

SUPPORTING INFORMATION

Synthesis of Tricyclic Heterocycles via a Tandem Aryl Alkylation/Heck Coupling Sequence

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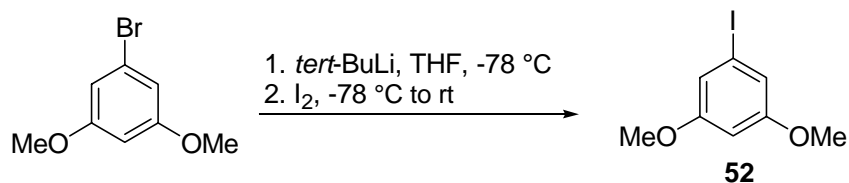
General Experimental

The following includes general experimental procedures, specific details for representative reactions, isolation and spectroscopic information for new compounds. Microwave-assisted reactions were performed in an Emrys Liberator model from Biotage (formerly Personal Chemistry) using Biotage Microwave Vials (2-5 mL). Microwave irradiation time was conducted using ramp time and hold time at the final temperature. ^1H NMR spectra were measured on spectrometers at 400 MHz or 300 MHz. ^{13}C NMR spectra were measured on spectrometers at 100 MHz or 75 MHz. ^1H spectra were referenced to tetramethylsilane (TMS, 0 ppm) or solvent hydrogens (3.31 ppm for CD_3OD and 2.50 for DMSO-d_6). ^{13}C spectra were referenced to solvent carbons (77.23 ppm for CDCl_3 , 49.86 ppm for CD_3OD or 39.43 ppm for DMSO-d_6).

Diethyl ether, toluene, and tetrahydrofuran (THF) were distilled under nitrogen from Na/benzophenone immediately prior to use. 1,2-Dimethoxyethane (DME), benzene and dichloromethane (CH_2Cl_2) was distilled under nitrogen from CaH_2 immediately prior to use. All other solvents were used as received. Triphenylphosphine was recrystallized using hexane. Reactions were performed under an atmosphere of nitrogen.

Synthesis of Aryl Iodides

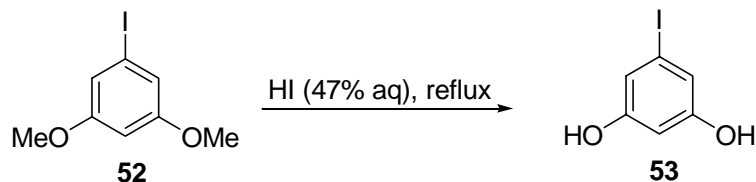
1-Iodo-3,5-dimethoxybenzene (52).



To a -78 °C solution of 1-bromo-3,5-dimethoxybenzene (10.0 g, 46.1 mmol, 1 equiv) in THF (60 mL) was added dropwise *tert*-butyllithium (61 mL, 104 mmol, 1.7 M in pentane, 2.25 equiv). The reaction was stirred for 1 h at -78 °C then iodine (35.1 g, 138 mmol, 3 equiv) in THF (70 mL)

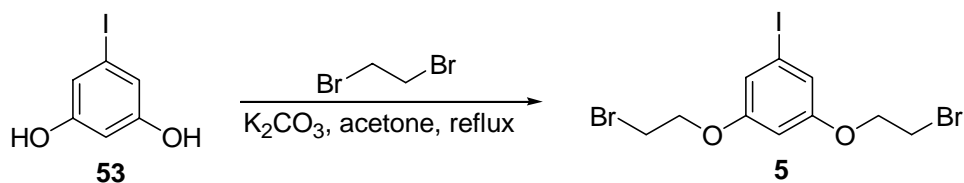
was added *via* cannula. The resulting mixture was stirred at -78 °C for 1 h then warmed to rt, quenched with water (100 mL) and diluted with CH₂Cl₂ (300 mL). The organic layer was washed with saturated aqueous Na₂S₂O₃, brine, dried with anhydrous MgSO₄, filtered and concentrated. The crude mixture was purified by flash chromatography using 10% EtOAc/hexanes as eluant to yield **52** (11.8 g, 98%) as a white solid, mp = 74-75 °C. R_f = 0.69 on silica gel (10% EtOAc/hexanes). IR (neat) ν = 1577, 1425, 1294, 1199, 1164, 1032 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.85 (d, 2H, *J* = 2.2 Hz), 6.40 (t, 1H, *J* = 2.2 Hz), 3.76 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 161.2, 116.0, 100.8, 94.3, 55.7; HRMS calcd for C₈H₉IO₂ [M]⁺ 263.9654, found 263.9647.

5-Iodobenzene-1,3-diol (**53**).¹



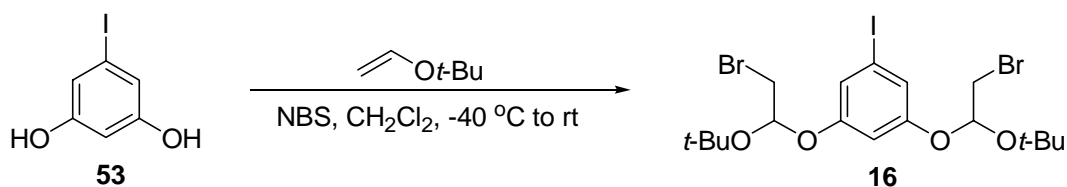
A solution of **52** (8.30 g, 31.4 mmol, 1 equiv) and HI (47 wt. % in water, 75 mL) was refluxed for 24 h. The solution was cooled to rt and diluted with water (100 mL) followed by the addition of ether (100 mL). The organic layer was separated and washed with 1 M sodium thiosulfate solution (2 × 75 mL) and once with water (50 mL). After drying with MgSO₄, removal of the solvent gave a crude oil that was purified by flash chromatography using 25% EtOAc/hexanes yielding **53** (6.90 g, 93%) as a white solid, mp = 93-95 °C. R_f = 0.21 on silica gel (25% EtOAc/hexanes). Spectral data match the previously reported data.¹

1,3-Bis(2-bromoethoxy)-5-iodobenzene (**5**).



To a solution of **53** (8.00 g, 33.9 mmol, 1 equiv) and 1,2-dibromoethane (44 mL, 508 mmol, 15 equiv) in acetone (70 mL) was added K₂CO₃ (23.4 g, 170 mmol, 5 equiv). The mixture was stirred at reflux for 36 h. The reaction was cooled to rt and filtered through celite. Distillation of excess 1,2-dibromoethane gave a crude oil that was purified by flash chromatography using 10% EtOAc/hexanes as eluant yielding **5** (9.30 g, 62%) as a white solid, mp = 97-98 °C. *R*_f = 0.75 on silica gel (25% EtOAc/hexanes). IR (neat) ν = 1421, 1168, 1052 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.89 (s, 2H), 6.44 (s, 1H), 4.24 (t, 4H, *J* = 6.0 Hz), 3.61 (t, 4H, *J* = 6.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 159.8, 117.4, 102.3, 94.3, 68.3, 28.9; HRMS calcd for C₁₀H₁₁Br₂IO₂ [M]⁺ 447.8161, found 447.8170.

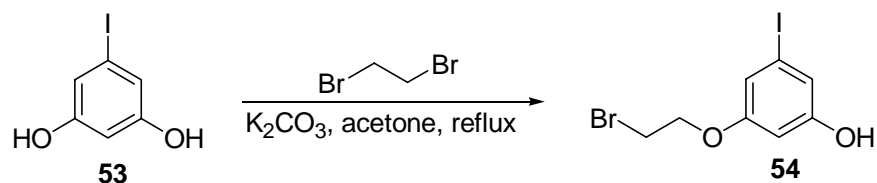
1,3-Bis(2-bromo-1-*tert*-butoxyethoxy)-5-iodobenzene (**16**)



tert-Butyl vinyl ether (0.51 mL, 3.9 mmol, 2 equiv) was added to a solution of NBS (686 mg, 3.9 mmol, 2 equiv) in CH₂Cl₂ (2 mL) at -40 °C. The reaction mixture was stirred at this temperature for 45 minutes. A solution of **53** (500 mg, 2.1 mmol, 1 equiv) in CH₂Cl₂ (2 mL) and DMF (0.5 mL) was added to the reaction mixture at -40 °C and the mixture was further stirred at this temperature for 2 h. The mixture was washed successively with 5% aq NaOH (5 mL), water (5 mL) and brine (5 mL). The organic layer was dried with anhydrous MgSO₄, filtered and

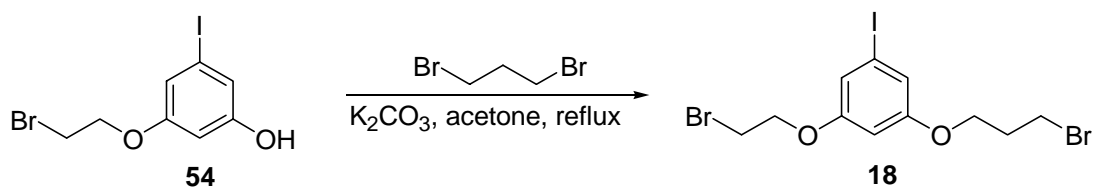
concentrated. The crude product was purified by flash chromatography using 5% EtOAc/hexanes eluant to afford **16** (375 mg, 30%) as a yellow oil, 1:1 mixture of diastereomers. $R_f = 0.73$ on silica gel (25% EtOAc/hexanes). IR (neat) $\nu = 1587, 1568, 1471, 1431, 1394, 1367, 1263, 1241, 1177, 1124, 1060, 1044, 1011, 968, 940, 921, 827 \text{ cm}^{-1}$; ^1H NMR (300 MHz, CDCl_3) δ 7.00 (d, 4H, $J = 1.9 \text{ Hz}$), 6.64 (d, 1H, $J = 2.2 \text{ Hz}$), 6.62 (d, 1H, $J = 2.2 \text{ Hz}$), 5.45 (dd, 2H, $J = 1.7, 4.2 \text{ Hz}$), 5.43 (dd, 2H, $J = 1.7, 4.2 \text{ Hz}$), 3.47 (dd, 4H, $J = 4.2, 10.7 \text{ Hz}$), 3.40 (dd, 4H, $J = 4.2, 10.7 \text{ Hz}$), 1.26 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.1, 157.1, 120.8, 107.5, 107.4, 97.2, 94.3, 76.7, 32.4, 28.7; HRMS calcd for $\text{C}_{18}\text{H}_{27}\text{Br}_2\text{IO}_4$ $[\text{M}]^+$ 591.9321, found 591.9319.

3-(2-Bromoethoxy)-5-iodophenol (**54**).



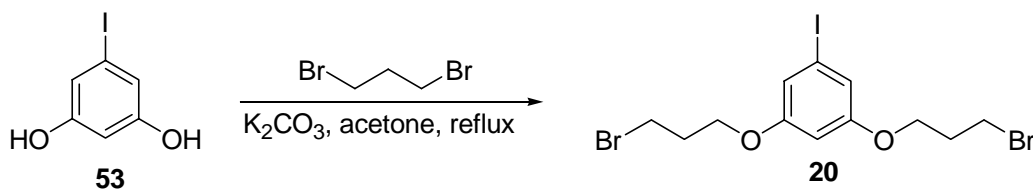
To a solution of **53** (2.75 g, 11.6 mmol, 1 equiv) and 1,2-dibromoethane (7.0 mL, 81.6 mmol, 7 equiv) in acetone (20 mL) was added K_2CO_3 (2.10 g, 15.1 mmol, 1.3 equiv). The mixture was stirred at reflux for 24 h. The reaction was cooled to room temperature and filtered through celite. Distillation of excess 1,2-dibromoethane gave a crude oil that was purified by flash chromatography using 10% EtOAc/hexanes as eluant yielding the desired product (1.33 g, 34%) as a white solid, mp = 139-141 °C. $R_f = 0.39$ on silica gel (25% EtOAc/hexanes). IR (neat) $\nu = 3385, 1596, 1493, 1279, 1148 \text{ cm}^{-1}$; ^1H NMR (300 MHz, CDCl_3) δ 6.83 (m, 2H), 6.36 (t, 1H, $J = 2.2 \text{ Hz}$), 4.89 (brs, 1OH), 4.21 (t, 2H, $J = 6.2 \text{ Hz}$), 3.59 (t, 2H, $J = 6.2 \text{ Hz}$); ^{13}C NMR (75 MHz, CDCl_3) δ 159.8, 157.2, 118.3, 116.8, 102.6, 94.3, 68.2, 28.9; HRMS calcd for $\text{C}_8\text{H}_8\text{BrIO}_2$ $[\text{M}]^+$ 341.8752, found 341.8752.

1-(2-Bromoethoxy)-3-(3-bromopropoxy)-5-iodobenzene (18).



To a solution of **54** (1.88 g, 5.48 mmol, 1 equiv) and 1,2-dibromopropane (5.6 mL, 54.8 mmol, 10 equiv) in acetone (15 mL) was added K_2CO_3 (2.27 g, 16.4 mmol, 3 equiv). The mixture was stirred at reflux for 36 h. The reaction was cooled to room temperature and filtered through celite. Distillation of excess 1,2-dibromopropane gave a crude oil that was purified by flash chromatography using 10% EtOAc/hexanes as eluant yielding **18** (1.00 g, 40%) as a white solid, mp = 63-64 °C. R_f = 0.50 (50% CH_2Cl_2 /hexanes). IR (neat) ν = 1574, 1434, 1277, 1163 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.90 (m, 1H), 6.86 (m, 1H), 6.43 (t, 1H, J = 2.4 Hz), 4.24 (t, 2H, J = 6.2 Hz), 4.06 (t, 2H, J = 6.0 Hz), 3.61 (t, 2H, J = 2.7 Hz), 3.56 (t, 2H, J = 6.4 Hz), 2.29 (quint, 2H, J = 6.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 160.4, 159.7, 117.4, 116.9, 102.1, 94.3, 68.2, 65.8, 32.3, 29.9, 28.9; HRMS calcd for $\text{C}_{11}\text{H}_{13}\text{Br}_2\text{IO}_2$ $[\text{M}]^+$ 461.8333, found 461.8327.

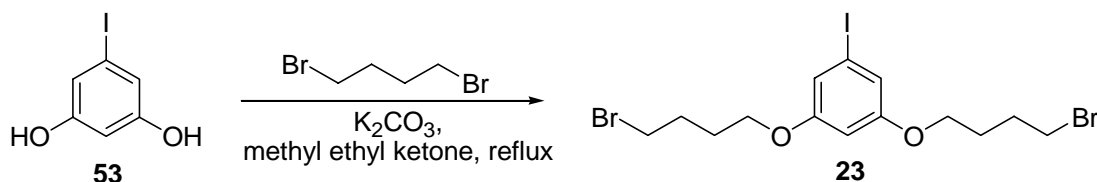
1,3-Bis(3-bromopropoxy)-5-iodobenzene (20).



To a solution of **53** (1.24 g, 5.25 mmol, 1 equiv) and 1,2-dibromopropane (5.3 mL, 52.5 mmol, 10 equiv) in acetone (15 mL) was added K_2CO_3 (3.63 g, 26.3 mmol, 5 equiv). The mixture was stirred at reflux for 36 h. The reaction was cooled to room temperature and filtered through celite. Distillation of excess 1,2-dibromopropane gave a crude oil that was purified by flash chromatography using 10% EtOAc/hexanes as eluant yielding **20** (1.46 g, 58%) as a white solid,

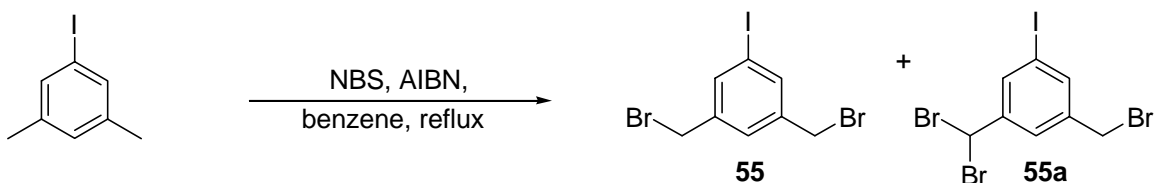
mp = 62 °C. R_f = 0.40 (10% EtOAc/hexanes). IR (neat) ν = 1593, 1434, 1166, 1053 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.87 (d, 2H, J = 2.2 Hz), 6.42 (t, 1H, J = 2.2 Hz), 4.06 (t, 4H, J = 5.8 Hz), 3.58 (t, 4H, J = 6.4 Hz), 2.29 (quint, 4H, J = 6.4 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 160.3, 116.8, 101.8, 94.3, 65.8, 32.4, 29.9; HRMS calcd for $\text{C}_{12}\text{H}_{15}\text{Br}_2\text{IO}_2$ $[\text{M}]^+$ 475.8477, found 475.8483.

1,3-Bis(4-bromobutoxy)-5-iodobenzene (23).



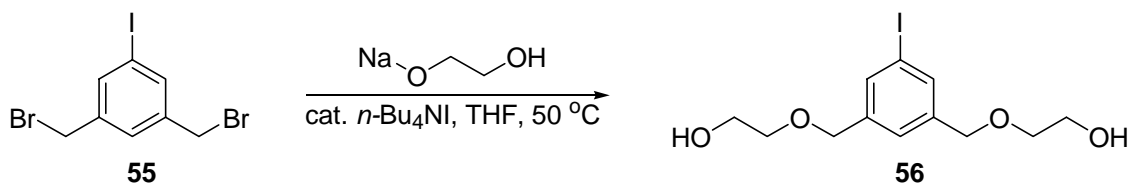
To a solution of **53** (3.5 g, 14.8 mmol, 1 equiv) and 1,4-dibromobutane (27 mL, 222 mmol, 15 equiv) in methyl ethyl ketone (30 mL) was added K_2CO_3 (10.3 g, 74.1 mmol, 5 equiv). The mixture was stirred at reflux for 24 h. The reaction was cooled to room temperature and filtered through celite. Distillation of excess 1,4-dibromobutane gave a crude oil that was purified by flash chromatography using 10% EtOAc/hexanes as eluant yielding **23** (3.67 g, 50%) as a white solid, mp = 51-53 °C. R_f = 0.48 (25% EtOAc/hexanes). IR (neat) ν = 1592, 1433, 1168, 1050 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.89 (d, 2H, J = 2.2 Hz), 6.37 (t, 1H, J = 2.2 Hz), 3.93 (t, 4H, J = 6.0 Hz), 3.48 (t, 4H, J = 6.3 Hz), 1.98-2.10 (m, 4H), 1.85-1.97 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.5, 116.5, 101.6, 94.3, 67.2, 33.6, 29.5, 27.9; HRMS calcd for $\text{C}_{14}\text{H}_{19}\text{Br}_2\text{IO}_2$ $[\text{M}]^+$ 503.8778, found 503.8785.

1,3-Bis-bromomethyl-5-iodobenzene (**55**).



A mixture of 3,5-dimethyliodobenzene (5.00 g, 21.5 mmol, 1 equiv), NBS (8.44 g, 47.4 mmol, 2.2 equiv) and AIBN (0.71 g, 4.3 mmol, 0.2 equiv) was refluxed in benzene (150 mL) for 6 h. The reaction mixture was cooled to room temperature, diluted with ether (150 mL) and washed with water (150 mL). The aqueous layer was extracted with ether (3×) and the combined organic layers were dried with anhydrous MgSO_4 and filtered. Removal of the solvent gave a crude oil that was purified by flash chromatography using 2-5% CH_2Cl_2 /hexanes to afford **55** and **55a** as an inseparable mixture (**55**:**55a** = 3:1, 4.55 g, 54%); white solid, mp = 75-80 °C. R_f = 0.33 on silica gel (5% ether/hexanes). IR (neat **55/55a**) ν = 1640, 1432, 1252, 1208 cm^{-1} ; **55**: ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, 2H, J = 1.5 Hz), 7.37 (s, 1H), 4.38 (s, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.4, 138.0, 129.2, 94.5, 31.5; HRMS $[\text{M}]^+$ not found. **55a**: ^1H NMR (400 MHz, CDCl_3) δ 7.82 (t, 1H, J = 1.5 Hz), 7.69 (t, 1H, J = 1.3 Hz), 7.54 (t, 1H, J = 1.5 Hz), 6.52 (s, 1H), 4.39 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 144.1, 139.3, 135.5, 132.1, 126.7, 94.1, 38.5, 31.1; HRMS calcd for $\text{C}_8\text{H}_6\text{Br}_3\text{I}$ $[\text{M}]^+$ 465.7064, found 465.7071.

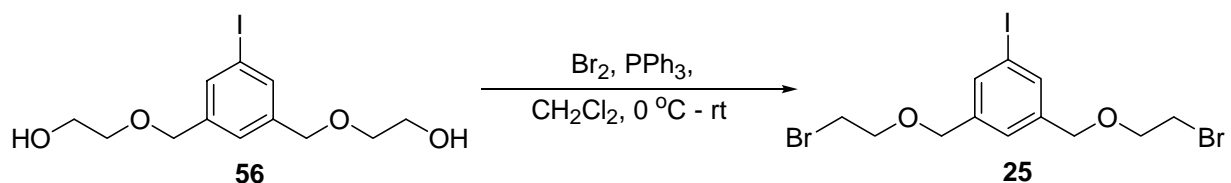
2-[3-(2-Hydroxy-ethoxymethyl)-5-iodo-benzyloxy]-ethanol (**56**).



Ethylene glycol (3.0 mL, 54 mmol, 6 equiv) was added to a suspension of sodium hydride (95% dispersion in mineral oil, 0.7 g, 27 mmol, 3 equiv) in THF (75 mL) at 0 °C. The solution was warmed to room temperature and stirred for an additional 30 min. In a separate round-bottom

flask, a catalytic amount of *n*-Bu₄NI was added to a solution of **55** (3.5 g, 9 mmol, 1 equiv) in THF (100 mL). This solution was cannulated into the solution of sodioethylene glycolate at room temperature. The reaction mixture was heated to 50 °C for 20 h, cooled to room temperature and quenched with saturated aq NH₄Cl (50 mL). THF was removed under reduced pressure and the aqueous layer was extracted with ether (3×75 mL). The combined organic layers were dried with anhydrous MgSO₄ and filtered. Removal of the solvent afforded a crude oil that was purified by flash chromatography using 2/38/60 – 5/35/60 MeOH/EtOAc/CH₂Cl₂ yielding **56** (1.85 g, 58%) as a light yellow oil. *R*_f = 0.31 on silica gel (5/35/60 MeOH/EtOAc/CH₂Cl₂). IR (neat) ν = 3386, 1602, 1569, 1442, 1352, 1246, 1156, 1118, 1069, 890, 854, 806 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.60 (s, 2H), 7.30 (s, 1H), 4.48 (s, 4H), 3.73 (bs, 4H), 3.57 (t, 4H, *J* = 4.6 Hz), 2.84 (bs, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 140.7, 136.0, 126.2, 94.6, 72.3, 71.9, 62.0; HRMS calcd for C₁₂H₁₇IO₄ [M]⁺ 352.0172, found 352.0174.

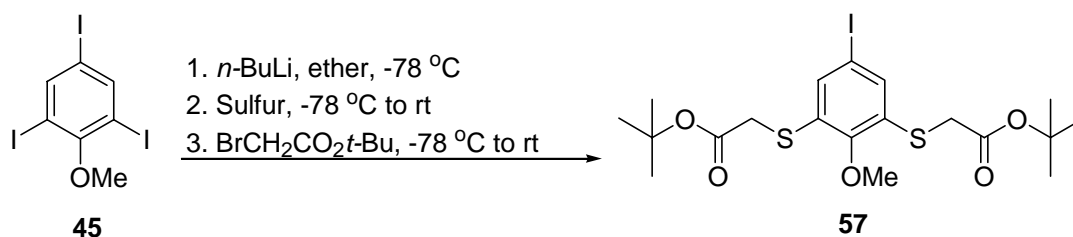
1,3-Bis-(2-bromo-ethoxymethyl)-5-iodobenzene (**25**).



Bromine (0.35 mL, 6.8 mmol, 2.4 equiv) was added slowly to a solution of triphenylphosphine (1.79 g, 6.8 mmol, 2.4 equiv) in CH₂Cl₂ (15 mL) at 0 °C. The resulting yellow suspension was stirred for an additional 10 min at 0 °C. A solution of **56** (1 g, 2.8 mmol, 1 equiv) and Et₃N (0.95 mL, 6.8 mmol, 2.4 equiv) in CH₂Cl₂ (15 mL) was added to the suspension at 0 °C and the resulting yellow solution was stirred at 0 °C for 30 min, then at room temperature for an additional 30 min. The solvent was removed from the reaction mixture and the crude residue was purified by flash chromatography using 50% CH₂Cl₂/hexanes to afford **25** (0.96 g, 71%) as a colourless oil. *R*_f = 0.31 on silica gel (50% CH₂Cl₂/hexanes). IR (neat) ν = 1644, 1570, 1440,

1355, 1276, 1112, 907, 730 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.64 (s, 2H), 7.31 (s, 1H), 4.53 (s, 4H), 3.80 (t, 4H, $J = 6.1$ Hz), 3.50 (t, 4H, $J = 6.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 140.5, 136.0, 126.1, 94.7, 72.2, 70.4, 30.5; HRMS calcd for $\text{C}_{12}\text{H}_{15}\text{Br}_2\text{IO}_2$ $[\text{M}]^+$ 475.8484, found 475.8494.

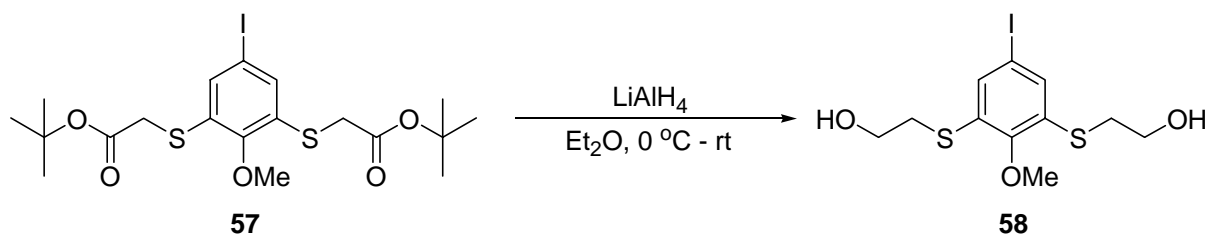
(3-*tert*-Butoxycarbonylmethylsulfanyl-5-iodo-2-methoxy-phenylsulfanyl)-acetic acid *tert*-butyl ester (57**).**



A solution of **45** (10.2 g, 21 mmol, 1 equiv) in ether (200 mL) was cooled to -78 °C. *n*-BuLi (1.6 M solution in hexanes, 29 mL, 46 mmol, 2.2 equiv) was added slowly and the reaction mixture was stirred at -78 °C for 1 hr. Sulfur (1.4 g, 42 mmol 2 equiv) was added in one portion and the reaction mixture was stirred again at -78 °C for 10 min. The mixture was then warmed to room temperature and stirred for an additional 3 h. The reaction mixture was cooled back down to -78 °C and *tert*-butyl bromoacetate (6.2 mL, 42 mmol, 2 equiv) was added. The mixture was stirred at this temperature for 5 minutes, and then warmed back up to room temperature and stirred for an additional hour. The reaction was quenched with saturated aq NH_4Cl (100 mL) and the aqueous layer was extracted with ether (3×100 mL). The combined organic layers were washed with brine (100 mL), dried with anhydrous MgSO_4 , filtered and concentrated. The crude product was purified by flash chromatography using 5% EtOAc/hexanes as an eluant to afford **57** (5.7 g, 51%) as a yellow oil. $R_f = 0.2$ (10% EtOAc/hexanes). IR (neat) $\nu = 1728, 1542, 1453, 1402, 1368, 1294, 1238, 1133, 991, 849$ cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.42 (s, 2H), 3.89 (s, 3H),

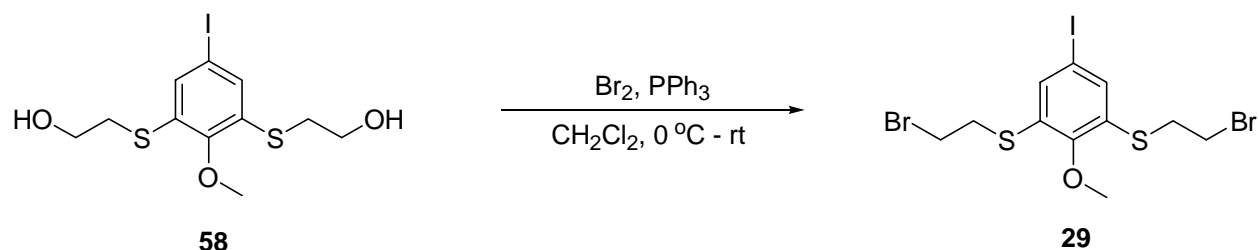
3.56 (s, 4H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.4, 155.1, 134.9, 132.9, 88.2, 82.6, 60.1, 35.8, 28.1; HRMS calcd for $\text{C}_{19}\text{H}_{27}\text{IO}_5\text{S}_2\text{Na}$ (ESI) 549.0236, found 549.0232.

2-[3-(2-Hydroxy-ethylsulfanyl)-5-iodo-2-methoxy-phenylsulfanyl]-ethanol (58**).**



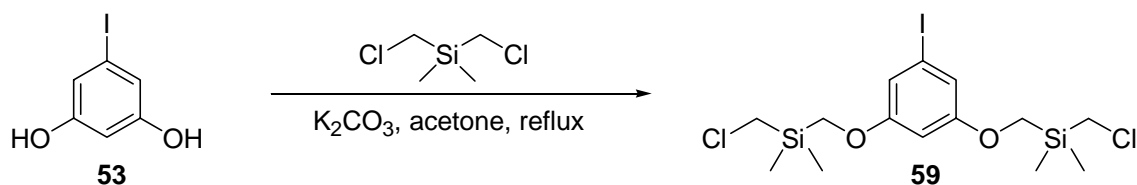
LiAlH_4 (1.02 g, 26.9 mmol, 2.5 equiv) was suspended in ether (20 mL) and cooled to 0 °C. A solution of **57** (5.66 g, 10.8 mmol, 1 equiv) in ether (40 mL) was added to the LiAlH_4 at 0 °C and the mixture was stirred at this temperature for 30 min, then at room temperature for 1 hour. To work-up the reaction: 1 mL water/g of LiAlH_4 was slowly added to the reaction mixture and stirred at room temperature for 10 minutes; followed by 1 mL 15% (w/w) NaOH /g LiAlH_4 and stir for 10 minutes; finally 3 mL water/g LiAlH_4 was added to the reaction mixture for 10 minutes, or until a fluffy white precipitate formed. The precipitate was filtered off and the ether was removed under reduced pressure. Crude product was purified by flash chromatography using 50% - 100% EtOAc/hexanes eluant to afford **58** (3 g, 72%) as a colourless oil. R_f = 0.17 (25% EtOAc/hexanes). IR (neat) ν = 3385, 1538, 1450, 1398, 1234, 1044, 990 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.48 (s, 2H), 3.89 (s, 3H), 3.75 (t, 4H, J = 5.6 Hz), 3.07 (t, 4H, J = 6.0 Hz), 2.56 (bs, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.9, 136.7, 132.6, 88.7, 60.7, 60.5, 36.1; HRMS calcd for $\text{C}_{11}\text{H}_{15}\text{IO}_3\text{S}_2$ $[\text{M}]^+$ 385.9507, found 385.9506.

1,3-Bis-(2-bromo-ethylsulfanyl)-5-iodo-2-methoxy-benzene (29).



Bromine (0.9 mL, 17.4 mmol, 2.4 equiv) was added slowly to a solution of triphenylphosphine (4.56 g, 17.4 mmol, 2.4 equiv) in CH_2Cl_2 (45 mL) at $0\text{ }^\circ\text{C}$. The resulting yellow suspension was stirred for an additional 10 min at $0\text{ }^\circ\text{C}$. A solution of **58** (2.8 g, 7.3 mmol, 1 equiv) and Et_3N (2.4 mL, 17.4 mmol, 2.4 equiv) in CH_2Cl_2 (45 mL) was added to the suspension at $0\text{ }^\circ\text{C}$ and the resulting yellow solution was stirred at $0\text{ }^\circ\text{C}$ for 30 min, then at room temperature for an additional 30 min. The solvent was removed from the reaction mixture and the crude residue was purified by flash chromatography using 2 to 5% Et_2O /hexanes to afford **29** (1.52 g, 41%) as a colourless oil. $R_f = 0.18$ on silica gel (2% Et_2O /hexanes). IR (neat) $\nu = 1587, 1534, 1447, 1388, 1222, 1185, 1097, 986\text{ cm}^{-1}$; ^1H NMR (400 MHz, CDCl_3) δ 7.44 (s, 2H), 3.87 (s, 3H), 3.51-3.29 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.7, 136.5, 132.2, 88.6, 60.3, 34.5, 29.6; HRMS calcd for $\text{C}_{11}\text{H}_{13}\text{Br}_2\text{IOS}_2$ $[\text{M}]^+$ 509.7819, found 509.7821.

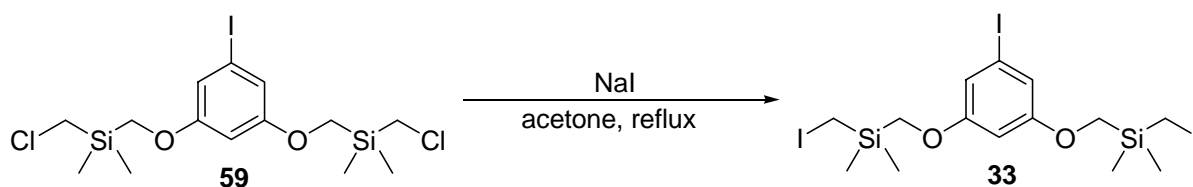
1,3-Bis-[(chloromethyl-dimethyl-silanyl)-methoxy]-5-iodo-benzene (59)



A solution of **53** (1 g, 4.2 mmol, 1 equiv) and K_2CO_3 (1.76 g, 12.7 mmol, 3 equiv) was stirred in acetone (45 mL) for 30 min at room temperature. Bis(chloromethyl)dimethylsilane (5.4 mL, 37.3 mmol, 9 equiv) and a catalytic amount of $n\text{-Bu}_4\text{NI}$ (155 mg, 0.4 mmol, 0.1 equiv) were added to

this solution and the reaction mixture was heated to 65 °C for 20 h. The acetone was removed under reduced pressure and the residue was partitioned between water and Et₂O (50 mL each). The aqueous layer was extracted with Et₂O (3× 50 mL) and the combined organic layers were washed with brine (50 mL), dried with anhydrous MgSO₄, filtered and concentrated. The crude product was purified by flash chromatography using 0 – 5% EtOAc/hexanes eluant to afford **59** (1.43 g, 71%) as a colourless oil. *R*_f = 0.84 on silica gel (10% EtOAc/hexanes). IR (neat) ν = 1590, 1569, 1420, 1252, 1153, 1047, 1014, 847 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.90 (d, 2H, *J* = 2.2 Hz), 6.50 (t, 1H, *J* = 2.2 Hz), 3.67 (s, 4H), 2.92 (s, 4H), 0.26 (s, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 116.2, 100.9, 94.1, 58.9, 28.5, -5.8; HRMS calcd for C₁₄H₂₃Cl₂IO₂Si₂ [M]⁺ 475.9658, found 475.9650.

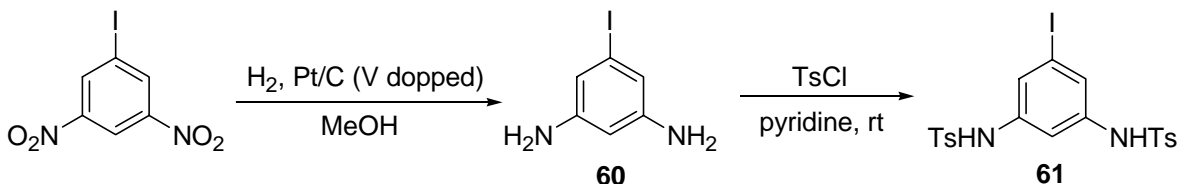
1-Iodo-3,5-bis-[(iodomethyl-dimethyl-silanyl)-methoxy]-benzene (**33**)



Sodium iodide (3.96 g, 26 mmol, 10 equiv) was added to a solution of **59** (1.26 g, 2.6 mmol, 1 equiv) in acetone (30 mL). The reaction mixture was heated to 65 °C for 6 h, during which time a white precipitate had formed. The solvent was removed under reduced pressure and the residue was partitioned between water and Et₂O (50 mL each). The aqueous layer was extracted with Et₂O (3× 50 mL) and the combined organic layers were washed with brine (50 mL), dried with anhydrous MgSO₄, filtered and concentrated. The crude product was purified by flash chromatography using 0 – 4% EtOAc/hexanes eluant to afford **33** (1.51 g, 87%) as a yellow oil. *R*_f = 0.43 on silica gel (2% Et₂O/hexanes). IR (neat) ν = 1589, 1568, 1418, 1251, 1153, 1047, 1009, 842 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.90 (d, 2H, *J* = 2.2 Hz), 6.50 (t, 1H, *J* = 2.2 Hz),

3.67 (s, 4H), 2.12 (s, 4H), 0.28 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.9, 116.2, 100.9, 94.1, 59.9, -4.20, -16.4; HRMS calcd for $\text{C}_{14}\text{H}_{23}\text{I}_3\text{O}_2\text{Si}_2$ $[\text{M}]^+$ 659.8371, found 659.8372.

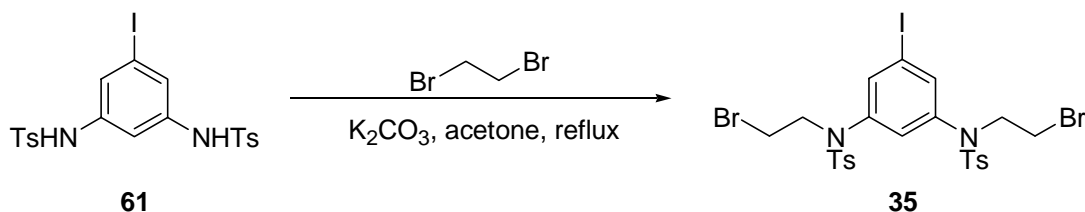
***N*-(3-Iodo-5-[[*(4-methylphenyl)sulfonyl*]amino}phenyl)-4-methylbenzenesulfonamide (61).**



To a solution of 1-iodo-3,5-dinitrobenzene (2.9 g, 9.9 mmol, 1 equiv) in MeOH (100 mL) was added 1% platinum on activated carbon (vanadium doped) (200 mg). The reaction mixture was placed under an atmosphere of hydrogen (30 psi) for 12 hr. The reaction mixture was filtered over Celite[®] and concentrated to afford crude **60** as brown solid, which was used without further purification. To a solution of **60** in pyridine (15 mL) was added *p*-toluenesulfonyl chloride (4.2 g, 21.8 mmol, 2.2 equiv). The reaction mixture was stirred at room temperature for 1 hr and then quenched with water (20 mL). The solution was extracted with CH_2Cl_2 (3×20 mL) and the combined organic extracts were washed with aqueous CuSO_4 (2×20 mL), dried with anhydrous MgSO_4 , filtered and concentrated. The crude product was purified by flash chromatography using 25% EtOAc/ CH_2Cl_2 eluant to afford **61** (3.9 g, 72%); tan solid, mp = 230 °C (decomposed). R_f = 0.34 on silica gel (25% EtOAc/ CH_2Cl_2). IR (Nujol) ν = 3251, 3221, 1601, 1581, 1462, 1377, 1156 cm^{-1} ; ^1H NMR (400 MHz, DMSO) δ 10.41 (s, 1H), 7.59 (d, 4H, J = 8.2 Hz), 7.35 (d, 4H, J = 8.2 Hz), 7.16 (t, 1H, J = 1.9 Hz), 6.97 (d, 2H, J = 1.9 Hz), 2.36 (s, 6H); ^{13}C NMR (100 MHz, DMSO) δ 143.5, 139.8, 136.1, 129.6, 126.6, 122.1, 108.2, 94.7, 20.9; HRMS calcd for $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_4\text{NaS}_2\text{I}$ (ESI) 564.9723, found 564.9735. Data for **60**: Brown solid, mp = 128-130 °C. R_f = 0.58 on silica gel (EtOAc). IR (neat) ν = 3433, 3304, 3195, 1565, 977, 800 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.46 (d, 2H, J = 2.0 Hz), 5.93 (t, 1H, J = 2.0 Hz), 3.55 (bs, 4H); ^{13}C NMR

(100 MHz, CDCl₃) δ 148.7, 115.0, 101.1, 95.7; HRMS calcd for C₆H₈N₂I (ESI) 234.9726, found 234.9738.

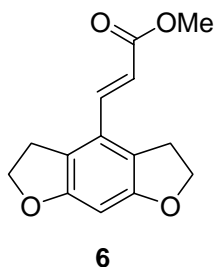
***N,N'*-Bis(2-Bromomethyl)-5-iodobenzene-1,3-di-*p*-toluylsulfonamide (**35**).**



To a suspension of **61** (2 g, 3.7 mmol, 1 equiv) in acetonitrile (35 mL) was added 1,2-dibromoethane (4.8 mL, 55.3 mmol, 15 equiv) and K₂CO₃ (1.53 g, 11.1 mmol, 3 equiv). The suspension was heated to reflux and stirred at this temperature for 8 hr. The reaction was then quenched with water (20 mL) and extracted with Et₂O (3 × 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated. The crude product was purified by flash chromatography using 25% EtOAc/hexanes eluant to afford **35** (2.3 g, 83%); white solid, mp = 117-118 °C. *R*_f = 0.47 on silica gel (25% EtOAc). IR (neat) ν = 3441, 1645, 1350, 1160 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.45 (d, 4H, *J* = 8.2 Hz), 7.42 (d, 2H, *J* = 1.9 Hz), 7.30 (d, 4H, *J* = 8.2 Hz), 6.71 (t, 1H, *J* = 1.9 Hz), 3.76 (t, 4H, *J* = 7.0 Hz), 3.33 (t, 4H, *J* = 7.0 Hz), 2.44 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 144.7, 141.0, 138.1, 134.5, 130.1, 128.8, 127.8, 93.3, 52.4, 29.0, 21.8; HRMS calcd for C₂₄H₂₅Br₂IN₂NaO₄S₂ [M]⁺ 776.8559 (ESI), found 776.8539.

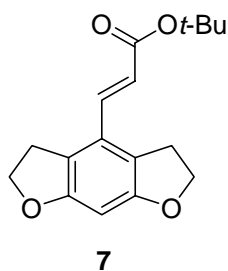
Alkylation/Alkenylation Reactions

3-(2,3,5,6-Tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylic acid methyl ester (**6**).



Following the general procedure for the alkylation/alkenylation reaction using **5** and methyl acrylate, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **6** (32 mg, 80%) as a yellow solid, mp = 157-158 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). R_f = 0.40 on silica gel (10% EtOAc/hexanes). IR (neat) 1716, 1635, 1452, 1294, 1182 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.66 (d, 1H, J = 16.3 Hz), 6.34 (s, 1H), 6.25 (d, 1H, J = 16.3 Hz), 4.62 (t, 4H, J = 8.6 Hz), 3.81 (s, 3H), 3.25 (t, 4H, J = 8.6 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.6, 161.1, 141.6, 127.1, 121.0, 118.5, 94.6, 72.2, 52.0, 29.7; HRMS calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4$ $[\text{M}]^+$ 246.0898, found 246.0892.

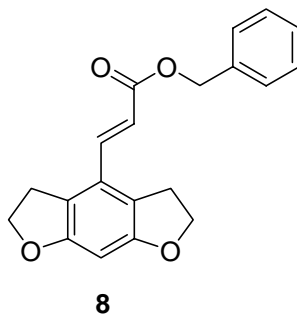
3-(2,3,5,6-Tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylic acid *tert*-butyl ester (**7**).



Following the general procedure for the alkylation/alkenylation reaction using **5** and *tert*-butyl acrylate, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **7** (49 mg, 85%) as a pale yellow solid, mp = 108-109 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). R_f = 0.35 on silica gel (10% EtOAc/hexanes). IR (neat) 1707, 1593, 1440, 1293, 1154 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.66 (d, 1H, J = 16.3 Hz),

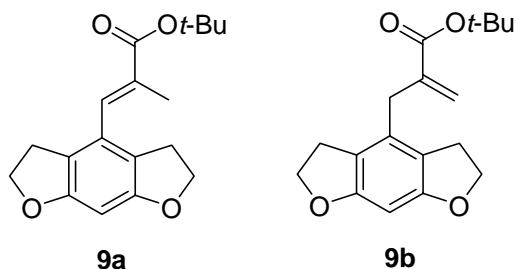
6.32 (s, 1H), 6.17 (d, 1H, $J = 16.3$ Hz), 4.61 (t, 4H, $J = 8.6$ Hz), 3.25 (t, 4H, $J = 8.6$ Hz), 1.53 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.6, 160.9, 140.4, 127.3, 123.2, 118.4, 94.3, 81.0, 72.2, 29.6, 28.4; HRMS calcd for $\text{C}_{17}\text{H}_{20}\text{O}_4$ $[\text{M}]^+$ 288.1363, found 288.1361.

3-(2,3,5,6-Tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylic acid benzyl ester (8).



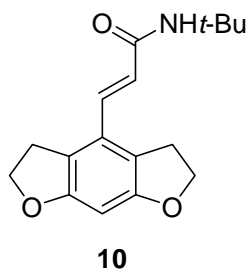
Following the general procedure for the alkylation/alkenylation reaction using **5** and benzyl acrylate, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **8** (47 mg, 77%) as a pale yellow solid, mp = 68-70 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). $R_f = 0.55$ on silica gel (10% EtOAc/hexanes). IR (neat) 2959, 1712, 1633, 1592, 1439, 1289 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.69 (d, 1H, $J = 16.3$ Hz), 7.40 (m, 5H), 6.33 (s, 1H), 6.27 (d, 1H, $J = 16.3$ Hz), 5.25 (s, 2H), 4.60 (t, 4H, $J = 8.5$ Hz), 3.24 (t, 4H, $J = 8.6$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 166.8, 160.8, 141.7, 135.9, 128.6, 128.4, 128.3, 126.8, 120.7, 118.3, 94.4, 66.5, 29.5; HRMS calcd for $\text{C}_{20}\text{H}_{18}\text{O}_4$ $[\text{M}]^+$ 322.1198, found 322.1205.

2-Methyl-3-(2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylic acid *tert*-butyl ester (9a) and 2-(2,3,5,6-Tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-ylmethyl)-acrylic acid *tert*-butyl ester (9b).



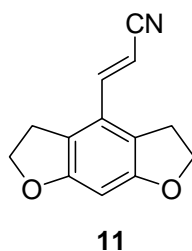
Following the general procedure for the alkylation/alkenylation reaction using **5** and *tert*-butyl methacrylate, and purification by flash chromatography using 5% EtOAc/hexanes as eluant resulted in an inseparable mixture of **9a** and **9b** in a 1:1 ratio (**9a:9b**) (34 mg, 57%) as a white solid, mp = 75-77 °C (the resulting solid from the evaporation of 5% EtOAc/hexanes). R_f = 0.33 on silica gel (5% EtOAc/hexanes). IR (neat) 2973, 1707, 1596, 1444 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.42 (s, 1H in **9a**), 6.27 (s, 1H in **9b**), 6.21 (s, 1H in **9a**), 6.09 (s, 1H in **9b**), 5.17 (s, 1H in **9b**), 4.57 (t, 4H, J = 8.5 Hz), 4.55 (t, 4H, J = 8.7 Hz), 3.44 (s, 2H in **9b**), 2.99 (t, 4H, J = 8.5 Hz), 2.95 (t, 4H, J = 8.5 Hz), 1.80 (brs, 2H in **9a**), 1.54 (s, 9H), 1.50 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 167.3, 166.5, 160.5, 160.4, 139.0, 135.0, 132.5, 131.0, 130.0, 124.3, 118.0, 117.0, 92.3, 91.2, 81.1, 80.9, 72.3, 72.1, 33.4, 29.0, 28.3, 28.2, 27.8, 14.9 HRMS calcd for $\text{C}_{18}\text{H}_{22}\text{O}_4$ $[\text{M}]^+$ 302.1519, found 302.1518.

***N*-tert-Butyl-3-(2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylamide (10).**



Following the general procedure for the alkylation/alkenylation reaction using **5** and *N*-tert-butylacrylamide, and purification by flash chromatography using 25% EtOAc/hexanes as eluant resulted in **10** (35 mg, 61%) as a white solid, mp = 83-84 °C (the resulting solid from the evaporation of 25% EtOAc/hexanes). R_f = 0.14 (25% EtOAc/hexanes). IR (neat) 1619, 1450, 1298, 1062 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.42 (d, 1H, J = 15.8 Hz), 6.30 (s, 1H), 6.13 (d, 1H, J = 15.8 Hz), 5.51 (brs, 1H), 4.59 (t, 4H, J = 8.6 Hz), 3.23 (t, 4H, J = 8.6 Hz), 1.44 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.3, 160.9, 137.2, 127.6, 124.8, 118.1, 93.9, 72.2, 51.9, 29.7, 29.1; HRMS calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_3$ $[\text{M}]^+$ 287.1528, found 287.1521.

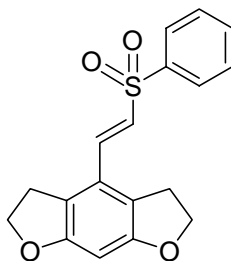
3-(2,3,5,6-Tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylonitrile (11).



Following the general procedure for the alkylation/alkenylation reaction using **5** and acrylonitrile, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **11** (30 mg, 71%) as a white solid, mp = 200-201 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). R_f = 0.23 (10% EtOAc/hexanes). IR (neat) 2910, 2211, 1738, 1592, 1442 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.36 (d, 1H, J = 16.8 Hz), 6.36 (s, 1H), 5.69 (d, 1H, J = 16.8 Hz), 4.63 (t, 4H, J = 8.6 Hz), 3.20 (t, 4H, J = 8.6 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 161.3, 147.7,

126.3, 118.4, 118.1, 99.5, 95.4, 72.2, 29.5; HRMS calcd for $C_{13}H_{11}NO_2$ $[M]^+$ 213.0785, found 213.0789.

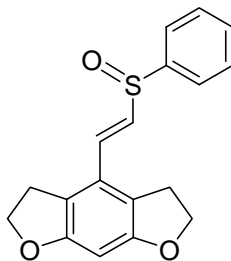
4-(2-Benzenesulfonyl-vinyl)-2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran (12).



12

Following the general procedure for the alkylation/alkenylation reaction using **5** and phenyl vinyl sulfone, and purification by flash chromatography using 25% EtOAc/hexanes as eluant resulted in **12** (24 mg, 38%) as a yellow solid, mp = 153-155 °C (the resulting solid from the evaporation of 25% EtOAc/hexanes). R_f = 0.31 on silica gel (25% EtOAc/hexanes). IR (neat) 1586, 1444, 1302, 1143 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, 2H, J = 7.0 Hz), 7.58 (m, 4H), 6.67 (d, 1H, J = 15.7 Hz), 6.35 (s, 1H), 4.61 (t, 4H, J = 8.6 Hz), 3.21 (t, 4H, J = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 140.8, 139.1, 133.7, 130.1, 129.6, 127.8, 125.0, 118.9, 95.5, 72.2, 29.6; HRMS calcd for $C_{18}H_{16}O_4S$ $[M]^+$ 328.0757, found 328.0769.

4-(2-Benzenesulfinyl-vinyl)-2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran (13).

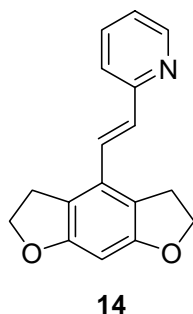


13

Following the general procedure for the alkylation/alkenylation reaction using **5** and phenyl vinyl sulfoxide, and purification by flash chromatography using 25% EtOAc/hexanes as eluant resulted

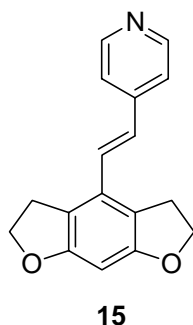
in **13** (23 mg, 37%) as a yellow solid, mp = 150-151 °C (the resulting solid from the evaporation of 25% EtOAc/hexanes). R_f = 0.31 on silica gel (25% EtOAc/hexanes). IR (neat) 2897, 1586, 1441, 1304, 1155, 1062 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.68 (m, 2H), 7.54 (m, 3H), 7.33 (d, 1H, J = 15.8 Hz), 6.67 (d, 1H, J = 15.8 Hz), 6.31 (s, 1H), 4.59 (t, 4H, J = 8.5 Hz), 3.19 (t, 4H, J = 8.5 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 161.0, 144.0, 136.2, 132.6, 131.5, 129.7, 126.2, 125.0, 117.9, 94.2, 72.1, 29.5; HRMS calcd for $\text{C}_{18}\text{H}_{16}\text{O}_3\text{S}$ $[\text{M}]^+$ 312.0828, found 312.0820.

2-[2-(2,3,5,6-Tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-vinyl]-pyridine (14**).**



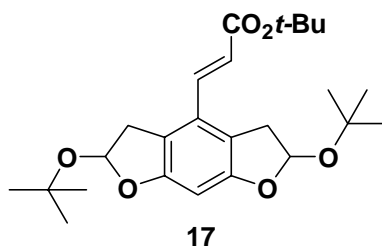
Following the general procedure for the alkylation/alkenylation reaction using **5** and 2-vinyl pyridine, and purification by flash chromatography using 50% EtOAc/hexanes as eluant resulted in **14** (30 mg, 57%) as a yellow solid, mp = 97-98 °C (the resulting solid from the evaporation of 50% EtOAc/hexanes). R_f = 0.37 on silica gel (25% EtOAc/hexanes). IR (neat) 2917, 1592, 1439, 1156, 1061 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.62 (brs, 1H), 7.67 (t, 1H, J = 7.6 Hz), 7.59 (d, 1H, J = 16.2 Hz), 7.37 (brd, 1H, J = 7.2 Hz), 7.17 (m, 1H), 7.00 (d, 1H, J = 16.3 Hz), 6.29 (s, 1H), 4.62 (t, 4H, J = 8.6 Hz), 3.34 (t, 4H, J = 8.6 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 160.9, 155.8, 149.9, 136.8, 131.62, 129.9, 129.4, 122.5, 122.6, 117.2, 92.9, 72.2, 29.9; HRMS calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_2$ $[\text{M}]^+$ 265.1103, found 265.1107.

4-[2-(2,3,5,6-Tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-vinyl]-pyridine (15**).**



Following the general procedure for the alkylation/alkenylation reaction using **5** and 4-vinyl pyridine, and purification by flash chromatography using 50% EtOAc/hexanes as eluant resulted in **15** (23 mg, 43%) as a yellow solid, mp = 136-137 °C (the resulting solid from the evaporation of 50% EtOAc/hexanes). R_f = 0.22 on silica gel (50% EtOAc/hexanes). IR (neat) 2921, 1593, 1439, 1061 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.60 (brs, 2H), 7.34 (d, 2H, J = 5.2 Hz), 7.23 (d, 1H, J = 16.7 Hz), 6.83 (d, 1H, J = 16.8 Hz), 6.31 (s, 1H), 4.64 (t, 4H, J = 8.5 Hz), 3.30 (t, 4H, J = 8.5 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 161.0, 150.5, 144.9, 130.4, 129.6, 128.8, 121.1, 117.1, 93.3, 72.2, 29.7; HRMS calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_2$ $[\text{M}]^+$ 265.1102, found 265.1099.

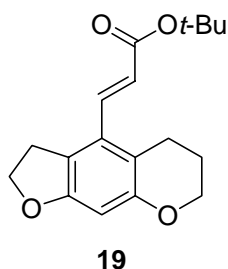
3-(2,6-Di-*tert*-butoxy-2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylic acid *tert*-butyl ester (17**).**



Following the general procedure for the alkylation/alkenylation reaction using **16** and *tert*-butyl acrylate, followed by purification by flash chromatography using 5-10% Et_2O /hexanes as eluant resulted **17** (45 mg, 52%) as a colourless oil, 1:1 mixture of diastereomers. R_f = 0.1 on silica gel (5% Et_2O /hexanes). IR (neat) ν = 1707, 1635, 1595, 1452, 1392, 1367, 1293, 1151, 1096, 1050,

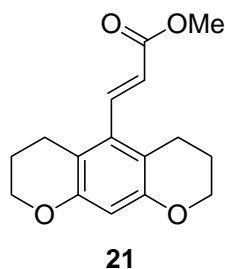
948, 928 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.52 (d, 1H, $J = 16.3$ Hz), 7.51 (d, 1H, $J = 16.3$ Hz), 6.35 (s, 1H), 6.34 (s, 1H), 6.12 (d, 1H, $J = 16.3$ Hz), 6.12 (d, 1H, $J = 16.3$ Hz), 6.02 (dt, 4H, $J = 2.3$ and 6.5 Hz), 3.37 (dd, 2H, $J = 2.9$ and 6.9 Hz), 3.33 (dd, 2H, $J = 2.9$ and 6.9 Hz), 3.06 (dd, 2H, $J = 2.5$ Hz), 3.02 (dd, 2H, $J = 2.5$ Hz), 1.52 (s, 18H), 1.31 (s, 18H), 1.30 (s, 18H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.6, 158.8, 158.8, 140.4, 127.0, 123.0, 117.2, 117.1, 102.2, 102.1, 94.9, 80.8, 75.7, 75.7, 37.7, 29.0, 28.4; HRMS calcd for $\text{C}_{25}\text{H}_{36}\text{O}_6$ $[\text{M}]^+$ 432.2512, found 432.2500.

***tert*-Butyl (2*E*)-3-(2,3,6,7-tetrahydro-5*H*-furo[3,2-*g*]chromen-4-yl)acrylate (**19**).**



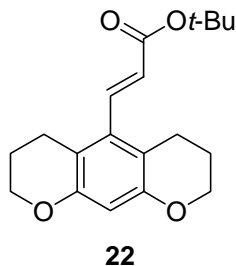
Following the general procedure for the alkylation/alkenylation reaction (irradiated for 10 min instead of 5 min) using **18** and *tert*-butyl acrylate, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **19** (45 mg, 80%) as a white solid, mp = 103-104 $^{\circ}\text{C}$ (the resulting solid from the evaporation of 10% EtOAc/hexanes). $R_f = 0.46$ on silica gel (10% EtOAc/hexanes). IR (neat) 2976, 1713, 1604, 1456, 1367, 1119 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.73 (d, 1H, $J = 16.2$ Hz), 6.33 (s, 1H), 6.17 (d, 1H, $J = 16.2$ Hz), 4.55 (t, 2H, $J = 8.6$ Hz), 4.12 (t, 2H, $J = 5.5$ Hz), 3.25 (t, 2H, $J = 8.6$ Hz), 2.77 (t, 2H, $J = 6.4$ Hz), 2.00 (quintet, 2H, $J = 6.1$ Hz), 1.53 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.4, 159.2, 155.3, 140.1, 130.5, 124.0, 118.5, 113.4, 99.7, 80.7, 71.4, 66.0, 30.4, 28.2, 22.9, 22.4; HRMS calcd for $\text{C}_{18}\text{H}_{22}\text{O}_4$ $[\text{M}]^+$ 302.1522, found 302.1518.

3-(3,4,7,8-Tetrahydro-2H,6H-pyrano[3,2-g]chromen-5-yl)-acrylic acid methyl ester (21).



Following the general procedure for the alkylation/alkenylation reaction (irradiated for 10 min instead of 5 min) using **20** and methyl acrylate, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **21** (36 mg, 67%) as a white solid, mp = 102-103 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). R_f = 0.43 on silica gel (10% EtOAc/hexanes). IR (neat) 2948, 1719, 1602, 1461, 1295, 1138 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.68 (d, 1H, J = 16.5 Hz), 6.32 (s, 1H), 6.05 (d, 1H, J = 16.5 Hz), 4.12 (t, 4H, J = 5.3 Hz), 3.81 (s, 3H), 2.66 (t, 4H, J = 6.4 Hz), 1.95 (quintet, 4H, J = 5.3 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 167.1, 154.1, 142.6, 135.0, 124.4, 113.7, 105.3, 66.2, 52.0, 23.8, 22.7; HRMS calcd for $\text{C}_{16}\text{H}_{18}\text{O}_4$ $[\text{M}]^+$ 274.1206, found 274.1205.

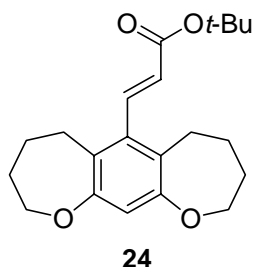
3-(3,4,7,8-Tetrahydro-2H,6H-pyrano[3,2-g]chromen-5-yl)-acrylic acid *tert*-butyl ester (22).



Following the general procedure for the alkylation/alkenylation reaction (irradiated for 10 min instead of 5 min) using **20** and *tert*-butyl acrylate, and purification by flash chromatography using 25% EtOAc/hexanes as eluant resulted in **22** (44 mg, 70%) as a white solid, mp = 116-117 °C (the resulting solid from the evaporation of 25% EtOAc/hexanes). R_f = 0.55 on silica gel (10% EtOAc/hexanes). IR (neat) 1711, 1602, 1462, 1296, 1140 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ

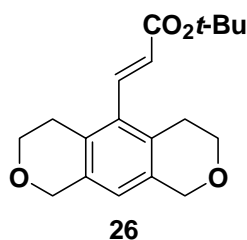
7.57 (d, 1H, $J = 16.4$ Hz), 6.30 (s, 1H), 5.96 (d, 1H, $J = 16.5$ Hz), 4.11 (t, 4H, $J = 5.1$ Hz), 2.67 (t, 4H, $J = 6.4$ Hz), 1.95 (quintet, 4H, $J = 6.4$ Hz), 1.54 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.1, 154.1, 141.1, 135.3, 126.6, 113.7, 105.0, 80.9, 66.2, 28.4, 23.8, 22.8; HRMS calcd for $\text{C}_{19}\text{H}_{24}\text{O}_4$ $[\text{M}]^+$ 316.1680, found 316.1675.

3-(2,3,4,5,7,8,9,10-Octahydro-1,11-dioxo-benzo[1,2;4,5]dicyclohepten-6-yl)-acrylic acid *tert*-butyl ester (24).



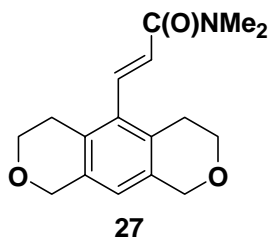
Following the general procedure for the alkylation/alkenylation reaction (irradiated for 20 min instead of 5 min) using **23** and *tert*-butyl acrylate, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **24** (42 mg, 68%) as a white solid, mp = 108-109 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). $R_f = 0.53$ on silica gel (10% EtOAc/hexanes). IR (neat) 2932, 1728, 1591, 1455, 1367, 1256, 1150 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, 1H, $J = 16.2$ Hz), 6.66 (s, 1H), 5.75 (d, 1H, $J = 16.2$ Hz), 3.99 (t, 4H, $J = 5.1$ Hz), 2.76 (m, 4H), 1.93 (quintet, 4H, $J = 5.6$ Hz), 1.65 (quintet, 4H, $J = 5.3$ Hz), 1.59 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.9, 159.5, 143.7, 135.7, 129.3, 127.1, 114.3, 81.0, 73.9, 32.3, 29.6, 28.4, 25.9; HRMS calcd for $\text{C}_{21}\text{H}_{28}\text{O}_4$ $[\text{M}]^+$ 344.1986, found 344.1988.

3-(4,5,6,8-Tetrahydro-1H,3H-2,7-dioxanthracen-10-yl)-acrylic acid *tert*-butyl ester (26).



Following the general procedure for the alkylation/alkenylation reaction using **25**, *tert*-butyl acrylate and 5 equiv of norbornene (1.00 mmol), followed by purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **26** (45 mg, 80%) as a white solid (the resulting solid from the evaporation of 10% EtOAc/hexanes), mp = 115-116 °C. R_f = 0.29 on silica gel (20% EtOAc/hexanes). IR (neat) ν = 1710, 1639, 1469, 1384, 1367, 1327, 1281, 1259, 1232, 1153, 1114, 1071, 982 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, 1H, J = 16.4 Hz), 6.62 (s, 1H), 6.00 (d, 1H, J = 16.4 Hz), 4.74 (s, 4H), 3.94 (t, 4H, J = 5.7 Hz), 2.80 (t, 4H, J = 5.7 Hz), 1.54 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.8, 140.2, 134.0, 132.9, 130.3, 126.7, 120.8, 80.9, 68.0, 65.4; HRMS calcd for $\text{C}_{19}\text{H}_{24}\text{O}_4$ $[\text{M}]^+$ 316.1675, found 316.1673.

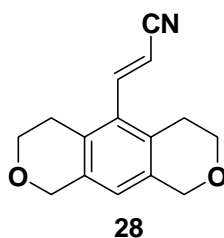
***N,N*-Dimethyl-3-(4,5,6,8-tetrahydro-1H,3H-2,7-dioxanthracen-10-yl)-acrylamide (27).**



Following the general procedure for the alkylation/alkenylation reaction using **25**, *N,N*-dimethyl acrylamide and 5 equiv of norbornene (1.00 mmol), followed by purification by flash chromatography using 50-75% EtOAc/ CH_2Cl_2 + 1% Et_3N as eluant resulted in **27** (34 mg, 58%) as a white solid (the resulting solid from the evaporation of EtOAc), mp = 165-167 °C. R_f = 0.1 on silica gel (50% EtOAc/ CH_2Cl_2). IR (neat) ν = 2360, 2333, 1651, 1607, 1466, 1394, 1386,

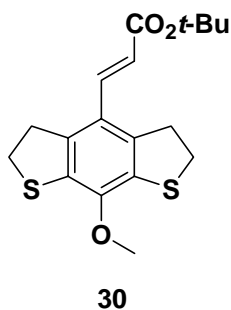
1129, 1112, 1070, 996, 982, 892 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, 1H, $J = 15.8$ Hz), 6.62 (s, 1H), 6.52 (d, 1H, $J = 15.8$ Hz), 4.74 (s, 4H), 3.93 (t, 4H, $J = 5.7$ Hz), 3.12 (s, 3H), 3.08 (s, 3H), 2.80 (t, 4H, $J = 5.7$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 166.3, 139.2, 135.3, 133.1, 130.1, 124.6, 120.5, 68.1, 65.6, 37.6, 36.1, 27.6; HRMS calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_3$ $[\text{M}]^+$ 287.1521, found 287.1524.

3-(4,5,6,8-Tetrahydro-1*H*,3*H*-2,7-dioxanthracen-10-yl)-acrylonitrile (28).



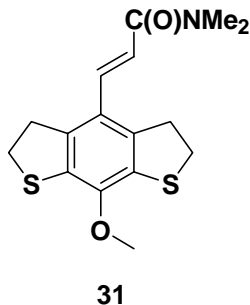
Following the general procedure for the alkylation/alkenylation reaction using **25**, acrylonitrile, and 5 equiv of norbornene (1.00 mmol), followed by purification by flash chromatography using 20-30% EtOAc/hexanes as eluant resulted in **28** (20 mg, 39%) as a white solid (the resulting solid from the evaporation of EtOAc), mp = 192-194 $^{\circ}\text{C}$. $R_f = 0.14$ on silica gel (20% EtOAc/hexanes). IR (neat) $\nu = 2215, 1614, 1471, 1130, 1112, 972$ cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.46 (d, 1H, $J = 17.0$ Hz), 6.67 (s, 1H), 5.59 (d, 1H, $J = 17.0$ Hz), 4.73 (s, 4H), 3.94 (t, 4H, $J = 5.6$ Hz), 2.76 (t, 4H, $J = 5.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 147.9, 133.3, 132.8, 130.1, 121.9, 117.4, 103.7, 67.8, 65.1, 27.2; HRMS calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_2$ $[\text{M}]^+$ 241.1103, found 241.1110.

3-(8-Methoxy-2,3,5,6-tetrahydro-1,7-dithia-s-indacen-4-yl)-acrylic acid *tert*-butyl ester (30).



Following the general procedure for the alkylation/alkenylation reaction (irradiated for 10 min instead of 5 min) using **29** and *tert*-butyl acrylate, purification by flash chromatography followed using 0-5% EtOAc/hexanes as eluant, resulted in **30** (30 mg, 43%) as a yellow solid (the resulting solid from evaporation of EtOAc), mp = 92-94 °C. R_f = 0.29 on silica gel (10% EtOAc/hexanes). IR (neat) ν = 1707, 1630, 1560, 1457, 1417, 1367, 1309, 1256, 1150, 1086, 980, 732 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, 1H, J = 16.3 Hz), 5.97 (d, 1H, J = 16.3 Hz), 3.88 (s, 3H), 3.35 (t, 8H, J = 1.5 Hz), 1.53 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.2, 149.1, 140.8, 138.4, 133.3, 124.0, 123.7, 80.8, 58.6, 35.9, 33.3, 28.2; HRMS calcd for $\text{C}_{18}\text{H}_{22}\text{O}_3\text{S}_2$ $[\text{M}]^+$ 350.1010, found 350.1013.

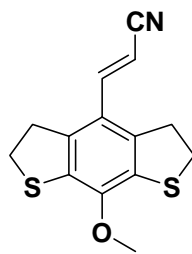
3-(8-Methoxy-2,3,5,6-tetrahydro-1,7-dithia-s-indacen-4-yl)-*N,N*-dimethyl-acrylamide (31).



Following the general procedure for the alkylation/alkenylation reaction (irradiated for 10 min instead of 5 min) using **29** and *N,N*-dimethylacrylamide, purification by flash chromatography followed using 2-5% acetone/ CH_2Cl_2 as eluant, resulted in **31** (16 mg, 26%) as a off-white oil. R_f = 0.34 on silica gel (5% acetone/ CH_2Cl_2). IR (neat) ν = 1648, 1639, 1632 cm^{-1} ; ^1H NMR (400

MHz, CDCl₃) δ 7.66 (d, 1H, J = 15.7 Hz), 6.47 (d, 1H, J = 15.7 Hz), 3.88 (s, 3H), 3.35 (t, 8H, J = 3.8 Hz), 3.12 (s, 3H), 3.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 166.6, 148.9, 139.8, 138.1, 133.4, 125.2, 121.8, 58.9, 36.1, 33.7, 30.0; HRMS calcd for C₁₆H₂₀NO₂S₂ (ESI) 322.0929, found 322.0934.

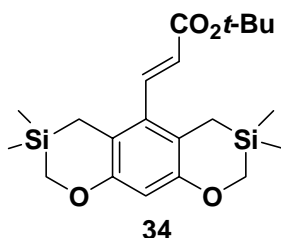
3-(8-Methoxy-2,3,5,6-tetrahydro-1,7-dithia-s-indacen-4-yl)-acrylonitrile (32).



32

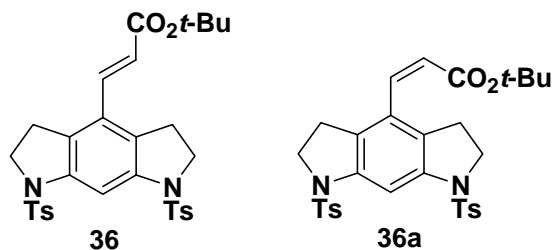
Following the general procedure for the alkylation/alkenylation reaction (irradiated for 10 min instead of 5 min) using **29** and acrylonitrile, purification by flash chromatography followed using 5-10% EtOAc/hexanes as eluant, resulted in **32** (10 mg, 19%) as an off-white solid (the resulting solid from the evaporation of EtOAc), mp = 164-166 °C. R_f = 0.16 on silica gel (10% EtOAc/hexanes). IR (neat) ν = 2216, 1616, 1553, 1456, 1417, 1315, 1270, 1088, 965 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.42 (d, 1H, J = 16.9 Hz), 5.50 (d, 1H, J = 16.9 Hz), 3.89 (s, 3H), 3.41 - 3.26 (m, 8H); ¹³C NMR (75 MHz, CDCl₃) δ 149.9, 148.1, 138.1, 133.9, 123.0, 118.0, 100.1, 58.7, 35.7, 33.2; HRMS calcd for C₁₄H₁₃NOS₂ [M]⁺ 275.0439, found 275.0435.

3-(3,3,6,6-Tetramethyl-3,4,6,7-tetrahydro-2H,5H-1,8-dioxa-3,6-disila-anthracen-10-yl)-acrylic acid *tert*-butyl ester (34).



Following the general procedure for the alkylation/alkenylation reaction using **33** and *tert*-butyl acrylate at 160 °C, followed by purification by flash chromatography using 0-5% EtOAc/hexanes as eluant resulted in **34** (48 mg, 60%) as a colourless oil. $R_f = 0.19$ on silica gel (5% EtOAc/hexanes). IR (neat) $\nu = 1711, 1640, 1586, 1442, 1367, 1290, 1251, 1151, 1113, 911, 842, 733 \text{ cm}^{-1}$; ^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, 1H, $J = 16.3 \text{ Hz}$), 6.58 (s, 1H), 5.80 (d, 1H, $J = 16.3 \text{ Hz}$), 3.70 (s, 4H), 1.91 (s, 4H), 1.57 (s, 9H), 0.14 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.1, 156.5, 143.7, 137.3, 126.9, 121.3, 111.4, 80.9, 64.0, 28.5, 13.4, -3.0; HRMS calcd for $\text{C}_{21}\text{H}_{32}\text{O}_4\text{Si}_2 [\text{M}]^+$ 404.1839, found 404.1832.

3-[1,7-Bis-(toluene-4-sulfonyl)-1,2,3,5,6,7-hexahydro-pyrrolo[3,2-*f*]indol-4-yl]-acrylic acid *tert*-butyl ester (36).

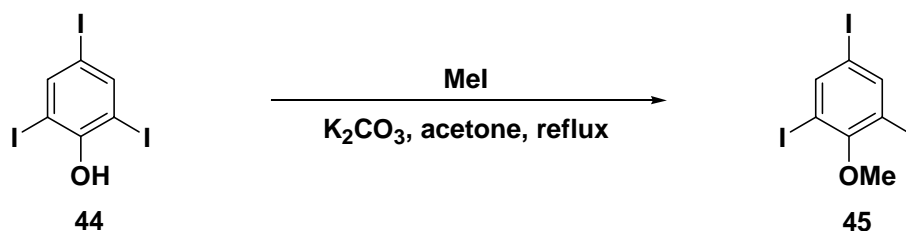


Following the general procedure for the alkylation/alkenylation reaction using **35** and *tert*-butyl acrylate and 5 equiv of norbornene (1.00 mmol), the reaction vessel was subjected to microwave irradiation at 160 °C for 5 min. Purification by flash chromatography followed using 5/35/60

Et₂O/CH₂Cl₂/hexanes as eluant, resulted in **36** (47 mg, 39%) as a colorless oil. *R_f* = 0.15 on silica gel (20% EtOAc/hexanes). **trans-isomer**: IR (neat) ν = 1652, 1635, 1354, 1267, 1164, 1096 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.90 (s, 1H), 7.74 (d, 4H, *J* = 8.3 Hz), 7.34 (d, 1H, *J* = 16.3 Hz), 7.25 (d, 4H, *J* = 8.3 Hz), 5.94 (d, 1H, *J* = 16.3 Hz), 3.99 (t, 4H, *J* = 8.4 Hz), 2.92 (t, 4H, *J* = 8.4 Hz), 2.39 (s, 6H), 1.47 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 166.1, 144.5, 142.8, 138.8, 134.1, 130.1, 128.0, 127.9, 126.6, 124.4, 103.3, 81.3, 50.8, 28.4, 27.7, 21.8; HRMS calcd for C₃₁H₃₄N₂O₆S₂ [M]⁺ 594.185831, found 594.185481. **cis-isomer (36a)**: *R_f* = 0.15 on silica gel (20% EtOAc/hexanes). IR (neat) ν = 1715, 1699, 1597, 1352, 1164, 1094, 815, 668 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.83 (s, 1H), 7.76 (d, 4H, *J* = 8.3 Hz), 7.25 (d, 4H, *J* = 8.3 Hz), 6.57 (d, 1H, *J* = 12.0 Hz), 5.88 (d, 1H, *J* = 12.0 Hz), 3.92 (t, 4H, *J* = 8.4 Hz), 2.65 (t, 4H, *J* = 8.4 Hz), 2.39 (s, 6H), 1.09 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 164.8, 144.2, 141.8, 137.4, 134.1, 130.9, 129.9, 127.9, 126.1, 124.6, 101.3, 80.7, 50.9, 27.8, 26.6, 21.8; HRMS calcd for C₃₁H₃₄N₂O₆S₂ [M]⁺ 594.185831, found 594.186567.

Synthesis of Mescaline Analogue 2

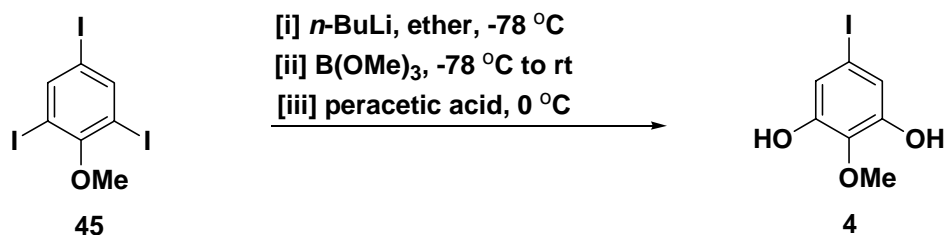
1,3,5-Triiodo-2-methoxybenzene (**45**).



To a solution of 2,4,6-triiodophenol (**44**) (10.0 g, 21.2 mmol, 1 equiv) in acetone (175 mL) was added K₂CO₃ (4.40 g, 31.8 mmol, 1.5 equiv). The mixture was stirred at rt for 30 min then iodomethane (2.00 mL, 31.8 mmol, 1.5 equiv) was added. The mixture was heated at reflux for 3 h, cooled to rt and filtered through Celite™. Evaporation of the volatiles gave a crude product that

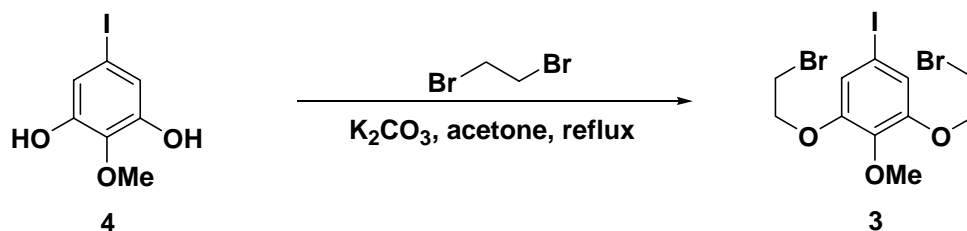
was purified by flash chromatography using 10% EtOAc/hexanes as eluant yielding **45** (10 g, 98%) as a pale yellow solid, mp = 93-94 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). R_f = 0.79 (10% EtOAc/hexanes). IR (neat) 1455, 1402 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.05 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.3, 147.5, 91.9, 89.5, 61.0; HRMS calcd for $\text{C}_7\text{H}_5\text{I}_3\text{O}$ $[\text{M}]^+$ 485.7481, found 485.7474.

5-Iodo-2-methoxybenzene-1,3-diol (**4**).



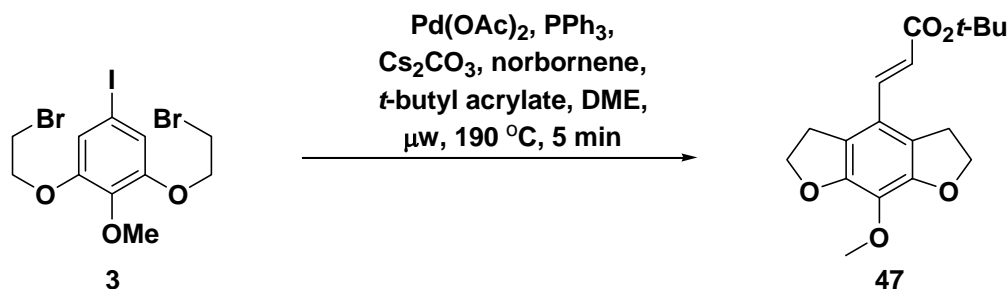
To a -78 °C solution of **45** (8.61 g, 17.7 mmol, 1 equiv) in ether (165 mL) was added dropwise *n*-BuLi (24.4 mL, 38.9 mmol, 1.6 M in hexanes, 2.2 equiv). The mixture was stirred at -78 °C for 1 h then trimethyl borate (20.0 mL, 177 mmol, 10 equiv) was added at once. The reaction was warmed to rt over 16 h then cooled to 0 °C. Peracetic acid solution (12.0 mL, 177 mmol, 32 wt% in dilute acetic acid, 10 equiv) was added dropwise. The reaction was stirred at 0 °C for 30 min then quenched with saturated aqueous NaHCO_3 (12 mL) and then warmed to rt. Water (170 mL) and ether (170 mL) were added and the organic layer was washed with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$, brine, dried with MgSO_4 , filtered, and concentrated. The crude mixture was purified by flash chromatography using 25% EtOAc/hexanes as eluant to yield **4** (3.6 g, 77%) as a pale yellow solid, mp = 90-91 °C (the resulting solid from the evaporation of 25% EtOAc/hexanes). R_f = 0.23 on silica gel (25% EtOAc/hexanes). IR (neat) 3395, 1582, 1487, 1161 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.87 (s, 2H), 5.93 (brs, 2OH), 3.85 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 149.8, 135.0, 117.9, 87.2, 61.4; HRMS calcd for $\text{C}_7\text{H}_7\text{IO}_3$ $[\text{M}]^+$ 265.9439, found 265.9440.

1,3-Bis(2-bromoethoxy)-5-iodo-2-methoxybenzene (3).



To a solution of **4** (5.16 g, 19.4 mmol, 1 equiv) and 1,2-dibromoethane (25.0 mL, 291 mmol, 15 equiv) in acetone (35 mL) was added K_2CO_3 (13.5 g, 97.1 mmol, 5 equiv). The mixture was heated at reflux for 36 h. The reaction was cooled to rt and filtered through Celite™. Distillation of the excess 1,2-dibromoethane gave a crude oil that was purified by flash chromatography using 10% EtOAc/hexanes as eluant yielding **3** (7.8 g, 84%) as a white solid, mp = 82-83 °C (the resulting solid from the evaporation of 10% EtOAc/hexanes). R_f = 0.55 on silica gel (10% EtOAc/hexanes). IR (neat) 1581, 1496, 1417, 1128 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.92 (s, 2H), 4.24 (t, 4H, J = 6.1 Hz), 3.87 (s, 3H), 3.65 (t, 4H, J = 6.1 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 153.1, 140.1, 118.3, 85.9, 69.6, 61.5, 29.2; HRMS calcd for $\text{C}_{11}\text{H}_{13}\text{Br}_2\text{IO}_3$ $[\text{M}]^+$ 477.8283, found 477.8276.

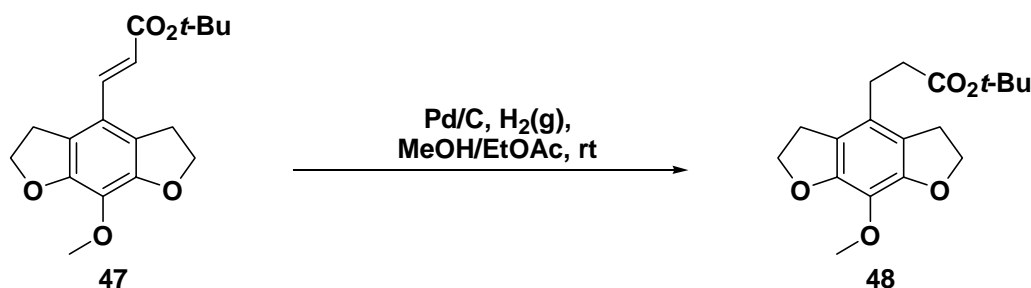
3-(8-Methoxy-2,3,5,6-tetrahydro-benzo[1,2-*b*:5,4-*b'*]difuran-4-yl)-acrylic acid *tert*-butyl ester (47).



Following the general procedure for the alkylation/alkenylation reaction using **3** (96.0 mg, 0.200 mmol) and *tert*-butyl acrylate, and purification by flash chromatography using 10% EtOAc/hexanes as eluant resulted in **47** (51 mg, 81%) as a pale yellow solid, mp = 116-117 °C

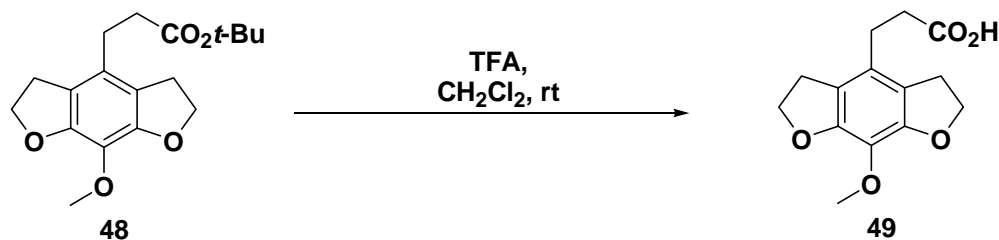
(the resulting solid from the evaporation of 10% EtOAc/hexanes). $R_f = 0.31$ on silica gel (10% EtOAc/hexanes). IR (neat) 1702, 1604, 1500, 1421 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.53 (d, 1H, $J = 16.2$ Hz), 6.07 (d, 1H, $J = 16.2$ Hz), 4.65 (t, 4H, $J = 8.8$ Hz), 4.00 (s, 3H), 3.27 (t, 4H, $J = 8.8$ Hz), 1.53 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.8, 150.7, 140.1, 131.3, 121.3, 121.0, 120.8, 80.7, 72.7, 60.4, 30.2, 28.3; HRMS calcd for $\text{C}_{18}\text{H}_{22}\text{O}_5$ $[\text{M}]^+$ 318.1469, found 318.1467.

3-(8-Methoxy-2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-propionic acid *tert*-butyl ester (48**).**



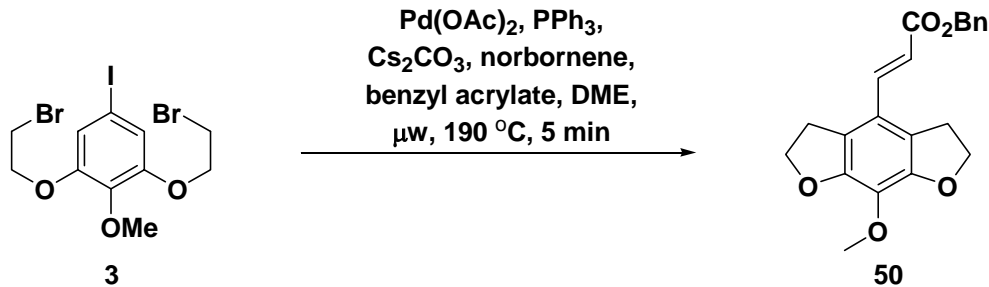
A solution of **47** (270 mg, 0.848 mmol, 1 equiv) and palladium on carbon (90 mg, 0.0848 mmol, [loading: 10 wt%, support activated carbon], 10 mol%), in MeOH/EtOAc 1:1 (20 mL) was hydrogenated at 40 psi in a Parr hydrogenator for 12 h. The mixture was filtered through Celite™ and concentrated. Purification by flash chromatography using 5% EtOAc/hexanes as eluant resulted in **48** (270 mg, 98%) as a white solid, mp = 62-63 °C (the resulting solid from the evaporation of 5% EtOAc/hexanes). $R_f = 0.24$ on silica gel (10% EtOAc/hexanes). IR (neat) 2978, 1728, 1605, 1504, 1422, 1336 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.60 (t, 4H, $J = 8.5$ Hz), 3.93 (s, 3H), 3.10 (t, 4H, $J = 8.5$ Hz), 2.73 (t, 2H, $J = 7.6$ Hz), 2.40 (t, 2H, $J = 8.5$ Hz), 1.42 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.4, 150.7, 128.4, 126.5, 119.1, 80.7, 72.7, 60.5, 34.8, 28.7, 28.2, 26.7; HRMS calcd for $\text{C}_{18}\text{H}_{24}\text{O}_5$ $[\text{M}]^+$ 320.1623, found 320.1624.

3-(8-Methoxy-2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-propionic acid (49**) from *tert*-butyl ester **48**.**



To a solution of **48** (110 mg, 0.343 mmol, 1 equiv) in CH_2Cl_2 (5 mL) was added trifluoroacetic acid (5 mL). The mixture was stirred at rt for 12 h. Toluene (25 mL) was added and the solution was concentrated yielding pure **49** (78 mg, 87%) as a white solid, mp = 133-134 °C (the resulting solid from the evaporation of toluene). R_f = 0.10 on silica gel (50% EtOAc/hexanes). IR (neat) 2921, 1694, 1606, 1506, 1429 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.61 (t, 4H, J = 8.6 Hz), 3.93 (s, 3H), 3.10 (t, 4H, J = 8.6 Hz), 2.78 (t, 2H, J = 7.3 Hz), 2.56 (t, 2H, J = 7.4 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 179.1, 150.9, 128.5, 125.9, 119.1, 72.7, 60.5, 33.5, 28.7, 26.6; HRMS calcd for $\text{C}_{14}\text{H}_{16}\text{O}_5$ $[\text{M}]^+$ 264.0999, found 264.0998.

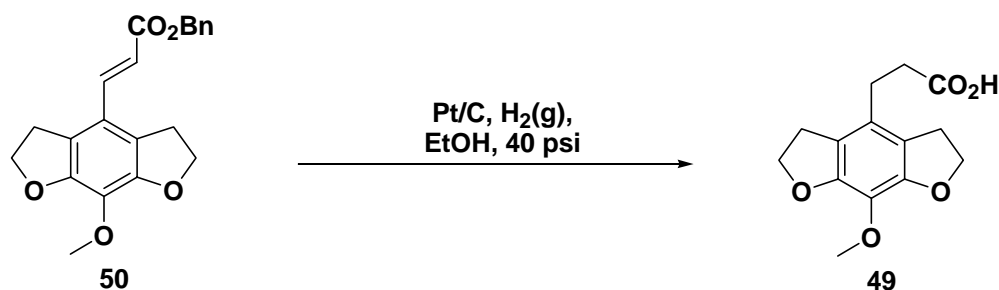
3-(8-Methoxy-2,3,5,6-tetrahydro-benzo[1,2-*b*;5,4-*b'*]difuran-4-yl)-acrylic acid benzyl ester (50**).**



Following the general procedure for the alkylation/alkenylation reaction using **3** (96.0 mg, 0.200 mmol) and benzyl acrylate, and purification by flash chromatography using 25% EtOAc/hexanes as eluant resulted in **50** (51 mg, 73%) as a white solid, mp = 113-115 °C (the resulting solid from the evaporation of 25% EtOAc/hexanes). R_f = 0.25 on silica gel (25% EtOAc/hexanes). IR (neat)

2953, 1713, 1581, 1504, 1426, 1335, 1164 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.66 (d, 1H, $J = 16.3$ Hz), 7.40 (m, 5H), 6.18 (d, 1H, $J = 16.3$ Hz), 5.24 (s, 2H), 4.65 (t, 4H, $J = 8.6$ Hz), 4.01 (s, 3H), 3.27 (t, 4H, $J = 8.6$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 167.3, 150.8, 141.8, 136.2, 131.6, 128.8, 128.6, 128.5, 121.1, 120.7, 118.9, 72.3, 66.6, 60.5, 30.2; HRMS calcd for $\text{C}_{21}\text{H}_{20}\text{O}_5$ $[\text{M}]^+$ 352.1305, found 352.1310.

3-(8-Methoxy-2,3,5,6-tetrahydro-benzo[1,2-b;5,4-b']difuran-4-yl)-propionic acid (49) from benzyl ester 50.



A solution of **50** (220 mg, 0.624 mmol, 1 equiv) and platinum on charcoal (487 mg, 0.124 mmol, [loading: 5 wt%, charcoal], 20 mol %), in EtOH (25 mL) was hydrogenated at 40 psi in a Parr hydrogenator for 12 h. The mixture was filtered through Celite™ and concentrated yielding **49** (130 mg, 79%), which was pure by NMR (see above for spectral data).

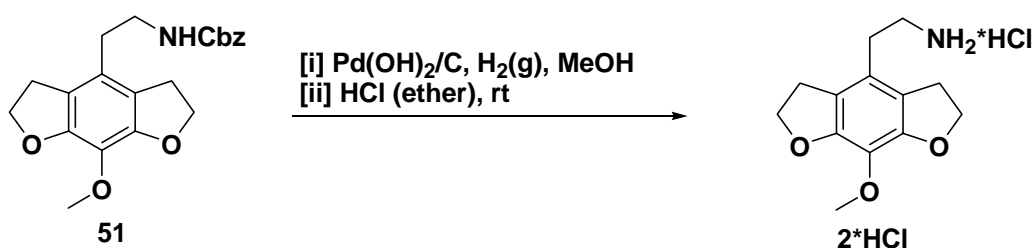
[2-(8-Methoxy-2,3,5,6-tetrahydro-benzo[1,2-b;5,4-b']difuran-4-yl)-ethyl]-carbamic acid benzyl ester (51).



A solution of **49** (100 mg, 0.378 mmol, 1 equiv), diphenyl phosphoryl azide (100 μL , 0.454 mmol, 1.2 equiv), and triethylamine (52.7 μL , 0.378 mmol, 1 equiv) in toluene (3 mL) was stirred at rt for 30 min and then heated at reflux for 30 min. Benzyl alcohol (47.0 μL , 0.454 mmol, 1.2

equiv) was added and the reaction was heated at reflux for 18 h. The organic layer was washed with 5% aqueous citric acid, water, saturated aqueous NaHCO₃, brine, dried with anhydrous Na₂SO₃, filtered, and concentrated. The crude mixture was purified by flash chromatography using 40% EtOAc/hexanes as eluant yielding **51** (90 mg, 65%) as a colourless oil. *R*_f = 0.22 on silica gel (40% EtOAc/hexanes). IR (neat) 3354, 2933, 1720, 1508, 1428, 1246 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.35 (m, 5H), 5.10 (s, 2H), 4.86 (brs, 1NH), 4.55 (t, 4H, *J* = 8.6 Hz), 3.92 (s, 3H), 3.34 (dd, 2H, *J* = 13.4, 6.8 Hz), 3.03 (t, 4H, *J* = 8.6 Hz), 2.65 (t, 2H, *J* = 7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 156.5, 150.8, 136.7, 128.7, 128.6, 128.4, 124.5, 119.6, 72.7, 66.8, 60.5, 40.4, 31.8, 28.8; HRMS calcd for C₂₁H₂₃NO₅ [M]⁺ 369.1577, found 369.1576.

2-(8-Methoxy-2,3,5,6-tetrahydro-benzo[1,2-b;5,4-b']difuran-4-yl)-ethylamine (2•HCl).



A solution of **51** (80.0 mg, 0.217 mmol, 1 equiv) and palladium hydroxide on carbon (30.4 mg, 0.0435 mmol, [loading: 20 wt%, support carbon wet], 20 mol%), in MeOH (10 mL) was hydrogenated at 40 psi in a Parr hydrogenator for 12 h. The mixture was filtered through Celite™ and concentrated. The crude solid was dissolved in MeOH (0.5 mL) and HCl (1 M in ether, 5 mL) was added. The solution was stirred at rt for 2 h and filtration of the precipitate provided pure **2•HCl** (56 mg, 94%) as a white solid, mp = 275-278 °C (recrystallized in ether). IR (neat) 2893, 2359, 1608, 1505, 1428, 1337 cm⁻¹; ¹H NMR (400 MHz, CD₃OD) δ 4.60 (t, 4H, *J* = 8.6 Hz), 3.82 (s, 3H), 3.13 (t, 4H, *J* = 8.6 Hz), 3.06 (dd, 2H, *J* = 8.6, 5.8 Hz), 2.83 (dd, 2H, *J* = 8.6,

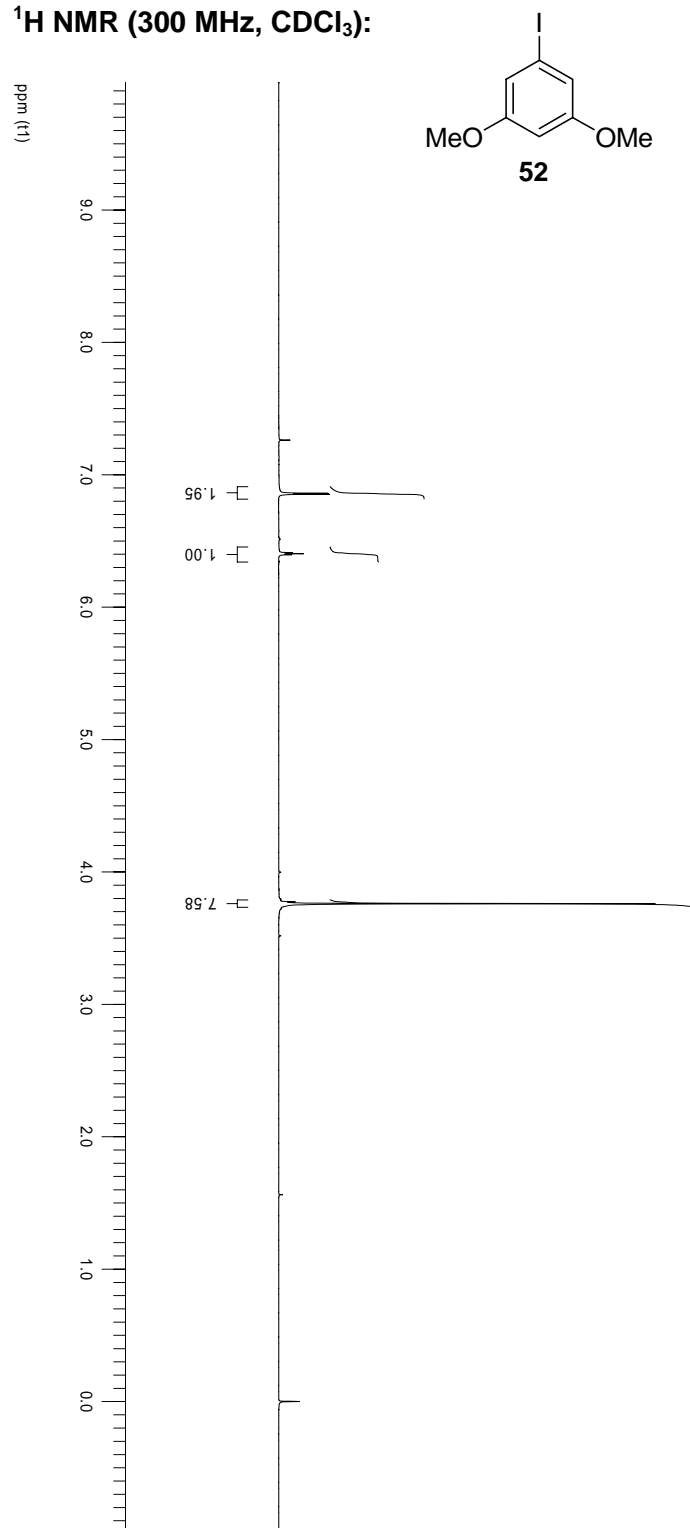
5.9 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 152.5, 130.3, 123.7, 121.1, 73.8, 60.7, 39.9, 30.2, 29.5;
HRMS calcd for $\text{C}_{13}\text{H}_{18}\text{ClNO}_3$ $[\text{M}-\text{HCl}]^+$ 235.1217, found 235.1208.

References

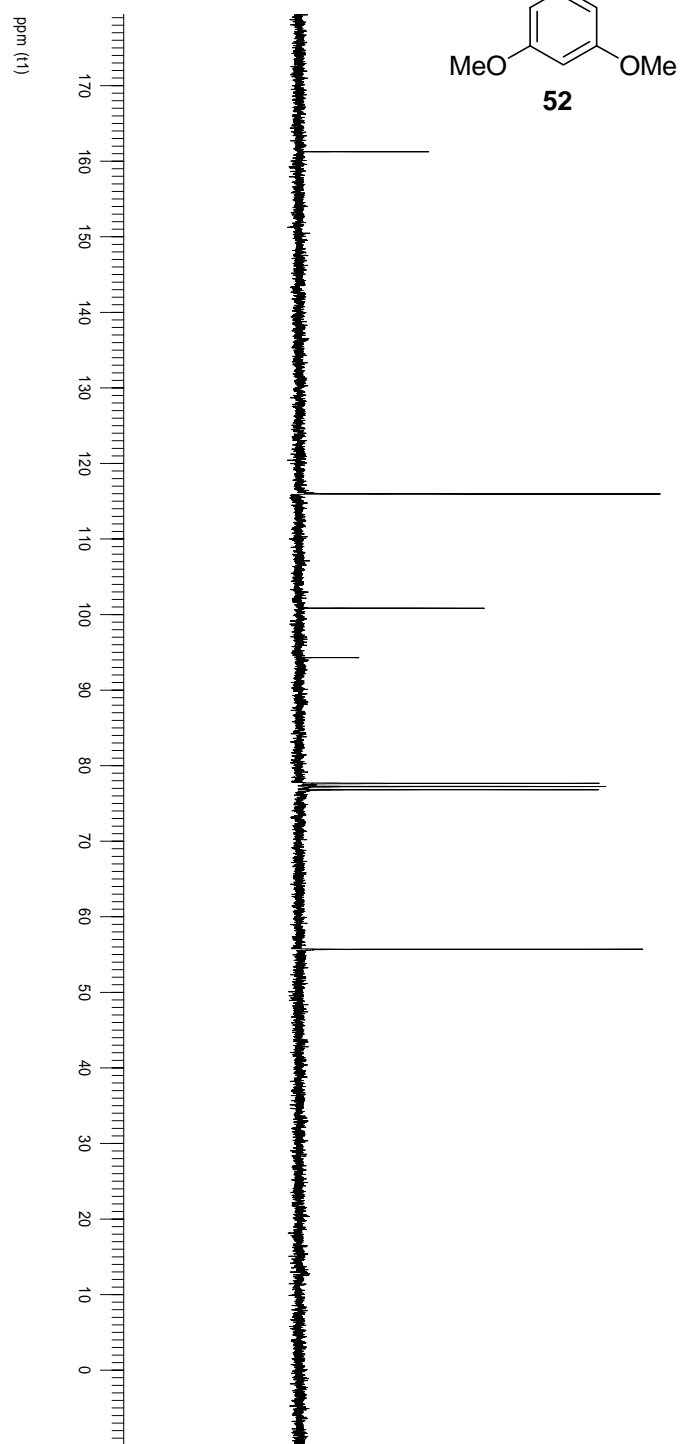
1. Prepared according to the literature procedure; Dol, C. C.; Kamer, C. J.; van Leeuwen, P. W. N. M. *Eur. J. Org. Chem.* **1998**, 359.

NMR Spectra

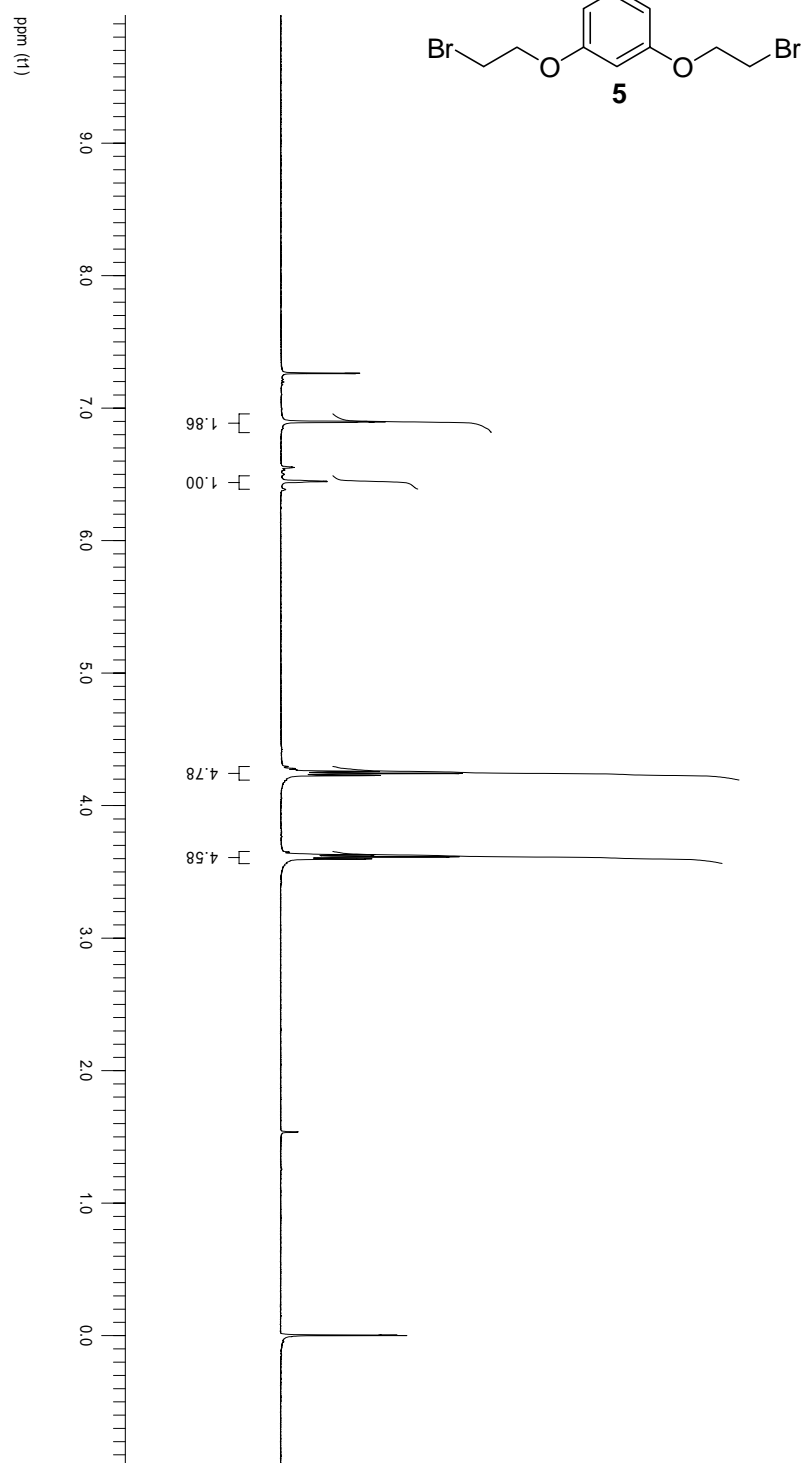
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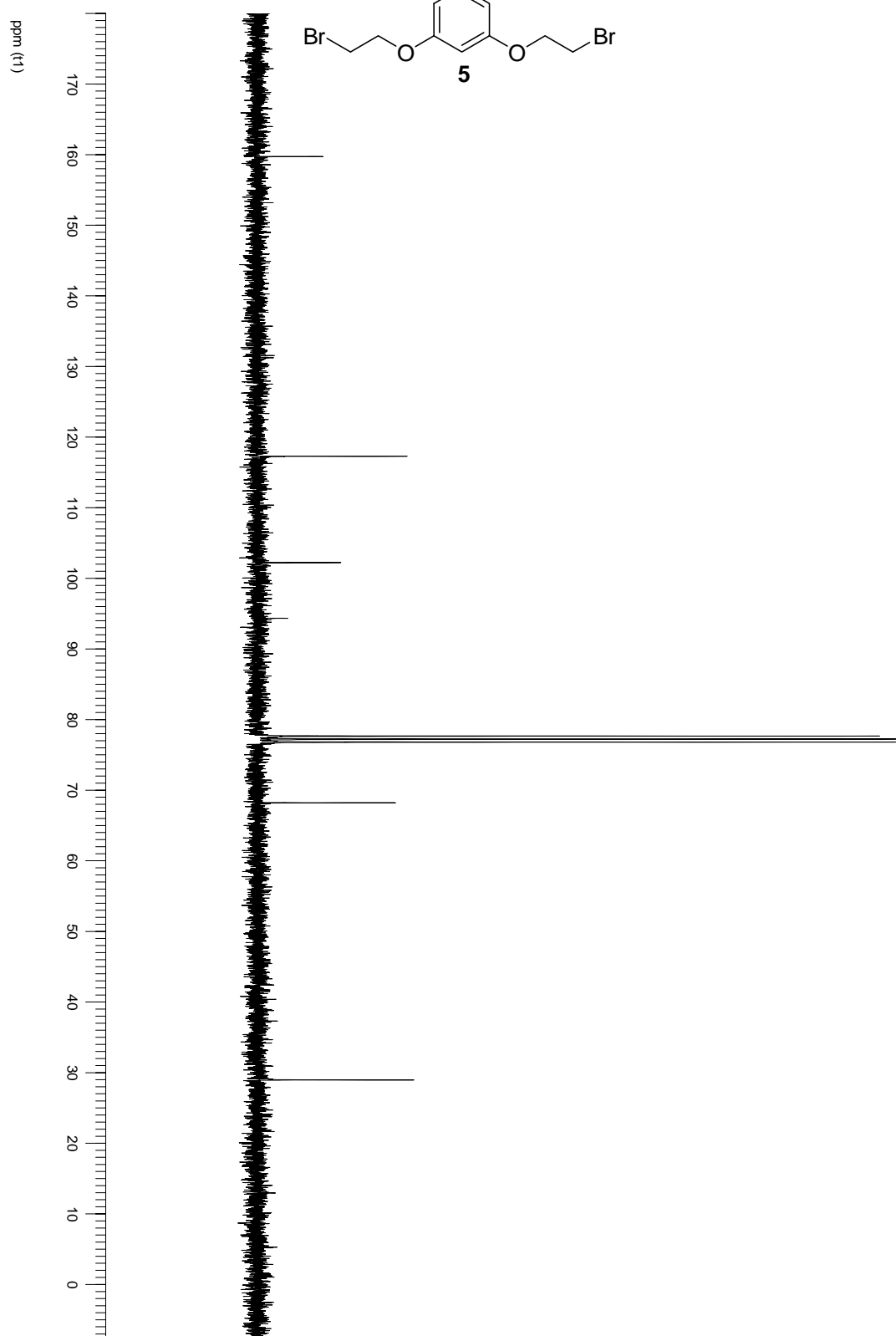
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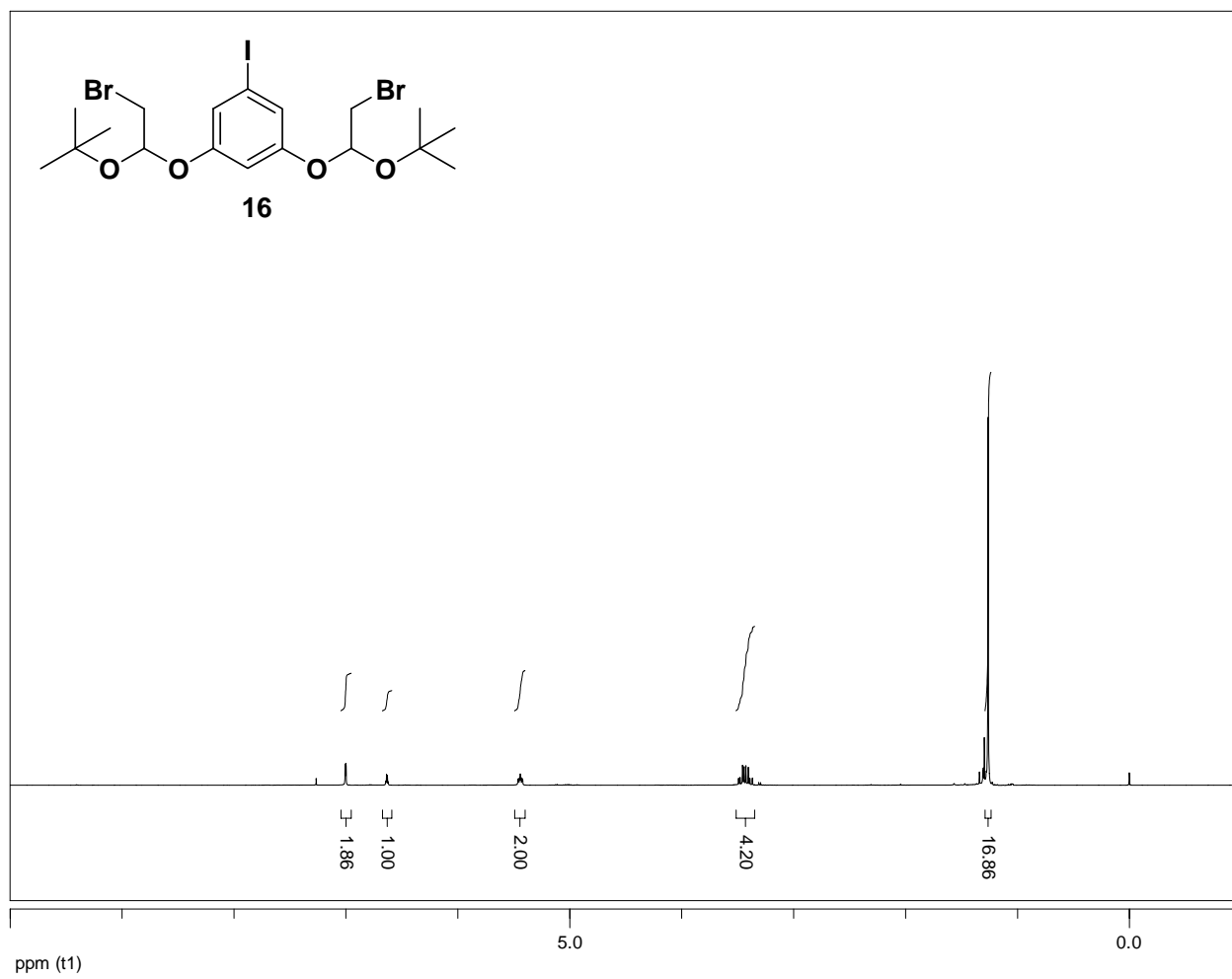
ppm (t1)



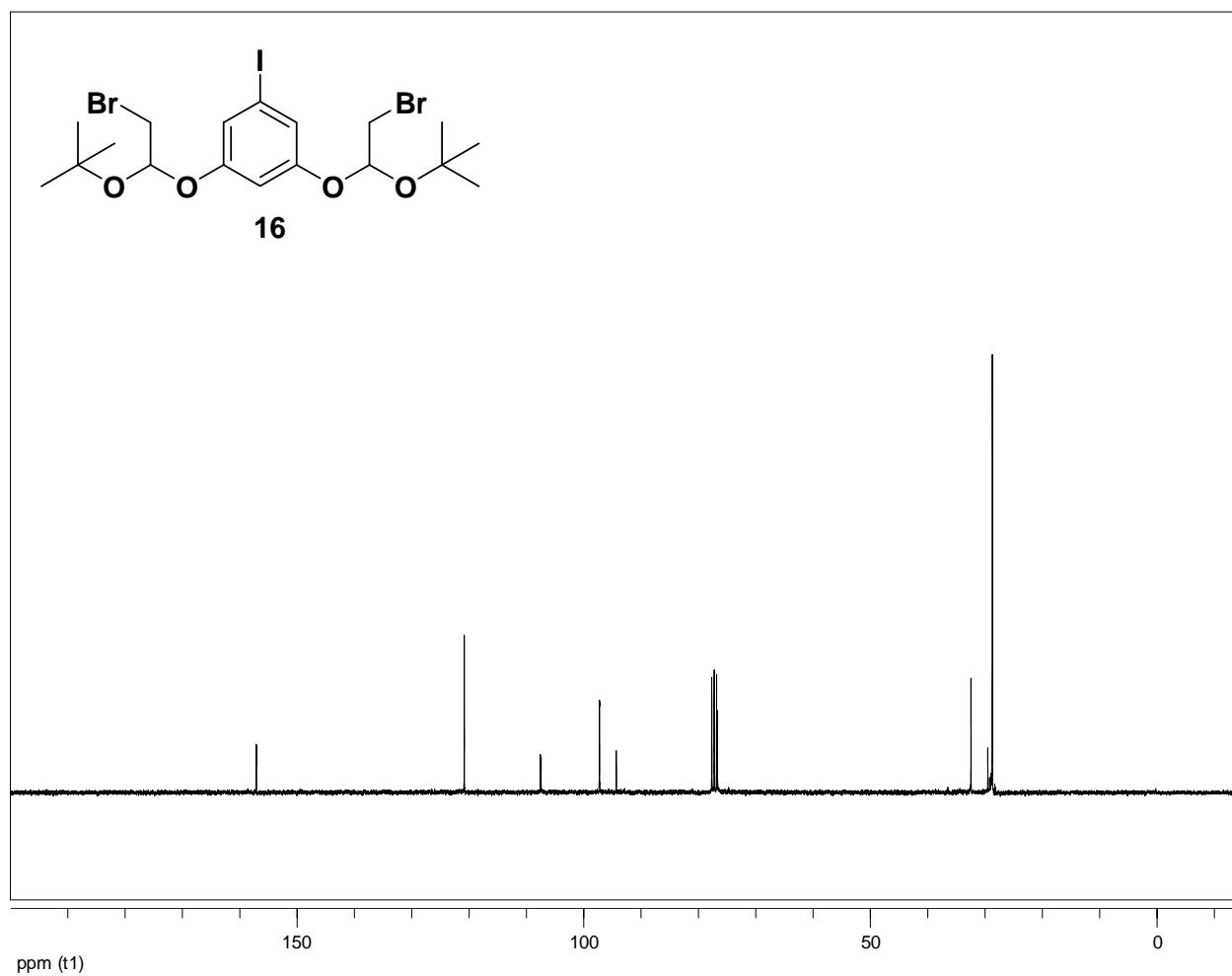
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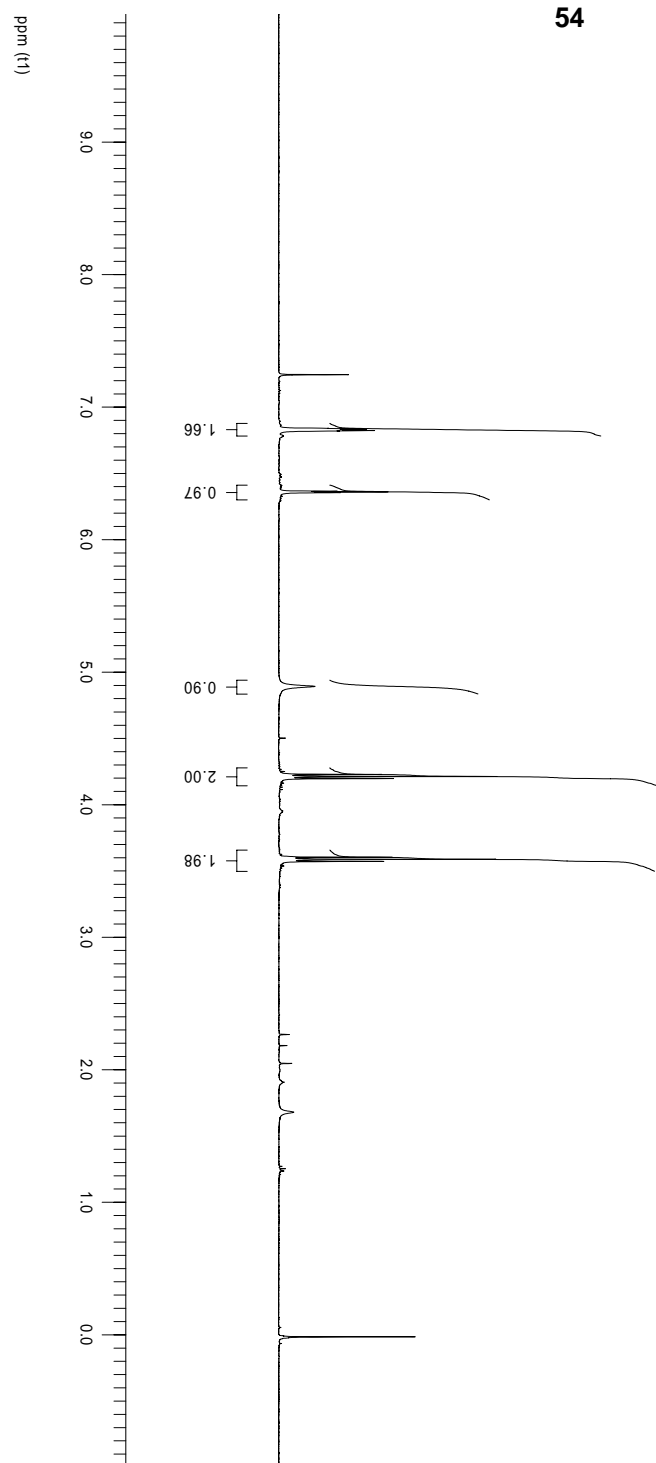
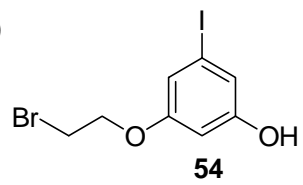
¹H NMR (300 MHz, CDCl₃)



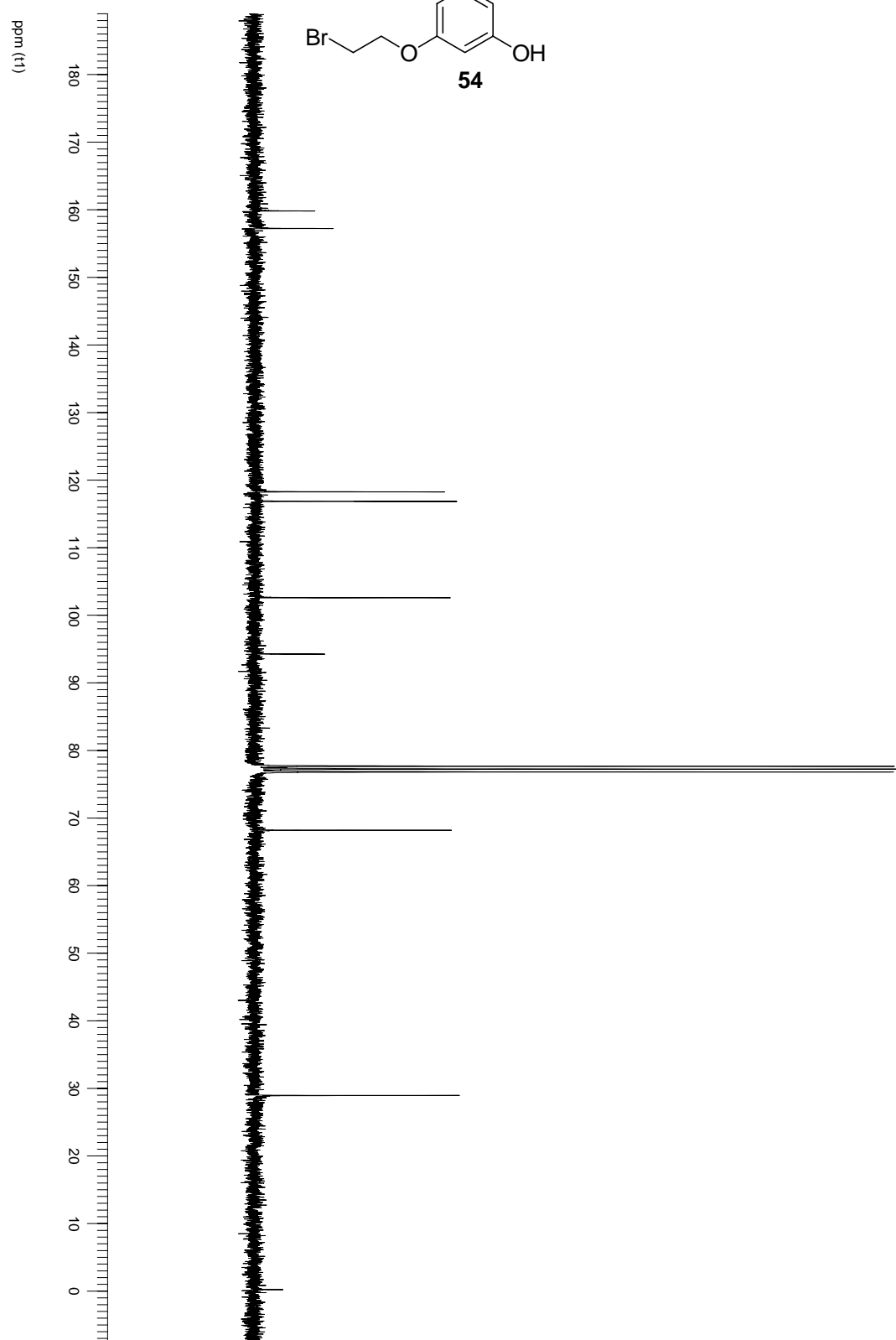
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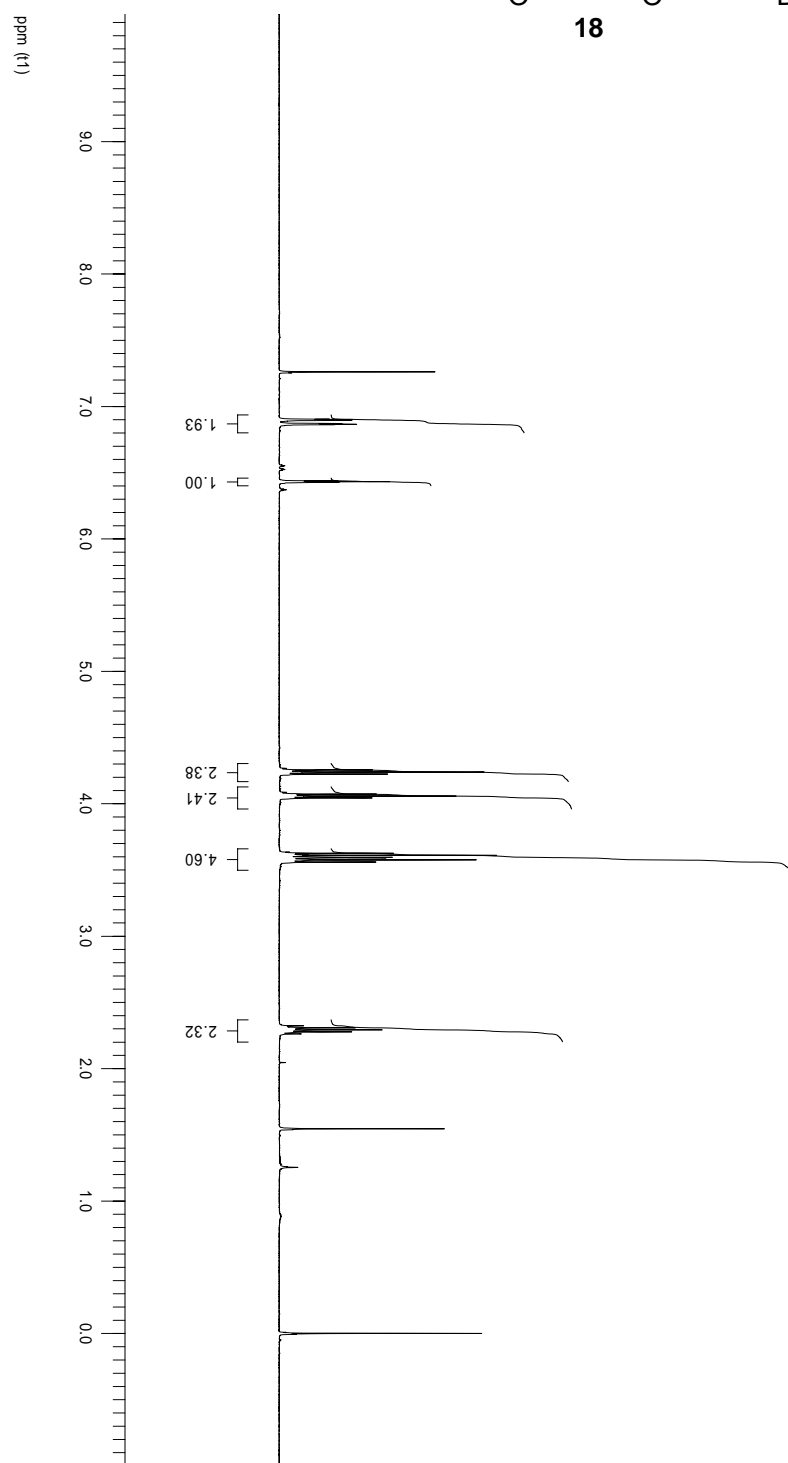
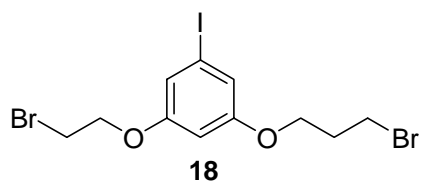
^1H NMR (300 MHz, CDCl_3)



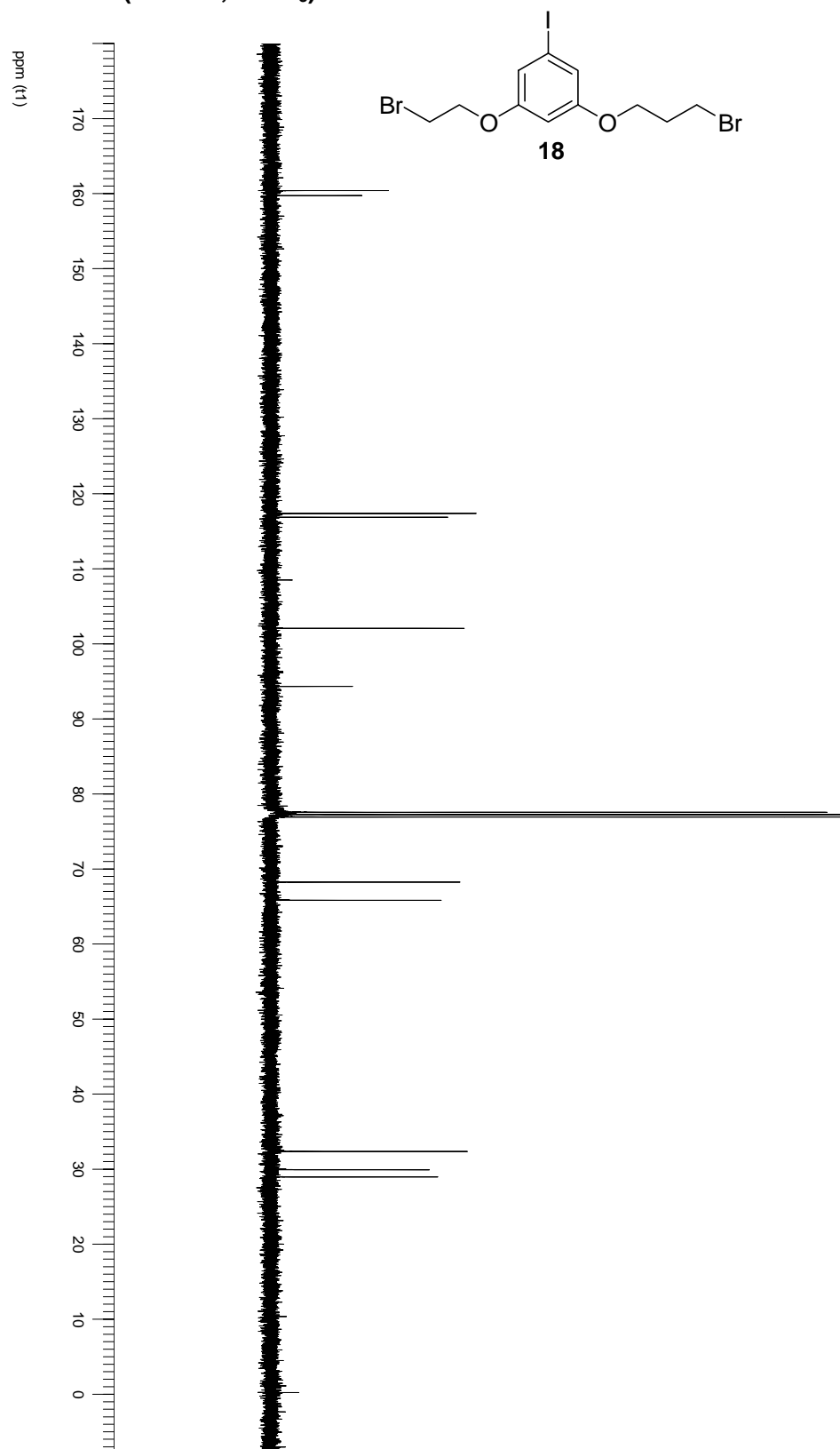
^{13}C NMR (75 MHz, CDCl_3)



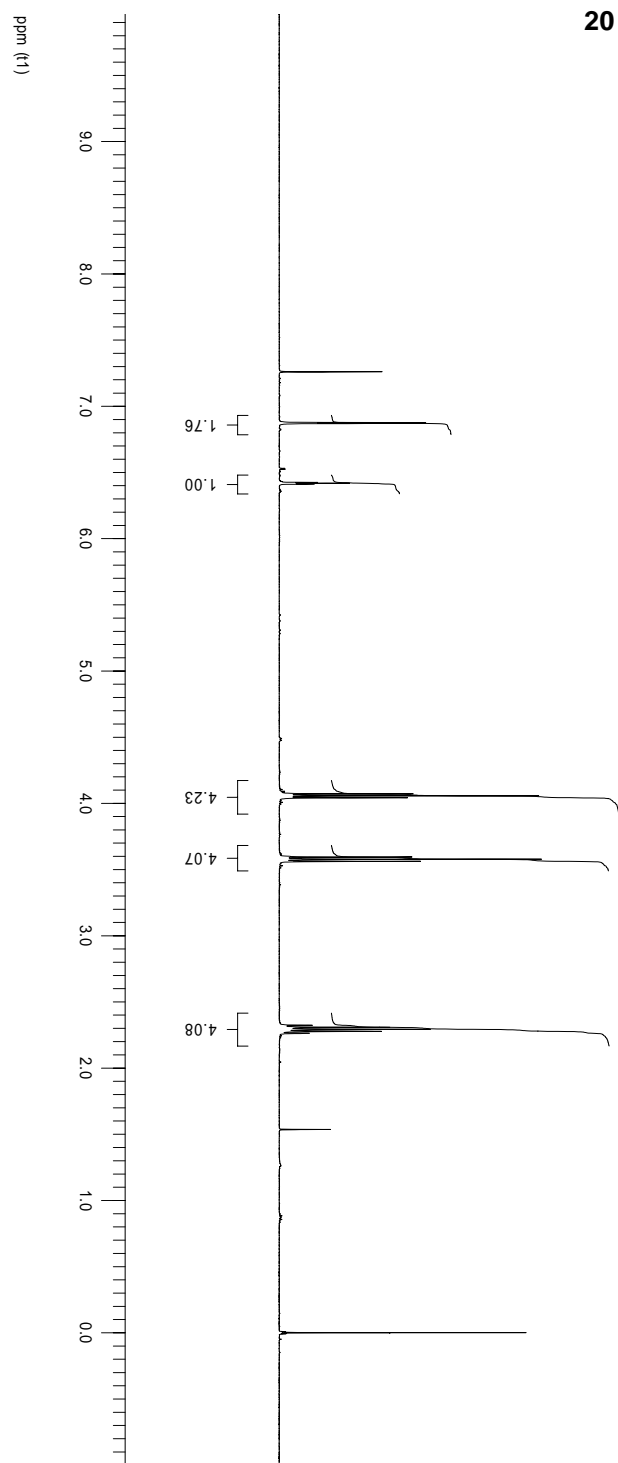
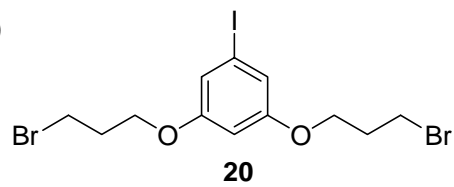
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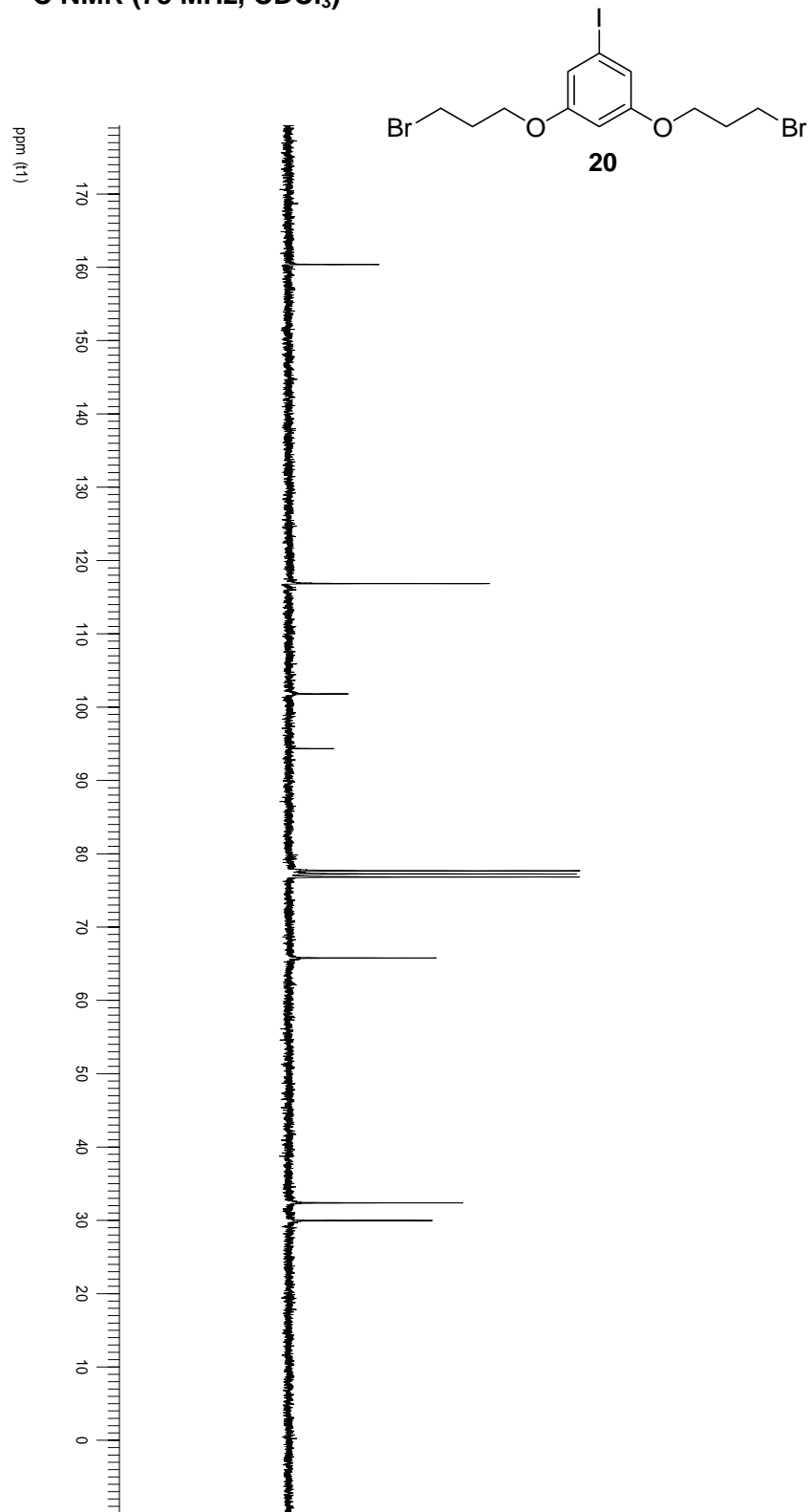
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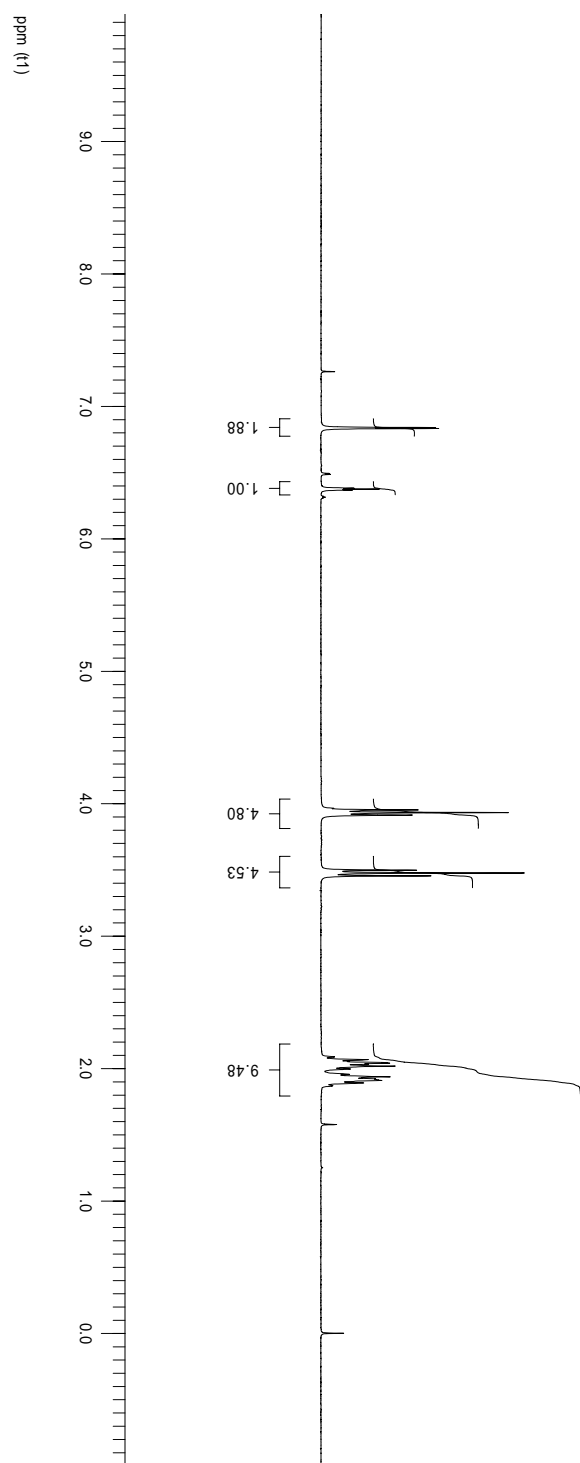
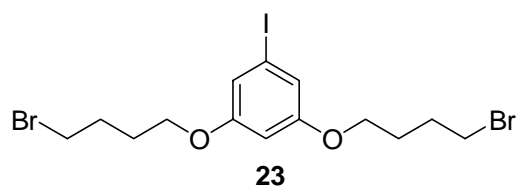
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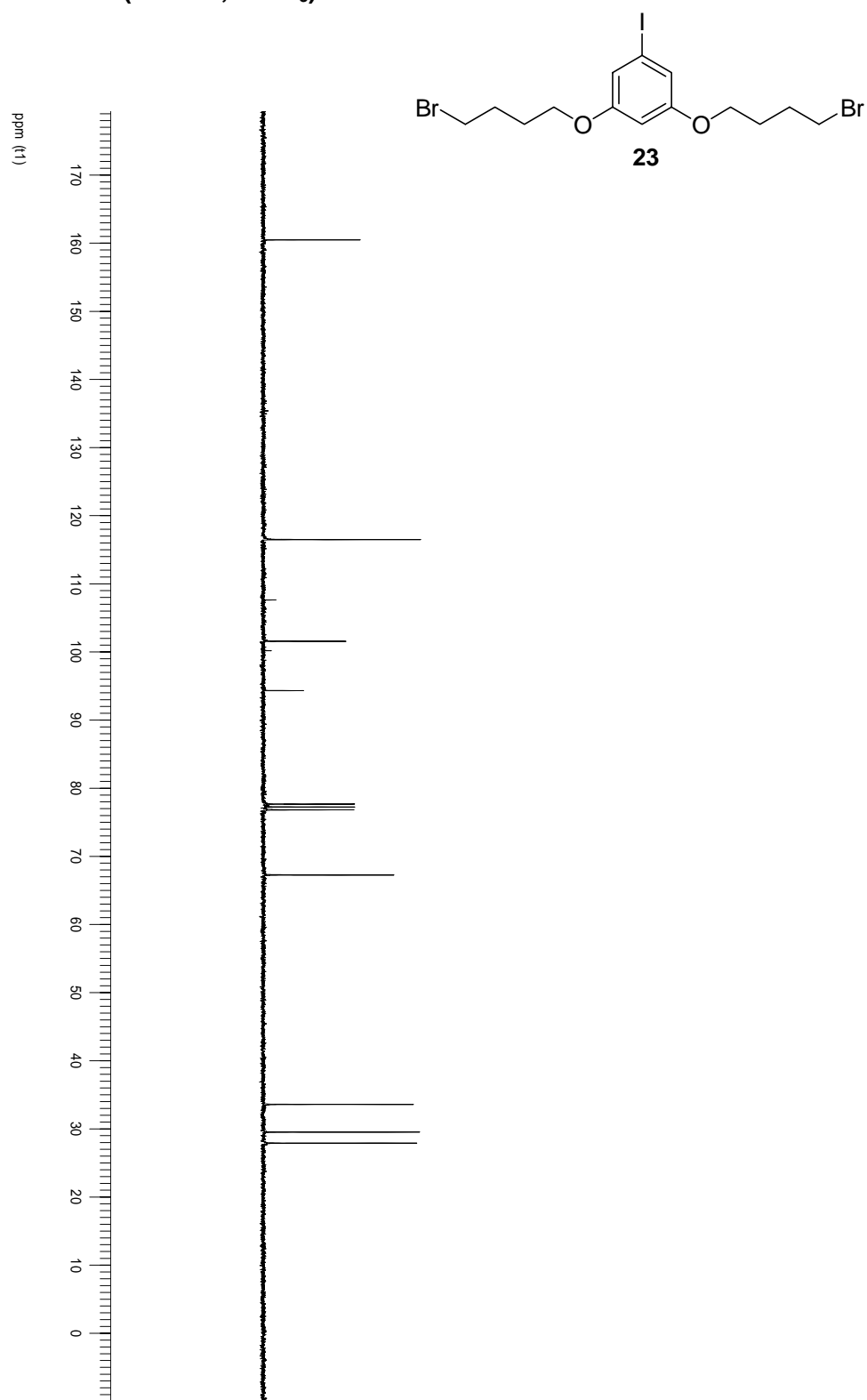
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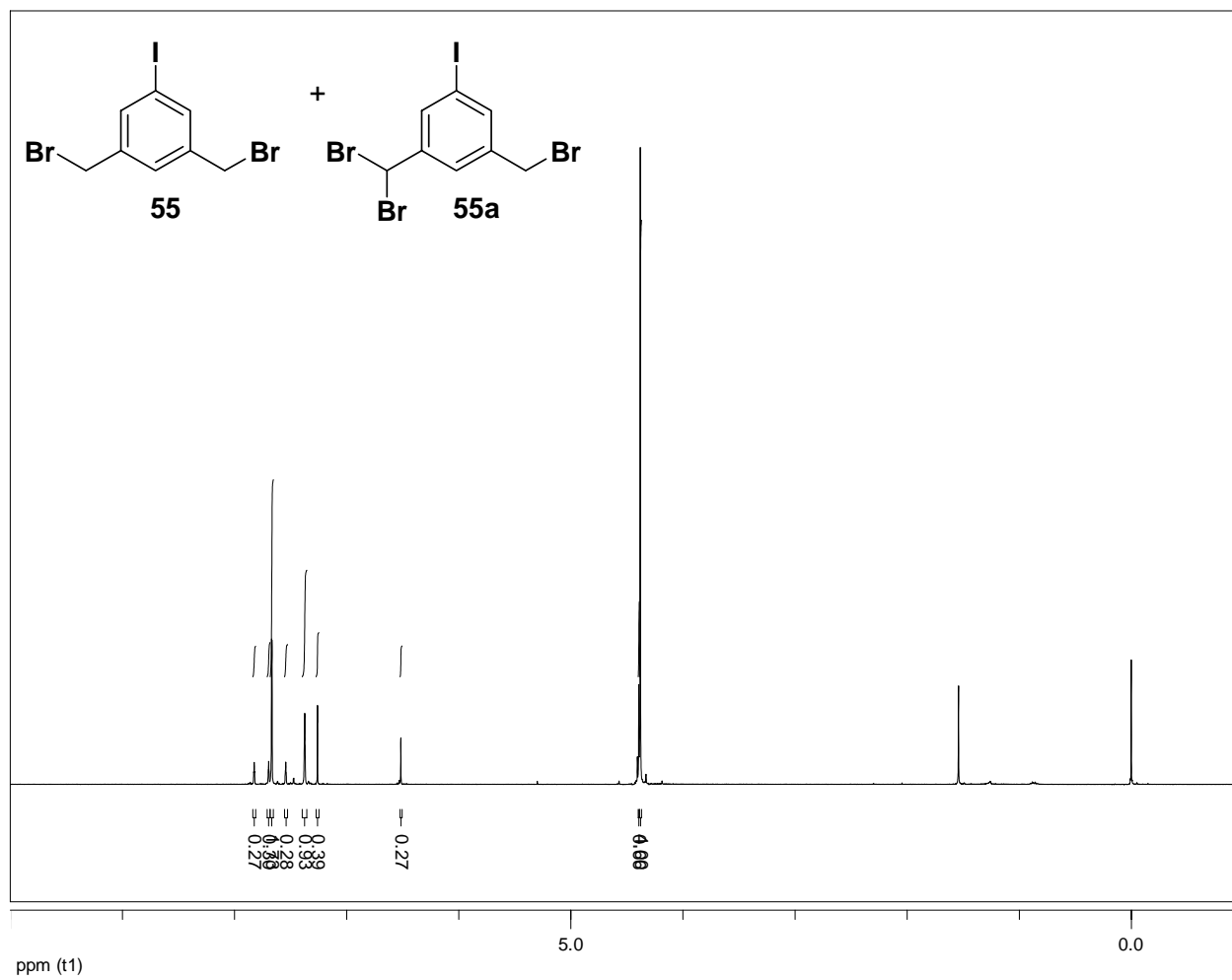
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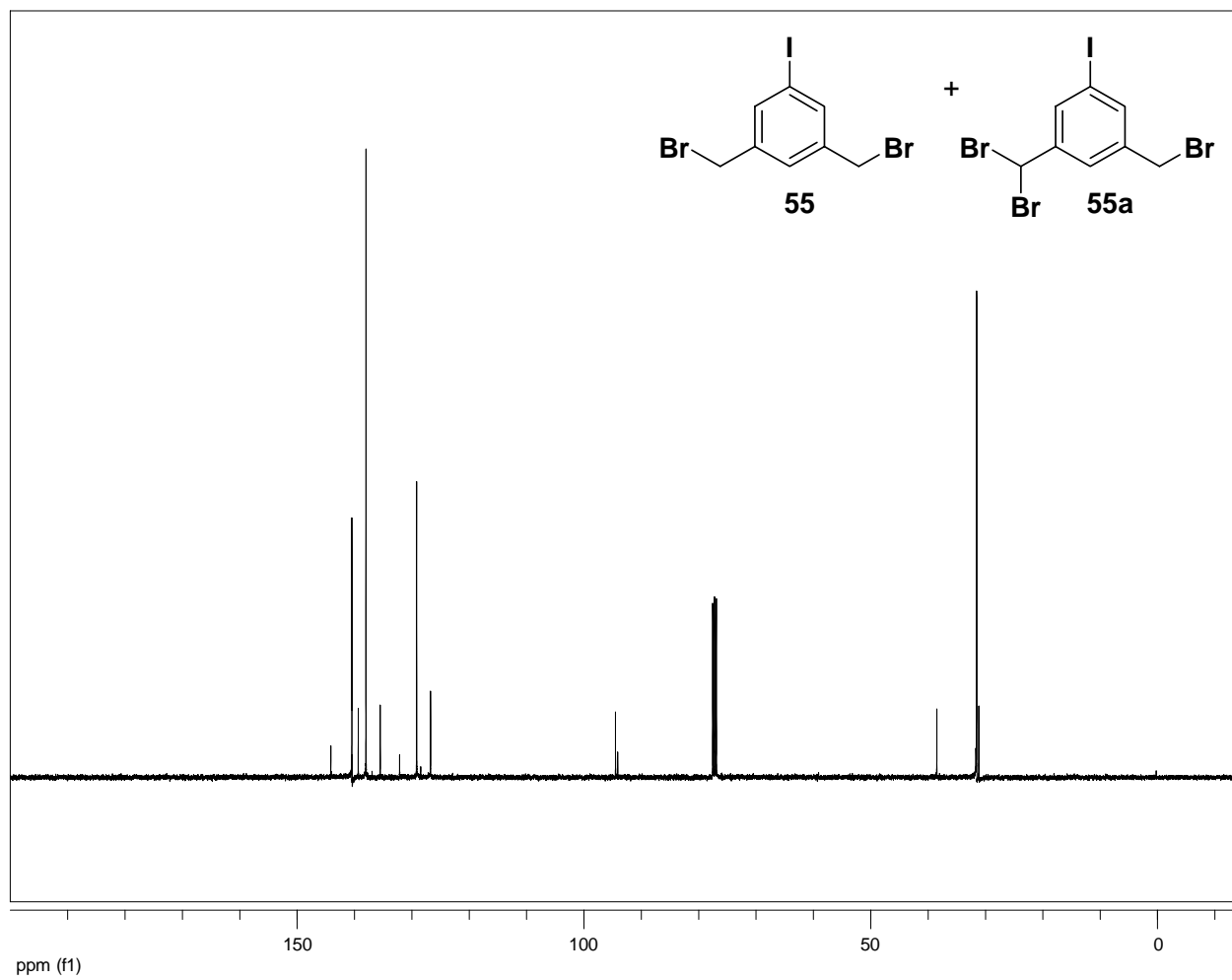
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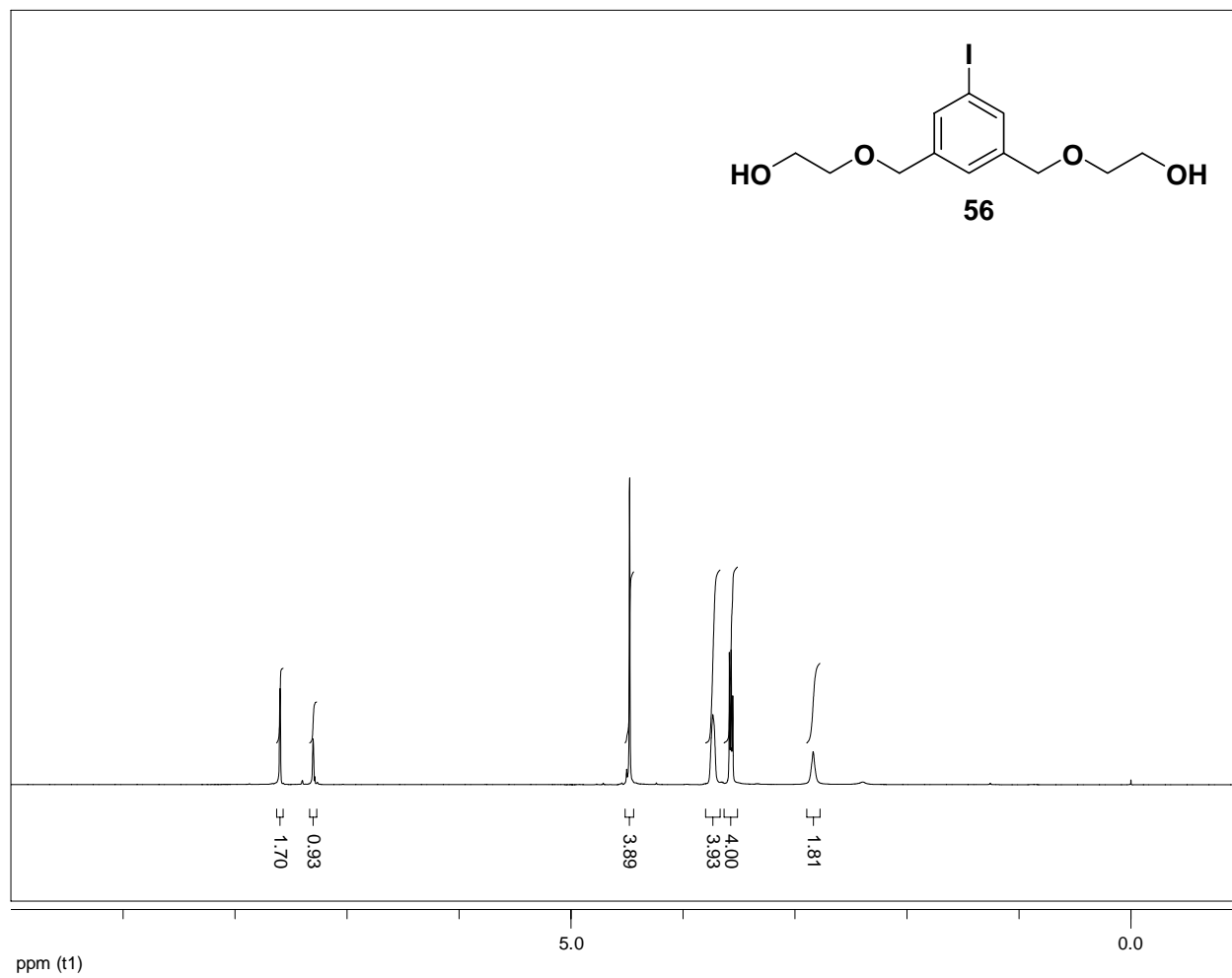
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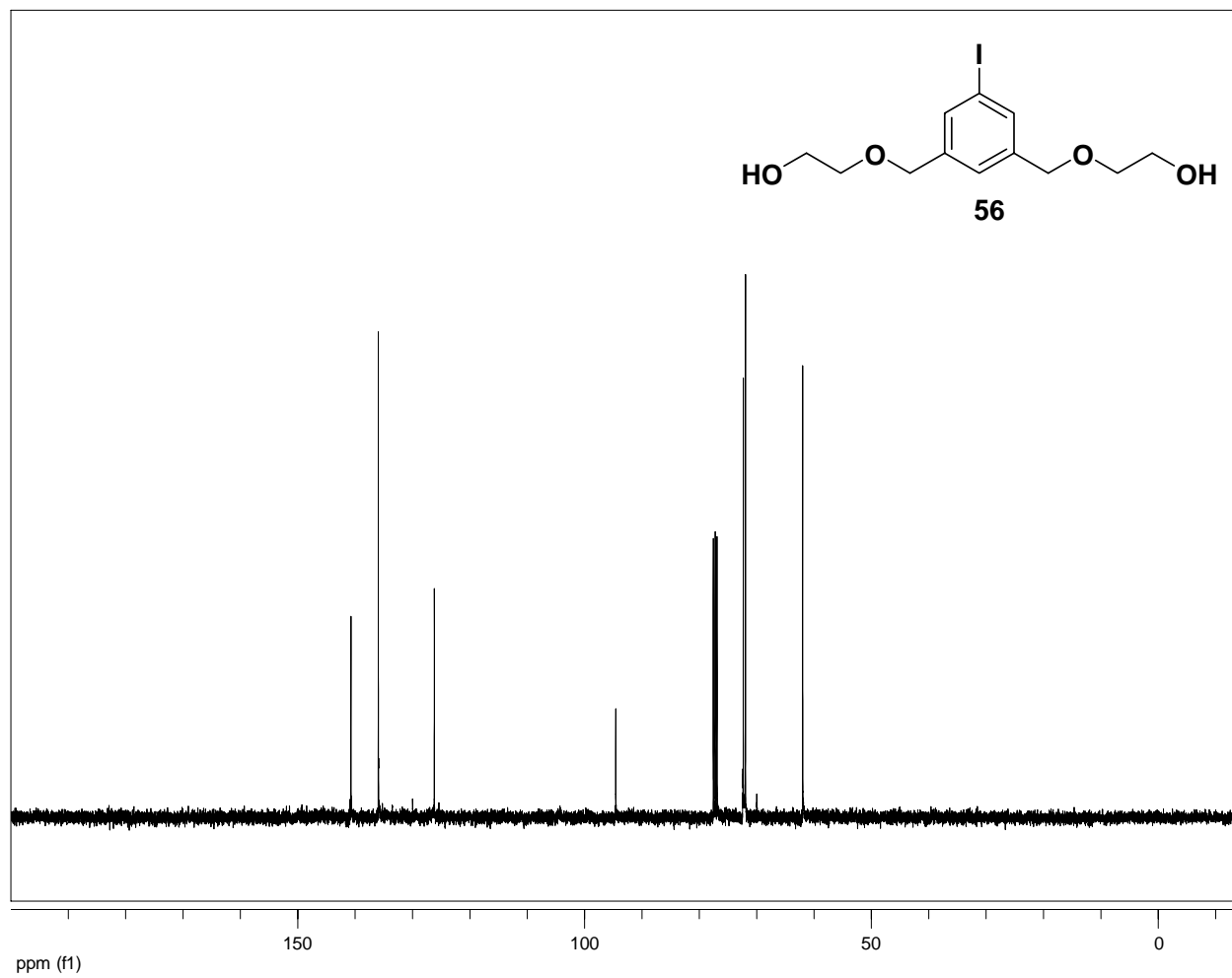
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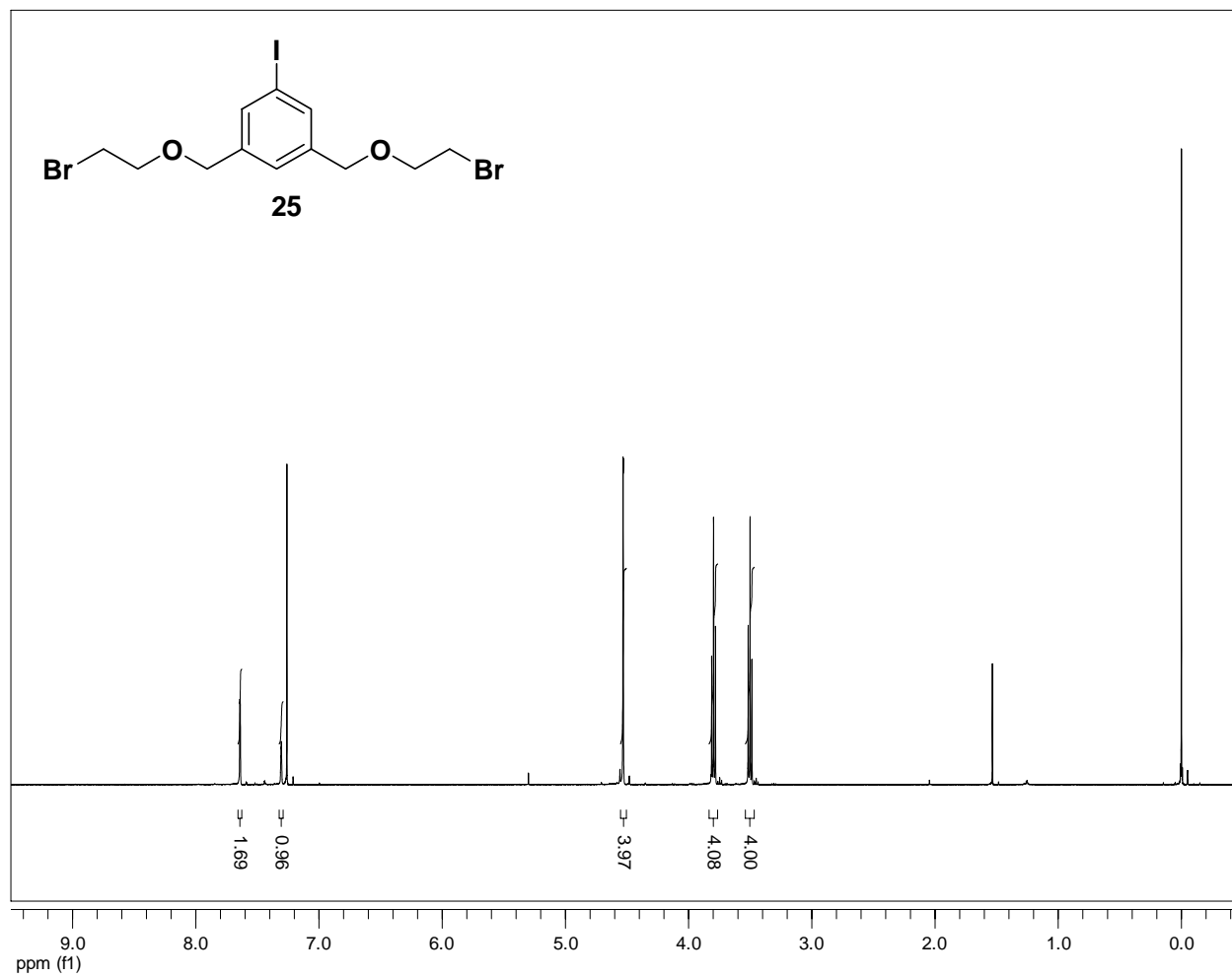
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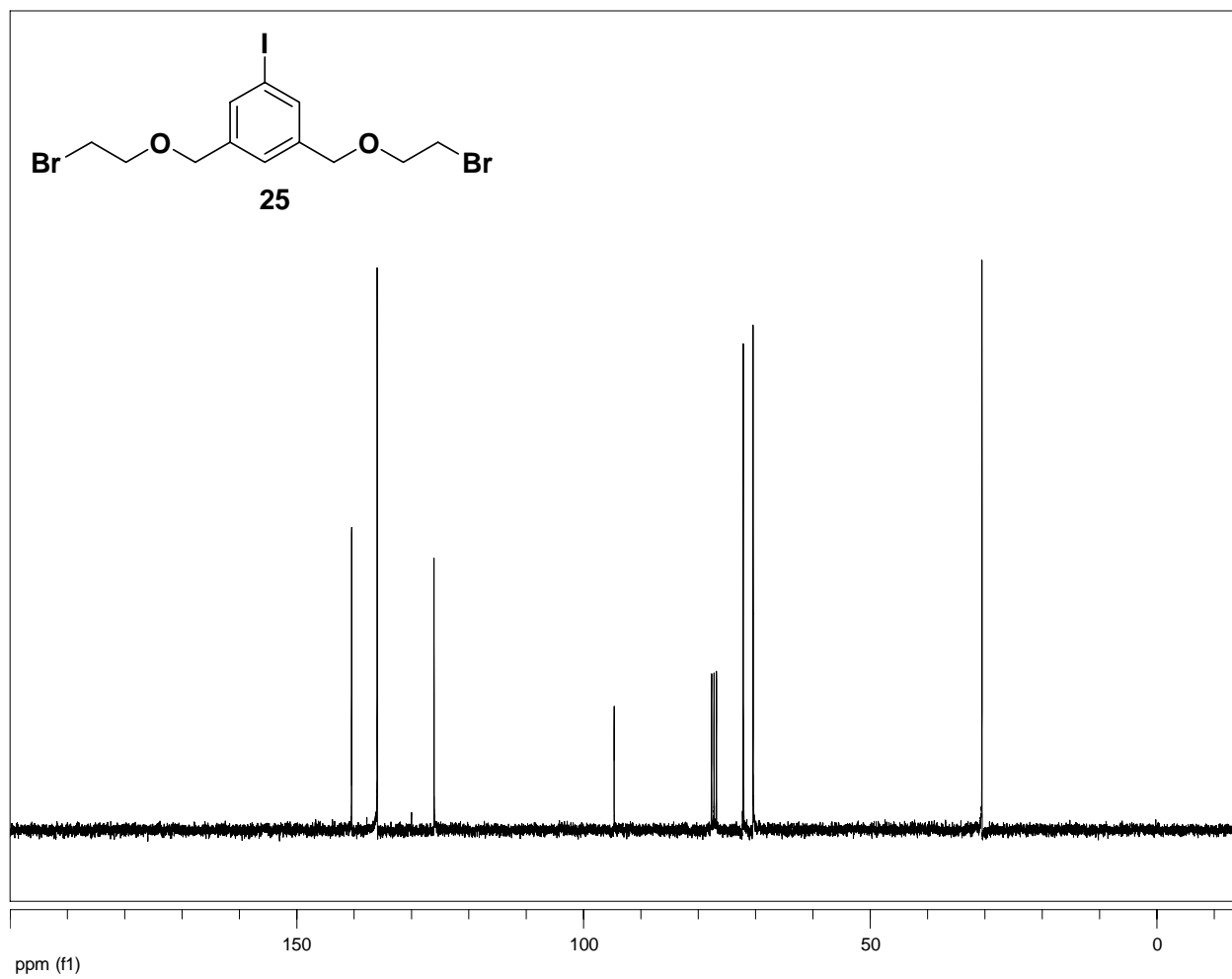
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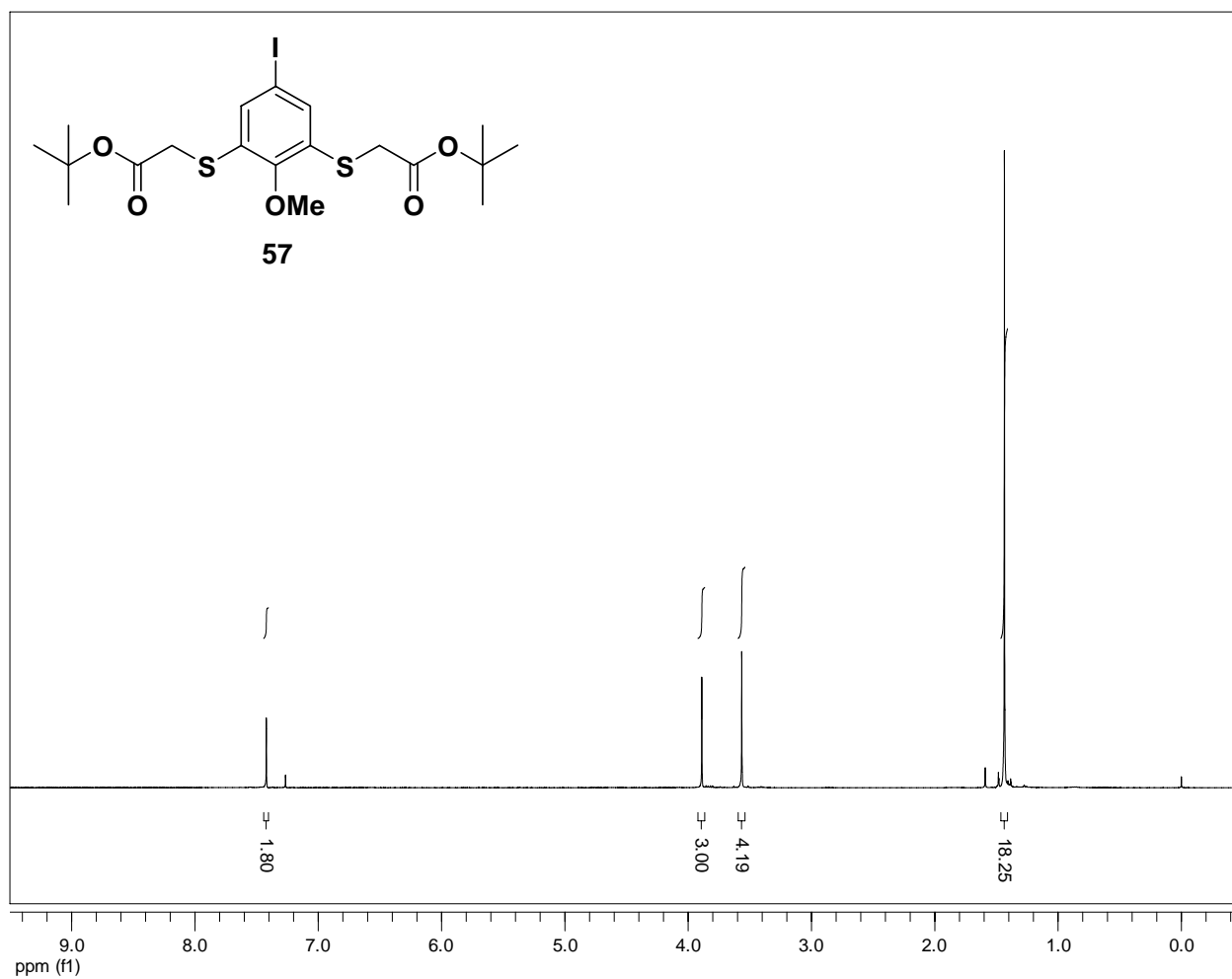
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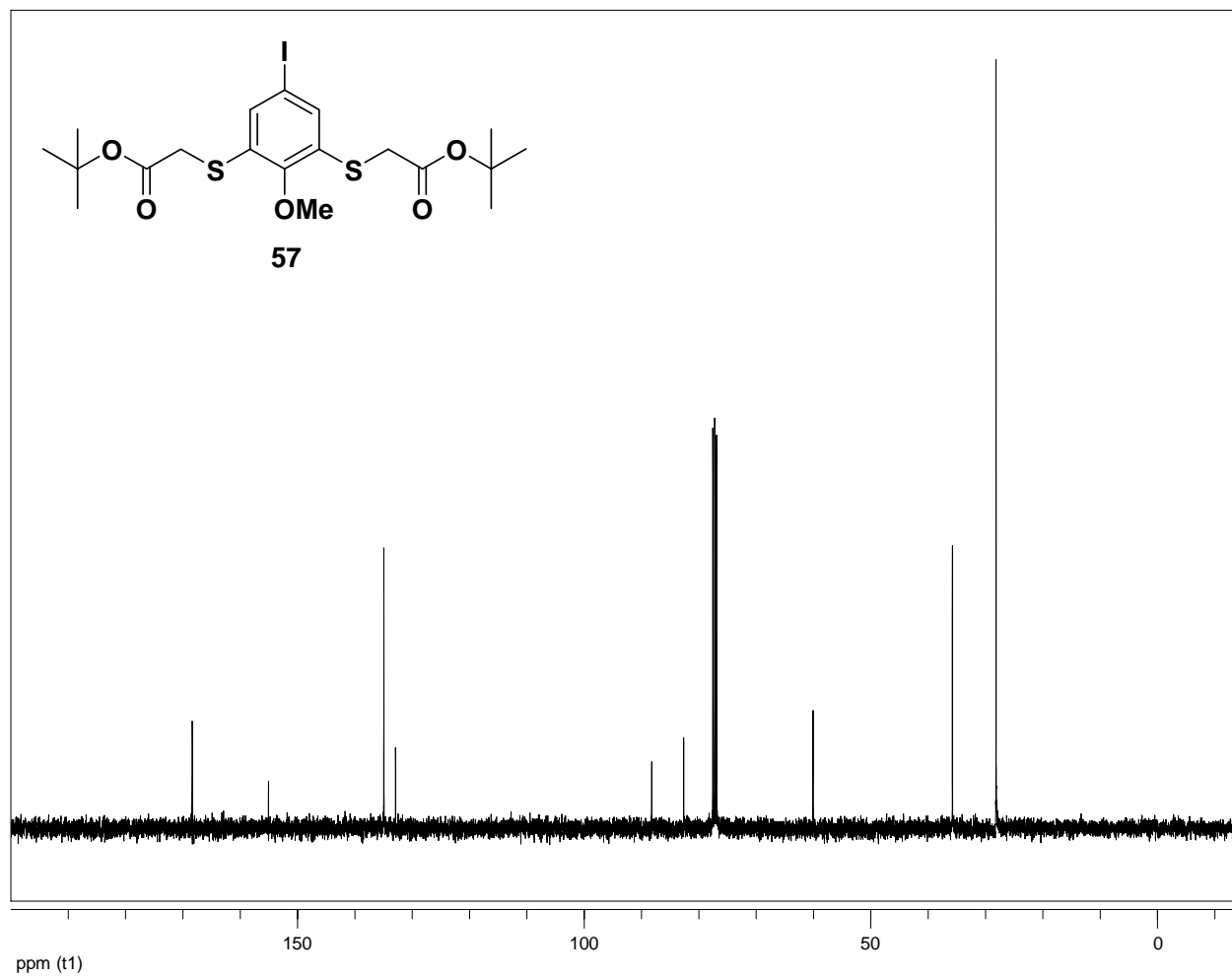
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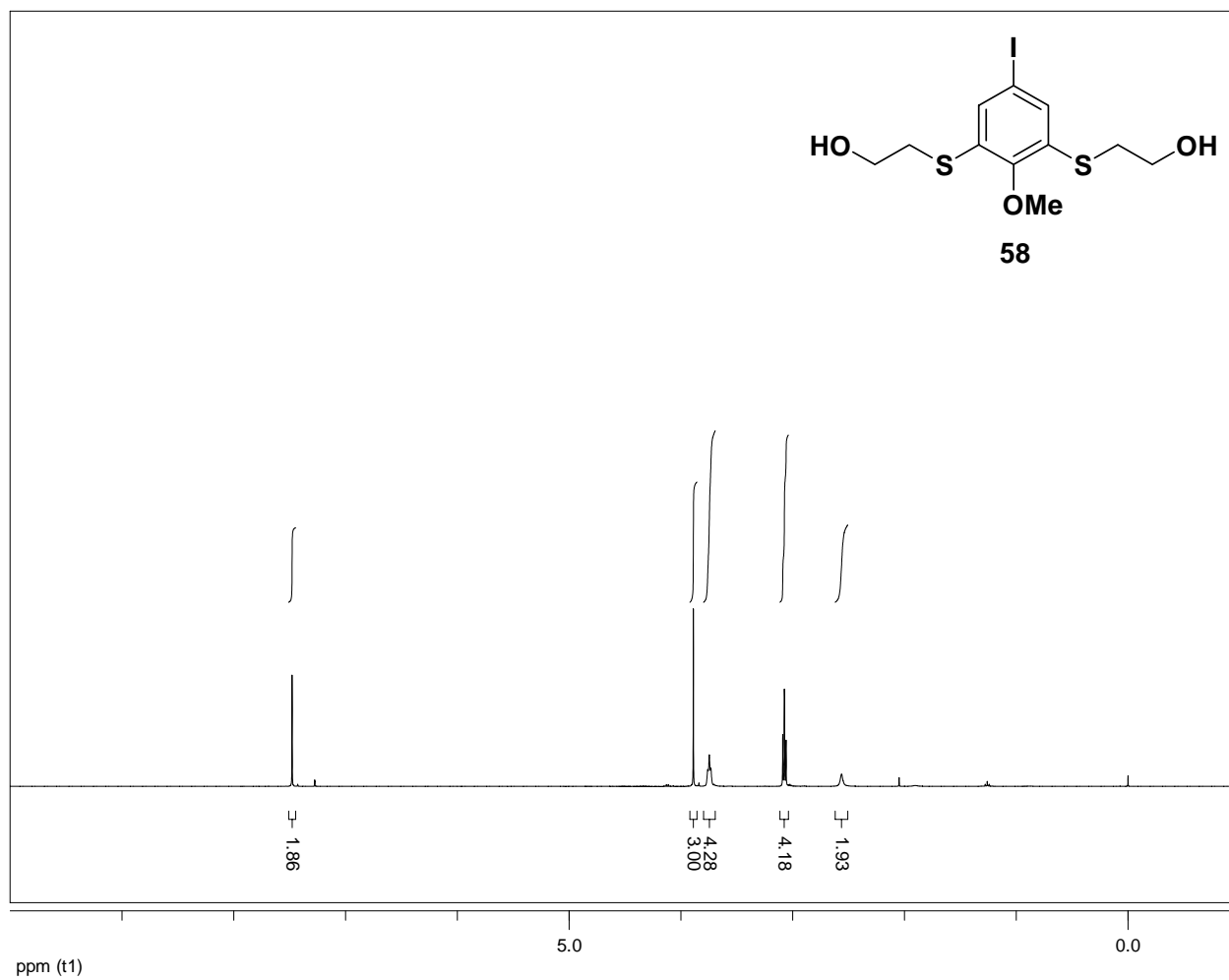
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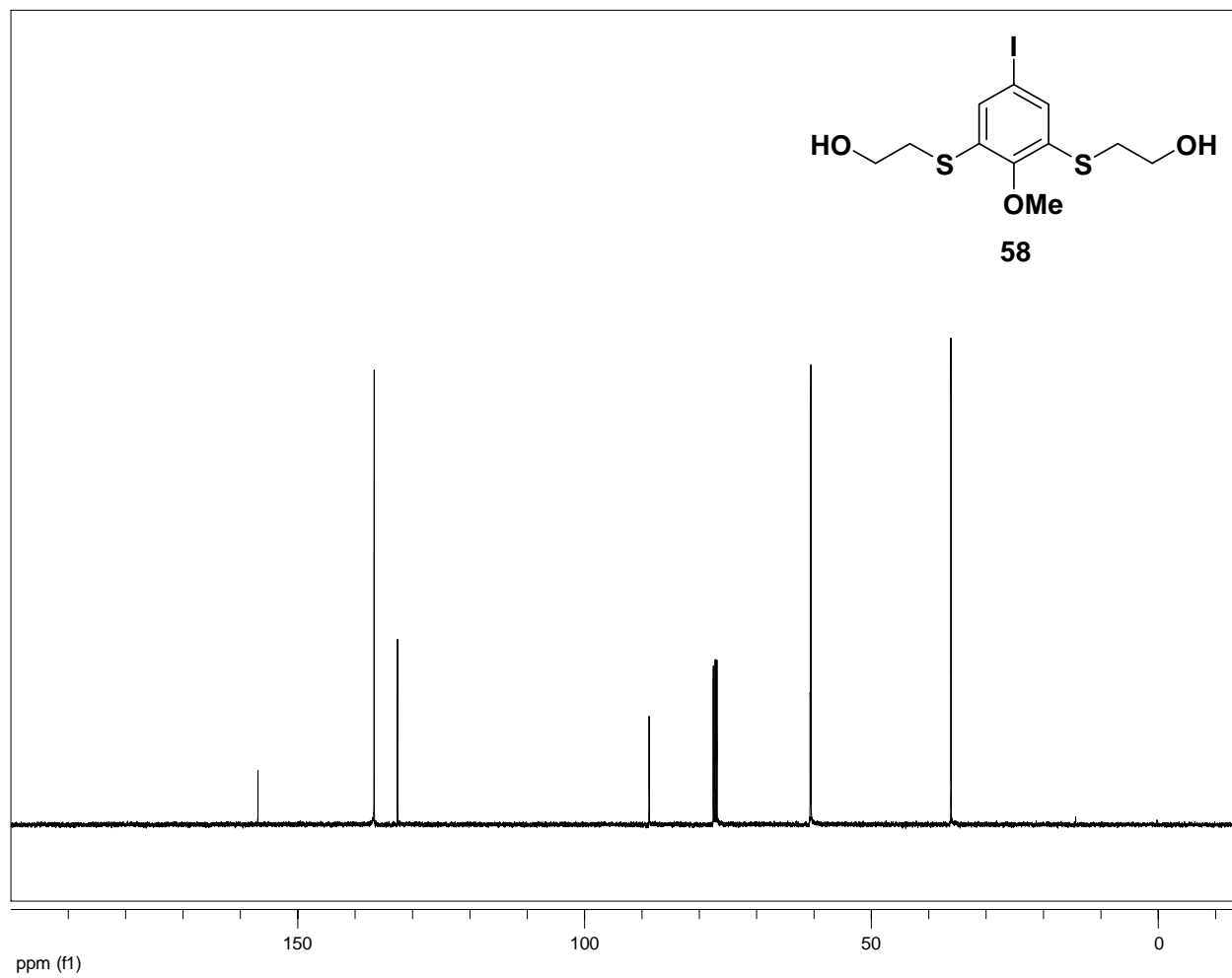
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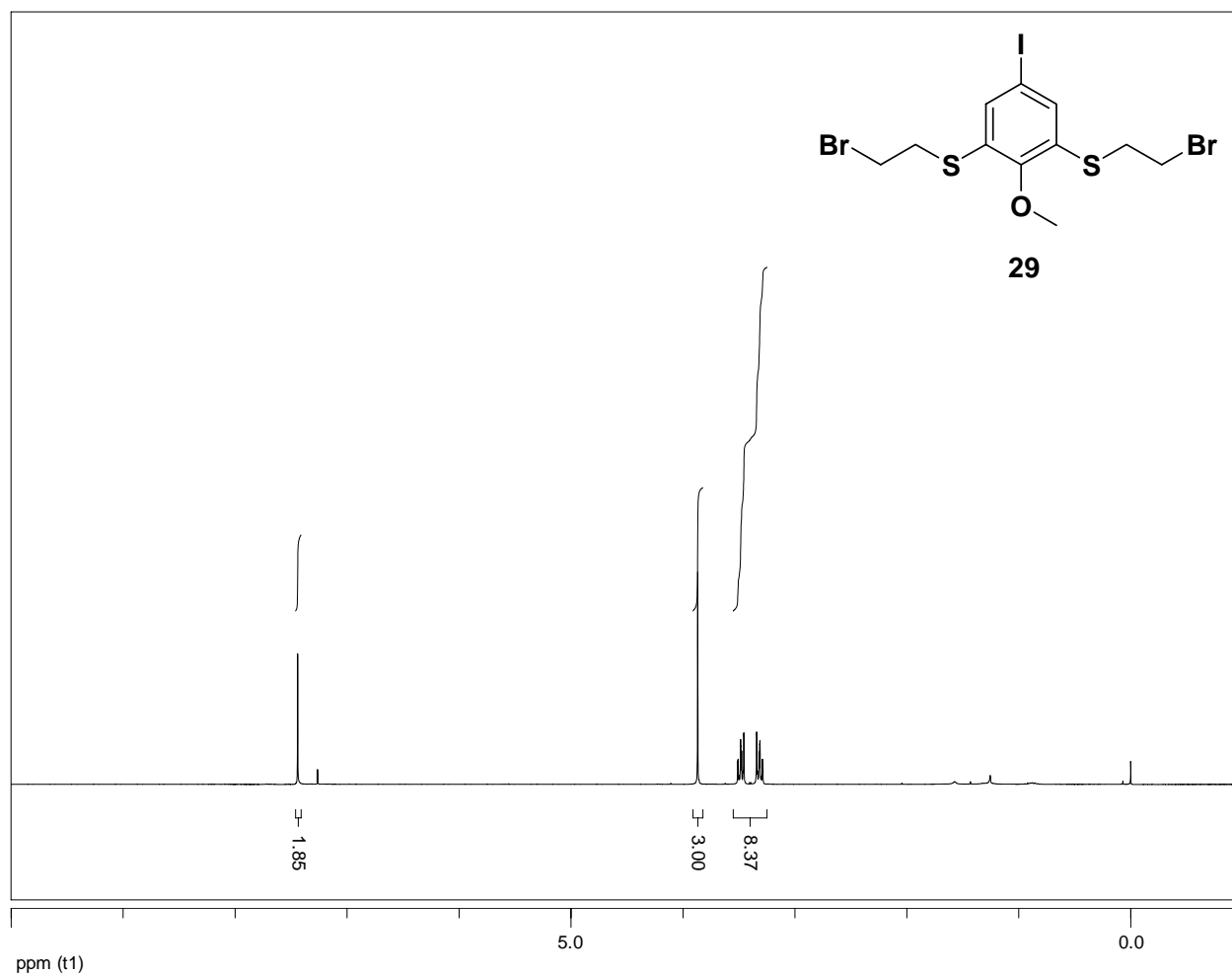
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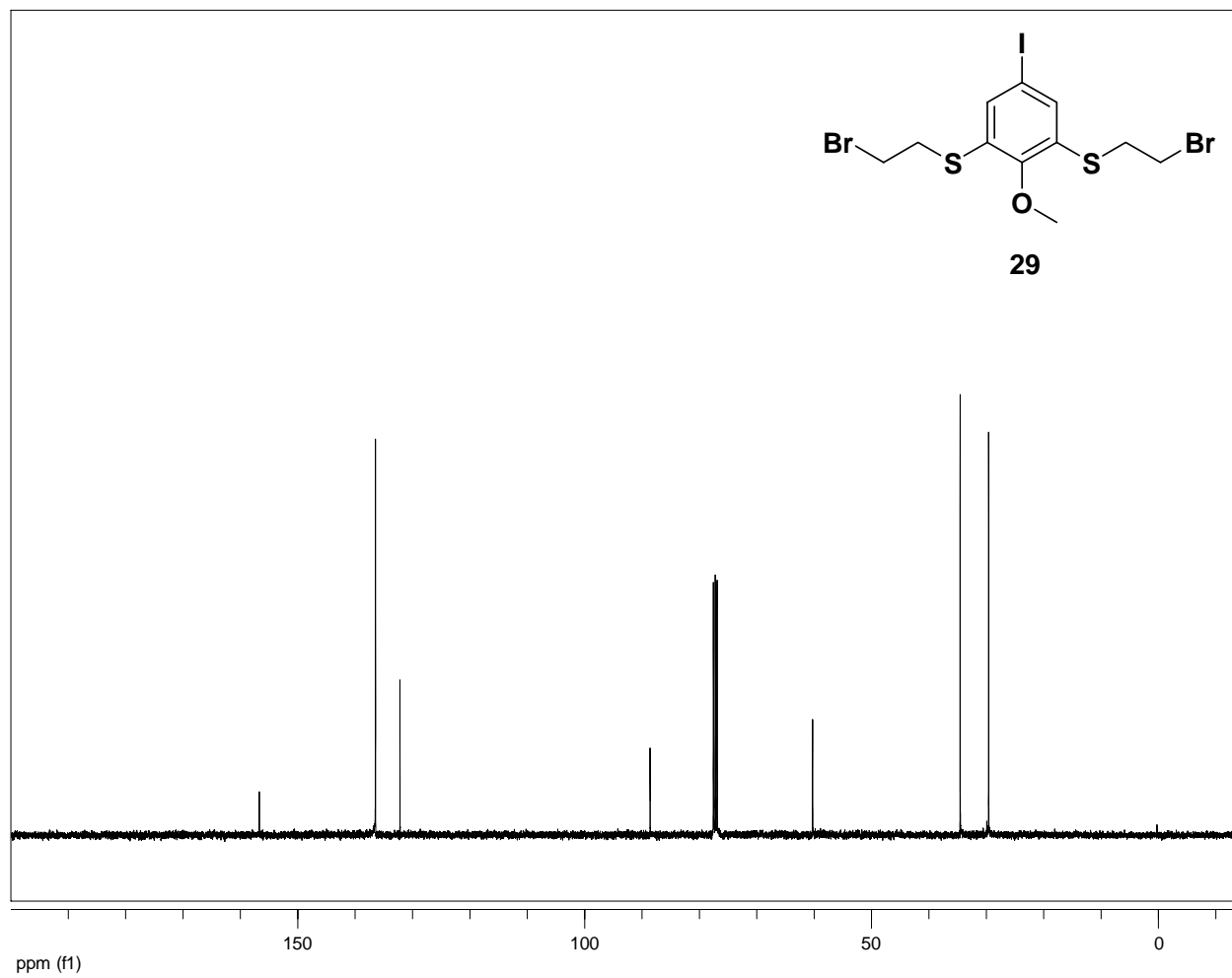
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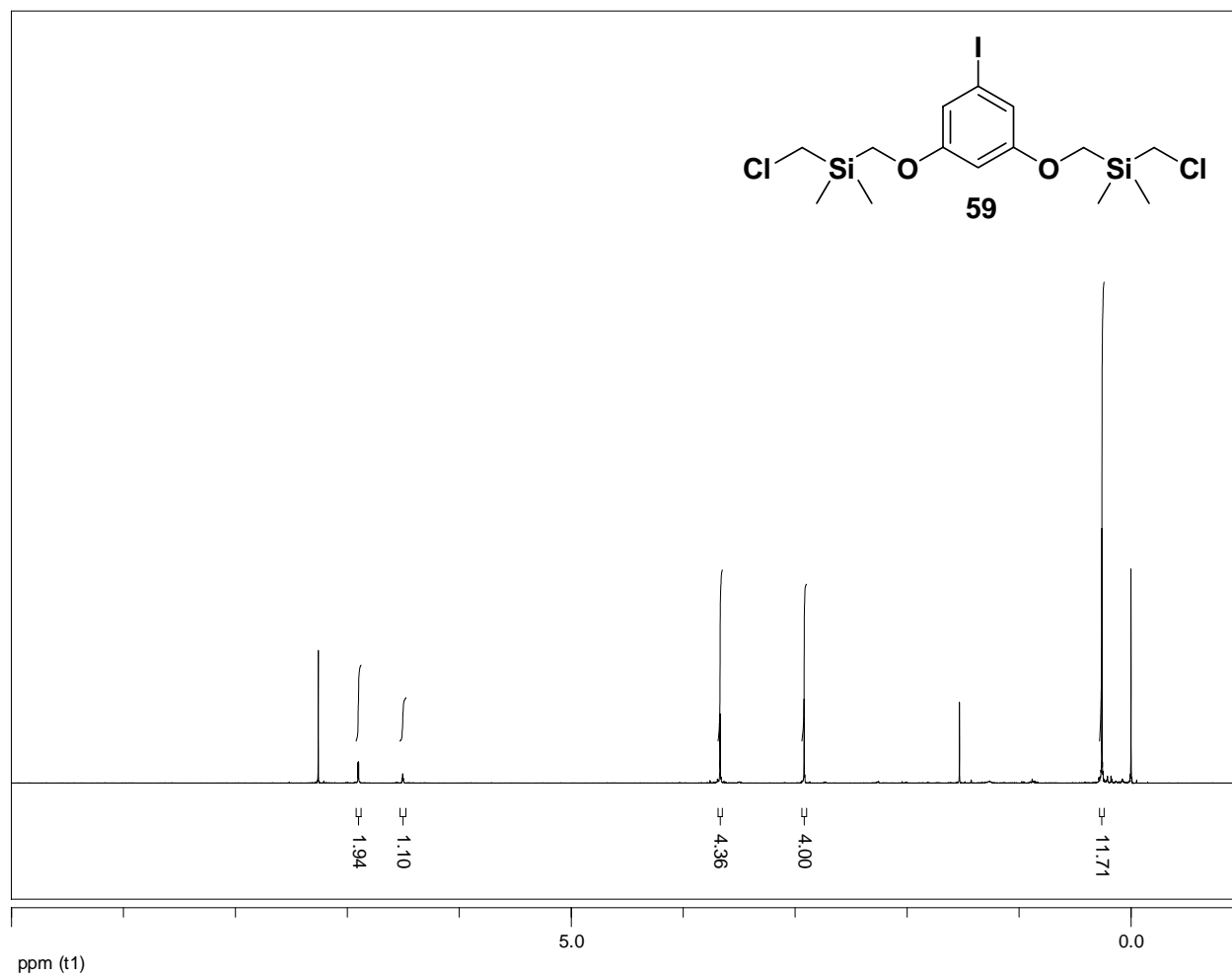
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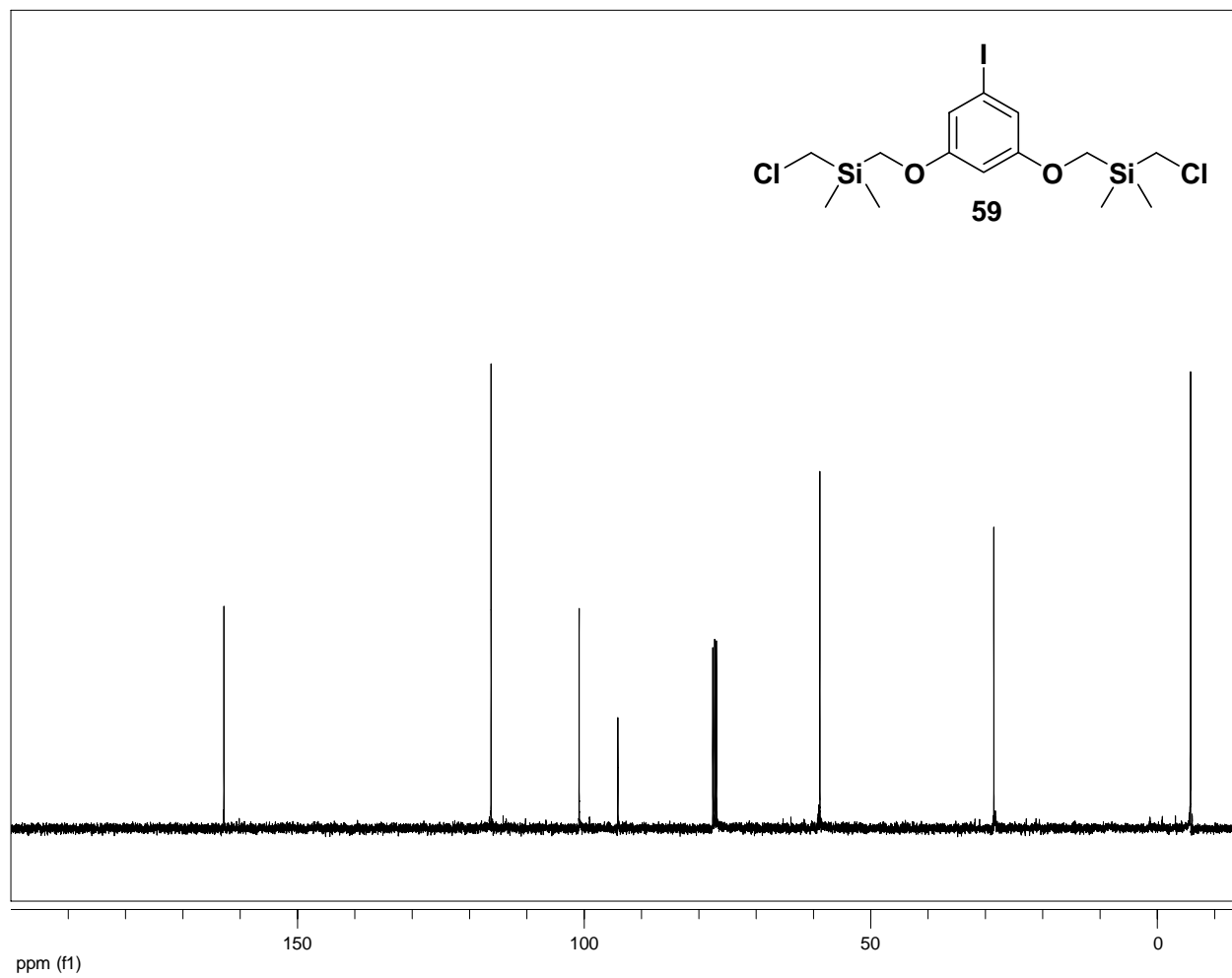
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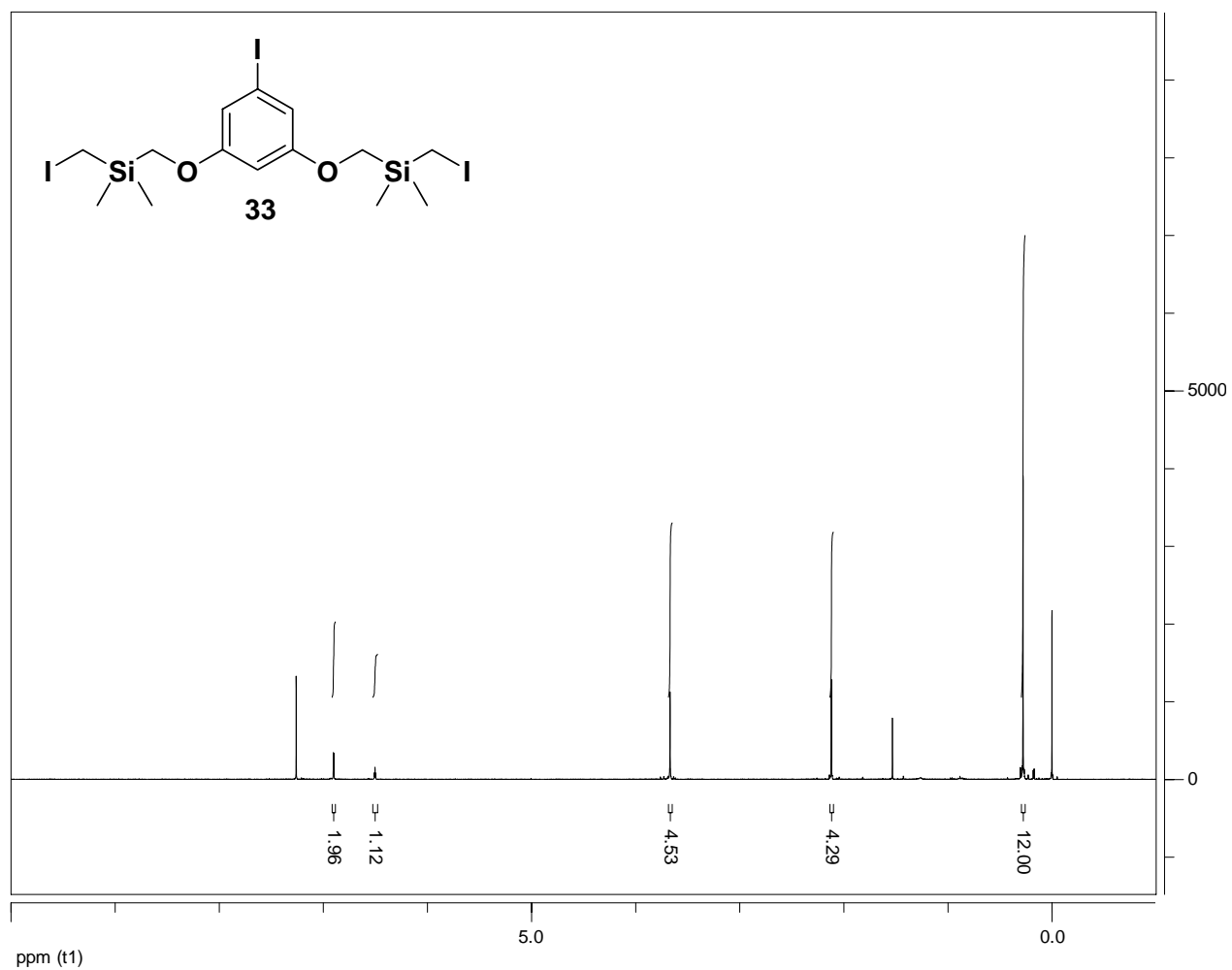
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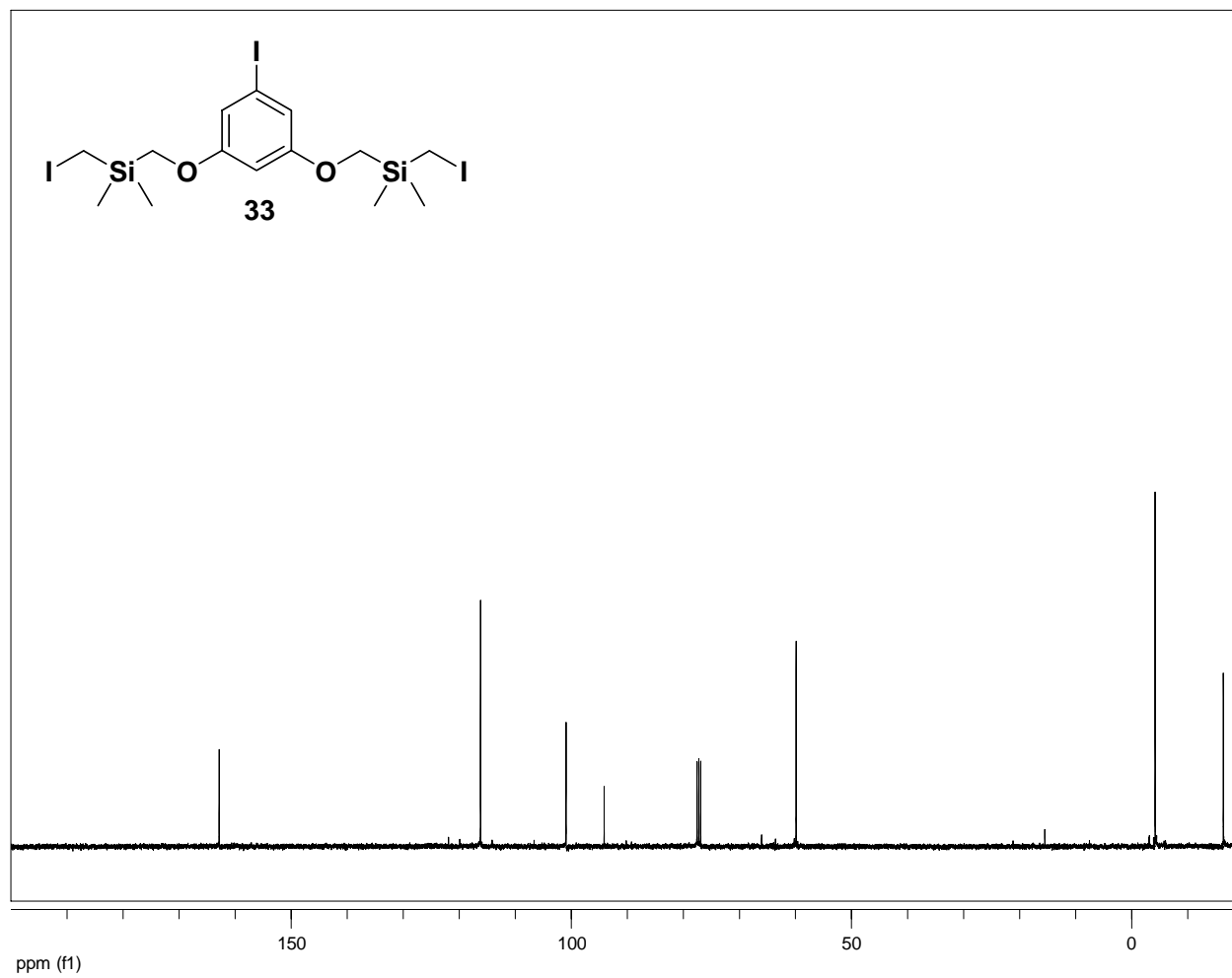
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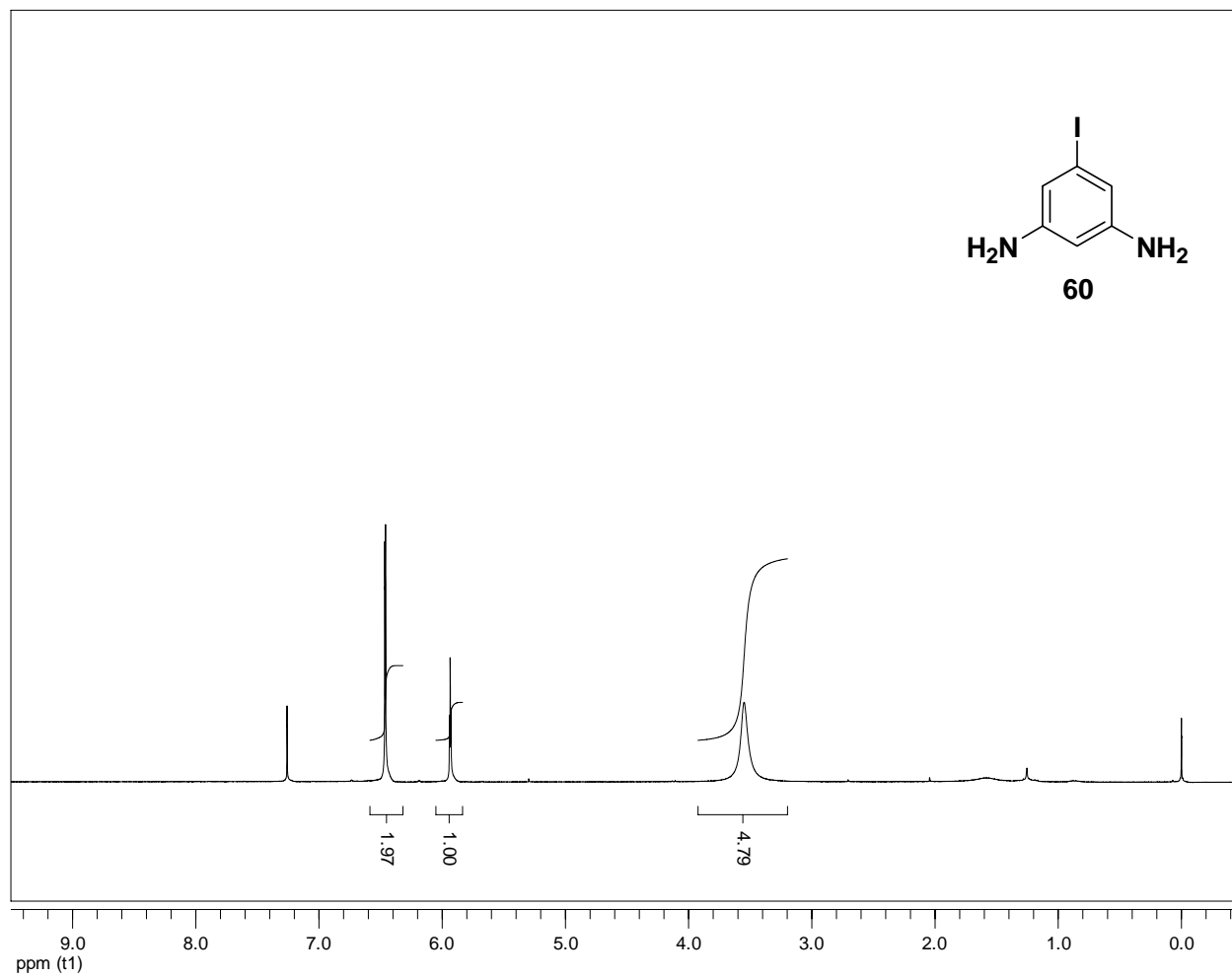
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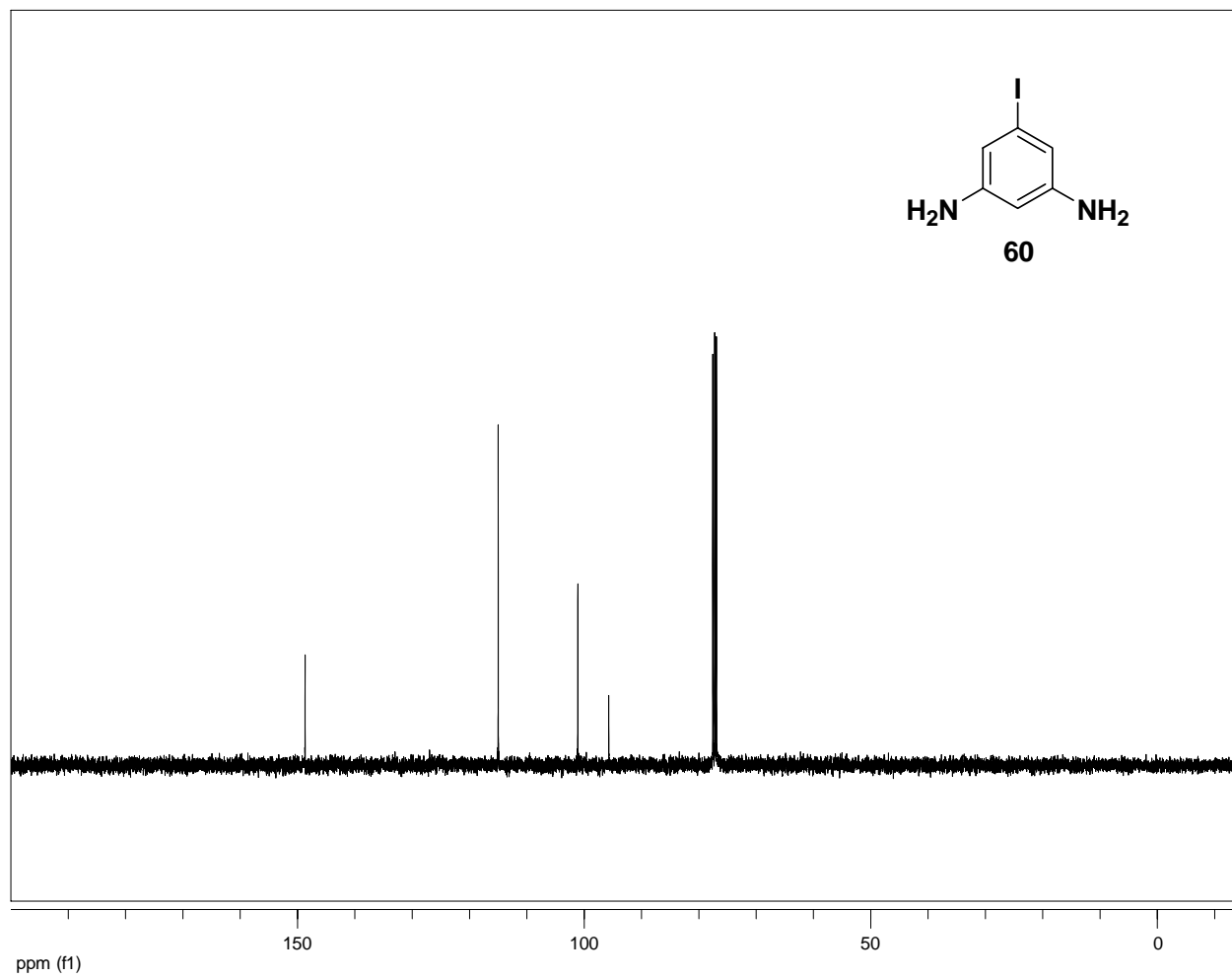
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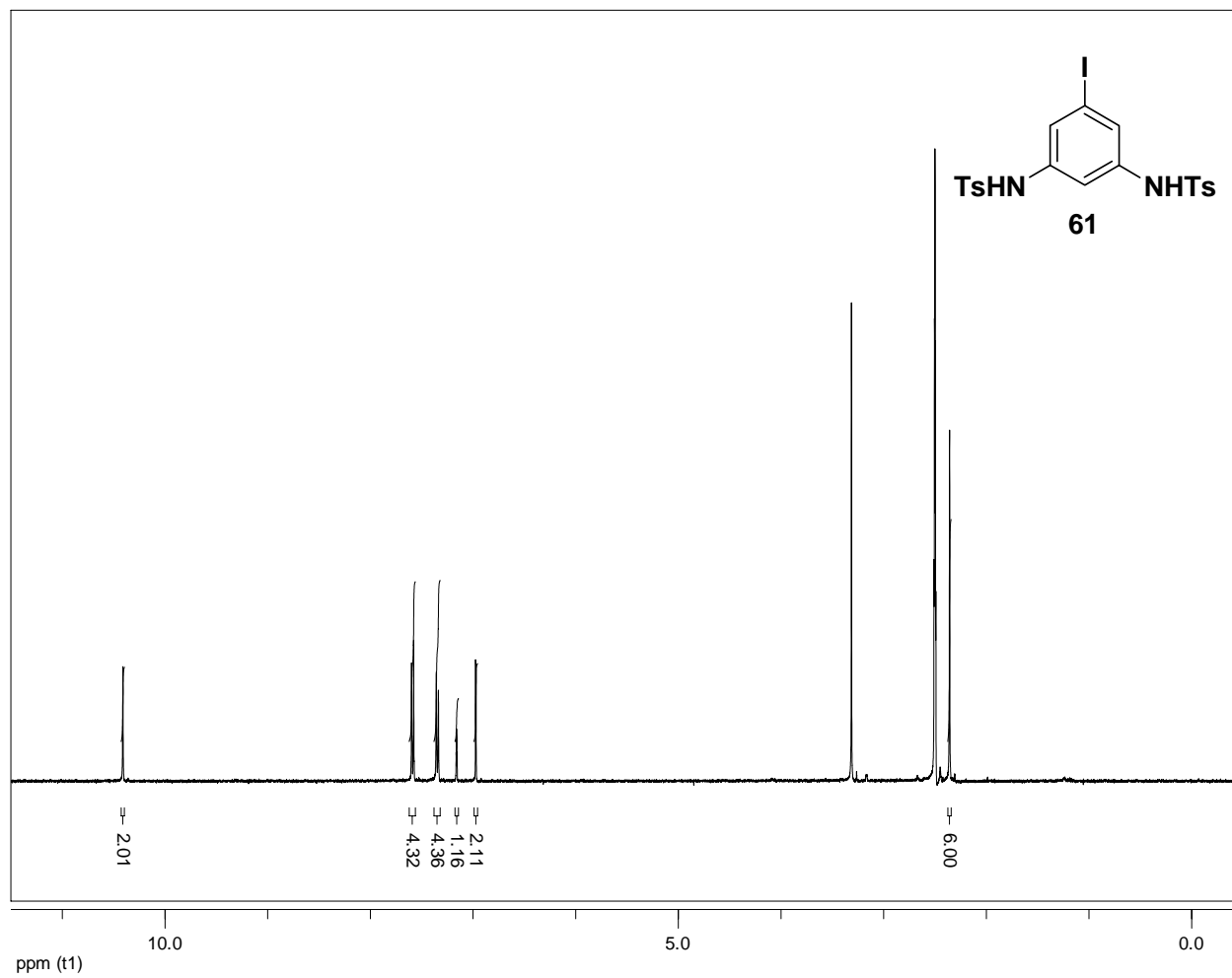
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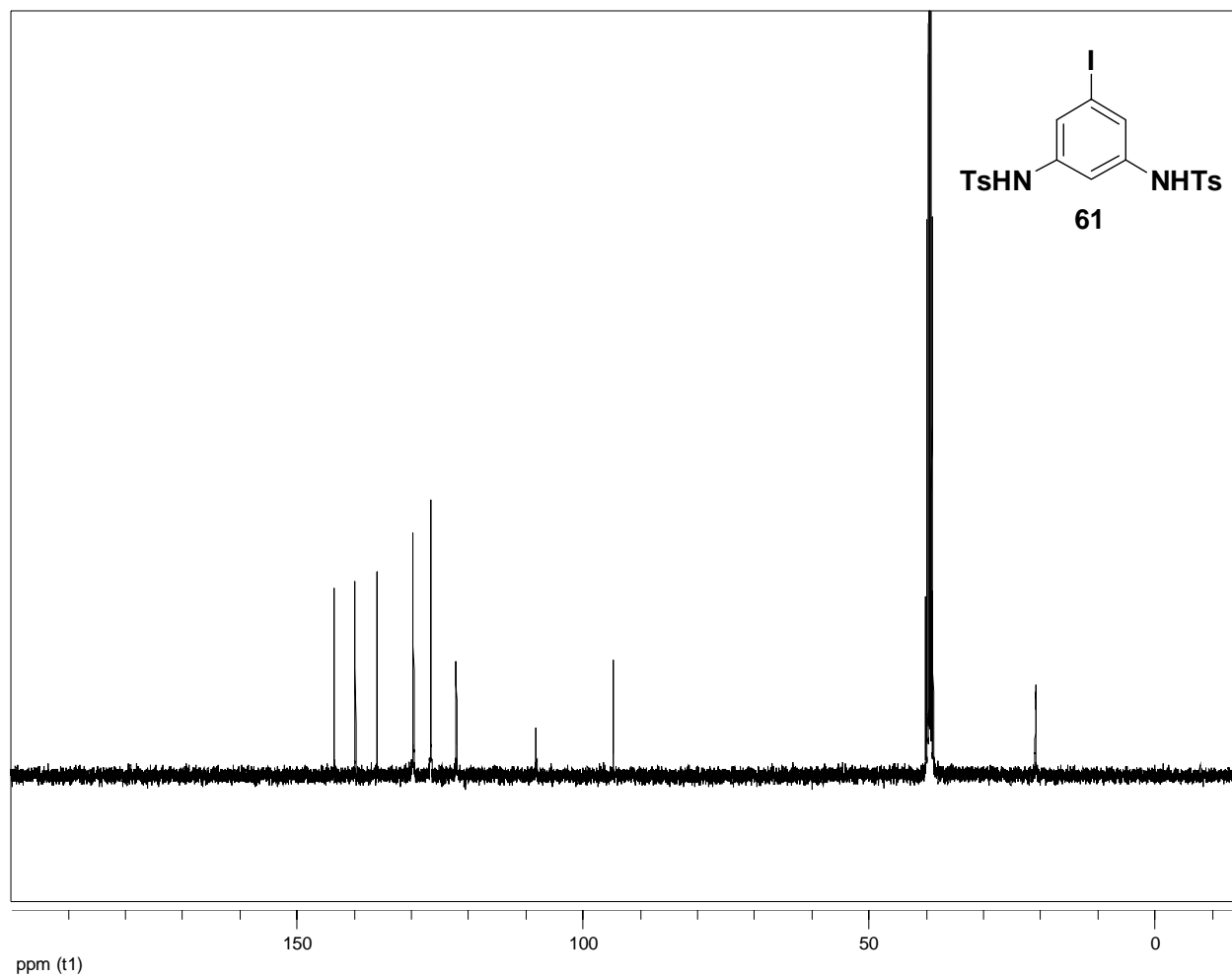
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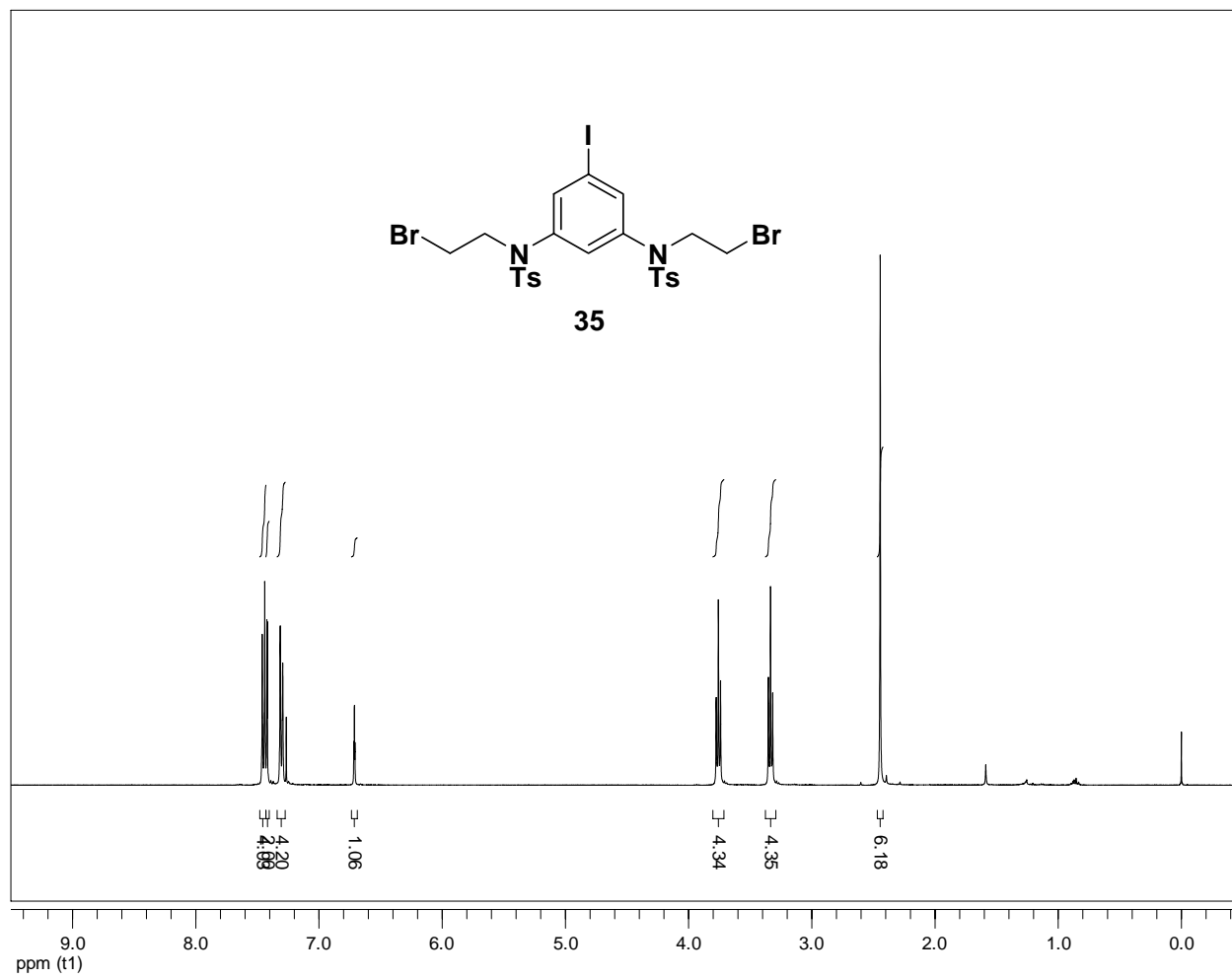
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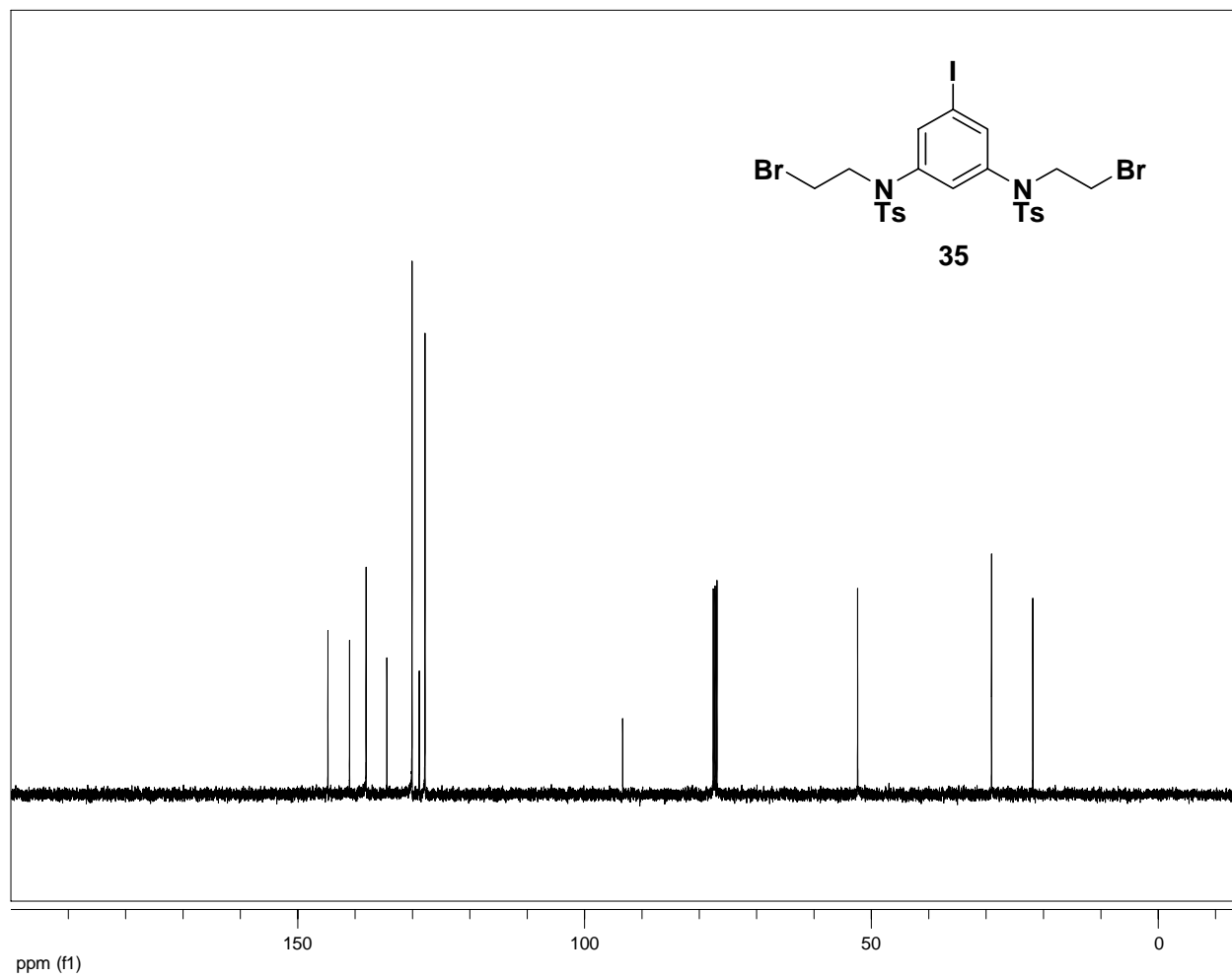
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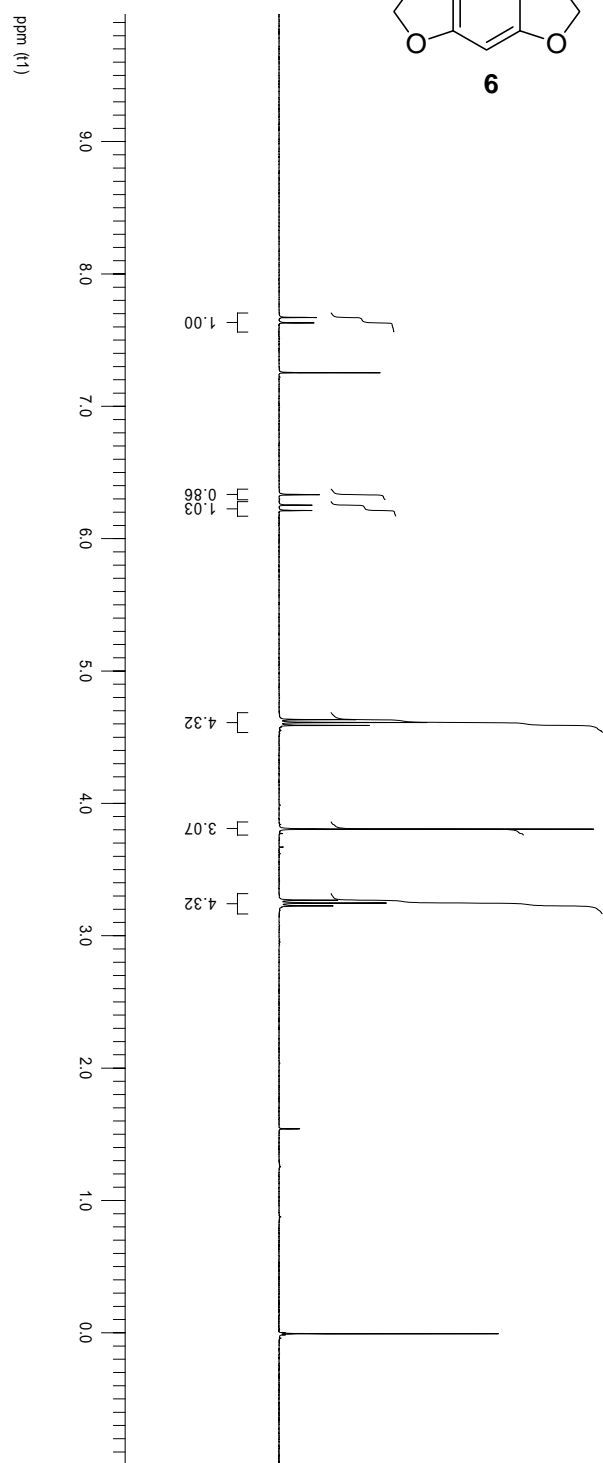
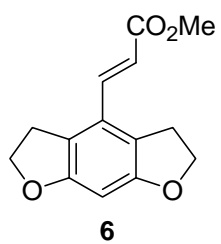
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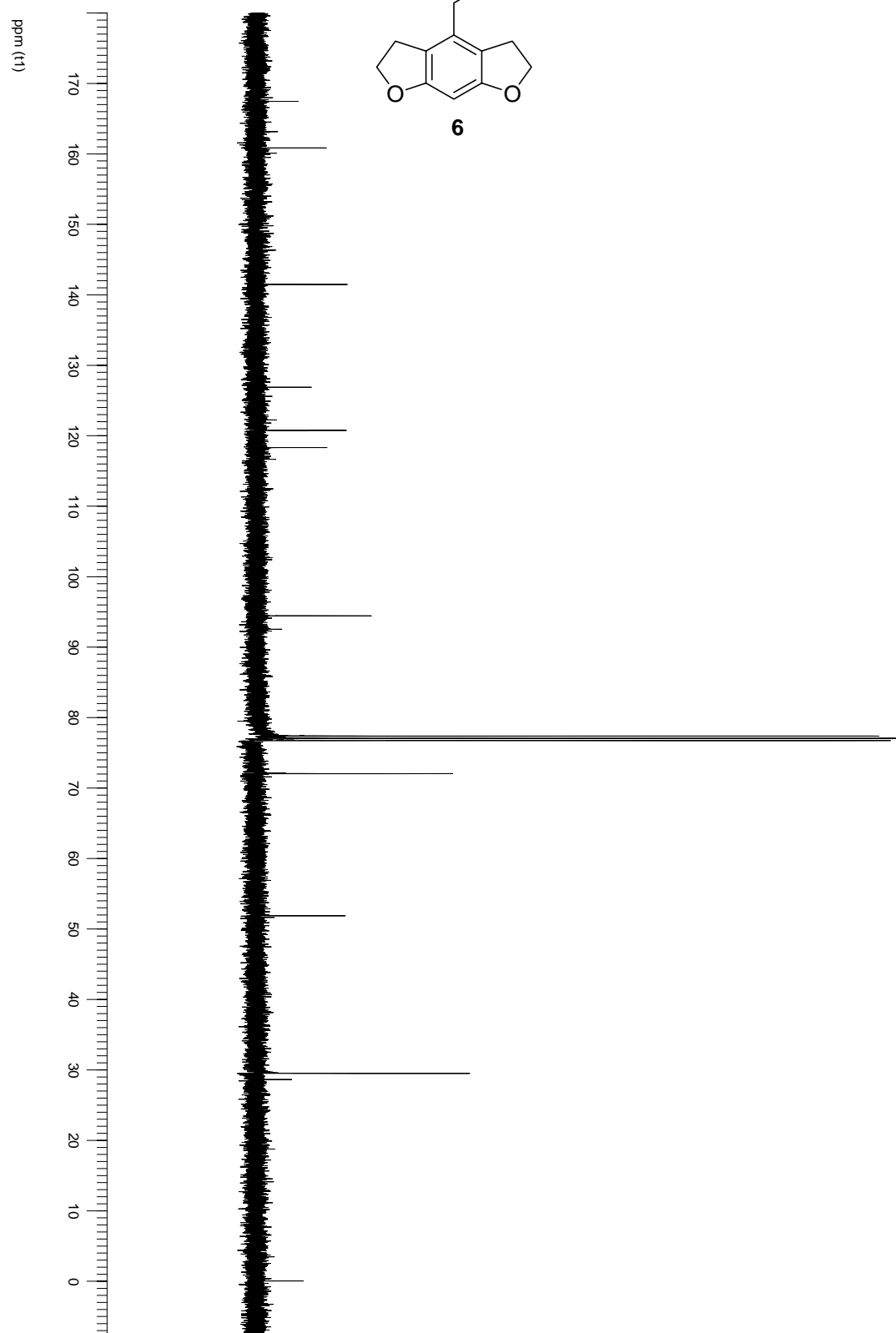
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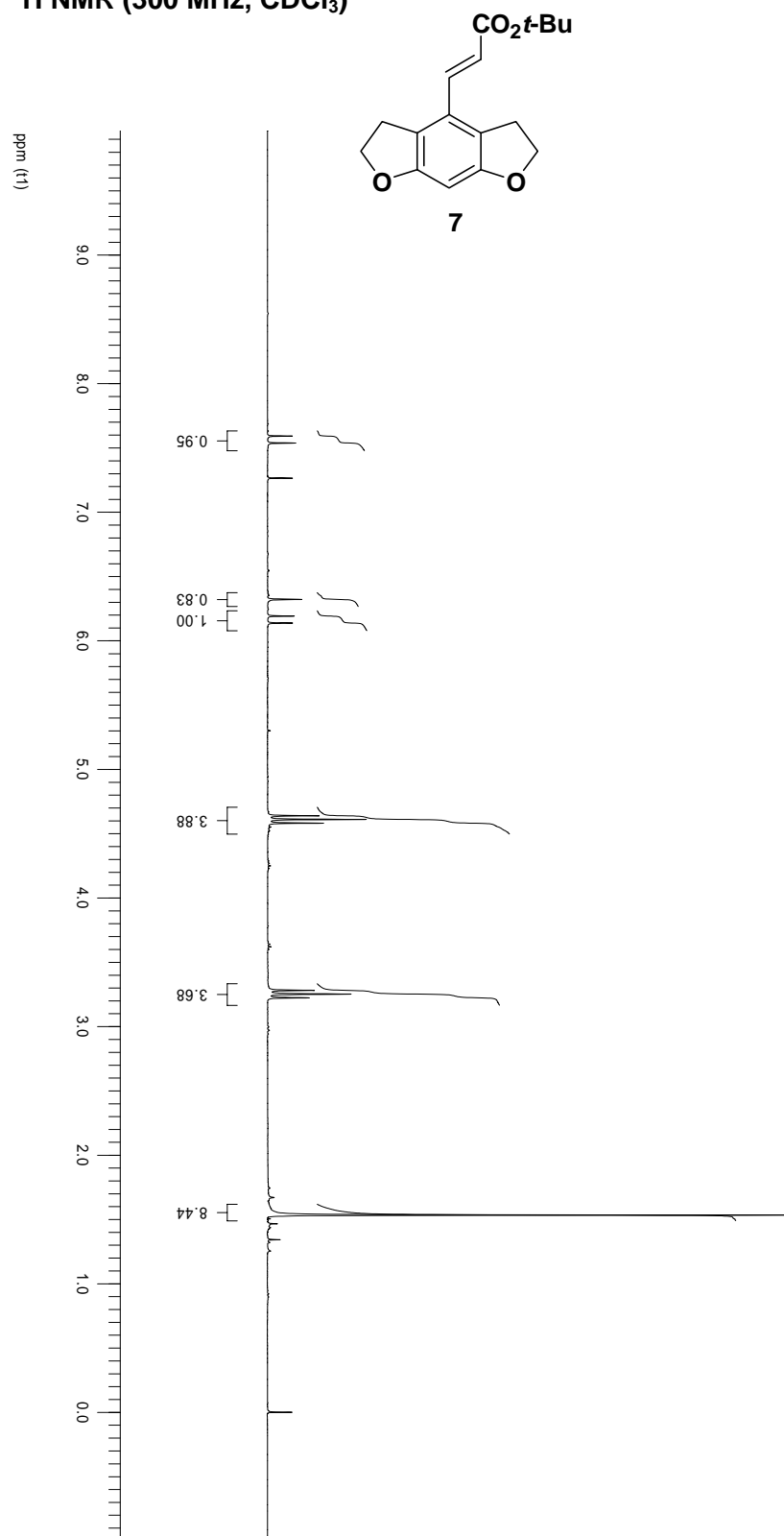
¹H NMR (400 MHz, CDCl₃)



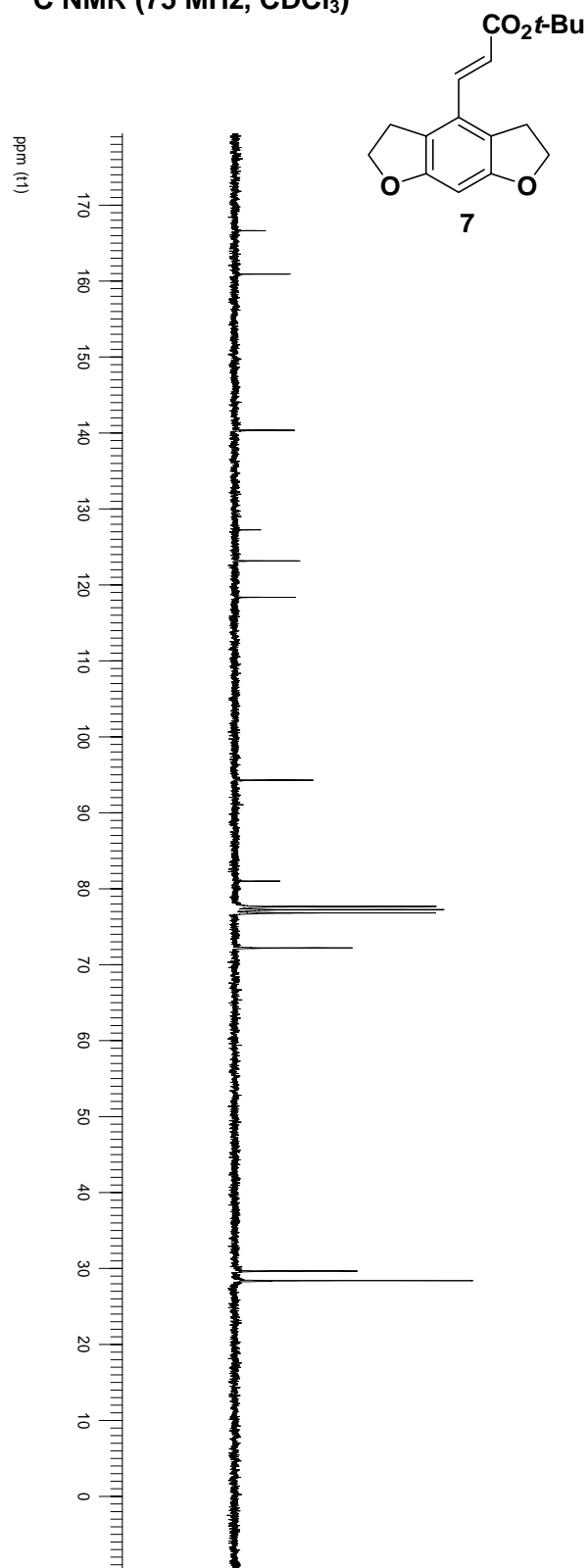
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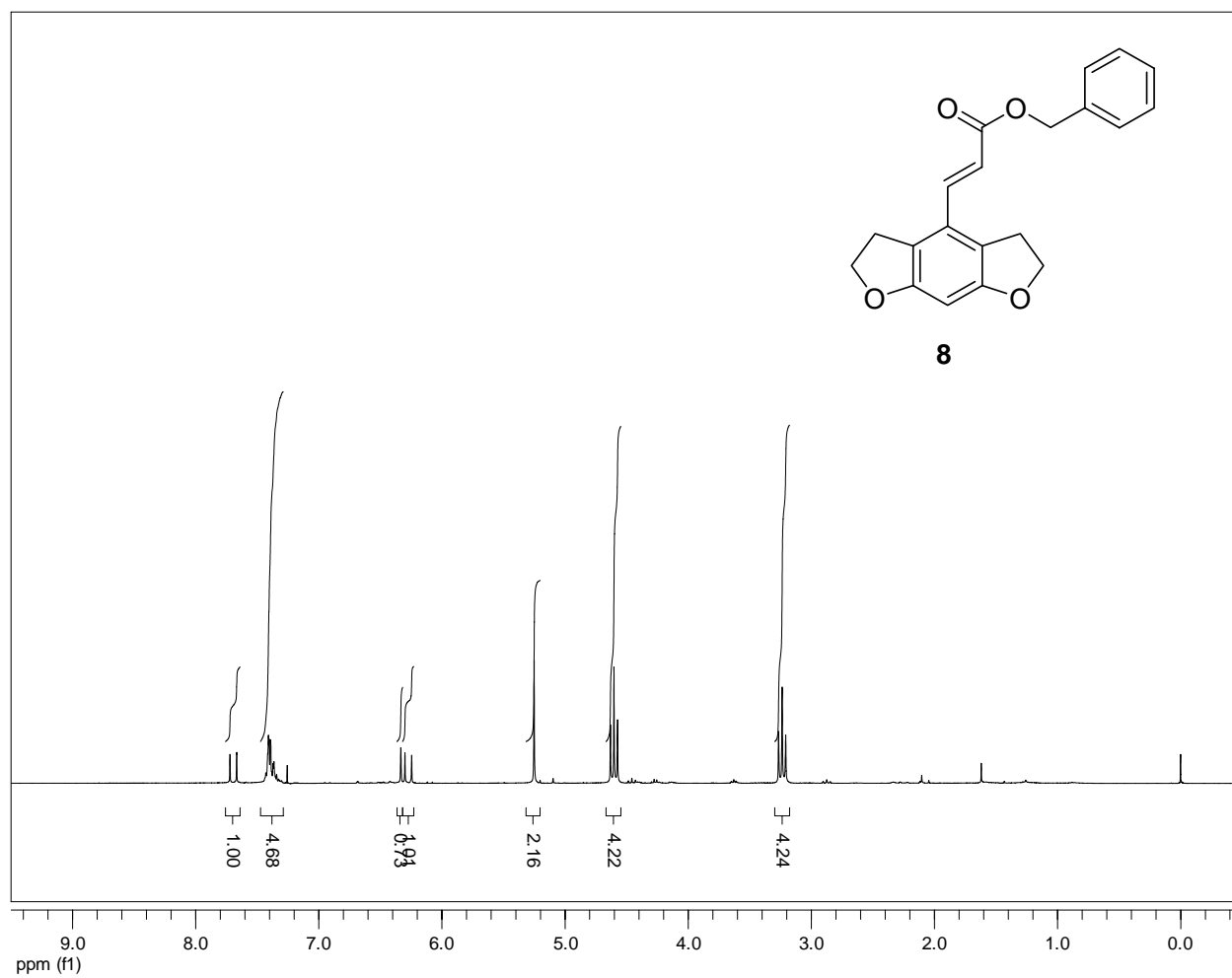
¹H NMR (300 MHz, CDCl₃)



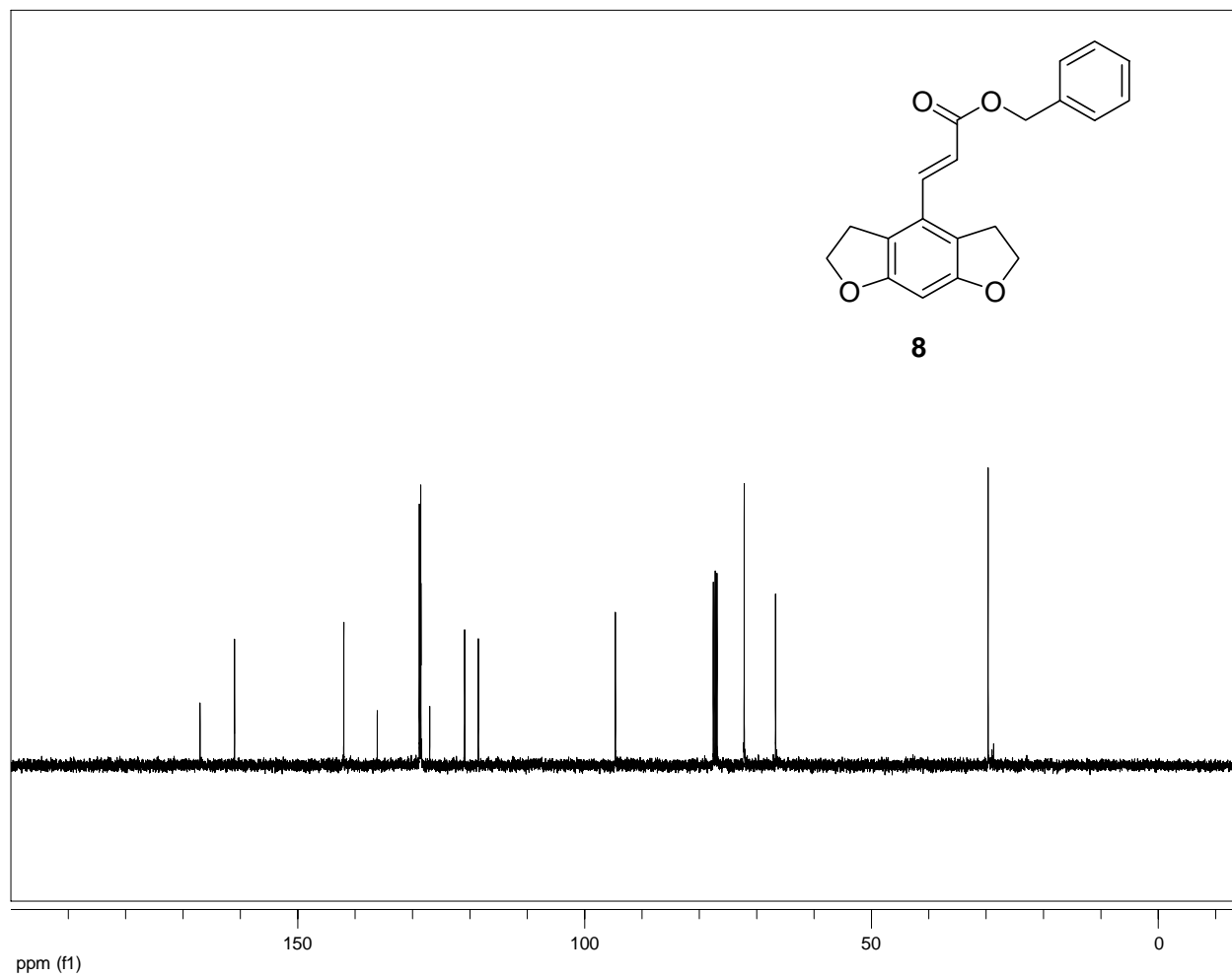
¹³C NMR (75 MHz, CDCl₃)



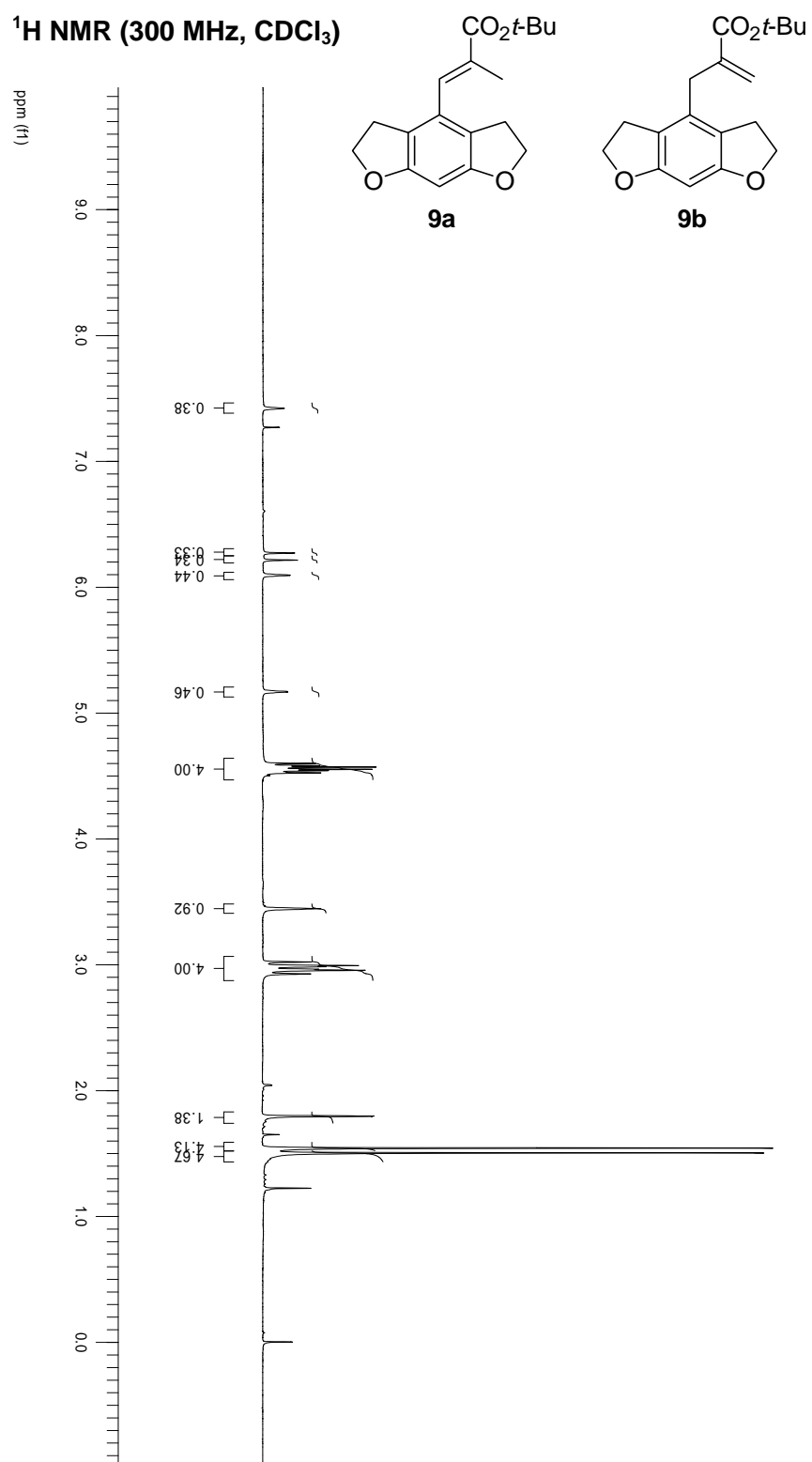
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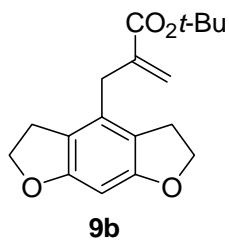
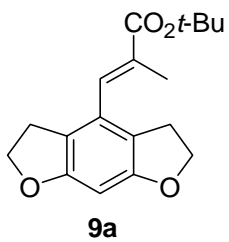
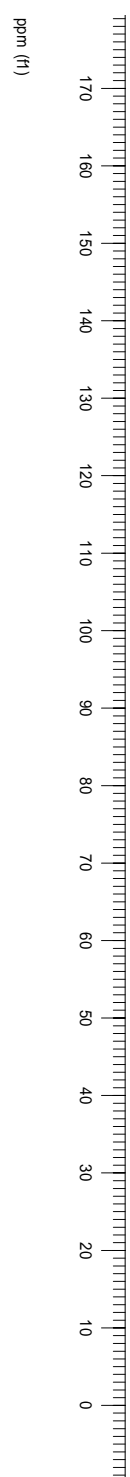
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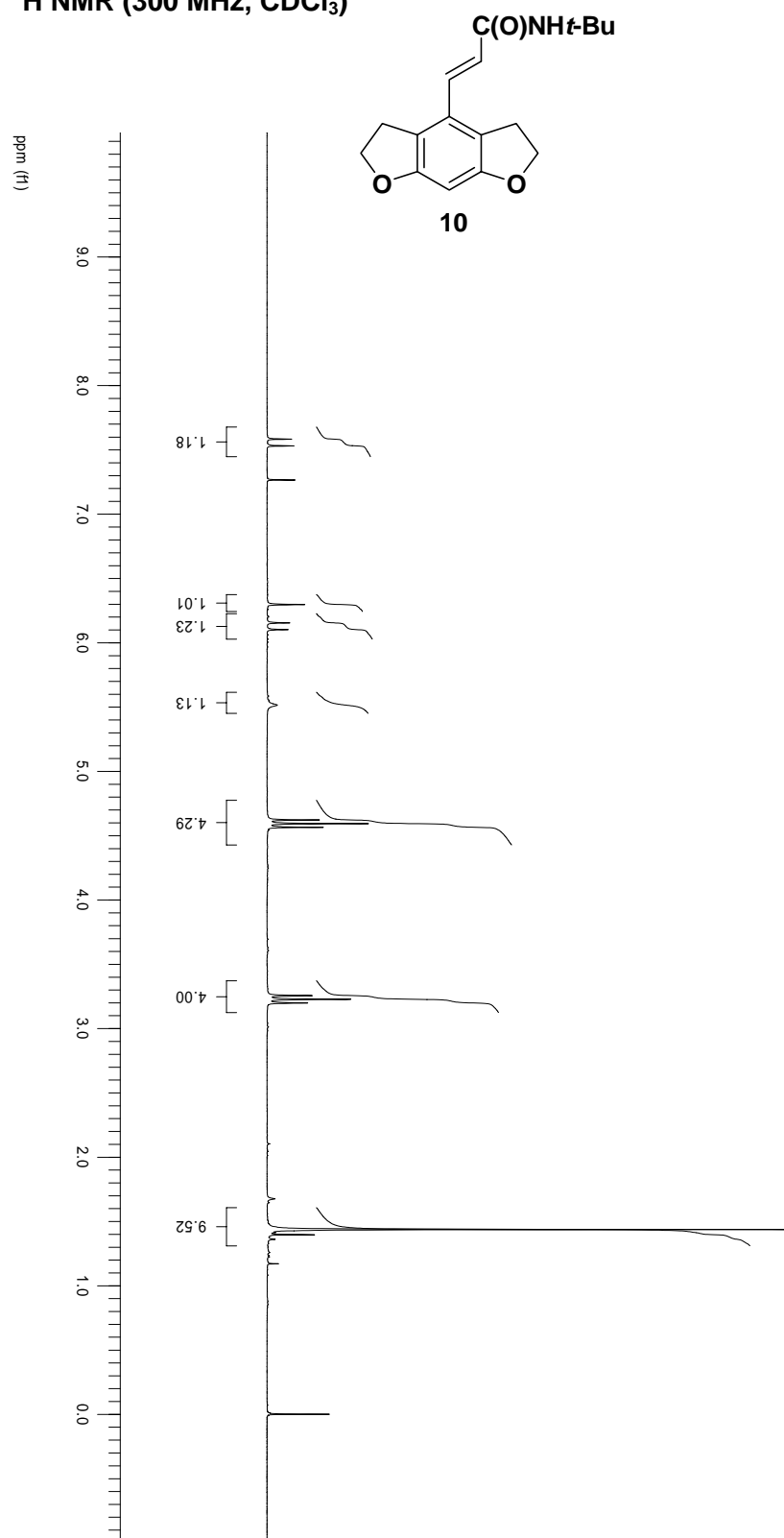
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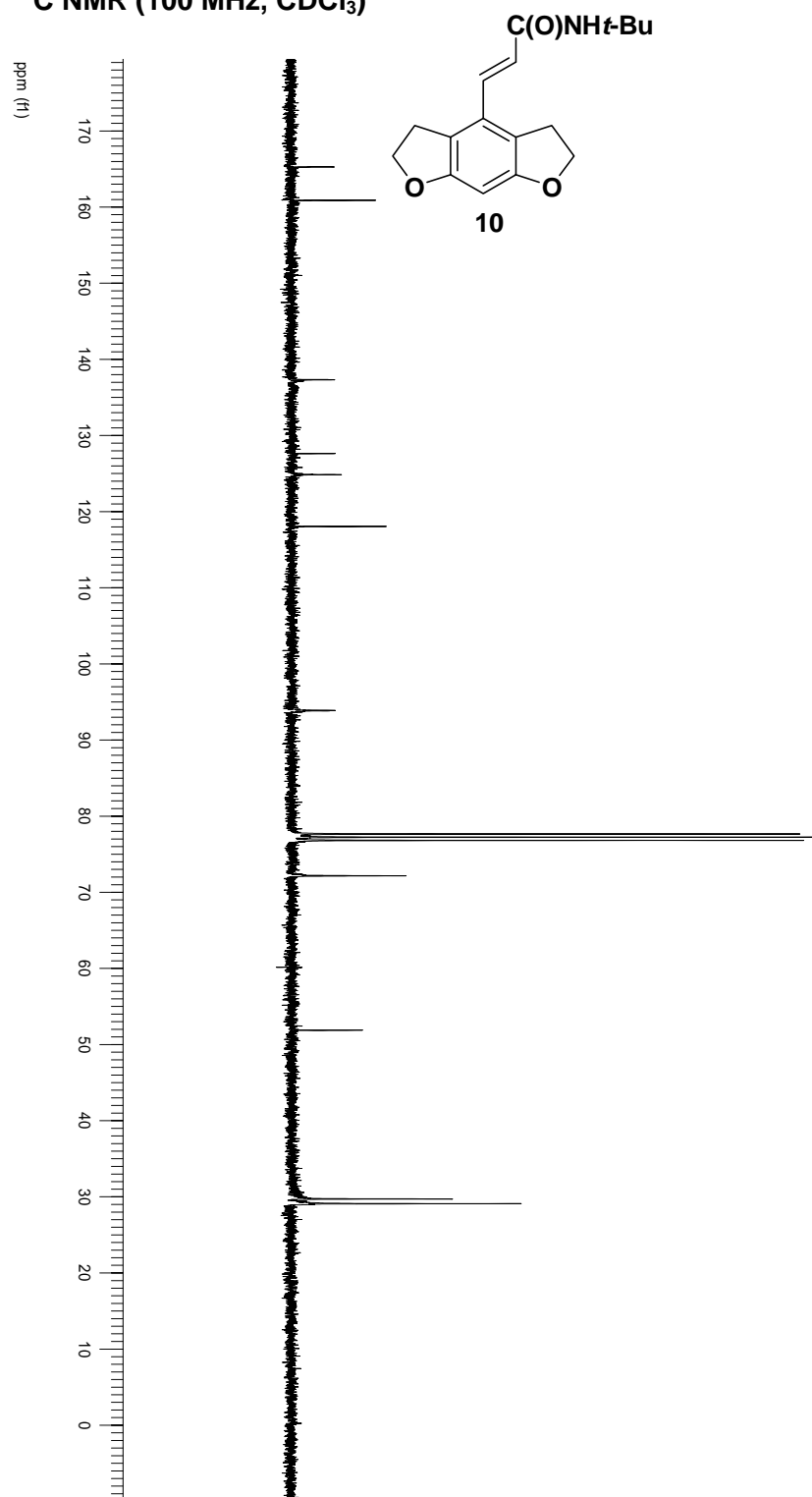
^{13}C NMR (75 MHz, CDCl_3)



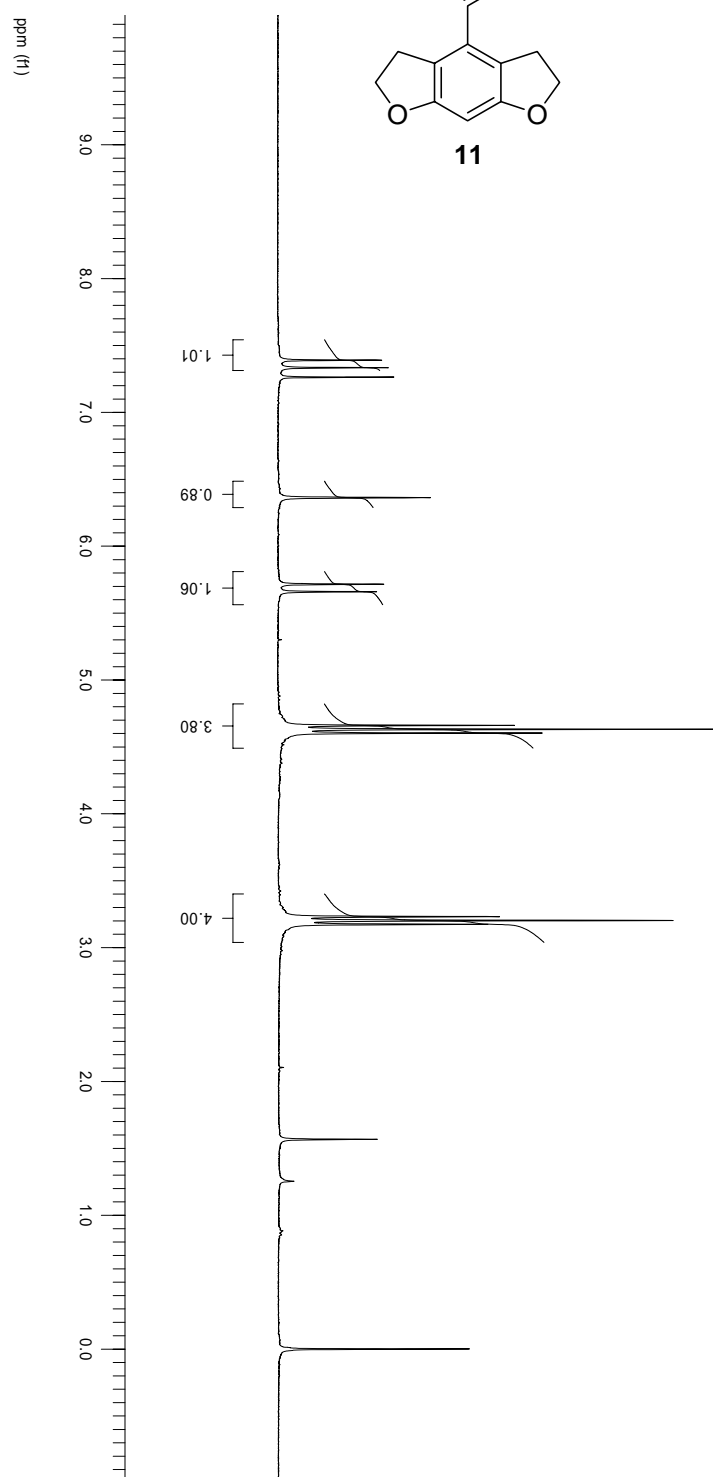
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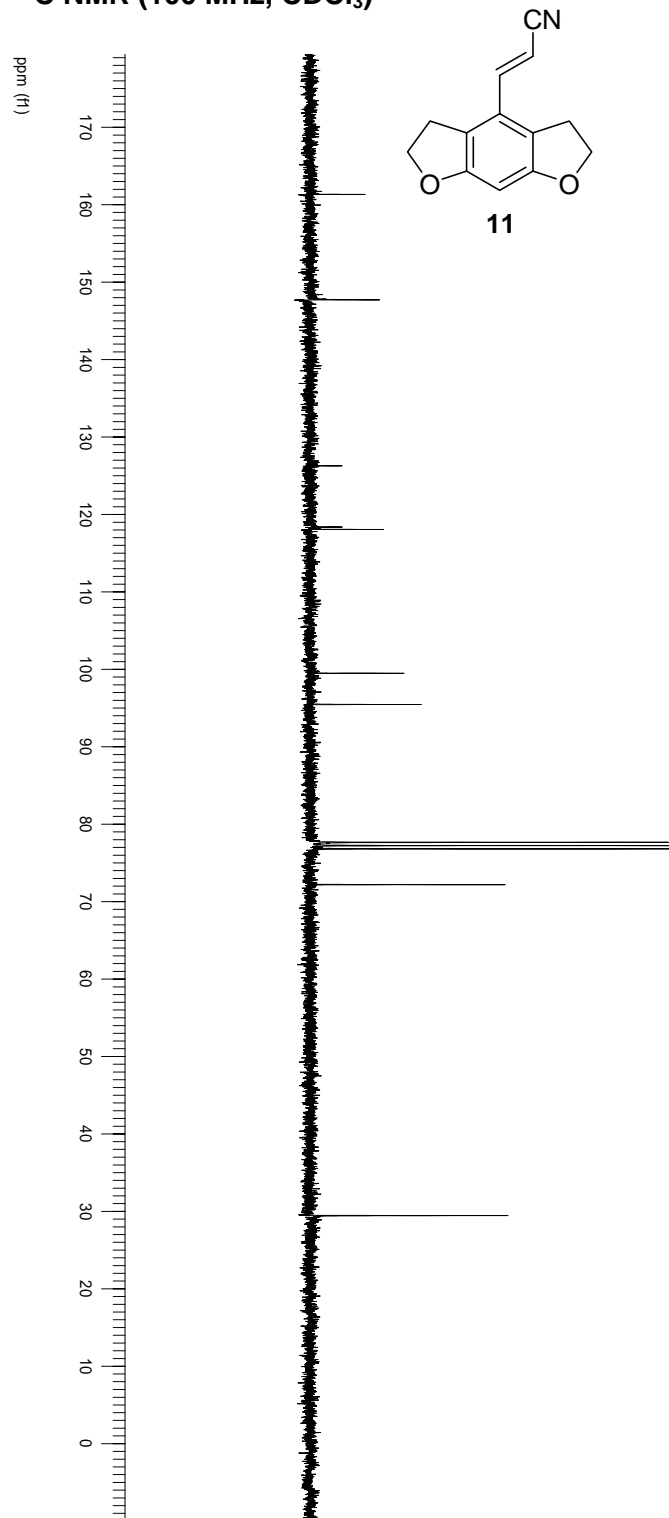
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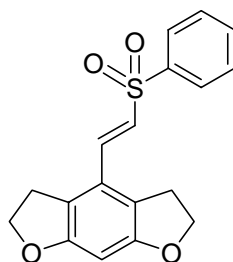
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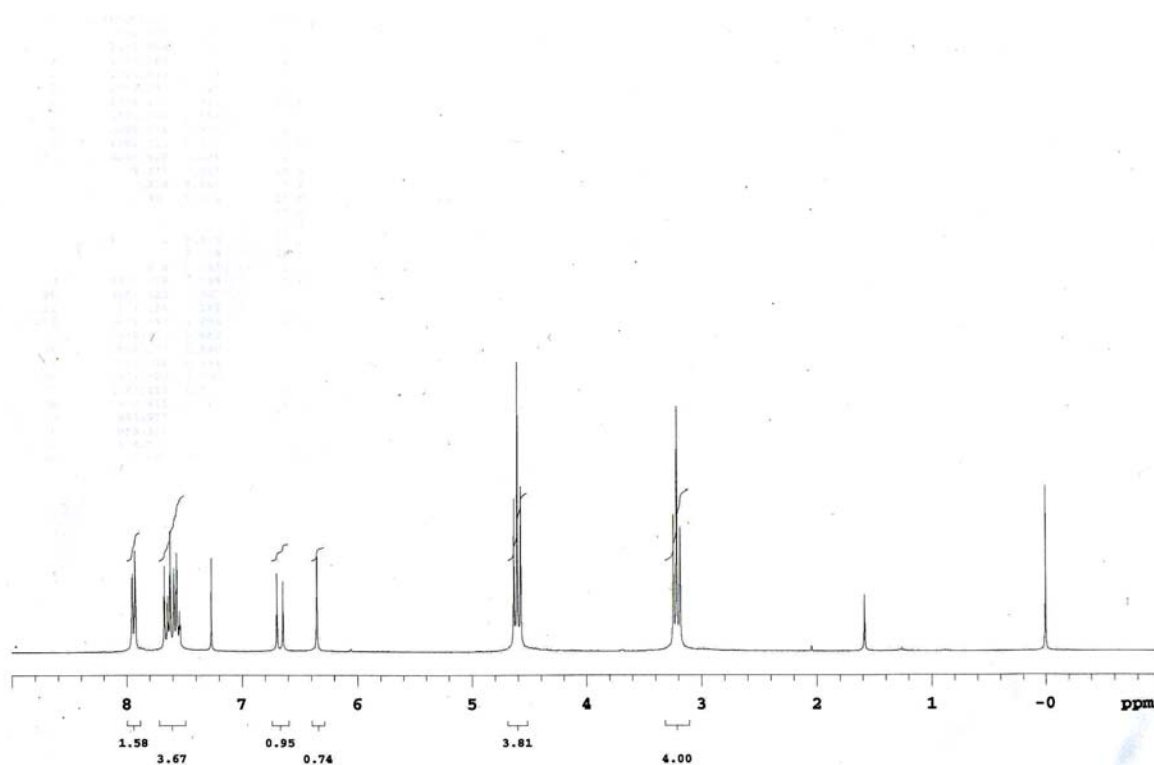
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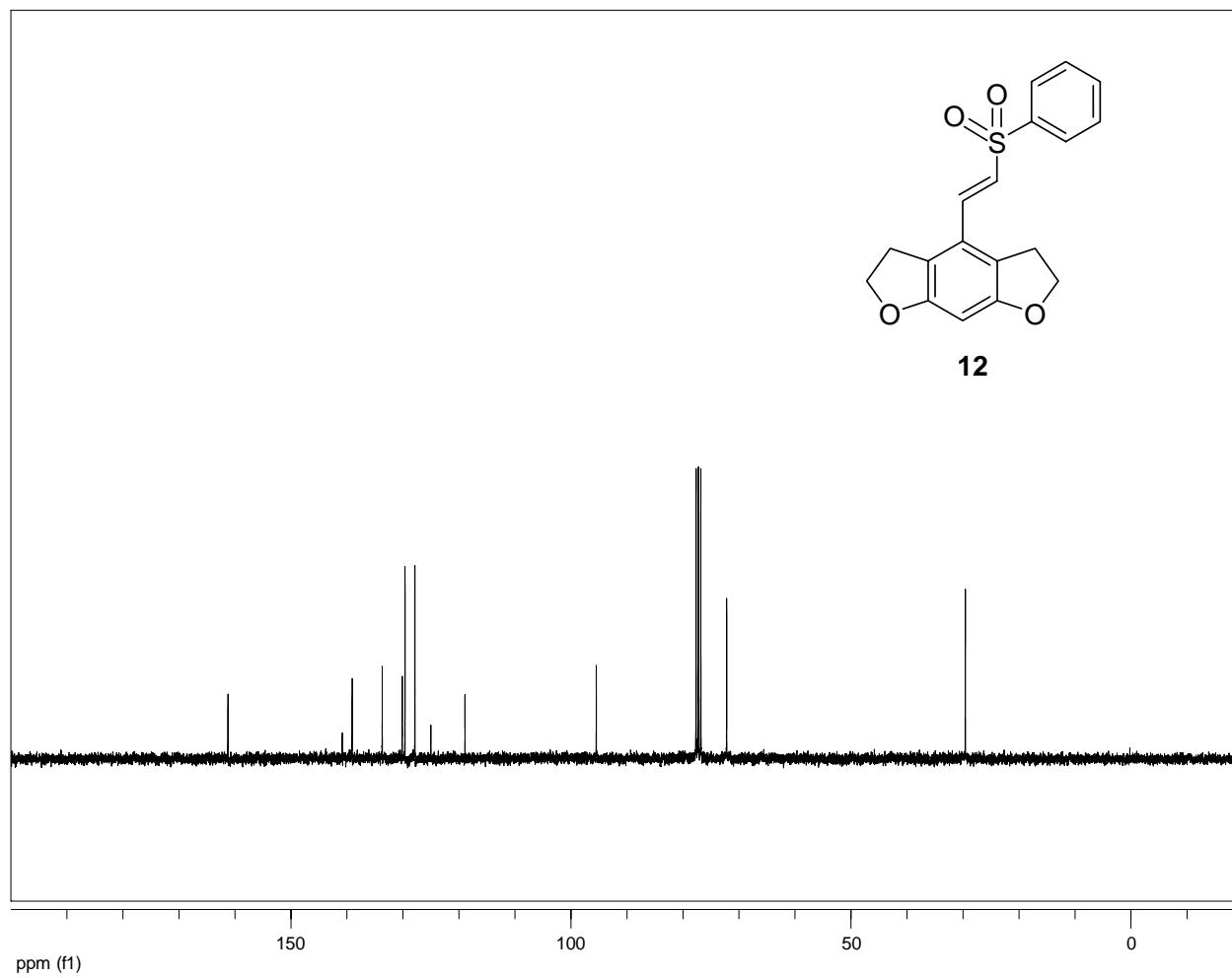
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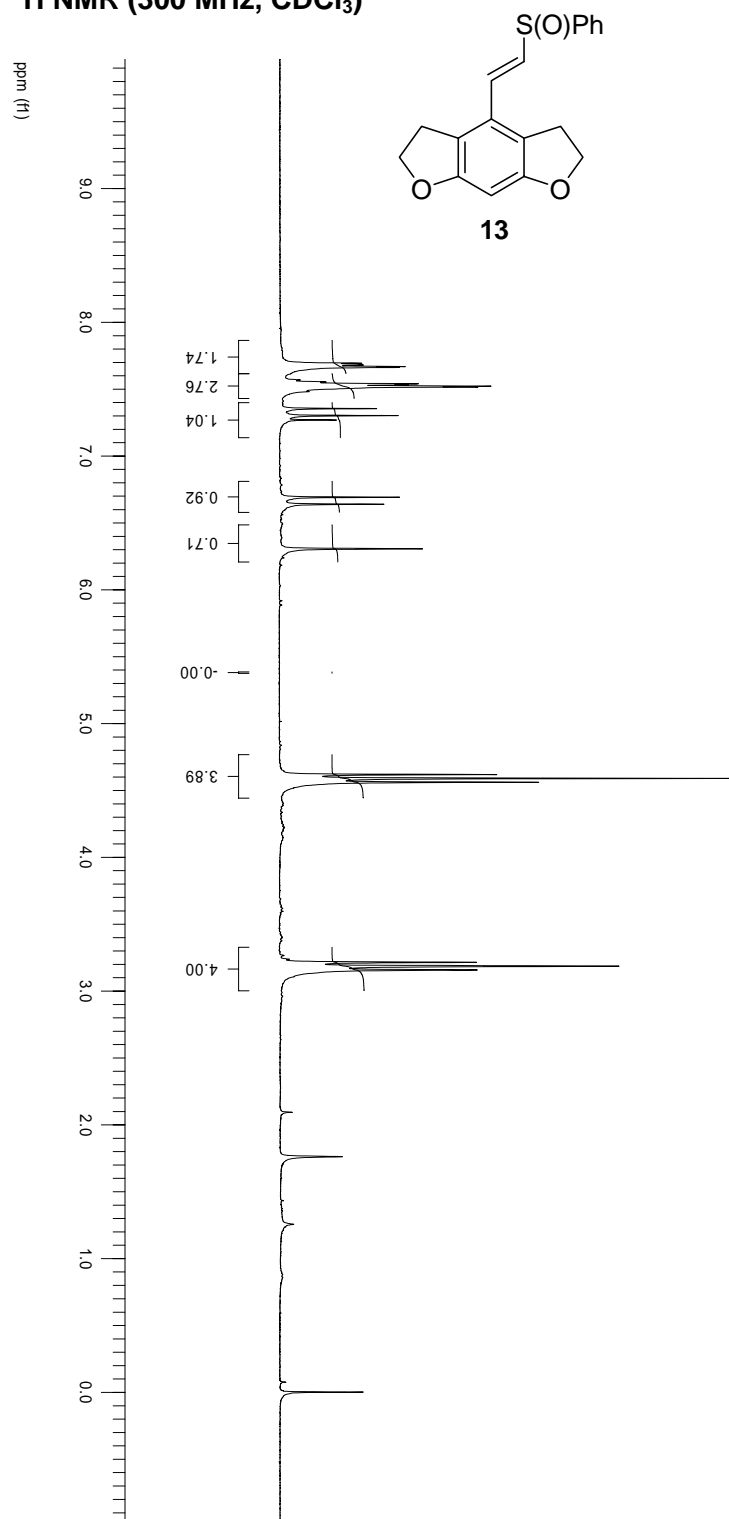
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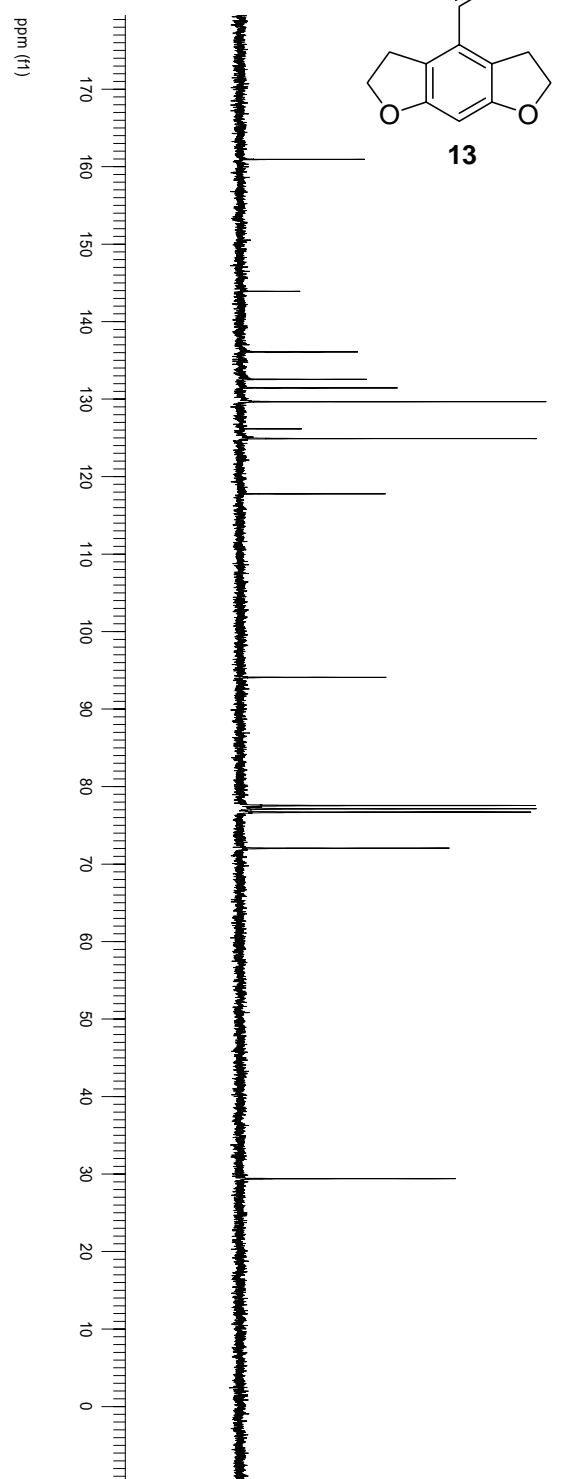
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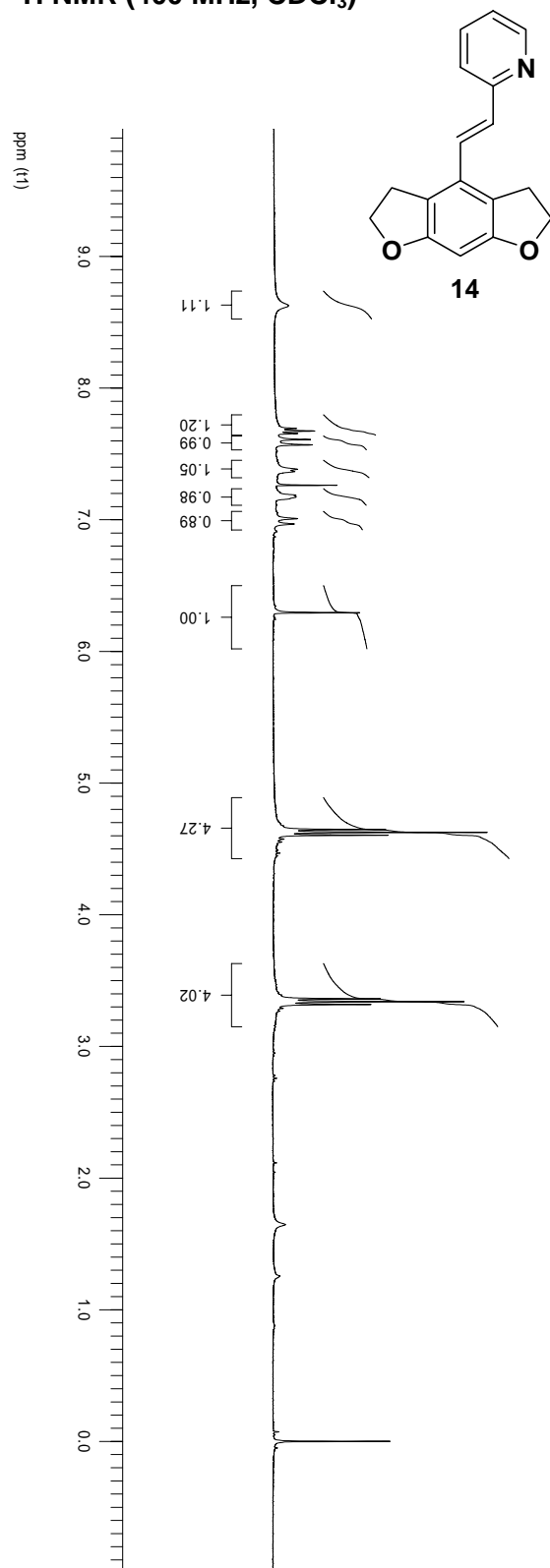
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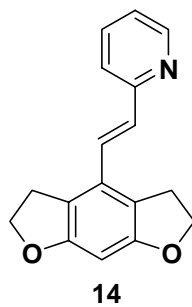
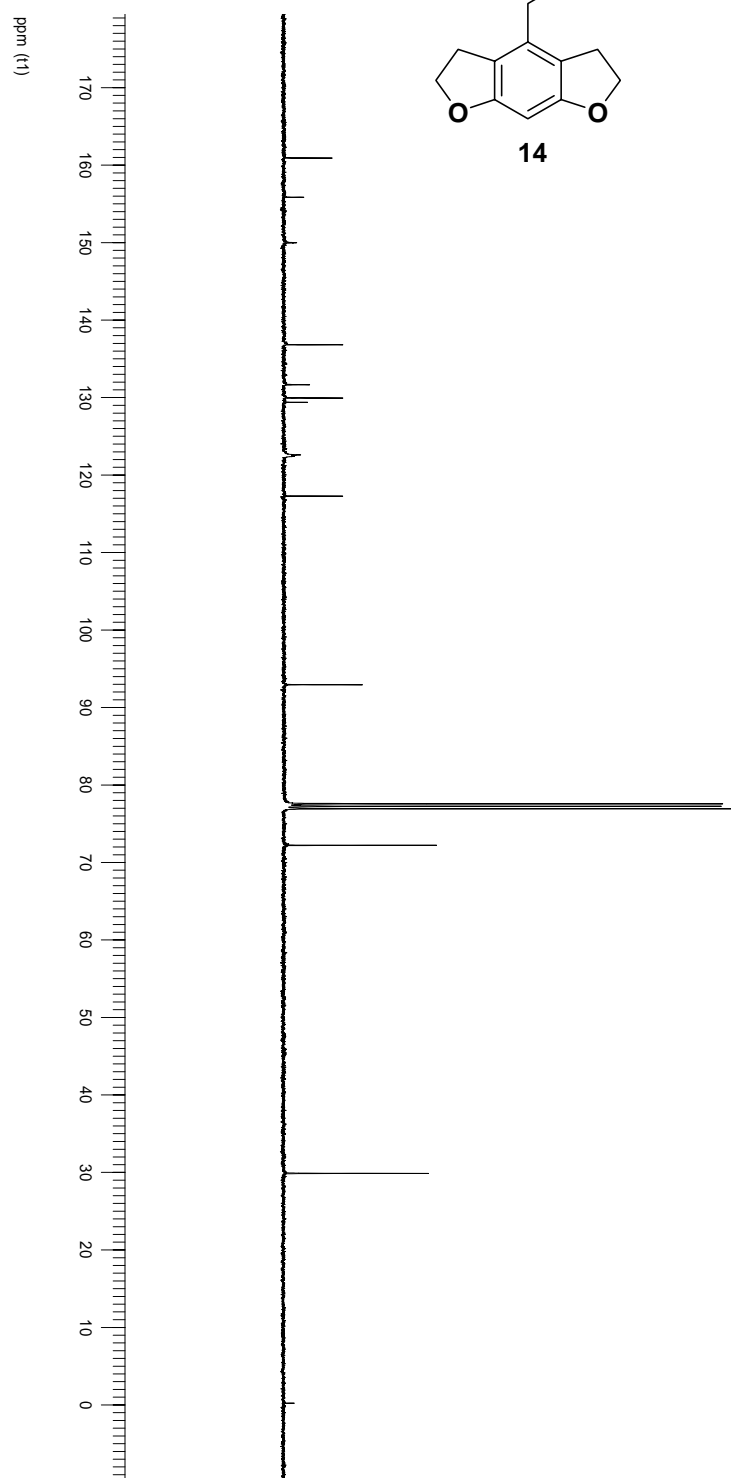
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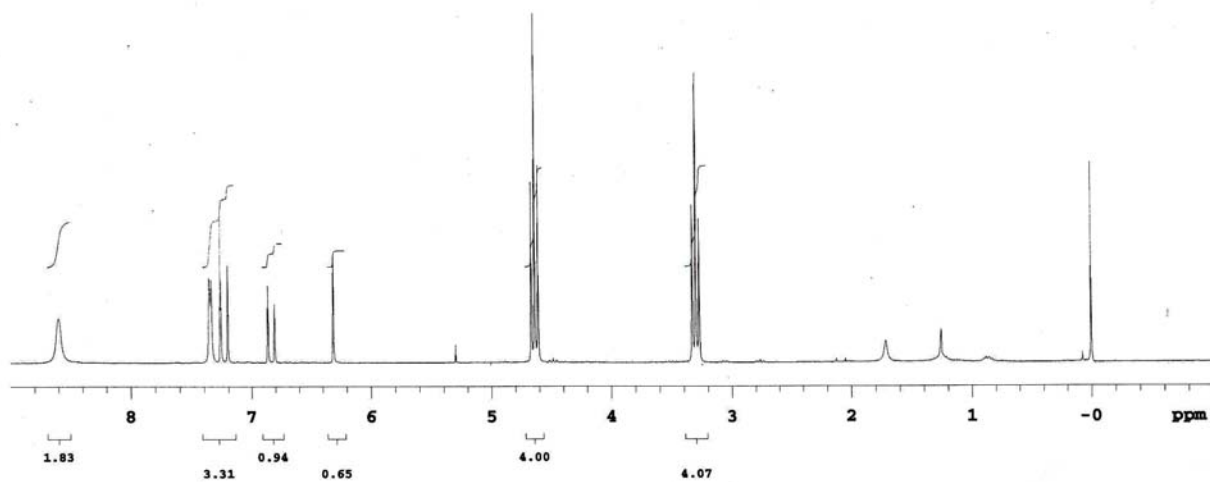
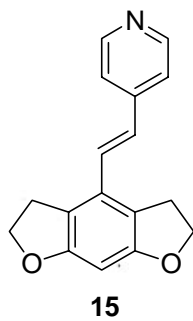
^1H NMR (400 MHz, CDCl_3)



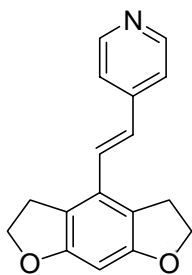
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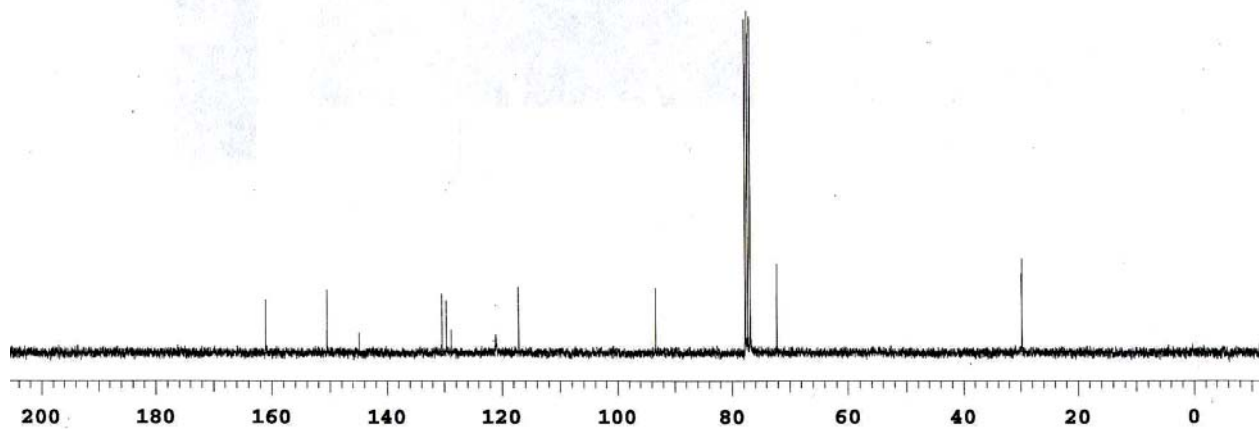
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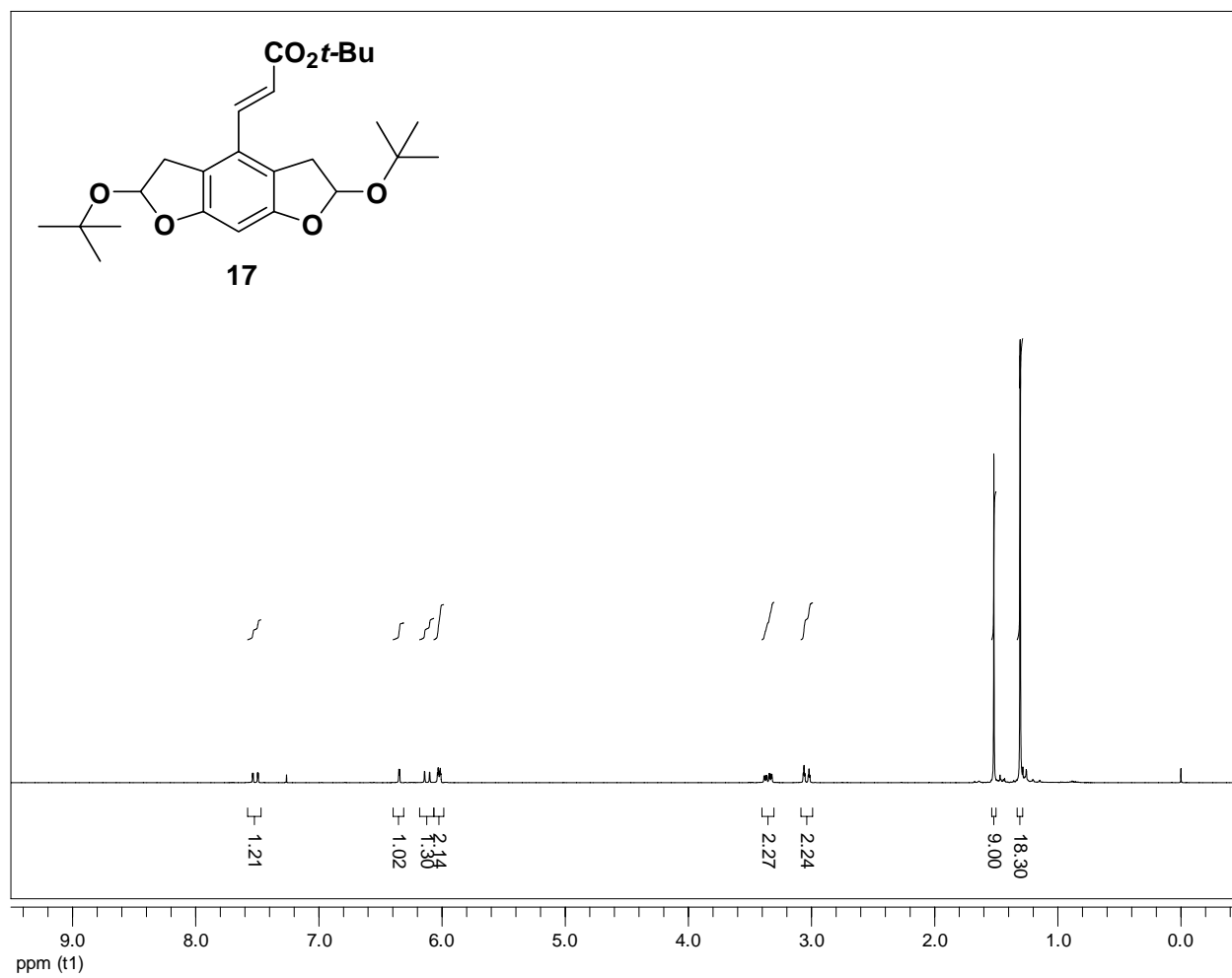
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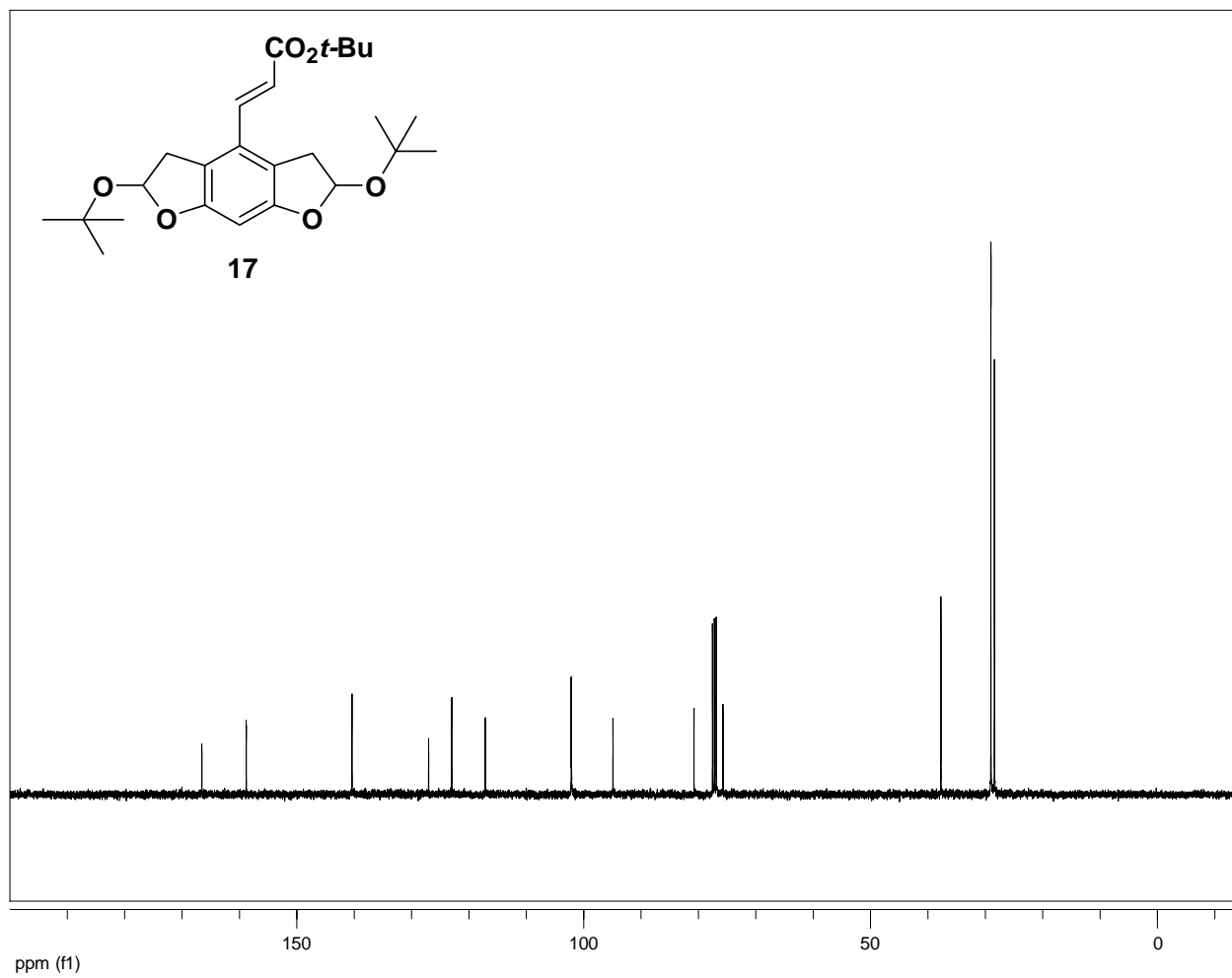
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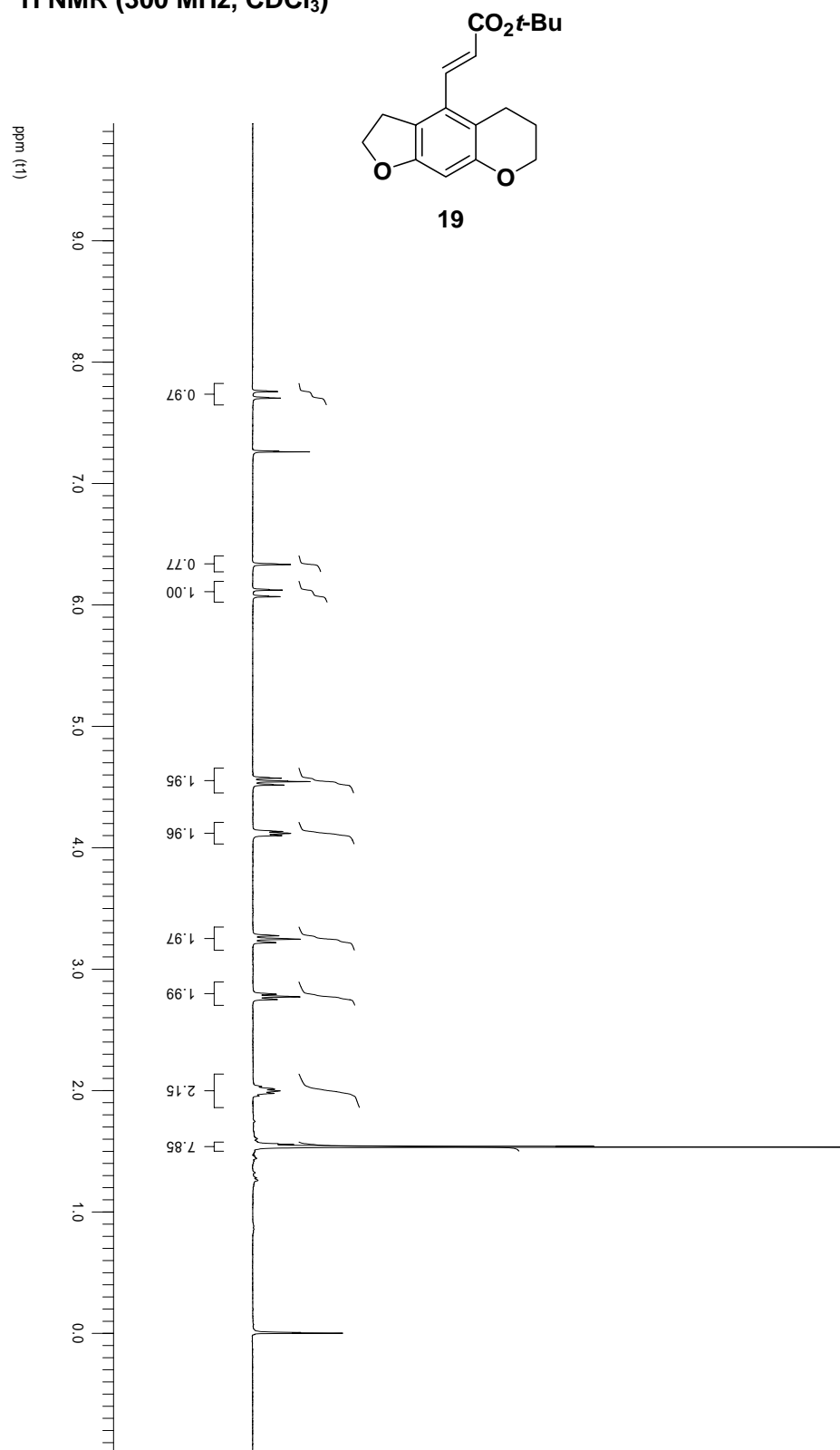
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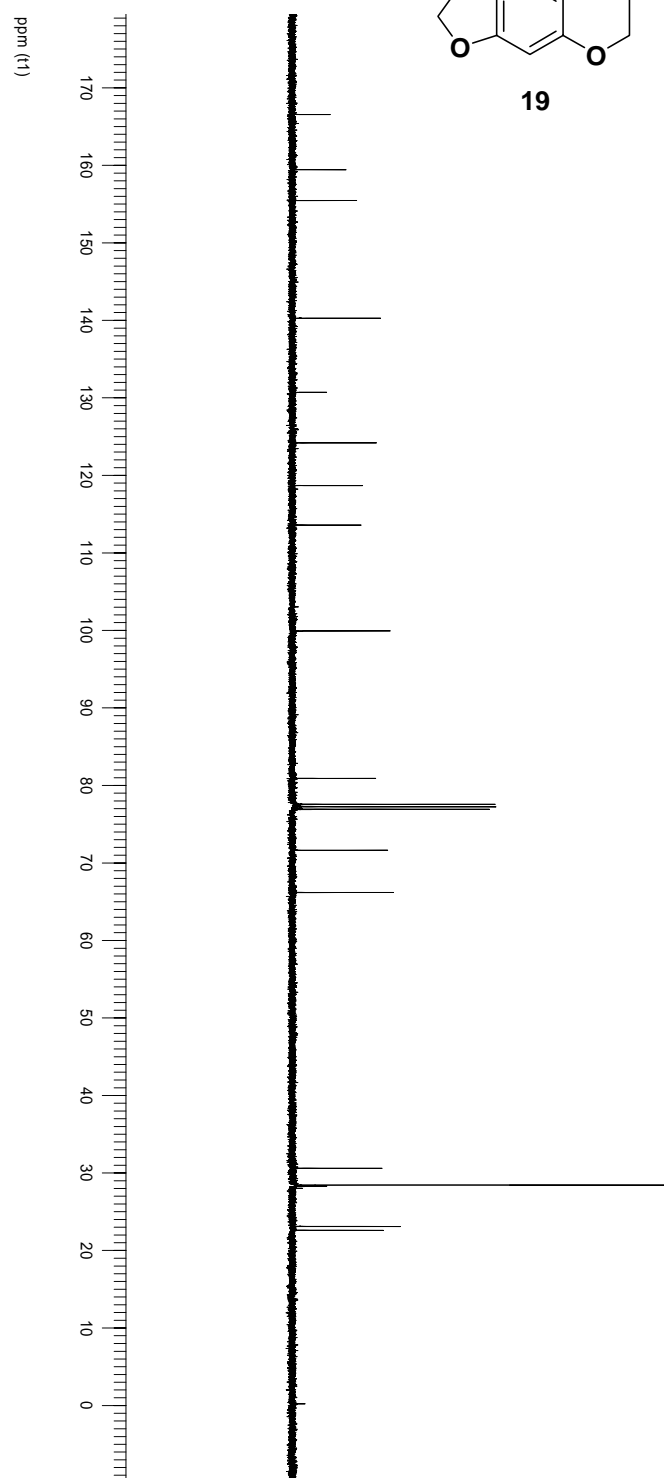
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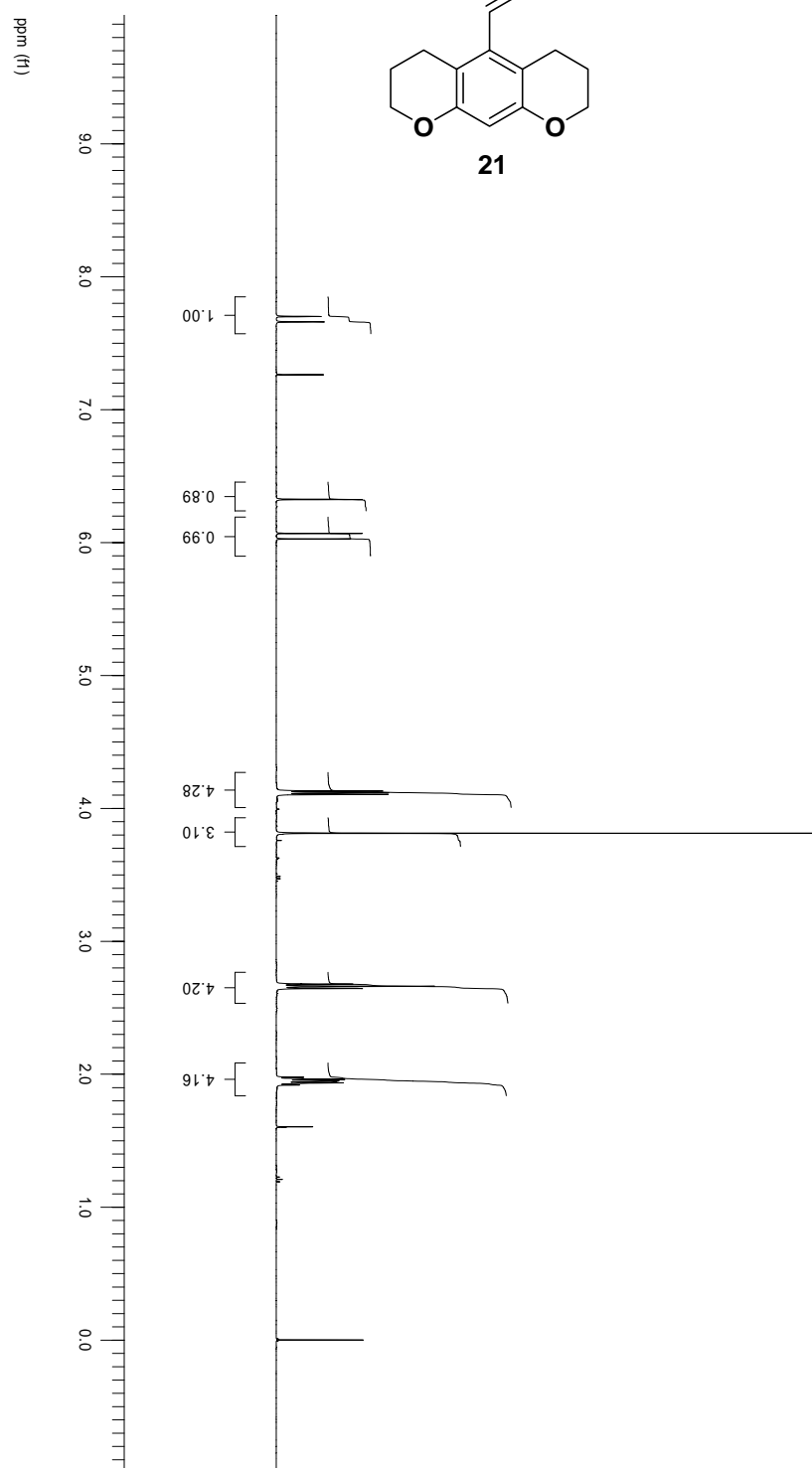
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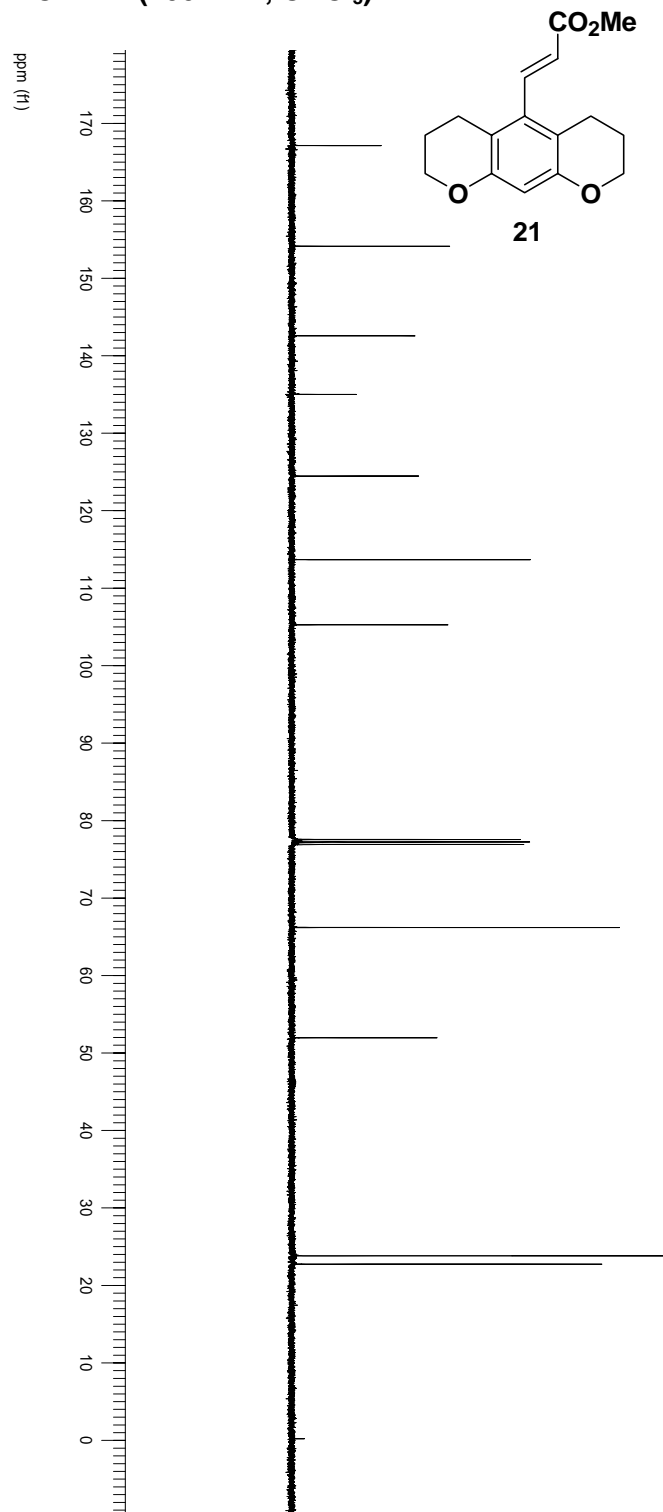
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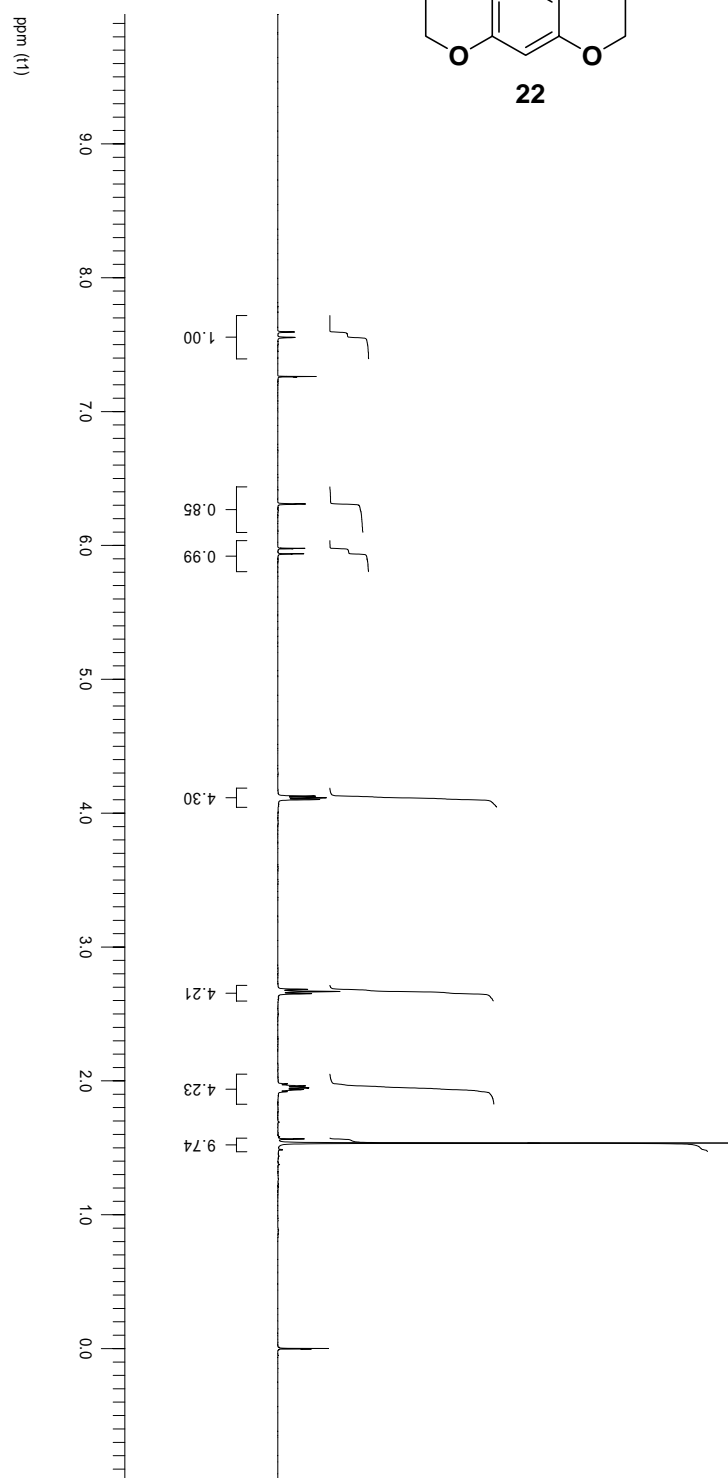
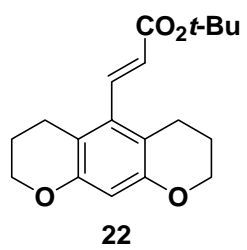
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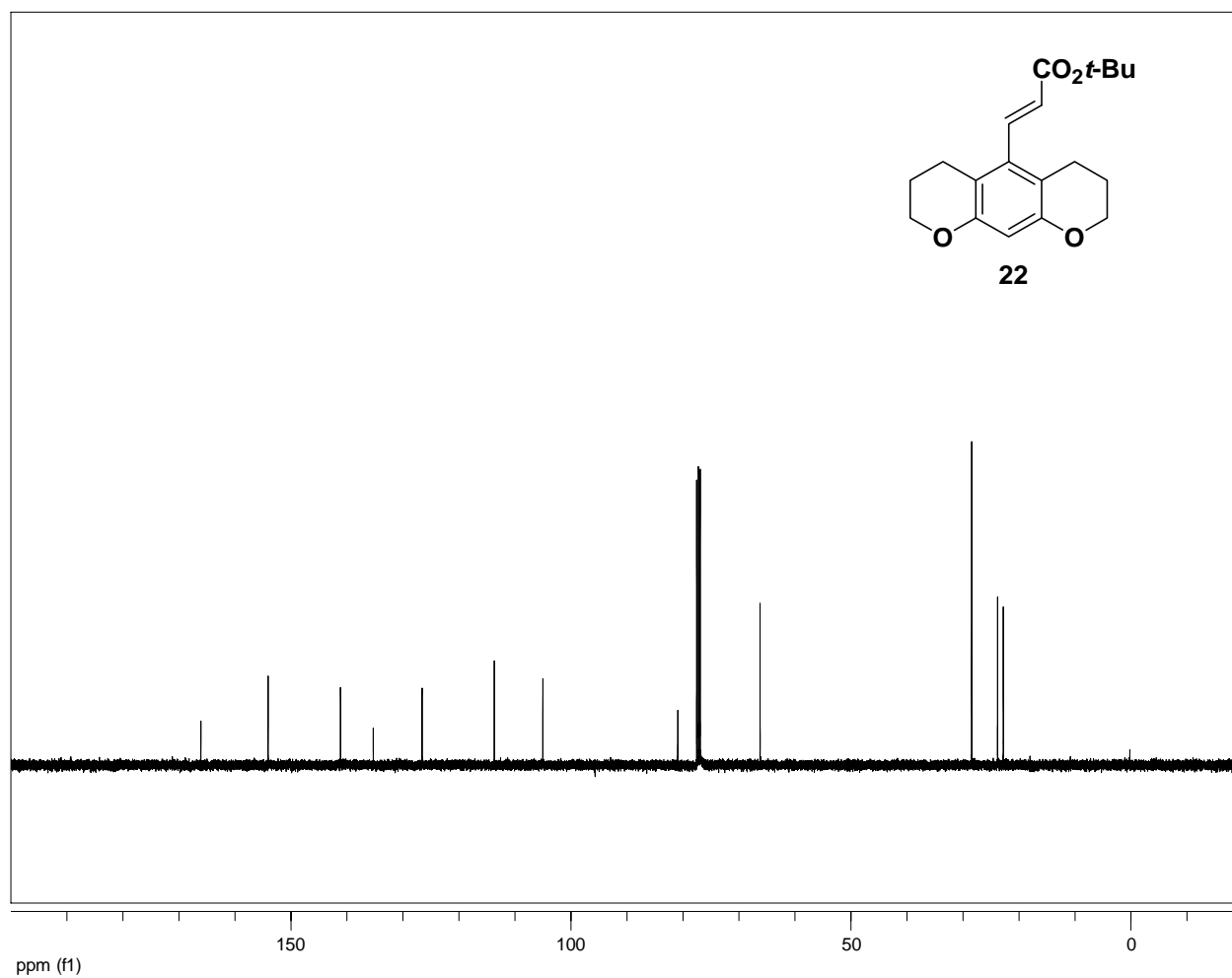
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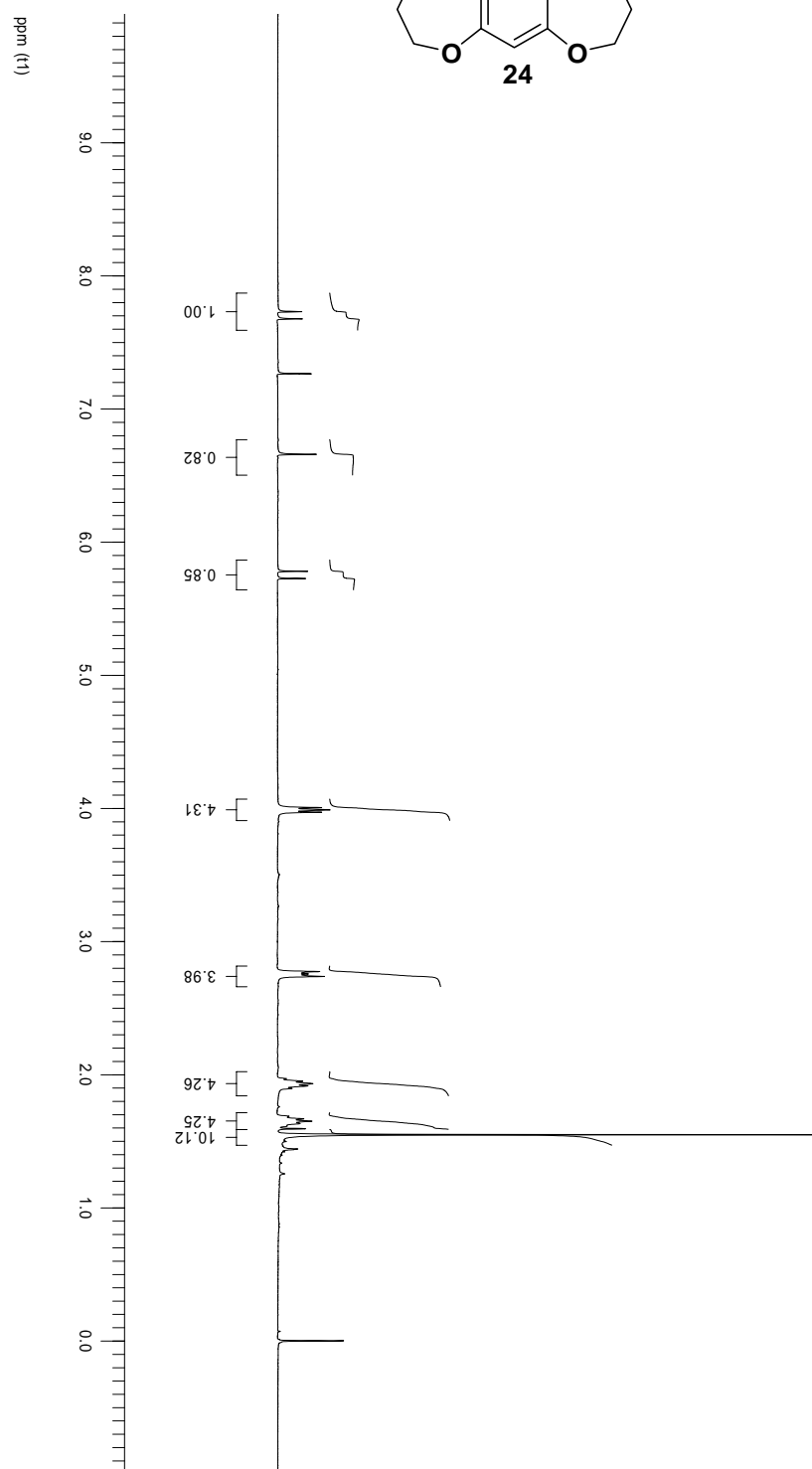
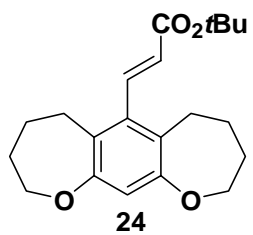
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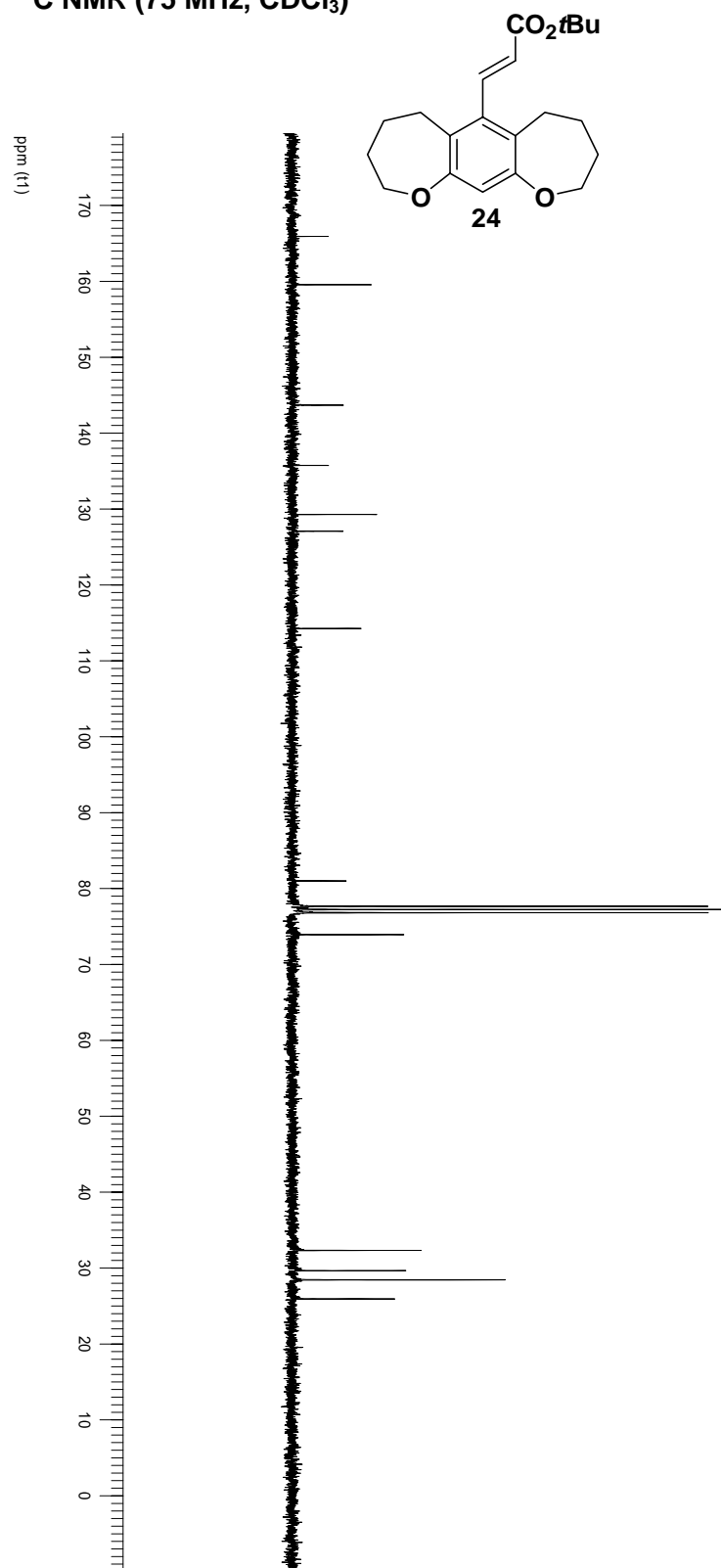
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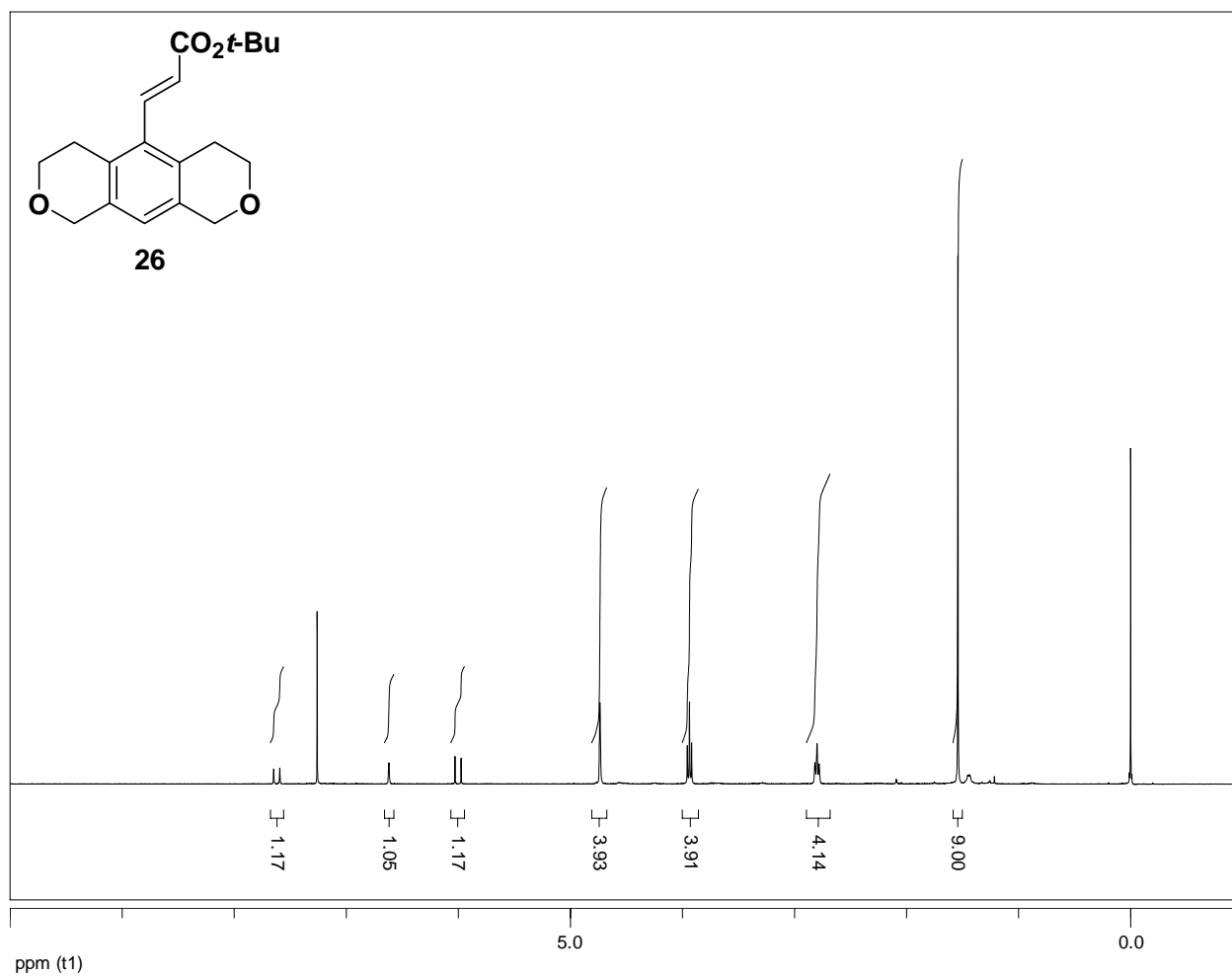
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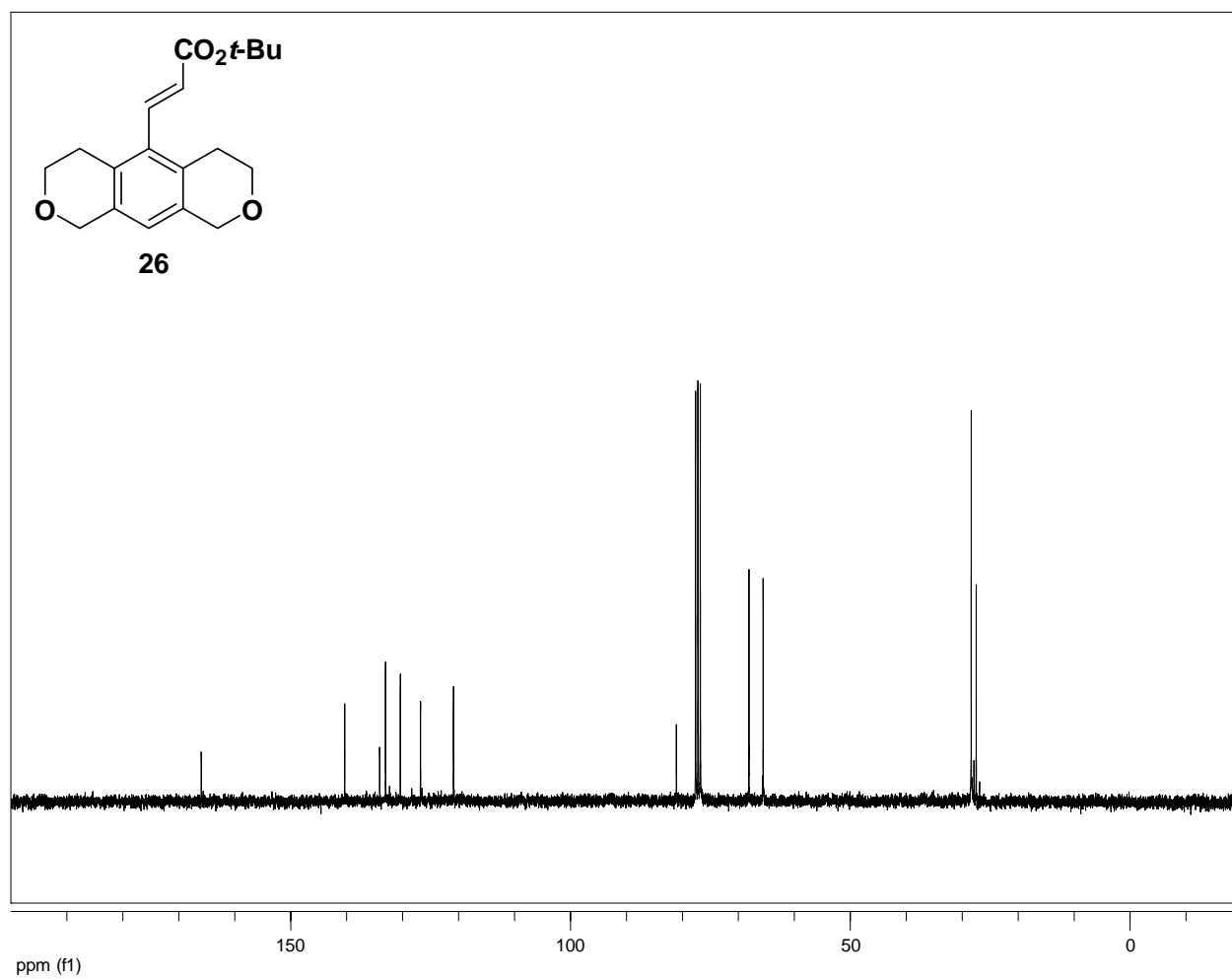
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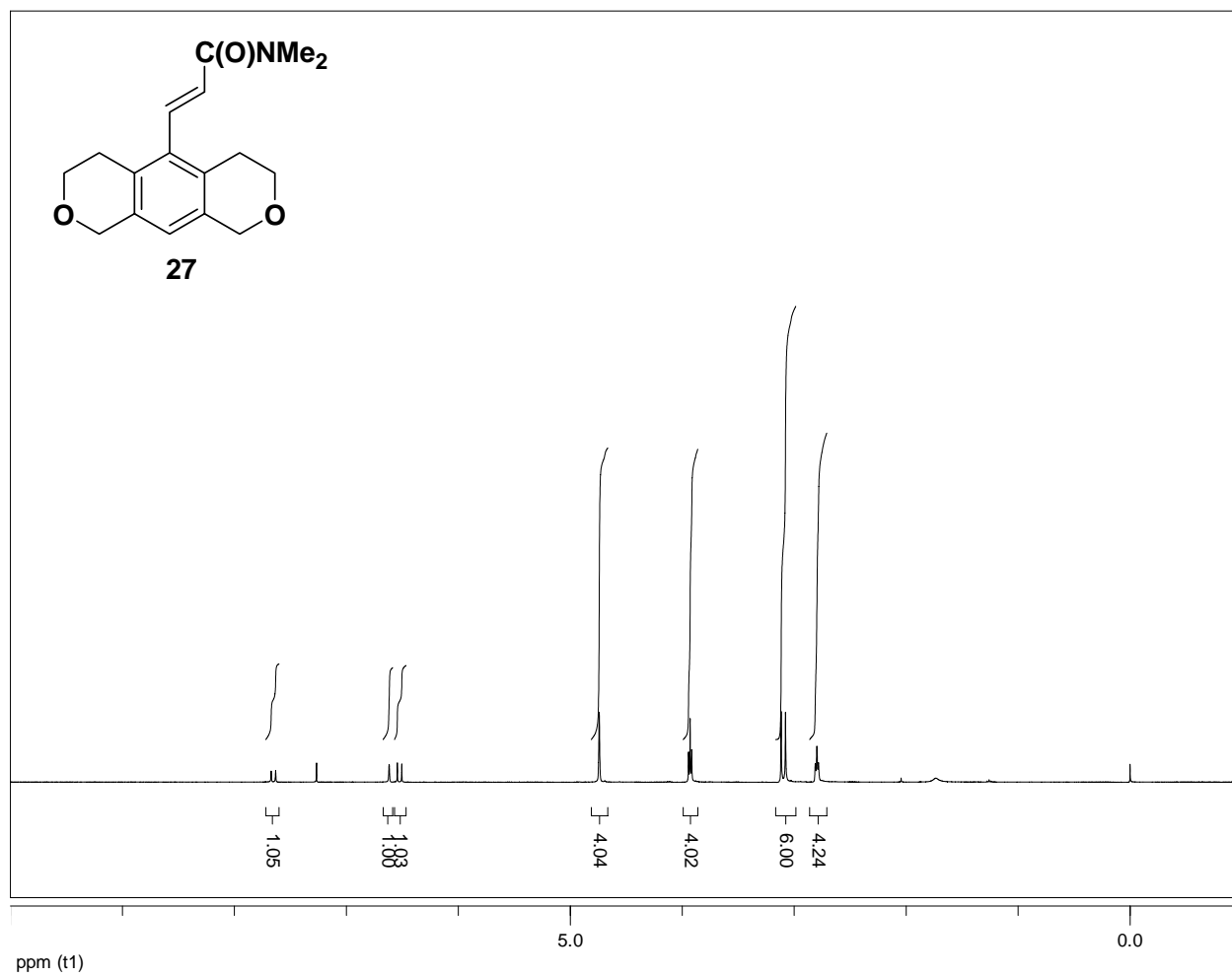
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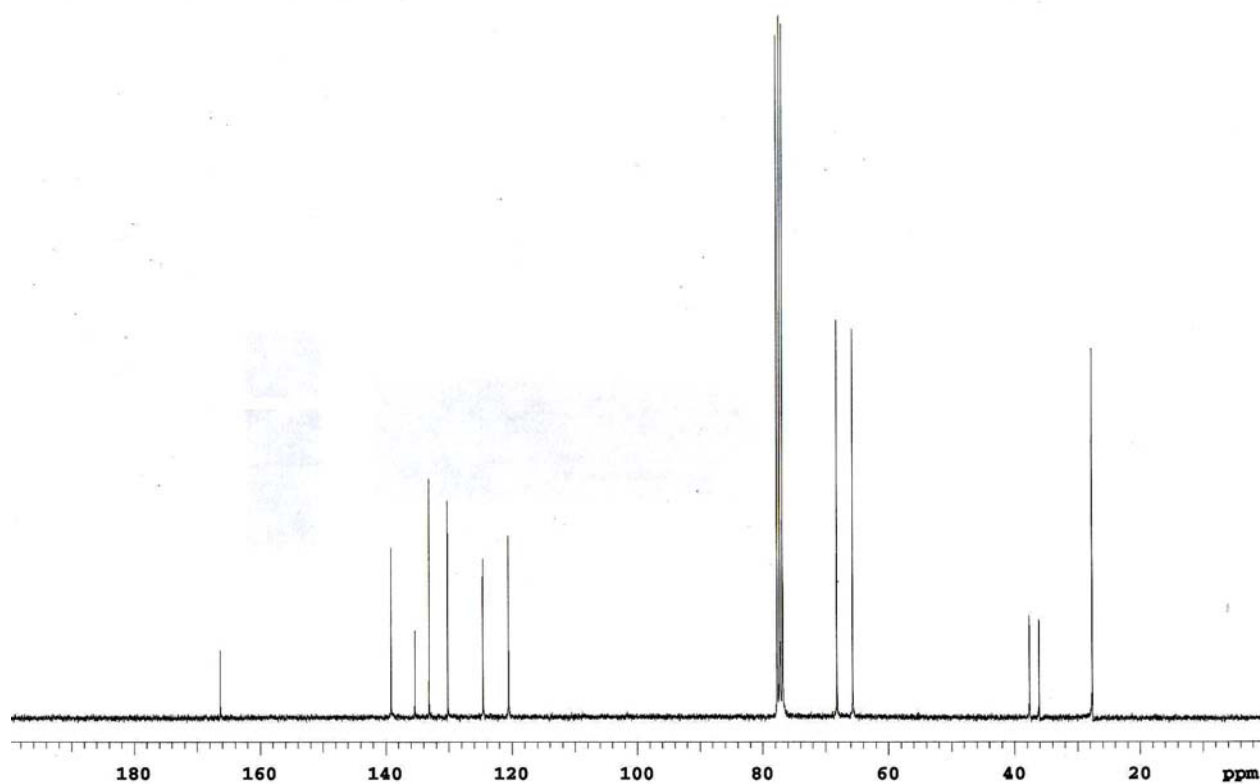
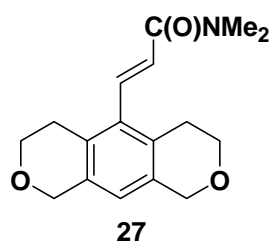
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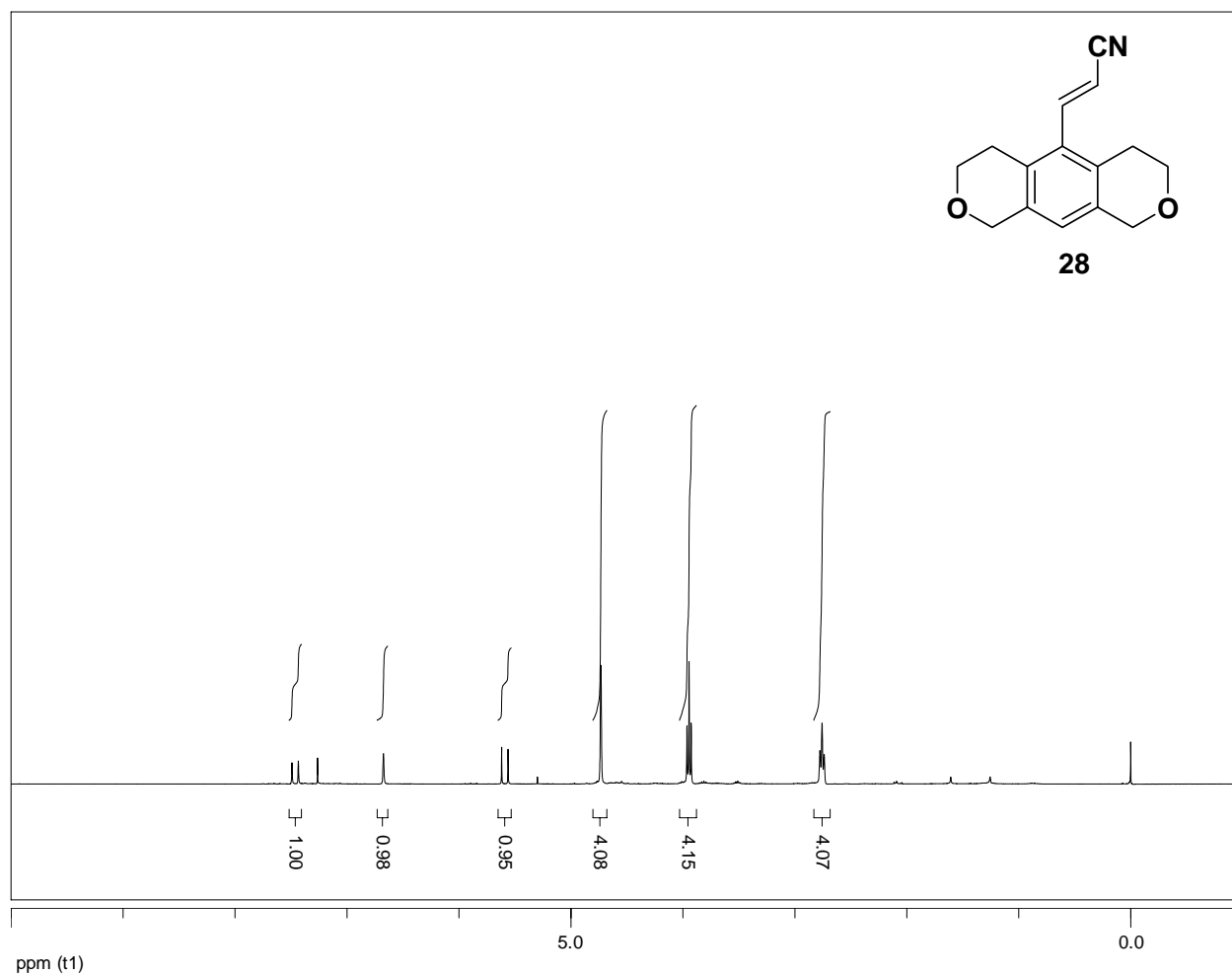
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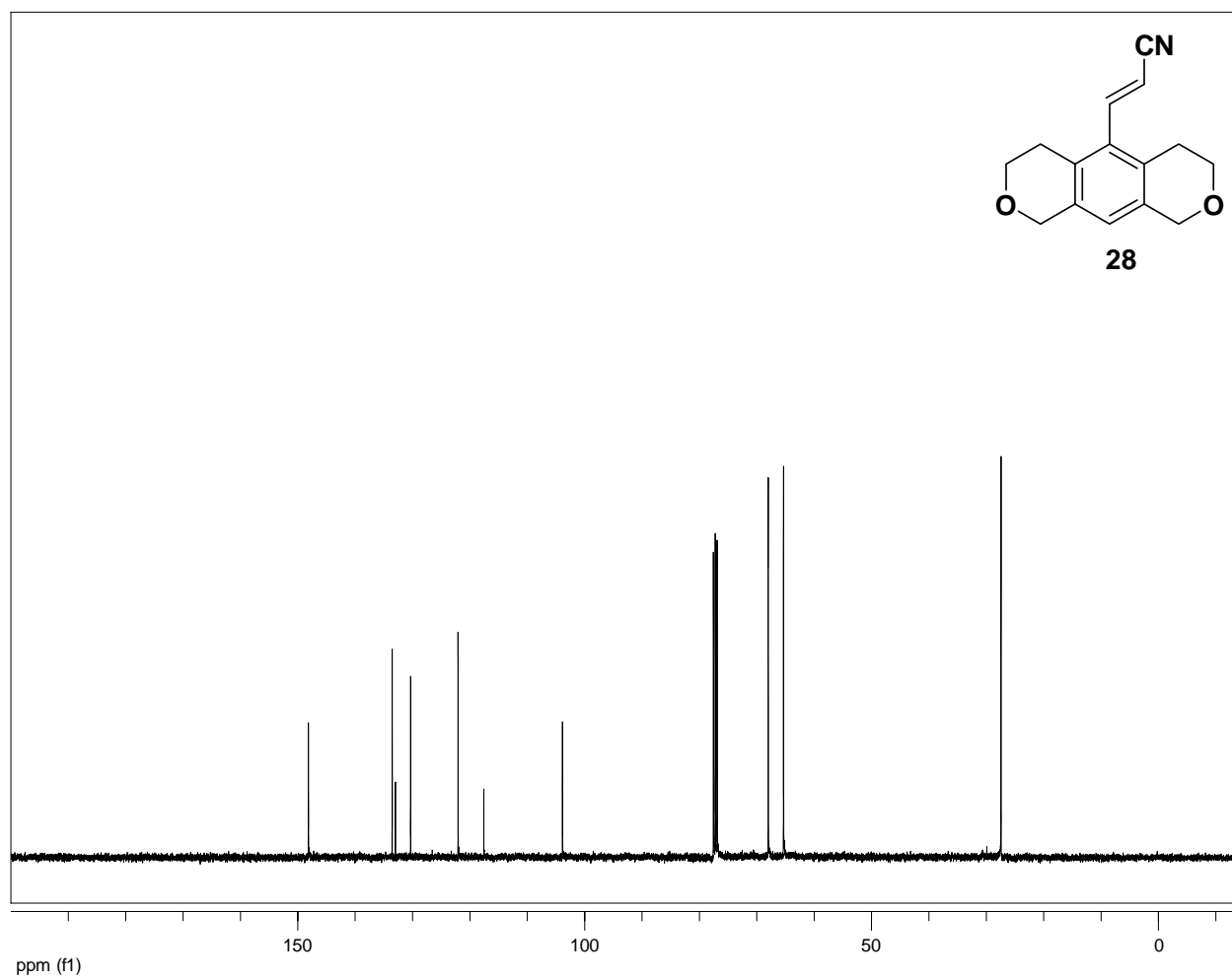
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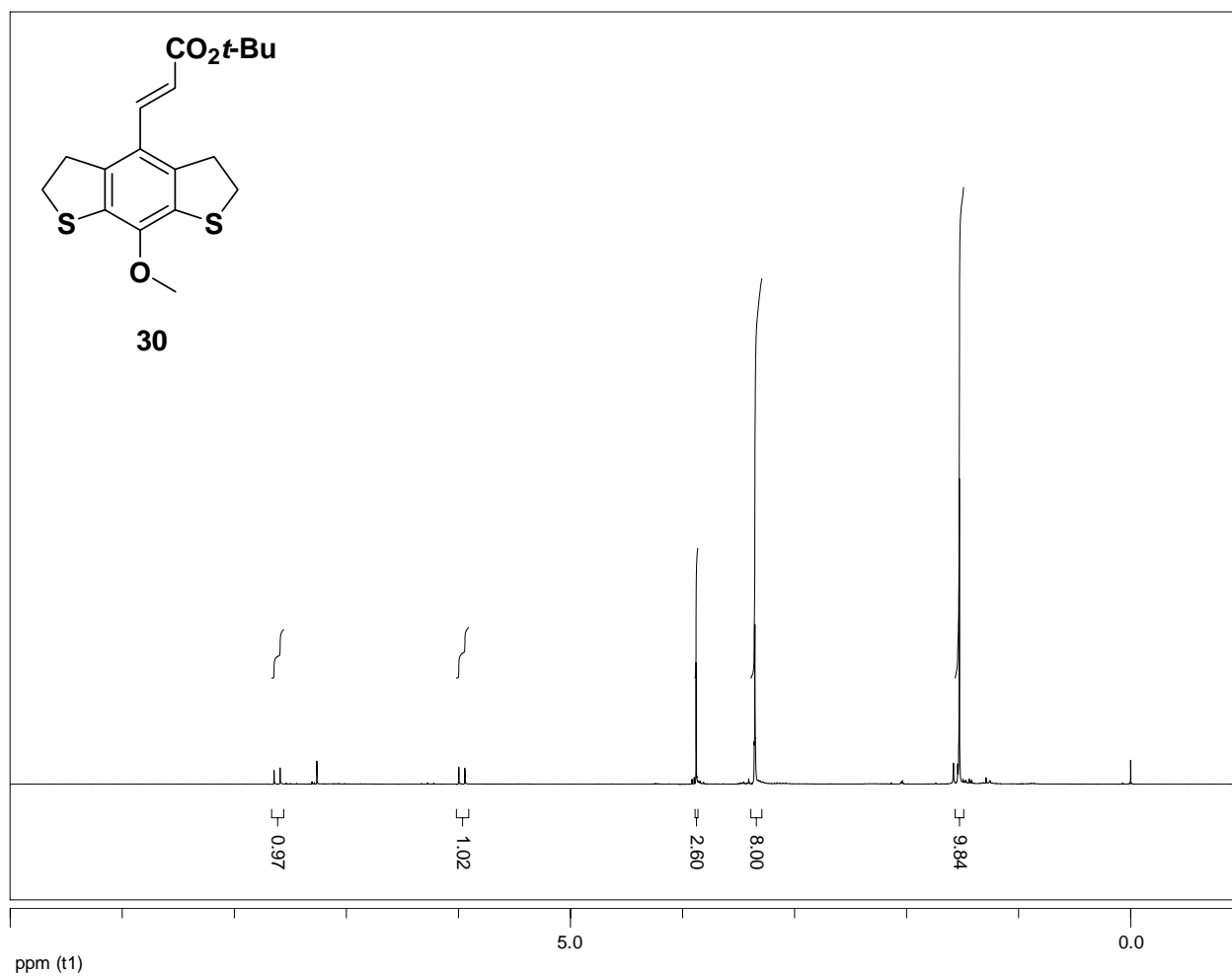
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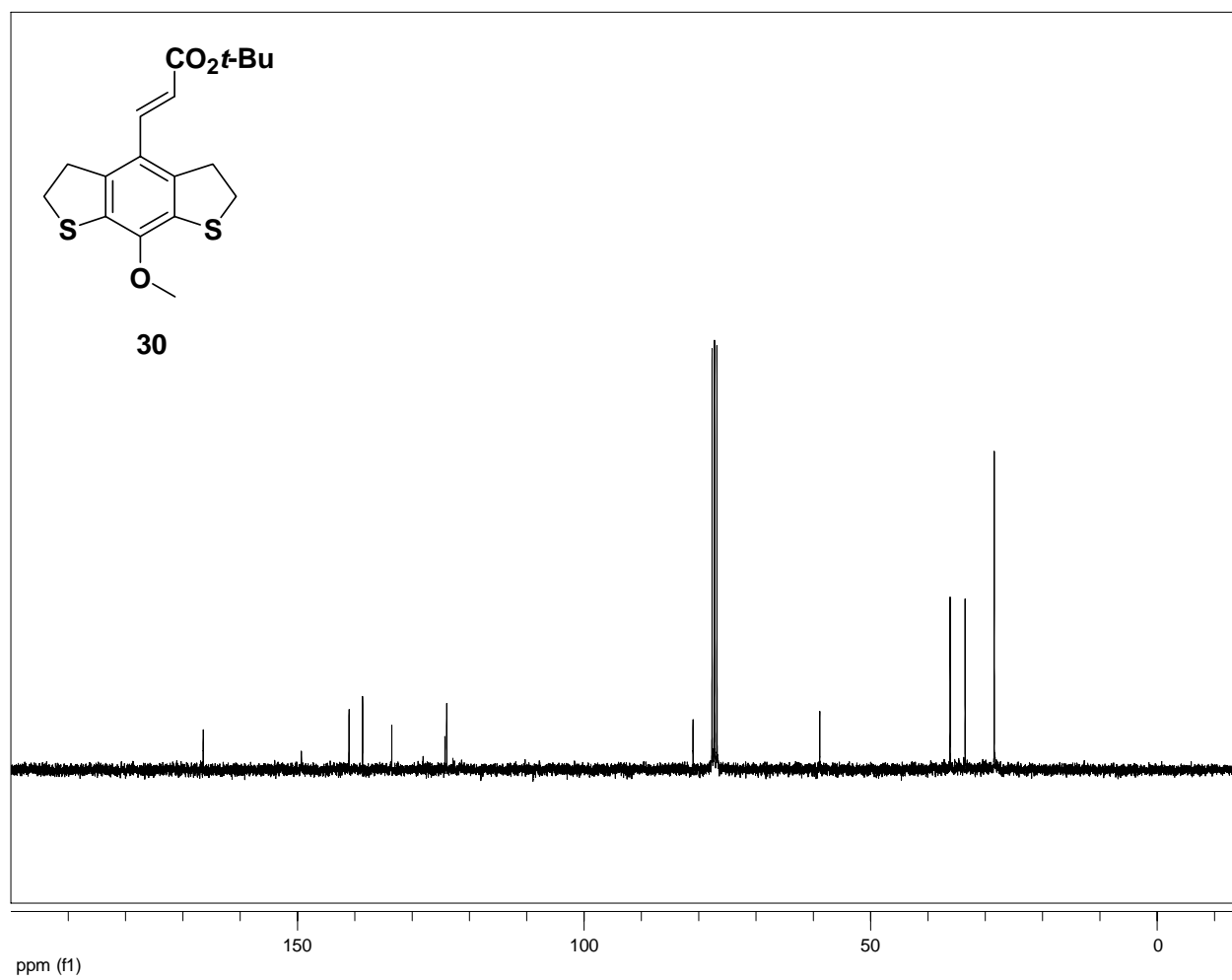
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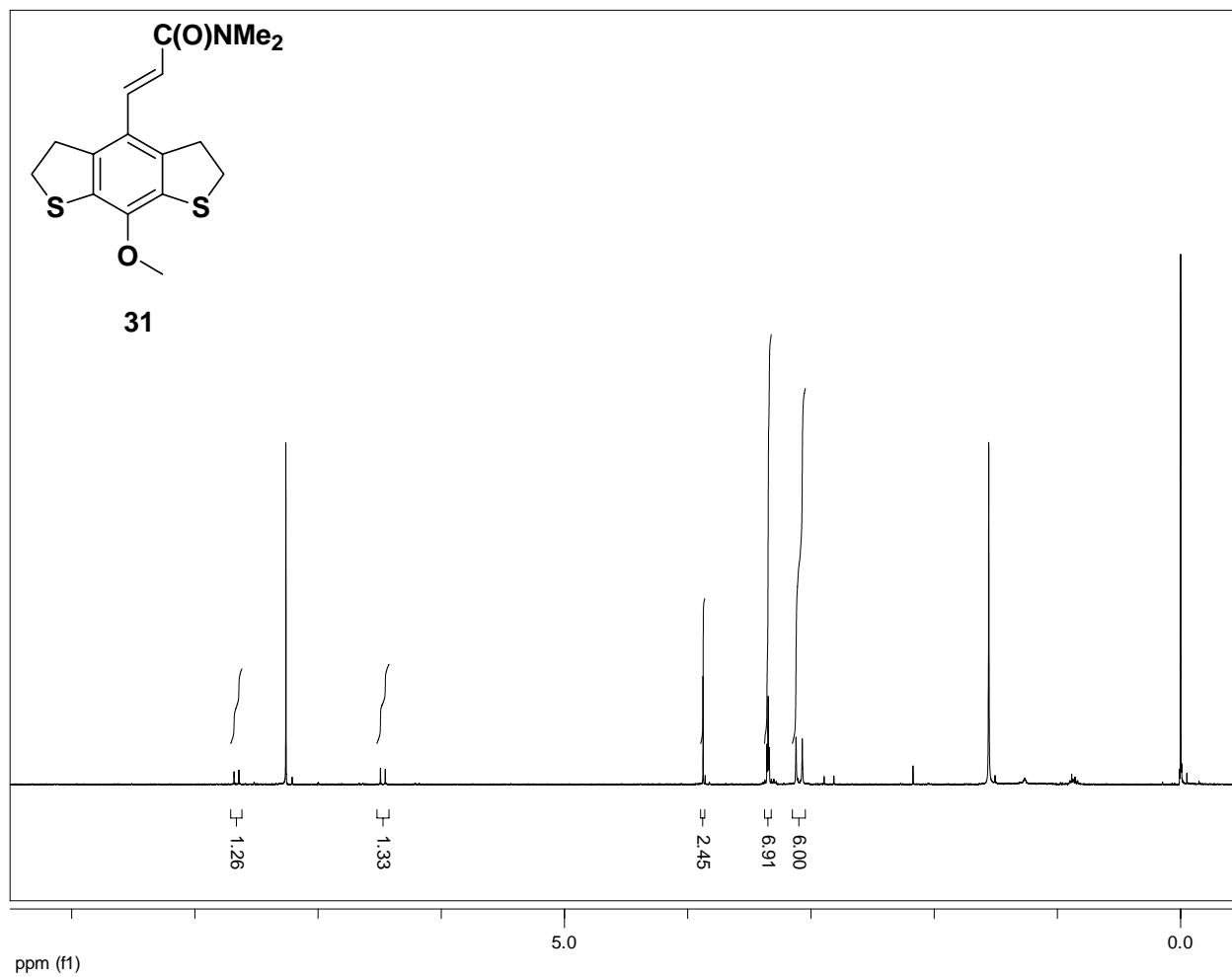
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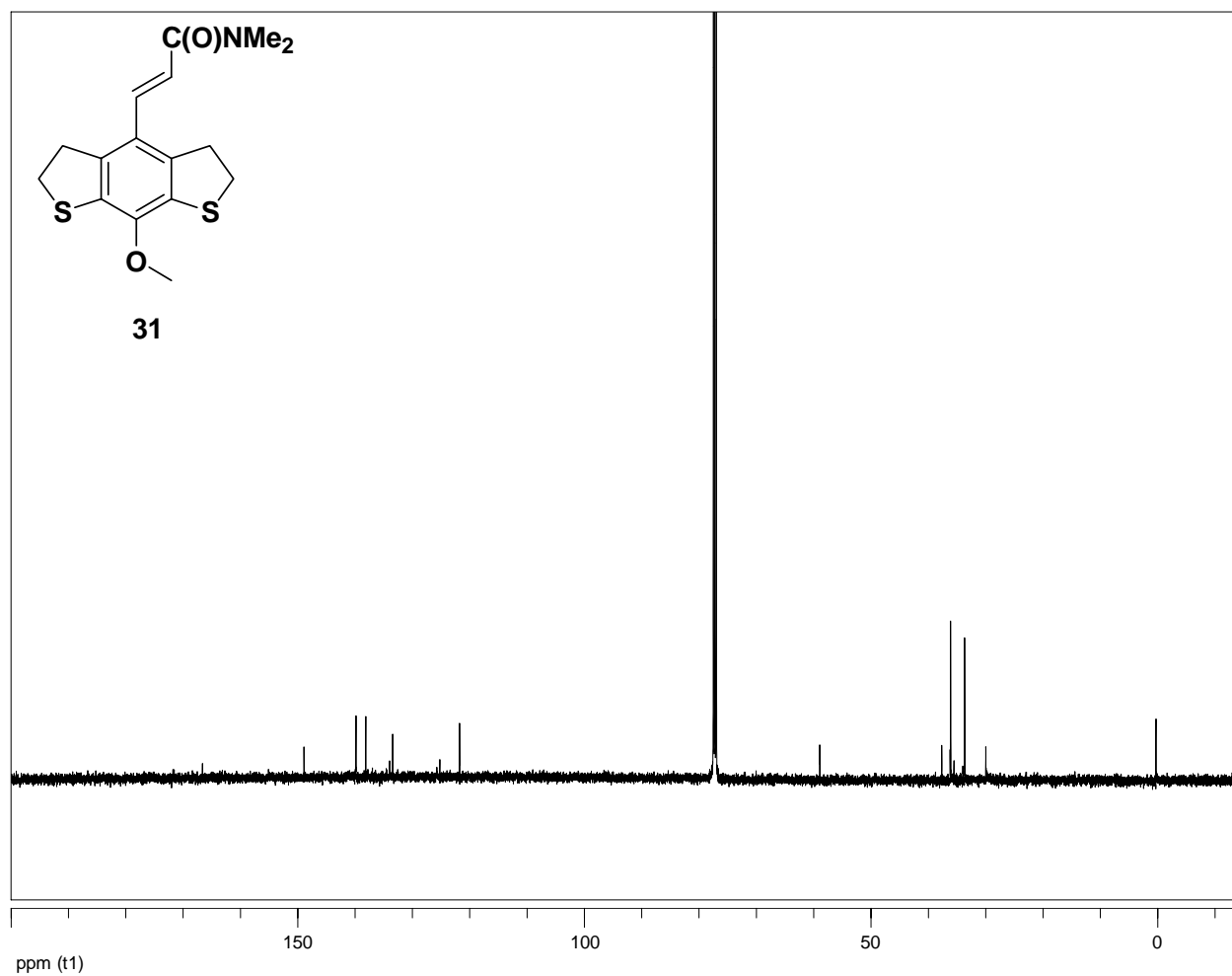
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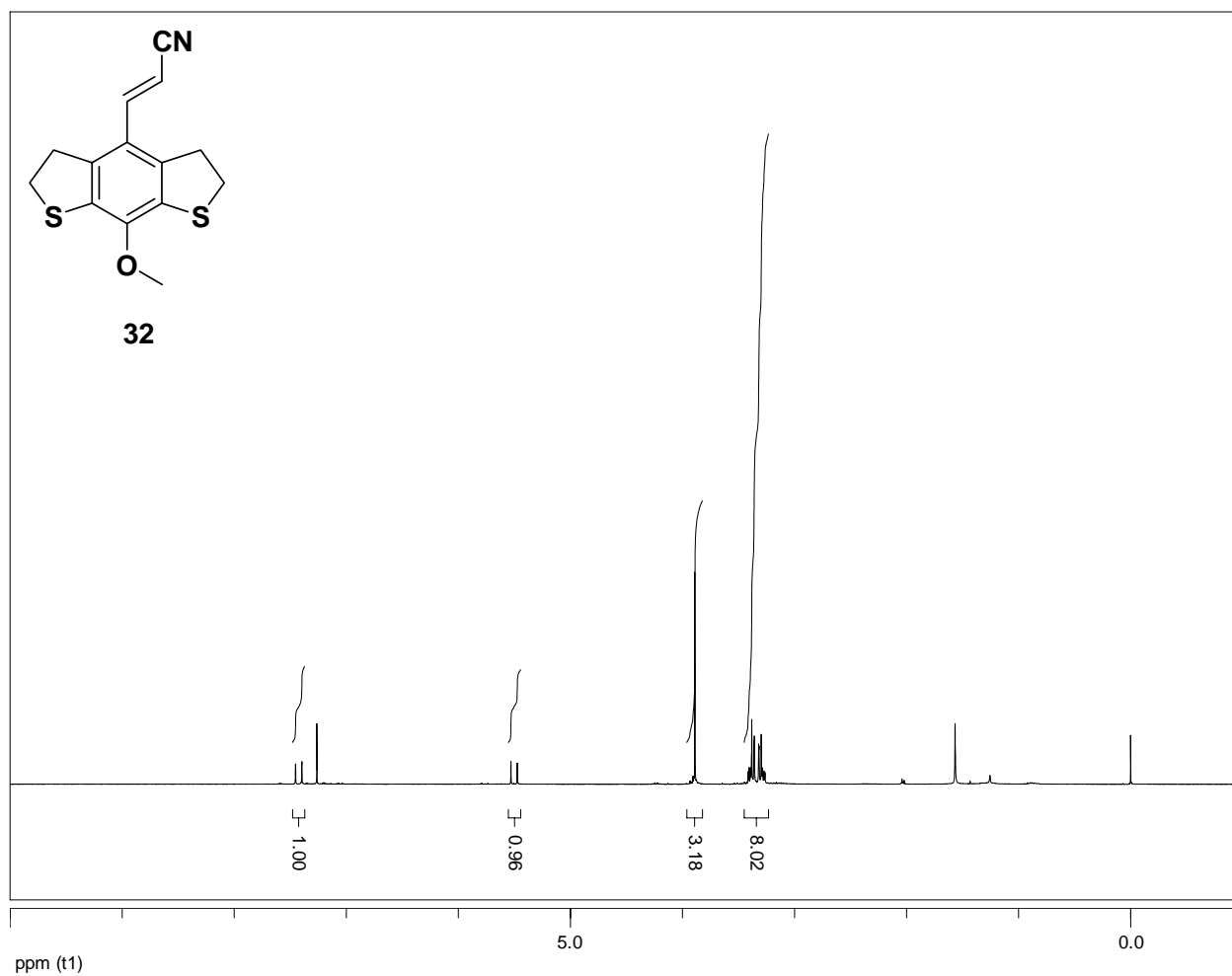
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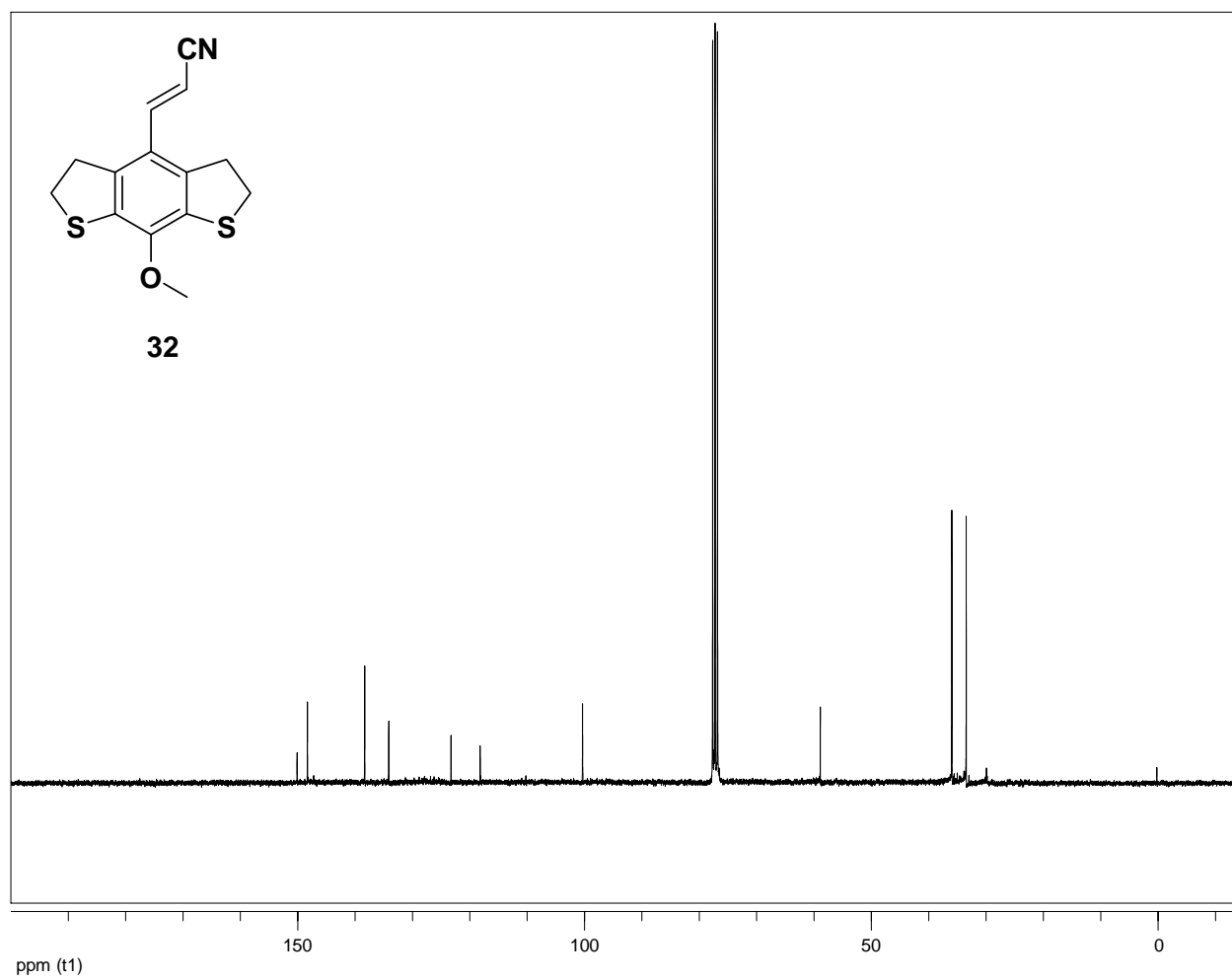
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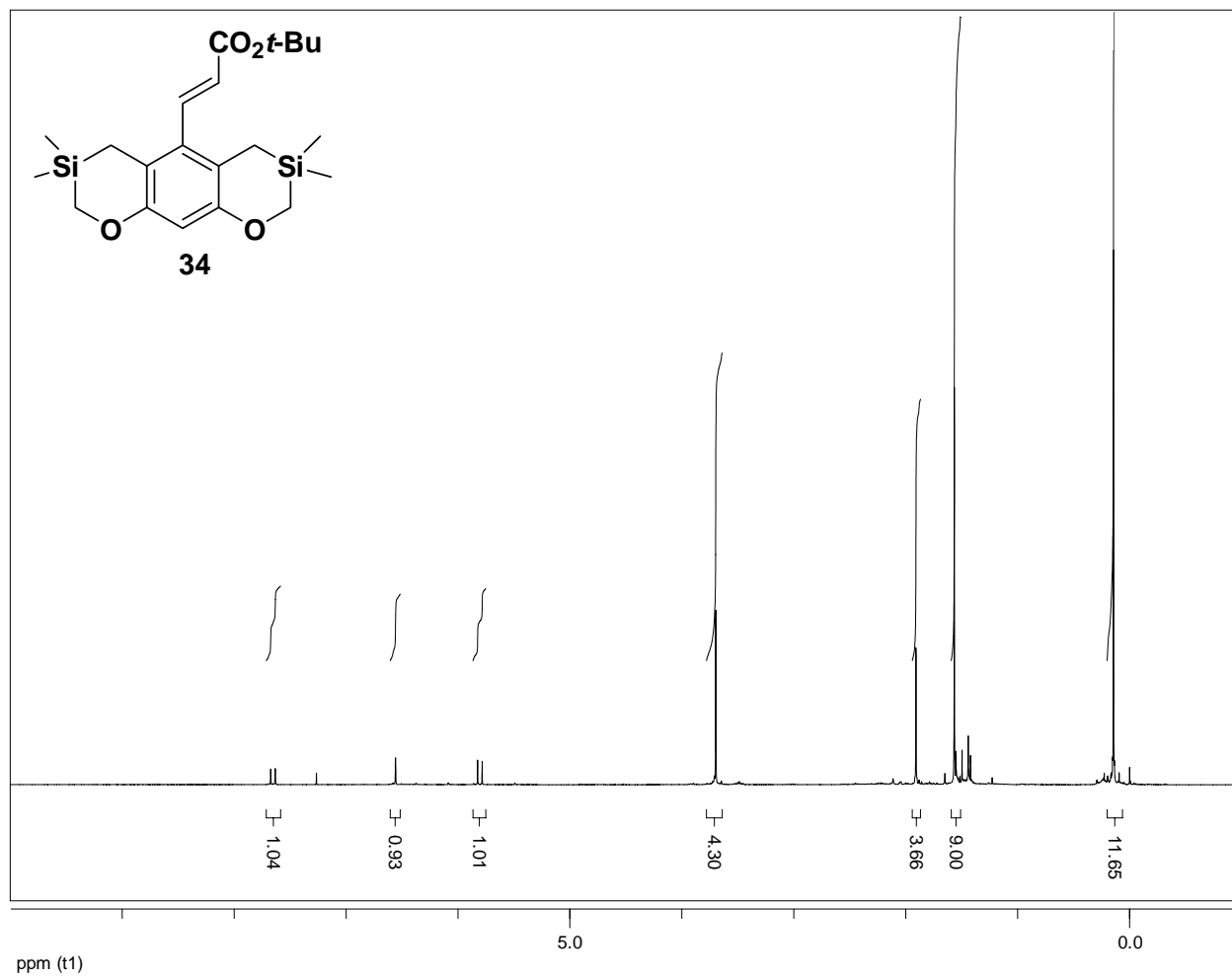
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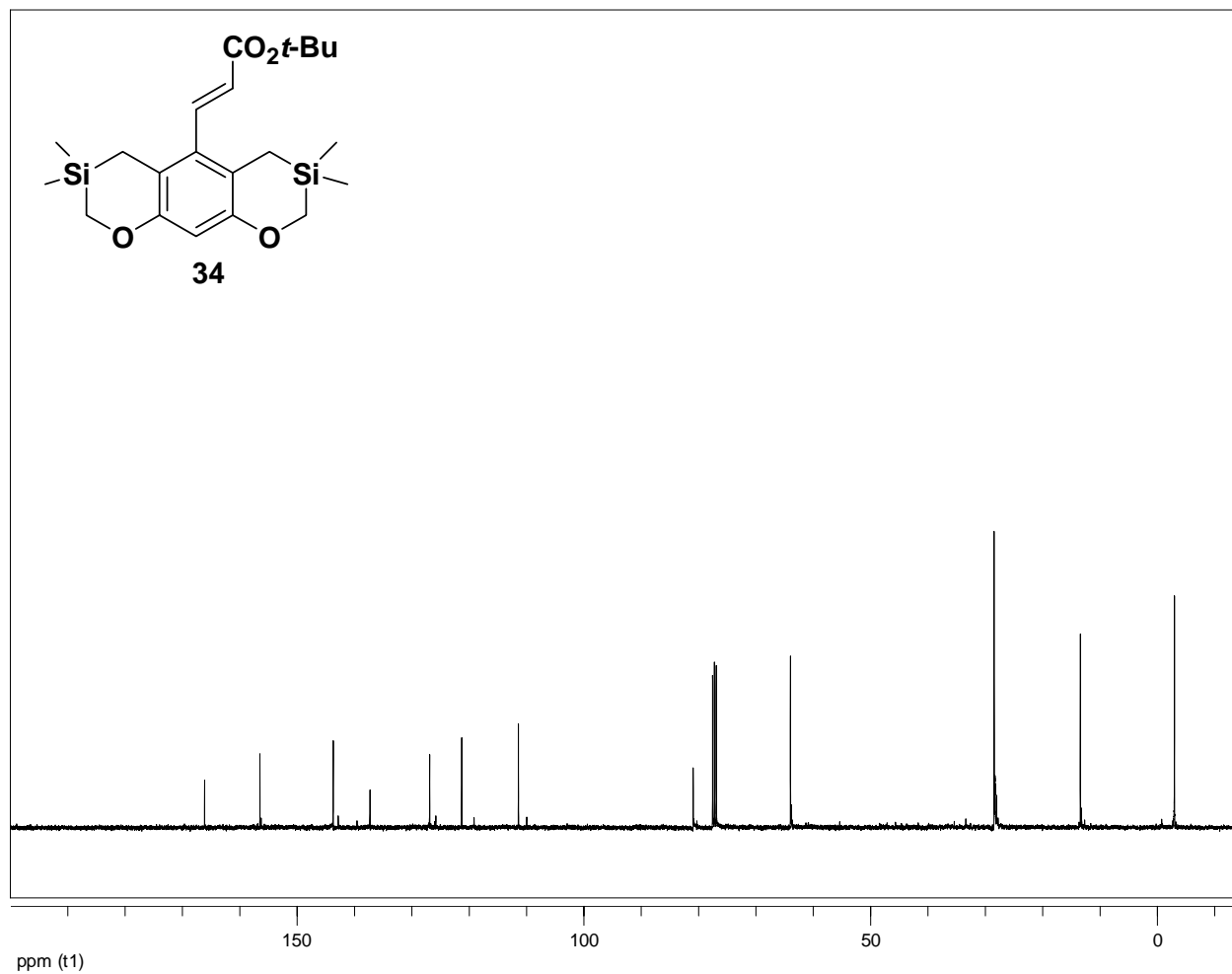
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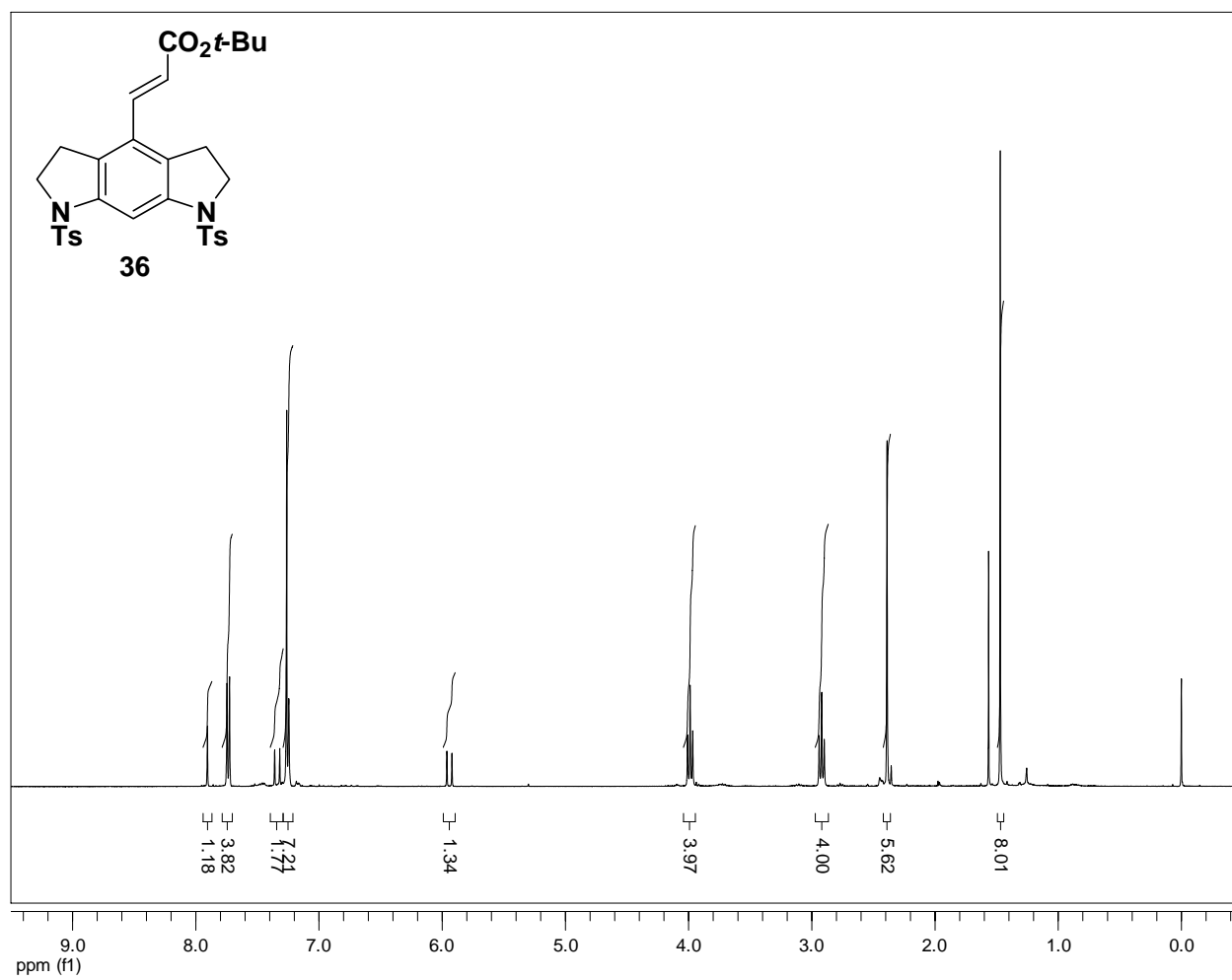
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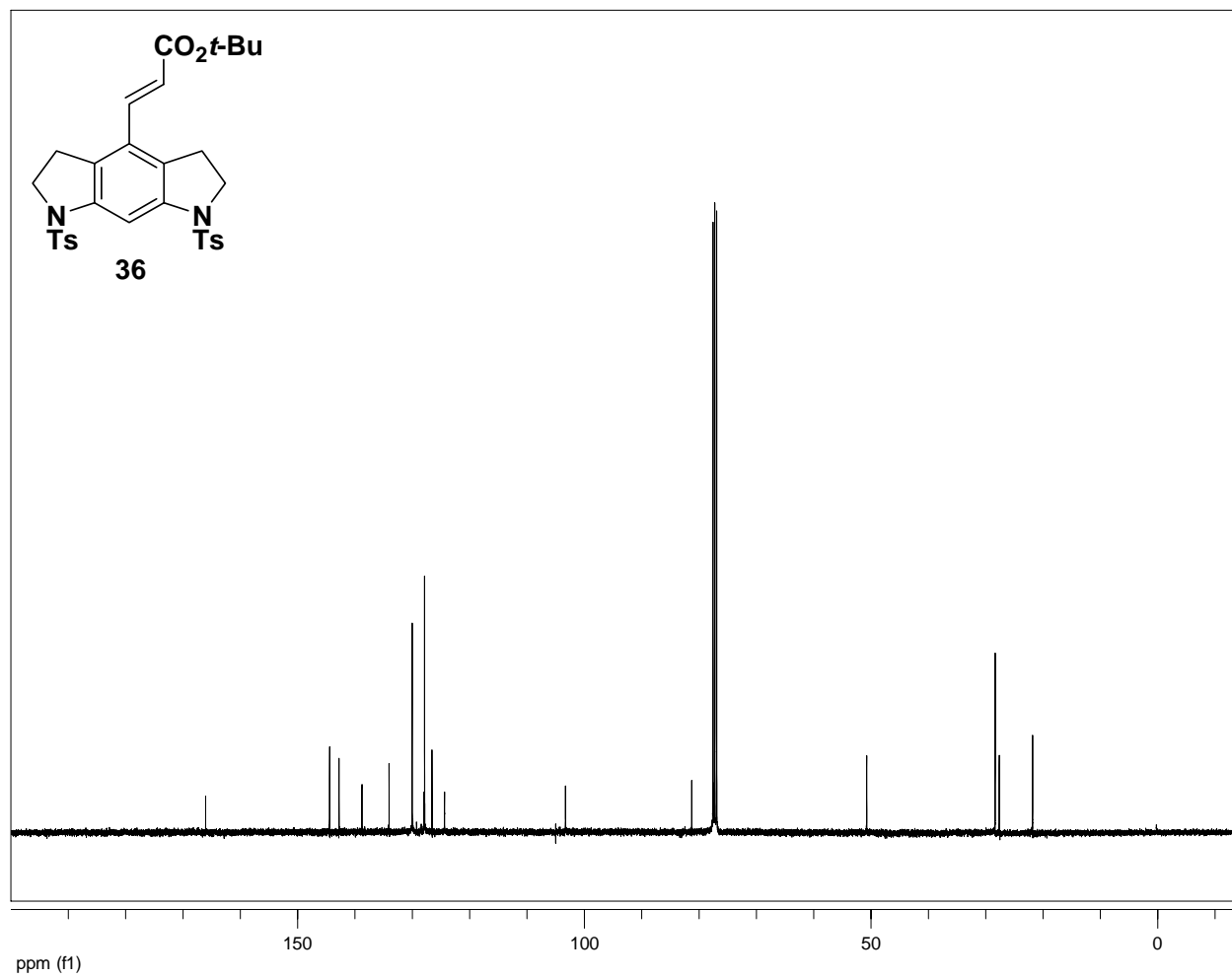
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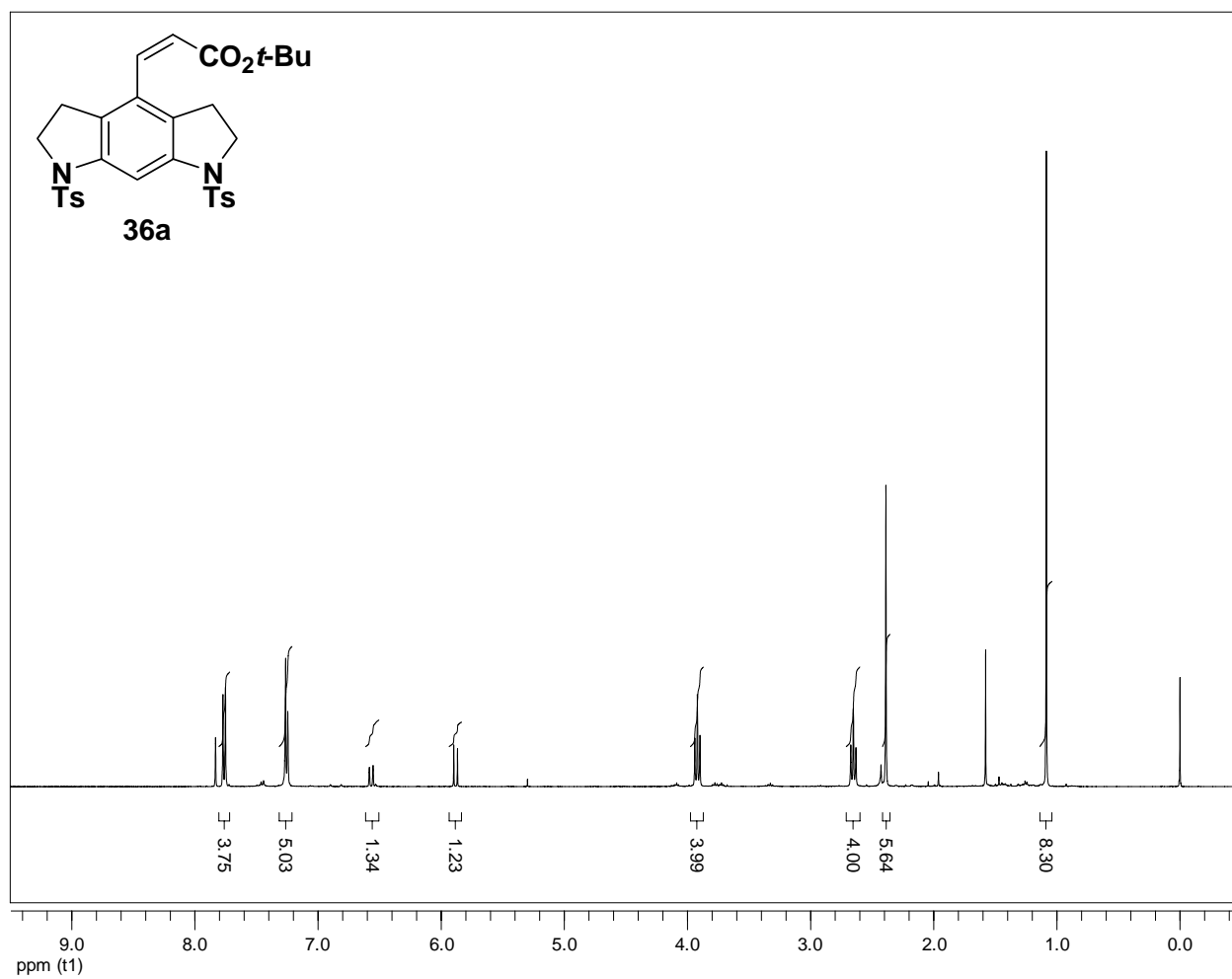
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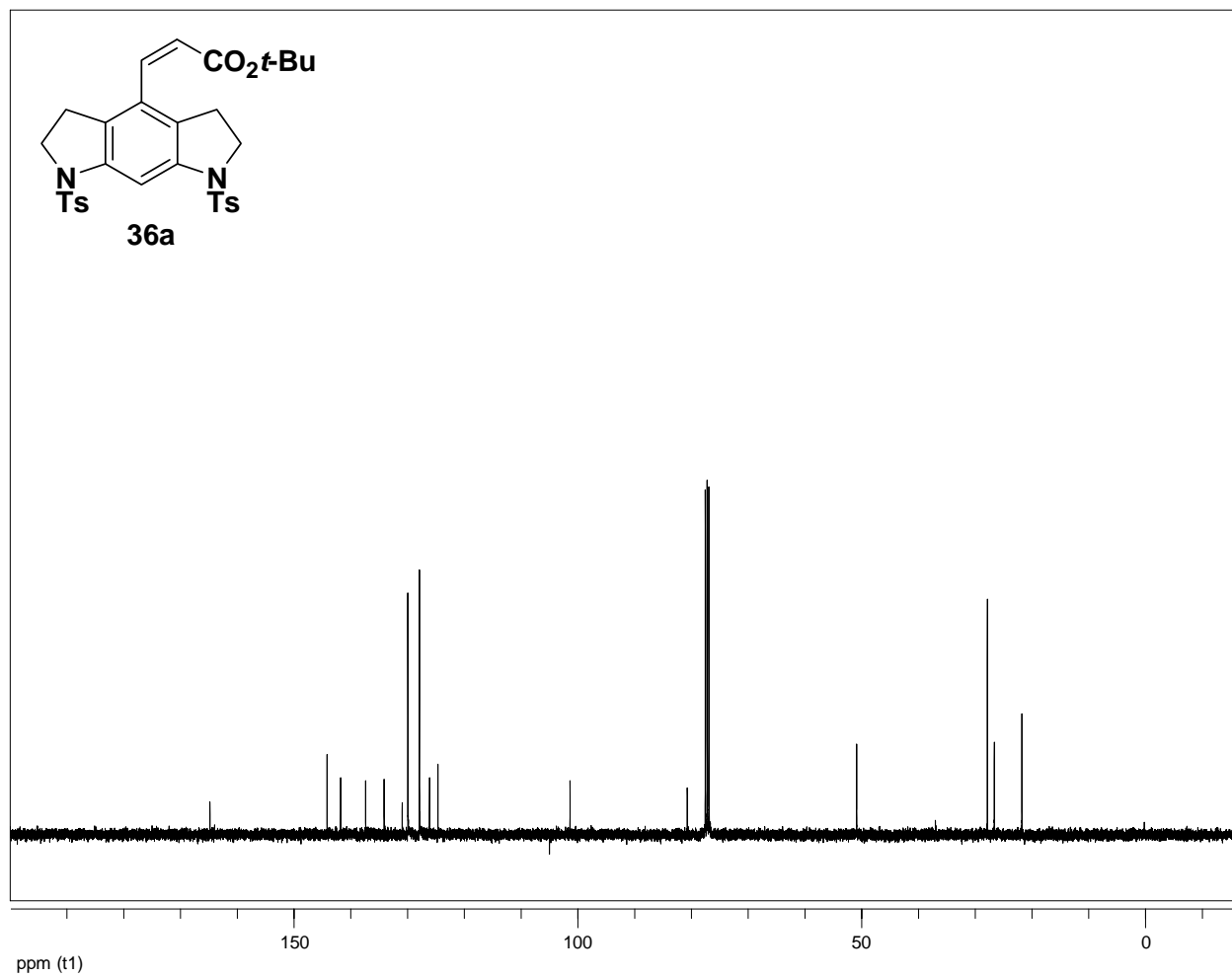
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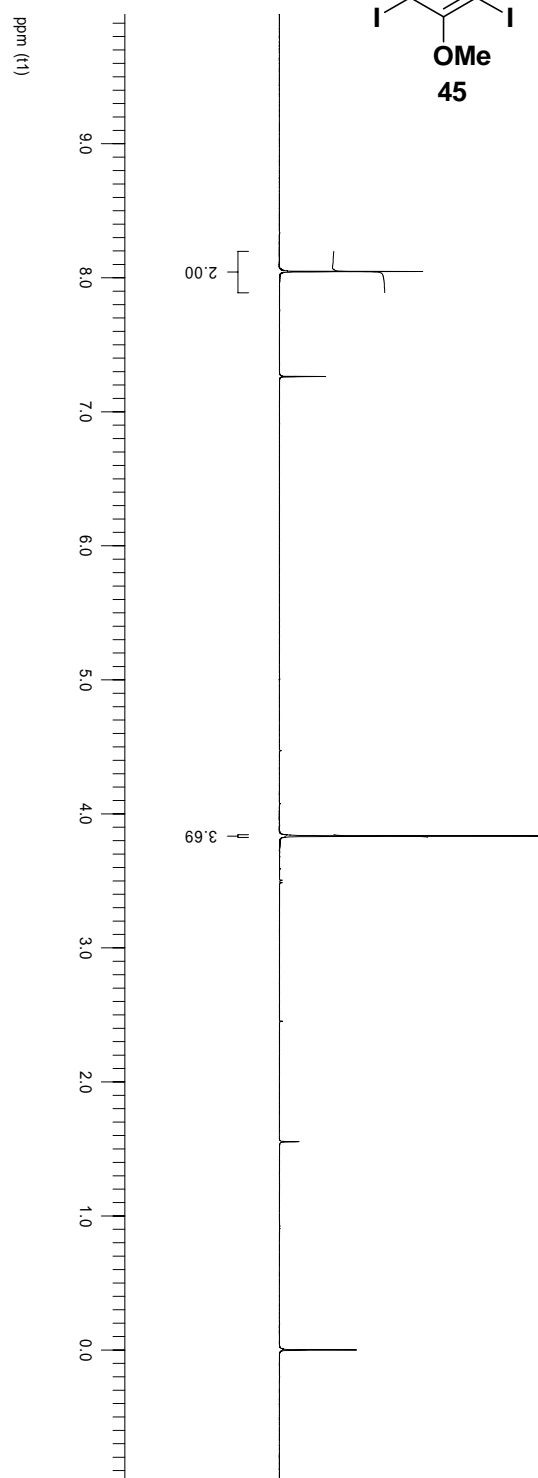
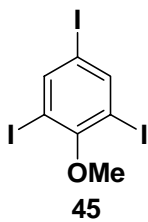
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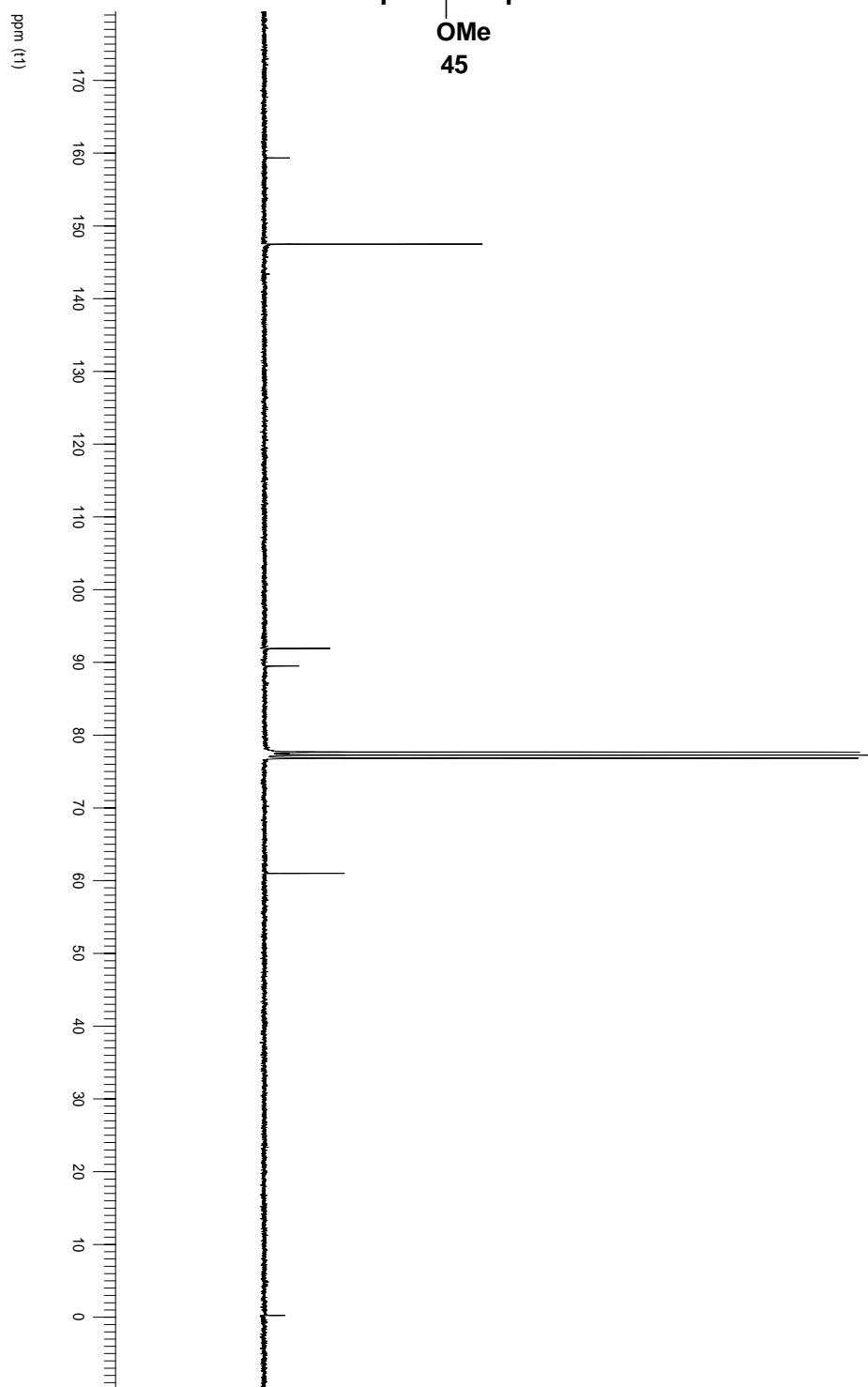
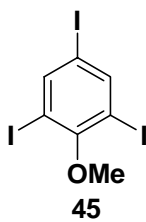
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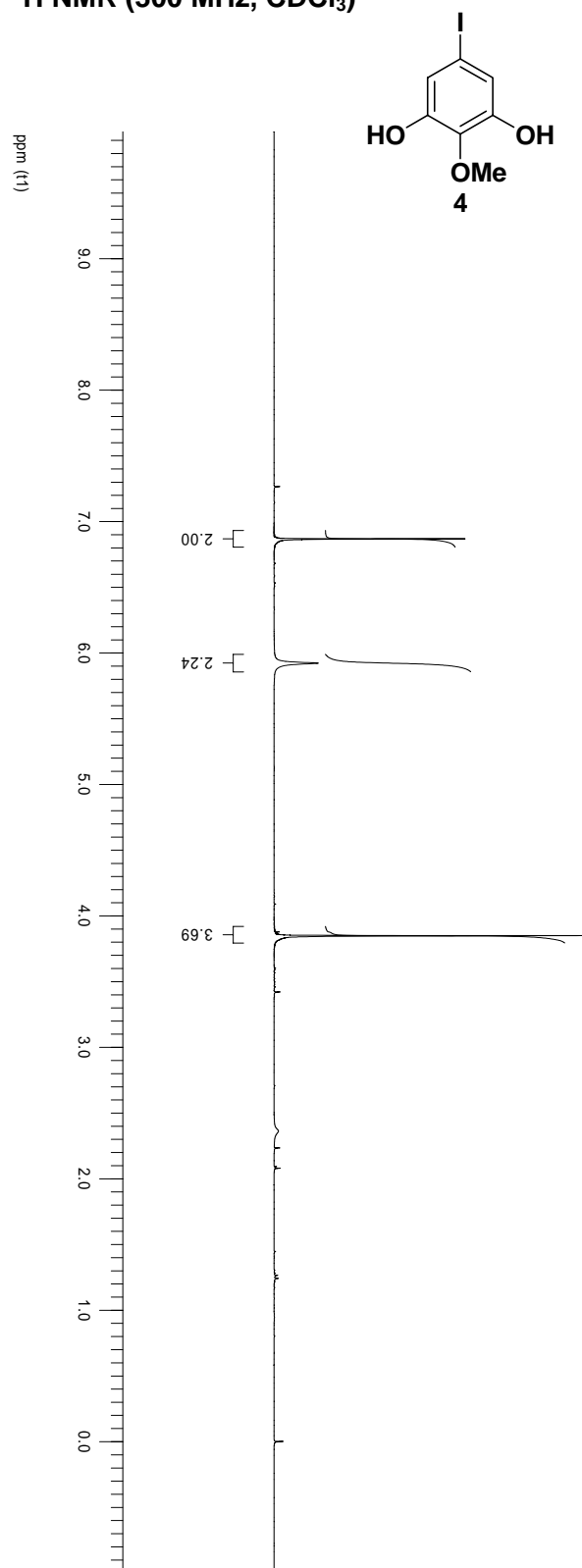
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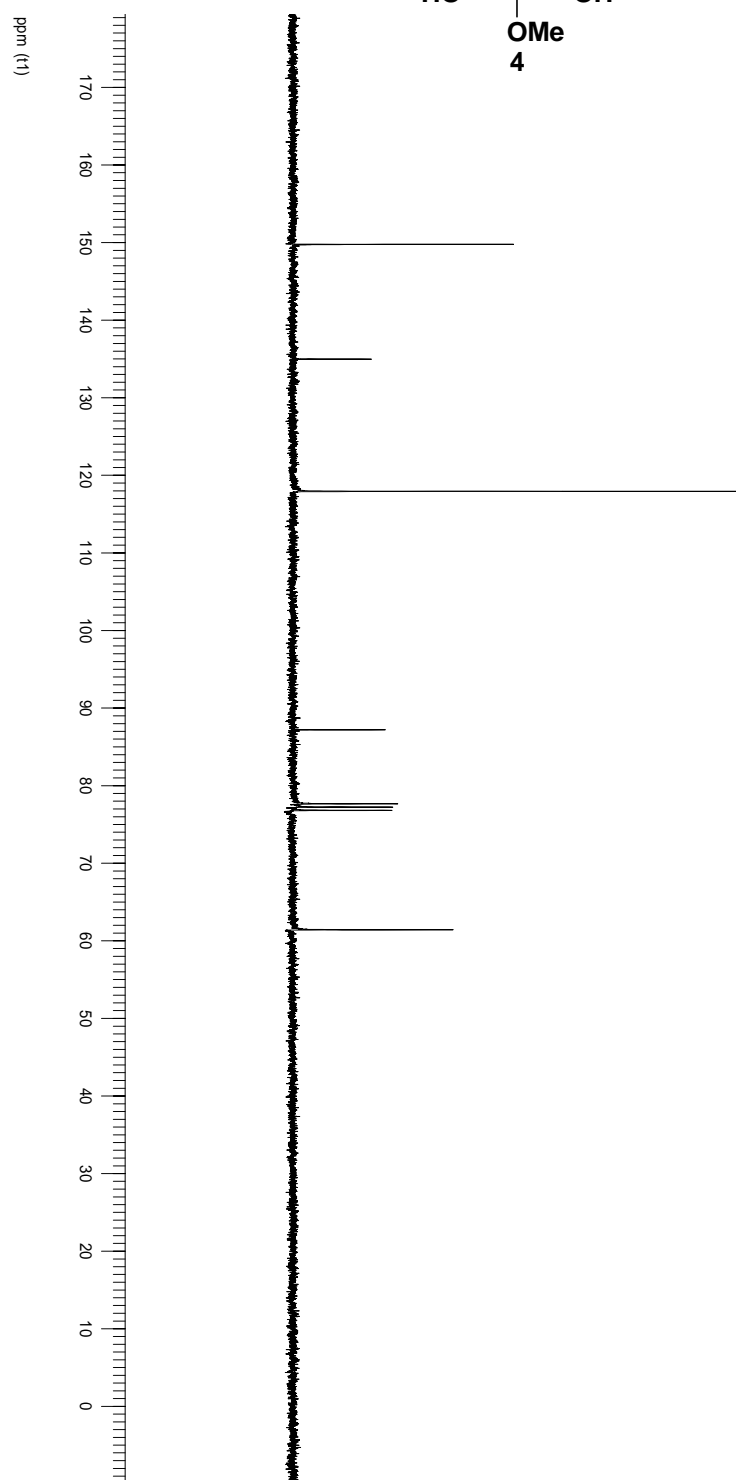
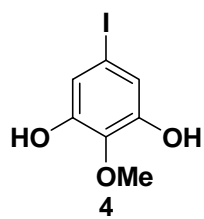
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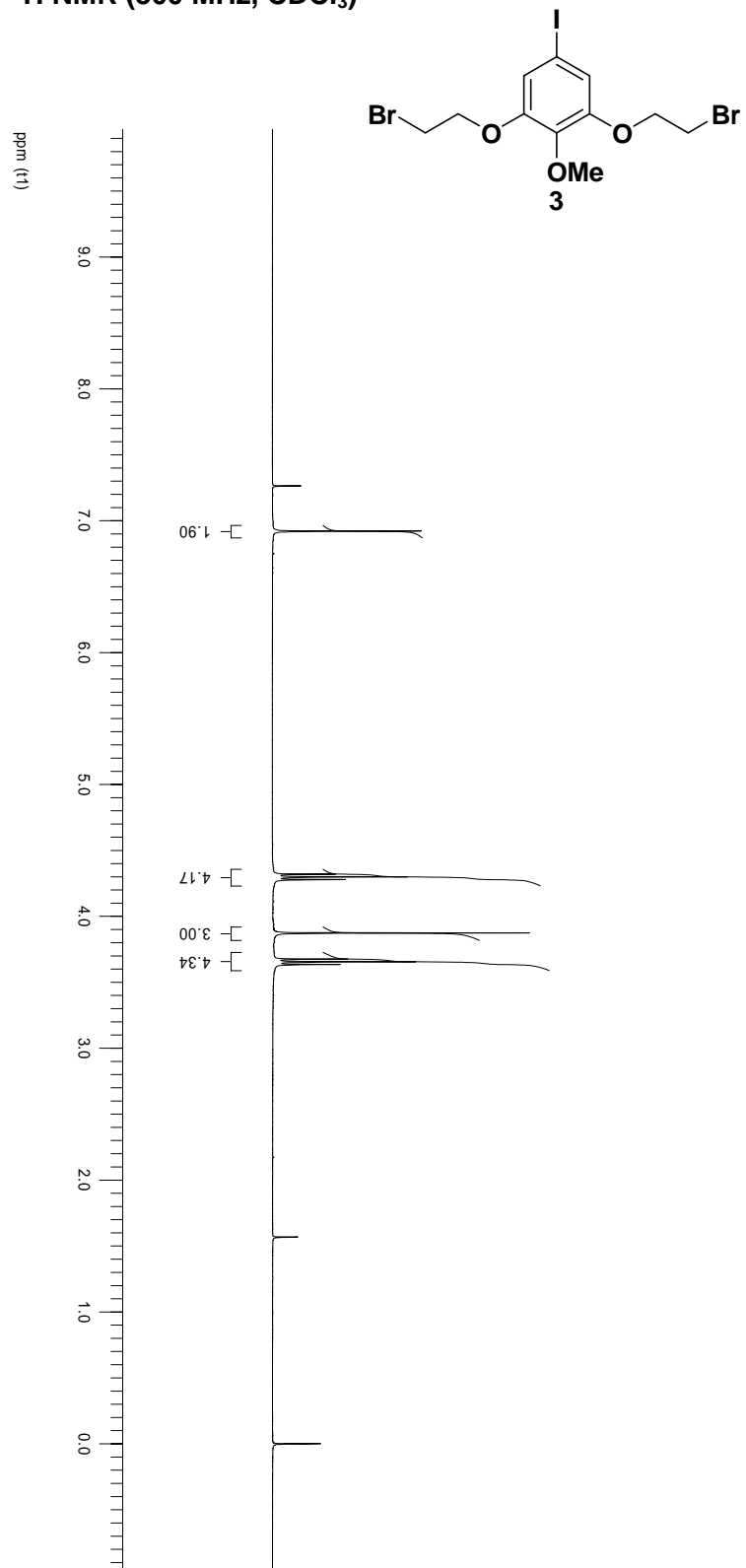
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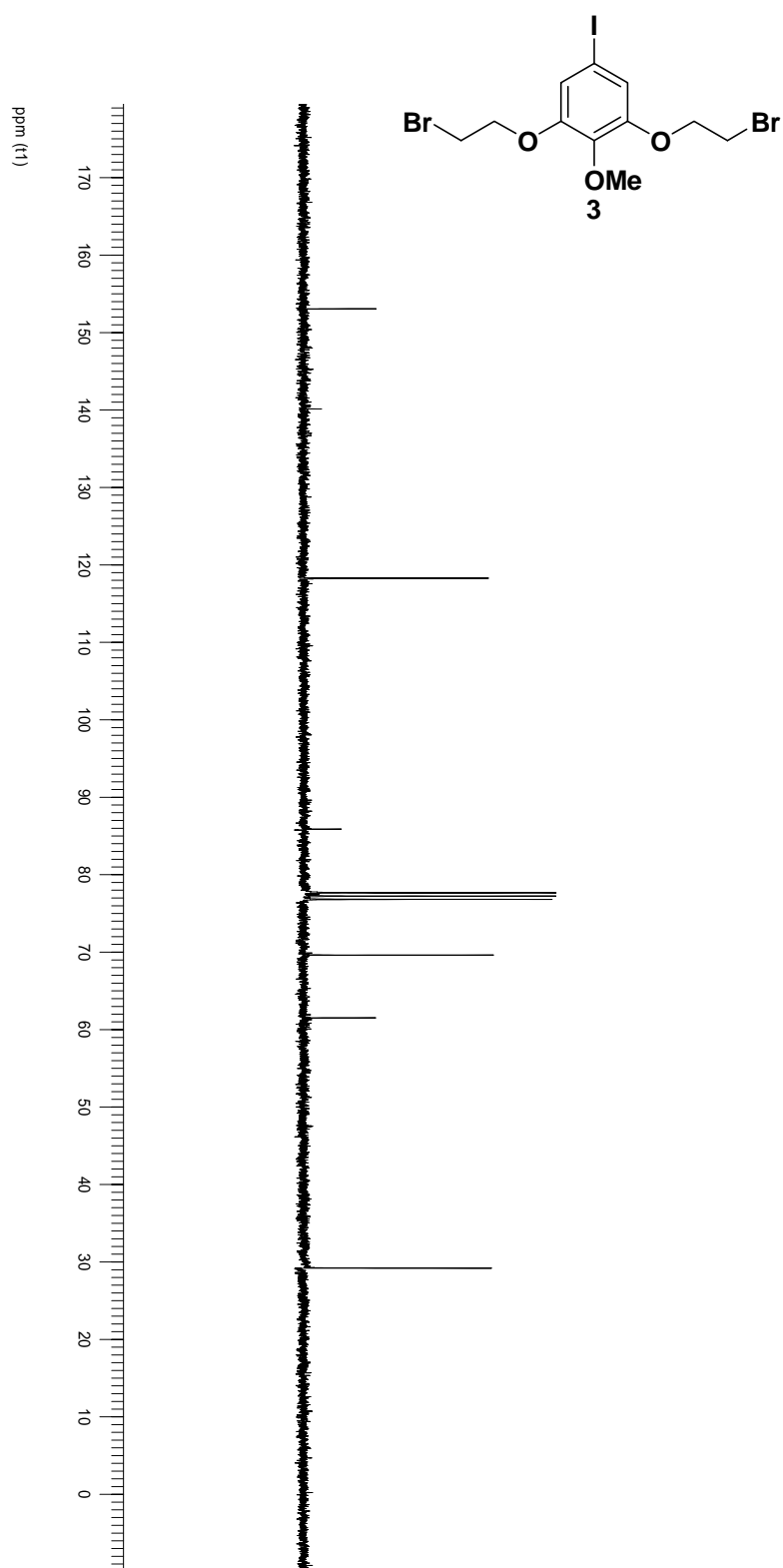
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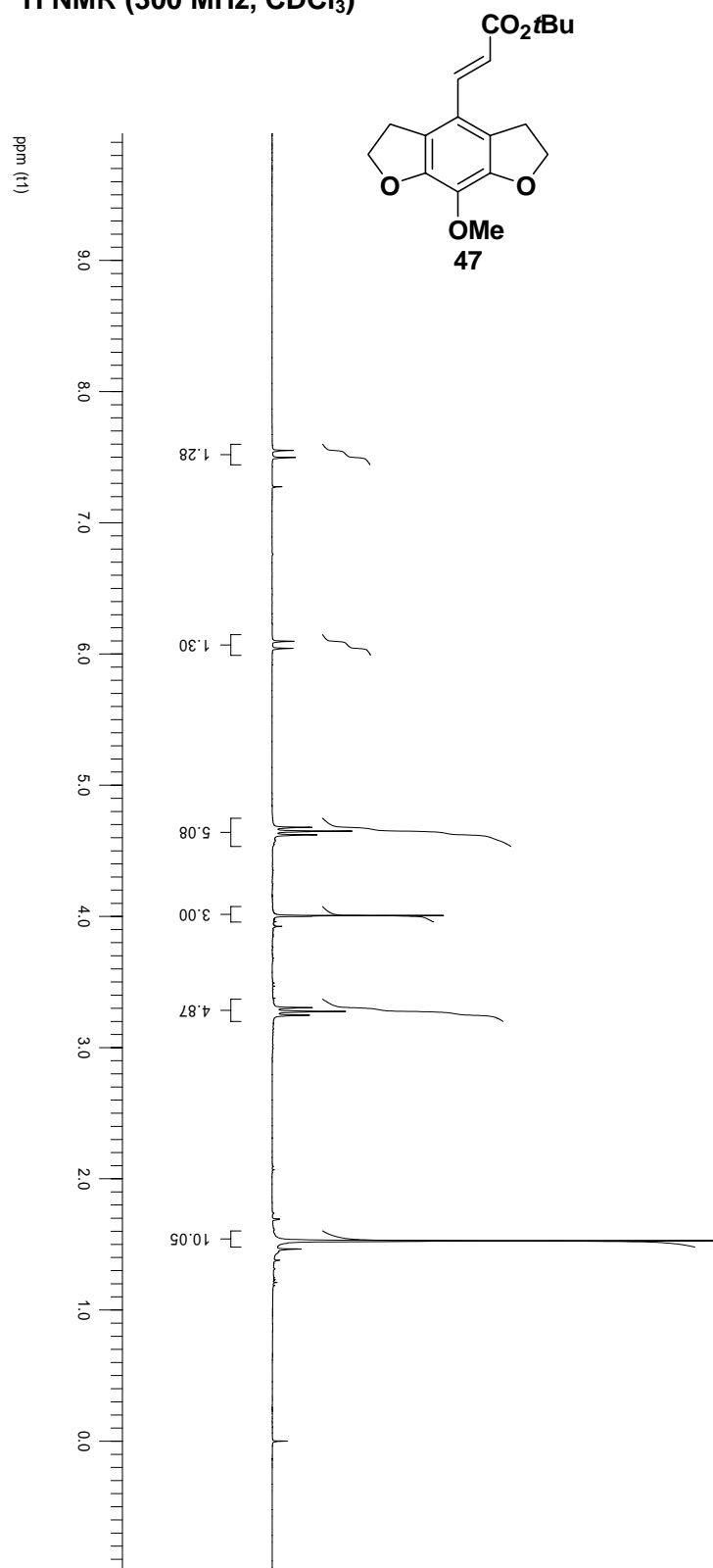
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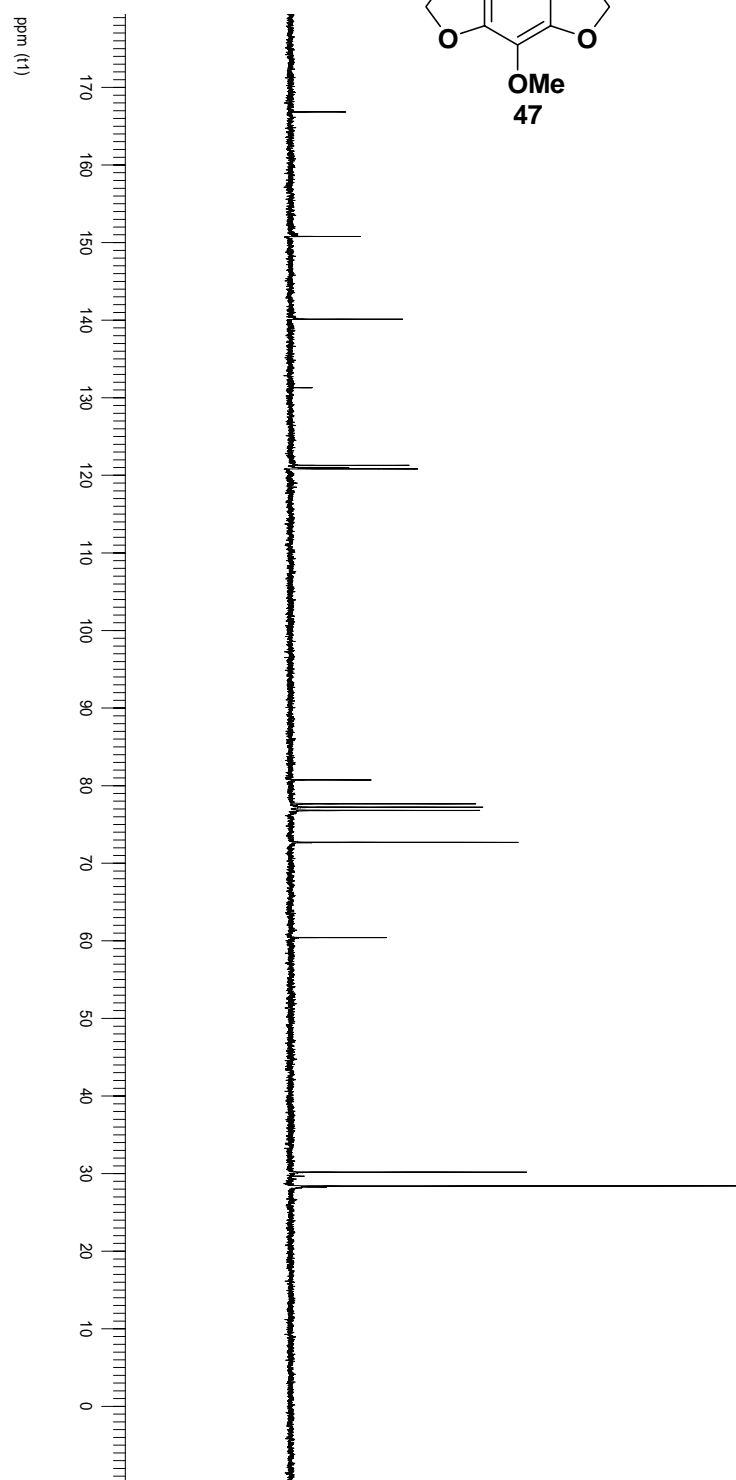
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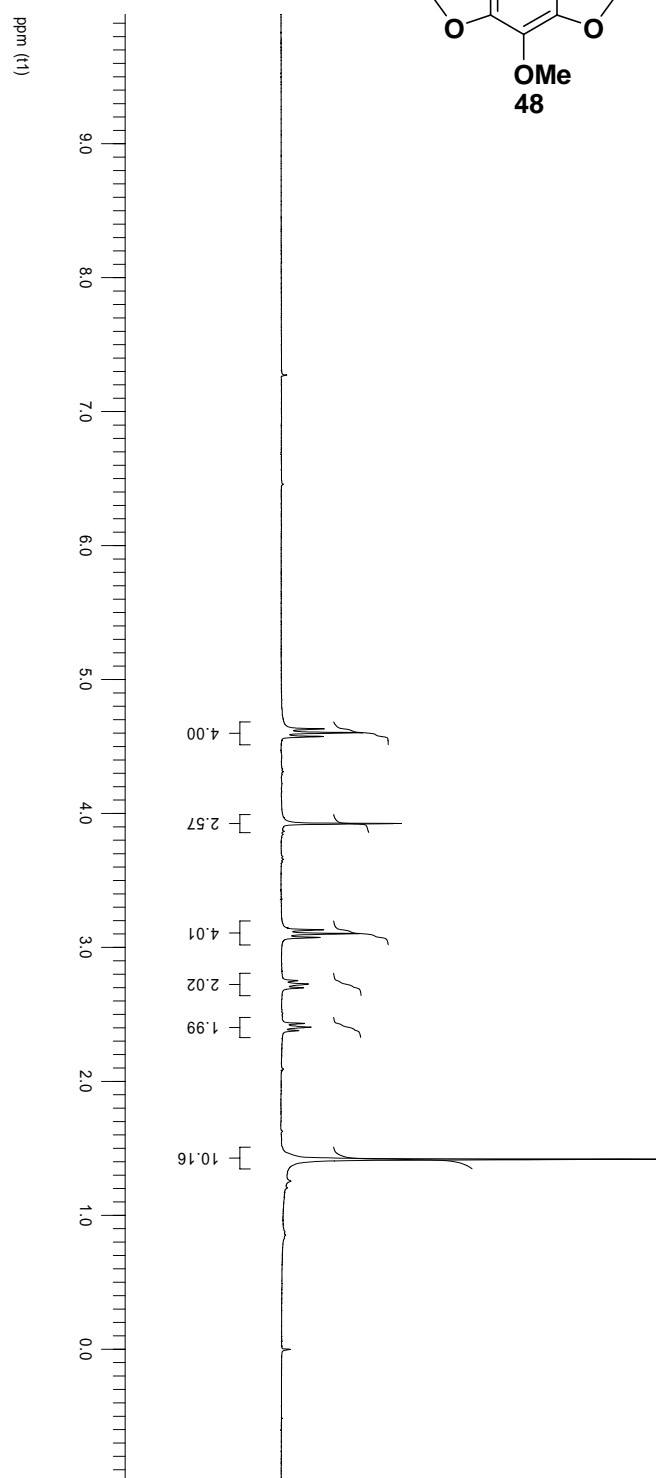
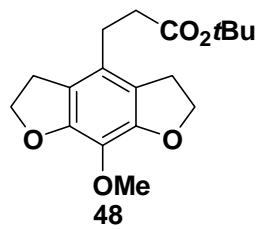
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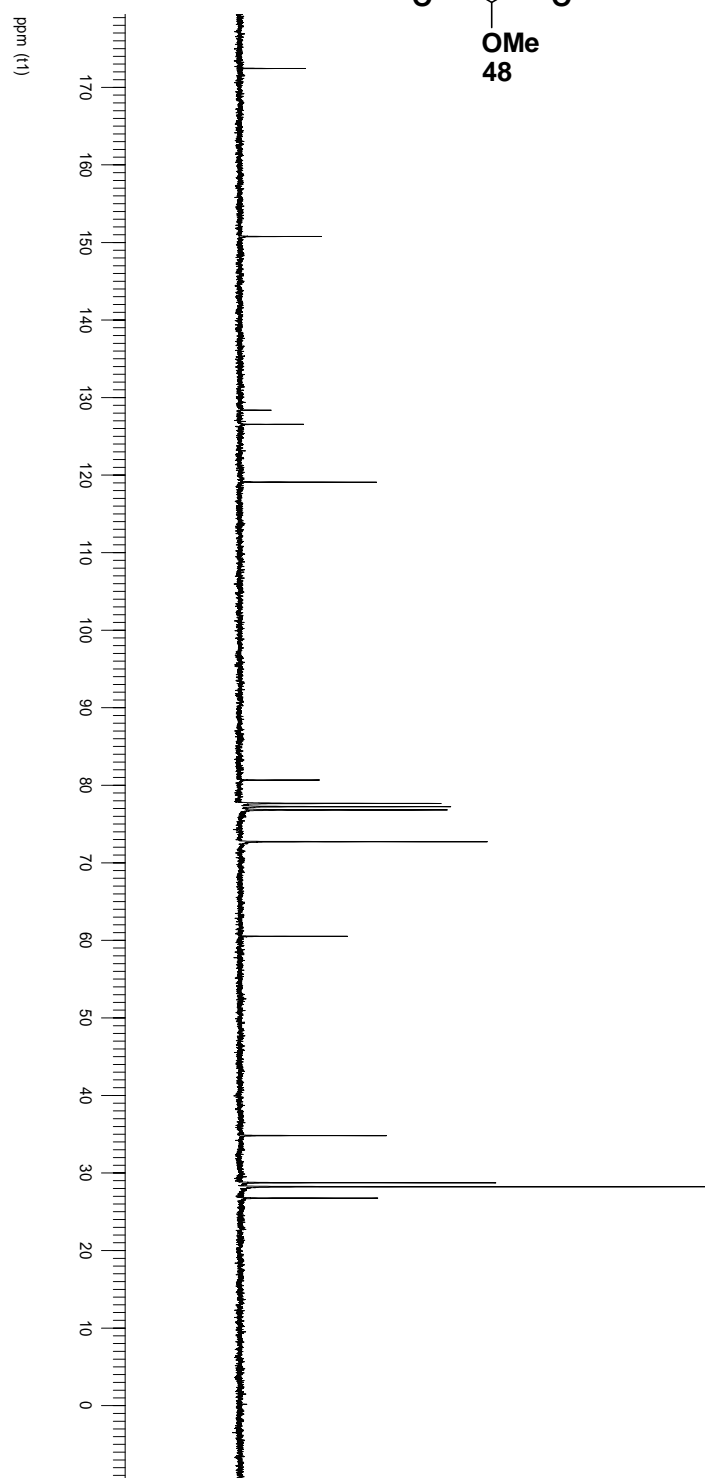
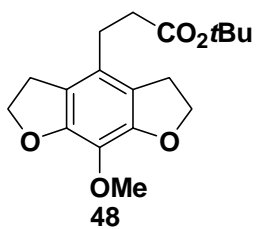
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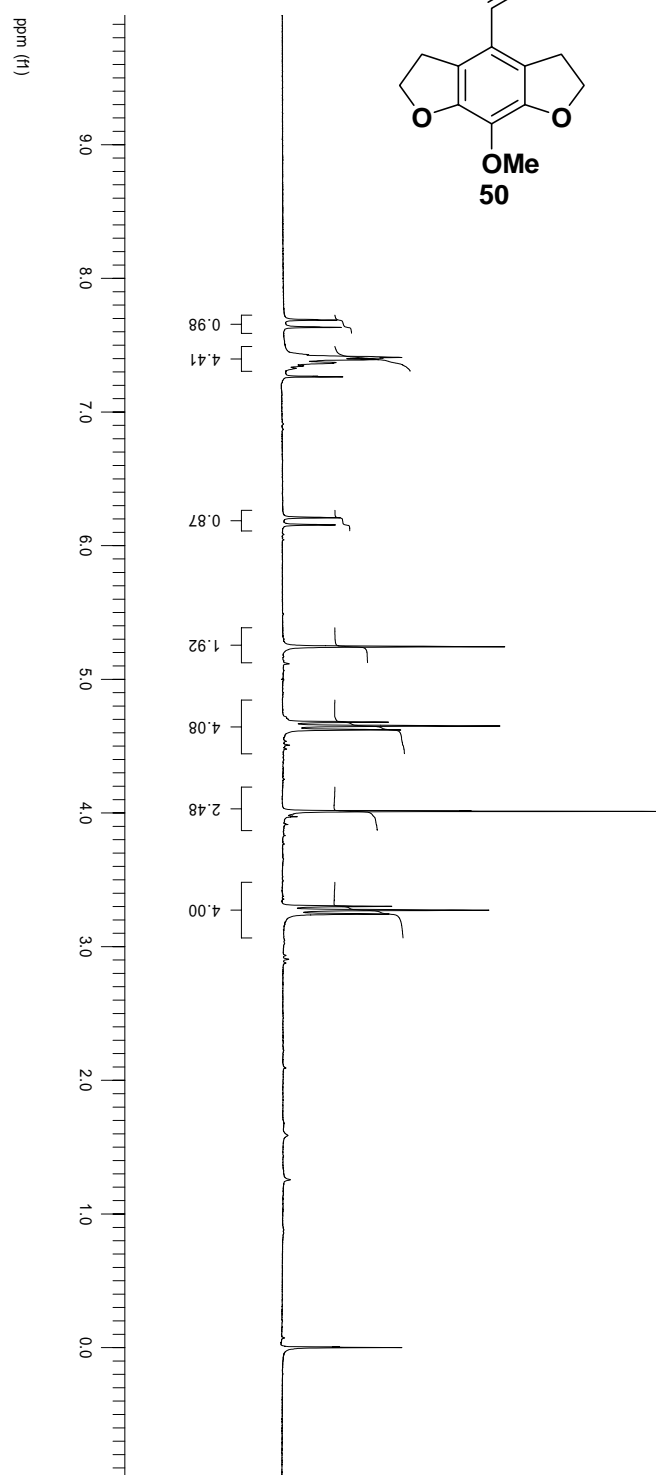
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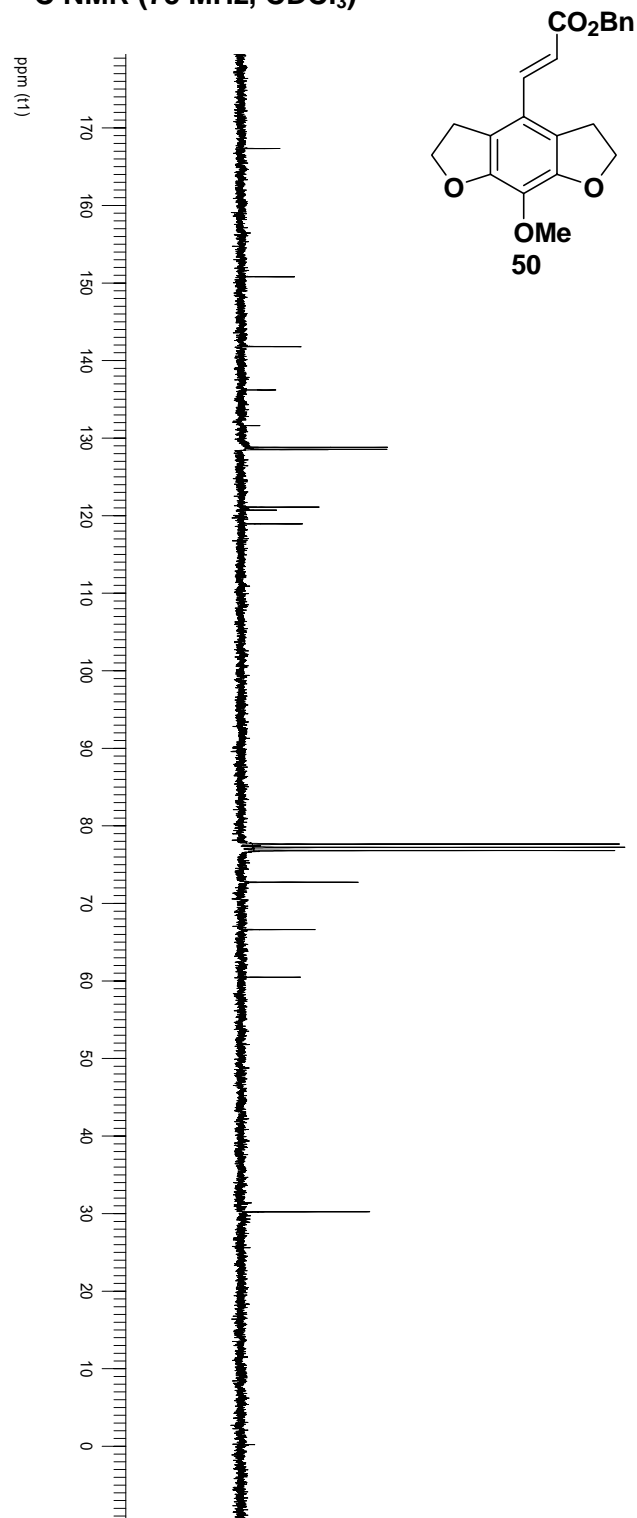
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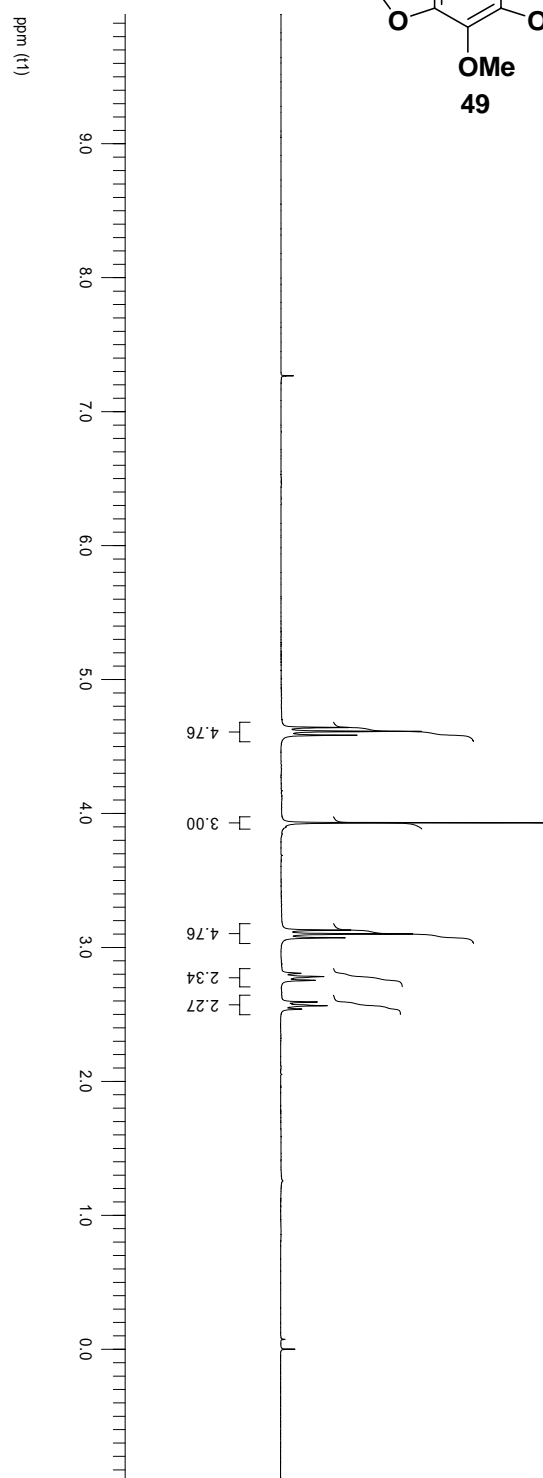
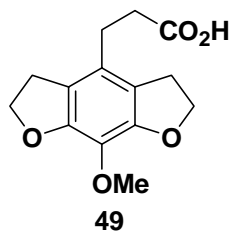
¹H NMR (300 MHz, CDCl₃)



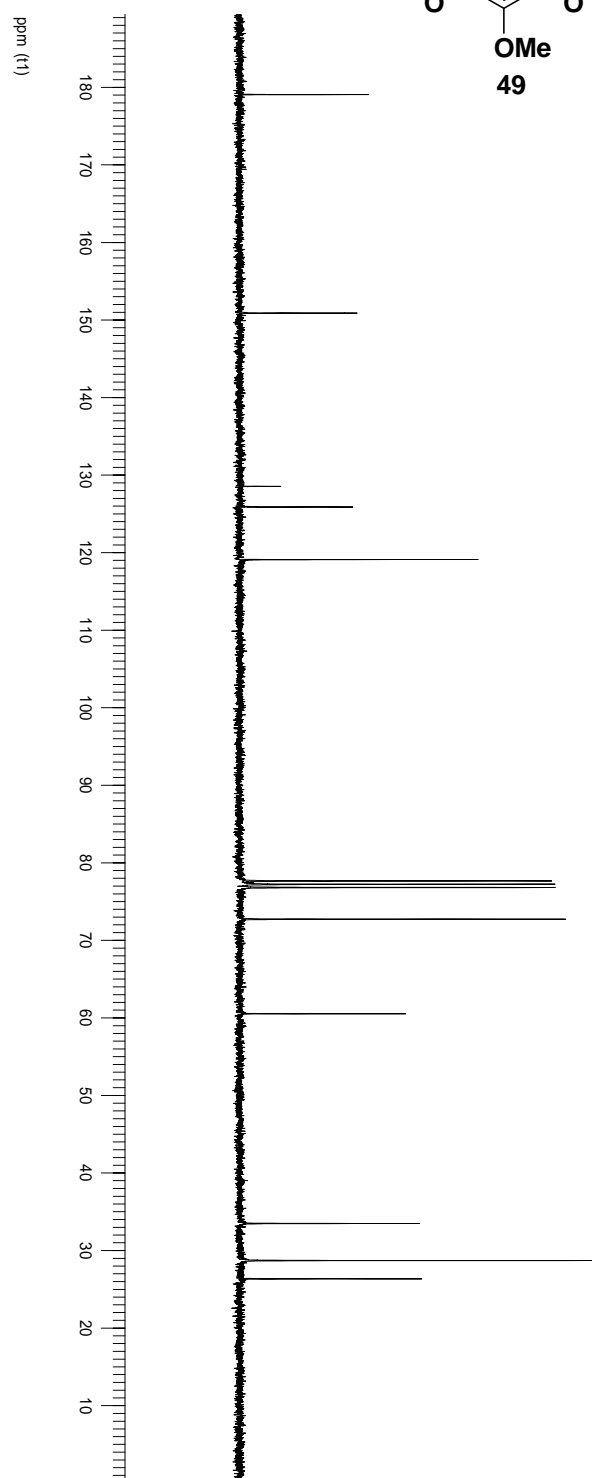
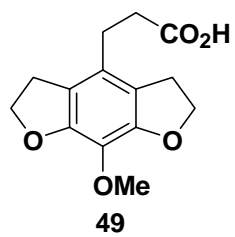
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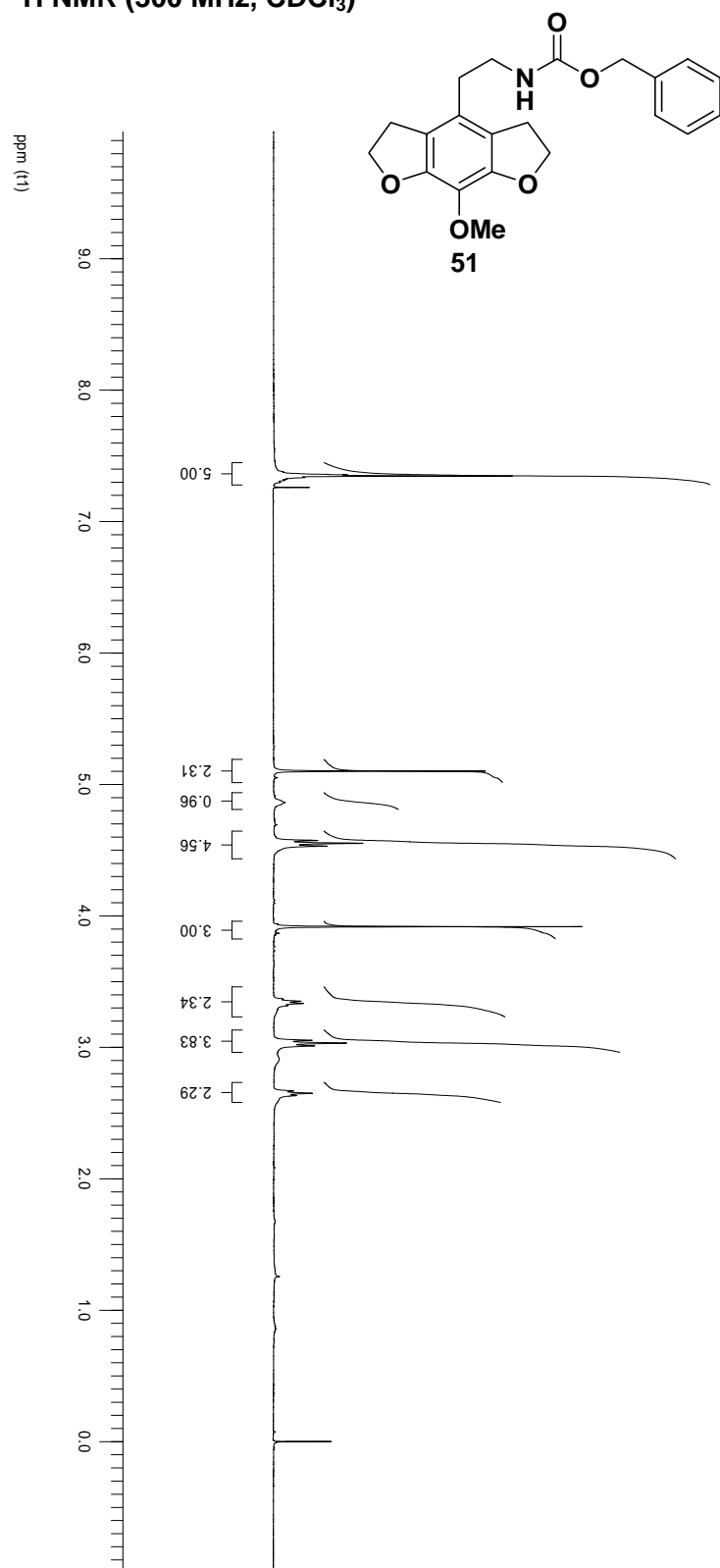
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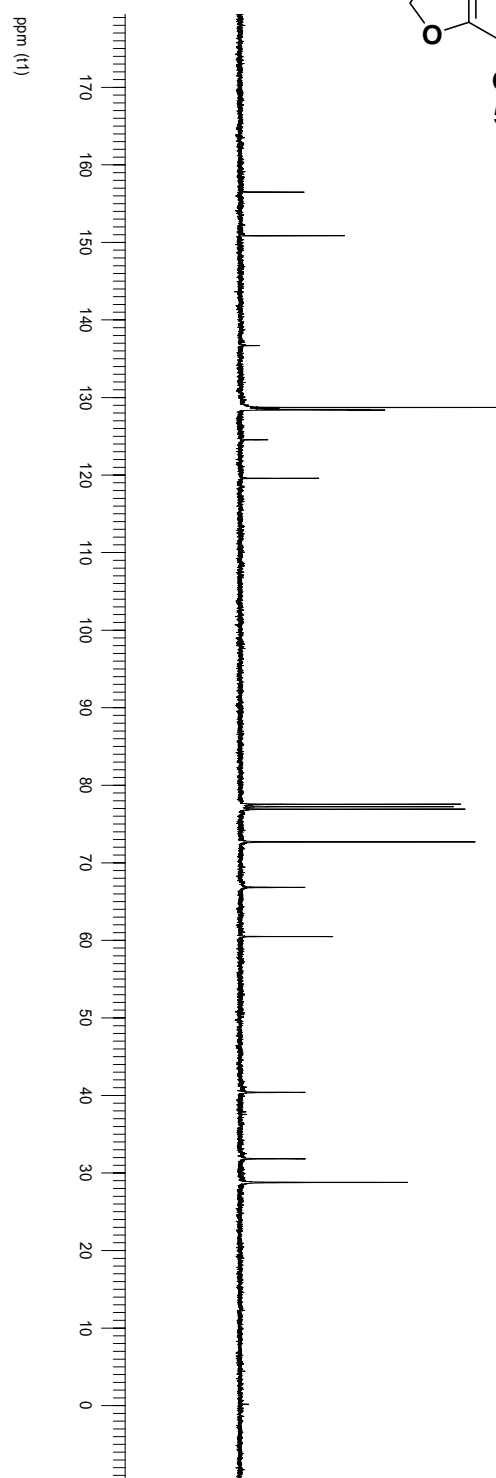
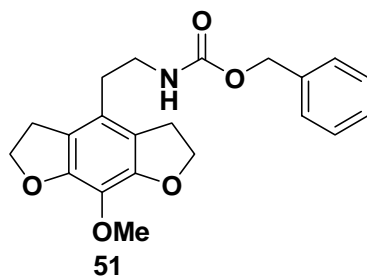
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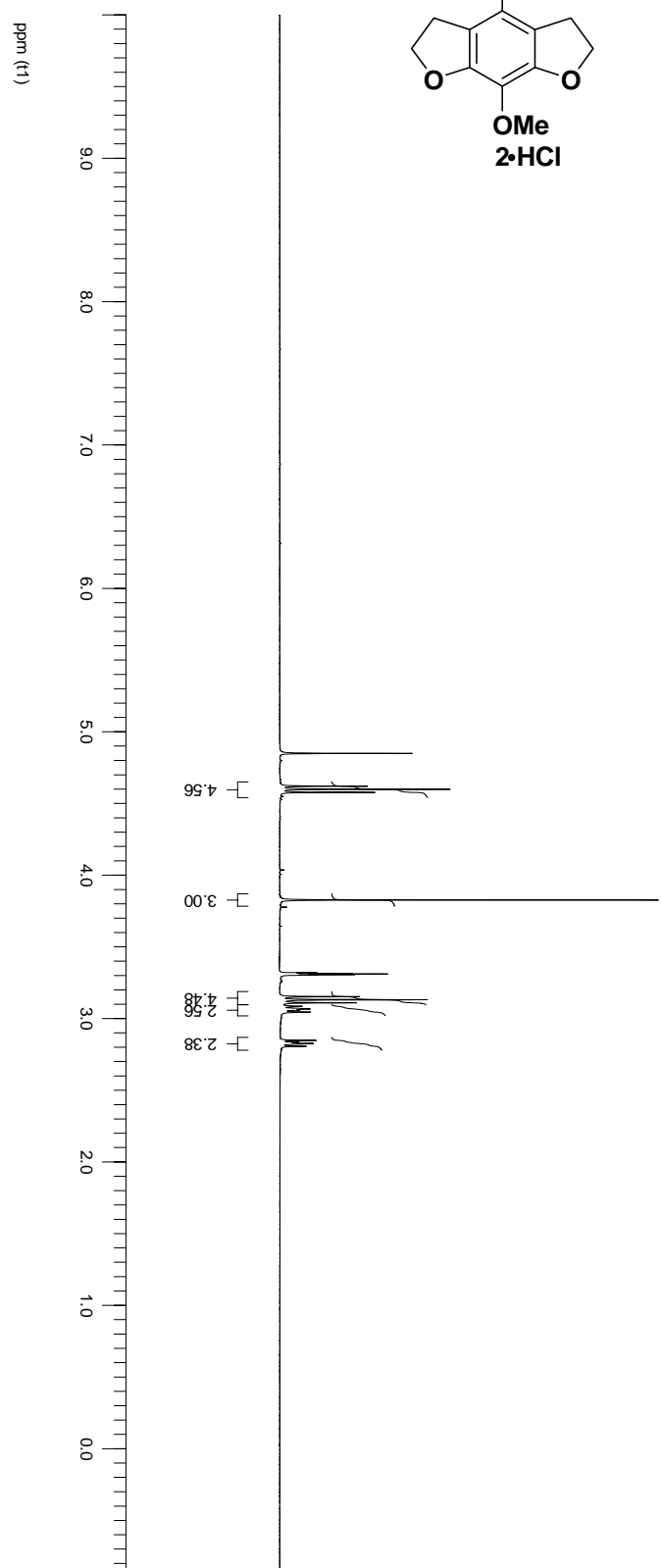
^1H NMR (300 MHz, CDCl_3)



^{13}C NMR (75 MHz, CDCl_3)



¹H NMR (400 MHz, CD₃OD)



¹³C NMR (100 MHz, CD₃OD)

