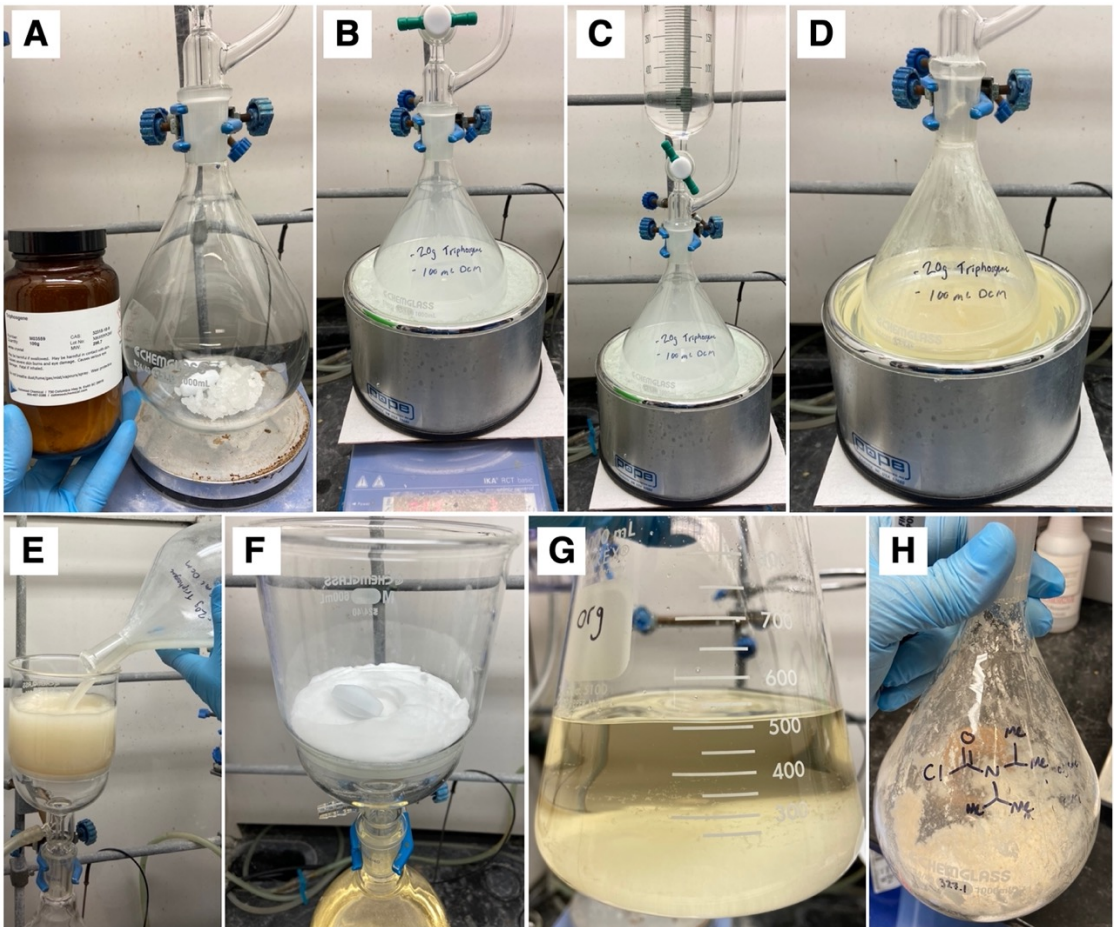
In a 1 L round-bottom flask equipped with a stir bar, septum capped addition funnel (500 mL) and argon balloon was added triphosgene (20 g, 16.9 mmol, 1 eq.) followed by DCM (100 mL) then cooled to 0 °C. A solution of DIPA (20.5 g, 28.6 mL, 202 mmol, 3 eq.) and Et_3N (20.5 g, 28.2 mL, 202 mmol, 3 eq.) in DCM (240 mL) was added to the addition funnel (directly poured using a funnel and recapped) then added over 10 minutes. The reaction mixture stirred at 0 °C for 1.5 hours, removed from the ice bath, filtered through a sintered glass funnel (removal of Et_3N-HCl) and rinsed with DCM (50 mL x 3). The filtrate was concentrated under reduced pressure to remove DCM (rotary evaporator bath set to 25 ºC) then taken up in hexanes (450 mL), washed with water (3 x 200 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated (rotary evaporator bath set to 25 ºC) to give the desired carbamoyl chloride (31.1 g, 190 mmol, 94% yield) as an off-white solid that was sufficiently pure by NMR and used in the next step without further purification.

Notes:

- DCM, DIPA and Et_3N were directly obtained from an anhydrous solvent system (PPT Glass Contour Solvent Purification System) under an atmosphere of argon.
- Triphosgene was purchased from Oakwood Chemicals and directly used.
- Thorough continuous mixing is required to obtain high overall conversion and yield.
- Slower additions of DIPA and Et_3N in DCM produced reaction mixtures and products having a yellow color. The source of the yellow discoloring was not identified.

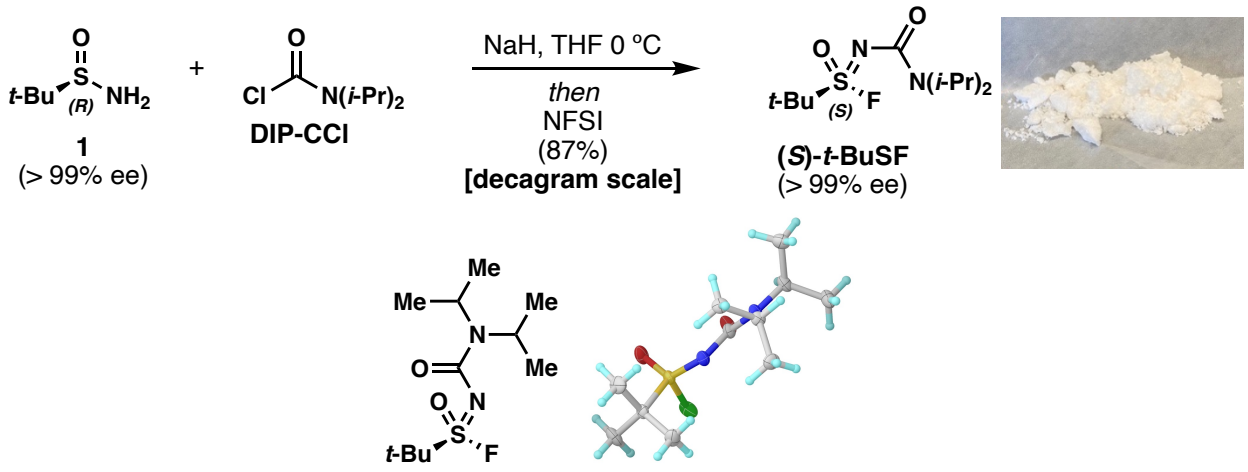
- Switching work-up organic solvent from DCM to hexanes provides a whiter solid in high purity, however, DCM can be used and the crude solid recrystallized from hexanes to afford DIP-CCl in high purity and yields (>95% purity; 85-90% yields).
- An alternative method using $NaHCO_3$ (reported to give 87% yield of DIP-CCl)[1] as the base resulted in a diminished yield of 20% in our hands.

Physical characteristics: Off-white solid
^{1}H NMR: (500 MHz, $CDCl_3$) δ 4.53 (q, *J* = 6.9 Hz, 1H), 3.66 – 3.50 (m, 1H), 1.36 (d, *J* = 6.9 Hz, 6H), 1.21 (d, *J* = 6.9 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 146.0, 52.9, 48.6, 20.4, 19.9. ppm



Graphical Procedure 1: A 20 gram-scale synthesis of **DIP-CCl**. **A.** Addition of triphosgene to the reaction flask. **B.** Triphosgene dissolved in DCM (100 mL) at 0 °C. **C.** Addition of DIPA/Et_3N solution in DCM (240 mL) to the reaction mixture via addition funnel. **D.** Reaction mixture after stirring for 1.5 hours. **E.** Filtration of the reaction mixture through a sintered glass funnel. **F.** Solid (Et_3N-HCl) collected and removed by filtration prior to work-up. **G.** Crude organic layer after work-up. **H.** Solid DIP-CCl obtained after removal of solvent from work-up.

Ib. Decagram synthesis of enantiopure (*S*)-t-BuSF.



Scheme S3: Synthesis of enantiopure *tert*-butyl sulfonimidoyl fluoride (*t*-BuSF) on a decagram scale displaying the bench stable crystalline solid and single crystal X-ray structure.

In a septum capped 1 L round-bottom flask equipped with a stir bar and argon balloon was added (*R*)-*t*-Bu sulfinamide **1** (10.3 g, 41.4 mmol, 1 eq.) followed by THF (400 mL, 0.21 M) then cooled to 0 °C. NaH (8.50 g, 212 mmol, 2.5 eq., 60% wt) was added portion-wise (3 portions) then stirred for 20 minutes until H_2 gas evolution ceased. **DIPC-CCl** (13.9 g, 84.9 mmol, 1 eq.) was added portion-wise (3 portions) then stirred at 0 °C for 1.5 hours until H_2 gas evolution ceased (reaction monitored by TLC and LC–MS for the disappearance of sulfinamide). NFSI (28.1 g, 89.2 mmol, 1.05 eq.) was added in one portion then stirred at 0 °C for an additional 1 hour (reaction monitored by TLC and LC–MS for the disappearance of sulfinyl urea intermediate). The reaction mixture was removed from the ice bath and diluted with 10% EtOAc in hexanes (300 mL) then filtered through a medium porous sintered glass funnel while rinsing with 10% EtOAc in hexanes. The organic solution was washed with 10% KI aqueous solution (150 mL x 3: for removal of unreacted NFSI) and brine (150 mL x 3). The solvent was dried over anhydrous Na_2SO_4, filtered and solvents removed under reduced pressure to give a yellow oil. Further purification by silica gel column chromatography using hexanes/EtOAc (0% to 20% EtOAc) provided **(*S*)-*t*-BuSF** (19.8 g, 74.3 mmol, 87% yield) as a clear colorless oil that solidified to a white crystalline solid under reduced pressure.

Physical characteristics: White crystalline solid
TLC: R_f = 0.33 (hexane/EtOAc, 20% EtOAc, PMA).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 4.03 (s, 1H), 3.88 (s, 1H), 1.59 (d, *J* = 0.7 Hz, 9H), 1.38 – 1.10 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 153.9, 62.8 (d, *J* = 11.7 Hz), 47.8, 45.9, 24.7, 21.4, 20.7, 20.6 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ 33.20 ppm.

Specific rotation: $[\alpha]_D^{23}$ = +78.17 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{11}H_{23}FN_2NaO_2S$ [M+Na^+] 289.1356; found 289.1363.

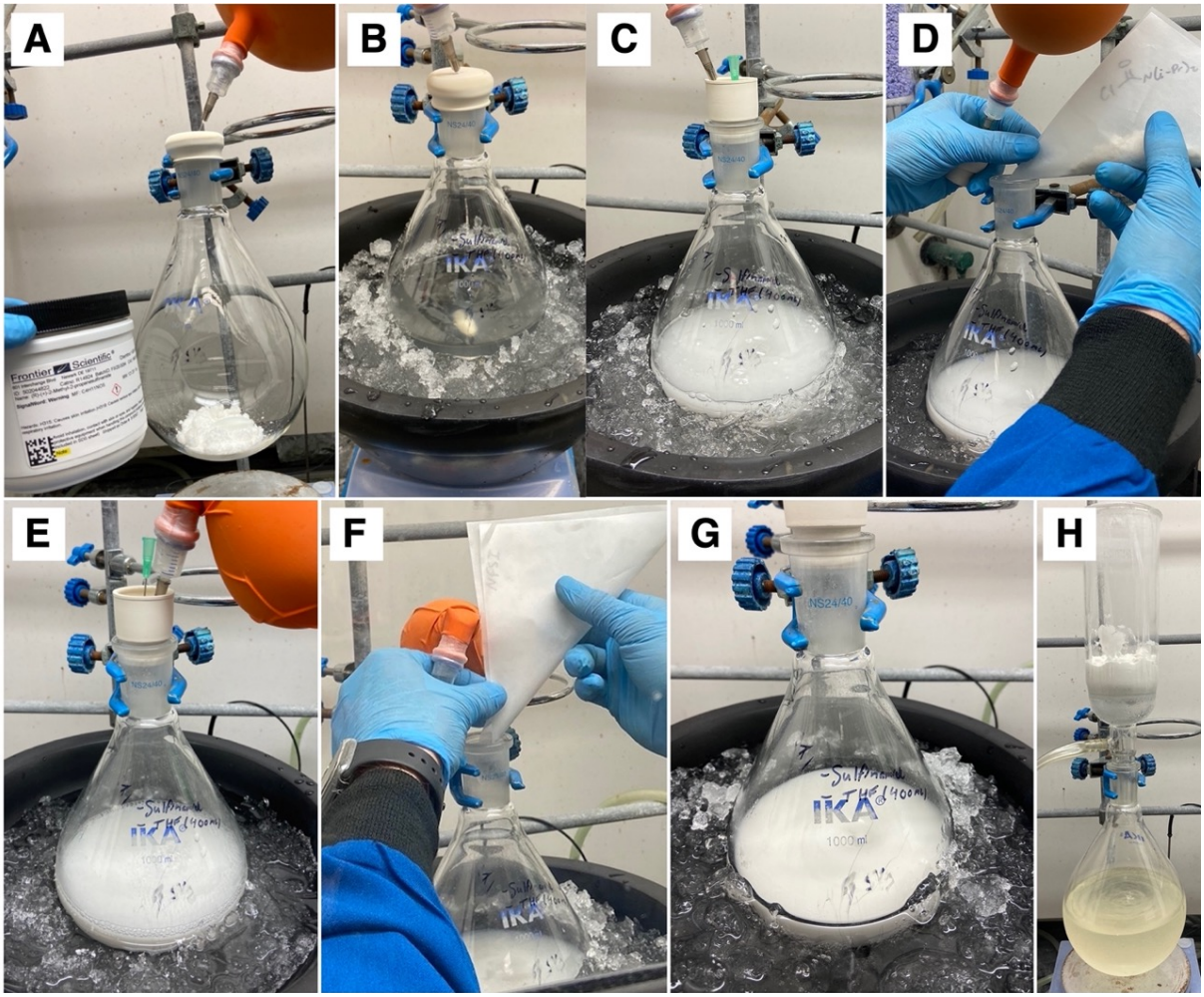
Enantiomeric excess: >99%

HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 13.0 min, major: 16.7 min.

CCDC deposition Number: 2243804

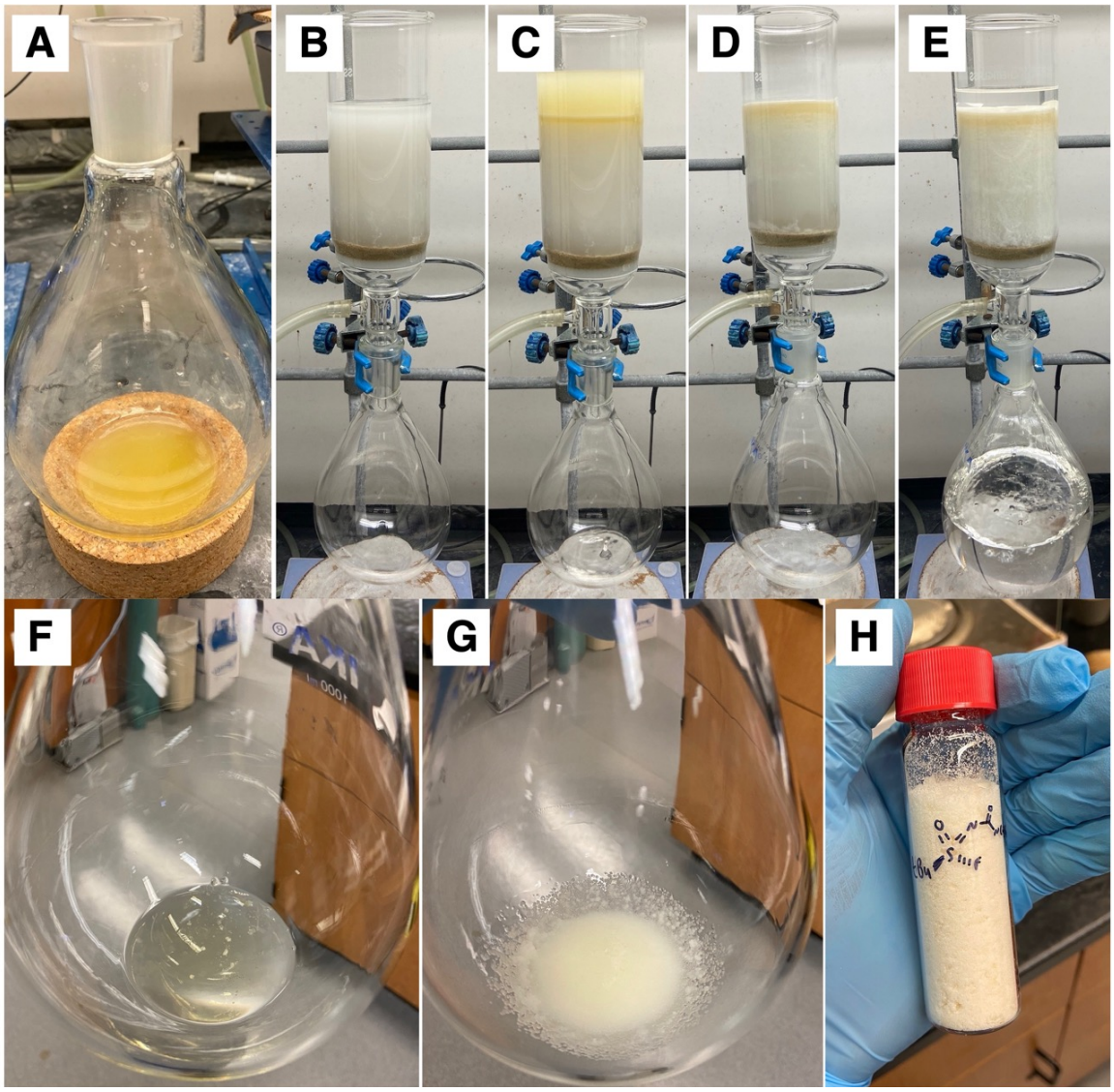
Notes:

1. When performing the reaction at this scale (10 g of *t*-Bu sulfinamide), the reaction concentration was increased from 0.1 to 0.2 M. Upon addition of the NFSI, the reaction mixture becomes a thick slurry that is difficult to stir with a traditional stir bar.
2. When performing the reaction on smaller scales (5 g of *t*-Bu sulfinamide), the reaction concentration was 0.1 M and yields of 90-94% (~10 g of *t*-BuSF) have been reproducibly obtained.
3. The sulfonimidoyl fluoride is weakly UV active; *p*-anisaldehyde or PMA stain should be used to visualize by TLC.
4. The sulfinyl urea intermediate is not stable under aqueous conditions but can be detected by LC-MS (reverse phase H_2O/MeCN 0.1% formic acid).
5. The solid filtered is the sodium salt by-product from NFSI. On smaller scales (< 1 g of *t*-Bu sulfinamide) workups without filtration were employed.
6. Removal of unreacted NFSI by washing with KI (10% aqueous solution) allows for easier purification and filtration through a silica plug of silica using hexanes/EtOAc (0-20% EtOAc) is sufficient if long-term storage of *t*-BuSF is not required (*vide infra*).
7. Racemic *t*-BuSF was prepared using the same method from commercially available racemic sulfinamide.
8. When Selectfluor (1.2 eq.) was used as the fluorinating agent, ***t*-BuSF** was obtained in 82% yield and 93.5% ee.



Graphical Procedure 2: Decagram scale synthesis of **(*S*)-*t*-BuSF**. **A.** Addition of (*R*)-*t*-Bu sulfinamide to the reaction flask. **B.** (*R*)-*t*-Bu sulfinamide dissolved in THF (400 mL) at 0 ºC. **C.** Reaction mixture after portion-wise addition of NaH. **D.** First addition of **DIP-CCl** to the reaction mixture. **E.** Reaction mixture after addition of **DIP-CCl** (evolution of H_2 gas). **F**. Addition of NFSI in a single portion. **G.** Reaction mixture after the addition of NFSI (thick slurry). **H.** Filtration of NFSI by-product from reaction mixture through a sintered glass funnel prior to aqueous workup.

Expedient purification of t-BuSF using a silica gel plug.



Graphical Procedure 3: Filter purification of **(*S*)-*t*-BuSF**. **A.** Crude reaction mixture after aqueous workup. **B.** Silica gel plug (250 g) slurry with hexanes. **C.** Addition of crude reaction mixture to silica gel plug using hexanes. **D.** After filtering with hexanes (100 mL) and 10% EtOAc in hexanes (100 mL). **E.** Elution of *t*-BuSF using 20% EtOAc in hexanes (500 mL) to give the first fraction. **F.** Concentrated first collected fraction of *t*-BuSF to give an oil. **G.** Crystallization of *t*-BuSF upon standing. **H.** Final collection and storage of *t*-BuSF.

II. Stability study of N–protected sulfonimidoyl fluorides

IIa. Bench stability analysis of *t*-BuSF.

***t*-BuSF** was prepared following the general procedure and stored on the lab bench in a colorless 20 mL capped vial (no exchange with argon). Room temperature was variable (23–26 °C) and humidity was roughly 55%. *t*-BuSF samples were prepared from the same batch, separated into three different vials and compared with freshly prepared material. Stability analysis using ^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR were used and accompanied by a reaction performance analysis (% yield and % ee) using phenyl lithium as the nucleophile over the course of 7 months.

Based on the NMR analysis, no significant decomposition was observed over seven months. The only identifiable peaks were that of diisopropyl amine (presumably forms via decomposition pathway). Reaction performance analysis provided identical enantiopurity of products with slightly diminished yields (up to 10%). The data collected from this stability study and our hands-on use of *t*-BuSF over the course of this study, *t*-BuSF is bench stable for >7 months and a single batch has been routinely used for over a year.

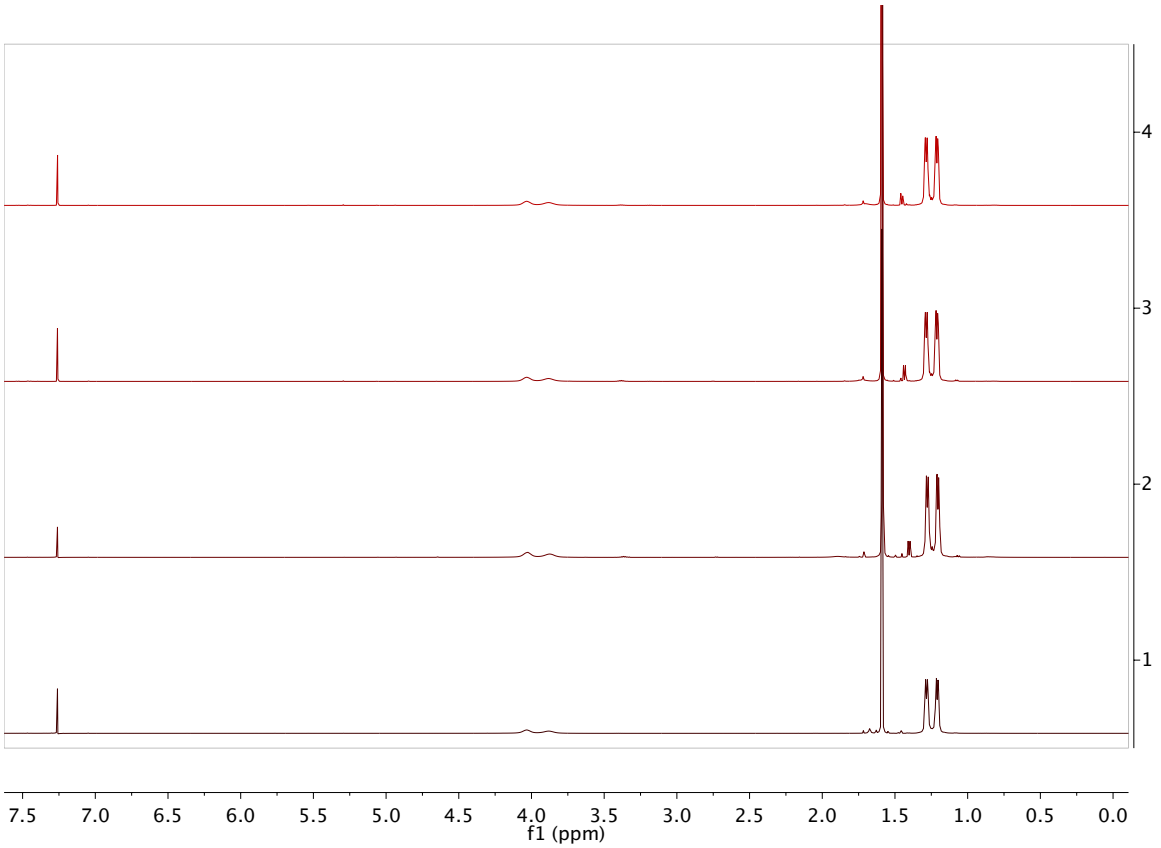


Figure S1: ^{1}H NMR analysis of *t*-BuSF stored at room temperature under an atmosphere of air. 1) *t*-BuSF control that was freshly prepared. Entries 2–4 are the three different samples used to determine bench stability after 7 months. All samples were prepared using $CDCl_3$.

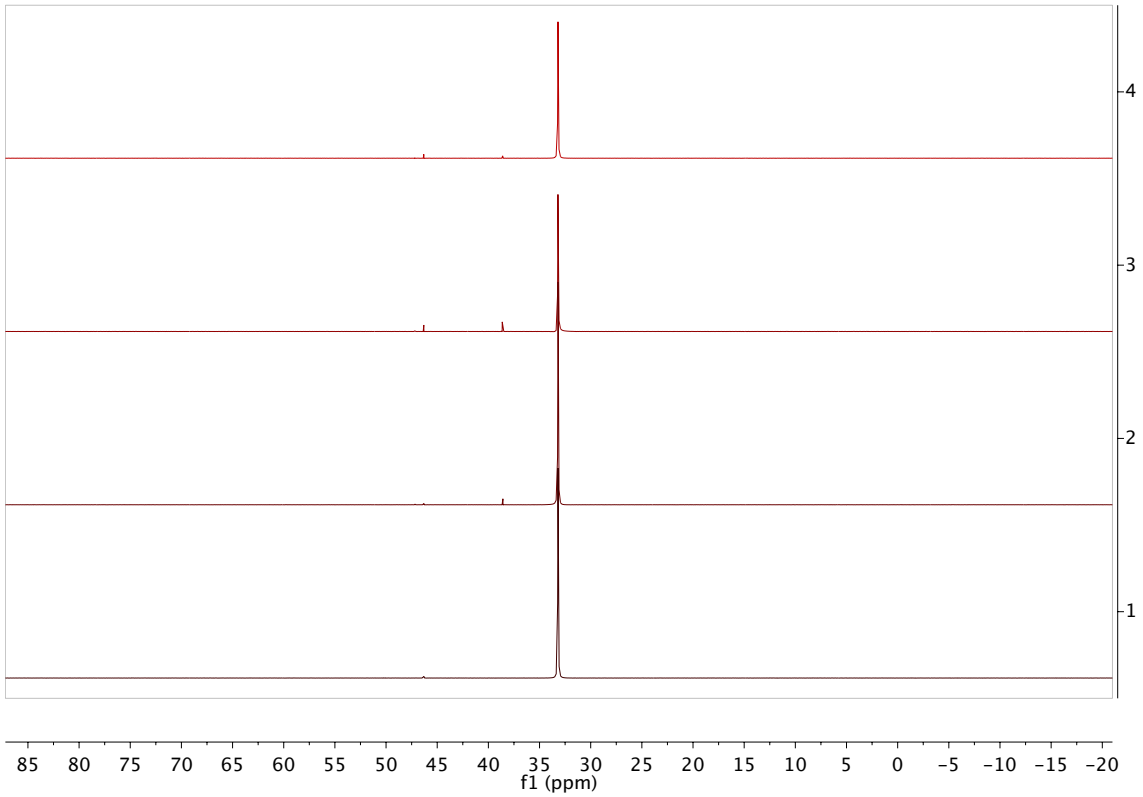


Figure S2: ^{19}F NMR analysis of *t*-BuSF stored at room temperature under an atmosphere of air. 1) *t*-BuSF control that was freshly prepared. Entries 2–4 are the three different samples used to determine bench stability after 7 months. All samples were prepared using $CDCl_3$.

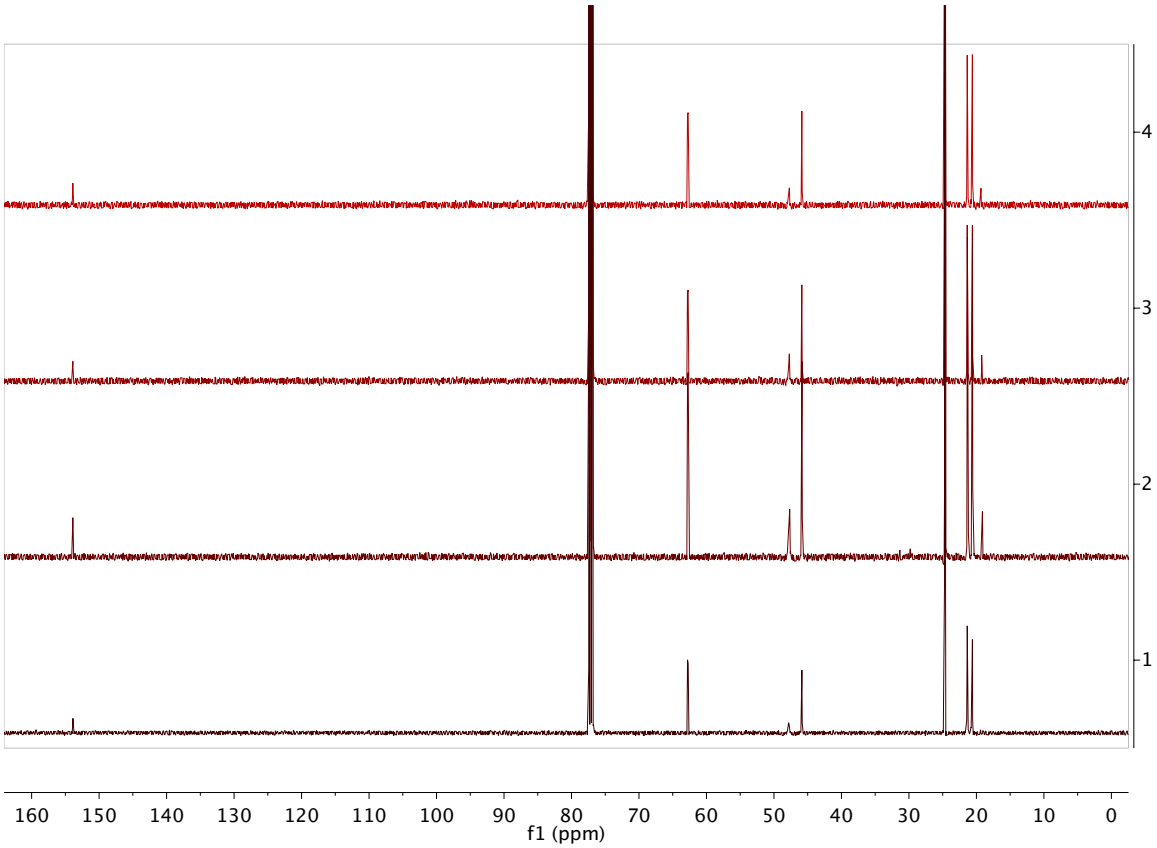


Figure S3: ^{13}C NMR analysis of *t*-BuSF stored at room temperature under an atmosphere of air. 1) *t*-BuSF control that was freshly prepared. Entries 2–4 are the three different samples used to determine bench stability after 7 months. All samples were prepared using $CDCl_3$.

IIb. Thermal stability of *tert*-butyl sulfonimidoyl fluoride reagents.

The thermal stability of ***t*-BuSF** was performed and compared to other protected *t*-Bu sulfonimidoyl fluorides. Three different solvents were used as a thermal distribution of 35–110 ºC. Each sample (0.2 mmol, 0.1 M) was refluxed in the respective solvent: Et_2O (35 °C), THF (66 °C) and toluene (110 °C) for 24 hours. ***Note:*** *anhydrous solvents and conditions were not employed.* After 24 hours of heating, the reactions were cooled to room temperature, the solvent was removed under reduced pressure, and the remaining residue dissolved in $CDCl_3$ then analyzed by NMR (^1H and ^{19}F).

IIb-1. Thermal stability of t-BuSF.

Based on the NMR analysis of *t*-BuSF, significant decomposition was only observed when heating at 110 ºC in toluene for 24 hours. We were unable to identify the by-products besides diisopropyl amine. Decomposition was not observed at room temperature in all solvents used.

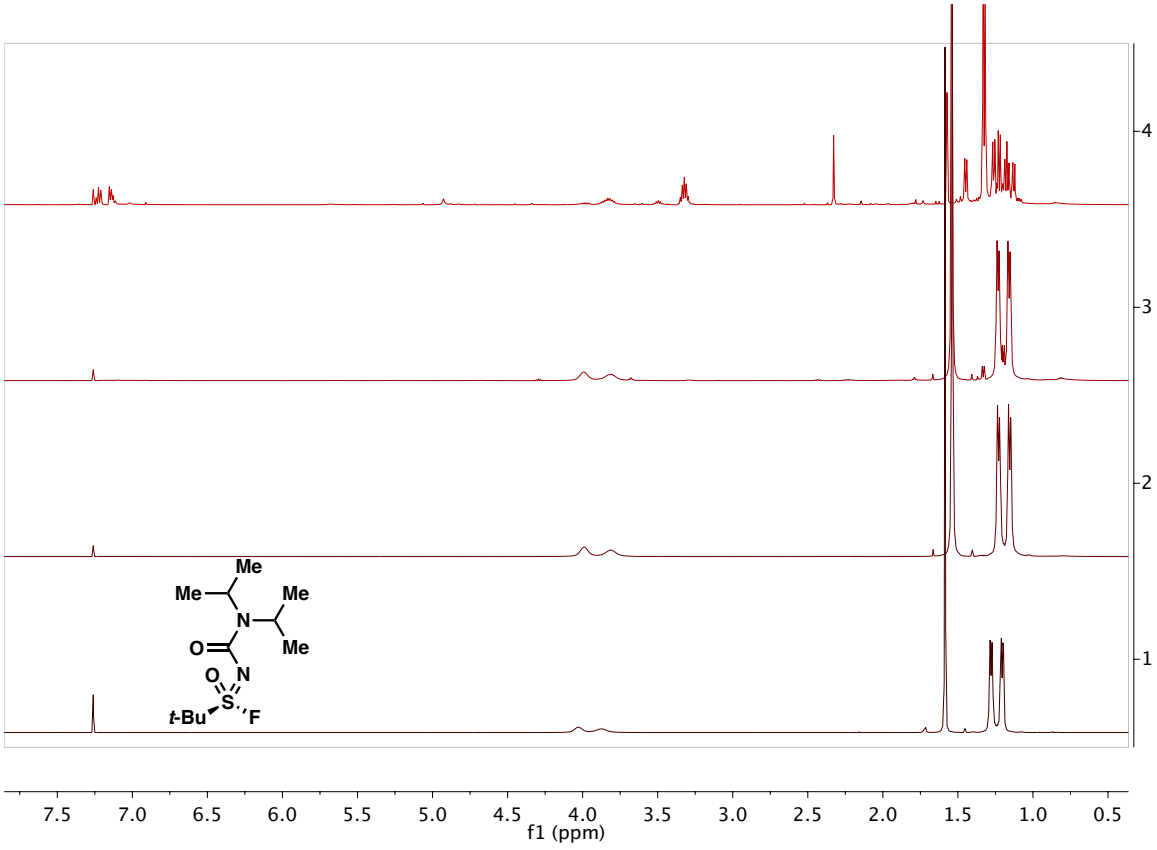


Figure S4: ^1H NMR analysis of *t*-BuSF after refluxing in three different solvents over 24 hours. 1) *t*-BuSF control. 2) *t*-BuSF refluxed (35 ºC) in Et_2O. 3) *t*-BuSF refluxed (66 ºC) in THF. 4) *t*-BuSF refluxed (110 ºC) in toluene. All samples were prepared using $CDCl_3$.

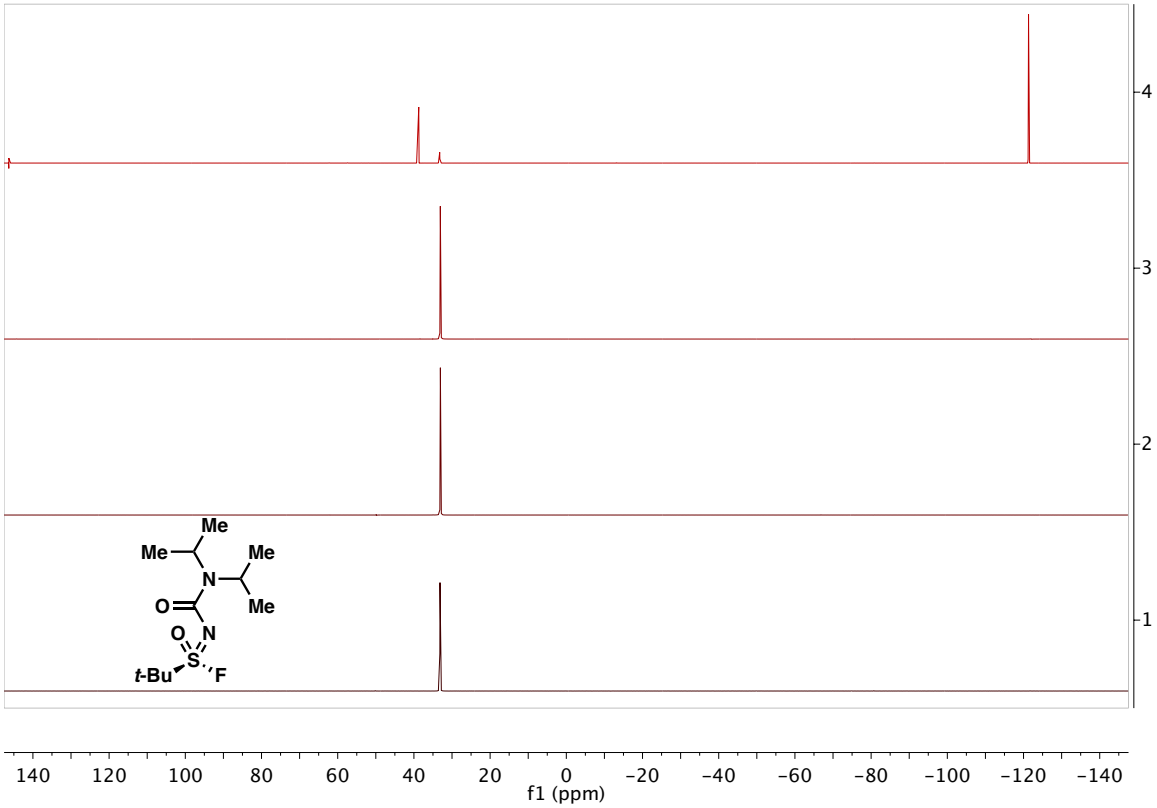


Figure S5: ^{19}F NMR analysis of *t*-BuSF after refluxing in three different solvents over 24 hours. 1) *t*-BuSF control. 2) *t*-BuSF refluxed (35 ºC) in Et_2O. 3) *t*-BuSF refluxed (66 ºC) in THF. 4) *t*-BuSF refluxed (110 ºC) in toluene. All samples were prepared using $CDCl_3$.

IIb-2. Thermal stability comparison of different protecting groups.

Four different protecting groups were evaluated for their thermal stability: two urea-based (–CON(*i*-Pr)$_2$, –CONEt$_2$) one carbamate (–Boc) and one acyl (–Piv). Other protecting groups including silyl (–TBS, –TBDPS), –tosyl, and –benzyl were unable to be prepared and evaluated due to reactivity or stability issues of the sulfinamide precursors and/or sulfonimidoyl fluoride products.

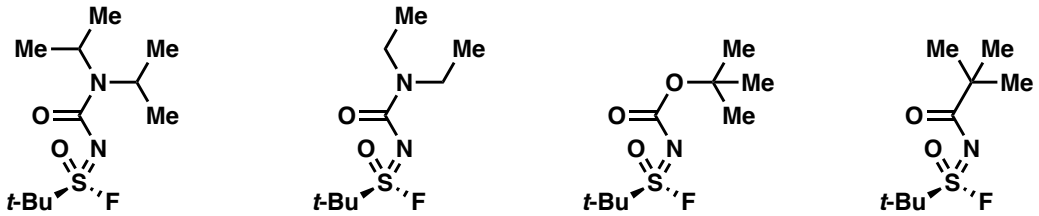


Figure S6: *t*-Bu sulfonimidoyl fluorides prepared and analyzed for thermal stability.

Experimental procedures and analyses were identical to those described above for ***t*-BuSF**. ^{1}H NMR was found to provide greater diagnostic evidence of decomposition compared to ^{19}F NMR. The urea protecting groups were both found to have increased stability under the thermal conditions relative to carbamate and acyl protecting groups. Both –Boc and –Piv protecting groups exhibited significant decomposition after refluxing (66 ºC) in THF for 24 hours. No obvious decomposition was observed when refluxing (35 ºC) in Et$_2$O for 24 hours across all four protected sulfonimidoyl fluorides.

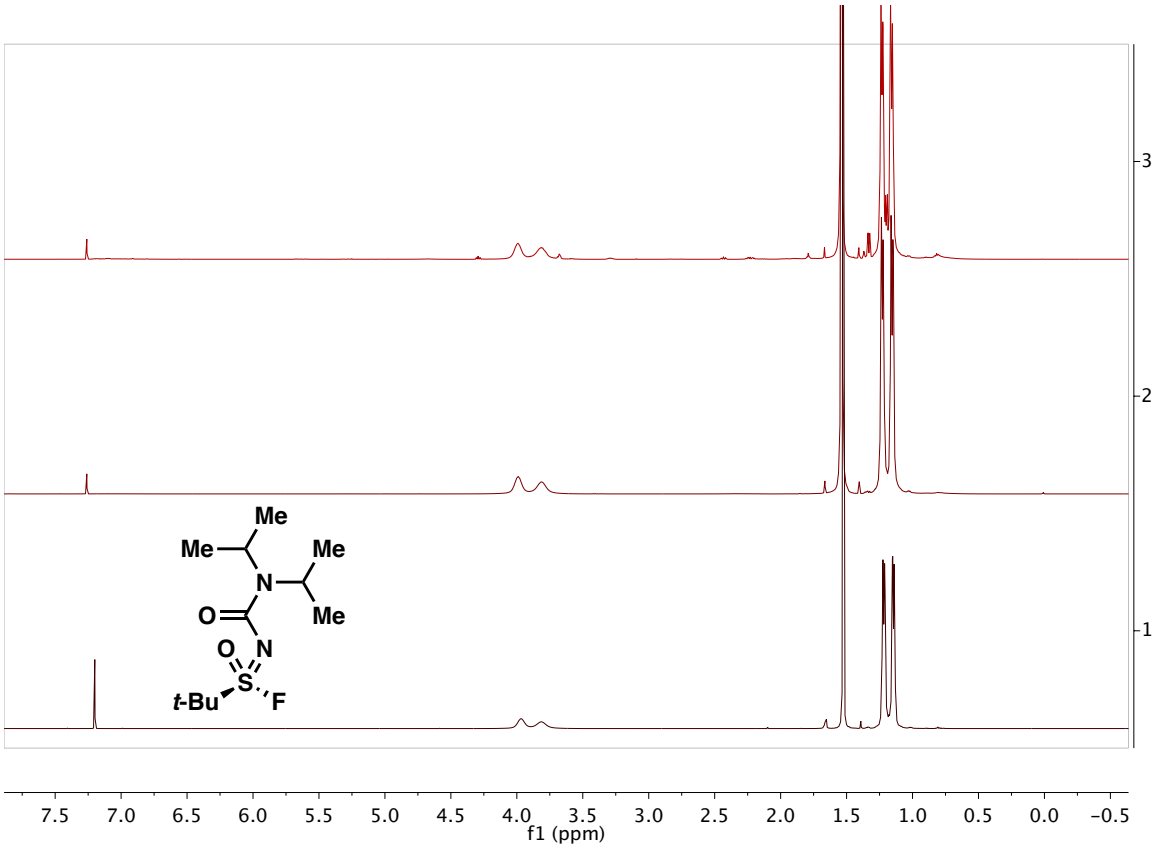


Figure S7: ^{1}H NMR analysis of *t*-BuSF after refluxing in Et_2O and THF over 24 hours. 1) *t*-BuSF control. 2) *t*-BuSF refluxed (35 ºC) in Et_2O. 3) *t*-BuSF refluxed (66 ºC) in THF. All samples were prepared using $CDCl_3$.

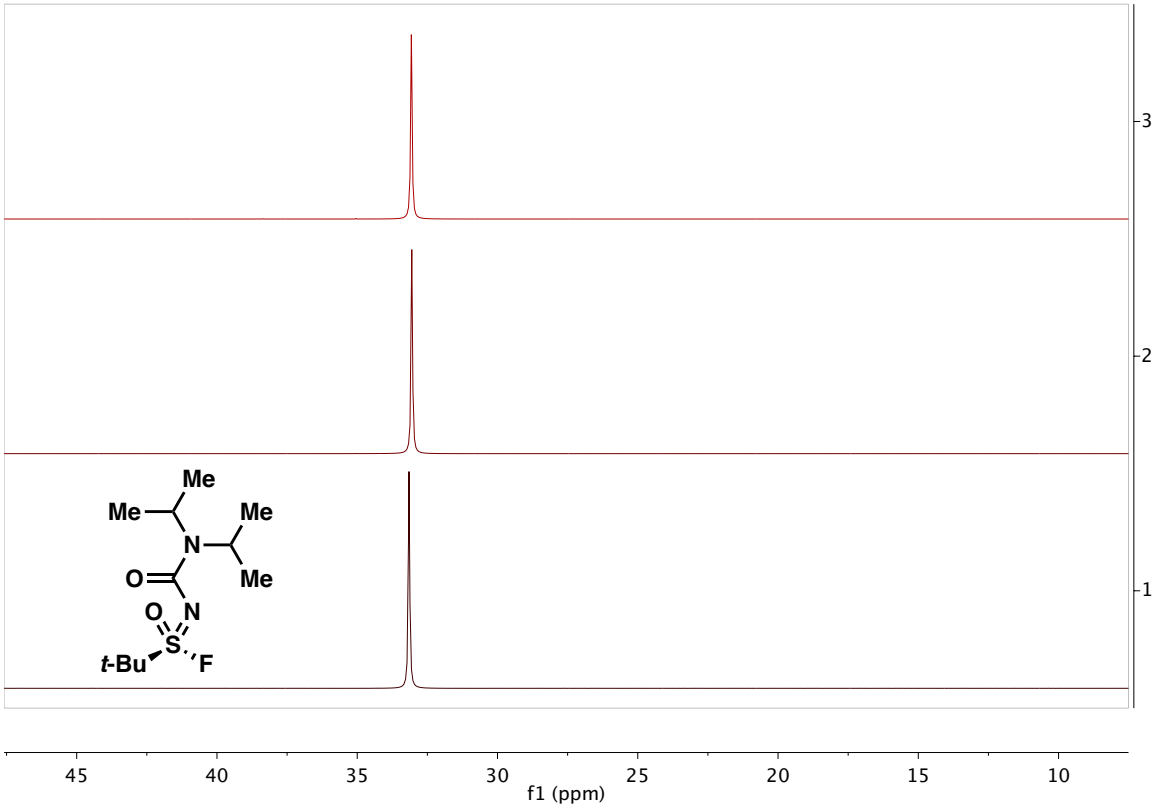


Figure S8: ^{19}F NMR analysis of *t*-BuSF after refluxing in Et_2O and THF over 24 hours. 1) *t*-BuSF control. 2) *t*-BuSF refluxed (35 ºC) in Et_2O. 3) *t*-BuSF refluxed (66 ºC) in THF. All samples were prepared using $CDCl_3$.

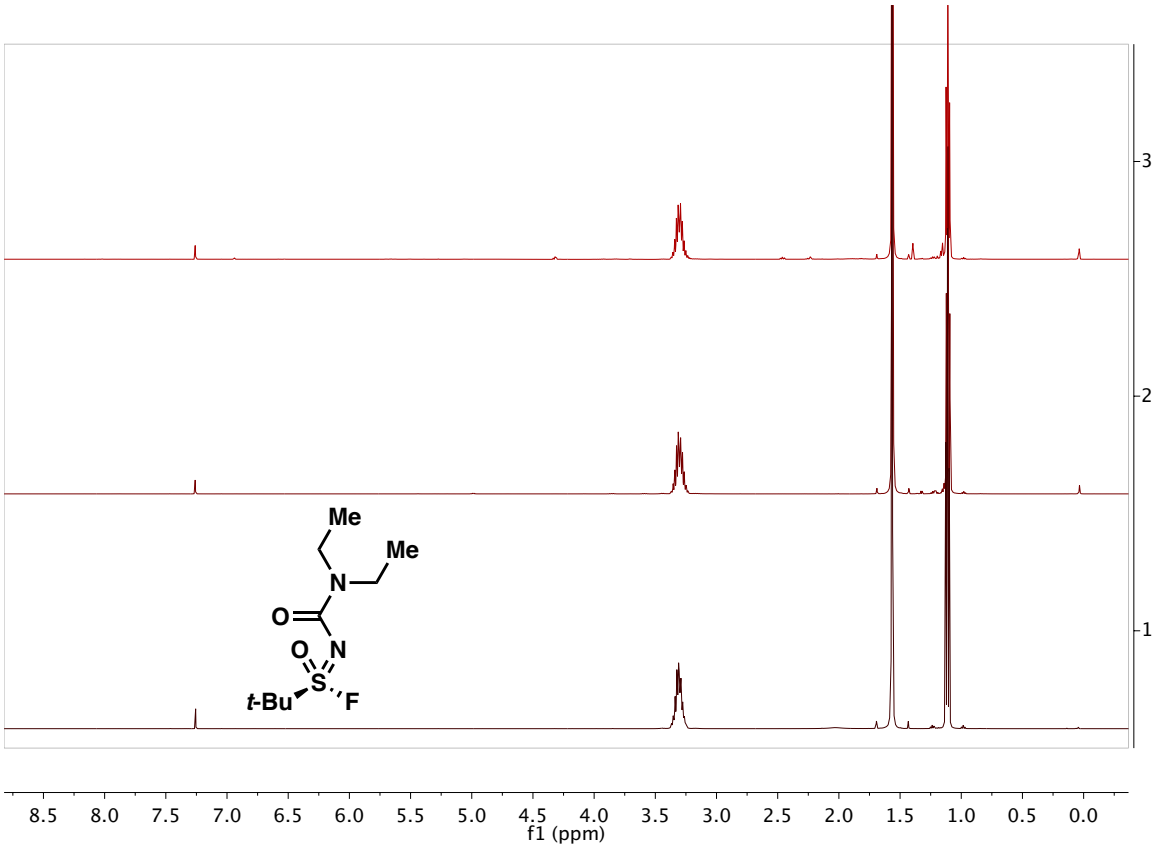


Figure S9: ^{1}H NMR analysis of –CONEt$_2$ urea protected *t*-Bu sulfonimidoyl fluoride after refluxing in Et$_2$O and THF over 24 hours. 1) CONEt$_2$ protected *t*-Bu sulfonimidoyl fluoride control. 2) after refluxing (35 ºC) in Et$_2$O. 3) after refluxing (66 ºC) in THF. All samples were prepared using CDCl$_3$.

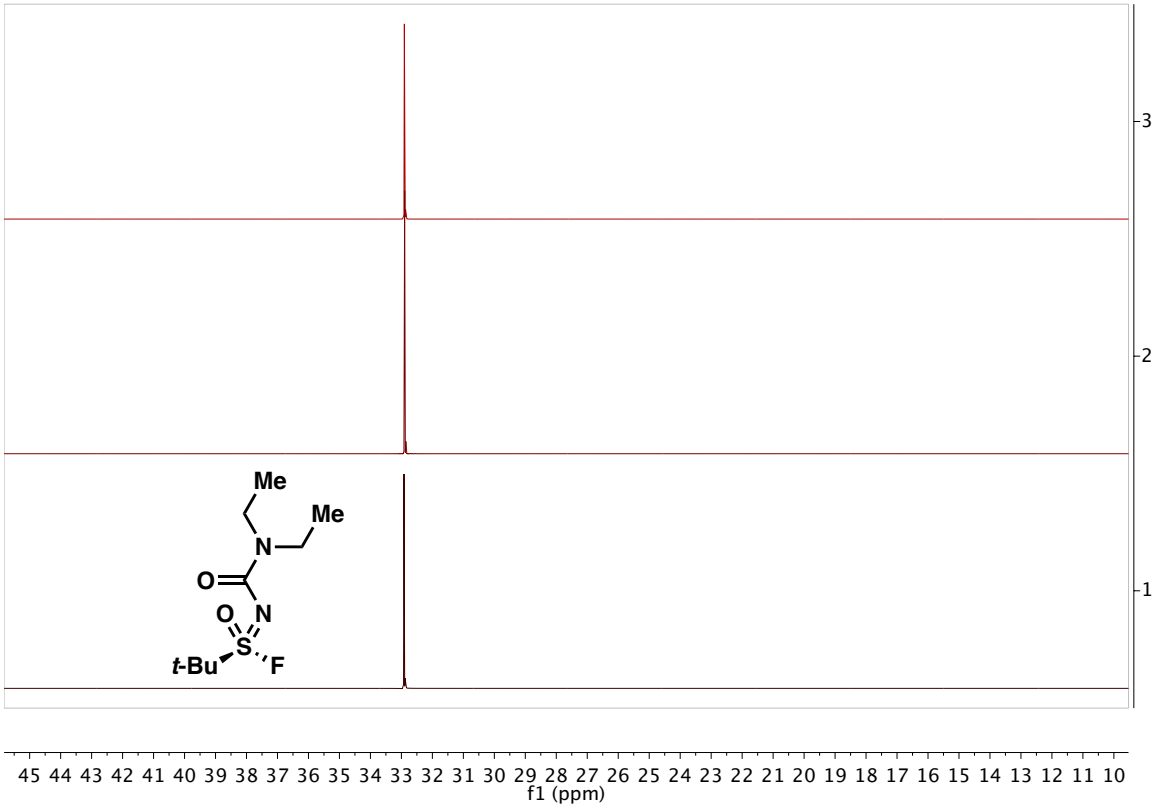


Figure S10: ^{19}F NMR analysis of –$CONEt_2$ urea protected *t*-Bu sulfonimidoyl fluoride after refluxing in Et_2O and THF over 24 hours. 1) $CONEt_2$ protected *t*-Bu sulfonimidoyl fluoride control. 2) after refluxing (35 ºC) in Et_2O. 3) after refluxing (66 ºC) in THF. All samples were prepared using $CDCl_3$.

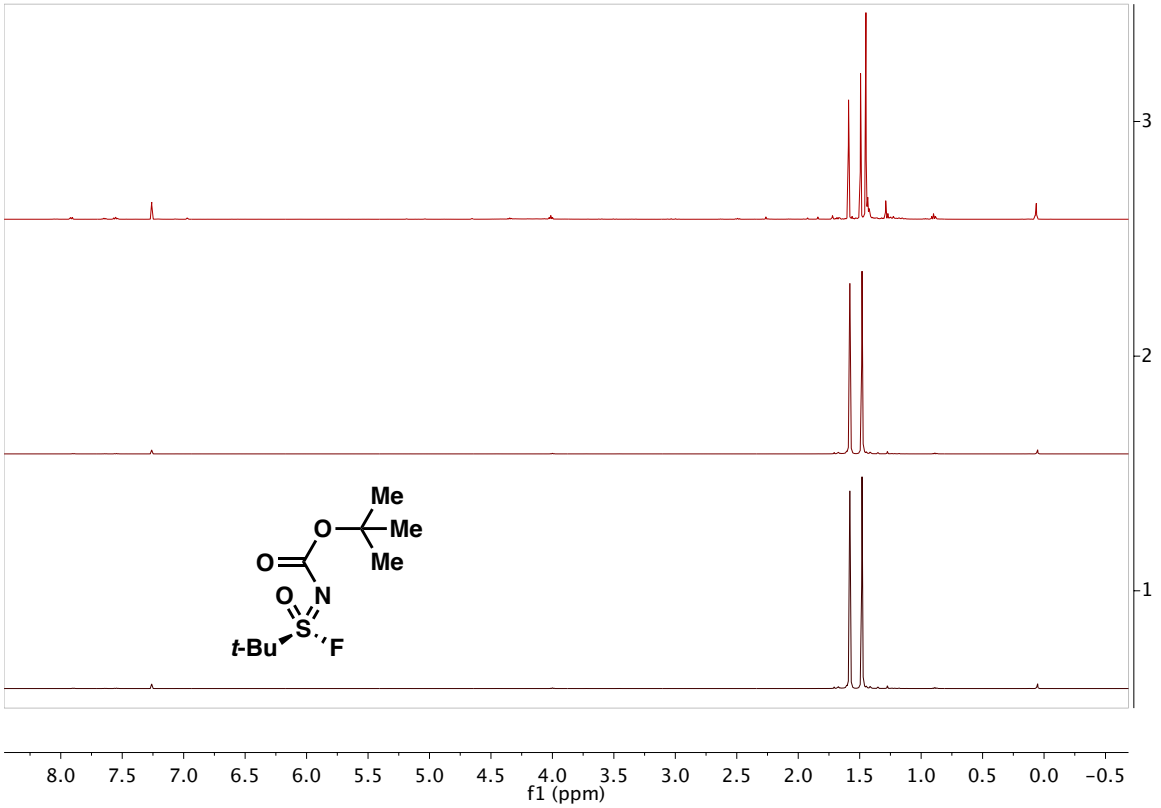


Figure S11: ^{1}H NMR analysis of –Boc protected *t*-Bu sulfonimidoyl fluoride after refluxing in Et_2O and THF over 24 hours. 1) –Boc protected *t*-Bu sulfonimidoyl fluoride control. 2) after refluxing (35 ºC) in Et_2O. 3) after refluxing (66 ºC) in THF. All samples were prepared using $CDCl_3$.

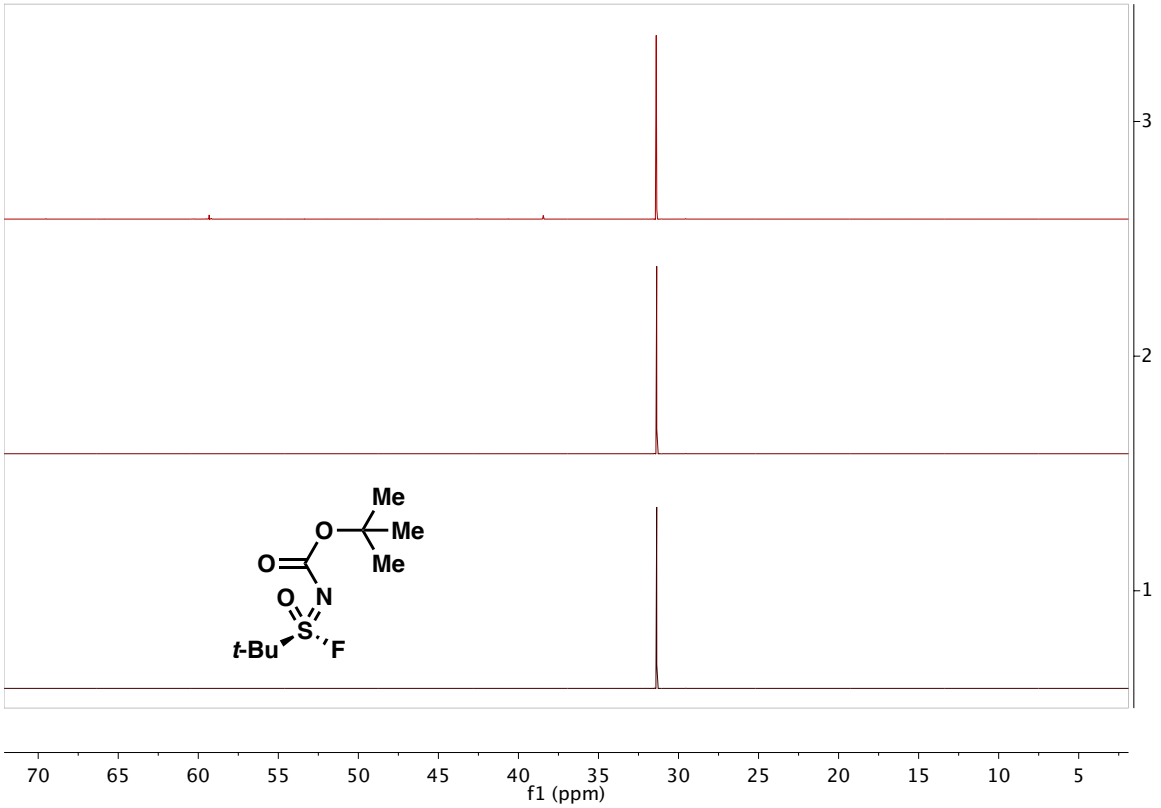


Figure S12: ^{19}F NMR analysis of –Boc protected *t*-Bu sulfonimidoyl fluoride after refluxing in Et_2O and THF over 24 hours. 1) –Boc protected *t*-Bu sulfonimidoyl fluoride control. 2) after refluxing (35 ºC) in Et_2O. 3) after refluxing (66 ºC) in THF. All samples were prepared using $CDCl_3$.

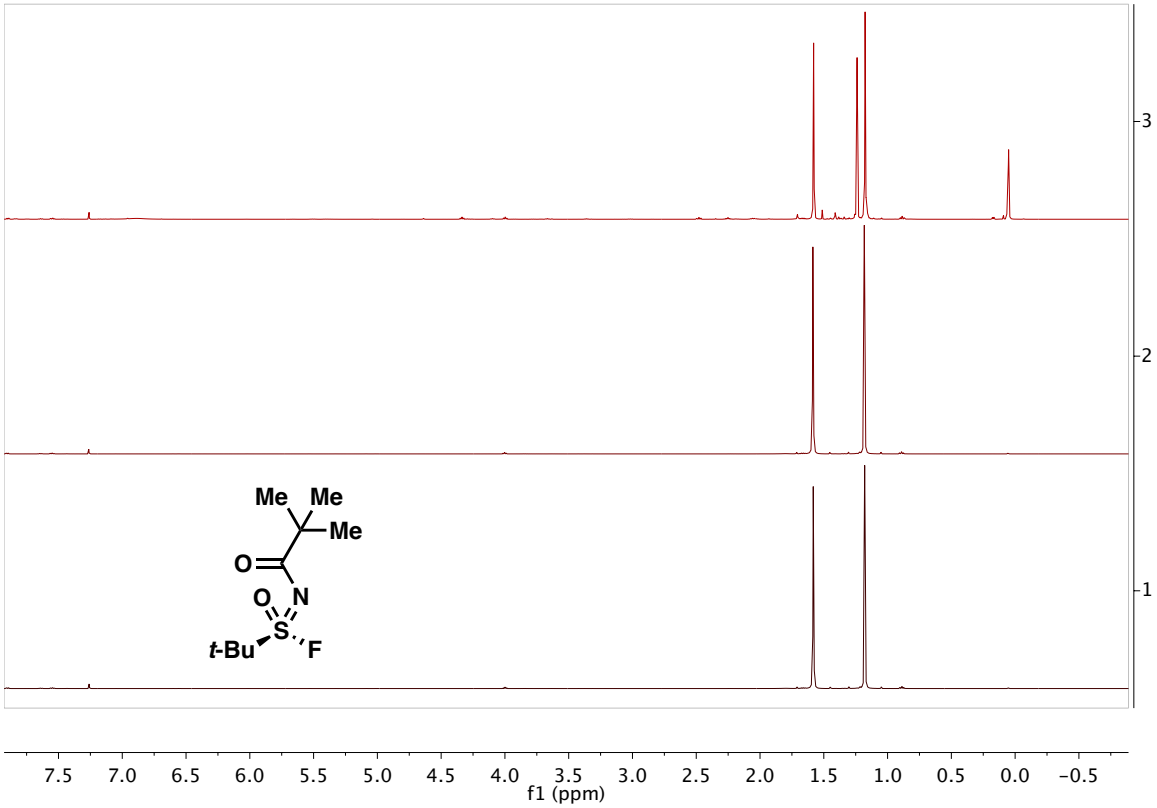


Figure S13: ^{1}H NMR analysis of –Piv protected *t*-Bu sulfonimidoyl fluoride after refluxing in Et_2O and THF over 24 hours. 1) –Piv protected *t*-Bu sulfonimidoyl fluoride control. 2) after refluxing (35 ºC) in Et_2O. 3) after refluxing (66 ºC) in THF. All samples were prepared using $CDCl_3$.

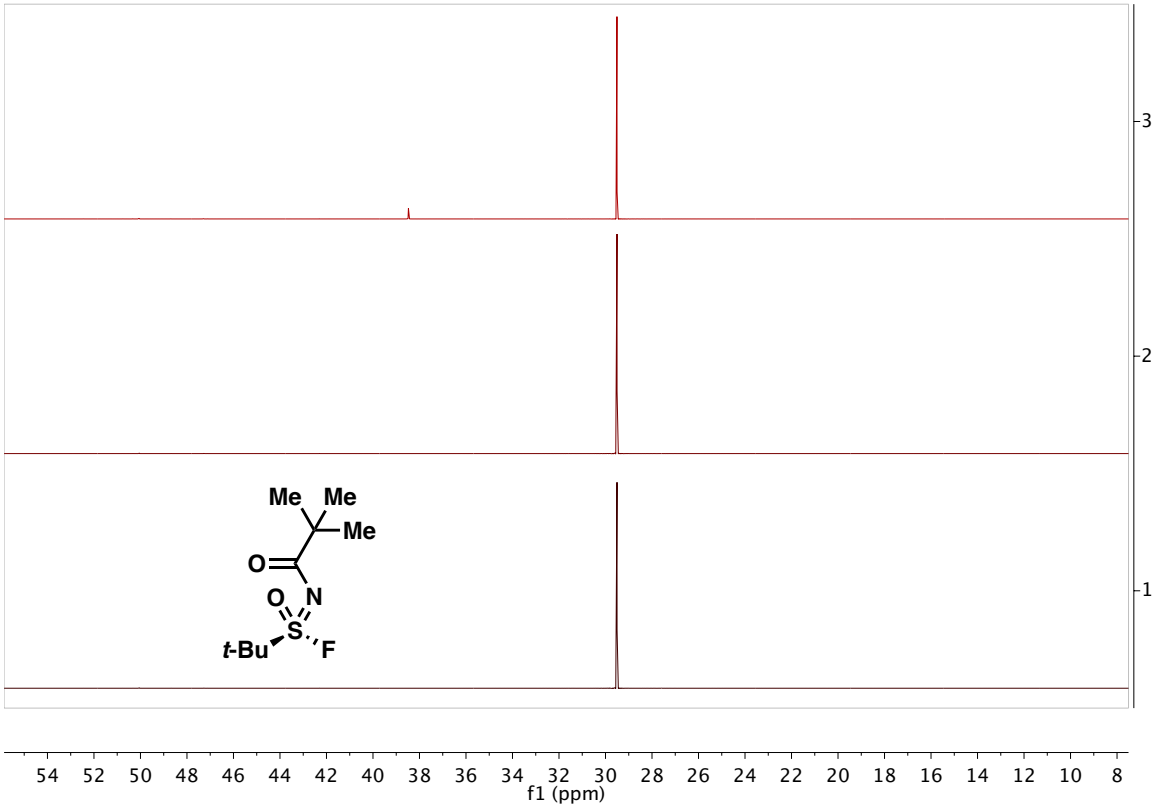
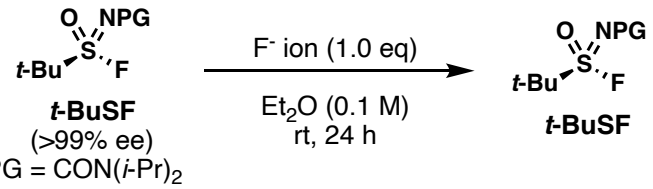


Figure S14: ^{19}F NMR analysis of –Piv protected *t*-Bu sulfonimidoyl fluoride after refluxing in Et_2O and THF over 24 hours. 1) –Piv protected *t*-Bu sulfonimidoyl fluoride control. 2) after refluxing (35 ºC) in Et_2O. 3) after refluxing (66 ºC) in THF. All samples were prepared using $CDCl_3$.

IIc. Stereogenic stability of *t*-BuSF in the presence of fluoride ions.

Stereogenic stability analysis of ***t*-BuSF** was performed in the presence of different fluoride ions. NaF, KF and TBAF were used as the fluoride sources. One blank sample was set as the control.

To a solution of ***t*-BuSF** (0.2 mmol) in Et_2O (0.1 M), the fluoride source (1.0 eq) was added. Stirred at room temperature for 24 h. The reaction mixture was filtered, and an aliquot was transferred into a HPLC vial then concentrated under reduced pressure. HPLC samples were prepared by dissolution in *i*-PrOH prior to analysis. **Note:** samples were prepared from reaction mixtures and not from crude solids.

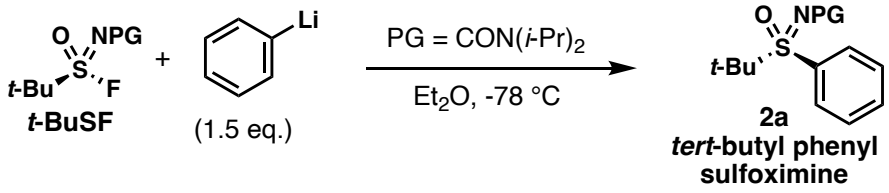


Entry	Fluoride Source	Enantiopurity (% ee)
1	None	> 99
2	NaF	> 99
3	KF	> 99
4	TBAF	97.3

Table S1: All reactions were performed with 0.2 mmol of ***t*-BuSF** in Et_2O (0.1 M) and 1.0 eq. of the fluoride source. Reactions were stirred at room temperature for 24 h. Enantiomeric excess (% ee) was determined by chiral HPLC analysis.

III. Sulfonimidoyl transfer: First *S*-functionalization of *t*-BuSF.

IIIa. Reaction optimization using phenyl lithium.



Entry	Variations	Enantiopurity (% ee)	Yield (%)[a]
1	**None[c]**	**98.3**	**87**
2	THF	NA[b]	<5
3	2-Me-THF	96.4	15
4	CPME	98.3	80
5	DME[d]	96.0	75
6	MTBE	95.6	42
7	PhMe	96.5	50
8	dibutyl ether	95.6	45
9	Et_2O/THF= 8:1	97.4	67
10	Et_2O/hexane= 8:1	96.2	60
11	PhLi (1.0 eq.)	98.2	55
12	0 °C	91.1	83
13	-50 °C	96.3	85
14	TMEDA (1.5 eq.) as additive	93	75
15	HMPA (1.0 eq.) as additive	96	74
16	HMPA (10 eq.) as additive	NA[b]	0
17	DMPU (1 eq.) as additive	97.4	74
18	TBAB (1.0 eq.) as additive	95	73
19	TBAI (1.0 eq.) as additive	96	73
20	LiBr (2.0 eq.) as additive	97.5	80
21	$LiClO_4$ (1.0 eq.) as additive	98.2	48
22	$LiClO_4$ (2.0 eq.) as additive	96.2	32
23	NFSI (0.15 eq.) as additive	91.3[e]	79

23	*t*-BuSF added (0.1 mL/min)	98.4	81
24	*t*-BuSF added (0.05 mL/min)	98.3	83
25	*t*-BuSF added (0.025 mL/min)	98.3	81
26	*t*-BuSF added (0.01 mL/min), 0.05 M	98.2	75
27	*t*-BuSF added (0.01 mL/min), 0.2 M	98.3	74
28	PhLi added (0.1 mL/min)	97.6	80
29	PhLi added (0.05 mL/min)	98.2	92
30	PhLi added (0.025 mL/min)	98.4	83
31	PhLi added (0.01 mL/min)	98.5	91
32	PhLi added (0.01 mL/min), 0.05 M	98.2	81
33	PhLi added (0.01 mL/min), 0.2 M	97.5	73
34	PG = $CON(Me)_2$	NA[b]	0
35	PG = $CON(Et)_2$	NA[b]	< 5
36	PG = Piv	NA[b]	0
37	PG = Boc	NA[b]	< 5
38	PG = Bz	NA[b]	0

Table S2: All reactions were performed on a 0.3 mmol scale and ***t*-BuSF** added dropwise to PhLi (1.9 M in dibutyl ether) at -78 ºC unless otherwise stated. Reactions were quenched within 1 hour after addition. Enantiopurity was determined by chiral HPLC relative to a racemic standard. [a]Isolated yield. [b]Not available. [c]No observable difference in yield or % ee when forming PhLi *in situ* using GP-1 or GP-2. [d]1,2-dimethoxyethane (DME) was warmed to -50 °C due to its melting point. [e]*t*-BuSF (93.5% ee) prepared using Selectfluor instead of NFSI. Addition rates (entries 23-33) were controlled via syringe pump.

During reagent development, we noticed the choice of solvent played a crucial role in reactivity and stereospecificity sulfonimidoyl transfers. Polar and non-polar aprotic solvents were evaluated (entries 1-10) where Et_2O and cyclopropylmethyl ether (CPME, entry 4) were found to give the highest isolated yields (87% and 80% yield) and identical enantiopurity (98.3% ee). Surprisingly, THF (entry 2) provided no observable conversion at -78 ºC or after warming to room temperature, despite additional equivalents of nucleophile (up to 5 eq.)—while 2-MeTHF (entry 3) gave a 15% yield with 96% ee. However, when THF was used as a co-solvent (8:1 Et_2O/THF, entry 9) reactivity was recovered with a slight decrease in enantiopurity. Other ethereal solvents including 1,2-dimethoxyethane (DME, entry 5), methyl *tert*-butyl ether ether (MTBE, entry 6), dibutyl ether (entry 8) and a mixture of Et_2O/hexanes (8:1, entry 9) delivered the desired sulfoximine, albeit in lower yields and slightly lower enantiopurities. When a non-polar aprotic solvent such as toluene was used (entry 7), the target sulfoximine was isolated in

a 50% yield with 96% ee. The temperature at which the reaction is initiated was found to have an even greater negative influence on the stereochemistry (entries 11 and 12) while maintaining good reactivity.

Based on the solvent screen data, we hypothesized that the aggregation and coordination of the organolithium species in solution influences both reactivity and the stereochemical outcome (*t*-BuSF was fully soluble in all solvents at cryogenic temperatures). To this end, additives known to form chelates in solution were explored such as TMEDA (entry 14), HMPA (entries 15 and 16), DMPU (entry 17), and tetrabutylammonium counterions (entries 18 and 19). The complexing ability of TMEDA, HMPA and DMPU was thought to increase the nucleophilicity of PhLi at -78 ºC in hopes of preserving stereochemical purity. Unfortunately, enantiomeric excess did not increase in the presence of additional chelating agents but decreased by 5% with TMEDA and to a lesser extent with HMPA (2%) and DMPU (0.6%)—increasing the equivalents of HMPA from 1–10 eq. resulted in no observable product. The tetrabutylammonium counterions of TBAB and TBAI also resulted in a decrease in enantiomeric excess of 3% and 2% respectively.

Given that the additive chelates and counterions failed to improve the stereospecificity of the addition–elimination at sulfur, we turned to increasing the concentration of soluble Li^+ cations to facilitate weakening the S–F bond and act as a Lewis acid to improve the reactivity at sulfur under cryogenic temperatures. A surprising decrease in t-BuSF consumption was observed when 1 eq. of $LiClO_4$ (entry 20), albeit with nearly identical enantiopurity. Additionally, 2 eq. of $LiClO_4$ (entry 21) resulted in a 1.8% decrease of ee. It is important to note that a solution of $LiClO_4$ in Et_2O was added to the PhLi at -78 ºC prior to *t*-BuSF addition—the addition of an ethereal solution of $LiClO_4$ to *t*-BuSF at room temperature resulted in full decomposition prior to organolithium addition.

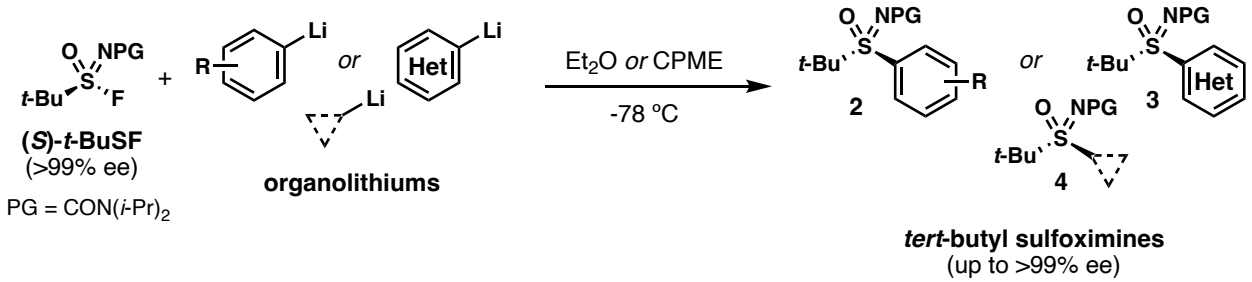
Due to the small decrease in enantiopurity from the starting sulfonimidoyl fluoride (99.4% ee; 99.7:0.3 er) to the *tert*-butylphenyl sulfoximine product (98.3% ee; 99.15:0.85 er), we found it plausible that a trace impurity within the *t*-BuSF could contribute to the 0.55% increase of the undesired enantiomer during the reaction. It was found that the addition of NFSI to the PhLi solution at -78 ºC prior to adding *t*-BuSF reduced the enantiopurity from 93.5% to 91.4% ee accompanied by the addition of phenyl sulfonamide (by-product of NFSI reacting with PhLi) to *t*-BuSF (observed by LC–MS). With careful analysis by HPLC and NMR, we determined the purity level has maintained $\geq$ 99% with routine storage (-20 ºC, under argon)—lower grade *t*-BuSF (< 95% pure) has shown slightly lower yields (5-10% less) but ***no*** decrease in stereochemical purity of sulfoximine products. These results suggest that unreacted NFSI could lower the stereochemical purity of *tert*-butyl sulfoximine products and both should be removed via work-up and column chromatography prior to use.

Since no improvement to the stereochemical yield was achieved by changing solvents, temperatures, or including additives, a thorough investigation into the order of addition and rate of addition was implemented (entries 23-33). We found that the order of addition did not significantly impact the enantiopurity or yield, but we strongly suggest slow addition of *t*-BuSF to an organolithium (especially an organolithium that has not been

well studied). It appears that slow addition of *t*-BuSF (0.1 mL/min) is ideal and was used as a standard throughout this manuscript (*a syringe pump was only used for reaction optimization*). Interestingly, addition of PhLi to *t*-BuSF at -78 ºC at a rate of 0.1 mL/min gave 97.6% ee while slower additions (0.05 to 0.01 mL/min) give >98% ee. The overall concentration of the reaction mixture did not appear to influence the stereochemical distribution of products, however, a concentration of at least 0.1 M is highly suggested.

The robustness of our –CON(*i*-Pr)$_2$ sulfonimidoyl protecting group has been demonstrated against two urea analogs (*N*,*N*-dimethyl, entry 34; *N*,*N*-diethyl, entry 35) and the three commonly encountered protecting groups –Boc (entry 36), –Piv (entry 37) and –Bz (entry 38). Out of the three different functional groups (urea, carbamate, acyl), the urea-based groups provided the increased electron density and enough steric bulk (*N*,*N*-diisopropyl) to completely diminish the reactivity at the carbonyl center of the protecting group. The discovery of *N*,*N*-diisopropyl sulfonimidoyl urea groups has enabled the first functionalization of *t*-BuSF, giving rise to stable and diversifiable S(VI) and S(IV) intermediates to be further functionalized. ***During the course of this optimization, unreacted t-BuSF was analyzed (not for every entry) and was determined to be >99% ee in every case.***

IIIb. General procedures for the first *S*-functionalization of *t*-BuSF.



Scheme S4: General scheme for the synthesis of *tert*-butyl sulfoximines from *t*-BuSF and organolithium reagents.

During the course of this study, we have found that sulfonimidoyl transfer of *t*-BuSF is compatible with a wide range of organolithiums including aryl, heteroaryl and alkyl examples with good to high yields and excellent stereochemical purity. Although many alkyl organolithiums provide the desired sulfoximine in high yields and enantiomeric excess (ee), the subsequent functionalization at sulfur results in an undesirable decrease in percent ee, thus we focused on aryl and heteroaryl sulfonimidoyl transfers for the first functionalization using *t*-BuSF followed by functionalization with aliphatic nucleophiles (Grignards and turbo-Grignards). Sulfoximines bearing two aliphatic substitutions and alkyl sulfonimidamides can be prepared using this method, however, a thorough investigation of the stereochemical purity of these products was not conducted and we cannot guarantee favorable stereochemical outcomes.

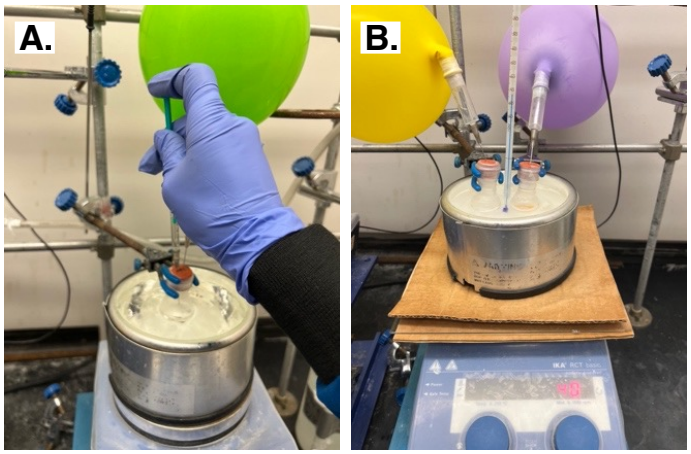
IIIb-1. General procedure 1 (GP-1): Stepwise addition.

All reactions were performed on a 0.25 mmol scale unless otherwise stated with a final reaction volume of 0.1 M in Et_2O or CPME.

To a 10 mL flame dried round-bottom flask equipped with magnetic stir bar and argon balloon was added aryl bromide (0.375 mmol, 1.5 eq.) followed by anhydrous Et_2O (2 mL) then cooled to -78 ºC. *n*-BuLi (0.375 mmol, 1.5 eq., 2.5 M in hexane) was added dropwise and stirred for 1 hour (lithium-halogen exchange) then ***t*-BuSF** (66.5 mg, 0.25 mmol, 1 eq.) in Et_2O (0.5 mL) was added dropwise. The reaction mixture stirred at -78 ºC for 1 hour (unless otherwise stated; *vide infra*). Upon completion (checked by TLC and LC–MS) MeOH (0.2 mL) and saturated aqueous NH_4Cl (5 mL) were added to quench the reaction. The mixture was transferred to separatory funnel and extracted with EtOAc (5 ml x 3), then washed with water (10 mL x 3) and brine (10 mL x 3). Dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Further purification was performed by silica gel column chromatography to give the desired *tert*-butyl sulfoximines.

Notes:

1. In some cases, lithium–halogen exchange was warmed up to -40–0 ˚C for 20 mins to achieve full exchange; see specific example for more details.
2. Dry ice/acetone bath can be used to maintain different temperatures by subsequent addition of dry-ice and monitored using a thermometer.
3. Excess organolithium nucleophile (1.5 eq.) was used unless otherwise stated in the specific example.
4. Full lithium–halogen exchange was not always observed and can be further optimized in a substrate specific manner to increase overall conversion and yield.
5. MeOH was used to quench the reaction efficiently to prevent immediate freezing when quenched with only saturated aqueous NH_4Cl.
6. *n*-BuLi (2.5 M in hexanes) was purchased from Sigma-Aldrich and used without further titration. We recommend using 25 mL bottles that have not been open for more than 3 months with storage at -20 ºC (unless titration in Et_2O was performed before use).
7. All the *tert*-butyl sulfoximines prepared could be visualized by TLC using a PMA stain.
8. All racemic sulfoximines were prepared using the same method as the chiral examples.



Graphical Procedure 4: General procedure (GP-1) for the synthesis of *tert*-butyl sulfoximines. **A.** Addition of *t*-BuSF to a pre-generated organolithium at -78 ºC. **B.** Two reactions side-by-side after the addition of *t*-BuSF.

IIIb-2. General procedure 2 (GP-2): One-pot lithiation/S(VI) transfer.

All reactions were performed on a 0.25 mmol scale unless otherwise stated with a final reaction volume of 0.1 M in Et_2O or CPME.

To a 10 mL flame dried round-bottom flask equipped with magnetic stir bar and argon balloon was added aryl/alkyl bromide (0.375 mmol, 1.5 eq.) followed by ***t*-BuSF** (66.5 mg, 0.25 mmol, 1 eq.) and anhydrous Et_2O (2.5 mL). Cooled to -78 ºC and *t*-BuLi (0.22 mL, 1.7 M in pentane, 1.5 eq.) was added dropwise. The reaction mixture was stirred at -78 ºC for 1 hour (some substrates required longer Li–X exchange times; *vide infra*). Upon completion (checked by TLC and LC–MS) MeOH (0.2 mL) and saturated aqueous NH_4Cl (5 mL) were added to quench the reaction. The mixture was transferred to separatory funnel and extracted with EtOAc (5 ml x 3), then washed with water (10 mL x 3) and brine (10 mL x 3). Dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Further purification was performed by silica gel column chromatography to give the desired *tert*-butyl sulfoximines.

Notes:

1. *t*-BuLi (1.7 M in pentane) was purchased from Sigma-Aldrich and used without further titration. We recommend using 25 mL bottles that have with uncompromised septa and have been stored at -20 ºC (unless titration in Et_2O was performed before use).
2. Dry ice-acetone bath can be used to maintain different temperatures by subsequent addition of dry-ice and monitored using a thermometer.
3. Longer reaction times and elevated temperatures were required (prior to ***t*-BuSF** addition) for some substrates to provide satisfactory lithium–halogen exchange and overall conversions (*vide infra*).
4. GP-1 was used for most substrates. GP-2 was spot checked with various examples without notable diminished yields and conversion.

5. We recommend using GP-1 as the initial lithiation method; however, some substrates are more compatible with *t*-BuLi and either a stepwise (GP-1 with *t*-BuLi) or premixed (GP-2) should be compatible.
6. The nucleophilic addition of *t*-BuLi to *t*-BuSF (di-*tert*-butyl sulfoximine) occurs at elevated temperatures (around -10 ºC) and did not significantly interfere with the lithium–halogen exchange within the reaction scope.
7. If a substrate is known to undergo lithium–halogen exchange with *t*-BuLi at temperatures higher than -20 ºC, we recommend using the stepwise method with *t*-BuLi (GP-1).
8. For some cases (noted below), 2 eq. of *t*-BuLi with respect to the organohalide was required to obtain efficient Li-X exchange.
9. Use of *n*-BuLi instead of *t*-BuLi for this procedure does not provide sufficient lithium–halogen exchange over *n*-butyl addition to ***t*-BuSF**, in which case *tert*-butyl(*n*-butyl) sulfoximine is observed.
10. All racemic sulfoximines were prepared using the same method as the chiral examples.

IIIb-3. General procedure 3 (GP-3): Lithiation of (hetero)aryl halides and more challenging substrates.

All reactions were performed on a 0.25 mmol scale unless otherwise stated with a final reaction volume of 0.1 M in Et_2O or CPME.

To a flame dried round-bottom flask equipped with magnetic stir bar under argon was added (hetero)aryl halide (0.375 mmol,1.5 eq.) followed by Et_2O (2.0 mL) then cooled to -78 °C. *n*-BuLi (0.150 mL, 0.375 mmol, 2.5 M in hexane, 1.5 eq.) was added dropwise and stirred at -78 °C for 30 minutes then warmed to -20–0 °C gradually and stirred for another 30 minutes then cooled to -78 °C. A solution of ***t*-BuSF** (0.25 mmol, 1 eq.) in Et_2O (0.5 mL) was added dropwise. The reaction mixture was stirred at -78 ºC for 1 hour (or warmed to the temperature noted below). Upon completion (checked by TLC and LC–MS) MeOH (0.2 mL) and saturated aqueous NH_4Cl (5 mL) were added to quench the reaction. The mixture was transferred to separatory funnel and extracted with EtOAc (5 ml x 3), then washed with water (10 mL x 3) and brine (10 mL x 3). Dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Further purification was performed by silica gel column chromatography to give the desired *tert*-butyl sulfoximines.

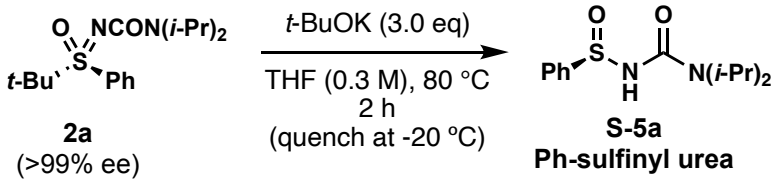
Notes:

1. Most organolithiums were stable at 0 °C during the preparation period.
2. This procedure was used to deprotonate heterocycles such as thiophenes and thiazoles.
3. Some substrates require higher temperatures (>0 °C) for Li-X—they are noted specifically in the substrate characterization section.
4. Dry ice-acetone bath can be used to maintain different temperature by subsequent addition of dry-ice and monitored using a thermometer.

5. The successful preparation of organolithiums is crucial for reaction with ***t*-BuSF**. Lithium–halogen exchange is substrate dependent and can be checked by LC–MS and/or TLC to determine the progress of the exchange. Full exchange was not always observed and can be further optimized to increase overall conversion and yield.
6. All racemic sulfoximines were prepared using the same method as the chiral examples.

IV. *S*-Activation of *tert*-butyl sulfoximines for further functionalization.

IVa. Reaction optimization: Reductive de-*tert*-butylation of sulfoximines



Entry	Variations	Enantiopurity (% ee)	Yield (%)[a]
1	**None**	**>99**	**88**
2	4 h	>99	87
3	8 h	>99	88
4	dioxane	>99	60
5	DMF	91	75
6	quench at 0 °C	97	84
7	quench at rt	93	83
8	TFA (0.2–1.5 eq.), DCM (0.25 M), rt	NA	decomposed
9	4.0 M HCl in Dioxane (5–20 eq.) DCM (0.2 M), -78 to 0 °C	NA	decomposed
10	BF_3•OEt_2 (1.0 eq.), THF (0.1 M), 0 to 50 ºC[b]	NA	decomposed
11	$Mg(ClO_4)_2$ (1.0 eq.), THF (0.2 M), rt to 80 ºC[b]	NA	NR
12	BH_3 (2.0 eq.), THF (0.2 M), rt	NA	NR
13	Selectfluor (2.0 eq.), MeCN (0.1 M) rt to 50 ºC, 48 h	NA	(< 20%)[c]

Table S3: Optimization of a reductive de-t*ert*-butylation of *N,N*-diispropyl urea protected chiral tert-butyl sulfoximines to sulfinyl ureas. All reactions were performed on a 0.3 mmol scale in a flame dried flask under argon with anhydrous solvents. Enantiopurity was determined by chiral HPLC. Reactions were quenched with solvated (THF/DCM) silica gel. [a]Isolated yield.

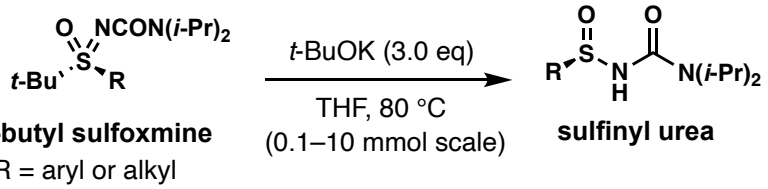
[b]Decomposed upon heating. [c]Relative yield based on LC–MS. NA = not available. NR = no reaction.

The reduction of various N–substituted *tert*-butyl sulfoximines to sulfinamides by de-*tert*-butylation has been previously described in the literature for N–alkyl and N–acyl sulfoximines.[2-6] Known reaction conditions were screened with enantiopure *tert*-butyl phenyl sulfoximine bearing the *N*,*N*-diisopropyl urea protecting group. We found one condition to be superior with the sulfonimidoyl urea protecting group (*t*-BuOK, THF, 80 ºC; entries 1-3), providing clean (quantitative by LC–MS analysis) conversion to the desired sulfinyl urea in high isolated yield and excellent stereochemical purity (>99%). The choice of solvent proved critical for both yield and stereospecificity. When dioxane was used, longer reaction times were required with lower isolated yield while maintaining excellent enantiopurity (entry 4). DMF led to enantio-erosion (75% ee) when applied to our sulfonimidoyl ureas (entry 5).

We found that the quench and work-up conditions were directly related to enantiopurity of the sulfinyl urea product. Quenching the reaction mixture with a mild aqueous acid such as NH_4Cl results in decomposition of target sulfinyl urea whereas quenching with diluted silica gel (wet with DCM and THF) or AcOH (2 1.5–2 eq.) in THF at -20 ºC provides the desired enantiopure product after filtration through a silica gel plug. When the reactions are quenched at temperatures above -20 ºC (entries 6 and 7), a decrease in enantiopurity is observed, *which we speculate is a result of the exotherm generated upon quenching excess t-BuOK in solution.*

Bronsted acids that have been reported to reduce *tert*-butyl sulfoximines such as TFA (entry 8) and HCl (entry 9) resulted in decomposition of either the sulfoximine or sulfinamide (the sulfinyl urea is not stable under strong acidic conditions). The strong Lewis acidity of BF_3 (entry 10) gave decomposition at elevated temperatures while no appreciable consumption was observed at room temperature. In addition, no reaction was observed when $Mg(ClO_4)_2$ was heated in THF at 80 ºC (entry 11). Reductive conditions using BH_3 were ineffective regardless of the source of BH_3 used (commercial solutions or generated *in situ* from $NaBH_4/I_2$). Interestingly, upon treatment with Selectfluor in MeCN (entry 13), the sulfinyl urea can be observed by LC–MS along with decomposition side-products. Attempts to optimization the Selectfluor condition were unsuccessful with respect to the sulfinyl urea—further investigation toward a one-pot de-*tert*-butylation/fluorination method is discussed in a later section.

IVb. General procedure 4 (GP-4): reductive de-*tert*-butylation of sulfoximines to sulfinyl urea using *t*-BuOK.



***tert*-butyl sulfoxmine**
R = aryl or alkyl

sulfinyl urea

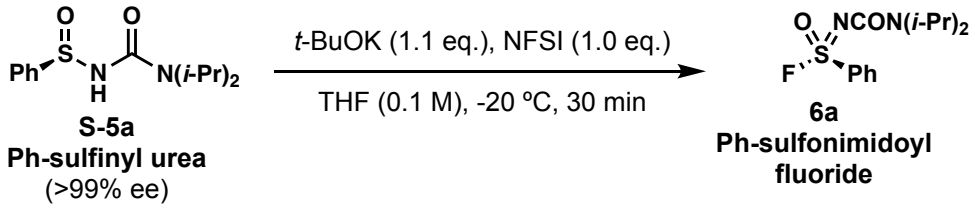
Scheme S5: General reaction condition for the reductive de-*tert*-butylation of *N*,*N*-diisopropyl urea protected chiral *tert*-butyl sulfoximines to sulfinyl ureas.

In a septum capped flame dried round-bottom flask equipped with a stir bar and argon balloon was added *tert*-butyl sulfoximine (1 eq.) followed by THF (0.3 M). Solid *t*-BuOK (3 eq.) was added, and the reaction stirred at room temperature for 2-5 minutes. The argon balloon was removed, and the reaction placed in a pre-heated oil bath set to 80 ºC for 2 hours (behind a blast shield). Upon competition (checked by TLC) the reaction was cooled to -20 ºC then quenched by adding a solution of AcOH (2 eq.) in THF (1-2 M) followed by silica gel (10:1, silica gel to starting material by mass) *or* by adding wet (THF and DCM) silica gel (20:1, silica gel to starting material by mass) with continual stirring at -20 ºC for 2-5 minutes. The reaction mixture containing silica was filtered a plug of silica gel (wet with DCM) and rinsed with DCM. The filtrate was concentrated under reduced pressure via rotary evaporated with a water bath set to 25 ºC to give the desired sulfinyl urea in 80-90% yields with high purity.

Notes:

1. Anhydrous THF was used. *t*-BuOK was purchased from Oakwood Chemical company and stored in a desiccator under argon. Pure AcOH was used, not an aqueous solution.
2. The argon balloon is removed to prevent evaporation of THF and contamination (from the solvent condensing in the balloon) during the reaction.
3. A blast shield is used as a safety precaution when heating any closed vessel higher than the solvent's boiling point.
4. The reactions were very clean with only the desired product detected by LC–MS (once full consumption was achieved).
5. Larger scale reactions (up to 10 mmol) provided >90% yields.
6. The reaction mixture can be adsorbed to silica gel and purified by column chromatography if desired. We found filtering through a plug of silica gel to be more convenient.
7. We avoided heating chiral sulfinamides under neutral or acidic conditions, regardless of the substitution at sulfur or nitrogen, due to their known stereochemical instability.
8. If a sulfonimidoyl fluoride is the desired synthetic target or intermediate, see the following sections for alternative methods.

IVc. Reaction optimization: Enantiospecific *S*-fluorination of sulfinyl ureas to sulfonimidoyl fluorides



S-5a
Ph-sulfinyl urea
(>99% ee)

6a
Ph-sulfonimidoyl fluoride

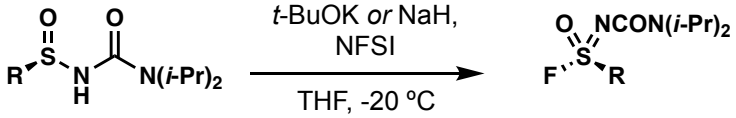
Entry	Variations	Enantiopurity (% ee)	Yield (%)[a]
1	**None**	**> 99**	**91**
2	0 °C, 5 min	98	60
3	0 °C, 30 min	98	93
4	-78°C, 2 h	> 99	65
5	DMF	96	81
6	NaH (1.5 eq.), 0 °C	97	90
7	**NaH (1.5 eq.), -20 °C**	**> 99**	**89**
8	EtOH (0.2 M), AcOK (2.0 eq.) selectfluor(2.0 eq.), 0 °C to rt, 24 h	97	87
9	DME, 0 °C, NaOH (1.5 eq.)	98	83

Table S4: Optimization of *S*-fluorination of chiral sulfinyl ureas to *N*,*N*-diisopropyl urea protected sulfonimidoyl fluorides. All reactions were performed on 0.3 mmol scale in a flame dried flask under argon. Enantiopurity was determined by using chiral HPLC. [a]Isolated yield.

The selective asymmetric *S*-fluorination of *N*,*N*-diisopropyl sulfinyl ureas to protected sulfonimidoyl fluorides is a key step to enable the *t*-BuSF reagent bifunctional. With enantiopure sulfinyl urea in hand, we determined two suitable conditions to achieve high yields and stereochemical preservation at sulfur (entries 1 and 7). The temperature used for *S*-fluorination influences stereochemical outcome. At 0 ºC, excellent enantiopurity (97% to 98% ee) regardless of reaction time (entries 2 and 3) or the base used (entry 6). Decreasing the temperature to -78 ºC provides >99% ee while reducing the reaction rate (entry 4). When the solvent was replaced with DMF (entry 5) both yield and enantiomeric excess dropped to 81% and 96% respectively.

The reported condition for *S*-fluorination of enantiopure N-Boc sulfinyl carbamates to sulfonimidoyl fluorides developed by Bull and Lücking[7] was found to give high yields (87%) with a reduction in enantiopurity (97% ee) when translated to our sulfinyl ureas (entry 8). Lastly, we employed the conditions used for Maruoka's S-alkylation of enantiopure *N*-Piv sulfinamides (entry 9),[8] which gave the desired sulfonimidoyl fluoride with slight erosion in enantiopurity (98% ee).

IVd. General procedure 5 (GP-5): synthesis of *N,N*-diisopropyl urea protected chiral sulfonimidoyl fluorides from sulfinyl ureas.



sulfinyl urea **sulfonimidoyl fluoride**

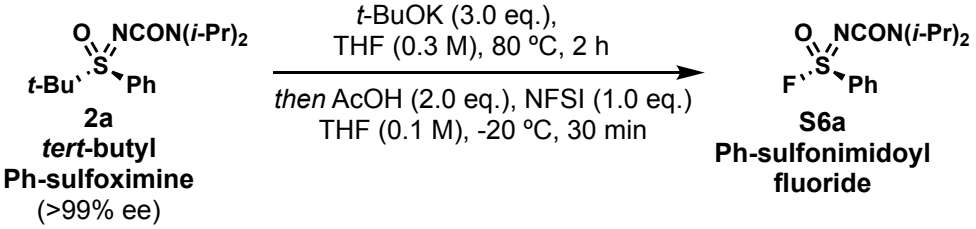
Scheme S6: General reaction conditions for the *S*-fluorination of chiral sulfinyl ureas to *N,N*-diisopropyl urea protected sulfonimidoyl fluorides.

In a septum capped flask or reaction vial equipped with a stir bar and argon balloon was added sulfinyl urea (1 eq.) and THF (0.1 M) then cooled to -20 ºC. Either solid *t*-BuOK (1.1 eq.) *or* NaH (1.5 eq., 60% wt) was added (in one portion for small scale reactions, portion wise for >5 mmol scales) and the reaction stirred for 15 minutes at -20 ºC. NFSI (1 eq.) was added in one portion and the reaction continued to stir for 30 minutes at -20 ºC. Upon completion (checked by TLC) the reactions were quenched with saturated aqueous NH_4Cl and extracted with EtOAc (x 3). Combined organic layers were washed with water and brine, dried over Na_2SO_4, filtered and concentrated. Further purification by silica gel column chromatography provided the desired sulfonimidoyl fluorides.

Notes:

1. Anhydrous solvent and reagents were used.
2. The choice of base did not affect the yield or enantiopurity on any scale up to 7 mmol (the largest performed).
3. Portion wise addition of base at larger scales was chosen to minimize the amount of heat generate from exotherms produced from deprotonation as well as vigorous hydrogen gas evolution when NaH was employed.
4. Quenching at temperatures higher than -20 ºC did not affect yield or enantiopurity.
5. Although this method can provide high yields and enantiopurity, the stereogenic liability of sulfinamides (under neutral and acidic conditions) prompted an alternative method for sulfonimidoyl fluoride preparation.

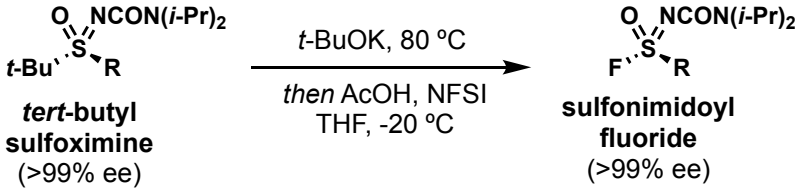
IVe. Reaction optimization: Enantiospecific S-activation of *tert*-butyl sulfoximines to sulfonimidoyl fluorides.



Entry	Variations	Enantiopurity (% ee)	Yield (%)[a]
1	**None**	**> 99**	**81**
2	**None**	**> 99**	**84[b]**
3	**None**	**> 99**	**78[c]**
4	2.5 eq. AcOH	> 99	73
5	1.5 eq. AcOH	> 99	75
6	0°C insteand of -20°C	98	80
7	no AcOH	NA[d]	ND[e]
8	Selectfluor (2.2 eq.), MeCN (0.1 M) 50 ºC, 48 h	40	62

Table S5: Optimization of a one-pot transformation of chiral *N,N*-diisopropyl urea protected *tert*-butyl sulfoximines to sulfonimidoyl ureas. All reactions were performed on 0.3 mmol scale in a flame dried flask under argon. Enantiopurity was determined by using chiral HPLC. [a]Isolated yield. [b]reaction performed on 1.5 mmol scale (500 mg). [c]reaction performed on >3 mmol scale (>1 g). [d]Not available. [e]Not detected.

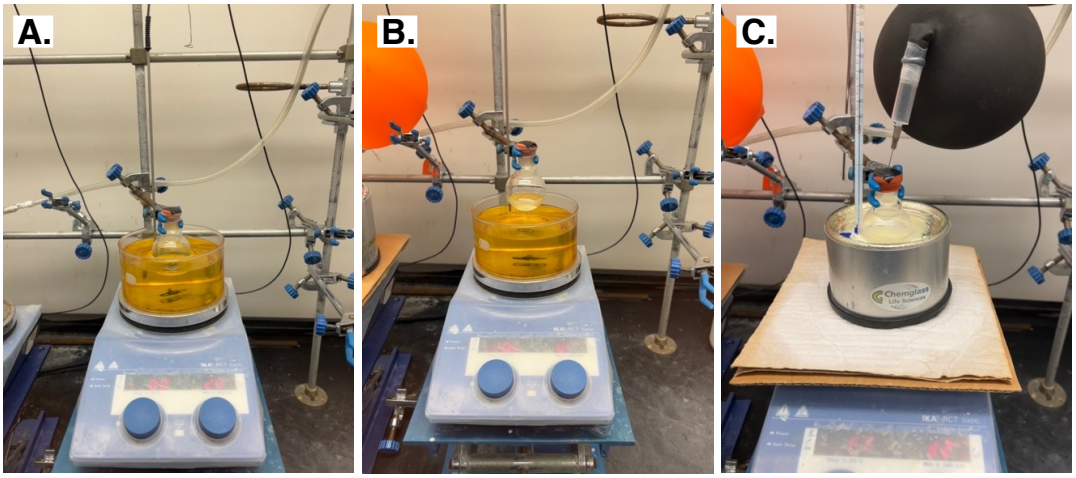
IVf. General procedure 6 (GP-6): enantiospecific de-*tert*-butylation/S-fluorination of *tert*-butyl sulfoximines to sulfonimidoyl fluorides



Scheme S7: General reaction condition for the one-pot transformation of chiral *N,N*-diisopropyl urea protected *tert*-butyl sulfoximines to sulfonimidoyl ureas.

To a flame dried round-bottom flask equipped with magnetic stir bar and argon balloon was added
t-Bu sulfoximine (1.0 eq) and anhydrous THF (0.3 M). Once dissolved, solid anhydrous *t*-BuOK (3.0 eq) was added, and the reaction stirred at room temperature for 2-5 minutes. The argon balloon was removed, and the reaction placed in a pre-heated oil bath set to 80 ºC for 2 hours (behind a blast shield). After 2 h (or upon completion; checked by TLC),

the argon balloon was replaced then the reaction was cooled to -20°C with dry ice and acetone bath. AcOH (2.0 eq) dissolved in anhydrous THF was added slowly to dilute the reaction to 0.1 M. Solid NSFI (1.0 eq) was added in one portion, and the reaction stirred at -20°C for 30 mins. Upon completion (checked by TLC) the reaction was quenched with saturated aqueous NH_4Cl solution at -20 °C and extracted with EtOAc (x 3). Combined organic layers were washed with water (x 3) and brine (x 3), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Further purification was performed by silica gel column chromatography to provide the desired sulfonimidoyl fluoride.

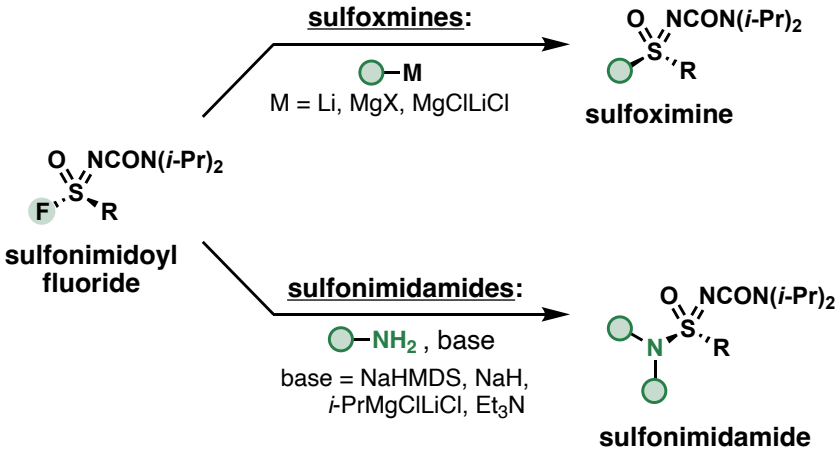


Graphical set-up 1: One-pot transformation of chiral *N,N*-diisopropyl urea protected *tert*-butyl sulfoximines to sulfinyl ureas. **A.** Reduction of *t*-butyl sulfoximines via de-*tert*-butylation using *t*-BuOK, heating at 80 ºC in THF. **B.** Cooling to room temperature after 2 hours at 80 ºC. **C.** Cooling to -20 ºC and quenching with AcOH (2 eq.) followed by addition of NFSI (1 eq.).

Notes:

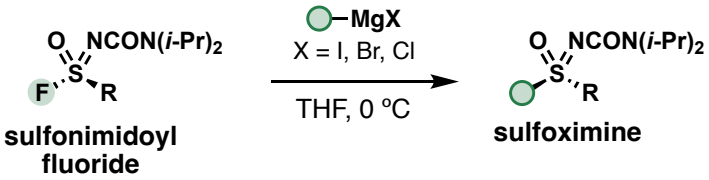
1. Anhydrous solvent and reagents were used.
2. Each step can be monitored by TLC (UV or PMA).
3. -20 ºC or lower is crucial for maintaining enantiopurity.
4. AcOH was used to quench excess *t*-BuOK present in the reaction mixture prior to addition of NFSI. If not quenched, the desired product is only observed in trace amounts—*t*-BuOK reacts with NFSI prior to the sulfinamide *and/or* degrades the sulfonimidoyl fluoride formed.
5. The first step doesn't typically show significant color change; we usually observed a change from colorless to light-yellow.
6. A white precipitate is observed after the addition of NFSI and is an indication that the fluorination reaction is proceeding.

V. Second *S*-functionalization: Enantiospecific synthesis of sulfoximines and sulfonimidamides from sulfonimidoyl fluorides.



Scheme S8: Divergent synthesis of chiral sulfoximine and sulfonimidamides from *N,N*-diisopropyl urea protected sulfonimidoyl fluorides.

Va. General procedure 7 (GP-7): Enantiospecific synthesis of sulfoximines from sulfonimidoyl fluorides using Grignard reagents.



Scheme S9: General reaction conditions for the synthesis of chiral sulfoximine from *N,N*-diisopropyl urea protected sulfonimidoyl fluorides using Grignard reagents.

The Grignard reagents were used as purchased or prepared as follows:
In a 10 mL flame dried round-bottom flask equipped a stir bar and argon balloon was added Mg turnings (73 mg, 3 mmol, 1.5 eq.) and I_2 (approx. 5 mg, 0.02 mmol, 0.01 eq.) then vacuumed and refilled with argon. A portion of alkyl bromide or iodide (2 mmol, 1 eq.) solution in anhydrous THF (4 mL) was added with gentle heat until I_2 color disappeared, the rest of solution was then added dropwise.

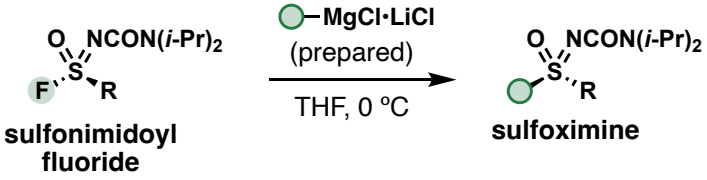
After titration with iodine, the proper amount of the Grignard reagent (0.275 mmol, 1.1 eq.) was added dropwise to a solution of the sulfonimidoyl fluoride (0.25 mmol, 1.0 eq.) in THF (2.5 mL) in a separate 5 mL flame dried septum capped vial equipped a stir bar and argon balloon at 0 ºC. The reaction was stirred at 0 ºC for 30 minutes then warmed to room temperature (unless otherwise stated below). Upon completion (checked by TLC) the reaction was quenched with saturated aqueous NH_4Cl (5 mL) then extracted with EtOAc (10 mL x 3). The combined organic layers were washed with water (5 mL x 3) then brine (5 mL x 3), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced

pressure. Further purification by silica gel column chromatography provided the desired sulfoximines.

Notes:

1. Most Grignard reactions were complete within 30 minutes at 0 ºC.
2. No significant decrease in yield or enantiopurity was observed if the reactions stirred at room temperature overnight.
3. Titrations were performed using a 0.2 M solution of I_2 in anhydrous THF.
4. All other Grignard reagents were directly purchased from Sigma-Aldrich or Acros Organics as described for each example below.

Vb. General procedure 8 (GP-8): Enantiospecific synthesis of sulfoximines from sulfonimidoyl fluorides using turbo-Grignard reagents.



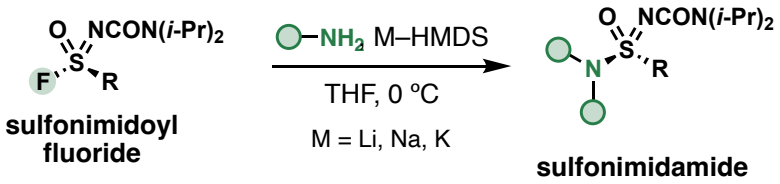
Scheme S10: General reaction conditions for the synthesis of chiral sulfoximine from *N*,*N*-diisopropyl urea protected sulfonimidoyl fluorides using turbo-Grignard reagents.

The preparation of turbo-Grignard reagents was modified from the Knochel methods, with slight variations depending on each substrate. In a 5 mL flame dried vial equipped with a stir bar and argon balloon was added isopropylmagnesium chloride lithium chloride (*i*-PrMgClLiCl) complex solution (0.21 mL, 0.275 mmol, 1.1 eq., 1.3 M in THF) followed by aryl bromide/iodide (0.275 mmol, 1.1 eq.) dissolved in dry THF (0.2 mL) at indicated temperature and exchange for indicated time (*vide infra*). Upon complete Mg-halogen exchange, a solution of sulfonimidoyl fluoride (0.25 mmol, 1 eq.) in THF (2.5 mL) was added dropwise at 0 ºC, stirred for 30 minutes then warmed to room temperature. Upon completion (checked by TLC) the reaction was quenched with saturated aqueous NH_4Cl (5 mL) then extracted with EtOAc (10 mL x 3). The combined organic layers were washed with water (5 mL x 3) then brine (5 mL x 3), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Further purification by silica gel column chromatography provided the desired sulfoximines.

Notes:

1. The completion of Mg-halogen exchange is monitored by TLC and LCMS for the complete consumption of aryl halide.
2. Isopropylmagnesium chloride lithium chloride complex solution (1.3 M in THF) was purchased from Sigma-Aldrich.
3. Some halogen exchanges require prolonged stirring at room temperature.
4. No significant decrease in yield or enantiopurity was observed if the reactions stirred at room temperature overnight.

Vc. General procedure 9 (GP-9): Enantiospecific synthesis of sulfonimidamides from sulfonimidoyl fluorides using Li/Na/KHMDS.



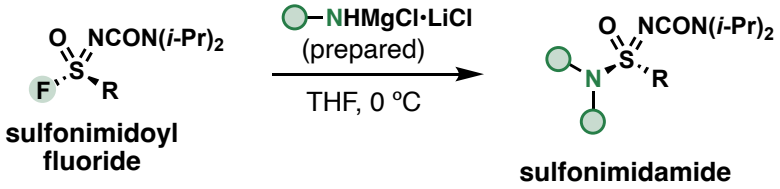
Scheme S11: General reaction conditions for the synthesis of chiral sulfonimidamides from *N,N*-diisopropyl urea protected sulfonimidoyl fluorides using Li/Na/K-HMDS as a base.

To a flame dried round-bottom flask equipped with magnetic stir bar and argon balloon, sulfonimidoyl fluoride (0.25 mmol, 1.0 eq.) and amine (1.0 eq.) were in anhydrous THF (0.1 M) at 0 °C. M-HMDS (2.0 eq.) was added dropwise to the stirring mixture at 0 °C. The reaction slowly warmed to room temperature where it stirred. Upon completion (checked by TLC) the reaction was quenched with silica gel then DCM was added, and solvent removed to adsorb the crude material to silica gel. Purification by column chromatography provided the desired sulfonimidamides.

Notes:

1. LiHMDS (1.0 M in THF), NaHMDS (2.0 M in THF) and KHMDS (0.7 M in toluene) were purchased from Acros Organics and used without titration. We found it important to use these bases within 6 months of the first use for optimal performance—older reagents provided decreased yields without affecting the enantiopurity of sulfonimidamide products.
2. We found that the counter ion (Li^+, Na^+, K^+) did not affect the enantiopurity of sulfonimidamide products.
3. Reactions can be quenched with water, brine, or saturated aqueous NH_4Cl but should be worked up immediately.
4. No significant decrease in yield or enantiopurity was observed if the reactions stirred at room temperature overnight.
5. Although this method works for most amine substrates (aromatic 1°/2° and aliphatic 1°/2° amines) we typically used this method for aromatic amines.

Vd. General procedure 10 (GP-10): Enantiospecific synthesis of sulfonimidamides from sulfonimidoyl fluorides using turbo-amides



Scheme S12: General reaction conditions for the synthesis of chiral sulfonimidamides from *N,N*-diisopropyl urea protected sulfonimidoyl fluorides using turbo-amides.

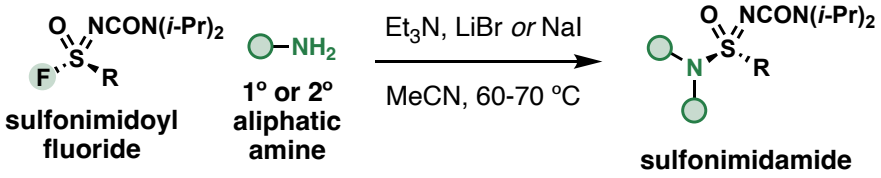
For aliphatic amines: To a flame dried round-bottom flask equipped with magnetic stir bar and argon balloon was amine (2 eq. for 1º amines, 1 eq. for 2º amines) in anhydrous THF (0.1 M) at 0 °C. *i*-PrMgCl-LiCl (2 eq. for 1º amines, 1:1; 1 eq. for 2º amines, 1:1) was added dropwise under 0 °C. After 30 minutes of stirring, sulfonimidoyl fluoride (1.0 eq.) in THF (0.5 M) was added dropwise then warmed to room temperature. Upon completion (checked by TLC) the reaction was quenched with saturated aqueous NH_4Cl then extracted with EtOAc (x 3). The combined organic layers were washed with water (x 3) then brine (x 3), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Further purification by silica gel column chromatography provided the desired sulfonimidamides.

For ammonium chloride or bromide: To a flame dried round-bottom flask equipped with magnetic stir bar and argon balloon was charged with ammonium chloride or bromide (3.0 eq.) in anhydrous THF (0.1 M) at 0 °C. *i*-PrMgCl-LiCl (6.0 eq.) was added dropwise to the vigorously stirring mixture at 0 °C (cloudy mixture) then warmed to room temperature where the reaction mixture stirred until it became nearly clear (1 hour). The reaction mixture was cooled to 0 ºC then sulfonimidoyl fluoride (1 eq.) in THF (0. 5 M) was added dropwise and slowly warmed to room temperature. Upon completion (checked by TLC) the reaction was quenched with saturated aqueous NH_4Cl then extracted with EtOAc (x 3). The combined organic layers were washed with water (x 3) then brine (x 3), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Further purification by silica gel column chromatography provided the desired sulfonimidamides.

Notes:

1. *i*-PrMgCl-LiCl was purchased from Sigma-Aldrich and used without titration.
2. Two equivalents of 1º turbo-amide were required due to the acidity of the sulfonimidamide products (**H**–N). Full consumption of the sulfonimidoyl fluoride was not achieved if one equivalent of the turbo-amide was used. Use of additional bases (NaH, NaHMDS, Et_3N) did not improve the reactions when one equivalent of turbo-amide was used.
3. Ammonium chloride or bromide reacted with turbo reagents generated gas. Releasing the gas would not affect the overall reaction. During the preparation of turbo amide, ammonium salt was slowly dissolved into the solution.

Ve. General procedure 11 (GP-11): Enantiospecific synthesis of sulfonimidamides from sulfonimidoyl fluorides under thermal conditions



Scheme S13: General reaction conditions for the synthesis of chiral sulfonimidamides from *N,N*-diisopropyl urea protected sulfonimidoyl fluorides using Et_3N as a base with LiBr or NaI organic soluble salts.

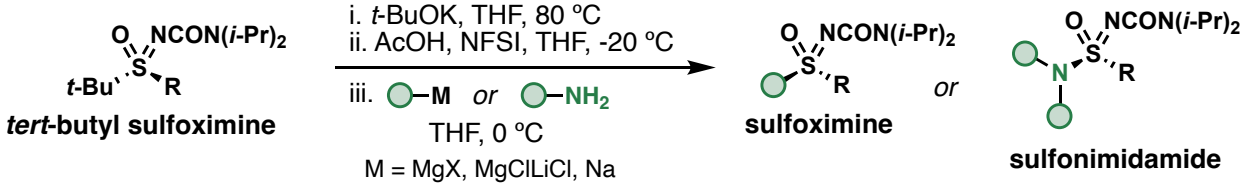
This reaction condition was adopted from the report by Bull and Luecking,[7] and slightly modified.

In a flame dried septum capped vial equipped with a stir bar and argon balloon was added sulfonimidoyl fluoride (1 eq.) followed by MeCN (0.3 M). The amine (1-1.5 eq.), LiBr (2 eq.) or NaI (2 eq.), and Et_3N (2 eq.) were added. The argon balloon was removed, and the reaction was heated to 60-70 °C for the indicated reaction time (3-48 hours). Upon completion (checked by TLC and/or LC–MS) the solvent was removed under reduced pressure and the crude material was purified by silica gel column chromatography.

Notes:

1. Anhydrous solvent and reagents were found to be necessary to achieve full consumption of the sulfonimidoyl fluoride.
2. A less hygroscopic salt (NaI) was found to be performing equally as well to give good to high yields and excellent stereospecificity. In one instance (noted below) NaI provided the desired sulfonimidamide product in higher enantiopurity compared to LiBr (>99% ee vs. 98% ee).
3. If an amine salt form is used (e.g. HCl or citrate), an extra molar equivalent (with respect to the amine salt) of Et_3N was required. Secondary amine salts provided cleaner reactions than primary amine salts.
4. The use of soluble salts such as LiBr and NaI was found to be crucial for the consumption of sulfonimidoyl fluorides. The enantiospecific was not determined without an additive salt.

Vf. General procedure 12 (GP-12): Enantiospecific synthesis of sulfoximines and sulfonimidamides from *tert*-butyl sulfoximines

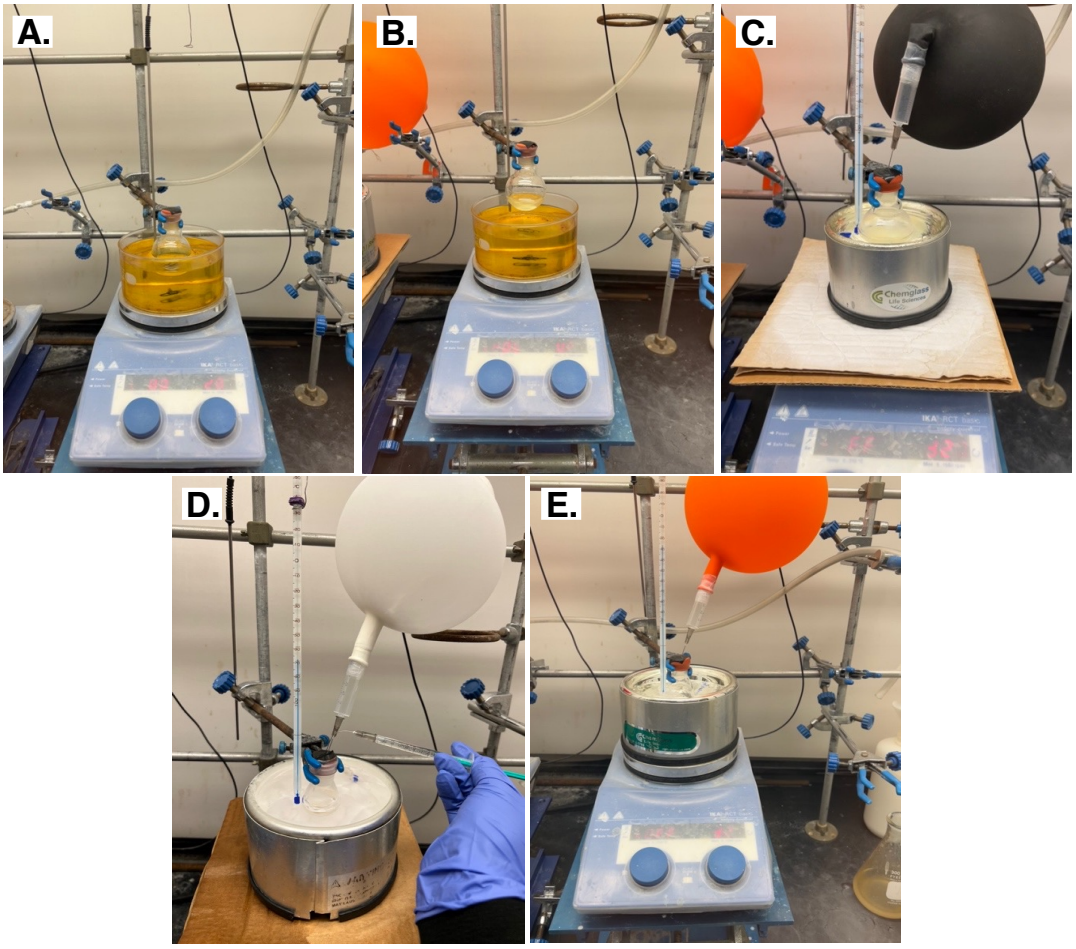


Scheme S14: General reaction conditions for a one-pot synthesis of chiral sulfoximine and sulfonimidamides from *N,N*-diisopropyl urea protected *tert*-sulfoximines.

To a flame dried round-bottom flask equipped with magnetic stir bar and argon balloon was added *tert*-butyl sulfoximine (1 eq.) followed by anhydrous THF (0.3 M). Once dissolved, solid anhydrous *t*-BuOK (3.0 eq) was added, and the reaction was stirred at room temperature for 2-5 minutes. The argon balloon was removed, and the reaction was placed in a pre-heated oil bath set to 80 ºC for 2 hours (behind a blast shield). After 2 h (or upon completion; checked by TLC), the argon balloon was replaced then the reaction was cooled to -20°C with dry ice and acetone bath. AcOH (2.0 eq) dissolved in anhydrous THF was added slowly to dilute the reaction to 0.1 M. Solid NSFI (1.0 eq) was added in one portion, and the reaction was stirred at -20°C for 30 mins. Upon completion (checked by TLC) either the Grignard or amine nucleophile was added.

Grignard nucleophiles:
The Grignard reagent (2 eq.) was added dropwise to the reaction mixture and stirred for one hour at -20 ºC (for certain case -78 °C was used instead, see substrate part for additional details). Upon completion (checked by TLC) the reaction was quenched with saturated aqueous NH_4Cl solution then extracted with EtOAc (x 3). The combined organic layers were washed with water (x 3) then brine (x 3), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Further purification by silica gel column chromatography provided the desired sulfoximines.

Amine nucleophiles:
While the reaction was still at -20 ºC from the fluorination step, the amine (1 eq.) and NaHMDS (2 eq.) were sequentially added to the reaction then slowly warmed to room temperature (2.0 eq turbo amide were used instead of 1.0 eq). Upon completion (checked by TLC) the reaction was quenched with silica gel then DCM was added, and solvent removed to adsorb the crude material to silica gel. Purification by column chromatography provided the desired sulfonimidamides.



Graphical Procedure 5: One-pot transformation of chiral *tert*-butyl sulfoximines to sulfoximines or sulfonimidamides. **A.** Reduction of *tert*-butyl sulfoximines via de-*tert*-butylation using *t*-BuOK, heating at 80 ºC in THF. **B.** Cooling to room temperature after 2 hours at 80 ºC. **C.** Cooling to -20 ºC and quenching with AcOH (2 eq.) followed by addition of NFSI (1 eq.). **D.** cooling to -78 ºC then adding Grignard or turbo-Grignard reagent. **E**. While at -20 ºC the desired turbo-amide or amine/NaHMDS was added then warmed to room temperature.

Notes:

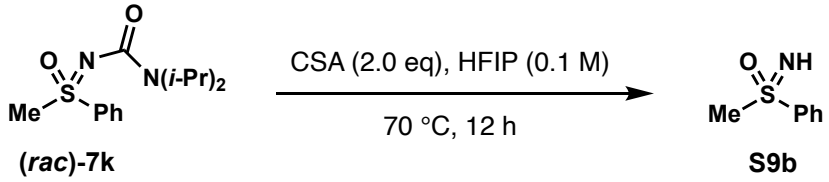
1. Each step can be monitored by TLC (UV or PMA).
2. -20°C or lower is crucial for maintaining enantiopurity for the fluorination step and the addition of amines.
3. Two equivalents of the Grignard reagents were required due to the presence of *t*-BuOH in the reaction mixture (after quenching with AcOH). The use of a sacrificial Grignard was investigated but the reaction rate for the nucleophilic addition to sulfonimidoyl fluorides and deprotonation appeared to be very similar.
4. Amine nucleophiles can be deprotonated first and then added to the reaction in the form of amides without reduction of enantiopurity. The turbo amide was prepared from *i*-PrMgCl-LiCl and amine. And 2.0 eq turbo amide were added.

5. Reactions can be quenched with water, brine, or saturated aqueous NH_4Cl but should be worked up immediately.
6. We did not observe a reduction in enantiopurity using this one-pot transformation versus the stepwise synthesis.

VI. Deprotection of *N,N*-diisopropyl urea protecting group from sulfoximines and sulfonimidamides

The development of a useful and practical sulfonimidoyl transfer reagent requires access to the free N–H derivatives that are more commonly investigated within the chemical sciences. We have demonstrated that the use of a sterically demanding urea-type sulfonimidoyl group enables synthesis of chiral sulfonimidoyl urea compounds in an expedient manner from a common bench stable reagent (*t*-BuSF). This section further demonstrates the unique features of the *N,N*-diisopropyl urea sulfonimidoyl group by its removal to N–H sulfoximines and sulfonimidamides under various reaction conditions, providing a new protecting group for the synthesis of sulfonimidoyl compounds.

VIa. Reaction optimization: Deprotection of *N,N*-diisopropyl sulfonimidoyl ureas to N–H sulfoximines and sulfonimidamides



(*rac*)-7k S9b

Entry	Variations	Conversion (%)[a]	Yield (%)[b]
1	**None**	**100**	**93**
2	**60 °C, 36 h**	**100**	**93**
3	4.0 M HCl (aq., 8.0 eq.): AcOH= 1:1, 100 °C, 12 h	100	87
4	4.0 M HCl (aq., 8.0 eq.): Dioxane= 1:1, 100 °C, 12 h	100	87
5	PTSA (4.0 eq.), EtOH (0.1 M) 80 °C, 20 h	< 5	NA[c]
6	MsOH (4.0 eq.), EtOH (0.1 M) 80 °C, 20 h	< 5	NA[c]
7	TfOH (4.0 eq.), EtOH (0.1 M) 80 °C, 20 h	< 5	NA[c]
8	LiOH (1.0 M, aq, 3.0 eq.) THF (0.1 M), 80 °C, 24 h	0	NA[c]
9	NH_4OH (aq., 30% w/w, 3.0 eq.) Dioxane (0.1 M), 100 °C, 24 h	0	NA[c]

10	$LiAlH_4$ (3.0 eq.), THF (0.1 M) rt, 12 h	64	57
11	SmI_2-H_2O-LiBr (5:100:100 eq.) THF (0.05 M), rt, 8 h	0	NA[c]
12	SmI_2-H_2O-Et_3N (6: 72: 72 eq.) THF (0.05 M), rt, 8 h	0	NA[c]
13	NaH (3.0 eq.), ZnI_2 (1.0 eq.) NaI (1.0 eq.), THF (0.2 M) 40 °C, 12 h	0	NA[c]
14	$(Ir(COE)_2Cl)_2$ (5 %), Et_2SiH_2 (4.0 eq.) THF (0.3 M), rt, 24 h	0	NA[c]
15	9-BBN (2.0 eq.), THF (0.1 M) rt, 12 h	0	NA[c]
16	$Ti(OiPr)_4$ (1.0 eq.), $PhSiH_3$ (1.1 eq.) THF (0.5 M), rt, 3 h	0	NA[c]
17	DMSO/H_2O= 10: 1(0.1 M) 80 °C, 12 h[d]	0	NA[c]

Table S6: Optimization for the cleavage of *N,N*-diisopropyl urea group from methyl phenyl sulfoximine. All reactions were performed on 0.1 mmol scale in a flame dried flask or vial under argon. [a]Determined by LC-MS. [b]Isolated yield. [c]Not available. [d]This condition works for secondary sulfonimidamides.

Our investigation to deprotect the *N,N*-diisopropyl urea group to give N–H sulfonimidoyl compounds used phenyl methyl sulfoximine as a model substrate (Table 5). Different hydrolysis conditions were evaluated including acidic (entries 1–7) and basic (entries 8 and 9) conditions. The optimal acidic conditions were found to be a combination of camphor sulfonic acid (CSA) in hexafluoroisopropyl alcohol (HFIP) at 60–70 ºC (entries 1 and 2), removing the *N,N*-diisopropyl carbonyl group to give free N–H sulfoximine in excellent yield (93%). Other acidic conditions were also compatible but required harsher acidic and thermal conditions (entries 3 and 4) to give the desired deprotected sulfoximine in good yields. Stronger acids such as methane sulfonic acid (MsOH; entry 6) and triflic acid (TfOH; entry 7) were evaluated in ethanol under thermal conditions with little conversion to the desired product. The sulfonimidoyl urea group was stable under basic hydrolysis conditions with no conversion observed (entries 8 and 9).

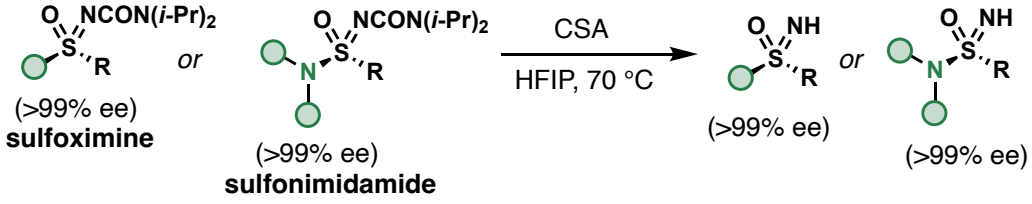
Reductive conditions known to remove the N–Piv protecting group of sulfoximines was found to be compatible (entry 10) albeit in lower conversion and yield (heating to 60 ºC increased the conversion to >90%, not shown). We further investigated methods reported to reduce secondary amides (entries 11-16) using a variety of conditions—all resulting in no conversion to the desired product.

We concurrently discovered that secondary sulfonimidamides (those containing an acidic proton **H**–N, *vide infra*) protected with the *N,N*-diisopropyl urea group were readily removed using CSA/HFIP and by heating in mixture of DMSO and water (10:1) at 80 ºC

(entry 17), however, sulfoximines and tertiary sulfonimidamides are unable to be deprotected under such mild conditions.

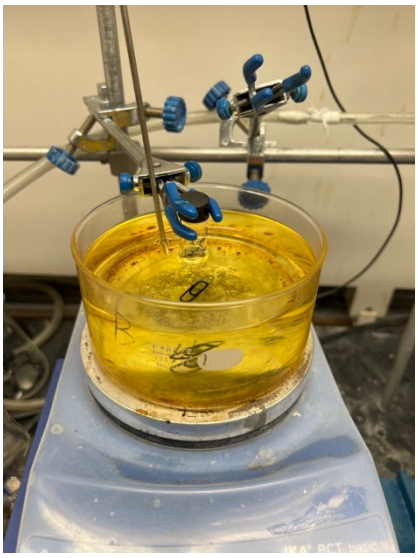
A variety of deprotection conditions were found for either sulfoximines and/or sulfonimidamides to give the free N–H derivatives (entries 1–4, entry 10, entry 17). *The preferred general method to deprotect the N,N-diisopropyl urea groups from sulfoximines and sulfonimidamides the use of CSA in HFIP at 60–70 ºC (Figure 15).* In the case of secondary sulfonimidamides, a milder condition (DMSO/H_2O, heat) can be employed if desired which won't interfere with other protecting groups that may be sensitive to weak acids such as CSA. Other deprotection methods are currently being explored ofr other sulfonimidoyl groups.

VIb. General procedure 13 (GP-13): Deprotection of *N,N*-diisopropyl urea from sulfoximines and sulfonimidamide using CSA



Scheme S15: General reaction conditions for the deprotection of *N,N*-diisopropyl urea protected sulfoximines and sulfonimidamides using CSA.

In a flask or vial equipped with a stir bar was added sulfoximine or sulfonimidamide (1eq.) followed by CSA (2.0 eq) and HFIP (0.1 M). The reaction vessel was tightly capped then heated to 70 °C and stirred overnight (typically 12 h). Upon completion (checked by TLC) the reaction was cooled to room temperature then quenched with saturated aqueous $NaHCO_3$ to adjust the pH to neutral. The mixture was extracted with EtOAc (x 4), washed with brine and purified by column chromatography to give the desired deprotected sulfoximine or sulfonimidamides.

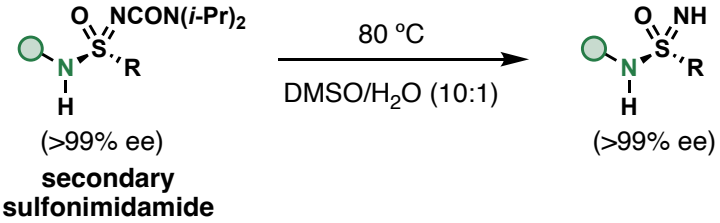


Graphical set-up 2: Deprotection of *N,N*-diisopropyl sulfonimidoyl ureas to N–H sulfonimidoyl groups using CSA in HFIP at 70 ºC.

Notes:

1. Extraneous anhydrous conditions were not necessary for this reaction and did not affect the yield or enantiopurity of the products.
2. No erosion of enantiopurity was observed during the deprotection.
3. Lower temperatures (<70 ºC) can be used with longer reaction times.

VIc. General procedure 14 (GP-14): Deprotection of *N,N*-diisopropyl urea from secondary sulfonimidamide using DMSO/H_2O and heat



Scheme S16: General reaction conditions for the deprotection of *N,N*-diisopropyl urea protected secondary sulfonimidamides.

In a flask or vial equipped with a stir bar was added the primary sulfonimidamide (1 eq.) followed by DMSO/H_2O (10:1, 0.1 M) then heated to 80 °C (typically 8 hours). Upon completion (checked by TLC) the reaction was cooled to room temperature, diluted with water, and extracted with EtOAc (x 4). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. Further purification by silica gel column chromatography gave the desired deprotected products.

Notes:

1. This reaction condition works very well with secondary aromatic and aliphatic sulfonimidamides. No reaction occurs with tertiary sulfonimidamides and sulfoximines.
2. Aromatic secondary sulfonimidamides react faster than aliphatic derivatives.
3. Other water miscible solvents besides DMSO (MeCN and MeOH) produce the desired deprotected products but require longer reaction time. The enantiopurity of the deprotected products in other solvents was not determined.

VII. Recrystallization of *tert*-butyl sulfoximines for further enantioenrichment

VIIa. General procedure 15 (GP-15): Recrystallization methods

For the cases in which organolithium additions to *t*-BuSF do not give the desired enantiopurity, recrystallizations can be performed to further enhance the enantiopurity of *tert*-butyl sulfoximines. We have found that nearly all *N,N*-diisopropyl urea protected chiral *tert*-butyl sulfoximines prepared from *t*-BuSF are solids at room temperature and have the potential to further enhance enantiopurity if desired.

For example: *tert*-butyl phenyl sulfoximine was used as our model substrate to demonstrate the bifunctional property of the *t*-BuSF sulfonimidoyl transfer reagents. The addition of PhLi (commercial or *in situ* generated) to *t*-BuSF provides *tert*-butyl phenyl sulfoximine in 98% ee as a white solid which was enhanced to >99% ee via recrystallization.

The general procedure (GP-15) for typical recrystallizations is as follows:
Pure *tert*-butyl sulfoximine was dissolved in a minimum amount of acetone, with the help of ultrasonic bath or heat. Hexanes (three times the volume of acetone used) was slowly added to prevent complete mixing of the two solvents. The mixture was transformed to -20 °C freezer to settle overnight to induce recrystallization. After 12 hours the recrystallized material was collected by filtration and washed with hexanes (x 3) to give 60–70% recovery yield and >99% ee after a single recrystallization. This process can be repeated two more times to give up to 90% recovery yield with >99% ee.

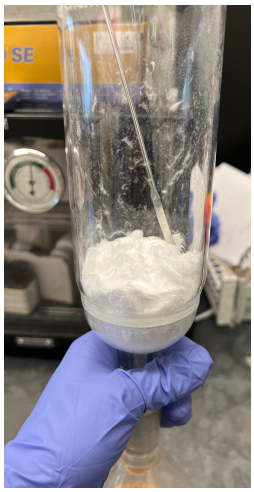


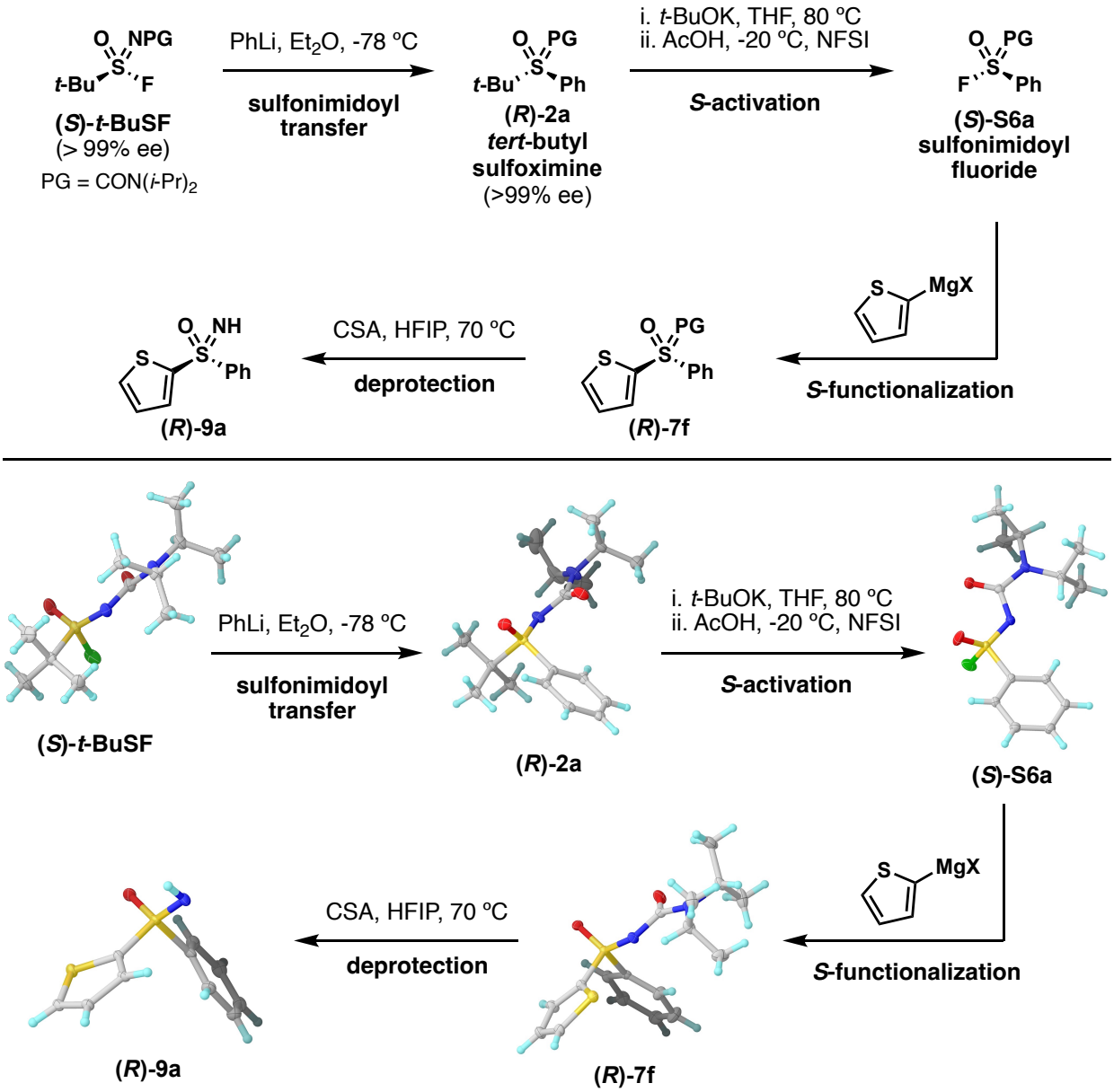
Image 1: Filtration of *tert*-butyl phenyl sulfoximine **2a** after first crop of recrystallization.

Other examples:
tert-butyl cyclopropyl sulfoximine (>90% recovery, 97 to >99% ee, three crops).
tert-butyl 4-chlrophenyl sulfoximine (>90% recovery, 95 to >99% ee; three crops).

Notes:

1. Acetone/hexanes solvent system worked for most recrystallizations. While for some cases, EtOAc/hexanes gave similar or better results—recrystallization is substrate-dependent.
2. General recovery yield was around 60–70% for all substrates.
3. The limit of recrystallization we observed was using an 80% ee mother liquor that gave roughly 60% recovery yield and >99% ee. A mother liquor lower than 80% ee became difficult to enhance further without seeding (using >99 % crystal).
4. Starting with 10 grams of *tert*-butyl phenyl sulfoximine, three rounds of recrystallization provided >90% recovery yield and >99% ee

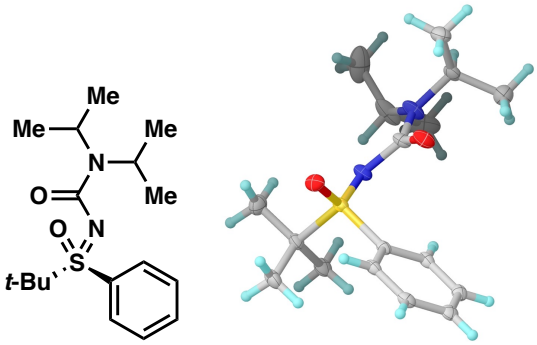
VIII. Verification of stereochemical assignment via X-ray crystallography



Scheme S17: Confirmation of stereogenic assignment for the synthesis of enantiopure sulfoximine **9** from ***t*-BuSF** by single crystal X-ray crystallography.

IX. Compound characterization data.

IXa. Sulfonimidoyl transfer scope and specific procedures.



2a

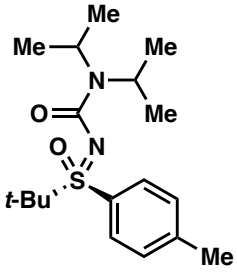
GP-1 and GP-2 were used with commercially available bromobenzene (0.375 mmol, 1.5 eq.) with no further modifications. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (70 mg, 217 µmol, 87% yield) as a white crystalline solid.
*There were no significant differences in yield or enantiopurity between the two procedures. Phenyl lithium can be used instead of generating phenyl lithium from *n*-BuLi or *t*-BuLi with no decrease in yield or enantiopurity.

Different scale reactions:
GP-1 was followed with commercial PhLi (5.33 mL, 10.1 mmol, 1.9 M, dibutylether, 1.5 eq.) and *t*-BuSF (1.80 g, 6.76 mmol, 1 eq.), produced (1.77 g, 5.45 mmol, 81% yield, 98% ee).

GP-1 was followed with commercial PhLi (8.89 mL, 16.9 mmol, 1.9 M, dibutylether, 1.5 eq.) and *t*-BuSF (3.0 g, 16.9 mmol, 1 eq.), produced (3.30 g, 10.2 mmol, 90% yield, 98% ee).

Physical characteristics: White crystalline solid.
TLC: R_f = 0.27 (hexane/EtOAc, 50% EtOAc, UV).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 – 7.73 (m, 2H), 7.61 – 7.56 (m, 1H), 7.55 – 7.50 (m, 2H), 4.06 (s, 2H), 1.37 (s, 9H), 1.27 (d, *J* = 8.3 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.6, 135.2, 132.9, 130.2, 128.9, 60.8, 45.9, 23.8, 21.4 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +28.85 (c 0.50, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{29}N_2O_2S$ [M+H$^+$] 325.1944; found 325.1951.
Melting Point: 177-178 °C
Enantiomeric excess: 98% ee. Recrystallized to >99% ee with >90% recovery.

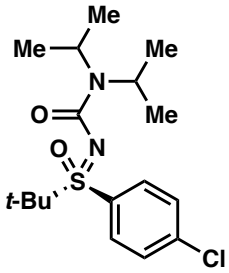
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 17.1 min, minor: 26.1 min.
CCDC deposition Number: 2243801



2b

GP-1 was followed with no additional modifications: Commercially available 4-bromotoluene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (71 mg, 209 µmol, 84% yield) as a white amorphous solid.
GP-2 was also followed and showed no significant difference on yield or enantiopurity.

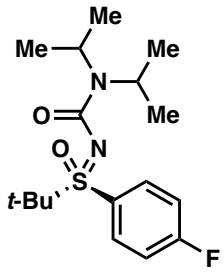
Physical characteristics: White amorphous solid.
TLC: R_f = 0.27 (hexane/EtOAc, 33% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.67 (d, 2H), 7.33 (d, 2H), 4.12 (d, *J* = 31.4 Hz, 2H), 2.44 (s, 3H), 1.39 (s, 15H), 1.20 (d, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.66, 143.65, 132.06, 130.21, 129.68, 60.67, 46.40, 45.17, 23.74, 21.86, 21.66, 20.88 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -9.12 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{31}N_2O_2S$ [M+H$^+$] 339.2101; found 339.2101.
Enantiomeric excess: 97% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 27.5 min, minor: 36.6 min.



2c

GP-1 was followed with no additional modifications: Commercially available 1-bromo-4-chlorobenzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (75 mg, 208 µmol, 85% yield) as a white crystalline solid.
GP-2 was also followed and showed no significant difference on yield or enantiopurity.

Physical characteristics: White crystalline solid.
TLC: R_f = 0.39 (hexane/EtOAc, 30% EtOAc, UV).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 2H), 4.06 (d, 2H), 1.37 (s, 21H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.4, 139.7, 134.0, 131.6, 129.3, 60.9, 46.5, 45.4, 23.7, 21.9, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -5.53 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{28}ClN_2O_2S$ [M+H$^+$] 359.1555; found 359.1560.
Melting Point: 178-180 °C
Enantiomeric excess: 96% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 15.8 min, minor: 18.0 min.

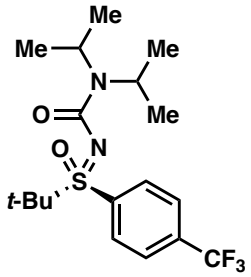


2d

GP-1 was followed with no additional modifications: Commercially available 1-bromo-4-fluorobenzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (71 mg, 207 µmol, 83% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.4 (hexane/EtOAc, 30% EtOAc, UV).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 – 7.72 (m, 2H), 7.21 (dd, *J* = 9.1, 8.2 Hz, 2H), 4.05 (s, 2H), 1.37 (s, 9H), 1.34 – 1.18 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 165.6 (d, *J* = 254.8 Hz), 159.4, 132.7 (d, *J* = 9.4 Hz), 131.1 (d, *J* = 3.2 Hz), 116.3 (d, *J* = 22.6 Hz), 60.9, 45.9, 23.7, 21.4 ppm.
^{19}F NMR: (471 MHz, CDCl3) δ -105.86 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -15.24 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{27}FN_2NaO_2S$ [M+Na$^+$] 365.1669; found 365.1666.

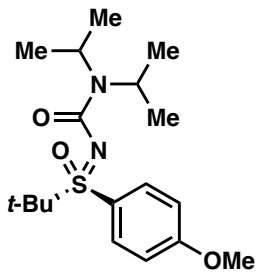
Enantiomeric excess: 97% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 13.7 min, major: 17.1 min.



2e

GP-1 was followed with no additional modifications: Commercially available 1-bromo-4-(trifluoromethyl)benzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (71.6 mg, 183 µmol, 73% yield) as a white amorphous solid.

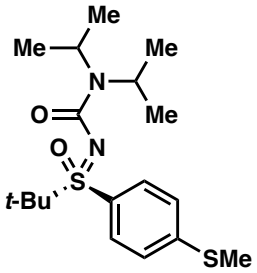
Physical characteristics: White amorphous solid.
TLC: R_f = 0.27 (hexane/EtOAc, 25% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.91 (d, 2H), 7.79 (d, 2H), 4.08 (d, 2H), 1.39 (s, 9H), 1.36 (s, 6H), 1.16 (dd, *J* = 23.0, 6.7 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.3, 139.6, 134.6 (q, *J* = 32.8 Hz), 130.7, 126.04 (q, *J* = 3.7 Hz), 123.5 (q, *J* = 273.0 Hz), 61.0, 46.6, 45.5, 24.7, 23.7, 21.8, 20.9, 20.8 ppm.
^{19}F NMR: (471 MHz, CDCl3) δ -63.07 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -8.76 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{28}F_3N_2O_2S$ [M+H$^+$] 393.1818; found 393.1824.
Enantiomeric excess: 95% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 8.3 min, minor: 9.4 min.



2f

GP-1 was followed with no additional modifications: Commercially available 4-bromoanisole (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (72.6 mg, 206 µmol, 82% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.25 (hexane/EtOAc, 33% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 9.1 Hz, 2H), 4.30 – 3.90 (m, 2H), 3.86 (s, 3H), 1.42 – 1.08 (m, 21H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 163.3, 159.6, 132.1, 126.2, 114.4, 60.8, 55.7, 45.24, 23.7, 21.8, 21.1 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -1.51 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{31}N_2O_3S$ [M+H$^+$] 355.2050; found 355.2051.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 40.2 min, minor: 46.9 min.

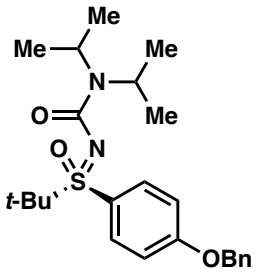


2g

GP-1 was followed with no additional modifications: Commercially available 4-bromothioanisole (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (69 mg, 187 µmol, 75% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.19 (hexane/EtOAc, 33% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 2H), 4.06 (s, 2H), 2.51 (s, 3H), 1.37 (s, 9H), 1.25 (t, *J* = 8.0 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.5, 146.0, 130.8, 130.4, 125.4, 60.9, 46.0, 23.7, 21.3, 14.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +10.10 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{31}N_2O_2S_2$ [M+H$^+$] 371.1821; found 371.1823.
Enantiomeric excess: 98% ee.

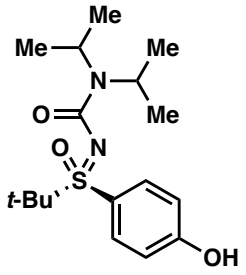
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 40.5 min, minor: 45.5 min.



2h

GP-1 was followed with no additional modifications: Commercially available 1-(benzyloxy)-4-bromobenzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (43 mg, 102 µmol, 40% yield) as a white amorphous solid.

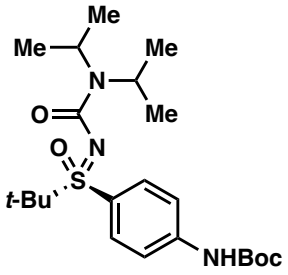
Physical characteristics: White amorphous
TLC: R_f = 0.25 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.5 Hz, 2H), 7.44 – 7.32 (m, 5H), 7.10 – 7.03 (m, 2H), 5.13 – 5.05 (m, 2H), 4.07 (m, 2H), 1.42 – 1.27 (m, 15H), 1.25 – 1.09 (m, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 162.6, 159.6, 136.1, 132.2, 128.9, 128.5, 127.8, 126.5, 115.1, 70.5, 60.8, 45.5, 23.8, 21.9, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +47.35 (c 0.50, $CHCl_3$)
HRMS: Calc'd for $C_{24}H_{35}N_2O_3S$ [M+H$^+$] 431.2363; found 431.2359.
Enantiomeric excess: 97% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 36.4 min, minor: 52.9 min.



2i

GP-1 was followed with no additional modifications: Commercially available 4-bromophenol (or with -TBS protection) (0.375 mmol, 1.5 eq.) were used. Purified by silica gel column chromatography using DCM/MeOH (0% to 10% MeOH gradient) to give the product (63.9 mg, 188 µmol, 75% yield) as a white amorphous solid.
Note: The OTBS protected phenol gave similar yield and exact enantiopurity. The silyl protecting group is removed during the reaction.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.20 (DCM/MeOH, 10% MeOH).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.36 (d, *J* = 8.3 Hz, 2H), 6.66 – 6.59 (m, 2H), 4.12 (d, *J* = 121.9 Hz, 2H), 1.42 (d, *J* = 6.8 Hz, 6H), 1.33 (s, 9H), 1.21 (dd, *J* = 14.0, 6.8 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 162.3, 161.1, 131.8, 122.2, 116.5, 61.2, 46.2, 45.9, 23.6, 21.9, 21.7, 21.0, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -66.29 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{28}N_2NaO_3S$ [M+Na$^+$] 363.1713; found 363.1705.
Enantiomeric excess: 97% ee.
HPLC Conditions: (hydroxy group was methylated for HPLC analysis) Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 36.5 min, minor: 43.7 min.

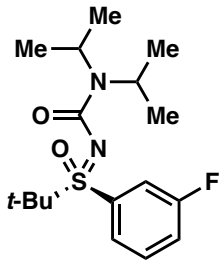


2j

GP-1 was followed with additional modifications mentioned below: Commercially available *tert*-butyl (4-bromophenyl) carbamate (0.375 mmol, 1.5 eq.) was used and equivalents of *n*-BuLi was increased (from 1.5 to 3 eq.). For halogen-Li exchange, the reaction was removed from bath for 15 min. Then cooled down to -78 °C and repeat the process with another 15 min to complete full exchange. The reaction was. warmed to -40 °C after addition of ***t*-BuSF** where it stirred for one hour. Purified by silica gel column chromatography using hexane/Acetone (0% to 30% Acetone gradient) to give the product (65.9 mg, 150 µmol, 60% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.35 (hexane/Acetone, 30% Acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.64 (d, 2H), 7.50 (d, 2H), 6.95 (s, 1H), 4.02 (d, 2H), 1.52 (s, 9H), 1.35 (s, 15H), 1.19 (d, 6H) ppm.

