

Supporting Information

for

Stable and Easily Available Sulfide Surrogates Allow a Stereoselective Activation of Alcohols

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Abstract: Isothiouronium salts are easily accessible and stable compounds. Herein, we report their use as versatile deoxasulfonylating agents enabling a stereoselective, thiol-free protocol for synthesis of thioethers from alcohols. The method is simple, scalable and tolerates a broad range of functional groups otherwise incompatible with other methods. Late-stage modification of several pharmaceuticals provides access to multiple analogues of biologically relevant molecules. Performed experiments give insight into the reaction mechanism.

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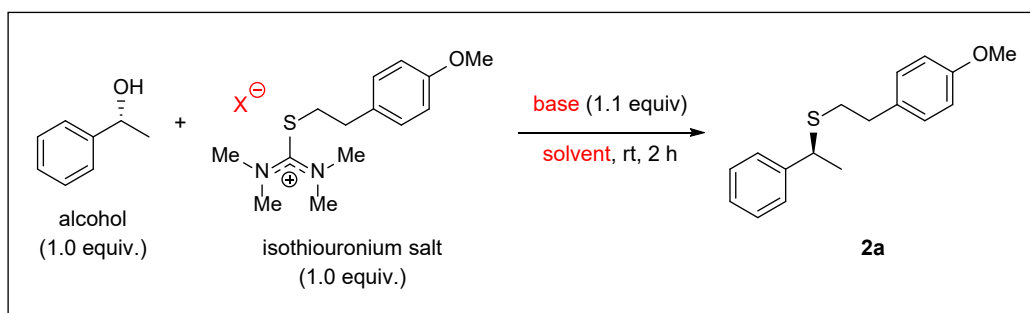
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I. General information

Unless otherwise stated, all glassware was flame-dried before use and all reactions were performed under an atmosphere of argon. All solvents were distilled from appropriate drying agents prior to use or directly taken from commercial sealed bottles under an atmosphere of argon. All reagents and some substrates (alcohols, carboxylic acids, amines and alkyl halides) were used as received from commercial suppliers unless otherwise stated. Reaction progress was monitored by thin layer chromatography (TLC) performed on aluminum plates coated with silica gel F254 with 0.2 mm thickness. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm or by staining using potassium permanganate. Flash column chromatography was performed using silica gel 60 (230-400 mesh, Merck and co.). Neat infra-red spectra were recorded using a Bruker Vertex 70 FT-IR spectrometer. Wavenumbers are reported in cm^{-1} . Mass spectra were obtained using a Bruker maXis UHR-TOF spectrometer, using electrospray ionization (ESI) and by Agilent 7200B GC/Q-TOF spectrometer, using electron impact (EI). All ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded using a Bruker AV III 400, AV NEO 500, AV III 600 or AV III HD 700 spectrometer in CDCl_3 . Chemical shifts were given in parts per million (ppm, δ), referenced to the solvent peak of CDCl_3 , defined at $\delta = 7.26$ ppm (^1H NMR) and $\delta = 77.16$ (^{13}C NMR). Coupling constants are quoted in Hz (J). ^1H NMR splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m), apparent (app) or broad (br). Enantiomeric excess was measured on a Shimadzu LC-8A preparative HPLC system using Lux Cellulose-1 or Lux Cellulose-3 chiral columns.

II. Optimization of reaction conditions



A base (0.33 mmol, 1.1 equiv.) was added dropwise to a solution of (R)-1-phenylethan-1-ol (37 mg, 0.30 mmol, 1.0 equiv., >99% ee) and the corresponding isothiuronium salt (0.30 mmol, 1.0 equiv.) in anhydrous solvent (2.2 mL) under an Ar atmosphere. The reaction mixture was then stirred at rt for 2 h before excess base was quenched by addition of a saturated solution of NH_4Cl . The mixture was then extracted with CH_2Cl_2 (3x), the combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification on silica gel (heptane/ Et_2O = 24:1). Enantiomeric excess was determined using chiral HPLC.

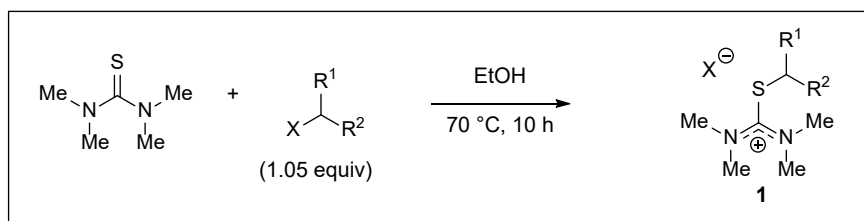
Table 1: Optimization of reaction conditions

Entry	X ⁻	Base	Solvent	Yield	ee
1	Br ⁻	BTMG ^a	CHCl_3	71%	73%
2	SbF_6^-	BTMG	CHCl_3	73%	96%
3	SbF_6^-	BTMG	Toluene	0%	n.d. ^b
4	SbF_6^-	BTMG	THF	20% ^c	n.d.
5	SbF_6^-	BTMG	CH_3CN	38%	86%
6	SbF_6^-	BTMG	DMF	52%	91%
7	SbF_6^-	NEt_3	CHCl_3	0%	n.d.
8	SbF_6^-	DBU ^d	CHCl_3	23% ^c	n.d.
9	SbF_6^-	2,6-lutidine	CHCl_3	0%	n.d.
10	SbF_6^-	imidazole	CHCl_3	0%	n.d.
11	SbF_6^-	TMG ^e	CHCl_3	28% ^c	n.d.
12	BF_4^-	BTMG	CHCl_3	53%	96%
13	PF_6^-	BTMG	CHCl_3	58%	97%

^a 2-*tert*-Butyl-1,1,3,3-tetramethylguanidine, Barton's base; ^b not determined; ^c NMR yield based on crude material, determined using trimethoxybenzene as an internal standard; ^d 1,8-Diazabicyclo[5.4.0]undec-7-en; ^e 1,1,3,3-Tetramethylguanidine.

III. Isothiuronium salts synthesis

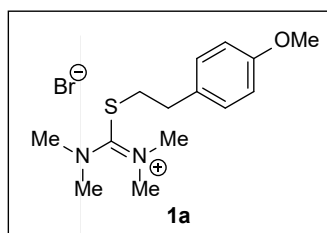
a. General procedure A : synthesis of isothiuronium salts



The procedure was adapted from the literature with changes.¹ Alkyl halide (1.05–5.0 equiv.) was added onto a solution of *N,N,N,N*-tetramethylthiourea (TMTU) (1.0 equiv.) in the EtOH [1 M]. The mixture was then heated at 70 °C for 10 h. After cooling to room temperature, the volatiles were evaporated on a rotavap followed by further drying under high vacuum to give the desired salt with acceptable purity.

b. Isothiuronium salts characterization

2-(4-methoxyphenethyl)-1,1,3,3-tetramethylisothiuronium bromide (1a)



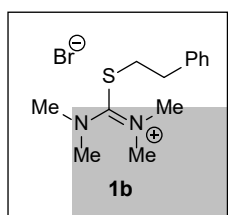
Prepared according to general procedure **A** from TMTU (132 mg, 1.0 mmol, 1.0 equiv.) and 1-(2-bromoethyl)-4-methoxybenzene (226 mg, 1.05 mmol, 1.05 equiv.). White solid (340 mg, 0.98 mmol, 98% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.22 – 7.16 (m, 2H), 6.90 – 6.83 (m, 2H), 3.78 (s, 3H), 3.45 (t, *J* = 7.1 Hz, 2H), 3.39 (s, 12H), 3.00 (t, *J* = 7.1 Hz, 2H).;

¹³C-NMR (101 MHz, CDCl₃): δ 176.1, 158.9, 130.1, 129.9, 114.4, 55.5, 44.9,

37.2, 34.6; **IR** (neat): ν 1595, 1511, 1393, 1246, 1178, 1111, 1032, 726, 696 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M⁺] calculated for [C₁₄H₂₃N₂OS⁺]: 267.1526, found: 267.1522. Mp.: 105–107 °C.

1,1,3,3-tetramethyl-2-phenethylisothiuronium bromide (1b)



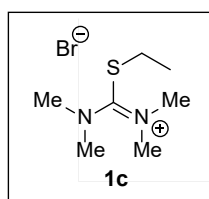
Prepared according to general procedure **A** from TMTU (661 mg, 5.0 mmol, 1.0 equiv.) and (2-bromoethyl)benzene (0.75 mL, 5.5 mmol, 1.1 equiv.). White solid (1.56 g, 4.9 mmol, 99% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.38 – 7.21 (m, 5H), 3.53 (t, *J* = 7.1 Hz, 2H), 3.40 (s, 12H), 3.10 (t, *J* = 7.1 Hz, 2H); **¹³C-NMR** (101 MHz, CDCl₃): δ 175.9, 138.1,

129.0, 128.9, 127.3, 44.9, 36.9, 35.5; **IR** (neat) ν 1264, 750, 732, 701 cm⁻¹;

HRMS (ESI⁺, *m/z*): [M⁺] calculated for [C₁₃H₂₁N₂S⁺]: 237.1420, found: 237.1419. Mp.: 146–148 °C.

2-ethyl-1,1,3,3-tetramethylisothiuronium bromide (1c)

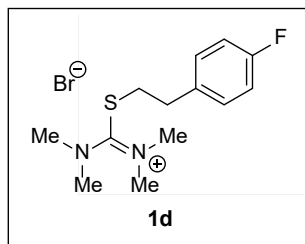


Prepared according to general procedure **A** from TMTU (530 mg, 4.0 mmol, 1.0 equiv.) and ethyl bromide (1.50 mL, 20.0 mmol, 5.0 equiv.). White crystalline solid (950 mg, 3.9 mmol, 98% yield).

¹H NMR (600 MHz, CDCl₃) δ 3.41 (s, 12H), 3.12 (q, *J* = 7.5 Hz, 2H), 1.33 (t, *J* = 7.5 Hz, 3H); **¹³C NMR** (151 MHz, CDCl₃) δ 175.5, 44.9, 29.8, 14.8; **IR** (neat) ν 2921, 2852,

1460, 1377, 761 cm^{-1} ; **HRMS** (ESI^+ , m/z): [M^+] calculated for [$\text{C}_7\text{H}_{17}\text{N}_2\text{S}^+$]: 161.1107, found: 161.1115. Mp.: 90–92 °C.

2-(4-fluorophenethyl)-1,1,3,3-tetramethylisothiuronium bromide (1d)

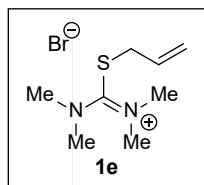


Prepared according to general procedure **A** from TMTU (264 mg, 2.0 mmol, 1.0 equiv.) and 1-(2-bromoethyl)-4-fluorobenzene (447 mg, 2.2 mmol, 1.1 equiv.). White solid (658 mg, 2.0 mmol, 98% yield).

^1H -NMR (400 MHz, CDCl_3): δ 7.34 – 7.28 (m, 2H), 7.07 – 6.92 (m, 2H), 3.52 (t, J = 7.3 Hz, 2H), 3.39 (s, 12H), 3.06 (t, J = 7.3 Hz, 2H); **^{13}C -NMR** (101 MHz, CDCl_3): δ 176.1, 162.1 (d, J = 245.7 Hz), 134.0 (d, J = 3.2 Hz),

130.6 (d, J = 7.9 Hz), 115.8 (d, J = 21.3 Hz), 45.0, 37.1, 34.7; **IR** (neat): ν 1264, 729, 700 cm^{-1} ; **HRMS** (ESI^+ , m/z): [M^+] calculated for [$\text{C}_{13}\text{H}_{20}\text{FN}_2\text{S}^+$]: 255.1326, found: 255.1322. Mp.: 117–119 °C.

2-allyl-1,1,3,3-tetramethylisothiuronium bromide (1e)

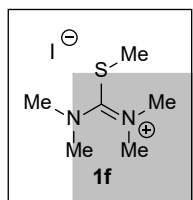


Prepared according to a modified general procedure **A** from TMTU (400 mg, 3.0 mmol, 1.0 equiv.) and ally bromide (0.52 mL, 6.0 mmol, 2.0 equiv.). Slightly brown solid (758 mg, 3.0 mmol, quant. yield).

^1H NMR (400 MHz, CDCl_3) δ 5.88 (ddt, J = 17.0, 10.0, 7.2 Hz, 1H), 5.35 (dd, J = 17.0, 1.0 Hz, 1H), 5.24 (dd, J = 10.0, 1.0 Hz, 1H), 3.78 (d, J = 7.2 Hz, 2H), 3.45 (s, 12H);

^{13}C NMR (101 MHz, CDCl_3) δ 174.8, 131.1, 121.1, 45.0, 38.0; **IR** (neat): ν 3503, 1602, 1398, 1262, 963, 884, 731 cm^{-1} ; **HRMS** (ESI^+ , m/z): [M^+] calculated for [$\text{C}_8\text{H}_{17}\text{N}_2\text{S}^+$]: 173.1107, found: 175.1108. Mp.: 143–145 °C.

1,1,2,3,3-pentamethylisothiuronium iodide (1f)

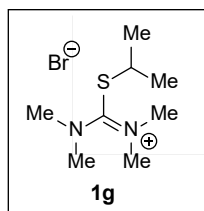


Prepared according to a slightly modified general procedure **A** from TMTU (400 mg, 3.0 mmol, 1.0 equiv.) and iodomethane (0.93 mL, 3.0 mmol, 5.0 equiv.). Orange solid (566 mg, 2.1 mmol, 69% yield).

^1H NMR (400 MHz, CDCl_3) δ 3.43 (s, 12H), 2.71 (s, 3H); **^{13}C NMR** (101 MHz, CDCl_3) δ 177.1, 45.4, 18.6; **IR** (neat) ν 3444, 3001, 2923, 2852, 1595, 1509, 1465, 1395, 1321,

1255, 1206, 1171, 1114, 1062, 873, 726 cm^{-1} ; **HRMS** (ESI^+ , m/z): [M^+] calculated for [$\text{C}_6\text{H}_{15}\text{N}_2\text{S}^+$]: 147.0950, found: 147.0949. Mp.: 132–134 °C.

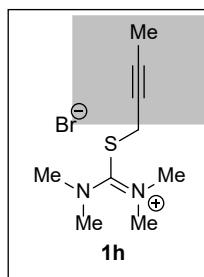
2-isopropyl-1,1,3,3-tetramethylisothiuronium bromide (1g)



Prepared according to a modified general procedure **A** from TMTU (400 mg, 3.0 mmol, 1.0 equiv.) and 3-bromopropane (1.4 mL, 15 mmol, 5.0 equiv.) in *tert*-amyl alcohol at 80 °C. After cooling at rt the solvent was evaporated under vacuum and the crude product was washed several times with EtOAc to give the desired salt as a white solid (275 mg, 1.1 mmol, 36% yield).

^1H NMR (400 MHz, CDCl_3) δ 3.67 – 3.56 (m, 1H), 3.48 (s, 12H), 1.36 (d, 3J = 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, CDCl_3) δ 174.2, 45.0, 41.1, 23.7; **IR** (neat) ν 3376, 2971, 2932, 1594, 1505, 1452, 1394, 1246, 1206, 1167, 1113, 1055 cm^{-1} ; **HRMS** (ESI^+ , m/z): [M^+] calculated for [$\text{C}_8\text{H}_{19}\text{N}_2\text{S}^+$]: 175.1263, found: 175.1263.

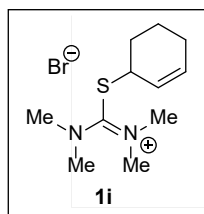
2-(but-2-yn-1-yl)-1,1,3,3-tetramethylisothiuronium bromide (1h)



Prepared according to general procedure **A** from TMTU (264 mg, 2.0 mmol, 1.0 equiv.) and 1-bromobut-2-yne (279 mg, 2.1 mmol, 1.05 equiv.). Yellow solid (528 mg, 2.0 mmol, quant. yield).

¹H-NMR (400 MHz, CDCl₃): δ 3.89 (q, *J* = 2.5 Hz, 2H), 3.49 (s, 12H), 1.85 (t, *J* = 2.5 Hz, 3H); **¹³C-NMR** (101 MHz, CDCl₃): δ 174.3, 83.0, 71.4, 45.0, 24.4, 4.0; **IR** (neat): ν 1600, 1395, 1263, 1056, 763, 749, 726, 697 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [*M*⁺] calculated for [C₉H₁₇N₂S⁺]: 185.1107, found: 185.1103.

2-(cyclohex-2-en-1-yl)-1,1,3,3-tetramethylisothiuronium bromide (1i)

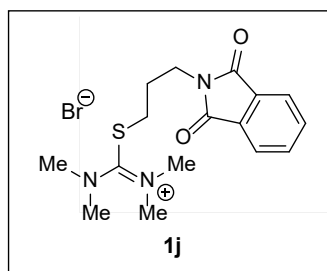


Prepared according to general procedure **A** from TMTU (400 mg, 3.0 mmol, 1.0 equiv.) and 3-bromocyclohexene (0.36 mL, 3.15 mmol, 1.05 equiv.). White solid (850 mg, 2.9 mmol, 97% yield).

¹H NMR (400 MHz, CDCl₃) δ 6.00 – 5.91 (m, 1H), 5.67 – 5.57 (m, 1H), 4.13 – 3.99 (m, 1H), 3.48 (s, 12H), 2.12 – 1.98 (m, 3H), 1.92 – 1.58 (m, 3H); **¹³C NMR** (101 MHz, CDCl₃) δ 174.2, 134.2, 123.7, 46.4, 45.1, 29.8, 24.5, 19.1; **IR** (neat) ν 3394, 3023,

2928, 1596, 1504, 1446, 1392, 1256, 1206, 1168, 1112, 1058, 1036, 993, 866, 749, 612 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [*M*⁺] calculated for [C₁₁H₂₁N₂S⁺]: 213.1420, found: 213.1416.

2-(3-(1,3-dioxo-2,3-dihydro-1H-inden-2-yl)propyl)-1,1,3,3-tetramethylisothiuronium bromide (1j)



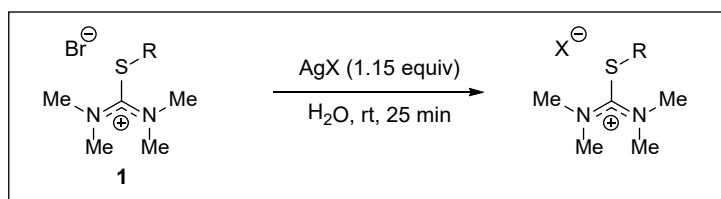
Prepared according to general procedure **A** from TMTU (793 mg, 6.0 mmol, 1.0 equiv.) and N-(3-bromopropyl)phthalimide (1.77 g, 6.6 mmol, 1.1 equiv.). White solid (2.15 g, 5.4 mmol, 90% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.83 (app dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (app dd, *J* = 5.5, 3.0 Hz, 2H), 3.85 (t, *J* = 6.4 Hz, 2H), 3.48 (s, 12H), 3.18 (t, *J* = 6.8 Hz, 2H), 2.11 (p, *J* = 6.6 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 175.8, 168.5, 134.5, 131.9, 123.6, 45.0, 36.1, 32.9, 28.6; **IR** (neat) ν 3390, 2937,

1768, 1703, 2597, 1504, 1435, 1393, 1258, 1189, 1169, 1106, 1057, 1015, 871, 722 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [*M*⁺] calculated for [C₁₆H₂₂N₃O₂S⁺]: 320.1427, found: 320.1425. Mp.: 61–63 °C.

IV. Stereospecific thioetherification of optically active alcohols

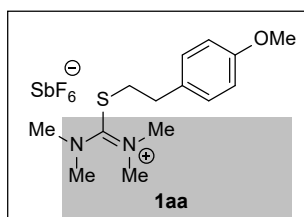
a. General procedure B : Counteranion exchange of isothiuronium salts (synthesis of SbF₆⁻, BF₄⁻ and PF₆⁻ salts)



Corresponding silver salt (AgX, 1.15 equiv.) was added in one portion into a solution of bromide salt of isothiuronium **1** (1 equiv.) in H₂O (0.35 M) and the solution was stirred at rt for 30 min. Formed precipitate was filtered off and the mixture was then extracted with CH₂Cl₂ (3x), the combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure to provide X⁻ thiuronium salt.

b. Thiuronium salt characterization

2-(4-methoxyphenethyl)-1,1,3,3-tetramethylisothiuronium hexafluoroantimonate (**1aa**)



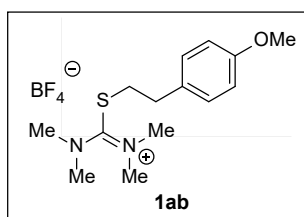
Prepared according to general procedure **B** from **1a** (800 mg, 2.30 mmol, 1.0 equiv.) and AgSbF₆ (910 mg, 2.65 mmol, 1.15 equiv.) as a thick yellowish oil (976 mg, 1.94 mmol, 84% yield).

¹H-NMR (700 MHz, CDCl₃) δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.24 (t, *J* = 7.1 Hz, 2H), 3.21 (s, 12H), 2.95 (t, *J* = 7.1 Hz, 2H);

¹³C-NMR (176 MHz, CDCl₃) δ 176.1, 159.0, 129.9, 129.8, 114.5, 55.5, 44.0,

36.6, 34.6; **¹⁹F NMR** (659 MHz, CDCl₃) δ -112.59 – -134.63 (m); **IR** (neat): ν 2950, 2921, 2853, 1455, 1376, 1247, 760 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [*M*⁺] calculated for [C₁₄H₂₃N₂OS]⁺: 267.1526, found: 267.1523.

2-(4-methoxyphenethyl)-1,1,3,3-tetramethylisothiuronium tetrafluoroborate (**1ab**)

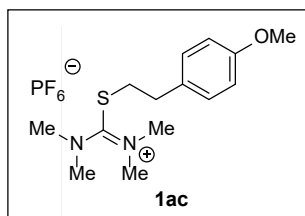


Prepared according to general procedure **B** from **1a** (695 mg, 2.0 mmol, 1.0 equiv.) and AgBF₄ (448 mg, 2.3 mmol, 1.15 equiv.) as a white-off solid (683 mg, 1.93 mmol, 96% yield).

¹H-NMR (400 MHz, CDCl₃) δ 7.15 (t, *J* = 5.7 Hz, 2H), 6.91 – 6.83 (m, 2H), 3.79 (s, 3H), 3.33 – 3.24 (m, 14H), 2.98 (dd, *J* = 7.8, 6.4 Hz, 2H); **¹³C-NMR** (101 MHz, CDCl₃) δ 176.0, 158.9, 130.1, 129.9, 114.4, 55.5, 44.1, 36.6, 34.6;

¹⁹F NMR (376 MHz, CDCl₃) δ -153.08 – -153.21 (m); **IR** (neat): ν 2938, 1598, 1512, 1467, 1397, 1246, 1050, 1034, 822, 536 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [*M*⁺] calculated for [C₁₄H₂₃N₂OS]⁺: 267.1526, found: 267.1523. Mp.: 89–91 °C.

2-(4-methoxyphenethyl)-1,1,3,3-tetramethylisothiuronium hexafluorophosphate (**1ac**)



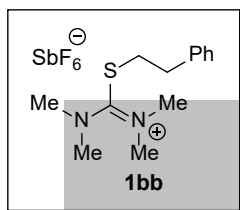
Prepared according to general procedure **B** from **1a** (764 mg, 2.20 mmol, 1.0 equiv.) and AgPF₆ (640 mg, 2.53 mmol, 1.15 equiv.) as a thick yellowish oil (740 mg, 1.97 mmol, 82% yield).

¹H-NMR (600 MHz, CDCl₃) δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.27 – 3.22 (m, 2H), 3.22 (s, 12H), 2.95 (t, *J* = 7.1 Hz, 2H).;

¹³C-NMR (176 MHz, CDCl₃) δ 176.0, 158.9, 130.0, 129.8, 114.4, 55.5, 44.0,

36.5, 34.5; **¹⁹F NMR** (565 MHz, CDCl₃) δ -72.87 (d, *J* = 713.1 Hz); **³¹P NMR** (243 MHz, CDCl₃) δ -134.57 – -154.28 (m). **IR** (neat): ν 2937, 1595, 1512, 1394, 1247, 1112, 1031, 829, 750, 555 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M⁺] calculated for [C₁₄H₂₃N₂OS]⁺: 267.1526, found: 267.1522.

1,1,3,3-tetramethyl-2-(2-phenylethyl)isothiouronium hexafluoroantimonate (1bb)

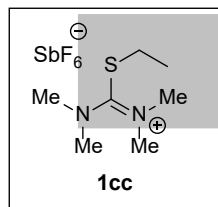


Prepared according to general procedure **B** from **1b** (317 mg, 1.00 mmol, 1.0 equiv.) and AgSbF₆ (395 mg, 1.15 mmol, 1.15 equiv.) as a thick yellowish oil (460 mg, 0.97 mmol, 97% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.33 (t, *J* = 7.5 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 2H), 3.28 (t, *J* = 7.1 Hz, 2H), 3.19 (s, 12H), 3.02 (t, *J* = 7.1 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 176.1, 138.0, 129.1, 128.8, 127.5, 44.0, 36.3,

35.5; **¹⁹F NMR** (565 MHz, CDCl₃) δ -112.14 – -133.82 (m); **IR** (neat) ν 2923, 2851, 1593, 1505, 1454, 1394, 1257, 1206, 1166, 1112, 1055, 869, 7753, 701, 651 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M⁺] calculated for [C₁₃H₂₁N₂S]⁺: 237.1420, found: 237.1427.

2-ethyl-1,1,3,3-tetramethylisothiouronium hexafluoroantimonate (1cc)

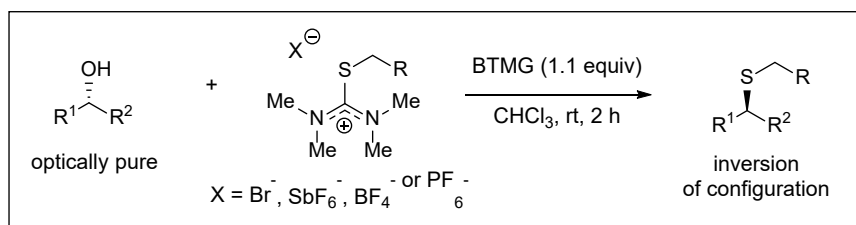


Prepared according to general procedure **B** from **1c** (957 mg, 3.97 mmol, 1.0 equiv.) and AgSbF₆ (1570 mg, 4.56 mmol, 1.15 equiv.) as a thick colorless oil (1010 mg, 2.54 mmol, 64% yield).

¹H-NMR (600 MHz, CDCl₃) δ 3.47 (s, 12H), 3.22 (q, *J* = 7.5 Hz, 2H), 1.42 (t, *J* = 7.4 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃) δ 176.1, 45.6, 30.6, 14.9; **¹⁹F NMR** (377 MHz,

CDCl₃) δ -106.52 – -139.77 (m); **IR** (neat): ν 3503, 2941, 1595, 1396, 1255, 1057, 619 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M⁺] calculated for [C₇H₁₇N₂S]⁺: 161.1107, found: 161.1106.

c. General procedure C : Thioetherification of chiral secondary alcohols

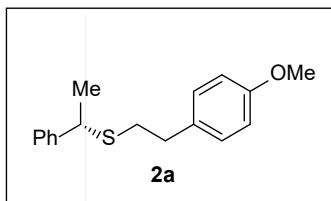


BTMG (2-*tert*-butyl-1,1,3,3-tetramethylguanidine, Barton's base) (68 μL, 0.33 mmol, 1.1 equiv.) was added dropwise to a solution of alcohol (0.30 mmol, 1.0 equiv.) and isothiouronium salt (0.30 mmol, 1.0 equiv.) in dry CHCl₃ (2.2 mL) under an Ar atmosphere. The reaction mixture was then stirred at rt for 2 h before excess base was quenched by addition of a saturated solution of NH₄Cl. The mixture was then extracted

with CH₂Cl₂ (3x), the combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography.

d. Chiral thioether characterization

(S)-(4-methoxyphenethyl)(1-phenylethyl)sulfane (2a)

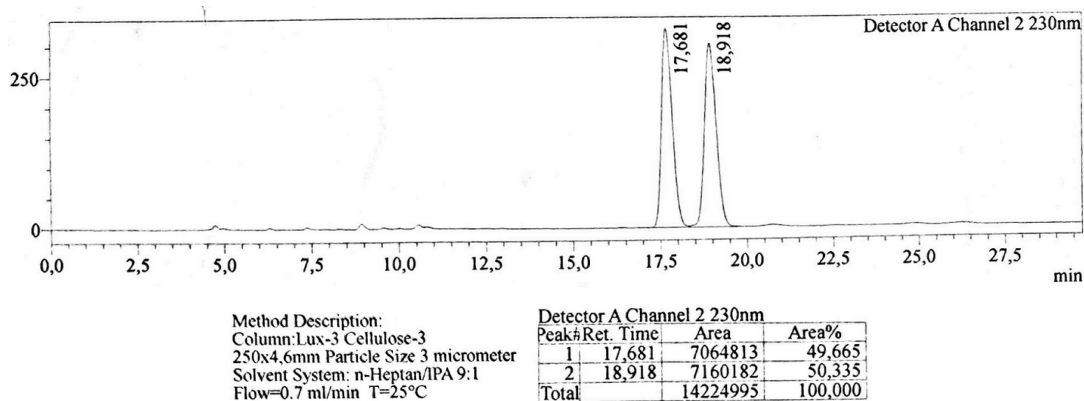


Prepared according to general procedure **C** from (*R*)-1-phenylethan-1-ol (37 mg, 0.30 mmol, 1.0 equiv., >99% ee) and **1a** or **1aa** (1.0 equiv.).

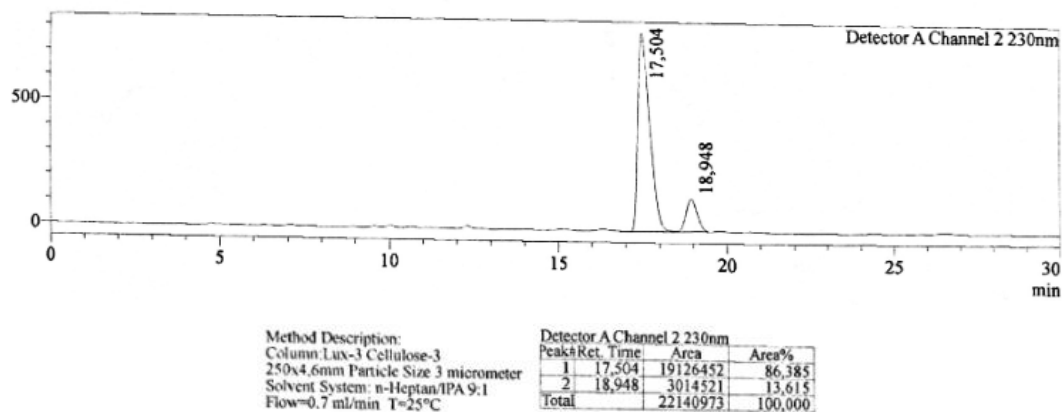
Purification on silica gel (heptane/Et₂O = 24:1). Colorless oil (from **1a**: 58 mg, 0.21 mmol, 71%, 73% ee; from **1aa**: 60 mg, 0.22 mmol, 73% yield, 96% ee).

¹H NMR (600 MHz, CDCl₃) δ 7.35 – 7.30 (m, 4H), 7.25 – 7.21 (m, 1H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 3.95 (q, *J* = 7.0 Hz, 1H), 3.77 (s, 3H), 2.77 – 2.60 (m, 2H), 2.59 – 2.46 (m, 2H), 1.56 (d, *J* = 7.0 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃) δ 158.2, 144.2, 132.9, 129.5, 128.6, 127.5, 127.2, 113.9, 55.4, 44.4, 35.4, 33.2, 22.7; **IR** (neat): ν 2960, 2833, 1611, 1510, 1451, 1244, 1176, 1034, 848, 763, 698 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₇H₂₀OSNa]⁺: 295.1127, found: 295.1126.

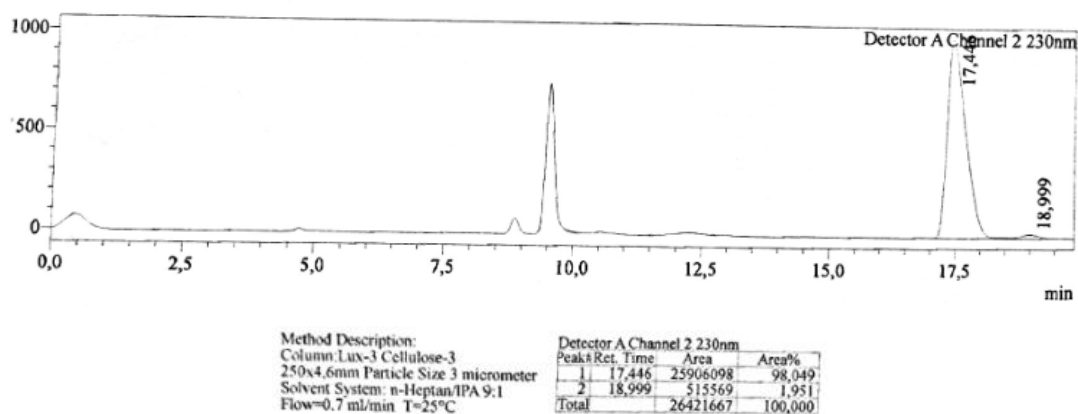
Racemic standard:



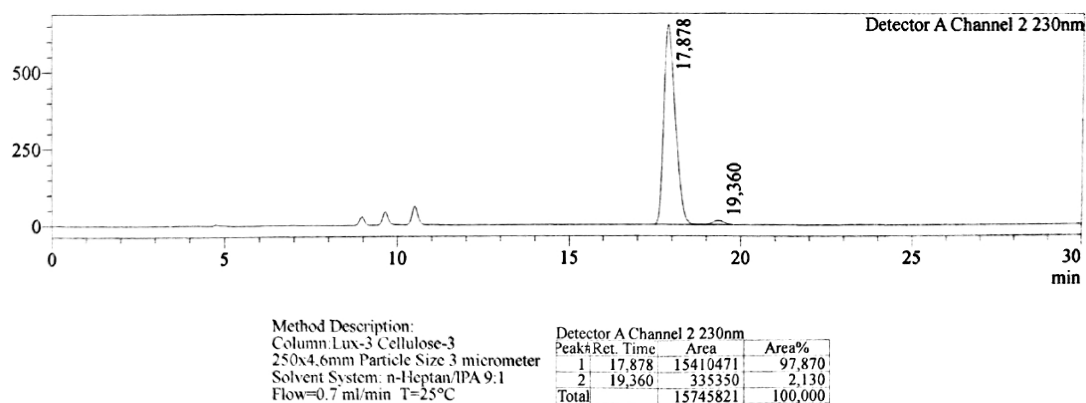
From **1a**:



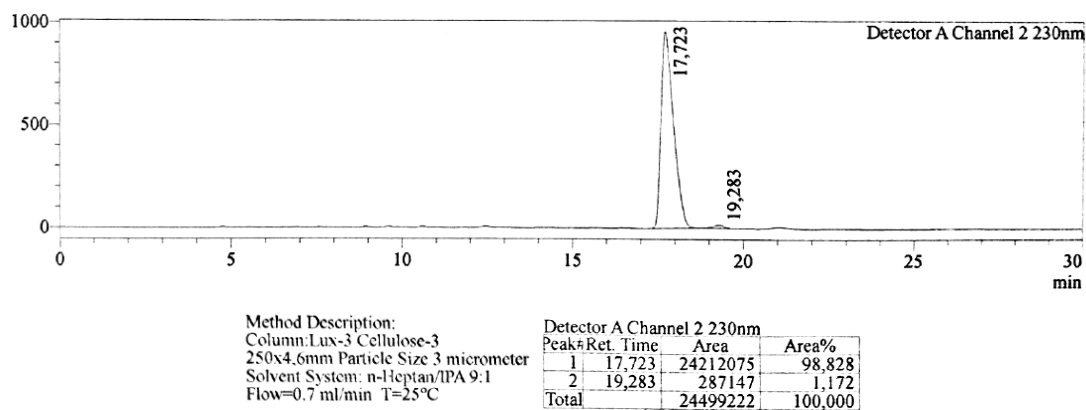
From **1aa**:



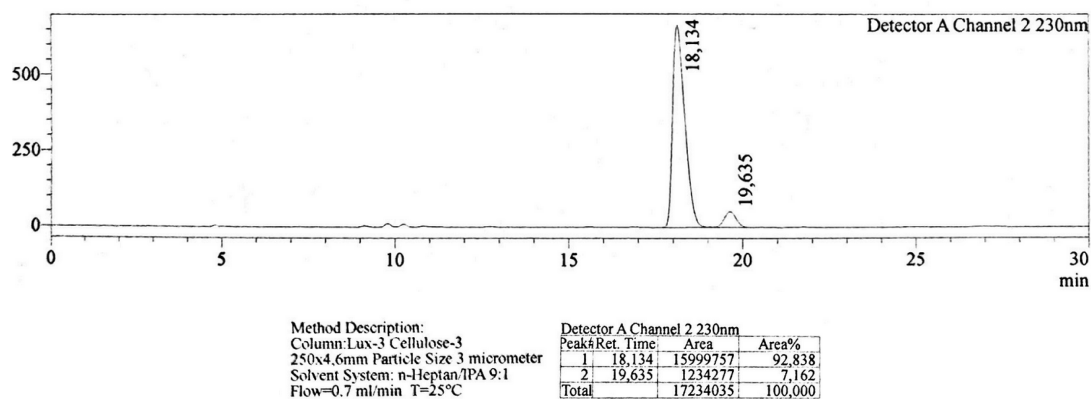
From **1ab**:



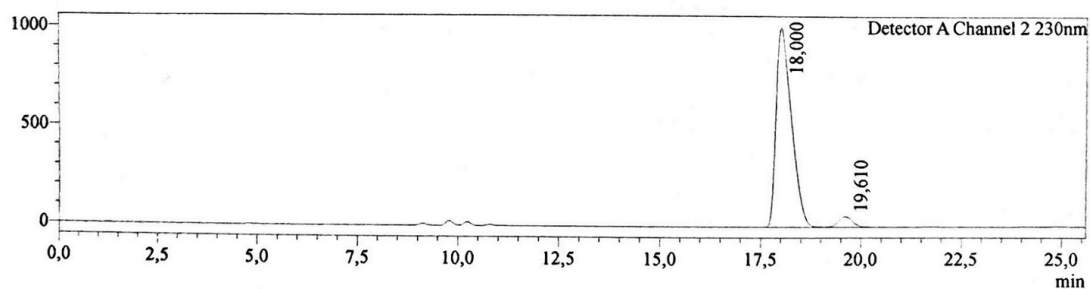
From **1ac**:



CH₃CN used as reaction solvent (from **1aa**):



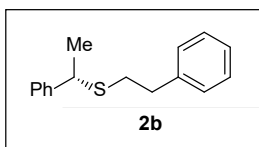
DMF used as reaction solvent (from **1aa**):



Method Description:
Column: Lux-3 Cellulose-3
250x4,6mm Particle Size 3 micrometer
Solvent System: n-Heptan/TPA 9:1
Flow=0.7 ml/min T=25°C

Peak#	Ret. Time	Area	Area%
1	18.000	26633172	95.212
2	19.610	1339398	4.788
Total		27972569	100.000

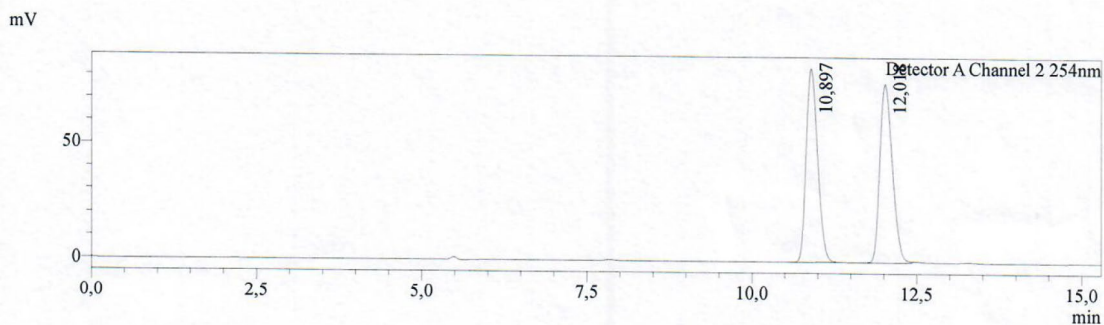
(S)-(4-methoxyphenethyl)(1-phenylethyl)sulfane (**2b**)



Prepared according to general procedure **C** from (*R*)-1-phenylethan-1-ol (37 mg, 0.30 mmol, 1.0 equiv., >99% ee) and **1bb** (1.0 equiv.). Purification on silica gel (heptane/EtOAc = 99:1). Colorless oil (56 mg, 0.22 mmol, 77%, 97% ee).

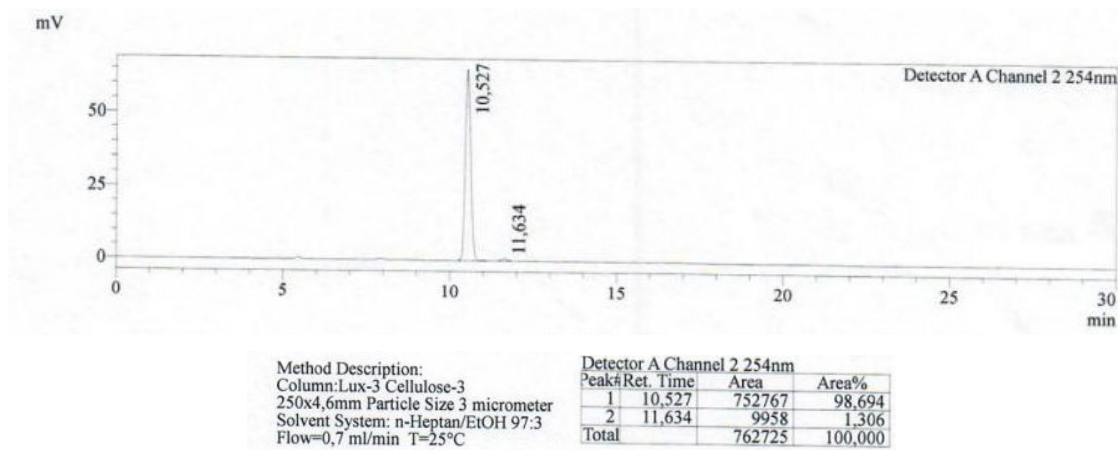
¹H NMR (600 MHz, CDCl₃) δ 7.35 – 7.30 (m, 4H), 7.27 – 7.22 (m, 3H), 7.21 – 7.17 (m, 1H), 7.11 – 7.07 (m, 2H), 3.96 (q, *J* = 7.0 Hz, 1H), 2.84 – 2.68 (m, 2H), 2.61 – 2.51 (m, 2H), 1.57 (d, *J* = 7.0 Hz, 3H); **¹³C-NMR** (150 MHz, CDCl₃) δ 144.1, 140.8, 128.64, 128.60, 128.5, 127.5, 127.2, 126.4, 44.4, 36.3, 32.9, 22.7; **IR** (neat): ν 1255, 748, 723, 699 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₆H₁₈SNa]⁺: 265.1021, found: 265.1019.

Racemic standard:

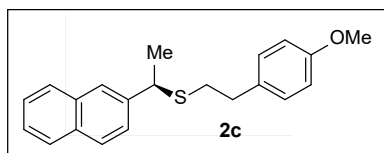


Peak#	Ret. Time	Area	Area%
1	10.897	1013158	49.894
2	12.018	1017467	50.106
Total		2030626	100.000

Method Description:
Column: Lux-3 Cellulose-3
250x4,6mm Particle Size 3 micrometer
Solvent System: n-Heptan/EtOH 97:3
Flow=0.7 ml/min T=25°C



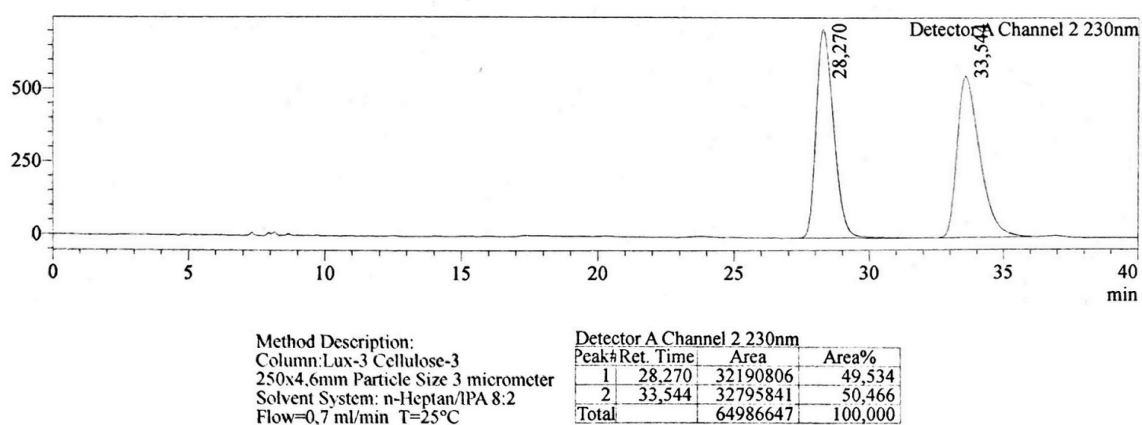
(R)-(4-methoxyphenethyl)(1-(naphthalen-2-yl)ethyl)sulfane (2c)

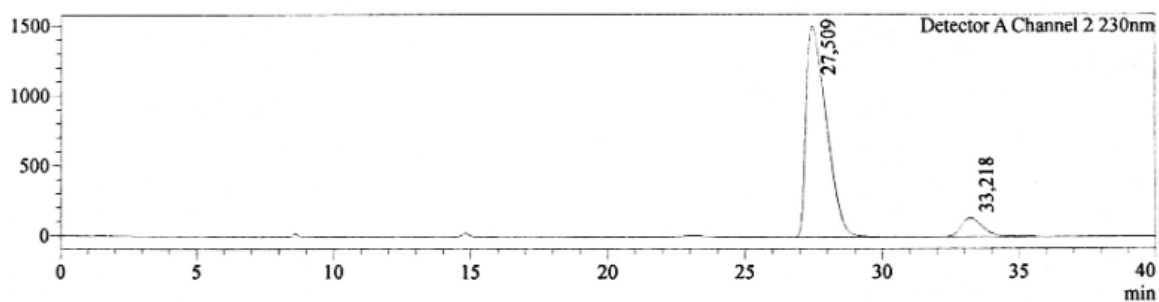


Prepared according to general procedure **C** from (S)-1-(naphthalen-2-yl)ethan-1-ol (52 mg, 0.30 mmol, 1.0 equiv., >98% ee) and **1a** (151 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/Et₂O = 24:1). Colorless oil (67 mg, 0.21 mmol, 69% yield, 82% ee).

¹H NMR (600 MHz, CDCl₃) δ 7.85 – 7.78 (m, 3H), 7.67 (bs, 1H), 7.55 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.50 – 7.44 (m, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 4.11 (q, *J* = 7.0 Hz, 1H), 3.76 (s, 3H), 2.77 – 2.62 (m, 2H), 2.58 – 2.46 (m, 2H), 1.64 (d, *J* = 7.0 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃) δ 158.2, 141.4, 133.3, 132.9, 132.8, 129.5, 128.7, 127.8, 127.8, 126.3, 126.0, 125.9, 125.5, 113.9, 55.4, 44.7, 35.4, 33.2, 22.6; **IR** (neat): ν 2951, 2833, 1610, 1510, 1440, 1243, 1175, 1034, 817, 747 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₂₁H₂₂OSNa]⁺: 345.1284, found: 345.1282.

Racemic standard:

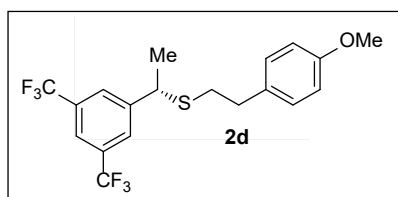




Method Description:
 Column: Lux-3 Cellulose-3
 250x4.6mm Particle Size: 3 micrometer
 Solvent System: n-Heptan/IPA 8:2
 Flow=0,7 ml/min T=25°C

Peak#	Ret. Time	Area	Area%
1	27.509	76665151	91,093
2	33.218	7495929	8,907
Total		84161080	100,000

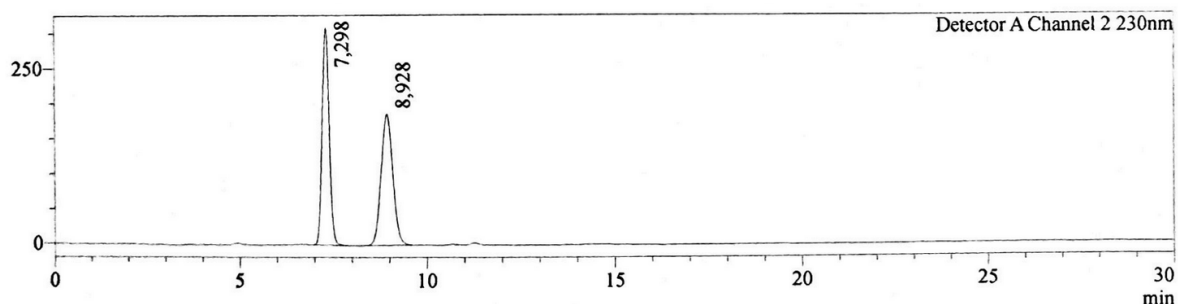
(S)-(1-(3,5-bis(trifluoromethyl)phenyl)ethyl)(4-methoxyphenethyl)sulfane (2d)



Prepared according to general procedure **C** from (*R*)-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol (77 mg, 0.30 mmol, 1.0 equiv., >98% ee) and **1aa** (151 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/Et₂O = 24:1). Colorless oil (78 mg, 0.19 mmol, 64% yield, >99% ee).

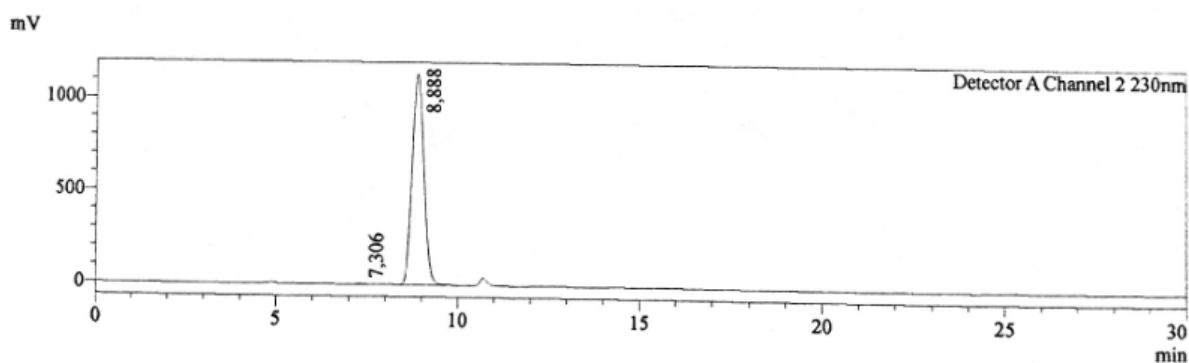
¹H NMR (600 MHz, CDCl₃) δ 7.75 (s, 3H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 3.96 (q, *J* = 7.1 Hz, 1H), 3.78 (s, 3H), 2.77 – 2.71 (m, 2H), 2.57 – 2.48 (m, 2H), 1.56 (d, *J* = 7.1 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃) δ 158.4, 147.2, 132.2, 131.9 (q, *J* = 33.2 Hz), 129.6, 127.7 (d, *J* = 2.6 Hz), 123.4 (q, *J* = 273.3 Hz), 121.3 (dt, *J* = 7.5, 3.6), 114.1, 55.4, 43.8, 35.3, 33.3, 22.7; **¹⁹F NMR** (659 MHz, CDCl₃) δ -62.79. **IR** (neat): ν 2929, 1612, 1512, 1373, 1301, 1246, 1168, 1126, 1036, 896, 705, 680 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₉H₁₈F₆OSNa]⁺: 431.0875, found: 431.0878.

Racemic standard:



Method Description:
 Column: Lux-3 Cellulose-3
 150x4.6mm Particle Size: 3 micrometer
 Solvent System: n-Heptan/IPA 95:5
 Flow=0,7 ml/min T=25°C

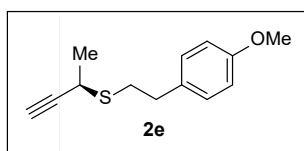
Peak#	Ret. Time	Area	Area%
1	7.298	4011556	49,749
2	8.928	4051994	50,251
Total		8063551	100,000



Method Description:
 Column: Lux-3 Cellulose-3
 250x4.6mm Particle Size 3 micrometer
 Solvent System: n-Heptan/IPA 95:5
 Flow=0.7 ml/min T=25°C

Peak#	Ret. Time	Area	Area%
1	7.306	38262	0.149
2	8.888	25578937	99.851
Total		25617199	100.000

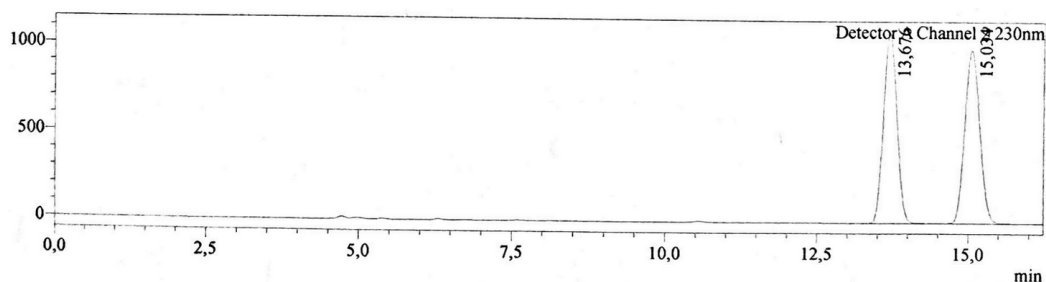
(R)-but-3-yn-2-yl(4-methoxyphenethyl)sulfane (2e)



Prepared according to general procedure **C** from (S)-3-butyne-2-ol (21 mg, 0.30 mmol, 1.0 equiv., >98% ee) and **1aa** (151 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/Et₂O = 49:1). Colorless oil (38 mg, 0.17 mmol, 58% yield, 98% ee).

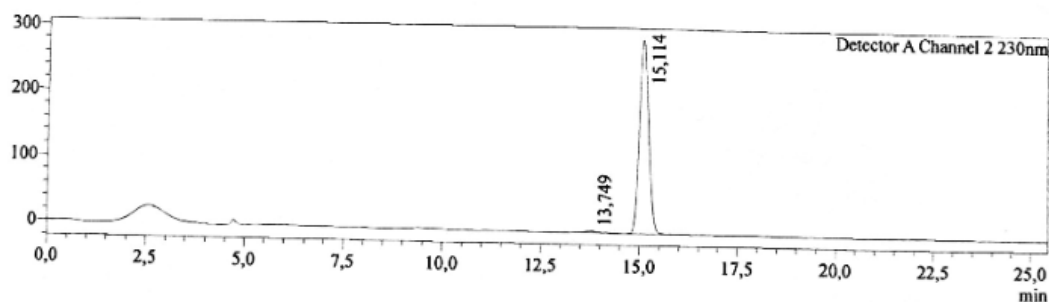
¹H NMR (600 MHz, CDCl₃) δ 7.14 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.61 (qd, *J* = 7.0, 2.3 Hz, 1H), 3.02 – 2.94 (m, 1H), 2.93 – 2.84 (m, 3H), 2.36 (d, *J* = 2.4 Hz, 1H), 1.50 (d, *J* = 7.0 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃) δ 158.3, 132.7, 129.6, 114.0, 84.8, 71.0, 55.4, 35.2, 33.2, 29.1, 21.6; **IR** (neat): ν 3286, 2930, 1610, 1511, 1442, 1244, 1176, 1034, 848, 635 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₃H₁₆OSNa]⁺: 243.0814, found: 243.0814.

Racemic standard:



Method Description:
 Column: Lux-3 Cellulose-3
 250x4.6mm Particle Size 3 micrometer
 Solvent System: n-Heptan/IPA 9:1
 Flow=0.7 ml/min T=25°C

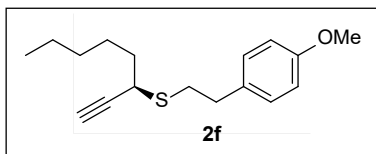
Peak#	Ret. Time	Area	Area%
1	13.676	16941297	49.685
2	15.034	17156249	50.315
Total		34097547	100.000



Method Description:
 Column: Lux-3 Cellulose-3
 250x4.6mm Particle Size 3 micrometer
 Solvent System: n-Heptan/IPA 9:1
 Flow=0.7 ml/min T=25°C

Peak	Ret. Time	Area	Area%
1	13.749	50165	1.030
2	15.114	4820965	98.970
Total		4871130	100.000

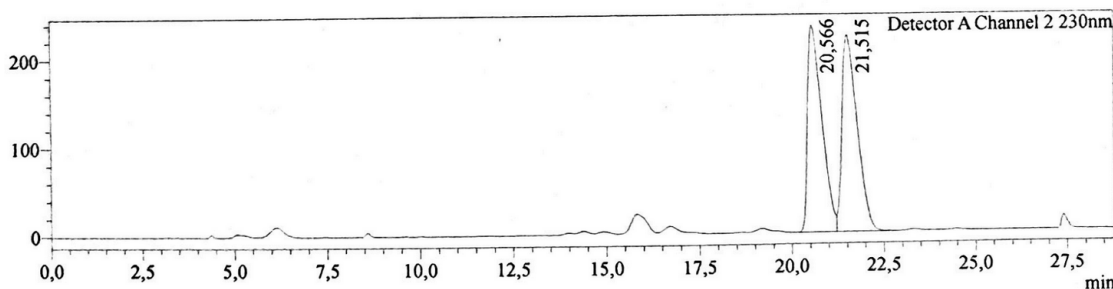
(*R*)-(4-methoxyphenethyl)(oct-1-yn-3-yl)sulfane (**2f**)



Prepared according to general procedure **C** from (*S*)-1-Octyn-3-ol (38 mg, 0.30 mmol, 1.0 equiv., 99% ee) and **1aa** (151 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/Et₂O = 49:1). Colorless oil (42 mg, 0.15 mmol, 51% yield, >97% ee).

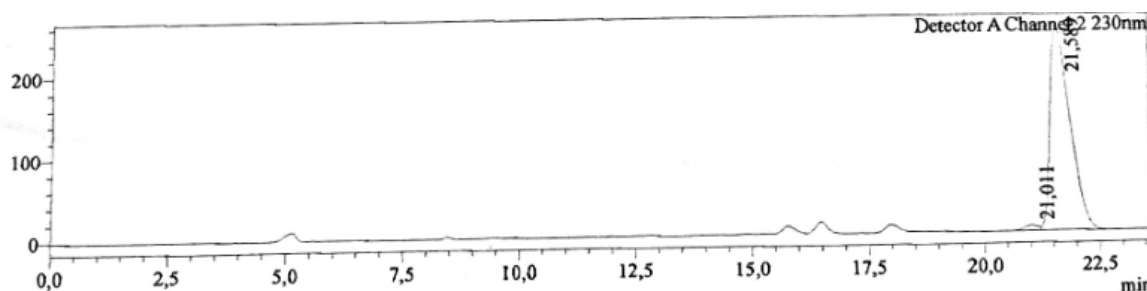
¹H NMR (700 MHz, CDCl₃) δ 7.14 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.50 – 3.47 (m, 1H), 3.00 – 2.94 (m, 1H), 2.92 – 2.81 (m, 3H), 2.36 (d, *J* = 2.3 Hz, 1H), 1.77 – 1.67 (m, 2H), 1.57 – 1.45 (m, 2H), 1.36 – 1.25 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H); **¹³C-NMR** (176 MHz, CDCl₃) δ 158.3, 132.8, 129.6, 114.0, 83.8, 71.7, 55.4, 35.3, 35.2, 34.6, 33.1, 31.4, 27.1, 22.6, 14.1; **IR** (neat): ν 3284, 2923, 2857, 1611, 1511, 1464, 1301, 1245, 1176, 1035, 820, 636 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₇H₂₄OSNa]⁺: 299.1440, found: 299.1436.

Racemic standard:



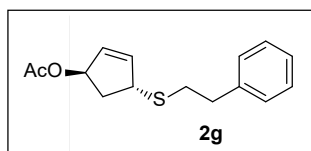
Method Description:
 Column: Lux-Cellulose1 (Chiralcel OD-H) 250x4.6mm
 Solvent System: n-Heptan+0.1%IPA
 Flow: 1 ml/min

Peak	Ret. Time	Area	Area%
1	20.566	6342907	49.736
2	21.515	6410291	50.264
Total		12753198	100.000



Method Description:
 Column: Lux-Cellulose1 (Chiralcel OD-H) 250x4.6mm
 Solvent System: n-Heptan+0.1%IPA
 Flow: 1 ml/min

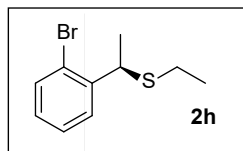
Peak	Ret. Time	Area	Area%
1	21.011	133056	1.739
2	21.589	7519103	98.261
Total		7652159	100.000

(1*R*,4*R*)-4-(phenethylthio)cyclopent-2-en-1-yl acetate (2g)

Prepared according to general procedure **C** from (1*R*,4*S*)-4-hydroxycyclopent-2-en-1-yl acetate (43 mg, 0.30 mmol, 1.0 equiv., >99%) and **1b** or **1bb** (1.0 equiv.). Purification on silica gel (heptane/Et₂O = 9:1). Colorless oil (from **1b**: 54 mg, 0.21 mmol, 69% yield, d.r. 94:6; from **1bb**:

58 mg, 0.22 mmol, 74% yield, one diastereomer).

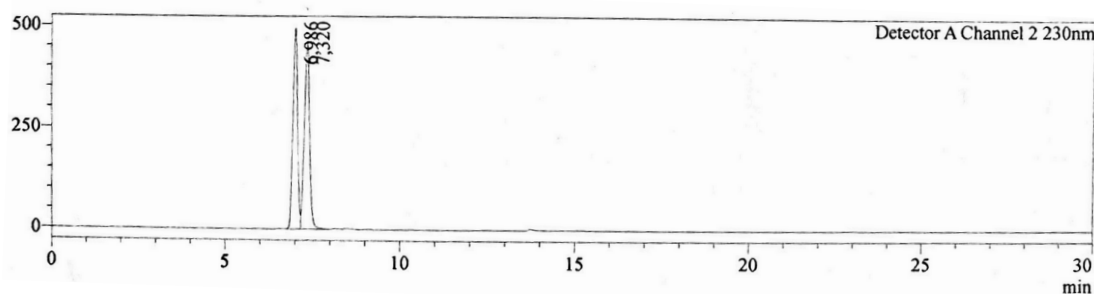
¹H NMR (700 MHz, CDCl₃) δ 7.30 (t, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 7.4 Hz, 2H), 6.04 (ddd, *J* = 5.5, 2.1, 0.9 Hz, 1H), 5.91 (dt, *J* = 5.5, 2.0 Hz, 1H), 5.77 – 5.74 (m, 1H), 4.01 – 3.98 (m, 1H), 2.93 – 2.82 (m, 2H), 2.81 – 2.70 (m, 2H), 2.34 – 2.25 (m, 2H), 2.03 (s, 3H); **¹³C-NMR** (176 MHz, CDCl₃) δ 171.0, 140.5, 138.6, 131.0, 128.7, 128.6, 126.6, 79.6, 48.2, 39.1, 36.5, 32.2, 21.3; **IR** (neat): ν 3027, 3920, 1728, 1496, 1357, 1235, 1174, 1017, 982, 722, 696 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₅H₁₈O₂SNa]⁺: 285.0920, found: 285.0917.

(*R*)-(1-(2-bromophenyl)ethyl)(ethyl)sulfane (2h)

Prepared according to general procedure **C** from (*S*)-1-(2-bromophenyl)ethan-1-ol (40 mg, 0.20 mmol, 1.0 equiv., >98%) and **1cc** (1.0 equiv.). Purification on silica gel (pentane). Yellowish oil (33 mg, 0.14 mmol, 67% yield, >98% ee).

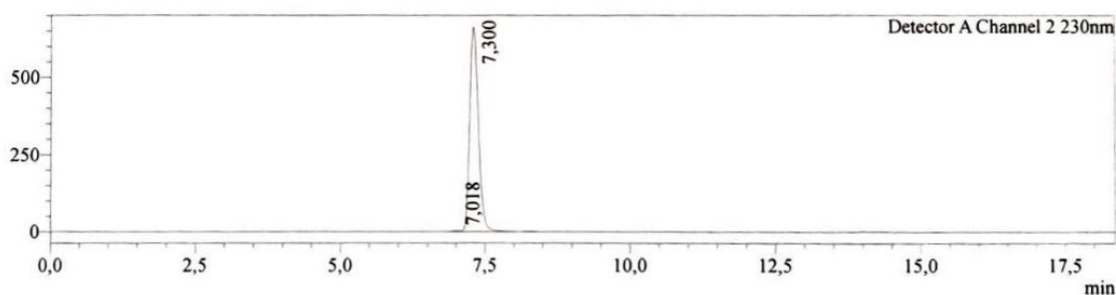
¹H NMR (600 MHz, CDCl₃) δ 7.63 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.52 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.35 – 7.29 (m, 1H), 7.10 – 7.05 (m, 1H), 4.57 (q, *J* = 7.0 Hz, 1H), 2.51 – 2.32 (m, 2H), 1.51 (d, *J* = 7.0 Hz, 3H), 1.19 (t, *J* = 7.4 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃) δ 143.5, 132.7, 128.8, 128.4, 128.1, 124.0, 42.3, 25.5, 22.3, 14.8; **IR** (neat): ν 2967, 2925, 1467, 1020, 753, 726, 658 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+H]⁺ calculated for [C₁₀H₁₄S(⁷⁹Br)]⁺: 244.9994, found: 244.9994; calculated for [C₁₀H₁₄S(⁸¹Br)]⁺: 246.9974, found: 246.9973. [α]_D²⁰ = - 57.4 (*c* = 1, CHCl₃) [lit. [α]_D²⁰ = - 54.7 (*c* = 1, CHCl₃)]¹

Racemic standard:



Method Description:
Column: Lux-3 Cellulose-3
250x4.6mm Particle Size 3 micrometer
Solvent System: n-Heptan+0.1%IPA/n-Heptan+2%IPA50:50
Flow=0.7 ml/min T=25°C

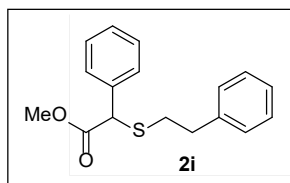
Detector A Channel 2 230nm			
Peak#	Ret. Time	Area	Area%
1	6.986	4623068	49.243
2	7.320	4765293	50.757
Total		9388361	100.000



Method Description:
 Column: Lux-3 Cellulose-3
 250x4,6mm Particle Size 3 micrometer
 Solvent System: n-Heptan+0,1%IPA/n-Heptan+2%IPA50:50
 Flow=0,7 ml/min T=25°C

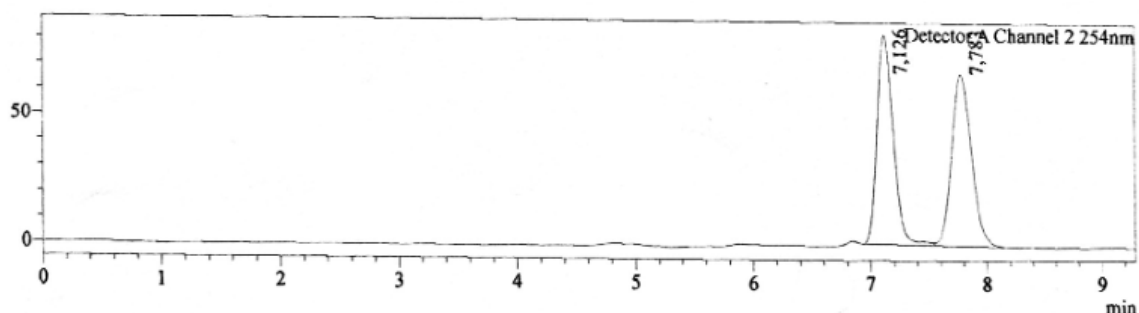
Detector A Channel 2 230nm			
Peak#	Ret. Time	Area	Area%
1	7,018	23369	0,335
2	7,300	6948940	99,665
Total		6972310	100,000

Methyl 2-(phenethylthio)-2-phenylacetate (2i)



Prepared according to general procedure **C** from methyl L-mandelate (50 mg, 0.30 mmol, 1.0 equiv., >99%) and **1bb** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 19:1). Colorless oil (61 mg, 0.21 mmol, 71% yield, 0% ee).

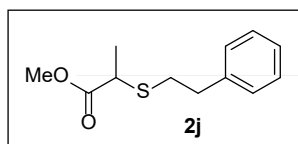
¹H NMR (600 MHz, CDCl₃) δ 7.45 (d, J = 7.5 Hz, 2H), 7.38 – 7.25 (m, 5H), 7.21 (t, J = 7.5 Hz, 1H), 7.14 (d, J = 7.5 Hz, 2H), 4.58 (s, 1H), 3.73 (s, 3H), 2.89 – 2.63 (m, 4H); **¹³C-NMR** (151 MHz, CDCl₃) δ 171.4, 140.3, 136.1, 128.9, 128.67, 128.65 (2xC), 128.4, 126.6, 52.9, 52.4, 35.9, 33.4.; **IR** (neat): ν 3027, 2950, 1735, 1496, 1453, 1301, 1146, 1006, 729, 695 cm⁻¹; **HRMS** (ESI⁺, m/z): [M+Na]⁺ calculated for [C₁₇H₁₈O₂SNa]⁺: 309.0920, found: 309.0918.



Method Description:
 Column: Lux-Cellulose1 (Chiralcel OD-H) 250x4,6mm
 Solvent System: n-Heptan+0,1%IPA/EtOH 8:2
 Flow:0,7ml/min

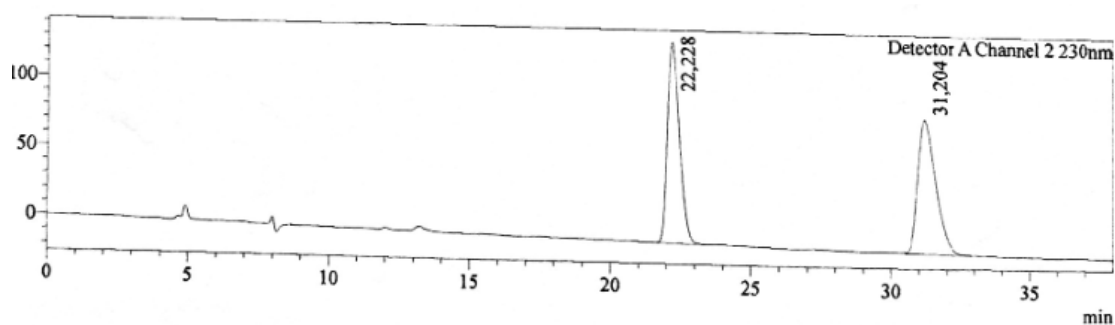
Detector A Channel 2 254nm			
Peak#	Ret. Time	Area	Area%
1	7,126	783053	49,659
2	7,783	793818	50,341
Total		1576870	100,000

Methyl 2-(phenethylthio)propanoate (2j)



Prepared according to general procedure **C** from methyl L-lactate (31 mg, 0.30 mmol, 1.0 equiv., >97%) and **1bb** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 19:1). Colorless oil (44 mg, 0.20 mmol, 66% yield, 0% ee).

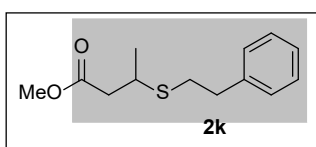
¹H NMR (600 MHz, CDCl₃) δ 7.30 (t, J = 7.3 Hz, 2H), 7.24 – 7.18 (m, 3H), 3.74 (s, 3H), 3.43 (q, J = 7.1 Hz, 1H), 2.96 – 2.79 (m, 4H), 1.45 (d, J = 7.1 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃) δ 173.7, 140.4, 128.6 (2xC), 126.6, 52.4, 41.2, 36.1, 33.0, 17.3; **IR** (neat): ν 2950, 1711, 1451, 1327, 1260, 1157, 1065, 697 cm⁻¹; **HRMS** (ESI⁺, m/z): [M+Na]⁺ calculated for [C₁₂H₁₆O₂SNa]⁺: 247.0763, found: 247.0760.



Method Description:
 Column: Lux-3 Cellulose-3
 250x4,6mm Particle Size 3 micrometer
 Solvent System: (n-Heptan+0,1%IPA)/IPA 85:15
 Flow=0,7ml/min T=25°C

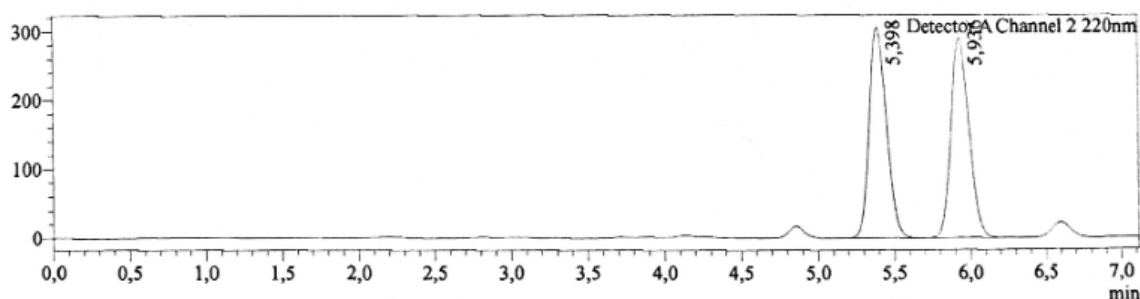
Peak	Ret. Time	Area	Area%
1	22.228	4248750	49.562
2	31.204	4323896	50.438
Total		8572646	100.000

Methyl 3-(phenethylthio)butanoate (2k)



Prepared according to general procedure **C** from methyl *S*-3-hydroxybutyrate (35 mg, 0.30 mmol, 1.0 equiv., 99%) and **1bb** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 19:1). Colorless oil (30 mg, 0.13 mmol, 42% yield, 0% ee).

¹H NMR (700 MHz, CDCl₃) δ 7.30 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.19 (m, 3H), 3.69 (s, 3H), 3.30 – 3.17 (m, 1H), 2.88 (dd, *J* = 9.3, 6.4 Hz, 2H), 2.85 – 2.78 (m, 2H), 2.63 (dd, *J* = 15.5, 6.3 Hz, 1H), 2.46 (dd, *J* = 15.5, 8.1 Hz, 1H), 1.33 (d, *J* = 6.8 Hz, 3H); **¹³C-NMR** (176 MHz, CDCl₃) δ 172.1, 140.6, 128.63, 128.60, 126.5, 51.9, 42.3, 36.5, 36.4, 32.4, 21.6; **IR** (neat): ν 2953, 1733, 1497, 1453, 1435, 1221, 1158, 1028, 747, 697 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₃H₁₈O₂SNa]⁺: 261.0920, found: 261.0920.

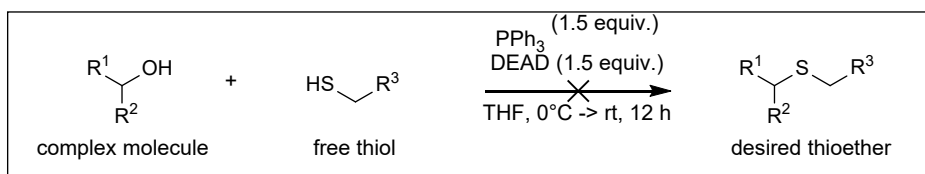


Method Description:
 Column: Lux-Cellulose1 (Chiralcel OD-H) 250x4,6mm
 Solvent System: n-Heptan+0,1%IPA/IPA 9:1
 Flow: 1 ml/min

Peak	Ret. Time	Area	Area%
1	5.398	2383393	49.995
2	5.936	2383914	50.005
Total		4767307	100.000

V. Late-stage transformation of biologically relevant molecules

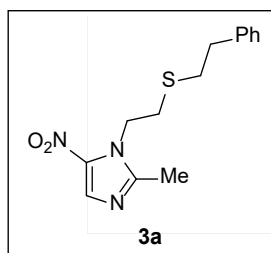
a. General procedure D: attempted thioether synthesis using thio-Mitsunobu reaction conditions



Reaction conditions were adapted from the literature with changes.³ To a stirred solution of alcohol (0.2 mmol, 1.0 equiv.) and PPh₃ (0.3 mmol, 1.5 equiv.) in dry THF (2 mL), diethyl azodicarboxylate (55 μ L, 0.3 mmol, 1.5 equiv.) was added dropwise at 0°C. Stirring continued for 10 min at 0°C, after which thiol (0.2 mmol, 1.0 equiv.) was added and the resulting mixture was stirred at rt for 12h. Volatiles were evaporated and ¹H NMR spectra of the remaining crude mixture was measured.

b. Thioether characterization

2-methyl-5-nitro-1-(2-(phenethylthio)ethyl)-1H-imidazole (3a)

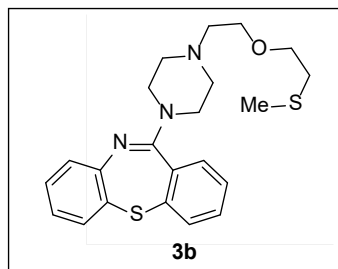


Prepared according to general procedure **C** from metronidazole (51 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 2:1). Pale yellow oil (55 mg, 0.19 mmol, 63% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.87 (s, 1H), 7.25 – 7.19 (m, 2H), 7.17 – 7.08 (m, 3H), 4.42 – 4.18 (m, 2H), 2.83 – 2.73 (m, 4H), 2.69 (ddd, J = 8.1, 6.2, 1.2 Hz, 2H), 2.41 (s, 3H); **¹³C-NMR** (101 MHz, CDCl₃): δ 150.6, 139.9, 138.4, 133.3, 128.7, 128.6, 126.7, 46.4, 36.4, 34.1, 31.9, 14.6; **IR** (neat): ν 2912, 1275, 1221,

1057, 895, 815, 769 cm⁻¹; **HRMS** (ESI⁺, m/z): [M+Na]⁺ calculated for [C₁₄H₁₇N₃O₂SNa]⁺: 314.0934, found: 314.0935.

11-(4-(2-(2-(methylthio)ethoxy)ethyl)piperazin-1-yl)dibenzo[b,f][1,4]thiazepine (3b)

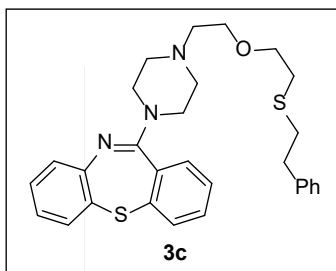


Prepared according to general procedure **C** from quetiapine (115 mg, 0.30 mmol, 1.0 equiv.) and **1f** (82 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 3:1 to 100% EtOAc). White solid (73 mg, 0.18 mmol, 59% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.47 – 7.39 (m, 1H), 7.31 (dd, J = 7.7, 1.4 Hz, 1H), 7.27 – 7.18 (m, 3H), 7.09 (ddd, J = 8.0, 7.3, 1.5 Hz, 1H), 6.99 (dd, J = 8.0, 1.3 Hz, 1H), 6.80 (td, J = 7.6, 1.5 Hz, 1H), 3.62 – 3.52

(m, 4H), 3.48 (bs, 4H), 2.66 – 2.41 (m, 8H), 2.06 (s, 3H); **¹³C-NMR** (101 MHz, CDCl₃): δ 160.9, 149.1, 140.1, 134.3, 132.28, 132.25, 130.8, 129.19, 129.12, 128.3, 128.1, 125.4, 122.9, 70.5, 68.8, 58.0, 53.6, 46.9 (bs), 33.7, 16.2; **IR** (neat): ν 2958, 1425, 1235, 789, 755, 668 cm⁻¹; **HRMS** (ESI⁺, m/z): [M+H]⁺ calculated for [C₂₂H₂₈N₃OS₂]⁺: 414.1668, found: 414.1665.

11-(4-(2-(2-(phenethylthio)ethoxy)ethyl)piperazin-1-yl)dibenzo[b,f][1,4]thiazepine (3c)

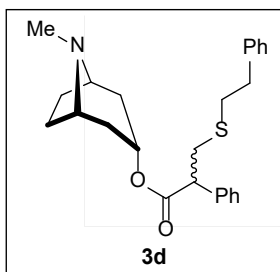


Prepared according to general procedure **C** from quetiapine (115 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 2:1). White solid (80 mg, 0.16 mmol, 53% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.46 – 7.38 (m, 1H), 7.30 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.27 – 7.16 (m, 5H), 7.16 – 7.05 (m, 4H), 6.99 (dd, *J* = 8.0, 1.4 Hz, 1H), 6.79 (td, *J* = 7.5, 1.5 Hz, 1H), 3.62 – 3.34 (m, 8H), 2.84 – 2.78 (m, 2H),

2.77 – 2.70 (m, 2H), 2.64 (td, *J* = 6.9, 2.4 Hz, 2H), 2.59 – 2.41 (m, 6H); **¹³C-NMR** (101 MHz, CDCl₃): δ 160.8, 149.1, 140.6, 140.0, 134.3, 132.26, 132.23, 130.8, 129.17, 129.10, 128.6, 128.3, 128.1, 126.5, 125.4, 122.8, 71.0, 68.8, 58.0, 53.5, 46.8 (bs), 36.5, 34.2, 31.8; **IR** (neat): ν 2959, 2930, 1453, 1264, 755, 748, 698 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+H]⁺ calculated for [C₂₉H₃₄N₃OS₂]⁺: 504.2138, found: 504.2106.

8-methyl-8-azabicyclo[3.2.1]octan-3-yl 3-(phenethylthio)-2-phenylpropanoate (3d)

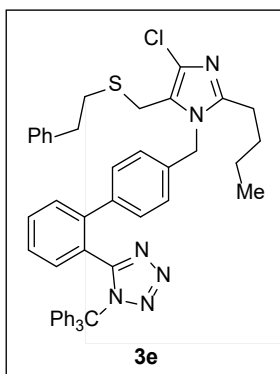


Prepared according to general procedure **C** from atropine (87 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (CH₂Cl₂/MeOH = 50:1). Yellow solid (72 mg, 0.18 mmol, 59% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.29 – 7.16 (m, 7H), 7.16 – 7.05 (m, 3H), 4.92 (t, *J* = 5.4 Hz, 1H), 3.65 (dd, *J* = 9.2, 6.2 Hz, 1H), 3.18 (dd, *J* = 13.2, 9.2 Hz, 1H), 2.99 – 2.94 (m, 1H), 2.89 – 2.84 (m, 1H), 2.84 – 2.65 (m, 5H), 2.14 (s, 3H), 2.06 – 1.90 (m, 2H), 1.86 – 1.66 (m, 3H), 1.61 (d, *J* = 14.7 Hz, 1H),

1.42 (d, *J* = 14.8 Hz, 1H), 1.37 – 1.28 (m, 1H); **¹³C-NMR** (101 MHz, CDCl₃): δ 171.8, 140.4, 137.9, 128.9, 128.6, 127.85, 127.82, 126.5, 68.4, 59.8, 59.7, 52.9, 40.4, 36.6, 36.4, 36.3, 35.1, 34.3, 25.6, 25.3; **IR** (neat): ν 1726, 1452, 1265, 1208, 1155, 1078, 1026, 749, 728, 698 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+H]⁺ calculated for [C₂₅H₃₂NO₂S]⁺: 410.2148, found: 410.2153.

5-(4'-((2-butyl-4-chloro-5-((phenethylthio)methyl)-1H-imidazol-1-yl)methyl)-[1,1'-biphenyl]-2-yl)-1-trityl-1H-tetrazole (3e)

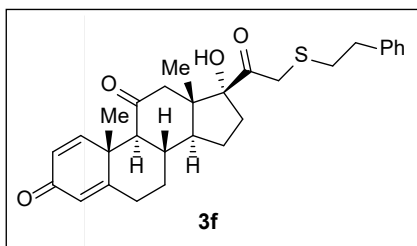


Prepared according to general procedure **C** from trityl losartan (obtained based on literature procedure)⁴ (200 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/acetone = 2:8). White foam (187 mg, 0.24 mmol, 79% yield).

¹H-NMR (700 MHz, CDCl₃): δ 7.96 (dd, *J* = 7.0, 1.4 Hz, 1H), 7.49 (td, *J* = 7.0, 1.4 Hz, 1H), 7.46 (td, *J* = 7.0, 1.4 Hz, 1H), 7.35 – 7.33 (m, 3H), 7.28 – 7.19 (m, 13H), 7.14 (d, *J* = 7.0 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 7.0 Hz, 4H), 6.70 (d, *J* = 8.4 Hz, 2H), 5.09 (s, 2H), 3.35 (s, 2H), 2.80 (t, *J* = 7.7 Hz, 2H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.50 (t, *J* = 7.7 Hz, 2H), 1.66 (q, *J* = 7.7 Hz, 2H),

1.29 (sextet, *J* = 7.7 Hz, 2H), 0.86 (t, *J* = 7.7 Hz, 3H). **¹³C-NMR** (175 MHz, CDCl₃): δ 164.0, 148.5, 141.4, 141.2, 140.4, 134.5, 130.9, 130.3, 130.1 (2 carbons), 128.7, 128.6, 128.5, 127.9, 127.8, 126.5, 126.4, 125.2, 121.4, 47.0, 36.3, 32.4, 29.9, 27.0, 24.0, 22.6, 13.9; **IR** (neat) ν 2958, 2930, 2866, 2704, 1604, 1568, 1456, 1413, 1348, 1256, 1151, 1067, 1028, 989, 906, 822, 775, 757, 726 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+H]⁺ calculated for [C₄₉H₄₆ClN₆S]⁺: 785.3188, found: 785.3185.

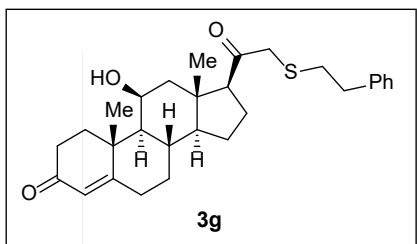
(8S,9S,10R,13S,14S,17R)-17-hydroxy-10,13-dimethyl-17-(2-(phenethylthio)acetyl)-7,8,9,10,12,13,14,15,16,17-decahydro-3H-cyclopenta[a]phenanthrene-3,11(6H)-dione (3f)



Prepared according to general procedure **C** from prednisone (108 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/acetone = 1:1). White flaky solid (124 mg, 0.26 mmol, 86% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.66 (d, *J* = 10.2 Hz, 1H), 7.30 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 6.19 (d, *J* = 10.2 Hz, 1H), 6.07 (br s, 1H), 3.52 – 3.48 (m, 1H), 3.24 – 3.20 (m, 1H), 2.89 – 2.70 (m, 8H), 2.50 (td, *J* = 12.8, 4.4 Hz, 1H), 2.43 – 2.35 (m, 2H), 2.16 – 1.88 (m, 4H), 1.75 – 1.68 (m, 1H), 1.51 – 1.45 (m, 1H), 1.42 (s, 3H), 1.33 – 1.18 (m, 1H), 0.70 (s, 3H); **¹³C-NMR** (151 MHz, CDCl₃): δ 209.3, 205.8, 186.5, 166.6, 155.3, 140.0, 128.7, 128.6, 127.8, 126.6, 124.8, 88.9, 60.2, 51.9, 50.0, 49.6, 38.7, 37.4, 36.3, 35.7, 33.8, 33.4, 32.4, 23.7, 18.9, 16.3; **IR** (neat) ν 3310, 2939, 1703, 1658, 1617, 1512, 1452, 1381, 1329, 1307, 1265, 1239, 1201, 1180, 1149, 1120, 1088, 1065, 1047, 1029, 976, 935, 615, 889, 817, 780, 732 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+H]⁺ calculated for [C₂₉H₃₅O₄S]⁺: 479.2251 found: 479.2243.

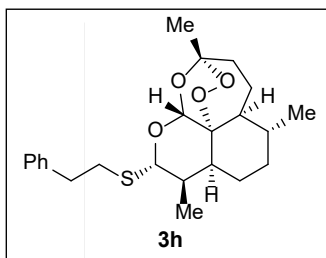
(8S,9S,10R,11S,13S,14S,17S)-11-hydroxy-10,13-dimethyl-17-(2-(phenethylthio)acetyl)-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3H-cyclopenta[a]phenanthren-3-one (3g)



Prepared according to general procedure **C** from corticosterone (104 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/acetone = 1:1). White flaky solid (136 mg, 0.29 mmol, 97% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.31 – 7.28 (m, 2H), 7.23 – 7.19 (m, 3H), 5.68 (s, 1H), 4.41 – 4.37 (m, 1H), 3.24 – 3.15 (m, 2H), 2.92 – 2.82 (m, 2H), 2.81 – 2.72 (m, 3H), 2.53 – 2.44 (m, 2H), 2.35 (dt, *J* = 16.8, 4.0 Hz, 1H), 2.27 – 2.25 (m, 1H), 2.25 – 2.15 (m, 2H), 2.12 – 2.07 (m, 1H), 2.04 – 1.94 (m, 2H), 1.89 – 1.81 (m, 1H), 1.80 – 1.69 (m, 2H), 1.63 (dd, *J* = 13.6, 3.2 Hz, 1H), 1.44 (s, 3H), 1.41 – 1.34 (m, 1H), 1.16 – 1.08 (m, 2H), 1.06 – 0.98 (m, 2H), 0.93 (s, 3H); **¹³C-NMR** (101 MHz, CDCl₃): δ 205.6, 199.5, 171.9, 128.7 (2xC), 126.6, 122.6, 68.3, 60.5, 57.6, 56.5, 48.3, 41.9, 35.8, 35.2, 34.0, 33.6, 32.7, 32.2, 31.5, 24.6, 23.6, 21.1, 16.3; **IR** (neat) ν 3439, 3409, 2929, 2855, 1701, 1659, 1618, 1497, 1452, 1414, 1389, 1347, 1270, 1232, 1186, 1152, 1119, 1092, 1046, 949, 914, 890, 870, 731 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₂₉H₃₈O₃SNa]⁺: 489.2434, found: 489.2431.

(3R,6R,8aS,9R,10R,12aR)-3,6,9-trimethyl-10-(phenethylthio)decahydro-12H-3,12-epoxy[1,2]dioxepino[4,3-*i*]isochromene (3h)



Prepared according to general procedure **C** from dihydroartemisinin (85 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/acetone = 2:8). Colorless oil (75 mg, 0.19 mmol, 62% yield).

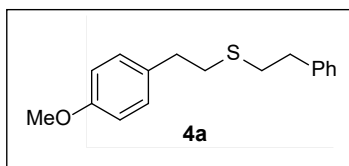
Preparation of **3h** was also attempted following general procedure **D** using dihydroartemisinin (58 mg, 0.20 mmol, 1.0 equiv.) and phenethyl mercaptan (27 μL, 0.20 mmol, 1.0 equiv.). ¹H NMR of the reaction mixture showed no formation of the desired product.

¹H-NMR (700 MHz, CDCl₃): δ 7.30 – 7.28 (m, 2H), 7.27 – 7.26 (m, 2H), 7.21 – 7.19 (m, 1H), 5.25 (s, 1H), 4.46 (d, *J* = 10.5 Hz, 1H), 3.10 – 3.04 (m, 2H), 2.99 – 2.94 (m, 1H), 2.89 – 2.85 (m, 1H), 2.65 – 2.60 (m, 1H), 2.37 (td, *J* = 14.7, 4.2 Hz, 1H), 2.03 – 2.00 (m, 1H), 1.90 – 1.86 (m, 1H), 1.72 – 1.67 (m, 2H), 1.60 – 1.57 (m, 1H), 1.51 – 1.44 (m, 1H), 1.42 (s, 3H), 1.35 – 1.22 (m, 3H), 1.05 – 0.99 (m, 1H), 0.95 (d, *J* = 6.3 Hz, 3H), 0.89 (d, *J* = 7.0 Hz, 3H); **¹³C-NMR** (175 MHz, CDCl₃): δ 141.2, 128.9, 128.5, 126.3, 104.4, 92.4, 80.7, 80.6, 51.9, 46.2, 37.5, 37.0, 36.4, 34.2, 31.7, 29.9, 26.1, 24.9, 21.4, 20.4, 15.1; **IR** (neat) ν 2924, 2870, 1452, 1377, 1278, 1229, 1195, 1181, 1151, 1127, 1094, 1085, 1069, 1034, 978, 961, 940, 927, 879, 854, 828, 730 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₂₃H₃₂O₄SNa]⁺: 427.1914, found: 427.1904.

VI. Thioetherification of primary and secondary alcohols

a. Thioether characterization

(4-methoxyphenethyl)(phenethyl)sulfane (4a)

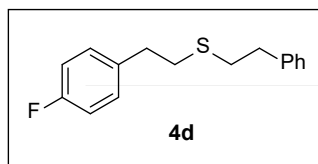


Prepared according to general procedure **C** from 2-(4-methoxyphenyl)ethan-1-ol (46 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 40:1). Colorless oil (61 mg, 0.22 mmol, 74% yield).

Alternative: The same product can be obtained according to general procedure **C** from 2-phenylethan-1-ol (37 mg, 0.30 mmol, 1.0 equiv.) and **1a** (104 mg, 0.30 mmol, 1.0 equiv.) in a slightly decreased yield (56 mg, 0.22 mmol, 68%).

¹H-NMR (400 MHz, CDCl₃): δ 7.26 – 7.19 (m, 2H), 7.16 – 7.09 (m, 3H), 7.05 – 7.00 (m, 2H), 6.79 – 6.71 (m, 2H), 3.71 (s, 3H), 2.84 – 2.63 (m, 8H); **¹³C-NMR** (101 MHz, CDCl₃): δ 158.3, 140.7, 132.8, 129.6, 128.6, 128.6, 126.5, 114.0, 55.4, 36.5, 35.6, 34.2, 33.9; **IR** (neat): ν 1511, 1496, 1452, 1243, 1176, 1033, 819, 747, 729, 697 cm⁻¹; **HRMS**-(ESI⁺, m/z): [M+Na]⁺ calculated for [C₁₇H₂₀OSNa]⁺: 295.1127, found: 295.1127.

(4-fluorophenethyl)(phenethyl)sulfane (4b)

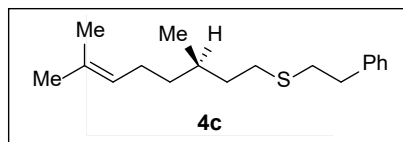


Prepared according to general procedure **C** from 2-(4-fluorophenyl)ethan-1-ol (42 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless oil (53 mg, 0.22 mmol, 67% yield).

Alternative: The same product can be obtained according to general procedure **C** from 2-phenylethan-1-ol (37 mg, 0.30 mmol, 1.0 equiv.) and **1d** (101 mg, 0.30 mmol, 1.0 equiv.) in a lower yield (36 mg, 0.14 mmol, 46%).

¹H-NMR (700 MHz, CDCl₃) δ 7.31 (t, *J* = 7.5 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 7.4 Hz, 2H), 7.14 (dd, *J* = 8.2, 5.5 Hz, 2H), 6.98 (t, *J* = 8.6 Hz, 2H), 2.96 – 2.82 (m, 4H), 2.82 – 2.71 (m, 4H); **¹³C-NMR** (101 MHz, CDCl₃): δ 161.7 (d, *J* = 244.4 Hz), 140.6, 136.3 (d, *J* = 2.6 Hz), 130.0 (d, *J* = 7.9 Hz), 128.6 (d, *J* = 2.5 Hz), 126.5, 115.4 (d, *J* = 21.1 Hz), 36.5, 35.6, 34.1, 34.0; **¹⁹F-NMR** (376 MHz, CDCl₃): δ -116.8; **IR** (neat): ν 1509, 1264, 1221, 1158, 823, 733, 700 cm⁻¹; **HRMS** (ESI⁺, m/z): [M+H]⁺ calculated for [C₁₆H₁₈FS]⁺: 261.1108, found: 261.1105.

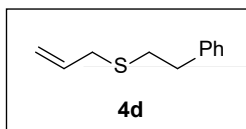
(*R*)-(3,7-dimethyloct-6-en-1-yl)(phenethyl)sulfane (4c)



Prepared according to general procedure **C** from (*R*)-β-citronellol (47 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 100:1). Pale yellow oil (62 mg, 0.23 mmol, 75% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.32 – 7.27 (m, 2H), 7.24 – 7.17 (m, 3H), 5.14 – 5.05 (m, 1H), 2.89 (dd, *J* = 9.1, 6.0 Hz, 2H), 2.77 (ddd, *J* = 8.4, 6.3, 1.1 Hz, 2H), 2.63 – 2.43 (m, 2H), 2.07 – 1.88 (m, 2H), 1.68 (d, *J* = 1.0 Hz, 3H), 1.66 – 1.62 (m, 1H), 1.60 (s, 3H), 1.60 – 1.54 (m, 1H), 1.46 – 1.28 (m, 2H), 1.16 (dddd, *J* = 13.5, 9.4, 7.6, 6.1 Hz, 1H), 0.89 (d, *J* = 6.5 Hz, 3H); **¹³C-NMR** (101 MHz, CDCl₃): δ 140.9, 131.4, 128.62, 128.61, 126.5, 124.9, 36.98, 36.96, 36.6, 33.8, 32.1, 30.2, 25.9, 25.6, 19.4, 17.8; **IR** (neat): 1452, 1264, 748, 698 cm⁻¹; **HRMS** (ESI⁺, m/z): [M+H]⁺ calculated for [C₁₈H₂₉S]⁺: 277.1984, found: 277.1983.

allyl(phenethyl)sulfane (4d)

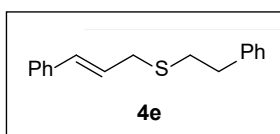


Prepared according to general procedure **C** from prop-2-en-1-ol (17 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (53 mg, 0.30 mmol, 99% yield).

Alternative: The same product can be obtained according to general procedure **C** from 2-phenylethan-1-ol (37 mg, 0.30 mmol, 1.0 equiv.) and **1e** (76 mg, 0.30 mmol, 1.0 equiv.) in a slightly decreased yield (31 mg, 0.17 mmol, 58%).

¹H-NMR (400 MHz, CDCl₃): δ 7.36 – 7.28 (m, 2H), 7.26 – 7.19 (m, 3H), 5.82 (ddt, *J* = 16.8, 9.6, 7.2 Hz, 1H), 5.17 – 5.08 (m, 2H), 3.19 – 3.13 (m, 2H), 2.89 (dd, *J* = 9.2, 6.3 Hz, 2H), 2.77 – 2.70 (m, 2H); **¹³C-NMR** (101 MHz, CDCl₃): δ 140.7, 134.6, 128.63, 128.57, 126.4, 117.1, 36.2, 35.0, 32.2; **IR** (neat): ν 1263, 764, 749, 703 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+H]⁺ calculated for [C₁₁H₁₅S]⁺: 179.0889, found: 179.0883.

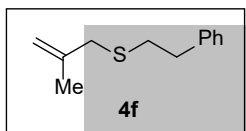
cinnamyl(phenethyl)sulfane (4e)



Prepared according to general procedure **C** from (*E*)-3-phenylprop-2-en-1-ol (40 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (67 mg, 0.26 mmol, 87% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.35 – 7.02 (m, 10H), 6.33 (d, *J* = 15.7 Hz, 1H), 6.09 (dt, *J* = 15.6, 7.4 Hz, 1H), 3.21 (dd, *J* = 7.4, 1.1 Hz, 2H), 2.80 (dd, *J* = 9.1, 6.4 Hz, 2H), 2.69 – 2.63 (m, 2H); **¹³C-NMR** (101 MHz, CDCl₃): δ 140.7, 136.8, 132.3, 128.70, 128.66, 128.57, 127.7, 126.5, 126.4, 126.1, 36.4, 34.6, 32.3; **IR** (neat): ν 1263, 749, 732, 699 cm⁻¹; **HRMS** (EI, *m/z*): [M]⁺⁺ calculated for [C₁₇H₁₈S]⁺⁺: 254.1124, found: 254.1122 ([M]⁺⁺).

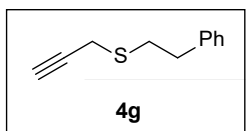
(2-methylallyl)(phenethyl)sulfane (4f)



Prepared according to general procedure **C** from 2-methylprop-2-en-1-ol (22 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (48 mg, 0.26 mmol, 87% yield).

¹H-NMR (600 MHz, CDCl₃): δ 7.35 – 7.29 (m, 2H), 7.25 – 7.19 (m, 3H), 4.90 – 4.87 (m, 1H), 4.87 – 4.84 (m, 1H), 3.15 (d, *J* = 0.7 Hz, 2H), 2.88 (dd, *J* = 9.2, 6.7 Hz, 2H), 2.70 – 2.66 (m, 2H), 1.86 – 1.81 (m, 3H); **¹³C-NMR** (150 MHz, CDCl₃): δ 141.4, 140.8, 128.62, 128.54, 126.4, 113.7, 39.5, 36.0, 32.3, 20.7; **IR** (neat): ν 1276, 1261, 764, 750 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₂H₁₆SNa]⁺: 215.0865, found: 215.0871.

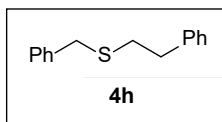
phenethyl(prop-2-yn-1-yl)sulfane (4g)



Prepared according to general procedure **C** from prop-2-yn-1-ol (17 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (48 mg, 0.27 mmol, 91% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.26 – 7.19 (m, 2H), 7.17 – 7.10 (m, 3H), 3.17 (d, *J* = 2.6 Hz, 2H), 2.90 – 2.83 (m, 4H), 2.17 (t, *J* = 2.6 Hz, 1H); **¹³C-NMR** (101 MHz, CDCl₃): δ 140.4, 128.7, 128.6, 126.6, 80.0, 71.2, 35.8, 33.1, 19.4; **IR** (neat): ν 904, 724, 647 cm⁻¹; **HRMS** (EI, *m/z*): [M]⁺⁺ calculated for [C₁₁H₁₂S]⁺⁺: 176.0654, found: 176.0657.

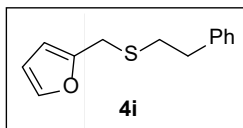
benzyl(phenethyl)sulfane (4h)



Prepared according to general procedure **C** from benzyl alcohol (32 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 99:1). Colorless liquid (64 mg, 0.28 mmol, 93% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.31 – 7.05 (m, 10H), 3.67 (s, 2H), 2.79 (t, *J* = 2.8 Hz, 2H), 2.61 (t, *J* = 2.8 Hz, 2H). According to literature data.⁵

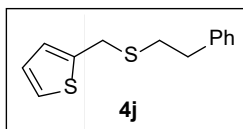
2-((phenethylthio)methyl)furan (4i)



Prepared according to general procedure **C** from furfuryl alcohol (29 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (49 mg, 0.23 mmol, 75% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.39 (dd, *J* = 1.9, 0.8 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.27 – 7.18 (m, 3H), 6.34 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.22 – 6.18 (m, 1H), 3.74 (s, 2H), 2.90 – 2.84 (m, 2H), 2.80 – 2.75 (m, 2H). According to literature data.⁵

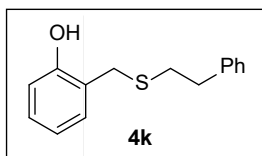
2-((phenethylthio)methyl)thiophene (4j)



Prepared according to general procedure **C** from thiophen-2-ylmethanol (34 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (59 mg, 0.25 mmol, 83% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.25 – 7.15 (m, 2H), 7.14 – 7.05 (m, 4H), 6.87 – 6.73 (m, 2H), 3.81 (s, 2H), 2.77 (dd, *J* = 9.0, 6.1 Hz, 2H), 2.65 (ddd, *J* = 8.3, 6.4, 1.1 Hz, 2H); ¹³C-NMR (101 MHz, CDCl₃): δ 142.1, 140.5, 128.62, 128.57, 126.8, 126.5, 126.2, 125.0, 36.1, 33.0, 30.8; IR (neat): ν 1263, 1095, 836, 764, 748, 736, 698 cm⁻¹; HRMS (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₃H₁₄S₂Na]⁺: 257.0429, found: 257.0422.

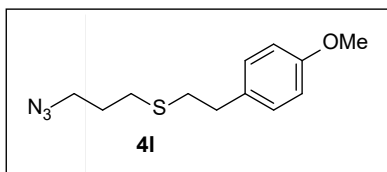
2-((phenethylthio)methyl)phenol (4k)



Prepared according to a modified general procedure **C** from 2-(hydroxymethyl)phenol (37 mg, 0.30 mmol, 1.0 equiv.), **1b** (95 mg, 0.30 mmol, 1.0 equiv.) and BTMG (136 μL, 0.66 mmol, 2.2 equiv.) Purification on silica gel (heptane/EtOAc = 10:1). Yellow oil (36 mg, 0.15 mmol, 50% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.31 – 7.27 (m, 2H), 7.24 – 7.17 (m, 2H), 7.14 – 7.09 (m, 2H), 7.06 (dd, *J* = 7.4, 1.4 Hz, 1H), 6.92 – 6.84 (m, 2H), 6.51 (s, 1H), 3.79 (s, 2H), 2.84 (dd, *J* = 8.9, 6.6 Hz, 2H), 2.66 (dd, *J* = 8.8, 6.5 Hz, 2H); ¹³C-NMR (101 MHz, CDCl₃): δ 155.6, 140.2, 130.7, 129.4, 128.7, 126.6, 122.5, 120.8, 117.4, 36.0, 33.0, 32.3; IR (neat): ν 1263, 749, 703 cm⁻¹; HRMS (ESI⁻, *m/z*): [M-H]⁻ calculated for [C₁₅H₁₅OS]⁻: 243.0849, found: 243.0849.

(3-azidopropyl)(phenethyl)sulfane (4l)

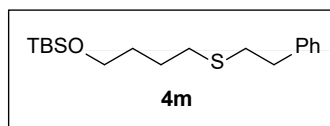


Prepared according to general procedure **C** from 3-azidopropan-1-ol (30 mg, 0.30 mmol, 1.0 equiv.) and **1a** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Pale yellow oil (35 mg, 0.16 mmol, 53% yield).

Preparation of **4l** was also attempted following general procedure **D** using 3-azidopropan-1-ol (20 mg, 0.20 mmol, 1.0 equiv.) and 2-(4-methoxyphenyl)ethanethiol (34 mg, 0.20 mmol, 1.0 equiv.). ¹H NMR of the reaction mixture showed no formation of the desired product.

¹H-NMR (700 MHz, CDCl₃) δ 7.12 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.2 Hz, 2H), 3.79 (s, 3H), 3.40 (t, *J* = 6.6 Hz, 2H), 2.83 (t, *J* = 7.7 Hz, 2H), 2.75 (t, *J* = 7.7 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 1.85 (p, *J* = 6.8 Hz, 2H); **¹³C-NMR** (176 MHz, CDCl₃): δ 158.3, 132.6, 129.6, 114.0, 55.4, 50.2, 35.5, 34.2, 29.3, 28.9; **IR** (neat): ν 2932, 2092, 1510, 1243, 1176, 1033, 819 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₂H₁₇N₃SONa]⁺: 274.0985, found: 274.0981.

***tert*-butyldimethyl(4-(phenethylthio)butoxy)silane (4m)**

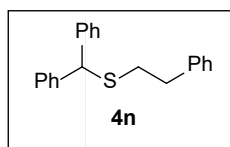


Prepared according to general procedure **C** from 4-((*tert*-butyldimethylsilyl)oxy)butan-1-ol (obtained based on literature procedure)⁶ (61 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (70.5 mg,

0.22 mmol, 72% yield).

¹H-NMR (400 MHz, CDCl₃) δ 7.34 – 7.27 (m, 2H), 7.25 – 7.14 (m, 3H), 3.62 (dd, *J* = 7.1, 5.0 Hz, 2H), 2.89 (dd, *J* = 8.8, 6.2 Hz, 2H), 2.82 – 2.73 (m, 2H), 2.60 – 2.50 (m, 2H), 1.72 – 1.55 (m, 4H), 0.90 (s, 9H), 0.05 (s, 6H); **¹³C-NMR** (101 MHz, CDCl₃): δ 140.9, 128.62, 128.60, 126.5, 62.8, 36.6, 33.7, 32.3, 32.2, 26.2, 26.1, 18.5; **IR** (neat): ν 1263, 1030, 750, 698 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₈H₃₂OSiNa]⁺: 347.1835, found: 347.1834.

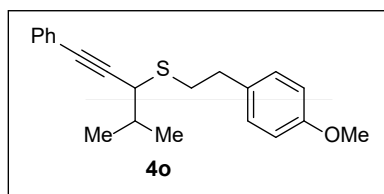
phenethyl(1-phenylethyl)sulfane (4n)



Prepared according to general procedure **C** from diphenylmethanol (55 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless oil (64 mg, 0.22 mmol, 74% yield).

¹H-NMR (400 MHz, CDCl₃): δ 7.32 (d, *J* = 7.2 Hz, 4H), 7.27 – 7.09 (m, 9H), 7.03 (d, *J* = 7.1 Hz, 2H), 5.03 (s, 1H), 2.79 – 2.73 (m, 2H), 2.59 – 2.52 (m, 2H); **¹³C-NMR** (101 MHz, CDCl₃): δ = 141.5, 140.6, 128.68, 128.68, 128.55, 128.47, 127.3, 126.4, 54.4, 36.1, 33.9; **IR** (neat): ν 1291, 1155, 802, 784, 733 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₂₁H₂₀SNa]⁺: 327.1178, found: 327.1179.

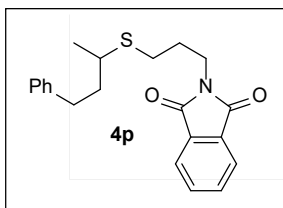
(4-methoxyphenethyl)(4-methyl-1-phenylpent-1-yn-3-yl)sulfane (4o)



Prepared according to general procedure **C** from 4-methyl-1-phenylpent-1-yn-3-ol (35 mg, 0.20 mmol, 1.0 equiv.) and **1a** (95 mg, 0.20 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Pale yellow oil (48 mg, 0.15 mmol, 74% yield).

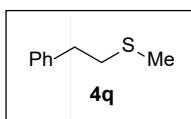
¹H-NMR (400 MHz, CDCl₃): δ 7.48 – 7.40 (m, 2H), 7.34 – 7.27 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.87 – 6.81 (m, 2H), 3.79 (s, 3H), 3.69 (d, *J* = 5.4 Hz, 1H), 3.09 – 2.84 (m, 4H), 2.04 (dq, *J* = 13.3, 6.7 Hz, 1H), 1.15 (dd, *J* = 8.8, 6.7 Hz, 6H); **¹³C-NMR** (101 MHz, CDCl₃): δ 158.3, 132.9, 131.8, 129.6, 128.4, 128.1, 123.4, 114.0, 87.9, 85.1, 55.4, 43.1, 35.6, 33.6, 33.1, 21.2, 19.4; **IR** (neat): ν 2957, 1611, 1511, 1442, 1300, 1245, 1176, 1034, 819, 755, 690 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₂₁H₂₄OSNa]⁺: 347.1440, found: 347.1423.

2-(3-((4-phenylbutan-2-yl)thio)propyl)isoindoline-1,3-dione (4p)



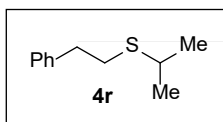
Prepared according to general procedure **C** from 4-phenylbutan-2-ol (30 mg, 0.20 mmol, 1.0 equiv.) and **1j** (80 mg, 0.20 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 25:2). Pale yellow oil (23.5 mg, 0.7 mmol, 33% yield). **¹H-NMR** (600 MHz, CDCl₃): δ 7.87 – 7.83 (m, 2H), 7.74 – 7.69 (m, 2H), 7.28 – 7.24 (m, 2H), 7.19 – 7.14 (m, 3H), 3.79 (t, *J* = 7.1 Hz, 2H), 2.78 – 2.69 (m, 3H), 2.56 (t, *J* = 7.4 Hz, 2H), 1.98 – 1.92 (m, 2H), 1.89 – 1.74 (m, 2H), 1.30 (d, *J* = 6.8 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃): δ 168.5, 142.0, 134.1, 132.3, 128.6, 128.5, 126.0, 123.4, 39.6, 38.7, 37.5, 33.3, 28.9, 27.7, 21.7; **IR** (neat): ν 3001, 1704, 1644, 1611, 1538, 1413, 1296, 1277, 844, 780, 681 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₂₁H₂₃NO₂SNa]⁺: 376.1342, found: 376.1340.

methyl(phenethyl)sulfane (4q)



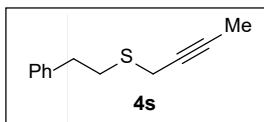
Prepared according to general procedure **C** from 2-phenylethyl alcohol (37 mg, 0.30 mmol, 1.0 equiv.) and **1f** (82 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless oil (64 mg, 0.22 mmol, 73% yield). **¹H NMR** (400 MHz, CDCl₃) δ 7.34 – 7.28 (m, 2H), 7.22 (dd, *J* = 7.1, 4.9 Hz, 2H), 2.91 (dd, *J* = 9.1, 6.4 Hz, 2H), 2.78 – 2.73 (m, 2H), 2.13 (s, 3H). According to literature data.⁷

isopropyl(phenethyl)sulfane (4r)



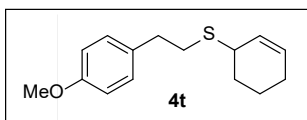
Prepared according to general procedure **C** from 2-phenylethyl alcohol (37 mg, 0.30 mmol, 1.0 equiv.) and **1g** (77 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless oil (40 mg, 0.22 mmol, 74% yield). **¹H NMR** (400 MHz, CDCl₃) δ 7.34 – 7.28 (m, 2H), 7.25 – 7.19 (m, 2H), 2.97 (hept, *J* = 6.7 Hz, 1H), 2.90 – 2.85 (m, 2H), 2.84 – 2.77 (m, 2H), 1.29 (d, *J* = 6.7 Hz, 6 H). According to literature data.⁸

but-2-yn-1-yl(phenethyl)sulfane (4s)



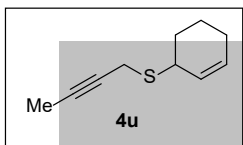
Prepared according to general procedure **C** from 2-phenylethyl alcohol (37 mg, 0.30 mmol, 1.0 equiv.) and **1h** (80 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Pale yellow oil (42 mg, 0.22 mmol, 73% yield). **¹H-NMR** (400 MHz, CDCl₃): δ 7.26 – 7.20 (m, 2H), 7.18 – 7.10 (m, 3H), 3.16 (q, *J* = 2.5 Hz, 2H), 2.85 (s, 4H), 1.76 (dd, *J* = 3.3, 1.7 Hz, 3H). According to literature data.⁹

cyclohex-2-en-1-yl(4-methoxyphenethyl)sulfane (4t)



Prepared according to general procedure **C** from 2-(4-methoxyphenyl)ethan-1-ol (46 mg, 0.30 mmol, 1.0 equiv.) and **1i** (88 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/CH₂Cl₂ = 70:30). Colorless liquid (69 mg, 0.24 mmol, 80% yield). **¹H NMR** (400 MHz, CDCl₃) δ 7.17 – 7.10 (m, 2H), 6.93 – 6.78 (m, 2H), 5.84 – 5.74 (m, 1H), 5.73 – 5.67 (m, 1H), 3.79 (s, 2H), 3.44 – 3.31 (m, 1H), 2.87 – 2.74 (m, 4H), 2.03 – 1.91 (m, 3H), 1.91 – 1.80 (m, 1H), 1.79 – 1.70 (m, 1H), 1.64 – 1.54 (m, 1H); **¹³C NMR** (101 MHz, CDCl₃) δ 158.3, 133.0, 129.8, 129.5, 128.0, 114.0, 55.4, 41.0, 35.9, 32.9, 29.7, 25.0, 20.1; **IR** (neat) ν 3024, 2927, 2833, 1610, 1586, 1510, 1441, 1300, 1243, 1176, 1102, 1034, 871, 819, 751, 722, 634 cm⁻¹; **HRMS** (ESI⁺, *m/z*): [M+Na]⁺ calculated for [C₁₅H₂₀OSNa]⁺: 271.1127, found: 271.1130.

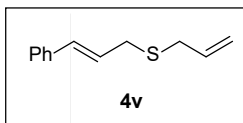
but-2-yn-1-yl(cyclohex-2-en-1-yl)sulfane (4u)



Prepared according to general procedure **C** from 2-butyne-1-ol (21 mg, 0.30 mmol, 1.0 equiv.) and **1i** (88 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Yellow liquid (44 mg, 0.27 mmol, 89% yield).

¹H-NMR (400 MHz, CDCl₃) δ 5.85 – 5.77 (m, 1H), 5.71 (ddt, *J* = 9.9, 3.7, 1.9 Hz, 1H), 3.63 – 3.54 (m, 1H), 3.24 (qq, *J* = 16.5, 2.5 Hz, 2H), 2.05 – 1.91 (m, 3H), 1.86 (ddd, *J* = 12.5, 6.3, 3.1 Hz, 1H), 1.82 (t, *J* = 2.5 Hz, 3H), 1.81 – 1.75 (m, 1H), 1.67 – 1.54 (m, 1H); **¹³C-NMR** (101 MHz, CDCl₃): δ 130.3, 127.2, 78.8, 75.4, 40.5, 28.9, 25.1, 19.8, 19.2, 3.8; **IR** (neat): ν 1264, 733, 698 cm⁻¹; **HRMS** (EI, *m/z*): [M]⁺⁺ calculated for [C₁₀H₁₄S]⁺⁺: 166.0811, found: 166.0812.

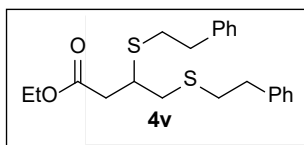
allyl(cinnamyl)sulfane (4v)



Prepared according to general procedure **C** from (*E*)-3-phenylprop-2-en-1-ol (40 mg, 0.30 mmol, 1.0 equiv.) and **1e** (76 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless liquid (40 mg, 0.21 mmol, 70% yield).

¹H-NMR (400 MHz, CDCl₃) δ 7.38 (dd, *J* = 5.3, 3.4 Hz, 2H), 7.35 – 7.29 (m, 2H), 7.27 – 7.19 (m, 1H), 6.43 (d, *J* = 15.7 Hz, 1H), 6.17 (dt, *J* = 15.7, 7.3 Hz, 1H), 5.88 – 5.73 (m, 1H), 5.15 (s, 1H), 5.13 – 5.10 (m, 1H), 3.28 (dd, *J* = 7.3, 1.2 Hz, 2H), 3.14 (dt, *J* = 7.1, 1.0 Hz, 2H); **¹³C-NMR** (101 MHz, CDCl₃): δ 136.9, 134.5, 132.6, 128.7, 127.7, 126.4, 126.0, 117.4, 33.7, 33.2; **IR** (neat): ν 1276, 1261, 764, 751 cm⁻¹; **HRMS** (EI, *m/z*): [M]⁺⁺ calculated for [C₁₂H₁₄S]⁺⁺: 190.0811, found: 190.0815.

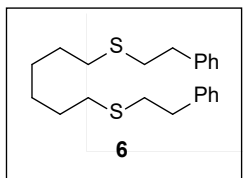
ethyl 3,4-bis(phenethylthio)butanoate (4w)



Prepared according to general procedure **C** from ethyl (*E*)-4-hydroxybut-2-enoate (obtained based on literature procedure)¹⁰ (**5c**, 39 mg, 0.30 mmol, 1.0 equiv.) and **1b** (95 mg, 0.30 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 97:3). Colorless liquid (41 mg, 0.11 mmol, 70% yield).

¹H-NMR (600 MHz, CDCl₃) δ 7.29 (t, *J* = 7.5 Hz, 4H), 7.24 – 7.18 (m, 6H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.27 – 3.18 (m, 1H), 2.94 – 2.86 (m, 6H), 2.86 – 2.77 (m, 4H), 2.74 – 2.65 (m, 1H), 2.51 (dd, *J* = 16.0, 8.1 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 3H); **¹³C-NMR** (151 MHz, CDCl₃): δ 171.6, 140.45, 140.43, 128.65 (6C), 128.63 (2C), 126.58 (2C), 60.9, 41.9, 39.3, 38.2, 36.50, 36.45, 34.5, 33.1, 14.4; **IR** (neat): ν 2914, 1729, 1204, 1136, 1030, 731, 696 cm⁻¹; **HRMS** (EI, *m/z*): [M+Na]⁺ calculated for [C₂₂H₂₈O₂S₂Na]⁺: 411.1423, found: 411.1422.

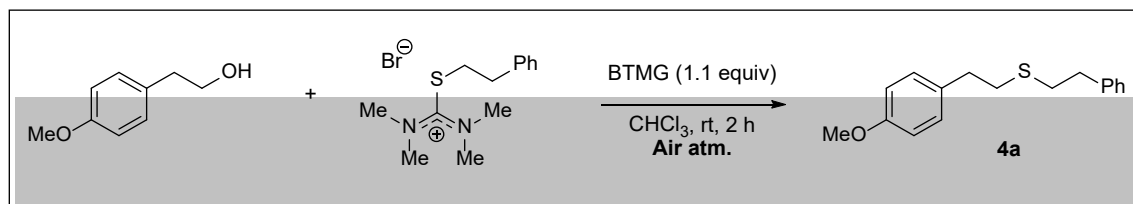
1,6-bis(phenethylthio)hexane (6)



Prepared following general procedure **C** from 6-bromohexan-1-ol (36 mg, 0.2 mmol, 1.0 equiv.) and **1b** (64 mg, 0.2 mmol, 1.0 equiv.). Purification on silica gel (heptane/EtOAc = 50:1). Colorless oil (11 mg, 0.03 mmol, 32% yield).

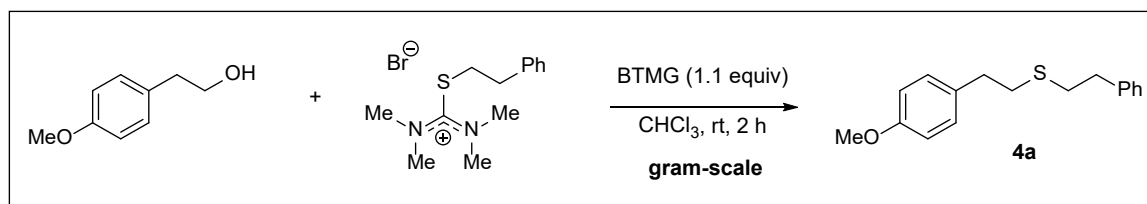
¹H-NMR (400 MHz, CDCl₃) δ 7.33 – 7.27 (m, 4H), 7.21 (t, *J* = 6.6 Hz, 6H), 2.88 (dd, *J* = 9.2, 6.2 Hz, 4H), 2.81 – 2.71 (m, 4H), 2.58 – 2.46 (m, 4H), 1.64 – 1.55 (m, 4H), 1.44 – 1.33 (m, 4H); **¹³C-NMR** (101 MHz, CDCl₃): δ 140.8, 128.6(4C), 126.5, 36.6, 33.8, 32.4, 29.7, 28.6; **IR** (neat): ν 3085, 3062, 3026, 3001, 2925, 2854, 1603, 1496, 1453, 1305, 1266, 1253, 1223, 1030, 739, 698 cm⁻¹; **HRMS** (EI, *m/z*): [M+Na]⁺ calculated for [C₂₂H₃₀S₂Na]⁺: 381.1681, found: 381.1675.

b. Synthesis of 4a under open-to-air conditions.



BTMG (2-*tert*-butyl-1,1,3,3-tetramethylguanidine, Barton's base) (68 μL , 0.33 mmol, 1.1 equiv.) was added dropwise to a solution of 2-(4-methoxyphenyl)ethan-1-ol (46 mg, 0.30 mmol, 1.0 equiv.) and 1,1,3,3-tetramethyl-2-phenethylisothiuronium bromide (95 mg, 0.30 mmol, 1.0 equiv.) in dry CHCl_3 (2.2 mL) under air atmosphere (balloon filled with air on the septum cap). The reaction mixture was then stirred at rt for 2 h, before excess base was quenched by addition of a saturated solution of NH_4Cl . The mixture was then extracted with CH_2Cl_2 (3x), the combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (heptane/EtOAc = 40:1) to provide **4a** as a colorless oil (61 mg, 0.22 mmol, 74% yield).

c. Gram-scale synthesis of 4a.

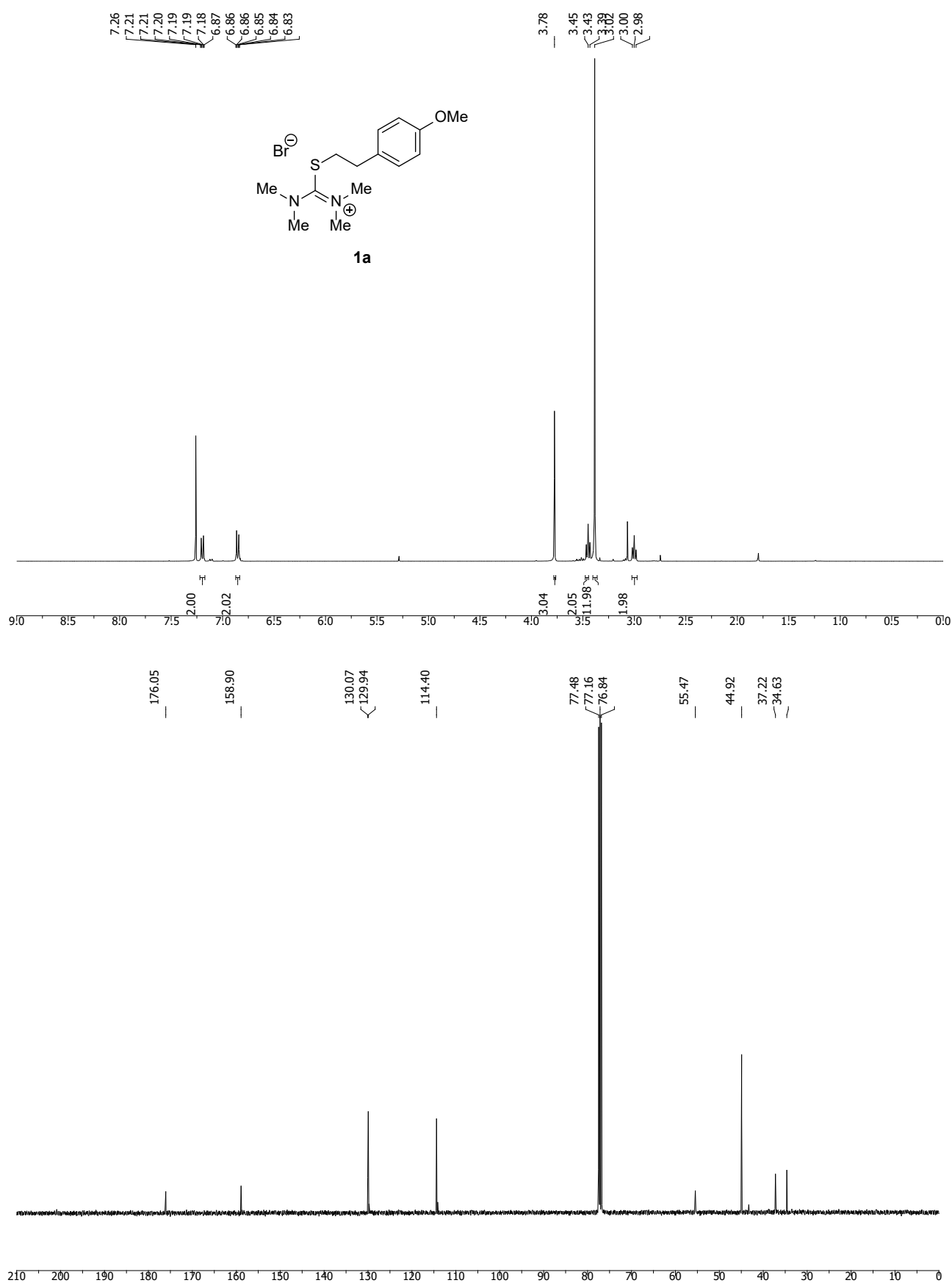


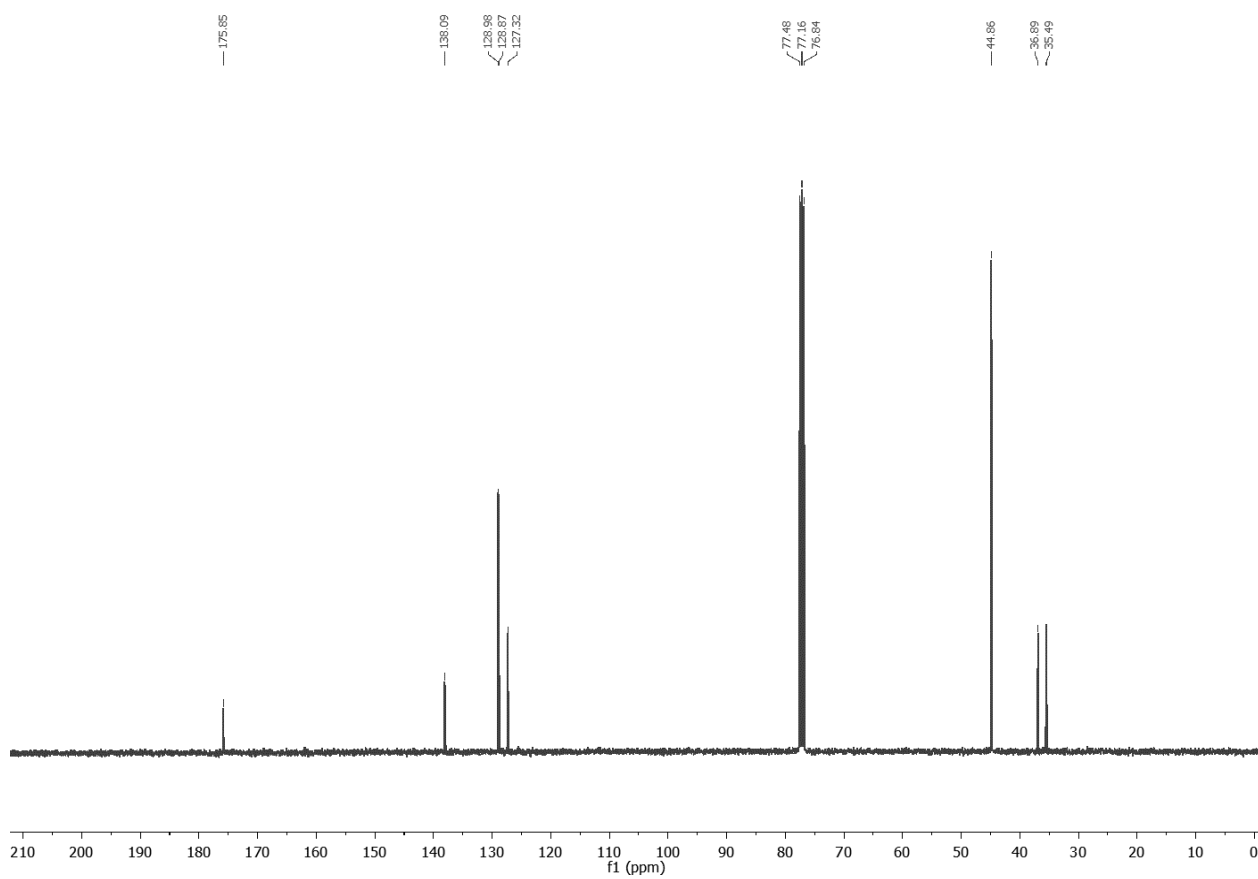
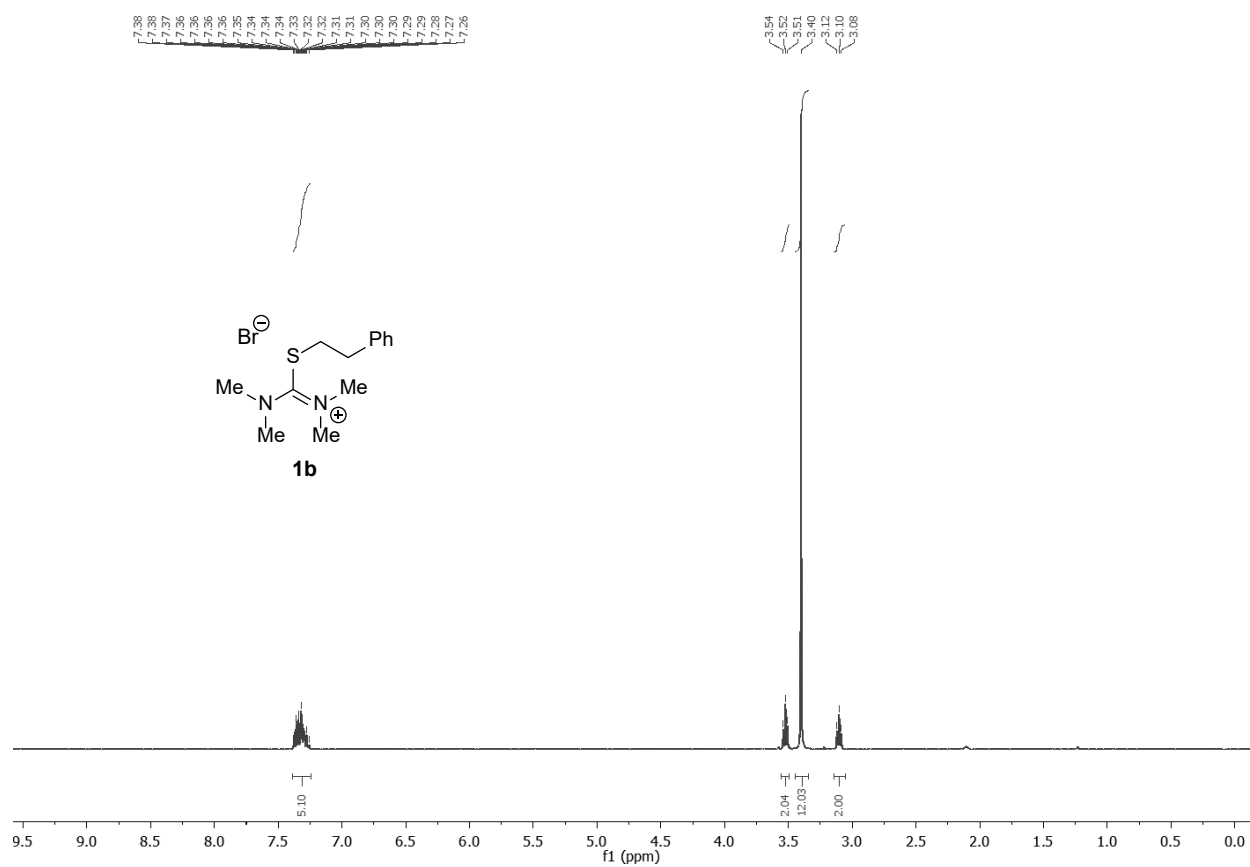
BTMG (2-*tert*-butyl-1,1,3,3-tetramethylguanidine, Barton's base) (1.5 mL, 7.2 mmol, 1.1 equiv.) was added dropwise to a solution of 2-(4-methoxyphenyl)ethan-1-ol (1.0 g, 6.6 mmol, 1.0 equiv.) and 1,1,3,3-tetramethyl-2-phenethylisothiuronium bromide (2.1 g, 6.6 mmol, 1.0 equiv.) in dry CHCl_3 (44 mL) under an Ar atmosphere. The reaction mixture was then stirred at rt for 2 h, before excess base was quenched by addition of a saturated solution of NH_4Cl (75 mL). The mixture was then extracted with CH_2Cl_2 (3x), the combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (heptane/EtOAc = 40:1) to provide **4a** as a colorless oil (1.37 g, 5.0 mmol, 74% yield).

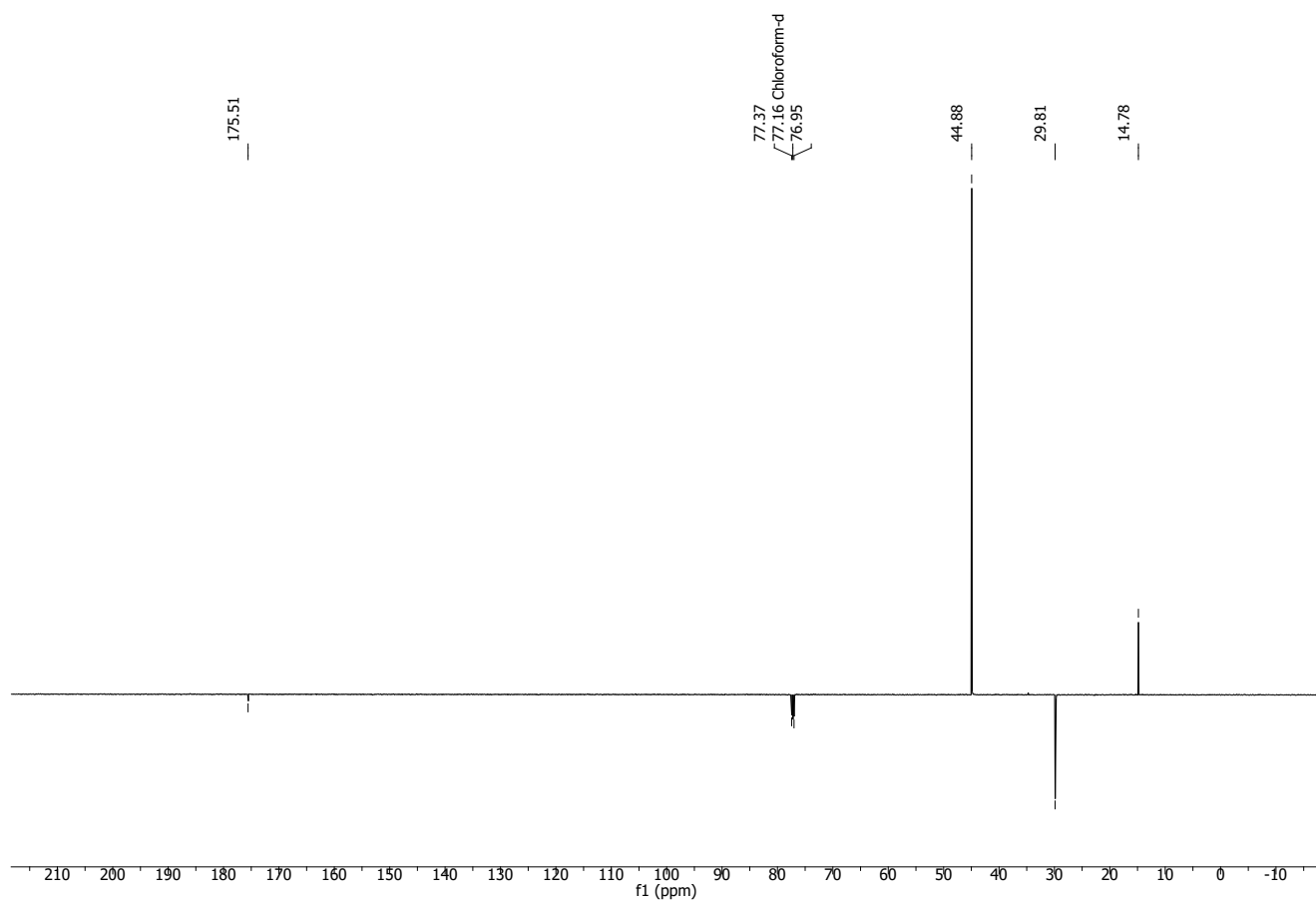
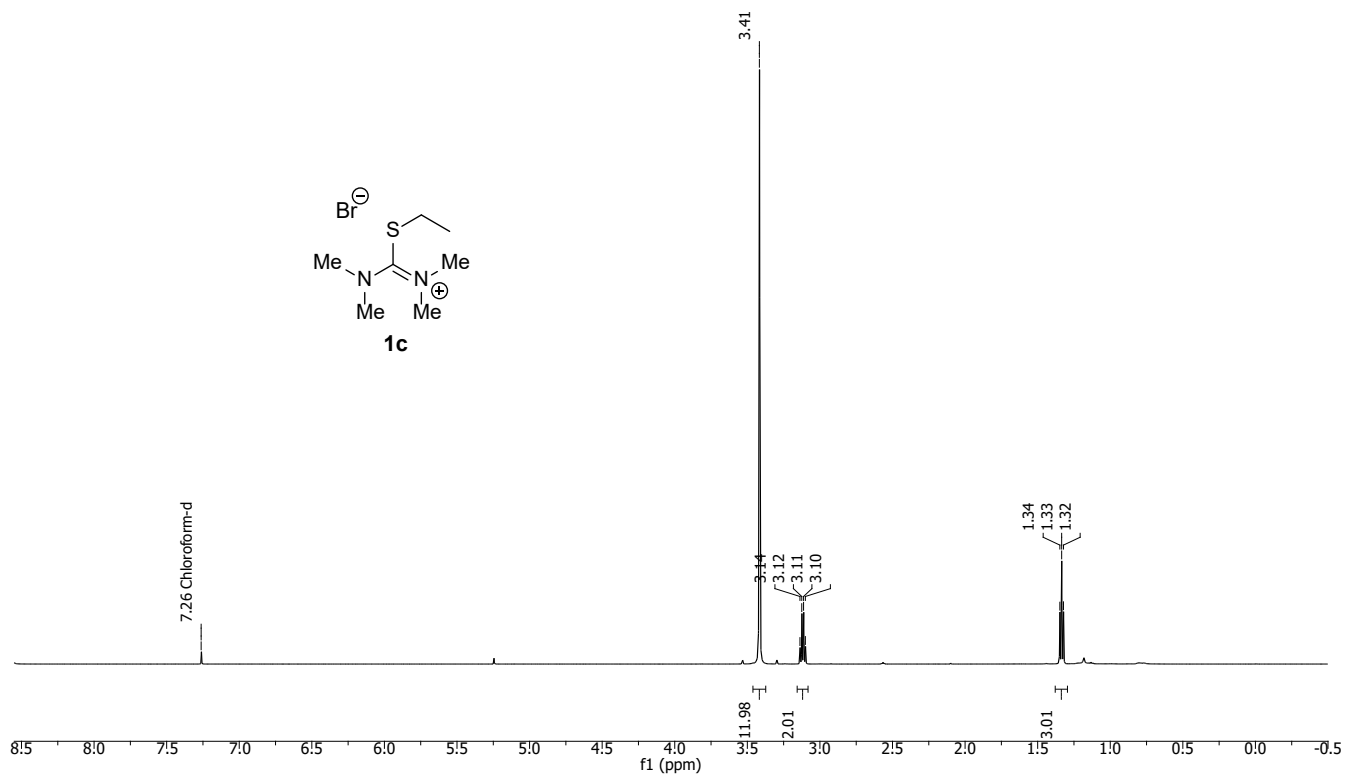
VII. References

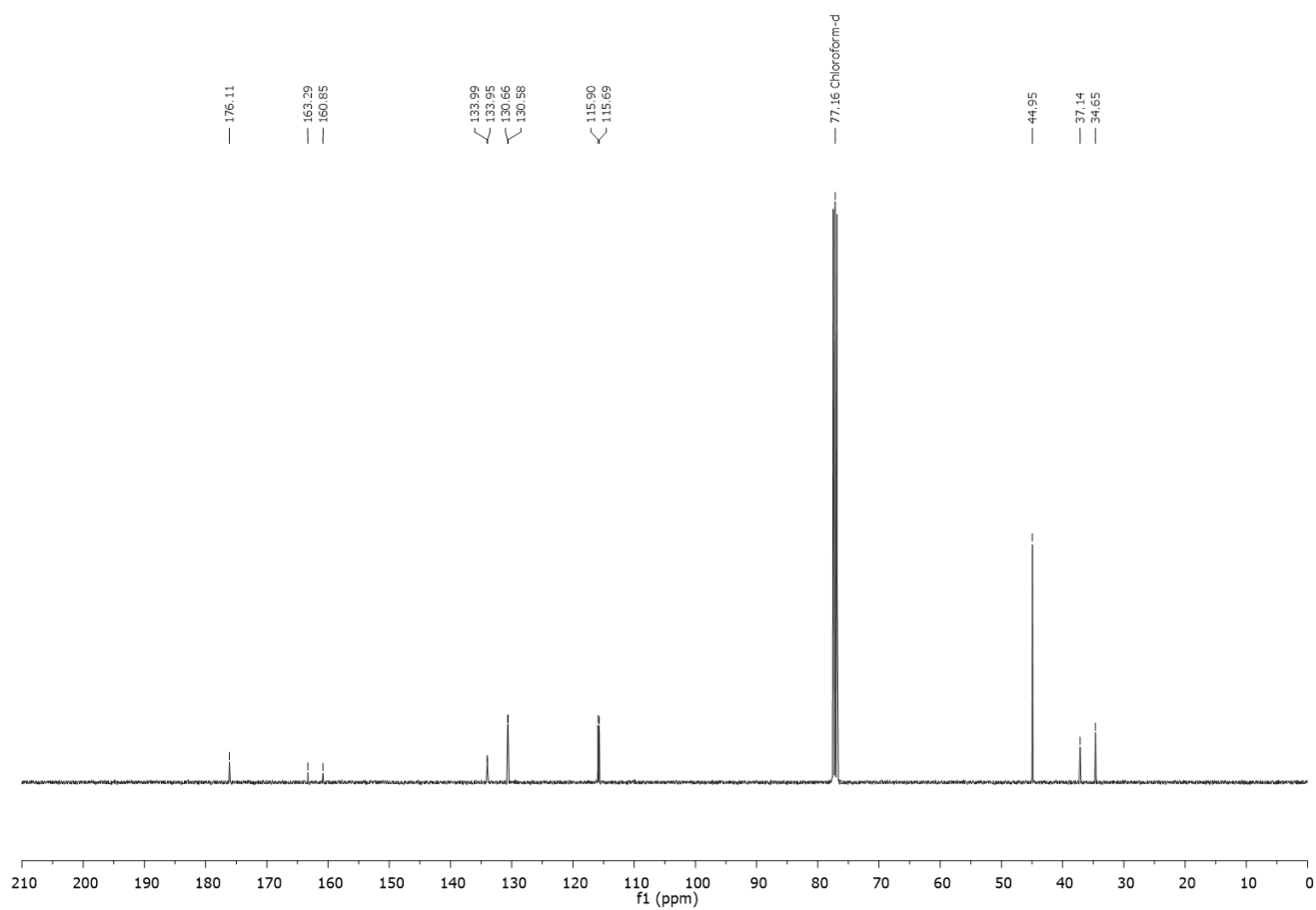
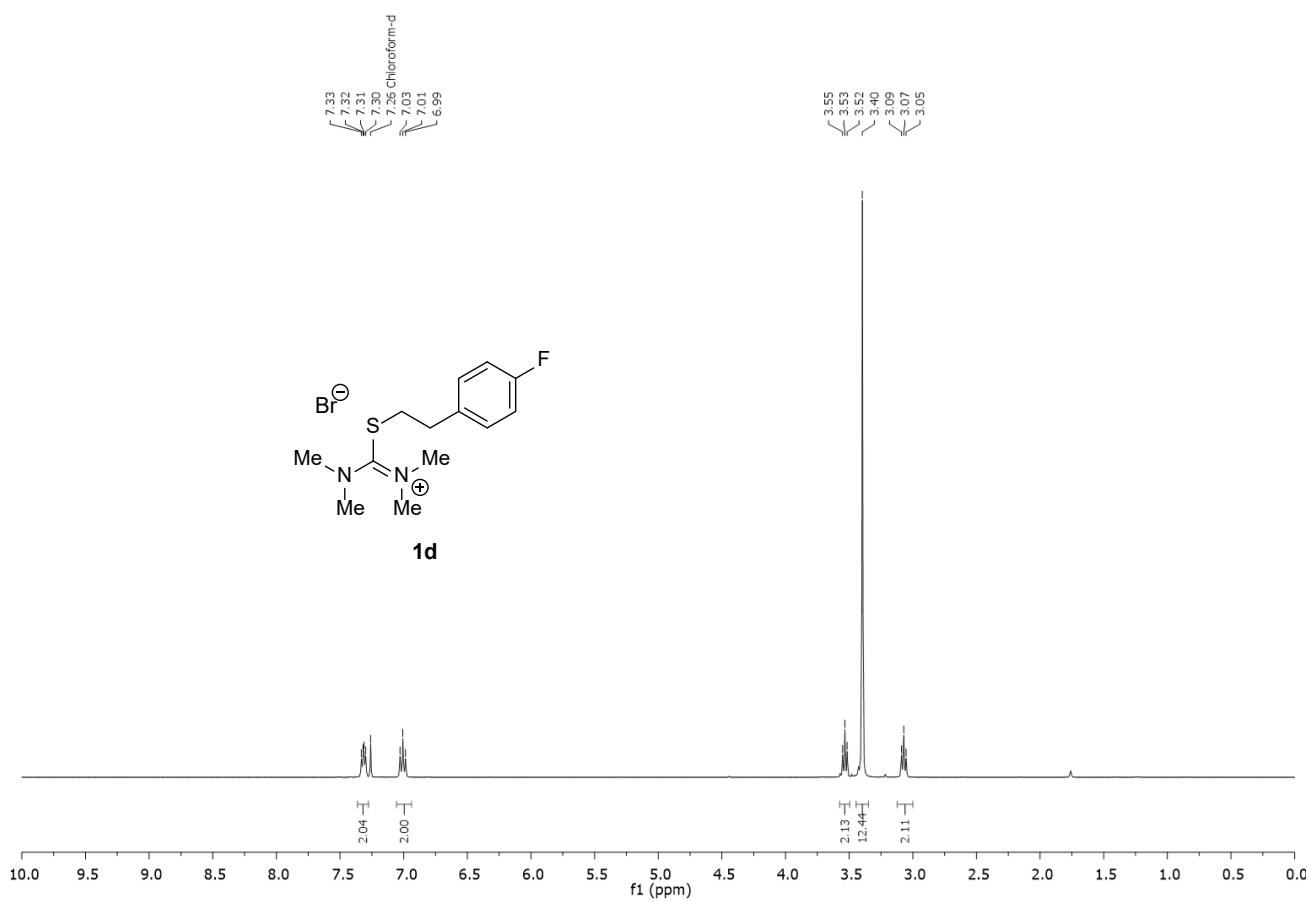
- ¹ S. Tong, M. Zhang, S. Wang, R. Yin, R. Yu, S. Wan, T. Jiang and L. Zhang, *Eur. J. Med. Chem.*, 2016, **123**, 849.
- ² S. S. Khokhar and T. Wirth, *Eur. J. Org. Chem.*, 2004, 4567.
- ³ Q. Yao and Y. Zhang, *J. Am. Chem. Soc.*, 2004, **126**, 74.
- ⁴ T. Hadizad, J. Collins, R. E. Antoun, R. S. Beanlands and J. N. DaSilva, *J. Label Compd. Radiopharm.*, 2011, **54**, 754.
- ⁵ D. Limnios and C. G. Kokotos, *Adv. Synth. Catal.*, 2017, **359**, 323.
- ⁶ A. Throup, L. H. Patterson and H. M. Sheldrake, *Org. Biomol. Chem.*, 2016, **14**, 9554.
- ⁷ S. K. Kristensen, S. L. R. Laursen, E. Taarning and T. Skrydstrup, *Angew. Chem. Int. Ed.*, 2018, **57**, 13887.
- ⁸ R. S. Glass, J. L. Boecker and M. E. Jatcko, *Tetrahedron*, 1989, **45**, 1263.
- ⁹ C. S. Holzwarth, I. Alt and B. Pletker, *Angew. Chem. Int. Ed.*, 2012, **51**, 5351.
- ¹⁰ L. Hutchings-Goetz, C. Yang and T. N. Snaddon, *ACS Catal.*, 2018, **8**, 10537.

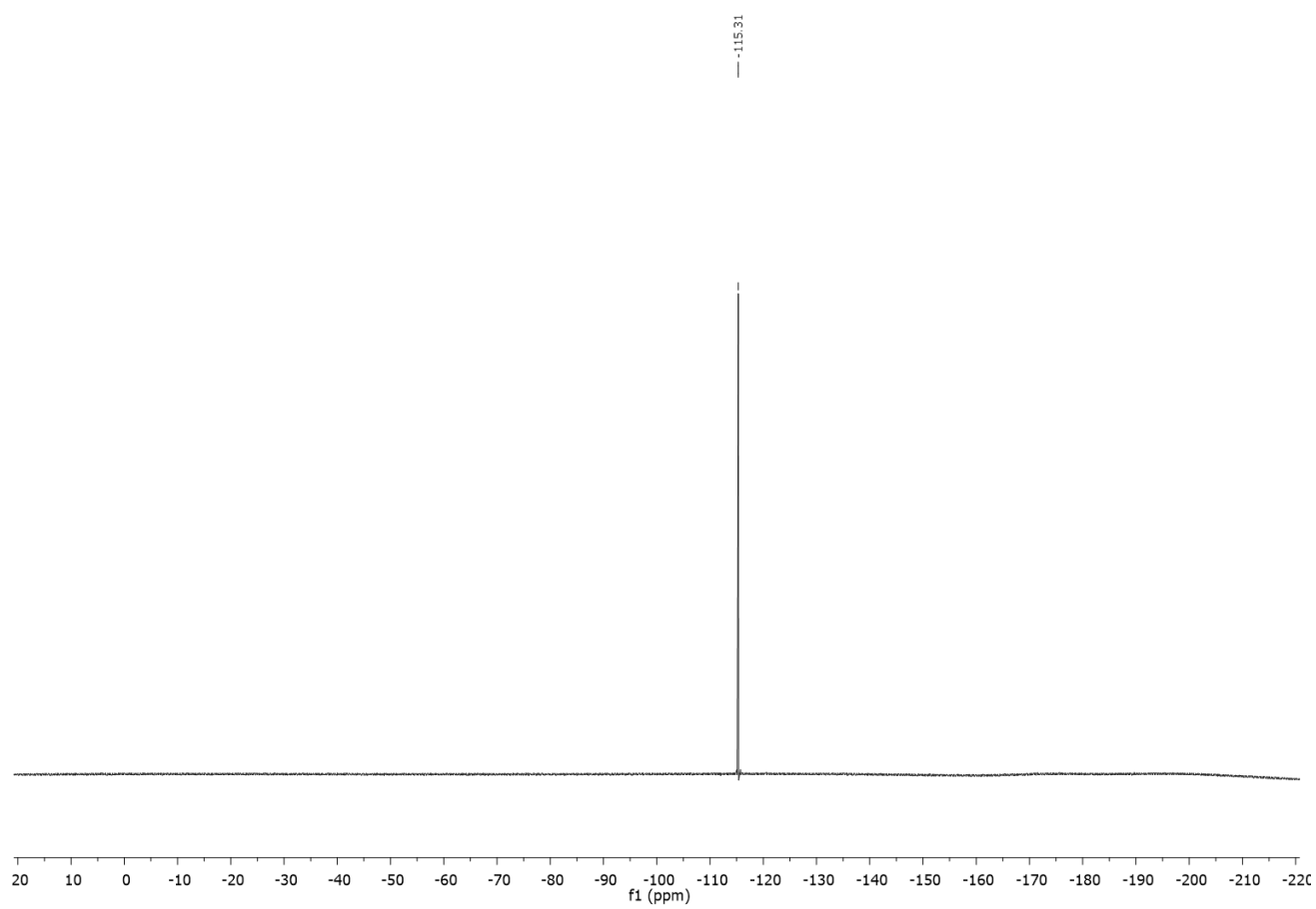
VIII. NMR spectra

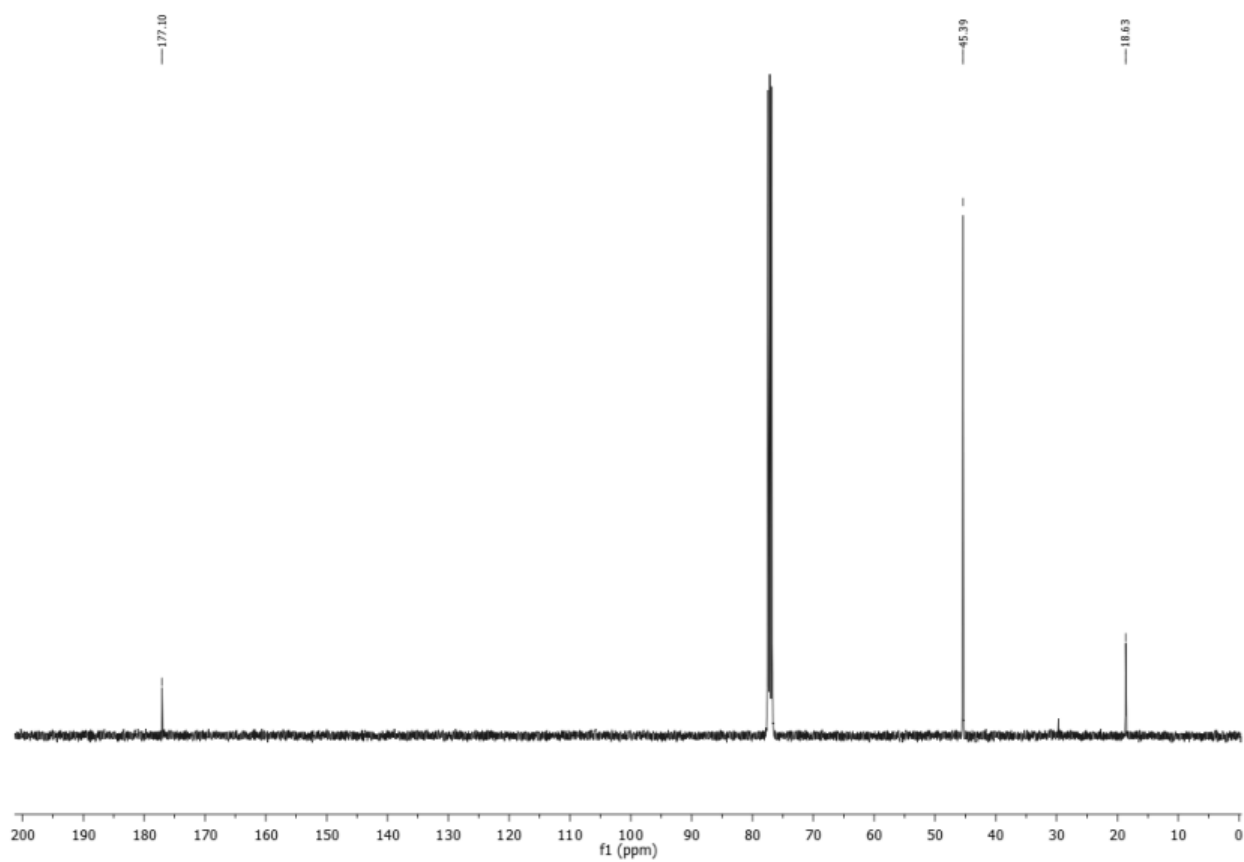
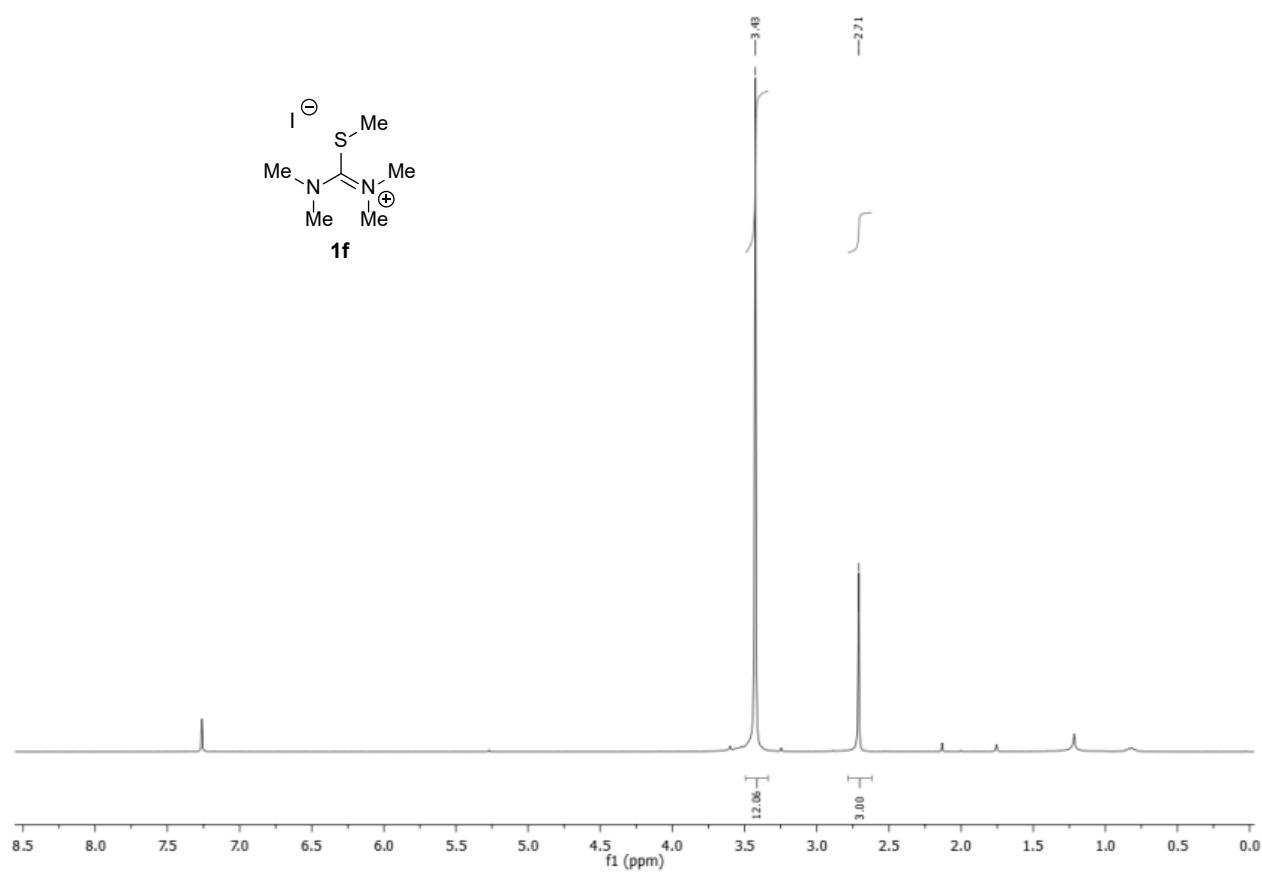


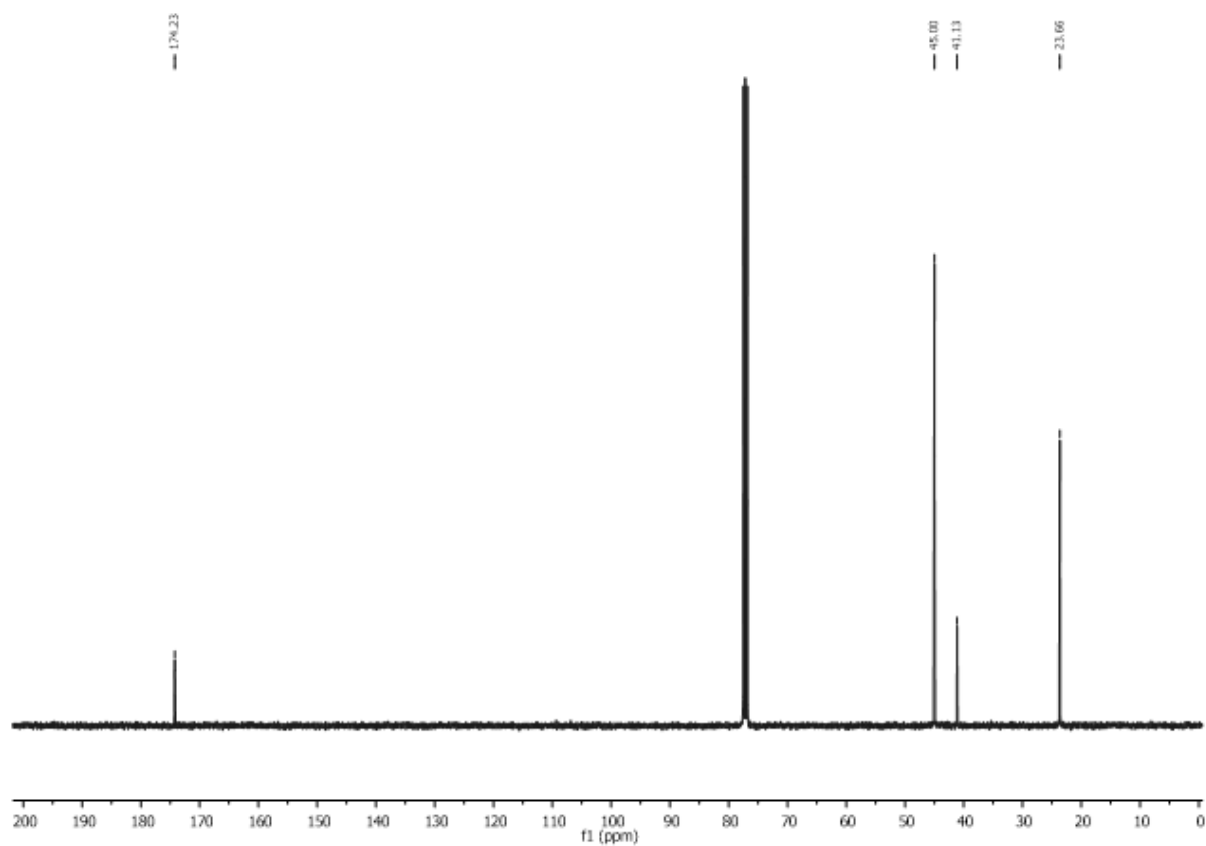
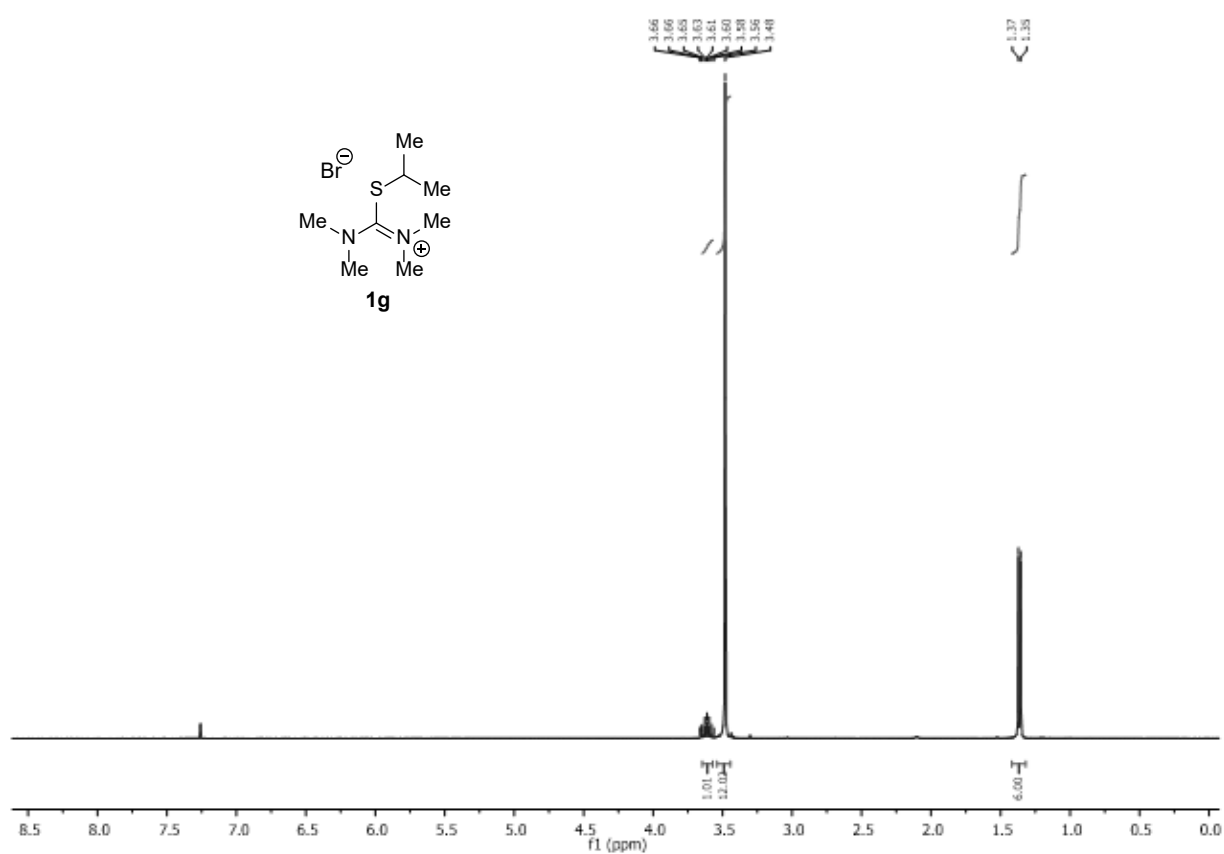


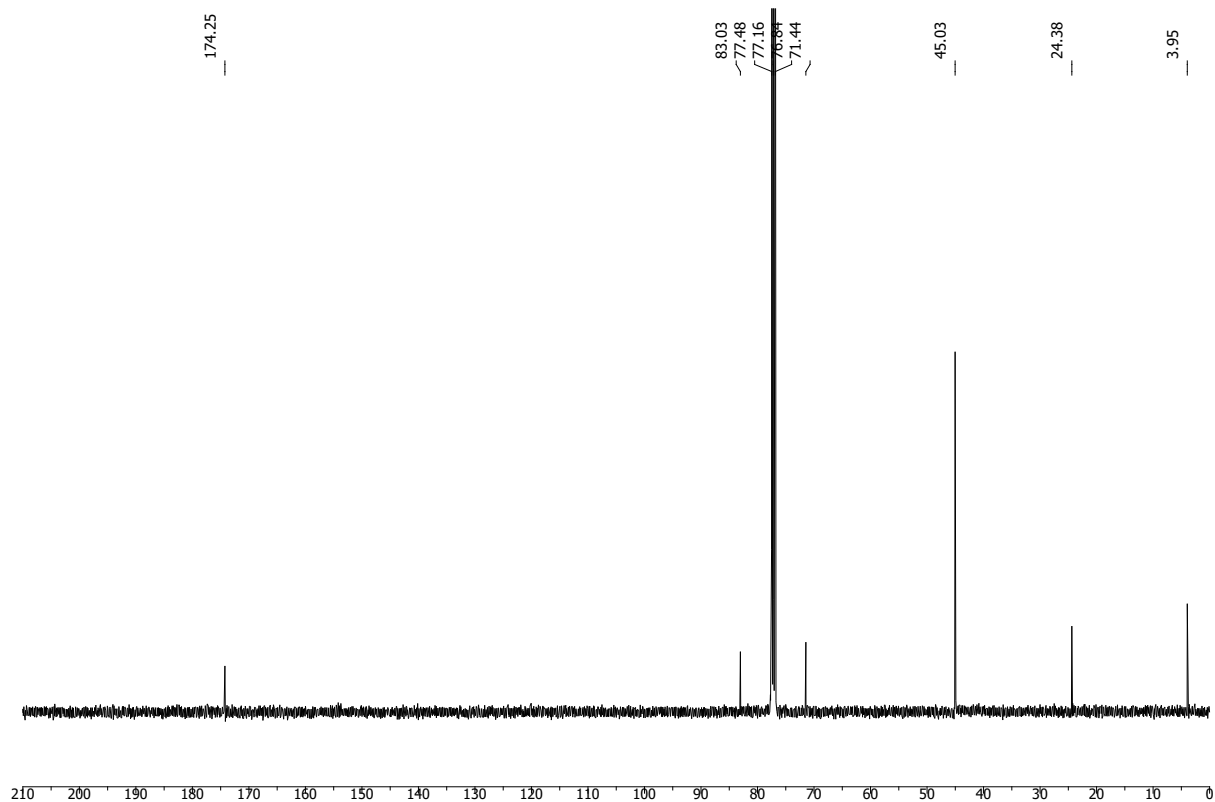
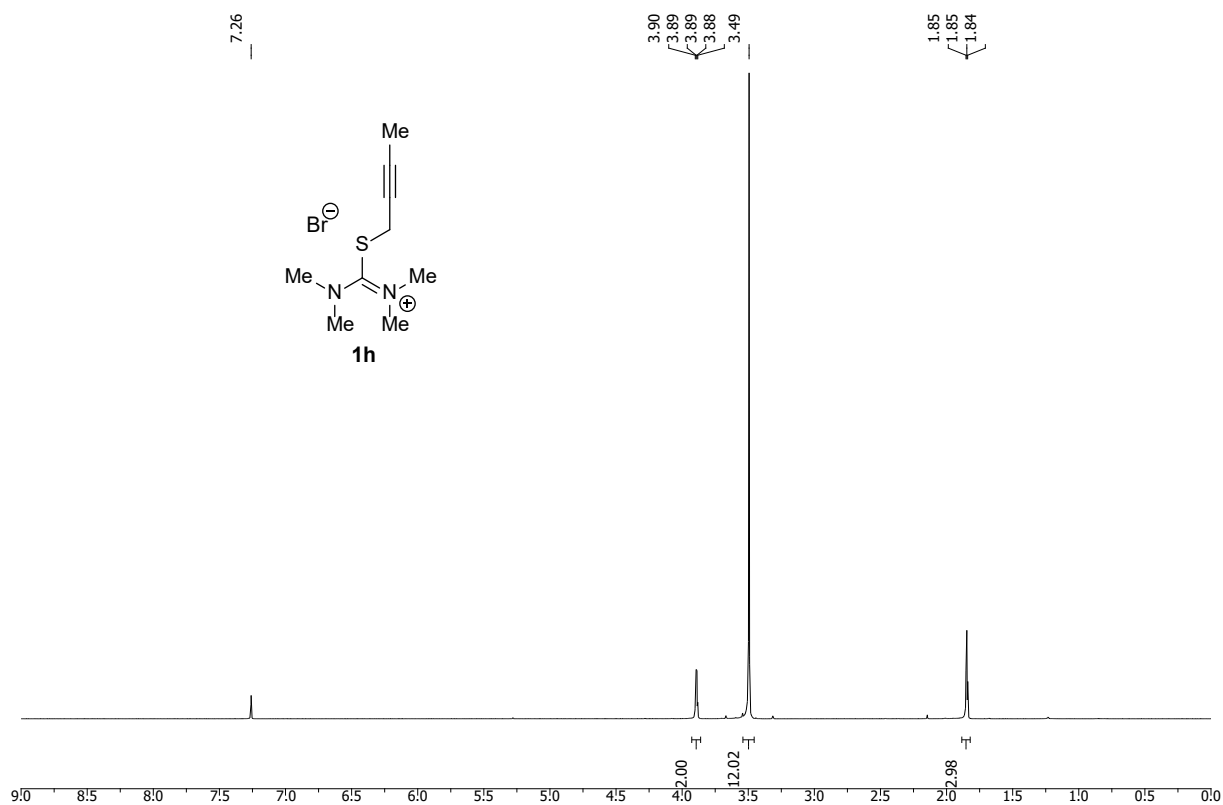


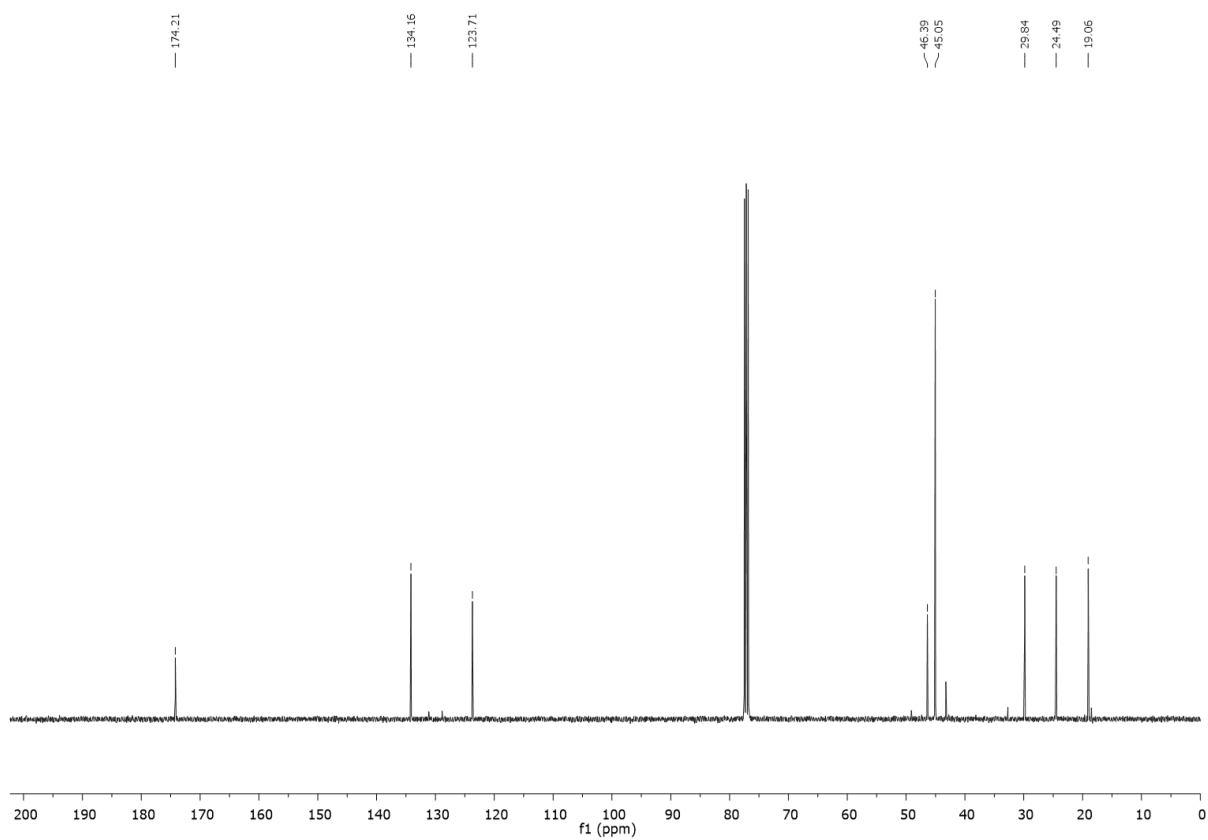
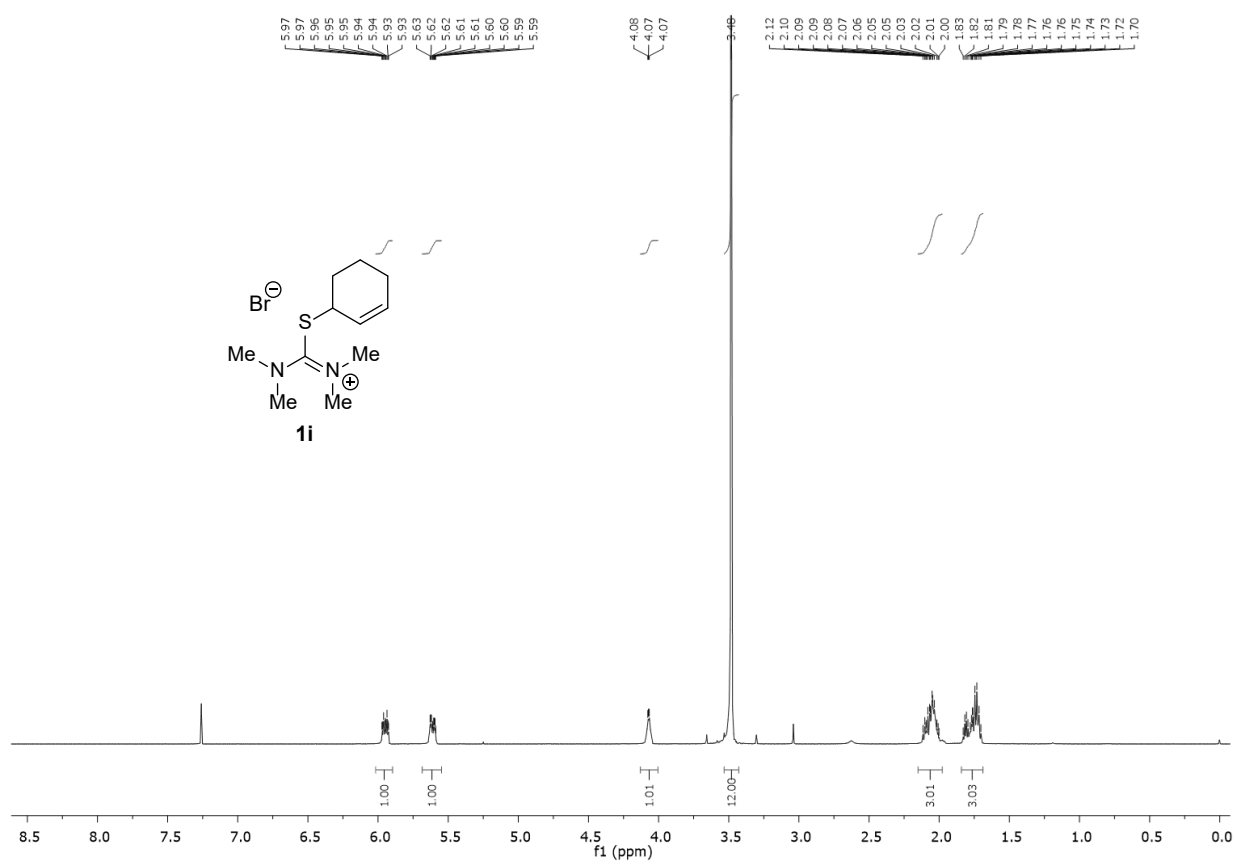


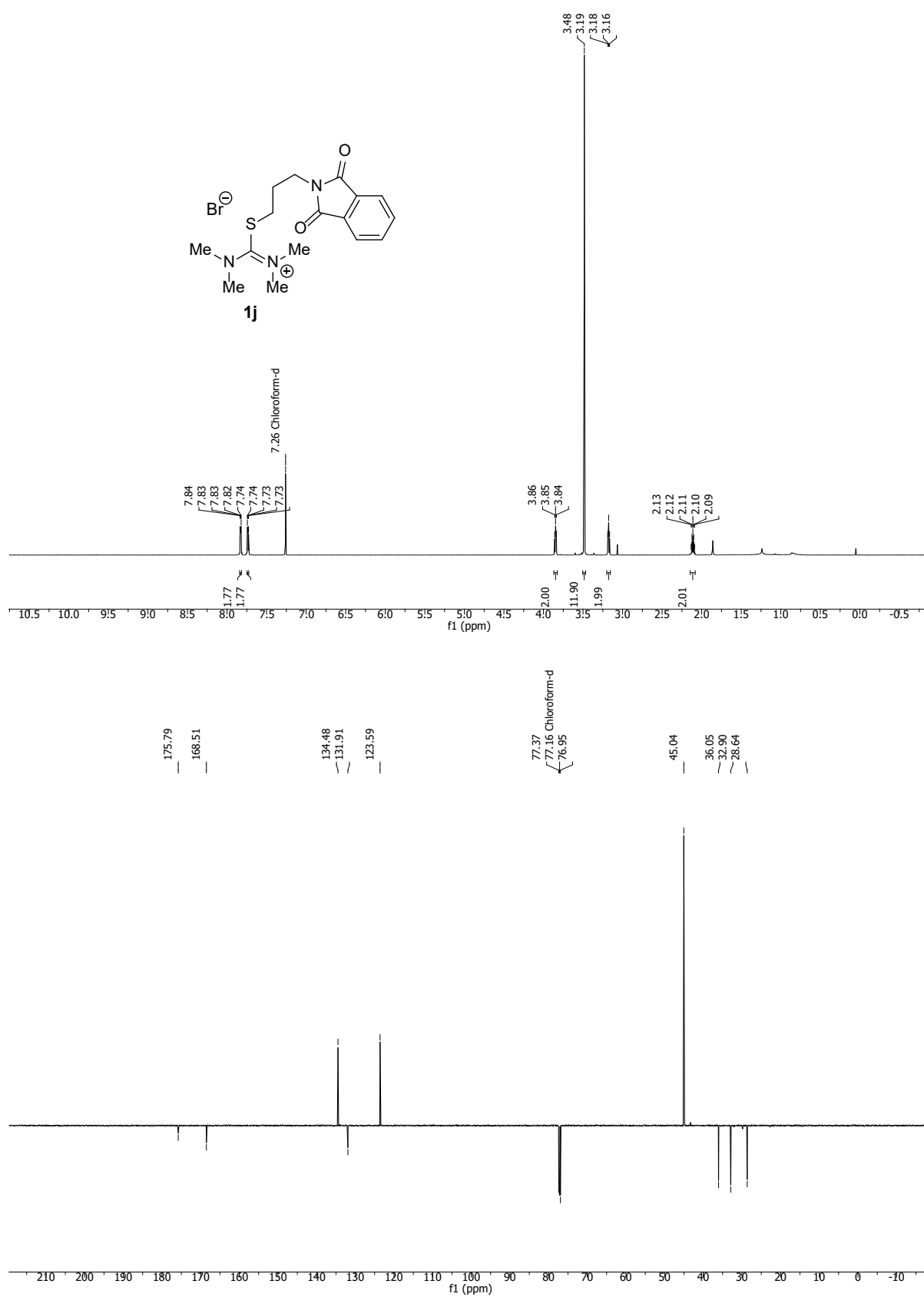


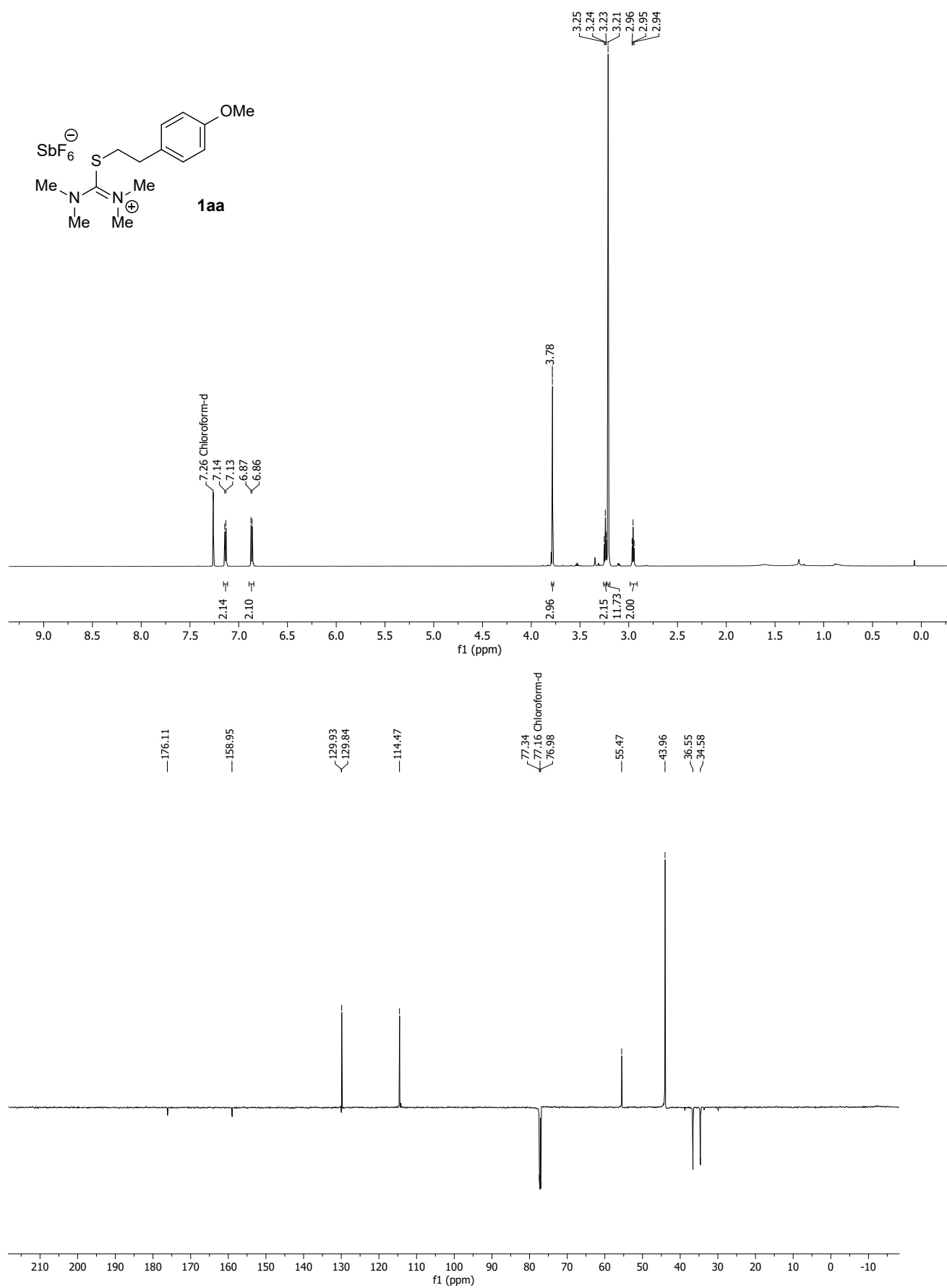


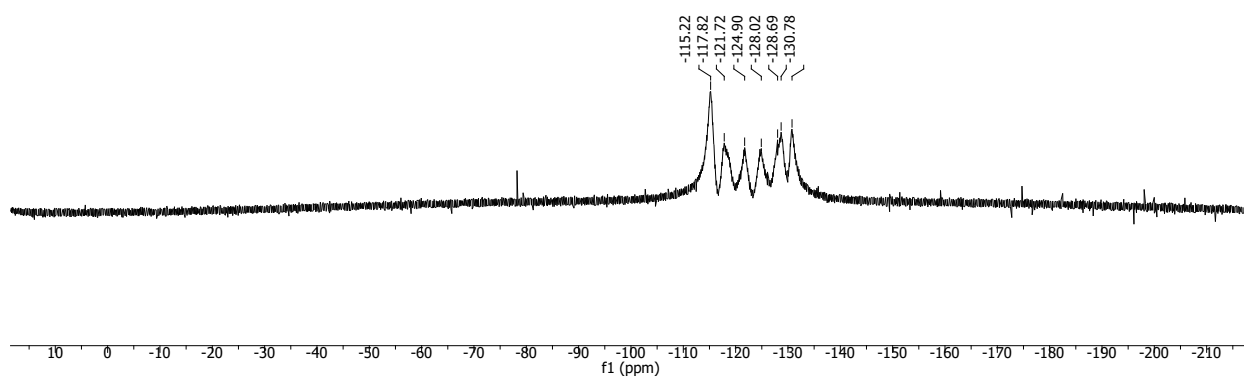
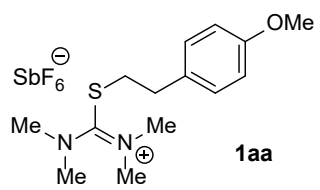


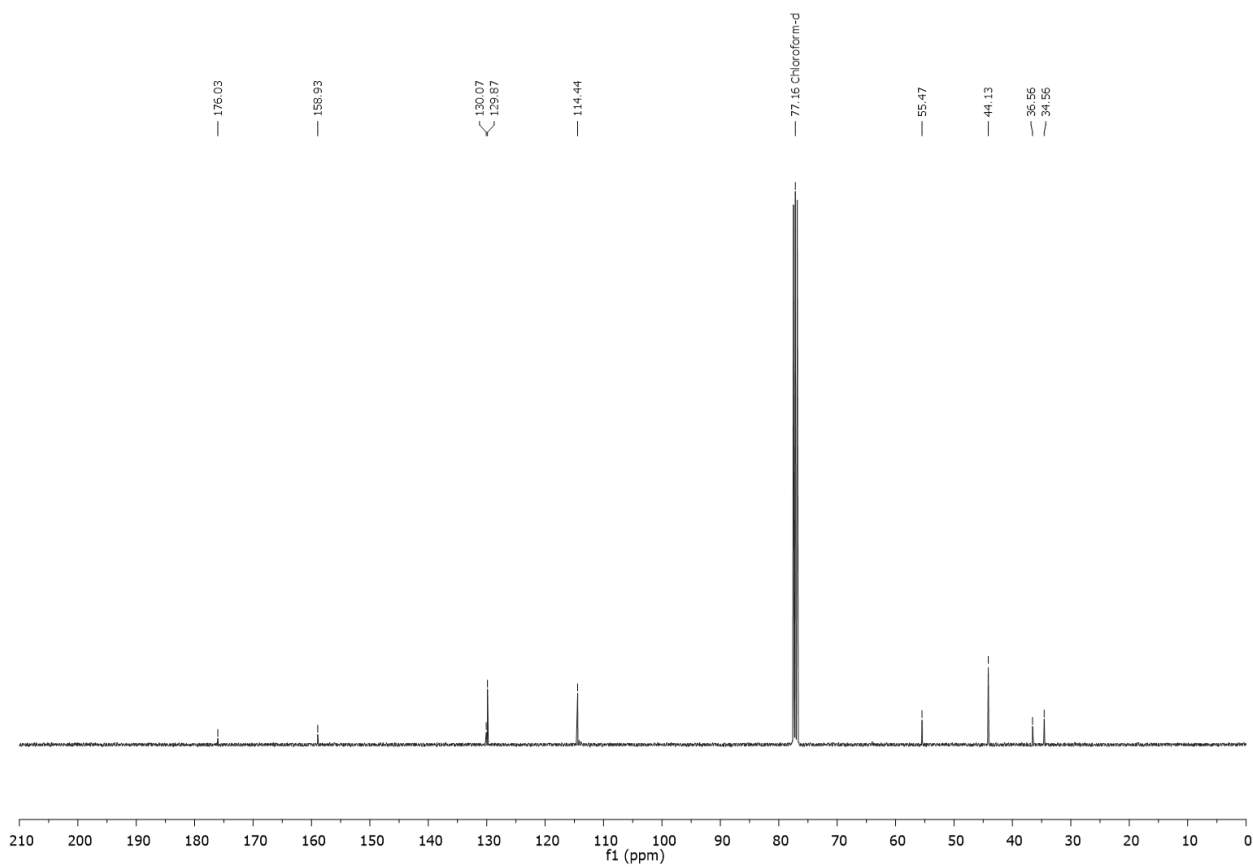
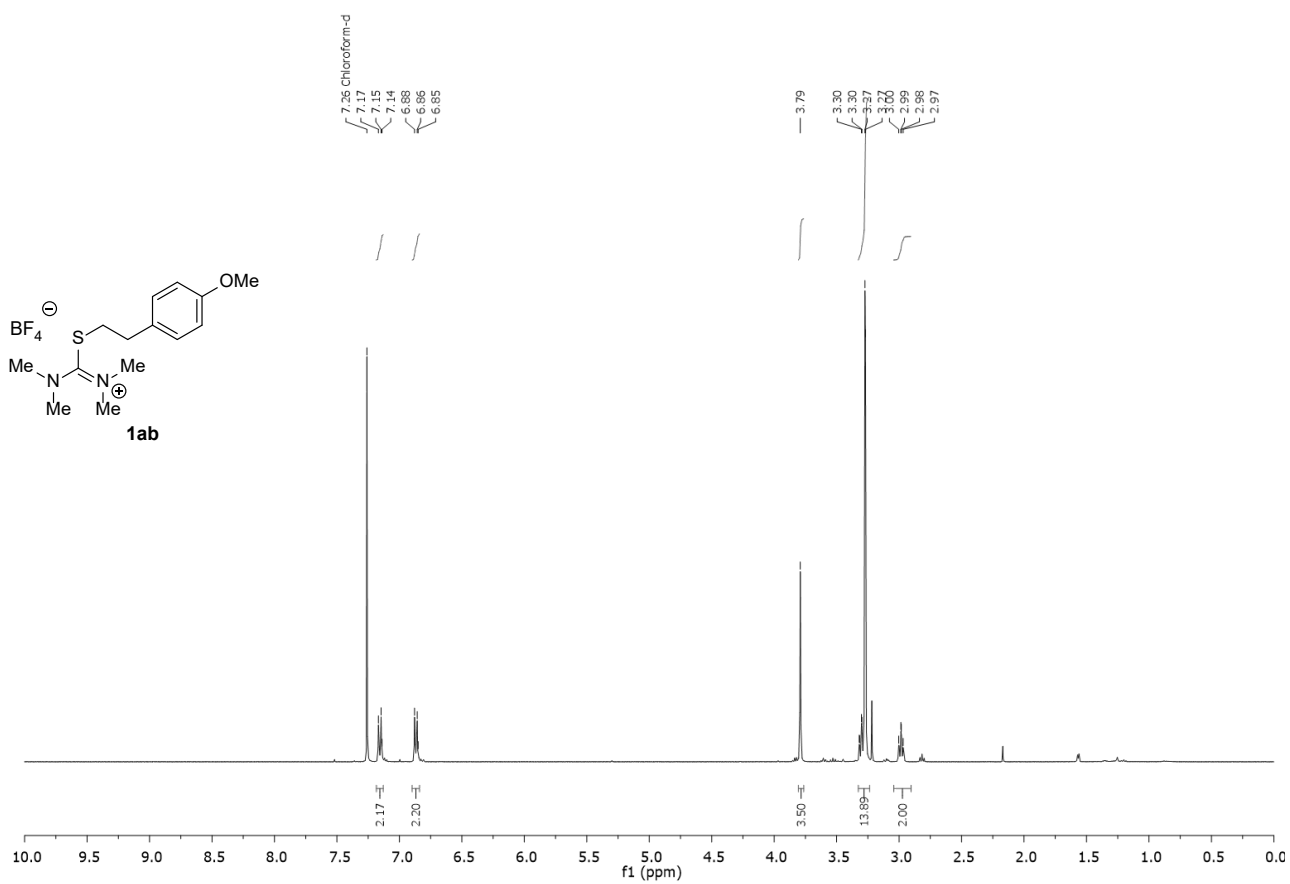


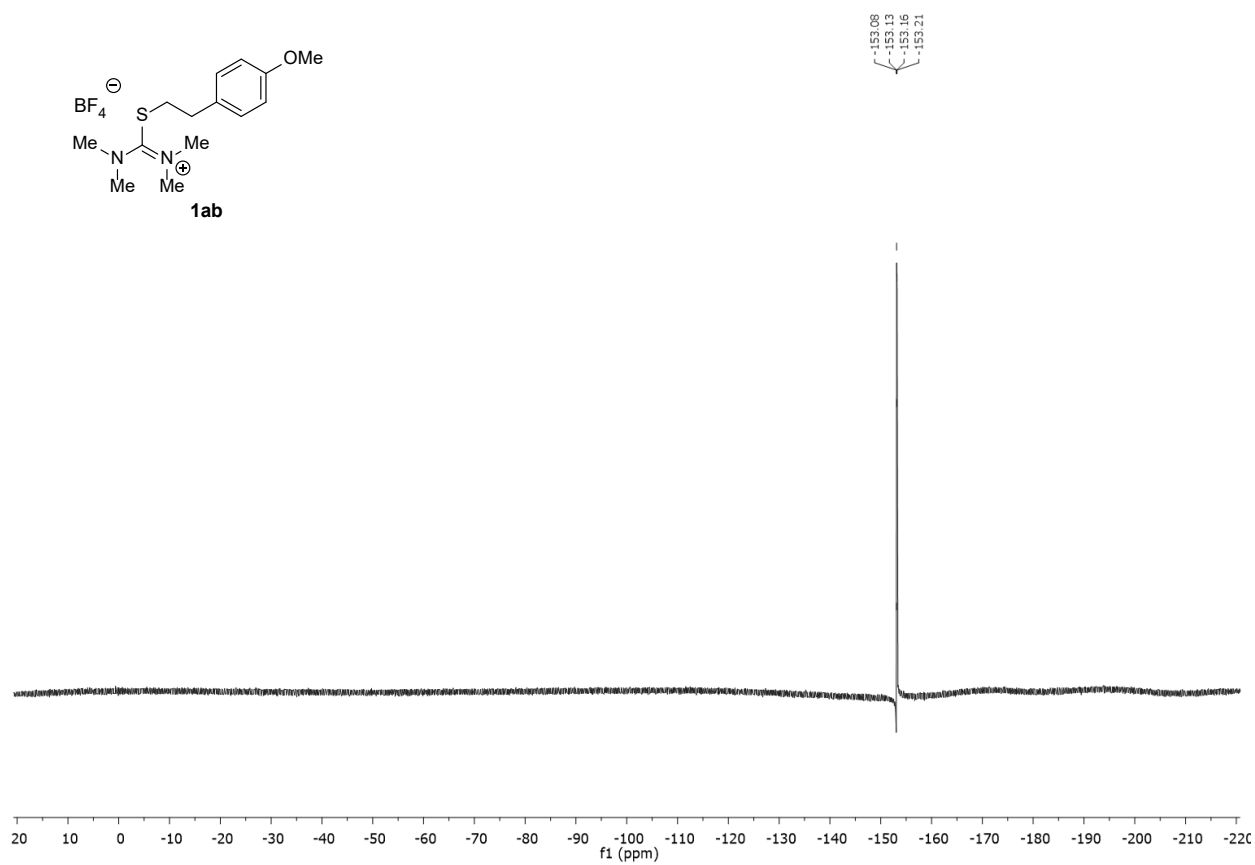


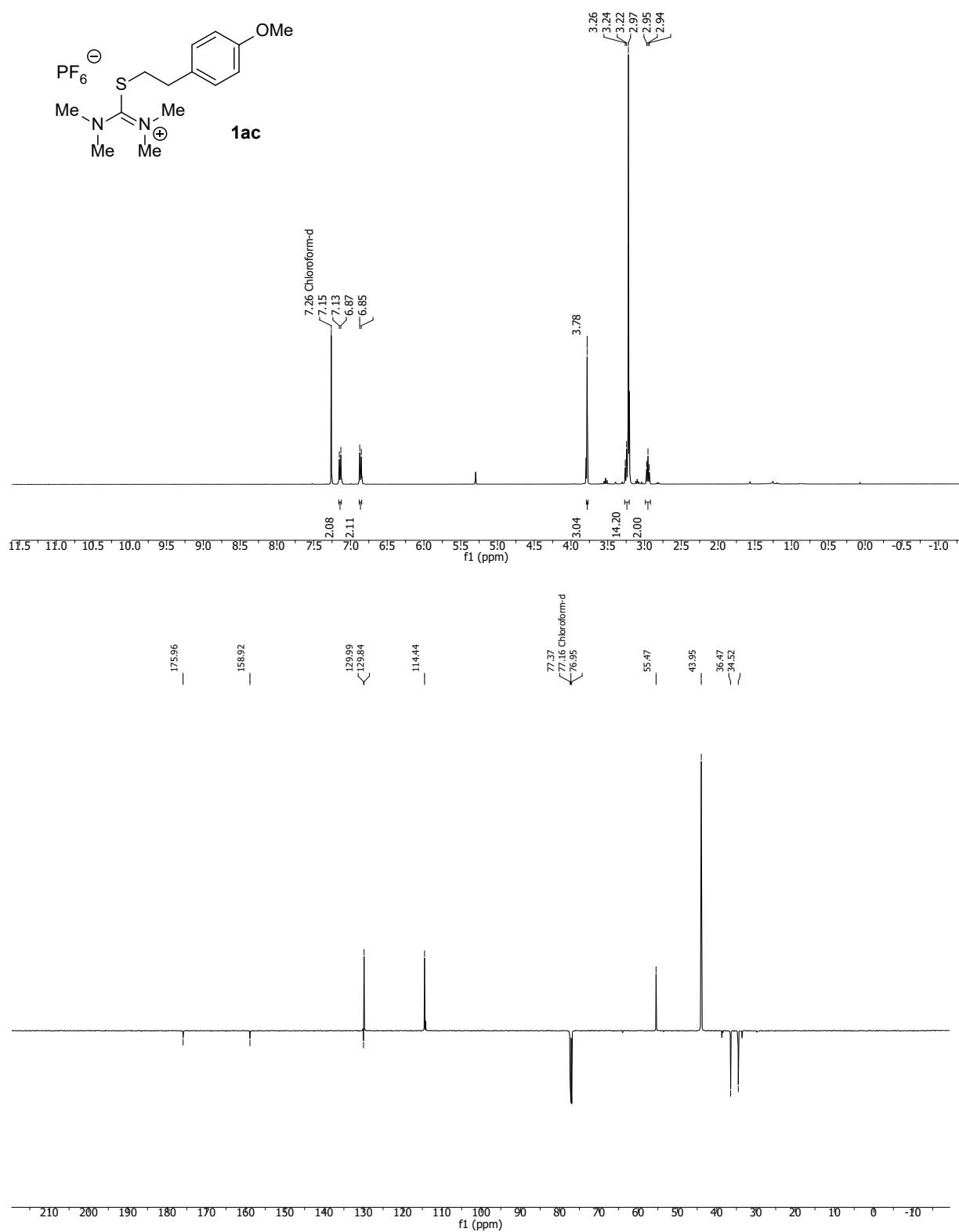


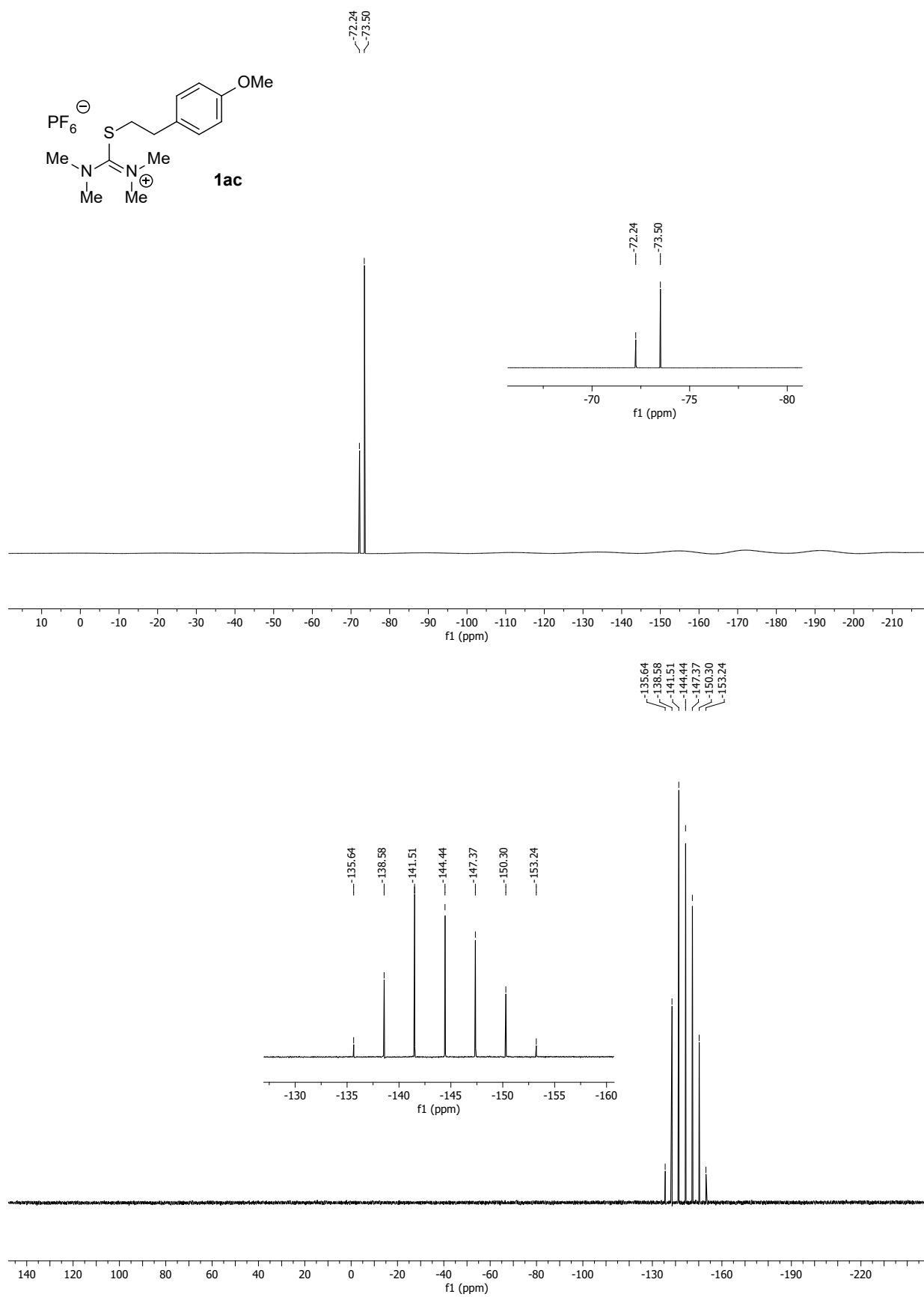


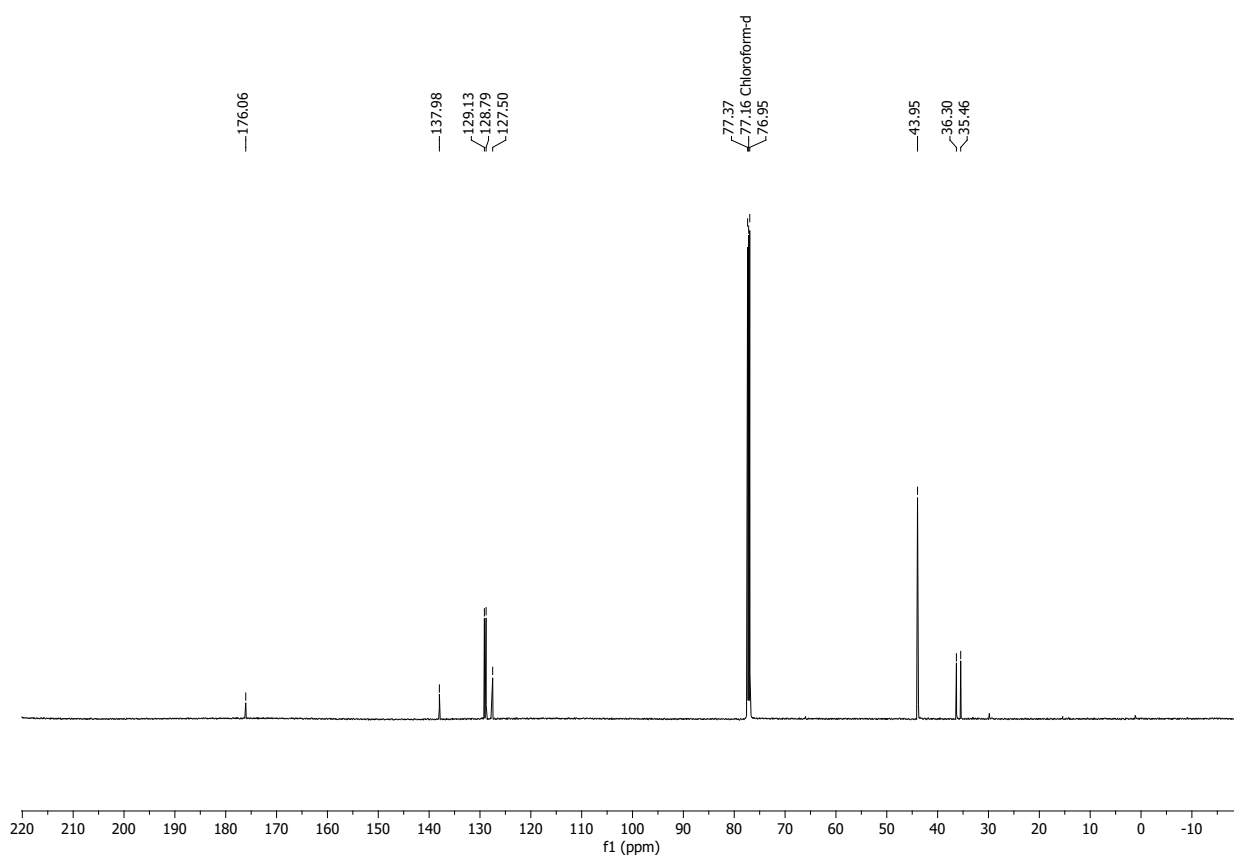
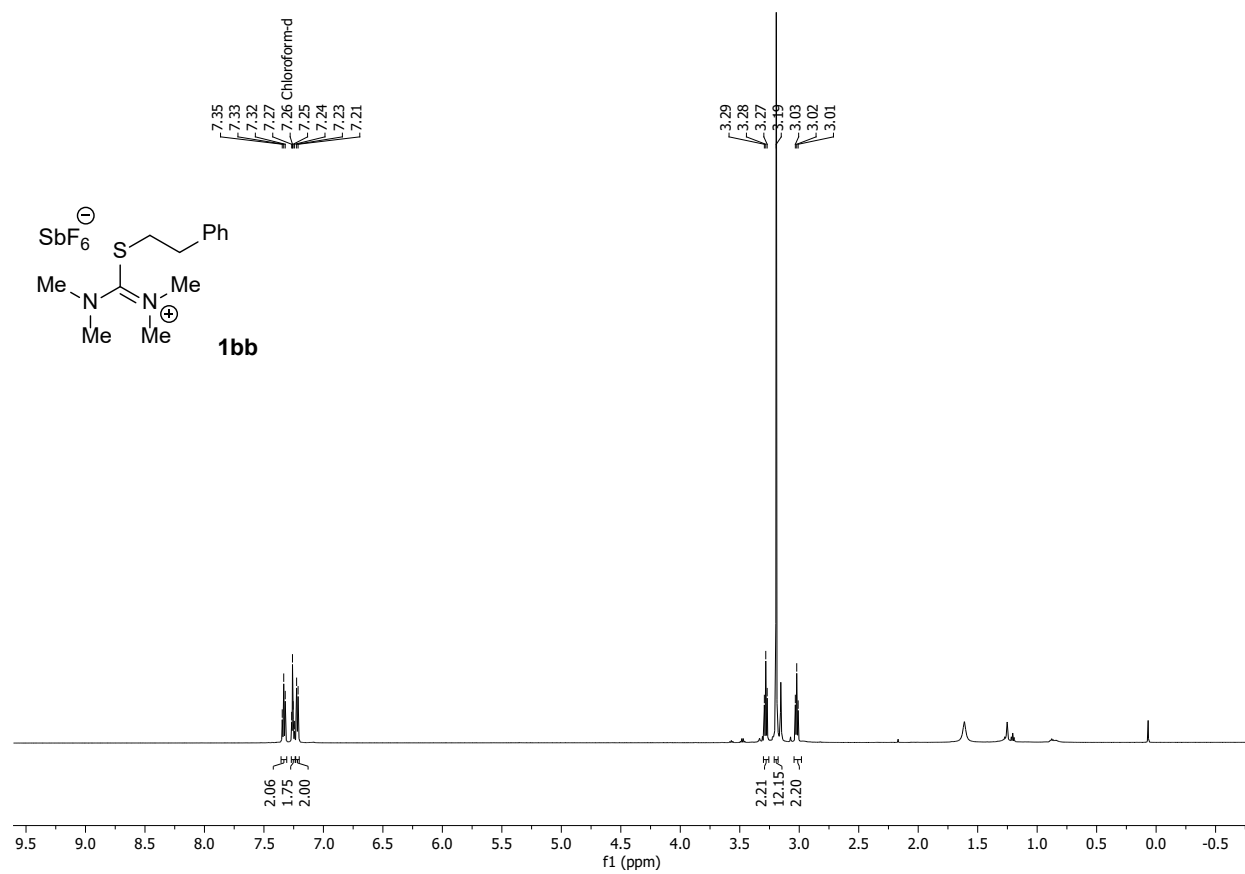


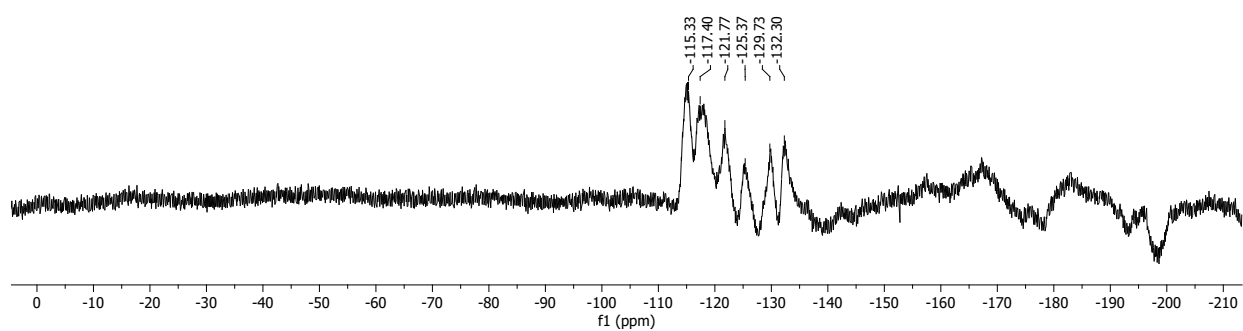
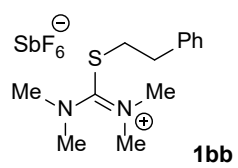


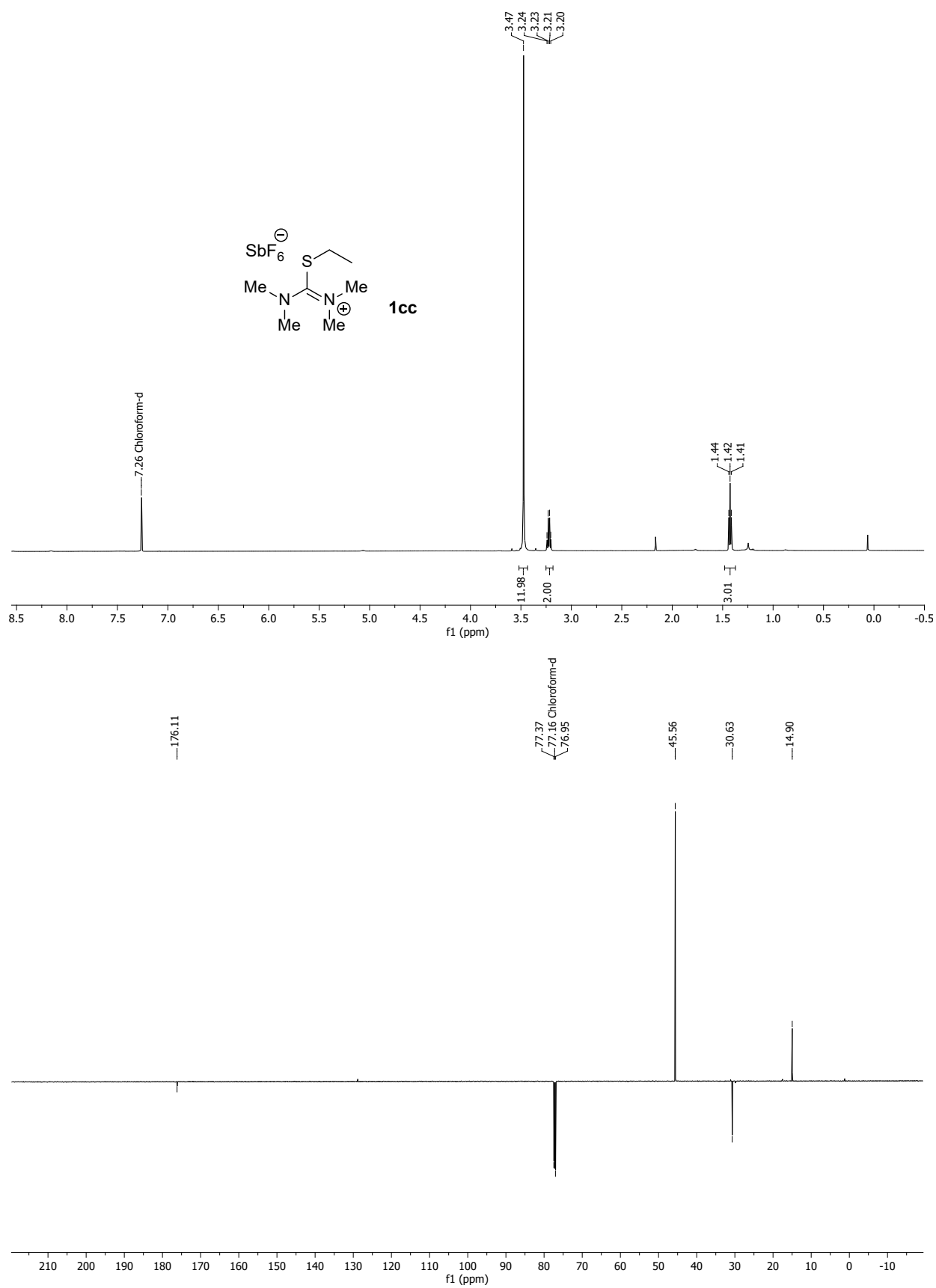


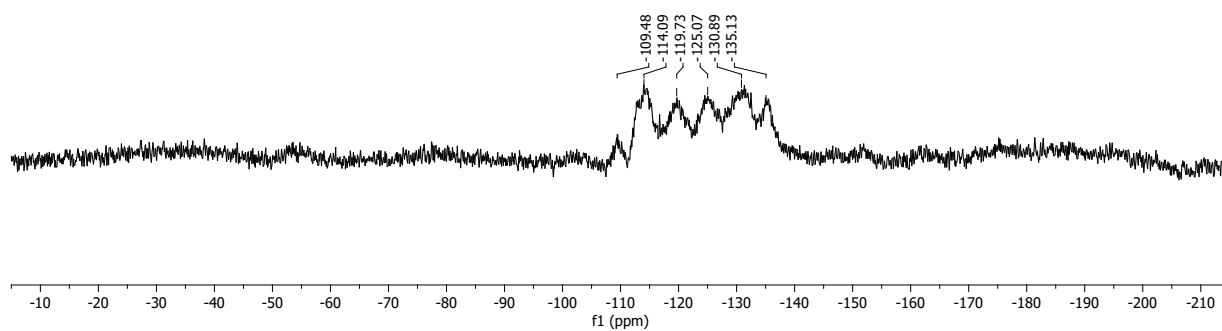
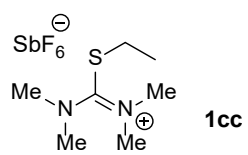


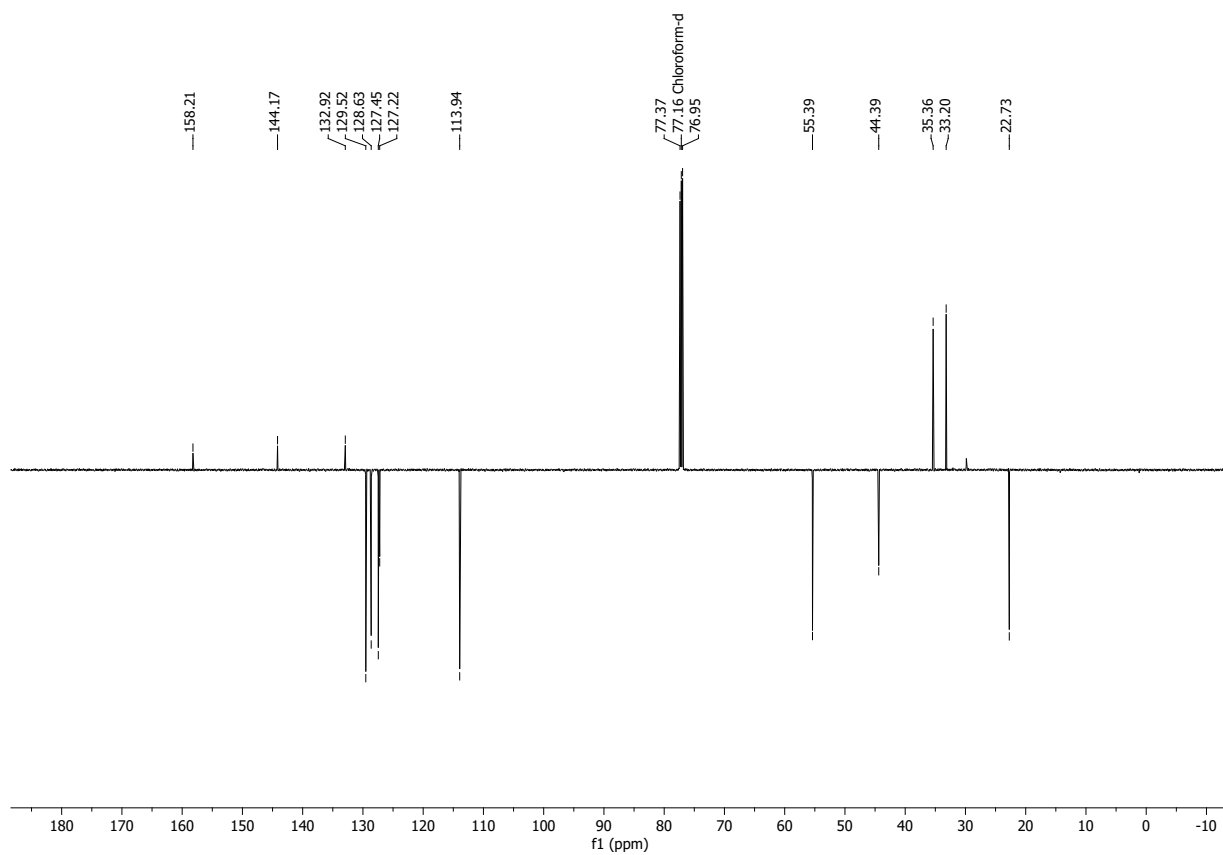
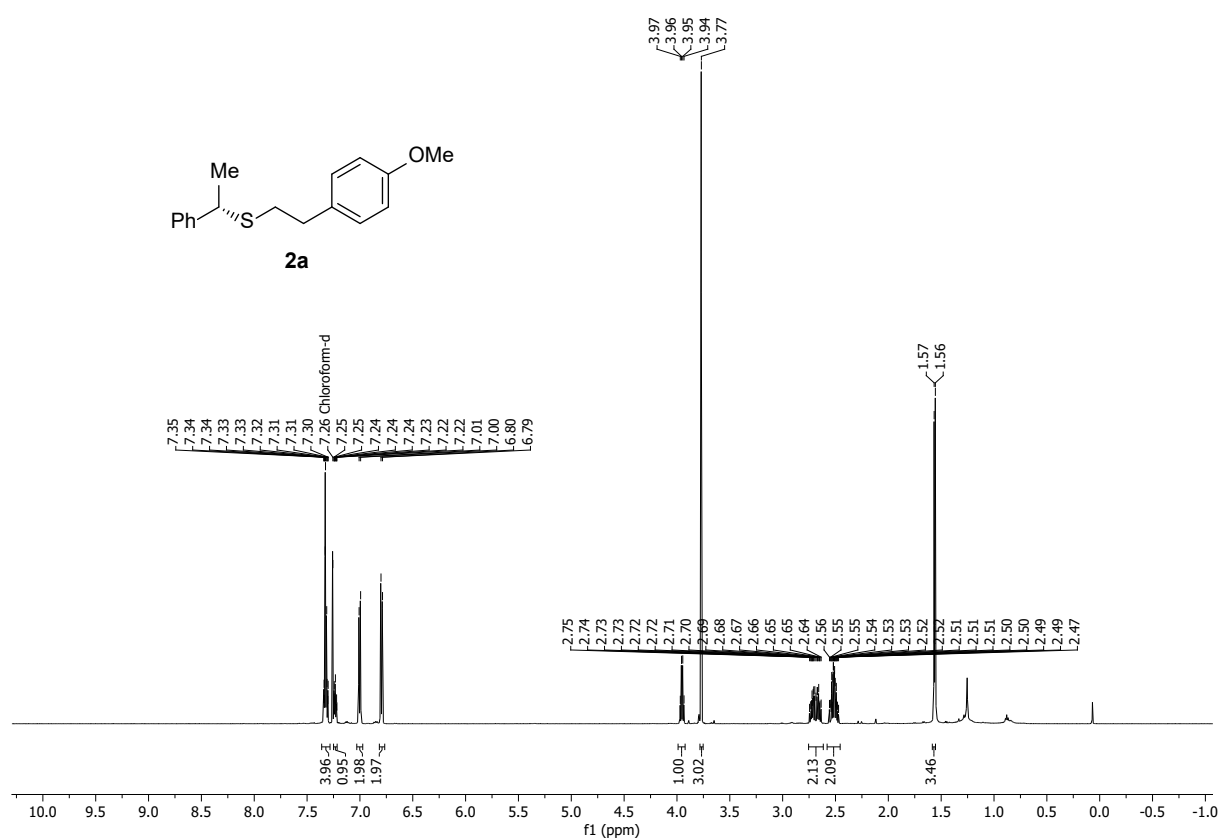


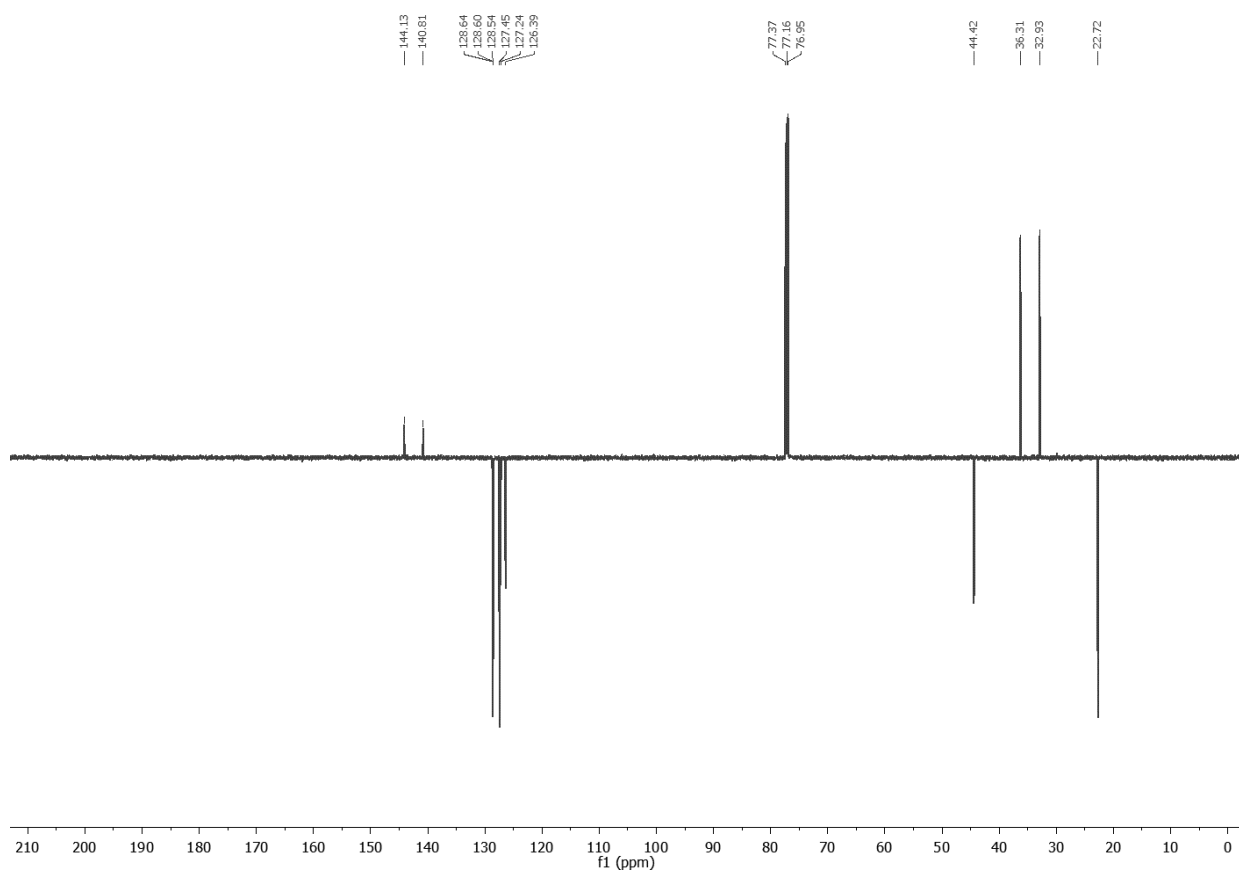
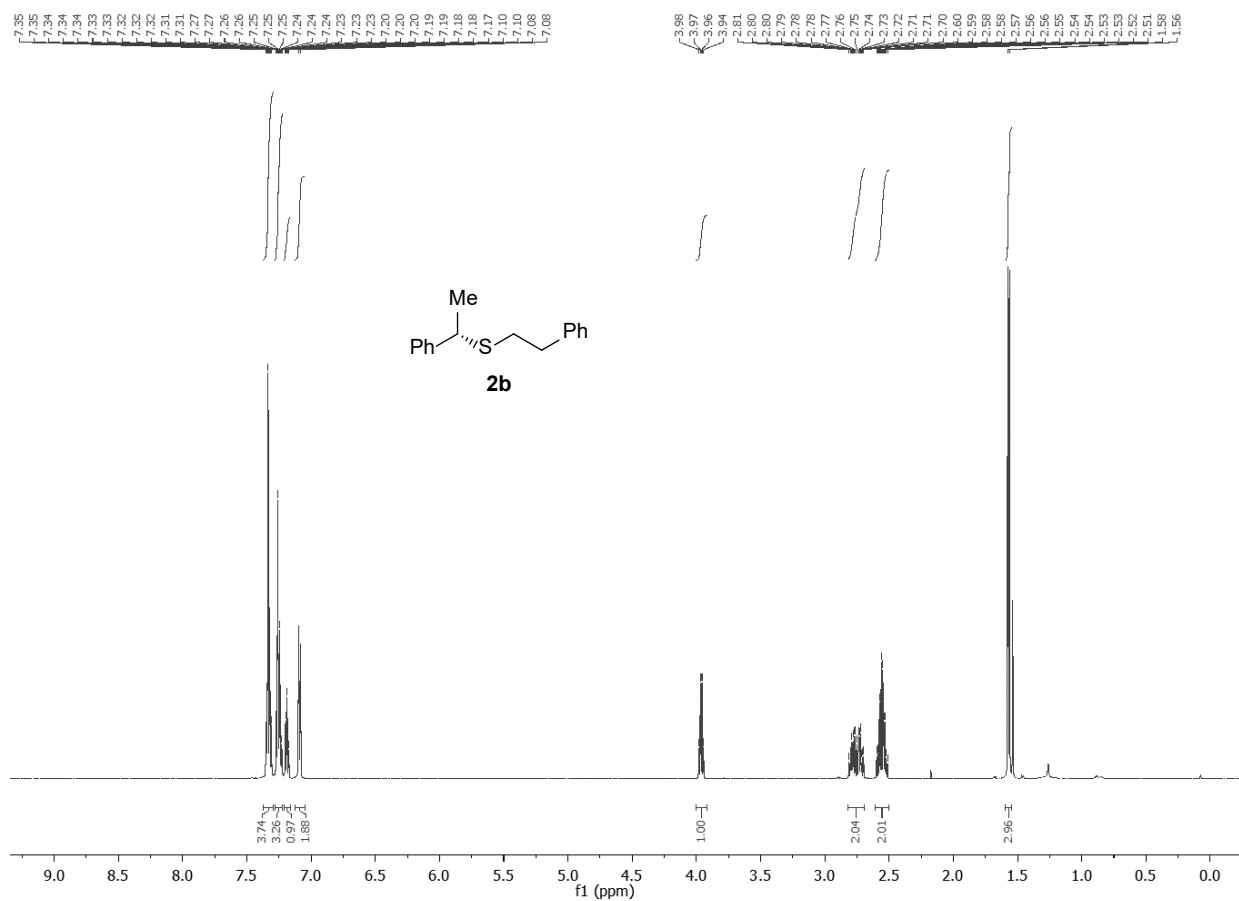


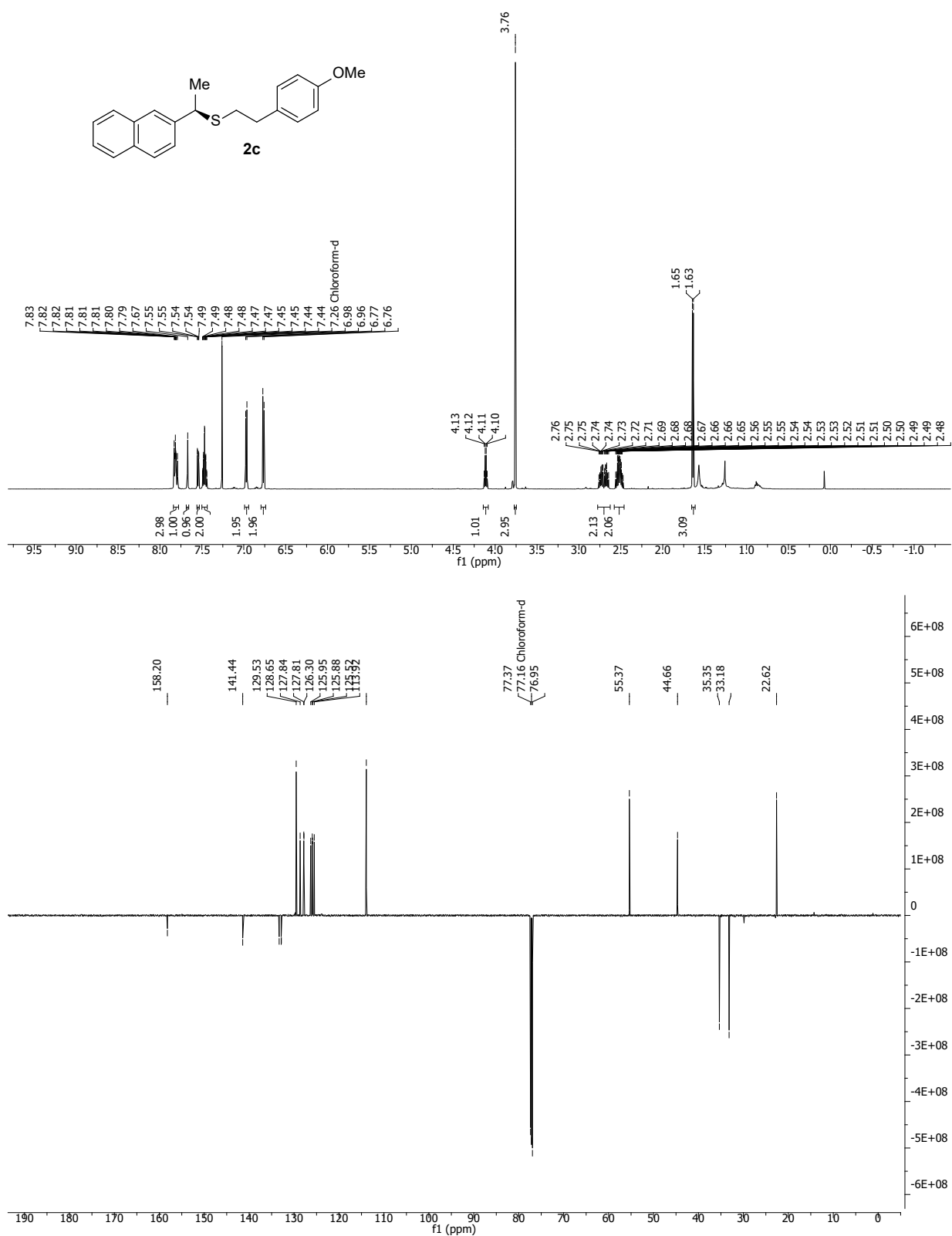


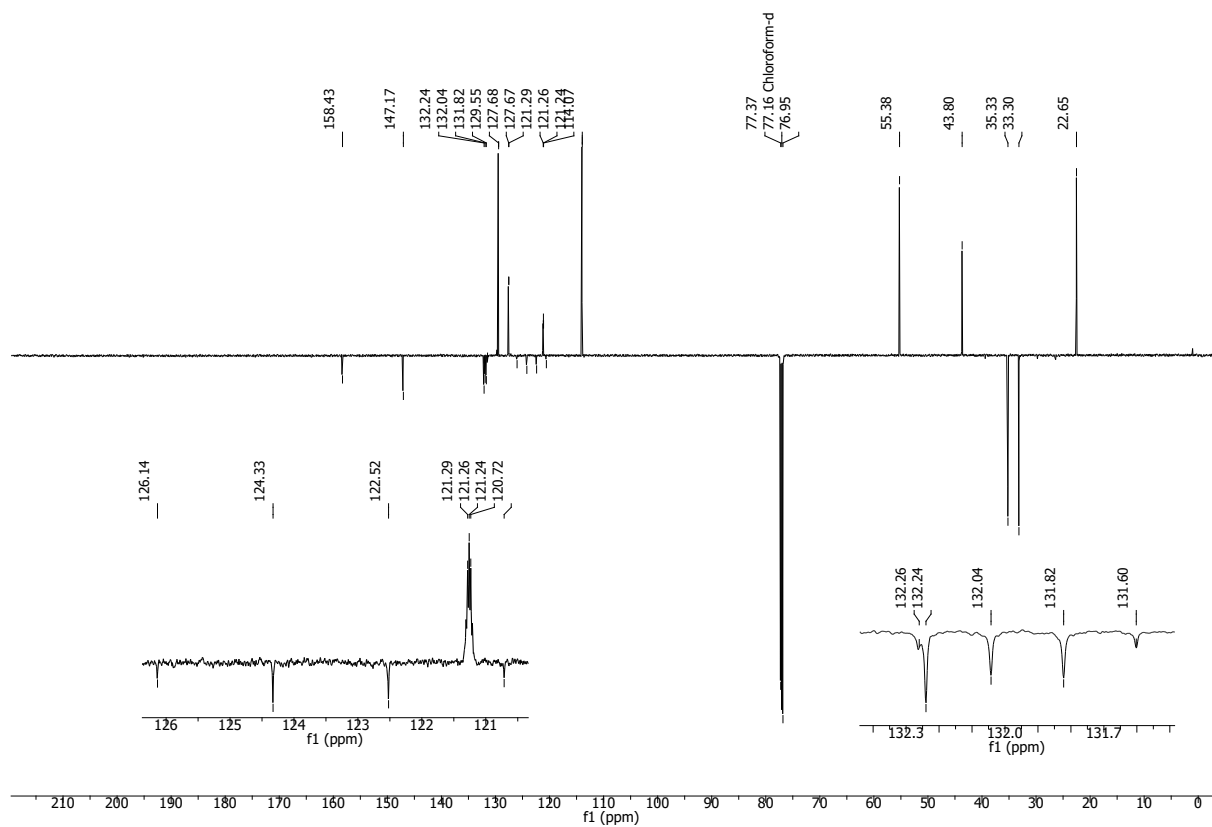
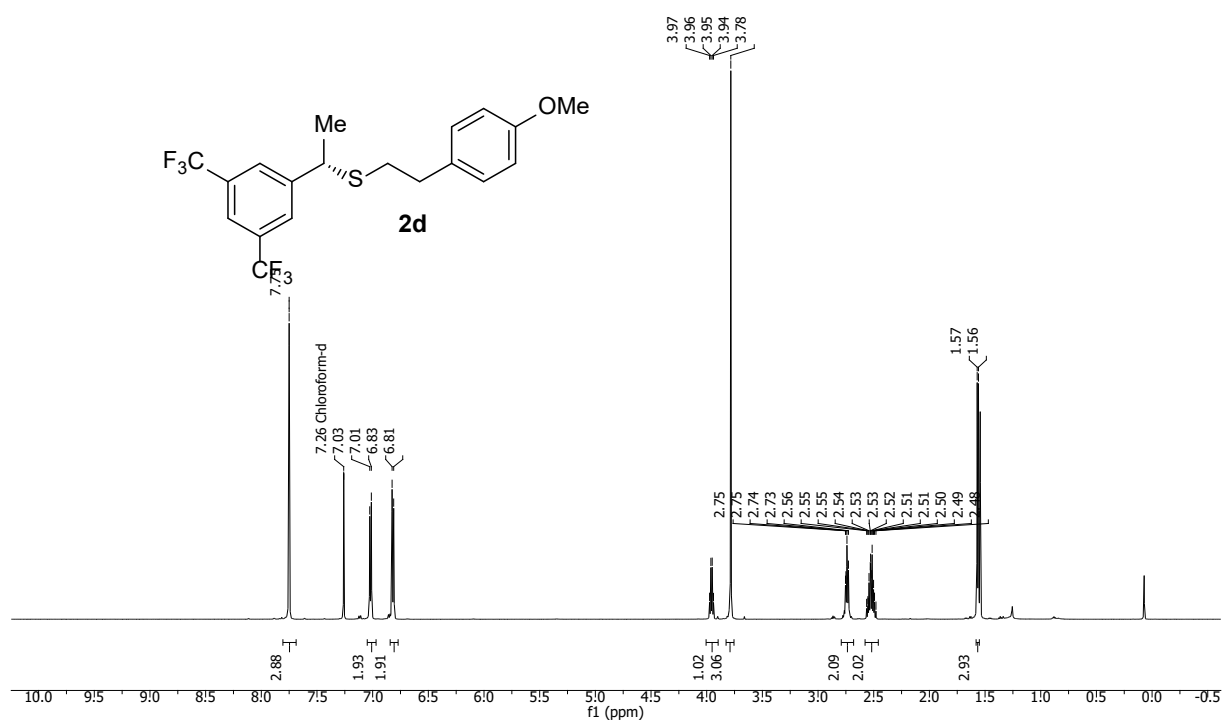


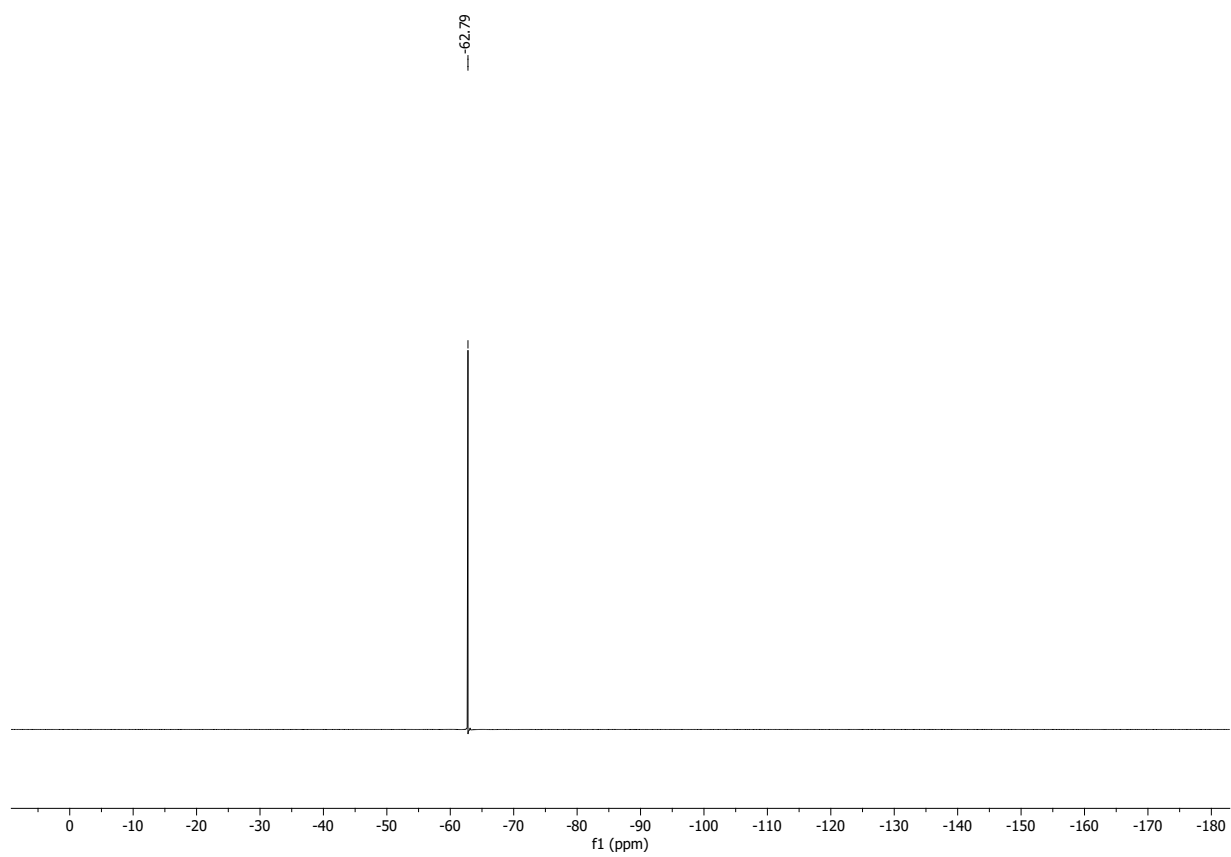


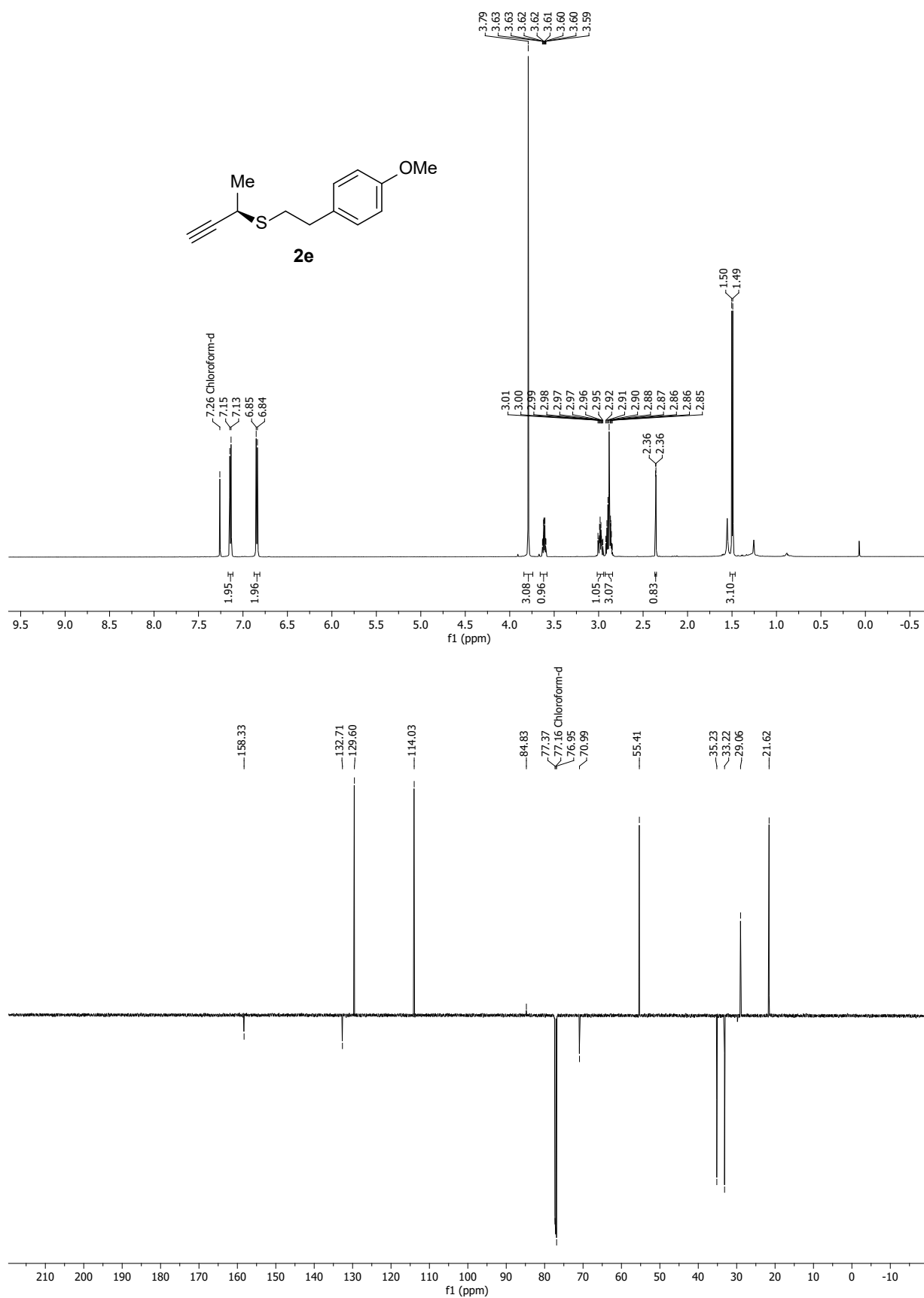


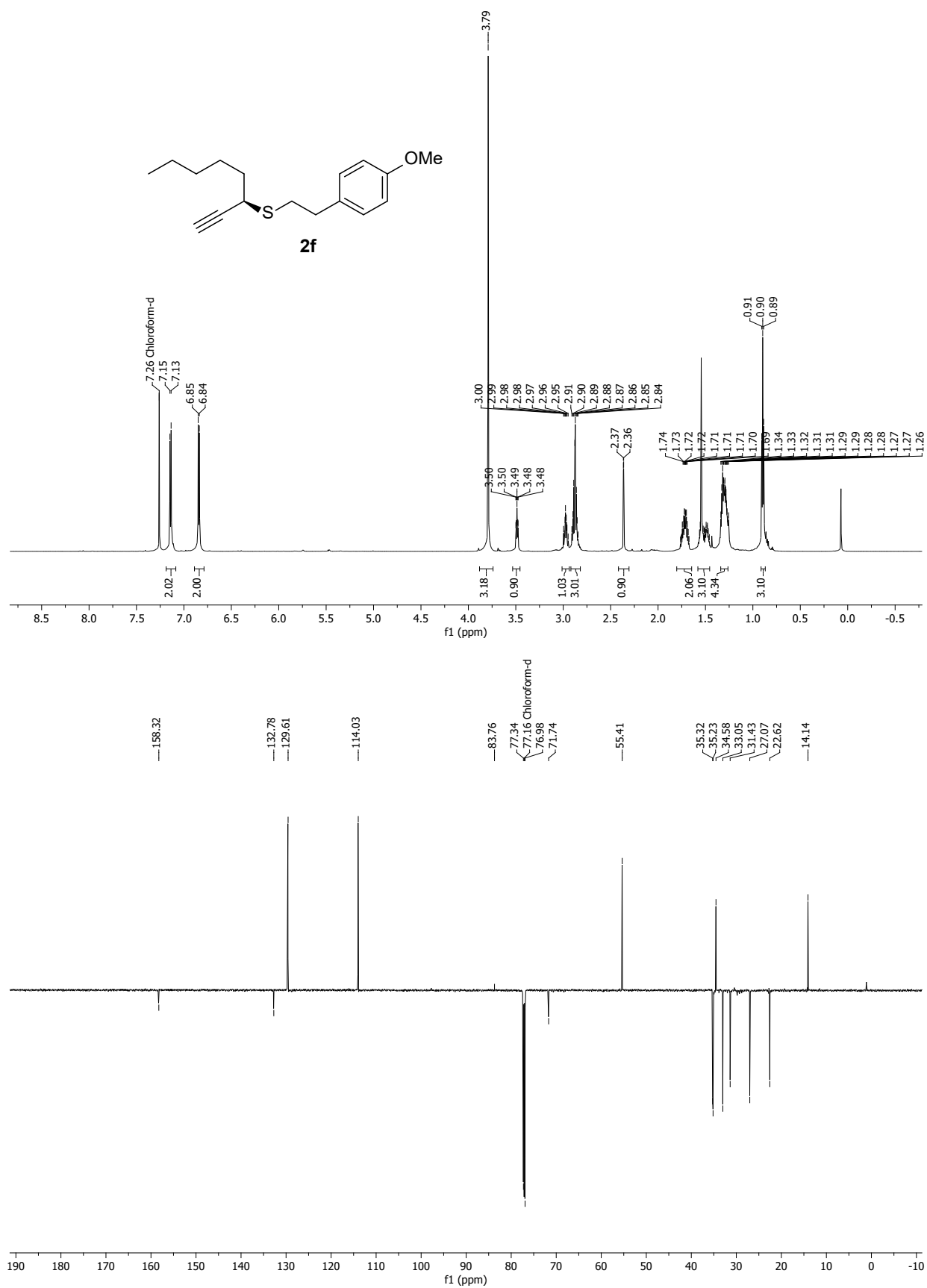


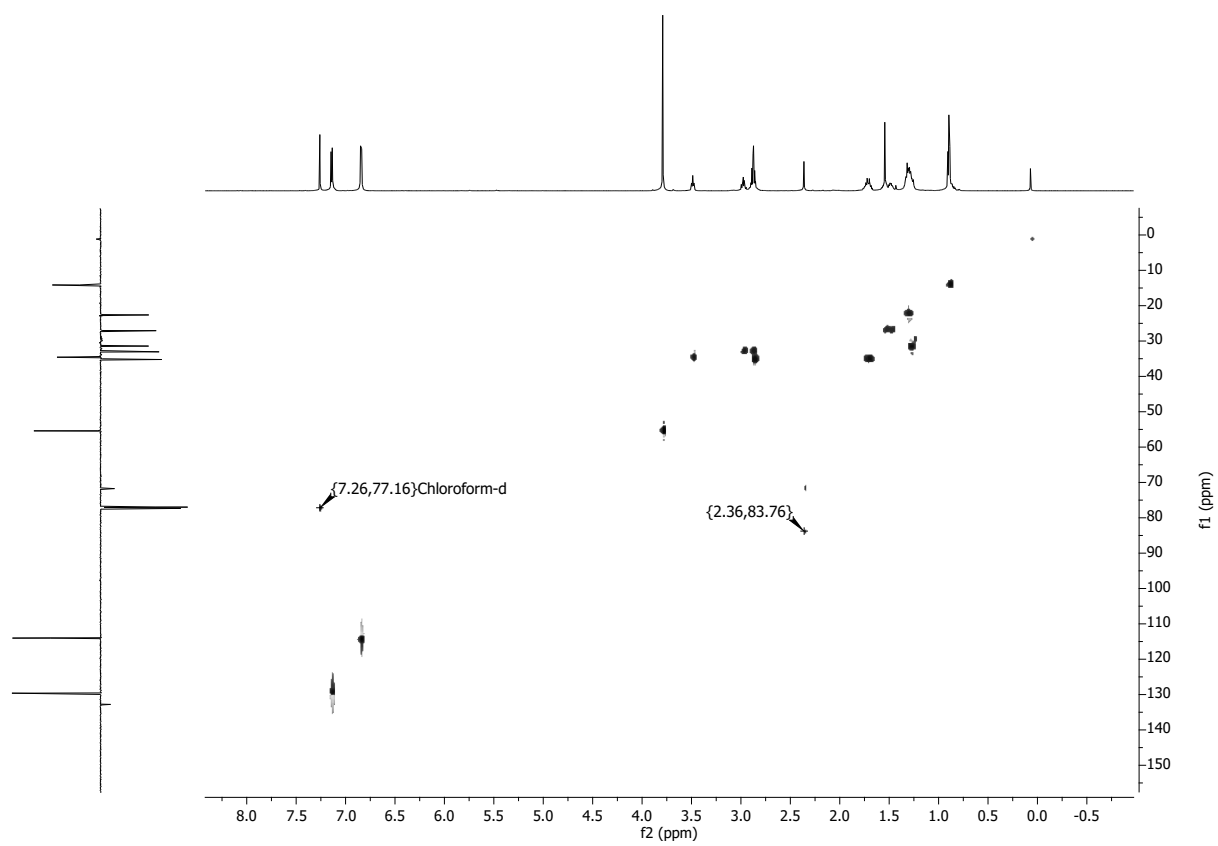


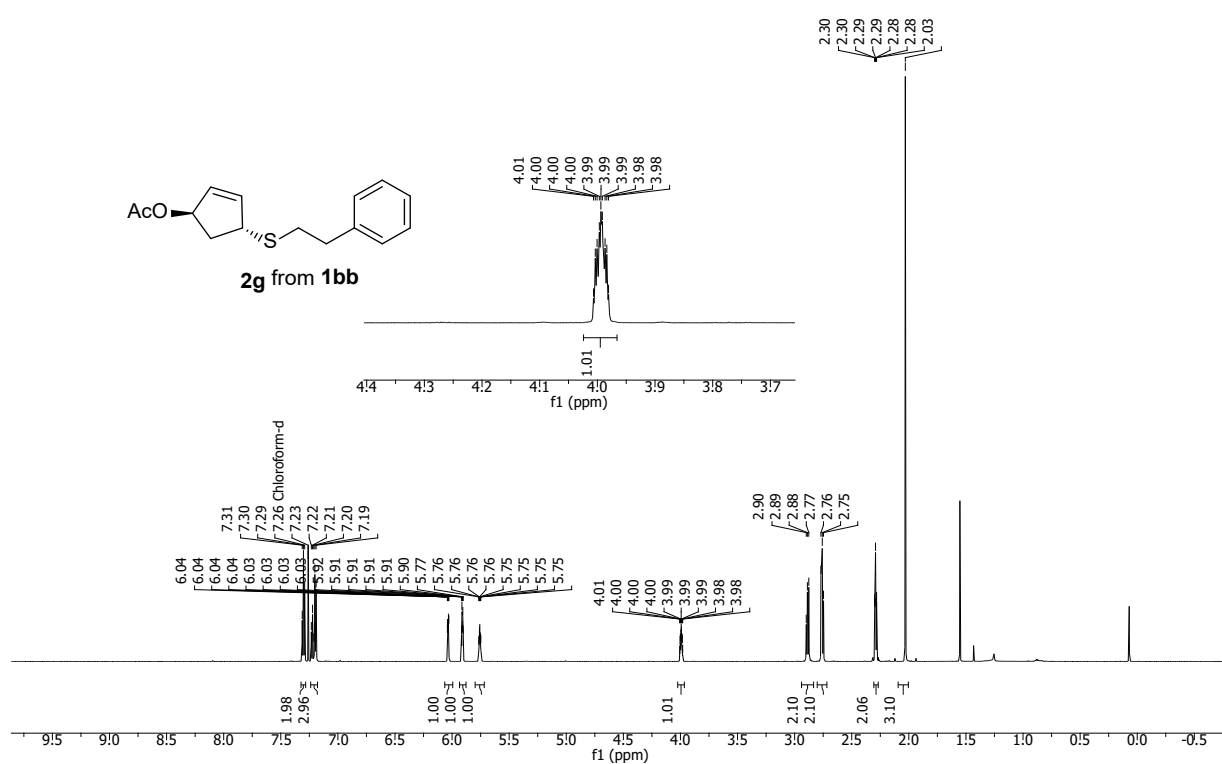
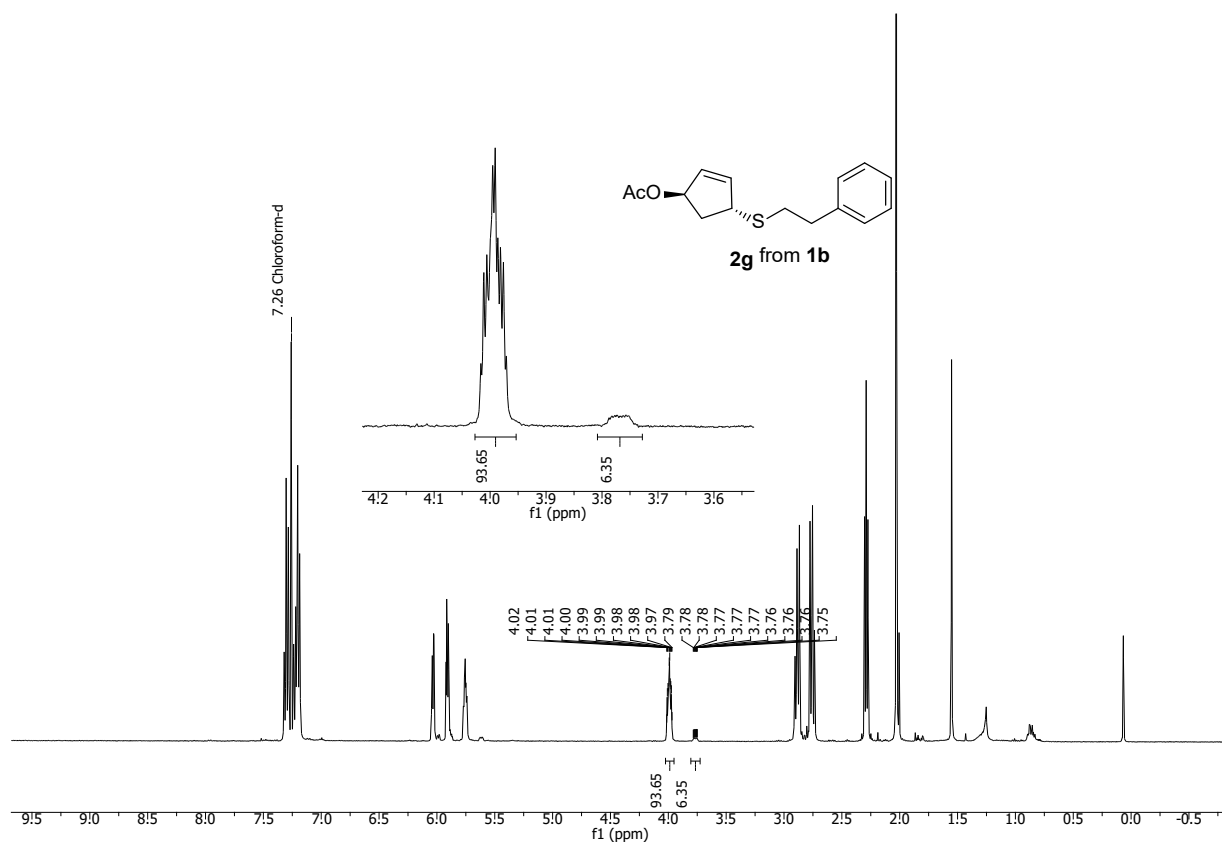


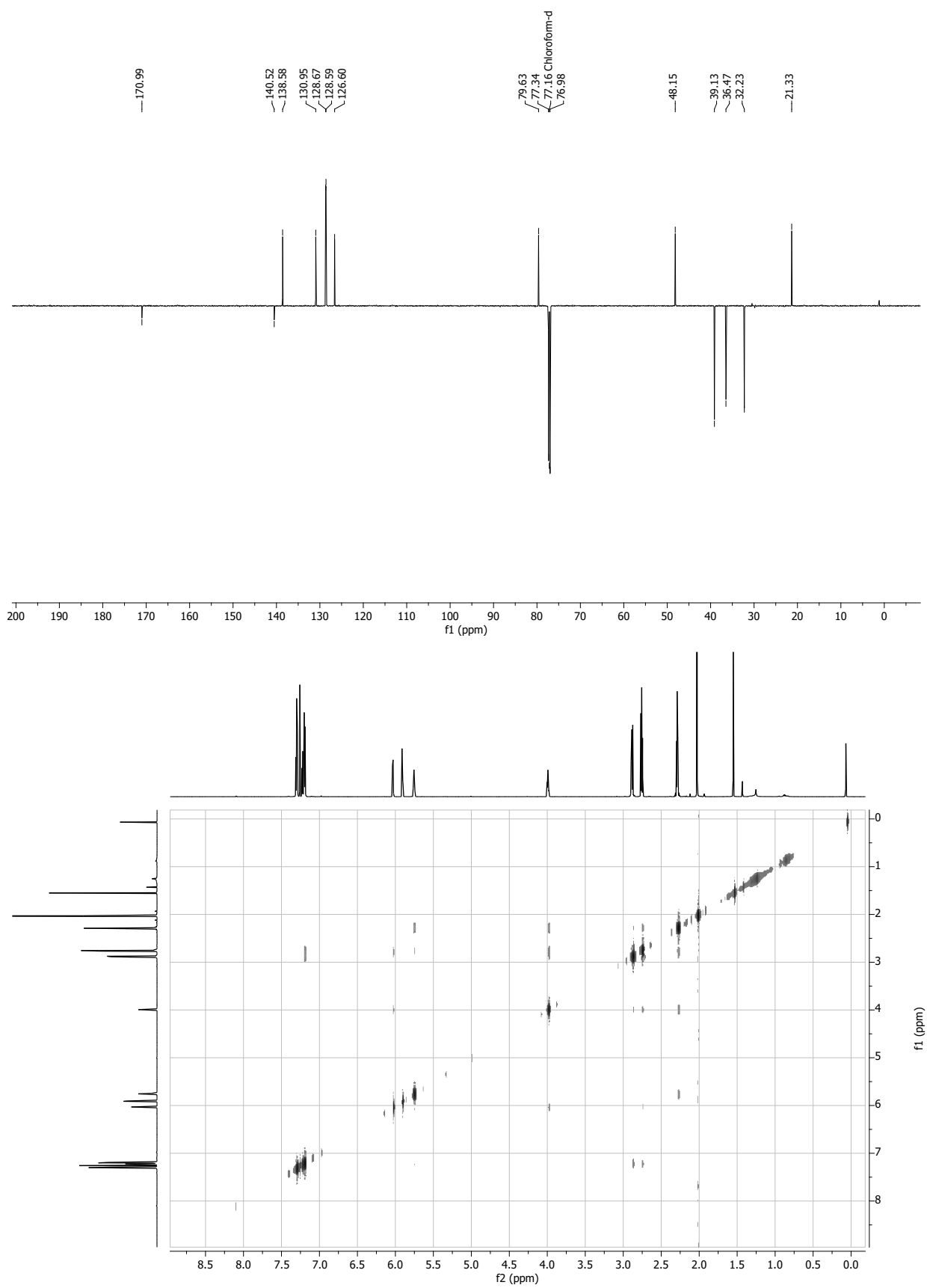


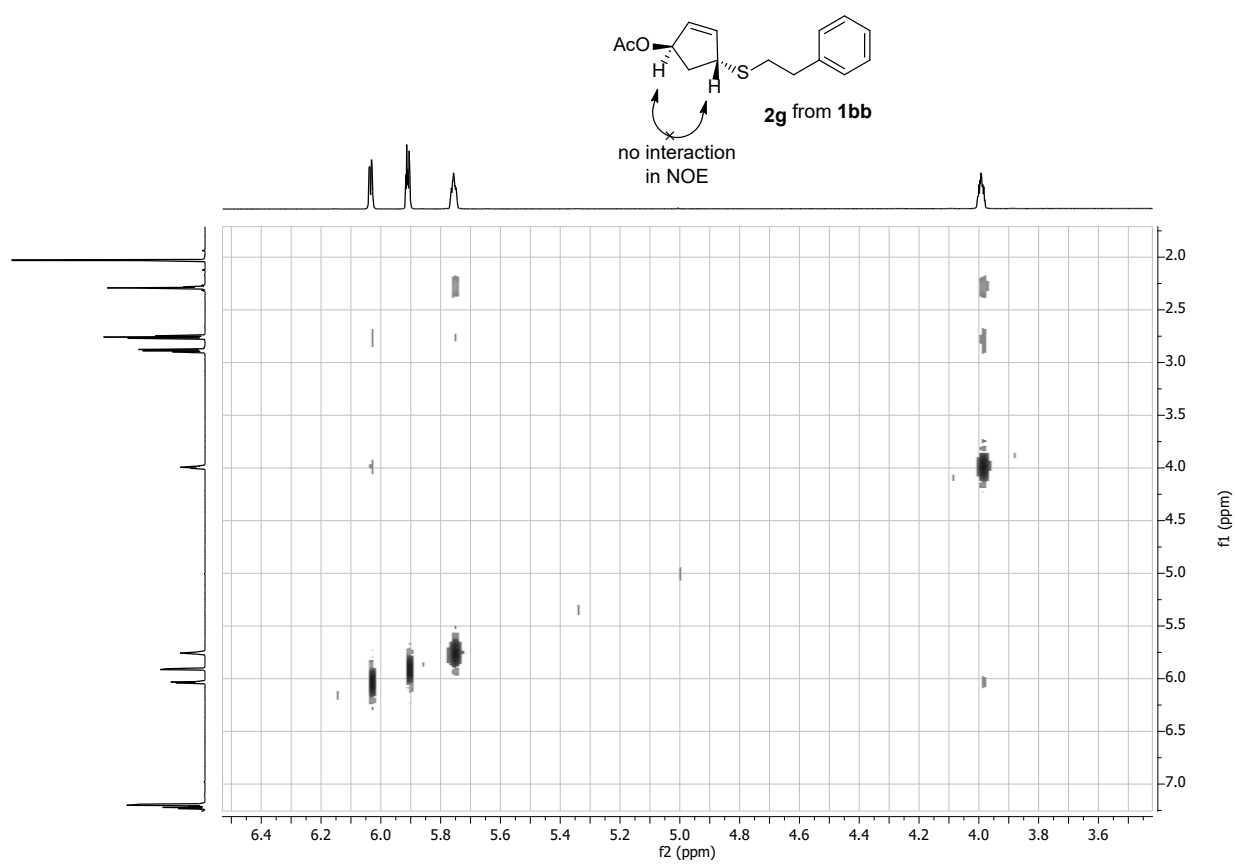


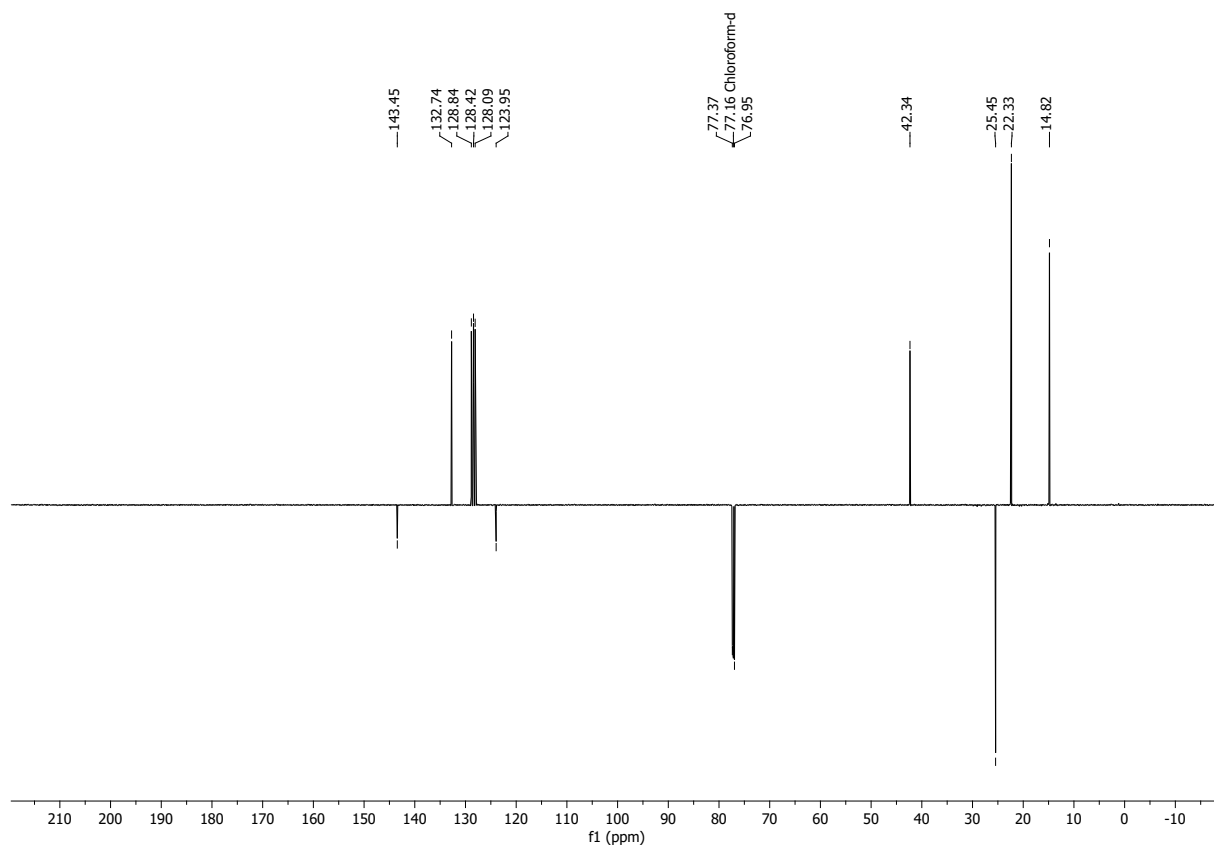
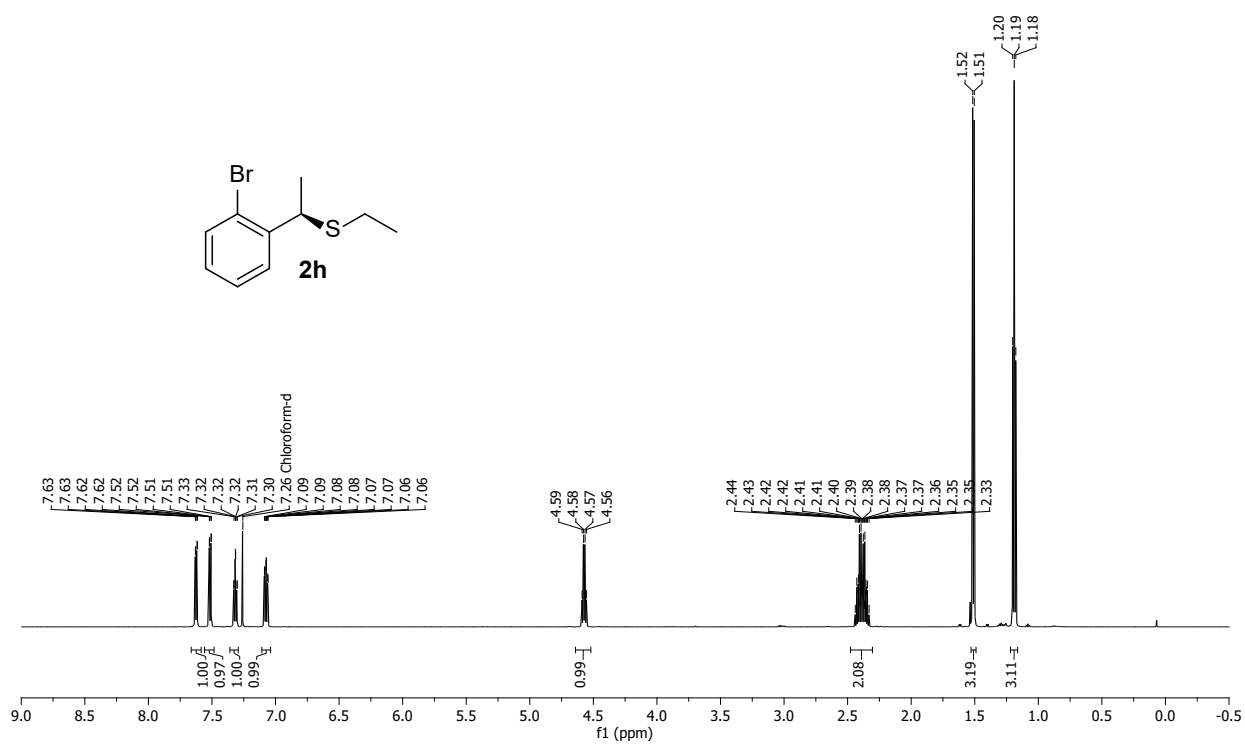


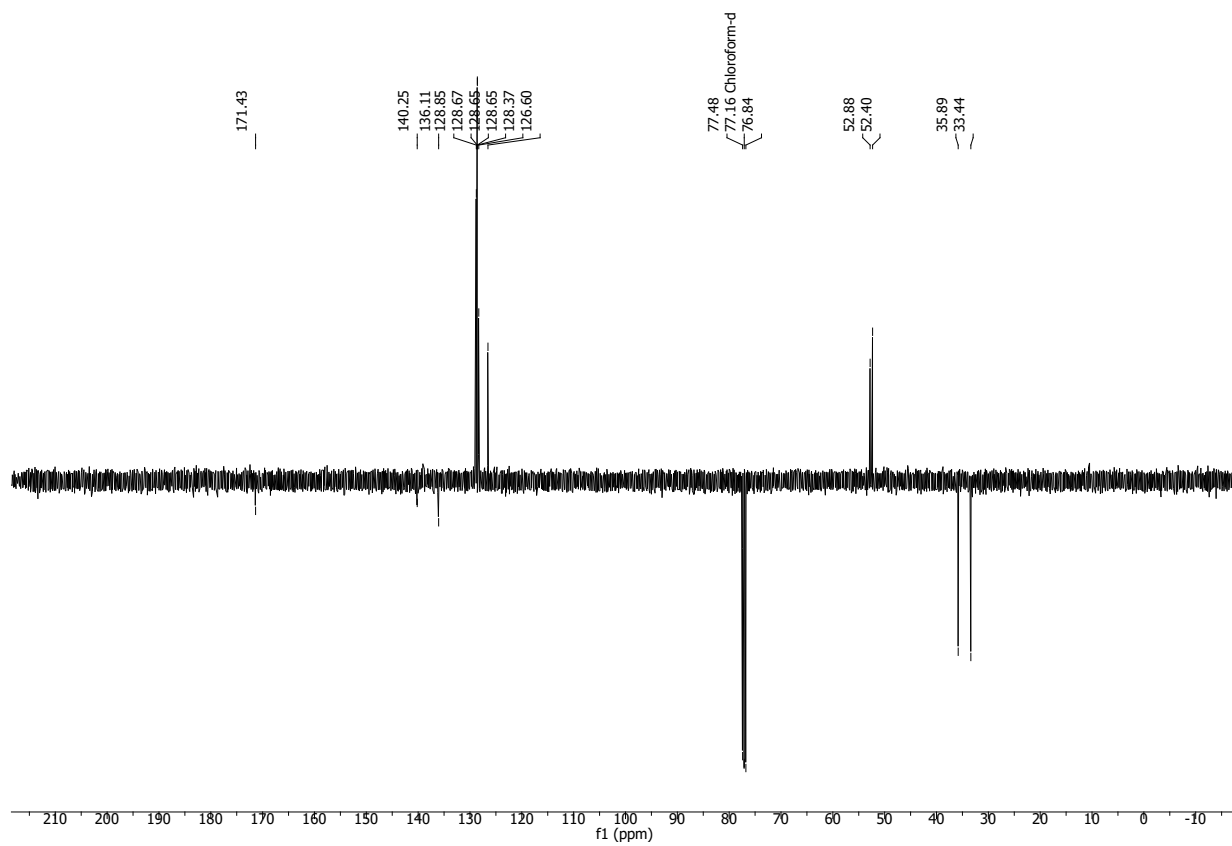
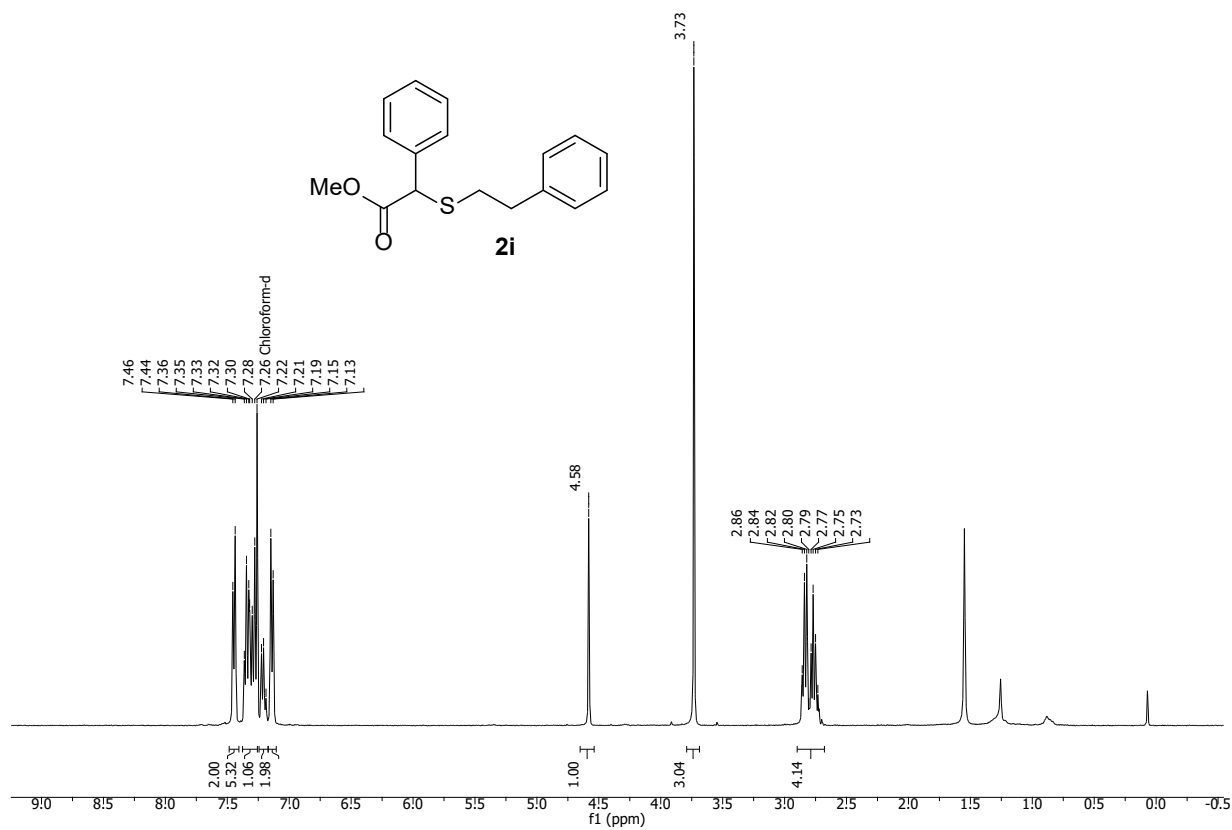


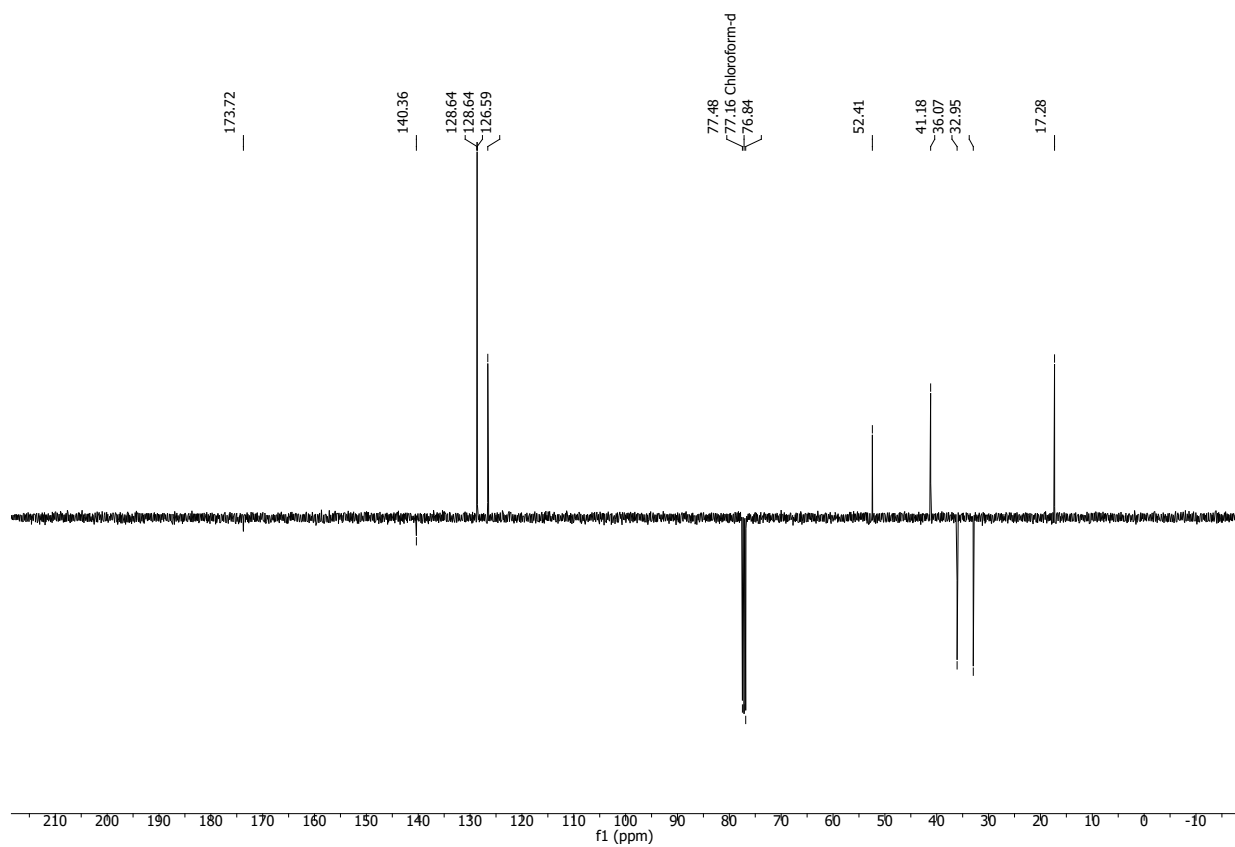
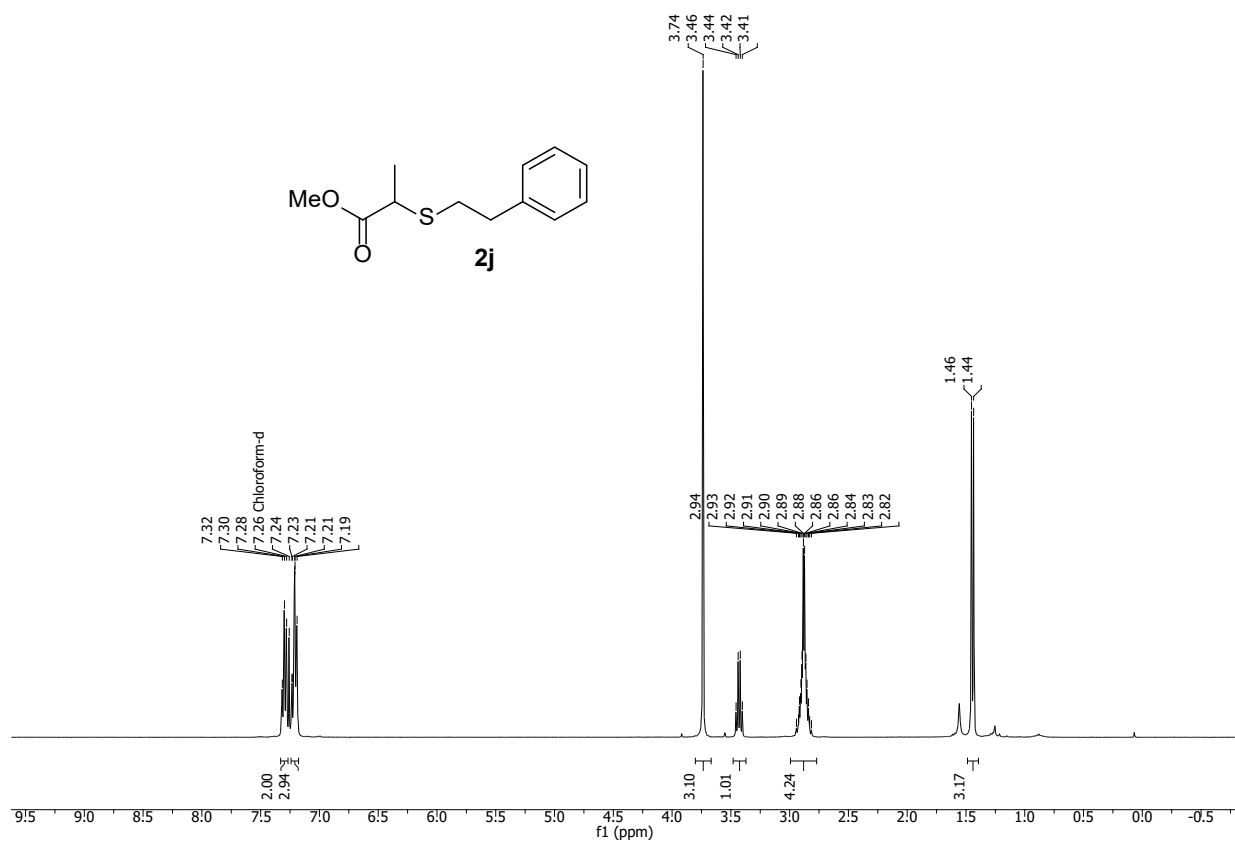


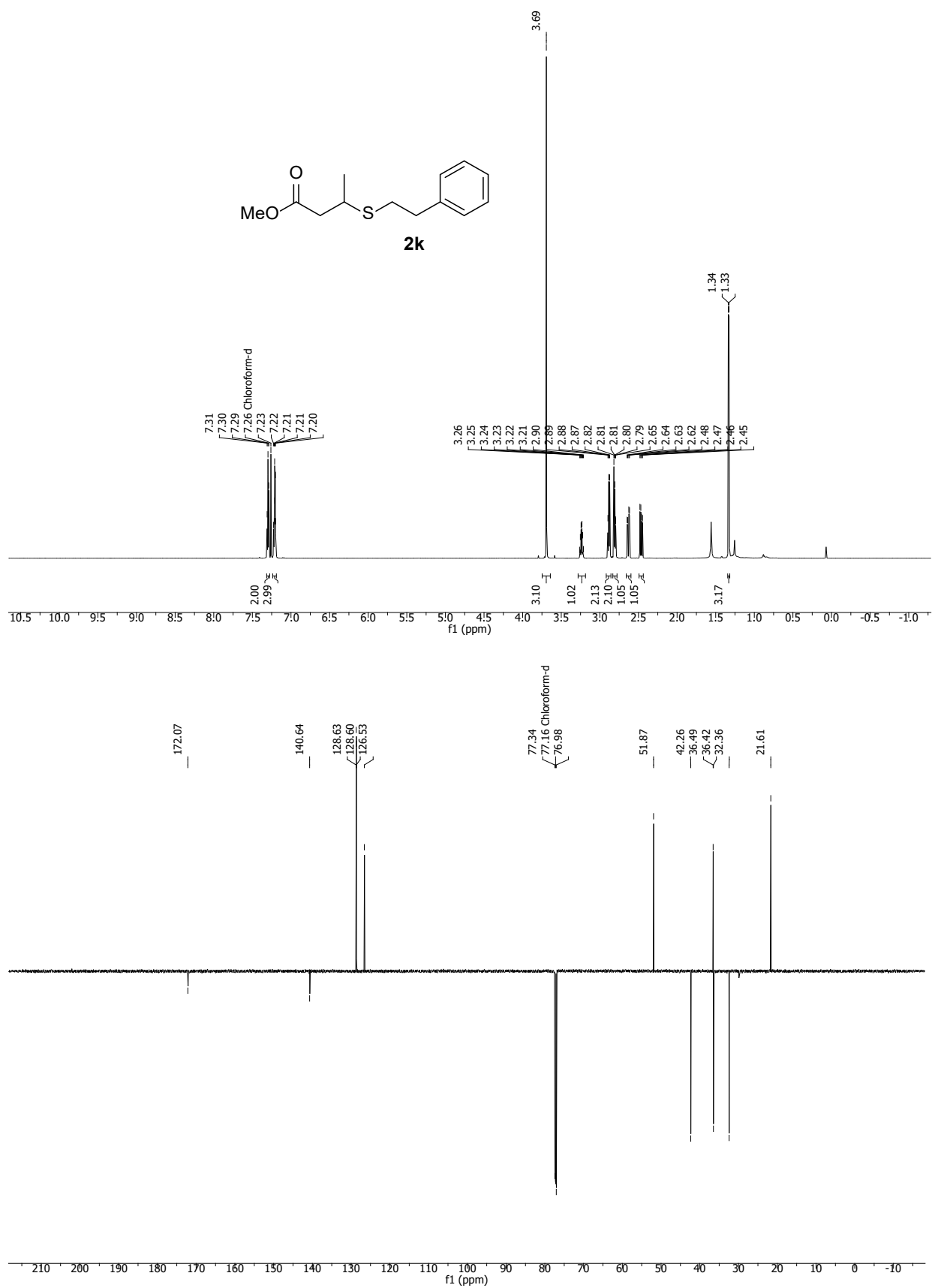


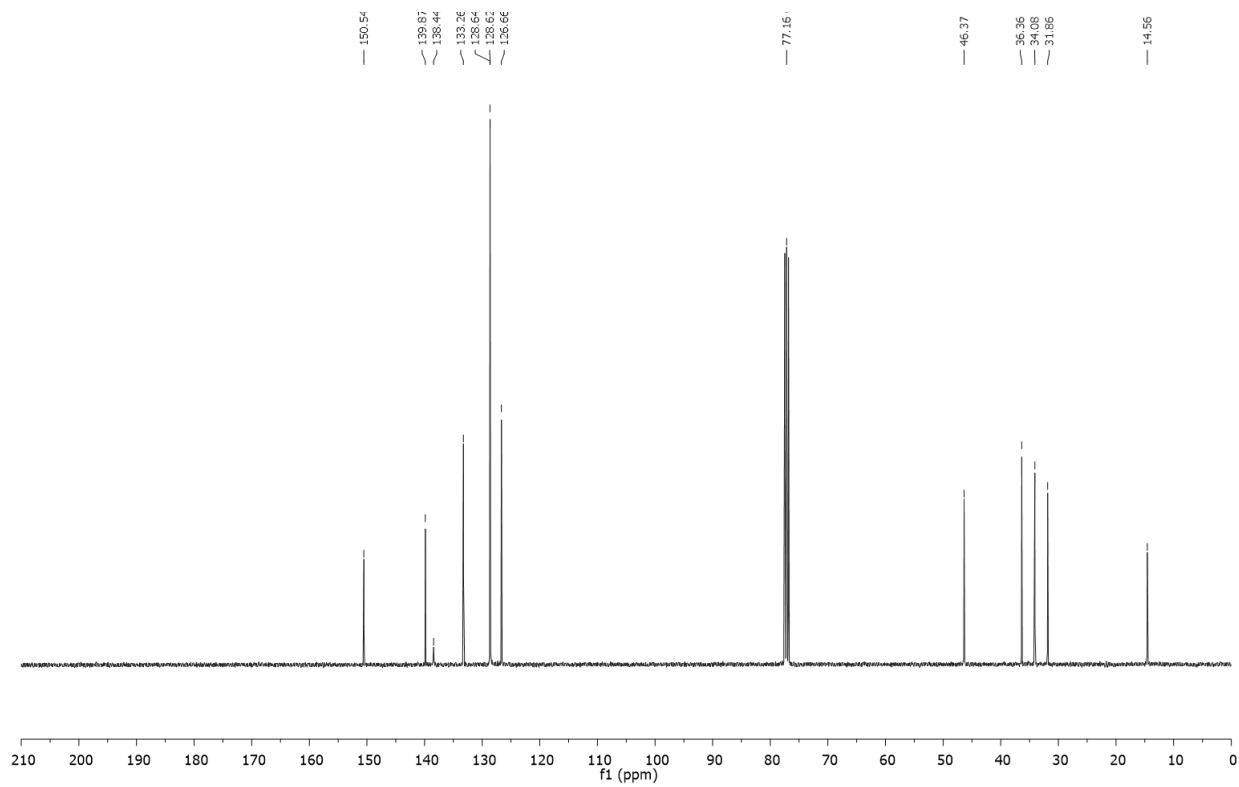
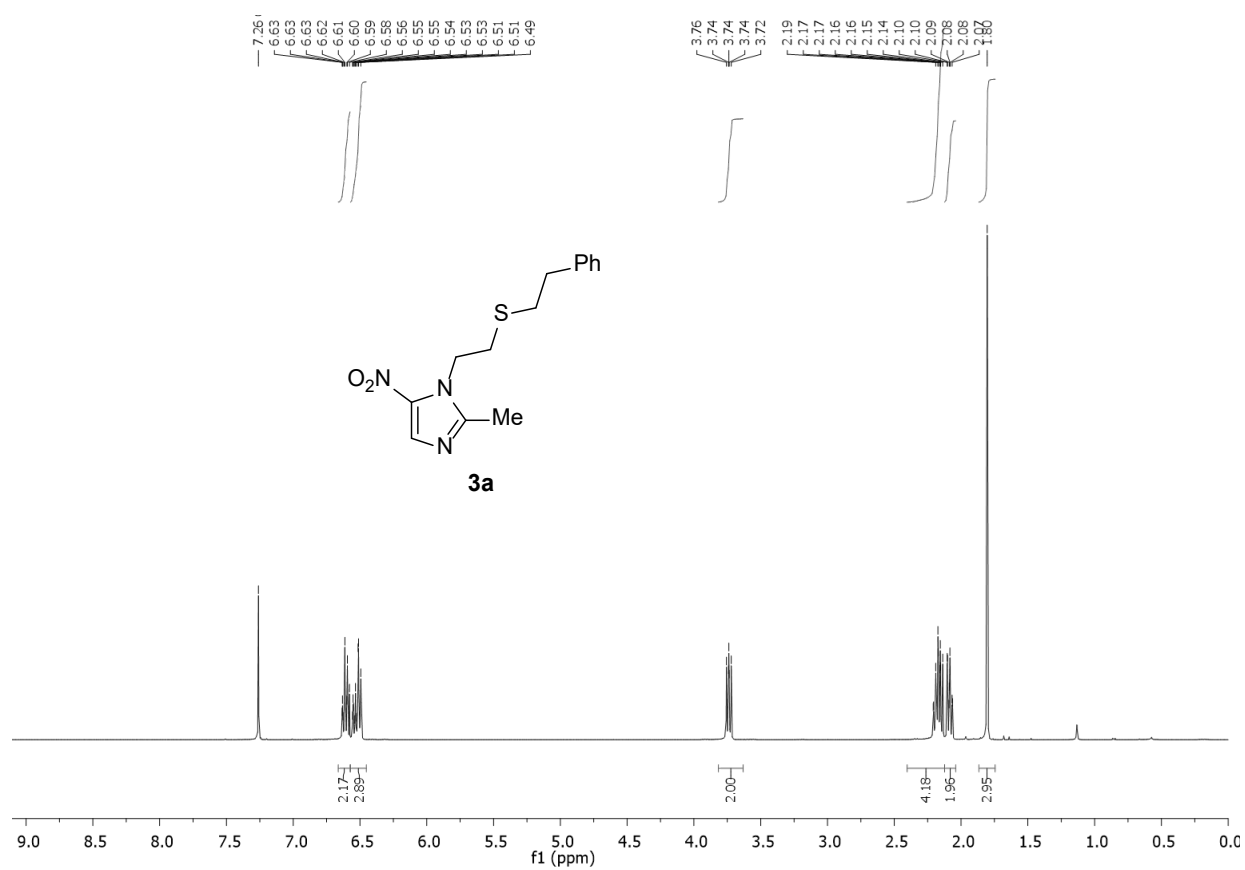


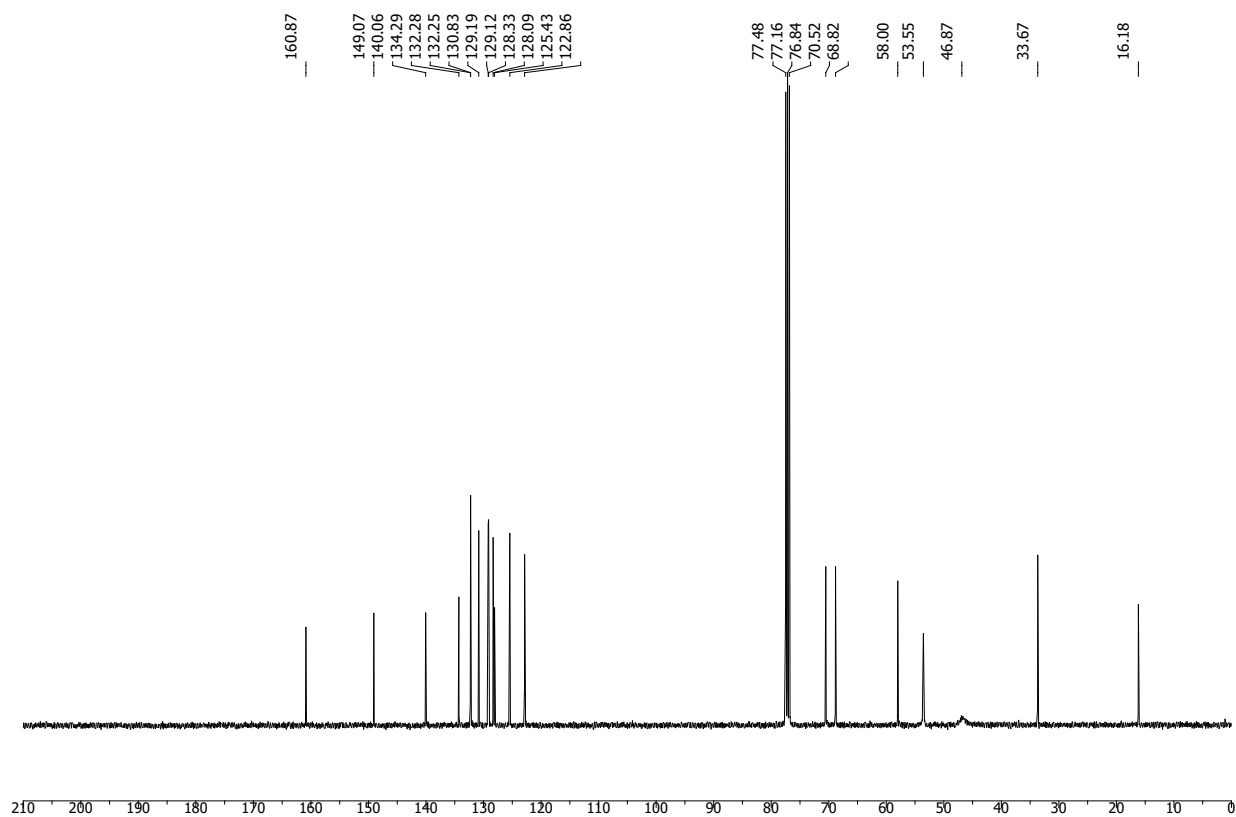
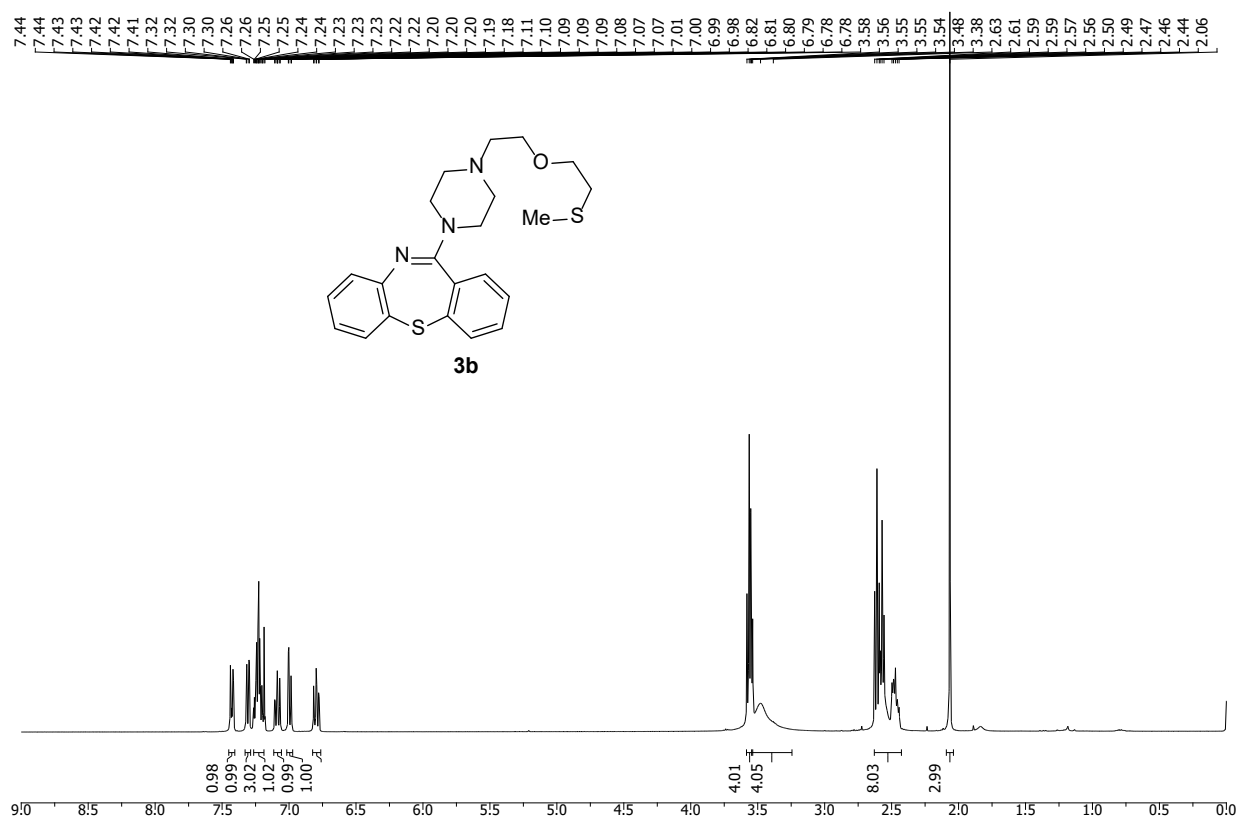


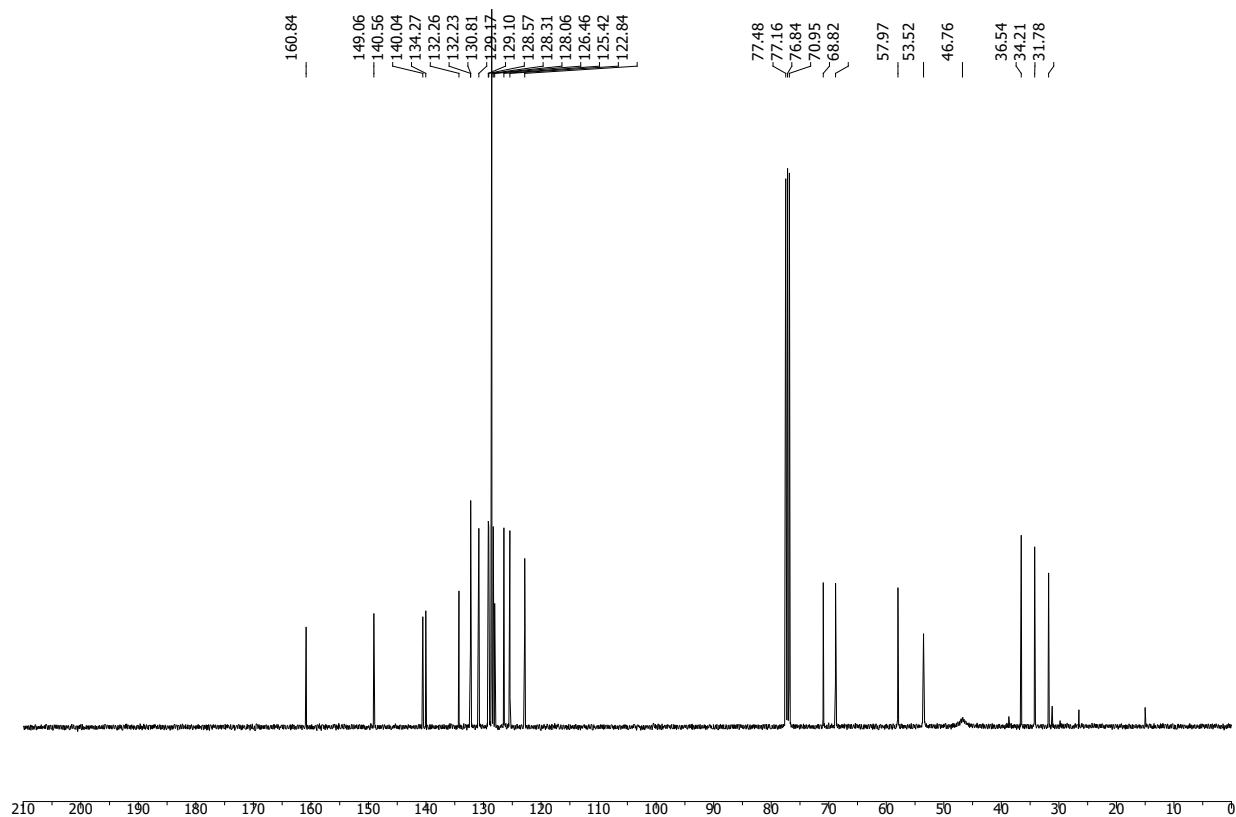
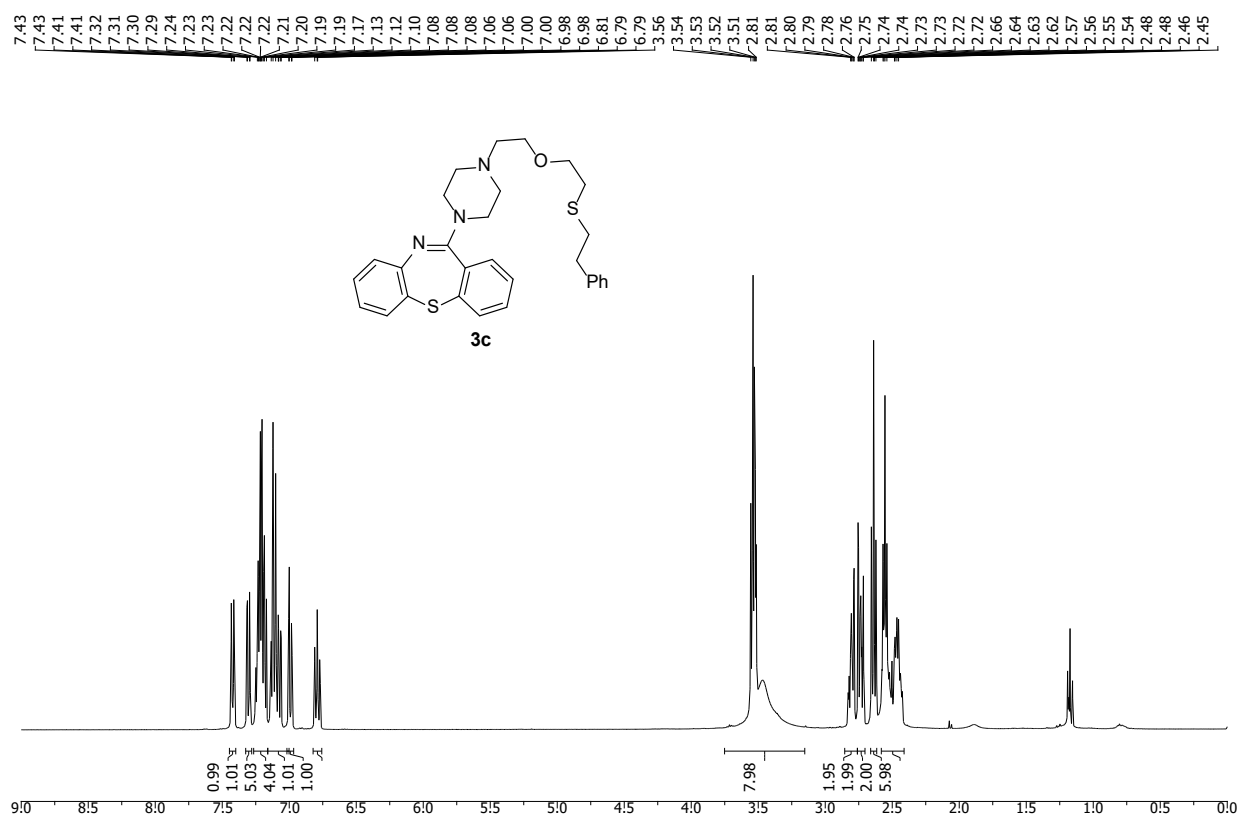


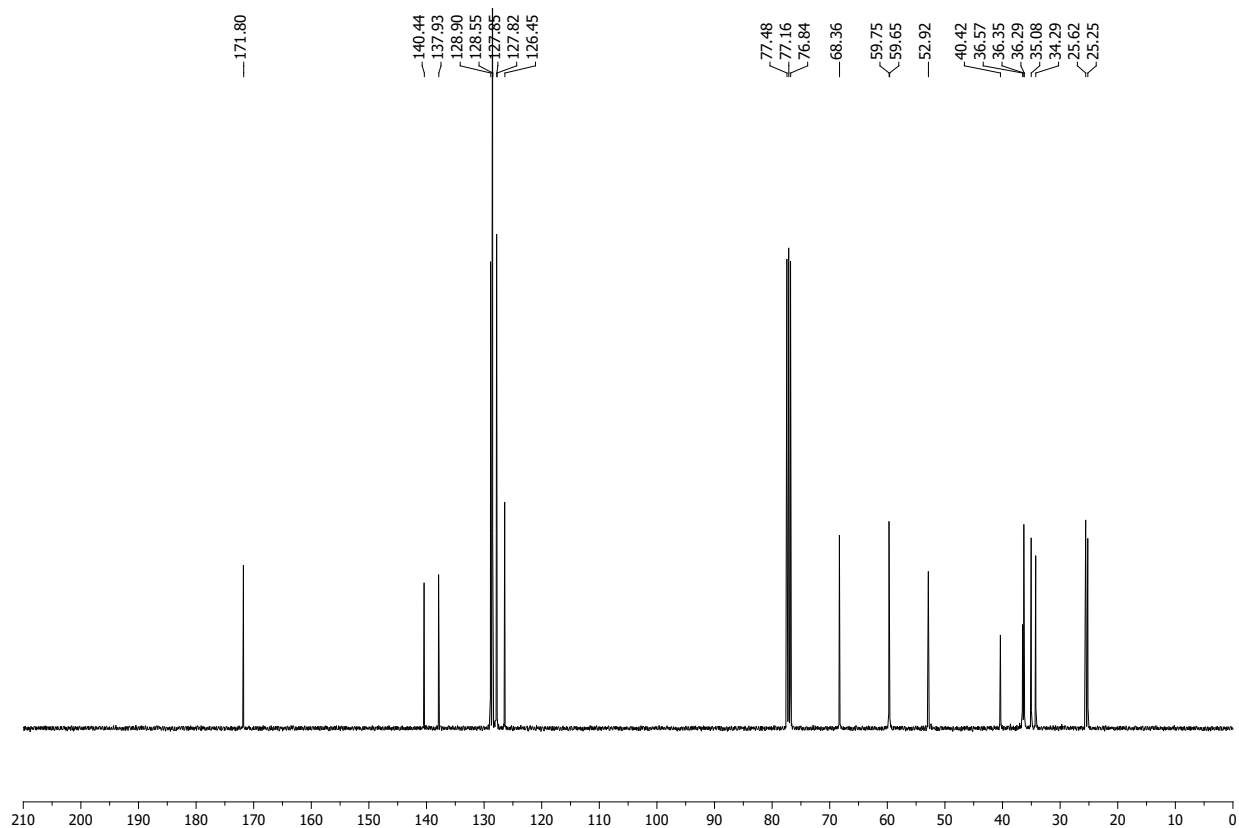
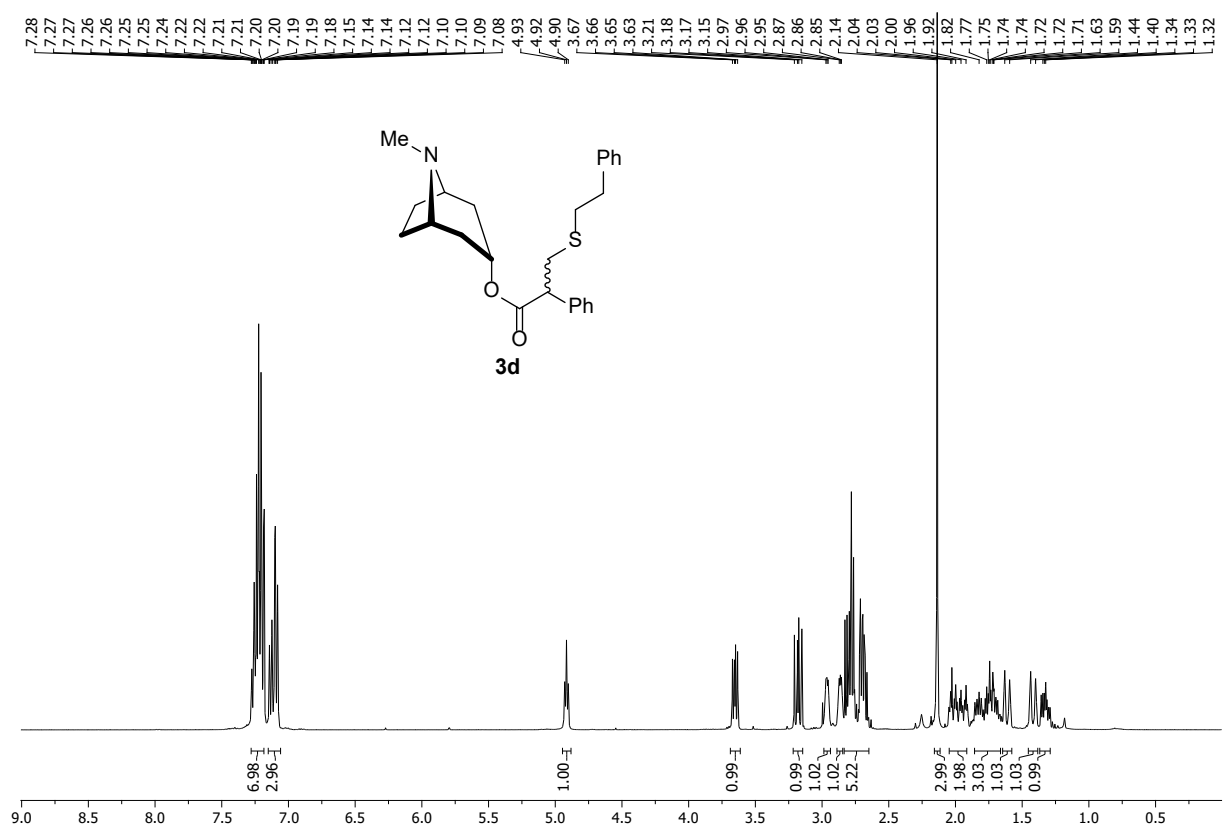


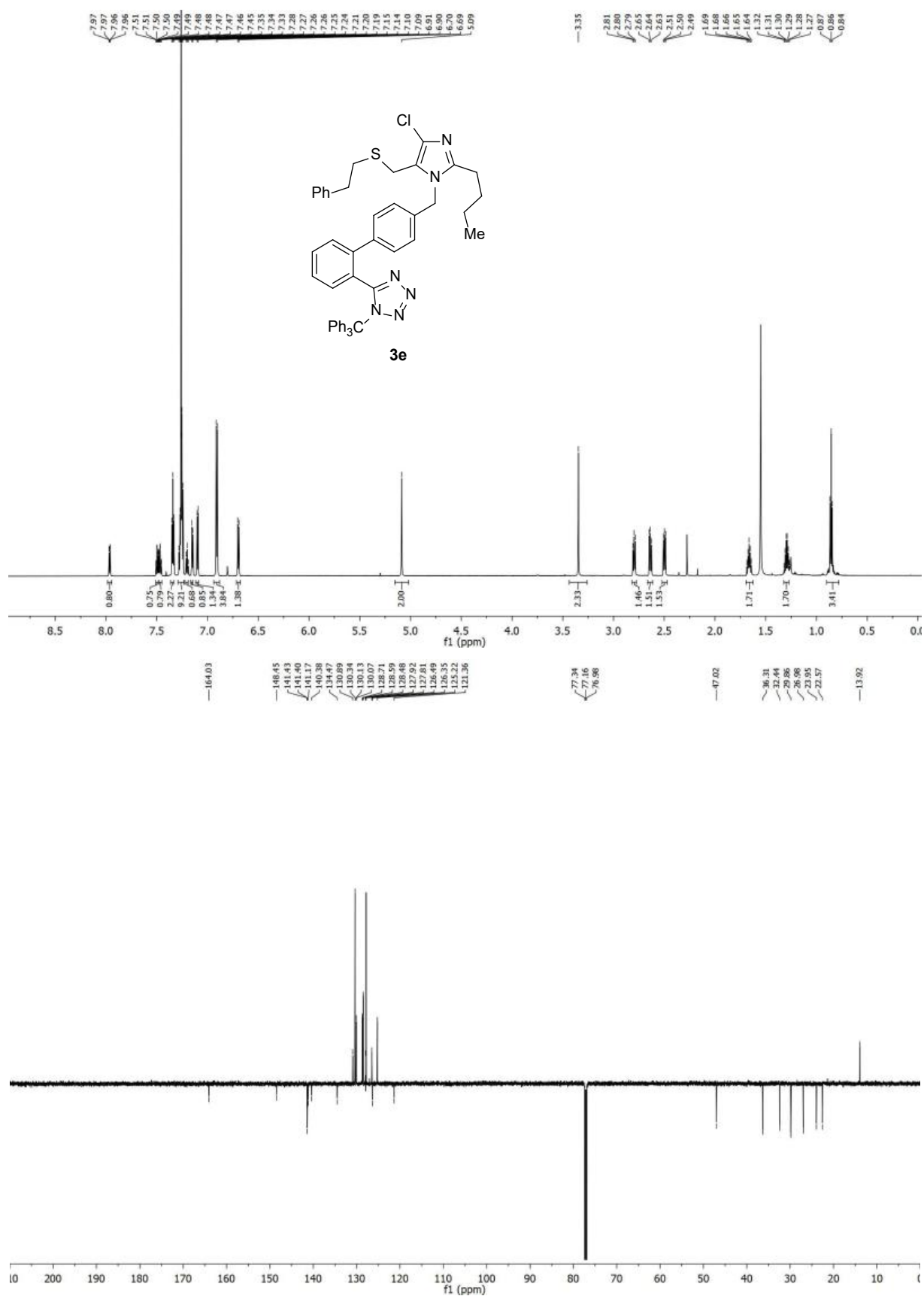


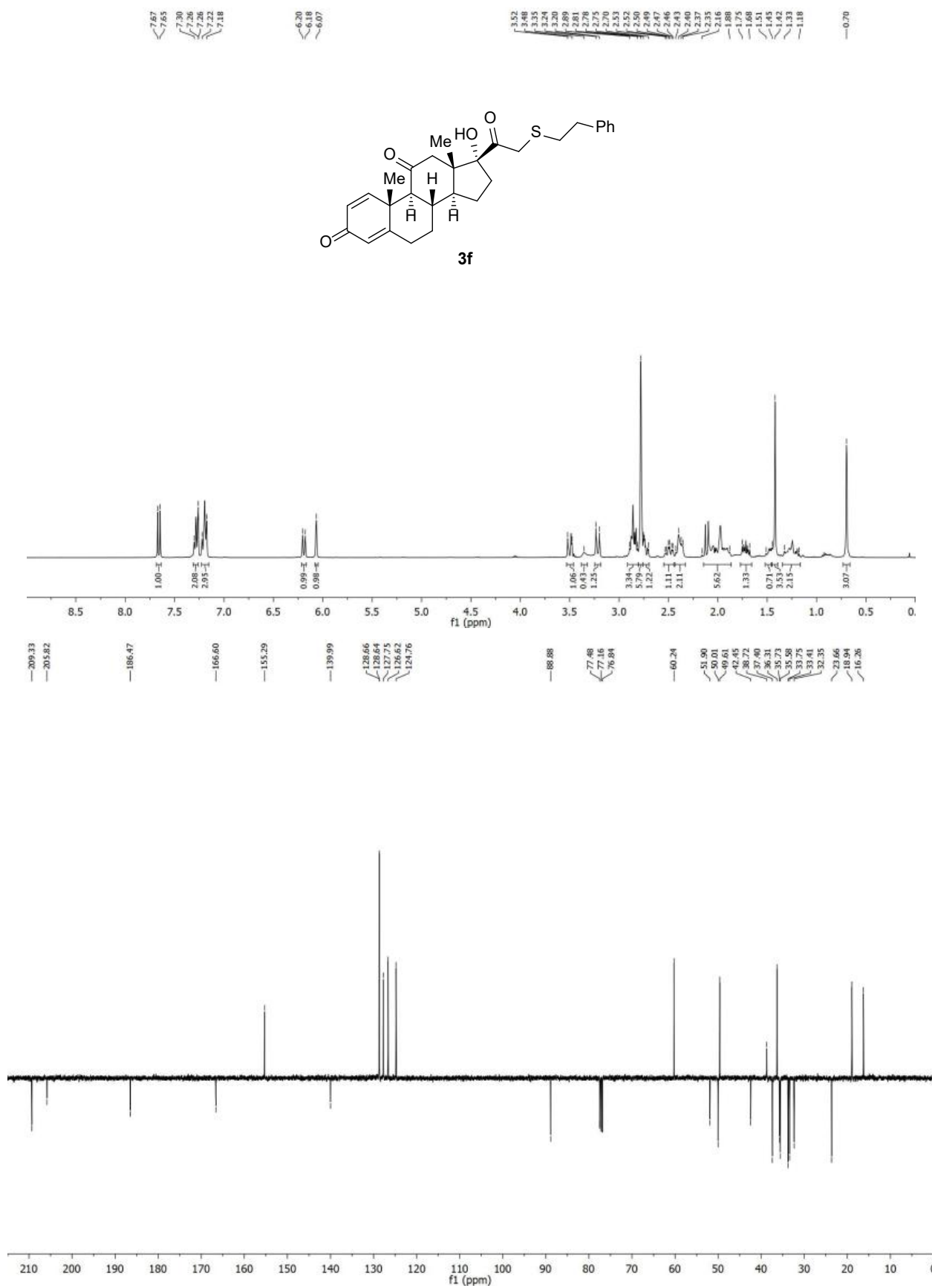


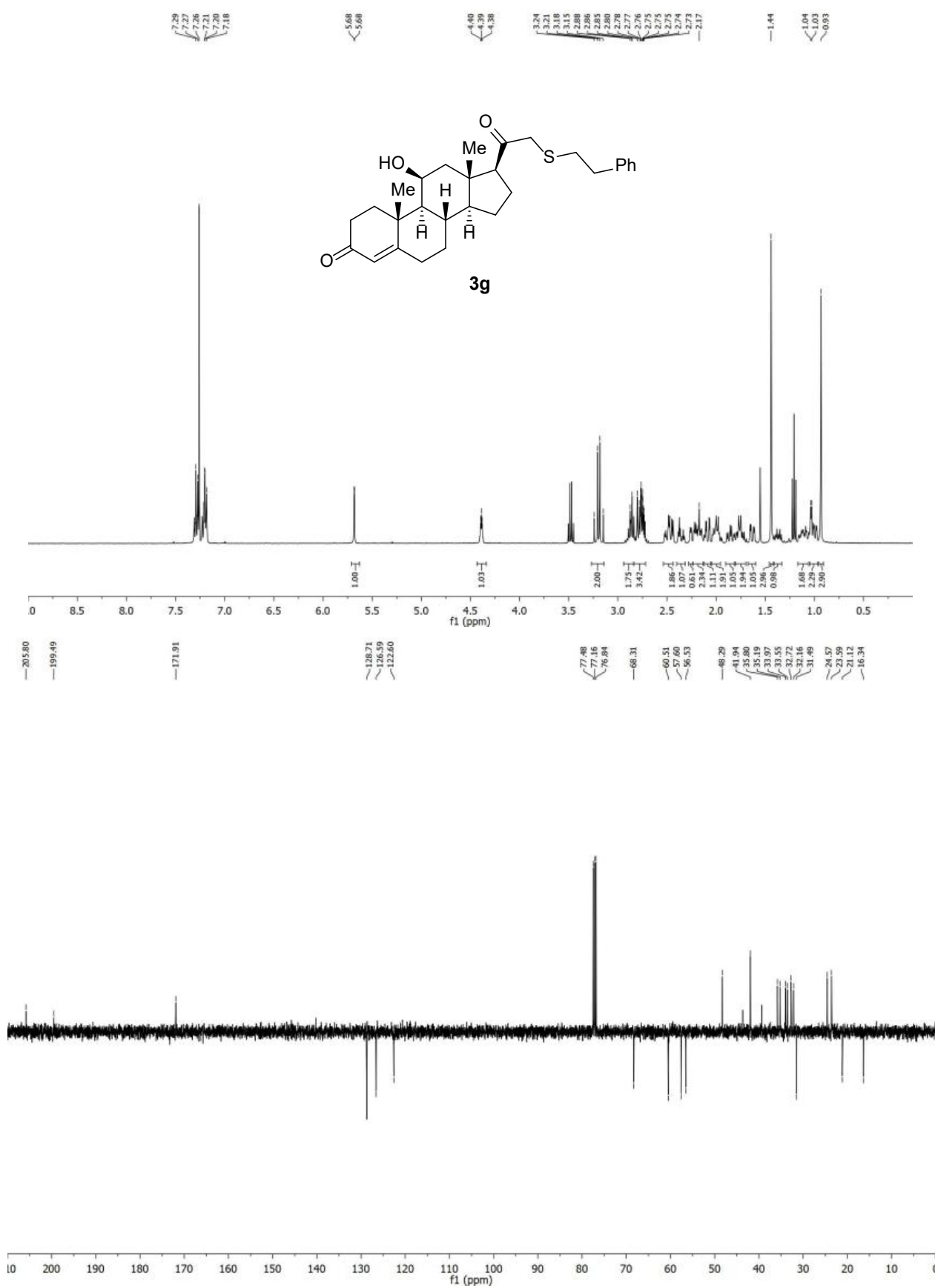


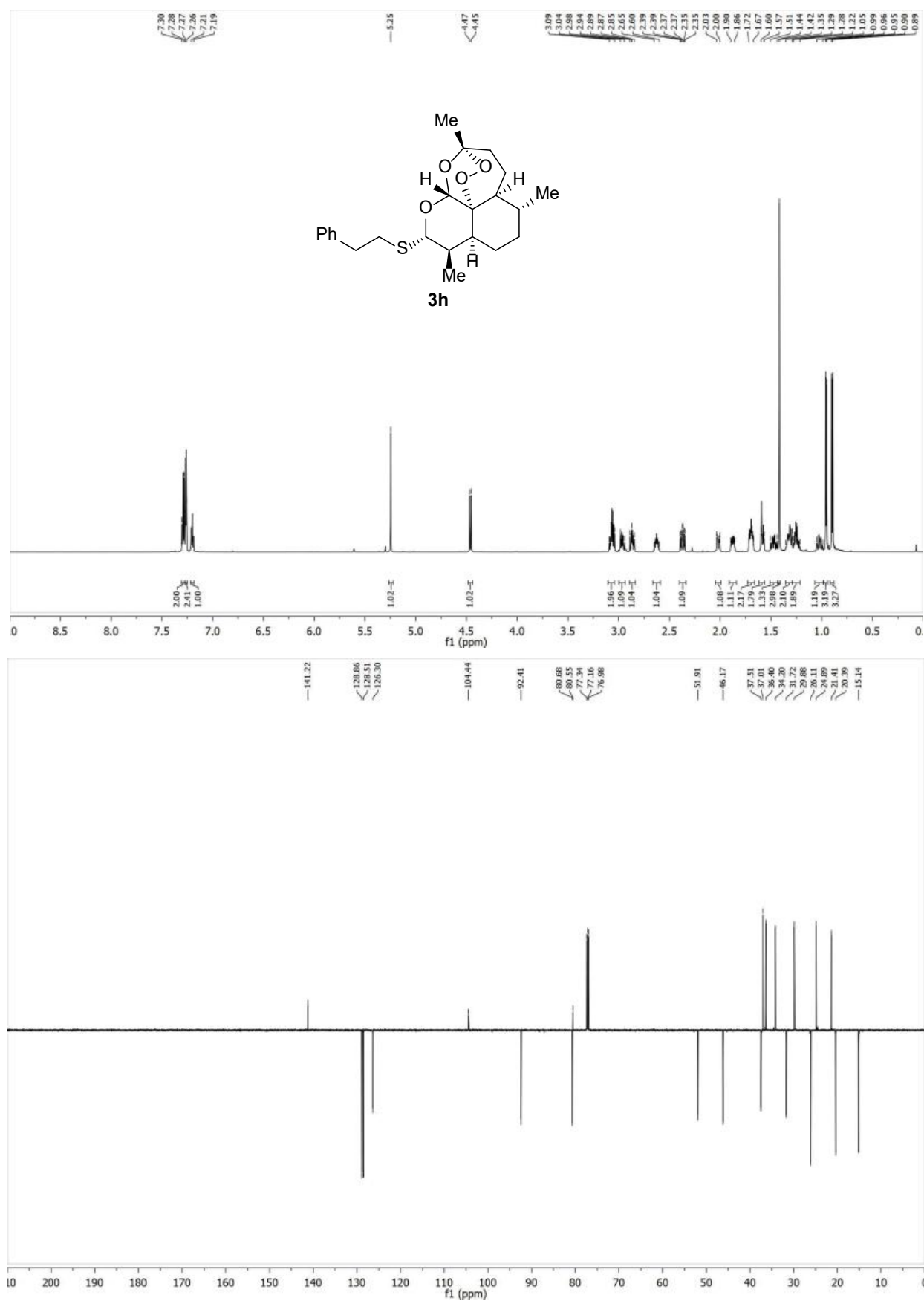


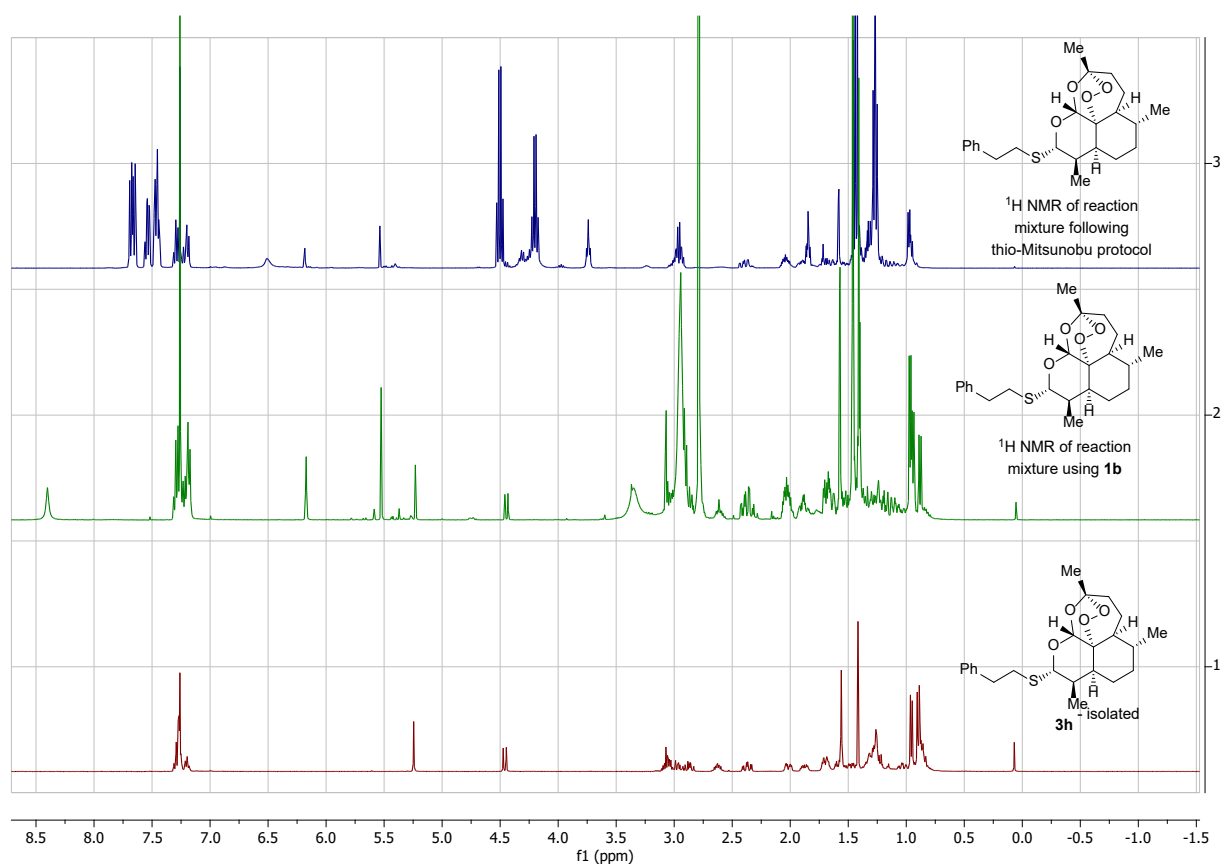


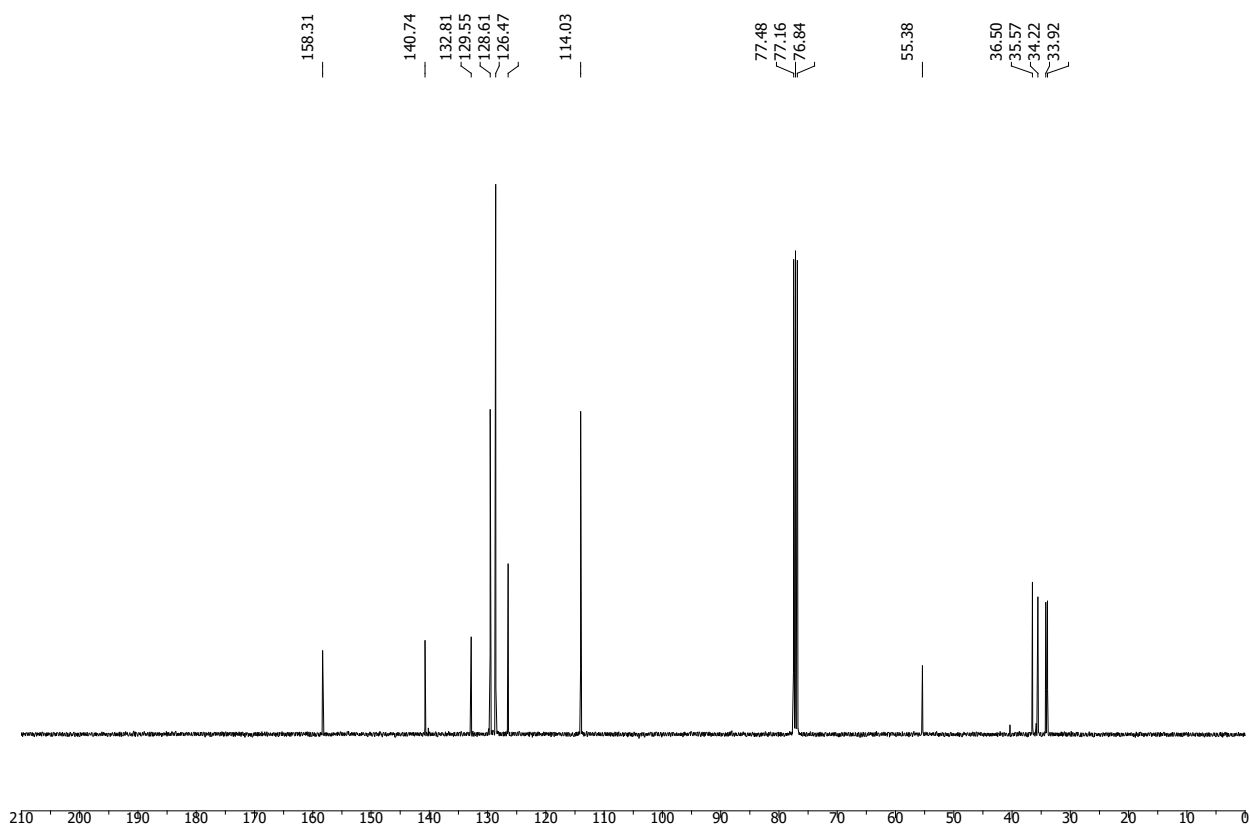
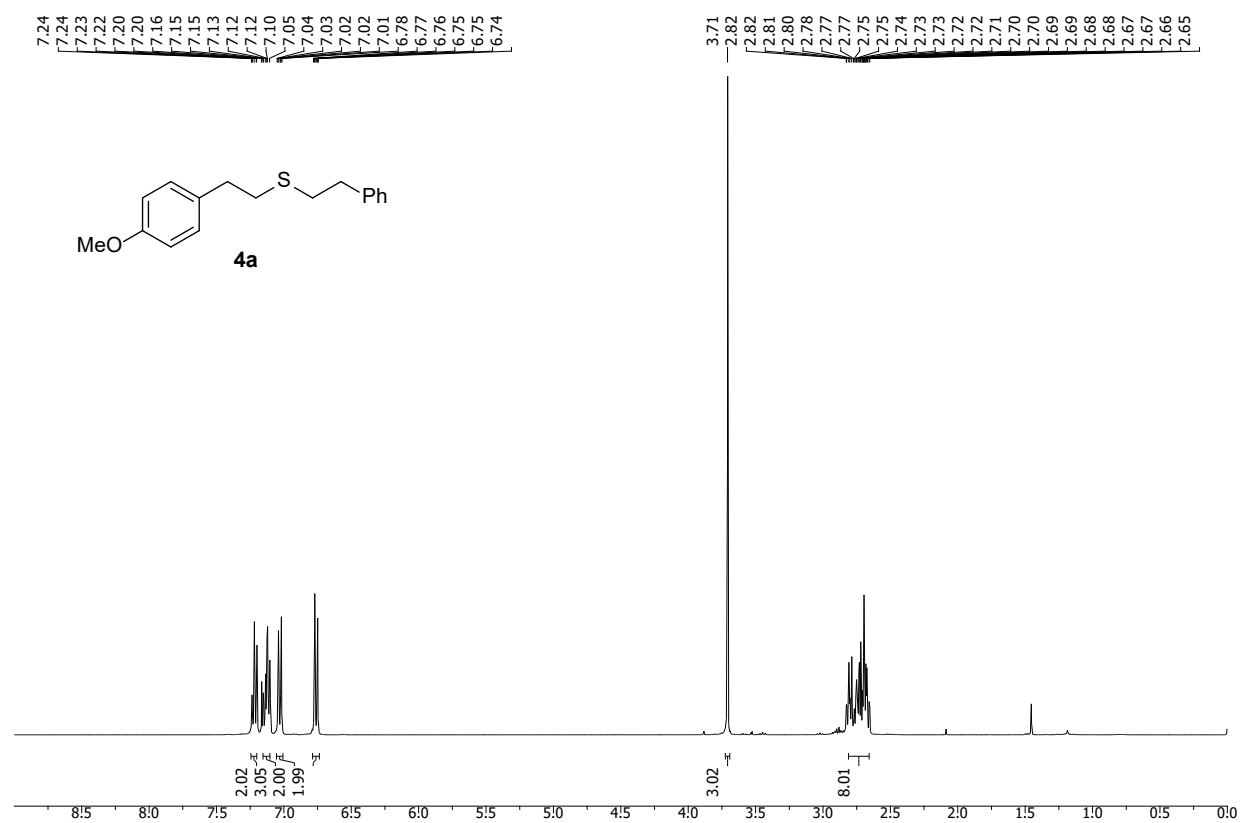


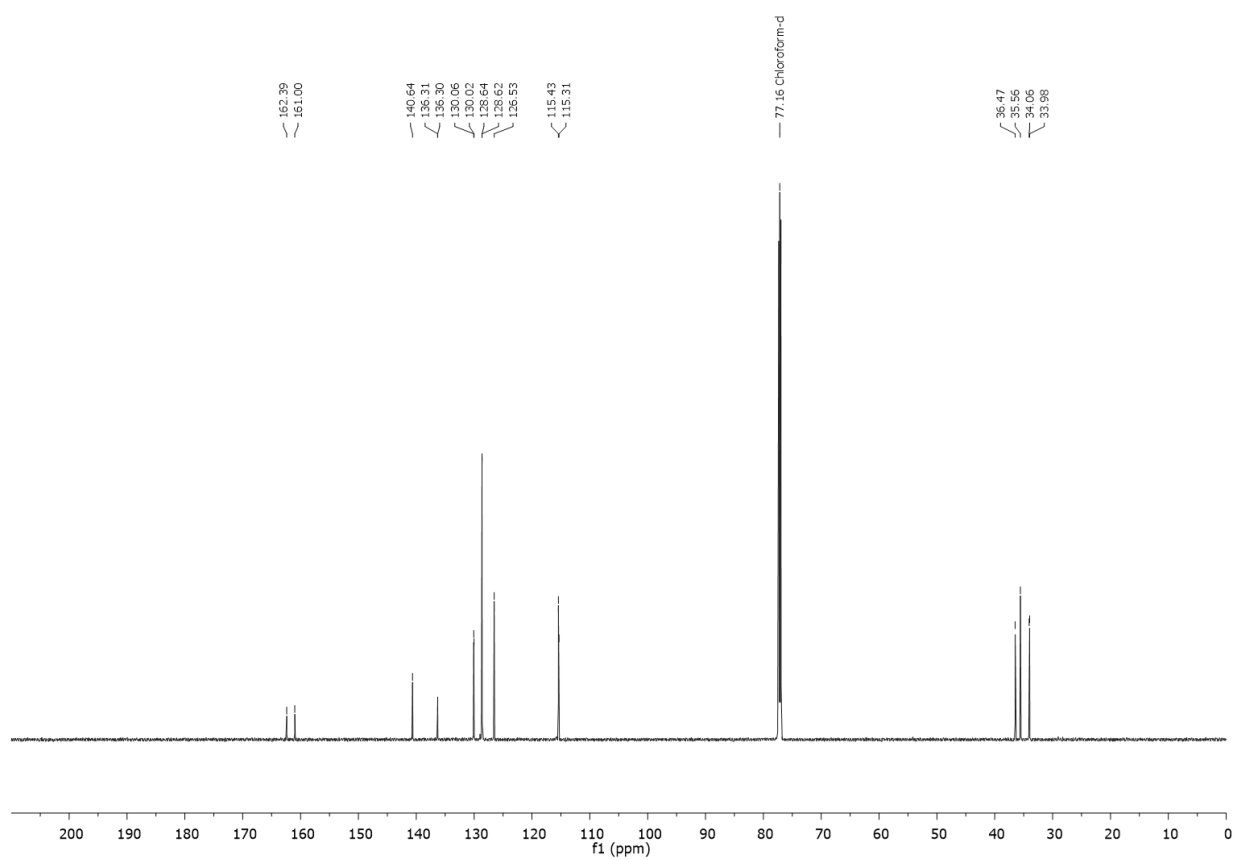
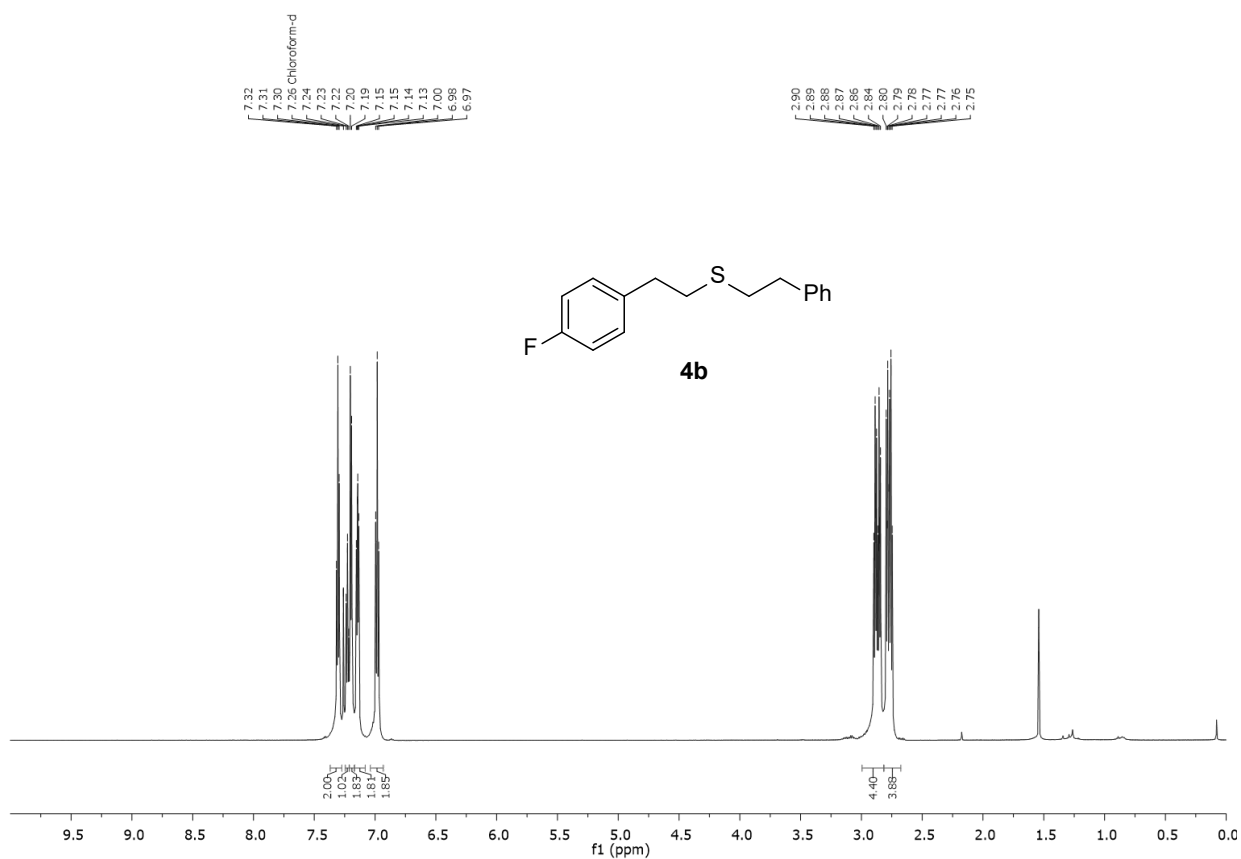


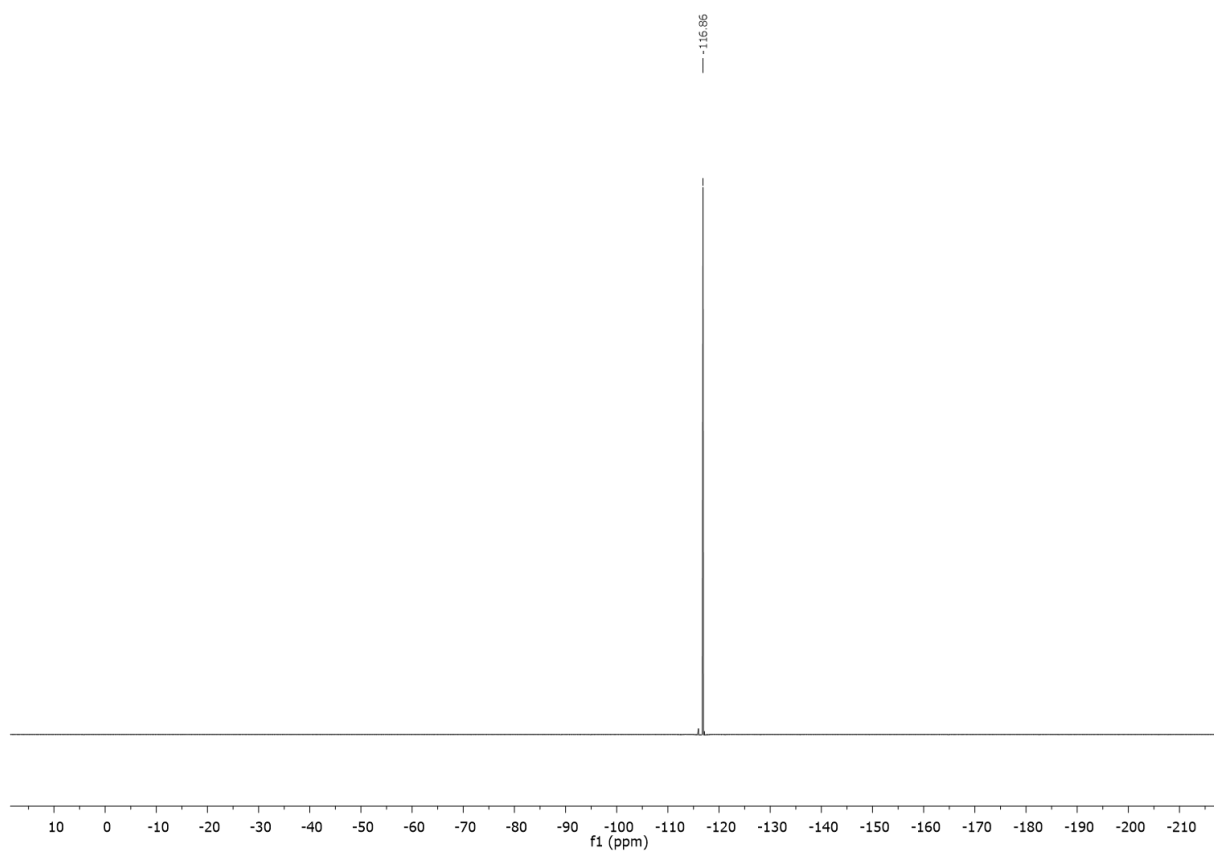


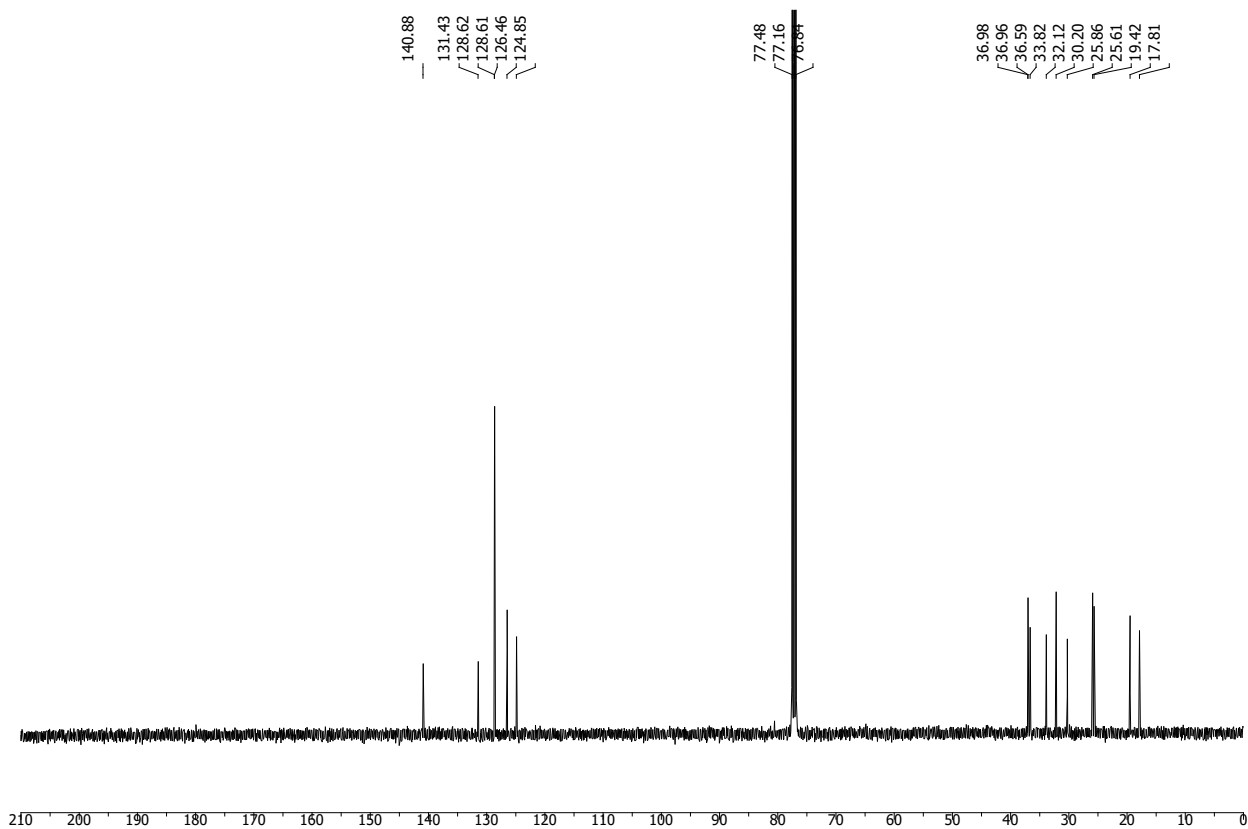
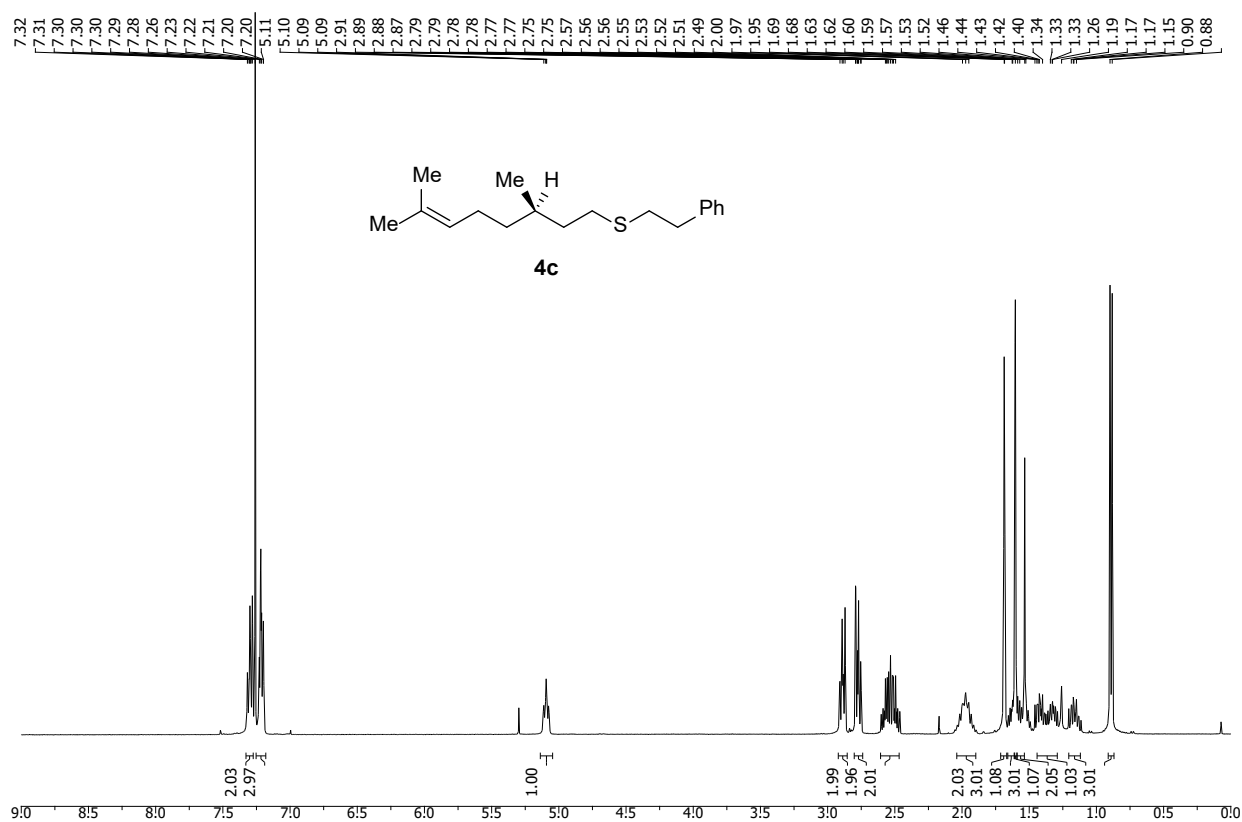


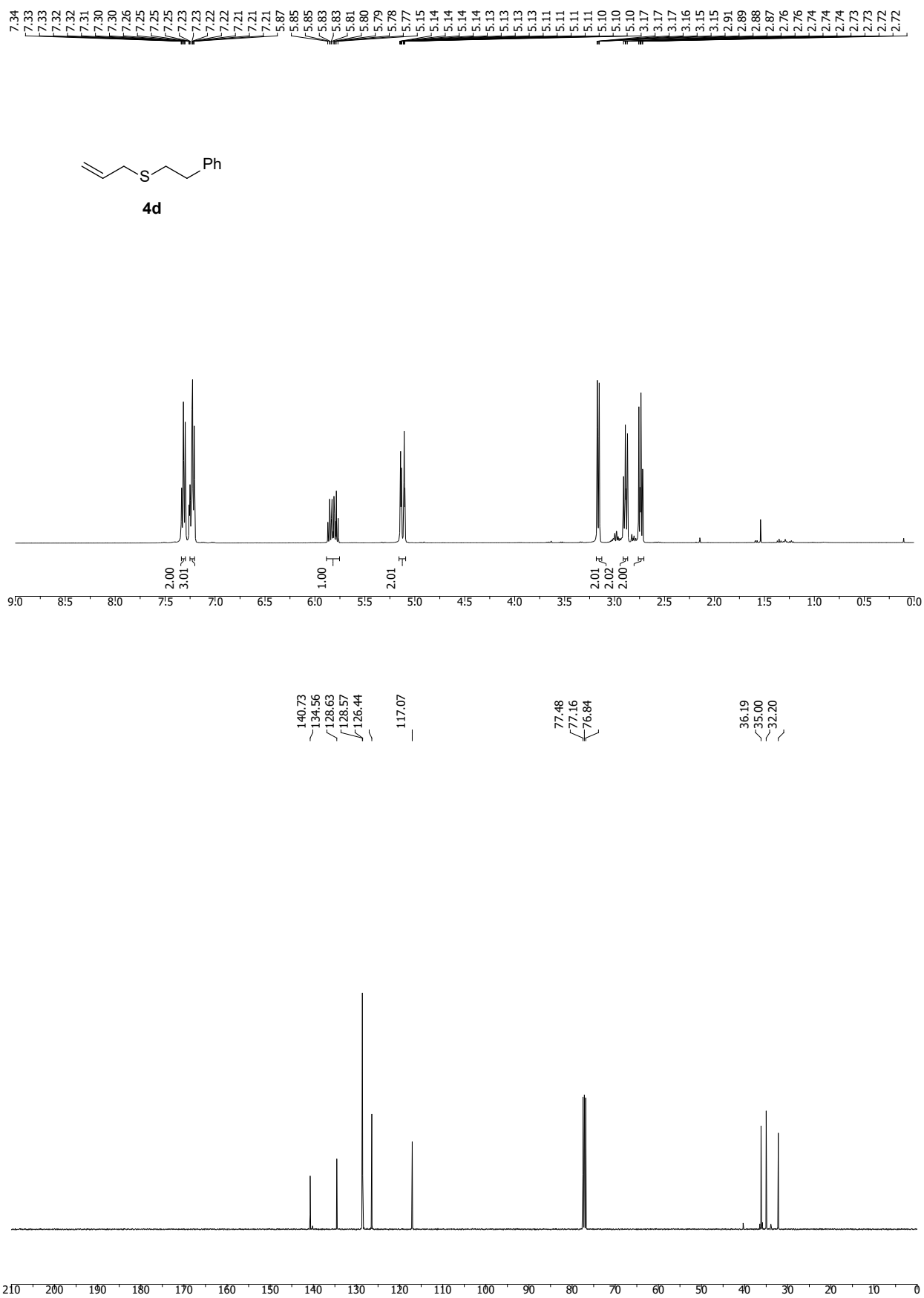


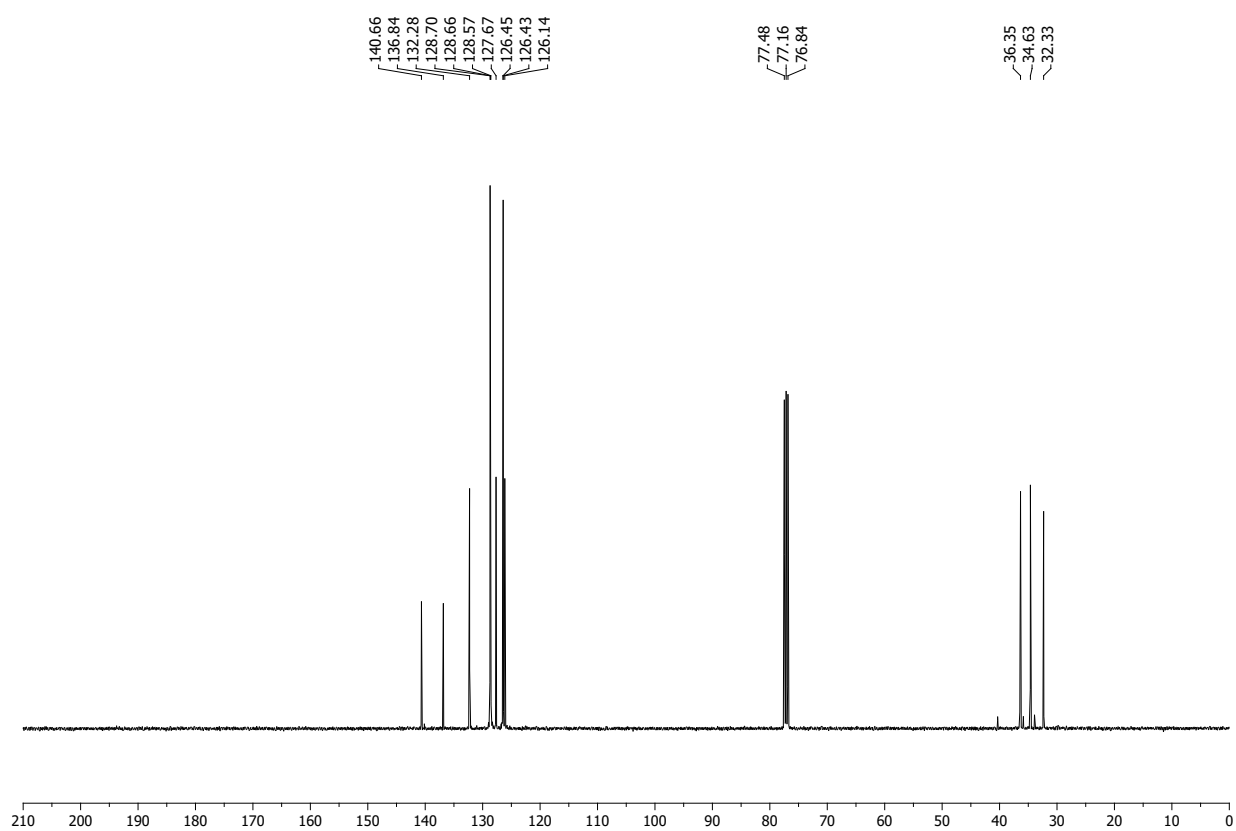
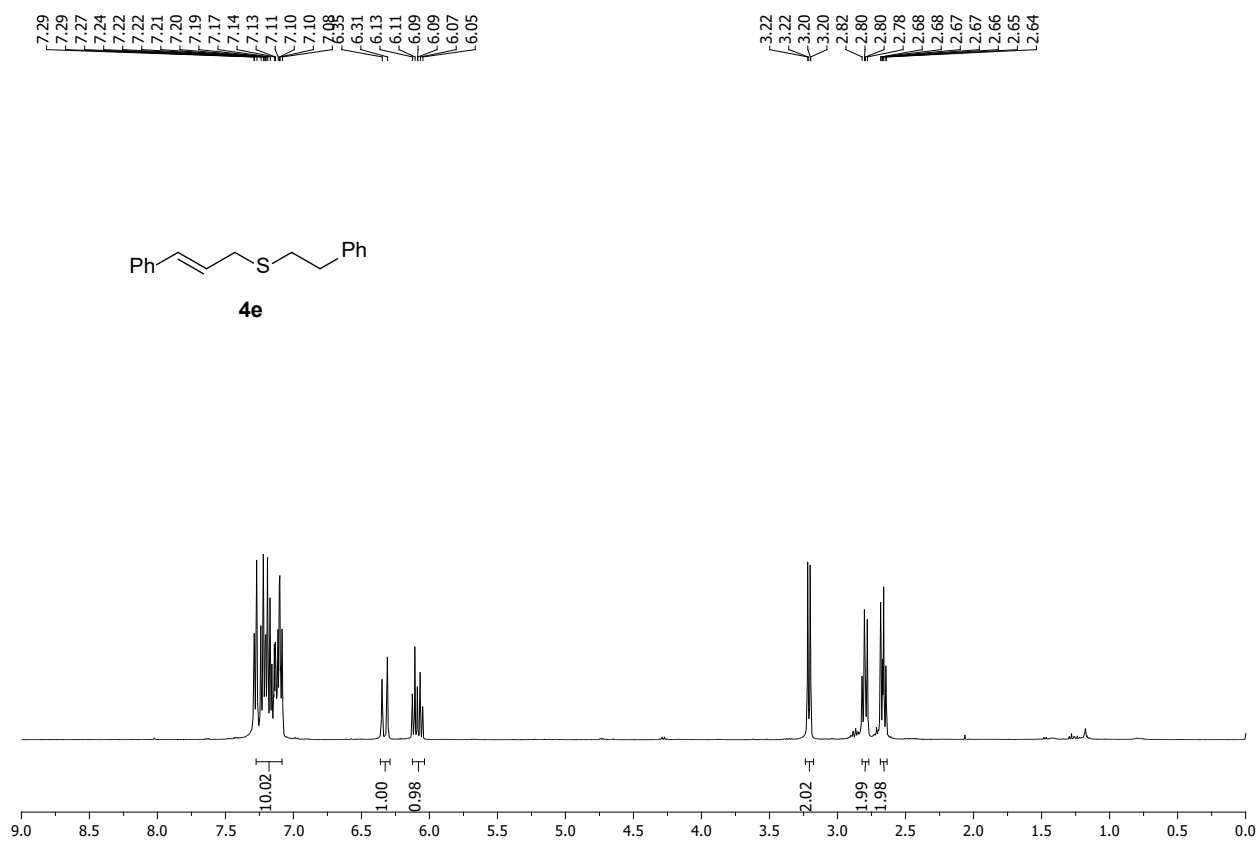


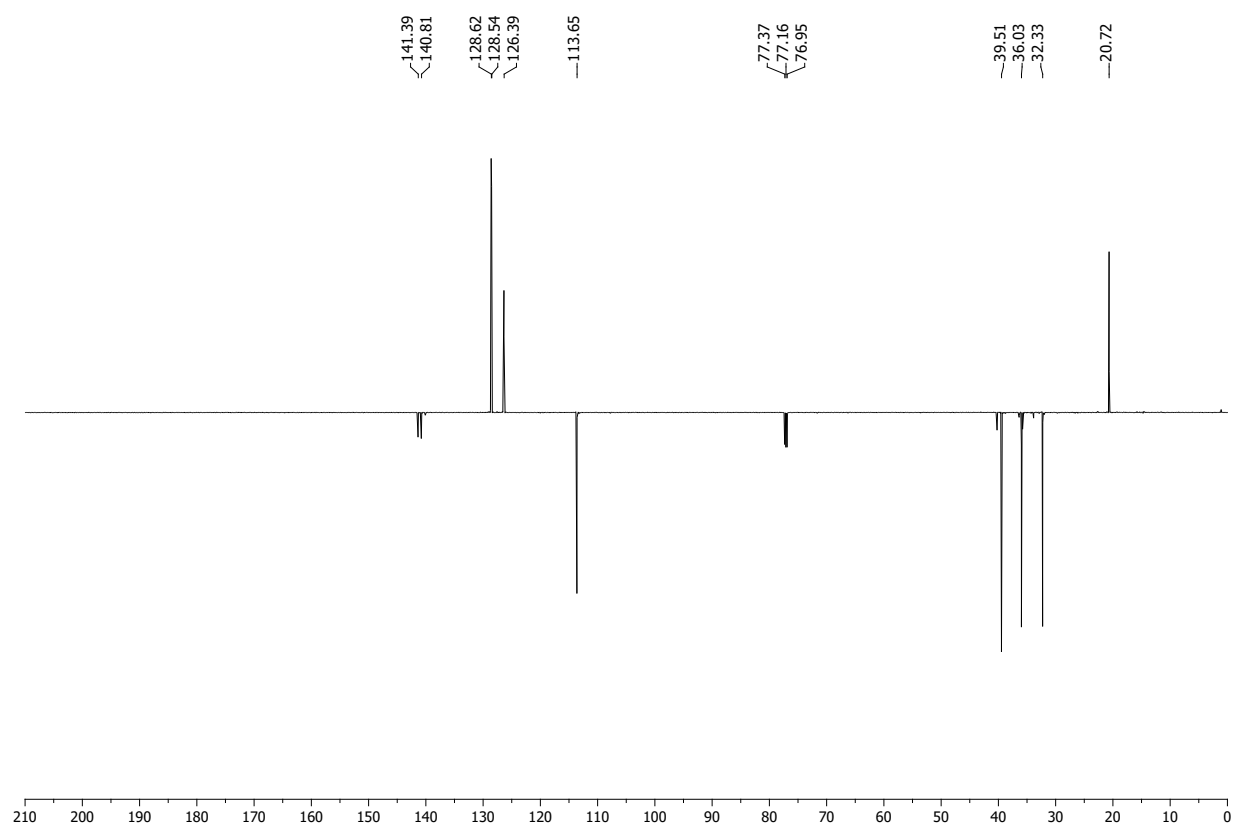
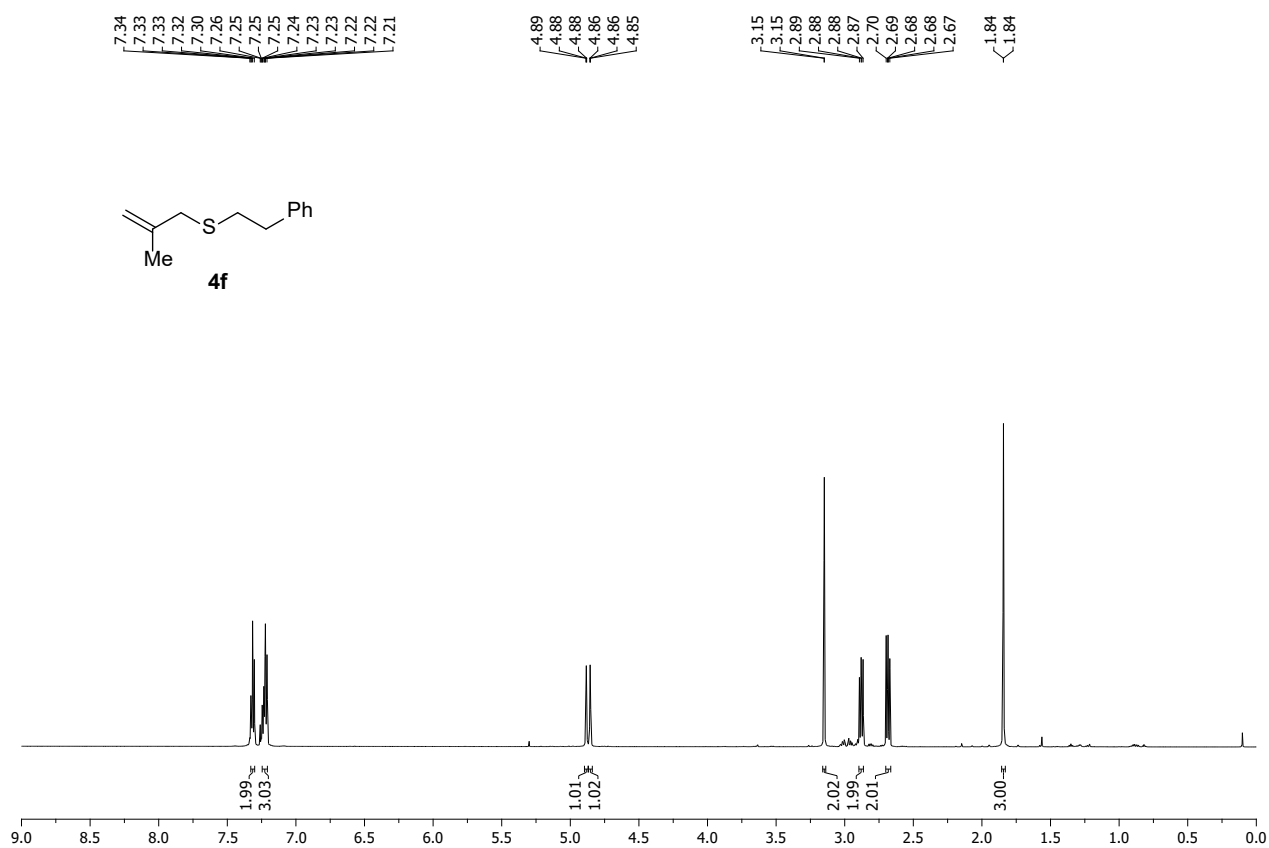


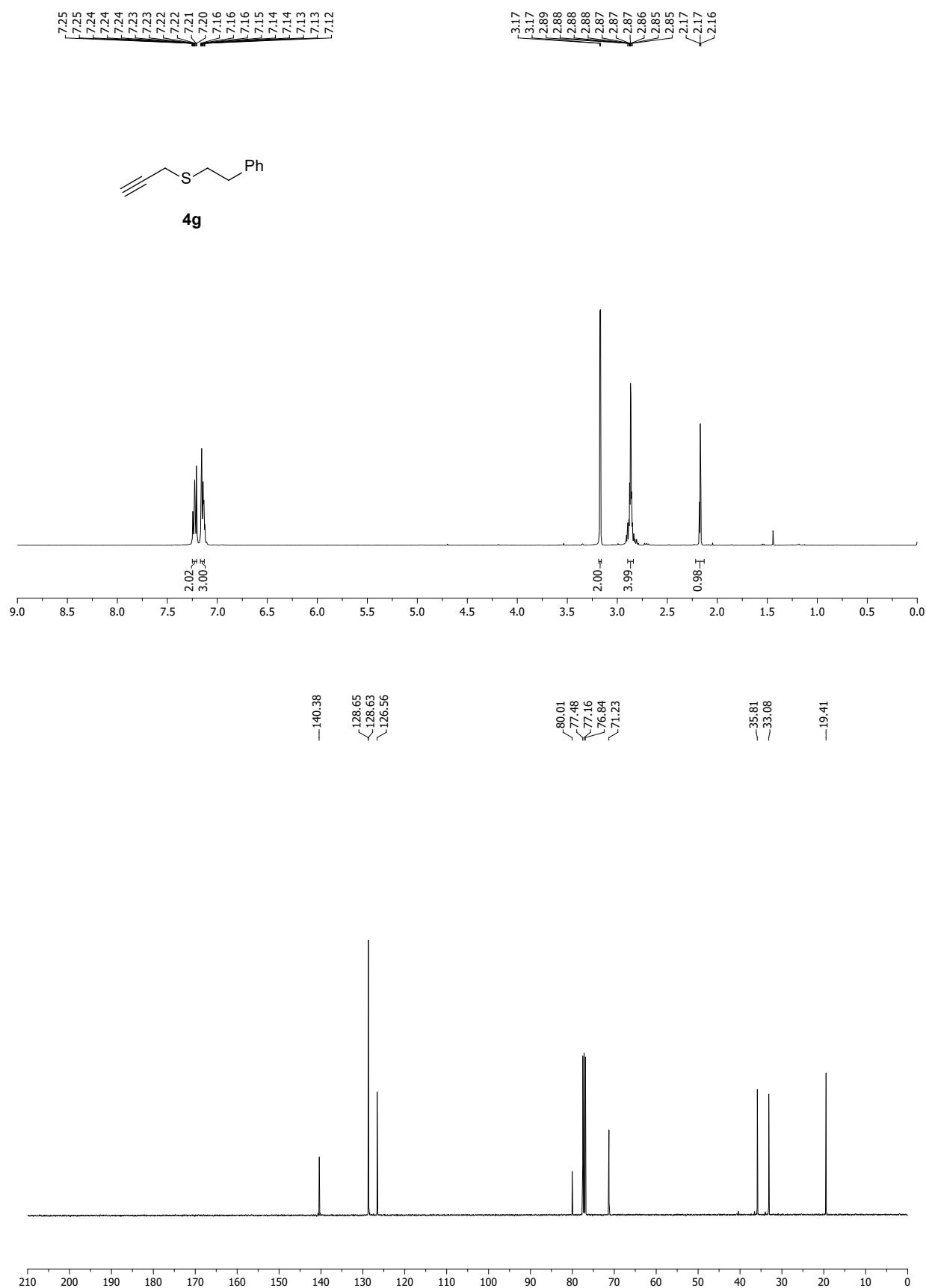


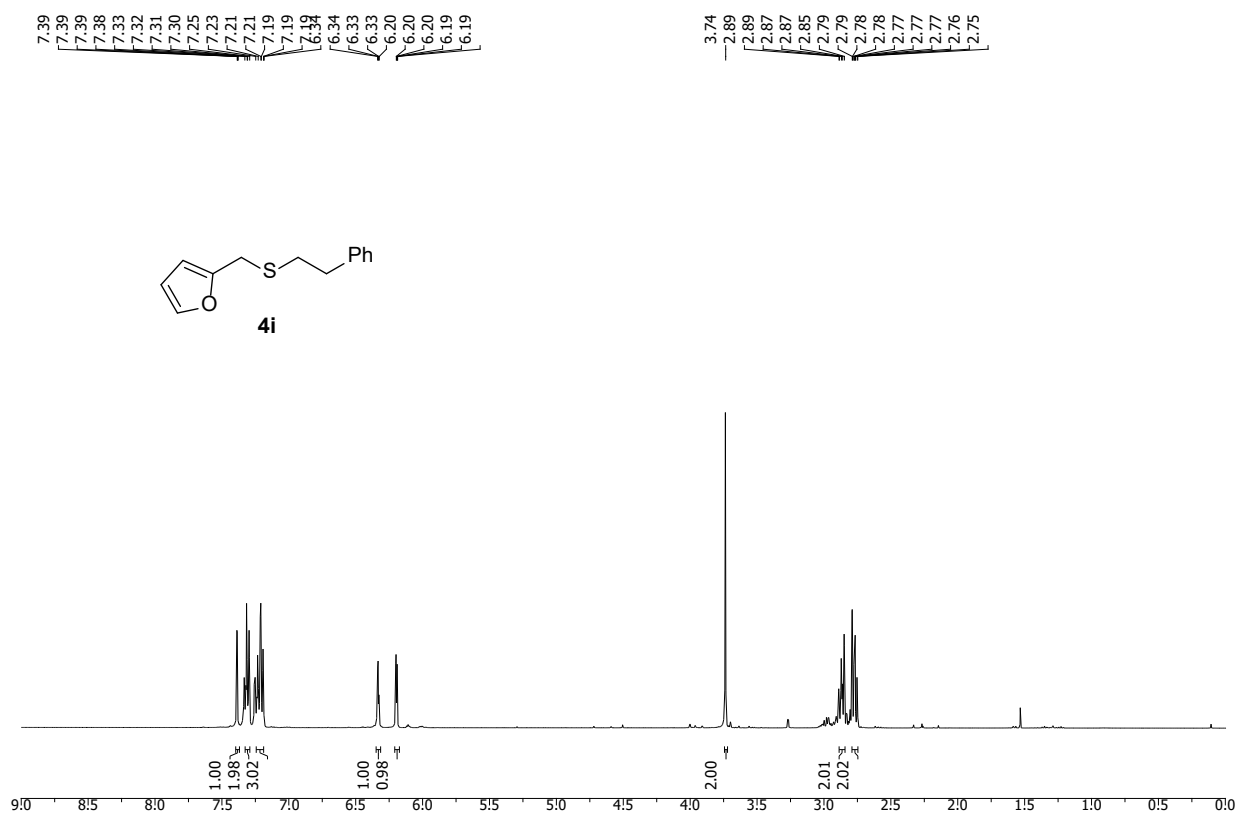
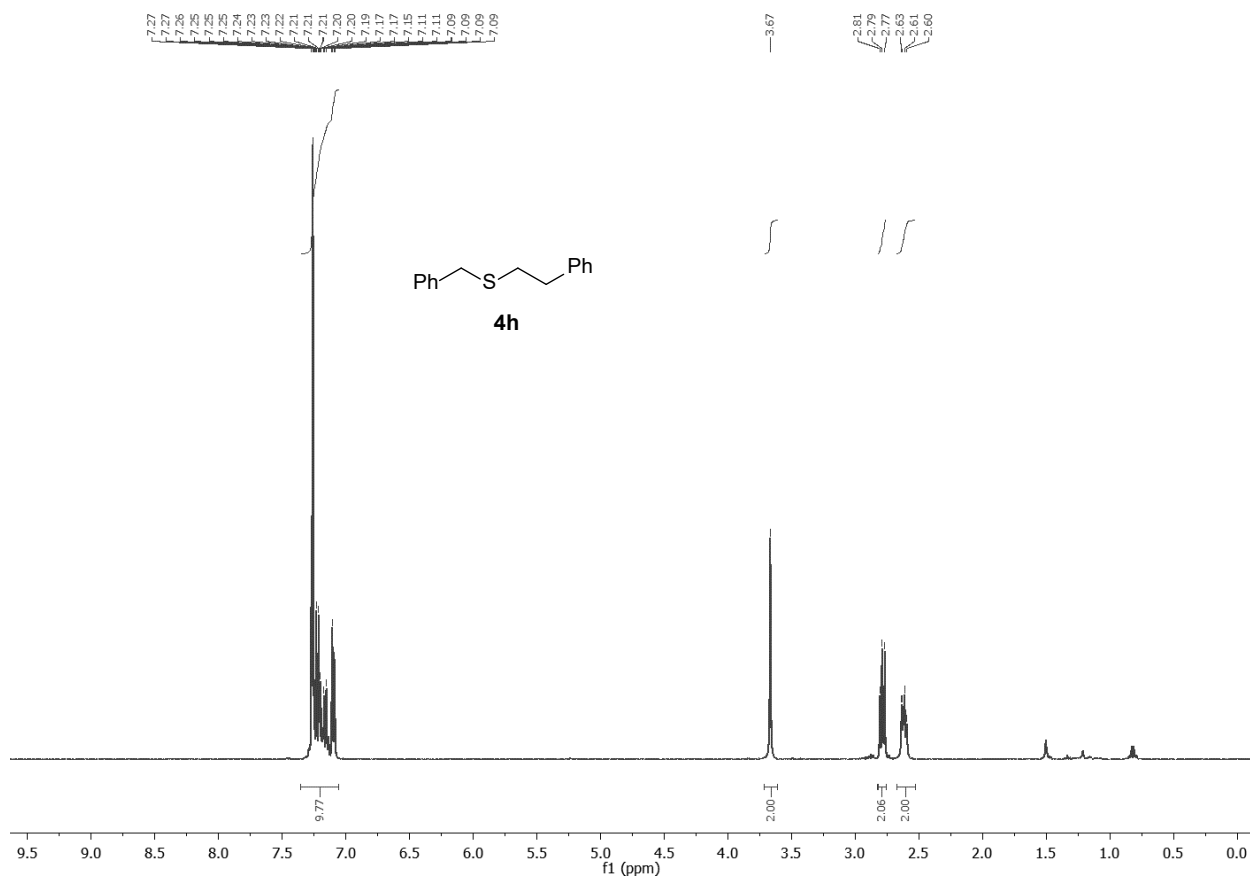


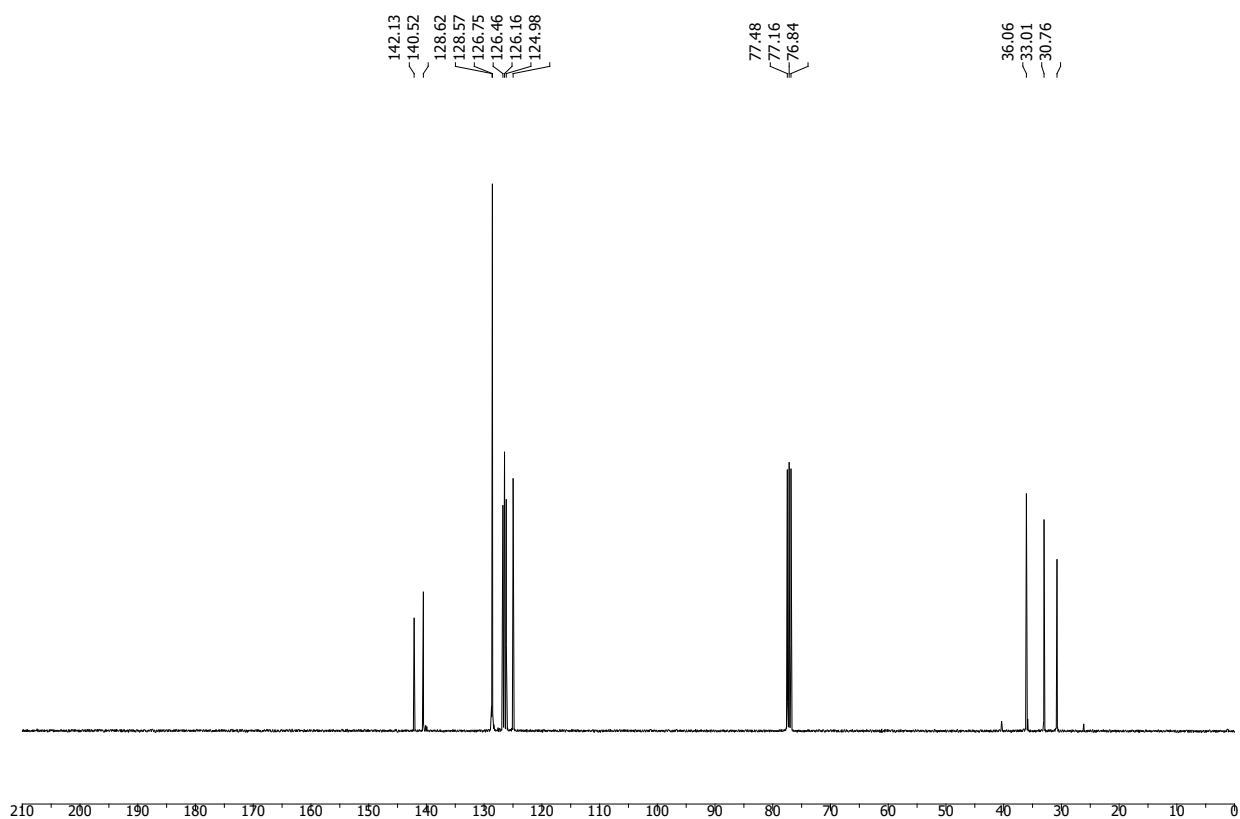
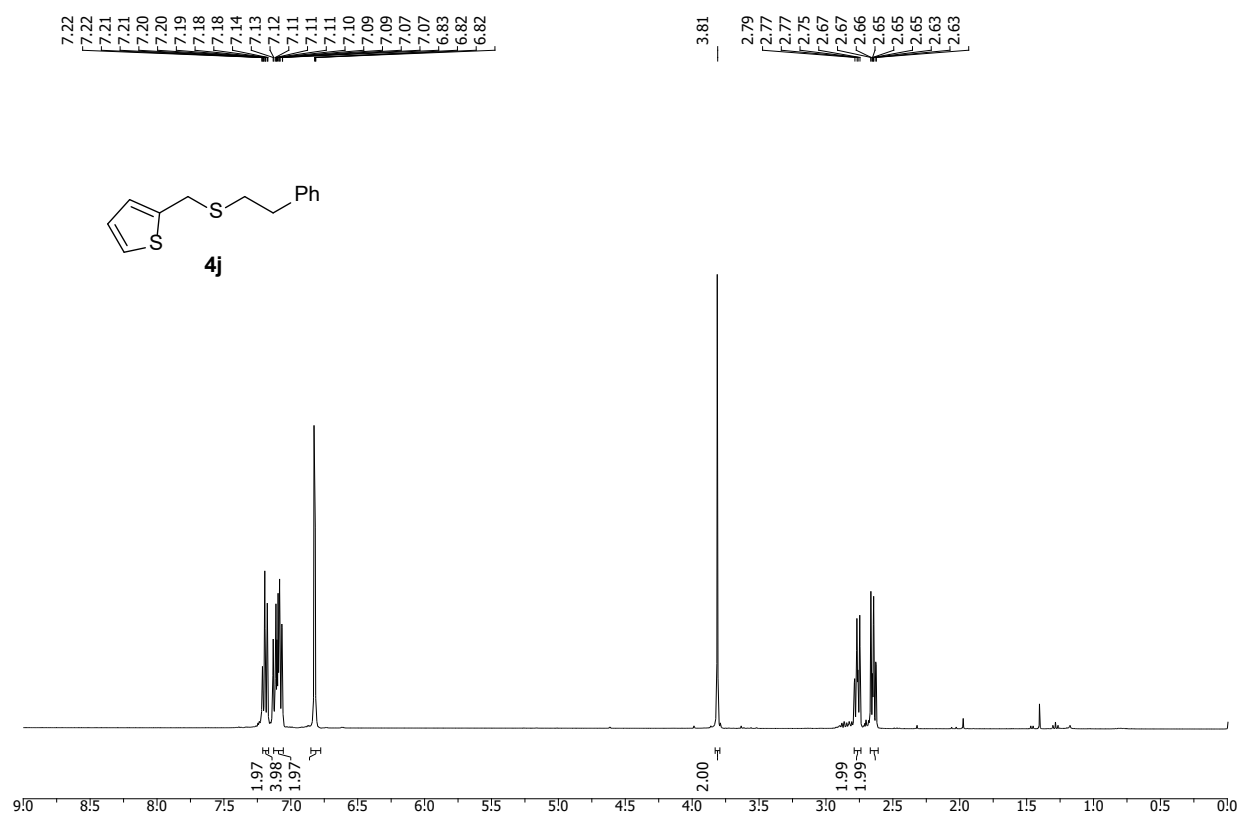


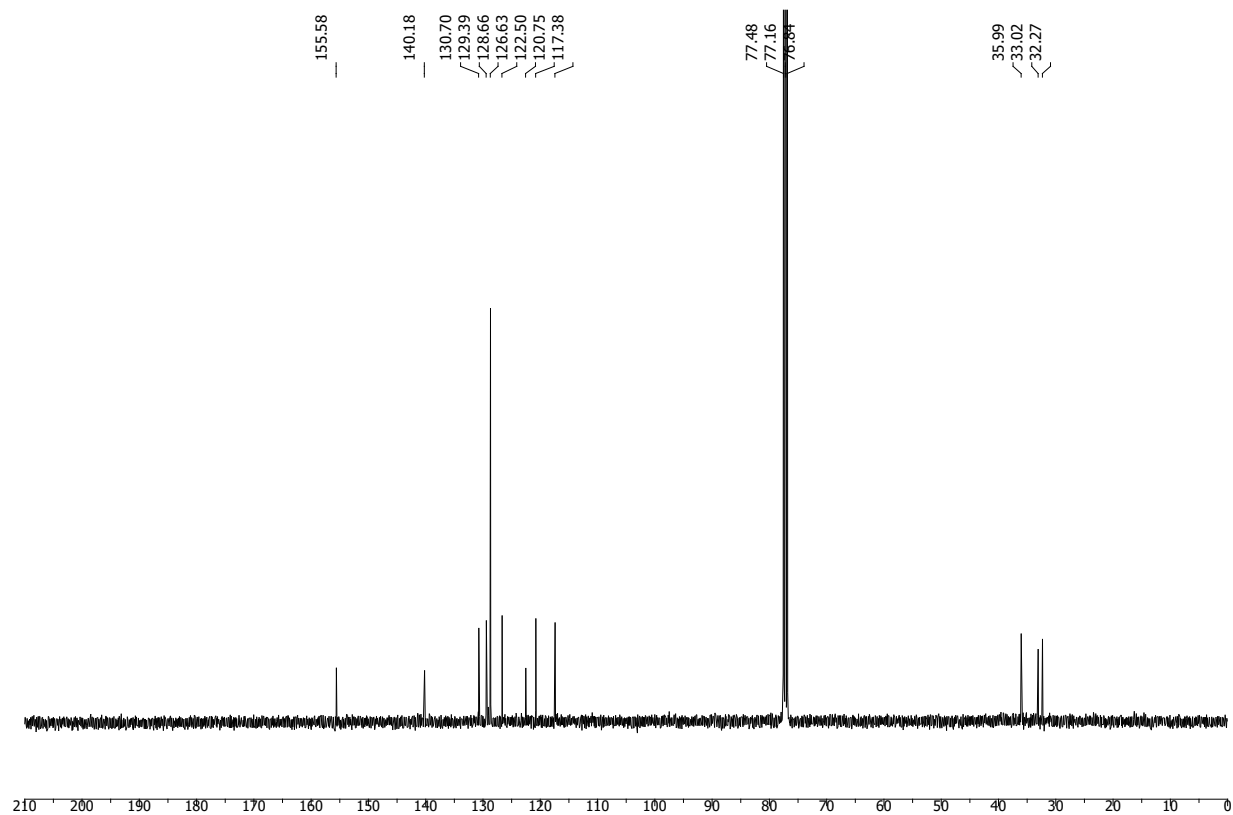
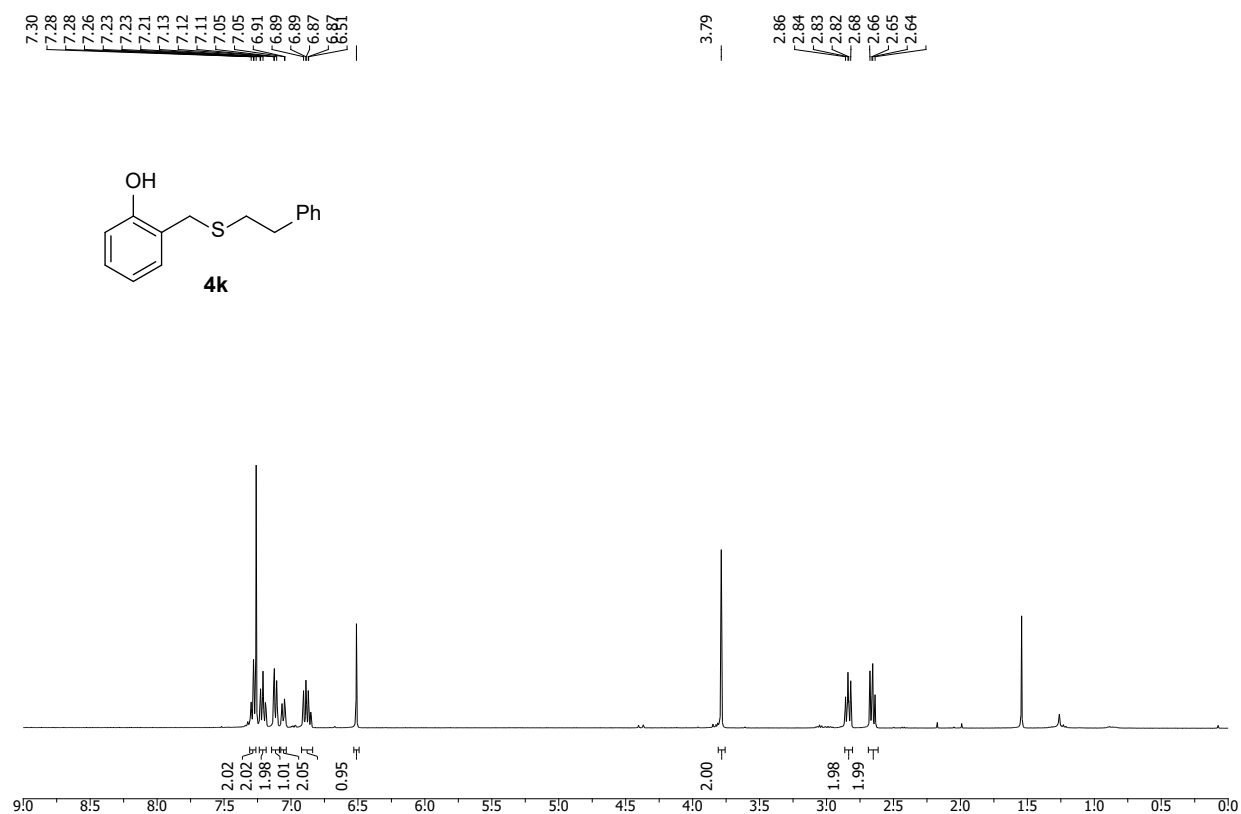


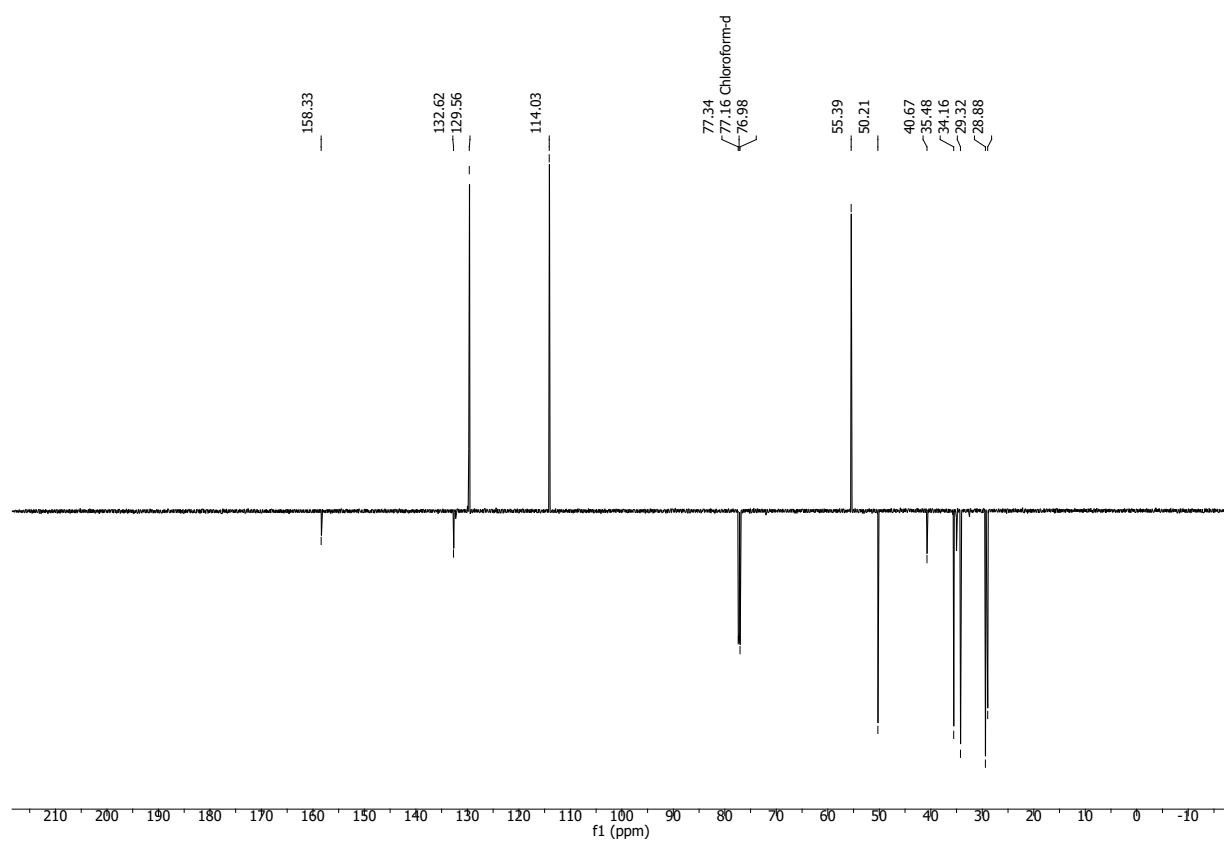
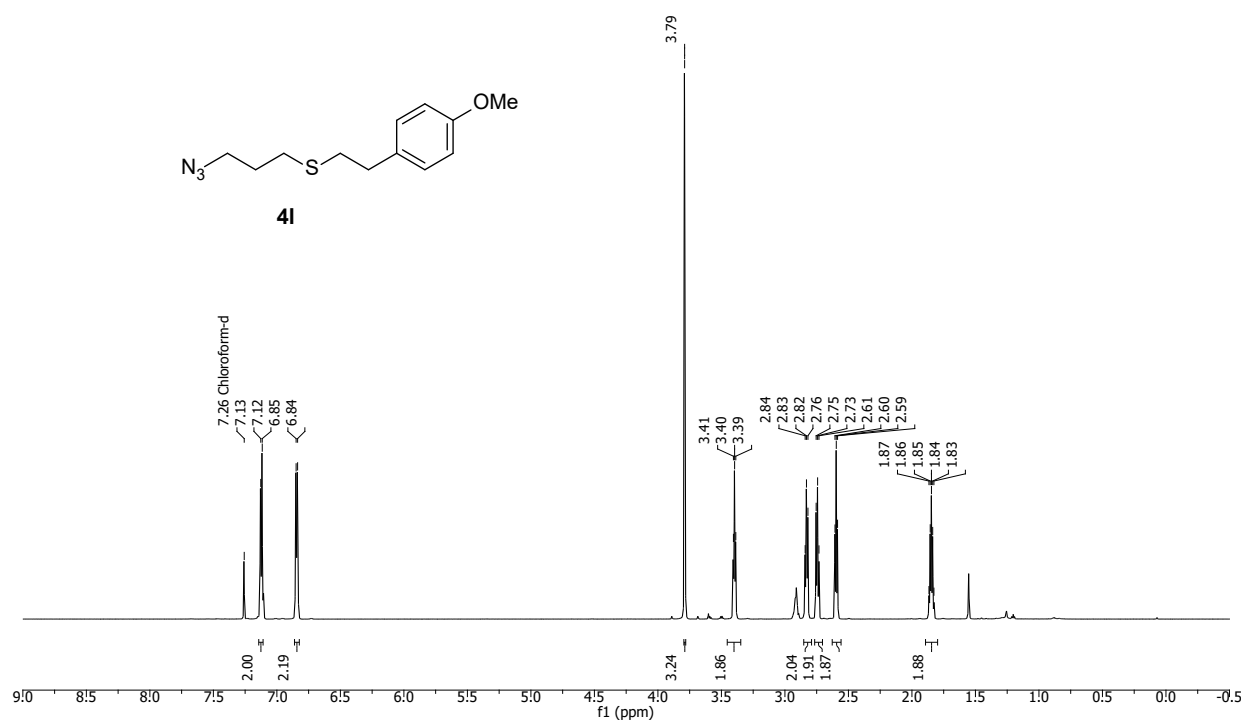


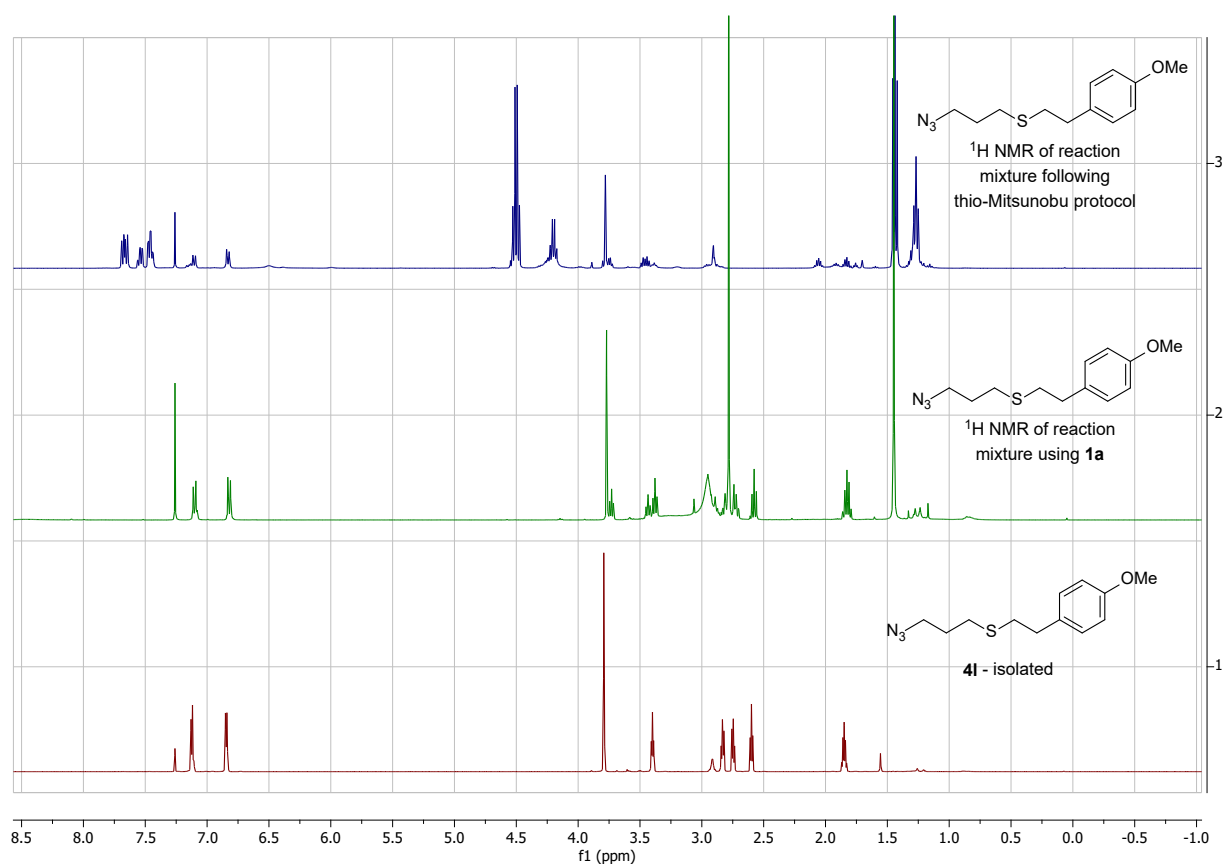


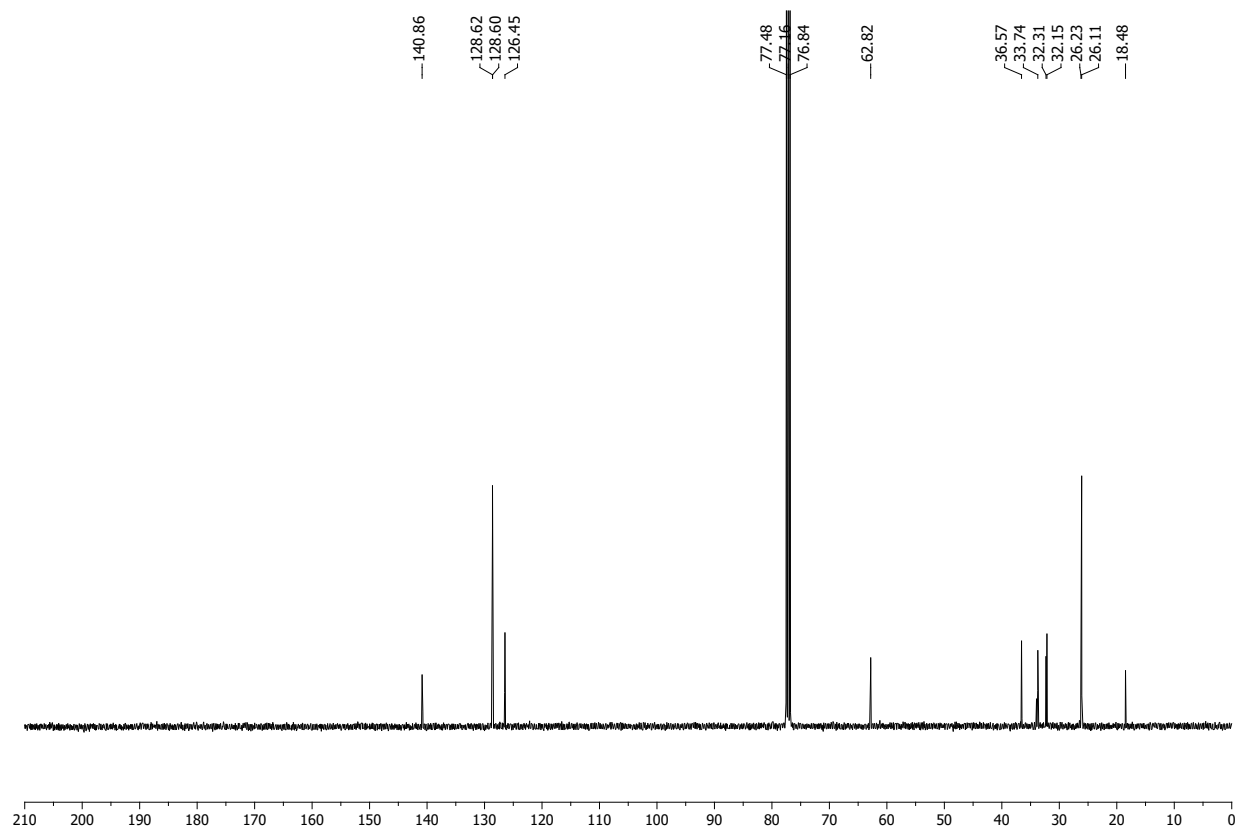
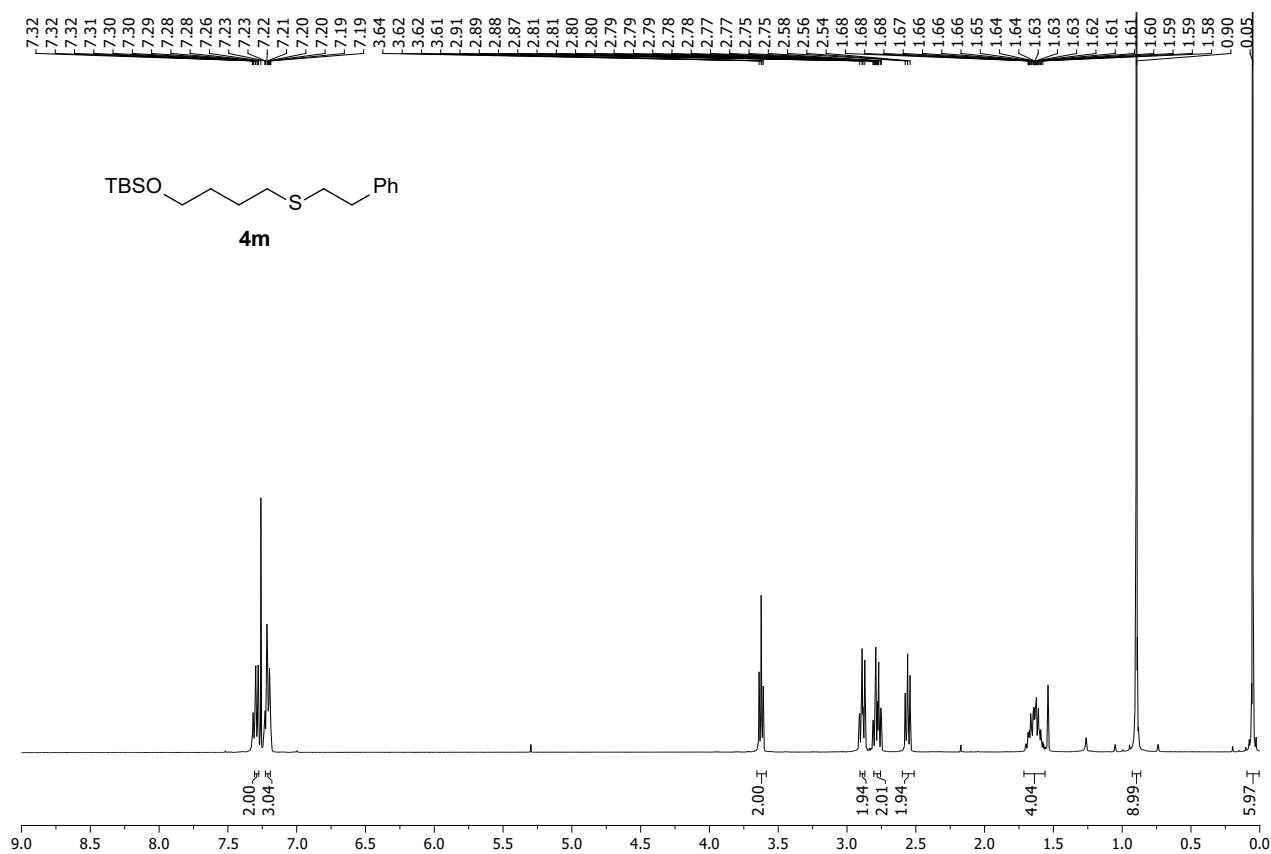


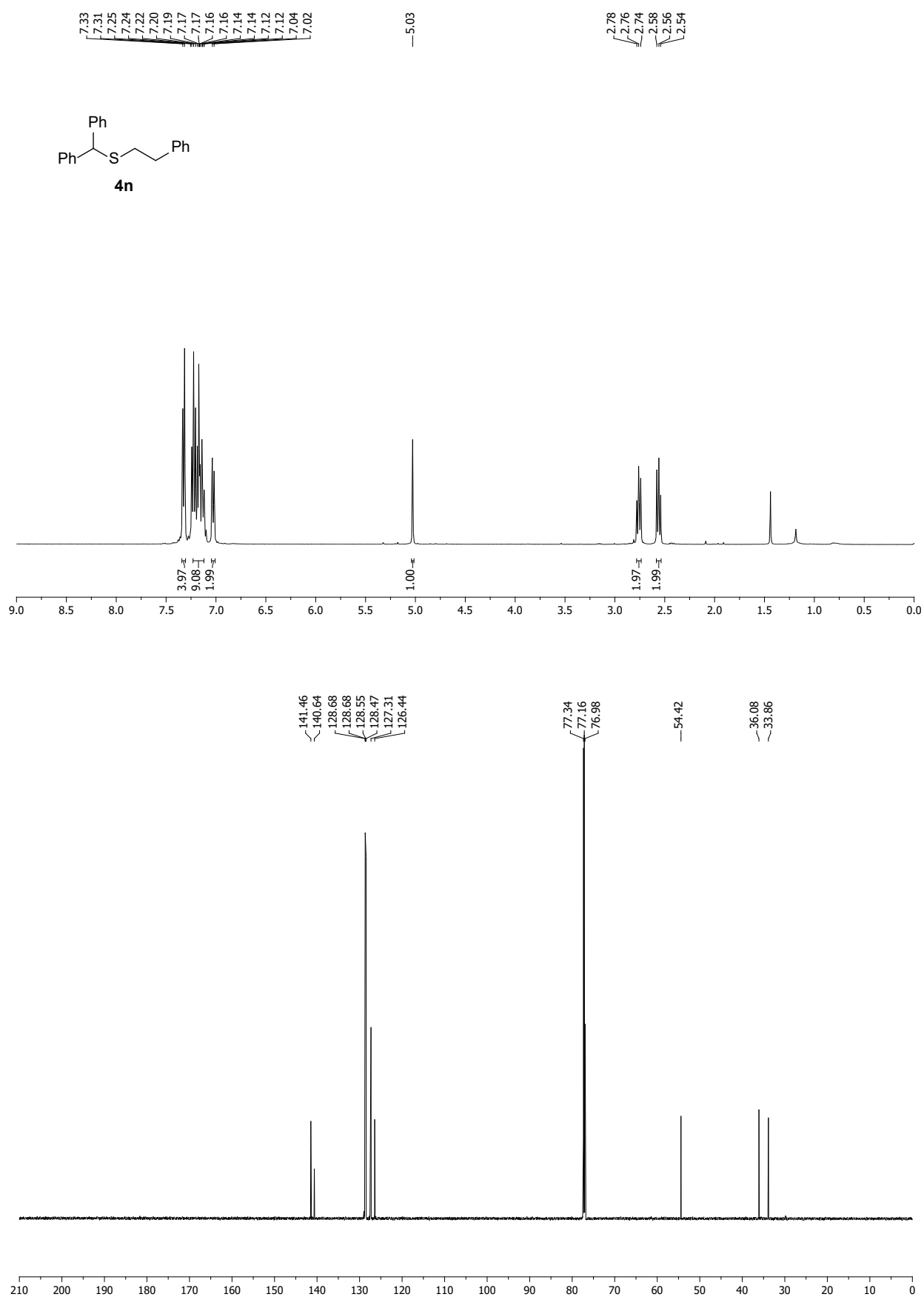


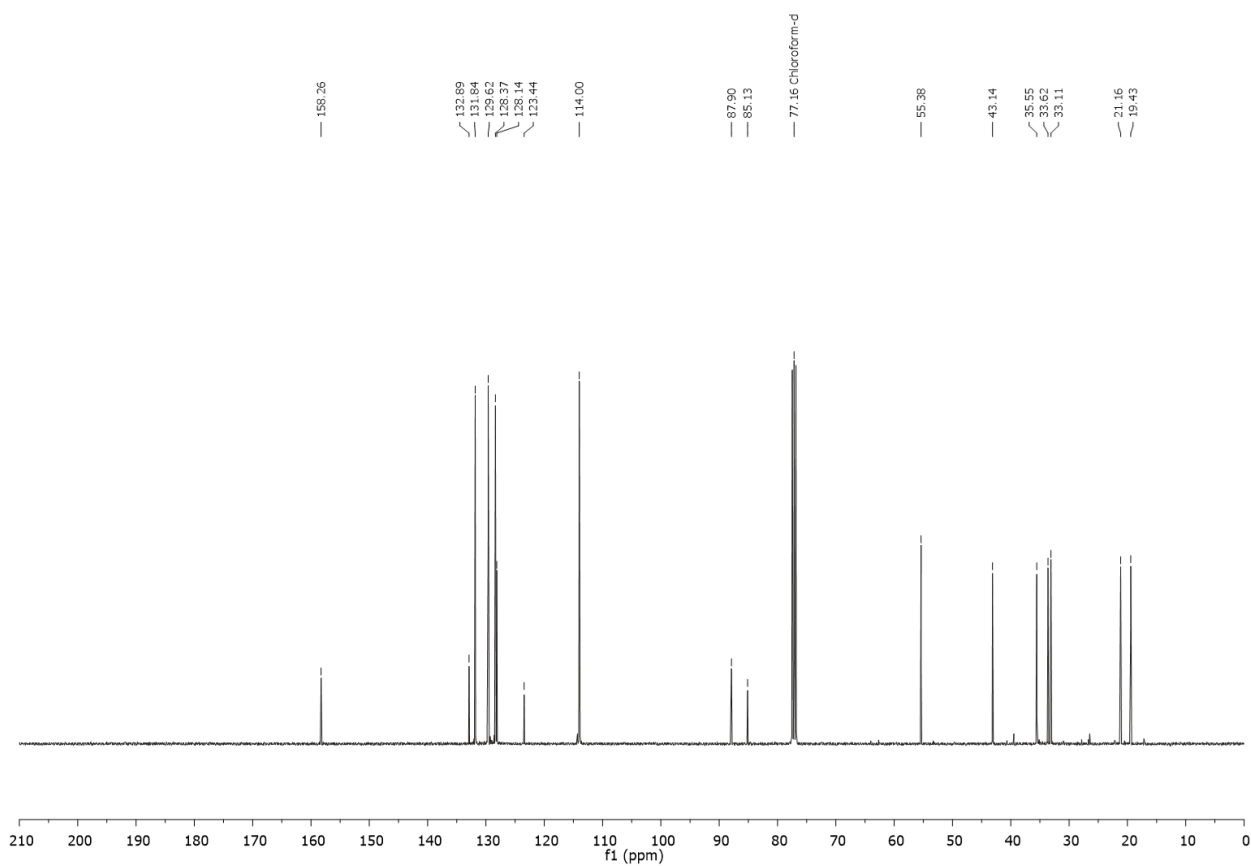
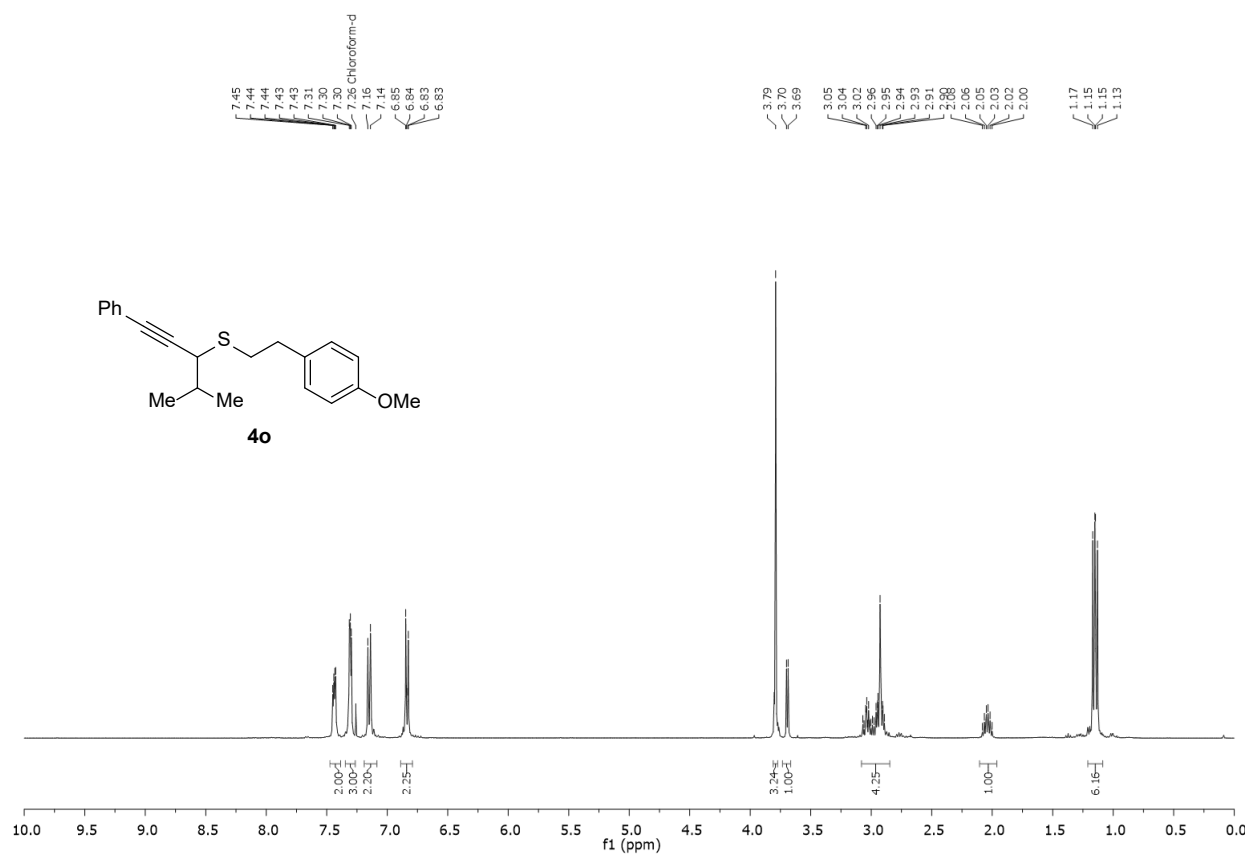


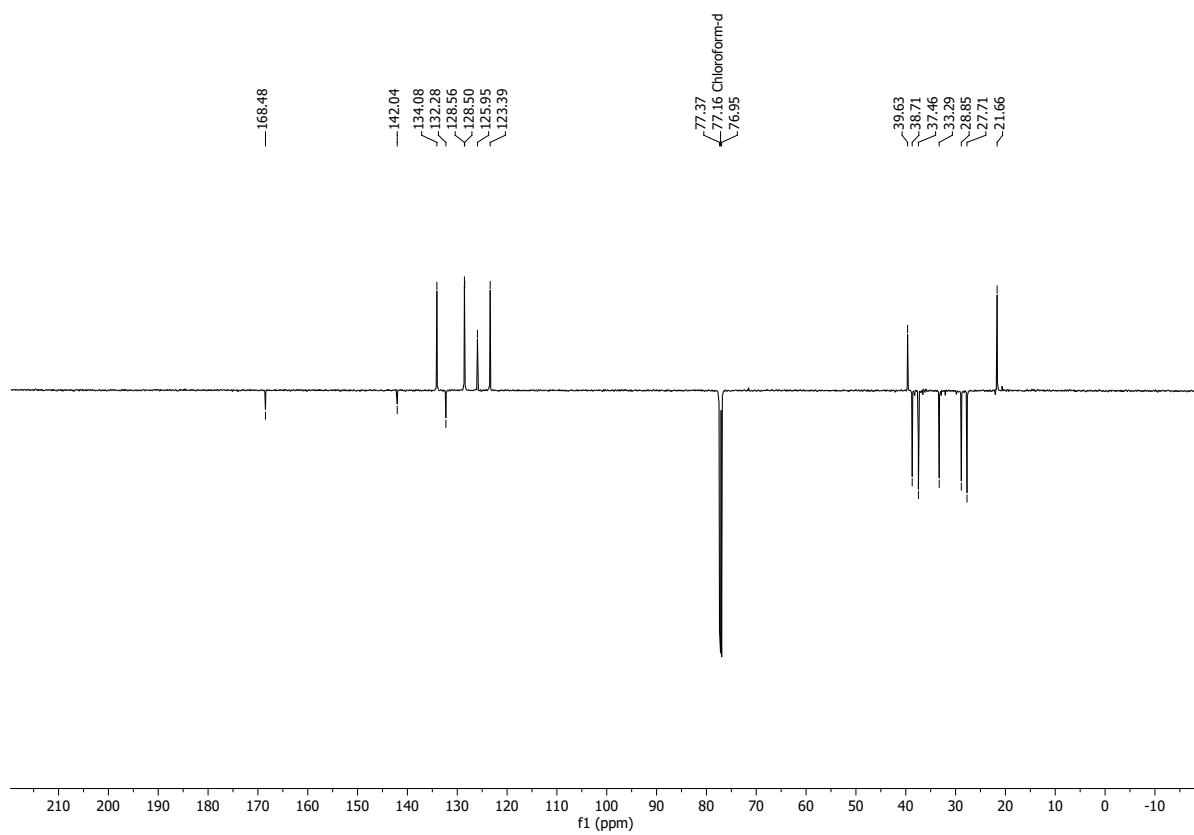
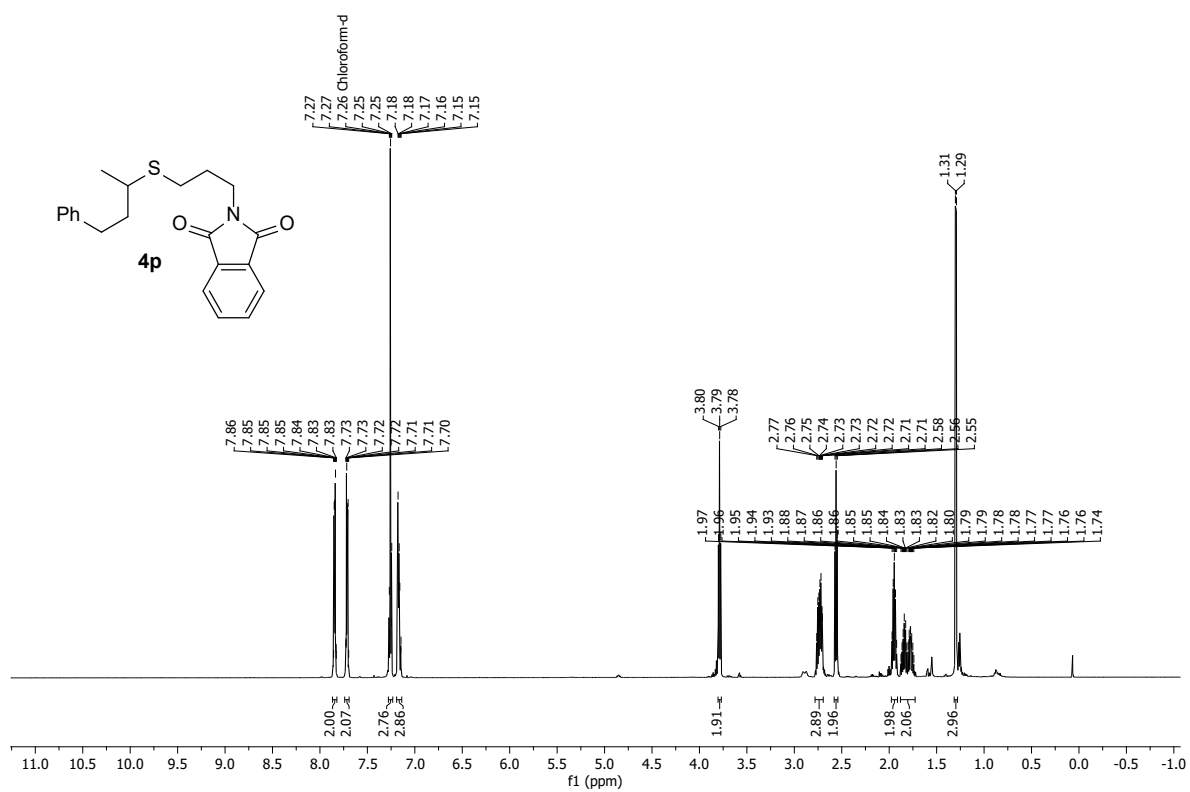


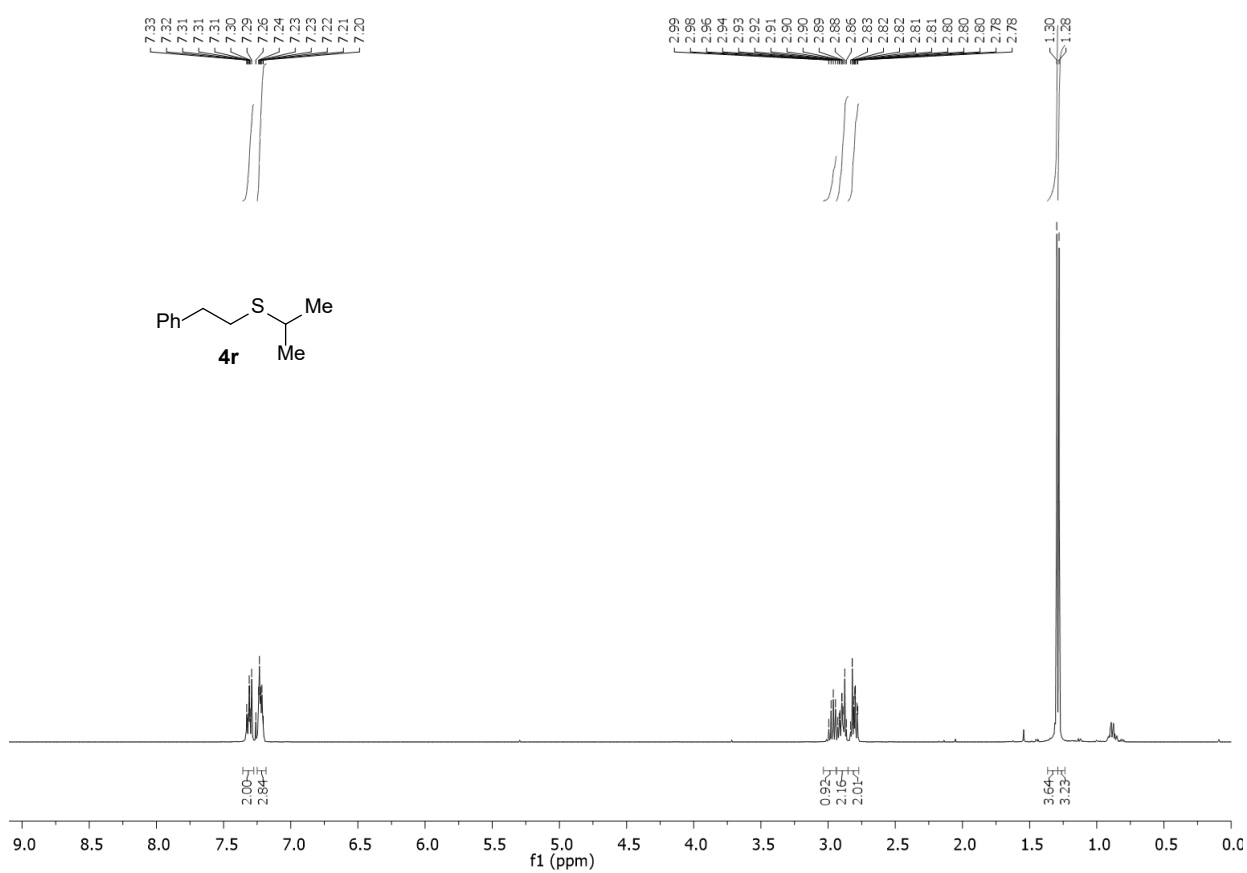
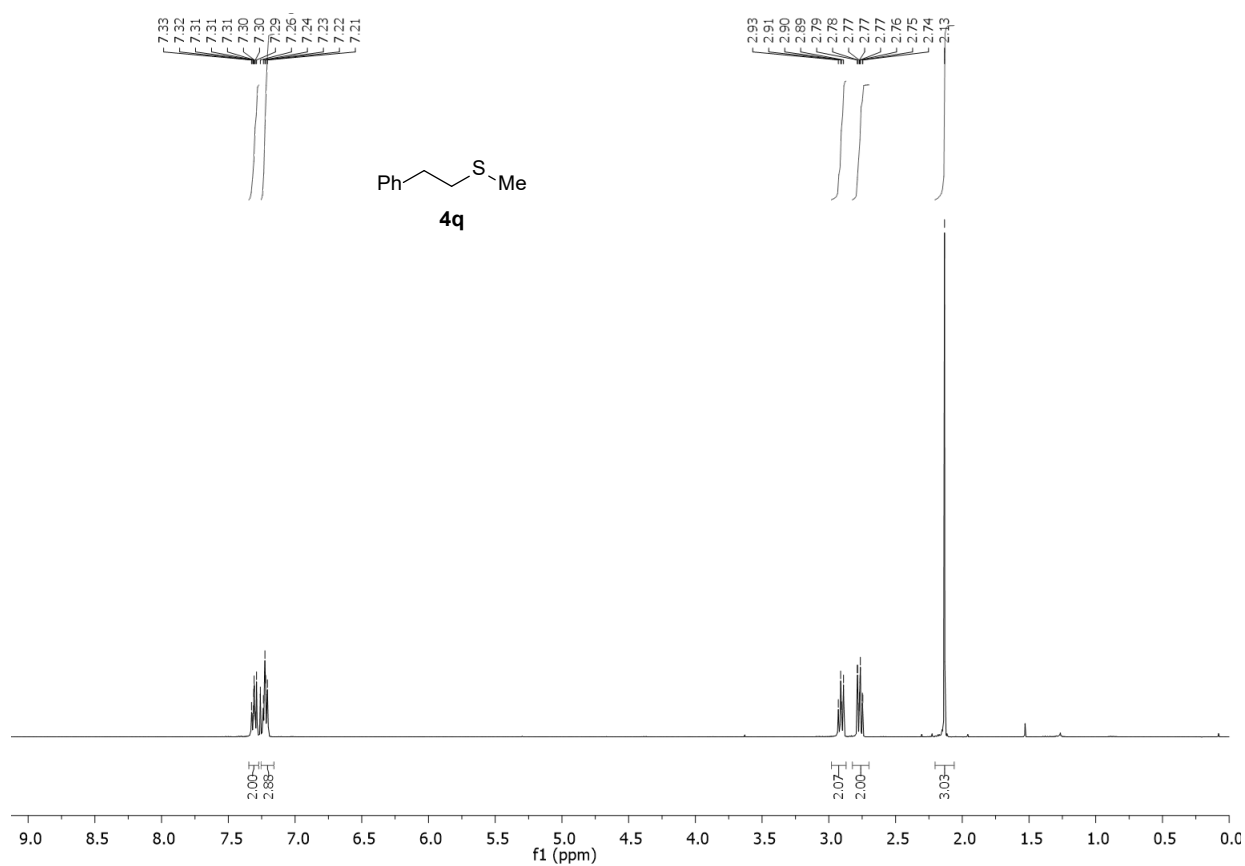


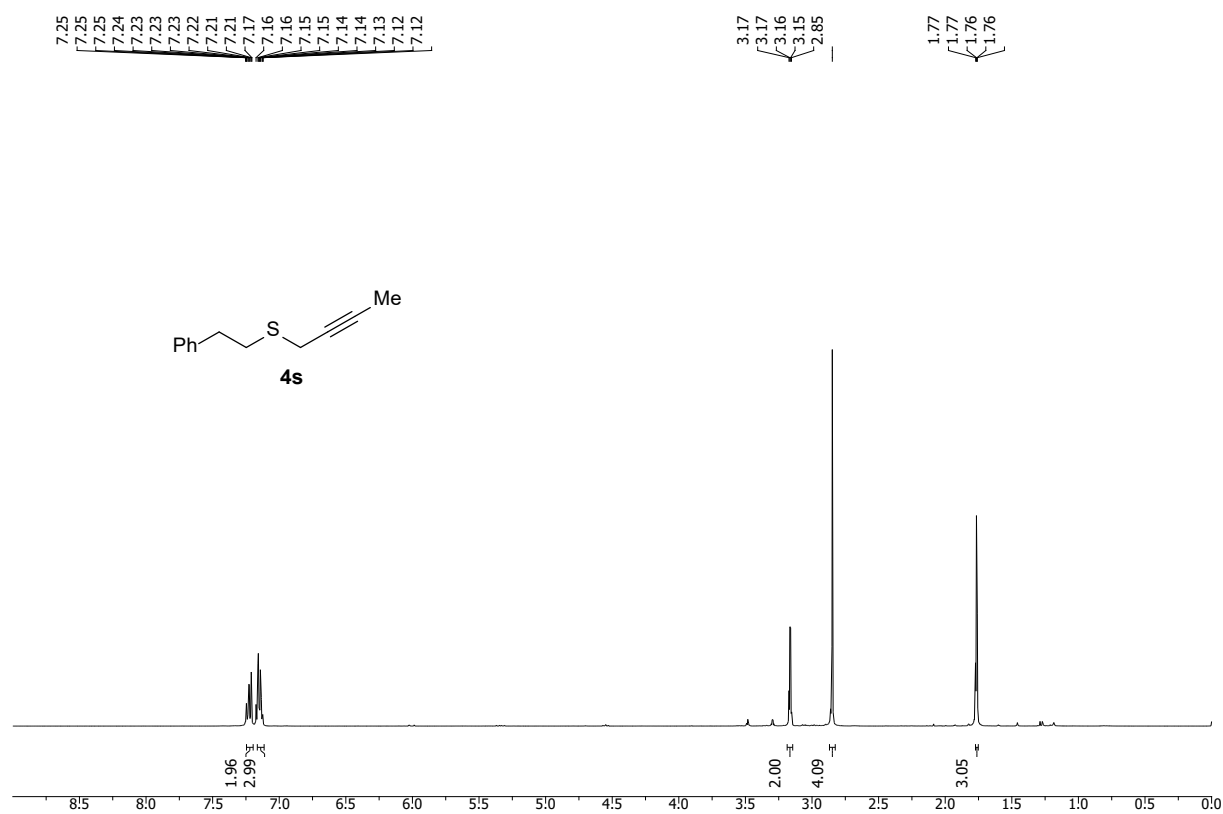


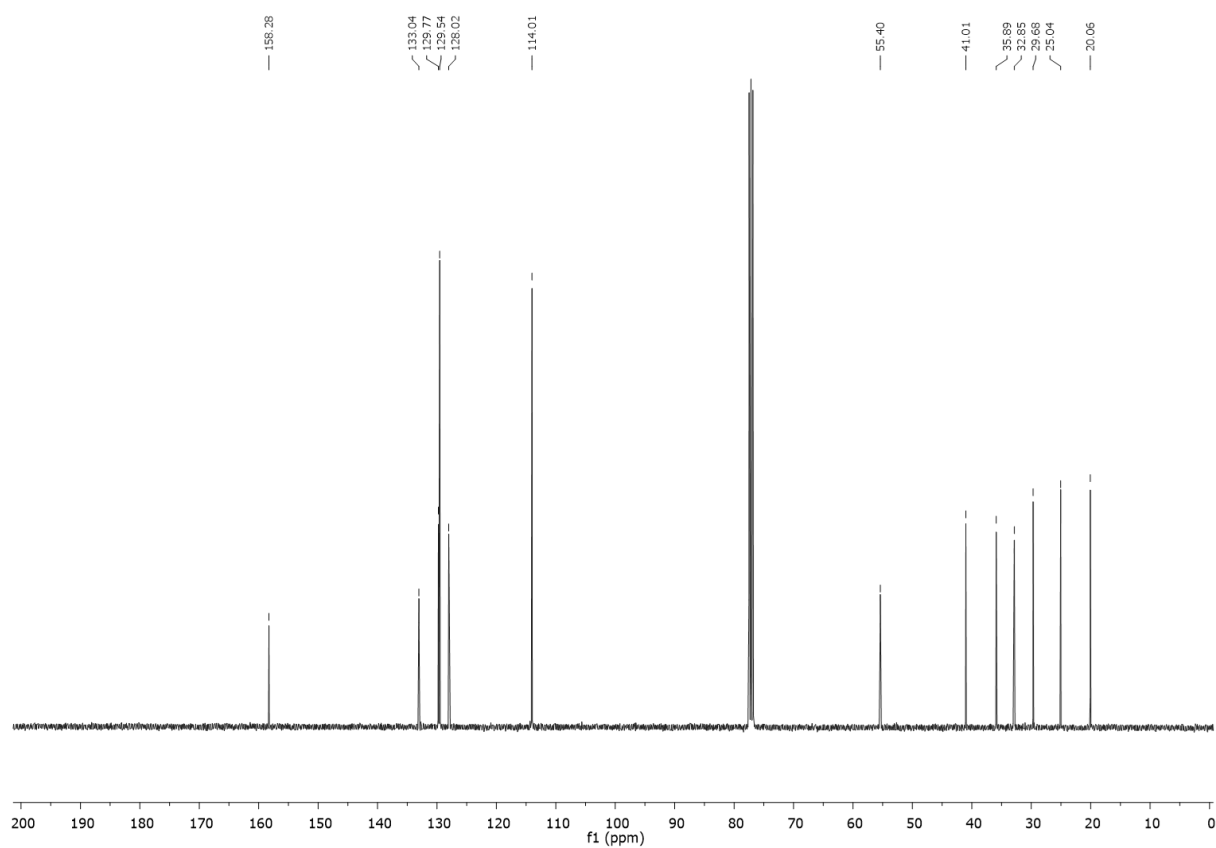
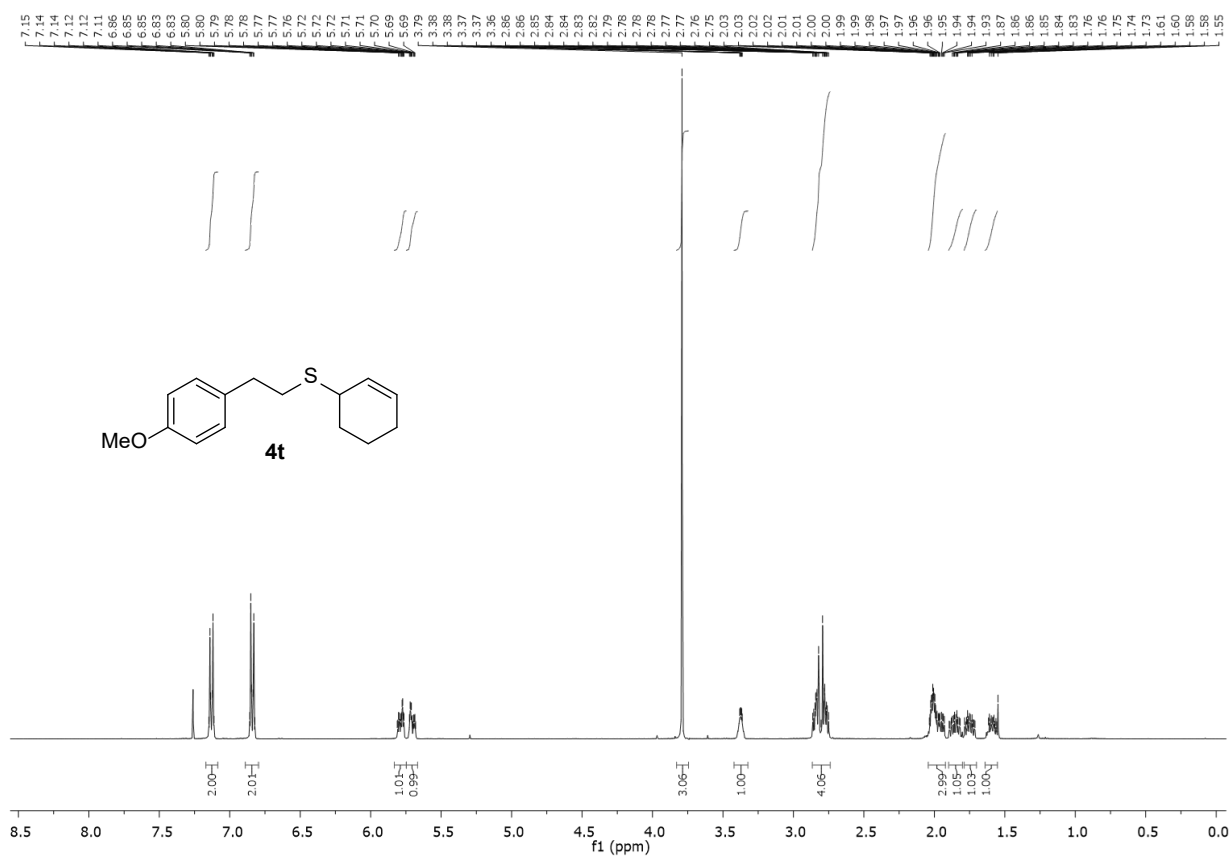


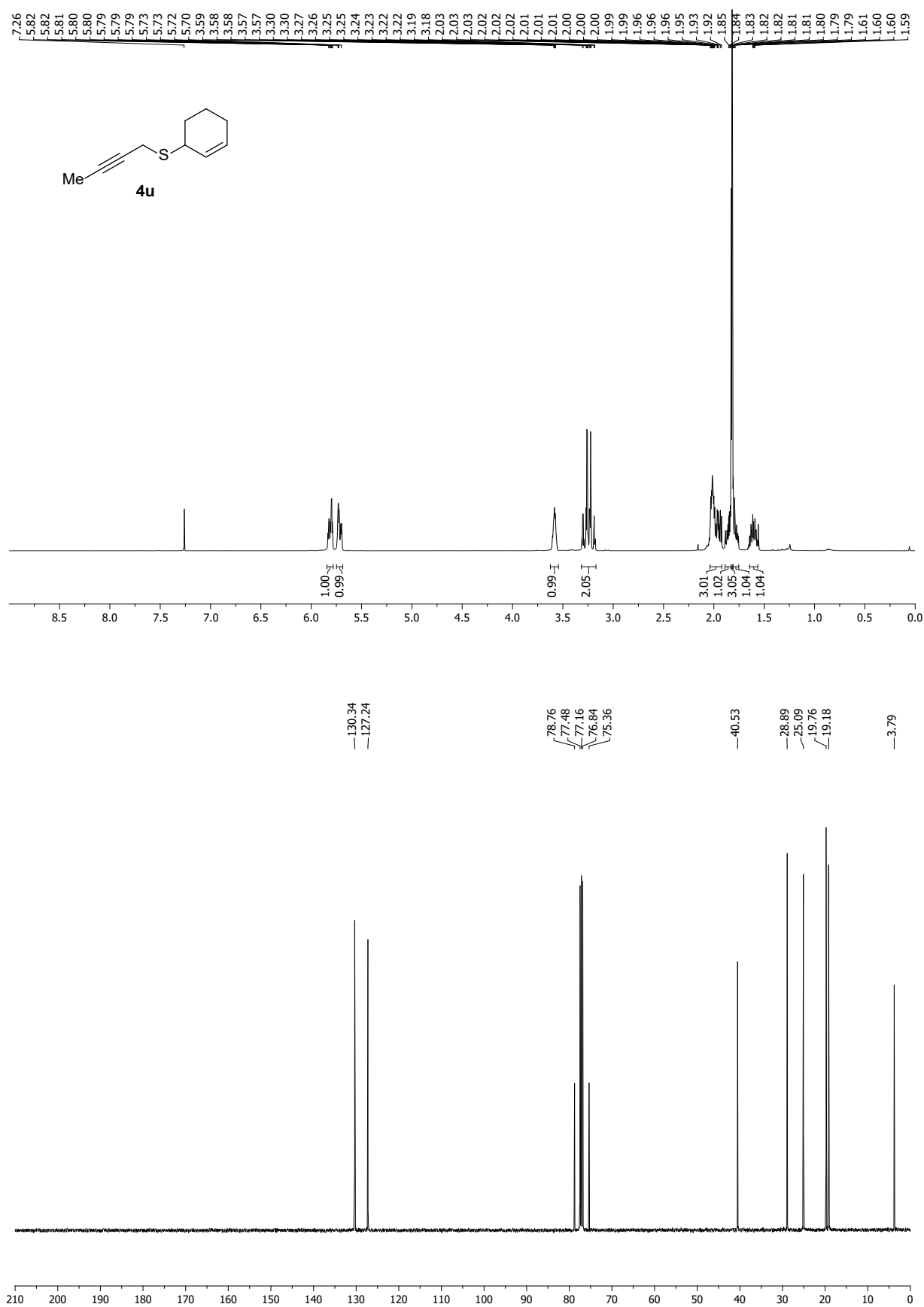


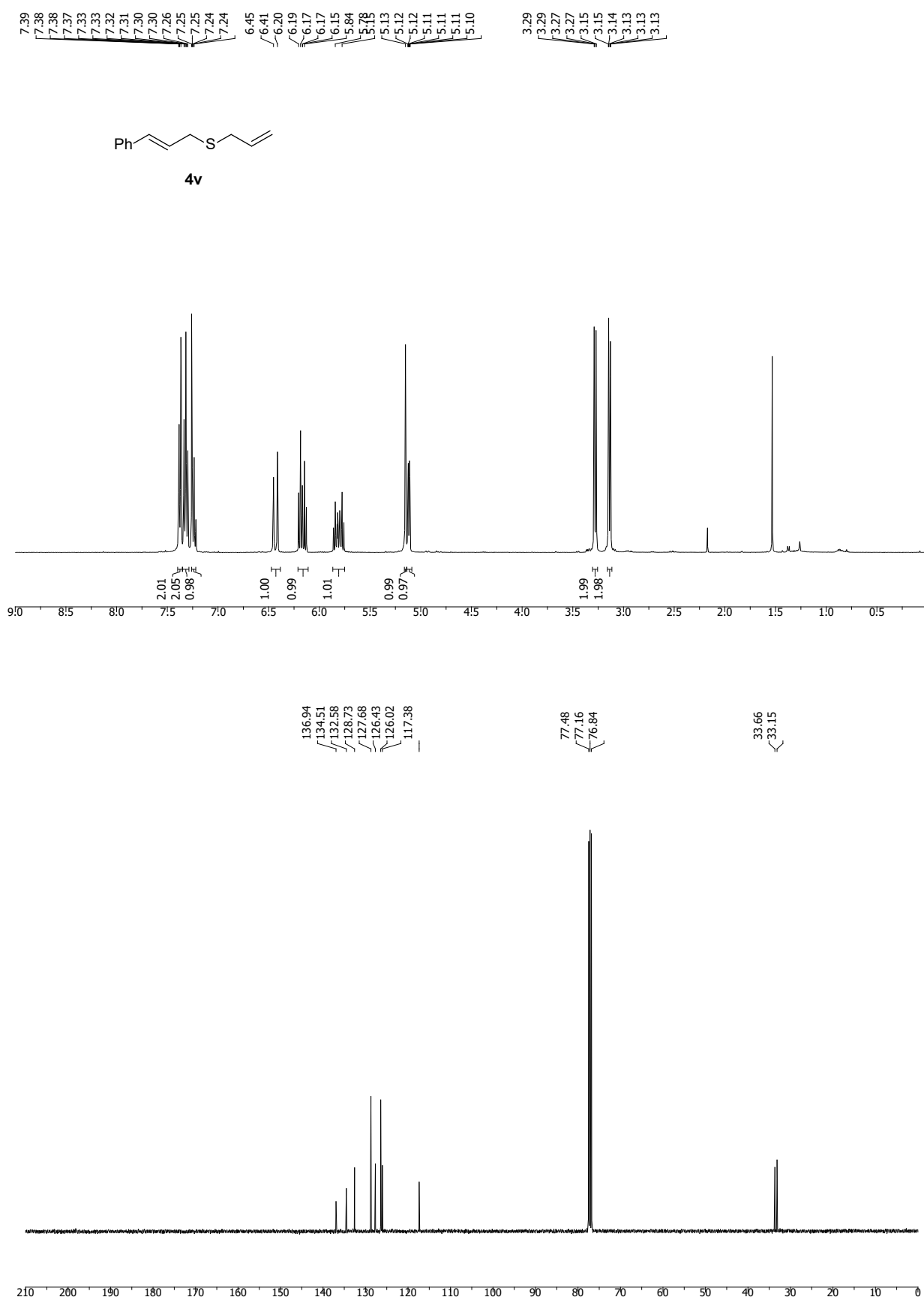


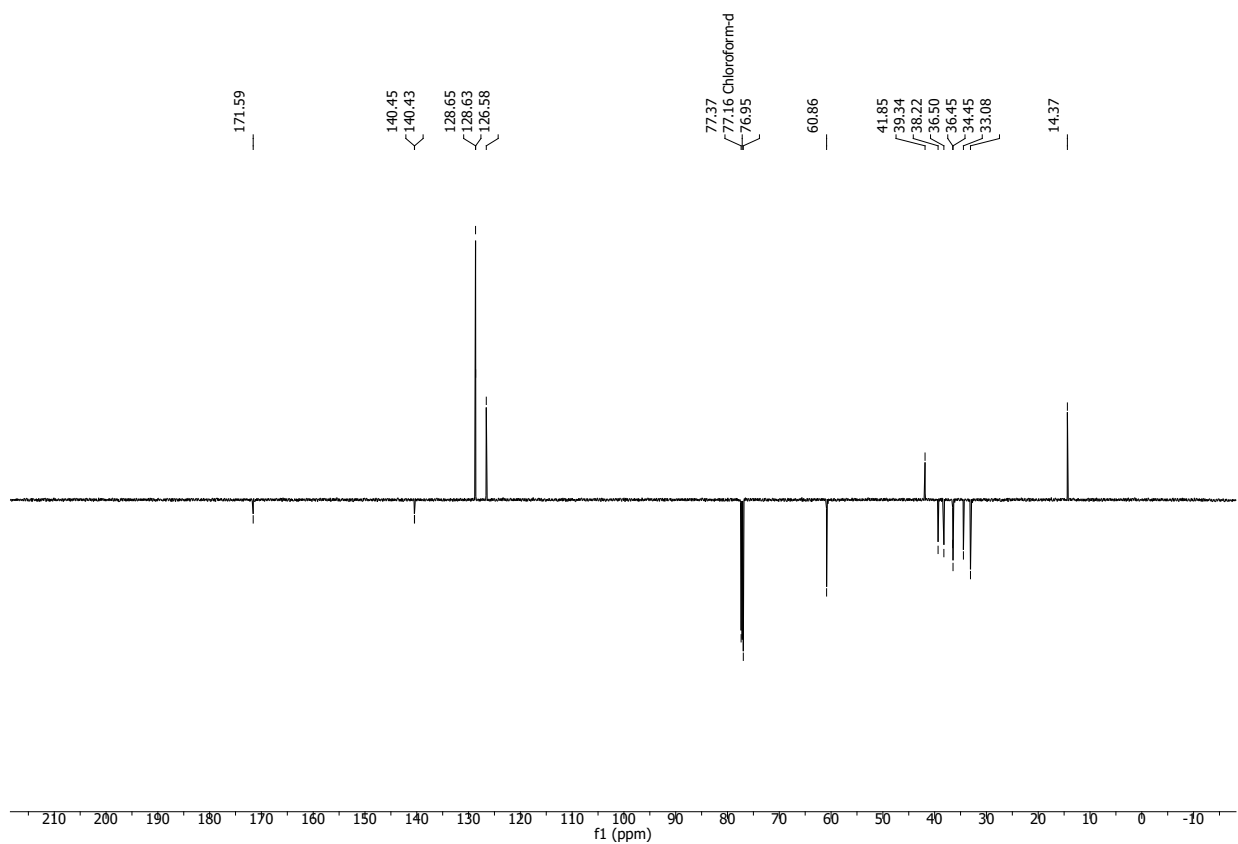
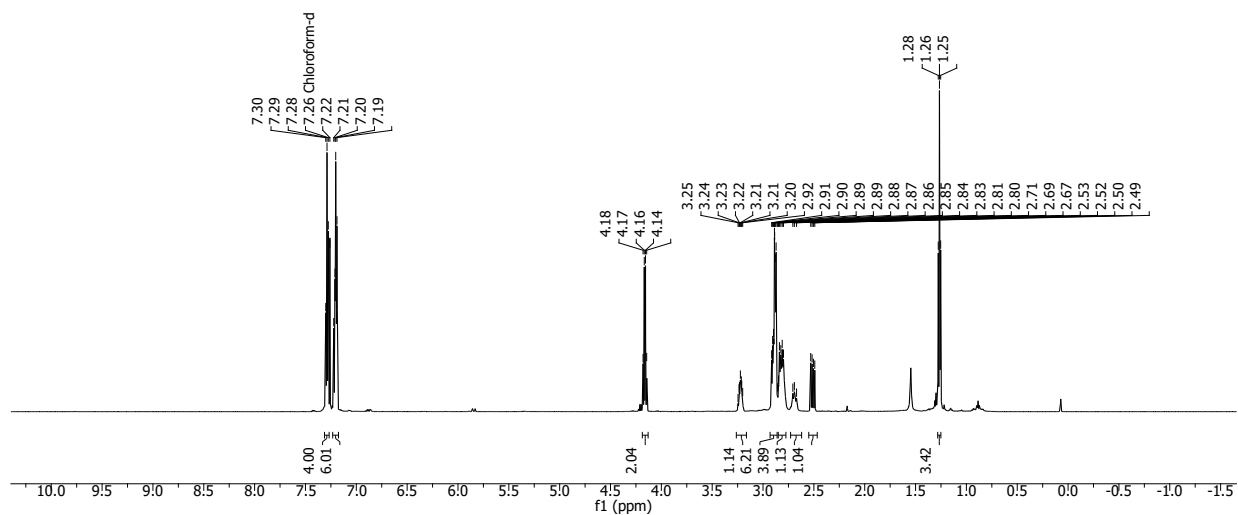
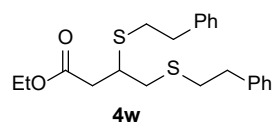


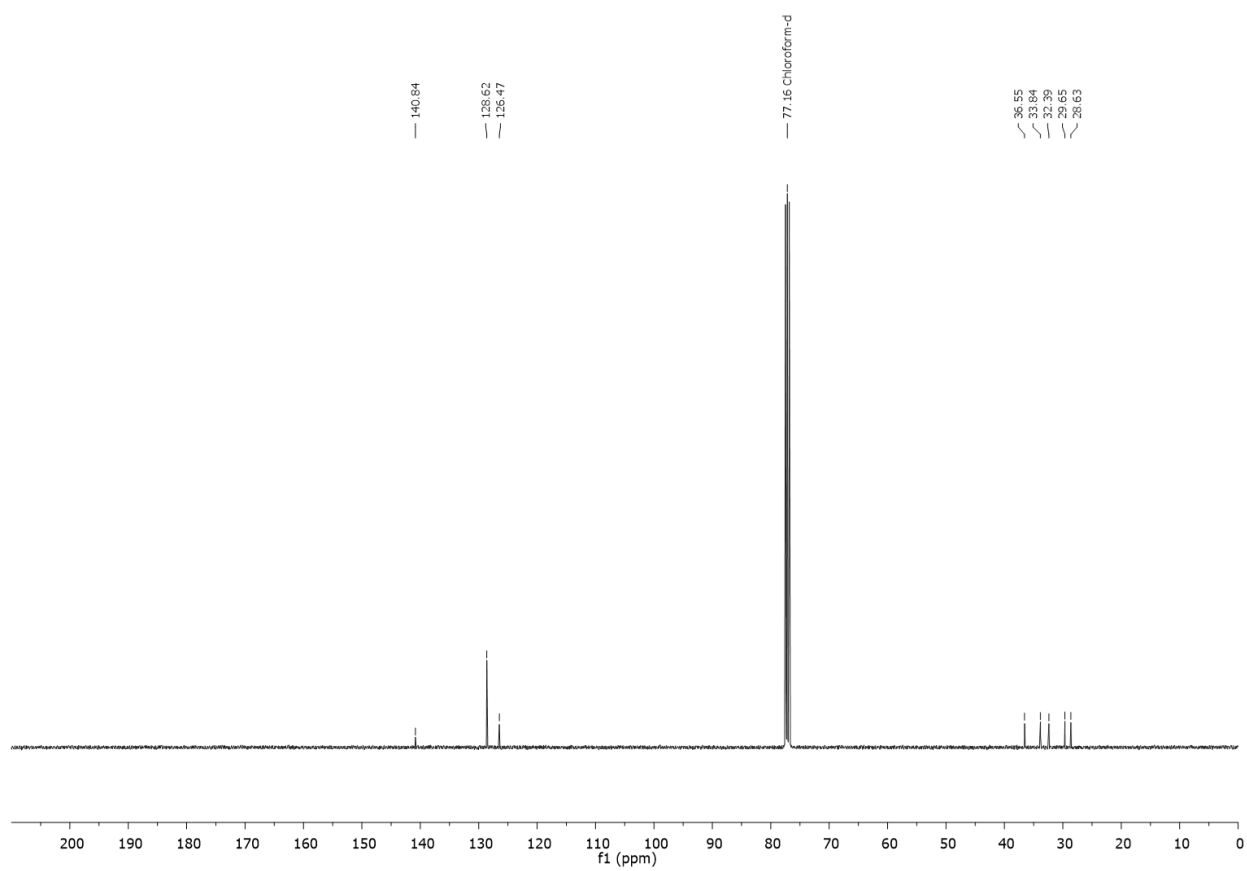
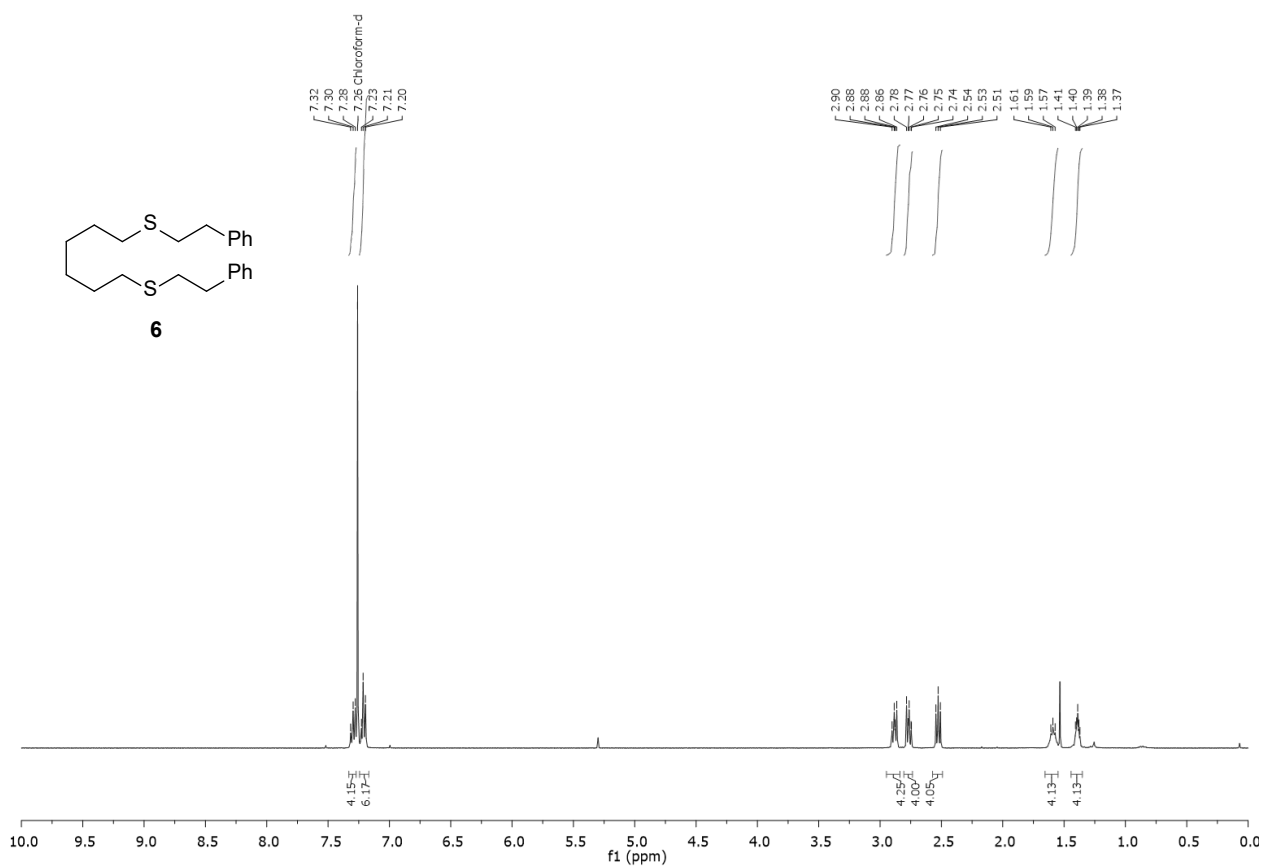


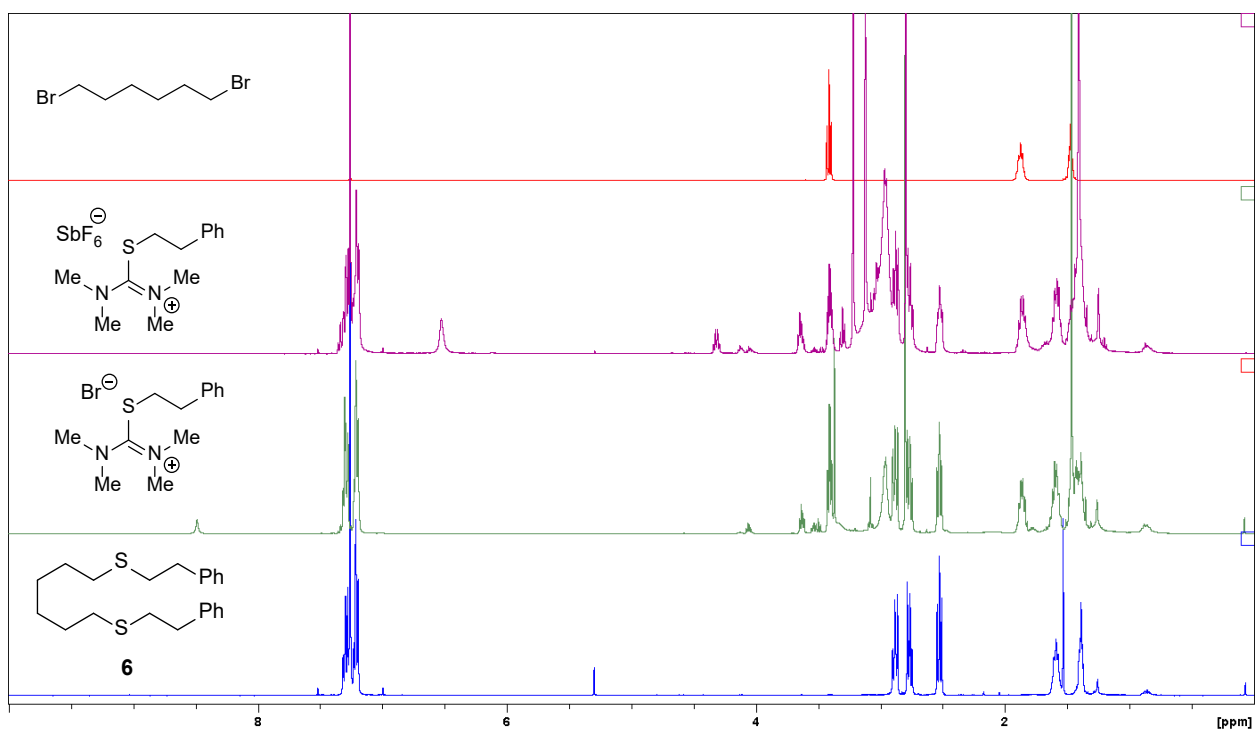












From top to bottom: a) ¹H-NMR of 1,6-dibromohexane, b) crude mixture from 6-bromo-1-hexanol and SbF₆⁻ salt, c) crude mixture from 6-bromo-1-hexanol and Br⁻ salt, d) double substitution product. Zoomed-in version below:

