

Supplemental Material for:

**Synthesis of the Tetracyclic Core of Tetrapetalone A Enabled by a Pyrrole Reductive Alkylation**

Andrew P. Marcus and Richmond Sarpong\*

*email:* [rsarpong@berkeley.edu](mailto:rsarpong@berkeley.edu)

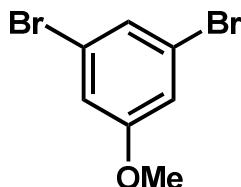
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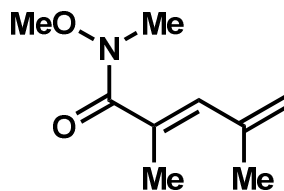
## Materials and Methods.

Unless otherwise stated, reactions were performed in flame-dried glassware sealed with rubber septa under a nitrogen atmosphere using dry solvents. Tetrahydrofuran (THF) and ether were distilled over sodium/benzophenone ketyl; dichloromethane, toluene, benzene and acetonitrile were distilled over calcium hydride; 1,4-dioxane was obtained from a Seca Solvent System by GlassContour (solvent dried over alumina under a N<sub>2</sub> atmosphere). Reaction temperatures were controlled by an IKAmag® temperature modulator. Determinations of pH were obtained by Color pHast® Indicator Strips pH = 0 – 14. Thin layer chromatography was performed using SiliCycle silica gel 60 Å F-254 precoated plates (0.25 mm) and visualized by UV and either anisaldehyde or ceric ammonium molybdate (CAM) stain. Sorbent silica gel 230-400 mesh (particle size 0.040 – 0.063 mm) was used for flash chromatography. <sup>1</sup>H NMR spectra were recorded on Bruker spectrometers (at 300, 400, 500 and 600 MHz), as were <sup>13</sup>C NMR (at 75, 100, 125 and 150 MHz, respectively). Chemical shifts (δ ppm) are reported relative to Me<sub>4</sub>Si (δ = 0.0) or CHCl<sub>3</sub> (δ = 7.26 for <sup>1</sup>H NMR and δ = 77.2 for <sup>13</sup>C NMR). Data for <sup>1</sup>H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, m = multiplet, br = broad), integration and coupling constant (Hz). IR spectra were recorded on a Nicolet MAGNA-IR 850 spectrometer and are reported in frequency of absorption (cm<sup>-1</sup>). Both low and high resolution mass spectra were obtained from the University of California, Berkeley Mass Spectral Facility.

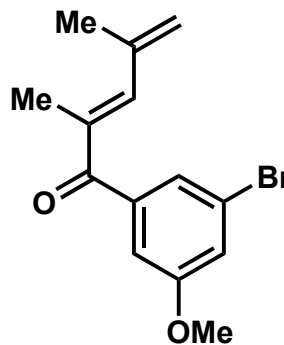
## Experimental Procedures.



**1,3-dibromo-5-methoxybenzene (9).**<sup>[1]</sup> To a 500-mL Schlenk flask equipped with a stir bar was added 98% 1,3,5-trimethoxybenzene (17.2 g, 53.4 mmol) and DMF (100 mL). In a separate 250-mL round-bottom flask, freshly cut sodium (1.29 g, 56.1 mmol) was added to methanol (100 mL, pre-dried over potassium carbonate). Once the sodium was dissolved, DMF (45 mL) was added, and the methanol was removed by rotary evaporation. The sodium methoxide solution was then added via cannula to the Schlenk flask, which was then sealed. The reaction mixture was stirred at 100 °C for 12 h, then cooled to room temperature and quenched with aqueous 1 N HCl (200 mL). The mixture was extracted with ether (3 x 150 mL), then the combined organic phase was washed with water (2 x 150 mL) and brine (100 mL). The organic phase was dried over MgSO<sub>4</sub>, filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (100% hexanes) to afford 11.8 g of colorless solid (83% yield). *R*<sub>f</sub> 0.50 (100% hexanes). <sup>1</sup>H NMR (500 MHz): δ 7.25 (t, 1H, *J* = 1.6 Hz), 6.99 (d, 1H, *J* = 1.6 Hz), 3.78 (s, 3H). <sup>13</sup>C NMR (125 MHz): δ 160.9, 126.5, 123.3, 116.6, 55.9. The data match literature values.

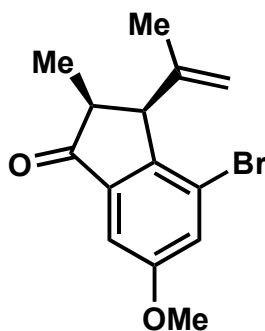


**(E)-N-methoxy-N,2,4-trimethylpenta-2,4-dienamide (10).** This compound was prepared from a literature procedure.<sup>[2]</sup> <sup>1</sup>H NMR (300 MHz): δ 6.18 (s, 1H), 5.09 (t, 1H, *J* = 1.5 Hz), 4.95 (s, 1H), 3.63 (s, 3H), 3.21 (s, 3H), 2.01 (d, 3H, *J* = 1.5 Hz), 1.89 (s, 3H). <sup>13</sup>C NMR (75 MHz): δ 173.6, 140.7, 133.6, 131.9, 118.0, 63.3, 33.9, 23.3, 15.9. MS (EI): *m/z* 169 (M<sup>+</sup>); HRMS (EI): found 169.1103, calcd for [C<sub>9</sub>H<sub>15</sub>NO<sub>2</sub>]<sup>+</sup> 169.1103. IR: ν 3493 (br), 3084, 2971, 2937, 2819, 1651, 1443, 1377 cm<sup>-1</sup>.



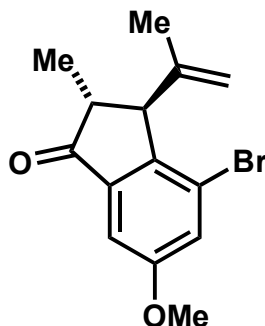
**(E)-1-(3-bromo-5-methoxyphenyl)-2,4-dimethylpenta-2,4-dien-1-one (8).** To a 100-mL round-bottom flask equipped with a stir bar was added **9** (3.00 g, 11.3 mmol) and ether (25 mL).

The reaction flask was cooled to  $-78^{\circ}\text{C}$ , then butyllithium (2.5 M in hexanes, 4.64 mL) was added over 20 min. The reaction mixture was stirred at  $-78^{\circ}\text{C}$  for 5 min, at which point a solution of **10** (1.82 g, 10.8 mmol) in THF (5 mL) was added over 5 min. Stirring was continued at  $-78^{\circ}\text{C}$  for 45 min, then the reaction mixture was quenched with saturated aqueous ammonium chloride (30 mL). The organic layer was diluted with ether (100 mL), extracted and washed with brine (25 mL). The organic phase was dried over  $\text{MgSO}_4$ , filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (30:1 hexanes:ethyl acetate, then 25:1, then 20:1) to afford 2.78 g of a yellow oil (88% yield).  $R_f$  0.25 (19:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.33 (t, 1H,  $J = 1.5$  Hz), 7.19 (t, 1H,  $J = 2.0$  Hz), 6.86 (dd, 1H,  $J = 1.5$  Hz, 2.5 Hz), 6.61 (s, 1H), 5.28 (s, 1H), 5.13 (s, 1H), 3.83 (s, 3H), 2.13 (s, 3H), 1.97 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  198.1, 160.2, 144.9, 141.3, 140.8, 135.7, 124.6, 122.7, 121.1, 120.4, 113.6, 55.9, 23.0, 14.1. MS (ESI+):  $m/z$  295 ( $\text{MH}^+$ ); HRMS (ESI+): found 295.0325, calcd for  $[\text{C}_{14}\text{H}_{16}\text{BrO}_2]^+$  295.0328. IR:  $\nu$  3081, 2965, 2933, 1657, 1643, 1591, 1565, 1452, 1277, 1219  $\text{cm}^{-1}$ .

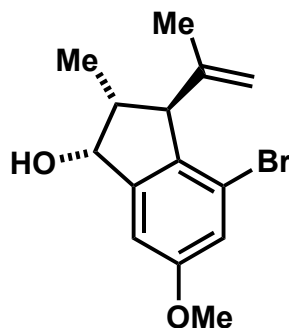


**cis-4-bromo-6-methoxy-2-methyl-3-(prop-1-en-2-yl)-2,3-dihydro-1H-inden-1-one (syn-11).** To a 250-mL round-bottom flask equipped with a stir bar was added aluminum chloride (4.59 g, 34.4 mmol) and toluene (60 mL). Aryl dienone **8** (10.2 g, 34.4 mmol) in toluene (40 mL) was added via syringe. The reaction mixture immediately turned red. It was stirred at room temperature for 2 h before being quenched with saturated aqueous ammonium chloride (100 mL). The aqueous phase was extracted with ether (3 x 100 mL), then the combined organic phase was washed with brine (75 mL), dried over  $\text{MgSO}_4$ , filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (30:1 hexanes:ethyl acetate, then 25:1, then 23:1) to afford 7.94 g of a yellow solid (78% yield, an inseparable 9:1 *syn:anti* mixture of diastereomers).  $R_f$  0.23 (19:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.36 (d, 1H,  $J = 2.0$  Hz), 7.18 (d, 1H,  $J = 2.5$  Hz), 5.01 (s, 1H), 4.68 (broad s, 1H), 4.08 (d, 1H,  $J = 8.0$  Hz), 3.83 (s, 3H), 2.90 (quint, 1H,  $J = 7.5$  Hz), 1.32 (broad s, 3H), 1.20 (d, 3H,  $J = 7.5$  Hz).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  207.4, 160.5, 146.6, 142.5, 139.4, 126.3, 122.6, 115.9, 113.2, 104.9, 56.1, 51.3, 48.1, 10.5. MS (ESI+):  $m/z$  295 ( $\text{MH}^+$ ); HRMS (ESI+): found 295.0330, calcd for  $[\text{C}_{14}\text{H}_{16}\text{BrO}_2]^+$  295.0328. IR:  $\nu$  3078, 2972, 2936, 1721, 1713, 1653, 1606, 1565, 1506, 1475, 1433, 1377, 1323, 1284, 1266  $\text{cm}^{-1}$ .

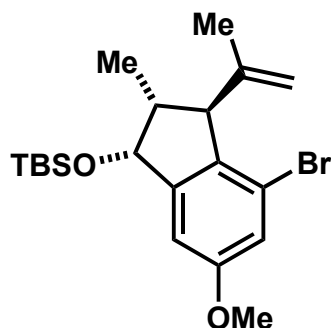




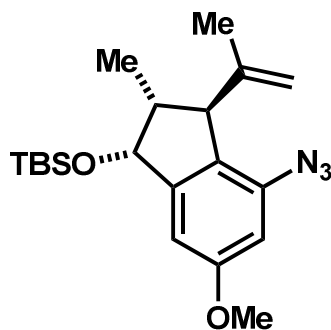
***trans*-4-bromo-6-methoxy-2-methyl-3-(prop-1-en-2-yl)-2,3-dihydro-1*H*-inden-1-one (*anti*-11).** To a 250-mL round-bottom flask equipped with a stir bar was added an 9:1 mixture of *syn:anti*-11 (7.94 mg, 26.9 mmol), potassium carbonate (744 mg, 5.38 mmol), and dioxane (90 mL). The reaction was stirred at 80 °C for 10 h, at which point the solvent was removed by rotary evaporation. The residue was dissolved in ether and filtered through Celite to afford a 1:4 mixture of *syn:anti* diastereomers, which were carried forward without further purification.  $R_f$  0.23 (19:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.39 (d, 1H,  $J = 2.5$  Hz), 7.18 (d, 1H,  $J = 2.5$  Hz), 4.88 (t, 1H,  $J = 1.5$  Hz), 4.76 (s, 1H), 3.84 (s, 3H), 3.51 (d, 1H,  $J = 3.0$  Hz), 2.50 (dq, 1H,  $J = 3.0$  Hz, 7.5 Hz), 1.60 (s, 3H), 1.32 (d, 3H,  $J = 7.5$  Hz).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  207.8, 160.7, 146.0, 144.4, 139.2, 127.2, 123.0, 113.2, 105.2, 56.1, 55.5, 50.4, 20.0, 16.7. IR:  $\nu$  3078, 2968, 2933, 1721, 1713, 1653, 1606, 1565, 1506, 1476, 1432, 1377, 1321, 1293, 1266  $\text{cm}^{-1}$ .



**(1*R*,2*R*,3*S*)-4-bromo-6-methoxy-2-methyl-3-(prop-1-en-2-yl)-2,3-dihydro-1*H*-inden-1-ol (S1).** To a 100-mL round-bottom flask equipped with a stir bar was added 11 (1.96 g, 6.64 mmol) in methanol (20 mL). The reaction flask was cooled to 0 °C, then sodium borohydride (251 mg, 6.64 mmol) was added as a solid in one portion. The reaction mixture was stirred at 0 °C for 30 min, then it was quenched with saturated aqueous ammonium chloride (50 mL). The aqueous layer was extracted with ether (2 x 50 mL), then the combined organic phase was washed with brine (30 mL), dried over  $\text{MgSO}_4$ , filtered through a frit, and concentrated by rotary evaporation. The residue was carried forward without further purification.  $R_f$  0.26 (4:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.05 (d, 1H,  $J = 2.0$  Hz), 6.93 (d, 1H,  $J = 2.0$  Hz), 4.87 (s, 1H), 4.63 (s, 1H), 4.59 (dd, 1H,  $J = 4.5$  Hz, 8.5 Hz), 3.81 (s, 3H), 3.78 (d, 1H,  $J = 8.5$  Hz), 3.21 (d, 1H,  $J = 5.0$  Hz), 2.12 (dq, 1H,  $J = 4.5$  Hz, 7.5 Hz), 1.72 (s, 3H), 1.17 (d, 3H,  $J = 7.5$  Hz).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  160.3, 147.7, 147.2, 134.7, 121.5, 118.9, 112.6, 109.2, 82.6, 58.8, 55.9, 49.3, 20.7, 18.0. MS (ESI+):  $m/z$  319 ( $\text{MNa}^+$ ); HRMS (ESI+): found 319.0313, calcd for  $[\text{C}_{14}\text{H}_{17}\text{BrO}_2\text{Na}]^+$  319.0304. IR:  $\nu$  3384 (br), 3074, 2958, 2930, 2872, 2835, 1607, 1566, 1470, 1436, 1375, 1314, 1266, 1181, 1140, 1110  $\text{cm}^{-1}$ .

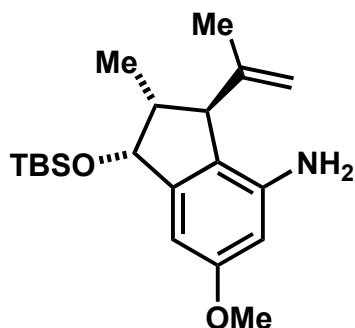


**((1R,2R,3S)-4-bromo-6-methoxy-2-methyl-3-(prop-1-en-2-yl)-2,3-dihydro-1H-inden-1-yloxy)(tert-butyl)dimethylsilane (S2).** To a 250-mL round-bottom flask equipped with a stir bar was added **S1** (7.46 g, 25.1 mmol), 98% *tert*-butyldimethylsilyl chloride (4.25 g, 27.6 mmol), imidazole (2.56 g, 37.7 mmol) and DMF (75 mL). The reaction flask was heated at 80 °C for 12 h, then the reaction mixture was cooled to room temperature. Water (150 mL) and ether (150 mL) were added, then the aqueous layer was separated and extracted with ether (2 x 100 mL). The combined organic phase was washed with water (3 x 100 mL) and brine (50 mL), then dried over MgSO<sub>4</sub>, filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (100% hexanes, then 35:1 hexanes:ethyl acetate) to yield 8.61 g of a colorless oil (83% over three steps). *R*<sub>f</sub> 0.45 (19:1 hexanes:ethyl acetate). <sup>1</sup>H NMR (500 MHz): δ 6.95 (d, 1H, *J* = 2.5 Hz), 6.77 (d, 1H, *J* = 2.0 Hz), 4.90 (s, 1H), 4.87 (s, 1H), 4.60 (d, 1H, *J* = 6.5 Hz), 3.79 (s, 3H), 3.21 (d, 1H, *J* = 7.5 Hz), 2.12 (sext, 1H, *J* = 7.0 Hz), 1.63 (s, 3H), 1.16 (d, 3H, *J* = 6.5 Hz), 0.94 (s, 9H), 0.19 (s, 3H), 0.15 (s, 3H). <sup>13</sup>C NMR (125 MHz): δ 160.0, 149.0, 145.6, 133.9, 121.0, 117.9, 113.5, 109.1, 82.2, 58.8, 55.7, 49.5, 26.0, 19.5, 18.2, 17.2, -3.91, -3.96. MS (EI): *m/z* 410 (M<sup>+</sup>); HRMS (EI): found 410.1275, calcd for [C<sub>20</sub>H<sub>31</sub>BrO<sub>2</sub>Si]<sup>+</sup> 410.1277. IR: ν 3582, 3400 (br), 2956, 2929, 2856, 1723, 1605, 1566, 1469, 1432, 1315, 1259, 1148, 1115 cm<sup>-1</sup>.

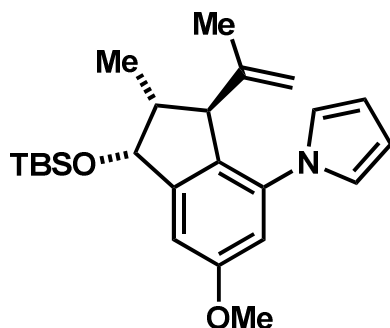


**((1R,2R,3S)-4-azido-6-methoxy-2-methyl-3-(prop-1-en-2-yl)-2,3-dihydro-1H-inden-1-yloxy)(tert-butyl)dimethylsilane (12).** To a 250-mL round-bottom flask equipped with a stir bar was added **S2** (8.61 g, 20.9 mmol) and THF (50 mL). The reaction flask was cooled to -78 °C, then *t*-butyllithium (1.6 M in pentane, 26.8 mL, 42.9 mmol) was added via syringe pump over 40 min. The reaction mixture turned pink, then reddish-orange, over the course of the addition. Tosyl azide (4.95 g, 25.1 mmol) in THF (10 mL) was then added via cannula over 15 min, leading to a deep red colored reaction mixture. Stirring at -78 °C was continued for 20 min, then the reaction mixture was allowed to equilibrate to room temperature over 2 h, slowly turning the color to brown. It was then quenched with saturated aqueous ammonium chloride (100 mL) and extracted with ether (150 mL). The organic phase was washed with brine (50 mL), dried over

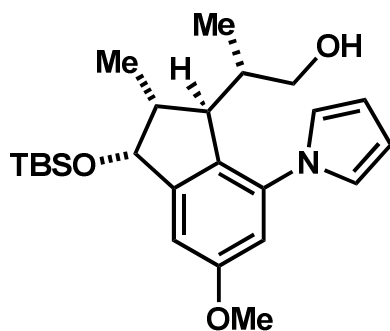
MgSO<sub>4</sub>, filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (35:1 hexanes:ethyl acetate) to yield 7.40 g of a red oil, as a 12:1 mixture of **12** to the desbromo product (87%). *R*<sub>f</sub> 0.48 (19:1 hexanes:ethyl acetate). <sup>1</sup>H NMR (500 MHz): δ 6.63 (d, 1H, *J* = 2.0 Hz), 6.55 (d, 1H, *J* = 2.0 Hz), 4.88 (s, 1H), 4.87 (s, 1H), 4.59 (d, 1H, *J* = 7.5 Hz), 3.81 (s, 3H), 3.14 (d, 1H, *J* = 8.5 Hz), 2.02 (sext, 1H, *J* = 7.5 Hz), 1.61 (s, 3H), 1.15 (d, 3H, *J* = 6.5 Hz), 0.98 (s, 9H), 0.21 (s, 3H), 0.15 (s, 3H). <sup>13</sup>C NMR (125 MHz): δ 160.6, 149.6, 145.7, 137.2, 125.5, 112.6, 105.7, 104.2, 81.8, 55.9, 55.7, 49.7, 26.0, 25.8, 18.8, 18.3, 16.3, -3.86, -3.93. MS (EI): *m/z* 373 (M<sup>+</sup>); HRMS (EI): found 373.2183, calcd for [C<sub>20</sub>H<sub>31</sub>N<sub>3</sub>O<sub>2</sub>Si]<sup>+</sup> 373.2186. IR: ν 3583, 3390 (br), 2956, 2929, 2857, 2107, 1722, 1643, 1611, 1591, 1483, 1463, 1440, 1360, 1337, 1255, 1220, 1148, 1103 cm<sup>-1</sup>.



**(1R,2R,3S)-1-(tert-butyldimethylsilyloxy)-6-methoxy-2-methyl-3-(prop-1-en-2-yl)-2,3-dihydro-1H-inden-4-amine (S3).** To a 250-mL round-bottom flask equipped with a stir bar was added **12** (92% pure, 7.34 g, 18.3 mmol) and THF (50 mL). The reaction flask was cooled to 0 °C, then lithium aluminum hydride (463 mg, 12.2 mmol) was added as a solid; gas evolved upon addition. After having been stirred for 30 min, the reaction mixture was quenched with water (463 μL), followed by 15% aqueous sodium hydroxide (463 μL), then water (1.39 mL). Once the gray color faded to a light yellow, the mixture was filtered through a funnel, and the solvent was removed by rotary evaporation. The residue was purified by silica gel chromatography (35:1 hexanes:ethyl acetate, then 11:1) to afford 4.63 g of a yellow oil (73%), plus 891 mg of the all-*cis* diastereomer (13%), carried though from the epimerization step. *R*<sub>f</sub> 0.21 (9:1 hexanes:ethyl acetate). <sup>1</sup>H NMR (500 MHz): δ 6.29 (d, 1H, *J* = 1.5 Hz), 6.06 (d, 1H, *J* = 1.5 Hz), 5.07 (d, 1H, *J* = 2.0 Hz), 4.96 (t, 1H, *J* = 1.5 Hz), 4.59 (d, 1H, *J* = 7.5 Hz), 3.84 (broad s, 2H), 3.75 (s, 3H), 3.17 (d, 1H, *J* = 8.0 Hz), 2.02 (sext, 1H, *J* = 8.0 Hz), 1.66 (s, 3H), 1.15 (d, 3H, *J* = 7.0 Hz), 0.97 (s, 9H), 0.21 (s, 3H), 0.15 (s, 3H). <sup>13</sup>C NMR (125 MHz): δ 160.7, 148.3, 147.1, 144.5, 118.3, 114.0, 100.4, 98.9, 82.2, 56.2, 55.3, 49.1, 26.1, 18.3, 16.2, -3.78, -3.92. MS (EI): *m/z* 347 (M<sup>+</sup>); HRMS (EI): found 347.2285, calcd for [C<sub>20</sub>H<sub>33</sub>NO<sub>2</sub>Si]<sup>+</sup> 347.2281. IR: ν 3583, 3476 (br), 3380 (br), 3071, 2954, 2929, 2856, 1641, 1620, 1612, 1492, 1468, 1360, 1255, 1207, 1151 cm<sup>-1</sup>.