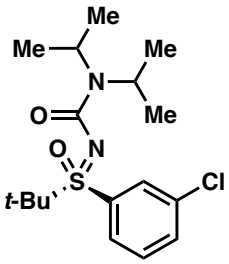
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.6, 152.4, 143.1, 131.4, 127.9, 118.1, 81.4, 60.9, 46.6, 45.3, 28.4, 23.7, 21.8, 21.0 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -15.31 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{22}H_{38}N_3O_4S$ [M+H$^+$] 440.2578; found 440.2574.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 9.7 min, minor: 13.4 min.



2k

GP-1 was followed with no additional modifications: Commercially available 1-bromo-3-fluorobenzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (70.1 mg, 205 µmol, 82% yield) as a white solid.

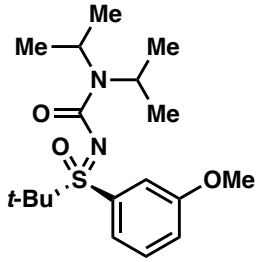
Physical characteristics: White amorphous solid.
TLC: R_f = 0.25 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.57 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.29 (tdd, *J* = 8.2, 2.6, 1.1 Hz, 1H), 4.27 – 3.82 (m, 2H), 1.39 (s, 9H), 1.34 (s, 6H), 1.15 (d, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 162.6 (d, *J* = 251.2 Hz), 159.3, 137.8 (d, *J* = 6.3 Hz), 130.5 (d, *J* = 7.6 Hz), 125.9 (d, *J* = 3.2 Hz), 120.2 (d, *J* = 21.2 Hz), 117.5 (d, *J* = 24.2 Hz), 61.0, 46.6, 45.4, 23.8, 21.8, 20.9, 20.8 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -110.39 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -13.65 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{28}FN_2O_2S$ [M+H$^+$] 343.1850; found 343.1853.
Enantiomeric excess: 95% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 12.1 min, minor: 13.7 min.



2l

GP-1 was followed with no additional modifications: Commercially available 1-bromo-3-chlorobenzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (74.3 mg, 207 µmol, 83% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.30 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.64 (dt, *J* = 8.0, 1.3 Hz, 1H), 7.55 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1H), 7.47 (t, *J* = 7.9 Hz, 1H), 4.29 – 3.86 (m, 2H), 1.38 (s, 9H), 1.35 – 1.16 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.3, 137.4, 135.3, 133.1, 130.2, 130.1, 128.3, 61.1, 46.7, 45.47, 23.8, 21.6, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -7.86 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{28}ClN_2O_2S$ [M+H$^+$] 359.1555; found 359.1560.
Enantiomeric excess: 97% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 12.2 min, minor: 14.3 min.

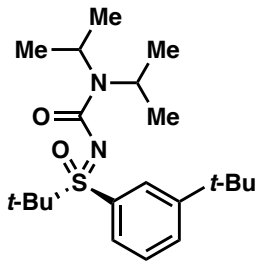


2m

GP-1 was followed with no additional modifications: Commercially available 3-bromoanisole (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (71.7 mg, 202 µmol, 81% yield) as a white solid.

Physical characteristics: White amorphous solid.

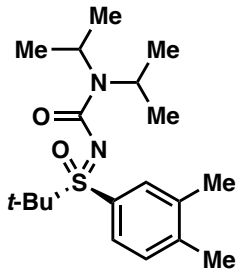
TLC: R_f = 0.20 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.42 (t, J = 8.0 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.11 (ddd, J = 8.2, 2.5, 1.0 Hz, 1H), 4.30 – 3.88 (m, 2H), 3.83 (s, 3H), 1.38 (s, 9H), 1.36 – 1.06 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.9, 159.6, 136.5, 129.8, 122.4, 119.4, 115.0, 60.9, 55.7, 46.35, 45.4, 23.8, 21.8, 21.0 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -1.76 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{27}F_3N_2O_2S$ [M+H$^+$] 355.2050; found 355.2051.
Enantiomeric excess: 97% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 23.8 min, minor: 30.9 min.



2n

GP-1 was followed with no additional modifications: Commercially available 1-bromo-3-(*tert*-butyl) benzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (68.4 mg, 180 µmol, 72% yield) as a white solid.

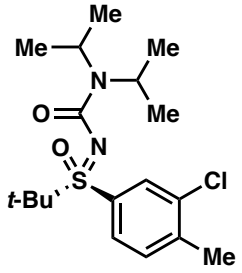
Physical characteristics: White amorphous solid.
TLC: R_f = 0.20 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) 7.76 (t, *J* = 2.0 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 1H), δ 3.96 (s, 1H), 4.19 (s, 1H), 1.32 (s, 9H), 1.35 (s, 15H), 1.16 (dd, *J* = 21.0, 7.0 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.6, 152,0 134.5, 129.9, 128.7, 127.6, 127.1, 60.6, 46.52, 45.2, 35.0, 31.3, 23.7, 21.8, 21.0, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -14.47 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{21}H_{37}N_2O_2S$ [M+H$^+$] 381.2570; found 381.2572.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 9.7 min, minor: 14.6 min.



2o

GP-1 was followed with no additional modifications: Commercially available 4-bromo-1,2-dimethylbenzene was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (73.3 mg, 207 µmol, 83% yield) as a white amorphous solid.

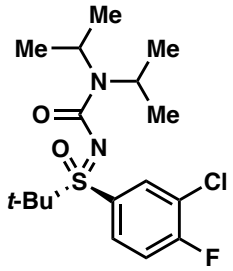
Physical characteristics: White amorphous solid.
TLC: R_f = 0.15 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 2.0 Hz, 1H), 7.45 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.26 (d, 1H, partly overlapped with chloroform peak, see corresponding spectrum for details), 4.13 (s, 1H), 3.99 (s, 1H), 2.30 (t, *J* = 1.1 Hz, 6H), 1.37 (s, 15H), 1.16 (dd, *J* = 25.2, 6.8 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.8, 142.4, 137.6, 132.1, 131.2, 130.2, 127.6, 60.6, 46.4, 45.21, 23.8, 21.8, 21.0, 20.9, 20.1, 20.0 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +1.08 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{19}H_{33}N_2O_2S$ [M+H$^+$] 353.2257; found 353.2260.
Enantiomeric excess: 98% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 30.8 min, minor: 43.5 min.



2p

GP-1 was followed with no additional modifications: Commercially available 4-bromo-1,2-dimethylbenzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (71.6 mg, 192 µmol, 77% yield) as a white amorphous solid.

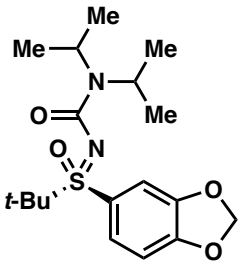
Physical characteristics: White amorphous solid.
TLC: R_f = 0.20 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 1.9 Hz, 1H), 7.53 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.38 (dd, *J* = 8.0, 0.9 Hz, 1H), 4.26 – 4.05 (m, 1H), 3.97 (s, 1H), 2.43 (s, 3H), 1.38 (s, 9H), 1.37 – 1.30 (m, 6H), 1.23 – 1.11 (m, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.4, 141.8, 135.4, 134.3, 131.4, 130.7, 128.2, 60.9, 46.7, 45.4, 23.8, 21.8, 20.9, 20.8, 20.4 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -2.06 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{30}ClN_2O_2S$ [M+H$^+$] 373.1711; found 373.1714.
Enantiomeric excess: 98% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 18.4 min, minor: 21.0 min.



2q

GP-1 was followed with no additional modifications: Commercially available 4-bromo-1-chloro-2-fluorobenzene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (71.5 mg, 190 µmol, 76% yield) as a white amorphous solid.

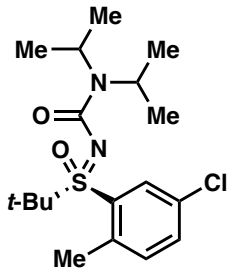
Physical characteristics: White amorphous solid.
TLC: R_f = 0.30 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 6.7, 2.3 Hz, 1H), 7.64 (ddd, *J* = 8.7, 4.3, 2.3 Hz, 1H), 7.29 (t, *J* = 8.5 Hz, 1H), 4.04 (d, *J* = 96.8 Hz, 2H), 1.39 (s, 9H), 1.33 (s, 6H), 1.17 (dd, *J* = 24.9, 6.7 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 162.0, 159.6 (d, *J* = 104.2 Hz), 132.9, 132.4 (d, *J* = 4.0 Hz), 130.4 (d, *J* = 8.3 Hz), 122.6 (d, *J* = 18.7 Hz), 117.3 (d, *J* = 22.5 Hz), 61.2, 46.7, 45.4, 23.7, 21.8, 20.9, 20.8 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -107.84 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -5.67 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{27}ClFN_2O_2S$ [M+H$^+$] 377.1460; found 377.1454.
Enantiomeric excess: 96% ee.
HPLC Conditions: Daicel Chiralpak IA column, 95:05 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 11.1 min, major: 14.6 min.



2r

GP-1 was followed with no additional change: Commercially available 5-bromobenzo[*d*][1,3]dioxole (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (68.1 mg, 185 µmol, 74% yield) as a white amorphous solid.
GP-2 was also used to give no significant change in yield or enantiopurity of the product.

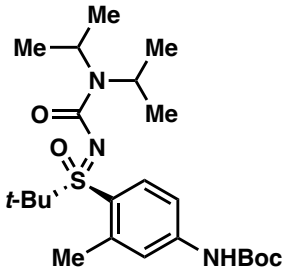
Physical characteristics: White amorphous solid.
TLC: R_f = 0.20 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.17 (s, 1H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.09 – 6.03 (m, 2H), 4.06 (d, *J* = 35.2 Hz, 2H), 1.37 (s, 9H), 1.36 – 1.29 (m, 6H), 1.16 (dd, *J* = 21.9, 6.8 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.6, 151.9, 148.3, 128.2, 125.8, 110.2, 108.5, 102.4, 61.0, 46.3, 45.3, 23.8, 21.9, 21.8, 21.0, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +1.57 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{29}N_2O_4S$ [M+H$^+$] 369.1843; found 369.1840.
Enantiomeric excess: 98% ee.
HPLC Conditions: Daicel Chiralpak IB column, 95:05 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 19.6 min, minor: 23.0 min.



2s

GP-1 was followed with no additional modifications: Commercially available 2-bromo-4-chlorotoluene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (67.2 mg, 180 µmol, 72% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.25 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.39 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.30 – 7.18 (m, 1H), 4.22 (s, 1H), 3.90 (s, 1H), 2.63 (d, *J* = 9.5 Hz, 3H), 1.40 (d, *J* = 9.4 Hz, 9H), 1.35 – 1.14 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.5, 135.4, 134.6, 132.7, 132.2, 62.6, 46.9, 45.3, 23.8, 21.7, 21.0, 20.8, 20.6 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -36.40 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{30}ClN_2O_2S$ [M+H$^+$] 373.1711; found 373.1710.
Enantiomeric excess: 98% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minorr: 8.6 min, major: 11.9 min.

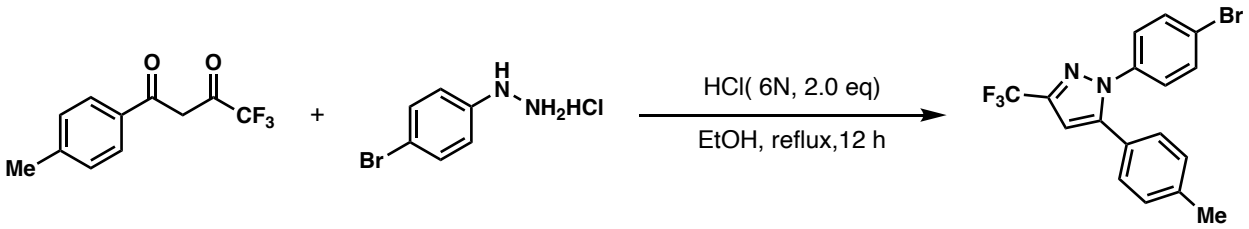


2t

GP-1 was followed with additional modifications mentioned below: Commercially available *tert*-butyl (4-bromo-3-methylphenyl) carbamate (0.375 mmol, 1.5 eq.) was used. Equivalents of *n*-BuLi was increased (from 1.5 to 3 eq.). For halogen-Li exchange, the reaction was removed from bath for 15 min. Then cooled down to -78 °C and repeat the process with another 15 min to complete full exchange. The reaction was. warmed to -40 °C after addition of ***t*-BuSF** where it stirred for one hour. Purified by silica gel column chromatography using hexane/Acetone (0% to 30% Acetone gradient) to give the product (75.7 mg, 167 µmol, 67% yield) as a white amorphous solid.

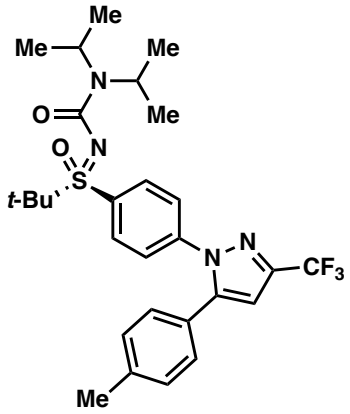
Physical characteristics: White amorphous solid.
TLC: R_f = 0.25 (hexane/Acetone, 30% Acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.47 (s, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.71 (s, 1H), 4.35 – 3.79 (m, 2H), 2.58 (s, 3H), 1.49 (s, 9H), 1.38 (s, 9H), 1.34 – 1.16 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.6, 152.5, 136.9, 133.6, 123.1, 122.7, 80.6, 62.3, 46.75, 45.1, 28.3, 23.7, 21.7, 21.5, 20.9, 20.8, 20.3 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -33.81 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{23}H_{39}N_3NaO_4S$ [M+Na$^+$] 476.2553; found 476.2549.
Enantiomeric excess: 95% ee.

HPLC Conditions: Daicel Chiralpak IB column, 95:05 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 5.8 min, minor: 7.1 min.



Prepared from a known procedure[9] to afford a white amorphous solid (3.5 g, 92%). Spectroscopic data was in accordance to the literature.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.35 (hexane/EtOAc, 10% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 (dd, J = 6.7, 2.3 Hz, 1H), 7.64 (ddd, J = 8.7, 4.3, 2.3 Hz, 1H), 7.29 (t, J = 8.5 Hz, 1H), 4.04 (d, J = 96.8 Hz, 2H), 1.39 (s, 9H), 1.33 (s, 6H), 1.17 (dd, J = 24.9, 6.7 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 145.0, 143.6 (q, J = 38.4 Hz), 139.5, 138.5, 132.4, 129.7, 128.8, 127.0, 126.1, 122.3, 121.3 (q, J = 269.0 Hz), 105.8 (d, J = 2.2 Hz), 21.5 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -107.84 ppm.
HRMS: Calc'd for $C_{17}H_{13}BrF_3N_2$ [M+H$^+$] 381.0209; found 381.0206.

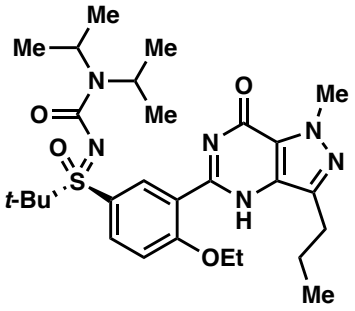


2u

GP-1 was followed with no additional modifications: The aryl bromide prepared above (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using DCM/EtOAc (0% to 10% EtOAc gradient) to give the product (95.9 mg, 175 µmol, 70% yield) as a white solid.

TLC: R_f = 0.35 (hexane/EtOAc, 30% EtOAc).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.49 (d, 2H), 7.18 – 7.09 (m, 4H), 6.73 (s, 1H), 4.37 – 3.58 (m, 2H), 2.34 (s, 3H), 1.34 (s, 9H), 1.25 (d, *J* = 6.8 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.2, 145.4, 144.1 (q, *J* = 38.5 Hz), 142.7, 139.8, 134.8, 131.2, 129.8, 128.8, 125.7, 125.0, 121.2 (q, *J* = 269.2 Hz), 106.5 – 106.2 (m), 61.0, 47.1, 45.3, 23.6, 21.4 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -62.42 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +42.52 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{28}H_{35}F_3N_4NaO_2S$ [M+Na^+] 571.2325 found 571.2330.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 7.7 min, minor: 12.4 min.



2v

GP-3 was followed with additional modifications mentioned: The aryl bromide was prepared using a known procedure.[10] MeLi (0.124 mL, 0.384 mmol, 3.1 M, 1.2 eq.) was added to a solution of the aryl bromide (0.320 mmol, 1 eq.) in Et_2O (2.5 mL) at -78 ºC and stirred for 30 minutes followed by the addition of *n*-BuLi (0.30 mL, 0.48 mmol, 1.6 M, 1.5 eq.). The reaction mixture stirred at -78 ºC for 1 hour before warming to -40 ºC where it stirred for an additional 30 minutes before cooling to -78 ºC. A solution of ***t*-BuSF** (128 mg, 0.48 mmol, 1.5 eq.) in Et_2O (0.7 mL) was added dropwise at -78 ºC then warmed to -20 ºC over 1.5 hours. No modification to the quench and work-up were made. Purification by silica gel column chromatography using Hex/EtOAc (0% to 60% EtOAc gradient) provided the product (96.0 mg, 0.172 mmol, 54% yield) as a white amorphous solid.

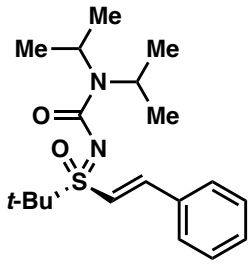
Physical characteristic: White amorphous solid.
TLC: R_f = 0.39 (DCM/MeOH, 5% MeOH).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 10.93 (s, 1H), 8.80 (d, *J* = 2.4 Hz, 1H), 7.94 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 4.37 (qd, *J* = 7.0, 1.3 Hz, 2H), 4.26 (s, 3H), 4.15 – 4.06 (m, 1H), 4.06 – 3.93 (m, 1H), 2.87 (t, *J* = 7.5 Hz, 2H), 1.86 – 1.77 (m, 2H), 1.64 (t, *J* = 7.0 Hz, 3H), 1.42 (s, 9H), 1.40 (d, *J* = 7.6 Hz, 6H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 159.5, 153.7, 146.8, 146.8, 138.4, 134.3, 132.9, 128.2, 124.5, 120.8, 113.2, 66.1, 60.9, 45.2, 38.2, 29.7, 27.6, 23.6, 22.3, 21.8, 20.8, 20.7, 14.6, 14.0 ppm.

Specific rotation: $[\alpha]_D^{22.5}$ = -55.56 (c 0.8, $CHCl_3$)

HRMS: Calc'd for $C_{28}H_{42}N_6O_4SNa$ [M+Na$^+$] 581.2880 found 581.2886.

Enantiomers were unable to be separated.



2w

GP-1 was followed with no additional modifications: Commercially available β-bromostyrene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (49.0 mg, 140 µmol, 56% yield) as a white amorphous solid. Only *Z* isomer was detected after purification.

Physical characteristics: White amorphous solid.

TLC: R_f = 0.20 (hexane/EtOAc, 30% EtOAc).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.56 – 7.51 (m, 3H), 7.41 – 7.37 (m, 3H), 6.92 (d, J = 15.5 Hz, 1H), 4.05 (s, 2H), 1.46 (s, 9H), 1.35 – 1.14 (m, 12H) ppm.

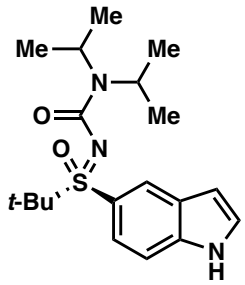
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.5, 146.2, 133.3, 130.8, 129.0, 128.7, 122.1, 60.5, 45.3, 23.7, 21.6, 20.9 ppm.

Specific rotation: $[\alpha]_D^{23}$ = +0.64 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{19}H_{31}N_2O_2S$ [M+H$^+$] 351.2101; found 351.2105.

Enantiomeric excess: 98% ee.

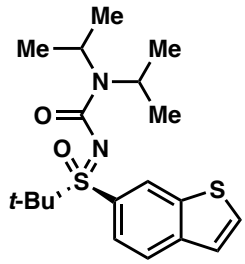
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 14.6 min, major: 16.0 min.



3a

GP-3 was followed with additional changes mentioned: Commercially available 5-iodo-1*H*-indole (0.275 mmol, 1.1 eq.) was used. CPME was used instead of Et_2O and 2.5 eq. of *t*-BuLi was used for the Li-I exchange (-78 ºC, 75 minutes). Warmed to -20 ºC and held for 1 hour before quenching. No modifications to the quench or work-up procedure were made. Purified by silica gel column chromatography using Hex/EtOAc (0% to 60% EtOAc gradient) to give the product (58 mg, 0.160 mmol, 64% yield) as a white amorphous solid.

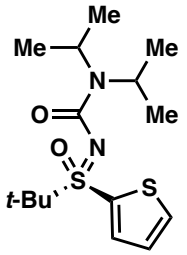
Physical characteristics: White amorphous solid.
TLC: R_f = 0.16 (hexanes/EtOAc, 60% EtOAc)
^{1}H NMR: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.31 (s, 1H), 7.84 (d, *J* = 2.0 Hz, 1H), 7.10 – 7.04 (m, 2H), 6.66 (d, *J* = 8.5 Hz, 1H), 6.28 (s, 1H), 4.49 – 4.23 (m, 1H), 4.16 – 3.96 (m, 1H), 1.46 – 1.38 (m, 6H), 1.35 (s, 9H), 1.34 – 1.28 (m, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 160.5, 137.8, 127.5, 127.2, 124.0, 122.5, 120.7, 111.7, 102.3, 61.0, 46.9, 45.2, 23.6, 21.6, 21.1 ppm.
Specific rotation: $[\alpha]_D^{22.2}$ = -37.62 (c 0.90, $CHCl_3$)
HRMS: Calc'd for $C_{19}H_{29}N_3O_2SNa$ [M+Na$^+$] 386.1873; found 386.1871.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IB column, 90:10 *n*-hexane:*i*-PrOH, flow rate: 1 mL/min, 25 °C, UV detection wavelength: 254 nm, retention time: major: 6.9 min, minor: 7.9 min.



3b

GP-1 was followed with no additional change: Commercially available 6-bromobenzo[*b*]thiophene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (62.7 mg, 165 µmol, 66% yield) as a white amorphous solid.

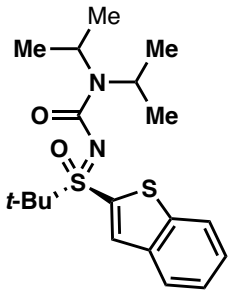
Physical characteristics: White amorphous solid.
TLC: R_f = 0.37 (hexanes/EtOAc, 50% EtOAc)
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.71 – 7.60 (m, 2H), 7.38 (d, *J* = 5.5 Hz, 1H), 4.17 (s, 1H), 3.96 (s, 1H), 1.46 – 1.30 (m, 15H), 1.14 (dd, *J* = 27.1, 6.8 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.5, 142.7, 139.9, 131.1, 130.8, 125.5, 124.9, 123.7, 61.1, 46.5, 45.2, 23.8, 21.9, 20.9, 20.8 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +7.58 (c 0.58, $CHCl_3$)
HRMS: Calc'd for $C_{19}H_{29}N_2O_2S_2$ [M+H$^+$] 381.1665; found 381.1666.
Enantiomeric excess: 97% ee.
HPLC Conditions: Daicel Chiralpak IA column, 50:50 *n*-hexane:DCM, flow rate: 1 mL/min, 25 °C, UV detection wavelength: 254 nm, retention time: major: 7.4 min, minor: 10.8 min.



3c

GP-1 was followed with no additional change: Commercially available thiophene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (66.0 mg, 200 µmol, 80% yield) as a white amorphous solid.

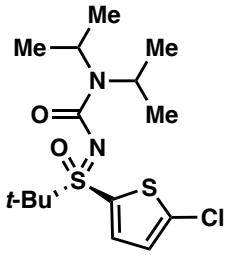
Physical characteristics: White amorphous solid.
TLC: R_f = 0.25 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.55 (dd, *J* = 3.7, 1.4 Hz, 1H), 7.15 (dd, *J* = 5.0, 3.7 Hz, 1H), 4.23 – 3.84 (m, 2H), 1.45 (s, 9H), 1.30 (d, *J* = 7.2 Hz, 6H), 1.20 (d, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.1, 136.1, 135.7, 134.4, 127.9, 61.7, 46.8, 45.3, 23.9, 21.70, 21.0, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -28.81 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{15}H_{27}N_2O_2S_2$ [M+H$^+$] 331.1508; found 331.1509.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 20.7 min, minor: 23.8 min.



3d

GP-1 was followed with no additional change: Commercially available benzo[*b*]thiophene (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (85.5 mg, 225 µmol, 90% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.10 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.90 – 7.81 (m, 3H), 7.48 – 7.40 (m, 2H), 4.08 (s, 2H), 1.51 (s, 9H), 1.26 (s, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.1, 143.6, 138.4, 137.1, 133.2, 127.0, 125.8, 125.3, 122.6, 62.1, 45.5, 24.0, 21.8, 21.0 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -11.42 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{19}H_{29}N_2O_2S_2$ [M+H$^+$] 381.1665; found 381.1668.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 33.6 min, major: 40.7 min.

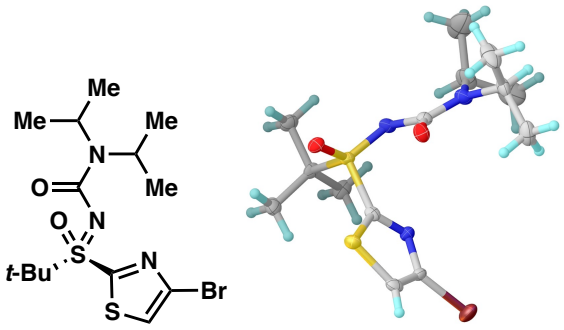


3e

GP-1 was followed with additional modifications mentioned below: Commercially available 2-bromo-5-chloro-thiophene (0.375 mmol, 1.5 eq.) was used. The reaction was warmed up to -40 °C. Purification was performed immediately after work-up by silica gel column chromatography using hexane/EtOAc (0% to 45% EtOAc gradient) to give the product (74.6 mg, 205 µmol, 82% yield) as a white amorphous solid.
GP-2 was used for a gram scale synthesis with no change in yield or enantiopurity of product.

Note: The product showed stability issues in the crude reaction mixture after quenching unlike other *tert*-butyl sulfoximines. The stability was no longer an issue once the product was isolated after column chromatography.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.50 (hexane/EtOAc, 33% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 4.0 Hz, 1H), 6.99 (d, *J* = 4.0 Hz, 1H), 4.03 (s, 2H), 1.47 – 1.44 (m, 9H), 1.28 – 1.20 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.9, 139.3, 135.1, 134.1, 127.7, 62.0, 46.1, 23.8, 21.3 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -33.04 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{15}H_{26}ClN_2O_2S_2$ [M+H$^+$] 365.1119; found 365.1122.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IA column, 95:05 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 12.8 min, major: 14.9 min.



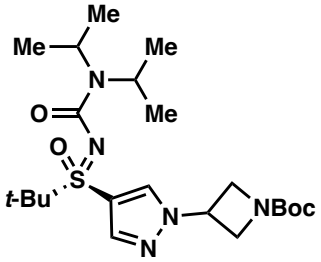
3f

GP-1 was followed with no additional change: Commercially available 4-bromothiazole (0.375 mmol, 1.5 eq.) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (72.8 mg, 178 µmol, 71% yield) as a white crystalline solid.

Physical characteristics: White crystalline solid.
TLC: R_f = 0.30 (hexane/EtOAc, 40% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 4.01 (s, 2H), 1.53 (s, 9H), 1.34 – 1.27 (m, 6H), 1.15 (dd, *J* = 21.5, 6.8 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 165.7, 158.4, 126.8, 125.5, 62.5, 46.8, 45.6, 24.0, 21.8, 20.8, 20.6 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -32.43 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{14}H_{24}BrN_3NaO_2S_2$ [M+Na$^+$] 432.0386; found 432.0383.
Melting Point: 140-142 °C
Enantiomeric excess: >99% ee.

HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 8.6 min, minor: 10.3 min.

CCDC deposition Number: 2243803



3g

GP-3 was followed with additional changes mentioned: *tert*-butyl 3-(4-bromo-1*H*-pyrazol-1-yl)azetidine-1-carboxylate (0.30 mmol, 1.2 eq.) was prepared by a known procedure.[11] CPME was used as the solvent instead of Et_2O and 2.2 eq. of *t*-BuLi was used. The reaction was warmed to -20 ºC and stirred for 30 minutes before quenching (2 hours total time after addition of ***t*-BuSF**. Full Li–Br exchange was not achieved). Purified by silica gel column chromatography using Hex/EtOAc (0% to 100% EtOAc gradient) to give the product (65 mg, 0.138 mmol, 55% yield) as a colorless foam.

Physical characteristics: Colorless foam.

TLC: R_f = 0.19 (hexanes/EtOAc, 80% EtOAc)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.60 (s, 1H), 4.99 (tt, *J* = 7.7, 5.5 Hz, 1H), 4.34 – 4.26 (m, 4H), 4.06 (s, 1H), 3.83 (s, 1H), 1.39 (s, 9H), 1.34 (s, 9H), 1.19 (d, *J* = 6.9 Hz, 6H), 1.14 (d, *J* = 5.5 Hz, 3H), 1.11 (d, *J* = 5.8 Hz, 3H) ppm.

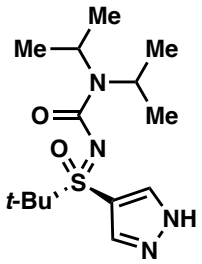
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.2, 156.0, 141.1, 133.5, 116.8, 80.4, 60.4, 56.3, 50.9, 46.6, 45.2, 28.3, 23.3, 21.5, 21.1, 20.8 ppm.

Specific rotation: $[\alpha]_D^{22.4}$ = -63.03 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{22}H_{40}N_5O_4S$ [M+H$^+$] 470.2796; found 470.2787.

Enantiomeric excess: >99% ee.

HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 35.5 min, minor: 57.9 min,



3h

GP-3 was followed with additional changes mentioned: Commercially available 4-bromopyrazole (0.375 mmol, 1.5 eq.) was used with an increased equivalence of *n*-BuLi (from 1.5 to 3 eq.). For halogen-Li exchange, the reaction was removed from bath for 15 min. Then cooled down to -78 °C and repeat this process with another 15 min to complete full exchange. The reaction was warmed to room temperate after addition of ***t*-BuSF** and stirred for 30 minutes. The compound is not UV active and PMA stain was used for TLC visualization. Purified by silica gel column chromatography using DCM/MeOH (0% to 10% MeOH gradient) to give the product (62 mg, 197.5 µmol, 79% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.

TLC: R_f = 0.40 (DCM/MeOH, 10% MeOH)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.62 (s, 2H), 4.36 – 3.78 (m, 2H), 1.38 (s, 9H), 1.30 (d, *J* = 7.5 Hz, 12H) ppm.

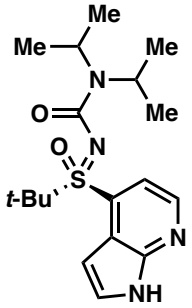
^{13}C NMR: (126 MHz, $CDCl_3$) δ 160.6, 137.2, 113.7, 60.5, 47.1, 45.6, 23.2, 21.4, 20.9 ppm.

Specific rotation: $[\alpha]_D^{23}$ = -76.09 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{14}H_{27}N_4O_2S$ [M+H$^+$] 315.1849; found 315.1840.

Enantiomeric excess: 95% ee.

HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 13.3 min, major: 14.9 min.



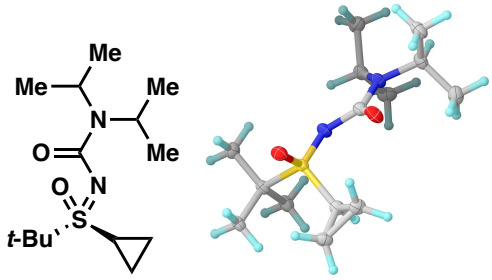
3i

GP-3 was followed with additional changes mentioned: Commercially available 4-bromo-1*H*-pyrrolo[2,3-*b*]pyridine (0.275 mmol, 1.1 eq.) was used. CPME was used instead of Et_2O and 2.5 eq. of *t*-BuLi was used for the Li-I exchange (-78 ºC, 70 minutes: full exchange). Warmed to -10 ºC and held for 2 hours before quenching (3 hours total time after addition of ***t*-BuSF**). No modifications to the quench or work-up procedure were made. Purified by silica gel column chromatography using Hex/EtOAc (0% to 60% EtOAc gradient) to give the product (75 mg, 0.208 mmol, 82% yield) as a clear colorless oil.

Physical characteristics: Clear colorless oil.

TLC: R_f = 0.24 (hexanes/EtOAc, 60% EtOAc)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 10.55 (s, 1H), 8.35 (d, *J* = 4.9 Hz, 1H), 7.50 – 7.29 (m, 1H), 7.24 (t, *J* = 2.9 Hz, 1H), 6.75 – 6.70 (m, 1H), 4.41 – 4.16 (m, 1H), 4.08 – 3.86 (m, 1H), 1.41 (d, *J* = 6.7 Hz, 6H), 1.39 (s, 9H), 1.23 (d, *J* = 6.7 Hz, 3H), 1.16 (d, *J* = 6.6 Hz, 3H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.7, 149.6, 141.6, 134.5, 128.7, 119.1, 117.1, 101.1, 62.0, 46.7, 45.4, 23.7, 21.9, 21.7, 20.9, 20.8 ppm.
Specific rotation: $[\alpha]_D^{25.6}$ = -3.57 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{28}N_4O_2SNa$ [M+Na$^+$] 387.1825; found 387.1829.
Enantiomeric excess: 97% ee.
HPLC Conditions: Daicel Chiralpak IB column, 95:5 *n*-hexane:*i*-PrOH, flow rate: 1 mL/min, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 22.3 min, major: 25.6 min.



4a

GP-2 was followed with additional changes mentioned: commercially available cyclopropylbromide (0.375 mmol, 1.5 eq.) was used and lithiated with *t*-BuLi (3 eq.) at -78 ºC. The reaction was warmed to -40 °C after addition of ***t*-BuSF** and stirred for one hour. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (51.0 mg, 176 µmol, 70% yield) as a white crystalline solid.

Different scale reactions:

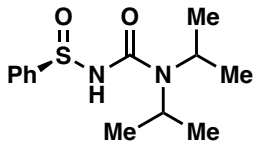
GP-2 was used with *t*-BuSF (2.0 g, 7.51 mmol, 1 eq.), cyclopropyl bromide (1.20 mL, 15.0 mmol, 2 eq.), and *t*-BuLi (8.8 mL, 15.0 mmol, 1.7 M, 2 eq.) to give (1.71 g, 5.93 mmol, 79% yield, 97% ee).

GP-2 was used with *t*-BuSF (5.65 g, 21.2 mmol, 1 eq.), cyclopropyl bromide (3.40 mL, 42.4 mmol, 2 eq.), and *t*-BuLi (25 mL, 42.4 mmol, 1.7 M, 2 eq.) to give (4.28g, 14.8 mmol, 70% yield, 97% ee).

Physical characteristics: White crystalline solid.
TLC: R_f = 0.2 (hexane/EtOAc, 40% EtOAc).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 4.00 (s, 2H), 2.51 – 2.40 (m, 1H), 1.60 (ddt, *J* = 10.2, 7.5, 5.1 Hz, 1H), 1.48 (s, 9H), 1.29 – 1.12 (m, 14H), 1.11 – 1.01 (m, 1H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.8, 62.5, 46.5, 45.1, 24.7, 24.3, 21.5, 20.9, 7.4, 5.1. ppm.
Specific rotation: $[\alpha]_D^{23}$ = +15.99 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{14}H_{29}N_2O_2S$ [M+H$^+$] 289.1944; found 289.2952.
Melting Point: 175-177 °C
Enantiomeric excess: 97% ee. Recrystallized to >99% ee with >90% recovery.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 10.8 min, major: 11.9 min.
CCDC deposition Number: 2243800

IXb. *S*-Activation and functionalization.

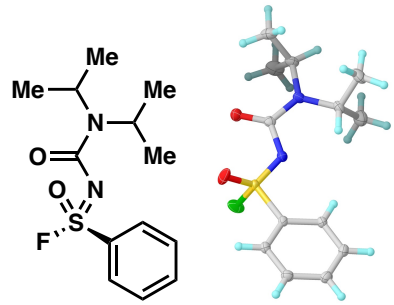


S5a

GP-4 was followed with no additional change: *tert*-butyl phenyl sulfoximine of >99% ee was used (97 mg, 0.30 mmol, 1 eq.). Purified by a short plug of silica gel eluting with DCM to give the product (71.0 mg, 0.264 mmol, 88% yield) as a white amorphous solid.

Different scale reactions:
(1.24 g, 3.82 mmol, >99% ee) produced (0.88 g, 3.28 mmol, 86% yield, >99% ee)
(3.01 g, 9.28 mmol, >99% ee) produced (2.22g, 8.27 mmol, 89% yield, >99% ee)

Physical characteristics: White amorphous solid.
TLC: R_f = 0.33 (hexane/acetone, 33% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.48 – 7.42 (m, 3H), 7.37 (s, 1H), 3.74 (hept, *J* = 6.8 Hz, 2H), 1.24 (d, *J* = 4.1 Hz, 6H), 1.23 (d, *J* = 4.1 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 153.7, 144.4, 131.3, 129.2, 125.2, 46.9, 21.3, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -149.55 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{13}H_{20}N_2O_2SNa$ [M+Na$^+$] 291.1138; found 291.1144.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IA column, 50:50 *n*-hexane:DCM, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 16.2 min, major: 20.1 min.

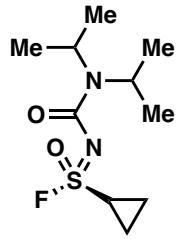


S6a

GP-6 was followed and no additional change: *tert*-butyl phenyl sulfoximine of >99% ee was used (500 mg, 1.5 mmol, 1.0 eq). Purified by silica gel column chromatography using hexane/EtOAc (0% to 25% EtOAc gradient) to give the product (370 mg, 1.3 mmol, 84% yield) as a white crystalline solid.

Different scale reactions:
(1.0 g, 3.08 mmol, >99% ee) produced (689 mg, 2.41 mmol, 78% yield, >99% ee)
(2.0 g, 6.16 mmol, >99% ee) produced (1.31 g, 4.57 mmol, 74% yield, >99% ee)

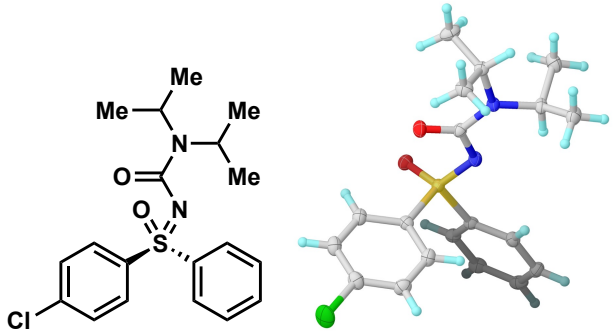
Physical characteristics: White crystalline solid.
TLC: R_f = 0.3 (hexane/EtOAc, 20% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 2H), 7.76 – 7.69 (m, 1H), 7.61 (t, *J* = 7.9 Hz, 2H), 4.16 (s, 1H), 3.84 (s, 1H), 1.31 (dd, *J* = 6.9, 3.4 Hz, 6H), 1.21 (t, *J* = 6.6 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 153.3 (d, *J* = 3.2 Hz), 135.4 (d, *J* = 22.6 Hz), 135.0, 129.6, 127.7, 48.3, 45.9, 21.3, 20.6, 20.5 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ 69.53 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +30.26 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{13}H_{20}FN_2O_2S$ [M+H$^+$] 287.1224; found 287.1224.
Melting Point: 102-105 °C
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 13.0 min, major: 15.1 min.
CCDC deposition Number: 2243798



S6b

GP-6 was followed and no additional change: *tert*-butyl cyclopropyl sulfoximine of >99% ee (1.04 mmol, 1.0 eq) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 25% EtOAc gradient) to give the product (232 mg, 0.927 mmol, 89% yield) as colorless oil which slowly solidified into a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.3 (hexane/EtOAc, 20% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 4.15 (s, 1H), 3.80 (s, 1H), 3.36 (dq, *J* = 8.2, 3.9 Hz, 1H), 1.55 – 1.43 (m, 2H), 1.33 – 1.27 (m, 6H), 1.25 (dq, *J* = 7.9, 1.7 Hz, 2H), 1.19 (d, J = 6.4 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 154.1 (d, *J* = 3.3 Hz), 48.1, 45.7, 30.1 (d, *J* = 27.0 Hz), 20.9 (d, *J* = 72.0 Hz), 7.2, 6.5 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ 62.06 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +38.58 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{10}H_{20}N_2O_2S$ [M+H$^+$] 251.1224; found 251.1218.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 7.4 min, major: 8.2 min.



7a

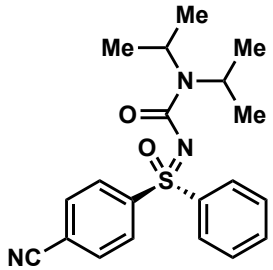
GP-7 (Grignard reagent) was followed with no additional modification: Commercially available 4-chlorophenylmagnesium bromide (0.275 mmol, 1.1 eq., 1.0 M solution in Et_2O) from Sigma-Aldrich was used with Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.). Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (89.8 mg, 0.237 mmol, 95% yield, >99% ee) as a white amorphous solid.

GP-8 (turbo-Grignard reagent) was followed with additional modifications mentioned: Commercially available 4-chloro-bromobenzene (0.275 mmol, 1.1 eq.) in dry THF (0.2 mL) was added at room temperature in one portion to the stirring isopropylmagnesium chloride lithium chloride complex solution (0.21 mL, 0.275 mmol, 1.1 eq. 1.3 M in THF), exchange takes about 12 hours. Purified by silica gel column chromatography using

hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (56.7 mg, 0.15 mmol, 60% yield, >99% ee) as a white amorphous solid.

GP-1 (organolithium) was followed with no additional modificaitons: Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (75.6 mg, 0.2 mmol, 80% yield, 94% ee) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.6 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.88 – 7.84 (m, 2H), 7.56 – 7.52 (m, 1H), 7.52 – 7.48 (m, 2H), 7.46 – 7.42 (m, 2H), 4.12 (br, 2H), 1.28 (s, 12H) ppm.
^{13}C NMR: (151 MHz, $CDCl_3$) δ 158.7, 141.0, 140.2, 139.3, 132.9, 129.7, 129.6, 129.1, 127.7, 46.3, 21.3 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -3.42 (c 1.00, $CHCl_3$)
Melting Point: 129-131 ºC
HRMS: Calc'd for $C_{19}H_{24}ClN_2O_2S^+$ [M+H$^+$] 379.1242; found 379.1242.
Enantiomeric excess: >99% ee for both Grignard and turbo-Grignard reagents. 94% ee for organolithium reagent.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 18.9 min, major: 22.4 min.
CCDC deposition Number: 2243808

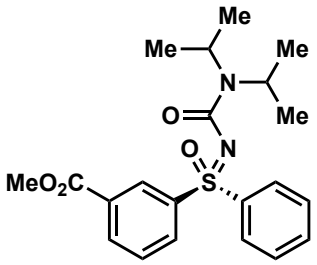


7b

GP-8 was used with additional modifications mentioned: A solution of commercially available 4-iodobenzonitrile (63 mg, 0.275 mmol, 1.1 eq.) in dry THF (0.25 ml) was added to isopropylmagnesium chloride lithium chloride complex solution (0.21 mL, 0.275 mmol, 1.1 eq. 1.3 M in THF) dropwise at -78 ºC. Upon gradual warming to -10 ºC for 4 hours (the reaction mixture turned yellow), then a solution of Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.25 mL) was added, workup procedure as described in GP-8. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (90.4 mg, 0.245 mmol, 98% yield) as a colorless oil.

GP-12 was followed with the Mg–X exchange as described above with 2 equivalents of turbo-Grignard reagent: Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) was used to provide (65 mg, 176 mmol, 70% yield) as colorless oil.

Physical characteristics: Colorless oil.
TLC: R_f = 0.71 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.03 – 7.99 (m, 2H), 7.99 – 7.95 (m, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.59 – 7.54 (m, 1H), 7.51 (dd, *J* = 8.4, 6.7 Hz, 2H), 4.28 (br, 1H), 3.92 (br, 1H), 1.55 – 0.96 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.3, 146.6, 139.5, 133.5, 133.1, 129.7, 128.1, 127.9, 117.4, 116.0, 47.1, 45.6, 21.3, 21.2, 21.1, 21.0 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -19.16 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{20}H_{24}N_3O_2S^+$ [M+H$^+$] 370.1584; found 370.1576.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 254 nm, retention time: minor: 28.3 min, major: 35.3 min.

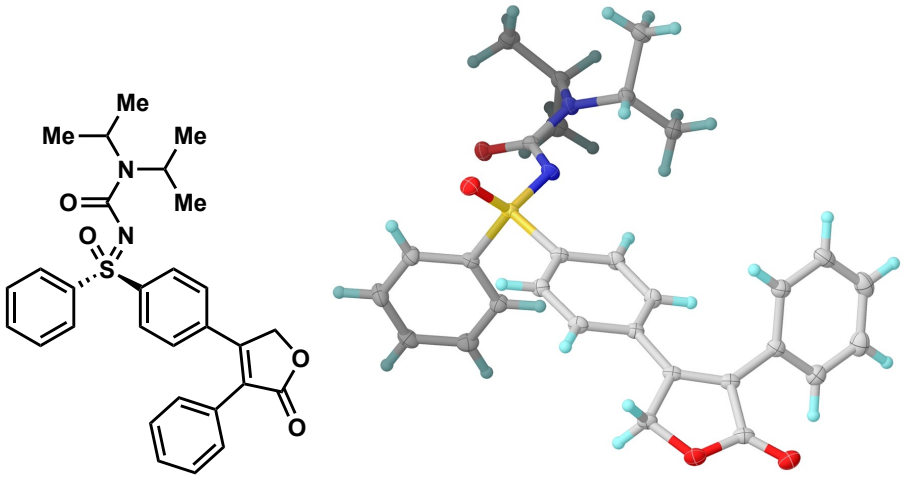


7c

GP-8 was used with additional modifications mentioned: A solution of commercially available methyl 3-iodobenzoate (72.1 mg, 0.275 mmol, 1.1 eq.) in dry THF (0.25 mL) was added to isopropylmagnesium chloride lithium chloride complex solution (0.21 mL, 0.275 mmol, 1.1 eq. 1.3 M in THF) dropwise at -78 ºC, to. Upon gradual warming to -10 ºC for 4 hours (the reaction mixture turned yellow) then a solution of Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.25 mL) was added. Work-up procedure as described in GP-8. Purified by silica gel column chromatography using DCM/acetone, (0% to 10% Acetone gradient) to give the product (63.4 mg, 0.158 mmol, 63% yield) as a colorless oil.

Physical characteristics: Colorless oil.
TLC: R_f = 0.84 (DCM/acetone, 10% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.58 (t, *J* = 1.8 Hz, 1H), 8.15 (dt, *J* = 7.8, 1.4 Hz, 1H), 8.11 (ddd, *J* = 8.0, 2.0, 1.2 Hz, 1H), 8.01 – 7.93 (m, 2H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.53 – 7.46 (m, 3H), 4.19 (br, 2H), 3.90 (s, 3H), 1.29 (s, 12H) ppm.

^{13}C NMR: (126 MHz, $CDCl_3$) δ 165.4, 158.6, 142.4, 140.6, 133.4, 132.9, 131.6, 131.5, 129.6, 129.5, 128.8, 127.7, 52.6, 46.1, 21.2 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -8.82 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{21}H_{27}N_2O_4S^+$ [M+H$^+$] 403.1686; found 403.1675.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IB column, 95:05 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 26.7 min, minor: 29.4 min.

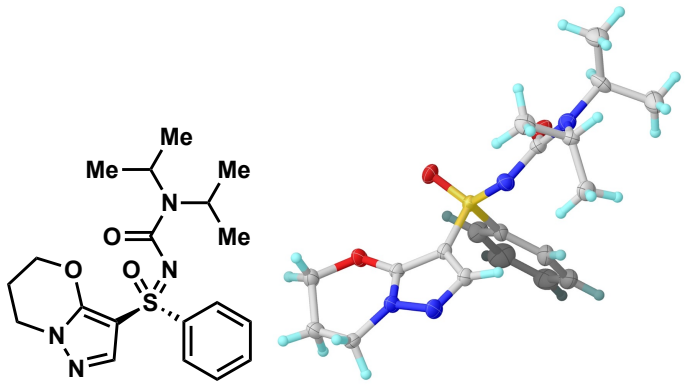


7d

GP-8 was used with additional changes mentioned: 4-(4-iodophenyl)-3-phenylfuran-2(5H)-one (60.5 mg, 0.25 mmol, 1 eq.) in 0.3 mL dry THF was added at room temperature in one portion to the stirring isopropylmagnesium chloride lithium chloride complex solution (0.38 mL, 0.5 mmol, 2 eq. 1.3 M in THF), the reaction mixture turned turbid orange and exchange takes about 2 hours. Upon complete Mg-halogen exchange, a solution of Sulfonimidoyl fluoride **S6a** (107.3 mg, 0.375 mmol, 1.5 eq.) in THF (0.5 mL) was added, workup procedure as described in Method 2.
Purified by silica gel column chromatography using DCM/acetone (0% to 6% acetone gradient) to give the product (77.8 mg, 0.155 mmol, 62% yield) as a colorless crystalline solid.

Physical characteristics: Colorless crystalline solid.
TLC: R_f = 0.72 (DCM/acetone, 10% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.98 – 7.93 (m, 2H), 7.90 – 7.86 (m, 2H), 7.57 – 7.53 (m, 1H), 7.50 (dd, *J* = 8.3, 6.6 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.36 (s, 5H), 5.13 (d, *J* = 3.5 Hz, 2H), 4.30 (br, 1H), 3.90 (br, 1H), 1.36 – 1.32 (m, 6H), 1.19 (t, *J* = 7.4 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 172.8, 158.5, 153.6, 143.5, 140.4, 134.8, 133.1, 129.5, 129.5, 129.3, 129.2, 129.0, 128.9, 128.5, 128.4, 128.2, 127.8, 70.4, 47.2, 45.4, 21.6, 20.7 ppm.

Specific rotation: $[\alpha]_D^{23}$ = +8.57 (c 1.00, $CHCl_3$)
Melting Point: 192-193 ºC
HRMS: Calc'd for $C_{29}H_{31}N_2O_4S^+$ [M+H$^+$] 503.2000; found 503.2006.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 19.7 min, major: 22.6 min.
CCDC deposition Number: 22243809

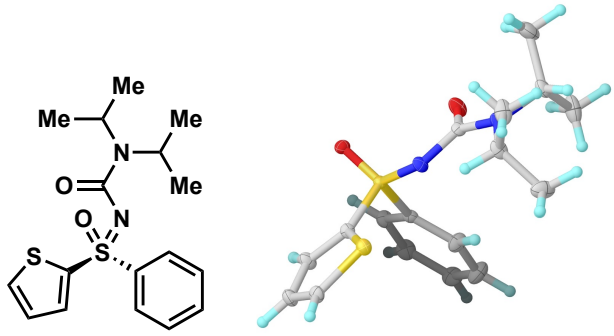


7e

GP-8 was followed with additional modifications mentioned: 3-iodo-6,7-dihydro-5H-pyrazolo[5,1-b][1,3]oxazine (62.5 mg, 0.25 mmol) in 0.5 mL dry THF was added at 0 ºC dropwise to the stirring isopropylmagnesium chloride lithium chloride complex solution (0.21 mL, 0.275 mmol, 1.1 eq. 1.3 M in THF) which was slowly warmed to room temperature (exchange takes about 6 hours, turning into a white emulsion). Then a solution of Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.25 mL) was added. Purified by silica gel column chromatography using DCM/acetone (0% to 15% acetone gradient) to give the product (87.7 mg, 0.225 mmol, 90% yield) as a white crystalline solid.

Physical characteristics: White crystalline solid.
TLC: R_f = 0.46 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.64 (s, 1H), 7.49 – 7.41 (m, 3H), 4.29 (dddd, *J* = 36.7, 11.1, 6.6, 4.0 Hz, 2H, overlay with br, 1H), 4.05 (t, *J* = 6.2 Hz, 2H), 3.85 (br, 1H), 2.25 – 2.13 (m, 2H), 1.28 (d, *J* = 6.9 Hz, 6H), 1.17 (t, *J* = 8.2 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.7, 149.7, 142.9, 138.9, 132.1, 129.0, 126.8, 102.2, 66.6, 46.9, 45.0, 44.4, 21.4, 21.4, 21.0, 20.8, 20.7 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +4.55 (c 1.00, $CHCl_3$)
Melting Point: 124-125 ºC
HRMS: Calc'd for $C_{19}H_{27}N_4O_3S^+$ [M+H$^+$] 391.1798; found 391.1793.
Enantiomeric excess: >99% ee.

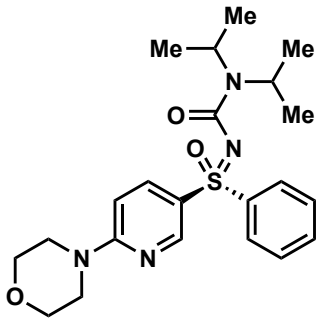
HPLC Conditions: Daicel Chiralpak IB column, 90:10 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 34.3 min, major: 42.6 min.
CCDC deposition Number: 2243805



7f

GP-8 was followed with additional modifications mentioned: Commercially available 2-bromothiophene (0.25 mmol, 1 eq.) was added at room temperature in one portion to a stirring isopropylmagnesium chloride lithium chloride complex solution (0.21 mL, 0.275 mmol, 1.1 eq. 1.3 M in THF) (exchange takes about 12 hours) then cooled to 0 ºC. A solution of Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.25 mL) was added dropwise at 0 ºC then warmed to room temperature. Work-up procedure as described in GP-8. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (81.4 mg, 0.233 mmol, 93% yield) as a light-pink crystalline solid.

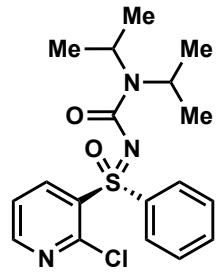
Physical characteristics: Light-pink crystalline solid
TLC: R_f = 0.46 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.99 – 7.95 (m, 2H), 7.59 (d, *J* = 4.4 Hz, 2H), 7.53 – 7.46 (m, 3H), 7.04 (t, *J* = 4.4 Hz, 1H), 4.09 (br, 2H), 1.29 (s, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.4, 142.4, 142.1, 133.7, 133.1, 132.6, 129.4, 128.2, 127.3, 45.8, 21.1 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +61.32 (c 1.00, $CHCl_3$)
Melting Point: 177-179 ºC
HRMS: Calc'd for $C_{17}H_{23}N_2O_2S_2^+$ [M+H$^+$] 351.1195; found 351.1189.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 254 nm, retention time: minor: 25.9 min, major: 29.9 min.
CCDC deposition Number: 2243806



7g

GP-8 was followed with additional changes mentioned: 4-(5-bromopyridin-2-yl)morpholine (60.5 mg, 0.25 mmol, 1 eq.) in 0.3 mL dry THF was added at room temperature in one portion to the stirring isopropylmagnesium chloride lithium chloride complex solution (0.38 mL, 0.5 mmol, 2 eq. 1.3 M in THF) at 0 ºC then warmed to room temperature where it stirred for 12 hours (reaction mixture turned turbid orange). Upon complete Mg-halogen exchange, a solution of Sulfonimidoyl fluoride **S6a** (107.3 mg, 0.375 mmol, 1.5 eq.) in THF (0.5 mL) was added at 0 ºC then warmed to room temperature while monitoring by TLC. Work-up conditions were the same as described in GP-8.
Purified by silica gel column chromatography using DCM/acetone (0% to 9% acetone gradient) to give the product (64.5 mg, 0.15 mmol, 60% yield) as a colorless crystalline solid.

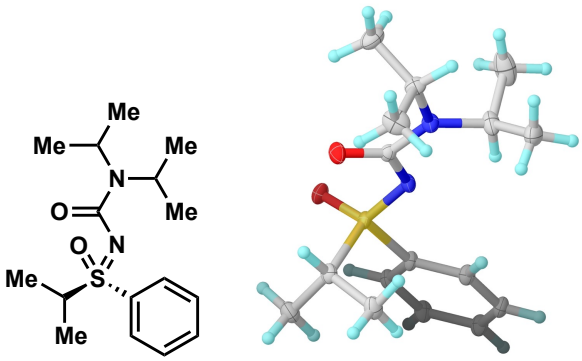
Physical characteristics: Colorless crystalline solid.
TLC: R_f = 0.2 (hexane/EtOAc, 50% EtOAc, light purple spot under 254 nm UV).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 2.5 Hz, 1H), 7.91 (dd, *J* = 8.0, 1.8 Hz, 2H), 7.88 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.51 – 7.43 (m, 3H), 6.58 (d, *J* = 9.2 Hz, 1H), 4.29 (s, 1H), 3.94 (s, 1H), 3.76 – 3.73 (m, 4H), 3.60 (dd, *J* = 5.8, 4.1 Hz, 4H), 1.35 (d, *J* = 6.9 Hz, 6H), 1.19 (t, *J* = 7.9 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 160.1, 158.7, 148.7, 142.3, 136.8, 132.3, 129.3, 127.1, 124.9, 105.8, 66.5, 46.9, 45.2, 44.9, 21.6, 20.8 ppm.
Specific rotation: $[\alpha]_D^{23}$ = 21.08 (c 1.00, $CHCl_3$)
Melting Point: 118-120 ºC
HRMS: Calc'd for $C_{22}H_{31}N_4O_3S^+$ [M+H$^+$] 431.2111; found 431.2101.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IB column, 90:10 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 34.6 min, major: 38.7 min.



7h

GP-8 was followed and additional changes mentioned: A solution of isopropylmagnesium chloride lithium chloride complex solution (0.21 mL, 0.275 mmol, 1.1 eq. 1.3 M in THF) was added dropwise at -40 ºC, to a solution of commercially available 3-iodo-2-chloropyridine (52.9 mg, 0.275 mmol, 1.1 eq.) in 0.25 mL dry THF. Upon gradual warming up to 0 ºC over 1 hour, the reaction mixture turned yellow, then a solution of Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.25 mL) was added, workup procedure as described in GP-8.
Purified by silica gel column chromatography using DCM/acetone (0% to 9% acetone gradient) to give the product (70.2 mg, 0.185 mmol, 74% yield) as a light-yellow amorphous solid.

Physical characteristics: Light-yellow amorphous solid.
TLC: R_f = 0.73 (DCM/acetone, 10% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 7.9, 1.9 Hz, 1H), 8.46 (dd, *J* = 4.7, 1.9 Hz, 1H), 8.08 – 7.98 (m, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.55 – 7.45 (m, 3H), 4.38 (br, 1H), 3.84 (br, 1H), 1.34 (d, *J* = 7.0 Hz, 6H), 1.20 (dd, *J* = 21.1, 6.9 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.9, 152.5, 146.9, 141.2, 137.5, 137.3, 133.7, 129.1, 129.1, 123.5, 47.4, 45.4, 21.5, 21.4, 20.7, 20.5 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -60.07 (c 1.00, $CHCl_3$)
Melting Point: 96-97 ºC
HRMS: Calc'd for $C_{18}H_{23}ClN_3O_2S^+$ [M+H$^+$] 380.1194; found 380.1188.
Enantiomeric excess: 98.7 % ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 254 nm, retention time: minor: 15.0 min, major: 18.1 min.



7i

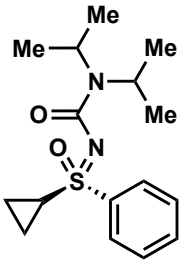
GP-7 was followed with no additional change: Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) and commercially available isopropylmagnesium chloride from Sigma-Aldrich were used.
Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (69.8 mg, 0.225 mmol, 90% yield) as a white amorphous solid.

GP-8 was used with no additional change: Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) and commercially available isopropylmagnesium chloride lithium chloride complex solution (1.3 M in THF) from Sigma-Aldrich. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (73.6 mg, 0.237 mmol, 95% yield) as a white amorphous solid.

GP-12 was followed with no additional change: Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) and commercially available isopropylmagnesium chloride lithium chloride complex solution (0.385 mL, 2 eq., 1.3 M in THF) from Sigma-Aldrich were used to provide (53 mg, 171 mmol, 68% yield) as white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.44 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.83 – 7.80 (m, 2H), 7.61 – 7.57 (m, 1H), 7.53 (dd, *J* = 8.5, 6.7 Hz, 2H), 4.05 (d, *J* = 70.6 Hz, 2H), 3.58 (pd, *J* = 6.9, 1.0 Hz, 1H), 1.36 – 1.13 (m, 18H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.2, 136.2, 132.9, 129.1, 128.9, 56.1, 46.5, 45.2, 21.6, 20.8, 16.0, 15.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +6.00 (c 1.00, $CHCl_3$)
Melting Point: 99-110 ºC
HRMS: Calc'd for $C_{16}H_{27}N_2O_2S^+$ [M+H$^+$] 311.1788; found 311.1779.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 20.2 min, major: 23.3 min.

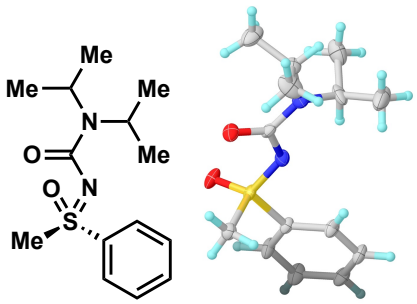
CCDC deposition Number: 2243802



7j

GP-7 was followed with no additional change: Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) and commercially available cyclopropylmagnesium chloride from Sigma-Aldrich were used.
Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (75.4 mg, 0.245 mmol, 98% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.4 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.2, 1.9 Hz, 2H), 7.57 – 7.53 (m, 1H), 7.50 (dd, *J* = 8.3, 6.4 Hz, 2H), 4.07 (br, 1H), 3.92 (br, 1H), 2.51 (tt, *J* = 8.0, 4.8 Hz, 1H), 1.47 (ddt, *J* = 10.2, 7.3, 5.0 Hz, 1H), 1.32 – 1.20 (m, 7H), 1.18 – 1.07 (m, 7H), 0.90 (dtd, *J* = 9.1, 7.5, 5.2 Hz, 1H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.7, 140.9, 132.6, 129.3, 127.2, 46.5, 45.1, 33.9, 21.6, 20.7, 6.7, 5.4 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +21.43 (c 1.00, $CHCl_3$)
Melting Point: 80-81 °C
HRMS: Calc'd for $C_{16}H_{25}N_2O_2S^+$ [M+H$^+$] 309.1632; found 309.1632.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 18.7 min, major: 22.2 min.

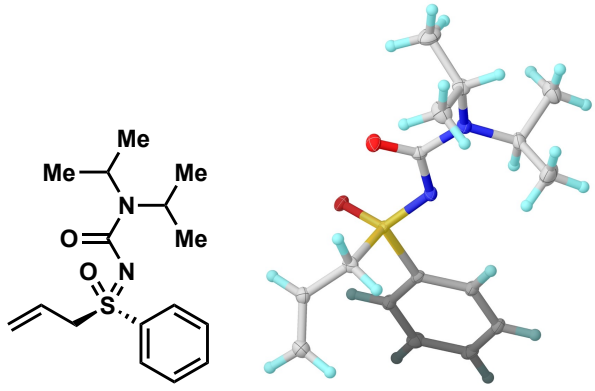


7k

GP-7 was followed with no additional change: Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) and commercially available methylmagnesium bromide from Sigma-Aldrich were used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (64.2 mg, 0.227 mmol, 91% yield) as a white crystalline solid.

GP-12 was followed with no additional change: Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) and commercially available methylmagnesium chloride (0.50 mmol, 2 eq.) from Sigma-Aldrich were used to provide (52 mg, 184 mmol, 74% yield) as white crystalline solid.

Physical characteristics: White crystalline solid.
TLC: R_f = 0.3 (hexane/EtOAc, 33% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 2H), 7.63 – 7.59 (m, 1H), 7.57 – 7.52 (m, 2H), 4.15 (s, 1H), 3.91 (s, 1H), 3.30 (s, 3H), 1.29 – 1.16 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.1, 140.4, 133.1, 129.4, 127.2, 46.8, 45.1, 44.9, 21.5, 21.4, 20.8 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -14.51 (c 1.00, $CHCl_3$)
Melting Point: 169-170 °C
HRMS: Calc'd for $C_{14}H_{23}N_2O_2S^+$ [M+H$^+$] 283.1475; found 283.1474.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 18.7 min, minor: 29.9 min.
CCDC deposition Number: 2243799

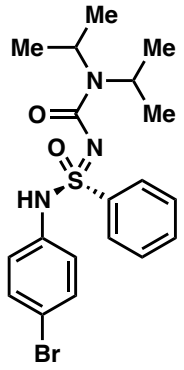


7l

GP-7 was followed with additional changed mentioned: Allylmagnesium bromide prepared following literature procedure[12] and added dropwise to a solution of Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) at -78 °C over 5 minutes to give a gold

solution, reaction completed after 1 hour at -78 ºC and quenched with MeOH. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (76 mg, 0.247 mmol, 98 % yield) as a white crystalline solid.

Physical characteristics: White crystalline solid.
TLC: R_f = 0.53 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.51 (dd, *J* = 8.5, 7.0 Hz, 2H), 5.64 (ddt, *J* = 17.5, 10.2, 7.5 Hz, 1H), 5.23 (d, *J* = 10.1 Hz, 1H), 5.03 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.40 (dd, *J* = 13.6, 7.5 Hz, 1H), 4.18 (s, 1H), 4.10 (dd, *J* = 13.6, 7.4 Hz, 1H), 3.89 (s, 1H), 1.23 (d, *J* = 6.8 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.1, 137.4, 133.3, 129.1, 129.0, 128.5, 125.2, 124.6, 60.4, 47.0, 45.1, 21.4, 20.8 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -99.33 (c 1.00, $CHCl_3$)
Melting Point: 79-80 ºC
HRMS: Calc'd for $C_{16}H_{25}N_2O_2S^+$ [M+H$^+$] 309.1632; found 309.1632.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 16.6 min, minor: 21.7 min.
CCDC deposition Number: 2243807



8a

GP-9 was followed with no additional change: Commercially available 4-bromoaniline (1.0 eq, 0.25 mmol) was used. NaHMDS (2.0 eq) was used as base. Purified by silica gel column chromatography using hexane/EtOAc (0% to 35% EtOAc gradient) to give the product (89 mg, 203 µmol, 81% yield) as a white solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.6 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 11.17 (s, 1H), 7.82 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.53 – 7.46 (m, 1H), 7.42 (dd, *J* = 8.5, 7.1 Hz, 2H), 7.32 – 7.27 (m, 2H), 7.01 – 6.95 (m, 2H), 4.32 (s, 1H), 3.86 (s, 1H), 1.33 (d, *J* = 6.8 Hz, 6H), 1.15 (d, *J* = 6.9 Hz, 6H) ppm.

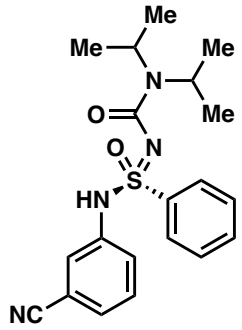
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.7, 140.7, 136.1, 132.9, 132.4, 129.2, 127.0, 118.0, 47.4, 45.5, 21.2, 21.1, 20.9, 20.8 ppm.

Specific rotation: $[\alpha]_D^{23}$ = -128.38 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{19}H_{25}BrN_3O_2S$ [M+H$^+$] 438.0845; found 438.0852.

Enantiomeric excess: >99% ee.

HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 4.9 min, major: 5.4 min.



8b

GP-9 was followed with no additional change: Commercially available 3-aminobenzonitrile (1.0 eq., 0.25 mmol) was used. NaHMDS (2.0 eq) was used as base. Purified by silica gel column chromatography using hexane/EtOAc (0% to 30% EtOAc gradient) to give the product (83 mg, 216 µmol, 86% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.

TLC: R_f = 0.28 (hexane/EtOAc, 25% EtOAc).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.5, 1.8 Hz, 2H), 7.53 (dd, *J* = 8.4, 6.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.37 (d, *J* = 2.2 Hz, 1H), 7.34 – 7.26 (m, 3H), 4.31 (s, 1H), 3.85 (s, 1H), 1.33 (d, *J* = 6.9 Hz, 6H), 1.15 (d, *J* = 6.6 Hz, 6H) ppm.

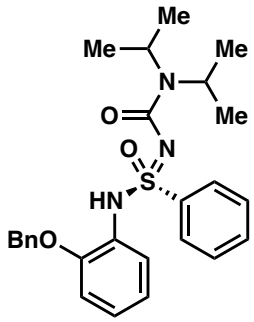
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.5, 140.5, 138.3, 133.2, 130.3, 129.4, 127.9, 126.9, 125.4, 123.9, 118.2, 113.4, 47.4, 45.6, 21.1, 21.0, 20.9, 20.8 ppm.

Specific rotation: $[\alpha]_D^{23}$ = -153.17 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{20}H_{25}N_4O_2S$ [M+H$^+$] 385.1693; found 385.1690.

Enantiomeric excess: >99% ee.

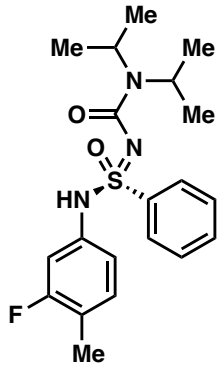
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 8.7 min, major: 9.3 min.



8c

GP-9 was followed with no additional change: Commercially available 2-(benzyloxy)aniline (1.0 eq) was used. NaHMDS (2.0 eq) was used as base. Purified by silica gel column chromatography using hexane/EtOAc (0% to 20% EtOAc gradient) to give the product (104 mg, 223 µmol, 89% yield) as a colorless oil, which solidified to a white amorphous solid.

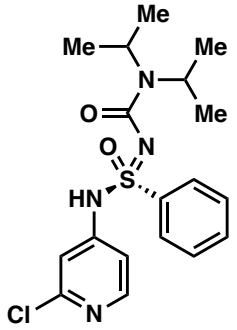
Physical characteristics: White amorphous solid.
TLC: R_f = 0.36 (hexane/EtOAc, 20% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 11.16 (s, 1H), 7.82 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.60 – 7.53 (m, 2H), 7.46 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.44 – 7.35 (m, 3H), 7.35 – 7.27 (m, 3H), 6.96 (td, *J* = 7.8, 1.6 Hz, 1H), 6.82 (t, *J* = 7.4 Hz, 2H), 5.10 (d, *J* = 12.1 Hz, 1H), 4.98 (d, *J* = 12.2 Hz, 1H), 4.40 (s, 1H), 3.79 (s, 1H), 1.36 (dd, *J* = 7.0, 3.6 Hz, 6H), 1.14 (dd, *J* = 21.3, 6.8 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.4, 149.1, 141.4, 136.6, 132.4, 128.8, 128.6, 127.8, 127.0, 126.9, 126.8, 125.0, 122.1, 121.3, 112.3, 70.4, 47.4, 45.3, 21.2, 21.1, 21.0, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +6.49 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{26}H_{32}N_3O_3S$ [M+H$^+$] 466.2159; found 466.2154.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 6.3 min, major: 7.1 min.



8d

GP-9 was followed with no additional change: Commercially available 3-fluoro-4-methylaniline (1.0 eq, 0.2 mmol) was used. NaHMDS (2.0 eq) was used as base. Purified by silica gel column chromatography using hexane/EtOAc (0% to 20% EtOAc gradient) to give the product (68 mg, 174 µmol, 69% yield) as a colorless oil.

Physical characteristics: Colorless oil.
TLC: R_f = 0.36 (hexane/EtOAc, 20% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 6.96 (t, *J* = 8.3 Hz, 1H), 6.82 (dd, *J* = 10.8, 2.2 Hz, 1H), 6.75 (dd, *J* = 8.1, 2.2 Hz, 1H), 4.32 (s, 1H), 3.98 – 3.77 (m, 1H), 2.13 (s, 3H), 1.33 (d, *J* = 6.9 Hz, 6H), 1.15 (d, *J* = 6.9 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 162.3, 160.3, 157.9, 140.9, 135.9 (d, *J* = 10.2 Hz), 132.9, 131.9 (d, *J* = 6.3 Hz), 129.2, 127.1, 121.4 (d, *J* = 17.4 Hz), 117.4 (d, *J* = 3.4 Hz), 109.1 (d, *J* = 25.8 Hz), 47.4, 45.6, 21.3, 21.2, 21.0, 20.9, 14.2 (d, *J* = 3.2 Hz) ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -115.20 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -135.45 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{20}H_{27}FN_3O_2S$ [M+H$^+$] 392.1803; found 392.1803.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 5.1 min, major: 5.6 min.

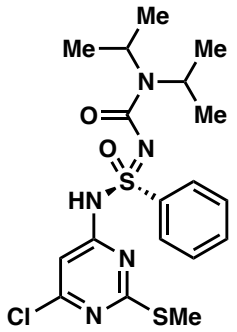


8e

GP-9 was followed with additional changes mentioned: Commercially available 2-chloropyridin-4-amine (1.0 eq, 0.2 mmol) and NaHMDS (2.0 eq) were used. The reaction was quenched after stirring at room temperature for 1.5 hours. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (71 mg, 0.180 mmol, 90% yield) as a clear colorless oil.

Physical characteristics: Clear colorless oil.
TLC: R_f = 0.36 (hexane/EtOAc, 40% EtOAc).

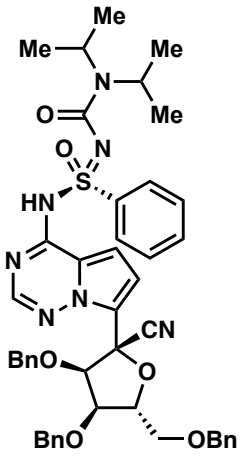
^{1}H NMR: (500 MHz, $CDCl_3$) δ 12.54 (s, 1H), 8.10 (d, *J* = 5.6 Hz, 1H), 7.94 – 7.89 (m, 2H), 7.61 – 7.55 (m, 1H), 7.53 – 7.48 (m, 2H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.91 (dd, *J* = 5.6, 2.0 Hz, 1H), 4.30 (s, 1H), 3.84 (s, 1H), 1.33 (d, *J* = 3.8 Hz, 6H), 1.14 (d, *J* = 3.5 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.1, 152.3, 150.2, 147.0, 140.3, 133.4, 129.4, 126.8, 113.0, 112.3, 47.4, 45.6, 21.0, 20.9, 20.8, 20.6 ppm.
Specific rotation: $[\alpha]_D^{22.8}$ = -65.23 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{23}ClN_4O_2SNa$ [M+Na$^+$] 417.1122; found 417.1122.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL/min, 25 °C, UV detection wavelength: 254 nm, retention time: minor: 6.9 min, major: 12.7 min.



8f

GP-9 was followed with additional changes mentioned: Commercially available 6-chloro-2-(methylthio)pyrimidin-4-amine (1.0 eq, 0.20 mmol) and NaHMDS (2.0 eq) were used. The reaction was quenched after stirring at room temperature for 1.5 hours. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (76 mg, 0.172 mmol, 86% yield) as a white amorphous solid.

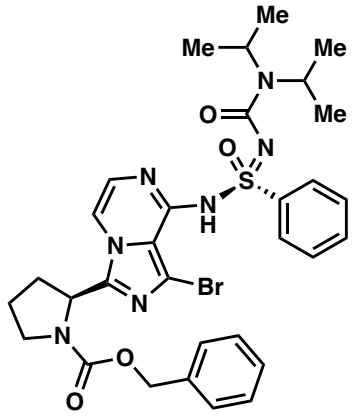
Physical characteristics: White amorphous solid.
TLC: R_f = 0.41 (hexane/EtOAc, 40% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.00 – 7.95 (m, 2H), 7.60 – 7.57 (m, 1H), 7.54 – 7.50 (m, 2H), 6.59 (s, 1H), 4.39 – 4.16 (m, 1H), 4.00 – 3.78 (m, 1H), 2.36 (s, 3H), 1.35 – 1.12 (m, 12H) ppm.
^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 164.2, 160.3, 141.0, 133.4, 129.3, 128.97, 127.1, 107.8, 47.4, 20.9, 20.8, 19.3, 14.1 ppm.
Specific rotation: $[\alpha]_D^{23.3}$ = -4.62 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{16}H_{24}ClN_5O_2S_2Na$ [M+Na$^+$] 464.0952; found 464.0957.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL/min, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 5.8 min, major: 8.4 min.



8g

GP-9 was followed with no additional change: Commercially available (2*R*,3*R*,4*R*,5*R*)-2-(4-aminopyrrolo[2,1-*f*][1,2,4]triazin-7-yl)-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-carbonitrile (0.1 mmol, 1 eq.) and NaHMDS (2.0 eq) were used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 35% EtOAc gradient) to give the product (66 mg, 79.7 µmol, 80% yield) as a light-yellow amorphous solid.

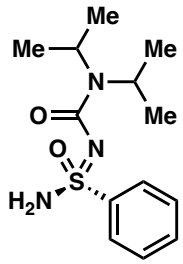
Physical characteristics: light-yellow amorphous solid.
TLC: R_f = 0.67 (hexane/EtOAc, 40% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.6 Hz, 2H), 7.63 – 7.53 (m, 3H), 7.49 (s, 1H), 7.33 – 7.23 (m, 15H), 6.92 – 6.84 (m, 2H), 4.84 (s, 2H), 4.65 (d, *J* = 4.9 Hz, 1H), 4.57 – 4.46 (m, 4H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.23 (s, 1H), 4.02 (t, *J* = 5.8 Hz, 1H), 3.93 (s, 1H), 3.76 (dd, *J* = 11.0, 3.5 Hz, 1H), 3.60 (dd, *J* = 11.0, 3.9 Hz, 1H), 1.34 (dd, *J* = 12.3, 6.8 Hz, 6H), 1.26 – 1.18 (m, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 160.1, 157.3, 146.1, 145.5, 143.3, 141.4, 138.0, 137.9, 137.5, 136.8, 135.7, 132.7, 132.2, 128.8, 128.7, 128.6, 128.4, 128.3, 128.3, 127.7, 127.6, 126.4, 126.1, 120.4, 116.3, 113.2, 107.8, 103.9, 82.1, 79.1, 78.4, 75.9, 73.3, 73.2, 73.1, 72.5, 72.2, 68.3, 47.5, 45.6, 21.0, 20.7 ppm.
Specific rotation: $[\alpha]_D^{22.7}$ = +62.96 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{48}H_{50}N_7O_6S$ [M+H$^+$] 828.3538; found 828.3529.
Diastereomeric excess: >99% de, determined by ^{1}H NMR. Comparison was made using the racemic starting material giving a mixture of diastereomers.



8h

GP-9 was followed with additional changed mentioned: Reaction scale changed to 0.20 mmol. Commercially available benzyl (2S)-2-[8-amino-1-bromoimidazo[1,5-a]pyrazin-3-yl]pyrrolidine-1-carboxylate (0.20 mmol, 1.0 eq) and NaHMDS (2.0 eq) were used. Purified by silica gel column chromatography using hexane/acetone (0% to 45% acetone gradient) to give the product (110 mg, 161 µmol, 80% yield) as a white amorphous solid. *Note:* The starting material exists as a mixture of rotamers which is also observed in the sulfonimidamide product.

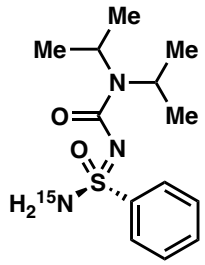
Physical characteristics: White amorphous solid.
TLC: R_f = 0.30 (hexane/acetone, 30% acetone).
^{1}H NMR: (500 MHz, DMSO) δ 12.45 – 11.84 (m, 1H), 8.19 – 8.06 (m, 2H), 7.83 (d, *J* = 5.8 Hz, 0H, another diastereomer), 7.67 – 7.58 (m, 3H), 7.38 – 7.27 (m, 2H), 7.11 – 7.01 (m, 2H), 6.86 (d, *J* = 5.8 Hz, 1H), 6.76 (d, *J* = 7.0 Hz, 1H), 5.33 – 5.22 (m, 1H), 5.09 – 4.58 (m, 2H), 4.27 – 3.97 (m, 1H), 3.96 – 3.71 (m, 1H), 3.62 – 3.45 (m, 2H), 2.35 – 1.84 (m, 4H), 1.20 – 1.09 (m, 12H) ppm.
^{13}C NMR: (126 MHz, DMSO) δ 159.2, 154.5, 153.7, 147.1, 147.0, 145.7, 145.6, 143.8, 143.7, 137.3, 136.5, 132.5, 129.3, 128.9, 128.5, 128.2, 128.2, 127.9, 127.7, 126.4, 117.6, 117.5, 116.9, 116.5, 108.1, 107.3, 66.5, 52.6, 51.9, 47.4, 46.8, 44.8, 32.9, 31.7, 24.6, 23.8, 21.5, 21.4, 21.3, 21.2 ppm. All rotameric carbons were reported.
Specific rotation: $[\alpha]_D^{23}$ = -19.56 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{31}H_{37}BrN_7O_4S$ [M+H$^+$] 682.1806; found 682.1810.
Diastereomeric Excess: >99 de, determined by ^{1}HNMR. Comparison was made using the racemic starting material giving a mixture of diastereomers and associated rotamers.



8i

GP-10 was followed with no additional change: Commercially available NH_4Cl (3.0 eq) was used as a nitrogen source. i-PrMgCl-LiCl (6.0 eq) was used as base. NH_4Cl and *i*-PrMgClLiCl were mixed at room temperature in THF (2.5 mL) and stirred the mixture for 30 min, Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.5 mL) was added to the reaction slowly. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (58 mg, 204 µmol, 82% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.3 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 7.5, 1.7 Hz, 2H), 7.58 – 7.52 (m, 1H), 7.49 (dd, *J* = 8.4, 6.7 Hz, 2H), 6.50 (s, 2H), 4.29 (s, 1H), 3.81 (s, 1H), 1.29 – 1.15 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.3, 143.3, 132.7, 129.1, 126.4, 47.2, 45.2, 21.3, 21.2, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -24.24 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{13}H_{22}N_3O_2S$ [M+H$^+$] 284.1427; found 284.1427.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 7.7 min, minor: 8.7 min.

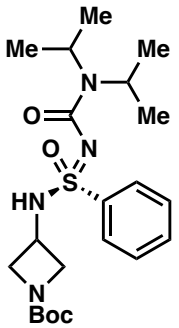


8j

GP-10 was followed with no additional change: Commercially available $^{15}NH_4Br$ (3.0 eq) was used as a nitrogen source. i-PrMgCl-LiCl (6.0 eq) was used as base. $^{15}NH_4Br$ and *i*-PrMgClLiCl were mixed at room temperature in THF (2.5 mL) and stirred the mixture for

30 min, Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.5 mL) was added to the reaction slowly. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (58 mg, 204 µmol, 82% yield) as a white solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.3 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.99 – 7.90 (m, 2H), 7.54 (t, *J* = 4.6 Hz, 1H), 7.48 (td, *J* = 7.9, 7.5, 2.2 Hz, 2H), 6.53 (d, *J* = 53.6 Hz, 2H), 4.28 (s, 1H), 3.80 (s, 1H), 1.21 (dd, *J* = 32.2, 7.5 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.3, 143.3, 132.7, 129.1, 126.4, 47.3, 45.2, 21.3, 21.2, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -22.10 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{13}H_{22}N_2{}^{15}NO_2S$ [M+H$^+$] 285.1398; found 285.1398.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 7.4 min, major: 8.3 min.



8k

GP-11 (LiBr) was followed with no addition change: Commercially available *tert*-butyl 3-aminoazetidine-1-carboxylate (1.0 eq. 0.1 mmol) was used. Heated the reaction at 60 ºC for 13 hours. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (34.6 mg, 78.9 µmol, 79% yield) as a clear colorless oil.

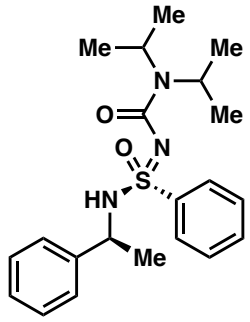
Physical characteristics: Clear colorless oil.
TLC: R_f = 0.41 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 8.8 Hz, 1H), 7.92 – 7.87 (m, 2H), 7.61 – 7.55 (m, 1H), 7.53 – 7.48 (m, 2H), 4.37 – 4.19 (m, 1H), 4.20 – 4.13 (m, 1H), 4.08 – 4.00 (m, 1H), 3.95 (dd, *J* = 9.1, 5.6 Hz, 1H), 3.91 – 3.79 (m, 1H), 3.78 – 3.72 (m, 1H), 3.54 (dd, *J* = 9.3, 5.7 Hz, 1H), 1.39 (s, 9H), 1.31 (d, *J* = 6.8 Hz, 6H), 1.15 (d, *J* = 6.9 Hz, 6H) ppm.
^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 155.8, 141.0, 133.0, 129.2, 126.9, 79.9, 57.4, 47.2, 45.3, 41.5, 28.3, 21.1, 21.0, 20.8, 20.8 ppm.

Specific rotation: $[\alpha]_D^{23}$ = -26.86 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{21}H_{34}N_4O_4SNa$ [M+Na$^+$] 461.2193; found 461.2195.

Enantiomeric excess: >99% ee.

HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL/min, 25 °C, UV detection wavelength: 254 nm, retention time: minor: 10.4 min, major: 13.5 min.



8l

GP-10 was followed with no additional change: commercially available (*S*)-1-phenylethan-1-amine (2 eq. 0.40 mmol) and Sulfonimidoyl fluoride **S6a** (0.20 mmol, 1 eq.) were used; deprotonation for 30 minutes. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (60 mg, 0.155 mmol, 77% yield) as a clear colorless oil that solidified upon standing.

Physical characteristics: Clear colorless oil.

TLC: R_f = 0.2 (hexane/acetone, 20% acetone).

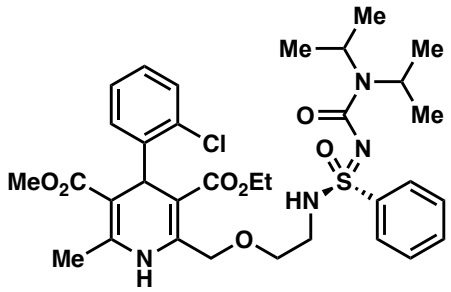
^{1}H NMR: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (d, *J* = 6.5 Hz, 1H), 7.95 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.58 – 7.53 (m, 1H), 7.52 – 7.47 (m, 2H), 7.36 – 7.27 (m, 4H), 7.25 – 7.20 (m, 1H), 4.40 (p, *J* = 6.8 Hz, 1H), 4.32 – 4.08 (m, 1H), 4.00 – 3.74 (m, 1H), 1.30 (d, *J* = 6.9 Hz, 3H), 1.34 – 1.23 (m, 6H), 1.19 – 1.06 (m, 6H) ppm.

^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.1, 143.2, 142.1, 132.5, 129.0, 128.6, 127.4, 126.4, 52.8, 47.0, 45.2, 23.4, 21.3, 21.2, 20.9, 20.9. ppm.

Specific rotation: $[\alpha]_D^{23.3}$ = -93.43 (c 1.00, $CHCl_3$)

HRMS: Calc'd for $C_{21}H_{30}N_3O_2S$ [M+H$^+$] 388.2053; found 388.2054.

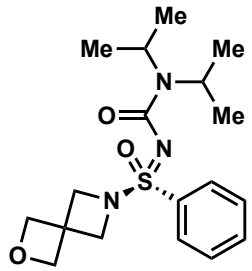
Diastereomeric excess: >99% de, determined by ^{1}H NMR. Comparison was made using the racemic starting material giving a mixture of diastereomers.



8m

GP-11 (LiBr) was followed with additional changes mentioned: Sulfonimidoyl fluoride **S6a** (1.1 eq., 0.11 mmol) was used. Commercially available *rac*-amlodipine (1 eq., 0.1 mmol) was used. The reaction was heated at 70 ºC for 13 hours. Purified by silica gel column chromatography using hexane/EtOAc (0% to 35% EtOAc gradient) to give an inseparable mixture of diastereomers (47 mg, 69.6 µmol, 70% yield) as a light-yellow oil.

Physical characteristic: Light-yellow oil.
TLC: R_f = 0.38 (hexane/EtOAc, 40% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.91 – 8.75 (m, 1H), 7.94 (d, *J* = 7.9 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.54 – 7.39 (m, 4H), 7.22 (d, *J* = 7.9 Hz, 1H), 7.14 (q, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 5.41 (d, *J* = 2.1 Hz, 1H), 4.79 – 4.59 (m, 2H), 4.32 – 4.10 (m, 1H), 4.09 – 3.98 (m, 2H), 3.98 – 3.79 (m, 1H), 3.73 – 3.64 (m, 1H), 3.62 (s, 3H), 3.58 – 3.51 (m, 1H), 3.35 – 3.23 (m, 1H), 3.13 – 3.03 (m, 1H), 2.43 (d, *J* = 2.6 Hz, 3H), 1.27 (s, 6H), 1.21 – 1.12 (m, 9H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 168.2, 167.3, 158.1, 158.1, 146.1, 146.0, 145.2, 145.2, 145.0, 144.9, 140.9, 140.8, 132.7, 132.7, 132.3, 132.2, 131.5, 131.5, 129.2, 129.1, 129.1, 127.3, 127.3, 127.0, 126.9, 103.7, 103.7, 101.6, 101.6, 69.6, 69.5, 68.0, 67.9, 59.8, 59.8, 50.7, 46.9, 45.3, 41.9, 37.0, 36.9, 29.7, 21.2, 21.1, 20.7, 19.4, 19.3, 14.3 ppm. *Note:* all diastereomeric carbons are listed.
Note: The primary amine nucleophile used was racemic.
HRMS: Calc'd for $C_{33}H_{44}ClN_4O_7S$ [M+H$^+$] 675.2614; found 675.2611.

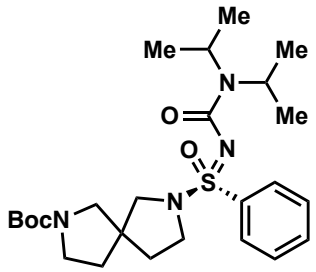


8n

GP-11 (NaI) was followed with addition changes mentioned: Commercially 2-oxa-6-azaspiro[3.3]heptane oxalate (1.0 eq., 0.1 mmol) was used. The equivalents of Et_3N were increased from 2 to 6 equivalents and the reaction was heated to 60 ºC for 24 hours; no

further modifications were made. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (30 mg, 82 µmol, 82% yield) as a white amorphous solid.

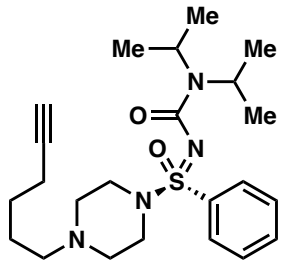
Physical characteristics: White amorphous solid.
TLC: R_f = 0.32 (hexane/EtOAc, 60% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.91 – 7.85 (m, 2H), 7.62 – 7.55 (m, 1H), 7.56 – 7.48 (m, 2H), 4.71 (d, *J* = 7.2 Hz, 2H), 4.67 (d, *J* = 7.3 Hz, 2H), 4.18 (d, *J* = 8.5 Hz, 2H), 4.16 – 4.07 (m, 1H), 3.98 (d, *J* = 8.5 Hz, 2H), 3.94 (s, 1H), 1.29 – 1.21 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.7, 138.0, 132.8, 129.1, 127.6, 80.9, 59.7, 47.0, 45.2, 37.4, 21.5, 20.7 ppm.
Specific rotation: $[\alpha]_D^{23.2}$ = -5.21 (c 0.90, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{27}N_3O_3S$ [M+Na$^+$] 388.1665; found 388.1666.
Enantiomeric excess: >99% ee. *Note:* When LiBr was used, 98% ee was obtained
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL/min, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 33.7 min, major: 57.8 min.



8o

GP-9 (NaHMDS) was followed with no additional change: Commercially available *tert*-butyl 2,7-diazaspiro[4.4]nonane-2-carboxylate (1.0 eq, 0.2 mmol) and NaHMDS (1.0 eq) were used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give an inseparable mixture of diastereomers (92 mg, 187 mmol, 93% yield) as a colorless foam.

Physical characteristics: Colorless foam
TLC: R_f = 0.58 (hexane/EtOAc, 60% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 6.9 Hz, 2H), 7.61 – 7.49 (m, 3H), 4.31 – 4.06 (m, 1H), 4.03 – 3.76 (m, 1H), 3.60 – 3.41 (m, 1H), 3.39 – 2.98 (m, 7H), 1.89 – 1.75 (m, 3H), 1.69 – 1.63 (m, 1H), 1.42 (s, 9H), 1.30 – 1.21 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.5, 154.4, 138.5, 132.5, 129.1, 127.1, 79.5, 56.2, 56.1, 54.8, 54.2, 49.0, 48.1, 47.2, 47.1, 45.1, 45.0, 44.7, 35.1, 34.9, 34.8, 34.3, 28.5, 21.5, 20.8 ppm.
Note: The spirocyclic amine nucleophile used was racemic.
HRMS: Calc'd for $C_{25}H_{41}N_4O_4S$ [M+H$^+$] 493.2843; found 493.2849.

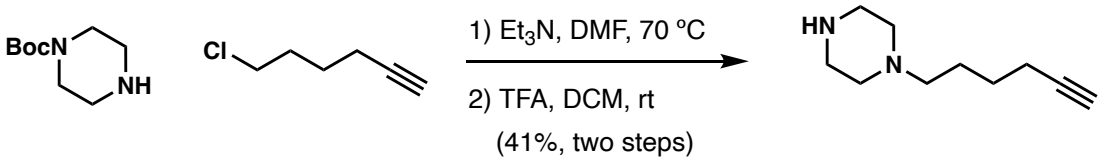


8p

GP-11 (LiBr) was followed with no additional change: 1-(hex-5-yn-1-yl)piperazine (1.1 eq. 0.220 mmol) was used (prepared from the procedure below). Heated the reaction at 70 ºC for 13 hours. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (85 mg, 0.196 mmol, 98% yield) as a clear light-yellow oil.

Physical characteristics: Clear light-yellow oil.
TLC: R_f = 0.2 (hexane/EtOAc, 60% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 2H), 7.58 – 7.48 (m, 3H), 4.23 (s, 1H), 3.88 (s, 1H), 3.20 – 3.06 (m, 4H), 2.56 – 2.47 (m, 4H), 2.34 (t, *J* = 7.0 Hz, 2H), 2.17 (td, *J* = 6.8, 2.6 Hz, 2H), 1.92 (t, *J* = 2.6 Hz, 1H), 1.59 – 1.44 (m, 4H), 1.30 – 1.20 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.2, 136.7, 132.5, 129.0, 127.6, 84.2, 68.5, 57.5, 52.3, 47.1, 45.8, 45.1, 26.2, 25.8, 21.5, 20.8, 18.3 ppm.
Specific rotation: $[\alpha]_D^{23.3}$ = -37.98 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{23}H_{37}N_4O_2S$ $[M+H^+]$ 433.2632; found 433.2636.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IA column, 90:10 *n*-hexane:*i*-PrOH, 0.1% Et_2NH as additive. flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 254 nm, retention time: minor: 11.1 min, major: 12.6 min.

Synthesis of 1-(hex-5-yn-1-yl)piperazine:

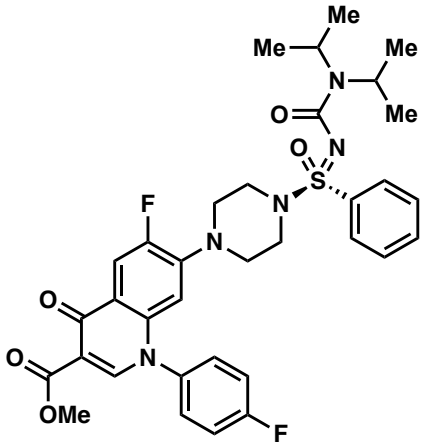


Step 1:
In a 200 mL round-bottom flask equipped with a stir bar was *tert*-butyl piperazine-1-carboxylate (2.55 g, 21.9 mmol, 1 eq.) in DMF (60 mL, 0.36 M). 6-chlorohex-1-yne (4.48 g, 24.1 mmol, 1.1 eq.) and Et_3N (3.66 mL, 26.3 mmol, 1.2 eq.) were added then the reaction vessel was capped with a septum and heated to 70 °C for 21 hours. The reaction mixture was cooled to room temperature and DMF was removed under vacuum to give a crude residue that was taken up in EtOAc (100 mL) and half saturated aqueous NaCl (150 mL). The aqueous layer was extracted with EtOAc (100 mL x 3), combined organic layers were dried over Na_2SO_4, filtered and concentrated. Further purification by silica gel column chromatography using DCM/MeOH (0% to 3% MeOH gradient) gave *tert*-butyl 4-(hex-5-yn-1-yl)piperazine-1-carboxylate (2.49 g, 9.35 mmol, 43% yield) as a colorless foam that was used in the next step.

Physical characteristics: Colorless foam.
TLC: R_f = 0.38 (DCM/MeOH, 5% MeOH).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 3.55 – 3.39 (m, 4H), 2.54 – 2.36 (m, 6H), 2.22 (td, *J* = 6.9, 2.6 Hz, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.69 – 1.61 (m, 2H), 1.58 – 1.52 (m, 2H), 1.45 (s, 9H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 154.7, 84.1, 79.8, 68.6, 57.9, 52.9, 42.9, 28.4, 26.3, 25.5, 18.3 ppm.
HRMS: Calc'd for $C_{15}H_{27}N_2O_2$ [M+H$^+$] 267.2067; found 267.2063.

Step 2:
In a 100 mL septum capped round-bottom flask equipped with a stir bar and argon balloon was *tert*-butyl 4-(hex-5-yn-1-yl)piperazine-1-carboxylate (2.49 g, 9.35 mmol, 1 eq.) in DCM (9.4 mL, 1.0 M) was added TFA (9.37 mL, 122 mmol, 13 eq.) at room temperature. The reaction mixture stirred at room temperature for 3 hours at which time the solvents were removed under reduced pressure to give a crude oil that was taken up in DCM (250 mL), washed with saturated Na_2CO_3 (100 mL x 3), dried over Na_2SO_4, filtered and concentrated to give 1-(hex-5-yn-1-yl)piperazine (1.48 g, 8.90 mmol, 95% yield) as an off-white amorphous solid that was used without further purification.

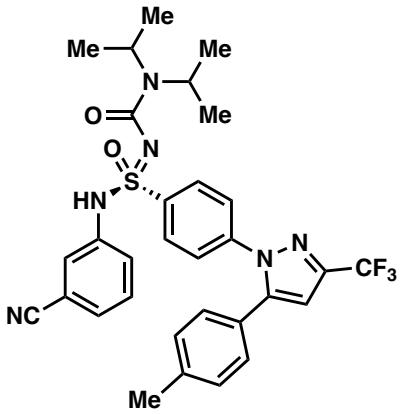
Physical characteristics: Off-white amorphous solid.
TLC: R_f = 0.18 (DCM/MeOH, 5% MeOH).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 2.88 (t, *J* = 4.8 Hz, 4H), 2.50 – 2.34 (m, 4H), 2.33 – 2.28 (m, 2H), 2.19 (td, *J* = 6.8, 2.6 Hz, 2H), 2.13 (s, 1H), 1.92 (t, *J* = 2.5 Hz, 1H), 1.64 – 1.49 (m, 4H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 84.34, 68.40, 58.64, 54.44, 46.01, 26.45, 25.71, 18.35.
HRMS: Calc'd for $C_{10}H_{19}N_2$ [M+H$^+$] 167.1543; found 167.1538.



8q

GP-11 (LiBr) was followed with no additional change: Commercially available sarafloxacin HCl salt was used to prepare the methyl ester analog of sarafloxacin,[13] which was used as the secondary amine nucleophile (1 eq., 0.1 mmol). The reaction was heated to 70 ºC for 10 hours. Purified by silica gel column chromatography using hexanes/acetone (0% to 50% acetone gradient) to give the product (54 mg, 81.1 µmol, 81% yield) as a light-yellow oil.

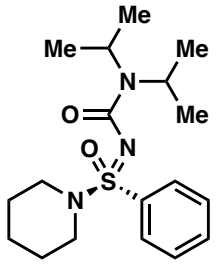
Physical characteristics: Light-yellow oil.
TLC: R_f = 0.48 (hexanes/acetone, 50% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.03 (d, *J* = 12.9 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.61 – 7.57 (m, 1H), 7.56 – 7.51 (m, 2H), 7.44 – 7.39 (m, 2H), 7.33 (t, *J* = 8.3 Hz, 2H), 6.23 (d, *J* = 6.9 Hz, 1H), 4.28 – 4.12 (m, 1H), 3.97 – 3.82 (m, 4H), 3.24 (dd, *J* = 6.5, 3.5 Hz, 4H), 3.09 (dd, *J* = 6.4, 3.7 Hz, 4H), 1.31 – 1.18 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 173.0 (d, *J* = 2.1 Hz), 166.1, 164.1, 162.1, 156.8, 154.3, 152.3, 148.6, 144.1 (d, *J* = 10.8 Hz), 138.1, 136.9, 136.5 (d, *J* = 3.5 Hz), 132.8, 129.3 (d, *J* = 9.0 Hz), 129.1, 127.4, 123.3 (d, *J* = 7.0 Hz), 117.8 (d, *J* = 23.2 Hz), 113.4 (d, *J* = 23.2 Hz), 110.7, 106.2 (d, *J* = 2.7 Hz), 52.2, 49.3 (d, *J* = 4.1 Hz), 47.2, 45.6, 45.3, 21.5, 20.8, 20.7 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -108.84, -123.42 ppm.
HRMS: Calc'd for $C_{34}H_{38}F_2N_5O_5S$ [M+H$^+$] 666.2556; found 666.2560.
Enantiomeric excess: Unable to separate enantiomers by HPLC chromatography.



8r

GP-12 was followed with no additional change: Commercially available 3-aminobenzonitrile (0.25 mmol, 1.0 eq) was used. NaHMDS (2.0 eq) was used as base. Purified by silica gel column chromatography using hexane/EtOAc (0% to 30% EtOAc gradient) to give the product (115 mg, 189 µmol, 75% yield) as a white amorphous solid.

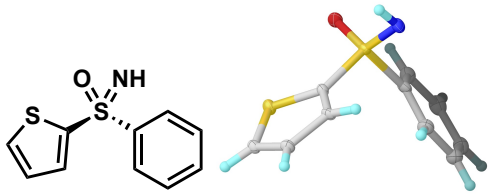
Physical characteristics: White amorphous solid.
TLC: R_f = 0.4 (hexane/EtOAc, 35% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.7 Hz, 2H), 7.43 – 7.37 (m, 3H), 7.37 – 7.29 (m, 3H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.04 – 6.98 (m, 2H), 6.71 (s, 1H), 4.31 (s, 1H), 3.86 (s, 1H), 2.38 (s, 3H), 1.32 (t, *J* = 5.8 Hz, 6H), 1.16 (d, *J* = 6.8 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.4, 145.4, 144.3 (q, *J* = 38.6 Hz), 142.7, 140.1, 139.9, 138.1, 130.4, 129.8, 128.8, 128.2, 127.9, 125.7, 125.5, 124.0, 121.1 (q, *J* = 269.1 Hz), 118.1, 113.6, 106.5 (d, *J* = 2.3 Hz), 47.5, 45.7, 21.4, 20.9 (dd, *J* = 39.0, 20.4 Hz) ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -62.52.ppm.
Specific rotation: $[\alpha]_D^{23}$ = -171.85 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{31}H_{32}N_6O_2S$ [M+H$^+$] 609.2254; found 609.2254.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IA column, 90:10 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 11.9 min, major: 16.8 min.



8s

GP-12 was followed with no additional change: Commercially available piperidine (1.0 eq) was used. i-PrMgCl-LiCl (1.1 eq) was used as base. *i*-PrMgCl-LiCl was added to a solution of piperidine in THF (2.5 mL) under -20 °C and stirred the mixture for 30 min, Sulfonimidoyl fluoride **S6a** (0.25 mmol, 1 eq.) in THF (0.5 mL) was added to the reaction slowly. Purified by silica gel column chromatography using hexane/EtOAc (0% to 60% EtOAc gradient) to give the product (76 mg, 216 µmol, 86% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.3 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.2, 1.8 Hz, 2H), 7.58 – 7.52 (m, 1H), 7.50 (dd, *J* = 8.3, 6.5 Hz, 2H), 4.21 (s, 1H), 3.92 (s, 1H), 3.20 – 2.99 (m, 4H), 1.61 (p, *J* = 5.6 Hz, 4H), 1.50 – 1.40 (m, 2H), 1.34 – 1.18 (m, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.6, 138.4, 132.3, 128.9, 127.6, 47.0, 46.7, 45.2, 25.5, 23.8, 21.6, 20.9, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -26.24 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{30}N_3O_2S$ [M+H$^+$] 352.2053; found 352.2047.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IA column, 98:02 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 26.5 min, minor: 30.1 min.

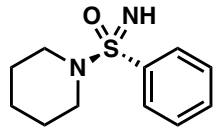


9a

GP-13 was followed with no additional modification: *N*,*N*-diisopropyl urea protected thiophene phenyl sulfoximine (87.6 mg, 0.25 mmol, 1 eq.) was used. Purified by silica gel column chromatography using DCM/acetone (0% to 10% acetone) to give the product (41.6 mg, 112 mmol, 75% yield) as a white crystalline solid.

Physical characteristics: White crystalline solid.
TLC: R_f = 0.7 (DCM/acetone, 10% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 7.5, 1.8 Hz, 2H), 7.65 (dd, *J* = 3.8, 1.4 Hz, 1H), 7.59 (dd, *J* = 4.9, 1.4 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.49 (dd, *J* = 8.4, 6.6 Hz, 2H), 7.04 (dd, *J* = 5.0, 3.8 Hz, 1H), 3.34 (s, 1H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 146.1, 143.3, 133.8, 133.2, 132.7, 129.2, 128.0, 127.7. ppm.
Specific rotation: $[\alpha]_D^{23}$ = +14.20 (c 1.00, $CHCl_3$)

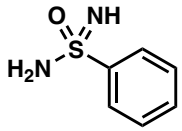
Melting Point: 123-125 ºC
HRMS: Calc'd for $C_{10}H_{10}NOS_2^+$ [M+H$^+$] 224.0198; found 224.0198.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IB column, 90:10 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 254 nm, retention time: minor: 28.7 min, major: 29.8 min.
CCDC deposition Number: 2243810



9b

GP-13 was followed with no additional change: Purified by silica gel column chromatography using hexane/acetone (0% to 50% acetone gradient) to give the product (20.5 mg, 91.3µmol, 91% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.28 (hexane/acetone, 50% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.58 – 7.53 (m, 1H), 7.53 – 7.48 (m, 2H), 2.98 (t, *J* = 5.5 Hz, 4H), 2.44 (s, 1H), 1.68 – 1.55 (m, 4H), 1.42 – 1.29 (m, 2H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 136.4, 132.3, 128.8, 128.1, 48.1, 25.8, 23.8 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +28.98 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{11}H_{17}N_2OS$ [M+H$^+$] 225.1056; found 225.1056.
Enantiomeric excess: >99% ee.
HPLC Conditions: Chiralpak IB column, 95:05 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 27.1 min, major: 29.0 min.

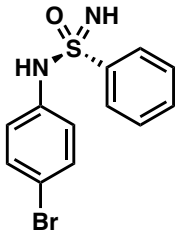


10a

GP-13 was followed with no additional modification: *N,N*-diisopropyl urea protected amino phenyl sulfonimidamide (50 mg, 0.176 mmol, 1 eq.) was used. Purified by silica gel column chromatography using hexane/acetone (0% to 80% acetone) to give the product (15 mg, 96 µmol, 54% yield) as a colorless amorphous solid. The NMR is matched with the literature. *(Org. Biomol. Chem., 2021, 19, 9470–9475)*

Physical characteristics: Colorless amorphous solid.

TLC: R_f = 0.15 (hexane/acetone, 50% acetone).
^{1}H NMR: (500 MHz, DMSO-d_6) δ 7.96 – 7.86 (m, 2H), 7.59 – 7.44 (m, 3H), 6.31 (br s, 2H) [NH-proton not detected] ppm.

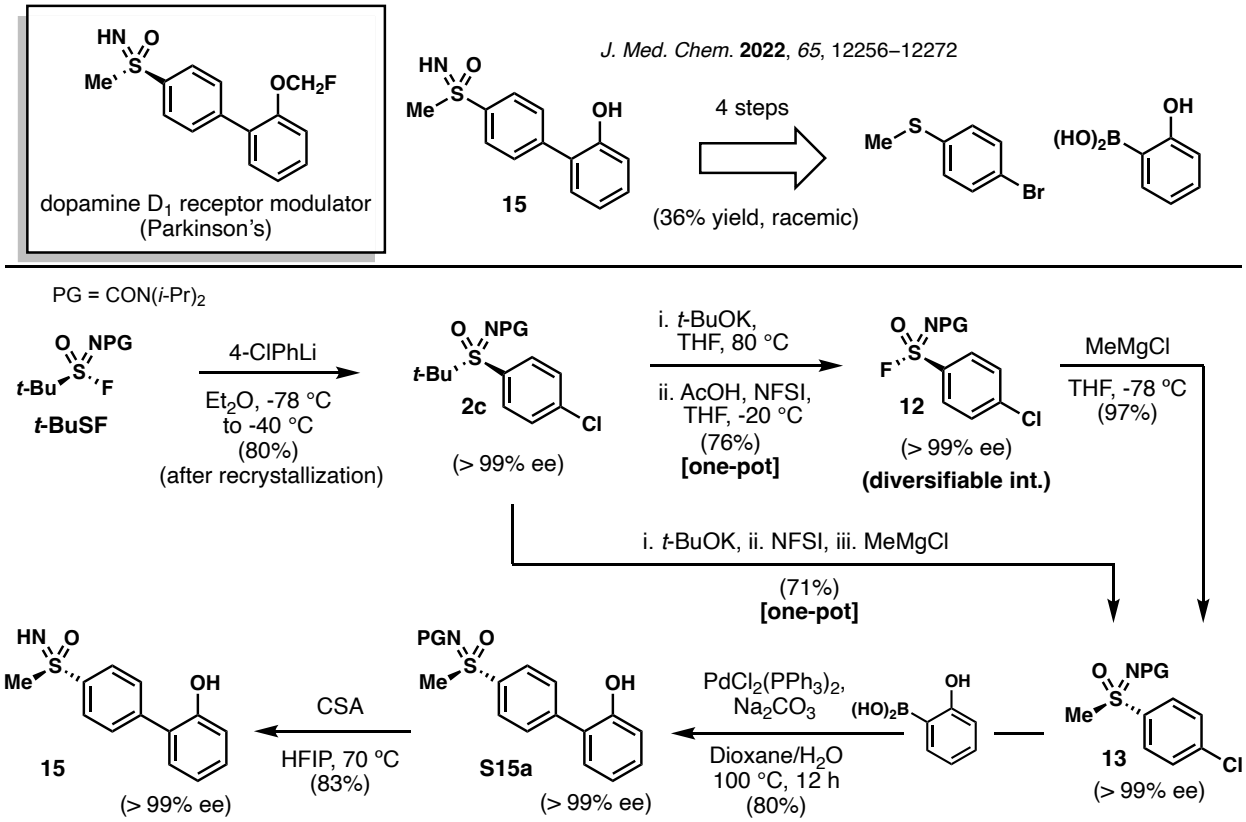


10b

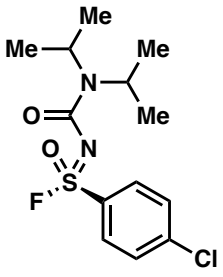
GP-14 was followed with no additional change: Purified by silica gel column chromatography using hexane/acetone (0% to 50% acetone gradient) to give the product (26 mg, 84 µmol, 84% yield) as a white a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.30 (hexane/acetone, 35% acetone).
^{1}H NMR: (500 MHz, DMSO-d_6) δ 7.93 (d, 2H), 7.62 – 7.53 (m, 3H), 7.37 – 7.26 (m, 4H), 6.93 (d, J = 8.2 Hz, 2H) ppm.
^{13}C NMR: (126 MHz, DMSO-d_6) δ 144.9, 143.7, 131.7, 131.4, 128.9, 126.4, 124.8, 112.2 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +262.22 (c 0.5, $CHCl_3$)
HRMS: Calc'd for $C_{12}H_{12}N_2OS$ [M+H$^+$] 310.9848; found 310.9848.
ee>99%
HPLC Conditions: Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 6.2 min, major: 6.6 min.

IXc. Asymmetric synthesis of dopamine D_1 receptor agonist intermediate.



Scheme 19: Asymmetric formal synthesis of a biaryl sulfoximine allosteric modulator of the dopamine D_1 receptor.

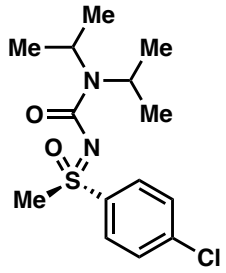


12

N,N-diisopropyl urea protected *tert*-butyl 4-chlorophenyl sulfoximine **2c** (552 mg, 1.54 mmol) with >99% ee was obtained by recrystallization of 95% ee material and >90% recovery. GP-15 was applied for the recrystallization using hexanes/EtOAc as a solvent system.

GP-6 was followed for the fluorination with an increased reaction time of step 1 (*t*-BuOK, THF, 80 ºC) from 2 to 3 hours. Purified by silica gel column chromatography using

hexane/EtOAc (0% to 20% EtOAc gradient) to give the product (380 mg, 1.18 mmol, 76% yield) as a white amorphous solid.
Physical characteristics: White amorphous solid.
TLC: R_f = 0.43 (hexane/EtOAc, 20% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.04 – 7.98 (m, 2H), 7.62 – 7.56 (m, 2H), 4.15 (s, 1H), 3.83 (s, 1H), 1.32 (dd, *J* = 6.8, 3.8 Hz, 6H), 1.22 (dd, *J* = 6.9, 5.2 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 153.1 (d, *J* = 3.0 Hz), 141.9, 133.9 (d, *J* = 24.1 Hz), 130.0, 129.3, 48.4, 46.0, 21.3, 20.6, 20.6 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ 69.70 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +14.43 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{13}H_{19}ClFN_2O_2S$ [M+H$^+$] 321.0834; found 321.0829.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 12.9 min, major: 15.0 min.



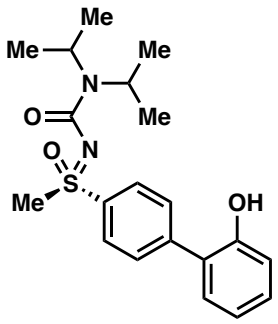
13

GP-7 was followed on a larger scale, -78 °C instead of 0 °C: *N,N*-diisopropyl urea protected sulfonimidoyl fluoride **12** (321mg, 1.0 mmol, 1.0 eq) was used with commercially available MeMgCl (0.367 mL, 1.1 eq, 3.0 M in THF, used without titration). Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (310 mg, 0.978 mmol, 97% yield) as a white amorphous solid.

The one-pot chiral sulfoximine synthesis was employed using modified GP-12 (addition of MeMgCl 3 eq., at -78 ºC) with **2c** to prepare urea protected chiral methyl sulfoximine **13** (215 mg, 0.60 mmol, 71% yield, >99% ee).

Physical characteristics: White amorphous solid.
TLC: R_f = 0.15 (hexane/EtOAc, 30% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.91 – 7.87 (m, 2H), 7.56 – 7.52 (m, 2H), 4.04 (s, 2H), 3.31 (s, 3H), 1.24 (dd, *J* = 6.9, 2.7 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.9, 139.9, 139.2, 129.9, 128.9, 45.1, 21.2 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -13.14 (c 1.00, $CHCl_3$)

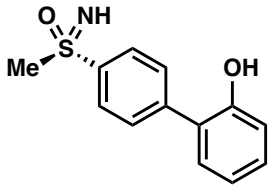
HRMS: Calc'd for $C_{14}H_{22}ClN_2O_2S$ [M+H$^+$] 317.1805; found 317.1801.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 14.4 min, major: 26.5 min.



S15a

General Suzuki coupling conditions were used. To a flame dried round-bottom flask with magnetic stir bar and under argon, *N,N*-diisopropyl urea protected 4-Cl-phenyl methyl sulfoximine (95mg, 0.3 mmol, 1 eq.), commercially available 2-Hydroxyphenylboronic acid (62 mg, 1.5 eq), $PdCl_2(PPh_3)_2$ (10.5 mg, 10%) and Na_2CO_3 (95.4 mg, 3.0 eq) were added. Then dissolved the mixture with degassed dioxane/H_2O (2:1) solution. Heated to 100 °C and stirred for 12 h in oil bath. Removed for bath and cooled to room temperature. Quenched the reaction with water and extracted with EtOAc (10 mL x 3). Washed the combined organic layer with water (10 mL x 3) and brine (10 mL x 3). Dried over anhydrous Na_2SO_4. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (90 mg, 240 µmol, 80% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.26 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 4.0 Hz, 1H), 7.29 – 7.22 (m, 2H), 7.04 (dd, *J* = 8.6, 1.2 Hz, 1H), 6.98 (td, *J* = 7.4, 1.3 Hz, 1H), 4.16 (d, *J* = 68.5 Hz, 2H), 3.34 (s, 3H), 1.34 (dt, *J* = 43.8, 6.6 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.4, 154.0, 144.0, 137.7, 130.4, 130.3, 129.8, 127.1, 126.2, 120.3, 117.0, 46.9, 45.5, 45.4, 21.6, 21.5, 20.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -2.78 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{20}H_{27}N_2O_3S$ [M+H$^+$] 375.1737; found 375.1730.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 9.5 min, minor: 11.8 min.



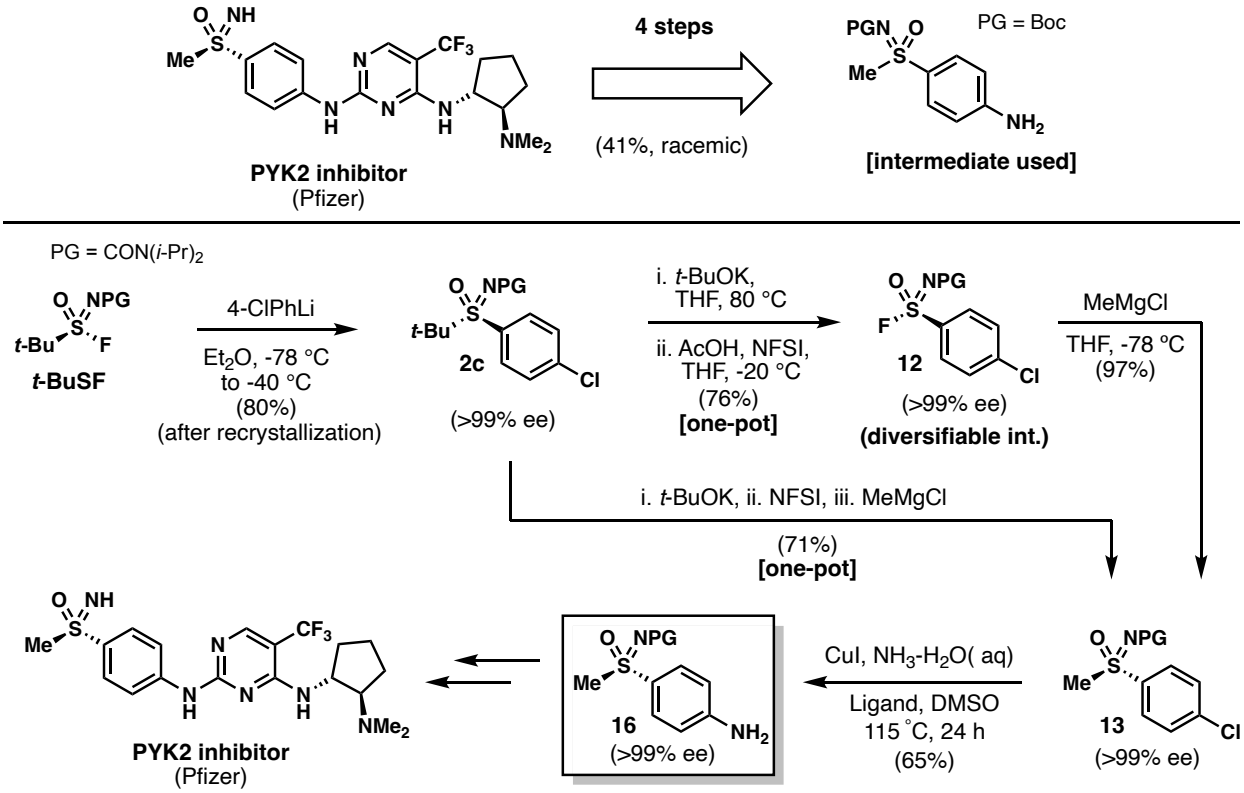
15

GP-13 was followed and no additional change: *N*,*N*-diisopropyl urea protected methyl biaryl sulfoximine (0.1 mmol) was used. Purified by silica gel column chromatography using hexane/acetone (0% to 60% acetone gradient) to give the product (20.6 mg, 83 µmol, 83% yield) as a white solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.2 (hexane/acetone, 50% acetone).
^{1}H NMR: (500 MHz, DMSO-d_6) δ 9.74 (s, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.29 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.20 (ddd, *J* = 8.2, 7.3, 1.7 Hz, 1H), 6.96 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.90 (td, *J* = 7.5, 1.2 Hz, 1H), 4.17 (s, 1H), 3.08 (s, 3H) ppm.
^{13}C NMR: (126 MHz, DMSO-d_6) δ 154.5, 142.7, 141.9, 130.4, 129.5, 129.5, 127.0, 126.2, 119.6, 116.2, 45.9 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +5.53 (c 1.00, MeOH)
HRMS: Calc'd for $C_{13}H_{14}NO_2S$ [M+H$^+$] 248.0740; found 248.0740.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 12.4 min, minor: 20.9 min.

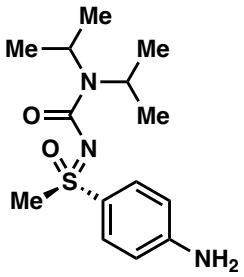
IXd. Asymmetric synthesis of a PYK2 inhibitor intermediate.

Bioorg. Med. Chem. Lett., **2009**, *19*, 3253–3258



Scheme 18: Asymmetric formal synthesis of a PYK2 inhibitor developed by Pfizer starting from *t*-BuSF.

Note: Sulfoximine **13** was used as the starting material from the methods described above.



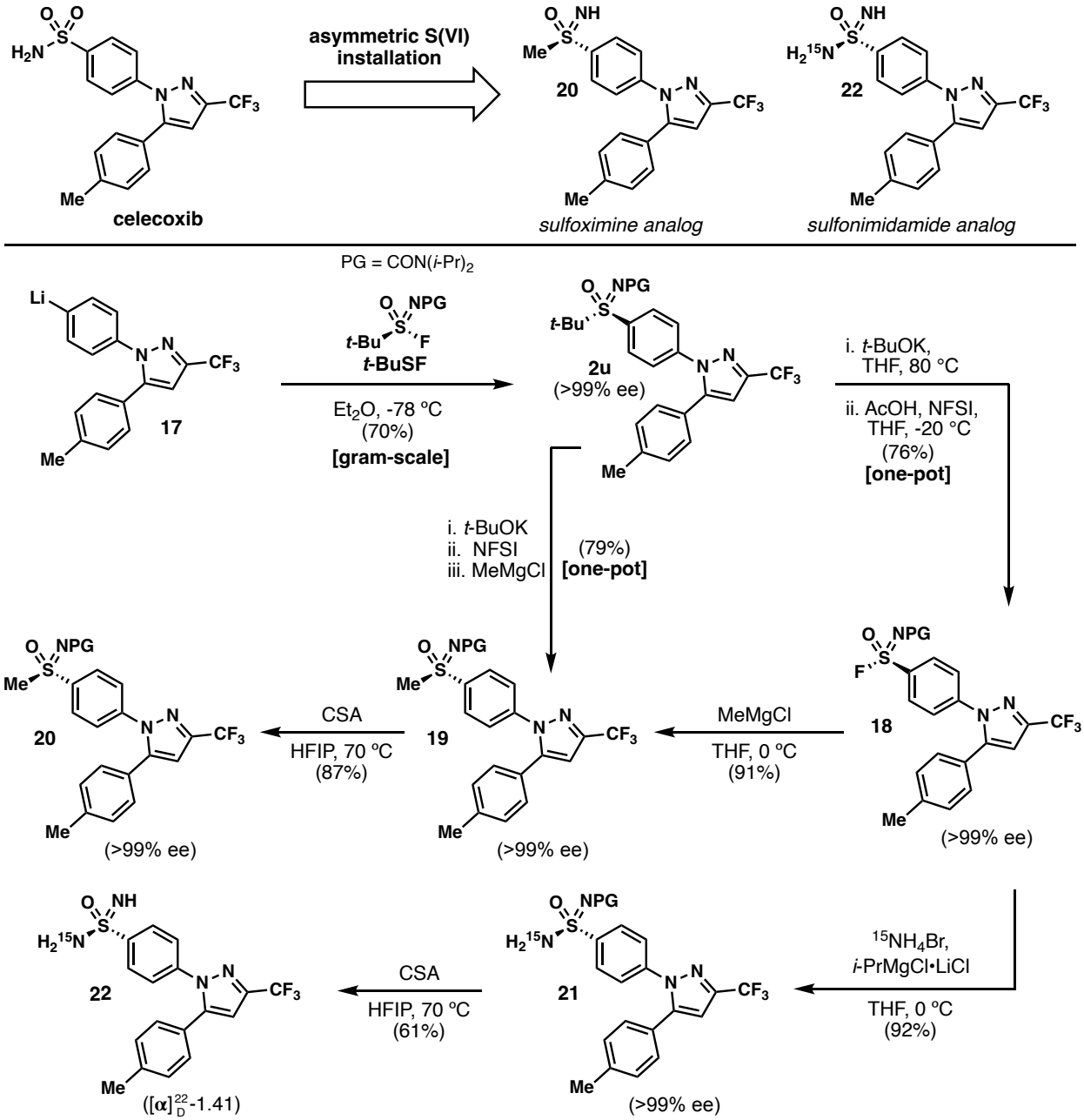
16

Used modified conditions from the reported method.[14] To a flame dried sealed tube with magnetic stir bar, added *N*,*N*-diisopropyl urea protected 4-chlrophenyl methyl sulfoximine **13** (158 mg, 0.5 mmol, 1 eq.), CuI (9.5 mg, 10 mol%), ligand prepared from above reference (16.2 mg, 10 mol%) and K_3PO_4 (117 mg, 1.1 eq). The flask was evacuated and back filled with argon three times then anhydrous DMSO (0.5 mL, 1.0 M) was added to

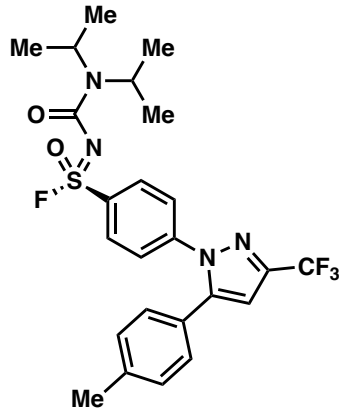
the mixture, followed by aqueous ammonia solution (133 µL, 2.0 eq, 30% w/w). The reaction tube was tightly sealed and heated to 115 °C in oil bath (blast shield was placed in front of the reaction). After 24 hours, the reaction was cooled to room temperature then diluted with EtOAc and brine, extracted with EtOAc (15 mL x 3). Combined organic layers were washed with water (10 mL x 3) and brine (10 mL x 3), dried over Na_2SO_4, filtered and concentrated. Further purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (97 mg, 0.326 mmol, 65% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.16 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, DMSO-d_6) δ 7.49 (d, 2H), 6.69 – 6.61 (m, 2H), 6.05 (s, 2H), 4.18 (s, 1H), 3.91 – 3.55 (m, 1H), 3.25 (s, 3H), 1.15 (dd, *J* = 7.0, 3.7 Hz, 12H) ppm.
^{13}C NMR: (126 MHz, DMSO-d_6) δ 158.5, 153.2, 128.8, 124.2, 112.9, 46.2, 44.7, 43.9, 21.1, 20.8 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -21.01 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{14}H_{24}N_3O_2S$ [M+H$^+$] 298.1584; found 289.1573.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 18.2 min, minor: 31.0 min.

IXe. Asymmetric synthesis of celecoxib sulfoximine analog.



Scheme 17: Asymmetric synthesis of sulfoximine Celebrex analog in three steps from *t*-BuSF.

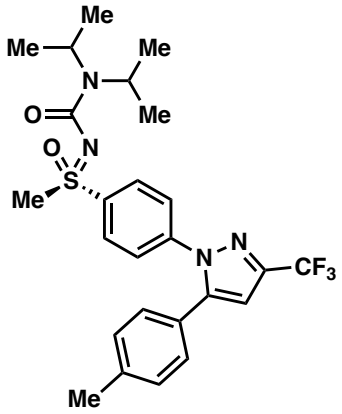


18

The requisite *tert*-butyl sulfoximine **2u** was prepared as described above using GP-1 on a gram-scale (1.54 g, 2.81 mmol, 70% yield, >99% ee).

GP-6 was followed with no additional change: *N*,*N*-diisopropyl urea protected *tert*-butyl celebrex sulfoximine **2u** (0.5 g, 0.91 mmol, 1.0 eq) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 30% EtOAc gradient) to give the product (400 mg, 0.78 mmol, 84% yield) as colorless oil which solidified into a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.4 (hexane/EtOAc, 40% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.8 Hz, 2H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.75 (s, 1H), 4.15 (s, 1H), 3.82 (s, 1H), 2.39 (s, 3H), 1.31 (dd, *J* = 6.8, 4.7 Hz, 6H), 1.21 (t, *J* = 6.6 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 152.92 (d, *J* = 3.2 Hz), 145.55, 144.64 (q, *J* = 38.7 Hz), 144.35, 140.20, 134.42 (d, *J* = 24.1 Hz), 130.01, 128.86 (d, *J* = 1.8 Hz), 125.66, 125.45, 121.04 (q, *J* = 269.2 Hz), 106.94 (d, *J* = 2.2 Hz), 48.44, 45.98, 21.44, 21.36 – 21.12 (m), 20.52 (d, *J* = 6.0 Hz) ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ 70.21, -62.58 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +7.62 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{24}H_{27}F_4N_4O_2S$ [M+H$^+$] 511.1785; found 511.1788.
Enantiomeric excess: >99% ee. (Based on later methylation or amination)
HPLC Conditions: Unable to separate enantiomers by HPLC chromatography.

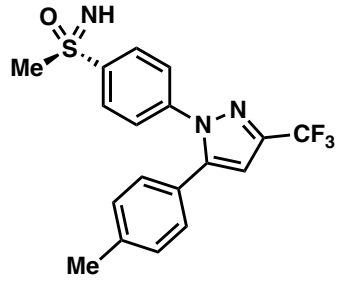


19

GP-7 was followed: *N*,*N*-diisopropyl urea protected sulfonimidoyl fluoride **18** (127 mg, 0.25 mmol, 1.0 eq) was used with commercially available MeMgCl (1.1 eq, 3.0 M in THF, used without titration). Purified by silica gel column chromatography using hexane/EtOAc (0% to 40% EtOAc gradient) to give the product (116 mg, 0.23 mmol, 91% yield, >99% ee) as a white amorphous solid.

The one-pot chiral sulfoximine synthesis was employed using GP-12 with **2u** and MeMgCl (3 eq.) to prepare urea protected chiral methyl sulfoximine analog of celecoxib **19** (220 mg, 0.431 mmol, 79% yield, >99% ee).

Physical characteristics: White amorphous solid.
TLC: R_f = 0.38 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.74 (s, 1H), 4.44 – 3.67 (m, 2H), 3.33 (s, 3H), 2.38 (s, 3H), 1.24 (t, *J* = 6.4 Hz, 12H). ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 158.9, 145.4, 144.3 (q, *J* = 38.5 Hz), 143.1, 140.0, 139.9, 129.9, 128.9, 128.5, 125.8, 125.7, 121.2 (q, *J* = 269.2 Hz), 106.6 (d, *J* = 2.0 Hz), 45.0, 21.4, 21.2 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -62.49.ppm.
Specific rotation: $[\alpha]_D^{23}$ = -18.22 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{25}H_{29}F_3N_4NaO_2S$ [M+Na^+] 529.1856; found 529.1854.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: major: 12.9 min, minor: 22.5 min.

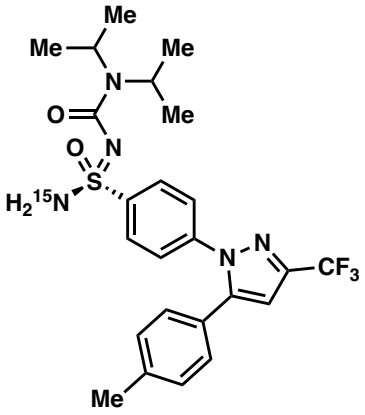


20

Deprotection of **19** (50.7 mg, 100 μmol, 1 eq) using GP-13 was followed with no additional changes. Purified by silica gel column chromatography using hexane/EtOAc (0% to 50% EtOAc gradient) to give the product (33 mg, 87 μmol, 87% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.28 (hexane/EtOAc, 50% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.7 Hz, 2H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.74 (s, 1H), 3.14 (s, 3H), 3.02 (s, 1H), 2.37 (s, 3H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 145.4, 144.3 (q, *J* = 38.5 Hz), 143.2, 142.4, 139.9, 129.9, 128.9, 128.8, 125.8, 125.7, 121.1 (q, *J* = 269.2 Hz), 106.5 (d, *J* = 2.1 Hz), 46.2, 21.4 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -65.50ppm.
Specific rotation: $[\alpha]_D^{23}$ = +42.33 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{18}H_{17}N_3OS$ [M+H$^+$] 380.1039; found 380.1039.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 21.6 min, major: 31.3 min.

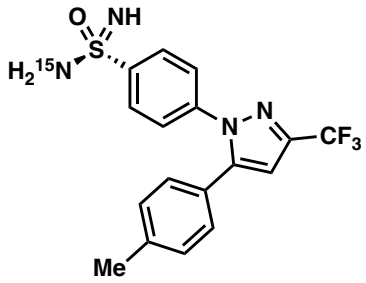
Xf. Asymmetric synthesis of isotopically labeled $^{15}NH_2$ celecoxib sulfonimidamide analog.



21

GP-10 was followed with no additional change: Commercially available $^{15}NH_4Br$ (3.0 eq) was used as a nitrogen source. *i*-PrMgCl-LiCl (6.0 eq) was used as base. $^{15}NH_4Br$ and *i*-PrMgClLiCl were mixed at room temperature in THF (2.5 mL) and stirred the mixture for 30 min, sulfonimidoyl fluoride **18** (0.25 mmol, 1 eq.) in THF (0.5 mL) was added to the reaction slowly. Purified by silica gel column chromatography using hexane/EtOAc (0% to 25% EtOAc gradient) to give the product (117 mg, 230 µmol, 92% yield) as a white amorphous solid.

Physical characteristics: White amorphous solid.
TLC: R_f = 0.4 (hexane/acetone, 33% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 6.85 – 6.35 (m, 3H), 4.26 (s, 1H), 3.78 (s, 1H), 2.36 (s, 3H), 1.29 – 1.21 (m, 6H), 1.16 (d, *J* = 6.9 Hz, 6H) ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -62.43 ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.96, 145.27, 144.06 (q, *J* = 38.5 Hz), 142.91 (d, *J* = 4.3 Hz), 142.30, 139.78, 129.79, 128.81, 127.31, 125.85, 125.35, 121.16 (q, *J* = 269.2 Hz), 106.33 (d, *J* = 2.3 Hz), 47.29, 45.22, 21.37, 21.19, 21.08, 20.85, 20.78 ppm.
Specific rotation: $[\alpha]_D^{22}$ = -19.62 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{24}H_{29}F_3N_4{}^{15}NO_2S$ [M+H$^+$] 509.1959; found 509.1955.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 254 nm, retention time: major: 5.9 min, minor: 6.8 min.



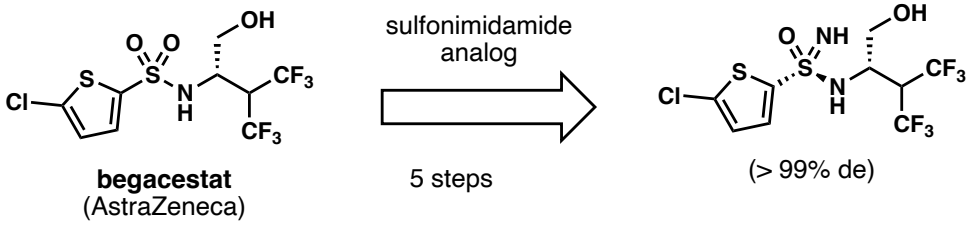
22

GP-13 was followed, reaction time was 30 h: *N,N*-diisopropyl urea protected sulfonimidamide **21** (50 mg, 98.3 µmol, 1 eq.) was used. Purified by silica gel column chromatography using hexane/acetone (0% to 80% acetone) to give the product (23 mg, 60.3 µmol, 61% yield) as a colorless amorphous solid.

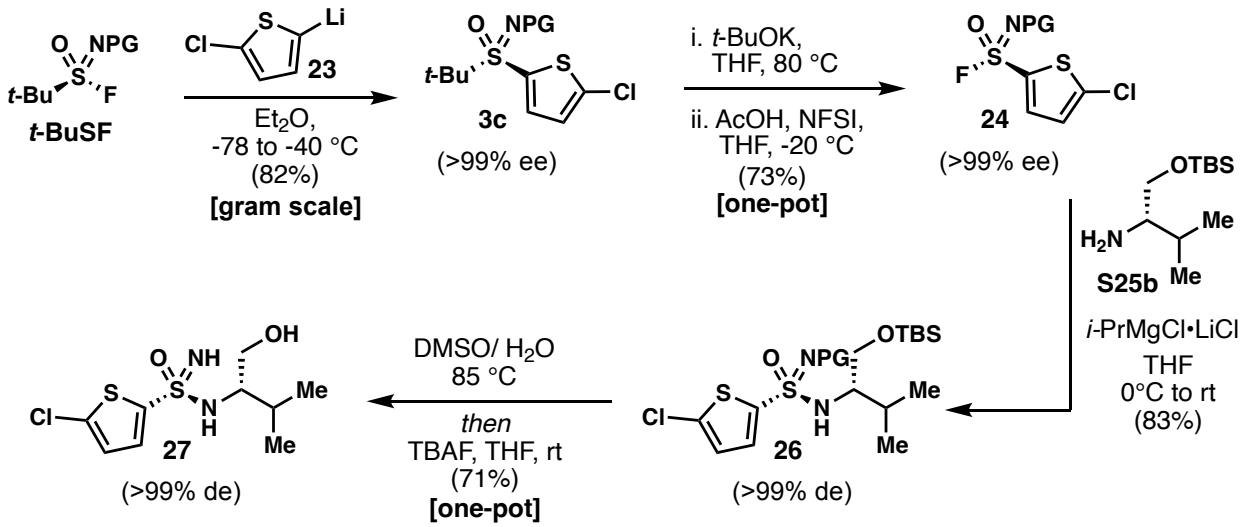
Physical characteristics: Colorless amorphous solid.
TLC: R_f = 0.40 (hexane/acetone, 50% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.7 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 6.73 (s, 1H), 3.95 (s, 3H), 2.37 (s, 3H) ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ -62.42 ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 145.34, 144.16 (q, *J* = 38.6 Hz), 143.49 (d, *J* = 4.4 Hz), 142.38, 139.87, 129.88, 128.87, 127.74, 125.89, 125.56, 121.21 (q, *J* = 269.2 Hz), 106.41 (d, *J* = 2.2 Hz), 21.46 ppm.
Specific rotation: $[\alpha]_D^{22}$ = -1.41 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{17}H_{16}F_3N_3{}^{15}NOS$ $[M+H^+]$ 382.0962; found 382.0960.

IXg. Asymmetric synthesis of begacestat sulfonimidamide analog.

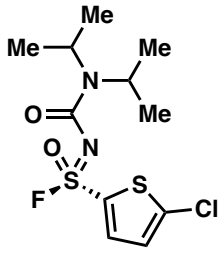
ChemMedChem, **2012**, *7*, 396–399



PG = $CON(i\text{-}Pr)_2$



Scheme 20: Asymmetric synthesis of a sulfonimidamide analog of begacestat in four steps from t-BuSF.

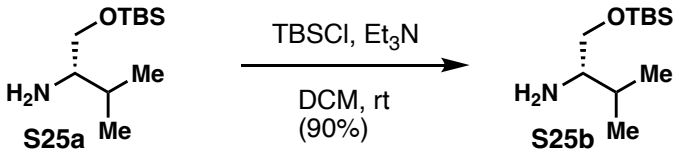


24

GP-6 was followed with no additional change: *N*,*N*-diisopropyl urea protected *tert*-butyl 5-Cl-thiophene sulfoximine **3c** (1.2 g, 3.29 mmol, 1.0 eq) was used. Purified by silica gel column chromatography using hexane/EtOAc (0% to 30% EtOAc gradient) to give the product (790 mg, 2.42 mmol, 73% yield) as colorless oil which solidified into a white amorphous solid.

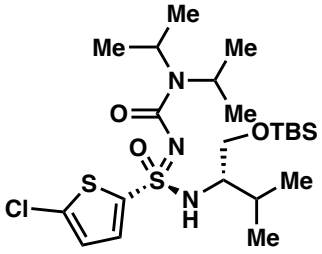
Physical characteristics: White amorphous solid.

TLC: R_f = 0.75 (hexane/EtOAc, 40% EtOAc).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 4.2 Hz, 1H), 7.03 (d, *J* = 4.2 Hz, 1H), 4.12 (s, 1H), 3.86 (s, 1H), 1.31 (d, *J* = 6.8 Hz, 6H), 1.23 (dd, *J* = 6.8, 4.2 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 153.2, 142.0 (d, *J* = 2.1 Hz), 135.3, 131.6 (d, *J* = 30.0 Hz), 127.2, 48.4, 46.0, 21.3, 20.6 ppm.
^{19}F NMR: (471 MHz, $CDCl_3$) δ 77.11 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +7.23 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{11}H_{17}ClFN_2O_2S$ [M+H$^+$] 327.0399; found 327.0399.
Enantiomeric excess: >99% ee.
HPLC Conditions: Daicel Chiralpak IC column, 70:30 *n*-hexane:*i*-PrOH, flow rate: 1 mL min-1, 25 °C, UV detection wavelength: 220 nm, retention time: minor: 9.2 min, major: 10.9 min.



Alcohol protection of **S25a** was performed using a reported method[15] with no modification and to give **S25b**. Spectroscopic data was in accordance with the literature.

^{1}H NMR: (500 MHz, $CDCl_3$) δ 3.65 (dd, *J* = 9.8, 4.1 Hz, 1H), 3.40 (dd, *J* = 9.8, 7.6 Hz, 1H), 2.59 (ddd, *J* = 7.6, 6.2, 4.0 Hz, 1H), 2.14 (s, 2H), 1.72 – 1.57 (m, 1H), 0.92 (dd, *J* = 7.7, 6.8 Hz, 6H), 0.89 (s, 9H), 0.05 (s, 6H) ppm.

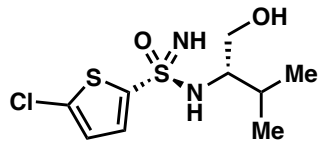


26

GP-10 was followed with no additional change: *N*,*N*-diisopropyl urea protected sulfonimidoyl fluoride **24** (98 mg, 0.3 mmol, 1.0 eq) was used with OTBS protected primary amine **S25b** (2 eq.). Purified by silica gel column chromatography using hexane/EtOAc (0% to 15% EtOAc gradient) to give the product (130 mg, 248 µmol, 83% yield) as a colorless oil.

Physical characteristics: Colorless oil.
TLC: R_f = 0.55 (hexane/EtOAc, 10% EtOAc).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 1H), 7.43 (d, *J* = 4.1 Hz, 1H), 7.39 (d, *J* = 4.0 Hz, 0.01H, from *S*-diastereomer), 6.84 (d, *J* = 4.1 Hz, 1H), 4.33 (s, 1H), 3.69 (s, 1H), 3.45 (dd, *J* = 10.2, 3.8 Hz, 1H), 3.30 (dd, *J* = 10.2, 5.3 Hz, 1H), 3.16 – 3.06 (m, 1H), 2.02 (dp, *J* = 13.6, 6.8 Hz, 1H), 1.29 (t, *J* = 8.0 Hz, 6H), 1.13 (dd, *J* = 11.8, 6.8 Hz, 6H), 0.95 (dd, *J* = 7.0, 2.6 Hz, 6H), 0.86 (s, 9H), -0.00 (s, 3H), -0.02 (s, 3H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.7, 141.6, 136.8, 130.9, 125.9, 61.4, 59.9, 47.6, 45.2, 29.5, 25.9, 21.2, 21.1, 20.8, 19.1, 18.5, 18.3, -5.5, -5.6 ppm.
Specific rotation: $[\alpha]_D^{23}$ = -42.01 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_{22}H_{43}ClN_3O_3S_2Si$ [M+H$^+$] 524.2198; found 524.2196.
Diastereomeric excess: >99% de, determined by ^{1}HNMR. Comparison was made using the racemic starting material giving a mixture of diastereomers.



27

Modified GP-14 was used to telescope OTBS deprotection: To a 5 mL vial with magnetic stir bar, dissolved protected sulfonimidamide **26** (105 mg, 0.2 mmol, 1.0 eq) in DMSO (0.1 M, 2.0 mL) then added water (0.2 mL) and heated to 80 °C for 12 h. Cooled to room temperature then TBAF (1.0 mL, 5.0 eq, 1.0 M in THF, used as received) was added slowly to the mixture. Upon completion (checked by TLC) water (10 mL) was added and extracted with EtOAc (15 mL x 3), washed with water (10 mL x 3) and brine (10 mL x 3), dried over N_2SO_4, filtered and concentrated. Purified by silica gel column chromatography using hexane/acetone (0% to 50% acetone gradient) to give the product (40 mg, 141 µmol, 71% yield) as a colorless oil.

Physical characteristics: Colorless oil.
TLC: R_f = 0.51 (hexane/EtOAc, 50% acetone).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 4.1 Hz, 1H), 6.90 (d, *J* = 4.0 Hz, 1H), 3.72 (m, *J* = 14.3, 12.2, 6.3, 3.7 Hz, 2H), 3.62 – 3.54 (m, 2H), 3.21 (td, *J* = 6.5, 4.0 Hz, 1H), 3.15 (d, *J* = 4.1 Hz, 0.01 H, from *S*-diastereomer) 1.77 (dq, *J* = 13.5, 6.8 Hz, 1H), 0.83 (t, *J* = 6.4 Hz, 6H) ppm.
^{13}C NMR: (126 MHz, $CDCl_3$) δ 142.8, 137.1, 131.3, 127.0, 63.7, 62.3, 30.1, 19.3, 18.5 ppm.
Specific rotation: $[\alpha]_D^{23}$ = +39.44 (c 1.00, $CHCl_3$)
HRMS: Calc'd for $C_9H_{16}N_2O_2S_2$ [M+H$^+$] 283.0336; found 283.0336.
Diastereomeric excess: >99% de, determined by ^{1}HNMR. Comparison was made using the racemic starting material giving a mixture of diastereomers.

X. Single crystal X-ray crystallography data

X-ray diffraction data were measured on Bruker D8 Venture PHOTON II CMOS diffractometer equipped with a Cu Kα INCOATEC ImuS micro-focus source (λ = 1.54178 Å). Indexing was performed using APEX4 [1] (Difference Vectors method). Data integration and reduction were performed using SaintPlus [2]. Absorption correction was performed by multi-scan method implemented in SADABS.[16] Space group was determined using XPREP implemented in APEX3 [1]. Structure was solved using SHELXT[17] and refined using SHELXL-2019/1[18] (full-matrix least-squares on F2) through OLEX2 interface program[19]. Ellipsoid plot was made with Platon [3].[20] Disorder was modeled using restraints and constraints. Data and refinement conditions are shown in Table 1.

[1] Bruker (2022). APEX4. Bruker AXS LLC, Madison, Wisconsin, USA.
[2] Bruker SAINT. Bruker AXS LLC, Madison, Wisconsin, USA.
[3] A.L.Spek, The Program PLATON is designed as a Multipurpose Crystallographic Tool. 1980-2021 A.L.Spek, Utrecht University, Utrecht, The Netherlands.

Notes:

S1DIPA_F (***t*-BuSF**): Structure was solved using SHELXT[17] and refined using SHELXL-2018/3[18] (full-matrix least-squares on F2) through OLEX2 interface program[19]. All hydrogen atoms were refined using riding model. The apparent higher (pseudo)-symmetry involving n and a glide planes is not feasible as sample is composed of single enantiomer. The SN_2/AE products of this compound were checked with chiral HPLC (Daicel Chemical, Chiralcel OJ-H, Hexane/*i*-PrOH= 95: 5, 1mL/ min), single enantiomers were found. This compound was verified to be enantiopure. (*S*)- [α]25 = +78.17 (c 1.00, $CHCl_3$). Although possible, the structure solution in Pna2(1) results in significantly higher R and Rmerge factors and the presence of racemic mixture in the model. Observed pseudosymmetry arises from the presence of pseudo mirror-plane in molecules with only SFO group breaking the mirror symmetry.

2136B (**2a**): While structure shows strong pseudotranslational symmetry, there are many weak reflections violating it and larger cell was used for data processing. The model shows less disorder of -CH_3 and -Ph groups than the one derived using smaller unit cell. ADDSYM detects pseudotranslation along B direction above ~0.15A translational deviation criteria.

S1_CP (**4a**), S1_4BrTA (**3e**), 2172 (**7k**), 2191C (**7i**), 2238B (**7f**): Structure was solved using SHELXT[17] and refined using SHELXL-2018/3[18] (full-matrix least-squares on F2) through OLEX2 interface program[20]. All hydrogen atoms were refined using riding model. Disordered atoms were refined with restraints.

2174B (**7a**): Structure was solved using SHELXT[17] and refined using SHELXL-2018/3[18] (full-matrix least-squares on F2) through OLEX2 interface program[19]. All hydrogen atoms

were refined using riding model. Disordered atoms were refined with restraints. The type and the amount of heavily disordered solvent in the channel is tentative.

4184A (**7e**): Structure was solved using SHELXT[17] and refined using SHELXL-2019/1[18] (full-matrix least-squares on F2) through OLEX2 interface program[19]. Ellipsoid plot was made with Platon [3][20]. Disorder was modeled using restraints and constraints. The contribution of heavily disordered content (crystal was obtained from THF/DCM/chloroform mixture) in structural voids was treated as diffuse using solvent mask procedure implemented in Olex2 program[19].

