Synthesis and Anticancer Activity of Sclerophytin-Inspired Isobenzofurans

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Supporting Information

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Materials and Instrumentation. All commercially available compounds were purchased from Aldrich Chemical Co., Alfa Aesar Organics, or TCI and used as received unless otherwise noted. Ether, THF, CH_3CN, and CH_2Cl_2 were dried over alumina using the Solv-Tec® ST-002 solvent purification system. Microwave reactions were carried out using a CEM Discover® series reactor. Bruker 300 and 400 MHz spectrometers and a JEOL 270 MHz spectrometer were employed for NMR data collection.

Experimental Procedures

***Anti*-alcohol 3a.** To a solution of diisopropylamine (49.9 mmol, 1.5 eq) in dry THF (200 mL) was added n-BuLi (3.20 g, 49.9 mmol, 1.5 eq, 2.81 M in hexane) dropwise at -78 ºC. After 15 min, (*S*)-(+)-carvone (5.00 g, 33.3 mmol, 1 eq) was added dropwise, followed after 30 min by slow addition of 2-bromobenzaldehyde (7.4 g, 39.9 mmol, 1.2 eq) over 45 min. The mixture was allowed to stir at -78 ºC until no starting material was observed by TLC (~ 6 h). Glacial HOAc (3.00 g, 49.9 mmol, 1.5 eq) was then added to the reaction mixture at -78 ºC. After ~5 min the reaction mixture was warmed to rt and diluted with ether (100 mL), washed with water (150 mL) and extracted with ether (3 x 100 mL). The combined organic extracts were then washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified via flash chromatography over silica gel (10:90 EtOAc/hexanes) to deliver the desired *anti*-alcohol **3a** as a colorless oil in 77 % yield (8.56 g, 28.6 mmol). ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.74−7.62 (d, J=7.55 Hz, 1H), 7.60−7.47 (d, J=7.99 Hz, 1H), 7.36-7.34 (t, J=7.55 Hz, 1H), 7.14-7.11 (t, 1H), 6.70 (s, 1H), 5.22-5.18 (t, J=6.15 Hz, 1H), 4.85 (s, 1H), 4.80 (s, 1H), 3.20-3.18 (d, J=5.93 Hz, 1H), 3.00-2.98 (m, 1H), 2.64-2.68 (m, 2H), 1.77 (s, 3H), 1.67 (s, 3H). ^{13}C-NMR (67 MHz, $CDCl_3$) δ 200.7, 145.1, 143.7, 141.3, 135.3, 132.7, 129.3, 129.1, 127.6, 113.1, 72.5, 55.1, 44.3, 29.4, 20.9, 15.8. IR (film) 3435, 1659 cm^{-1}. HRMS calculated for $C_{17}H_{19}BrO_2Na$ 357.0466, found 357.0466.

***Anti*-alcohol 3b.** Prepared as for **3a.** The desired alcohol **3b** was obtained as a colorless oil in 58% yield (3.89 g, 11.6 mmol) from 3.00 g (20.0 mmol) of (*S*)-(+)-carvone. ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.35−7.31 (m, 1H), 7.23-7.20 (t, *J*=7.79 Hz, 1H), 6.71-6.68 (m, 1H), 4.91-4.89 (d, *J*=6.38 Hz, 2H), 4.81-4.76 (dd, *J*=8.60, 3.50 Hz, 1H), 3.22 (d, *J*=8.86 Hz, 1H), 2.94-2.85 (m, 2H), 2.40-2.43 (m, 2H), 1.74 (s, 3H), 1.53 (s, 3H). ^{13}C- NMR (67 MHz, $CDCl_3$) δ 202.50, 145.91, 144.64, 143.92, 135.95, 130.90, 130.50, 129.83, 129.61, 126.20, 122.04, 114.66, 77.34, 77.02, 76.71, 73.94, 53.62, 44.35, 31.26, 19.05, 15.63. Anal. ($C_{17}H_{19}BrO_2$) C 60.94, H 5.66.

***Anti*-alcohol 3c.** Prepared as for **3a.** The desired alcohol **3c** was obtained as a colorless oil in 75% yield (8.17 g, 25.1 mmol) from 5.00 g (33.2 mmol) of (*S*)-(+)-carvone. ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.66−7.63 (d, 1H), 7.38-7.36 (d, 1H), 7.28-7.25 (t, 1H), 6.71-6.69 (m, 1H), 5.24-5.21 (dd, J=7.32 Hz, 4.55 Hz, 1H), 4.89-4.87 (m, 2H), 3.28-3.25 (d, J=7.32 Hz, 1H), 3.05-3.00 (dd, J=9.20, 4.55 Hz, 2H), 2.87-2.79 (m, 1H), 2.53-2.52 (m, 1H), 1.74 (s, 1H), 1.39 (s, 3H). ^{13}C-NMR (67 MHz, $CDCl_3$) δ 202.50, 145.91, 144.64, 143.92, 135.95, 130.90, 130.50, 129.83, 129.61, 126.20, 122.04, 114.66, 77.34, 77.02, 76.71, 73.94, 53.62, 44.35, 31.26, 19.05, 15.63. Anal. ($C_{17}H_{18}Cl_2O_2$) C 62.65, H 5.64.

***Anti*-alcohol 3d.** Prepared as for **3a.** The desired alcohol **3d** was obtained as a white solid in 66% yield (7.13 g, 21.9 mmol) from 5.00 g (33.2 mmol) of (*S*)-(+)-carvone; mp 110-112 °C; ^{1}H-NMR (300 MHz, CDCl3) δ 7.65 (d, 1H), 7.31-7.24 (m, 2H), 6.74-6.65 (m, 1H), 5.15-5.08 (dd, *J*=7.32, 4.75 Hz, 1H), 4.88 (s, 1H), 3.26 (d, J=7.32 Hz, 1H), 3.01-2.95 (dd, J=4.75, 9.3Hz, 1H), 2.89-2.79 (m, 1H), 2.49 (m, 2H), 1.74 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 200.65, 145.04, 144.81, 138.07, 135.55, 133.51, 133.15, 130.29, 128.92, 126.66, 113.62, 77.46, 77.04, 76.61, 69.46, 52.83, 43.19, 30.52, 19.12, 16.07.

***Anti*-alcohol 3e.** Prepared as above for **3a.** The desired alcohol **3e** was obtained in 65% yield as a solid (2.22 g, 7.25 mmol) from 1.96 g (13.1 mmol) of (*S*)-(+)-carvone; mp 123-124 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, J = 7.6 Hz, 1H), 8.13 (d, J = 7.5 Hz, 0H), 7.94 – 7.78 (m, 3H), 7.62 (d, J = 7.2 Hz, 1H), 7.60 – 7.41 (m, 5H), 6.72 (s, 1H), 5.58 (t, J = 6.1 Hz, 1H), 5.16 (s, 1H), 4.82 (d, J = 18.7 Hz, 2H), 3.38 (d, J = 6.5 Hz, 1H), 3.30 – 3.20 (m, 1H), 2.72 – 2.61 (m, 1H), 2.61 – 2.32 (m, 2H), 1.84 (d, J = 1.4 Hz, 3H), 1.61 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 201.86, 145.62, 143.77, 137.80, 135.55, 131.34, 128.85, 128.75, 126.52, 126.05, 125.59, 125.50, 123.84, 113.38, 71.11, 63.87, 44.66, 29.39, 21.09, 16.16. Anal. ($C_{21}H_{22}O_2$) C 82.23, H, 7.36.

***Anti* -alcohol 3f.** Prepared as above for **3a.** The desired alcohol **3f** was obtained in 28 % yield as an oil (1.92 g, 7.5 mmol) from 4.00 g (26.6 mmol) of (*S*)-(+)-carvone. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, J = 4.8 Hz, 1H), 7.68 (td, J = 1.7, 7.7 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.13 (dd, J = 4.9, 7.4 Hz, 1H), 6.74 – 6.65 (m, 1H), 4.94 (dd, J = 10.4, 11.8 Hz, 2H), 4.84 (d, J = 7.9 Hz, 1H), 3.90 (d, J = 9.1 Hz, 1H), 3.50 (dd, J = 2.1, 12.4 Hz, 1H), 3.13 (ddd, J = 5.1, 10.5, 12.4 Hz, 1H), 2.65 – 2.47 (m, 1H), 2.39 (dt, J = 5.2, 9.5 Hz, 1H), 1.85 (s, 3H), 1.68 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 200.91, 163.01, 148.18, 145.60, 144.46, 136.58, 135.88, 121.65, 119.69, 114.48, 72.07, 54.52, 46.27, 31.26, 19.12, 15.84. Anal. ($C_{16}H_{19}NO_2$) C 74.45, H, 7.50.

***Anti*-alcohol 3g.** Prepared as for **3a**. The desired alcohol **3g** was obtained as an oil in 47% yield (1.15 g, 4.7 mmol) from 1.5 g (10.0 mmol) of (*S*)-(+)-carvone. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.30 (dd, J = 0.8, 1.8 Hz, 1H), 6.78 (ddd, J = 1.3, 2.4, 6.1 Hz, 1H), 6.29 (dd, J = 1.8, 3.2 Hz, 1H), 6.16 (d, J = 3.3 Hz, 1H), 5.20 (d, J = 10.9 Hz, 1H), 4.91 – 4.83 (m, 1H), 4.75 (dd, J = 4.5, 11.0 Hz, 2H), 2.95 (dd, J = 4.4, 12.8 Hz, 1H), 2.64 – 2.50 (m, 1H), 2.50 – 2.34 (m, 1H), 2.33 – 2.19 (m, 1H), 1.81 (dt, J = 1.3, 2.4 Hz, 3H), 1.74 (s, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 202.69,154.94, 154.81, 144.03, 141.68, 135.78, 114.37, 110.23, 108.17, 68.24, 52.10, 45.29, 31.17, 18.74, 15.74. Anal. ($C_{15}H_{18}O_3$) C 73.39, H, 7.43.

***Anti*-alcohol 3h.** Prepared as for **3a**. The desired alcohol **3h** was obtained in 50% yield as an oil (1.79 g, 6.52 mmol) from 1.96 g (13.1 mmol) of (*S*)-(+)-carvone. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.35 (td, J = 1.7, 7.6 Hz, 1H), 7.30-7.14 (m, 1H), 7.07 (dt, J = 3.8, 7.5 Hz, 1H), 6.96 (ddd, J = 1.2, 8.2, 10.6 Hz, 1H), 6.72 (ddd, J = 1.4, 3.6, 4.9 Hz, 1H), 5.39 (dd, J = 5.1, 8.1 Hz, 1H), 4.71 (dd, J = 12.7, 14.1 Hz, 2H), 4.12 (d, J = 8.2 Hz, 1H), 3.03 (dd, J = 5.1, 9.8 Hz, 1H), 2.84 – 2.68 (m, 1H), 2.51 – 2.25 (m, 2H), 1.77 (s, 3H), 1.58 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 202.01, 161.92, 158.66, 145.11, 135.90, 129.28, 129.16, 129.11, 128.99, 124.07, 115.49, 115.19, 113.26, 67.87, 53.89, 43.54, 30.52, 19.83, 16.04. Anal. ($C_{17}H_{19}FO_2$) C 74.70, H 7.03.

Glycolate 4a. To a stirring solution of alcohol **3a** (8.65 g, 25.80 mmol) in anhydrous DMF (75mL) was added Ag_2O (9.00 g, 38.7 mmol, 1.5 eq), followed by dropwise addition of ethyl bromoacetate (6.46 g, 38.7 mmol, 1.5 eq) at rt. After stirring ~10 min, 2,6-lutidine (4.15 g, 38.7 mmol) was added via syringe pump (~2 mL/h) and stirring was continued for 24 h at rt. The crude mixture was then filtered through a short silica gel column eluted with diethyl ether (100 mL). The filtrate was washed with 3N HCl (100 mL) and extracted with hexane (3x60 mL). The combined extracts were washed sequentially with saturated aqueous $NaHCO_3$ and brine, then dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified via flash chromatography over silica gel (20:80 EtOAc/hexanes) to deliver glycolate **4a** as a yellow oil in 77 % yield (8.47 g, 20.1 mmol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (dd, J = 1.7, 7.8 Hz, 1H),

7.48 (dd, J = 1.1, 8.0 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.23 – 7.10 (m, 1H), 6.69 (s, 1H), 5.45 (d, J = 7.0 Hz, 1H), 4.71 (dd, J = 8.1, 9.3 Hz, 3H), 4.33 – 4.14 (m, 3H), 4.02 (d, J = 16.4 Hz, 1H), 3.84 (d, J = 16.4 Hz, 1H), 3.33 (s, 1H), 3.08 – 2.89 (m, 2H), 2.45 (d, J = 19.3 Hz, 1H), 1.75 (d, J = 1.4 Hz, 3H), 1.57 (s, 3H), 1.37 – 1.21 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) 198.3, 169.9, 141.7, 129.8, 129.0, 128.8, 128.1, 127.6, 112.2, 80.7, 77.6, 77.1, 76.6, 65.6, 64.9, 60.7, 55.4, 43.5, 28.4, 21.4, 16.3, 14.2. IR (film) 1750, 1671 cm^{-1}. HRMS Calcd for $C_{21}H_{25}BrNaO_4$: 443.0834, found 443.0830.

Glycolate 4b. Prepared as for **4a.** Glycolate **4b** was obtained as a colorless oil in 77% yield (1.56 g, 3.70 mmol) from 1.61 g (4.80 mmol) of alcohol **3b**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.34 (m, 2H), 7.20 (q, J = 7.7 Hz, 2H), 6.69 (s, 1H), 4.89 (d, J = 7.0 Hz, 1H), 4.74 (s, 1H), 4.67 (s, 1H), 4.26 – 4.13 (m, 2H), 4.08 (d, J = 16.6 Hz, 1H), 3.84 (d, J = 16.6 Hz, 1H), 3.25 (s, 1H), 3.04 – 2.90 (m, 1H), 2.80 (dd, J = 4.0, 7.0 Hz, 1H), 2.44 (d, J = 19.6 Hz, 1H), 1.71 (s, 4H), 1.58 (d, J = 14.2 Hz, 6H), 1.27 (t, J = 7.1 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) 197.8, 170.1, 146.1, 143.4, 138.0, 135.5, 132.6, 129.6, 129.4, 127.6, 112.3, 79.4, 72.6, 68.0, 66.2, 61.0, 55.7, 41.5, 28.2, 21.2, 16.3, 14.3.

Glycolate 4c. Prepared as for **4a**. Glycolate **4c** was obtained as a colorless oil in 83% yield (7.41 g, 18.0 mmol) from 7.06 g of alcohol **3c** (21.7 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 1.5, 7.9 Hz, 1H), 7.45 (dd, J = 1.6, 7.9 Hz, 1H), 7.30 (dd, J = 4.7, 12.7 Hz, 2H), 6.67 (s, 1H), 5.22 (d, J = 5.7 Hz, 1H), 4.83 (dd, J = 7.9, 9.2 Hz, 2H), 4.28 – 4.10 (m, 2H), 4.03 (d, J = 16.3 Hz, 1H), 3.73 (d, J = 16.3 Hz, 1H), 2.99 (t, J = 5.6 Hz, 1H), 2.89 – 2.69 (m, 2H), 2.43 (d, J = 18.5 Hz, 1H), 1.82 (s, 3H), 1.73 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.71, 169.62, 145.56, 142.22, 139.41, 135.71, 132.88, 131.37, 129.87, 127.68, 127.47, 112.89, 79.45, 77.35, 77.03, 76.71, 66.40, 60.83, 54.26, 44.36, 28.82, 20.74, 16.19, 14.18.

Glycolate 4d. Prepared as for **4a.** Glycolate **4d** was obtained as a colorless oil in 80% yield (9.60 g, 23.3 mmol) from 9.48 g (29.2 mmol) of alcohol **3d**. ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.53−7.49 (d, 1H), 7.44-7.40 (d, 1H), 7.30-7.26 (m, 1H), 6.64 (s, 1H), 5.20-5.18 (d, 1H), 4.81-4.76 (d, 2H) 4.20-4.11 (m, 2H), 4.03-3.97 (d, J=16.03 Hz, 1H), 3.72-3.66 (d, J=16.03 Hz, 1H), 3.31-3.25 (m, 1H), 2.94-2.90 (m, 2H), 2.44-2.34 (m, 1H), 1.72, (s, 3H), 1.48 (s, 3H), 1.31-1.26 (t, J=7.07 Hz, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 198.12, 170.14, 145.91, 143.38, 141.50, 135.24, 131.18, 130.27, 129.96, 125.78, 122.56, 112.21, 80.74, 77.33, 77.01, 76.70, 66.00, 60.85, 57.54, 41.25, 29.71, 28.11, 21.23, 16.14, 14.16.

Glycolate 4e. Prepared as for **4a.** Glycolate **4e** was obtained as an oil in 25% yield (8.17 g, 25.13 mmol) from *anti* alcohol **1g** (3.27 mmol). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 7.6 Hz, 1H), 7.91 – 7.83 (m, 1H), 7.79 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 7.0 Hz, 1H), 7.56 – 7.41 (m, 3H), 6.75 (s, 1H), 5.86 (d, J = 5.1 Hz, 1H), 4.59 (s, 2H), 4.13 (d, J = 16.4 Hz, 1H), 3.92 (d, J = 10.3 Hz, 1H), 3.70 (s, 3H), 3.28 (dd, J = 4.4, 9.8 Hz, 1H), 3.09 – 2.90 (m, 2H), 2.47 – 2.31 (m, 1H), 1.72 (s, 3H), 1.27 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.92, 170.89, 146.63, 144.20, 135.41, 134.25, 133.96, 131.11, 129.22, 128.72, 126.54, 125.73, 125.26, 125.22, 122.98, 112.11, 79.47, 66.40, 55.66, 51.85, 41.25, 29.00, 20.97, 16.37. HRMS Calcd for $C_{24}H_{26}O_4Na$: 401.1729, found: 401.1719.

Glycolate 4f. Prepared as for **4a.** Glycolate **4f** was obtained as an oil in 86% yield (1.43 g, 4.34 mmol) from 1.3g (5.05 mmol) of alcohol **3f**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.50 (d, J = 4.8, 1H), 7.70 (dt, J = 7.0, 20.6 Hz, 2H), 7.23 – 7.10 (m, 1H), 6.63 (s, 1H), 4.83 (s, 1H), 4.75 (d, J = 5.2 Hz, 1H), 4.20 (d, J = 16.2 Hz, 1H), 3.93 (d, J = 16.2 Hz, 1H), 3.69 (s, 3H), 3.17 (dd, J = 5.2, 8.0 Hz, 1H), 2.89 – 2.70 (m, 1H), 2.50 (m, 2H), 1.80 – 1.71 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 197.99, 170.30, 160.59, 148.74 145.81, 142.32, 136.52, 135.60, 122.39, 121.32, 113.28, 83.42, 67.59, 55.15, 51.80, 44.20, 29.28, 20.03, 16.15. Anal. ($C_{19}H_{23}NO_4$) C 68.99, H 7.09.

Glycolate 4g. Prepared as for **4a.** Glycolate **4g** was obtained as an oil in 48% yield (679 mg, 2.13 mmol) from 1.1 g (4.46 mmol) of alcohol **3g**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, J = 0.7 Hz, 1.7, 1H), 6.68 – 6.59 (m, 1H), 6.33 – 6.20 (m, 2H), 4.88 (d, J = 7.6 Hz, 1H), 4.74 (d, J = 1.2 Hz, 1H), 4.66 (s, 1H), 4.12 (d, J = 16.8 Hz, 1H), 3.96 – 3.87 (m, 1H), 3.73 – 3.66 (m, 3H), 3.21 (dd, J = 4.4, 9.4 Hz, 1H), 3.09 (dd, J = 4.4, 7.5 Hz, 1H), 2.98 – 2.81 (m, 1H), 2.42 (ddd, J = 2.5, 5.6, 19.6 Hz, 1H), 1.68 (s, 7H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.03, 171.00, 151.32, 145.97, 143.28, 143.06, 112.17, 110.34, 110.18, 74.74, 65.50, 54.79, 51.92, 41.73, 28.02, 21.52, 16.28. Anal. ($C_{18}H_{22}O_5$) C 67.71, H 6.96.

Glycolate 4h. Prepared as for **4a.** Glycolate **4h** was obtained as an oil in 19 % yield (0.25 g, 0.71 mmol) from 1.05 g of alcohol **3h** (3.8 mmol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (td, J = 1.8, 7.5 Hz, 1H), 7.31 – 7.21 (m, 2H), 7.15 (t, J = 7.0 Hz, 1H), 6.97 (dd, J = 8.4, 10.1 Hz, 1H), 6.66 (s, 1H), 5.26 (d, J = 7.6 Hz, 1H), 4.68 (d, J = 11.6 Hz, 2H), 4.08 (d, J = 16.5 Hz, 1H), 3.87 (d, J = 16.5 Hz, 1H), 3.73 (s, 3H), 3.31 (s, 1H), 3.06 – 2.80 (m, 2H), 2.43 (d, J = 19.6 Hz, 1H), 1.72 (s, 3H), 1.59 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.18, 170.72, 162.47, 159.21, 146.07, 143.16, 135.39, 129.84, 128.75, 126.14, 125.97, 124.48, 124.43, 115.46, 115.18, 112.2574.74, 66.05, 56.64, 51.90, 41.50, 27.91, 21.48, 16.24. Anal. ($C_{20}H_{23}FO_4$) C 68.98, H 6.61.

Isobenzofuran 5a. To a solution of glycolate **4a** (4.13 g, 9.80 mmol) in dry THF (100 mL) was added KHMDS (2.35 g, 11.8 mmol, 1.1 eq, 0.5 M soln. in toluene) quickly at -78 ^{o}C, followed immediately by rapid addition of 1.2 eq HOAc (0.71 g, 11.8 mmol). The reaction mixture was allowed to warm to rt, then water (100 mL) was added. The organic layer was extracted with ether (3 x 60 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified via flash chromatography over silica gel (10:90 EtOAc/hexanes) to yield cycloaldol product **5a** as a colorless oil in 80% yield (3.30 g, 7.84 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, J = 1.6, 7.9 Hz, 1H), 7.52 (d, J = 8.0, 1H), 7.43 (t, J = 7.6, 1H), 7.22 – 7.14 (m, 1H), 5.78 (s, 1H), 5.24 (d, J = 8.8 Hz, 1H), 4.84 (d, J = 3.3 Hz, 2H), 4.46 (s, 1H), 4.37 – 4.22 (m, 2H), 3.08 (s, 1H), 2.76 (dd, J = 5.3, 8.8 Hz, 1H), 2.54 (d, J = 15.8 Hz, 1H), 2.31 (d, J = 4.6 Hz, 2H), 1.86 (s, 3H), 1.58 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) 171.0, 147.0, 139.4, 132.9, 132.4, 130.4, 129.7, 128.3, 125.6, 123.9, 112.2, 82.6, 81.9, 80.7, 61.3, 55.5, 39.1, 27.7, 21.4, 17.7, 14.2. IR (film) 3536, 1743 cm^{-1}. HRMS Calcd for $C_{21}H_{25}BrO_4Na^{+}$: 443.0834, found 443.0834.

Isobenzofuran 5b. Prepared as for **5a.** Isobenzofuran **5b** was obtained as a white solid in 73% yield (0.56 g, 1.34 mmol) from 0.77g (1.83 mmol) of glycolate **4b**. mp 131-136 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 7.1 Hz, 1H), 7.08

(d, *J* = 7.7 Hz, 1H), 5.70 (s, 1H), 5.60 (s, 1H), 4.64 (s, 1H), 4.30 (d, *J* = 4.0 Hz, 2H), 4.20 (d, *J* = 15.9 Hz, 2H), 3.12 (s, 1H), 2.74 – 2.58 (m, 1H), 2.46 – 2.29 (m, 1H), 2.00-1.77 (m, 6H), 1.61 (s, 1H), 1.42 – 1.26 (m, 7H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.41, 145.68, 141.05, 133.43, 130.42, 130.26, 128.94, 125.89, 125.72, 121.90, 111.83, 83.50, 83.46, 82.88, 77.35, 77.03, 76.71, 61.53, 53.84, 40.35, 31.67, 19.40, 18.00, 14.15. Anal. ($C_{21}H_{25}BrO_4$) C 60.13, H 6.04.

Isobenzofuran 5c. Prepared as for **5a.** Isobenzofuran **5c** was obtained as a pale yellow oil in 77% yield (2.61 g, 6.34 mmol) from 3.39 g (8.24 mmol) of glycolate **4c**. ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.22 (dd, J = 1.7, 7.8 Hz, 1H), 7.38 (dd, J = 1.7, 7.9 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 5.70 (s, 1H), 5.30 (d, J = 8.2 Hz, 1H), 4.80 (s, 3H), 4.42 (s, 1H), 4.25 (qd, J = 2.7, 7.1 Hz, 2H), 3.06 (s, 1H), 2.74 – 2.59 (m, 1H), 2.27 (s, 3H), 1.79 (s, 3H), 1.53 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C-NMR (67 MHz, $CDCl_3$) 171.1, 146.7, 140.8, 132.9, 132.6, 131.5, 130.1, 128.4, 128.1, 125.7, 112.5, 81.9, 80.9, 80.7, 61.4, 55.4, 39.7, 27.7, 21.3, 17.7, 14.2.

Isobenzofuran 5d. Prepared as for **5a.** Isobenzofuran **5d** was obtained as a pale yellow oil in 74% yield (3.50 g, 8.51 mmol) from 4.73 g (11.5 mmol) of glycolate **4d**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, J = 9.1, 1H), 7.41 – 7.34 (m, 2H), 5.77 (s, 1H), 5.26 (d, J = 8.3 Hz, 1H), 4.85 (s, 2H), 4.46 (s, 1H), 4.31 (ddd, J = 5.6, 8.3, 16.5 Hz, 3H), 3.16 (s, 1H), 2.69 (dd, J = 5.9, 8.3 Hz, 1H), 2.36 (m, 4H), 1.85 (d, J = 1.5 Hz, 4H), 1.58 (d, J = 6.7 Hz, 9H), 1.42 – 1.21 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.10, 146.70, 136.85, 134.34, 132.78, 131.21, 128.77, 128.06, 126.96, 125.72, 112.41, 81.72, 80.77, 79.71, 77.33, 77.21, 77.01, 76.70, 61.46, 59.84, 55.17, 39.68, 27.73, 21.23, 17.68, 14.13.

Isobenzofuran 5e. Prepared as for **5a.** Isobenzofuran **5e** was obtained in 59 % yield (0.22 g, 0.59 mmol) as an oil from 0.41 g (1.08 mmol) of glycolate **4e**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.2 Hz, 1H), 7.86 (t, J = 9.1 Hz, 2H), 7.52 (dt, J = 6.9, 14.5 Hz, 3H), 5.76 (s, 1H), 5.62 (d, J = 7.2 Hz, 1H), 4.91 (s, 1H), 4.83 (s, 1H), 4.59 (s, 1H), 3.85 (s, 3H), 3.26 (s, 1H), 3.03 (t, J = 7.2 Hz, 1H), 2.39 (dd, J = 6.5, 12.7 Hz, 1H), 2.29 (s, 2H), 1.87 (s, 3H), 1.55 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 172.29, 146.85, 135.72, 133.92, 133.46, 131.85, 128.99, 128.86, 126.11, 125.74, 125.63, 125.60, 125.52, 123.60, 113.03, 82.77, 81.51, 80.99, 53.68, 52.36, 42.04, 28.22, 20.68, 17.79. Anal. ($C_{24}H_{26}O_4$) C 76.09, H 6.95.

Isobenzofuran 5f. Prepared as for **5a.** Isobenzofuran **5f** was obtained in 81 % yield (0.30 g, 0.90 mmol) as a solid from 0.36 g (1.10 mmol) of glycolate **4f**; mp 67-69 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.53 (d, J = 4.0 Hz, 1H), 7.64 (td, J = 1.8, 7.7 Hz, 1H), 7.19 (ddd, J = 3.6, 6.0, 7.8 Hz, 2H), 5.58 (d, J = 1.5 Hz, 1H), 4.88 (s, 1H), 4.82 (s, 1H), 4.55 (s, 1H), 3.69 (s, 3H), 2.55 – 2.32 (m, 2H), 2.07 (d, J = 3.1, 2H), 1.89 – 1.73 (m, 3H), 1.50 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 170.36, 159.63, 149.19, 146.18, 137.80, 133.65, 125.22, 123.42, 123.23, 113.50, 87.12, 84.83, 82.53, 54.58, 52.07, 46.56, 30.98, 19.36, 17.95. Anal. ($C_{19}H_{23}NO_4$) C 68.98, H 6.86.

Methyl ester 5a.i. To a solution of ethyl ester **5a (**0.10 g, 0.24 mmol) in 15 mL of methanol was added 0.04 g (0.28 mmol, 1.2 eq) of K_2CO_3 at room temperature. The reaction mixture was stirred at rt until no starting material was observed by TLC (ca. 20 min). The mixture was then and diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were then washed with brine (50 mL), extracted with CH_2Cl_2 (40 mL), dried over

$MgSO_4$, and concentrated in vacuo. The crude product was filtered through a short silica gel column (EtOAc/Hexanes 1:1) to deliver methyl ester **5a.i** as a colorless oil in 97 % yield (94.8 mg, 23.3 mmol). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.30 (dd, J = 1.7, 7.9 Hz, 1H), 7.54 (dd, J = 1.2, 8.0 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.24 – 7.15 (m, 1H), 5.79 (s, 1H), 5.25 (d, J = 9.2 Hz, 1H), 4.90 – 4.81 (m, 2H), 4.51 (s, 1H), 3.85 (s, 3H), 2.93 (s, 1H), 2.77 (dd, J = 4.9, 9.2 Hz, 1H), 2.66 – 2.51 (m, 1H), 2.32 (d, J = 15.0 Hz, 2H), 1.88 (d, J = 1.6 Hz, 3H), 1.58 (d, J = 5.8 Hz, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 171.54, 147.20, 139.28, 132.82, 132.46, 130.27, 129.79, 128.39, 125.67, 123.84, 112.00, 82.51, 81.76, 80.50, 77.47, 77.05, 76.62, 73.47, 55.22, 52.22, 38.31, 27.49, 21.61, 17.67. Anal. ($C_{20}H_{23}BrO_4$) C 59.16, H 5.80.

Cyclopropylmethyl ester 5a.ii. A mixture of ethyl ester **5a** (0.14 g, 0.33 mmol), cyclopropyl methanol (2.66 mL, 33.22 mmol, 100 eq), and Bu_2SnO (0.06 g, 0.24 mmol, 0.75eq) was sealed in an 8 mL microwave reaction vessel. The mixture was irradiated for 30 min. at 150 °C and 300 W with continuous stirring. The mixture was then cooled to rt, diluted with ethyl acetate (10 mL), washed with sat. $NaHCO_3$ (30 mL) and extracted with EtOAc (3x20 mL). The combined organic extracts were then washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified via flash chromatography over silica gel (10:90 EtOAc/hexanes) to deliver ester **5a.ii** as a colorless oil in 84% yield (0.125 g, 0.28 mmol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (dd, J = 1.7, 7.9 Hz, 1H), 7.53 (dd, J = 1.2, 8.0 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.24 – 7.11 (m, 1H), 5.78 (s, 1H), 5.26 (d, J = 8.6 Hz, 1H), 4.85 (s, 2H), 4.49 (s, 1H), 4.16 – 3.99 (m, 2H), 3.16 (s, 1H), 2.77 (dd, J = 5.7, 8.6 Hz, 1H), 2.53 (d, J = 15.6 Hz, 1H), 2.30 (d, J = 10.1 Hz, 2H), 2.19 (s, 1H), 1.88 (d, J = 1.4 Hz, 3H), 1.59 (d, J = 6.8 Hz, 3H), 1.30 – 1.13 (m, 2H), 0.62 (dt, J = 5.4, 5.9 Hz, 2H), 0.35 (q, J = 4.7 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) 171.0, 146.8, 139.4, 132.9, 132.4, 130.4, 129.7, 128.3, 125.7, 112.2, 82.7, 81.9, 80.7, 70.2, 55.5, 39.5, 27.8, 21.27, 17.7, 9.6, 3.4.

Cyclopentylmethyl ester 5a.iii. Prepared as for **5a.ii.** Ester **5a.iii** was obtained in 91% yield as an oil (0.11 g, 0.24 mmol) from 0.11 g (0.26 mmol) of ester **5a.** ^{1}H-NMR (270 MHz, $CDCl_3$) 8.29 (d, J = 6.2 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.19 (dd, J = 4.5, 10.8 Hz, 1H) 5.79 (s, 1H), 5.25 (d, J = 9.0 Hz, 1H), 4.85 (s, 2H), 4.49 (s, 1H), 4.17 – 4.04 (m, 2H), 2.99 (s, 1H), 2.76 (dd, J = 5.0, 9.1 Hz, 1H), 2.64-2.52 (m, 1H), 2.32 (d, J = 7.3 Hz, 3H), 1.89-1.74 (m, 6H), 1.68-1.54 (m, 8H), 1.39-1.26 (m, 3H). ^{13}C-NMR (67 MHz, $CDCl_3$) 171.1, 147.1, 139.5, 132.9, 132.4, 130.3, 129.7, 128.3, 125.5, 123.8, 112.0, 82.5, 81.9, 80.6, 69.3, 55.5, 38.5, 38.3, 29.3, 27.5, 25.4, 21.5, 17.6.

Acid 5a.iv. To a solution of 3:2:1 THF/H_2O/MeOH and ester **5a** (0.18 g, 0.43 mmol) was added 0.02 g (0.85 mmol, 2 eq) of LiOH at rt. The reaction mixture was allowed to stir at rt until no starting material was observed by TLC (~1.5 h), then acidified to pH 2 with 3N HCl. The mixture was diluted with CH_2Cl_2 (30 mL), extracted with CH_2Cl_2 (3 x 30 mL), washed with brine (40 mL), dried over $MgSO_4$ and concentrated in vacuo to yield a yellow foam. The crude material was eluted through a plug of silica gel (1:1 EtOAc/hexanes) to deliver acid **5a.iv** as a white solid in 95% yield (0.16 g, 0.41 mmol); mp 52-56 °C. ^{1}H-NMR (270 MHz, $CDCl_3$) δ 8.14- 8.09 (d, J=7.86 Hz, 1H), 7.59-7.54 (d, J=8.03 Hz, 1H), 7.47-7.40 (t, J=7.55 Hz, 1H), 7.25-7.18 (dd, J=4.47, 10.85 Hz, 1H), 5.81 (s, 1H), 5.28 (s, 1H), 5.25 (d, J=8.87 Hz, 1H), 4.85 (s, 2H), 4.51 (s, 1H), 2.79-2.72 (dd, J=5.18, 8.84 Hz, 1H), 2.60-2.47 (m, 1H), 2.35-2.24 (m, 2H), 1.94 (s,

3H), 1.59 (s, 3H). ^{13}C-NMR (67 MHz, $CDCl_3$) 146.6, 138.6, 132.9, 132.7, 130.0, 129., 128.4, 125.9, 124.1, 112.4, 82.7, 55.6, 27.6, 21.4, 17.7. IR (film) 3450, 1638 cm^{-1}.

Diene 6a. Preparation was carried out as above for **5a** from glycolate **4a** (3.5 g, 8.31 mmol), but the reaction mixture was allowed to stir for 5 minutes before quenching with HOAc. Purification of the crude product via flash chromatography over silica gel (10:90 EtOAc/hexanes) delivered diene **6a** as a yellow oil in 15 % yield (0.42 g, 1.27 mmol) as well as isobenzofuran **5a** in 41% yield (1.43 g, 3.41 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 6.5, 1H), 7.34 – 7.08 (m, 3H), 6.62 (s, 1H), 4.95 (s, 1H), 4.73 (s, 1H), 3.62 (s, 1H), 2.74 – 2.48 (m, 1H), 2.19 (s, 1H), 1.95 – 1.82 (m, 2H), 1.77 (s, 2H), 1.59 (s, 1H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 189.40, 145.37, 141.23, 139.35, 136.66, 136.31, 134.83, 132.82, 129.65, 129.62, 127.04, 125.00, 114.21, 77.35, 77.03, 76.71, 43.88, 29.72, 29.18, 21.78, 16.34.

Diene 6e. Prepared as for **6a.** Diene **6e** was obtained in 33% yield (0.10 g, 0.33 mmol) as a solid from 0.41 g (1.08 mmol) of glycolate **4e**; ; mp 113-115 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.2 Hz, 1H), 7.86 (dd, J = 8.2, 10.1 Hz, 2H), 7.61 – 7.42 (m, 3H), 5.76 (s, 1H), 5.62 (d, J = 7.2 Hz, 1H), 4.87 (d, J = 26.1 Hz, 2H), 4.59 (s, 1H), 3.83 (s, 3H), 3.26 (s, 1H), 3.03 (t, J = 7.2 Hz, 1H), 2.39 (dd, J = 6.5, 12.7 Hz, 1H), 2.34 – 2.21 (m, 2H), 1.87 (s, 3H), 1.55 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 189.94, 146.02, 141.49, 140.18, 136.87, 133.88, 133.65, 133.24, 132.32, 128.97, 128.70, 126.58, 126.32, 126.02, 125.37, 124.92, 114.15, 44.28, 29.57, 22.06, 16.59. Anal: ($C_{22}H_{22}O$) C 87.78, H 7.26.

Diene 6g. Prepared as for **6a.** Diene **6g** was obtained in 41% yield (0.05 g, 0.19 mmol) as a solid from 0.15 g (0.46 mmol) of glycolate **4g**; mp 71-73 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 1.6 Hz, 1H), 7.42 (s, 1H), 6.70 – 6.61 (m, 1H), 6.58 (d, J = 3.4 Hz, 1H), 6.47 (dd, J = 1.8, 3.4 Hz, 1H), 4.87 – 4.74 (m, 1H), 4.65 (s, 1H), 4.37 (d, J = 6.1 Hz, 1H), 2.77 – 2.45 (m, 2H), 1.86 (s, 3H), 1.81 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 188.77, 152.31, 145.57, 144.27, 141.82, 136.68, 134.43, 122.87, 116.05, 112.65, 112.24, 43.29, 28.94, 22.11, 16.77. Anal. ($C_{16}H_{18}O_2$) C 79.23, H 7.24.

Diene 6h. Prepared as for **10a.** Diene **6h** was obtained in 45% yield (0.07 g, 0.26 mmol) as an oil from 0.20 g (0.58 mmol) of glycolate **4h**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.33 (dt, J = 4.5, 14.2 Hz, 2H), 7.12 (dd, J = 8.3, 16.2 Hz, 2H), 6.67 – 6.59 (m, 1H), 4.96 (s, 1H), 4.74 (s, 1H), 3.75 (s, 1H), 2.72 – 2.50 (m, 2H), 1.90 (s, 3H), 1.81 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 189.45, 162.81,159.50, 145.36, 141.33, 140.24, 136.68, 130.42, 130.31, 129.93, 129.90, 128.54, 128.49, 124.03, 123.98, 123.86, 115.88, 115.59, 114.30, 44.28, 29.24, 21.92, 16.50. Anal. ($C_{18}H_{19}FO$) C 79.58, H 6.72.

Enone 8a. Isobenzofuran **5a** (0.37 g, 0.87 mmol) in anhydrous CH_2Cl_2 (9.0 mL) was added to a mixture of finely ground pyridinium chlorochromate (2.00 g, 8.70 mmol) and silica gel (2.00 g) in dry CH_2Cl_2 (20.0 mL) at rt. The reaction mixture was stirred at rt for 24 h. The crude solution was then filtered through a short silica gel column with ether (100 mL) and concentrated in vacuo. The dark brown residue was purified via flash chromatography over silica gel (15/85, EtOAc/hexanes) to deliver enone **6a** as a white solid in 55 % yield (0.20 g, 0.48 mmol) mp 126-127 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 – 7.98 (m, 1H), 7.49 (dd, *J* = 1.0, 8.1 Hz, 1H), 7.41

(t, *J* = 7.6 Hz, 1H), 7.18 (td, *J* = 1.7, 8.0 Hz, 1H), 5.28 (s, 1H), 5.21 (d, *J* = 10.0 Hz, 1H), 4.74 (s, 1H), 4.47 (s, 1H), 4.40 – 4.25 (m, 2H), 3.26 (t, *J* = 10.3 Hz, 1H), 2.93 – 2.70 (m, 1H), 2.54 – 2.30 (m, 2H), 2.01 – 1.87 (m, 3H), 1.58 (d, *J* = 8.2 Hz, 1H), 1.36 (q, *J* = 7.1 Hz, 3H), 1.27 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) 198.0, 171.0, 146.0, 142.0, 138.0, 132.9, 130.4, 130.0, 129.7, 128.3, 125.6, 114.2, 85.2, 78.5, 62.3, 51.5, 47.5, 42.0, 18.5, 14.7, 12.2. IR (film) 1743, 1674 cm^{-1}. HRMS Calcd for $C_{21}H_{24}BrO_4^+$: 419.0858, found 419.0836. Anal. ($C_{21}H_{23}BrO_4$) C 60.31, H 5.47.

Enone 8b. Prepared as for **8a.** Enone **8b** was obtained as a white foam in 54 % yield (0.07 g, 0.16 mmol) from 0.12g (0.29 mmol) of isobenzofuran **5b**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 8.8 Hz, 1H), 7.18 (dd, J = 5.0, 10.5 Hz, 2H), 6.98 (d, J = 7.8 Hz, 1H), 5.61 (d, J = 8.9 Hz, 1H), 5.56 (s, 1H), 4.92 (s, 1H), 4.77 (s, 1H), 4.30 (q, J = 7.1 Hz, 2H), 3.70 (s, 1H), 2.50 (dd, J = 3.9, 16.3 Hz, 1H), 2.23 (dd, J = 13.9, 16.3 Hz, 1H), 1.98 (d, J = 2.0 Hz, 3H), 1.93 – 1.80 (m, 1H), 1.61 (s, 1H), 1.53 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H).^{13}C-NMR (75 MHz, $CDCl_3$) 183.6, 156.0, 142.3, 132.6, 129.9, 127.9, 113.9, 85.0, 78.1, 66.6, 62.0, 58.0, 46.7, 42.4, 22.7, 18.02, 14.2, 11.4.

Enone 8c. Prepared as for **8a.** Enone **8c** was obtained as a white solid in 56% yield (0.22 g, 0.54 mmol) from 0.40 g (0.97 mmol) of isobenzofuran **5c**; mp 41-45 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.93 (dd, J = 1.6, 7.8, 1H), 7.38 (dd, J = 1.7, 7.9, 1H), 7.25 (t, J = 7.9, 1H), 5.31 – 5.10 (m, 2H), 4.61 (s, 1H), 4.47 – 4.36 (m, 1H), 4.25 (qd, J = 1.3, 7.1, 2H), 3.14 (d, J = 10.4, 1H), 2.84 – 2.63 (m, 1H), 2.48 – 2.21 (m, 2H), 1.86 (dd, J = 0.9, 2.5, 3H), 1.30 (t, J = 7.1, 3H), 1.21 (s, 4H). ^{13}C-NMR (67 MHz, $CDCl_3$) 197.5, 169.8, 154.7, 142.1, 139.0, 132.5, 129.9, 127.4, 113.4, 82.6, 62.0, 50.4, 46.9, 42.3, 18.2, 14.1, 11.1.

Enone 8d. Prepared as for **8a.** Enone **8d** was obtained as a white solid in 67% yield (0.11 g, 0.27 mmol) from 0.17 g (0.41 mmol) of isobenzofuran **5d**; mp 96-100 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.93 (dd, J = 1.6, 7.8 Hz, 1H), 7.38 (dd, J = 1.7, 7.9 Hz, 1H), 7.25 (t, J = 7.9 Hz, 1H), 5.31 – 5.10 (m, 2H), 4.61 (s, 1H), 4.47 – 4.36 (m, 1H), 4.25 (qd, J = 1.3, 7.1 Hz, 2H), 3.14 (d, J = 10.4 Hz, 1H), 2.84 – 2.63 (m, 1H), 2.48 – 2.21 (m, 2H), 1.86 (dd, J = 0.9, 2.5 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H), 1.21 (s, 3H). ^{13}C-NMR (67 MHz, $CDCl_3$) 198.1, 169.8, 155.5, 142.4, 135.6, 134.7, 130.5, 130.4, 129.0, 127.8, 114.0, 82.0, 62.2, 50.2, 46.7, 42.3, 18.2, 14.3, 11.5.

Tosylhydrazone 9a. HOAc (0.01 g, 0.16 mmol) was added to a solution of enone **8a** (0.10 g, 0.24 mmol) and tosylhydrazide (0.06 g, 0.31 mmol) in CH_2Cl_2 (2.20 mL). The reaction mixture stirred at rt for 24 h, then was washed with water (5.00 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified via flash chromatography on silica gel (80:20, hexanes/EtOAc) to afford tosylhydrazone **9a** as white solid in 92 % yield (0.13 g, 0.22 mmol); mp 162-165 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.79 (m, 3H), 7.46 (d, J = 9.5 Hz, 2H), 7.36 (t, J = 8.7 Hz, 3H), 7.14 (t, J = 7.7 Hz, 1H), 5.28 (s, 1H), 5.07 (d, J = 9.8 Hz, 1H), 4.70 (s, 1H), 4.48 (s, 1H), 4.25 (q, J = 7.1 Hz, 2H), 2.99 (s, 1H), 2.58 – 2.34 (m, 6H), 2.10 – 1.85 (m, 4H), 1.34 (t, J = 7.1 Hz, 3H), 1.22 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.44, 153.31, 144.28, 143.92, 142.66, 138.39, 135.01, 132.51, 129.73, 129.69, 129.49, 128.25, 127.80, 127.78, 124.74, 114.17, 85.49, 78.23, 77.35, 77.04, 76.72, 61.70, 49.10, 44.80, 29.37, 21.66, 18.00, 14.18, 13.07. IR (film) 3210, 3070, 2980, 2919, 2256, 1739 cm^{-1}. HRMS Calcd for $C_{28}H_{31}BrN_2O_5S^+$: 587.1215, found: 587.1201.

Ester 10a. Catecholborane (0.10 mL, 0.80 mmol)) was added to a solution of tosylhydrazone **9a** (0.40 g, 0.70 mmol) in $CHCl_3$ (3.00 mL) at 0 °C. The reaction mixture stirred at 0 °C for 1 h, then $NaOAc.3H_2O$ (0.19 g, 1.30 mmol) was added in one portion. The reaction mixture was maintained for 1 h at 0 °C, diluted with $CHCl_3$ (1.80 mL), and heated under reflux for 12 h. The mixture was then cooled to rt and filtered through a pad of Celite. The filtrate was concentrated in vacuo and the residue was purified via flash chromatography over silica gel (90:10, hexanes/ EtOAc) to afford ester **10a** as white solid in 68 % yield (0.17 g, 0.48 mmol); mp 37-40 °C; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 7.97 (d, J = 6.2 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 7.0 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 5.59 (s, 1H), 5.34 (d, J = 6.4 Hz, 1H), 4.79 (s, 2H), 4.38 (d, J = 6.4 Hz, 1H), 4.25 (dd, J = 4.9, 7.1 Hz, 2H), 3.01 (s, 1H), 2.37 (m, 3H), 2.21 – 2.04 (m, 1H), 1.73 (s, 3H), 1.60 (s, 4H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C-NMR (67 MHz, $CDCl_3$) δ 173.01, 146.94, 140.85, 132.70, 130.21, 129.58, 129.37, 128.04, 123.25, 123.10, 112.16, 83.50, 81.30, 77.56, 77.09, 76.62, 61.33, 49.14, 47.31, 39.39, 28.04, 22.08, 21.00, 14.22.

