Supplementary Material (ESI) for Chemical Communications

Concise Total Syntheses of (±)-Aspidospermidine and Formal Syntheses of Related Compounds

Cyrille Sabot, Kimiaka Guérard and Sylvain Canesi*

Laboratoire de Méthodologie et Synthèse de Produit Naturels.
Université du Québec à Montréal, C.P.8888, Succ. Centre-Ville, Montréal. H3C 3P8, Québec, Canada.

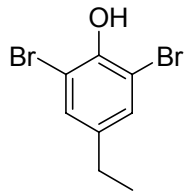
Supporting Information

Table of Contents

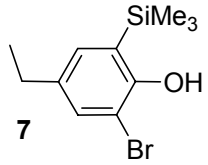
I. General information and materials

Unless otherwise indicated, ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ solutions. Chemical shifts are reported in ppm on the δ scale. Multiplicities are described as s (singlet), d (doublet), dd, ddd, etc. (doublet of doublets, doublet of doublets of doublets, etc.), t (triplet), q (quartet), p (pentuplet), m (multiplet), and further qualified as app (apparent) br (broad) c (complex). Coupling constants, J, are reported in Hz. IR spectra (cm–1) were recorded from thin films. Mass spectra (m/e) were measured in the electrospray (ESI) mode.

II. Experimental procedures for all compounds



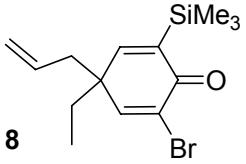
2,6-dibromo-4-ethylphenol: To a stirred solution of 4-ethylphenol (2.00 g, 16.3 mmol) in dry dichloromethane (20 mL) at 0 °C, was added bromine (1.755 mL, 34.4 mmol, 2.1 equiv.). The solution was allowed to warm to room temperature and stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure and purified by chromatography over silica gel (n-hexane/EtOAc, 95:5) to give 4.541 g (99%) of the desired product as a colorless oil. IR υ (cm^{-1}) 3499, 2965, 1476, 1163; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.93 (s, 2H), 5.38 (br, 1H), 2.21 (q, J = 7.6 Hz, 2H), 0.86 (t, J = 7.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 138.7, 131.2, 109.4, 27.4, 15.4; HRMS (ESI): Calc. for $C_8H_7Br_2O$: 278.8842 $(M-H)^-$; found: 278.8838.



7

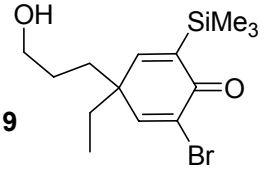
Compound **7**: To a solution of the compound dibromophenol (4.530 g, 16.2 mmol) in dry THF (30 mL) at room temperature, was added hexamethyldisilazane (7.50 mL, 35.6 mmol, 2.2 equiv.). The reaction mixture was stirred at reflux for 45 min. The resulting reaction mixture was concentrated under reduced pressure to remove the excess of hexamethyldisilazane. Dry THF was added (30 ml) and a solution of n-BuLi (7.21 mL at 2.5 mol/L in hexane, 17.8 mmol, 1.1 equiv.) was added at -78 °C. The reaction was warmed slowly at room temperature and stirred overnight. The mixture was quenched with sat. aq. $NaHCO_3$ (30 ml), diluted with ethyl acetate (40 mL), washed with sat. aq. NH_4Cl (30 mL) and

brine (2 x 30 mL). The organic layer was dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The resulting oil was purified by chromatography over silica gel (hexanes/EtOAc, 98:2) to yield 3.766 g (87%) of the compound **7** as a pale yellow oil. IR υ (cm^{-1}) 3521, 2957, 1562, 1450, 1403, 1246; ^1H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, *J* = 1.8 Hz, 1H), 7.09 (d, *J* = 1.8 Hz, 1H), 5.54 (br, 1H), 2. 56 (d, *J* = 8.2 Hz, 12H), 1.71 (q, *J* = 7.6 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H), 0.30 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.0, 137.4, 133.9, 131.9, 126.6, 110.2, 27.7, 15.8, -1.1; HRMS (ESI): Calc. for $C_{11}H_{16}BrOSi$ $(M-H)^-$: 271.0159; found: 271.0156.



8

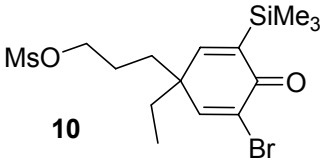
Compound **8**: To a stirred solution of phenol **7** (300 mg, 1.1 mmol), allylsilane (0.35 mL, 2.2 mmol, 1 equiv.) and $NaHCO_3$ (280 mg, 3.3 mmol, 3 equiv.) in HFIP (3 mL) at 0 °C was added DIB (353 mg, 1.1 mmol, 1 equiv.) dissolved in HFIP (1 mL), over 10 seconds. The reaction mixture was stirred at room temperature for 2 min and allylsilane (0.35 mL, 2.2 mmol, 2 equiv.) was added, followed by DIB (353 mg, 1.1 mmol, 1 equiv.) dissolved in HFIP (1 mL) at 0°C. This successive addition was repeated three more times, *i.e.* a total of 10 equiv. of allylsilane and 5 equiv. of DIB were added. Then the solution was treated with sat. aq. $NaHCO_3$ (30 mL). The aqueous phase was extracted with EtOAc (3 x 25 mL), the combined organic layers were washed with brine (30 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography over silica gel (n-hexane/CH_2Cl_2, from 100:0 to 70:30) to afford 193 mg (56%) of the corresponding dienone **8** as a yellow oil. IR υ (cm^{-1})2964, 1651, 1247; ^1H (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 2.7 Hz, 1H), 6.82 (d, *J* = 2.7 Hz, 1H), 5.55 (m, 1H), 5.06 (d, *J* = 10.4 Hz, 1H), 5.06 (d, *J* = 10.4 Hz, 1H), 5.03 (dd, 1H, *J* = 16.5, 1.6 Hz, 1H), 2. 36 (d, *J* = 8.2 Hz, 2H), 1.71 (q, *J* = 7.6 Hz, 2H), 0.75 (t, *J* = 7.6 Hz, 3H), 0.19 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 181.7, 161.7, 153.6, 141.4, 131.9, 125.9, 119.0, 50.4, 43.5, 31.6, 9.1, -1.5; HRMS (ESI): Calc. for $C_{14}H_{22}BrOSi$ $(M+H)^+$: 313.0618; found: 313.0616 .



9

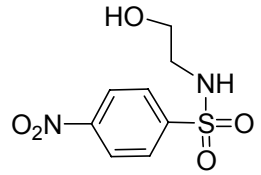
Compound **9**: To a solution of the dienone **8** (338 mg, 1.7mmol) in dry THF (1.5 mL) at 0 °C, was added 9-borabicyclo[3.3.1]nonane (0.5 M in toluene, 5.38 mL 2.7 mmol, 2.5 equiv.). The reaction mixture was stirred at room temperature for 2 hours and a solution of H_2O_2 (30% w/w in water, 0.82 mL, 8.6 mmol, 8 equiv.) was added at 0°C, followed by K_2CO_3 (1.158 g, 8.4 mmol, 7.8 equiv.) dissolved in a minimum of

water. After 10 min stirring, the solution was treated with sat. aq. NH_4Cl (15 mL). The aqueous phase was extracted with EtOAc (3 x 20 mL), the combined organic layers were washed with brine (15 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography over silica gel (n-hexane/EtOAc, from 15:85 to 30:70) to afford 258 mg (72%) of the corresponding product **9** as an oil. IR υ (cm^{-1})3416, 2935, 1647, 1348, 1248; ^1H (300 MHz, $CDCl_3$) δ 7.13 (d, *J* = 2.7 Hz, 1H), 6.81 (d, *J* = 2.7 Hz, 1H), 3.60 (t, *J* = 6.4 Hz, 2H), 1.76 (t, *J* = 7.6 Hz, 2H), 1.71 (q, *J* = 7.6 Hz, 2H), 1.37 (m, 2H), 0.75 (t, *J* = 7.6 Hz, 3H), 0.19 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 181.8, 162.2, 154.3, 141.7, 125.9, 62.3, 50.5, 35.6, 32.5, 27.7, 9.0, -1.5; HRMS (ESI): Calc. for $C_{14}H_{24}BrO_2Si$ $(M+H)^+$: 331.0723; found: 331.0719.



10

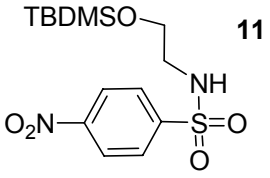
Compound **10**: To a solution of the alcohol **9** (240 mg, 0.72 mmol) in dry CH_2Cl_2 (1.5 mL) at 0 °C was added 2,6-lutidine (0.34 mL, 2.90 mmol, 4 equiv.) and mesyl chloride (0.11 mL, 1.44 mmol, 2 equiv.). The solution was stirred at room temperature for 2 hours. The resulting reaction mixture was filtrated directly over silica gel (n-hexane/CH_2Cl_2, from 50:50 to 0:100) to afford 288 mg (97%) of the product **10** as a colorless oil. IR υ (cm^{-1}) 2961, 1648, 1534, 1354, 1247, 1175; ^1H (300 MHz, $CDCl_3$) δ 7.10 (d, *J* = 2.7 Hz, 1H), 6.80 (d, *J* = 2.7 Hz, 1H), 4.16 (t, *J* = 6.4 Hz, 2H), 3.01 (s, 3H), 1.80 (t, *J* = 7.6 Hz, 2H), 1.71 (q, *J* = 7.6 Hz, 2H), 1.53 (m, 2H), 0.76 (t, *J* = 7.6 Hz, 3H), 0.20 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.5, 161.2, 153.4, 142.4, 126.4, 69.3, 50.2, 37.3, 35.0, 32.6, 24.6, 8.9, -1.5; HRMS (ESI): Calc. for $C_{15}H_{26}BrO_4SSi$ $(M+H)^+$: 409.0499; found: 409.0495.



2-*para*-Nosylamidoethanol

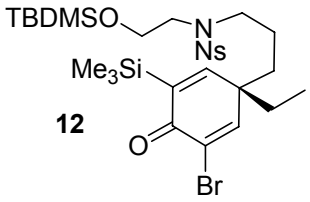
2-*para*-Nosylamidoethanol: To a stirred solution of 2-aminoethan-1-ol (0.20 mL, 3.3 mmol) in dry CH_2Cl_2 (8 mL) cooled at 0 °C were added triethylamine (0.69 mL, 5.0 mmol, 1.5 equiv.) and *para*-nosyl chloride (741 mg, 3.4 mmol, 1.05 equiv.). The reaction mixture was stirred for 3 hours at room temperature and then was treated with sat. aq. $NaHCO_3$ (10 ml). The aqueous phase was extracted with CH_2Cl_2 (4 x 20 mL) and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, concentrated under reduced pressure. 746 mg (92%) of a white solid were obtained. Mp = 126 °C; IR υ (cm^{-1}) 3300, 1529, 1351, 1310, 1162; ^1H (300 MHz, DMSO-d_6) δ 8.42 (d, *J* = 7.2 Hz, 2H), 8.06 (d, *J* = 7.2 Hz, 2H), 7.91 (br, 1H), 4.75 (t, *J* = 5.5 Hz, 1H), 3.37 (q, *J* = 5.5 Hz, 2H), 2.86 (t, *J* = 6.0 Hz, 2H);

^{13}C NMR (75 MHz, DMSO-d_6) δ 149.4, 146.2, 127.9, 124.4, 59.7, 45.0; HRMS (ESI): Calc. for $C_8H_{11}N_2O_3S$ $(M+H)^+$: 247.0383; found: 247.0382.



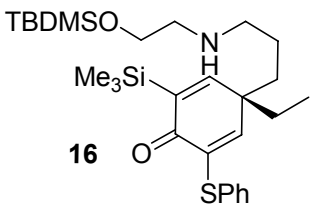
11

Compound **11**: To a solution of 2-*para*-Nosylamidoethanol (744 mg, 3.03 mmol) in dry DMF at 0 °C were added imidazole (308 mg, 4.53 mmol, 1.5 equiv.) and *tert*-butyldimethylsilyl chloride (544 mg, 3.62 mmol, 1.2 equiv.). The resulting solution was stirred at room temperature for 2 hours and then was treated with sat. aq. $NaHCO_3$ (10 mL). The aqueous phase was extracted with EtOAc (4 x 20 mL) and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by chromatography over silica gel (n-hexane/EtOAc, 80:20) to afford 1.055 g (97%) of the product as a white solid. Mp = 72 °C; IR υ (cm^{-1}) 3266, 2925, 2854, 1533, 1350, 1161; ^{1}H (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 9.4 Hz, 2H), 8.06 (d, *J* = 9.4 Hz, 2H), 4.95 (t, *J* = 5.3 Hz, 1H), 3.65 (t, *J* = 5.3 Hz, 1H), 3.12 (q, *J* = 5.3 Hz, 2H), 0.84 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 145.8, 128.2, 124.3, 61.2, 45.2, 25.7, 18.1, -5.5; HRMS (ESI): Calc. for $C_{14}H_{25}N_2O_5SSi$ $(M+H)^+$: 361.1248; found: 361.1250.



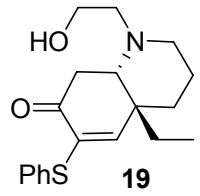
12

Compound **12**: To a stirred solution of compound **11** (670 mg, 1.86 mmol, 2.7 equiv) in dry DMF (2 mL) at 0 °C, was added sodium hydride (60% w/w in oil, 72 mg,1.79 mmol, 2.6 equiv.) by portion. The reaction mixture was stirred for one hour at room temperature before the dropwise addition of the mesylate **10** (282 mg, 0.69 mmol) dissolved in THF (1.5 mL). The reaction mixture was stirred at 65 °C for 12 hours. The resulting solution was directly filtrated over silica gel (n-hexane/EtOAc, 85:15) to remove DMF. The resulting crude mixture was purified over silica gel (toluene) to give 414 mg (89%) of the product **12** as a yellow oil. IR υ (cm^{-1}) 2949, 2854, 1647, 1531, 1348, 1163, 1107; ^{1}H (300 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 2.7 Hz, 1H), 6.77 (d, *J* = 2.7 Hz, 1H), 3.68 (t, *J* = 5.9 Hz, 2H), 3.24 (t, *J* = 5.9 Hz, 2H), 3.22 (m, 2H), 1.69 (q, *J* = 7.6 Hz, 2H), 1.68 (m, 2H), 1.37 (m, 2H), 0.84 (s, 9H), 0.75 (t, *J* = 7.6 Hz, 3H), 0.19 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 181.6, 161.4, 153.5, 149.9, 145.8, 142.3, 128.1, 126.3, 124.4, 61.9, 50.4, 49.9, 49.2, 35.9, 32.7, 25.7, 23.6, 18.1, 9.0, -1.4, -5.4; HRMS (ESI): Calc. for $C_{28}H_{46}BrN_2O_6SSi$ $(M+H)^+$:673.1793; found: 673.1779.



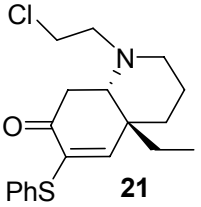
16

Compound **16**: To a solution of **12** (101 mg, 0.15 mmol) in degassed acetonitrile (1 mL) was added solid K_2CO_3 (104 mg, 0.75 mmol, 5 equiv.) and thiophenol (77 µL, 0.75 mmol, 5 equiv.). The solution was stirred overnight and filtrated directly over celite (EtOAc) to remove the insolubilities. The resulting crude product **16**, was purified by chromatography over silica gel (n-hexane/EtOAc, 80:20 to remove sulphur-containing by-product and then EtOAc/MeOH, 95:5 for the product) to afford 66 mg (85%) of the product **16** as an orange oil. IR υ (cm^{-1}) 2951, 2856, 1634, 1246, 1106; ^1H (600 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.2 Hz, 2H), 7.38 (m, 3H), 6.80 (d, *J* = 2.9 Hz, 1H), 5.91 (d, *J* = 2.9 Hz, 1H), 3.71 (t, *J* = 5.3 Hz, 2H), 2.67 (t, *J* = 5.3 Hz, 2H), 2.55 (t, *J* = 7.0 Hz, 2H), 1.80 (br, 1H), 1.60 (m, 2H), 1.52 (m, 2H), 1.23 (m, 2H), 0.89 (s, 9H), 0.63 (t, *J* = 7.6 Hz, 3H), 0.20 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 185.4, 162.8, 146.0, 141.4, 139.7, 134.5, 131.5, 129.4, 128.4, 61.8, 51.2, 49.4, 48.2, 37.3, 32.8, 25.8, 24.9, 18.1, 8.9, -1.4, -5.3; LRMS (ESI): 518, 410 and 408; HRMS (ESI): Calc. for $C_{28}H_{48}NO_2SSi$ $(M+H)^+$:518.2939; found: 518.2928.