Table 1 Crystal data and structure refinement for S1DIPA_F (*t*-BuSF).	
Identification code	S1DIPA_F
Empirical formula	$C_{11}H_{23}FN_2O_2S$
Formula weight	266.37
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	11.2391(3)
b/Å	15.0285(4)
c/Å	17.1814(5)
α/°	90
β/°	90.5020(10)
γ/°	90
Volume/Å^3	2901.94(14)
Z	8
ρ_{calc}g/cm^3	1.219
μ/mm^{-1}	2.047
F(000)	1152.0
Crystal size/mm^3	0.2 × 0.2 × 0.08
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	5.144 to 160.632
Index ranges	-13 ≤ h ≤ 14, -19 ≤ k ≤ 19, -21 ≤ l ≤ 21
Reflections collected	58544
Independent reflections	12252 [R_{int} = 0.0416, R_{sigma} = 0.0365]
Data/restraints/parameters	12252/1/641
Goodness-of-fit on F^2	1.023
Final R indexes [I>=2σ (I)]	R_1 = 0.0256, wR_2 = 0.0665
Final R indexes [all data]	R_1 = 0.0262, wR_2 = 0.0670
Largest diff. peak/hole / e Å^{-3}	0.31/-0.28
Flack parameter	0.029(4)

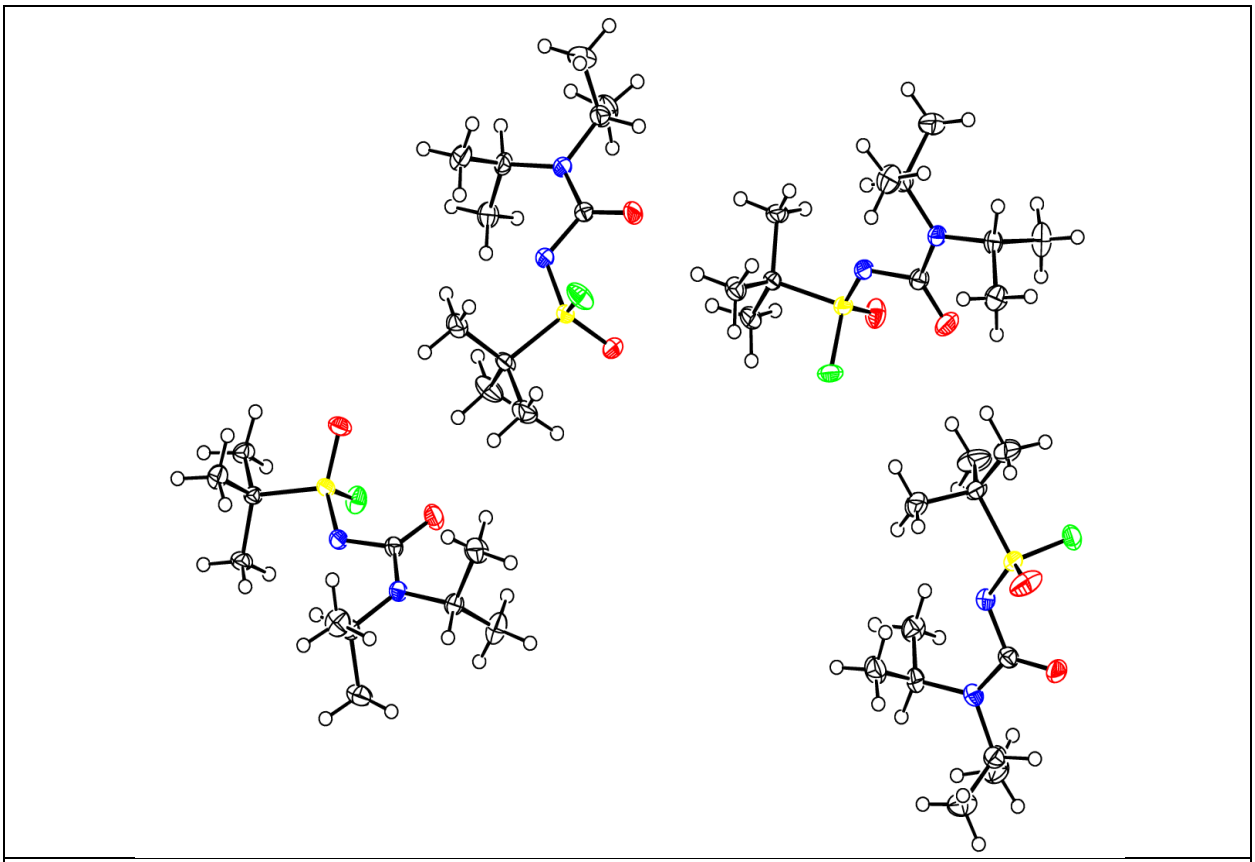


Fig.1. Ellipsoid plot of **S1DIPA_F (*t*-BuSF)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243804

Table 1 Crystal data and structure refinement for TBUPH (2a).	
Identification code	TBUPH
Empirical formula	$C_{17}H_{28}N_2O_2S$
Formula weight	324.47
Temperature/K	100.00
Crystal system	monoclinic
Space group	$P2_1$
a/Å	16.5691(5)
b/Å	6.0854(2)
c/Å	19.6317(6)
α/°	90
β/°	113.528(1)
γ/°	90
Volume/Å^3	1814.9(1)
Z	4
ρ_{calc}g/cm^3	1.188
μ/mm^{-1}	1.647
F(000)	704.0
Crystal size/mm^3	0.6 × 0.06 × 0.03
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	4.91 to 144.758
Index ranges	-20 ≤ h ≤ 20, -7 ≤ k ≤ 7, -24 ≤ l ≤ 24
Reflections collected	34970
Independent reflections	7027 [R_{int} = 0.0546, R_{sigma} = 0.0438]
Data/restraints/parameters	7027/432/482
Goodness-of-fit on F^2	1.033
Final R indexes [I>=2σ (I)]	R_1 = 0.0346, wR_2 = 0.0920
Final R indexes [all data]	R_1 = 0.0352, wR_2 = 0.0926
Largest diff. peak/hole / e Å^{-3}	0.21/-0.43
Flack parameter	0.107(6)

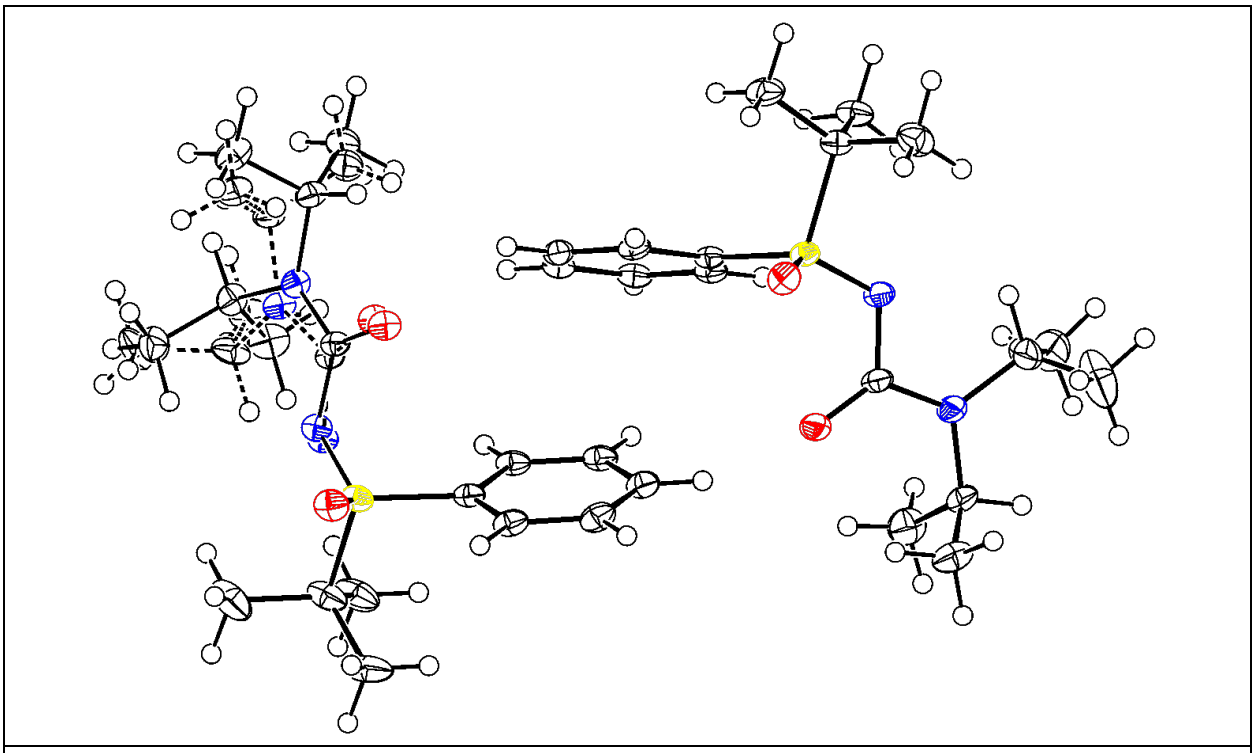


Fig.1. Ellipsoid plot of **TBUPH (2a)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243801

Table 1 Crystal data and structure refinement for S1_4BrTA (3e).	
Identification code	S1_4BrTA
Empirical formula	$C_{14}H_{24}BrN_3O_2S_2$
Formula weight	410.39
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	7.9955(3)
b/Å	11.2096(4)
c/Å	11.0513(4)
α/°	90
β/°	96.378(2)
γ/°	90
Volume/Å^3	984.36(6)
Z	2
ρ_{calc}g/cm^3	1.385
μ/mm^{-1}	4.905
F(000)	424.0
Crystal size/mm^3	0.12 × 0.1 × 0.05
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.05 to 160.25
Index ranges	-10 ≤ h ≤ 10, -14 ≤ k ≤ 14, -14 ≤ l ≤ 14
Reflections collected	16529
Independent reflections	4114 [R_{int} = 0.0706, R_{sigma} = 0.0555]
Data/restraints/parameters	4114/1/207
Goodness-of-fit on F^2	1.161
Final R indexes [I>=2σ (I)]	R_1 = 0.0432, wR_2 = 0.0891
Final R indexes [all data]	R_1 = 0.0508, wR_2 = 0.0955
Largest diff. peak/hole / e Å^{-3}	0.41/-0.47
Flack parameter	0.068(17)

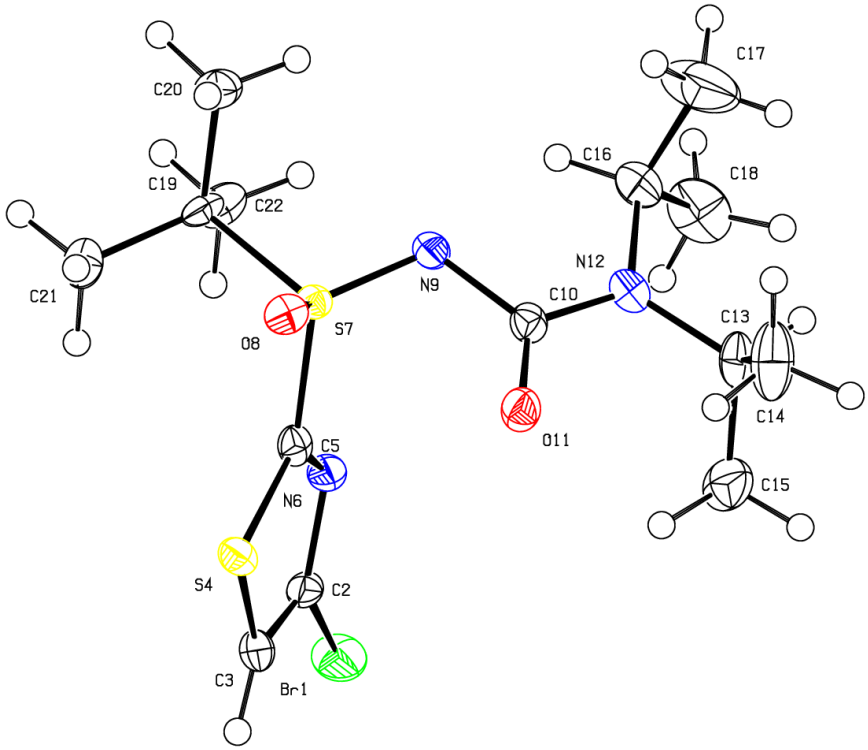


Fig.1. Ellipsoid plot of **S1_4BrTA (3e)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243803

Table 1 Crystal data and structure refinement for S1_CP (4a).	
Identification code	S1_CP
Empirical formula	$C_{14}H_{28}N_2O_2S$
Formula weight	288.44
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	6.0845(2)
b/Å	16.9812(6)
c/Å	7.8504(2)
α/°	90
β/°	99.469(2)
γ/°	90
Volume/Å^3	800.07(4)
Z	2
ρ_{calc}g/cm^3	1.197
μ/mm^{-1}	1.800
F(000)	316.0
Crystal size/mm^3	0.08 × 0.05 × 0.04
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	10.418 to 159.908
Index ranges	-6 ≤ h ≤ 7, -21 ≤ k ≤ 20, -10 ≤ l ≤ 10
Reflections collected	11983
Independent reflections	3300 [R_{int} = 0.0669, R_{sigma} = 0.0544]
Data/restraints/parameters	3300/1/179
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0423, wR_2 = 0.0916
Final R indexes [all data]	R_1 = 0.0475, wR_2 = 0.0949
Largest diff. peak/hole / e Å^{-3}	0.32/-0.35
Flack parameter	0.088(15)

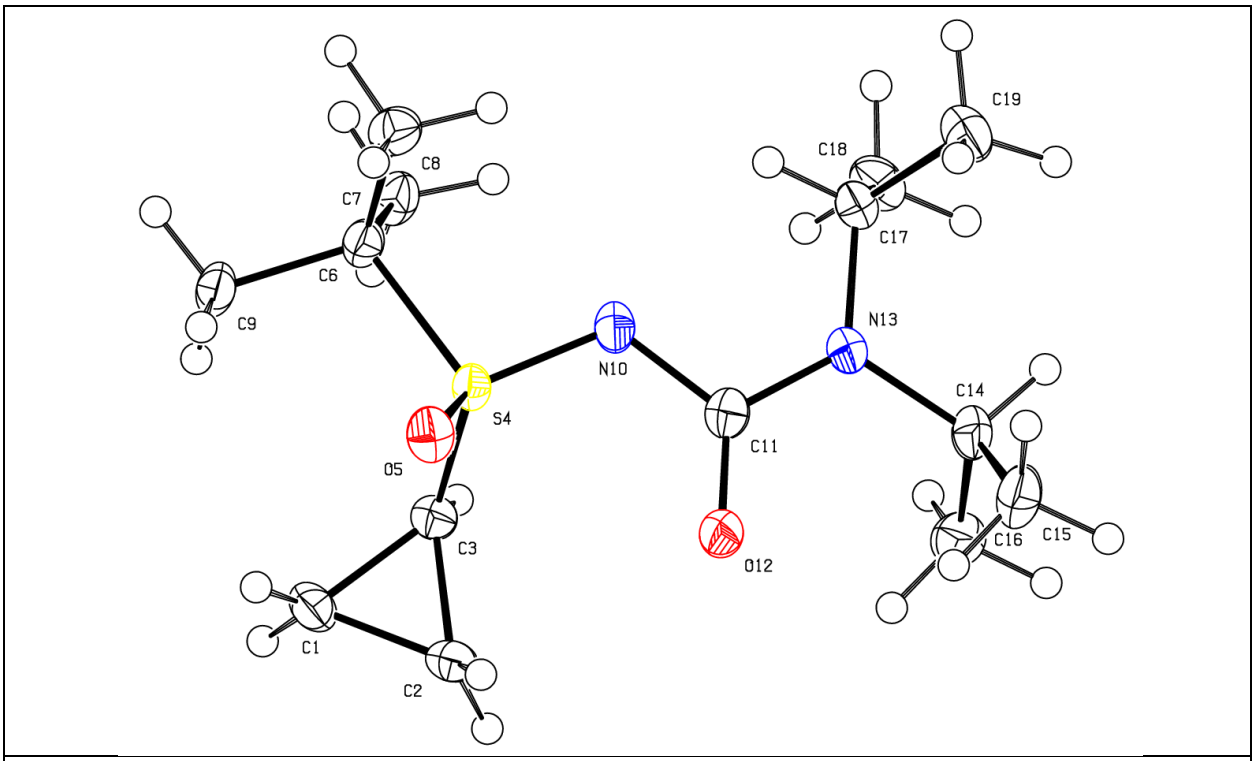


Fig.1. Ellipsoid plot of **S1_CP (4a)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243800

Table 1 Crystal data and structure refinement for 2136B (S6a).	
Identification code	2136B
Empirical formula	$C_{13}H_{19}FN_2O_2S$
Formula weight	286.36
Temperature/K	100.00
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.4950(2)
b/Å	10.7311(2)
c/Å	14.6795(2)
α/°	90
β/°	99.5221(6)
γ/°	90
Volume/Å^3	1475.11(5)
Z	4
ρ_{calc}g/cm^3	1.289
μ/mm^{-1}	2.062
F(000)	608.0
Crystal size/mm^3	0.54 × 0.25 × 0.11
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.104 to 160.002
Index ranges	-11 ≤ h ≤ 12, -13 ≤ k ≤ 13, -18 ≤ l ≤ 18
Reflections collected	20802
Independent reflections	5969 [R_{int} = 0.0360, R_{sigma} = 0.0428]
Data/restraints/parameters	5969/1/351
Goodness-of-fit on F^2	1.049
Final R indexes [I>=2σ (I)]	R_1 = 0.0274, wR_2 = 0.0719
Final R indexes [all data]	R_1 = 0.0287, wR_2 = 0.0729
Largest diff. peak/hole / e Å^{-3}	0.18/-0.35
Flack parameter	0.046(6)

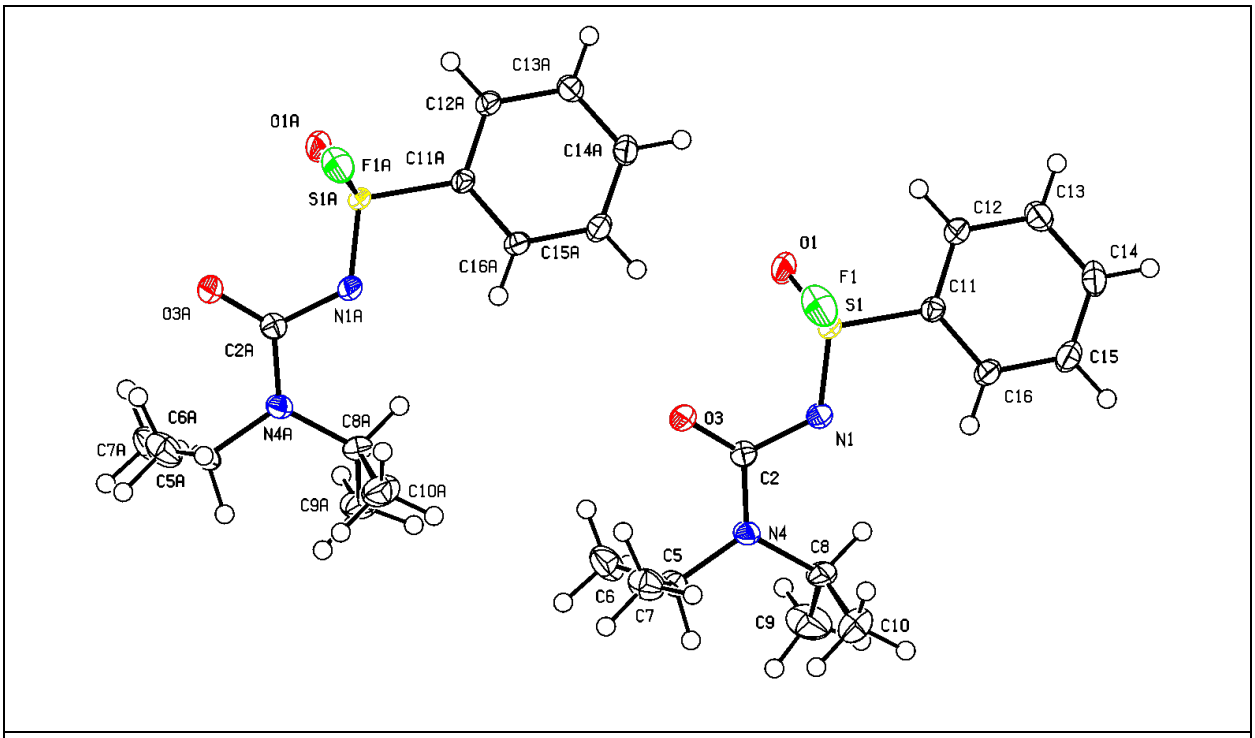


Fig.1. Ellipsoid plot of **2136B (S6a)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243798

Table 1 Crystal data and structure refinement for 2172 (7k).	
Identification code	2172
Empirical formula	$C_{14}H_{22}N_2O_2S$
Formula weight	282.39
Temperature/K	291.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.1841(1)
b/Å	11.5106(2)
c/Å	16.2095(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1527.00(4)
Z	4
ρ_{calc}g/cm^3	1.228
μ/mm^{-1}	1.885
F(000)	608.0
Crystal size/mm^3	0.24 × 0.08 × 0.07
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	9.424 to 160.112
Index ranges	-10 ≤ h ≤ 9, -13 ≤ k ≤ 13, -20 ≤ l ≤ 19
Reflections collected	18369
Independent reflections	3230 [R_{int} = 0.0684, R_{sigma} = 0.0381]
Data/restraints/parameters	3230/514/294
Goodness-of-fit on F^2	1.072
Final R indexes [I>=2σ (I)]	R_1 = 0.0317, wR_2 = 0.0685
Final R indexes [all data]	R_1 = 0.0379, wR_2 = 0.0721
Largest diff. peak/hole / e Å^{-3}	0.18/-0.27
Flack parameter	0.039(10)

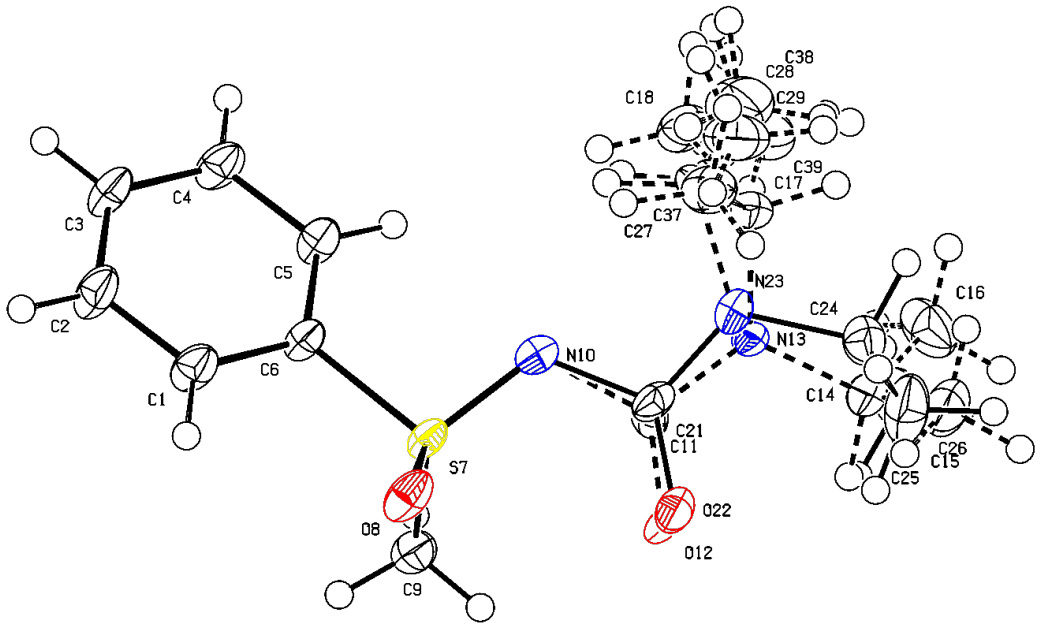


Fig.1. Ellipsoid plot of **2172 (7k)**. Anisotropic displacement parameters were drawn at 50% probability level.
CCDC deposition Number: 2243799

Table 1 Crystal data and structure refinement for 2174B (7a).	
Identification code	2174B
Empirical formula	$C_{19.165}H_{23.25}Cl_{1.42}N_2O_2S$
Moiety formula	$C_{19}H_{23}ClN_2O_2S$, 0.086($CHCl_3$), 0.079(CH_2Cl_2)
Formula weight	395.96
Temperature/K	291.0
Crystal system	hexagonal
Space group	$P6_3$
a/Å	23.8178(4)
b/Å	23.8178(4)
c/Å	6.0872(2)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	2990.55(14)
Z	6
ρ_{calc}g/cm^3	1.319
μ/mm^{-1}	3.313
F(000)	1250.0
Crystal size/mm^3	0.56 × 0.12 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	4.284 to 160.17
Index ranges	-29 ≤ h ≤ 30, -30 ≤ k ≤ 27, -7 ≤ l ≤ 7
Reflections collected	51722
Independent reflections	4305 [R_{int} = 0.0685, R_{sigma} = 0.0274]
Data/restraints/parameters	4305/131/284
Goodness-of-fit on F^2	1.046
Final R indexes [I>=2σ (I)]	R_1 = 0.0343, wR_2 = 0.0854
Final R indexes [all data]	R_1 = 0.0366, wR_2 = 0.0877
Largest diff. peak/hole / e Å^{-3}	0.33/-0.43
Flack parameter	0.050(6)

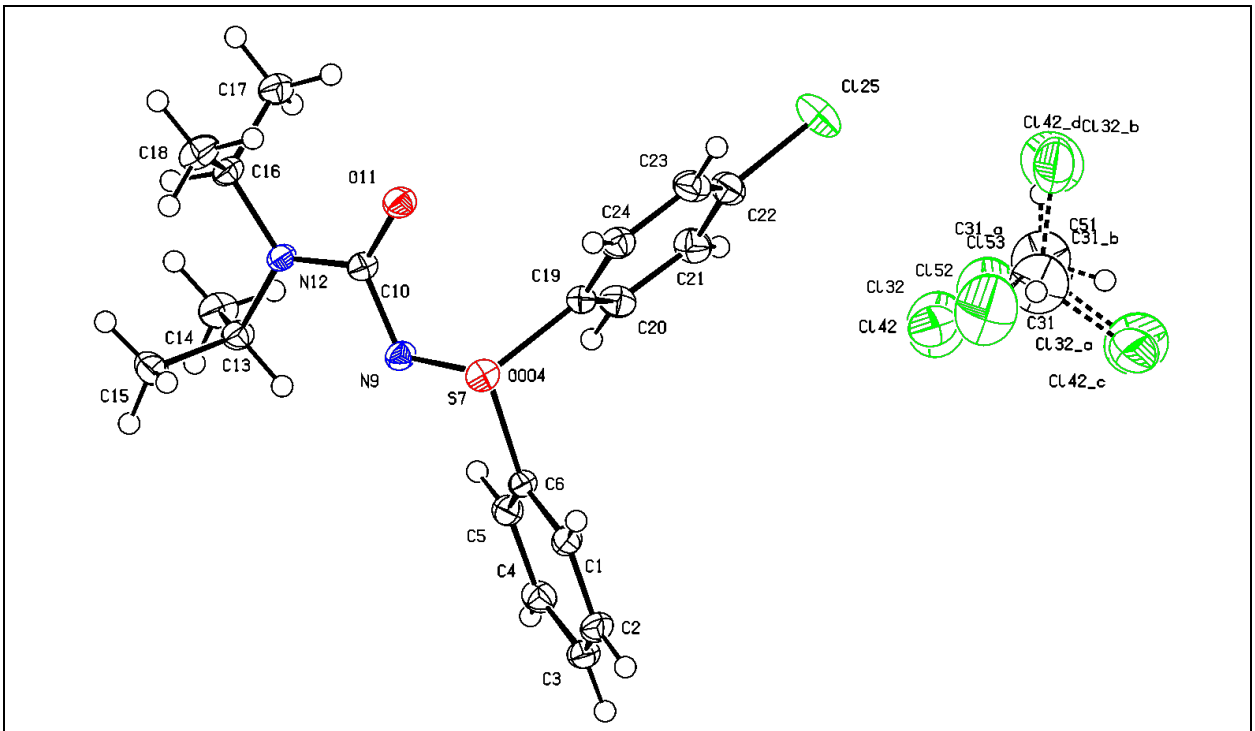


Fig.1. Ellipsoid plot of **2174B (7a)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243808

Table 1 Crystal data and structure refinement for 2191C (7i) .	
Identification code	2191C
Empirical formula	$C_{16}H_{26}N_2O_2S$
Formula weight	310.45
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	6.11810(10)
b/Å	19.5419(4)
c/Å	14.1505(3)
α/°	90
β/°	92.7190(10)
γ/°	90
Volume/Å^3	1689.92(6)
Z	4
ρ_{calc}g/cm^3	1.220
μ/mm^{-1}	1.747
F(000)	672.0
Crystal size/mm^3	0.34 × 0.1 × 0.06
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.252 to 159.81
Index ranges	-7 ≤ h ≤ 7, -24 ≤ k ≤ 24, -15 ≤ l ≤ 17
Reflections collected	47117
Independent reflections	7106 [R_{int} = 0.0972, R_{sigma} = 0.0478]
Data/restraints/parameters	7106/1/391
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0375, wR_2 = 0.0866
Final R indexes [all data]	R_1 = 0.0446, wR_2 = 0.0912
Largest diff. peak/hole / e Å^{-3}	0.28/-0.43
Flack parameter	0.069(8)

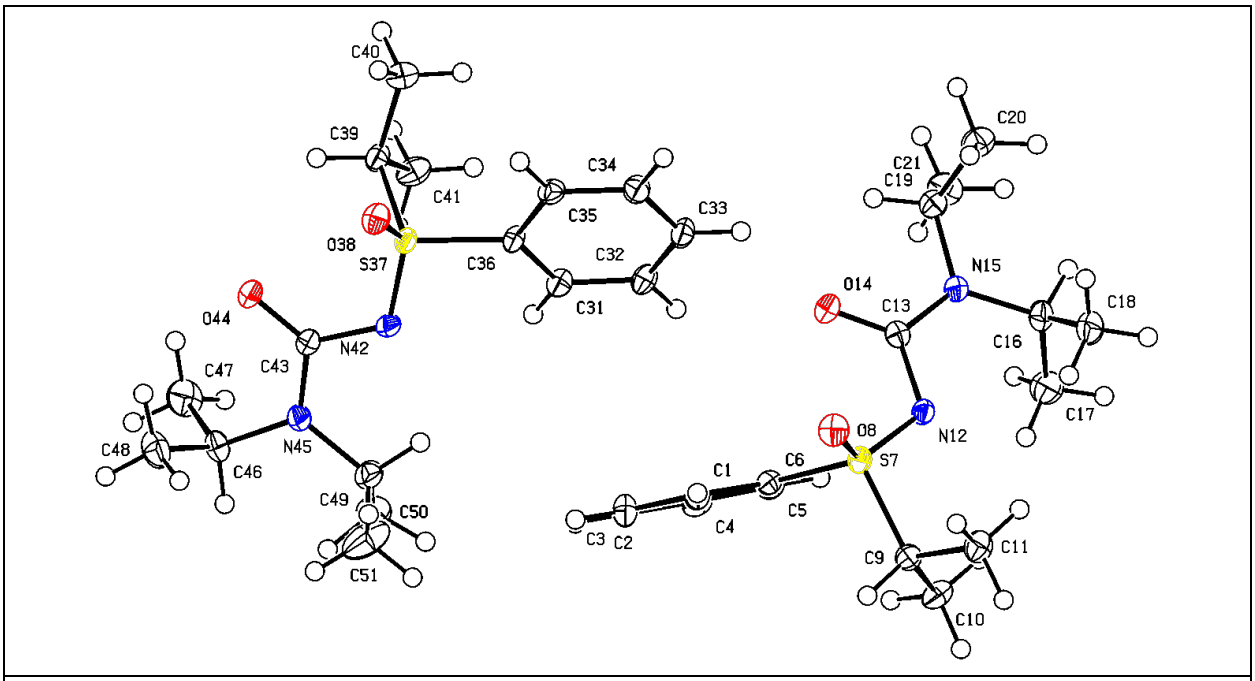


Fig.1. Ellipsoid plot of **2191C (7i)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243802

Table 1 Crystal data and structure refinement for 2238B (7f).	
Identification code	2238B
Empirical formula	$C_{17}H_{22}N_2O_2S_2$
Formula weight	350.48
Temperature/K	100.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.1124(2)
b/Å	11.2478(2)
c/Å	20.2004(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1843.22(6)
Z	4
ρ_{calc}g/cm^3	1.263
μ/mm^{-1}	2.699
F(000)	744.0
Crystal size/mm^3	0.6 × 0.37 × 0.09
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.754 to 160.352
Index ranges	-9 ≤ h ≤ 9, -14 ≤ k ≤ 14, -25 ≤ l ≤ 23
Reflections collected	23943
Independent reflections	3881 [R_{int} = 0.0393, R_{sigma} = 0.0261]
Data/restraints/parameters	3881/0/212
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0226, wR_2 = 0.0560
Final R indexes [all data]	R_1 = 0.0234, wR_2 = 0.0564
Largest diff. peak/hole / e Å^{-3}	0.21/-0.30
Flack parameter	0.025(5)

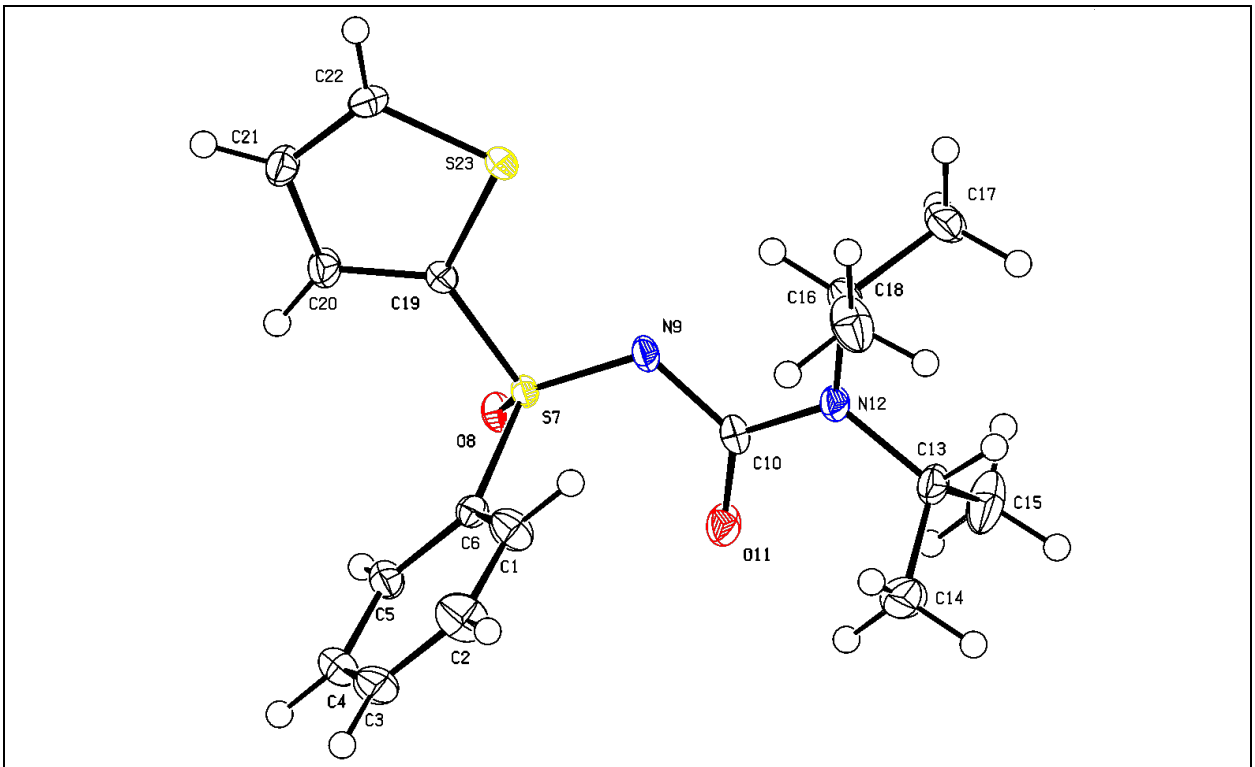


Fig.1. Ellipsoid plot of **2238B (7f)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243806

Table 1 Crystal data and structure refinement for 4121A (7l).	
Identification code	4121A
Empirical formula	C16H24N2O2S
Formula weight	308.43
Temperature/K	100.00
Crystal system	orthorhombic
Space group	P212121
a/Å	8.1411(2)
b/Å	10.6363(3)
c/Å	19.6540(6)
α/°	90
β/°	90
γ/°	90
Volume/Å3	1701.86(8)
Z	4
ρcalcg/cm3	1.204
μ/mm-1	1.734
F(000)	664.0
Crystal size/mm3	0.45 × 0.3 × 0.09
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.998 to 158.808
Index ranges	-10 ≤ h ≤ 10, -13 ≤ k ≤ 12, -24 ≤ l ≤ 25
Reflections collected	40568
Independent reflections	3645 [Rint = 0.0419, Rsigma = 0.0207]
Data/restraints/parameters	3645/0/202
Goodness-of-fit on F2	1.040
Final R indexes [I>=2σ (I)]	R1 = 0.0231, wR2 = 0.0607
Final R indexes [all data]	R1 = 0.0233, wR2 = 0.0609
Largest diff. peak/hole / e Å-3	0.23/-0.26
Flack parameter	0.046(3)

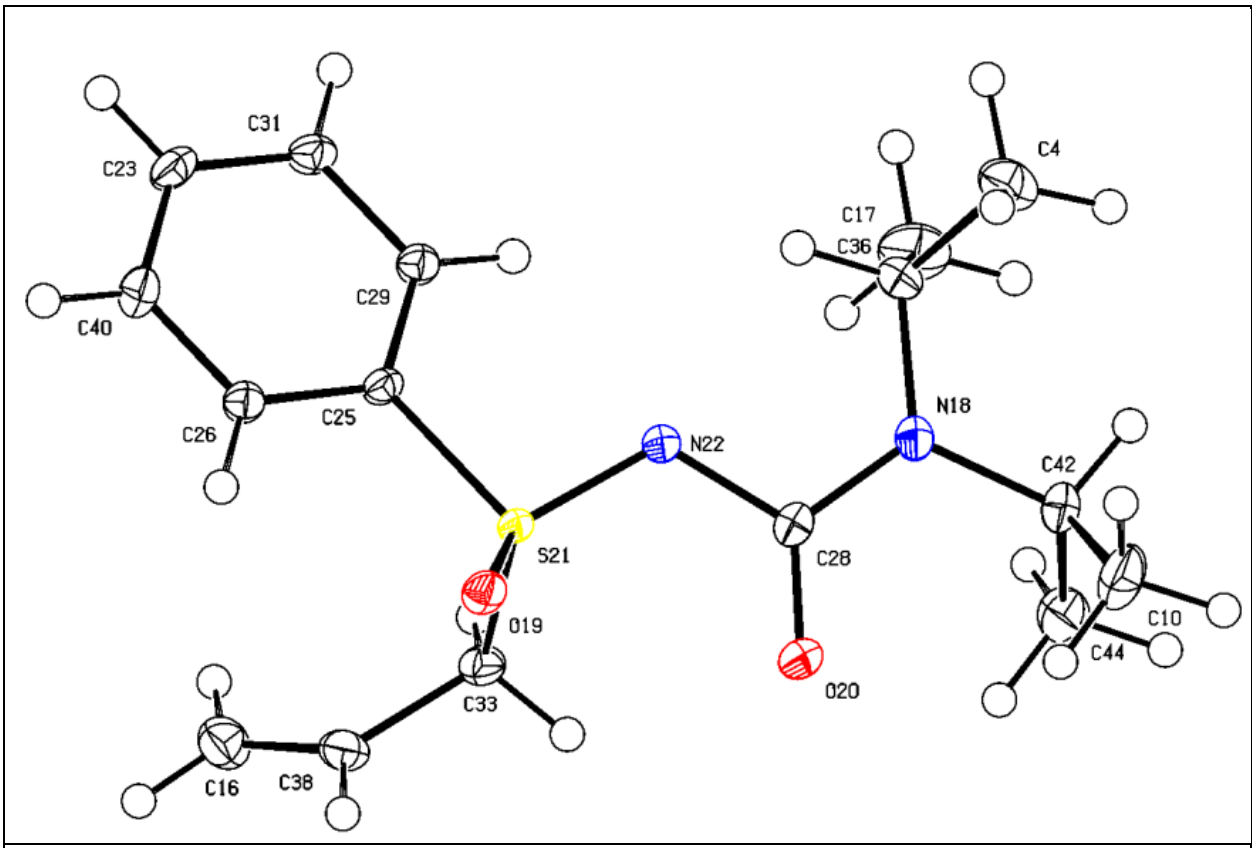


Fig.1. Ellipsoid plot of **4121A (7l)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243807

Table 1 Crystal data and structure refinement for 4184A (7e).	
Identification code	4184A
Empirical formula	$C_{19}H_{26}N_4O_3S$
Formula weight	390.50
Temperature/K	100.00
Crystal system	hexagonal
Space group	$P6_5$
a/Å	23.6795(3)
b/Å	23.6795(3)
c/Å	6.2938(1)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	3056.25(9)
Z	6
ρ_{calc}g/cm^3	1.273
μ/mm^{-1}	1.629
F(000)	1248.0
Crystal size/mm^3	0.6 × 0.03 × 0.02
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	4.308 to 160.326
Index ranges	-28 ≤ h ≤ 30, -30 ≤ k ≤ 29, -7 ≤ l ≤ 7
Reflections collected	64029
Independent reflections	4406 [R_{int} = 0.0667, R_{sigma} = 0.0270]
Data/restraints/parameters	4406/602/353
Goodness-of-fit on F^2	1.040
Final R indexes [I>=2σ (I)]	R_1 = 0.0263, wR_2 = 0.0693
Final R indexes [all data]	R_1 = 0.0271, wR_2 = 0.0698
Largest diff. peak/hole / e Å^{-3}	0.14/-0.30
Flack parameter	0.081(6)

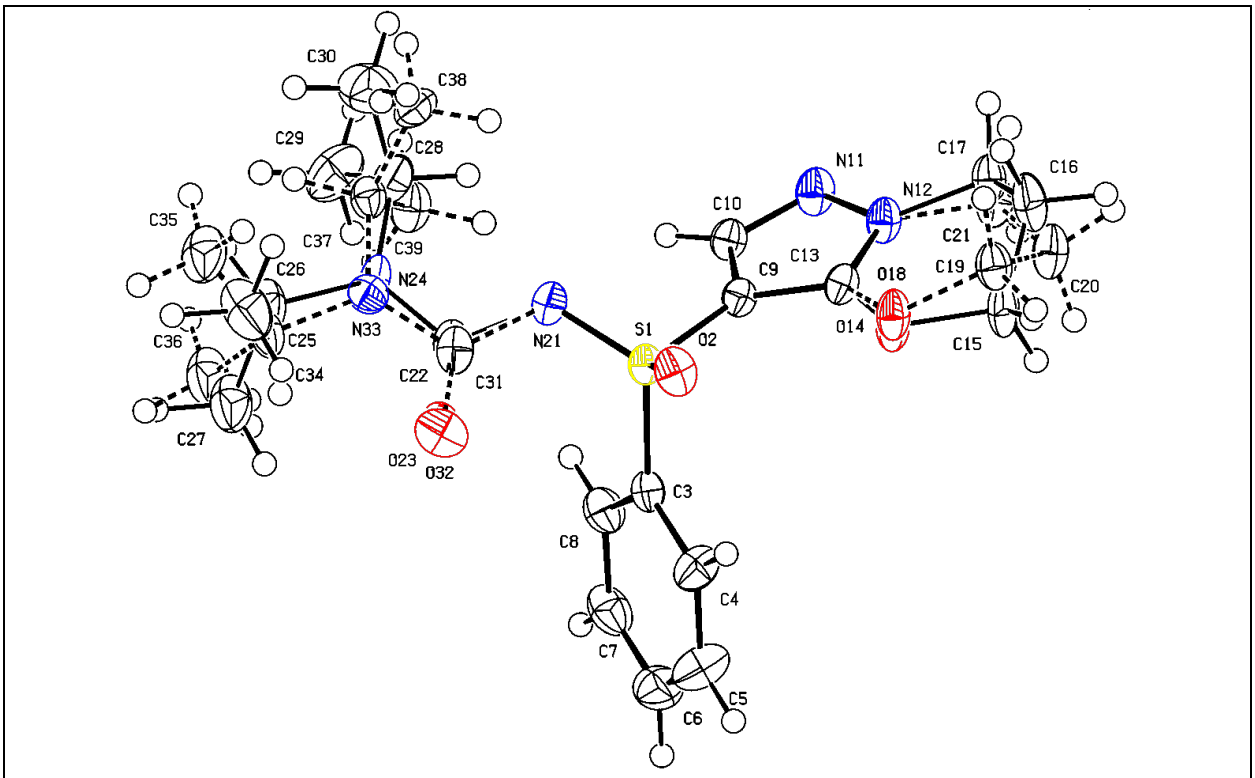


Fig.1. Ellipsoid plot of **4184A (7e)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243805

Table 1 Crystal data and structure refinement for 4292C (7d).	
Identification code	4292C
Empirical formula	$C_{29}H_{30}N_2O_4S$
Formula weight	502.61
Temperature/K	101.00
Crystal system	monoclinic
Space group	$P2_1$
a/Å	6.3511(2)
b/Å	17.4886(6)
c/Å	11.6191(4)
α/°	90
β/°	96.1890(10)
γ/°	90
Volume/Å^3	1283.03(7)
Z	2
ρ_{calc}g/cm^3	1.301
μ/mm^{-1}	1.428
F(000)	532.0
Crystal size/mm^3	0.25 × 0.2 × 0.08
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	9.174 to 159.728
Index ranges	$-7 \le h \le 8$, $-22 \le k \le 22$, $-14 \le l \le 14$
Reflections collected	25741
Independent reflections	5160 [R_{int} = 0.0418, R_{sigma} = 0.0381]
Data/restraints/parameters	5160/1/329
Goodness-of-fit on F^2	1.054
Final R indexes [I>=2σ (I)]	R_1 = 0.0307, wR_2 = 0.0788
Final R indexes [all data]	R_1 = 0.0309, wR_2 = 0.0790
Largest diff. peak/hole / e Å^{-3}	0.35/-0.28
Flack parameter	0.157(5)

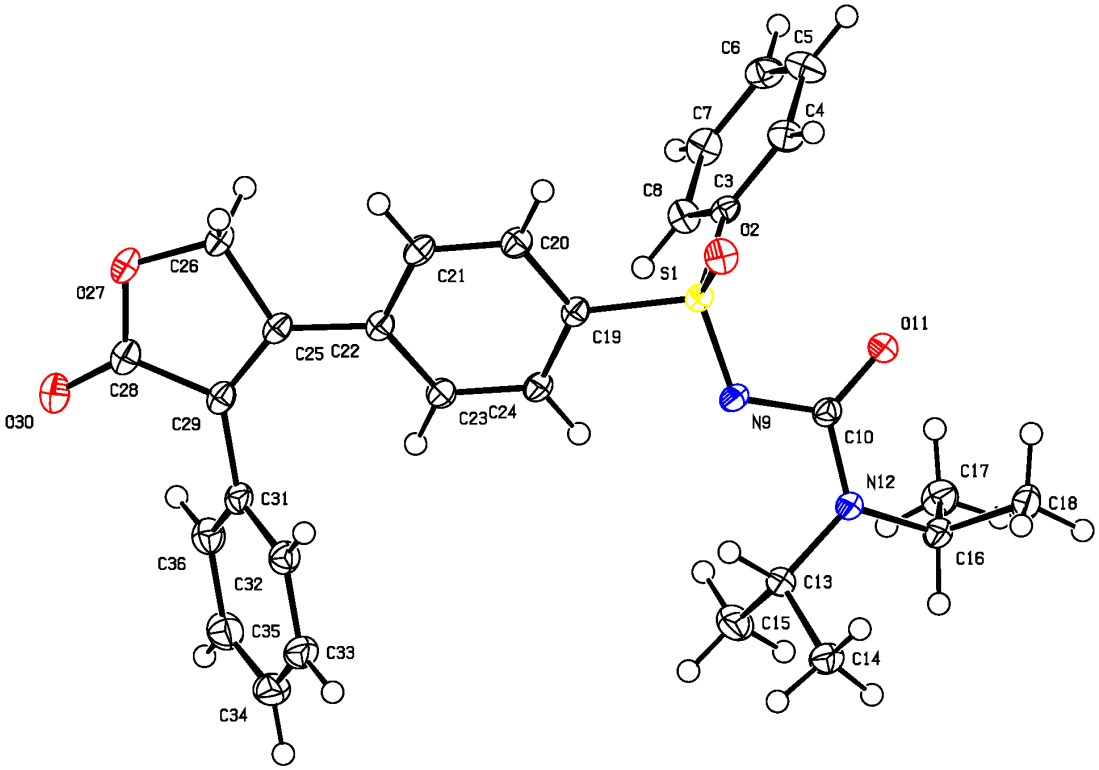


Fig.1. Ellipsoid plot of **4292C (7d)**. Anisotropic displacement parameters were drawn at 50% probability level.
CCDC deposition Number: 2243809

Table 1 Crystal data and structure refinement for **5115D (9a)**.	
Identification code	5115D
Empirical formula	C10H9NOS2
Formula weight	223.30
Temperature/K	100.00
Crystal system	orthorhombic
Space group	C2221
a/Å	6.0476(2)
b/Å	14.4290(4)
c/Å	22.6538(7)
α/°	90
β/°	90
γ/°	90
Volume/Å3	1976.79(10)
Z	8
ρcalcg/cm3	1.501
μ/mm-1	4.582
F(000)	928.0
Crystal size/mm3	0.22 × 0.15 × 0.06
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	12.878 to 159.214
Index ranges	-7 ≤ h ≤ 7, -17 ≤ k ≤ 18, -28 ≤ l ≤ 28
Reflections collected	18719
Independent reflections	2122 [Rint = 0.0388, Rsigma = 0.0252]
Data/restraints/parameters	2122/347/177
Goodness-of-fit on F2	1.085
Final R indexes [I>=2σ (I)]	R1 = 0.0231, wR2 = 0.0650
Final R indexes [all data]	R1 = 0.0231, wR2 = 0.0650
Largest diff. peak/hole / e Å-3	0.30/-0.32
Flack parameter	0.074(5)

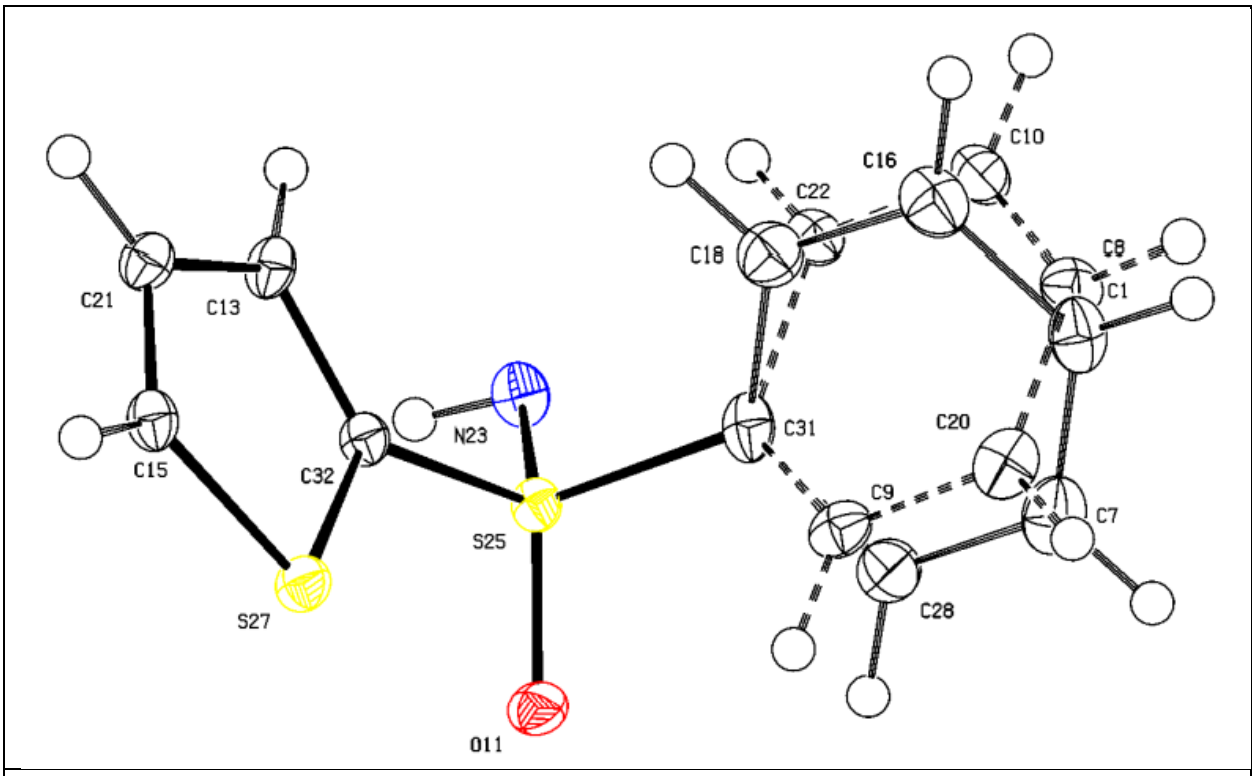


Fig.1. Ellipsoid plot of **5115D (9a)**. Anisotropic displacement parameters were drawn at 50% probability level. CCDC deposition Number: 2243810

XI. References

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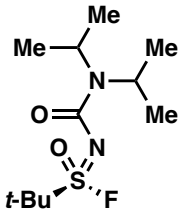
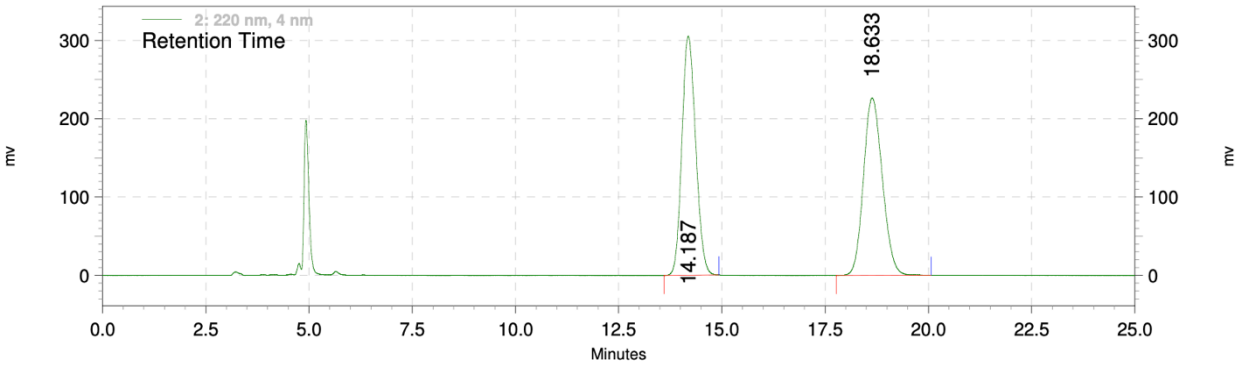
XII. Chiral HPLC chromatograms



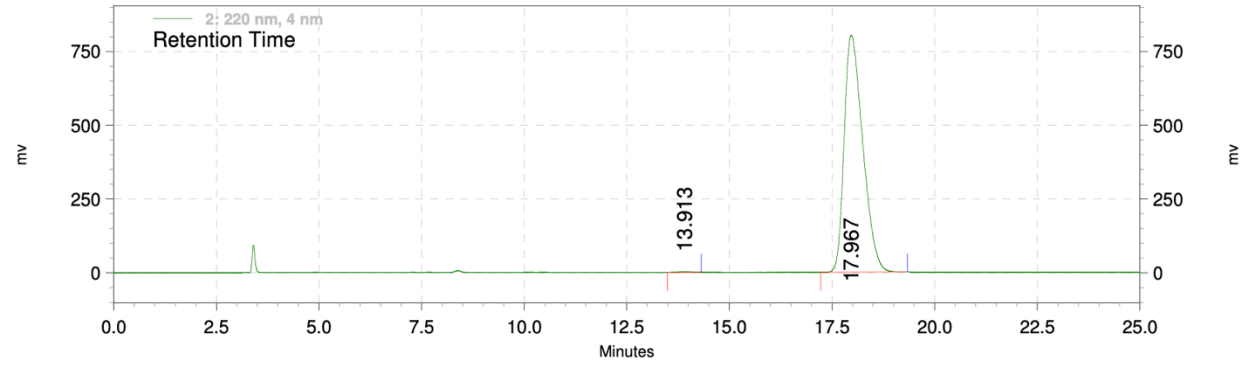
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for *t*-BuSF: (*rac*)



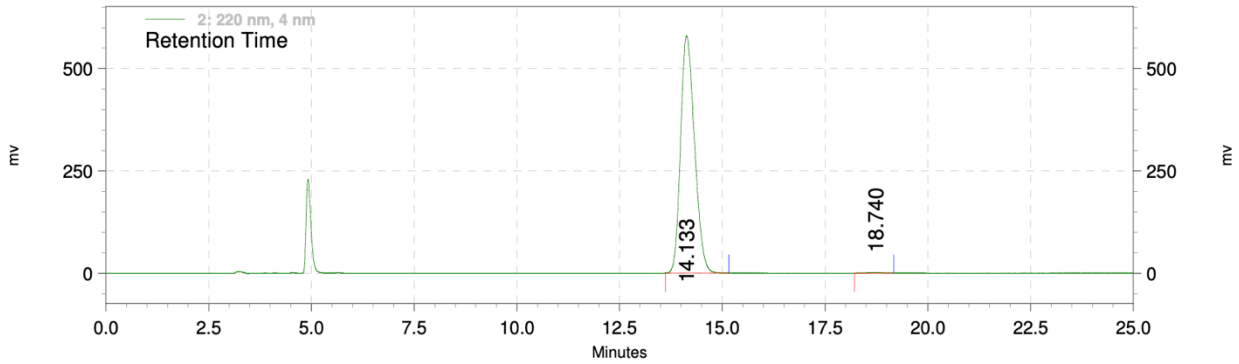
Retention Time	Area	Area %	Height	Height %
14.187	7104139	49.68	305451	57.42
18.633	7194660	50.32	226486	42.58
Totals	14298799	100.00	531937	100.00

Chromatogram for *t*-BuSF: (*S*)

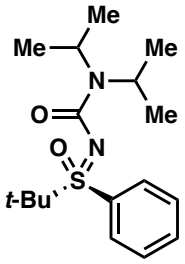


Retention Time	Area	Area %	Height	Height %
13.913	72121	0.28	3376	0.42
17.967	25319954	99.72	802998	99.58
Totals	25392075	100.00	806374	100.00

Chromatogram for *t*-BuSF: (*R*)

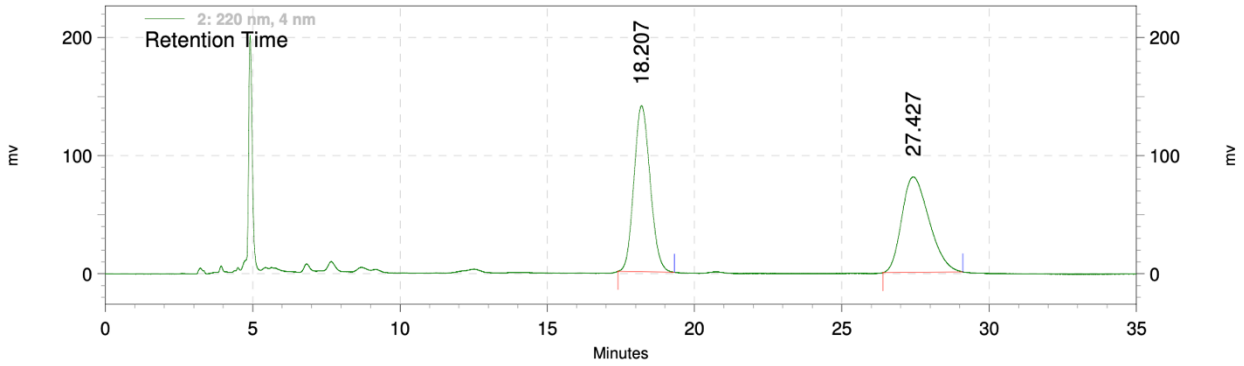


Retention Time	Area	Area %	Height	Height %
14.133	13699269	99.71	579838	99.75
18.740	40200	0.29	1454	0.25
Totals	13739469	100.00	581292	100.00



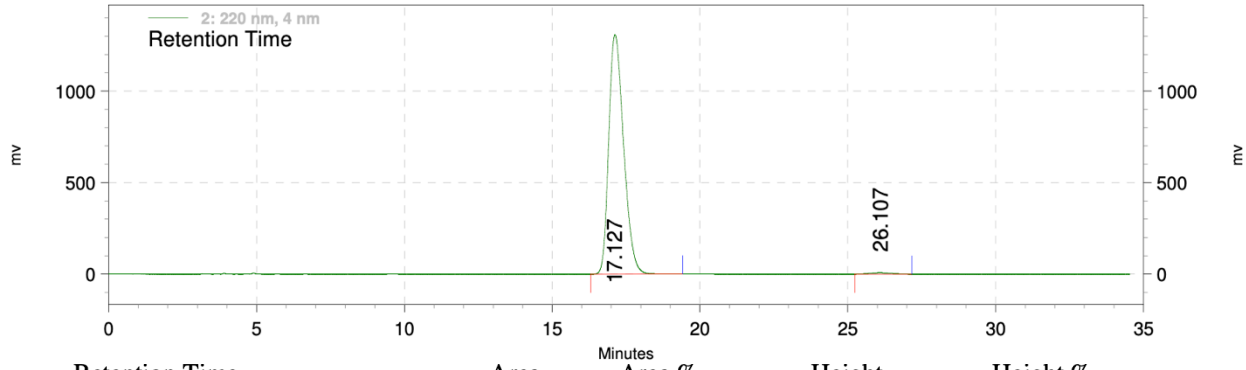
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2a



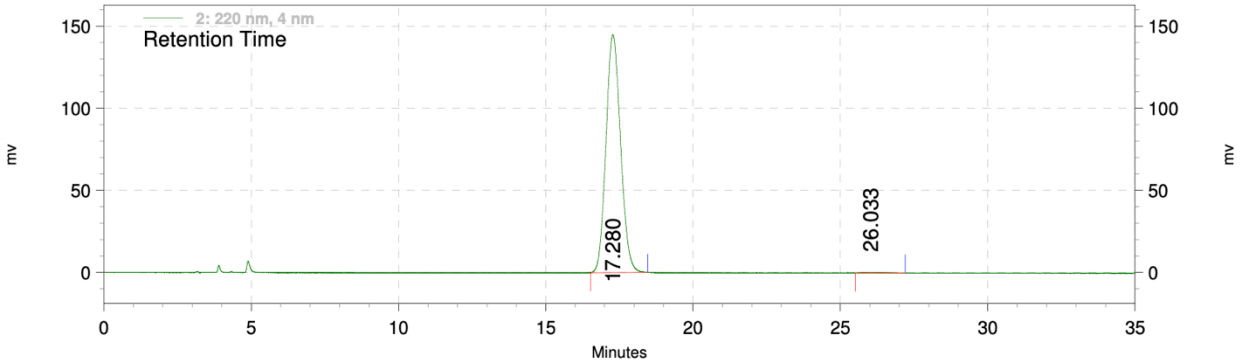
Retention Time	Area	Area %	Height	Height %
18.207	5376077	50.80	140872	63.54
27.427	5205791	49.20	80823	36.46
Totals	10581868	100.00	221695	100.00

Chromatogram for sulfoximine: (*R*)-2a

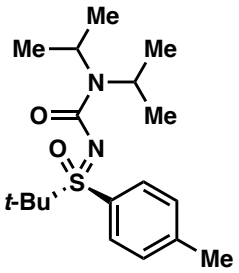


Retention Time	Area	Area %	Height	Height %
17.127	45889702	99.15	1309511	99.44
26.107	395120	0.85	7384	0.56
Totals	46284822	100.00	1316895	100.00

Chromatogram for sulfoximine: (*R*)-2a after single recrystallization

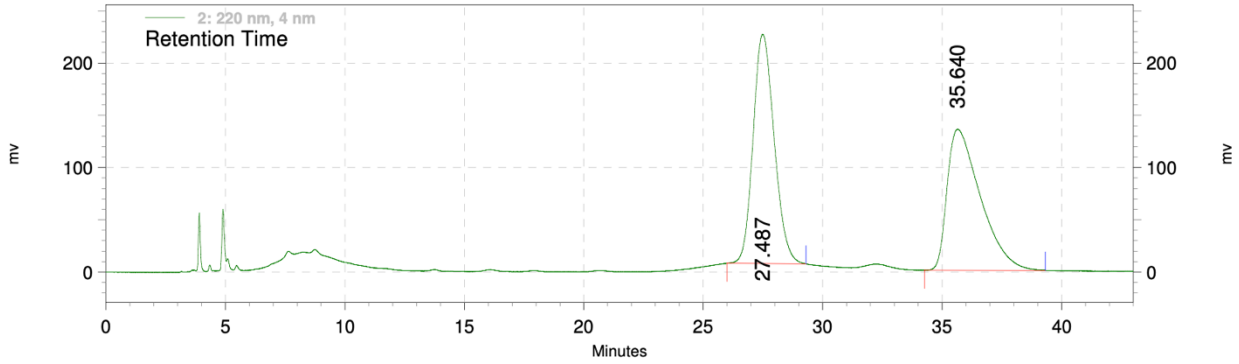


Retention Time	Area	Area %	Height	Height %
17.280	4976663	99.72	144771	99.81
26.033	14018	0.28	276	0.19
Totals	4990681	100.00	145047	100.00



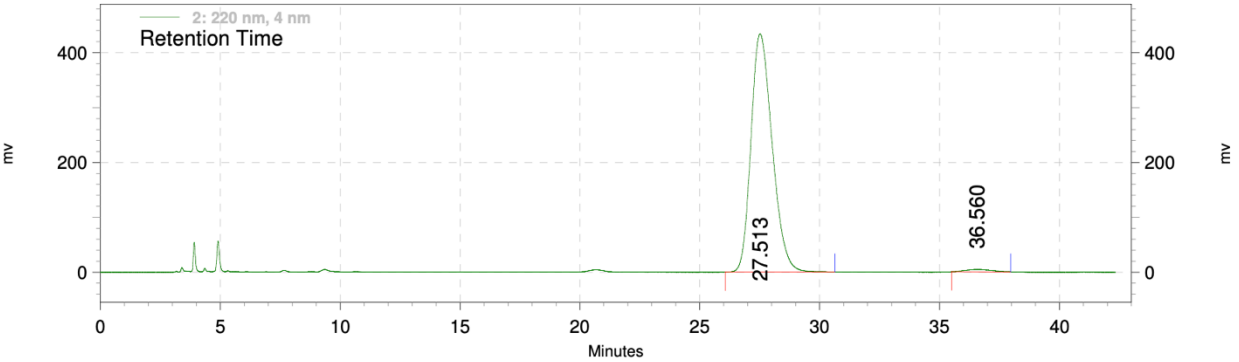
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2b

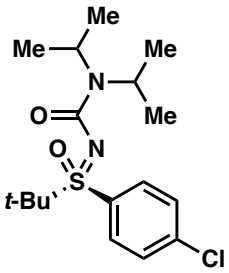


Retention Time	Area	Area %	Height	Height %
27.487	13478110	50.79	219540	61.91
35.640	13060489	49.21	135050	38.09
Totals	26538599	100.00	354590	100.00

Chromatogram for sulfoximine: (*R*)-2b

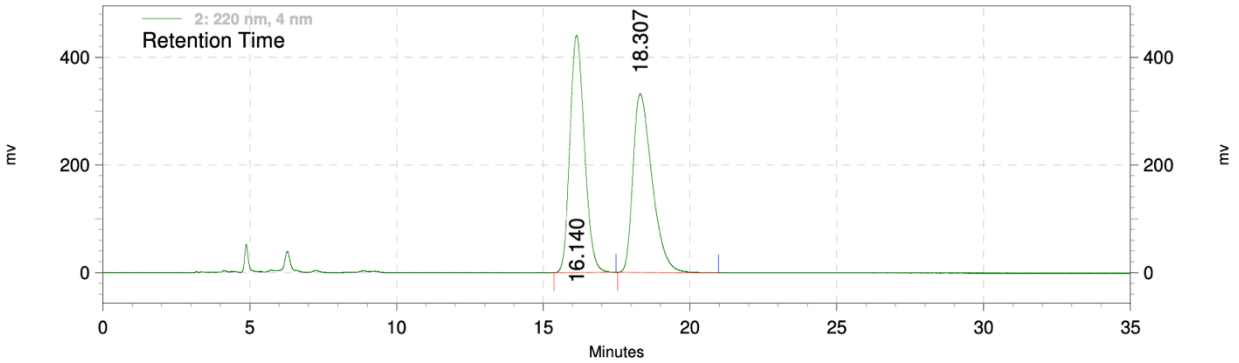


Retention Time	Area	Area %	Height	Height %
27.513	26673288	98.80	434388	99.02
36.560	324285	1.20	4278	0.98
Totals	26997573	100.00	438666	100.00



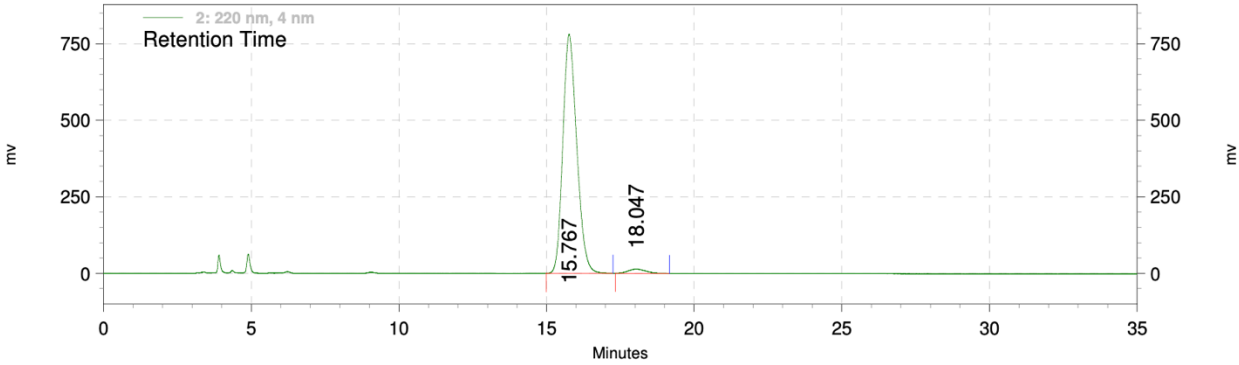
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2c



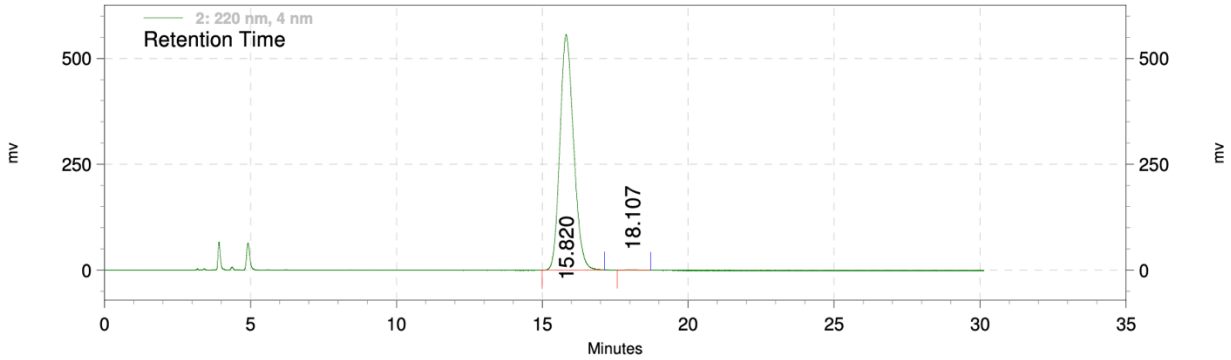
Retention Time	Area	Area %	Height	Height %
16.140	15250879	50.37	441178	57.07
18.307	15027789	49.63	331808	42.93
Totals	30278668	100.00	772986	100.00

Chromatogram for sulfoximine: (*R*)-2c



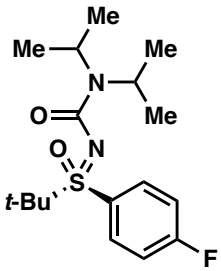
Retention Time	Area	Area %	Height	Height %
15.767	26057951	97.86	781281	98.28
18.047	568995	2.14	13697	1.72
Totals	26626946	100.00	794978	100.00

Chromatogram for sulfoximine: (*R*)-2c after single recrystallization



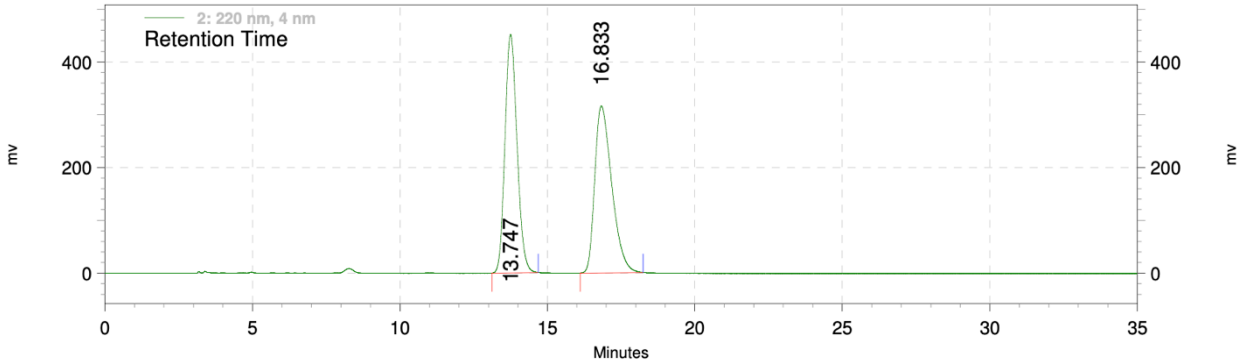
Retention Time	Area	Area %	Height	Height %
15.820	18478507	99.86	556555	99.84
18.107	25672	0.14	909	0.16

Totals	18504179	100.00	557464	100.00



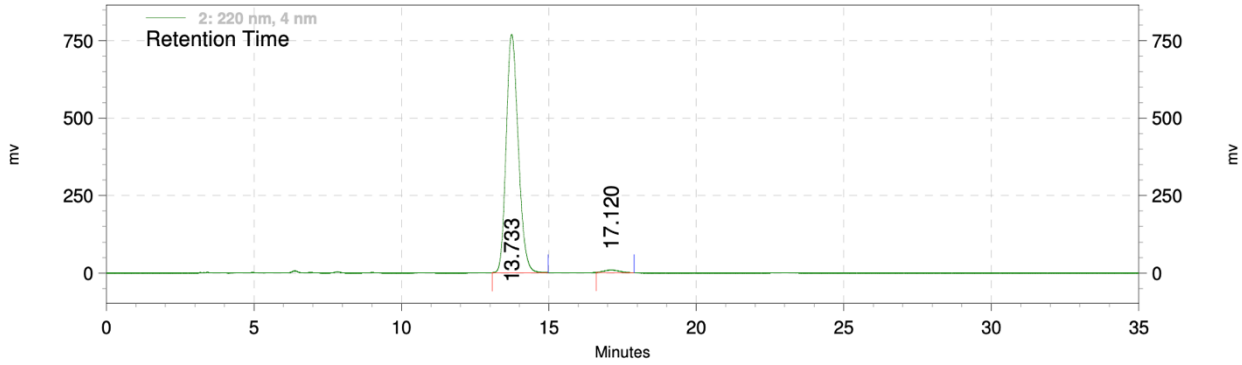
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2d

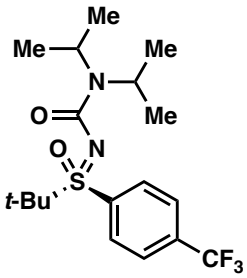


Retention Time	Area	Area %	Height	Height %
13.747	12843908	50.33	451843	58.81
16.833	12675693	49.67	316492	41.19
Totals	25519601	100.00	768335	100.00

Chromatogram for sulfoximine: (*R*)-2d

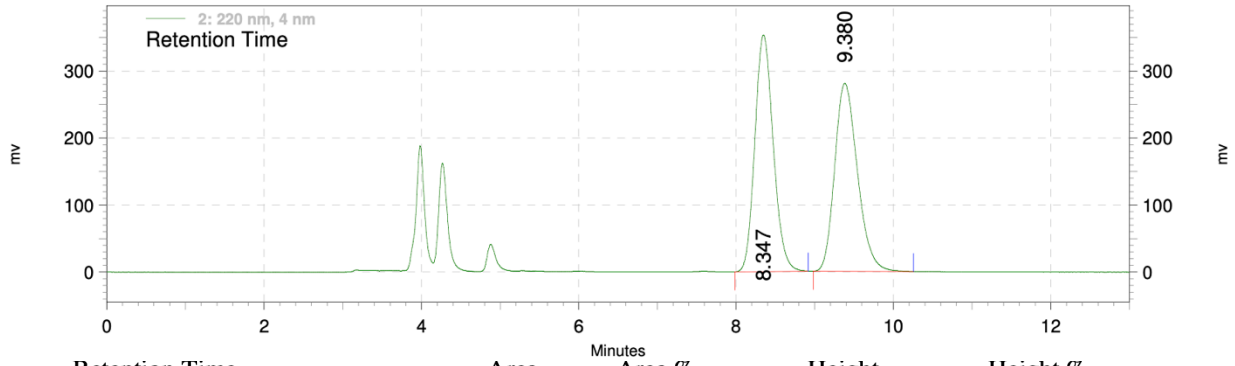


Retention Time	Area	Area %	Height	Height %
13.733	21889684	98.60	768960	98.90
17.120	310221	1.40	8546	1.10
Totals	22199905	100.00	777506	100.00



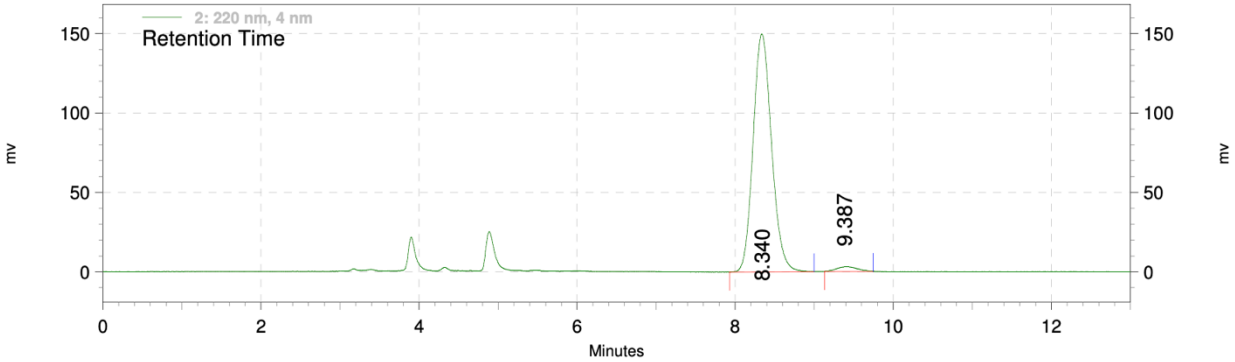
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2e

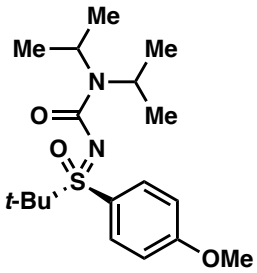


Retention Time	Area	Area %	Height	Height %
8.347	5746711	50.44	352935	55.72
9.380	5646088	49.56	280503	44.28
Totals	11392799	100.00	633438	100.00

Chromatogram for sulfoximine: (*R*)-2e

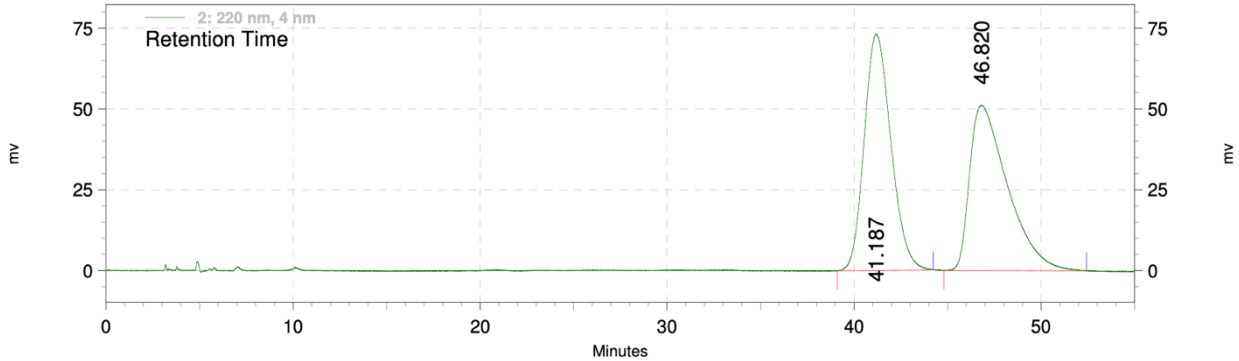


Retention Time	Area	Area %	Height	Height %
8.340	2431664	97.87	149919	98.05
9.387	52852	2.13	2987	1.95
Totals	2484516	100.00	152906	100.00



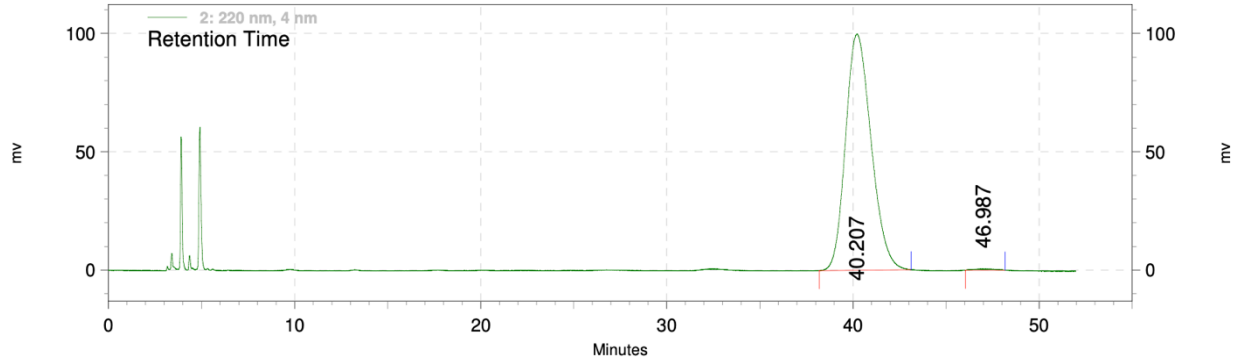
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2f

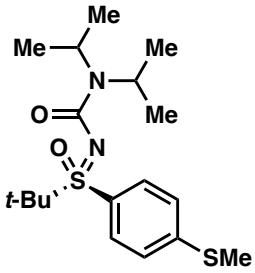


Retention Time	Area	Area %	Height	Height %
41.187	7257537	50.18	73123	58.81
46.820	7206635	49.82	51223	41.19
Totals	14464172	100.00	124346	100.00

Chromatogram for sulfoximine: (*R*)-2f

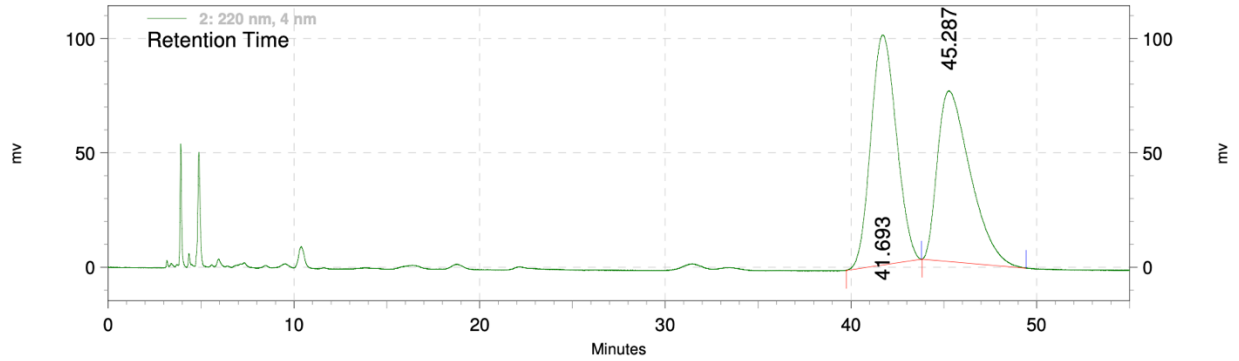


Retention Time	Area	Area %	Height	Height %
40.207	9544710	99.56	99888	99.43
46.987	42357	0.44	574	0.57
Totals	9587067	100.00	100462	100.00



Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

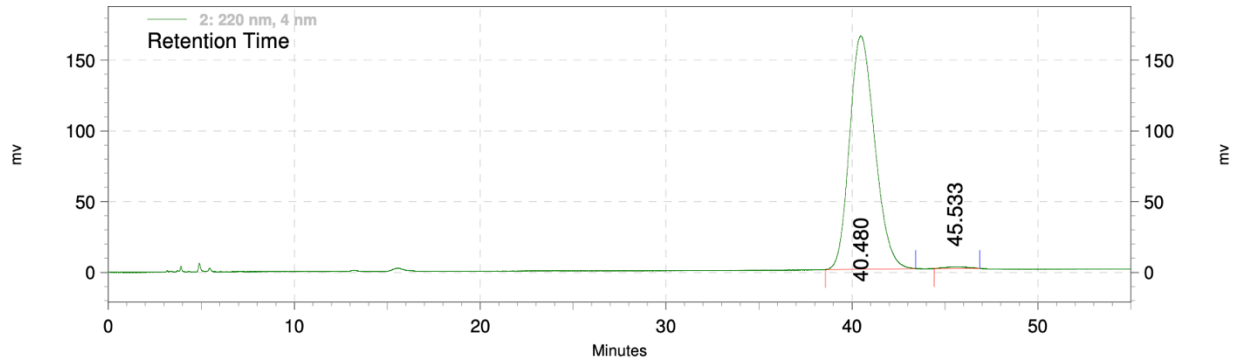
Chromatogram for sulfoximine: (*rac*)-2g



Retention Time	Area	Area %	Height	Height %
41.693	9613336	51.12	100606	57.40
45.287	9192250	48.88	74680	42.60

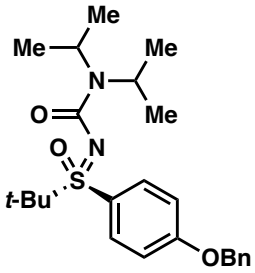
Totals	18805586	100.00	175286	100.00

Chromatogram for sulfoximine: (*R*)-2g



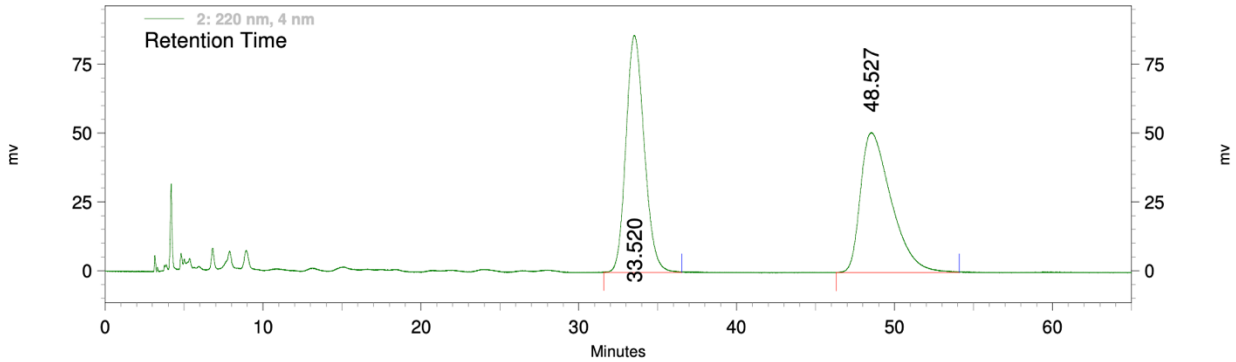
Retention Time	Area	Area %	Height	Height %
40.480	15582540	99.31	165090	99.22
45.533	108469	0.69	1298	0.78

Totals	15691009	100.00	166388	100.00



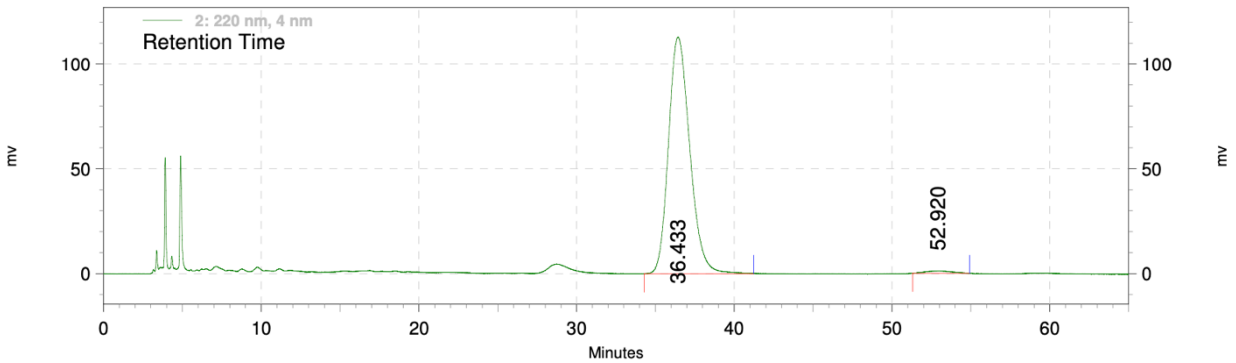
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2h

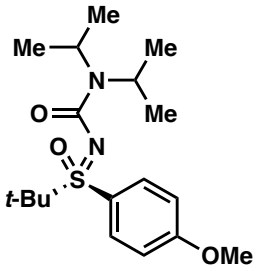


Retention Time	Area	Area %	Height	Height %
33.520	6921433	50.24	86134	62.89
48.527	6856277	49.76	50831	37.11
Totals	13777710	100.00	136965	100.00

Chromatogram for sulfoximine: (*R*)-2h

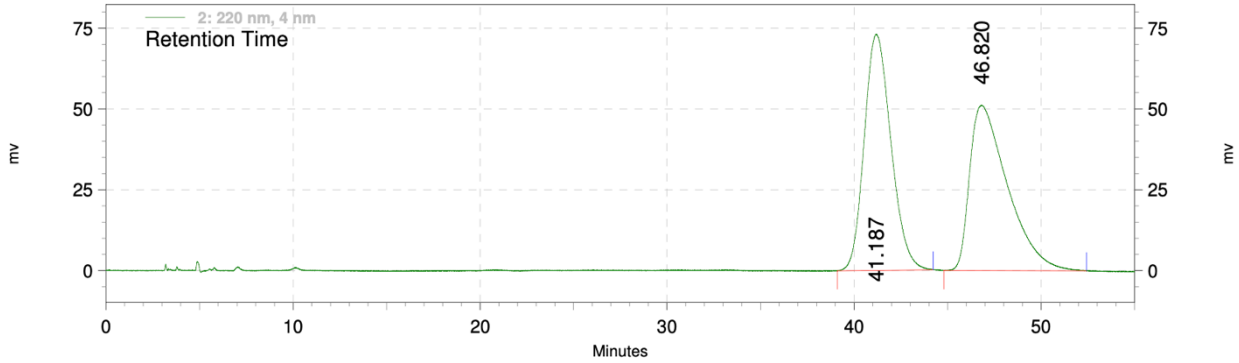


Retention Time	Area	Area %	Height	Height %
36.433	10612292	98.69	113013	98.93
52.920	140327	1.31	1225	1.07
Totals	10752619	100.00	114238	100.00



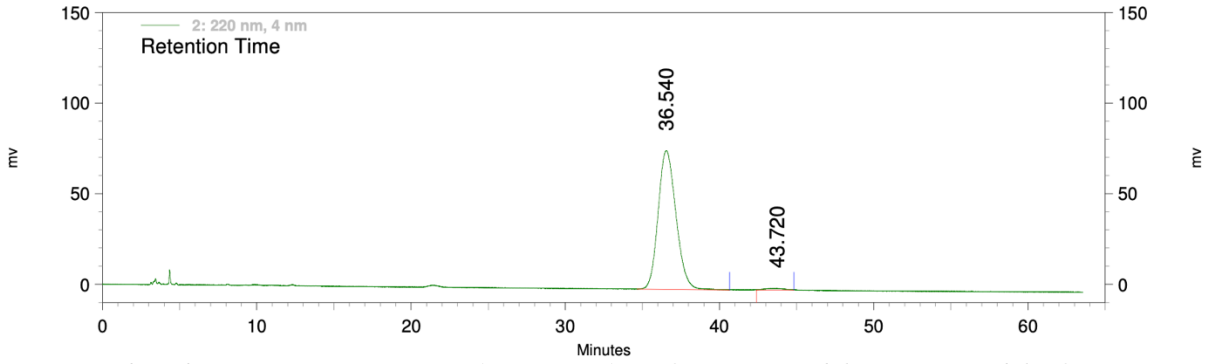
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2f (from (*rac*)-2i, methylated for HPLC analysis)



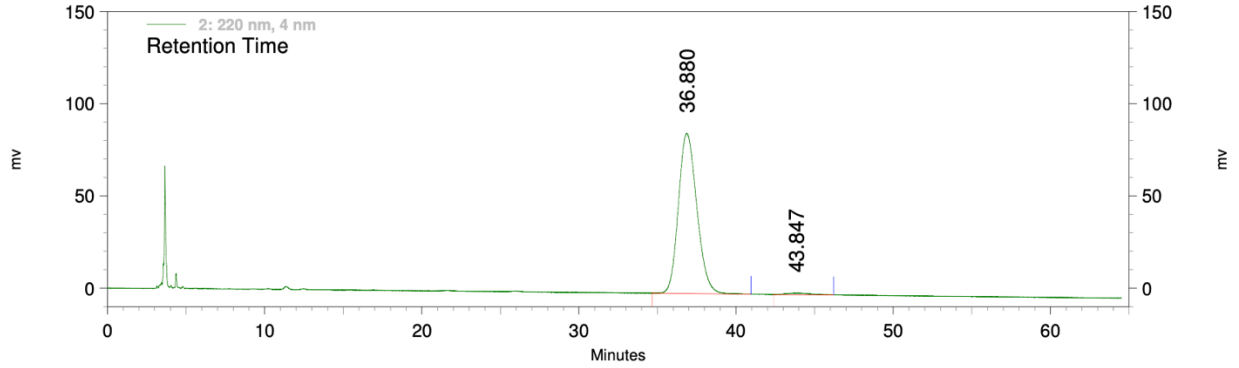
Retention Time	Area	Area %	Height	Height %
41.187	7257537	50.18	73123	58.81
46.820	7206635	49.82	51223	41.19
Totals	14464172	100.00	124346	100.00

Chromatogram for sulfoximine: (*R*)-2f (from 4-OH, methylated for HPLC analysis)

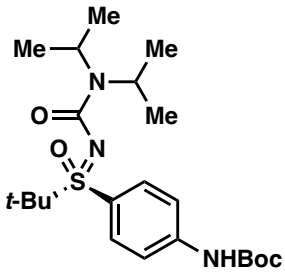


Retention Time	Area	Area %	Height	Height %
36.540	6171373	98.83	76592	98.79
43.720	73001	1.17	939	1.21
Totals	6244374	100.00	77531	100.00

Chromatogram for sulfoximine: (*R*)-2f (from 4-OTBS, methylated for HPLC analysis)

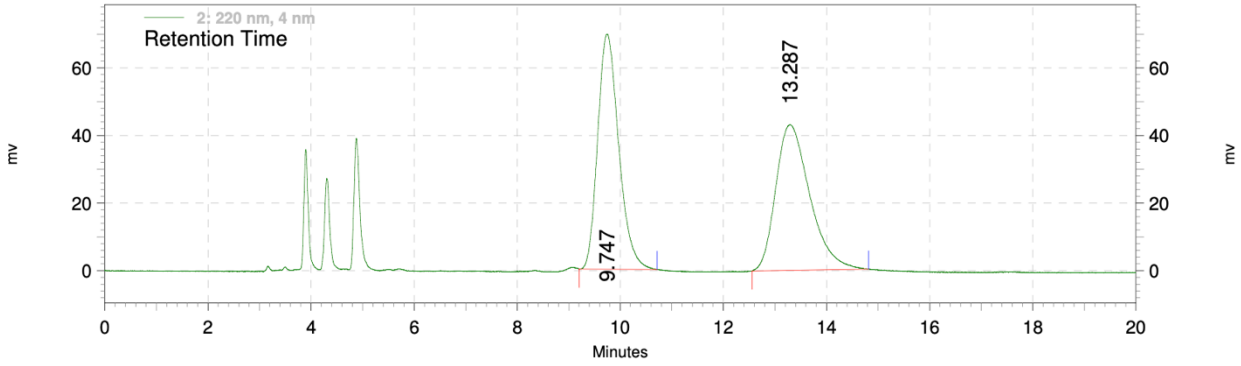


Retention Time	Area	Area %	Height	Height %
36.880	7089708	98.58	86901	98.90
43.847	102240	1.42	965	1.10
Totals	7191948	100.00	87866	100.00



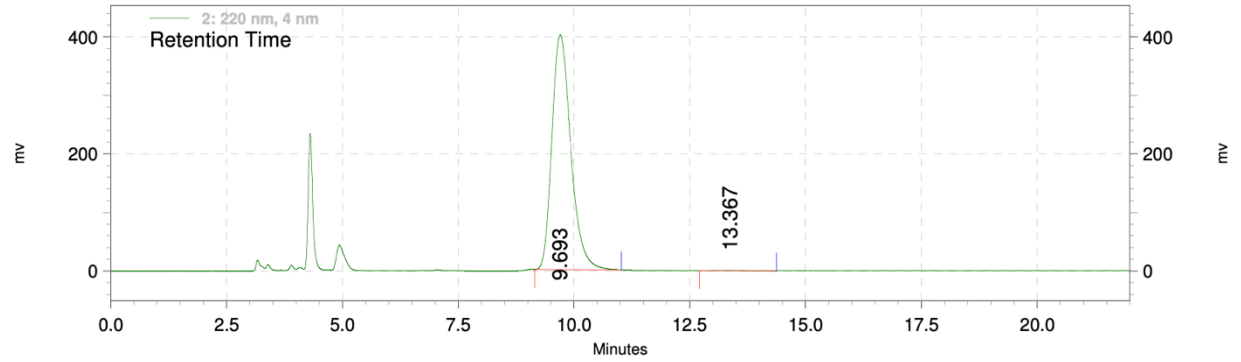
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2j

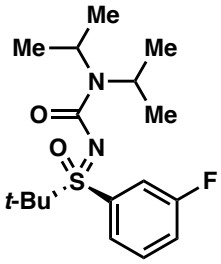


Retention Time	Area	Area %	Height	Height %
9.747	1975254	50.03	69573	61.75
13.287	1973186	49.97	43098	38.25
Totals	3948440	100.00	112671	100.00

Chromatogram for sulfoximine: (*R*)-2j

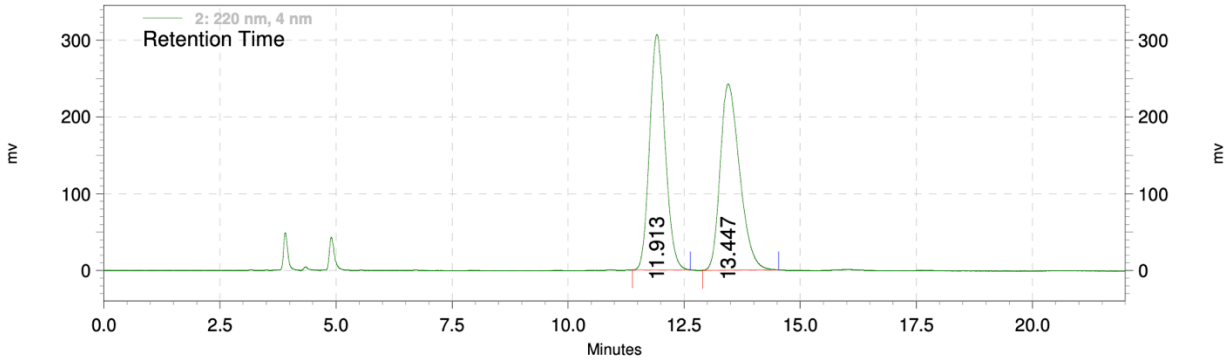


Retention Time	Area	Area %	Height	Height %
9.693	11450597	99.69	401092	99.80
13.367	35935	0.31	809	0.20
Totals	11486532	100.00	401901	100.00



Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

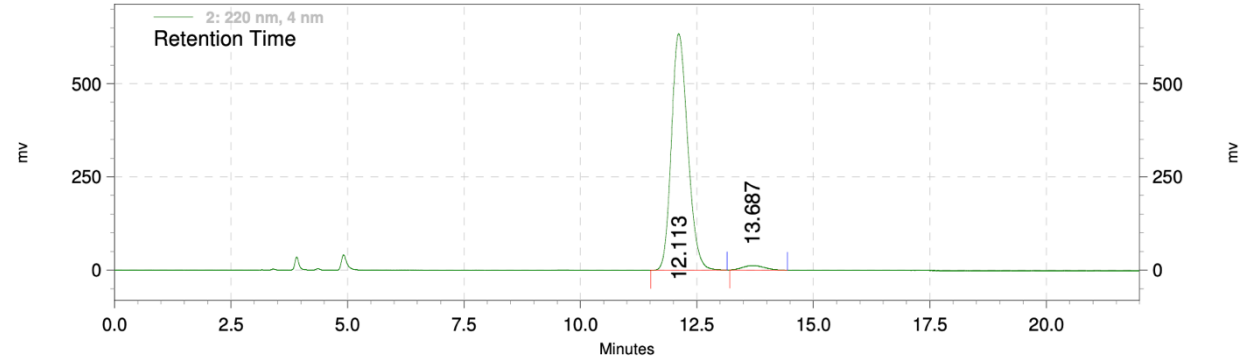
Chromatogram for sulfoximine: (*rac*)-2k



Retention Time	Area	Area %	Height	Height %
11.913	7127973	50.14	306635	55.82
13.447	7089082	49.86	242713	44.18

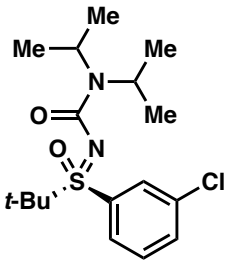
Totals				
	14217055	100.00	549348	100.00

Chromatogram for sulfoximine: (*R*)-2k

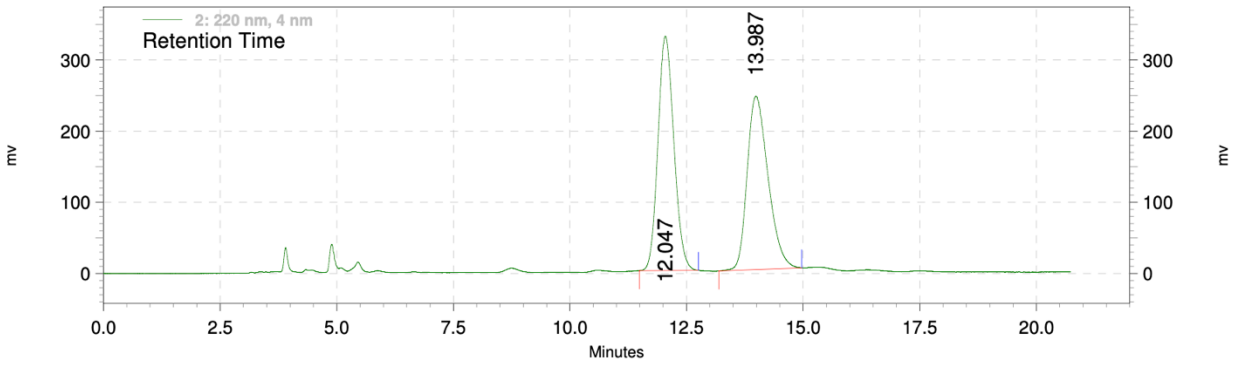


Retention Time	Area	Area %	Height	Height %
12.113	15485948	97.53	635313	98.12
13.687	392326	2.47	12205	1.88

Totals				
	15878274	100.00	647518	100.00

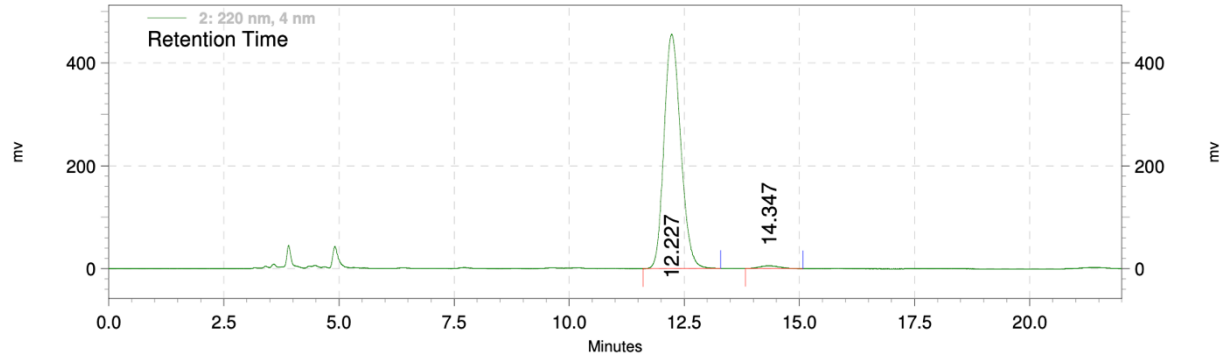


Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min
Chromatogram for sulfoximine: (*rac*)-2l

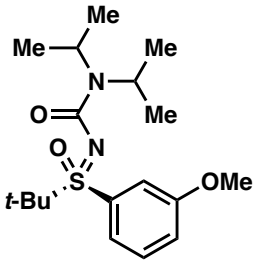


Retention Time	Area	Area %	Height	Height %
12.047	7873110	50.85	329382	57.48
13.987	7609700	49.15	243619	42.52
Totals	15482810	100.00	573001	100.00

Chromatogram for sulfoximine: (*R*)-2l

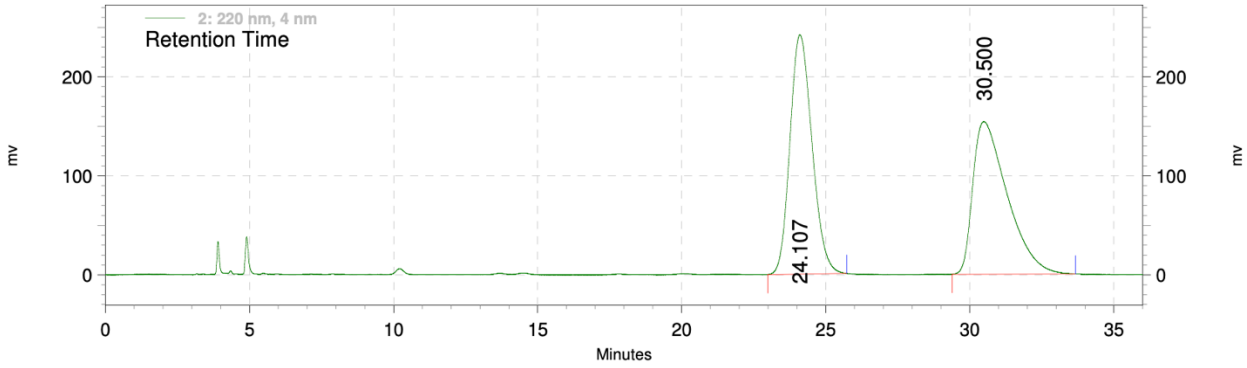


Retention Time	Area	Area %	Height	Height %
12.227	11366202	98.61	455096	98.87
14.347	160625	1.39	5202	1.13
Totals	11526827	100.00	460298	100.00



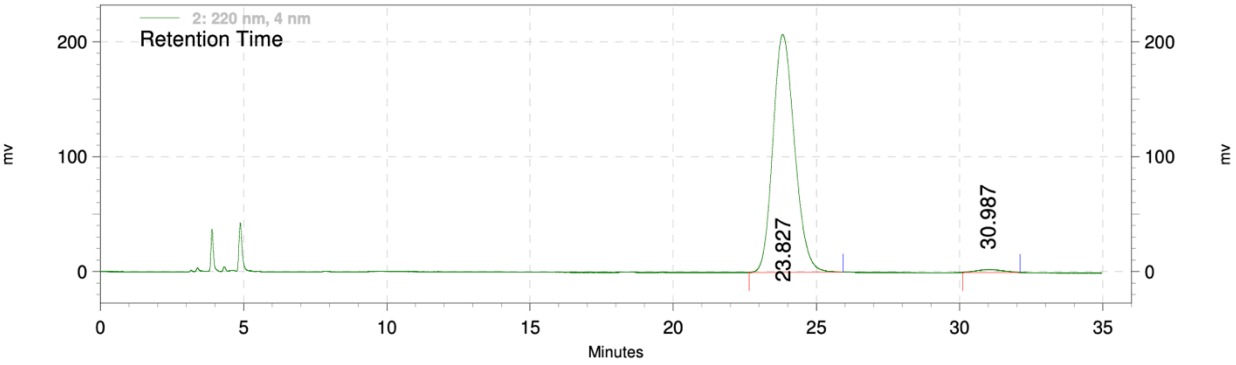
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2m

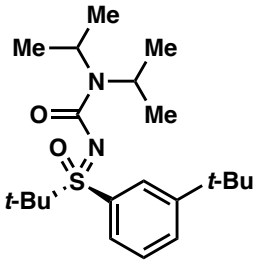


Retention Time	Area	Area %	Height	Height %
24.107	12873695	50.25	241545	61.07
30.500	12744512	49.75	153970	38.93
Totals	25618207	100.00	395515	100.00

Chromatogram for sulfoximine: (*R*)-2m

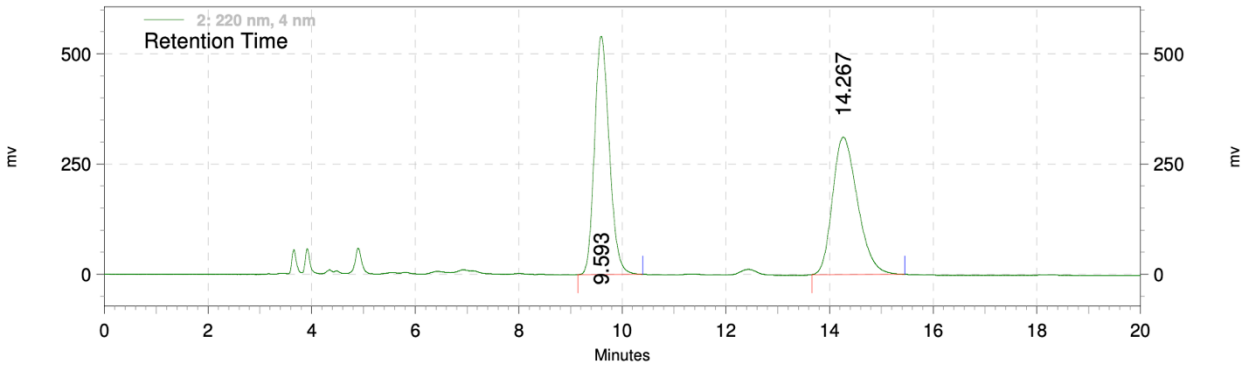


Retention Time	Area	Area %	Height	Height %
23.827	10846795	98.63	206903	98.87
30.987	151036	1.37	2366	1.13
Totals	10997831	100.00	209269	100.00



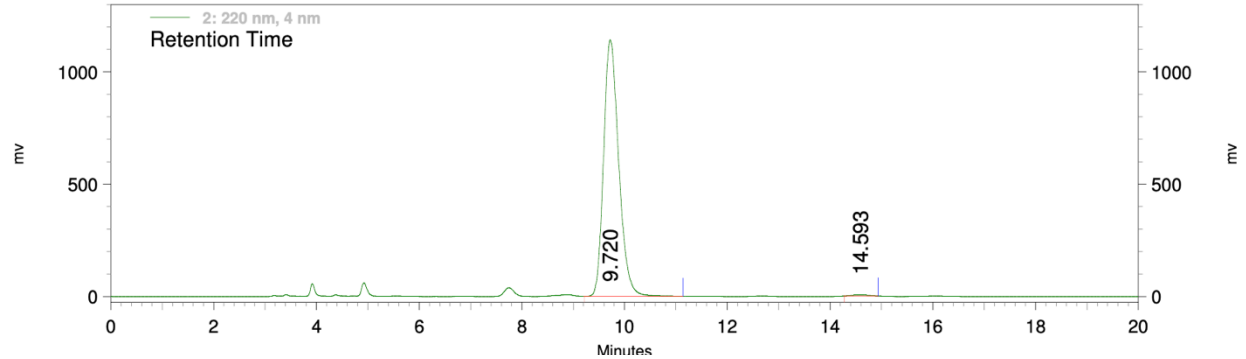
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2n

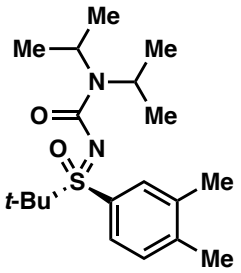


Retention Time	Area	Area %	Height	Height %
9.593	10729675	50.60	540421	63.42
14.267	10476809	49.40	311706	36.58
Totals	21206484	100.00	852127	100.00

Chromatogram for sulfoximine: (*R*)-2n

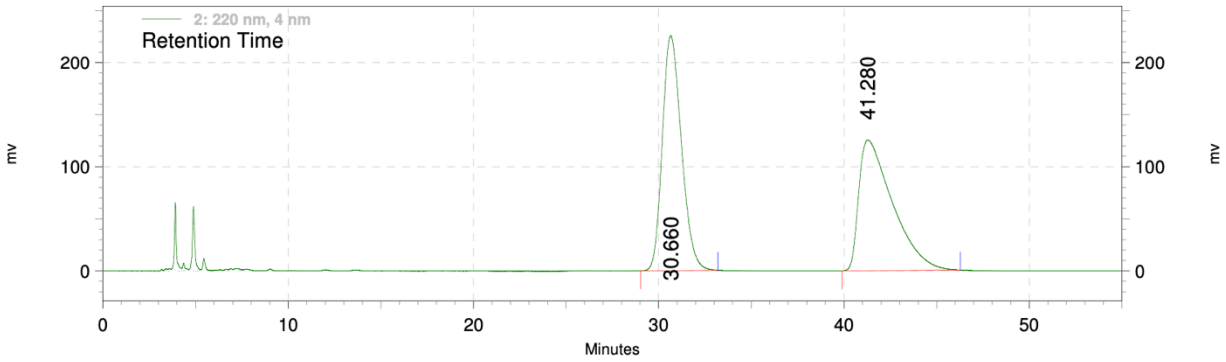


Retention Time	Area	Area %	Height	Height %
9.720	23355532	99.53	1141430	99.59
14.593	109182	0.47	4666	0.41
Totals	23464714	100.00	1146096	100.00



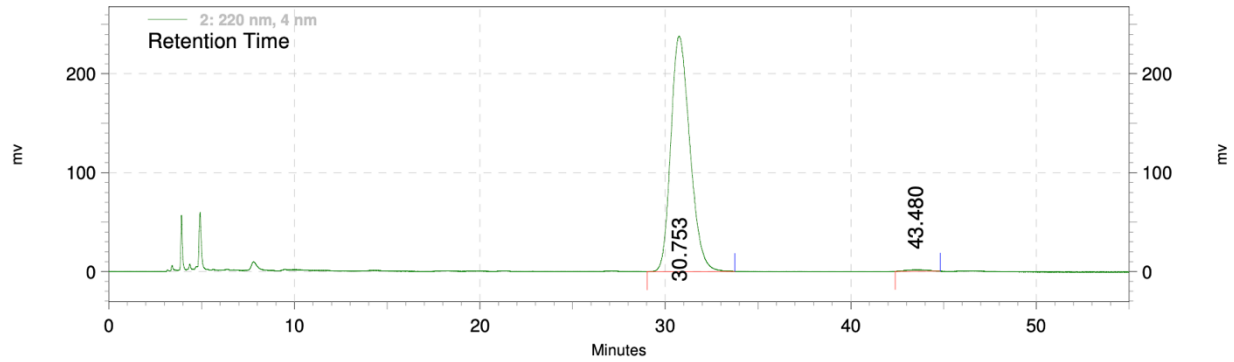
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2o

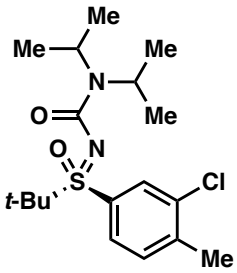


Retention Time	Area	Area %	Height	Height %
30.660	16161082	50.41	225802	64.26
41.280	15895738	49.59	125596	35.74
Totals	32056820	100.00	351398	100.00

Chromatogram for sulfoximine: (*R*)-2o

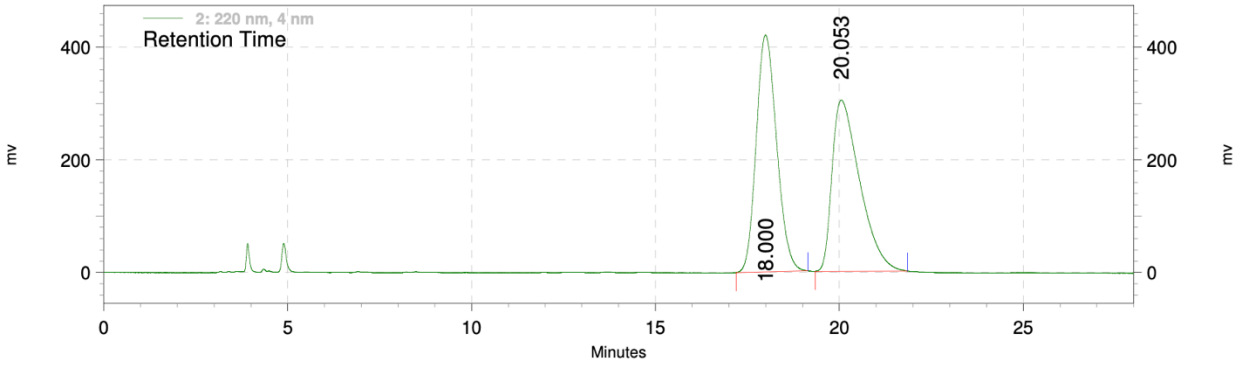


Retention Time	Area	Area %	Height	Height %
30.753	17015644	99.29	238565	99.36
43.480	121523	0.71	1527	0.64
Totals	17137167	100.00	240092	100.00



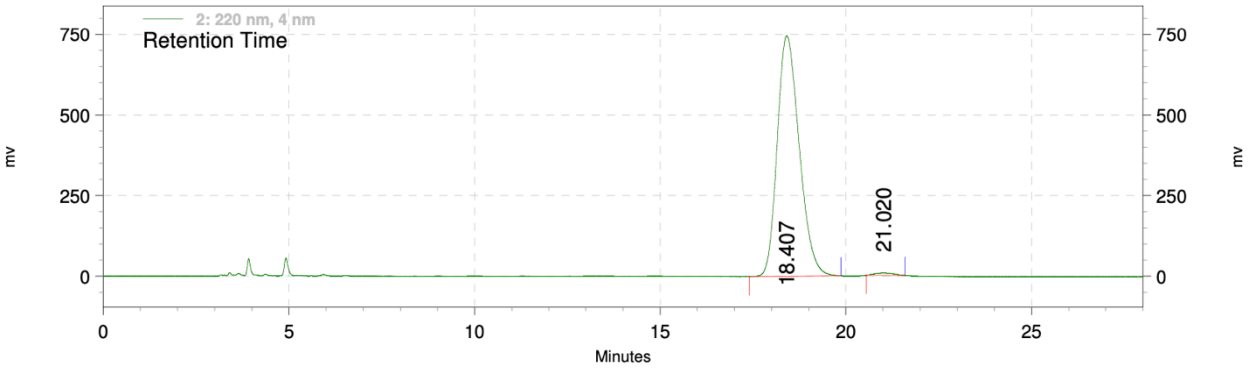
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2p

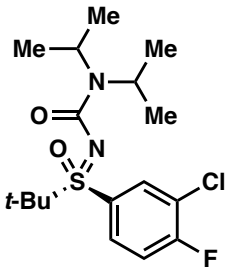


Retention Time	Area	Area %	Height	Height %
18.000	16260584	50.62	421071	58.07
20.053	15861123	49.38	304005	41.93
Totals	32121707	100.00	725076	100.00

Chromatogram for sulfoximine: (*R*)-2p

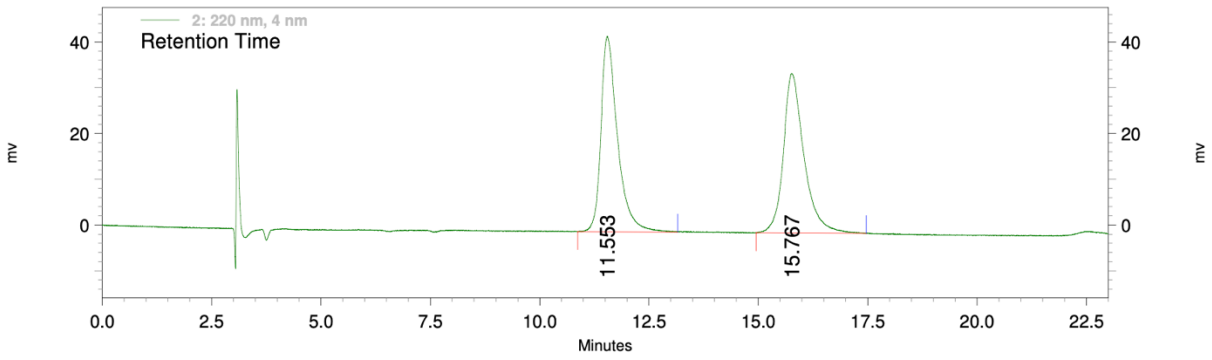


Retention Time	Area	Area %	Height	Height %
18.407	30741382	99.15	746204	99.03
21.020	264760	0.85	7280	0.97
Totals	31006142	100.00	753484	100.00



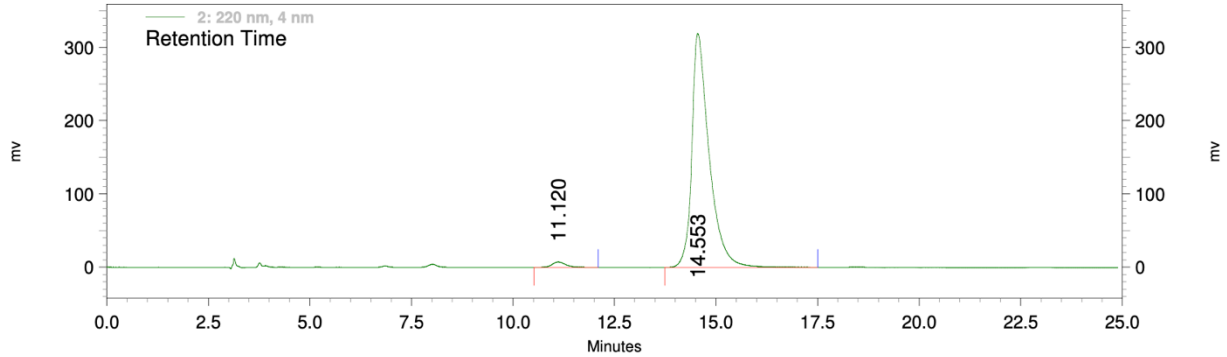
Column: Daicel Chiralpak IA; **Solvent:** *n*-hexane/IPA (95:05); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2q

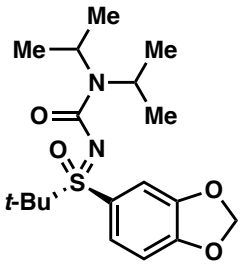


Retention Time	Area	Area %	Height	Height %
11.553	1127966	49.63	42757	55.07
15.767	1144810	50.37	34884	44.93
Totals	2272776	100.00	77641	100.00

Chromatogram for sulfoximine: (*R*)-2q

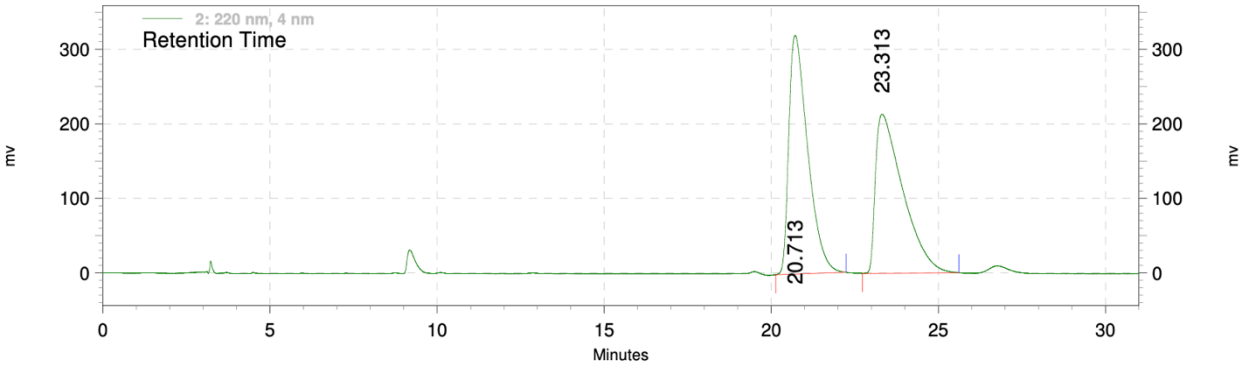


Retention Time	Area	Area %	Height	Height %
11.120	187862	1.94	7530	2.30
14.553	9485452	98.06	319510	97.70
Totals	9673314	100.00	327040	100.00



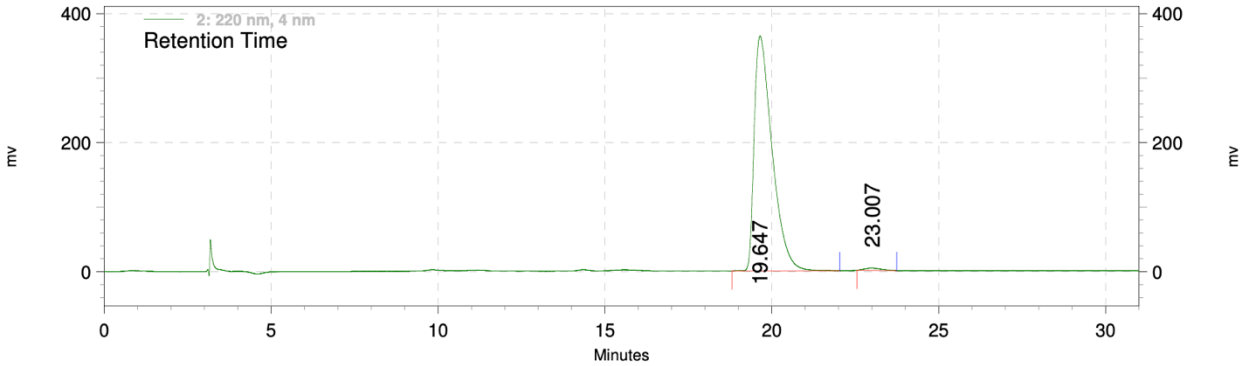
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (95:05); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2r

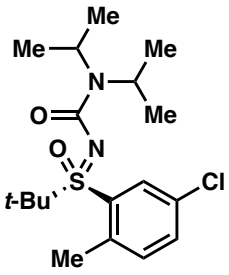


Retention Time	Area	Area %	Height	Height %
20.713	12573536	50.90	320350	60.02
23.313	12129290	49.10	213430	39.98
Totals	24702826	100.00	533780	100.00

Chromatogram for sulfoximine: (*R*)-2r

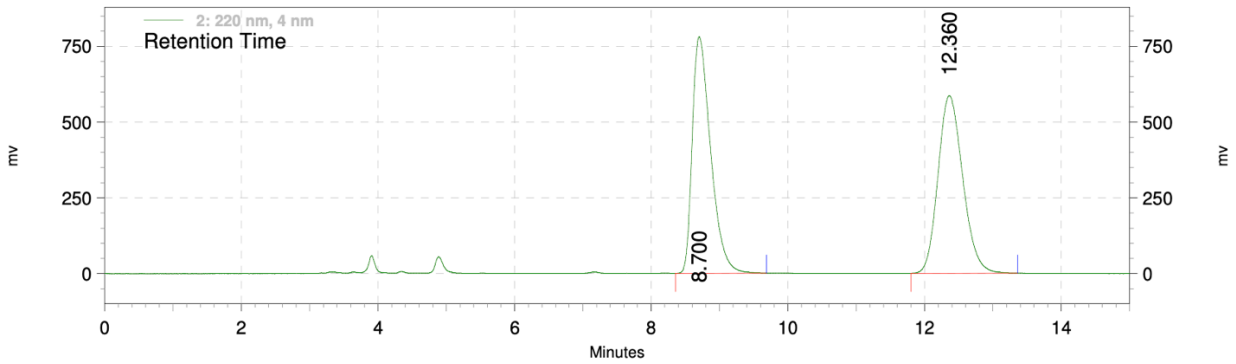


Retention Time	Area	Area %	Height	Height %
19.647	13531013	99.14	363715	99.06
23.007	117050	0.86	3450	0.94
Totals	13648063	100.00	367165	100.00



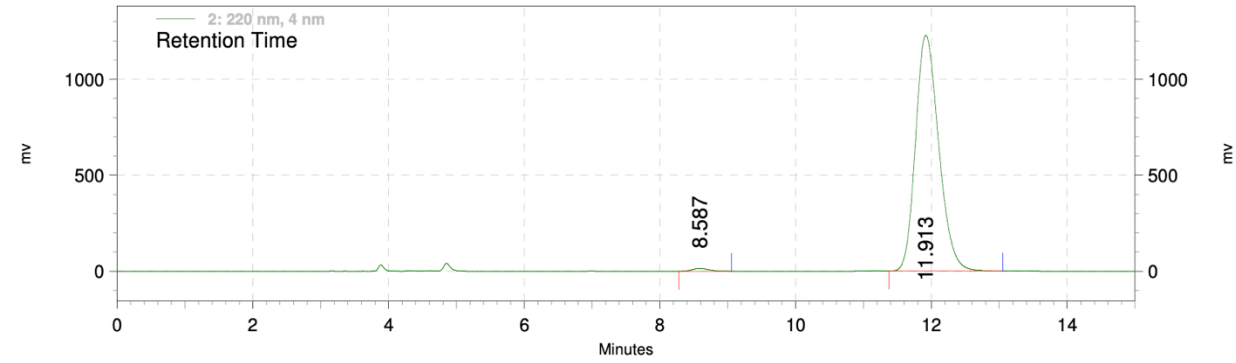
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2s

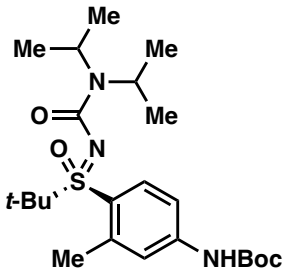


Retention Time	Area	Area %	Height	Height %
8.700	14592616	49.71	780940	57.13
12.360	14761527	50.29	586106	42.87
Totals	29354143	100.00	1367046	100.00

Chromatogram for sulfoximine: (*R*)-2s

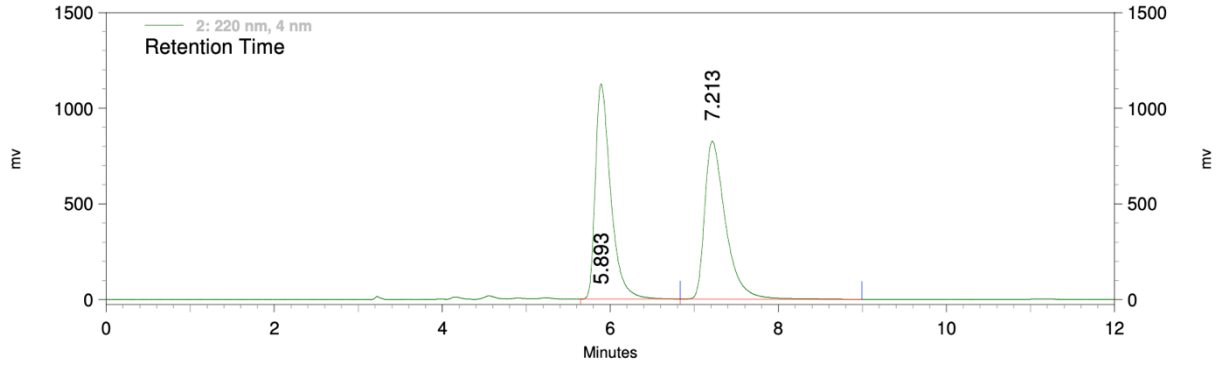


Retention Time	Area	Area %	Height	Height %
8.587	240682	0.82	14159	1.14
11.913	29157195	99.18	1227073	98.86
Totals	29397877	100.00	1241232	100.00



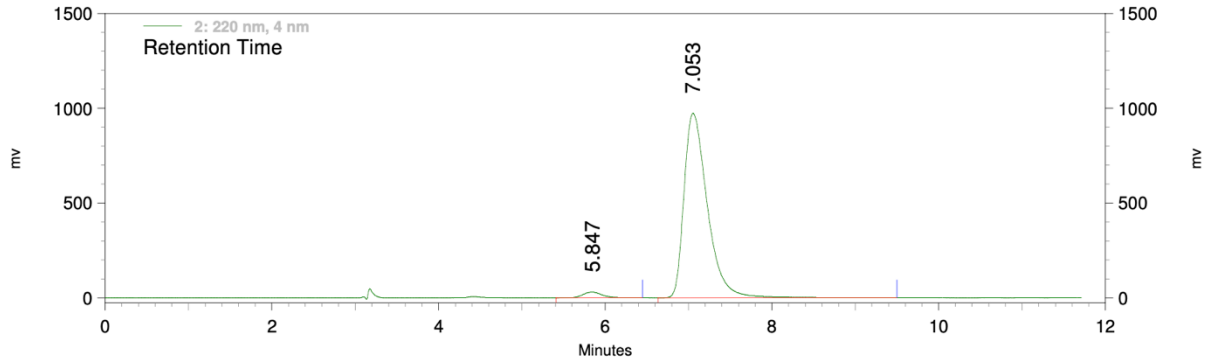
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (95:05); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2t

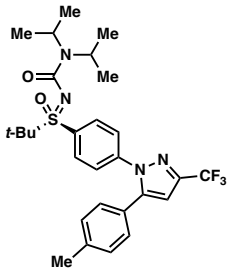


Retention Time	Area	Area %	Height	Height %
5.893	14297311	50.09	1122887	57.67
7.213	14245628	49.91	824236	42.33
Totals	28542939	100.00	1947123	100.00

Chromatogram for sulfoximine: (*R*)-2t

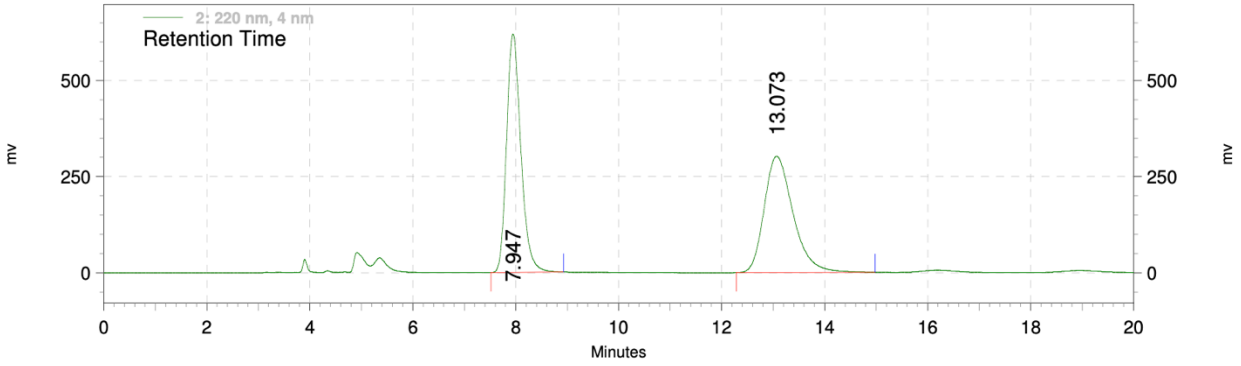


Retention Time	Area	Area %	Height	Height %
5.847	482316	2.48	30162	3.01
7.053	18929852	97.52	972768	96.99
Totals	19412168	100.00	1002930	100.00



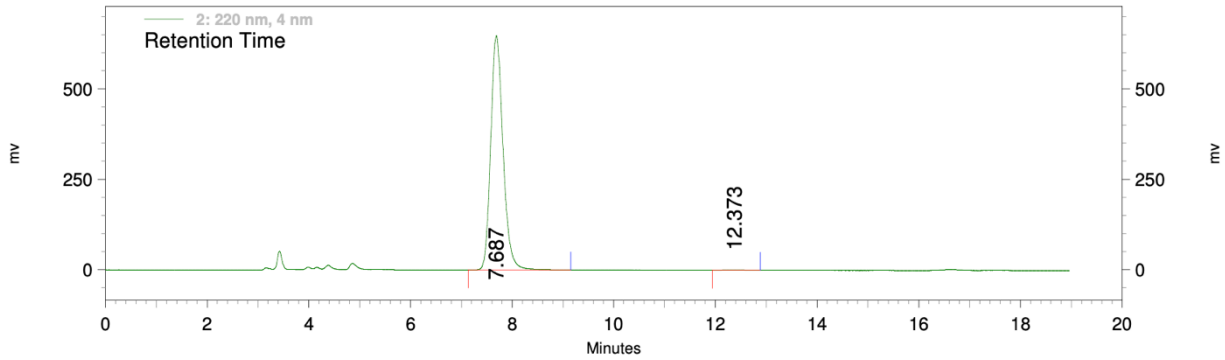
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-2u

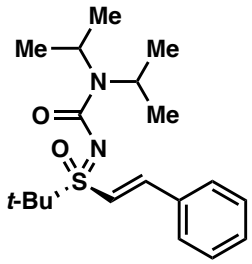


Retention Time	Area	Area %	Height	Height %
7.947	11960150	50.35	619813	67.20
13.073	11792391	49.65	302577	32.80
Totals	23752541	100.00	922390	100.00

Chromatogram for sulfoximine: (*R*)-2u

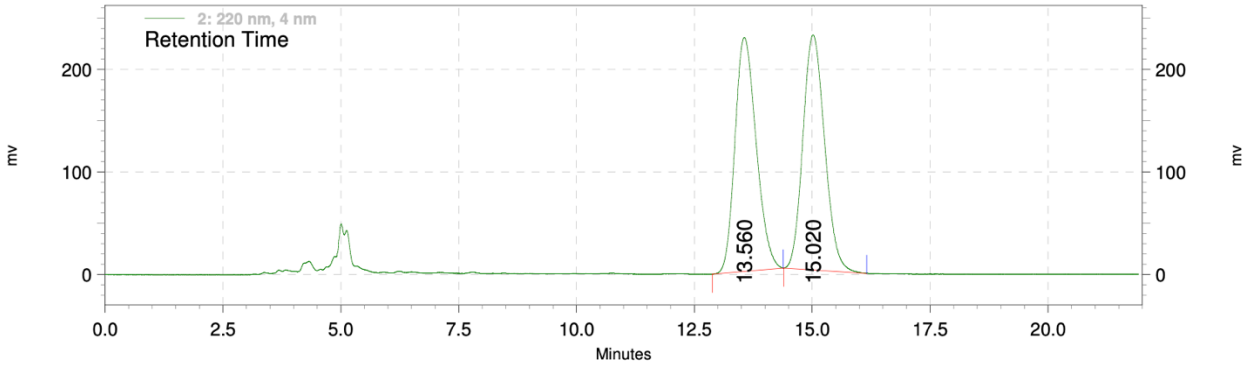


Retention Time	Area	Area %	Height	Height %
7.687	10930868	99.76	648328	99.86
12.373	26162	0.24	901	0.14
Totals	10957030	100.00	649229	100.00



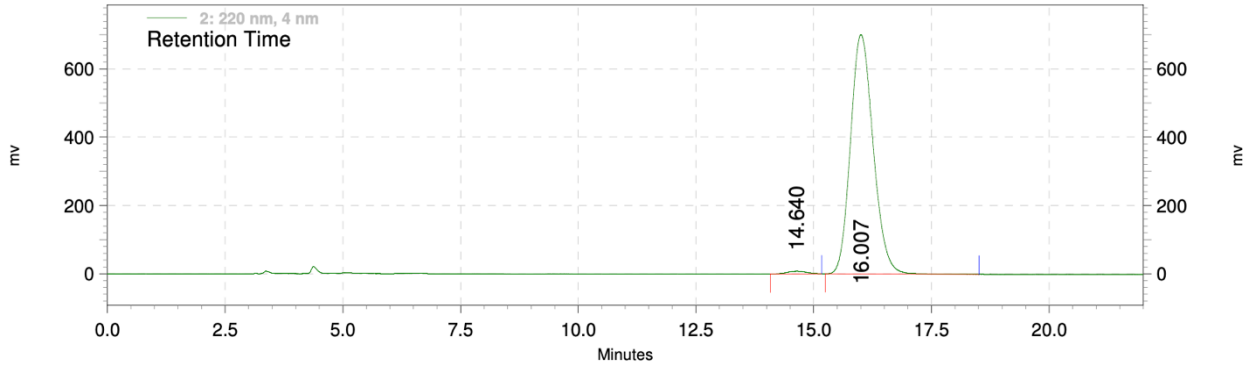
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac, E*)-2w

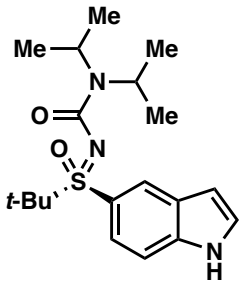


Retention Time	Area	Area %	Height	Height %
13.560	7138053	49.32	227951	49.89
15.020	7333937	50.68	228972	50.11
Totals	14471990	100.00	456923	100.00

Chromatogram for sulfoximine: (*S, E*)-2w

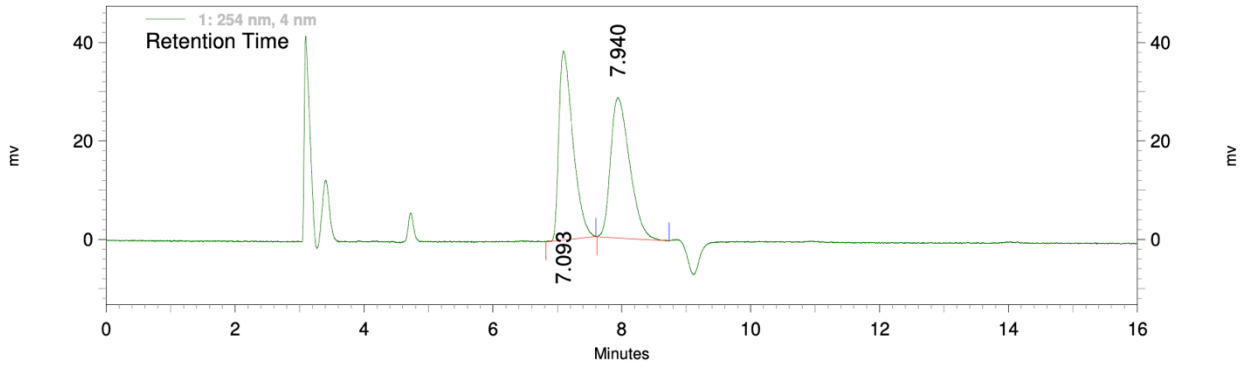


Retention Time	Area	Area %	Height	Height %
14.640	236281	1.00	7824	1.10
16.007	23455446	99.00	701049	98.90
Totals	23691727	100.00	708873	100.00



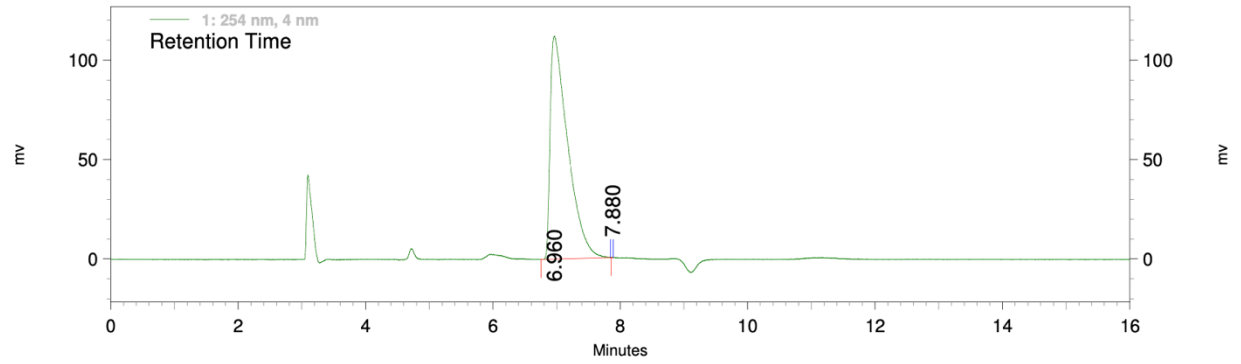
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (90:10); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3a

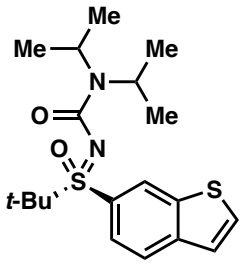


Retention Time	Area	Area %	Height	Height %
7.093	590055	50.09	38358	57.35
7.940	587885	49.91	28527	42.65
Totals	1177940	100.00	66885	100.00

Chromatogram for sulfoximine: (*R*)-3a

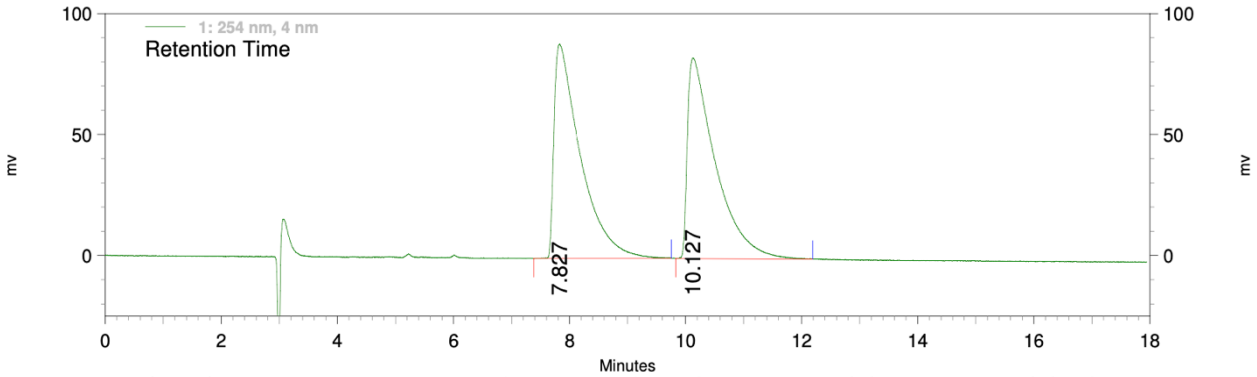


Retention Time	Area	Area %	Height	Height %
6.960	2167328	99.99	112218	99.87
7.880	132	0.01	144	0.13
Totals	2167460	100.00	112362	100.00



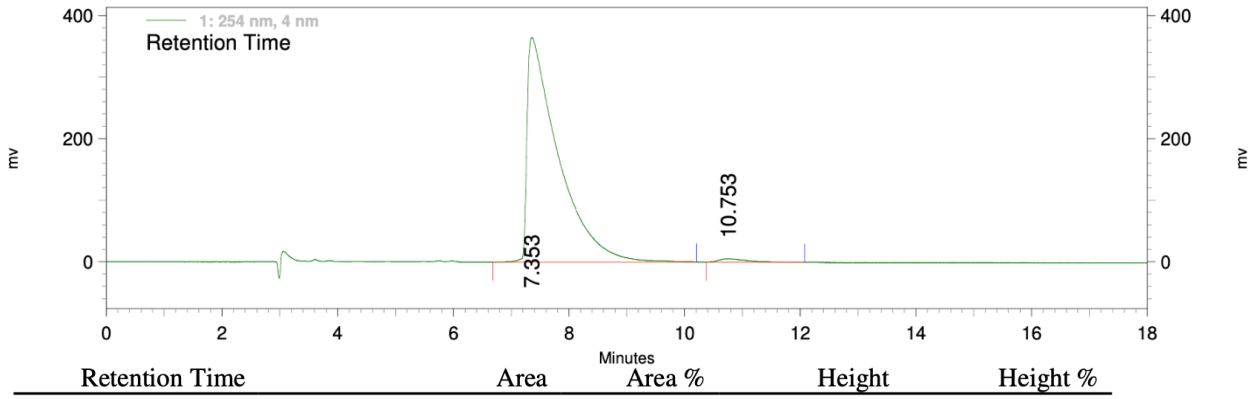
Column: Daicel Chiralpak IA; **Solvent:** *n*-hexane/DCM (50:50); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3b

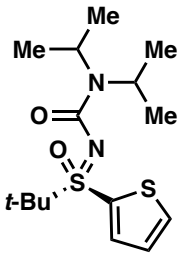


Retention Time	Area	Area %	Height	Height %
7.827	2808743	50.38	88659	51.69
10.127	2766316	49.62	82859	48.31
Totals	5575059	100.00	171518	100.00

Chromatogram for sulfoximine: (*R*)-3b

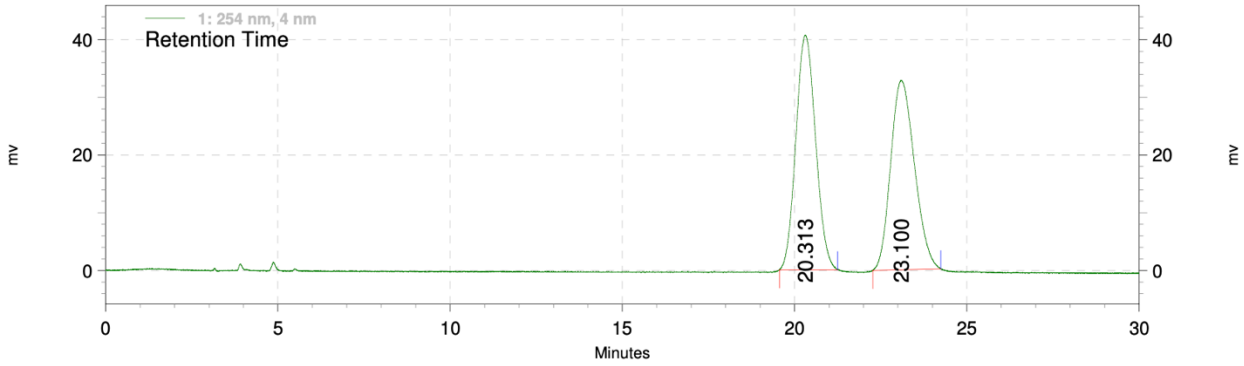


Retention Time	Area	Area %	Height	Height %
7.353	13710594	98.59	365215	98.49
10.753	196639	1.41	5594	1.51
Totals	13907233	100.00	370809	100.00



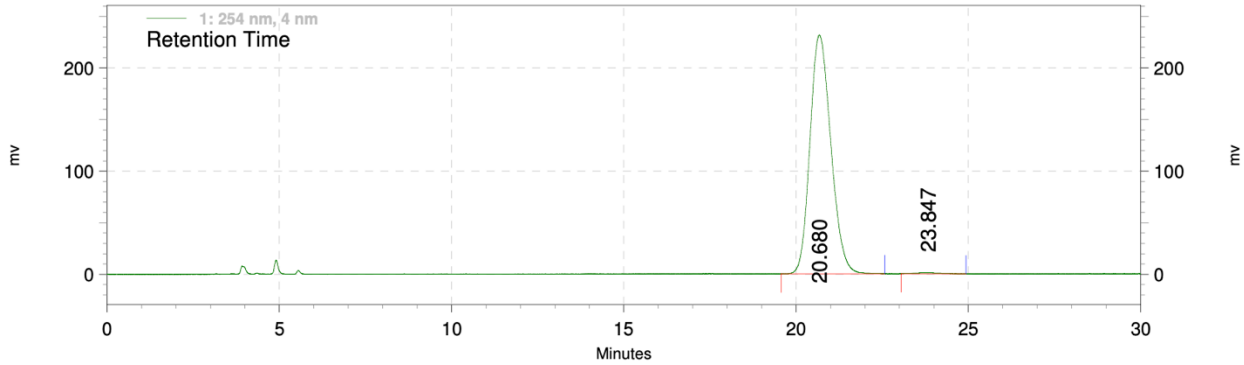
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3c

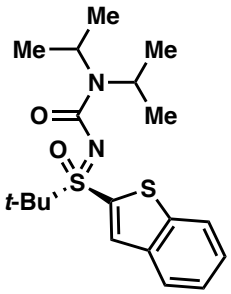


Retention Time	Area	Area %	Height	Height %
20.313	1616656	50.63	40705	55.36
23.100	1576432	49.37	32824	44.64
Totals	3193088	100.00	73529	100.00

Chromatogram for sulfoximine: (*R*)-3c

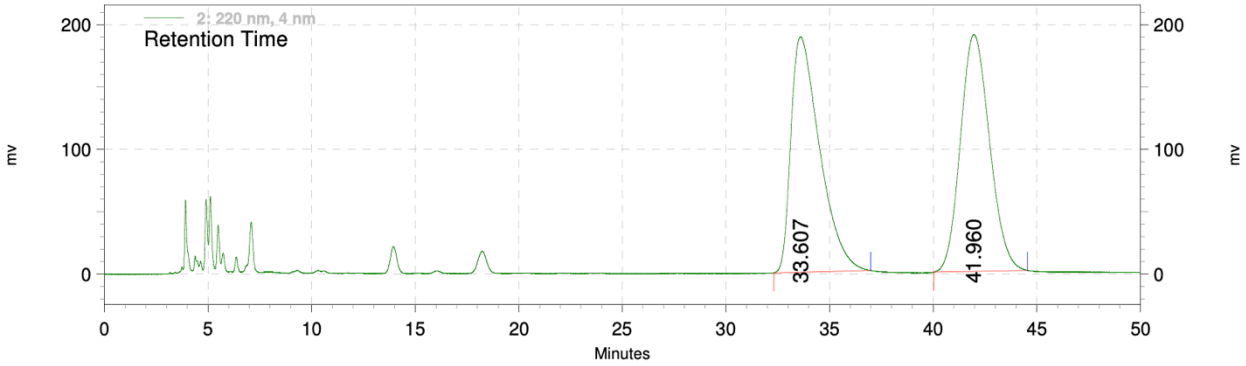


Retention Time	Area	Area %	Height	Height %
20.680	9763478	99.53	231520	99.59
23.847	46398	0.47	955	0.41
Totals	9809876	100.00	232475	100.00



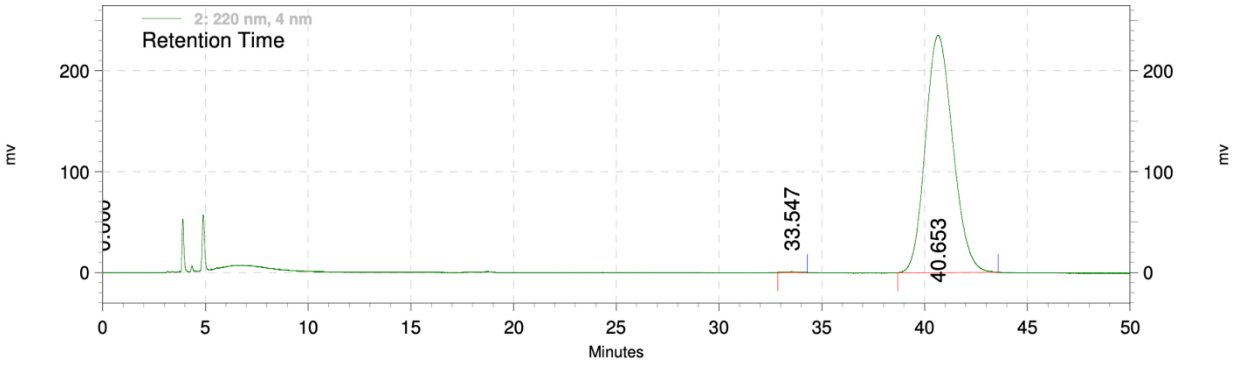
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3d

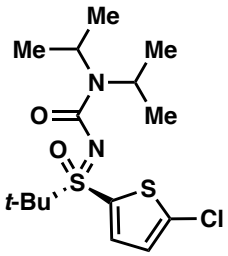


Retention Time	Area	Area %	Height	Height %
33.607	18223512	49.55	188859	49.84
41.960	18552831	50.45	190053	50.16
Totals	36776343	100.00	378912	100.00

Chromatogram for sulfoximine: (*R*)-3d

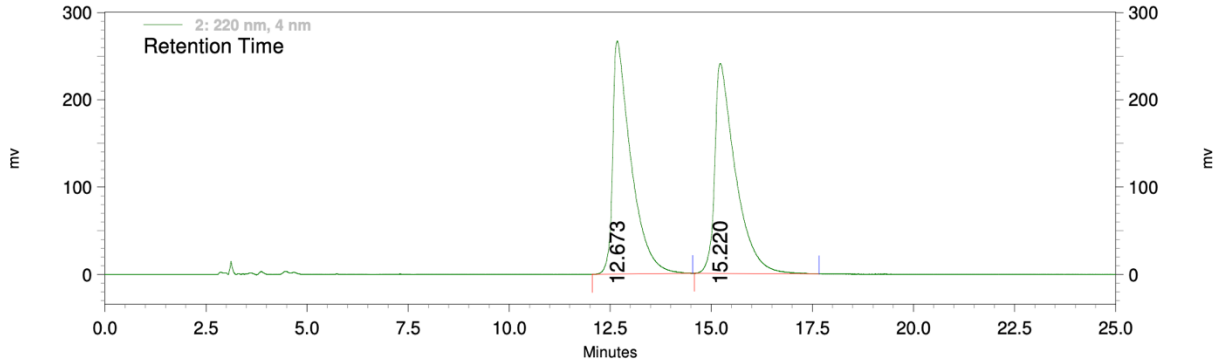


Retention Time	Area	Area %	Height	Height %
33.547	35438	0.16	676	0.29
40.653	21845505	99.84	235521	99.71
Totals	21880943	100.00	236197	100.00



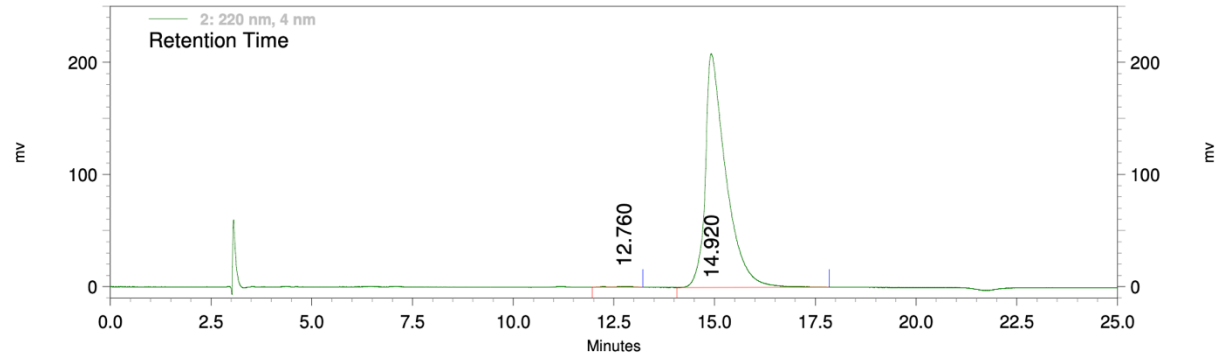
Column: Daicel Chiralpak IA; **Solvent:** *n*-hexane/IPA (95:05); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3e

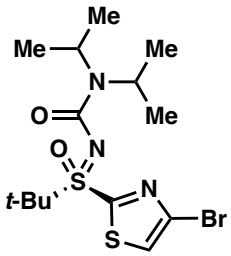


Retention Time	Area	Area %	Height	Height %
12.673	8451507	49.62	266879	52.58
15.220	8579596	50.38	240687	47.42
Totals	17031103	100.00	507566	100.00

Chromatogram for sulfoximine: (*R*)-3e

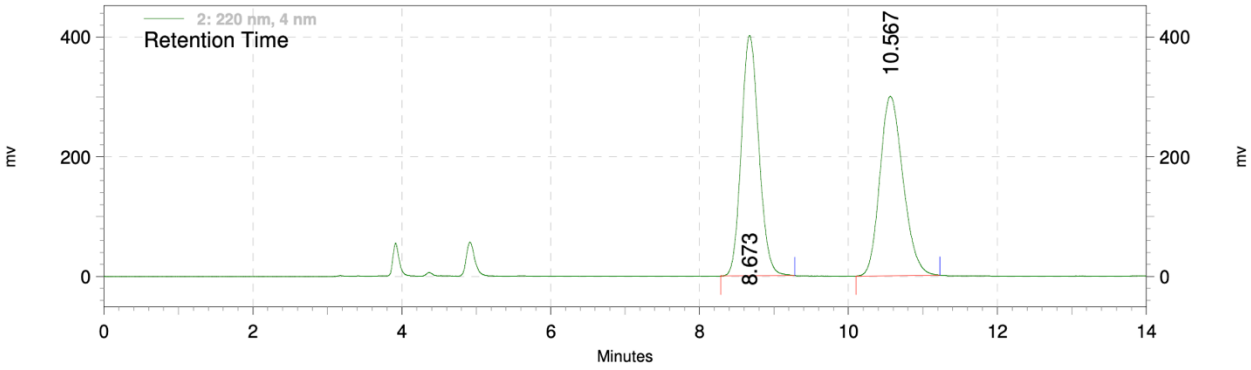


Retention Time	Area	Area %	Height	Height %
12.760	29254	0.39	797	0.38
14.920	7439335	99.61	208227	99.62
Totals	7468589	100.00	209024	100.00



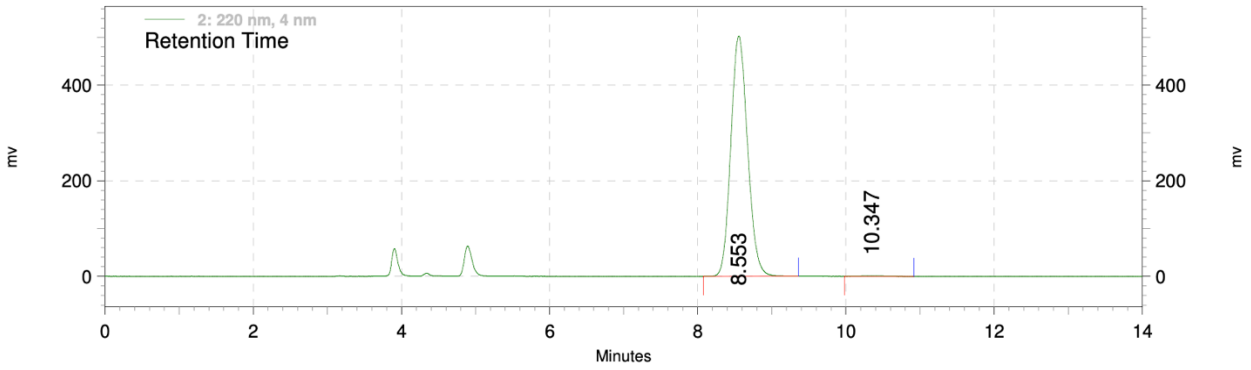
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3f

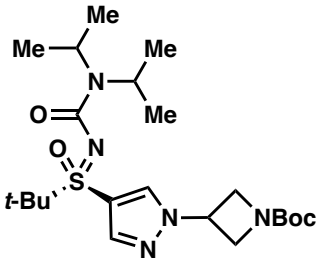


Retention Time	Area	Area %	Height	Height %
8.673	6556540	50.28	401759	57.27
10.567	6484514	49.72	299717	42.73
Totals	13041054	100.00	701476	100.00

Chromatogram for sulfoximine: (*R*)-3f

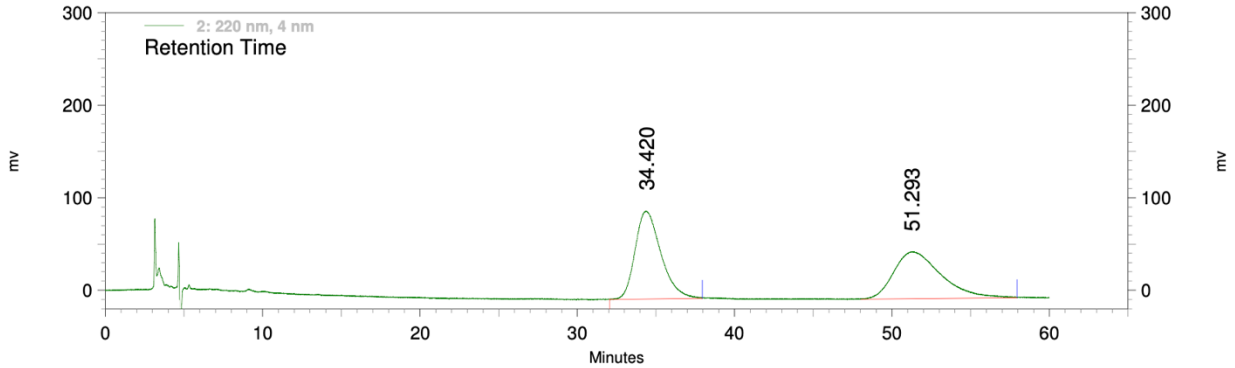


Retention Time	Area	Area %	Height	Height %
8.553	7898638	99.62	502837	99.73
10.347	30293	0.38	1365	0.27
Totals	7928931	100.00	504202	100.00