Biological Assays

KB3 Assays. All stock solutions of compounds were made at 10 mM in dimethyl sulfoxide (DMSO). DMSO and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) were from Sigma Chemical Co. (St. Louis, MO). Cell culture reagents were obtained from Life Technologies (Carlsbad, CA).

Cell Culture. The KB-3 human carcinoma cell line was maintained in monolayer culture at 37°C and 5% CO_2 in Dulbecco's Modified Eagle's Medium, supplemented with 10% fetal bovine serum, 2 mM L-glutamine, 50 units/mL penicillin, and 50 μg/mL streptomycin.

MTT colorimetric assay. Inhibition of cell proliferation was assessed by the MTT colorimetric assay. First described by Mosmann,[1] this assay is based on the ability of a mitochondrial dehydrogenase enzyme from viable cells to cleave the tetrazolium rings of the pale yellow MTT and form a dark blue formazan crystal product which is largely impermeable to cell membranes, thus resulting in its accumulation within healthy cells. Solubilization of the cells by the addition of solvent results in the liberation of the crystals which are solubilized. The level of the formazan product created is directly proportional to the number of living cells.

KB-3 cells (2000/well) were plated in 96-well dishes, and were treated after 24 h with different concentrations (0.1 nM -100 μM) of the compound being assayed. The final concentration of DMSO did not exceed 1%, and controls received vehicle alone. MTT assay was performed after 96 h as described.[2,3] Cells were incubated with 50 μg/well/0.2 mL MTT for 4 h at 37°C, the media was removed and the formazan crystals were dissolved in 150 μL of DMSO. The resulting color change was measured via spectrophotometry at a wavelength of 570 nm using an ELx800™ Absorbance Microplate Reader (Bio Tek Instruments, Inc., Winooski, VT). Values are the means of triplicate assays and are expressed as mean relative to untreated controls. IC_{50}

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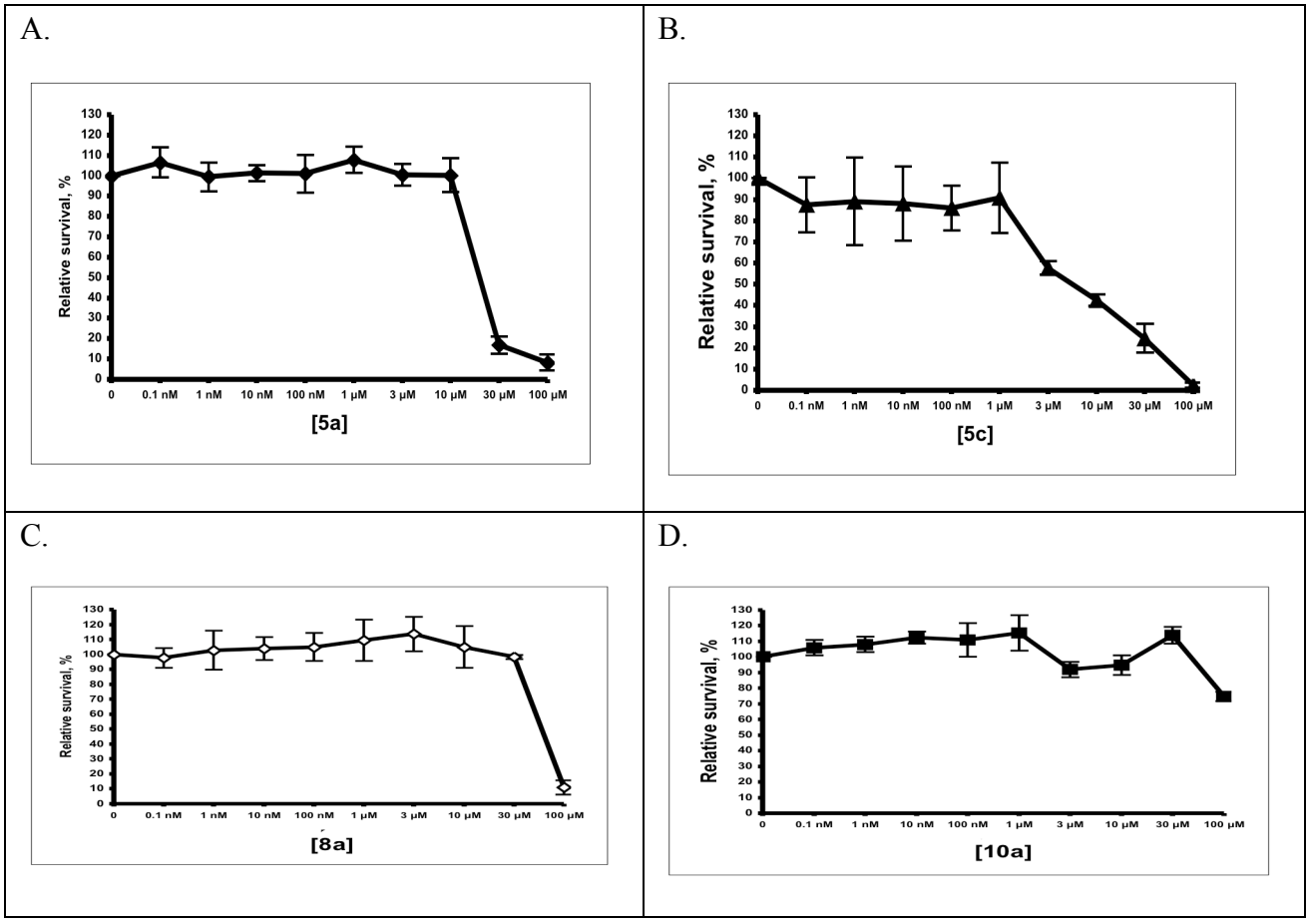
[1] Mosmann T. *J. Immunol. Methods* **1983**, *65*, 55-63.

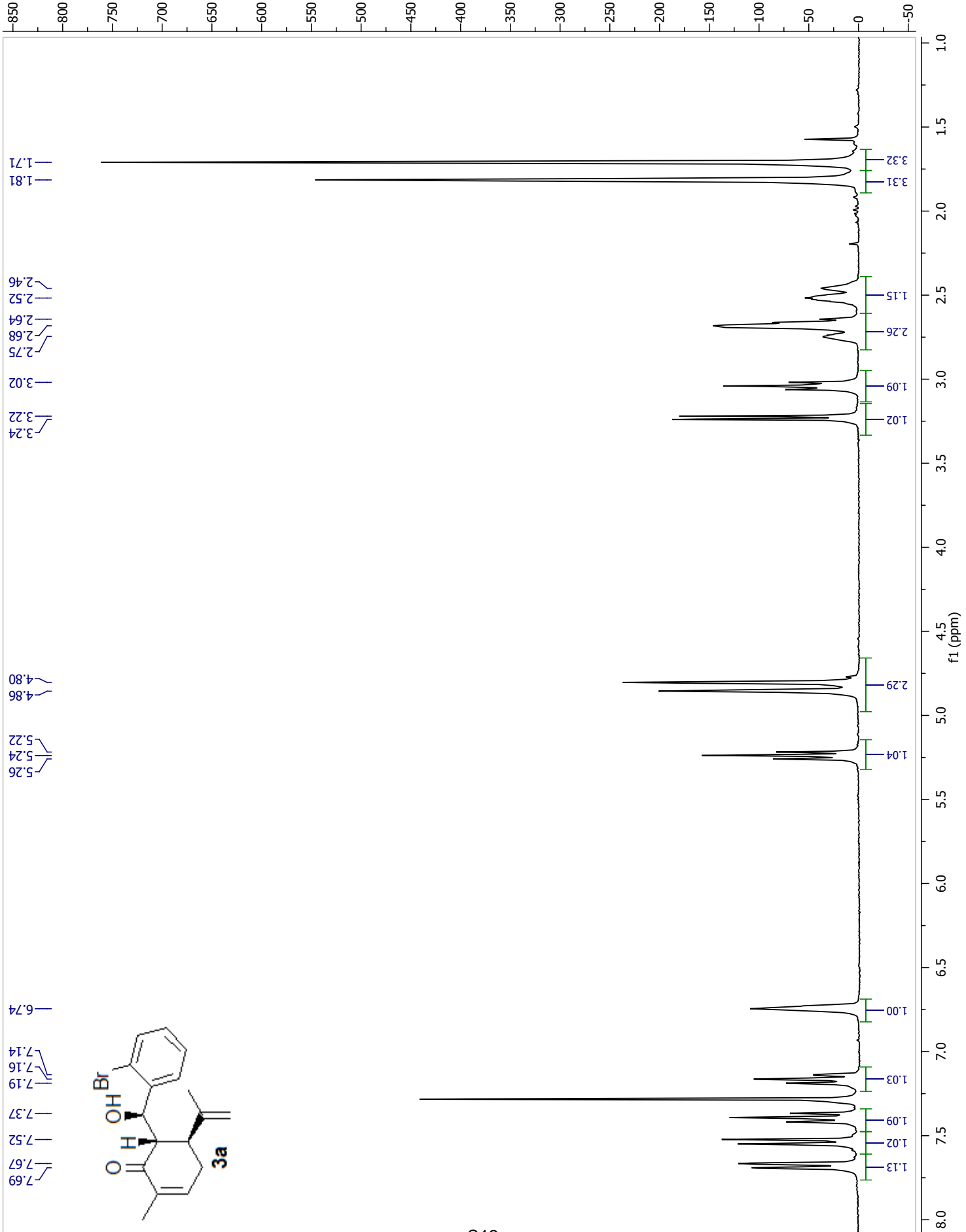
[2] Fan, M.; Du, L.; Stone, A. A.; Gilbert K. M.; Chambers, T. C. *Cancer Res*. **2000**, *60*, 6403-6407.

[3] Alley, M. C.; Scudiero, D. A.; Monks A.; Hursey, M. L.; Czerwinski, M. J.; Fine, D. L.; Abbott, B. J.; Mayo, J. G.; Shoemaker, R. H.; Boyd M. R. *Cancer Res*. **1988**, *48*, 589-601

is the concentration that reduced survival to 50% of the control (no drug). Representative concentrations curves are shown below (Figure).

Figure. Concentration curves of Sclerologs **5a**, **5c**, **8a** and **10a**.

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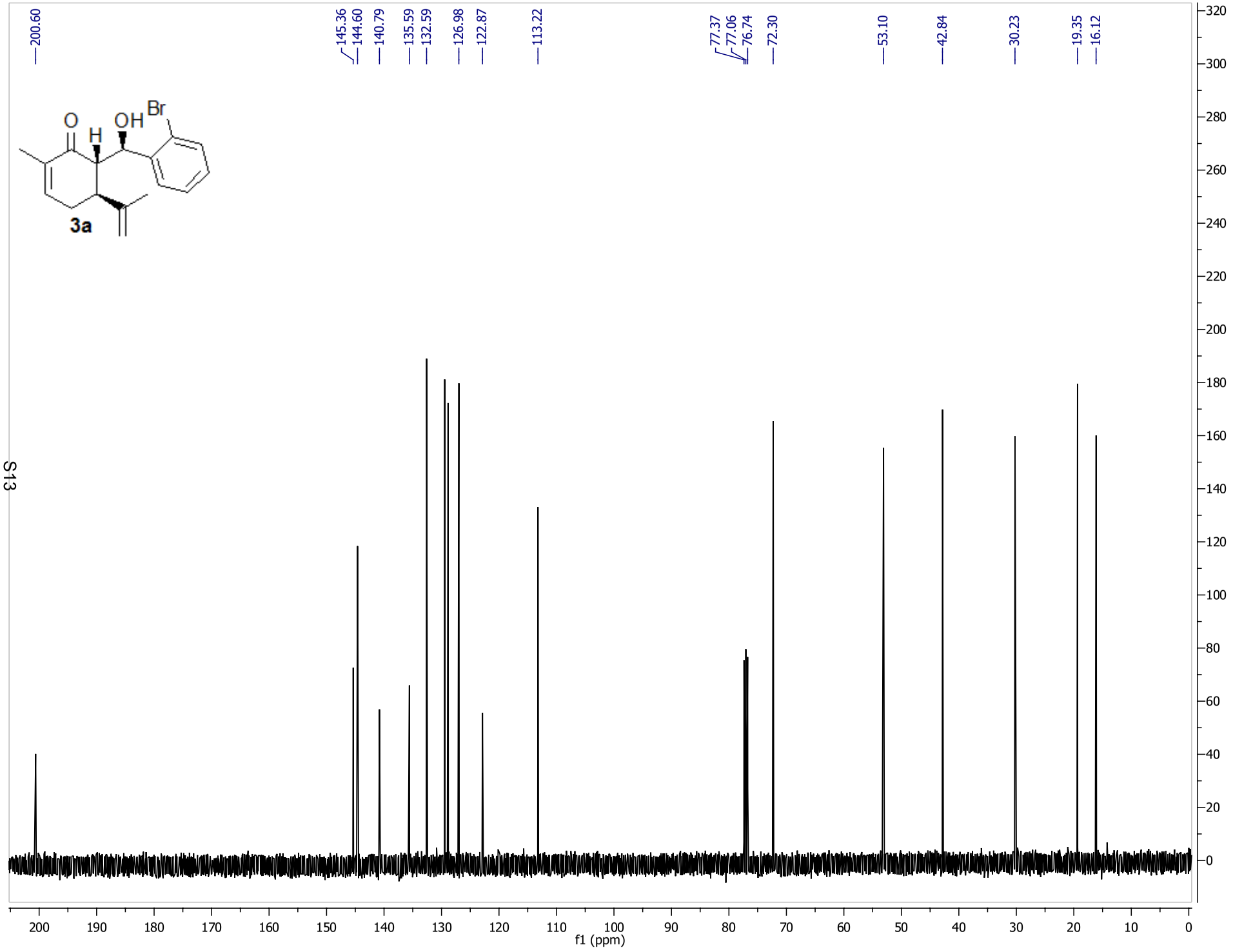
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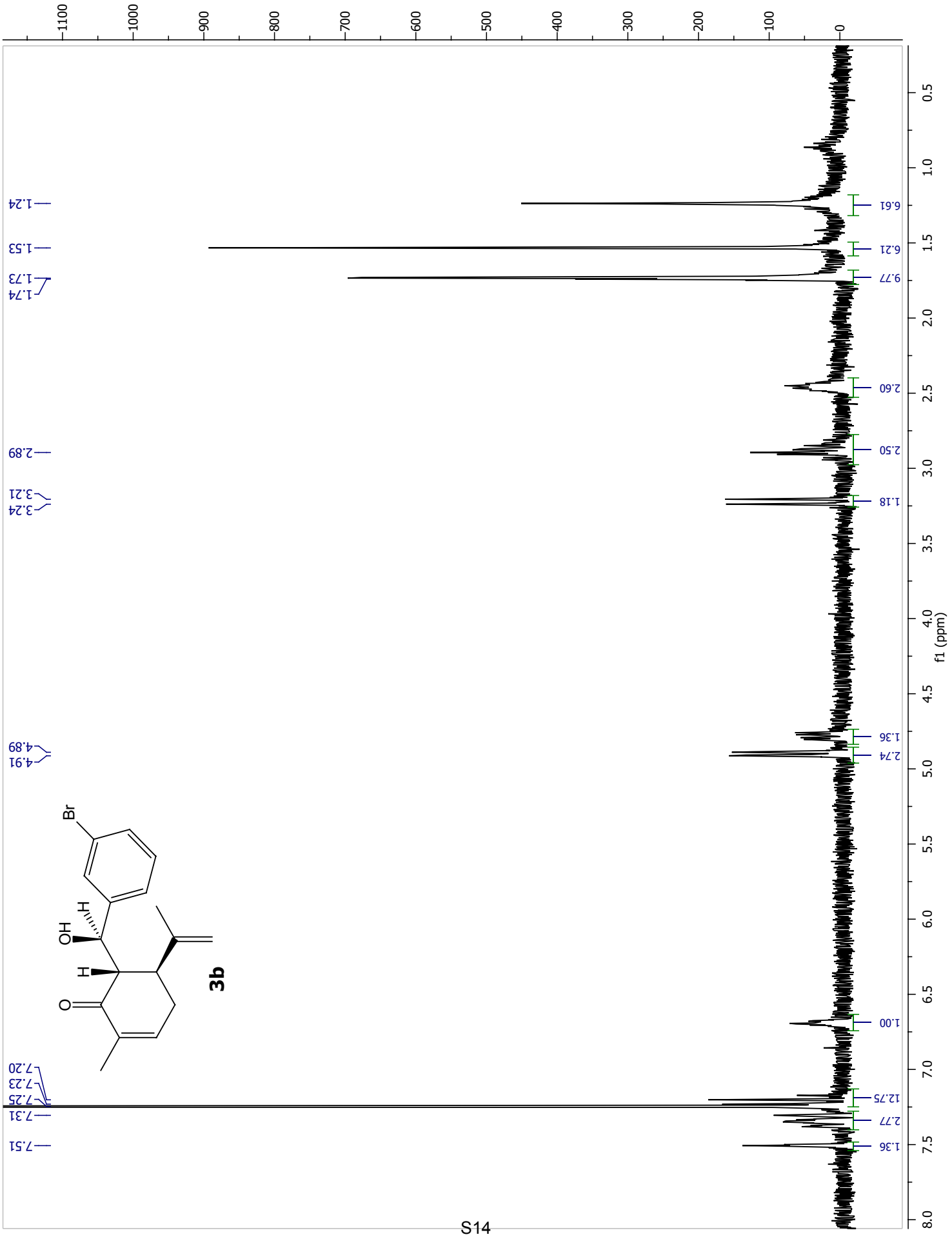
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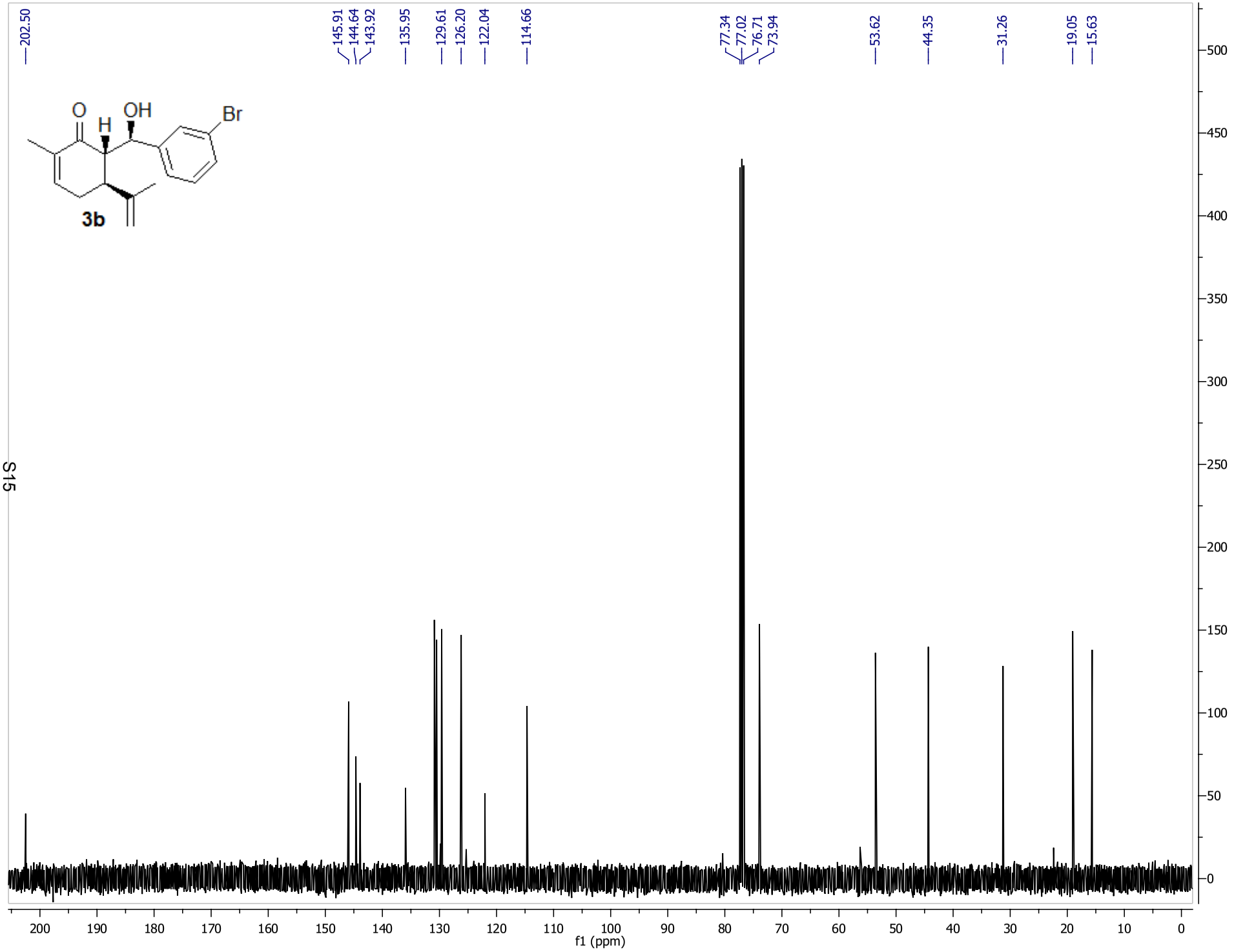
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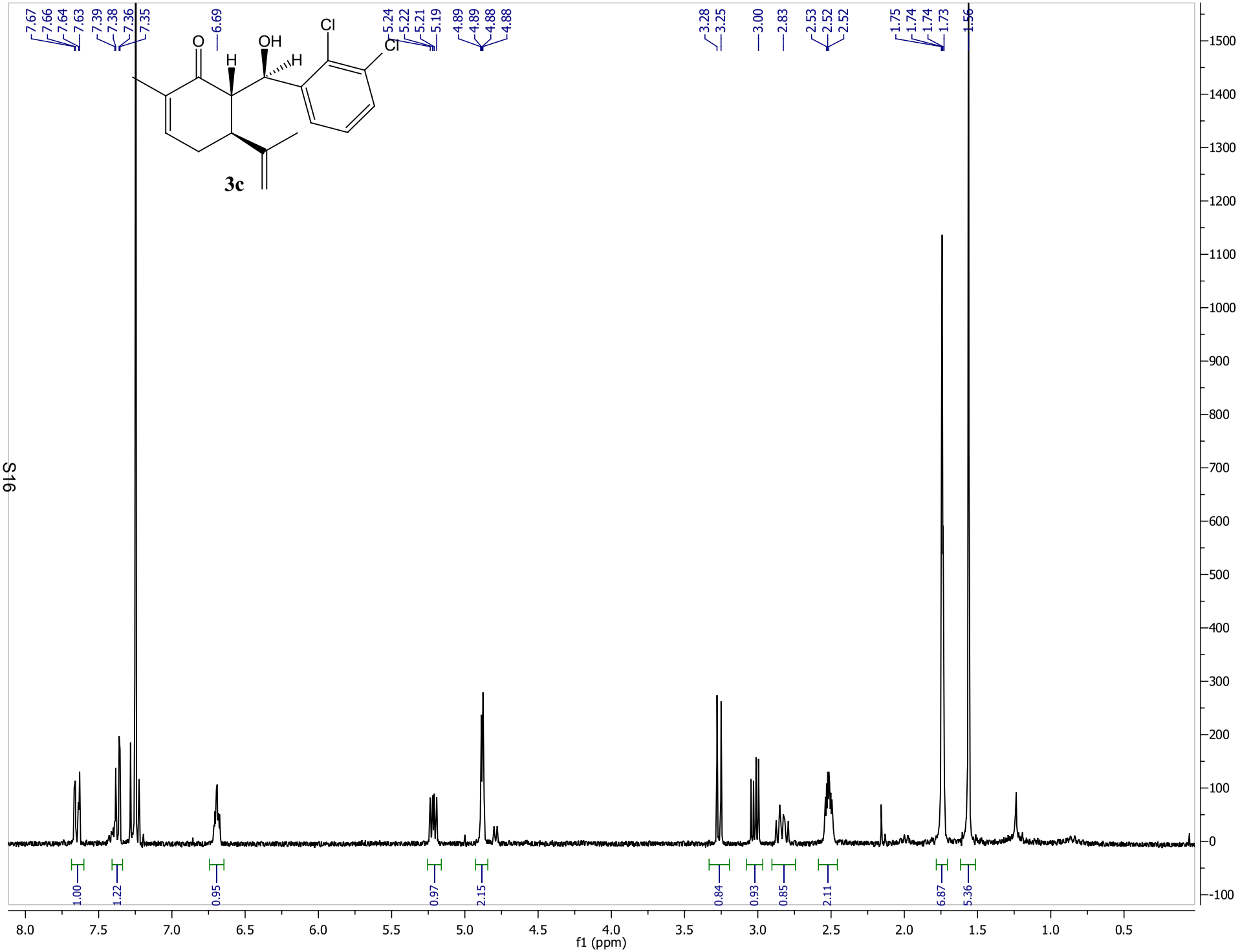
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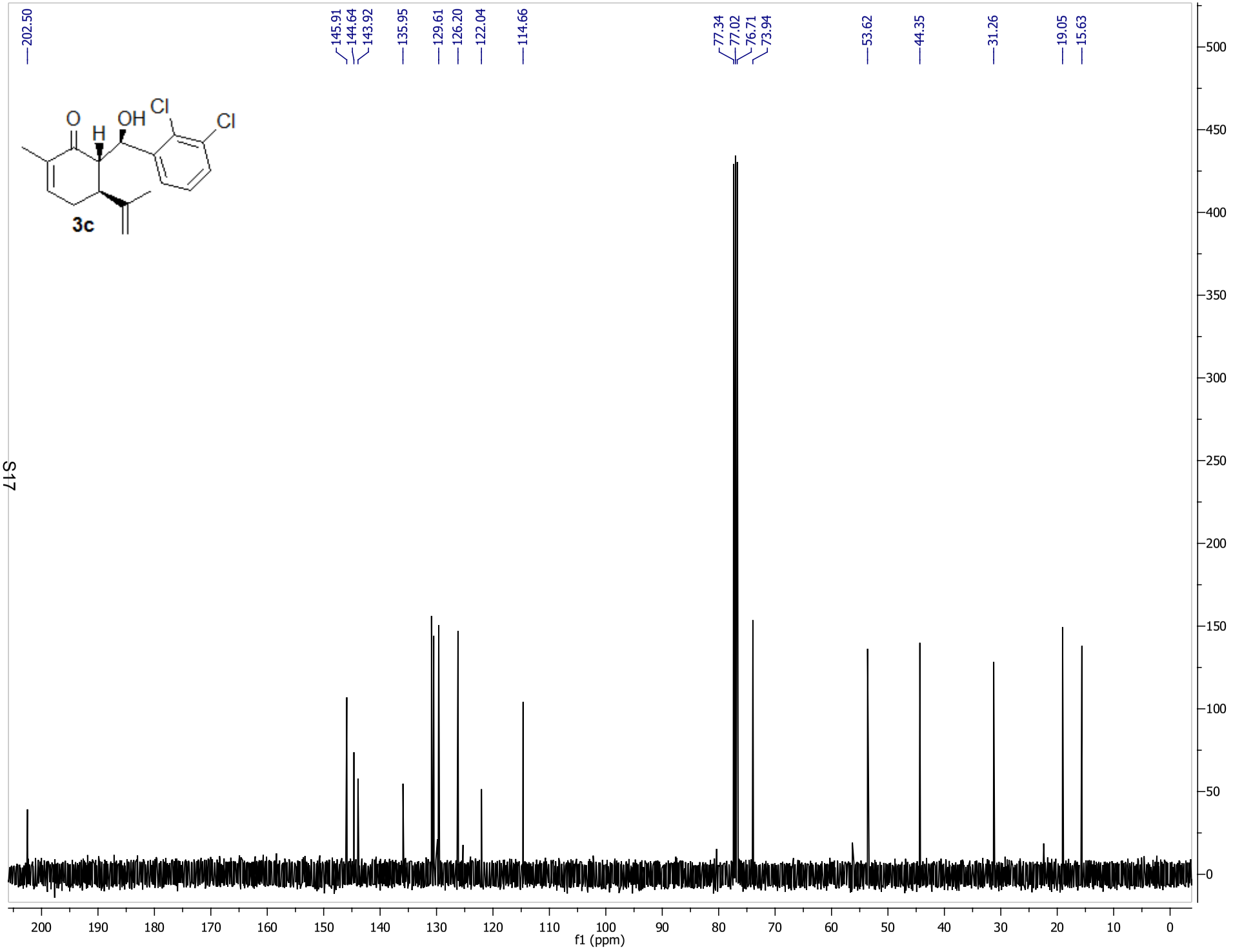
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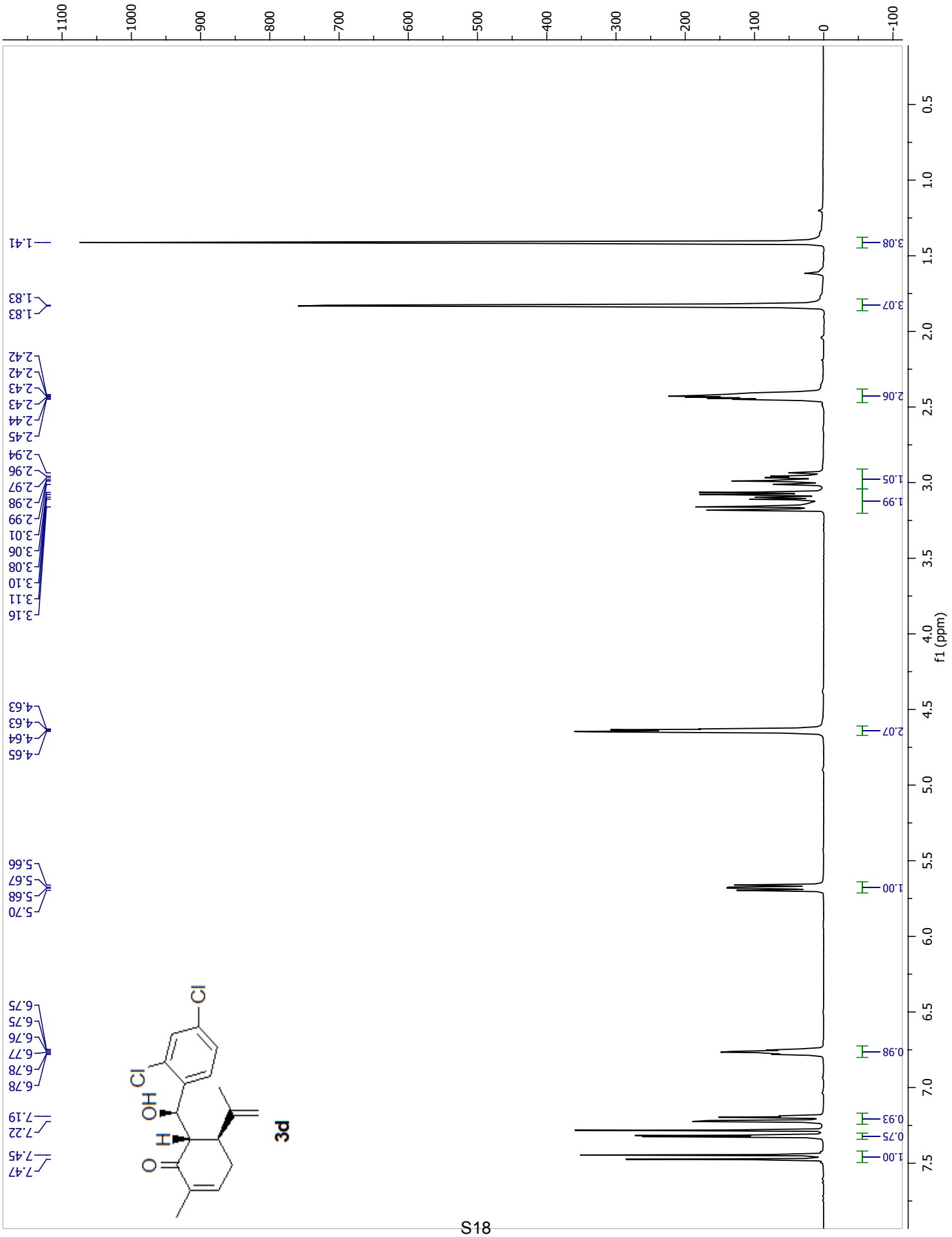
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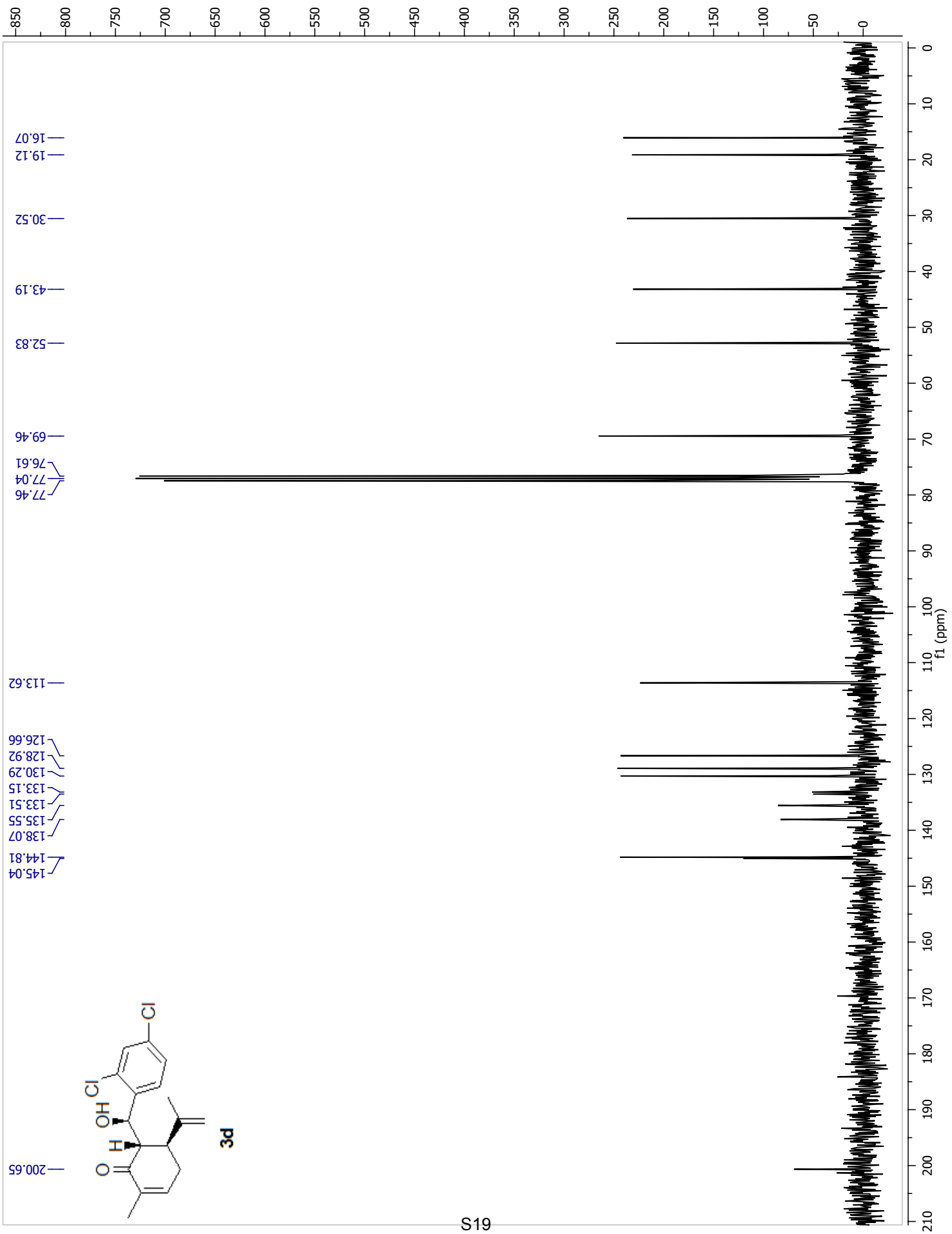
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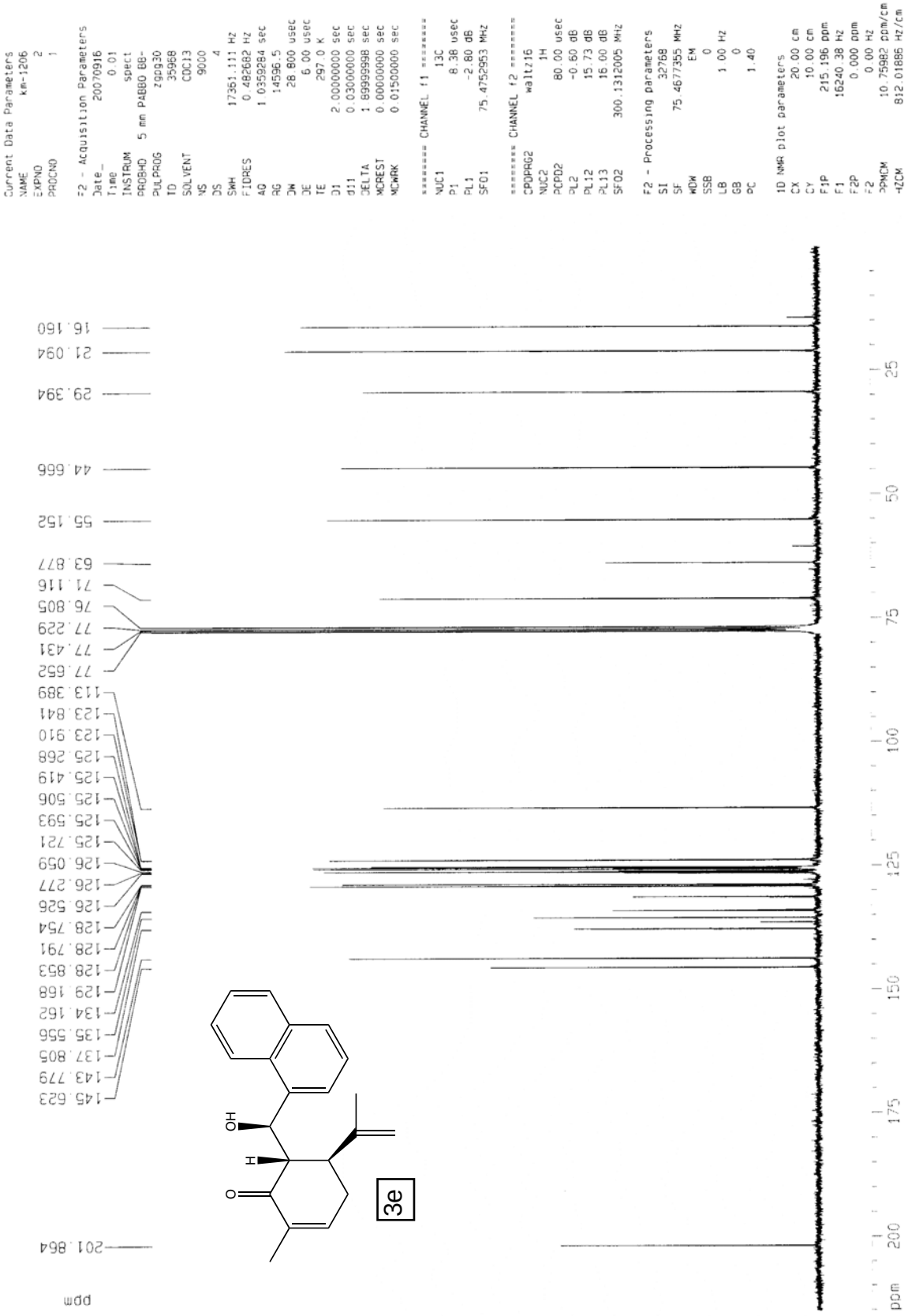
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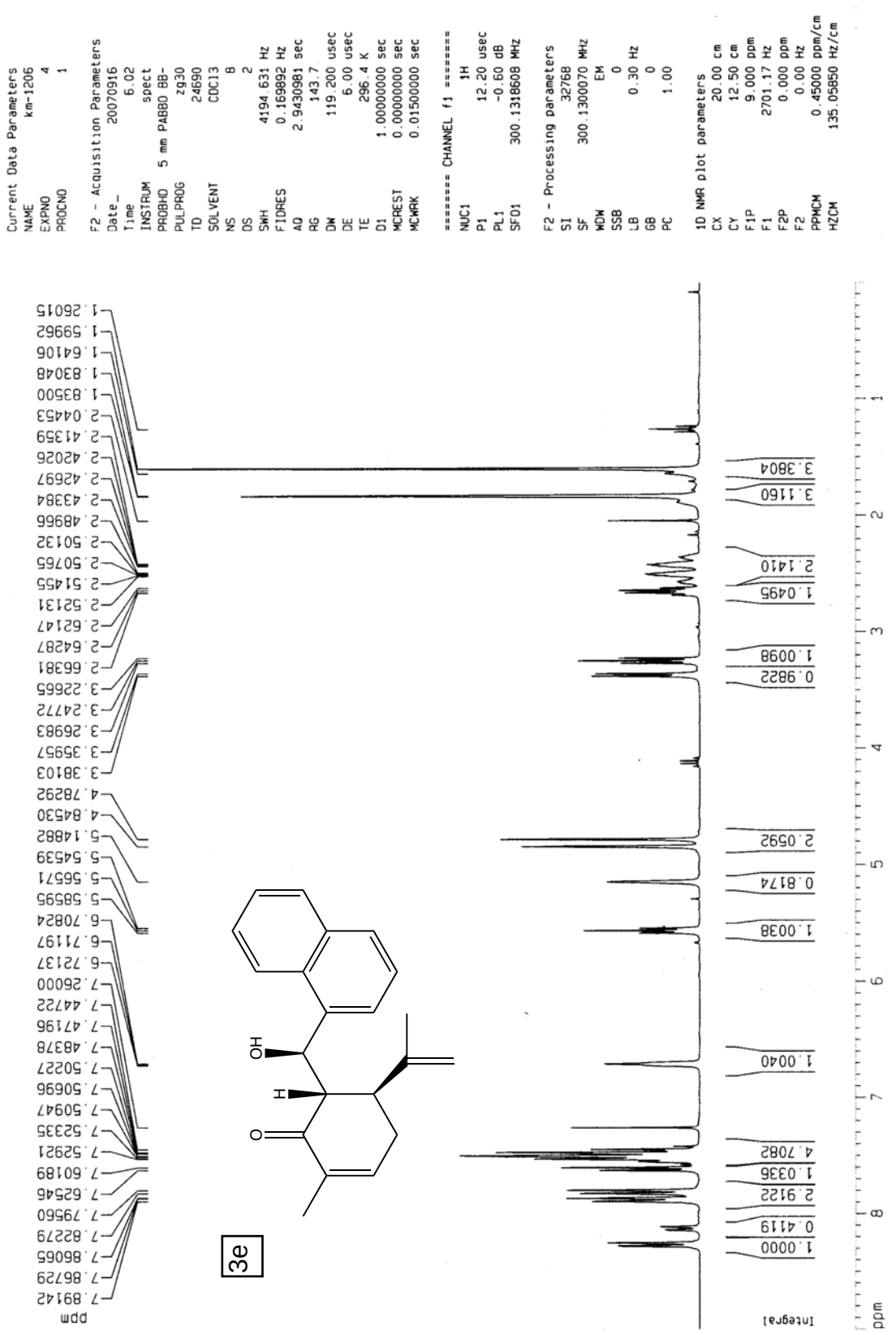
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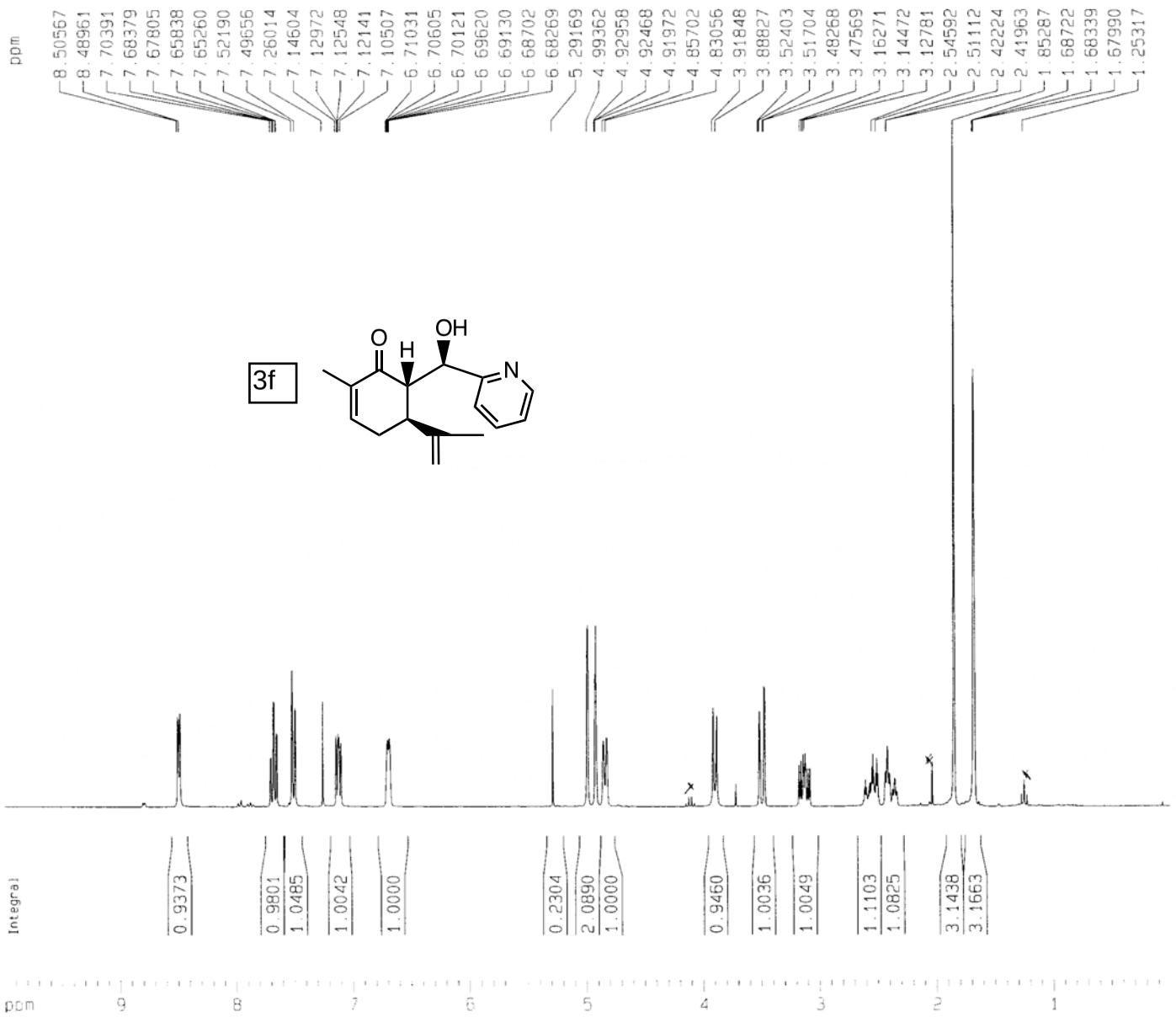