19

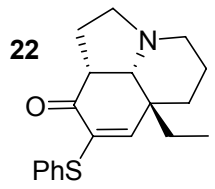
Compound **19**: To a solution of the amine **16** (95 mg, 0.18 mmol) in THF (0.3 mL) at 0 °C was added dropewise TBAF (1M in THF, 0.73 mL, 0.73 mmol, 4 equiv.). The reaction mixture was stirred at room temperature for 5 hours and then the solution was quickly filtrated over a short plug of silica gel (EtOAc 100%) to afford 53 mg (87%) of the alcohol **19** as an oil. IR υ (cm^{-1}) 3424, 2930, 1674, 1582, 1044; ^1H (600 MHz, C_6D_6) δ 7.43 (d, *J* = 7.6 Hz, 2H), 7.05 (t, *J* = 7.6 Hz, 2H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.12 (s, 1H), 3.33 (m, 2H), 2.73 (dd, *J* = 12.3, 3.5 Hz, 1H), 2.46 (dd, *J* = 15.8, 12.3 Hz, 1H), 2.31 (dd, *J* = 15.8, 4.1 Hz, 1H), 2.11 (m, 2H), 2.04 (dt, *J* = 12.9, 4.7 Hz, 1H), 1.91 (td, *J* = 11.7, 2.3 Hz, 1H), 1.66 (sex, *J* = 7.0 Hz, 1H), 1.24 (m, 1H), 0.98 (m, 5H), 0.51 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 194.5, 153.0, 136.6, 133.7, 133.5, 129.5, 128.0, 58.6, 55.8, 44.9, 41.9, 32.7, 29.4, 28.2, 26.0, 20.9, 8.3; LRMS (ESI^+): 332 and 222; HRMS (ESI): Calc. for $C_{19}H_{26}BrNO_2S$ $(M+H)^+$: 332.1679; found: 332.1682.



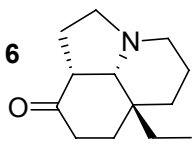
21

Compound **21**: To a solution the alcohol **19** (53 mg, 0.16 mmol) in dry CH_2Cl_2 (0.3 mL) at 0 °C, was added triethylamine (67µL, 0.48 mmol, 3 equiv.) and mesyl chloride (19 µL, 0.24 mmol, 1.5 equiv.) dropwise.

The reaction mixture was stirred for 2 hours at room temperature and quickly filtrated over a short plug of silica gel (n-hexane/EtOAc, 70:30) to give 44 mg (79%) of the compound **21** as a thick oil. IR υ (cm^{-1}) 2926, 1673, 1317, 1172; ^1H (600 MHz, C_6D_6) δ 7.45 (d, *J* = 7.6 Hz, 2H), 7.05 (t, *J* = 7.6 Hz, 2H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.16 (s, 1H), 3.00 (t, *J* = 6.4 Hz, 2H), 2.61 (dd, *J* = 8.2, 2.3 Hz, 1H), 2.40 (c, 1H), 2.21 (dd, *J* = 15,8 4.0 Hz, 1H), 2.16 (m, 2H), 1.98 (br, 1H), 1.92 (td, *J* = 11.1, 2.3 Hz, 1H), 1.75 (sex, *J* = 7.0 Hz, 1H), 1.28 (c, 1H), 1.08 (sex, *J* = 7.6 Hz, 1H), 0.97 (m, 3H), 0.54 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 194.2, 153.1, 136.4, 133.6, 129.5, 128.3, 128.1, 58.6, 55.9, 45.8, 42.2, 41.8, 32.9, 29.5, 28.2, 21.0, 8.3; LRMS (ESI): 352, 350 and 314; HRMS (ESI): Calc. for $C_{19}H_{25}ClNOS$ $(M+H)^+$:350.1340; found: 350.1338.

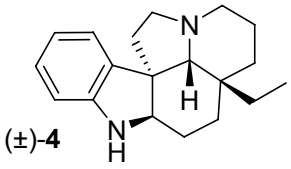


Compound **22**: To a solution of the product **21** (44 mg, 0.13 mmol) in dry toluene (1 mL) at room temperature, was added potassium tert-butanolate (42 mg, 0.38 mmol, 3 equiv.) by portion. The reaction mixture was stirred for 12 hours at room temperature and directly filtrated over silica gel (n-hexane/EtOAc, 70:30) to afford 33 mg (84%) of the product **22** as a yellow oil. IR υ (cm^{-1}) 2922, 1668, 1439, 1194; ^1H (600 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.26 (t, *J* = 7.3 Hz, 1H), 6.23 (s, 1H), 2.99 (t, *J* = 7.3 Hz, 2H), 2.92 (dm, *J* = 9.4 Hz, 1H), 2.20 (m, 1H), 2.11 (br, 1H), 2.06 (q, *J* = 8.2 Hz, 1H), 2.00 (t, *J* = 10.0, 2.3 Hz, 1H), 1.94 (td, *J* = 10.5, 2.3 Hz, 1H), 1.76 (d, *J* = 13.5 Hz, 1H), 1.64 (sex, *J* = 7.6 Hz, 1H), 1.56 (d, *J* = 13.5 Hz, 1H), 1.47 (sex, *J* = 7.6 Hz, 1H), 1.43 (d, *J* = 13.5 Hz, 1H), 1.17 (td, *J* = 13.5, 4.1 Hz, 1H), 0.85 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.7, 152.8, 135.4, 133.6, 132.5, 129.1, 127.4, 69.4, 52.2, 51.6, 46.5, 40.5, 35.7, 34.1, 25.8, 23.1, 8.1; LRMS (ESI): 314 and 204; HRMS (ESI): Calc. for $C_{19}H_{24}NOS$ $(M+H)^+$:314.1573; found: 314.1571.



Compound **6**: To a stirred solution of the compound **22** (15 mg, 0.048 mmol) in EtOH (0.4 mL) was added small amount of Ni (Raney) at room temperature until the reaction was completed as indicated by TLC (n-hexane/EtOAc, 70:30). The mixture was directly filtered over silicagel (n-hexane/EtOAc, 70:30) to give 8.5 mg (85%) of the tricylic compound **6** as a colorless oil. IR υ (cm^{-1}) 2932, 2786, 1439, 1194; ^1H (600 MHz, $CDCl_3$) δ 3.00 (m, 2H), 2.68 (m, 1H), 2.41 (m, 1H), 2.37 (dd, *J* = 15.2, 5.9 Hz, 1H), 2.30 (dm, *J* = 15.8 Hz, 1H), 2.25 (td, *J* = 14.1, 4.7 Hz, 1H), 1.94 (m, 2H), 1.89 (dd, *J* = 14.1, 7.6 Hz, 1H), 1.72 (td, *J* = 12.9, 3.5 Hz, 1H), 1.63 (m,

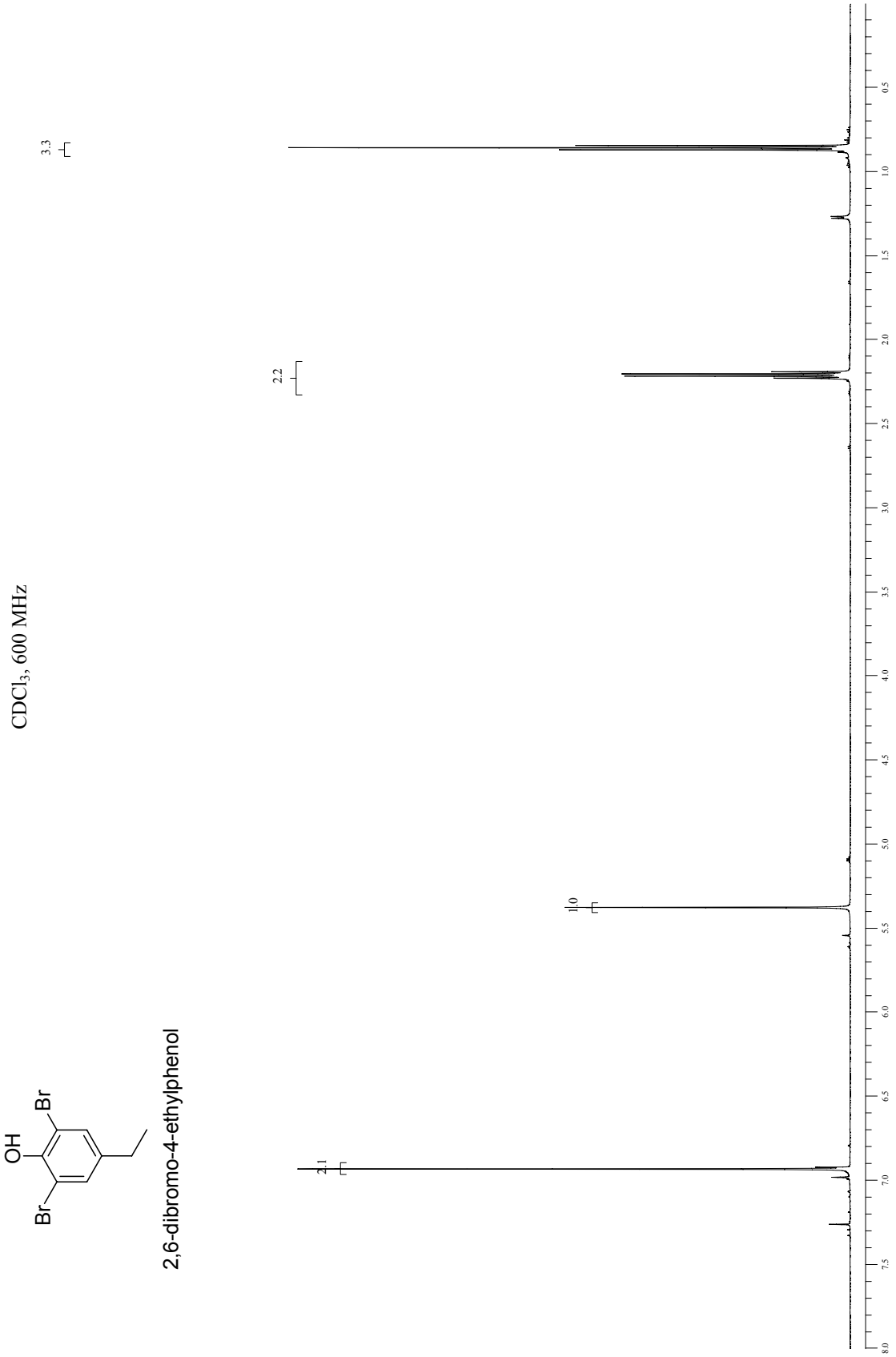
2H), 1.49 (m, 2H), 1.32 (sex, *J* = 7.6 Hz, 1H), 1.10 (td, *J* = 13.5, 4.1 Hz, 1H), 0.93 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.4, 73.5, 53.1, 52.9, 48.1, 36.7, 34.7, 32.8, 30.0, 26.0, 21.3, 21.2, 7.1; HRMS (ESI): Calc. for $C_{13}H_{22}NO$ $(M+H)^+$: 208.1696; found: 208.1700.

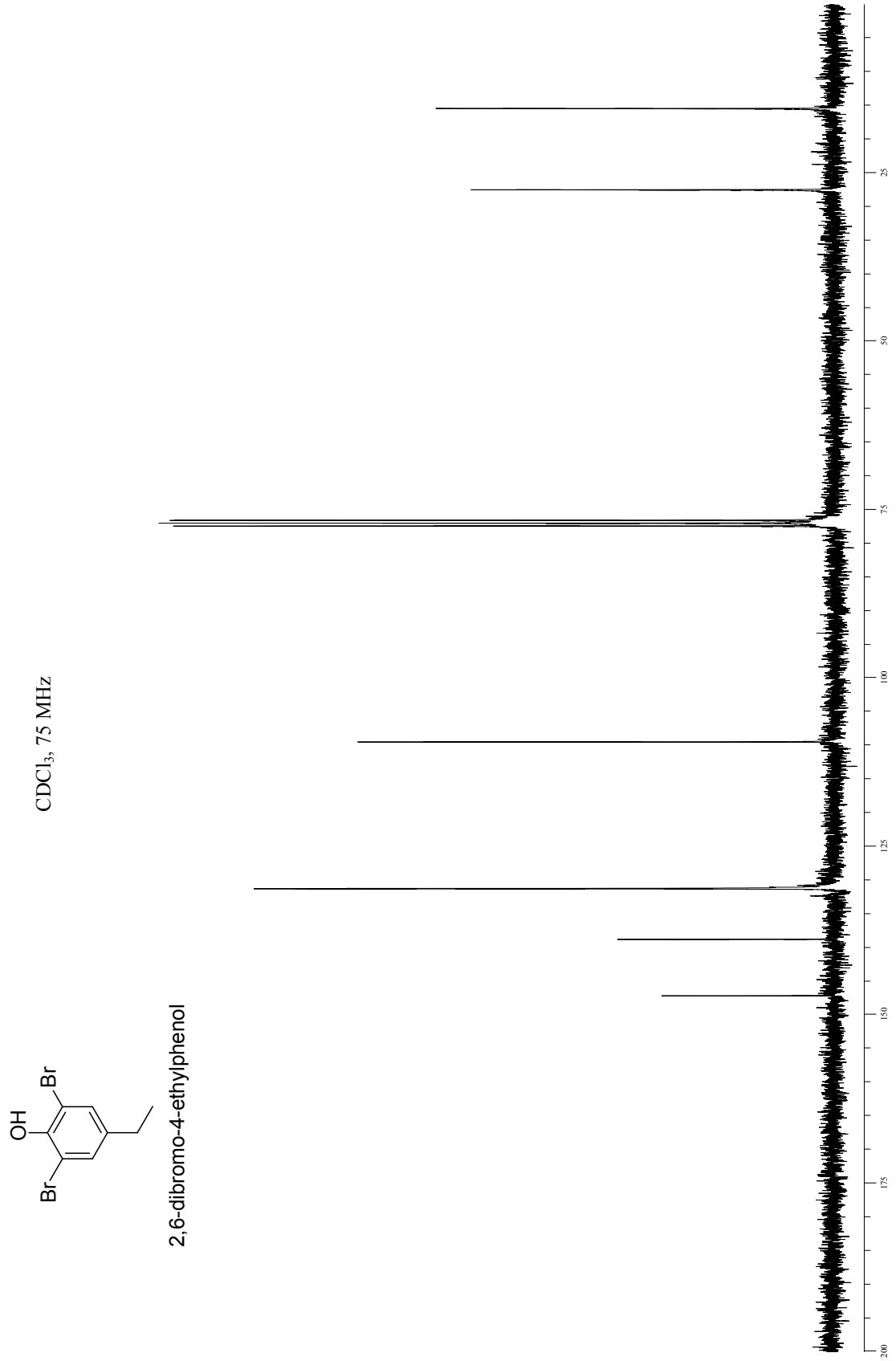


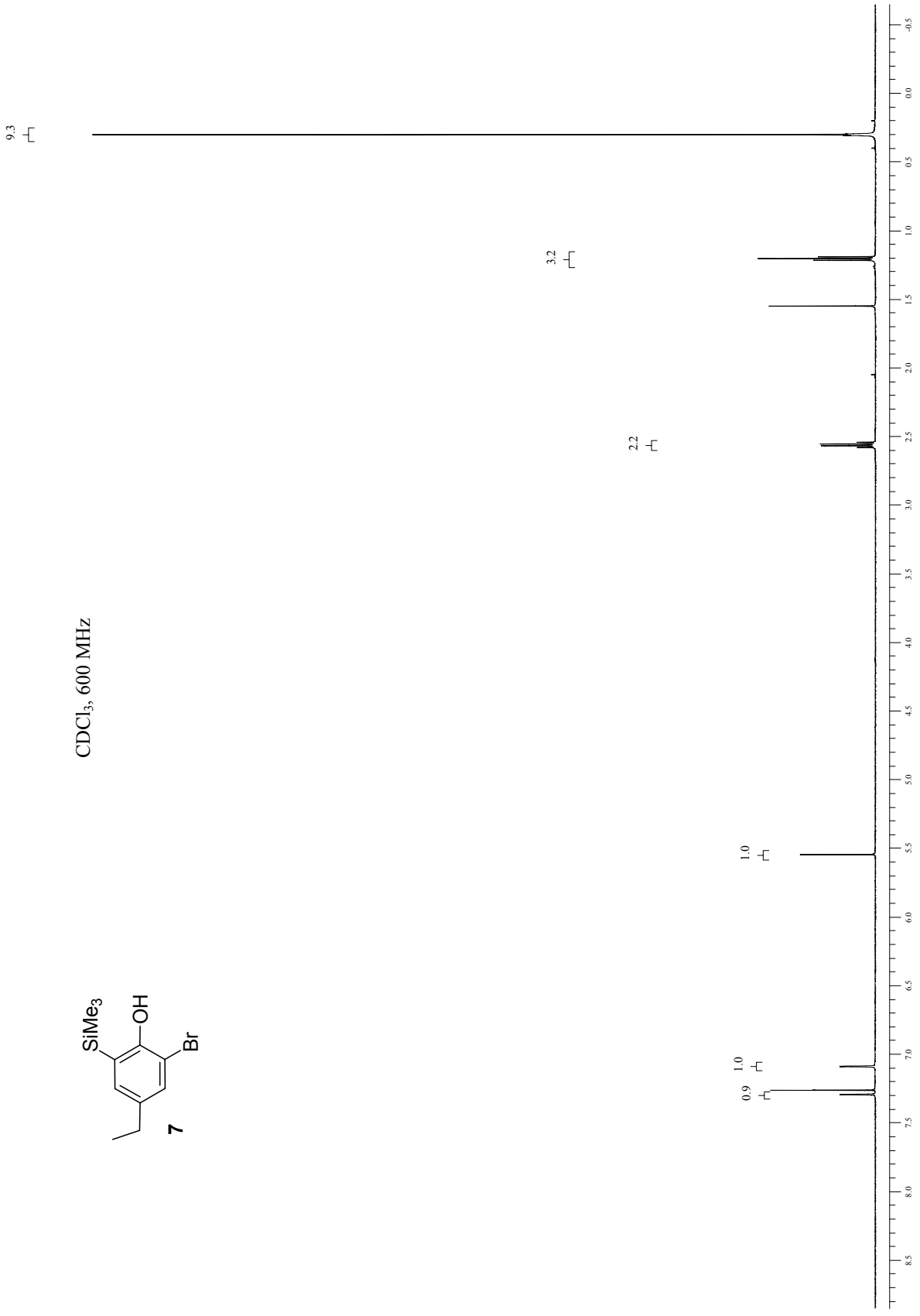
(±)-**4**

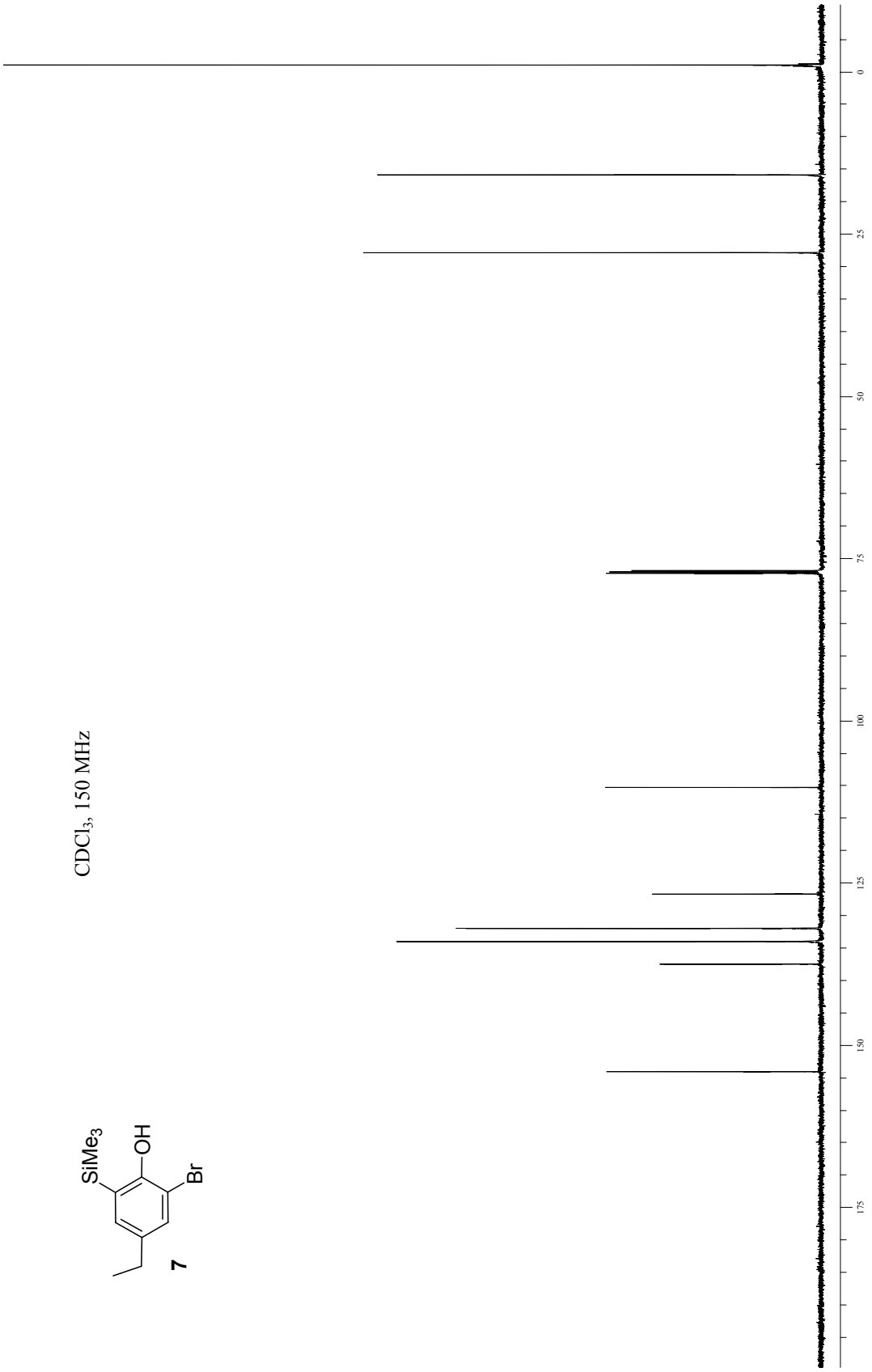
(±)-Aspidospermidine, 4: The ketone **6** (3 mg, 0.0145 mmol) in dry benzene (0.3 mL) and phenylhydrazine (2.4 mg, 0.022 mmol, 1.5 equiv.) was heated under reflux. After 2 hours, the mixture was cooled to room temperature, the solvent was evaporated. The crude was dissolved in dry benzene and solvent evaporated under reduced pressure to remove residual water. The mixture was redissolved in dry acetic acid (0.4 mL) and was heated under reflux. After 4 hours, the mixture was cooled to room temperature, the solvent was evaporated and the mixture dissolved in THF (0.5 mL). $LiAlH_4$ (5.5 mg, 0.145 mmol, 10 equiv.) was added at 0 °C, and the mixture was stirred at room temperature for 30 min. The mixture was cooled to 0 °C, water (0.5 mL) was added, the suspension was filtered through celite and was washed with EtOAc. The resulting crude mixture was purified over silica gel (triethylamine/MeOH/CH_2Cl_2, 0.1:7:93) to give 1.8 mg (43%) of aspidospermidine as a white solid. ^{1}H (600 MHz, C_6D_6) δ 7.06 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.80 (d, *J* = 7.3 Hz, 1H), 6.48 (d, *J* = 7.3 Hz, 1H), 3.42 (dd, *J* = 10.3, 6.6 Hz, 1H), 2.96 (td, *J* = 9.5, 3.7 Hz, 1H), 2.87 (d, *J* = 10.3 Hz, 1H), 2.36 (m, 1H), 2.16 (s, 1H), 2.10 (q, *J* = 8.1 Hz, 1H), 2.02 (td, *J* = 13.2, 4.4 Hz, 1H), 1.84 (td, *J* = 11.4, 2.2 Hz, 1H), 1.71 (qt, *J* = 12.5, 3.7 Hz, 1H), 1.59 (sex, *J* = 7.3 Hz, 1H), 1.49 (dd, *J* = 13.9, 3.7 Hz, 1H), 1.45 (d, *J* = 11.0 Hz, 1H), 1.32 (m, 4H), 0.96 (td, *J* = 13.2, 4.4 Hz, 1H), 0.92 (d, *J* = 13.2 Hz, 1H), 0.88 (sex, *J* = 7.3 Hz, 1H), 0.55 (t, *J* = 7.6 Hz, 3H); LRMS (ESI): Calc. for $C_{19}H_{27}N_2$ $(M+H)^+$: 283.

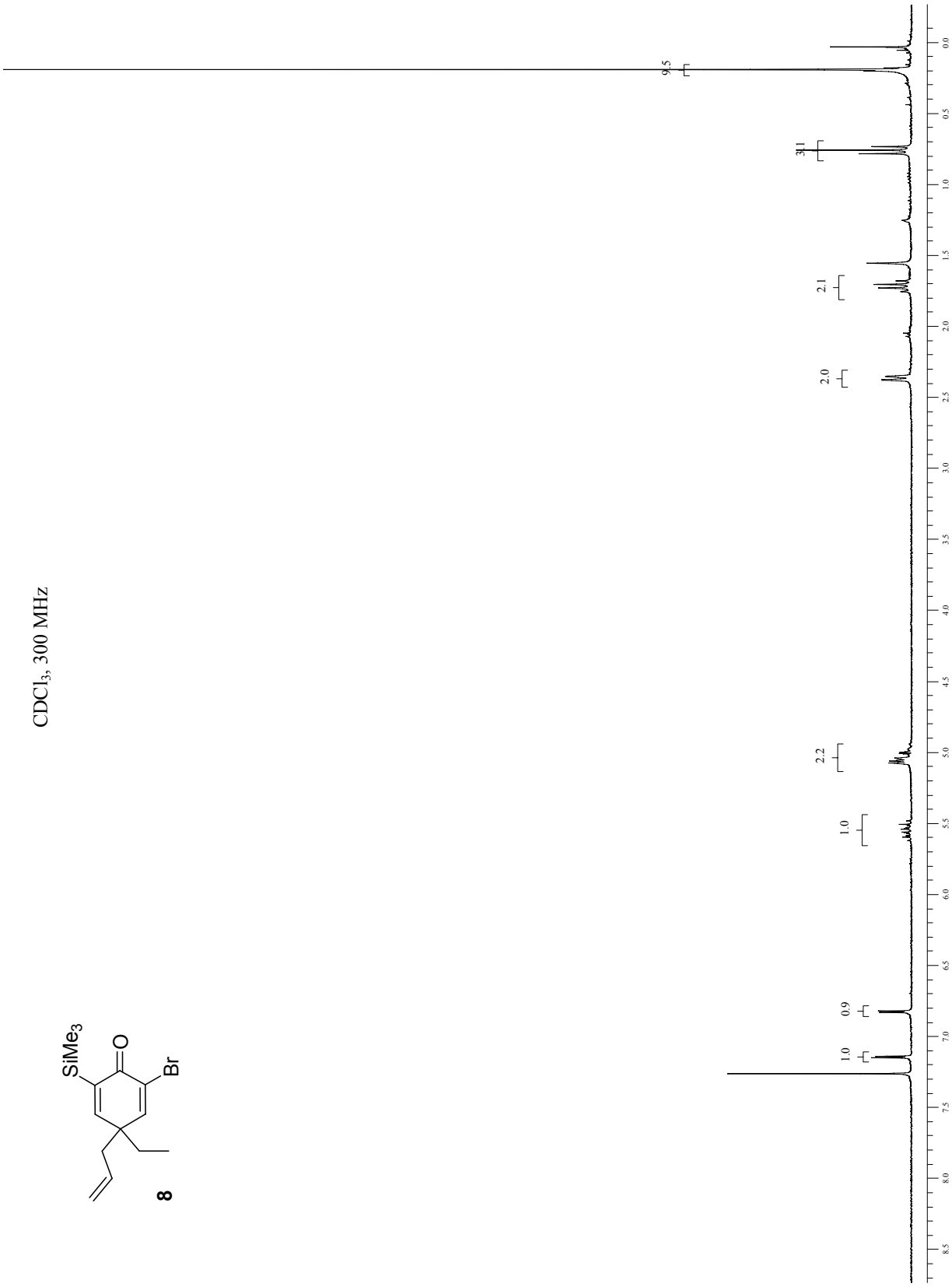
III. Copies of ^{1}H and ^{13}C NMR spectra for all compounds

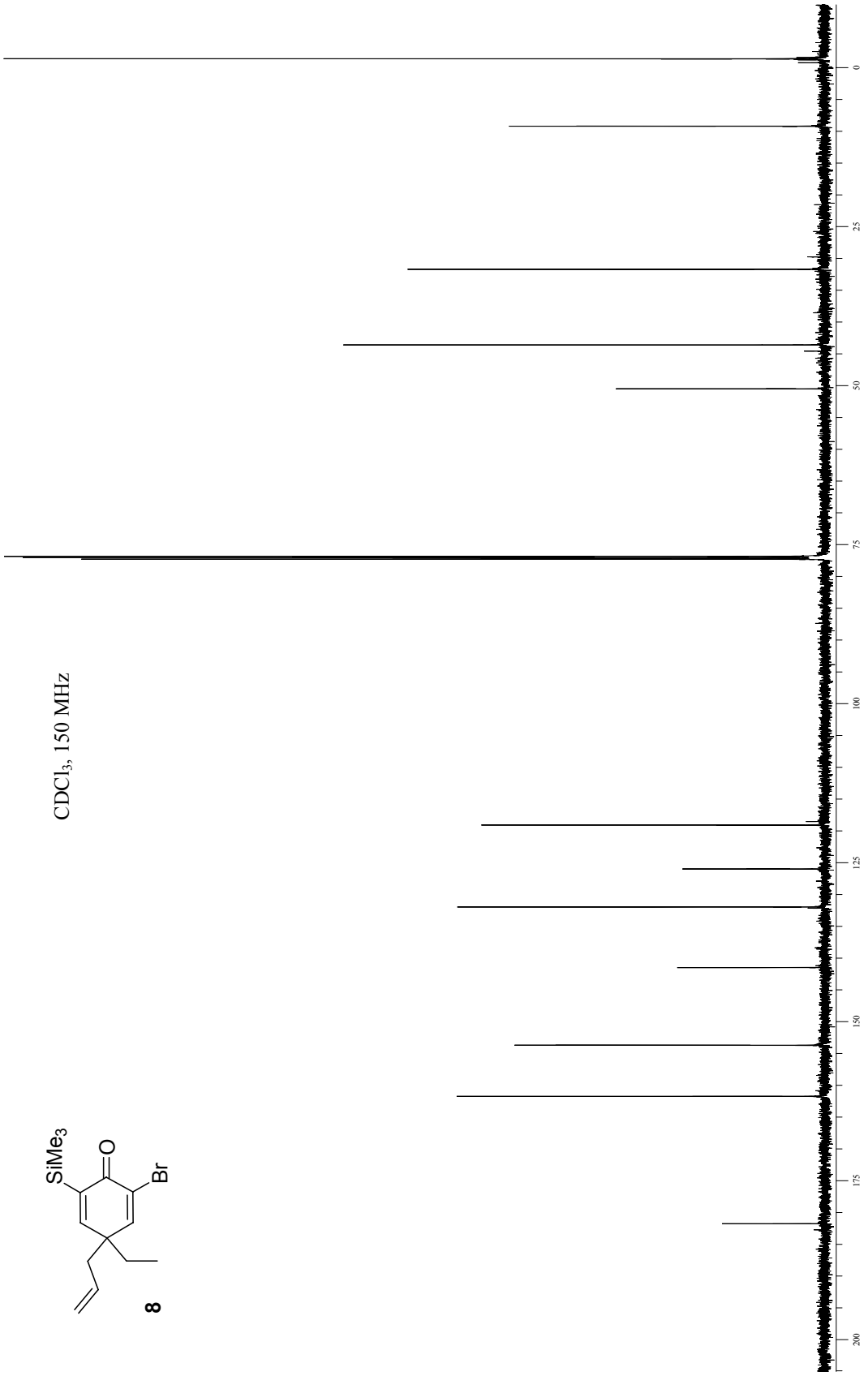

OH
Br
Br
2,6-dibromo-4-ethylphenol
CDCl3, 600 MHz
2.1
1.0
2.2
3.3

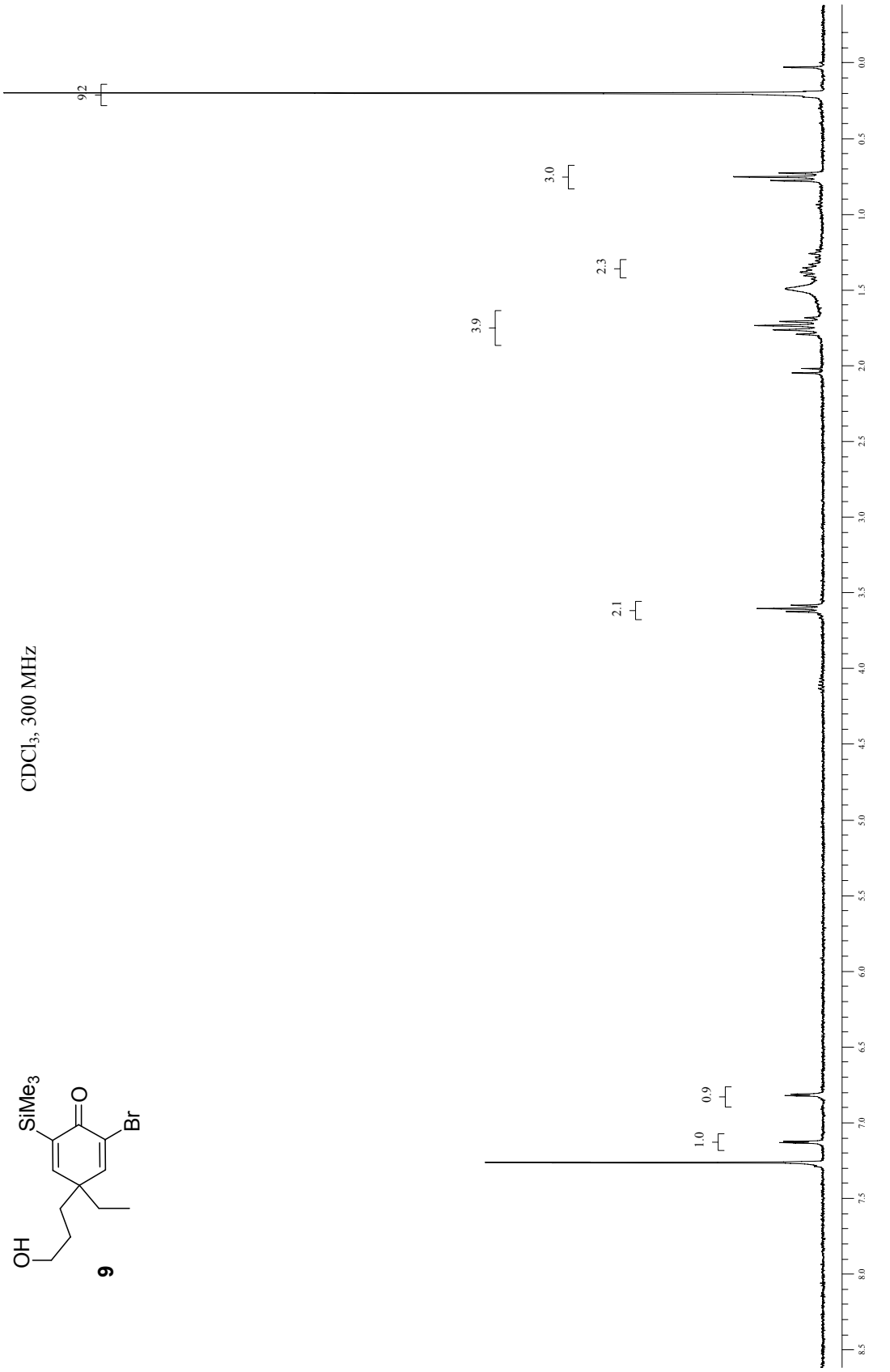

OH
Br
Br
2,6-dibromo-4-ethylphenol
$CDCl_3$, 75 MHz
200
175
150
125
100
75
50
25

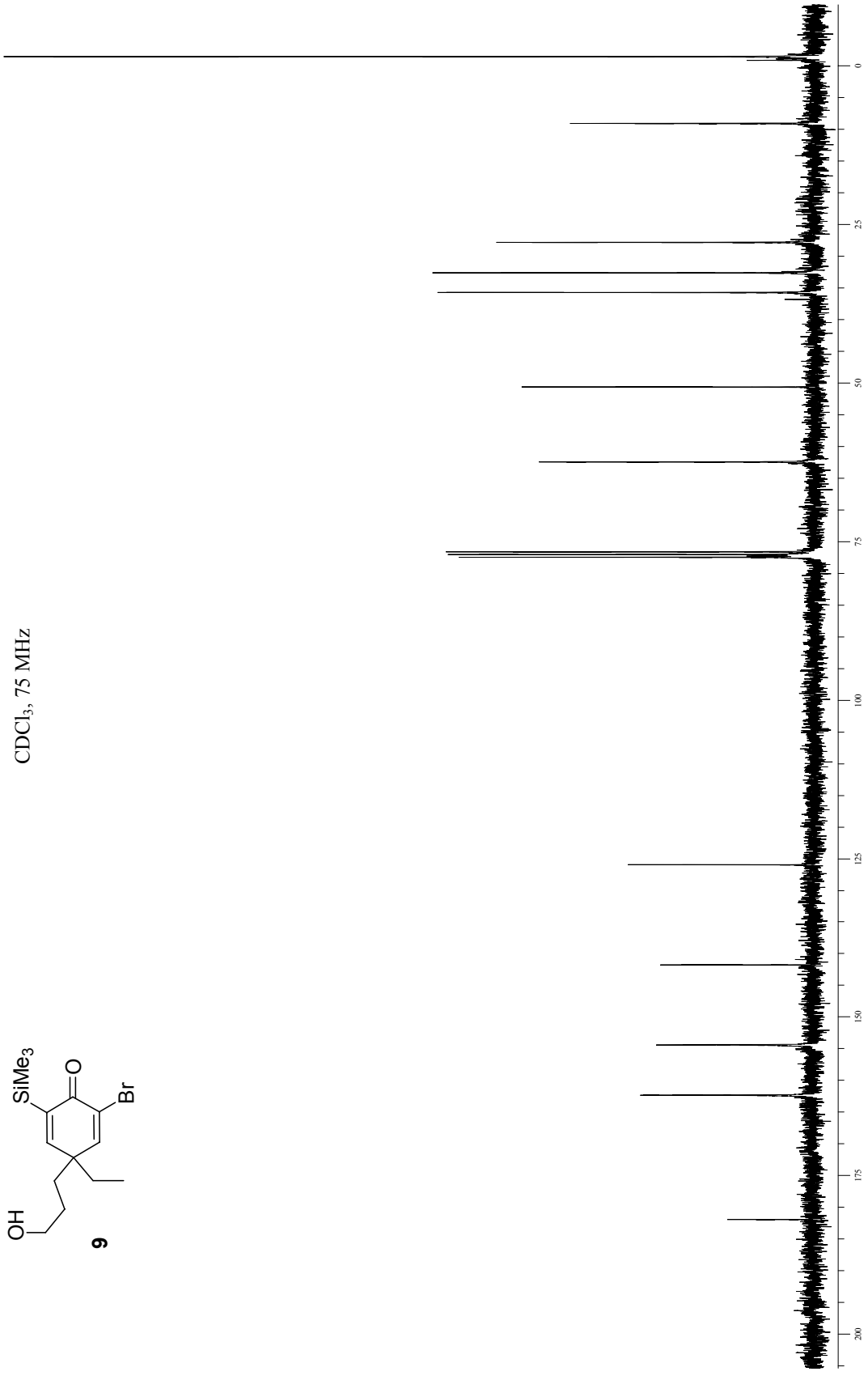

CDCl3, 600 MHz
SiMe3
OH
Br
7
9.3
3.2
2.2
1.0
1.0
0.9

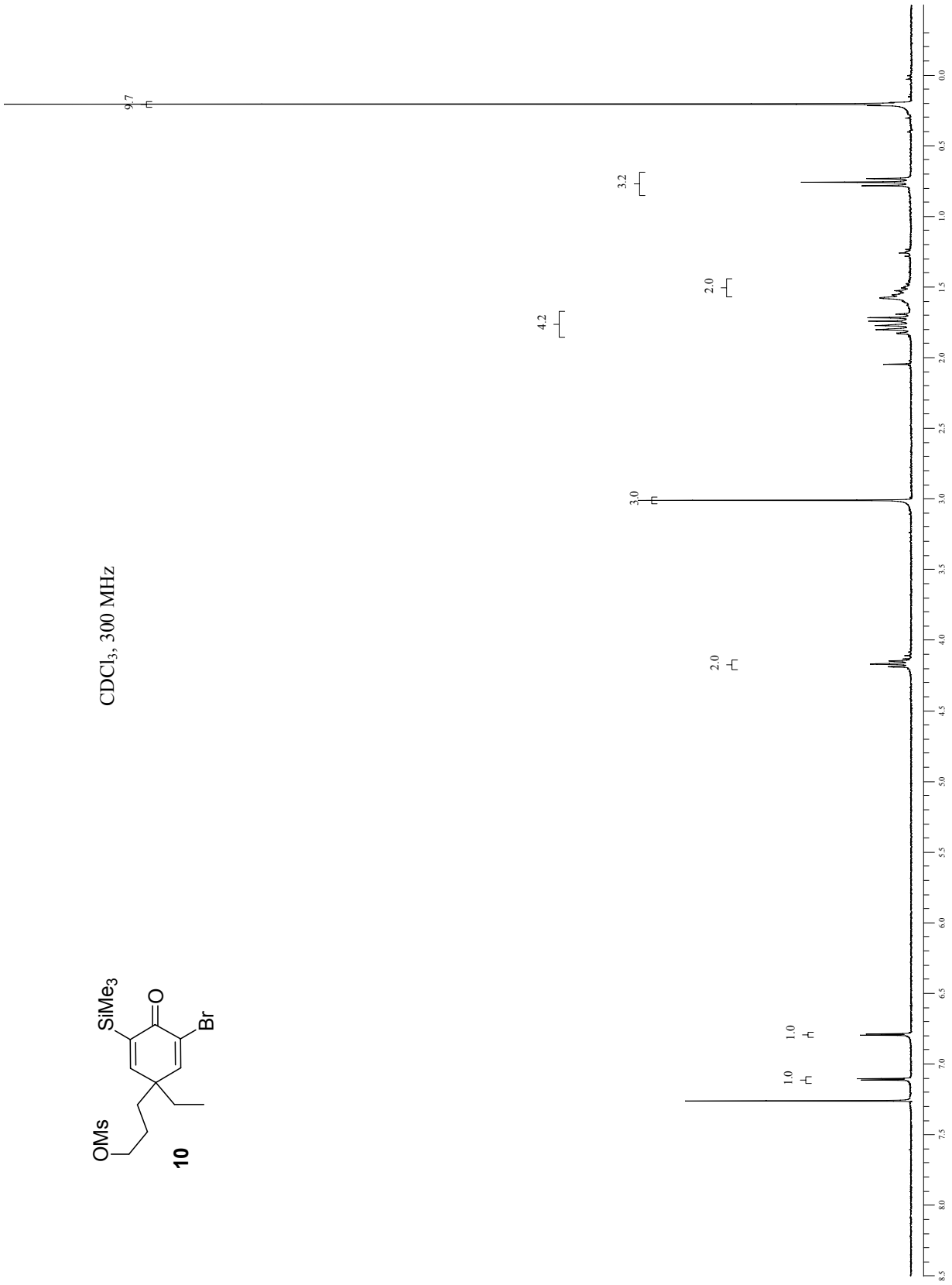


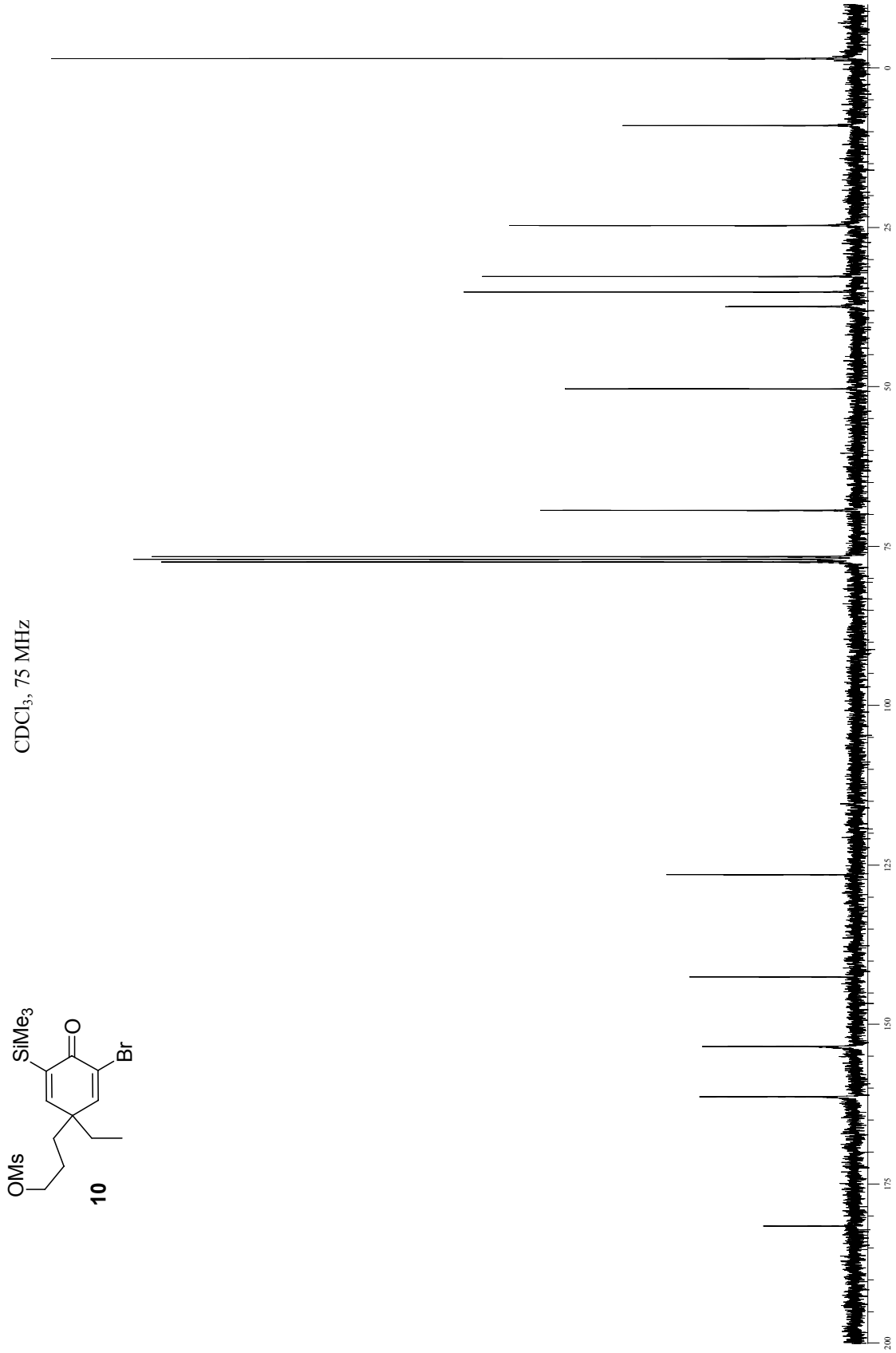

CDCl3, 300 MHz
SiMe3
O
Br
8
9.5
3.1
2.1
2.0
2.2
1.0
0.9
1.0

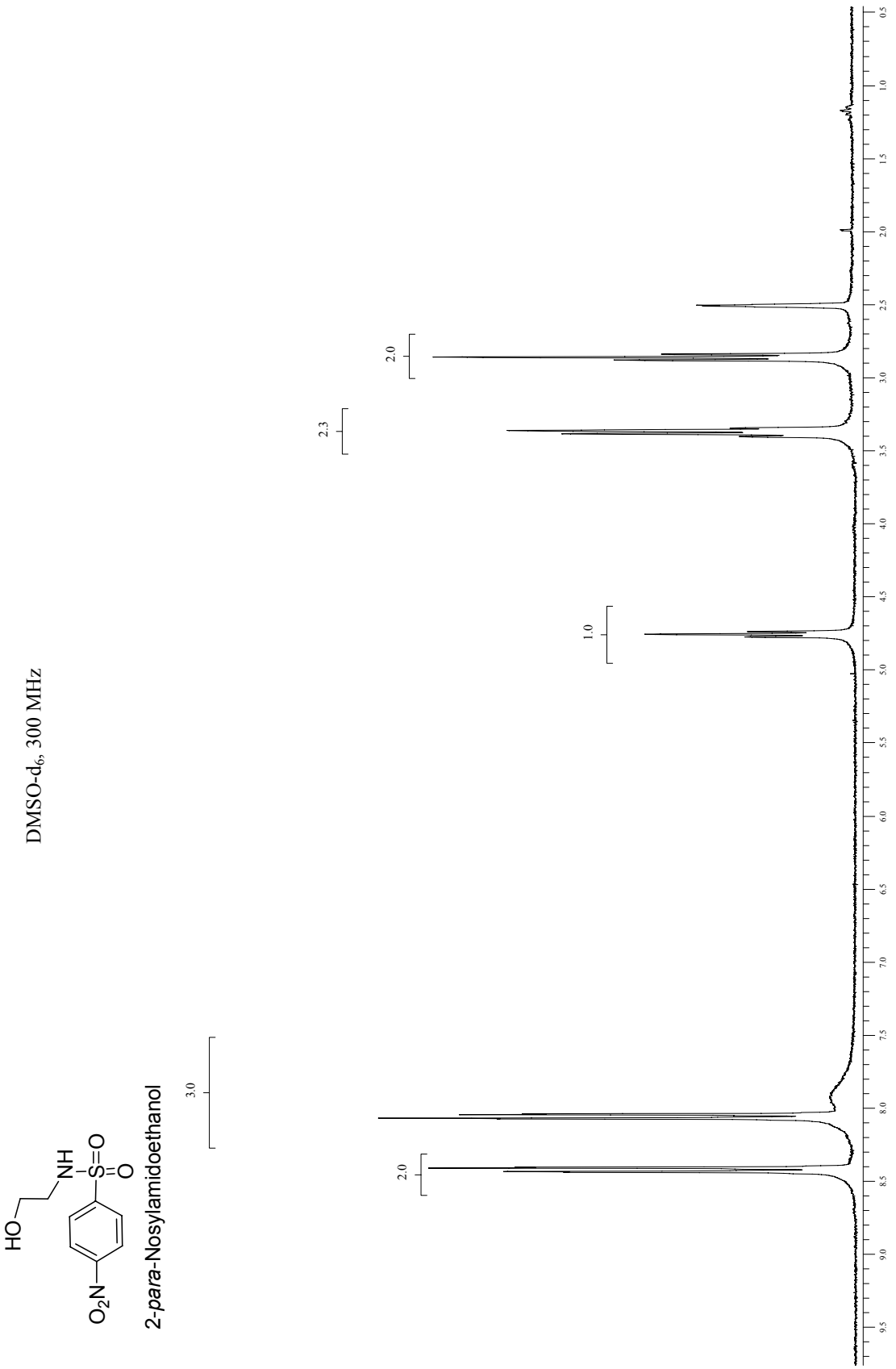

CDCl3, 150 MHz
SiMe3
O
Br
8
0
25
50
75
100
125
150
175
200

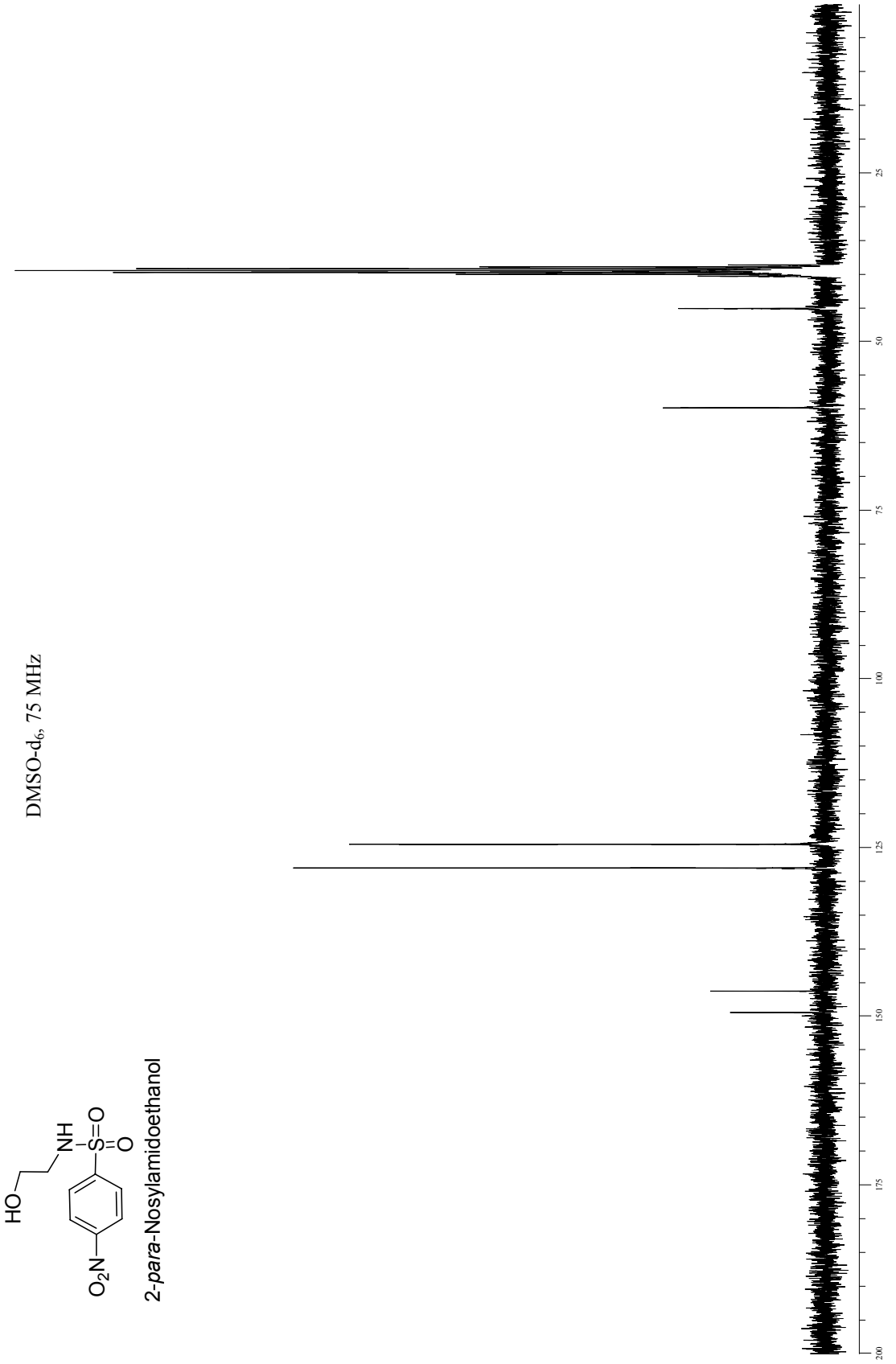

CDCl3, 300 MHz
SiMe3
O
Br
OH
9
9.2
3.0
2.3
3.9
2.1
0.9
1.0

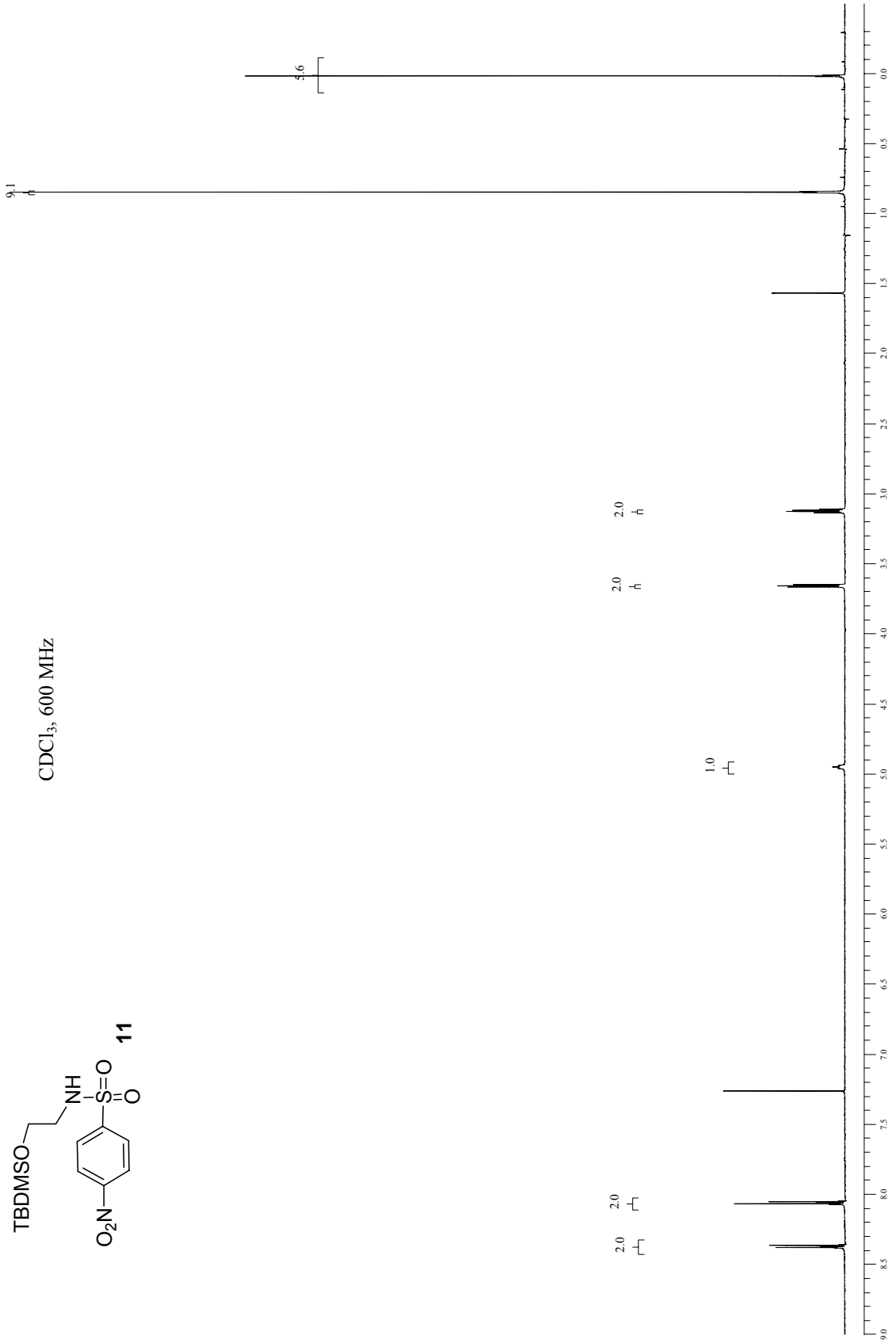

CDCl3, 75 MHz
SiMe3
O
Br
OH
9
0
25
50
75
100
125
150
175
200

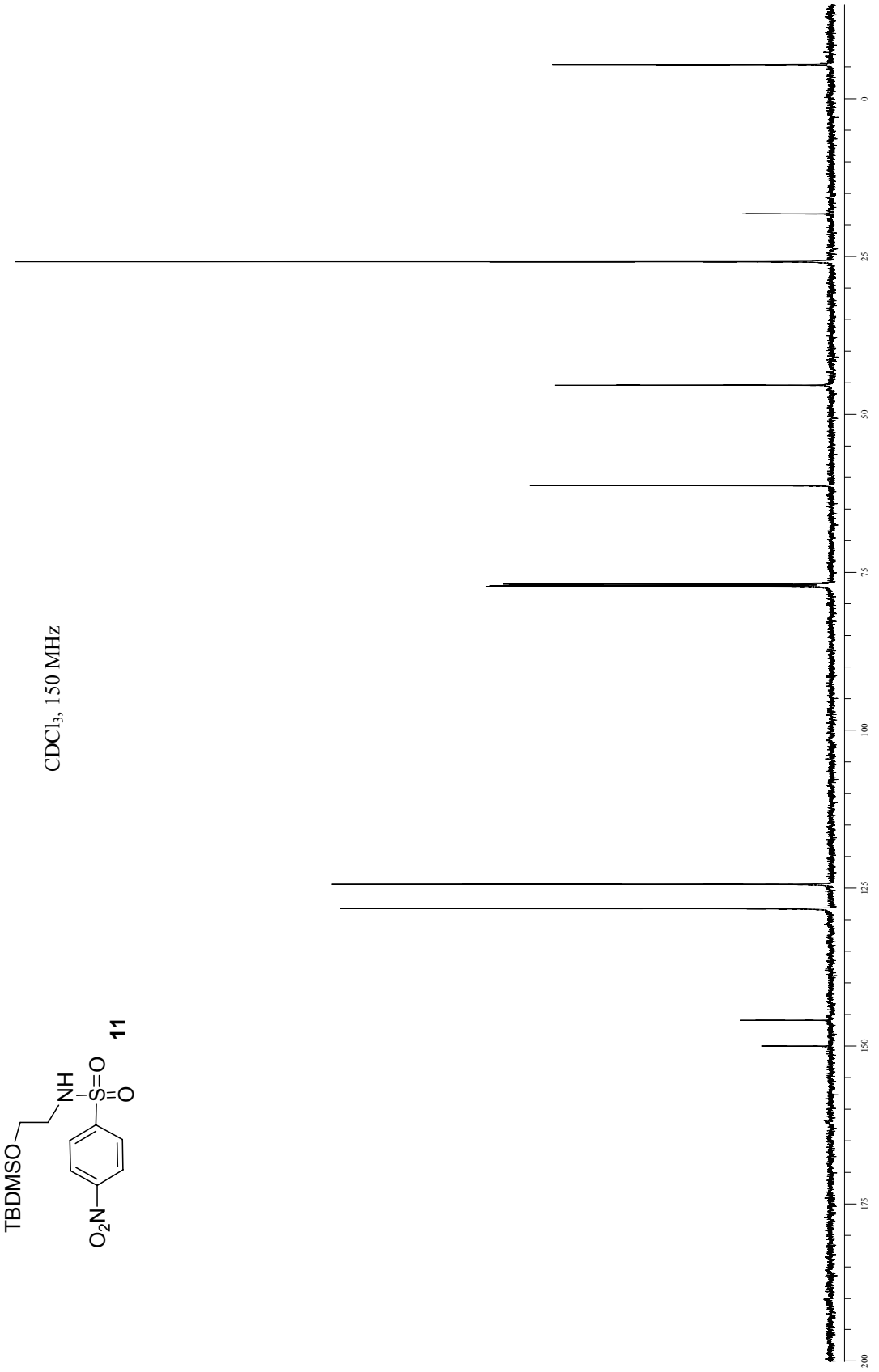

CDCl3, 300 MHz
SiMe3
O
Br
OMs
10
9.7
3.2
2.0
4.2
3.0
2.0
1.0
1.0

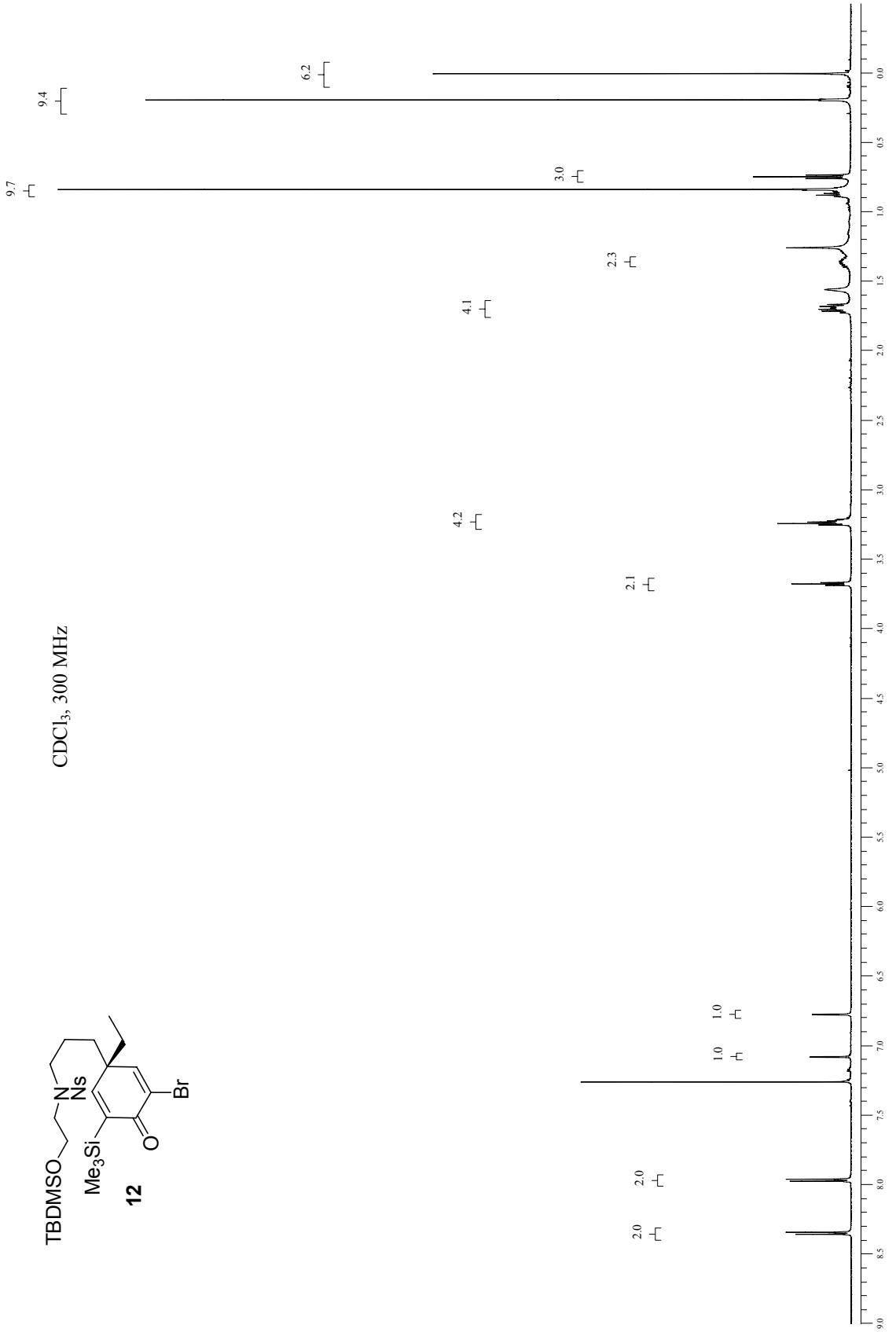

CDCl3, 75 MHz
SiMe3
O
Br
OMs
10

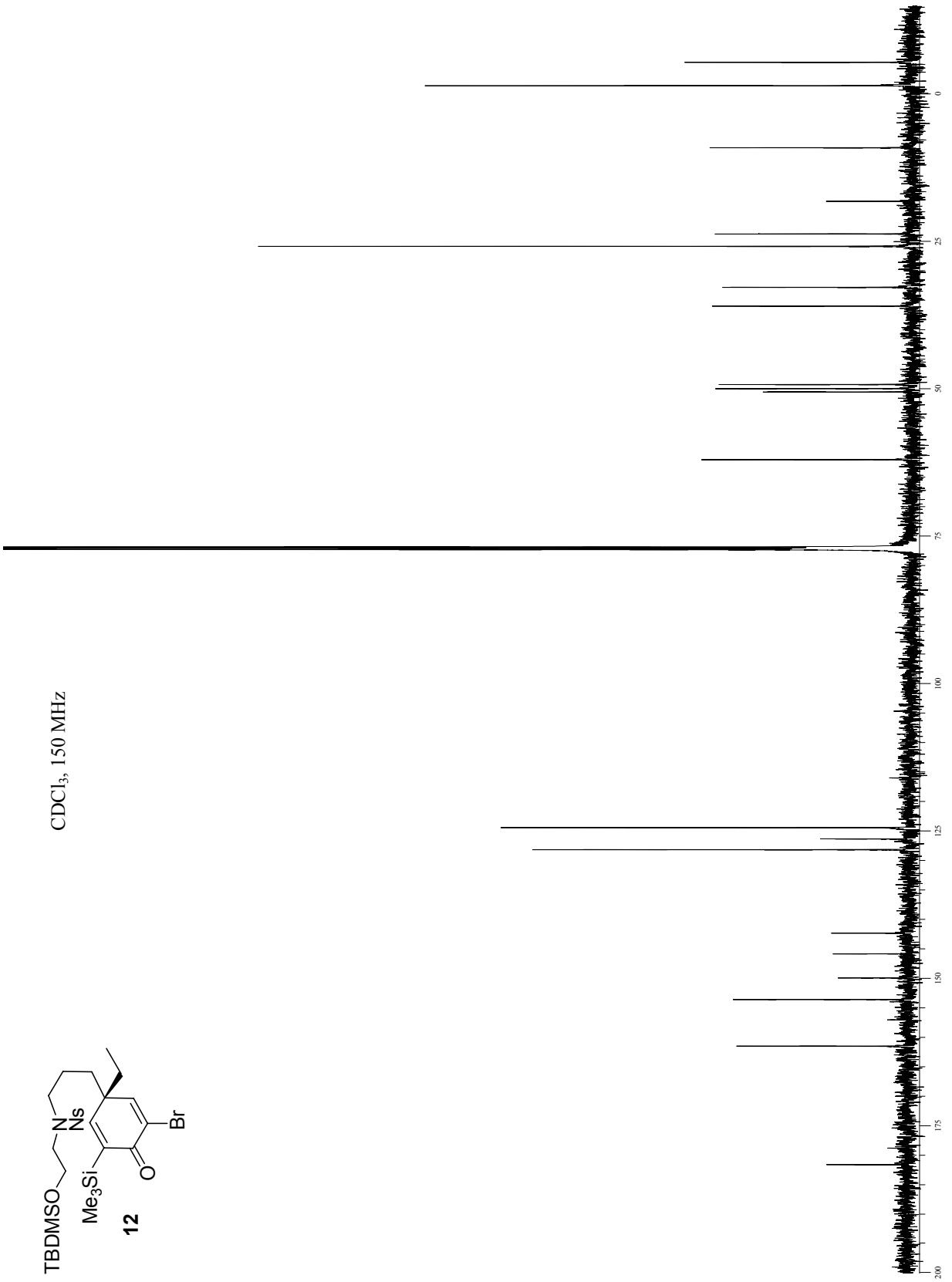

DMSO-d6, 300 MHz
HO
NH
S
O
O
O2N
2-para-Nosylamidoethanol
3.0
2.0
2.3
2.0
1.0

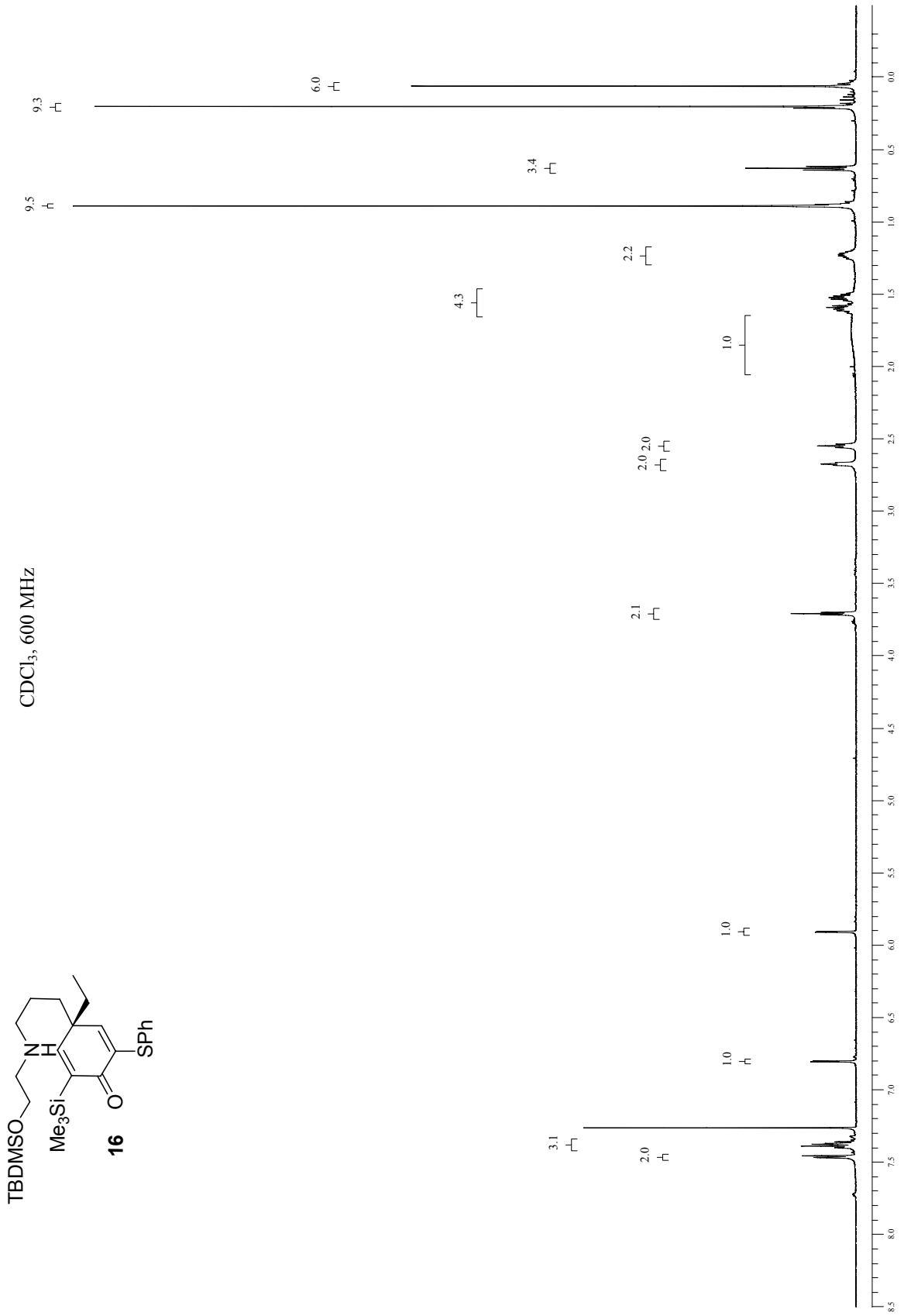

DMSO-d6, 75 MHz
HO
NH
S
O
O
O2N
2-para-Nosylamidoethanol
200
175
150
125
100
75
50
25

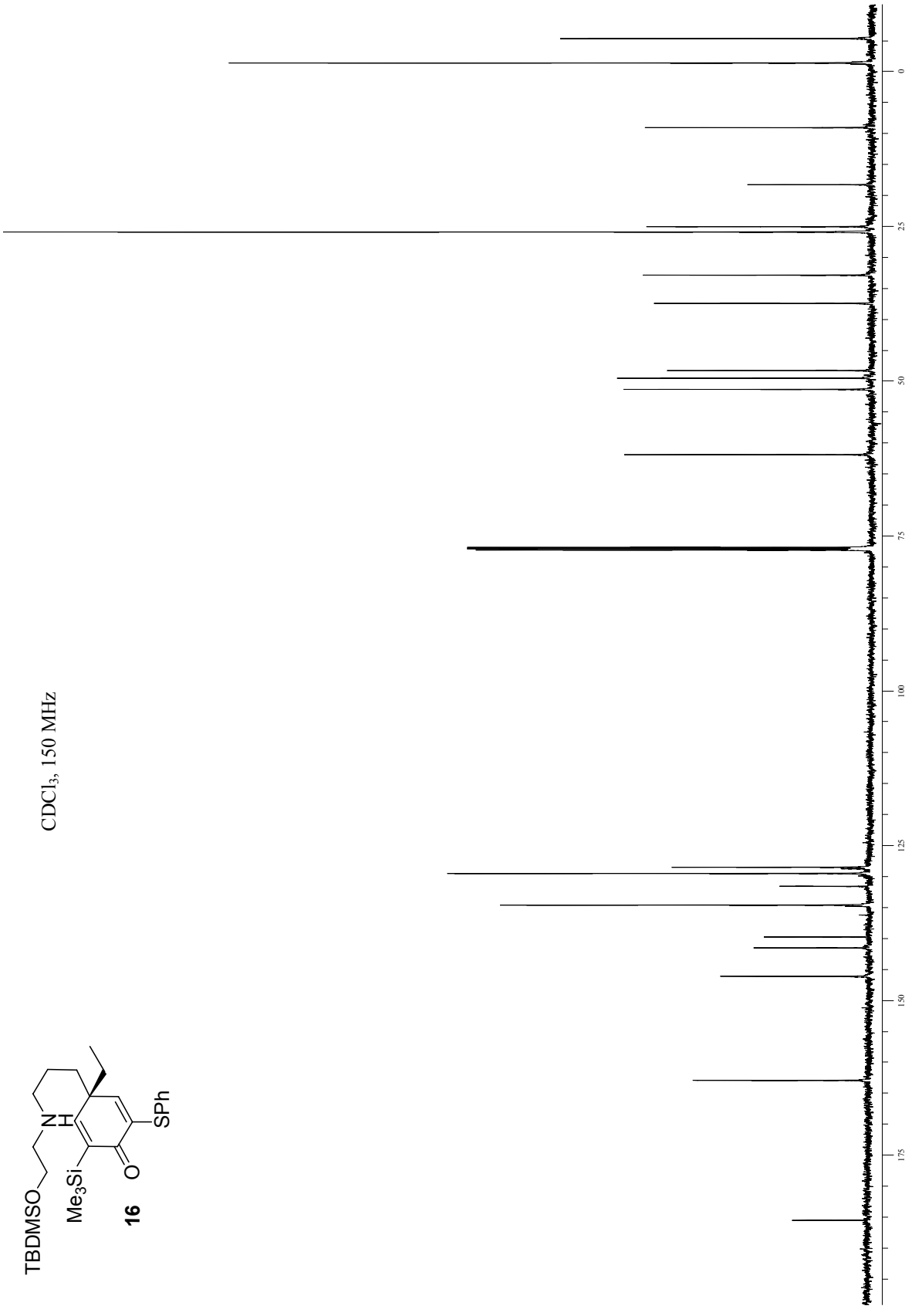

CDCl3, 600 MHz
TBDMSO
NH
S=O
O
O2N
11
9.1
5.6
2.0
2.0
2.0
2.0
1.0

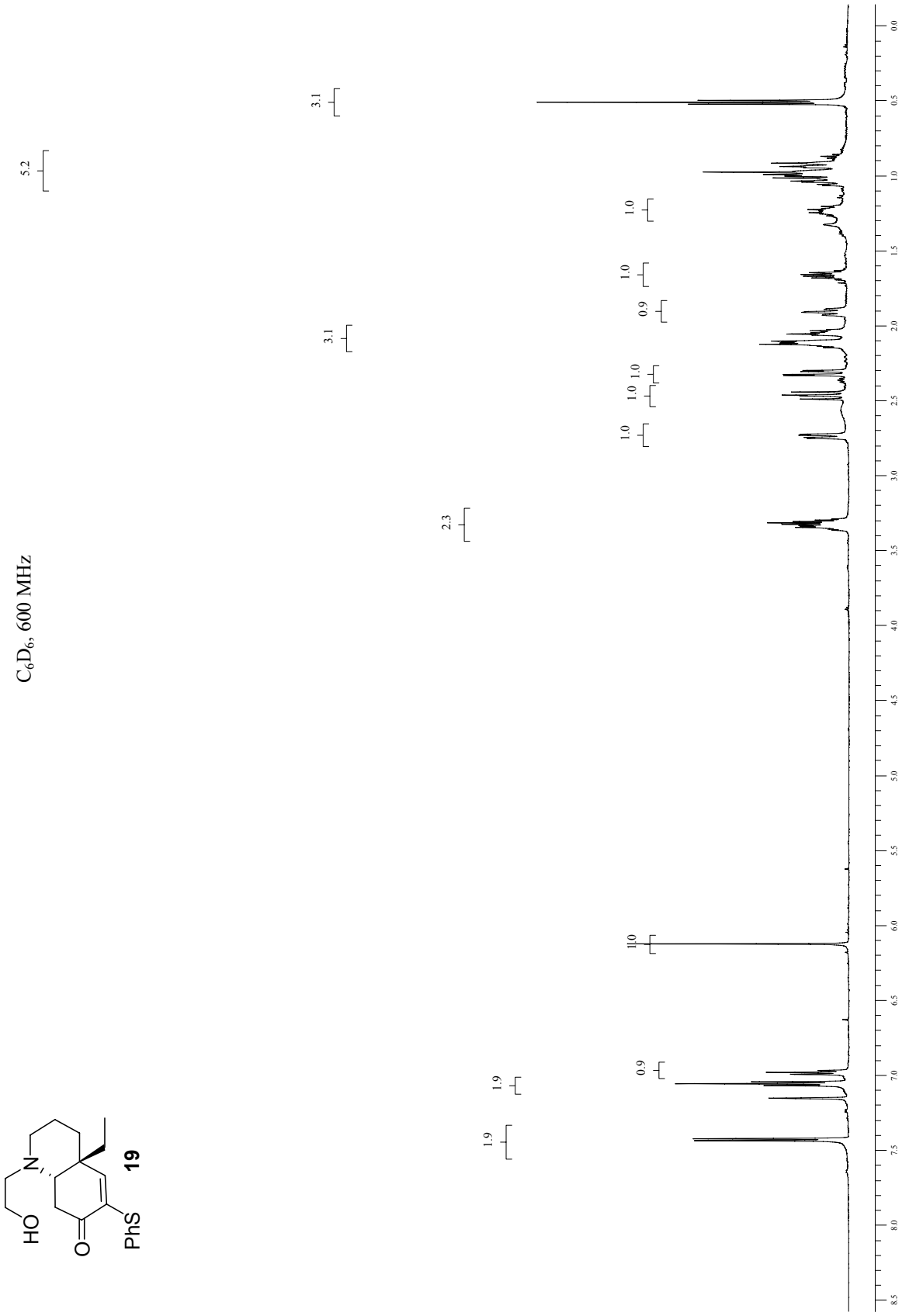

TBDMSO
NH
S
O
O
O2N
11
CDCl3, 150 MHz
0
25
50
75
100
125
150
175
200

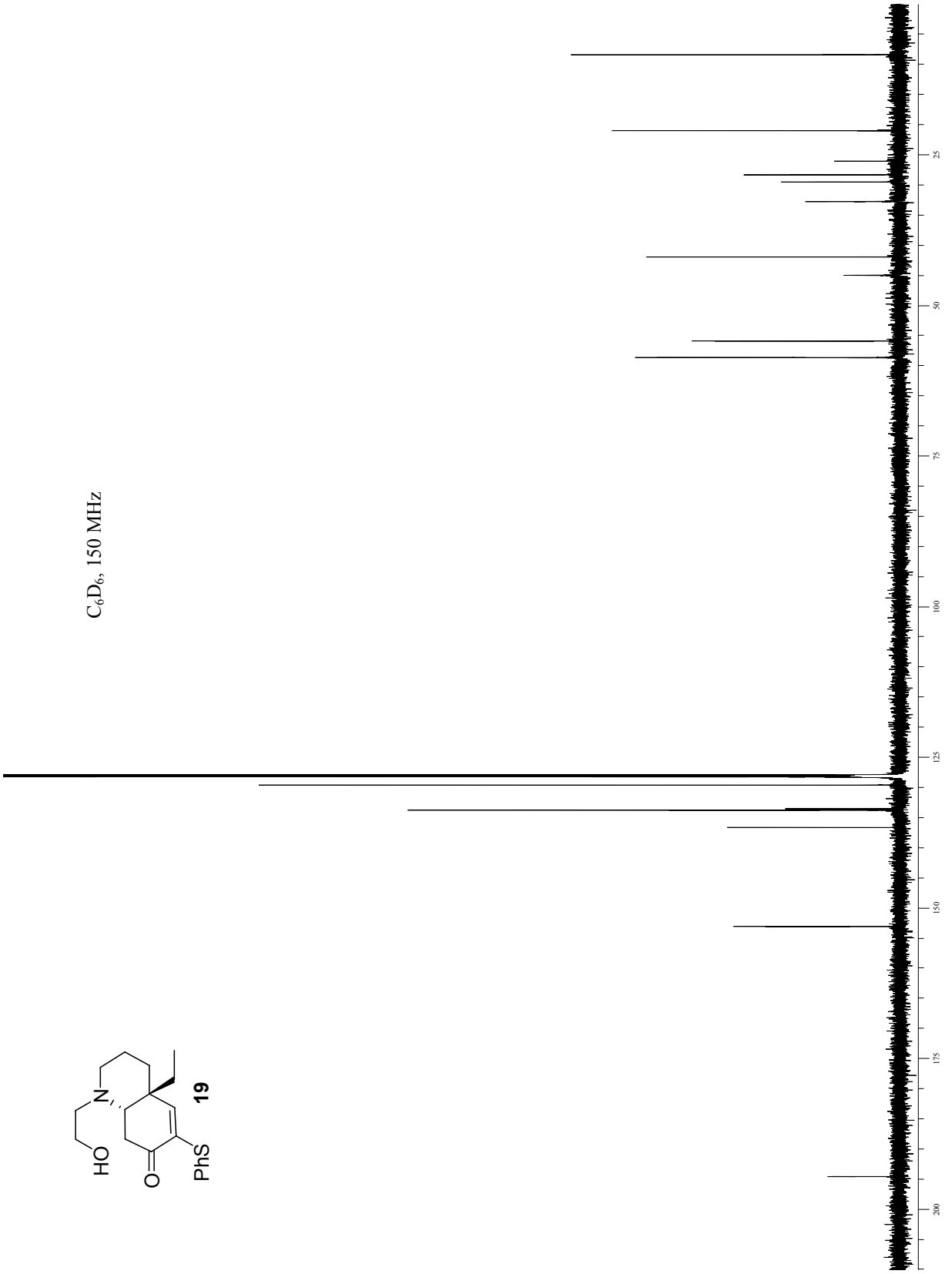

CDCl3, 300 MHz
TBDMSO
N
Ns
Me3Si
O
Br
12
9.7
9.4
6.2
3.0
2.3
4.1
4.2
2.1
1.0
1.0
2.0
2.0

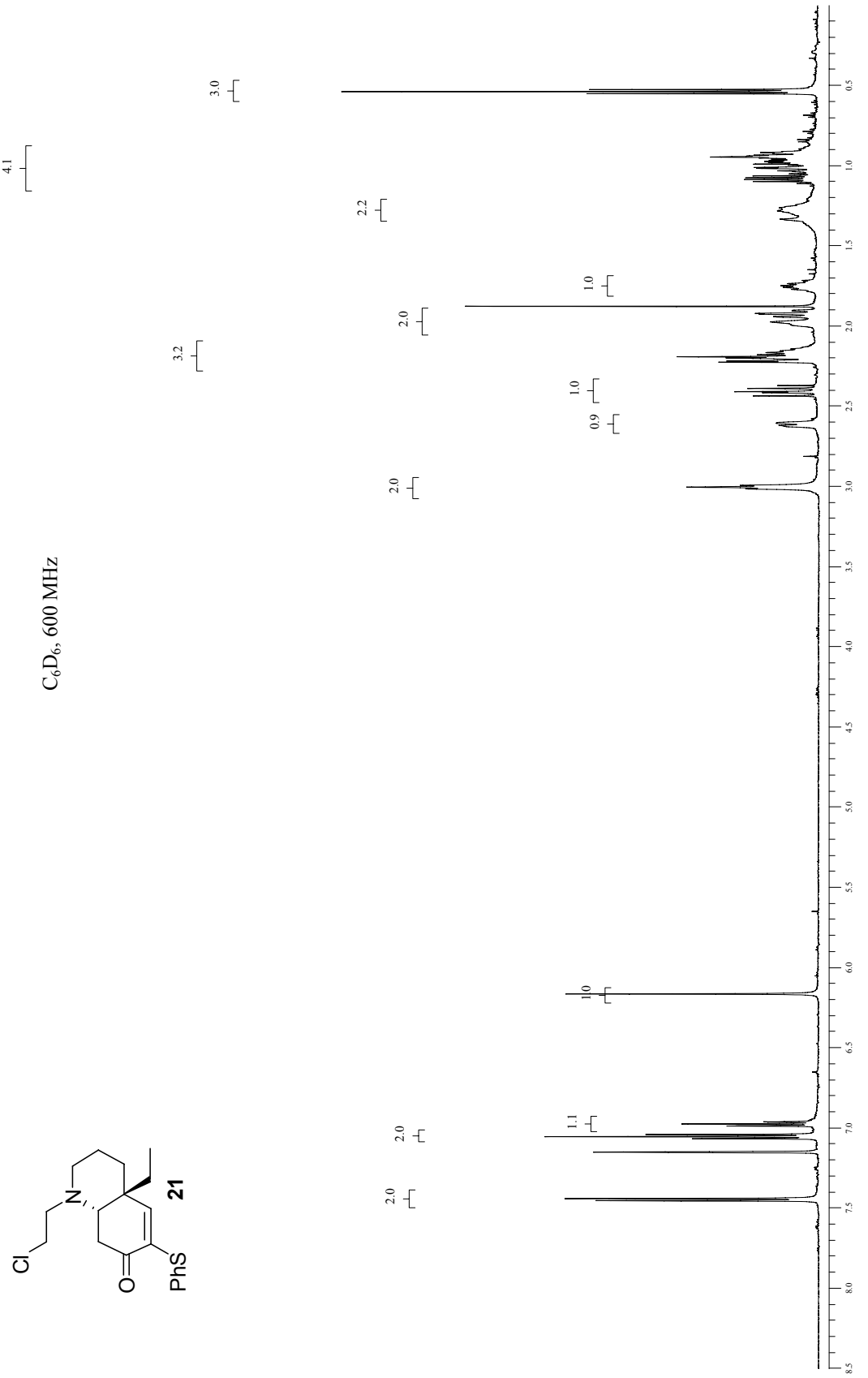

CDCl3, 150 MHz
TBDMSO
N
Ns
Me3Si
O
Br
12

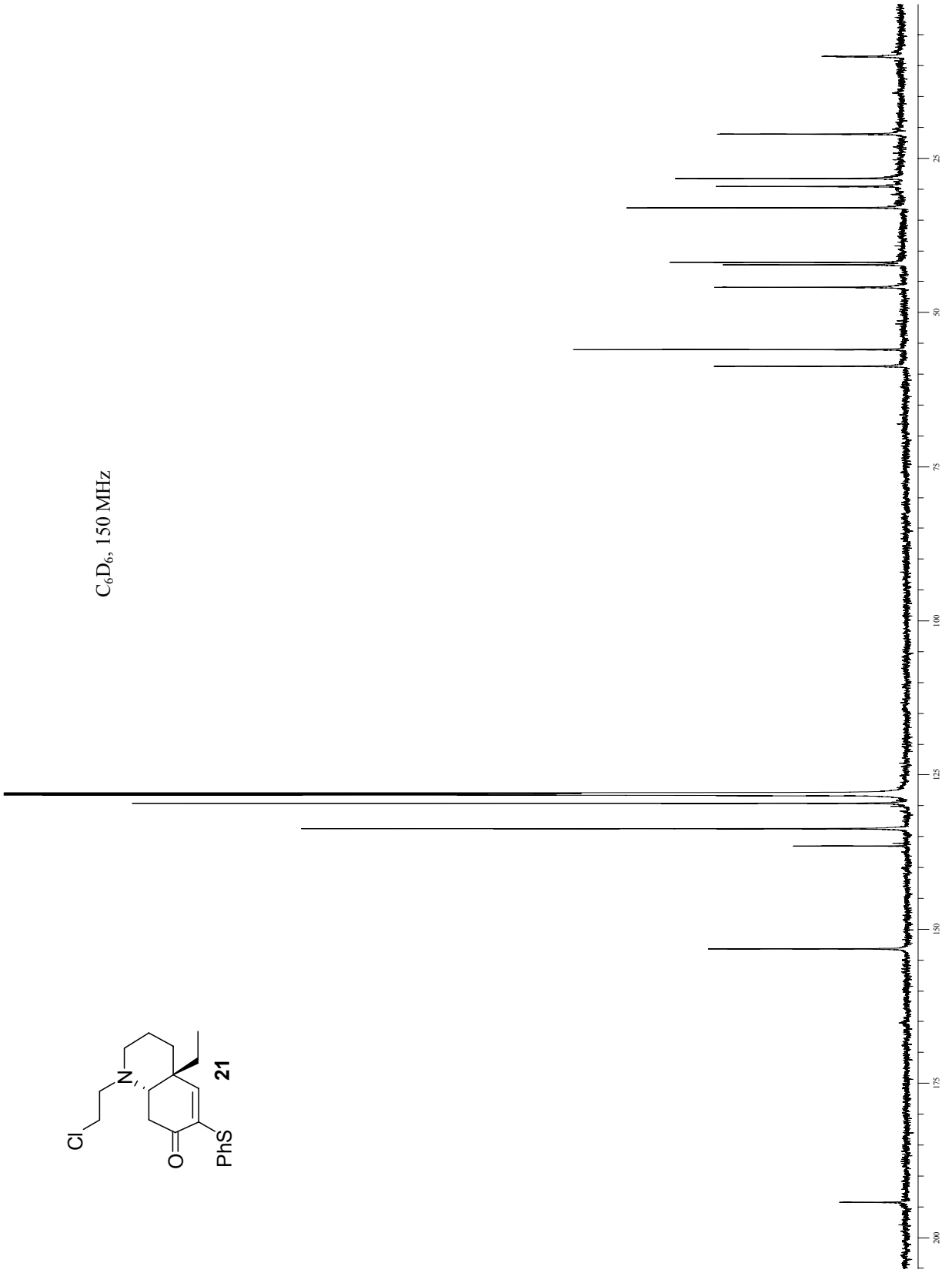

CDCl3, 600 MHz
TBDMSO
Me3Si
N
H
O
SPh
16
9.5
9.3
6.0
3.4
4.3
2.2
2.0
2.0
2.1
1.0
1.0
1.0
3.1
2.0