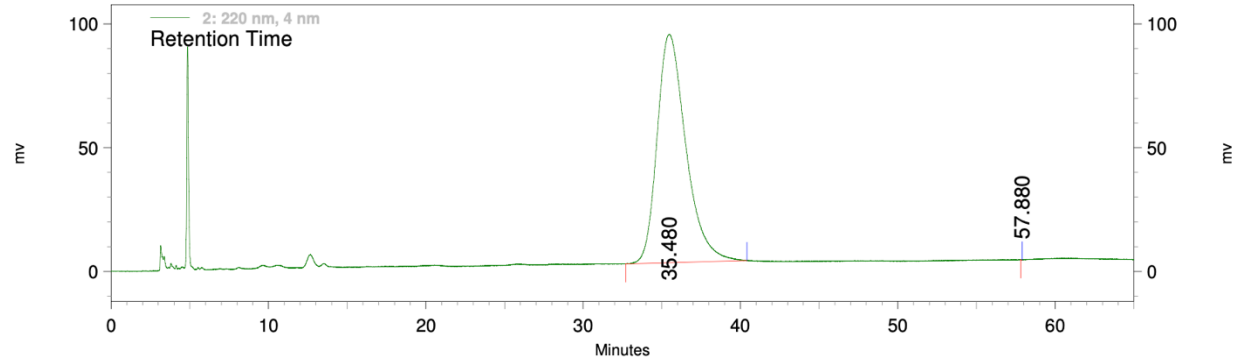
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3g

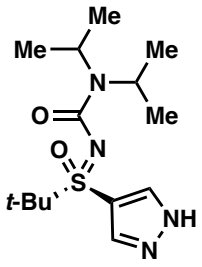


Retention Time	Area	Area %	Height	Height %
34.420	10867674	50.69	95291	65.17
51.293	10570699	49.31	50929	34.83
Totals	21438373	100.00	146220	100.00

Chromatogram for sulfoximine: (*R*)-3g

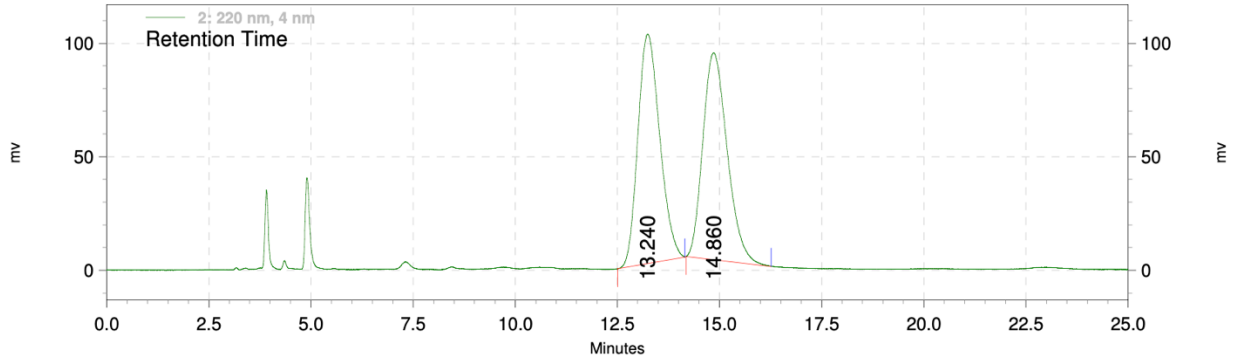


Retention Time	Area	Area %	Height	Height %
35.480	11739959	100.00	92381	99.80
57.880	488	0.00	185	0.20
Totals	11740447	100.00	92566	100.00



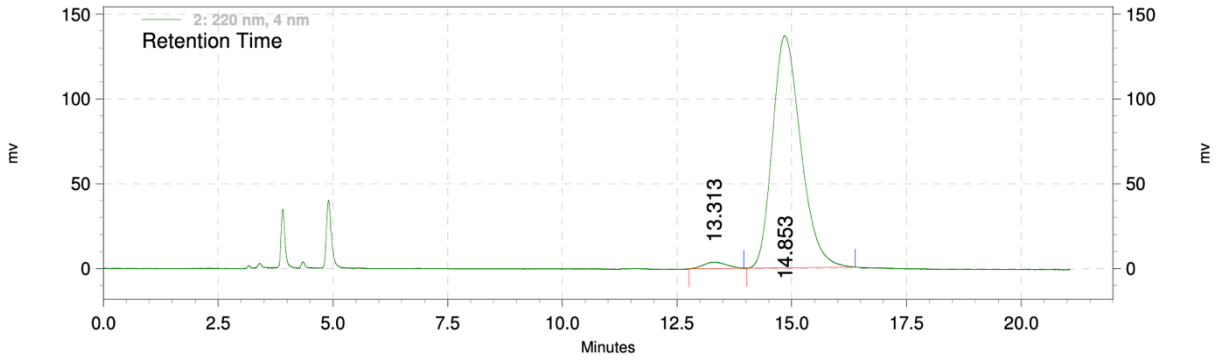
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3h

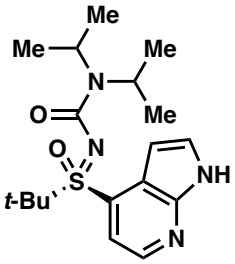


Retention Time	Area	Area %	Height	Height %
13.240	3751069	49.84	101118	52.60
14.860	3775646	50.16	91138	47.40
Totals	7526715	100.00	192256	100.00

Chromatogram for sulfoximine: (*R*)-3h

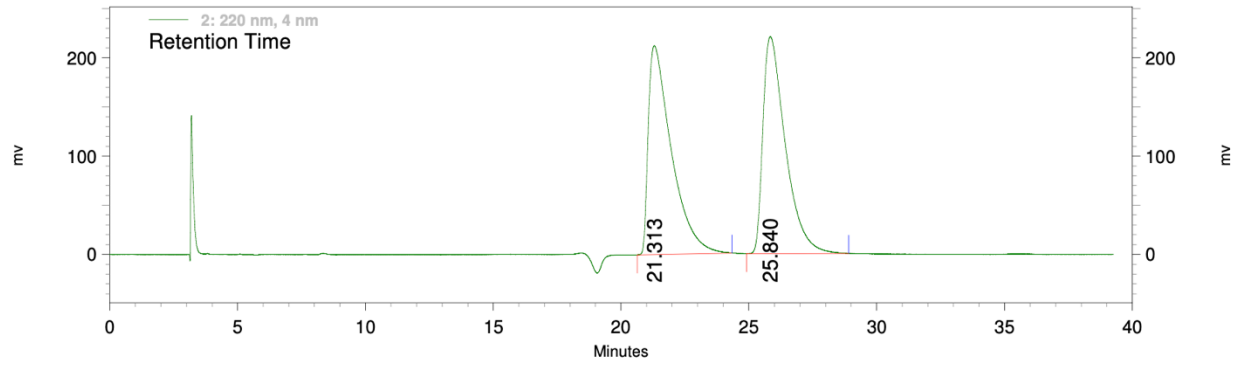


Retention Time	Area	Area %	Height	Height %
13.313	132251	2.20	3816	2.71
14.853	5880746	97.80	136821	97.29
Totals	6012997	100.00	140637	100.00



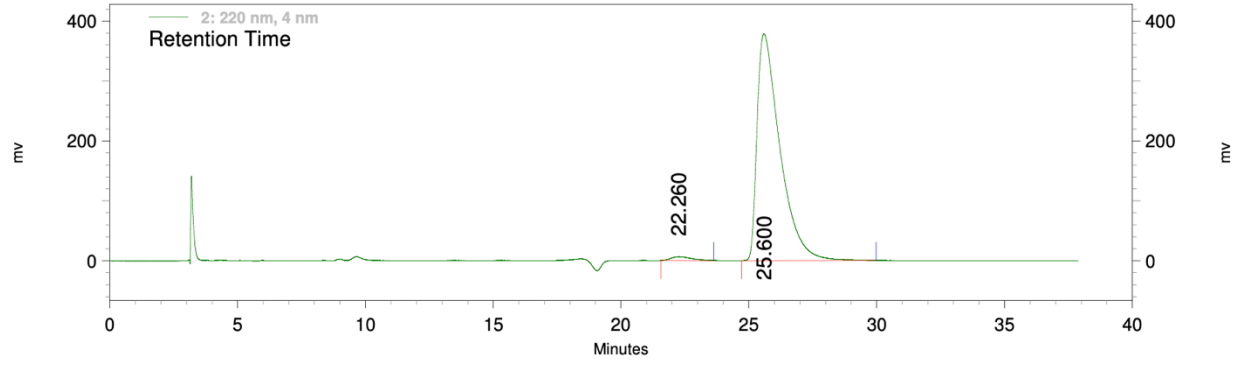
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (95:05); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-3i

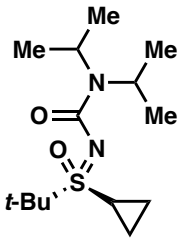


Retention Time	Area	Area %	Height	Height %
21.313	13334158	49.78	212434	49.01
25.840	13451042	50.22	221046	50.99
Totals	26785200	100.00	433480	100.00

Chromatogram for sulfoximine: (*R*)-3i

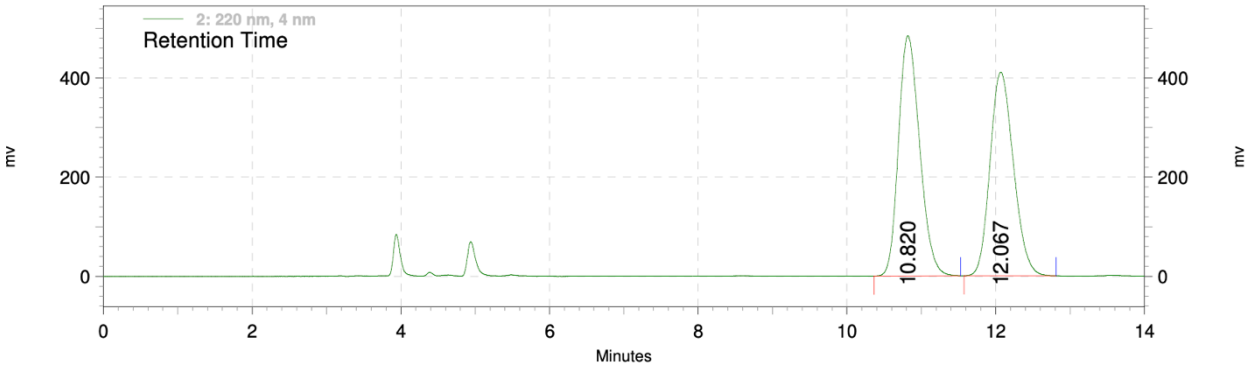


Retention Time	Area	Area %	Height	Height %
22.260	347220	1.46	6253	1.62
25.600	23485576	98.54	378749	98.38
Totals	23832796	100.00	385002	100.00



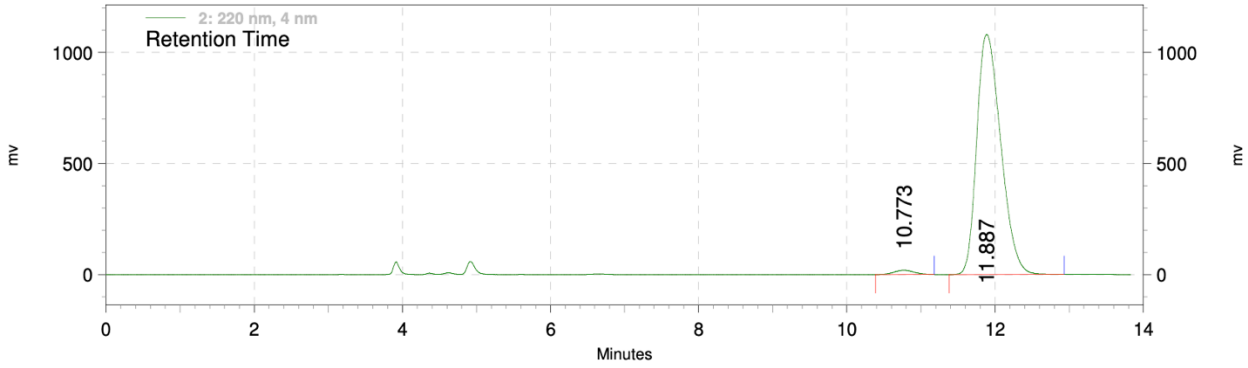
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-4a



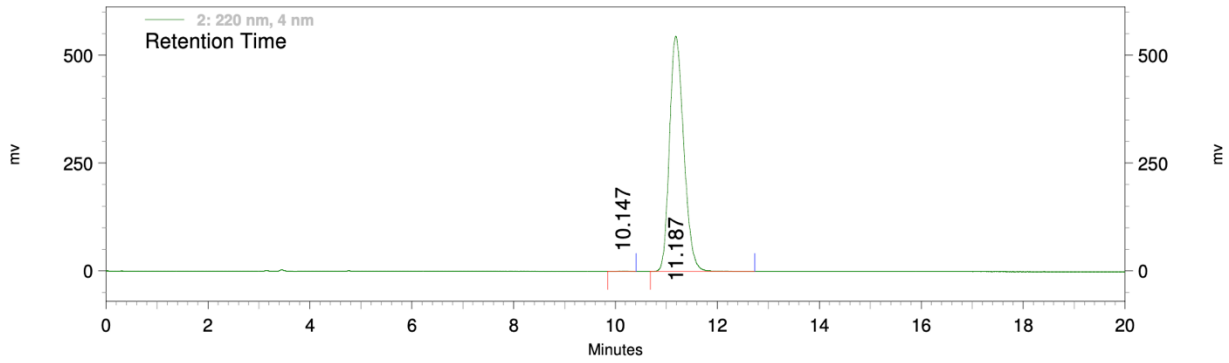
Retention Time	Area	Area %	Height	Height %
10.820	9577115	51.57	484524	54.13
12.067	8994233	48.43	410659	45.87
Totals	18571348	100.00	895183	100.00

Chromatogram for sulfoximine: (*S*)-4a



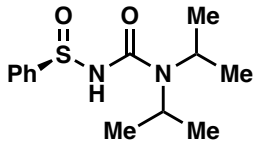
Retention Time	Area	Area %	Height	Height %
10.773	365838	1.48	19535	1.78
11.887	24321589	98.52	1080504	98.22
Totals	24687427	100.00	1100039	100.00

Chromatogram for sulfoximine: (*S*)-4a after single recrystallization



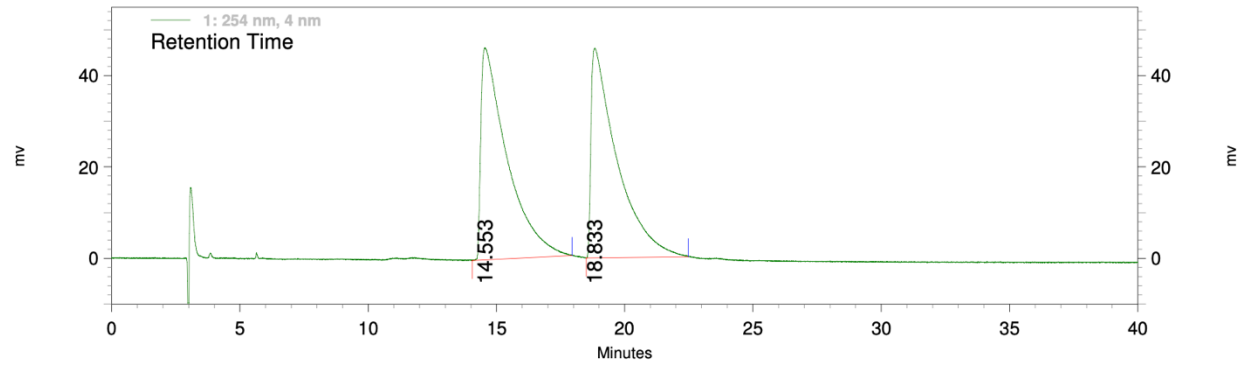
Retention Time	Area	Area %	Height	Height %
10.147	6230	0.06	399	0.07
11.187	10605693	99.94	545456	99.93

Totals	10611923	100.00	545855	100.00



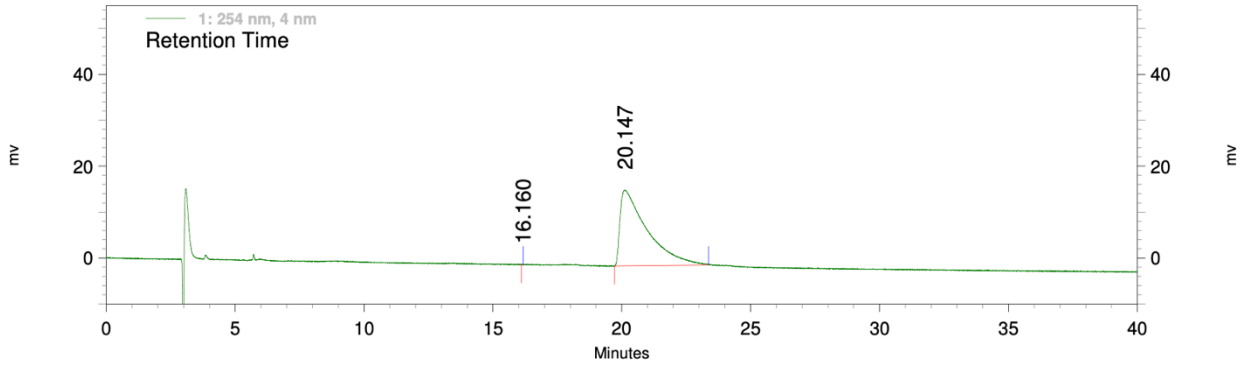
Column: Daicel Chiralpak IA; **Solvent:** *n*-hexane/DCM (50:50); **flowrate:** 1 mL/min

Chromatogram for sulfinamide: (*rac*)-phenyl sulfinyl urea (*rac*)-S5a

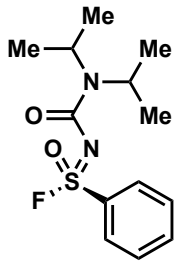


Retention Time	Area	Area %	Height	Height %
14.553	3276538	50.52	46410	50.26
18.833	3209149	49.48	45932	49.74
Totals	6485687	100.00	92342	100.00

Chromatogram for sulfinamide: (*R*)-phenyl sulfinyl urea (*R*)-S5a)

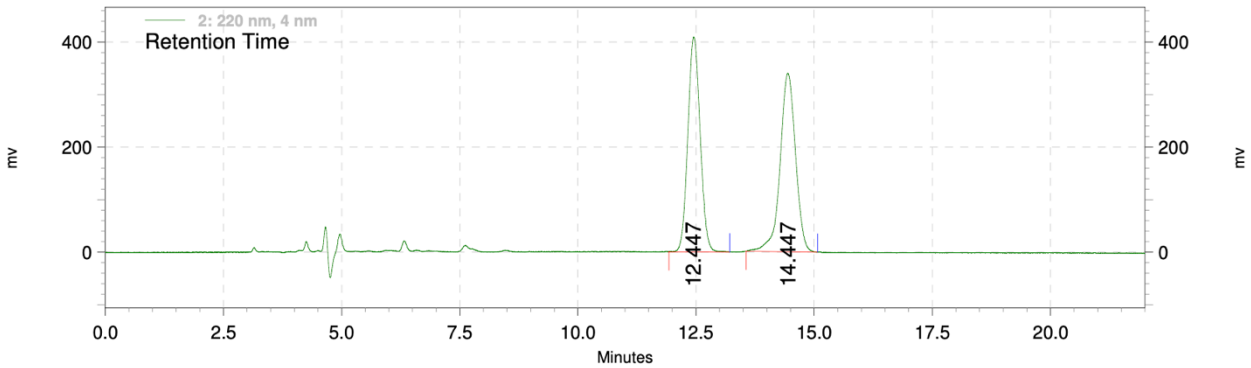


Retention Time	Area	Area %	Height	Height %
16.160	243	0.02	184	1.10
20.147	1194698	99.98	16472	98.90
Totals	1194941	100.00	16656	100.00



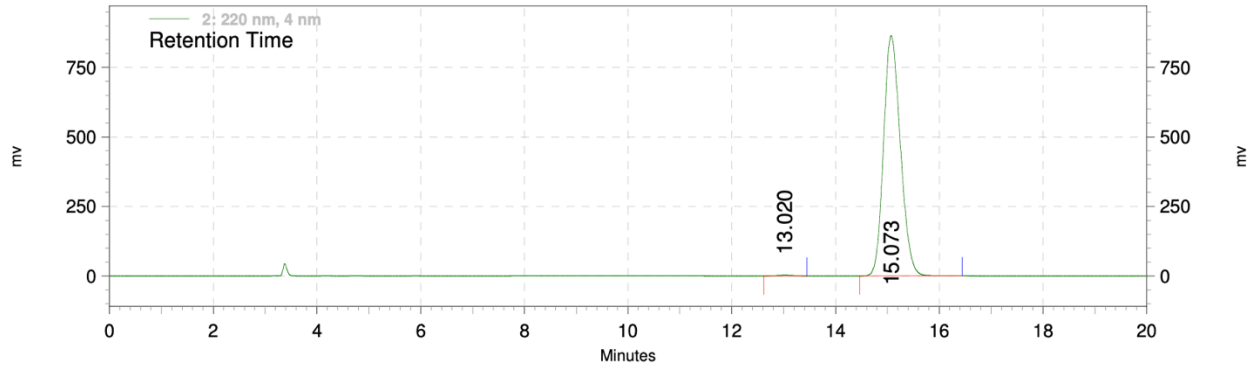
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidoyl fluoride: (*rac*)-S6a

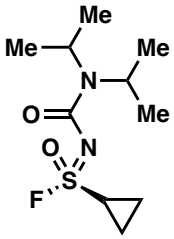


Retention Time	Area	Area %	Height	Height %
12.447	7379945	48.96	409106	54.62
14.447	7693588	51.04	339913	45.38
Totals	15073533	100.00	749019	100.00

Chromatogram for sulfonimidoyl fluoride: (*S*)-S6a

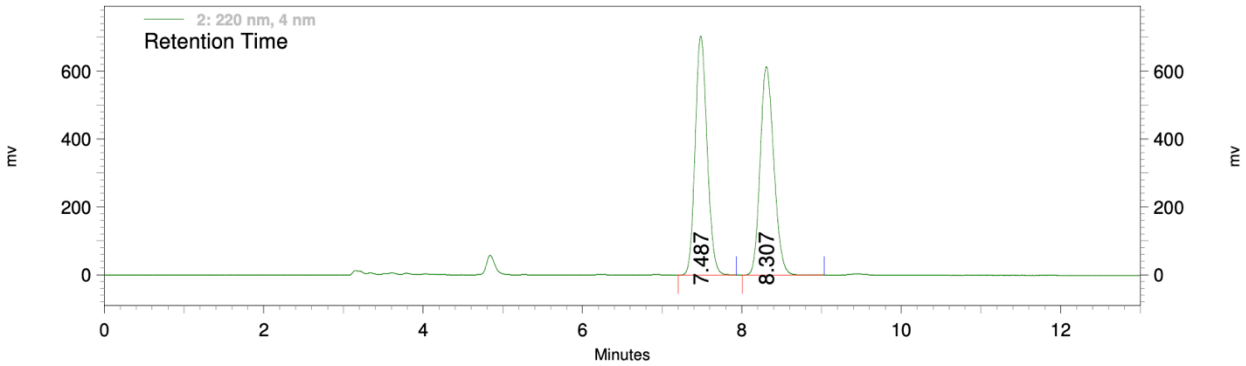


Retention Time	Area	Area %	Height	Height %
13.020	57920	0.30	2969	0.34
15.073	19475238	99.70	864434	99.66
Totals	19533158	100.00	867403	100.00



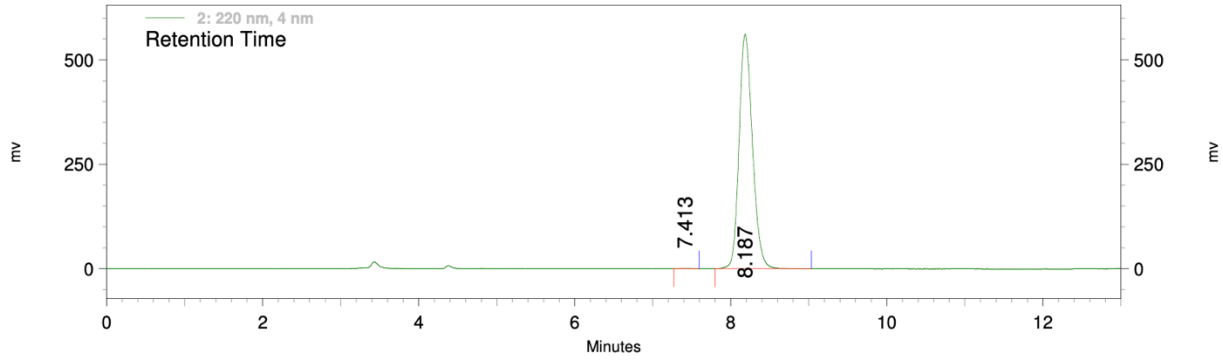
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidoyl fluoride: (*rac*)- cyclopropyl-SF

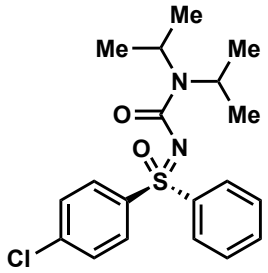


Retention Time	Area	Area %	Height	Height %
7.487	7344826	50.10	704121	53.42
8.307	7316847	49.90	613965	46.58
Totals	14661673	100.00	1318086	100.00

Chromatogram for sulfonimidoyl fluoride: (*S*)- cyclopropyl-SF

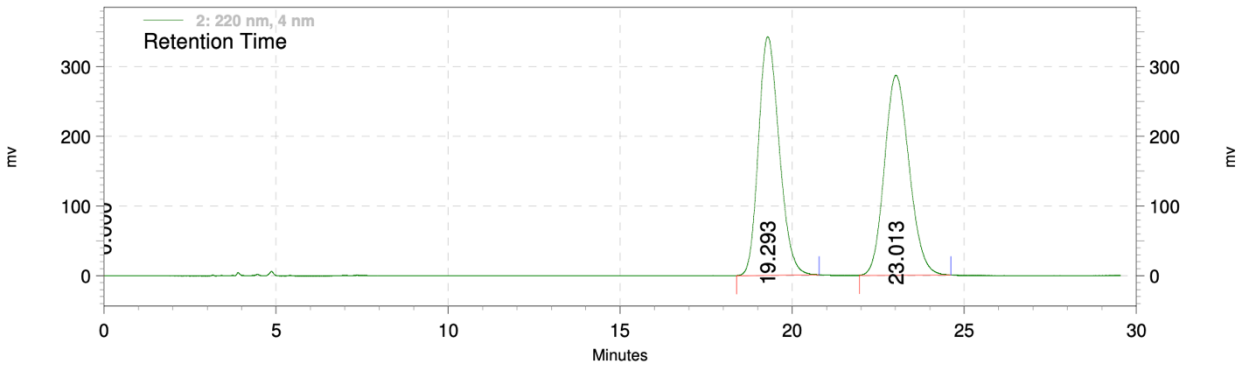


Retention Time	Area	Area %	Height	Height %
7.413	10523	0.16	1097	0.19
8.187	6712187	99.84	561816	99.81
Totals	6722710	100.00	562913	100.00



Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

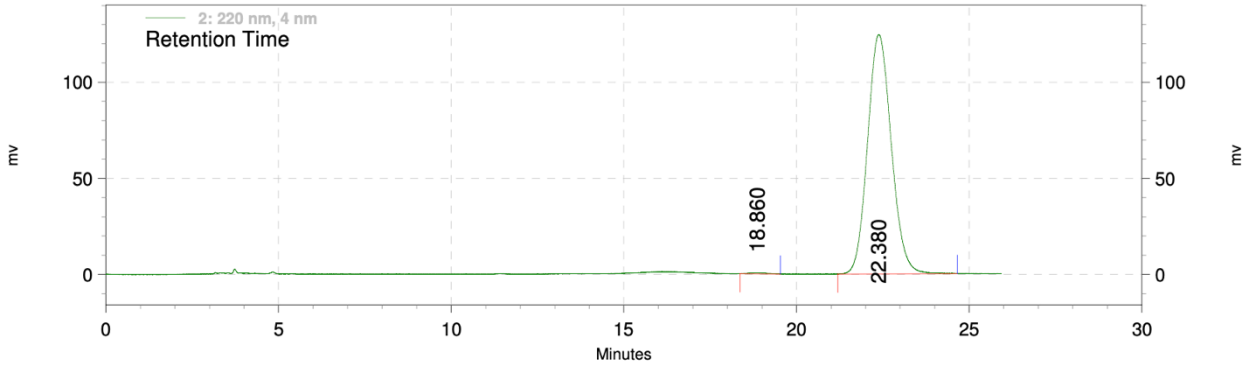
Chromatogram for sulfoximine: (*rac*)-7a



Retention Time	Area	Area %	Height	Height %
19.293	14355225	50.03	342360	54.41
23.013	14335407	49.97	286862	45.59

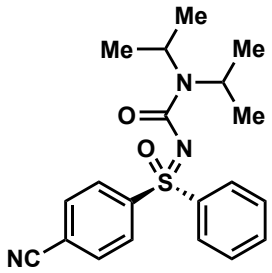
Totals				
	28690632	100.00	629222	100.00

Chromatogram for sulfoximine: (*R*)-7a



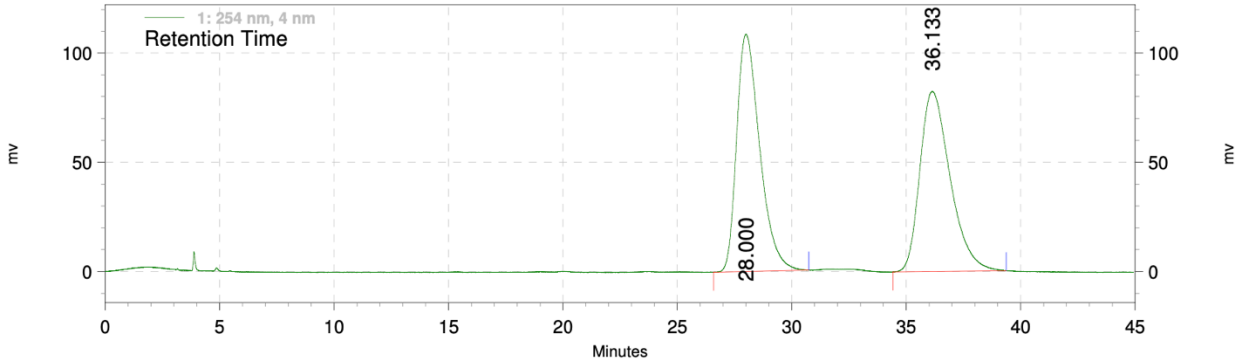
Retention Time	Area	Area %	Height	Height %
18.860	20170	0.34	538	0.43
22.380	5945664	99.66	124438	99.57

Totals				
	5965834	100.00	124976	100.00



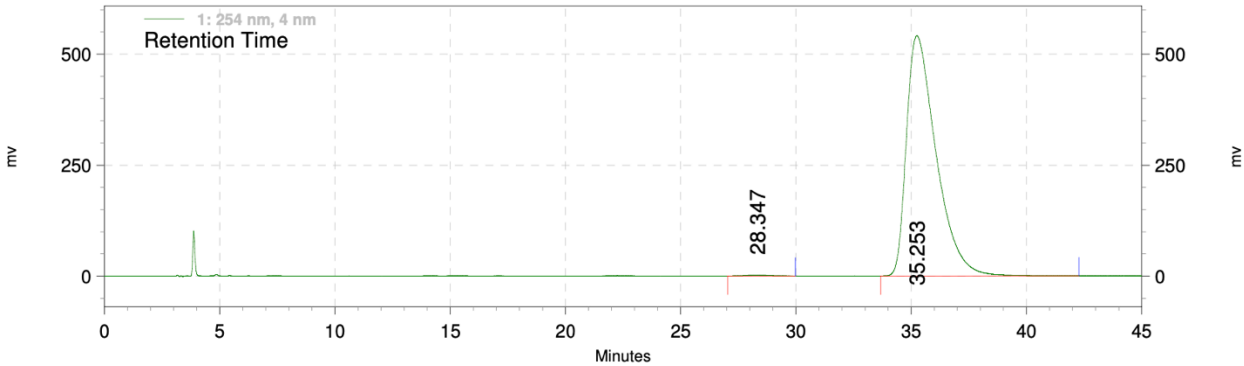
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7b

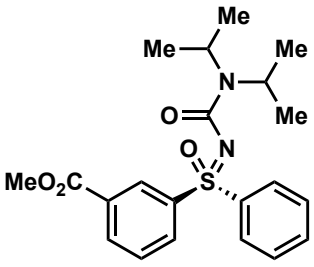


Retention Time	Area	Area %	Height	Height %
28.000	7624109	50.15	108717	56.85
36.133	7578306	49.85	82505	43.15
Totals	15202415	100.00	191222	100.00

Chromatogram for sulfoximine: (*R*)-7b

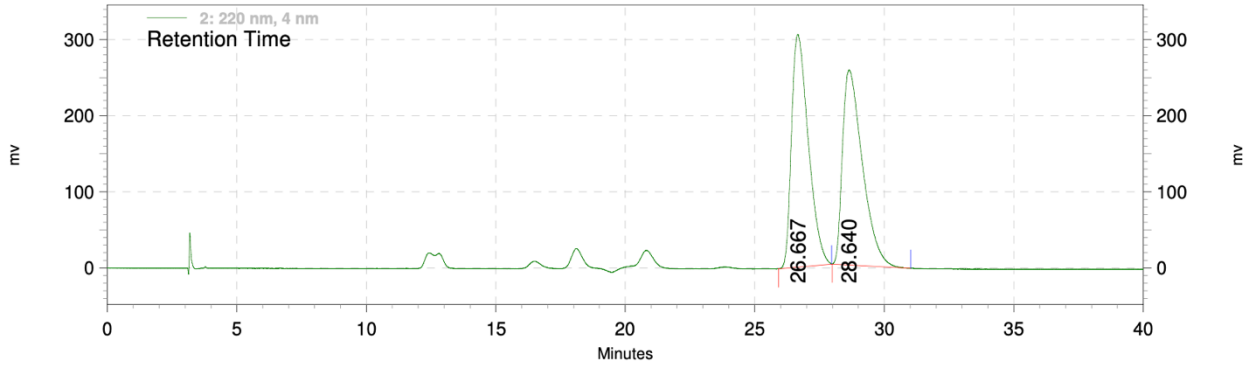


Retention Time	Area	Area %	Height	Height %
28.347	172915	0.36	2319	0.43
35.253	48407244	99.64	541447	99.57
Totals	48580159	100.00	543766	100.00



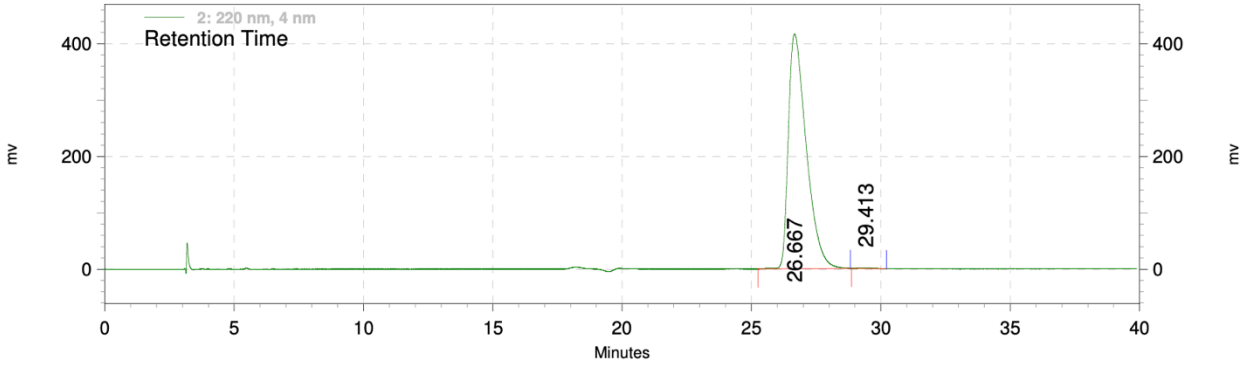
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (95:05); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7c

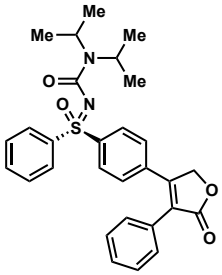


Retention Time	Area	Area %	Height	Height %
26.667	13777162	50.13	305667	54.41
28.640	13706613	49.87	256115	45.59
Totals	27483775	100.00	561782	100.00

Chromatogram for sulfoximine: (*R*)-7c

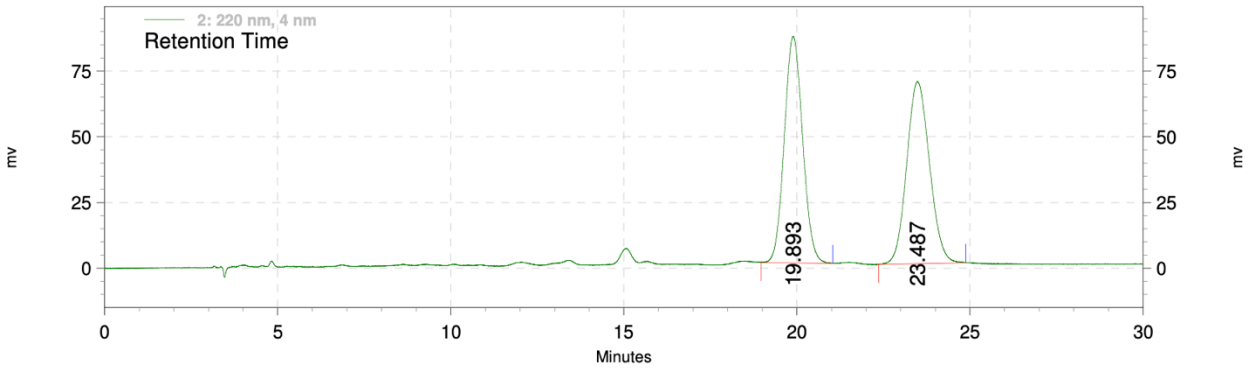


Retention Time	Area	Area %	Height	Height %
26.667	20001859	99.85	416392	99.81
29.413	30867	0.15	810	0.19
Totals	20032726	100.00	417202	100.00



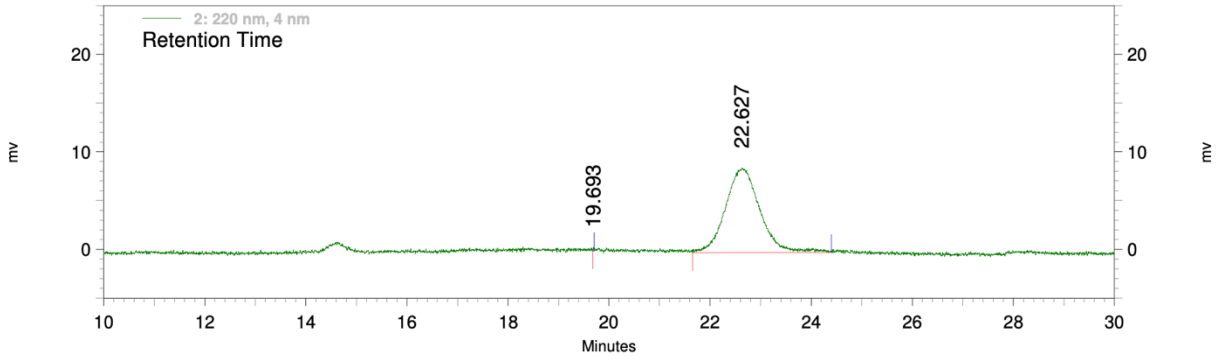
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7d

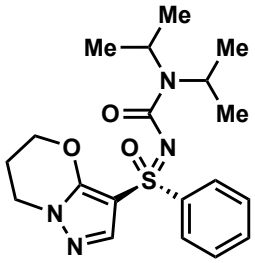


Retention Time	Area	Area %	Height	Height %
19.893	3176358	50.06	86173	55.42
23.487	3169151	49.94	69318	44.58
Totals	6345509	100.00	155491	100.00

Chromatogram for sulfoximine: (*R*)-7d

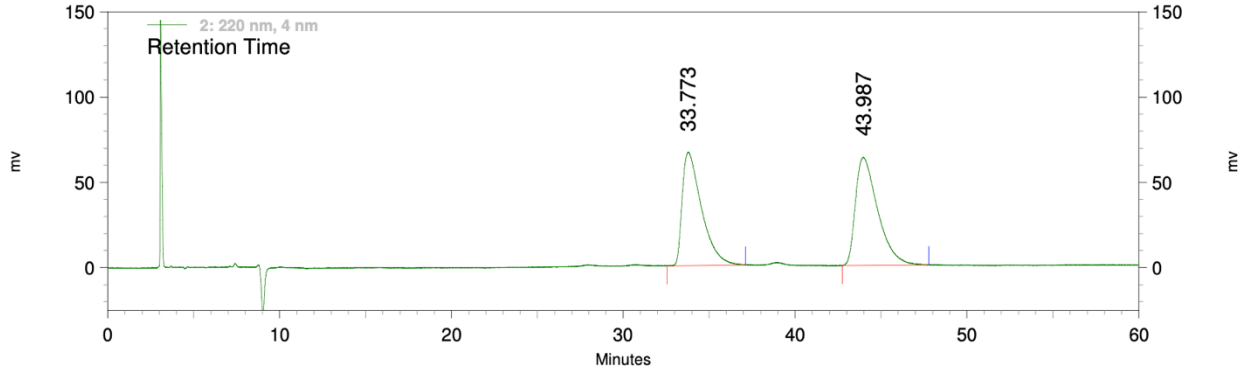


Retention Time	Area	Area %	Height	Height %
19.693	268	0.07	327	3.64
22.627	410447	99.93	8656	96.36
Totals	410715	100.00	8983	100.00



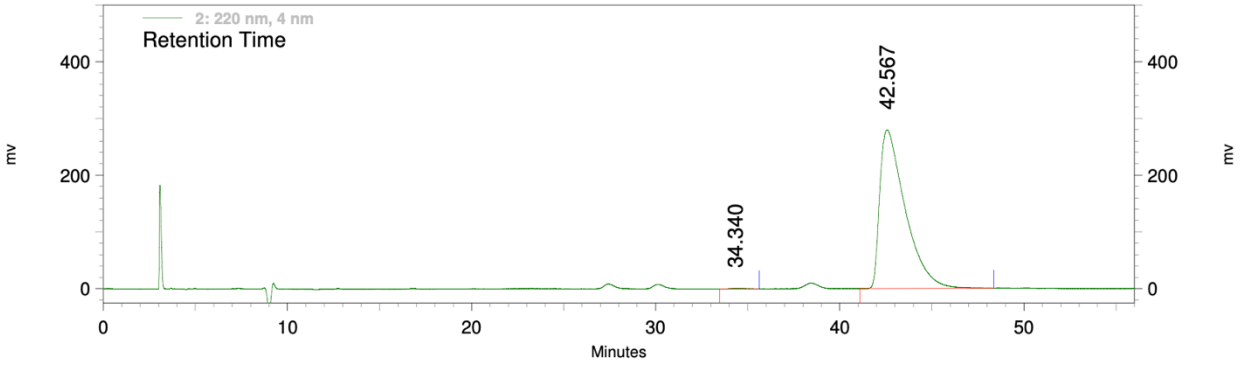
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (90:10); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7e

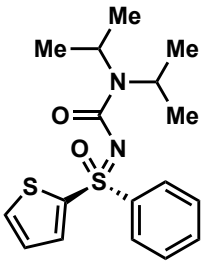


Retention Time	Area	Area %	Height	Height %
33.773	5196301	47.70	66668	51.23
43.987	5697621	52.30	63473	48.77
Totals	10893922	100.00	130141	100.00

Chromatogram for sulfoximine: (*R*)-7e

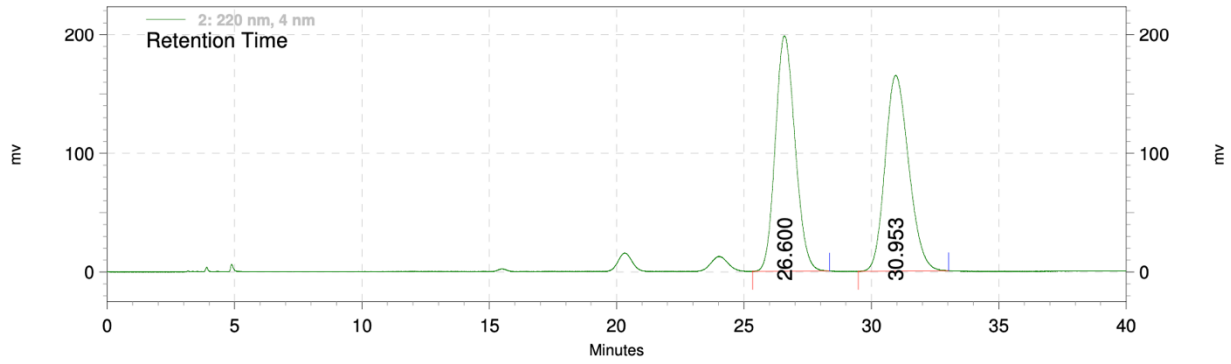


Retention Time	Area	Area %	Height	Height %
34.340	36609	0.14	618	0.22
42.567	26798078	99.86	279630	99.78
Totals	26834687	100.00	280248	100.00



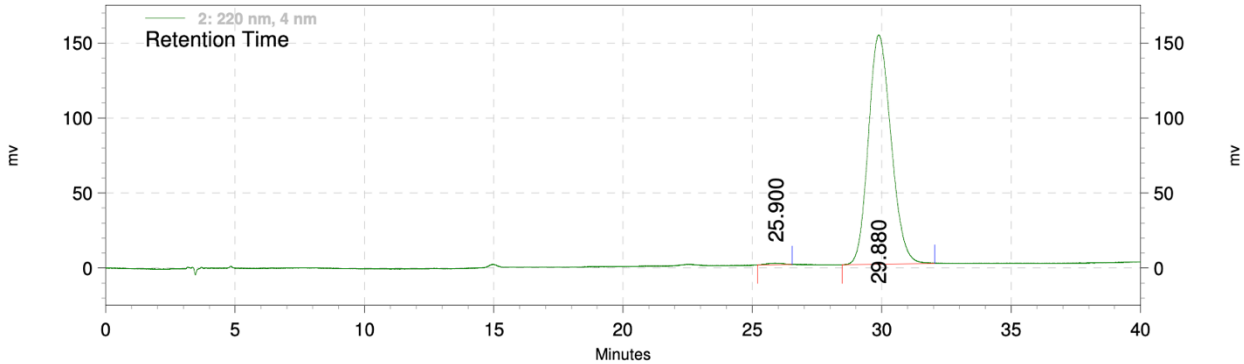
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7f

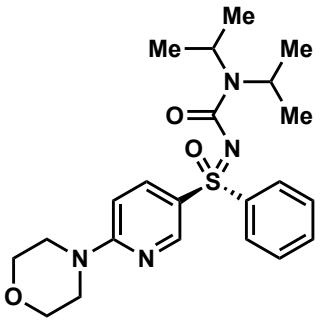


Retention Time	Area	Area %	Height	Height %
26.600	10694284	50.00	198338	54.58
30.953	10696261	50.00	165040	45.42
Totals	21390545	100.00	363378	100.00

Chromatogram for sulfoximine: (*R*)-7f

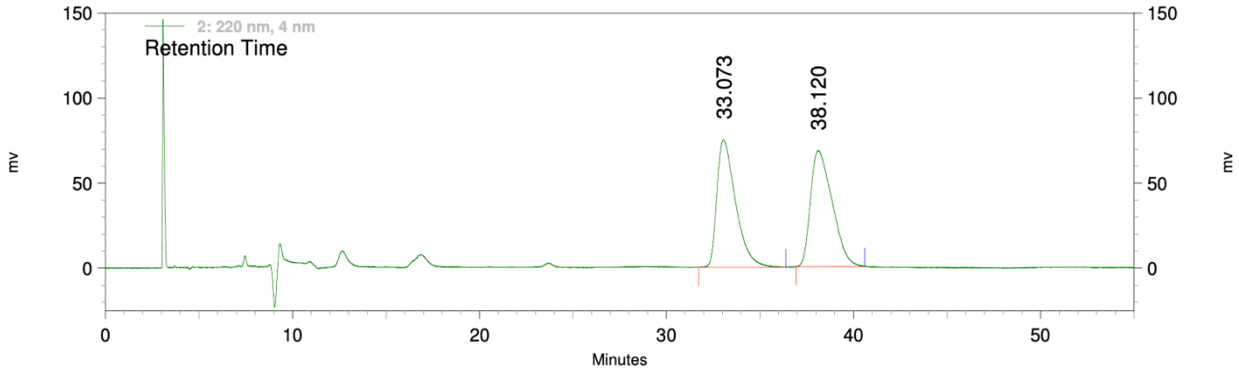


Retention Time	Area	Area %	Height	Height %
25.900	41837	0.45	1017	0.66
29.880	9315452	99.55	152884	99.34
Totals	9357289	100.00	153901	100.00



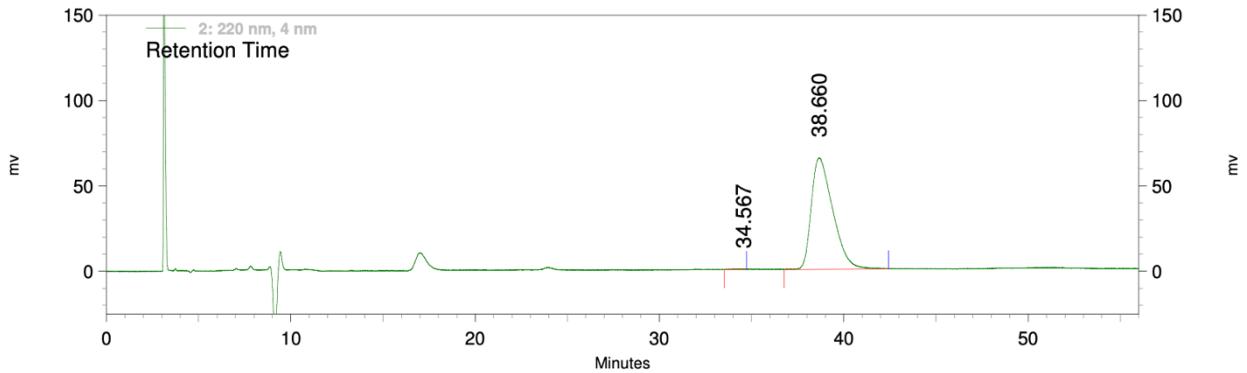
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (90:10); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7g

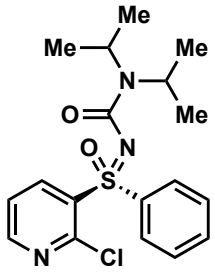


Retention Time	Area	Area %	Height	Height %
33.073	5242522	48.82	74948	52.34
38.120	5495849	51.18	68257	47.66
Totals	10738371	100.00	143205	100.00

Chromatogram for sulfoximine: (*R*)-7g

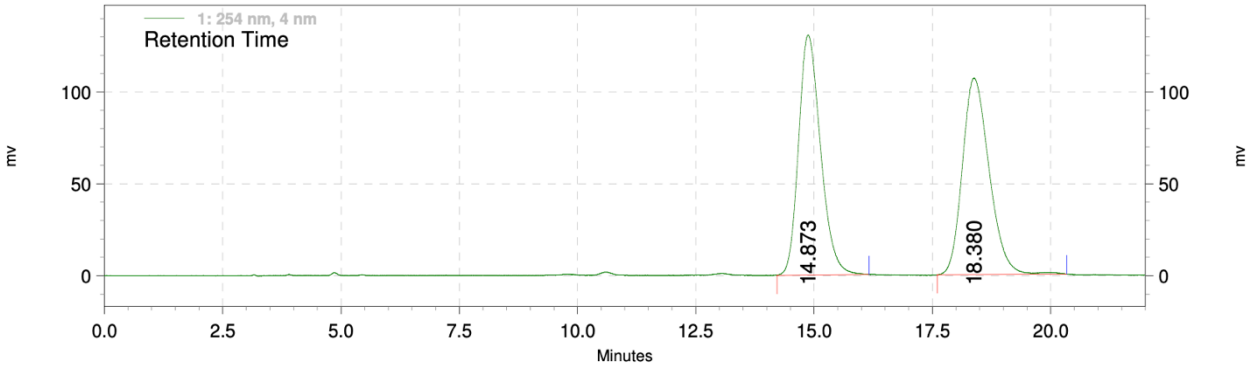


Retention Time	Area	Area %	Height	Height %
34.567	18309	0.34	479	0.73
38.660	5301866	99.66	65243	99.27
Totals	5320175	100.00	65722	100.00



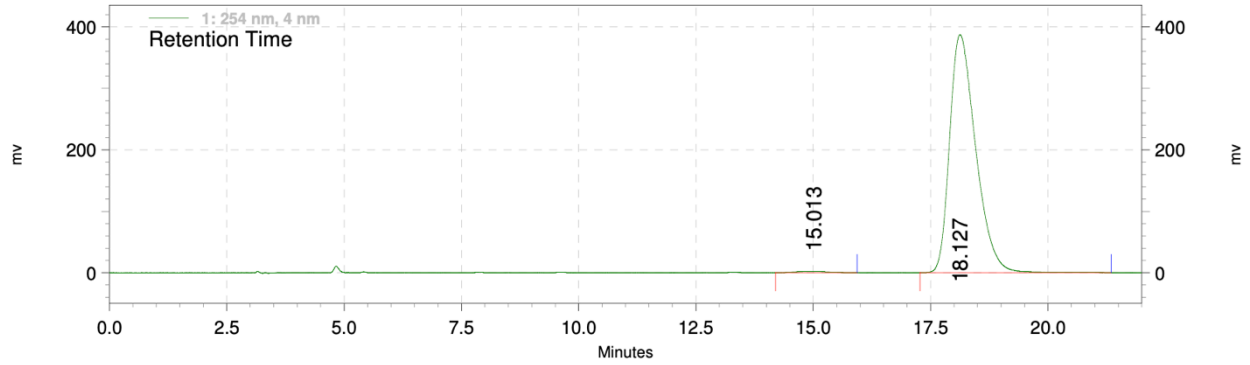
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7h

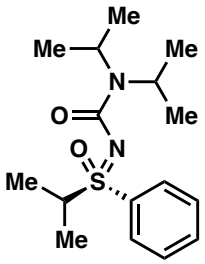


Retention Time	Area	Area %	Height	Height %
14.873	4227168	50.05	130663	54.98
18.380	4218514	49.95	107006	45.02
Totals	8445682	100.00	237669	100.00

Chromatogram for sulfoximine: (*R*)-7h

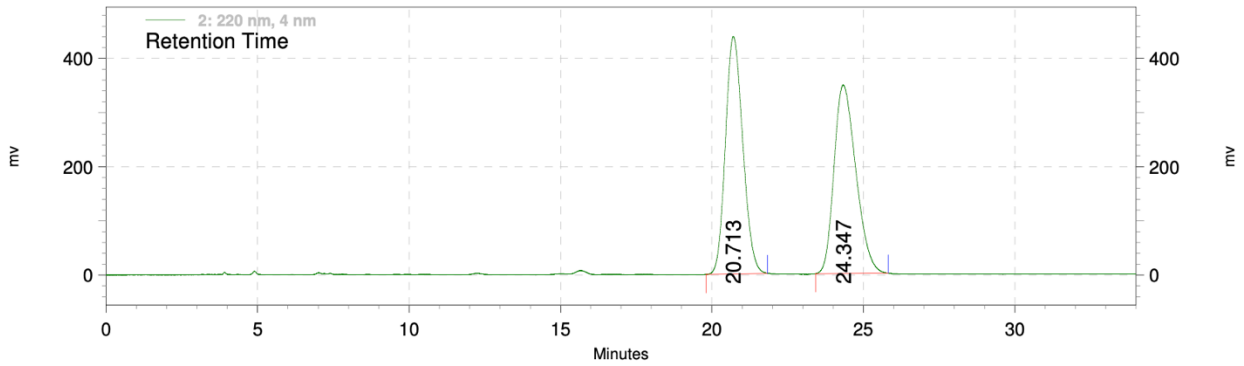


Retention Time	Area	Area %	Height	Height %
15.013	102107	0.68	2282	0.59
18.127	14908071	99.32	386986	99.41
Totals	15010178	100.00	389268	100.00



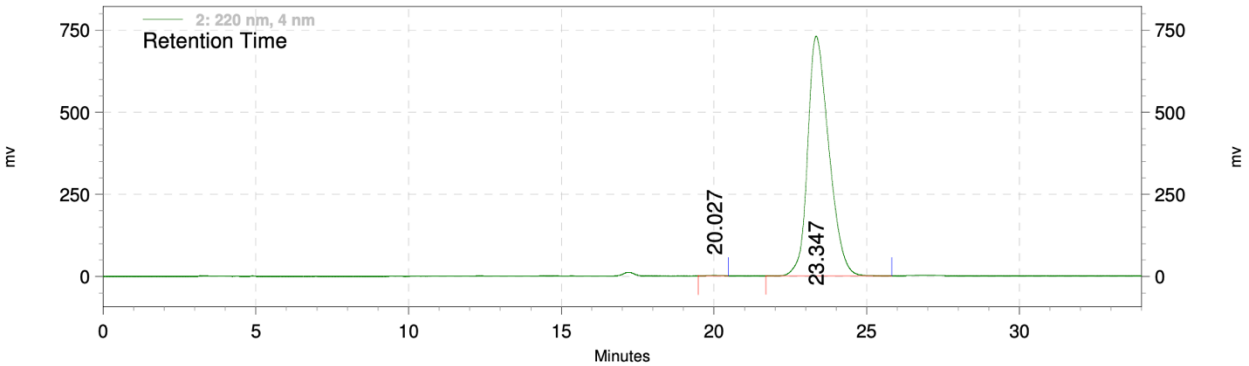
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-7i

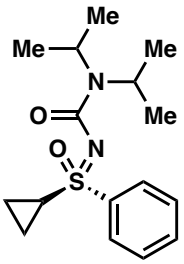


Retention Time	Area	Area %	Height	Height %
20.713	17541654	50.06	438687	55.75
24.347	17496114	49.94	348192	44.25
Totals	35037768	100.00	786879	100.00

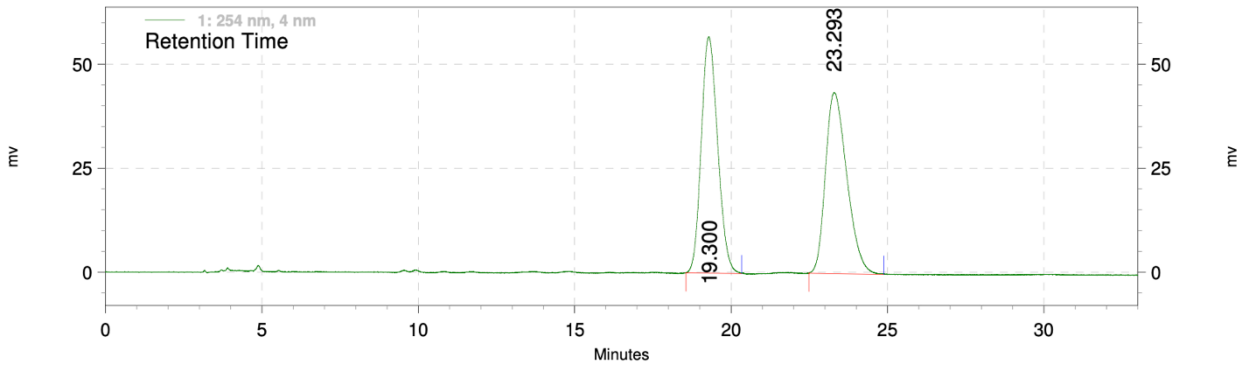
Chromatogram for sulfoximine: (*S*)-7i



Retention Time	Area	Area %	Height	Height %
20.027	53568	0.15	1760	0.24
23.347	35183762	99.85	729960	99.76
Totals	35237330	100.00	731720	100.00

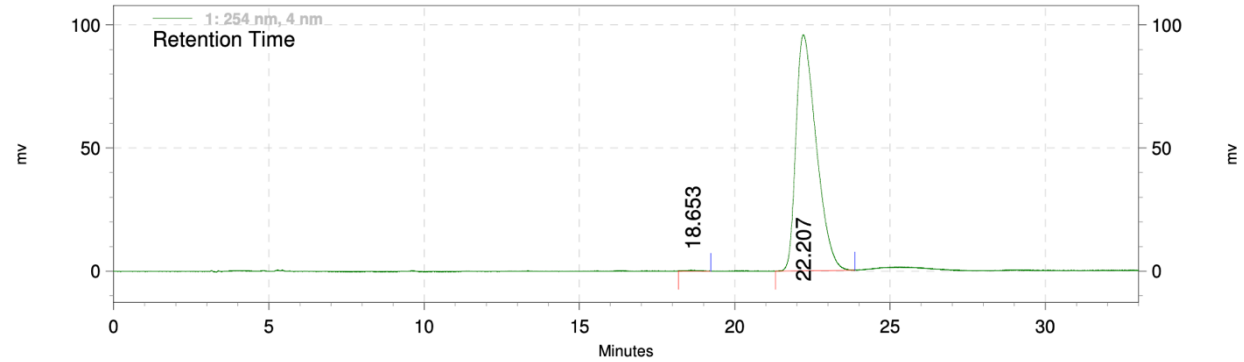


Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min
Chromatogram for sulfoximine: (*rac*)-7j

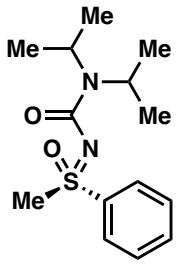


Retention Time	Area	Area %	Height	Height %
19.300	2074147	50.10	56888	56.63
23.293	2066057	49.90	43568	43.37
Totals	4140204	100.00	100456	100.00

Chromatogram for sulfoximine: (*S*)-7j

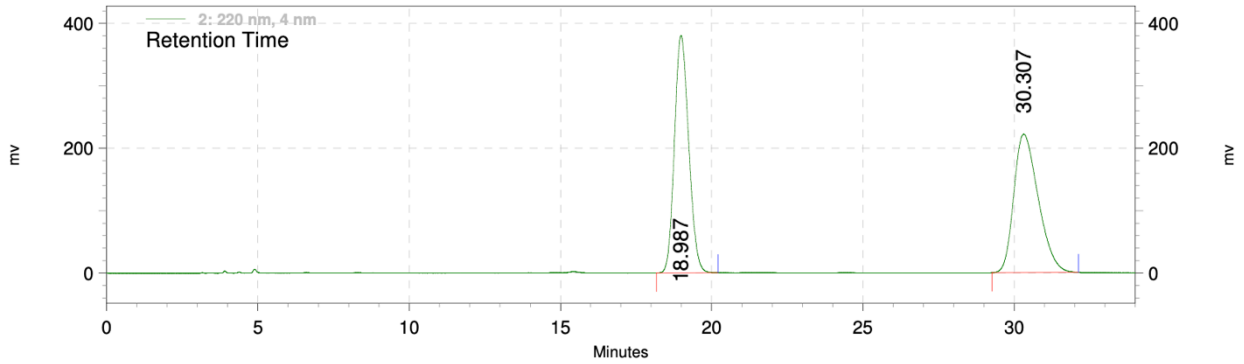


Retention Time	Area	Area %	Height	Height %
18.653	14640	0.33	453	0.47
22.207	4365410	99.67	95868	99.53
Totals	4380050	100.00	96321	100.00



Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

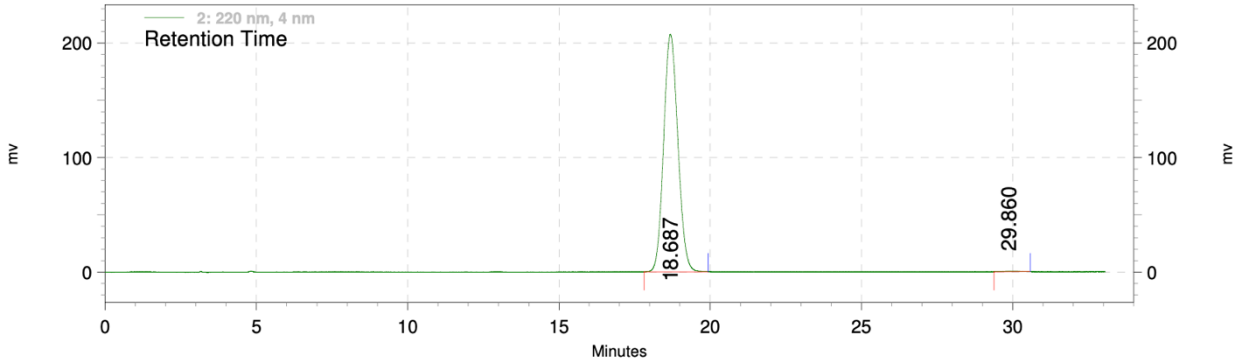
Chromatogram for sulfoximine: (*rac*)-7k



Retention Time	Area	Area %	Height	Height %
18.987	12469772	50.05	380217	63.16
30.307	12446386	49.95	221803	36.84

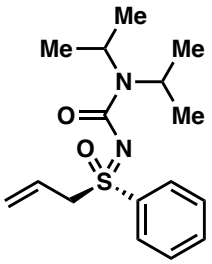
Totals	24916158	100.00	602020	100.00

Chromatogram for sulfoximine: (*S*)-7k



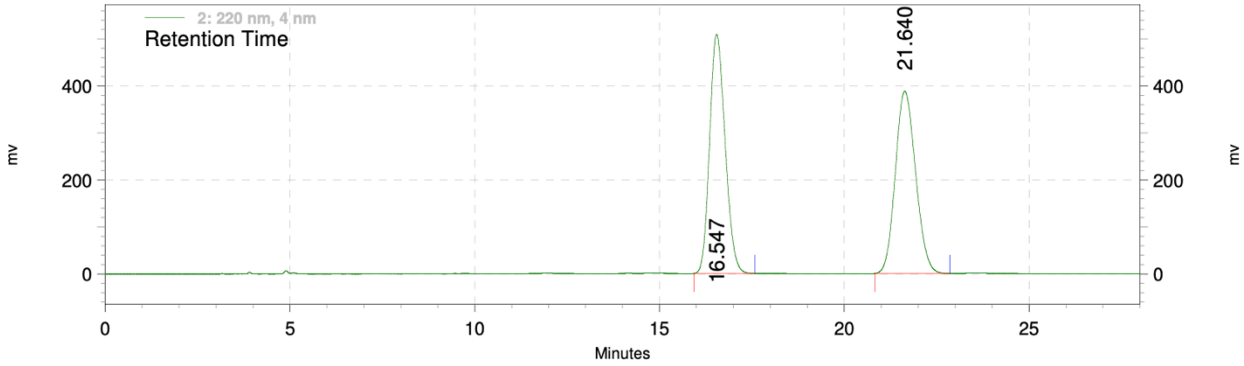
Retention Time	Area	Area %	Height	Height %
18.687	6764266	99.76	207329	99.79
29.860	16451	0.24	427	0.21

Totals	6780717	100.00	207756	100.00



Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

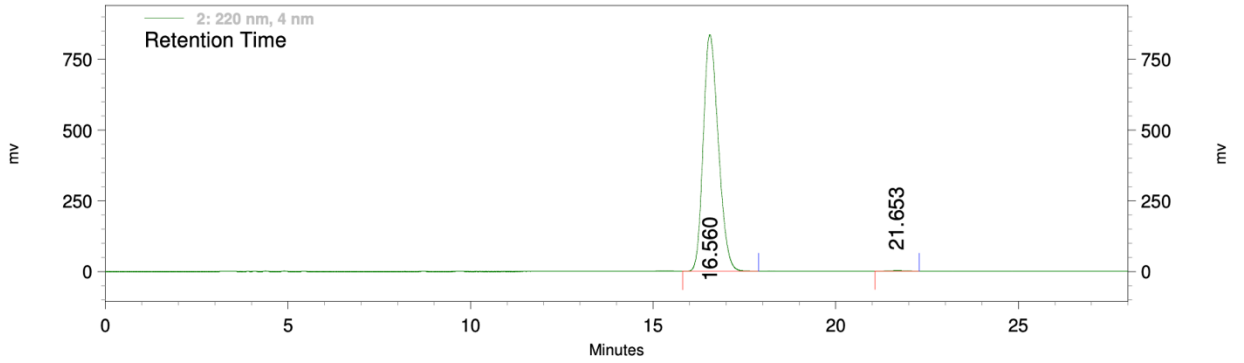
Chromatogram for sulfoximine: (*rac*)-7l



Retention Time	Area	Area %	Height	Height %
16.547	14871234	50.07	509026	56.74
21.640	14829699	49.93	388044	43.26

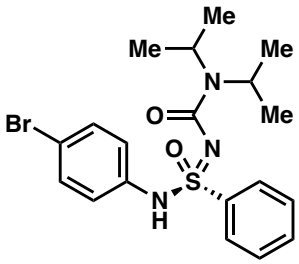
Totals				
	29700933	100.00	897070	100.00

Chromatogram for sulfoximine: (*S*)-7l



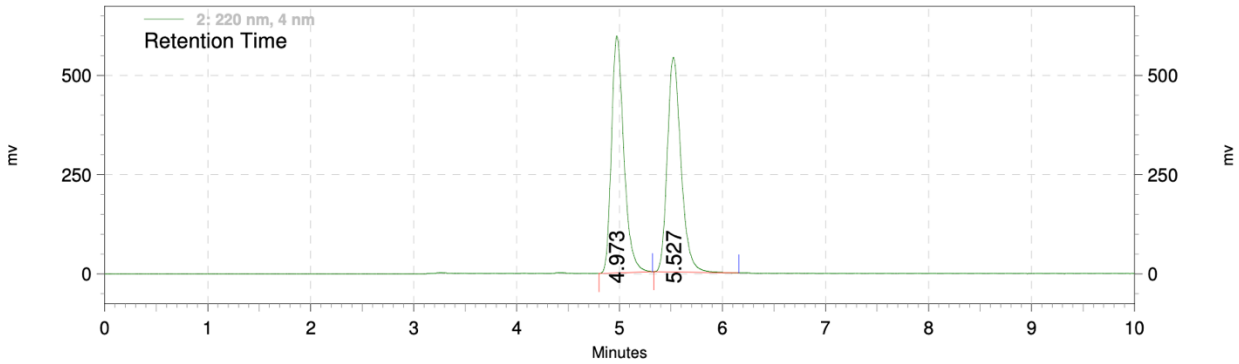
Retention Time	Area	Area %	Height	Height %
16.560	24116403	99.68	836424	99.73
21.653	76575	0.32	2248	0.27

Totals				
	24192978	100.00	838672	100.00



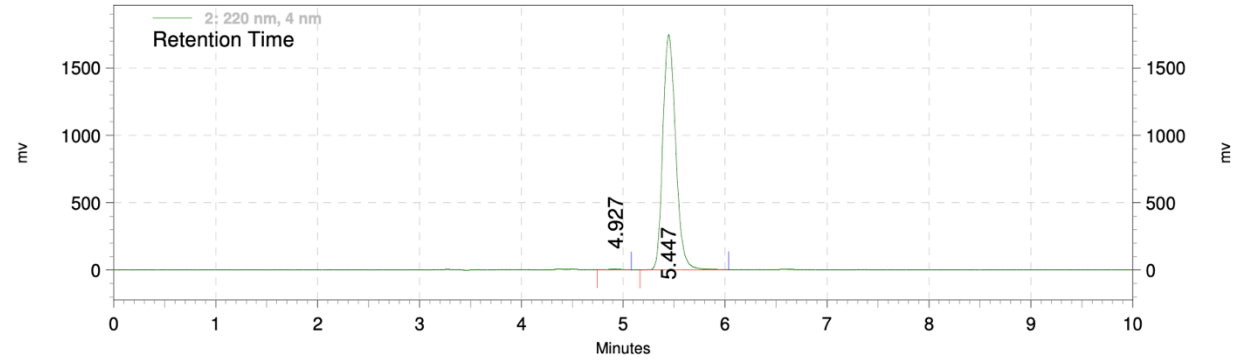
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8a

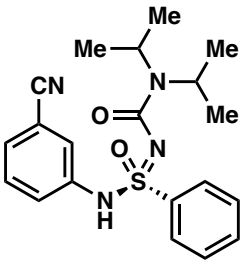


Retention Time	Area	Area %	Height	Height %
4.973	4964145	49.88	597920	52.52
5.527	4987388	50.12	540490	47.48
Totals	9951533	100.00	1138410	100.00

Chromatogram for sulfonimidamide: (*S*)-8a

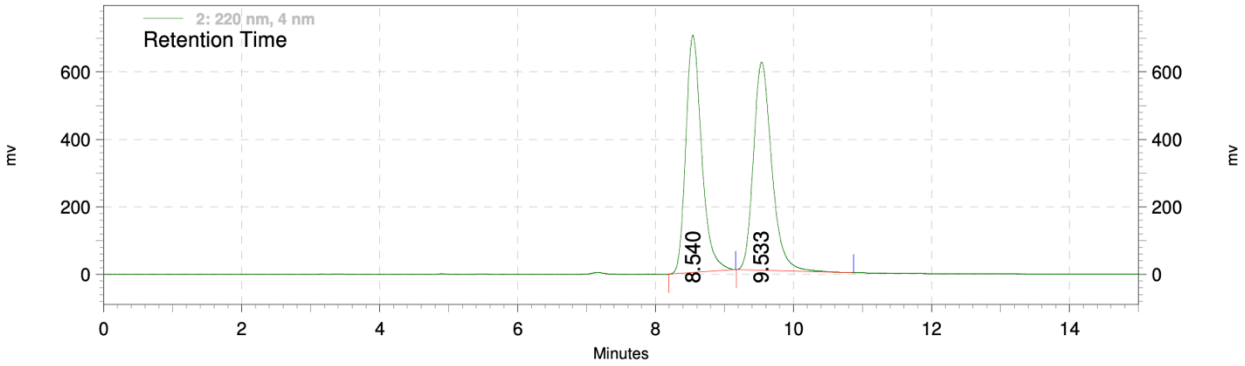


Retention Time	Area	Area %	Height	Height %
4.927	33745	0.22	4358	0.25
5.447	15227332	99.78	1747832	99.75
Totals	15261077	100.00	1752190	100.00



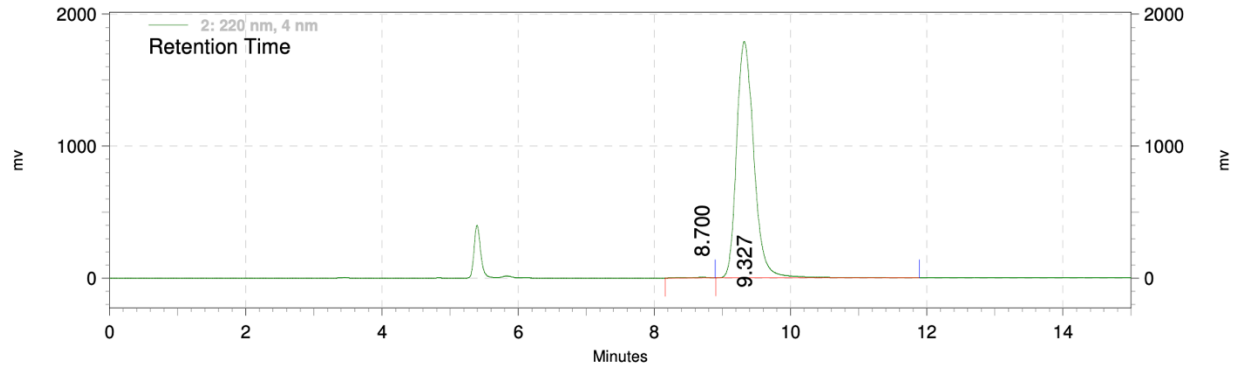
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8b

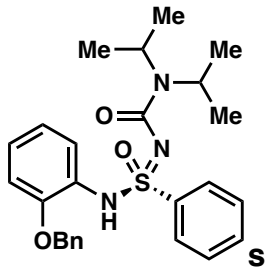


Retention Time	Area	Area %	Height	Height %
8.540	11207687	49.63	703908	53.29
9.533	11375507	50.37	616925	46.71
Totals	22583194	100.00	1320833	100.00

Chromatogram for sulfonimidamide: (*S*)-8b

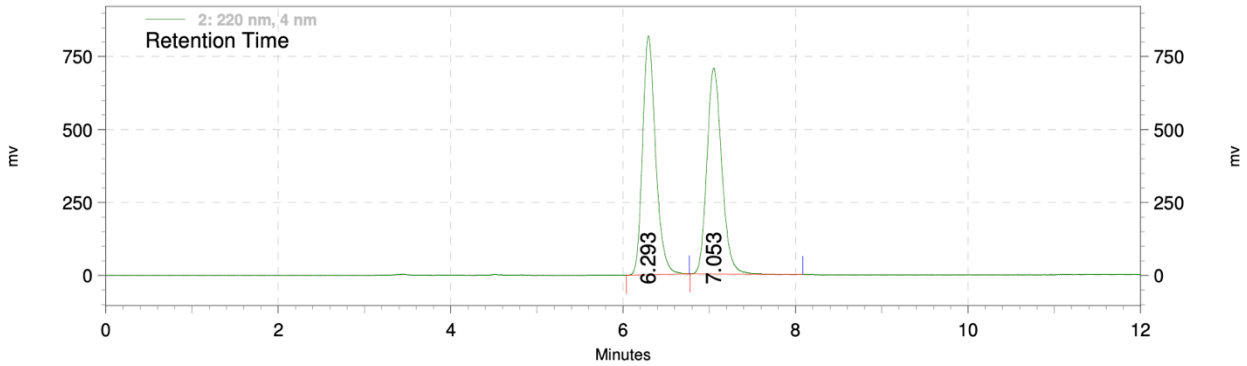


Retention Time	Area	Area %	Height	Height %
8.700	110363	0.35	5306	0.30
9.327	31717838	99.65	1790868	99.70
Totals	31828201	100.00	1796174	100.00



Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

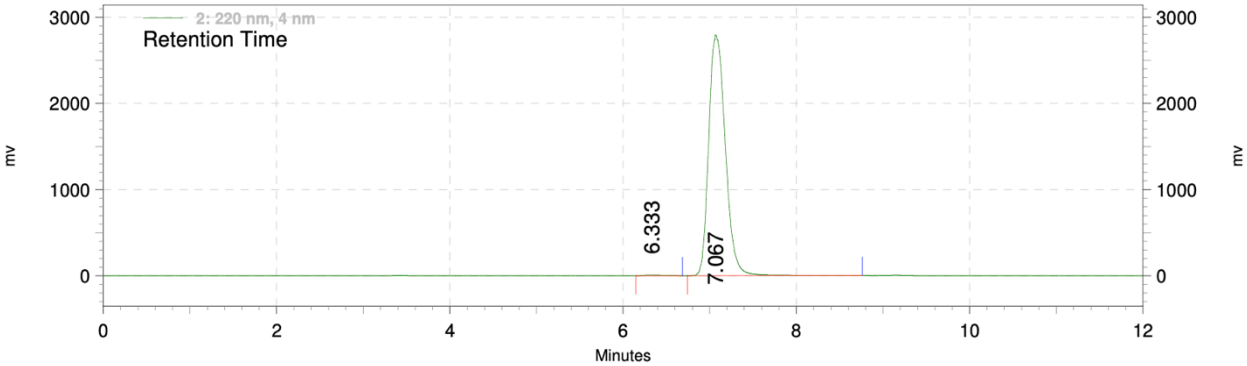
Chromatogram for sulfonimidamide: (*rac*)-8c



Retention Time	Area	Area %	Height	Height %
6.293	8588418	50.37	819326	53.68
7.053	8462676	49.63	707013	46.32

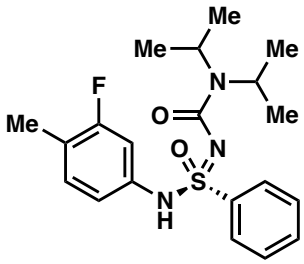
Totals	17051094	100.00	1526339	100.00

Chromatogram for sulfonimidamide: (*S*)-8c



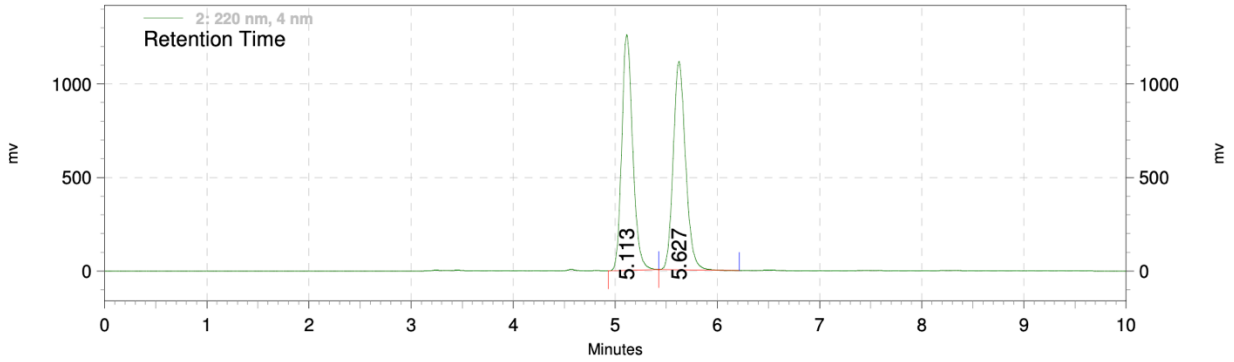
Retention Time	Area	Area %	Height	Height %
6.333	118755	0.32	8712	0.31
7.067	37232051	99.68	2796413	99.69

Totals	37350806	100.00	2805125	100.00



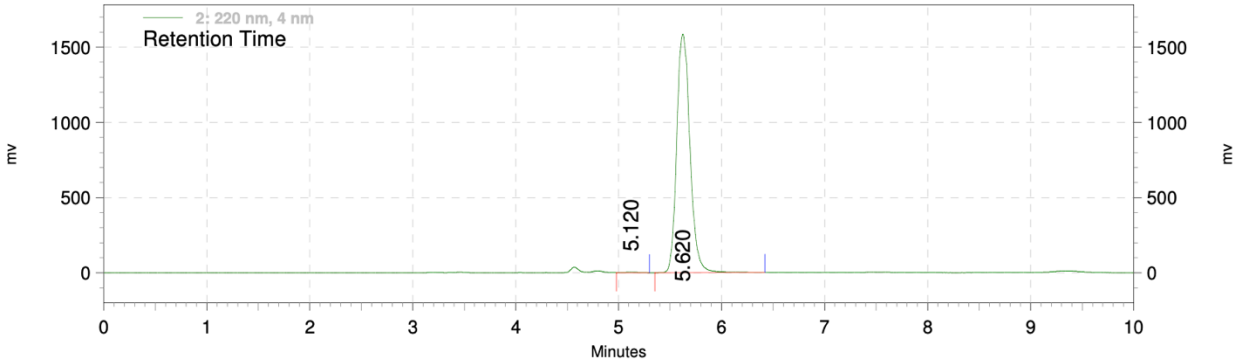
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8d

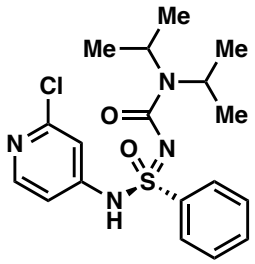


Retention Time	Area	Area %	Height	Height %
5.113	9374025	50.00	1259655	53.12
5.627	9372388	50.00	1111672	46.88
Totals	18746413	100.00	2371327	100.00

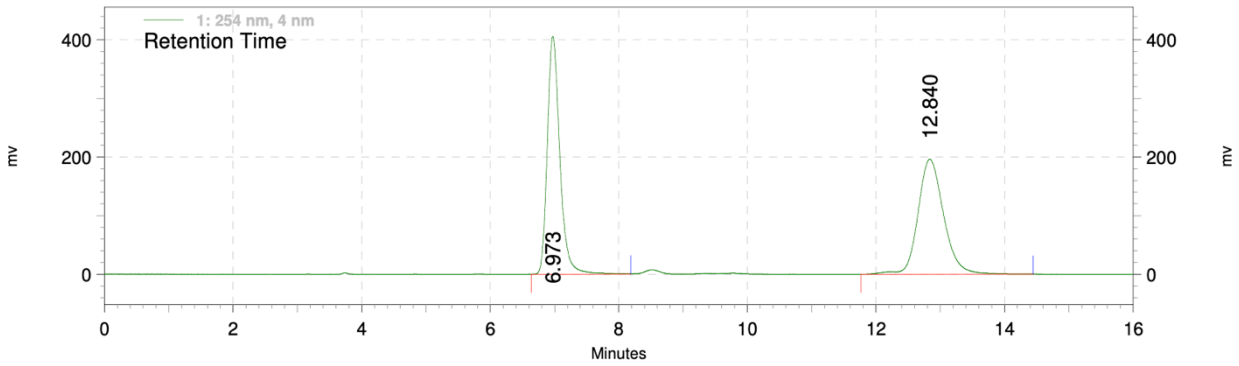
Chromatogram for sulfonimidamide: (*S*)-8d



Retention Time	Area	Area %	Height	Height %
5.120	28649	0.20	3773	0.24
5.620	14177995	99.80	1584519	99.76
Totals	14206644	100.00	1588292	100.00

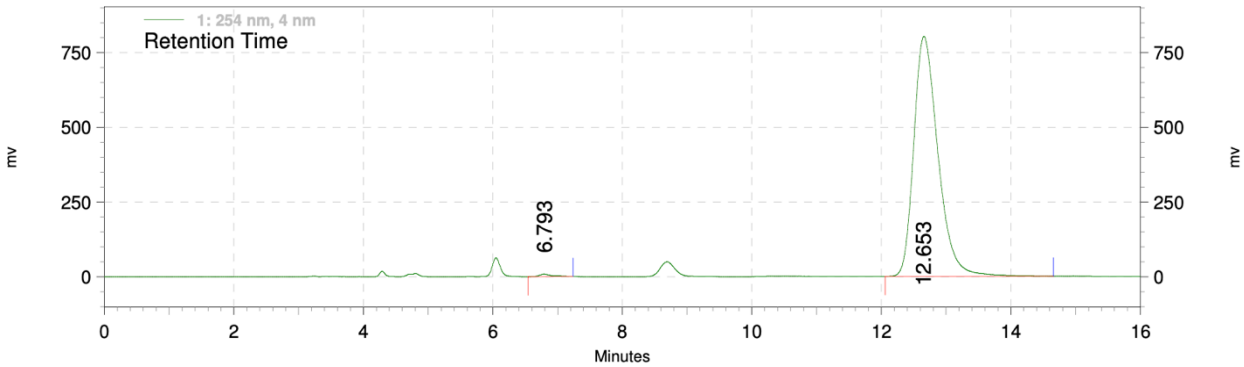


Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min
Chromatogram for sulfonimidamide: (*rac*)-8e

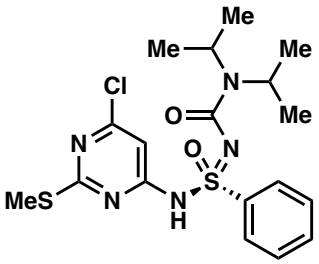


Retention Time	Area	Area %	Height	Height %
6.973	5488951	50.15	405547	67.37
12.840	5456704	49.85	196384	32.63
Totals	10945655	100.00	601931	100.00

Chromatogram for sulfonimidamide: (*S*)-8e

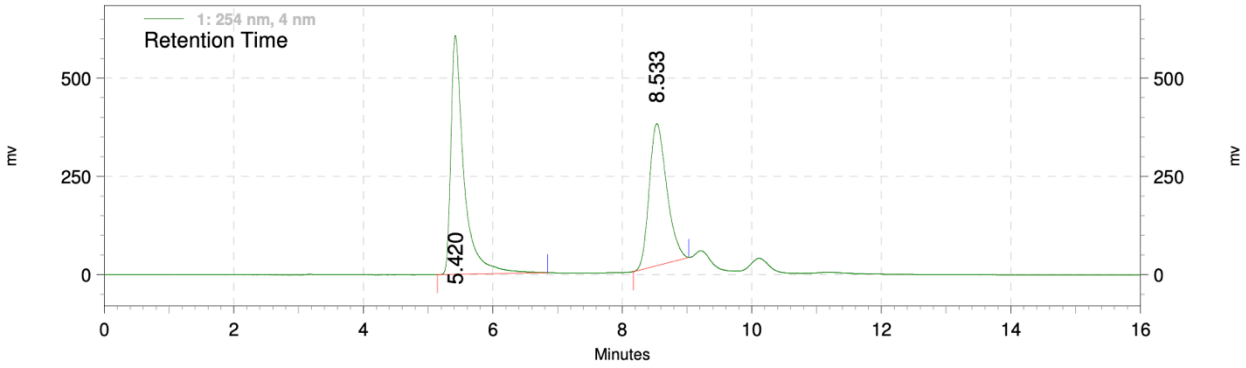


Retention Time	Area	Area %	Height	Height %
6.793	118308	0.56	8619	1.06
12.653	20872639	99.44	802755	98.94
Totals	20990947	100.00	811374	100.00



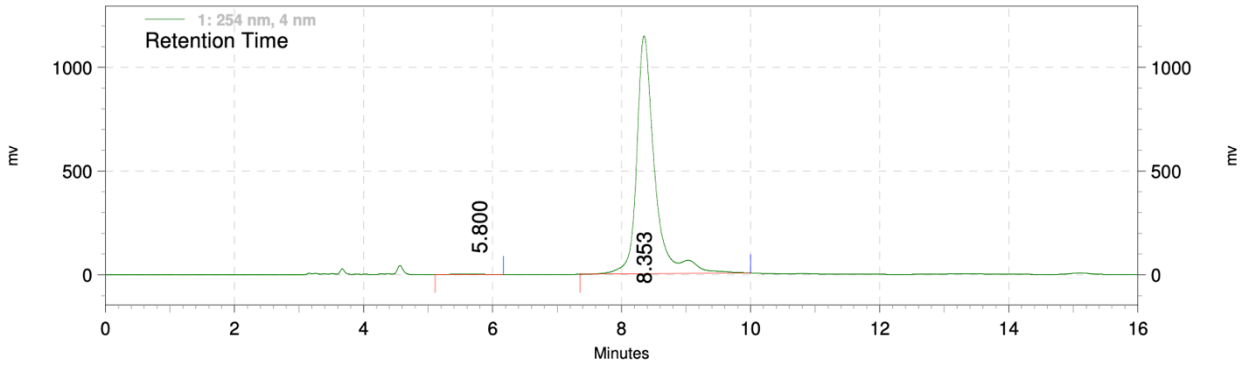
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8f

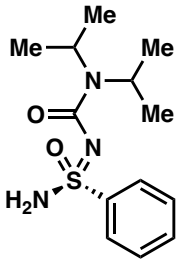


Retention Time	Area	Area %	Height	Height %
5.420	8490124	55.48	607956	62.72
8.533	6813812	44.52	361381	37.28
Totals	15303936	100.00	969337	100.00

Chromatogram for sulfonimidamide: (*S*)-8f

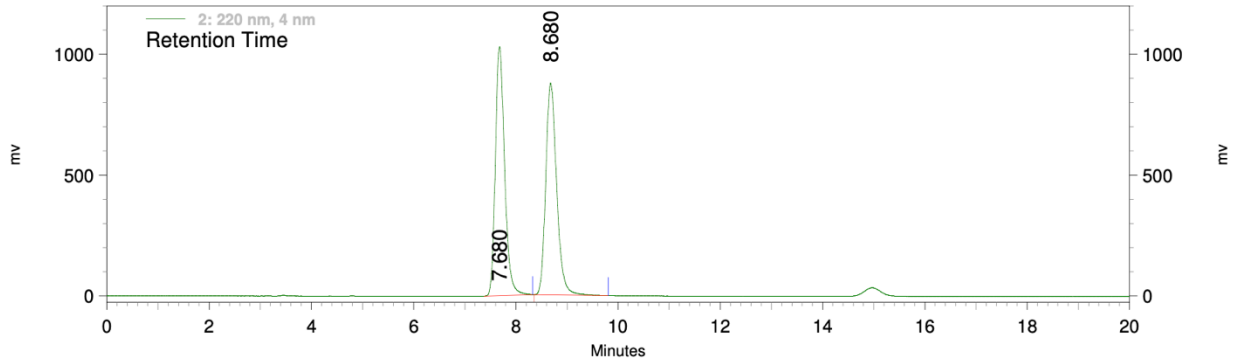


Retention Time	Area	Area %	Height	Height %
5.800	71247	0.32	2760	0.24
8.353	22389399	99.68	1146508	99.76
Totals	22460646	100.00	1149268	100.00



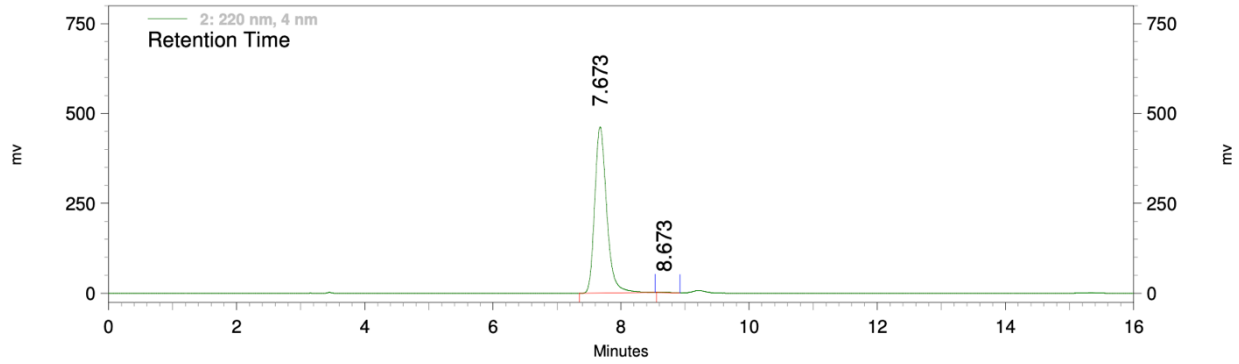
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8i

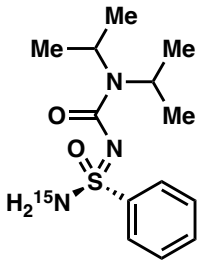


Retention Time	Area	Area %	Height	Height %
7.680	12986240	49.98	1029069	54.00
8.680	12995458	50.02	876640	46.00
Totals	25981698	100.00	1905709	100.00

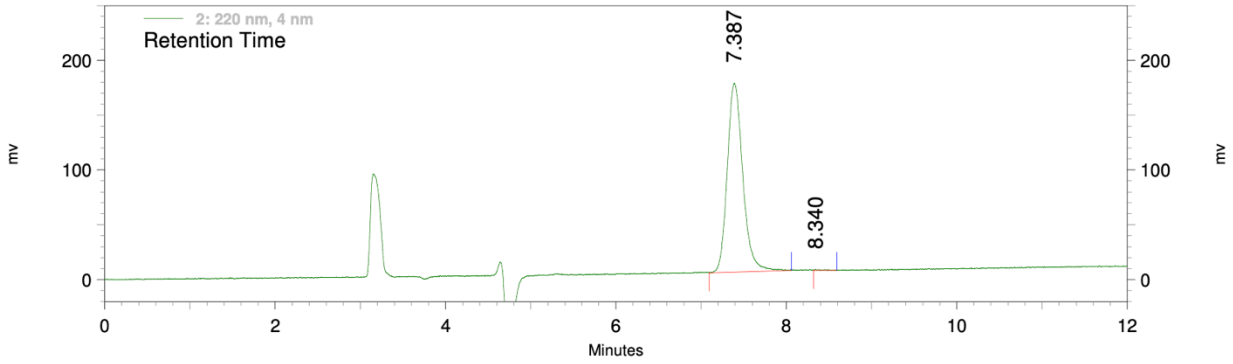
Chromatogram for sulfonimidamide: (*R*)-8i



Retention Time	Area	Area %	Height	Height %
7.673	6007994	99.89	462066	99.89
8.673	6810	0.11	504	0.11
Totals	6014804	100.00	462570	100.00

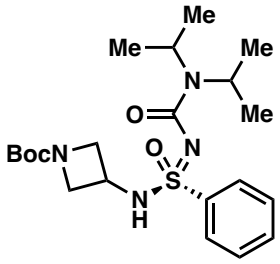


Chromatogram for sulfonimidamide: (*R*)-8j



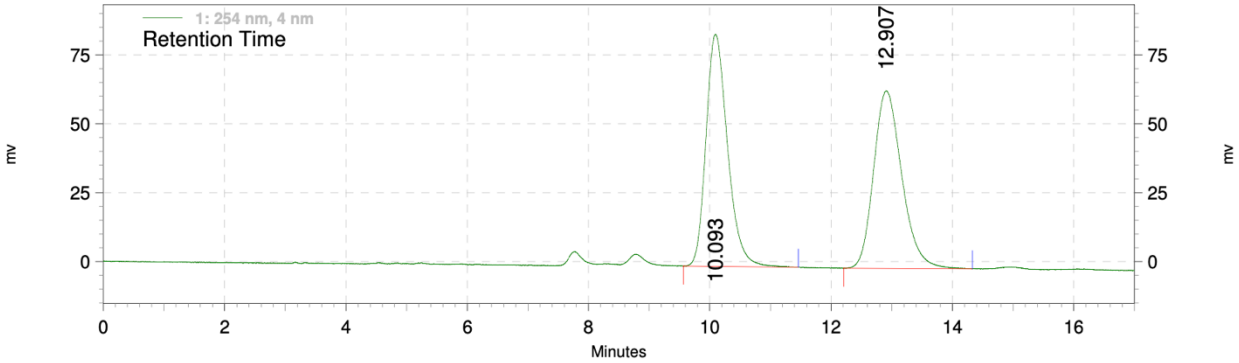
Retention Time	Area	Area %	Height	Height %
7.387	2184352	99.66	172448	99.47
8.340	7491	0.34	917	0.53

Totals	2191843	100.00	173365	100.00



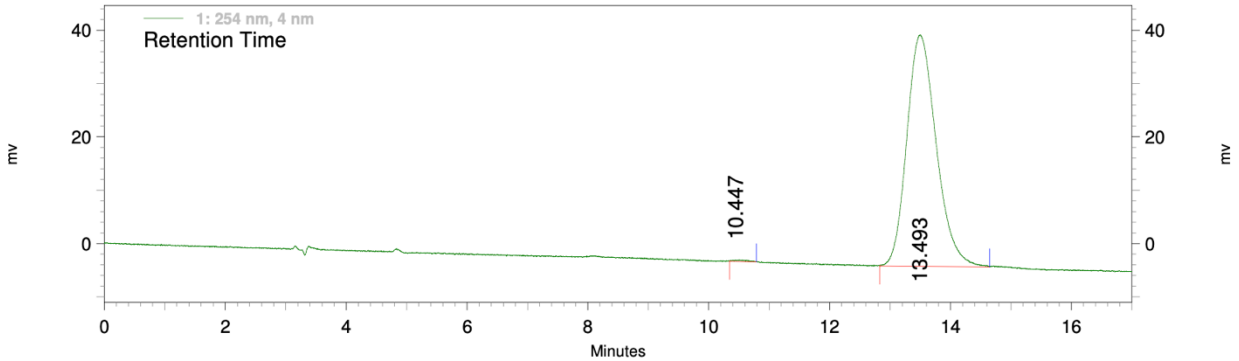
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8k

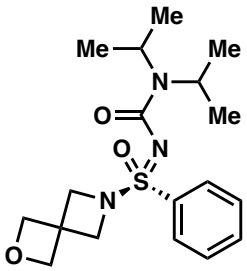


Retention Time	Area	Area %	Height	Height %
10.093	2080198	49.93	84151	56.62
12.907	2085898	50.07	64470	43.38
Totals	4166096	100.00	148621	100.00

Chromatogram for sulfonimidamide: (*S*)-8k

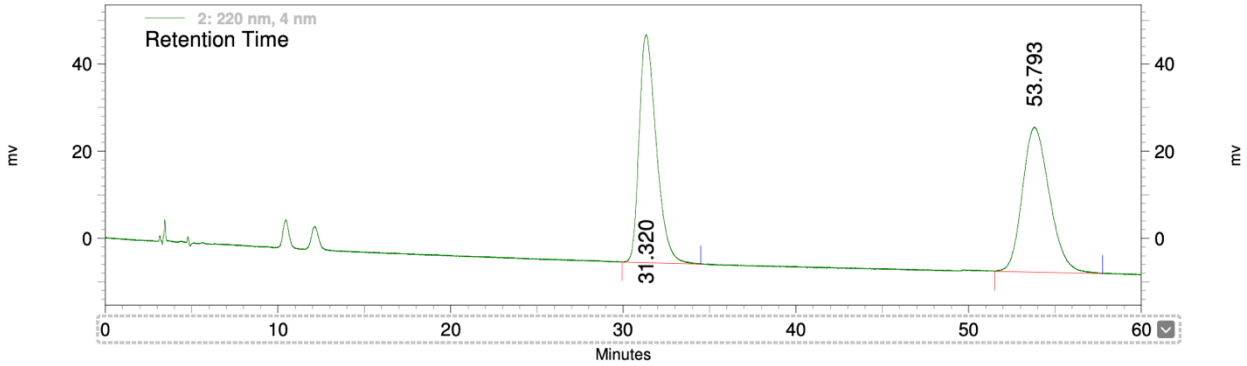


Retention Time	Area	Area %	Height	Height %
10.447	3779	0.26	251	0.57
13.493	1467239	99.74	43416	99.43
Totals	1471018	100.00	43667	100.00



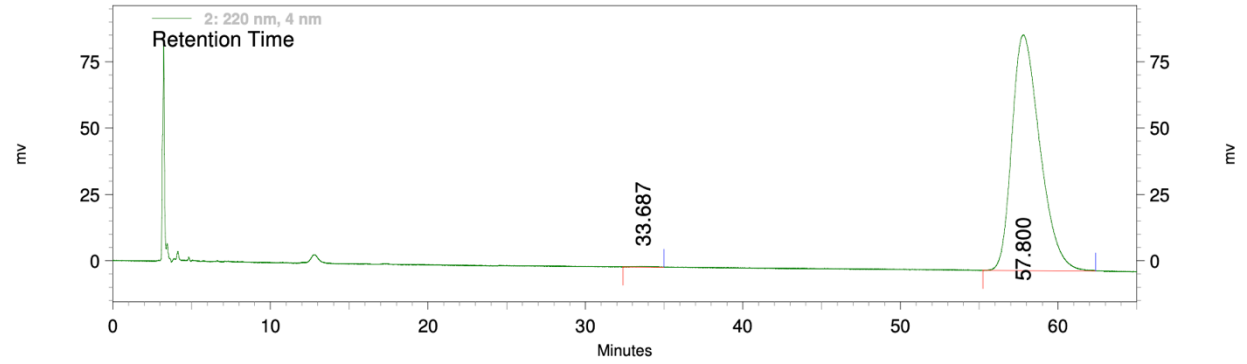
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8n

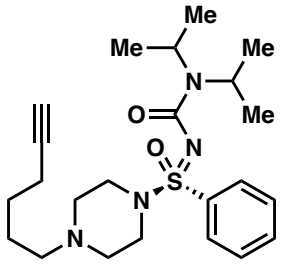


Retention Time	Area	Area %	Height	Height %
31.320	3614010	49.81	52388	61.15
53.793	3640876	50.19	33280	38.85
Totals	7254886	100.00	85668	100.00

Chromatogram for sulfonimidamide: (*S*)-8n

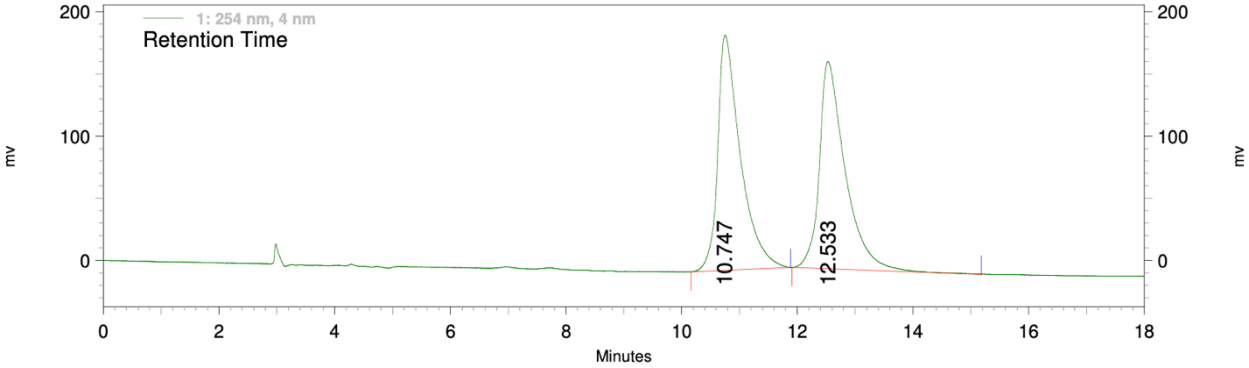


Retention Time	Area	Area %	Height	Height %
33.687	25045	0.23	318	0.36
57.800	10995279	99.77	88904	99.64
Totals	11020324	100.00	89222	100.00



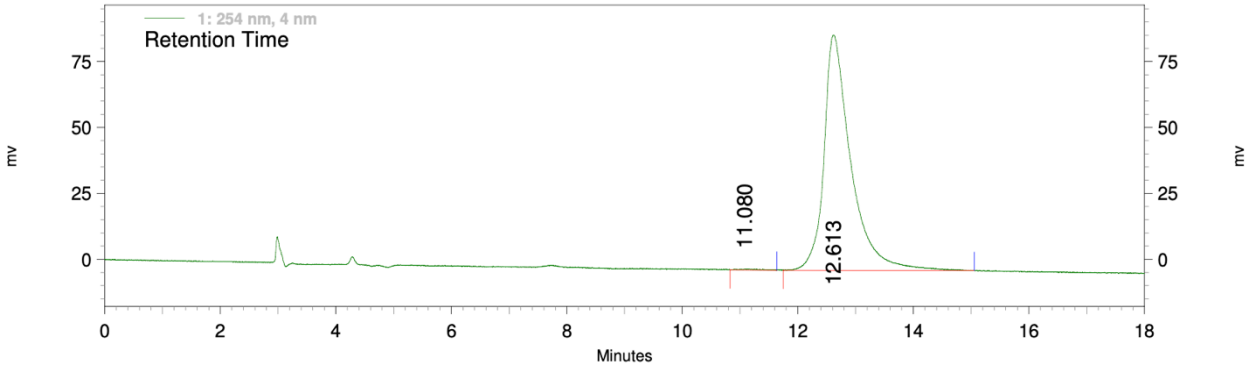
Column: Daicel Chiralpak IA; **Solvent:** *n*-hexane/IPA/Et_2NH (90:10:0.1%); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8p

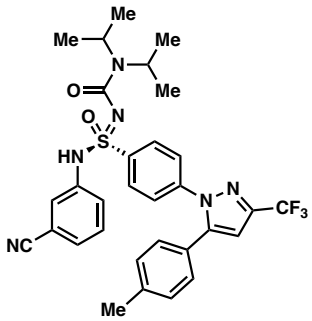


Retention Time	Area	Area %	Height	Height %
10.747	5152443	49.89	189200	53.18
12.533	5175277	50.11	166592	46.82
Totals	10327720	100.00	355792	100.00

Chromatogram for sulfonimidamide: (*S*)-8p

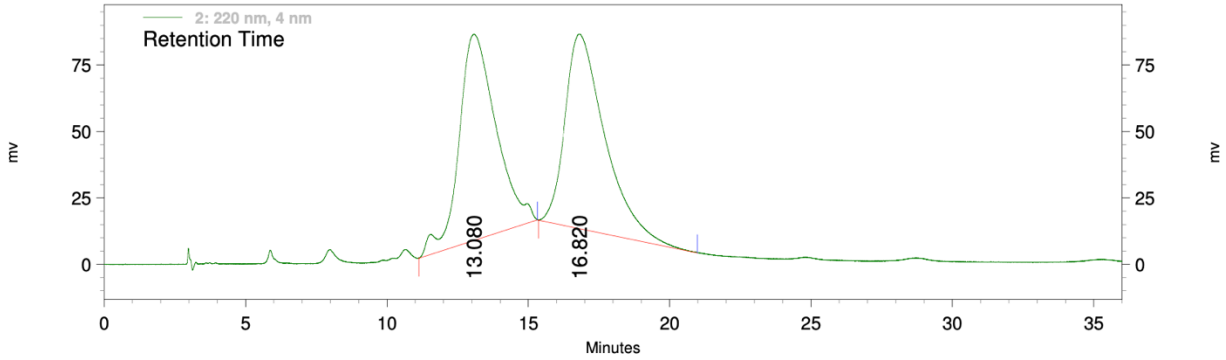


Retention Time	Area	Area %	Height	Height %
11.080	8848	0.30	356	0.40
12.613	2897547	99.70	89313	99.60
Totals	2906395	100.00	89669	100.00



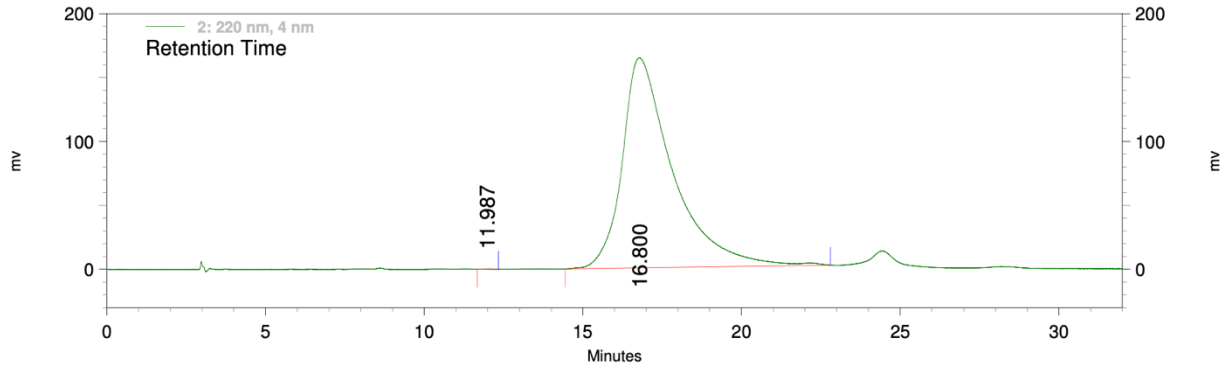
Column: Daicel Chiralpak IA; **Solvent:** *n*-hexane/IPA (90:10); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8r

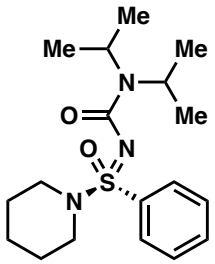


Retention Time	Area	Area %	Height	Height %
13.080	7067407	49.43	77665	51.47
16.820	7229537	50.57	73219	48.53
Totals	14296944	100.00	150884	100.00

Chromatogram for sulfonimidamide: (*S*)-8r

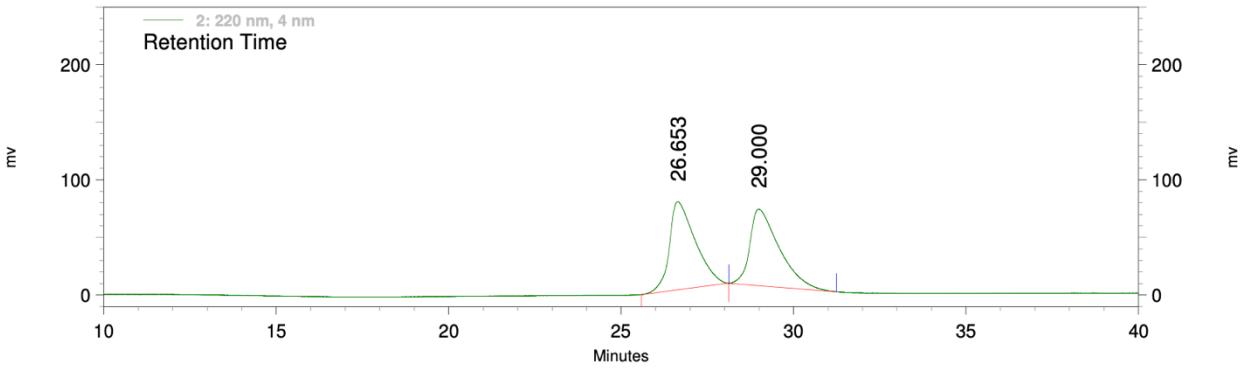


Retention Time	Area	Area %	Height	Height %
11.987	8688	0.05	416	0.25
16.800	18256017	99.95	164392	99.75
Totals	18264705	100.00	164808	100.00



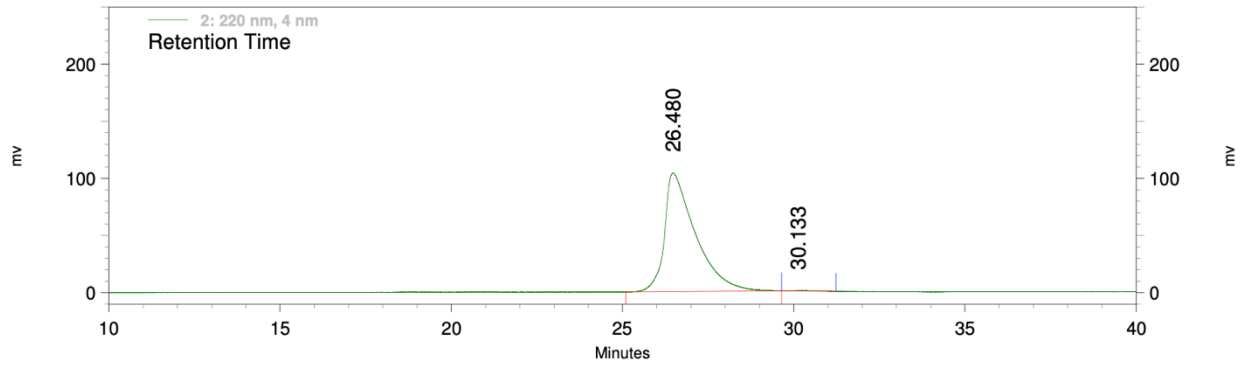
Column: Daicel Chiralpak IA; **Solvent:** *n*-hexane/IPA (98:02); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-8s

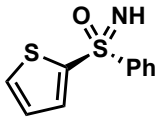


Retention Time	Area	Area %	Height	Height %
26.653	3998041	50.29	76536	53.53
29.000	3951793	49.71	66438	46.47
Totals	7949834	100.00	142974	100.00

Chromatogram for sulfonimidamide: (*S*)-8s

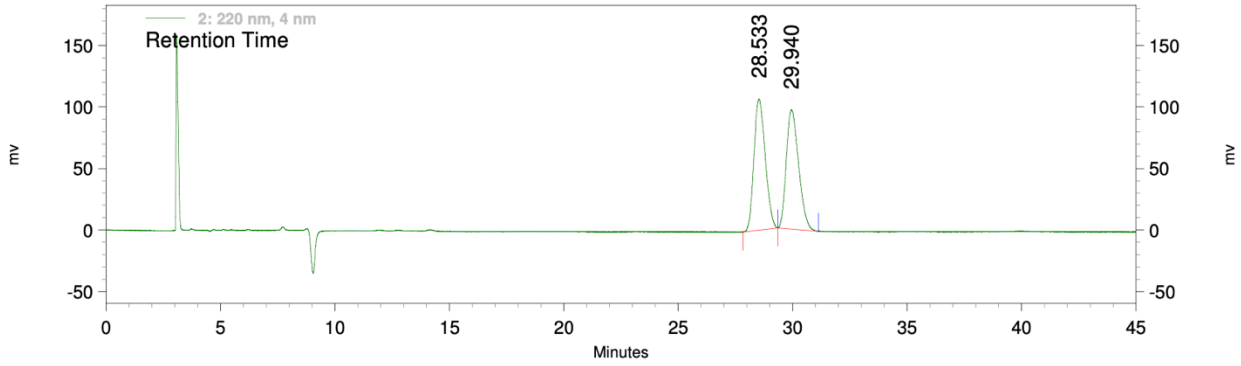


Retention Time	Area	Area %	Height	Height %
26.480	6540381	99.57	104030	99.53
30.133	28452	0.43	487	0.47
Totals	6568833	100.00	104517	100.00



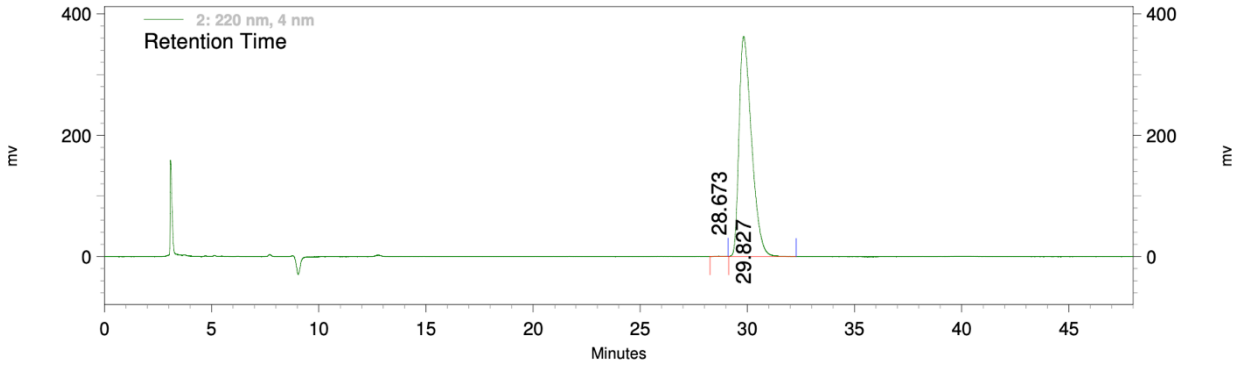
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (90:10); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-9a

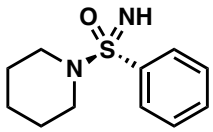


Retention Time	Area	Area %	Height	Height %
28.533	3662385	50.10	106586	52.35
29.940	3647198	49.90	97005	47.65
Totals	7309583	100.00	203591	100.00

Chromatogram for sulfoximine: (*R*)-9a

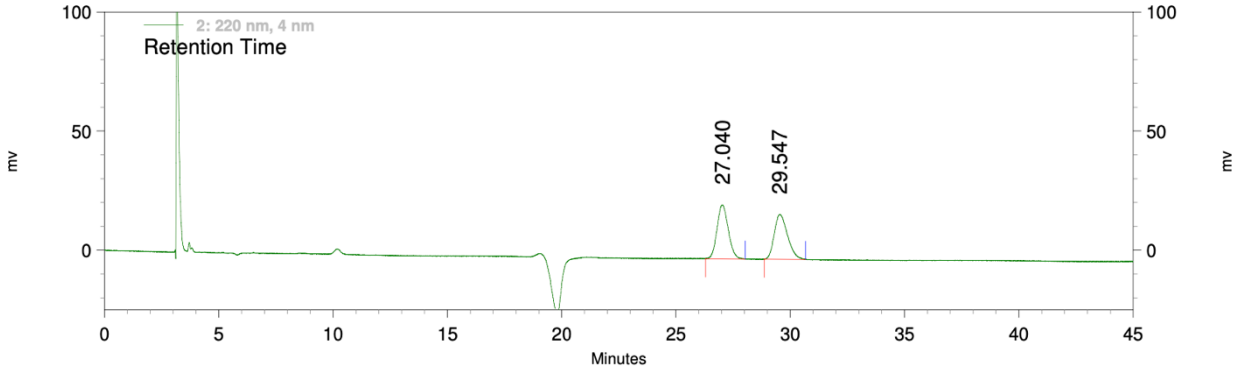


Retention Time	Area	Area %	Height	Height %
28.673	18267	0.12	758	0.21
29.827	14729473	99.88	363307	99.79
Totals	14747740	100.00	364065	100.00



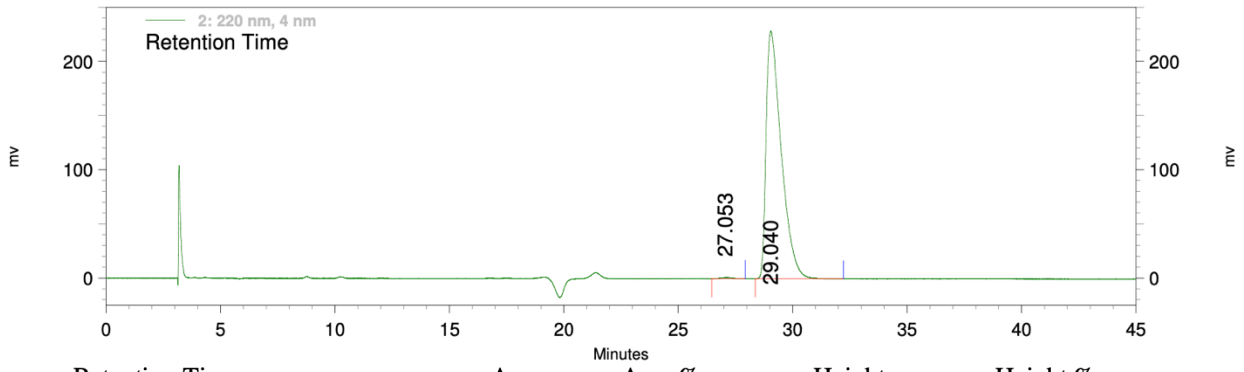
Column: Daicel Chiralpak IB; **Solvent:** *n*-hexane/IPA (95:05); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-9b

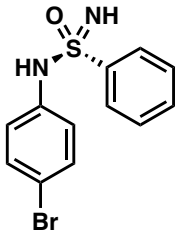


Retention Time	Area	Area %	Height	Height %
27.040	778429	50.63	22597	54.50
29.547	759135	49.37	18866	45.50
Totals	1537564	100.00	41463	100.00

Chromatogram for sulfonimidamide: (*S*)-9b

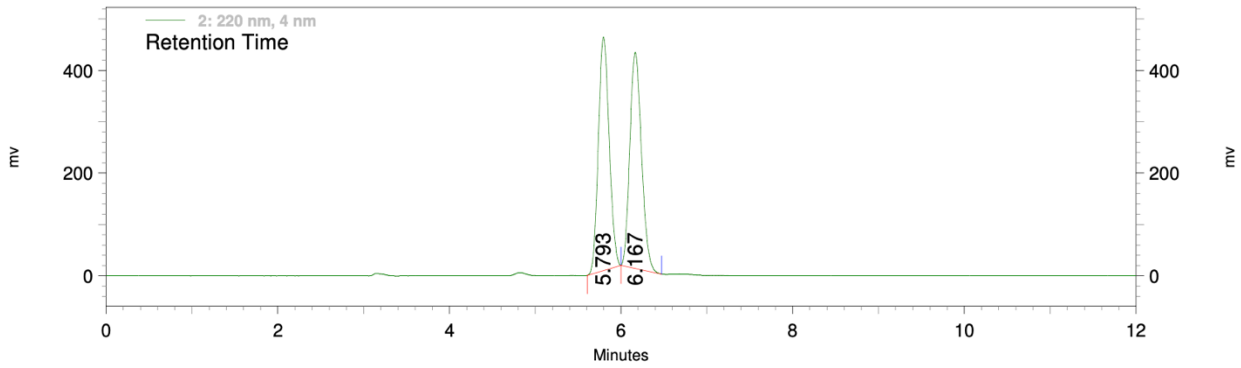


Retention Time	Area	Area %	Height	Height %
27.053	39700	0.38	1148	0.50
29.040	10488905	99.62	228803	99.50
Totals	10528605	100.00	229951	100.00



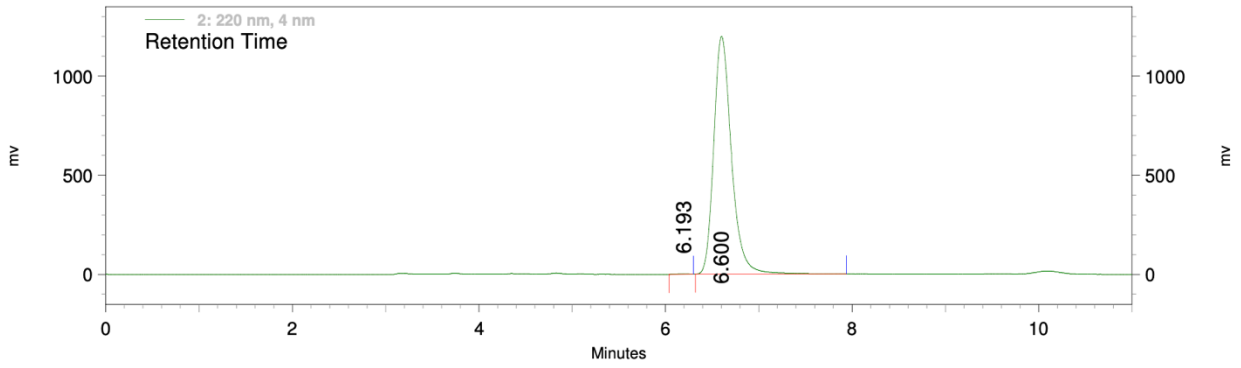
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-10b

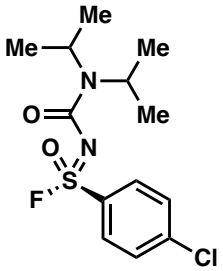


Retention Time	Area	Area %	Height	Height %
5.793	3983004	50.06	455000	51.95
6.167	3972717	49.94	420920	48.05
Totals	7955721	100.00	875920	100.00

Chromatogram for sulfonimidamide: (*S*)-10b

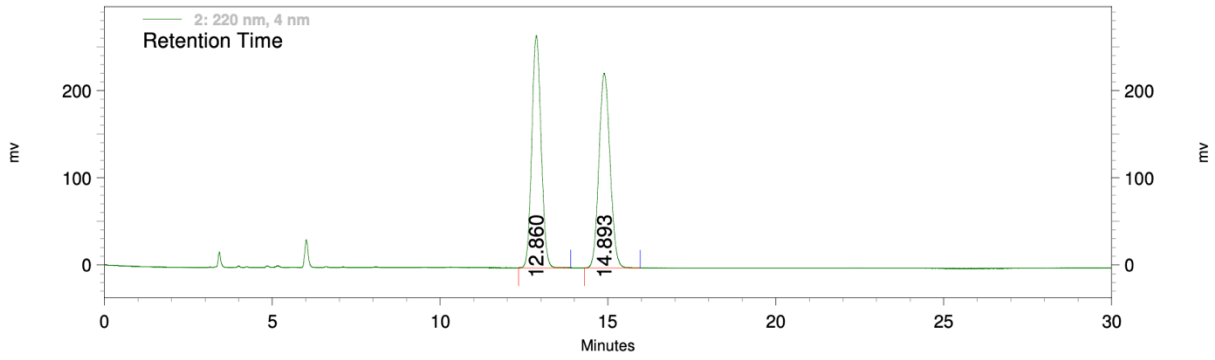


Retention Time	Area	Area %	Height	Height %
6.193	14581	0.09	1774	0.15
6.600	15832441	99.91	1199575	99.85
Totals	15847022	100.00	1201349	100.00



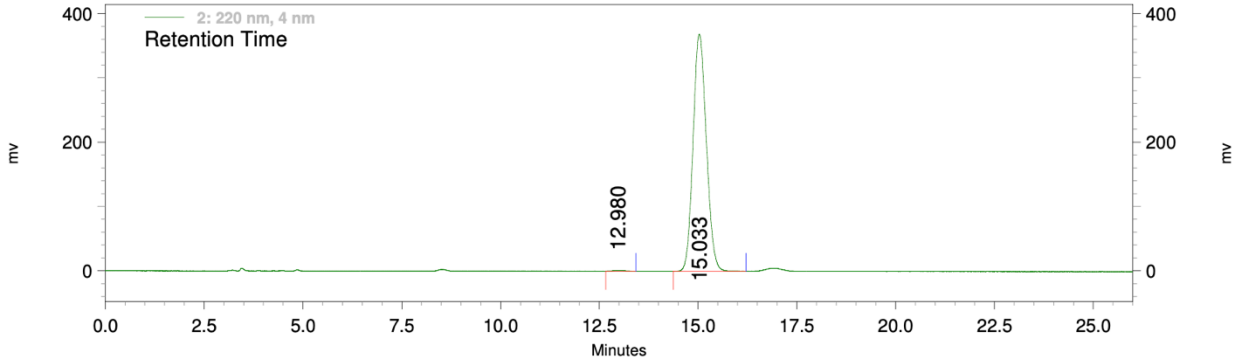
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidoyl fluoride: (*rac*)-12

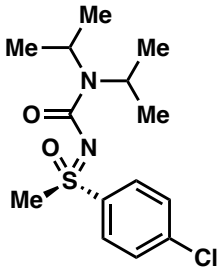


Retention Time	Area	Area %	Height	Height %
12.860	5155112	50.02	266423	54.40
14.893	5150530	49.98	223322	45.60
Totals	10305642	100.00	489745	100.00

Chromatogram for sulfonimidoyl fluoride: (*S*)-12

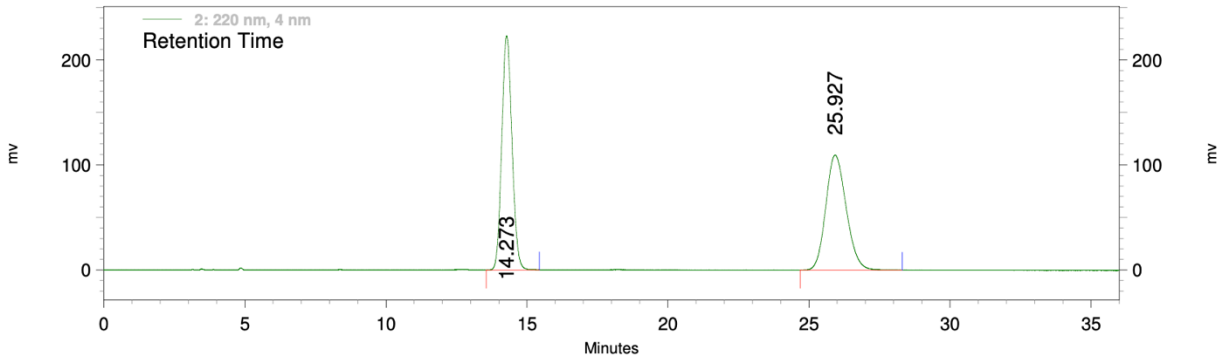


Retention Time	Area	Area %	Height	Height %
12.980	33091	0.38	1612	0.43
15.033	8640478	99.62	369199	99.57
Totals	8673569	100.00	370811	100.00



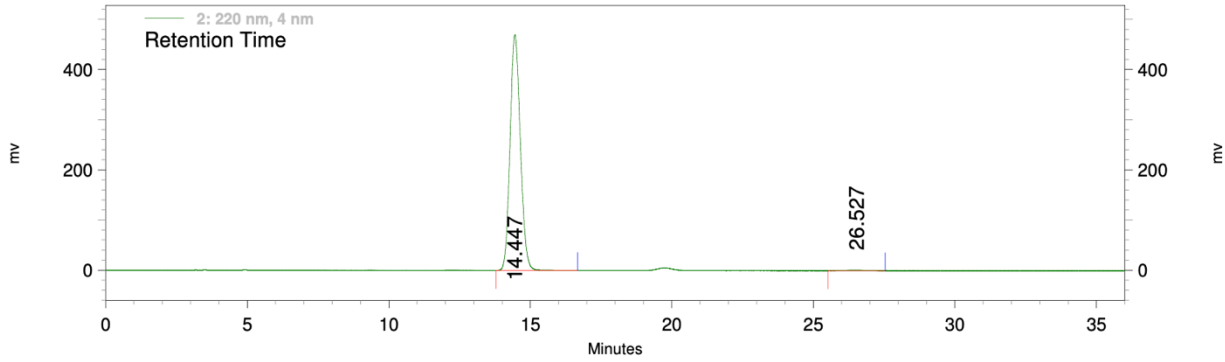
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-13

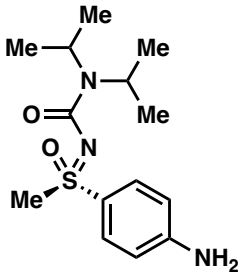


Retention Time	Area	Area %	Height	Height %
14.273	5642446	50.50	223116	67.06
25.927	5529976	49.50	109615	32.94
Totals	11172422	100.00	332731	100.00

Chromatogram for sulfoximine: (*S*)-13

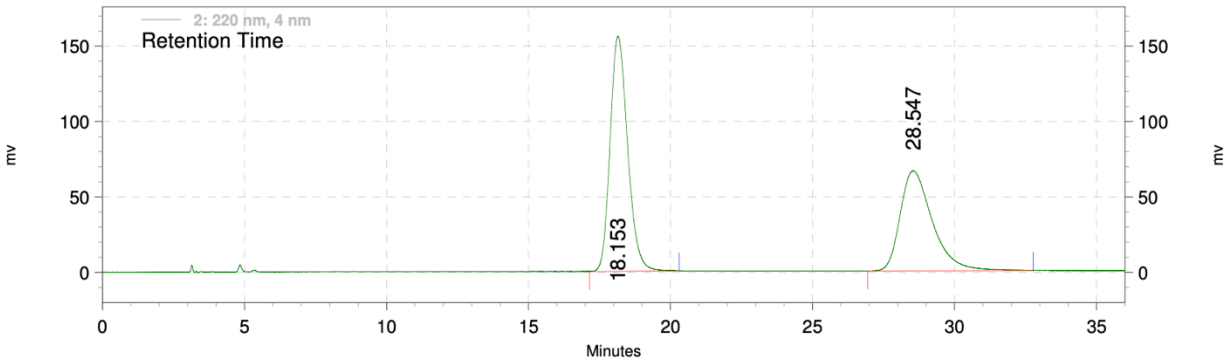


Retention Time	Area	Area %	Height	Height %
14.447	11928605	99.53	469990	99.78
26.527	56062	0.47	1032	0.22
Totals	11984667	100.00	471022	100.00



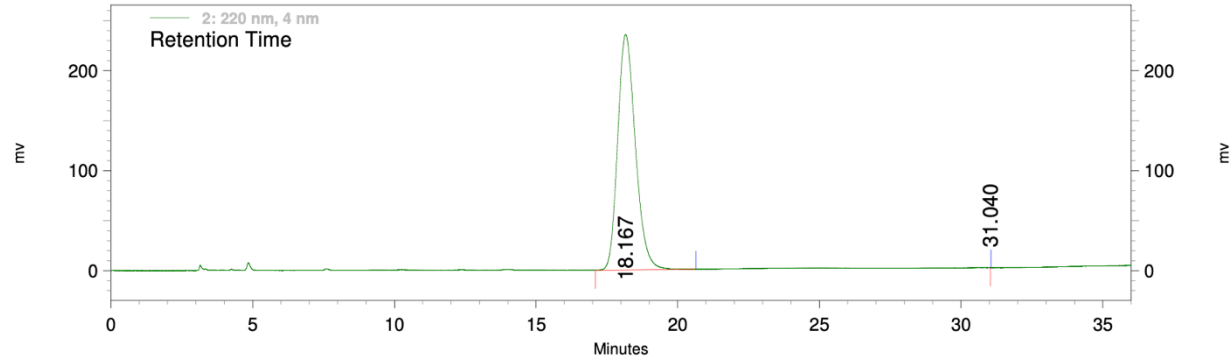
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-16

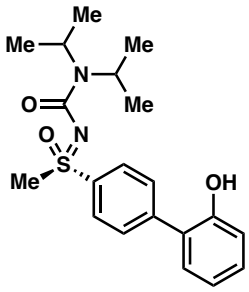


Retention Time	Area	Area %	Height	Height %
18.153	6693863	56.23	155934	70.17
28.547	5209753	43.77	66295	29.83
Totals	11903616	100.00	222229	100.00

Chromatogram for sulfoximine: (*S*)-16

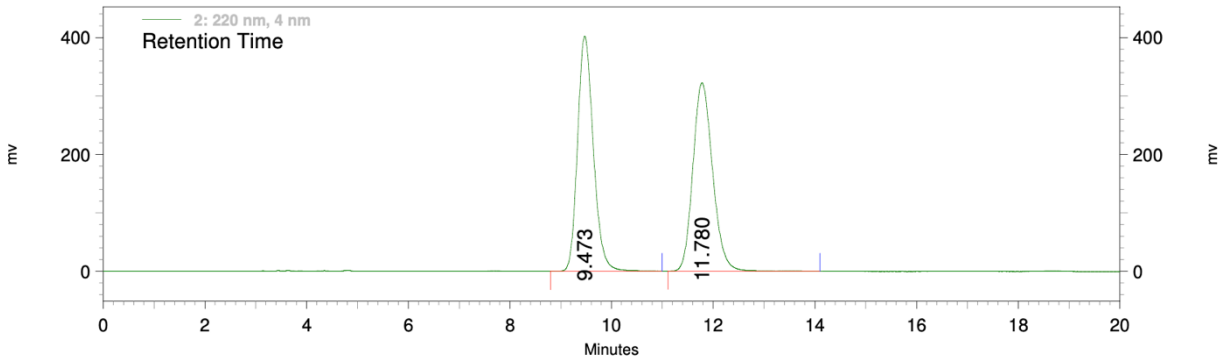


Retention Time	Area	Area %	Height	Height %
18.167	10257275	100.00	235677	99.93
31.040	104	0.00	158	0.07
Totals	10257379	100.00	235835	100.00



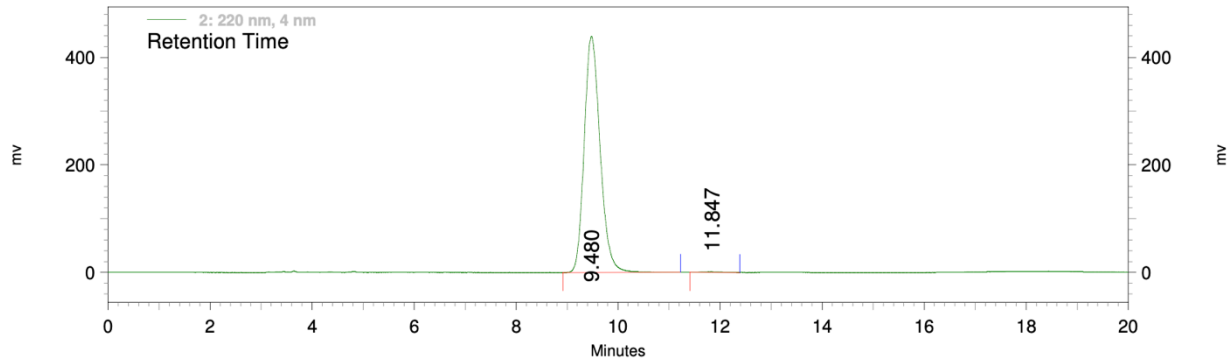
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-urea protected 15

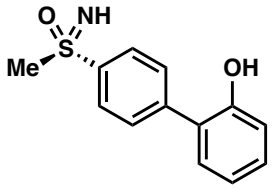


Retention Time	Area	Area %	Height	Height %
9.473	8711406	49.96	402538	55.53
11.780	8726869	50.04	322403	44.47
Totals	17438275	100.00	724941	100.00

Chromatogram for sulfoximine: (*S*)-urea protected 15

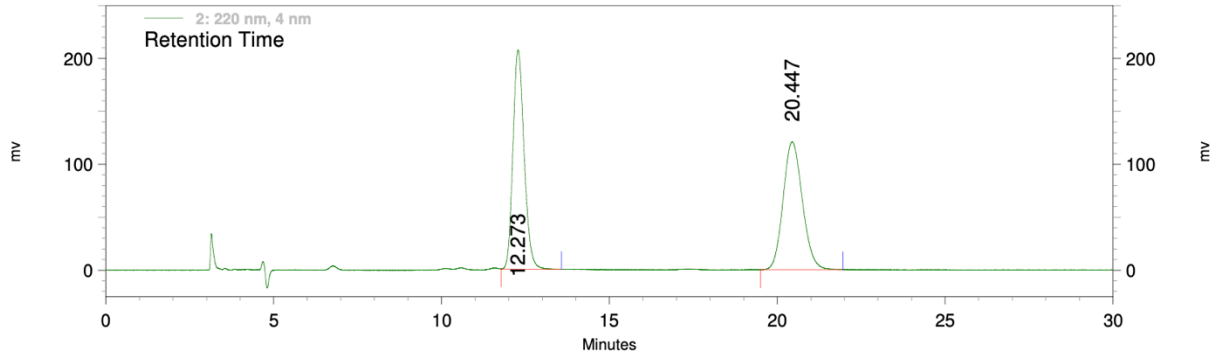


Retention Time	Area	Area %	Height	Height %
9.480	9527986	99.65	439718	99.71
11.847	33056	0.35	1279	0.29
Totals	9561042	100.00	440997	100.00



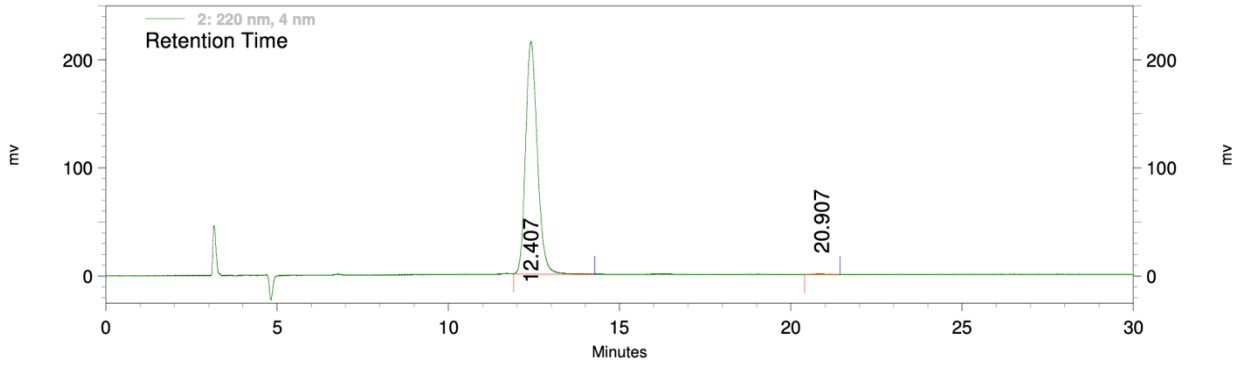
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-15

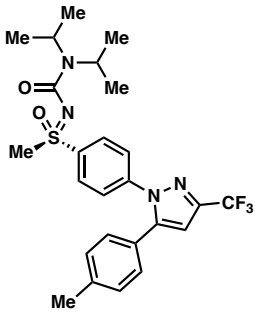


Retention Time	Area	Area %	Height	Height %
12.273	4810476	49.93	206899	63.11
20.447	4824227	50.07	120931	36.89
Totals	9634703	100.00	327830	100.00

Chromatogram for sulfoximine: (*S*)-15

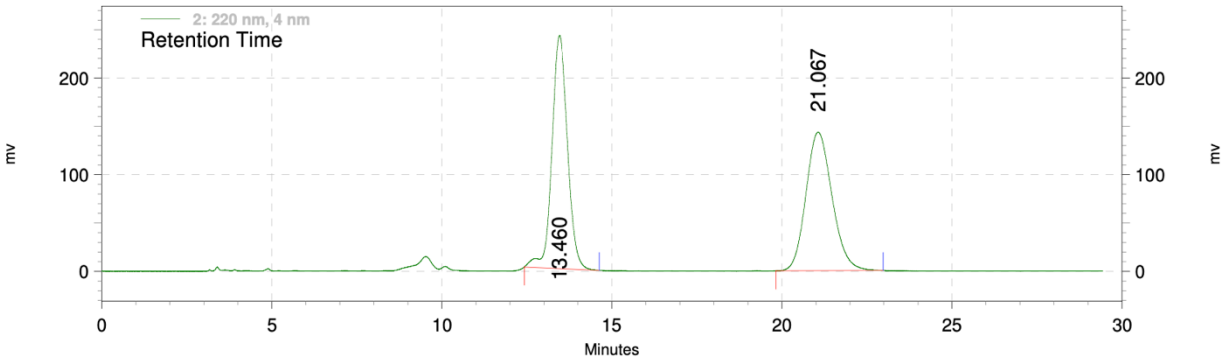


Retention Time	Area	Area %	Height	Height %
12.407	5129210	99.59	214841	99.71
20.907	21153	0.41	619	0.29
Totals	5150363	100.00	215460	100.00



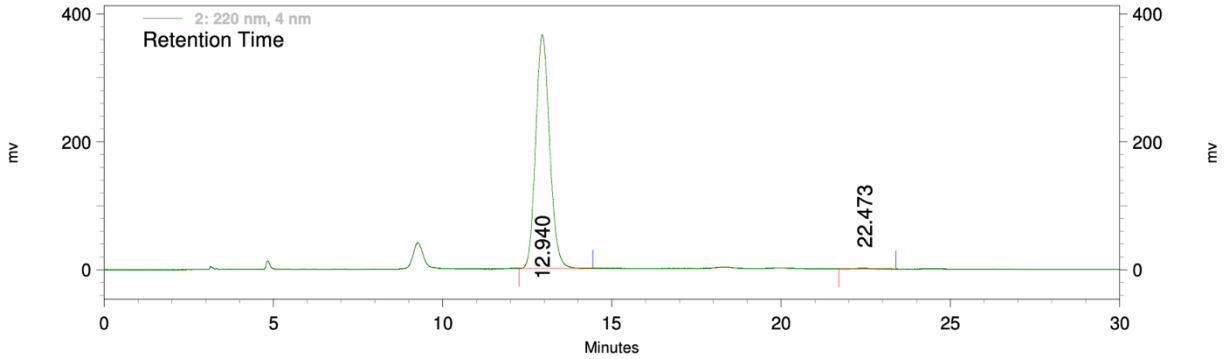
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-19

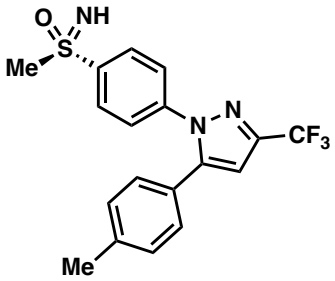


Retention Time	Area	Area %	Height	Height %
13.700	15976427	49.18	528282	62.68
21.347	16508974	50.82	314498	37.32
Totals	32485401	100.00	842780	100.00

Chromatogram for sulfoximine: (*S*)-19

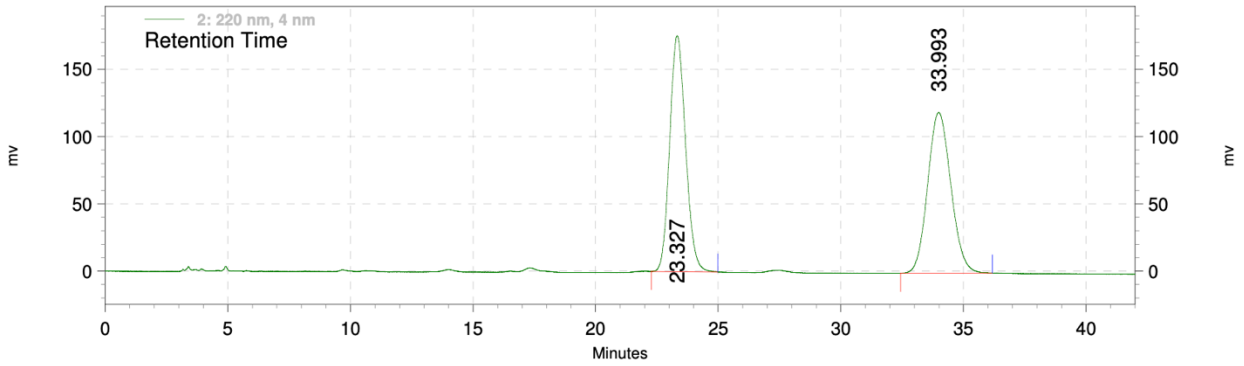


Retention Time	Area	Area %	Height	Height %
12.940	10446764	99.54	365306	99.70
22.473	48617	0.46	1096	0.30
Totals	10495381	100.00	366402	100.00



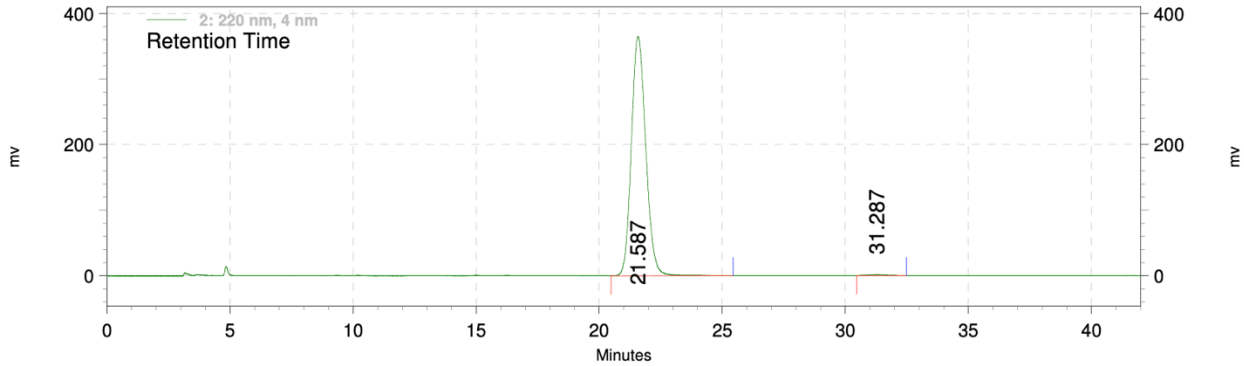
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfoximine: (*rac*)-20

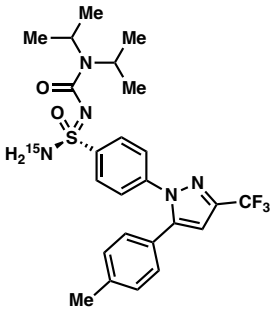


Retention Time	Area	Area %	Height	Height %
23.327	7891203	50.10	175310	59.46
33.993	7858739	49.90	119522	40.54
Totals	15749942	100.00	294832	100.00

Chromatogram for sulfoximine: (*S*)-20

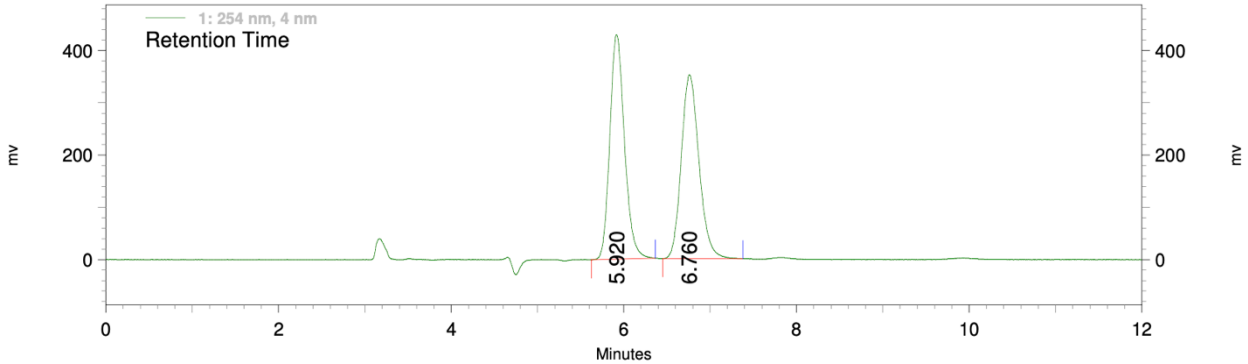


Retention Time	Area	Area %	Height	Height %
21.587	14833945	99.50	364841	99.62
31.287	75002	0.50	1391	0.38
Totals	14908947	100.00	366232	100.00



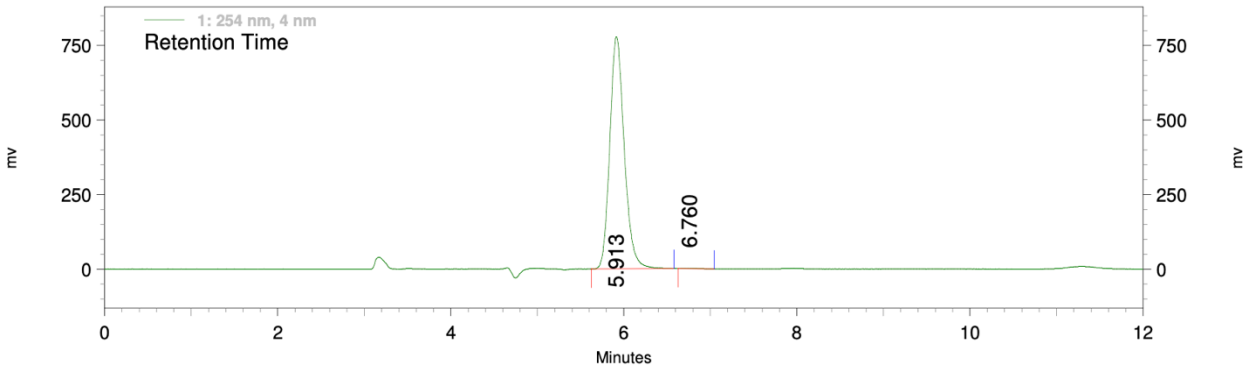
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidamide: (*rac*)-21

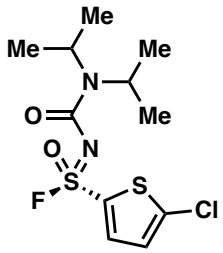


Retention Time	Area	Area %	Height	Height %
5.920	5064533	50.23	429288	54.98
6.760	5018726	49.77	351559	45.02
Totals	10083259	100.00	780847	100.00

Chromatogram for sulfonimidamide: (*R*)-21

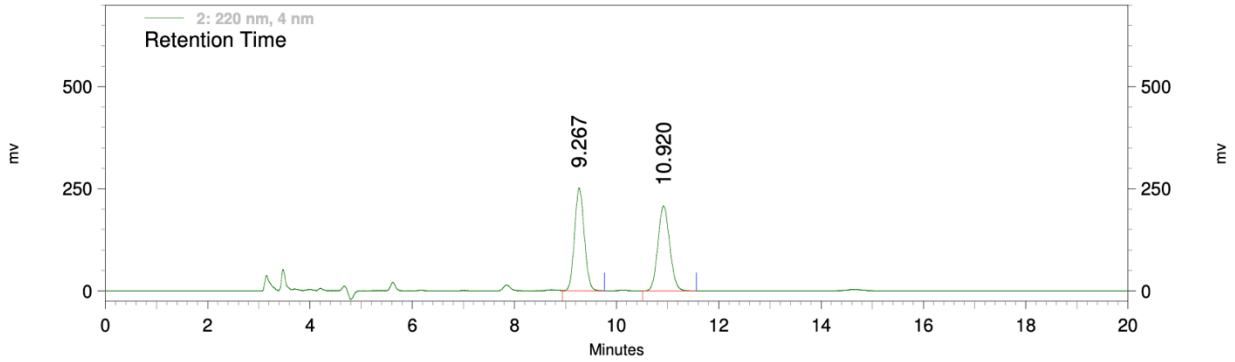


Retention Time	Area	Area %	Height	Height %
5.913	9055337	99.79	778548	99.81
6.760	18895	0.21	1494	0.19
Totals	9074232	100.00	780042	100.00



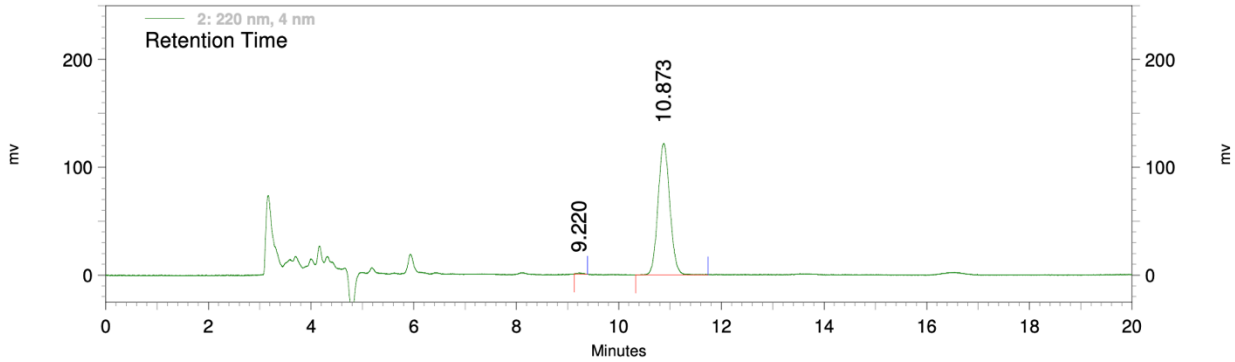
Column: Daicel Chiralpak IC; **Solvent:** *n*-hexane/IPA (70:30); **flowrate:** 1 mL/min

Chromatogram for sulfonimidoyl fluoride: (*rac*)-24



Retention Time	Area	Area %	Height	Height %
9.267	3322402	49.87	250933	54.71
10.920	3339908	50.13	207768	45.29
Totals	6662310	100.00	458701	100.00