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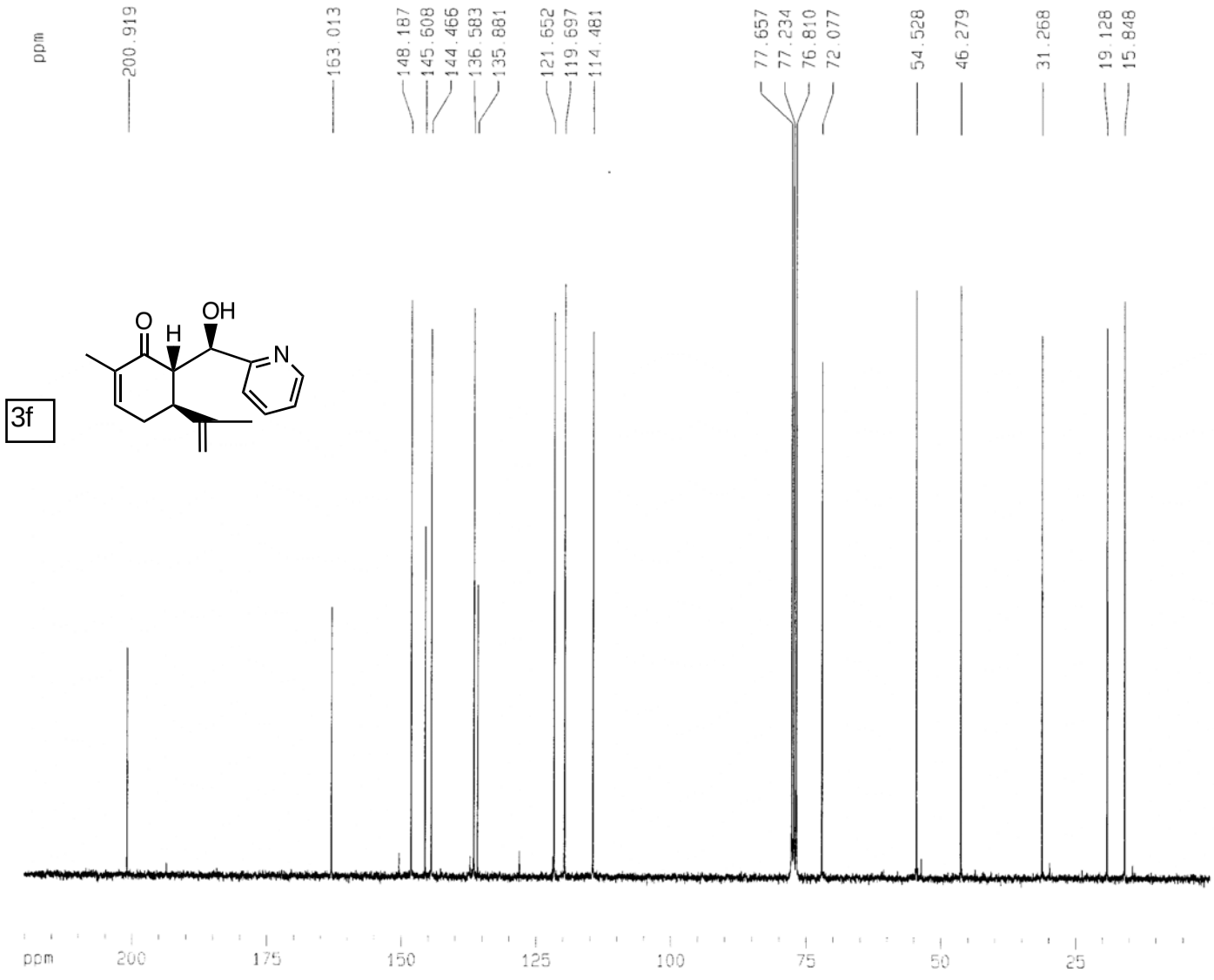


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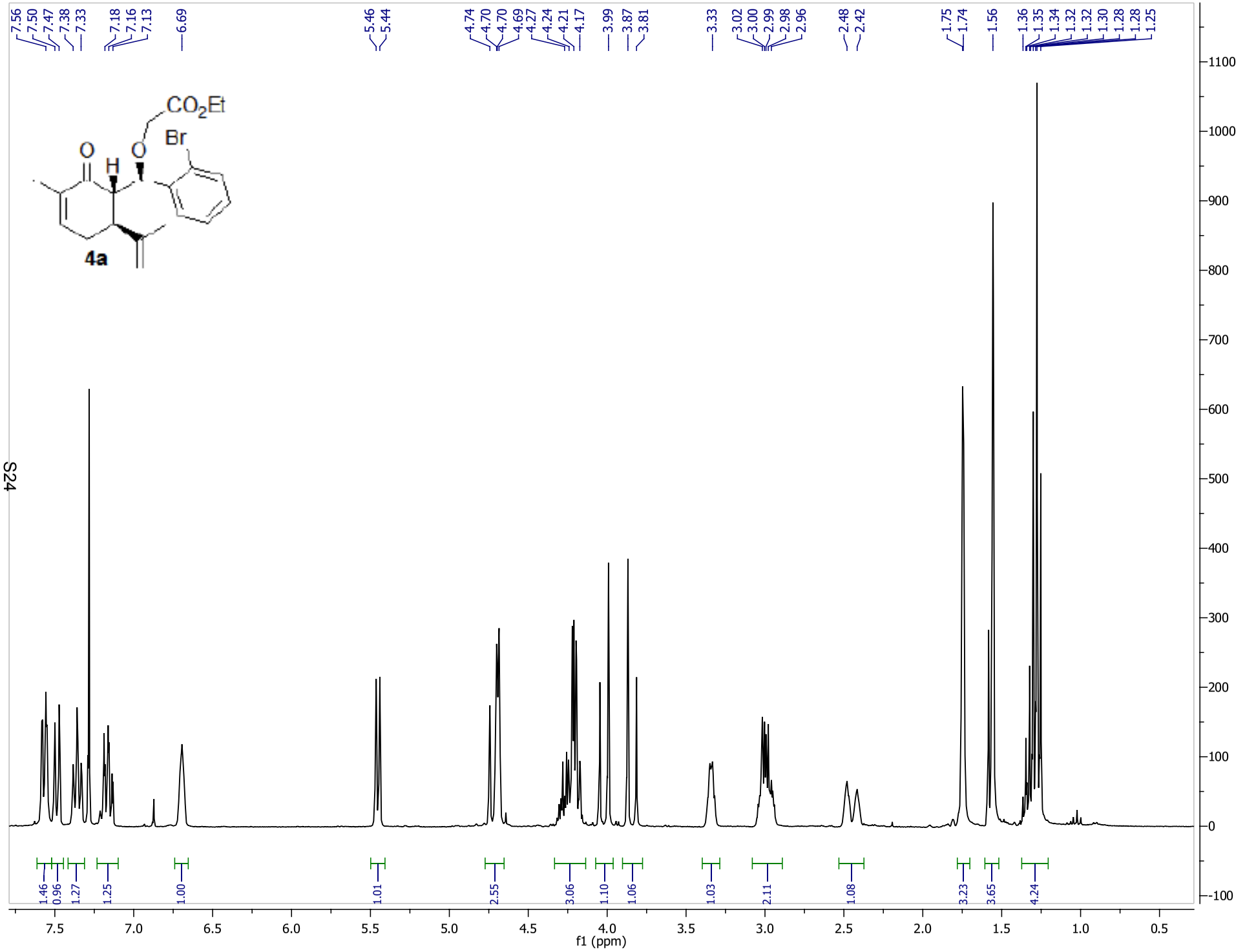
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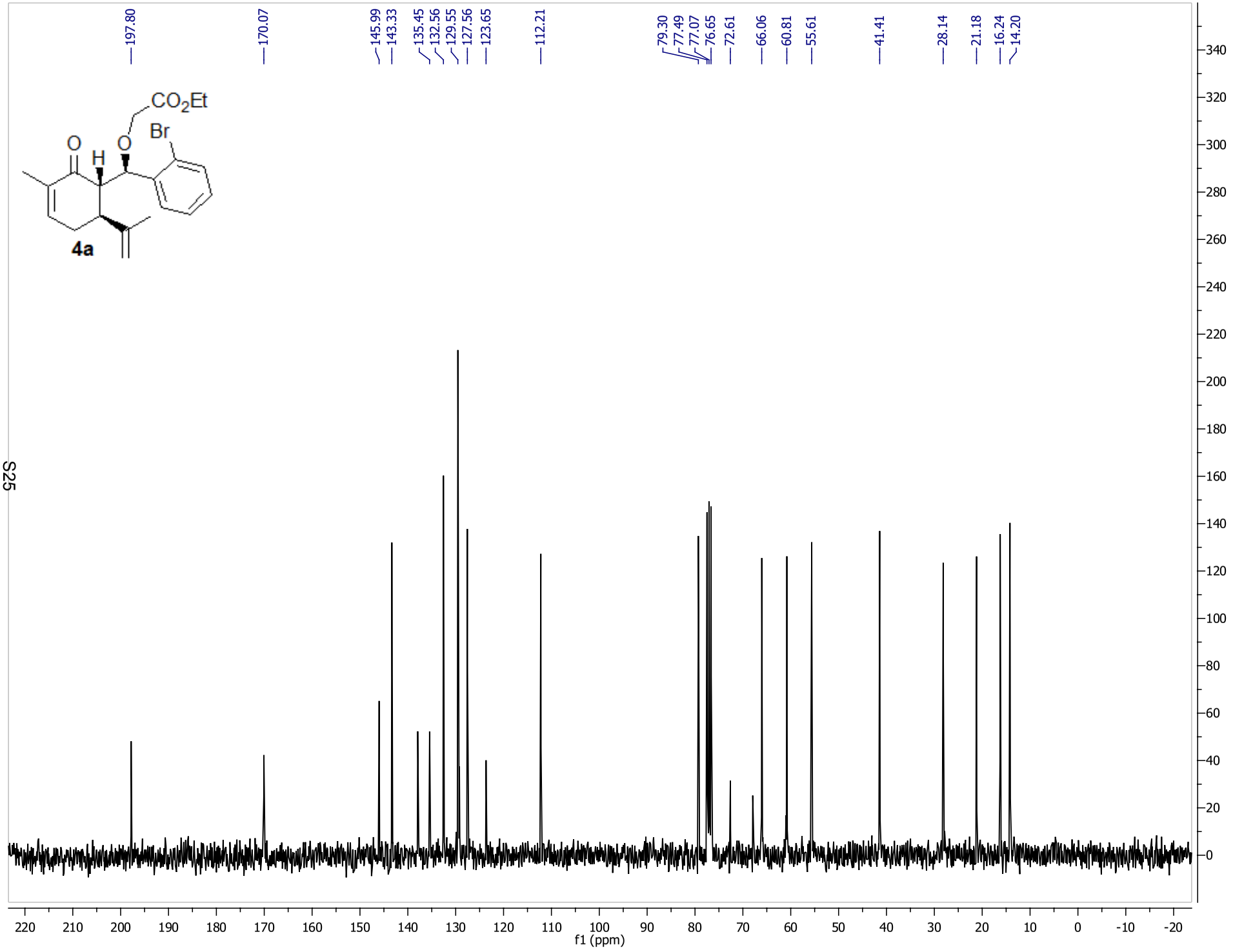
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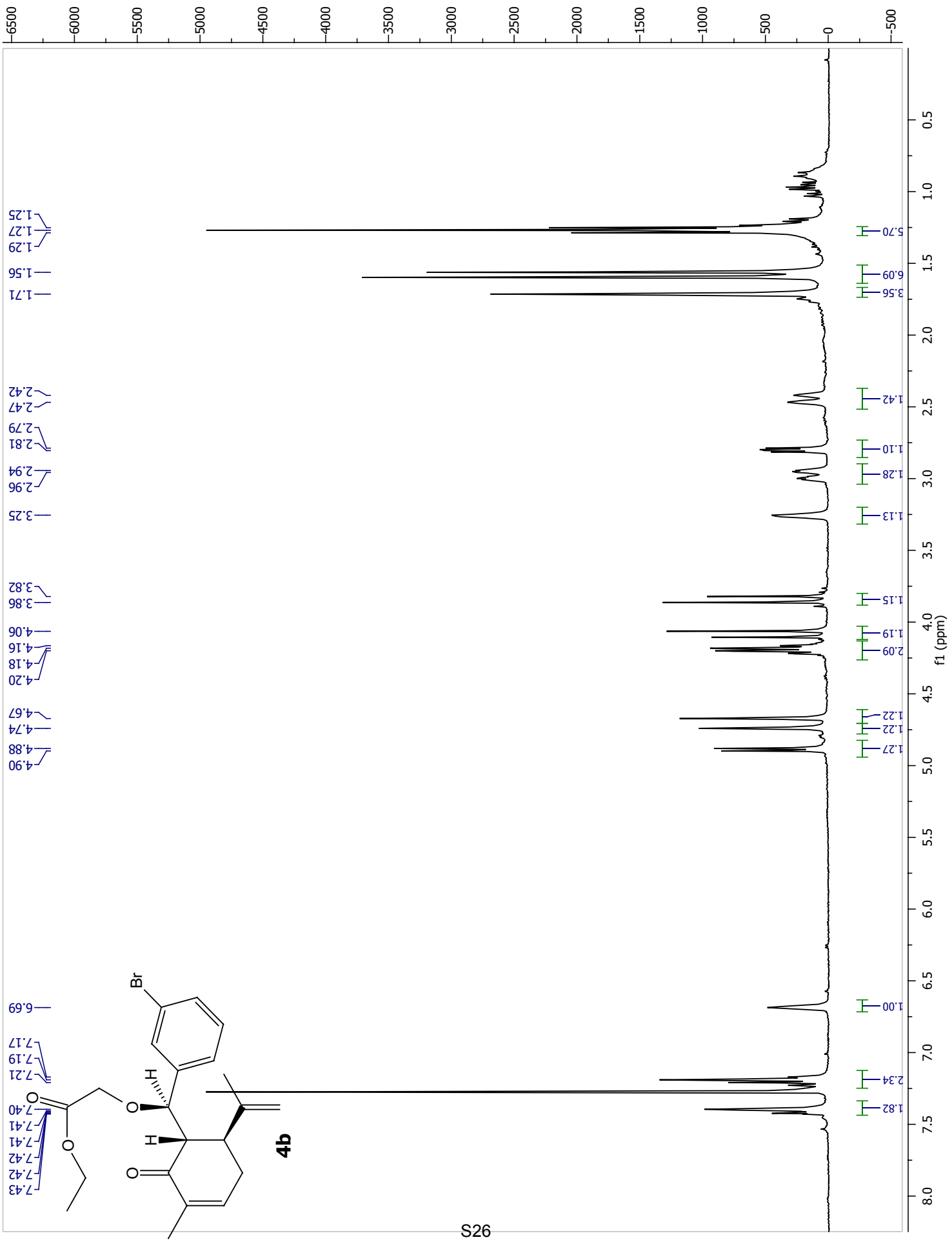
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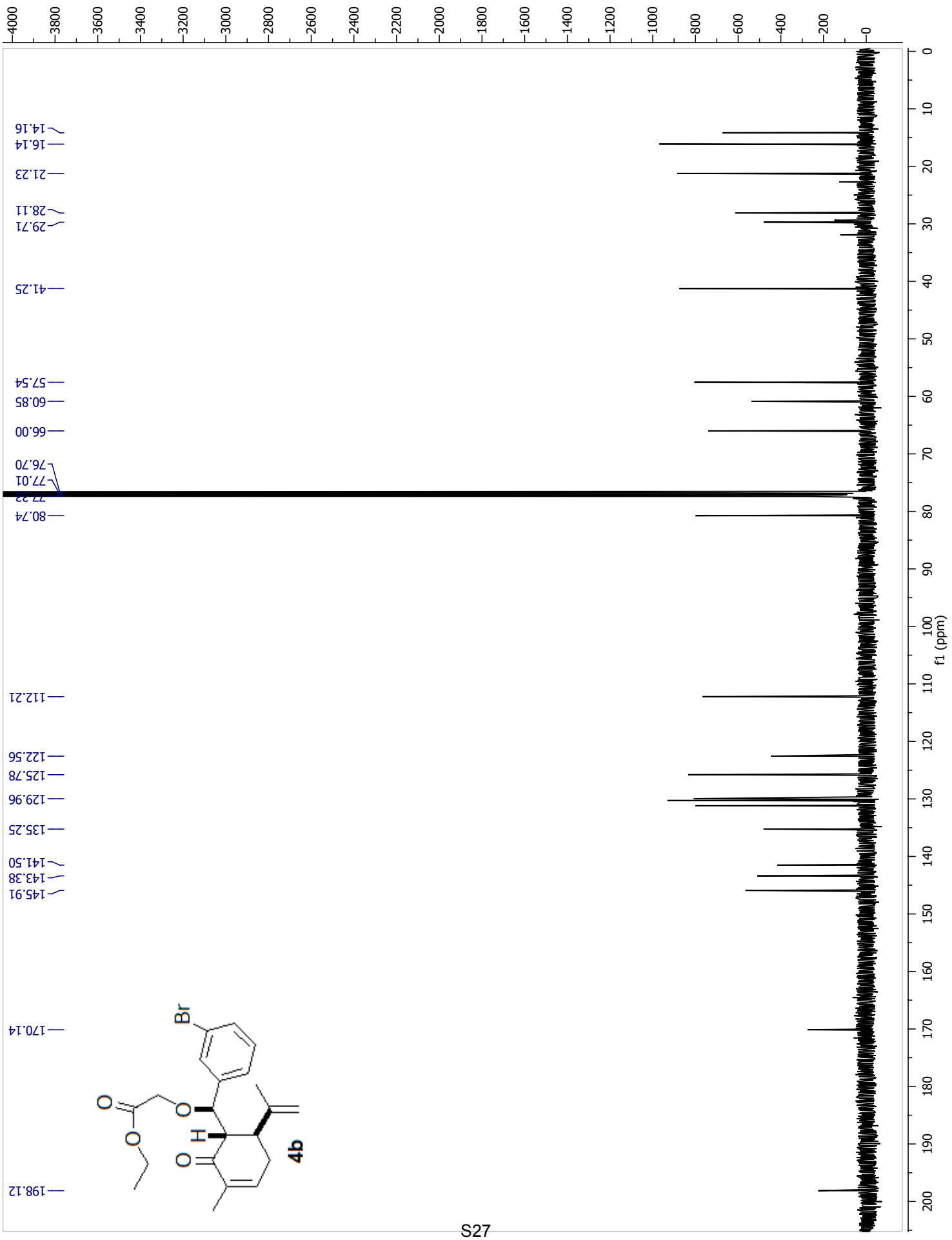
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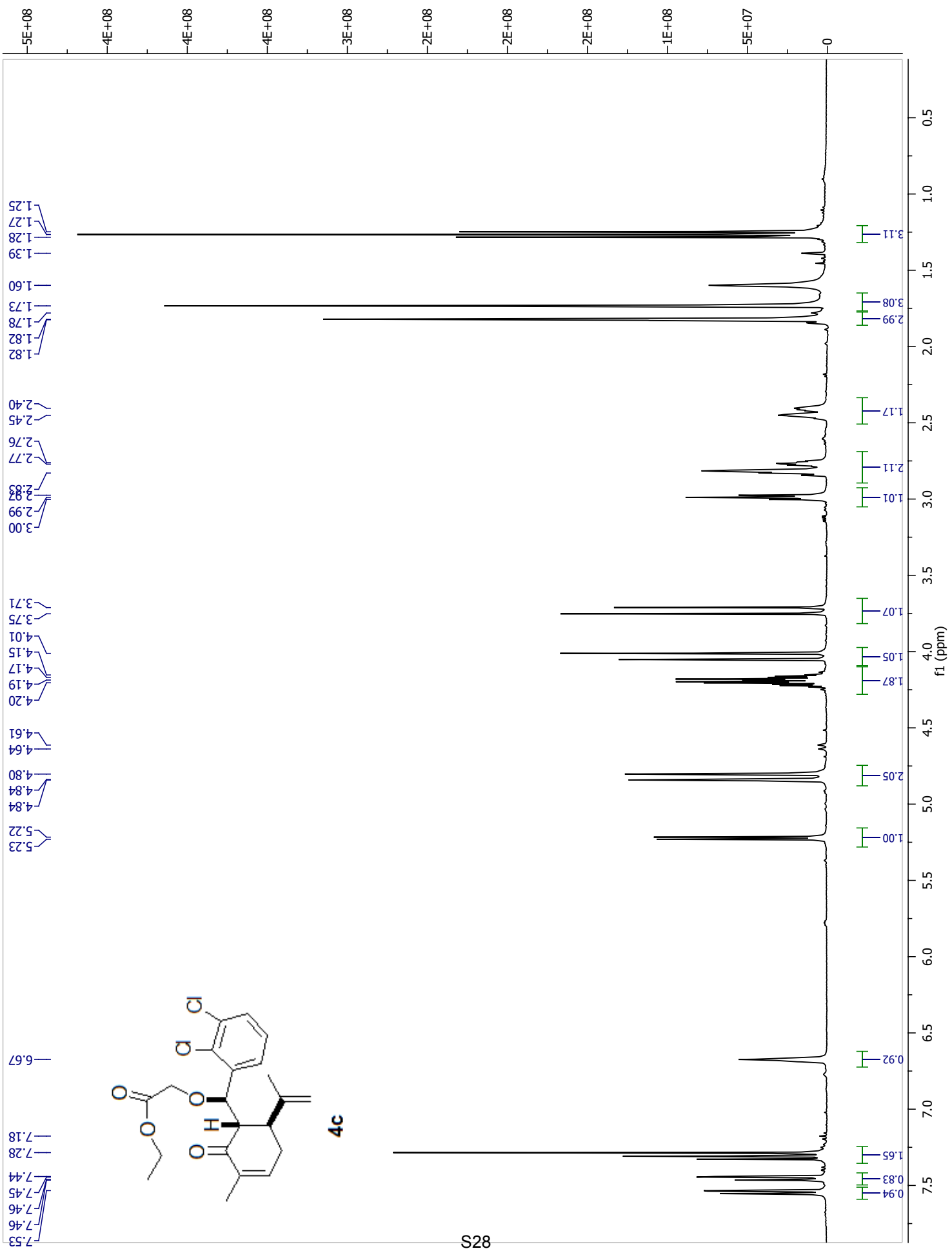
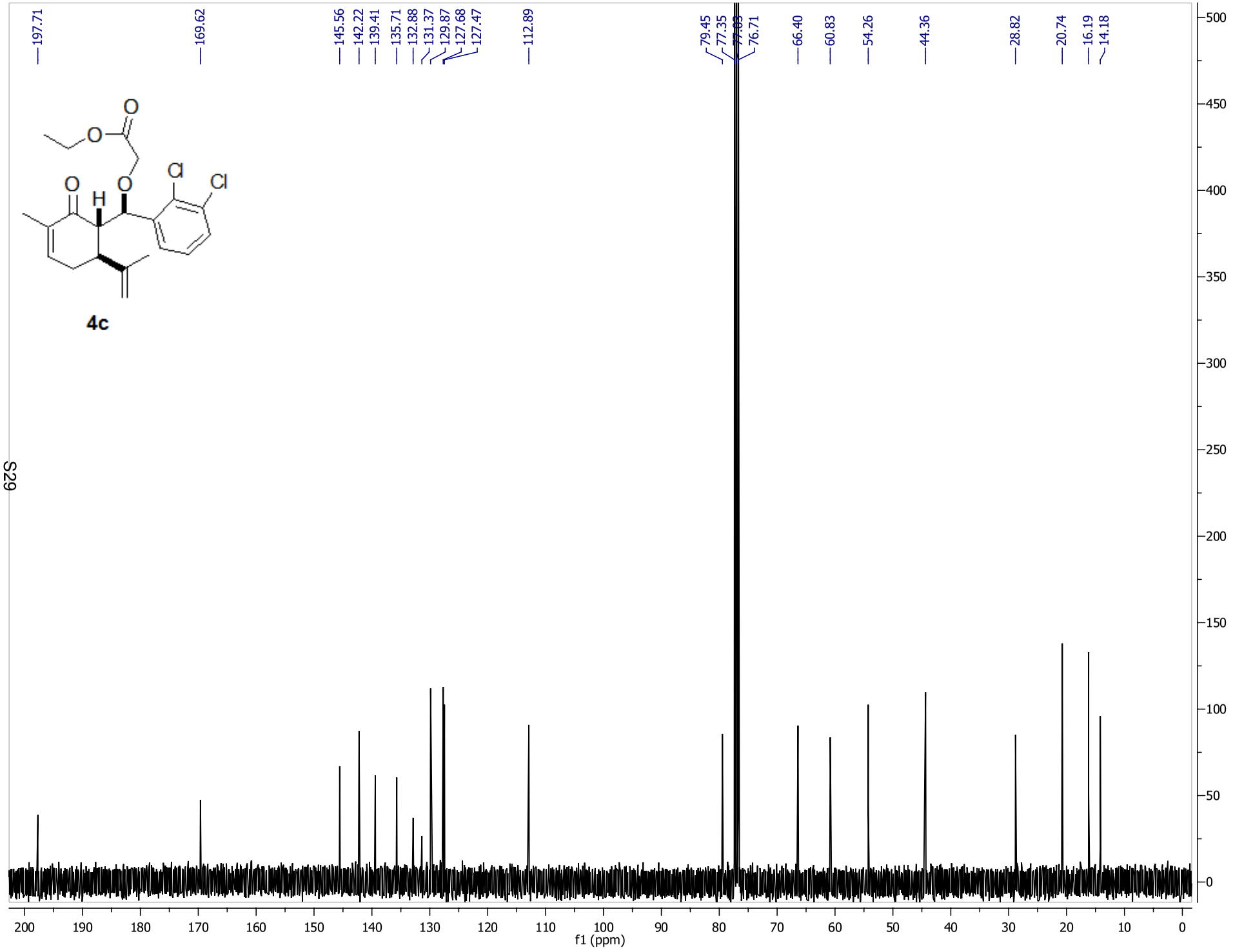
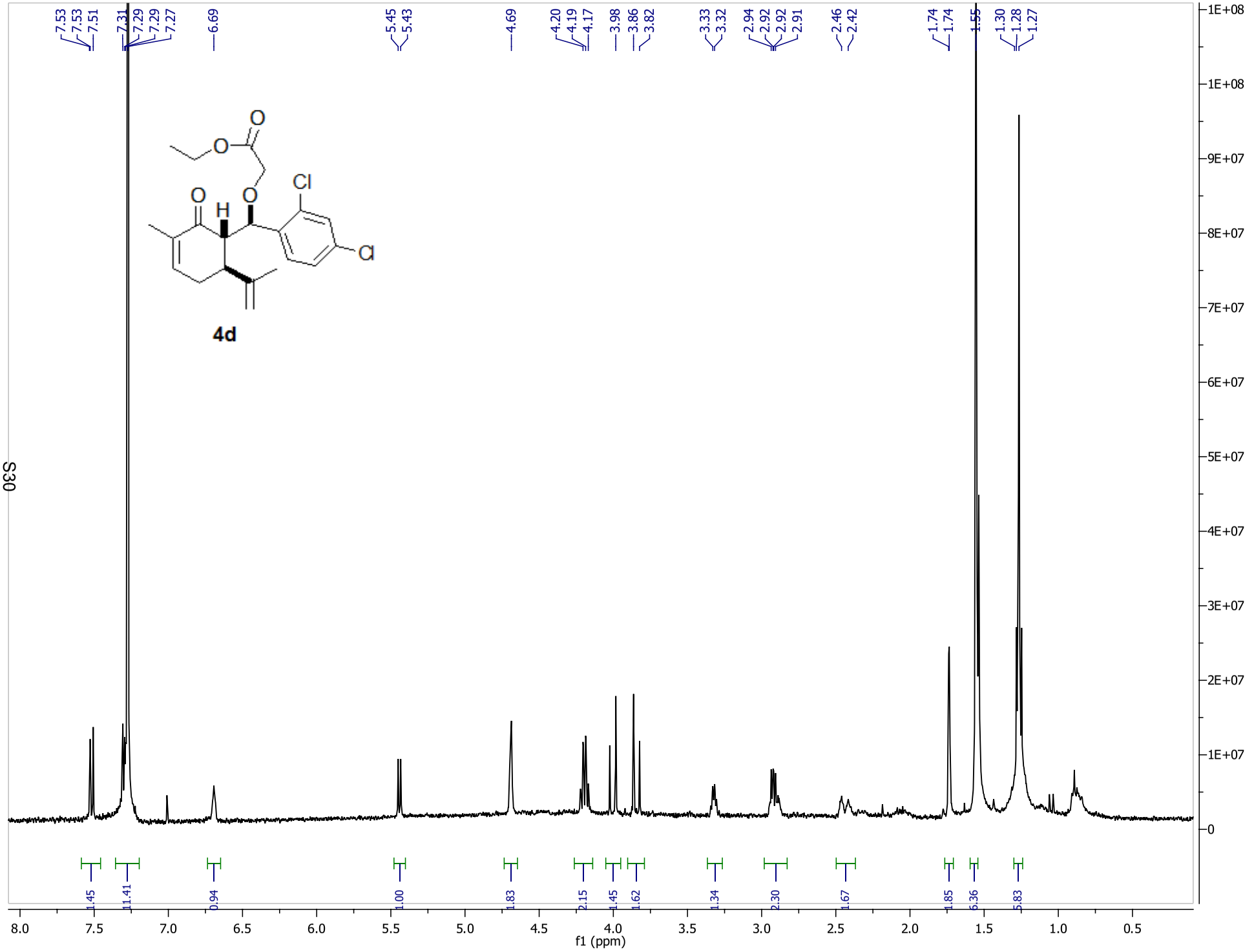
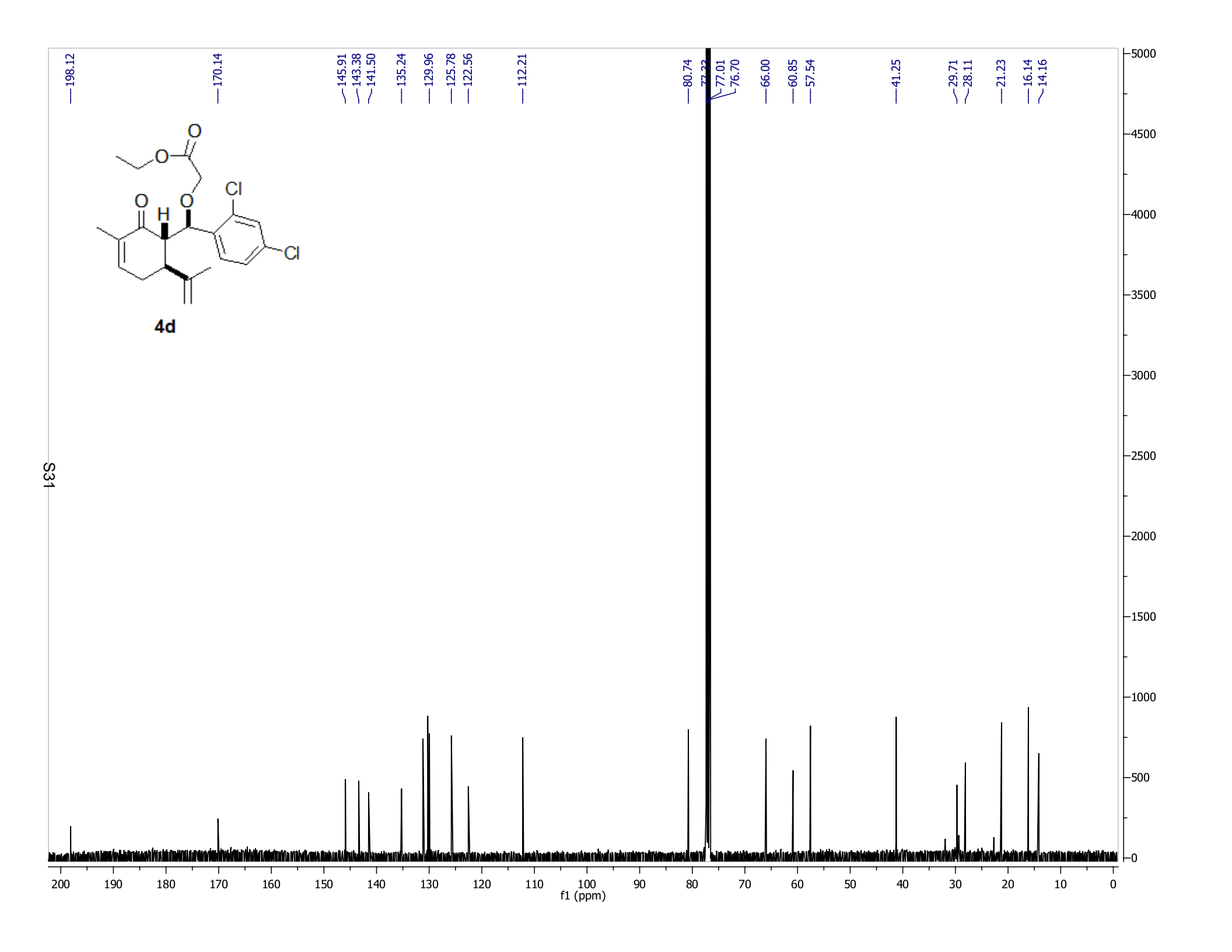
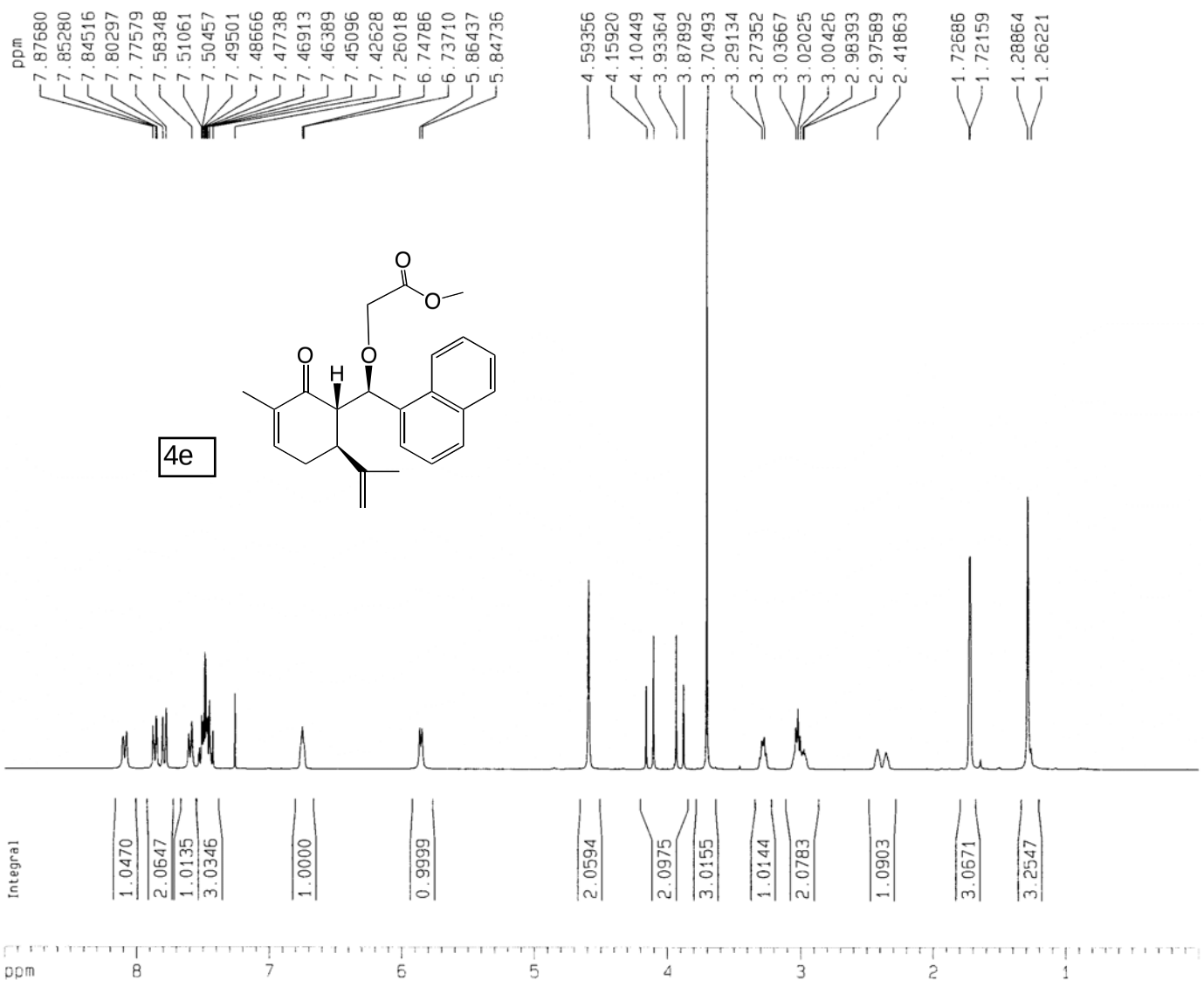
129.96
135.25
141.50
143.38
145.91
170.14
198.12
f1 (ppm)
Br
O
O
O
H
O
4b


4c
f1 (ppm)


197.71
169.62
145.56
142.22
139.41
135.71
132.88
131.37
129.87
127.68
127.47
112.89
79.45
77.35
77.03
76.71
66.40
60.83
54.26
44.36
28.82
20.74
16.19
14.18
O
O
O
O
H
Cl
Cl
4c
S29
f1 (ppm)


7.53
7.53
7.51
7.31
7.29
7.29
7.27
6.69
5.45
5.43
4.69
4.20
4.19
4.17
3.98
3.86
3.82
3.33
3.32
2.94
2.92
2.92
2.91
2.46
2.42
1.74
1.74
1.55
1.30
1.28
1.27
O
O
O
O
H
Cl
Cl
4d
S30
1E+08
1E+08
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
1.45
11.41
0.94
1.00
1.83
2.15
1.45
1.62
1.34
2.30
1.67
1.85
6.36
5.83
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


198.12
170.14
145.91
143.38
141.50
135.24
129.96
125.78
122.56
112.21
80.74
77.32
77.01
76.70
66.00
60.85
57.54
41.25
29.71
28.11
21.23
16.14
14.16
O
O
O
O
H
Cl
Cl
4d
S31
f1 (ppm)



Current Data Parameters

NAME	km-1387
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20080313
Time	11.13
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	23980
SOLVENT	CDCl3
NS	16
DS	2
SWH	5995.204 Hz
FIDRES	0.250008 Hz
AQ	1.9999820 sec
RG	90.5
DW	83.400 usec
DE	6.00 usec
TE	296.5 K
D1	1.00000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

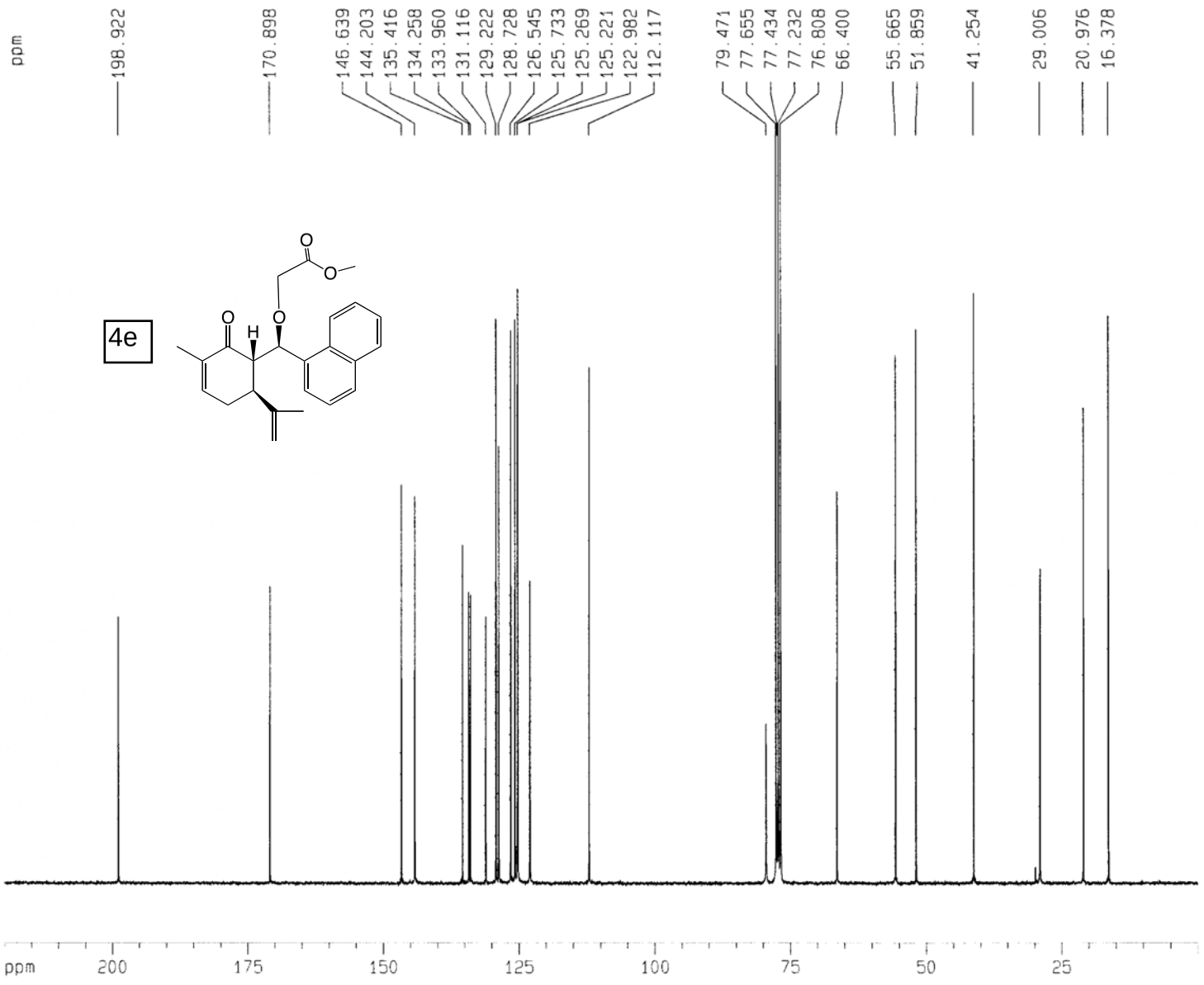
NUC1	1H
P1	12.20 usec
PL1	-1.00 dB
SFO1	300.1318608 MHz

F2 - Processing parameters

SI	32768
SF	300.1300066 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	12.00 cm
F1P	9.000 ppm
F1	2701.17 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



Current Data Parameters

NAME	km-1387
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20080313
Time	7.11
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	36230
SOLVENT	CDCl3
NS	16000
DS	4
SWH	18115.941 Hz
FIDRES	0.500026 Hz
AQ	0.9999980 sec
RG	14596.5
DW	27.600 usec
DE	6.00 usec
TE	297.0 K
D1	2.00000000 sec
d11	0.03000000 sec
DELTA	1.89999998 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.38 usec
PL1	-2.80 dB
SFO1	75.4760505 MHz

======== CHANNEL f2 ========

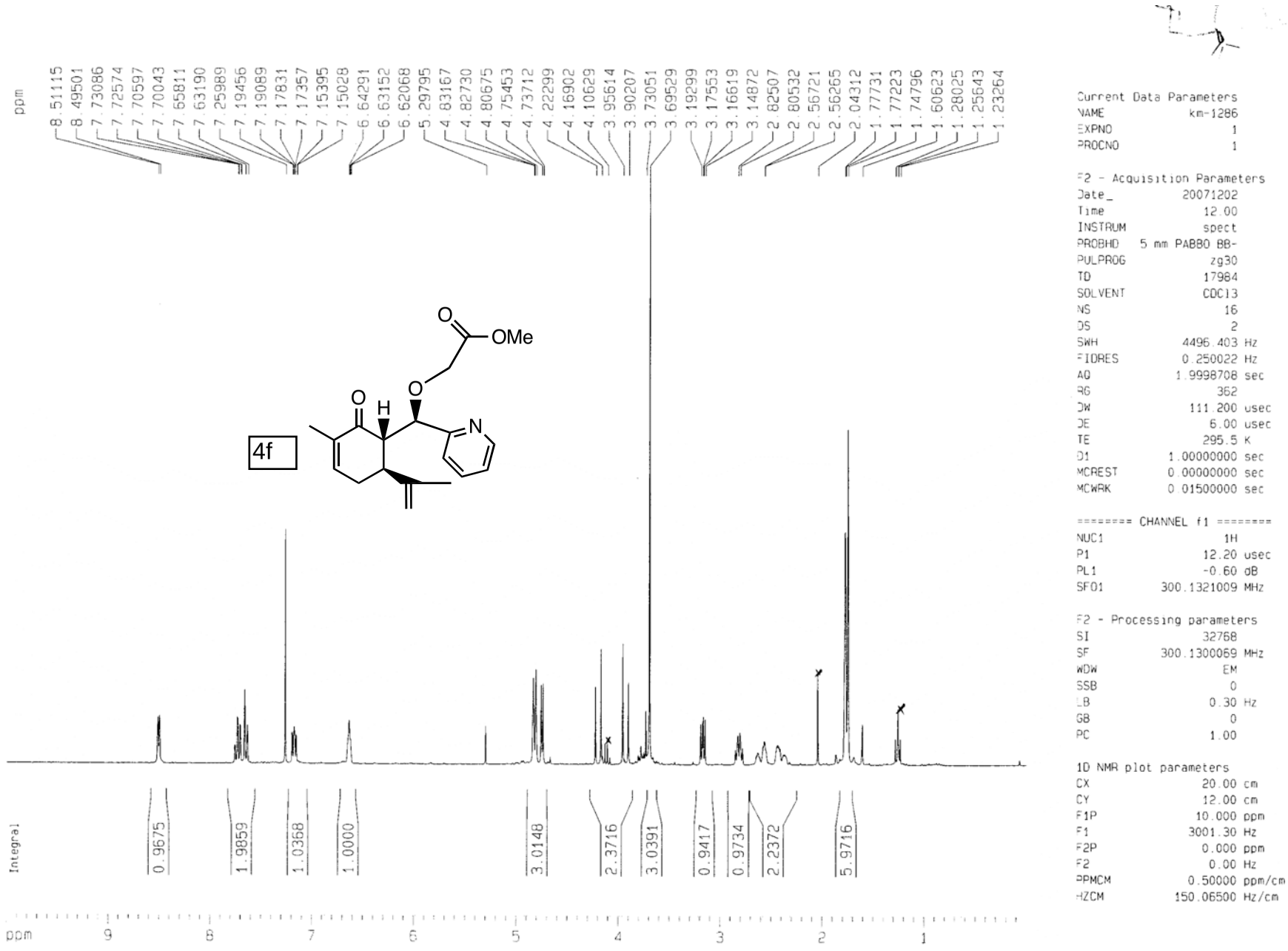
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-1.00 dB
PL12	15.33 dB
PL13	16.00 dB
SFO2	300.1312005 MHz

F2 - Processing parameters

SI	32768
SF	75.4677359 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	220.000 ppm
F1	16602.90 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	11.00000 ppm/cm
HZCM	830.14508 Hz/cm