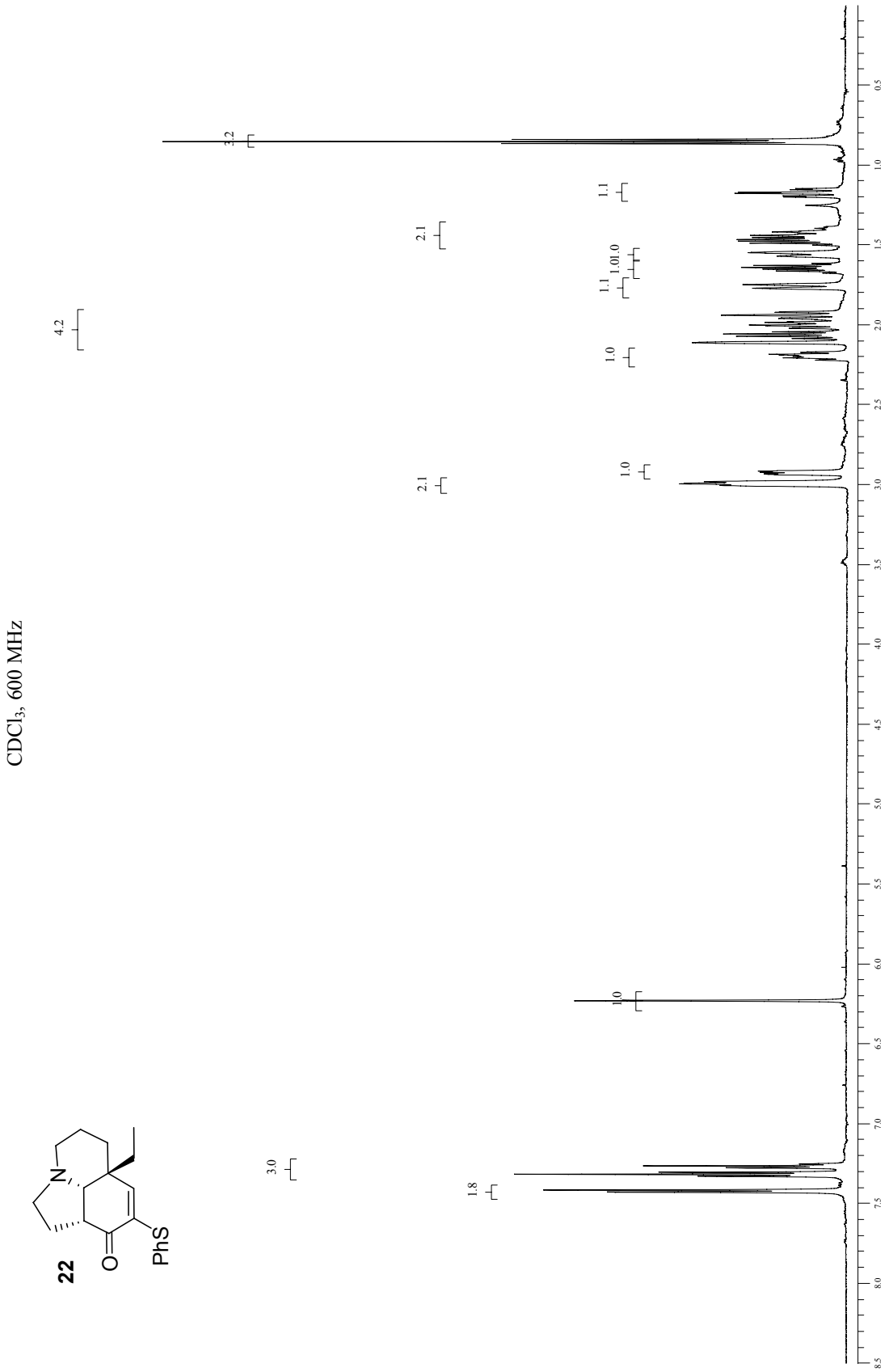

CDCl3, 150 MHz
TBDMSO
Me3Si
O
SPh
16

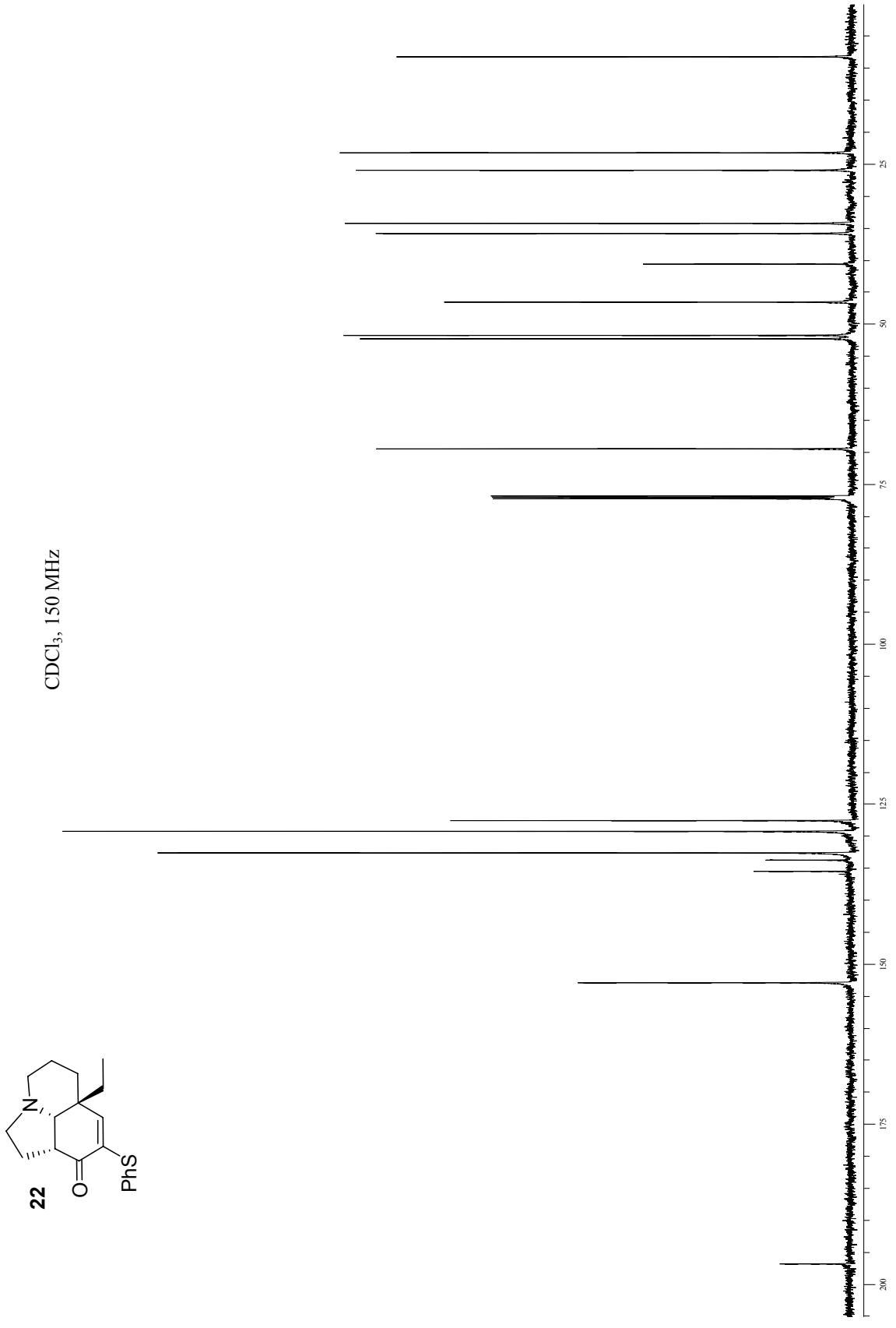

C_6D_6, 600 MHz
HO
N
O
PhS
19

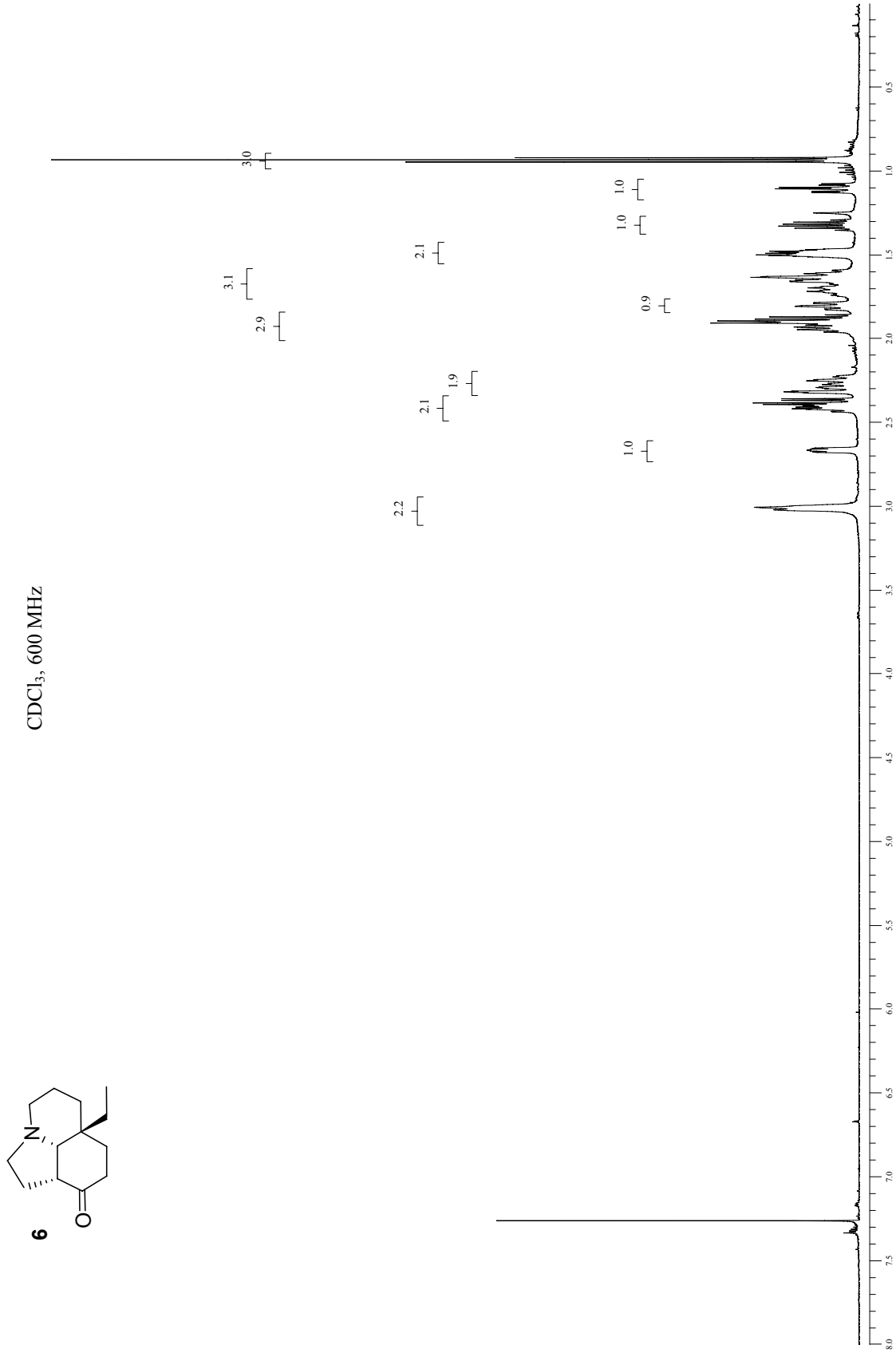

C6D6, 150 MHz
HO
N
O
PhS
19



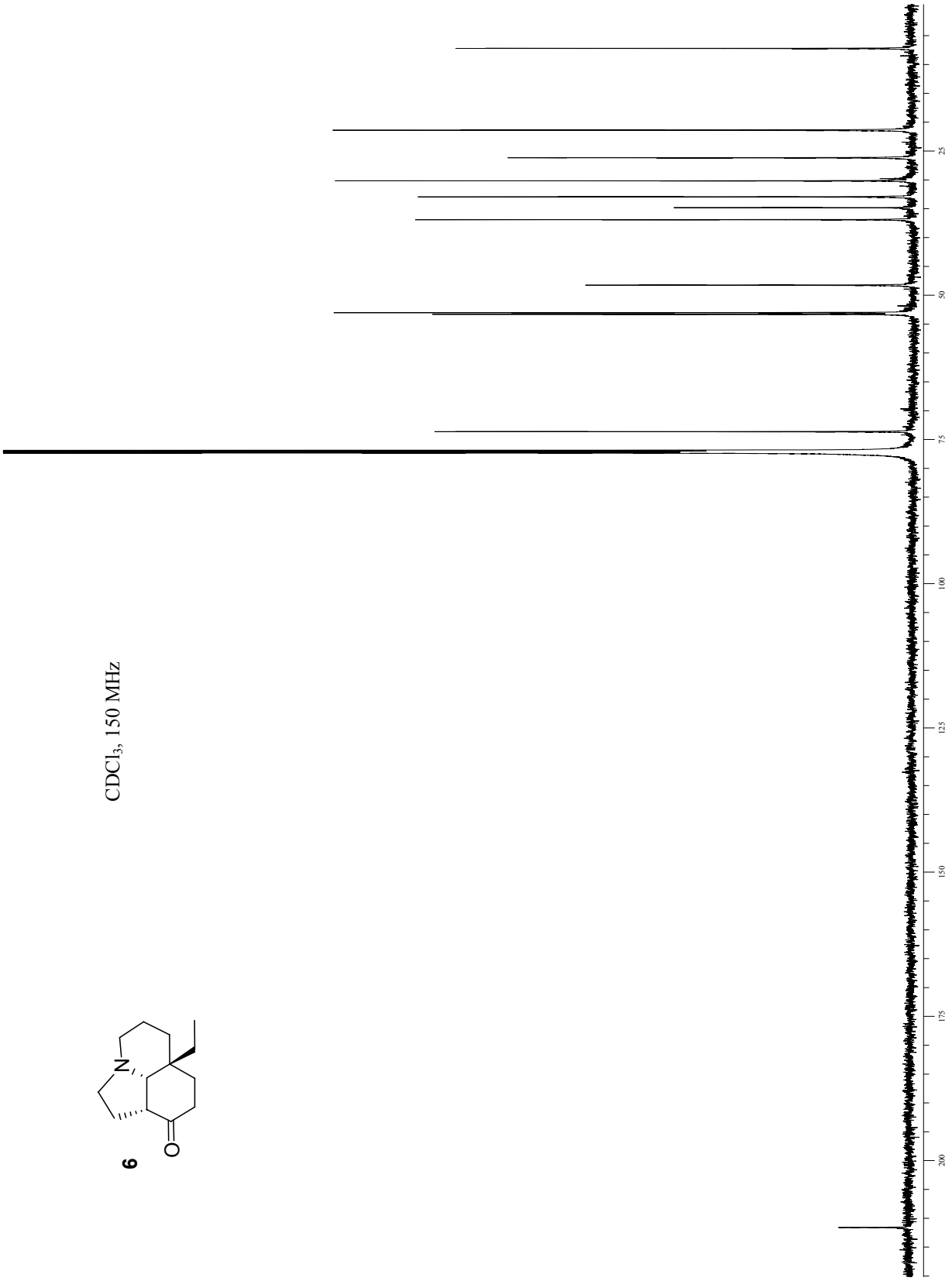

C_6D_6, 150 MHz
Cl
N
O
PhS
21
200
175
150
125
100
75
50
25

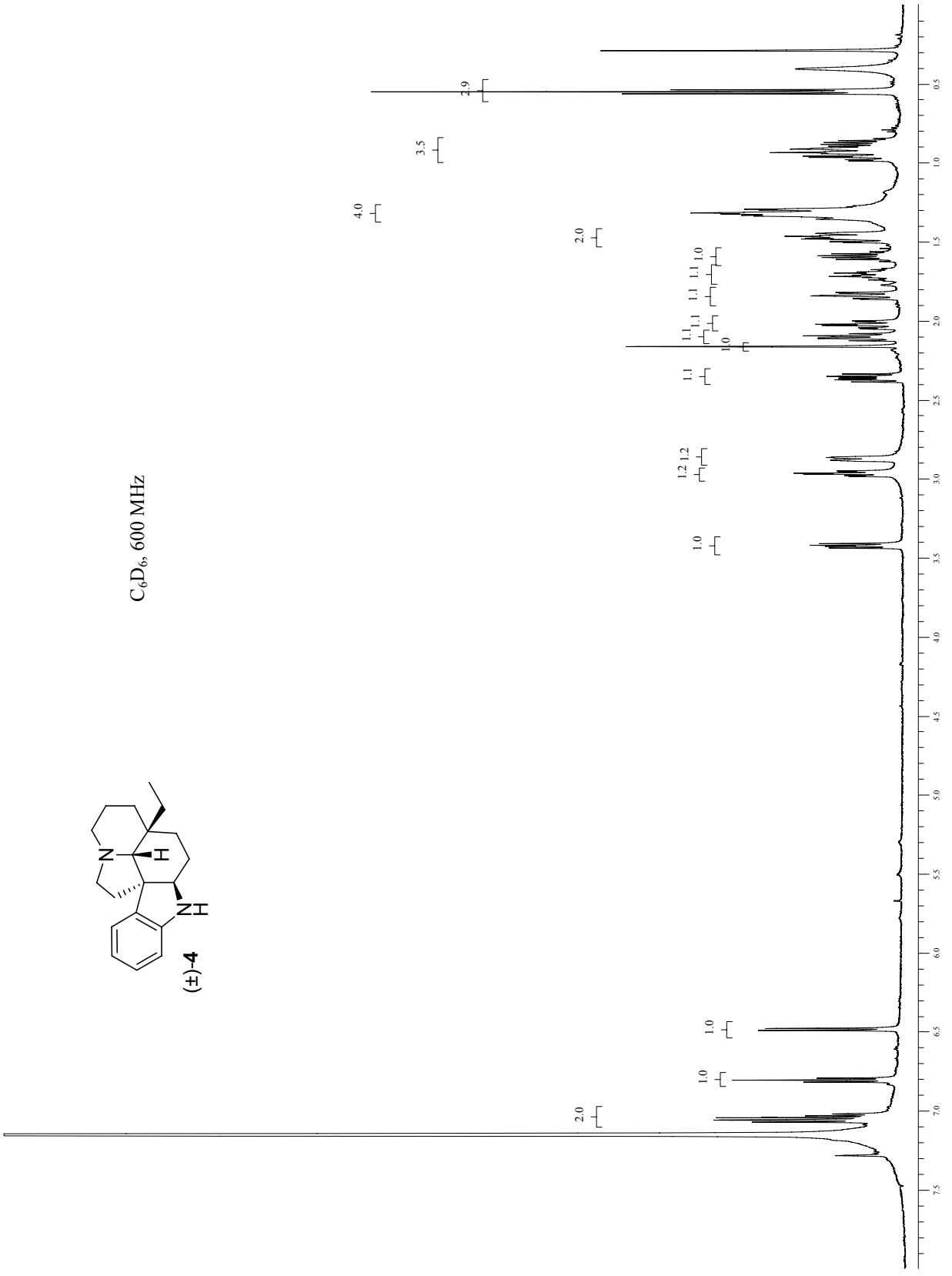

CDCl3, 600 MHz
22
N
O
PhS
3.2
1.1
2.1
1.1
1.01.0
4.2
1.0
2.1
1.0
1.0
3.0
1.8


CDCl3, 150 MHz
22
N
O
PhS
200
175
150
125
100
75
50
25



6


CDCl3, 150 MHz
6
N
O
200
175
150
125
100
75
50
25


C6D6, 600 MHz
(±)-4
2.9
3.5
4.0
2.0
1.0
1.1
1.1
1.1
1.0
1.1
1.2
1.2
1.0
1.0
1.0
2.0