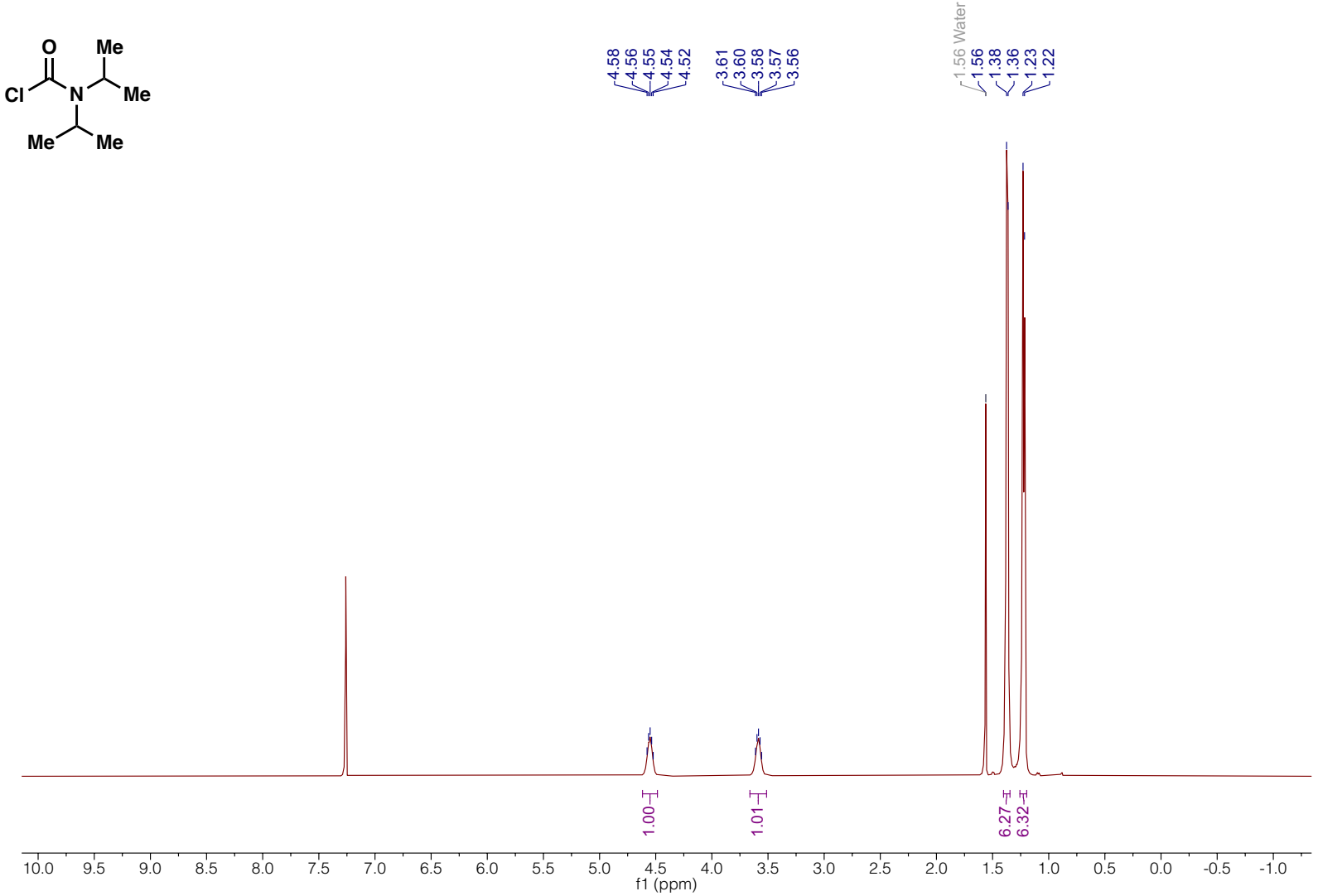
Chromatogram for sulfonimidoyl fluoride: (*S*)-24



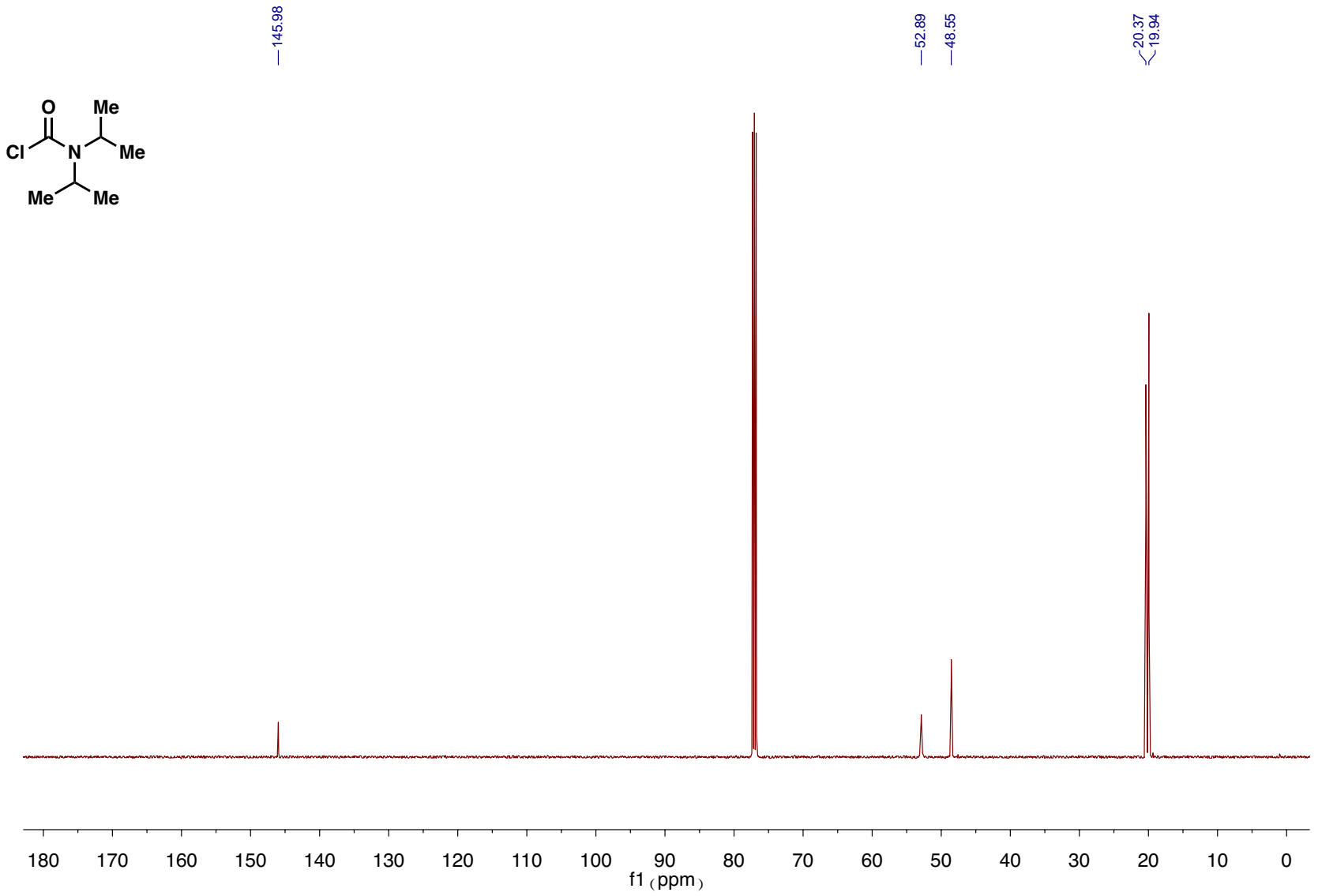
Retention Time	Area	Area %	Height	Height %
9.220	8254	0.42	1046	0.85
10.873	1946605	99.58	121833	99.15
Totals	1954859	100.00	122879	100.00

XIII. NMR Spectra

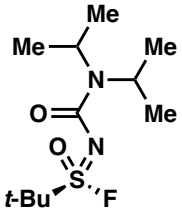
^{1}H NMR of *N,N*-diisopropyl carbamoyl chloride:



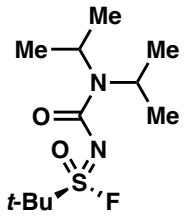
^{13}C NMR of *N,N*-diisopropyl carbamoyl chloride:



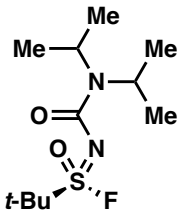
^{1}H NMR of compound (*S*)-*t*-BuSF:



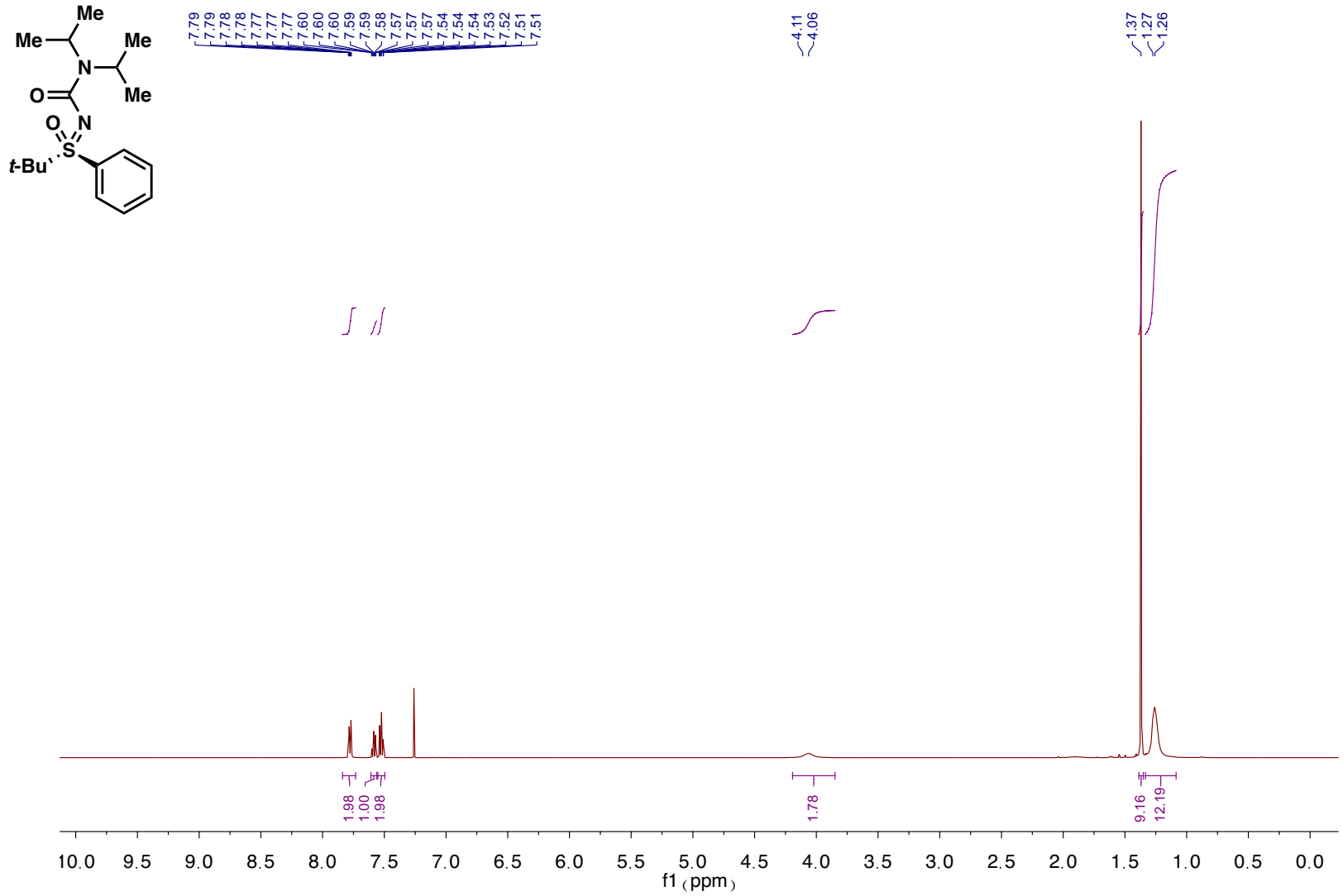
^{13}C NMR of compound (*S*)-*t*-BuSF:



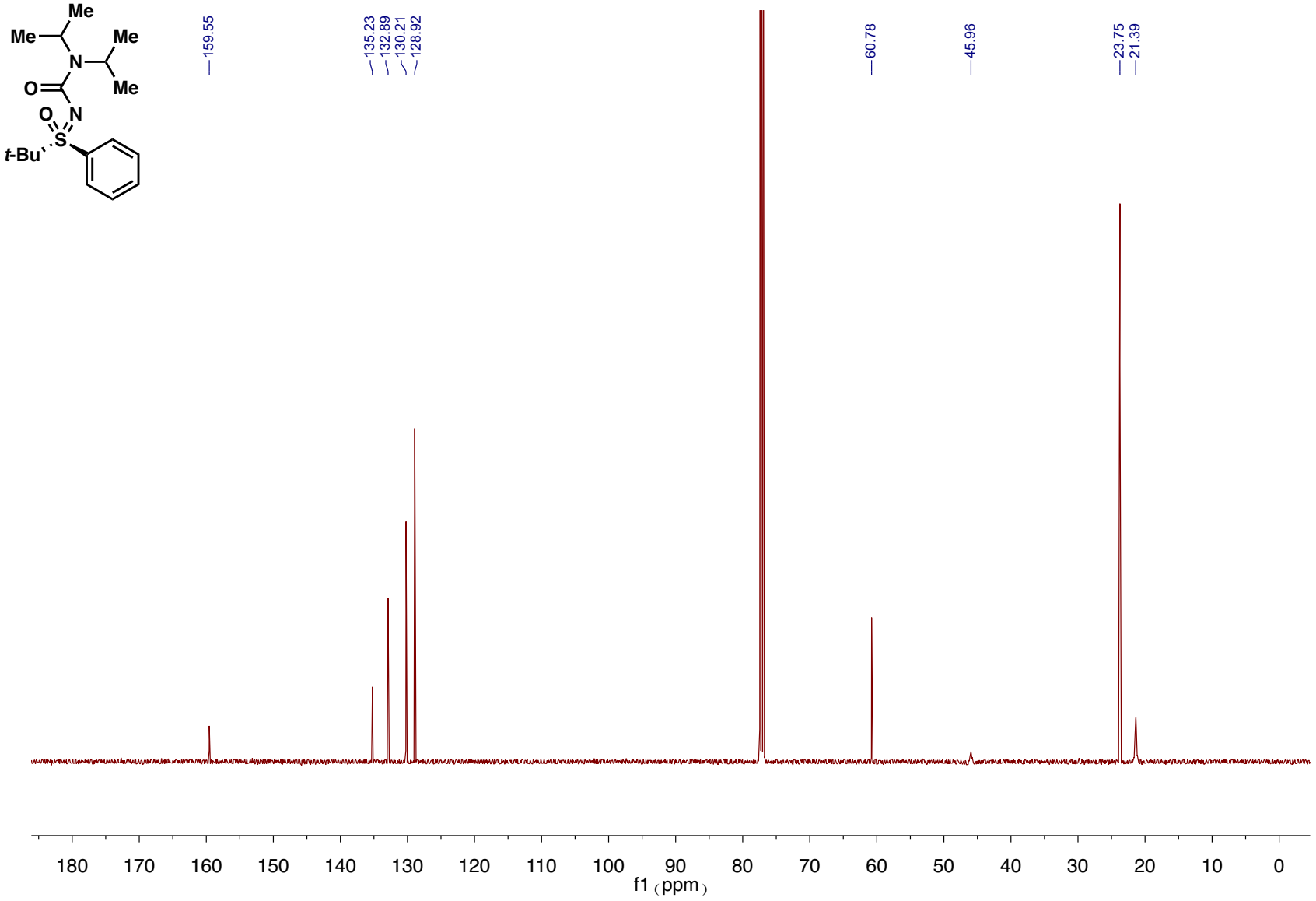
^{19}F NMR of compound (*S*)-*t*-BuSF:



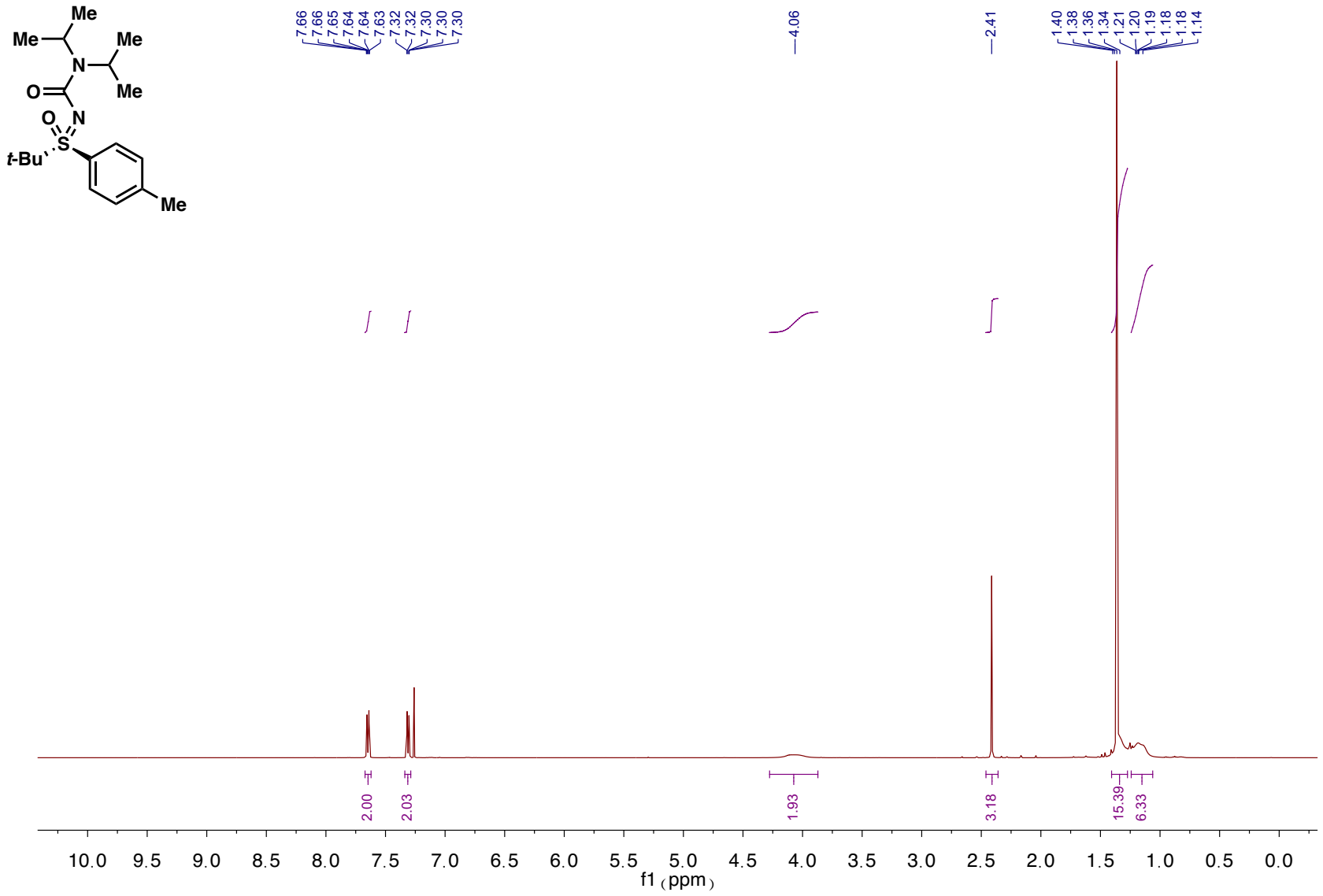
^{1}H NMR of compound 2a:



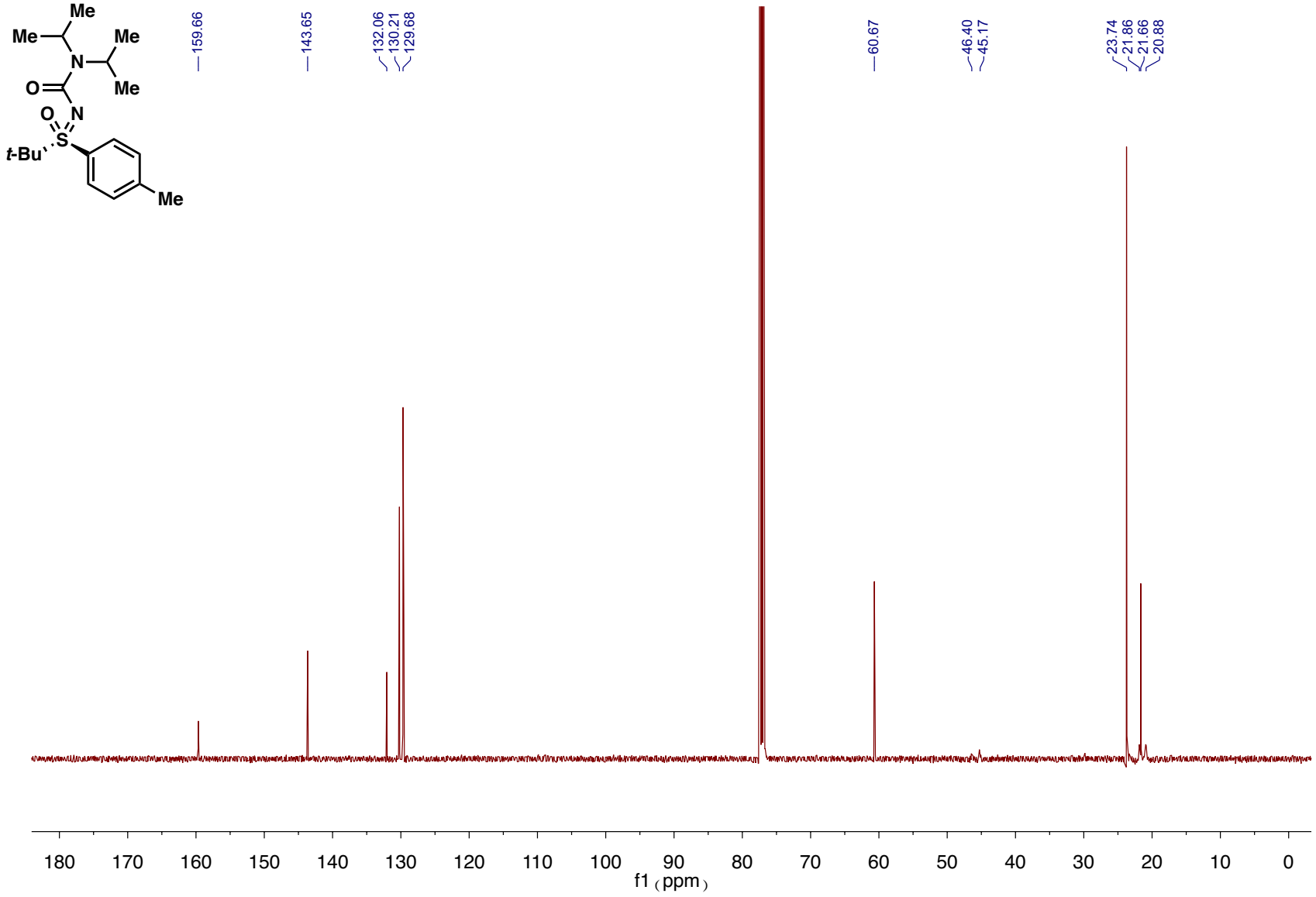
^{13}C NMR of compound 2a:



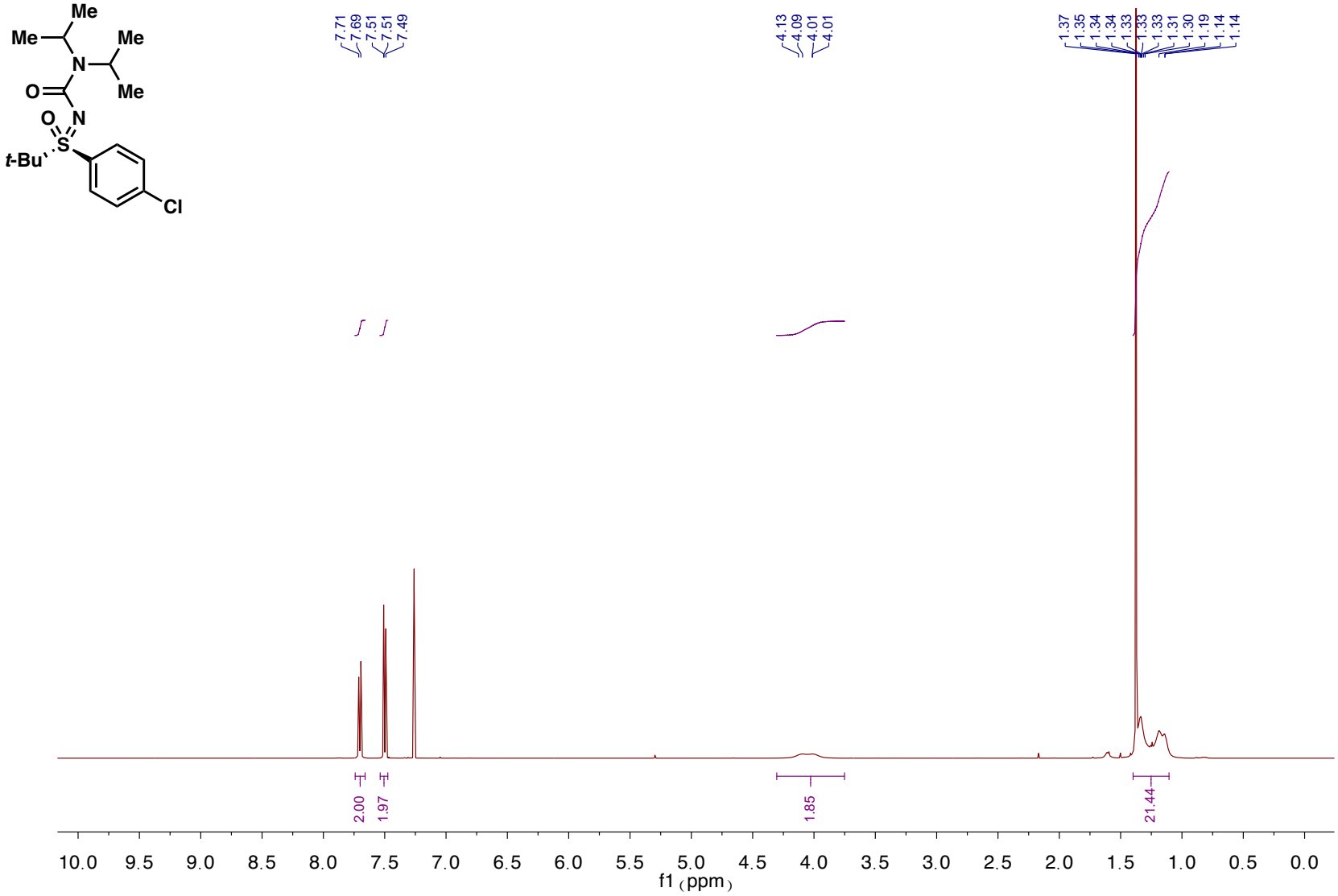
^{1}H NMR of compound 2b:



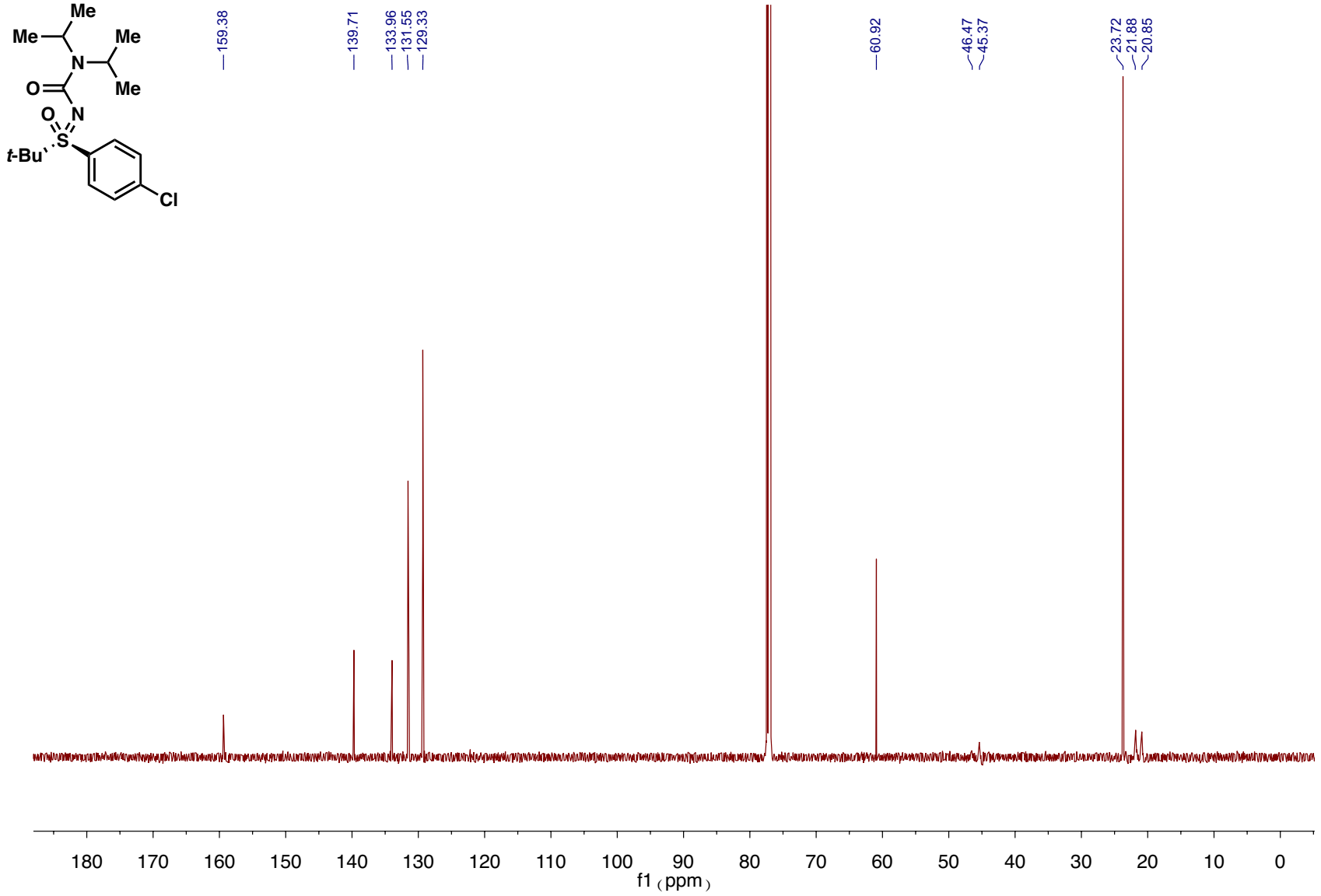
^{13}C NMR of compound 2b:



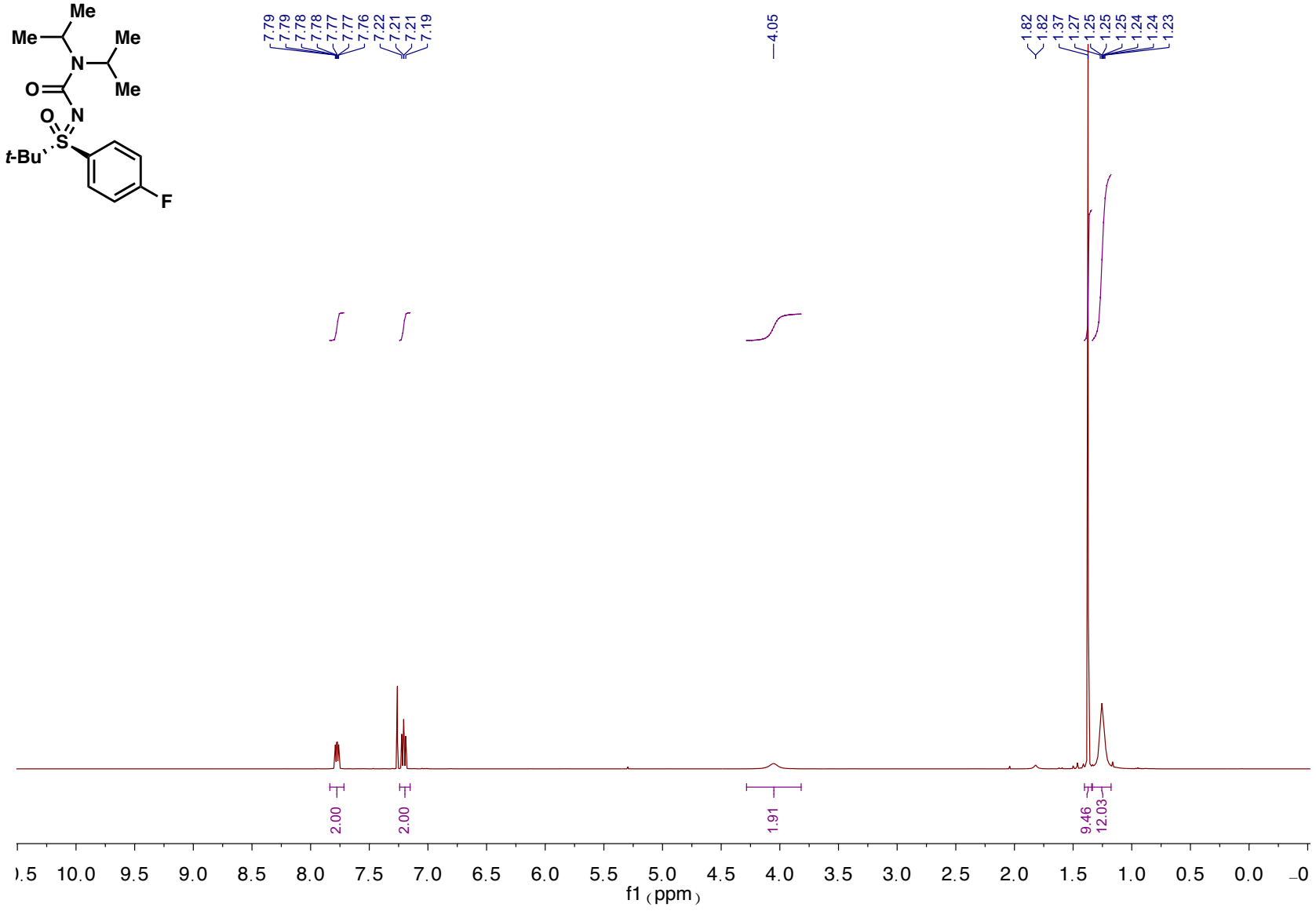
^{1}H NMR of compound 2c:



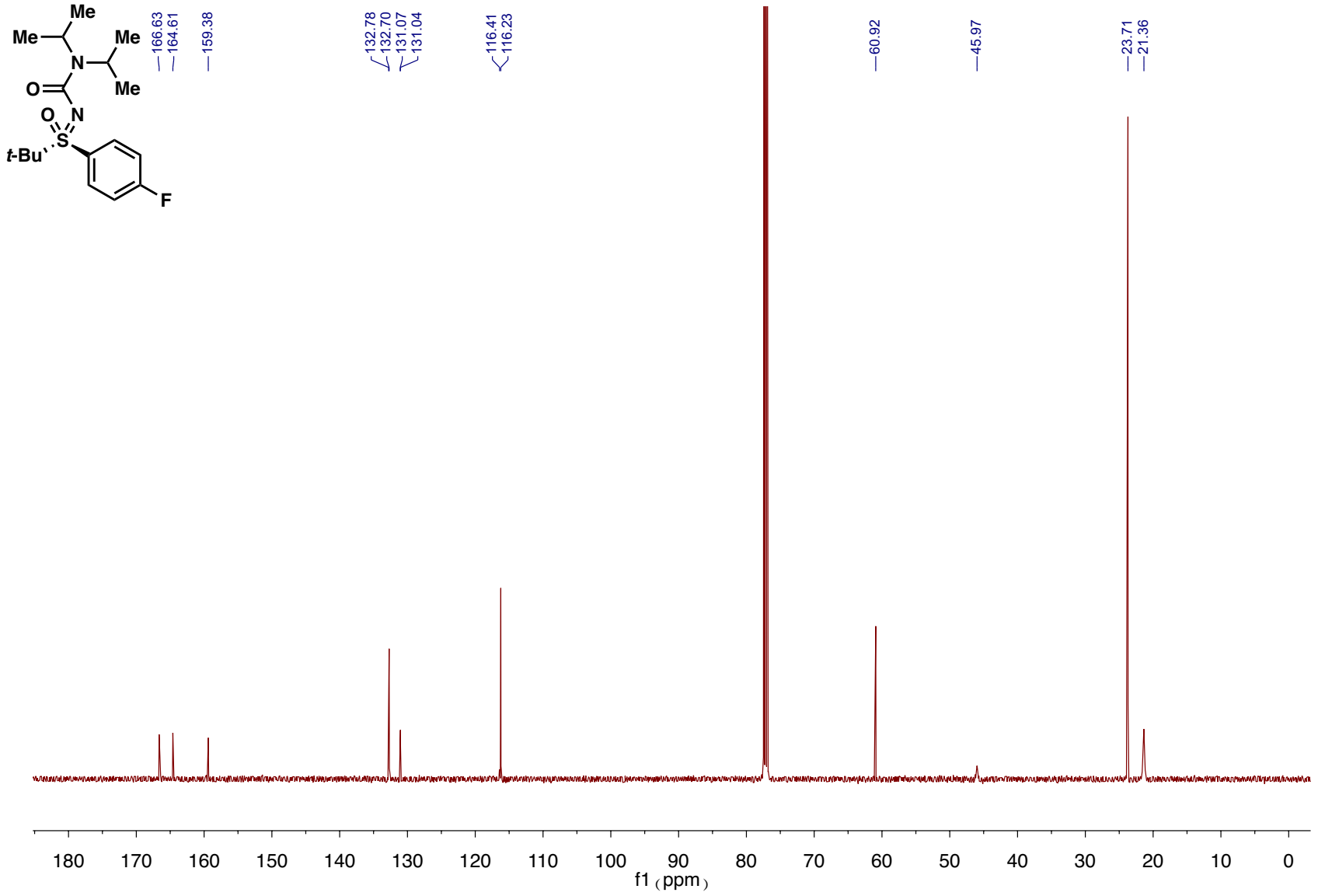
^{13}C NMR of compound 2c:



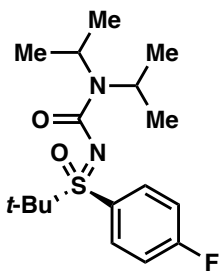
^{1}H NMR of compound 2d:



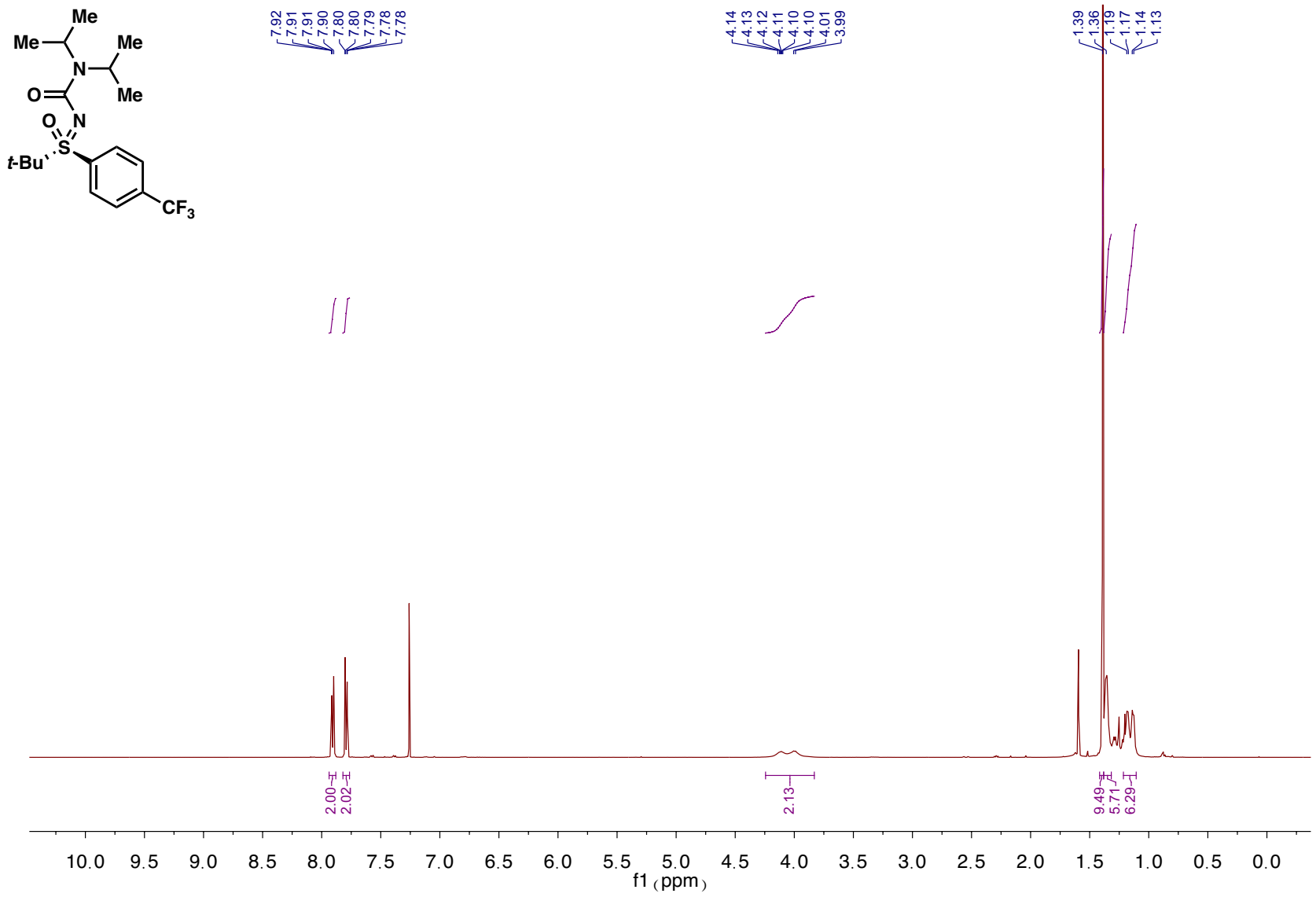
^{13}C NMR of compound 2d:



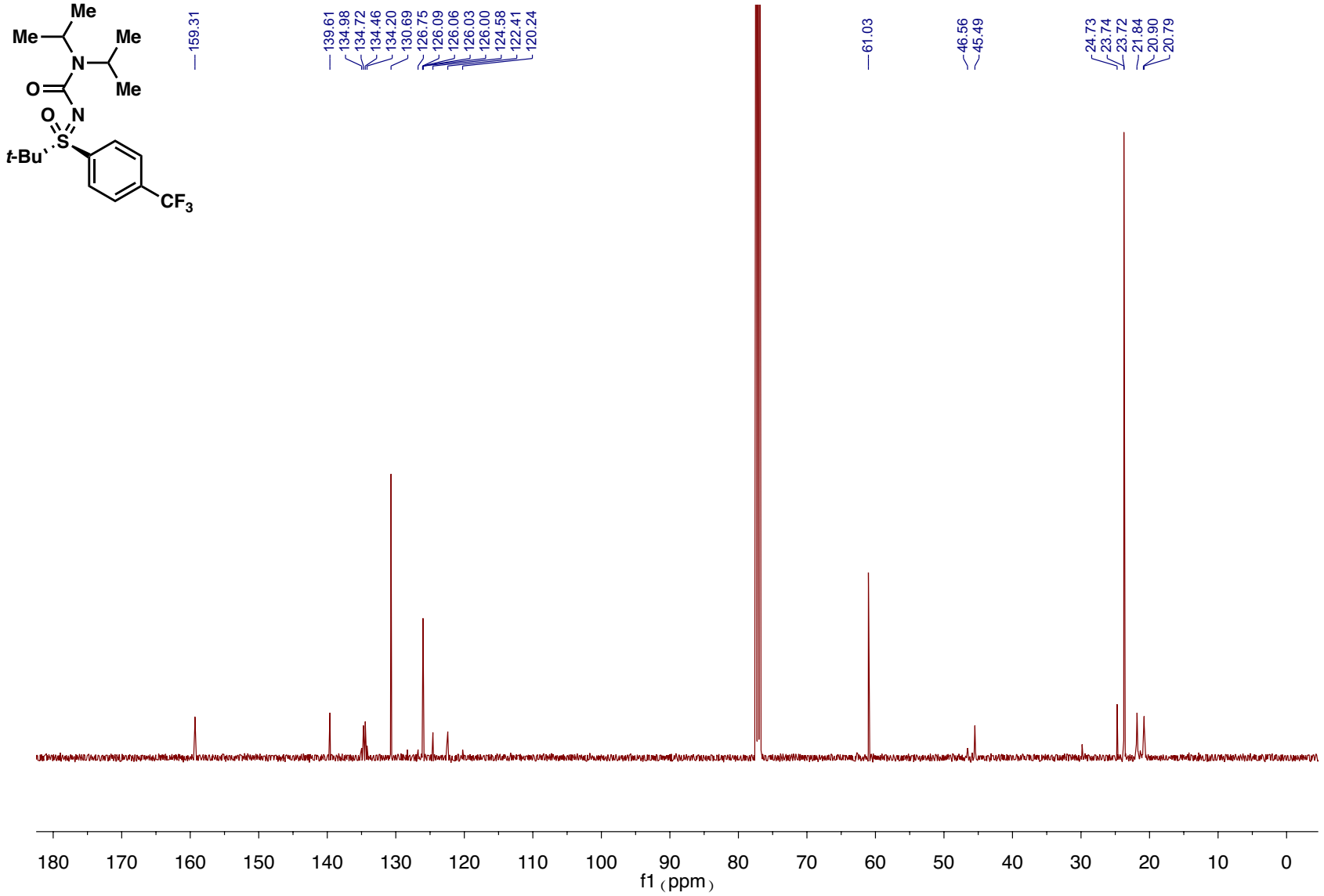
^{19}F NMR of compound 2d:



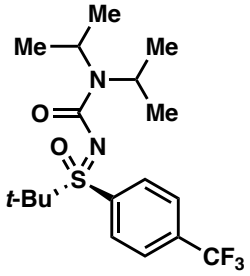
^{1}H NMR of compound 2e:



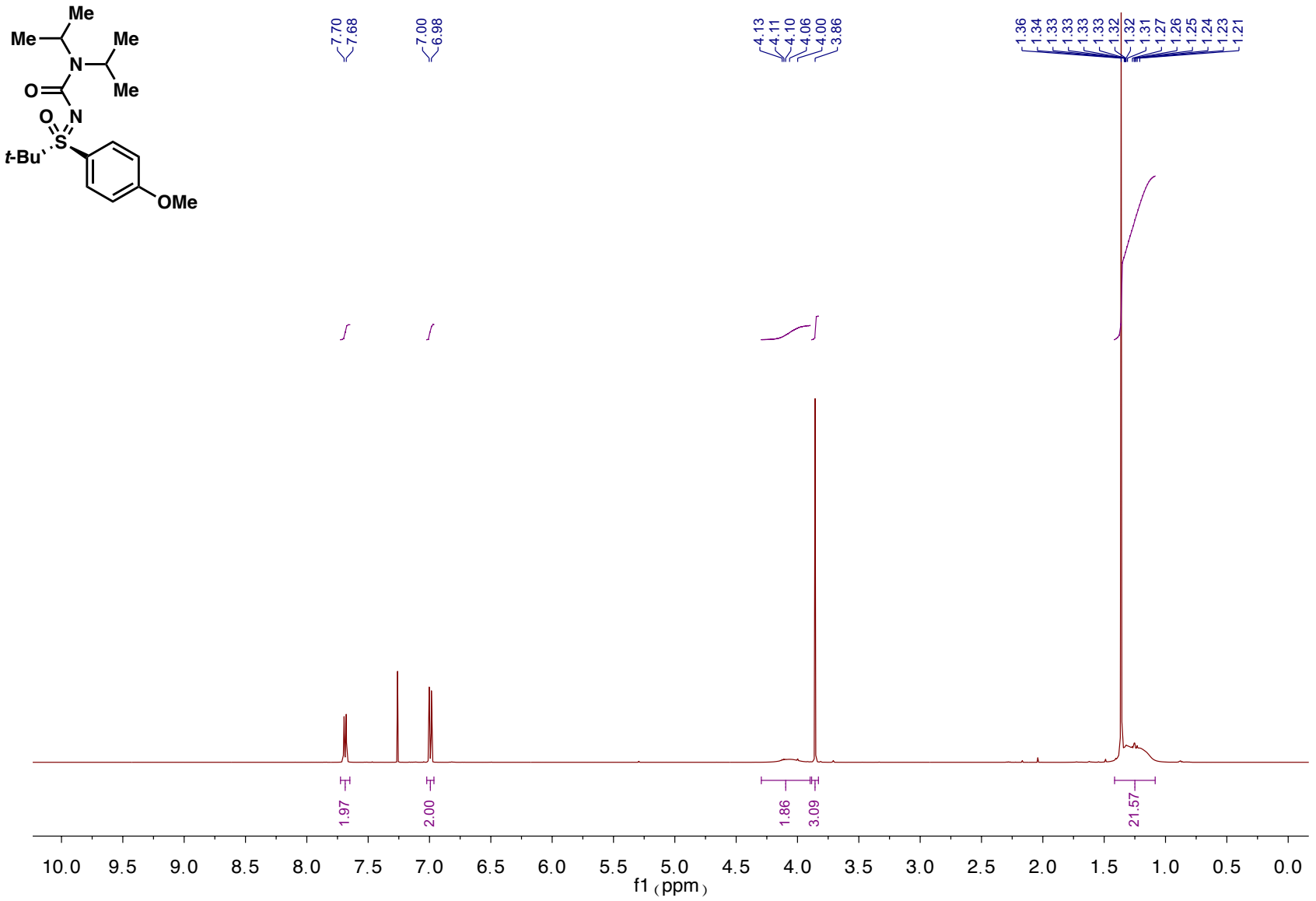
^{13}C NMR of compound 2e:



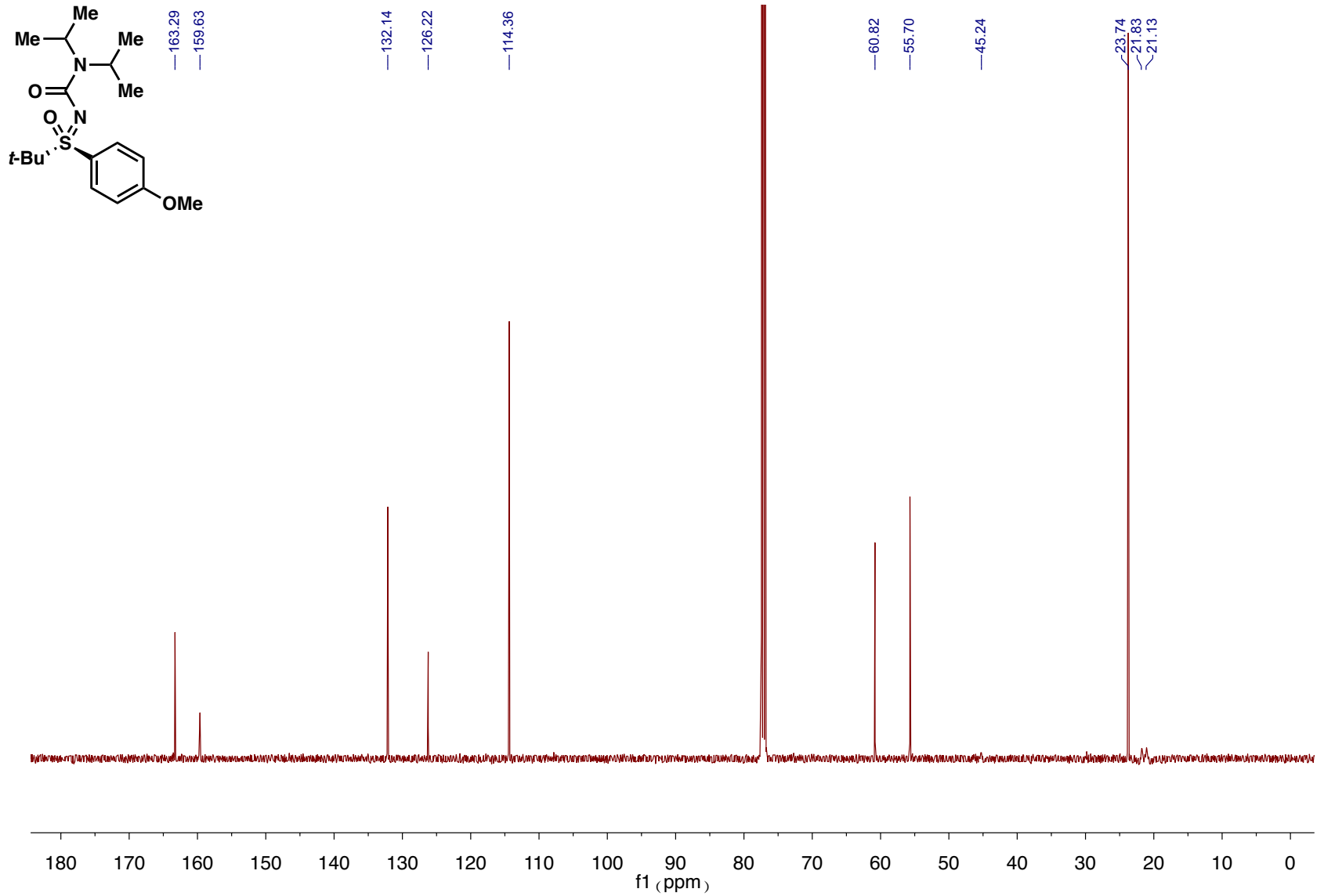
^{19}F NMR of compound 2e:



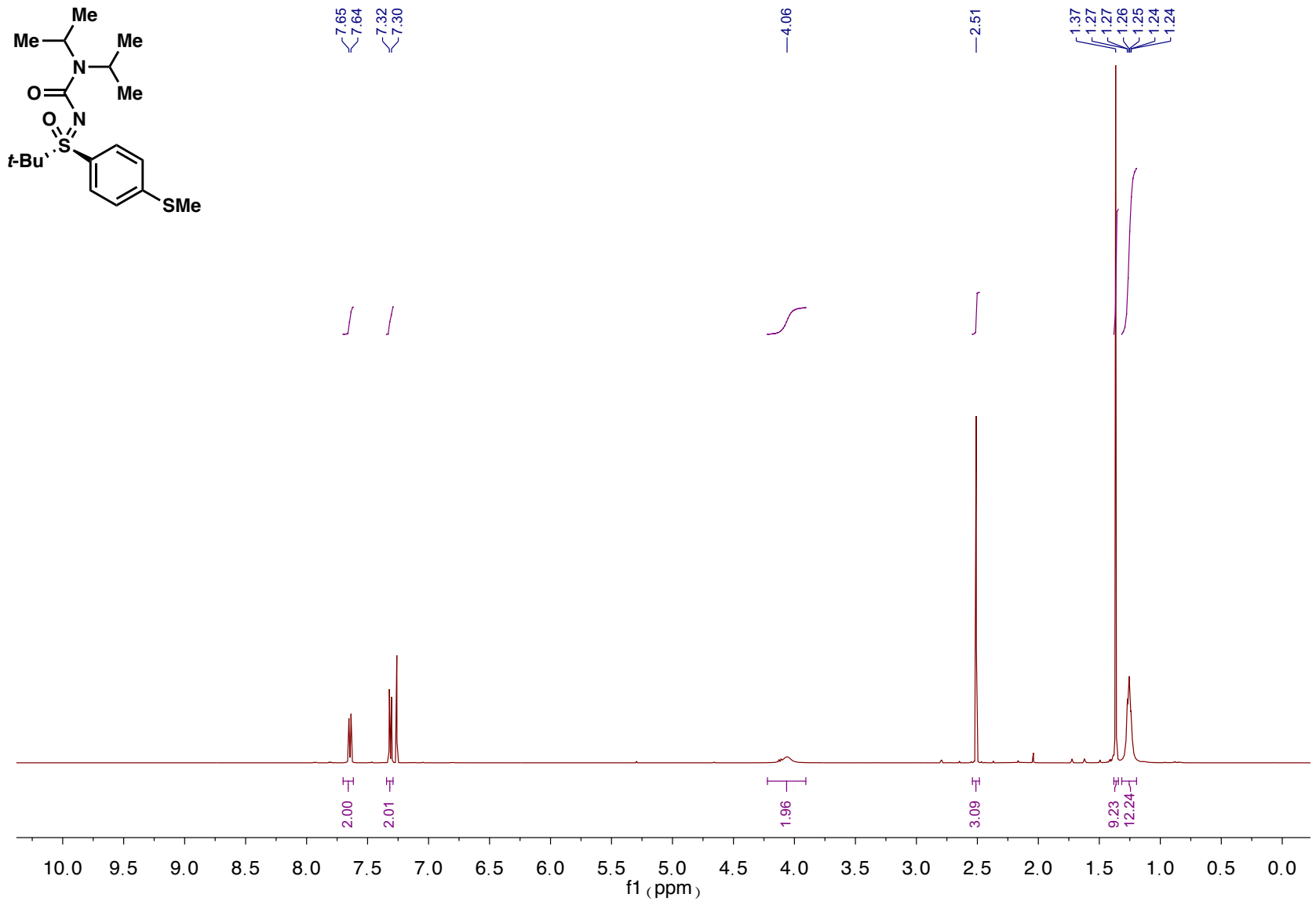
^{1}H NMR of compound 2f:



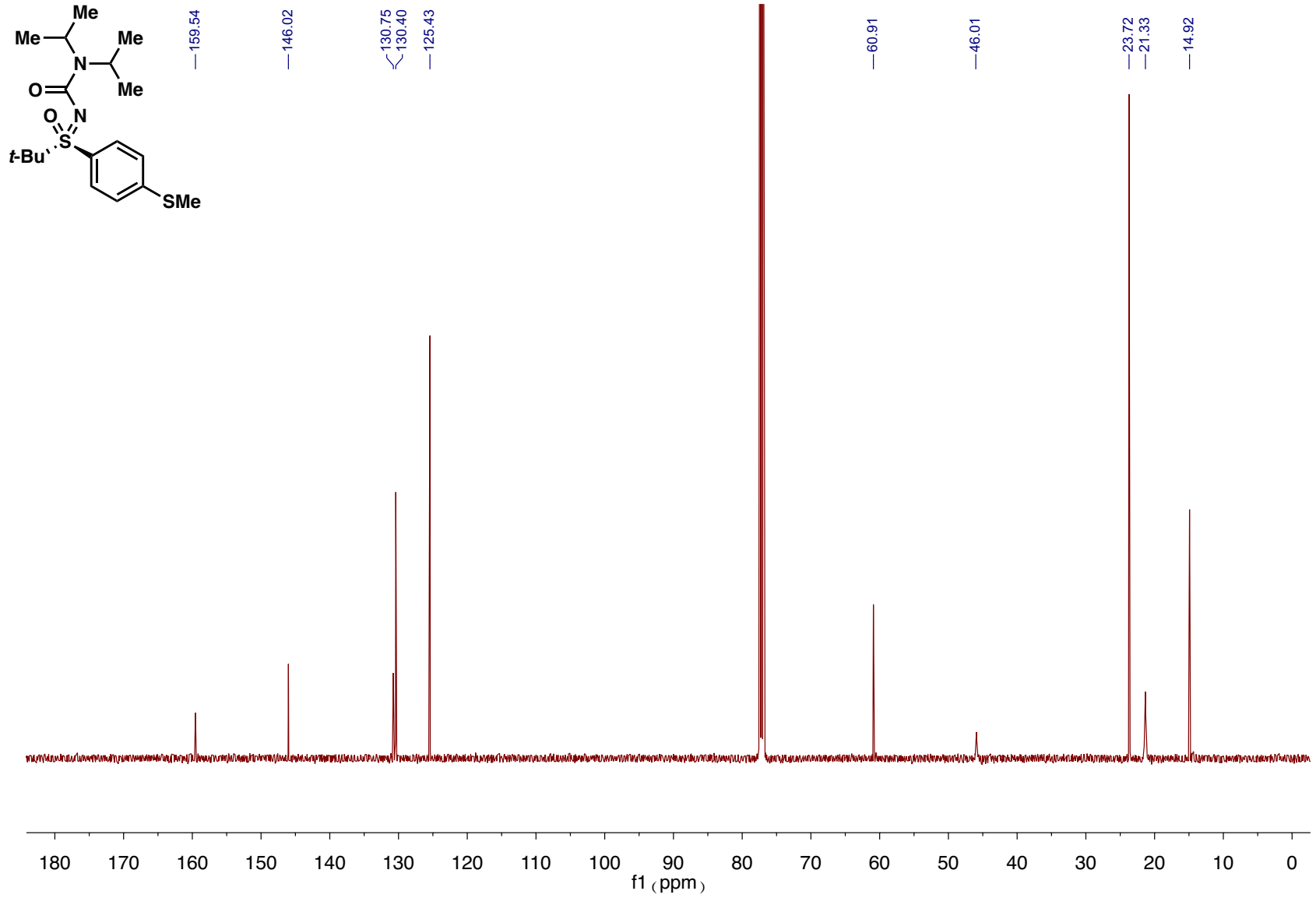
^{13}C NMR of compound 2f:



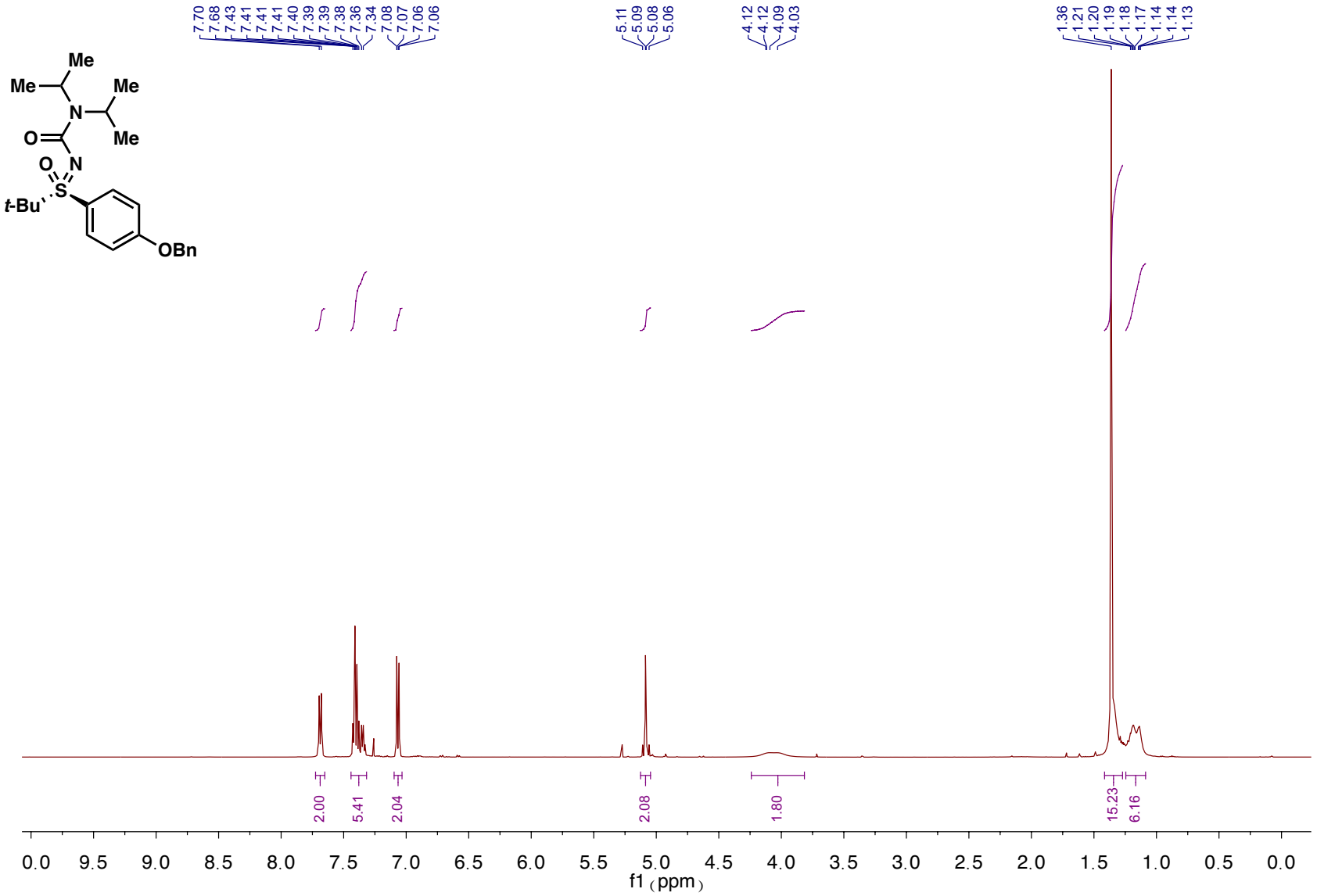
^{1}H NMR of compound 2g:



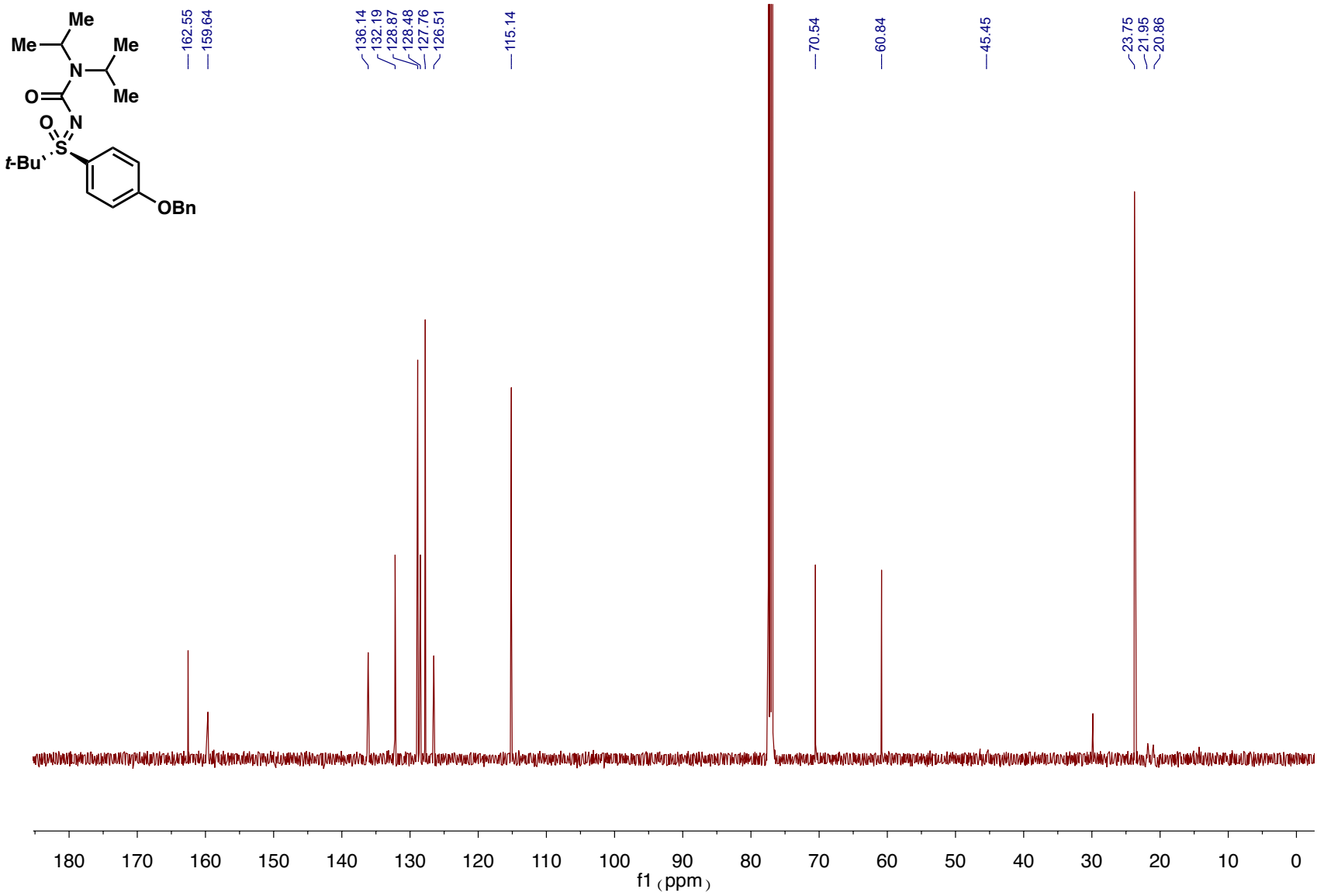
^{13}C NMR of compound 2g:



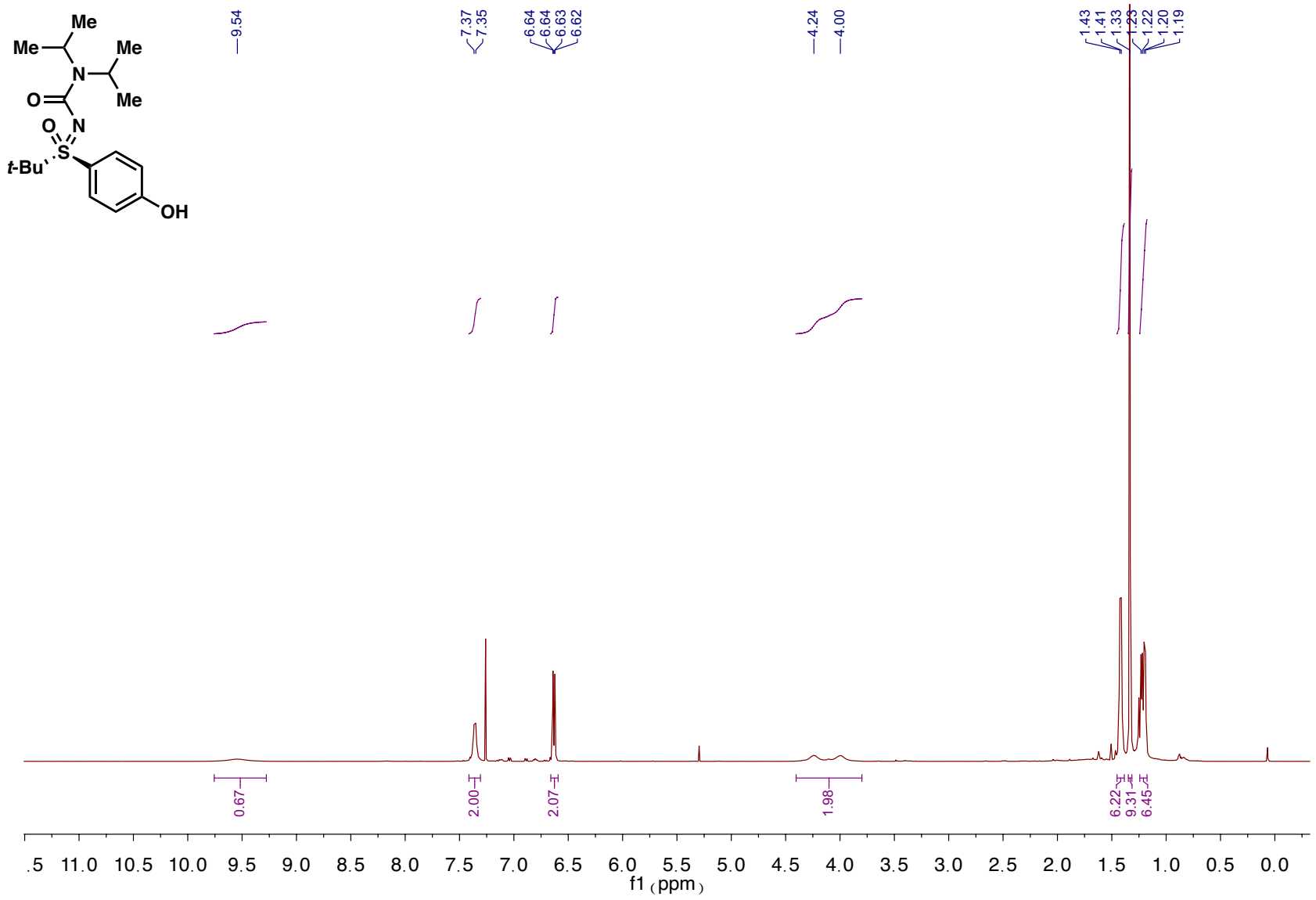
^{1}H NMR of compound 2h:



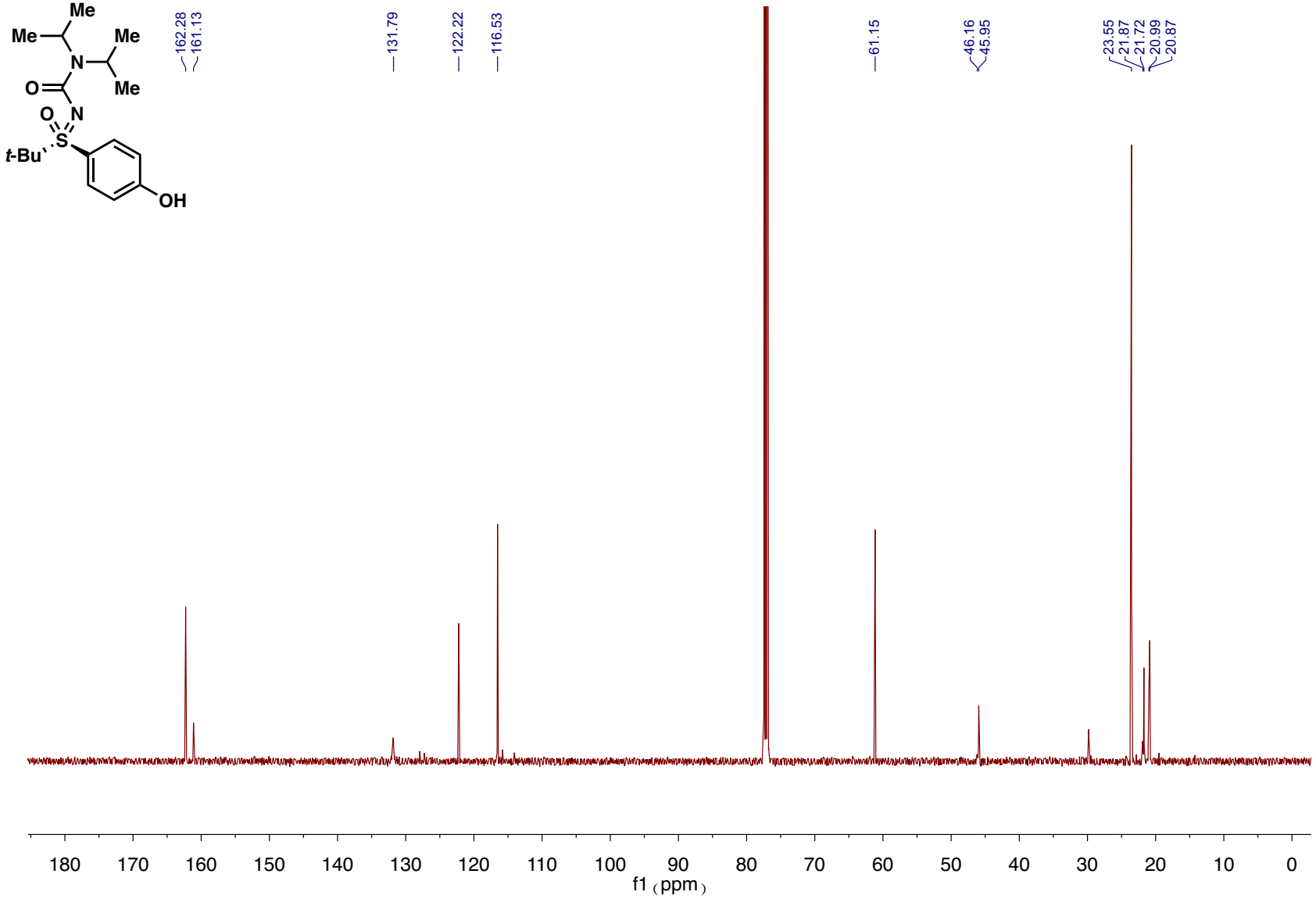
^{13}C NMR of compound 2h:



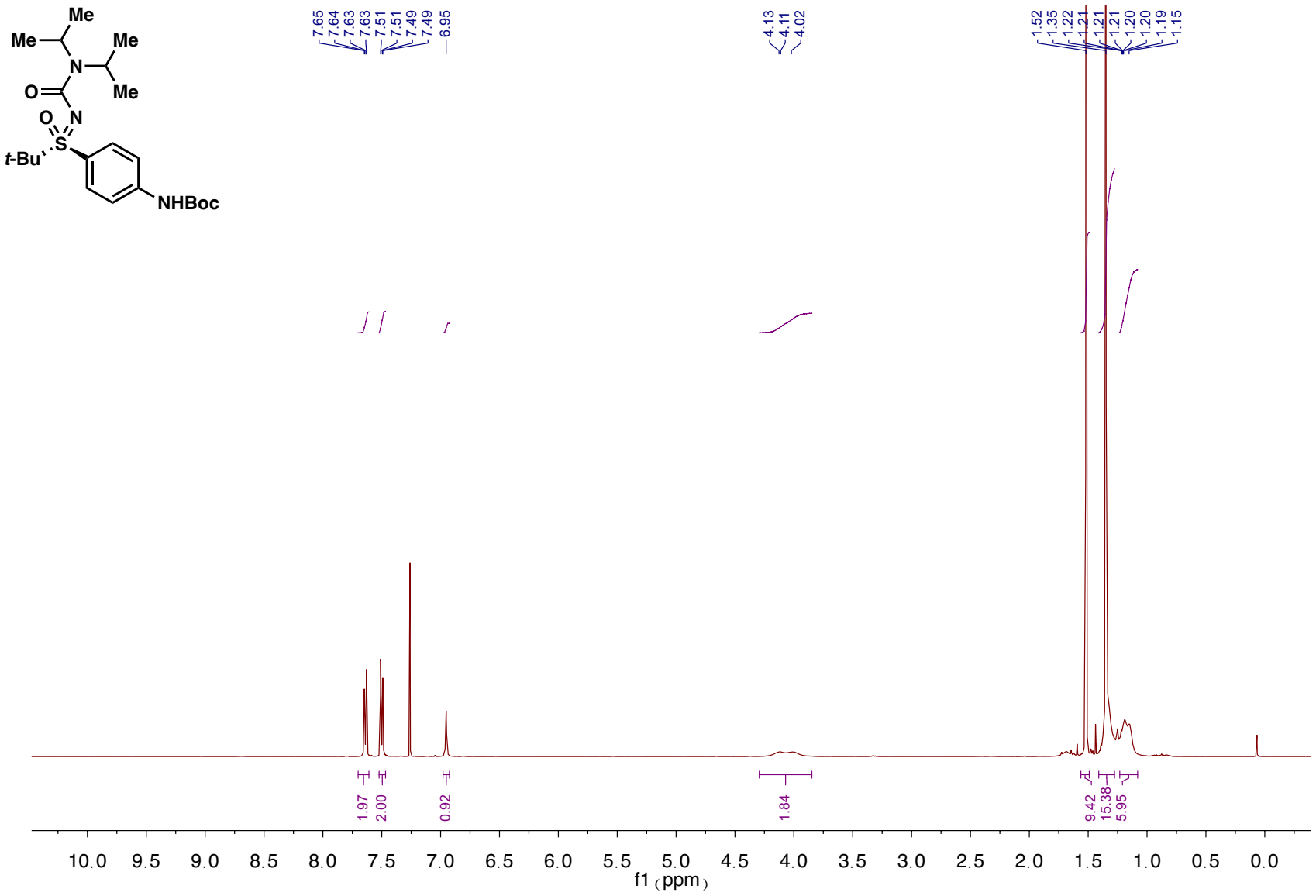
^{1}H NMR of compound 2i:



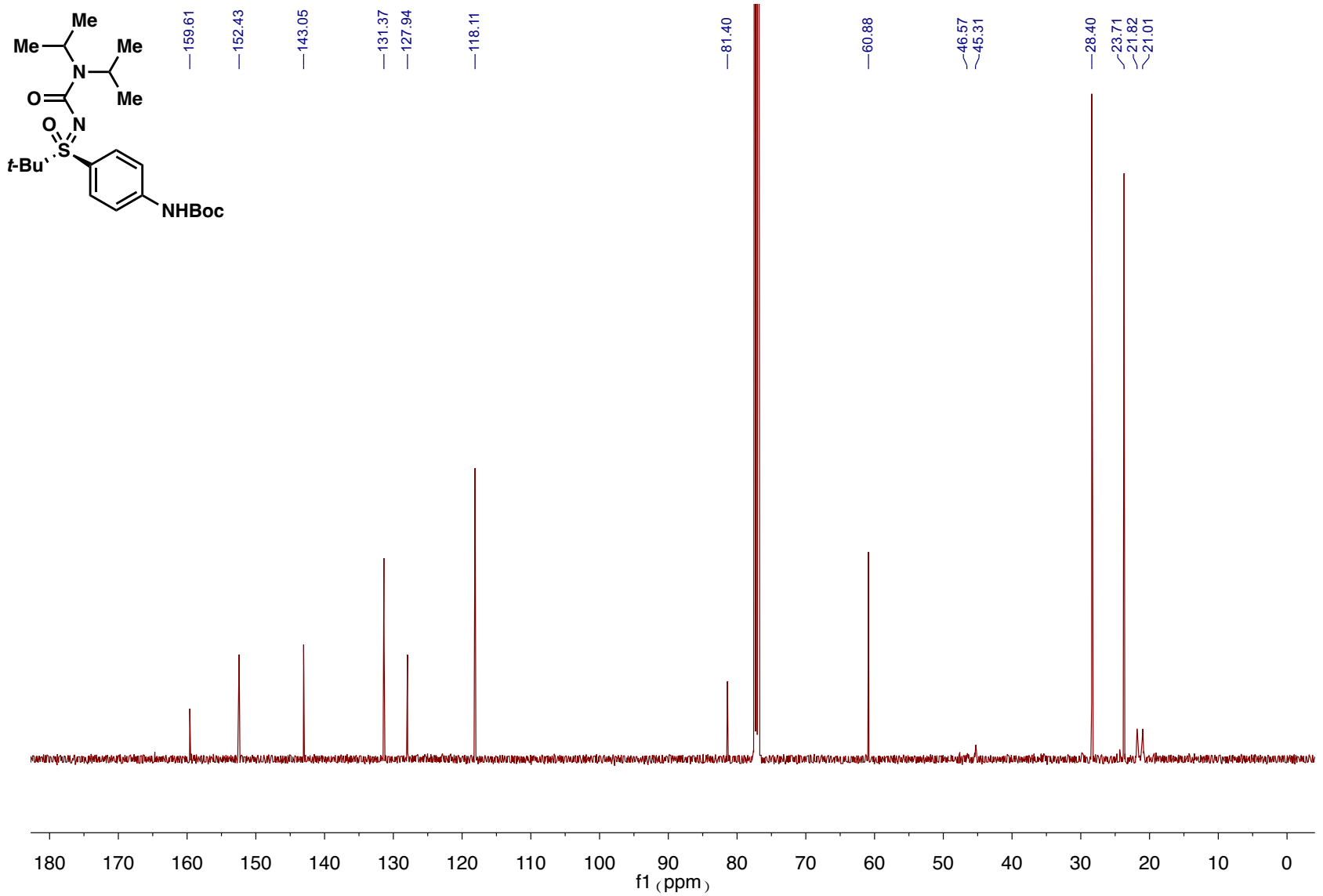
^{13}C NMR of compound 2i:



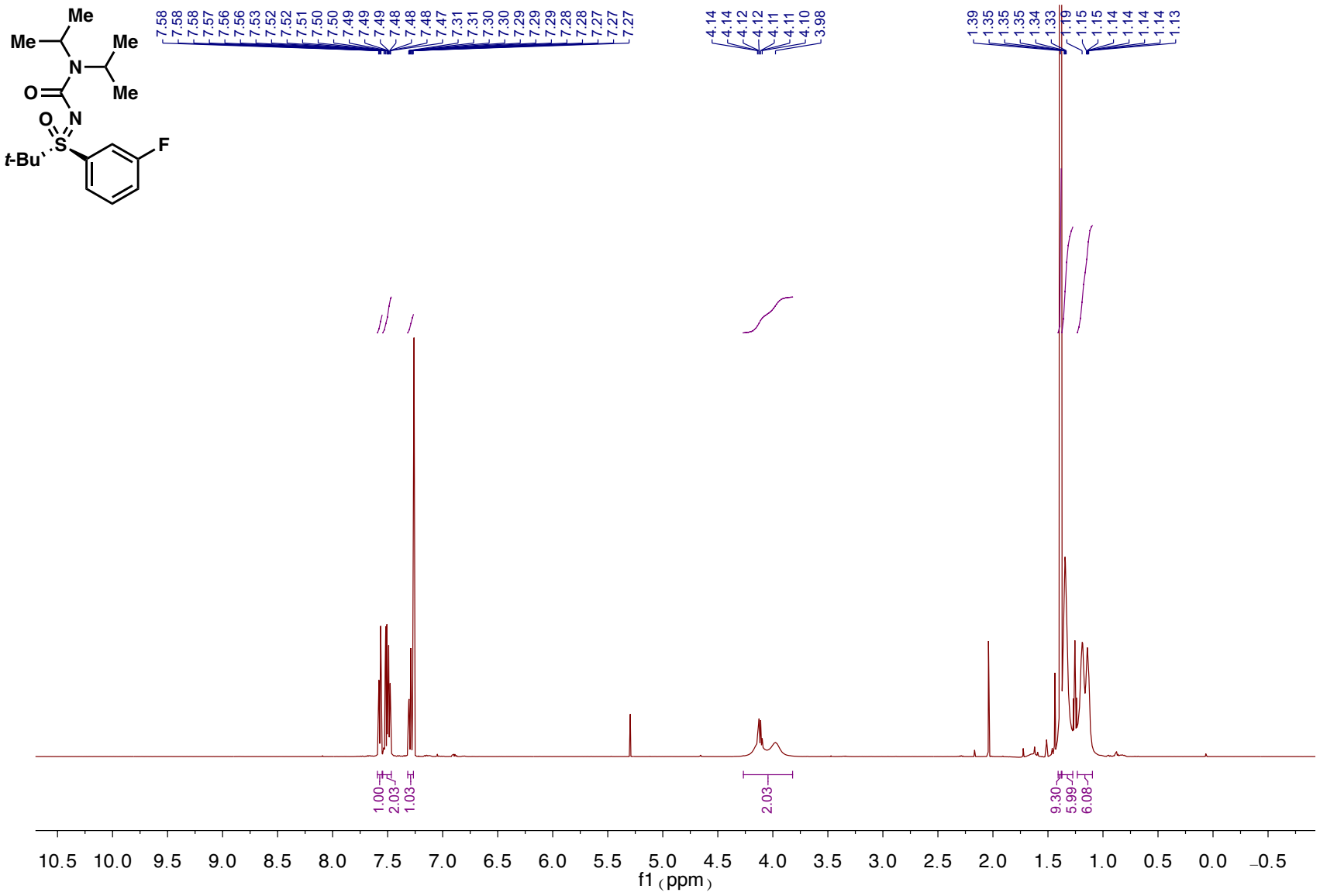
^{1}H NMR of compound 2j:



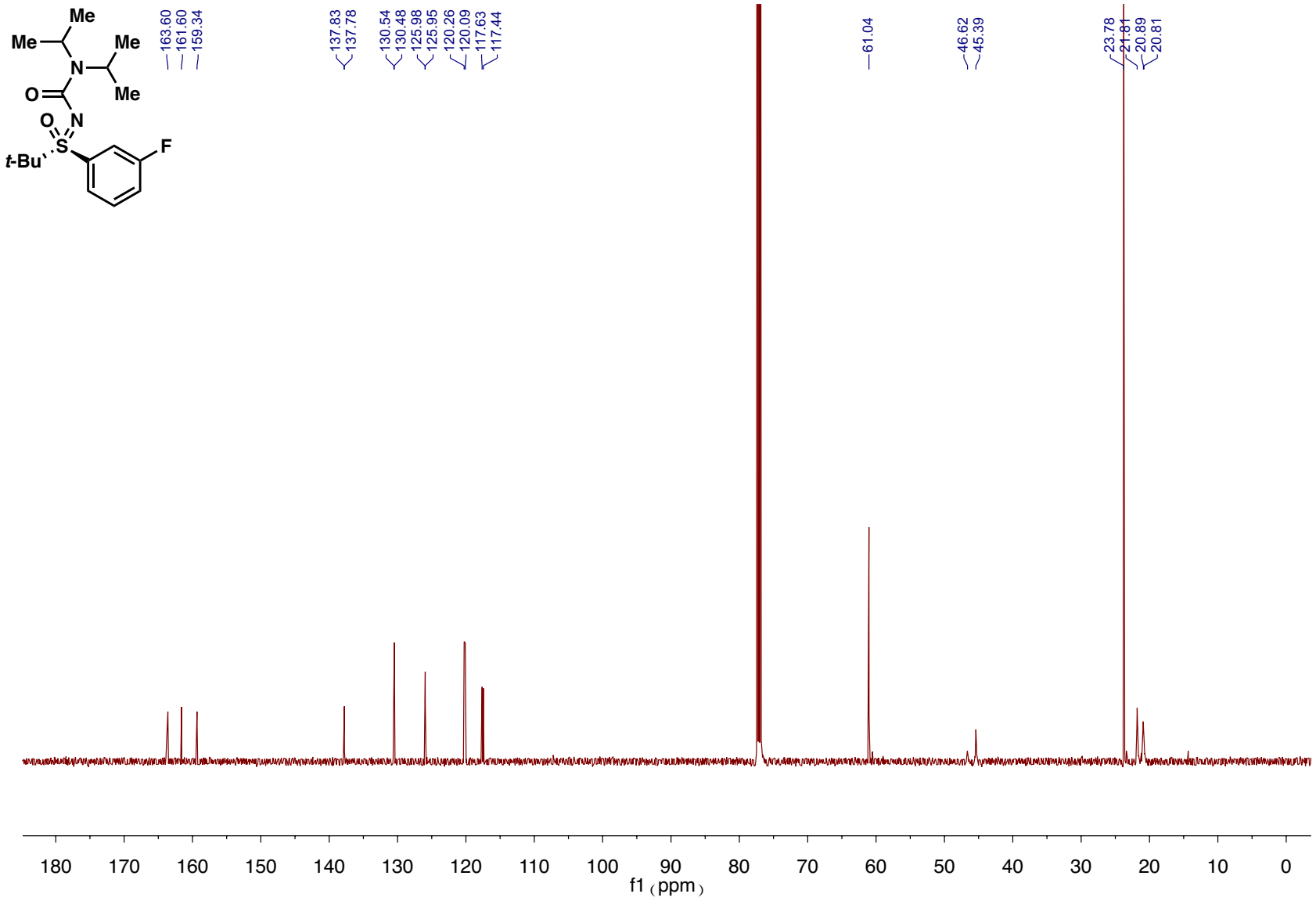
^{13}C NMR of compound 2j:



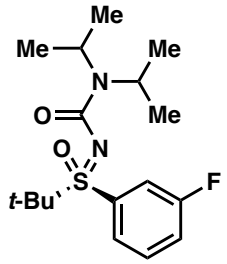
^{1}H NMR of compound 2k:



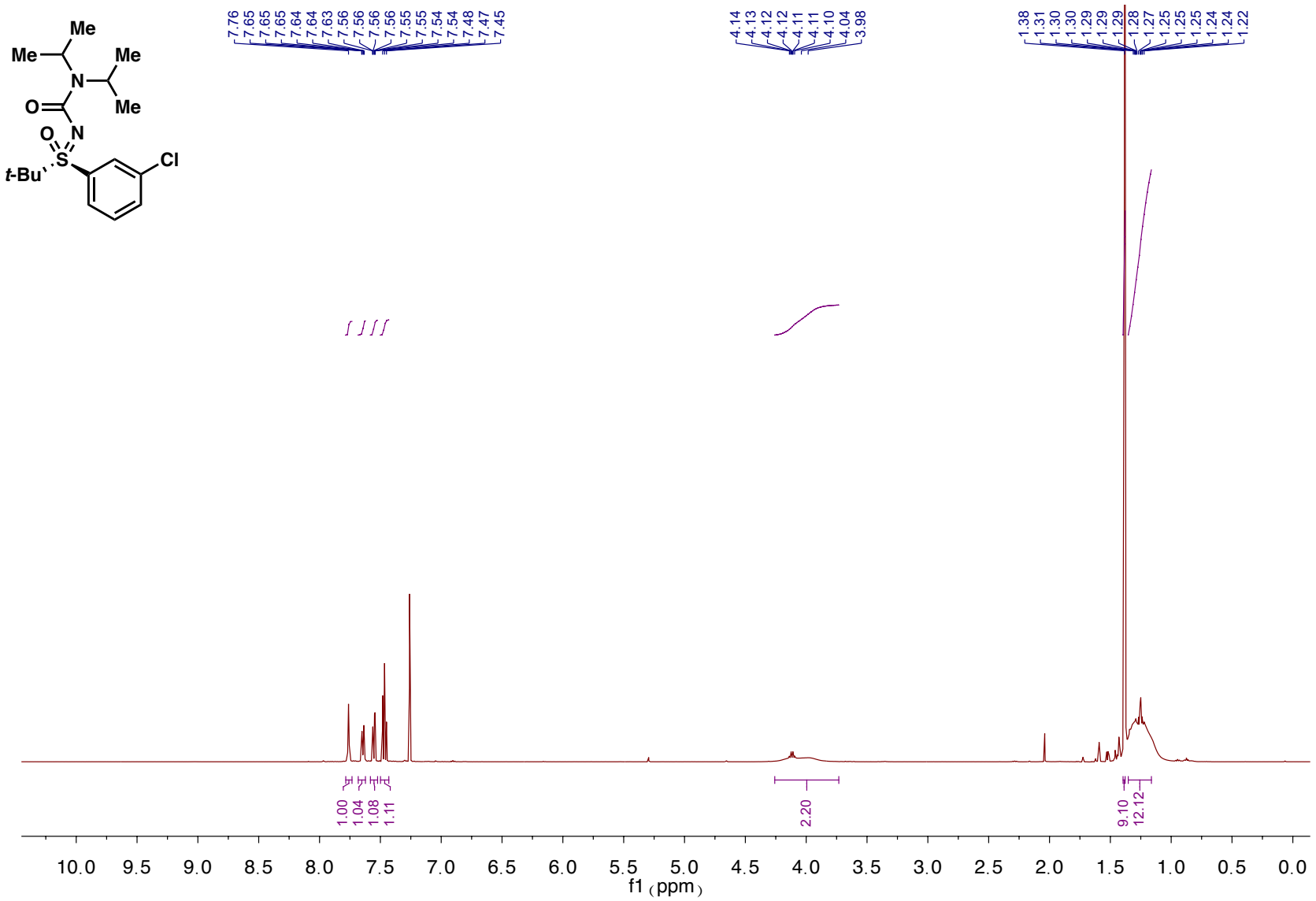
^{13}C NMR of compound 2k:



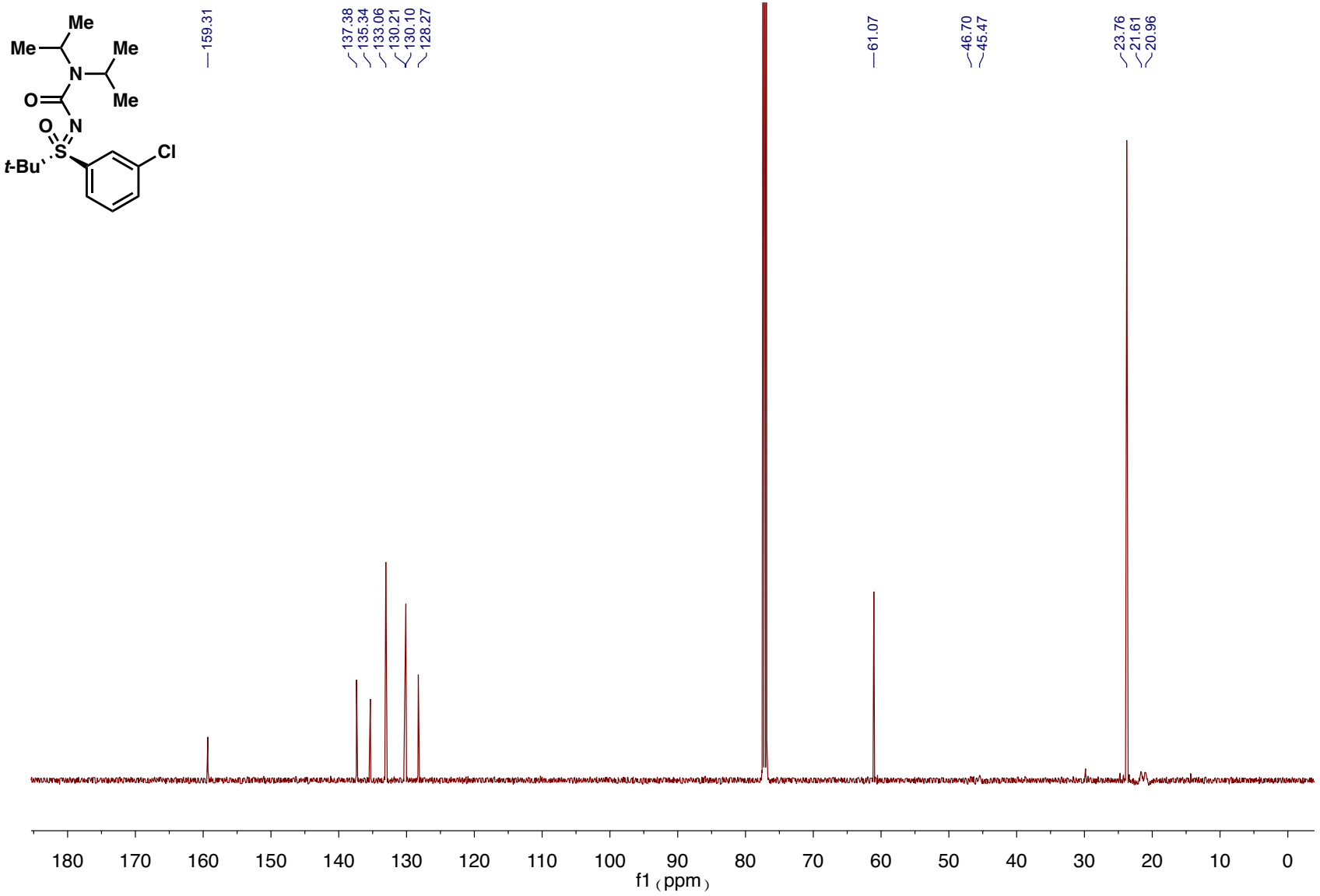
^{19}F NMR of compound 2k:



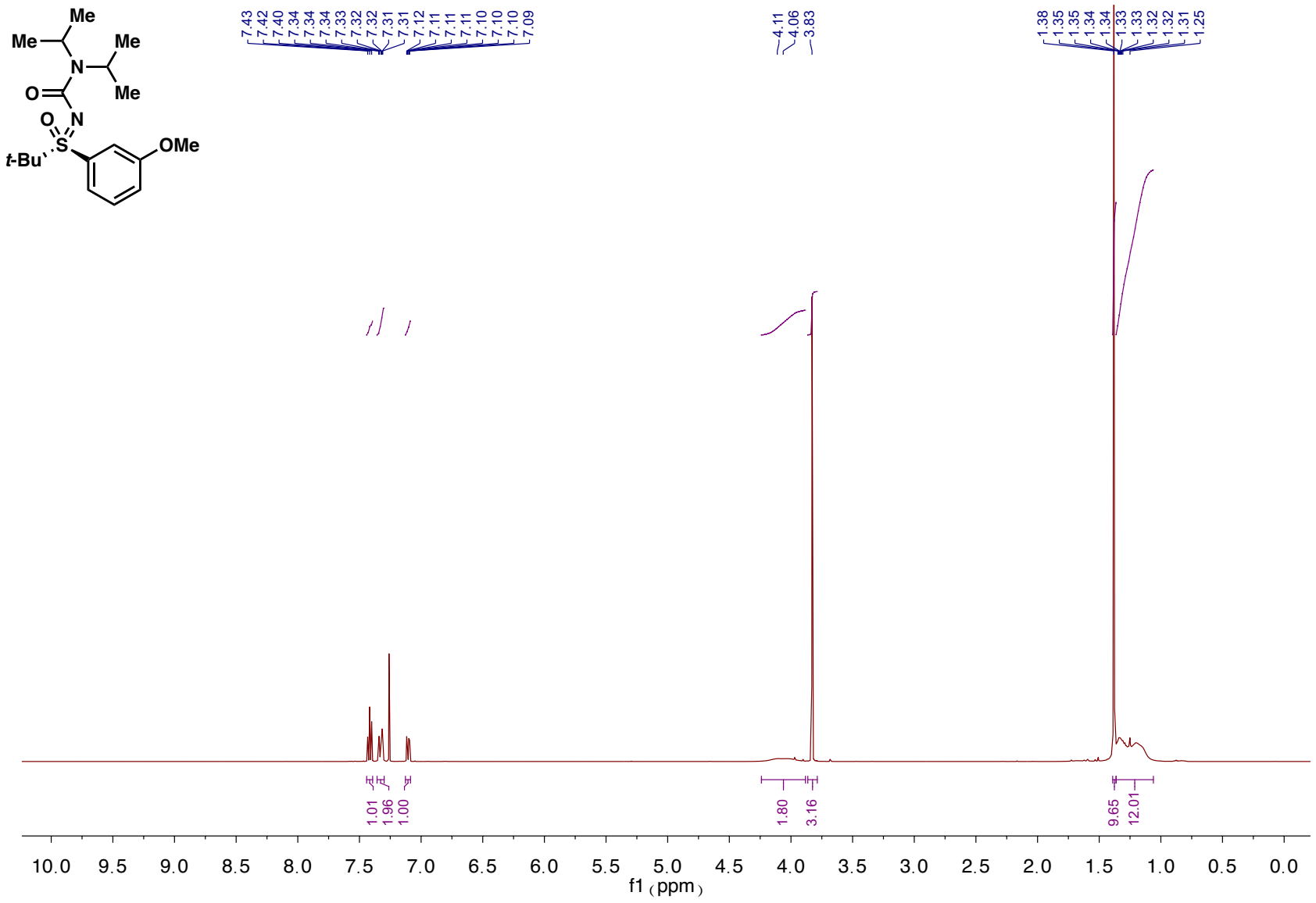
^{1}H NMR of compound 2l:



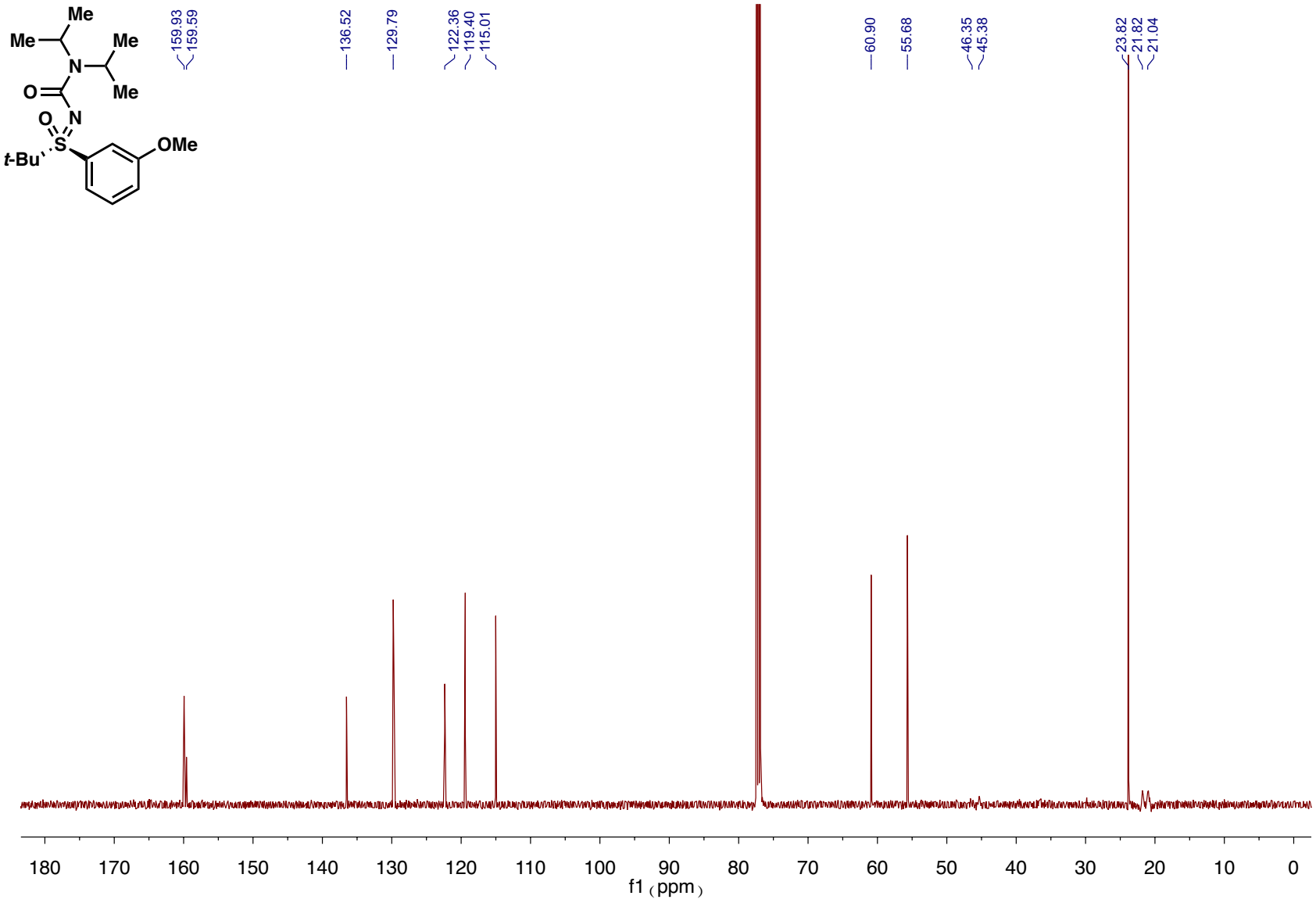
^{13}C NMR of compound 2l:



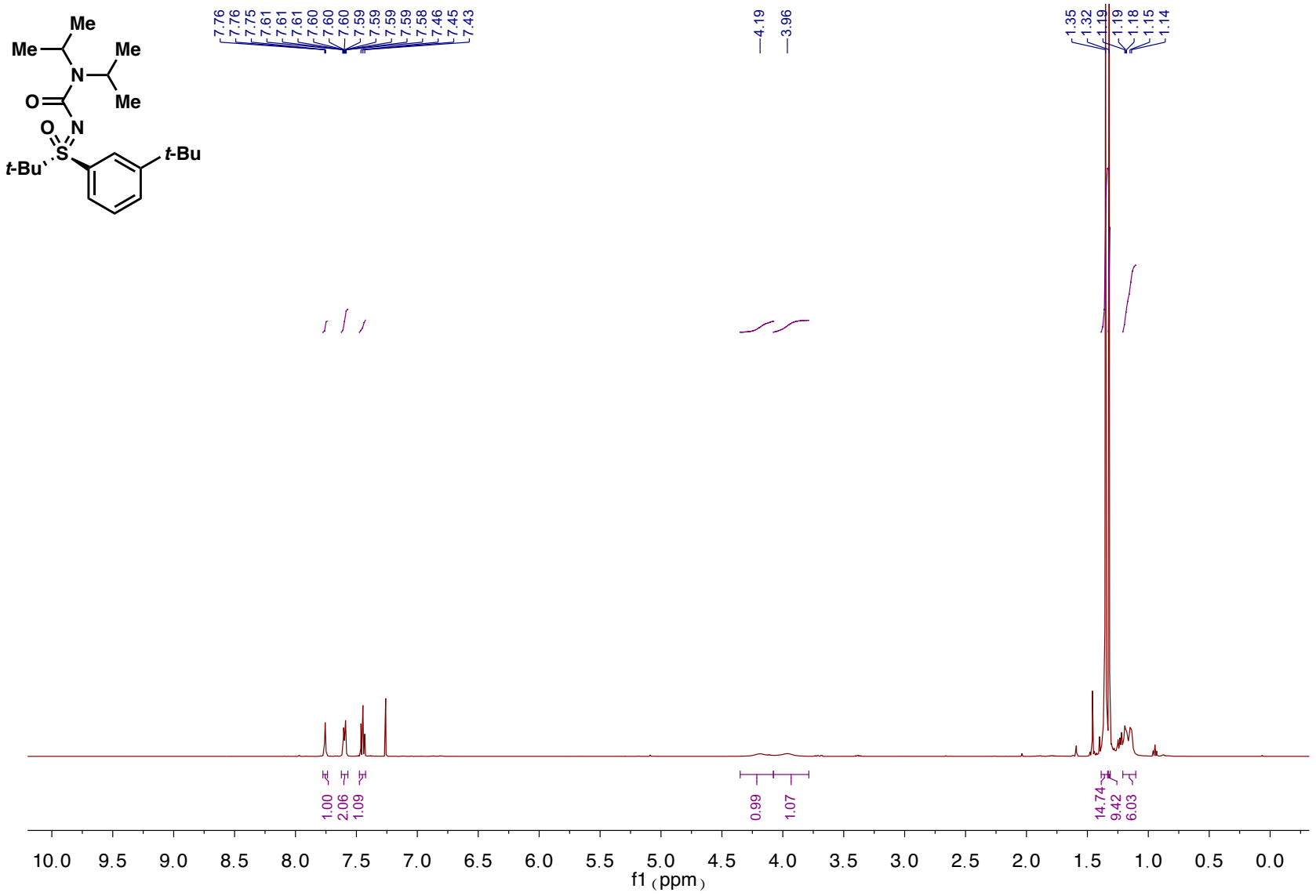
^{1}H NMR of compound 2m:



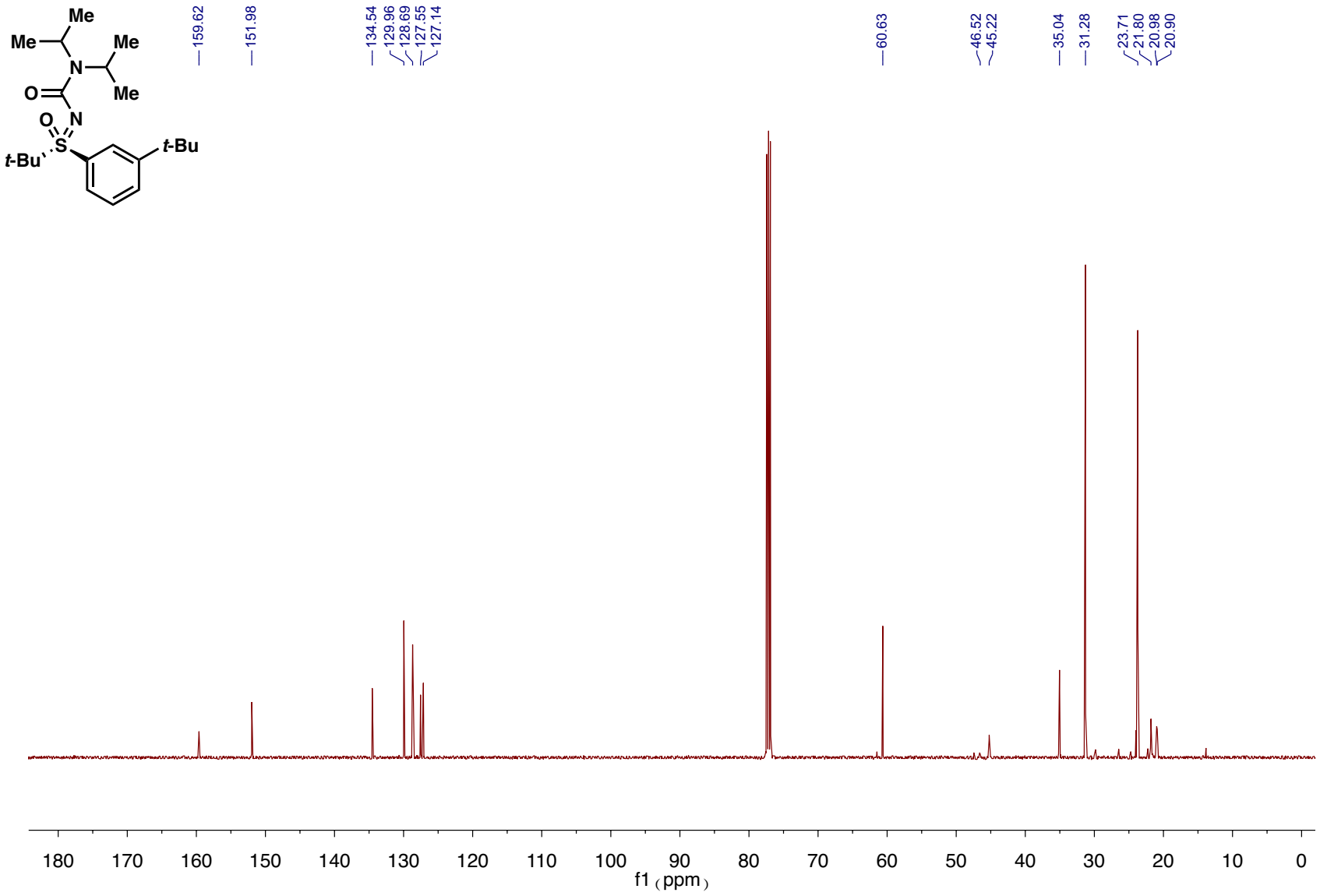
^{13}C NMR of compound 2m:



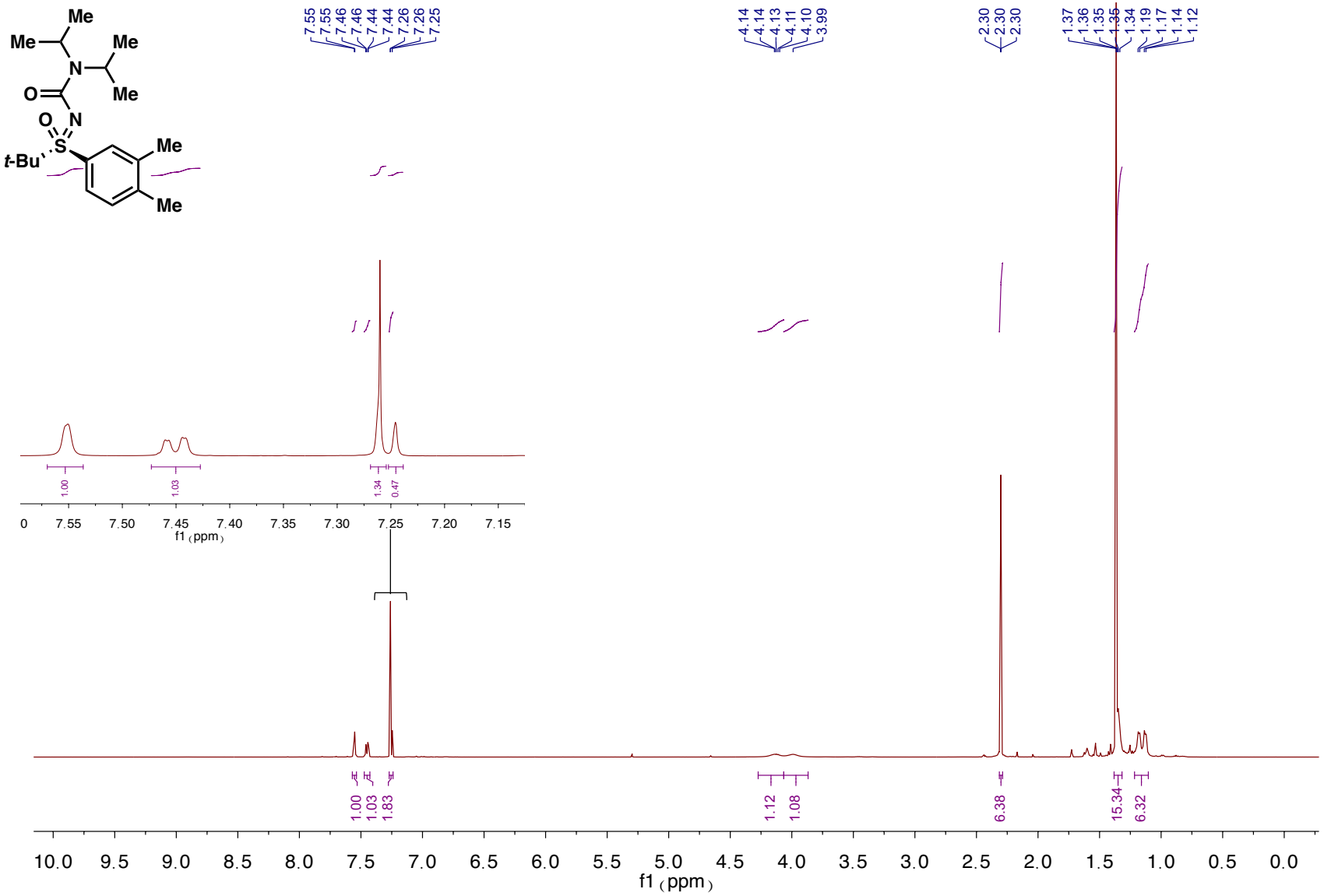
^{1}H NMR of compound 2n:



^{13}C NMR of compound 2n:



^{1}H NMR of compound 2o:



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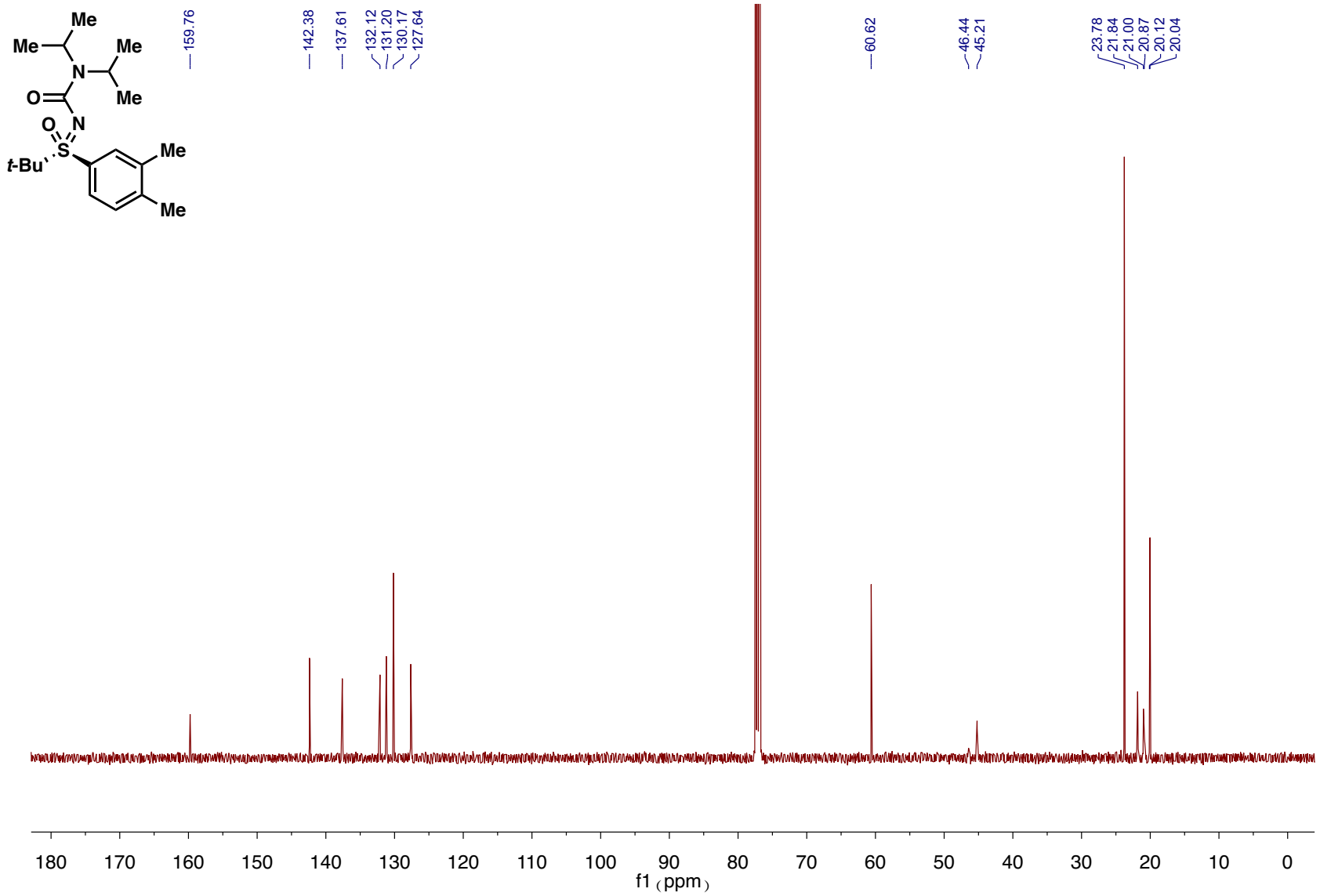
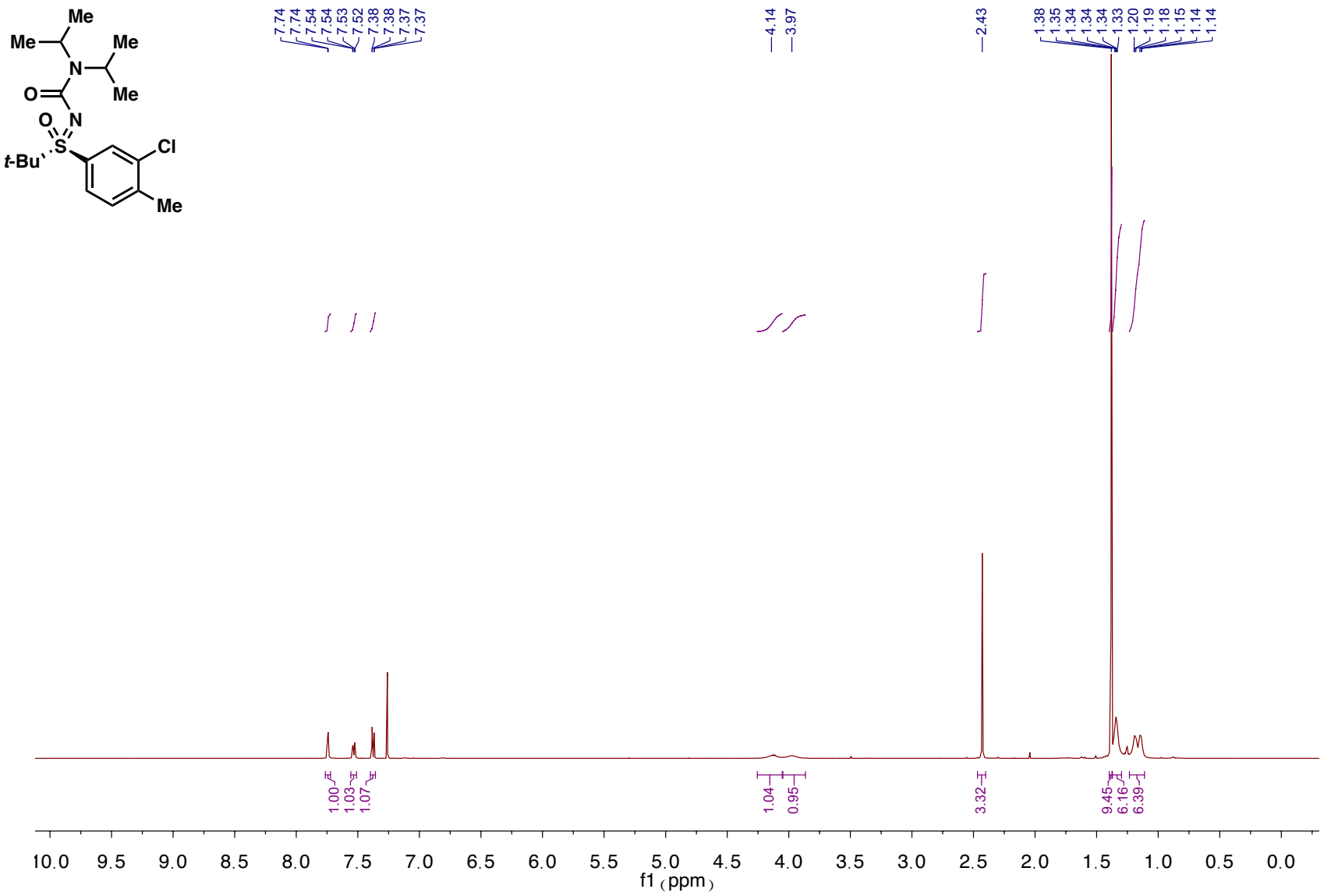


^{1}H NMR of compound 2p:



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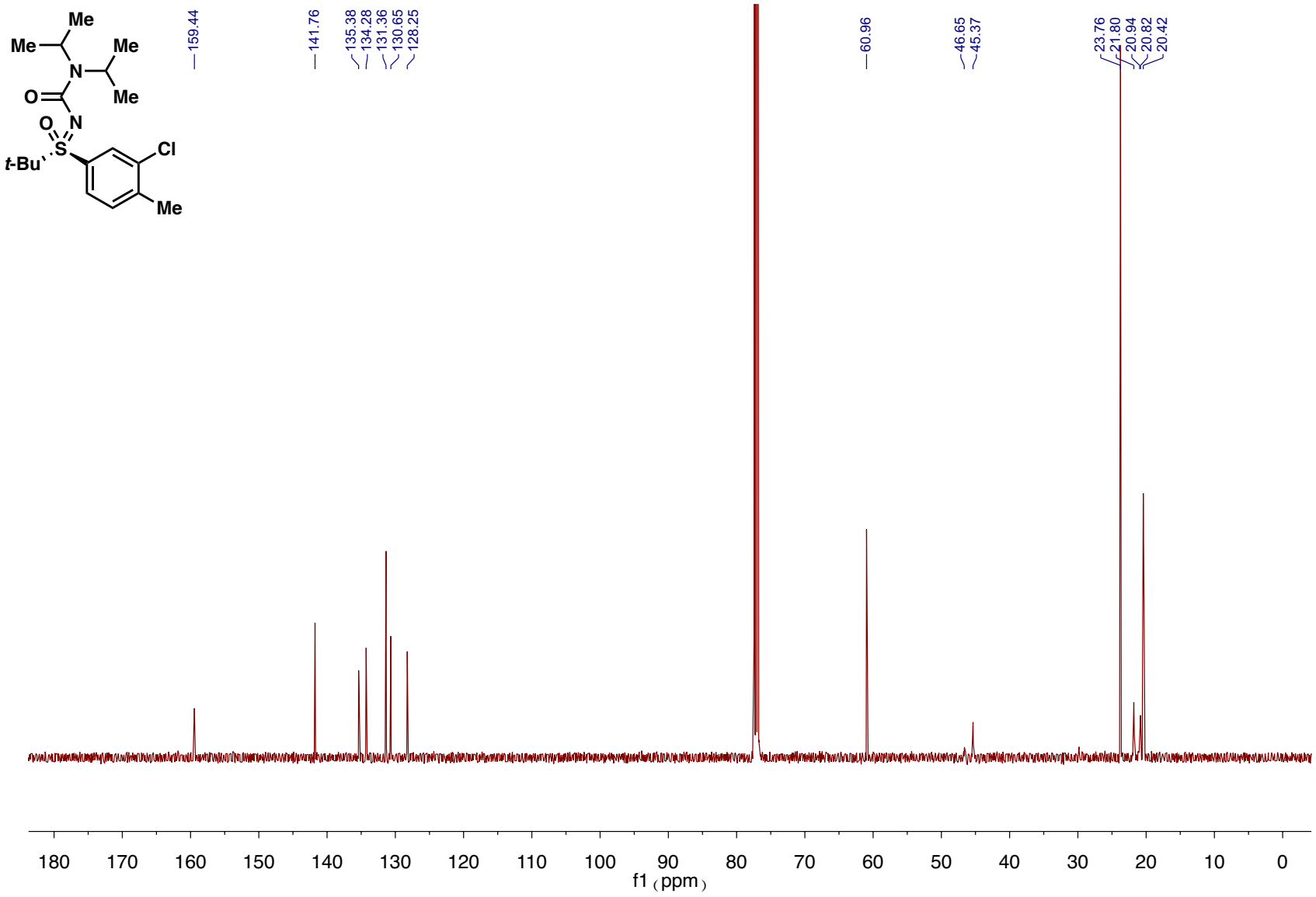
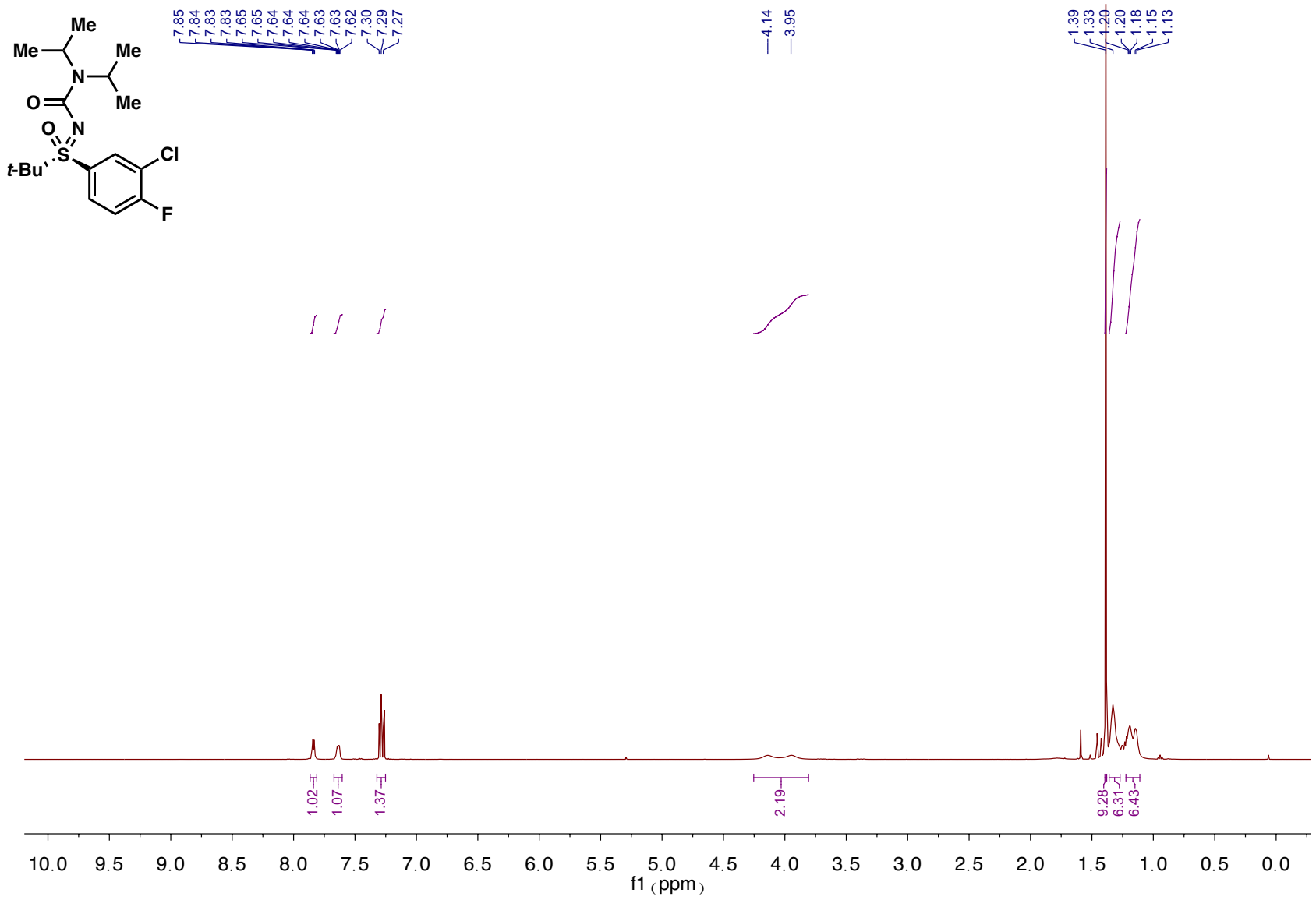


^{1}H NMR of compound 2q:



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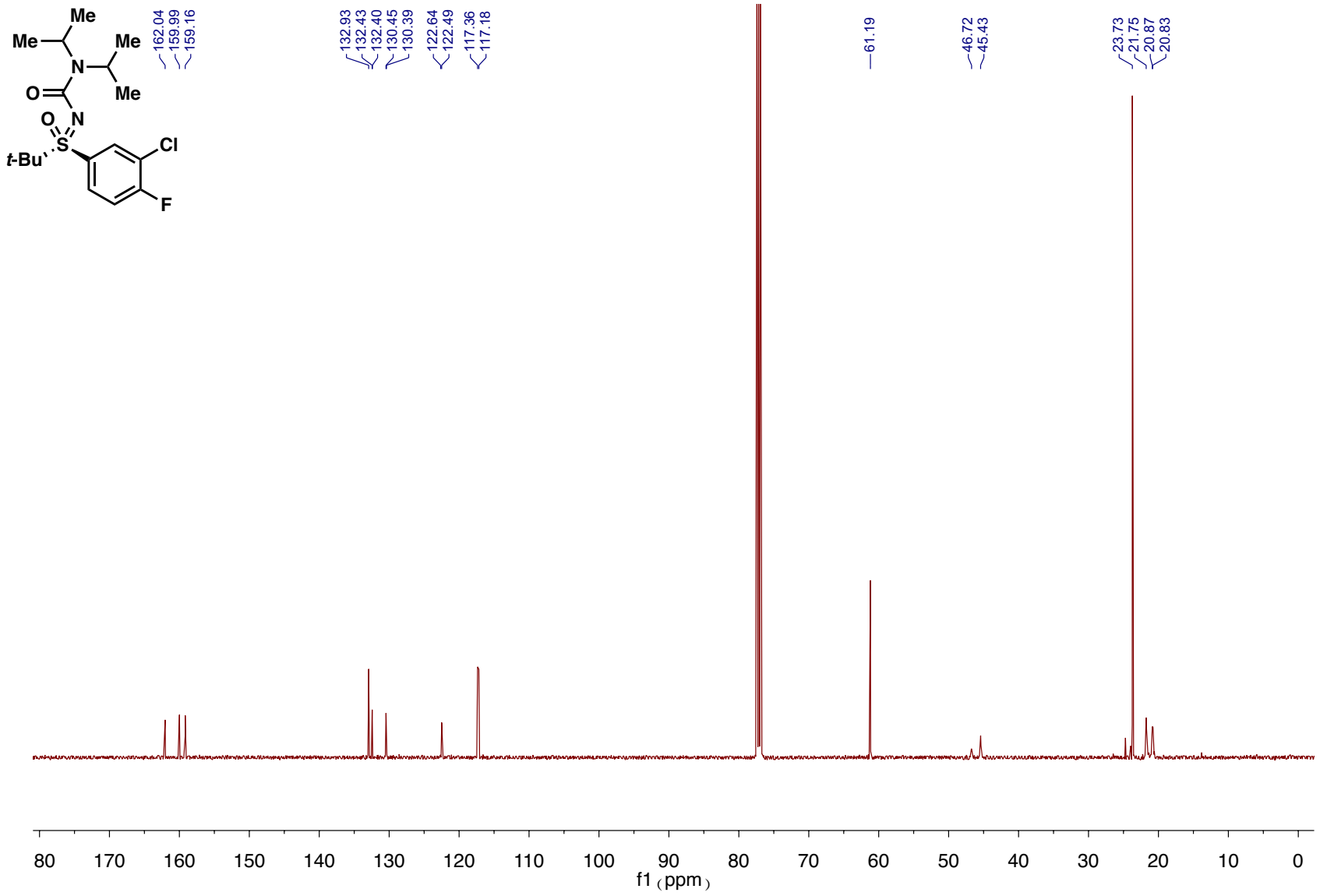
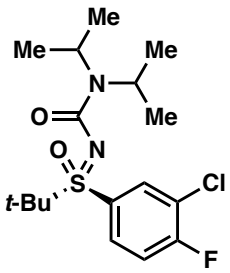
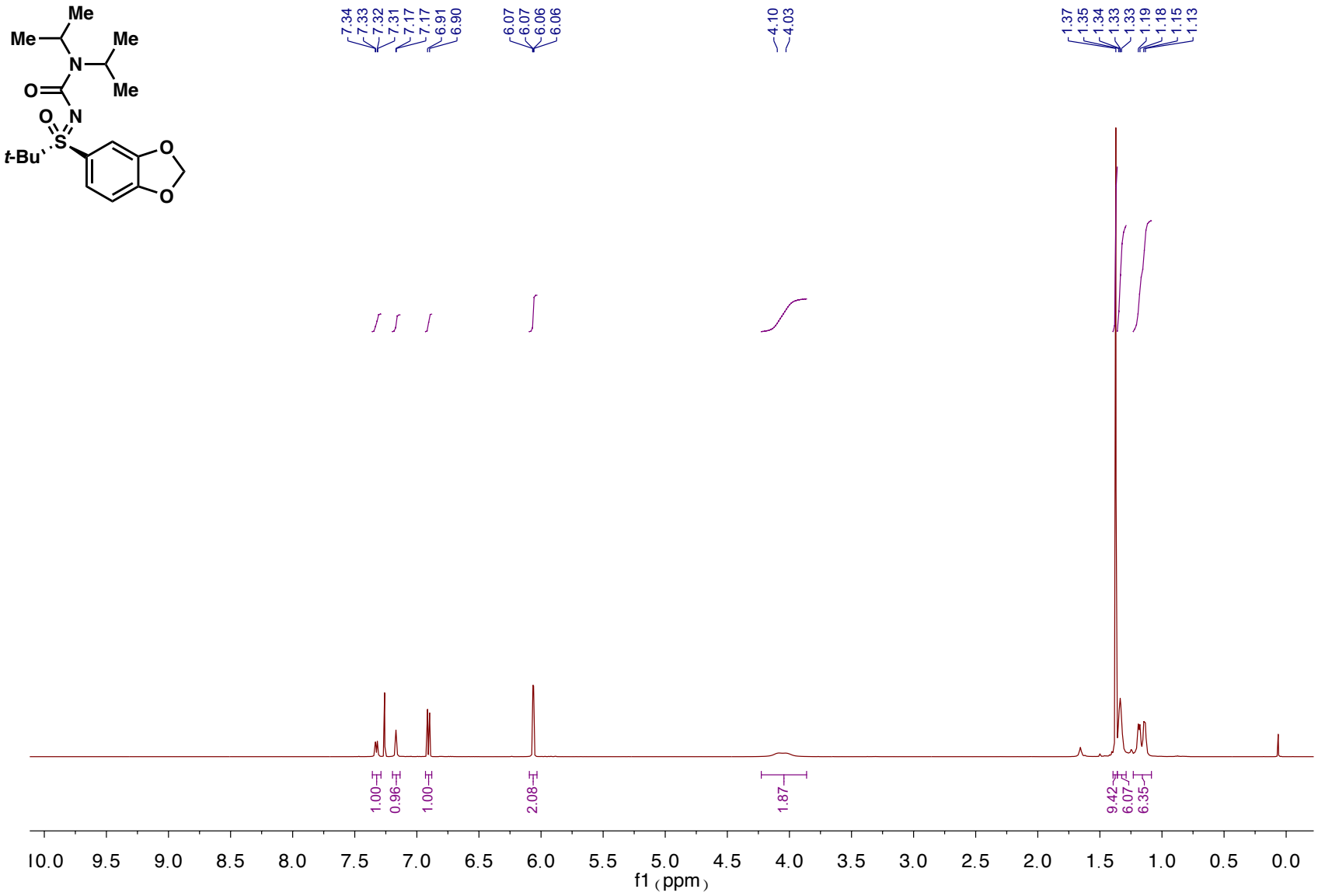


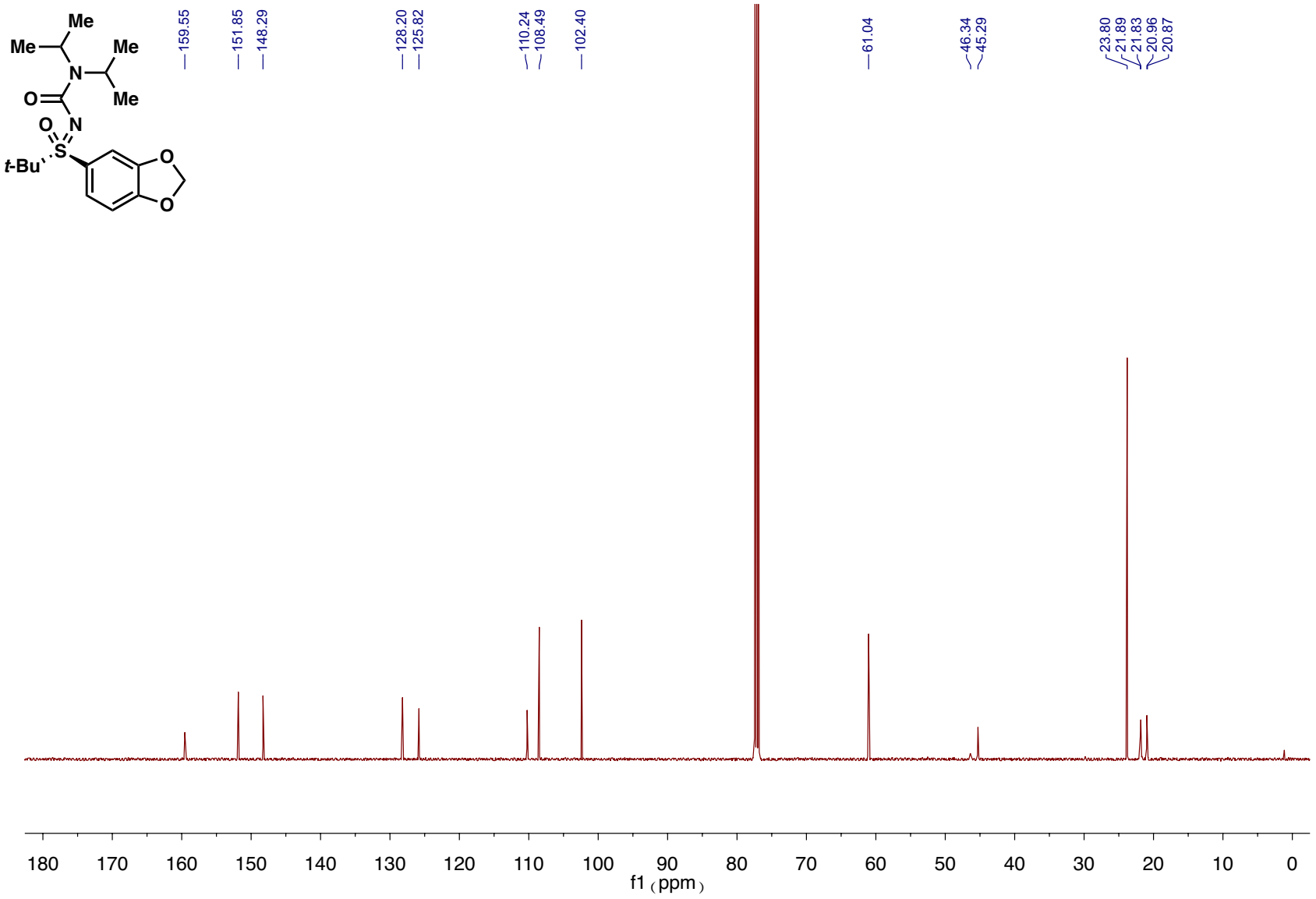
^{19}F NMR of compound 2q:



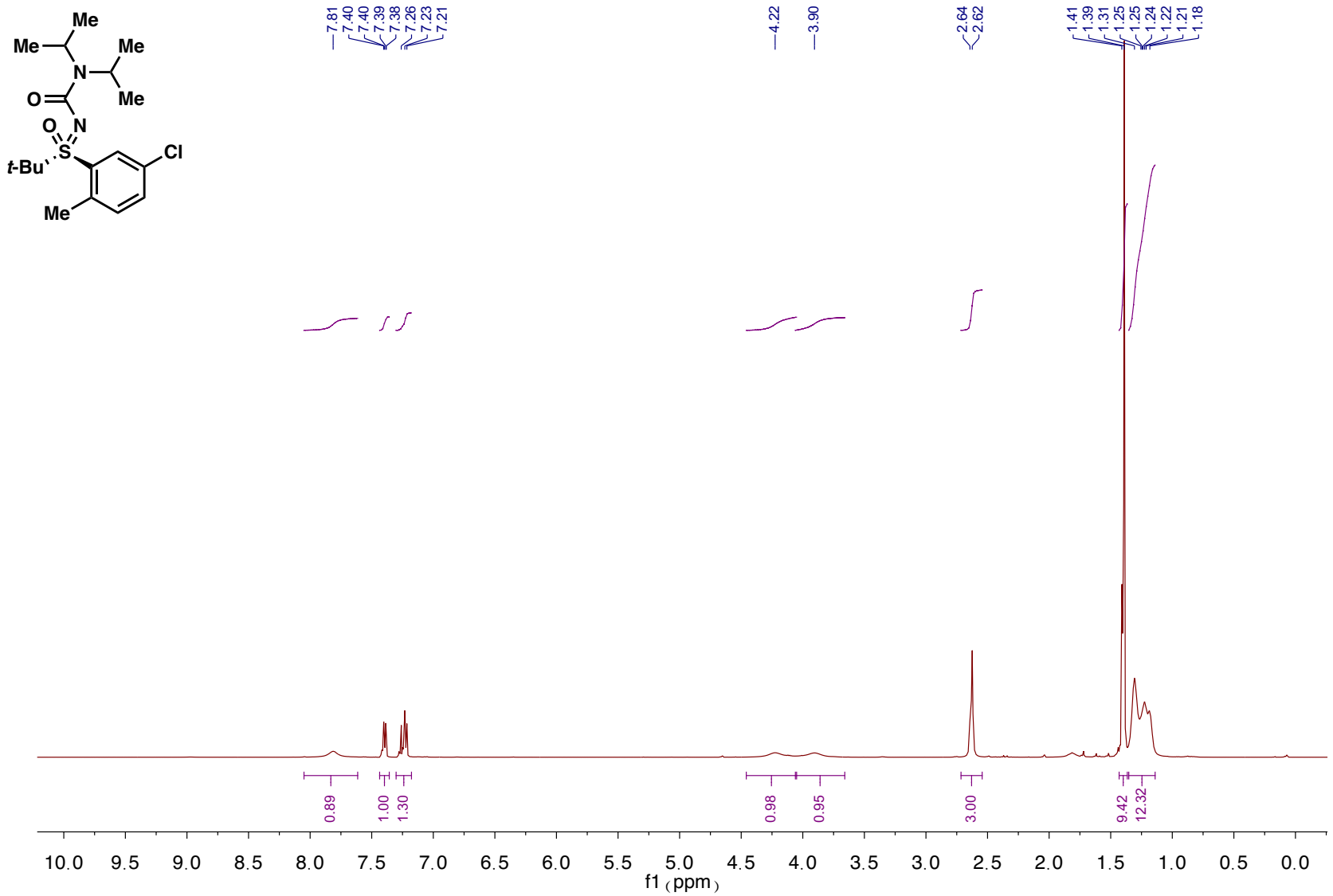
^{1}H NMR of compound 2r:



^{13}C NMR of compound 2r:



^{1}H NMR of compound 2s:



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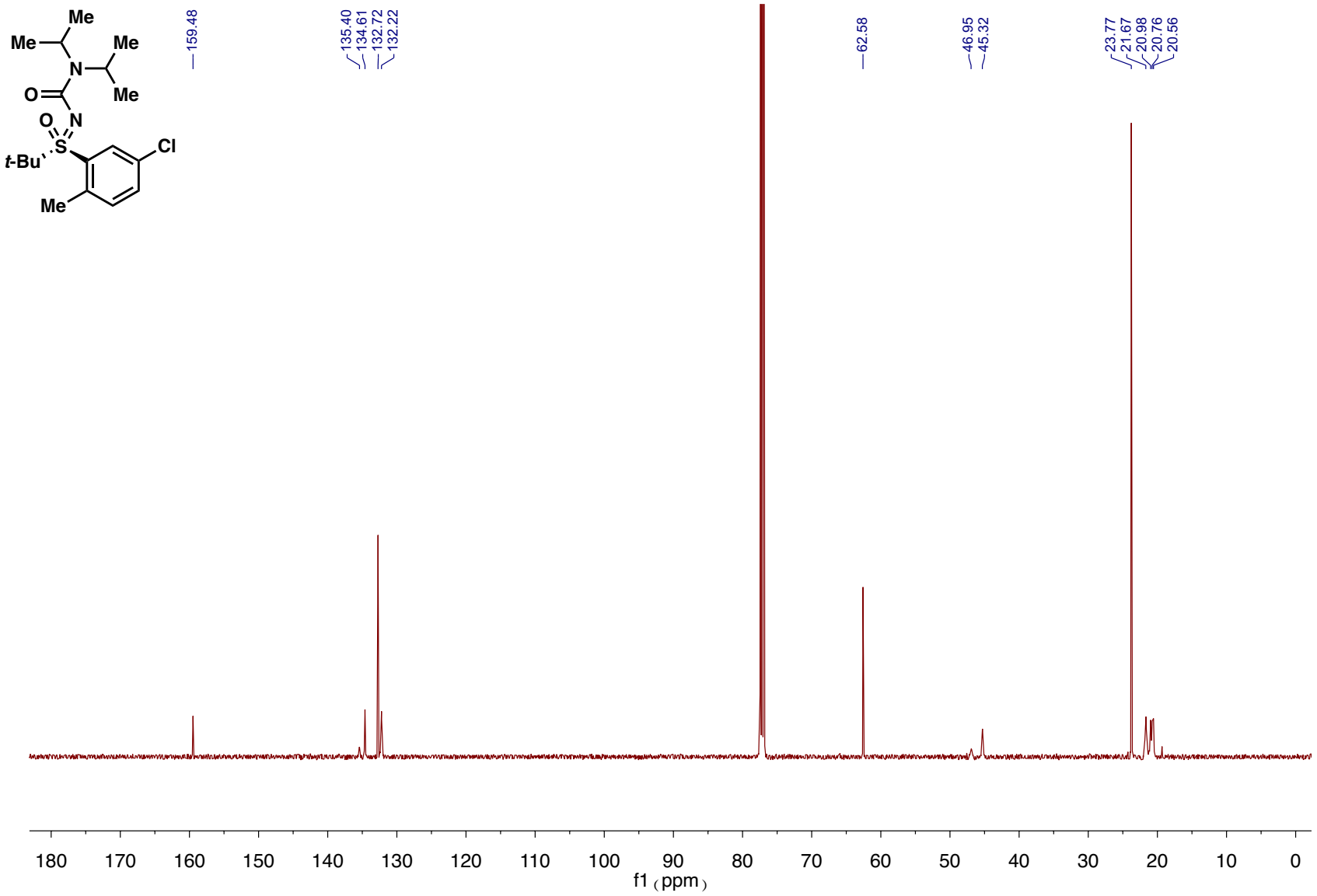
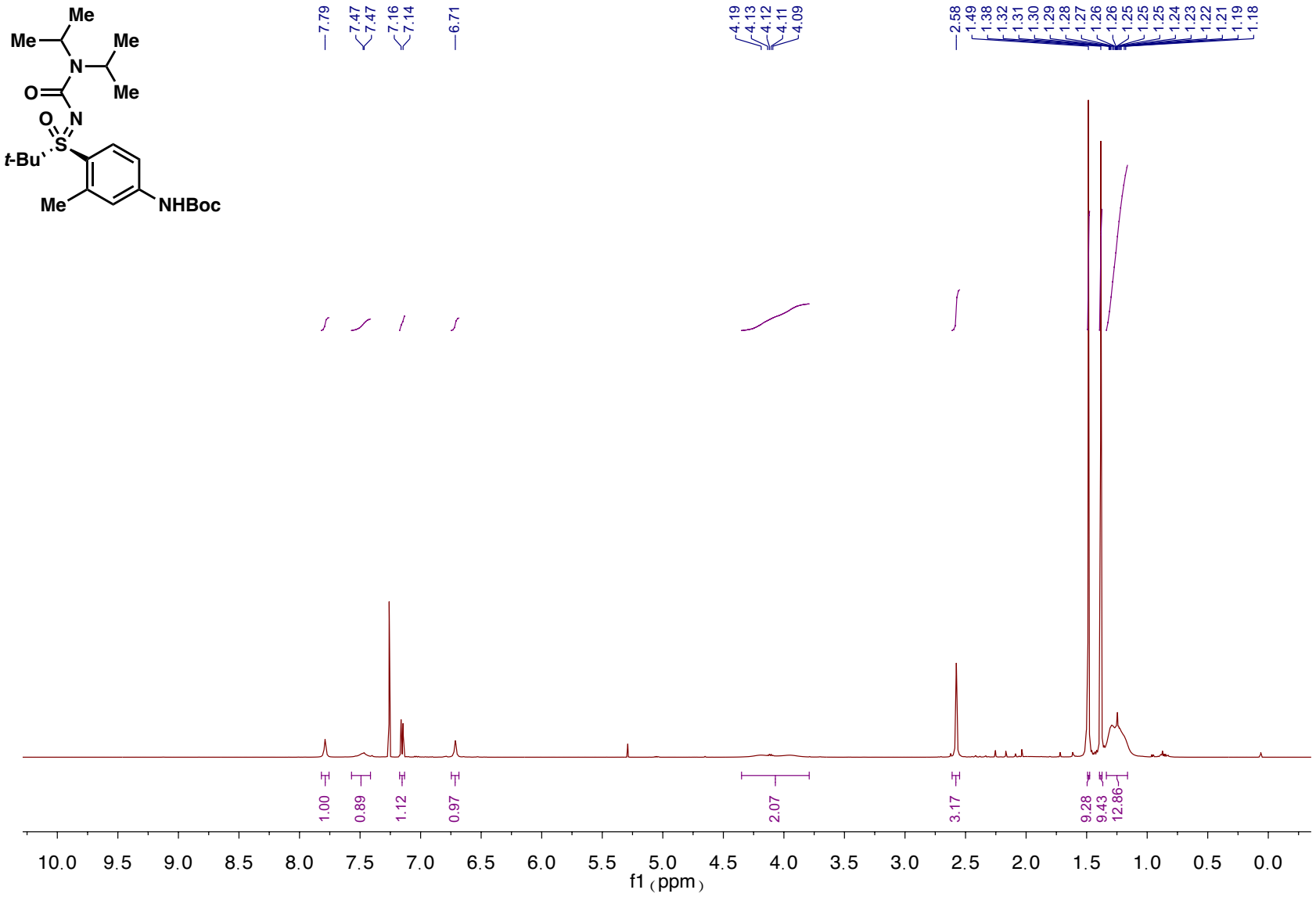


^{1}H NMR of compound 2t:



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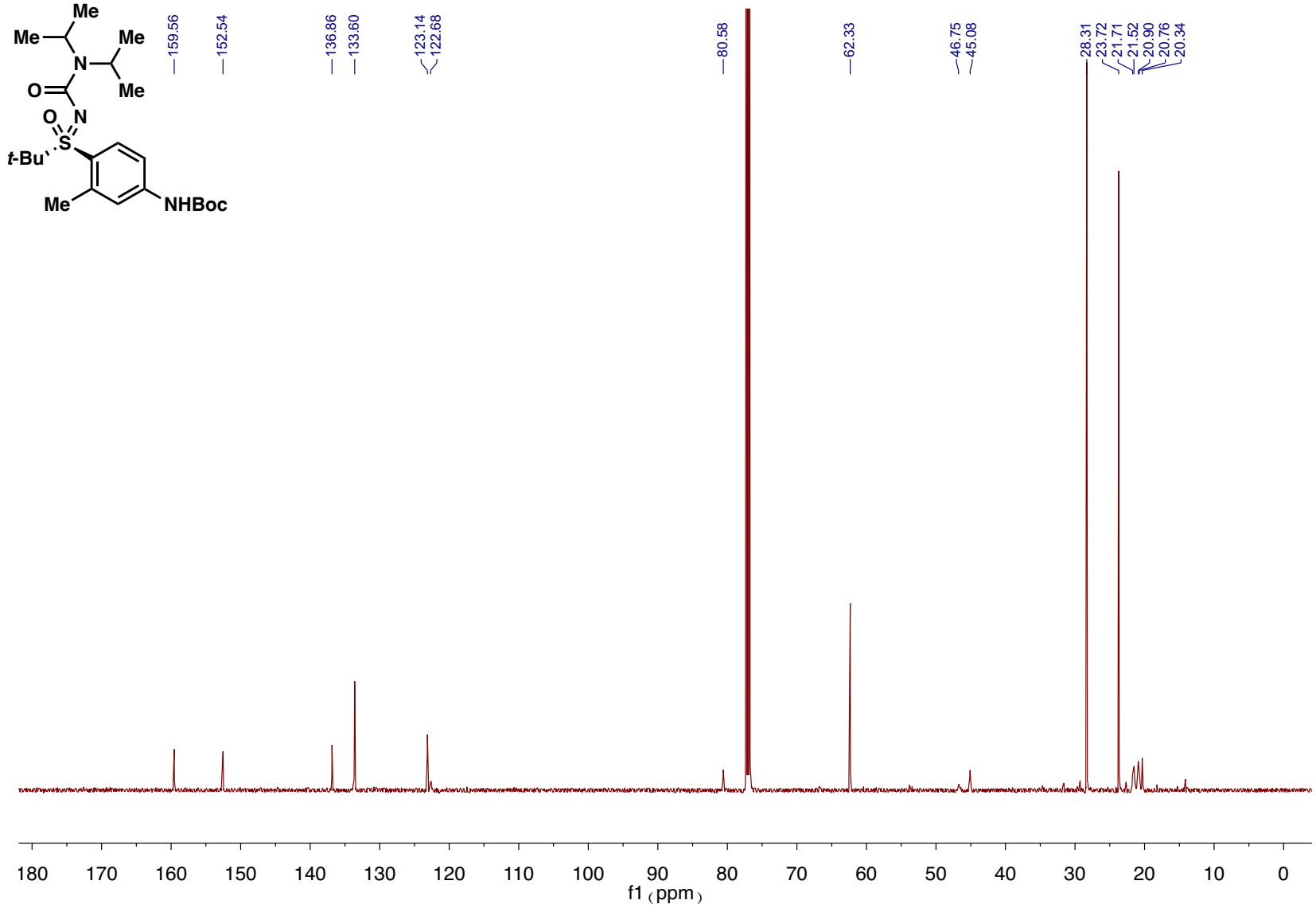
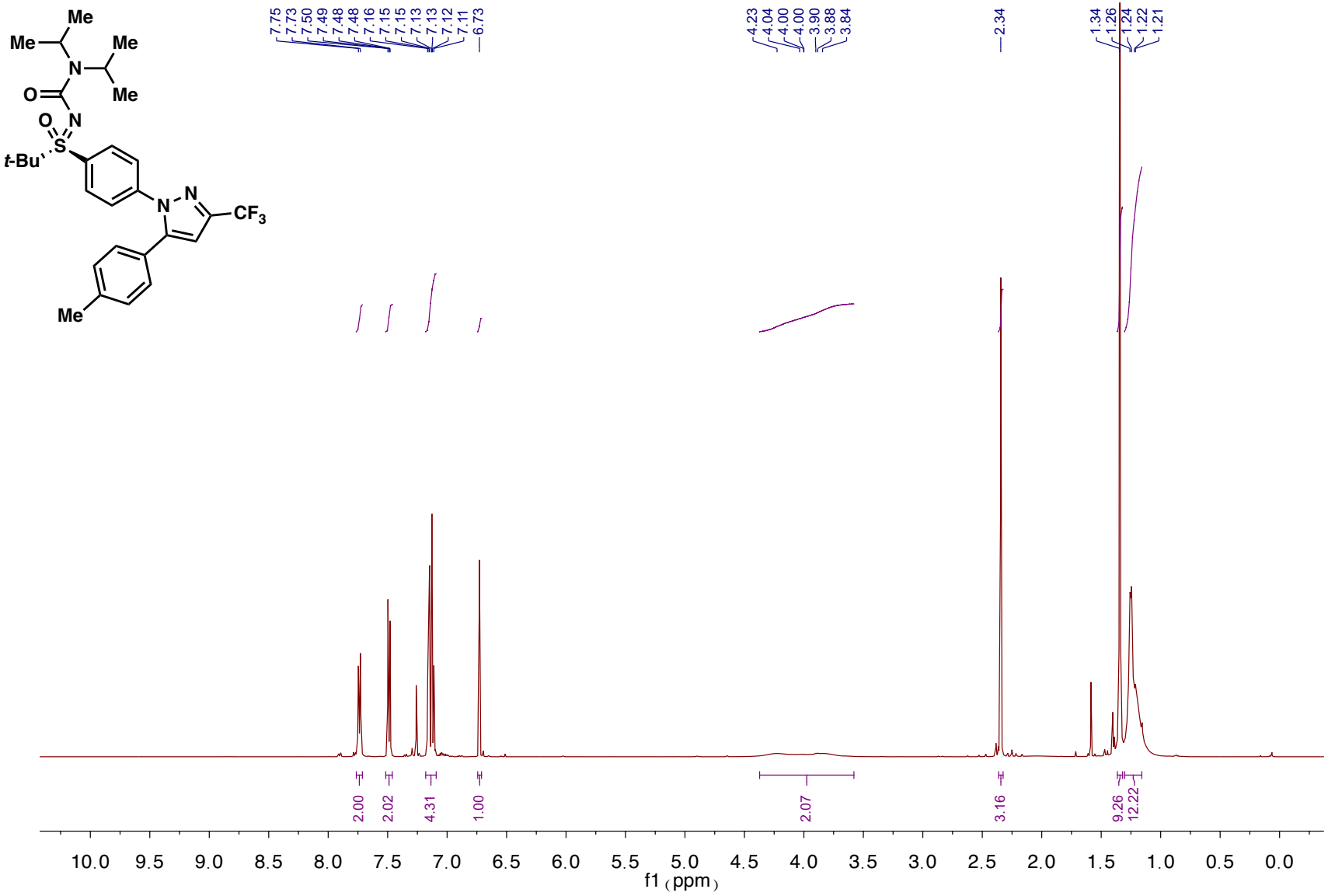