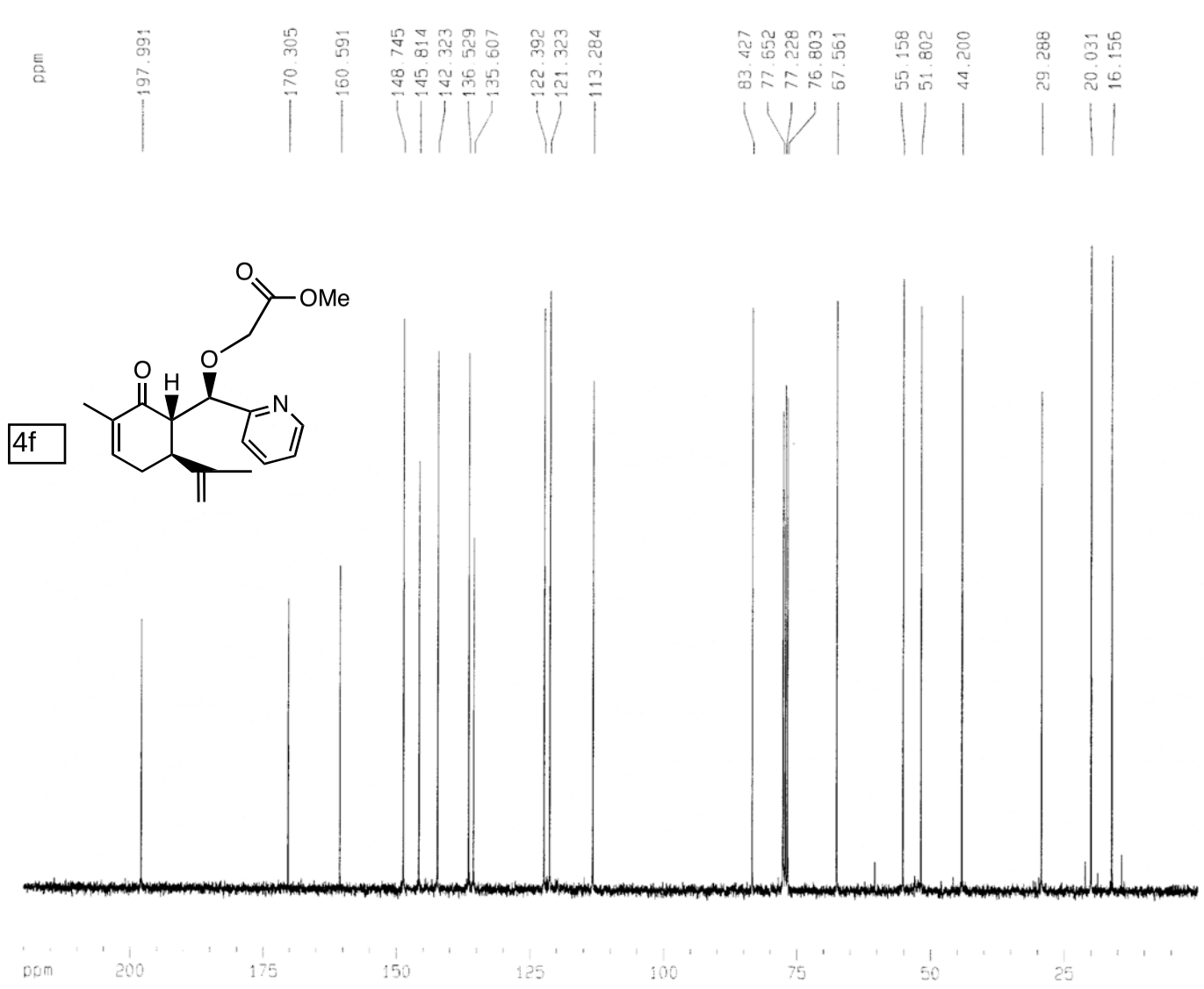
Current Data Parameters
NAME km-1286
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20071202
Time 12.00
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 17984
SOLVENT CDCl3
NS 16
DS 2
SWH 4496.403 Hz
FIDRES 0.250022 Hz
AQ 1.9998708 sec
RG 362
DW 111.200 usec
DE 6.00 usec
TE 295.5 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

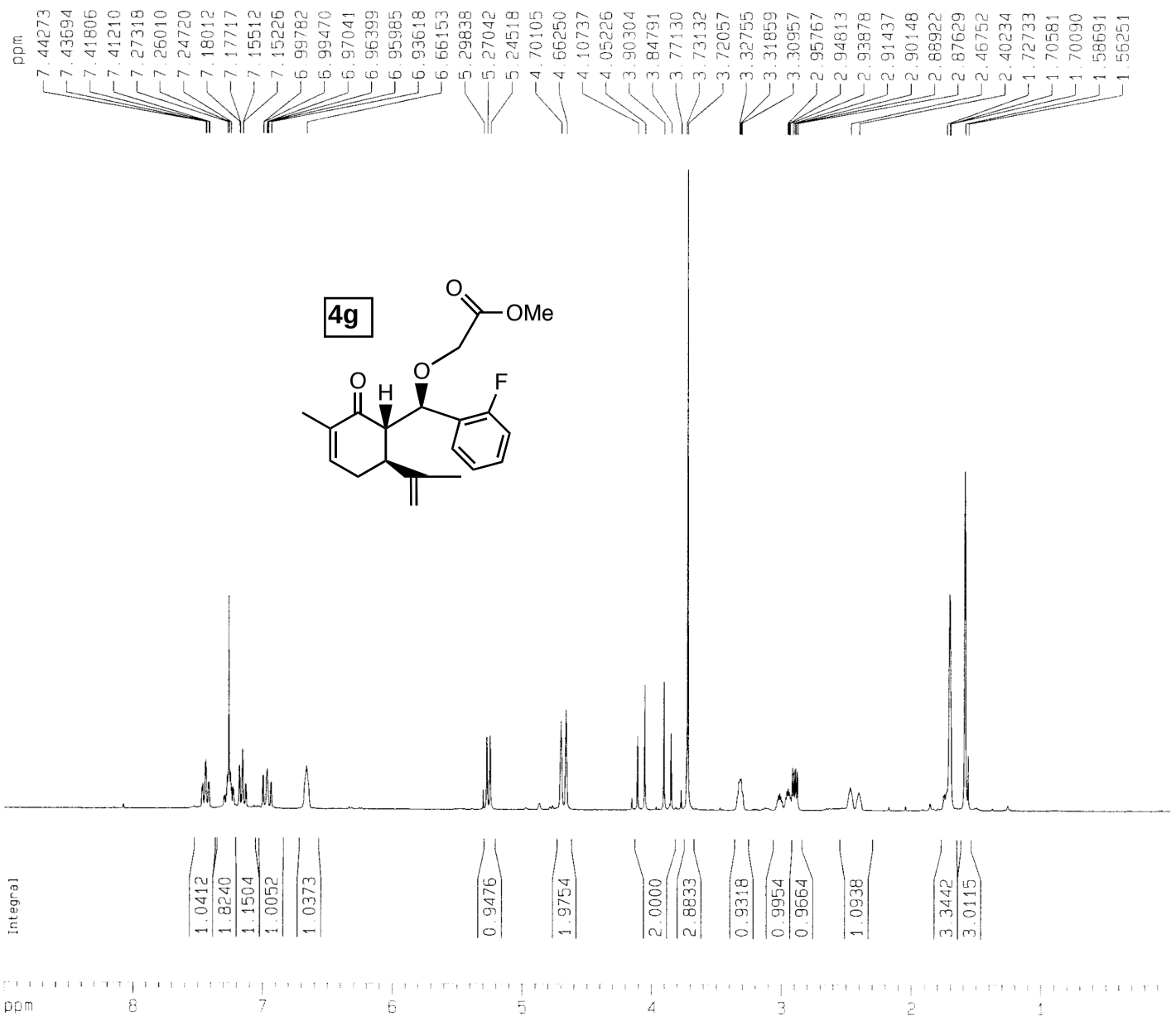
======== CHANNEL f1 ========
NUC1 1H
P1 12.20 usec
PL1 -0.60 dB
SFO1 300.1321009 MHz

F2 - Processing parameters
SI 32768
SF 300.1300069 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 12.00 cm
F1P 10.000 ppm
F1 3001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 150.06500 Hz/cm




```
Current Data Parameters
NAME                  km-1286
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20071203
Time                   11.18
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zgpg30
TD                      32372
SOLVENT                CDCl3
NS                        400
DS                          4
SWH                18115.941 Hz
FIDRES             0.559618 Hz
AQ                 0.8935172 sec
RG                   23170.5
DW                    27.600 usec
DE                     6.00 usec
TE                    297.0 K
D1                 2.00000000 sec
d11                0.03000000 sec
DELTA              1.89999998 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                       8.38 usec
PL1                     -2.80 dB
SFO1               75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   80.00 usec
PL2                     -0.60 dB
PL12                    15.73 dB
PL13                    16.00 dB
SFO2              300.1312005 MHz

F2 - Processing parameters
SI                        32768
SF                 75.4677415 MHz
WDW                          EM
SSB                           0
LB                       1.00 Hz
GB                            0
PC                       1.40

1D NMR plot parameters
CX                      20.00 cm
CY                      11.00 cm
F1P                   220.118 ppm
F1                  16611.81 Hz
F2P                    -0.000 ppm
F2                     -0.00 Hz
PPMCM                11.00590 ppm/cm
HZCM                830.59045 Hz/cm
```



Current Data Parameters

NAME	km-1240
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20071002
Time	8.39
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	17984
SOLVENT	CDCl3
NS	16
DS	2
SWH	4496.403 Hz
FIDRES	0.250022 Hz
AQ	1.9998708 sec
RG	322.5
DW	111.200 usec
DE	6.00 usec
TE	296.2 K
D1	1.00000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

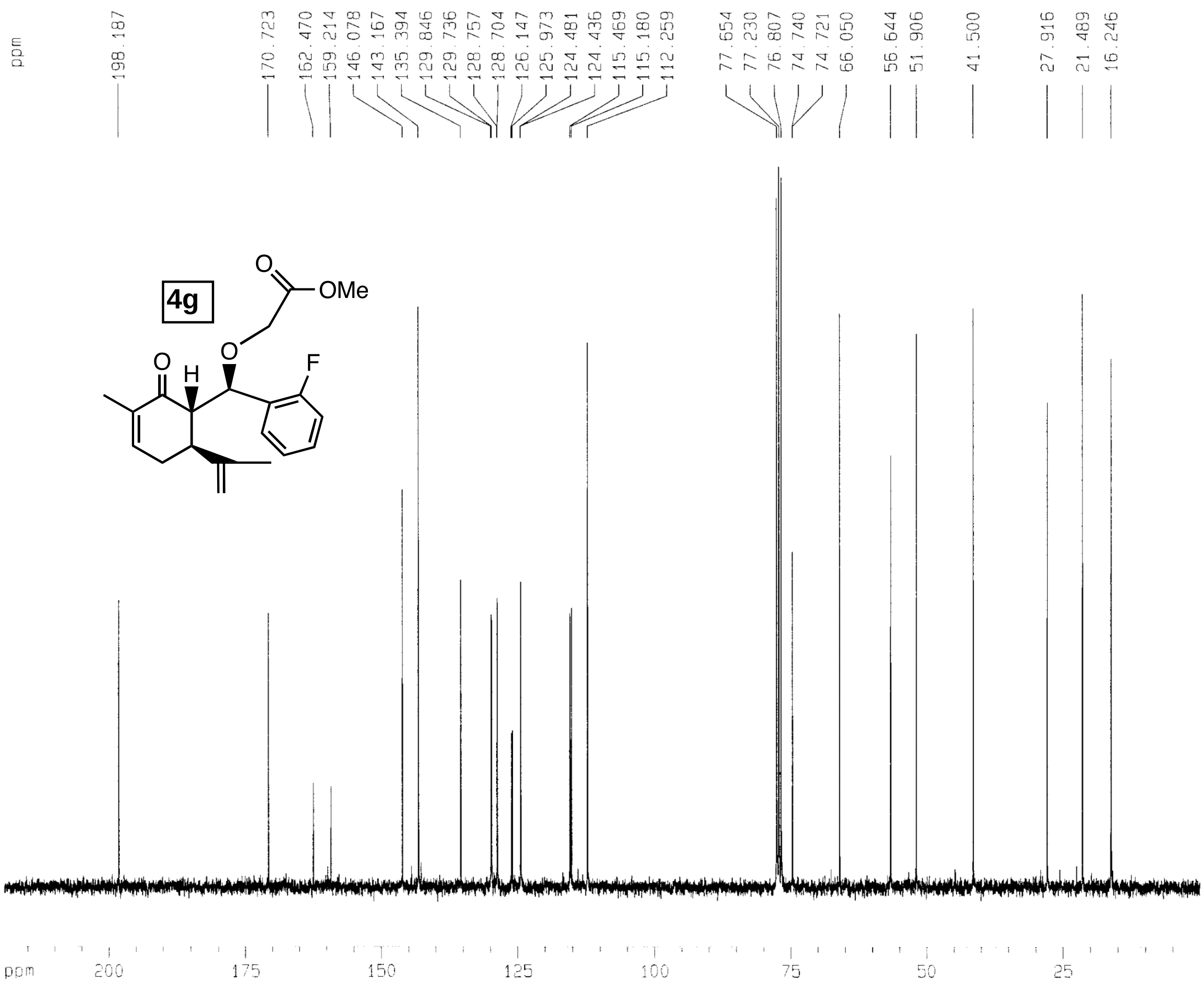
NUC1	1H
P1	12.20 usec
PL1	-0.60 dB
SFO1	300.1321009 MHz

F2 - Processing parameters

SI	32768
SF	300.1300066 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	11.00 cm
F1P	9.000 ppm
F1	2701.17 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



Current Data Parameters
NAME km-1240
EXPNO 2
PROCNO 1

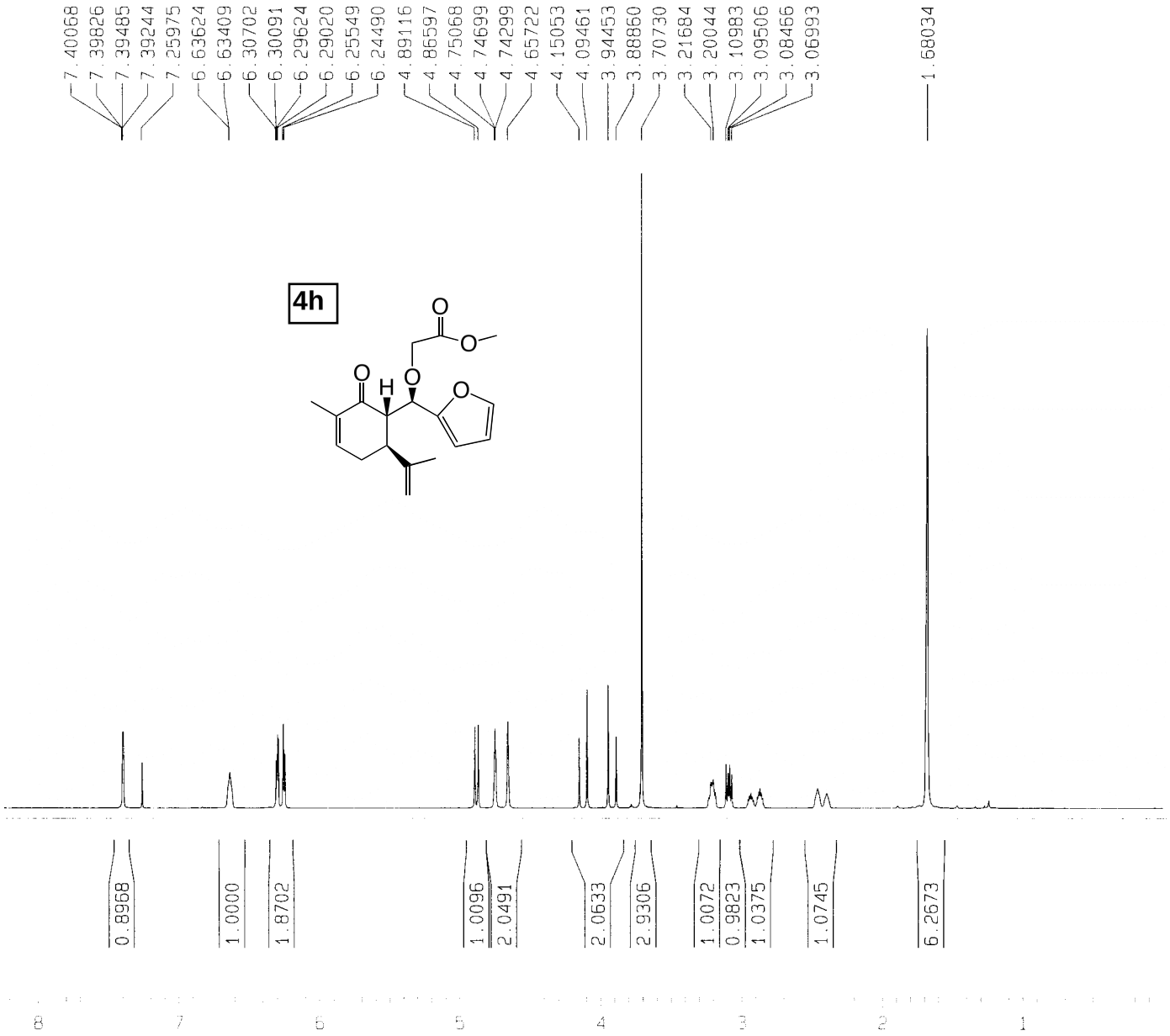
F2 - Acquisition Parameters
Date_ 20071003
Time 13.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 32372
SOLVENT CDCl3
NS 500
DS 4
SWH 17985.611 Hz
FIDRES 0.555592 Hz
AQ 0.8999916 sec
RG 18390.4
DW 27.800 usec
DE 6.00 usec
TE 296.8 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 8.38 usec
PL1 -2.80 dB
SFO1 75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -0.60 dB
PL12 15.73 dB
PL13 16.00 dB
SFO2 300.1312005 MHz

F2 - Processing parameters
SI 32768
SF 75.4677363 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 219.323 ppm
F1 16551.79 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.96613 ppm/cm
HZCM 827.58929 Hz/cm



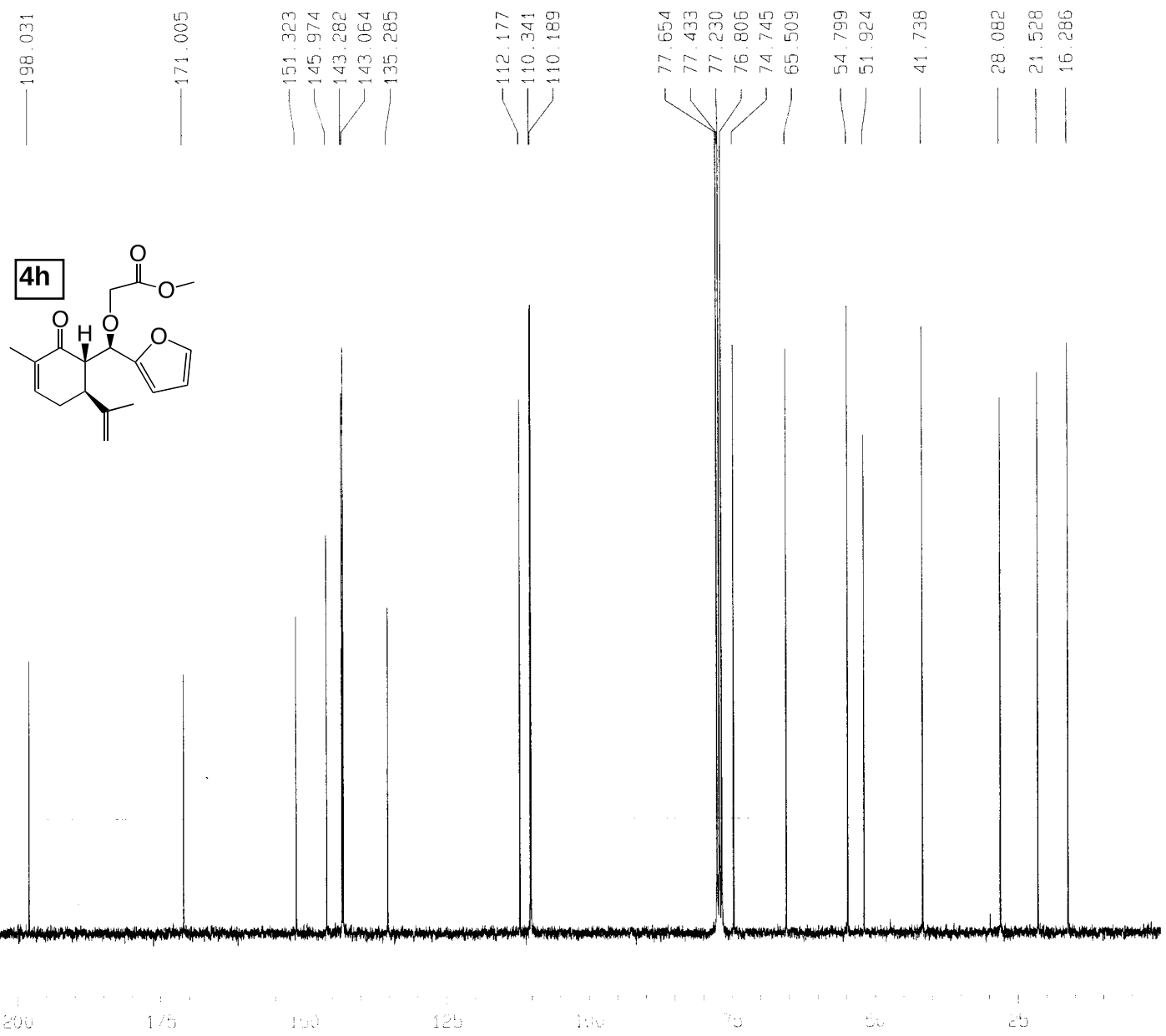
Current Data Parameters
NAME km-1354
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20080205
Time 17.30
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 23980
SOLVENT CDCl3
NS 16
DS 2
SWH 5995.204 Hz
FIDRES 0.250008 Hz
AQ 1.9999820 sec
RG 128
DW 83.400 usec
DE 6.00 usec
TE 296.3 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

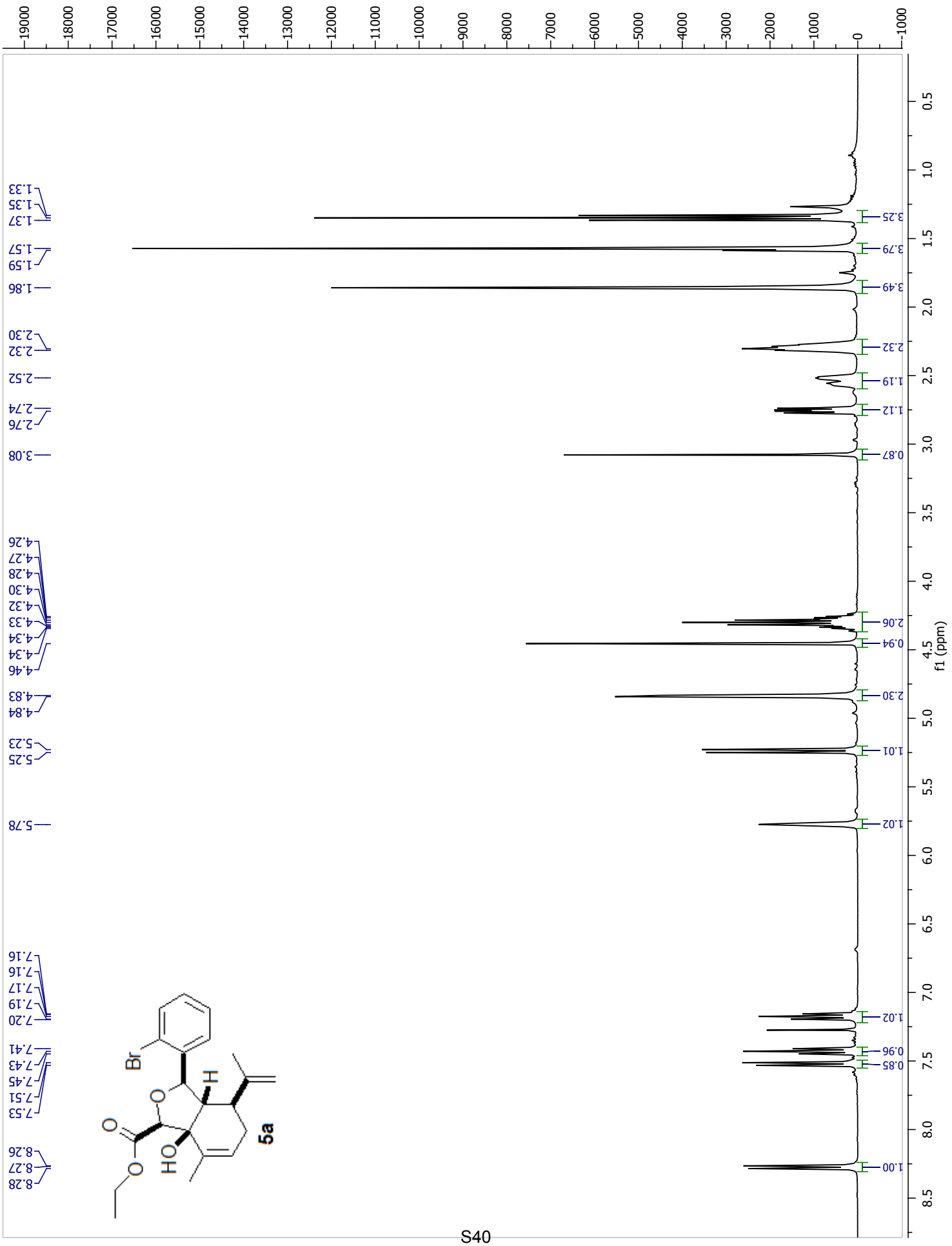
======== CHANNEL f1 ========
NUC1 1H
P1 12.20 usec
PL1 -1.00 dB
SFO1 300.1318608 MHz

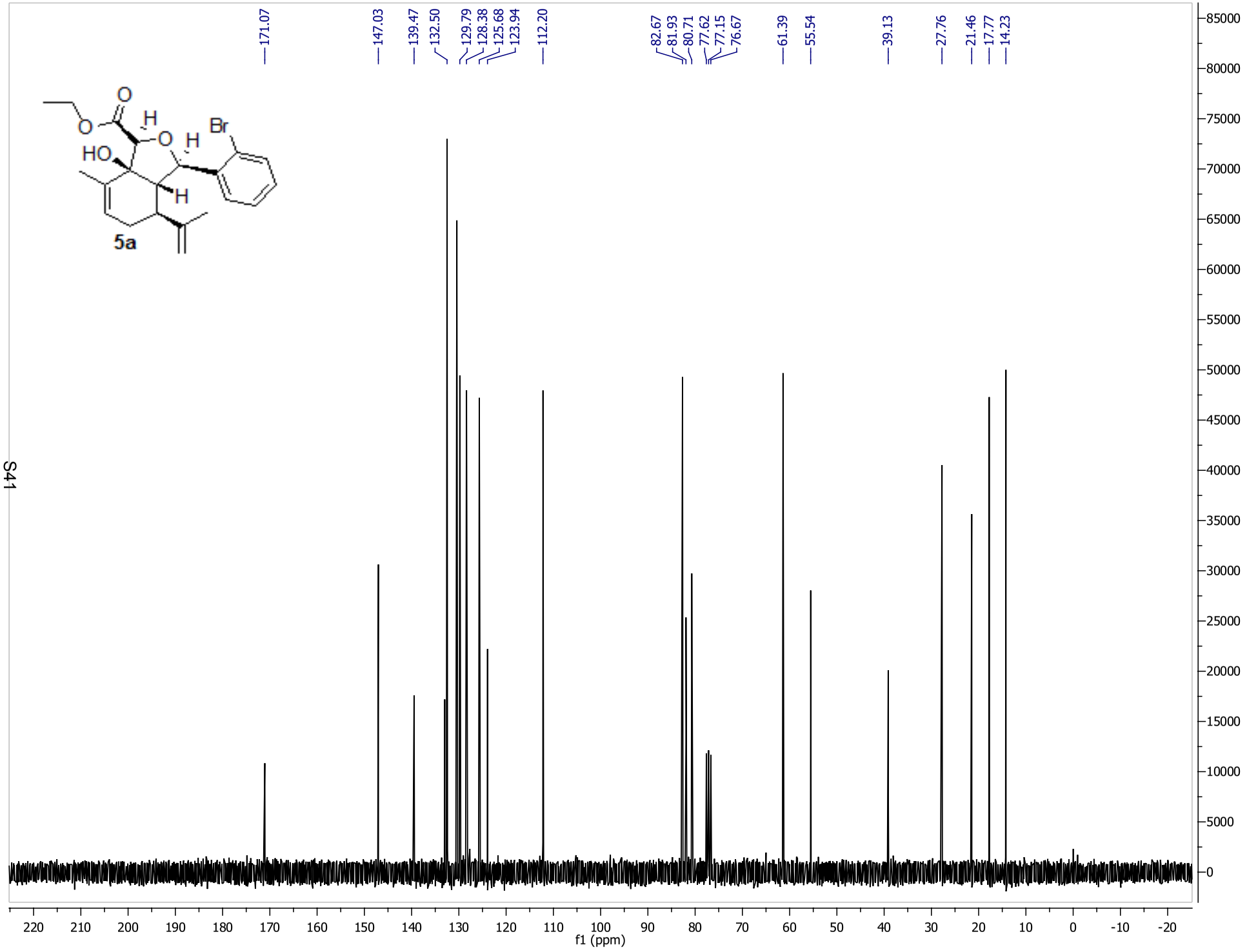
F2 - Processing parameters
SI 32768
SF 300.1300068 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

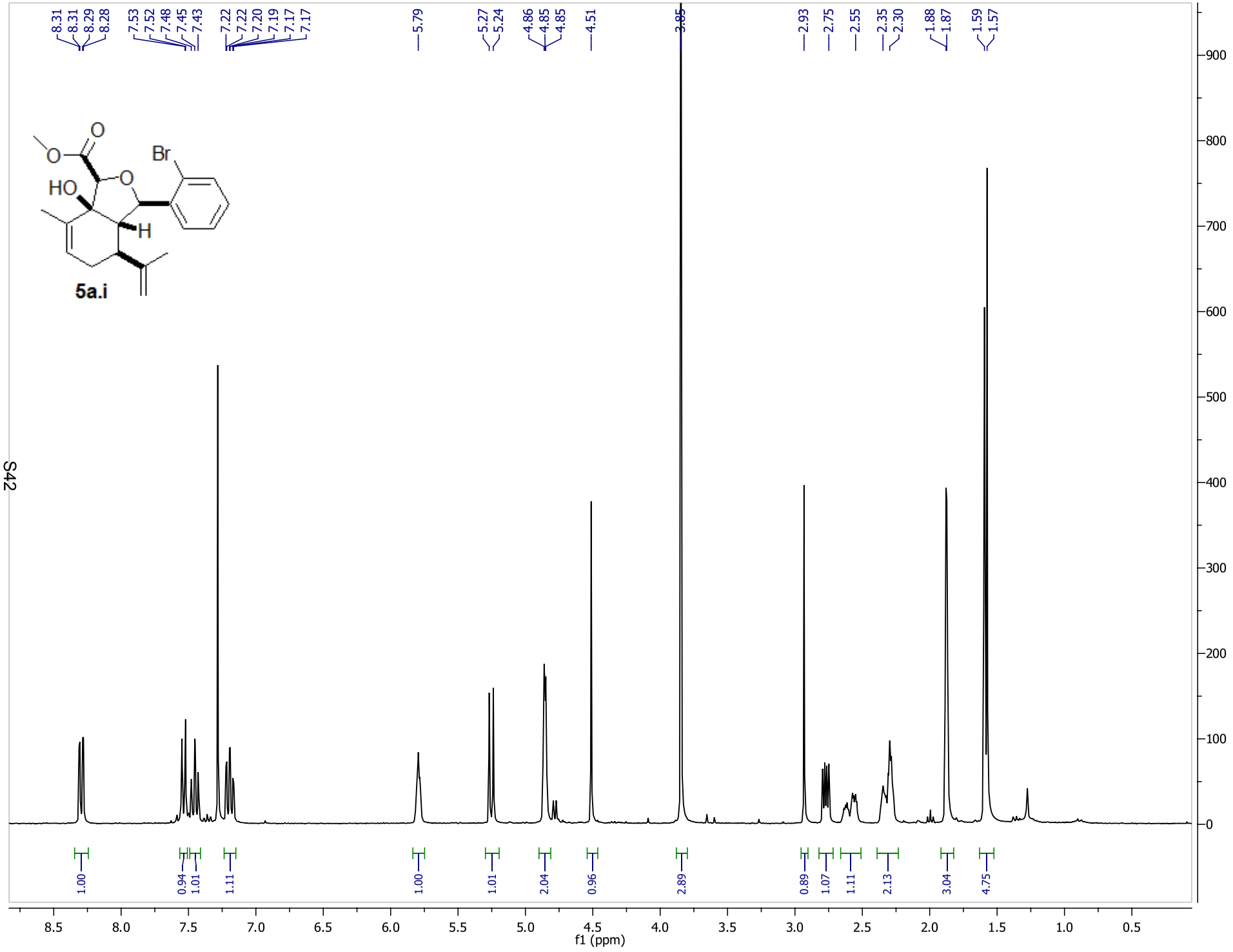
1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 9.000 ppm
F1 2701.17 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm

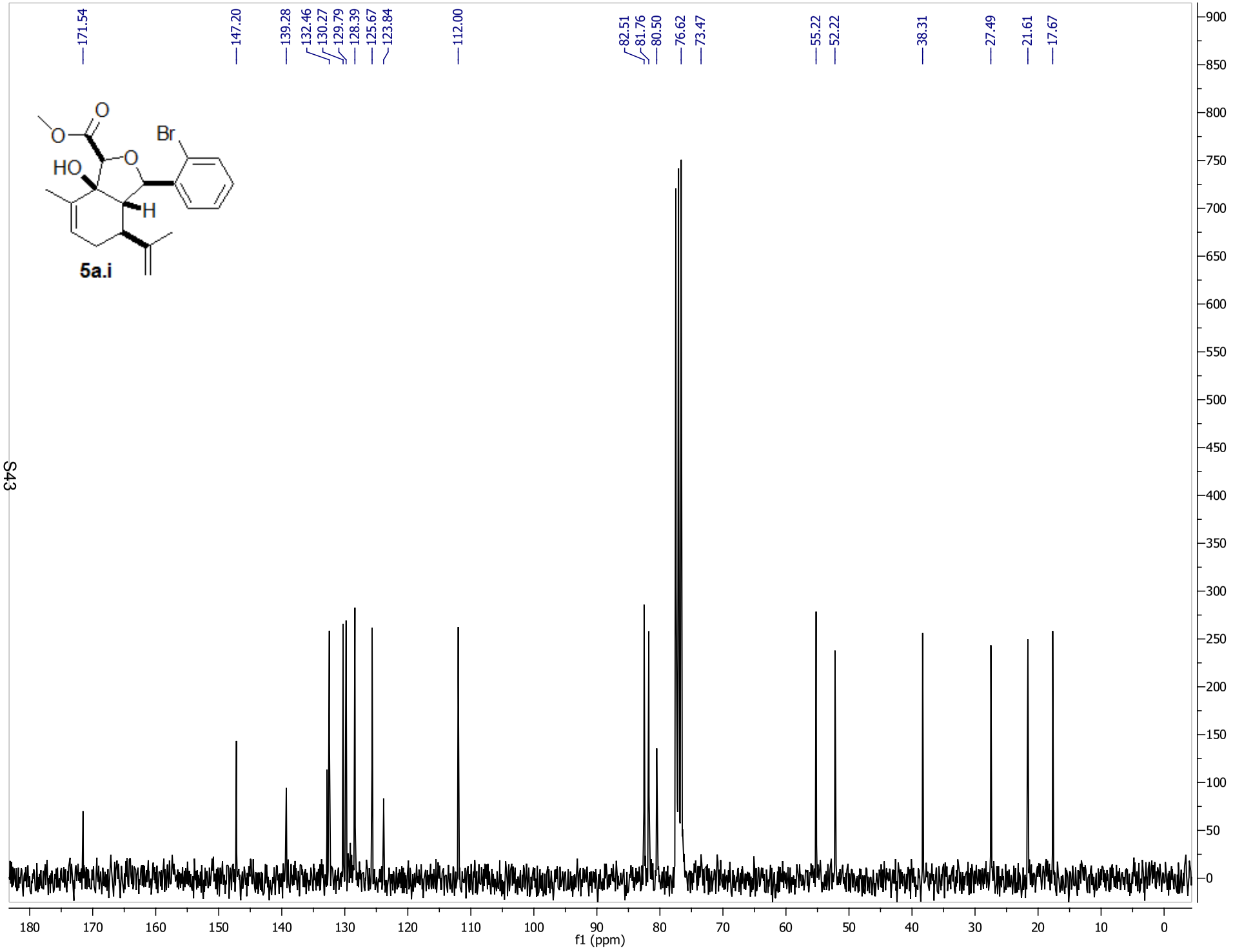


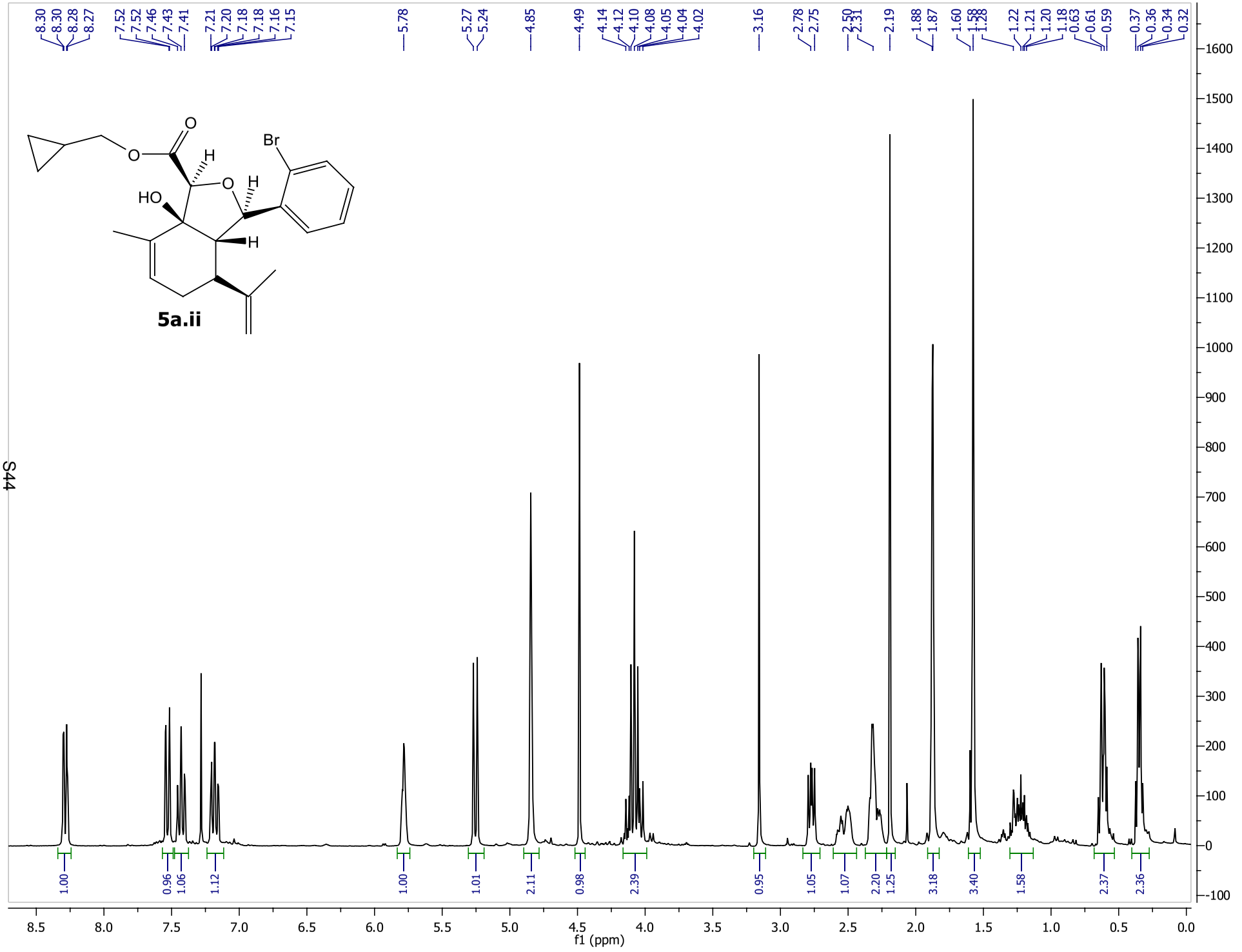

```
Current Data Parameters
NAME                  km-1354
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20080210
Time                    9.05
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                zgpg30
TD                      36230
SOLVENT                CDCl3
NS                        2000
DS                           4
SWH                18115.941 Hz
FIDRES                0.500026 Hz
AQ                    0.9999980 sec
RG                    23170.5
DW                     27.600 usec
DE                      6.00 usec
TE                     297.0 K
D1                    2.00000000 sec
D11                   0.03000000 sec
DELTA                 1.89999998 sec
MCREST                0.00000000 sec
MCWRK                 0.01500000 sec

======== CHANNEL f1 ========
NUC1                       13C
P1                        8.38 usec
PL1                      -2.80 dB
SFO1                75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   80.00 usec
PL2                      -1.00 dB
PL12                     15.33 dB
PL13                     16.00 dB
SFO2               300.1312005 MHz

F2 - Processing parameters
SI                         32768
SF                 75.4677348 MHz
WDW                           EM
SSB                            0
LB                          1.00 Hz
GB                             0
PC                          1.40

1D NMR plot parameters
CX                         20.00 cm
CY                         10.00 cm
F1P                       220.206 ppm
F1                      16618.44 Hz
F2P                       0.000 ppm
F2                        0.00 Hz
PPMCM                  11.01030 ppm/cm
HZCM                 830.92206 Hz/cm
```

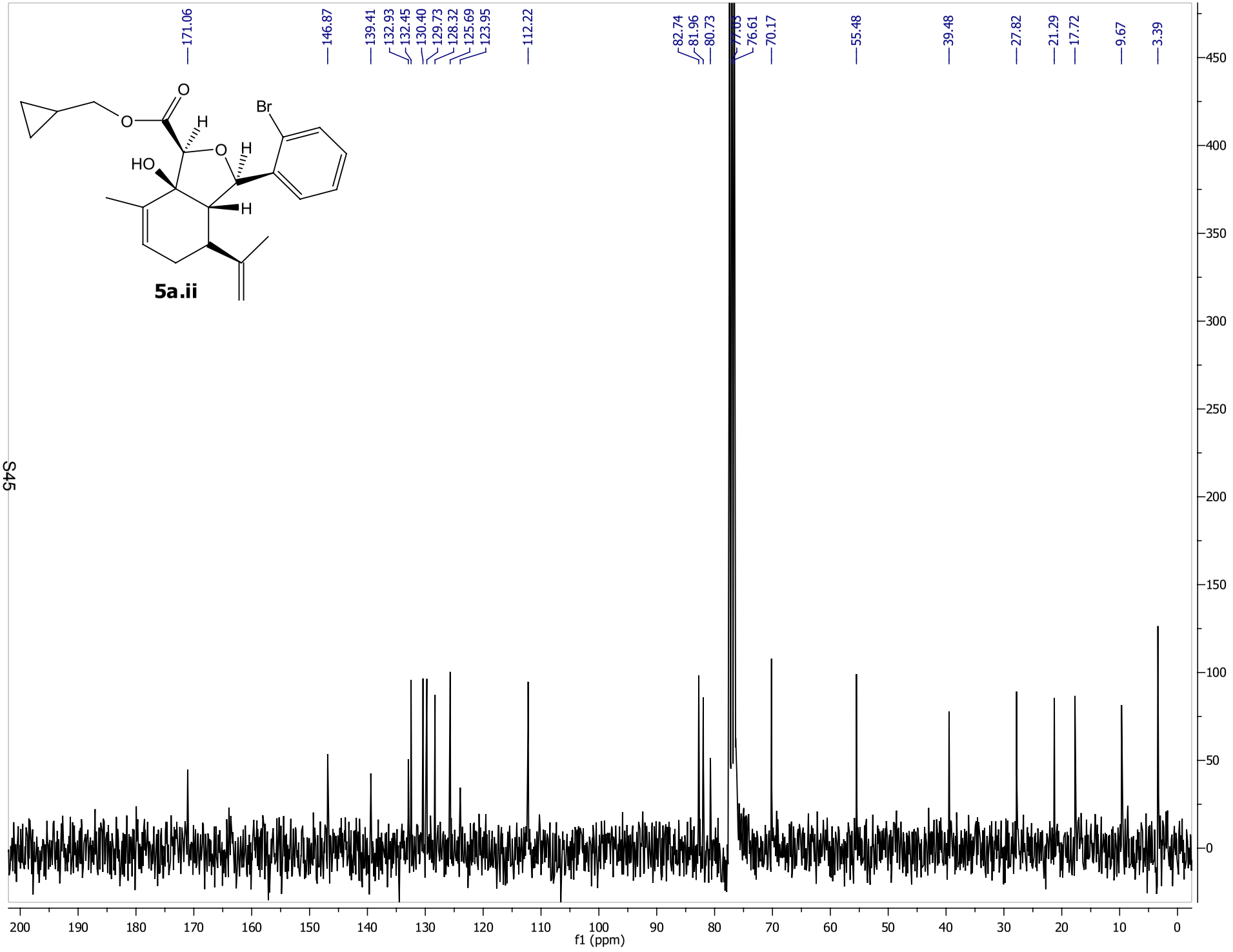

1.33
1.35
1.37
1.57
1.59
1.86
2.30
2.32
2.52
2.74
2.76
3.08
4.26
4.27
4.28
4.30
4.32
4.33
4.34
4.34
4.46
4.83
4.84
5.23
5.25
5.78
7.16
7.16
7.17
7.19
7.20
7.41
7.43
7.45
7.51
7.53
8.26
8.27
8.28
3.25
3.79
3.49
2.32
1.19
1.12
0.87
2.06
0.94
2.30
1.01
1.02
1.02
0.96
0.85
1.00
f1 (ppm)
Br
O
H
HO
O
O
5a

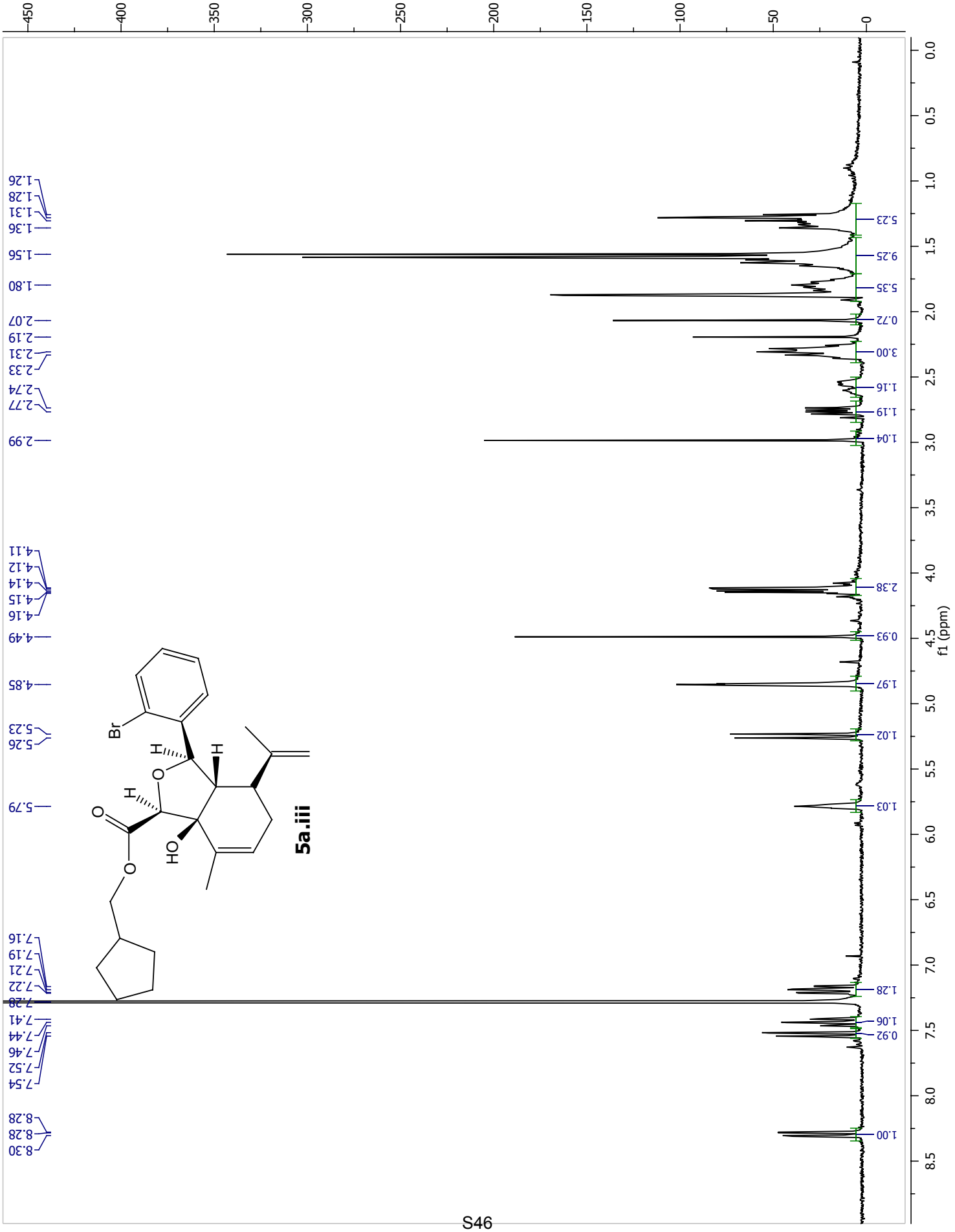

171.07
147.03
139.47
132.50
129.79
128.38
125.68
123.94
112.20
82.67
81.93
80.71
77.62
77.15
76.67
61.39
55.54
39.13
27.76
21.46
17.77
14.23
O
O
H
O
H
Br
HO
H
5a
f1 (ppm)

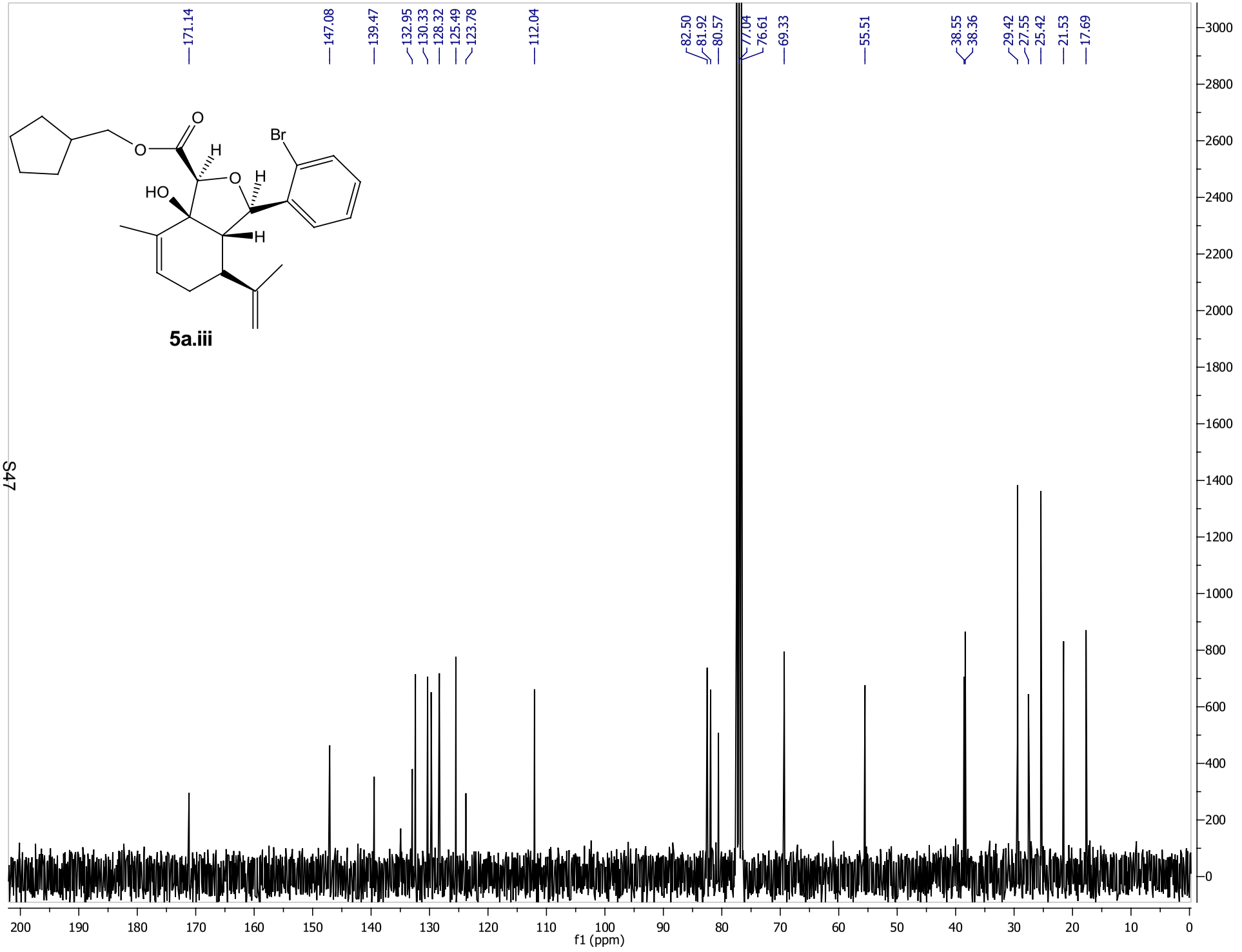

8.31
8.31
8.29
8.28
7.53
7.52
7.48
7.45
7.43
7.22
7.22
7.20
7.19
7.17
7.17
5.79
5.27
5.24
4.86
4.85
4.85
4.51
3.85
2.93
2.75
2.55
2.35
2.30
1.88
1.87
1.59
1.57
O
O
HO
O
Br
H
5a.i
1.00
0.94
1.01
1.11
1.00
1.01
2.04
0.96
2.89
0.89
1.07
1.11
2.13
3.04
4.75
f1 (ppm)

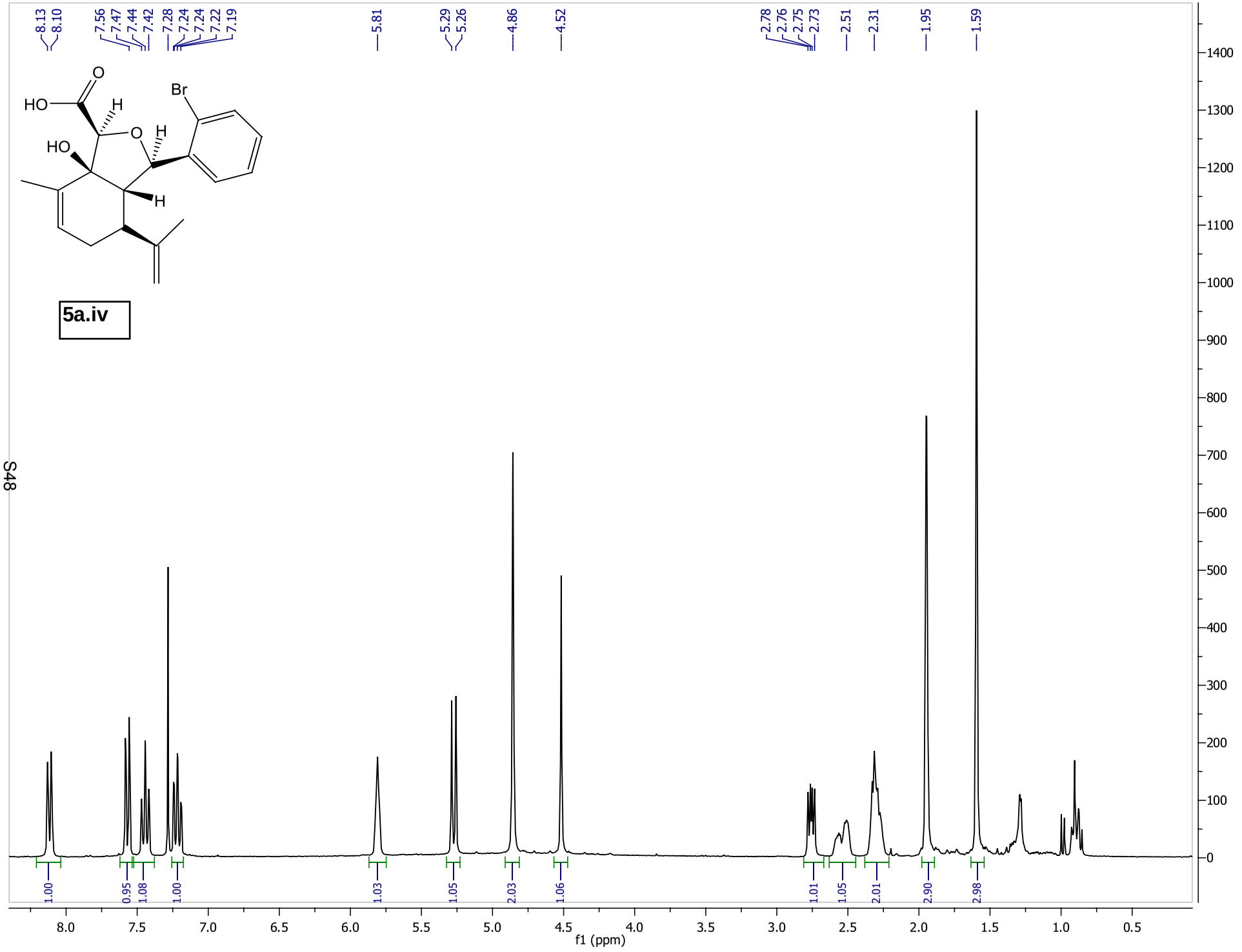

171.54
147.20
139.28
132.46
130.27
129.79
128.39
125.67
123.84
112.00
82.51
81.76
80.50
76.62
73.47
55.22
52.22
38.31
27.49
21.61
17.67
O
O
Br
HO
O
H
5a.i
f1 (ppm)

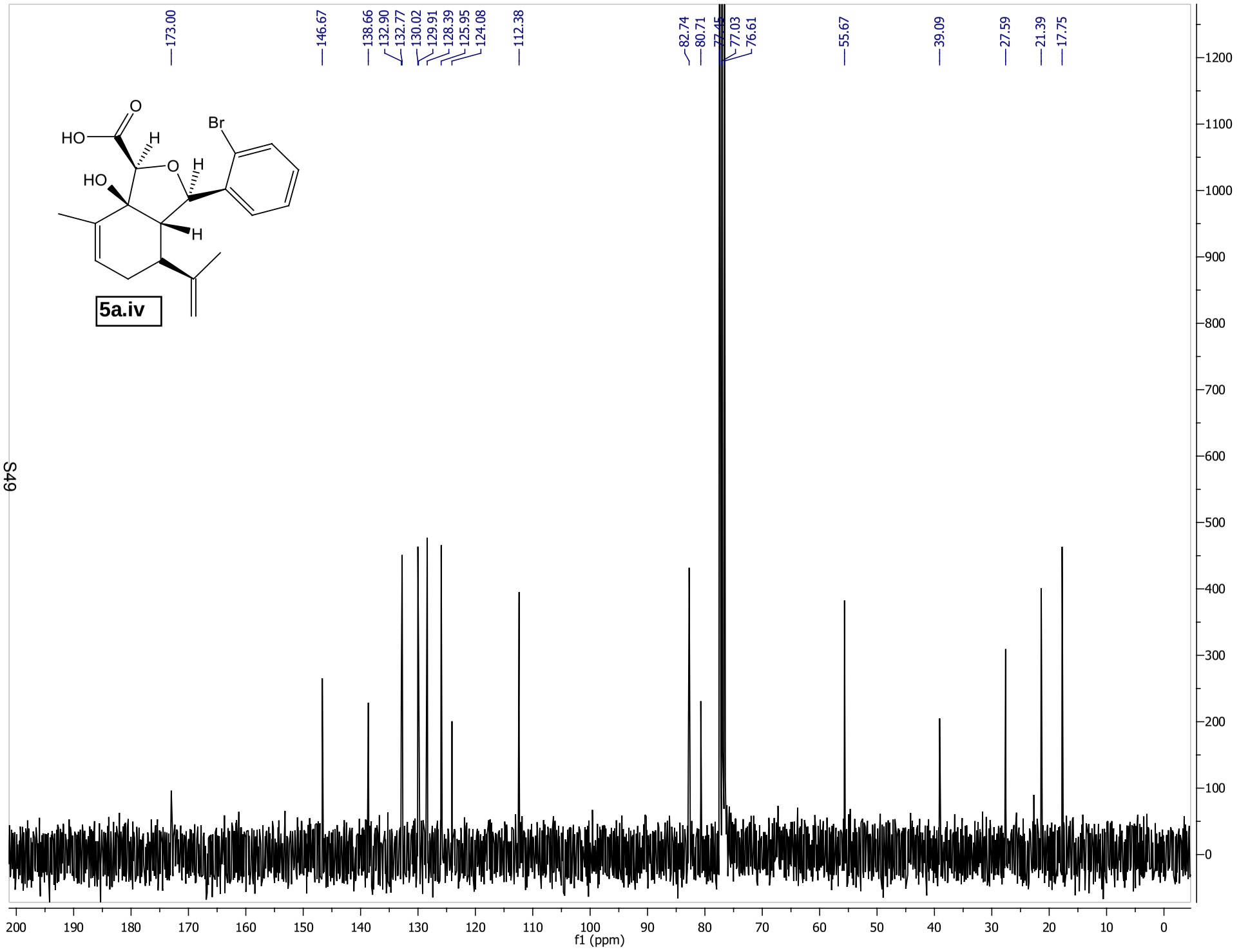

8.30
8.30
8.28
8.27
7.52
7.52
7.46
7.43
7.41
7.21
7.20
7.18
7.18
7.16
7.15
5.78
5.27
5.24
4.85
4.49
4.14
4.12
4.10
4.08
4.05
4.04
4.02
3.16
2.78
2.75
2.50
2.31
2.19
1.88
1.87
1.60
1.58
1.28
1.22
1.21
1.20
1.18
0.63
0.61
0.59
0.37
0.36
0.34
0.32
O
O
H
O
H
HO
Br
H
5a.ii
1.00
0.96
1.06
1.12
1.00
1.01
2.11
0.98
2.39
0.95
1.05
1.07
2.20
1.25
3.18
3.40
1.58
2.37
2.36
f1 (ppm)

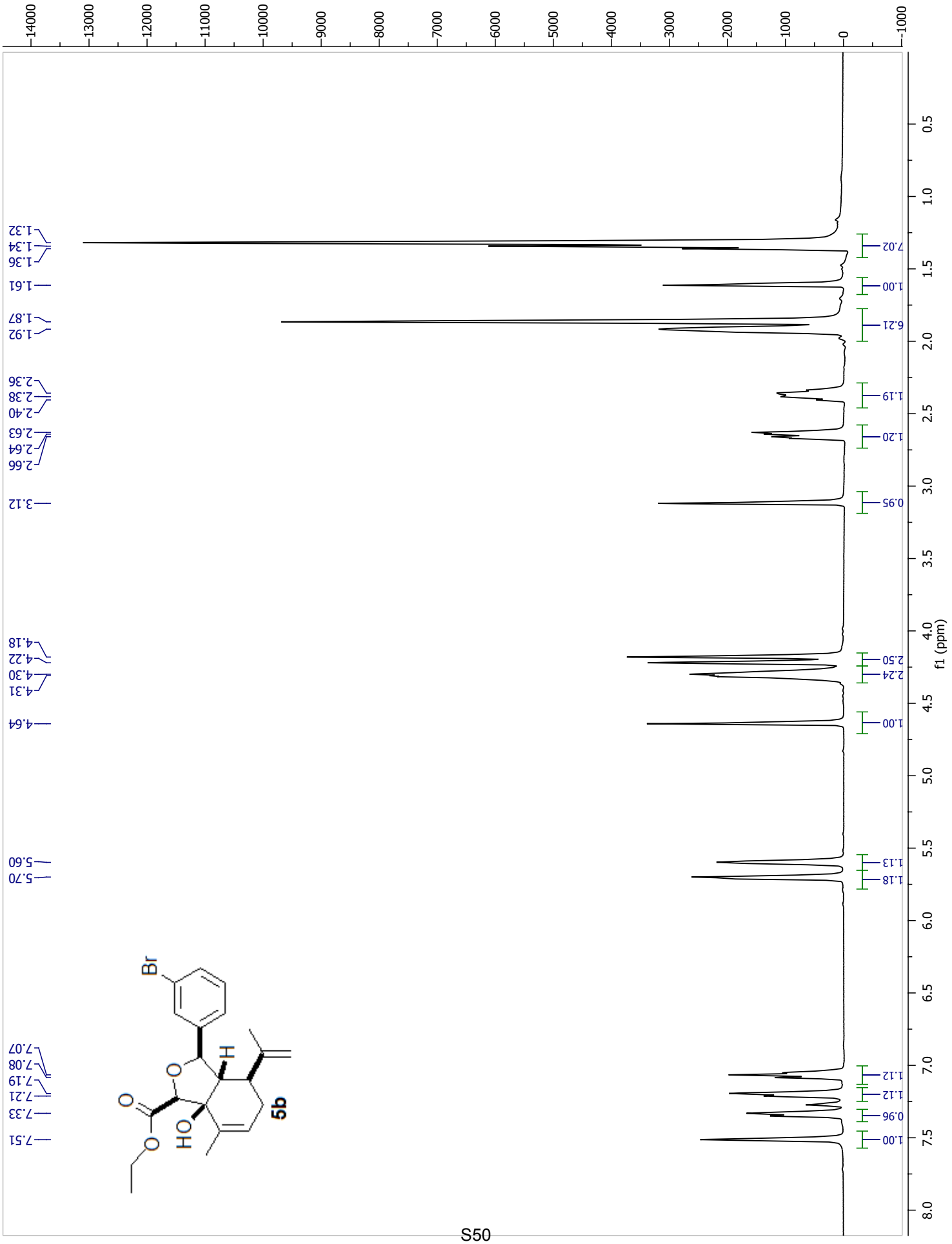

171.06
146.87
139.41
132.93
132.45
130.40
129.73
128.32
125.69
123.95
112.22
82.74
81.96
80.73
77.03
76.61
70.17
55.48
39.48
27.82
21.29
17.72
9.67
3.39
O
O
H
Br
O
H
HO
H
5a.ii
450
400
350
300
250
200
150
100
50
0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

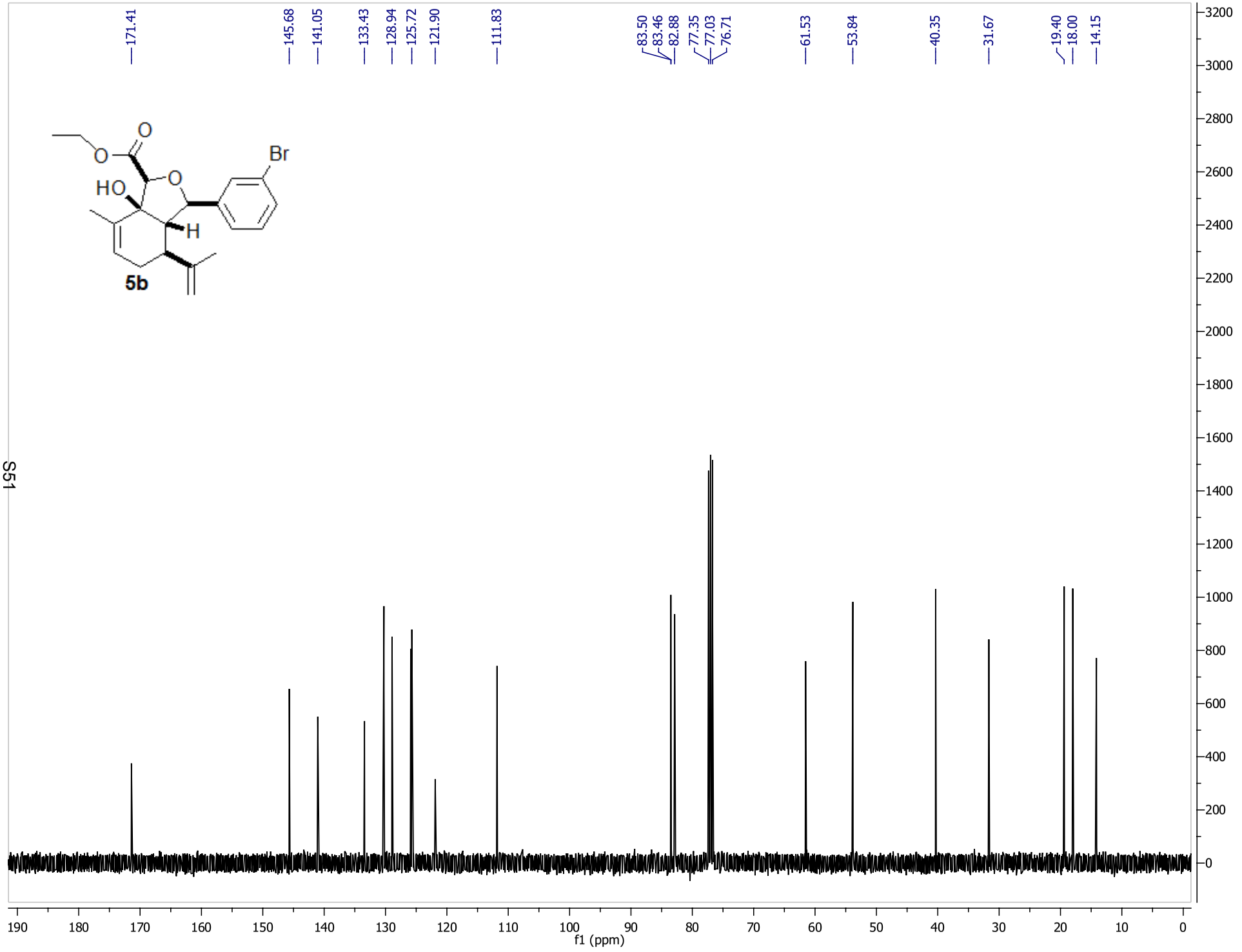

5a.iii
f1 (ppm)

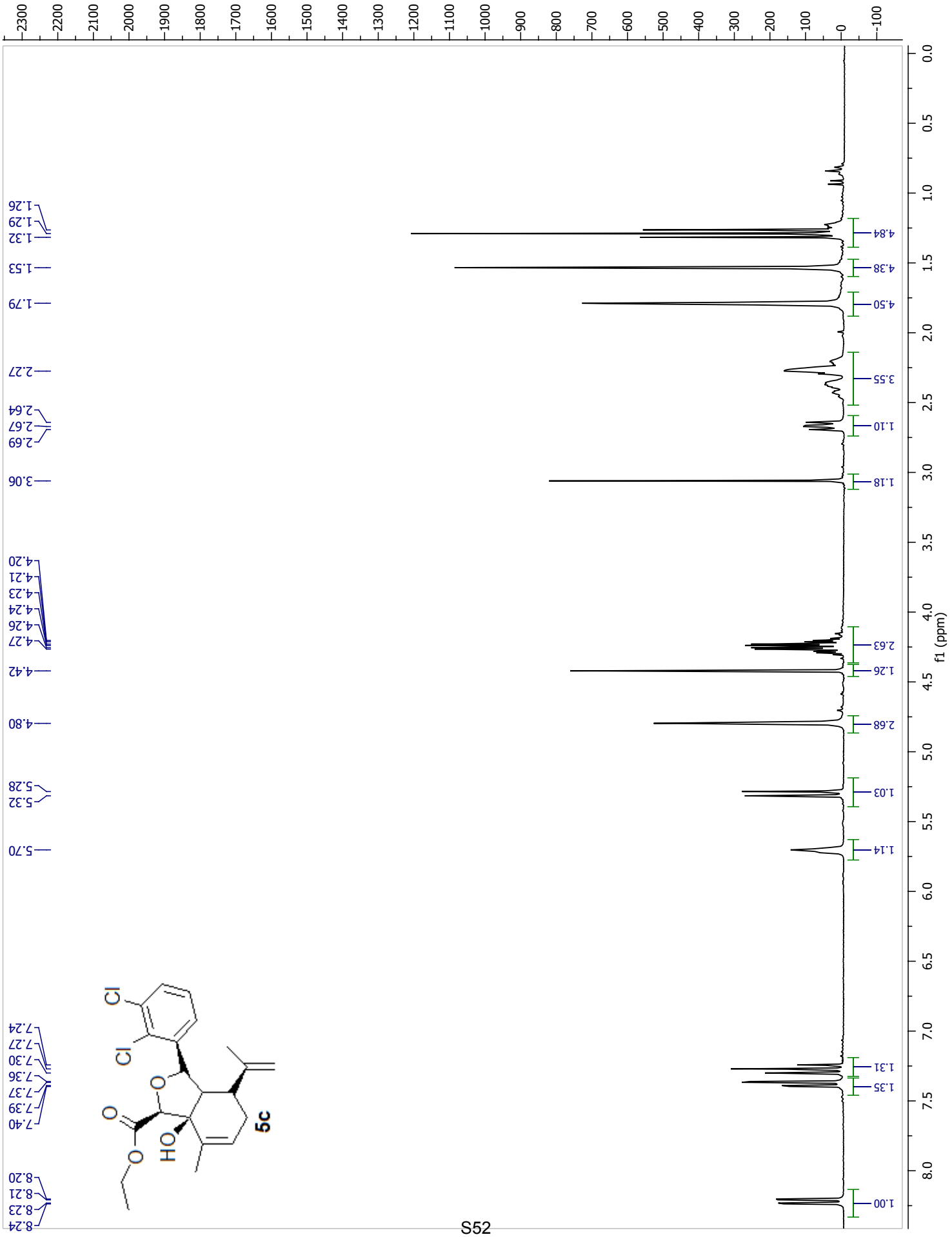

171.14
147.08
139.47
132.95
130.33
128.32
125.49
123.78
112.04
82.50
81.92
80.57
77.04
76.61
69.33
55.51
38.55
38.36
29.42
27.55
25.42
21.53
17.69
O
O
H
O
H
HO
H
Br
5a.iii
f1 (ppm)

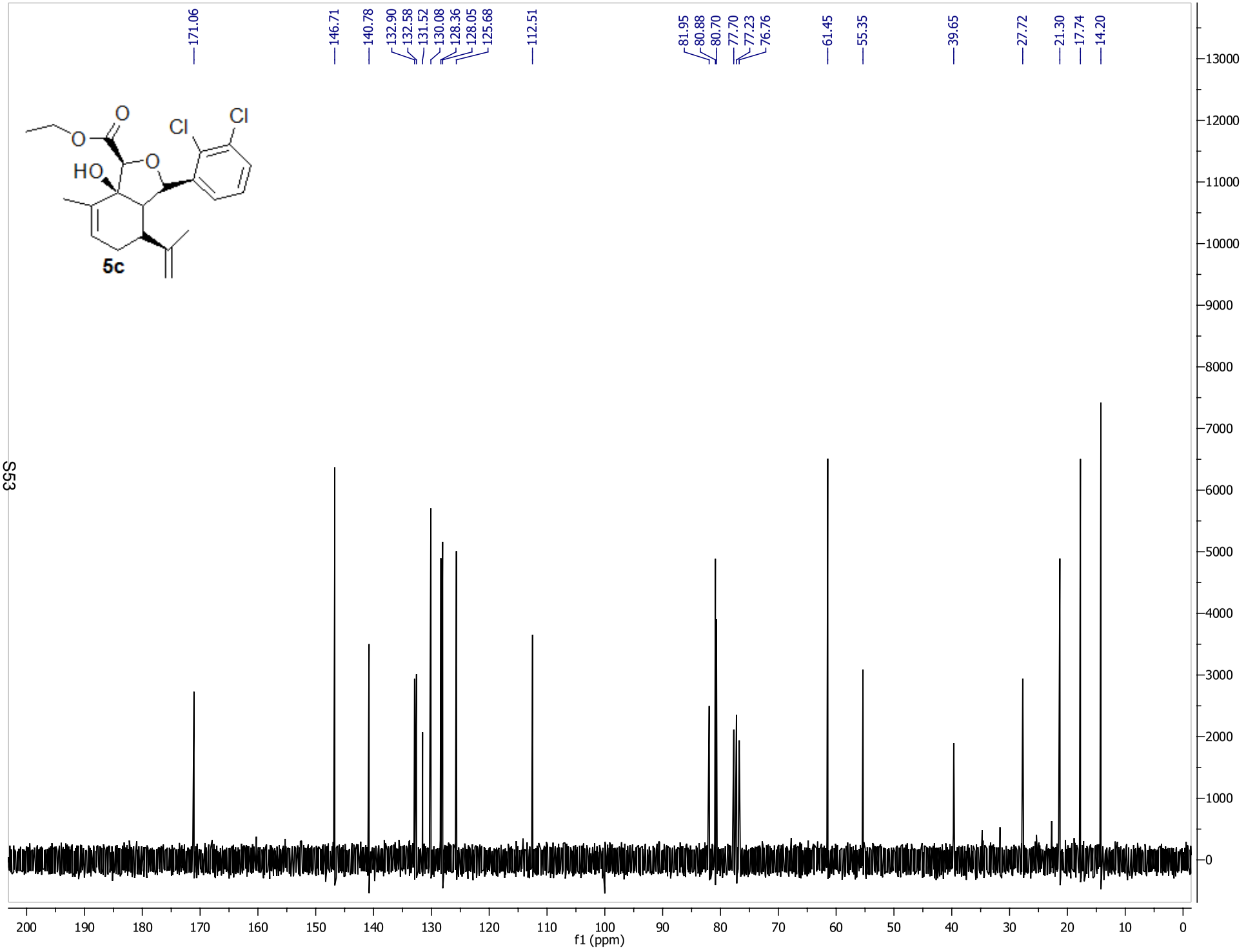

8.13
8.10
7.56
7.47
7.44
7.42
7.28
7.24
7.24
7.22
7.19
5.81
5.29
5.26
4.86
4.52
2.78
2.76
2.75
2.73
2.51
2.31
1.95
1.59
O
HO
H
Br
O
H
HO
H
5a.iv
1.00
0.95
1.08
1.00
1.03
1.05
2.03
1.06
1.01
1.05
2.01
2.90
2.98
f1 (ppm)

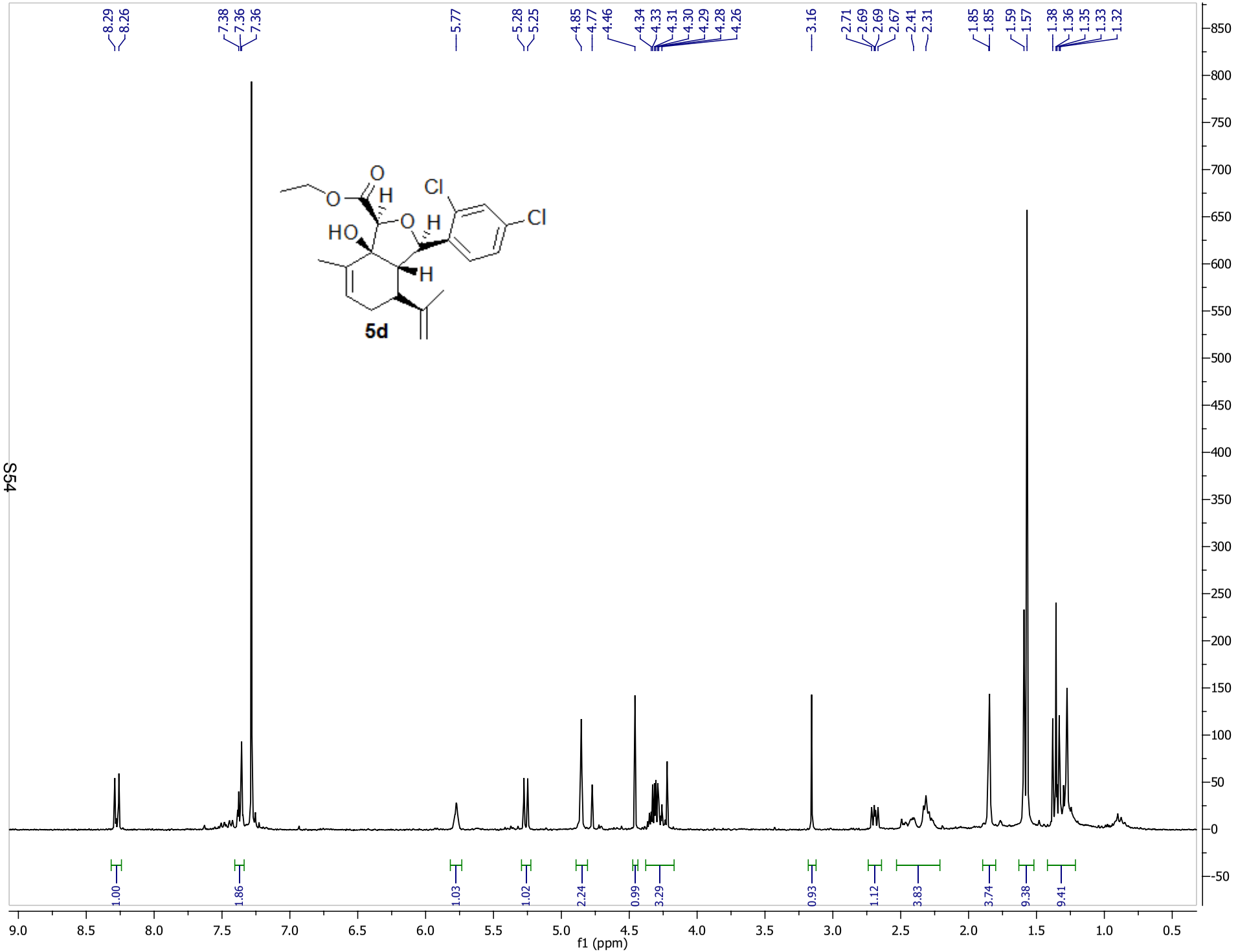

173.00
146.67
138.66
132.90
132.77
130.02
129.91
128.39
125.95
124.08
112.38
82.74
80.71
77.45
77.03
76.61
55.67
39.09
27.59
21.39
17.75
HO
O
H
Br
HO
O
H
H
5a.iv
f1 (ppm)

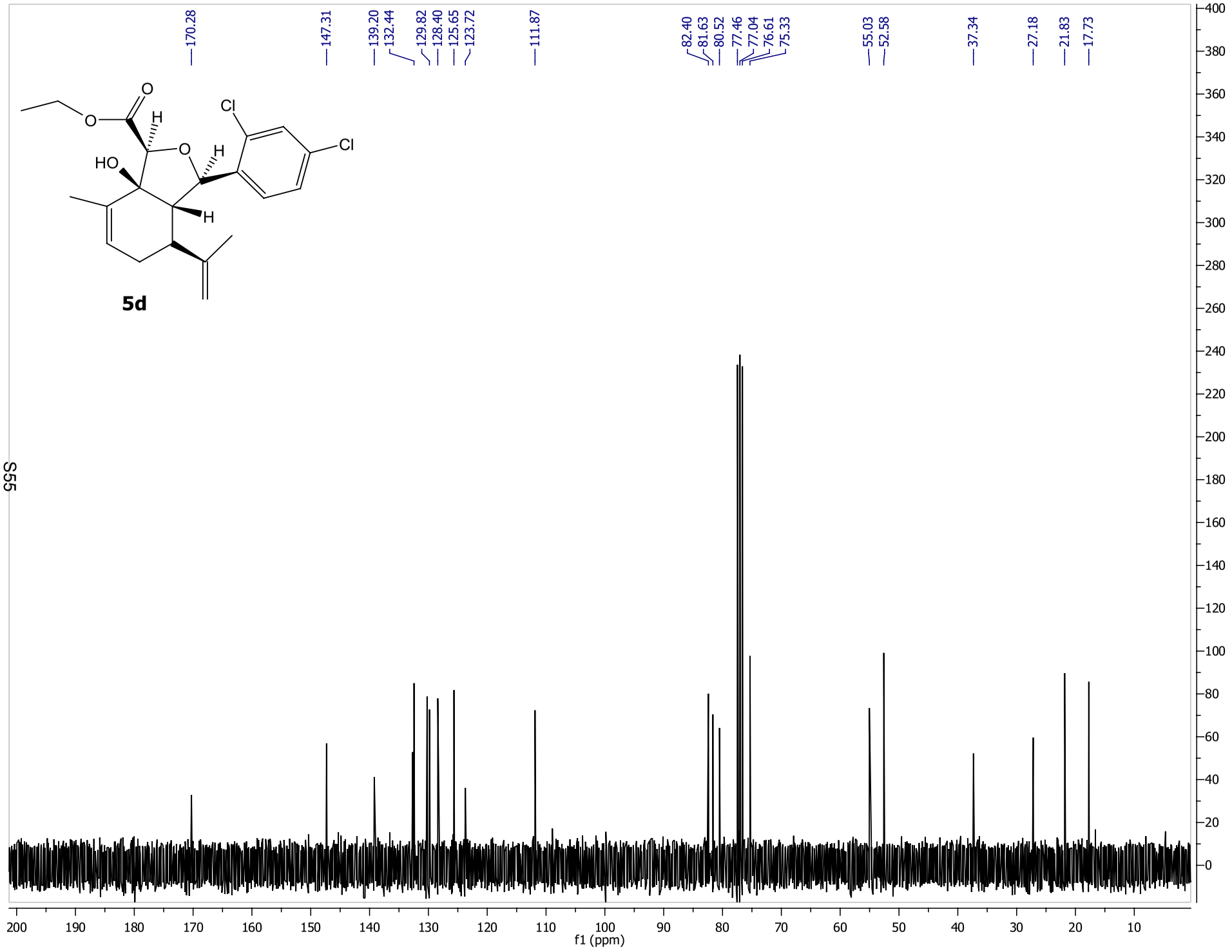

1.32
1.34
1.36
1.61
1.87
1.92
2.36
2.38
2.40
2.63
2.64
2.66
3.12
4.18
4.22
4.30
4.31
4.64
5.60
5.70
7.07
7.08
7.19
7.21
7.33
7.51
7.02
1.00
6.21
1.19
1.20
0.95
2.50
2.24
1.00
1.13
1.18
1.12
1.12
0.96
1.00
f1 (ppm)
Br
O
H
HO
O
O
5b

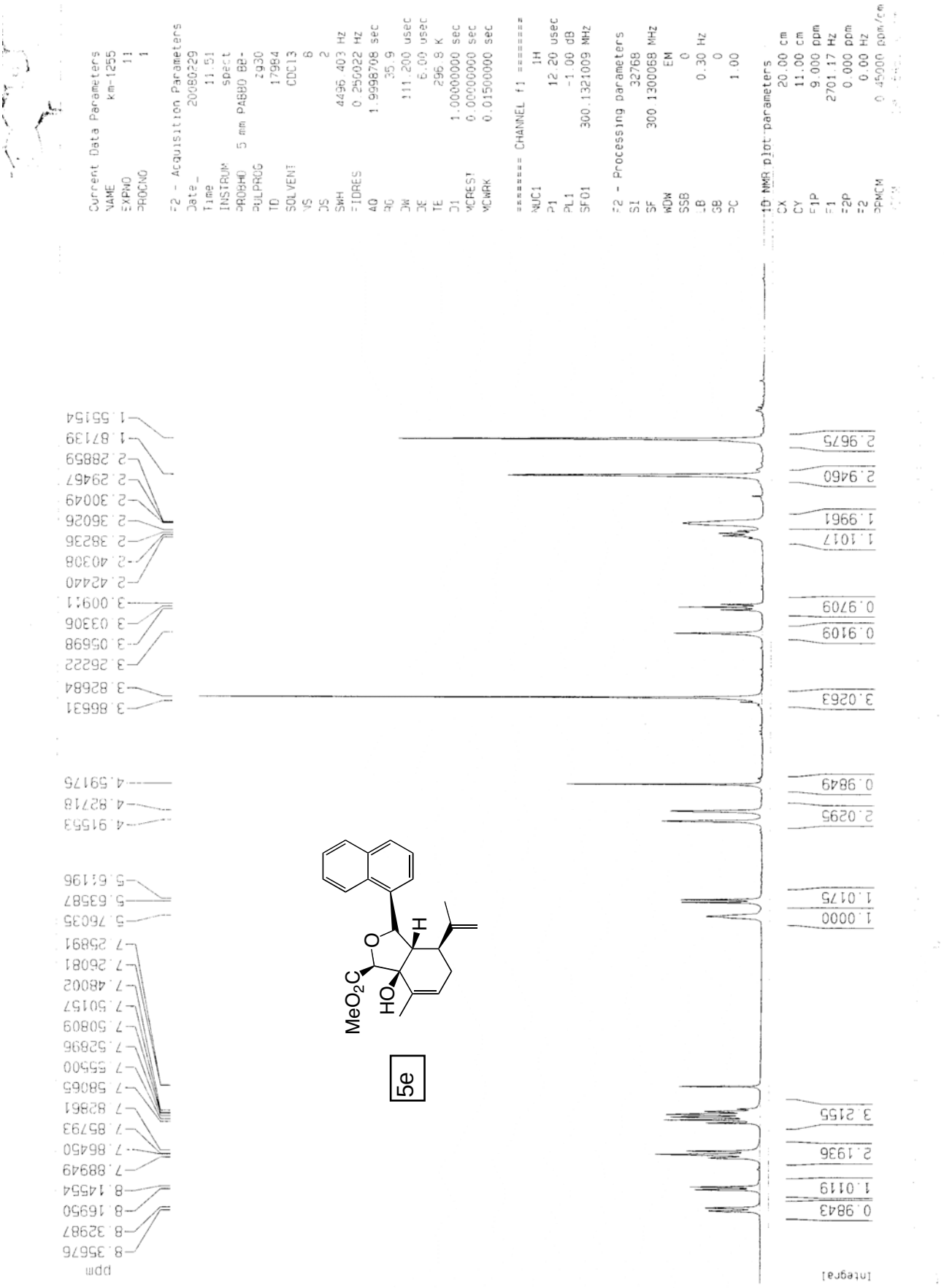

171.41
145.68
141.05
133.43
128.94
125.72
121.90
111.83
83.50
83.46
82.88
77.35
77.03
76.71
61.53
53.84
40.35
31.67
19.40
18.00
14.15
O
O
HO
O
Br
H
5b
f1 (ppm)

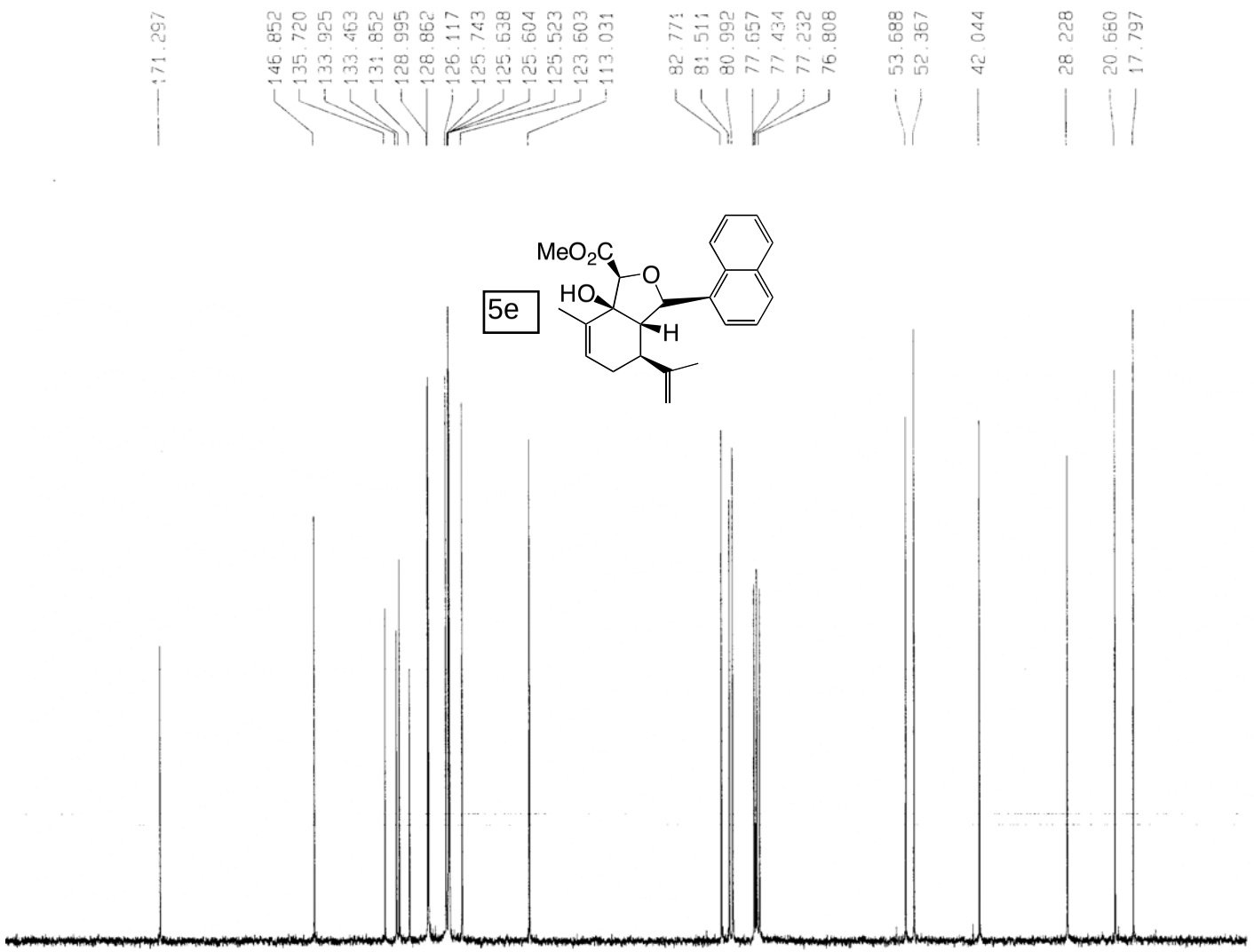

8.24
8.23
8.21
8.20
7.40
7.39
7.37
7.36
7.30
7.27
7.24
5.70
5.32
5.28
4.80
4.42
4.27
4.26
4.24
4.23
4.21
4.20
3.06
2.69
2.67
2.64
2.27
1.79
1.53
1.32
1.29
1.26
1.00
1.31
1.35
1.14
1.03
2.68
1.26
2.63
1.18
1.10
3.55
4.50
4.38
4.84
Cl
Cl
O
O
O
HO
5c
f1 (ppm)


171.06
146.71
140.78
132.90
132.58
131.52
130.08
128.36
128.05
125.68
112.51
81.95
80.88
80.70
77.70
77.23
76.76
61.45
55.35
39.65
27.72
21.30
17.74
14.20
O
O
HO
O
Cl
Cl
5c
S53
f1 (ppm)


8.29
8.26
7.38
7.36
7.36
5.77
5.28
5.25
4.85
4.77
4.46
4.34
4.33
4.31
4.30
4.29
4.28
4.26
3.16
2.71
2.69
2.69
2.67
2.41
2.31
1.85
1.85
1.59
1.57
1.38
1.36
1.35
1.33
1.32
O
O
H
Cl
HO
O
H
Cl
H
5d
1.00
1.86
1.03
1.02
2.24
0.99
3.29
0.93
1.12
3.83
3.74
9.38
9.41
f1 (ppm)


170.28
147.31
139.20
132.44
129.82
128.40
125.65
123.72
111.87
82.40
81.63
80.52
77.46
77.04
76.61
75.33
55.03
52.58
37.34
27.18
21.83
17.73
O
O
H
O
H
HO
H
Cl
Cl
5d
S55
f1 (ppm)


MeO2C
HO
H
O
5e



Current Data Parameters
NAME km-1255
EXPNO 10
PROCNO 1

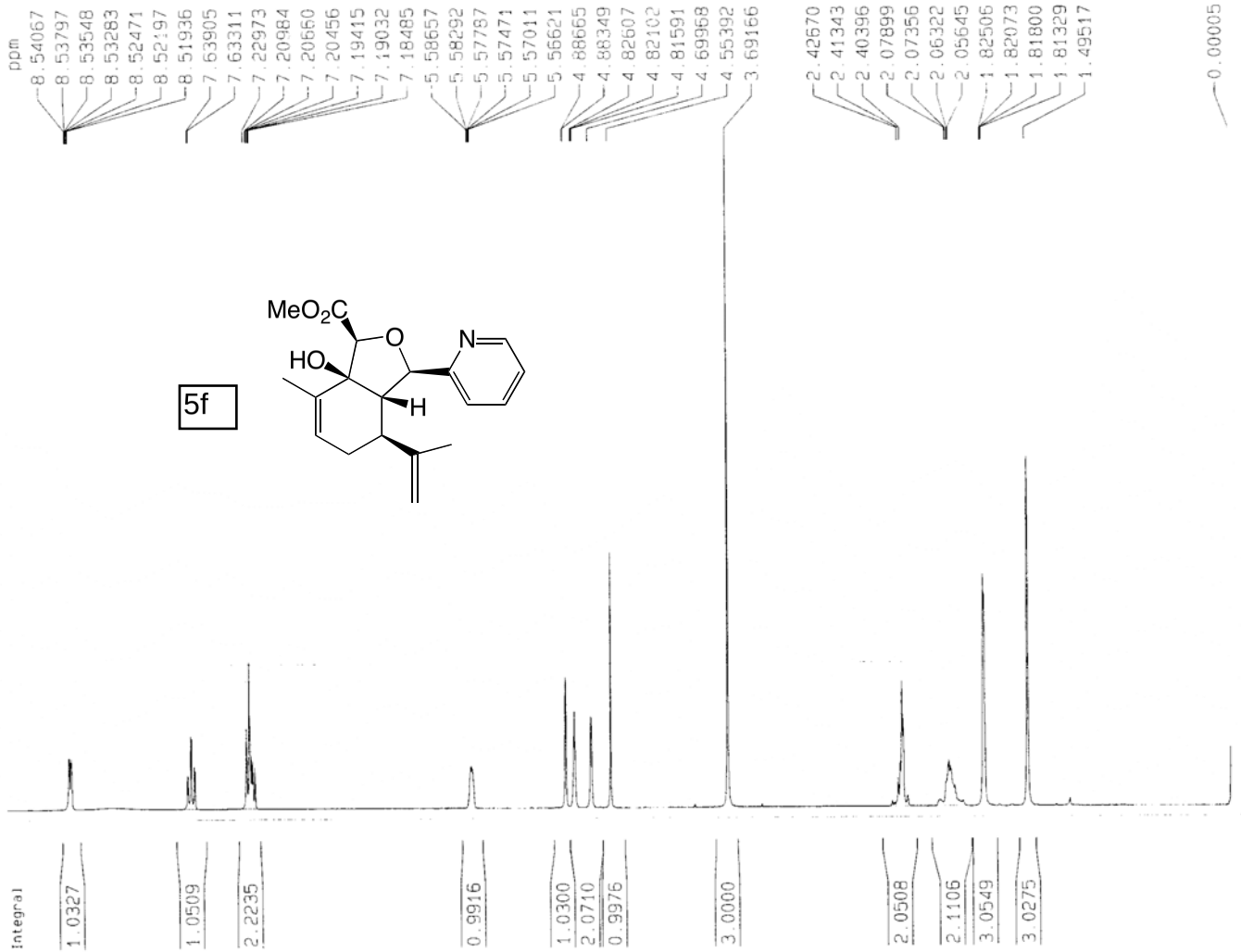
F2 - Acquisition Parameters
Date_ 20080229
Time 11.48
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 32606
SOLVENT CDCl3
NS 400
DS 4
SWH 18115.941 Hz
FIDRES 0.555601 Hz
AQ 0.8999756 sec
RG 23170.5
DW 27.600 usec
DE 6.00 usec
TE 297.1 K
D1 2.00000000 sec
D11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 8.38 usec
PL1 -2.80 dB
SFO1 75.4760505 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -1.00 dB
PL12 15.33 dB
PL13 16.00 dB
SFO2 300.1312005 MHz

F2 - Processing parameters
SI 32768
SF 75.4677447 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 200.000 ppm
F1 15093.55 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 10.00000 ppm/cm
HZCM 1504.61035 Hz/cm



Current Data Parameters

NAME	km-1290
EXPNO	7
PROCNO	1

F2 - Acquisition Parameters

Date_	20080229
Time	17.51
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	37036
SOLVENT	CDCl3
NS	8
DS	2
SWH	6172.839 Hz
FIDRES	0.166671 Hz
AQ	2.9999659 sec
RG	57
DW	81.000 usec
DE	6.00 usec
TE	296.2 K
D1	1.00000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

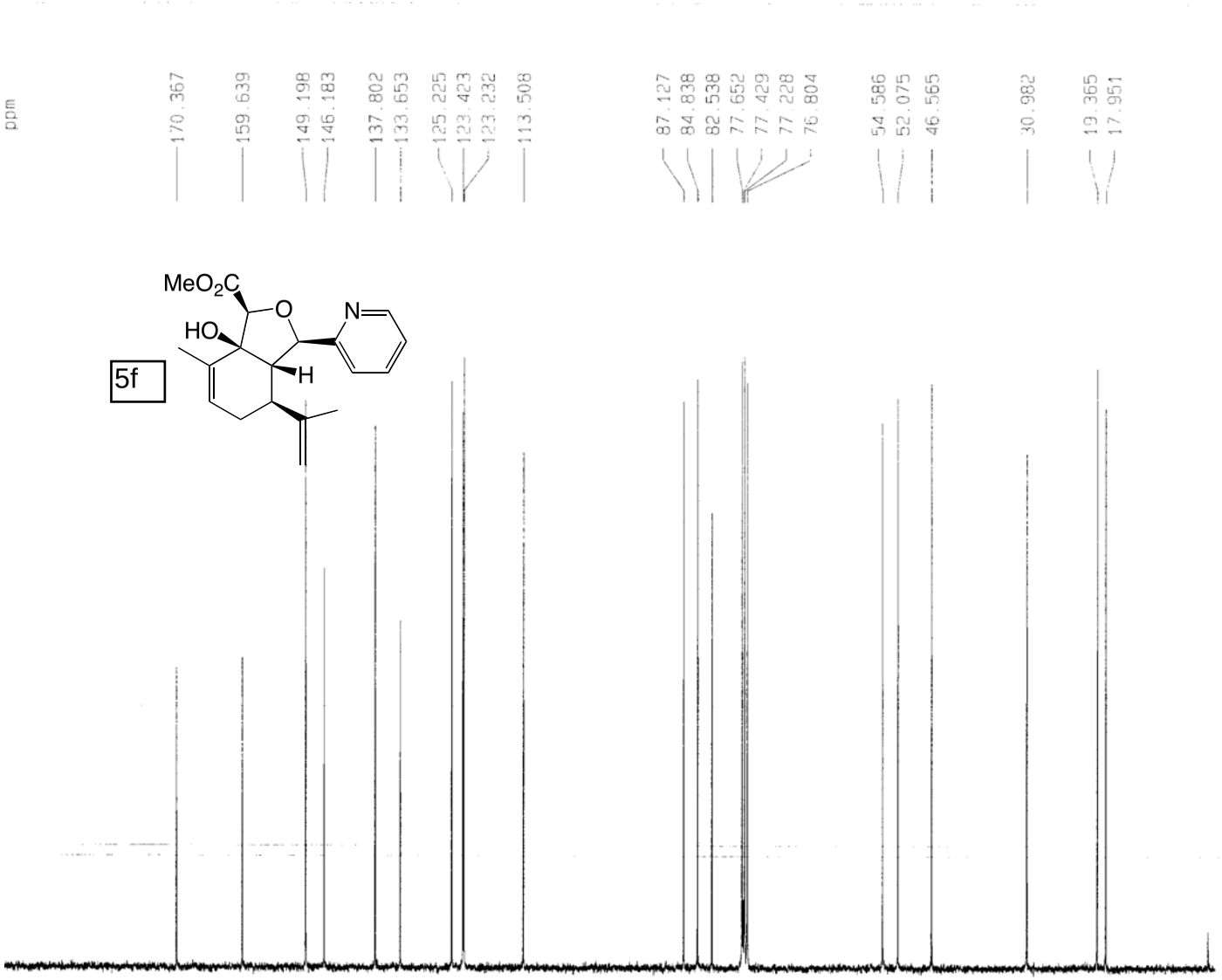
NUC1	1H
P1	12.20 usec
PL1	-1.00 dB
SFO1	300.1318534 MHz

F2 - Processing parameters

SI	32768
SF	300.1300218 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	9.000 ppm
F1	2701.17 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.45000 ppm/cm



Current Data Parameters
NAME km-1290
EXPNO 8
PROCNO 1

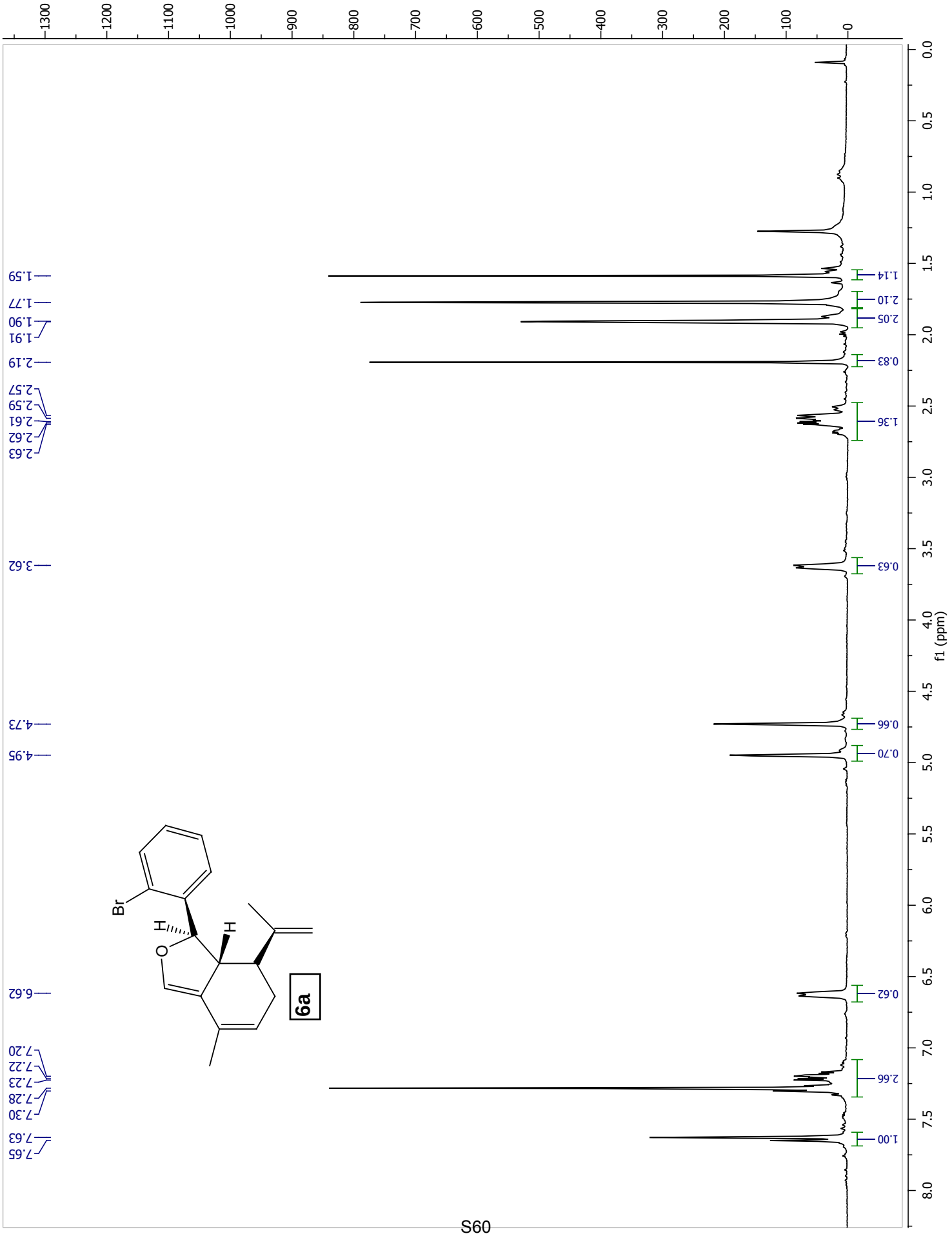
F2 - Acquisition Parameters
Date_ 20080229
Time 18.45
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 35968
SOLVENT CDCl3
NS 1024
DS 4
SWH 17985.611 Hz
FIDRES 0.500045 Hz
AQ 0.9999604 sec
RG 23170.5
DW 27.800 usec
DE 6.00 usec
TE 296.9 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

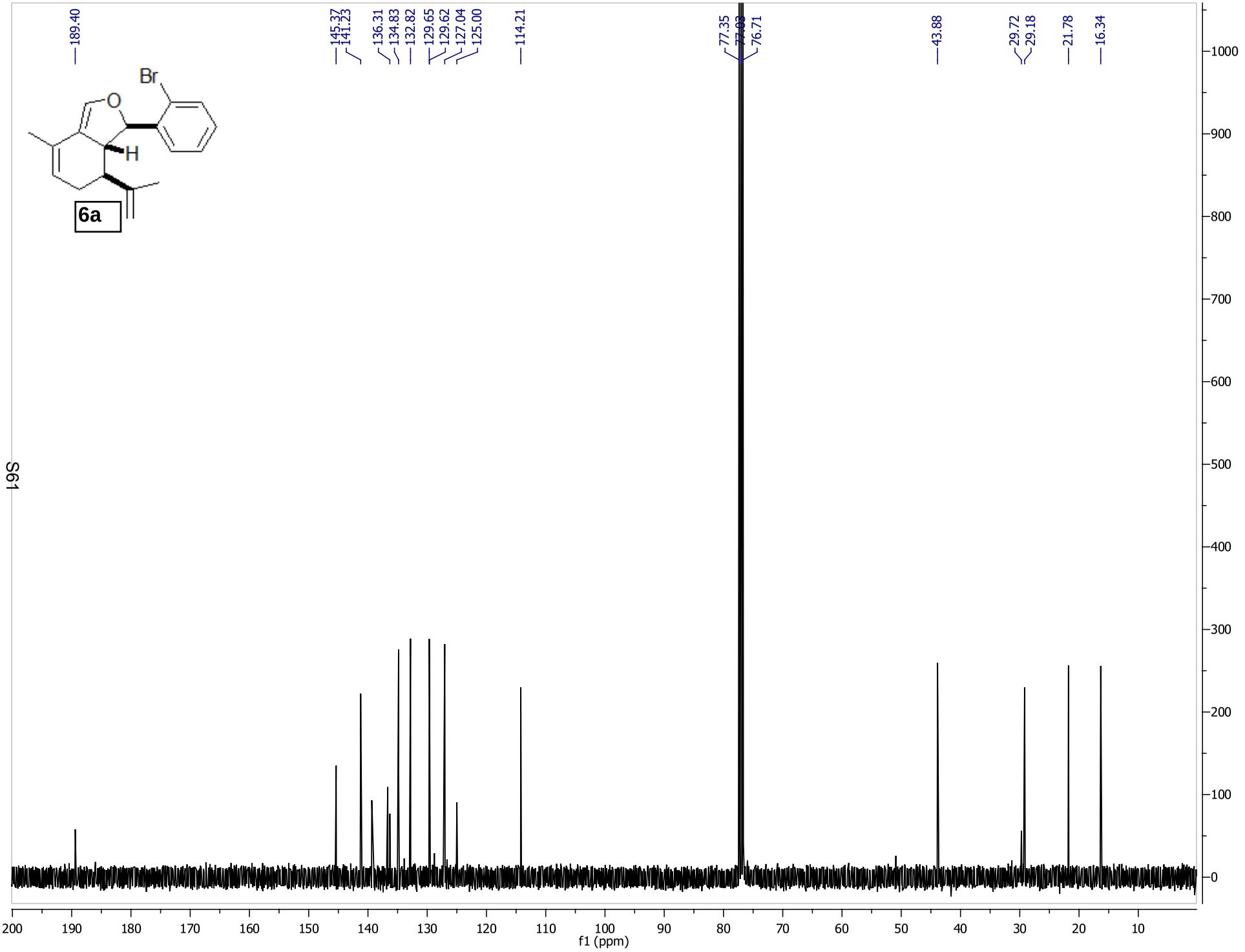
======== CHANNEL f1 ========
NUC1 13C
P1 8.38 usec
PL1 -2.80 dB
SFO1 75.4760505 MHz

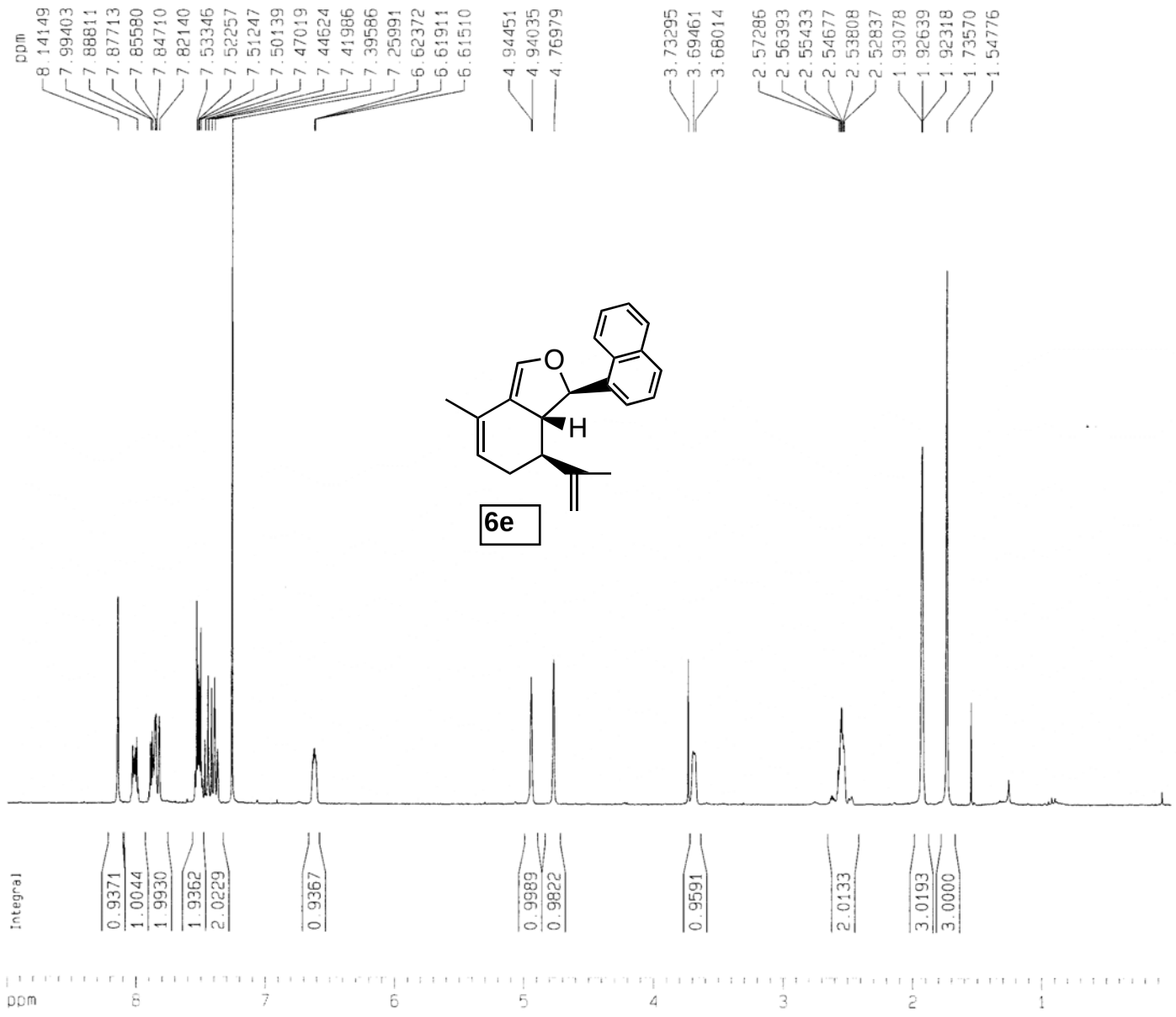
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -1.00 dB
PL12 15.33 dB
PL13 16.00 dB
SFO2 300.1312005 MHz

F2 - Processing parameters
SI 32768
SF 75.4677395 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 200.000 ppm


1.59
1.77
1.90
1.91
2.19
2.57
2.59
2.61
2.62
2.63
3.62
4.73
4.95
6.62
7.20
7.22
7.23
7.28
7.30
7.63
7.65
1.14
2.10
2.05
0.83
1.36
0.63
0.66
0.70
0.62
2.66
1.00
Br
H
O
H
6a
f1 (ppm)


189.40
145.37
141.23
136.31
134.83
132.82
129.65
129.62
127.04
125.00
114.21
77.35
77.03
76.71
43.88
29.72
29.18
21.78
16.34
Br
O
H
6a
S61
f1 (ppm)



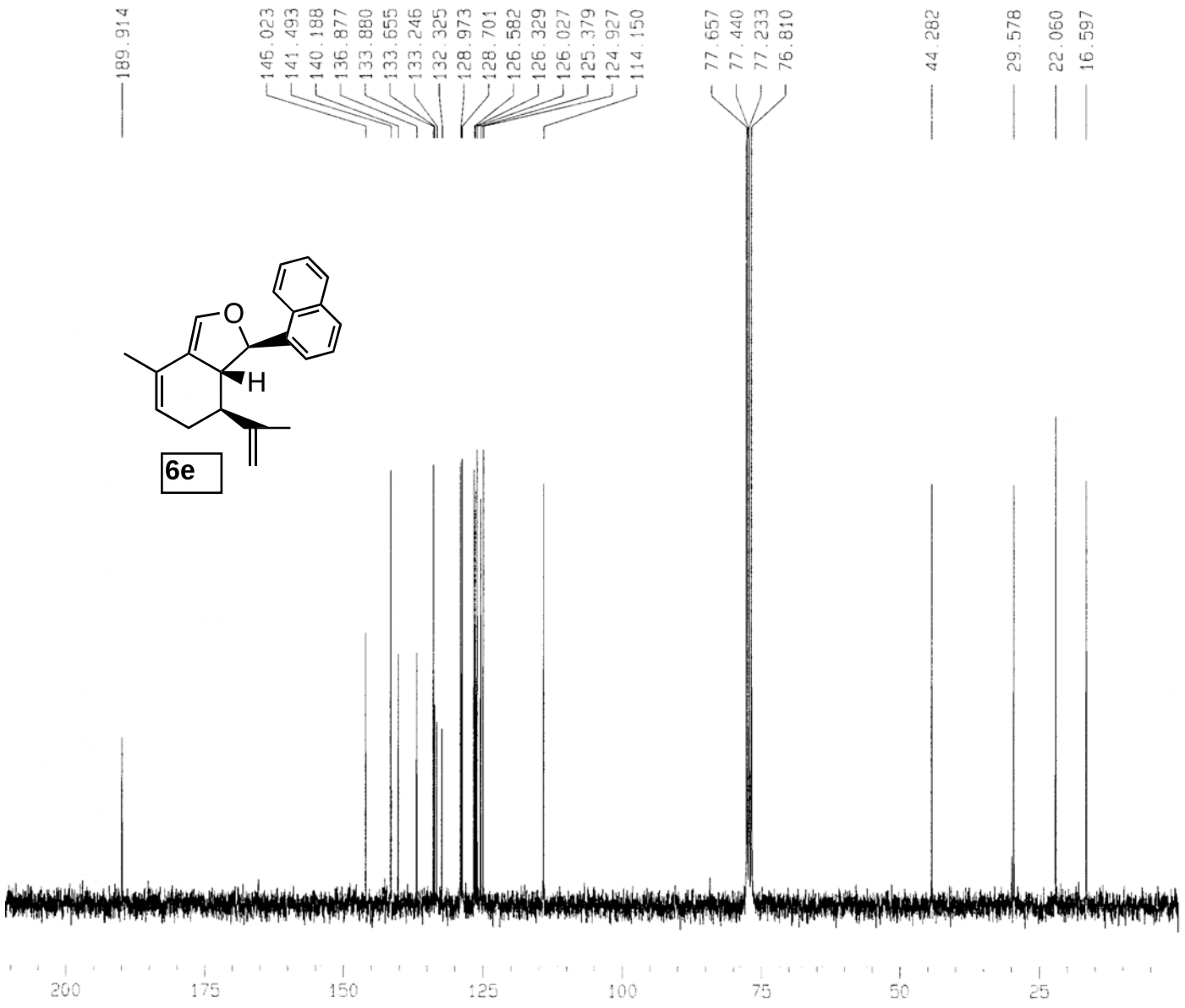
Current Data Parameters
NAME km-1257
EXPNO 9
PROCNO 1

F2 - Acquisition Parameters
Date_ 20071017
Time 9.07
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 17984
SOLVENT CDCl3
NS 32
DS 2
SWH 4496.403 Hz
FIDRES 0.250022 Hz
AQ 1.9998708 sec
RG 456.1
DW 111.200 usec
DE 6.00 usec
TE 296.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

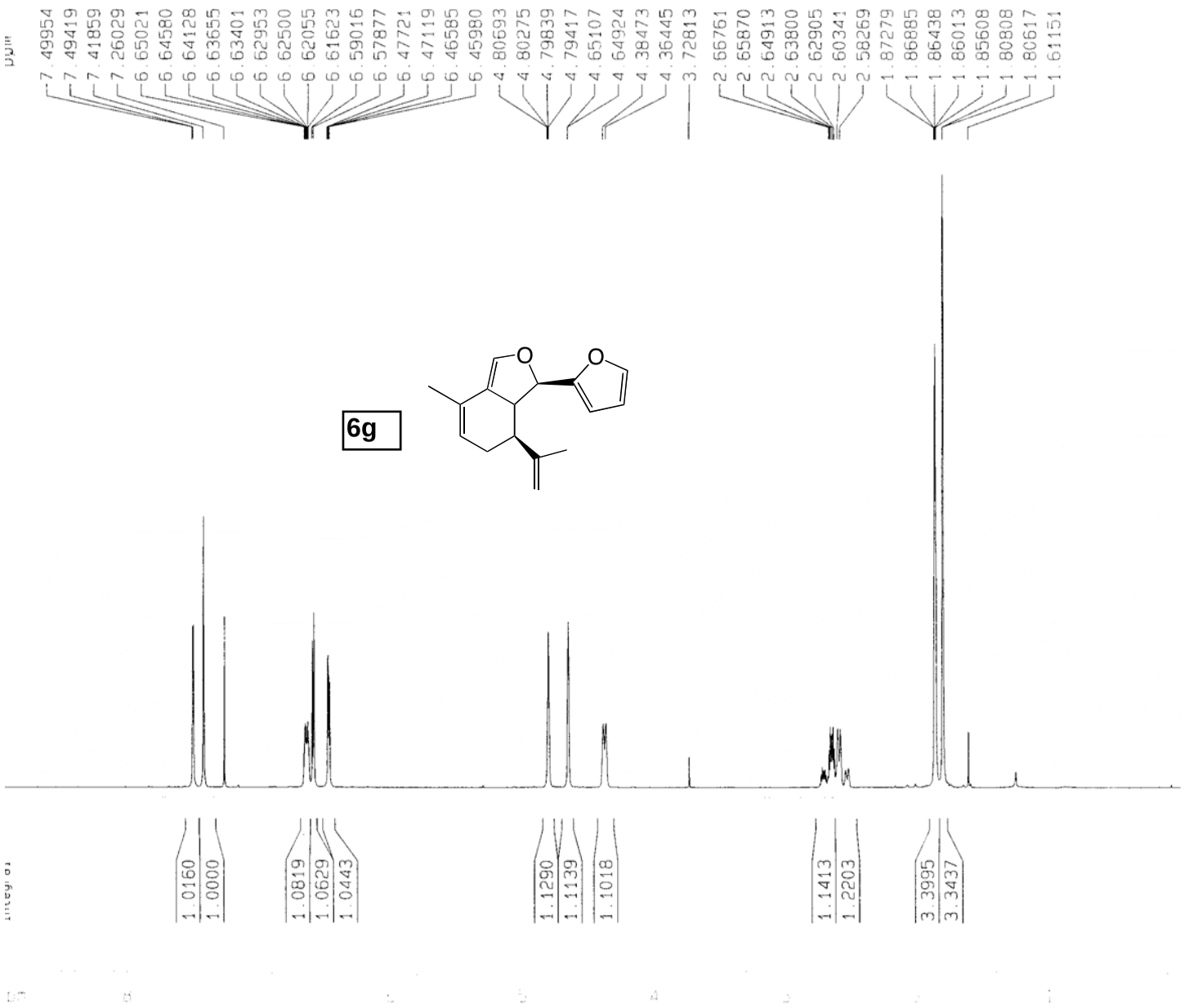
======== CHANNEL f1 ========
NUC1 1H
P1 12.20 usec
PL1 -0.60 dB
SFO1 300.1321009 MHz

F2 - Processing parameters
SI 32768
SF 300.1300068 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 12.00 cm
F1P 9.000 ppm
F1 2701.17 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm




```
Current Data Parameters
NAME                  km-1257
EXPNO                       8
PROCNO                      1

F2 - Acquisition Parameters
Date_              20071021
Time                   11.27
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zgpg30
TD                      35968
SOLVENT                CDCl3
NS                       1024
DS                          4
SWH               18115.941 Hz
FIDRES             0.503668 Hz
AQ                 0.9927668 sec
RG                      26008
DW                   27.600 usec
DE                    6.00 usec
TE                   297.0 K
D1                2.00000000 sec
D11               0.03000000 sec
DELTA             1.89999998 sec
MCREST            0.00000000 sec
MCWRK             0.01500000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                     8.38 usec
PL1                   -2.80 dB
SFO1             75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                80.00 usec
PL2                   -0.60 dB
PL12                  15.73 dB
PL13                  16.00 dB
SFO2            300.1312005 MHz

F2 - Processing parameters
SI                       32768
SF               75.4677337 MHz
WDW                         EM
SSB                          0
LB                    1.00 Hz
GB                           0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
CY                    8.00 cm
F1P                220.221 ppm
F1                16619.54 Hz
F2P                 -0.000 ppm
F2                   -0.00 Hz
PPMCM             11.01103 ppm/cm
HZCM             830.97717 Hz/cm
```



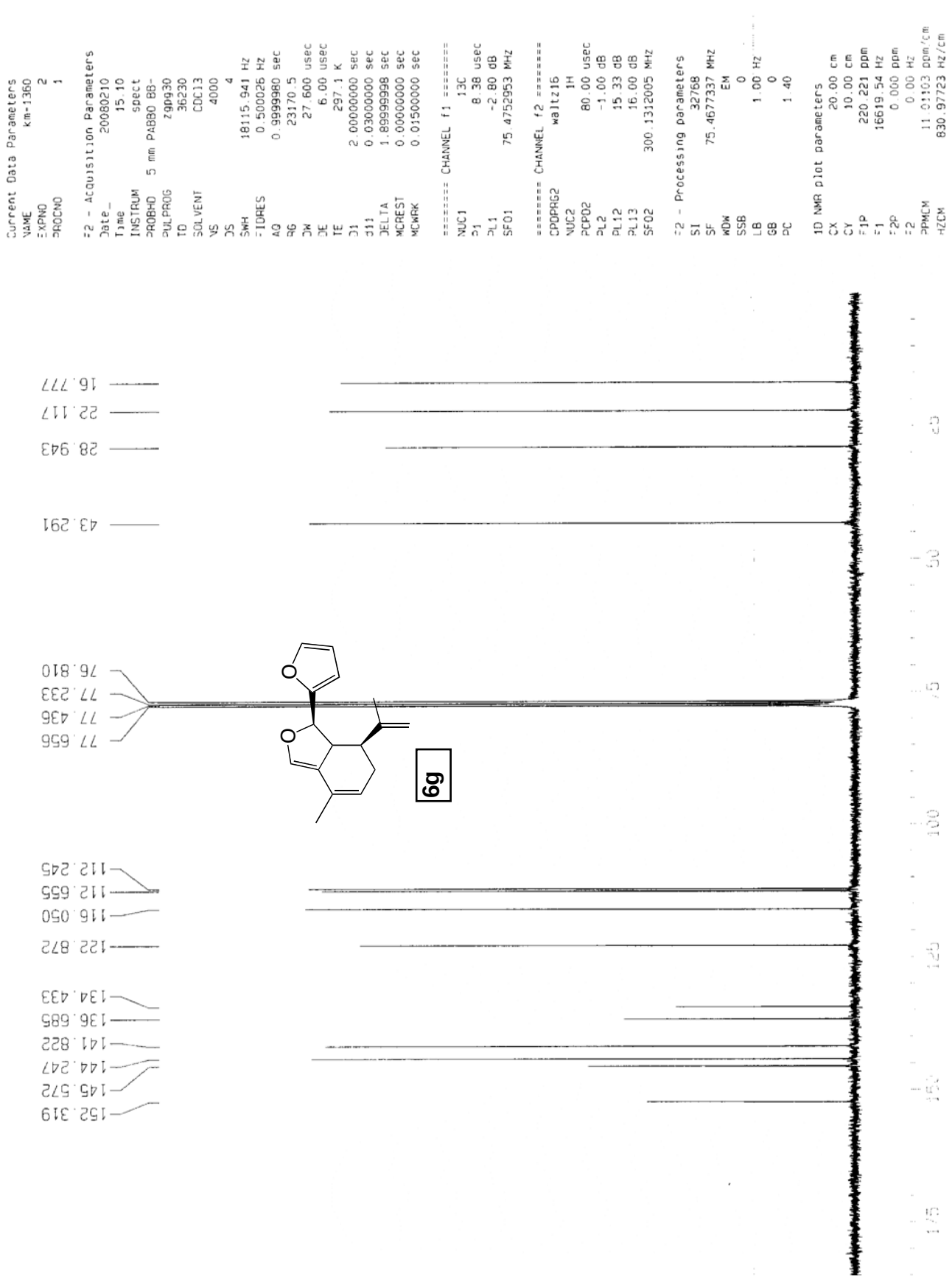
Current Data Parameters
NAME km-1360
EXPNO 2
PROCNO 1

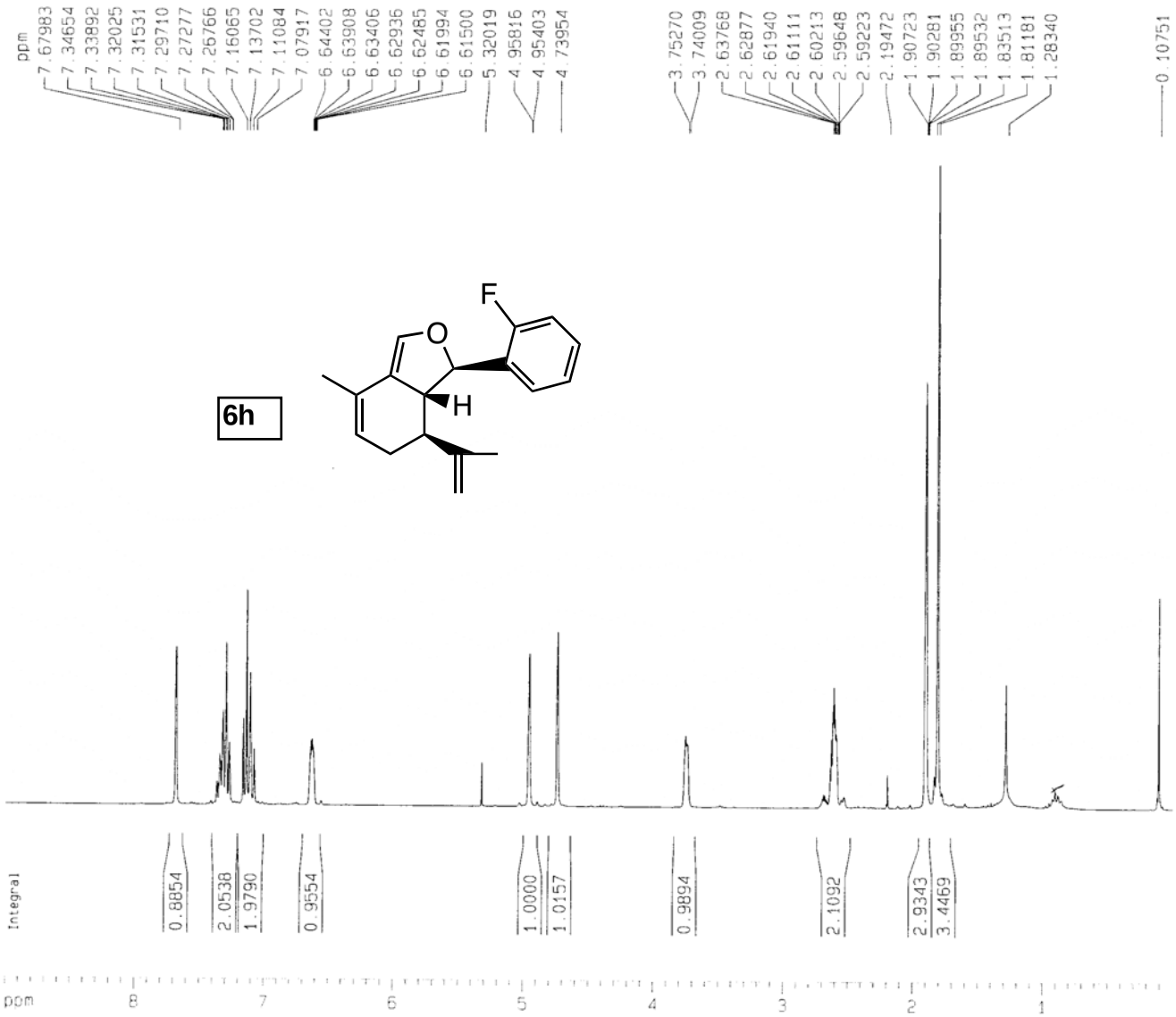
F2 - Acquisition Parameters
Date_ 20080207
Time 16.57
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 23980
SOLVENT CDCl3
NS 16
DS 2
SWH 5995.204 Hz
FIDRES 0.250008 Hz
AQ 1.9999820 sec
RG 256
DW 83.400 usec
DE 6.00 usec
TE 296.4 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 12.20 usec
PL1 -1.00 dB
SFO1 300.1318608 MHz

F2 - Processing parameters
SI 32768
SF 300.1300066 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 9.000 ppm
F1 2701.17 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.45000 ppm/cm
HZCM [illegible]


Current Data Parameters
NAME km-1360
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080210
Time 15.10
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 36230
SOLVENT CDCl3
NS 4000
DS 4
SWH 18115.941 Hz
FIDRES 0.500026 Hz
AQ 0.9999980 sec
RG 23170.5
DW 27.600 usec
DE 6.00 usec
TE 297.1 K
D1 2.00000000 sec
D11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 8.38 usec
PL1 -2.80 dB
SFO1 75.4752953 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -1.00 dB
PL12 15.33 dB
PL13 16.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677337 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 220.221 ppm
F1 16619.54 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 11.01103 ppm/cm
HZCM 830.97723 Hz/cm
16.777
22.117
28.943
43.291
76.810
77.233
77.436
77.656
112.245
112.655
116.050
122.872
134.433
136.685
141.822
144.247
145.572
152.319
6g



Current Data Parameters

NAME	km-1245
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20071006
Time	10.17
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	17984
SOLVENT	CDCl3
NS	8
DS	2
SWH	4496.403 Hz
FIDRES	0.250022 Hz
AQ	1.9998708 sec
RG	71.8
DW	111.200 usec
DE	6.00 usec
TE	296.3 K
D1	1.00000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

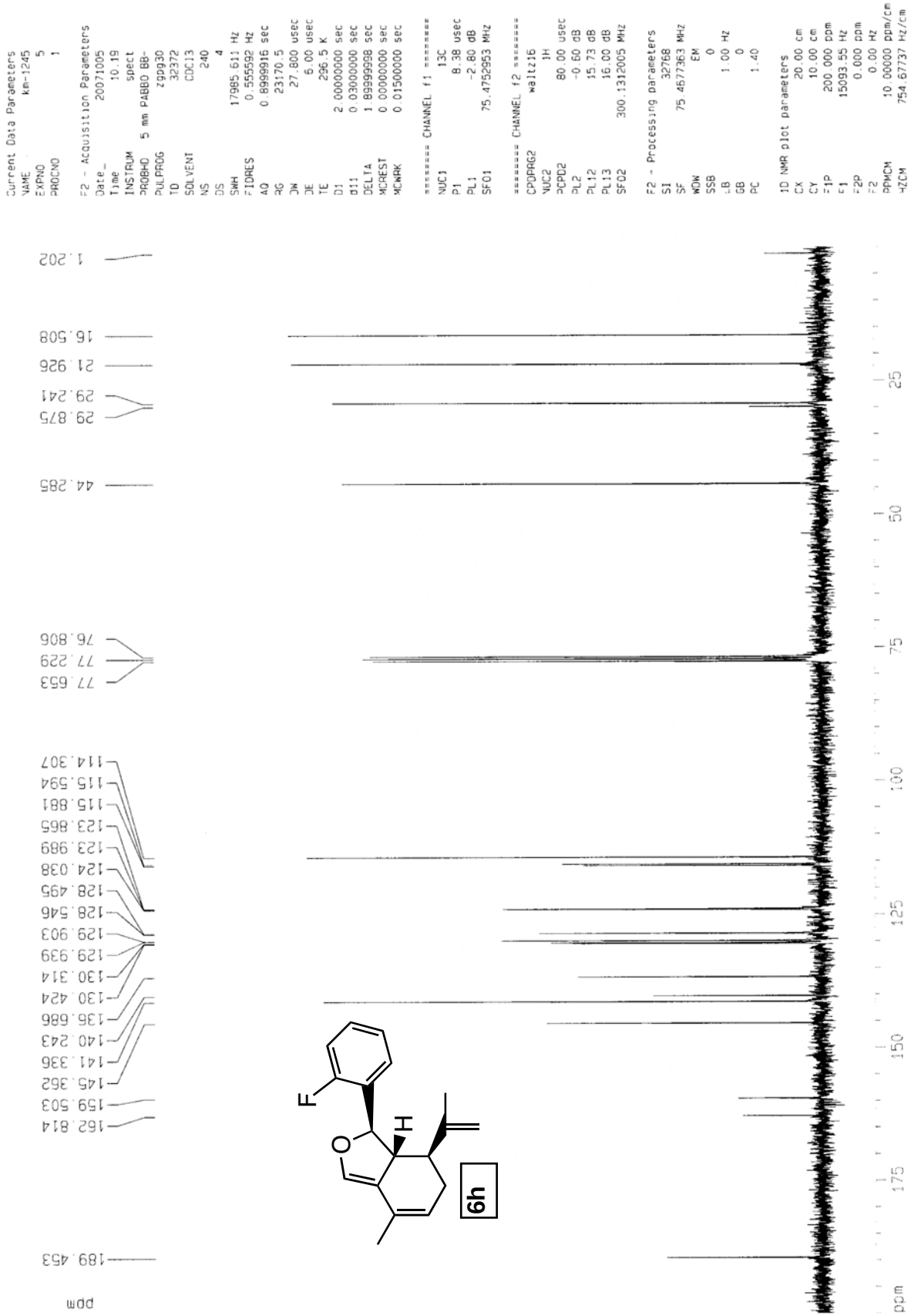
NUC1	1H
P1	12.20 usec
PL1	-0.60 dB
SFO1	300.1321009 MHz

F2 - Processing parameters

SI	32768
SF	300.1299955 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	11.00 cm
F1P	9.000 ppm
F1	2701.17 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm


Current Data Parameters
NAME km-1245
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071005
Time 10.19
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 32372
SOLVENT CDCl3
NS 240
DS 4
SWH 17985.611 Hz
FIDRES 0.555592 Hz
AQ 0.8999916 sec
RG 23170.5
DW 27.800 usec
DE 6.00 usec
TE 296.5 K
D1 2.00000000 sec
D11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 8.38 usec
PL1 -2.80 dB
SFO1 75.4752953 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -0.60 dB
PL12 15.73 dB
PL13 16.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677363 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 200.000 ppm
F1 15093.55 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 10.00000 ppm/cm
HZCM 754.67737 Hz/cm
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21.926
29.241
29.875
44.285
76.806
77.229
77.653
114.307
115.594
115.881
123.865
123.989
124.038
128.495
128.546
129.903
129.939
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F
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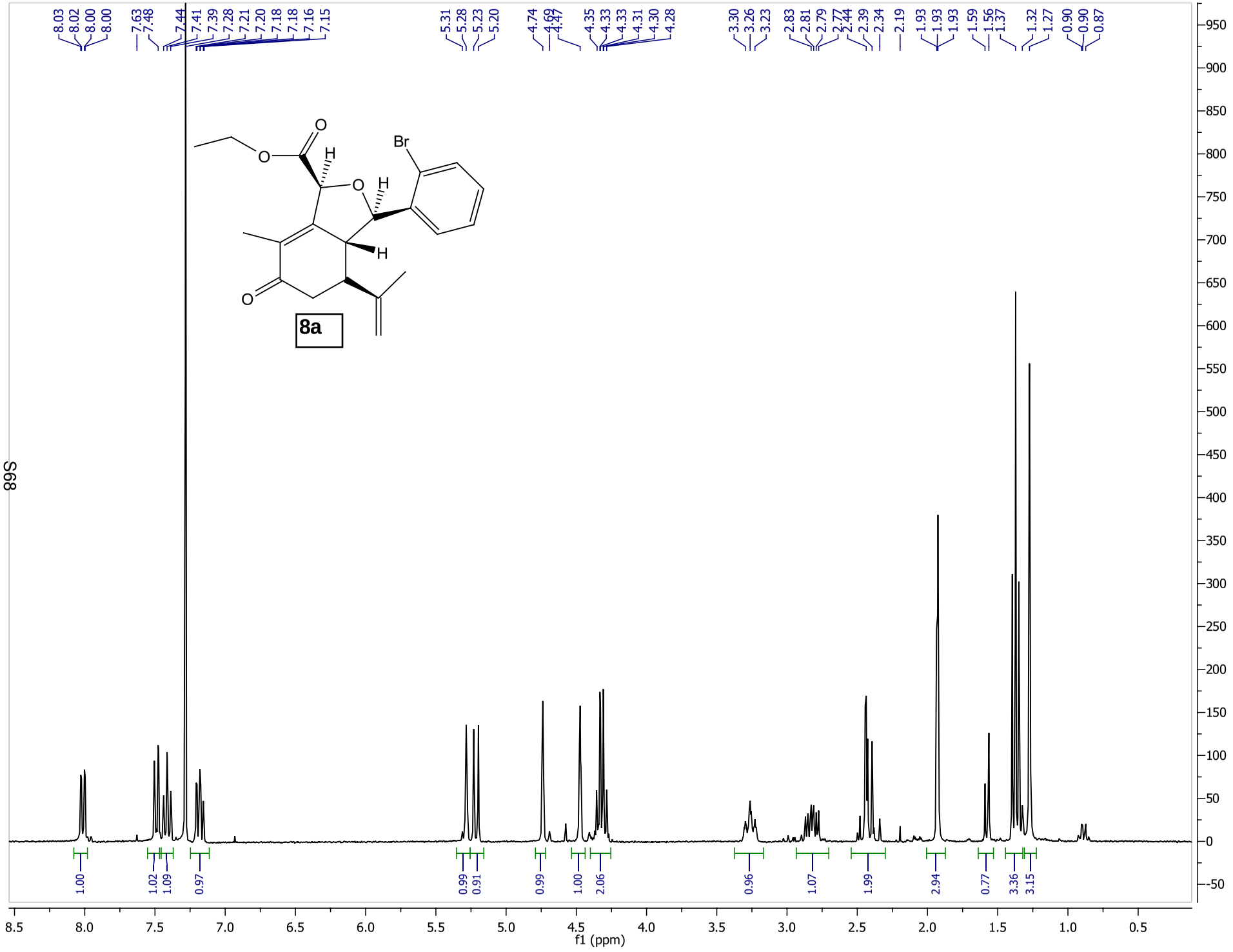
H
6h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5.28
5.23
5.20
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4.47
4.35
4.33
4.33
4.31
4.30
4.28
3.30
3.26
3.23
2.83
2.81
2.79
2.77
2.44
2.39
2.34
2.19
1.93
1.93
1.93
1.59
1.56
1.37
1.32
1.27
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0.90
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H
Br
H
O
8a
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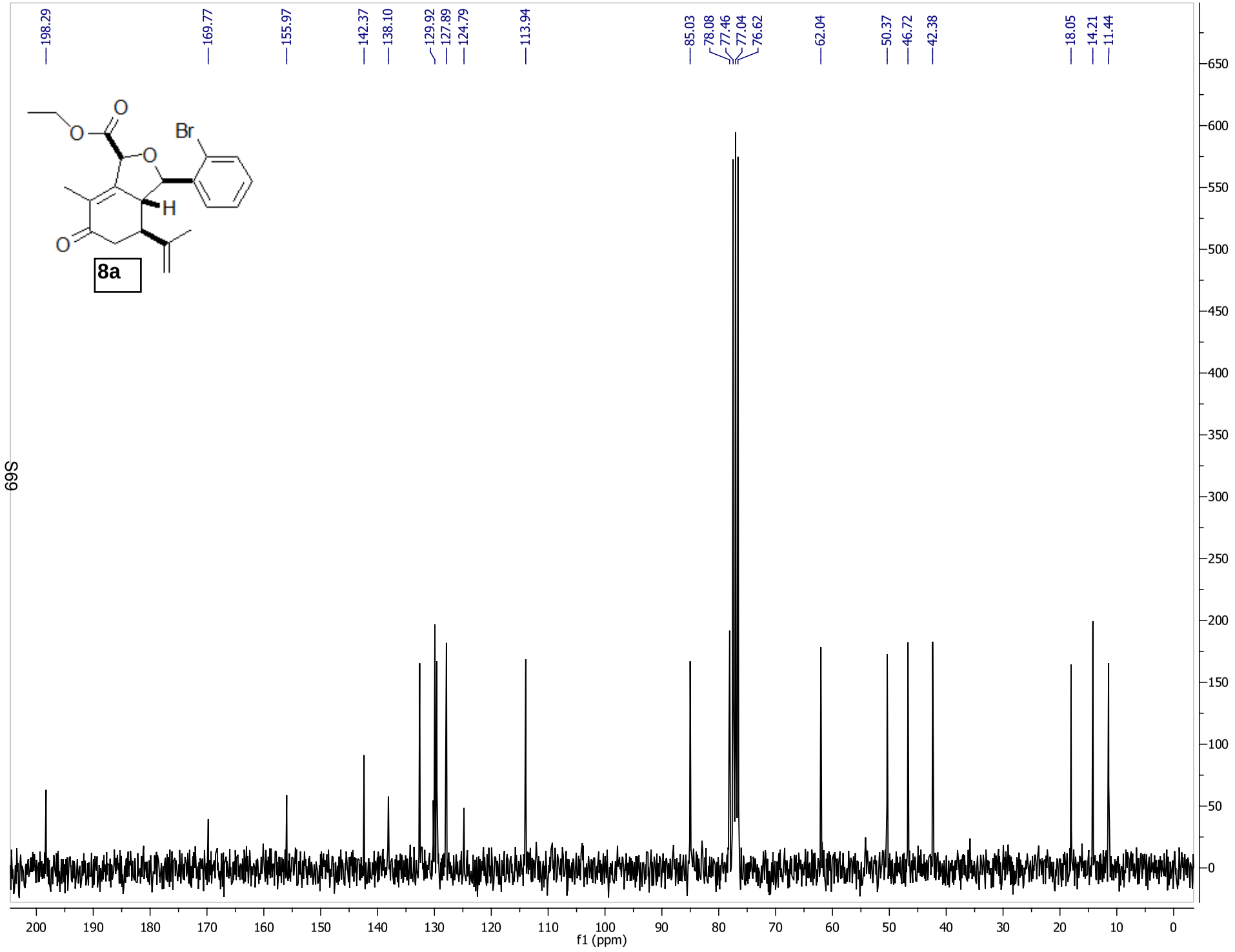
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76.62
62.04
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O
Br
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O
8a
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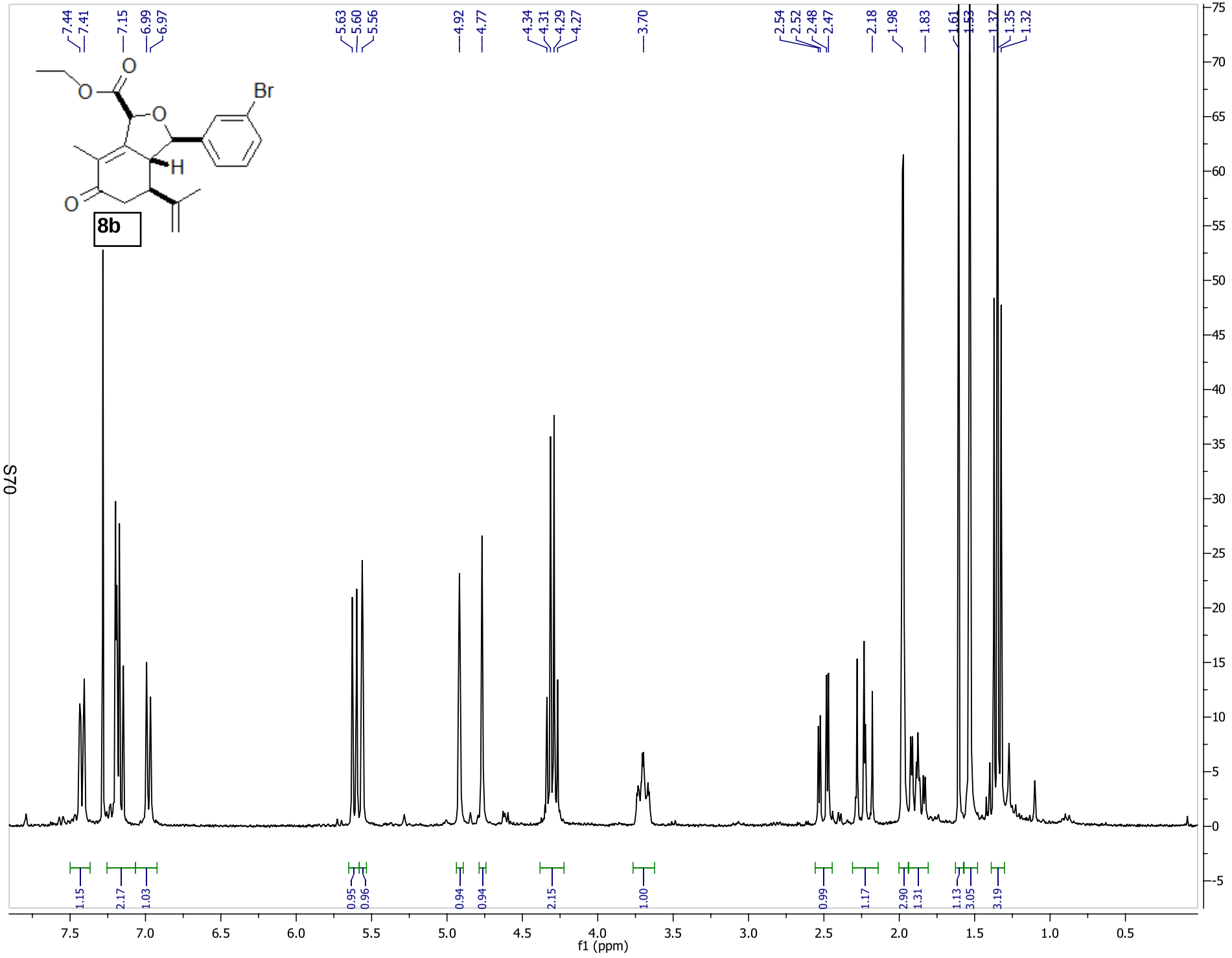
f1 (ppm)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4.27
3.70
2.54
2.52
2.48
2.47
2.18
1.98
1.83
1.61
1.53
1.37
1.35
1.32
Br
O
O
O
O
H
8b
S70
1.15
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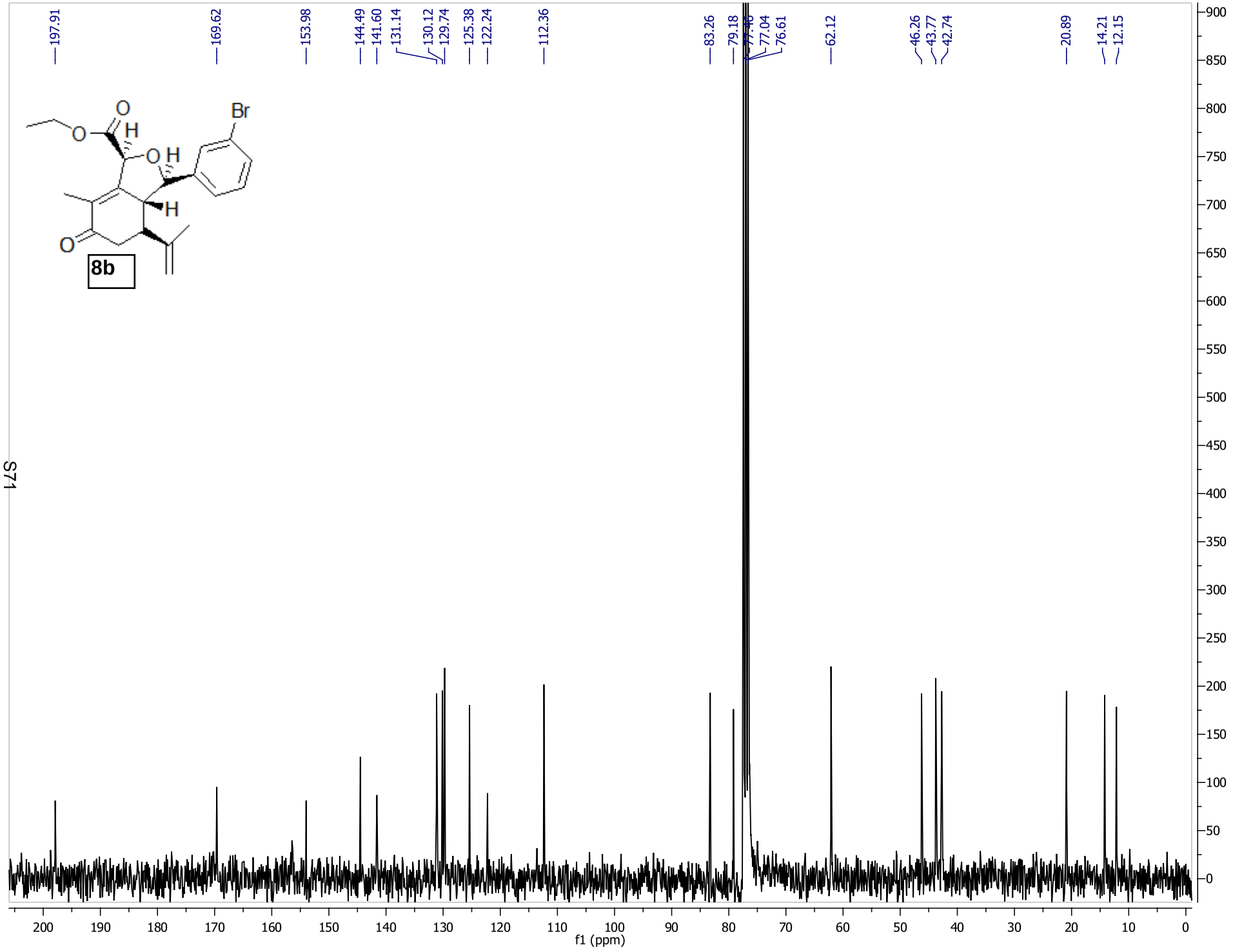
f1 (ppm)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77.04
76.61
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H
O
O
8b
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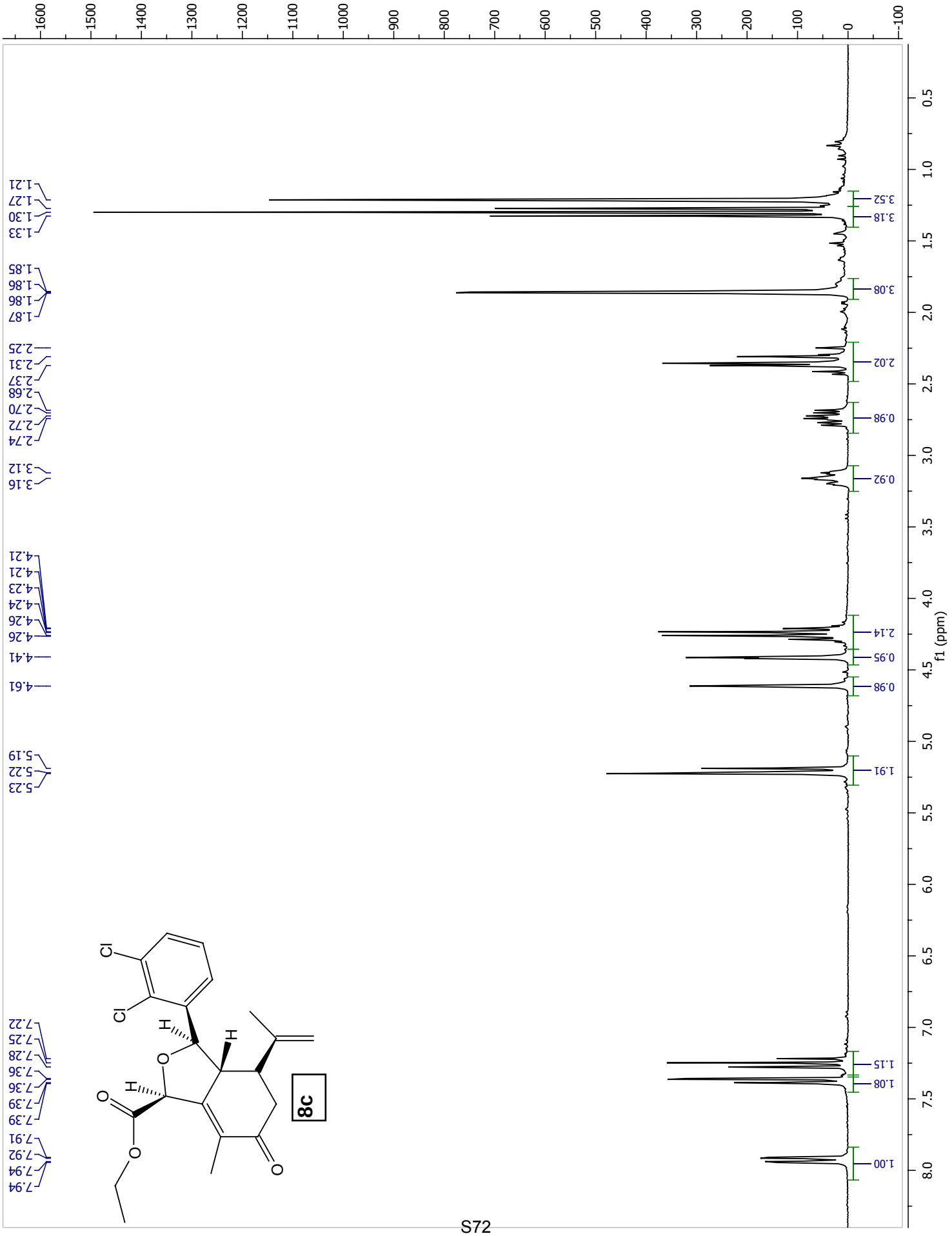
f1 (ppm)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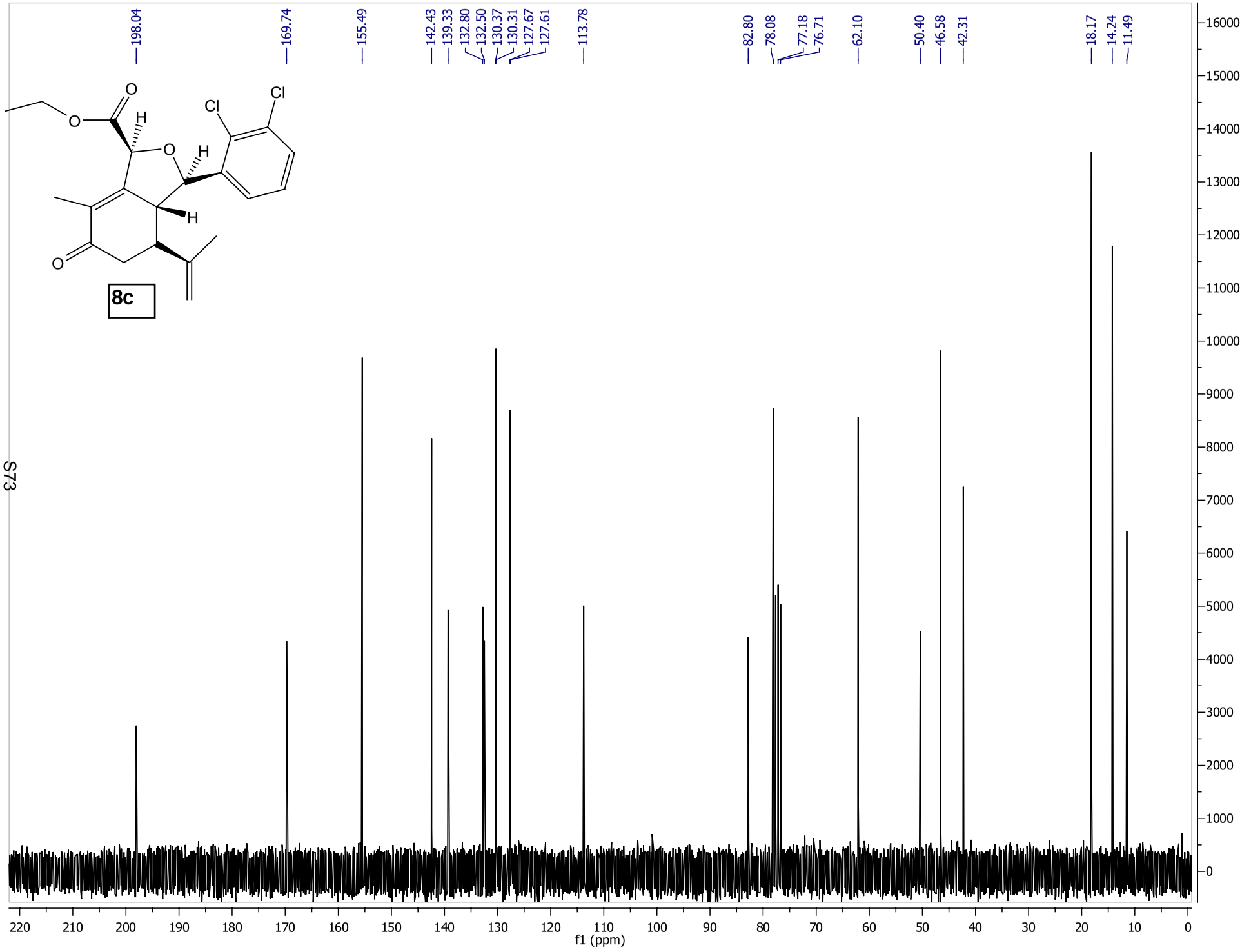
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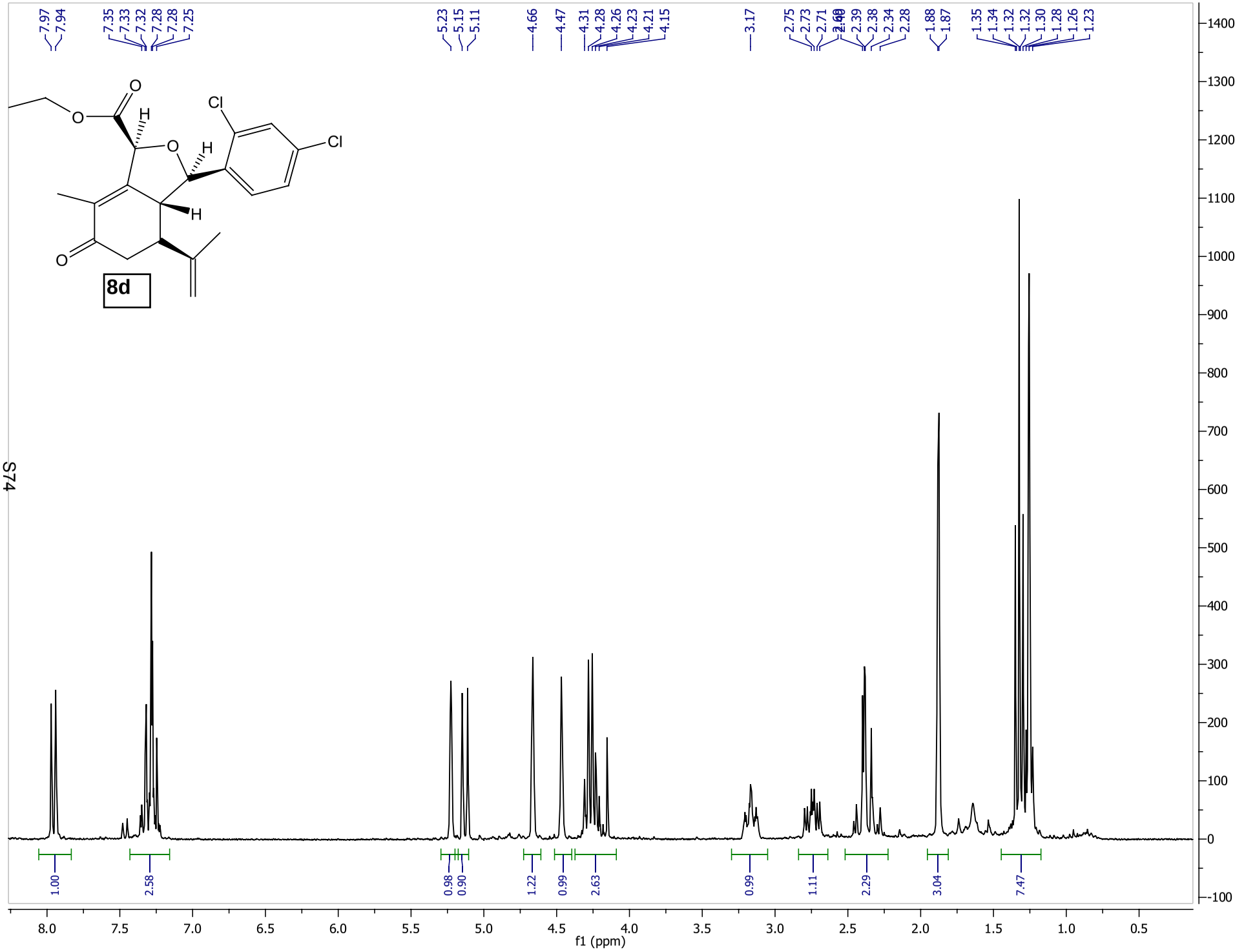
H
8c
f1 (ppm)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4.23
4.21
4.15
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2.73
2.71
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2.38
2.34
2.28
1.88
1.87
1.35
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1.23
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O
H
O
H
Cl
Cl
H
O
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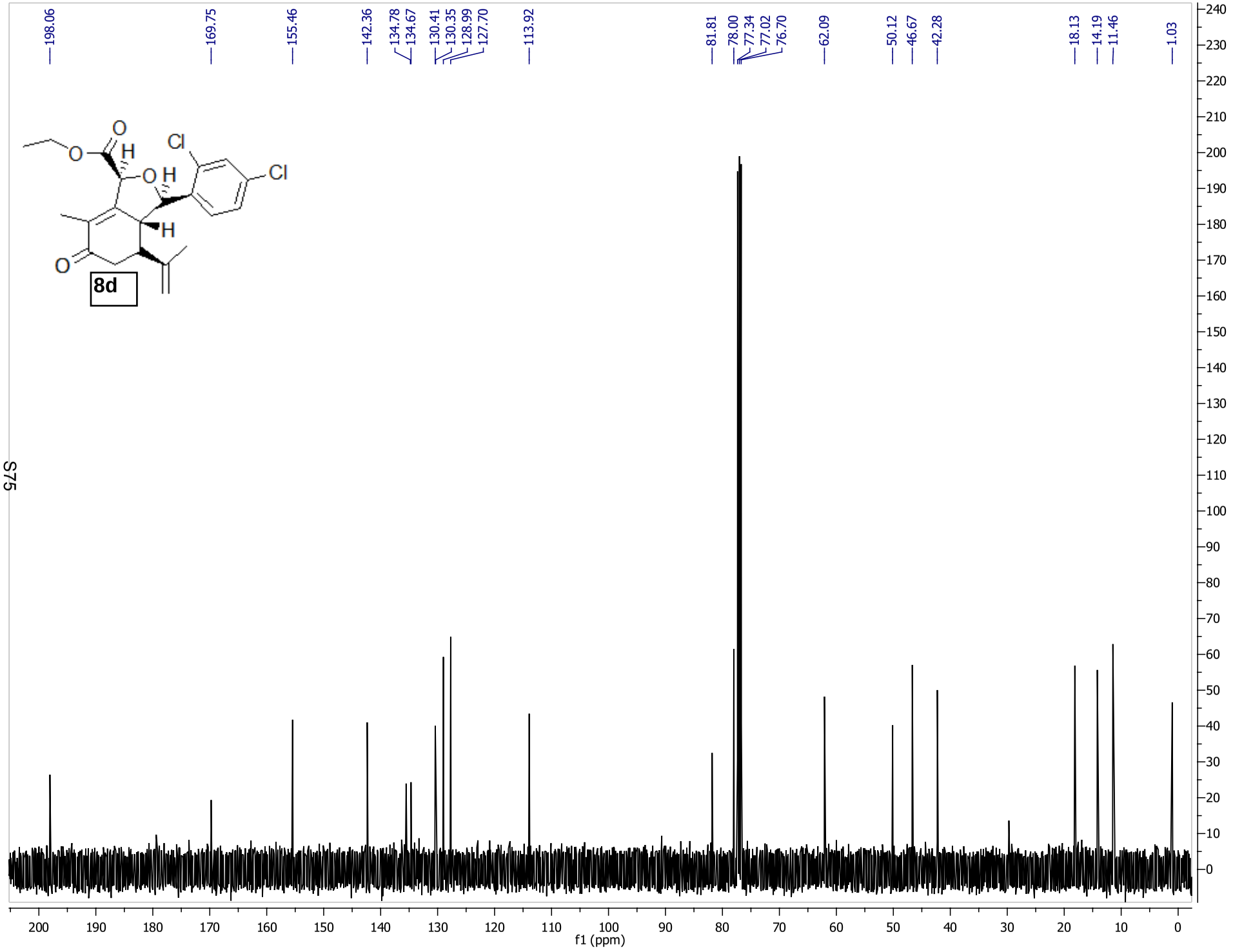
f1 (ppm)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50.12
46.67
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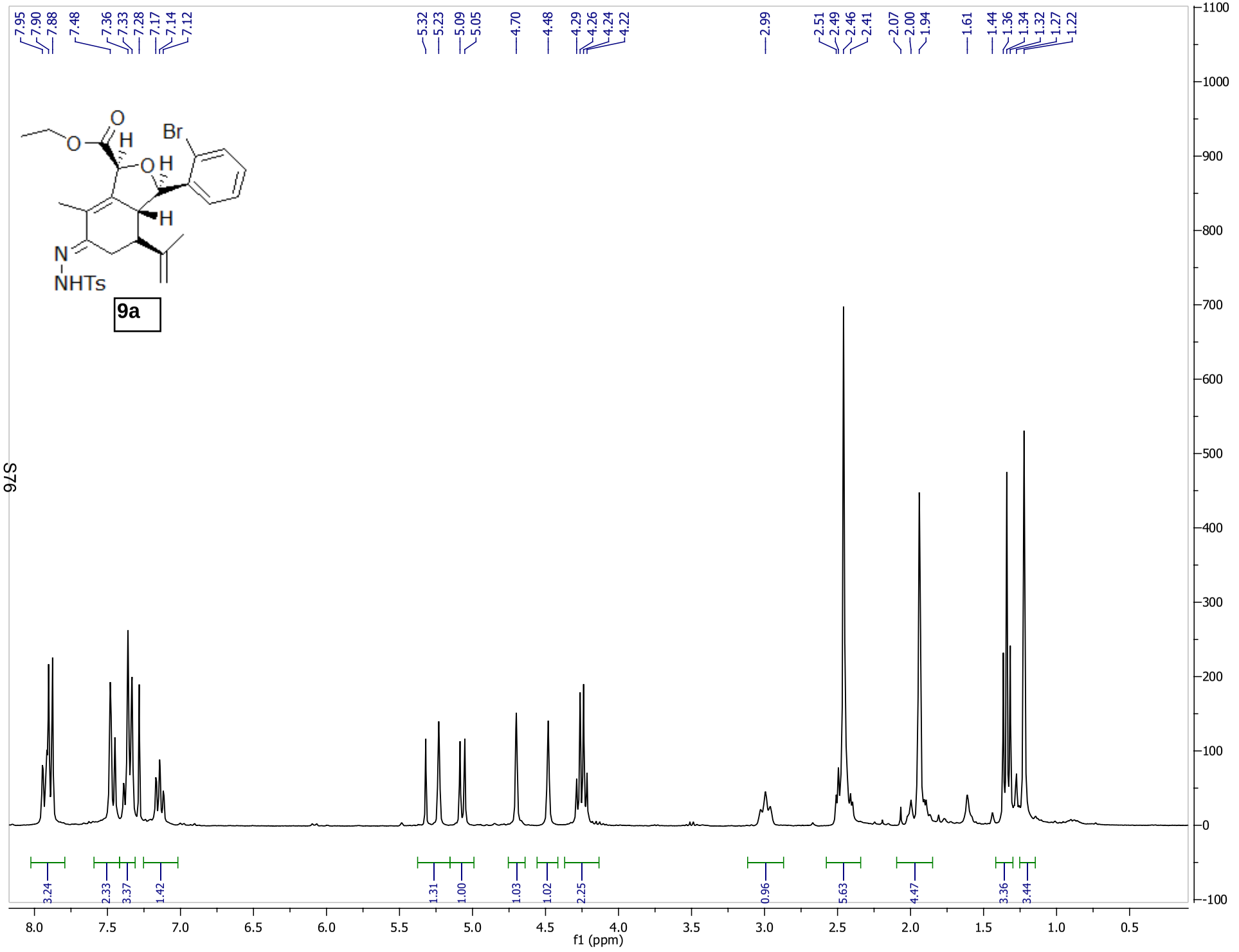
Cl
Cl
H
O
8d
f1 (ppm)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4.48
4.29
4.26
4.24
4.22
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2.49
2.46
2.41
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1.94
1.61
1.44
1.36
1.34
1.32
1.27
1.22
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O
H
H
N
NHTs
9a
S76
3.24
2.33
3.37
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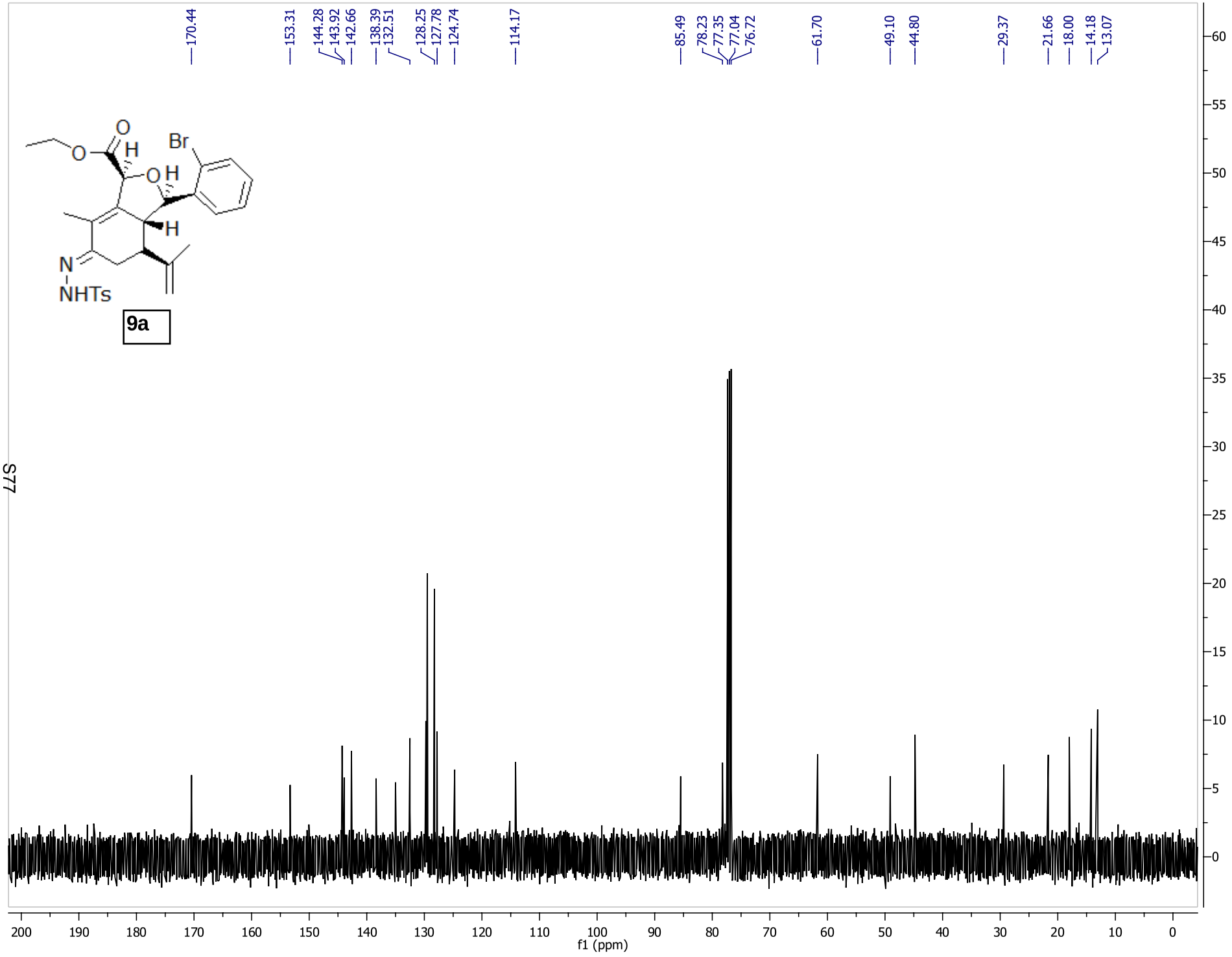
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114.17
85.49
78.23
77.35
77.04
76.72
61.70
49.10
44.80
29.37
21.66
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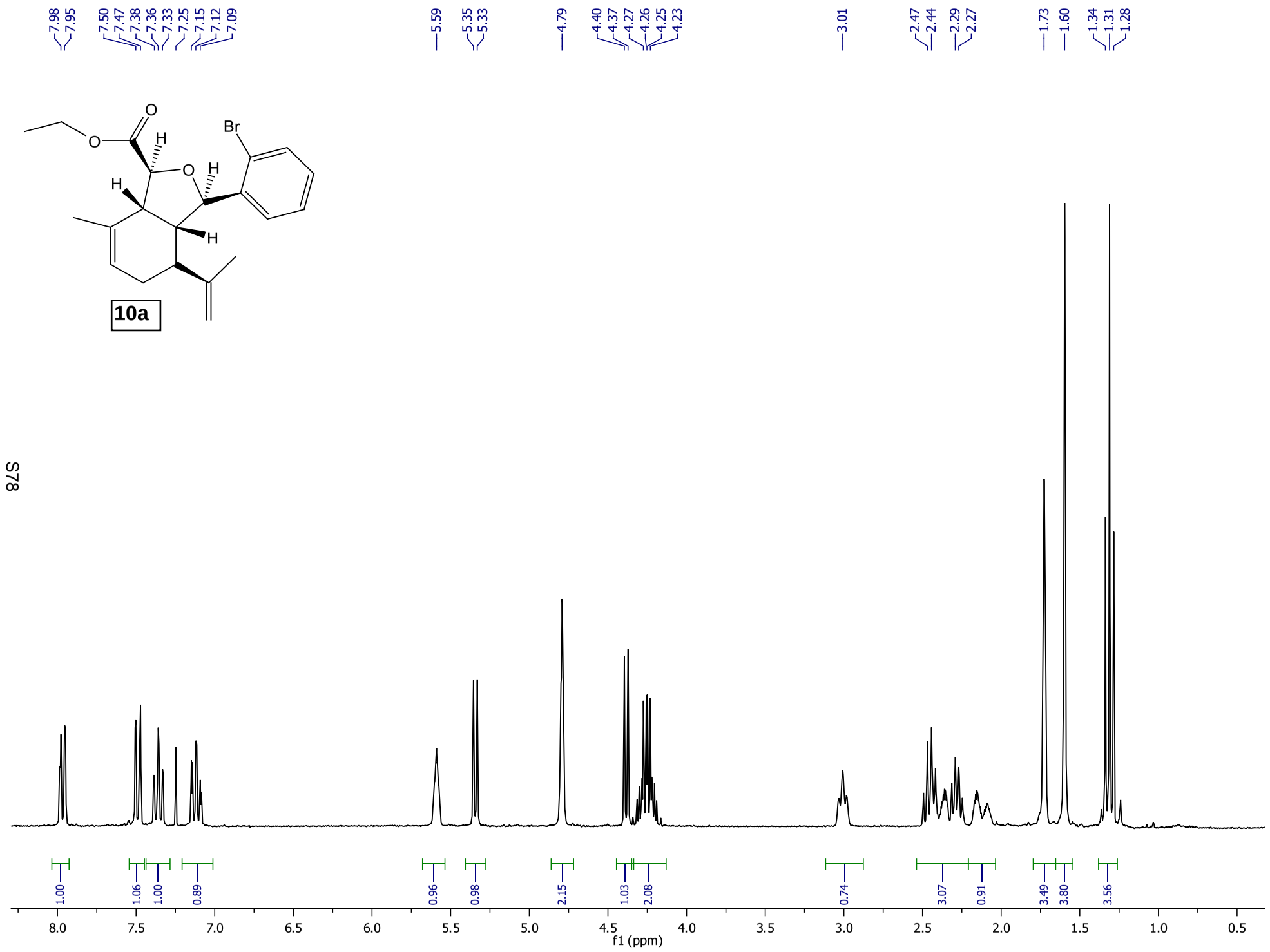
H
H
N
NHTs
9a
S77
f1 (ppm)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5.33
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4.27
4.26
4.25
4.23
3.01
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2.44
2.29
2.27
1.73
1.60
1.34
1.31
1.28
O
O
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O
H
H
H
Br
10a
S78
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0.98
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1.03
2.08
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3.07
0.91
3.49
3.80
3.56
8.0
7.5
7.0
6.5
6.0
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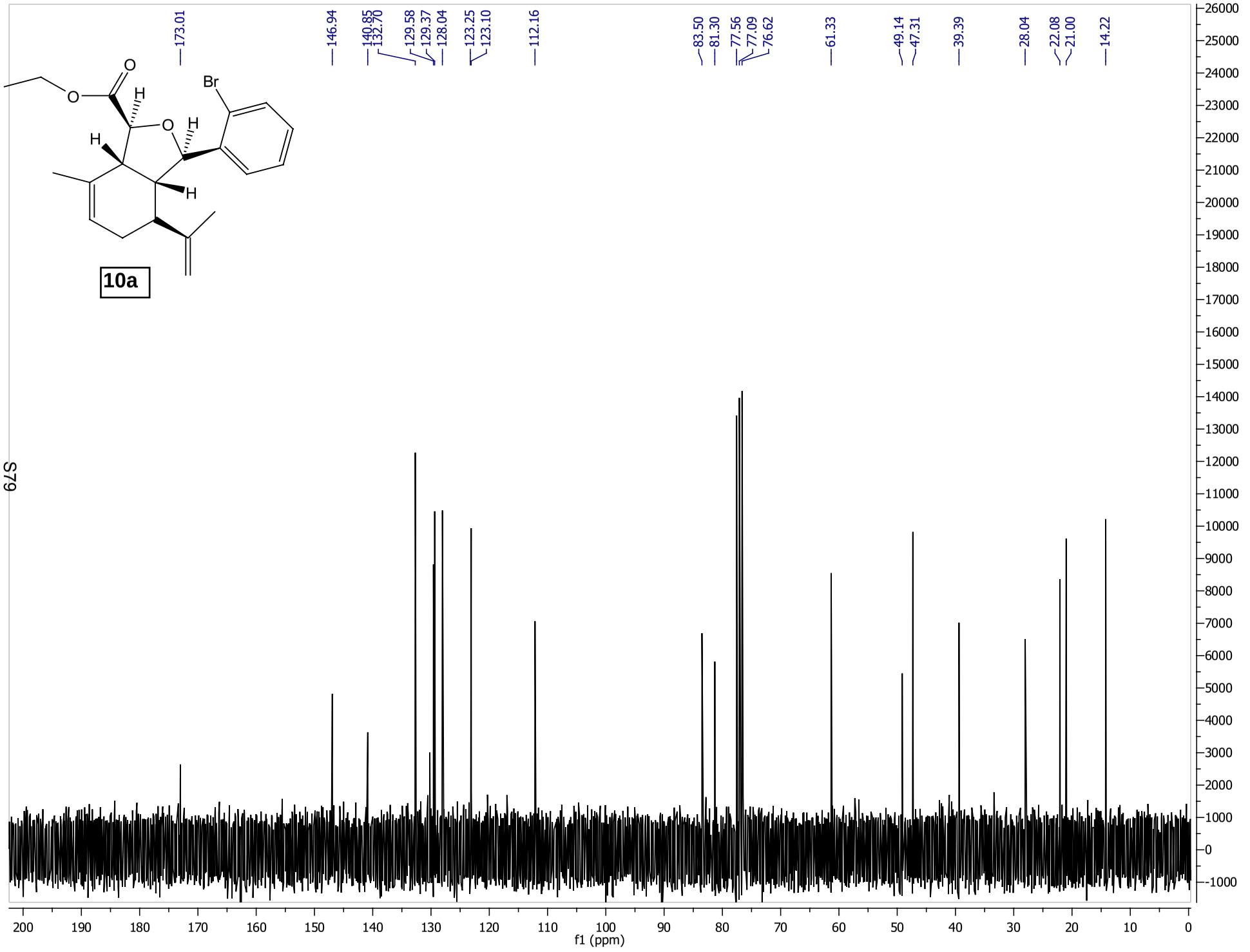
f1 (ppm)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39.39
28.04
22.08
21.00
14.22
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H
O
H
H
H
10a
S79
f1 (ppm)

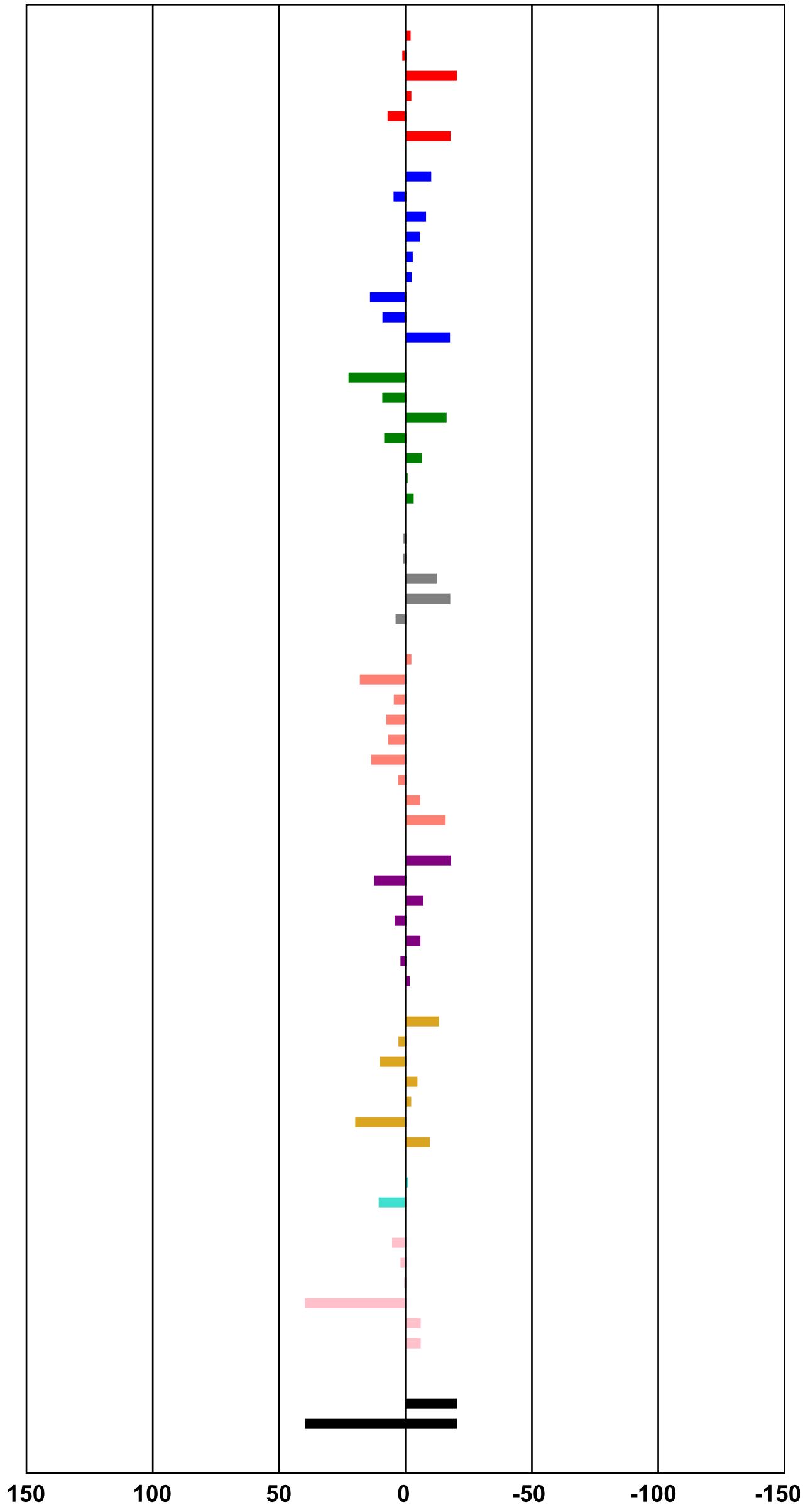
Developmental Therapeutics Program

One Dose Mean Graph

NSC: 749110 / 1	Conc: 1.00E-5 Molar	Test Date: Nov 17, 2008
Experiment ID: 0811OS91		Report Date: Dec 19, 2008

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	98.31
HL-60(TB)	100.94
K-562	79.96
MOLT-4	98.02
RPMI-8226	106.77
SR	82.50
Non-Small Cell Lung Cancer	
A549/ATCC	90.16
EKVX	104.39
HOP-62	92.21
HOP-92	94.71
NCI-H226	97.47
NCI-H23	97.89
NCI-H322M	113.73
NCI-H460	108.80
NCI-H522	82.73
Colon Cancer	
COLO 205	122.22
HCC-2998	108.86
HCT-116	84.08
HCT-15	108.10
HT29	93.83
KM12	99.49
SW-620	97.10
CNS Cancer	
SF-268	100.46
SF-539	100.60
SNB-19	87.90
SNB-75	82.61
U251	103.59
Melanoma	
LOX IMVI	98.00
MALME-3M	117.74
M14	104.29
MDA-MB-435	107.24
SK-MEL-2	106.54
SK-MEL-28	113.23
SK-MEL-5	102.55
UACC-257	94.54
UACC-62	84.48
Ovarian Cancer	
IGROV1	82.34
OVCAR-3	112.11
OVCAR-4	93.31
OVCAR-5	103.98
OVCAR-8	94.44
NCI/ADR-RES	101.67
SK-OV-3	98.68
Renal Cancer	
786-0	87.09
A498	102.47
ACHN	109.85
RXF 393	95.61
SN12C	98.08
TK-10	119.56
UO-31	90.72
Prostate Cancer	
PC-3	99.33
DU-145	110.29
Breast Cancer	
MCF7	104.98
MDA-MB-231/ATCC	101.68
HS 578T	100.26
BT-549	139.44
T-47D	94.32
MDA-MB-468	94.32
Mean	100.01
Delta	20.05
Range	59.48

Mean Growth Percent - Growth Percent



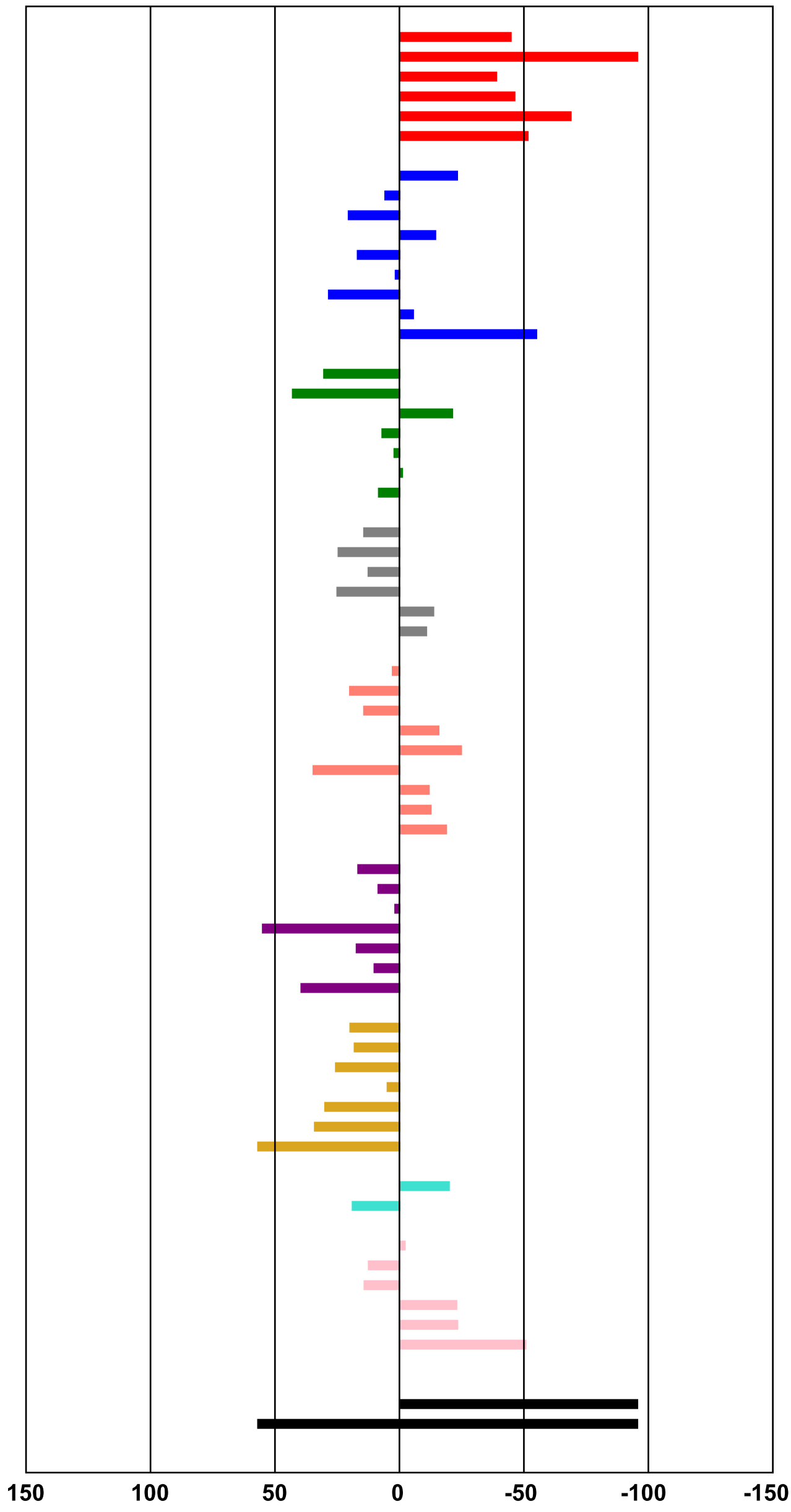
Developmental Therapeutics Program

One Dose Mean Graph

NSC: 749112 / 1	Conc: 1.00E-5 Molar	Test Date: Nov 17, 2008
Experiment ID: 0811OS91		Report Date: Dec 19, 2008

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	19.48
HL-60(TB)	-31.34
K-562	25.32
MOLT-4	17.98
RPMI-8226	-4.60
SR	12.69
Non-Small Cell Lung Cancer	
A549/ATCC	41.04
EKVX	69.98
HOP-62	84.64
HOP-92	49.80
NCI-H226	81.04
NCI-H23	65.80
NCI-H322M	92.62
NCI-H460	58.73
NCI-H522	9.23
Colon Cancer	
COLO 205	94.54
HCC-2998	107.11
HCT-116	42.99
HCT-15	71.15
HT29	66.30
KM12	63.13
SW-620	72.54
CNS Cancer	
SF-268	78.47
SF-295	88.75
SF-539	76.69
SNB-19	89.23
SNB-75	50.59
U251	53.44
Melanoma	
LOX IMVI	66.98
MALME-3M	84.13
M14	78.49
MDA-MB-435	48.50
SK-MEL-2	39.43
SK-MEL-28	98.82
SK-MEL-5	52.40
UACC-257	51.65
UACC-62	45.44
Ovarian Cancer	
IGROV1	80.84
OVCAR-3	72.74
OVCAR-4	65.97
OVCAR-5	119.16
OVCAR-8	81.47
NCI/ADR-RES	74.31
SK-OV-3	103.67
Renal Cancer	
786-0	84.02
A498	82.29
ACHN	89.80
RXF 393	69.05
SN12C	94.13
TK-10	98.26
UO-31	121.05
Prostate Cancer	
PC-3	44.34
DU-145	83.07
Breast Cancer	
MCF7	62.06
MDA-MB-231/ATCC	76.61
HS 578T	78.32
BT-549	41.32
T-47D	40.94
MDA-MB-468	13.57
Mean	64.24
Delta	95.58
Range	152.39

Mean Growth Percent - Growth Percent



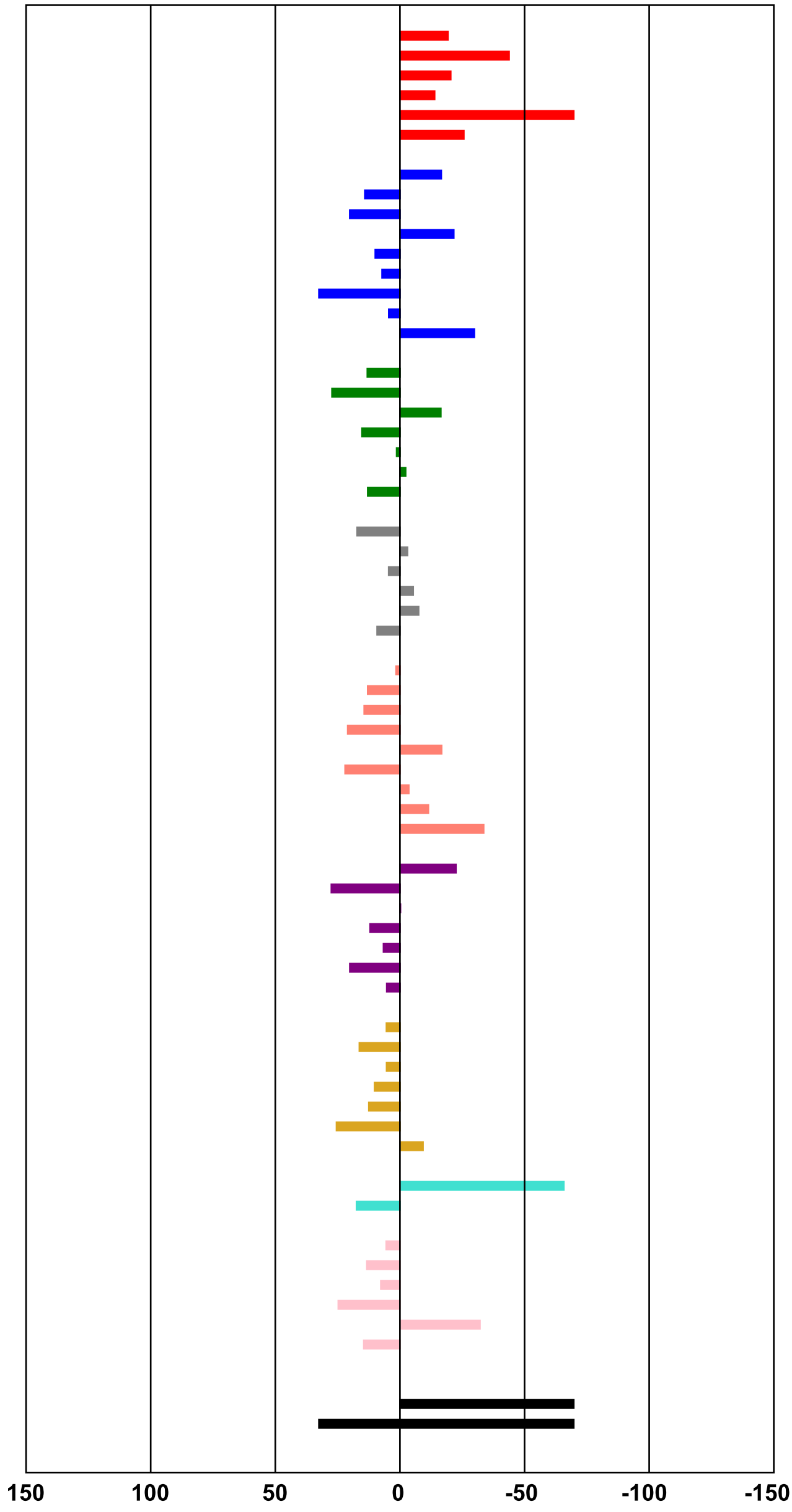
Developmental Therapeutics Program

One Dose Mean Graph

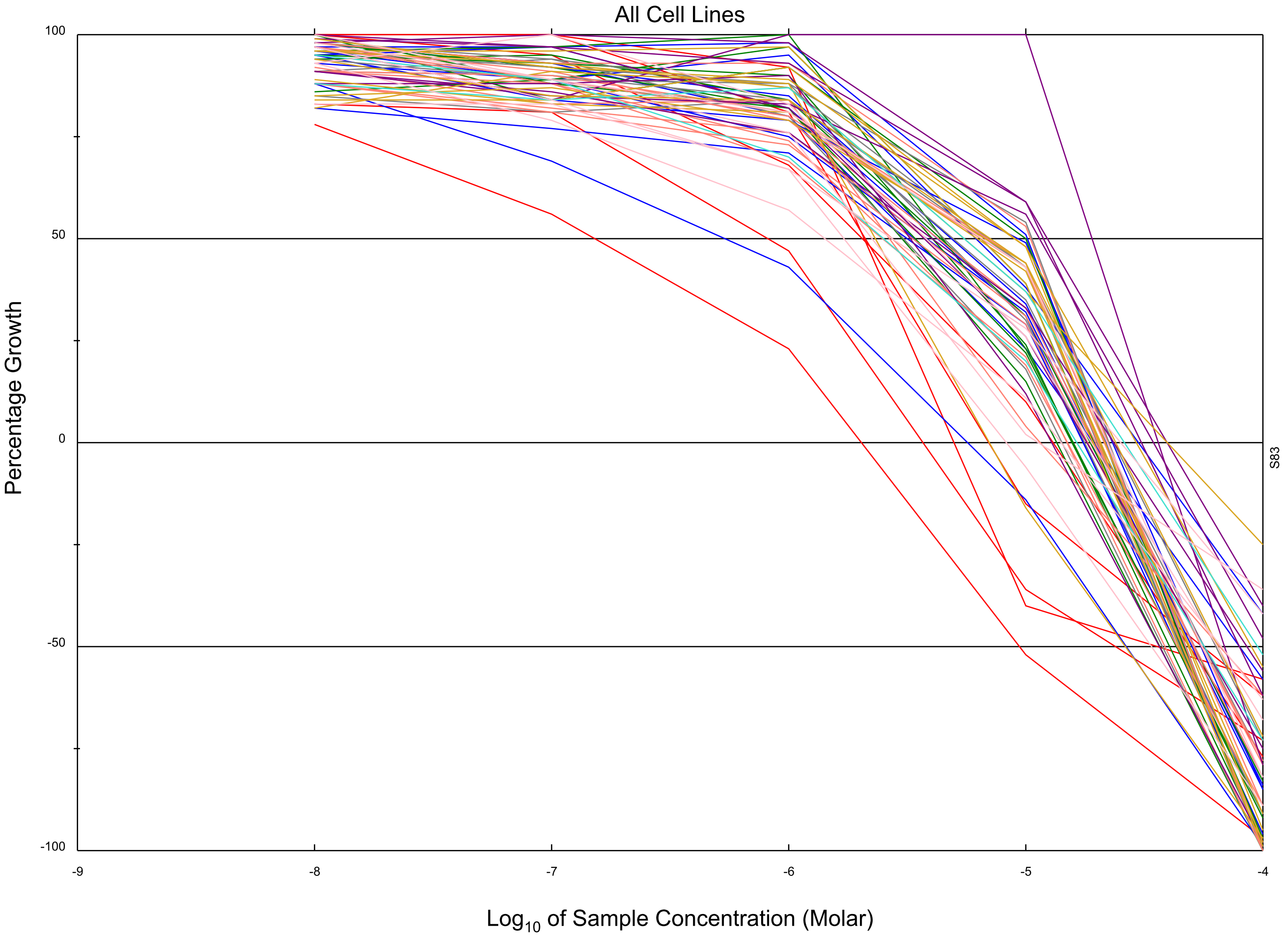
NSC: 749111 / 1	Conc: 1.00E-5 Molar	Test Date: Nov 17, 2008
Experiment ID: 0811OS91		Report Date: Dec 19, 2008

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	68.96
HL-60(TB)	44.43
K-562	67.84
MOLT-4	74.30
RPMI-8226	18.49
SR	62.58
Non-Small Cell Lung Cancer	
A549/ATCC	71.63
EKVX	102.28
HOP-62	108.33
HOP-92	66.62
NCI-H226	98.10
NCI-H23	95.40
NCI-H322M	120.70
NCI-H460	92.68
NCI-H522	58.36
Colon Cancer	
COLO 205	101.29
HCC-2998	115.46
HCT-116	71.81
HCT-15	103.41
HT29	89.53
KM12	85.93
SW-620	101.12
CNS Cancer	
SF-268	105.37
SF-295	85.19
SF-539	92.75
SNB-19	82.90
SNB-75	80.72
U251	97.35
Melanoma	
LOX IMVI	89.75
MALME-3M	101.14
M14	102.54
MDA-MB-435	109.16
SK-MEL-2	71.47
SK-MEL-28	110.20
SK-MEL-5	84.67
UACC-257	76.82
UACC-62	54.63
Ovarian Cancer	
IGROV1	65.74
OVCAR-3	115.72
OVCAR-4	88.01
OVCAR-5	100.16
OVCAR-8	94.80
NCI/ADR-RES	108.30
SK-OV-3	93.49
Renal Cancer	
786-0	93.62
A498	104.48
ACHN	93.56
RXF 393	98.38
SN12C	100.70
TK-10	113.66
UO-31	78.96
Prostate Cancer	
PC-3	22.47
DU-145	105.62
Breast Cancer	
MCF7	93.70
MDA-MB-231/ATCC	101.47
HS 578T	95.86
BT-549	112.93
T-47D	56.11
MDA-MB-468	102.71
Mean	88.21
Delta	69.72
Range	102.21

Mean Growth Percent - Growth Percent

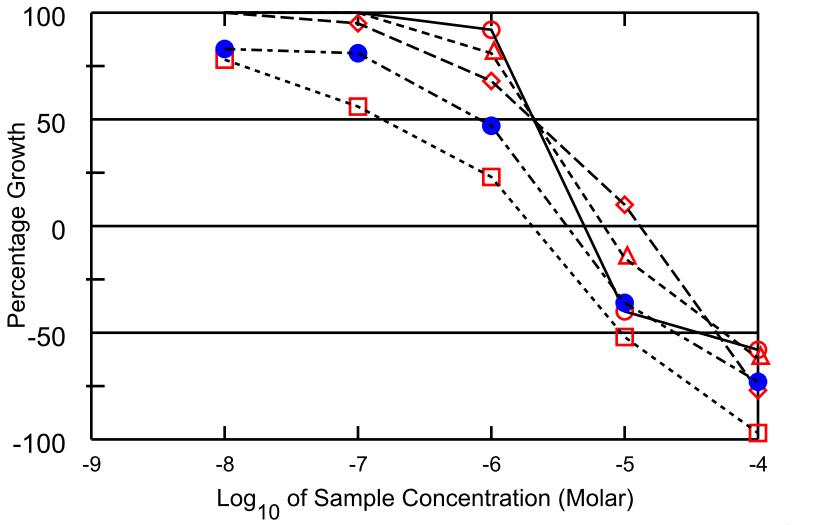


National Cancer Institute Developmental Therapeutics Program Dose Response Curves	NSC : D - 749112/1	SSPL:0XCV	EXP. ID:0902NS35
	Report Date:March 24, 2009	Test Date:February 02, 2009	



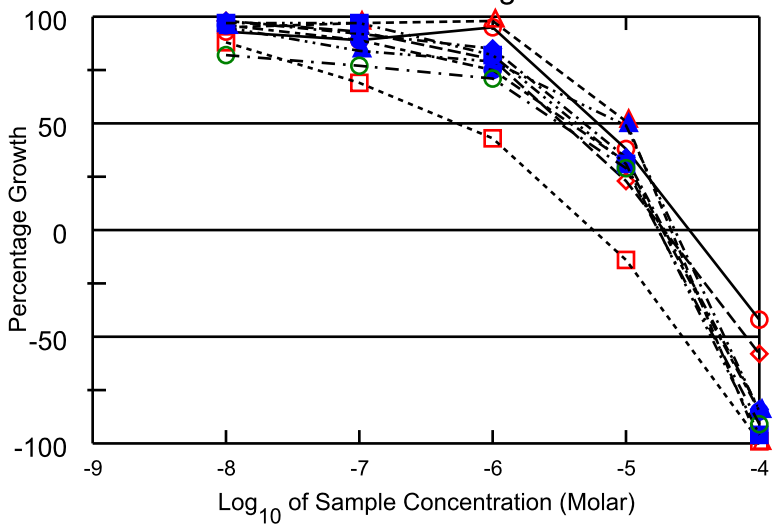
National Cancer Institute Developmental Therapeutics Program Dose Response Curves	NSC: D - 749112 / 1	SSPL: 0XCV	EXP. ID: 0902NS35
	Report Date: March 24, 2009	Test Date: February 02, 2009	

Leukemia



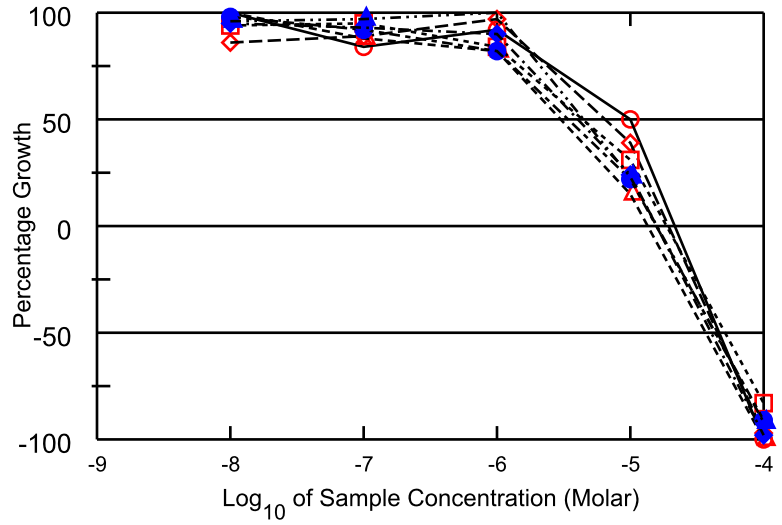
HL-60(TB) — K-562 — MOLT-4
RPMI-8226 — SR

Non-Small Cell Lung Cancer



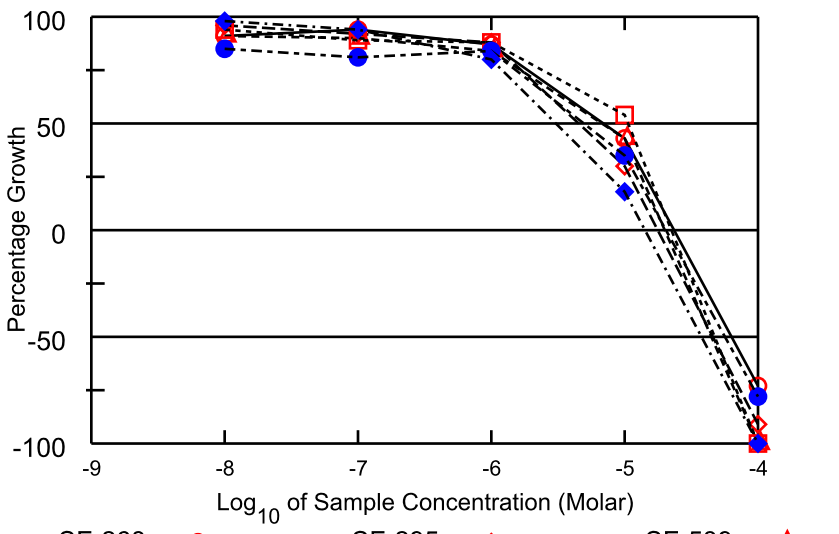
A549/ATCC — EKVX — HOP-62
HOP-92 — NCI-H226 — NCI-H23
NCI-H322M — NCI-H460 — NCI-H522

Colon Cancer



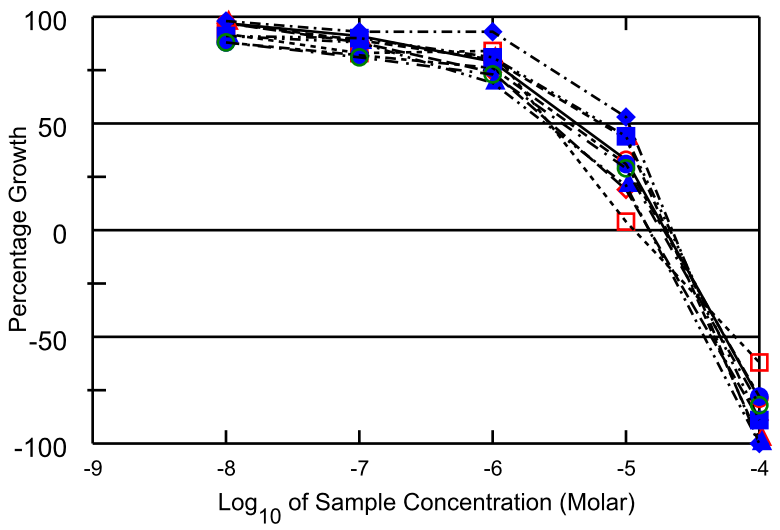
COLO 205 — HCC-2998 — HCT-116
HCT-15 — HT29 — KM12
SW-620

CNS Cancer



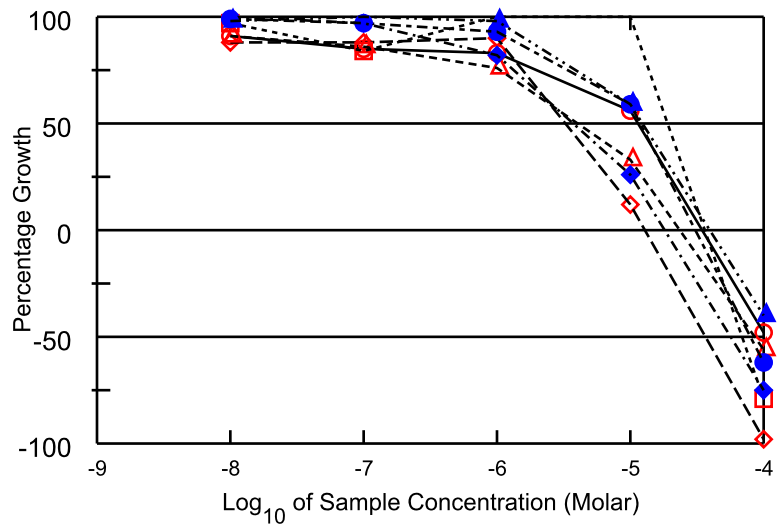
SF-268 — SF-295 — SF-539
SNB-19 — SNB-75 — U251

Melanoma



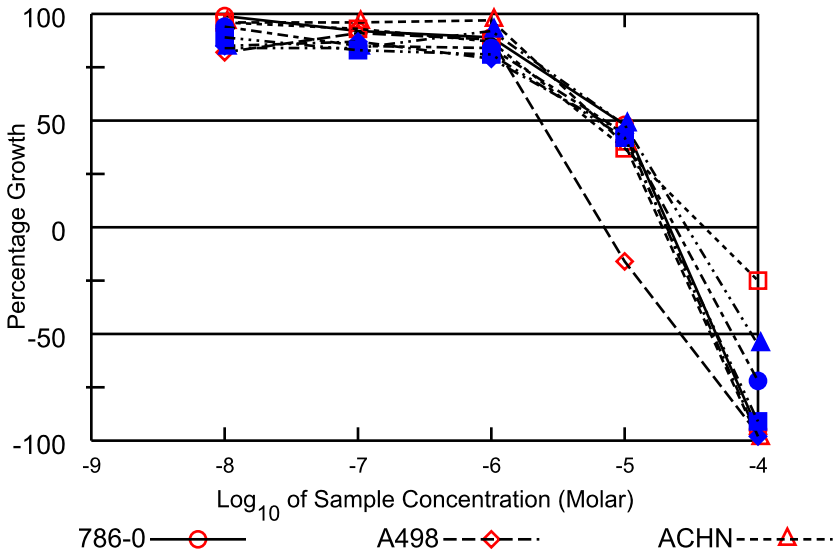
LOX IMVI — MALME-3M — M14
MDA-MB-435 — SK-MEL-2 — SK-MEL-28
SK-MEL-5 — UACC-257 — UACC-62

Ovarian Cancer



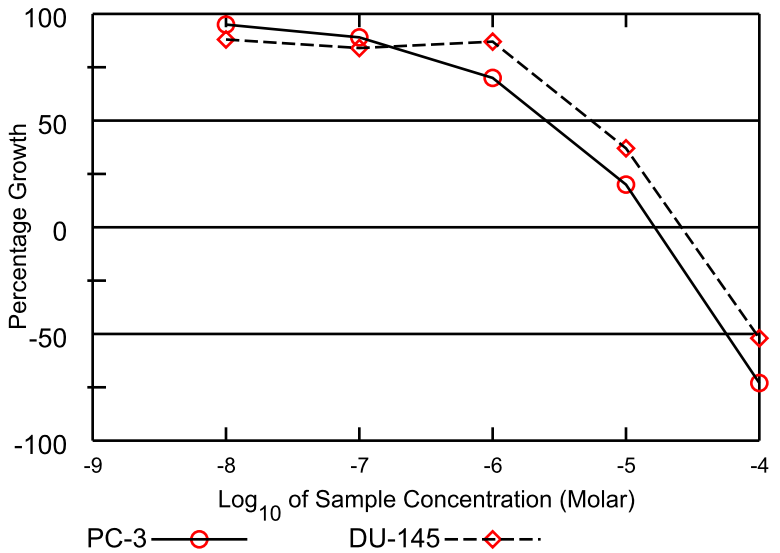
IGROV1 — OVCAR-3 — OVCAR-4
OVCAR-5 — OVCAR-8 — NCI/ADR-RES
SK-OV-3

Renal Cancer



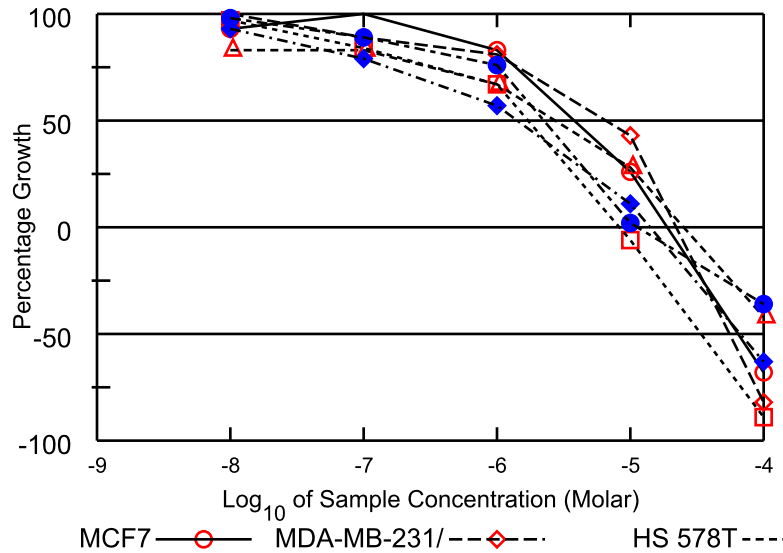
786-0 — A498 — ACHN
CAKI-1 — RXF 393 — SN12C
TK-10 — UO-31

Prostate Cancer



PC-3 — DU-145

Breast Cancer



MCF7 — MDA-MB-231/ — HS 578T
BT-549 — T-47D — MDA-MB-468

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 749112 / 1	Experiment ID : 0902NS35	Test Type : 08	Units : Molar
Report Date : March 24, 2009	Test Date : February 02, 2009	QNS :	MC :
COMI : DB.10h (81264)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0XCV	

		Log10 Concentration												
	Time	Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
HL-60(TB)	0.986	2.104	2.149	2.153	2.017	0.589	0.415	104	104	92	-40	-58	2.08E-6	4.97E-6	3.55E-5
K-562	0.252	1.205	1.210	1.156	0.897	0.352	0.059	101	95	68	10	-77	2.04E-6	1.32E-5	4.93E-5
MOLT-4	0.530	1.404	1.457	1.404	1.241	0.452	0.203	106	100	81	-15	-62	2.12E-6	7.03E-6	5.62E-5
RPMI-8226	0.854	1.741	1.548	1.348	1.056	0.409	0.028	78	56	23	-52	-97	1.48E-7	2.01E-6	9.36E-6
SR	0.425	0.820	0.753	0.744	0.609	0.273	0.114	83	81	47	-36	-73	7.98E-7	3.67E-6	2.39E-5
Non-Small Cell Lung Cancer															
A549/ATCC	0.245	1.246	1.178	1.135	1.193	0.627	0.143	93	89	95	38	-42	6.17E-6	3.01E-5	> 1.00E-4
EKVX	0.596	1.398	1.380	1.341	1.236	0.783	0.252	98	93	80	23	-58	3.37E-6	1.94E-5	8.03E-5
HOP-62	0.452	1.137	1.100	1.115	1.124	0.801	0.002	95	97	98	51	-100	1.01E-5	2.18E-5	4.68E-5
HOP-92	0.824	1.239	1.188	1.112	1.004	0.712	0.011	88	69	43	-14	-99	5.52E-7	5.76E-6	2.68E-5
NCI-H226	0.670	1.231	1.206	1.171	1.090	0.851	0.104	96	89	75	32	-85	3.82E-6	1.89E-5	5.06E-5
NCI-H23	0.665	1.820	1.792	1.723	1.648	1.060	0.105	98	92	85	34	-84	4.88E-6	1.94E-5	5.14E-5
NCI-H322M	0.621	1.739	1.686	1.557	1.507	1.173	0.091	95	84	79	49	-85	9.50E-6	2.32E-5	5.46E-5
NCI-H460	0.261	2.111	2.057	2.061	1.784	0.832	0.011	97	97	82	31	-96	4.24E-6	1.75E-5	4.34E-5
NCI-H522	0.396	1.269	1.111	1.069	1.013	0.649	0.036	82	77	71	29	-91	3.13E-6	1.74E-5	4.55E-5
Colon Cancer															
COLO 205	0.280	0.968	0.978	0.859	0.910	0.621	-0.011	101	84	92	50	-100	9.77E-6	2.15E-5	4.63E-5
HCC-2998	0.683	1.954	1.779	1.818	1.915	1.176	0.024	86	89	97	39	-97	6.40E-6	1.93E-5	4.53E-5
HCT-116	0.251	1.689	1.718	1.524	1.424	0.472	-0.014	102	88	82	15	-100	3.00E-6	1.36E-5	3.69E-5
HCT-15	0.376	2.159	2.057	2.072	1.878	0.927	0.063	94	95	84	31	-83	4.38E-6	1.86E-5	5.10E-5
HT29	0.149	0.997	0.976	0.928	0.845	0.334	0.013	98	92	82	22	-91	3.41E-6	1.56E-5	4.32E-5
KM12	0.466	2.085	2.011	1.964	1.921	0.853	0.010	95	93	90	24	-98	4.02E-6	1.57E-5	4.04E-5
SW-620	0.291	1.511	1.462	1.472	1.520	0.572	0.025	96	97	101	23	-92	4.49E-6	1.59E-5	4.34E-5
CNS Cancer															
SF-268	0.362	1.187	1.115	1.136	1.077	0.718	0.096	91	94	87	43	-73	6.95E-6	2.34E-5	6.29E-5
SF-295	1.371	3.235	3.161	3.095	3.020	1.921	0.124	96	92	88	30	-91	4.49E-6	1.76E-5	4.57E-5
SF-539	0.743	2.275	2.135	2.118	2.026	1.406	-0.001	91	90	84	43	-100	6.82E-6	2.00E-5	4.48E-5
SNB-19	0.642	1.499	1.445	1.403	1.398	1.107	-0.007	94	89	88	54	-100	1.07E-5	2.25E-5	4.74E-5
SNB-75	0.585	1.212	1.119	1.092	1.111	0.805	0.132	85	81	84	35	-78	4.94E-6	2.05E-5	5.69E-5
U251	0.235	1.379	1.353	1.309	1.153	0.442	-0.001	98	94	80	18	-100	3.06E-6	1.42E-5	3.77E-5
Melanoma															
LOX IMVI	0.270	1.964	1.911	1.807	1.603	0.835	0.058	97	91	79	33	-79	4.30E-6	1.98E-5	5.54E-5
MALME-3M	0.708	1.590	1.562	1.485	1.365	0.879	0.080	97	88	74	19	-89	2.78E-6	1.51E-5	4.38E-5
M14	0.256	0.915	0.897	0.846	0.785	0.540	0.005	97	89	80	43	-98	6.51E-6	2.02E-5	4.56E-5
MDA-MB-435	0.472	1.904	1.787	1.665	1.676	0.524	0.181	92	83	84	4	-62	2.65E-6	1.14E-5	6.63E-5
SK-MEL-2	0.507	0.967	0.913	0.886	0.856	0.649	0.111	88	82	76	31	-78	3.74E-6	1.92E-5	5.52E-5
SK-MEL-28	0.479	1.173	1.157	1.121	1.122	0.847	-0.001	98	93	93	53	-100	1.05E-5	2.22E-5	4.71E-5
SK-MEL-5	0.327	1.972	1.816	1.779	1.461	0.673	-0.015	91	88	69	21	-100	2.48E-6	1.49E-5	3.86E-5
UACC-257	0.602	1.345	1.280	1.272	1.201	0.926	0.067	91	90	81	44	-89	6.71E-6	2.13E-5	5.09E-5
UACC-62	0.265	0.930	0.852	0.804	0.748	0.459	0.048	88	81	73	29	-82	3.31E-6	1.83E-5	5.15E-5
Ovarian Cancer															
IGROV1	0.319	1.316	1.225	1.164	1.144	0.874	0.167	91	85	83	56	-48	1.13E-5	3.46E-5	> 1.00E-4
OVCAR-3	0.361	0.987	0.914	0.912	0.925	0.434	0.007	88	88	90	12	-98	3.24E-6	1.28E-5	3.65E-5
OVCAR-4	0.397	1.403	1.310	1.266	1.165	0.733	0.177	91	86	76	33	-56	4.10E-6	2.37E-5	8.66E-5
OVCAR-5	0.478	0.903	0.891	0.837	0.905	1.015	0.101	97	84	100	126	-79	2.36E-5	4.13E-5	7.23E-5
OVCAR-8	0.302	1.242	1.233	1.210	1.181	0.858	0.114	99	97	93	59	-62	1.19E-5	3.06E-5	7.90E-5
NCI/ADR-RES	0.556	1.619	1.667	1.589	1.423	0.829	0.137	105	97	82	26	-75	3.67E-6	1.79E-5	5.61E-5
SK-OV-3	0.621	1.326	1.309	1.323	1.314	1.037	0.372	98	100	98	59	-40	1.23E-5	3.93E-5	> 1.00E-4
Renal Cancer															
786-0	0.594	2.154	2.139	2.032	1.980	1.336	0.027	99	92	89	48	-95	8.73E-6	2.15E-5	4.81E-5
A498	1.150	1.457	1.402	1.430	1.422	0.970	0.035	82	91	88	-16	-97	2.34E-6	7.07E-6	2.65E-5
ACHN	0.334	1.372	1.332	1.333	1.344	0.734	0.002	96	96	97	39	-99	6.39E-6	1.90E-5	4.38E-5
CAKI-1	0.864	2.632	2.565	2.515	2.399	1.520	0.651	96	93	87	37	-25	5.50E-6	3.98E-5	> 1.00E-4
RXF 393	0.398	1.056	1.016	0.960	0.954	0.686	0.112	94	85	84	44	-72	7.00E-6	2.39E-5	6.47E-5
SN12C	0.544	1.869	1.668	1.703	1.593	1.123	0.012	85	87	79	44	-98	6.63E-6	2.03E-5	4.59E-5
TK-10	0.599	1.222	1.123	1.124	1.170	0.897	0.268	84	84	92	48	-55	8.93E-6	2.91E-5	8.89E-5
UO-31	0.460	1.368	1.264	1.217	1.193	0.845	0.041	89	83	81	42	-91	6.32E-6	2.08E-5	4.92E-5
Prostate Cancer															
PC-3	0.422	1.262	1.218	1.166	1.006	0.592	0.116	95	89	70	20	-73	2.49E-6	1.65E-5	5.72E-5
DU-145	0.297	1.210	1.104	1.061	1.089	0.637	0.142	88	84	87	37	-52	5.53E-6	2.61E-5	9.45E-5
Breast Cancer															
MCF7	0.265	1.401	1.317	1.441	1.209	0.557	0.084	93	103	83	26	-68	3.77E-6	1.88E-5	6.39E-5
MDA-MB-231/ATCC	0.489	1.367	1.378	1.271	1.204	0.871	0.090	101	89	81	43	-82	6.73E-6	2.23E-5	5.59E-5
HS 578T	0.689	1.300	1.194	1.194	1.099	0.858	0.397	83	83	67	28	-42	2.72E-6	2.48E-5	> 1.00E-4
BT-549	1.527	2.435	2.405	2.293	2.136	1.442	0.166	97	84	67	-6	-89	1.72E-6	8.37E-6	3.40E-5
T-47D	0.705	1.402	1.389	1.325	1.236	0.717	0.452	98	89	76	2	-36	2.24E-6	1.11E-5	> 1.00E-4
MDA-MB-468	0.404	1.289	1.227	1.106	0.911	0.502	0.148	93	79	57	11	-63	1.43E-6	1.41E-5	6.61E-5

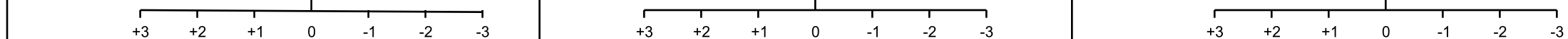
National Cancer Institute Developmental Therapeutics Program

Mean Graphs

NSC : D - 749112/1 | Units :Molar | SSPL :0XCV | EXP. ID :0902NS35

Report Date :March 24, 2009 | Test Date :February 02, 2009

Panel/Cell Line	Log_{10}GI50	GI50	Log_{10}TGI	TGI	Log_{10}LC50	LC50
Leukemia						
HL-60(TB)	-5.68		-5.30		-4.45	
K-562	-5.69		-4.88		-4.31	
MOLT-4	-5.67		-5.15		-4.25	
RPMI-8226	-6.83		-5.70		-5.03	
SR	-6.10		-5.43		-4.62	
Non-Small Cell Lung Cancer						
A549/ATCC	-5.21		-4.52		> -4.00	
EKVX	-5.47		-4.71		-4.10	
HOP-62	-4.99		-4.66		-4.33	
HOP-92	-6.26		-5.24		-4.57	
NCI-H226	-5.42		-4.72		-4.30	
NCI-H23	-5.31		-4.71		-4.29	
NCI-H322M	-5.02		-4.63		-4.26	
NCI-H460	-5.37		-4.76		-4.36	
NCI-H522	-5.50		-4.76		-4.34	
Colon Cancer						
COLO 205	-5.01		-4.67		-4.33	
HCC-2998	-5.19		-4.71		-4.34	
HCT-116	-5.52		-4.87		-4.43	
HCT-15	-5.36		-4.73		-4.29	
HT29	-5.47		-4.81		-4.36	
KM12	-5.40		-4.80		-4.39	
SW-620	-5.35		-4.80		-4.36	
CNS Cancer						
SF-268	-5.16		-4.63		-4.20	
SF-295	-5.35		-4.76		-4.34	
SF-539	-5.17		-4.70		-4.35	
SNB-19	-4.97		-4.65		-4.32	
SNB-75	-5.31		-4.69		-4.24	
U251	-5.51		-4.85		-4.42	
Melanoma						
LOX IMVI	-5.37		-4.70		-4.26	
MALME-3M	-5.56		-4.82		-4.36	
M14	-5.19		-4.70		-4.34	
MDA-MB-435	-5.58		-4.94		-4.18	
SK-MEL-2	-5.43		-4.72		-4.26	
SK-MEL-28	-4.98		-4.65		-4.33	
SK-MEL-5	-5.60		-4.83		-4.41	
UACC-257	-5.17		-4.67		-4.29	
UACC-62	-5.48		-4.74		-4.29	
Ovarian Cancer						
IGROV1	-4.95		-4.46		> -4.00	
OVCAR-3	-5.49		-4.89		-4.44	
OVCAR-4	-5.39		-4.62		-4.06	
OVCAR-5	-4.63		-4.38		-4.14	
OVCAR-8	-4.93		-4.51		-4.10	
NCI/ADR-RES	-5.44		-4.75		-4.25	
SK-OV-3	-4.91		-4.41		> -4.00	
Renal Cancer						
786-0	-5.06		-4.67		-4.32	
A498	-5.63		-5.15		-4.58	
ACHN	-5.19		-4.72		-4.36	
CAKI-1	-5.26		-4.40		> -4.00	
RXF 393	-5.16		-4.62		-4.19	
SN12C	-5.18		-4.69		-4.34	
TK-10	-5.05		-4.54		-4.05	
UO-31	-5.20		-4.68		-4.31	
Prostate Cancer						
PC-3	-5.60		-4.78		-4.24	
DU-145	-5.26		-4.58		-4.02	
Breast Cancer						
MCF7	-5.42		-4.73		-4.19	
MDA-MB-231/ATCC	-5.17		-4.65		-4.25	
HS 578T	-5.57		-4.61		> -4.00	
BT-549	-5.77		-5.08		-4.47	
T-47D	-5.65		-4.96		> -4.00	
MDA-MB-468	-5.84		-4.85		-4.18	
_MID	-5.38		-4.77		-4.29	
Delta	1.45		0.93		0.74	
Range	2.2		1.32		1.03	



S86