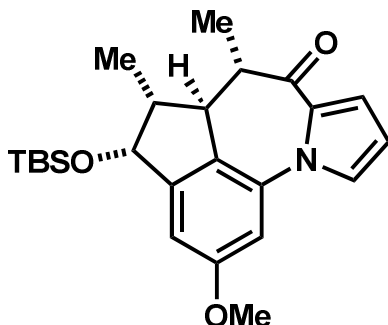


**1-((1R,2R,3S)-1-(tert-butyldimethylsilyloxy)-6-methoxy-2-methyl-3-(prop-1-en-2-yl)-2,3-dihydro-1H-inden-4-yl)-1H-pyrrole (13).** To a 250-mL round-bottom flask equipped with a stir bar was added **27** (4.05 g, 11.7 mmol), 2,5-dimethoxytetrahydrofuran (1.81 mL, 14.0 mmol), acetic acid (180  $\mu$ L), 1,2-dichloroethane (40 mL) and water (10 mL). The reaction mixture was stirred at 90  $^{\circ}$ C for 4 h, then it was cooled to room temperature and partitioned between ether (150 mL) and water (80 mL). The organic phase was extracted and washed with brine (50 mL), then dried over  $\text{MgSO}_4$ , filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (40:1 hexanes:ethyl acetate) to afford 4.54 g of a yellow oil (97%).  $R_f$  0.55 (19:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  6.82 (d, 1H,  $J$  = 1.5 Hz), 6.76 (t, 2H,  $J$  = 2.0 Hz), 6.73 (d, 1H,  $J$  = 2.0 Hz), 6.20 (d, 2H,  $J$  = 2.0 Hz), 4.71 (d, 1H,  $J$  = 7.5 Hz), 4.60 (d, 1H,  $J$  = 1.5 Hz), 4.59 (s, 1H), 3.82 (s, 3H), 3.37 (d, 1H,  $J$  = 8.5 Hz), 2.02 (sext, 1H,  $J$  = 7.5 Hz), 1.32 (s, 3H), 1.18 (d, 3H,  $J$  = 7.0 Hz), 0.98 (s, 9H), 0.24 (s, 3H), 0.18 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  160.0, 149.8, 144.4, 138.9, 127.8, 122.1, 113.2, 110.4, 108.8, 107.7, 81.7, 56.5, 55.7, 50.4, 26.1, 18.7, 18.3, 16.4, -3.86, -3.90. MS (EI):  $m/z$  397 ( $\text{M}^+$ ); HRMS (EI): found 397.2435, calcd for  $[\text{C}_{24}\text{H}_{35}\text{NO}_2\text{Si}]^+$  397.2437. IR:  $\nu$  3583, 3367 (br), 2956, 2929, 2856, 1721, 1711, 1692, 1613, 1590, 1493, 1470, 1450, 1365, 1256, 1215, 1148, 1103  $\text{cm}^{-1}$ .

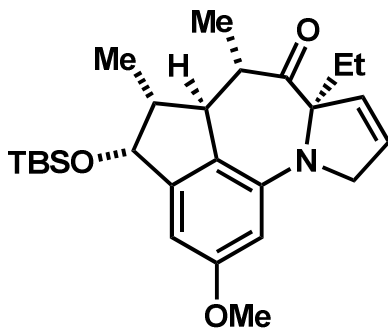


**(S)-2-((1R,2R,3R)-3-(tert-butyldimethylsilyloxy)-5-methoxy-2-methyl-7-(1H-pyrrol-1-yl)-2,3-dihydro-1H-inden-1-yl)propan-1-ol (14).** To a 500-mL round-bottom flask equipped with a stir bar was added **13** (2.31 g, 5.81 mmol), and borane-THF complex (1.0 M, 58.1 mL). The reaction mixture was stirred at room temperature for 12 h, then it was cooled to 0  $^{\circ}$ C before the successive addition of ethanol (20 mL), 10% aqueous sodium hydroxide (50 mL) and 30% aqueous hydrogen peroxide (150 mL). The reaction mixture was warmed to room temperature and stirred for 24 h. It was then extracted with ether (3 x 150 mL), then the combined organic phase was washed with brine (50 mL), dried over  $\text{MgSO}_4$ , filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (11:1 hexanes:ethyl acetate) to afford 2.09 g of a yellow oil (87%).  $R_f$  0.22 (9:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  6.85 (t, 2H,  $J$  = 2.5 Hz), 6.82 (d, 1H,  $J$  = 3.0 Hz), 6.80 (d, 1H,  $J$  = 3.0

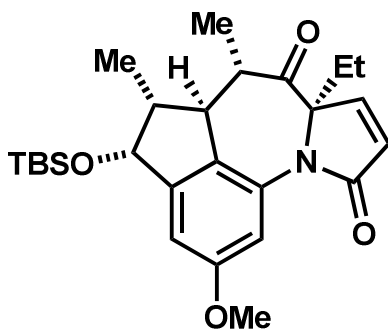
Hz), 6.30 (t, 2H,  $J = 2.5$  Hz), 4.72 (s, 1H), 3.82 (s, 3H), 3.16 (m, 2H), 2.96 (t, 1H,  $J = 2.5$  Hz), 2.81 (t, 1H,  $J = 9.0$  Hz), 2.42 (q, 1H,  $J = 9.0$  Hz), 1.15 (d, 3H,  $J = 9.0$  Hz), 0.92 (s, 9H), 0.88 (d, 3H,  $J = 8.5$  Hz), 0.98 (s, 9H), 0.22 (s, 6H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  160.2, 146.5, 139.1, 132.3, 121.1, 112.4, 109.8, 109.7, 83.9, 64.4, 55.7, 55.3, 42.3, 36.6, 26.0, 22.4, 18.3, 16.0, -3.43, -4.21. MS (FAB):  $m/z$  415 ( $M^+$ ); HRMS (FAB): found 415.2540, calcd for  $[\text{C}_{24}\text{H}_{37}\text{NO}_3\text{Si}]^+$  415.2543. IR:  $\nu$  3583, 3400 (br), 2955, 2928, 2856, 1721, 1711, 1613, 1590, 1494, 1469, 1364, 1256, 1151, 1121  $\text{cm}^{-1}$ .



**(4R,5R,5aS,6S)-4-(tert-butyldimethylsilyloxy)-2-methoxy-5,6-dimethyl-5a,6-dihydro-4H-indeno[1,7-ef]pyrrolo[1,2-a]azepin-7(5S)-one (7).** To a 250-mL round-bottom flask equipped with a stir bar was added **14** (1.70 g, 4.09 mmol), Dess-Martin periodinane (4.34 g, 10.2 mmol), water (184  $\mu\text{L}$ , 10.2 mmol) and dichloromethane (110 mL). The reaction flask was heated at 50  $^\circ\text{C}$  for 16 h, then the reaction mixture was cooled to room temperature and quenched with saturated aqueous sodium bicarbonate (100 mL). The organic layer was separated and washed sequentially with saturated aqueous sodium metabisulfate (100 mL), saturated aqueous sodium bicarbonate (100 mL), saturated aqueous sodium metabisulfate (100 mL) and brine (50 mL). The organic phase was dried over  $\text{MgSO}_4$ , filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (11:1 hexanes:ethyl acetate) to afford 1.53 g of a light yellow solid (91%).  $R_f$  0.22 (9:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.37 (t, 2H,  $J = 2.0$  Hz), 6.91 (d, 1H,  $J = 2.0$  Hz), 6.75 (d, 1H,  $J = 1.5$  Hz), 6.39 (t, 1H,  $J = 3.5$  Hz), 4.74 (d, 1H,  $J = 4.0$  Hz), 3.86 (s, 3H), 3.09 (dd, 1H,  $J = 2.5$  Hz, 6.5 Hz), 2.84 (dd, 1H,  $J = 2.5$  Hz, 7.0 Hz), 2.07 (q, 1H,  $J = 6.5$  Hz), 1.25 (d, 3H,  $J = 8.0$  Hz), 0.97 (s, 9H), 0.93 (d, 3H,  $J = 7.5$  Hz), 0.23 (s, 3H), 0.18 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  193.0, 160.6, 149.1, 136.8, 133.0, 126.4, 123.2, 122.5, 111.3, 106.5, 105.8, 82.6, 55.7, 48.6, 47.2, 47.0, 26.0, 18.2, 17.9, 11.9, -3.89, -3.94. MS (EI):  $m/z$  411 ( $M^+$ ); HRMS (EI): found 411.2235, calcd for  $[\text{C}_{24}\text{H}_{33}\text{NO}_3\text{Si}]^+$  411.2230. IR:  $\nu$  2955, 2930, 2856, 1642, 1596, 1530, 1493, 1473, 1449, 1435, 1411, 1366, 1284, 1231, 1205, 1148, 1112  $\text{cm}^{-1}$ .

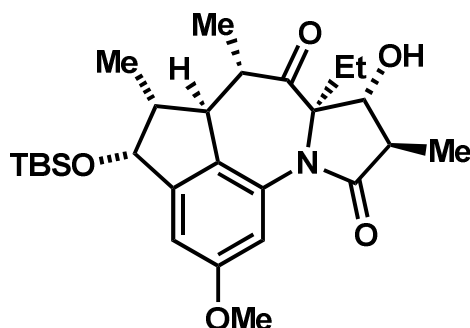


**(4*R*,5*R*,5*aS*,6*S*,7*aR*)-4-(tert-butyldimethylsilyloxy)-7*a*-ethyl-2-methoxy-5,6-dimethyl-5*a*,6,7*a*,10-tetrahydro-4*H*-indeno[1,7-*ef*]pyrrolo[1,2-*a*]azepin-7(5*H*)-one (17).** To a 100-mL round-bottom flask equipped with a stir bar was added **7** (312 mg, 758  $\mu$ mol), bis(methoxyethyl)amine (2.22 mL, 15.2 mmol) and THF (6 mL). The reaction mixture was cooled to -78 °C, then ammonia (25 mL) was added by cannula from a separate flask. Sodium (87.1 mg, 3.79 mmol) was added as several solid flakes, then the reaction flask was briefly removed from the -78 °C bath until the reaction maintained a greenish-blue color. The flask was returned to the -78 °C bath and stirred for 45 minutes. Isoprene (15 drops) was added until the blue color faded to yellow, then iodoethane (303  $\mu$ L, 3.79 mmol) was added. The reaction mixture was stirred at -78 °C for an additional 1 h, then it was quenched with saturated aqueous ammonium chloride (40 mL). The mixture was allowed to equilibrate to room temperature, then it was extracted with ethyl acetate (3 x 50 mL). The combined organic phase was washed with brine (30 mL), dried over MgSO<sub>4</sub>, filtered through a frit, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (15:1 hexanes:ethyl acetate, then 9:1) to afford 198 mg of a yellow oil (59% yield), plus 50.2 mg of **7** (16%). *R*<sub>f</sub> 0.40 (9:1 hexanes:ethyl acetate). <sup>1</sup>H NMR (500 MHz):  $\delta$  6.39 (d, 1H, *J* = 1.5 Hz), 6.13 (d, 1H, *J* = 1.5 Hz), 6.01 (d, 1H, *J* = 6.5 Hz), 5.94 (d, 1H, *J* = 6.5 Hz), 4.71 (d, 1H, *J* = 8.5 Hz), 4.40 (d, 1H, *J* = 14.0 Hz), 3.97 (d, 1H, *J* = 14.0 Hz), 3.81 (s, 3H), 2.85 (dd, 1H, *J* = 2.5 Hz, 10.0 Hz), 2.71 (dd, 1H, *J* = 2.5 Hz, 7.5 Hz), 2.01 (ddd, 1H, *J* = 2.5 Hz, 6.5 Hz, 9.0 Hz), 1.82 (m, 2H, *J* = 7.0 Hz), 1.18 (d, 3H, *J* = 6.5 Hz), 1.04 (d, 3H, *J* = 7.0 Hz), 0.99 (s, 9H), 0.66 (t, 3H, *J* = 7.0 Hz), 0.24 (s, 3H), 0.18 (s, 3H). <sup>13</sup>C NMR (125 MHz):  $\delta$  213.8, 160.7, 149.1, 142.6, 132.2, 125.7, 118.0, 100.4, 97.7, 83.7, 81.6, 57.2, 55.3, 49.6, 49.0, 47.2, 32.6, 26.1, 18.3, 15.1, 10.8, 7.72, -3.83, -3.93. MS (ESI<sup>+</sup>): *m/z* 440 (M-H<sup>+</sup>); HRMS (ESI<sup>+</sup>): found 440.2609, calcd for [C<sub>26</sub>H<sub>38</sub>NO<sub>3</sub>Si]<sup>+</sup> 440.2615. IR:  $\nu$  3583, 2956, 2925, 2854, 1703, 1611, 1462, 1377, 1258, 1173, 1113 cm<sup>-1</sup>.



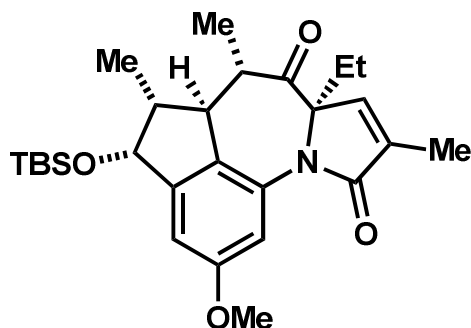
**(4*R*,5*R*,5*aS*,6*S*,7*aR*)-4-(tert-butyldimethylsilyloxy)-7*a*-ethyl-2-methoxy-5,6-dimethyl-5*a*,6-dihydro-4*H*-indeno[1,7-*ef*]pyrrolo[1,2-*a*]azepine-7,10(5*H*,7*aH*)-dione (18).** To a 50-mL round-bottom flask equipped with a stir bar was added **17** (228 mg, 516  $\mu$ mol), crushed 3Å molecular sieves (60 mg) and dry ethyl acetate (10 mL). *Tert*-butyl hydroperoxide (5.0-6.0 M in decane, 516  $\mu$ L, 2.58 mmol) was added, then the reaction mixture was stirred at room temperature for 30 min. Manganese (III) acetate dehydrate (13.8 mg, 51.6  $\mu$ mol) was added as a solid, then the reaction mixture was stirred in the dark for 48 h. The mixture was filtered through Celite and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (6:1 hexanes:ethyl acetate, then 7:2) to afford 132 mg of a yellow foamy solid (56% yield). *R*<sub>f</sub> 0.15 (4:1 hexanes:ethyl acetate). <sup>1</sup>H NMR (500 MHz):  $\delta$  7.31 (d, 1H, *J* = 2.0 Hz), 7.11 (d, 1H, *J* = 5.5 Hz), 6.77 (s, 1H), 6.32 (d, 1H, *J* = 6.0 Hz), 4.67 (d, 1H, *J* = 8.5 Hz), 3.85 (s, 3H), 2.86 (dq, 1H, *J* = 2.5 Hz, 7.0 Hz), 2.64 (dd, 1H, *J* = 2.0 Hz, 12.5 Hz), 2.18 (sext, 1H, *J* = 7.0 Hz),

2.08 (m, 1H), 1.79 (sext, 1H,  $J = 7.0$  Hz), 1.18 (d, 3H,  $J = 6.5$  Hz), 0.98 (s, 9H), 0.96 (d, 3H,  $J = 7.5$  Hz), 0.63 (t, 3H,  $J = 7.5$  Hz), 0.24 (s, 3H), 0.18 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz):  $\delta$  208.8, 169.8, 160.0, 148.8, 148.7, 132.2, 127.8, 123.2, 108.6, 107.6, 82.3, 81.1, 55.7, 49.3, 49.0, 46.6, 29.1, 26.0, 18.3, 14.8, 9.19, 6.73, -3.82, -3.94. MS (ESI<sup>+</sup>):  $m/z$  456 (MH<sup>+</sup>); HRMS (ESI<sup>+</sup>): found 456.2556, calcd for  $[\text{C}_{26}\text{H}_{38}\text{NO}_4\text{Si}]^+$  455.2492. IR:  $\nu$  3625, 3583, 2956, 2928, 2855, 2283, 1703, 1652, 1594, 1462, 1442, 1377, 1259, 1196, 1175, 1113  $\text{cm}^{-1}$ .



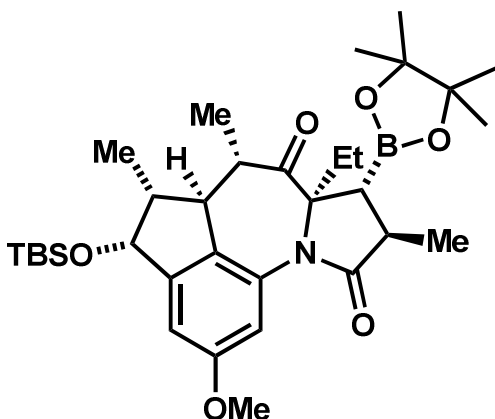
**(4*R*,5*R*,5*aS*,6*S*,7*aR*,8*R*,9*R*)-4-(*tert*-butyldimethylsilyloxy)-7*a*-ethyl-8-hydroxy-2-methoxy-5,6,9-trimethyl-5*a*,6,8,9-tetrahydro-4*H*-indeno[1,7-*ef*]pyrrolo[1,2-*a*]azepine-7,10(5*H*,7*aH*)-dione (20).** To a 10-mL round-bottom flask equipped with a stir bar was added diethylaminodiphenylchlorosilane (200  $\mu\text{L}$ , 793  $\mu\text{mol}$ ) and THF (3 mL). Lithium metal (21.9 mg, 3.17 mmol) was added as a solid in one portion. The reaction mixture was stirred at room temperature for 5 min, then the flask was cooled to 0  $^{\circ}\text{C}$ . Stirring was continued for 5 h at 0  $^{\circ}\text{C}$  during which time the color changed from light green to reddish-purple to brown. In a separate 4-mL vial equipped with a stir bar was added copper cyanide (3.6 mg, 40.2  $\mu\text{mol}$ ) and THF (200  $\mu\text{L}$ ). The reaction flask was cooled to 0  $^{\circ}\text{C}$ , at which point the silyllithium in THF (414  $\mu\text{L}$ , 96.5  $\mu\text{mol}$ ) was added dropwise via syringe. The reaction mixture was stirred at 0  $^{\circ}\text{C}$  for 10 min, then the flask was cooled to -78  $^{\circ}\text{C}$ . **18** (7.3 mg, 16.0  $\mu\text{mol}$ ) in THF (200  $\mu\text{L}$ ) was added via cannula. The reaction mixture was stirred at -78  $^{\circ}\text{C}$  for 30 min, then iodomethane (5.0  $\mu\text{L}$ , 80.3  $\mu\text{mol}$ ) was added. The reaction mixture was stirred for an additional 30 min, then it was quenched cold with saturated aqueous ammonium chloride (2 mL) and extracted with ethyl acetate (2 mL). The organic phase was washed with brine (1 mL), dried over  $\text{MgSO}_4$ , filtered through a cotton plug, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (6:1 hexanes:ethyl acetate, then 4:1) to yield 10.2 mg of an oil, as a mixture of **19** with phenylsilyl byproducts.  $R_f$  0.38 (4:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.74–7.60 (m, 4H), 7.48–7.36 (m, 6H), 6.92 (d, 1H,  $J = 2.0$  Hz), 6.72 (d, 1H,  $J = 1.5$  Hz), 5.23 (d, 1H,  $J = 1.5$  Hz), 4.60 (d, 1H,  $J = 8.5$  Hz), 3.90 (q, 2H,  $J = 7.0$  Hz), 3.75 (s, 3H), 2.92 (dq, 1H,  $J = 2.5$  Hz, 7.5 Hz), 2.72 (quint, 1H,  $J = 7.5$  Hz), 2.56 (dd, 1H,  $J = 2.5$  Hz, 12.5 Hz), 2.31 (dd, 1H,  $J = 1.5$  Hz, 8.5 Hz), 2.12 (sext, 1H,  $J = 7.5$  Hz), 2.06 (m, 1H), 1.80 (sext, 1H,  $J = 7.5$  Hz), 1.15 (d, 3H,  $J = 7.0$  Hz), 1.12 (d, 3H,  $J = 7.5$  Hz), 1.04 (d, 3H,  $J = 7.0$  Hz), 0.97 (s, 9H), 0.96 (d, 3H,  $J = 7.5$  Hz), 0.88 (t, 3H,  $J = 7.5$  Hz), 0.73 (t, 3H,  $J = 7.5$  Hz), 0.22 (s, 3H), 0.16 (s, 3H). Silane **19** (containing phenylsilyl byproducts) was then transferred to a 4-mL vial equipped with a stir bar and dissolved in DMF (200  $\mu\text{L}$ ), to which *m*-chloroperbenzoic acid (70%, 10.8 mg, 43.8  $\mu\text{mol}$ ), and potassium hydrogen fluoride (3.4 mg, 43.5  $\mu\text{mol}$ ) were added. The reaction mixture was stirred at room temperature for 16 h, at which point the mixture was quenched with saturated aqueous sodium bicarbonate (2 mL). Ethyl acetate (2 mL) was added, then the organic phase was separated and washed with water (1 mL) and brine (1 mL). The organic phase was dried over  $\text{MgSO}_4$ , filtered

through a cotton plug, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (9:1 hexanes:ethyl acetate, then 4:1, then 2:1) to afford 1.7 mg of **20** as a colorless oil (22% over two steps).  $R_f$  0.18 (2:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (600 MHz):  $\delta$  7.02 (d, 1H,  $J$  = 2.5 Hz), 6.76 (d, 1H,  $J$  = 1.0 Hz), 4.76 (t, 1H,  $J$  = 5.0 Hz), 4.68 (d, 1H,  $J$  = 8.5 Hz), 3.82 (s, 3H), 2.84 (dq, 1H,  $J$  = 3.0 Hz, 7.5 Hz), 2.79 (dd, 1H,  $J$  = 3.0 Hz, 10.5 Hz), 2.43 (m, 1H), 2.07 (m, 1H), 1.95 (quint, 1H,  $J$  = 7.5 Hz), 1.83 (sext, 1H,  $J$  = 7.5 Hz), 1.67 (d, 1H, 6.0 Hz), 1.28 (d, 3H,  $J$  = 7.5 Hz), 1.18 (d, 3H,  $J$  = 6.5 Hz), 0.98 (s, 9H), 0.96 (d, 3H,  $J$  = 7.5 Hz), 0.92 (t, 3H,  $J$  = 7.5 Hz), 0.23 (s, 3H), 0.17 (s, 3H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  211.6, 174.1, 159.9, 148.4, 132.8, 123.9, 110.3, 108.4, 81.1, 79.6, 72.0, 55.8, 49.1, 49.0, 46.2, 41.9, 26.0, 25.0, 24.8, 18.3, 14.8, 11.8, 8.73, 8.23, -3.80, -3.95. MS (ESI+):  $m/z$  488 ( $\text{MH}^+$ ); HRMS (ESI+): found 488.2819, calcd for  $[\text{C}_{27}\text{H}_{42}\text{NO}_5\text{Si}]^+$  488.2827. IR:  $\nu$  3380 (br), 2956, 2928, 2856, 1703, 1692, 1680, 1653, 1635, 1594, 1462, 1378, 1258, 1223, 1197  $\text{cm}^{-1}$ .

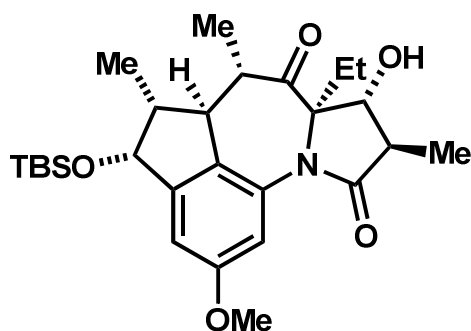


**(4R,5R,5aS,6S,7aR)-4-(tert-butyldimethylsilyloxy)-7a-ethyl-2-methoxy-5,6,9-trimethyl-5a,6-dihydro-4H-indeno[1,7-ef]pyrrolo[1,2-a]azepine-7,10(5H,7aH)-dione (21).** To a 5-mL round-bottom flask equipped with a stir bar was added diisopropylethylamine (15.9  $\mu\text{L}$ , 113  $\mu\text{mol}$ ) and THF (300  $\mu\text{L}$ ). The reaction mixture was cooled to 0  $^\circ\text{C}$ , then butyllithium (2.5 M in hexanes, 40.8  $\mu\text{L}$ , 102  $\mu\text{mol}$ ) was added dropwise. The reaction mixture was stirred at 0  $^\circ\text{C}$  for 30 min, then it was cooled to -78  $^\circ\text{C}$ , at which point **18** (15.5 mg, 34.0  $\mu\text{mol}$ ) in THF (300  $\mu\text{L}$ ) was added via cannula. The reaction mixture was stirred at -78  $^\circ\text{C}$  for 30 min, then iodomethane (12.7  $\mu\text{L}$ , 204  $\mu\text{mol}$ ) was added. Stirring was continued for 1 h, then the reaction mixture was quenched with saturated aqueous ammonium chloride (2 mL). Ethyl acetate (2 mL) was added, then the organic phase was separated, washed with brine (1 mL), dried over  $\text{MgSO}_4$ , filtered through a cotton plug, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (8:1 hexanes:ethyl acetate, then 7:1, then 7:2) to afford 9.3 mg of a white solid (58% yield), along with 1.9 mg of starting material (12%).  $R_f$  0.41 (4:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (600 MHz):  $\delta$  7.33 (d, 1H,  $J$  = 1.8 Hz), 6.76 (d, 1H,  $J$  = 1.2 Hz), 6.74 (d, 1H,  $J$  = 1.8 Hz), 4.67 (d, 1H,  $J$  = 9.0 Hz), 3.84 (s, 3H), 2.84 (dq, 1H,  $J$  = 2.4 Hz, 7.2 Hz), 2.64 (dd, 1H,  $J$  = 2.4 Hz, 10.8 Hz), 2.13 (sext, 1H,  $J$  = 7.2 Hz), 2.06 (m, 1H), 1.98 (d, 3H,  $J$  = 1.8 Hz), 1.74 (sext, 1H,  $J$  = 7.2 Hz), 1.18 (d, 3H,  $J$  = 6.6 Hz), 0.98 (s, 9H), 0.93 (d, 3H,  $J$  = 7.8 Hz), 0.59 (t, 3H,  $J$  = 7.2 Hz), 0.24 (s, 3H), 0.17 (s, 3H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  209.5, 170.5, 160.0, 148.7, 141.6, 135.6, 132.6, 123.6, 108.2, 107.8, 81.1, 79.9, 55.7, 49.4, 49.0, 46.8, 29.1, 26.0, 18.3, 14.8, 11.2, 9.20, 6.73, -3.80, -3.94. MS (ESI+):  $m/z$  470 ( $\text{MH}^+$ ); HRMS (ESI+): found 470.2722, calcd for  $[\text{C}_{27}\text{H}_{40}\text{NO}_4\text{Si}]^+$  470.2721. IR:  $\nu$  2956, 2928, 2856, 1703, 1697, 1653, 1613, 1594, 1484, 1463, 1442, 1377, 1247, 1210  $\text{cm}^{-1}$ .

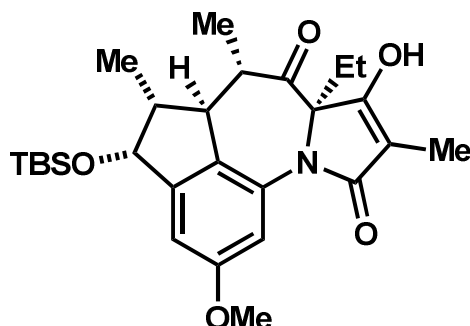




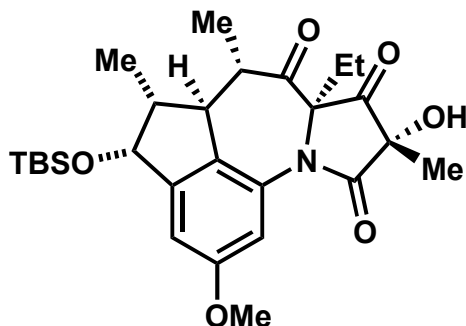
**(4R,5R,5aS,6S,7aR,8R,9R)-4-(tert-butyldimethylsilyloxy)-7a-ethyl-2-methoxy-5,6,9-trimethyl-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5a,6,8,9-tetrahydro-4H-indeno[1,7-ef]pyrrolo[1,2-a]azepine-7,10(5H,7aH)-dione (S4).** To an oven-dried 4-mL vial equipped with a stir bar in a glove box was added copper (I) chloride (132  $\mu\text{g}$ , 1.33  $\mu\text{mol}$ ), sodium *tert*-butoxide (261  $\mu\text{g}$ , 2.66  $\mu\text{mol}$ ), 1,3-dicyclohexylimidazolium chloride<sup>[3]</sup> (357  $\mu\text{g}$ , 1.33  $\mu\text{mol}$ ) and THF (150  $\mu\text{L}$ ). The reaction mixture was stirred at room temperature for 2 h, at which point a solution of **21** (7.8 mg, 16.6  $\mu\text{mol}$ ), bis(pinacolato)diboron (4.6 mg, 18.3  $\mu\text{mol}$ ) and THF (150  $\mu\text{L}$ ) was added. Stirring was continued for an additional 18 h, at which point the reaction mixture was quenched with saturated aqueous ammonium chloride (2 mL). Ethyl acetate (2 mL) was added, then the organic phase was separated, washed with brine (1 mL), dried over  $\text{MgSO}_4$ , filtered through a cotton plug, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (8:1 hexanes:ethyl acetate, then 7:1, then 4:1) to afford 5.2 mg of **S4** as a colorless oil (52% yield, a 2:1 mixture of *anti* diastereomers, major diastereomer shown), along with 3.7 mg of **21** (47%).  $R_f$  0.23 (4:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.01 (d, 1H,  $J = 2.0$  Hz), 6.76 (d, 1H,  $J = 1.0$  Hz), 4.66 (d, 1H,  $J = 8.5$  Hz), 3.84 (s, 3H), 2.86 (dq, 1H,  $J = 2.5$  Hz, 7.5 Hz), 2.81 (d, 1H,  $J = 8.5$  Hz), 2.75 (dd, 1H,  $J = 3.0$  Hz, 10.5 Hz), 2.40 (quint, 1H,  $J = 7.5$  Hz), 2.07 (m, 1H), 1.89 (sext, 1H,  $J = 7.5$  Hz), 1.75 (sext, 1H,  $J = 7.5$  Hz), 1.24 (s, 12H), 1.23 (d, 3H,  $J = 10.5$  Hz), 1.16 (d, 3H,  $J = 6.5$  Hz), 0.98 (s, 9H), 0.96 (d, 3H,  $J = 7.5$  Hz), 0.87 (t, 3H,  $J = 7.5$  Hz), 0.23 (s, 3H), 0.16 (s, 3H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  212.0, 176.0, 159.8, 148.3, 133.3, 124.4, 110.8, 107.8, 84.0, 81.1, 77.5, 55.8, 49.3, 48.6, 46.5, 38.6, 29.9, 28.1, 26.0, 25.3, 18.3, 14.8, 13.2, 11.7, 8.07, -3.83, -3.95. MS (ESI+):  $m/z$  598 ( $\text{MH}^+$ ); HRMS (ESI+): found 598.3721, calcd for  $[\text{C}_{33}\text{H}_{53}\text{BNO}_6\text{Si}]^+$  598.3730. IR:  $\nu$  2957, 2929, 2856, 1709, 1698, 1653, 1635, 1613, 1594, 1482, 1463, 1380, 1371, 1343, 1257, 1225, 1196  $\text{cm}^{-1}$ .



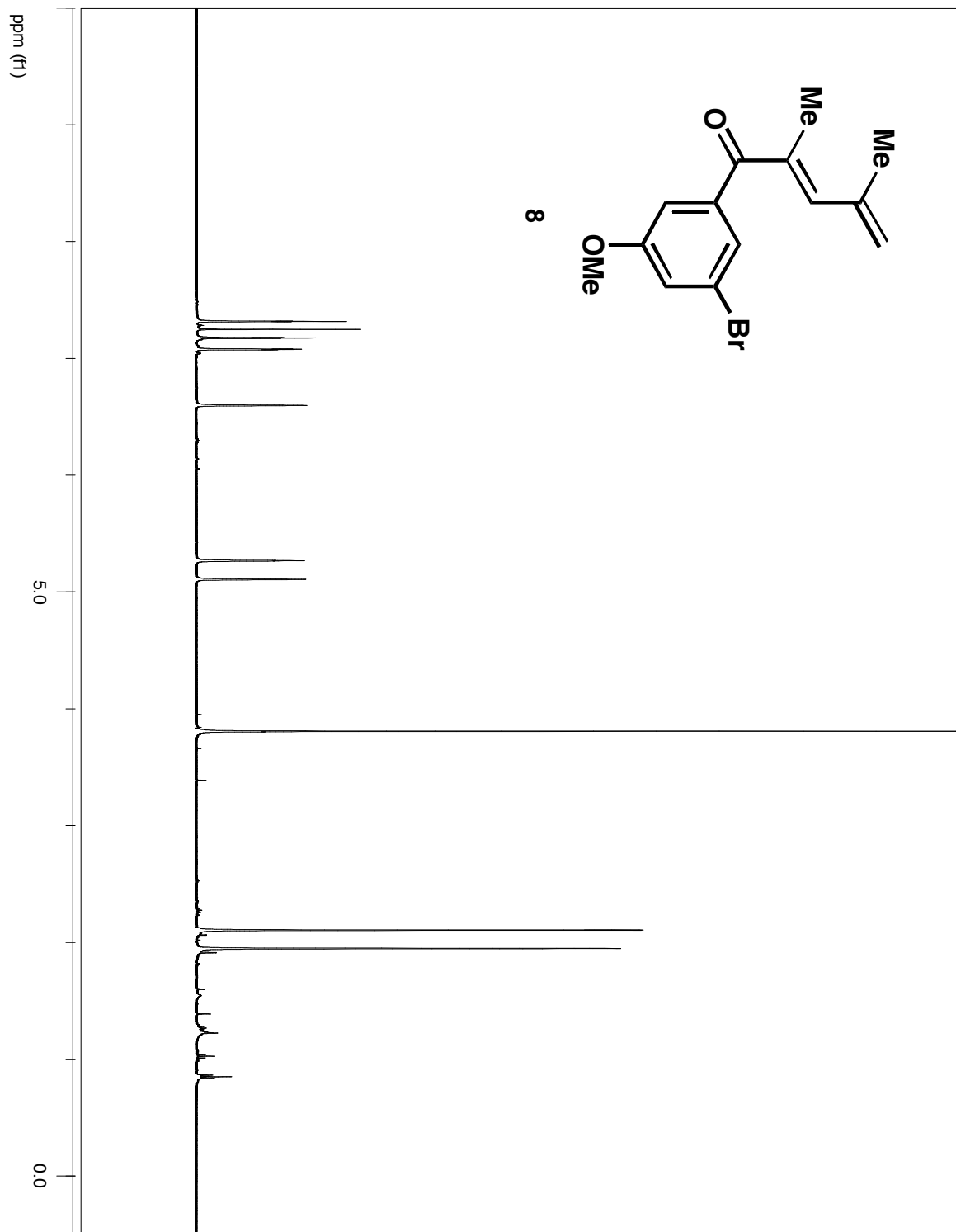
**(4*R*,5*R*,5*aS*,6*S*,7*aR*,8*R*,9*R*)-4-(*tert*-butyldimethylsilyloxy)-7*a*-ethyl-8-hydroxy-2-methoxy-5,6,9-trimethyl-5*a*,6,8,9-tetrahydro-4*H*-indeno[1,7-*ef*]pyrrolo[1,2-*a*]azepine-7,10(5*H*,7*aH*)-dione (20).** To a 4-mL vial equipped with a stir bar was added **S4** (7.9 mg, 13.2  $\mu$ mol), THF (200  $\mu$ L) and water (200  $\mu$ L). The reaction mixture was stirred at room temperature for 2 h, then it was partitioned between ethyl acetate (2 mL) and water (2 mL). The organic phase was separated, washed with brine (1 mL), dried over  $\text{MgSO}_4$ , filtered through a cotton plug, and concentrated by rotary evaporation to afford 6.4 mg of a colorless oil (quantitative yield).

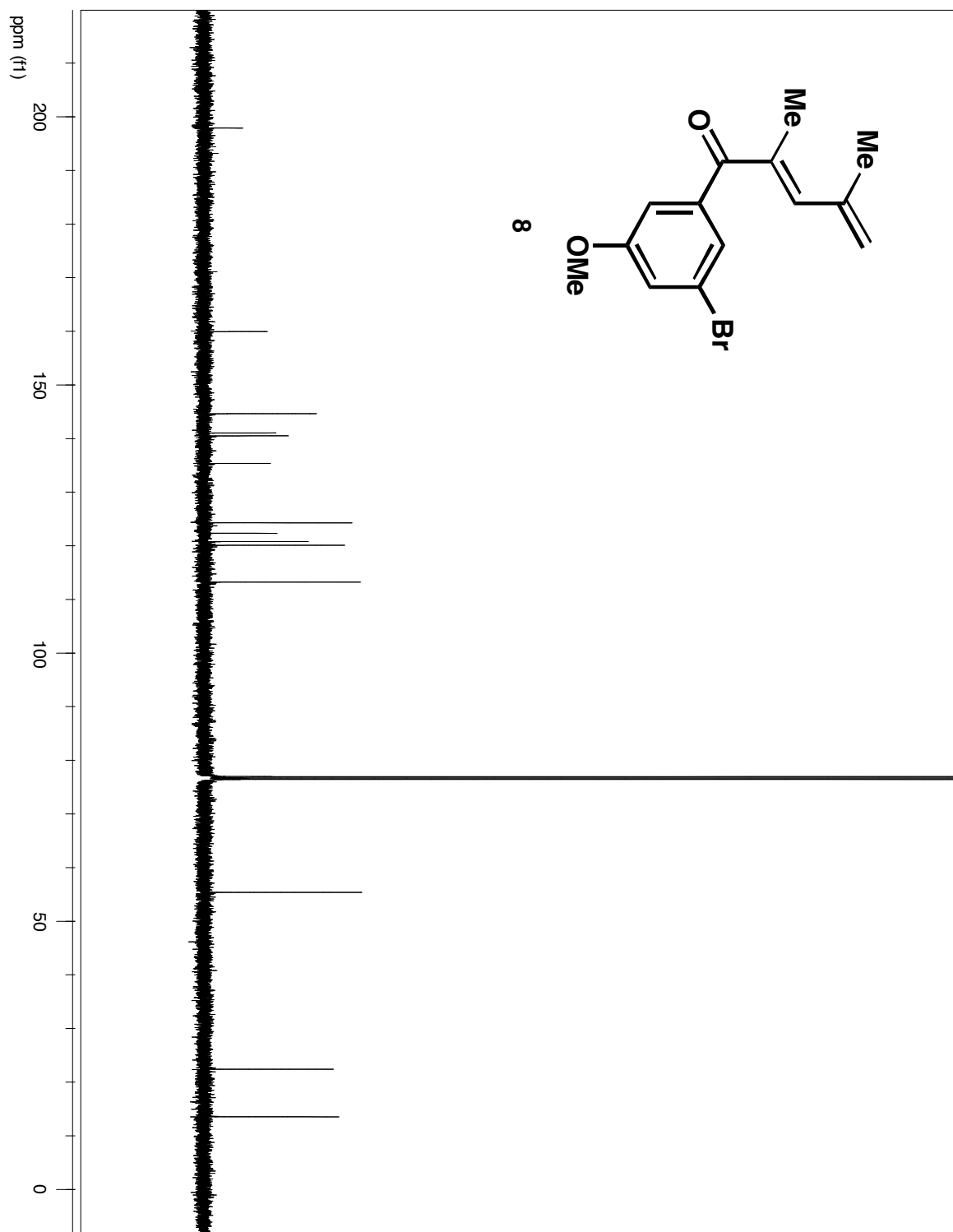


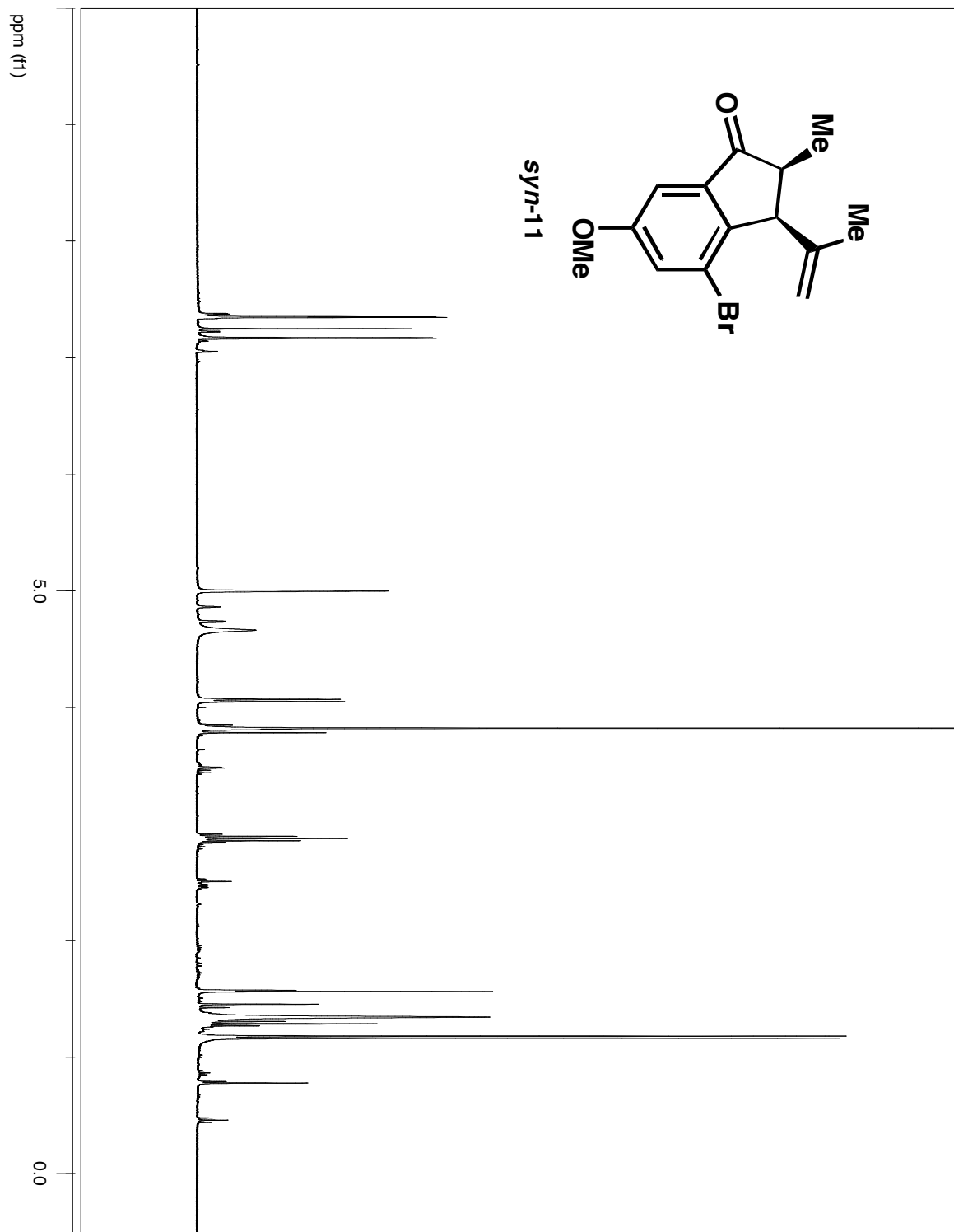
**(4*R*,5*R*,5*aS*,6*S*,7*aR*)-4-(*tert*-butyldimethylsilyloxy)-7*a*-ethyl-8-hydroxy-2-methoxy-5,6,9-trimethyl-5*a*,6-dihydro-4*H*-indeno[1,7-*ef*]pyrrolo[1,2-*a*]azepine-7,10(5*H*,7*aH*)-dione (22).** To a 4-mL vial equipped with a stir bar was added oxalyl chloride (1.1  $\mu$ L, 12.6  $\mu$ mol) in dichloromethane (200  $\mu$ L). The reaction flask was cooled to  $-78^\circ\text{C}$ , then dimethylsulfoxide (1.7  $\mu$ L, 23.9  $\mu$ mol) in dichloromethane (100  $\mu$ L) was added. Stirring at  $-78^\circ\text{C}$  was continued for 30 min, then **20** (2.0 mg, 4.1  $\mu$ mol) in dichloromethane (150  $\mu$ L) was added via cannula. Stirring at  $-78^\circ\text{C}$  was continued for an additional 30 min, then triethylamine (6.9  $\mu$ L, 49.5  $\mu$ mol) was added. After additional stirring at  $-78^\circ\text{C}$  for 1 h, the reaction mixture was quenched with saturated aqueous sodium bicarbonate (2 mL). It was extracted with ethyl acetate (2 mL), then the organic phase was washed with brine (1 mL), dried over  $\text{MgSO}_4$ , filtered through a cotton plug, and concentrated by rotary evaporation. The residue was purified by silica gel chromatography (5:1 hexanes:ethyl acetate) to yield 1.3 mg of a colorless oil (65%, appears to be 3:1 mixture of enol:keto tautomers).  $R_f$  0.63 (2:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (500 MHz):  $\delta$  7.21 (d, 1H,  $J$  = 2.0 Hz), 6.85 (d, 1H,  $J$  = 1.5 Hz), 4.67 (d, 1H,  $J$  = 8.5 Hz), 3.84 (s, 3H), 3.02 (dq, 1H,  $J$  = 3.0 Hz, 7.5 Hz), 2.67 (dd, 1H,  $J$  = 2.5 Hz, 10.5 Hz), 2.44 (sext, 1H,  $J$  = 7.0 Hz), 2.13 (m, 1H), 1.83 (sext, 1H,  $J$  = 7.0 Hz), 1.79 (s, 3H), 1.25 (d, 3H,  $J$  = 7.5 Hz), 1.19 (d, 3H,  $J$  = 6.5 Hz), 0.99 (s, 9H), 0.68 (t, 3H,  $J$  = 7.0 Hz), 0.25 (s, 3H), 0.18 (s, 3H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  203.8, 195.1, 167.7, 159.9, 149.3, 130.6, 124.1, 110.1, 109.3, 83.9, 80.9, 77.4, 55.9, 49.6, 49.3, 46.7, 29.9, 26.0, 19.6, 18.2, 14.7, 11.4, 8.55, -3.82, -3.93. MS (EI $^+$ ):  $m/z$  485 ( $\text{MH}^+$ ); HRMS (EI $^+$ ): found 485.2585, calcd for  $[\text{C}_{27}\text{H}_{39}\text{NO}_5\text{Si}]^+$  485.2597. IR:  $\nu$  3390 (br), 2950, 2928, 2855, 1788, 1725, 1708, 1618, 1591, 1462, 1377, 1287, 1250, 1202, 1147  $\text{cm}^{-1}$ .

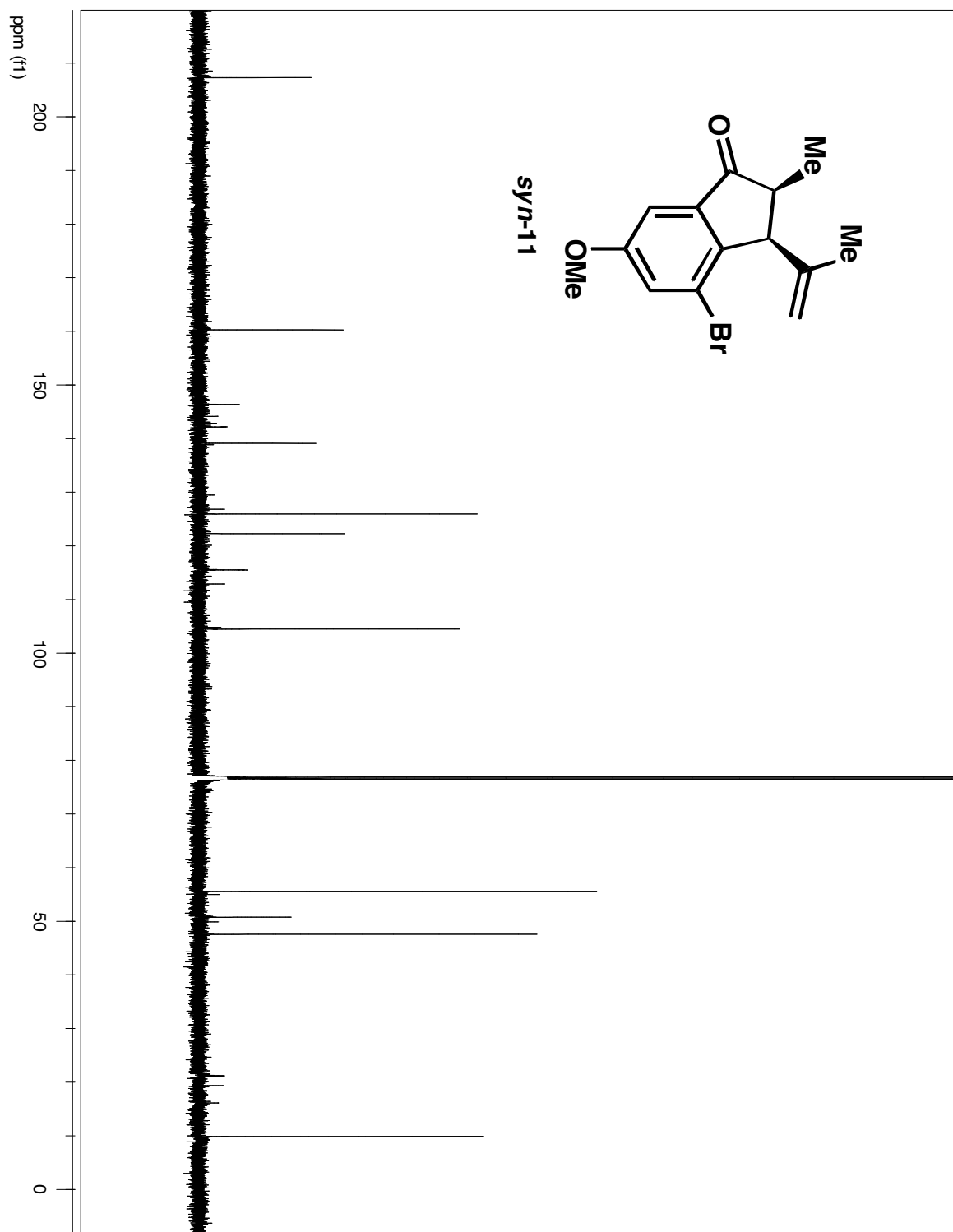


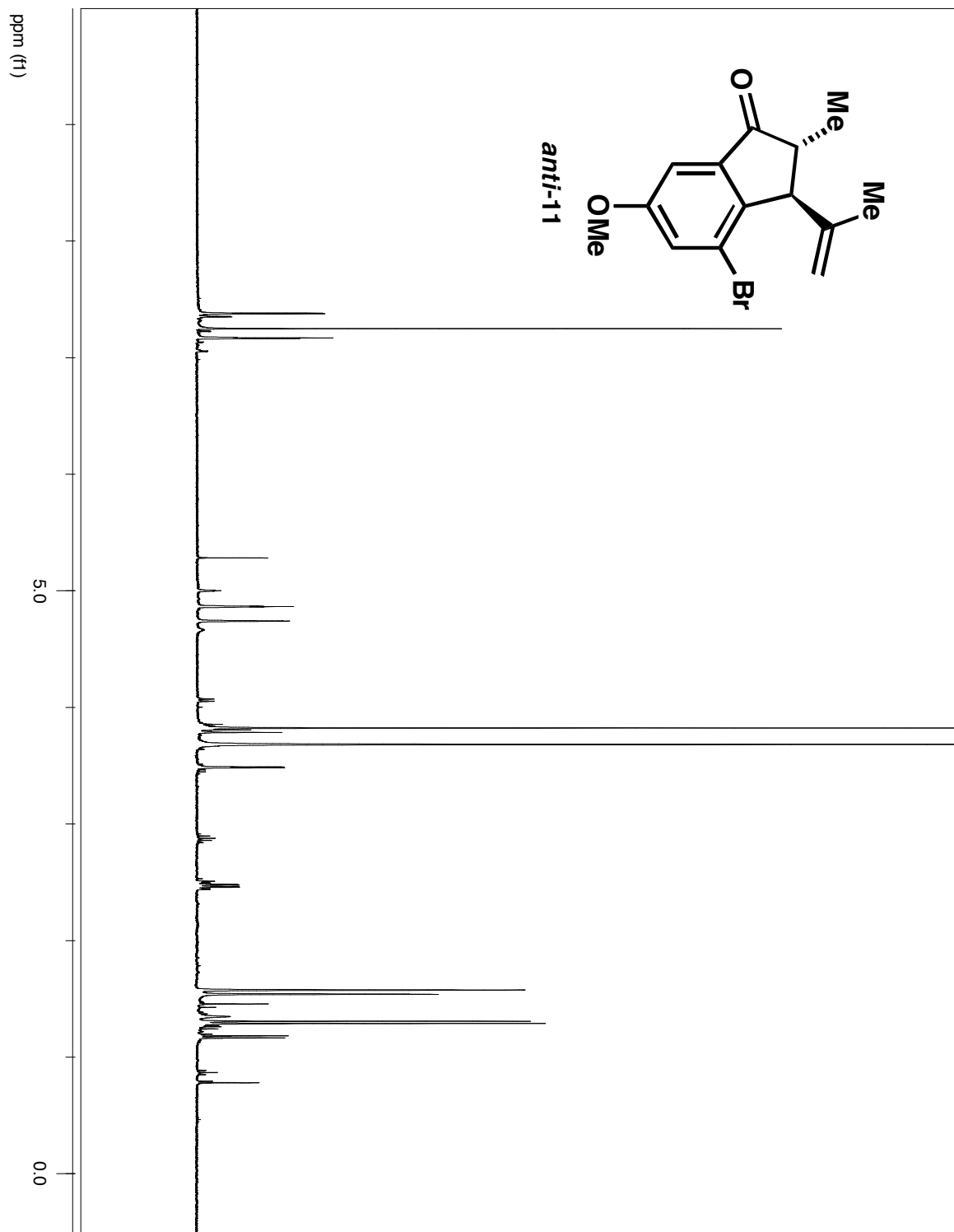
**(4*R*,5*R*,5*aS*,6*S*,7*aS*,9*S*)-4-(*tert*-butyldimethylsilyloxy)-7*a*-ethyl-9-hydroxy-2-methoxy-5,6,9-trimethyl-5*a*,6-dihydro-4*H*-indeno[1,7-*ef*]pyrrolo[1,2-*a*]azepine-7,8,10(5*H*,7*aH*,9*H*)-trione (24).** To a solution of **20** (3.4 mg, 7.0  $\mu$ mol) in dichloromethane (400  $\mu$ L) was added Dess-Martin periodinane (4.4 mg, 10.4  $\mu$ mol). The reaction mixture was stirred at room temperature for 16 h, then it was quenched with saturated aqueous sodium metabisulfate (3 mL). Ethyl acetate (3 mL) was added, then the organic layer was separated and washed with saturated aqueous sodium bicarbonate (3 mL) and brine (1 mL). The organic phase was dried over  $\text{MgSO}_4$ , filtered through a cotton plug, then concentrated by rotary evaporation. The residue was purified by silica gel chromatography (4:1 hexanes:ethyl acetate, then 2:1) to afford 1.3 mg of a colorless oil (37%).  $R_f$  0.25 (2:1 hexanes:ethyl acetate).  $^1\text{H}$  NMR (600 MHz):  $\delta$  7.05 (d, 1H,  $J$  = 2.4 Hz), 6.85 (t, 1H,  $J$  = 1.2 Hz), 4.67 (d, 1H,  $J$  = 8.4 Hz), 3.84 (s, 3H), 2.98 (dq, 1H,  $J$  = 2.4 Hz, 7.2 Hz), 2.67 (dd, 1H,  $J$  = 2.4 Hz, 10.8 Hz), 2.55 (s, 1H), 2.47 (sext, 1H,  $J$  = 7.2 Hz), 2.11 (m, 1H), 1.79 (sext, 1H,  $J$  = 7.2 Hz), 1.55 (s, 3H), 1.19 (d, 3H,  $J$  = 6.6 Hz), 1.17 (d, 3H,  $J$  = 7.2 Hz), 0.99 (s, 9H), 0.72 (t, 3H,  $J$  = 7.2 Hz), 0.25 (s, 3H), 0.18 (s, 3H).  $^{13}\text{C}$  NMR (150 MHz):  $\delta$  204.0, 199.2, 171.2, 156.0, 149.4, 130.6, 124.7, 110.6, 109.2, 84.4, 81.0, 69.9, 55.9, 49.6, 49.3, 46.8, 29.2, 26.0, 19.2, 18.3, 14.7, 10.2, 8.65, -3.83, -3.94. MS (EI $^+$ ):  $m/z$  501 ( $\text{M}^+$ ); HRMS (EI $^+$ ): found 501.2533, calcd for  $[\text{C}_{27}\text{H}_{39}\text{NO}_6\text{Si}]^+$  501.2547. IR:  $\nu$  3365 (br), 2955, 2927, 2854, 1788, 1722, 1710, 1693, 1653, 1636, 1620, 1593, 1421, 1380, 1291, 1251, 1226, 1202  $\text{cm}^{-1}$ .



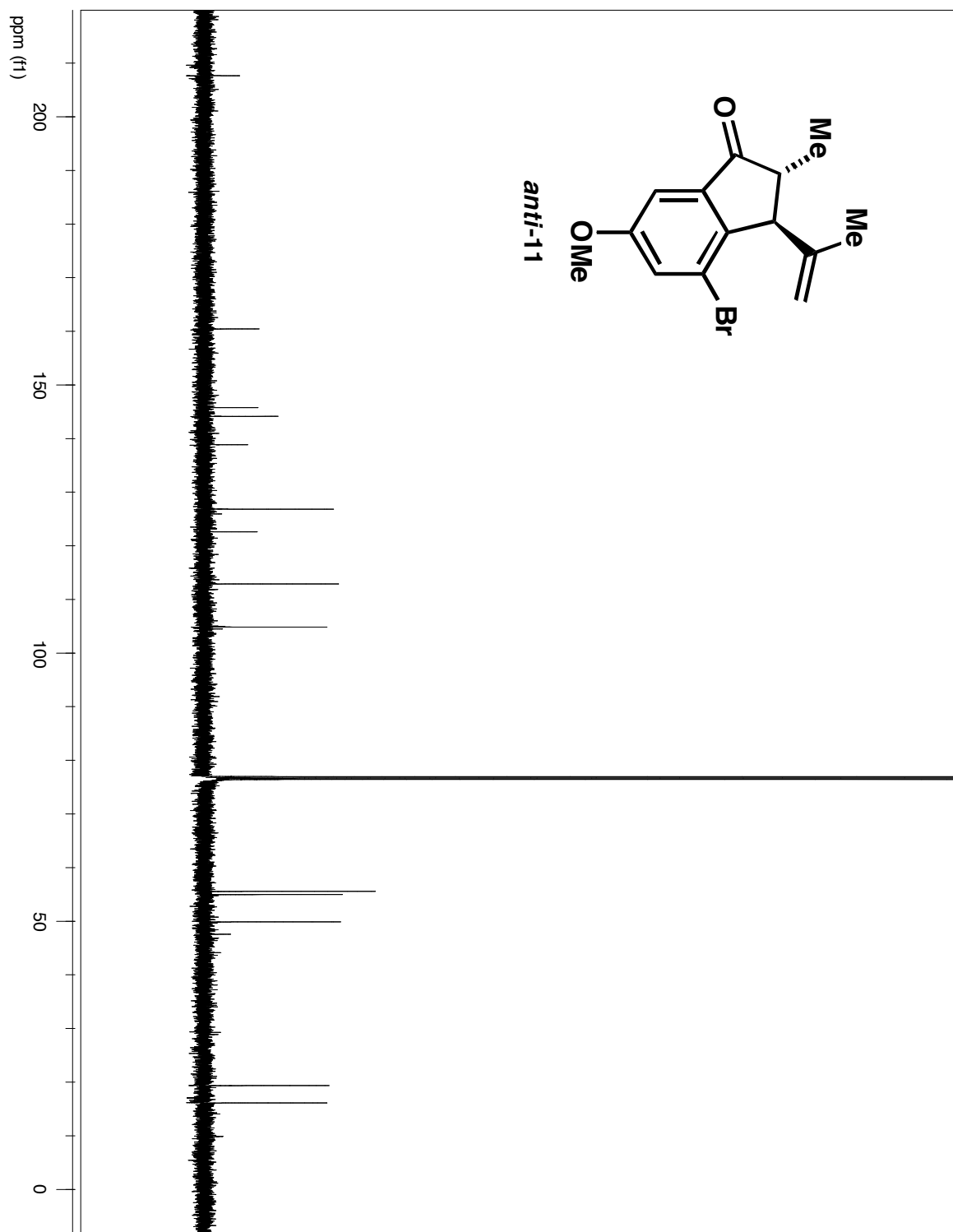


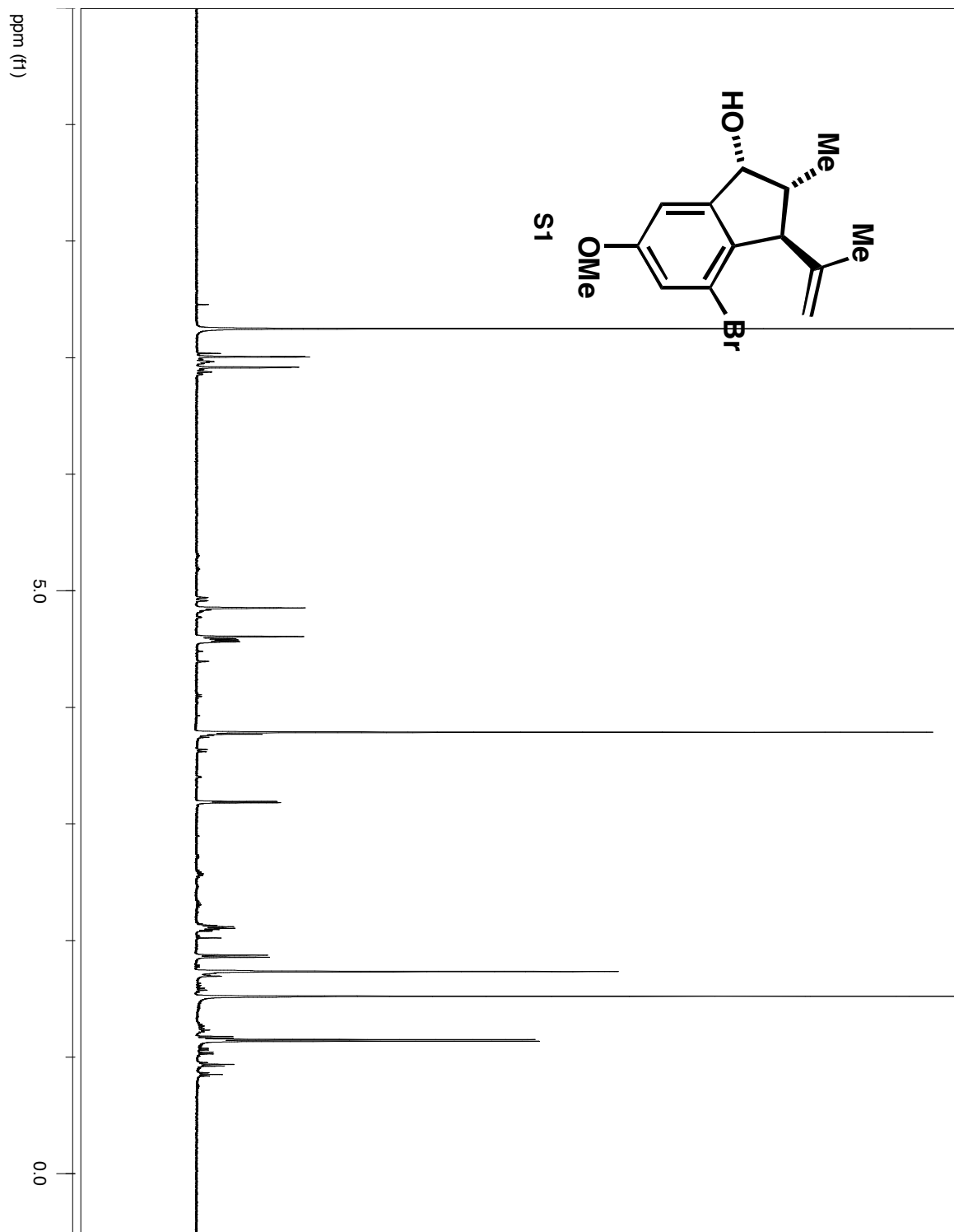


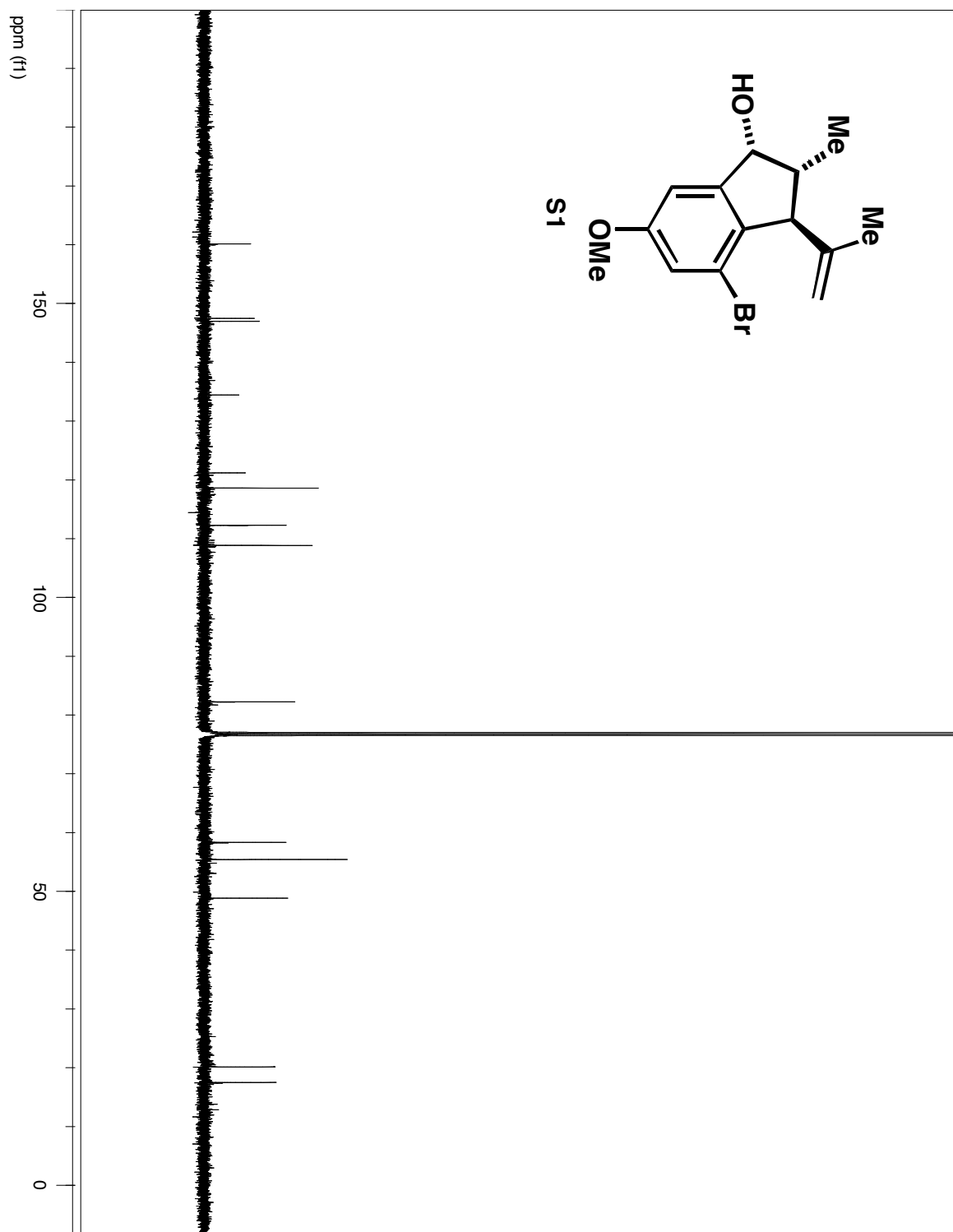


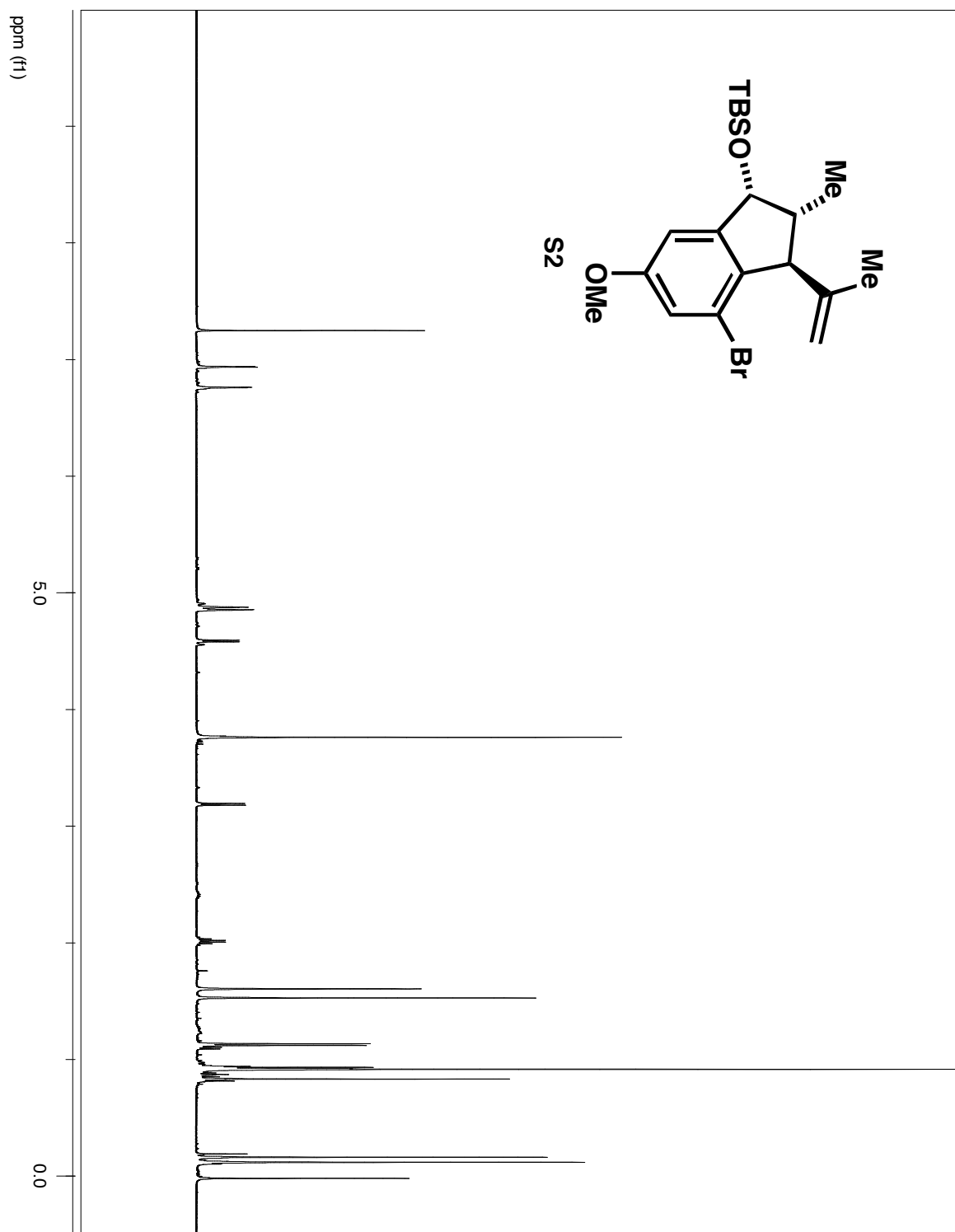


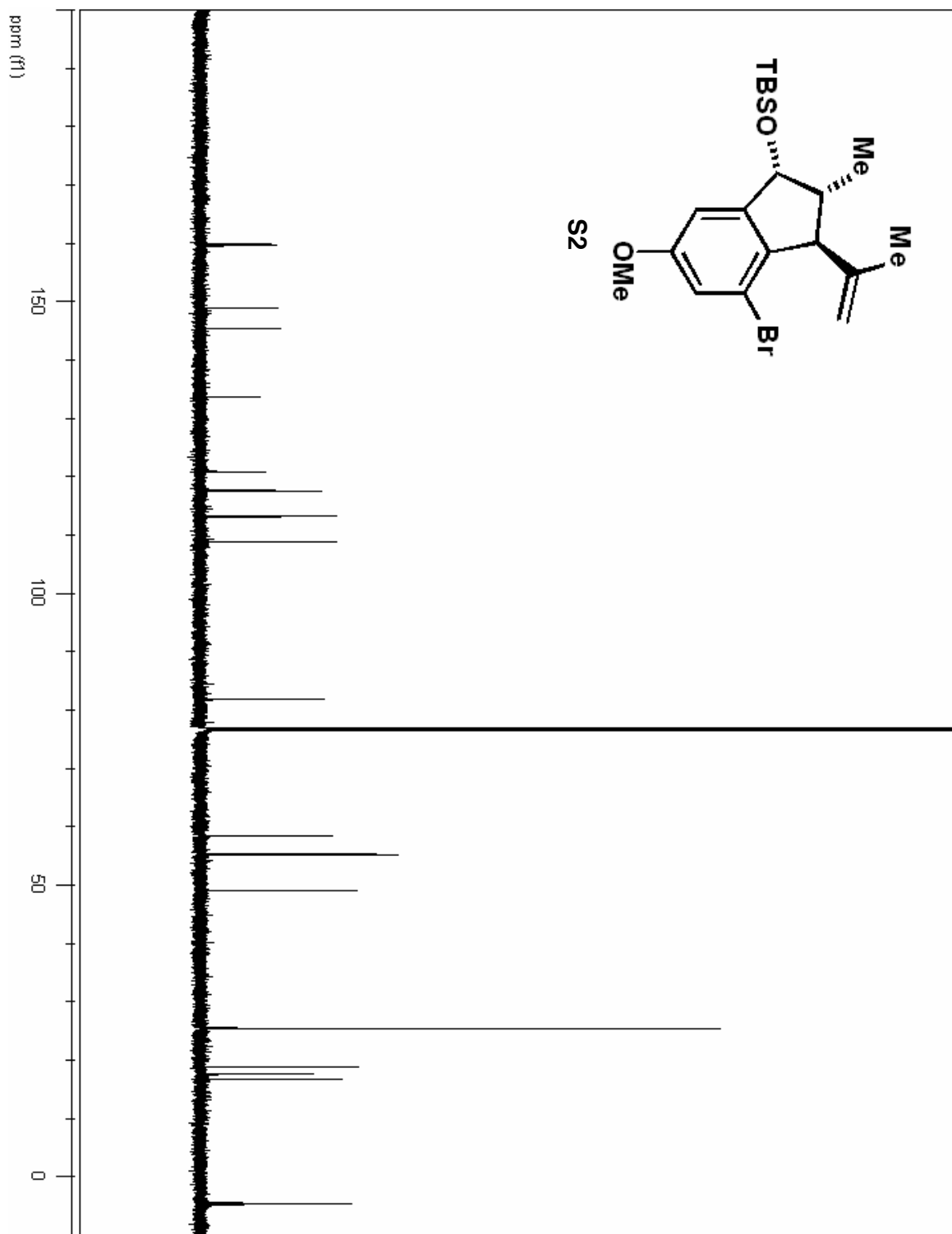


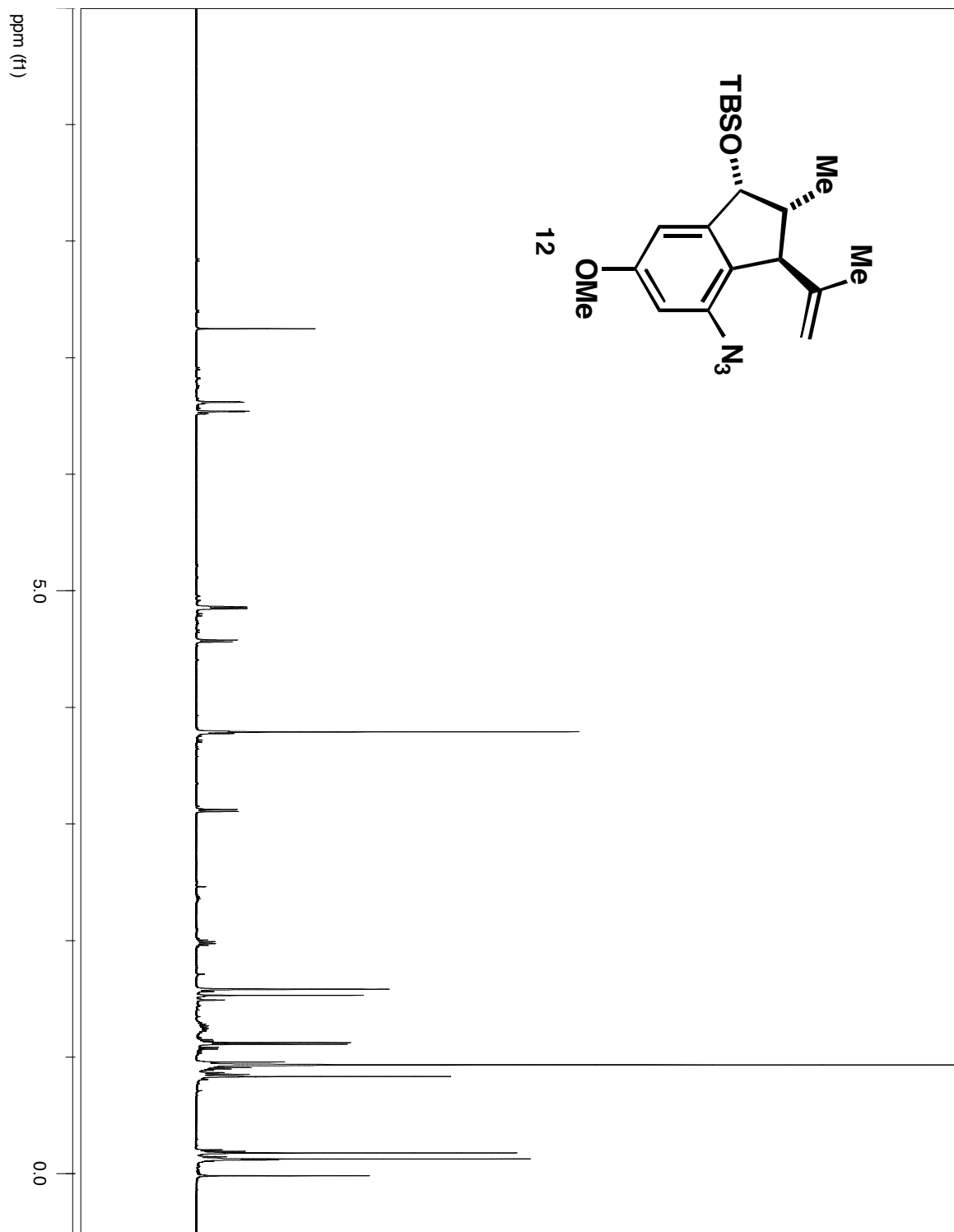


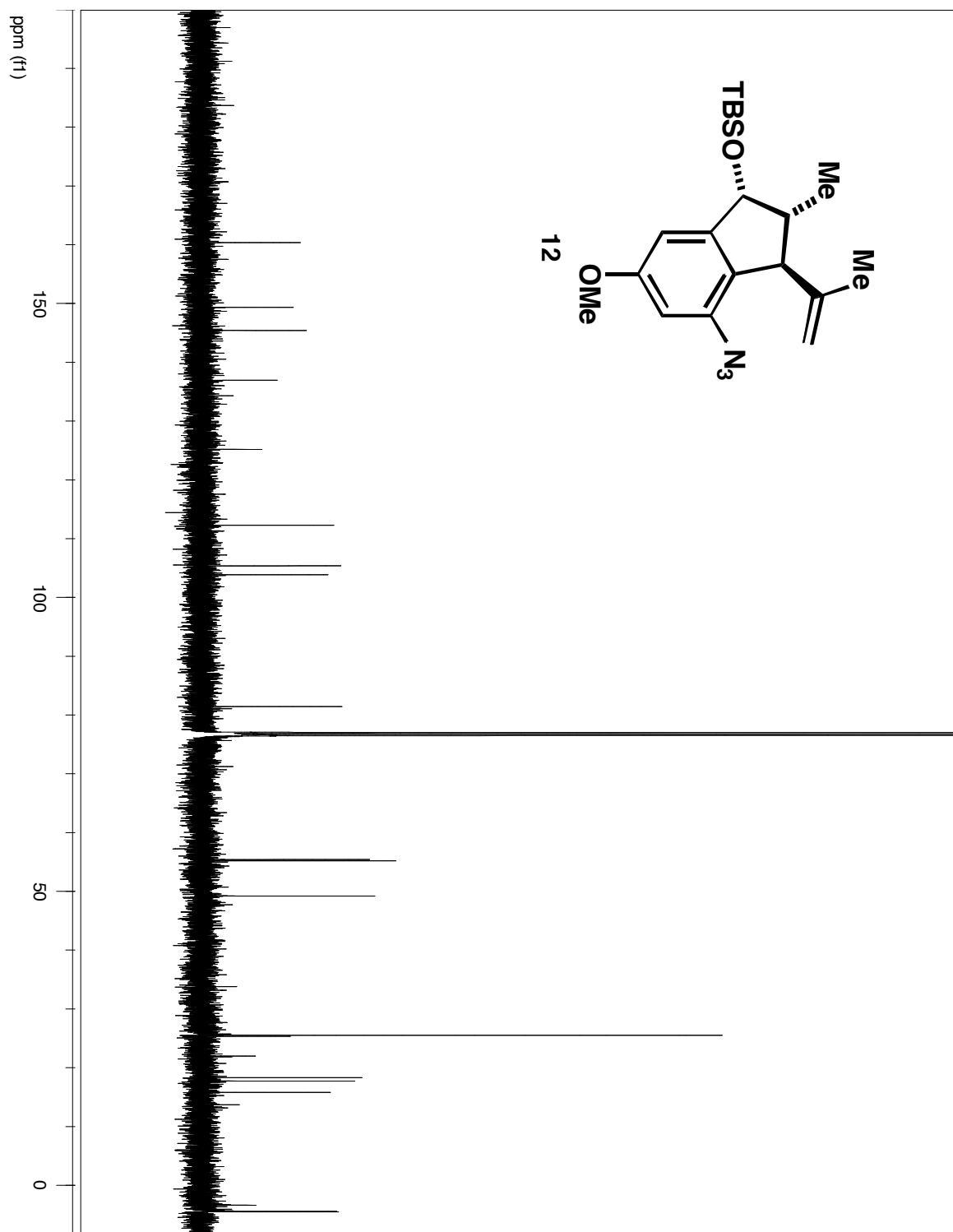


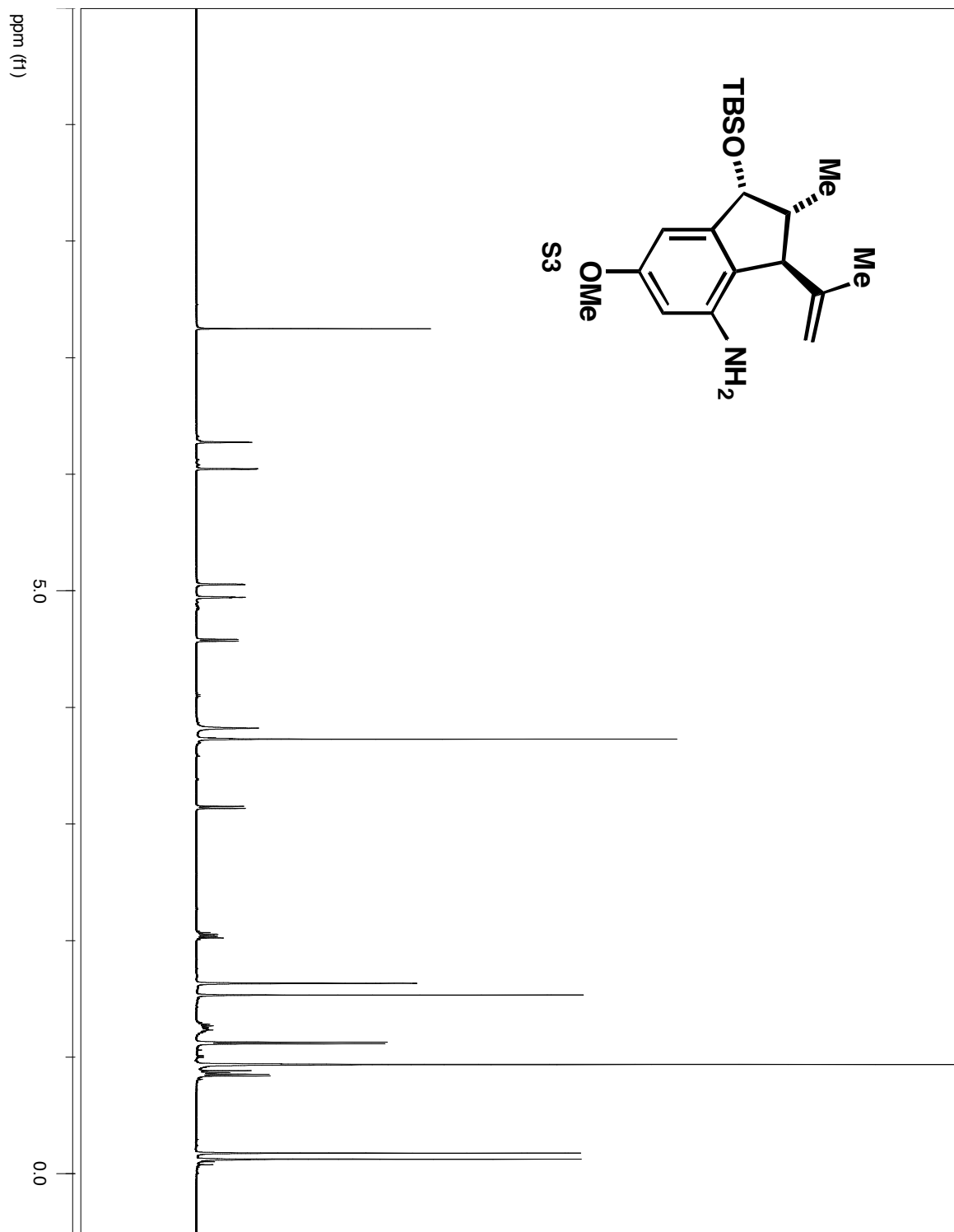




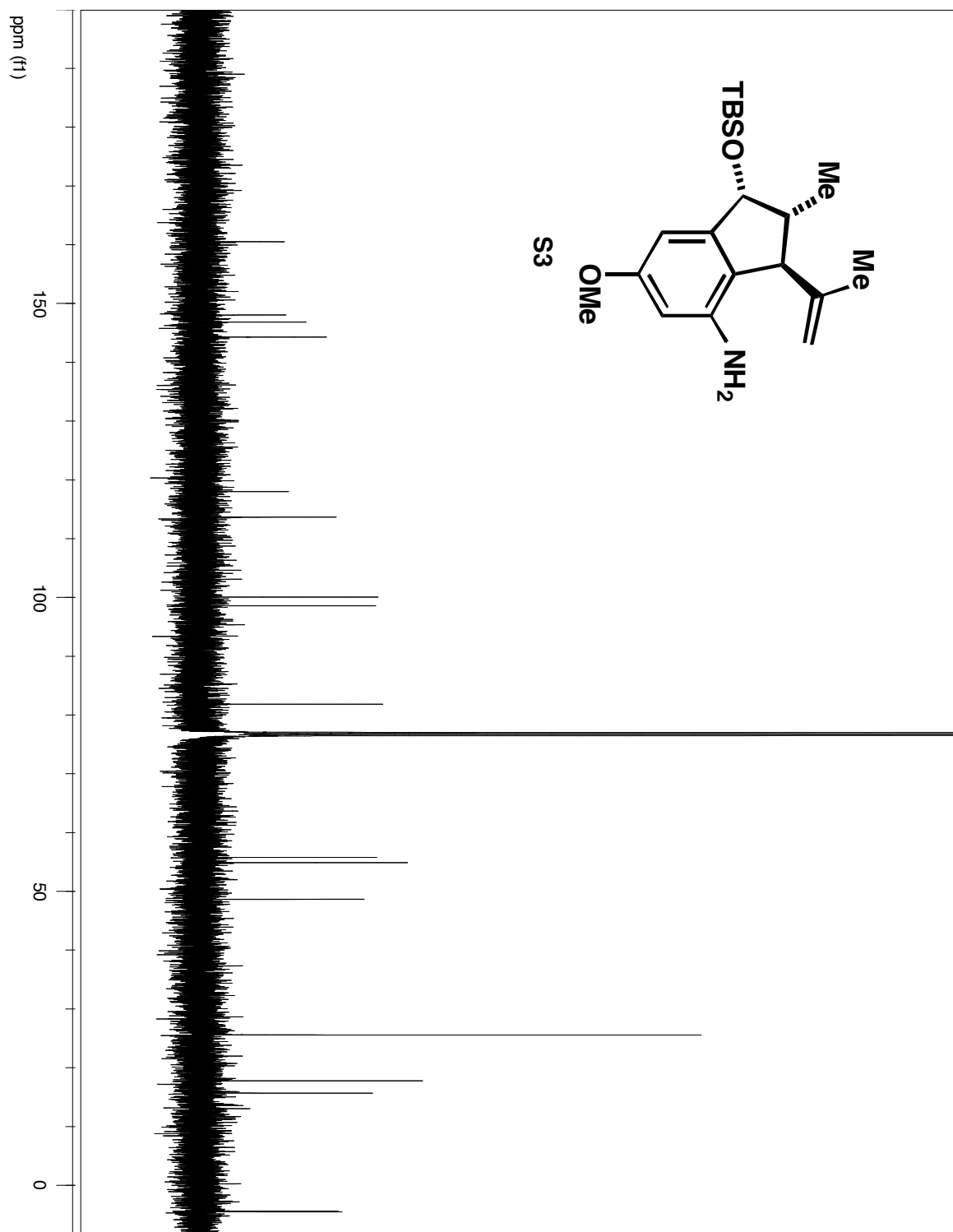


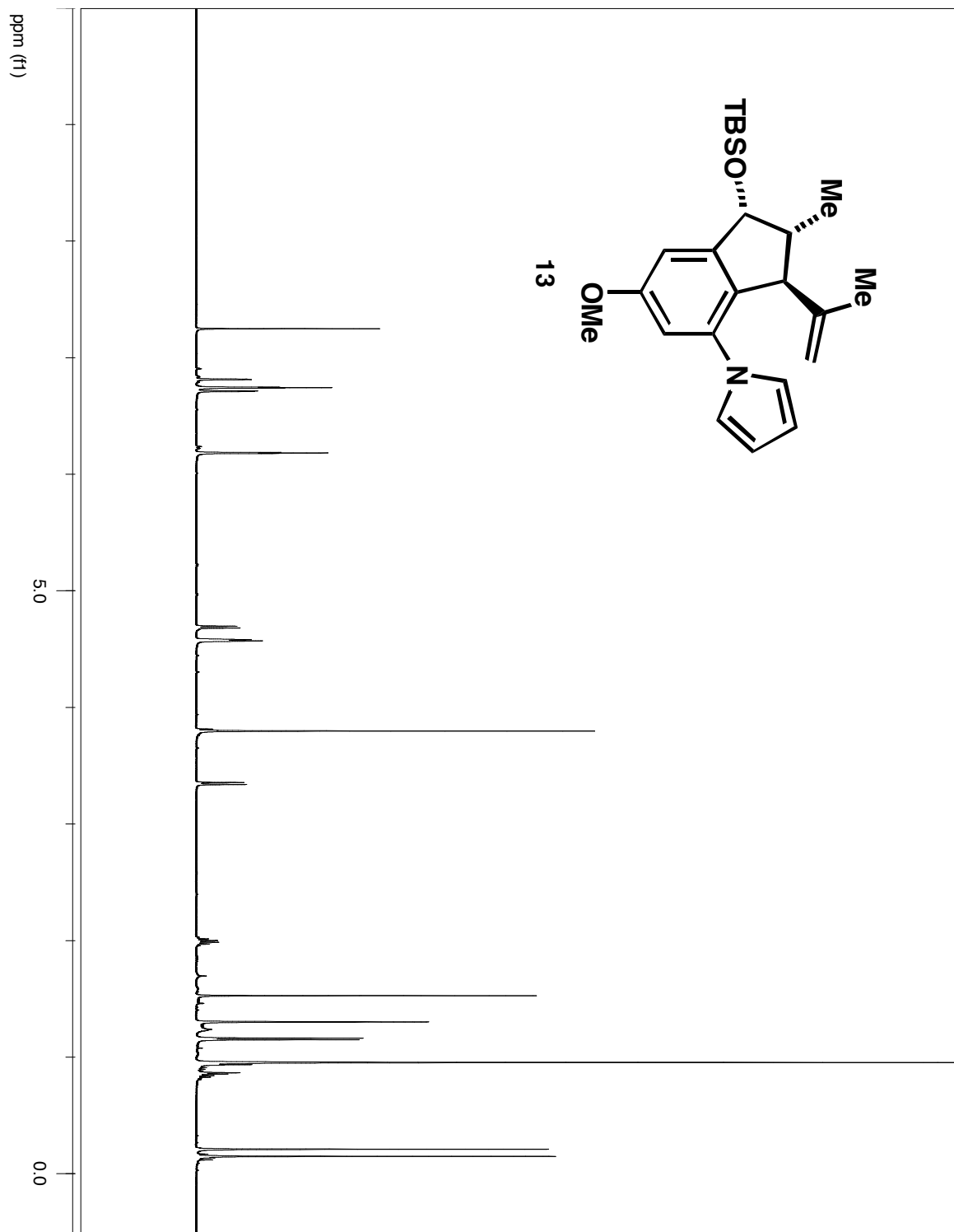


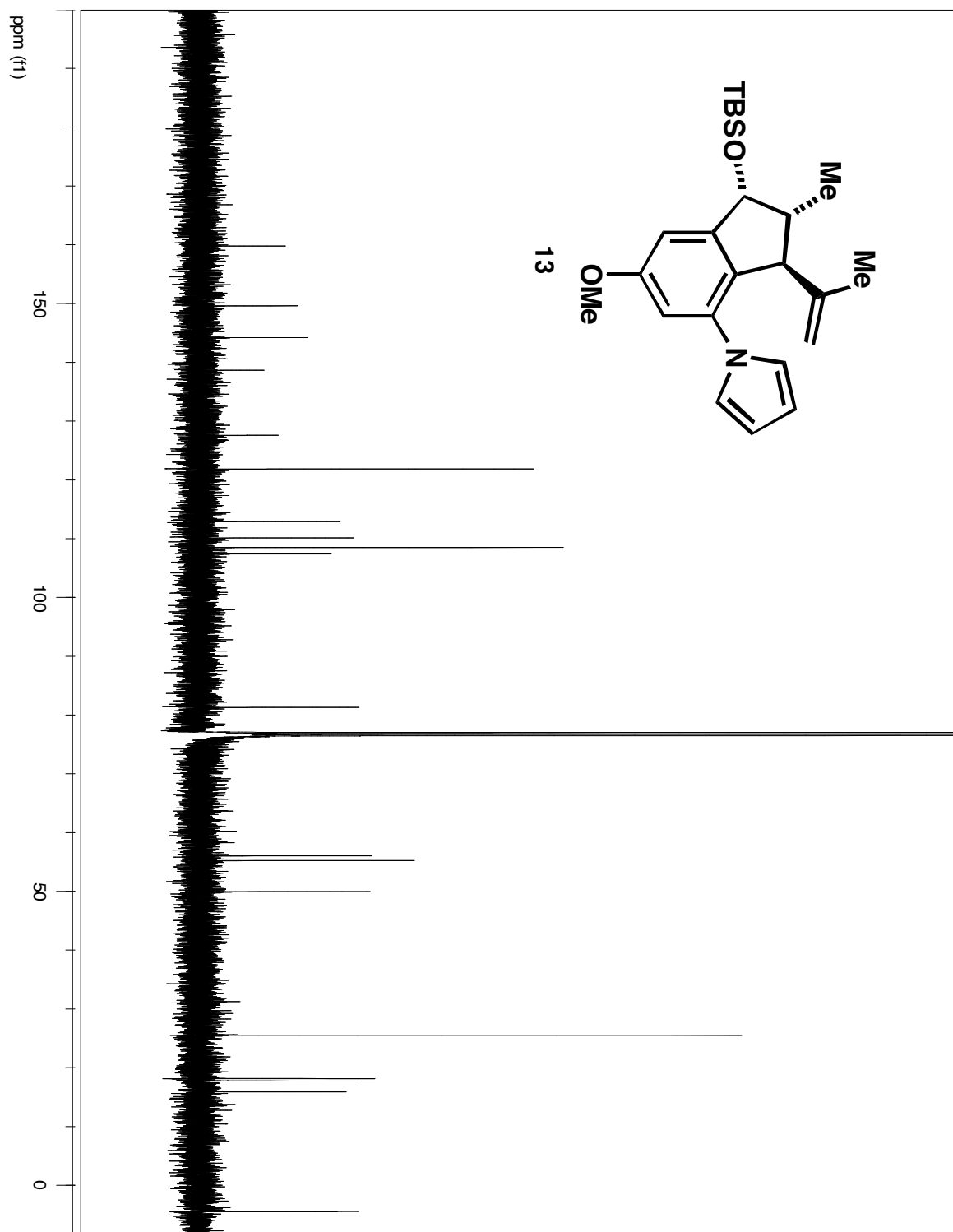


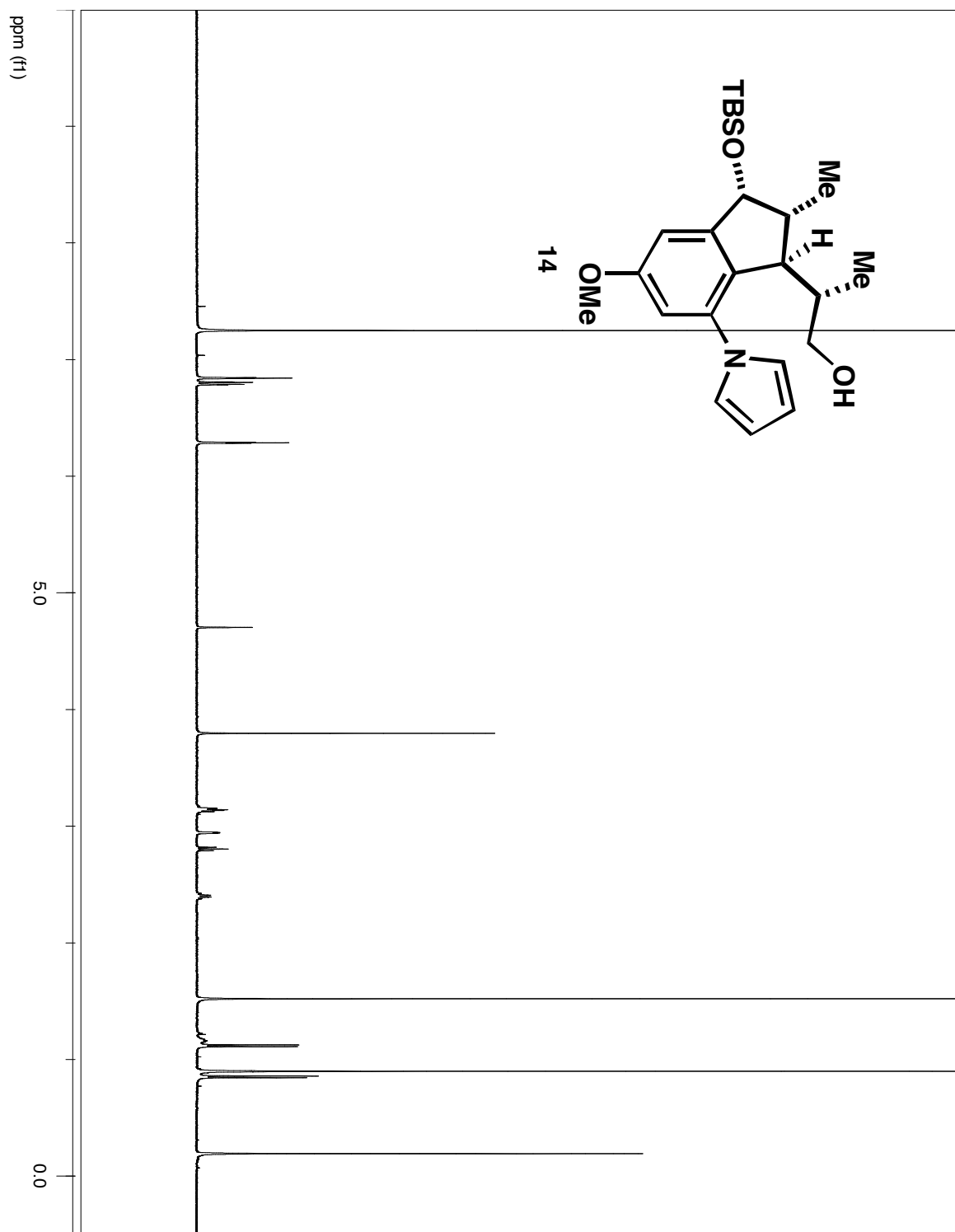


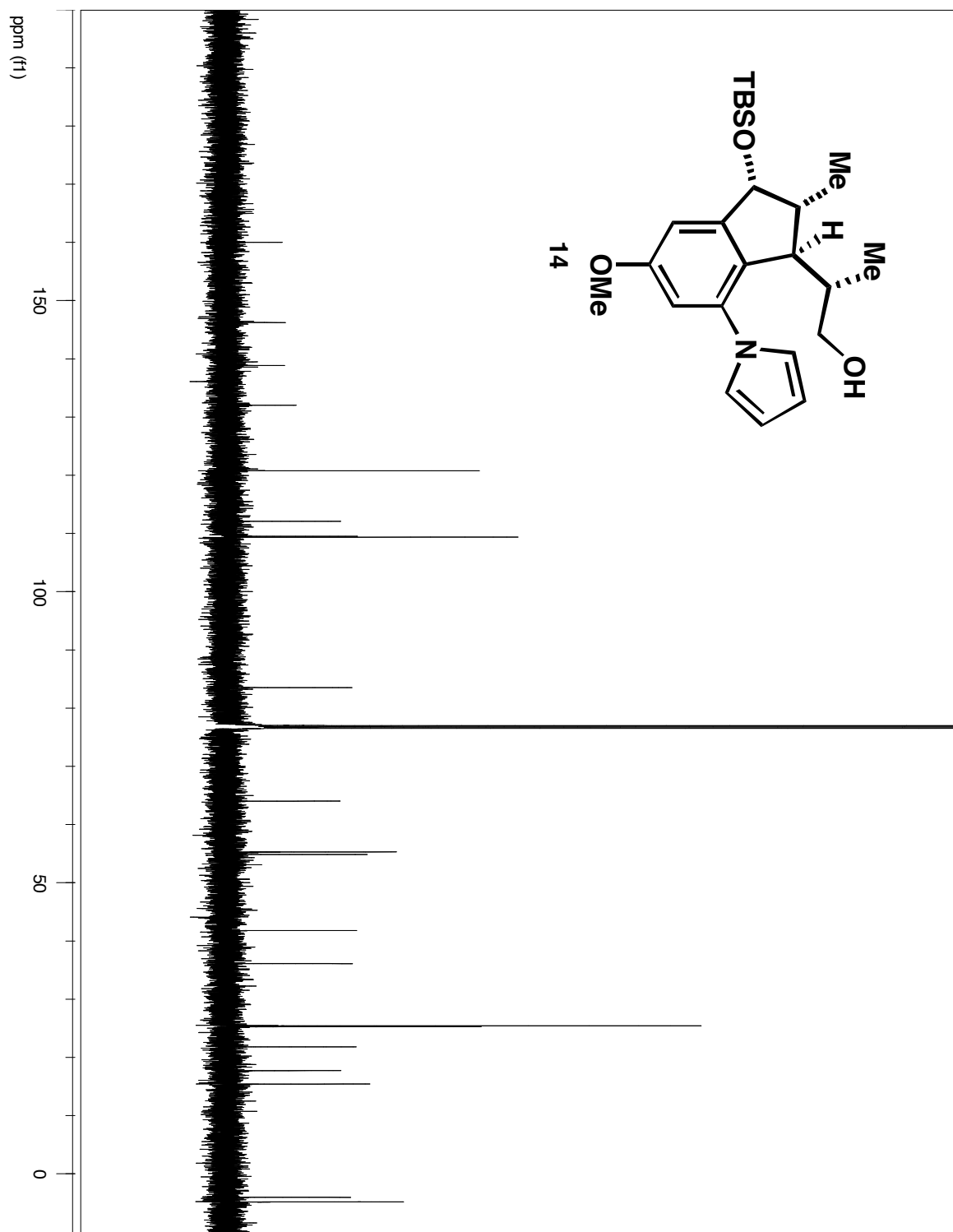


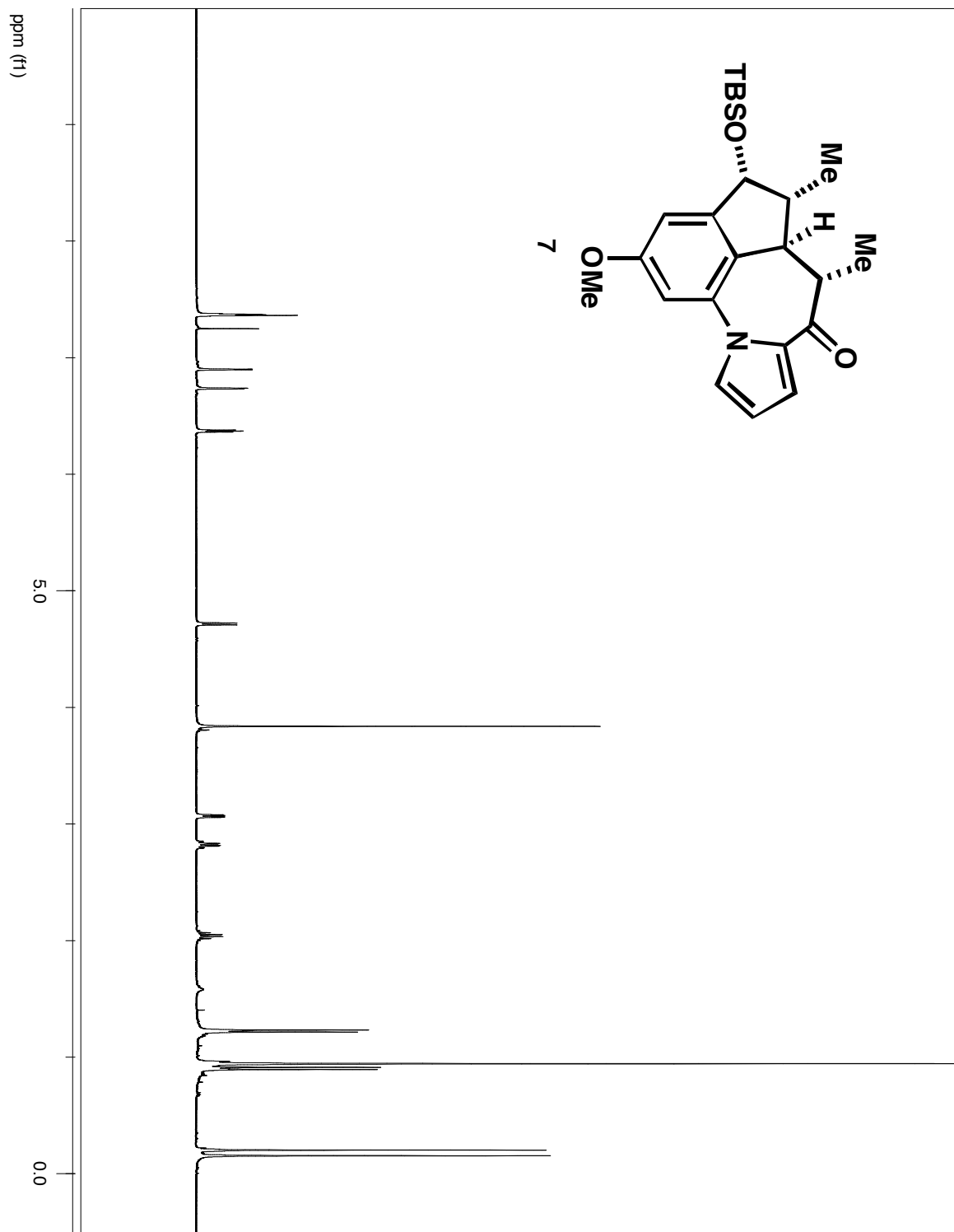


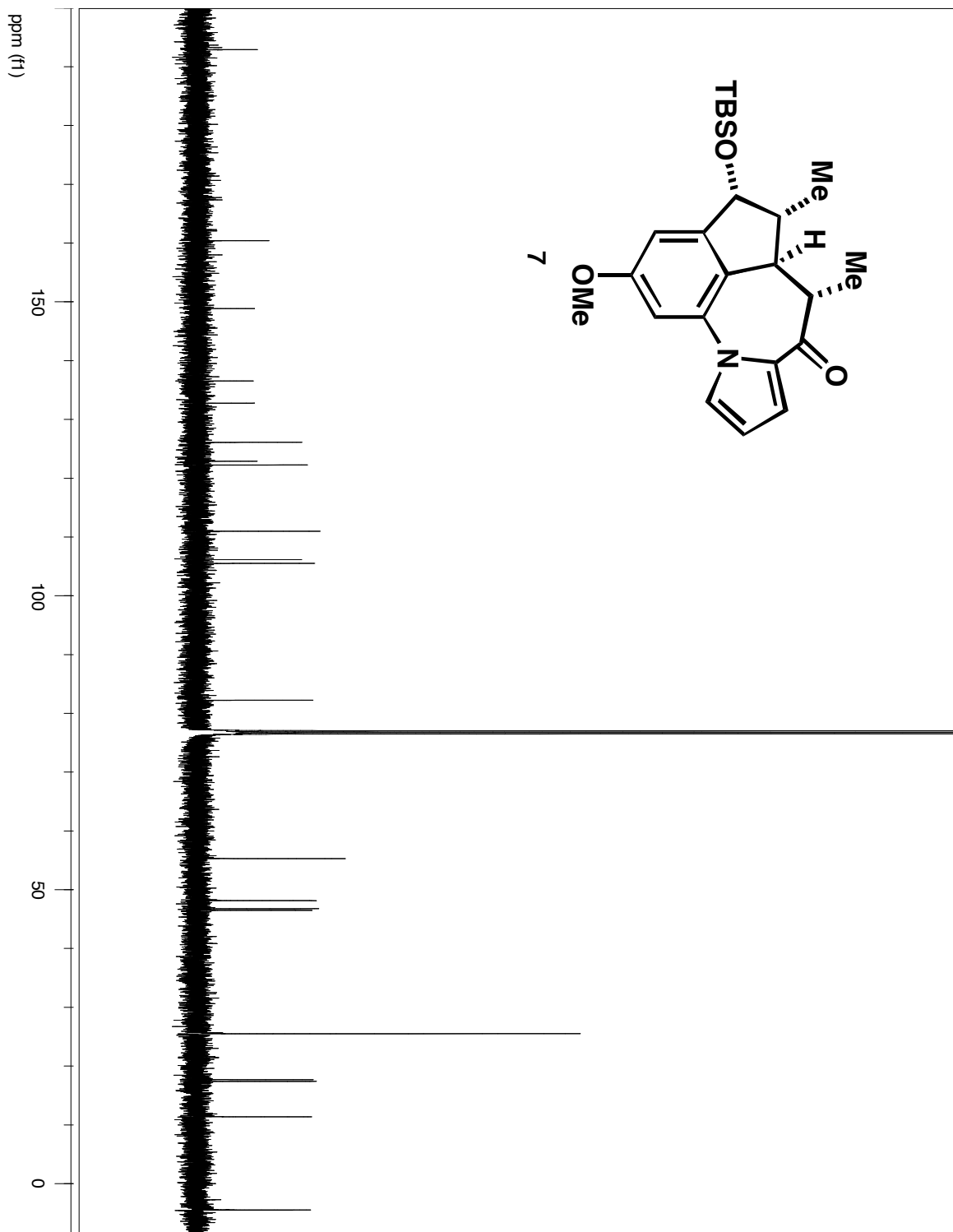


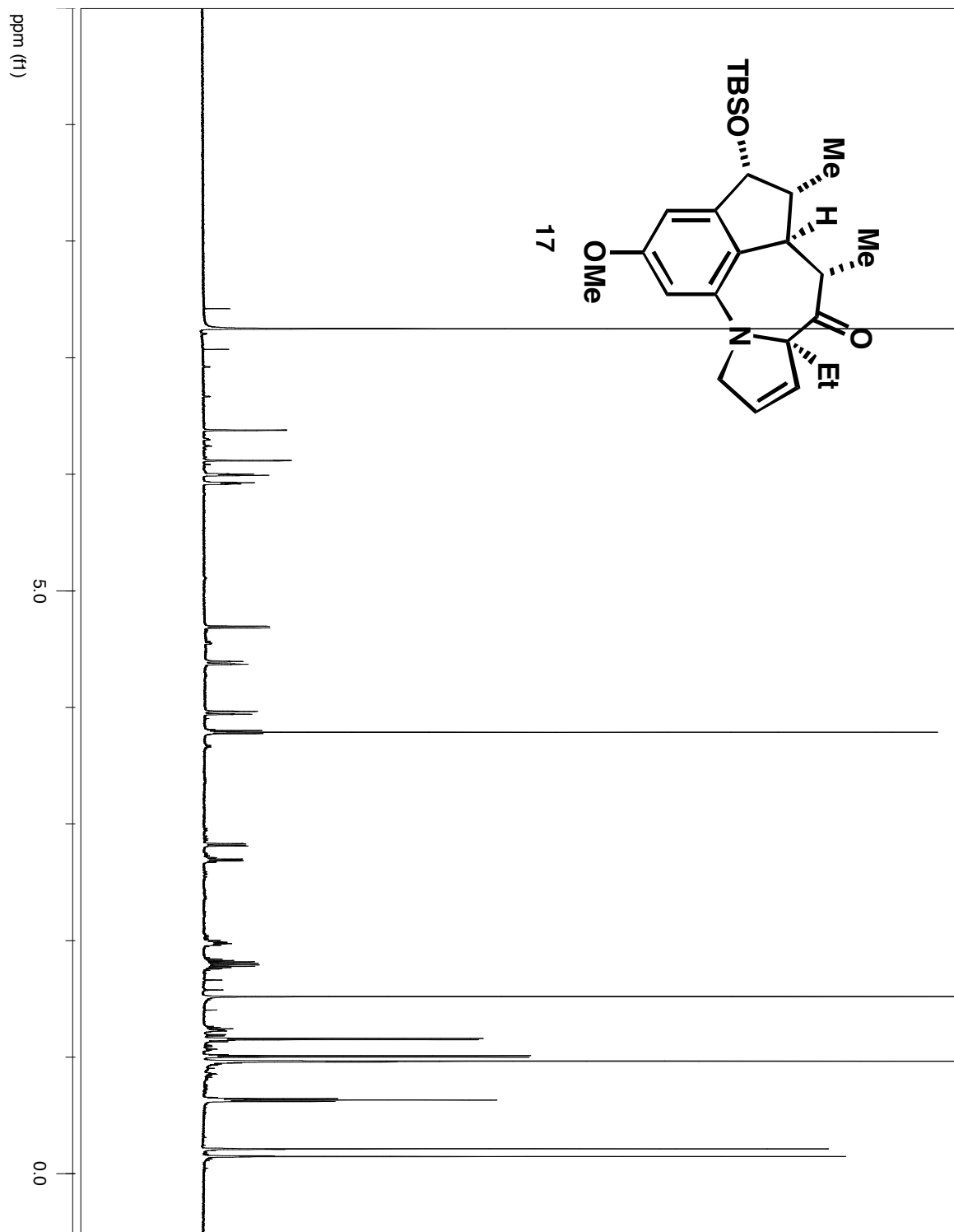




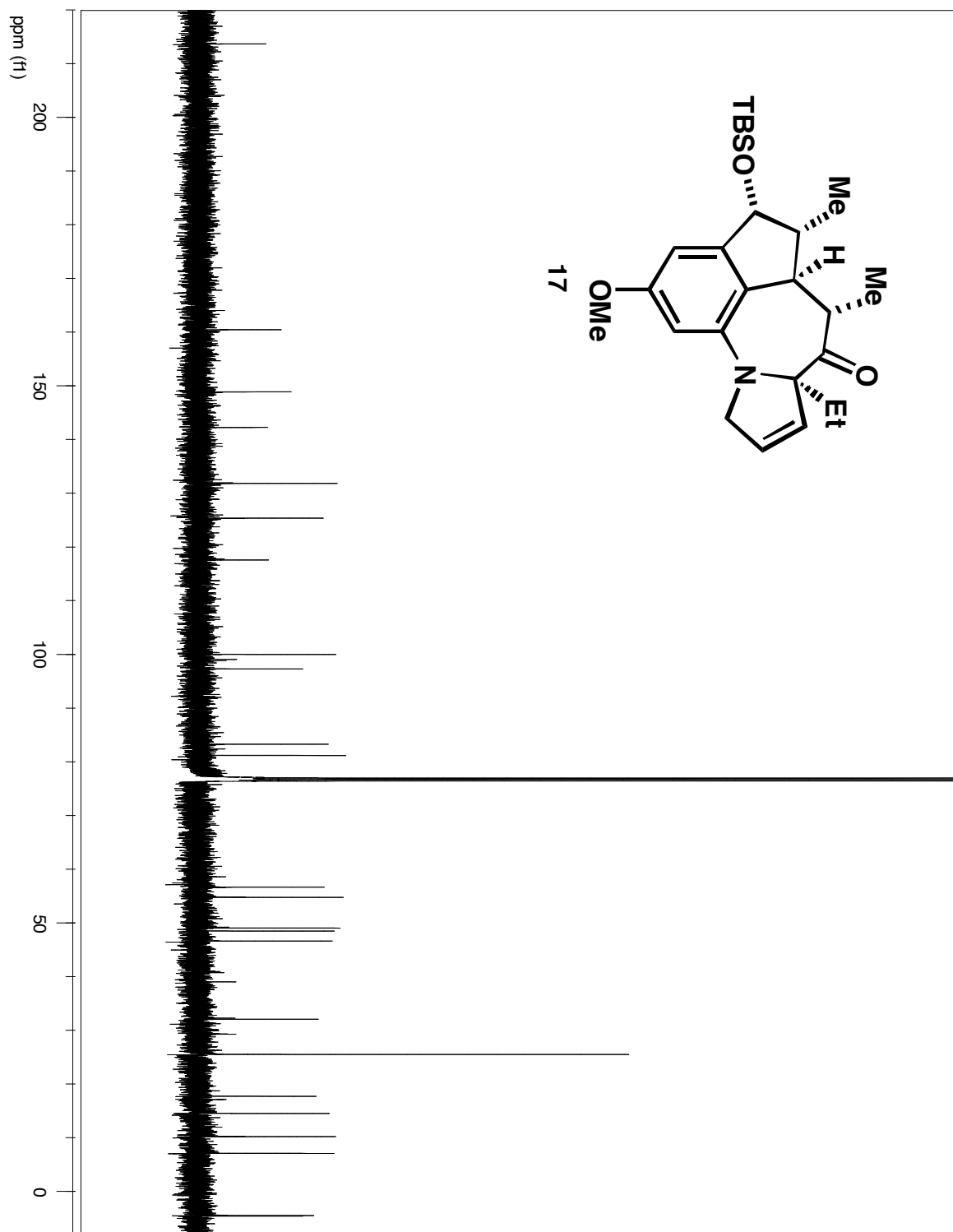


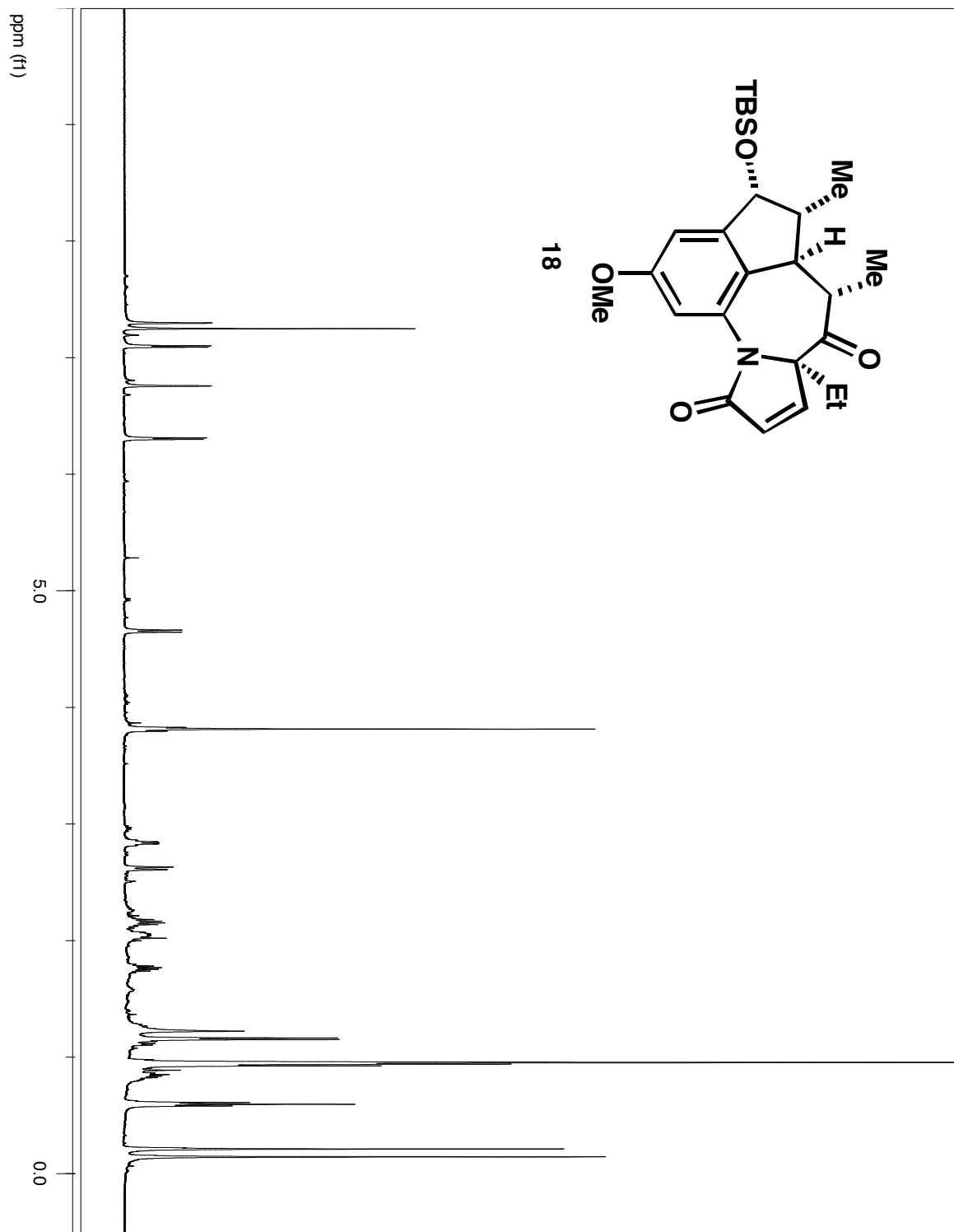


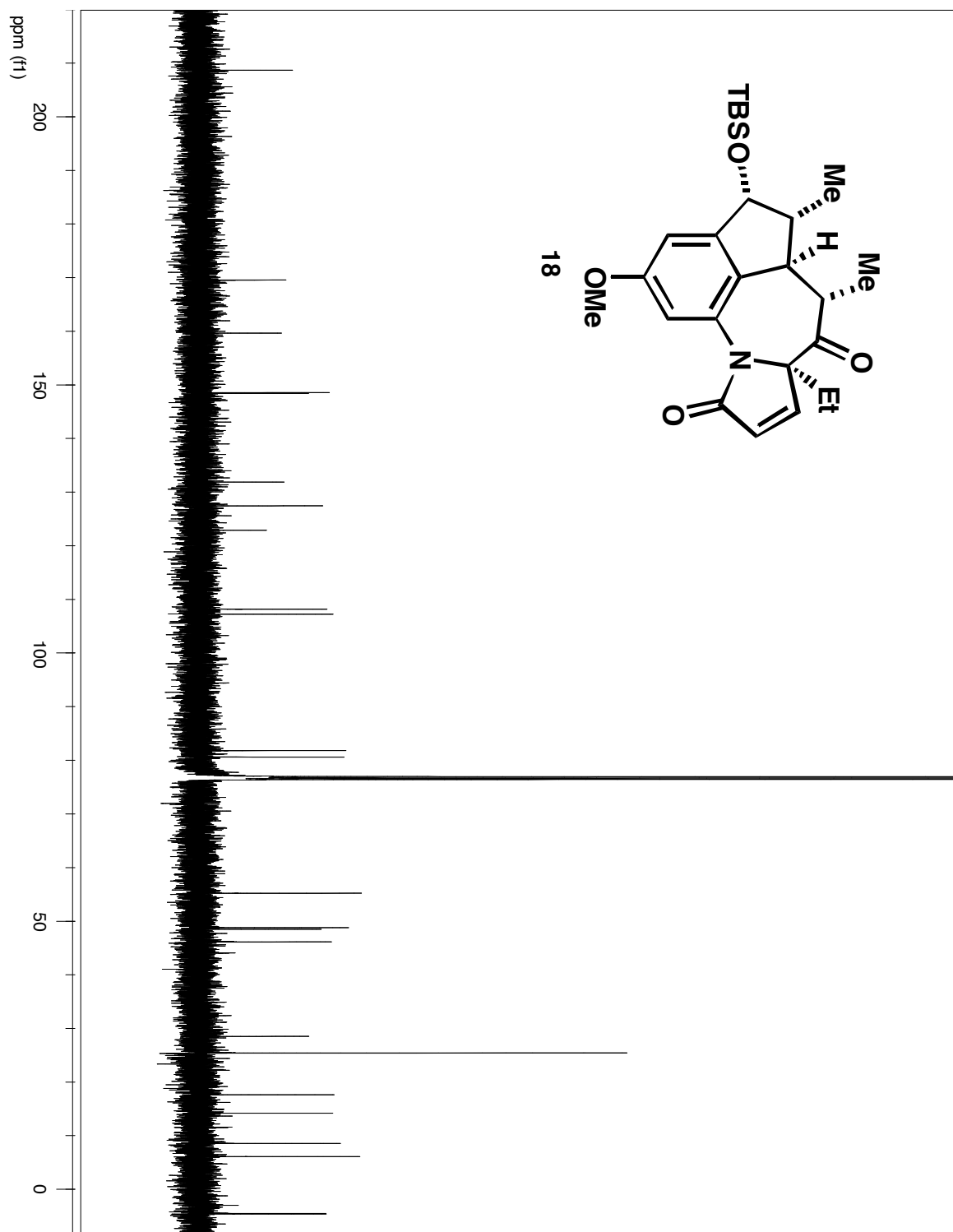


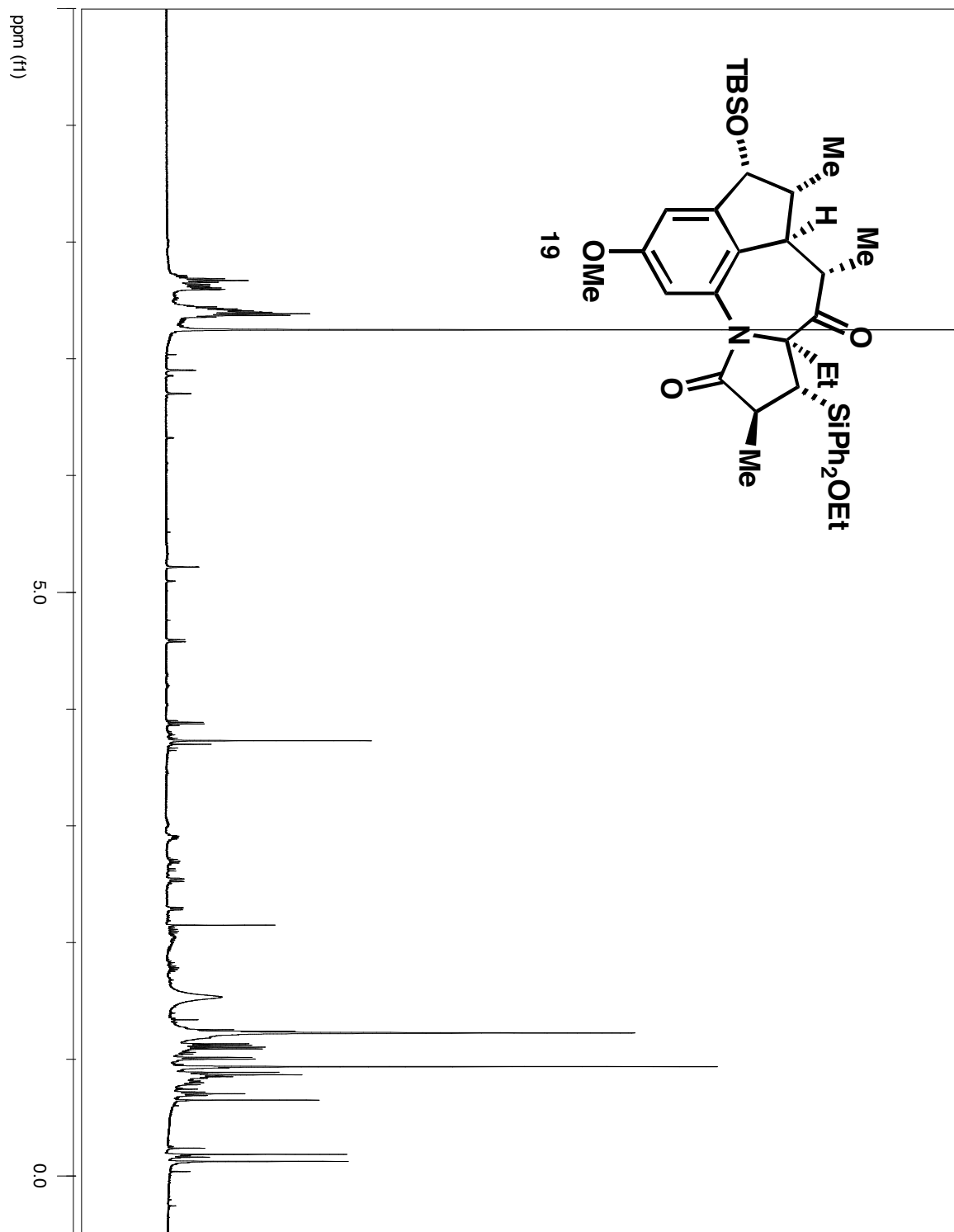


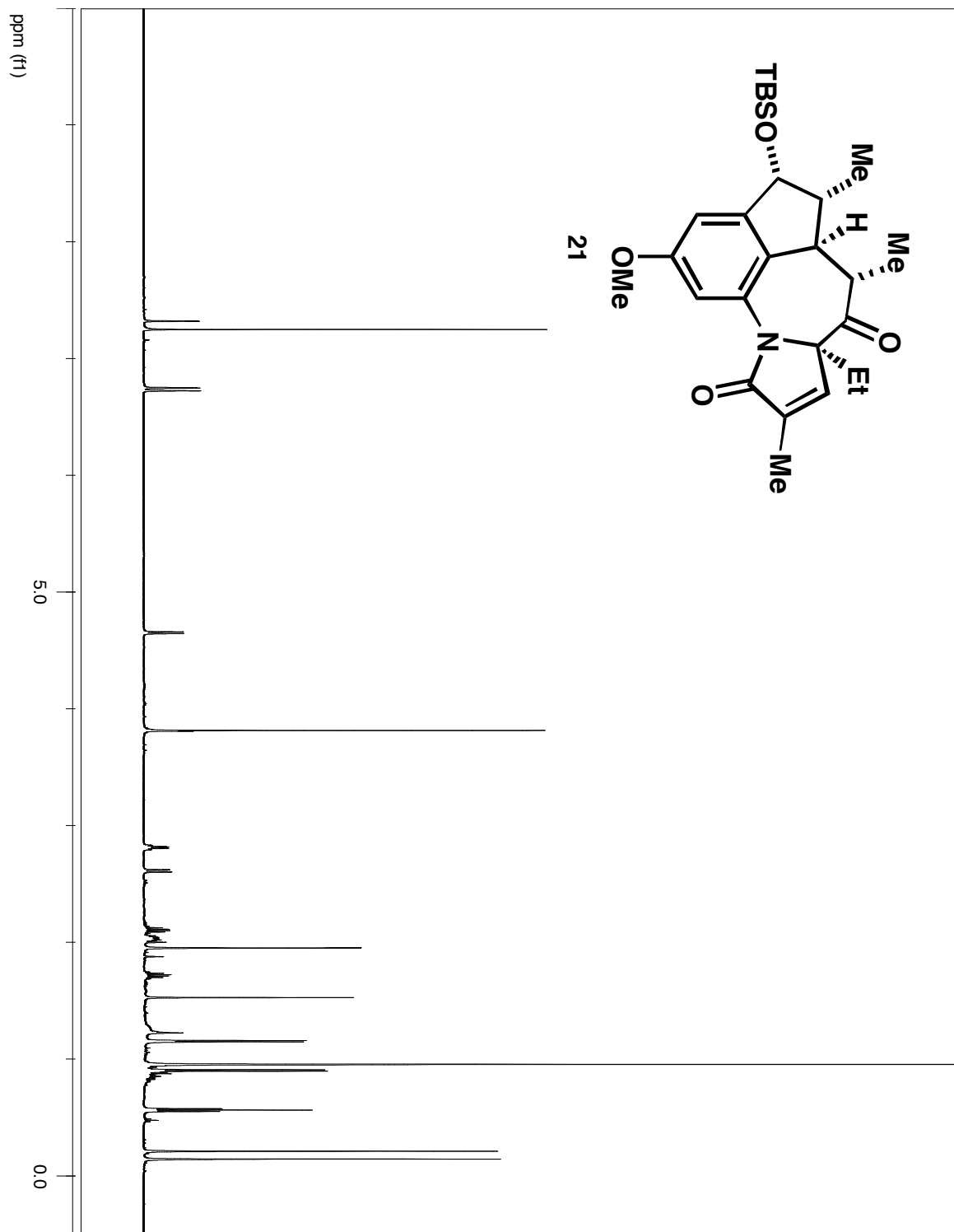


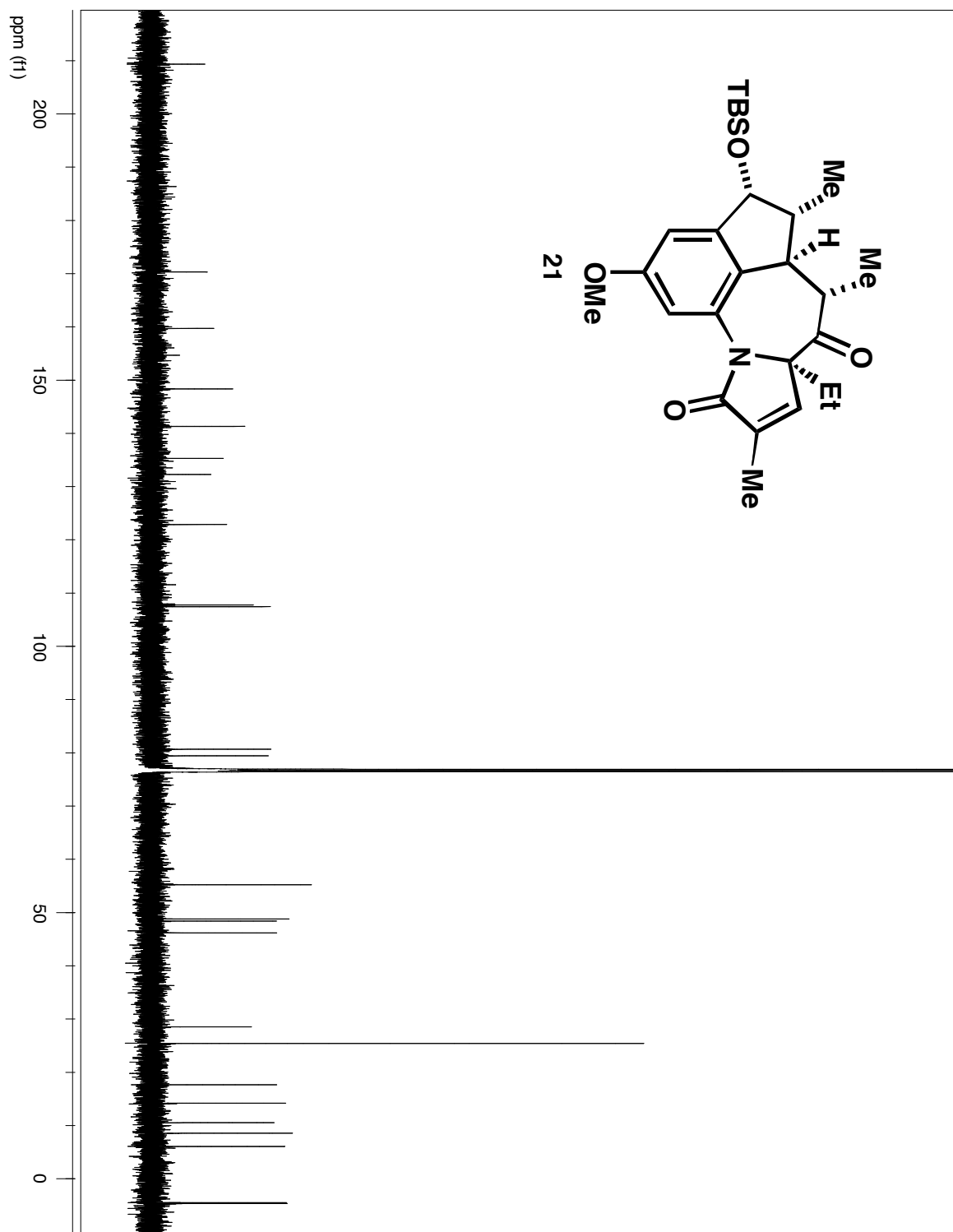


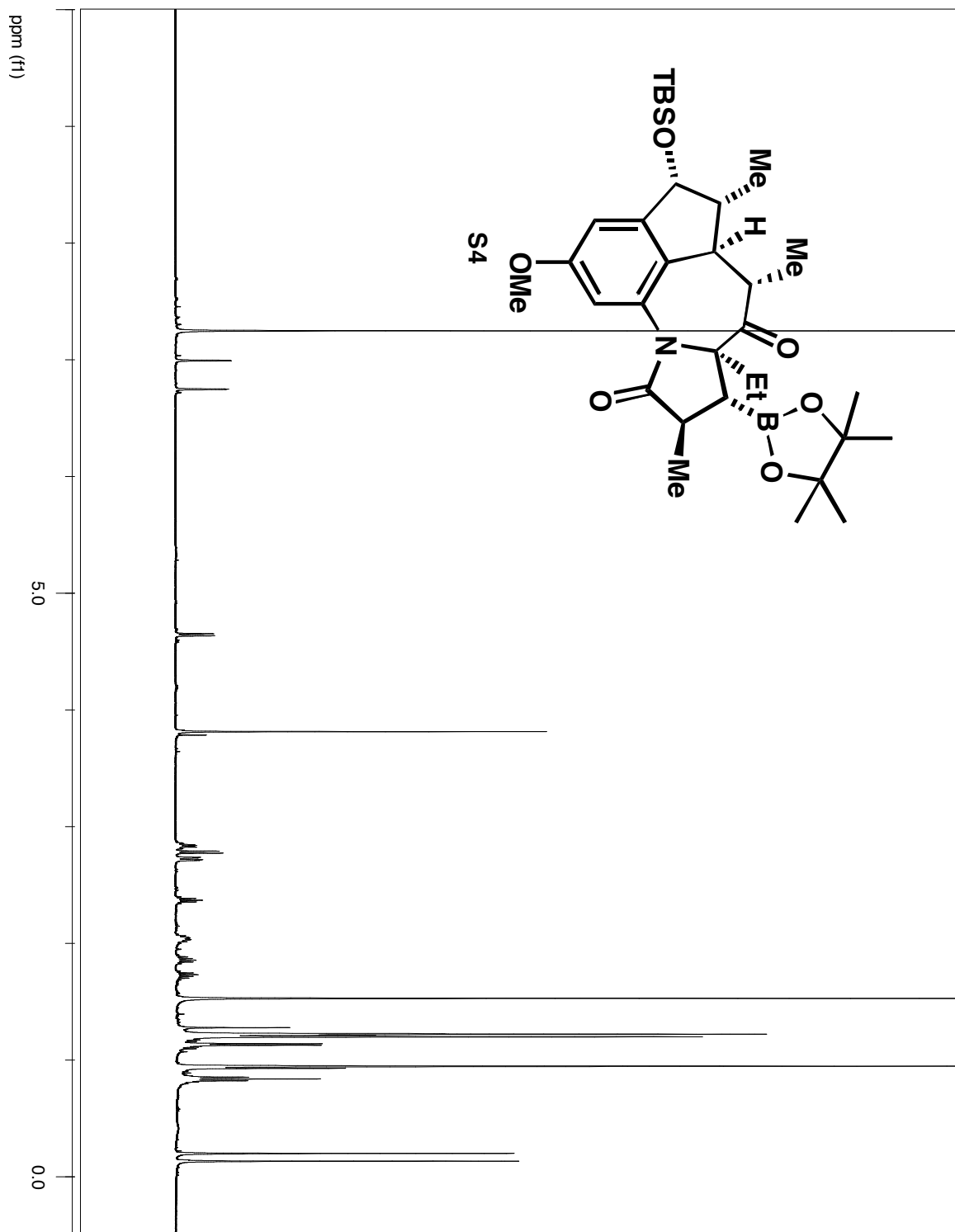


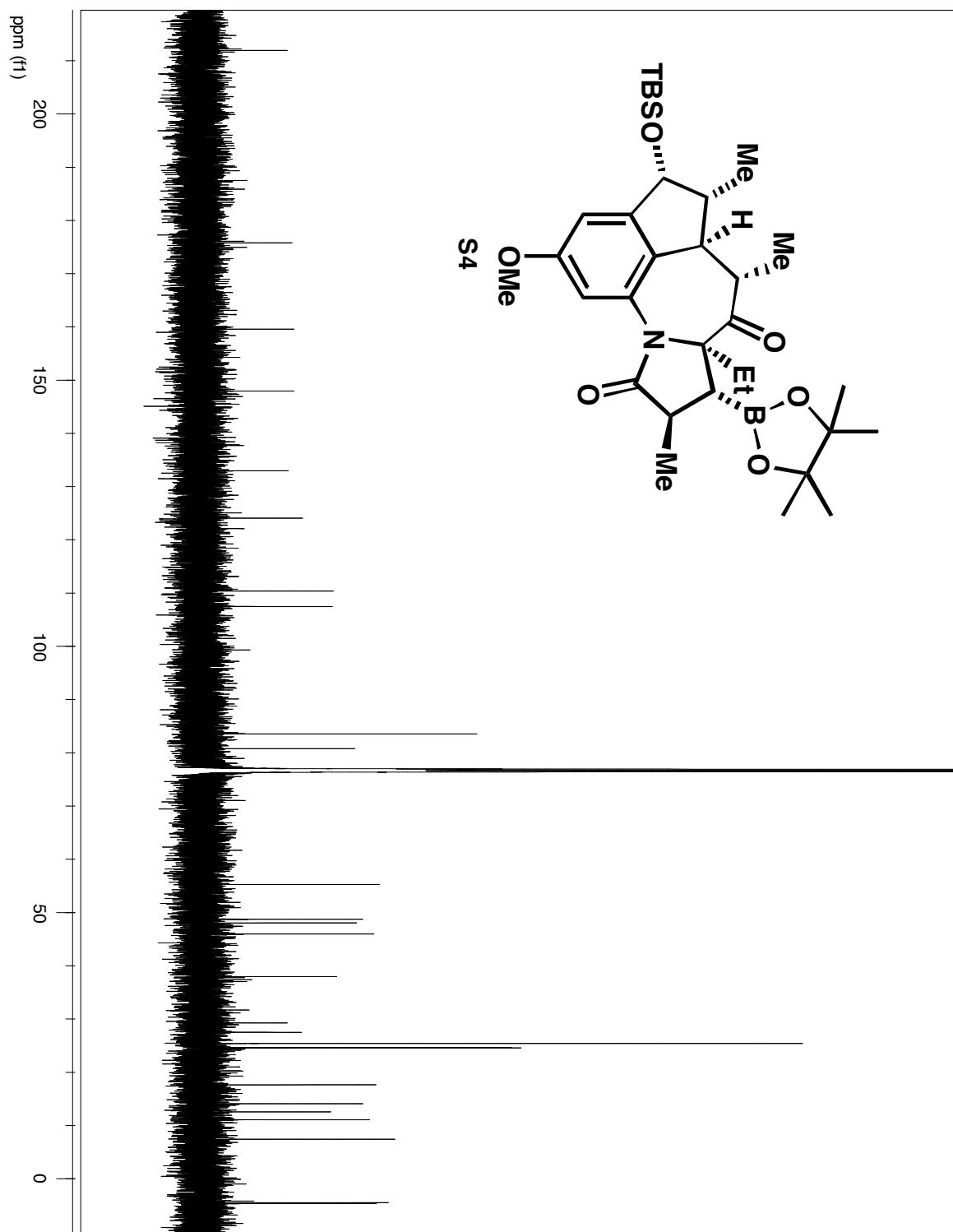




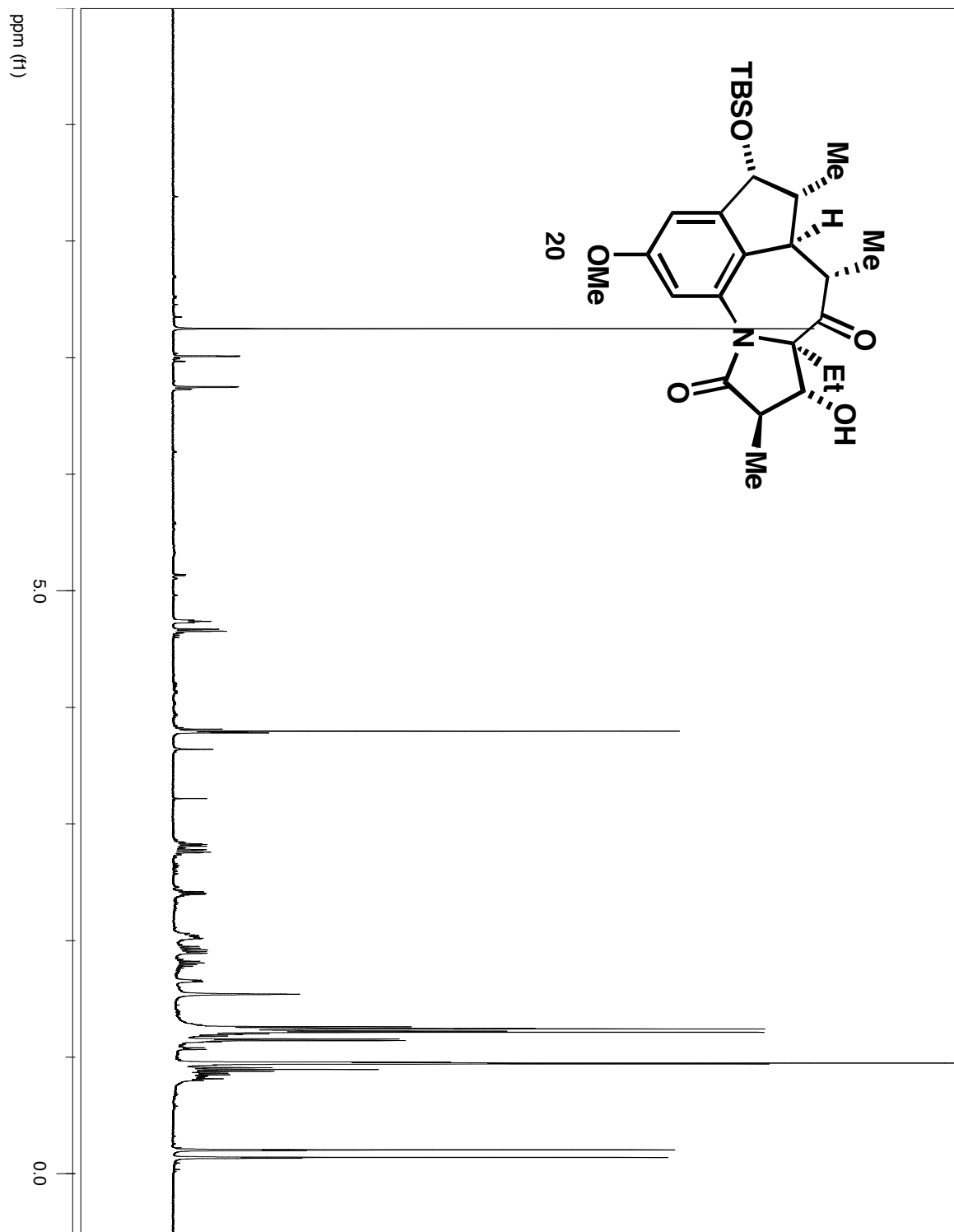


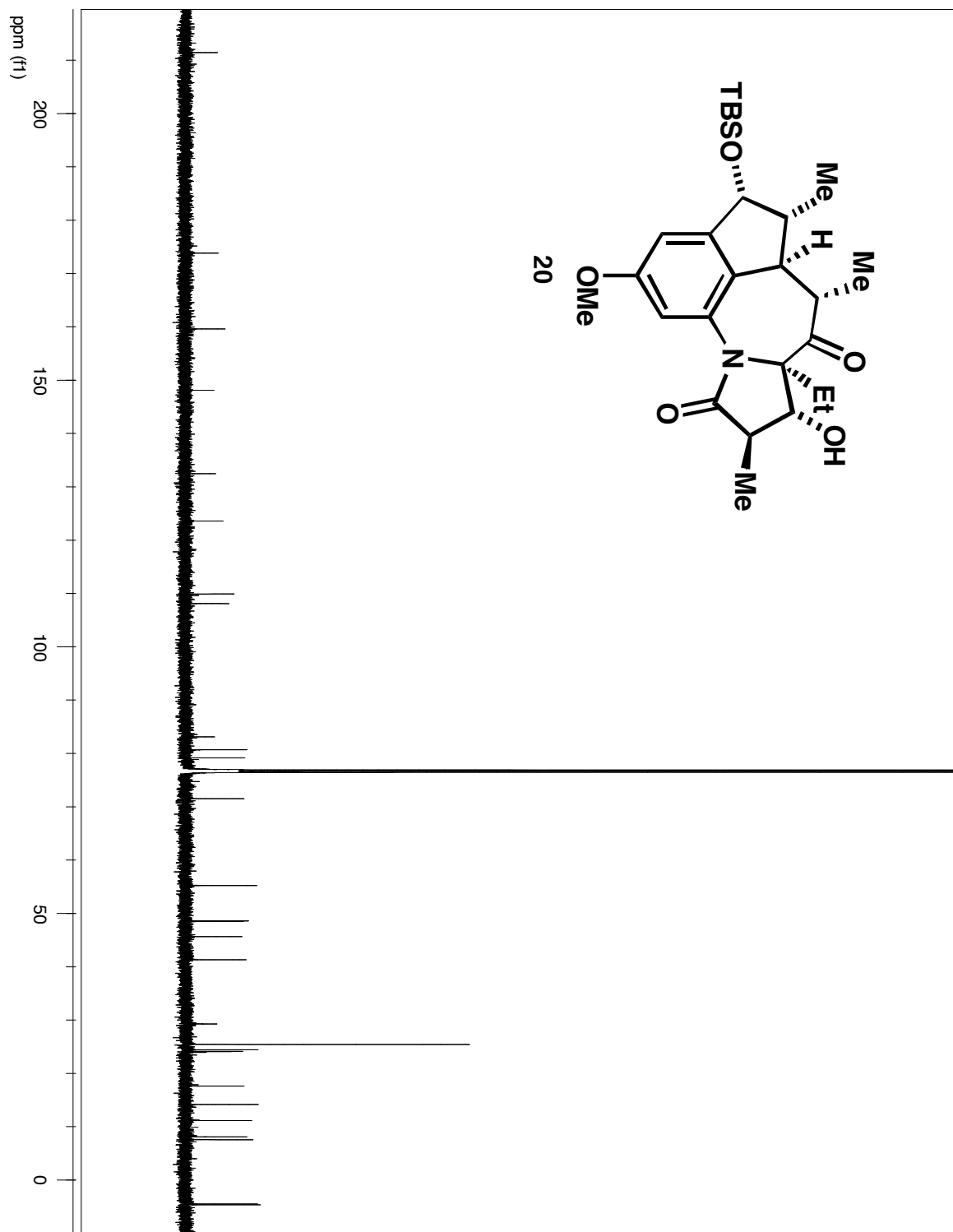


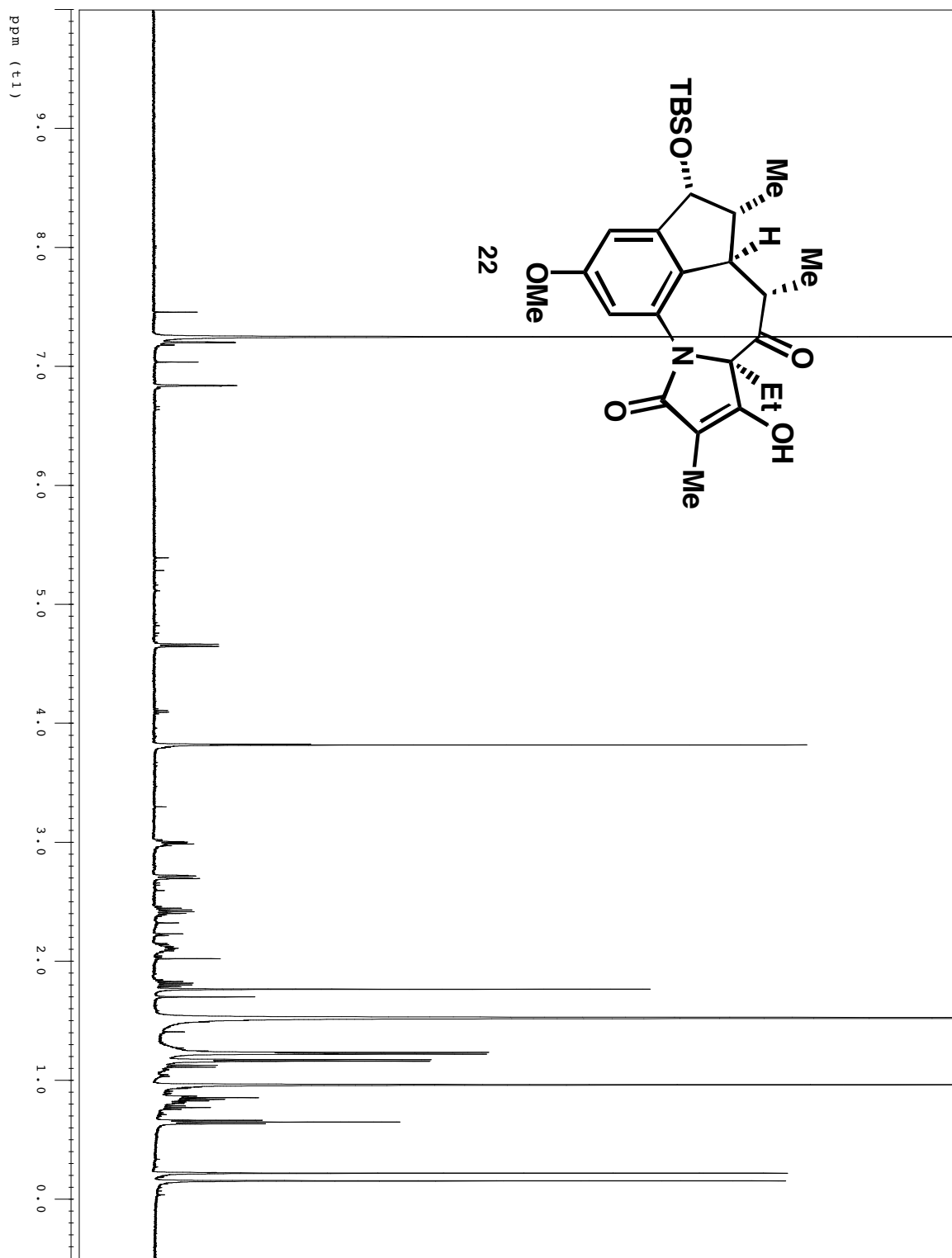


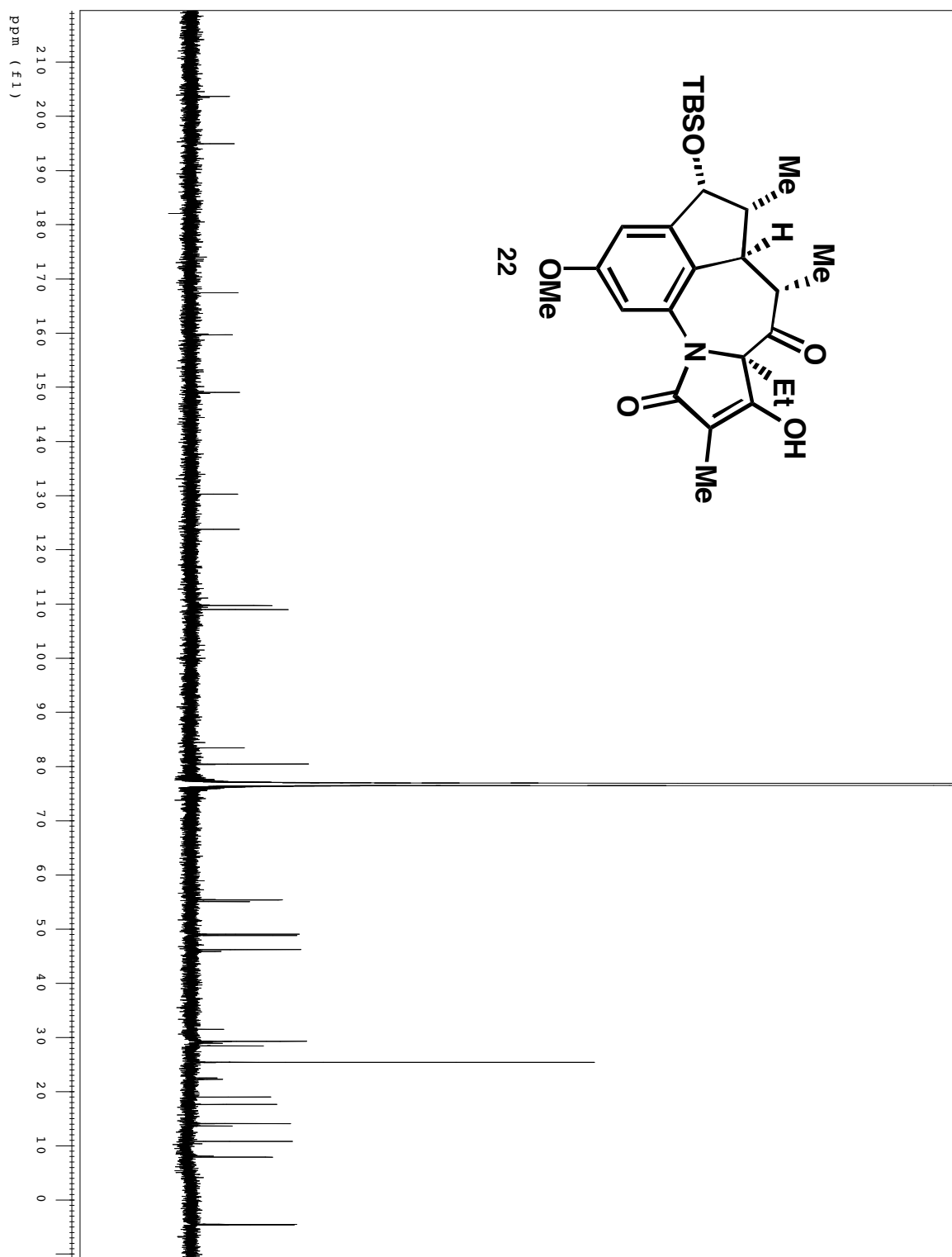


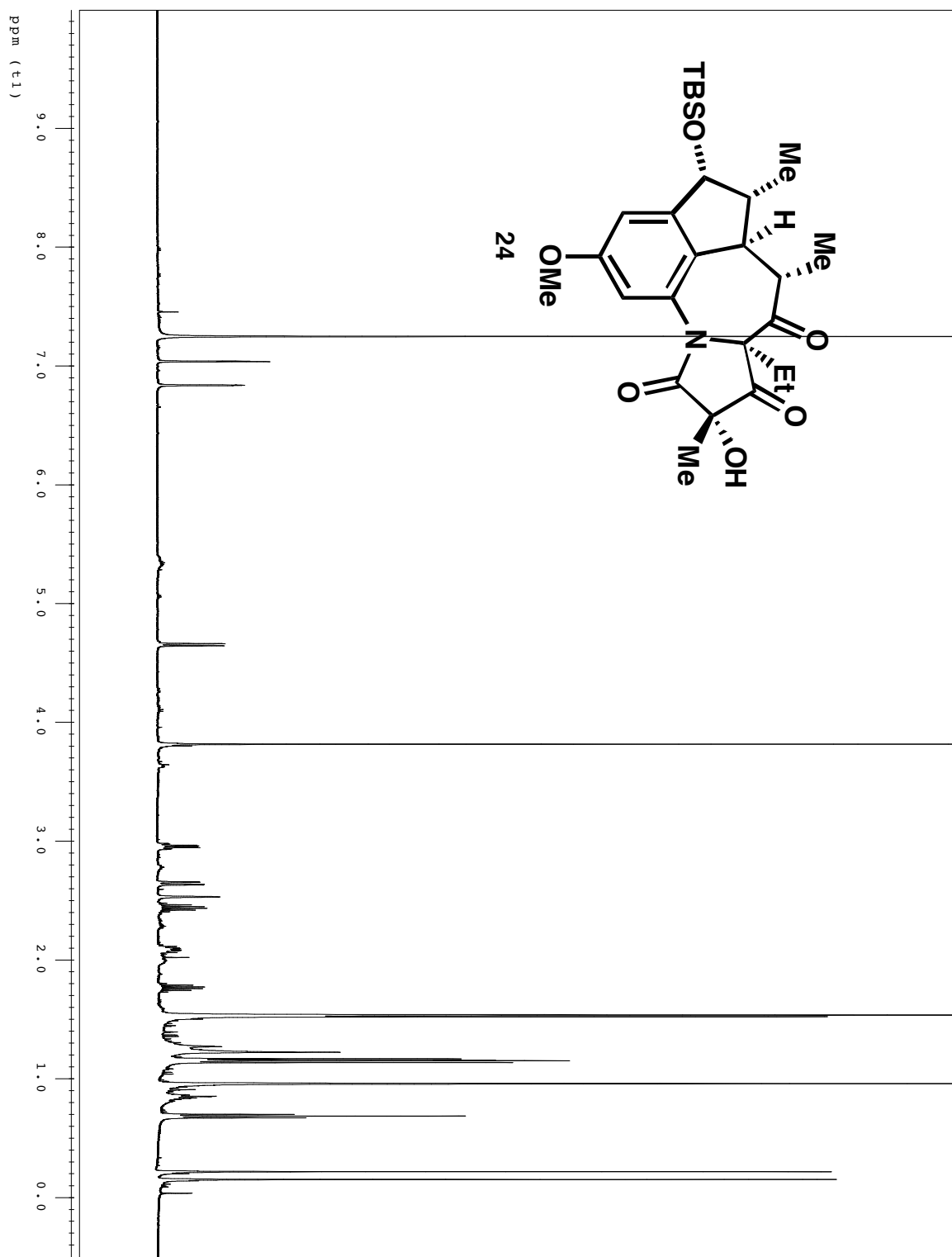


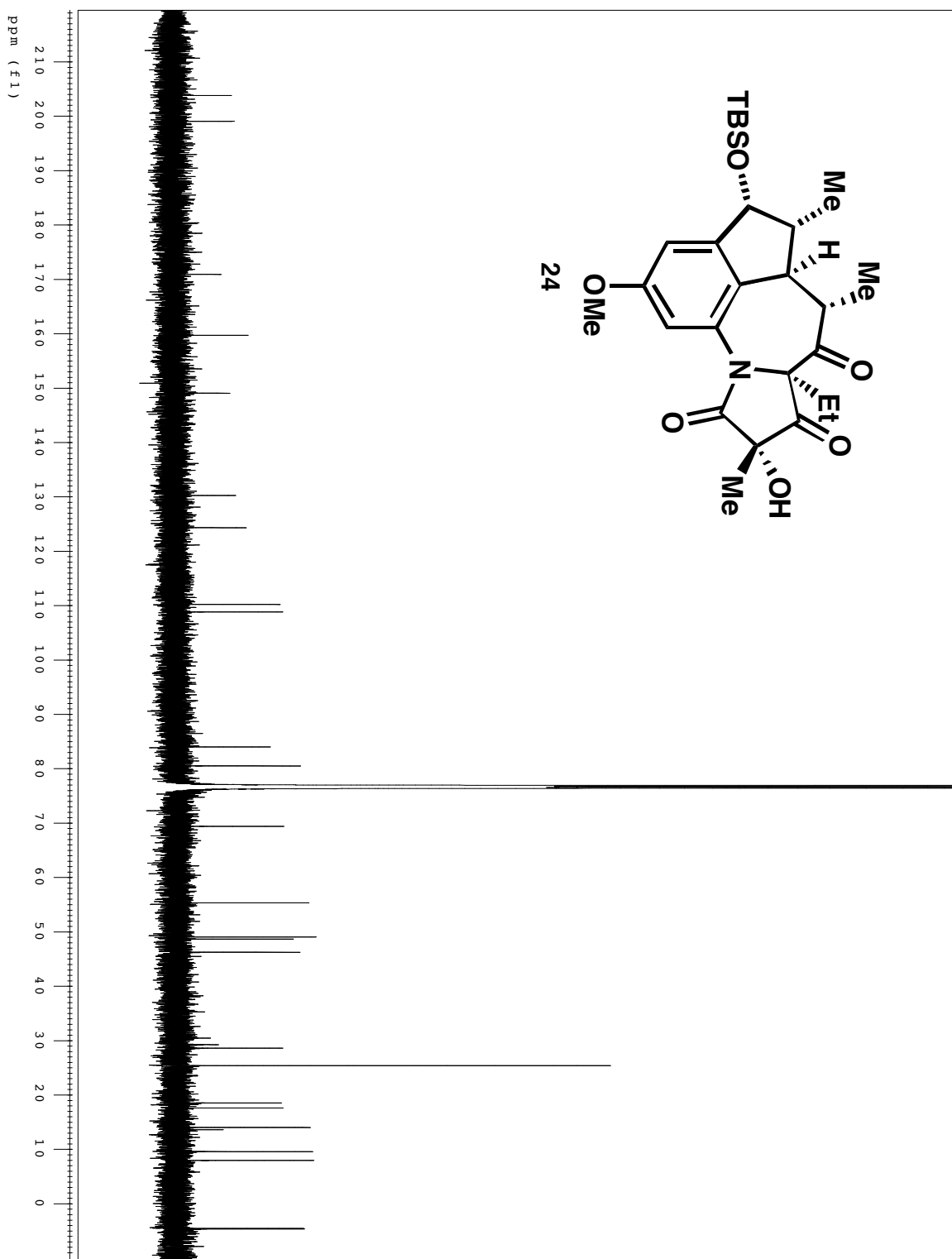












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- [2] Marcus, A. P. ; Lee, A. S.; Davis, R. L.; Tantillo, D. J.; Sarpong, R. *Angew. Chem. Int. Ed.* **2008**, 47, 6379-6383.
- [3] Herrmann, W. A.; Koecher, C.; Goossen, L. J.; Artus, G. R. J. *Chem. Eur. J.* **1996**, 2, 1627-1636.