^{1}H NMR of compound 2u:



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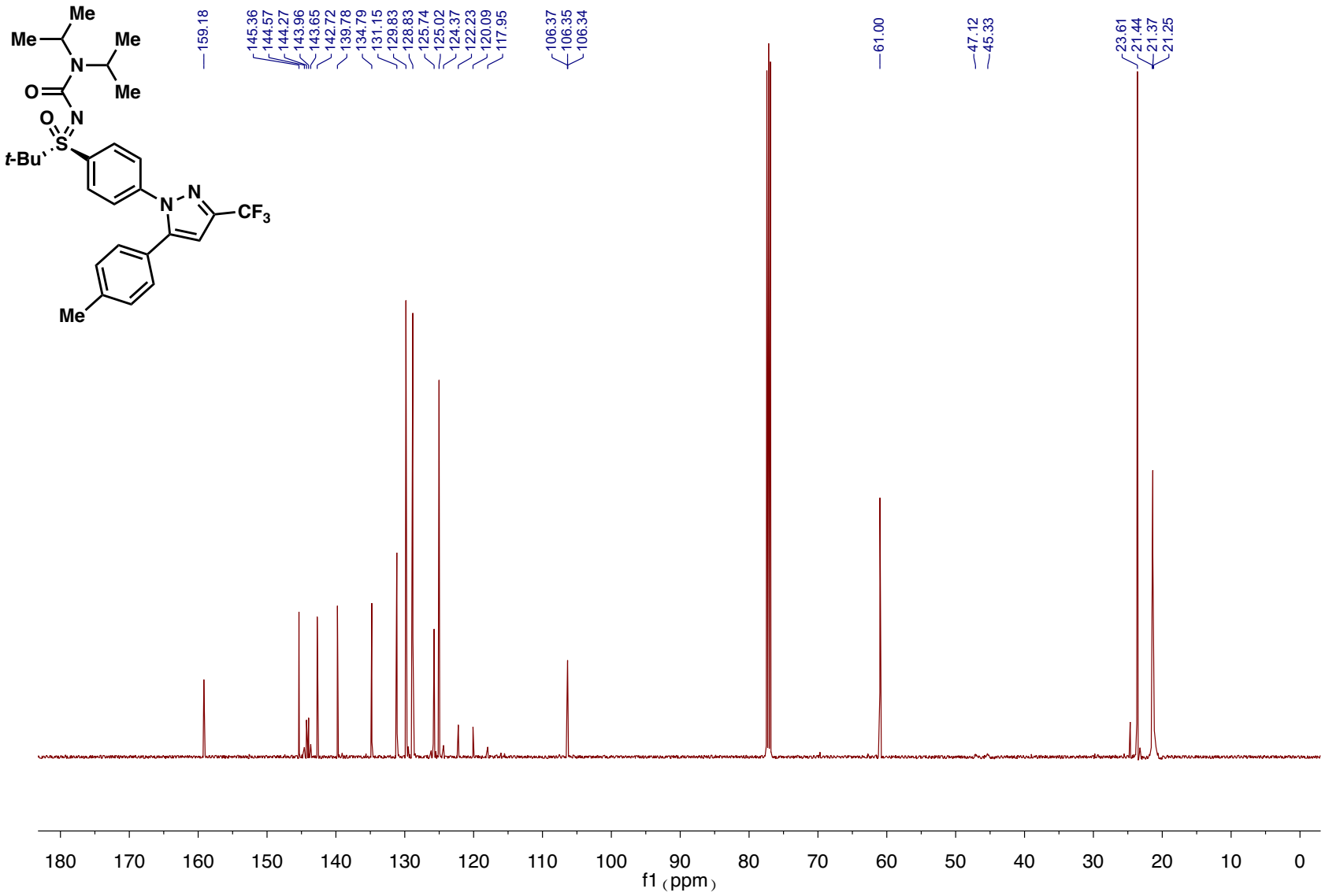
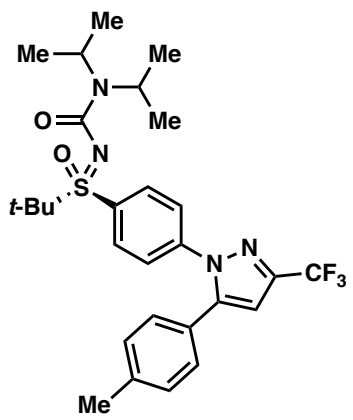
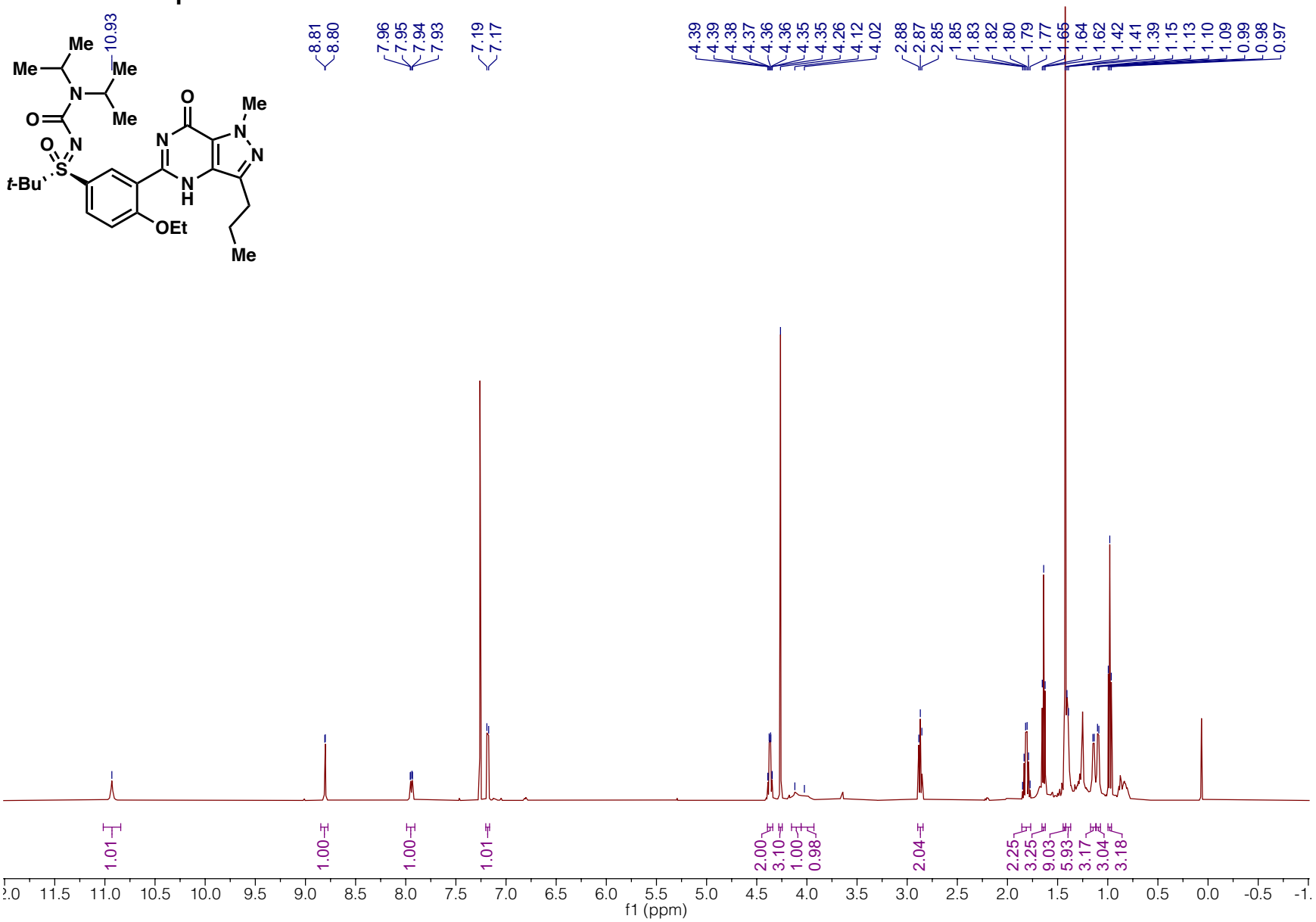


^{19}F NMR of compound 2u:



^{1}H NMR of compound 2v:



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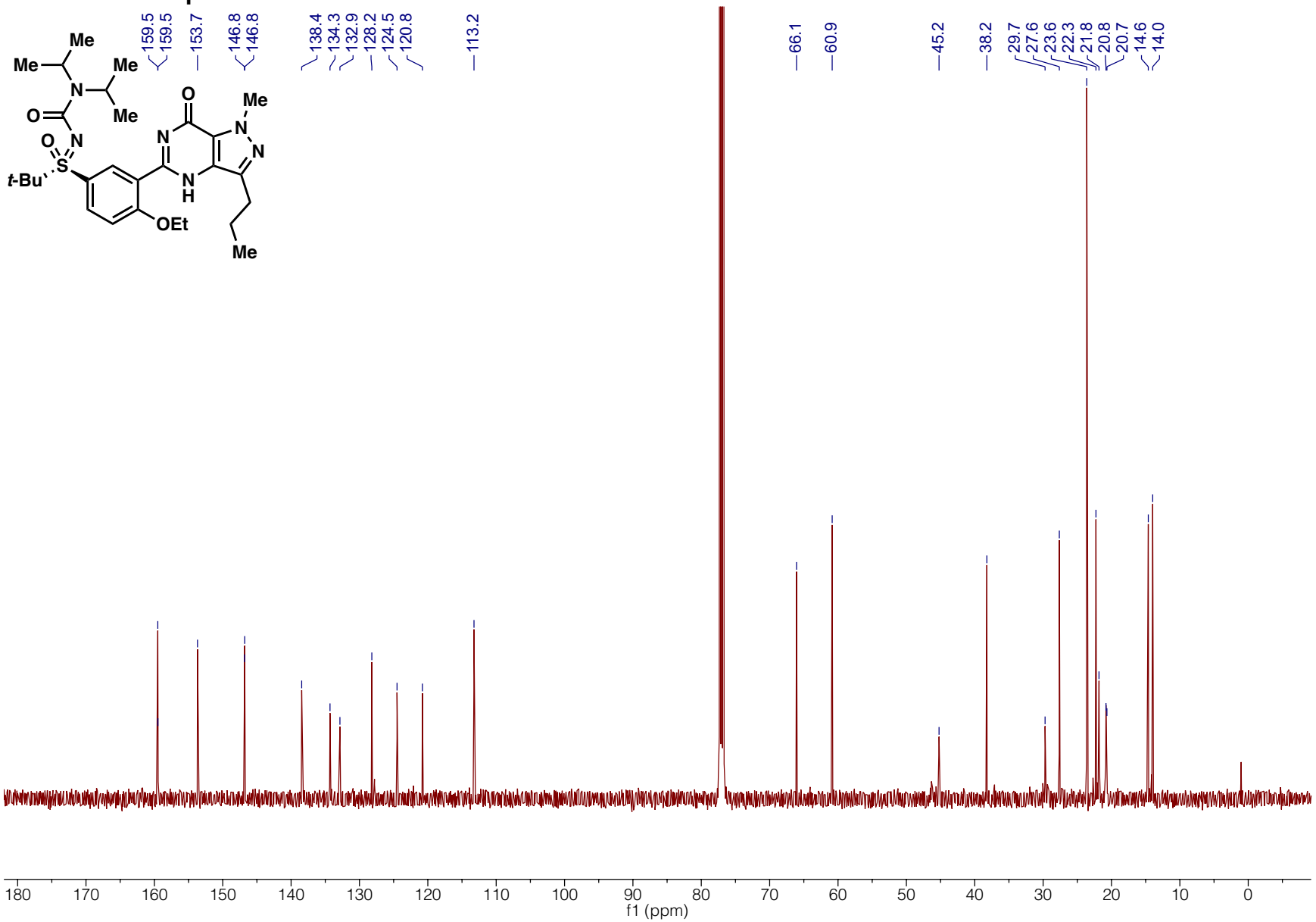
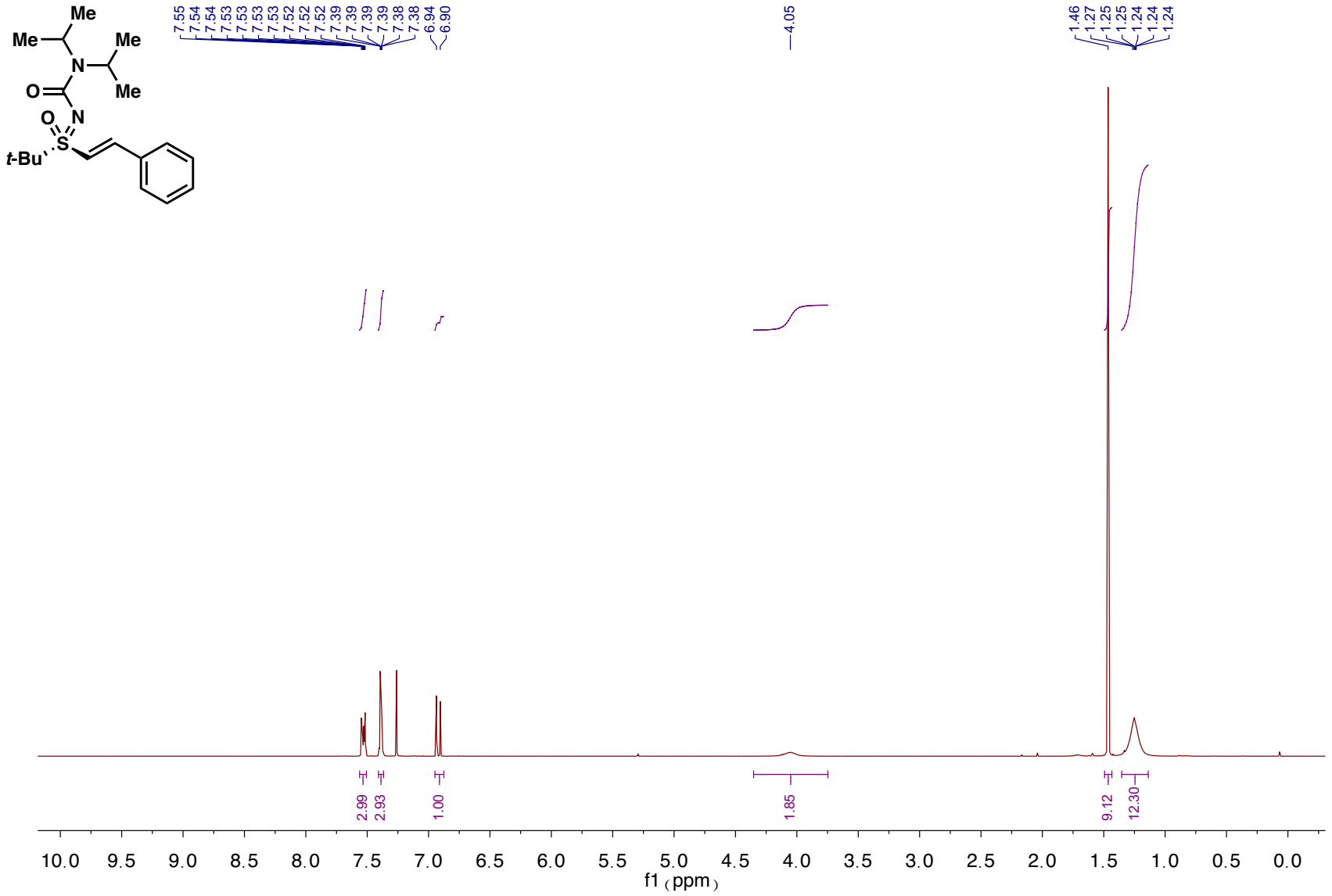
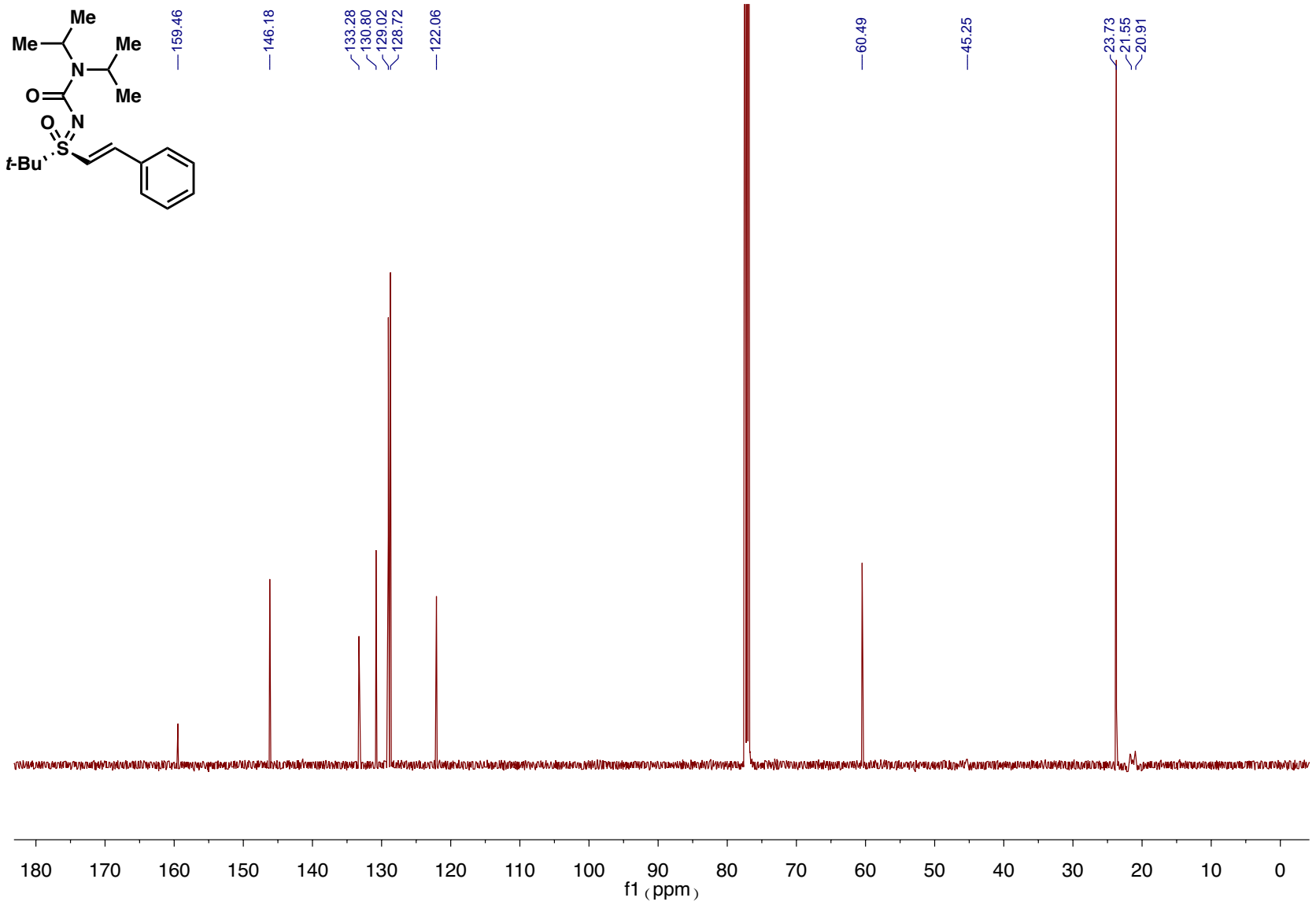


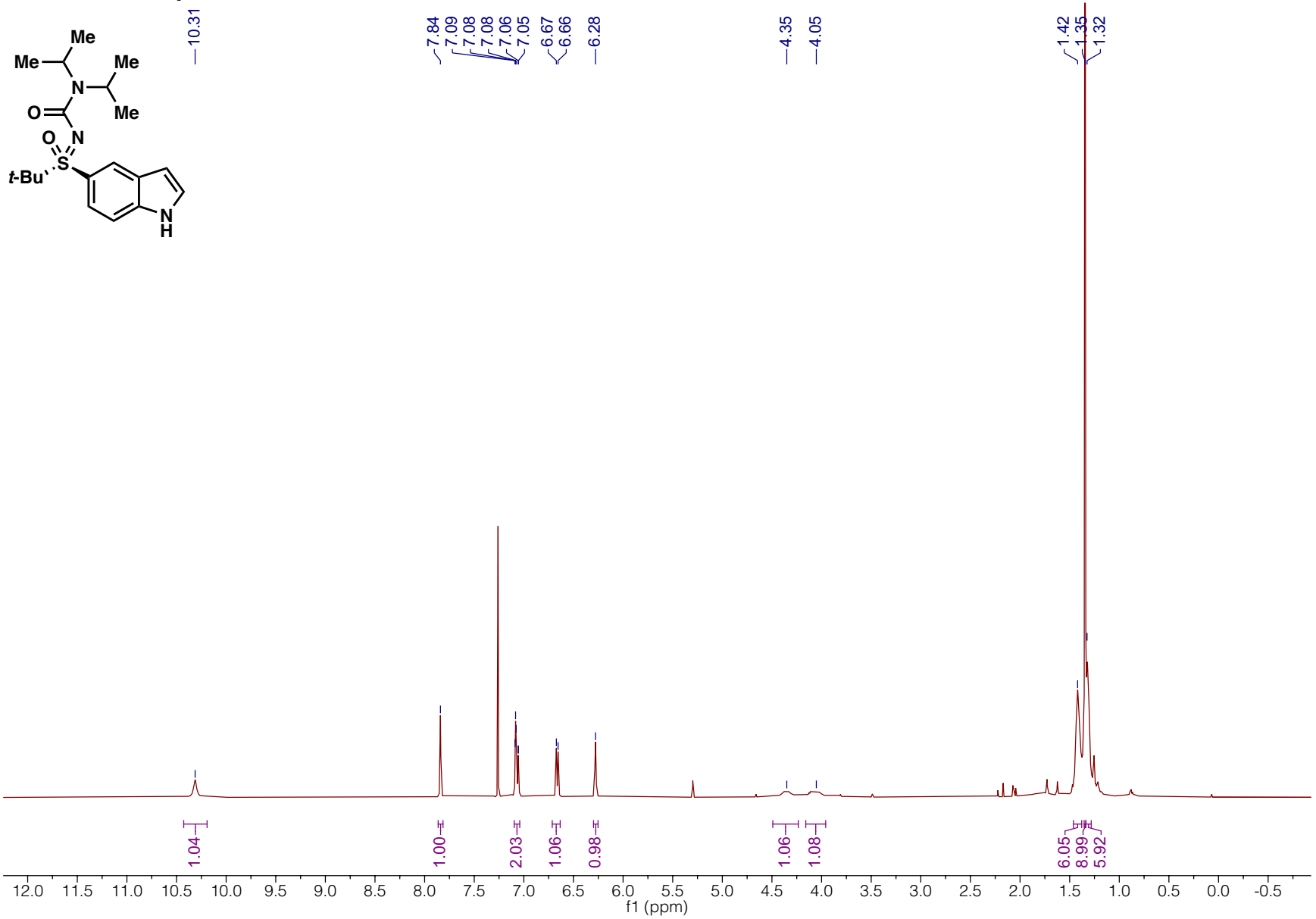
^{1}H NMR of compound 2w:



^{13}C NMR of compound 2w:



^{1}H NMR of compound 3a:



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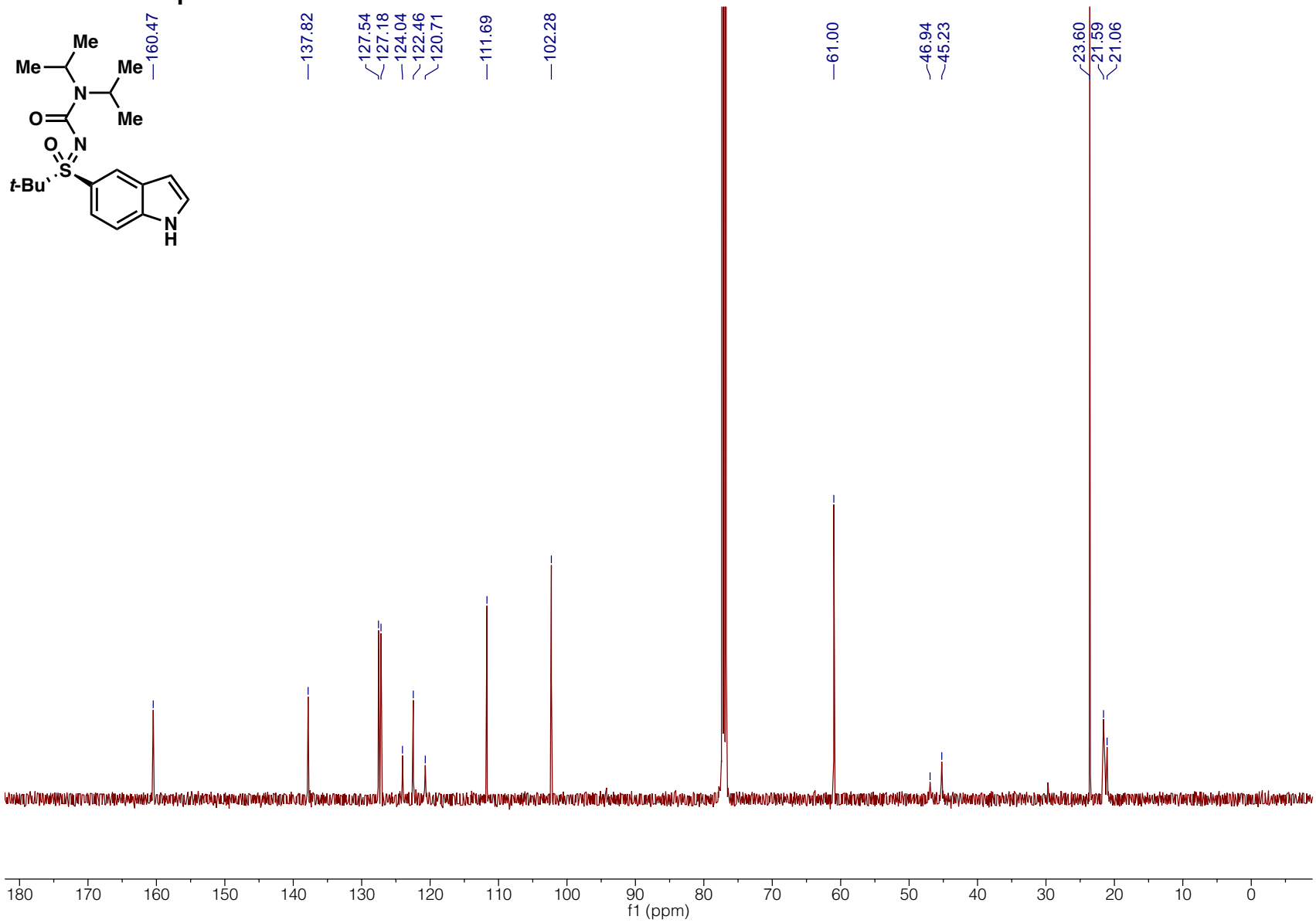
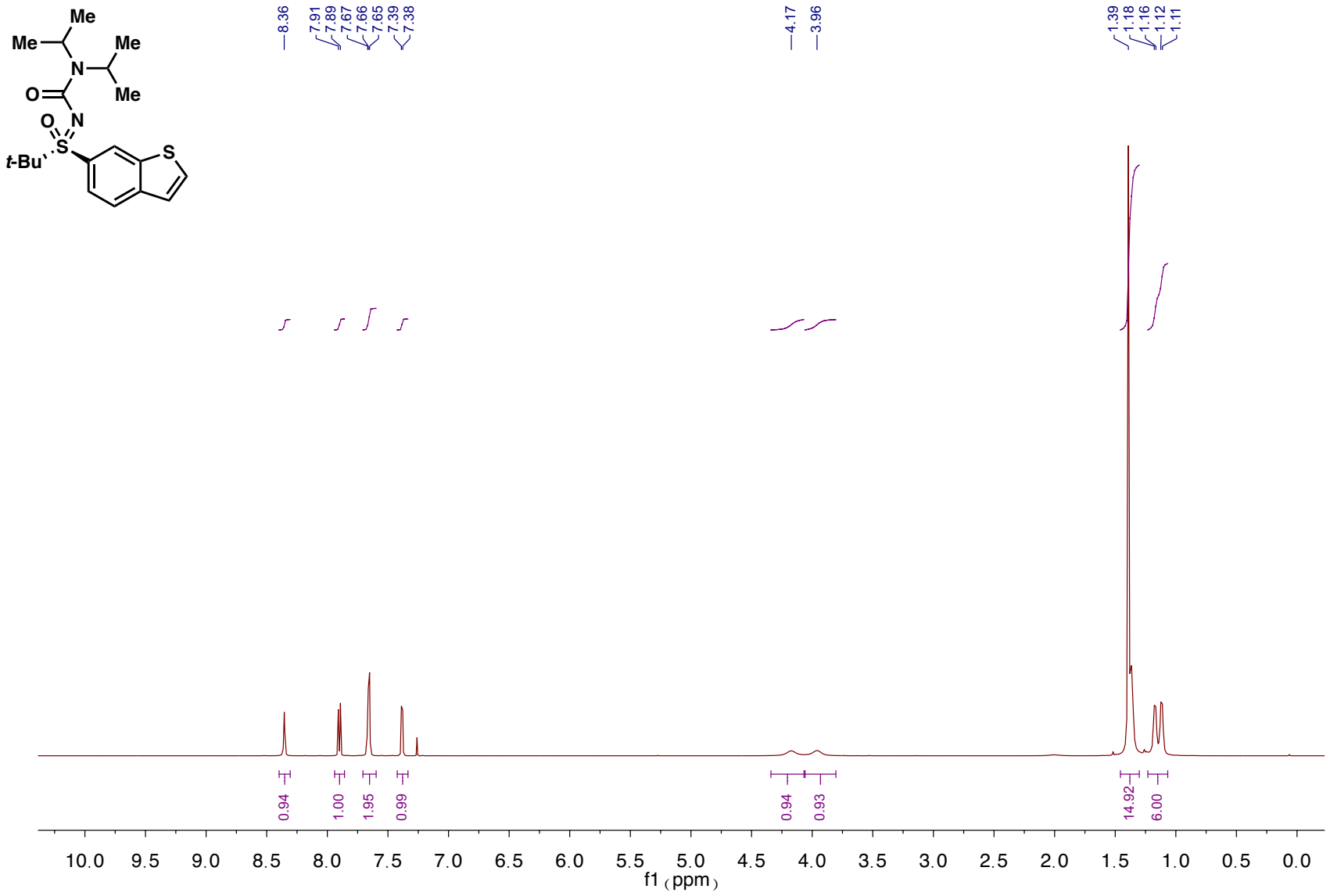


^{1}H NMR of compound 3b:



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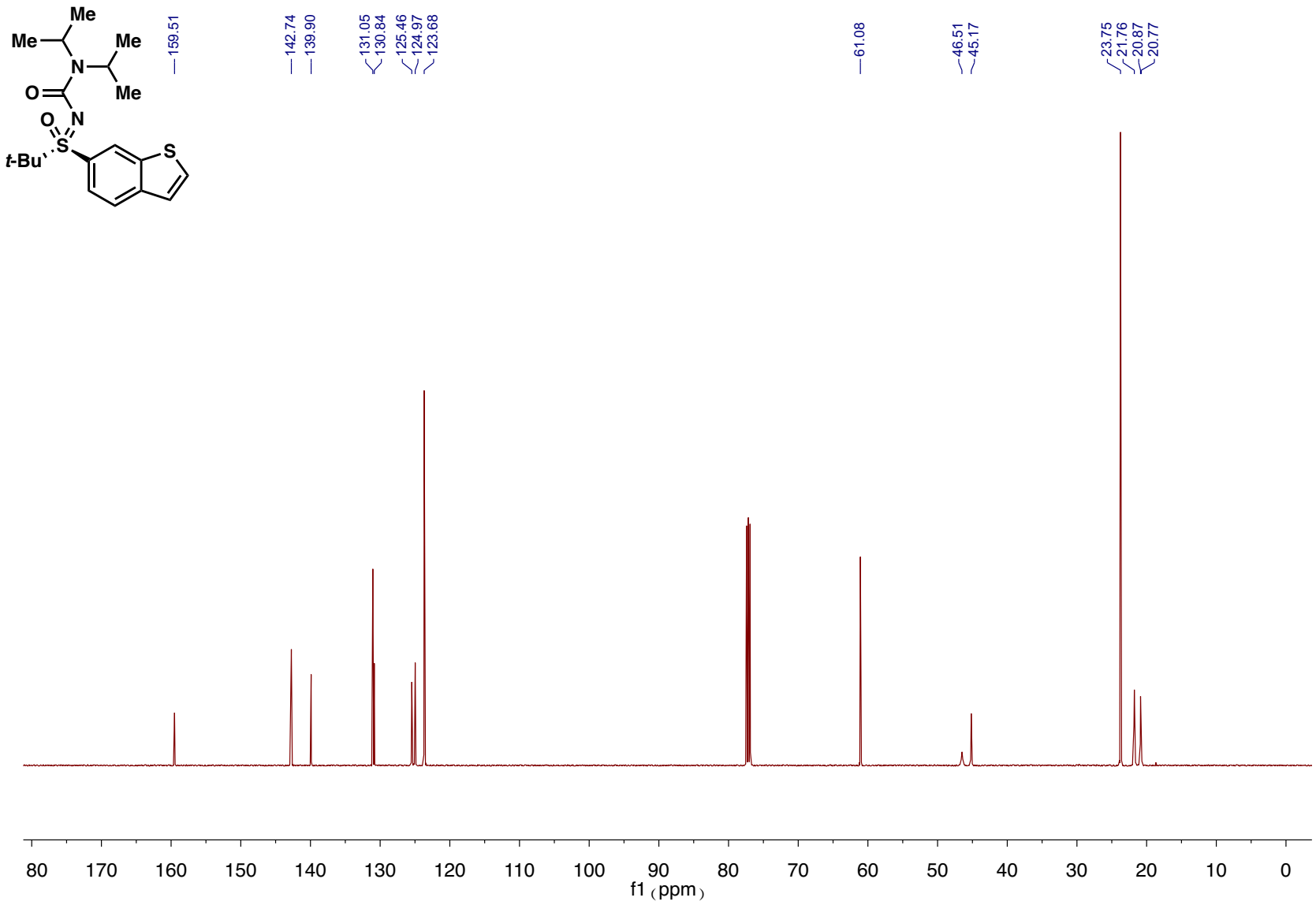
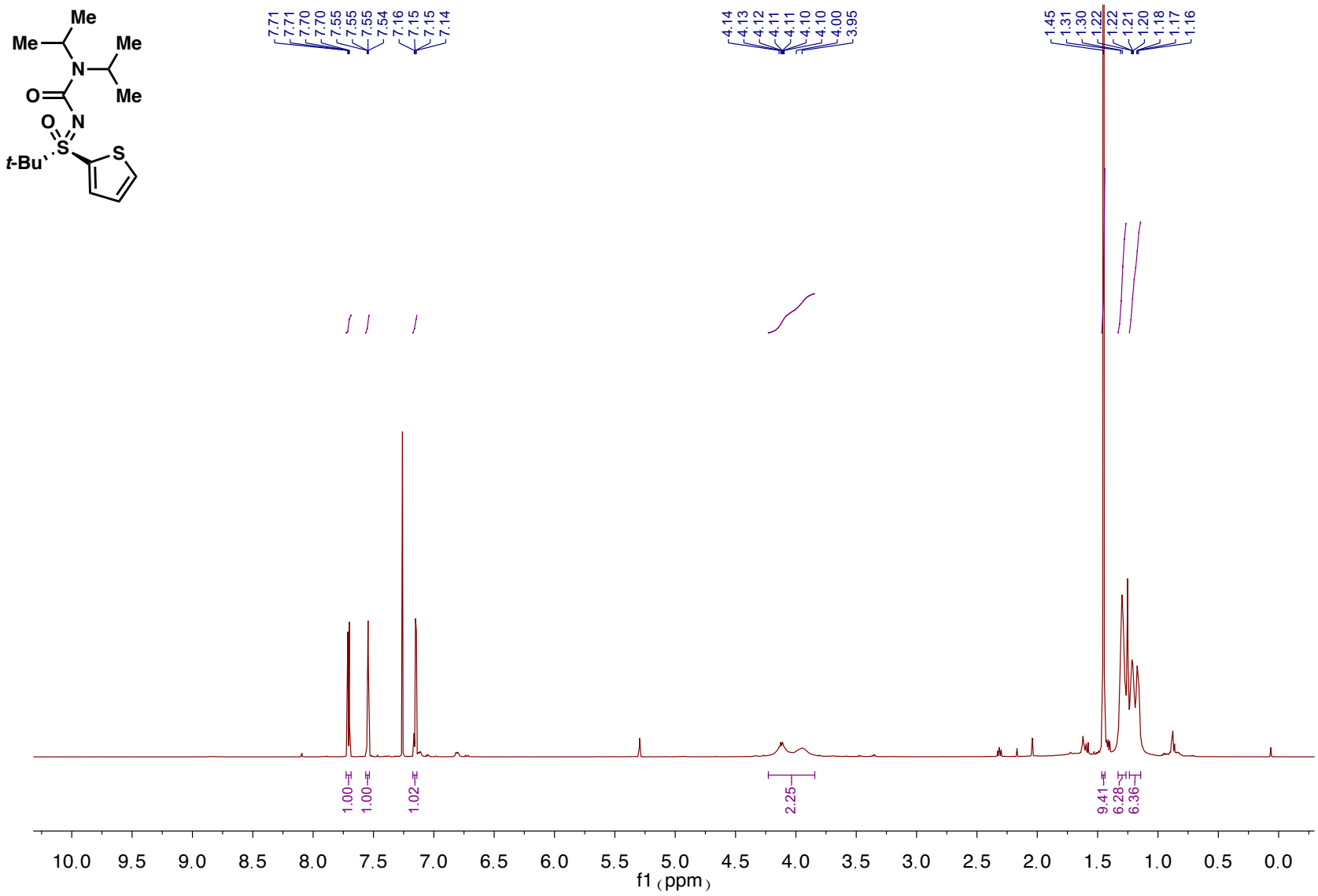
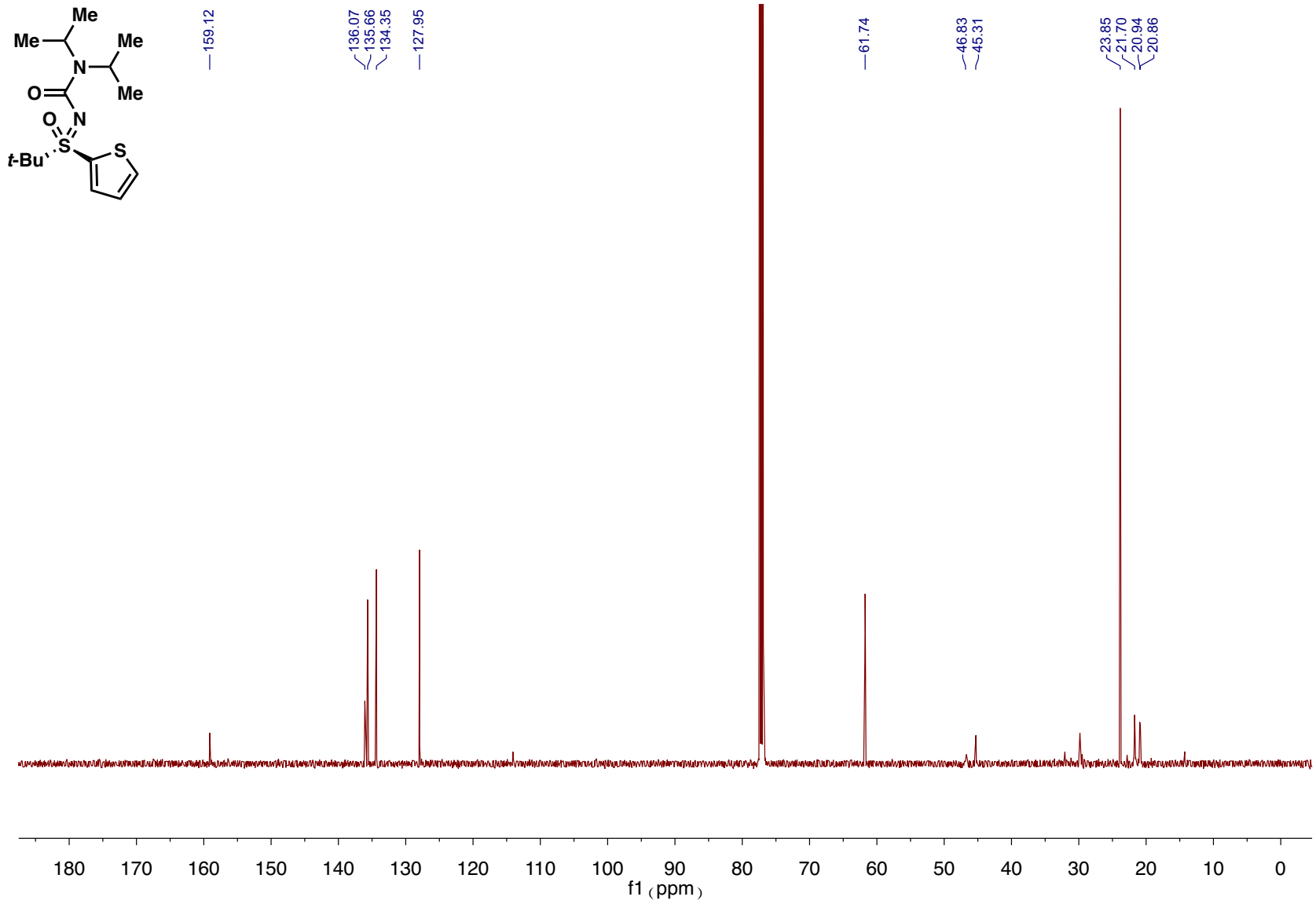


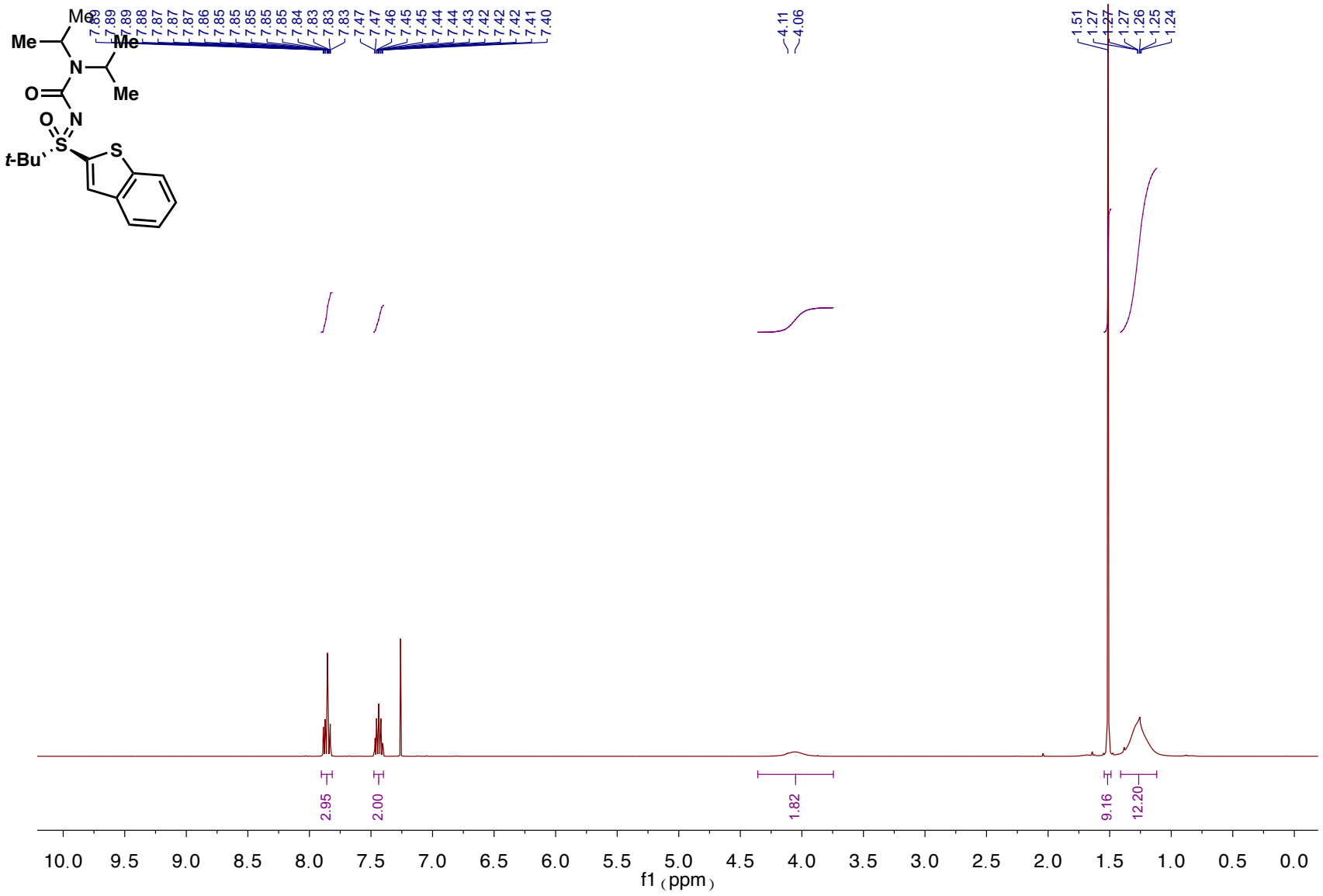
^{1}H NMR of compound 3c:



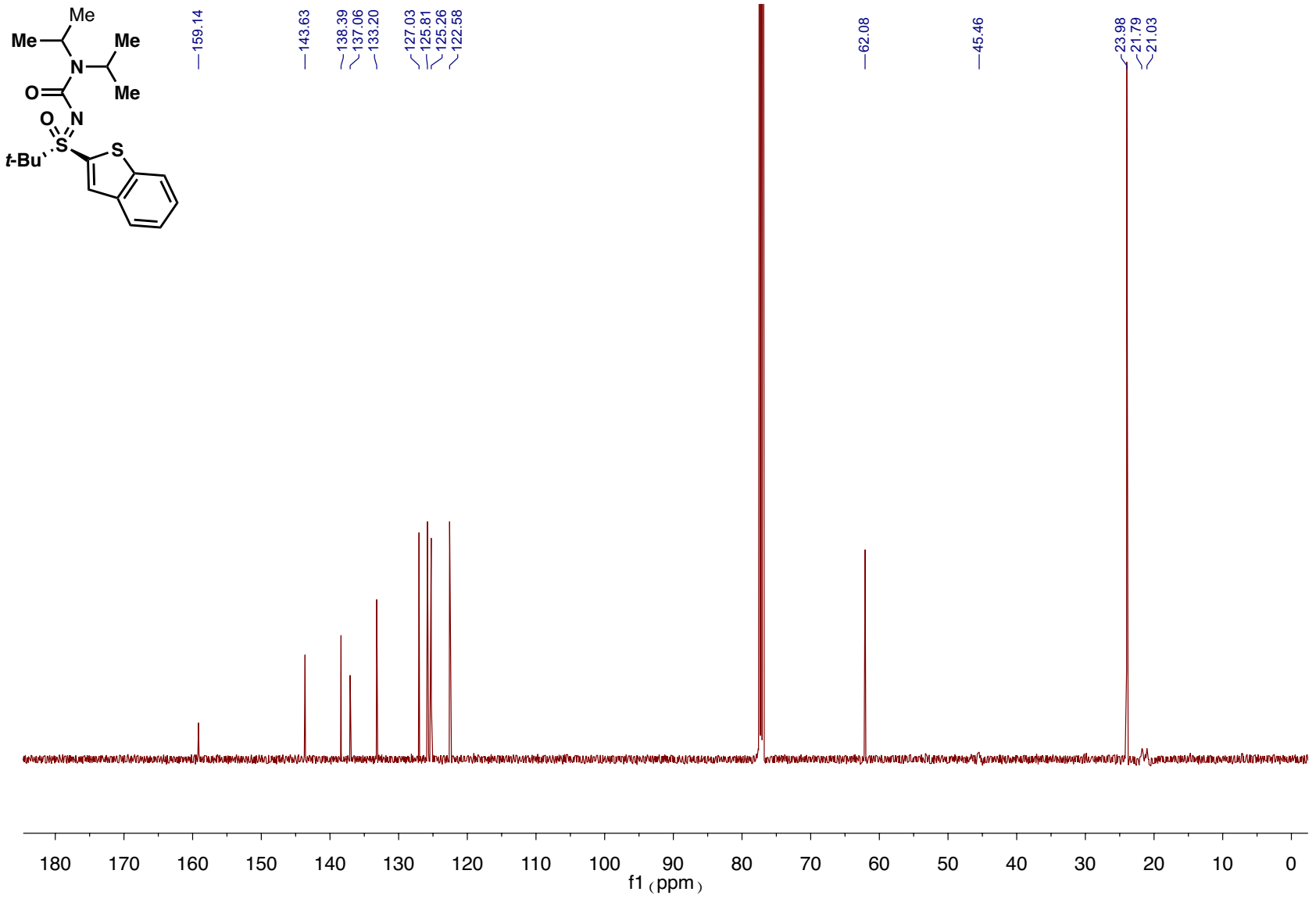
^{13}C NMR of compound 3c:



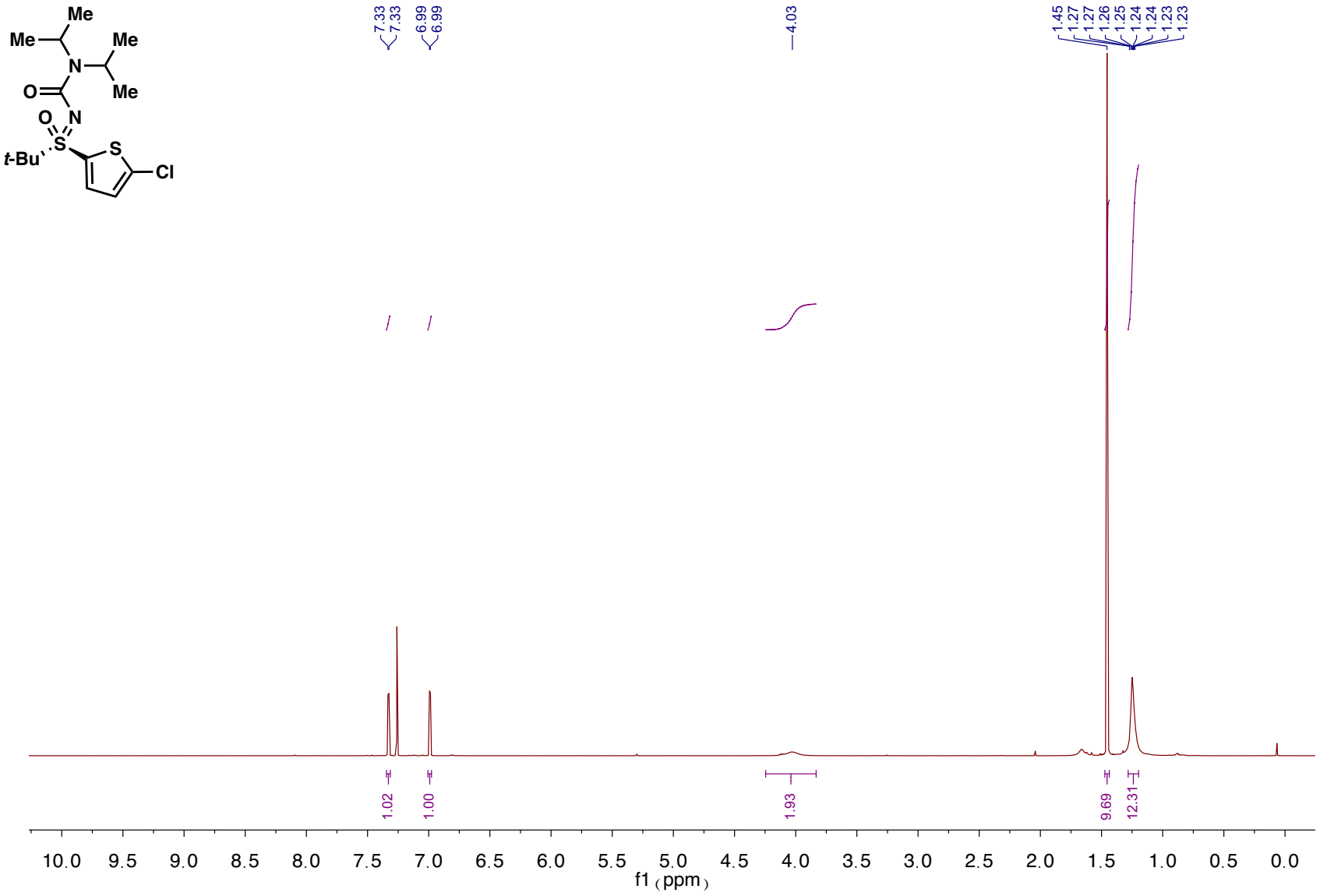
^{1}H NMR of compound 3d:



^{13}C NMR of compound 3d:



^{1}H NMR of compound 3e:



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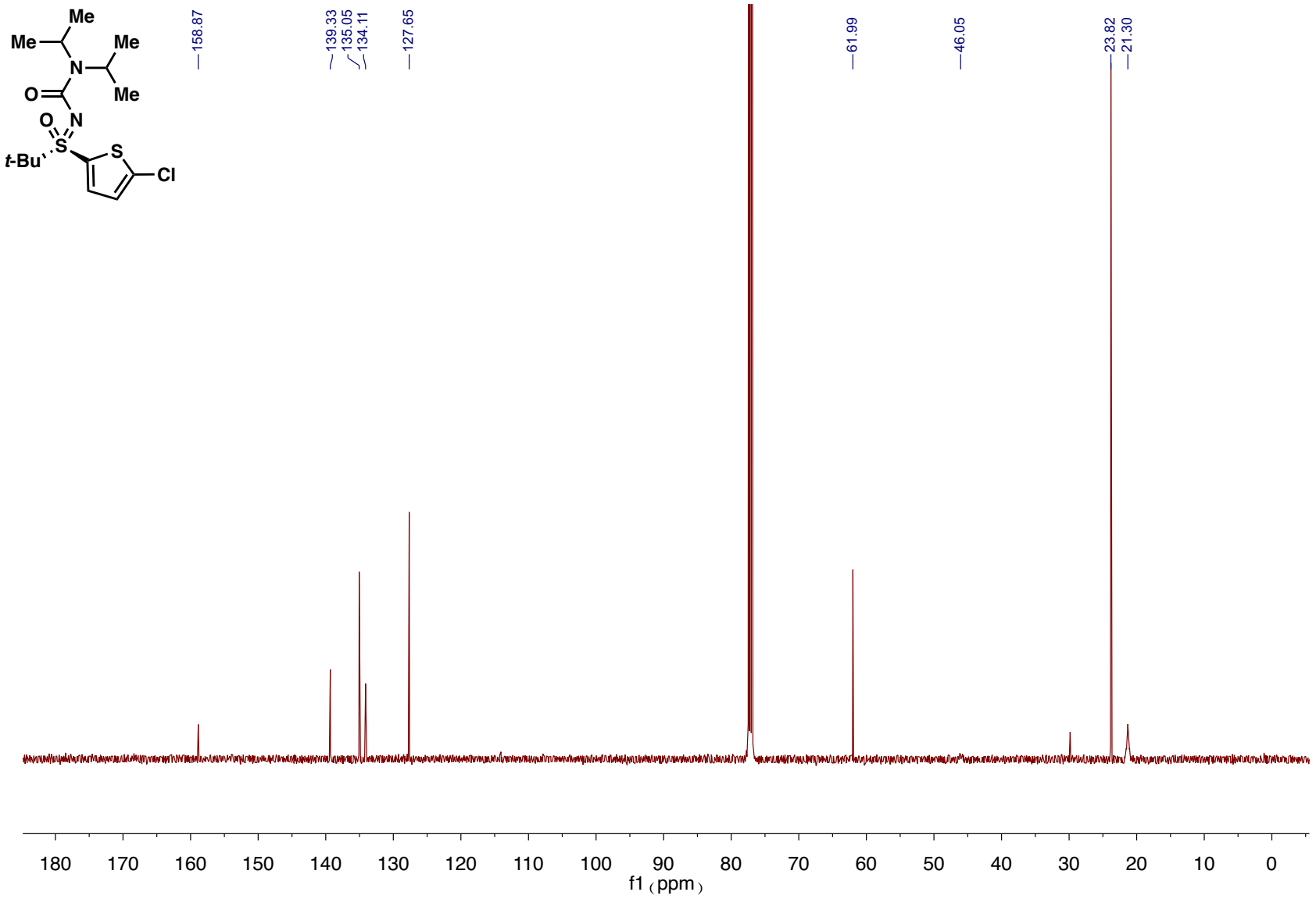
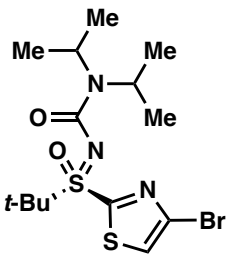


^{1}H NMR of compound 3f:



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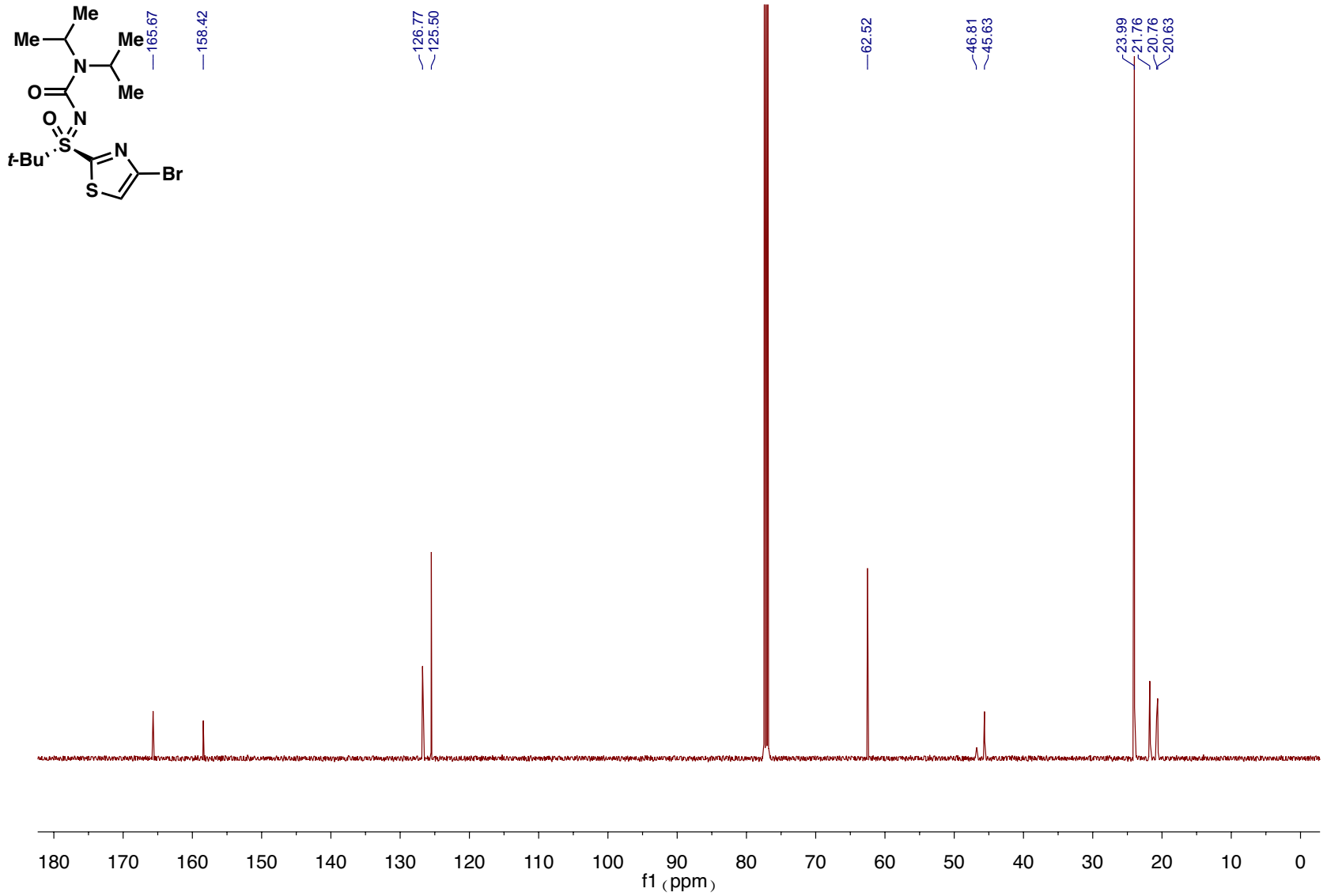
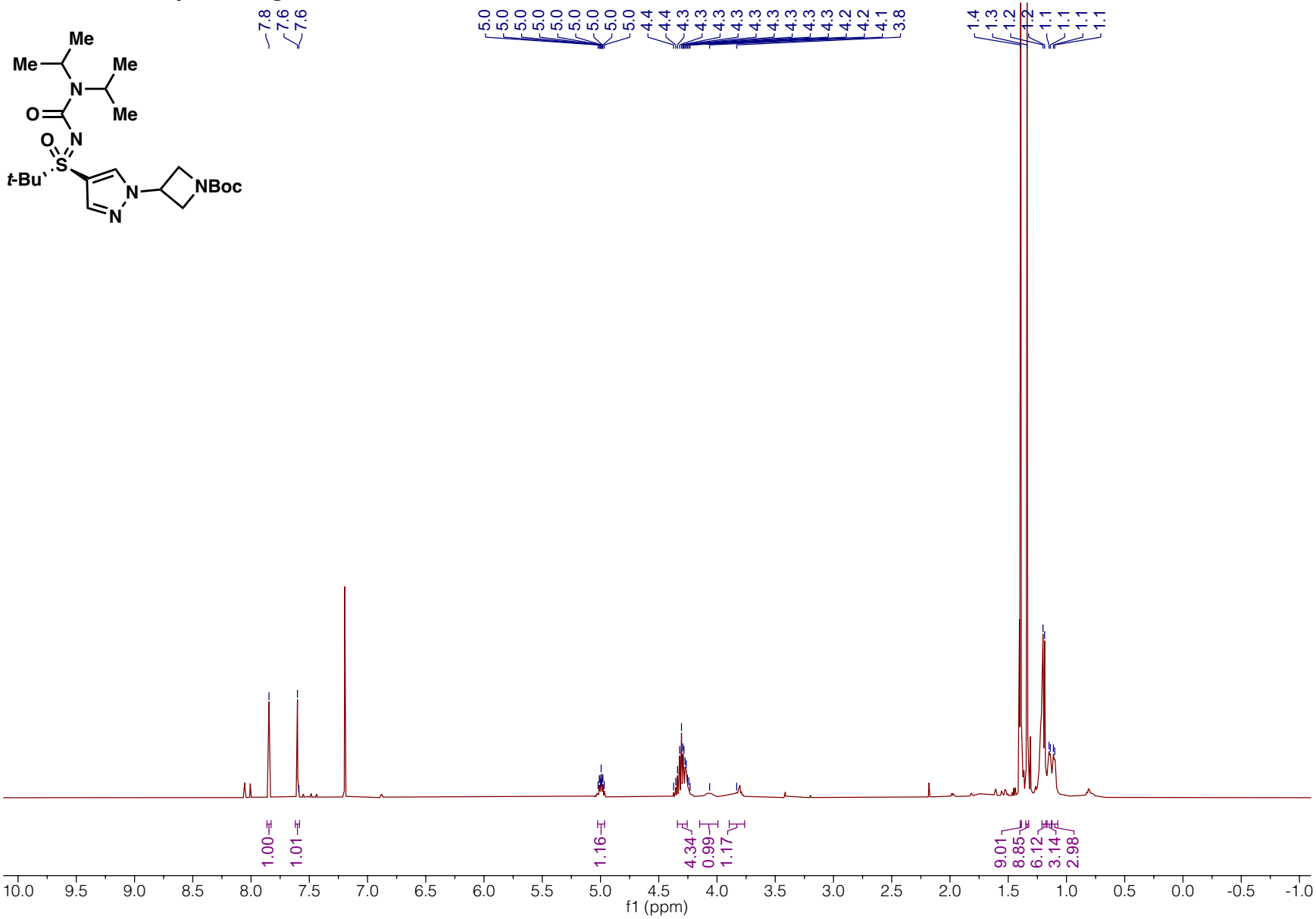


^{1}H NMR of compound 3g:



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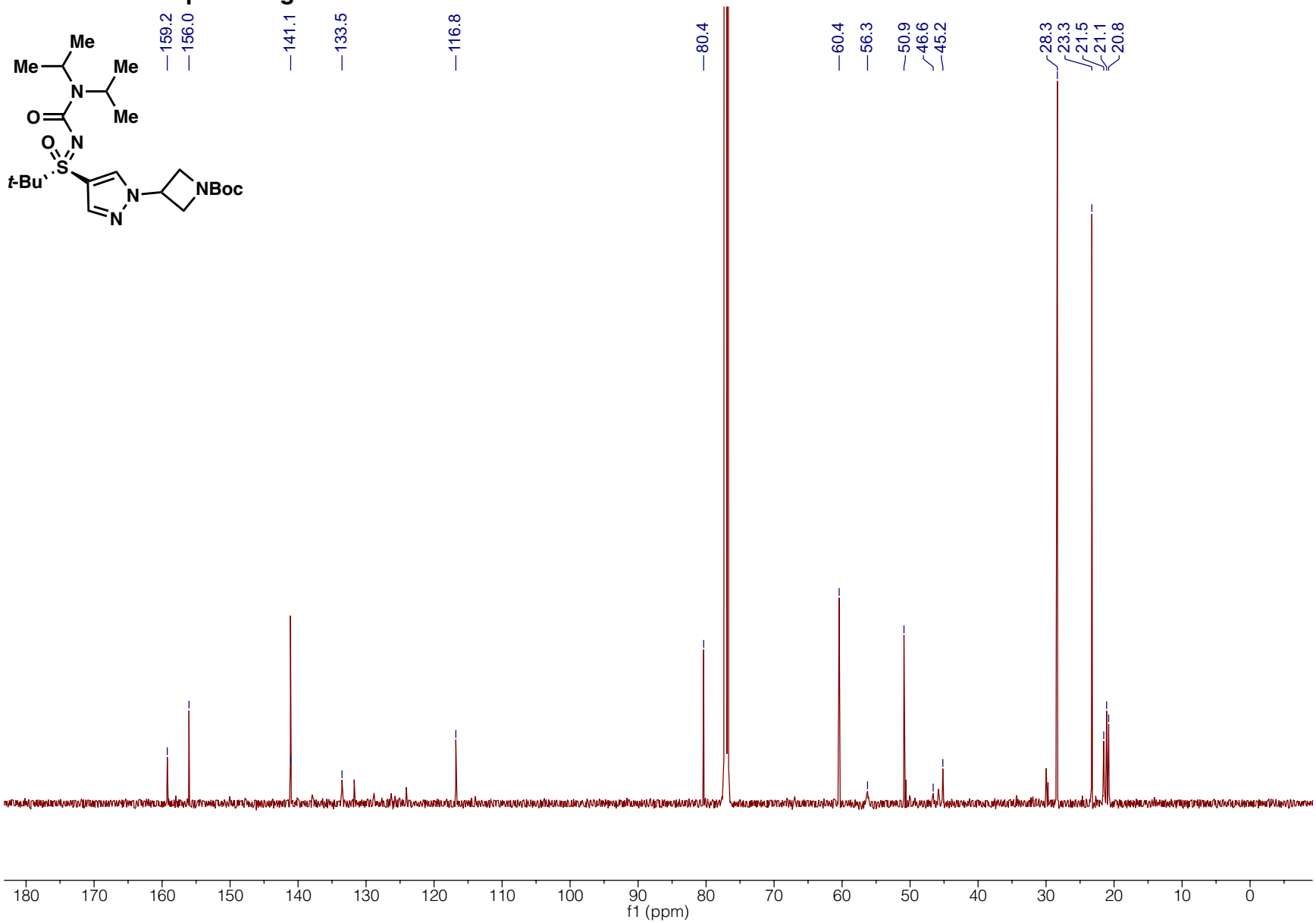
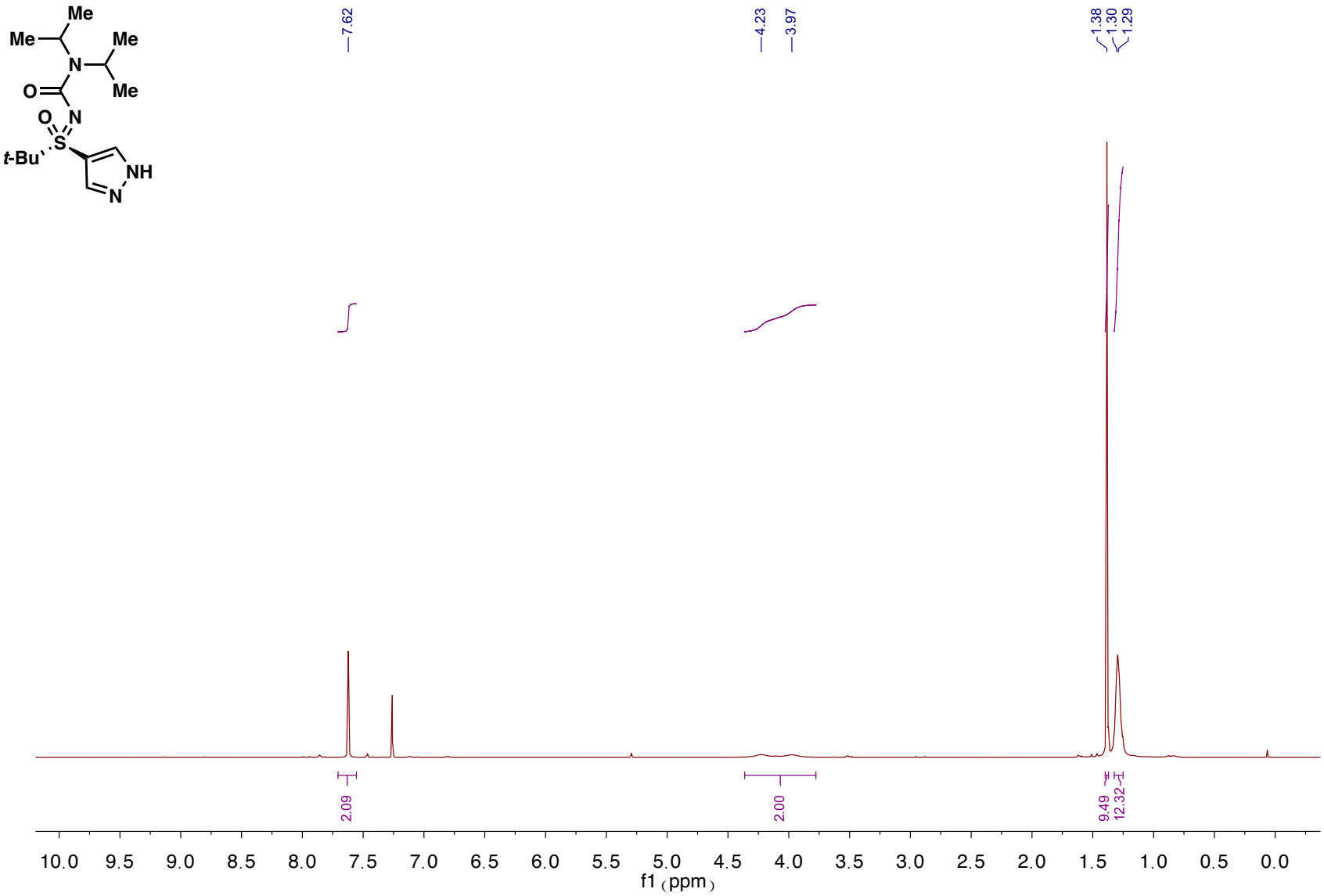


^{1}H NMR of compound 3h:



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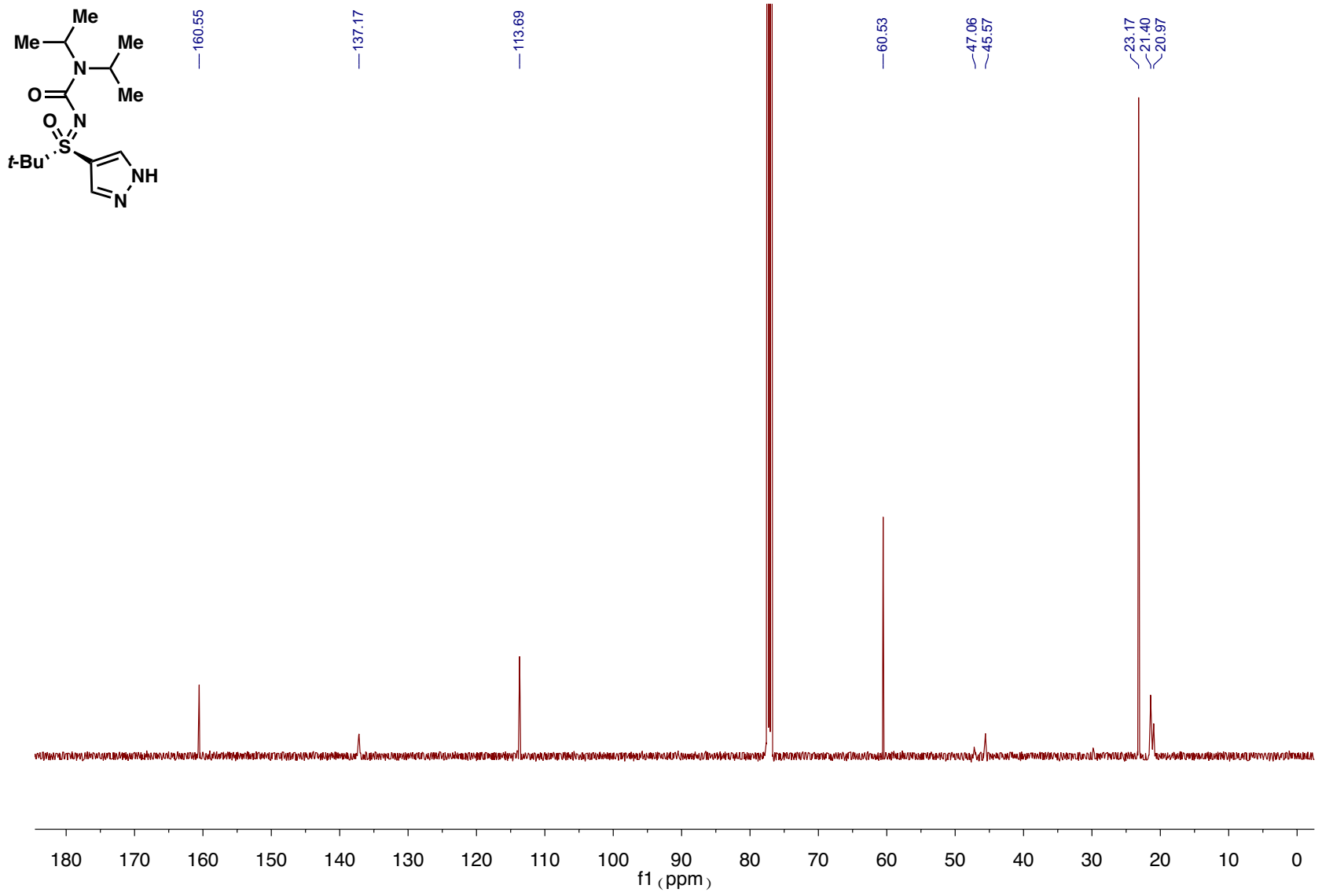
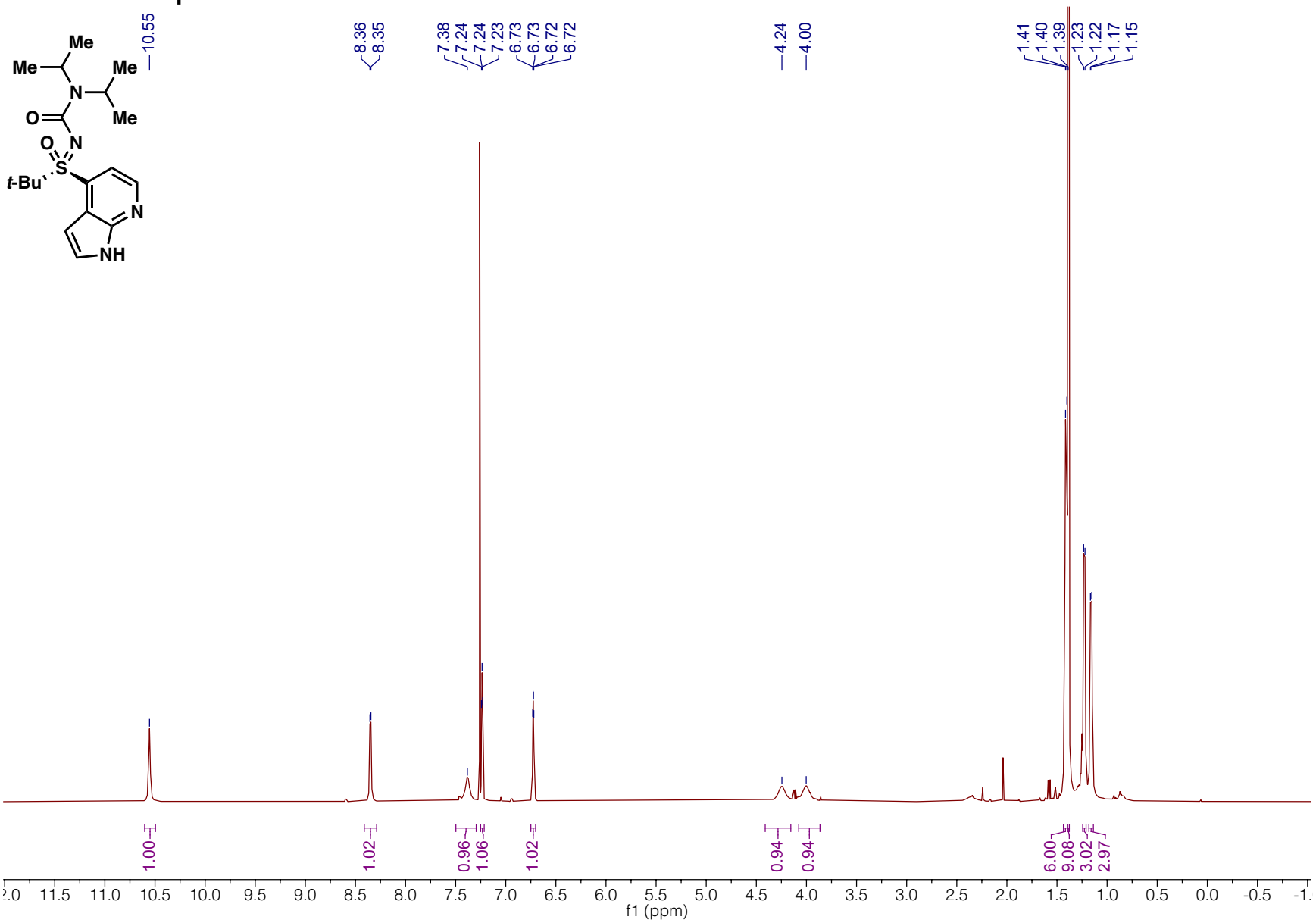


^{1}H NMR of compound 3i:



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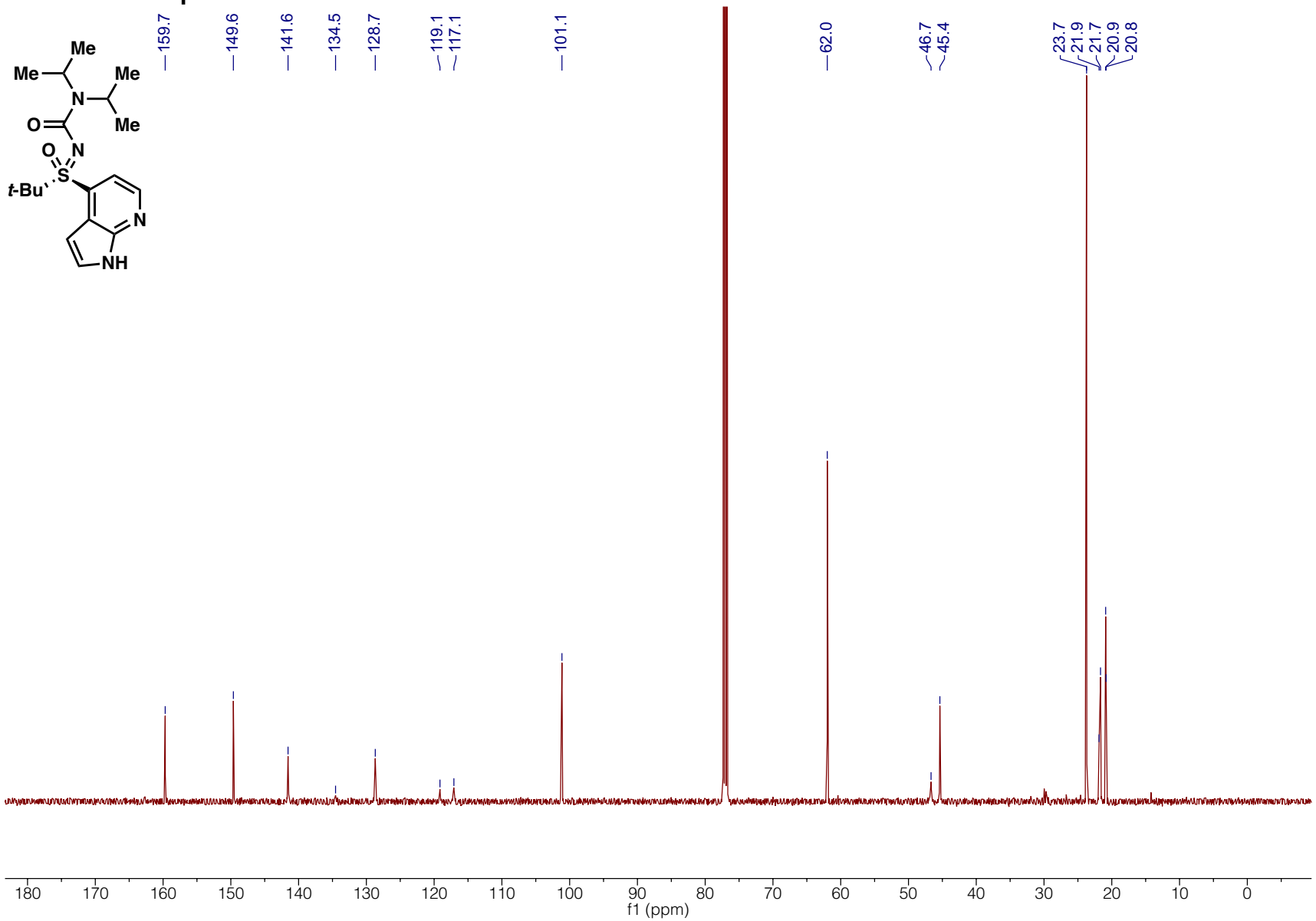
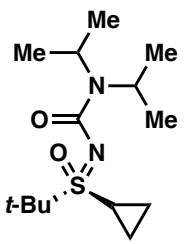
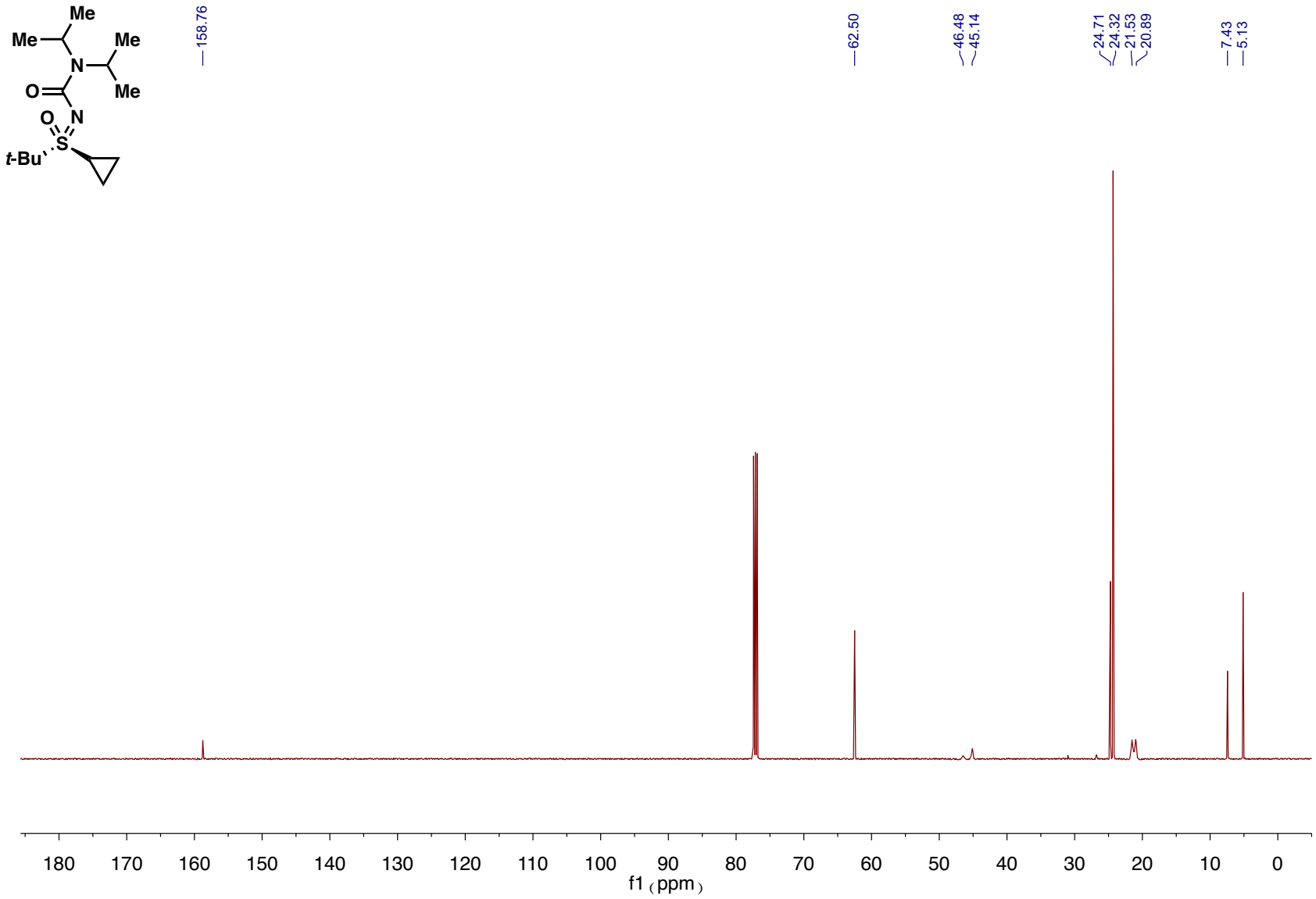


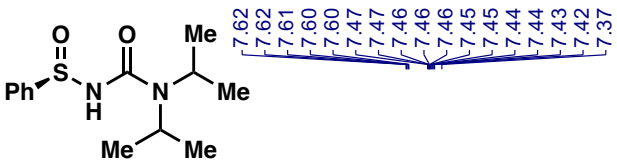
^{1}H NMR of compound 4a:



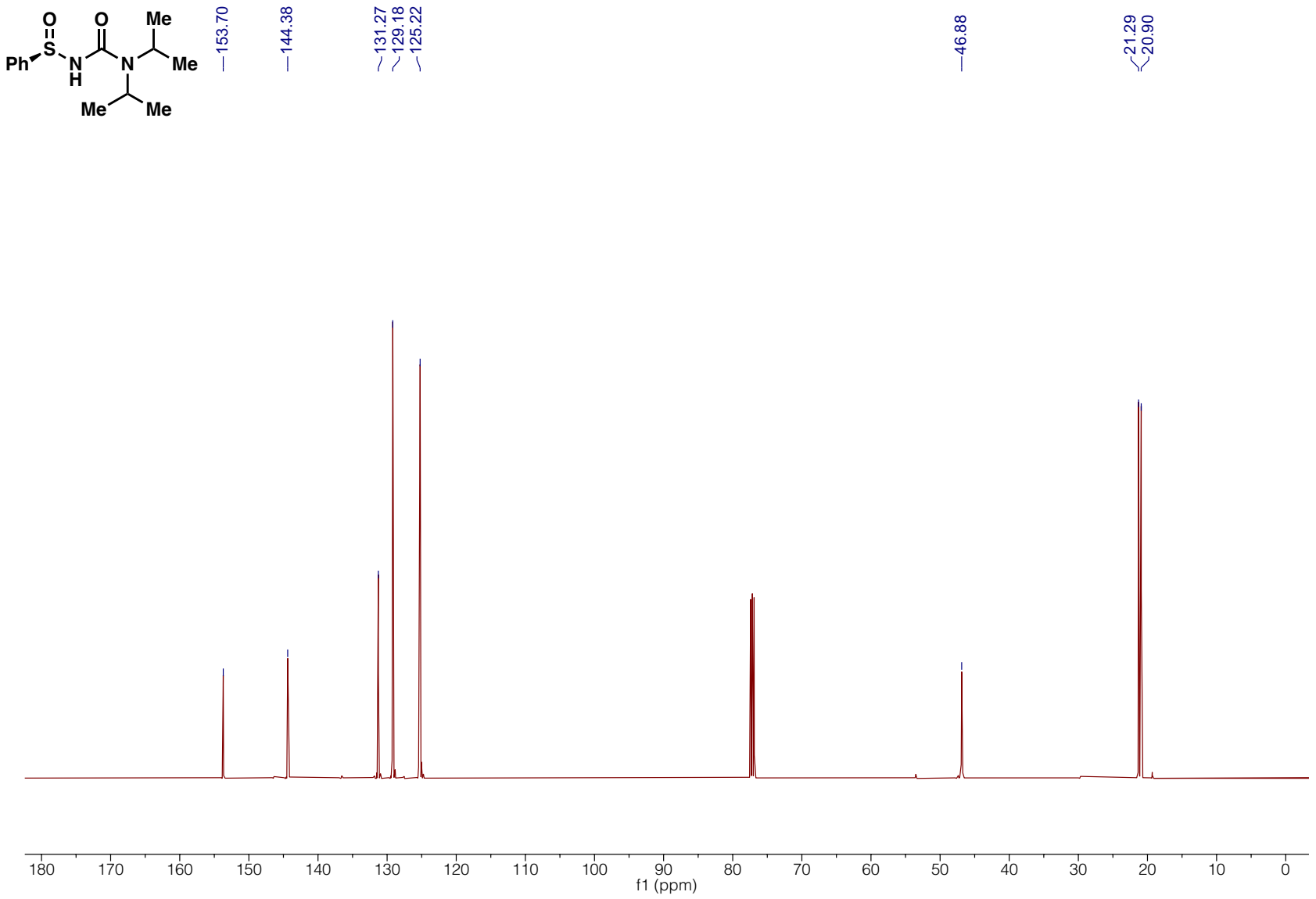
^{13}C NMR of compound 4a:



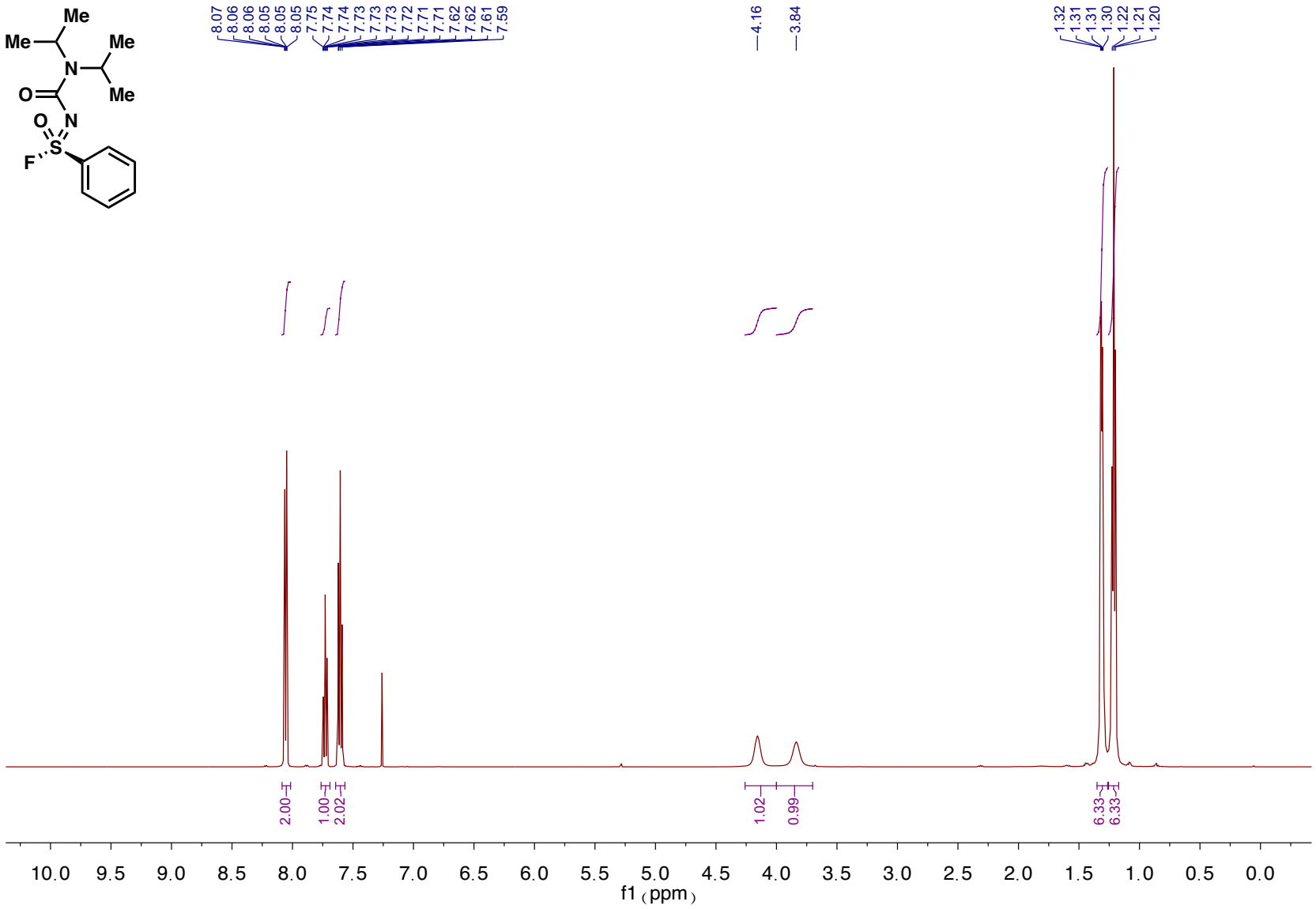
^{1}H NMR of phenyl sulfinyl urea:



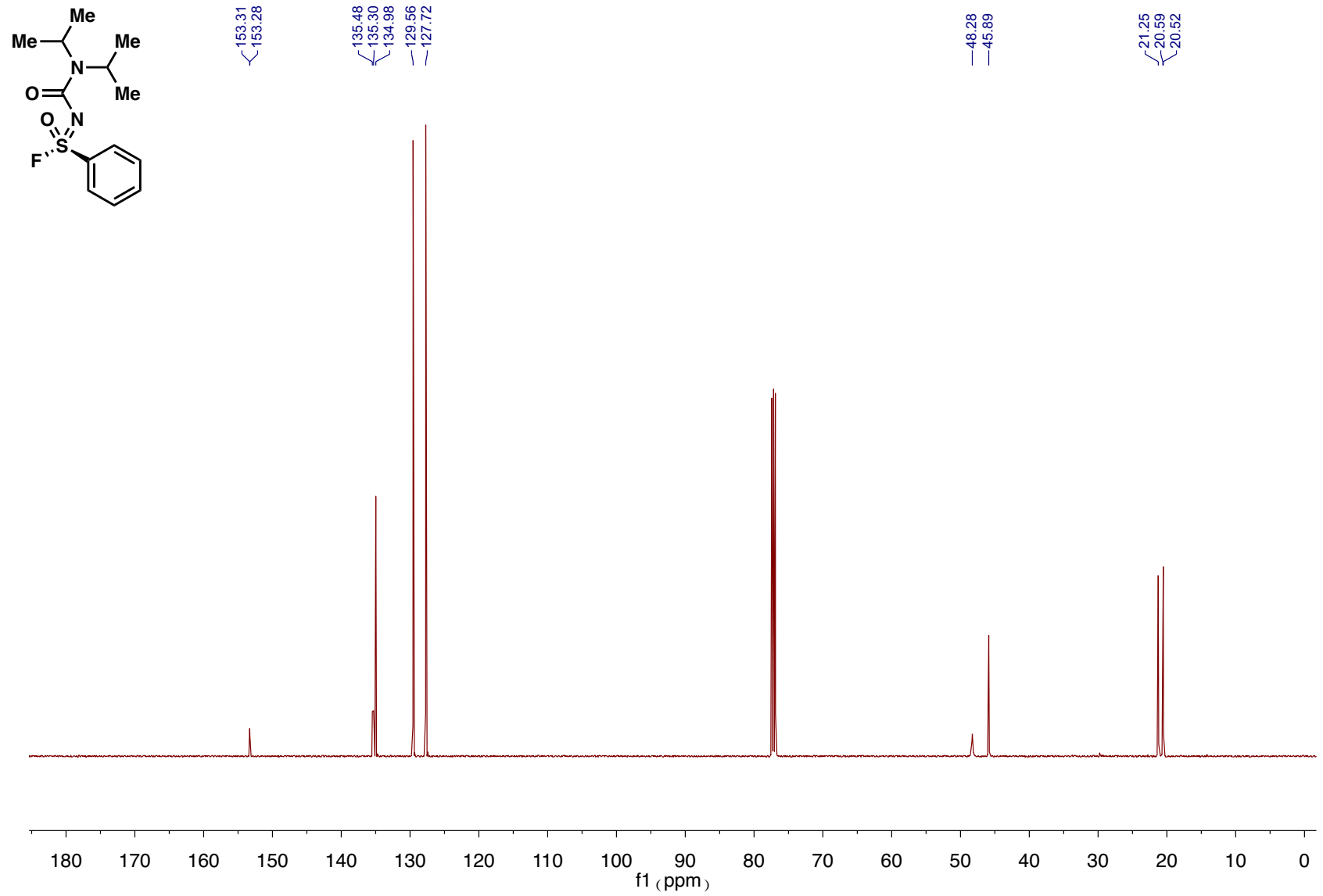
^{13}C NMR of phenyl sulfinyl urea:



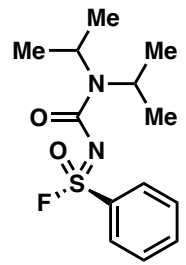
^{1}H NMR of compound S6a:



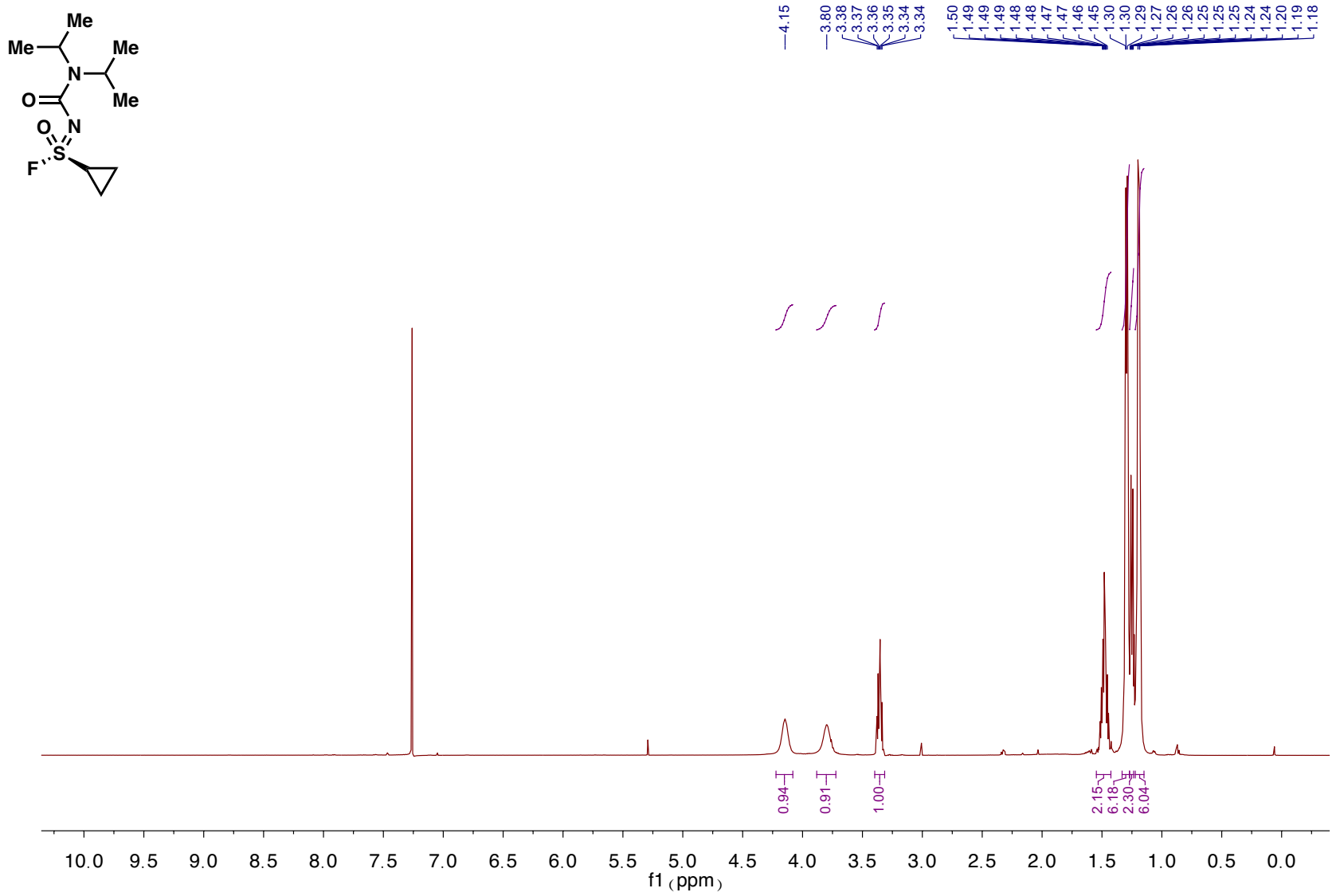
^{13}C NMR of compound S6a:



^{19}F NMR of compound S6a:



^{1}H NMR of 6b: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3.37
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3.34
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1.49
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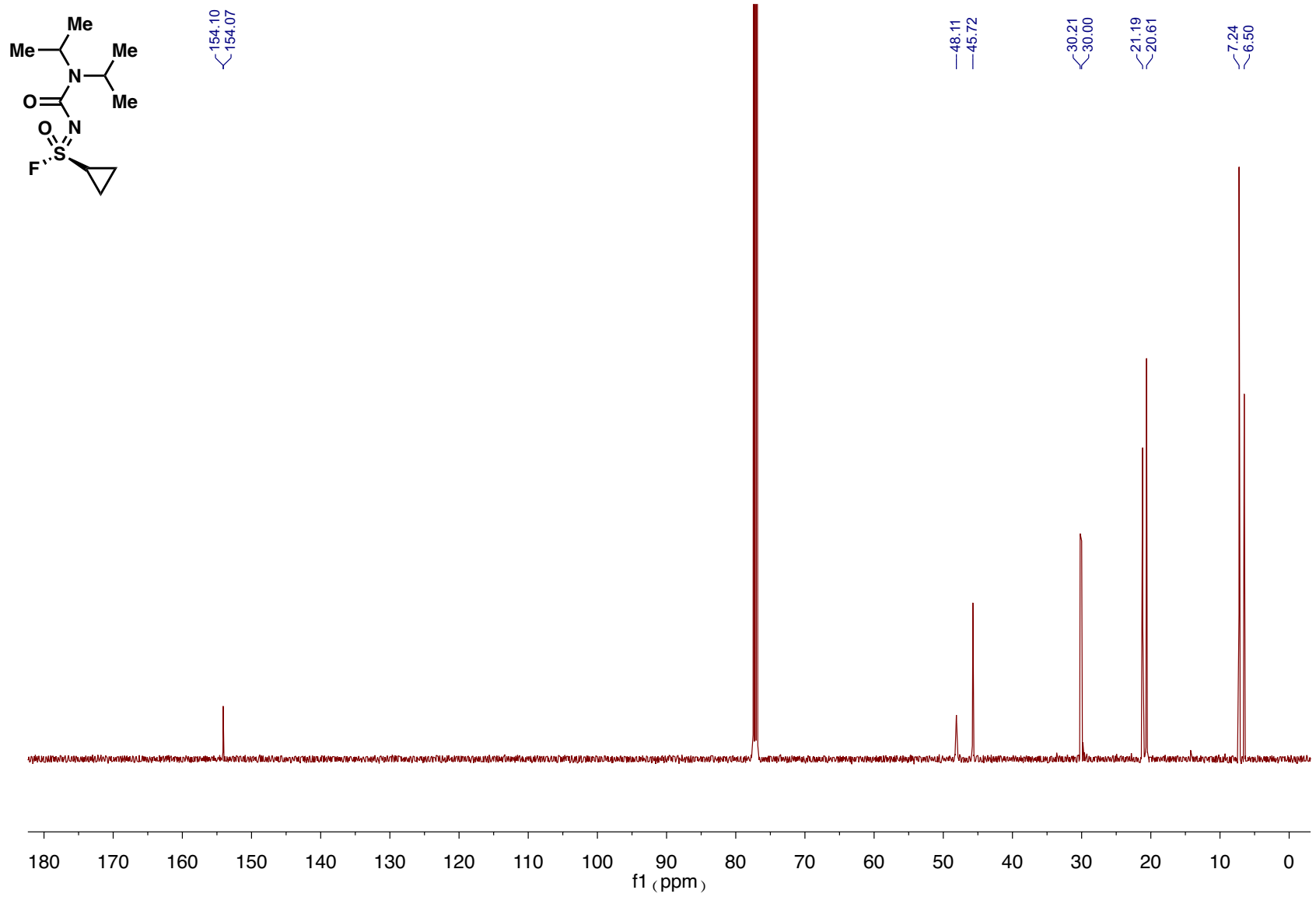
1.48
1.47
1.47
1.46
1.45
1.30
1.30
1.29
1.27
1.26
1.26
1.25
1.25
1.25
1.24
1.24
1.20
1.19
1.18
0.94
0.91
1.00
2.15
6.18
2.30
6.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C NMR of 6b: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Me
Me
N
Me
O
O
N
S
F
154.10
154.07
48.11
45.72
30.21
30.00
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20.61
7.24
6.50
180
170
160
150
140
130
120
110
100
90
80
70
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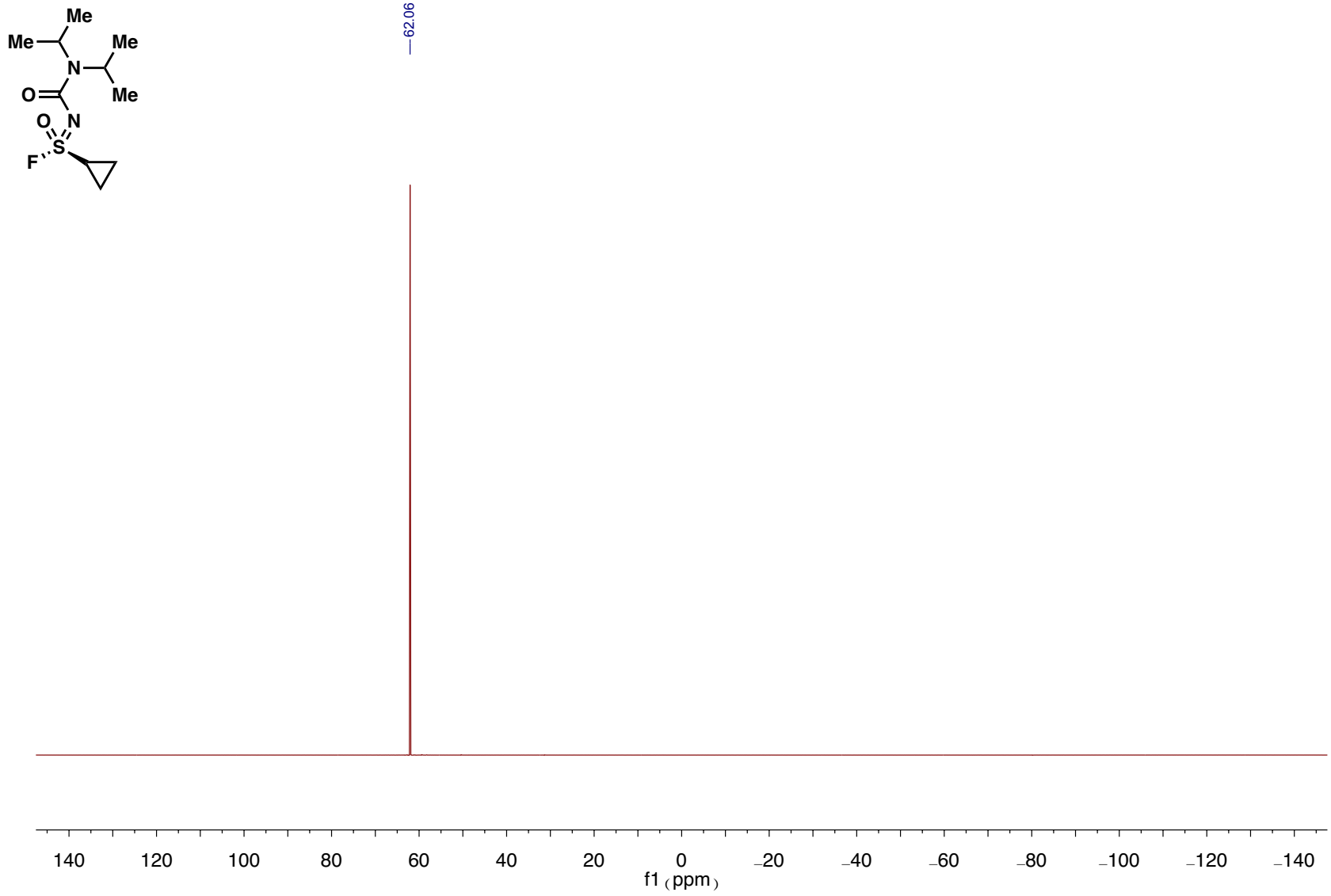
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR of 6b:


Me
Me
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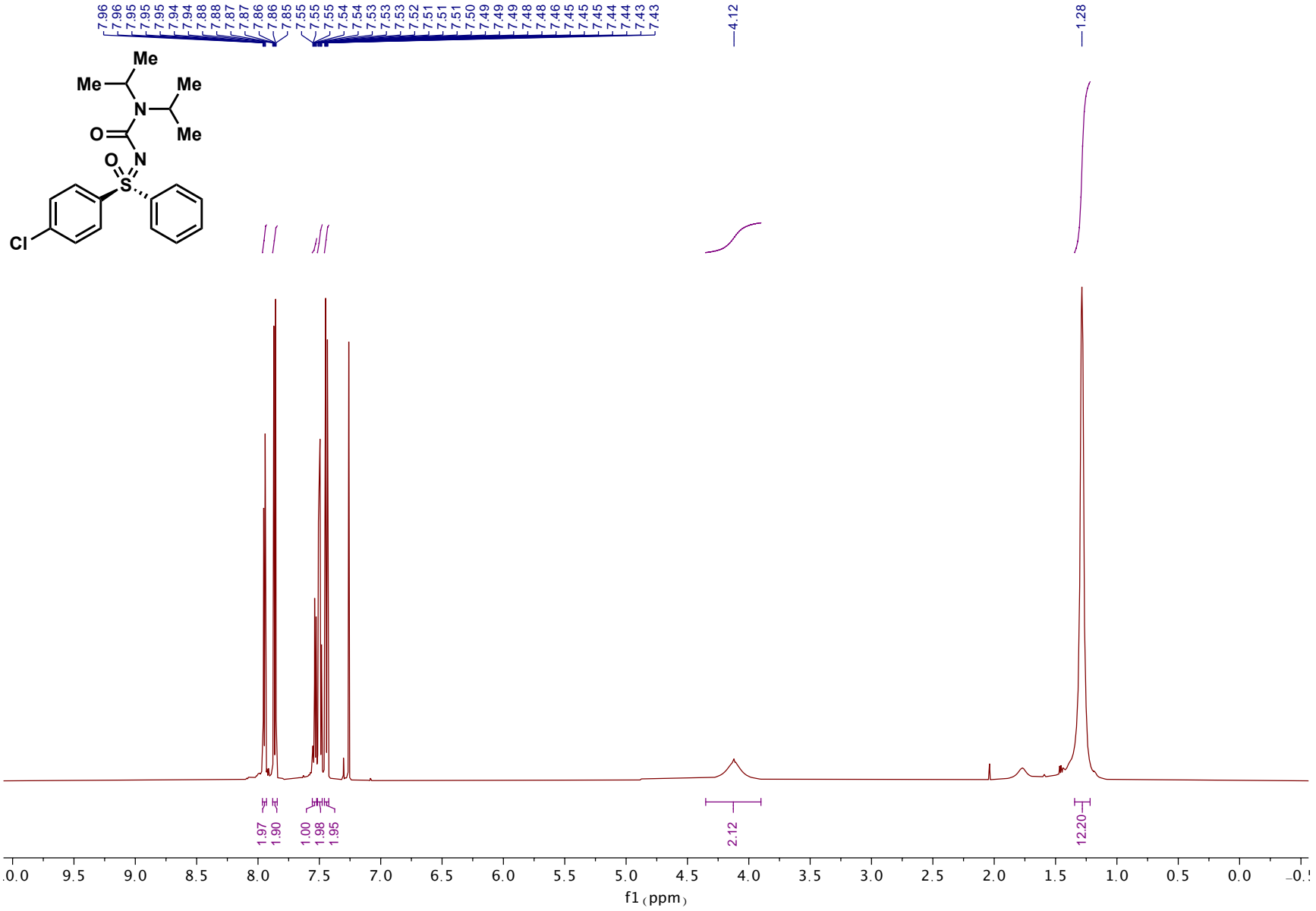
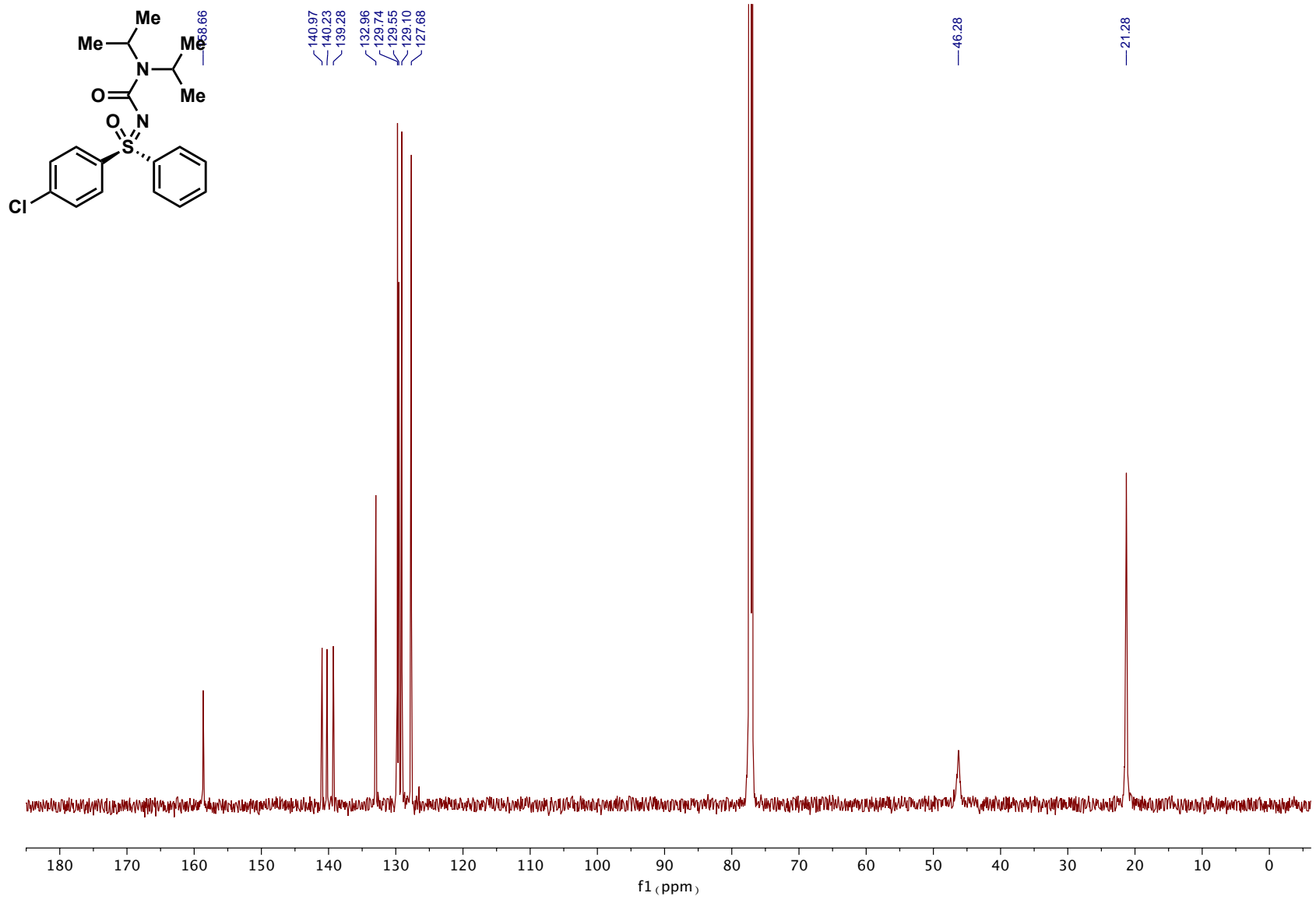
N
Me
O
O
N
S
F
62.06
140
120
100
80
60
40
20
0
−20
−40
−60
−80
−100
−120
−140
f1 (ppm)

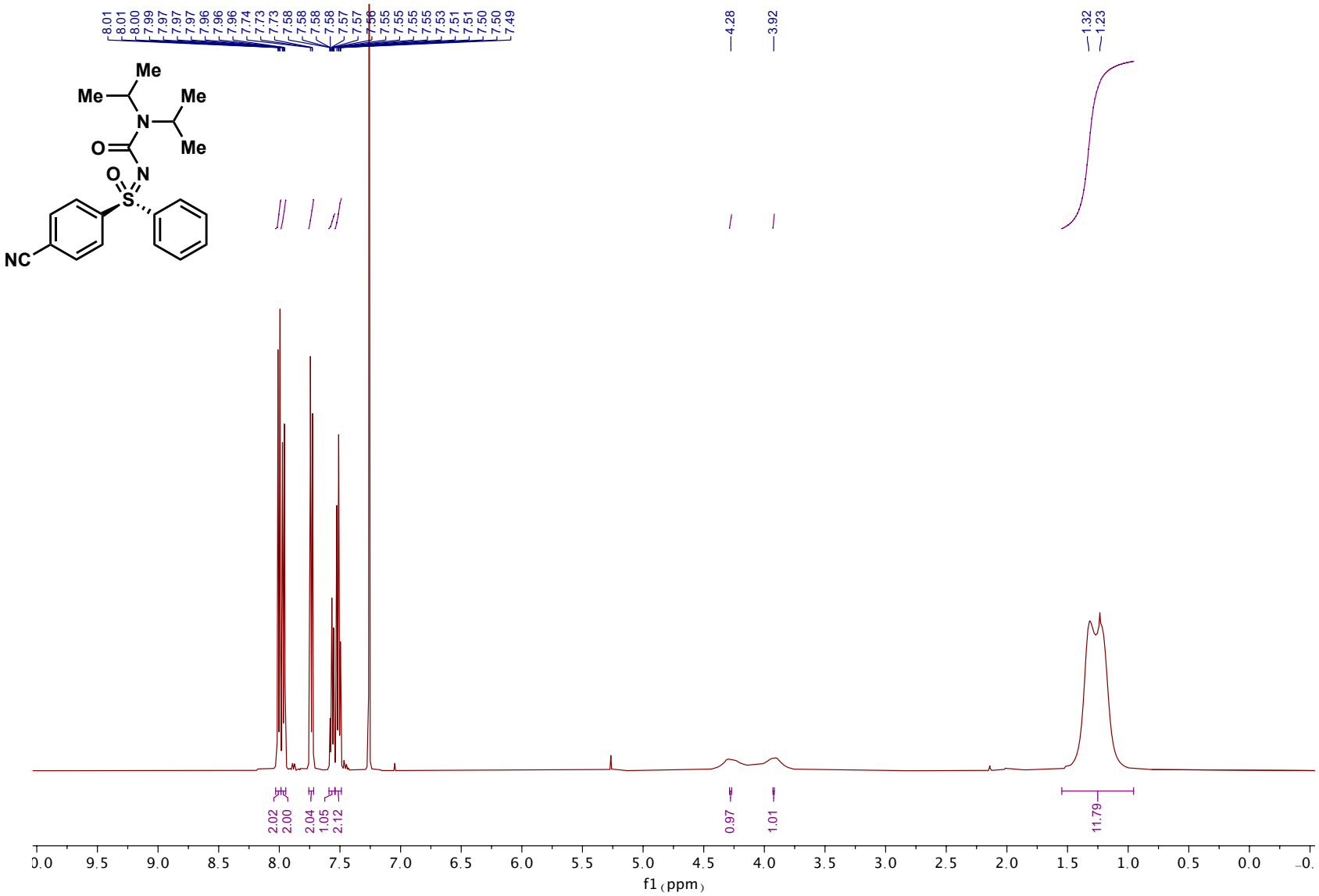
^{1}H NMR of compound 7a:



^{13}C NMR of compound 7a:



^{1}H NMR of compound 7b:



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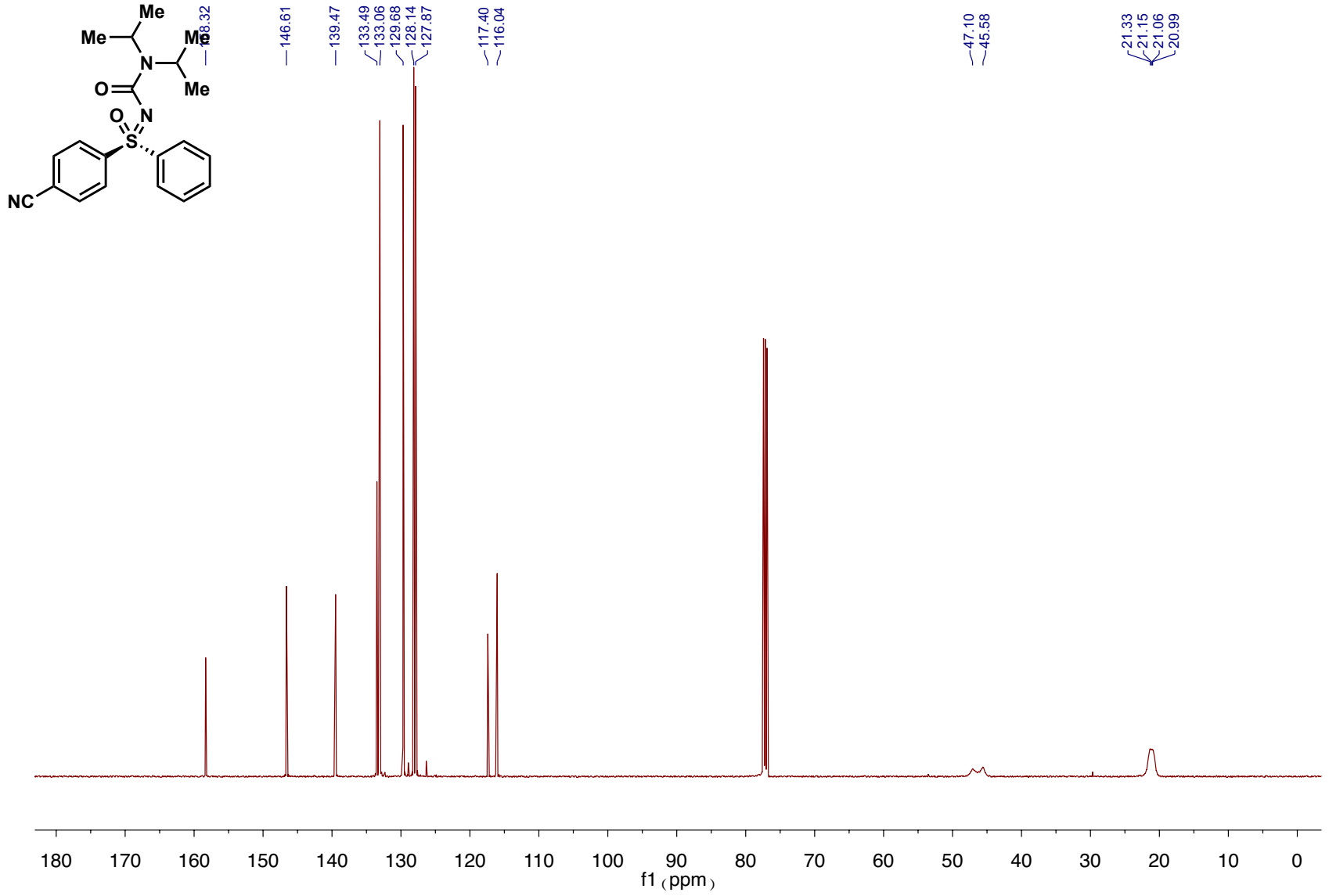

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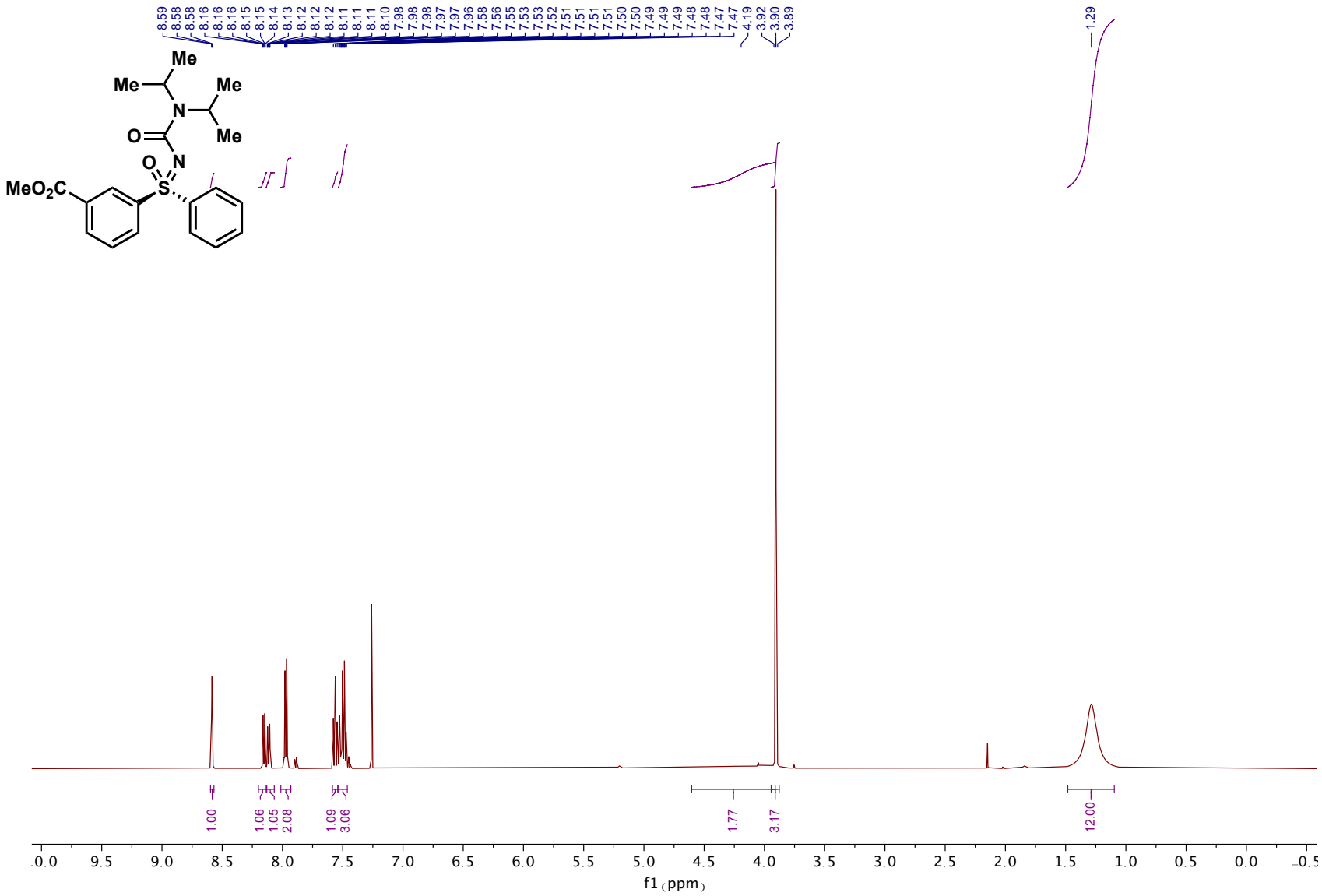
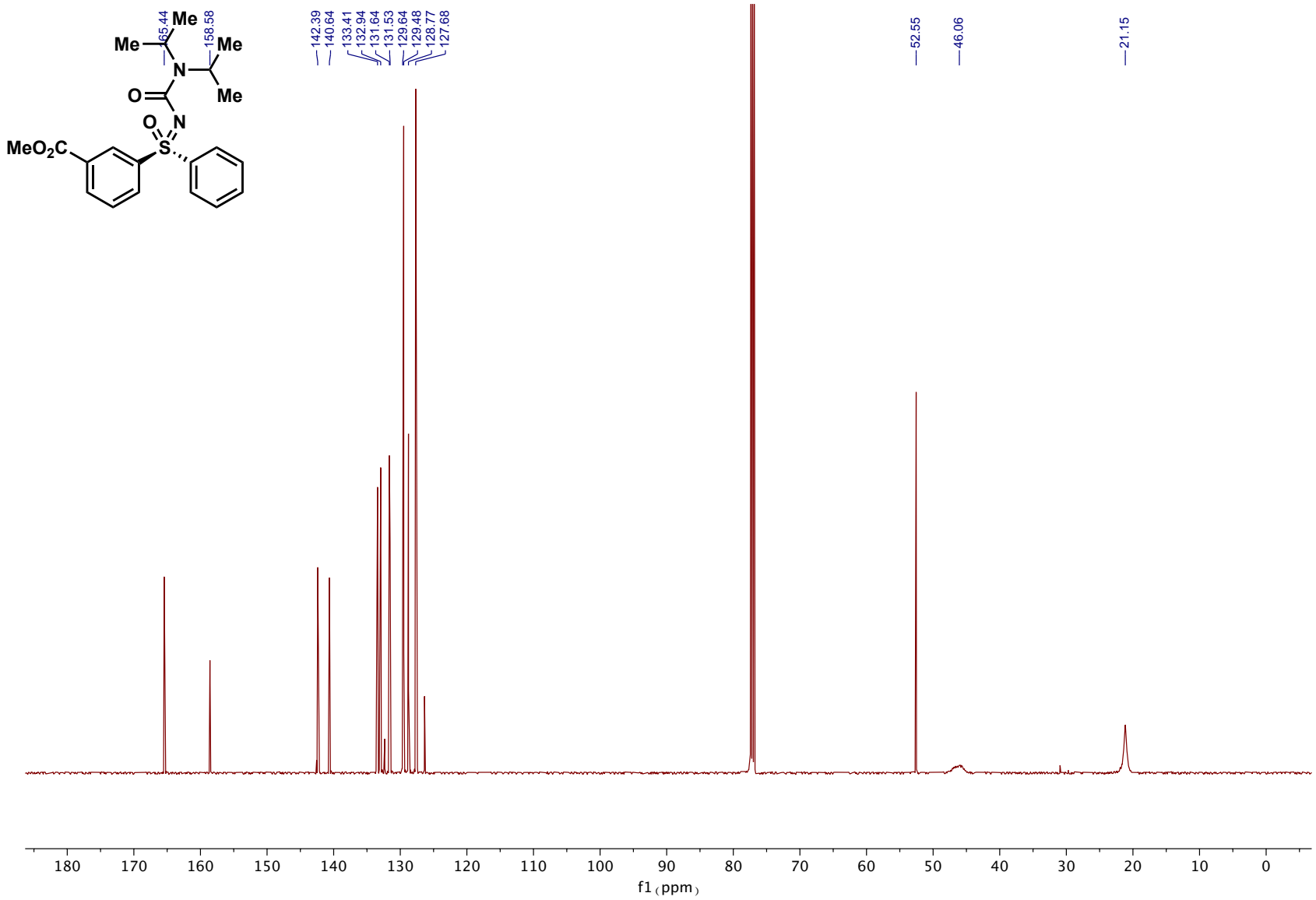
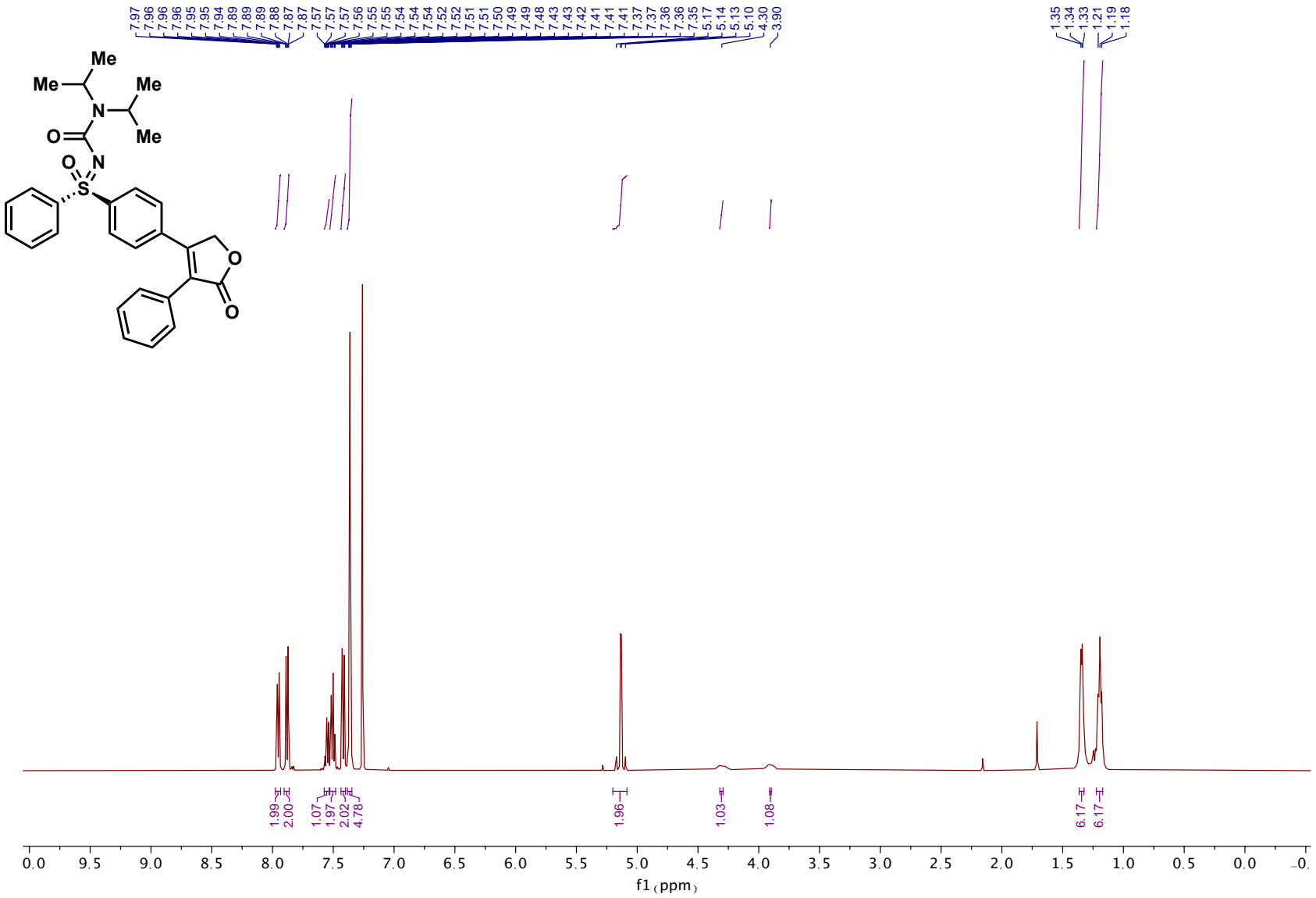


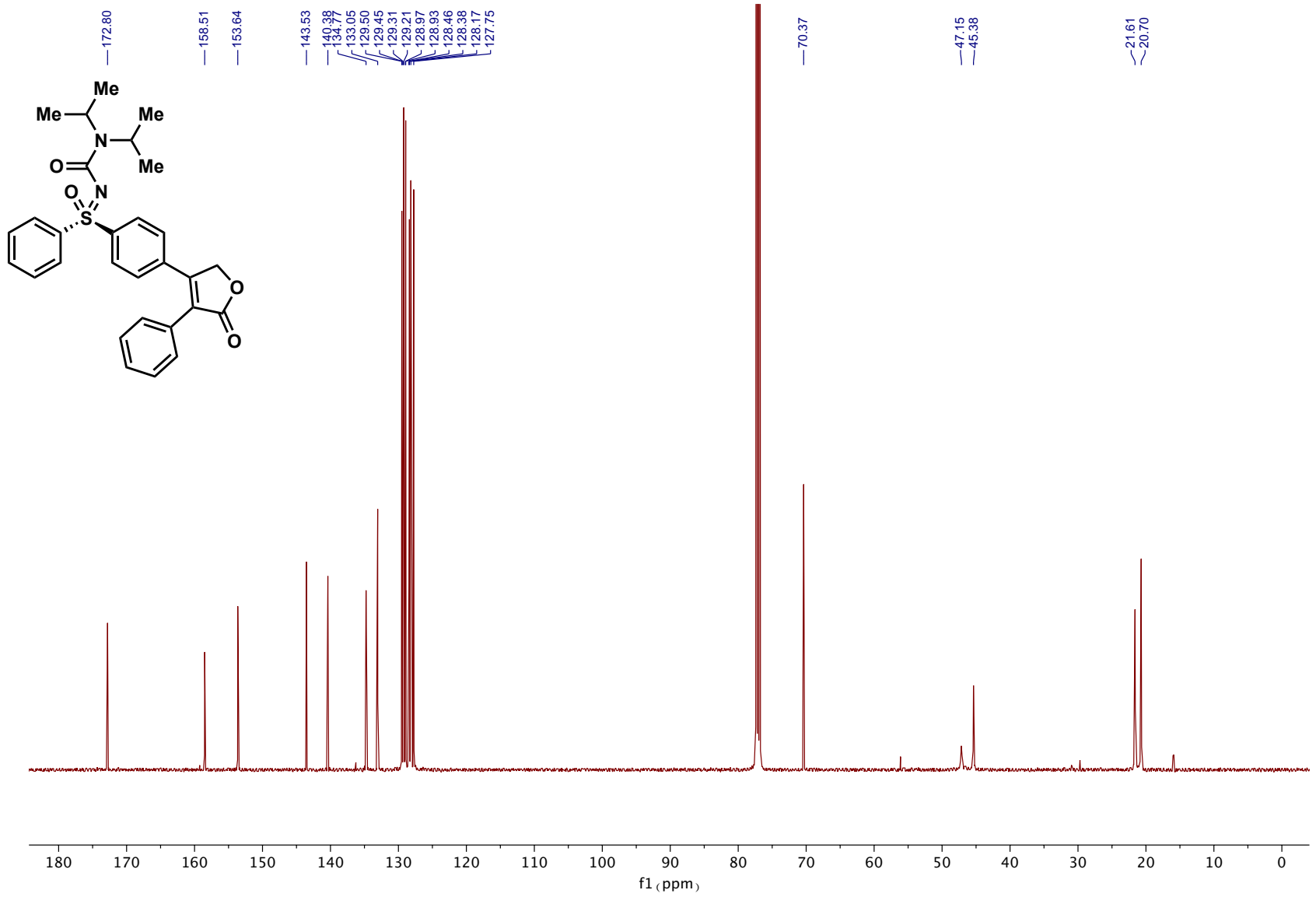
^{13}C NMR of compound 7c:



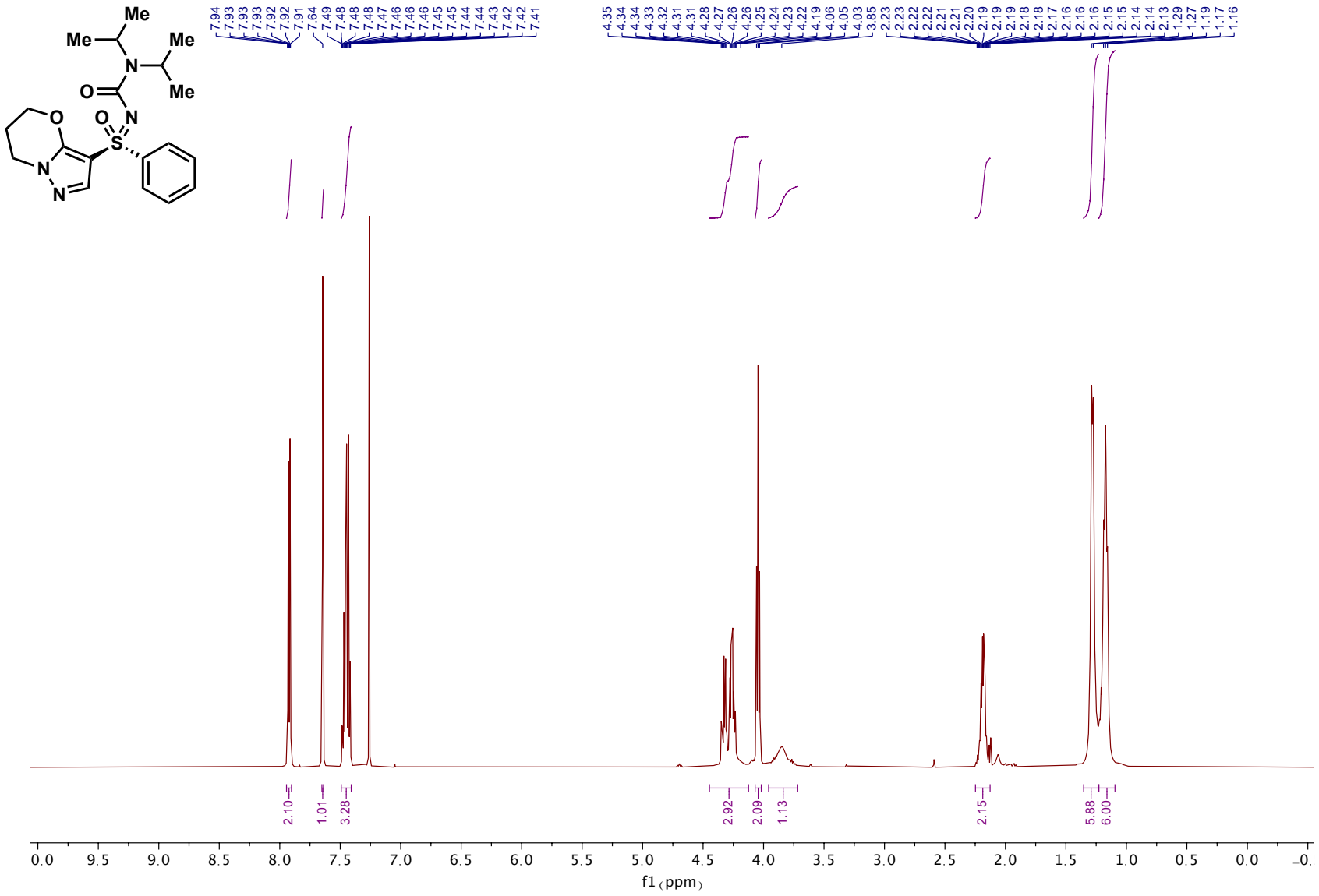
^{1}H NMR of compound 7d:



^{13}C NMR of compound 7d:



^{1}H NMR of compound 7e:



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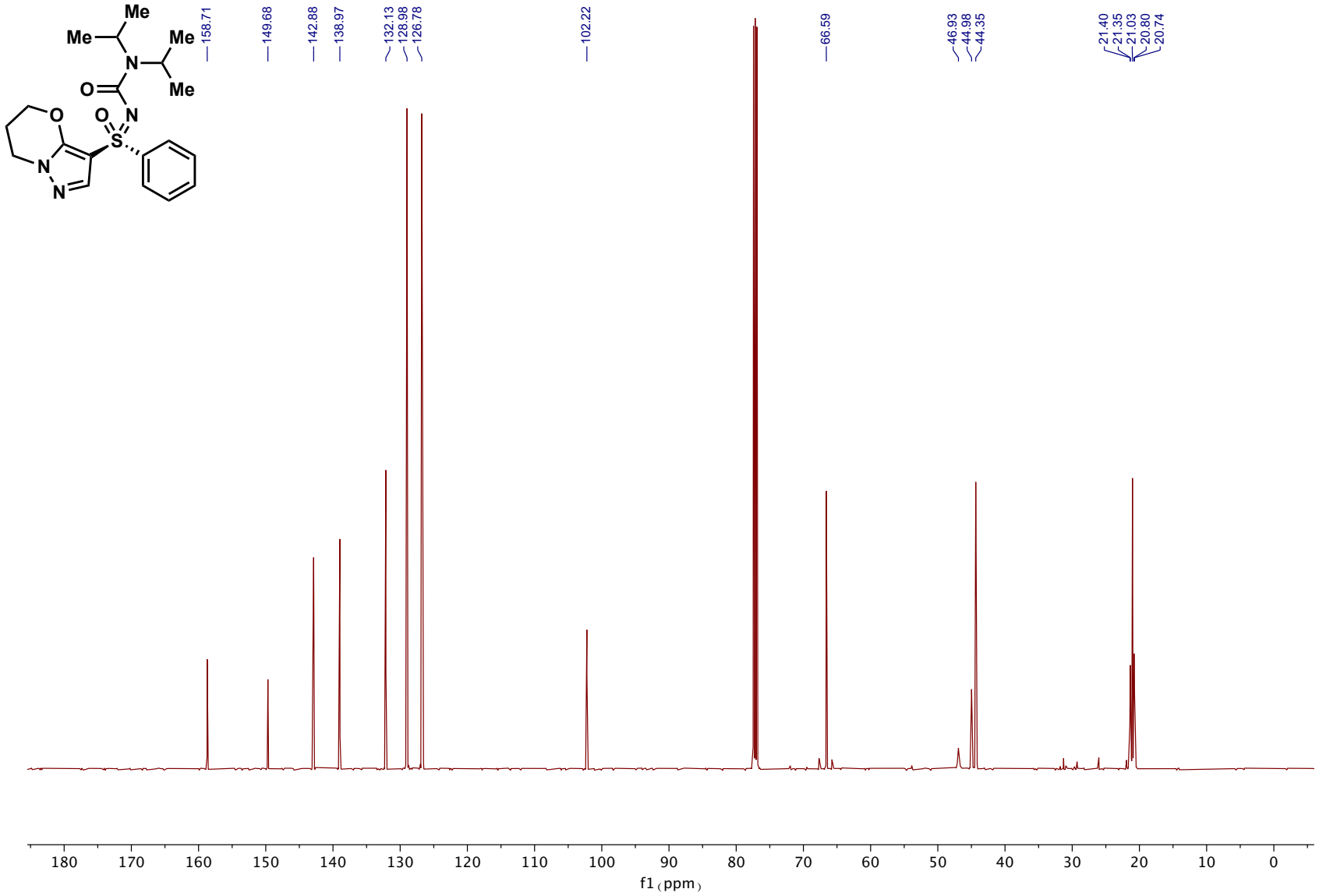
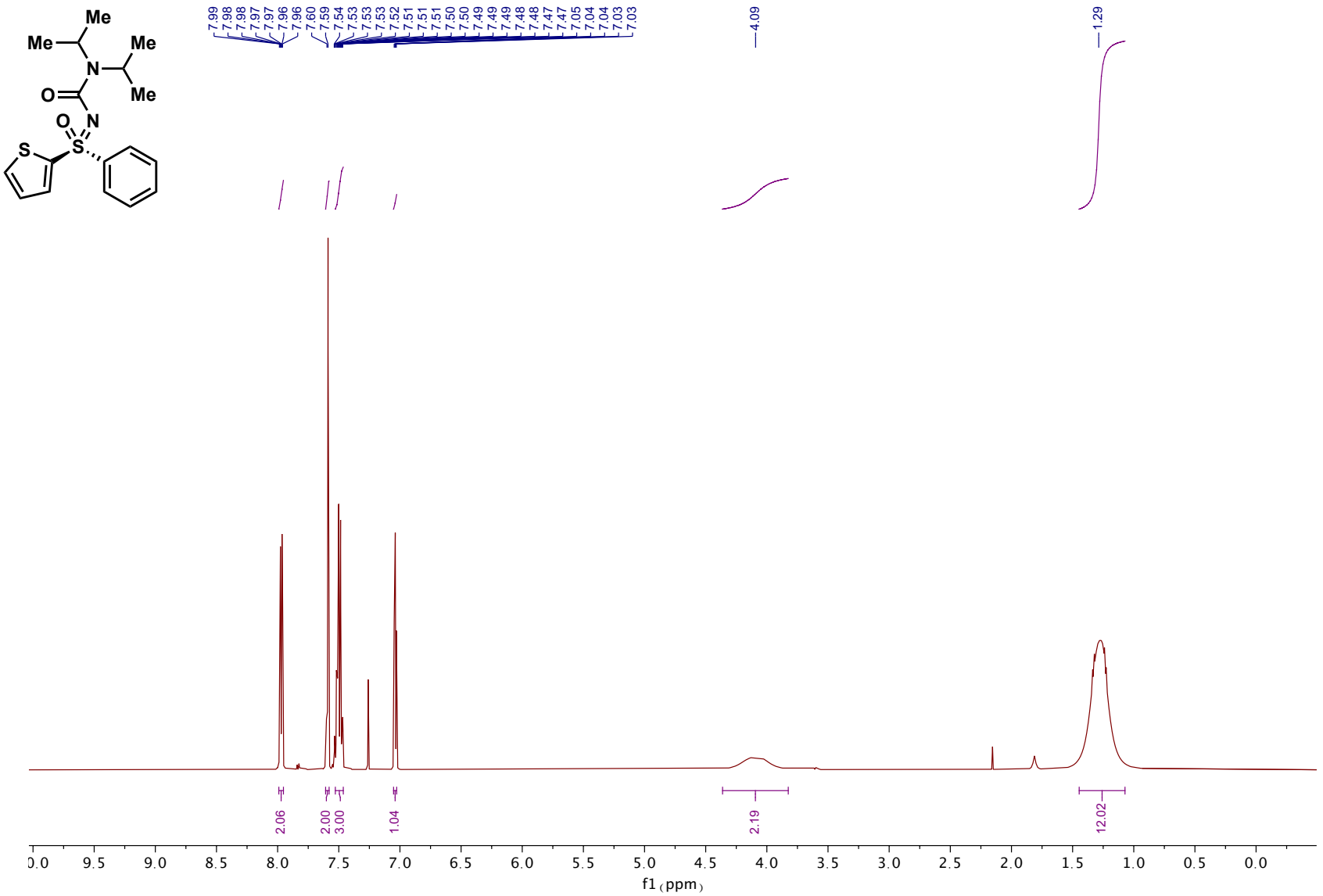
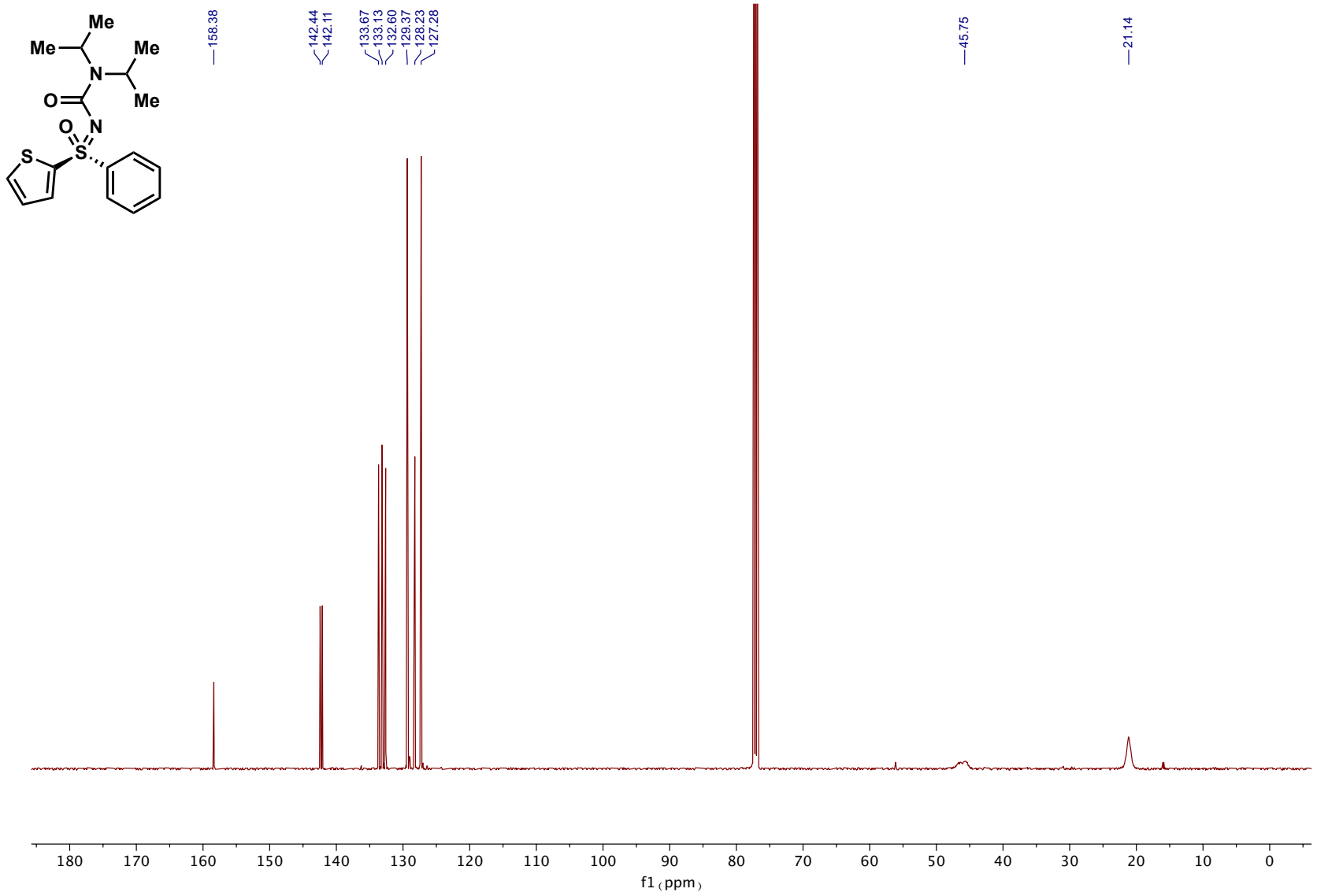


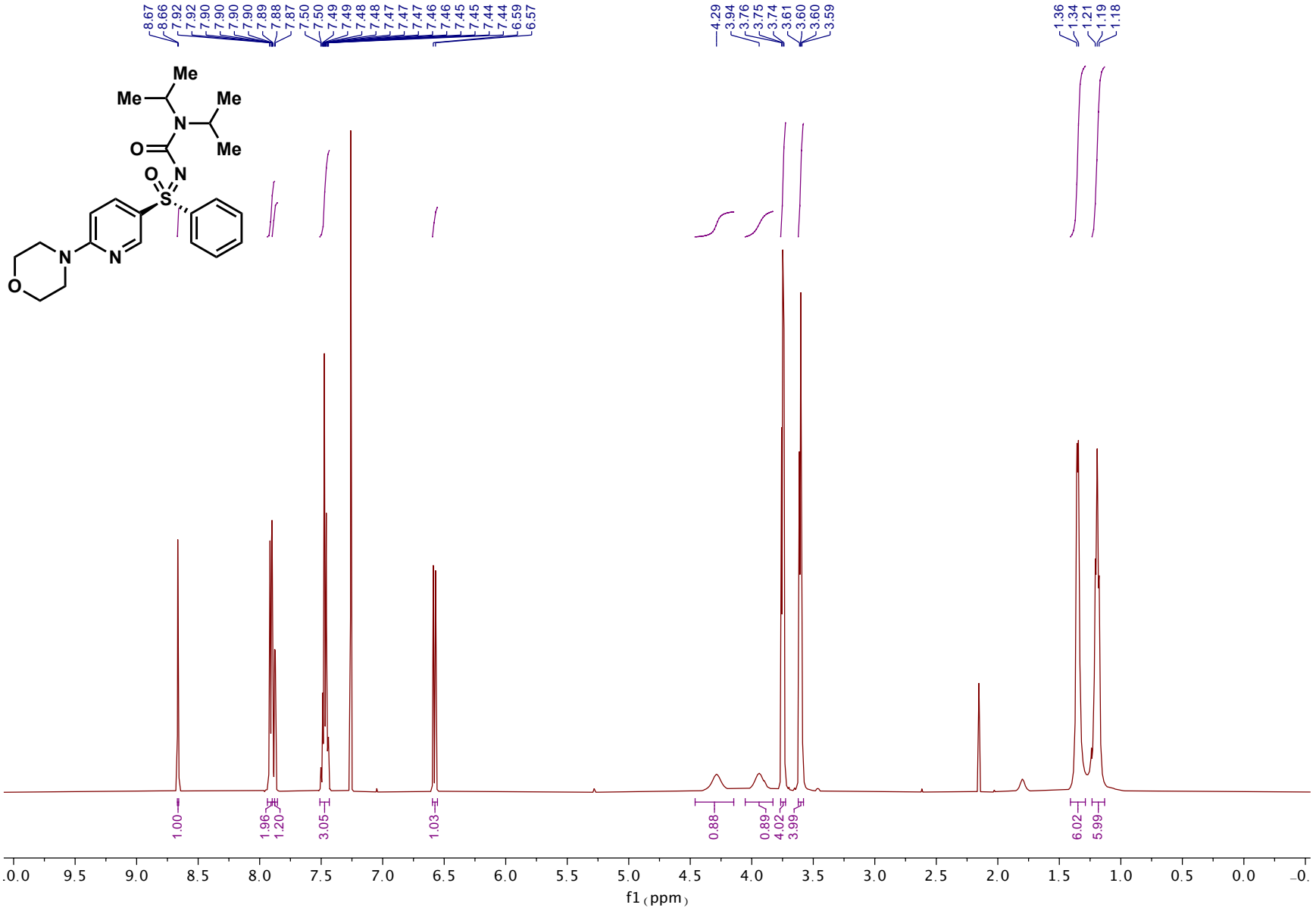
^{1}H NMR of compound 7f:



^{13}C NMR of compound 7f:



^{1}H NMR of compound 7g:



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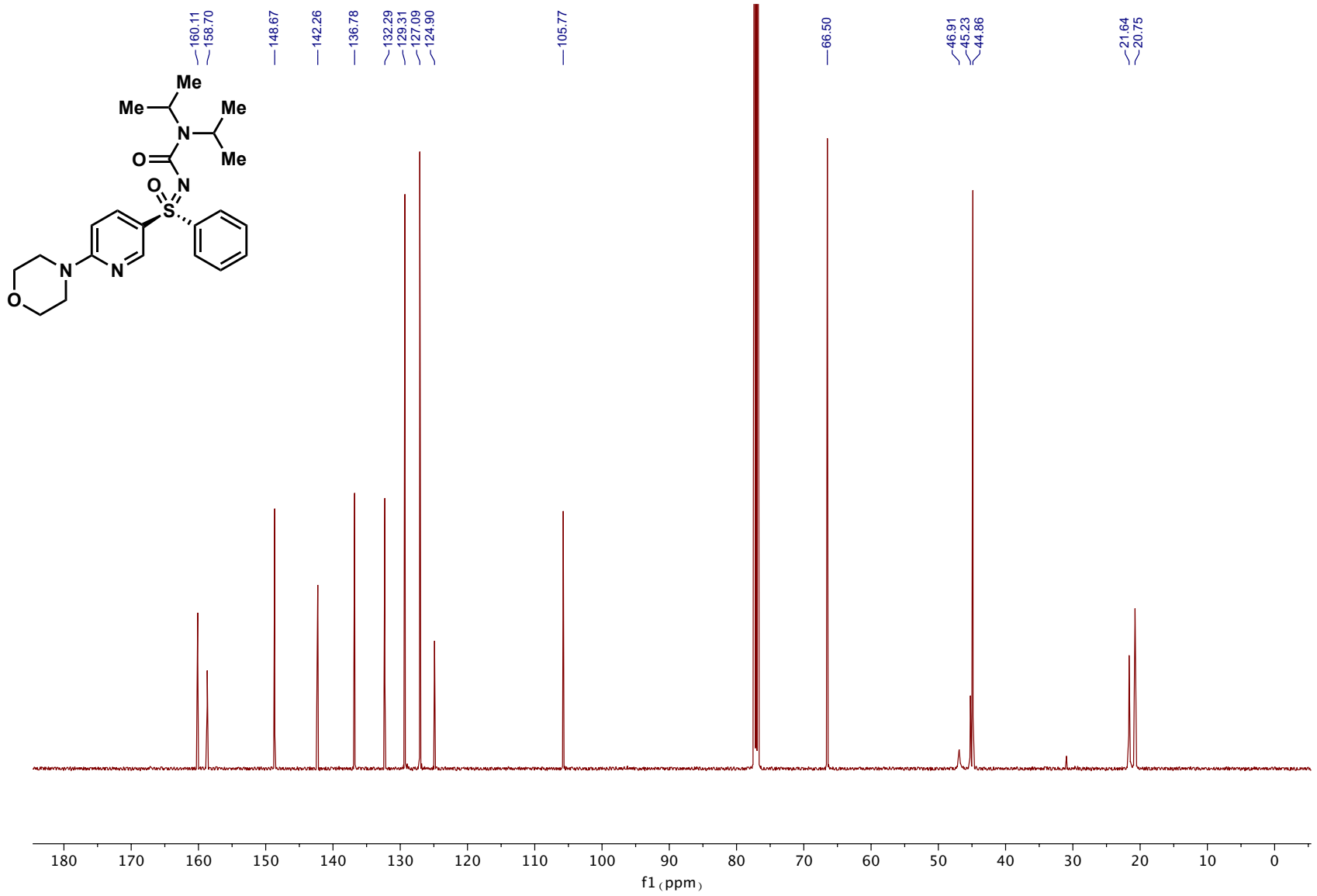
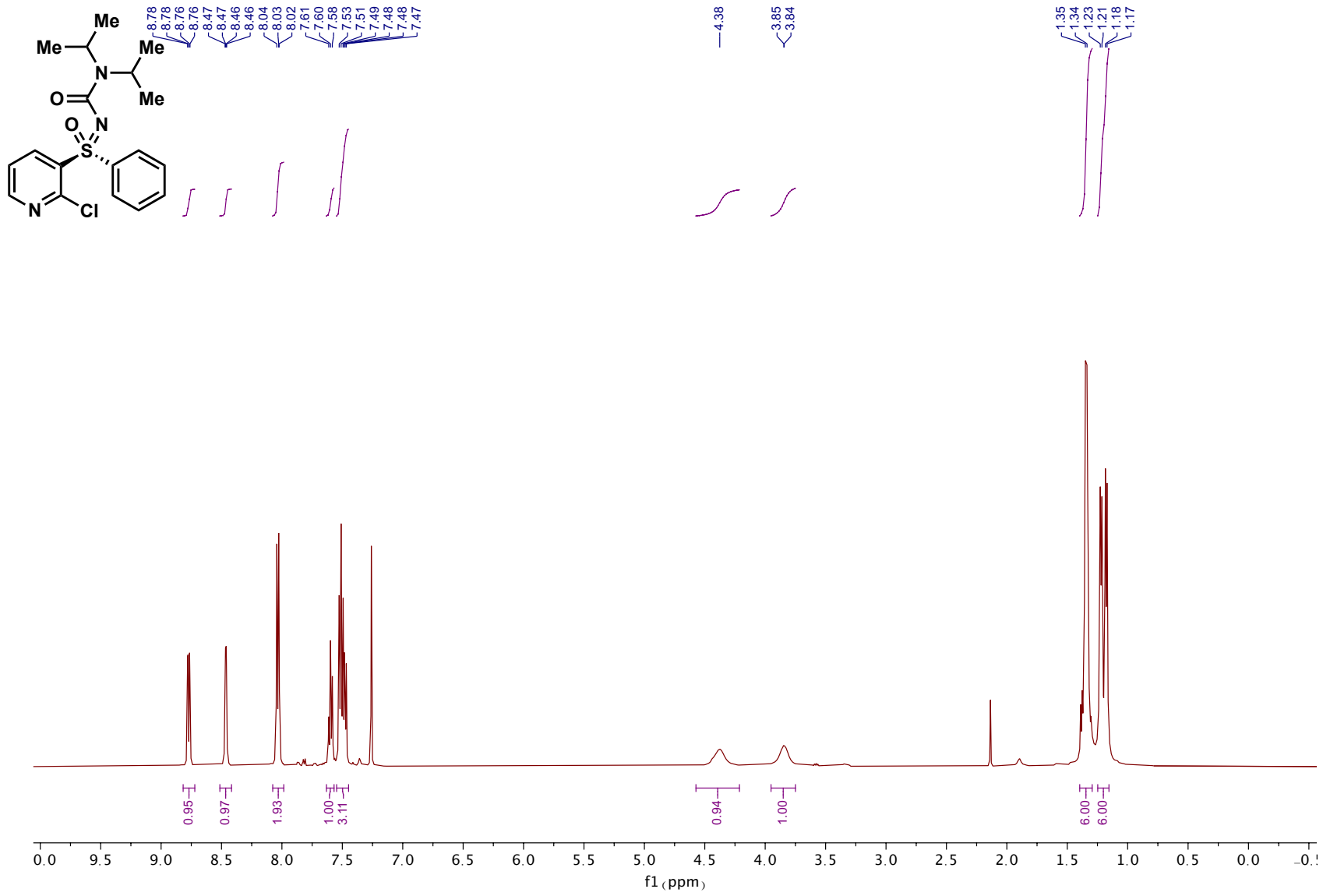
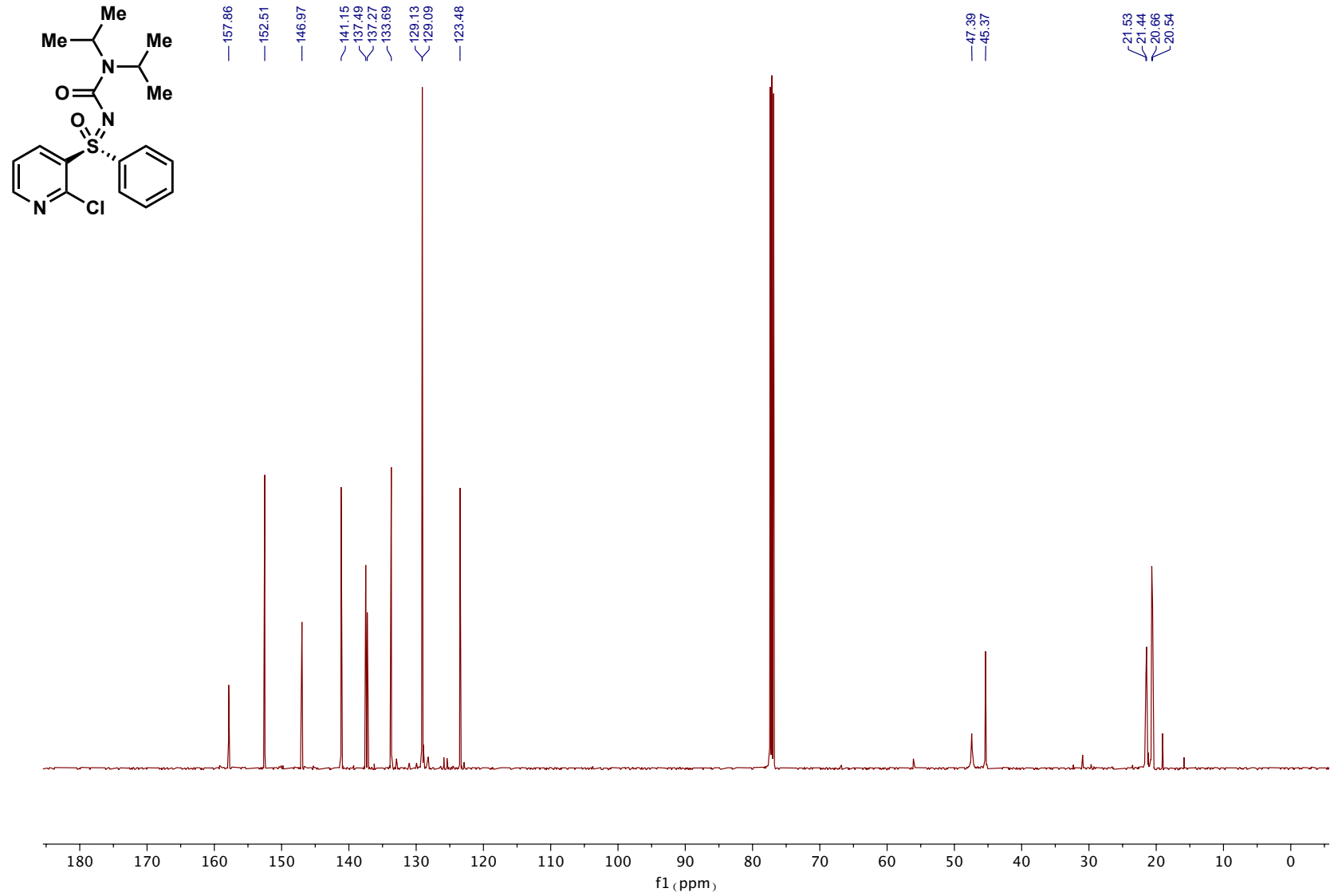


^{1}H NMR of compound 7h:



^{13}C NMR of compound 7h:



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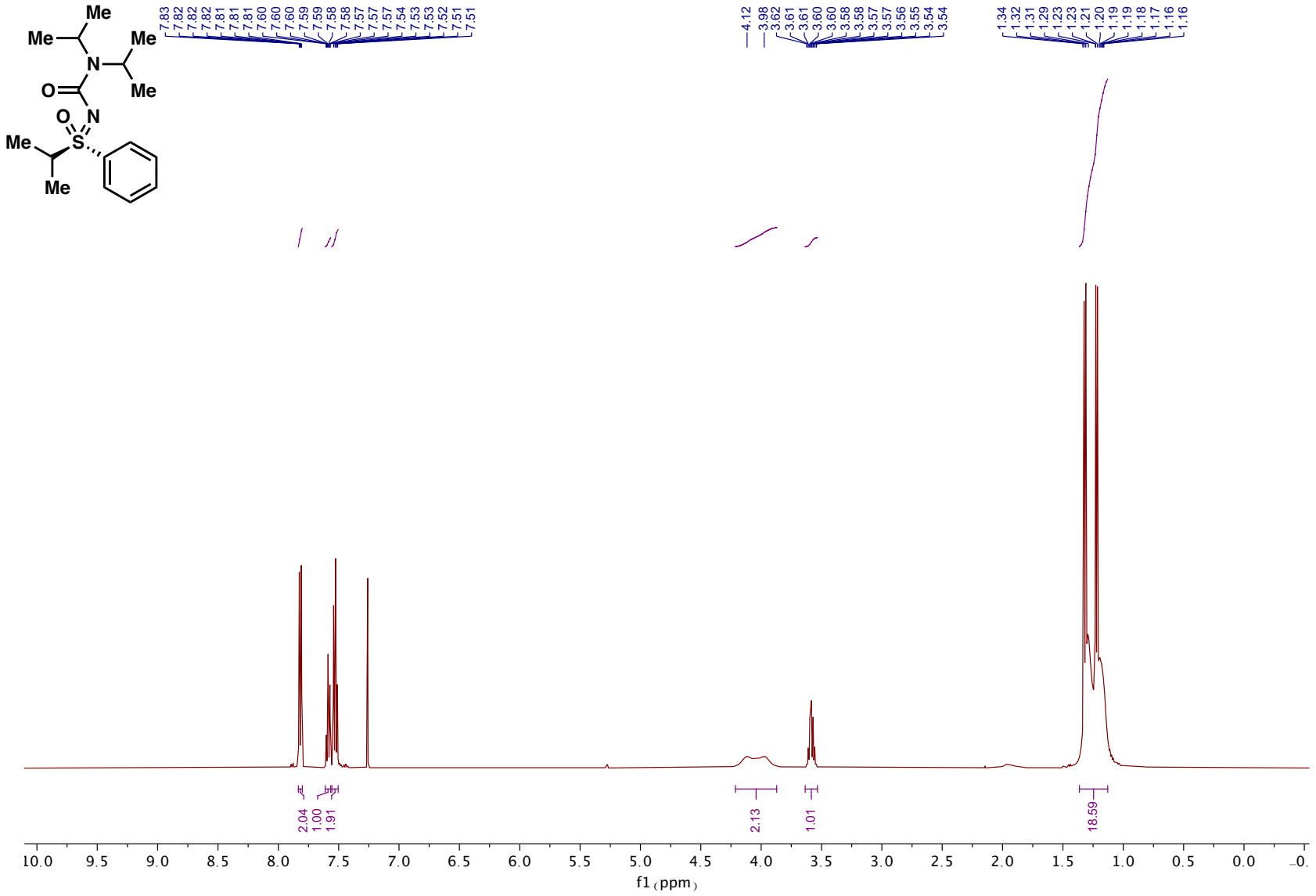

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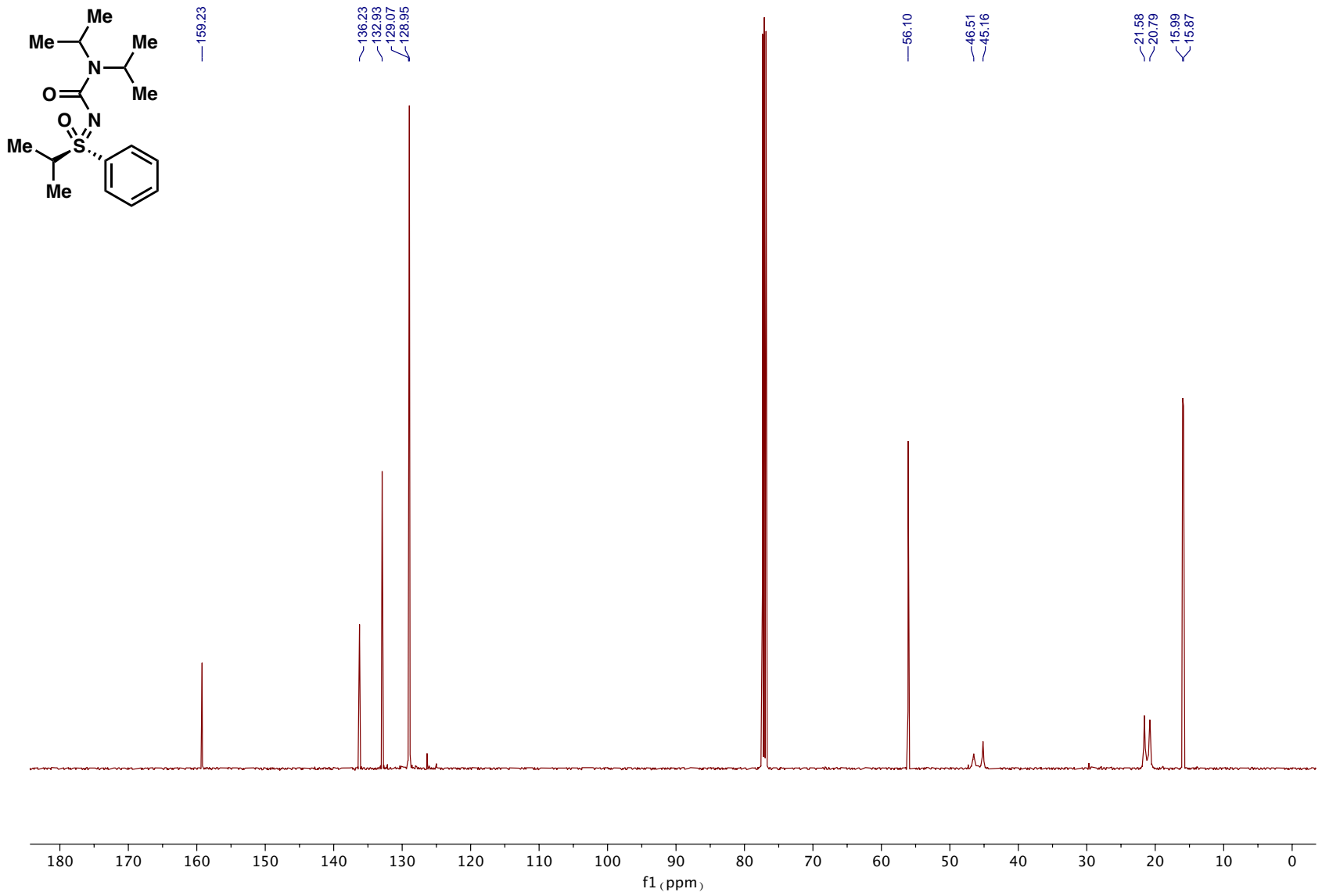

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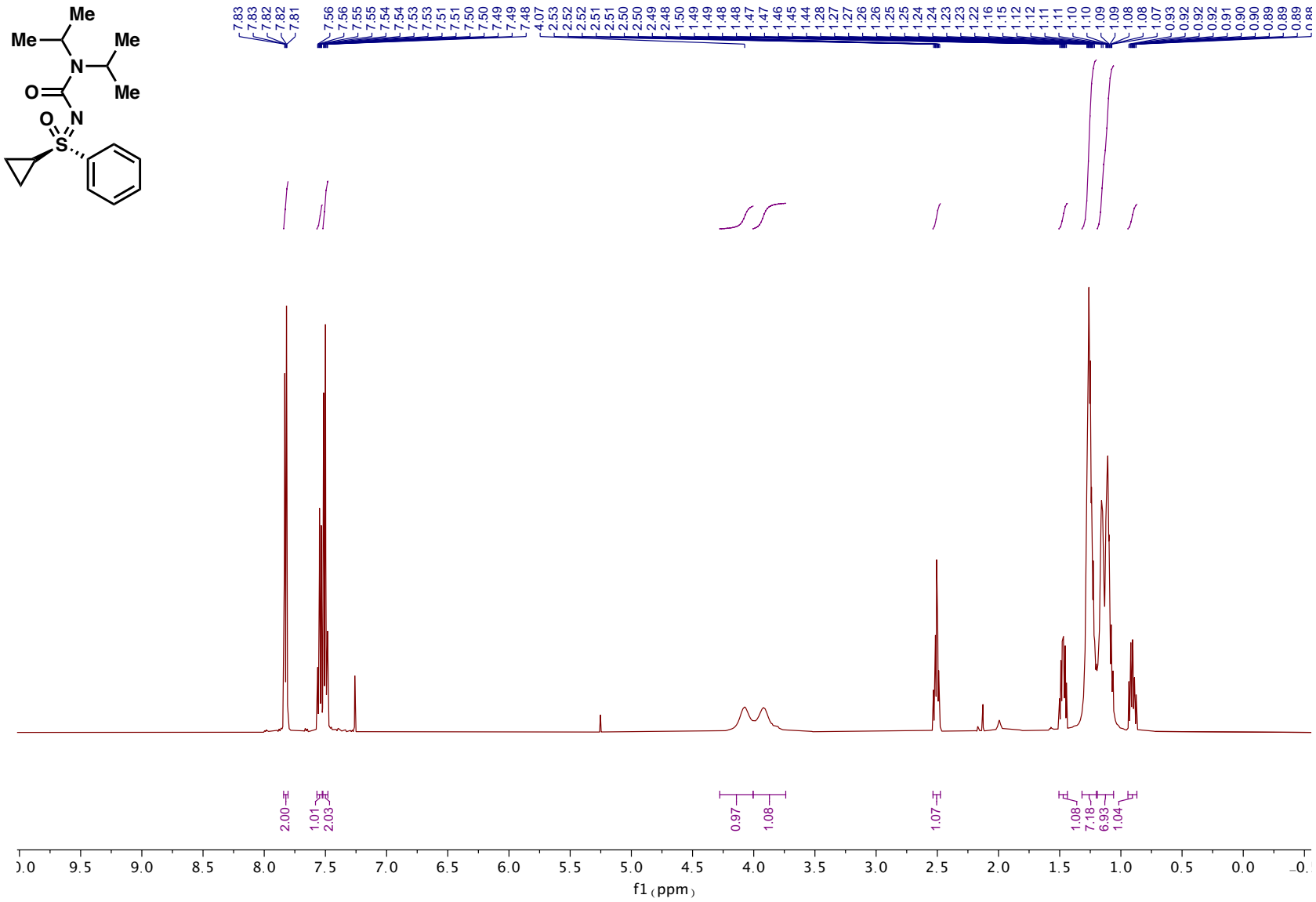

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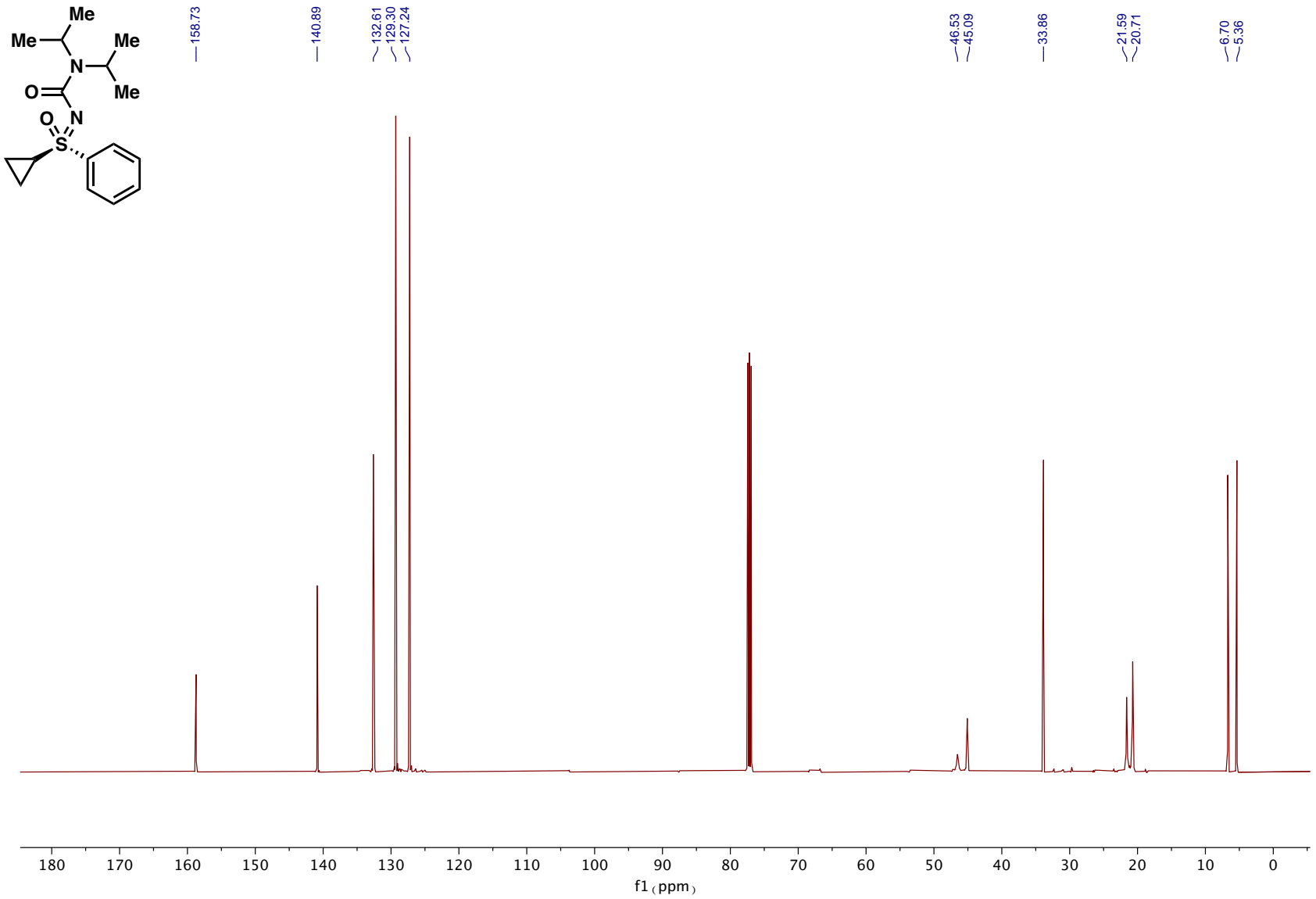

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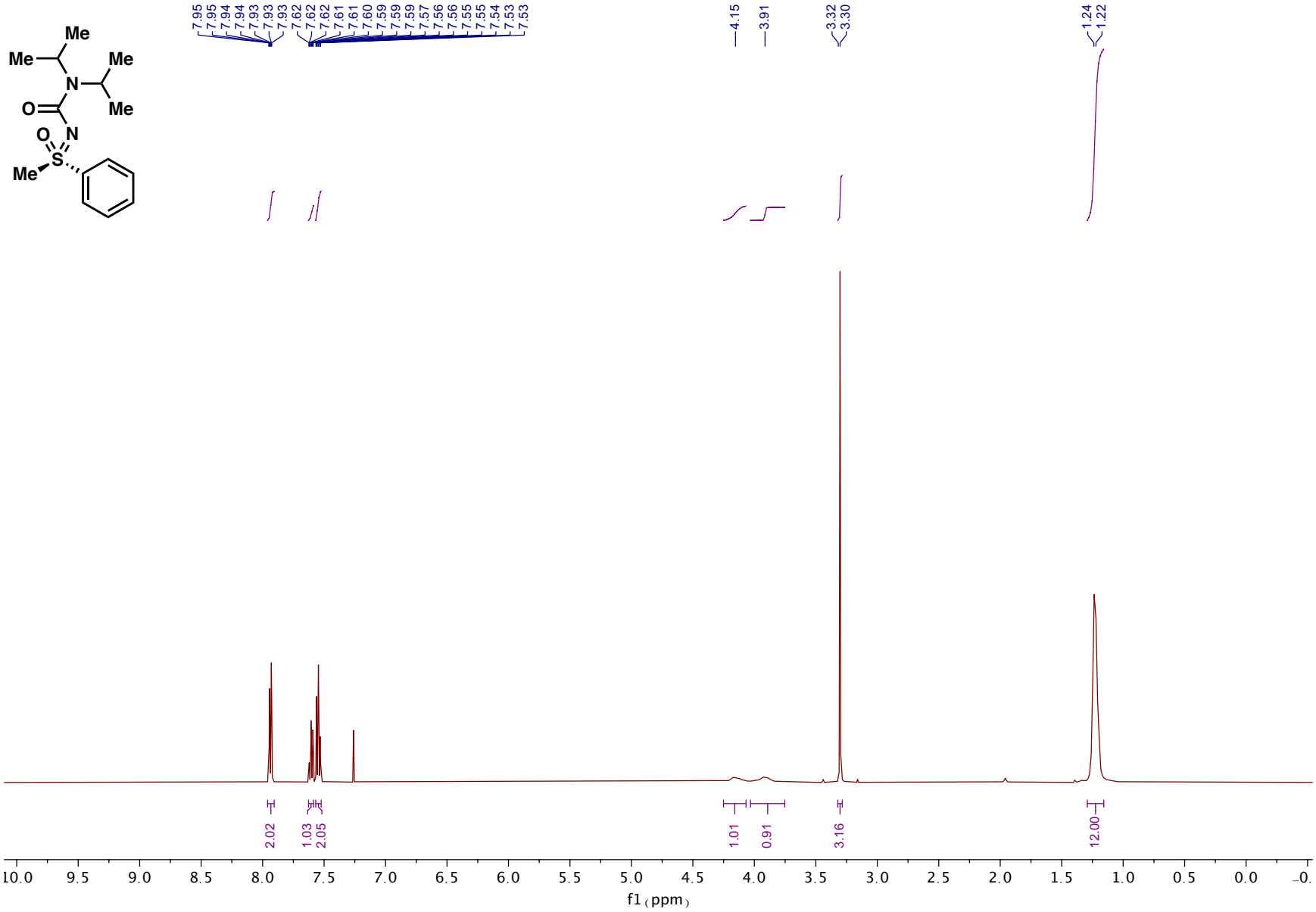
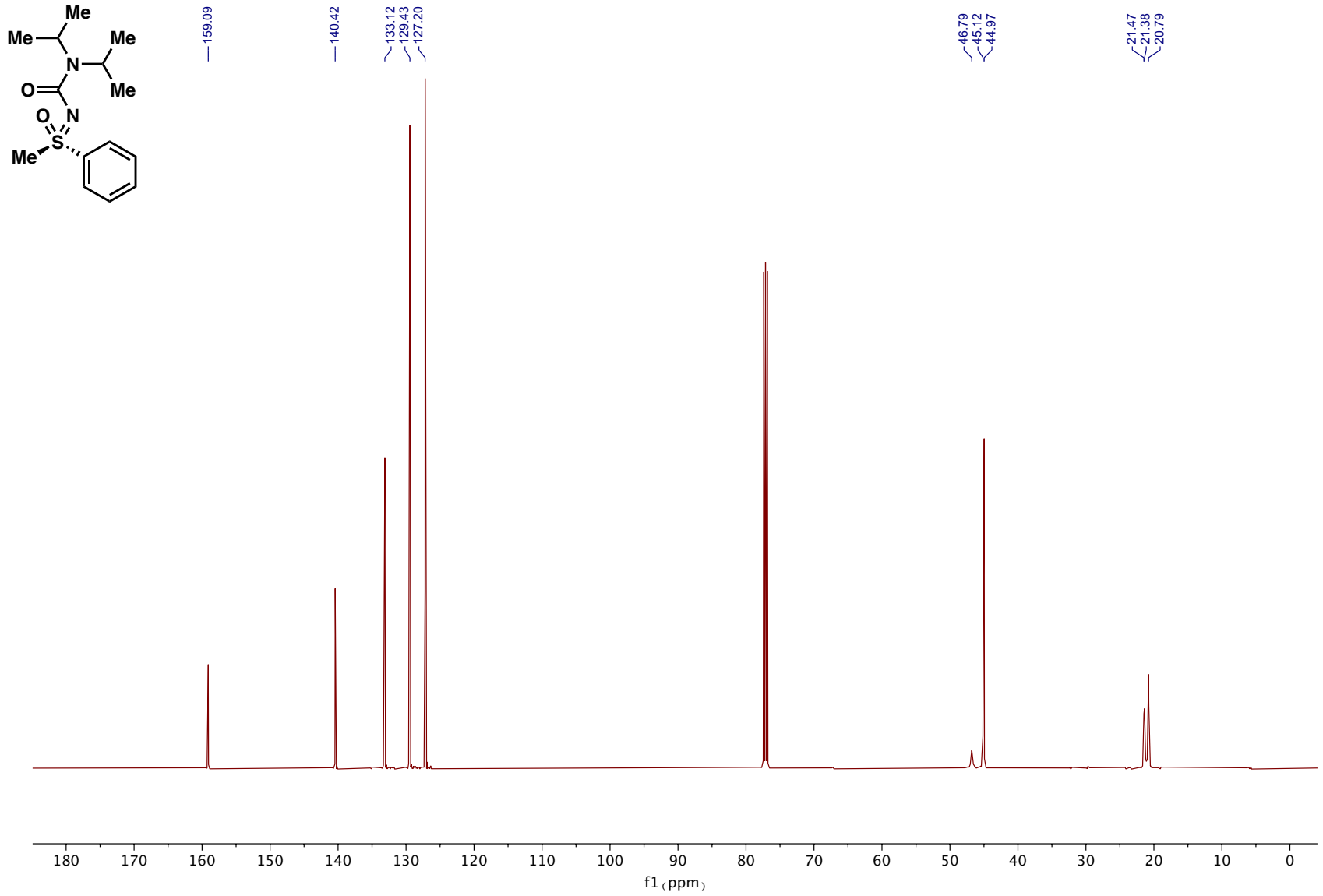


^{13}C NMR of compound 7k:



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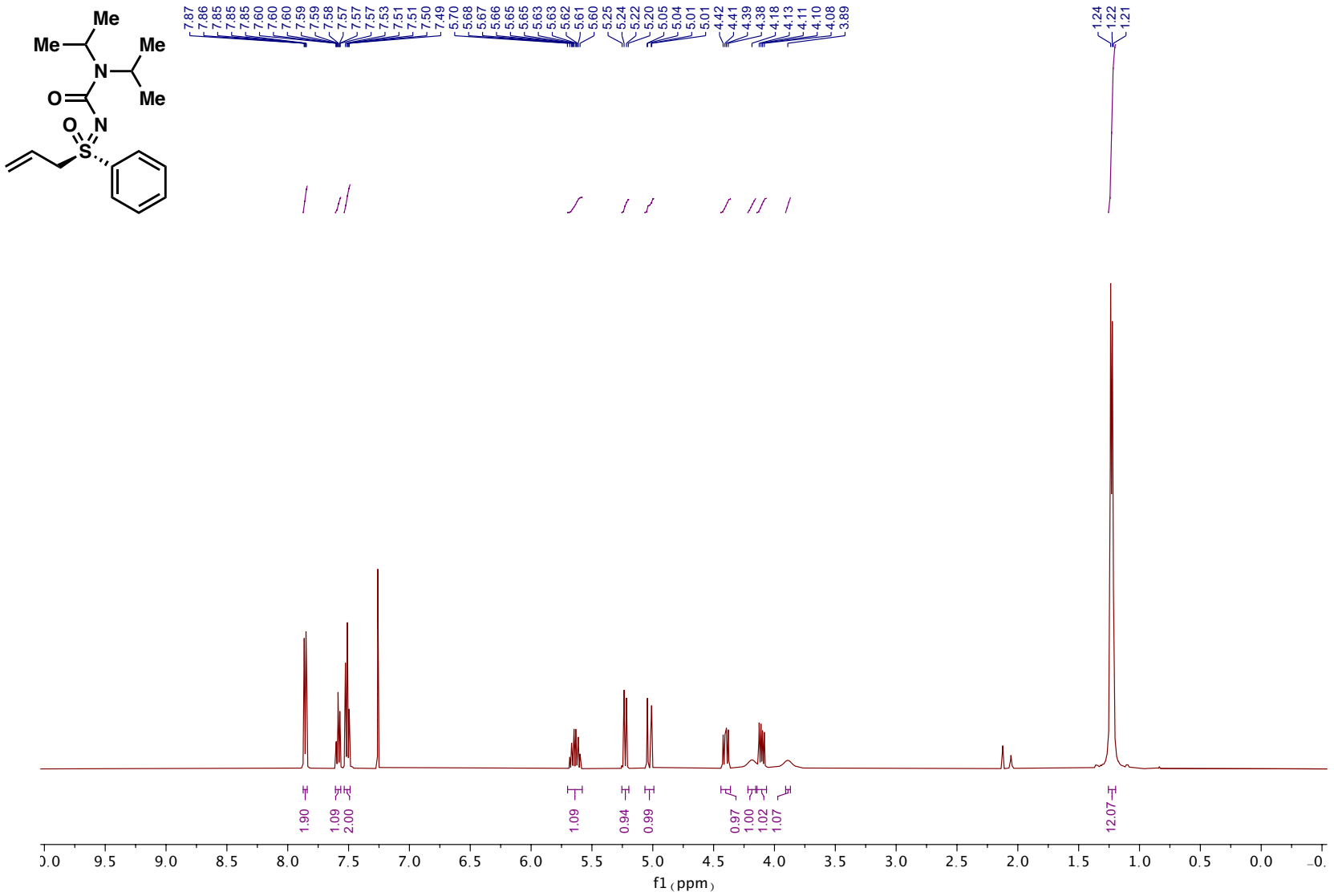

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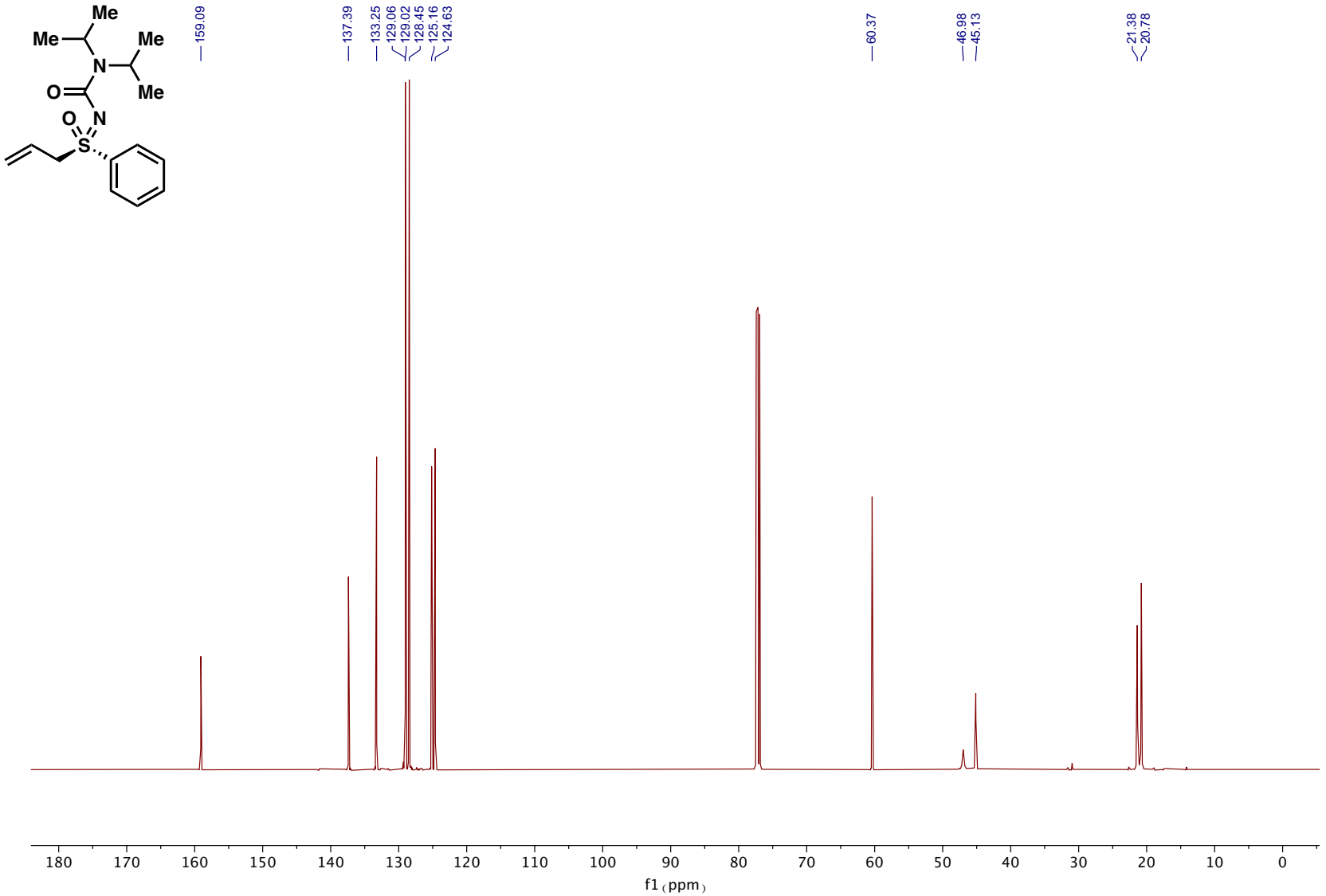
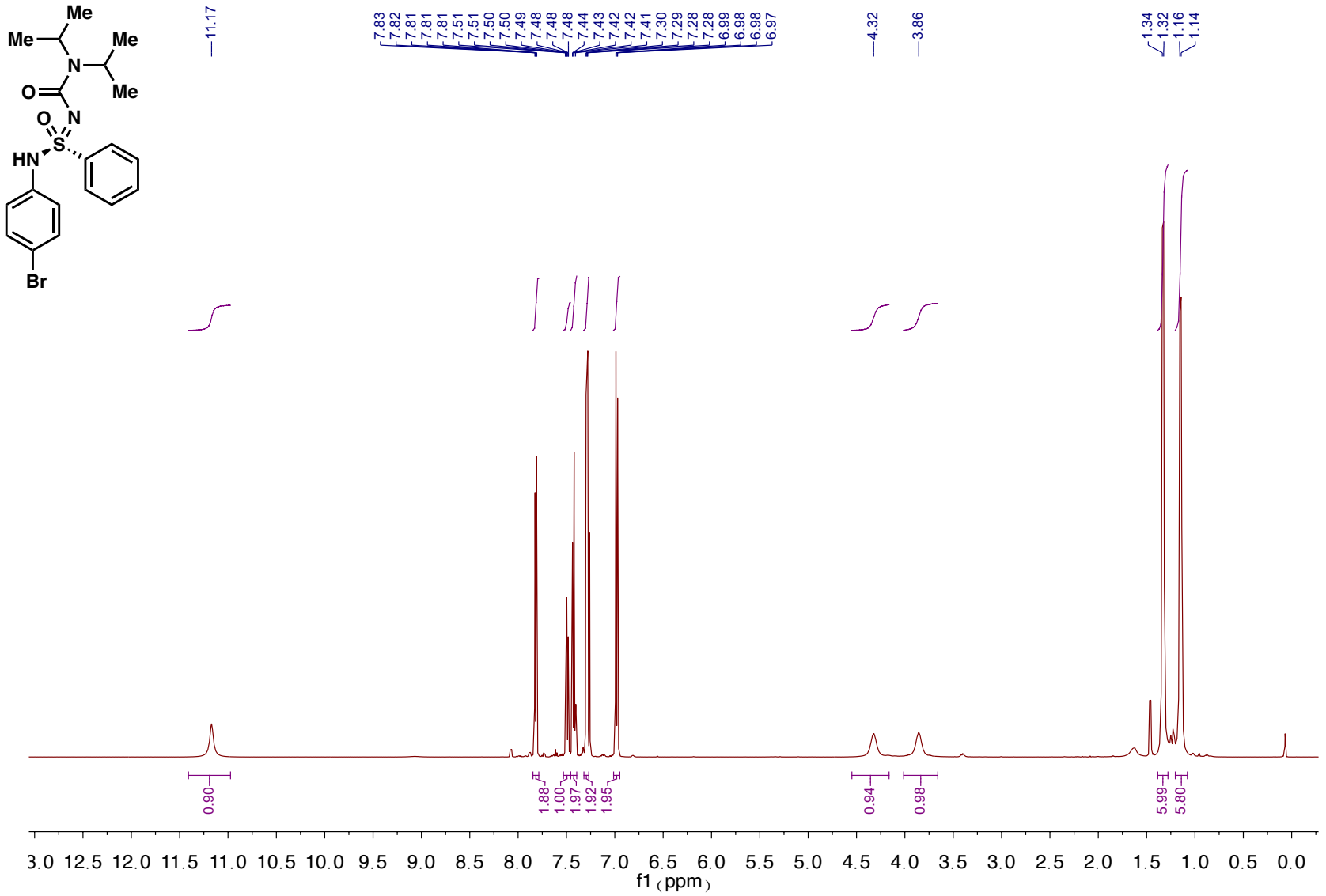
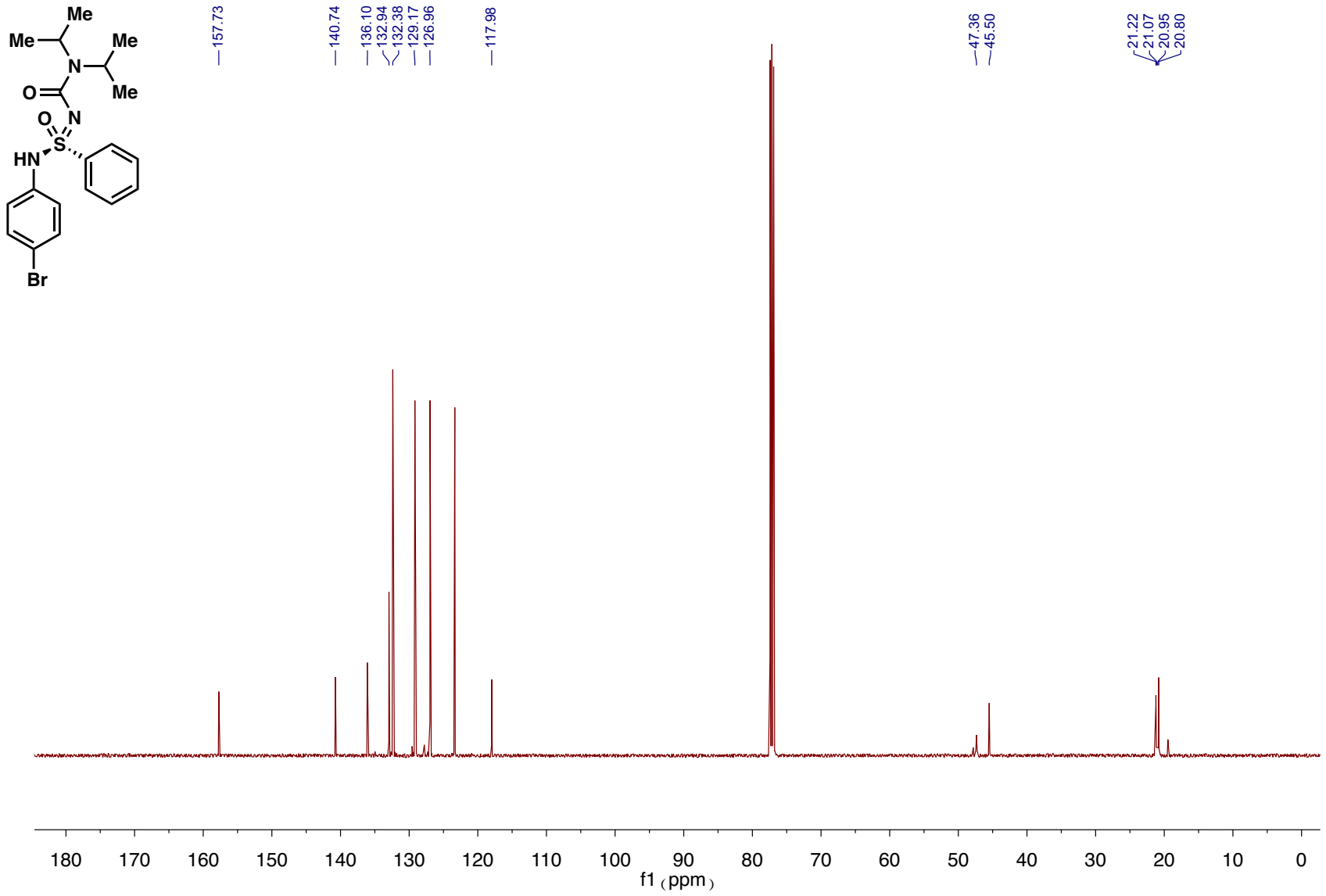


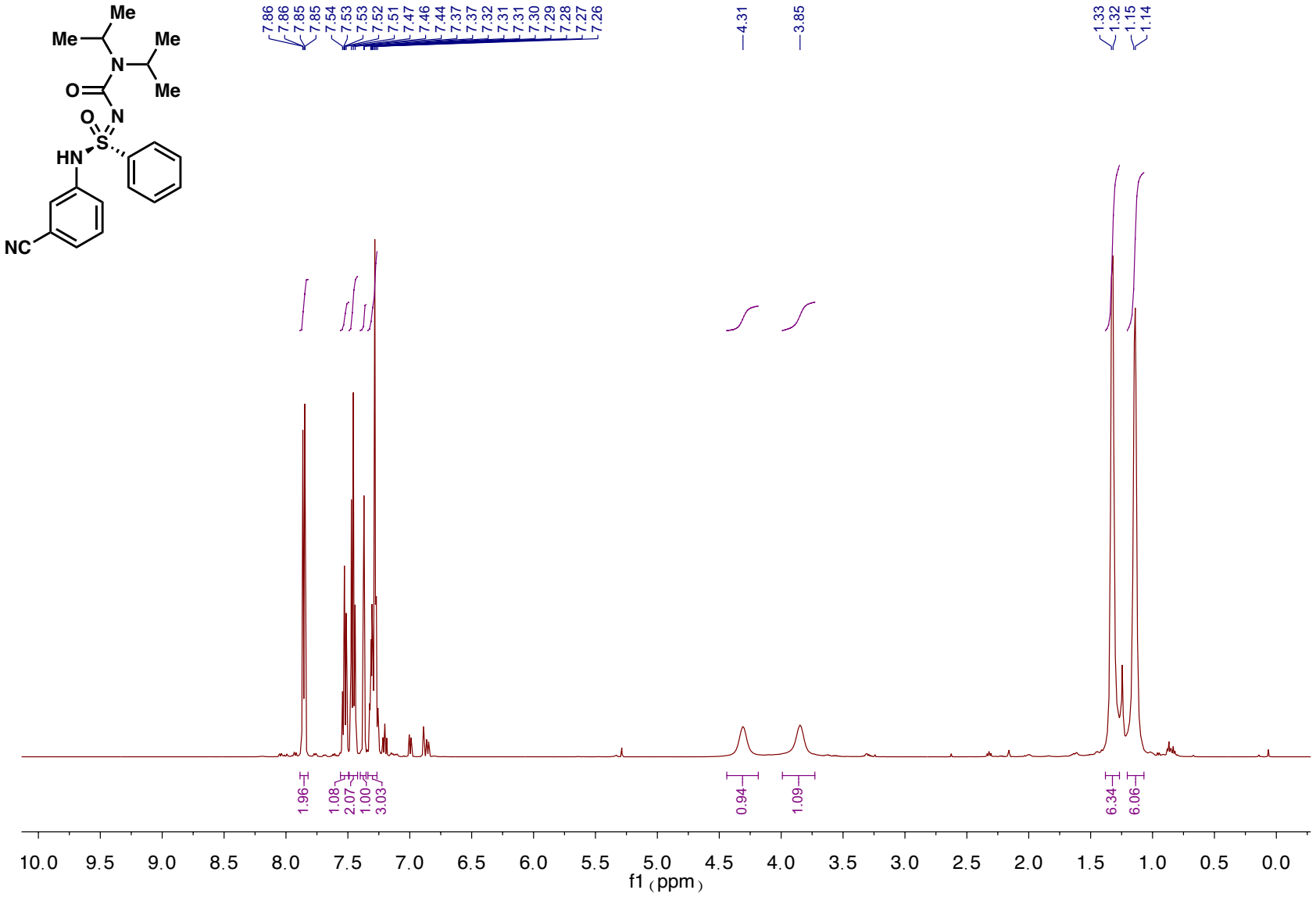
^{1}H NMR of compound 8a:



^{13}C NMR of compound 8a:



^{1}H NMR of compound 8b:



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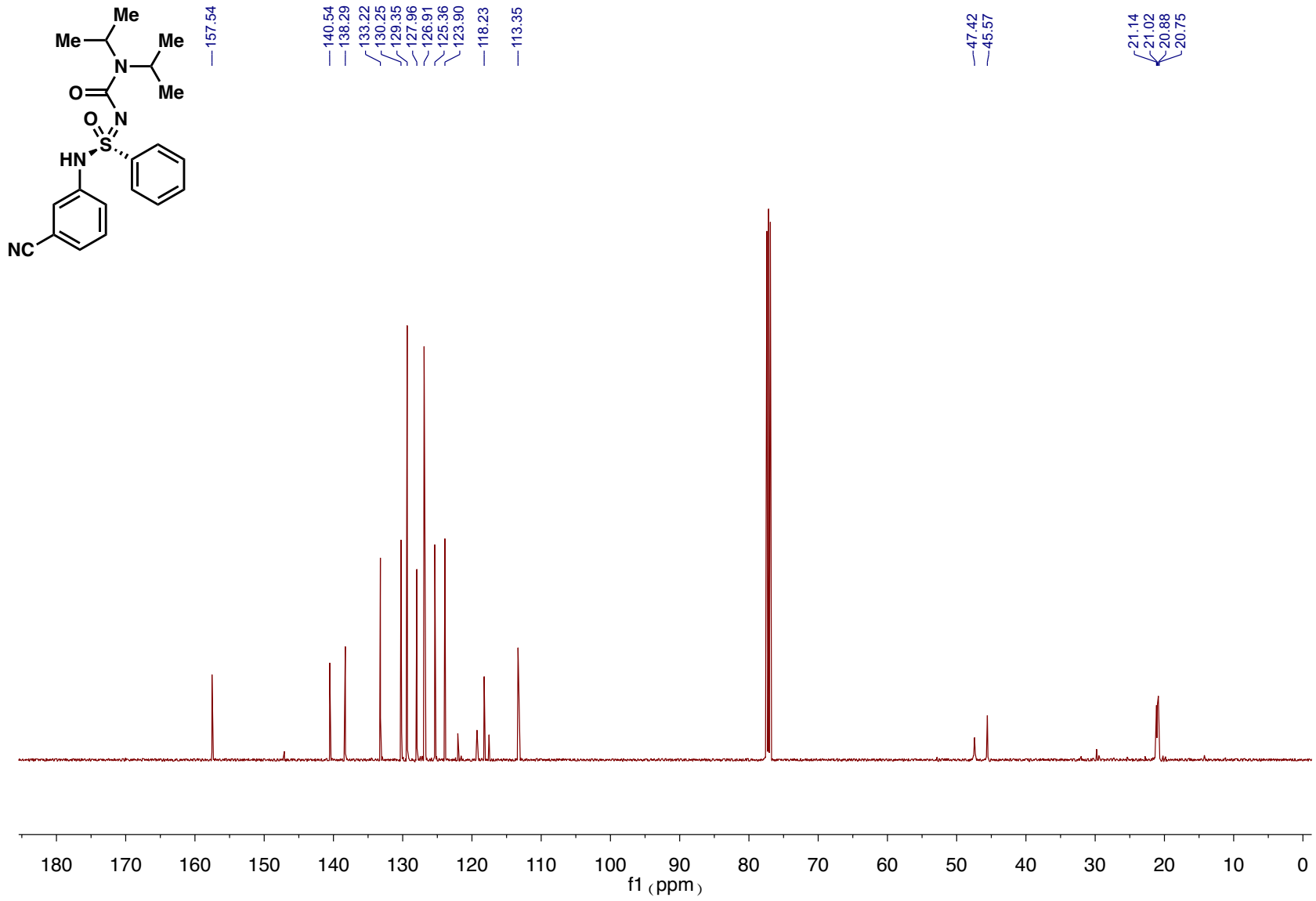
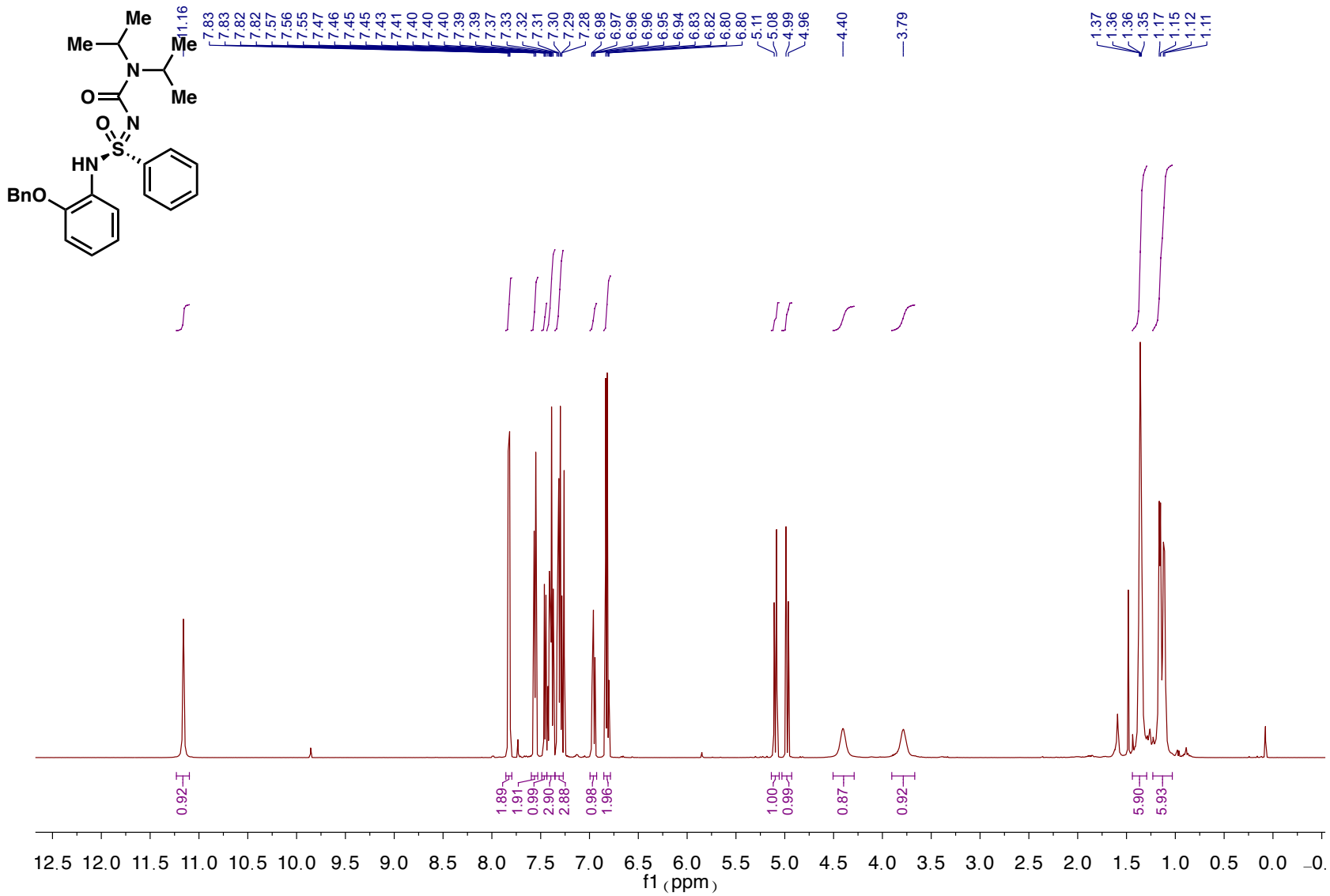


^{1}H NMR of compound 8c:



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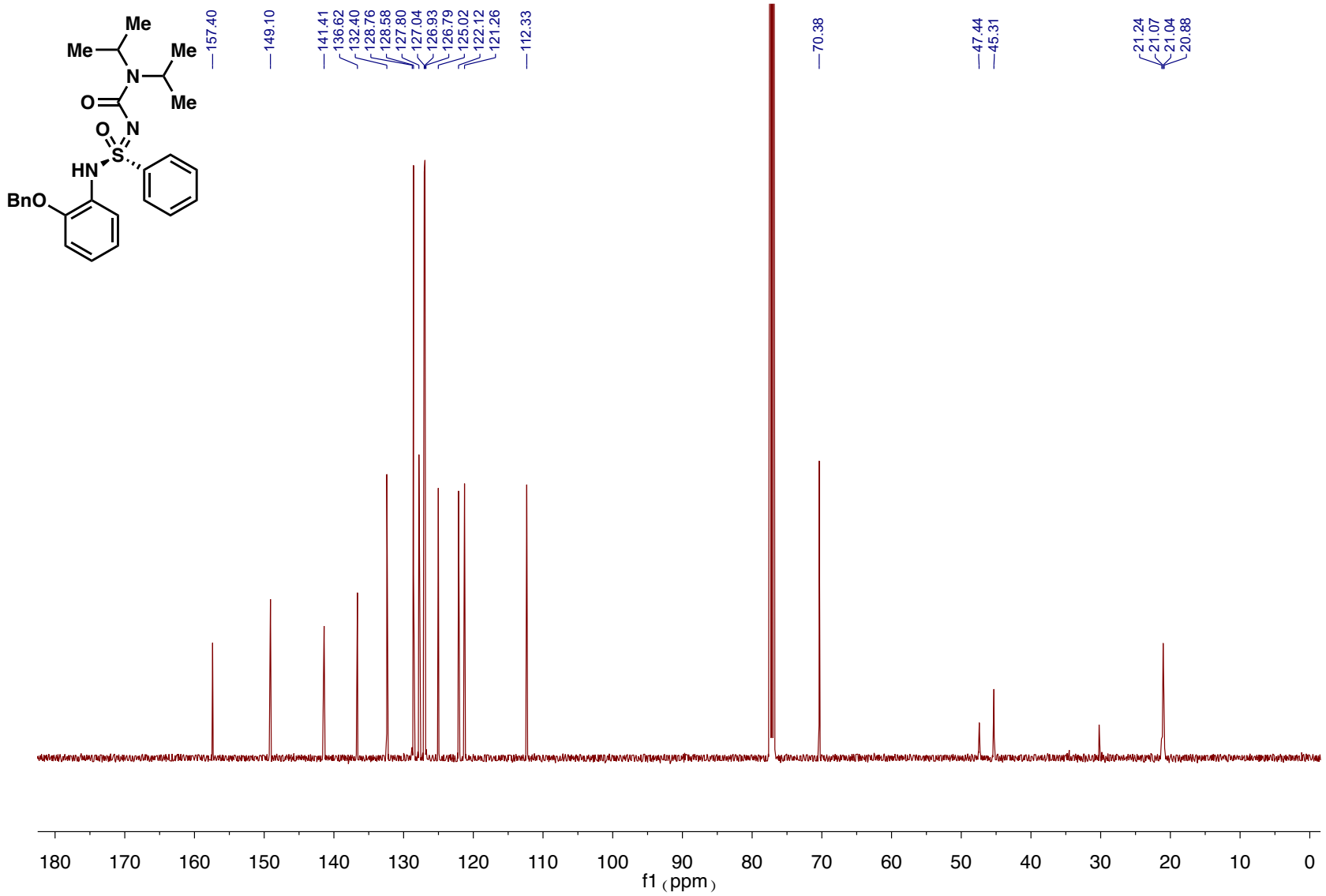

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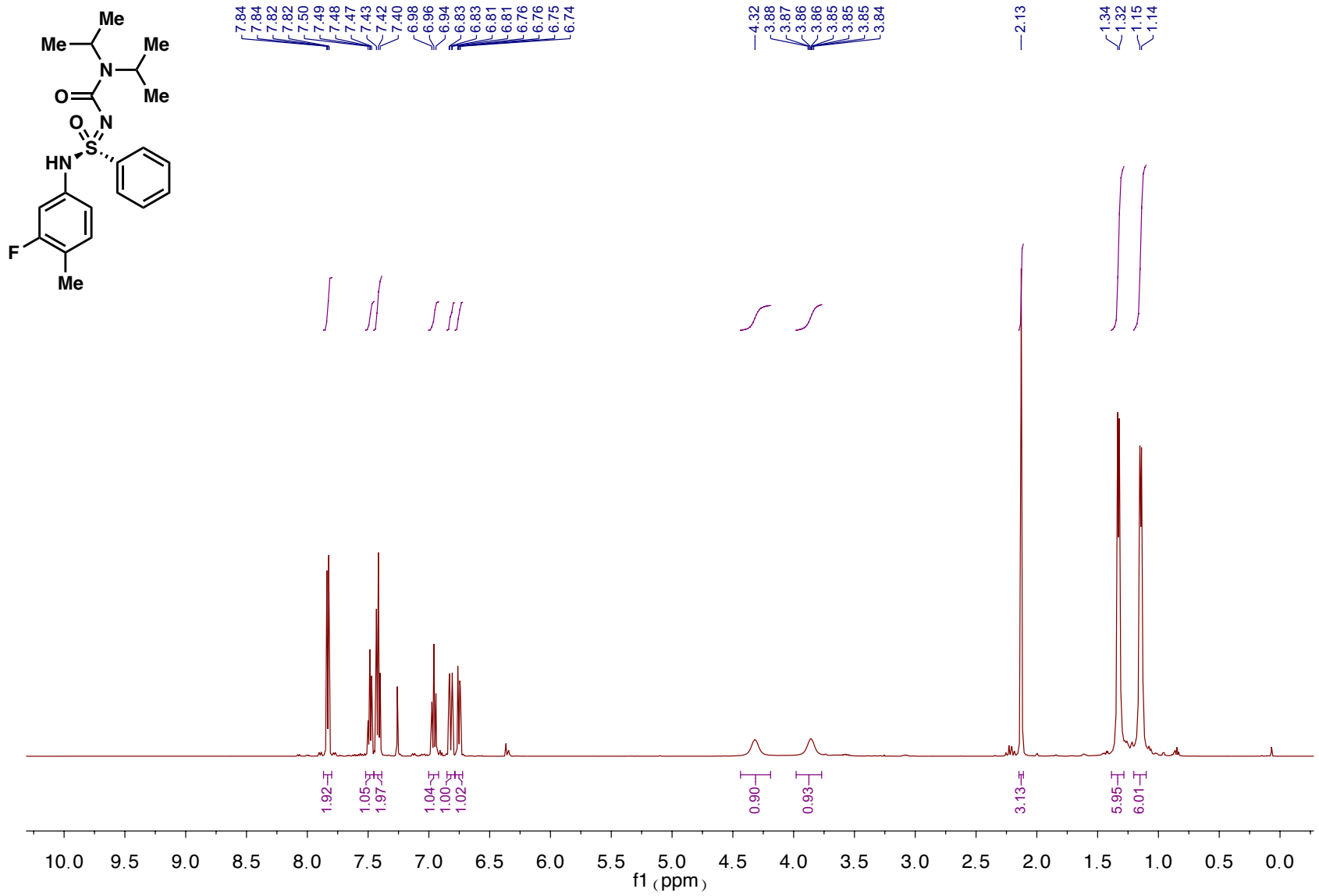

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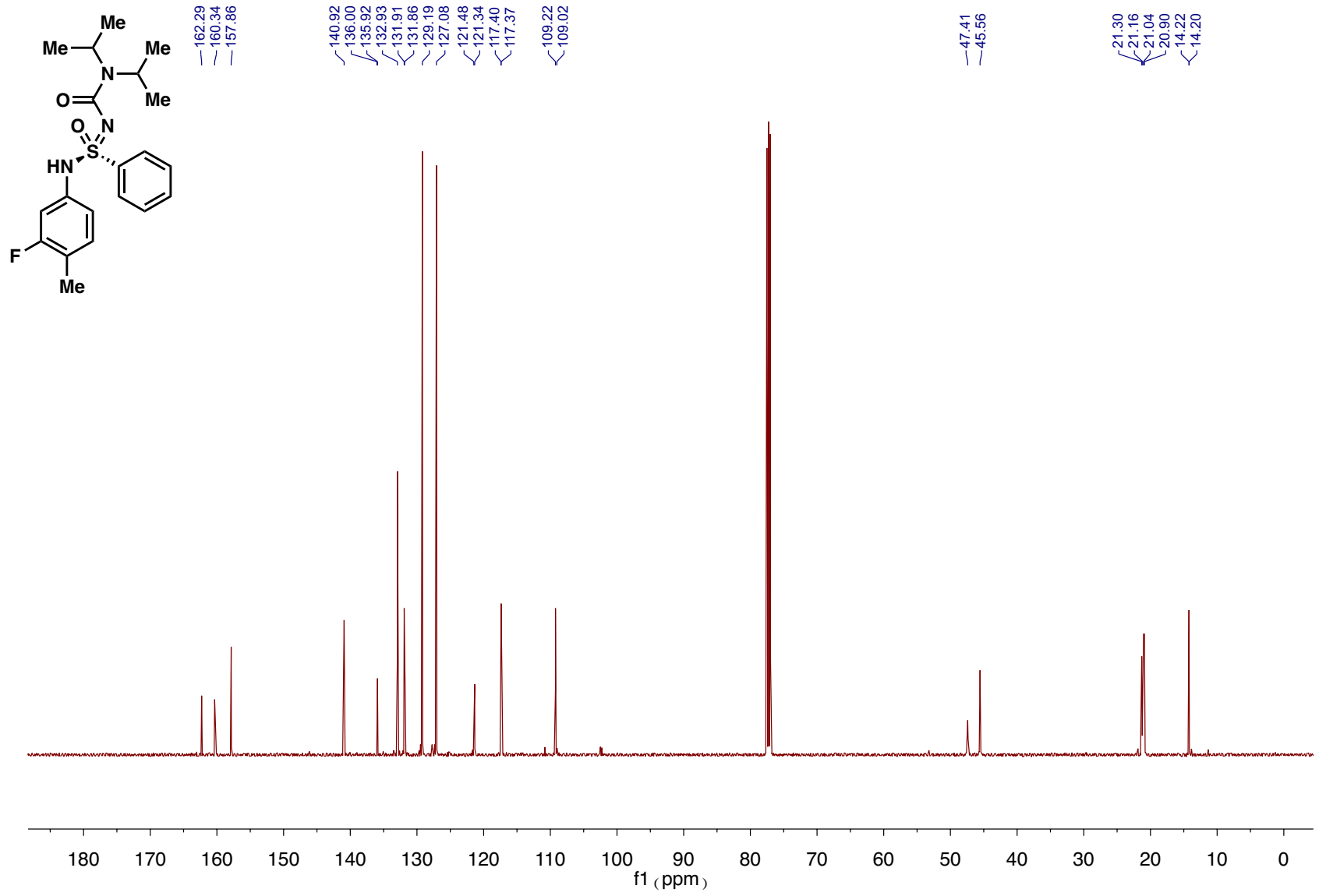
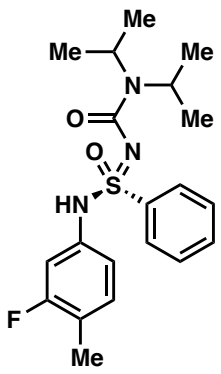


^{19}F NMR of compound 8d:



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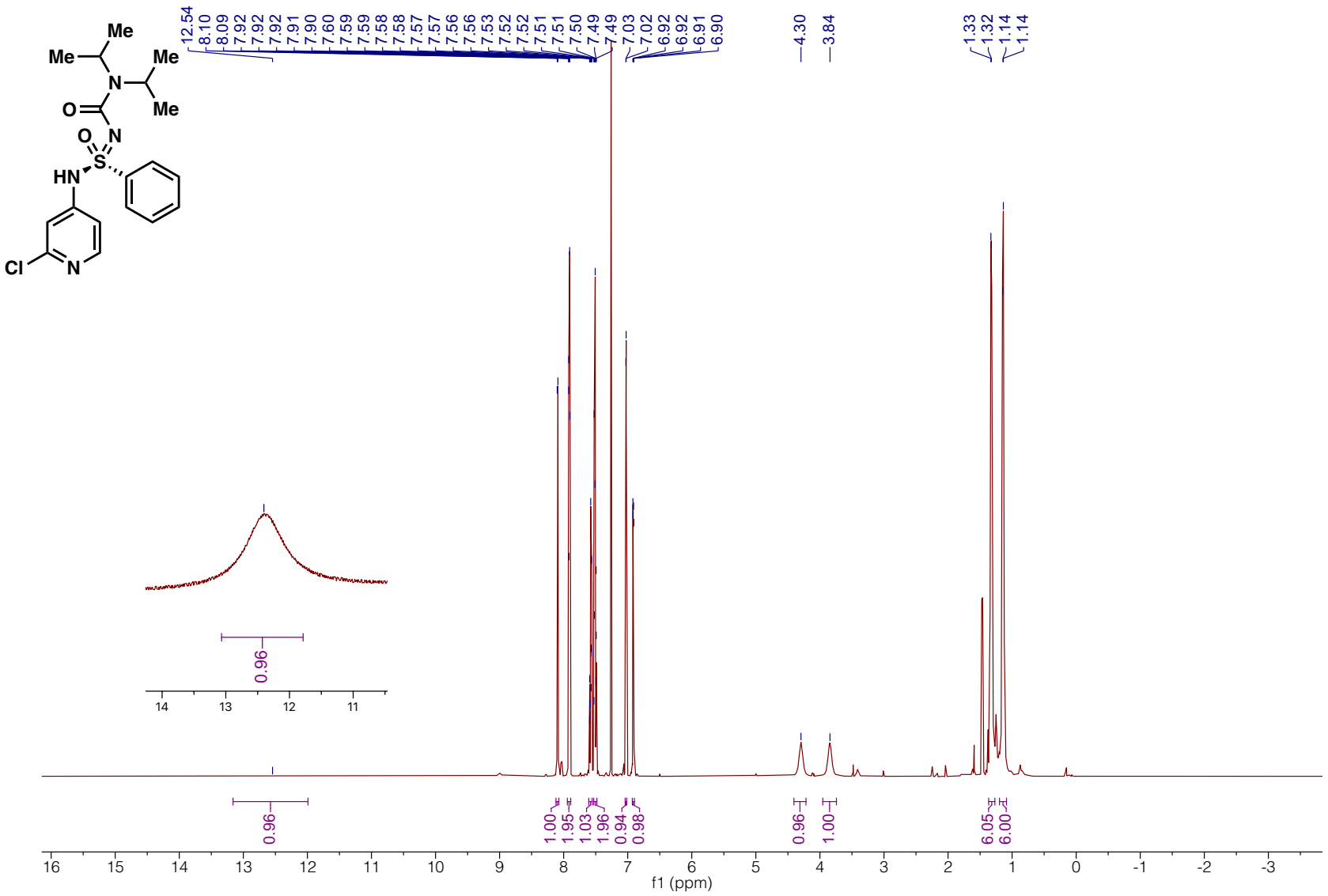

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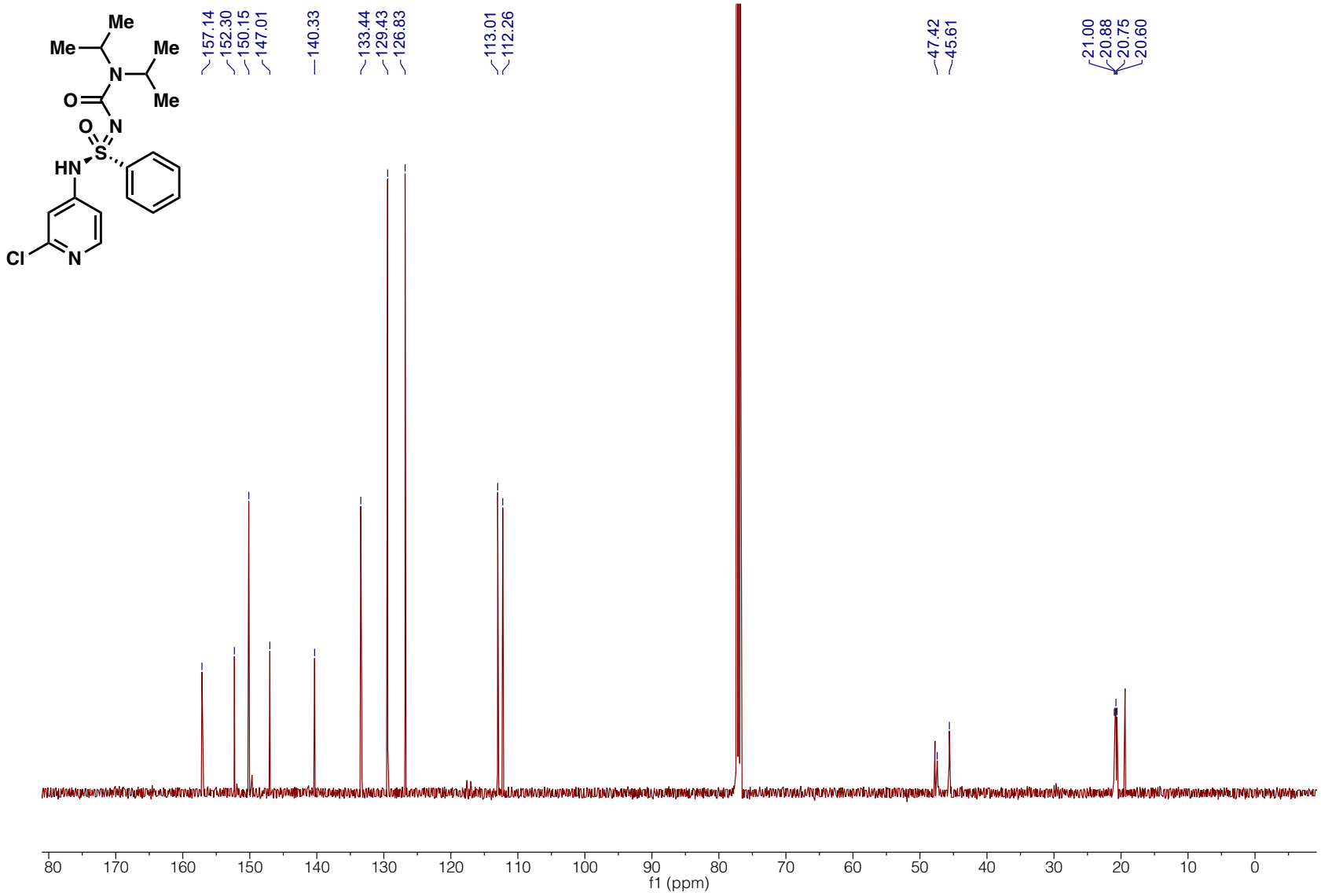

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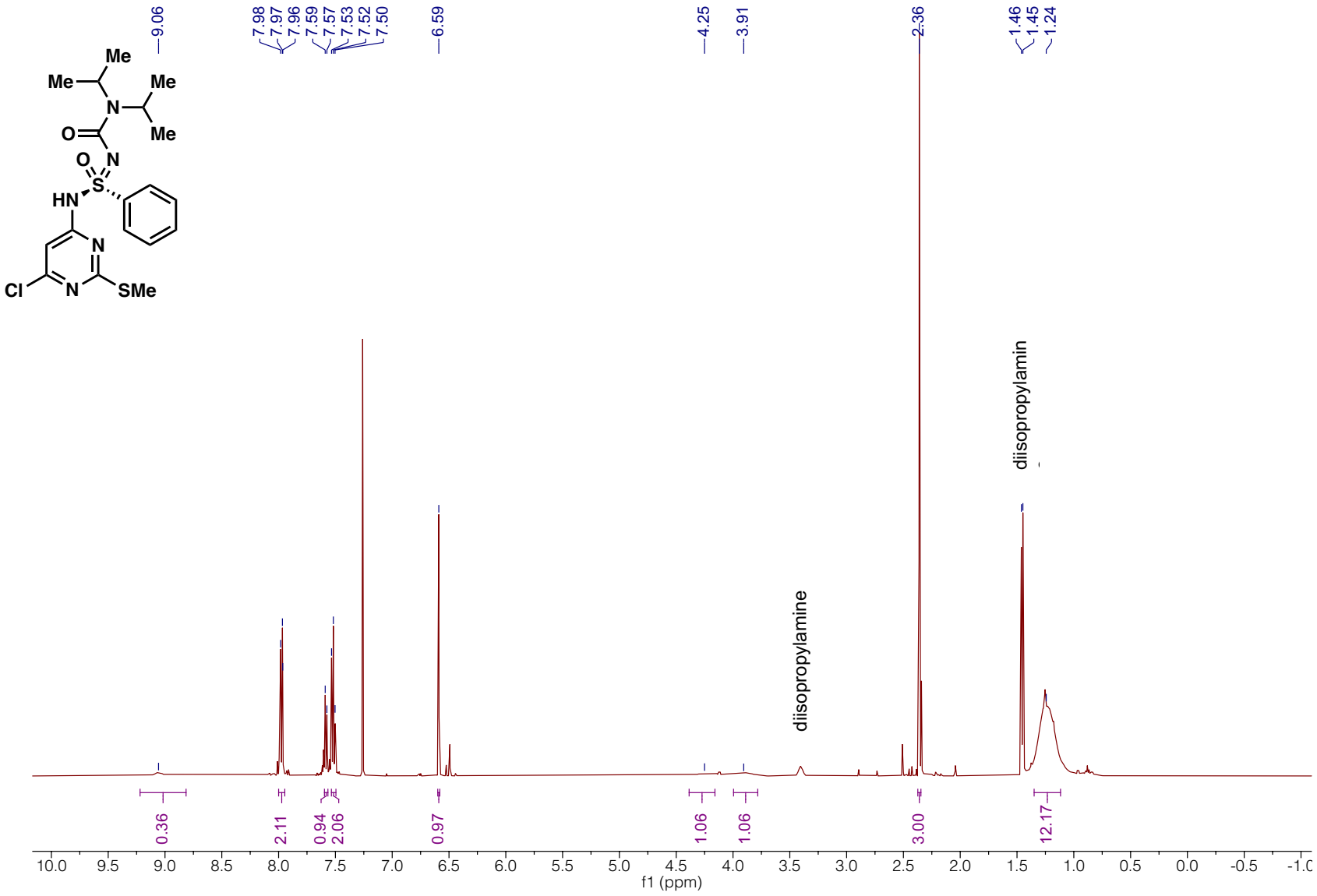

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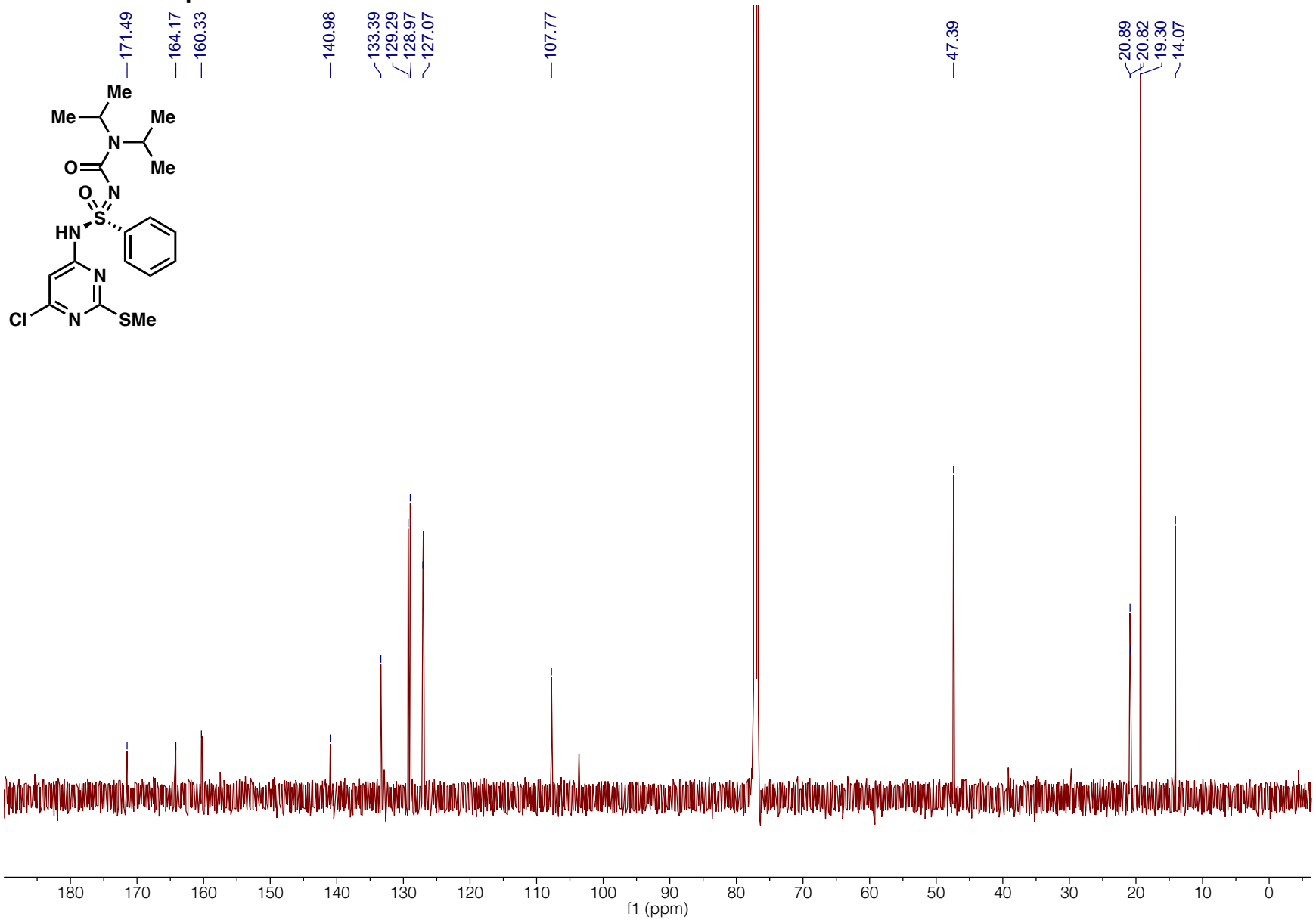
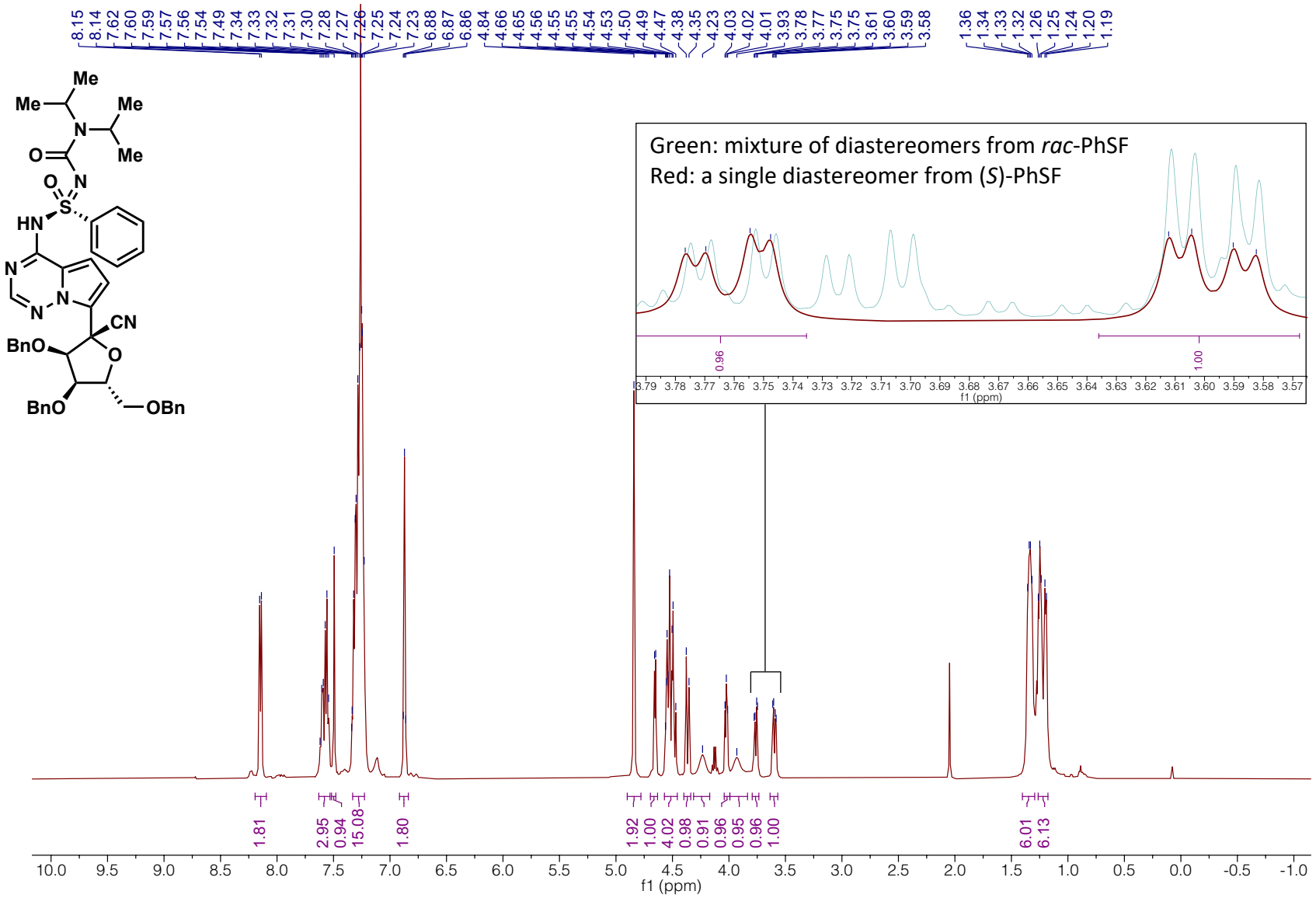
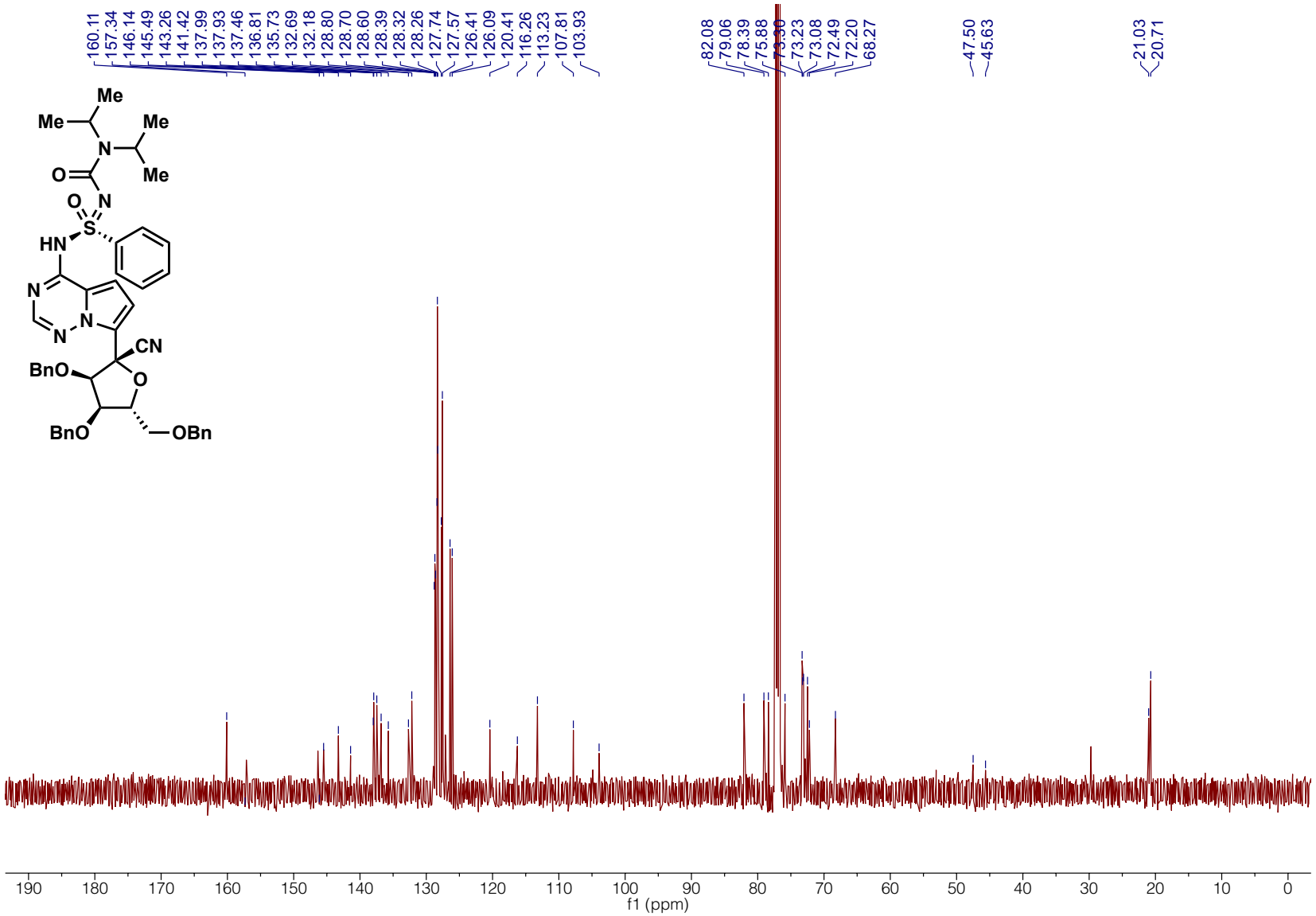


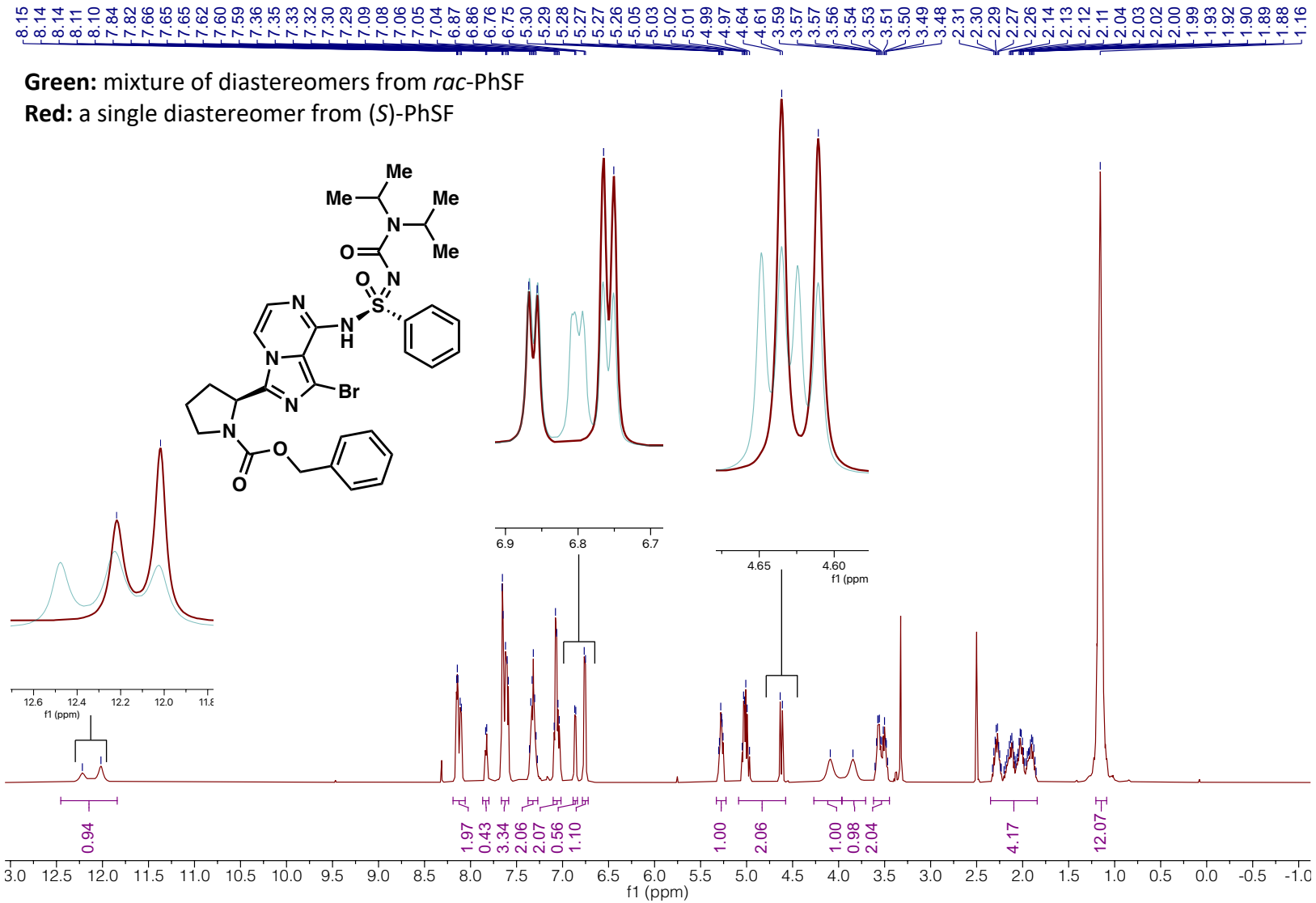
^{1}H NMR of compound 8g:



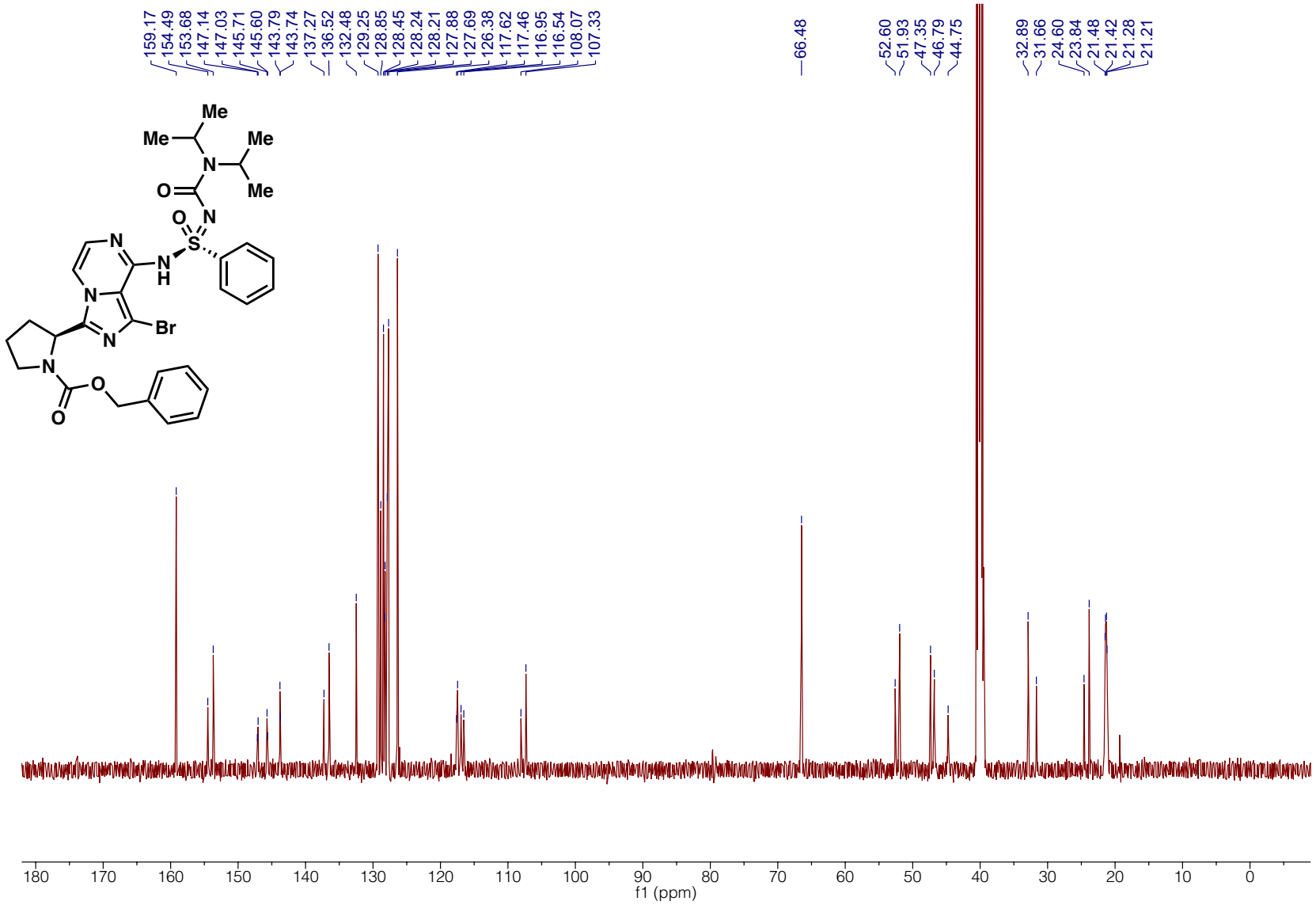
^{13}C NMR of compound 8g:



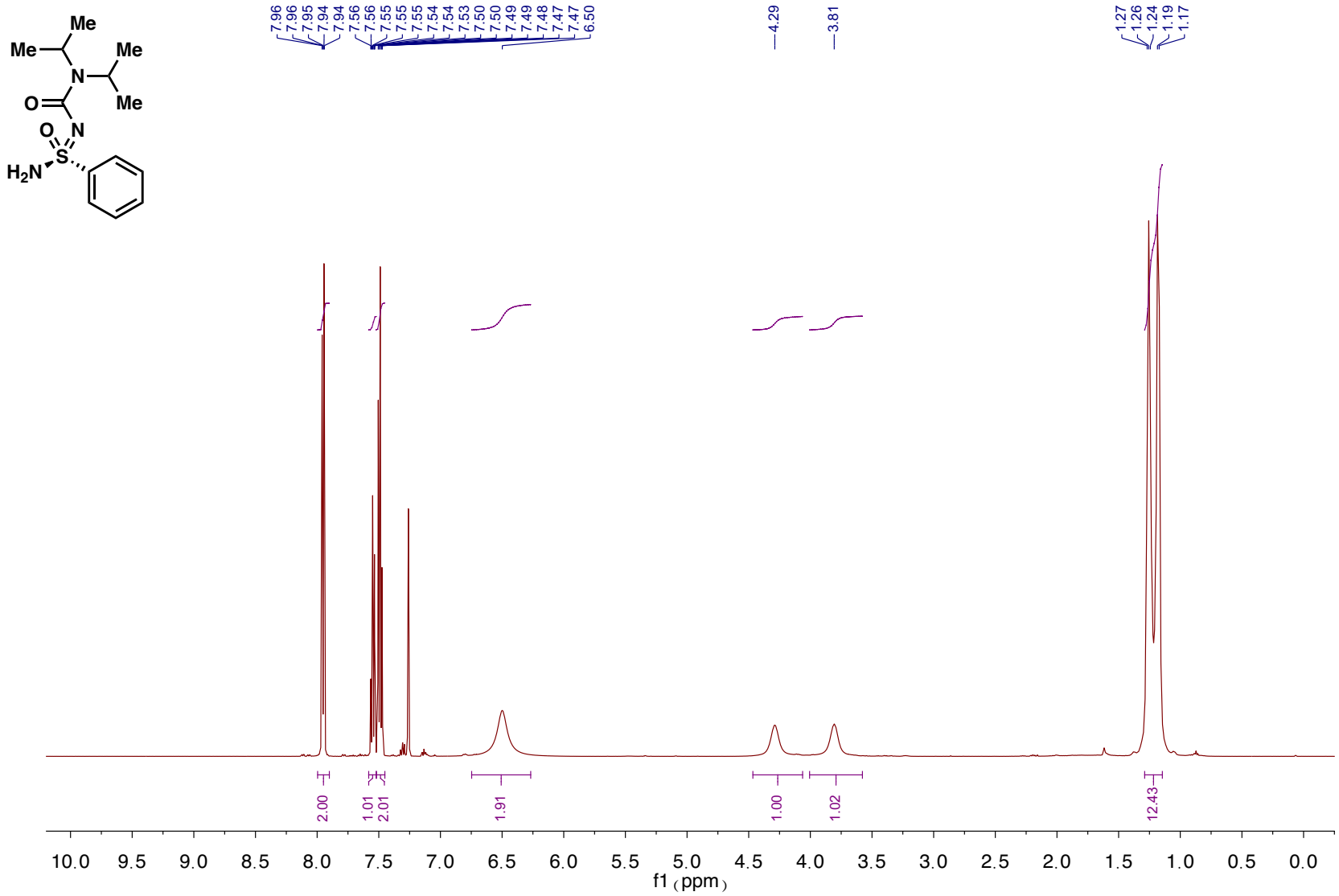
^{1}H NMR of compound 8h:



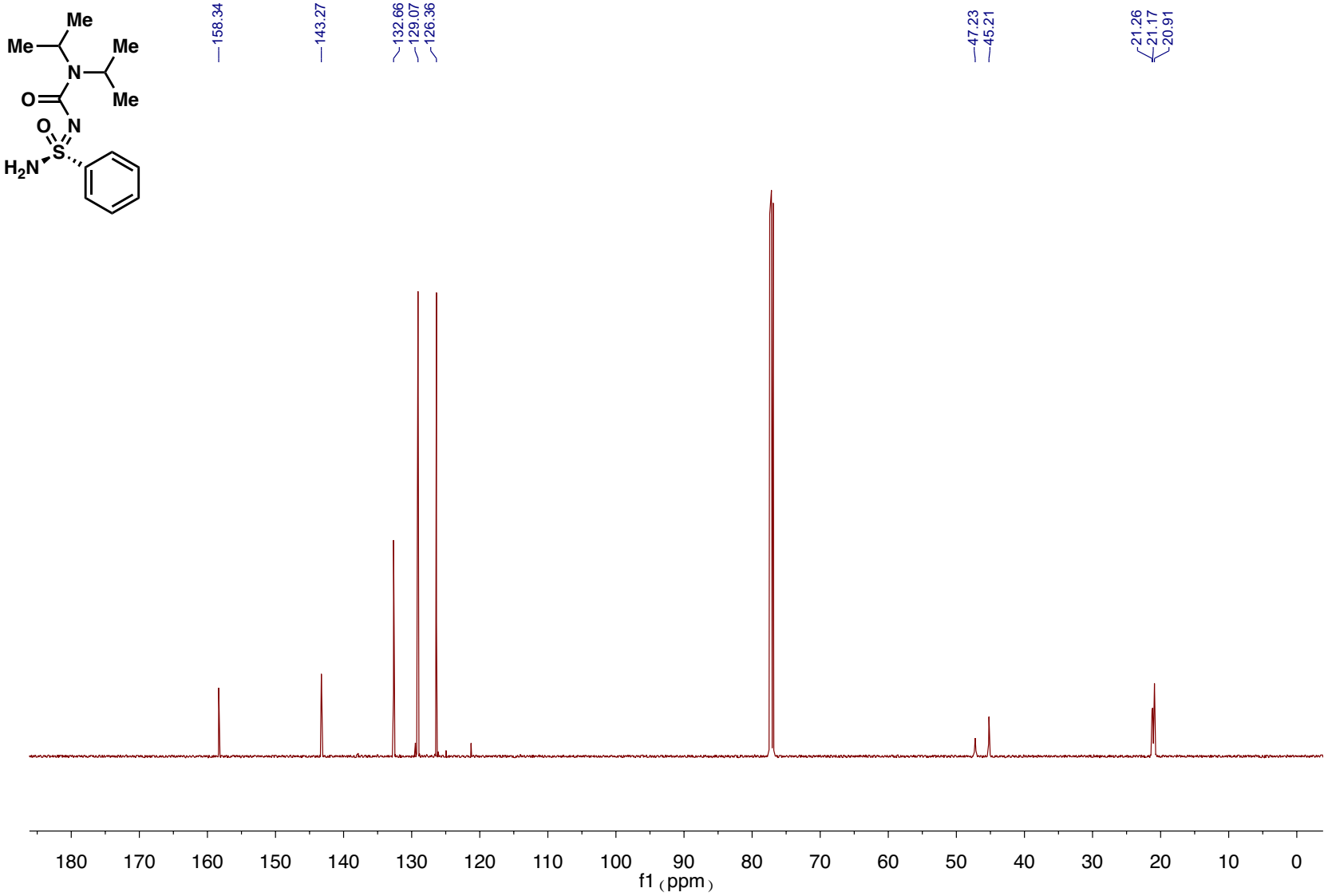
^{13}C NMR of compound 8h:



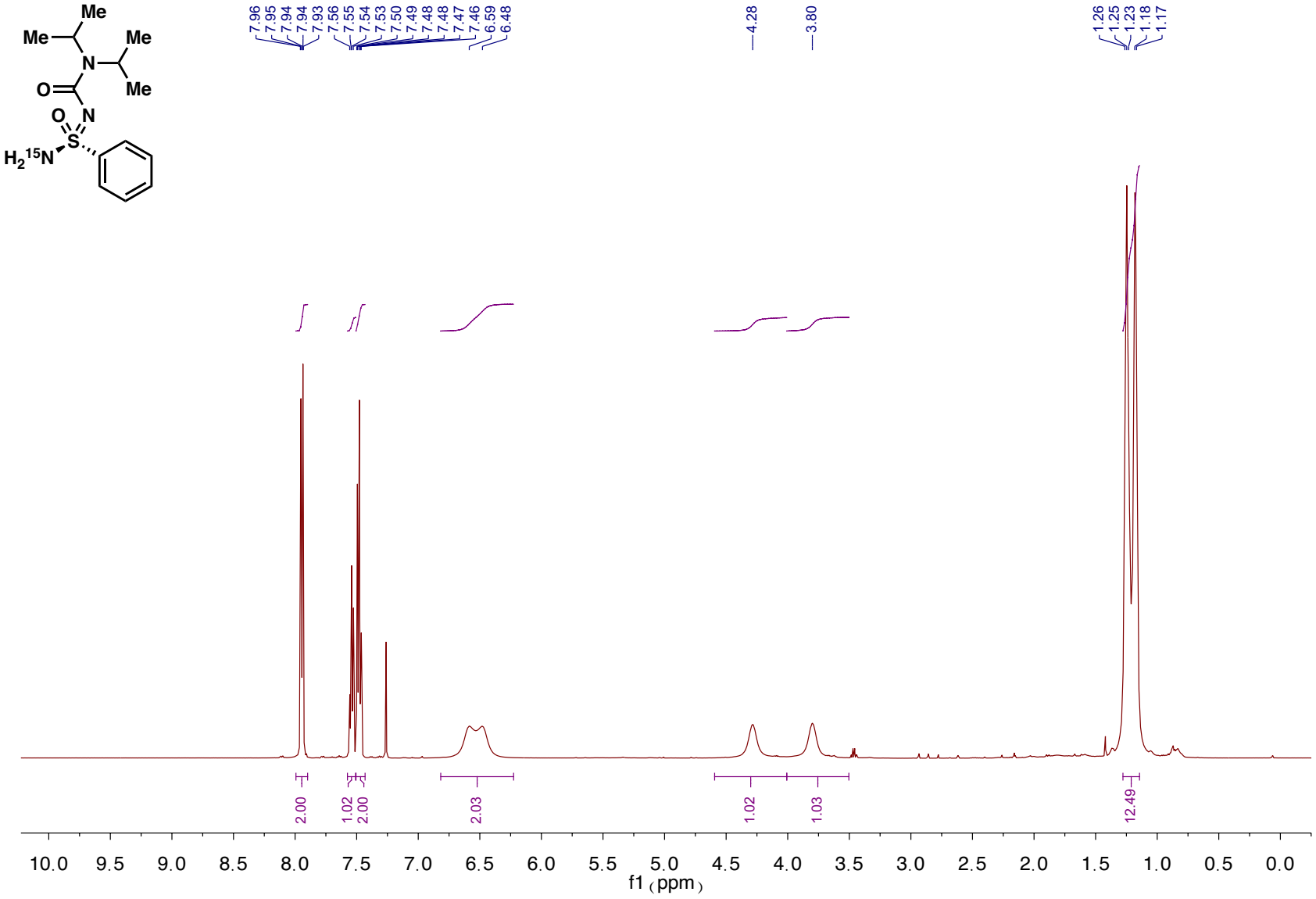
^{1}H NMR of compound 8i:



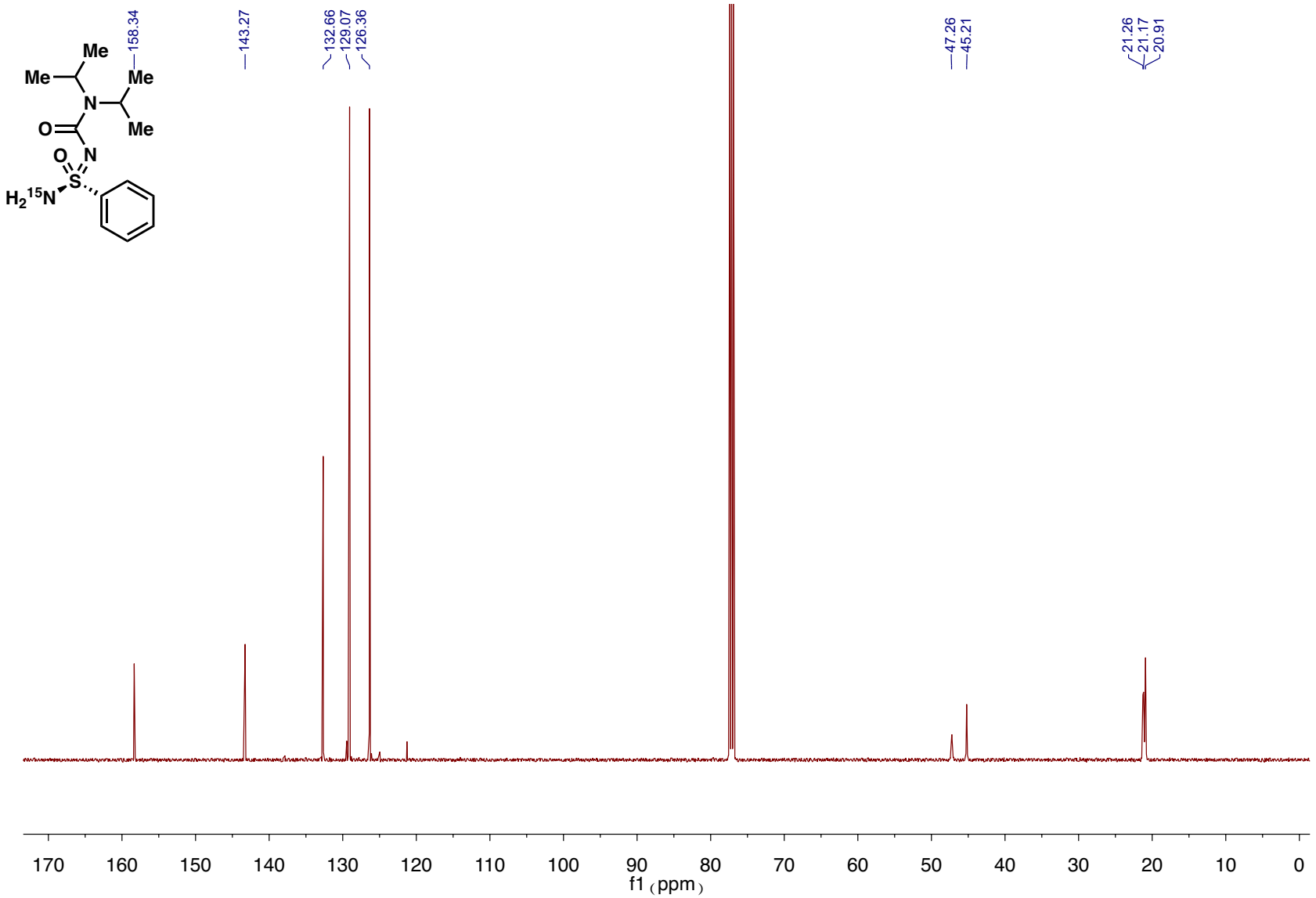
^{13}C NMR of compound 8i:



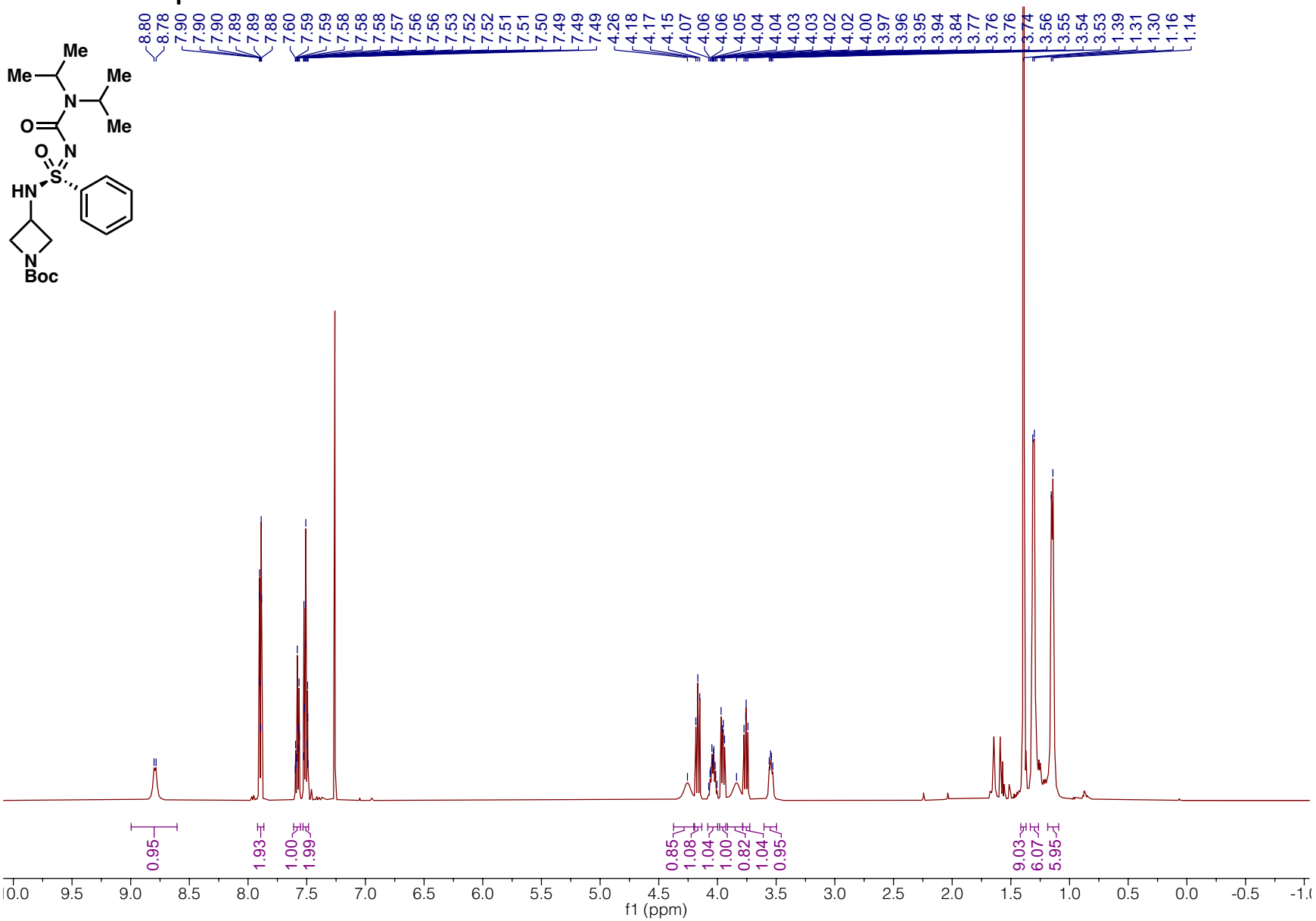
^{1}H NMR of compound 8j:



^{13}C NMR of compound 8j:



^{1}H NMR of compound 8k:



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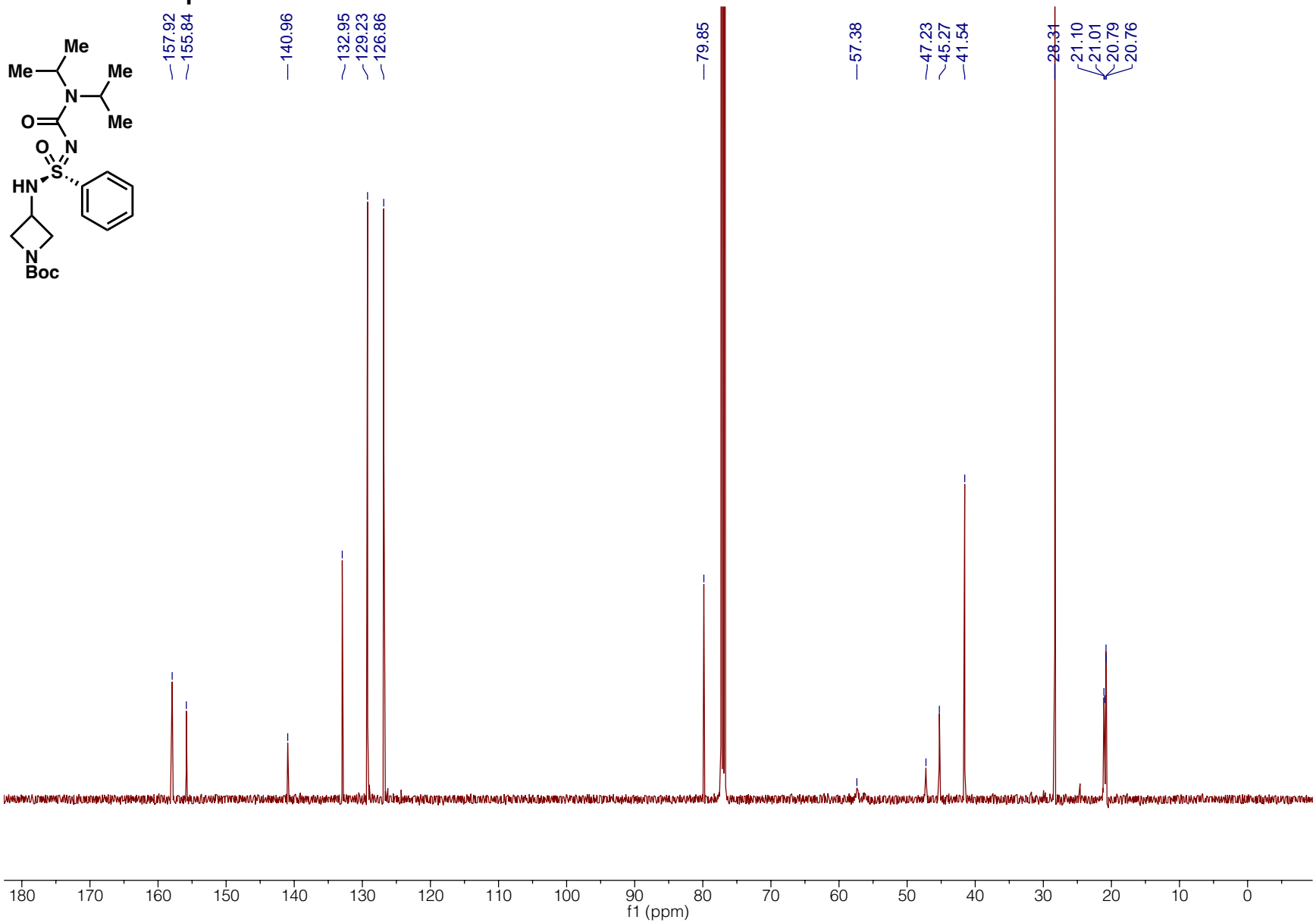
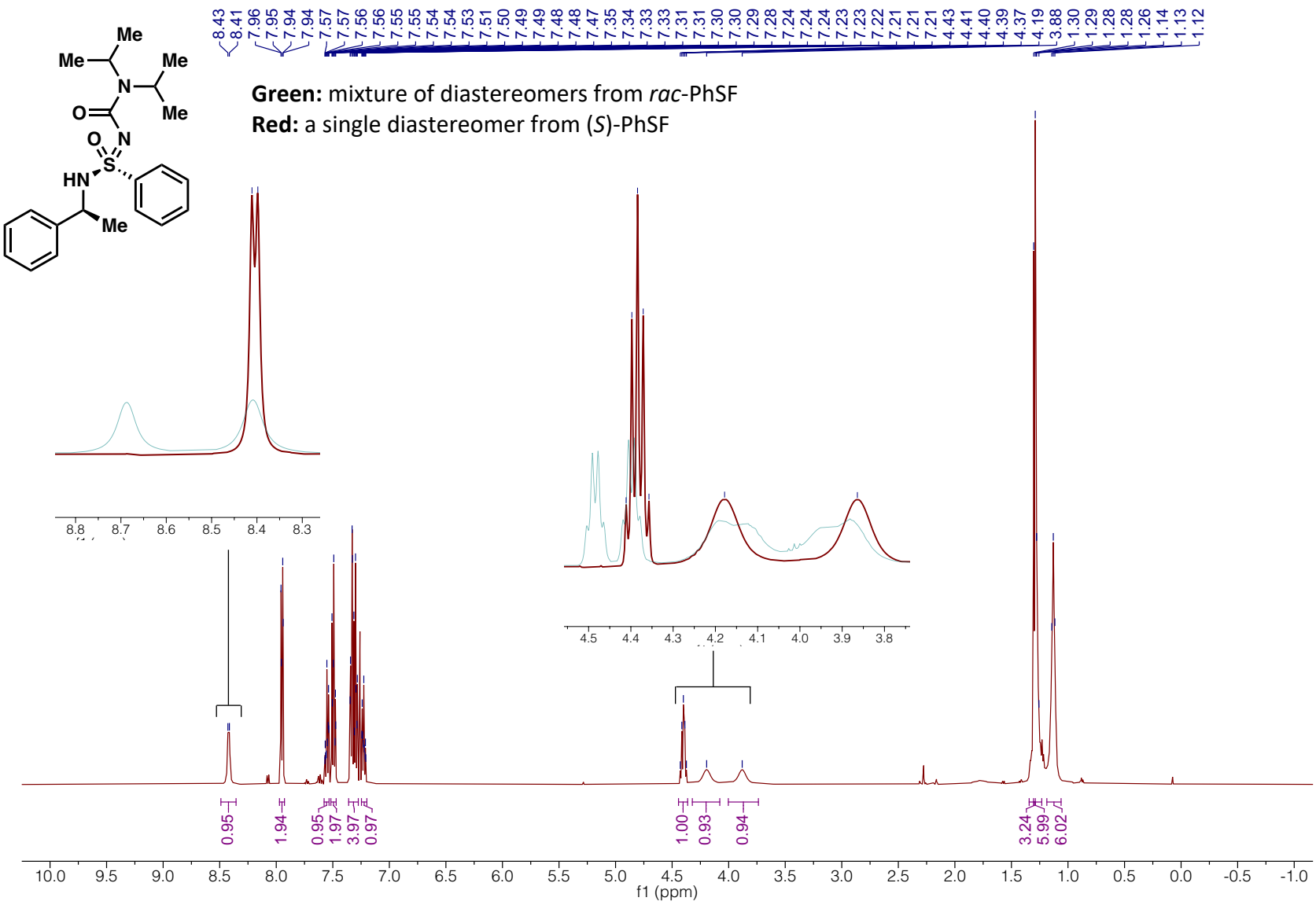
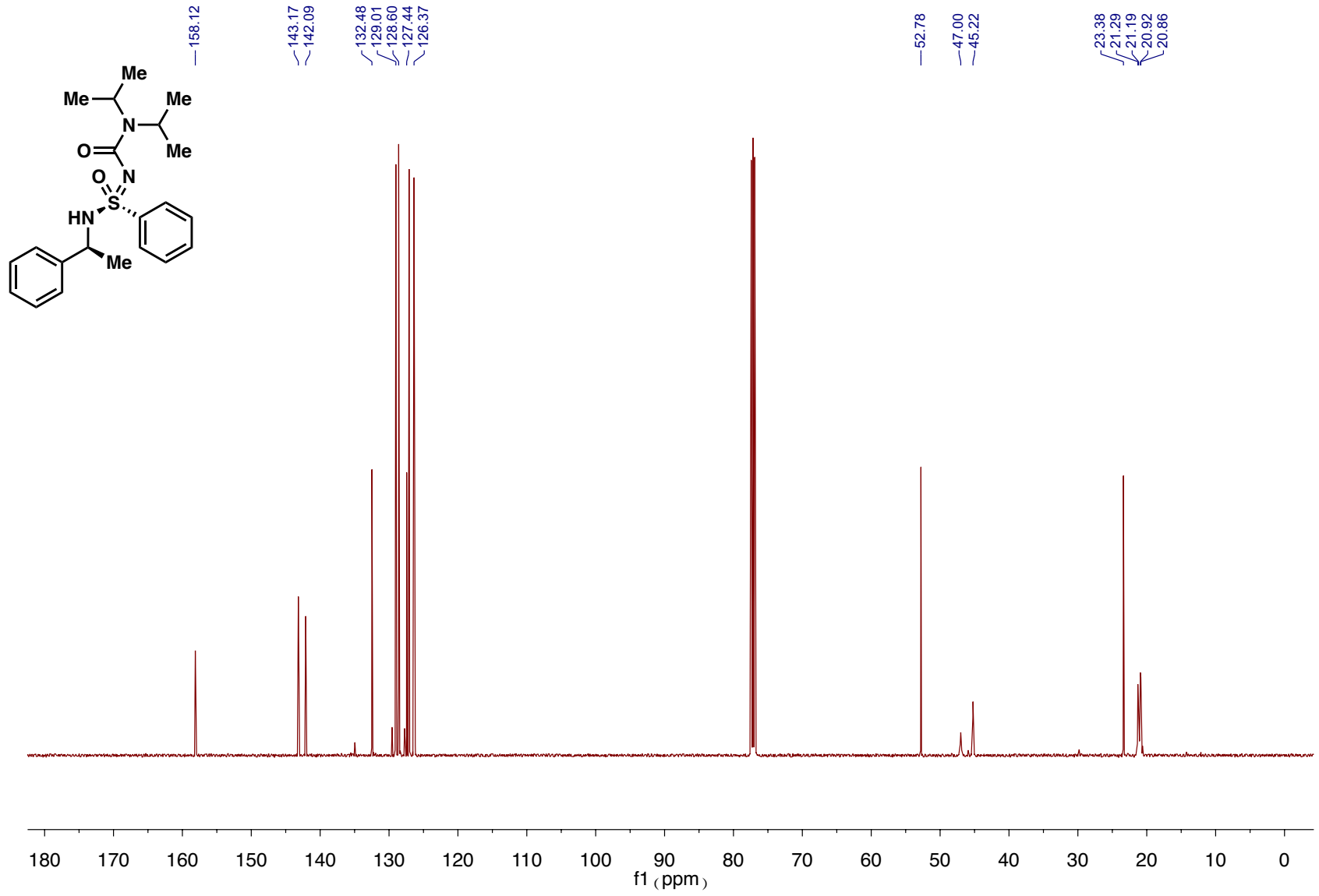


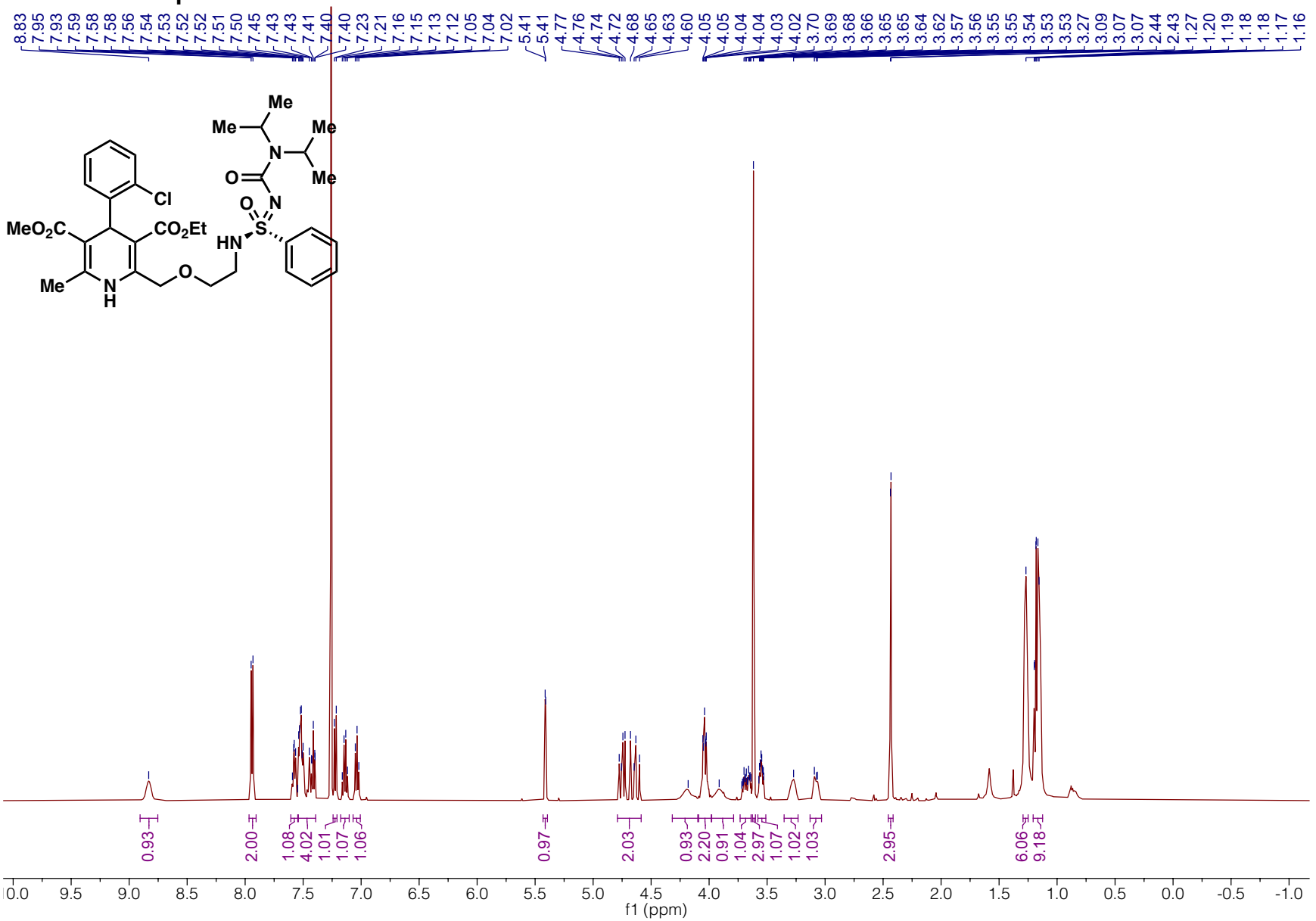
^{1}H NMR of compound 8l:



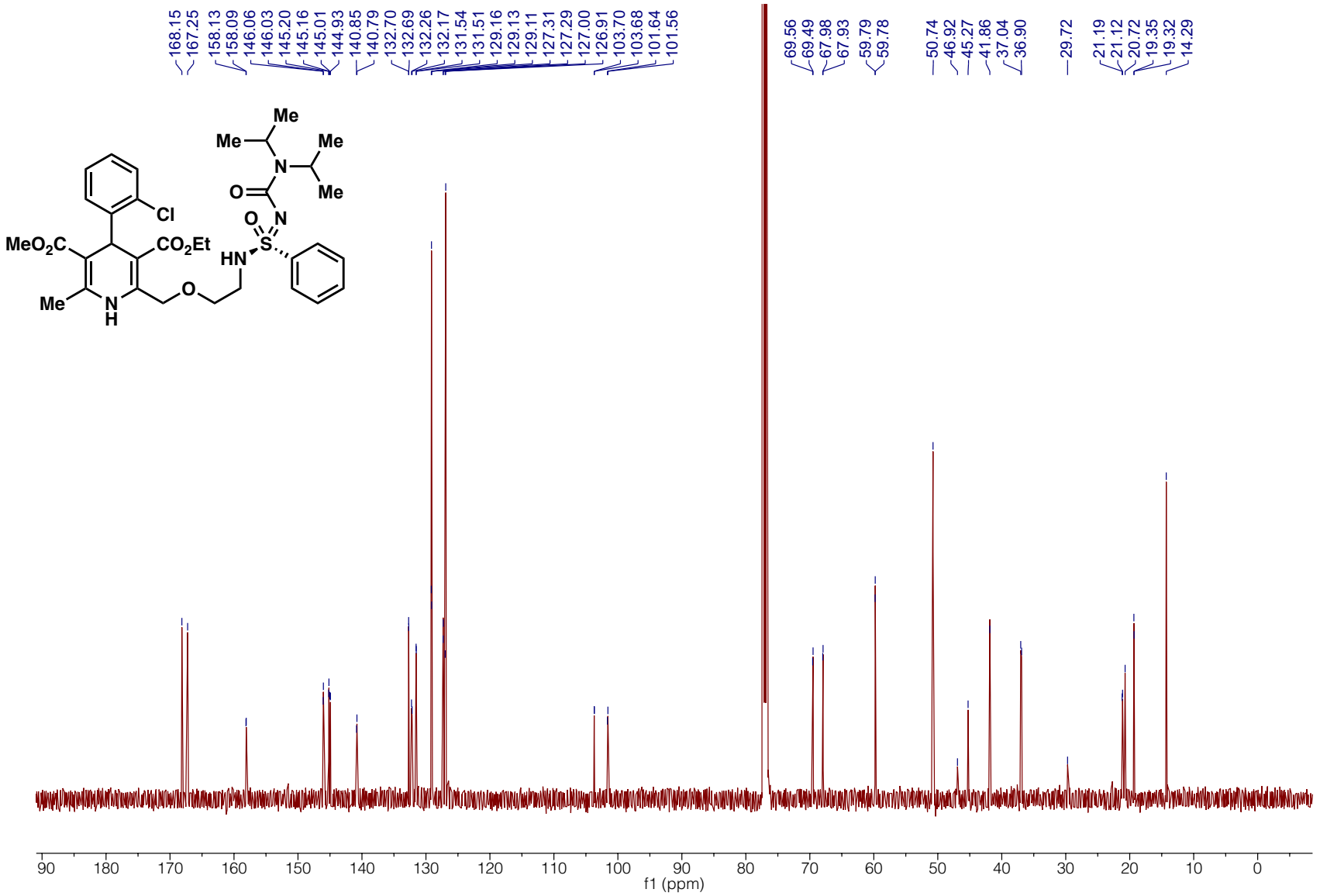
^{13}C NMR of compound 8l:



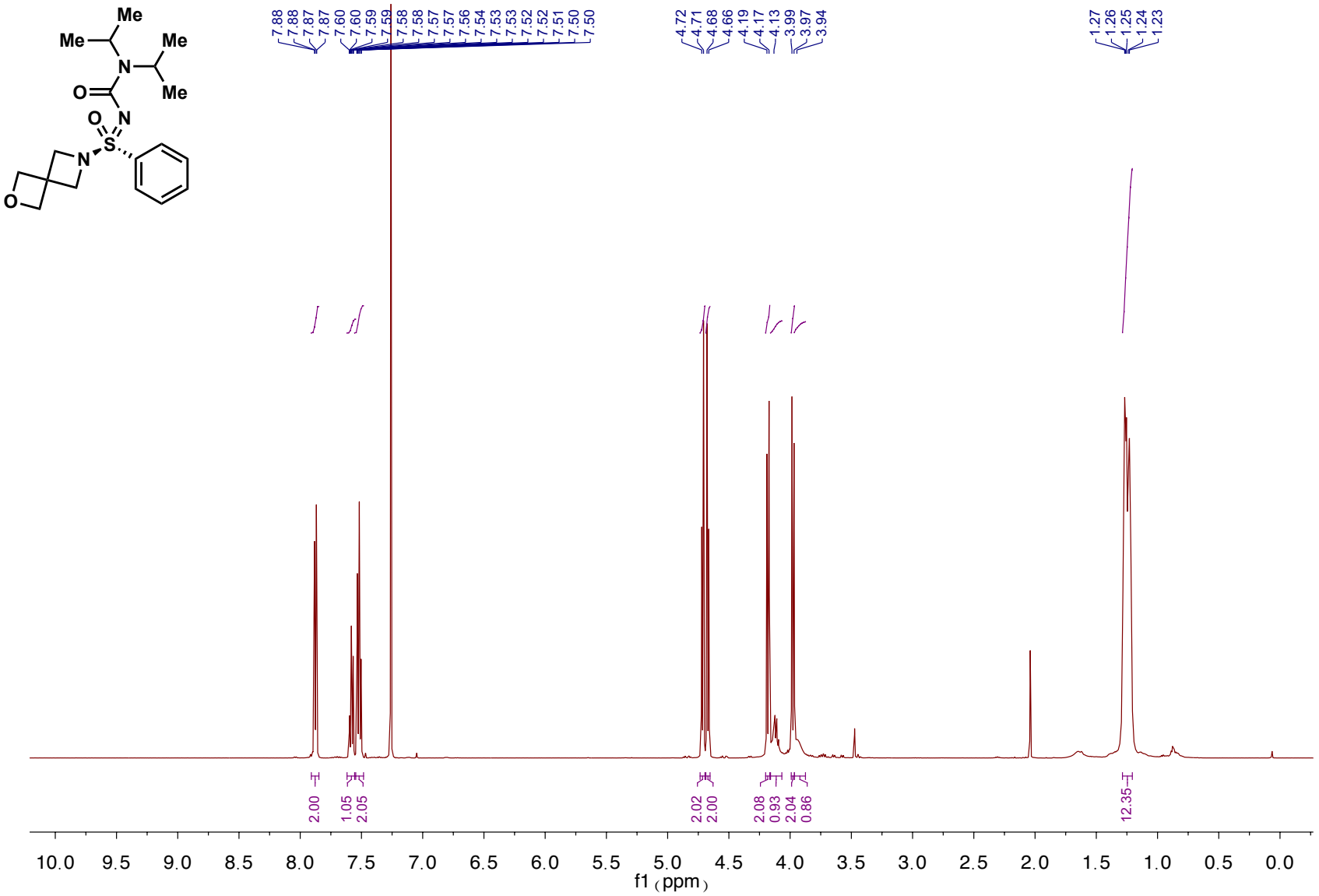
^{1}H NMR of compound 8m:



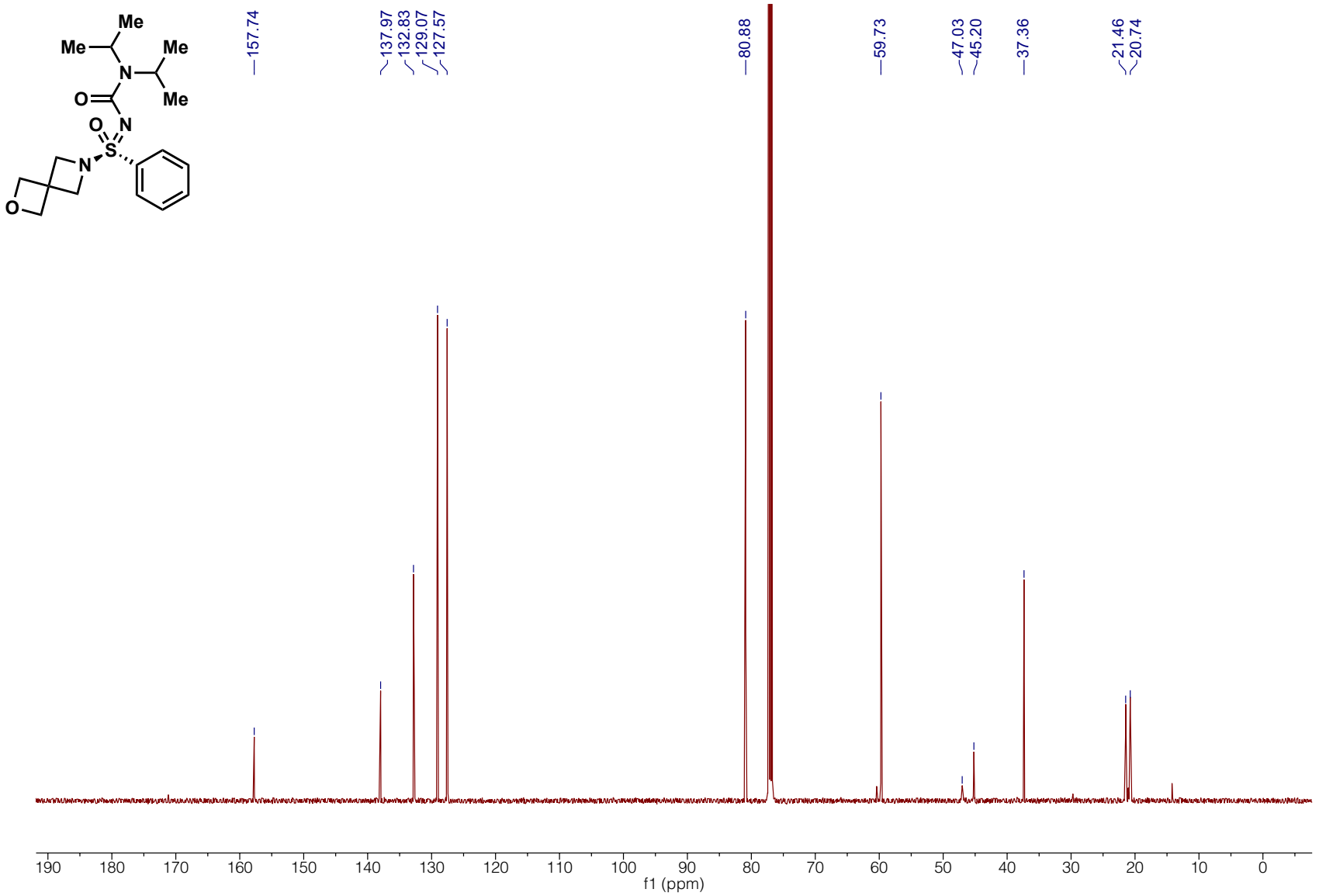
^{13}C NMR of compound 8m:



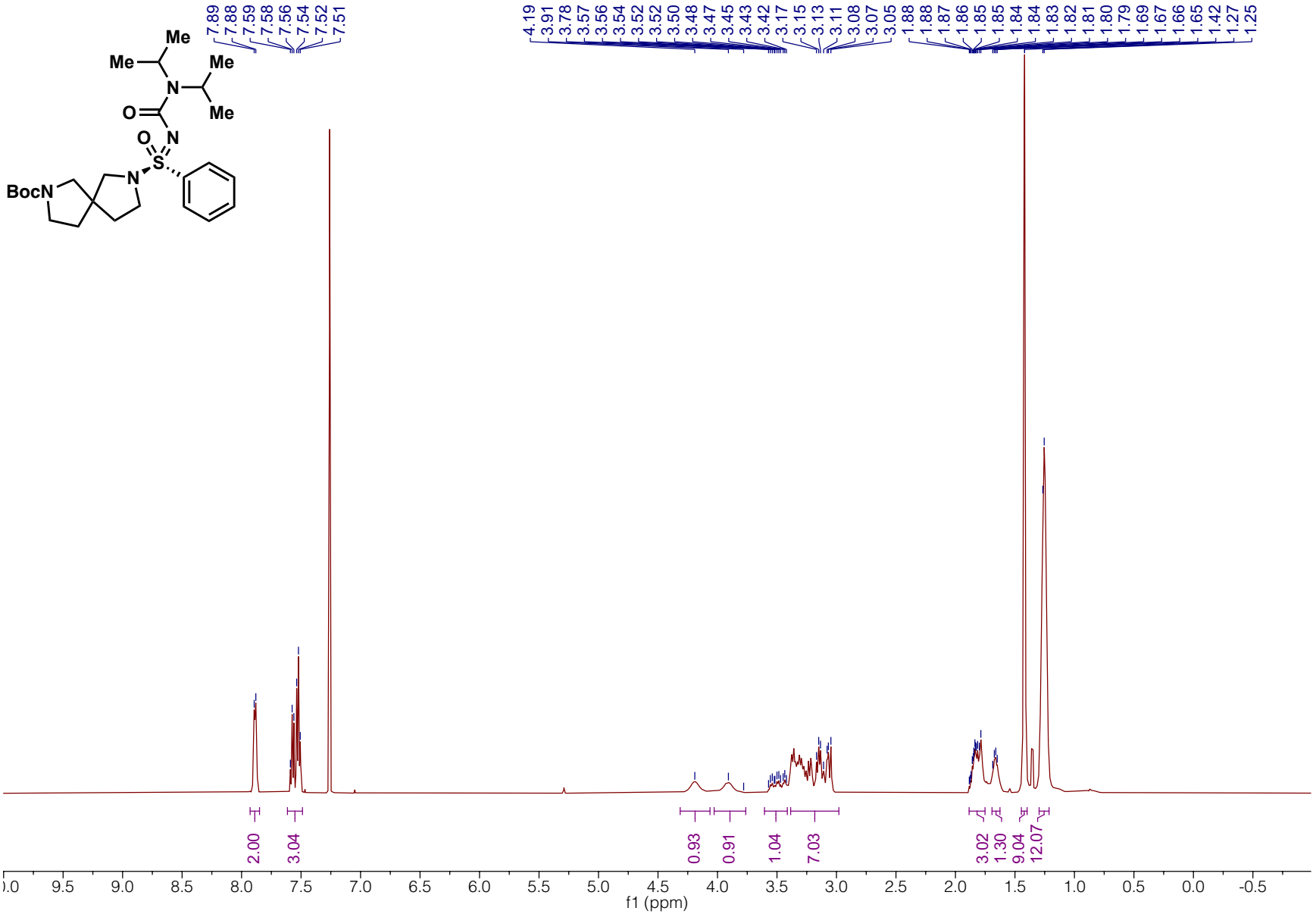
^{1}H NMR of compound 8n:



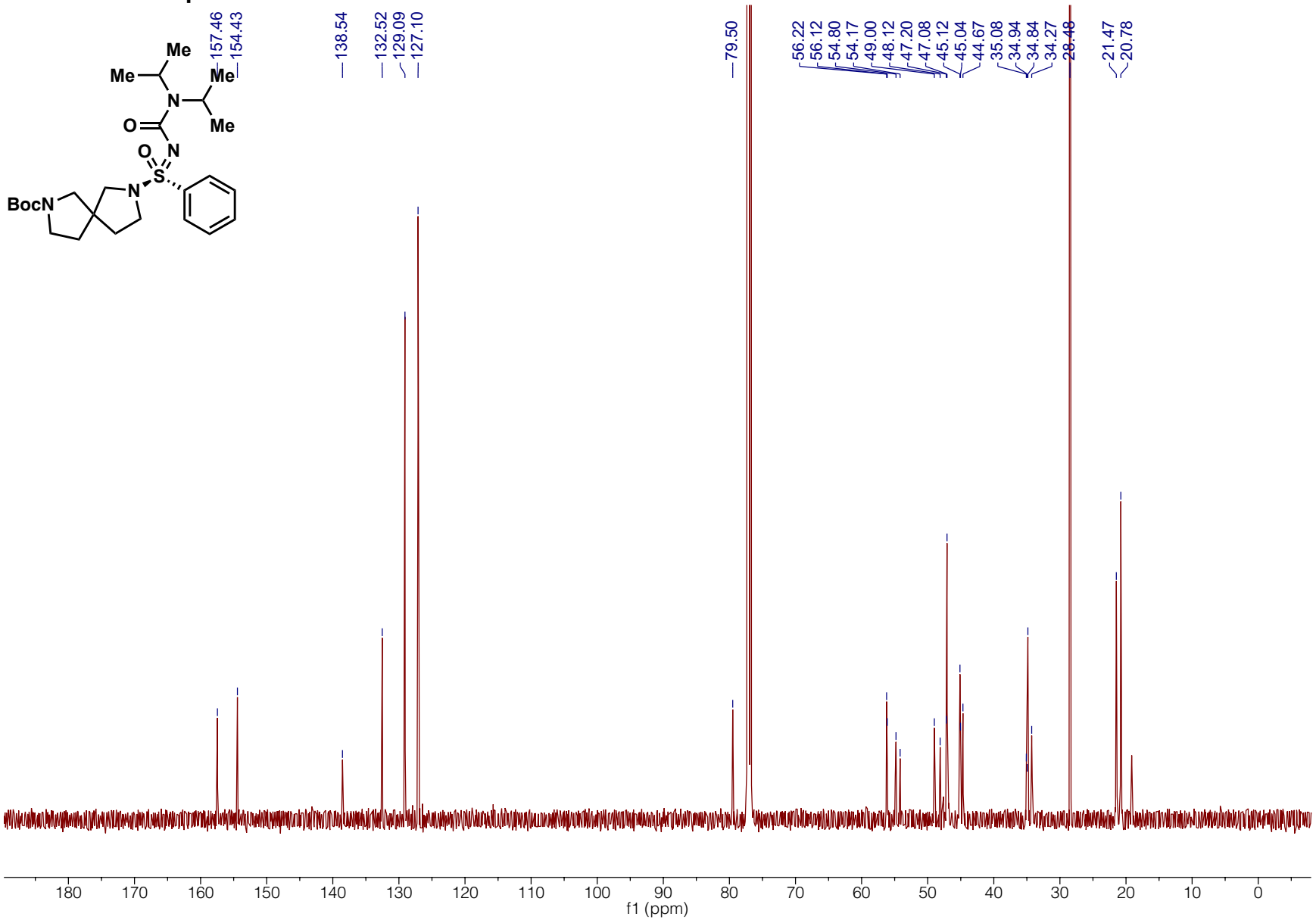
^{13}C NMR of compound 8n:



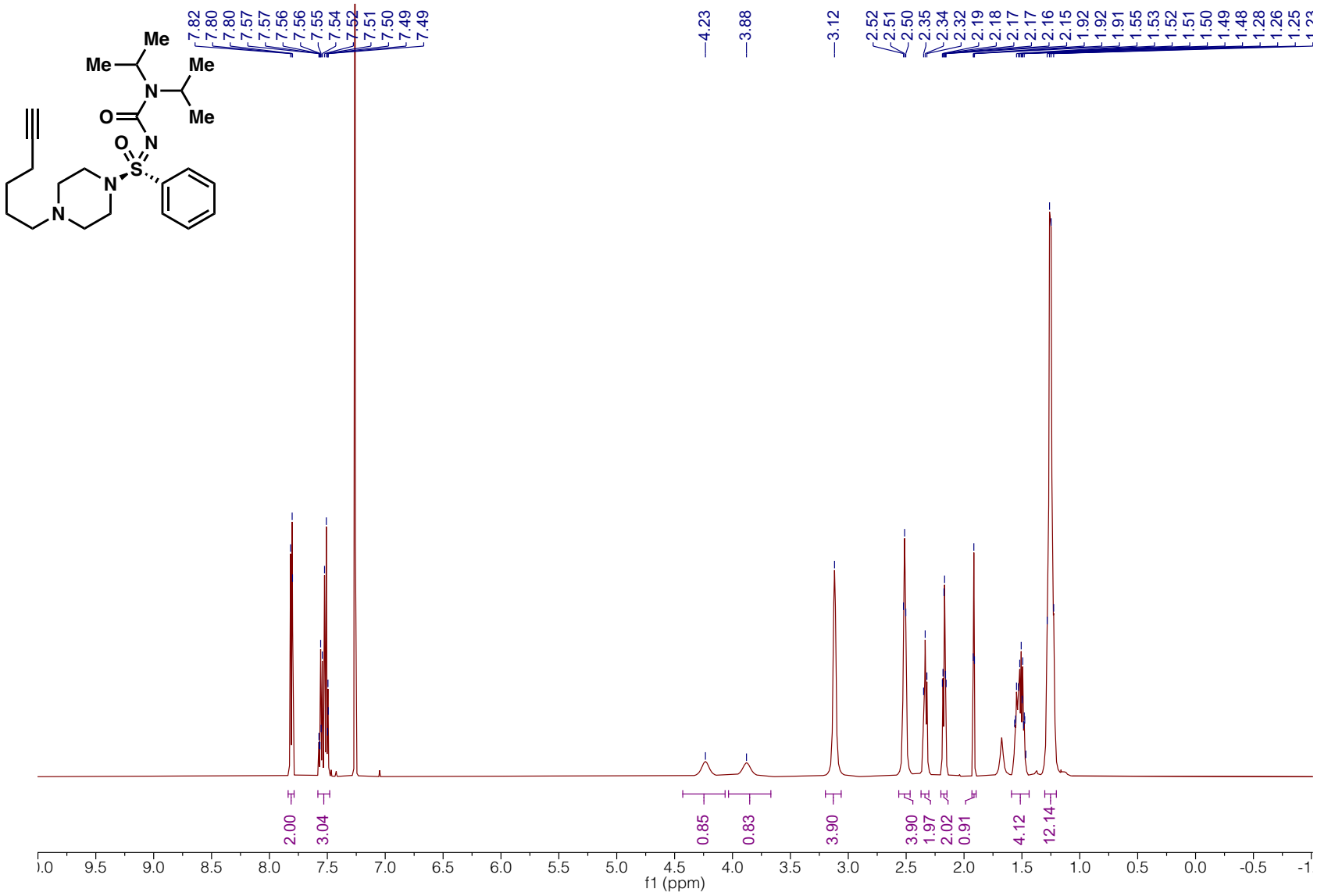
^{1}H NMR of compound 8o:



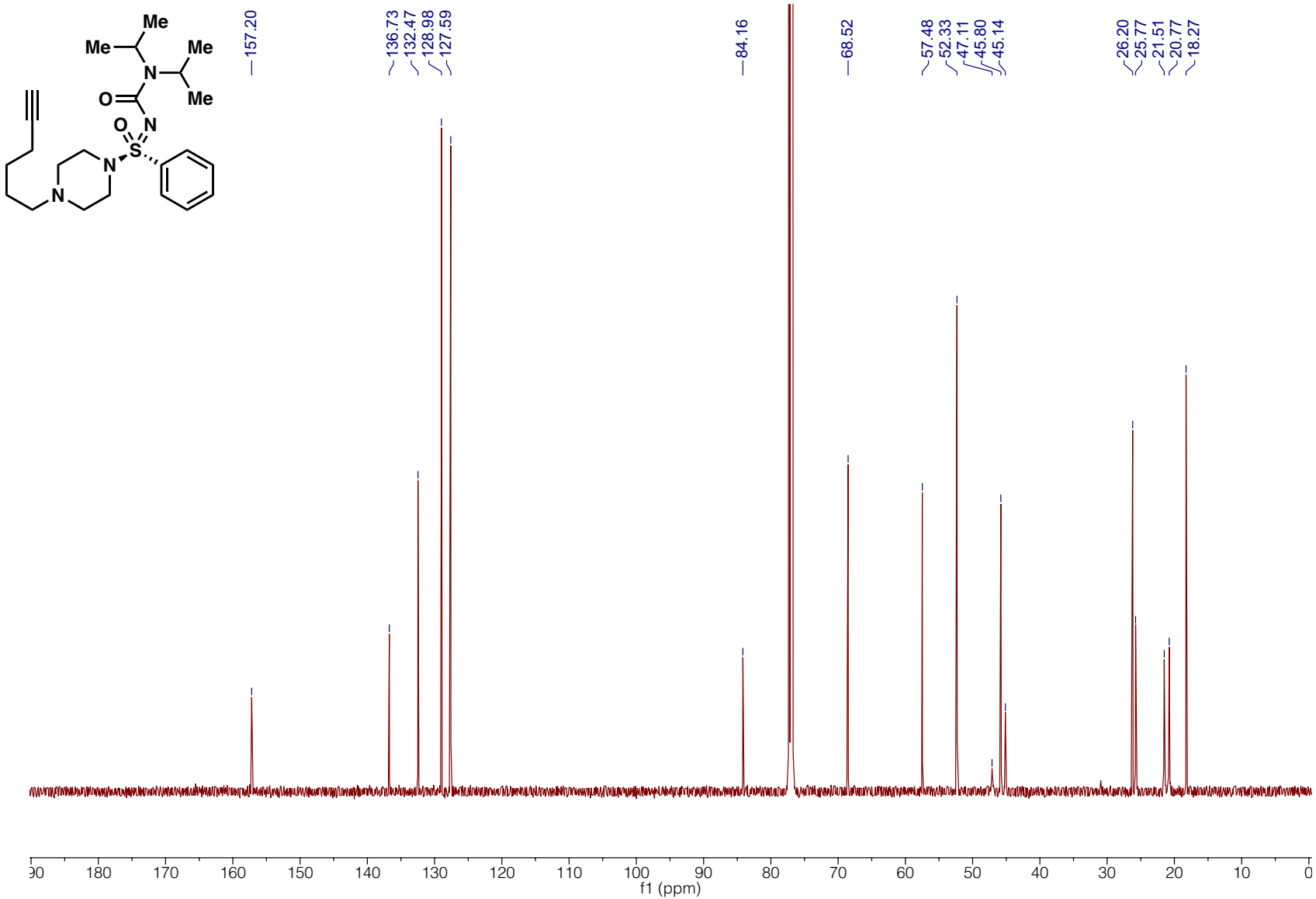
^{13}C NMR of compound 8o:



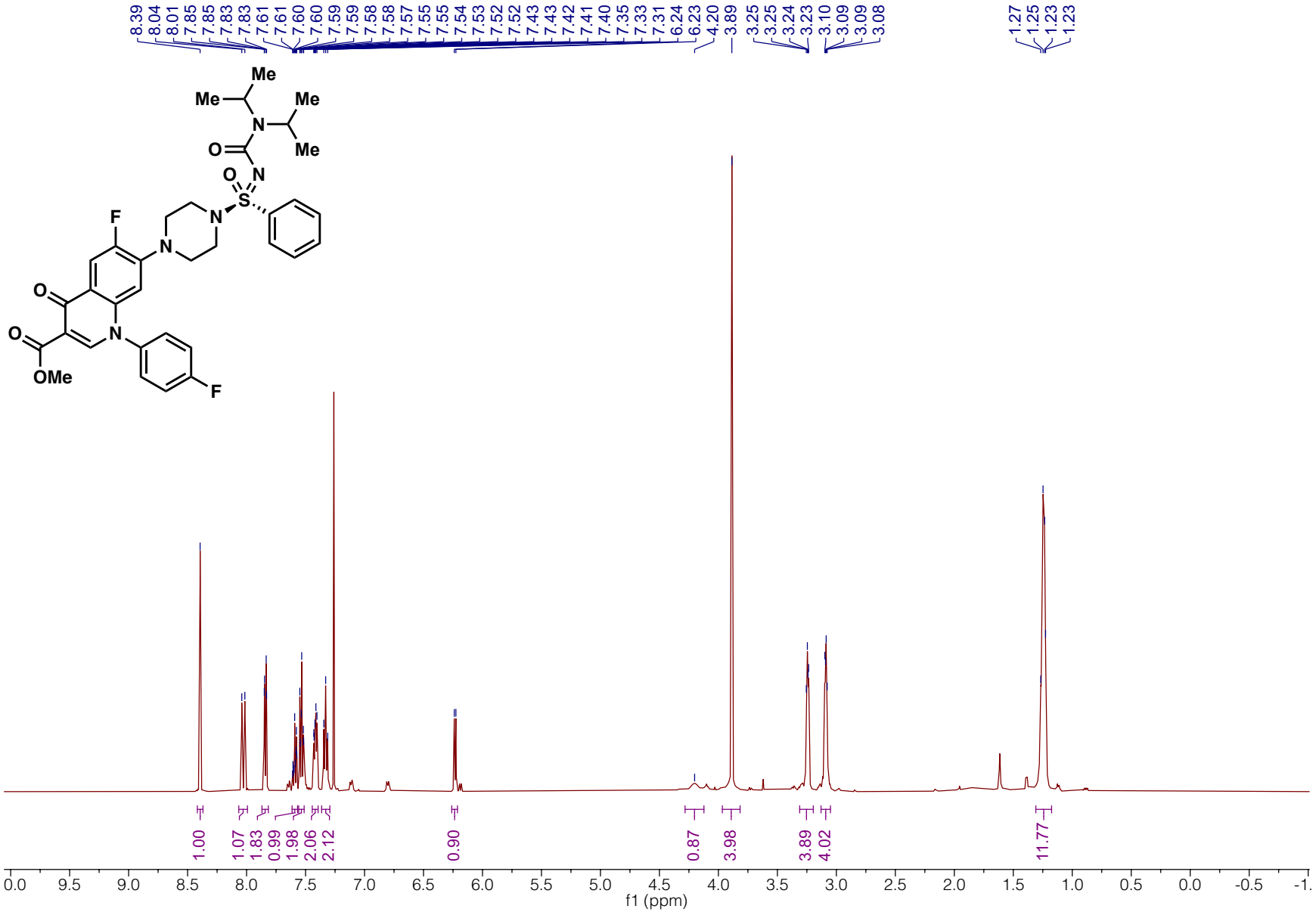
^{1}H NMR of compound 8p:



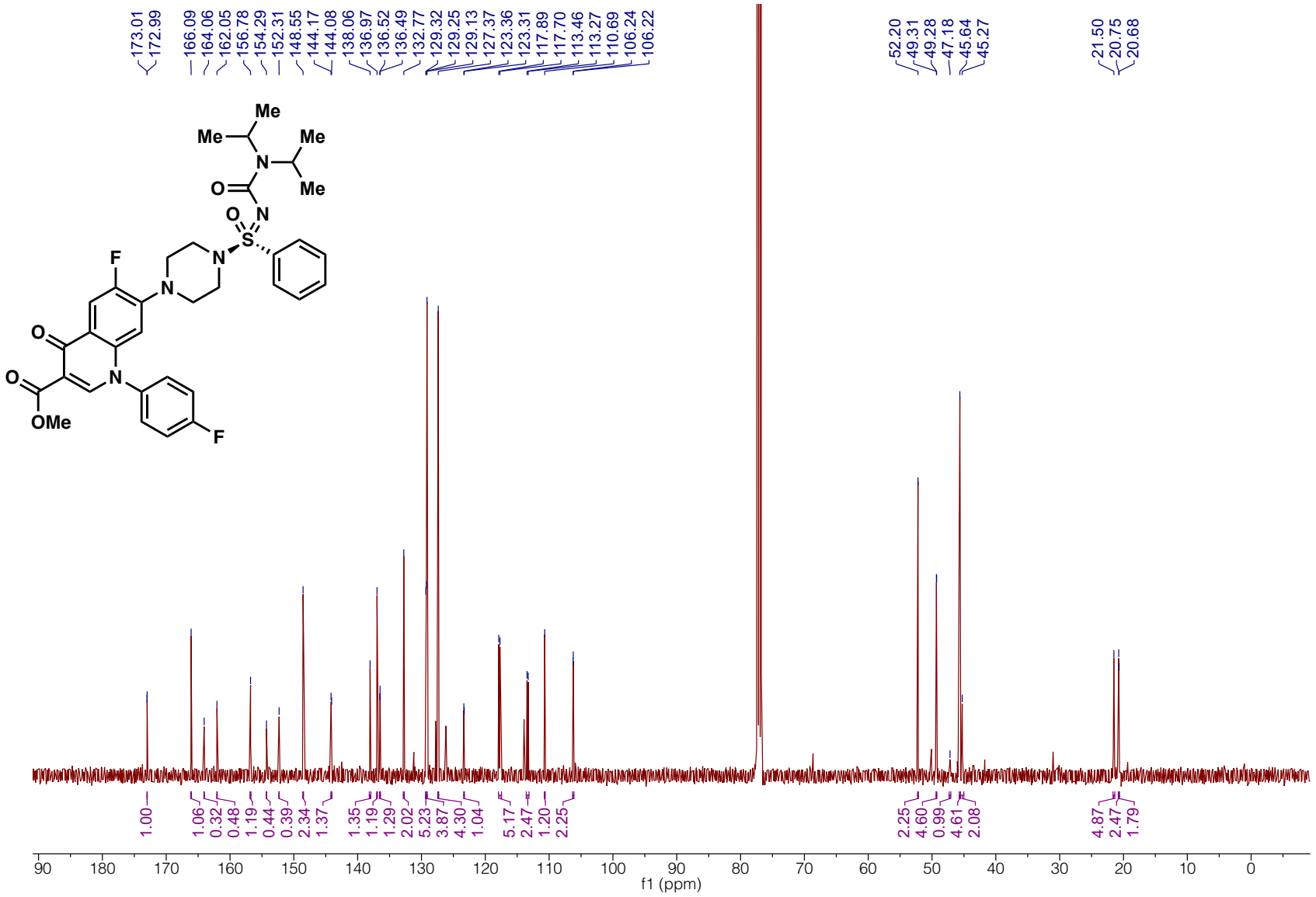
^{13}C NMR of compound 8p:



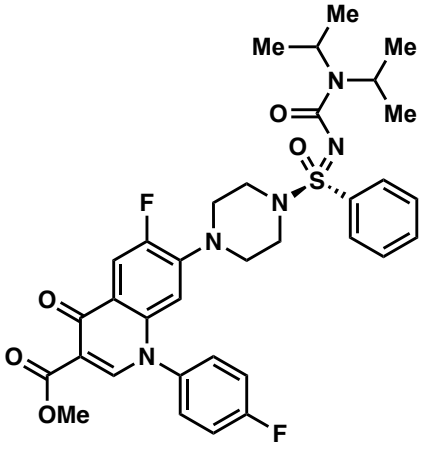
^{1}H NMR of compound 8q:



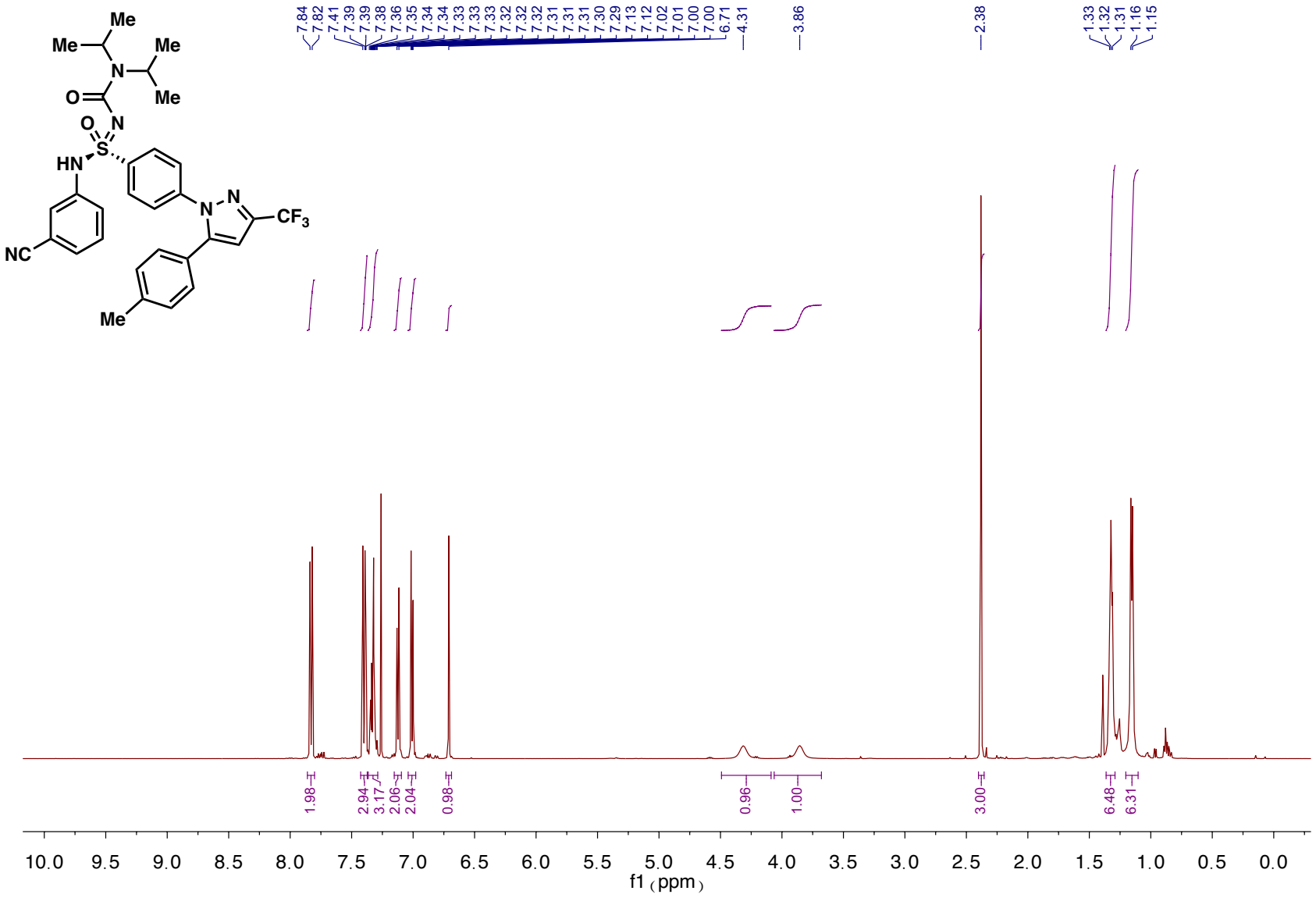
^{13}C NMR of compound 8q:



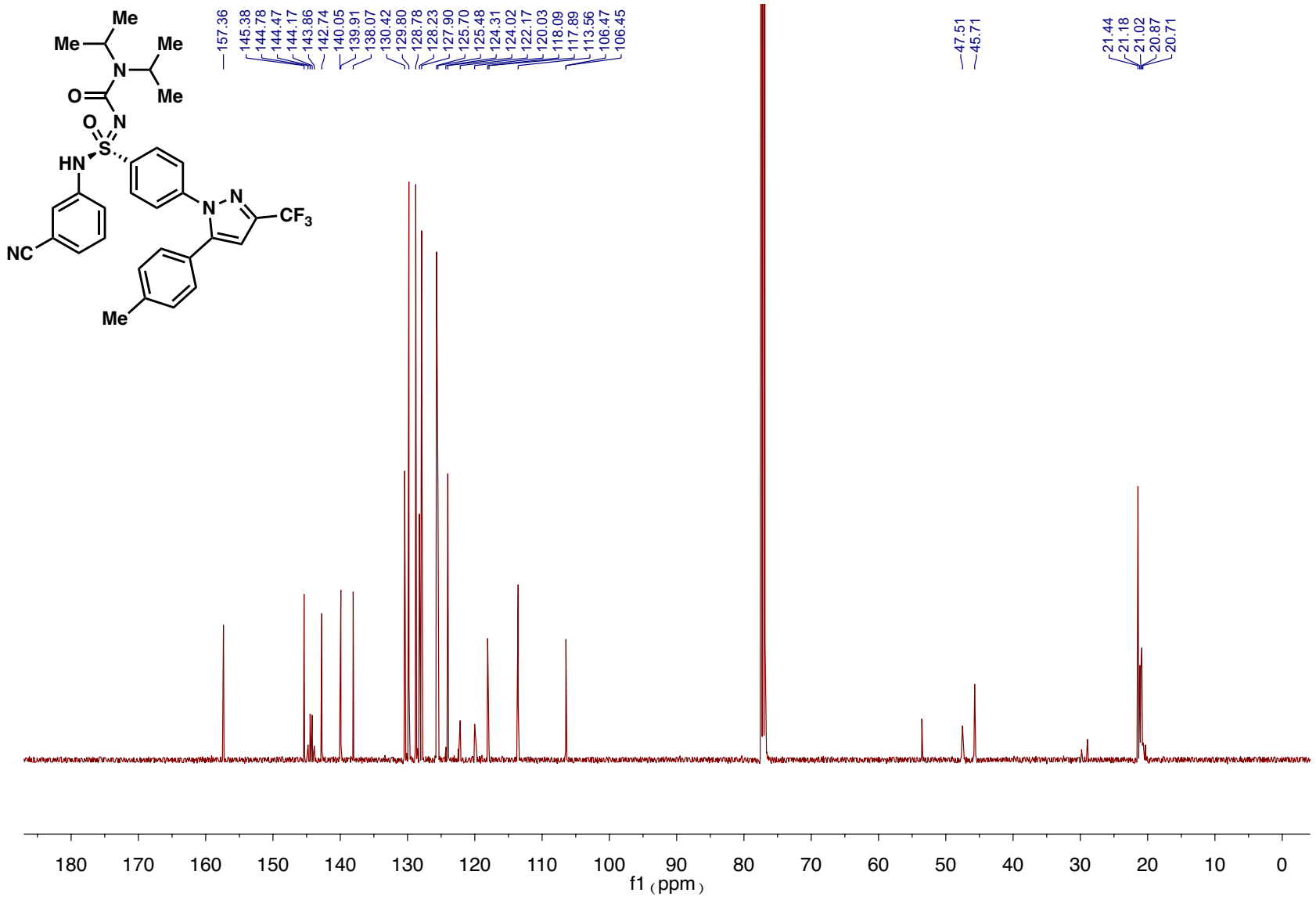
^{19}F NMR of compound 8q:



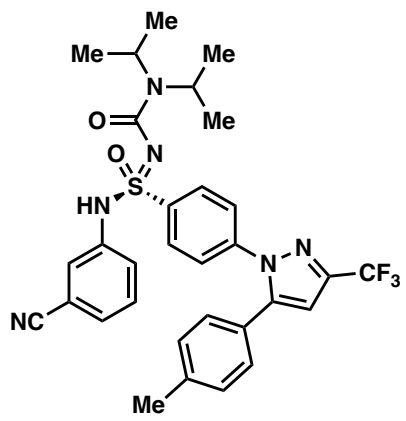
^{1}H NMR of compound 8r:



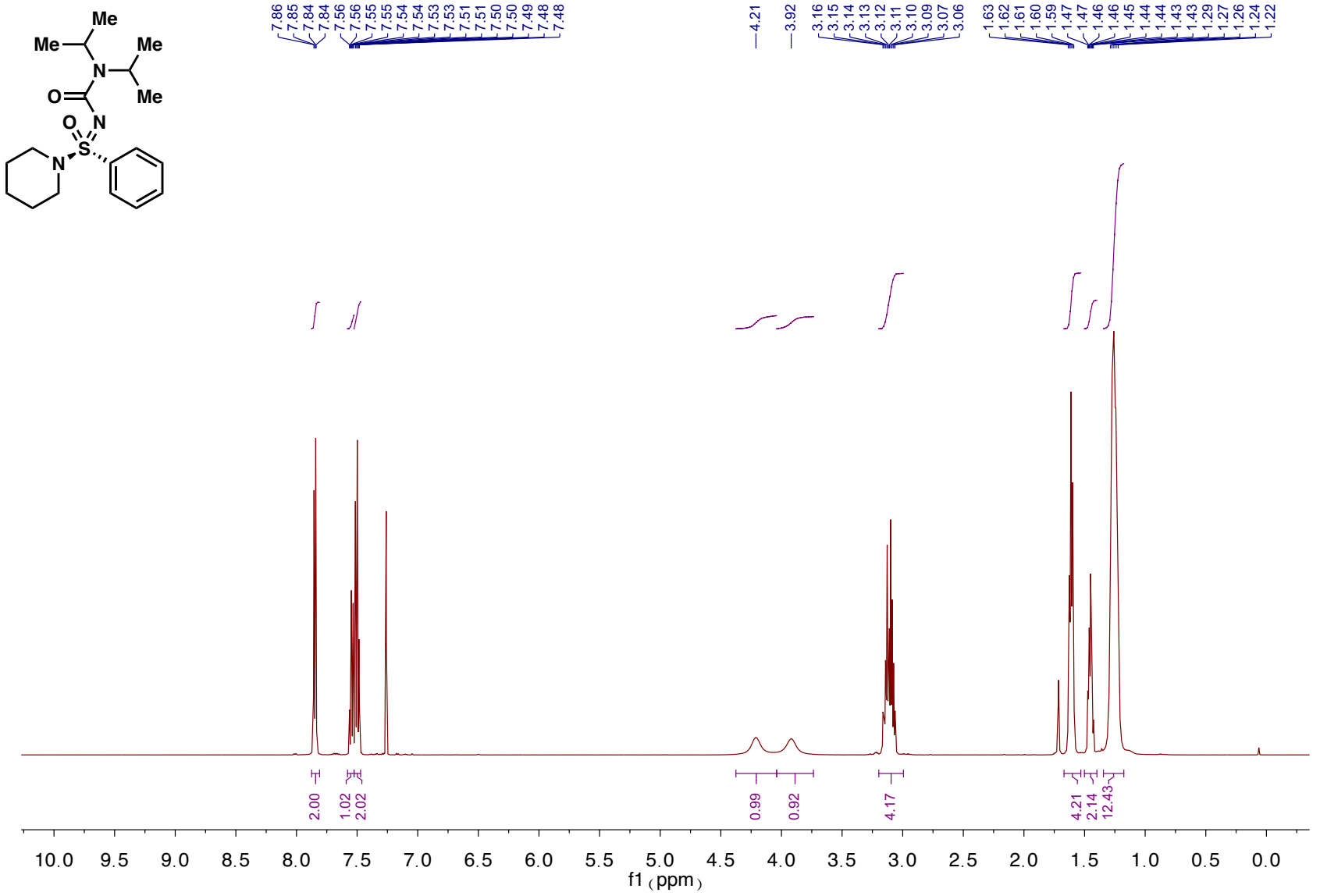
^{13}C NMR of compound 8r:



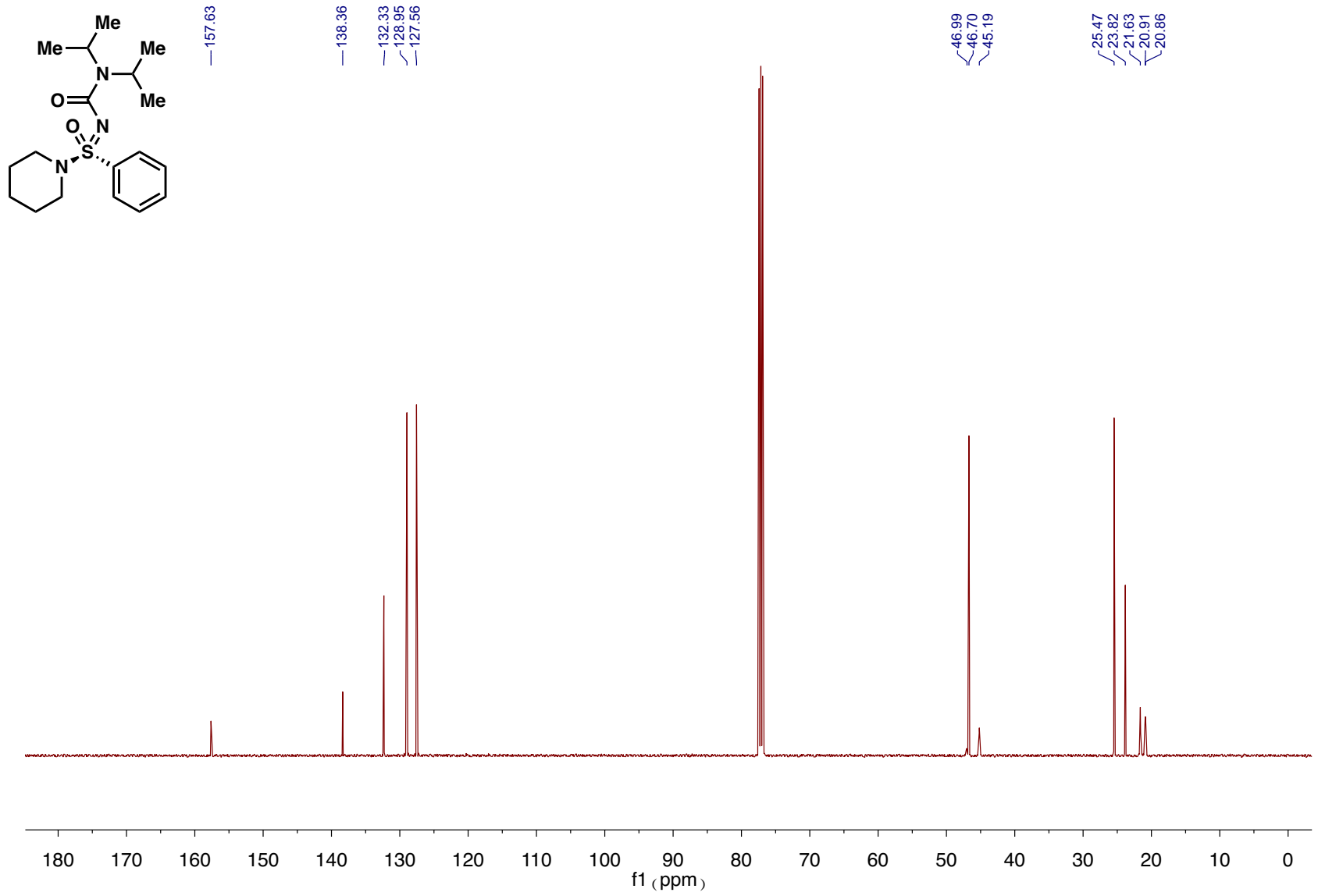
^{19}F NMR of compound 8r:



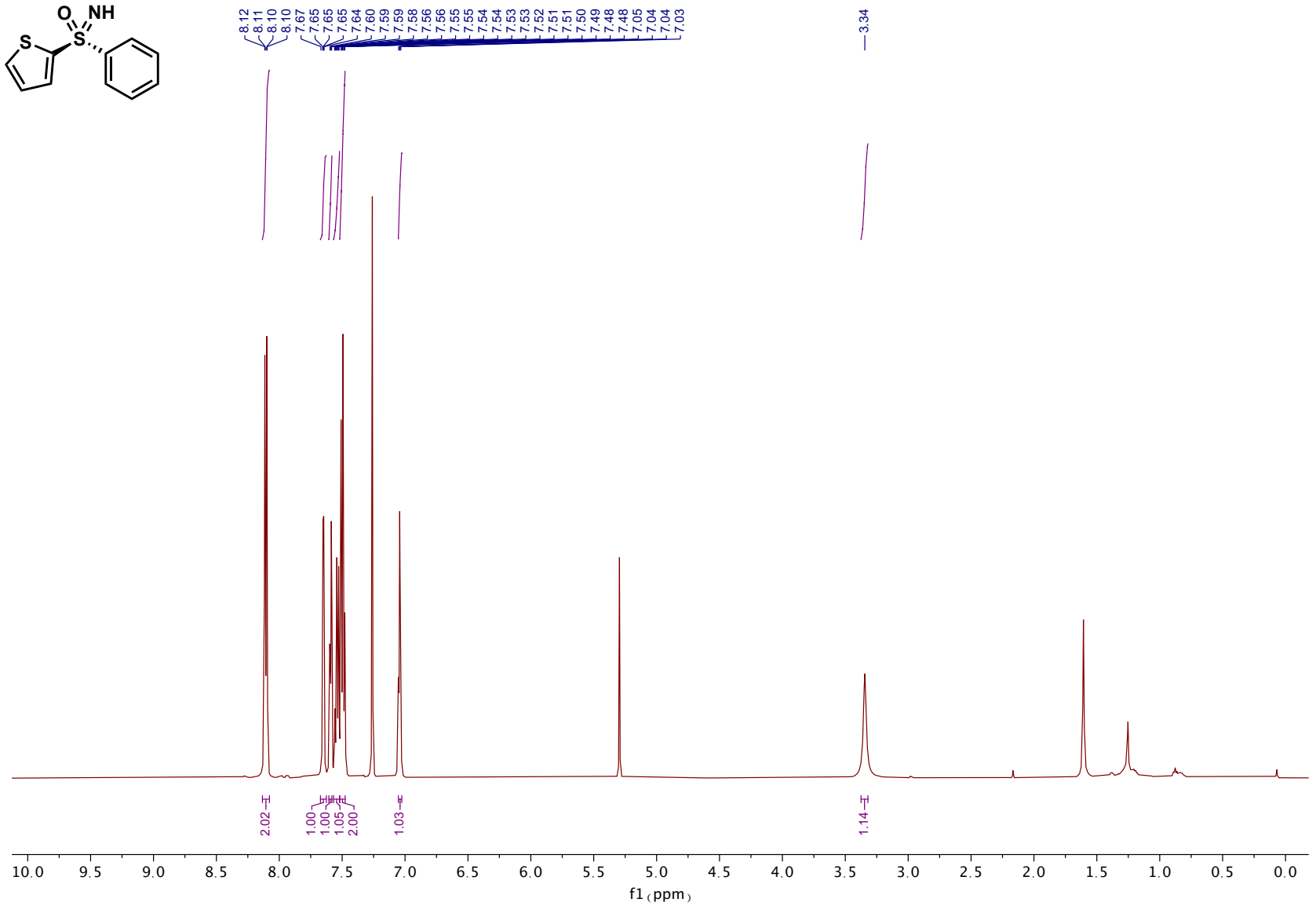
^{1}H NMR of compound 8s:



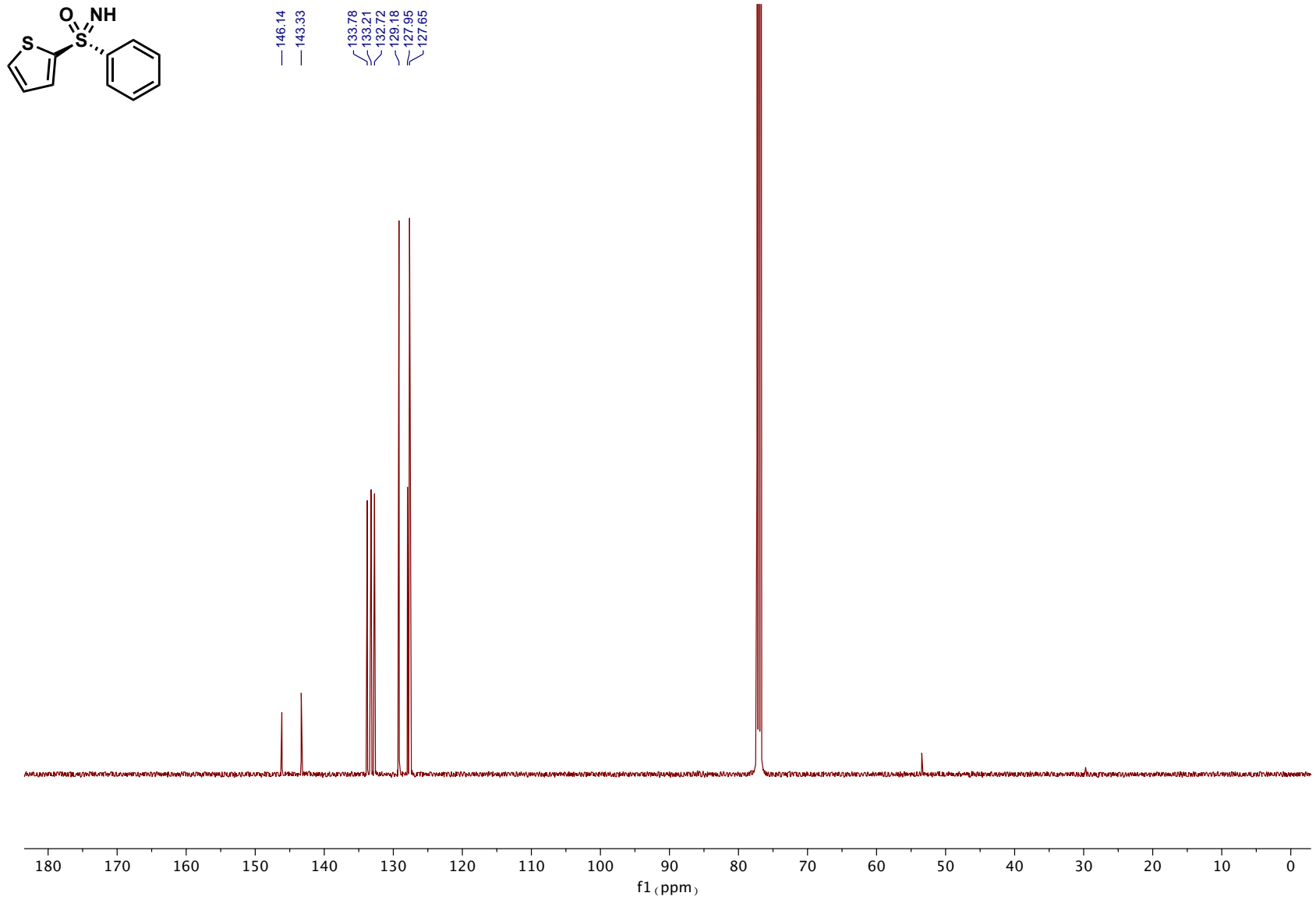
^{13}C NMR of compound 8s:



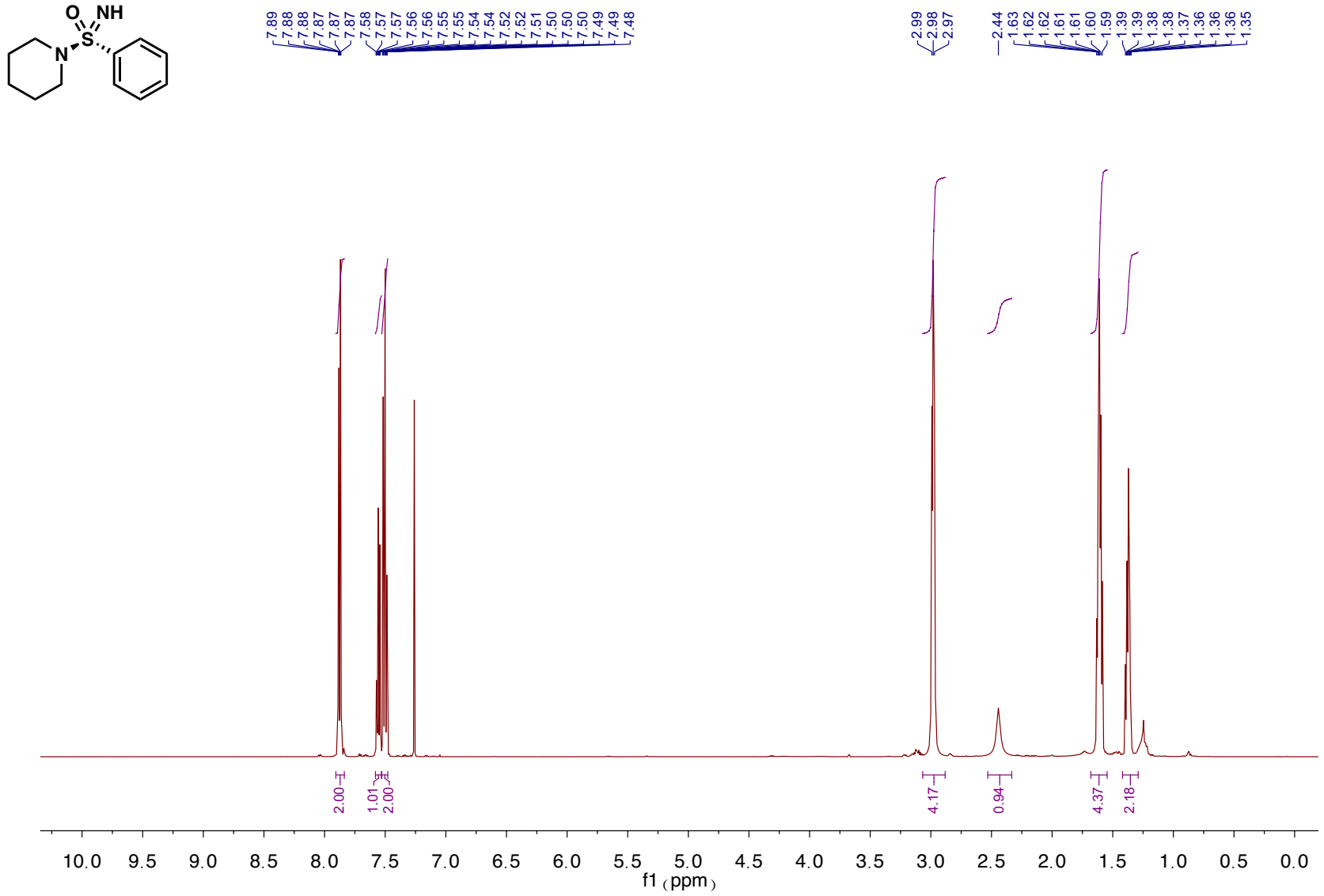
^{1}H NMR of compound 9a:



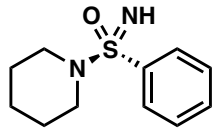
^{13}C NMR of compound 9a:



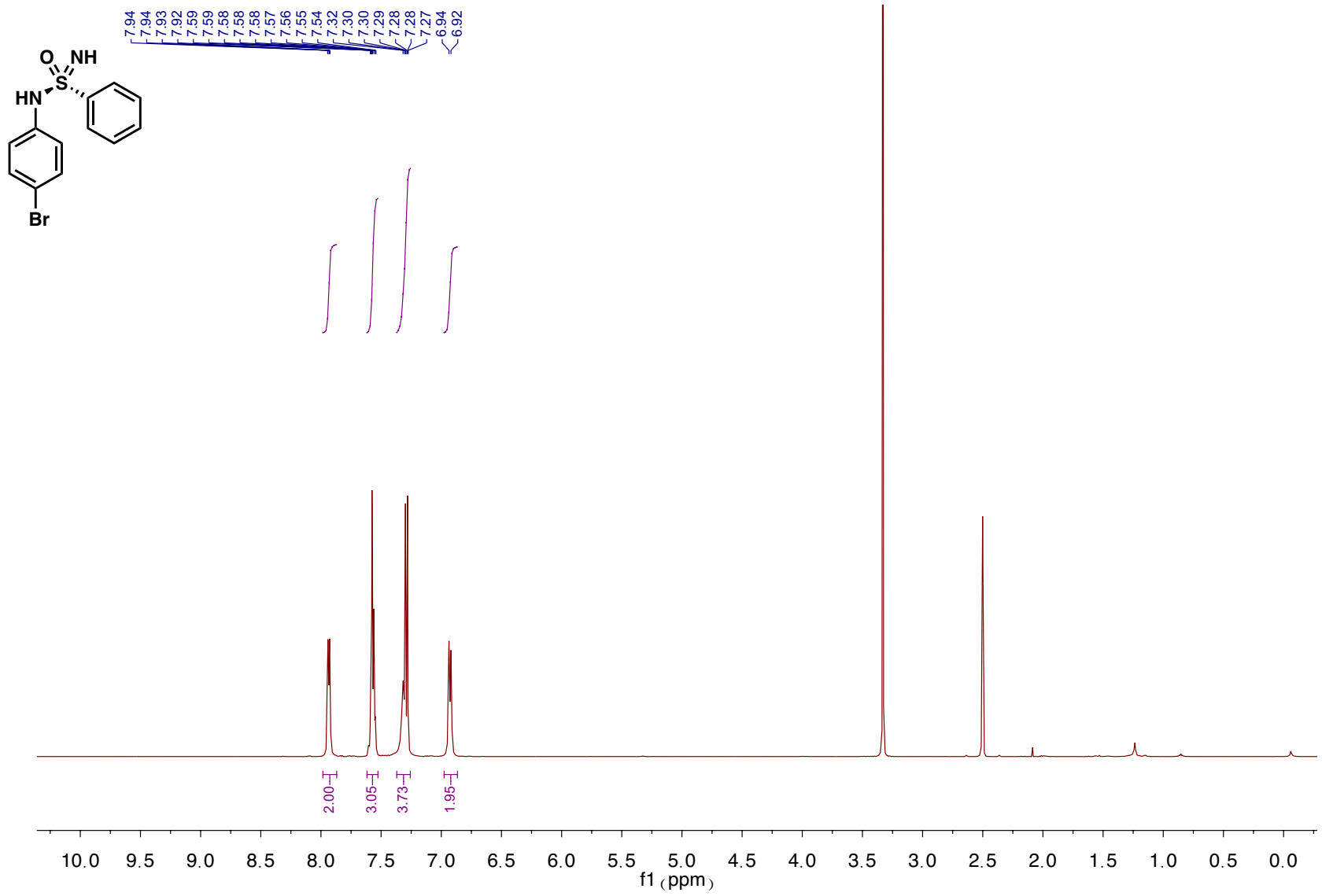
^{1}H NMR of compound 9b:



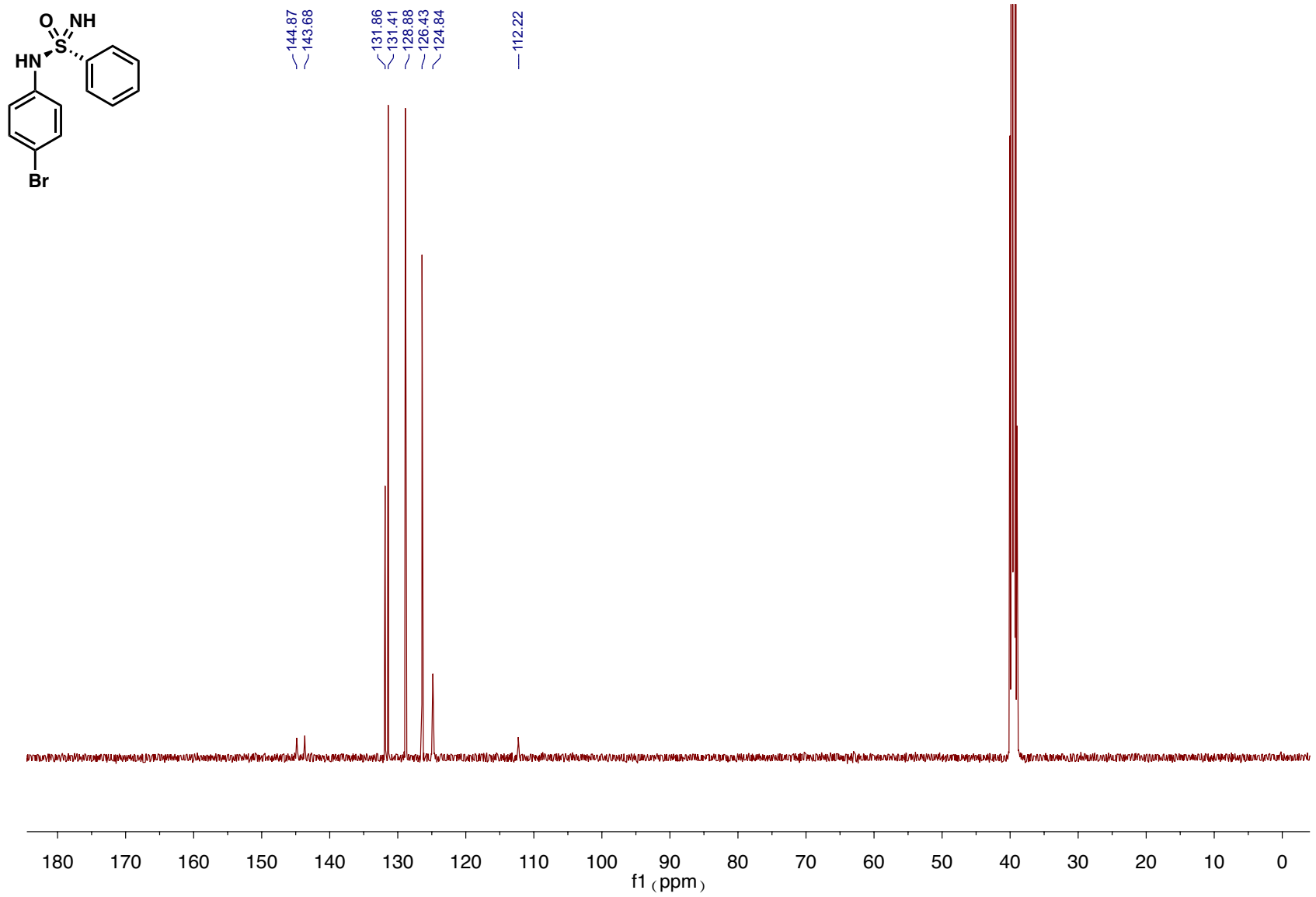
^{13}C NMR of compound 9b:



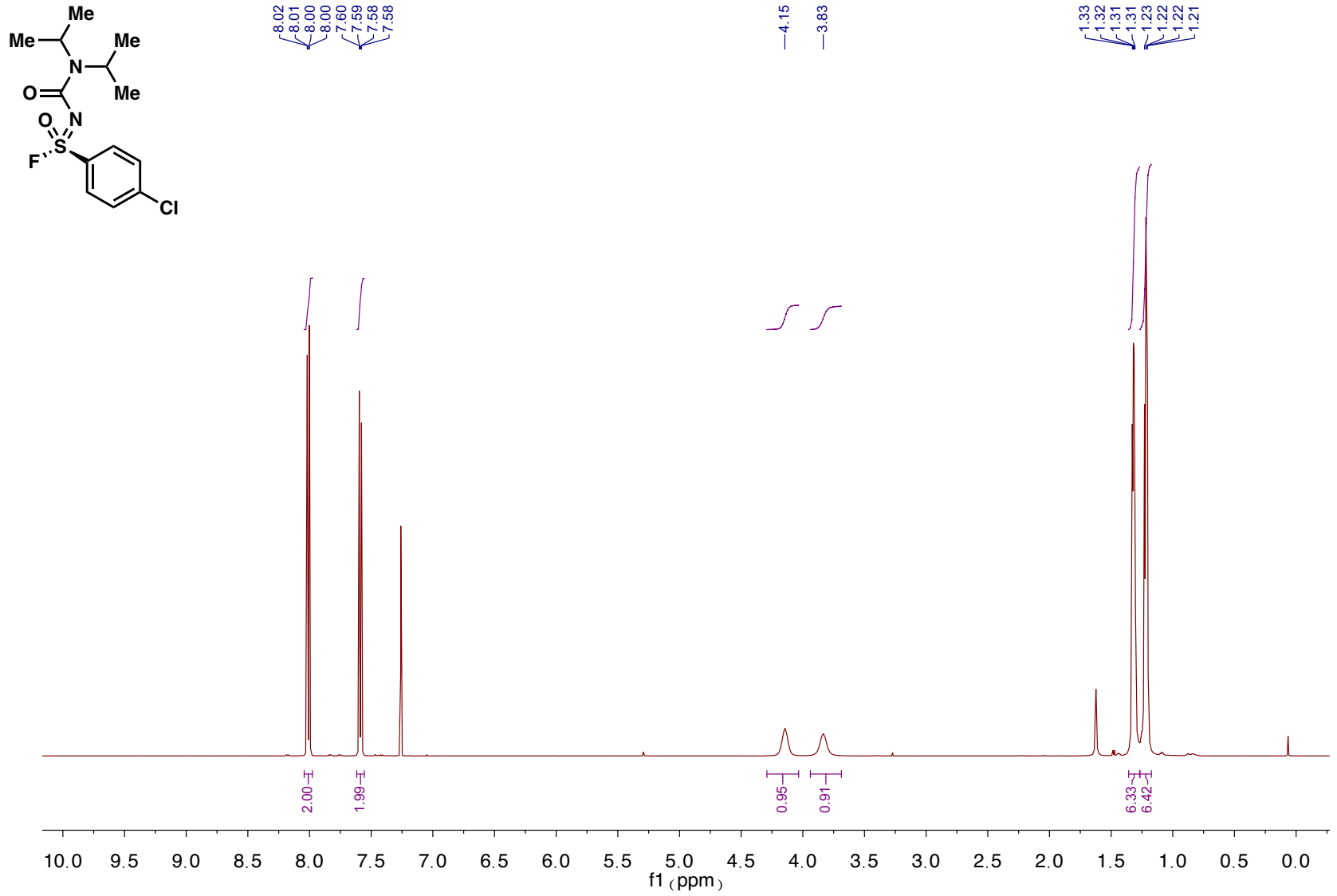
^{1}H NMR of compound 10b:



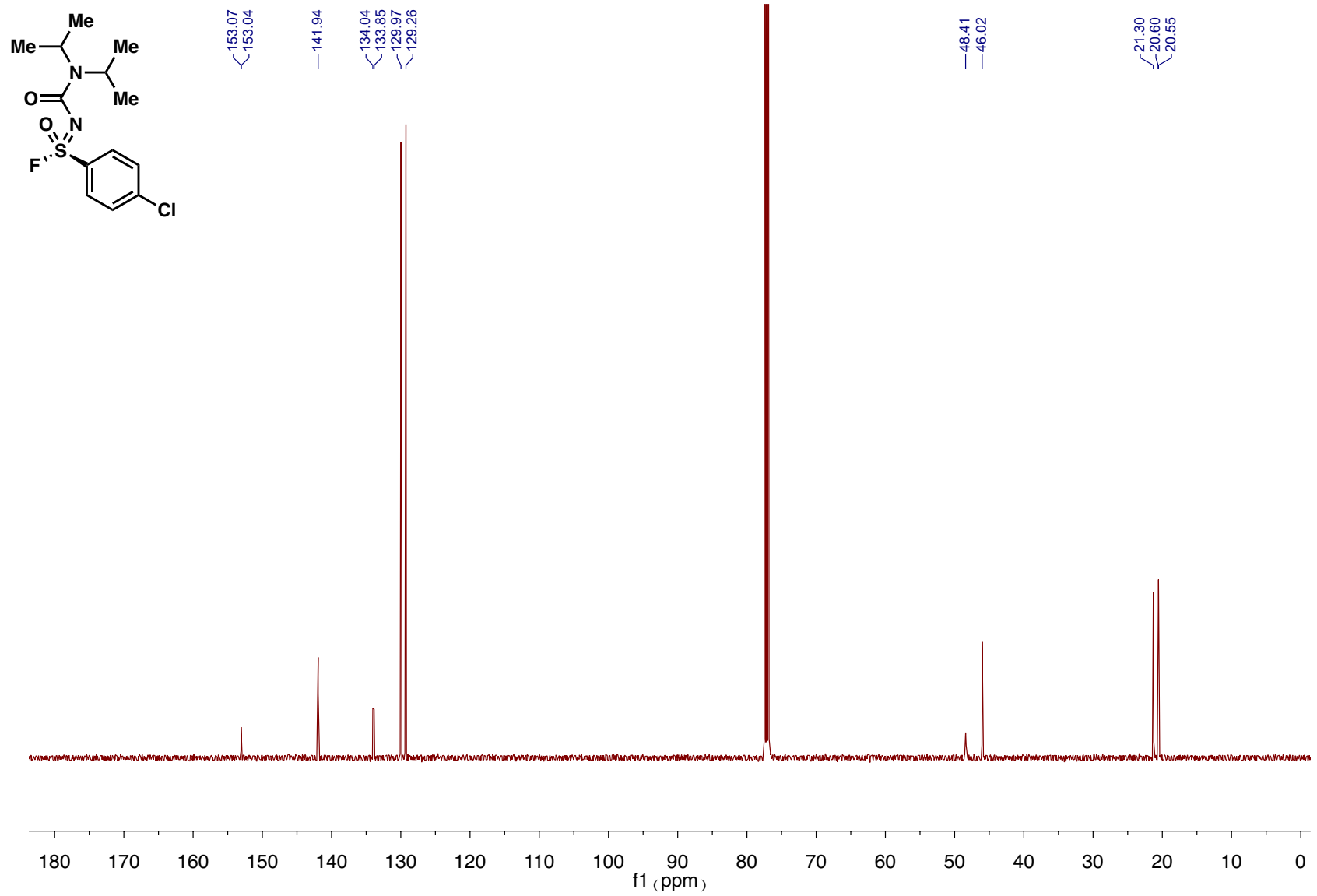
^{13}C NMR of compound 10b:



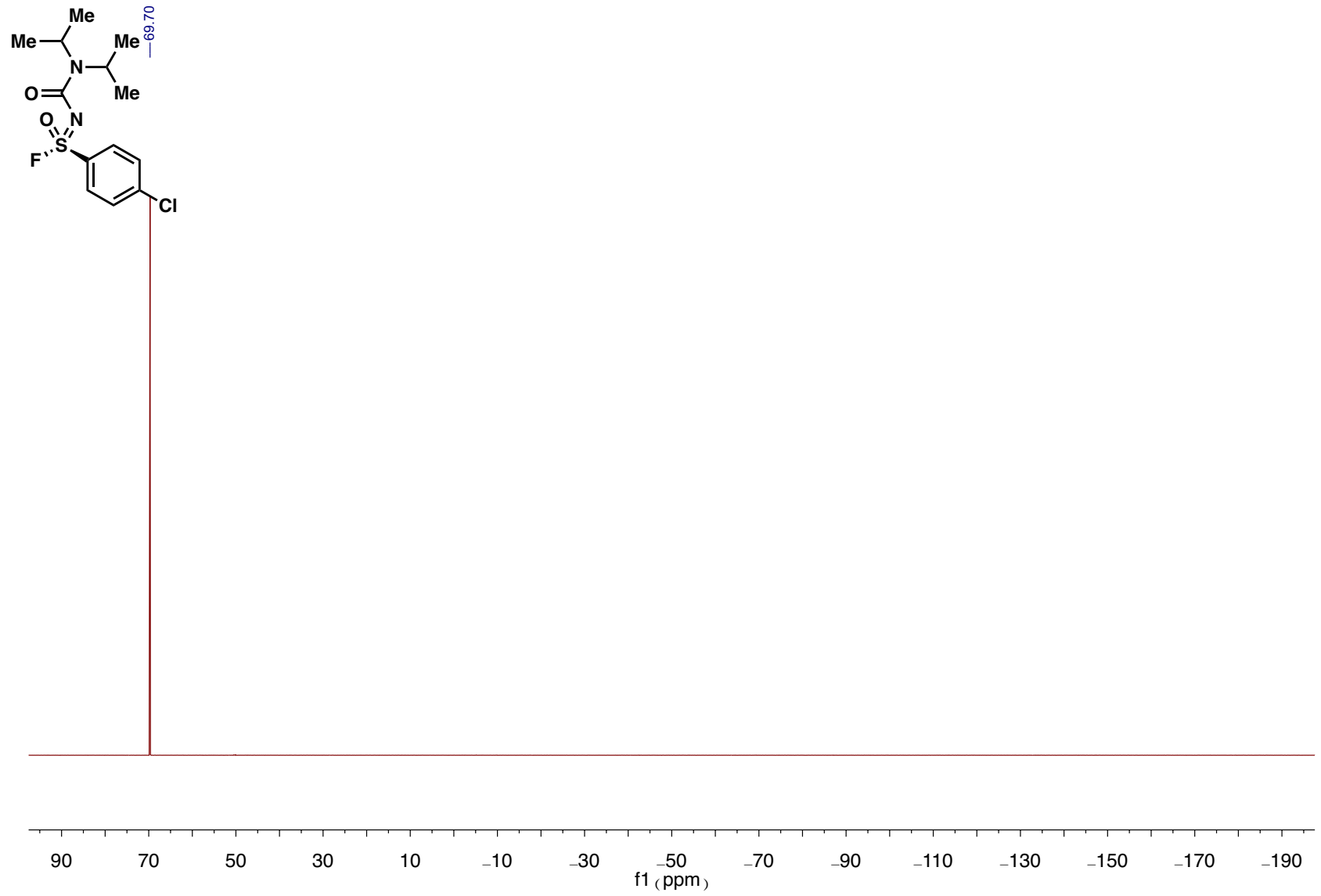
^{1}H NMR of compound 12:



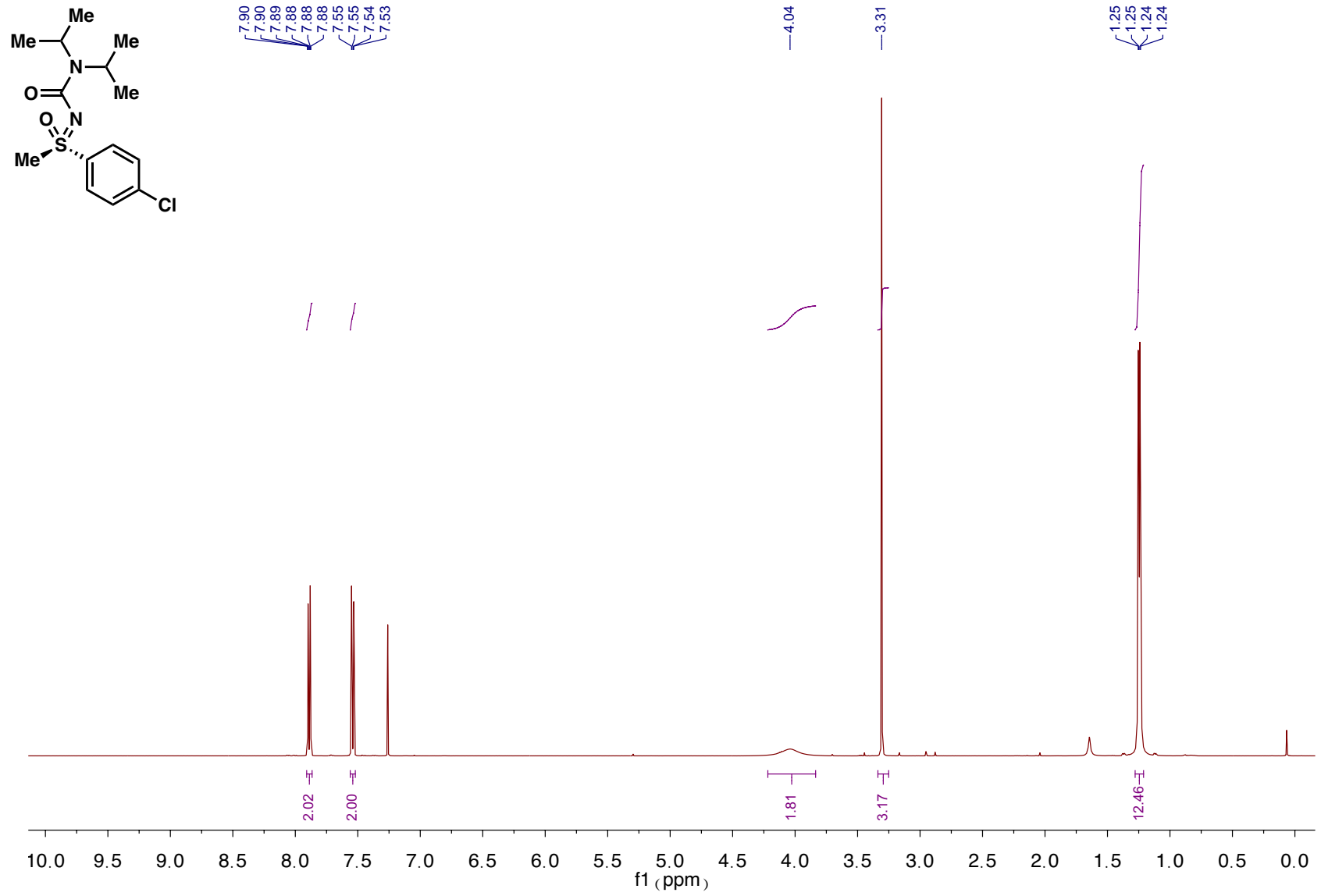
^{13}C NMR of compound 12:



^{19}F NMR of compound 12:



^{1}H NMR of compound 13:



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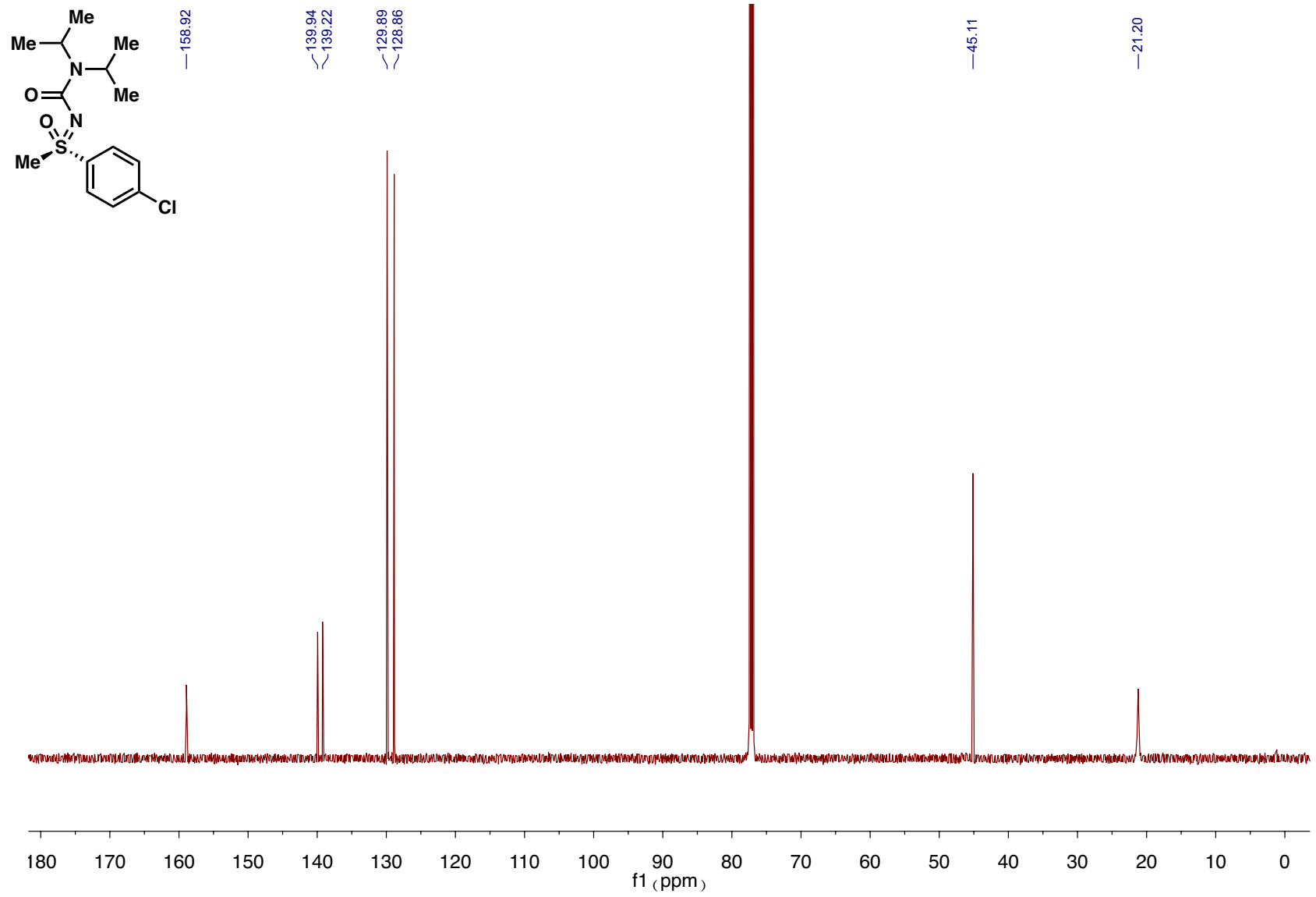
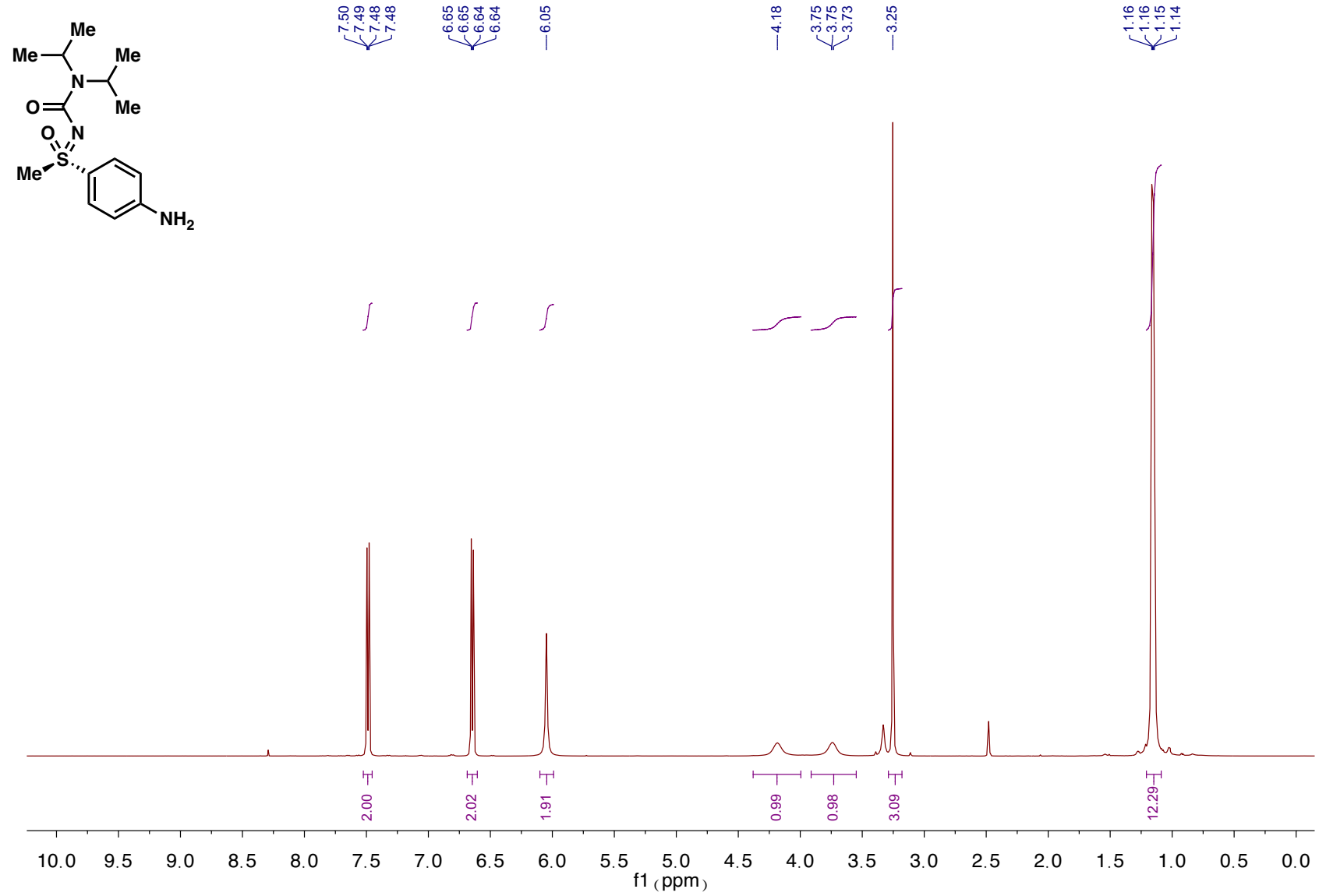


^{1}H NMR of compound 16:



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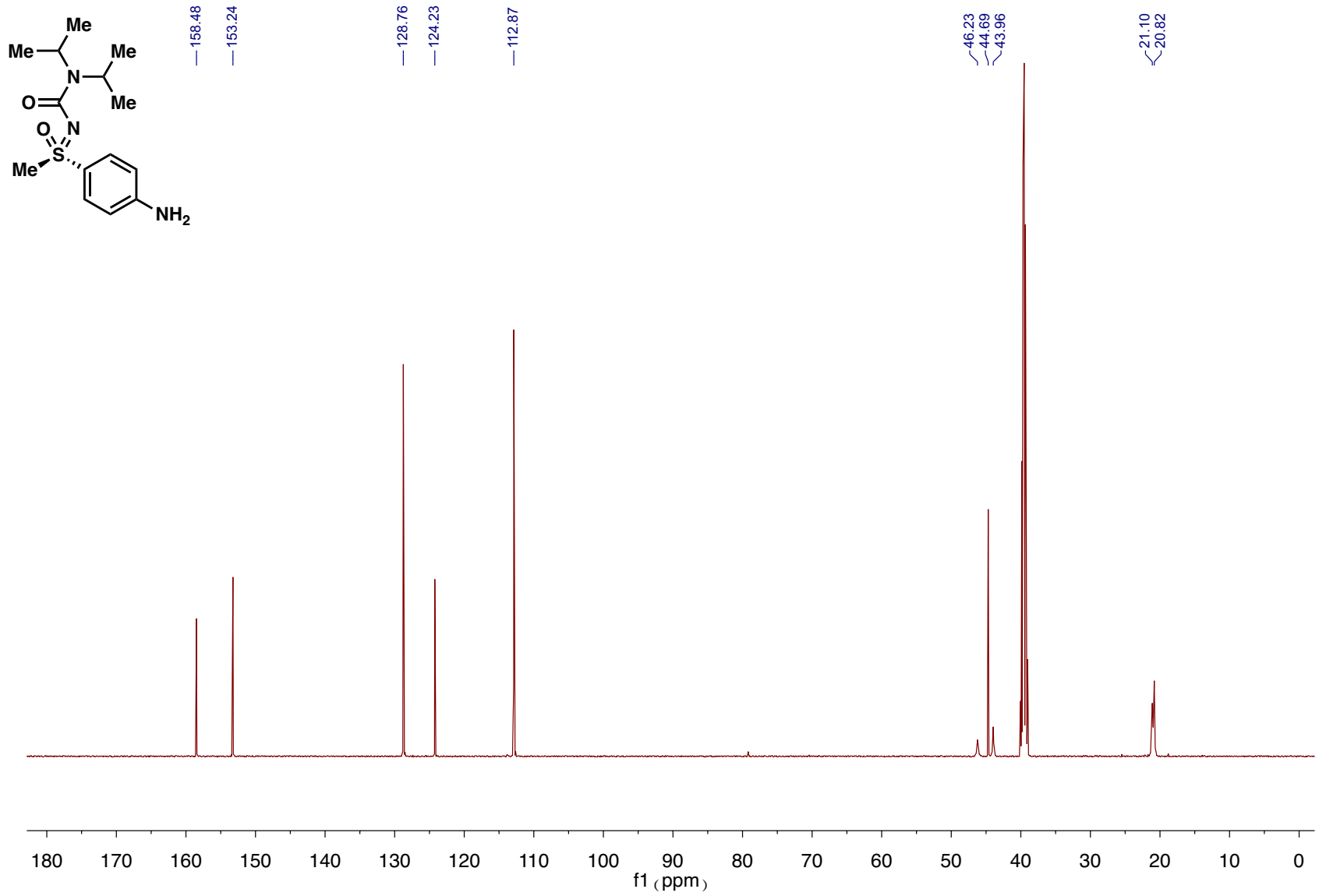
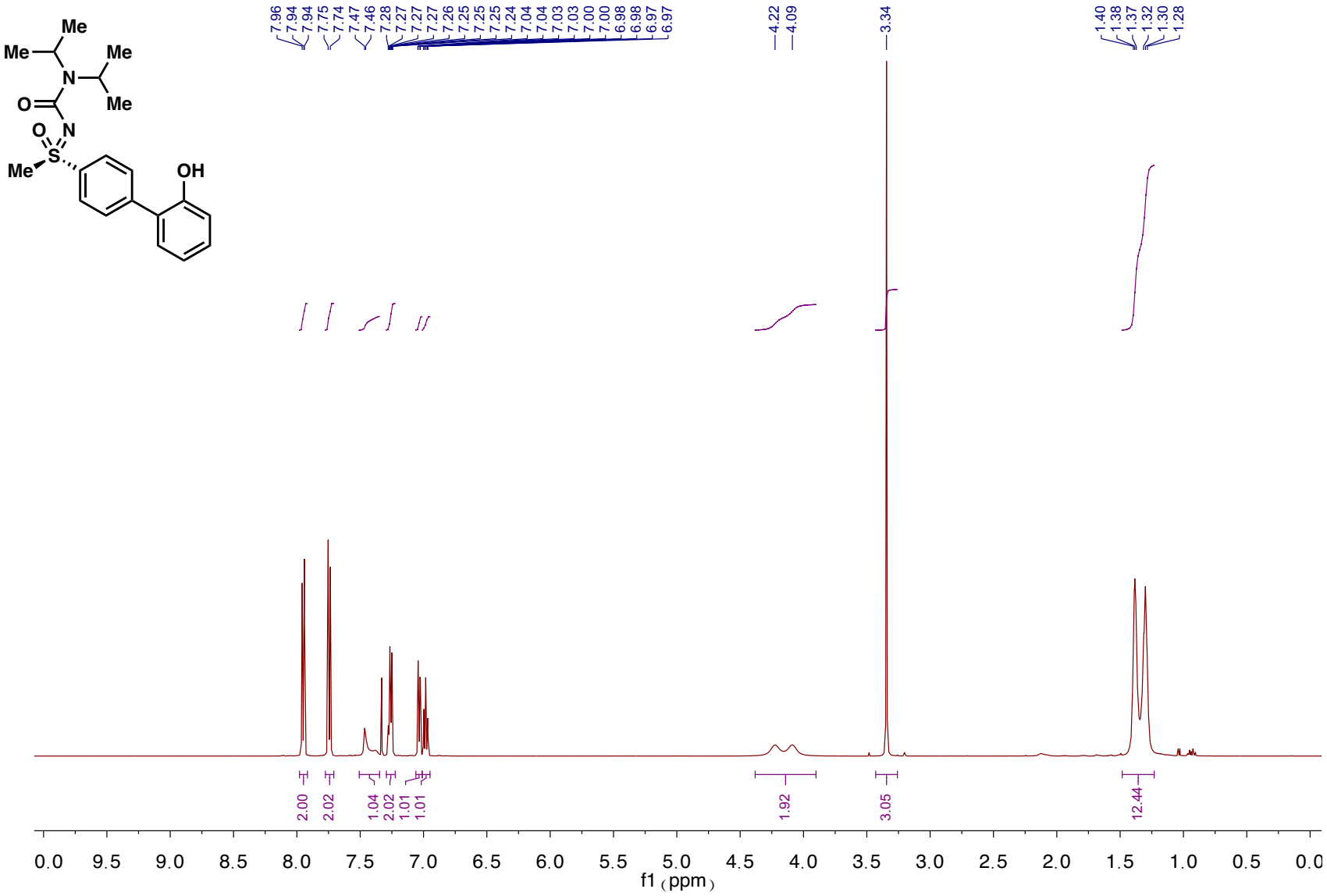
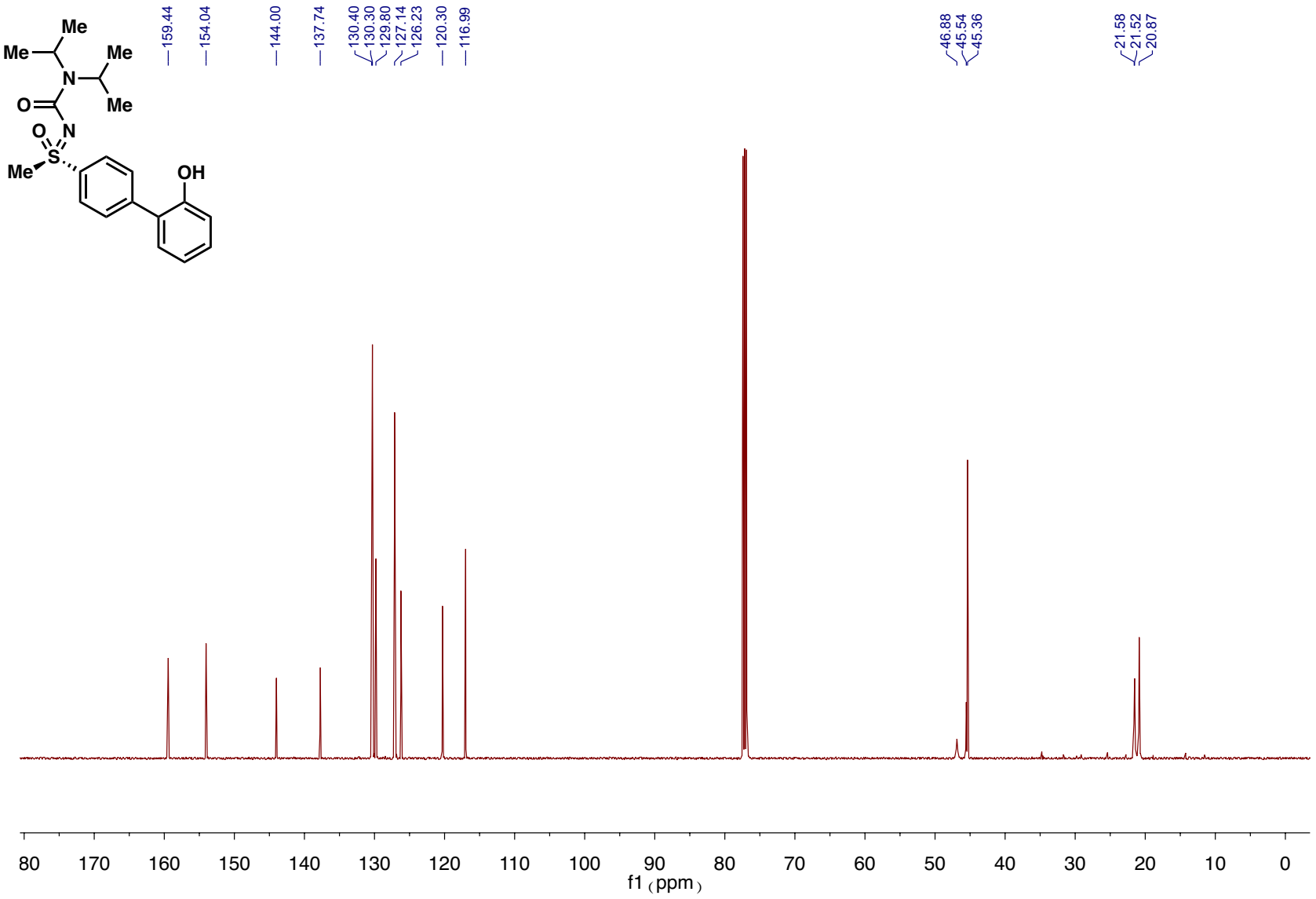


^{1}H NMR of urea protected 15:



^{13}C NMR of urea protected 15:



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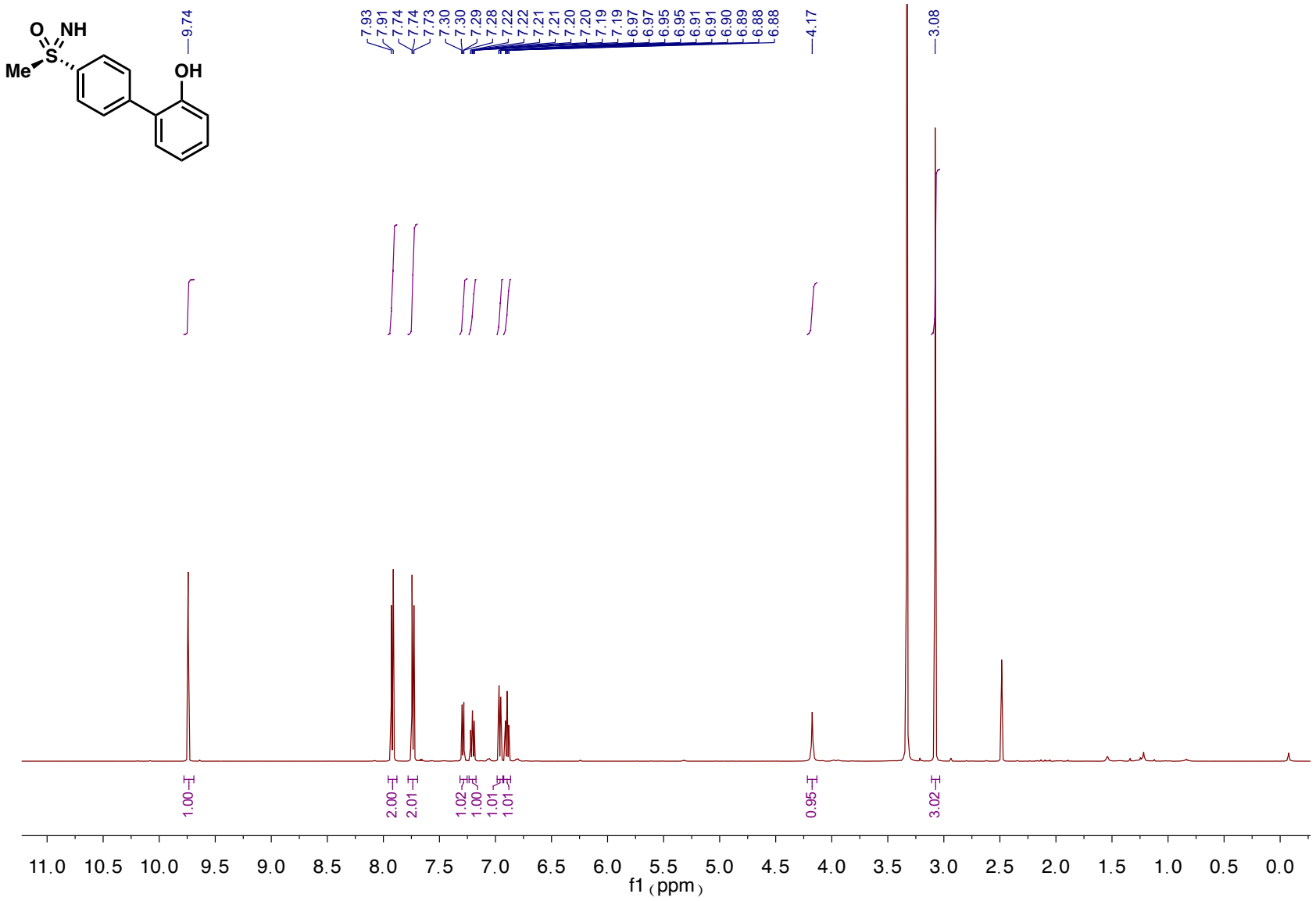

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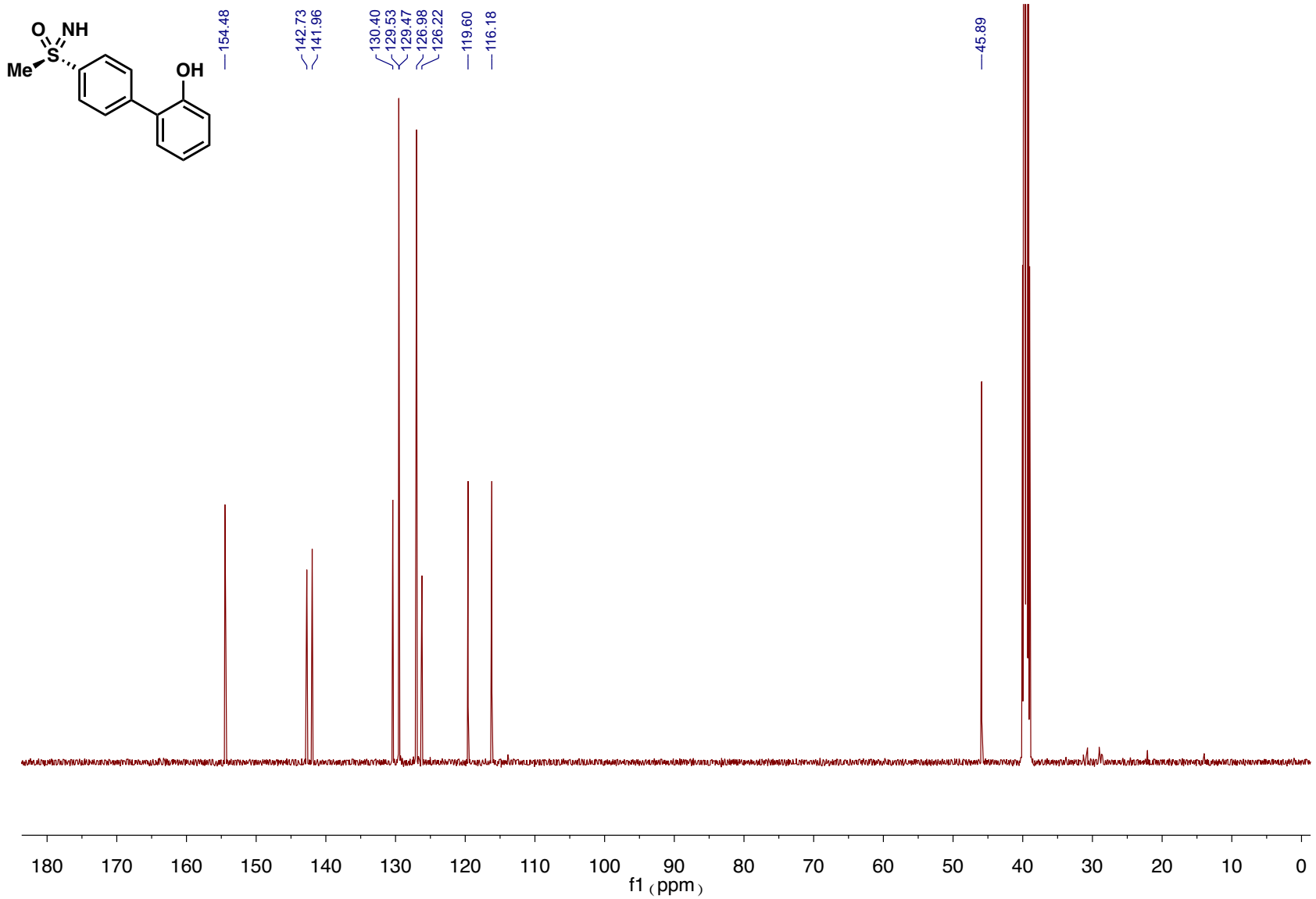
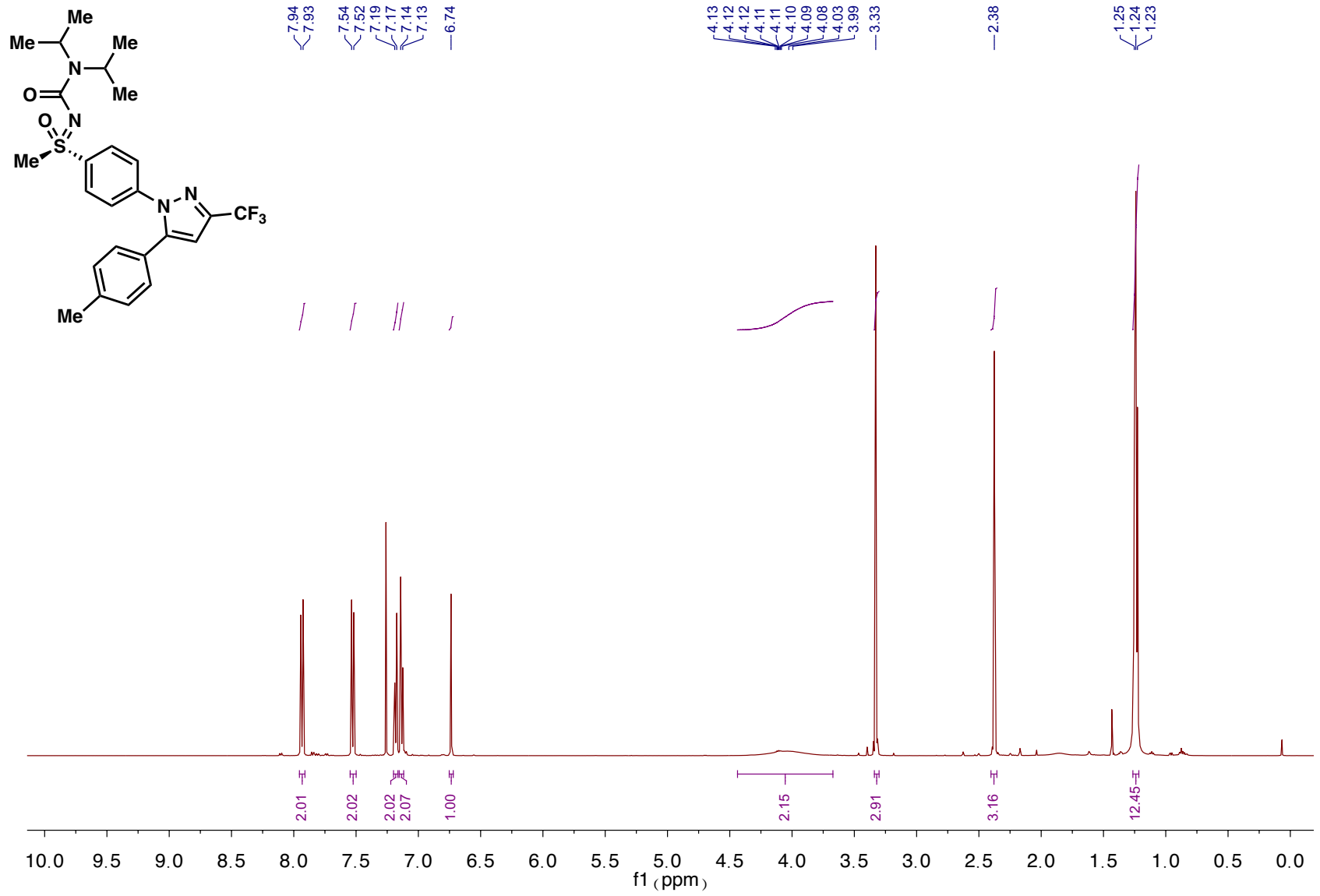


^{1}H NMR of compound 19:



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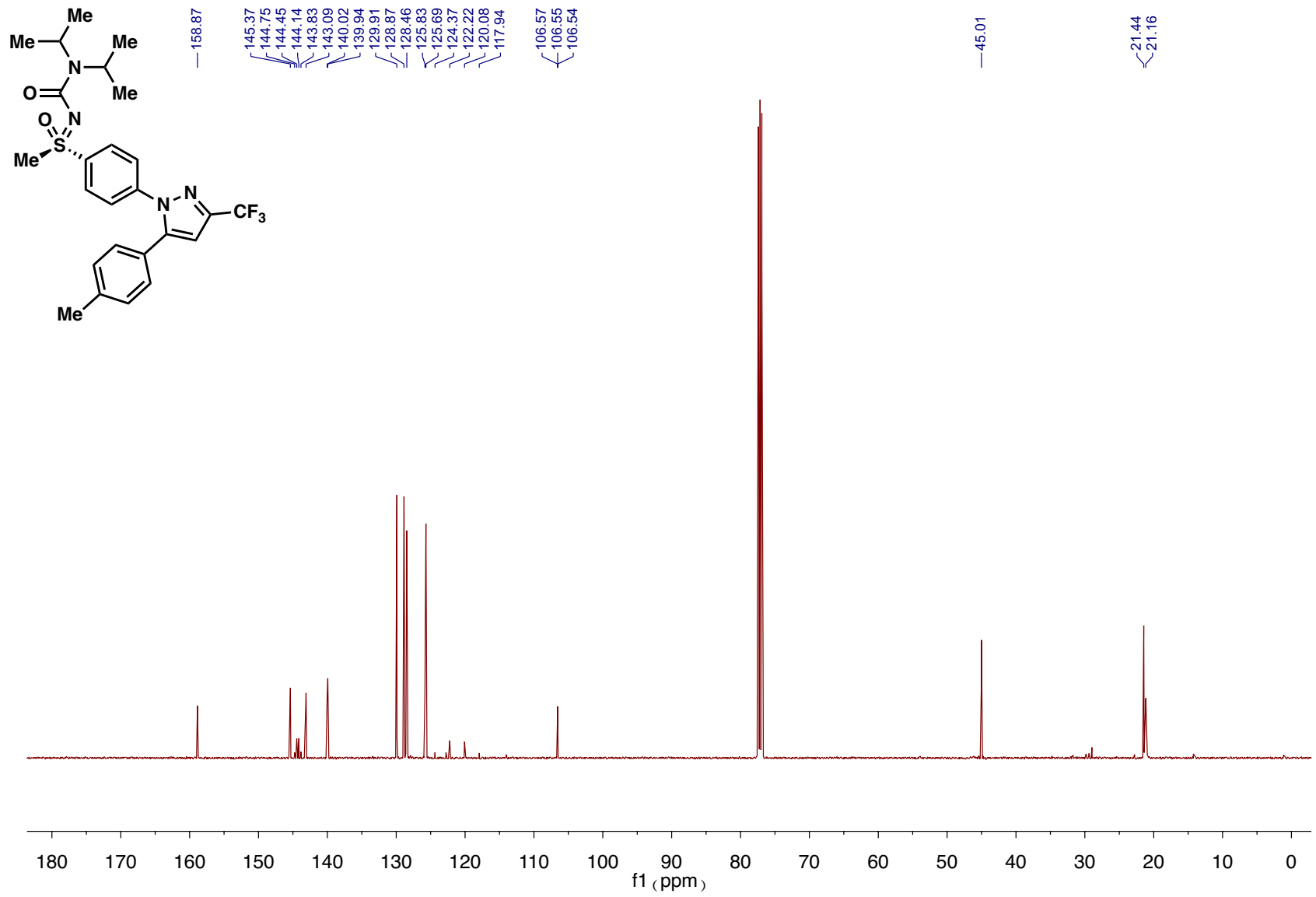
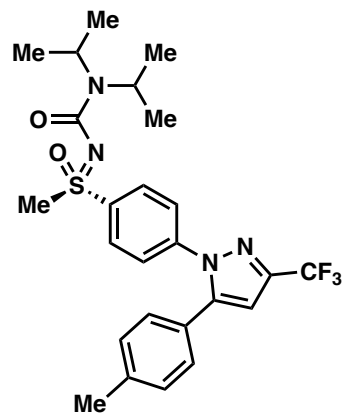
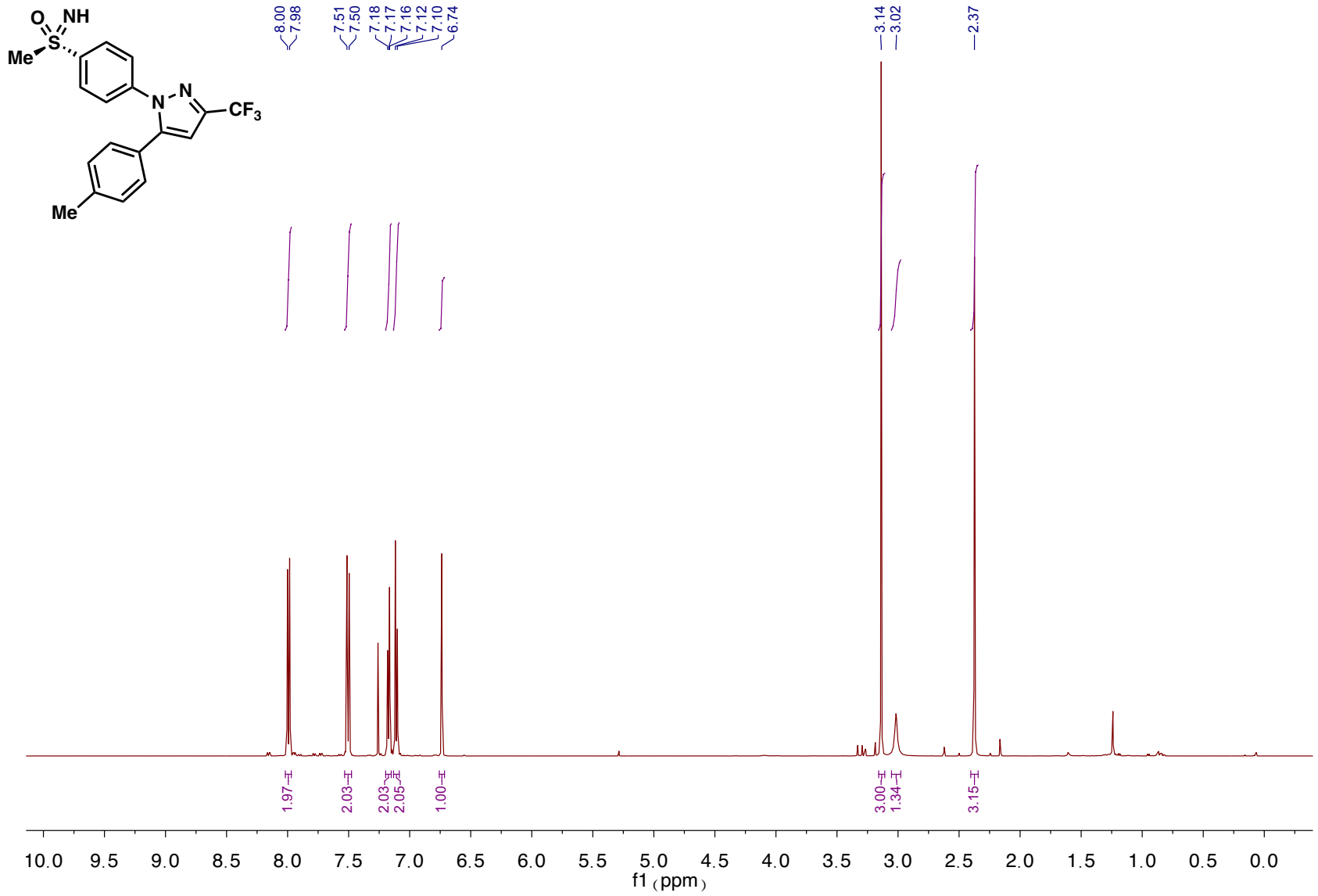


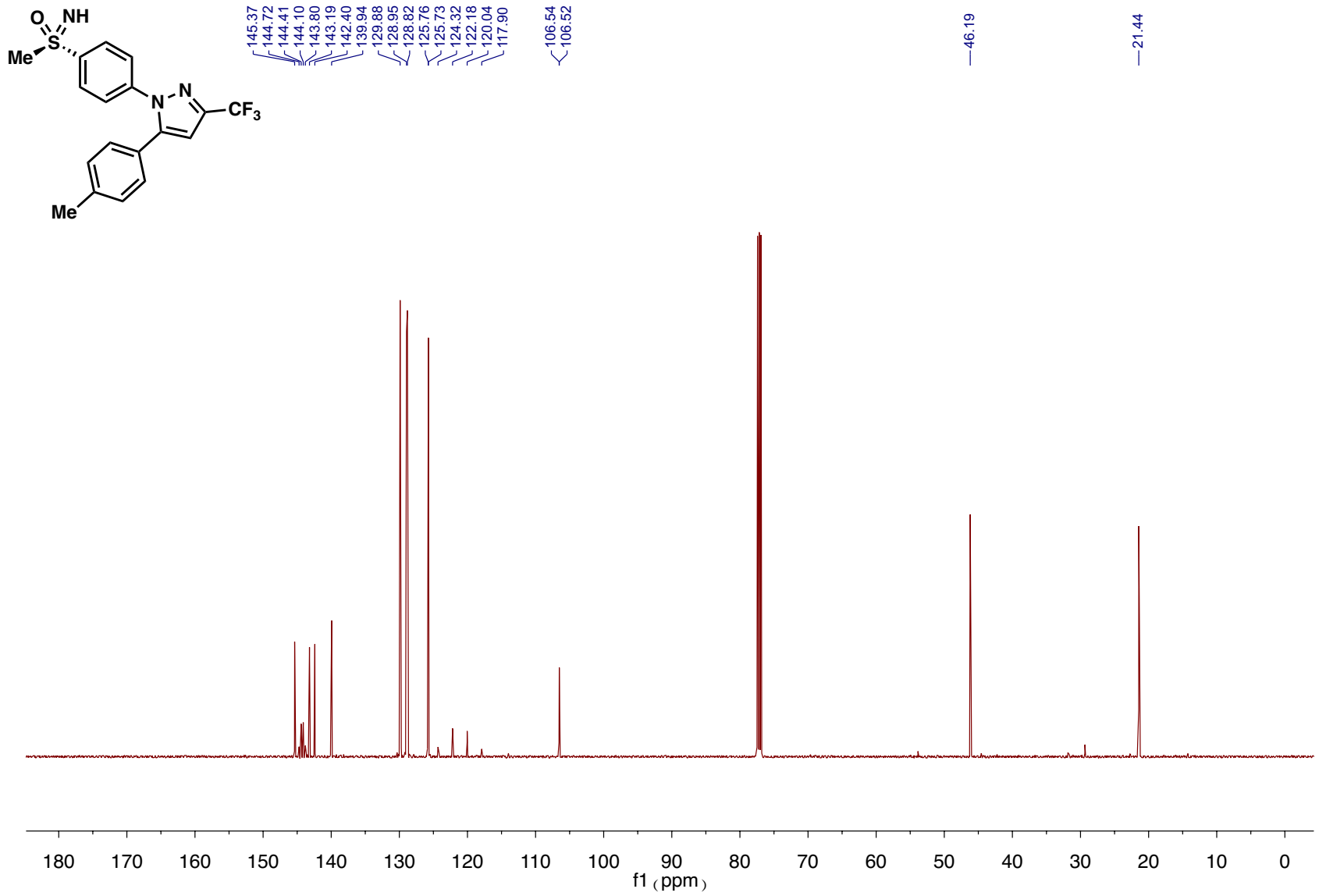
^{19}F NMR of compound 19:



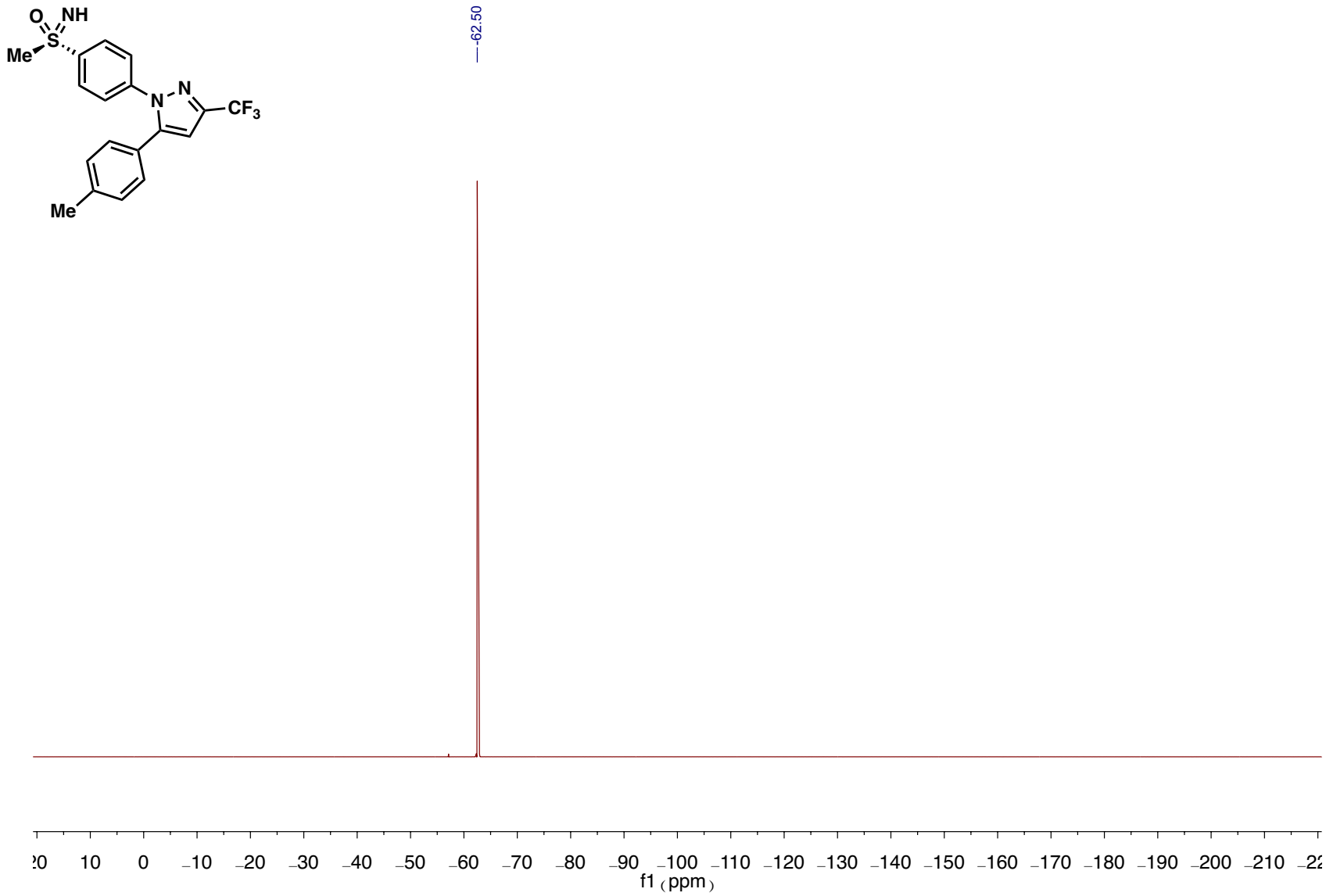
^{1}H NMR of compound 20:



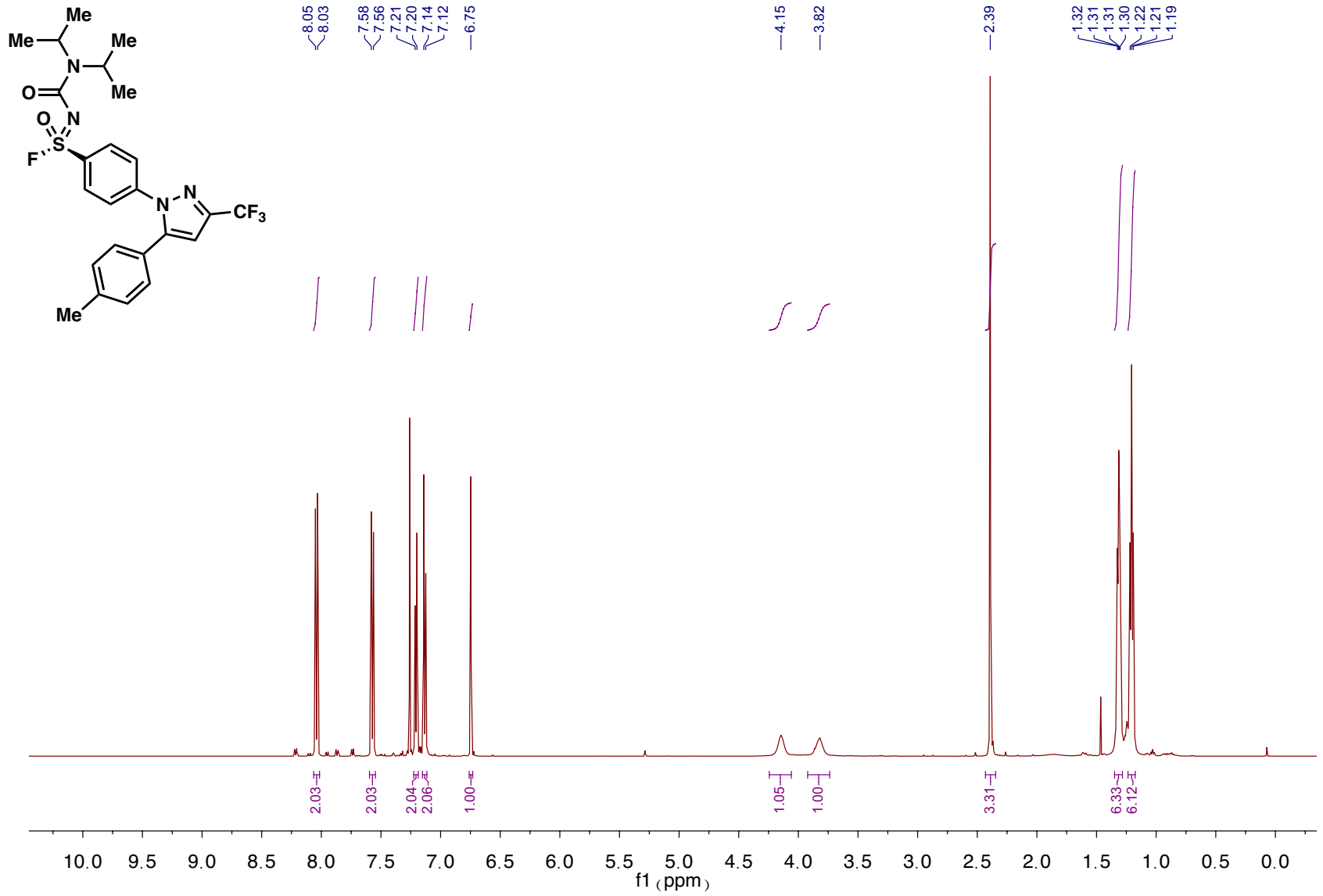
^{13}C NMR of compound 20:



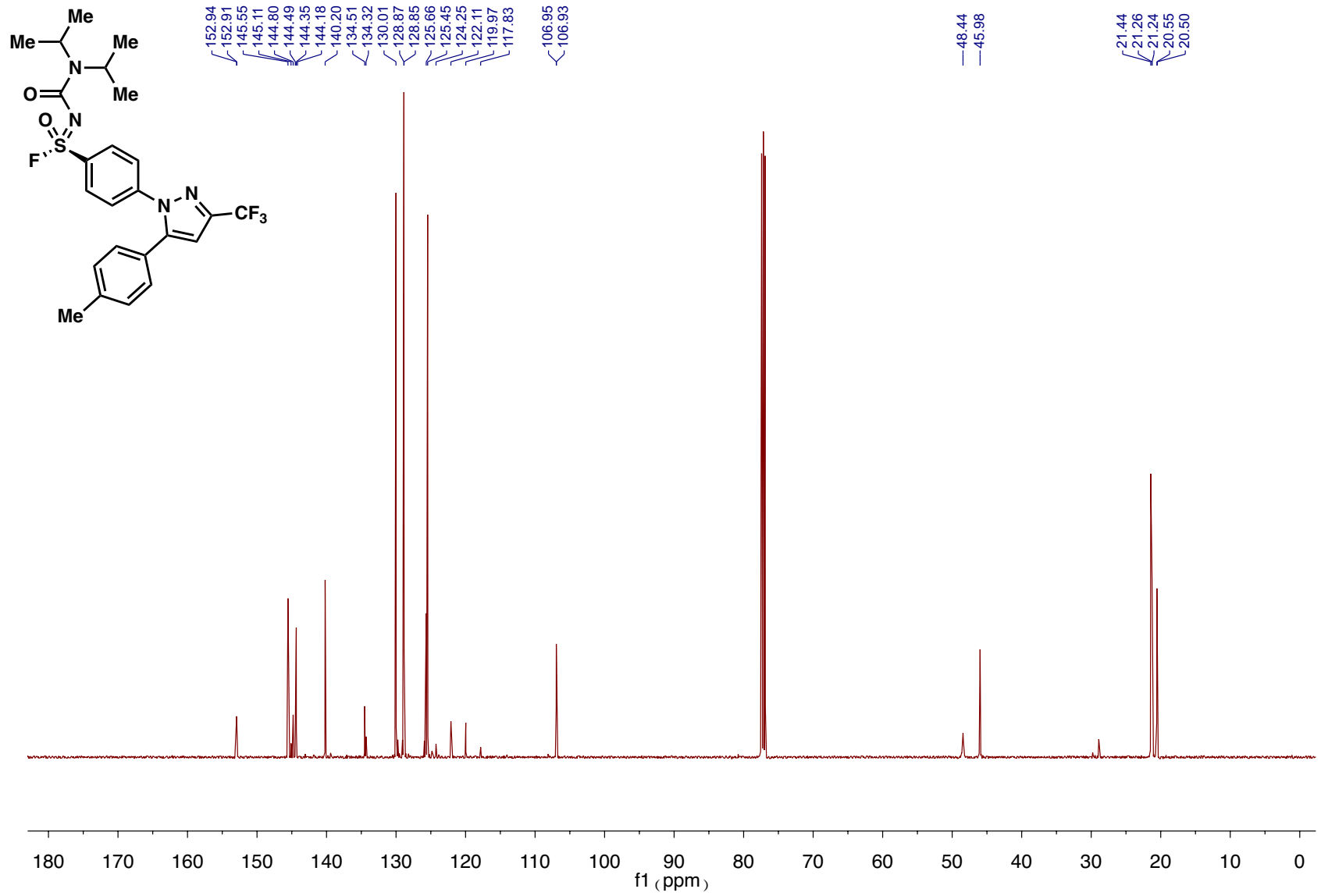
^{19}F NMR of compound 20:



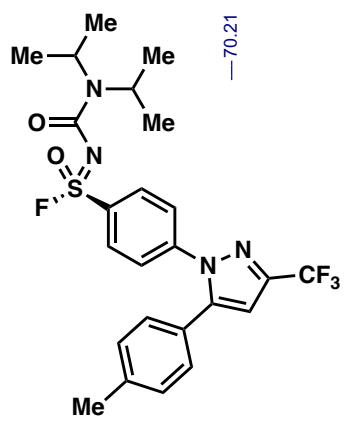
^{1}H NMR of compound 18:



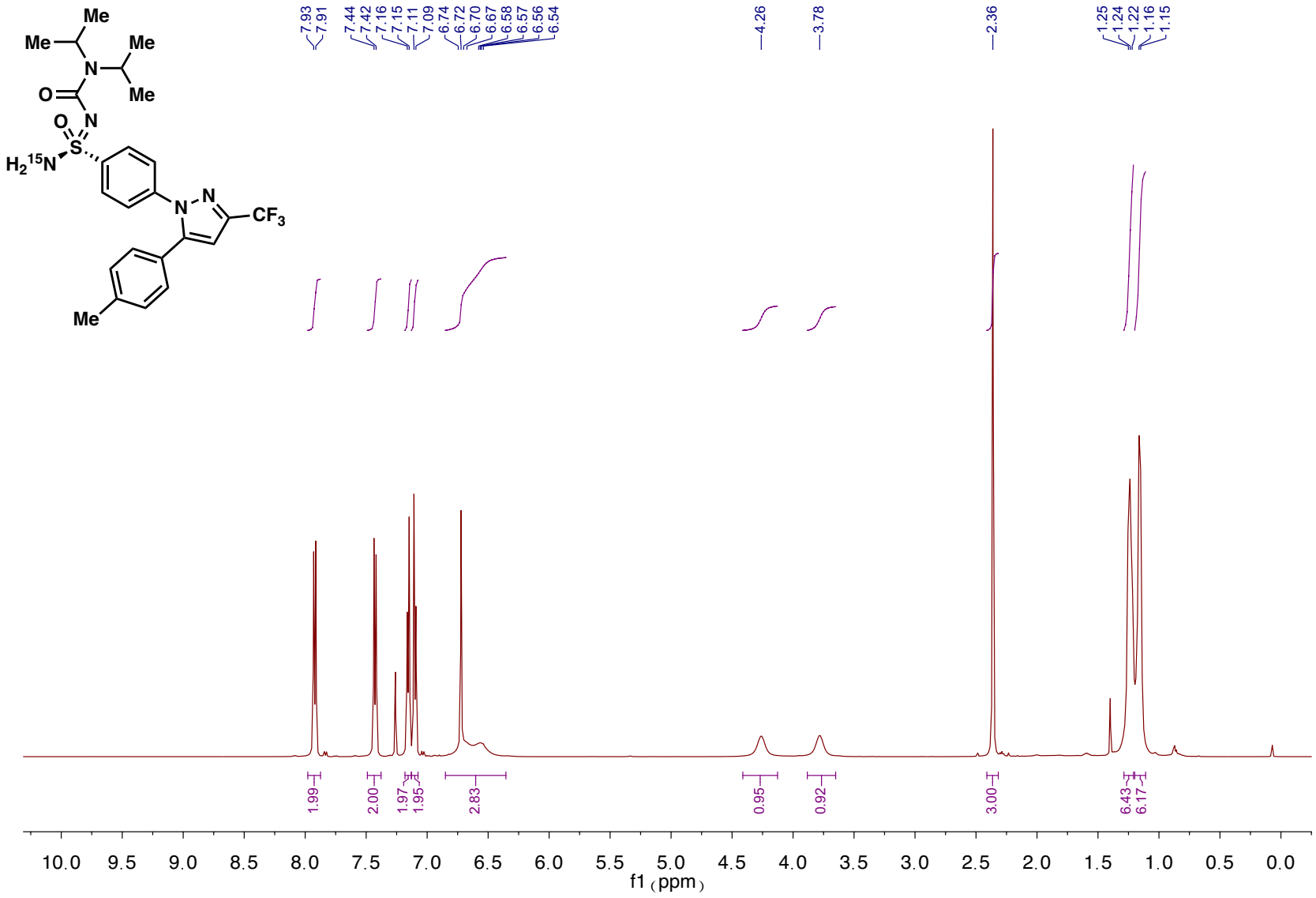
^{13}C NMR of compound 18:



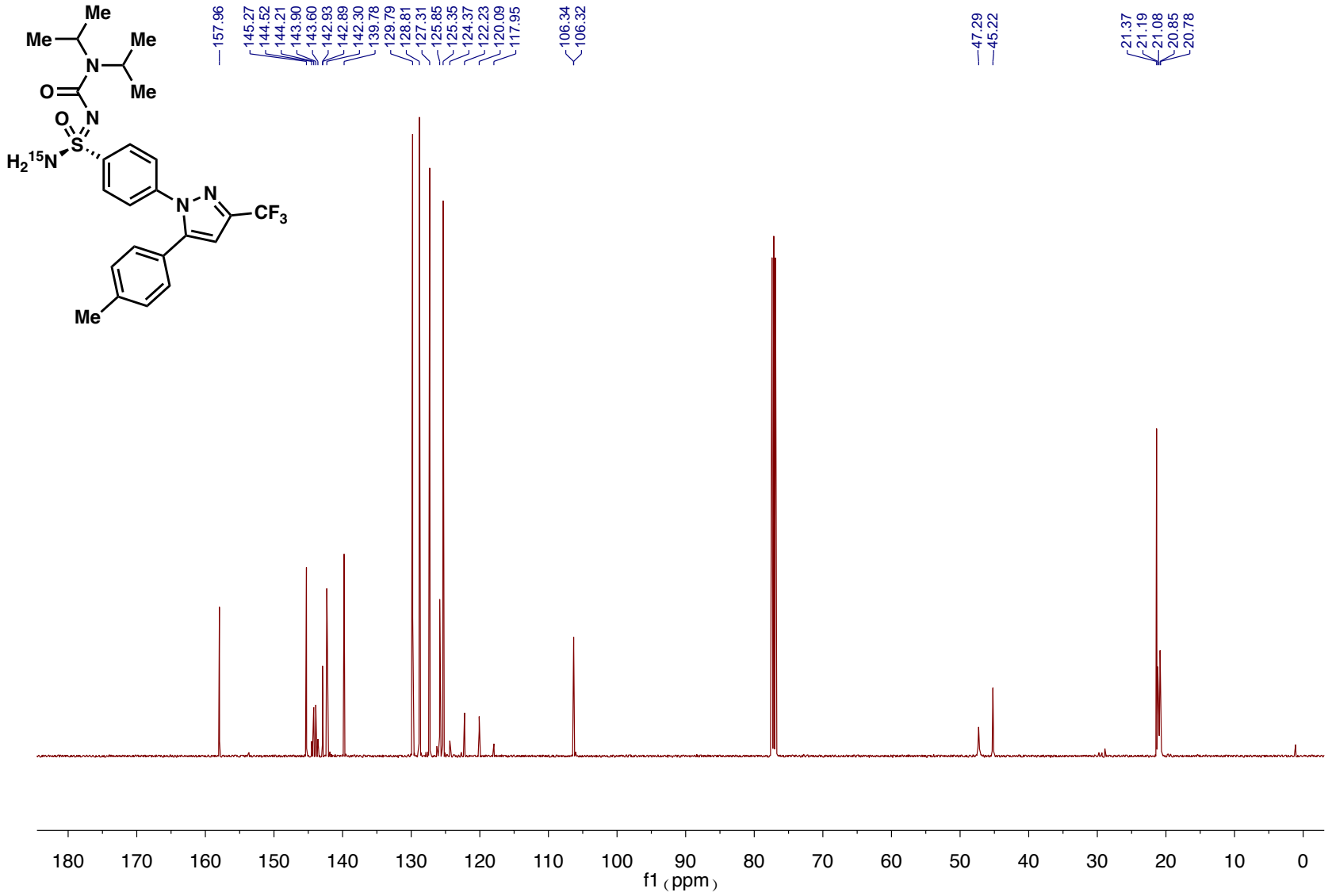
^{19}F NMR of compound 18:



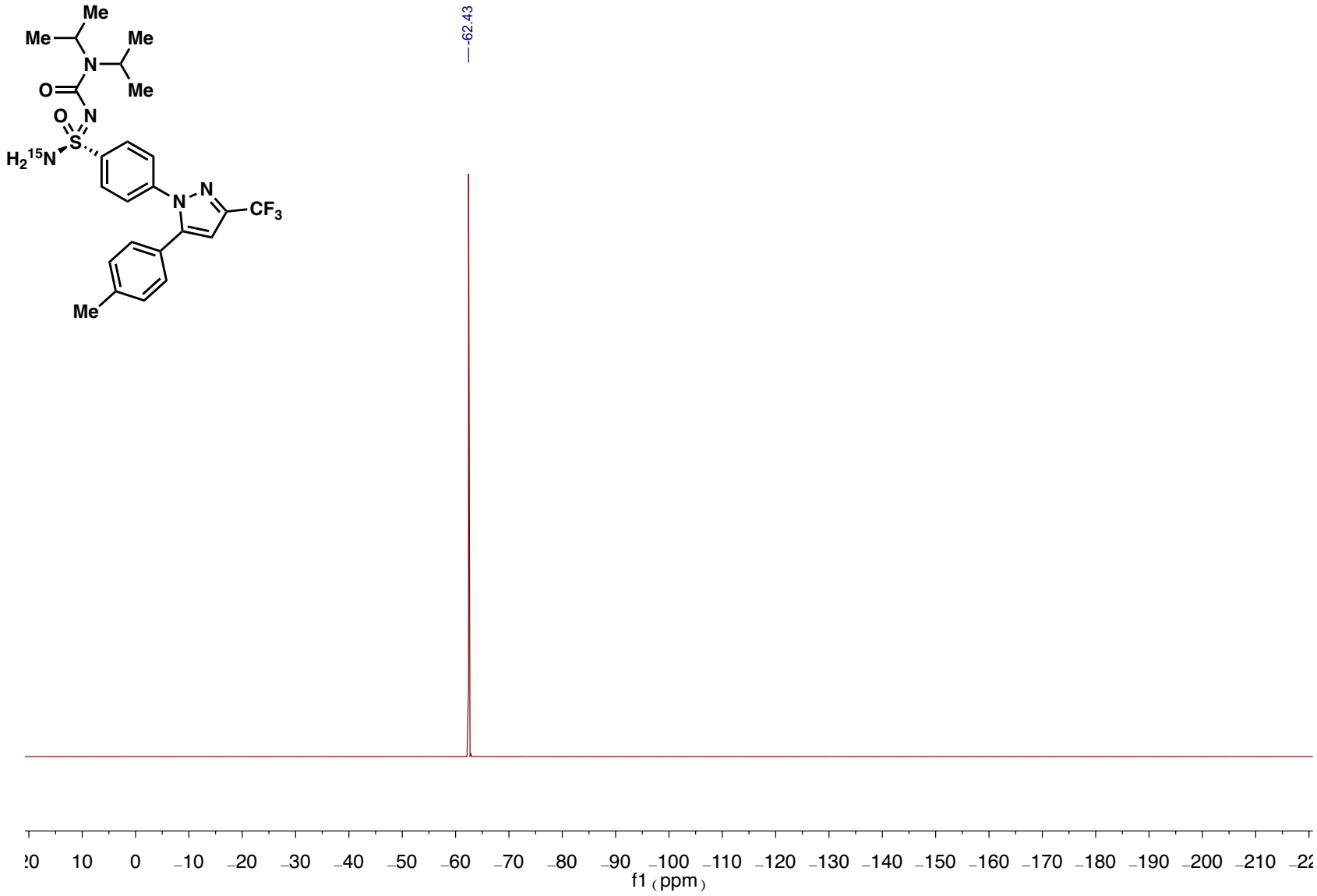
^{1}H NMR of compound 21:



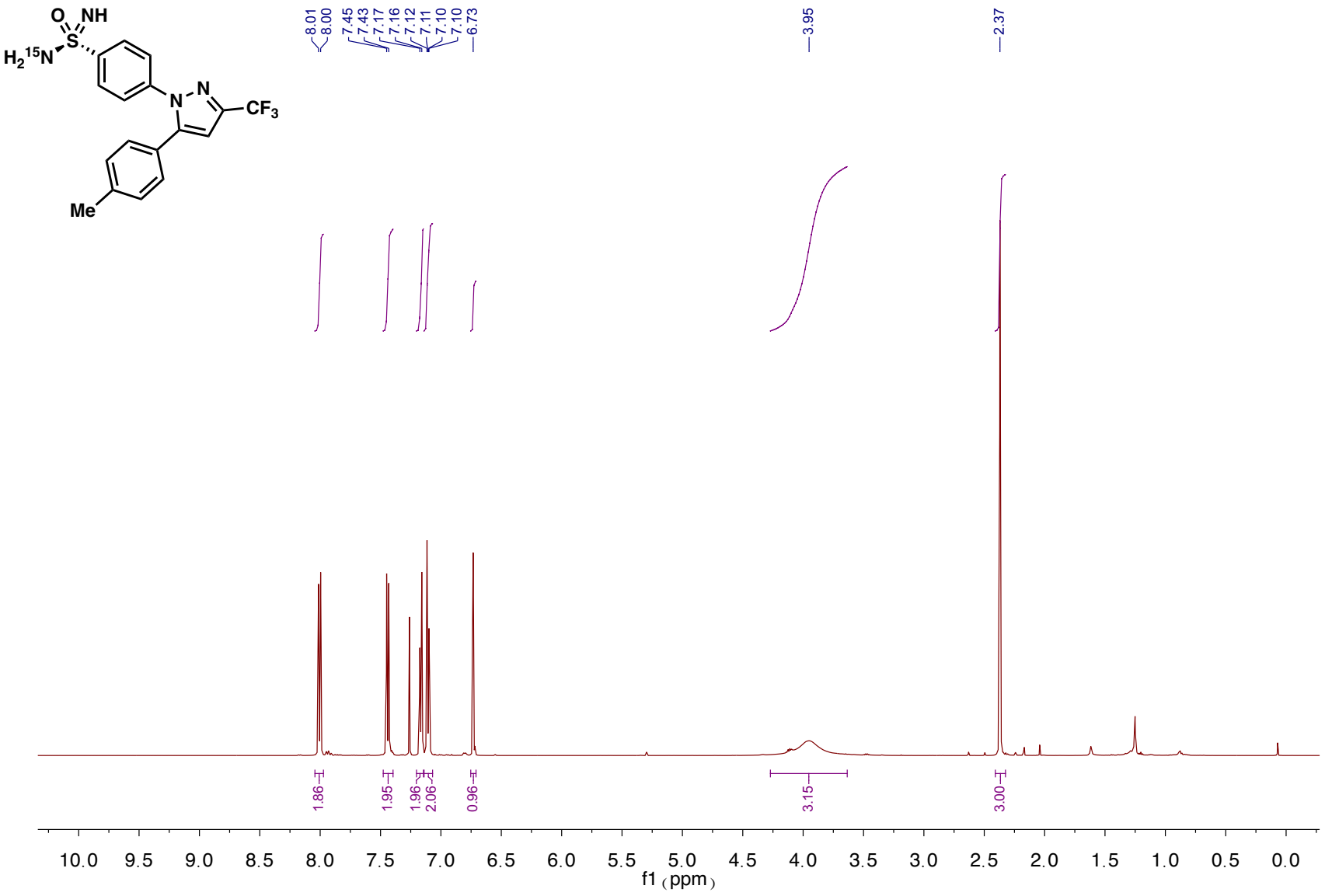
^{13}C NMR of compound 21:



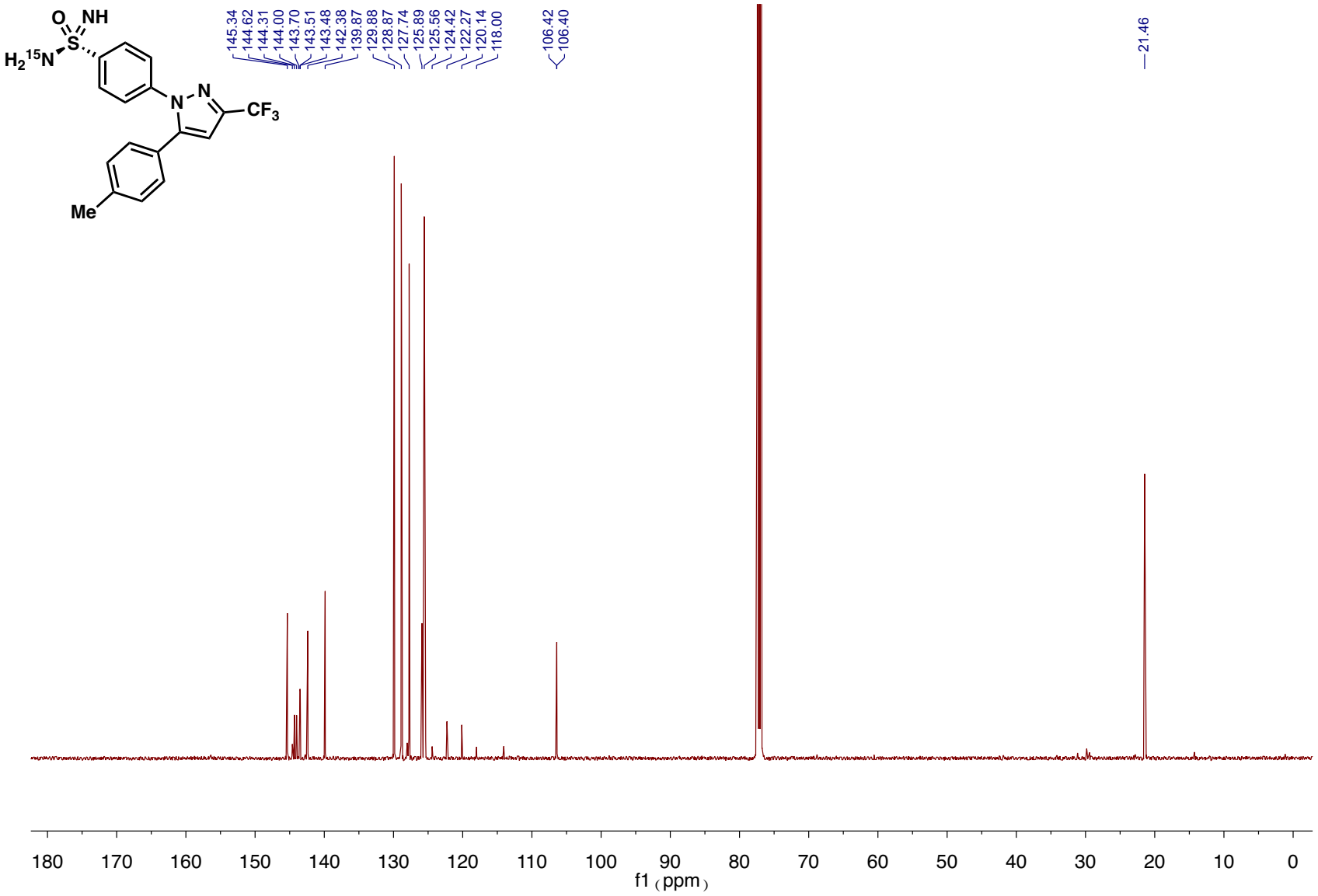
^{19}F NMR of compound 21:



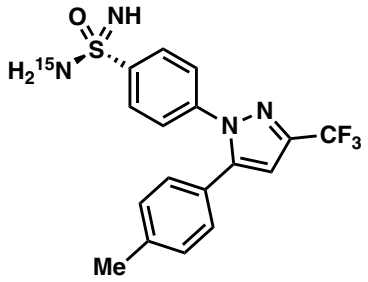
^{1}H NMR of compound 22:



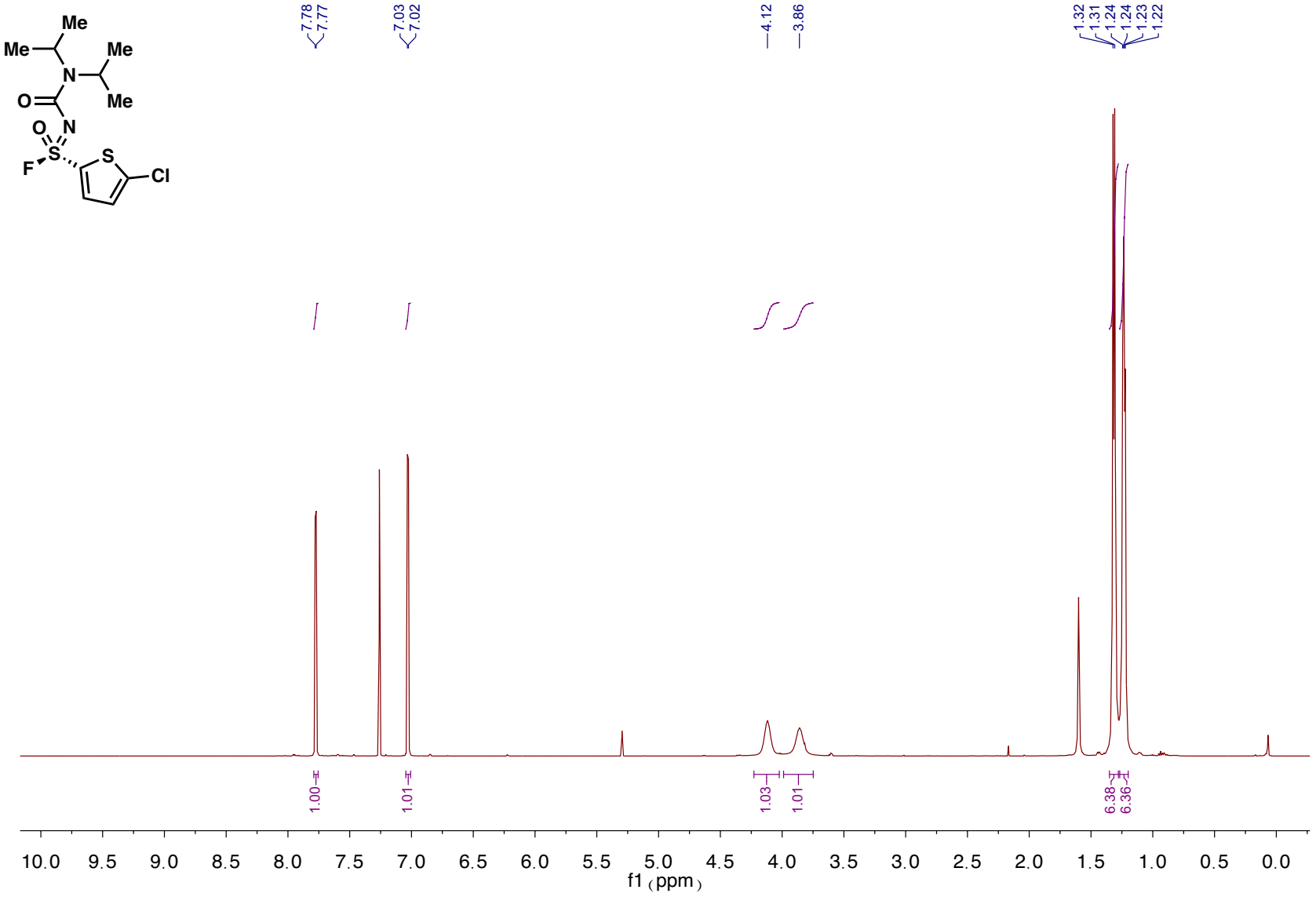
^{13}C NMR of compound 22:



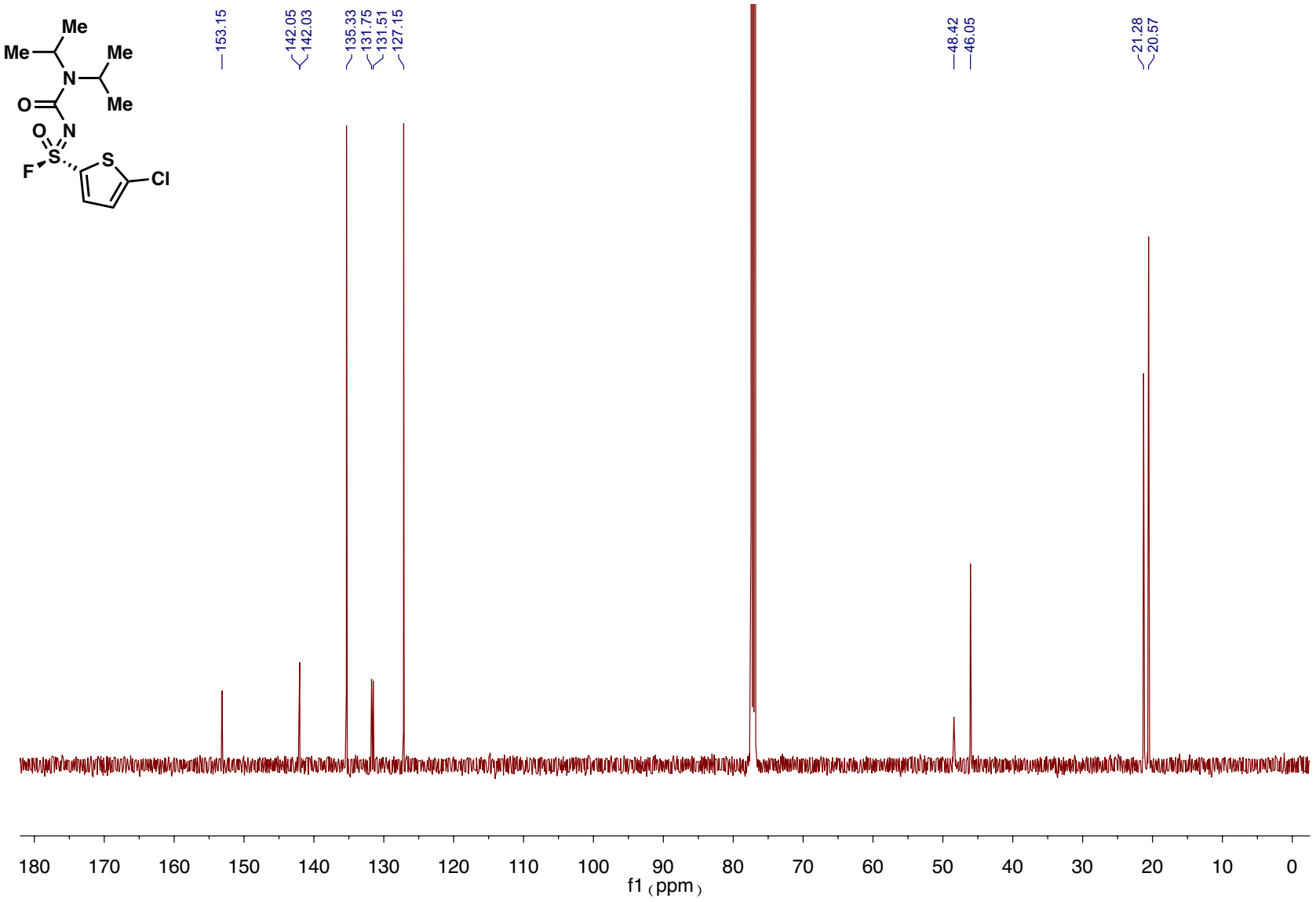
^{19}F NMR of compound 22:



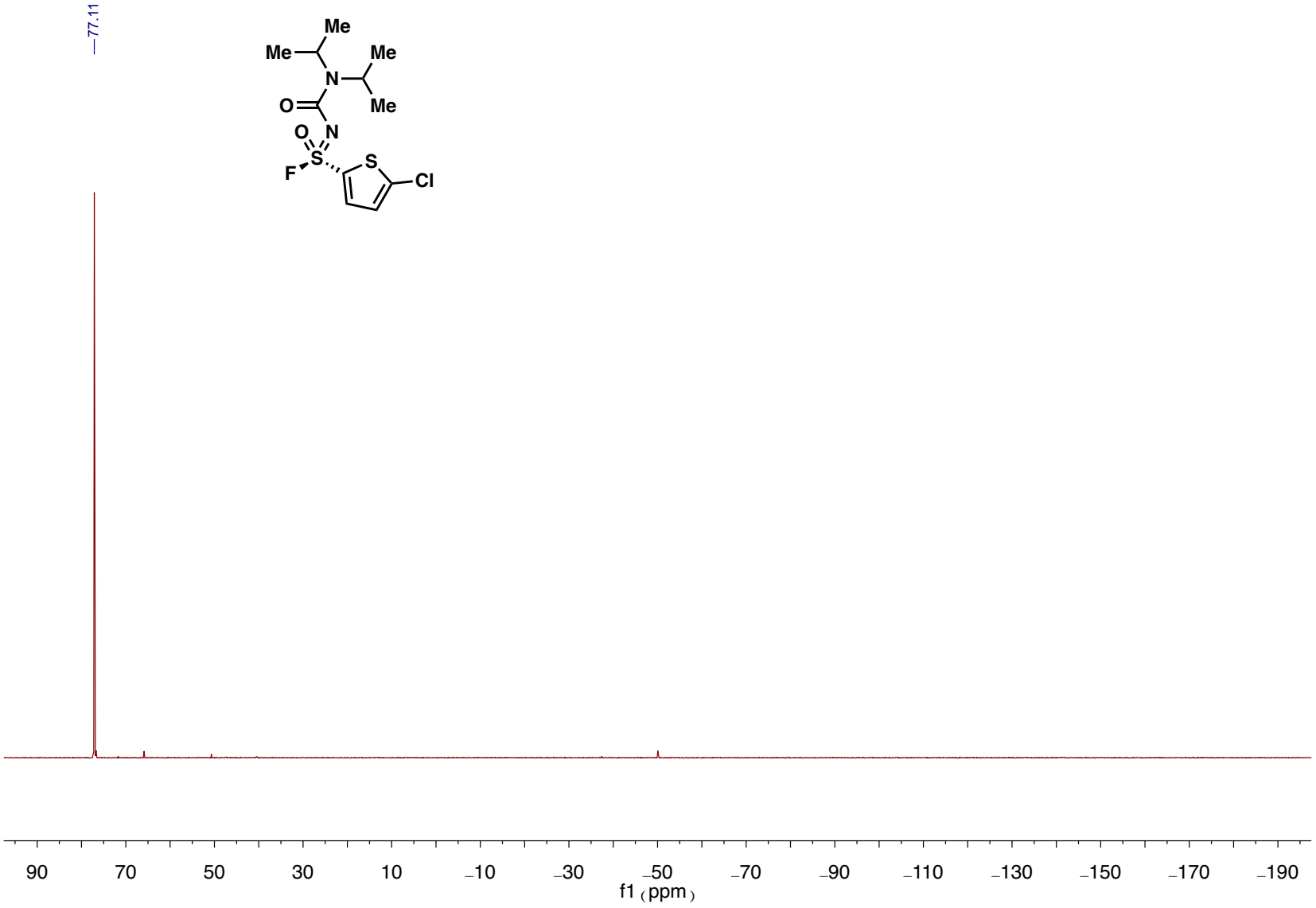
^{1}H NMR of compound 24:



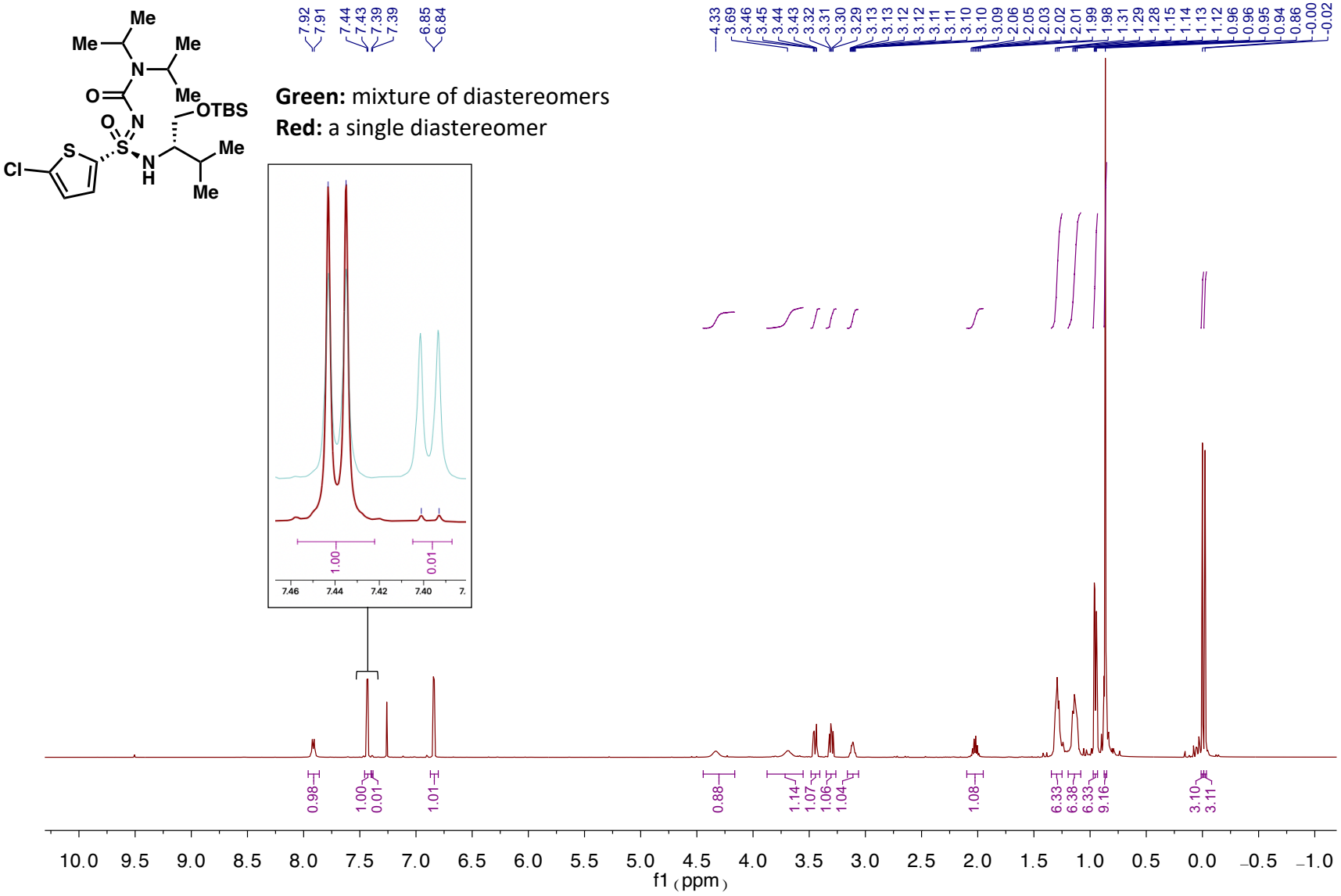
^{13}C NMR of compound 24:



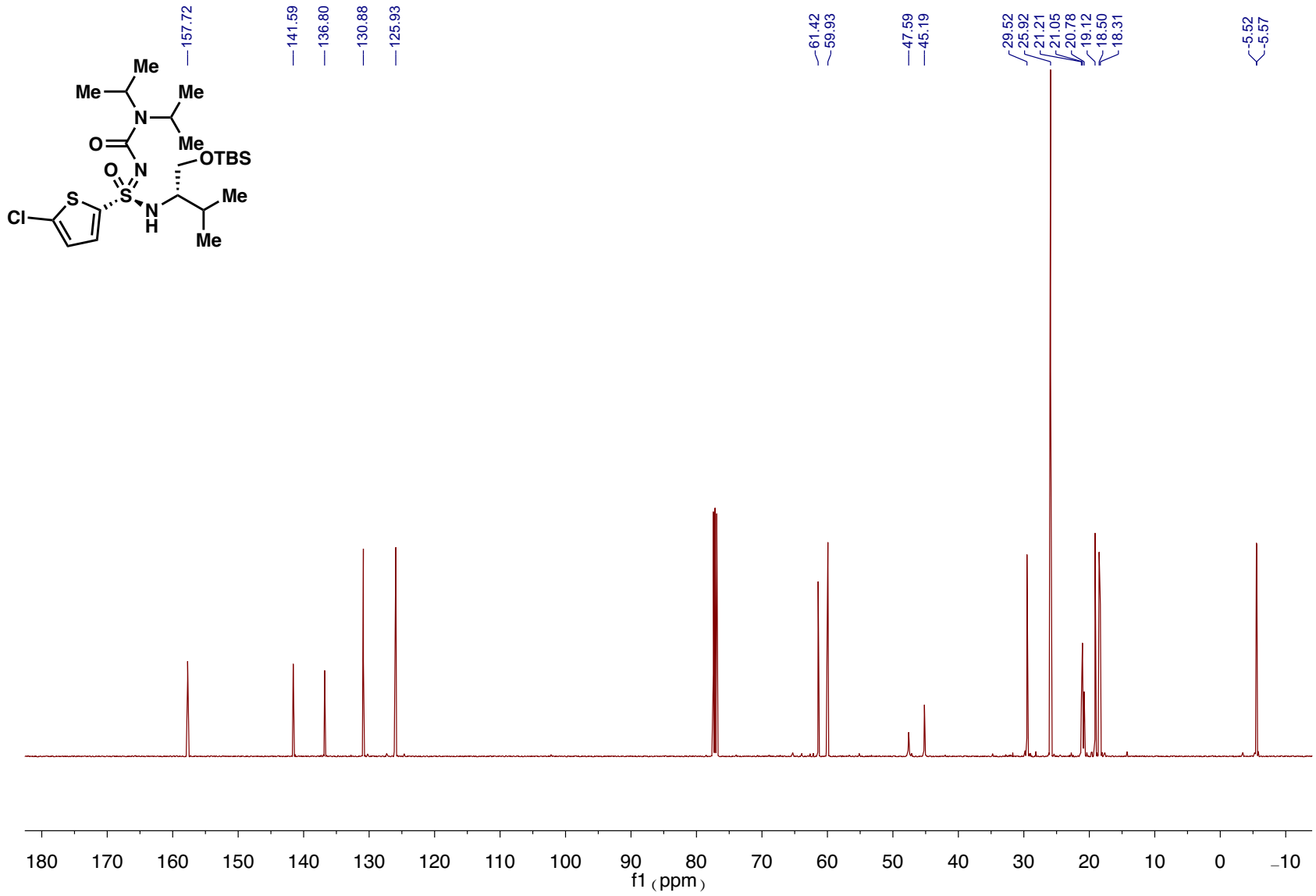
^{19}F NMR of compound 24:



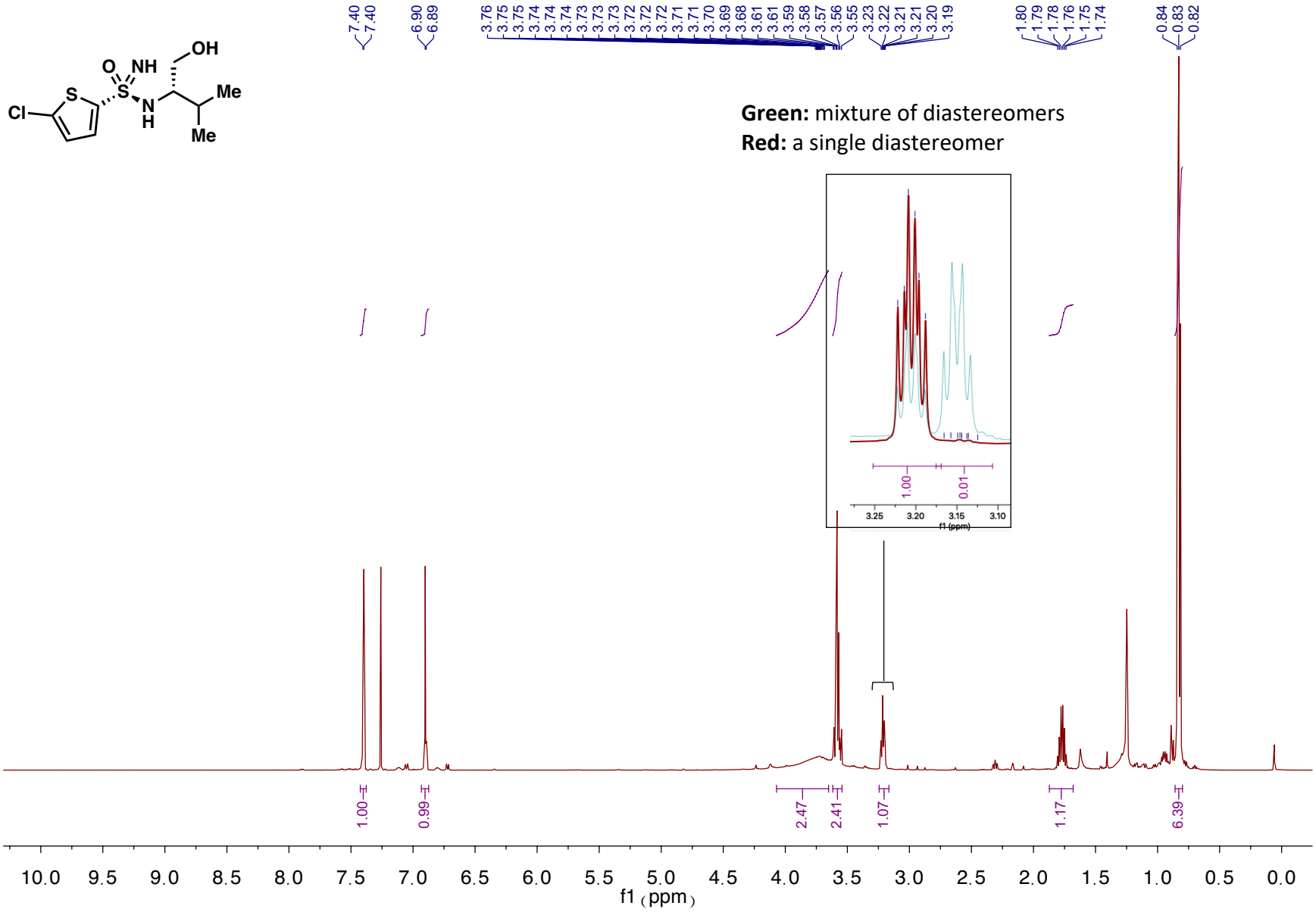
^{1}H NMR of compound 26:



^{13}C NMR of compound 26:



^{1}H NMR of compound 27:



^{13}C NMR of compound 27: