Supporting Information

Total Synthesis and Evaluation of Chlorofusin, its Seven Chromophore Diastereomers and Key Partial Structures

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NMR solvent residual peaks used in all data collection

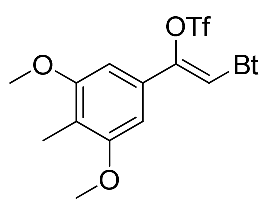
DMSO-d_6
- ^{1}H NMR: 2.52 ppm (As used by Williams)
- ^{13}C NMR: 39.6 ppm (As used by Williams)

$CDCl_3$
- ^{1}H NMR: 7.26 ppm
- ^{13}C NMR: 77.23 ppm

CD_3OD
- ^{13}C NMR: 49.05

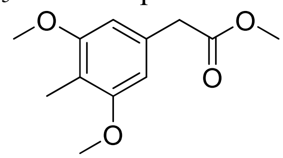
acetone-d_6
- ^{1}H NMR: 2.05 ppm
- ^{13}C NMR: 30.83 ppm

ROESY mixing time: 300 ms

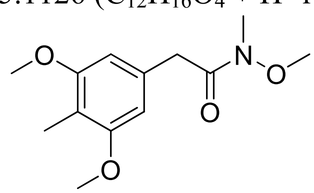


(*Z*)-2-(1*H*-Benzo[*d*]-1,2,3-triazol-1-yl)-1-(3,5-dimethoxy-4-methylphenyl)vinyl trifluoromethanesulfonate (6). A mixture of commercially available 3,5-dimethoxy-4-methylbenzoic acid (5.0 g, 25 mmol) in thionyl chloride (19 mL, 260 mmol) was warmed at 60 °C for 2 h. The volatiles were removed under reduced pressure to provide the crude acid chloride, which was dissolved in THF (30 mL), treated with 1-(trimethylsilylmethyl)benzotriazole (5.2 g, 25 mmol) and warmed at 85 °C for 24 h. The reaction mixture was cooled to 0 °C and the precipitate was collected. The residue was washed with cold THF (20 mL) and dried under reduced pressure to afford the crude *N*-(acylmethyl)benzotriazole as a gray solid which used in the next step without purification. A suspension of the crude intermediate (7.1 g) in anhydrous CH_2Cl_2 (46 mL) under nitrogen was cooled to 0 °C. The reaction mixture was treated with 2,6-lutidine (5.4 mL, l50 mmol), freshly distilled trifluoromethanesulfonic anhydride (4.3 mL, 25 mmol), and stirred at 23 °C for 4 h. The reaction mixture was quenched with the addition of saturated aqueous NH_4Cl (20 mL), extracted with EtOAc (3 × 20 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated under reduced pressure.

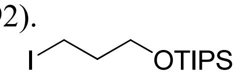
Flash chromatography (SiO_2, 15% EtOAc–hexanes) afforded **6** as a gray solid (86% over three steps, 9.9 g): mp 129–133 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.15 (d, J = 8.4 Hz, 1H), 7.61–7.65 (m, 2H), 7.61 (s, 1H), 7.48 (ddd, J = 8.1, 6.2, 1.7 Hz, 1H), 6.87 (s, 2H), 3.91 (s, 6H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 158.9 (2C), 145.6, 143.6, 132.8, 129.2, 128.9, 125.1, 120.7, 118.8, 118.2 (q, J = 321 Hz), 113.3, 110.3, 101.8 (2C), 56.1 (2C), 8.7; IR (film) ν_{max} 1584, 1456, 1417, 1215, 1140, 1047, 745 cm^{-1}; HR ESI-TOF m/z 444.0831 ($C_{18}H_{16}F_3N_3O_5S + H^+$ requires 444.0841).



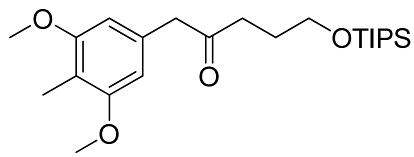
Methyl 2-(3,5-dimethoxy-4-methylphenyl)acetate (7). A solution of **6** (9.0 g, 20 mmol) in anhydrous MeCN (130 mL) was treated with NaOMe (2.7 g, 49 mmol) and stirred at 60 °C for 12 h. The reaction mixture was cooled and concentrated under reduced pressure. The residue was dissolved in MeOH (130 mL), treated with aqueous 12 N HCl (5.0 mL) and warmed at 70 °C for 18 h. The volatiles were removed under reduced pressure and the residue was dissolved in EtOAc (150 mL), washed with saturated aqueous $NaHCO_3$ (50 mL), H_2O (30 mL), saturated aqueous NaCl (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to yield **7** as a colorless oil (87% over two steps, 3.9 g): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.46 (s, 2H), 3.82 (s, 6H), 3.70 (s, 3H), 3.59 (s, 2H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.3, 158.4 (2C), 132.3, 113.5, 104.8 (2C), 55.9 (2C), 52.2, 41.8, 8.2; IR (film) ν_{max} 2952, 2839, 1738, 159, 1455, 1243, 1138 cm^{-1}; HR ESI-TOF m/z 225.1126 ($C_{12}H_{16}O_4 + H^+$ requires 225.1127).



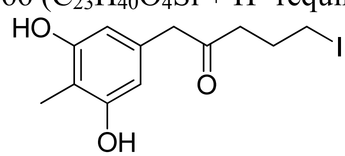
2-(3,5-Dimethoxy-4-methylphenyl)-*N*-methoxy-*N*-methylacetamide (8). A suspension of **7** (2.80 g, 12.5 mmol) and NH(OMe)Me·HCl (2.07 g, 21.2 mmol) in anhydrous THF (25 mL) at −20 °C under argon was treated with a solution of *i*-PrMgCl (2.0 M in THF, 21.2 mL, 42.4 mmol) over 30 min. The reaction mixture was stirred at −10 °C for 30 min before being quenched with the addition of saturated aqueous NH_4Cl. The resulting mixture was extracted with Et_2O (3 × 30 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2, 40% EtOAc–hexanes) to yield **8** as a white solid (95%, 3.01 g): mp 50–53 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.48 (s, 2H), 3.80 (s, 6H), 3.73 (s, 2H), 3.62 (s, 3H), 3.20 (s, 3H), 2.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 158.3 (2C), 133.2, 113.0, 104.8 (2C), 61.5, 55.9 (2C), 39.9, 32.4, 8.1,; IR (film) ν_{max} 2928, 2857, 1659, 1586, 1457, 1418, 1379, 1239, 1138, 1007 cm^{-1}; HR ESI-TOF m/z 254.1378 ($C_{13}H_{19}NO_4 + H^+$ requires 254.1392).



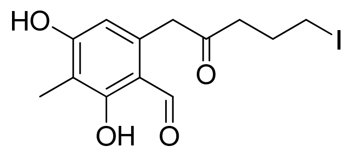
3-Iodo-1-triisopropylsilyloxypropane (9). Commercially available 3-iodopropan-1-ol (2.85 mL, 29.7 mmol) in anhydrous CH_2Cl_2 (30 mL) under argon was cooled to 0 °C, treated with 2,6-lutidine (7.60 mL, 65.3 mmol), triisopropylsilyl-trifluoromethanesulfonate (10.0 g, 32.6 mmol) and stirred at 23 °C for 18 h. The reaction mixture was diluted with EtOAc (100 mL), washed with aqueous 1 N HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), H_2O (30 mL), saturated aqueous NaCl (30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2, heptane) to yield **9** as a colorless oil (95%, 9.65 g): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.75 (t, J = 5.6 Hz, 2H), 3.32 (t, J = 6.7 Hz, 2H), 2.01 (m, 2H), 1.07 (m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 62.7, 36.5, 18.0 (6C), 11.9 (3C), 3.8; IR (film) ν_{max} 2941, 2861, 1463, 1104, 882, 682 cm^{-1}; HR ESI-TOF *m/z* 343.0950 ($C_{12}H_{27}IOSi$ + H^+ requires 343.0954).



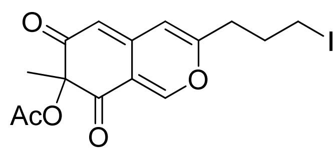
1-(3,5-Dimethoxy-4-methylphenyl)-5-(triisopropylsilyloxy)pentan-2-one (10). A solution of *tert*-butyl lithium (1.7 M in pentane, 17.3 mL, 29.4 mmol) in anhydrous Et_2O (83 mL) was cooled to −78 °C under argon, treated with **9** (4.58 g, 13.4 mmol) in Et_2O (27 mL) and stirred at −78 °C for 20 min before a solution of **8** (2.82 g, 11.2 mmol) in anhydrous THF (22 mL) was added. The reaction mixture was stirred at −78 °C for 3 h before being quenched with the addition of saturated aqueous NH_4Cl. The resulting mixture was stirred at 23 °C for 1 h, extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 10% EtOAc−hexanes) to afford **10** as a pale yellow oil (90%, 4.10 g): ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.37 (s, 2H), 3.80 (s, 6H), 3.65 (t, J = 5.6 Hz, 2H), 3.64 (s, 2H), 2.58 (t, J = 7.2 Hz, 2H), 2.06 (s, 3H), 1.78 (app quint, J = 6.6 Hz, 2H), 0.97–1.08 (m, 21H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 209.0, 158.6 (2C), 132.8, 113.3, 104.9 (2C), 62.4, 55.9 (2C), 51.1, 38.2, 27.1, 18.2 (6C), 12.1 (3C), 8.2; IR (film) ν_{max} 2932, 2868, 1713, 1590, 1463, 1413, 1137, 1100 cm^{-1}; HR ESI-TOF *m/z* 409.2766 ($C_{23}H_{40}O_4Si$ + H^+ requires 409.2774).



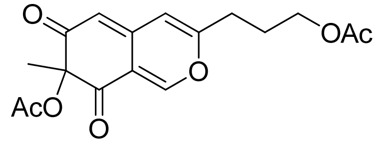
1-(3,5-Dihydroxy-4-methylphenyl)-5-iodopentan-2-one (11). A solution of **10** (412 mg, 1.01 mmol) in anhydrous MeCN (14.5 mL) was treated with iodotrimethylsilane (2.15 mL, 15.1 mmol) and warmed at 120 °C for 50 min at the normal absorption level in a microwave reactor. The cooled reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ (1 mL), stirred at 23 °C for 30 min and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), concentrated under reduced pressure and purified by flash chromatography (SiO_2, 3% MeOH−CH_2Cl_2) to afford **11** as an oil (95%, 321 mg): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.26 (s, 2H), 4.81 (br s, 2H), 3.54 (s, 1H), 3.17 (t, J = 6.7 Hz, 2H), 2.60 (t, J = 6.9 Hz, 2H), 2.11 (s, 3H), 2.03 (app quint, J = 6.8 Hz, 2H), one OH was not observed; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 208.7, 155.4 (2C), 132.4, 109.8, 108.8 (2C), 50.1, 42.3, 27.3, 8.1, 6.4; IR (film) ν_{max} 3383, 2922, 1702, 1598, 1431, 1371, 1081 cm^{-1}; HR ESI-TOF *m/z* 335.1042 ($C_{12}H_{15}IO_3$ + H^+ requires 335.0144).



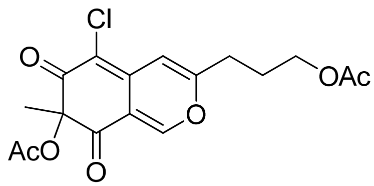
2,4-Dihydroxy-6-(5-iodo-2-oxopentyl)-3-methylbenzaldehyde (12). A suspension of $AlCl_3$ (1.06 g, 7.92 mmol) in anhydrous toluene (53 mL) was cooled to −45 °C under argon, treated with a solution of **11** (882 mg, 2.64 mmol) in triethyl orthoformate (8.80 mL, 52.8 mmol) and stirred at −30 °C for 1 h. The reaction mixture was treated at −15 °C with aqueous 2 N HCl (10 mL), warmed to 23 °C and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with saturated aqueous NaCl (30 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO_2, 3% MeOH−CH_2Cl_2) to provide **12** as a gray solid (75%, 717 mg): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.88 (s, 1H), 6.24 (s, 1H), 5.52 (br s, 1H), 3.92 (s, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.70 (t, *J* = 6.9 Hz, 2H), 2.10 (s, 3H), 2.06 (app quint, *J* = 6.7 Hz, 2H), one OH was not observed; ^{13}C NMR (CD_3OD, 125 MHz) δ 208.3, 194.9, 165.2, 164.6, 139.1, 113.8, 111.7, 111.5, 46.7, 43.5, 28.7, 7.3, 5.9; IR (film) ν_{max} 3335, 2923, 1712, 1620, 1428, 1303, 125,2 1121 cm^{-1}; HR ESI-TOF *m/z* 384.9913 ($C_{13}H_{15}IO_4 + Na^+$ requires 384.9913).



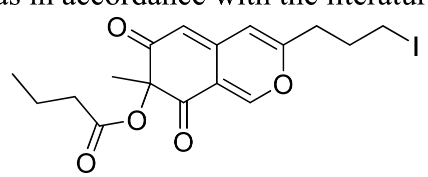
7-Acetoxy-3-(3-iodopropyl)-7-methyl-6*H*-isochromene-6,8-dione (13). A solution of **12** (547 mg, 1.51 mmol) in acetic acid (150 mL) was treated with *p*-TsOH (2.60 g, 15.1 mmol). The reaction mixture was stirred at 95 °C under argon. After 90 min, the reaction mixture was cooled to 15 °C, degassed with nitrogen for 30 min, treated portionwise with 95% lead tetraacetate (803 mg, 1.81 mmol) over 15 min, stirred at 15 °C for 30 min, and allowed to stand at 15−17 °C for 20 min. The reaction mixture was poured into ice water (200 mL), extracted with EtOAc (3 × 100 mL), and the combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 50% EtOAc−hexanes) afforded **13** as an oil (48%, 291 mg): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.86 (d, *J* = 0.8 Hz, 1H), 6.15 (s, 1H), 5.53 (d, *J* = 1.0 Hz, 1H), 3.18-3.26 (m, 2H), 2.56 (app t, *J* = 7.5 Hz, 2H), 2.16 (s, 3H), 2.11 (app quint, *J* = 6.7 Hz, 2H), 1.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.3, 192.9, 170.3, 160.3, 154.0, 142.4, 115.5, 109.8, 107.6, 84.6, 34.0, 29.9, 22.4, 20.3, 4.4; IR (film) ν_{max} 3458, 2926, 1720, 1641, 1444, 1249 cm^{-1}; HR ESI-TOF *m/z* 403. 0043 ($C_{15}H_{15}IO_5 + H^+$ requires 403.0042).



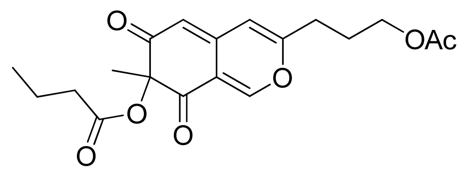
7-Acetoxy-3-(3-acetoxypropyl)-7-methyl-6*H*-isochromene-6,8-dione (15). A solution of **13** (140 mg, 0.35 mmol) in acetic acid (3.50 mL) was treated with silver acetate (174 mg, 1.05 mmol) and stirred at 50 °C for 4 h. The reaction mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. Chromatography (SiO_2, 50% EtOAc−hexanes) afforded **15** as an oil (87%, 86.0 mg): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.86 (d, *J* = 0.9 Hz, 1H), 6.12 (s, 1H), 5.52 (d, *J* = 1.1 Hz, 1H), 4.13 (t, *J* = 6.2 Hz, 2H), 2.50 (app t, *J* = 7.6 Hz, 2H), 2.16 (s, 3H), 2.06 (s, 3H), 1.93–2.00 (m, 2H), 1.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.4, 192.9, 171.1, 170.3, 161.1, 154.0, 142.5, 115.4, 109.3, 107.5, 84.6, 63.1, 30.1, 25.9, 22.5, 21.1, 20.3; IR (film) ν_{max} 3359, 2929, 1713, 1618, 1427, 1302, 1252, 1121 cm^{-1}; HR ESI-TOF *m/z* 335.1127 ($C_{17}H_{18}O_7 + H^+$ requires 335.1131).



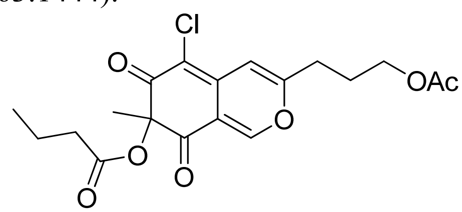
7-Acetoxy-3-(3-acetoxypropyl)-5-chloro-7-methyl-6*H*-isochromene-6,8-dione (17). A solution of **15** (91 mg 0.27 mmol) in acetic acid (2.7 mL) was treated with *N*-chlorosuccinimide (39 mg, 0.29 mmol). The reaction mixture was stirred at 23 °C for 24 h before being quenched with the addition of saturated aqueous $Na_2S_2O_3$ (0.5 mL). The reaction mixture was diluted with EtOAc (30 mL), washed with saturated aqueous $NaHCO_3$ (3 × 10 mL), H_2O (10 mL), saturated aqueous NaCl (10 mL) and the organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 40% EtOAc–hexanes) afforded **17** as a yellow solid (87%, 86 mg): mp 177–178 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.91 (s, 1H), 6.62 (s, 1H), 4.16 (t, *J* = 6.1 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.17 (s, 3H), 2.08 (s, 3H), 2.02 (m, 2H), 1.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 191.8, 186.5, 171.1, 170.4, 163.1, 153.1, 138.3, 115.1, 111.1, 106.5, 84.8, 63.1, 30.5, 26.0, 22.5, 21.1, 20.3; IR (film) ν_{max} 3212, 3086, 2959, 1743, 1647, 1558, 1472, 1241, 852, 773 cm^{-1}; HR ESI-TOF *m/z* 369.0729 ($C_{17}H_{17}ClO_7 + H^+$ requires 369.0741). Spectral data was in accordance with the literature values.[1]



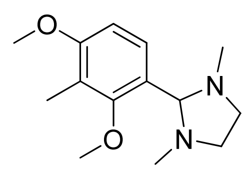
7-Butyryloxy-3-(3-iodopropyl)-7-methyl-6*H*-isochromene-6,8-dione (14). A solution of **12** (561 mg 1.55 mmol) in butyric acid (155 mL) was treated with *p*-TsOH (2.67 g, 15.5 mmol). The reaction mixture was stirred at 100 °C under argon. After 90 min, the reaction mixture was cooled to 15 °C, degassed with nitrogen for 30 min, treated portionwise with 95% lead tetraacetate (824 mg, 1.86 mmol) over 15 min, stirred at 15 °C for 30 min, and allowed to stand at 15–17 °C for 20 min. The reaction mixture was poured into ice water (200 mL), extracted with EtOAc (3 × 100 mL), and the combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 40% EtOAc–hexanes) afforded **14** as an oil (31%, 207 mg): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.86 (s, 1H), 6.16 (s, 1H), 5.54 (s, 1H), 3.22 (td, *J* = 1.8, 6.7 Hz, 2H), 2.56 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 2.12 (dt, *J* = 12.2, 6.0 Hz, 2H), 1.66 (m, 2H), 1.53 (s, 3H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.5, 193.2, 173.2, 160.2, 154.0, 142.4, 115.4, 109.8, 107.6, 84.3, 35.3, 34.0, 29.9, 22.3, 18.4, 13.7, 4.5; IR (film) ν_{max} 2917, 1728, 1645, 1626, 1449, 1249, 1177, 1081, 1028 cm^{-1}; HR ESI-TOF *m/z* 431.0351 ($C_{17}H_{19}IO_5 + H^+$ requires 431.0355).



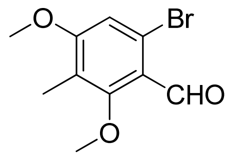
3-(3-Acetoxypropyl)-7-butyryloxy-7-methyl-6*H*-isochromene-6,8-dione (16). A solution of **14** (77 mg, 0.18 mmol) in butyric acid (1.80 mL) was treated with silver acetate (90 mg, 0.54 mmol) and stirred at 57 °C for 3 h. The reaction mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. Chromatography (SiO_2, 40% EtOAc–hexanes) afforded **16** as an oil (63%, 41 mg): ^1H NMR ($CDCl_3$, 400 MHz) δ 7.87 (d, J = 0.9 Hz, 1H), 6.13 (s, 1H), 5.53 (d, J = 1.1 Hz, 1H), 4.13 (t, J = 6.2 Hz, 2H), 2.50 (app t, J = 7.6 Hz, 2H), 2.42 (t, J = 7.3 Hz, 2H), 2.07 (s, 3H), 1.92–2.01 (m, 2H), 1.66 (app sext, J = 7.4 Hz, 2H), 1.52 (s, 3H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 193.5, 193.1, 173.2, 171.1, 161.0, 154.0, 142.5, 115.4, 109.3, 107.5, 84.3, 63.1, 35.3, 30.1, 25.9, 22.3, 21.1, 18.4, 13.7; IR (film) ν_{max} 2922, 2858, 1728, 1624, 1450, 1367, 1244, 1092 cm^{-1}; HR ESI-TOF m/z 363.1442 ($C_{19}H_{22}O_7 + H^+$ requires 363.1444).



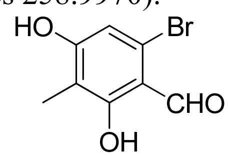
3-(3-Acetoxypropyl)-7-butyryloxy-5-chloro-7-methyl-6*H*-isochromene-6,8-dione (18). A solution of **16** (44 mg 0.11 mmol) in acetic acid (1.1 mL) at 23 °C was treated with *N*-chlorosuccinimide (16 mg, 0.12 mmol). The reaction mixture was stirred at 23 °C for 24 h before being quenched with the addition of saturated aqueous $Na_2S_2O_3$ (0.2 mL). The reaction mixture was diluted with EtOAc (15 mL), washed with saturated aqueous $NaHCO_3$ (3 × 5 mL), H_2O (5 mL), saturated aqueous NaCl (5 mL) and the organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 40% EtOAc–hexanes) afforded **18** as a yellow solid (85%, 37 mg): mp 89–91 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.89 (s, 1H), 6.61 (s, 1H), 4.14 (t, J = 6.2 Hz, 2H), 2.59 (app t, J = 7.6 Hz, 2H), 2.41 (td, J = 7.3, 1.0 Hz, 2H), 2.06 (s, 3H), 1.97–2.04 (m, 2H), 1.65 (app sext, J = 7.4 Hz, 2H), 1.54 (s, 3H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.9, 186.5, 173.2, 171.1, 163.0, 153.1, 138.2, 115.1, 111.0, 106.5, 84.5, 63.1, 35.2, 30.5, 25.9, 22.4, 21.1, 18.4, 13.7; IR (film) ν_{max} 2918, 1736, 1644, 1536, 1429, 1368, 1242, 1129, 1043 cm^{-1}; HR ESI-TOF m/z 397.1045 ($C_{19}H_{21}ClO_7 + H^+$ requires 397.1054).



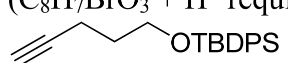
2-(2,4-Dimethoxy-3-methylphenyl)-1,3-dimethylimidazolidine (20). A solution of 2,4-dimethoxy-3-methylbenzaldehyde (50.7 g, 0.281 mol) in anhydrous toluene (500 mL) was treated with *N,N'*-dimethylethylenediamine (36 mL, 0.34 mol) and warmed at 130 °C for 3 h in a flask fitted with a Dean–Stark trap. The cooled reaction mixture was treated with Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the residue was purified by vacuum distillation (0.3 torr) at 165 °C to afford **20** as a clear colorless oil that crystallized on standing (67.0 g, 95%): mp 41 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (d, J = 8.6 Hz, 1H), 6.69 (d, J = 8.7 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 1H), 3.70 (s, 3H), 3.29–3.42 (m, 2H), 2.49–2.62 (m, 2H), 2.18 (s, 6H), 2.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.3, 158.6, 127.2, 124.4, 118.6, 107.1, 84.6, 61.5, 55.7, 53.5, 39.9, 9.3; IR (film) ν_{max} 2940, 2834, 2775, 1600, 1488, 1453, 1361, 1271, 1161, 1106, 1043, 1025, 1007, 991, 882, 805 cm^{-1}; HR ESI-TOF *m/z* 251.1750 ($C_{14}H_{22}N_2O_2 + H^+$ requires 251.1759).



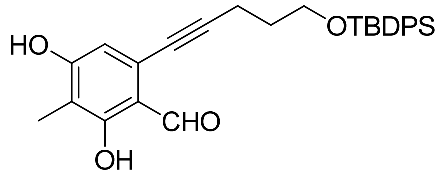
6-Bromo-2,4-dimethoxy-3-methylbenzaldehyde (21). A solution of **20** (5.00 g, 20.0 mmol) in anhydrous ether (95 mL) at −55 °C was treated with *tert*-butyl lithium (1.5 M in hexane, 14.6 mL, 22.0 mmol) and stirred at 0 °C for 1 h. The reaction mixture was cooled to −78 °C, treated with 1,2-dibromotetrafluoroethane (6.23 g, 24.0 mmol) in ether (15 mL) and stirred at 23 °C for 18 h. The reaction mixture was treated with aqueous 2 N HCl (100 mL), stirred for 30 min and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were washed with saturated aqueous NH_4Cl (2 × 200 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 5−10% EtOAc−hexanes gradient) to yield **21** as a white solid (3.70 g, 72%): mp 71 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.28 (s, 1H), 6.93 (s, 1H), 3.90 (s, 3H), 3.81 (s, 3H), 2.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 190.0, 162.9, 162.2, 124.4, 121.1, 121.1, 112.6, 62.8, 56.3, 8.6; IR (film) ν_{max} 2981, 2943, 2852, 1684, 1584, 1450, 1376, 1283, 1234, 1134, 1019, 988, 816 cm^{-1}; HR ESI-TOF *m/z* 258.9961 ($C_{10}H_{11}BrO_3 + H^+$ requires 258.9970).



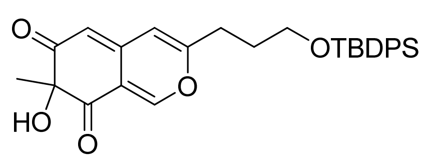
6-Bromo-2,4-dihydroxy-3-methylbenzaldehyde (22). A solution of **21** (6.43 g, 24.8 mmol) in anhydrous CH_2Cl_2 (400 mL) was cooled to −78 °C, treated with BBr_3 (1 M in CH_2Cl_2, 100 mL, 99.3 mmol) dropwise over 30 min, and stirred at 23 °C for 24 h. The reaction mixture was cooled to 0 °C, treated with H_2O (300 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The combined organic layers were washed with saturated aqueous NaCl (1 × 400 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 10−20% EtOAc−hexanes gradient) to yield **22** as a white solid (5.06 g, 88%): mp 175 °C; ^{1}H NMR (acetone-d_6, 500 MHz) δ 12.71 (s, 1H), 10.06 (s, 1H), 9.86 (s, 1H), 6.83 (s, 1H), 2.02 (s, 3H); ^{13}C NMR (acetone-d_6, 125 MHz) δ 197.5, 166.0, 164.9, 127.2, 114.7, 113.5, 113.2, 8.4; IR (film) ν_{max} 3127, 1602, 1461, 1314, 1251, 1122, 739, 568 cm^{-1}; HR ESI-TOF *m/z* 230.9651 ($C_8H_7BrO_3 + H^+$ requires 230.9657).



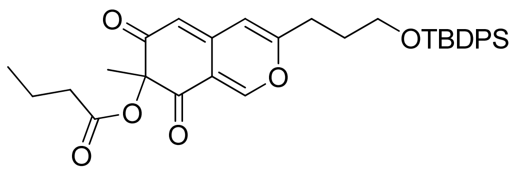
1-*tert*-Butyldiphenylsilyloxy-4-pentyne (23). A solution of 4-pentyn-1-ol (1.00 g, 11.9 mmol) and imidazole (2.03 g, 29.7 mmol) in THF (25 mL) was treated with TBDPSCl (3.7 mL, 14 mmol) over 5 min and stirred at 23 °C for 4 h. The reaction mixture was treated with saturated aqueous NH_4Cl (100 mL) and extracted with 1:1 Et_2O–hexanes (3 × 100 mL). The combined organic layers were washed with saturated aqueous NaCl (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 2–5% EtOAc–hexanes gradient) to afford **23** as a colorless oil (98%, 3.72 g): ^1H NMR ($CDCl_3$, 500 MHz) δ 7.65–7.69 (m, 4H), 7.35–7.45 (m, 6H), 3.75 (t, J = 6.0 Hz, 2H), 2.35 (dt, J = 7.2, 2.7 Hz, 2H), 1.91 (t, J = 2.7 Hz, 1H), 1.78 (tt, J = 7.2, 6.0 Hz, 2H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 135.8 (4C), 134.0 (2C), 129.8 (2C), 127.8 (4C), 84.5, 68.5, 62.5, 31.7, 27.1 (3C), 19.5, 15.2; IR (film) ν_{max} 3305, 3070, 2932, 2858, 1471, 1428, 1389, 1109, 981, 822, 739, 703, 614 cm^{-1}; HR ESI-TOF *m/z* 323.1829 ($C_{21}H_{26}OSi + H^+$ requires 323.1831).



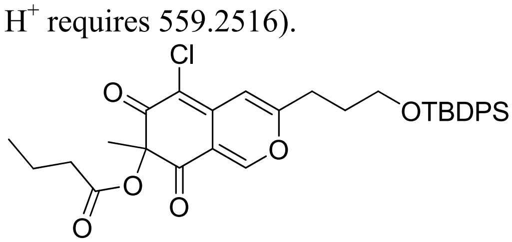
6-(5-(*tert*-Butyldiphenylsilyloxy)pent-1-ynyl)-2,4-dihydroxy-3-methylbenzaldehyde (24). A flask containing **22** (2.15 g, 9.31 mmol), **23** (4.50 g, 14.0 mmol), $PdCl_2(PPh_3)_2$ (653 mg, 0.931 mmol) and CuI (177 mg, 0.931 mmol) was evacuated and backfilled with argon three times, charged with degassed DMF (30 mL), treated with Et_3N (4.5 mL, 33 mmol) and stirred at 70 °C for 16 h. The reaction mixture was cooled and treated with saturated aqueous NH_4Cl (20 mL), stirred at 23 °C for 10 min and extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with saturated aqueous NaCl (40 mL), dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2, 5–20% EtOAc–hexanes gradient) to afford **24** as a white solid (3.20 g, 73%): mp 144 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ 12.33 (s, 1H), 10.15 (s, 1H), 7.65–8.00 (m, 4H), 7.39–7.44 (m, 2H), 7.35–7.39 (m, 4H), 6.39 (s, 1H), 5.46 (s, 1H), 3.80 (t, J = 5.9 Hz, 2H), 2.61 (t, J = 7.1 Hz, 2H), 2.11 (s, 3H), 1.86 (tt, J = 7.0, 6.0 Hz, 2H), 1.07 (s, 9H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 195.4, 163.1, 160.4, 135.8 (4C), 133.9 (2C), 129.9 (2C), 127.9 (4C), 127.5, 114.7, 112.5, 111.6, 97.1, 76.1, 62.5, 31.5, 27.1 (3C), 19.5, 16.3, 7.3; IR (film) ν_{max} 3178, 2930, 2861, 1770, 1601, 1472, 1428, 1284, 1250, 1180, 1132, 1061, 701 cm^{-1}; HR ESI-TOF *m/z* 473.2162 ($C_{29}H_{32}O_4Si + H^+$ requires 473.2148).



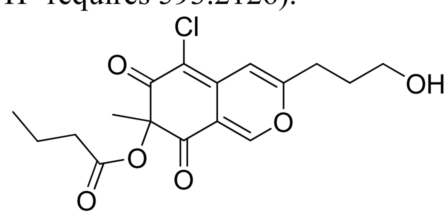
3-(3-*tert*-Butyldiphenylsilyloxypropyl)-7-hydroxy-7-methyl-6*H*-isochromene-6,8-dione (25). A suspension of **24** (1.63 g, 3.44 mmol) and $Au(OAc)_3$ (64 mg, 0.17 mmol) in dichloroethane (25 mL) was treated with trifluoroacetic acid (1.6 mL, 24 mmol) and stirred at 23 °C for 4 min before being treated with IBX (1.06 g, 3.79 mmol), tetrabutylammonium iodide (64 mg, 0.17 mmol) and stirred at 23 °C for 4 h. The reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ (25 mL), diluted with H_2O (50 mL) and extracted with EtOAc (3 × 75 mL). The combined organic layers were washed with saturated aqueous NaCl (75 mL), dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2 pretreated with 1% AcOH in 40% EtOAc–hexanes, 40–60% EtOAc–hexanes gradient) to yield **25** as a yellow oil (72%, 1.22 g). The enantiomers of **25** were resolved by semi-preparative chiral HPLC (Daicel CHIRALCEL® OD column, 2 × 25 cm, 20% EtOH−hexanes, 7 mL/min, 320 nm, t_R: 22.3 min (*R*)-**25**, 30.2 min (*S*)-**25**, α = 1.35). For (*R*)-**25**: CD (MeOH, 1 mM) λ_{ext} nm (Δε) 363 (–2.9), 280 (2.3), 241 (2.0); $[\alpha]^{23}_D$ –75 (*c* 0.64, MeOH); for (*S*)-**25**: CD (MeOH, 1 mM) λ_{ext} nm (Δε) 361 (3.1), 279 (–2.8), 240 (–2.8); $[\alpha]^{23}_D$ +77 (*c* 0.53, MeOH). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.83 (d, *J* = 0.7 Hz, 1H), 7.62−7.67 (m, 4H), 7.41−7.46 (m, 2H), 7.36−7.41 (m, 4H), 6.04 (s, 1H), 5.48 (d, *J* = 1.1 Hz, 1H), 3.91 (br s, 1H), 3.71 (t, *J* = 5.9 Hz, 2H), 2.56 (t, *J* = 7.4 Hz, 2H), 1.86 (tt, *J* = 7.1, 6.1 Hz, 2H), 1.54 (s, 3H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 196.5, 195.9, 162.8, 153.1, 144.2, 135.7 (4C), 133.6 (2C), 130.0 (2C), 128.0 (4C), 116.0, 108.7, 105.3, 83.7, 62.5, 30.0, 29.4, 28.7, 27.1 (3C), 19.4; IR (film) ν_{max} 3425, 3069, 2934, 2860, 1718, 1630, 1430, 1106, 737, 704 cm^{-1}; HR ESI-TOF *m/z* 489.2088 ($C_{29}H_{32}O_5Si + H^+$ requires 489.2097).



3-(3-*tert*-Butyldiphenylsilyloxypropyl)-7-butyryloxy-7-methyl-6*H*-isochromene-6,8-dione (26). A solution of **25** (697 mg, 1.43 mmol) in CH_2Cl_2 (20 mL) was treated with butyric anhydride (1.20 mL, 7.13 mmol), DMAP (17 mg, 0.14 mmol) and stirred at 23 °C for 24 h. The reaction mixture was treated with MeOH (3 mL), stirred at 23 °C for 15 min and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2 pretreated with 1% AcOH in 10% EtOAc–hexanes, 10–20% EtOAc–hexanes gradient) to yield **26** as an orange oil that solidified on standing (91%, 722 mg). The enantiomers of **26** were resolved by semi-preparative chiral HPLC (Daicel CHIRALCEL® OD column, 2 × 25 cm, 20% EtOH−hexanes, 7 mL/min, 320 nm, t_R: 22.3 min (*R*)-**26**, 24.2 min (*S*)-**26**, α = 1.09). For (*R*)-**26**: CD (MeOH, 0.2 mM) λ_{ext} nm (Δε) 349 (–4.3), 272 (3.4), 239 (1.3); $[\alpha]^{23}_D$ –133 (*c* 0.34, MeOH); for (*S*)-**26**: CD (MeOH, 0.2 mM) λ_{ext} nm (Δε) 351 (4.0), 272 (–3.1), 239 (–1.6); $[\alpha]^{23}_D$ +135 (*c* 0.31, MeOH). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.82 (s, 1H), 7.62−7.68 (m, 4H), 7.42−7.47 (m, 2H), 7.36−7.42 (m, 4H), 6.02 (s, 1H), 5.49 (s, 1H), 3.71 (t, *J* = 5.9 Hz, 2H), 2.53 (t, *J* = 7.5 Hz, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 1.77−1.90 (m, 2H), 1.67 (sext., *J* = 7.4 Hz, 2H), 1.52 (s, 3H), 1.06 (s, 9H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.6, 193.1, 173.1, 162.1, 154.1, 142.8, 135.7 (4C), 133.7 (2C), 130.0 (2C), 128.0 (4C), 115.3, 109.0, 107.1, 84.3, 62.5, 35.3, 29.9, 29.5, 27.1 (3C), 22.4, 19.4, 18.4, 13.7; IR (film) ν_{max} 2956, 2931, 2857, 1737, 1718, 1648, 1458, 1426, 1110, 704 cm^{-1}; HR ESI-TOF *m/z* 559.2506 ($C_{33}H_{38}O_6Si + H^+$ requires 559.2516).



3-(3-*tert*-Butyldiphenylsilyloxypropyl)-7-butyryloxy-5-chloro-7-methyl-6*H*-isochromene-6,8-dione (27). A solution of **26** (723 mg, 1.29 mmol) in glacial AcOH (20 mL) was treated with *N*-chlorosuccinimide (225 mg, 1.68 mmol) and stirred at 23 °C for 36 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2 pretreated with 1% AcOH in 10% EtOAc–hexanes, 10–20% EtOAc–hexanes gradient) to yield **27** as a yellow oil (89%, 686 mg). The enantiomers of **27** were resolved by semi-preparative chiral HPLC (Daicel CHIRALCEL® OD column, 2 × 25 cm, 20% EtOH−hexanes, 7 mL/min, 320 nm, t_R: 18.8 min (*S*)-**27**, 25.0 min (*R*)-**27**, α = 1.33). For (*S*)-**27**: CD (MeOH, 0.2 mM) λ_{ext} nm ($\Delta\varepsilon$) 363 (–7.1), 307 (1.5), 276 (2.4), 239 (2.6); $[\alpha]^{23}_D$ –132 (*c* 1.8, MeOH); for (*R*)-**27**: CD (MeOH, 0.2 mM) λ_{ext} nm ($\Delta\varepsilon$) 362 (7.0), 309 (–1.5), 273 (–2.2), 239 (–2.8); $[\alpha]^{23}_D$ +134 (*c* 2.4, MeOH). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.86 (s, 1H), 7.62–7.68 (m, 4H), 7.42–7.46 (m, 2H), 7.36–7.42 (m, 4H), 6.59 (s, 1H), 3.72 (t, *J* = 5.9 Hz, 2H), 2.65 (t, *J* = 7.5 Hz, 2H), 2.43 (dt, *J* = 7.3, 1.3 Hz, 2H), 1.84–1.94 (m, 2H), 1.67 (sext., *J* = 7.4 Hz, 2H), 1.54 (s, 3H), 1.07 (s, 9H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 192.1, 186.6, 173.1, 164.2, 153.3, 138.5, 135.7 (4C), 133.6 (2C), 130.0 (2C), 128.0 (4C), 115.1, 110.7, 106.3, 84.5, 62.4, 35.2, 30.3, 29.6, 27.1 (3C), 22.5, 19.4, 18.4, 13.7; IR (film) ν_{max} 2955, 2932, 2860, 1731, 1720, 1649, 1580, 1542, 1426, 1256, 1232, 1181, 1109, 704 cm^{-1}; HR ESI-TOF *m/z* 593.2123 ($C_{33}H_{37}ClO_6Si + H^+$ requires 593.2126).



7-Butyryloxy-5-chloro-3-(3-hydroxypropyl)-7-methyl-6*H*-isochromene-6,8-dione (28). A solution of **27** (230 mg, 0.388 mmol) in THF (4 mL) was cooled to 0 °C, treated with pyridine (800 μL), HF-pyridine (380 μL) and stirred at 23 °C for 2 h. The reaction mixture was added slowly to a stirred mixture of EtOAc (50 mL) and saturated aqueous $NaHCO_3$ (100 mL). The aqueous layer was extracted with EtOAc (1 × 50 mL) and the combined organic layers were washed with saturated aqueous NaCl (3 × 20 mL), dried ($NaSO_4$) and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2 pretreated with 1% AcOH in 40% EtOAc–hexanes, 40–75% EtOAc–hexanes gradient) to yield **28** as a yellow oil (72%, 98 mg). The enantiomers of **28** were resolved by semi-preparative chiral HPLC (Daicel CHIRALCEL® OD column, 2 × 25 cm, 20% EtOH−hexanes, 7 mL/min, 320 nm, t_R: 22.2 min (*S*)- **28**, 25.0 min (*R*)- **28**, α = 1.13). For (*S*)- **28**: CD (MeOH, 0.2 mM) λ_{ext} nm ($\Delta\varepsilon$) 361 (–6.6), 300 (1.2), 274 (1.8), 241 (1.7); $[\alpha]^{23}_D$ –236 (*c* 0.94, MeOH); for (*R*)- **28**: CD (MeOH, 0.2 mM) λ_{ext} nm ($\Delta\varepsilon$) 363 (6.7), 299 (–2.2), 275 (–2.4), 242 (–2.5); $[\alpha]^{23}_D$ +236 (*c* 1.1, MeOH). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.91 (s, 1H), 6.62 (s, 1H), 3.74 (t, *J* = 6.0 Hz, 2H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.42 (dt, *J* = 7.2, 1.5 Hz, 2H), 1.87–1.95 (m, 2H), 1.66 (sext., *J* = 7.4 Hz, 2H), 1.59 (s, 1H), 1.55 (s, 3H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 192.0, 186.6, 173.2, 164.0, 153.3, 138.5, 115.1, 110.8, 106.4, 84.6, 61.4, 35.2, 30.2, 29.5, 22.5, 18.4, 13.6; IR (film) ν_{max} 3495, 2935, 2884, 1719, 1642, 1536, 1449, 1431, 1257, 1181, 1128, 1086, 1061, 836 cm^{-1}; HR ESI-TOF *m/z* 355.0941 ($C_{17}H_{19}ClO_6 + H^+$ requires 355.0948).

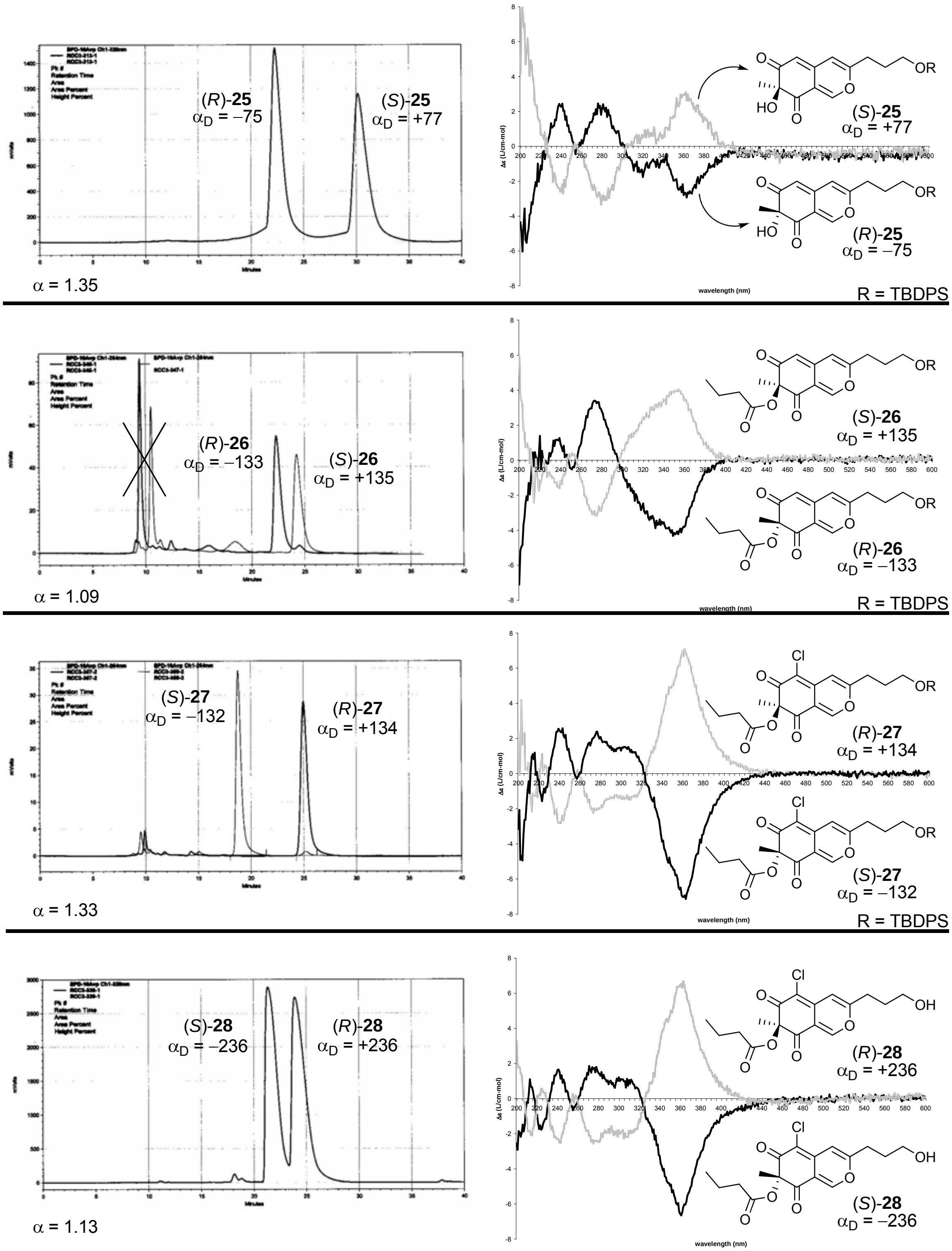
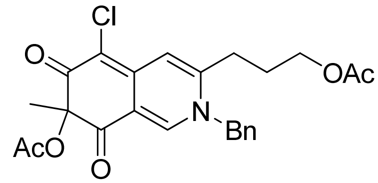
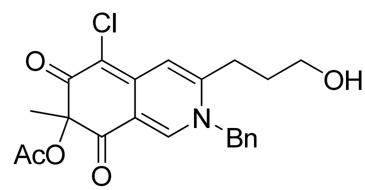


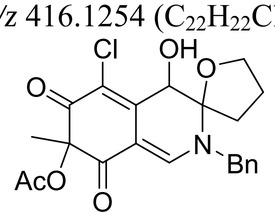
Figure S1. HPLC traces (CHIRALCEL® OD) and CD spectra (0.2 mM in MeOH) of **25**–**28**.



7-Acetoxy-3-(3-acetoxypropyl)-2-benzyl-5-chloro-7-methyl-2*H*,7*H*-isoquinoline-6,8-dione (34). A solution of **17** (63 mg, 0.17 mmol) in anhydrous CH_2Cl_2 (1.7 mL) was treated with benzylamine (21 μL, 0.19 mmol), stirred at 23 °C for 1 h and concentrated under reduced pressure. Chromatography (SiO_2, 70% EtOAc–hexanes) afforded **34** as a red solid (77 mg, 99%): mp 154–155 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.82 (s, 1H), 7.40 (m, 3H), 7.13 (d, *J* = 7.4 Hz, 2H), 6.80 (s, 1H), 5.04 (s, 2H), 4.10 (t, *J* = 6.0 Hz, 2H), 2.57 (m, 2H), 2.17 (s, 3H), 2.02 (s, 3H), 1.95 (dt, *J* = 6.4, 12.7 Hz, 2H), 1.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 193.9, 185.1, 171.0, 170.4, 149.8, 144.1, 142.1, 134.1, 129.9 (2C), 129.3, 126.3 (2C), 115.2, 113.9, 102.8, 85.0, 63.0, 57.1, 28.8, 27.6, 23.3, 21.1, 20.5; IR (film) ν_{max} 1729,1617, 1513, 1368, 1234, 1085, 855 cm^{-1}; HR ESI-TOF *m/z* 458.1360 ($C_{24}H_{24}ClNO_6$ + H^+ requires 458.1370). Spectral data was in accordance with the literature values.[1]



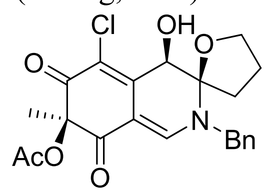
7-Acetoxy-2-benzyl-5-chloro-3-(3-hydroxypropyl)-7-methyl-2*H*,7*H*-isoquinoline-6,8-dione (35). A solution of **34** (40 mg, 0.087 mmol) in H_2O (90 μL) and MeOH (0.9 mL) was cooled to 0 °C and treated with K_2CO_3 (24 mg, 0.18 mmol). The reaction mixture was stirred at 0 °C for 30 min before being quenched with aqueous 0.1 N HCl (2.5 mL). The resulting mixture was acidified to pH 3 and extracted with EtOAc (3 × 3 mL). The combined organic phases were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 90% EtOAc–hexanes) afforded **35** as a red solid (75%, 27 mg) along with recovered **34** (25 %, 10 mg): mp 159–161 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (s, 1H), 7.35–7.46 (m, 3H), 7.14 (d, *J* = 6.9 Hz, 2H), 6.83 (s, 1H), 5.09 (s, 2H), 3.72 (t, *J* = 5.6 Hz, 2H), 2.66 (app t, *J* = 7.6 Hz, 2H), 2.17 (s, 3H), 1.82–1.91 (m, 2H), 1.56 (s, 3H), OH proton was not observed; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.9, 184.8, 170.4, 151.2, 144.7, 142.1, 134.3, 129.8 (2C), 129.2, 126.5 (2C), 115.4, 114.2, 102.7, 85.0, 61.1, 57.0, 31.5, 28.7, 23.4, 20.5; IR (film) ν_{max} 3400, 2925, 2853, 1704, 1593, 1503, 1234, 1146, 1081 cm^{-1}; HR ESI-TOF *m/z* 416.1254 ($C_{22}H_{22}ClNO_5$ + H^+ requires 416.1265).



36. A solution of **35** (12.3 mg, 0.0296 mmol) in H_2O (0.6 mL) and DMSO (3.0 mL) was treated with iodine (22.5 mg, 0.0887 mmol), silver trifluoroacetate (10.5 mg, 0.0473 mmol) and stirred at 23 °C for 2 days. The reaction mixture was quenched with the addition of saturated aqueous $Na_2S_2O_3$ (2 mL), diluted with EtOAc (50 mL), washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (10 mL), and saturated aqueous NaCl (10 mL). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (preparative TLC, SiO_2, 3 × 70% EtOAc–hexanes) afforded diastereomers **36A** (24%, 3.1 mg), **36B** (30%, 3.8 mg), **36C** (10%, 1.3 mg) and **36D** (6%, 0.8 mg) as well as recovered **35** (23%, 2.8 mg).

Isomerization of 36B to 36D: A solution of **36B** (4.8 mg, 0.011 mmol) in anhydrous CH_2Cl_2 (1.1 ml) at 23 °C was treated with anhydrous *p*-toluenesulfonic acid (5.7 mg, 0.033 mmol). The reaction mixture was stirred at 23 °C for 16 h and quenched with the addition of saturated aqueous $NaHCO_3$ (1 mL). The resulting mixture was extracted with CH_2Cl_2 (3 × 1 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (preparative TLC, SiO_2, 3 × 70% EtOAc–hexanes) afforded **36D** (0.3 mg, 11%) and recovered **36B** (2.0 mg, 74%).

Isomerization of 36C to 36A: A solution of **C** (1.7 mg, 0.004 mmol) in anhydrous MeCN (0.4 ml) at 23 °C was treated with anhydrous *p*-toluenesulfonic acid (3.4 mg, 0.020 mmol). The reaction mixture was stirred at 23 °C for 16 h and quenched with the addition of saturated aqueous $NaHCO_3$ (1 mL). The resulting mixture was extracted with CH_2Cl_2 (3 × 1 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (preparative TLC, SiO_2, 3 × 70% EtOAc–hexanes) afforded **36A** (0.9 mg, 51%) and recovered **36C** (0.3 mg, 18%).



= 36A

(relative stereochemistry depicted, confirmation of structure by X-ray[2])

For **36A**: Recrystallization from Et_2O (slow evaporation) provided **36A** as yellow needles from which a single-crystal X-ray structure was determined: mp 148–151 °C; ^1H NMR (DMSO-d_6, 600 MHz) δ 7.88 (s, 1H), 7.42–7.45 (m, 2H), 7.36–7.40 (m, 2H), 7.30–7.34 (m, 1H), 6.31 (d, *J* = 5.6 Hz, 1H), 4.79 (d, *J* = 15.1 Hz, 1H), 4.72 (d, *J* = 15.1 Hz, 1H), 4.53 (d, *J* = 5.5 Hz, 1H), 4.15–4.20 (m, 1H), 3.97 (dd, *J* = 14.9, 7.1 Hz, 1H), 2.07 (s, 3H), 1.85–1.99 (m, 3H), 1.75–1.84 (m, 1H), 1.43 (s, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.1, 188.9, 168.9, 150.2, 148.4, 137.4, 128.5 (2C), 128.1 (2C), 127.6, 113.9, 101.0, 97.9, 84.9, 70.3, 68.7, 52.1, 34.5, 24.5, 23.6, 20.0; IR (film) ν_{max} 3372, 2921, 2852, 1732, 1638, 1567, 1456, 1251, 1077 cm^{-1}; HR ESI-TOF *m/z* 432.1203 ($C_{22}H_{22}ClNO_6 + H^+$ requires 432.1214).

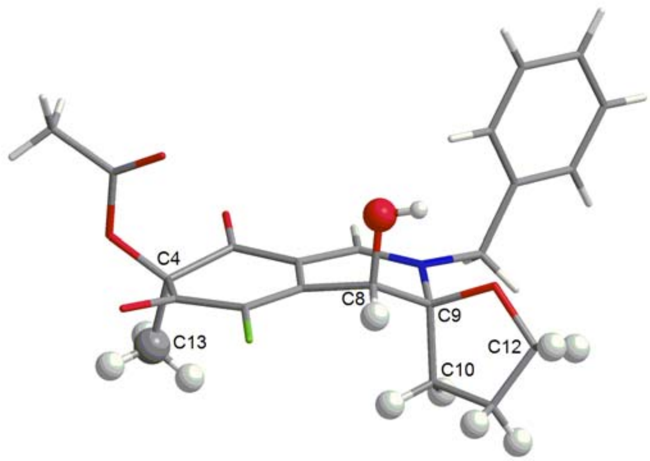
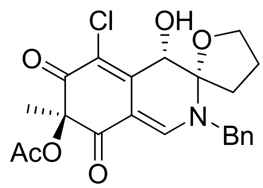


Figure S2. CIF file of **36A** viewed with Chem3D.



= **36B**

(relative stereochemistry depicted, confirmation of structure by X-ray[3])

For **36B**: Recrystallization from Et_2O (slow evaporation) provided **36B** as yellow needles from which a single-crystal X-ray structure was determined: mp 136–138 °C; ^1H NMR (DMSO-d_6, 600 MHz) δ 7.86 (s, 1H), 7.42–7.45 (m, 2H), 7.36–7.40 (m, 2H), 7.30–7.34 (m, 1H), 6.23 (d, *J* = 4.9 Hz, 1H), 4.79 (d, *J* = 15.0 Hz, 1H), 4.72 (d, *J* = 15.0 Hz, 1H), 4.58 (d, *J* = 4.9 Hz, 1H), 4.18 (m, 1H), 3.97 (dd, *J* = 15.2, 7.0 Hz, 1H), 2.08 (s, 3H), 1.87–1.95 (m, 1H), 1.71–1.86 (m, 3H), 1.40 (s, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.8, 188.4, 169.2, 149.8, 148.3, 137.4, 128.6 (2C), 128.2 (2C), 127.7, 114.1, 100.6, 97.9, 84.7, 70.4, 68.8, 52.2, 35.0, 24.5, 22.9, 20.0; IR (film) ν_{max} 3355, 2923, 2853, 1732, 1636, 1562, 1454, 1241, 1077, 1056, 703 cm^{-1}; HR ESI-TOF *m/z* 432.1206 ($C_{22}H_{22}ClNO_6$ + H^+ requires 432.1214).

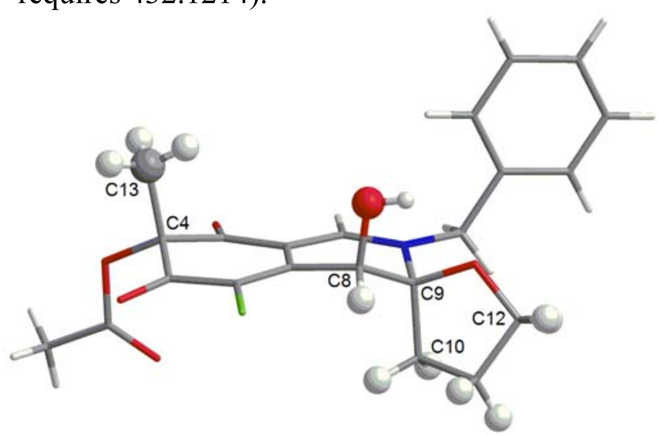
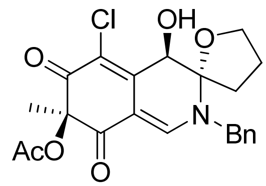


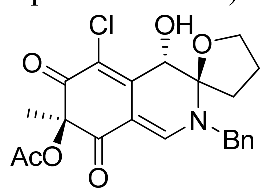
Figure S3. CIF file of **36B** viewed with Chem3D.



= **36C**

(relative stereochemistry depicted)

For **36C**: mp 135−138 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.88 (s, 1H), 7.37−7.43 (m, 4H), 7.31−7.35 (m, 1H), 6.59 (d, *J* = 6.4 Hz, 1H), 4.95 (d, *J* = 16.6 Hz, 1H), 4.82 (d, *J* = 16.6 Hz, 1H), 4.55 (d, *J* = 6.4 Hz, 1H), 3.85−3.90 (m, 1H), 3.80 (dd, *J* = 15.3, 7.1 Hz, 1H), 2.20–2.30 (m, 2H), 2.10 (s, 3H), 1.95–2.06 (m, 2H), 1.42 (s, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.4, 188.6, 168.9, 151.5, 148.0, 137.7, 128.7 (2C), 127.5, 126.7 (2C), 115.6, 102.0, 97.2, 84.9, 68.9, 68.6, 53.7, 30.6, 25.2, 23.5, 20.0; IR (film) ν_{max} 3369, 2920, 1736, 1687, 1638, 1563, 1240, 1077, 736 cm^{-1}; HR ESI-TOF *m/z* 432.1205 ($C_{22}H_{22}ClNO_6 + H^+$ requires 432.1214).



= **36D**

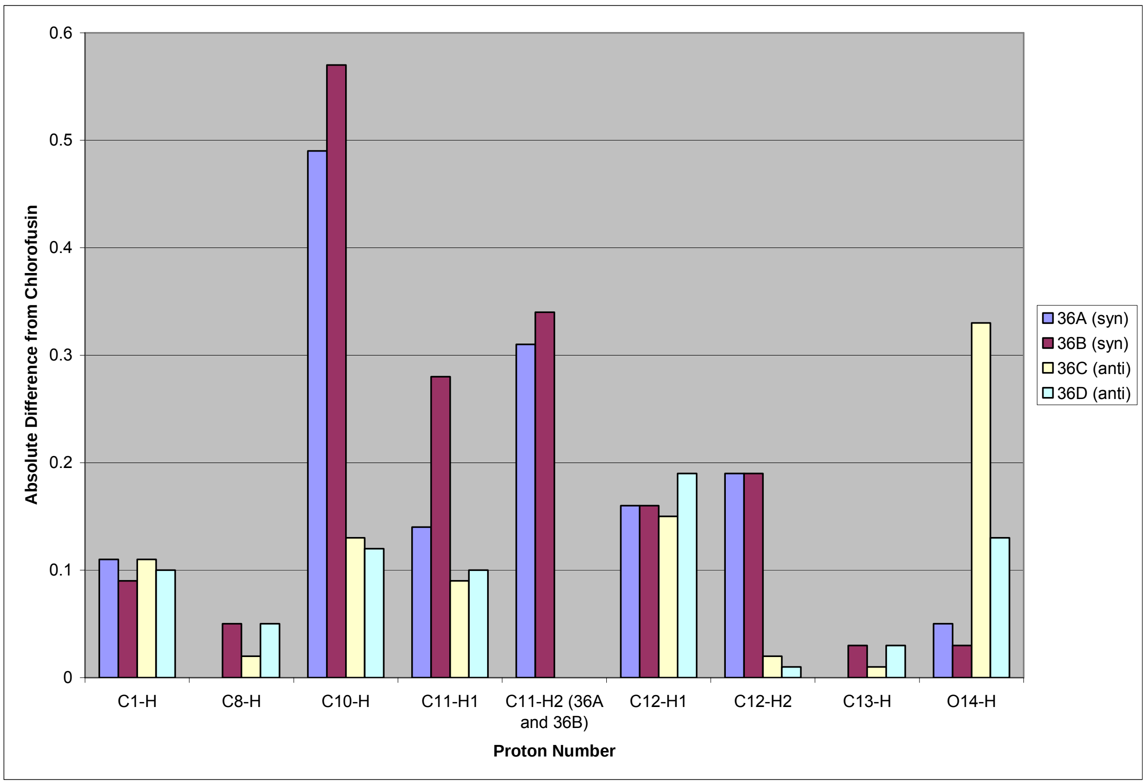
(relative stereochemistry depicted)

For **36D**: mp 131−135 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.88 (s, 1H), 7.37−7.43 (m, 4H), 7.31−7.35 (m, 1H), 6.39 (d, *J* = 5.2 Hz, 1H), 4.94 (d, *J* = 16.6 Hz, 1H), 4.83 (d, *J* = 16.6 Hz, 1H), 4.58 (d, *J* = 5.1 Hz, 1H), 3.80−3.85 (m, 1H), 3.77 (dd, *J* = 14.8, 7.1 Hz, 1H), 2.22–2.32 (m, 2H), 2.10 (s, 3H), 1.96–2.03 (m, 2H), 1.46 (s, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.8, 188.6, 169.1, 151.1, 147.5, 137.6, 128.7 (2C), 127.6, 126.7 (2C), 115.8, 101.5, 97.1, 85.0, 68.8, 68.7, 53.9, 30.5, 25.2, 23.1, 20.0; IR (film) ν_{max} 3318, 2922, 2853, 1737, 1642, 1571, 1453, 1249, 1077, 1043, 698 cm^{-1}; HR ESI-TOF *m/z* 432.1213 ($C_{22}H_{22}ClNO_6 + H^+$ requires 432.1214).

Table S1. Comparison of chromophore ^{1}H NMR data for **36A**–**36D** with Williams values.

Proton Number	δ (^{1}H NMR)[a]				
	chlorofusin	**36A** (*syn*)	**36B** (*syn*)	**36C** (*anti*)	**36D** (*anti*)
Configuration		*R*,R*,R**	*R*,S*,S**	*R*,R*,S**	*R*,S*,R**
C1-H	7.77 (s)	7.88 (s)	7.86 (s)	7.88 (s)	7.87 (s)
C8-H	4.53 (d)	4.53 (d)	4.58 (d)	4.55 (d)	4.58 (d)
C10-H	2.38 (br m)	1.89 (m)	1.81 (m)	2.25 (m)	2.26 (m)
C11-H	2.1 (br m)	1.79, 1.96 (m)	1.76, 1.82 (m)	2.01 (m)	2.00 (m)
C12-H[1]	4.02 (m)	4.18 (m)	4.18 (m)	3.87 (m)	3.83 (m)
C12-H[2]	3.78 (q)	3.97 (dd)	3.97 (dd)	3.80 (dd)	3.77 (m)
C13-H	1.43 (s)	1.43 (s)	1.40 (s)	1.42 (s)	1.46 (s)
O14-H	6.26 (d)	6.31 (d)	6.23 (d)	6.59 (d)	6.39 (d)

[a] Assignment was assisted by COSY and HMQC NMR.



Note: For comparison of geminal proton shifts that appear as one signal in Williams' work with shifts for the analogous protons that we observe as two signals, the value for the former is employed twice in determining the Abs(diff) values for the above chart. For comparison of shifts reported as a range in Williams' work or our experimental data, the center of the range was used in the above table and in calculations for the above chart.

Figure S4. ^{1}H NMR chemical shift difference from Williams' chlorofusin values for **36A**–**36D**.

Table S2. Comparison of chromophore ^{13}C NMR data for **36A–36D** with Williams values.

Carbon Number	δ (^{13}C NMR)[a]				
	chlorofusin	**36A** (*syn*)	**36B** (*syn*)	**36C** (*anti*)	**36D** (*anti*)
Configuration		*R*,R*,R**	*R*,S*,S**	*R*,R*,S**	*R*,S*,R**
C1	150.0	150.2	149.8	151.5	151.1
C2	115.2	113.9	114.1	115.6	115.8
C3	188.1	188.9[b]	188.4[b]	189.4[b]	188.6[b]
C4	84.7	84.9	84.7	84.9	85.0
C5	188.7	189.1[b]	188.8[b]	188.6[b]	188.8[b]
C6	101.3	101.0	100.6	102.0	101.5
C7	147.5	148.4	148.3	148.0	147.5
C8	68.4	68.7	68.8	68.6	68.7
C9	96.7	97.9	97.9	97.2	97.1
C10	30.3	34.5	35.0	30.6	30.5
C11	25.1	24.5	24.5	25.2	25.2
C12	68.4	70.3	70.4	68.9	68.8
C13	22.9	23.6	22.9	23.5	23.1

[a] Assignment was assisted by COSY and HMQC NMR.

[b] Assignments made by analogy to **48A**–**48D**.

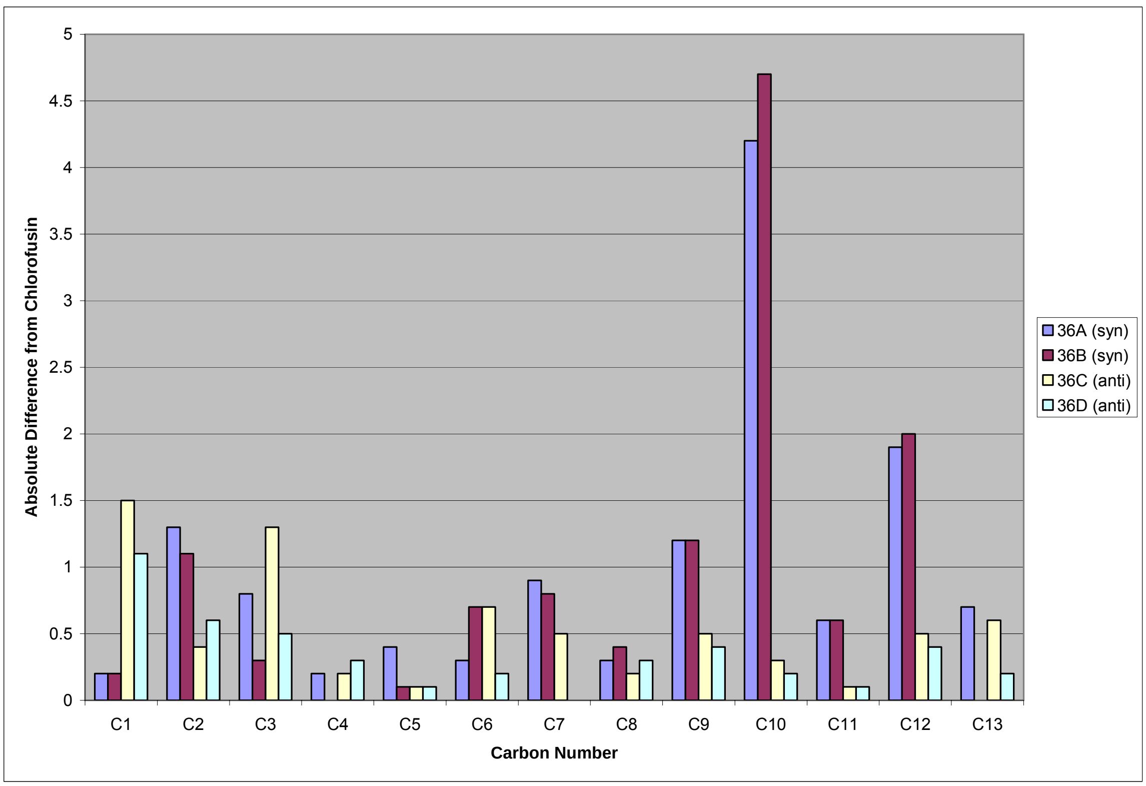
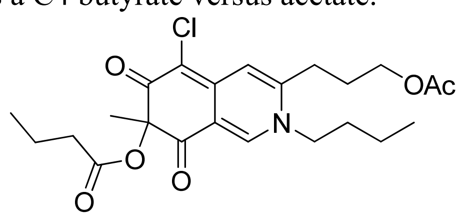
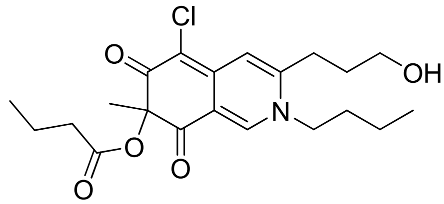


Figure S5. ^{13}C NMR chemical shift difference from Williams' chlorofusin values for **36A**–**36D**.

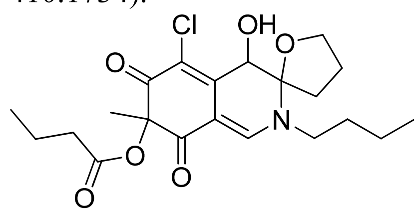
The X-ray crystal structures of the **36** diastereomers **36A**[2] and **36B**[3], the major products of the oxidative spirocyclization reaction, were determined and it was found that the C8 and C9 oxygen substituents of both compounds were oriented *syn* with respect to one another. *N*,*O*-Ketal equilibration studies defined the respective **36** *syn*/*anti* pairs and unambiguously established the structures and corresponding stereochemistry of **36C** and **36D**. Particularly indicative of the relative orientation of the C8 and C9 substituents were the ^{1}H NMR signals of the tetrahydrofuran ring. The chemical shifts of the C10-H signals for **36C** (m, 2.25 ppm) and **36D** (m, 2.26 ppm) are more similar to each other and to the C10-H signal reported for chlorofusin (br m, 2.38 ppm) compared to the analogous signals from the spectra of **36A** (m, 1.89) and **36B** (m, 1.81). Likewise the C11-H signals for **36C** (m, 2.01 ppm) and **36D** (m, 2.00 ppm) possess chemical shifts that are closer to chlorofusin (m, 2.0–2.2 ppm) than **36A** (m, 1.79 ppm; m, 1.96 ppm) and **36B** (m, 1.76 ppm; m, 1.82 ppm), and the C12-H signals for **36C** (m, 3.80 ppm; m, 3.87 ppm) and **36D** (m, 3.77 ppm; m, 3.83 ppm) were also similar to one another and chlorofusin (q, 3.78 ppm; m, 4.02 ppm), and different from those of **36A** (m, 3.97 ppm; m, 4.18 ppm) and **36B** (m, 3.97 ppm; m, 4.18 ppm). The ^{13}C NMR data show similar trends with the most striking difference coming at C10 with **36C** (30.6 ppm) and **36D** (30.5 ppm) being very similar to each other and to chlorofusin (30.3 ppm) but 4 ppm farther upfield than the C10 signals for **36A** (34.5 ppm) and **36B** (35.0 ppm). Although these initial results indicated that the C8 and C9 oxygen substituents of chlorofusin are oriented *anti* with respect to one another, the potential perturbation of the chromophore NMR signals by the appended benzyl ring led to the analogous examination of **42A–42D** incorporating an *N*-butyl substituent as well as a C4 butyrate versus acetate.



3-(3-Acetoxypropyl)-2-butyl-7-butyryloxy-5-chloro-7-methyl-2*H*,7*H*-isoquinoline-6,8-dione (40). A solution of **18** (31 mg, 0.078 mmol) in anhydrous CH_2Cl_2 (1.4 mL) was treated with *n*-butylamine (9.3 μL, 0.094 mmol) and SiO_2 (16 mg). The reaction mixture was stirred at 23 °C for 1 h and concentrated under reduced pressure. Chromatography (SiO_2, 60% EtOAc−hexanes) afforded **40** as a red foam (99%, 35 mg): ^{1}H NMR ($CDCl_3$, 600 MHz) 7.72 (s, 1H), 6.75 (s, 1H), 4.18 (t, *J* = 6.0 Hz, 2H), 3.77 (dd, *J* = 9.0, 6.6 Hz, 2H), 2.64 (app t, *J* = 7.9 Hz, 2H), 2.36−2.46 (m, 2H), 2.08 (s, 3H), 1.98−2.04 (m, 2H), 1.70−1.77 (m, 2H), 1.64 (app sext, *J* = 7.4 Hz, 2H), 1.51 (s, 3H), 1.41 (app sext, *J* = 7.5 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 194.0, 184.9, 173.1, 171.0, 149.3, 144.2, 141.2, 115.3, 113.8, 102.6, 84.7, 63.0, 53.2, 35.3, 33.3, 28.7, 27.9, 23.2, 21.0, 19.9, 18.4, 13.8, 13.7; IR (film) ν_{max} 2930, 1737, 1612, 1505, 1228, 1179 cm^{-1}; HR ESI-TOF *m/z* 452.1841 ($C_{23}H_{30}ClNO_6$ + H^+ requires 452.1840).

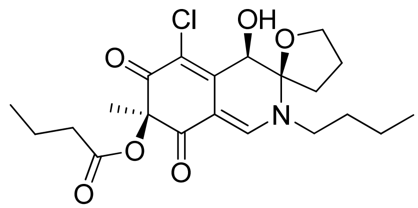


2-Butyl-7-butyryloxy-5-chloro-3-(3-hydroxypropyl)-7-methyl-2*H*,7*H*-isoquinoline-6,8-dione (41). A solution of **40** (51.7 mg, 0.115 mmol) in H_2O (0.12 mL) and MeOH (1.2 mL) was cooled to 0 °C and treated with K_2CO_3 (31.8 mg, 0.230 mmol) and stirred at 0 °C for 30 min. The reaction mixture was quenched with aqueous 0.2 N HCl (1.6 mL), acidified to pH 3 and extracted with EtOAc (3 × 5 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 60% EtOAc–hexanes) afforded **41** as a red solid (91%, 43.1 mg): mp 83–89 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.76 (s, 1H), 6.80 (s, 1H), 3.79–3.89 (m, 2H), 3.78 (t, *J* = 5.7 Hz, 2H), 2.73 (app t, *J* = 7.8 Hz, 2H), 2.38–2.48 (m, 2H), 1.84–1.95 (m, 3H), 1.75 (app quint, *J* = 7.7 Hz, 2H), 1.66 (app sext, *J* = 7.4 Hz, 2H), 1.54 (s, 3H), 1.41 (app sext, *J* = 7.5 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 194.1, 184.6, 173.2, 150.9, 144.9, 141.3, 115.5, 114.1, 102.2, 84.7, 61.1, 53.4, 35.4, 33.3, 31.6, 28.5, 23.3, 20.0, 18.4, 13.79, 13.77; IR (film) ν_{max} 3400, 2932, 2875, 1732, 1704, 1592, 1503, 1230, 1180, 1081 cm^{-1}; HR ESI-TOF *m/z* 410.1728 ($C_{21}H_{28}ClNO_5 + H^+$ requires 410.1734).



42. A solution of **41** (11.6 mg, 0.0284 mmol) in H_2O (0.28 mL) and DMSO (2.8 mL) was treated with iodine (21.6 mg, 0.0852 mmol), and silver nitrate (9.6 mg, 0.057 mmol), and the mixture was stirred at 23 °C for 2 days before being quenched with the addition of saturated aqueous $Na_2S_2O_3$ (2 mL). The resulting mixture was diluted with EtOAc (50 mL), washed with saturated aqueous $NaHCO_3$ (20 mL), H_2O (10 mL) and saturated aqueous NaCl (10 mL). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (preparative TLC, SiO_2, 3 × 50% EtOAc–hexanes) afforded diastereomers **42A** (24%, 2.9 mg), **42B** (22%, 2.7 mg), **42C** (7%, 0.9 mg), **42D** (6%, 0.7 mg) and recovered **41** (13%, 1.5 mg).

Isomerization of 42B to 42D: A solution of **42B** (2.7 mg, 0.006 mmol) in acetic acid (0.6 mL) at 23 °C was treated with CF_3CO_2H (5 μL, 0.06 mmol) and stirred at 23 °C for 16 h and quenched with the addition of saturated aqueous $NaHCO_3$ (2 mL). The resulting mixture was extracted with CH_2Cl_2 (3 × 1 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (preparative TLC, SiO_2, 3 × 60% EtOAc–hexanes) afforded **42D** (0.3 mg, 11%) and recovered **42B** (2.0 mg, 74%).



= **42A**

(relative stereochemistry depicted, confirmation of structure by X-ray[4])

For **42A**: Recrystallization from Et_2O (slow evaporation) provided **42A** as yellow prisms from which a single-crystal X-ray structure was determined: mp 158−160 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.86 (s, 1H), 6.18 (d, *J* = 5.6 Hz, 1H), 4.48 (d, *J* = 5.4 Hz, 1H), 4.19−4.25 (m, 1H), 4.03 (dd, *J* = 15.0, 7.0 Hz, 1H), 3.48−3.55 (m, 1H), 3.42−3.48 (m, 1H), 2.35 (t, *J* = 7.1 Hz, 2H), 1.91−2.06 (m, 3H), 1.82−1.89 (m, 1H), 1.58−1.69 (m, 2H), 1.55 (app sext, *J* = 7.3 Hz, 2H), 1.41 (s, 3H), 1.28−1.40 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.04, 188.97, 171.4, 149.9, 148.7, 113.1, 100.5, 98.0, 84.7, 70.5, 68.6, 49.7, 34.6, 34.5, 32.5, 24.7, 23.7, 19.2, 18.1, 13.7, 13.3; IR (film) ν_{max} 3438, 2925, 2855, 1737, 1644, 1574, 1454, 1236, 1181, 1075 cm^{-1}; HR ESI-TOF *m/z* 426.1671 ($C_{21}H_{28}ClNO_6 + H^+$ requires 426.1683).

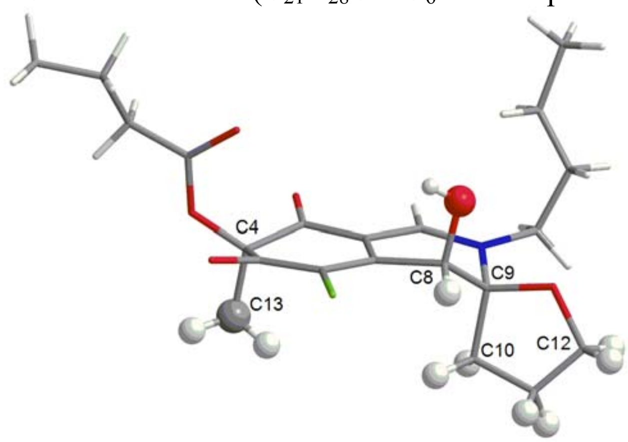
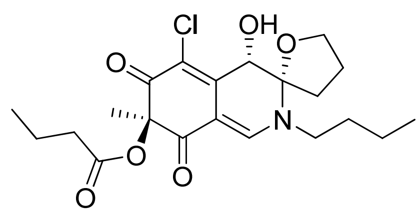


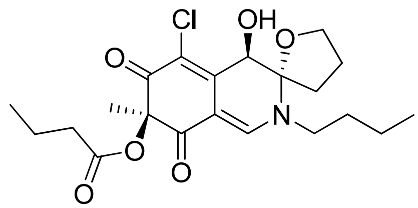
Figure S6. CIF file of **42A** viewed with Chem3D.



= **42B**

(relative stereochemistry depicted)

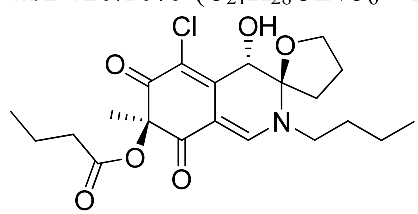
For **42B**: mp 155−158 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.80 (s, 1H), 6.11 (d, *J* = 4.8 Hz, 1H), 4.54 (d, *J* = 4.8 Hz, 1H), 4.22 (dd, *J* = 13.4, 7.4 Hz, 1H), 4.04 (dd, *J* = 14.9, 7.4 Hz, 1H), 3.49−3.56 (m, 1H), 3.40−3.47 (m, 1H), 2.34 (t, *J* = 7.1 Hz, 2H), 1.94−2.06 (m, 2H), 1.77−1.87 (m, 2H), 1.56−1.70 (m, 2H), 1.53 (app sext, *J* = 7.3 Hz, 2H), 1.40 (s, 3H), 1.27−1.39 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.3, 171.7, 149.6, 148.7, 113.5, 100.2, 97.9, 84.6, 70.6, 68.7, 49.8, 35.0, 34.6, 32.6, 24.6, 23.0, 19.2, 18.0, 13.7, 13.3; IR (film) ν_{max} 3416, 2928, 2874, 1734, 1644, 1573, 1454, 1236, 1076 cm^{-1}; HR ESI-TOF *m/z* 426.1671 ($C_{21}H_{28}ClNO_6 + H^+$ requires 426.1683).



= **42C**

(relative stereochemistry depicted)

For **42C**: mp 136–140 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.83 (s, 1H), 6.41 (d, J = 6.7 Hz, 1H), 4.49 (d, J = 6.5 Hz, 1H), 3.93–3.97 (m, 1H), 3.82 (dd, J = 7.0, 15.3 Hz, 1H), 3.54–3.60 (m, 1H), 3.46–3.53 (m, 1H), 2.32–2.42 (m, 2H), 2.36 (t, J = 7.1 Hz, 2H), 2.08 (app quint, J = 7.1 Hz, 2H), 1.51–1.61 (m, 4H), 1.38 (s, 3H), 1.34 (app sext, J = 7.4 Hz, 2H), 0.92 (t, J = 7.4 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.3, 188.8, 171.5, 150.9, 148.3, 115.0, 101.5, 96.9, 84.7, 68.6, 68.4, 50.5, 34.5, 32.9, 30.2, 25.3, 23.5, 19.2, 18.1, 13.7, 13.3; IR (film) ν_{max} 3370, 2923, 2853, 1695, 1650, 1576, 1459, 1237, 1080, 1042 cm^{-1}; HR ESI-TOF m/z 426.1675 ($C_{21}H_{28}ClNO_6 + H^+$ requires 426.1683).



= **42D**

(relative stereochemistry depicted, confirmation of structure by X-ray[5])

For **42D**: Recrystallization from Et_2O (slow evaporation) provided **42D** as yellow prisms from which a single-crystal X-ray structure was determined: mp 133–136 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.80 (s, 1H), 6.25 (d, J = 5.3 Hz, 1H), 4.53 (d, J = 5.1 Hz, 1H), 3.95 (dd, J = 14.9, 6.6 Hz, 1H), 3.80 (dd, J = 15.3, 7.1 Hz, 1H), 3.54–3.60 (m, 1H), 3.46–3.53 (m, 1H), 2.37–2.40 (m, 2H), 2.35 (t, J = 7.1 Hz, 2H), 2.05–2.12 (m, 2H), 1.51–1.62 (m, 4H), 1.43 (s, 3H), 1.34 (app sext, J = 7.5 Hz, 2H), 0.93 (t, J = 7.4 Hz, 3H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.5, 171.6, 150.5, 147.7, 115.2, 101.2, 96.8, 84.8, 68.5, 68.4, 50.6, 34.5, 33.0, 30.2, 25.3, 23.1, 19.2, 18.1, 13.7, 13.3; IR (film) ν_{max} 3440, 2924, 2849, 1735, 1693, 1645, 1574, 1454, 1236, 1077 cm^{-1}; HR ESI-TOF m/z 426.1677 ($C_{21}H_{28}ClNO_6 + H^+$ requires 426.1683).

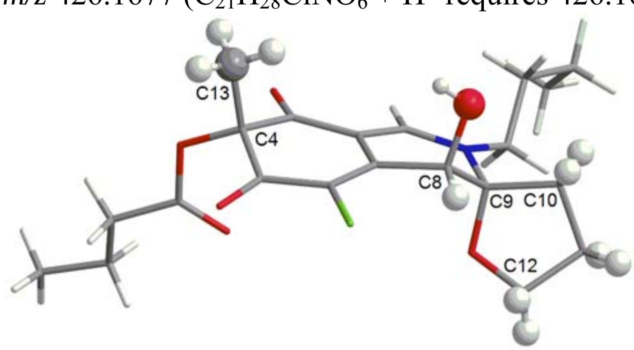
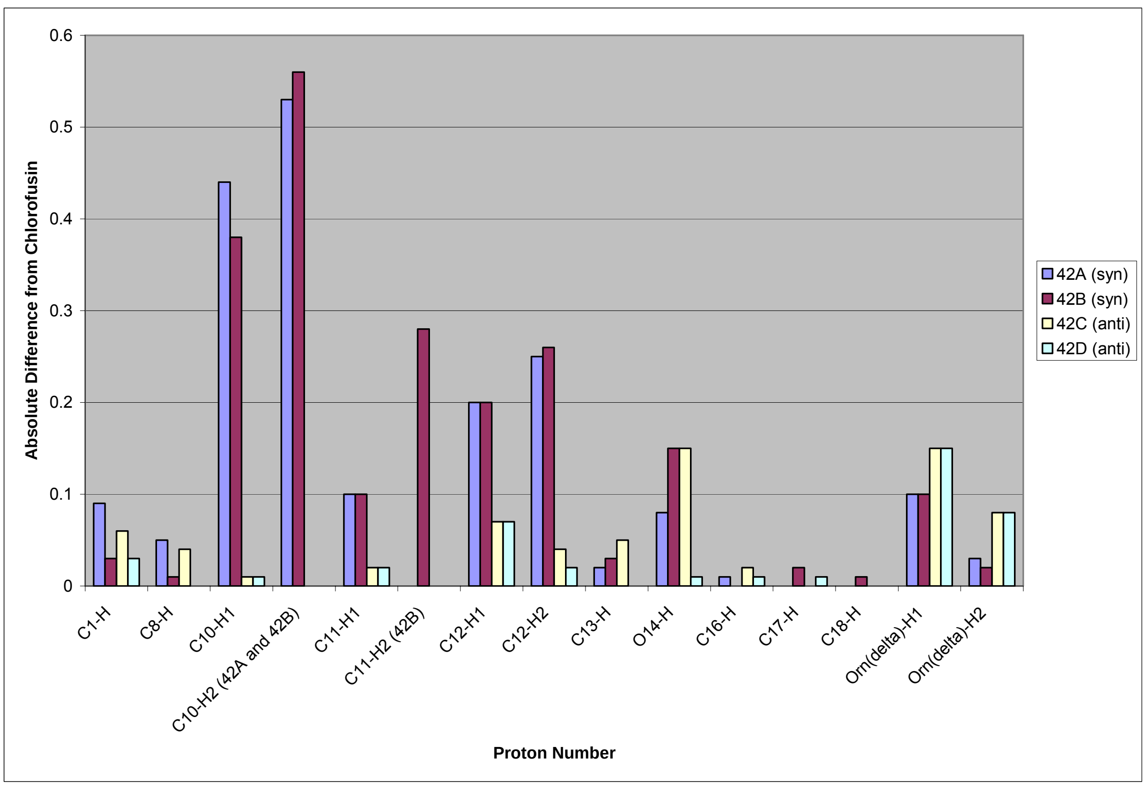


Figure S7. CIF file of **42D** viewed with Chem3D.

Table S3. Comparison of chromophore ^{1}H NMR data for **42A**–**42D** with Williams values.

Proton Number	δ (^{1}H NMR)[a]				
	chlorofusin	**42A** (*syn*)	**42B** (*syn*)	**42C** (*anti*)	**42D** (*anti*)
Configuration		*R*,R*,R**	*R*,S*,S**	*R*,R*,S**	*R*,S*,R**
C1-H	7.77 (s)	7.86 (s)	7.80 (s)	7.83 (s)	7.80 (s)
C8-H	4.53 (d)	4.48 (d)	4.54 (d)	4.49 (d)	4.53 (d)
C10-H	2.38 (br m)	1.85, 1.94 (m)	1.82, 2.00 (m)	2.37 (m)	2.39 (m)
C11-H	2.1 (br m)	2.00 (m)	1.82, 2.00 (m)	2.08 (app quint)	2.08 (m)
C12-H^1	4.02 (m)	4.22 (m)	4.22 (dd)	3.95 (m)	3.95 (dd)
C12-H^2	3.78 (q)	4.03 (dd)	4.04 (dd)	3.82 (dd)	3.80 (dd)
C13-H	1.43 (s)	1.41 (s)	1.40 (s)	1.38 (s)	1.43 (s)
O14-H	6.26 (d)	6.18 (d)	6.11 (d)	6.41 (d)	6.25 (d)
C16-H	2.34 (t)	2.35 (t)	2.34 (t)	2.36 (t)	2.35 (t)
C17-H	1.55 (sextet)	1.55 (app sext)	1.53 (app sext)	1.55 (m)	1.54 (m)
C18-H	0.92 (t)	0.92 (t)	0.91 (t)	0.92 (t)	0.92 (t)
Orn-CH_2^{δ}	3.42 (t)	3.45, 3.52 (m)	3.44, 3.52 (m)	3.50, 3.57 (m)	3.50, 3.57 (m)

[a] Assignment was assisted by COSY and HMQC NMR.



Note: For comparison of geminal proton shifts that appear as one signal in Williams' work with shifts for the analogous protons that we observe as two signals, the value for the former is employed twice in determining the Abs(diff) values for the above chart. For comparison of shifts reported as a range in Williams' work or our experimental data, the center of the range was used in the above table and in calculations for the above chart.

Figure S8. ^{1}H NMR chemical shift difference from Williams' chlorofusin values for **42A**–**42D**.

Table S4. Comparison of chromophore ^{13}C NMR data for **42A–42D** with Williams values.

Carbon Number	δ (^{13}C NMR)[a]				
	chlorofusin	**42A** (*syn*)	**42B** (*syn*)	**42C** (*anti*)	**42D** (*anti*)
Configuration		*R*,R*,R**	*R*,S*,S**	*R*,R*,S**	*R*,S*,R**
C1	150.0	149.9	149.5	150.9	150.5
C2	115.2	113.1	113.5	115.0	115.2
C3	188.1	189.0	188.3[b]	189.3[b]	188.5[b]
C4	84.7	84.7	84.6	84.7	84.8
C5	188.7	189.0	188.9[b]	188.8[b]	188.9[b]
C6	101.3	100.5	100.2	101.5	101.1
C7	147.5	148.7	148.7	148.3	147.7
C8	68.4	68.6	68.7	68.4	68.5
C9	96.7	97.9	97.9	96.9	96.8
C10	30.3	34.6	35.0	30.2	30.2
C11	25.1	24.7	24.6	25.3	25.3
C12	68.4	70.5	70.6	68.6	68.5
C13	22.9	23.7	23.0	23.5	23.1
C15	171.4	171.4	171.7	171.5	171.6
C16	34.4	34.5	34.6	34.5	34.5
C17	17.9	18.1	18.0	18.1	18.1
C18	13.2	13.3	13.3	13.3	13.3
Orn δ	50.5	49.7	49.8	50.5	50.6

[a] Assignment was assisted by COSY and HMQC NMR.

[c] Assignments made by analogy to **48A–48D**.

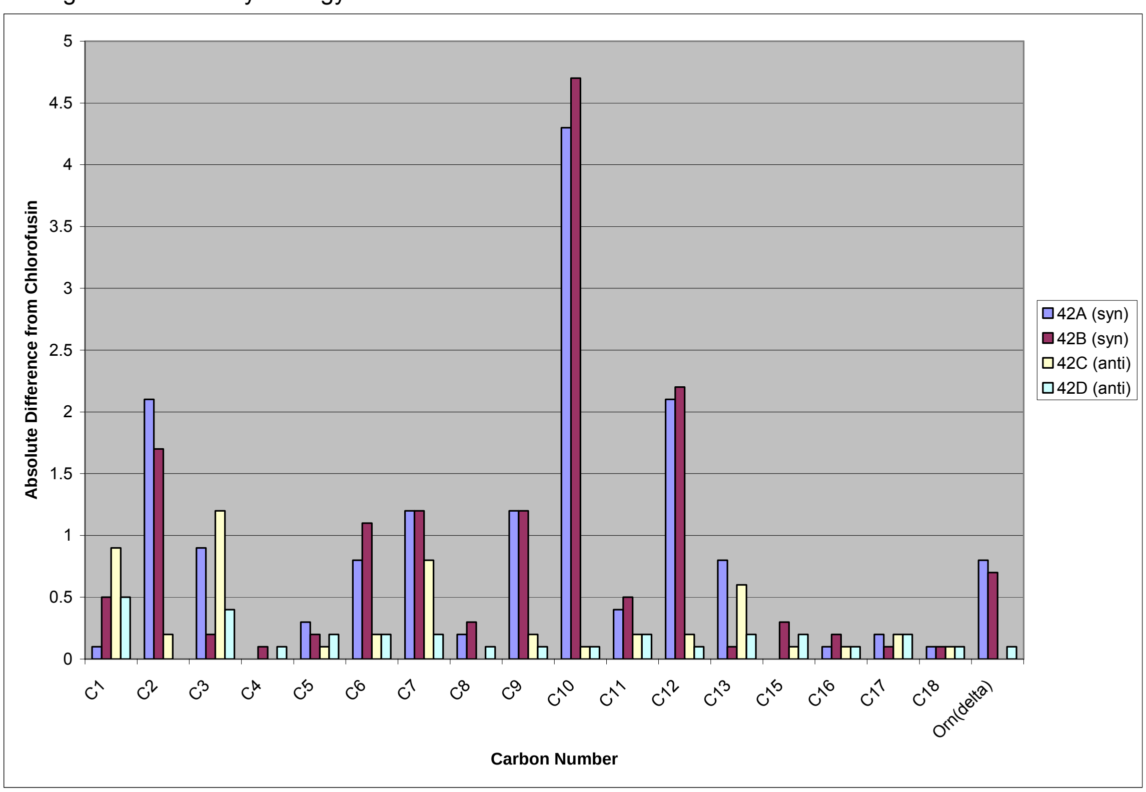
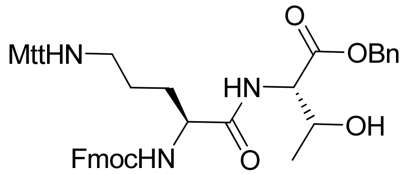


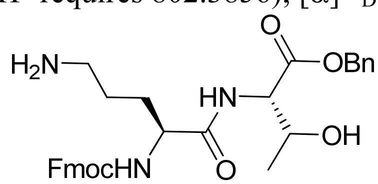
Figure S9. ^{13}C NMR chemical shift difference from Williams' chlorofusin values for **42A–42D**.

As with the benzylamine incorporated case, the NMR data collected from **42C** and **42D** in the **42** series better matched that of chlorofusin than **42A** or **42B**. An X-ray crystal structure of **D**, the best match with chlorofusin by NMR, confirmed that the relative orientation of the C8 and C9 oxygen substituents is *anti* and that the C4-methyl group is *cis* to the C8-OH and *trans* to the C9 oxygen of the tetrahydrofuran. As the similarity of the model to the chromophore of chlorofusin increased, the trends in the NMR data distinguishing the C8/C9 *syn* diastereomers from the *anti* diastereomers became even stronger. For C10-H, **42A** (m, 1.85 ppm; m, 1.94 ppm) and **42B** (m, 1.82 ppm; m, 2.00 ppm) each display two signals, neither of which is within 0.3 ppm of chlorofusin (br m, 2.38 ppm) whereas the signals for **42C** (m, 2.37 ppm) and **42D** (m, 2.39 ppm) only differ from chlorofusin by 0.01 ppm. In the same manner the C12-H signals, for **42A** (dd, 4.03 ppm; m, 4.22 ppm) and **42B** (dd, 4.04 ppm; dd, 4.22 ppm), are much farther downfield than the analogous signals seen for **42C** (dd, 3.82 ppm; m, 3.95 ppm), **42D** (dd, 3.80 ppm; dd, 3.95 ppm) and chlorofusin (q, 3.78 ppm; m, 4.02 ppm). An additional and important trend emerges linking **42B** with **42D**, which share the same relative stereochemistry at C8. The signals for C8-H observed in the spectra from **42A** (d, 4.48 ppm) and **42C** (d, 4.49 ppm) are similar to one another while the signals for **42B** (d, 4.54 ppm) and **42D** (d, 4.53 ppm) are not only similar to one another but also to that of chlorofusin (d, 4.53 ppm). This distinguishes the two *anti* diastereomers, with **42D** (not **42C**) being representative of the stereochemistry found in chlorofusin. Finally, the C8-OH signal in this series appears to diagnostically differentiate **42A** (d, 6.18 ppm), **42B** (d, 6.11 ppm), **42C** (d, 6.41 ppm) and **42D** (d, 6.25 ppm) as well as link the relative stereochemistry of **42D** with that of chlorofusin (d, 6.26 ppm). The ^{13}C NMR data show similar trends to both the proton NMR data and to the benzylamine incorporated diastereomers. Differences between the *syn* and *anti* compounds become either slightly more exaggerated or remain the same in this series for C10, C11, C12 and C9 in the absence of a proximal aryl ring. With X-ray structures of both represenative C8/C9 *syn* and *anti* diastereomers in hand, the dramatic difference seen between their ^{13}C NMR chemical shifts at C10 can be attributed to its axial (*syn*) or equatorial (*anti*) orientation with regard to the tetrahydropyridine ring of the chromophore. For C10, with **42C** (30.2 ppm) and **42D** (30.2 ppm) the shifts became closer to chlorofusin (30.3 ppm) but remained over 4 ppm farther upfield than the C10 signals for **42A** (34.6 ppm) and **42B** (35.0 ppm). The use of butylamine as an Orn side chain analog also allowed comparison of the chemical shift of the methylene adjacent to the chromophore ring system, with **42C** (50.5 ppm) and **42D** (50.6 ppm) matching chlorofusin (50.5 ppm) as opposed to **42A** (49.7 ppm) and **42B** (49.8 ppm).

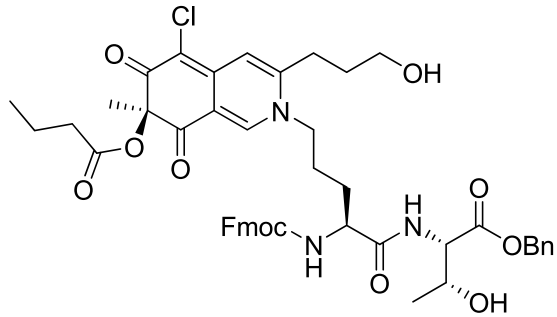
Although intuitively surprising but which may be expected from the X-ray crystal structure of **42D** which clearly shows an unobstructed path between C8-H and C4-Me (4.761 Å, C8-H–C13) the ROESY NMR data for **42D** shows a weak cross-peak between C4-Me and C8-H as seen by Williams as a long range NOE in chlorofusin. Also observed in the X-ray structure is the di-axial orientation of the C8 and C9 oxygen substituents. In this conformation, the equatorial C8-H can exhibit NOEs to both C10-H and C12-H. Although these NOEs were not quantitated, it is notable that C8-H is closer to C10-H (2.484 Å) than C12-H (2.592 Å) in this X-ray. With the data from both the **36** and **42** model systems in hand, the stereochemistry of the chlorofusin chromophore was confidently assigned as either (4*S*,8*R*,9*S*) or (4*R*,8*S*,9*R*).



Fmoc-L-Orn(Mtt)-L-Thr-OBn (43). A flask containing commercially available Fmoc-L-Orn(Mtt)-OH (1.50 g, 2.46 mmol), H-L-Thr-OBn·oxalate (591 mg, 2.58 mmol), HOAt (1.00 g, 7.37 mmol), and EDCI (1.41 g, 7.37 mmol) was cooled to 0 °C and treated with anhydrous DMF (8.2 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (100 mL), washed with aqueous 1 N HCl (2 × 10 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL), H_2O (10 mL) and saturated aqueous NaCl (20 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 40% EtOAc–hexanes) afforded **43** as a white foam (82%, 1.62 g): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.97 (d, J = 8.4 Hz, 1H), 7.91 (dd, J = 7.5, 3.3 Hz, 2H), 7.76 (dd, J = 10.8, 7.6 Hz, 2H), 7.57 (d, J = 8.3 Hz, 1H), 7.42 (m, 6H), 7.34 (m, 4H), 7.29 (m, 9H), 7.18 (t, J = 7.3 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 5.14 (d, J = 12.7 Hz, 1H), 5.10 (d, J = 12.8 Hz, 1H), 5.06 (d, J = 5.4 Hz, 1H), 4.37 (dd, J = 8.4, 3.1 Hz, 1H), 4.06–4.31 (m, 4H), 4.14 (m, 1H), 2.42 (t, J = 7.8 Hz, 1H), 2.26 (s, 3H), 1.95 (m, 2H), 1.65–1.77 (m, 1H), 1.54 (m, 3H), 1.09 (d, J = 6.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 172.8, 170.6, 160.0, 146.5 (2C), 144.0, 143.8, 143.3, 140.8 (2C), 136.0, 135.1, 128.41 (6C), 128.36 (3C), 128.3 (2C), 127.9 (2C), 127.7 (6C), 127.1 (2C), 126.0 (2C), 125.4 (2C), 120.2 (2C), 70.2, 66.3, 65.9, 65.7, 57.9, 54.7, 46.8, 43.2, 30.2, 26.8, 20.6, 20.2; IR (film) ν_{max} 3306, 3019, 2944, 1662, 1509, 1449, 1245, 1216, 1105, 752, 700 cm^{-1}; HR ESI-TOF m/z 802.3851 ($C_{51}H_{51}N_3O_6 + H^+$ requires 802.3856); $[\alpha]^{23}_D$ −8 (c 1.1, $CHCl_3$).



Fmoc-L-Orn-L-Thr-OBn (44). A solution of **43** (662 mg, 0.825 mmol) in anhydrous CH_2Cl_2 (30 mL) was treated with trifluoroacetic acid (0.30 mL) and stirred at 23 °C for 1 h. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography (SiO_2, $CHCl_3$(80):MeOH(20):H_2O(1):NH_4OH(1)) to provide **44** as a white foam (97%, 450 mg): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.10 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 7.6 Hz, 2H), 7.78 (s, 2H), 7.74 (dd, J = 7.2, 4.8 Hz, 2H), 7.64 (d, J = 8.5 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 7.33–7.39 (m, 7H), 5.16 (d, J = 12.7 Hz, 1H), 5.13 (d, J = 12.7 Hz, 1H), 4.38 (dd, J = 8.4, 3.1 Hz, 1H), 4.20–4.33 (m, 5H), 3.56 (brs, 1H), 2.77 (m, 2H), 1.72 (m, 1H), 1.60 (m, 3H), 1.09 (d, J = 6.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 172.5, 170.5, 156.1, 143.92, 143.86, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.39, 125.37, 120.2 (2C), 66.3, 66.0, 65.8, 57.9, 53.7, 46.7, 38.5, 28.8, 23.8, 20.9; IR (film) ν_{max} 3271, 3016, 1668, 1526, 1451, 1202, 1137, 756 cm^{-1}; HR ESI-TOF m/z 546.2606 ($C_{31}H_{35}N_3O_6 + H^+$ requires 546.2604); $[\alpha]^{23}_D$ −16 (c 1.7, $CHCl_3$).



45. A solution of (*R*)-**28** (273 mg, 0.770 mmol) in DMF (4 mL) and CH_2Cl_2 (4 mL) was treated with **44** (462 mg, 0.847 mmol), $NaHCO_3$ (194 mg, 2.31 mmol) and stirred at 23 °C for 24 h. The reaction mixture was diluted with CH_2Cl_2 (4 mL), treated with aqueous 1 N HCl (4 mL) and stirred vigorously at 23 °C for 4 h. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers dried (Na_2SO_4) for 15 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 80% EtOAc–hexanes – 3% MeOH–EtOAc gradient) to yield **45** as an orange foam (84%, 567 mg): mp 97–101 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.19 (s, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 7.90 (dd, *J* = 7.5, 3.6 Hz, 2H), 7.73 (t, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.27–7.46 (m, 9H), 6.76 (s, 1H), 5.03–5.20 (m, 3H), 4.69 (s, 1H), 4.14–4.41 (m, 6H), 3.94–4.09 (m, 2H), 3.52 (t, *J* = 5.9 Hz, 2H), 2.72 (t, *J* = 7.6 Hz, 2H), 2.33 (t, *J* = 7.0 Hz, 2H), 1.70–1.84 (m, 5H), 1.58–1.67 (m, 1H), 1.52 (sext, *J* = 7.3 Hz, 2H), 1.40 (s, 3H), 1.08 (d, *J* = 6.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 193.1, 182.6, 172.3, 171.7, 170.4, 155.9, 152.7, 144.7, 143.9, 143.8, 142.5, 140.7 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.69, 127.68, 127.12, 127.10, 125.3 (2C), 120.2, 120.1, 114.3, 112.1, 98.9, 84.7, 66.2, 66.0, 65.6, 59.5, 57.8, 53.7, 52.2, 46.7, 34.6, 31.5, 28.7, 27.6, 27.0, 23.0, 20.2, 18.0, 13.2; IR (film) ν_{max} 3333, 3060, 2935, 2872, 1730, 1713, 1661, 1589, 1504, 1449, 1267, 1220, 1146, 1081, 739 cm^{-1}; HR ESI-TOF *m/z* 882.3353 ($C_{48}H_{52}ClN_3O_{11}$ + H^+ requires 882.3368); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 375 (11.2), 301 (–9.6), 247 (6.2); $[\alpha]^{23}_D$ +148 (*c* 0.56, MeOH).

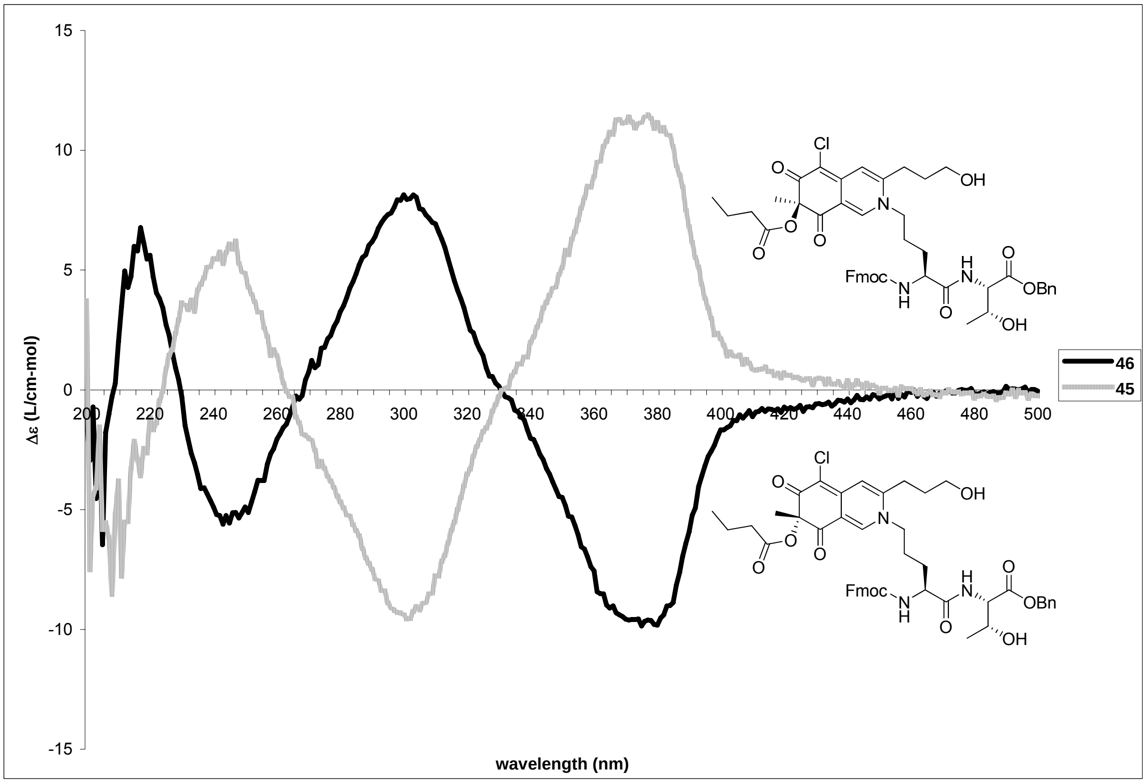
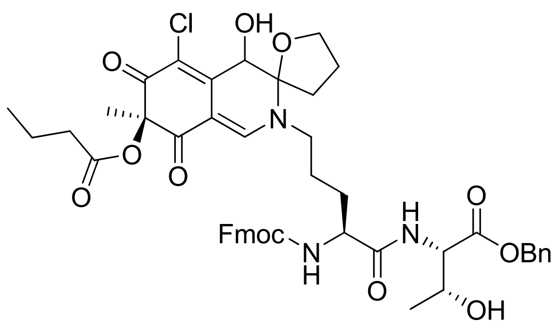


Figure S10. CD spectra (0.2 mM in MeOH) of **45** and **46**.

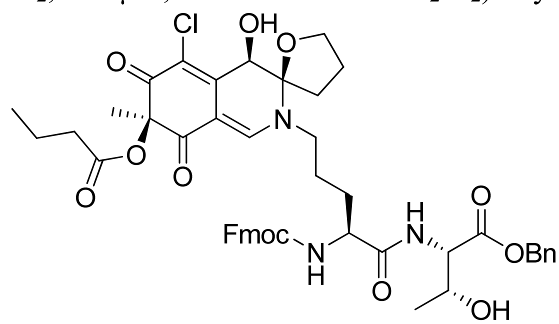


47A−47D. A solution of **45** (15.1 mg, 0.0171 mmol) in DMSO (1.7 mL) and H_2O (170 μL) was treated with I_2 (13.0 mg, 0.0513 mmol), $AgNO_3$ (5.8 mg, 0.034 mmol) and stirred at 23 °C for 3 d. The reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ (1 mL) and diluted with EtOAc (3 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (2 × 2 mL), saturated aqueous NaCl (2 mL), dried (Na_2SO_4) and the solvent was removed by a stream of nitrogen. The residue was purified by preparative TLC (SiO_2, 250 μm, 4 × 4% MeOH−CH_2Cl_2) to yield **47A** (23%, 3.5 mg), **47B** (25%, 3.8 mg), **47C** (6%, 1.0 mg), **47D** (7%, 1.1 mg) and recovered **45** (8%, 1.2 mg).

Isomerization of 47A to 47C: A solution of **47A** (33.0 mg, 0.0367 mmol) in AcOH (2 mL) was treated with CF_3CO_2H (0.2 mL) and stirred at 23 °C for 6 h. The solvent was removed by a stream of nitrogen and the residue was purified by preparative TLC (SiO_2, 250 μm, 2 × 4% MeOH−CH_2Cl_2) to yield **47C** (9%, 3.0 mg) and recovered **47A** (74%, 24.3 mg).

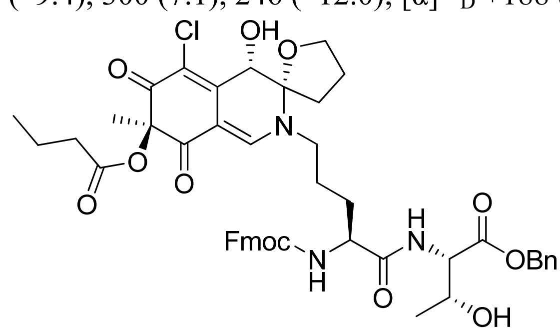
Isomerization of 47B to 47D: A solution of **47B** (82.7 mg, 0.0921 mmol) in AcOH (2 mL) was treated with CF_3CO_2H (0.2 mL) and stirred at 23 °C for 5 h. The solvent was removed by a stream of nitrogen and the residue was purified by preparative TLC (SiO_2, 250 μm, 2 × 4% MeOH–CH_2Cl_2) to yield **47D** (8%, 6.8 mg) and recovered **47B** (79%, 65.7 mg).

Isomerization of 47C to 47A: A solution of **47C** (1.9 mg, 0.0021 mmol) in 1,2-dichloroethane (0.5 mL) was treated with CF_3CO_2H (0.5 mL) and stirred at 23 °C for 5 h. The solvent was removed by a stream of nitrogen and the residue was purified by preparative TLC (SiO_2, 250 μm, 2 × 4% MeOH–CH_2Cl_2) to yield **47A** (89%, 1.7 mg).



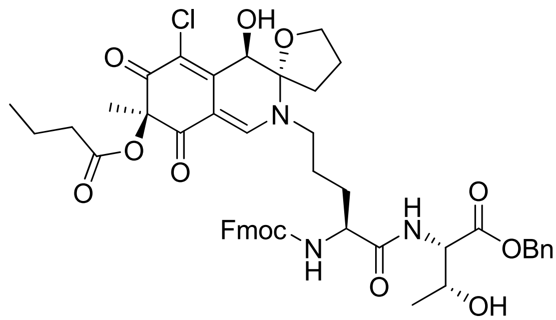
= 47A

For **47A**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.98 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 7.5 Hz, 2H), 7.87 (s, 1H), 7.75 (t, J = 7.5 Hz, 2H), 7.64 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.30–7.41 (m, 7H), 6.14 (d, J = 5.7 Hz, 1H), 5.11–5.19 (m, 3H), 4.49 (d, J = 5.8 Hz, 1H), 4.37 (dd, J = 8.4, 3.0 Hz, 1H), 4.17–4.34 (m, 6H), 4.00 (dd, J = 14.5, 6.9 Hz, 1H), 3.48–3.55 (m, 1H), 3.38–3.44 (m, 1H), 2.33 (dt, J = 7.0, 1.4 Hz, 2H), 1.91–2.04 (m, 3H), 1.80–1.87 (m, 1H), 1.71–1.80 (m, 2H), 1.49–1.69 (m, 2H), 1.53 (app sext, J = 7.3 Hz, 2H) 1.43 (s, 3H), 1.09 (d, J = 6.3 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.04, 188.99, 172.6, 171.4, 170.5, 156.1, 149.8, 148.6, 143.93, 143.85, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.4 (2C), 120.2 (2C), 113.4, 100.7, 97.8, 84.7, 70.4, 68.7, 66.3, 66.0, 65.8, 57.8, 53.8, 48.9, 46.7, 34.54, 34.51, 28.8, 26.8, 24.7, 23.7, 20.3, 18.1, 13.3; IR (film) ν_{max} 3340, 2920, 1736, 1719, 1701, 1686, 1654, 1573, 1458, 1239, 1101, 1079, 1055 cm^{-1}; HR ESI-TOF m/z 898.3305 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 406 (9.0), 348 (–9.4), 300 (7.1), 246 (–12.0); $[\alpha]^{23}_D$ +188 (c 0.76, MeOH).



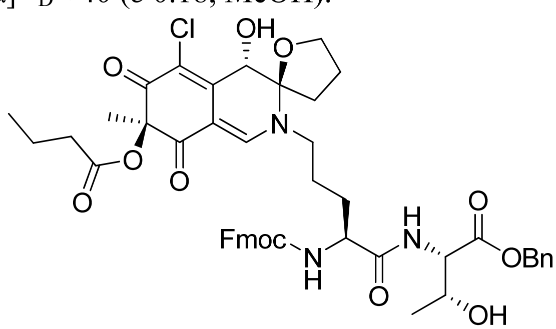
= 47B

For **47B**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.07 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 7.5 Hz, 2H), 7.81 (s, 1H), 7.74 (t, J = 7.7 Hz, 2H), 7.56 (d, J = 8.2 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.31–7.40 (m, 7H), 6.12 (d, J = 4.9 Hz, 1H), 5.15 (d, J = 12.6 Hz, 1H), 5.12 (d, J = 12.7 Hz, 1H), 5.09 (d, J = 5.2 Hz, 1H), 4.54 (d, J = 5.0 Hz, 1H), 4.37 (dd, J = 8.4, 3.1 Hz, 1H), 4.16–4.33 (m, 6H), 4.00 (dd, J = 15.1, 7.3 Hz, 1H), 3.37–3.49 (m, 2H), 2.34 (t, J = 7.1 Hz, 2H), 1.93–2.05 (m, 2H), 1.61–1.87 (m, 5H), 1.50–1.61 (m, 1H), 1.53 (app sext, J = 7.3 Hz, 2H), 1.40 (s, 3H), 1.08 (d, J = 6.3 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 188.4, 172.6, 171.7, 170.6, 155.9, 149.5, 148.6, 143.93, 143.85, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.4 (2C), 120.2 (2C), 113.6, 100.3, 97.8, 84.6, 70.6, 68.7, 66.3, 66.0, 65.7, 57.9, 54.0, 49.7, 46.7, 35.0, 34.6, 29.0, 27.2, 24.6, 23.0, 20.2, 18.0, 13.3; IR (film) ν_{max} 3335, 2922, 1731, 1695, 1649, 1572, 1453, 1268, 1237, 1079 cm^{-1}; HR ESI-TOF *m/z* 898.3294 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 404 (2.4), 344 (–20.1), 256 (13.3), 222 (–5.7); $[\alpha]^{23}_{D}$ –131 (*c* 0.18, MeOH).



= **47C**

For **47C**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.03 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 7.6 Hz, 2H), 7.83 (s, 1H), 7.74 (t, J = 7.6 Hz, 2H), 7.64 (d, J = 8.2 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.30–7.41 (m, 7H), 6.41 (d, J = 6.9 Hz, 1H), 5.16 (d, J = 12.6 Hz, 1H), 5.13 (d, J = 12.8 Hz, 1H), 5.10 (d, J = 5.1 Hz, 1H), 4.48 (d, J = 6.9 Hz, 1H), 4.37 (dd, J = 8.3, 3.0 Hz, 1H), 4.18–4.34 (m, 5H), 3.93 (dd, J = 14.0, 7.1 Hz, 1H), 3.78 (dd, J = 15.3, 7.3 Hz, 1H), 3.49–3.57 (m, 1H), 3.39–3.46 (m, 1H), 2.32–2.39 (m, 2H), 2.34 (t, J = 7.1 Hz, 2H), 1.99–2.09 (m, 2H), 1.62–1.78 (m, 3H), 1.50–1.62 (m, 1H), 1.53 (app sext, J = 7.3 Hz, 2H), 1.38 (s, 3H), 1.08 (d, J = 6.4 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.3, 188.7, 172.5, 171.4, 170.5, 156.0, 150.7, 148.2, 143.9, 143.8, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.4 (2C), 120.2 (2C), 115.2, 101.7, 96.9, 84.7, 68.6, 68.4, 66.3, 66.0, 65.8, 57.9, 53.9, 50.4, 46.7, 34.5, 30.3, 28.8, 27.4, 25.3, 23.5, 20.3, 18.1, 13.3; IR (film) ν_{max} 3342, 2922, 1731, 1693, 1653, 1576, 1451, 1240, 1081, 1043 cm^{-1}; HR ESI-TOF *m/z* 898.3309 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 400 (7.0), 344 (–12.8), 272 (2.5), 235 (–8.3); $[\alpha]^{23}_{D}$ +40 (*c* 0.18, MeOH).



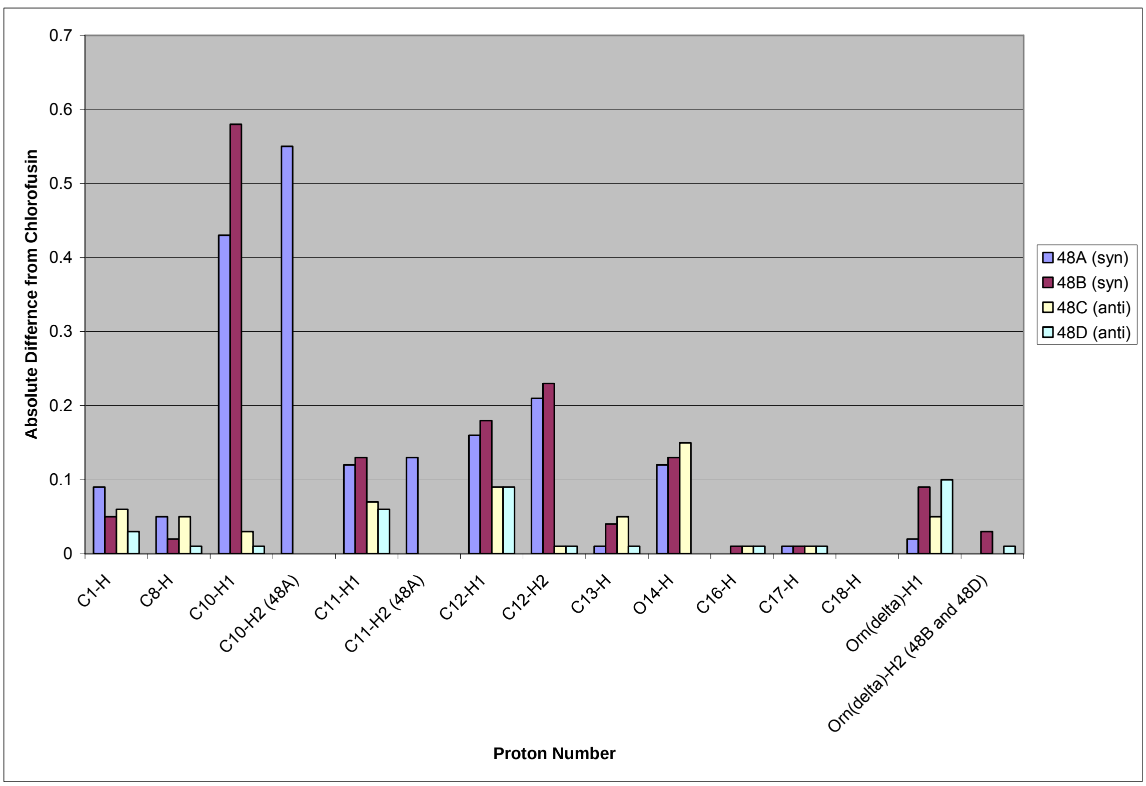
= **47D**

For **47D**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.05 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 7.5 Hz, 2H), 7.82 (s, 1H), 7.74 (t, J = 8.2 Hz, 2H), 7.64 (d, J = 8.3 Hz, 1H), 7.43 (t, J = 7.4 Hz, 2H), 7.31–7.41 (m, 7H), 6.27 (d, J = 5.5 Hz, 1H), 5.16 (d, J = 12.6 Hz, 1H), 5.13 (d, J = 12.7 Hz, 1H), 5.11 (d, J = 5.0 Hz, 1H), 4.52 (d, J = 5.5 Hz, 1H), 4.37 (dd, J = 8.4, 2.8 Hz, 1H), 4.18–4.34 (m, 5H), 3.92 (dd, J = 14.0, 6.6 Hz, 1H), 3.77 (dd, J = 15.1, 7.0 Hz, 1H), 3.43–3.49 (m, 2H), 2.34 (t, J = 7.0 Hz, 4H), 1.99–2.07 (m, 2H), 1.62–1.78 (m, 3H), 1.50–1.62 (m, 1H), 1.54 (app sext, *J* = 7.3 Hz, 2H), 1.43 (s, 3H), 1.09 (d, *J* = 6.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 188.5, 172.6, 171.6, 170.5, 156.0, 150.4, 147.7, 143.9, 143.8, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.4 (2C), 120.2 (2C), 115.4, 101.4, 96.8, 84.8, 68.5 (2C), 66.3, 66.0, 65.8, 57.9, 53.7, 50.5, 46.7, 34.5, 30.2, 28.8, 27.5, 25.3, 23.0, 20.3, 18.1, 13.3; IR (film) ν_{max} 3335, 2922, 1733, 1696, 1649, 1574, 1453, 1272, 1239, 1080, 1043 cm^{-1}; HR ESI-TOF *m/z* 898.3288 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 400 (6.0), 343 (–12.7), 292 (3.8), 255 (1.8), 221 (–2.8); $[\alpha]^{23}_{D}$ +71 (*c* 0.18, MeOH).

Table S5. Comparison of chromophore ^{1}H NMR data for **47A**–**47D** with Williams values.

Proton Number	δ (^{1}H NMR)[a]				
	chlorofusin	**47A** (*syn*)	**47B** (*syn*)	**47C** (*anti*)	**47D** (*anti*)
Configuration		4*R*, 8*R*, 9*R*	4*R*, 8*S*, 9*S*	4*R*, 8*R*, 9*S*	4*R*, 8*S*, 9*R*
C1-H	7.77 (s)	7.87 (s)	7.81 (s)	7.83 (s)	7.82 (s)
C8-H	4.53 (d)	4.49 (d)	4.54 (d)	4.48 (d)	4.52 (d)
C10-H	2.38 (br m)	1.77, 1.97 (m)	1.81 (m)	2.36 (m)	2.35 (m)
C11-H	2.1 (br m)	1.97 (m)	2.00 (m)	2.04 (m)	2.05 (m)
C12-H^1	4.02 (m)	4.20 (m)	4.19 (m)	3.93 (dd)	3.92 (dd)
C12-H^2	3.78 (q)	4.00 (dd)	4.00 (dd)	3.78 (dd)	3.77 (dd)
C13-H	1.43 (s)	1.43 (s)	1.40 (s)	1.38 (s)	1.43 (s)
O14-H	6.26 (d)	6.14 (d)	6.12 (d)	6.41 (d)	6.27 (d)
C16-H	2.34 (t)	2.33 (dt)	2.34 (t)	2.34 (t)	2.34 (t)
C17-H	1.55 (sext)	1.53 (app sext)	1.53 (app sext)	1.53 (app sext)	1.54 (app sext)
C18-H	0.92 (t)	0.90 (t)	0.91 (t)	0.91 (t)	0.91 (t)
Orn-CH_2^{δ}	3.42 (t)	3.40, 3.51 (m)	3.44 (m)	3.41, 3.52 (m)	3.45 (m)

[a] Assignment was assisted by COSY, HMQC, HMBC and ROESY NMR.



Note: For comparison of geminal proton shifts that appear as one signal in Williams' work with shifts for the analogous protons that we observe as two signals, the value for the former is employed twice in determining the Abs(diff) values for the above chart. For comparison of shifts reported as a range in Williams' work or our experimental data, the center of the range was used in the above table and in calculations for the above chart.

Figure S11. ^{1}H NMR chemical shift difference from Williams' chlorofusin values for **47A**–**47D**.

Table S6. Comparison of chromophore ^{13}C NMR data for **47A–47D** with Williams values.

Carbon Number	δ (^{13}C NMR)[a]				
	chlorofusin	**47A** (*syn*)	**47B** (*syn*)	**47C** (*anti*)	**47D** (*anti*)
Configuration		4*R*, 8*R*, 9*R*	4*R*, 8*S*, 9*S*	4*R*, 8*R*, 9*S*	4*R*, 8*S*, 9*R*
C1	150.0	149.8	149.5	150.7	150.4
C2	115.2	113.4	113.6	115.2	115.4
C3	188.1	189.0[b]	188.4[b]	189.3[b]	188.5
C4	84.7	84.7	84.6	84.7	84.8
C5	188.7	189.0[b]	188.9[b]	188.7[b]	188.9
C6	101.3	100.7	100.3	101.7	101.4
C7	147.5	148.6	148.6	148.2	147.7
C8	68.4	68.7	68.7	68.4	68.5
C9	96.7	97.8	97.8	96.9	96.8
C10	30.3	34.5	35.0	30.3	30.2
C11	25.1	24.7	24.6	25.3	25.3
C12	68.4	70.4	70.6	68.6	68.5
C13	22.9	23.7	23.0	23.5	23.0
C15	171.4	171.4	171.7	171.4	171.6
C16	34.4	34.5	34.6	34.5	34.5
C17	17.9	18.1	18.0	18.1	18.1
C18	13.2	13.3	13.3	13.3	13.3
Orn δ	50.5	48.9	49.7	50.4	50.5

[a] Assignment was assisted by COSY, HMQC, HMBC and ROESY NMR.

[b] Assignments made by analogy to **48A**–**48D**.

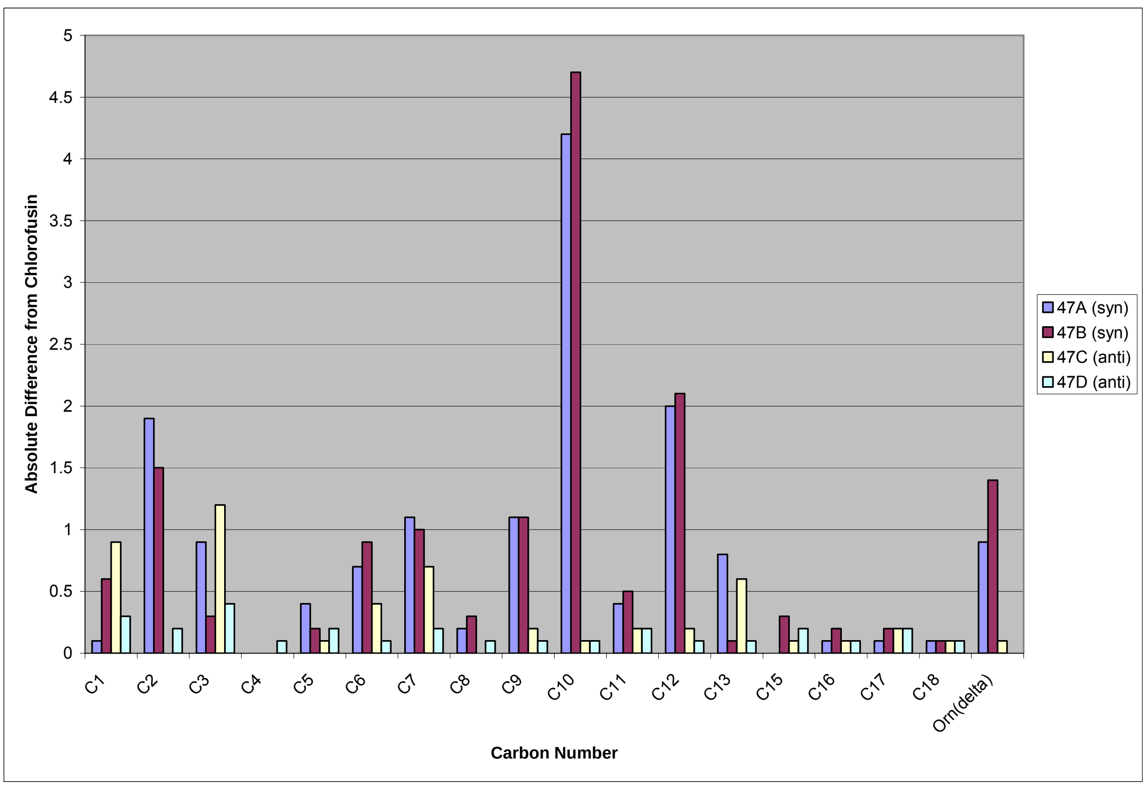
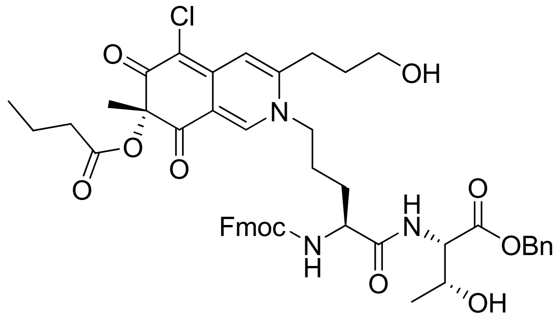
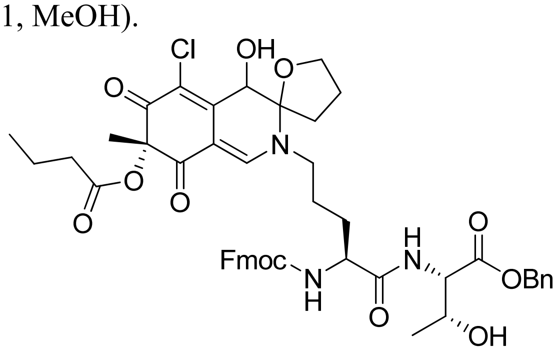


Figure S12. ^{13}C NMR chemical shift difference from Williams' chlorofusin values for **47A–47D**.



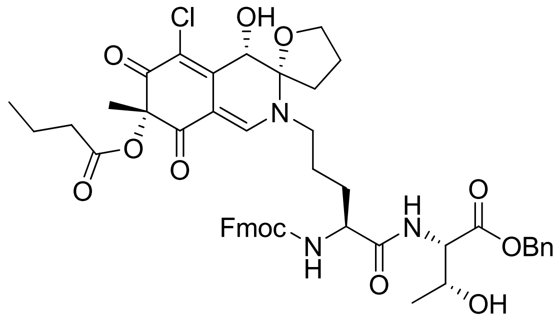
46. A solution of (*S*)-**28** (52 mg, 0.15 mmol) in DMF (0.75 mL) and CH_2Cl_2 (0.75 mL) was treated with **44** (96 mg, 0.18 mmol), $NaHCO_3$ (37 mg, 0.44 mmol) and stirred at 23 °C for 18 h. The reaction mixture was diluted with CH_2Cl_2 (1 mL), treated with aqueous 1 N HCl (1 mL) and stirred vigorously at 23 °C for 3 h. The aqueous layer was extracted with CH_2Cl_2 (3 × 1 mL) and the combined organic layers dried (Na_2SO_4) for 15 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 80% EtOAc–hexanes – 3% MeOH–EtOAc gradient) to yield **46** as an orange foam (71%, 92 mg): mp 97–101 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.17 (s, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.89 (dd, *J* = 7.5, 3.8 Hz, 2H), 7.72 (dd, *J* = 13.0, 7.5 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.26–7.47 (m, 9H), 6.76 (s, 1H), 5.03–5.20 (m, 3H), 4.70 (br s, 1H), 4.37 (dd, *J* = 8.4, 3.1 Hz, 1H), 4.18–4.35 (m, 5H), 3.96–4.07 (m, 2H), 3.52 (t, *J* = 6.0 Hz, 2H), 2.72 (t, *J* = 7.5 Hz, 2H), 2.34 (t, 7.1 Hz, 2H), 1.68–1.83 (m, 5H), 1.58–1.67 (m, 1H), 1.54 (sext., *J* = 7.3 Hz, 2H), 1.39 (s, 3H), 1.08 (d, *J* = 6.3 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 193.1, 182.6, 172.3, 171.7, 170.4, 155.9, 152.7, 144.7, 144.0, 143.8, 142.5, 140.7 (2C), 135.9, 128.4 (2C), 128.0, 127.8 (2C), 127.69, 127.67, 127.1 (2C), 125.3 (2C), 120.18, 120.15, 114.3, 112.1, 98.9, 84.7, 66.2, 65.9, 65.6, 59.5, 57.8, 53.7, 52.3, 46.7, 34.6, 31.5, 28.7, 27.6, 27.0, 22.9, 20.2, 18.0, 13.3; IR (film) ν_{max} 3333, 3060, 2935, 2872, 1730, 1713, 1666, 1648, 1589, 1504, 1449, 1267, 1220, 1146, 1081, 739 cm^{-1}; HR ESI-TOF *m/z* 882.3356 ($C_{48}H_{52}ClN_3O_{11}$ + H^+ requires 882.3368); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 375 (–9.9), 300 (8.1), 245 (–5.6); $[\alpha]^{23}_D$ –129 (*c* 0.71, MeOH).



48A–48D. A solution of **46** (15.0 mg, 0.0170 mmol) in DMSO (1.7 mL) and H_2O (175 μL) was treated with I_2 (13.0 mg, 0.0512 mmol), $AgNO_3$ (5.8 mg, 0.0341 mmol) and stirred at 23 °C for 3 d. The reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ (1 mL) and diluted with EtOAc (3 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (2 × 2 mL), saturated aqueous NaCl (2 mL), dried (Na_2SO_4) and the solvent was removed by a stream of nitrogen. The residue was purified by preparative TLC (SiO_2, 250 μm, 4 × 4% MeOH–CH_2Cl_2) to yield diastereomers **48A** (20%, 3.1 mg), **48B** (22%, 3.3 mg), **48C** (8%, 1.2 mg) and **48D** (7%, 1.1 mg).

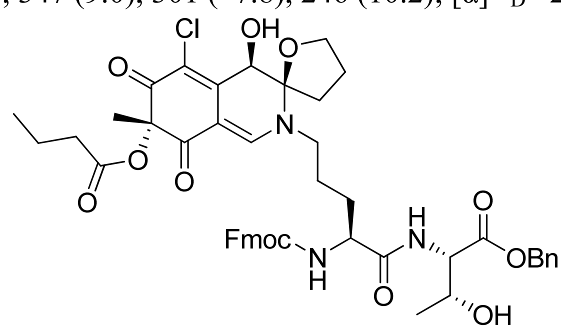
Isomerization of 48A to 48C: A solution of **48A** (10.0 mg, 0.0111 mmol) in AcOH (1 mL) was treated with CF_3CO_2H (50 μL) and stirred at 23 °C for 15 h. The reaction mixture was diluted with EtOAc (15 mL), washed with H_2O (2 × 3 mL), 50% saturated aqueous $NaHCO_3$ (2 × 3 mL), saturated aqueous NaCl (3 mL) and dried (Na_2SO_4). The solvent was removed by a stream of nitrogen and the residue was purified by preparative TLC (SiO_2, 250 µm, 2 × 4% MeOH–CH_2Cl_2) to yield **48C** (15%, 1.5 mg) and recovered **48A** (71%, 7.1 mg).

Isomerization of 48B to 48D: A solution of **48B** (10.0 mg, 0.0111 mmol) in AcOH (1 mL) was treated with CF_3CO_2H (100 μL) and stirred at 23 °C for 15 h. The reaction mixture was diluted with EtOAc (15 mL), washed with H_2O (2 × 3 mL), 50% saturated aqueous $NaHCO_3$ (2 × 3 mL), saturated aqueous NaCl (3 mL) and dried (Na_2SO_4). The solvent was removed by a stream of nitrogen and the residue was purified by preparative TLC (SiO_2, 250 µm, 2 × 4% MeOH–CH_2Cl_2) to yield **48D** (6%, 0.6 mg) and recovered **48B** (74%, 7.4 mg).



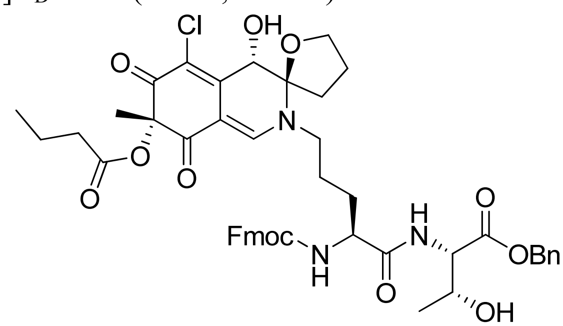
= 48A

For **48A**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.05 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 7.5 Hz, 2H), 7.86 (s, 1H), 7.74 (t, J = 7.3 Hz, 2H), 7.58 (d, J = 8.2 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.30–7.40 (m, 7H), 6.14 (d, J = 5.8 Hz, 1H), 5.16 (d, J = 12.7 Hz, 1H), 5.13 (d, J = 12.7 Hz, 1H), 5.08 (d, J = 5.2 Hz, 1H), 4.48 (d, J = 5.8 Hz, 1H), 4.37 (dd, J = 8.4, 3.1 Hz, 1H), 4.15–4.34 (m, 6H), 3.99 (dd, J = 14.8, 6.9 Hz, 1H), 3.39–3.48 (m, 2H), 2.34 (t, J = 7.1 Hz, 2H), 1.91–2.05 (m, 3H), 1.80–1.87 (m, 1H), 1.58–1.79 (m, 4H), 1.54 (app sext, J = 7.3 Hz, 2H), 1.42 (s, 3H), 1.08 (d, J = 6.4 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.1, 189.0, 172.6, 171.4, 170.6, 156.0, 149.9, 148.6, 143.91, 143.89, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.4 (2C), 120.2 (2C), 113.3, 100.6, 97.8, 84.7, 70.4, 68.6, 66.3, 66.0, 65.7, 57.9, 54.0, 49.6, 46.7, 34.5 (2C), 29.0, 27.1, 24.7, 23.7, 20.2, 18.0, 13.3; IR (film) ν_{max} 3358, 2918, 2845, 1732, 1715, 1695, 1684, 1649, 1572, 1454, 1270, 1236, 1102, 1076 cm^{-1}; HR ESI-TOF m/z 898.3307 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 407 (–9.5), 347 (9.0), 301 (–7.8), 246 (10.2); $[\alpha]^{23}_D$ –204 (c 0.18, MeOH).



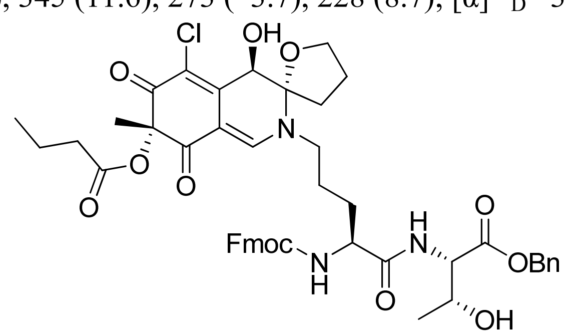
= X2B

For **48B**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.82 (s, 1H), 7.74 (dd, *J* = 12.8, 7.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.29–7.40 (m, 7H), 6.13 (d, *J* = 4.9 Hz, 1H), 5.08–5.18 (m, 3H), 4.55 (d, *J* = 4.8 Hz, 1H), 4.37 (dd, *J* = 8.4, 3.1 Hz, 1H), 4.15–4.33 (m, 6H), 4.01 (dd, *J* = 15.2, 7.3 Hz, 1H), 3.47–3.55 (m, 1H), 3.37–3.43 (m, 1H), 2.35 (t, *J* = 7.1 Hz, 2H), 1.89–2.04 (m, 2H), 1.70–1.88 (m, 4H), 1.56–1.69 (m, 2H), 1.54 (app sext, *J* = 7.3 Hz, 2H), 1.39 (s, 3H), 1.09 (d, *J* = 6.3 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.4, 172.5, 171.7, 170.5, 156.1, 149.4, 148.5, 144.0, 143.8, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.41, 125.37, 120.2 (2C), 113.7, 100.4, 97.8, 84.7, 70.5, 68.7, 66.3, 66.0, 65.8, 57.9, 53.8, 49.1, 46.7, 35.0, 34.6, 28.8, 26.9, 24.6, 23.0, 20.3, 18.1, 13.3; IR (film) ν_{max} 3355, 2918, 2850, 1716, 1649, 1571, 1559, 1455, 1273, 1101, 1077 cm^{-1}; HR ESI-TOF *m/z* 898.3307 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 405 (–2.8), 345 (18.0), 256 (–13.4), 221 (9.0); $[\alpha]^{23}_D$ +105 (*c* 0.44, MeOH).



= 48C

For **48C**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.05 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 2H), 7.83 (s, 1H), 7.74 (t, *J* = 8.6 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.30–7.40 (m, 7H), 6.41 (d, *J* = 7.0 Hz, 1H), 5.09–5.19 (m, 3H), 4.48 (d, *J* = 7.0 Hz, 1H), 4.37 (dd, *J* = 8.4, 3.0 Hz, 1H), 4.18–4.33 (m, 5H), 3.93 (dd, *J* = 14.7, 6.5 Hz, 1H), 3.79 (dd, *J* = 15.1, 7.2 Hz, 1H), 3.47 (t, *J* = 7.6 Hz, 2H), 2.35 (t, *J* = 7.1 Hz, 4H), 2.03 (app quint, *J* = 7.1 Hz, 2H), 1.63–1.77 (m, 3H), 1.50–1.63 (m, 1H), 1.54 (app sext, *J* = 7.3 Hz, 2H), 1.38 (s, 3H), 1.09 (d, *J* = 6.3 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.3, 188.8, 172.6, 171.5, 170.5, 156.0, 150.9, 148.2, 143.93, 143.85, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.4 (2C), 120.2 (2C), 115.2, 101.7, 96.9, 84.7, 68.6, 68.4, 66.3, 66.0, 65.8, 57.9, 53.8, 50.4, 46.7, 34.5, 30.2, 28.8, 27.4, 25.3, 23.5, 20.3, 18.1, 13.3; IR (film) ν_{max} 3361, 2919, 2854, 1733, 1717, 1699, 1685, 1651, 1574, 1559, 1456, 1271, 1240, 1080, 1043 cm^{-1}; HR ESI-TOF *m/z* 898.3307 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 397 (–6.7), 345 (11.6), 273 (–3.7), 228 (8.7); $[\alpha]^{23}_D$ –38 (*c* 0.18, MeOH).



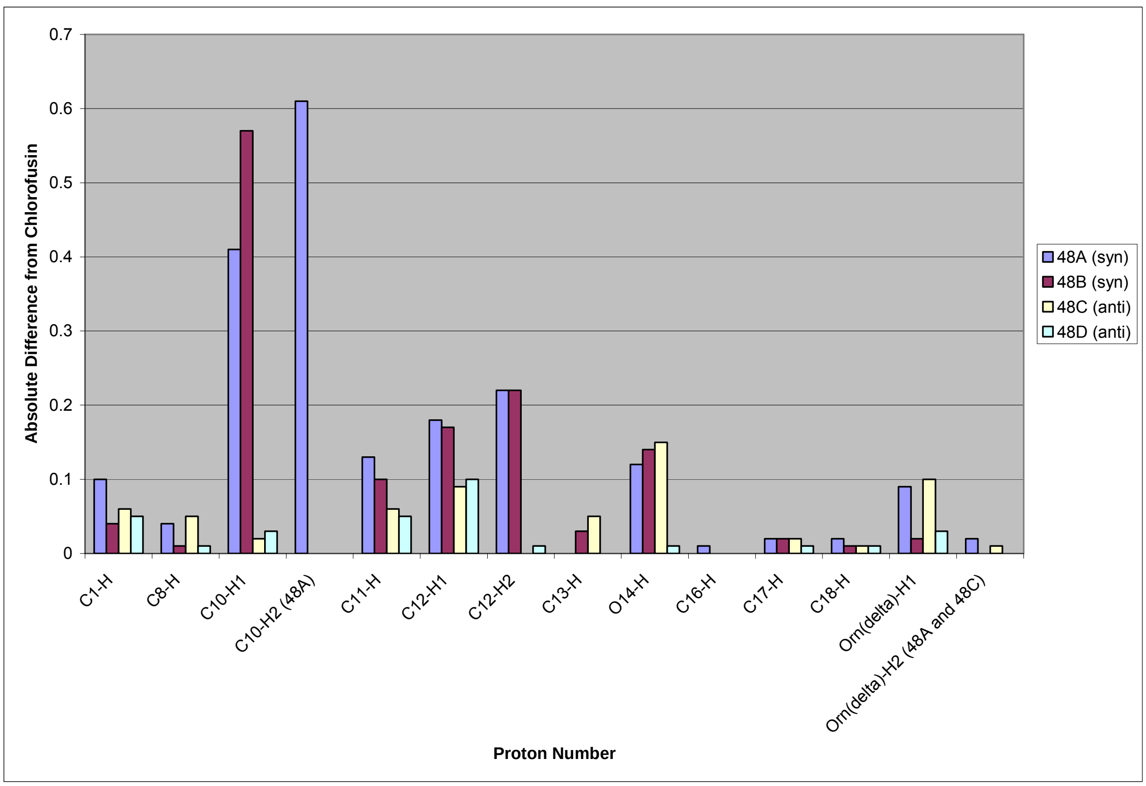
= 48D

For **48D**: ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 2H), 7.80 (s, 1H), 7.74 (dd, *J* = 11.8, 7.5 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.31–7.40 (m, 7H), 6.26 (d, *J* = 5.4 Hz, 1H), 5.16 (d, *J* = 19.2, 12.6 Hz, 1H), 5.15 (d, *J* = 12.6 Hz, 1H), 5.12 (d, *J* = 12.7 Hz, 1H), 5.11 (d, *J* = 5.1 Hz, 1H), 4.52 (d, *J* = 5.4 Hz, 1H), 4.37 (dd, *J* = 8.4, 3.1 Hz, 1H), 4.17–4.34 (m, 5H), 3.93 (dd, *J* = 13.9, 7.4 Hz, 1H), 3.77 (dd, *J* = 15.2, 7.2 Hz, 1H), 3.48–3.56 (m, 1H), 3.37–3.45 (m, 1H), 2.33–2.39 (m, 2H), 2.35 (t, *J* = 7.1 Hz, 2H), 1.99–2.09 (m, 2H), 1.62–1.78 (m, 3H), 1.51–1.62 (m, 1H), 1.54 (app sext, *J* = 7.3 Hz, 2H), 1.42 (s, 3H), 1.09 (d, *J* = 6.3 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.5, 172.5, 171.6, 170.5, 156.0, 150.3, 147.7, 143.9, 143.8, 140.8 (2C), 136.0, 128.4 (2C), 128.0, 127.8 (2C), 127.7 (2C), 127.2 (2C), 125.4 (2C), 120.2 (2C), 115.4, 101.4, 96.8, 84.8, 68.52, 68.49, 66.3, 66.0, 65.8, 57.9, 53.9, 50.5, 46.7, 34.5, 30.2, 28.8, 27.5, 25.3, 23.0, 20.3, 18.1, 13.3; IR (film) ν_{max} 3334, 2932, 1731, 1696, 1647, 1573, 1452, 1239, 1081, 1044, 739 cm^{-1}; HR ESI-TOF *m/z* 898.3303 ($C_{48}H_{52}ClN_3O_{12}$ + H^+ requires 898.3318); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 398 (–6.0), 346 (11.9), 291 (–4.4), 256 (–3.0), 220 (4.6); $[\alpha]^{23}_{D}$ –58 (*c* 0.18, MeOH).

Table S7. Comparison of chromophore ^{1}H NMR data for **48A**–**48D** with Williams values.

Proton Number	δ (^{1}H NMR)[a]				
	chlorofusin	**48A** (*syn*)	**48B** (*syn*)	**48C** (*anti*)	**48D** (*anti*)
Configuration		4*S*, 8*S*, 9*S*	4*S*, 8*R*, 9*R*	4*S*, 8*S*, 9*R*	4*S*, 8*R*, 9*S*
C1-H	7.77 (s)	7.86 (s)	7.82 (s)	7.83 (s)	7.80 (s)
C8-H	4.53 (d)	4.48 (d)	4.55 (d)	4.48 (d)	4.52 (d)
C10-H	2.38 (br m)	1.83, 1.95 (m)	1.80 (m)	2.35 (t)	2.37 (m)
C11-H	2.1 (br m)	1.97, 1.98 (m)	1.97 (m)	2.03 (app quint)	2.04 (m)
C12-H^1	4.02 (m)	4.18 (m)	4.20 (m)	3.93 (dd)	3.93 (dd)
C12-H^2	3.78 (q)	3.99 (dd)	4.01 (dd)	3.79 (dd)	3.77 (dd)
C13-H	1.43 (s)	1.42 (s)	1.39 (s)	1.38 (s)	1.42 (s)
O14-H	6.26 (d)	6.14 (d)	6.13 (d)	6.41 (d)	6.26 (d)
C16-H	2.34 (t)	2.34 (t)	2.35 (t)	2.35 (t)	2.35 (t)
C17-H	1.55 (sext)	1.54 (app sext)	1.54 (app sext)	1.54 (app sext)	1.54 (app sext)
C18-H	0.92 (t)	0.92 (t)	0.92 (t)	0.92 (t)	0.92 (t)
Orn-CH_2^{δ}	3.42 (t)	3.44 (m)	3.39, 3.51 (m)	3.47 (t)	3.41, 3.52 (m)

[a] Assignment was assisted by COSY, HMQC, HMBC and ROESY NMR.



Note: For comparison of geminal proton shifts that appear as one signal in Williams' work with shifts for the analogous protons that we observe as two signals, the value for the former is employed twice in determining the Abs(diff) values for the above chart. For comparison of shifts reported as a range in Williams' work or our experimental data, the center of the range was used in the above table and in calculations for the above chart.

Figure S13. ^{1}H NMR chemical shift difference from Williams' chlorofusin values for **48A**–**48D**.

Table S8. Comparison of chromophore ^{13}C NMR data for **48A**–**48D** with Williams values.

Carbon Number	δ (^{13}C NMR)[a]				
	chlorofusin	**48A** (*syn*)	**48B** (*syn*)	**48C** (*anti*)	**48D** (*anti*)
Configuration		4*S*, 8*S*, 9*S*	4*S*, 8*R*, 9*R*	4*S*, 8*S*, 9*R*	4*S*, 8*R*, 9*S*
C1	150.0	149.9	149.4	150.9	150.3
C2	115.2	113.3	113.7	115.2	115.4
C3	188.1	189.0	188.4	189.3	188.5
C4	84.7	84.7	84.7	84.7	84.8
C5	188.7	189.1	188.9	188.8	188.9
C6	101.3	100.6	100.4	101.7	101.4
C7	147.5	148.6	148.5	148.2	147.7
C8	68.4	68.6	68.7	68.4	68.5
C9	96.7	97.8	97.8	96.9	96.8
C10	30.3	34.5	35.0	30.2	30.2
C11	25.1	24.7	24.6	25.3	25.3
C12	68.4	70.4	70.5	68.6	68.5
C13	22.9	23.7	23.0	23.5	23.0
C15	171.4	171.4	171.7	171.5	171.6
C16	34.4	34.5	34.6	34.5	34.5
C17	17.9	18.0	18.1	18.1	18.1
C18	13.2	13.3	13.3	13.3	13.3
Orn δ	50.5	49.6	49.1	50.4	50.5

[a] Assignment was assisted by COSY, HMQC, HMBC and ROESY NMR.

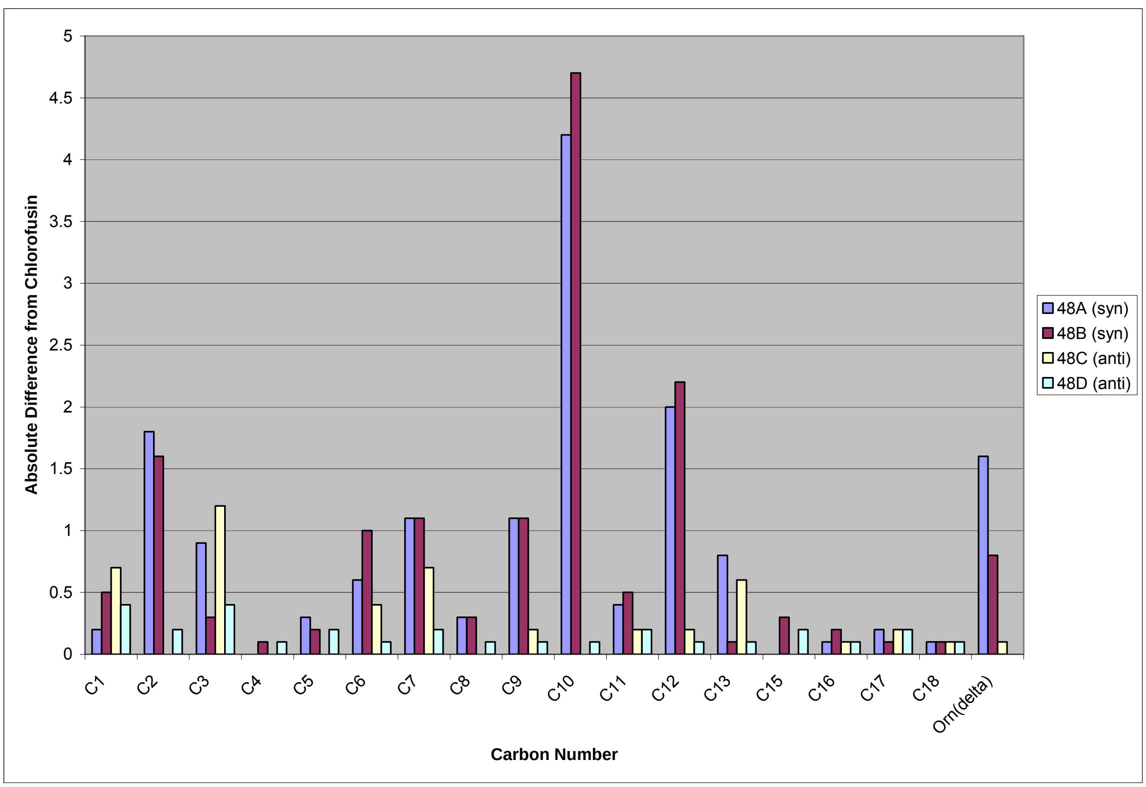
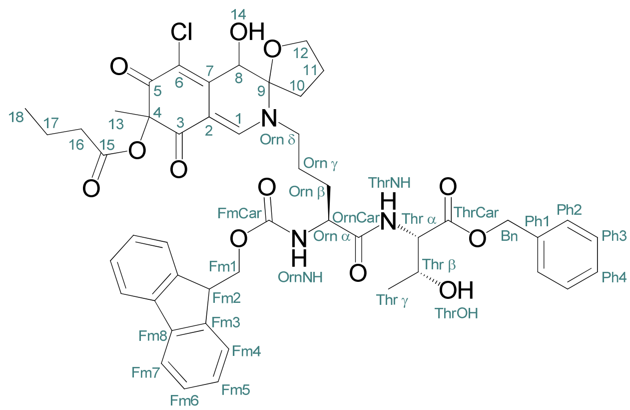


Figure S14. ^{13}C NMR chemical shift difference from Williams' chlorofusin values for **48A**–**48D**.



Stereochemical Assignment of Chlorofusin. For convenience of relating the spectroscopic properties and relative stereochemistries of the benzylamine and butylamine adducts discussed beforehand as well as for relating chromophore enantiomeric pairs, notations of **A–D** consistently refer to the same relative stereochemistry of the chromophore at C4, C8 and C9. Using the diagnostic spectroscopic properties of the two sets of four diastereomers along with the analogous *N*,*O*-ketal equilibrations that define the respective *syn*/*anti* pairs in each series allowed the full relative and absolute stereochemical assignments for all eight diastereomers. Moreover, only diastereomer **47D** (4*R*,8*S*,9*R*) matched all of the spectroscopic properties reported for the chlorofusin chromophore. With **47A–D** and **48A–D** the signals most diagnostic of a *syn* versus *anti* relationship between the C8 and C9 oxygen substituents are again those derived from C10-H and C12-H. The C10-H signals associated with **48C** (m, 2.35 ppm), **48D** (m, 2.37 ppm), **47C** (m, 2.36 ppm), **47D** (m, 2.35 ppm) and chlorofusin (br m, 2.38 ppm) are all very similar to one another, whereas those for **48A** (m, 1.83 ppm; m, 1.95 ppm) and **47A** (m, 1.77 ppm; m, 1.97 ppm) are similar and those for **48B** (m, 1.80 ppm) and **47B** (m, 1.81 ppm) are similar but distinct from chlorofusin. For C12-H, the signals are analogously diagnostic with **48C** (dd, 3.79 ppm; dd, 3.93 ppm), **48D** (dd, 3.77 ppm; dd, 3.93 ppm), **47C** (dd, 3.78 ppm; dd, 3.93 ppm), **47D** (dd, 3.77 ppm; dd, 3.92 ppm) and chlorofusin (q, 3.78 ppm; m, 4.02 ppm) being similar to one another, and **48A** (dd, 3.99 ppm; m, 4.18 ppm), **48B** (dd, 4.01 ppm; m, 4.20 ppm), **47A** (dd, 4.00 ppm; m, 4.20 ppm) and **47B** (dd, 4.00 ppm; m, 4.19 ppm) being similar to one another but distinct from chlorofusin. In the ^{13}C NMR data for these eight compounds, the chemical shifts of the C2 signals of **48C** (115.2 ppm), **48D** (115.4 ppm), **47C** (115.2 ppm), **47D** (115.4 ppm) and chlorofusin (115.2 ppm) are nearly 2 ppm downfield of the analogous signals for **48A** (113.3 ppm), **48B** (113.7 ppm), **47A** (113.4 ppm) and **47B** (113.6 ppm). [The assignments C6 and C2 appear to have been switched in the original Williams work based on the observance of much stronger HMBC correlations between the C1-H signals of **48A–D** and what were assigned as the C6 signals (four bond) while the C1-H correlations with what were assigned as the C2 signals were weak (two bond). This reassignment, which is inconsequential to the comparisons, would appear to be confirmed with HMQC data from a dechloro-derivative obtained during *N*,*O*-spiroketal isomerization. While this tentative reassignment is under continued investigation the data in this manuscript is reported in terms of the Williams assignment.] Other ^{13}C NMR data distinguishing *syn* from *anti*: For C6: **48C** (101.7 ppm), **48D** (101.4 ppm), **47C** (101.7 ppm), **47D** (101.4 ppm), chlorofusin (101.3 ppm), versus **48A** (100.6 ppm), **48B** (100.4

ppm), **47A** (100.7 ppm) and **47B** (100.3 ppm); C9: **48C** (96.9 ppm), **48D** (96.8 ppm), **47C** (96.9 ppm), **47D** (96.8 ppm), chlorofusin (96.7 ppm), versus **48A** (97.8 ppm), **48B** (97.8 ppm), **47A** (97.8 ppm) and **47B** (97.8 ppm); C10: **48C** (30.2 ppm), **48D** (30.2 ppm), **47C** (30.3 ppm), **47D** (30.2 ppm), chlorofusin (30.3 ppm), versus **48A** (34.5 ppm), **48B** (35.0 ppm), **47A** (34.5 ppm) and **47B** (35.0 ppm); C12: **48C** (68.6 ppm), **48D** (68.5 ppm), **47C** (68.6 ppm), **47D** (68.5 ppm), chlorofusin (68.4 ppm), versus **48A** (70.4 ppm), **48B** (70.5 ppm), **47A** (70.4 ppm) and **47B** (70.6 ppm); Orn delta: **48C** (50.4 ppm), **48D** (50.5 ppm), **47C** (50.4 ppm), **47D** (50.5 ppm), chlorofusin (50.5 ppm), versus **48A** (49.6 ppm), **48B** (49.1 ppm), **47A** (48.9 ppm) and **47B** (49.7 ppm). ^{1}H NMR data distinguishing **47C/48C** from **47D/48D** as well as *syn* versus *anti*: C8-H: **48C** (d, 4.48 ppm), **47C** (d, 4.48 ppm), versus **48D** (d, 4.52 ppm), **47D** (d, 4.52 ppm), chlorofusin (d, 4.53 ppm), [also versus **48A** (d, 4.48 ppm), **47A** (d, 4.49 ppm), **47B** (d, 4.55 ppm) and **48B** (d, 4.54 ppm)]; C13-H: **48C** (s, 1.38 ppm), **47C** (s, 1.38 ppm), versus **48D** (s, 1.42 ppm), **47D** (s, 1.43 ppm), chlorofusin (s, 1.43 ppm), [also versus **48A** (s, 1.42 ppm), **47A** (s, 1.43 ppm), **48B** (s, 1.39 ppm) and **47B** (s, 1.40 ppm),]; O14-H: **48C** (d, 6.41 ppm), **47C** (d, 6.41 ppm), versus **48D** (d, 6.26 ppm), **47D** (d, 6.27 ppm), chlorofusin (d, 6.26 ppm), [also versus **48A** (d, 6.14 ppm), **47A** (d, 6.14 ppm), **48B** (d, 6.13 ppm) and **47B** (d, 6.12 ppm)]. ^{13}C NMR data distinguishing **47C/48C** from **47D/48D** as well as *syn* versus *anti*: C1: **48C** (150.9 ppm), **47C** (150.7 ppm), versus **48D** (150.3 ppm), **47D** (150.4 ppm), chlorofusin (150.0 ppm), [also versus **48A** (149.9 ppm), **47A** (149.8 ppm), **48B** (149.4 ppm) and **47B** (149.5 ppm)]; C3: **48C** (189.3 ppm), **47C** (189.3 ppm), versus **48D** (188.5 ppm), **47D** (188.5 ppm), chlorofusin (188.1 ppm), [also versus **48A** (189.0 ppm), **47A** (189.0 ppm), **48B** (188.4 ppm) and **47B** (188.4 ppm)]; C6: **48C** (101.7 ppm), **47C** (101.7 ppm), versus **48D** (101.4 ppm), **47D** (101.4 ppm), chlorofusin (101.3 ppm), [also versus **48A** (100.6 ppm), **47A** (100.7 ppm), **48B** (100.4 ppm) and **47B** (100.3 ppm)]; C7: **48C** (148.2 ppm), **47C** (148.2 ppm), versus **48D** (147.7 ppm), **47D** (147.7 ppm), chlorofusin (147.5 ppm), [also versus **48A** (148.6 ppm), **47A** (148.6 ppm), **48B** (148.5 ppm) and **47B** (148.6 ppm)]; C13: **48C** (23.5 ppm), **47C** (23.5 ppm), versus **48D** (23.0 ppm), **47D** (23.0 ppm), chlorofusin (22.9 ppm), [also versus **48A** (23.7 ppm), **47A** (23.7 ppm), **48B** (23.0 ppm) and **47B** (23.0 ppm)]. ^{1}H NMR data distinguishing **48D** from **47D** allowing the absolute configuration assignment: Orn delta: **48D** (m, 3.41 ppm; m, 3.52 ppm, 1H each) versus **47D** (m, 3.45 ppm, 2H), chlorofusin (t, 3.42 ppm, 2H).

The ROESY NMR data for these eight diastereomers reveals a correlation only between C8-H and C4-Me (and not C4-Me/C8-OH) when those groups are *cis* with respect to one another (**48A**, **48C**, **47A** and **47C**) and a correlation between C4-Me and both C8-H and C8-OH when C4-Me is *trans* with respect to C8-H (**48B**, **48D**, **47B** and **47D**). Regardless of the relative stereochemistry of the chromophore, an NOE is seen between C4-Me and C8-H, and furthermore, the correlations are consistent with the ROESY NMR data for **42A** and **42D** (X-ray).

Comparison of the CD spectra of all eight diastereomers shows that the region between 250–470 nm is apparently dependent on the stereochemistry of the chromophore alone with nearly equal and opposite spectra observed for **48A** and **47A**, for **48B** and **47B**, for **48C** and **47C** and for **48D** and **47D** (See figure below). Of particular note is the sign of the longest wavelength Cotton effect (395–410 nm). As with azaphilones **25–28**, a positive longest wavelength Cotton effect is diagnostic of C4-*R* stereochemistry and a negative Cotton effect is diagnostic of C4-*S* stereochemistry.

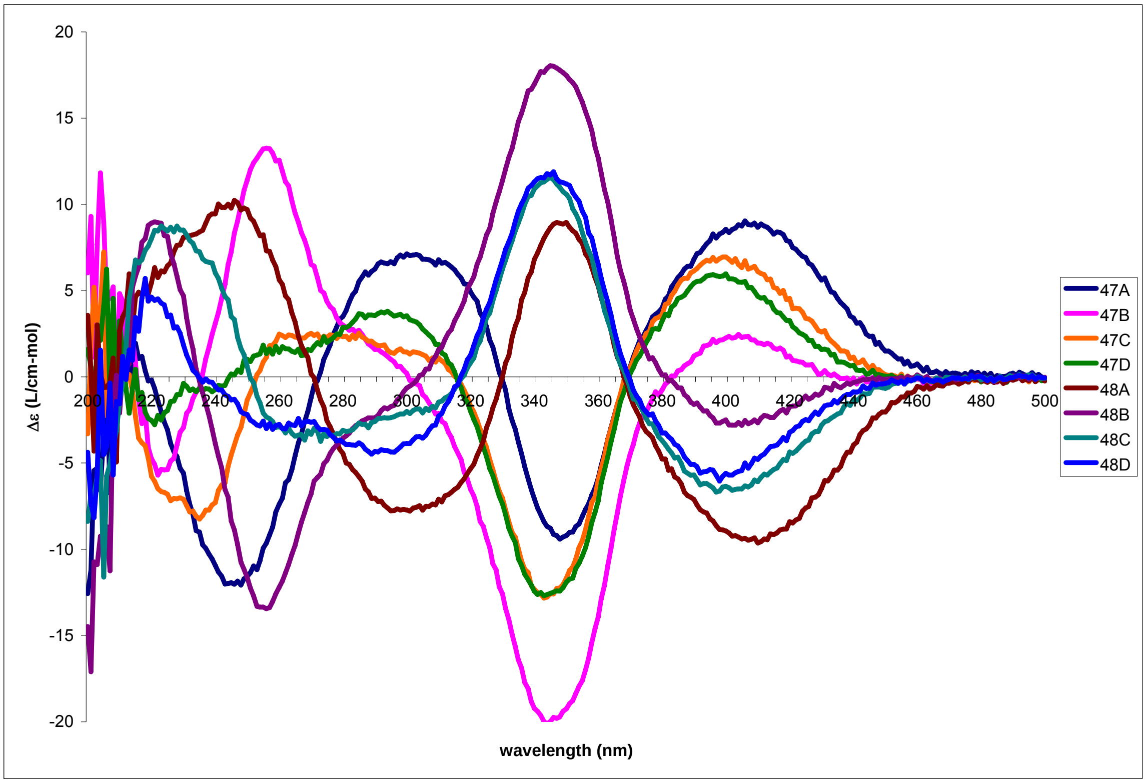
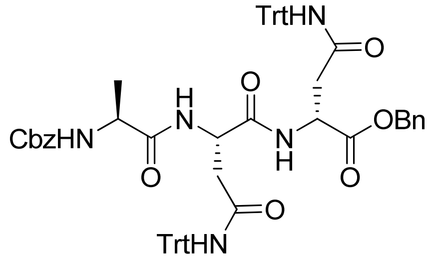
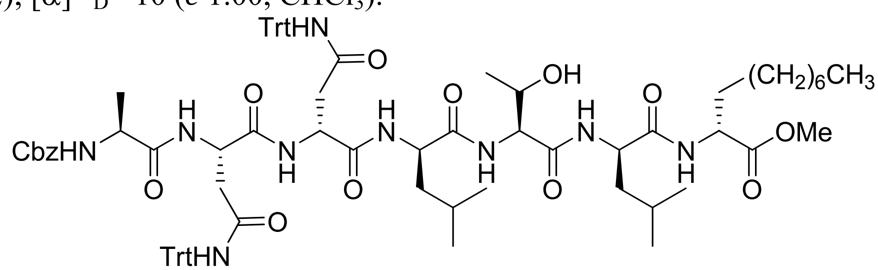


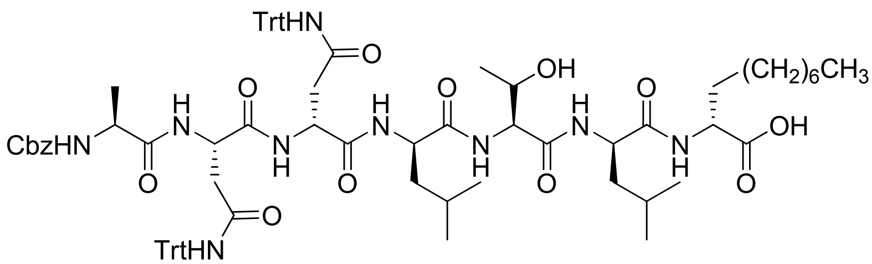
Figure S15. CD spectra (0.2 mM in MeOH) of **47A**–**47D** and **48A**–**48D**.



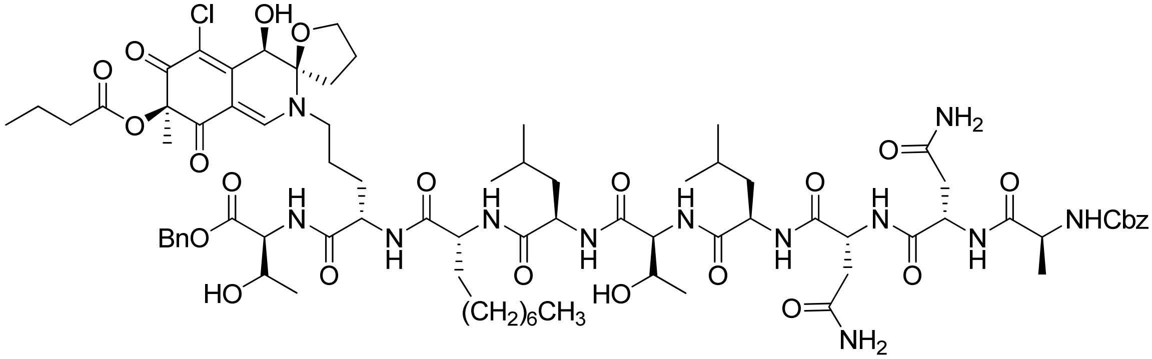
Cbz-L-Ala-L-Asn(Trt)-D-Asn(Trt)-OBn (55). A solution of Fmoc-L-Asn(Trt)-D-Asn(Trt)-OBn[5] (511 mg, 0.490 mmol) in anhydrous CH_2Cl_2 (4.9 mL) was treated with piperidine (0.15 mL, 1.5 mmol) and stirred at 23 °C for 100 min. Chromatography (SiO_2, 70% EtOAc−hexanes) afforded the crude dipeptide as a gray solid which was directly employed in the next reaction. A flask containing the intermediate dipeptide (401 mg, 0.490 mmol), commercially available Cbz-L-Ala-OH (142 mg, 0.637 mmol), HOAt (177 mg, 1.30 mmol) and EDCI (9.25 g, 1.30 mmol) at 0 °C was slowly treated with anhydrous DMF (3.3 mL), stirred at 0 °C for 1 h then stirred at 23 °C for 24 h under argon. The reaction mixture was diluted with EtOAc (50 mL) and washed with aqueous 0.1 N HCl (2 × 10 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL), H_2O (10 mL), and saturated aqueous NaCl (20 mL). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 70% EtOAc−hexanes) afforded **55** as a white solid (60%, 300 mg): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.76 (s, 1H), 8.57 (s, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 7.8 Hz, 1H), 7.32–7.38 (m, 11H), 7.14−7.29 (m, 30H), 5.07 (m, 4H), 4.69 (dd, J = 14.7, 8.0 Hz, 1H), 4.60 (dd, J = 13.7, 6.5 Hz, 1H), 4.15 (m, 1H), 2.74–2.84 (m, 3H), 2.58 (m, 1H), 1.22 (d, J = 7.1 Hz, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 172.3, 171.0, 170.9, 168.8, 168.7, 155.7, 144.8 (3C),144.7 (3C), 137.0, 135.9, 128.61 (6C), 128.59 (6C), 128.5 (3C), 128.4 (3C), 127.9. 127.8 (3C), 127.7 (2C), 127.53 (6C), 127.51 (6C), 126.41 (2C), 126.38 (2C), 69.5, 69.4, 66.1, 65.6, 50.1 (2C), 49.2, 39.0, 37.6, 18.8; IR (film) ν_{max} 3311, 3058, 3032, 1666, 1492, 1448, 1215, 751, 699 cm^{-1}; HR ESI-TOF *m/z* 1026.4412 ($C_{64}H_{59}N_5O_8 + H^+$ requires 1026.4442); $[\alpha]^{23}_D$ −10 (*c* 1.00, $CHCl_3$).



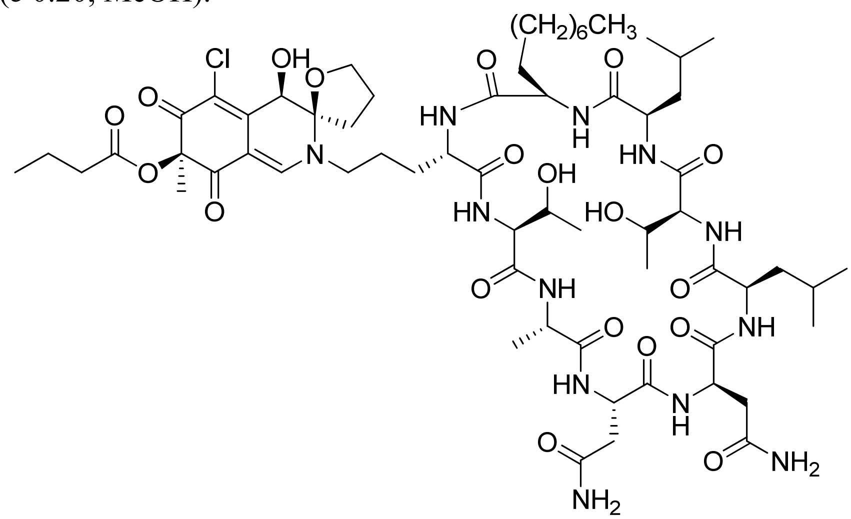
Cbz-L-Ala-L-Asn(Trt)-D-Asn(Trt)-D-Leu-L-Thr-D-Leu-D-ADA-OMe (59). A solution of **55** (356 mg, 0.347 mmol) in THF (4.4mL) was cooled to 0 °C, treated with a solution of LiOH·H_2O (146 mg, 3.47 mmol) in H_2O (4.4 mL) and stirred at 0 °C for 6 h. The reaction mixture was quenched with the addition of aqueous 2 N HCl (1.7 mL), acidified to pH 3 and extracted with EtOAc (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 7% MeOH−CH_2Cl_2) afforded the carboxylic acid as a white foam which was directly employed in the next reaction. Concurrently, Boc-D-Leu-L-Thr-D-Leu-D-ADA-OMe[6] (218 mg, 0.347 mmol) was treated with 4 N HCl−dioxane (1.0 mL). The reaction solution was stirred for 1 h, and the volatiles were removed with a stream of nitrogen. The residue was treated with Et_2O and concentrated under reduced pressure (2 × 2 mL) to afford the terminal amine as a sticky oil which was directly employed in the next reaction. A flask containing the carboxylic acid, the amine, HOAt (142 mg, 1.04 mmol), EDCI (200 mg, 1.04 mmol) and $NaHCO_3$ (88.0 mg, 1.04 mmol) was cooled to 0°C, treated with anhydrous DMF (2.3 mL) and stirred at 23 °C for 20 h. The reaction mixture was diluted with EtOAc (30 mL), washed with aqueous 1 N HCl (2 × 5 mL), saturated aqueous $NaHCO_3$ (2 × 5 mL), H_2O (5 mL), and saturated aqueous NaCl (10 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 9% MeOH–CH_2Cl_2) afforded **59** as a white solid (57%, 286 mg): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.62 (s, 1H), 8.60 (s, 1H), 8.38 (d, *J* = 7.3 Hz, 1H), 8.25 (d, *J* = 7.4 Hz, 1H), 8.22 (d, *J* = 7.1 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.37 (m, 5H), 7.33 (m, 1H), 7.15–7.28 (m, 30H), 5.11 (d, *J* = 12.5 Hz, 1H), 4.98 (d, *J* = 12.5 Hz, 1H), 4.75 (d, *J* = 5.4 Hz, 1H), 4.58 (m, 1H), 4.51 (m, 1H), 4.36 (m, 1H), 4.27 (dd, *J* = 14.1, 8.4 Hz, 1H), 4.13 (m, 3H), 3.93 (qd, *J* = 12.0, 6.2 Hz, 1H), 3.58 (s, 3H), 2.60–2.75 (m, 4H), 1.61 (m, 6H), 1.48 (m, 3H), 1.25 (m, 14H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.86 (m, 9H), 0.81 (m, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 172.9, 172.5, 172.3, 172.2, 171.4, 171.0, 170.0, 168.9, 168.8, 155.9, 144.82 (3C), 144.77 (3C), 136.9, 128.6 (12C), 128.4 (2C), 127.90, 127.88 (2C), 127.5(12C), 126.4 (6C), 69.50, 69.48, 66.6, 65.8, 59.8, 58.7, 52.2, 51.9, 51.7, 50.7, 50.4, 50.2, 40.9, 40.3, 38.5, 38.0, 36.3, 31.3, 30.7, 28.9, 28.7, 25.4, 24.2, 24.0, 23.2, 23.0, 22.2, 21.6, 21.5, 19.6, 18.3, 14.0; IR (film) ν_{max} 3307, 2926, 1661, 1518, 1448, 1242, 753, 700 cm^{-1}; HR ESI–TOF *m/z* 1446.7732 ($C_{84}H_{103}N_9O_{13}$ + H^+ requires 1446.7753); $[\alpha]^{23}_D$ –30 (*c* 0.20, MeOH).



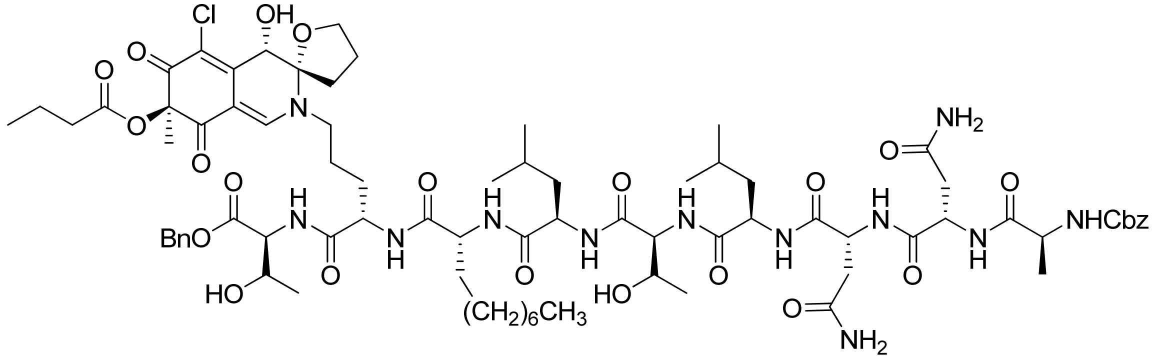
Cbz-L-Ala-L-Asn(Trt)-D-Asn(Trt)-D-Leu-L-Thr-D-Leu-D-ADA-OH (60). A solution of **59** (724 mg, 0.501 mmol) in THF (6.2 mL) was cooled to 0 °C, treated with a solution of LiOH·H_2O (210 mg, 5.01 mmol) in H_2O (6.2 mL) and stirred at 0 °C for 90 min before being quenched with addition of aqueous 2 N HCl (2.5 mL). The resulting mixture was acidified to pH 3 and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (SiO_2, 10% MeOH–CH_2Cl_2) afforded **60** as a white solid (85%, 464 mg): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.63 (s, 1H), 8.60 (s, 1H), 8.29 (d, *J* = 5.5 Hz, 1H), 7.94 (brs, 2H), 7.84 (s, 1H), 7.66 (brs, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 4.1 Hz, 5H), 7.33 (m, 1H), 7.15–7.28 (m, 30H), 5.12 (d, *J* = 12.5 Hz, 1H), 4.97 (d, *J* = 12.5 Hz, 1H), 4.61 (m, 1H), 4.50 (m, 1H), 4.30 (m, 1H), 4.24 (s, 1H), 4.11 (dd, *J* = 7.7, 4.4 Hz, 1H), 4.07 (m, 1H), 4.01 (s, 1H), 3.95 (m, 1H), 2.76 (m, 1H), 2.65 (m, 3H), 1.57 (m, 9H), 1.23 (m, 14H), 0.98 (d, *J* = 6.2 Hz, 3H), 0.86 (m, 9H), 0.80 (dd, *J* = 12.1, 6.3 Hz, 6H), the two OH protons were not observed; ^{13}C NMR (DMSO-d_6, 150 MHz) δ 173.8, 172.8, 172.2 (2C), 171.5, 171.1, 170.0, 169.0, 168.8, 160.0, 144.9 (3C), 144.8 (3C), 136.9, 128.6 (12C), 128.4 (2C), 127.9 (3C), 127.5(12C), 126.3 (6C), 69.5 (2C), 66.3, 65.7, 58.8, 52.9, 51.8, 51.2, 51.1, 50.6, 50.3, 40.7, 40.4, 38.6, 38.2, 31.4, 29.1, 29.0, 28.9, 28.8, 25.4, 24.3, 24.1, 23.2, 23.0, 22.2, 21.8, 21.4, 19.8, 18.3, 14.0; IR (film) ν_{max} 3326, 2927, 2855, 1655, 1524, 1496, 752, 699, 598 cm^{-1}; HR ESI-TOF *m/z* 1432.7575 ($C_{83}H_{101}N_9O_{13}$ + H^+ requires 1432.7597); $[\alpha]^{23}_D$ −20 (*c* 0.2, MeOH).



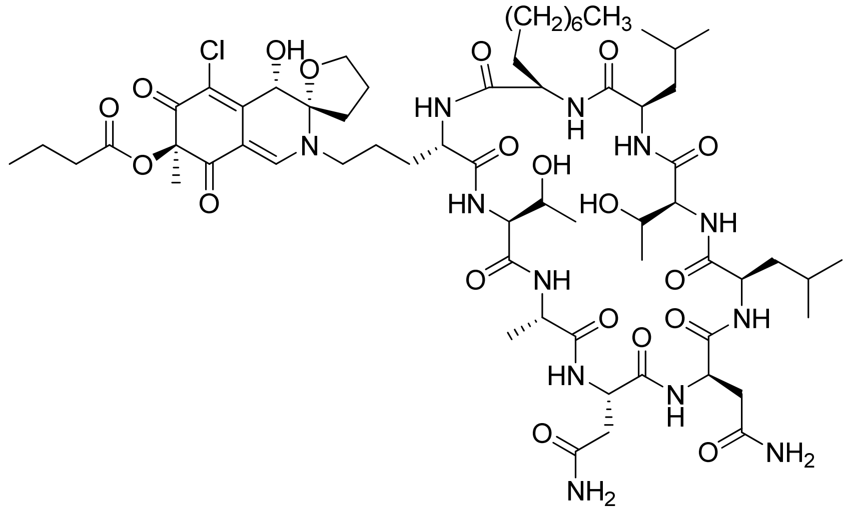
S1. A solution of **60** (42.1 mg, 0.0294 mmol) in trifluoroacetic acid (1.0 mL) and H_2O (50 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 2.0 mL) to provide crude **61** as a gray solid (27.5 mg), which was directly employed in the next step. A solution of **47A** (24.0 mg, 0.0267 mmol) in anhydrous CH_2Cl_2 (0.44 mL) and DMF (0.44 mL) was treated with piperidine (13 μL, 0.134 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine (17.0 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (27.5 mg), the free amine (17.0 mg), HOAt (14.6 mg, 0.107 mmol), EDCI (20.5 mg, 0.107 mmol), and $NaHCO_3$ (9.0 mg, 0.107 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.26 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (30 mL), washed with aqueous 1 N HCl (2 × 5.0 mL), saturated aqueous $NaHCO_3$ (2 × 5.0 mL), H_2O (5.0 mL) and saturated aqueous NaCl (10.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **S1** as a yellow solid (26.0 mg, 61%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.27 (d, *J* = 7.3 Hz, 1H), 8.14 (d, *J* = 7.5 Hz, 1H), 8.10 (d, *J* = 8.2 Hz, 1H), 7.95 (m, 3H), 7.85 (s, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.51 (s, 1H), 7.48 (d, *J* = 6.9 Hz, 1H), 7.43 (s, 1H), 7.30−7.41 (m, 10H), 7.03 (s, 1H), 6.98 (s, 1H), 6.09 (d, *J* = 5.6 Hz, 1H), 5.19 (d, *J* = 5.4 Hz, 1H), 5.14 (app q, *J* = 12.7 Hz, 2H), 5.08 (d, *J* = 12.5 Hz, 1H), 4.99 (d, *J* = 12.5 Hz, 1H), 4.90 (d, *J* = 6.0 Hz, 1H), 4.51 (m, 4H), 4.35 (dd, *J* = 8.3, 3.1 Hz, 1H), 4.31 (m, 1H), 4.18−4.26 (m, 4H), 4.09 (m, 2H), 4.01 (m, 2H), 3.49 (m, 1H), 3.40 (m, 1H), 2.63 (dd, *J* = 15.3, 5.6 Hz, 1H), 2.54 (m, 3H), 2.33 (t, *J* = 6.9 Hz, 2H), 1.98 (m, 3H), 1.80 (m, 2H), 1.46−1.73 (m, 12H), 1.41 (s, 3H), 1.23 (br m, 16H), 1.09 (d, *J* = 6.3 Hz, 3H), 1.03 (d, *J* = 6.2 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 9H), 0.81 (d, *J* = 6.2 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.0, 188.9, 172.8, 172.3, 172.13 (2C), 172.06, 171.7, 171.6, 171.3, 171.1, 170.8, 170.4, 170.4, 155.9, 149.6, 148.5, 136.9, 136.0, 128.4 (4C), 128.0, 127.9 (3C), 127.8 (2C), 113.4, 100.7, 97.8, 84.7, 70.4, 68.6, 66.8, 66.3, 66.0 (2C), 65.6, 59.2, 58.1, 53.0, 52.0, 51.2, 51.1, 50.1 (2C), 50.0, 48.8, 40.4, 40.1, 37.1, 36.3, 34.5, 32.0, 31.4, 29.03, 28.97, 28.8 (2C), 26.4, 25.5, 24.7, 24.1, 24.0, 23.6, 23.2, 23.1, 22.2, 21.40, 21.36, 20.2, 19.6, 18.1, 17.9, 14.0, 13.3; IR (film) ν_{max} 3273, 2922, 2849, 1734, 1632, 1555, 1467, 1238, 685 cm^{-1}; HR ESI-TOF *m/z* 1605.7834 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_D$ +58 (*c* 0.20, MeOH).



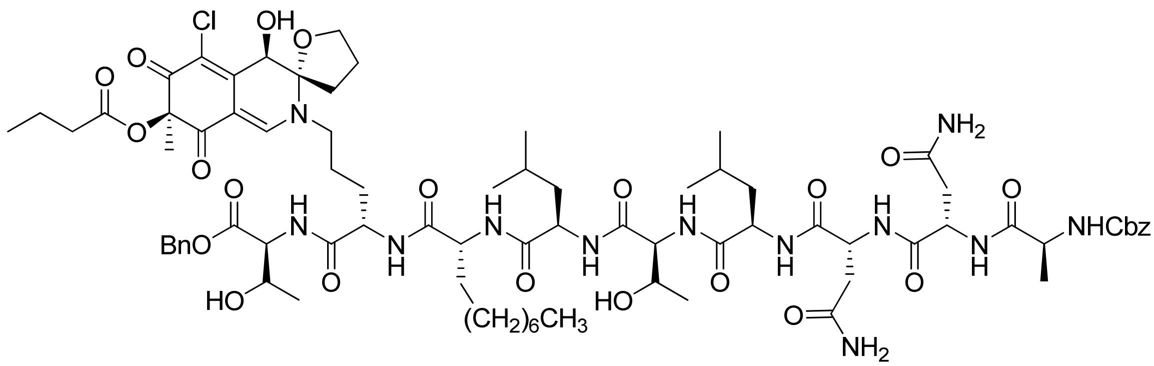
3. A solution of **S1** (26.0 mg, 0.0162 mmol) in anhydrous THF (5.4 mL) and DMF (2.7 mL) was treated with 10% Pd–C (39.0 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite, and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (22.0 mg, 0.162 mmol), EDCI (31.0 mg, 0.162 mmol), $NaHCO_3$ (13.6 mg, 0.162 mmol), cooled to 0 °C, treated with anhydrous DMF (5.4 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (60 mL), washed with aqueous 1 N HCl (2 × 10 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL), H_2O (10 mL) and saturated aqueous NaCl (20 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **3** as a yellow solid (13.6 mg, 62%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 9.09 (br s, 1H), 8.85 (br s, 1H), 8.72 (s, 1H), 7.88 (s, 1H), 7.82 (br s, 1H), 7.77 (d, *J* = 7.1 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.25 (s, 1H), 7.12 (s, 1H), 7.01 (s, 1H), 6.94 (s, 1H), 6.89 (s, 2H), 6.76 (br s, 1H), 5.98 (d, *J* = 2.8 Hz, 1H), 5.33 (d, *J* = 3.8 Hz, 1H), 5.01 (d, *J* = 4.9 Hz, 1H), 4.78 (m, 1H), 4.59 (m, 1H), 4.50 (d, *J* = 3.2 Hz, 1H), 4.48 (m, 1H), 4.38 (m, 1H), 4.23 (m, 1H), 4.10 (m, 1H), 3.88–4.04 (m, 6H), 3.63 (br s, 1H), 3.50 (m, 1H), 3.43 (m, 1H), 2.95 (br d, *J* = 13.0, 1H), 2.77 (dd, *J* = 15.3, 10.5 Hz, 1H), 2.58 (dd, *J* = 14.2, 11.5 Hz, 1H), 2.49 (m, HMQC, 1H), 2.34 (t, *J* = 7.0 Hz, 2H), 2.06 (m, 1H), 1.70–1.96 (m, 9H), 1.50–1.66 (m, 5H), 1.41 (s, 3H), 1.35–1.45 (m, 3H), 1.26 (br m, 14H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.10 (d, *J* = 5.9 Hz, 4H), 0.93 (d, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.2 Hz, 3H), 0.77 (d, *J* = 6.1 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.0, 188.9, 174.4, 173.22, 173.18, 173.1, 173.0, 172.6, 171.74, 171.70, 171.5, 171.3, 171.2, 170.4, 149.7, 148.3, 113.4, 100.6, 97.9, 84.7, 70.8, 69.0, 65.1, 64.9, 63.6 (HMQC), 62.4, 53.9, 52.6, 52.3, 51.6, 50.9, 49.7, 49.2, 49.1, 39.0 (HMQC), 38.9 (HMQC), 37.5, 36.2, 34.7, 34.5, 31.4, 29.9, 28.72, 28.68, 28.5, 28.3, 26.8, 26.1, 24.5, 24.4, 24.1, 23.6, 23.4, 23.2, 22.1, 20.7, 20.5, 20.4 (2C), 18.1, 16.5, 14.0, 13.3; IR (film) ν_{max} 3315, 2962, 2927, 2860, 1650, 1567, 1538, 1446, 1410, 1332, 1312, 1261, 1239, 1102, 1077, 1057 cm^{-1}; HR ESI-TOF *m/z* 1363.6896 ($C_{63}H_{99}ClN_{12}O_{19} + H^+$ requires 1363.6916); CD (MeOH, 0.20 mM) λ_{ext} nm ($\Delta\varepsilon$) 407 (9.0), 348 (−6.8), 302 (7.1), 240 (−11.1), 202 (20.8); $[\alpha]^{23}_{D}$ +270 (*c* 0.14, MeOH).



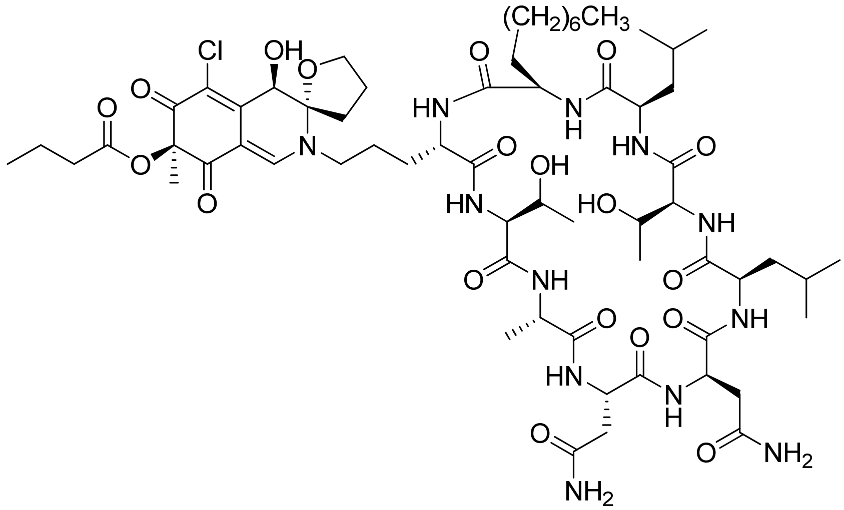
S2. A solution of **60** (74.0 mg, 0.0515 mmol) in trifluoroacetic acid (2.0 mL) and H_2O (100 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 3.0 mL) to provide crude **61** as a gray solid (52.1 mg), which was directly employed in the next step. A solution of **47B** (42.0 mg, 0.0468 mmol) in anhydrous CH_2Cl_2 (0.78 mL) and DMF (0.78 mL) was treated with piperidine (23 μL, 0.234 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine (28.3 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (52.1 mg), the free amine (28.3 mg), HOAt (26.0 mg, 0.192 mmol), EDCI (37.0 mg, 0.192 mmol), and $NaHCO_3$ (16.0 mg, 0.192 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.47 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (50 mL), washed with aqueous 1 N HCl (2 × 5.0 mL), saturated aqueous $NaHCO_3$ (2 × 5.0 mL), H_2O (5.0 mL) and saturated aqueous NaCl (10.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **S2** as a yellow solid (51.0 mg, 68%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.26 (d, *J* = 7.4 Hz, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 8.14 (d, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 7.2 Hz, 1H), 7.91 (t, *J* = 7.2 Hz, 2H), 7.80 (s, 1H), 7.79 (s, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.51 (s, 1H), 7.48 (d, *J* = 6.9 Hz, 1H), 7.43 (s, 1H), 7.31−7.40 (m, 10H), 7.03 (s, 1H), 6.98 (s, 1H), 6.06 (d, *J* = 4.9 Hz, 1H), 5.13 (dd, *J* = 12.7, 3.9 Hz, 2H), 5.08 (m, 2H), 4.99 (d, *J* = 12.5 Hz, 1H), 4.90 (d, *J* = 6.1 Hz, 1H), 4.53 (d, *J* = 5.0 Hz, 1H), 4.48 (m, 3H), 4.34 (dd, *J* = 8.3, 3.3 Hz, 1H), 4.30 (dd, *J* = 15.1, 8.1 Hz, 1H), 4.21 (m, 4H), 4.09 (m, 2H), 4.01 (m, 2H), 3.47 (m, 2H), 2.63 (dd, *J* = 15.7, 5.8 Hz, 1H), 2.54 (m, 3H), 2.32 (t, *J* = 7.0 Hz, 2H), 1.99 (m, 2H), 1.80 (m, 2H), 1.43−1.79 (m, 13H), 1.38 (s, 3H), 1.23 (m, 16H), 1.08 (d, *J* = 6.3 Hz, 3H), 1.03 (d, *J* = 6.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 9H), 0.81 (d, *J* = 6.3 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.8, 188.3, 172.8, 172.3, 172.2, 172.06, 172.05, 171.7, 171.6, 171.5, 171.1, 170.8, 170.43, 170.41, 155.9, 149.4, 148.6, 136.9, 136.0, 128.42 (2C), 128.41 (2C), 128.0, 127.9 (3C), 127.8 (2C), 113.6, 100.4, 97.7, 84.6, 70.5, 69.9, 68.7, 66.8, 66.3, 66.0 (2C), 65.6, 59.2, 58.1, 52.9, 52.0, 51.6, 51.2, 50.1, 50.0, 49.5, 40.4, 40.1, 37.1, 36.3, 35.6, 34.9, 34.6, 32.1, 31.4, 28.9, 28.81, 28.79, 26.7, 25.4, 24.6, 24.1, 24.0, 23.2, 23.1, 23.0, 22.2, 21.4, 20.2, 19.6, 18.0, 17.9, 14.1, 13.3; IR (film) ν_{max} 3287, 2910, 2849, 1735, 1628, 1465, 1352, 1235, 1174, 786 cm^{-1}; HR ESI-TOF *m/z* 1605.7870 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_{D}$ −14 (*c* 0.10, MeOH).



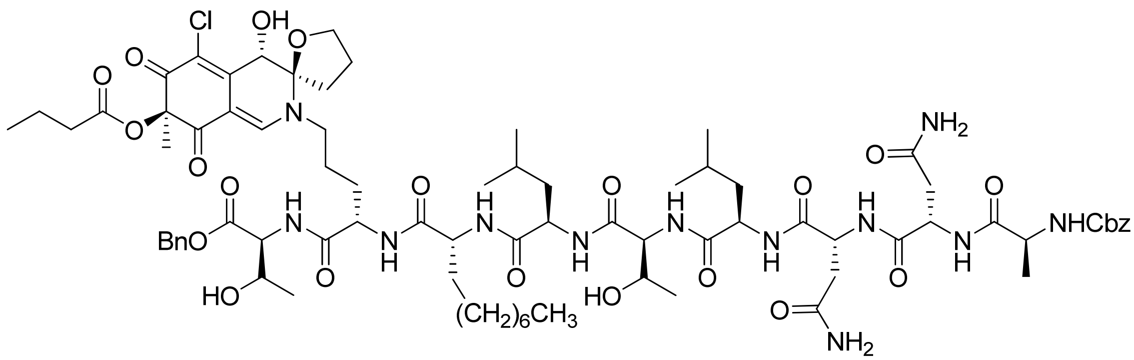
65. A solution of **S2** (45.0 mg, 0.0280 mmol) in anhydrous THF (9.0 mL) and DMF (4.5 mL) was treated with 10% Pd–C (67.5 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite, and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (38.0 mg, 0.280 mmol), EDCI (54.0 mg, 0.280 mmol), $NaHCO_3$ (24.0 mg, 0.280 mmol), cooled to 0 °C, treated with anhydrous DMF (9.3 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (120 mL), washed with aqueous 1 N HCl (2 × 20 mL), saturated aqueous $NaHCO_3$ (2 × 20 mL), H_2O (20 mL) and saturated aqueous NaCl (40 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **65** as a yellow solid (24.8 mg, 65%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 9.13 (br s, 1H), 8.72 (br s, 1H), 8.62 (s, 1H), 7.84 (br s, 1H), 7.81 (s, 1H), 7.72 (d, *J* = 6.2 Hz, 1H), 7.50 (d, *J* = 8.7 Hz, 1H), 7.25 (s, 1H), 7.08 (s, 1H), 7.01 (s, 1H), 6.93 (br s, 1H), 6.89 (s, 1H), 6.74 (br s, 1H), 6.67 (br s, 1H), 5.98 (d, *J* = 4.7 Hz, 1H), 5.30 (d, *J* = 4.5 Hz, 1H), 5.08 (d, *J* = 3.6 Hz, 1H), 4.74 (m, 1H), 4.56 (m, 1H), 4.54 (d, *J* = 4.8 Hz, 1H), 4.47 (m, 1H), 4.41 (m, 1H), 4.22 (dd, *J* = 13.6, 7.0 Hz, 1H), 3.90–4.06 (m, 7H), 3.65 (br s, 1H), 3.35 (m, HMQC, 2H), 2.93 (br d, *J* = 12.5 Hz, 1H), 2.75 (dd, *J* = 15.6, 10.3 Hz, 1H), 2.63 (dd, *J* = 15.4, 10.7 Hz, 1H), 2.49 (m, HMQC, 1H), 2.33 (t, *J* = 7.1 Hz, 2H), 1.93–2.07 (m, 2H), 1.73–1.89 (m, 6H), 1.50–1.70 (m, 8H), 1.41 (s, 3H), 1.38–1.45 (m, 2H), 1.26 (br m, 14H), 1.16 (d, *J* = 6.2 Hz, 4H), 1.10 (d, *J* = 5.4 Hz, 3H), 0.91 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.77 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.0, 173.3, 173.2, 172.8, 172.7, 172.5, 172.0, 171.7, 171.6, 171.5, 171.3, 170.9, 170.4, 149.4, 148.4, 113.7, 100.4, 97.7, 84.6, 70.6, 68.7, 65.1, 65.0, 63.5 (HMQC), 62.3, 54.0, 52.8, 52.1, 51.7, 50.9, 49.2 (2C), 49.0, 39.0 (HMQC), 38.9 (HMQC), 37.5, 36.2, 35.0, 34.6, 31.4, 30.0, 28.74, 28.69, 28.6, 28.3, 27.0, 26.0, 24.7, 24.2, 24.1, 23.4, 23.2, 23.0, 22.1, 20.7, 20.4 (2C), 20.2, 18.1, 16.4, 14.0, 13.3; IR (film) ν_{max} 3314, 2951, 2926, 2855, 1648, 1537, 1451, 1413, 1337, 1239, 1105, 1078, 1054 cm^{-1} HR ESI-TOF *m/z* 1363.6914 ($C_{63}H_{99}ClN_{12}O_{19}$ + H^+ requires 1363.6916); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 403 (1.4), 345 (−11.4), 255 (9.2), 222 (−8.5), 201 (22.8); $[\alpha]^{23}_{D}$ −94 (*c* 0.13, MeOH).



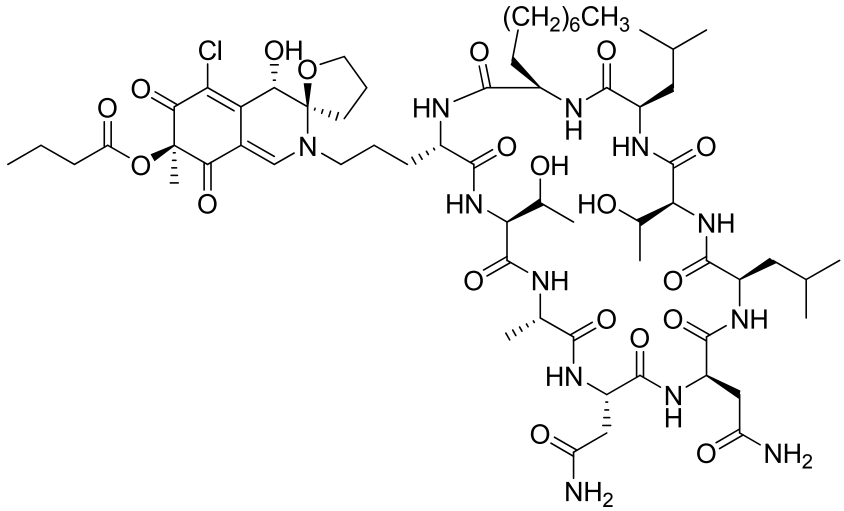
S3. A solution of **60** (21.6 mg, 0.0151 mmol) in trifluoroacetic acid (0.6 mL) and H_2O (30 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 1.0 mL) to provide crude **61** as a gray solid (15.0 mg), which was directly employed in the next step. A solution of **47C** (12.3 mg, 0.0137 mmol) in anhydrous CH_2Cl_2 (0.23 mL) and DMF (0.23 mL) was treated with piperidine (7 μL, 0.069 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine (8.2 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (15.0 mg), the free amine (8.2 mg), HOAt (7.5 mg, 0.055 mmol), EDCI (10.5 mg, 0.055 mmol), and $NaHCO_3$ (4.6 mg, 0.055 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.13 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (20 mL), washed with aqueous 1 N HCl (2 × 5.0 mL), saturated aqueous $NaHCO_3$ (2 × 5.0 mL), H_2O (5.0 mL) and saturated aqueous NaCl (5.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **S3** as a yellow solid (12.0 mg, 55%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.30 (d, *J* = 7.3 Hz, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 7.1 Hz, 1H), 7.95 (t, *J* = 9.0 Hz, 2H), 7.86 (d, *J* = 7. 5 Hz, 1H), 7.80 (s, 1H), 7.78 (m, 1H), 7.50 (m, 2H), 7.44 (s, 1H), 7.30–7.41 (m, 10H), 7.01 (s, 1H), 6.98 (s, 1H), 6.40 (d, *J* = 6.6 Hz, 1H), 5.14 (q, *J* = 12.7 Hz, 2H), 5.18 (m, 1H), 5.08 (d, *J* = 12.5 Hz, 1H), 5.05 (m, 1H), 4.99 (d, *J* = 12.5 Hz, 1H), 4.44–4.55 (m, 4H), 4.34 (dd, *J* = 8.2, 3.3 Hz, 1H), 4.29 (dd, *J* = 14.3, 8.5 Hz, 1H), 4.21 (m, 3H), 4.09 (m, 2H), 4.02 (m, 1H), 3.96 (dd, *J* = 14.0, 7.0 Hz, 1H), 3.78 (q, *J* = 7.4 Hz, 1H), 3.49 (m, 1H), 3.42 (m, 1H), 2.62 (m, 1H), 2.55 (m, 3H), 2.37 (m, 2H), 2.34 (t, *J* = 7.1 Hz, 2H), 2.01 (m, 2H), 1.72 (m, 1H), 1.44−1.67 (m, 12H), 1.37 (s, 3H), 1.23 (m, 16H), 1.08 (d, *J* = 6.3 Hz, 3H), 1.03 (d, *J* = 6.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.86 (m, 9H), 0.81 (d, *J* = 6.3 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.2, 188.7, 172.8, 172.3, 172.1 (2C), 172.0, 171.7, 171.6, 171.4, 171.1, 170.8, 170.6, 170.4, 155.9, 150.6, 148.2, 136.9, 136.0, 128.42 (2C), 128.41 (2C), 128.0, 127.9 (3C), 127.8 (2C), 115.1, 101.7, 96.9, 84.7, 69.9, 68.6, 68.4, 66.8, 66.2, 66.0, 65.6, 59.2, 58.1, 52.9, 52.0, 51.6, 51.3, 50.5, 50.1 (2C), 50.0, 40.4, 40.1, 37.1, 36.4, 34.5, 32.0, 31.4, 30.3, 29.1, 29.0, 28.8 (2C), 27.2, 25.4, 25.3, 24.1, 24.0, 23.4, 23.2, 23.1, 22.2, 21.4, 20.2, 19.6, 18.1, 18.0, 14.0, 13.3; IR (film) ν_{max} 3310, 2927, 2855, 1732, 1652, 1537, 1454, 1243, 1079, 698 cm^{-1}; HR ESI-TOF *m/z* 1605.7869 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_D$ +20 (*c* 0.30, MeOH).



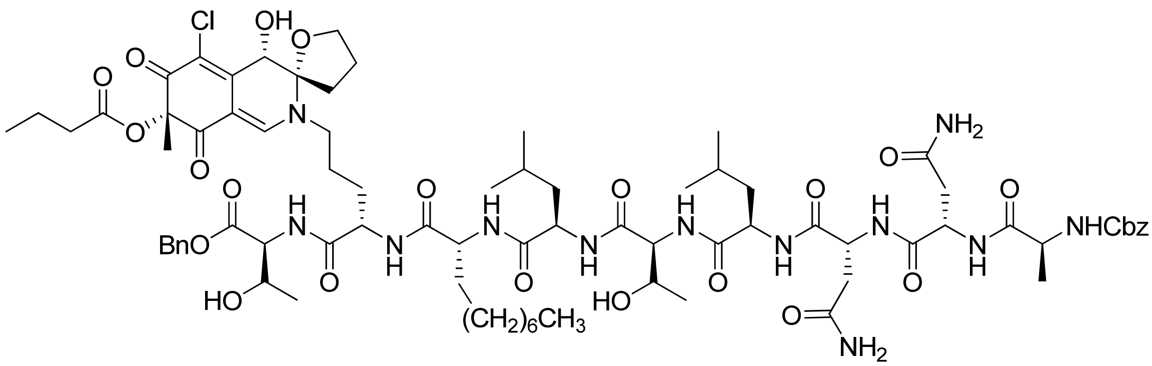
66. A solution of **S3** (12.4 mg, 0.0077 mmol) in anhydrous THF (2.5 mL) and DMF (1.3 mL) was treated with 10% Pd–C (18.6 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite, and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (10.5 mg, 0.077 mmol), EDCI (14.8 mg, 0.077 mmol), $NaHCO_3$ (6.5 mg, 0.077 mmol), cooled to 0 °C, treated with anhydrous DMF (2.6 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (30 mL), washed with aqueous 1 N HCl (2 × 5 mL), saturated aqueous $NaHCO_3$ (2 × 5 mL), H_2O (5 mL) and saturated aqueous NaCl (5 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **66** as a yellow solid (6.4 mg, 61%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 9.08 (br s, 1H), 8.88 (br s, 2H), 7.86 (br s, 1H), 7.78 (s, 1H), 7.71 (d, *J* = 6.2 Hz, 1H), 7.56 (d, *J* = 9.0 Hz, 1H), 7.26 (s, 1H), 7.22 (br s, 1H), 7.09 (s, 1H), 7.01 (s, 1H), 6.92 (br s, 1H), 6.84 (s, 1H), 6.67 (br s, 1H), 6.38 (d, *J* = 6.5 Hz, 1H), 5.38 (d, *J* = 4.3 Hz, 1H), 5.04 (d, *J* = 5.2 Hz, 1H), 4.75 (m, 1H), 4.56 (m, 1H), 4.48 (d, *J* = 6.3 Hz, 1H), 4.47 (m, 1H), 4.40 (m, 1H), 4.02 (m, 3H), 3.88–3.99 (m, 4H), 3.80 (dd, *J* = 15.3, 7.1 Hz, 1H), 3.69 (br s, 1H), 3.52 (m, 1H), 3.39 (m, 1H), 2.92 (br d, *J* = 14.8 Hz, 1H), 2.75 (m, 1H), 2.58 (m, 1H), 2.49 (m, HMQC, 1H), 2.40 (br m, 2H), 2.34 (t, *J* = 7.1 Hz, 2H), 2.03 (m, 2H), 1.65–1.85 (m, 6H), 1.50–1.62 (m, 6H), 1.38 (s, 3H), 1.37–1.43 (m, 2H), 1.26 (br m, 14H), 1.16 (d, *J* = 6.3 Hz, 4H), 1.09 (d, *J* = 5.9 Hz, 3H), 0.92 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H), 0.78 (app t, *J* = 5.7 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.1, 188.7, 174.1, 173.1, 173.0, 172.8, 172.6, 172.5, 172.0, 171.8, 171.5, 171.4, 171.1, 170.5, 150.6, 148.2, 115.1, 101.8, 96.9, 84.7, 68.6, 68.3, 65.2, 65.0, 63.2 (HMQC), 62.2, 54.0, 52.7, 52.1, 51.4, 50.84, 50.76, 49.3, 49.2, 39.0 (HMQC), 38.9 (HMQC), 37.4, 36.2, 34.5, 31.4, 30.3, 30.1, 28.73, 28.70, 28.6 (2C), 27.2, 26.0, 25.3, 24.2, 24.1, 23.5, 23.4, 23.3, 22.1, 20.7, 20.4, 20.3, 20.2, 18.1, 16.6, 14.0, 13.3; IR (film) ν_{max} 3309, 2923, 2852, 1646, 1536, 1452, 1411, 1367, 1238, 1179, 1078, 1030 cm^{-1}; HR ESI-TOF *m/z* 1363.6921 ($C_{63}H_{99}ClN_{12}O_{19}$ + H^+ requires 1363.6916); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 401 (3.6), 244 (–5.6), 281 (1.6), 227 (–7.1), 202 (16.9); $[\alpha]^{23}_D$ +48 (*c* 0.13, MeOH).



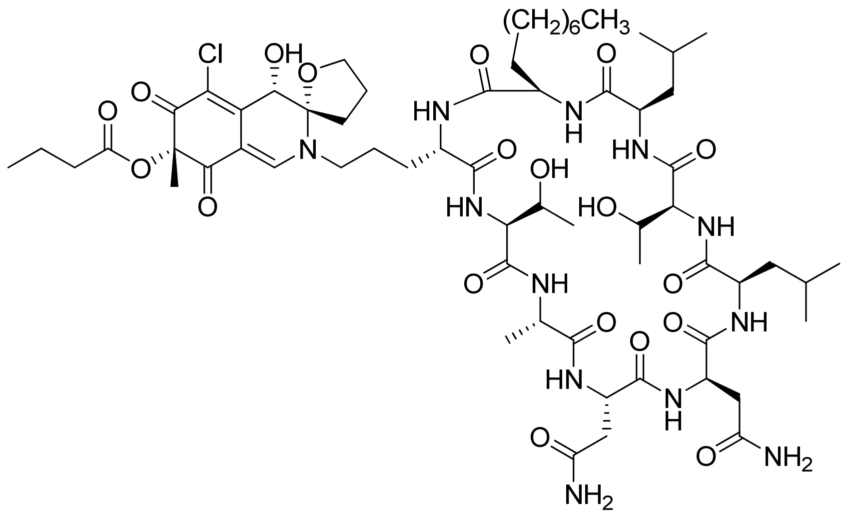
63. A solution of **60** (19.6 mg, 0.0137 mmol) in trifluoroacetic acid (1.1 mL) and H_2O (55 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 2.0 mL) to provide crude **61** as a gray solid (11.8 mg), which was directly employed in the next step. A solution of **47D** (10.2 mg, 0.0114 mmol) in anhydrous CH_2Cl_2 (0.19 mL) and DMF (0.19 mL) was treated with piperidine (5.6 μL, 0.057 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine **62** (7.3 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (11.8 mg), **62** (7.3 mg), HOAt (6.2 mg, 0.046 mmol), EDCI (8.7 mg, 0.046 mmol), and $NaHCO_3$ (3.8 mg, 0.046 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.11 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (10 mL), washed with aqueous 1 N HCl (2 × 2.0 mL), saturated aqueous $NaHCO_3$ (2 × 2.0 mL), H_2O (1.0 mL) and saturated aqueous NaCl (2.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **63** as a yellow solid (10.0 mg, 55%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.26 (d, J = 7.4 Hz, 1H), 8.19 (d, J = 8.2 Hz, 1H), 8.13 (d, J = 7.7 Hz, 1H), 7.97 (d, J = 7.5 Hz, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.79 (s, 2H), 7.64 (d, J = 7.6 Hz, 1H), 7.51 (s, 1H), 7.48 (d, J = 6.9 Hz, 1H), 7.43 (s, 1H), 7.31−7.40 (m, 10H), 7.03 (s, 1H), 6.98 (s, 1H), 6.24 (d, J = 5.4 Hz, 1H), 5.14 (app q, J = 12.7 Hz, 2H), 5.10 (d, J = 5.2 Hz, 1H), 5.02 (m, 2H), 4.90 (d, J = 6.1 Hz, 1H), 4.50 (m, 4H), 4.34 (dd, J = 8.2, 3.3 Hz, 1H), 4.31 (dd, J = 15.0, 7.9 Hz, 1H), 4.23 (m 3H), 4.09 (m, 2H), 4.01 (m, 1H), 3.95 (dd, J = 14.5, 6.7 Hz, 1H), 3.78 (q, J = 7.2 Hz, 1H), 3.44 (m, 2H), 2.63 (m, 1H), 2.55 (m, 3H), 2.35 (m, 2H), 2.34 (t, J = 7.1 Hz, 2H), 2.05 (m, 2H), 1.72 (m, 1H), 1.45−1.67 (m, 12H), 1.42 (s, 3H), 1.24 (m, 16H), 1.08 (d, J = 6.3 Hz, 3H), 1.03 (d, J = 6.2 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H), 0.87 (m, 9H), 0.81 (m, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.4, 172.8, 172.3, 172.15, 172.06 (2C), 171.7, 171.6, 171.5, 171.1, 170.8, 170.43, 170.40, 155.9, 150.3, 147.6, 136.9, 136.0, 128.42 (2C), 128.40 (2C), 128.1, 127.90 (3C), 127.85 (2C), 115.4, 101.4, 96.8, 84.7, 69.8, 68.5, 68.4, 66.8, 66.2, 66.0, 65.6, 59.1, 58.1, 52.9, 52.0, 51.4, 51.2, 50.5, 50.1 (2C), 50.0, 40.5, 40.3, 37.1, 36.3, 34.5, 32.1, 31.3, 30.2, 29.3, 29.0, 28.8 (2C), 27.1, 25.5, 25.3, 24.1, 24.0, 23.2, 23.1, 23.0, 22.2, 21.4, 20.2, 19.6, 18.0, 17.9, 14.0, 13.3; IR (film) ν_{max} 3271, 2923, 2853, 1735, 1624, 1558, 1455, 1367, 1247, 1081 cm^{-1}; HR ESI-TOF m/z 1605.7833 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_D$ +26 (c 0.12, MeOH).



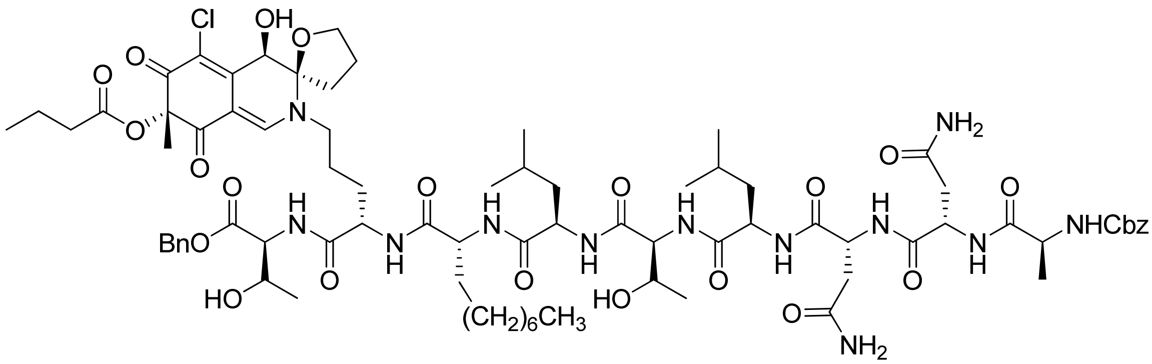
Chlorofusin (1). A solution of **63** (6.0 mg, 0.0037 mmol) in anhydrous THF (1.3 mL) and DMF (0.65 mL) was treated with 10% Pd–C (9.0 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (5.1 mg, 0.037 mmol), EDCI (7.2 mg, 0.037 mmol), $NaHCO_3$ (3.2 mg, 0.037 mmol), cooled to 0 °C, treated with anhydrous DMF (1.2 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (30 mL), washed with aqueous 1 N HCl (2 × 5 mL), saturated aqueous $NaHCO_3$ (2 × 5 mL), H_2O (5 mL) and saturated aqueous NaCl (10 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **1** as a yellow solid (3.0 mg, 60%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 9.09 (br s, 1H), 8.75 (br s, 1H), 8.62 (s, 1H), 7.84 (br s, 1H), 7.77 (s, 1H), 7.70 (d, J = 9.6 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.07 (s, 1H), 7.01 (s, 1H), 6.93 (br s, 1H), 6.91 (s, 1H), 6.82 (s, 1H), 6.69 (br s, 1H), 6.26 (d, J = 5.2 Hz, 1H), 5.29 (d, J = 4.2 Hz, 1H), 5.05 (d, J = 3.4 Hz, 1H), 4.75 (m, 1H), 4.59 (m, 1H), 4.53 (d, J = 5.1 Hz, 1H), 4.47 (m, 1H), 4.40 (m, 1H), 4.02 (m, 3H), 3.88–3.98 (m, 4H), 3.78 (dd, J = 7.7, 7.5 Hz, 1H), 3.66 (br s, 1H), 3.42 (br t, J = 7.8 Hz, 2H), 2.93 (br d, J = 13.6 Hz, 1H), 2.75 (dd, J = 14.4, 11.2 Hz, 1H), 2.63 (m, 1H), 2.49 (m, HMQC, 1H), 2.38 (br m, 2H), 2.34 (t, J = 7.0 Hz, 2H), 2.00–2.15 (m, 2H), 1.70–1.86 (m, 6H), 1.50–1.63 (m, 6H), 1.43 (s, 3H), 1.37–1.41 (m, 2H), 1.26 (br m, 14H), 1.16 (d, J = 6.1 Hz, 4H), 1.10 (d, J = 5.3 Hz, 3H), 0.92 (t, J = 7.3, 3H), 0.92 (d, J = 5.7, 3H), 0.87 (t, J = 7.2, 3H), 0.82 (d, J = 6.5 Hz, 3H), 0.78 (m, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.3, 174.2, 173.2, 173.1, 172.64, 172.61, 172.5, 172.0, 171.8, 171.5 (2C), 171.0, 170.4, 150.2, 147.7, 115.3, 101.4, 96.8, 84.8, 68.6, 68.5, 65.1, 65.0, 63.4 (HMQC), 62.3, 54.1, 52.8, 52.1, 51.2, 50.9, 50.6, 49.2, 49.1, 39.0 (HMQC), 38.9 (HMQC), 37.4, 36.2, 34.5, 31.4, 30.5, 30.0, 28.72, 28.70, 28.6, 28.4 (HMQC), 27.1, 26.0, 25.2, 24.2, 24.1, 23.4, 23.3, 23.0, 22.1, 20.7, 20.4, 20.3, 20.2, 18.1, 16.6, 14.0, 13.3; IR (film) ν_{max} 3320, 2926, 2855, 1655, 1536, 1205, 1184, 1138 cm^{-1}; HR ESI-TOF m/z 1363.6921 ($C_{63}H_{99}ClN_{12}O_{19}$ + H^+ requires 1363.6916); CD (MeOH, 0.13 mM) λ_{ext} nm (Δε) 397 (4.1), 345 (–7.7), 295 (3.3), 254 (2.4), 223 (–5.1), 201 (17.1); $[\alpha]^{23}_D$ +28 (c 0.05, MeOH).



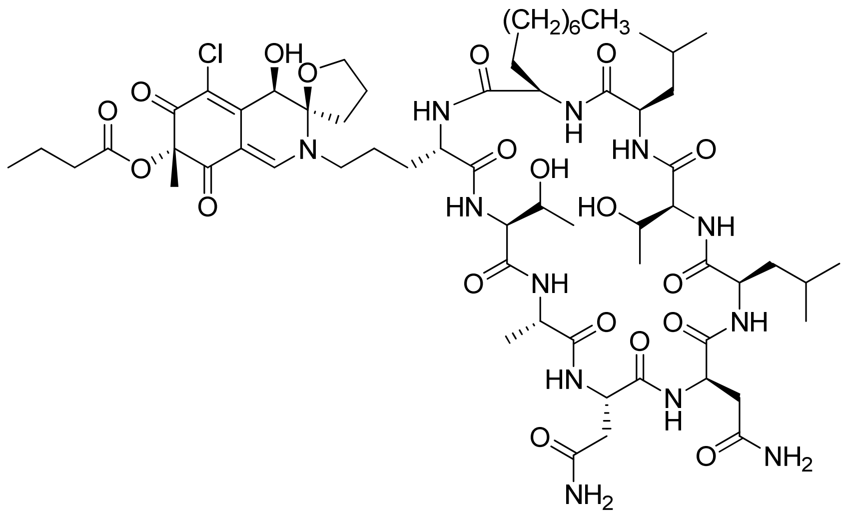
S4. A solution of **60** (63.0 mg, 0.043 mmol) in trifluoroacetic acid (1.8 mL) and H_2O (90 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 1.0 mL) to provide crude **61** as a gray solid (43.7 mg), which was directly employed in the next step. A solution of **48A** (32.0 mg, 0.036 mmol) in anhydrous CH_2Cl_2 (0.60 mL) and DMF (0.60 mL) was treated with piperidine (19 μL, 0.18 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine (21.3 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (43.7 mg), the free amine (21.3 mg), HOAt (19.4 mg, 0.14 mmol), EDCI (27.3 mg, 0.14 mmol), and $NaHCO_3$ (12.0 mg, 0.14 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.36 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (20 mL), washed with aqueous 1 N HCl (2 × 5.0 mL), saturated aqueous $NaHCO_3$ (2 × 5.0 mL), H_2O (15.0 mL) and saturated aqueous NaCl (5.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **S4** as a yellow solid (34.5 mg, 61%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.26 (d, J = 7.5 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.91 (m, 2H), 7.85 (s, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.51 (s, 1H), 7.48 (d, J = 6.9 Hz, 1H), 7.43 (s, 1H), 7.31–7.41 (m, 10H), 7.03 (s, 1H), 6.98 (s, 1H), 6.05 (d, J = 5.8 Hz, 1H), 5.14 (m, 2H), 5.07 (m, 2H), 4.99 (d, J = 12.4 Hz, 1H), 4.90 (d, J = 6.1 Hz, 1H), 4.44–4.53 (m, 4H), 4.35 (dd, J = 8.2, 3.4 Hz, 1H), 4.30 (m, 1H), 4.21 (br m, 4H), 4.09 (m, 2H), 4.01 (m, 2H), 3.48 (m, 1H), 3.41 (m, 1H), 2.63 (m, 1H), 2.54 (m, 3H), 2.33 (t, J = 7.1 Hz, 2H), 1.98 (m, 3H), 1.82 (m, 1H), 1.46–1.76 (m, 13H), 1.41 (s, 3H), 1.23 (m, 16H), 1.08 (d, J = 6.3 Hz, 3H), 1.03 (d, J = 6.2 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H), 0.86 (m, 9H), 0.81 (d, J = 6.3 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.0, 188.9, 172.8, 172.3, 172.14, 172.06 (2C), 171.7, 171.5, 171.3, 171.1, 170.8, 170.44, 170.40, 155.9, 149.8, 148.6, 136.9, 136.0, 128.4 (4C), 128.0, 127.9 (3C), 127.8 (2C), 113.4, 100.6, 97.7, 84.7, 70.3, 69.9, 68.6, 66.8, 66.3, 66.0 (2C), 65.6, 59.2, 58.1, 52.9, 52.0, 51.7, 51.2, 50.1, 50.0, 49.3, 40.4, 40.1, 37.1, 36.3, 35.8, 34.5 (2C), 32.0, 31.4, 29.0, 28.8 (2C), 26.6, 25.5, 24.6, 24.1, 24.0, 23.6, 23.2, 23.1, 22.2, 21.4, 20.2, 19.6, 18.0, 17.9, 14.0, 13.3; IR (film) ν_{max} 3275, 2926, 2855, 1662, 1622, 1566, 1450, 1379, 1243, 1198, 1077 cm^{-1}; HR ESI-TOF m/z 1605.7820 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_D$ −55 (c 0.10, MeOH).



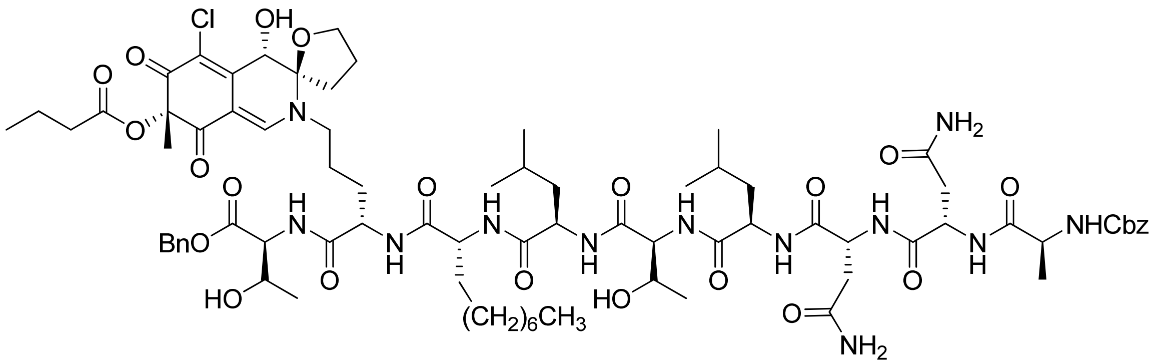
2. A solution of **S4** (34.5 mg, 0.022 mmol) in anhydrous THF (7.0 mL) and DMF (3.5 mL) was treated with 10% Pd–C (52.0 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite, and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (29.9 mg, 0.22 mmol), EDCI (42.1 mg, 0.22 mmol), $NaHCO_3$ (18.5 mg, 0.22 mmol), cooled to 0 °C, treated with anhydrous DMF (7.0 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (70 mL), washed with aqueous 1 N HCl (2 × 15 mL), saturated aqueous $NaHCO_3$ (2 × 15 mL), H_2O (10 mL) and saturated aqueous NaCl (15 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **2** as a yellow solid (16.8 mg, 58%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 9.16 (br s, 1H), 8.73 (br s, 1H), 8.51 (d, *J* = 3.4 Hz, 1H), 7.88 (s, 1H), 7.84 (br s, 1H), 7.73 (d, *J* = 7.1 Hz, 1H), 7.48 (d, *J* = 9.0 Hz, 1H), 7.24 (s, 1H), 7.07 (s, 1H), 7.01 (s, 1H), 6.90 (s, 1H), 6.87 (br s, 1H), 6.73 (br s, 1H), 6.65 (br s, 1H), 5.92 (d, *J* = 5.8 Hz, 1H), 5.32 (d, *J* = 4.7 Hz, 1H), 5.09 (d, *J* = 3.3 Hz, 1H), 4.75 (m, 1H), 4.61 (m, 1H), 4.48 (d, *J* = 5.8 Hz, 2H), 4.41 (m, 1H), 4.24 (dd, *J* = 12.6, 7.5 Hz, 1H), 4.07 (dd, *J* = 14.8, 8.2 Hz, 1H), 3.89–4.02 (m, 6H), 3.63 (br s, 1H), 3.45 (m, 1H), 3.35 (m, 1H, HMQC), 2.95 (br d, *J* = 13.3 Hz, 1H), 2.76 (dd, *J* = 15.5, 10.3 Hz, 1H), 2.66 (dd, *J* = 15.9, 11.2 Hz, 1H), 2.50 (m, 1H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.72–2.06 (m, 8H), 1.49–1.72 (m, 8H), 1.41 (s, 3H), 1.35–1.45 (m, 2H), 1.26 (br m, 14H), 1.16 (d, *J* = 6.3 Hz, 4H), 1.10 (d, *J* = 5.4 Hz, 3H), 0.92 (m, 6H), 0.87 (t, *J* = 7.0 Hz, 3H), 0.81 (d, *J* = 6.5 Hz, 3H), 0.77 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.0, 188.7, 174.3, 174.0, 173.2, 173.1, 172.9, 172.7, 172.4, 172.0, 171.6, 171.4, 170.8, 170.4, 149.9, 148.2, 113.4, 100.7, 97.6, 84.8, 70.5, 68.7, 65.1, 64.9, 63.5 (HMQC), 62.3, 53.9, 52.8, 52.2, 51.7, 50.9, 49.0, 48.9 (HMQC), 48.6, 39.0 (HMQC), 38.9 (HMQC), 36.9 (HMQC), 36.2, 34.7, 34.5, 31.4, 30.0, 28.8, 28.7, 28.5, 28.1, 27.1, 26.1, 24.7, 24.2, 24.0, 23.7, 23.4, 23.2, 22.1, 20.7, 20.42, 20.38, 20.3, 18.1, 16.3, 14.0, 13.3; IR (film) ν_{max} 3319, 2935, 1720, 1655, 1572, 1473, 1241, 1162, 1133, 1014, 807, 613 cm^{-1}; HR ESI-TOF *m/z* 1363.6889 ($C_{63}H_{99}ClN_{12}O_{19}$ + H^+ requires 1363.6916); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 409 (–4.9), 348 (3.6), 306(–3.9), 247 (5.8), 220 (–1.6), 201 (18.7); $[\alpha]^{23}_D$ –40 (*c* 0.07, MeOH).



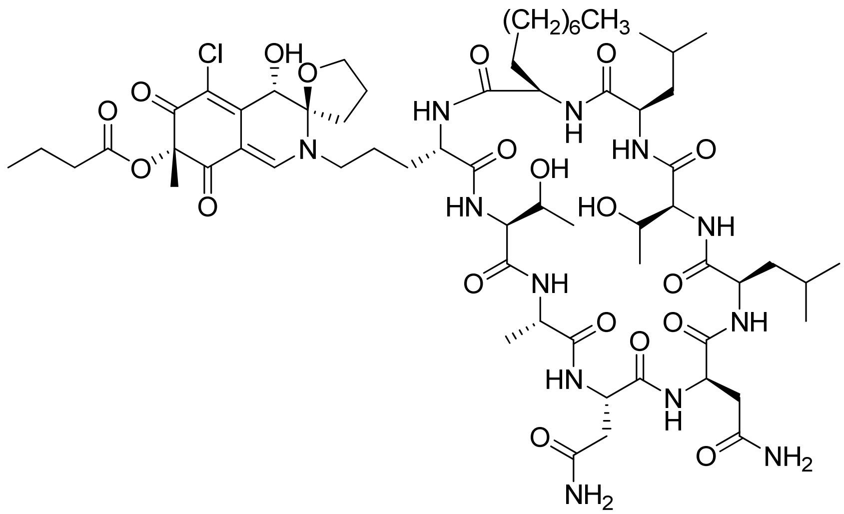
S5. A solution of **60** (38.6 mg, 0.027 mmol) in trifluoroacetic acid (1.0 mL) and H_2O (50 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 1.0 mL) to provide crude **61** as a gray solid (26.8 mg), which was directly employed in the next step. A solution of **48B** (22.0 mg, 0.025 mmol) in anhydrous CH_2Cl_2 (0.49 mL) and DMF (0.49 mL) was treated with piperidine (12 μL, 0.12 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine (14.6 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (26.8 mg), the free amine (14.6 mg), HOAt (14.3 mg, 0.098 mmol), EDCI (18.8 mg, 0.098 mmol), and $NaHCO_3$ (8.2 mg, 0.098 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.24 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (20 mL), washed with aqueous 1 N HCl (2 × 5.0 mL), saturated aqueous $NaHCO_3$ (2 × 5.0 mL), H_2O (5.0 mL) and saturated aqueous NaCl (5.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **S5** as a yellow solid (24.7 mg, 63%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.26 (d, J = 7.2 Hz, 1H), 8.14 (d, J = 7.5 Hz, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.96 (m, 3H), 7.79 (br m, 1H), 7.78 (s, 1H), 7.63 (d, J = 7.7 Hz, 1H), 7.51 (br s, 1H), 7.48 (d, J = 6.8 Hz, 1H), 7.43 (br s, 1H), 7.31–7.39 (m, 10H), 7.03 (s, 1H), 6.98 (s, 1H), 6.08 (d, J = 4.8 Hz, 1H), 5.14 (m, 3H), 5.08 (d, J = 12.5 Hz, 1H), 4.99 (d, J = 12.5 Hz, 1H), 4.89 (d, J = 6.1 Hz, 1H), 4.55 (d, J = 4.8 Hz, 1H), 4.50 (m, 3H), 4.35 (dd, J = 8.3, 3.2 Hz, 1H), 4.32 (br m, 1H), 4.22 (m, 4H), 4.09 (m, 2H), 4.01 (m, 2H), 3.49 (m, 1H), 3.38 (m, 1H), 2.63 (dd, J = 15.7, 6.0 Hz, 1H), 2.55 (m, 3H), 2.33 (t, J = 7.1 Hz, 2H), 1.98 (m, 2H), 1.68–1.87 (m, 3H), 1.44–1.66 (m, 12H), 1.39 (s, 3H), 1.23 (m, 16H), 1.08 (d, J = 6.4 Hz, 3H), 1.03 (d, J = 6.3 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H), 0.86 (m, 9H), 0.81 (d, J = 6.3 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.8, 188.3, 172.8, 172.3, 172.11 (2C), 172.07, 171.9, 171.7, 171.6, 171.6, 171.1, 170.8, 170.4, 155.9, 149.3, 148.5, 136.9, 136.0, 128.4 (4C), 128.0, 127.9 (3C), 127.8 (2C), 113.7, 100.4, 97.8, 84.6, 70.6, 69.9, 68.7, 66.8, 66.3, 66.0 (2C), 65.6, 59.2, 58.0, 53.0, 52.0, 51.8, 51.2, 51.1, 50.1, 50.0, 49.0, 40.5, 37.1, 36.3, 35.0, 34.6, 32.0, 31.3, 30.4, 29.0, 28.81, 28.79, 26.5, 25.5, 24.6, 24.1, 24.0, 23.2, 23.1, 23.0, 22.2, 21.4, 20.2, 19.6, 18.0, 17.9, 14.0, 13.3; IR (film) ν_{max} 3270, 2917, 1659, 1627, 1551, 1533, 1454, 1448, 1381, 1109, 1073 cm^{-1}; HR ESI-TOF m/z 1605.7834 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_{D}$ +40 (c 0.20, MeOH).



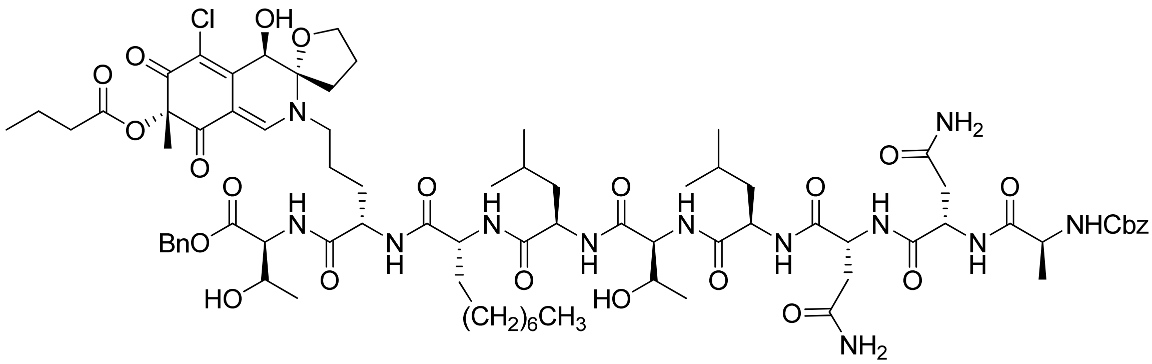
67. A solution of **S5** (10.5 mg, 0.0065 mmol) in anhydrous THF (2.2 mL) and DMF (1.1 mL) was treated with 10% Pd–C (15.8 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite, and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (8.9 mg, 0.065 mmol), EDCI (12.5 mg, 0.065 mmol), $NaHCO_3$ (5.5 mg, 0.065 mmol), cooled to 0 °C, treated with anhydrous DMF (2.2 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (25 mL), washed with aqueous 1 N HCl (2 × 5 mL), saturated aqueous $NaHCO_3$ (2 × 5 mL), H_2O (5 mL) and saturated aqueous NaCl (5 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **67** as a yellow solid (5.3 mg, 60%): ^1H NMR (DMSO-d_6, 600 MHz) δ 9.08 (br s, 1H), 8.77 (br s, 1H), 8.65 (s, 1H), 7.84 (br s, 1H), 7.83 (s, 1H), 7.78 (d, J = 6.2 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.25 (s, 1H), 7.12 (s, 1H), 7.01 (s, 1H), 6.96 (br s, 1H), 6.92 (br s, 1H), 6.90 (s, 1H), 6.76 (br s, 1H), 6.02 (s, 1H), 5.32 (s, 1H), 5.01 (d, J = 5.1 Hz, 1H), 4.78 (m, 1H), 4.60 (m, 1H), 4.56 (s, 1H), 4.48 (m, 1H), 4.38 (m, 1H), 4.24 (dd, J = 12.8, 7.4 Hz, 1H), 4.10 (m, 1H), 3.85–4.07 (m, 6H), 3.64 (br s, 1H), 3.50 (m, 1H), 3.42 (m, 1H), 2.94 (br d, J = 13.3 Hz, 1H), 2.77 (dd, J = 10.5, 15.7 Hz, 1H), 2.57 (dd, J = 11.3, 15.0 Hz, 1H), 2.50 (m, 1H), 2.34 (t, J = 7.1 Hz, 2H), 2.06 (m, 1H), 1.96 (m, 1H), 1.72–1.89 (m, 8H), 1.48–1.67 (m, 5H), 1.39 (s, 3H), 1.35–1.44 (m, 3H), 1.26 (br m, 14H), 1.16 (d, J = 9.3 Hz, 4H), 1.10 (d, J = 6.1 Hz, 3H), 0.92 (m, 6H), 0.87 (t, J = 7.0 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H), 0.78 (m, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.8, 188.2, 174.3, 173.2 (2C), 173.0, 172.6, 171.8, 171.7, 171.6, 171.5, 171.3, 171.2, 170.4, 149.5, 148.4, 113.6, 100.4, 97.8, 84.7, 71.0, 69.1, 65.1, 64.9, 63.5 (HMQC), 62.4, 54.0, 52.6, 52.2, 51.5, 50.9, 49.8, 49.19, 49.16, 39.4 (HMQC), 39.2 (HMQC), 37.4, 36.2, 35.2, 34.6, 31.4, 29.9, 28.72, 28.69, 28.5, 28.3, 27.0, 26.1, 24.5, 24.4, 24.1, 23.4, 23.2, 23.0, 22.1, 20.7, 20.5, 20.3 (2C), 18.0, 16.5, 14.0, 13.3; IR (film) ν_{max} 3316, 2928, 1656, 1561, 1535, 1238, 1078 cm^{-1}; HR ESI-TOF *m/z* 1363.6905 ($C_{63}H_{99}ClN_{12}O_{19} + H^+$ requires 1363.6916); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 403 (–0.2), 345 (9.0), 257 (–6.4), 202 (12.4); $[\alpha]^{23}_D$ +110 (*c* 0.12, MeOH).



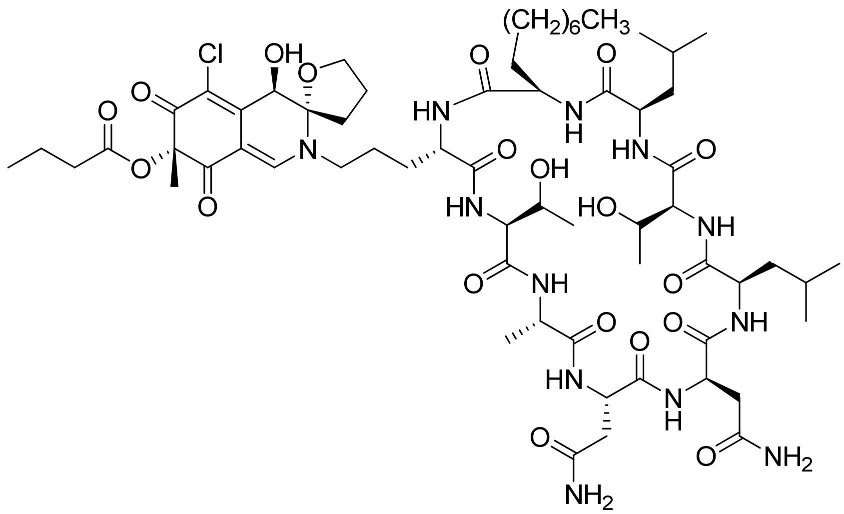
S6. A solution of **60** (37.5 mg, 0.027 mmol) in trifluoroacetic acid (1.0 mL) and H_2O (50 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 1.0 mL) to provide crude **61** as a gray solid (26.0 mg), which was directly employed in the next step. A solution of **48C** (19.6 mg, 0.022 mmol) in anhydrous CH_2Cl_2 (0.35 mL) and DMF (0.35 mL) was treated with piperidine (11 μL, 0.11 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine (13.0 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (26.0 mg), the free amine (13.0 mg), HOAt (11.9 mg, 0.087 mmol), EDCI (16.7 mg, 0.087 mmol), and $NaHCO_3$ (7.3 mg, 0.087 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.20 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (20 mL), washed with aqueous 1 N HCl (2 × 5.0 mL), saturated aqueous $NaHCO_3$ (2 × 5.0 mL), H_2O (5.0 mL) and saturated aqueous NaCl (5.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **S6** as a yellow solid (19.9 mg, 57%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.26 (d, J = 7.4 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.96 (t, J = 8.2 Hz, 2H), 7.90 (d, J = 7.8 Hz, 1H), 7.79 (s, 1H), 7.78 (br s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.51 (br s, 1H), 7.48 (d, J = 6.8 Hz, 1H), 7.43 (br s, 1H), 7.31−7.41 (m, 10H), 7.03 (s, 1H), 6.98 (s, 1H), 6.36 (d, J = 7.0 Hz, 1H), 5.14 (q, J = 12.7 Hz, 2H), 5.08 (m, 2H), 4.99 (d, J = 12.5 Hz, 1H), 4.90 (d, J = 6.1 Hz, 1H), 4.50 (m, 4H), 4.34 (dd, J = 8.2, 3.4 Hz, 1H), 4.31 (m, 1H), 4.22 (m, 3H), 4.09 (m, 2H), 4.01 (m, 1H), 3.96 (dd, J = 14.7, 6.5 Hz, 1H), 3.79 (dd, J = 15.0, 7.2 Hz, 1H), 3.46 (m, 2H), 2.63 (m, 1H), 2.55 (m, 3H), 2.34 (t, J = 6.7 Hz, 2H), 2.29–2.38 (m, 2H), 2.04 (m, 2H), 1.43−1.77 (m, 13H), 1.37 (s, 3H), 1.24 (br m, 16H), 1.08 (d, J = 6.3 Hz, 3H), 1.02 (d, J = 6.3 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 6.9 Hz, 9H), 0.81 (d, J = 6.3 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.3, 188.7, 172.8, 172.3, 172.2, 172.1 (2C), 171.7, 171.5, 171.4, 171.1, 170.8, 170.4, 170.4, 155.9, 150.7, 148.2, 136.9, 136.0, 128.4 (4C), 128.0, 127.9 (3C), 127.8 (2C), 115.2, 101.7, 96.9, 84.7, 69.8, 68.6, 68.4, 66. 8, 66.2, 66.0, 65.6, 59.2, 58.1, 52.9, 52.0, 51.5, 51.2, 50.5, 50.1 (2C), 50.0, 40.5, 40.1, 37.1, 36.3, 34.5, 32.1, 31.3, 30.2, 29.1, 29.0, 28.8 (2C), 27.1, 25.5, 25.3, 24.1, 24.0, 23.4, 23.2, 23.1, 22.2, 21.4, 20.2, 19.6, 18.0, 17.9, 14.0, 13.3; IR (film) ν_{max} 3278, 2923, 1736, 1660, 1537, 1454, 1249, 1175, 767 cm^{-1}; HR ESI-TOF m/z 1605.7794 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_D$ +40 (c 0.10, MeOH).



68. A solution of **S6** (30.0 mg, 0.019 mmol) in anhydrous THF (6.2 mL) and DMF (3.1 mL) was treated with 10% Pd–C (45.0 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite, and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (25.5 mg, 0.19 mmol), EDCI (35.8 mg, 0.19 mmol), $NaHCO_3$ (15.7 mg, 0.19 mmol), cooled to 0 °C, treated with anhydrous DMF (6.2 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (70 mL), washed with aqueous 1 N HCl (2 × 15 mL), saturated aqueous $NaHCO_3$ (2 × 15 mL), H_2O (15 mL) and saturated aqueous NaCl (15 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **68** as a yellow solid (14.2 mg, 56%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 9.08 (br s, 1H), 8.71 (br s, 1H), 8.59 (s, 1H), 7.84 (br s, 1H), 7.77 (s, 1H), 7.71 (d, *J* = 5.4 Hz, 1H), 7.52 (d, *J* = 8.6 Hz, 1H), 7.25 (s, 1H), 7.08 (s, 1H), 7.01 (s, 1H), 6.93 (s, 1H), 6.90 (br s, 1H), 6.88 (br s, 1H), 6.75 (br s, 1H), 6.37 (d, *J* = 6.8 Hz, 1H), 5.34 (d, *J* = 4.6 Hz, 1H), 5.03 (d, *J* = 4.7 Hz, 1H), 4.76 (m, 1H), 4.58 (m, 1H), 4.49 (d, *J* = 6.8 Hz, 1H), 4.47 (m, 1H), 4.40 (m, 1H), 4.08 (dd, *J* = 12.6, 7.5 Hz, 1H), 4.02 (m, 2H), 3.88–3.98 (m, 4H), 3.78 (dd, *J* = 15.2, 7.4 Hz, 1H), 3.66 (br s, 1H), 3.41 (m, 1H), 3.37 (m, 1H), 2.93 (br d, *J* = 13.5 Hz, 1H), 2.75 (dd, *J* = 15.6, 10.3 Hz, 1H), 2.61 (dd, *J* = 15.0, 11.3 Hz, 1H), 2.50 (m, 1H), 2.37 (br m, 2H), 2.35 (t, *J* = 7.1 Hz, 2H), 2.05 (br m, 2H), 1.65–1.87 (m, 6H), 1.45–1.65 (m, 6H), 1.39 (s, 3H), 1.36–1.45 (m, 2H), 1.26 (br m, 14H), 1.16 (d, *J* = 6.2 Hz, 4H), 1.09 (d, *J* = 5.7 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 6.6 Hz, 3H), 0.78 (m, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 189.2, 188.7, 174.2, 173.2, 173.1, 172.9, 172.6, 172.5, 172.0, 171.8, 171.5, 171.4, 171.1, 170.4, 150.4, 148.2, 115.1, 101.8, 96.9, 84.7, 68.7, 68.6, 65.1, 65.0, 63.2 (HMQC), 62.3, 54.0, 52.7, 52.2, 51.4, 50.9, 50.3, 49.2 (2C), 39.1, 39.0, 37.5, 36.2, 34.5, 31.4, 30.7, 30.0, 28.73, 28.70, 28.60, 28.57, 27.3, 26.1, 25.3, 24.2, 24.1, 23.5, 23.4, 23.3, 22.1, 20.7, 20.4, 20.30, 20.27, 18.1, 16.6, 14.0, 13.3; IR (film) ν_{max} 3314, 2956, 2928, 1648, 1537, 1240, 1079 cm^{-1}; HR ESI-TOF *m/z* 1363.6883 ($C_{63}H_{99}ClN_{12}O_{19}$ + H^+ requires 1363.6916); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 404 (–2.9), 343 (6.0), 275 (–1.7), 239 (2.4), 221 (–1.0), 202 (16.5); $[\alpha]^{23}_D$ –18 (*c* 0.2, MeOH).



S7. A solution of **60** (55.5 mg, 0.039 mmol) in trifluoroacetic acid (1.6 mL) and H_2O (80 μL) was stirred at 23 °C for 70 min. The volatiles were removed with a stream of nitrogen, and the residue was triturated with hexanes (3 × 2.0 mL) to provide crude **61** as a gray solid (38.0 mg), which was directly employed in the next step. A solution of **48D** (29.0 mg, 0.032 mmol) in anhydrous CH_2Cl_2 (0.54 mL) and DMF (0.54 mL) was treated with piperidine (16 μL, 0.16 mmol) and stirred at 23 °C for 40 min. The reaction mixture was concentrated with a stream of nitrogen and the residue was purified by flash chromatography (SiO_2, 10% MeOH−CH_2Cl_2) to afford the free amine (19.0 mg) as a yellow−orange solid which was directly used in next step. A flask containing **61** (38.0 mg), the free amine (19.0 mg), HOAt (17.6 mg, 0.13 mmol), EDCI (24.7 mg, 0.13 mmol), and $NaHCO_3$ (10.8 mg, 0.13 mmol) was cooled to 0 °C, treated with anhydrous DMF (0.30 mL) and stirred at 23 °C for 24 h. The reaction mixture was diluted with EtOAc (20 mL), washed with aqueous 1 N HCl (2 × 5.0 mL), saturated aqueous $NaHCO_3$ (2 × 5.0 mL), H_2O (5.0 mL) and saturated aqueous NaCl (5.0 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 8% MeOH−CH_2Cl_2) afforded **S7** as a yellow solid (31.6 mg, 617%): ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.26 (d, J = 7.3 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.96 (m, 2H), 7.91 (d, J = 7.5 Hz, 1H), 7.80 (d, J = 8.6 Hz, 1H), 7.77 (s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.51 (s, 1H), 7.48 (d, J = 6.6 Hz, 1H), 7.43 (s, 1H), 7.31–7.41 (m, 10H), 7.03 (s, 1H), 6.98 (s, 1H), 6.23 (d, J = 5.3 Hz, 1H), 5.14 (app q, J = 12.7 Hz, 2H), 5.09 (m, 2H), 4.99 (d, J = 12.6 Hz, 1H), 4.90 (d, J = 5.9 Hz, 1H), 4.52 (d, J = 5.3 Hz, 1H), 4.50 (m, 3H), 4.34 (dd, J = 8.1, 3.3 Hz, 1H), 4.30 (m, 1H), 4.23 (m, 3H), 4.09 (m, 2H), 4.01 (m, 1H), 3.95 (dd, J = 14.5, 6.7 Hz, 1H), 3.78 (q, J = 7.2 Hz, 1H), 3.50 (m, 1H), 3.41 (m, 1H), 2.63 (m, 1H), 2.54 (m, 3H), 2.36 (m, 2H), 2.34 (t, J = 7.1 Hz, 2H), 2.05 (m, 2H), 1.46–1.76 (m, 13H), 1.42 (s, 3H), 1.24 (m 16H), 1.08 (d, J = 6.3 Hz, 3H), 1.03 (d, J = 6.3 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H), 0.86 (m, 9H), 0.81 (m, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.4, 172.8, 172.3, 172.10, 172.07 (2C), 171.7, 171.53, 171.51, 171.1, 170.8, 170.5, 170.4, 155.9, 150.2, 147.7, 136.9, 136.0, 128.42 (2C), 128.40 (2C), 128.0, 127.9 (3C), 127.8 (2C), 115.3, 101.4, 96.8, 84.8, 69.8, 68.5, 68.4, 66.8, 66.2, 66.0, 65.6, 59.2, 58.1, 52.9, 52.0, 51.5, 51.2, 50.6, 50.1 (2C), 50.0, 40.4, 40.1, 37.1, 36.3, 34.5, 32.0, 31.4, 30.2, 29.3, 29.1, 28.9, 28.8, 27.2, 25.5, 25.3, 24.1, 24.0, 23.2, 23.1, 23.0, 22.2, 21.4, 20.2, 19.6, 18.0, 17.9, 14.0, 13.3; IR (film) ν_{max} 3321, 2921, 1737, 1658, 1537, 1451, 1259, 1079 cm^{-1}; HR ESI-TOF m/z 1605.7864 ($C_{78}H_{113}ClN_{12}O_{22}$ + H^+ requires 1605.7859); $[\alpha]^{23}_D$ –35 (c 0.10, MeOH).



4. A solution of **S7** (18.5 mg, 0.012 mmol) in anhydrous THF (3.8 mL) and DMF (1.9 mL) was treated with 10% Pd–C (27.8 mg) and stirred under H_2 (1 atm) at 23 °C for 4 h. The catalyst was removed by filtration through Celite, and the solvent was removed with a stream of nitrogen. The residue was treated with HOAt (15.7 mg, 0.12 mmol), EDCI (22.0 mg, 0.12 mmol), $NaHCO_3$ (9.7 mg, 0.12 mmol), cooled to 0 °C, treated with anhydrous DMF (3.8 mL) and stirred at 23 °C for 40 h. The reaction mixture was diluted with EtOAc (40 mL), washed with aqueous 1 N HCl (2 × 10 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL), H_2O (10 mL) and saturated aqueous NaCl (10 mL). The organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (SiO_2, 11% MeOH–CH_2Cl_2)[7] afforded **4** as a yellow solid (8.9 mg, 57%): ^1H NMR (DMSO-d_6, 600 MHz) δ 9.01 (br s, 1H), 8.62 (br s, 1H), 8.60 (s, 1H), 7.87 (br s, 1H), 7.77 (s, 1H), 7.73 (d, *J* = 4.8 Hz, 1H), 7.52 (d, *J* = 9.4 Hz, 1H), 7.26 (s, 1H), 7.09 (s, 1H), 7.01 (s, 1H), 6.96 (br s, 1H), 6.94 (s, 1H), 6.90 (br s, 1H), 6.82 (br s, 1H), 6.22 (d, *J* = 5.4 Hz, 1H), 5.29 (d, *J* = 4.7 Hz, 1H), 5.02 (d, *J* = 5.0 Hz, 1H), 4.74 (m, 1H), 4.56 (m, 1H), 4.52 (d, *J* = 5.4 Hz, 1H), 4.45 (m, 1H), 4.39 (m, 1H), 3.88–4.06 (m, 7H), 3.78 (dd, *J* = 15.0, 7.2 Hz, 1H), 3.68 (br s, 1H), 3.52 (m, 1H), 3.41 (m, 1H), 2.91 (br d, *J* = 14.1 Hz, 1H), 2.74 (dd, *J* = 15.7, 10.1 Hz, 1H), 2.57 (dd, *J* = 15.2, 10.9 Hz, 1H), 2.51 (m, 1H), 2.40 (m, 2H), 2.34 (t, *J* = 7.0 Hz, 2H), 2.04 (m, 2H), 1.67–1.86 (m, 6H), 1.48–1.63 (m, 6H), 1.42 (s, 3H), 1.37–1.45 (m, 2H), 1.26 (br m, 14H), 1.16 (d, *J* = 6.3 Hz, 4H), 1.09 (d, *J* = 5.9 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.91 (d, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.5 Hz, 3H), 0.78 (app t, *J* = 6.7 Hz, 6H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 188.9, 188.4, 174.1, 173.1, 172.9, 172.8, 172.54, 172.48, 172.0, 171.53, 171.47, 171.3, 171.1, 170.5, 150.3, 147.7, 115.3, 101.4, 96.8, 84.8, 68.49, 68.45, 65.2, 65.1, 63.3 (HMQC), 62.2, 54.0, 52.7, 52.1, 51.4, 50.8, 50.7, 49.3, 49.2, 39.1 (2C, HMQC), 37.4, 36.2, 34.5, 31.4, 30.3, 30.1, 28.73, 28.70, 28.6, 28.5 (HMQC), 27.2, 26.0, 25.2, 24.2, 24.1, 23.4, 23.3, 23.0, 22.1, 20.7, 20.34 (2C), 20.26, 18.0, 16.6, 14.0, 13.3; IR (film) ν_{max} 3308, 2956, 2927, 1652, 1541, 1244, 1080 cm^{-1}; HR ESI-TOF *m/z* 1363.6896 ($C_{63}H_{99}ClN_{12}O_{19} + H^+$ requires 1363.6916); CD (MeOH, 0.20 mM) λ_{ext} nm (Δε) 395 (–1.9), 345 (5.1), 293 (–1.5), 229 (–2.7), 201 (14.0); $[\alpha]^{23}_D$ –20 (*c* 0.2, MeOH).

Table S9. ^{1}H NMR shift comparsion of synthetic and natural chlorofusin (Williams' values)[8,a]

	^{1}H NMR shifts			^{1}H NMR shifts	
Position	**1**, natural	**1**, synthetic	Position	**1**, natural	**1**, synthetic
Thr-1			**Leu-7**		
NH	8.73 (br s)	8.75 (br s)	NH	9.08 (br s)	9.09 (br s)
α-CH	3.66 (br s)	3.66 (br s)	α-CH	3.95 (m)	3.95 (m)[b]
β-CH	4.02 (m)	4.02 (m)[b]	β-CH_2	1.60 (m)	1.60 (m)[b]
γ-CH_3	1.16 (d)	1.16 (d)	γ-CH	1.71–1.88 (m)	1.70–1.86 (m)
OH	5.28 (br s)	5.29 (d)	δ-CH_3^1	0.92 (d)	0.92 (d)[b]
Ala-2			δ-CH_3^2	0.82 (d)	0.82 (d)
NH	8.61 (d)	8.62 (s)	**ADA-8**		
α-CH	3.95 (m)	3.96 (m)[b]	NH	7.70 (d)	7.70 (d)
β-CH_3	1.26 (br m)	1.26 (br m)	α-CH	4.02 (m)	4.02 (m)[b]
Asn-3			β-CH_2	1.71–1.88 (m)	1.70–1.86 (m)
NH	6.93 (br s)	6.93 (br s)	γ-CH^1	1.38 (m)	1.38 (m)[b]
α-CH	4.75 (dt)	4.75 (m)	γ-CH^2	1.26 (br m)	1.26 (br m)
β-CH^1	2.93 (dd)	2.93 (br d)	δ-CH_2	1.26 (br m)	1.26 (br m)
β-CH^2	2.62 (dd)	2.63 (dd)	ε-CH_2	1.26 (br m)	1.26 (br m)
δ-NH^1	6.90 (br s)	6.91 (s)	ζ-CH_2	1.26 (br m)	1.26 (br m)
δ-NH^2	6.82 (br s)	6.82 (s)	η-CH_2	1.26 (br m)	1.26 (br m)
Asn-4			θ-CH_2	1.26 (br m)	1.26 (br m)
NH	7.84 (br s)	7.84 (br s)	ι-CH_3	0.87 (t)	0.87 (t)
α-CH	4.41 (ddd)	4.40 (m)	**Orn-9**		
β-CH^1	2.75 (dd)	2.75 (dd)	NH	6.69 (br s)	6.69 (br s)
β-CH^2	2.48 (dd)	2.49 (m)[b]	α-CH	4.59 (br t)	4.59 (m)
δ-NH^1	7.24 (br s)	7.25 (s)	β-CH_2	1.71–1.88 (m)	1.70–1.86 (m)
δ-NH^2	7.00 (br s)	7.01 (s)	γ-CH^1	1.71–1.88 (m)	1.70–1.86 (m)
Leu-5			γ-CH^2	1.55 (sextet)	1.52 (m)[b]
NH	7.51 (d)	7.51 (d)	δ-CH_2	3.42 (t, 2H)	3.42 (br t, 2H)
α-CH	4.48 (dt)	4.47 (m)	**Chromophore**		
β-CH^1	1.60 (m)	1.60 (m)[b]	1-CH	7.77 (s)	7.77 (s)
β-CH^2	1.13 (br m)	1.13 (m)[b]	8-CH	4.53 (d)	4.53 (d)
γ-CH	1.41 (m)	1.41 (m)[b]	10-CH_2	2.38 (br m)	2.38 (br m)
δ-CH_3^1	0.78 (d)	0.78 (d)	11-CH_2	2.0–2.2 (m)	2.00–2.15 (m)
δ-CH_3^2	0.77 (d)	0.77 (d)	12-CH^1	4.02 (m)	4.02 (m)[b]
Thr-6			12-CH^2	3.78 (q)	3.78 (dd)
NH	7.07 (br s)	7.07 (s)	13-CH_3	1.43 (s)	1.43 (s)
α-CH	3.92 (m)	3.92 (m)[b]	14-OH	6.26 (d)	6.26 (d)
β-CH	3.92 (m)	3.92 (m)[b]	16-CH_2	2.34 (t)	2.34 (t)
γ-CH_3	1.10 (d)	1.10 (d)	17-CH_2	1.55 (sextet)	1.54 (sextet)
OH	5.05 (br s)	5.05 (d)	18-CH_3	0.92 (t)	0.92 (m)

[a] Values reported in ppm. Assignments made by analogy to **47D**, chlorofusin and using HMQC NMR.

[b] Chemical shift value determined by HMQC NMR.

Table S10. ^{13}C NMR shift comparsion of synthetic and natural chlorofusin (Williams' values)[8,a]

	^{13}C NMR shifts			^{13}C NMR shifts	
Position	**1**, natural	**1**, synthetic	Position	**1**, natural	**1**, synthetic
Thr-1			**ADA-8**		
α-carbonyl	173.0	173.1	α-carbonyl	171.9	172.0
α-CH	63.1	63.4[b]	α-CH	53.9	54.1
β-CH	65.0	65.1	β-CH_2	30.0	30.0
γ-CH_3	20.3	20.4	γ-CH_2	25.9	26.0
Ala-2			δ-CH_2	28.6	28.7
α-carbonyl	171.6	171.6	ε-CH_2	28.5	28.7
α-CH	50.8	50.9	ζ-CH_2	28.4	28.6
β-CH_3	16.5	16.6	η-CH_2	31.2	31.4
Asn-3			θ-CH_2	22.0	22.1
α-carbonyl	170-174[8]	170-174	ι-CH_3	13.9	14.0
α-CH	49.0	49.1	**Orn-9**		
β-CH_2	37.3	37.4	α-carbonyl	170-174	170-174
γ-carbonyl	170.9[8]	171.0	α-CH	51.2	51.2
Asn-4			β-CH_2	28.3	28.4[b]
α-carbonyl	170-174	170-174	γ-CH_2	27.0	27.1
α-CH	52.0	52.1	δ-CH_2	50.5	50.6
β-CH_2	36.2	36.2	**Chromophore**		
γ-carbonyl	170.3	170.4	1-CH	150.0	150.2
Leu-5			2-C	115.2	115.3
α-carbonyl	173.1	173.2	3-carbonyl	188.1	188.3
α-CH	49.2	49.2	4-C	84.7	84.8
β-CH_2	38.7	39.0[b]	5-carbonyl	188.7	188.9
γ-CH	24.0	24.1	6-C	101.3	101.4
δ-$CH_3{}^1$	23.2	23.4	7-C	147.5	147.7
δ-$CH_3{}^2$	20.6	20.7	8-CH	68.4	68.6
Thr-6			9-C	96.7	96.8
α-carbonyl	170-174	170-174	10-CH_2	30.3	30.5
α-CH	62.1	62.3	11-CH_2	25.1	25.2
β-CH	64.9	65.0	12-CH_2	68.4	68.5
γ-CH_3	20.2	20.3	13-CH_3	22.9	23.0
Leu-7			15-carbonyl	171.4	171.5
α-carbonyl	172.4	172.5	16-CH_2	34.4	34.5
α-CH	52.7	52.8	17-CH_2	17.9	18.1
β-CH_2	38.7	38.9[b]	18-CH_3	13.2	13.3
γ-CH	24.1	24.2			
δ-$CH_3{}^1$	23.1	23.3			
δ-$CH_3{}^2$	20.1	20.2			

[a] Values reported in ppm. Assignments made by analogy to **47D**, chlorofusin and using HMQC NMR.

[b] Chemical shift value determined by HMQC NMR.

Table S11. ^{1}H NMR shift comparsion of all eight synthetic chlorofusin chromophore diastereomers to the natural product (Williams' values)[8,a]

Position	Natural chlorofusin	**1**, (4*R*,8*S*,9*R*)	**3**, (4*R*,8*R*,9*R*)	**65**, (4*R*,8*S*,9*S*)	**66**, (4*R*,8*R*,9*S*)	**2**, (4*S*,8*S*,9*S*)	**67**, (4*S*,8*R*,9*R*)	**68**, (4*S*,8*S*,9*R*)	**4**, (4*S*,8*R*,9*S*)
Thr-1									
NH	8.73 (br s)	8.75 (br s)	8.85 (br s)	8.72 (br s)	8.88 (br s)	8.73 (br s)	8.77 (br s)	8.71 (br s)	8.62 (br s)
α-CH	3.66 (br s)	3.66 (br s)	3.63 (br s)	3.65 (br s)	3.69 (br s)	3.63 (br s)	3.64 (br s)	3.66 (br s)	3.68 (br s)
β-CH	4.02 (m)	4.02 (m)[b]	4.01 (m)[b]	4.02 (m)[b]	4.02 (m)[b]	3.97 (m)[b]	4.02 (m)[b]	4.02 (m)[b]	4.02 (m)[b]
γ-CH$_3$	1.16 (d)	1.16 (d)	1.16 (d)	1.16 (d)	1.16 (d)	1.16 (d)	1.16 (d)	1.16 (d)	1.16 (d)
OH	5.28 (br s)	5.29 (d)	5.33 (d)	5.30 (d)	5.38 (d)	5.32 (d)	5.32 (s)	5.34 (d)	5.29 (d)
Ala-2									
NH	8.61 (d)	8.62 (s)	8.72 (s)	8.62 (s)	8.88 (br s)	8.51 (d)	8.65 (s)	8.59 (s)	8.60 (s)
α-CH	3.95 (m)	3.96 (m)[b]	4.10 (m)	3.95 (m)[b]	3.95 (m)[b]	3.96 (m)[b]	3.96 (m)[b]	3.93 (m)[b]	3.96 (m)[b]
β-CH$_3$	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)
Asn-3									
NH	6.93 (br s)	6.93 (br s)	6.94 (s)	6.93 (br s)	7.22 (br s)	6.90 (s)	6.96 (br s)	6.93 (s)	6.96 (br s)
α-CH	4.75 (dt)	4.75 (m)	4.78 (m)	4.74 (m)	4.75 (m)	4.75 (m)	4.78 (m)	4.76 (m)	4.74 (m)
β-CH^1	2.93 (dd)	2.93 (br d)	2.95 (br d)	2.93 (br d)	2.92 (br d)	2.95 (br d)	2.94 (br d)	2.93 (br d)	2.91 (br d)
β-CH^2	2.62 (dd)	2.63 (dd)	2.58 (dd)	2.63 (dd)	2.58 (m)	2.66 (dd)	2.57 (dd)	2.61 (dd)	2.57 (dd)
δ-NH^1	6.90 (br s)	6.91 (s)	6.89 (s)	6.89 (s)	6.92 (br s)	6.87 (br s)	6.92 (br s)	6.90 (br s)	6.94 (s)
δ-NH^2	6.82 (br s)	6.82 (s)	6.89 (s)	6.74 (br s)	6.84 (s)	6.73 (br s)	6.90 (s)	6.88 (br s)	6.90 (br s)
Asn-4									
NH	7.84 (br s)	7.84 (br s)	7.82 (br s)	7.84 (br s)	7.86 (br s)	7.84 (br s)	7.84 (br s)	7.84 (br s)	7.87 (br s)
α-CH	4.41 (ddd)	4.40 (m)	4.38 (m)	4.41 (m)	4.40 (m)	4.41 (m)	4.38 (m)	4.40 (m)	4.39 (m)
β-CH^1	2.75 (dd)	2.75 (dd)	2.77 (dd)	2.75 (dd)	2.75 (m)	2.76 (dd)	2.77 (dd)	2.75 (dd)	2.74 (dd)
β-CH^2	2.48 (dd)	2.49 (m)[b]	2.49 (m)[b]	2.49 (m)[b]	2.49 (m)[b]	2.50 (m)[b]	2.50 (m)[b]	2.50 (m)[b]	2.51 (m)[b]
δ-NH^1	7.24 (br s)	7.25 (s)	7.25 (s)	7.25 (s)	7.26 (s)	7.24 (s)	7.25 (s)	7.25 (s)	7.26 (s)
δ-NH^2	7.00 (br s)	7.01 (s)	7.01 (s)	7.01 (s)	7.01 (s)	7.01 (s)	7.01 (s)	7.01 (s)	7.01 (s)
Leu-5									
NH	7.51 (d)	7.51 (d)	7.52 (d)	7.50 (d)	7.56 (d)	7.48 (d)	7.51 (d)	7.52 (d)	7.52 (d)
α-CH	4.48 (dt)	4.47 (m)	4.48 (m)	4.47 (m)	4.47 (m)	4.48 (m)	4.48 (m)	4.47 (m)	4.45 (m)
β-CH^1	1.60 (m)	1.60 (m)[b]	1.60 (m)[b]	1.60 (m)[b]	1.59 (m)[b]	1.59 (m)[b]	1.59 (m)[b]	1.58 (m)[b]	1.59 (m)[b]
β-CH^2	1.13 (br m)	1.13 (m)[b]	1.12 (m)[b]	1.13 (m)[b]	1.13 (m)[b]	1.14 (m)[b]	1.14 (m)[b]	1.15 (m)[b]	1.15 (m)[b]
γ-CH	1.41 (m)	1.41 (m)[b]	1.41 (m)[b]	1.41 (m)[b]	1.41 (m)[b]	1.41 (m)[b]	1.41 (m)[b]	1.41 (m)[b]	1.43 (m)[b]
δ-CH$_3$^{1}	0.78 (d)	0.78 (d)	0.77 (d)	0.77 (d)	0.78 (d)	0.77 (d)	0.78 (d)	0.78 (d)	0.79 (d)
δ-CH$_3$^{2}	0.77 (d)	0.77 (d)	0.77 (d)	0.77 (d)	0.78 (d)	0.77 (d)	0.77 (d)	0.77 (d)	0.78 (d)
Thr-6									
NH	7.07 (br s)	7.07 (s)	7.12 (s)	7.08 (s)	7.09 (s)	7.07 (s)	7.12 (d)	7.08 (s)	7.09 (s)
α-CH	3.92 (m)	3.92 (m)[b]	3.92 (m)[b]	3.93 (m)[b]	3.91 (m)[b]	3.91 (m)[b]	3.91 (m)[b]	3.91 (m)[b]	3.90 (m)[b]
β-CH	3.92 (m)	3.92 (m)[b]	3.92 (m)[b]	3.93 (m)[b]	3.91 (m)[b]	3.93 (m)[b]	3.98 (m)[b]	3.93 (m)[b]	3.94 (m)[b]
γ-CH$_3$	1.10 (d)	1.10 (d)	1.10 (d)	1.10 (d)	1.09 (d)	1.10 (d)	1.10 (d)	1.09 (d)	1.09 (d)
OH	5.05 (br s)	5.05 (d)	5.01 (d)	5.08 (d)	5.04 (d)	5.09 (d)	5.01 (d)	5.03 (d)	5.02 (d)
Leu-7									
NH	9.08 (br s)	9.09 (br s)	9.09 (br s)	9.13 (br s)	9.08 (br s)	9.16 (br s)	9.08 (br s)	9.08 (br s)	9.01 (br s)
α-CH	3.95 (m)	3.95 (m)[b]	3.95 (m)[b]	3.95 (m)[b]	3.96 (m)[b]	3.95 (m)[b]	4.10 (m)	3.94 (m)[b]	3.98 (m)[b]
β-CH$_2$	1.60 (m)	1.60 (m)[b]	1.60 (m)[b]	1.60 (m)[b]	1.59 (m)[b]	1.59 (m)[b]	1.48–1.67 (m)	1.45–1.65 (m)	1.57 (m)[b]
γ-CH	1.71–1.88 (m)	1.70–1.86 (m)	1.70–1.96 (m)	1.73–1.89 (m)	1.65–1.85 (m)	1.72–2.06 (m)	1.72–1.89 (m)	1.65–1.87 (m)	1.67–1.86 (m)
δ-CH$_3$^{1}	0.92 (d)	0.92 (d)[b]	0.93 (d)[b]	0.92 (d)[b]	0.92 (d)	0.91 (d)	0.92 (d)	0.91 (d)	0.91 (d)[b]
δ-CH$_3$^{2}	0.82 (d)	0.82 (d)	0.85 (d)[b]	0.83 (d)	0.82 (d)	0.81 (d)	0.84 (d)	0.80 (d)	0.82 (d)
ADA-8									
NH	7.70 (d)	7.70 (d)	7.77 (d)	7.72 (d)	7.71 (d)	7.73 (d)	7.78 (d)	7.71 (d)	7.73 (d)
α-CH	4.02 (m)	4.02 (m)[b]	4.02 (m)[b]	4.02 (m)[b]	4.02 (m)[b]	4.07 (dd)	4.02 (m)[b]	4.02 (m)[b]	4.03 (m)[b]
β-CH$_2$	1.71–1.88 (m)	1.70–1.86 (m)	1.70–1.96 (m)	1.73–1.89 (m)	1.65–1.85 (m)	1.72–2.06 (m)	1.72–1.89 (m)	1.65–1.87 (m)	1.67–1.86 (m)
γ-CH^1	1.38 (m)	1.38 (m)[b]	1.38 (m)[b]	1.38 (m)[b]	1.38 (m)[b]	1.40 (m)[b]	1.40 (m)[b]	1.40 (m)[b]	1.40 (m)[b]
γ-CH^2	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)
δ-CH$_2$	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)
ε-CH$_2$	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)
ζ-CH$_2$	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)
η-CH$_2$	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)
θ-CH$_2$	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)	1.26 (br m)
ι-CH$_3$	0.87 (t)	0.87 (t)	0.87 (t)	0.87 (t)	0.87 (t)	0.87 (t)	0.87 (t)	0.87 (t)	0.87 (t)
Orn-9									
NH	6.69 (br s)	6.69 (br s)	6.76 (br s)	6.67 (br s)	6.67 (br s)	6.65 (br s)	6.76 (br s)	6.75 (br s)	6.82 (br s)
α-CH	4.59 (br t)	4.59 (m)	4.59 (m)	4.56 (m)	4.56 (m)	4.61 (m)	4.60 (m)	4.58 (m)	4.56 (m)
β-CH$_2$	1.71–1.88 (m)	1.70–1.86 (m)	1.70–1.96 (m)	1.66 (m)[b], 1.73–1.89	1.65–1.85 (m)	1.67 (m)[b], 1.72–2.06	1.72–1.89 (m)	1.65–1.87 (m)	1.67–1.86 (m)
γ-CH^1	1.71–1.88 (m)	1.70–1.86 (m)	1.70–1.96 (m)	1.59 (m)[b]	1.65–1.85 (m)	1.56 (m)[b]	1.72–1.89 (m)	1.65–1.87 (m)	1.67–1.86 (m)
γ-CH^2	1.55 (sextet)	1.52 (m)[b]	1.42 (m)[b]	1.59 (m)[b]	1.51 (m)[b]	1.56 (m)[b]	1.42 (m)[b]	1.50 (m)[b]	1.50 (m)[b]
δ-CH$_2$	3.42 (t, 2H)	3.42 (br t, 2H)	3.43 (m), 3.50 (m)	3.35 (m, 2H)[b]	3.39 (m), 3.52 (m)	3.35 (m)[b], 3.45 (m)	3.42 (m), 3.50 (m)	3.37 (m), 3.41 (m)	3.41 (m), 3.52 (m)
Chromophore									
1-CH	7.77 (s)	7.77 (s)	7.88 (s)	7.81 (s)	7.78 (s)	7.88 (s)	7.83 (s)	7.77 (s)	7.77 (s)
8-CH	4.53 (d)	4.53 (d)	4.50 (d)	4.54 (d)	4.48 (d)	4.48 (d)	4.56 (s)	4.49 (d)	4.52 (d)
10-CH$_2$	2.38 (br m)	2.38 (br m)	1.70–1.96 (m)	1.73–1.89 (m)	2.40 (br m)	1.72–2.06 (m)	1.72–1.89 (m)	2.37 (br m)	2.40 (m)
11-CH$_2$	2.0–2.2 (m)	2.00–2.15 (m)	1.93 (m)[b], 2.06 (m)	1.93–2.07 (m)	2.03 (m)	1.72–2.06 (m)	1.96 (m), 2.06 (m)	2.05 (br m)	2.04 (m)
12-CH^1	4.02 (m)	4.02 (m)[b]	4.23 (m)	4.22 (dd)	4.02 (m)[b]	4.24 (dd)	4.24 (dd)	4.08 (dd)	4.00 (m)[b]
12-CH^2	3.78 (q)	3.78 (dd)	4.02 (m)[b]	4.02 (m)[b]	3.80 (dd)	3.96 (m)[b]	3.92 (m)[b]	3.78 (dd)	3.78 (dd)
13-CH$_3$	1.43 (s)	1.43 (s)	1.41 (s)	1.41 (s)	1.38 (s)	1.41 (s)	1.39 (s)	1.39 (s)	1.42 (s)
14-OH	6.26 (d)	6.26 (d)	5.98 (d)	5.98 (d)	6.38 (d)	5.92 (d)	6.02 (s)	6.37 (d)	6.22 (d)
16-CH$_2$	2.34 (t)	2.34 (t)	2.34 (t)	2.33 (t)	2.34 (t)	2.35 (t)	2.34 (t)	2.35 (t)	2.34 (t)
17-CH$_2$	1.55 (sextet)	1.54 (sextet)	1.55 (sextet)	1.54 (sextet)	1.55 (sextet)	1.55 (sextet)	1.54 (sextet)	1.55 (sextet)	1.54 (sextet)
18-CH$_3$	0.92 (t)	0.92 (t)	0.92 (t)	0.91 (t)	0.92 (t)	0.92 (t)	0.92 (t)	0.92 (t)	0.92 (t)

[a] Values reported in ppm. Assignments made by analogy to **47A**–**47D**, **48A**–**48D** and chlorofusin and using HMQC NMR.

[b] Chemical shift value determined by HMQC NMR.

Table S12. ^{13}C NMR shift comparsion of all eight synthetic chlorofusin chromophore diastereomers to the natural product (Williams' values)[8,a]

Position	Natural chlorofusin	**1**, (4*R*,8*S*,9*R*)	**3**, (4*R*,8*R*,9*R*)	**65**, (4*R*,8*S*,9*S*)	**66**, (4*R*,8*R*,9*S*)	**2**, (4*S*,8*S*,9*S*)	**67**, (4*S*,8*R*,9*R*)	**68**, (4*S*,8*S*,9*R*)	**4**, (4*S*,8*R*,9*S*)
Thr-1									
α-carbonyl	173.0	173.1	173.0	173.2	173.0	173.1	173.0	173.1	172.9
α-CH	63.1	63.4[b]	63.6[b]	63.5[b]	63.2[b]	63.5[b]	63.5[b]	63.2[b]	63.3[b]
β-CH	65.0	65.1	65.1	65.1	65.2	65.1	65.1	65.1	65.2
γ-CH_3	20.3	20.4	20.4	20.4	20.3	20.4	20.3	20.4	20.3
Ala-2									
α-carbonyl	171.6	171.6	171.5	171.5	171.5	171.6	171.6	171.5	171.5
α-CH	50.8	50.9	50.9	50.9	50.8	50.9	50.9	50.9	50.8
β-CH_3	16.5	16.6	16.5	16.4	16.6	16.3	16.5	16.6	16.6
Asn-3									
α-carbonyl	170-174[g]	170-174	170-174	170-174	170-174	170-174	170-174	170-174	170-174
α-CH	49.0	49.1	49.1	49.0	49.3	48.9[b]	49.2	49.2	49.2
β-CH_2	37.3	37.4	37.5	37.5	37.4	36.9[b]	37.4	37.5	37.4
γ-carbonyl	170.9[g]	171.0	171.2	170.9	171.1	170.8	171.2	171.1	171.1
Asn-4									
α-carbonyl	170-174	170-174	170-174	170-174	170-174	170-174	170-174	170-174	170-174
α-CH	52.0	52.1	52.3	52.1	52.1	52.2	52.2	52.2	52.1
β-CH_2	36.2	36.2	36.2	36.2	36.2	36.2	36.2	36.2	36.2
γ-carbonyl	170.3	170.4	170.4	170.4	170.5	170.4	170.4	170.4	170.5
Leu-5									
α-carbonyl	173.1	173.2	173.1	173.3	173.1	173.2	173.2	173.2	173.1
α-CH	49.2	49.2	49.2	49.2[b]	49.2	49.0	49.2	49.2	49.3
β-CH_2	38.7	39.0[b]	39.0	39.0[b]	39.0[b]	39.0[b]	39.2[b]	39.0	39.1[b]
γ-CH	24.0	24.1	24.1	24.1	24.1	24.2	24.1	24.1	24.1
δ-CH_3^1	23.2	23.4	23.4	23.2	23.4	23.4	23.4	23.4	23.4
δ-CH_3^2	20.6	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7
Thr-6									
α-carbonyl	170-174	170-174	170-174	170-174	170-174	170-174	170-174	170-174	170-174
α-CH	62.1	62.3	62.4	62.3	62.2	62.3	62.4	62.3	62.2
β-CH	64.9	65.0	64.9	65.0	65.0	64.9	64.9	65.0	65.1
γ-CH_3	20.2	20.3	20.4	20.4	20.4	20.4	20.3	20.3	20.3
Leu-7									
α-carbonyl	172.4	172.5	172.6	172.5	172.5	172.4	172.6	172.5	172.5
α-CH	52.7	52.8	52.6	52.8	52.7	52.8	52.6	52.7	52.7
β-CH_2	38.7	38.9[b]	38.9[b]	38.9[b]	38.9[b]	38.9[b]	39.4[b]	39.1	39.1[b]
γ-CH	24.1	24.2	24.4	24.2	24.2	24.0	24.4	24.2	24.2
δ-CH_3^1	23.1	23.3	23.2	23.0	23.3	23.2	23.2	23.3	23.3
δ-CH_3^2	20.1	20.2	20.5	20.2	20.2	20.3	20.5	20.3	20.3
ADA-8									
α-carbonyl	171.9	172.0	171.7	172.0	172.0	172.0	171.8	172.0	172.0
α-CH	53.9	54.1	53.9	54.0	54.0	53.9	54.0	54.0	54.0
β-CH_2	30.0	30.0	29.9	30.0	30.1	30.0	29.9	30.0	30.1
γ-CH_2	25.9	26.0	26.1	26.0	26.0	26.1	26.1	26.1	26.0
δ-CH_2	28.6	28.7	28.7	28.7	28.7	28.8	28.7	28.7	28.7
ε-CH_2	28.5	28.7	28.7	28.7	28.7	28.7	28.7	28.7	28.7
ζ-CH_2	28.4	28.6	28.5	28.6	28.6	28.5	28.5	28.6	28.6
η-CH_2	31.2	31.4	31.4	31.4	31.4	31.4	31.4	31.4	31.4
θ-CH_2	22.0	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.1
ι-CH_3	13.9	14.0	14.0	14.0	14.0	14.0	14.0	14.0	14.0
Orn-9									
α-carbonyl	170-174	170-174	170-174	170-174	170-174	170-174	170-174	170-174	170-174
α-CH	51.2	51.2	51.6	51.7	51.4	51.7	51.5	51.4	51.4
β-CH_2	28.3	28.4[b]	28.3	28.3	28.6	28.1	28.3	28.6	28.5[b]
γ-CH_2	27.0	27.1	26.8	27.0	27.2	27.1	27.0	27.3	27.2
δ-CH_2	50.5	50.6	49.7	49.2[b]	50.8	48.6	49.8	50.3	50.7
Chromophore									
1-CH	150.0	150.2	149.7	149.4	150.6	149.9	149.5	150.4	150.3
2-C	115.2	115.3	113.4	113.7	115.1	113.4	113.6	115.1	115.3
3-carbonyl	188.1	188.3	188.9	188.0	189.1	188.7	188.2	189.2	188.4
4-C	84.7	84.8	84.7	84.6	84.7	84.8	84.7	84.7	84.8
5-carbonyl	188.7	188.9	189.0	188.9	188.7	189.0	188.8	188.7	188.9
6-C	101.3	101.4	100.6	100.4	101.8	100.7	100.4	101.8	101.4
7-C	147.5	147.7	148.3	148.4	148.2	148.2	148.4	148.2	147.7
8-CH	68.4	68.6	69.0	68.7	68.3	68.7	69.1	68.6	68.5
9-C	96.7	96.8	97.9	97.7	96.9	97.6	97.8	96.9	96.8
10-CH_2	30.3	30.5	34.7	35.0	30.3	34.7	35.2	30.7	30.3
11-CH_2	25.1	25.2	24.5	24.7	25.3	24.7	24.5	25.3	25.2
12-CH_2	68.4	68.5	70.8	70.6	68.6	70.5	71.0	68.7	68.5
13-CH_3	22.9	23.0	23.6	23.4	23.5	23.7	23.0	23.5	23.0
15-carbonyl	171.4	171.5	171.3	171.3	171.4	171.4	171.5	171.4	171.5
16-CH_2	34.4	34.5	34.5	34.6	34.5	34.5	34.6	34.5	34.5
17-CH_2	17.9	18.1	18.1	18.1	18.1	18.1	18.0	18.1	18.0
18-CH_3	13.2	13.3	13.3	13.3	13.3	13.3	13.3	13.3	13.3

[a] Values reported in ppm. Assignments made by analogy to **47A**–**47D**, **48A**–**48D** and chlorofusin and using HMQC NMR.

[b] Chemical shift value determined by HMQC NMR.

Authentic Natural Chlorofusin. An authentic, but aged, sample of natural chlorofusin (1 mg) received in 2003 from Dr. Stephen Wrigley of Cubist Pharmaceuticals [which had acquired Terragen Discovery Inc. which had in turn earlier aquired Xenova Discovery Ltd. that was responsible for the isolation of the natural product] was examined at the time of its receipt. A 0.4 mg portion of the sample failed to provide a discernable ^{1}H NMR spectrum (DMSO-d_6, S. S. Pfeiffer and P. Desai, unpublished, Figure attached) and proved inactive in a p53−MDM2 inhibition assay at the concentrations tested (I. Hwang, unpublished). We refrigerated this and the remaining untouched sample in hopes of returning to it at a later date for further purification once we had the chromatographic behavior and properties of such molecules well in hand. On May 3, 2007 following the Yao disclosure (web 5-2-07) as well as following the completion of our own studies detailed herein, we elected to begin a reexamination of this sample. The CD spectrum of the prior NMR sample (0.4 mg) was examined and it exhibited a positive long wavelength Cotton effect and empirically appeared nearly identical in shape to the CD spectrum of **47D** and synthetic **1**, but of an intensity that indicated that most of the material did not appear to be chlorofusin. The remaining untouched sample was purified by filtration and extensively dried (from a solution of anhydrous HPLC grade methanol by a stream of nitrogen (× 3), followed by reduced pressure for 48 h). This treatment provided a sample of natural chlorofusin that displayed a CD spectrum (sign and magnitude) identical to our synthetic material confirming the absolute configuration assignment. Its ^{1}H NMR spectrum, though broadened and still containing residual impurities, clearly matches that reported by Williams and is of a quality that insures its CD and ^{1}H NMR spectra represent those of the natural product reported by Williams.

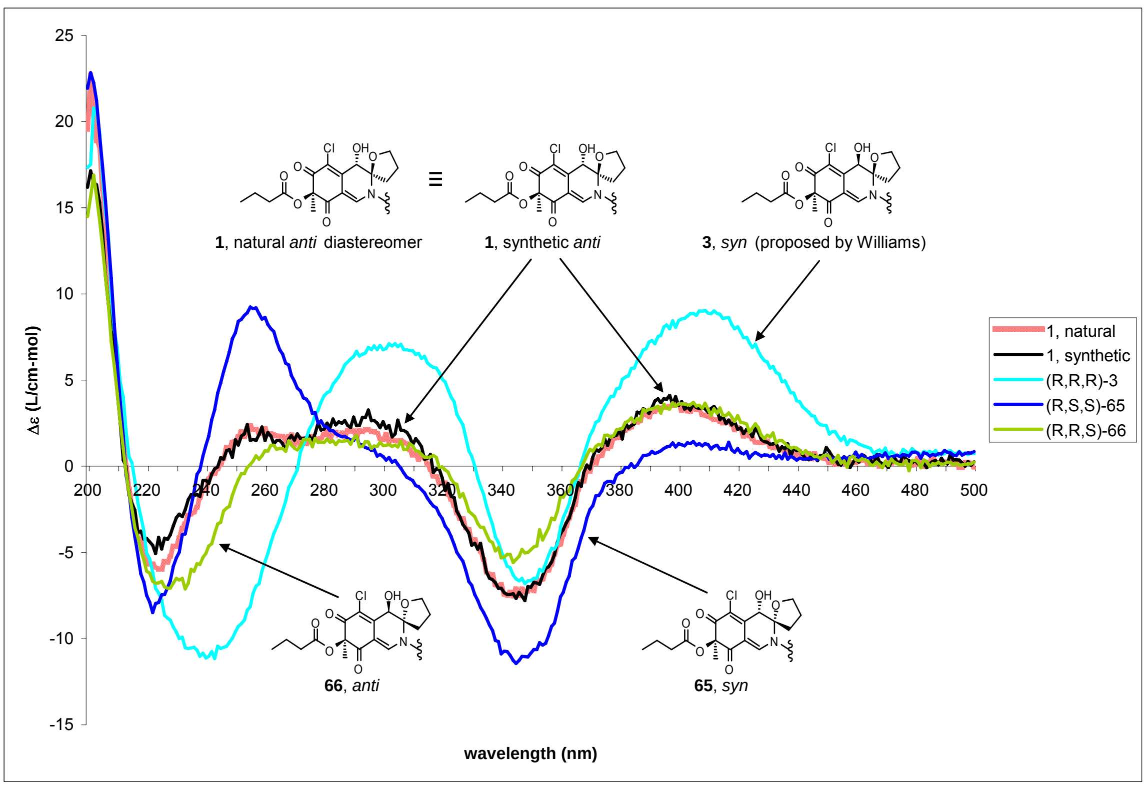


Figure S16. CD spectra (0.2 mM in MeOH) of **3**, **65**, **66**, **1** and natural chlorofusin.

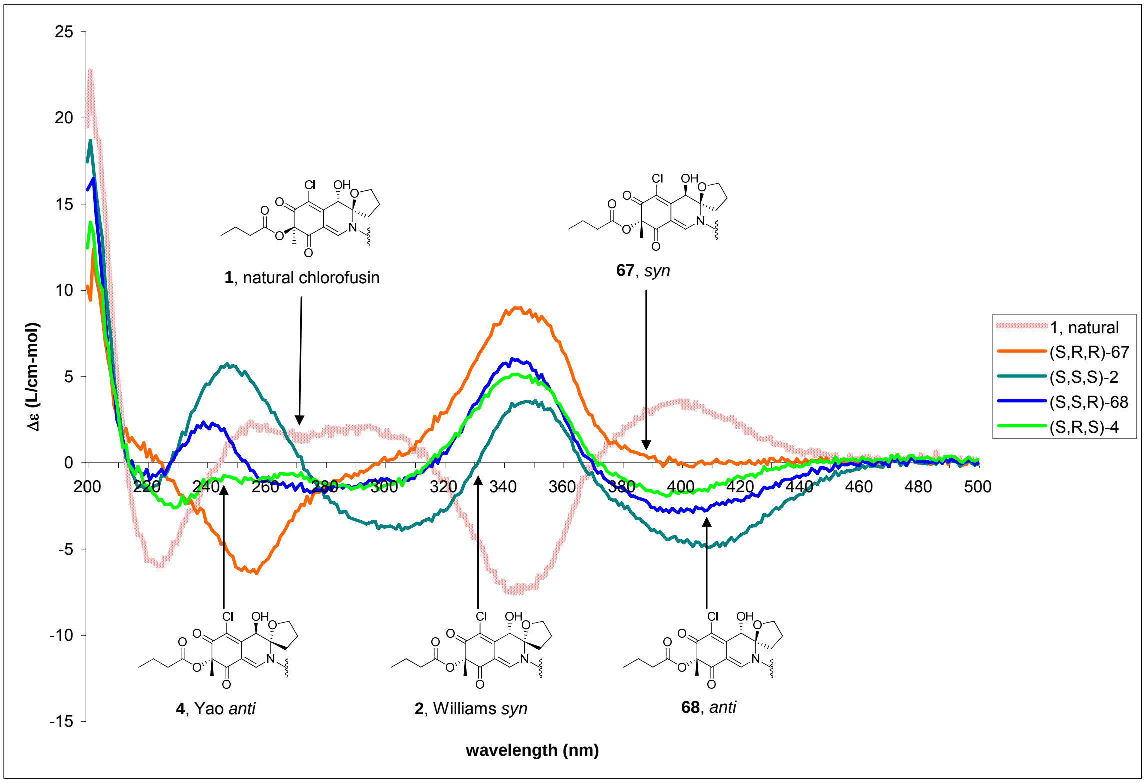
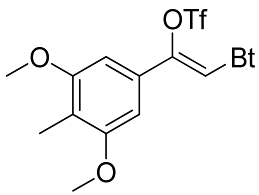


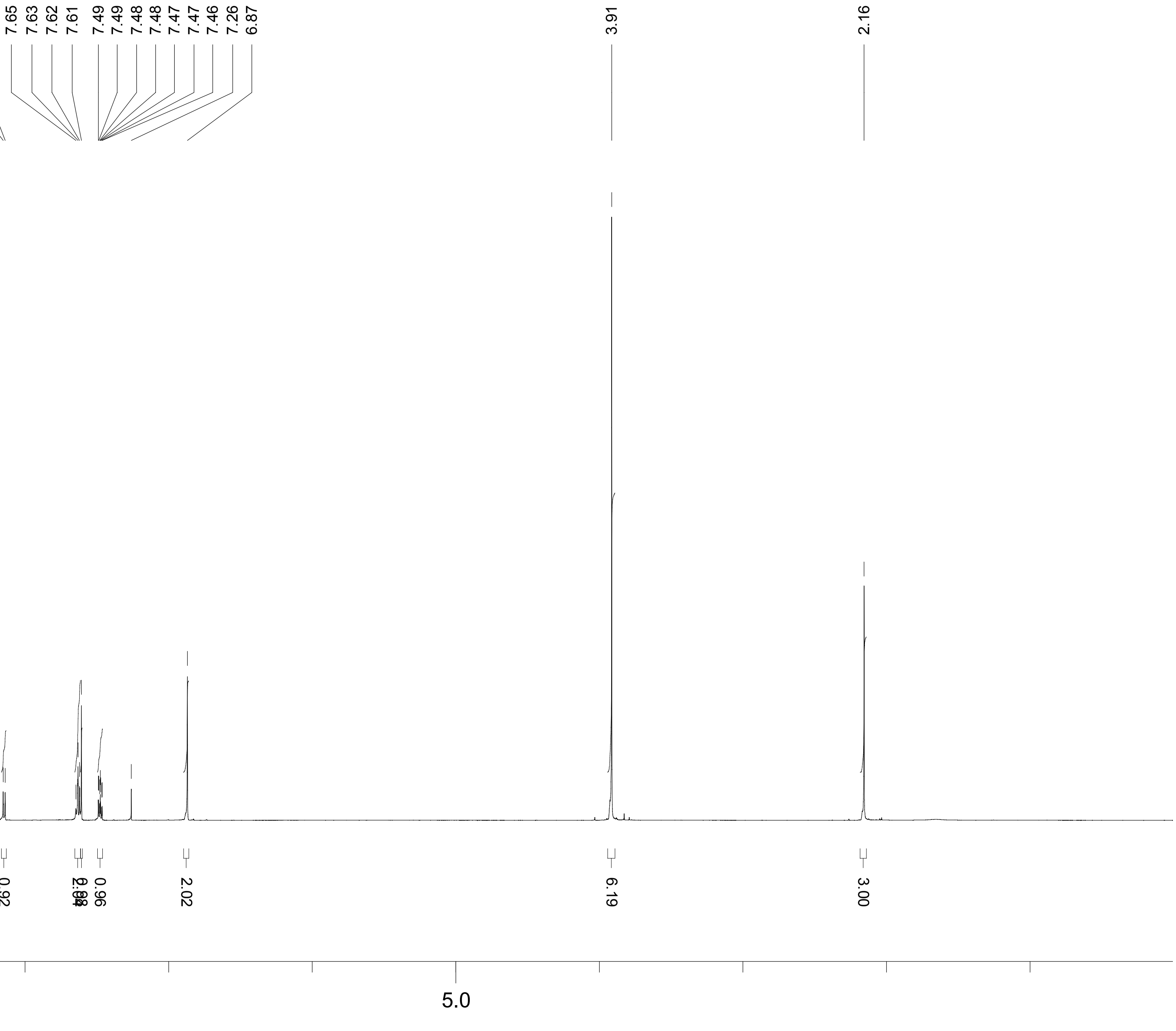
Figure S17. CD spectra (0.2 mM in MeOH) of **2**, **67**, **68**, **4** and natural chlorofusin.

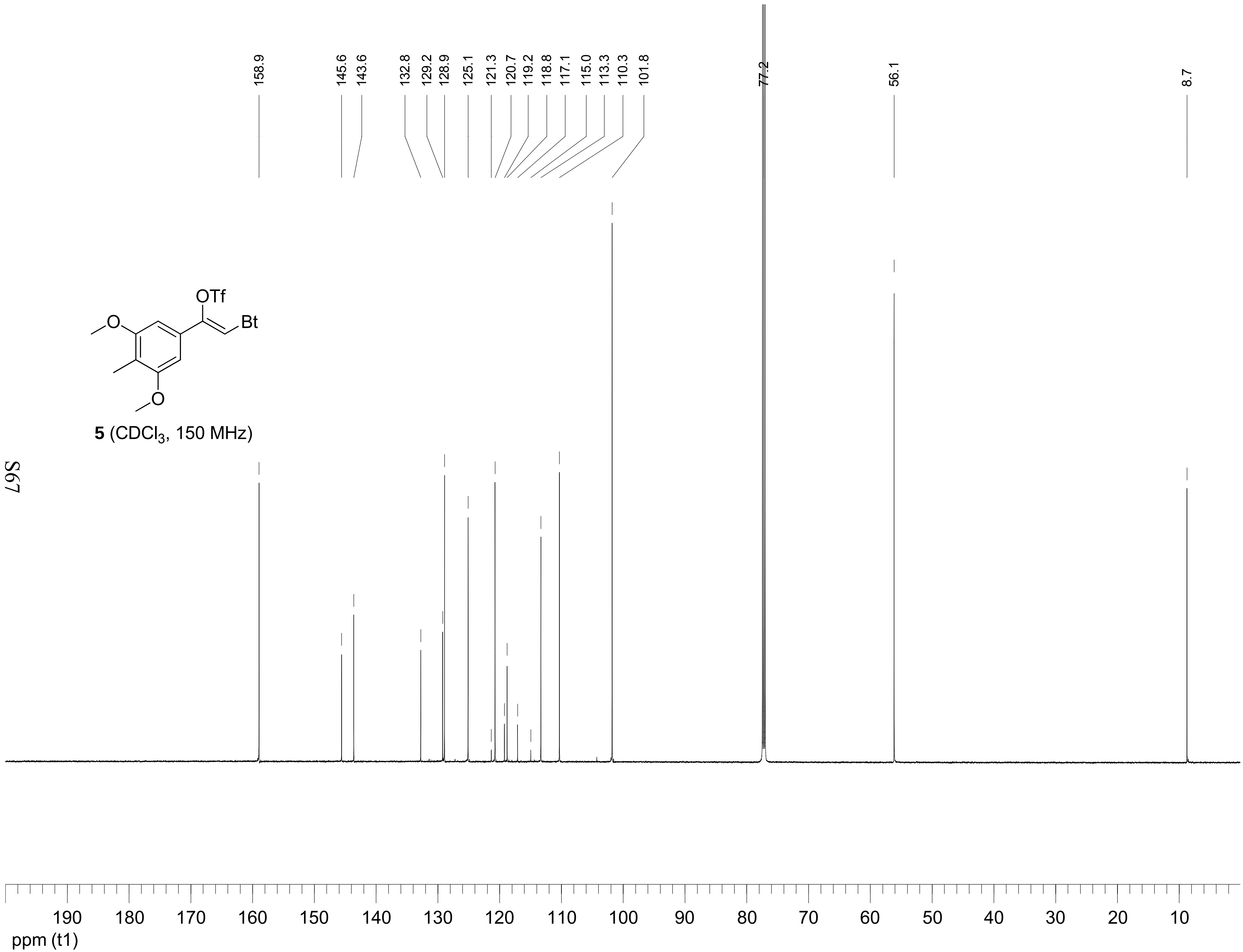
References:

1. Wei, W.-G.; Yao, Z.-J. *J. Org. Chem.* **2005**, *70*, 4585.
2. Atomic coordinates for **36A** (CCDC646443) have been deposited with the Cambridge Crystallographic Data Center.
3. Atomic coordinates for **36B** (CCDC646442) have been deposited with the Cambridge Crystallographic Data Center.
4. Atomic coordinates for **42A** (CCDC678265) have been deposited with the Cambridge Crystallographic Data Center.
5. Atomic coordinates for **42D** (CCDC646441) have been deposited with the Cambridge Crystallographic Data Center.
6. Desai, P.; Pfeiffer, S. S.; Boger, D. L. *Org. Lett.* **2003**, *5*, 5047.
7. Minor impurities observed on occasion in the NMR spectra could be removed by SiO_2 chromatography ($CHCl_3$(80):MeOH(20):H_2O(1):NH_4OH(1)) followed by C18 reverse phase chromatography (MeCN(1): H_2O(1)).
8. Duncan, S. J.; Grueschow, S.; Williams, D. H.; McNicholas, C.; Purewal, R.; Hajek, M.; Gerlitz, M.; Martin, S.; Wrigley, S. K.; Moore, M., *J. Am. Chem. Soc.* **2001**, *123*, 554. Correction: *J. Am. Chem. Soc.* **2002**, *124*, 14503.
9. Duncan, S. J.; Williams, D. H.; Ainsworth, M.; Martin, S.; Ford, R.; Wrigley, S. K. *Tetrahedron Lett.* **2002**, *43*, 1075.



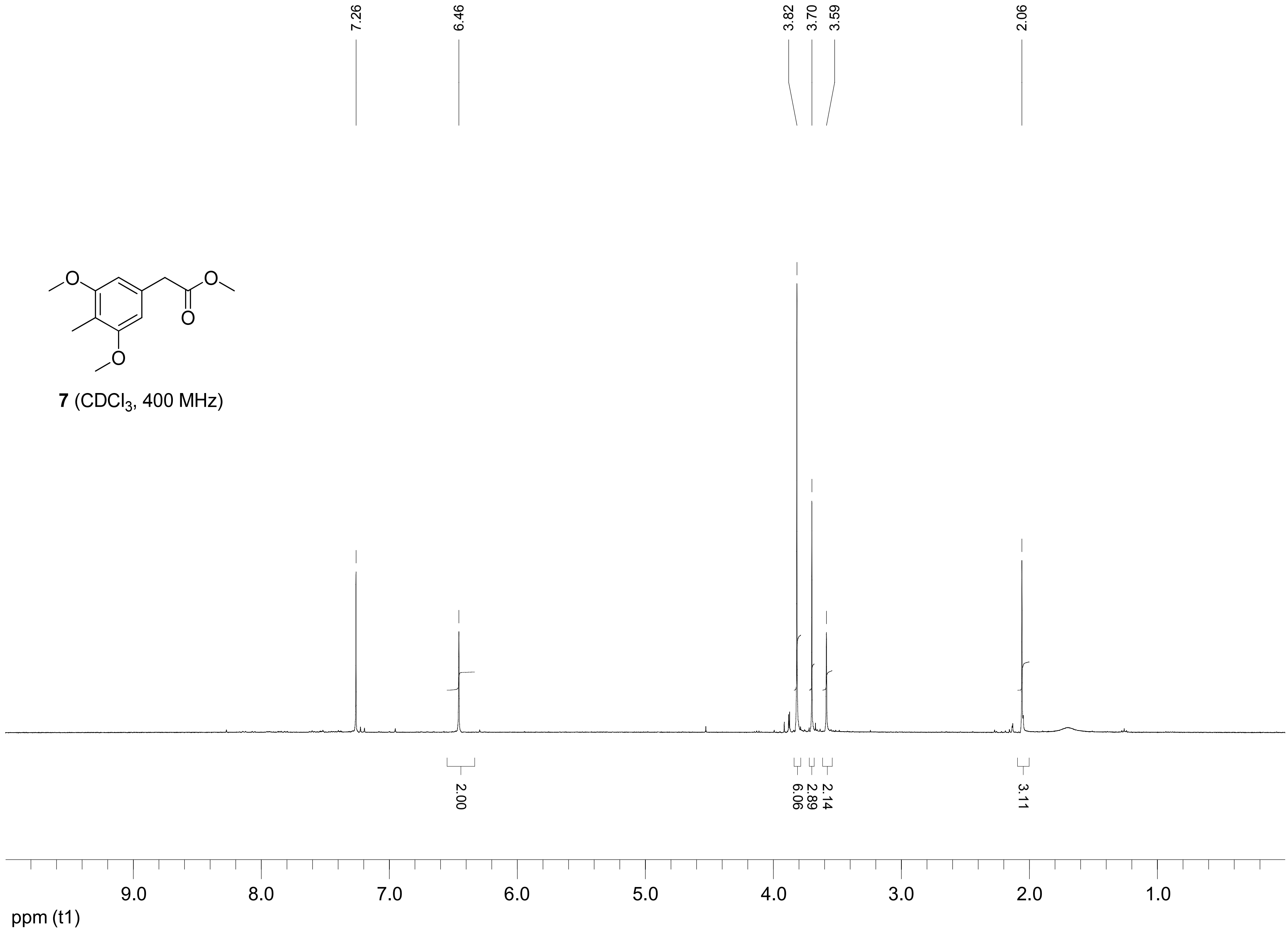
5 ($CDCl_3$, 600 MHz)

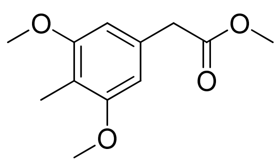




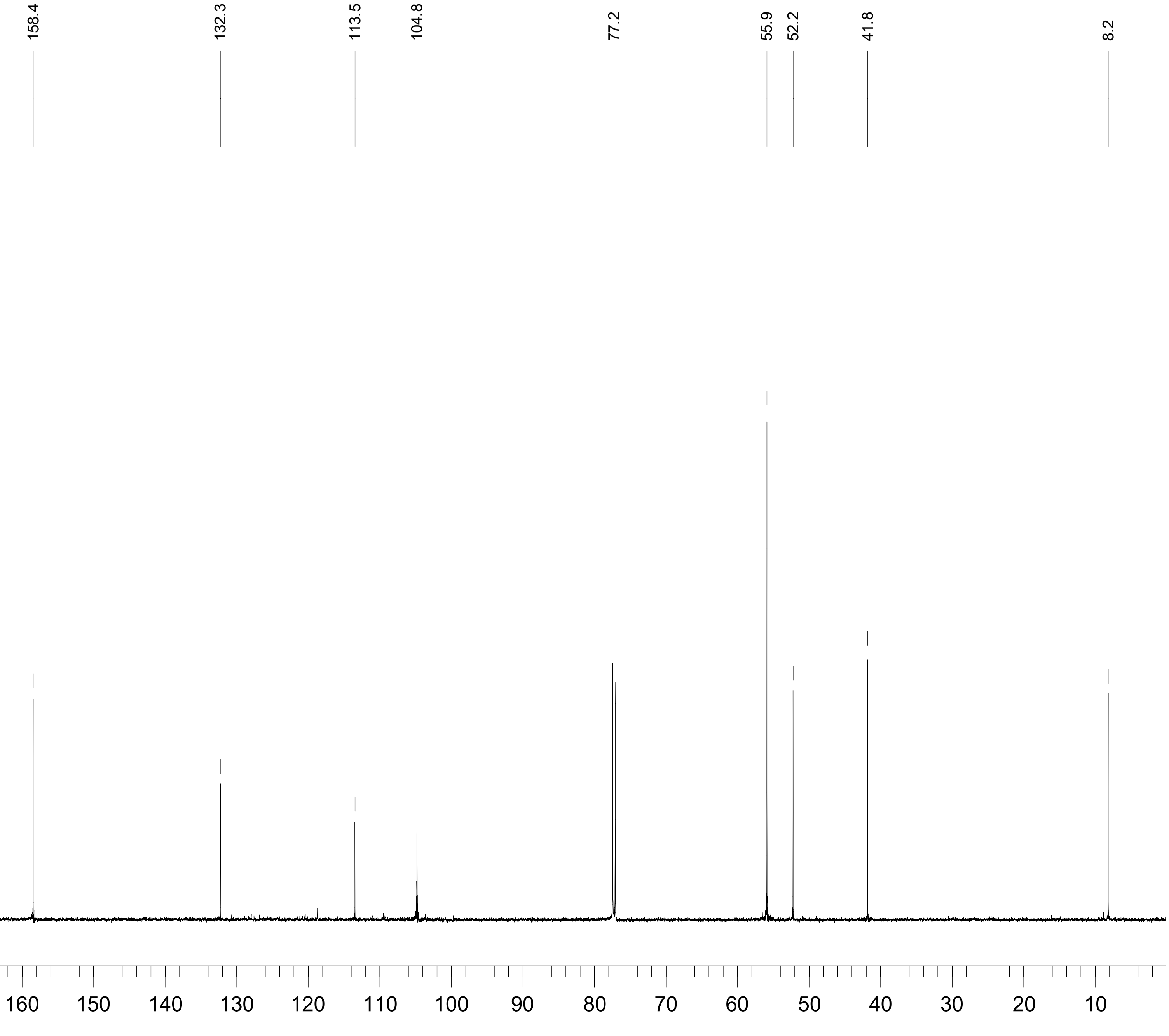
5 ($CDCl_3$, 150 MHz)

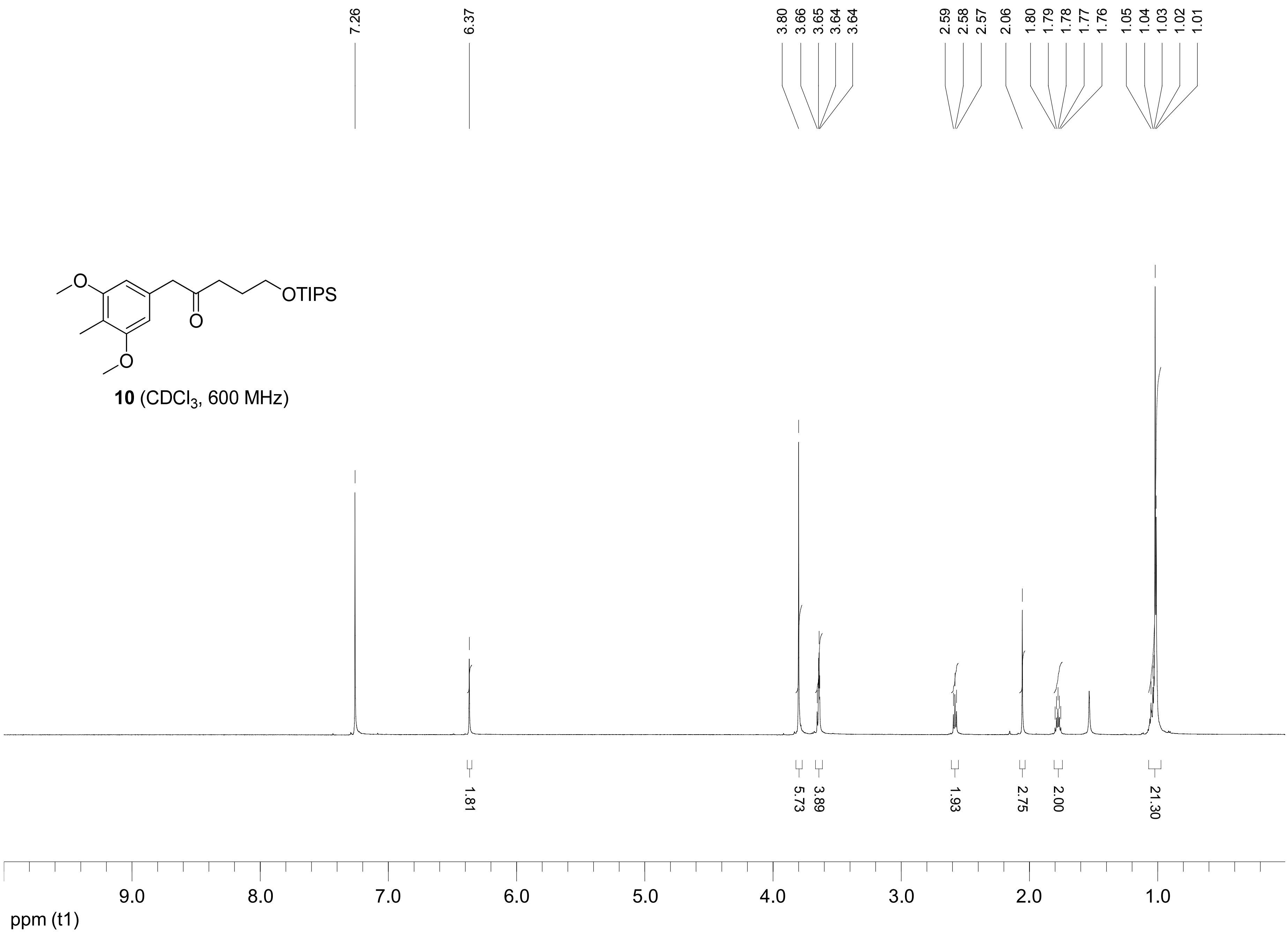
7 ($CDCl_3$, 400 MHz)



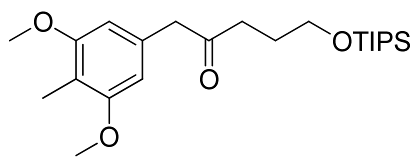


7 ($CDCl_3$, 150 MHz)

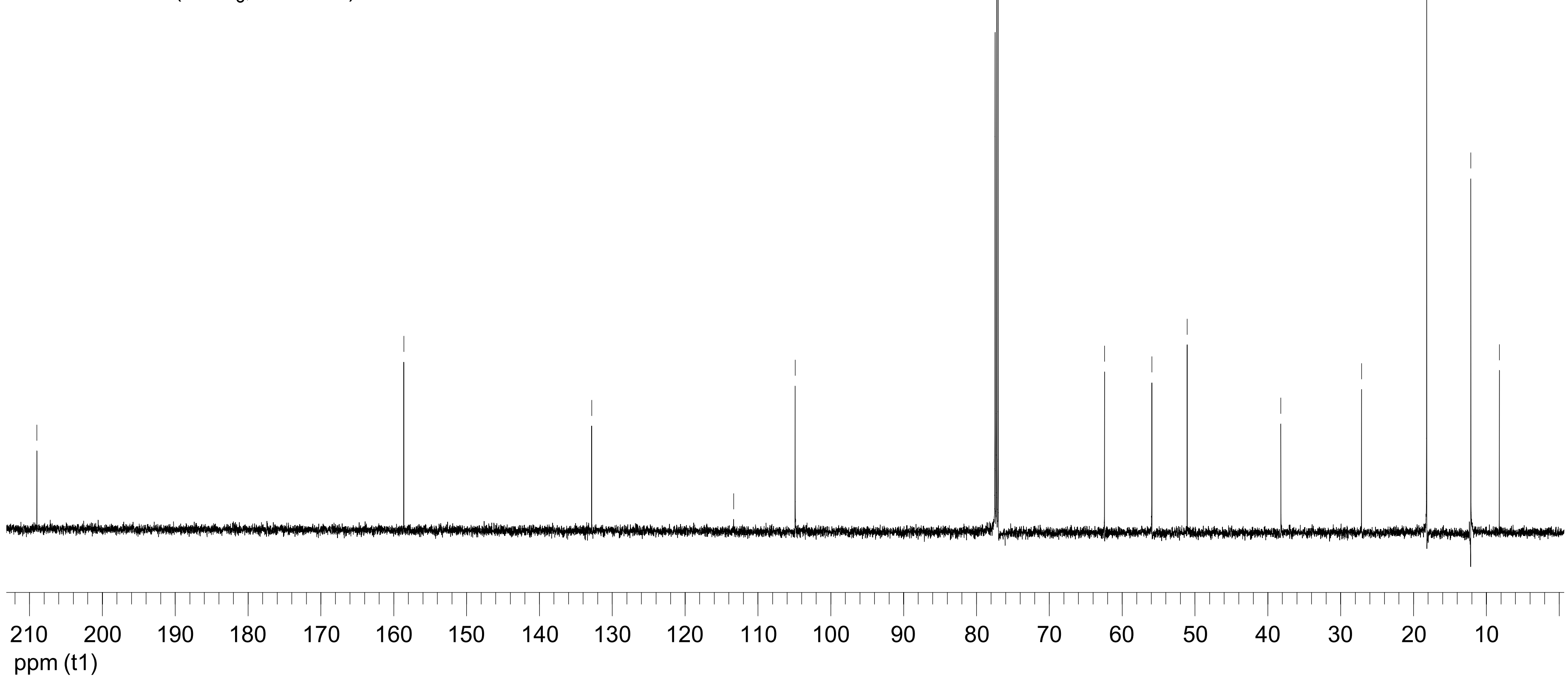


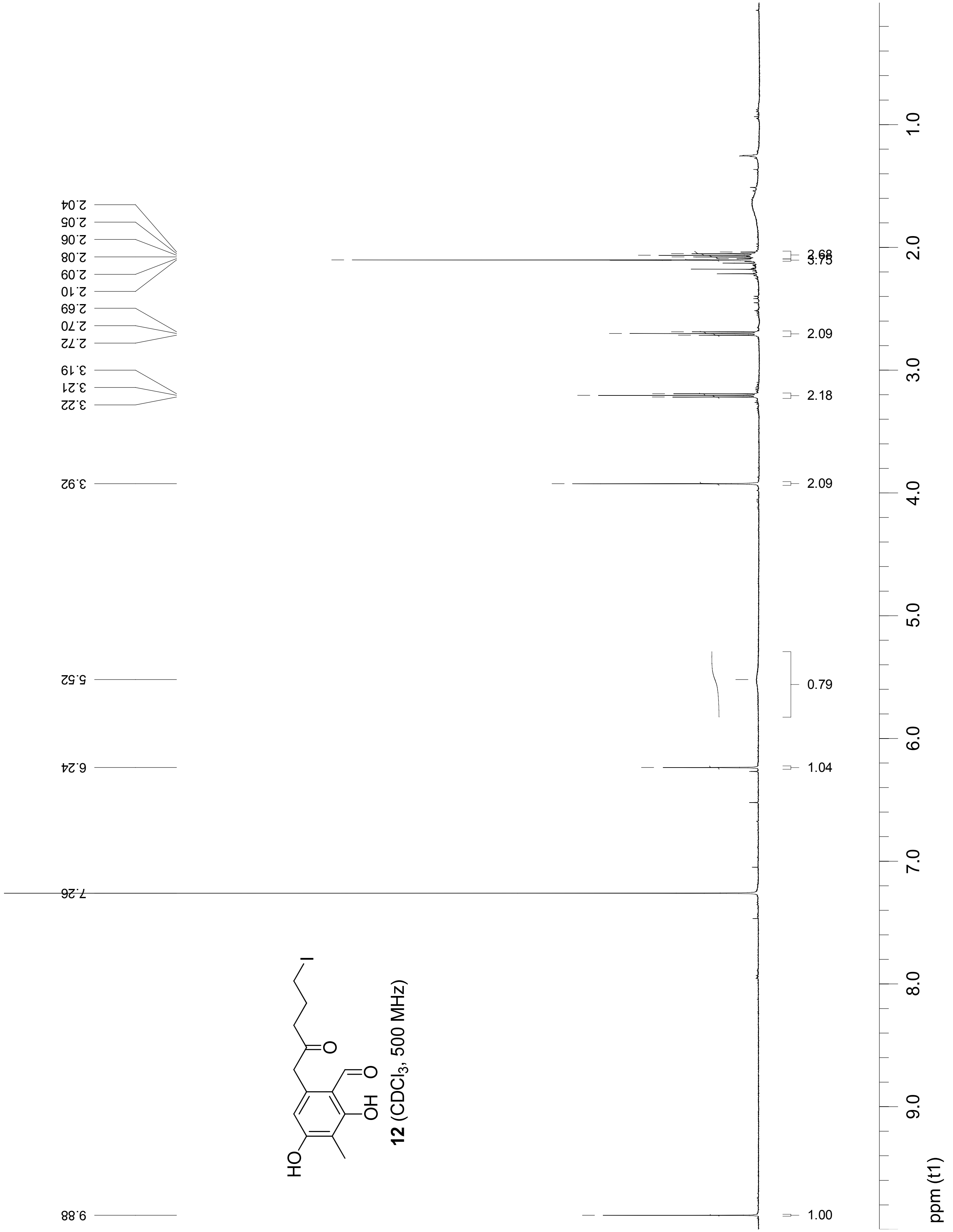


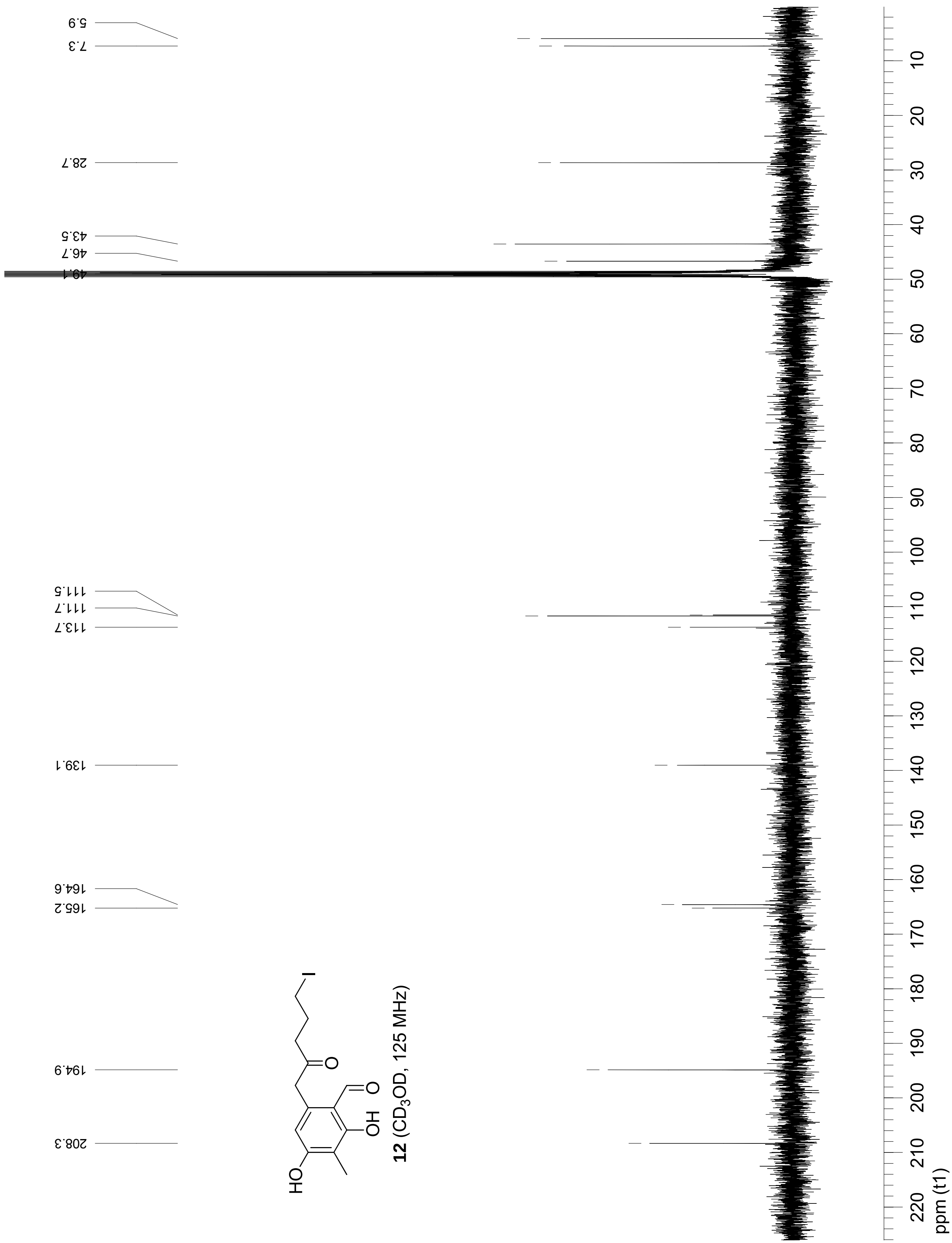
10 ($CDCl_3$, 600 MHz)



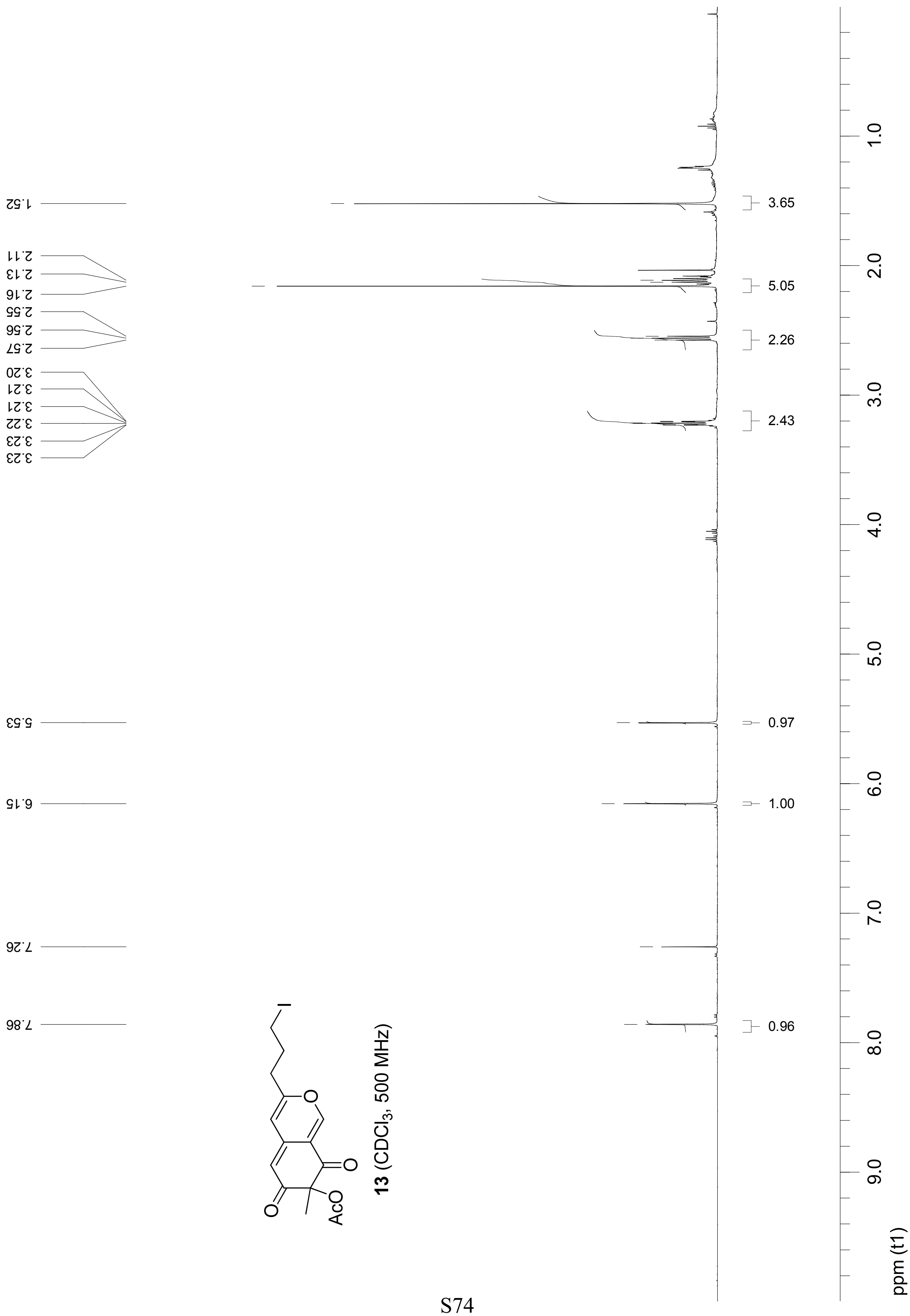
10 ($CDCl_3$, 150 MHz)



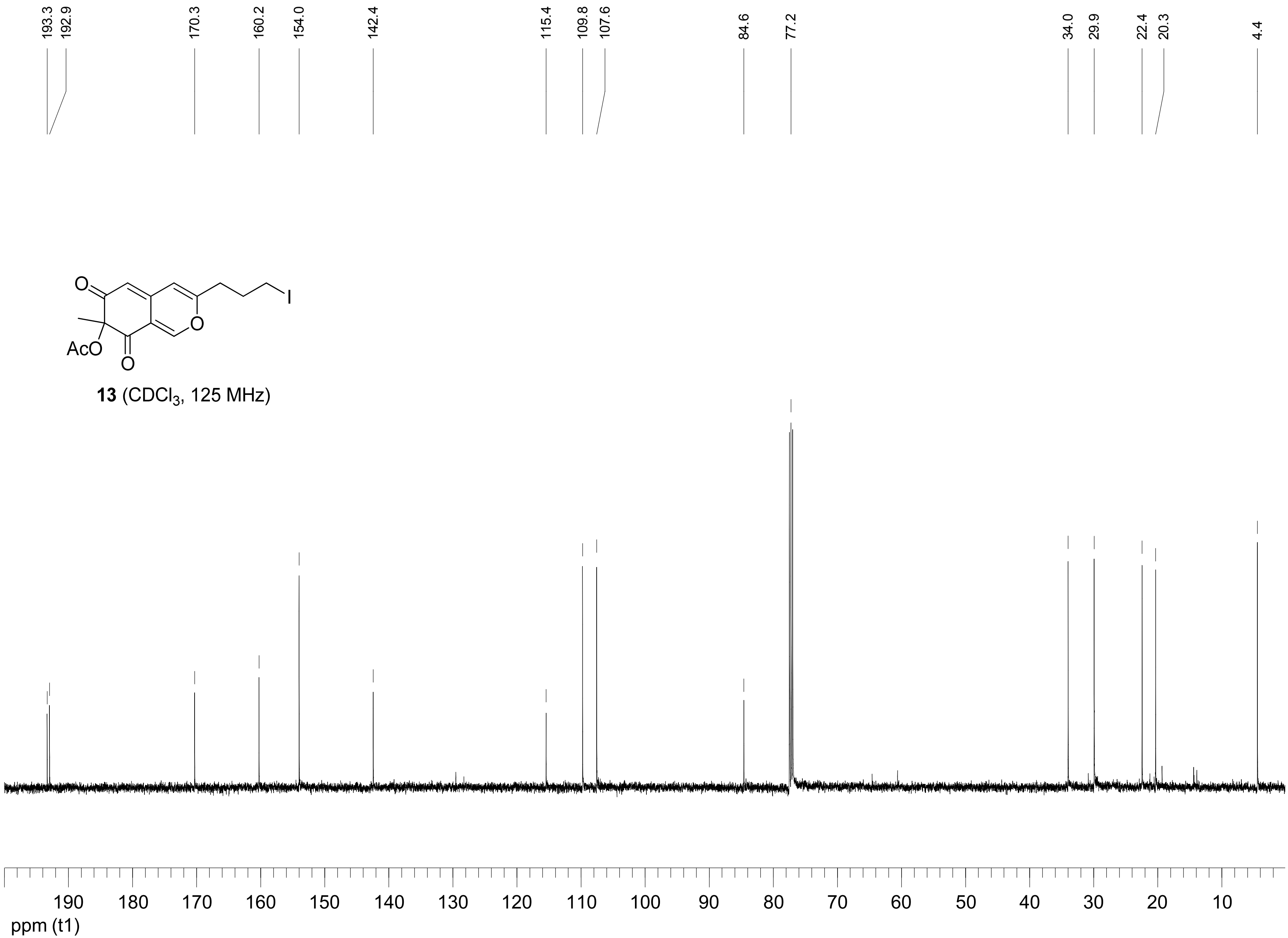

12 (CDCl$_3$, 500 MHz)
HO
OH
O
O
I
2.04
2.05
2.06
2.08
2.09
2.10
2.69
2.70
2.72
3.19
3.21
3.22
3.92
5.52
6.24
7.26
9.88
2.68
3.75
2.09
2.18
2.09
0.79
1.04
1.00
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
ppm (t1)



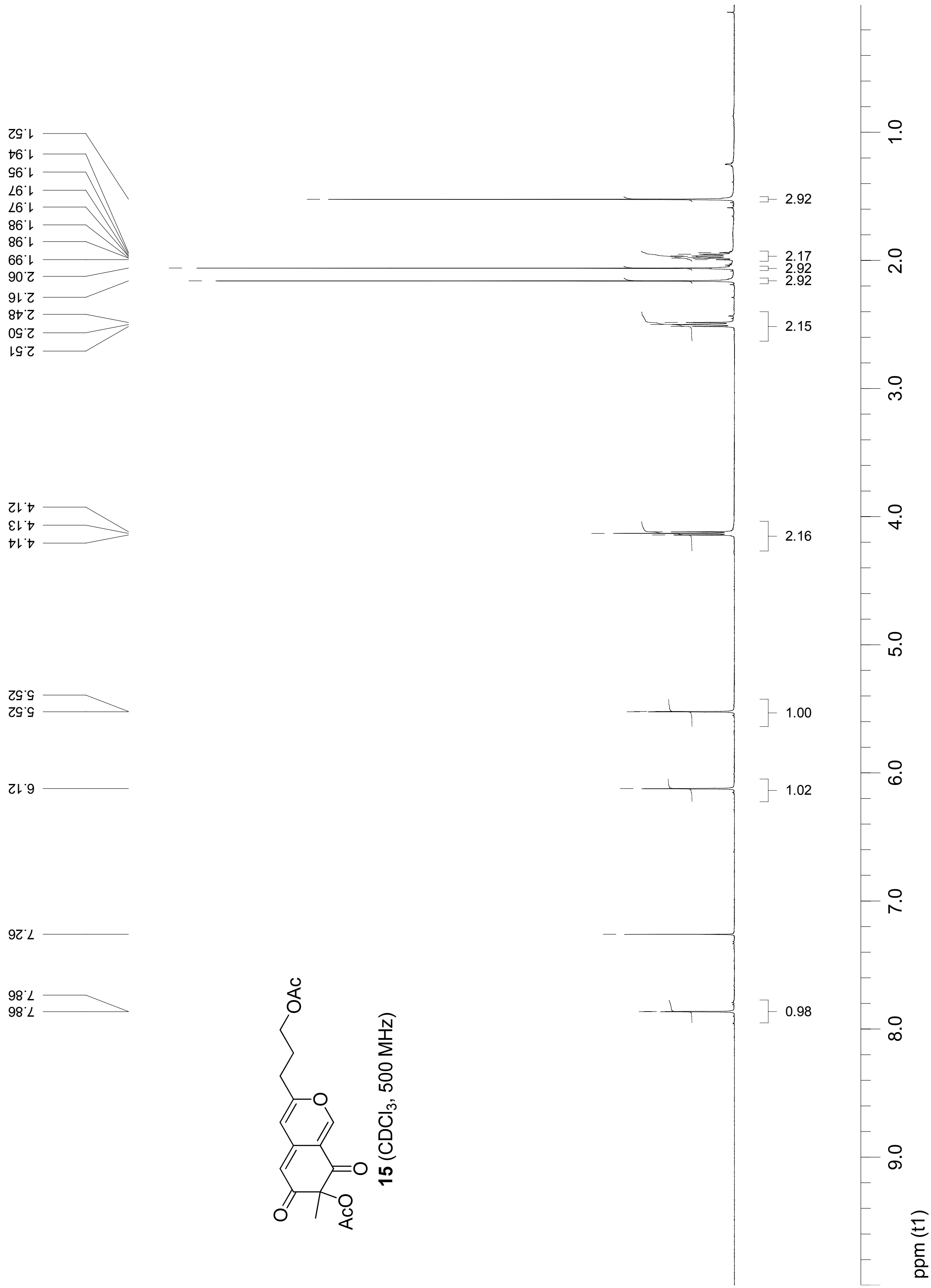
12 (CD_3OD, 125 MHz)



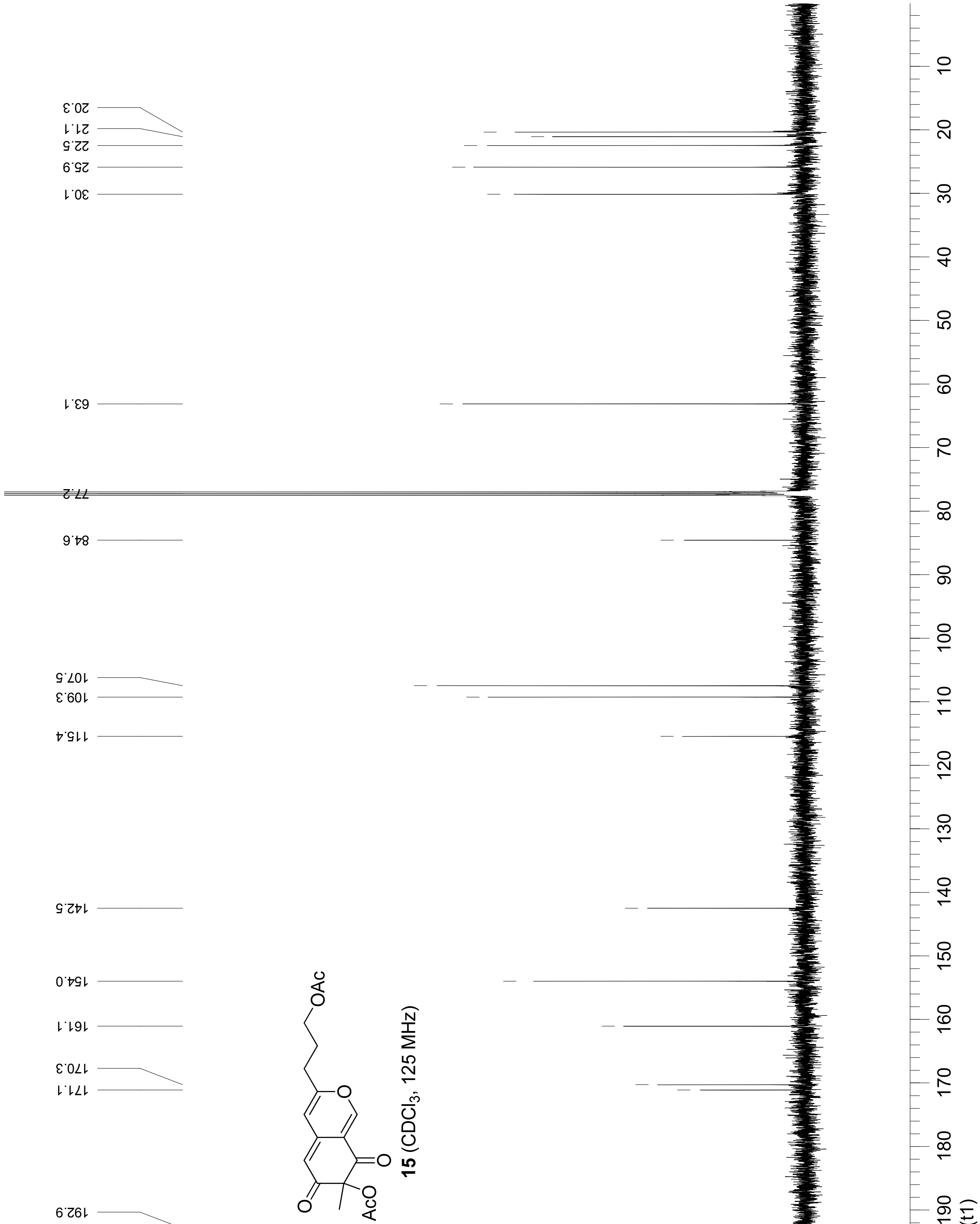
13 ($CDCl_3$, 500 MHz)



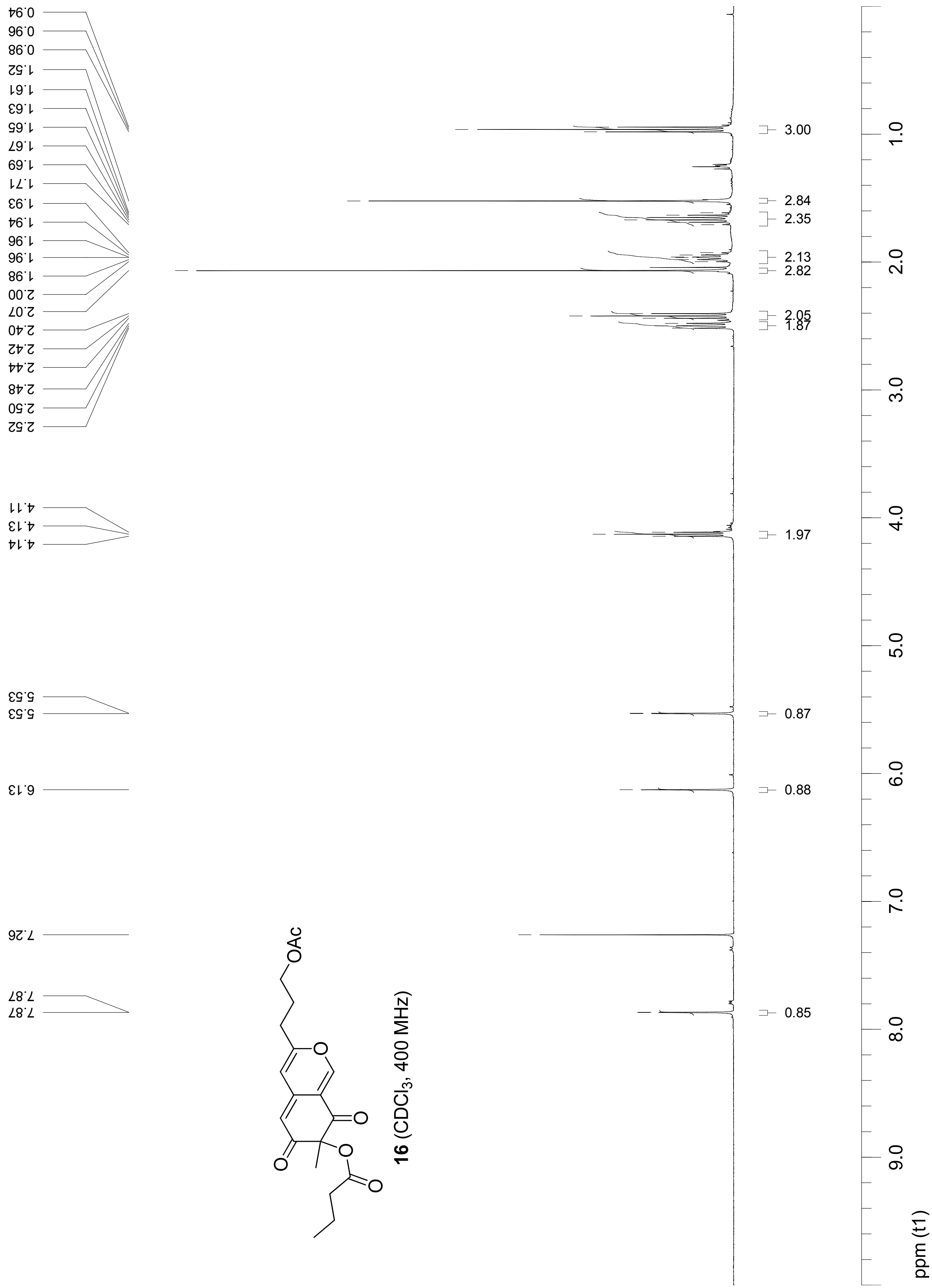
13 ($CDCl_3$, 125 MHz)



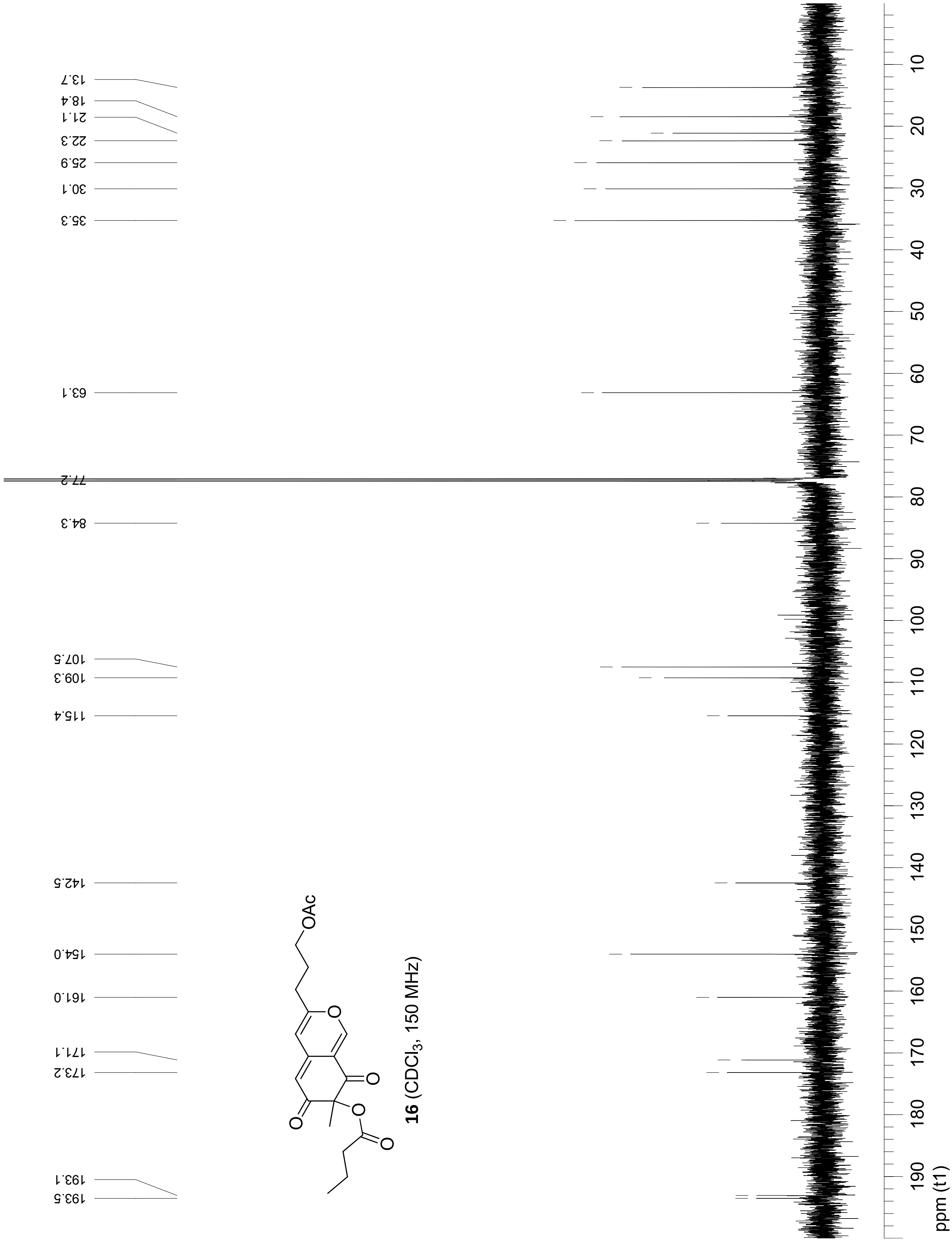
15 ($CDCl_3$, 500 MHz)



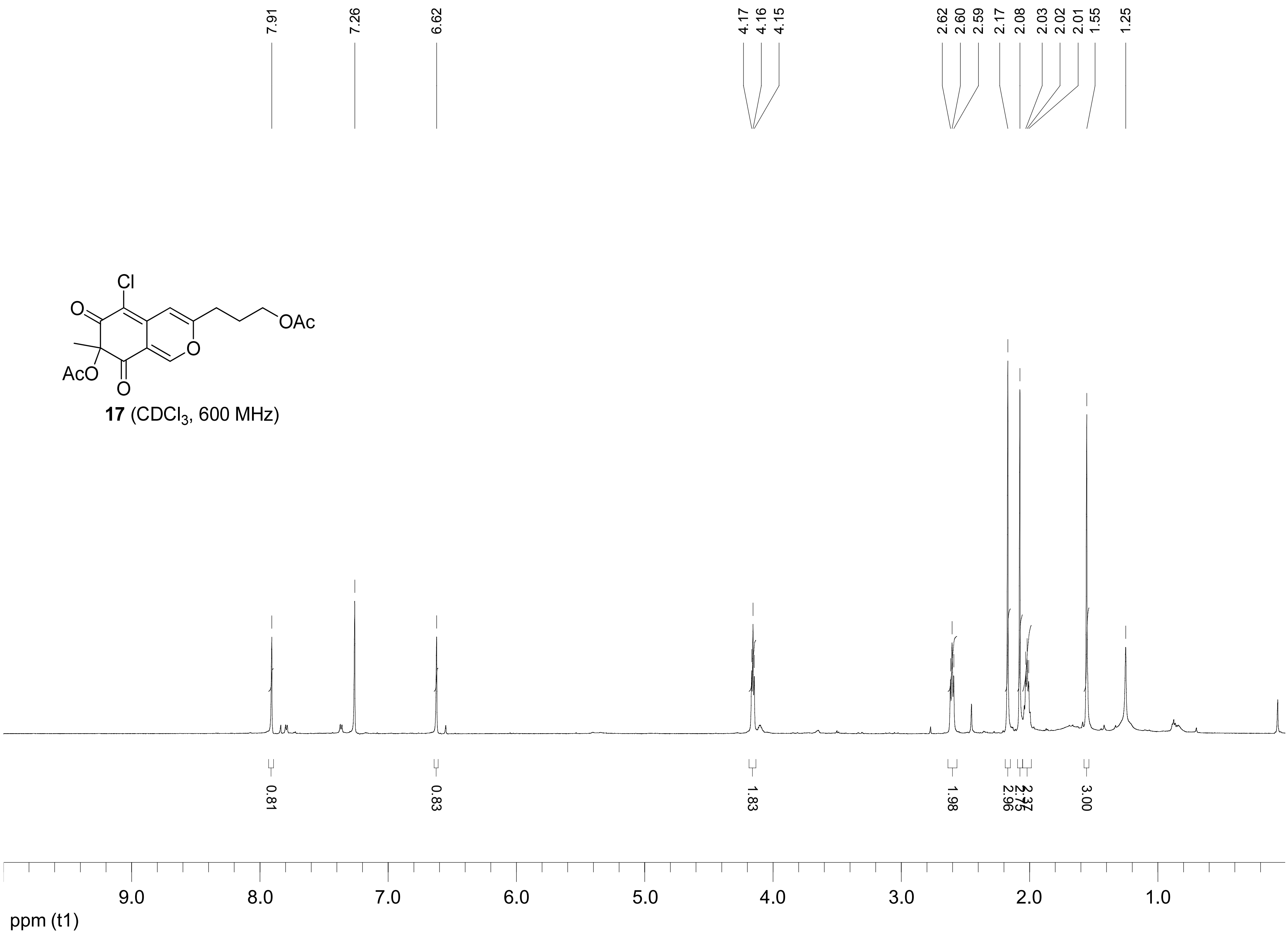
15 (CDCl$_3$, 125 MHz)



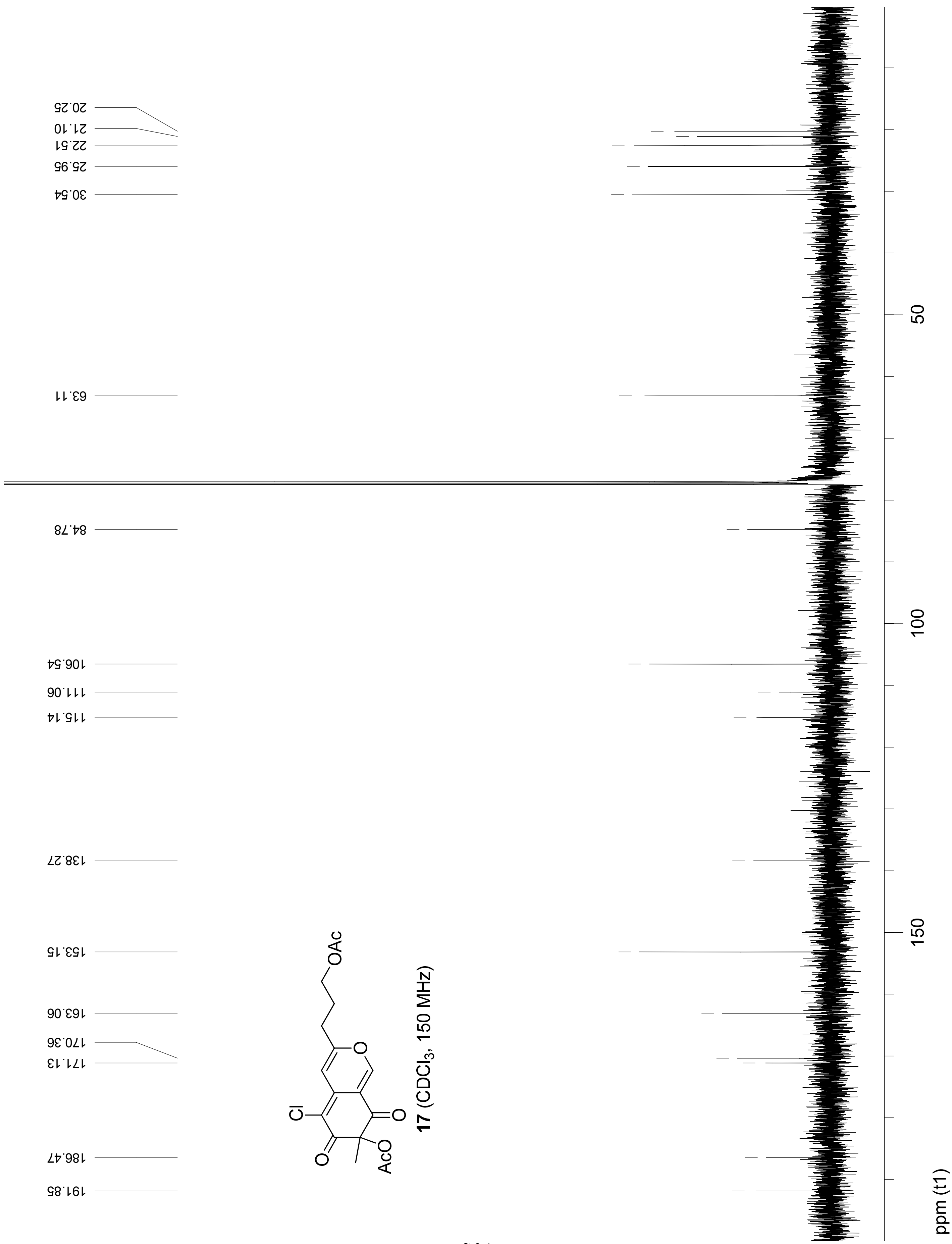
16 ($CDCl_3$, 400 MHz)



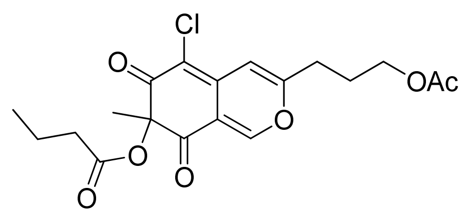
16 ($CDCl_3$, 150 MHz)



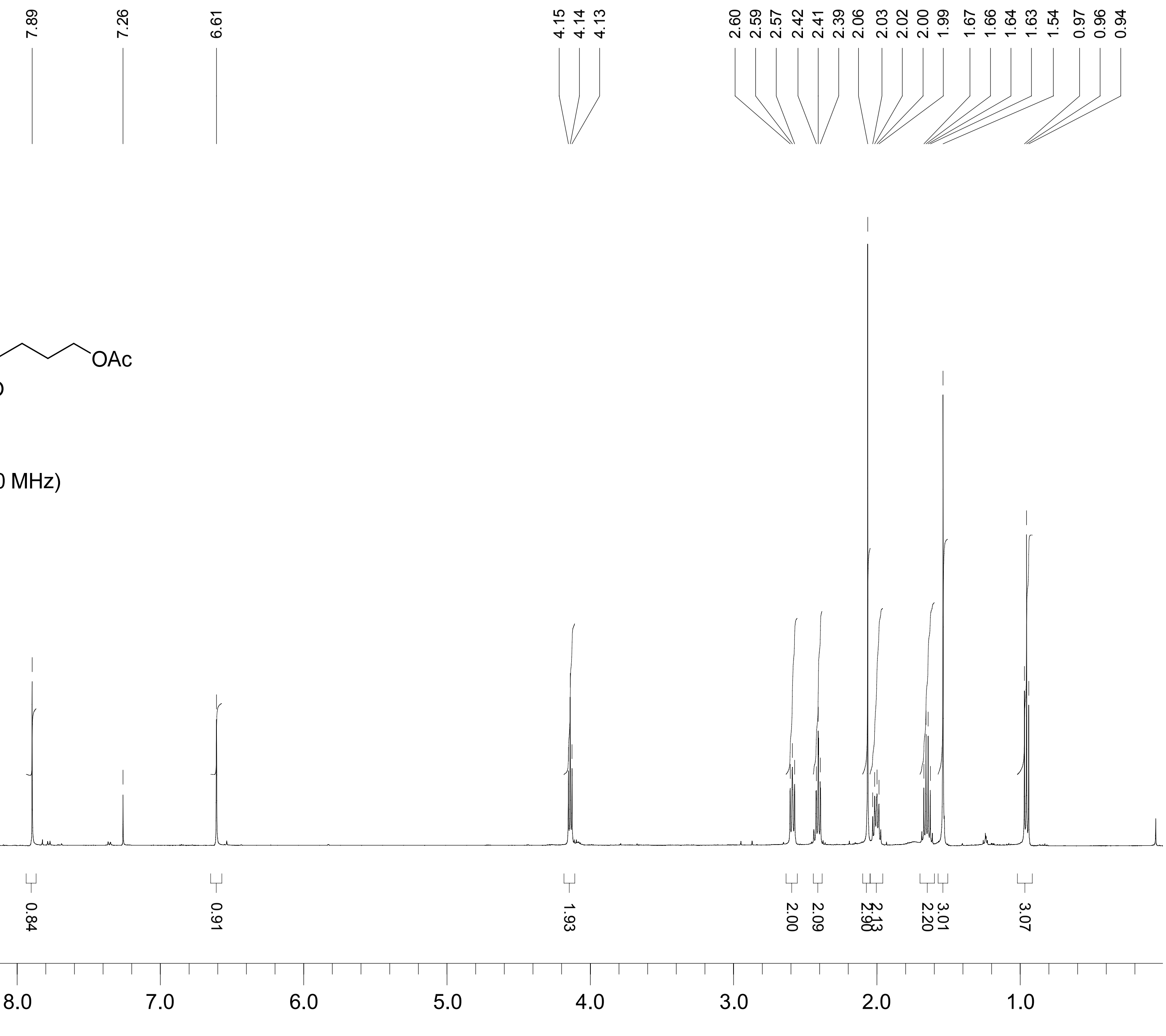
17 ($CDCl_3$, 600 MHz)

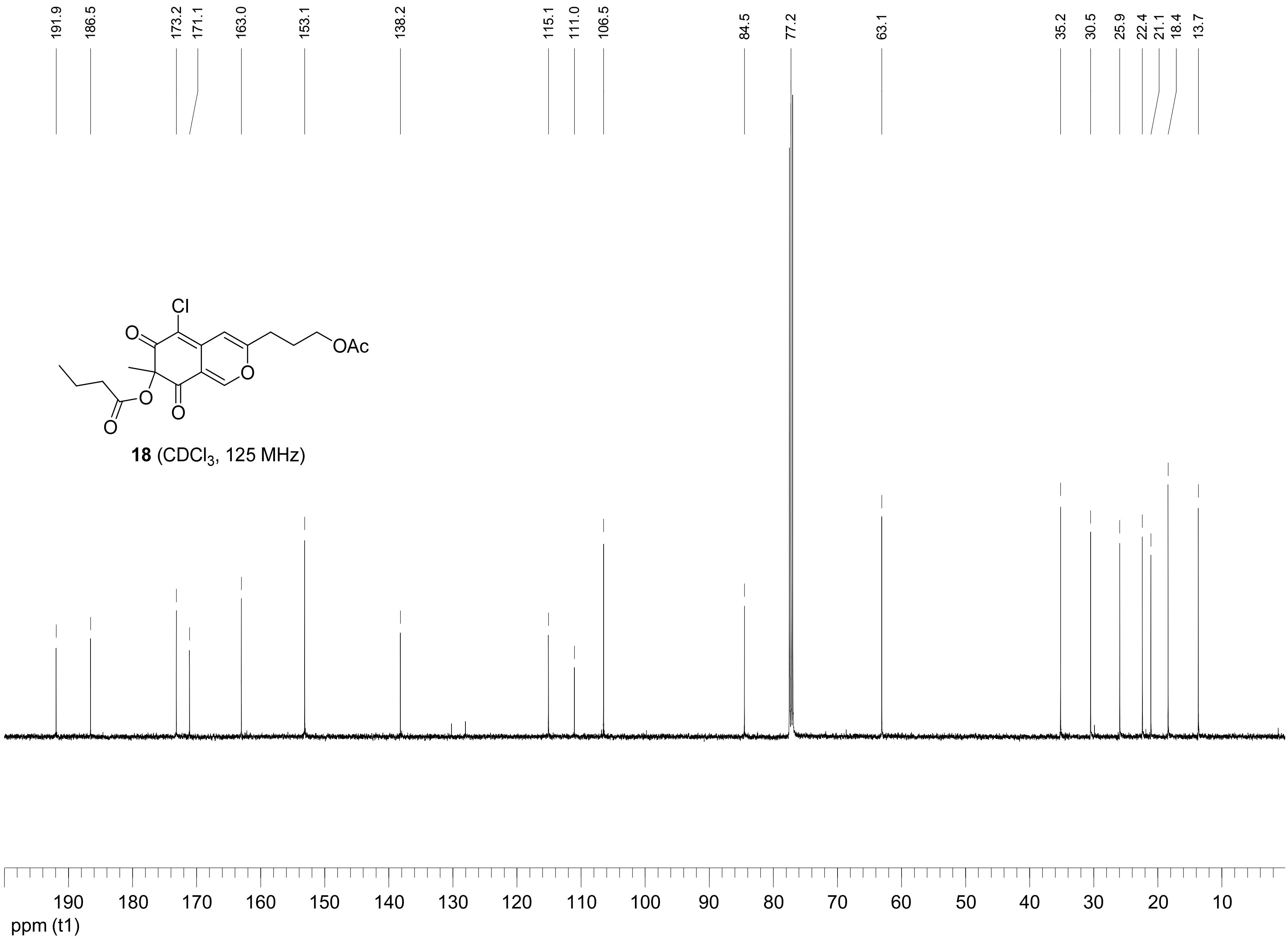


17 ($CDCl_3$, 150 MHz)

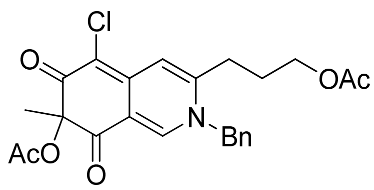


18 ($CDCl_3$, 500 MHz)

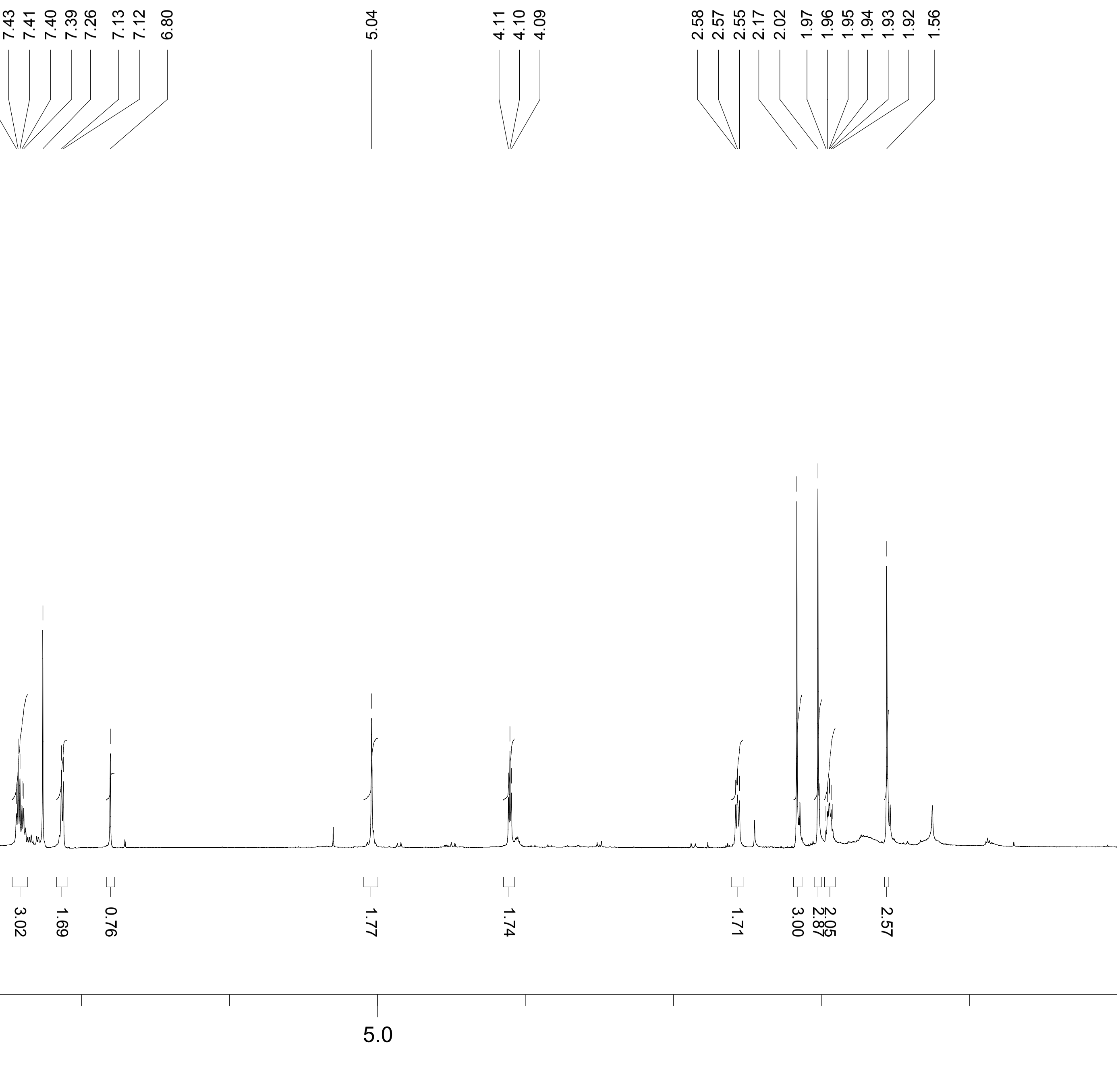


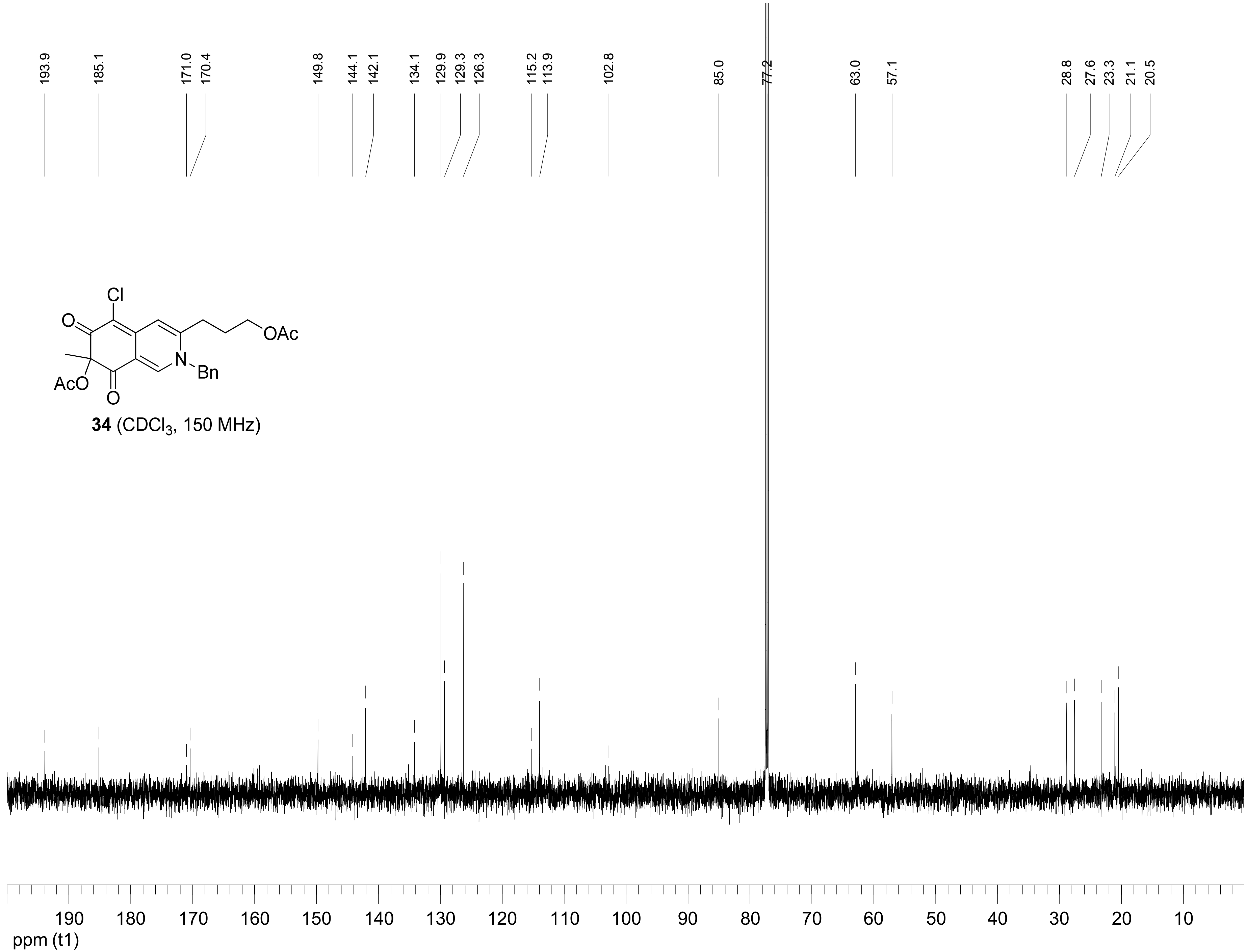


18 (CDCl$_3$, 125 MHz)

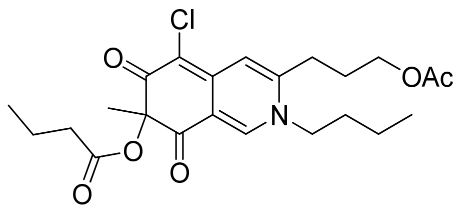


34 ($CDCl_3$, 600 MHz)

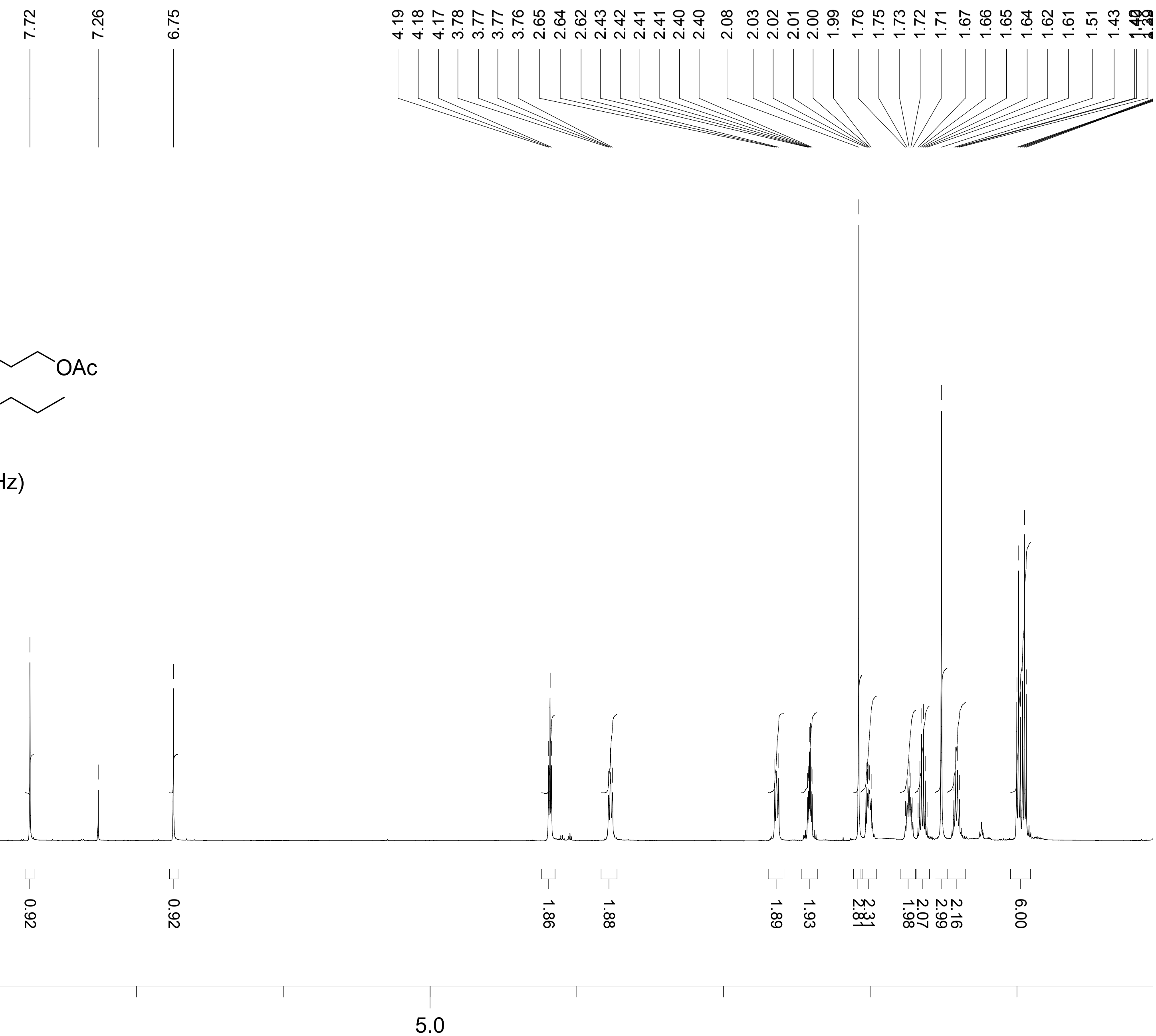


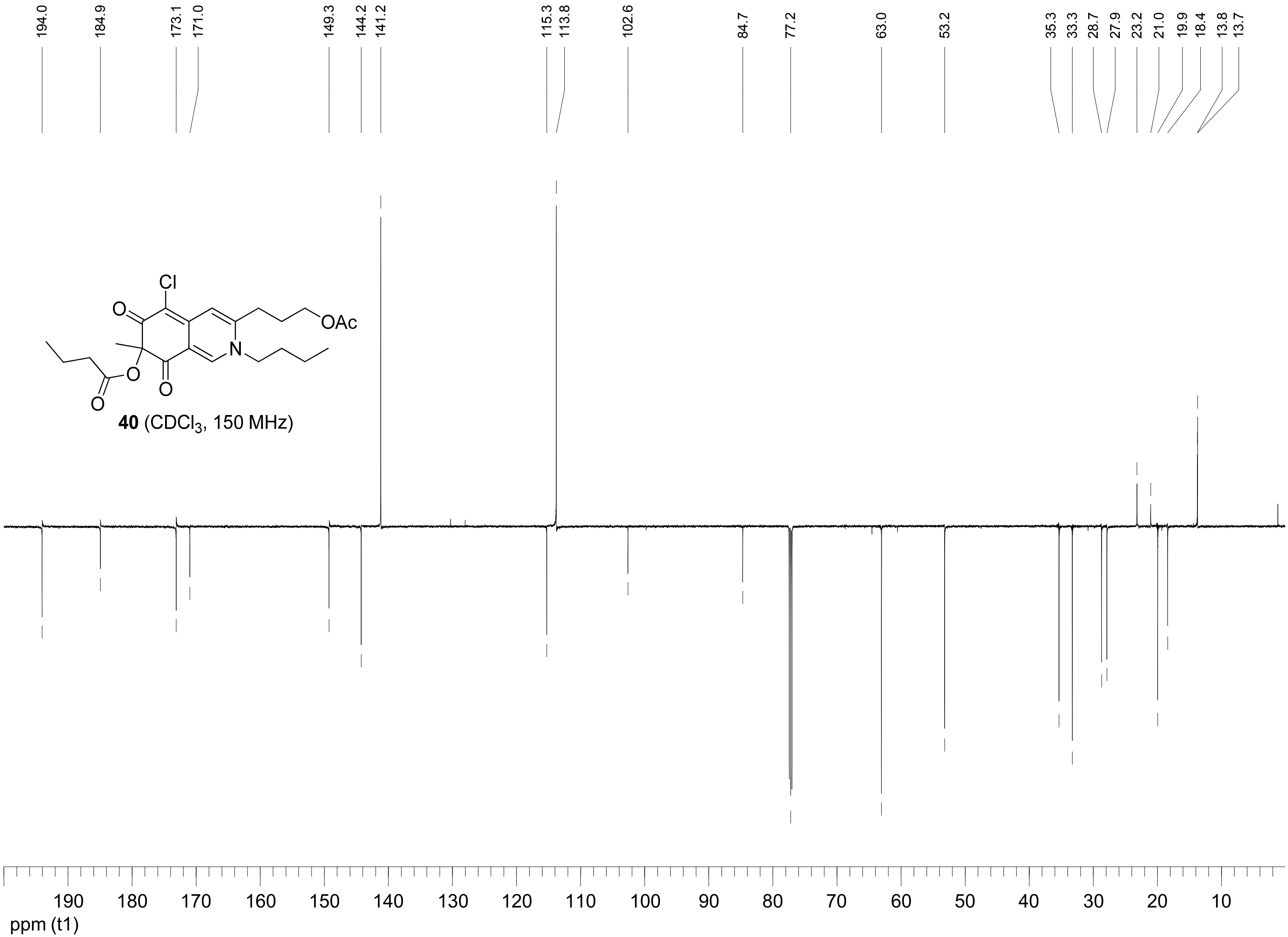


34 ($CDCl_3$, 150 MHz)



40 ($CDCl_3$, 600 MHz)





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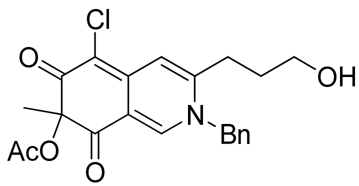

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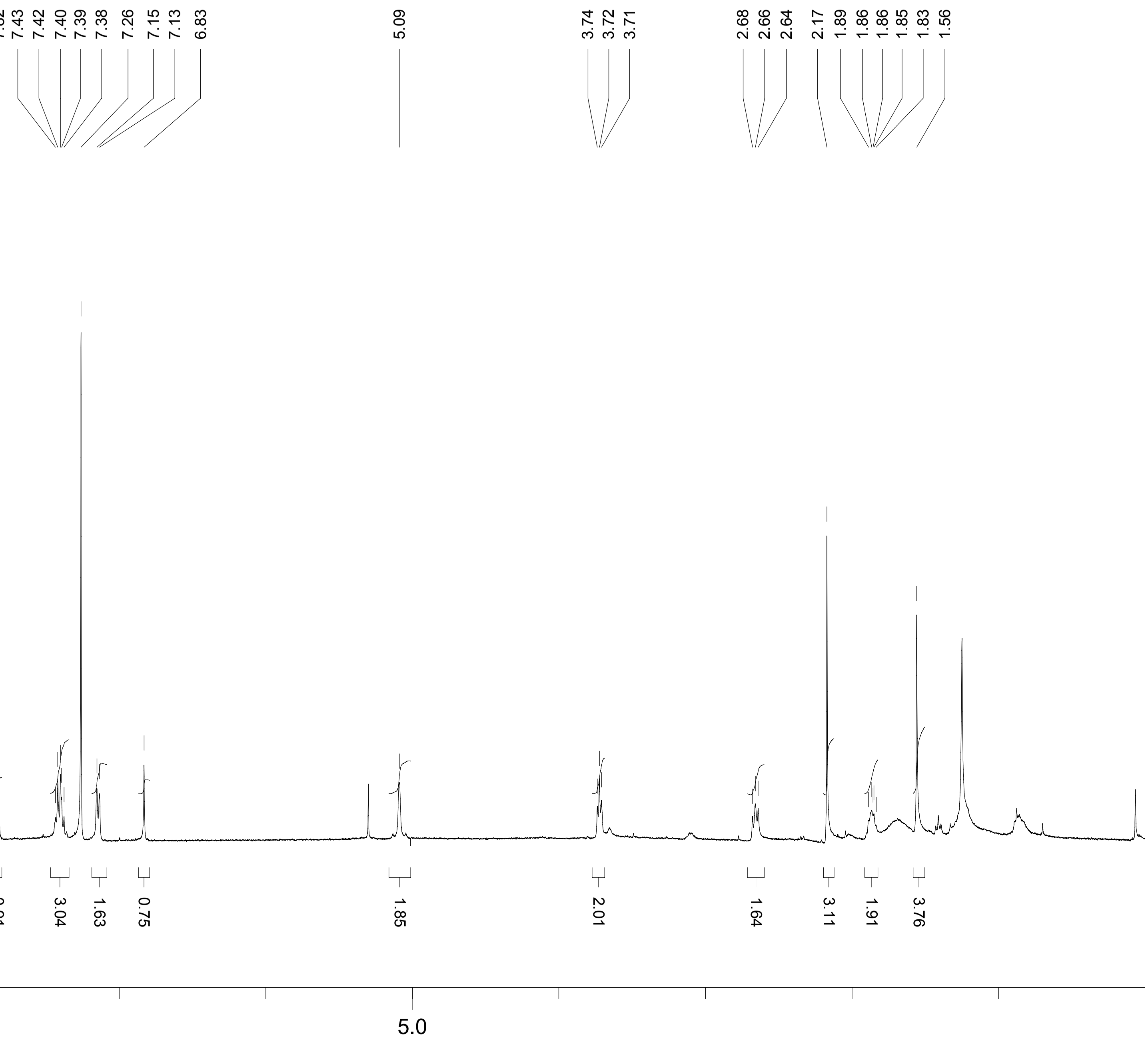

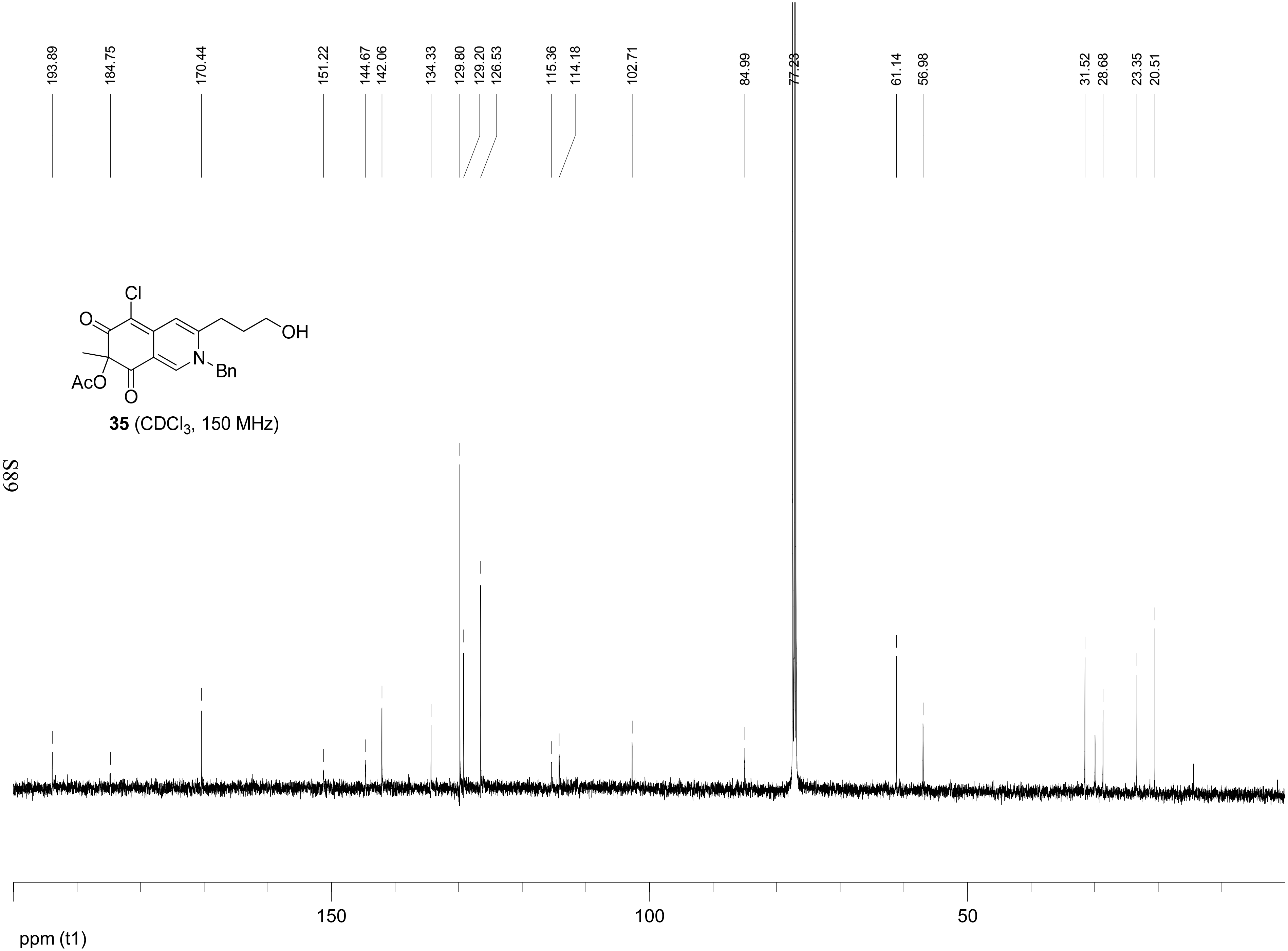

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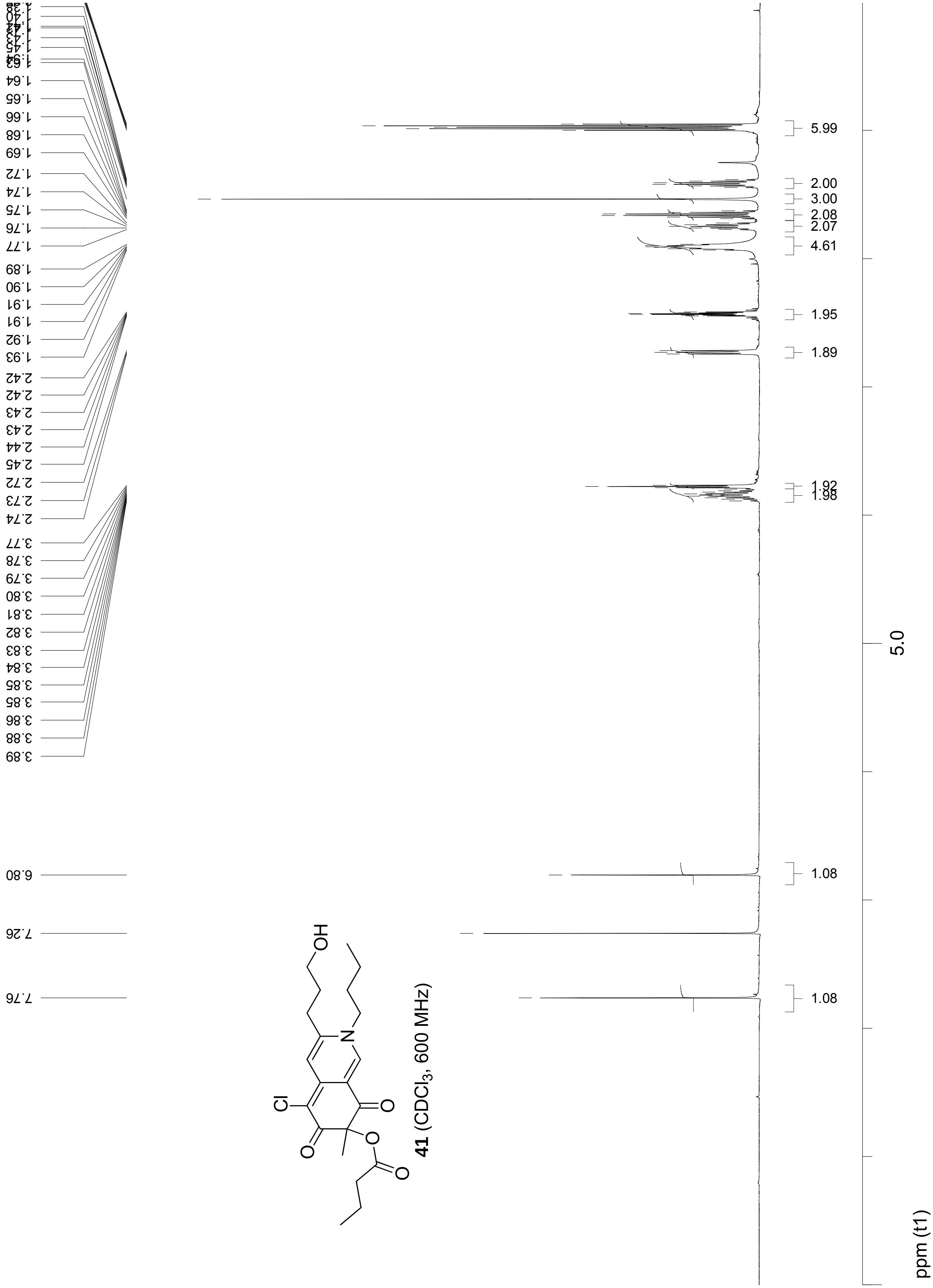
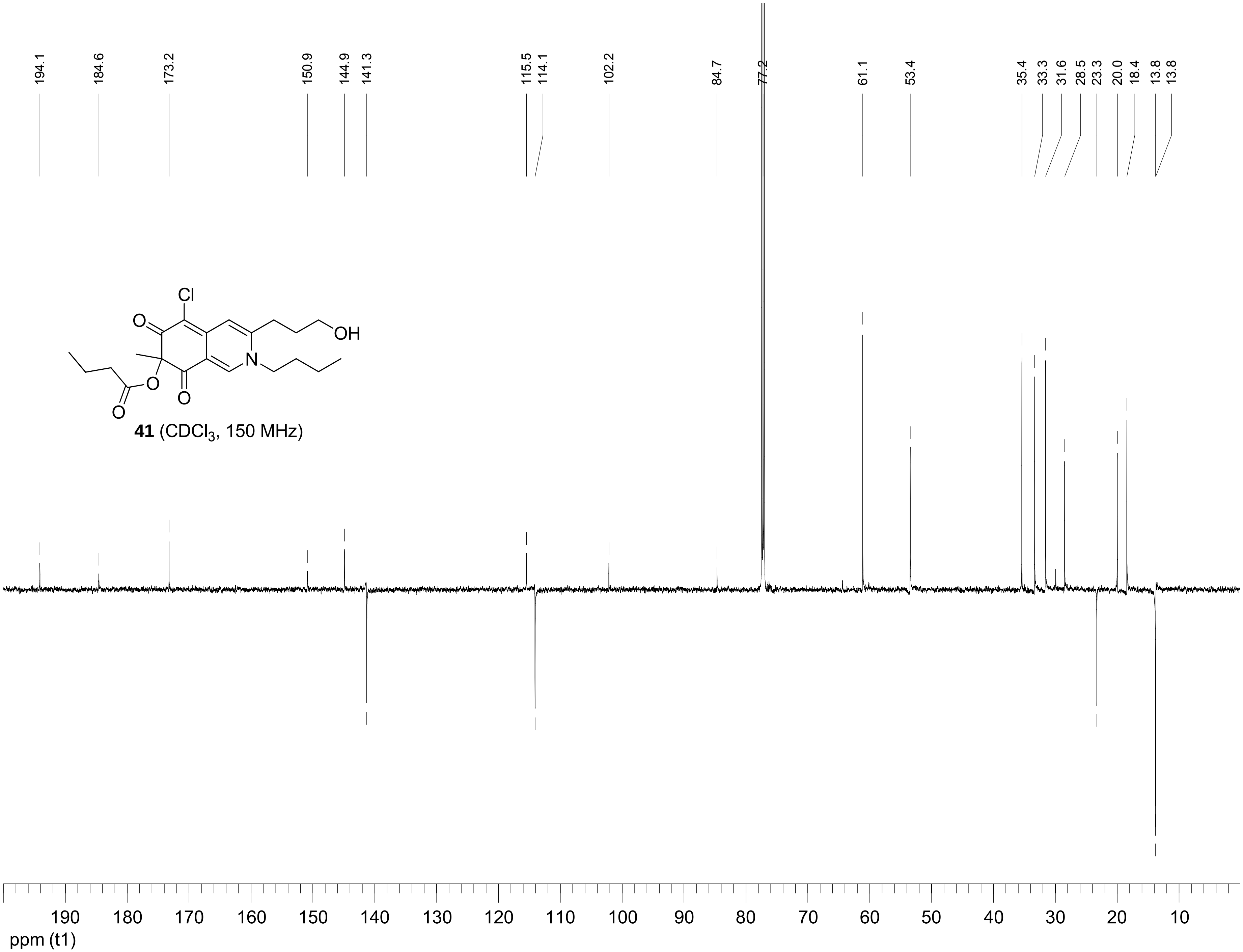
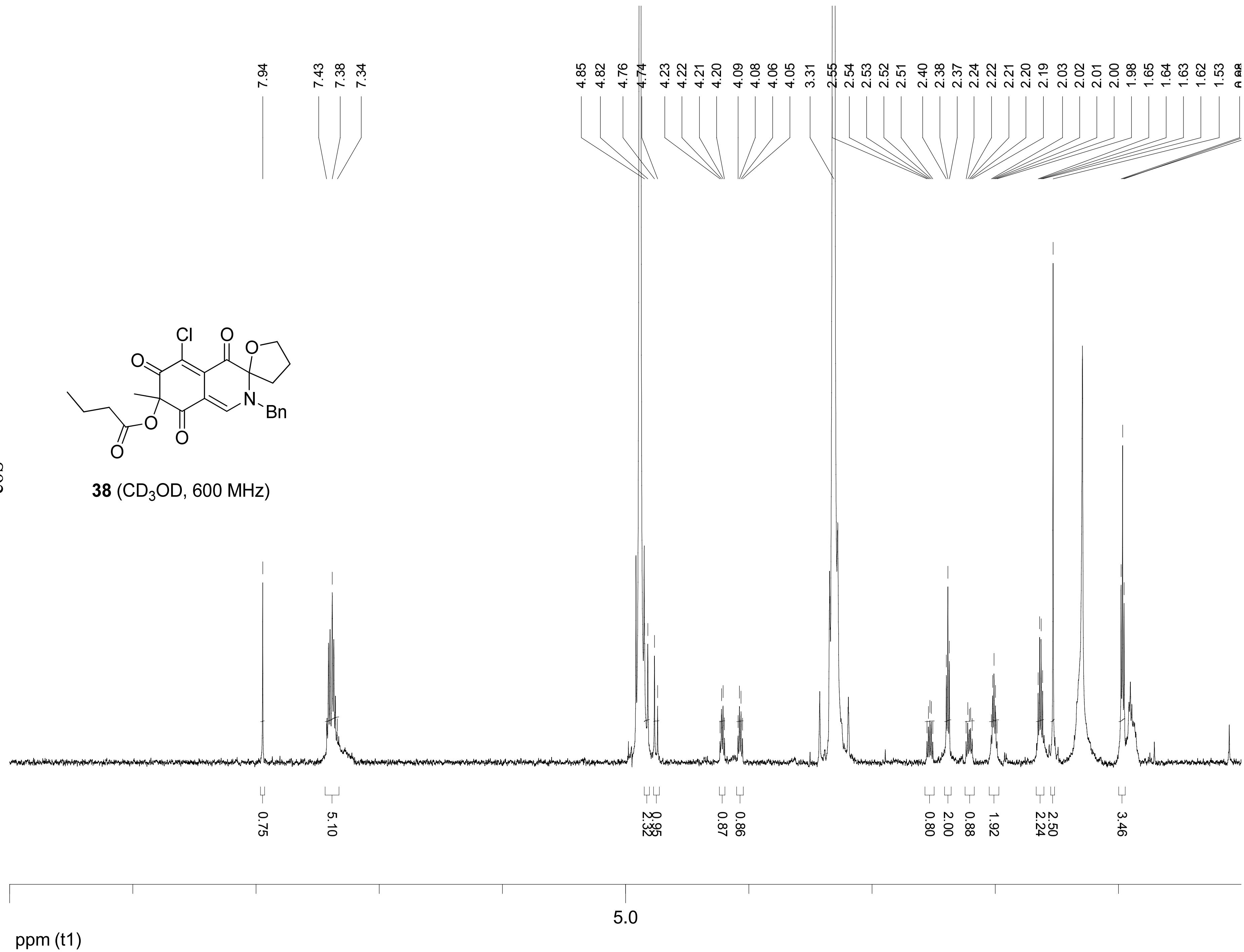


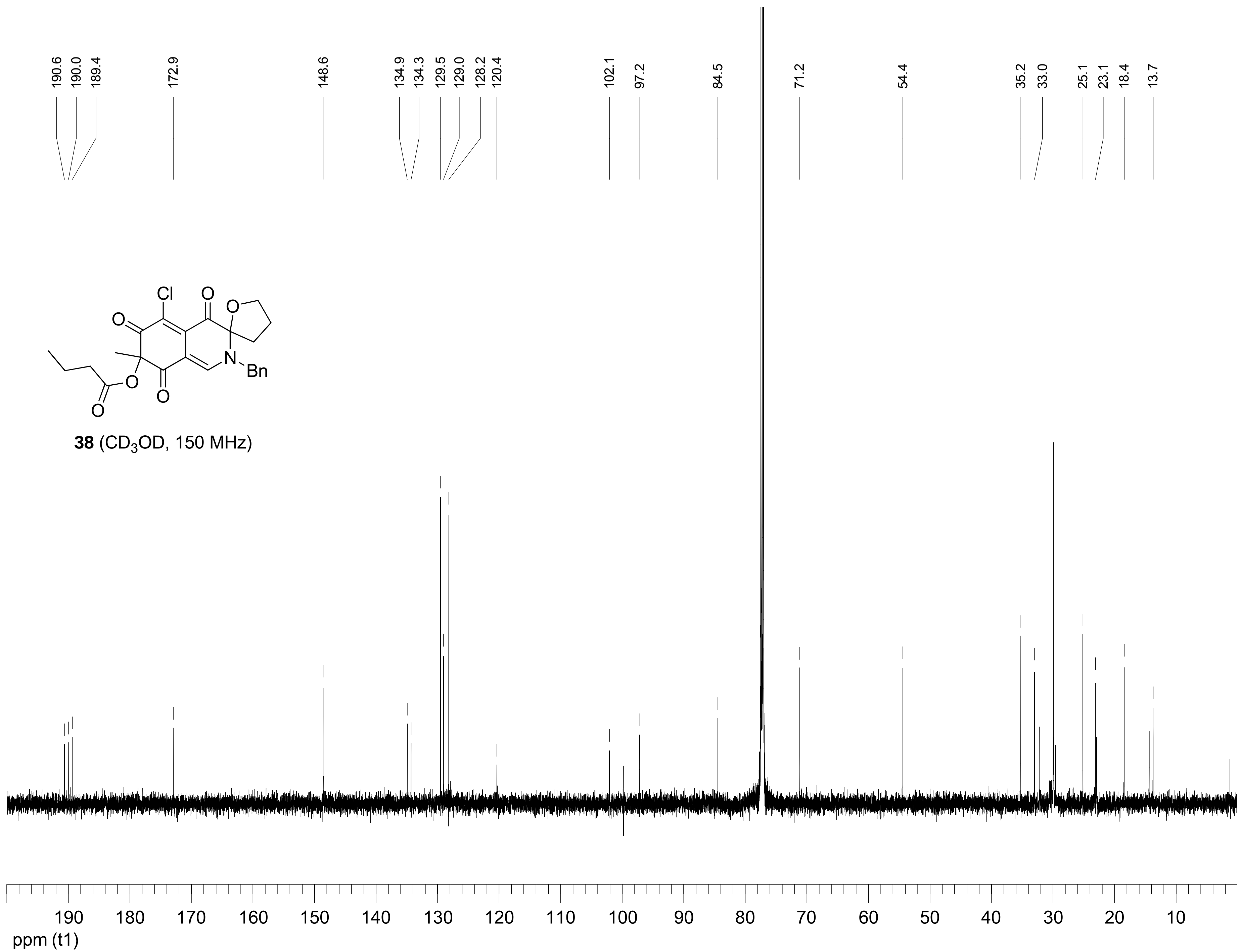
41 ($CDCl_3$, 600 MHz)



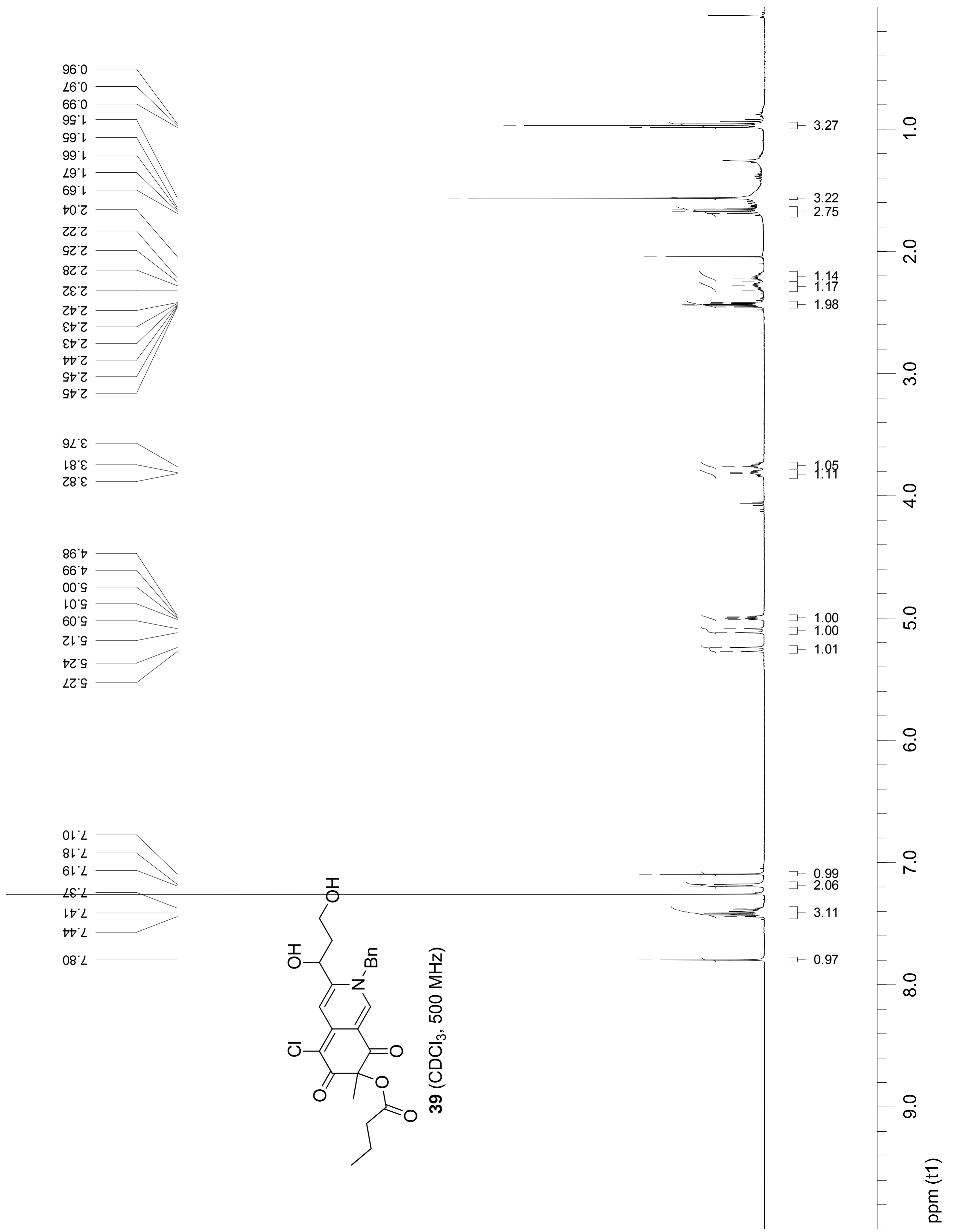
41 ($CDCl_3$, 150 MHz)



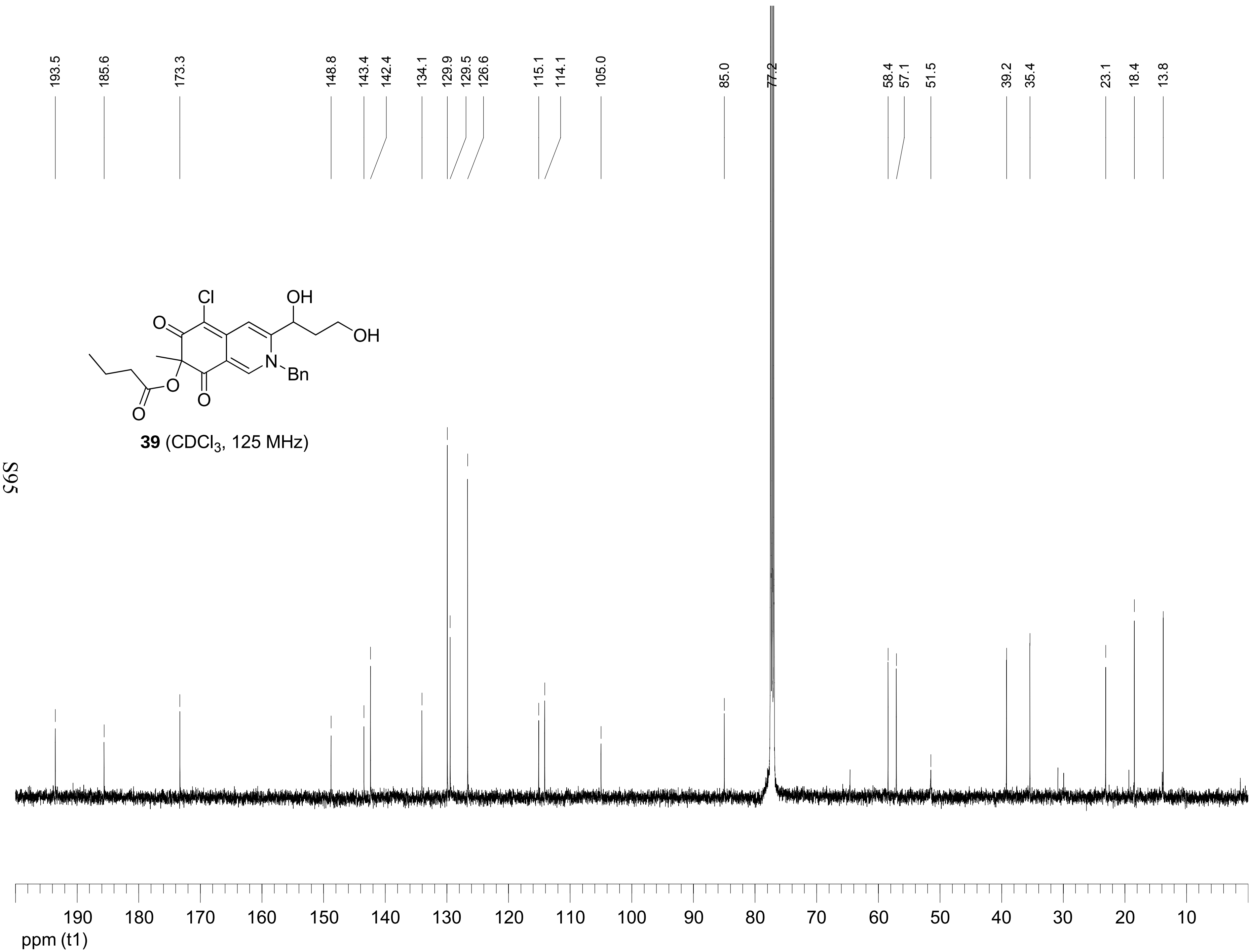
38 (CD_3OD, 600 MHz)



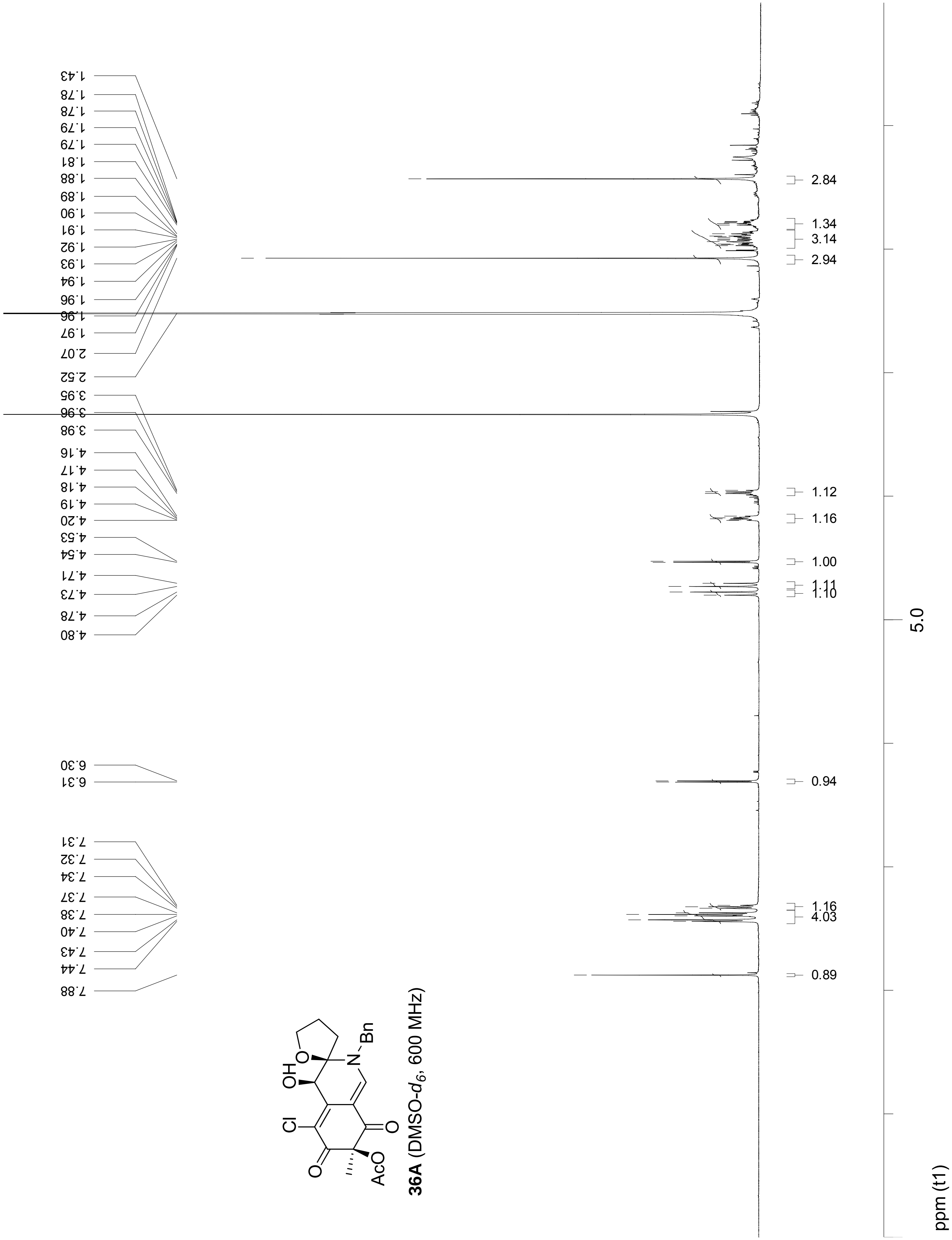
38 (CD_3OD, 150 MHz)



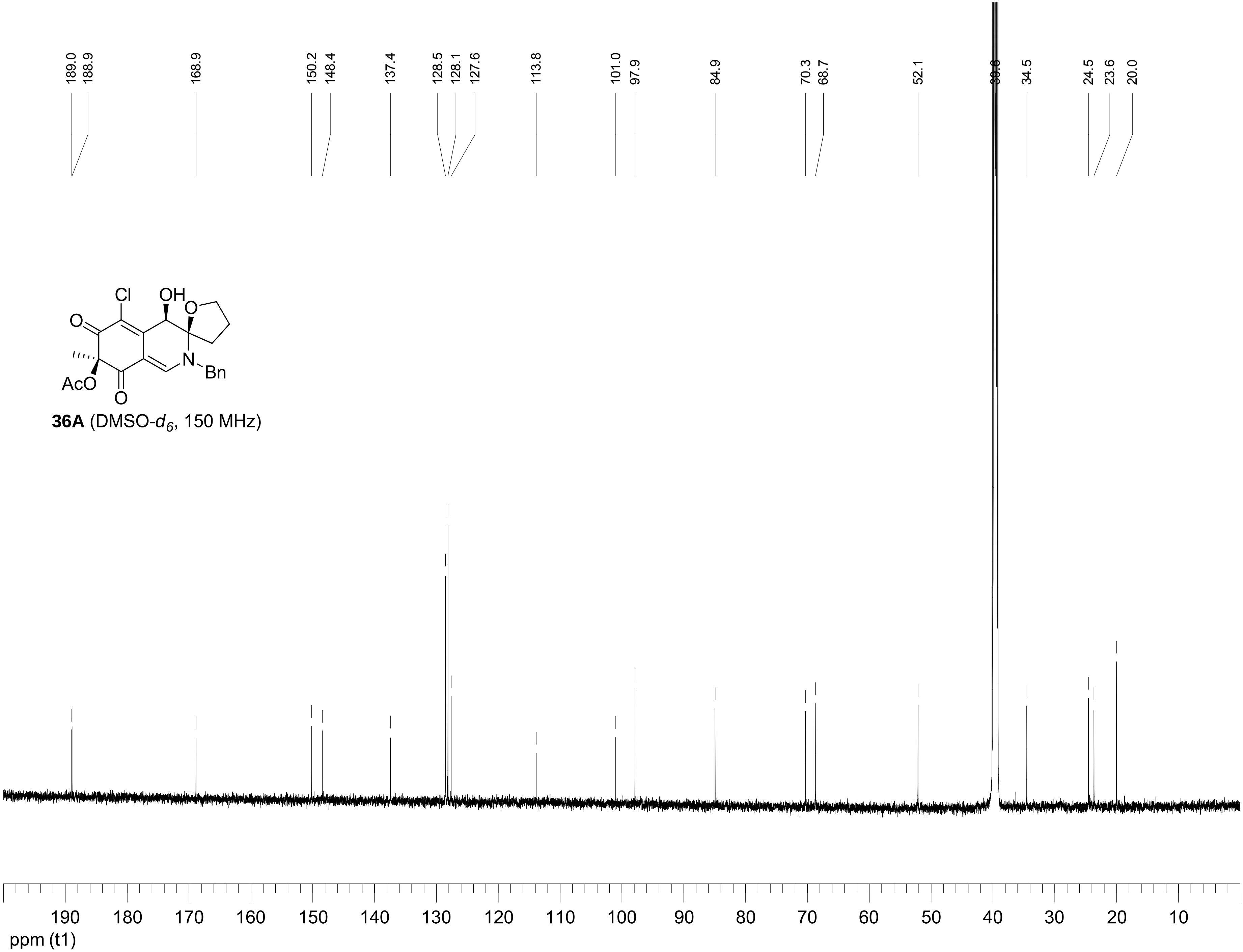
39 ($CDCl_3$, 500 MHz)



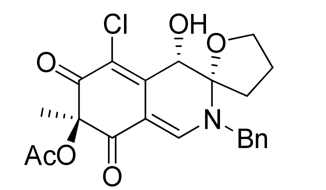
39 ($CDCl_3$, 125 MHz)



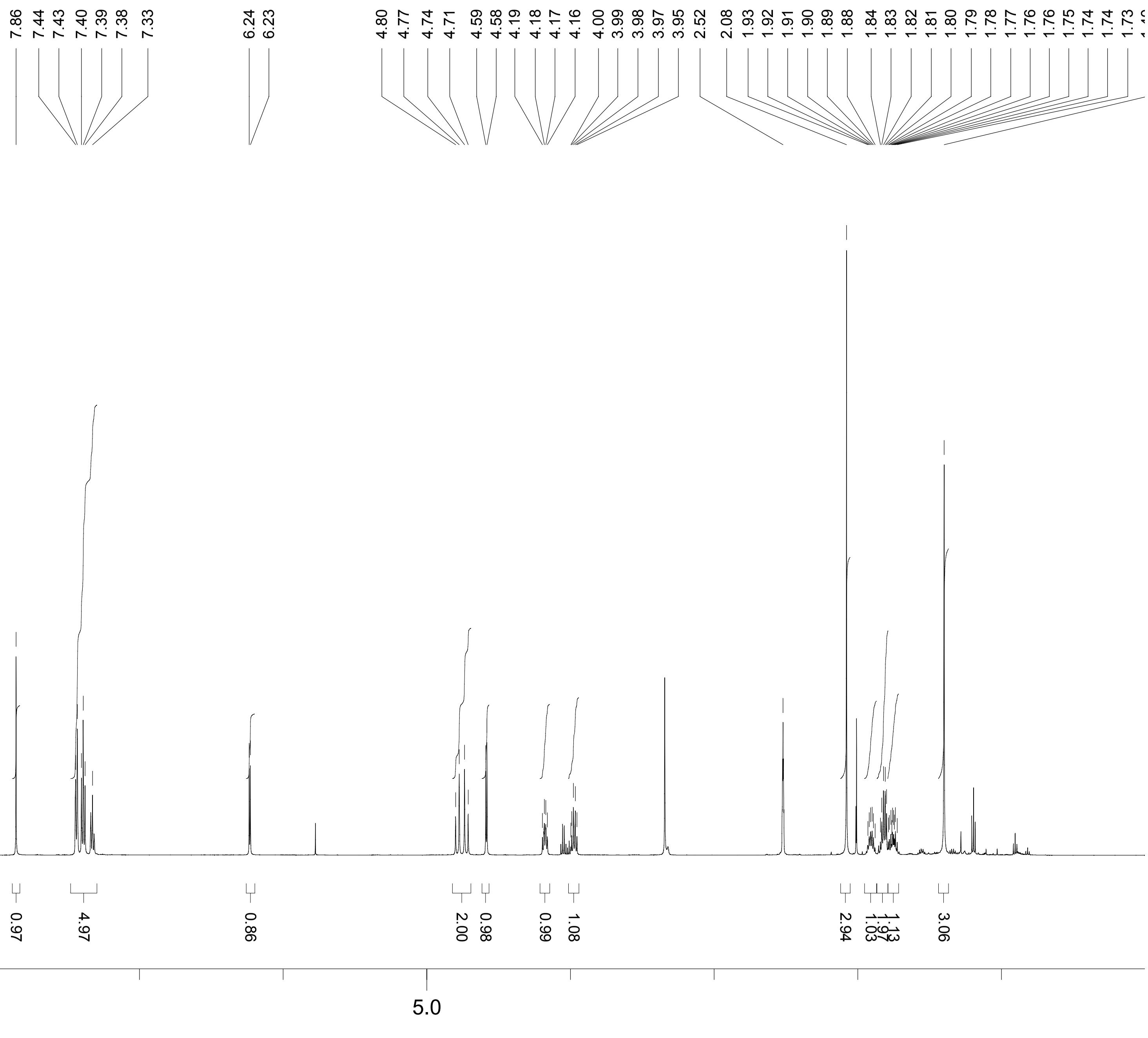
36A (DMSO-d_6, 600 MHz)

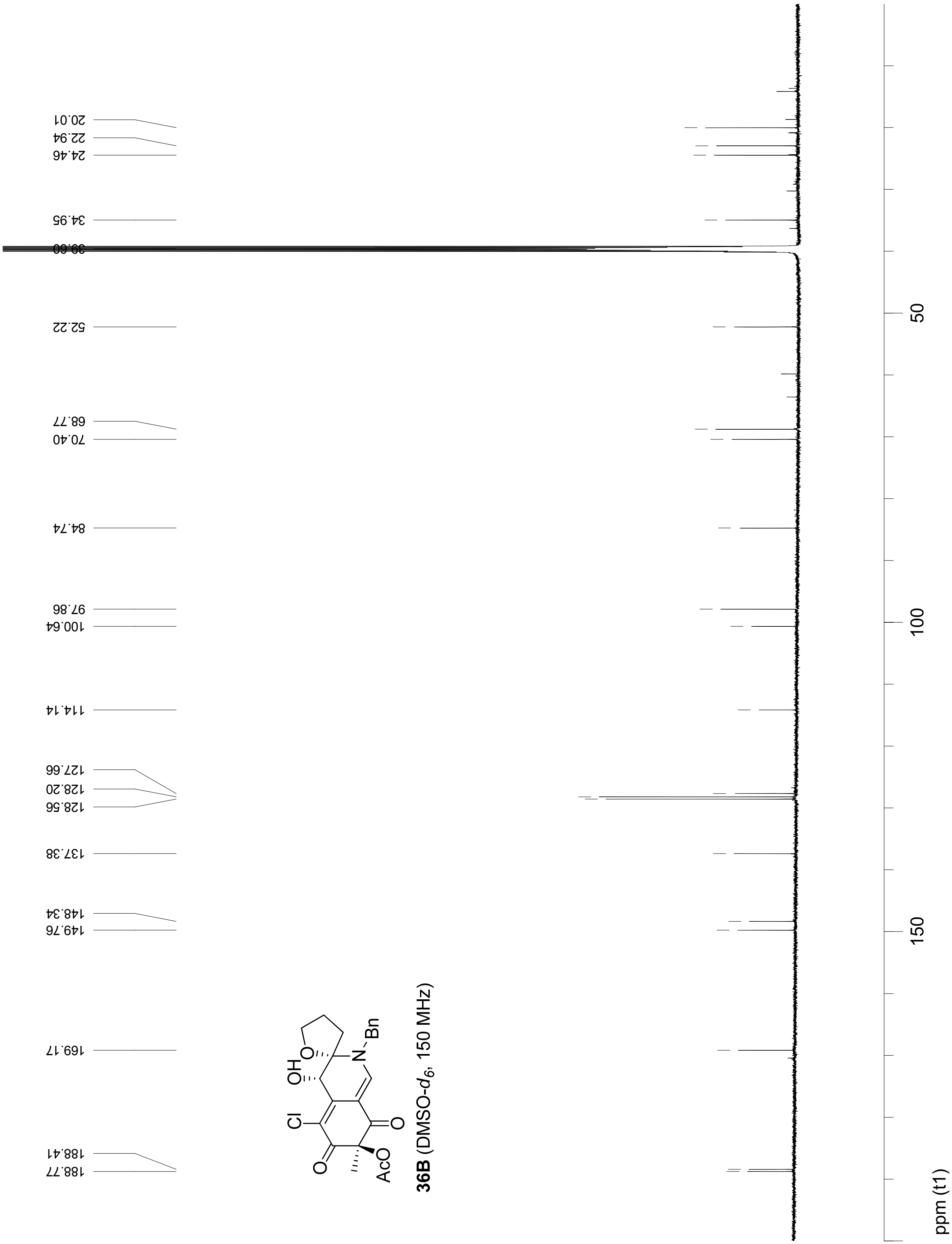


36A (DMSO-d_6, 150 MHz)

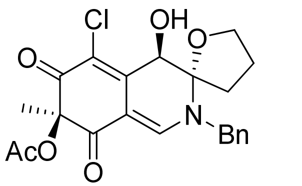


36B (DMSO-d_6, 600 MHz)

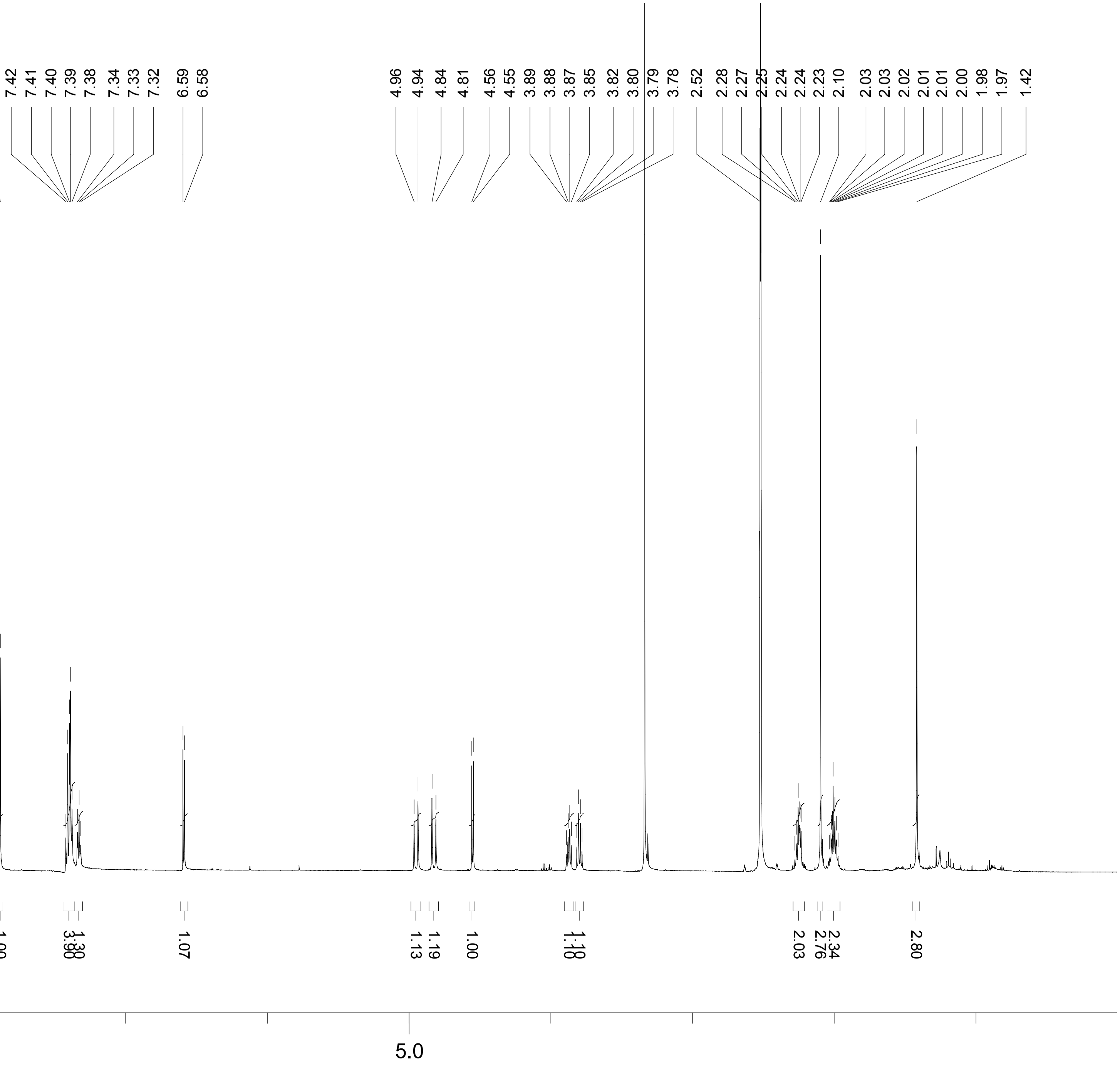


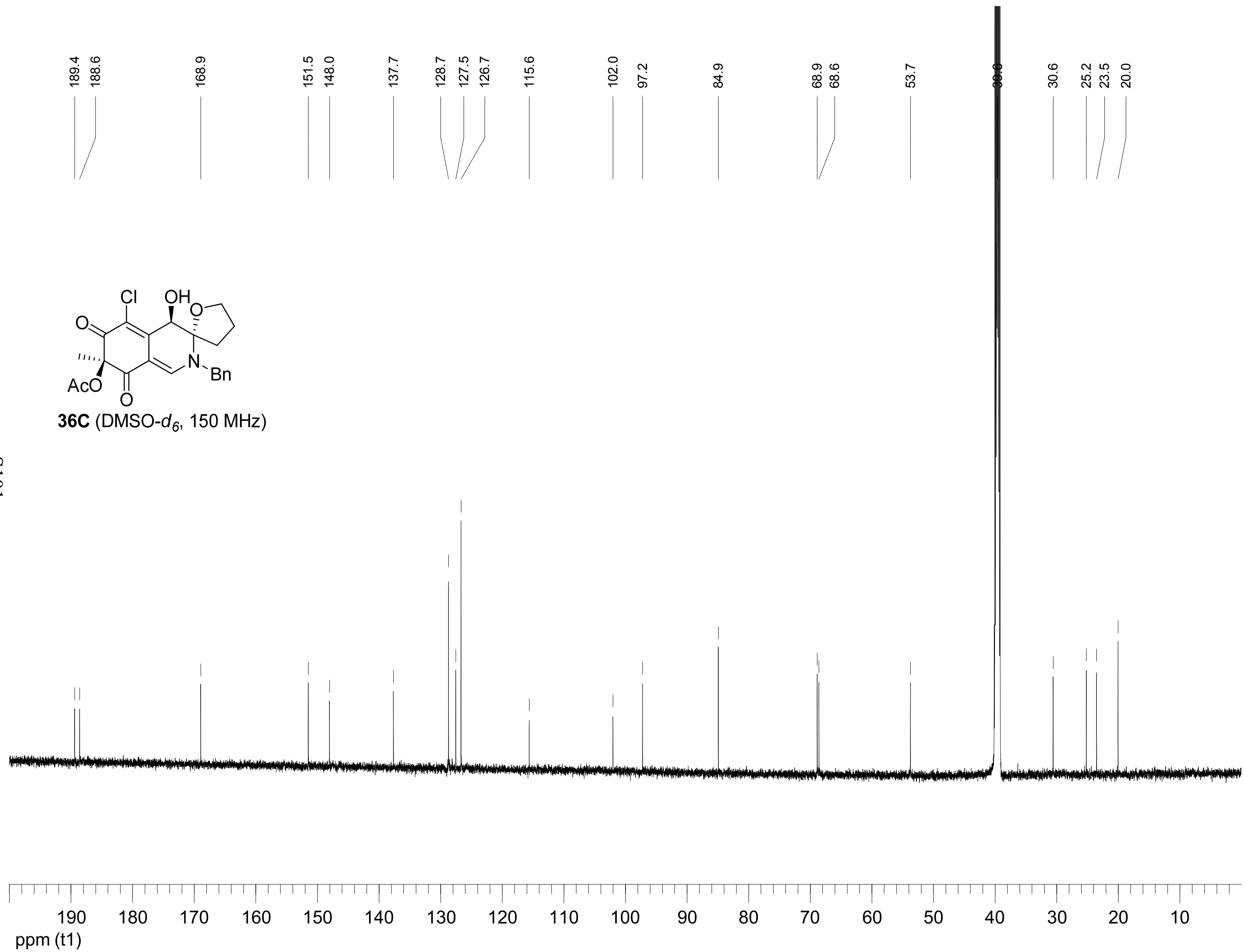


36B (DMSO-d_6, 150 MHz)

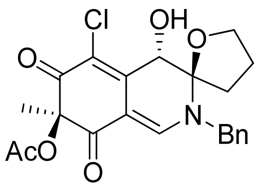


36C (DMSO-d_6, 600 MHz)

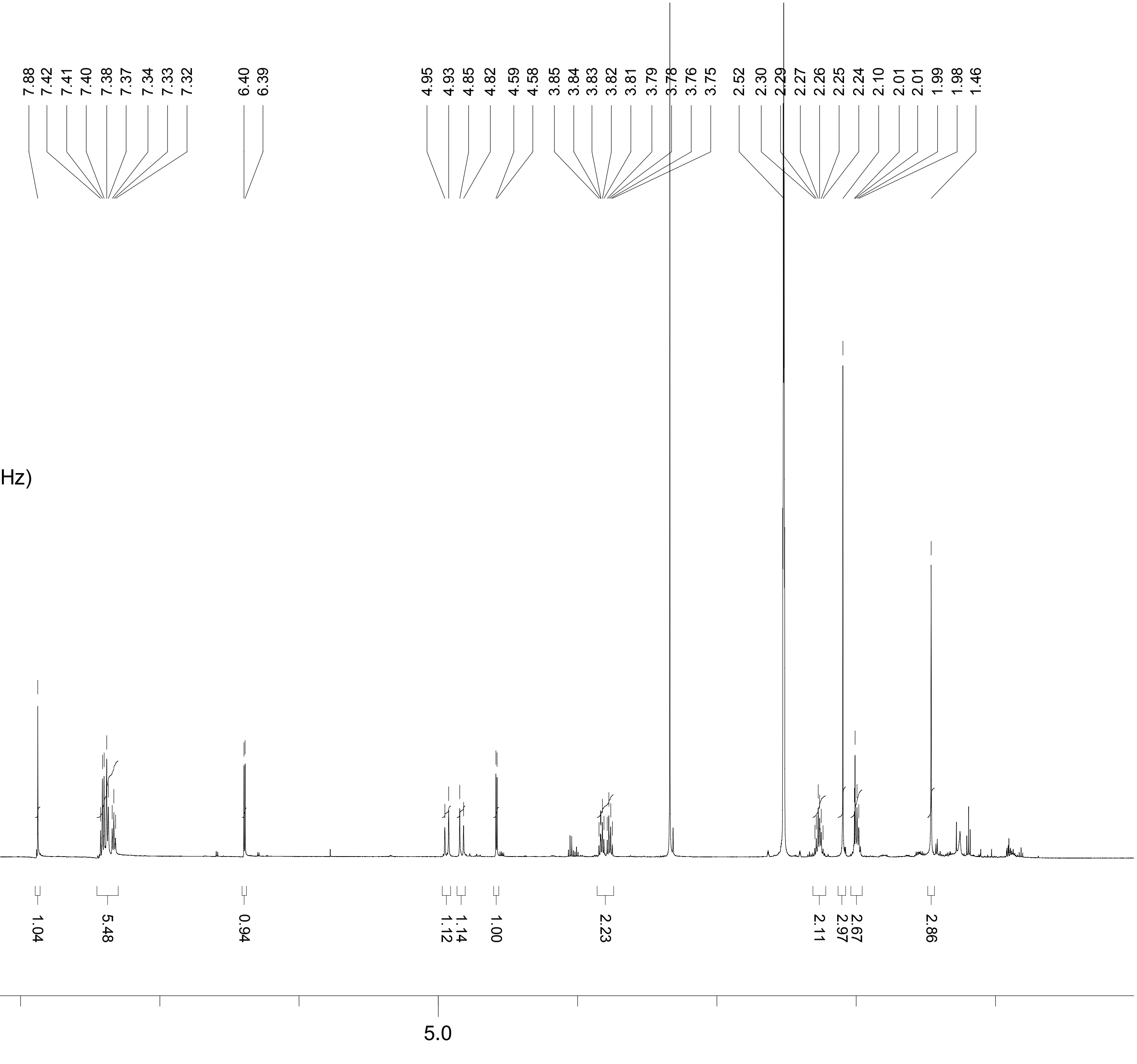


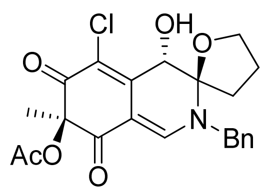


36C (DMSO-d_6, 150 MHz)

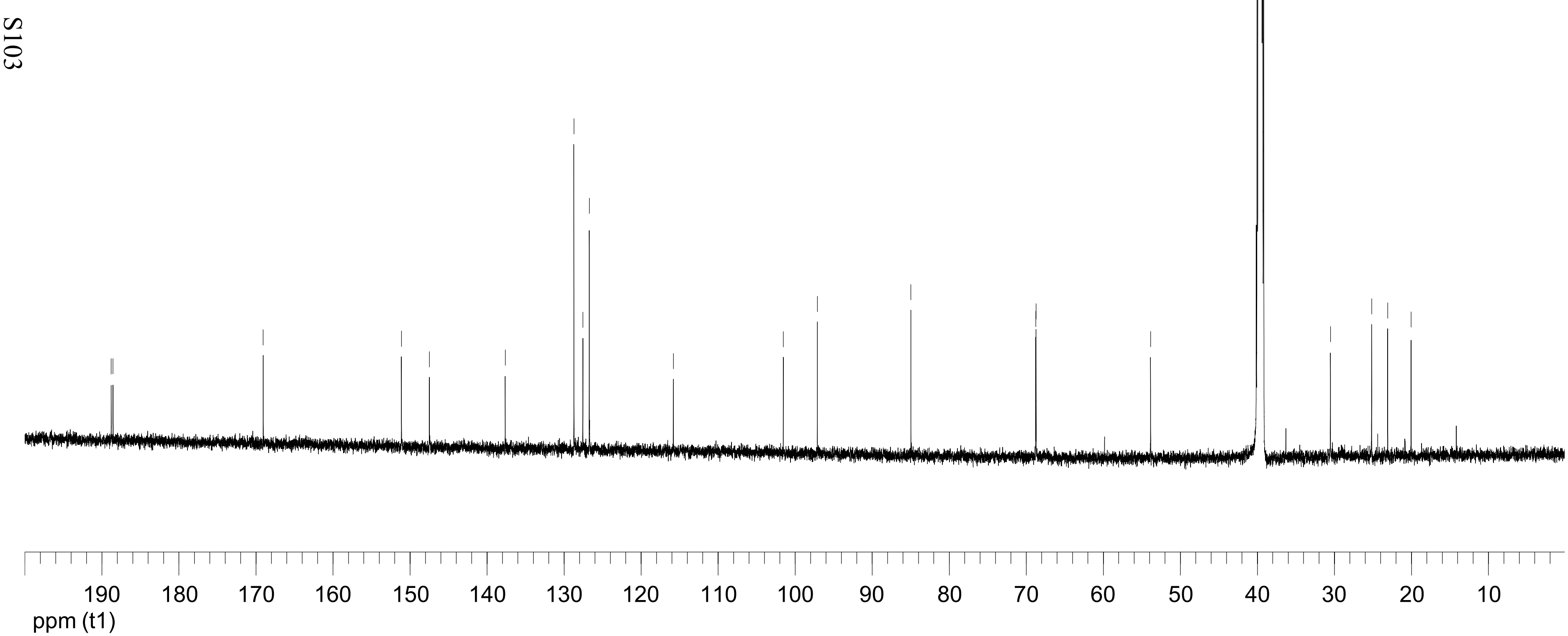


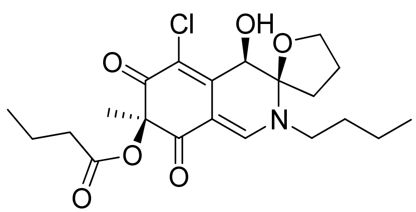
36D (DMSO-d_6, 600 MHz)



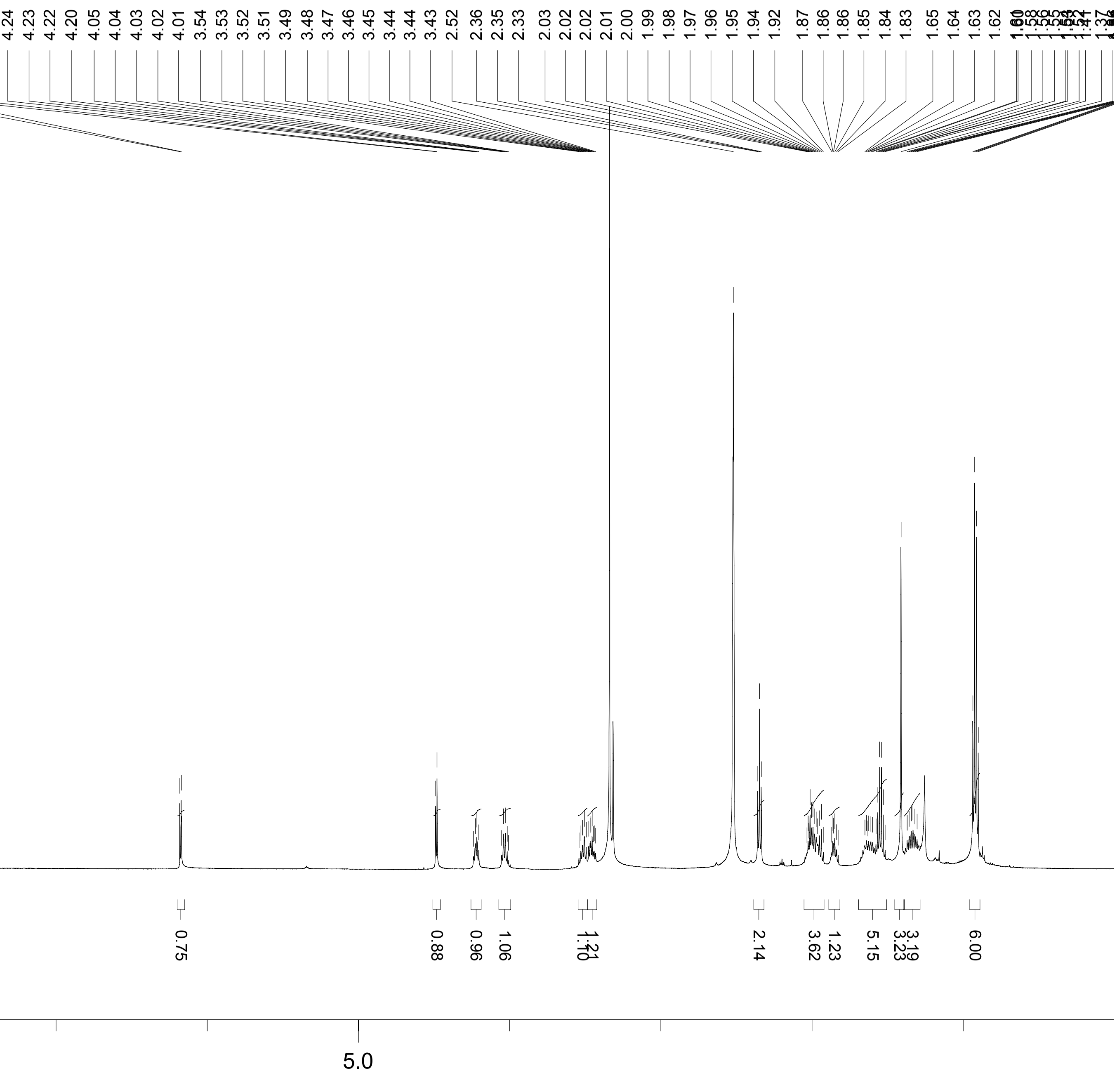


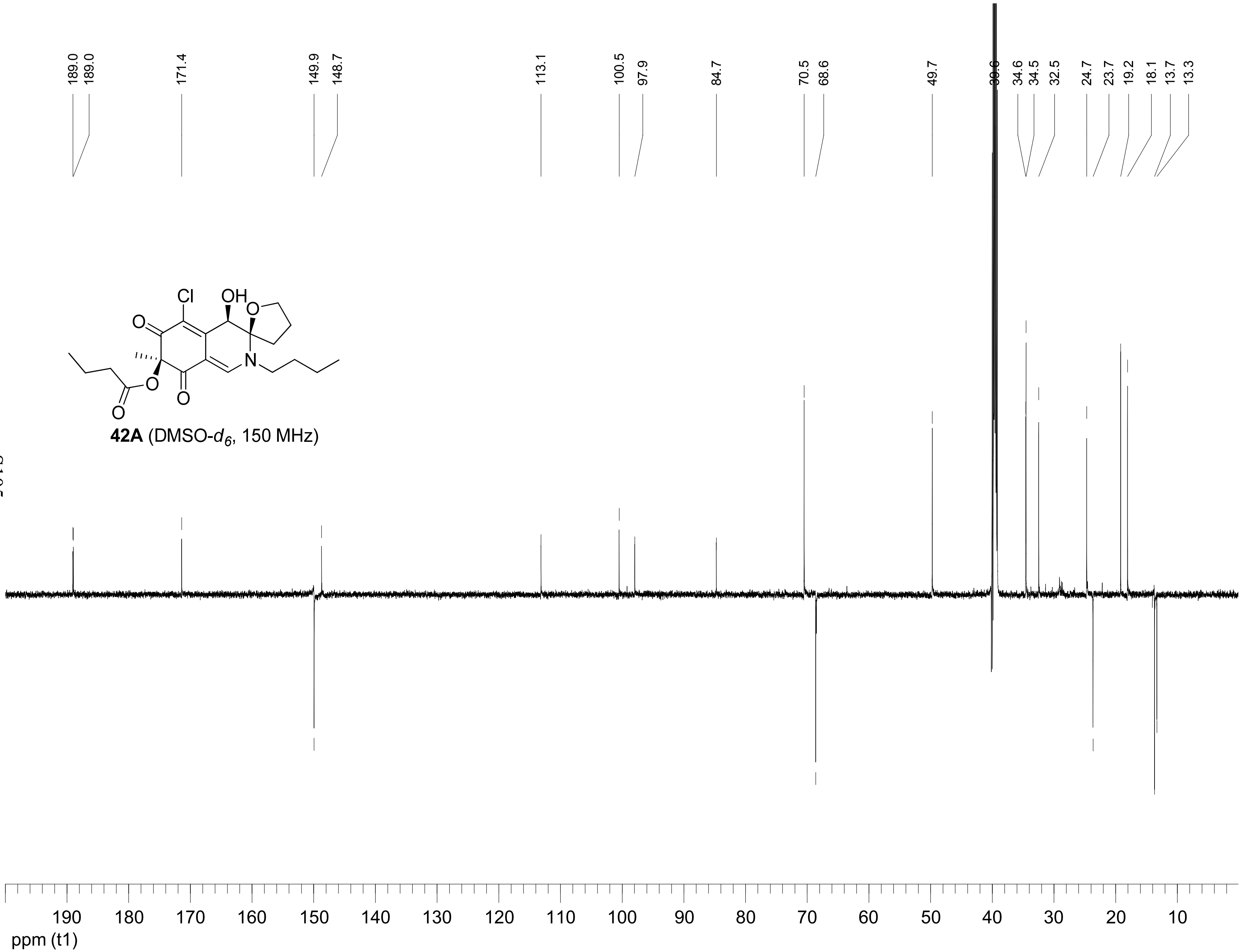
36D (DMSO-d_6, 150 MHz)



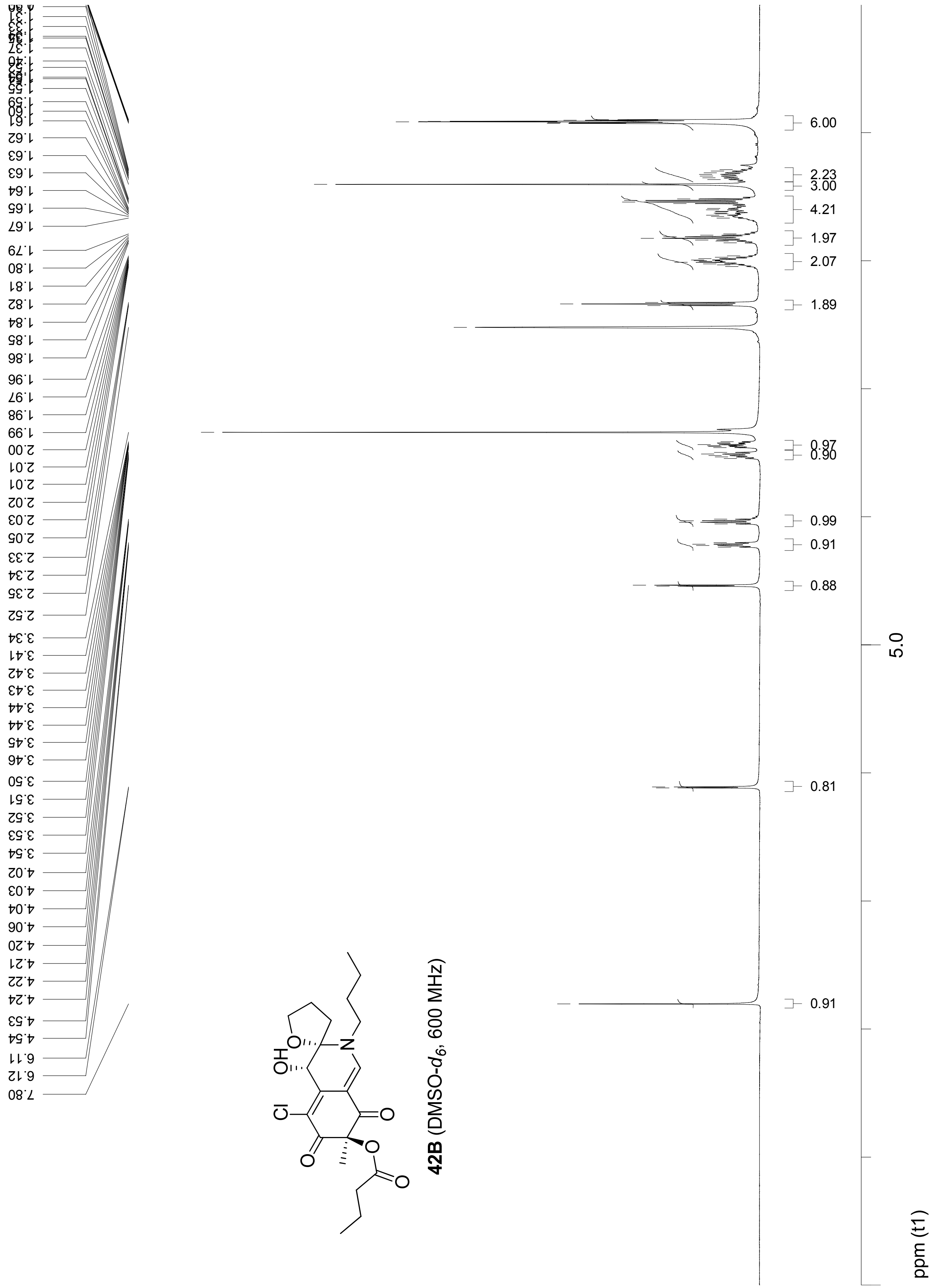


42A (DMSO-d_6, 600 MHz)

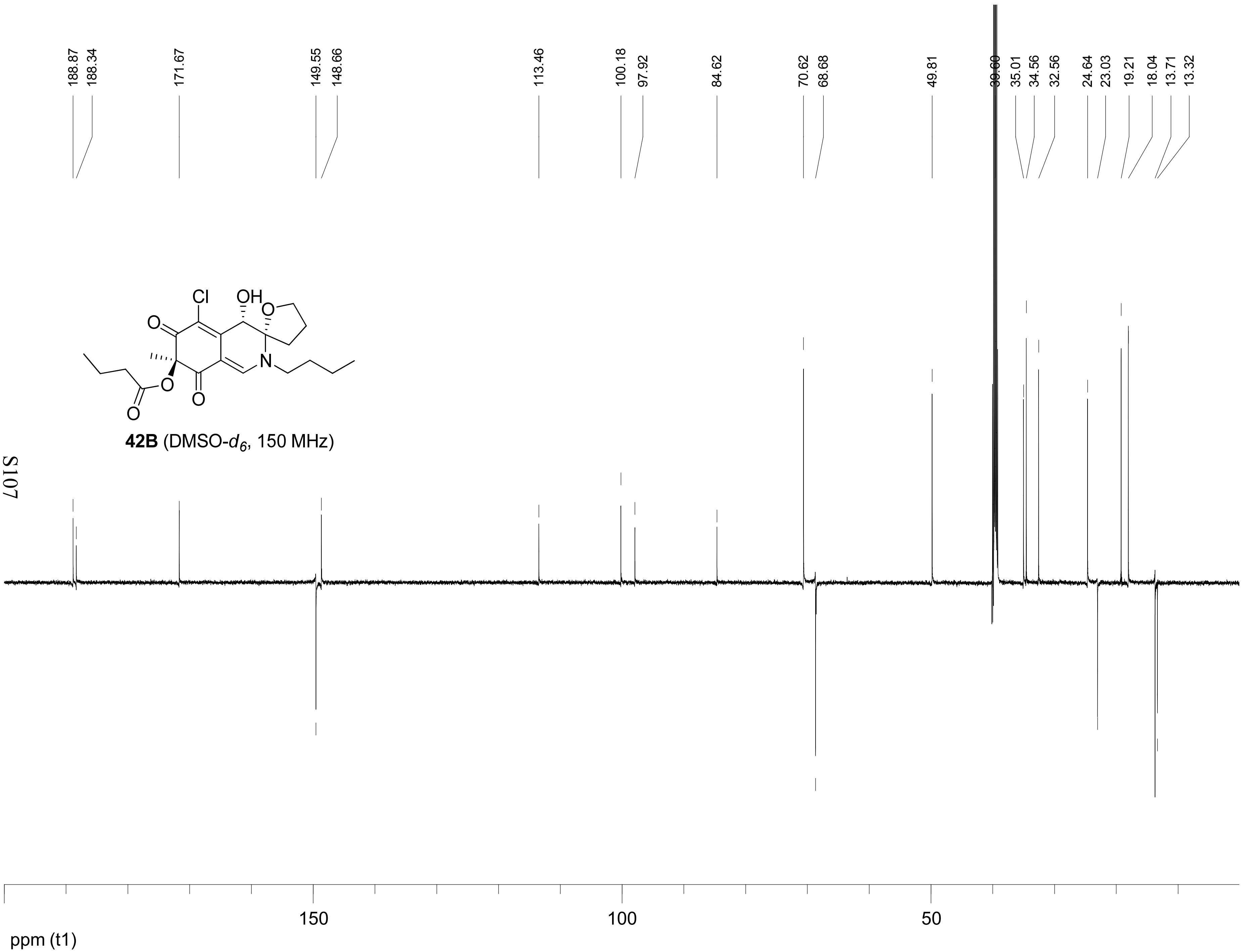




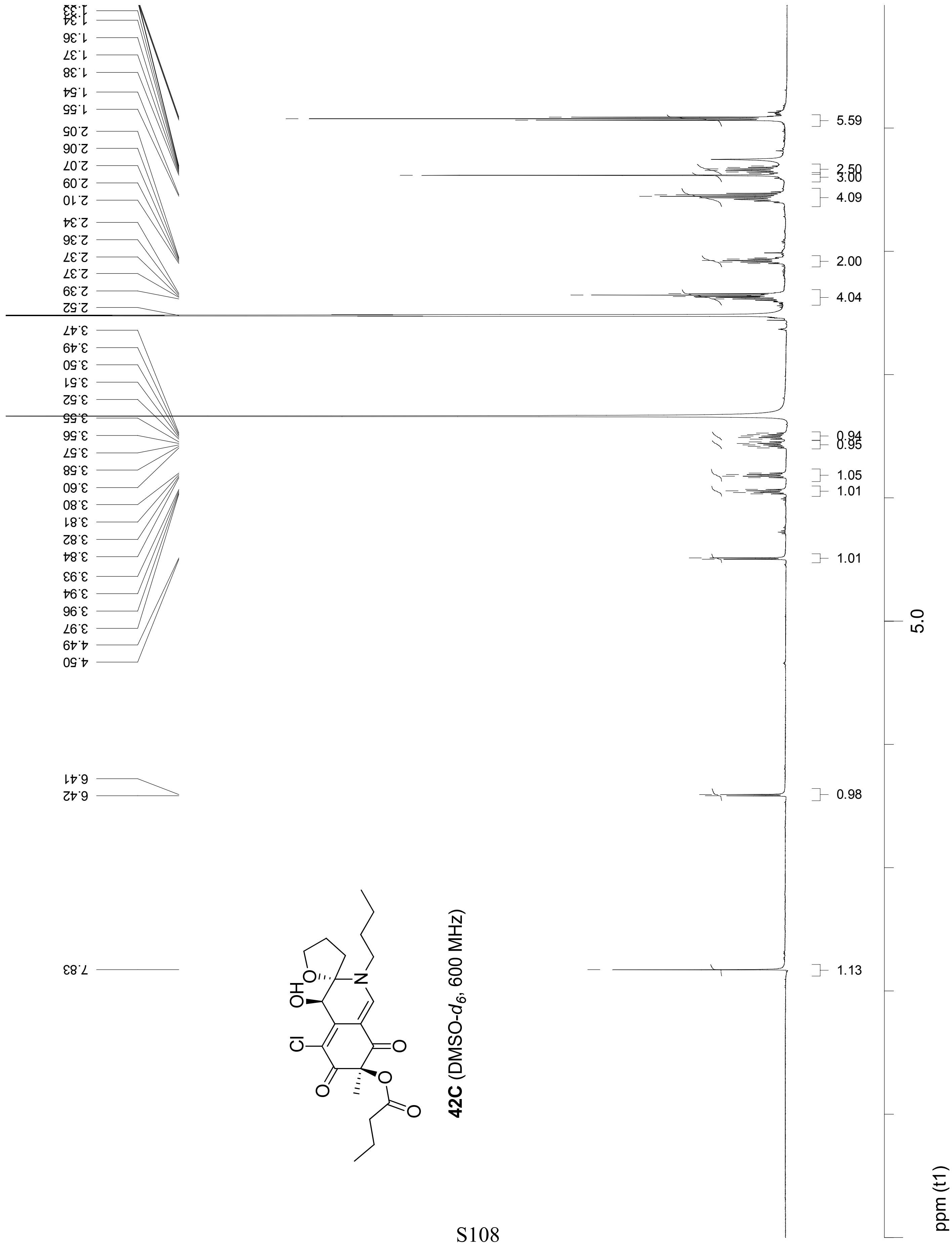
42A (DMSO-d_6, 150 MHz)



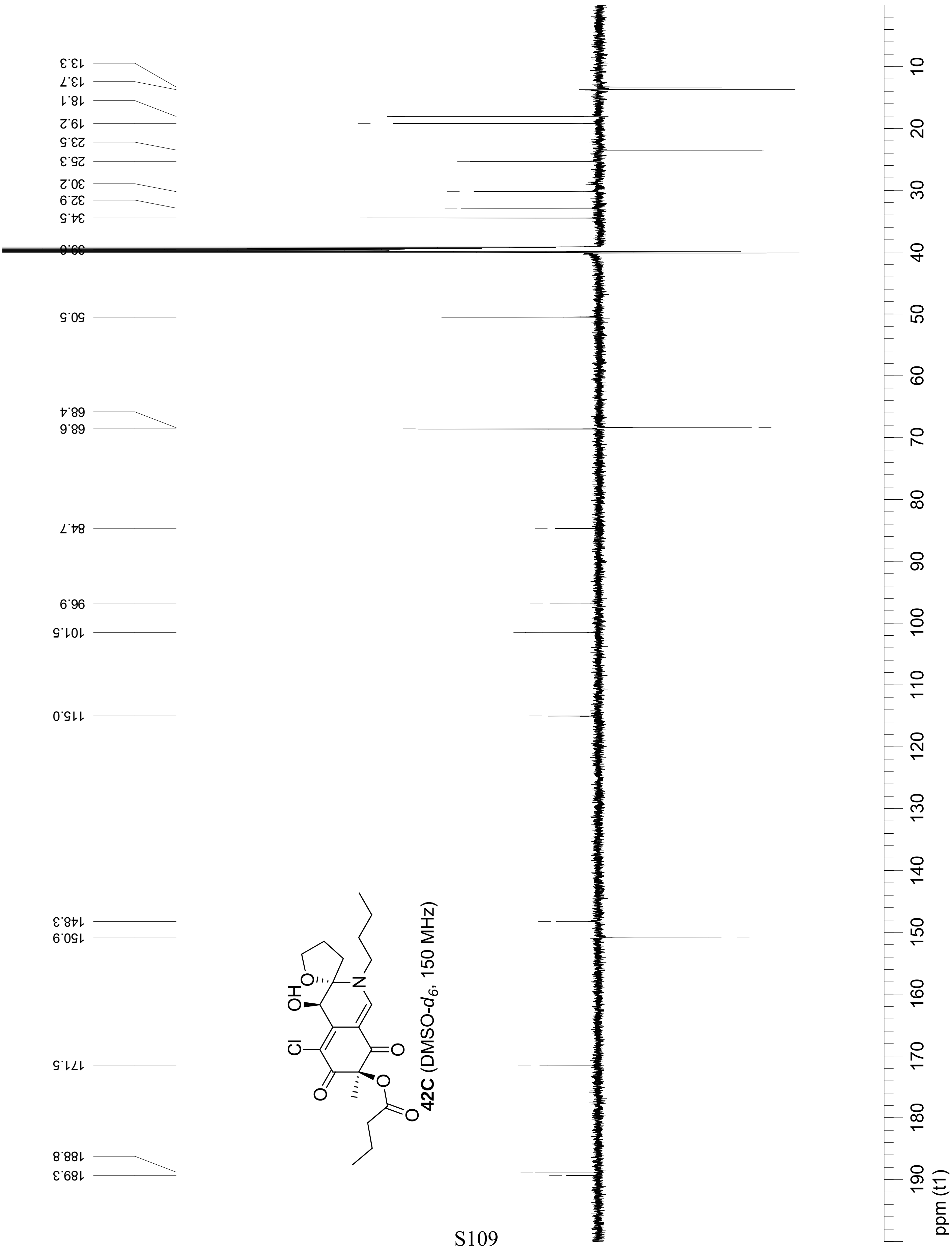
42B (DMSO-d_6, 600 MHz)



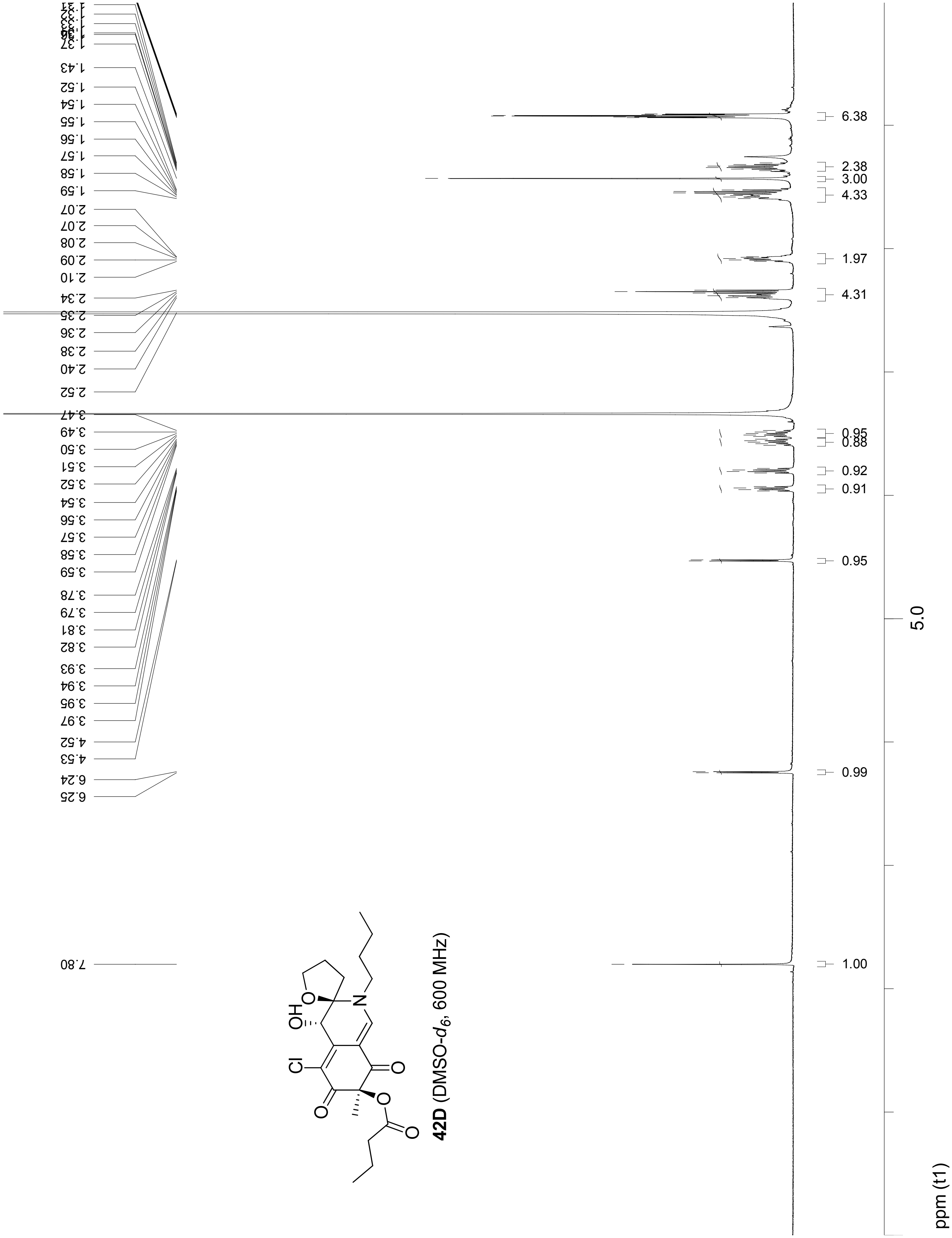
42B (DMSO-d_6, 150 MHz)



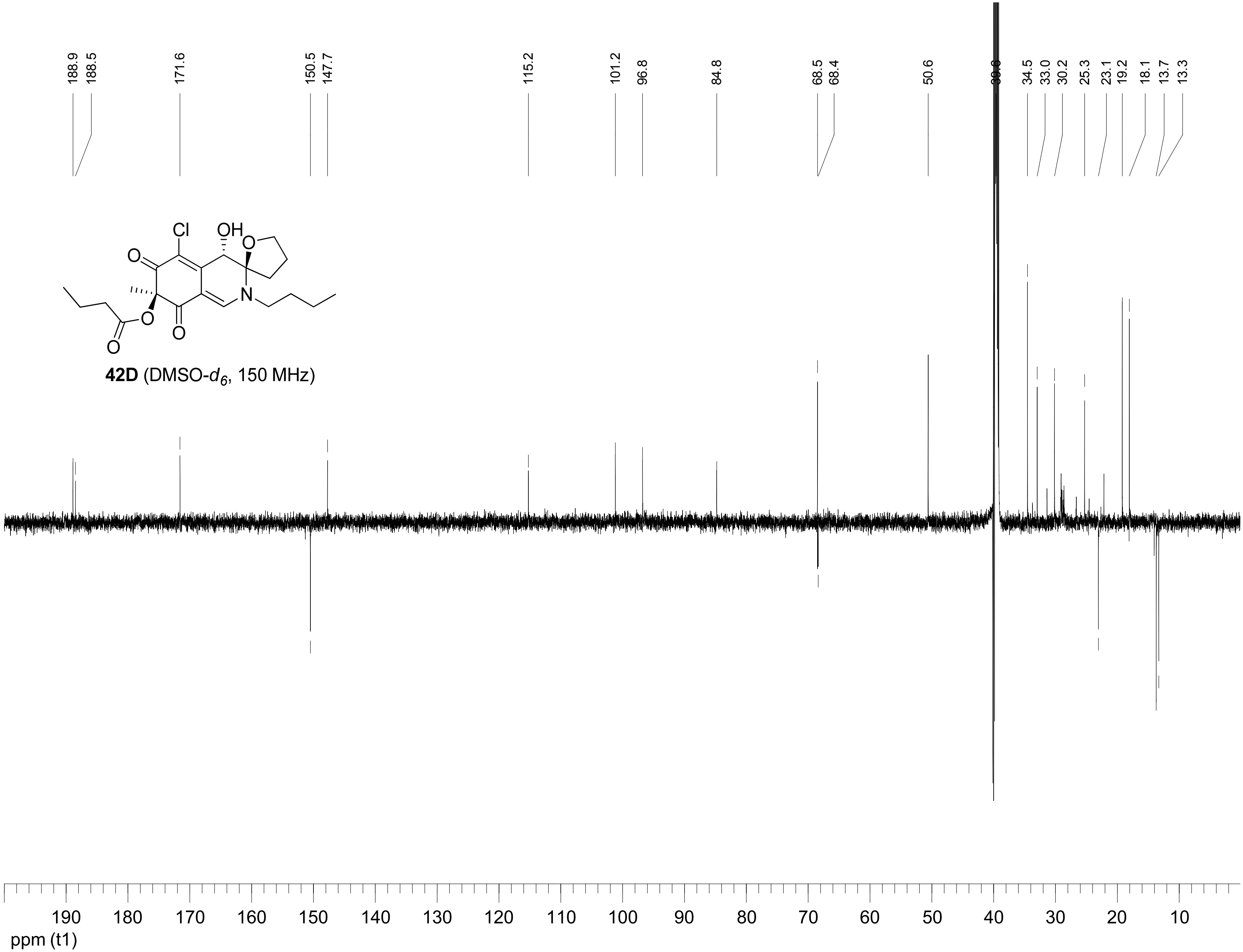
42C (DMSO-d_6, 600 MHz)



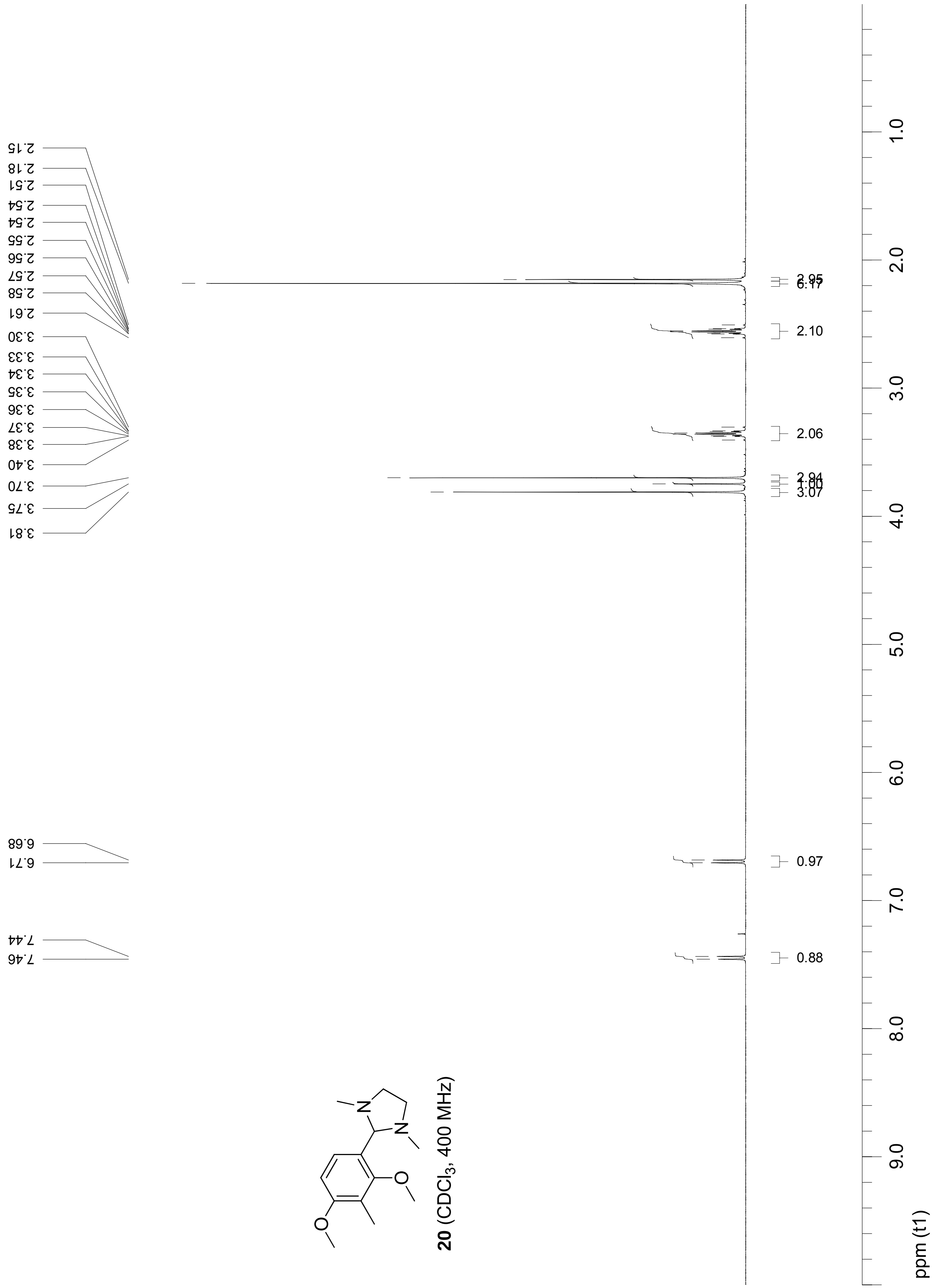
13.3
13.7
18.1
19.2
23.5
25.3
30.2
32.9
34.5
39.6
50.5
68.4
68.6
84.7
96.9
101.5
115.0
148.3
150.9
171.5
188.8
189.3
OH
Cl
O
N
42C (DMSO-d_6, 150 MHz)
ppm (t1)



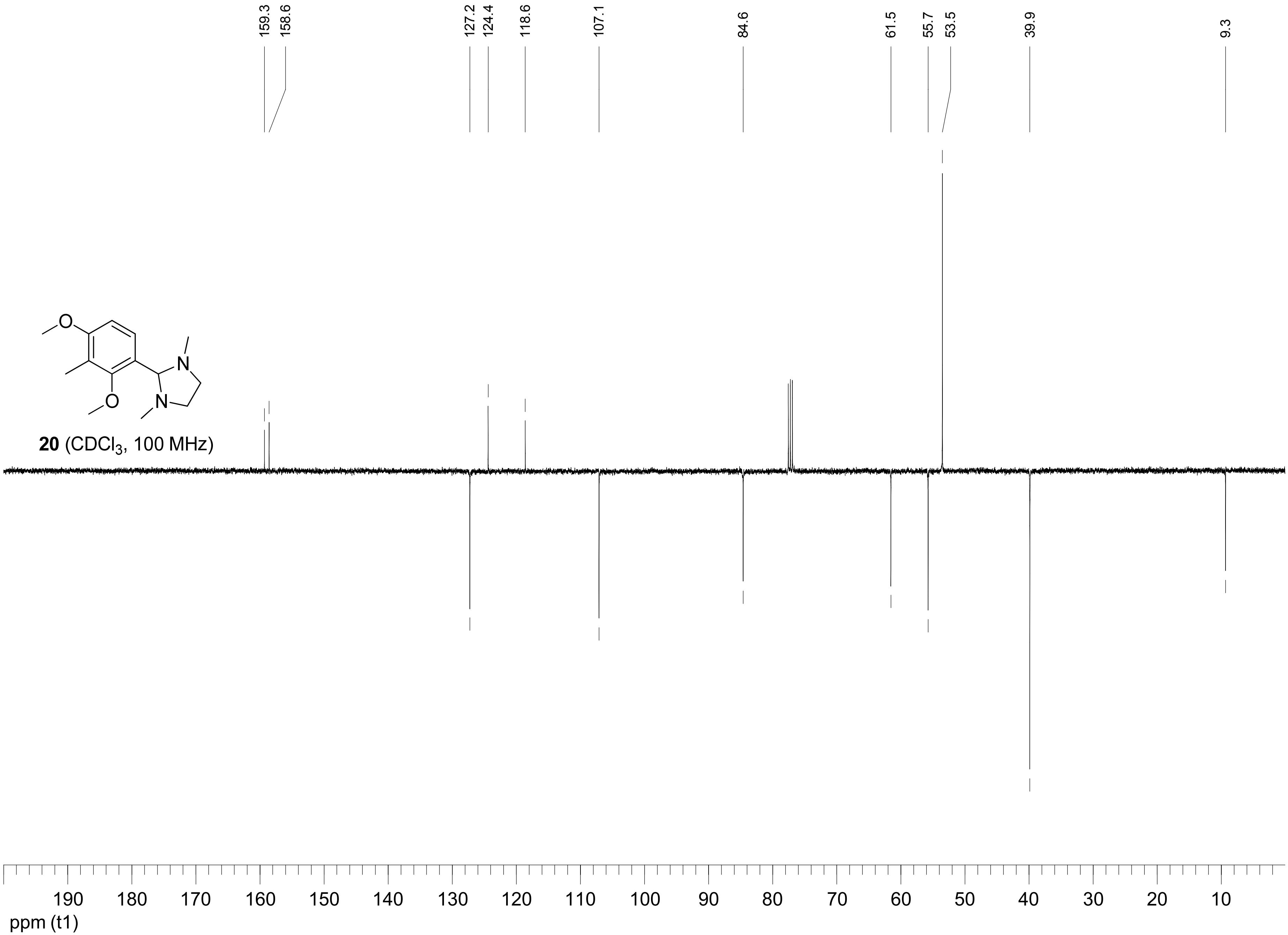
42D (DMSO-d_6, 600 MHz)



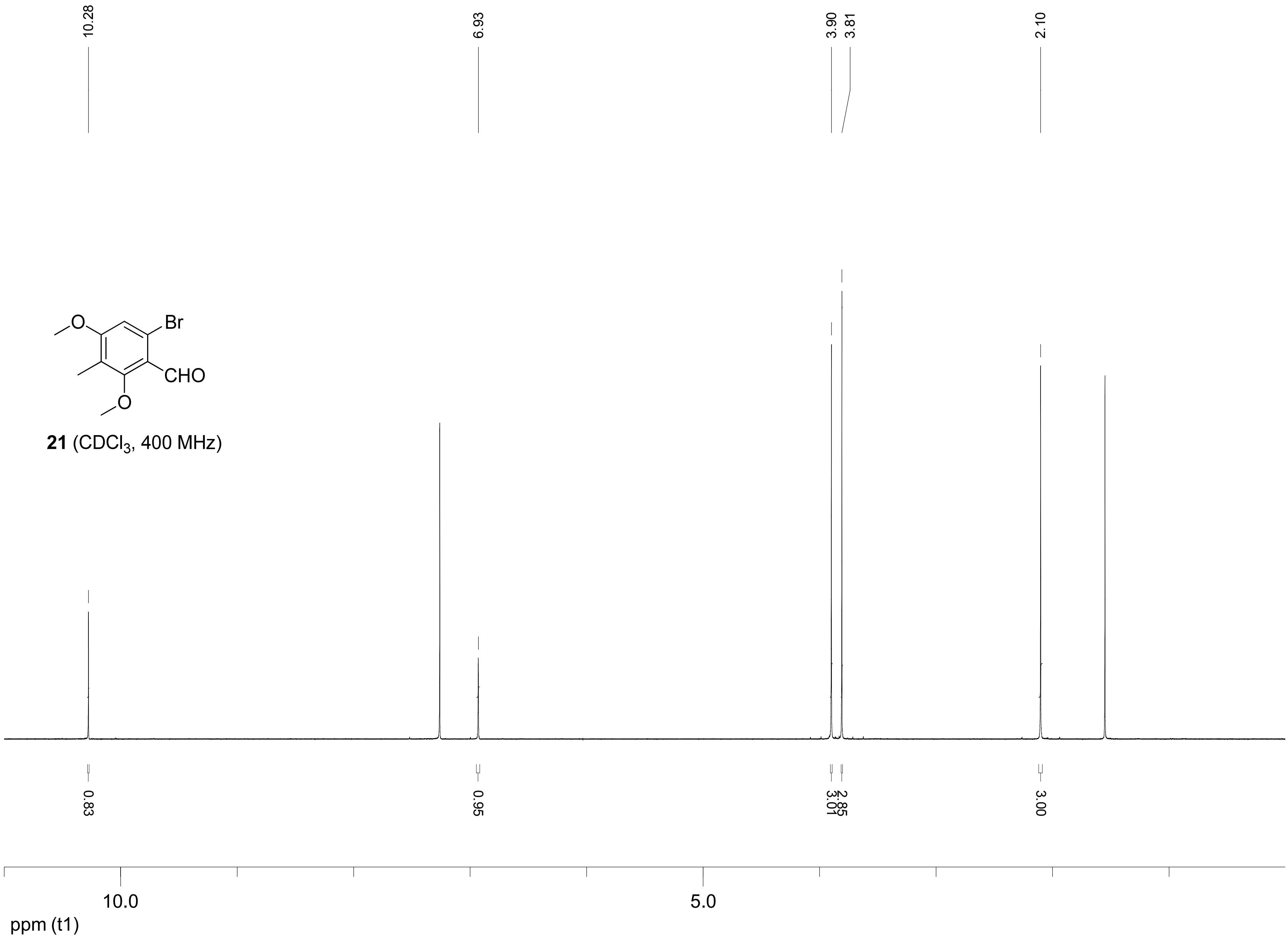
42D (DMSO-d_6, 150 MHz)



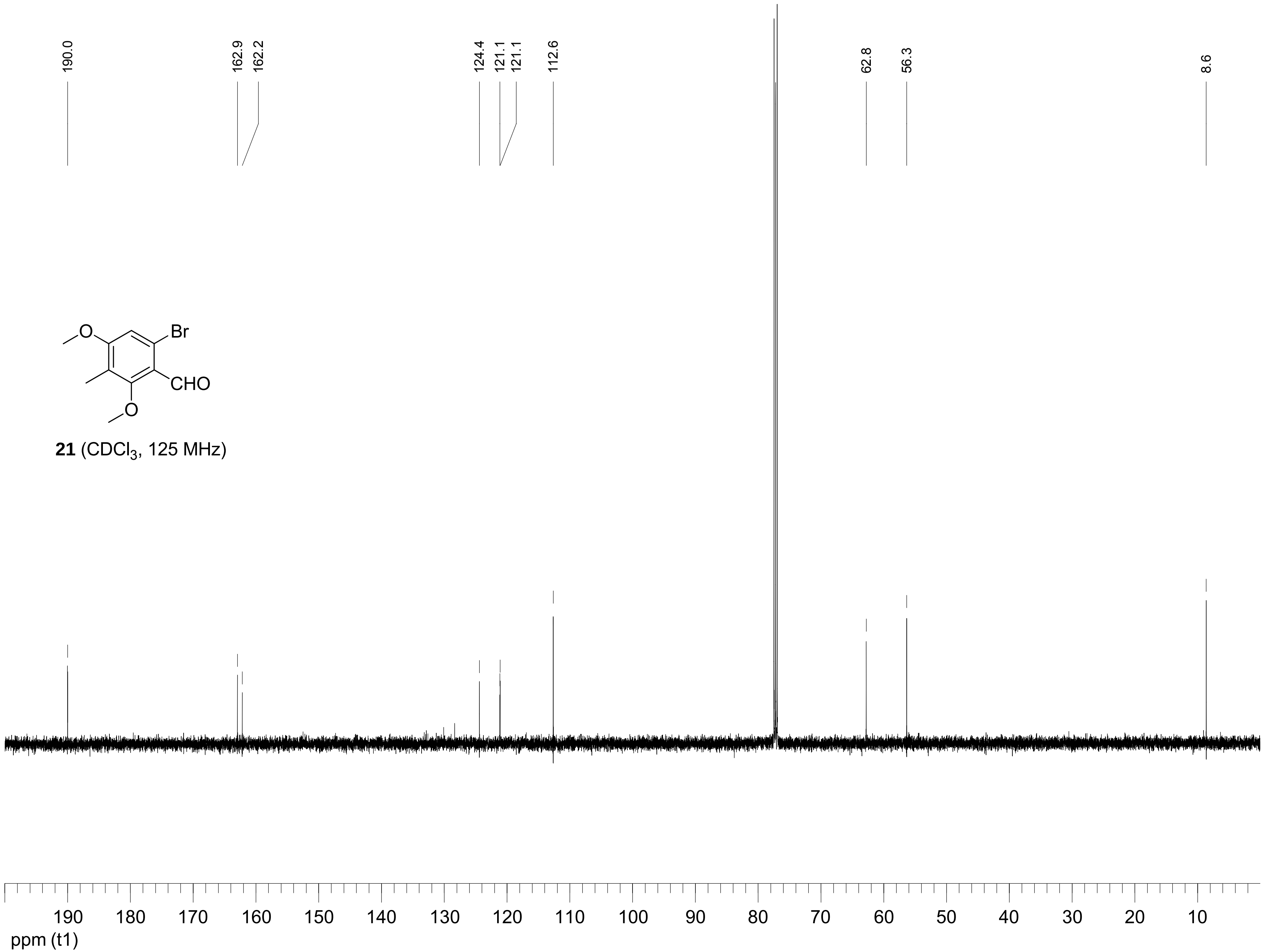
20 ($CDCl_3$, 400 MHz)



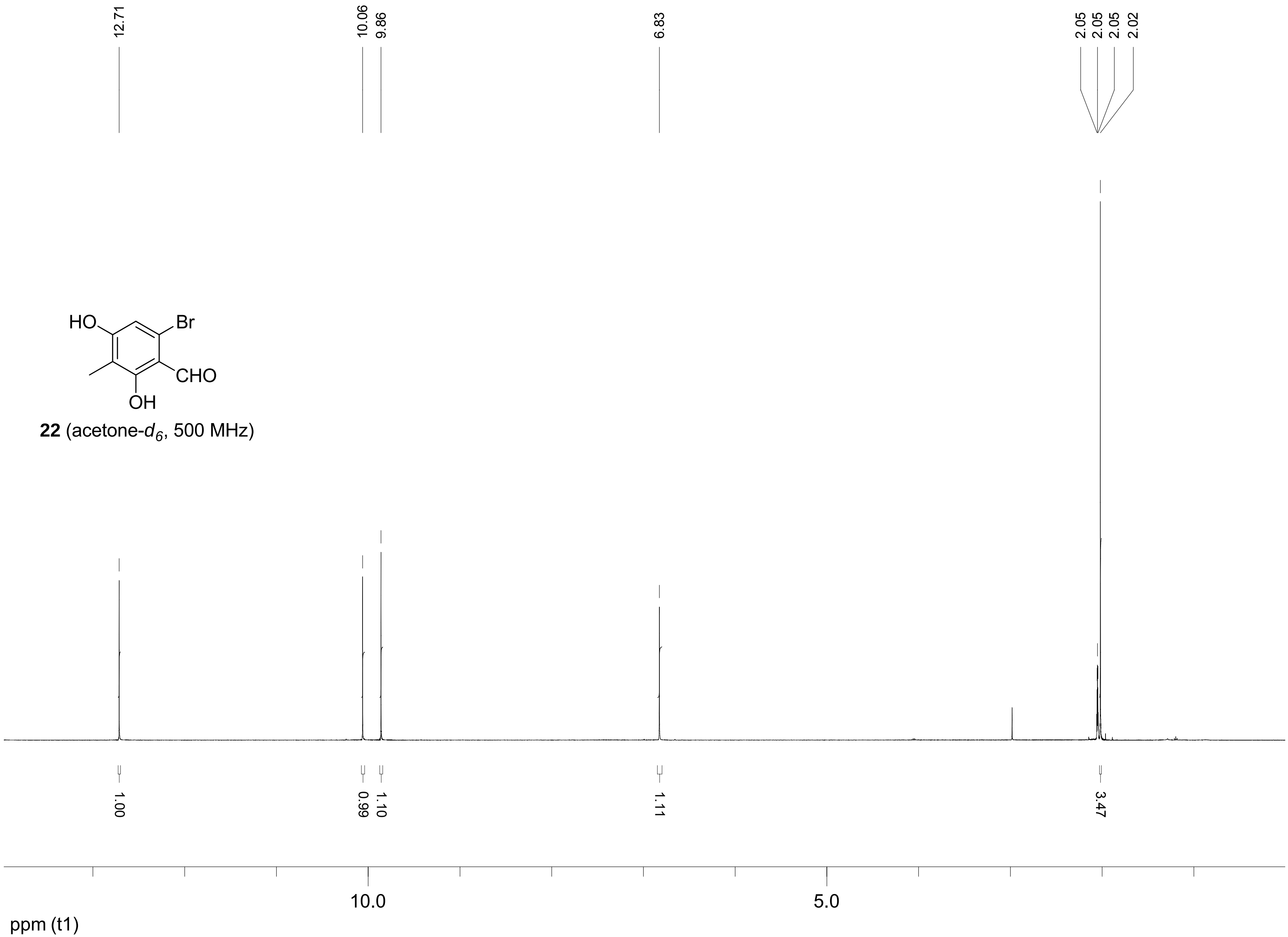
20 ($CDCl_3$, 100 MHz)



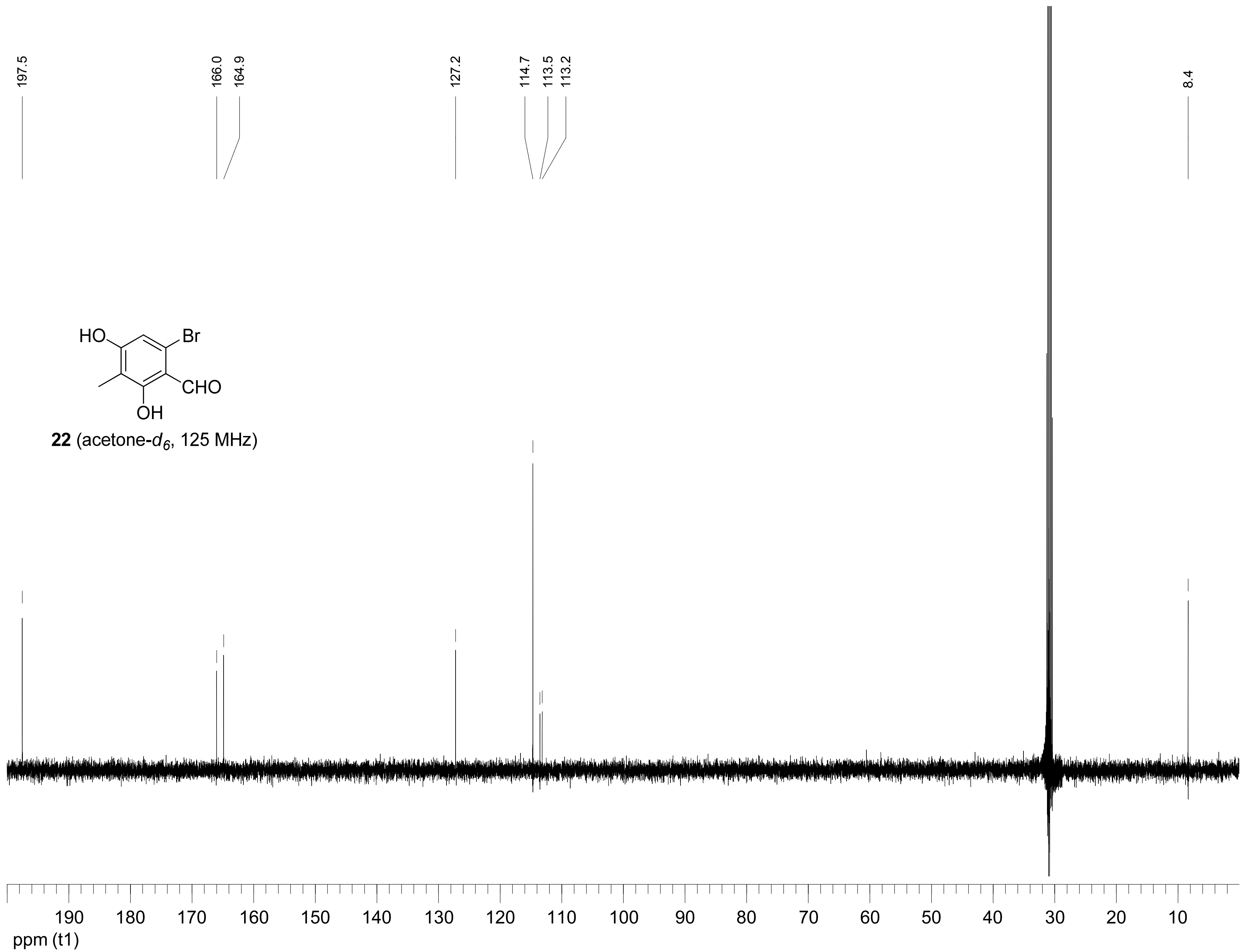
21 ($CDCl_3$, 400 MHz)



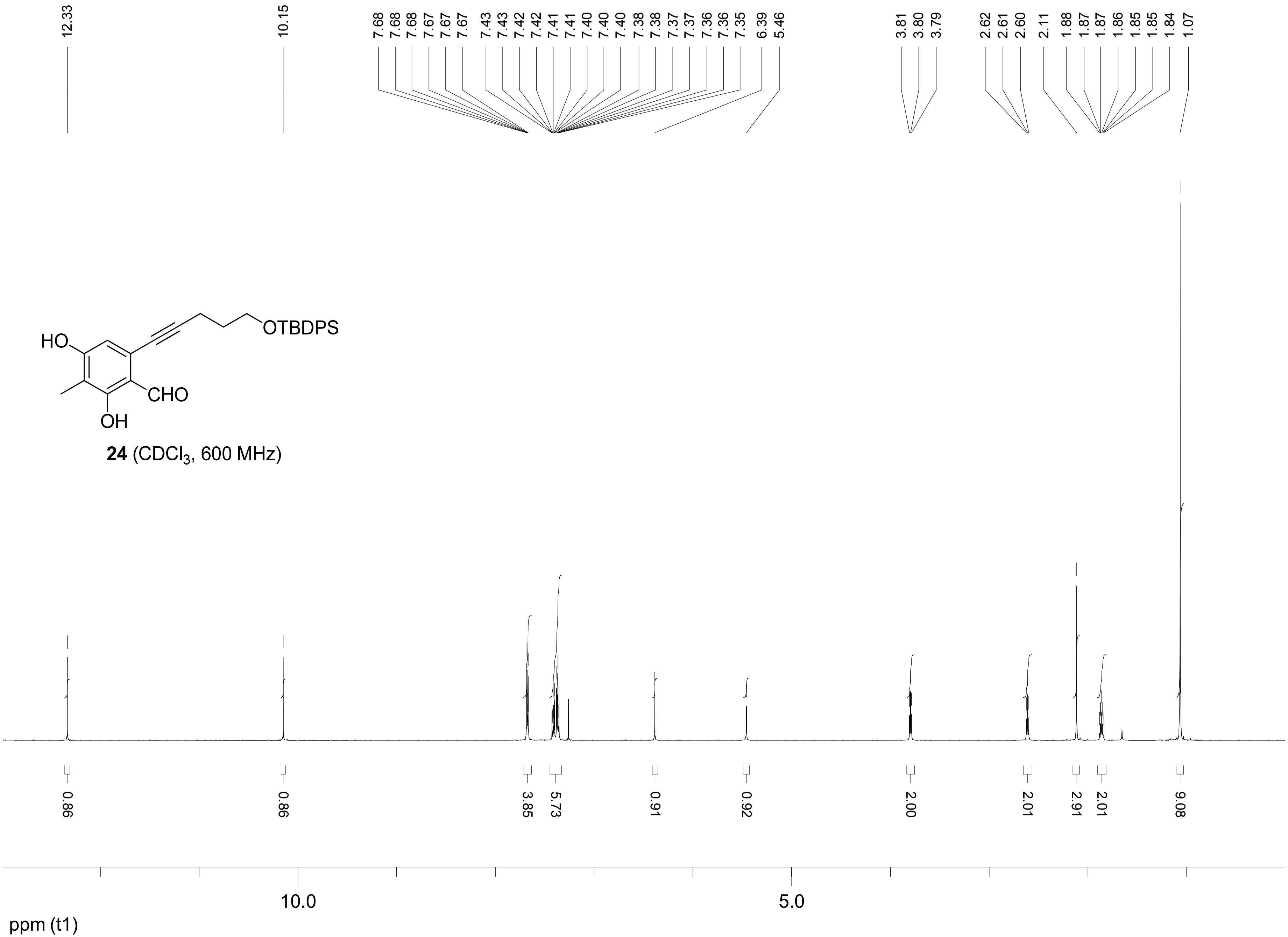
21 ($CDCl_3$, 125 MHz)



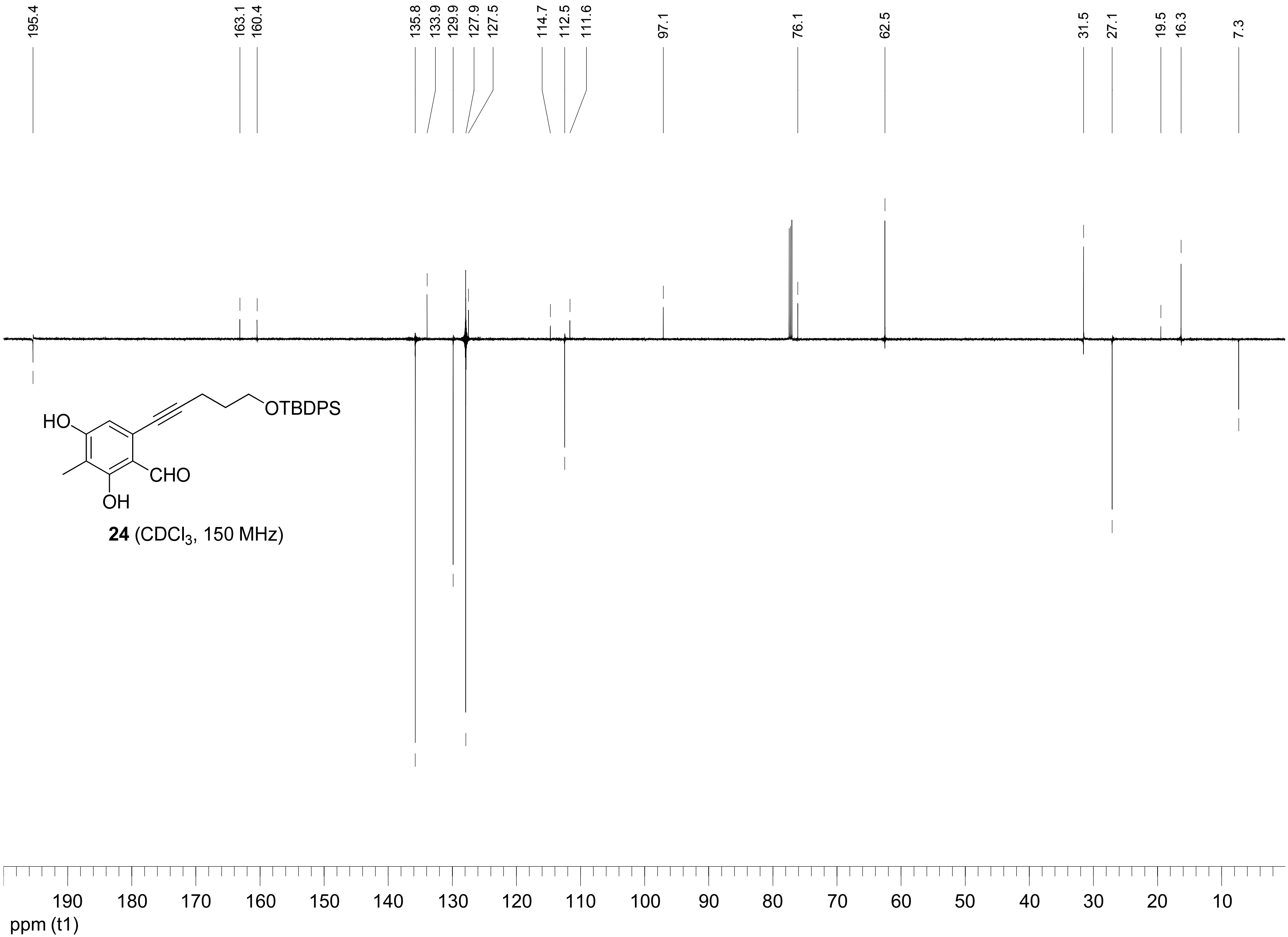
22 (acetone-d_6, 500 MHz)



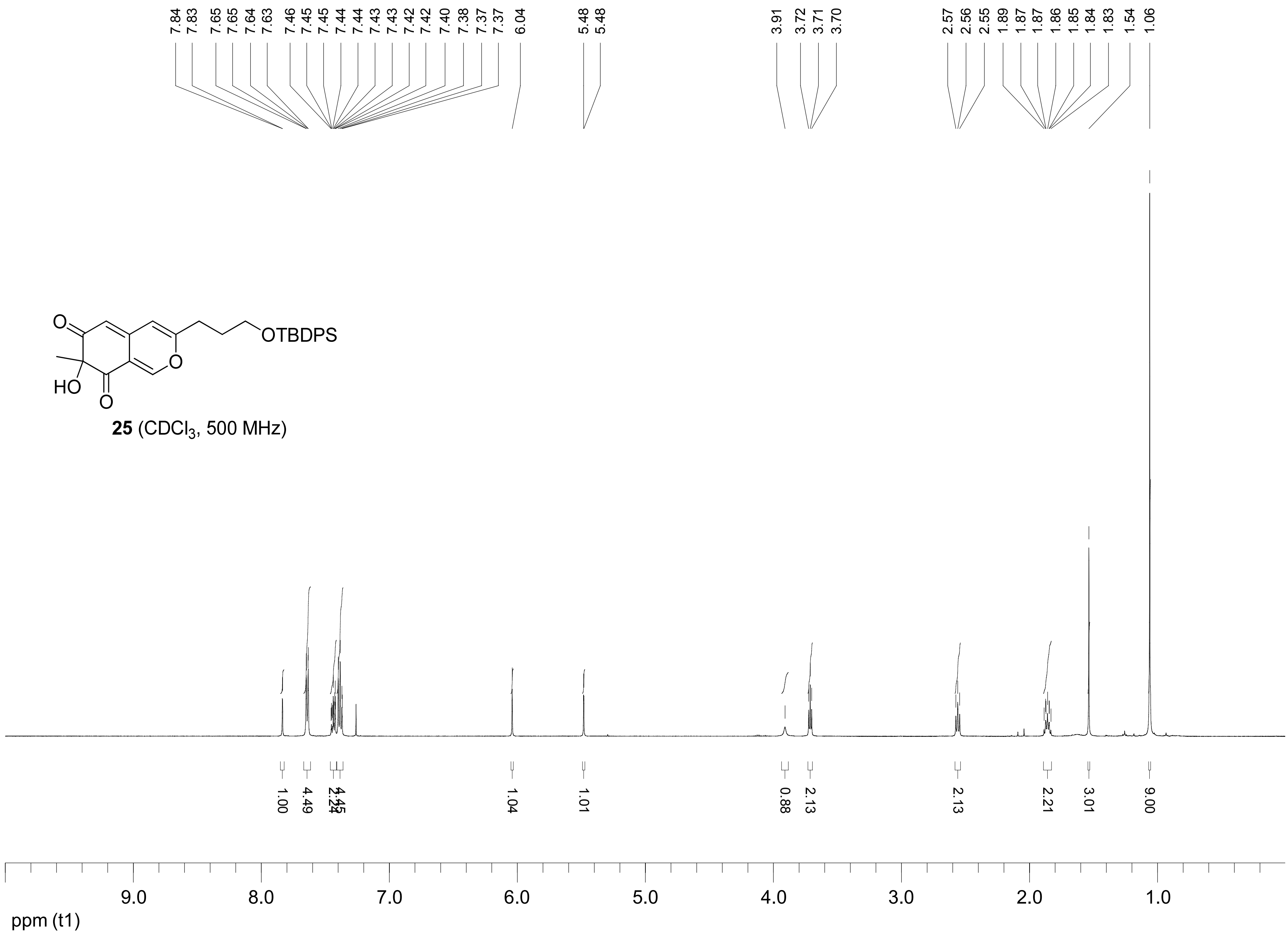
22 (acetone-d_6, 125 MHz)



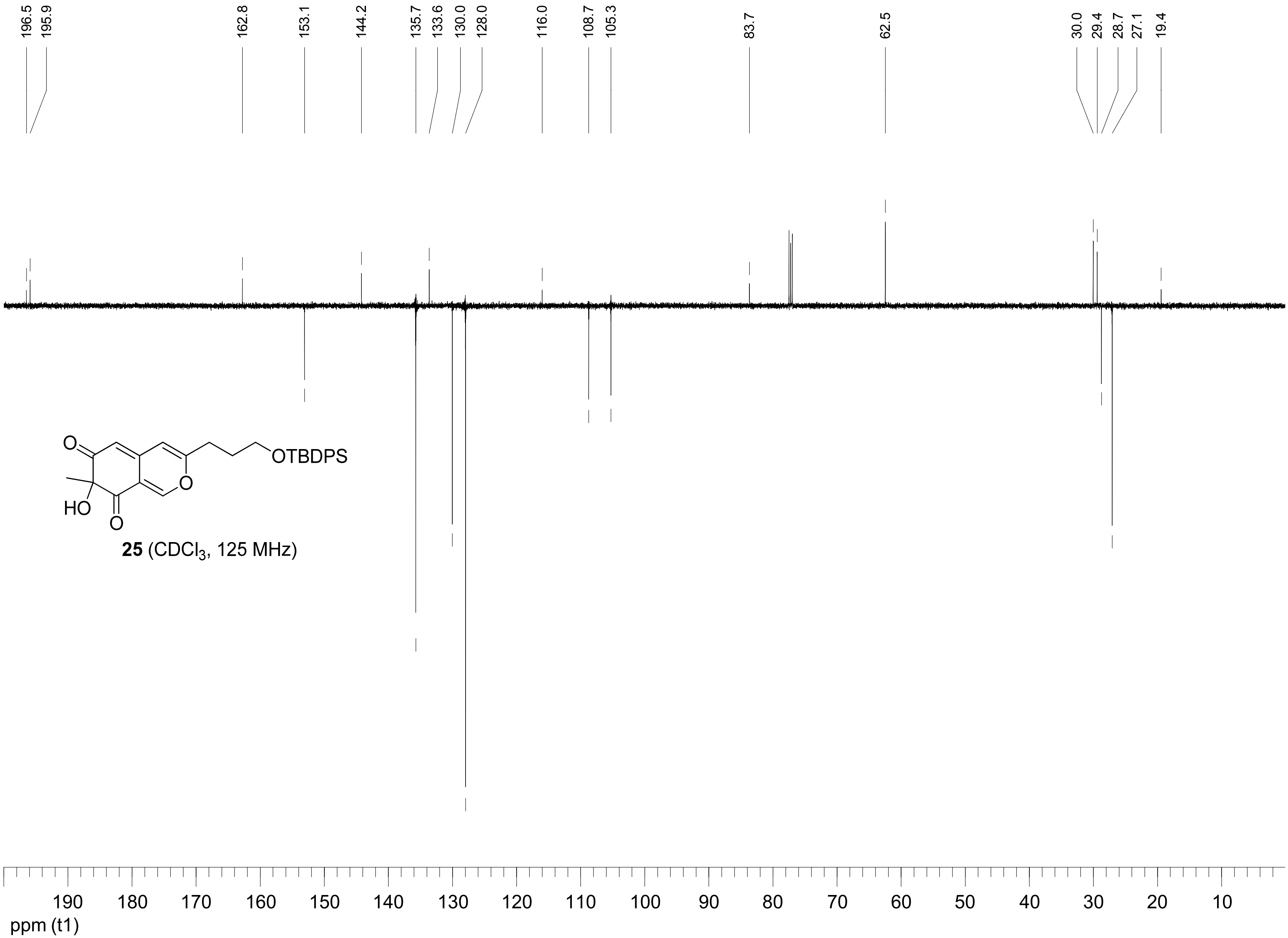
24 ($CDCl_3$, 600 MHz)



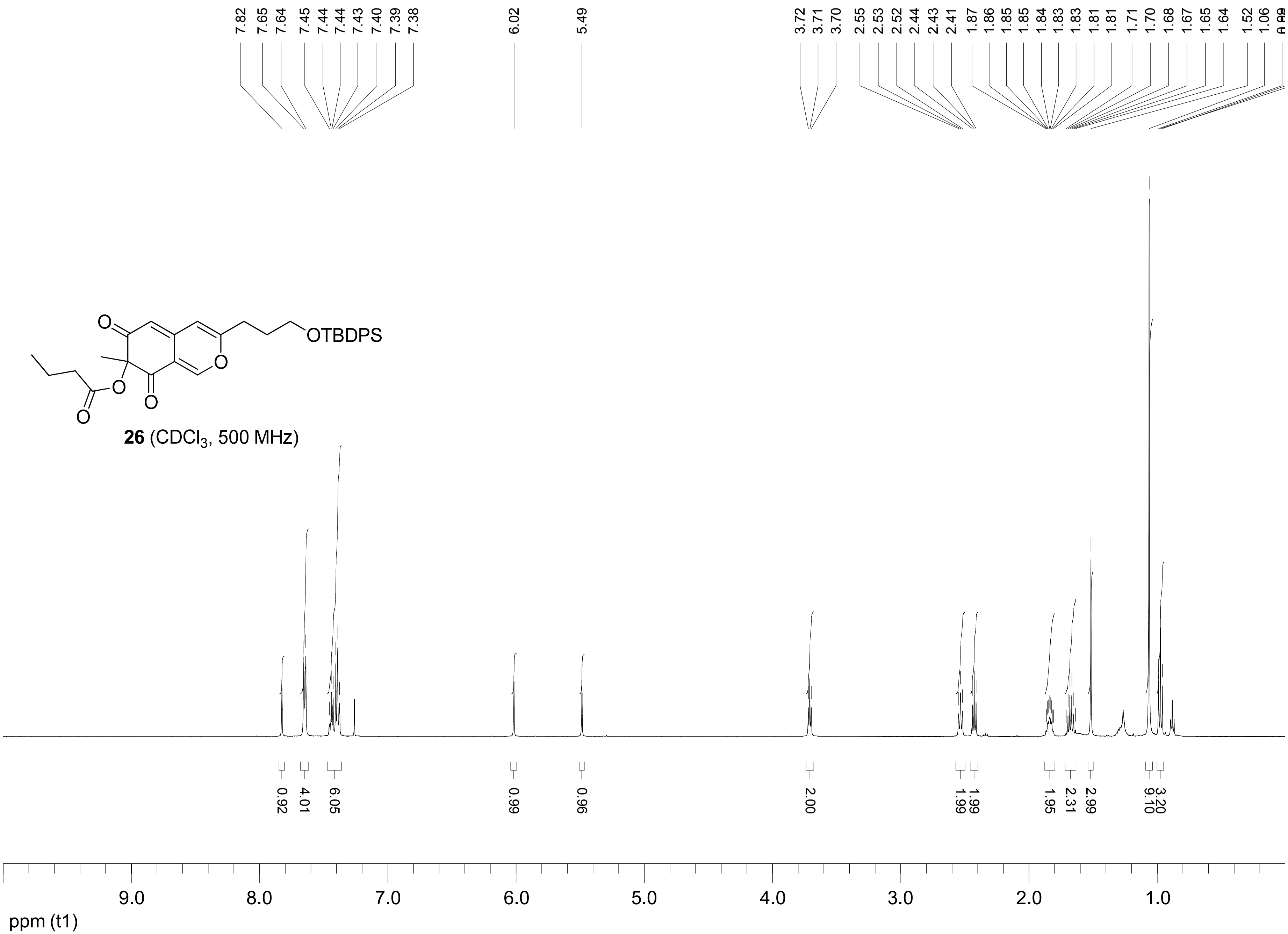
24 ($CDCl_3$, 150 MHz)

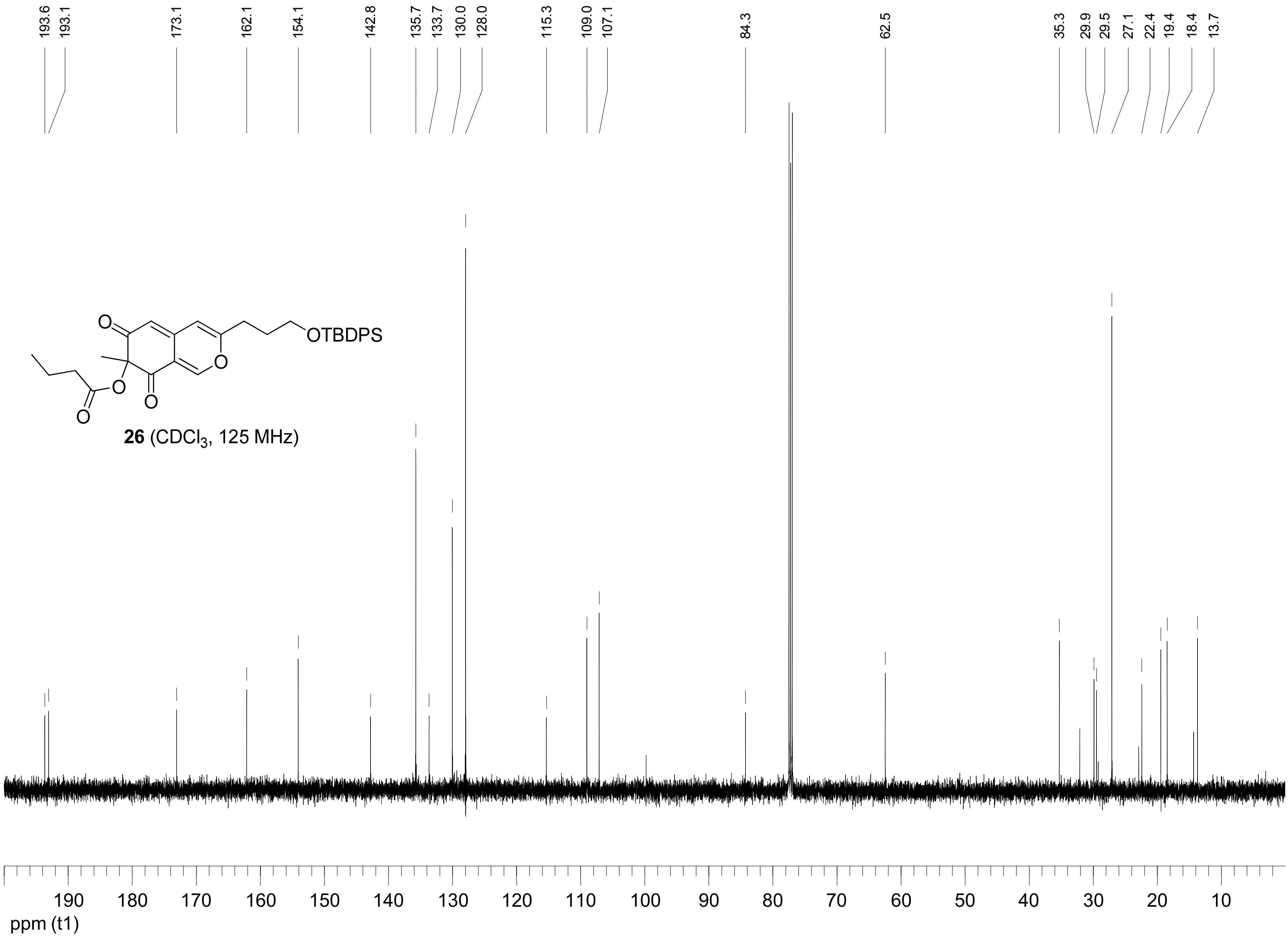


25 ($CDCl_3$, 500 MHz)

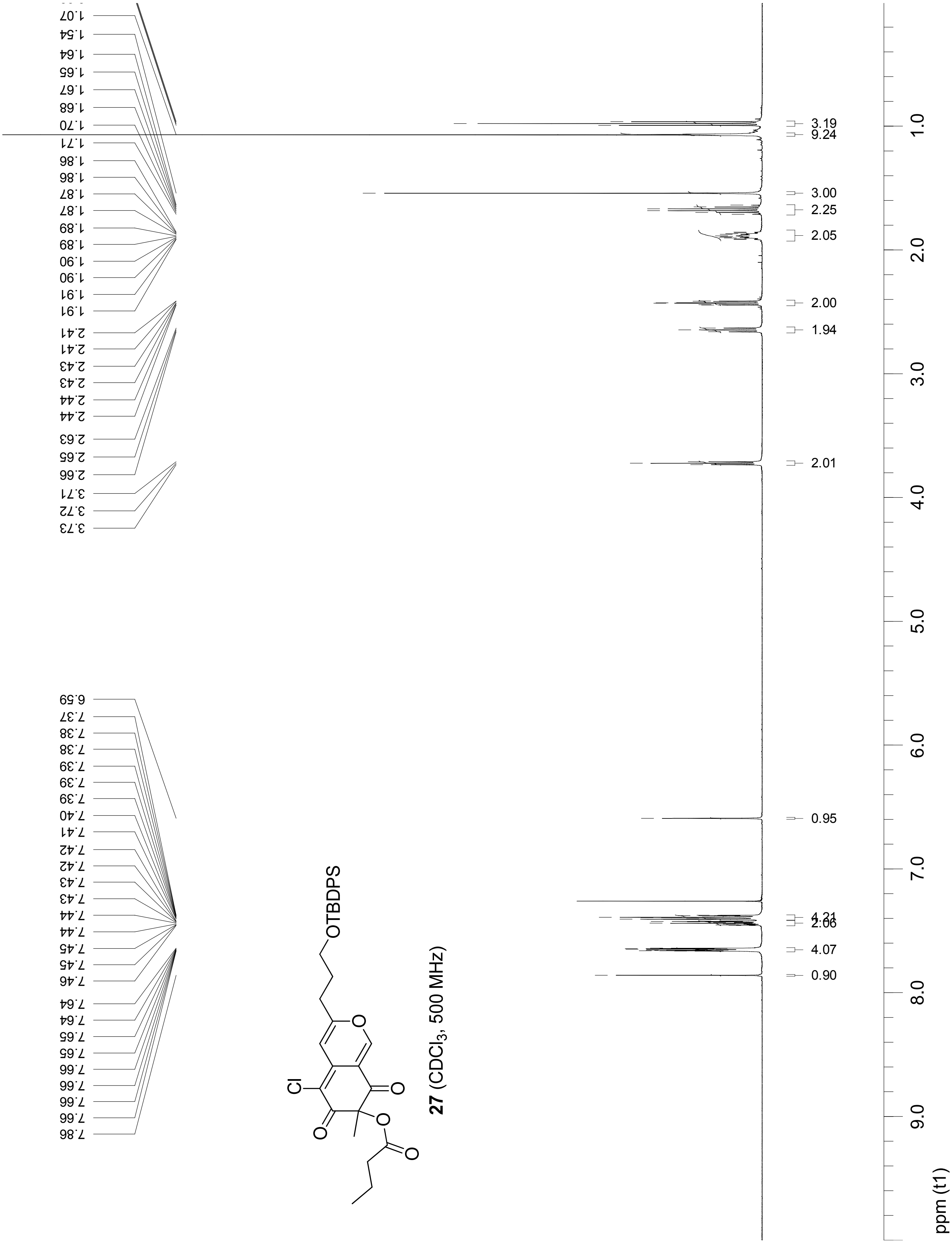


25 ($CDCl_3$, 125 MHz)

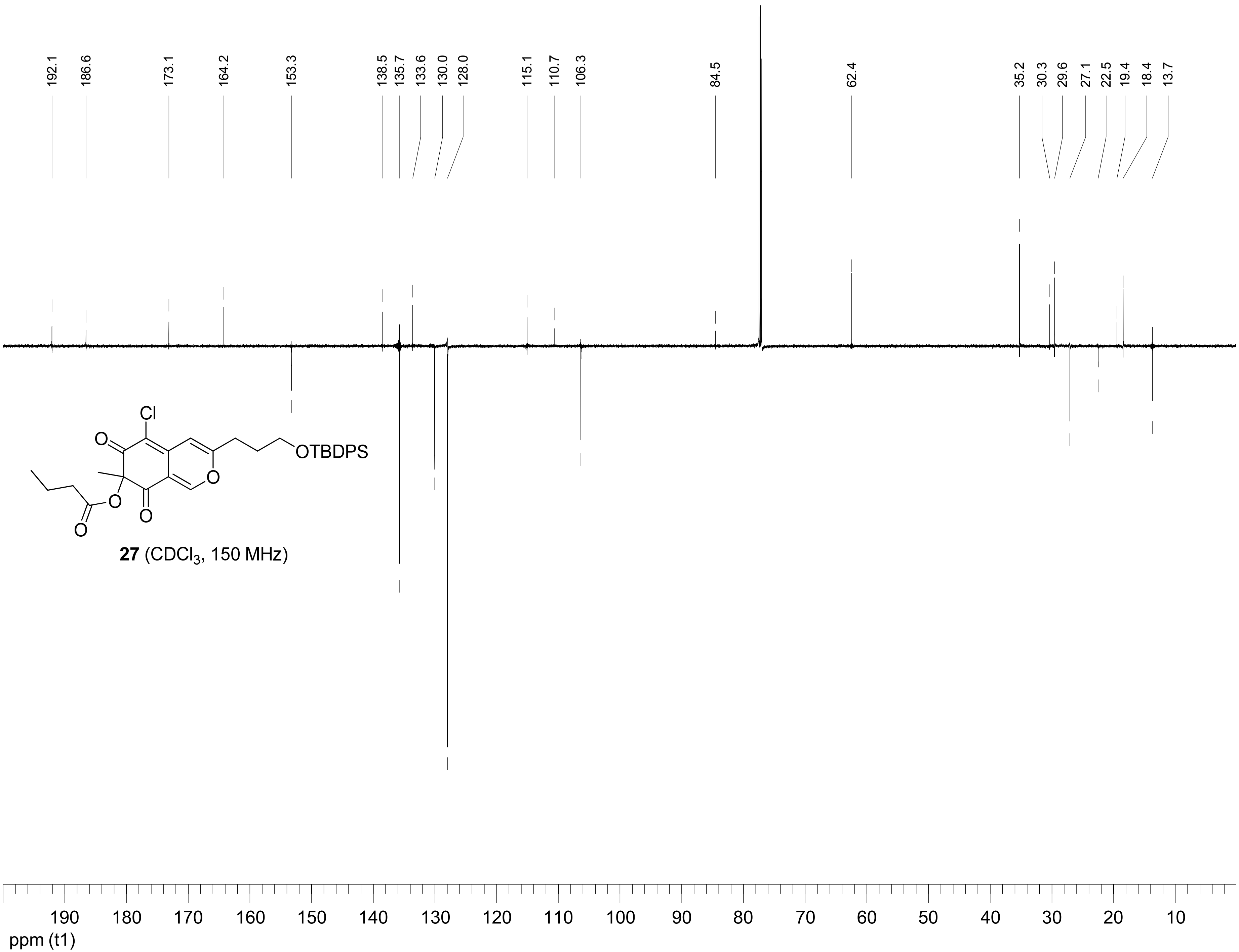

OTBDPS
26 (CDCl3, 500 MHz)
7.82
7.65
7.64
7.45
7.44
7.44
7.43
7.40
7.39
7.38
6.02
5.49
3.72
3.71
3.70
2.55
2.53
2.52
2.44
2.43
2.41
1.87
1.86
1.85
1.85
1.84
1.83
1.83
1.81
1.81
1.71
1.70
1.68
1.67
1.65
1.64
1.52
1.06
0.92
4.01
6.05
0.99
0.96
2.00
1.99
1.99
1.95
2.31
2.99
9.10
3.20
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)



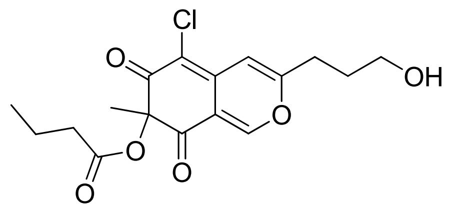
26 ($CDCl_3$, 125 MHz)



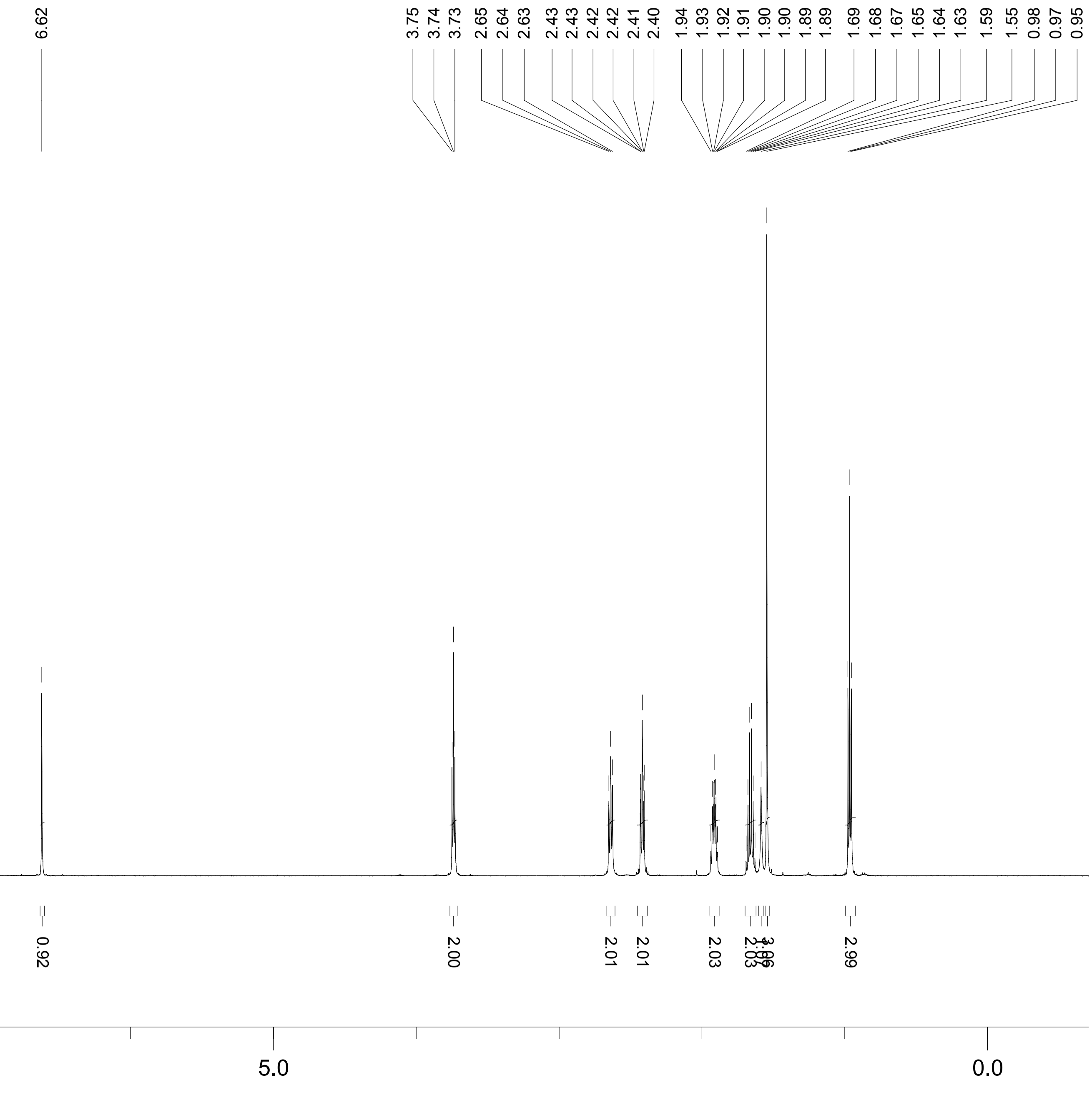
27 ($CDCl_3$, 500 MHz)

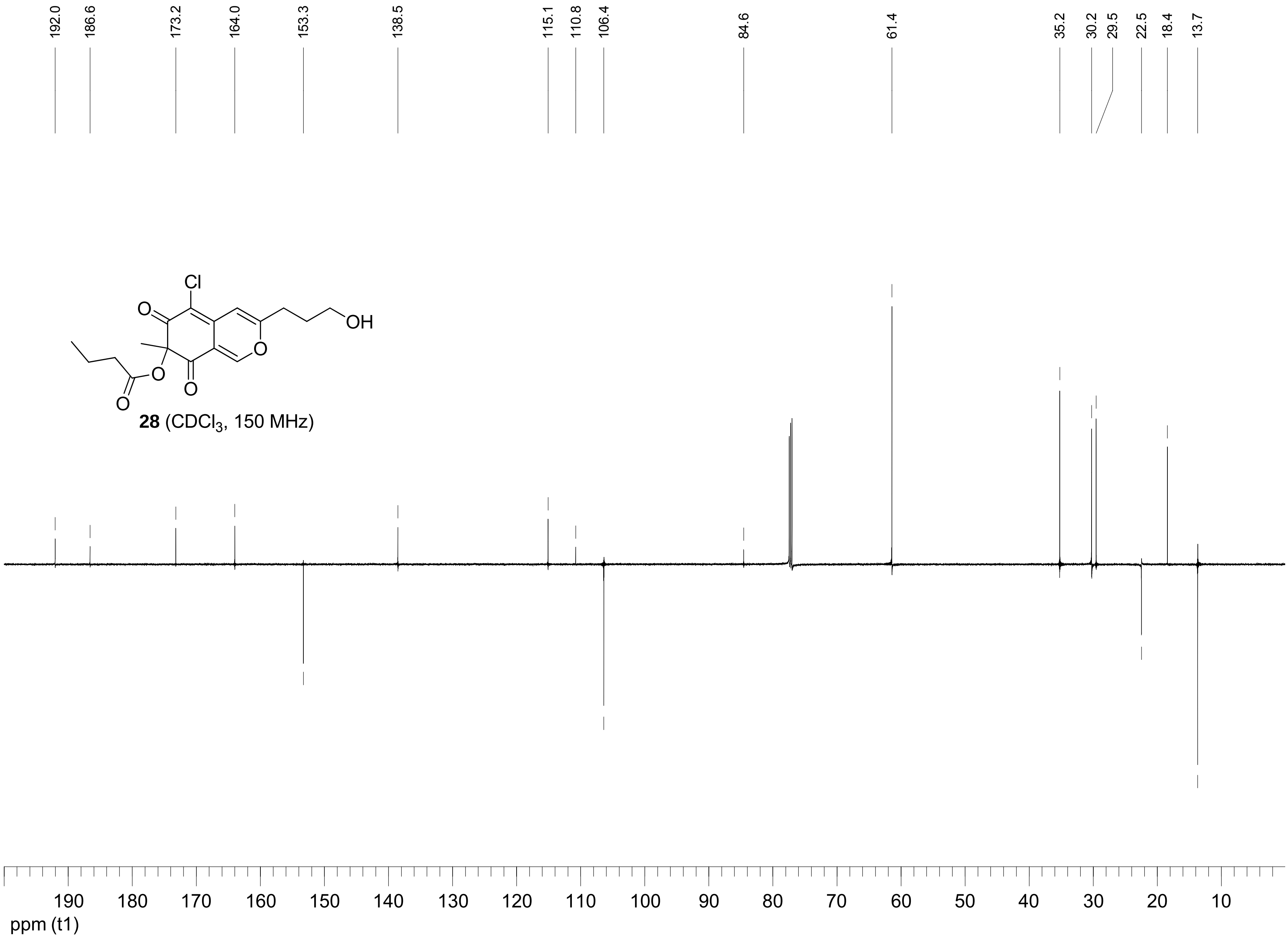


27 ($CDCl_3$, 150 MHz)

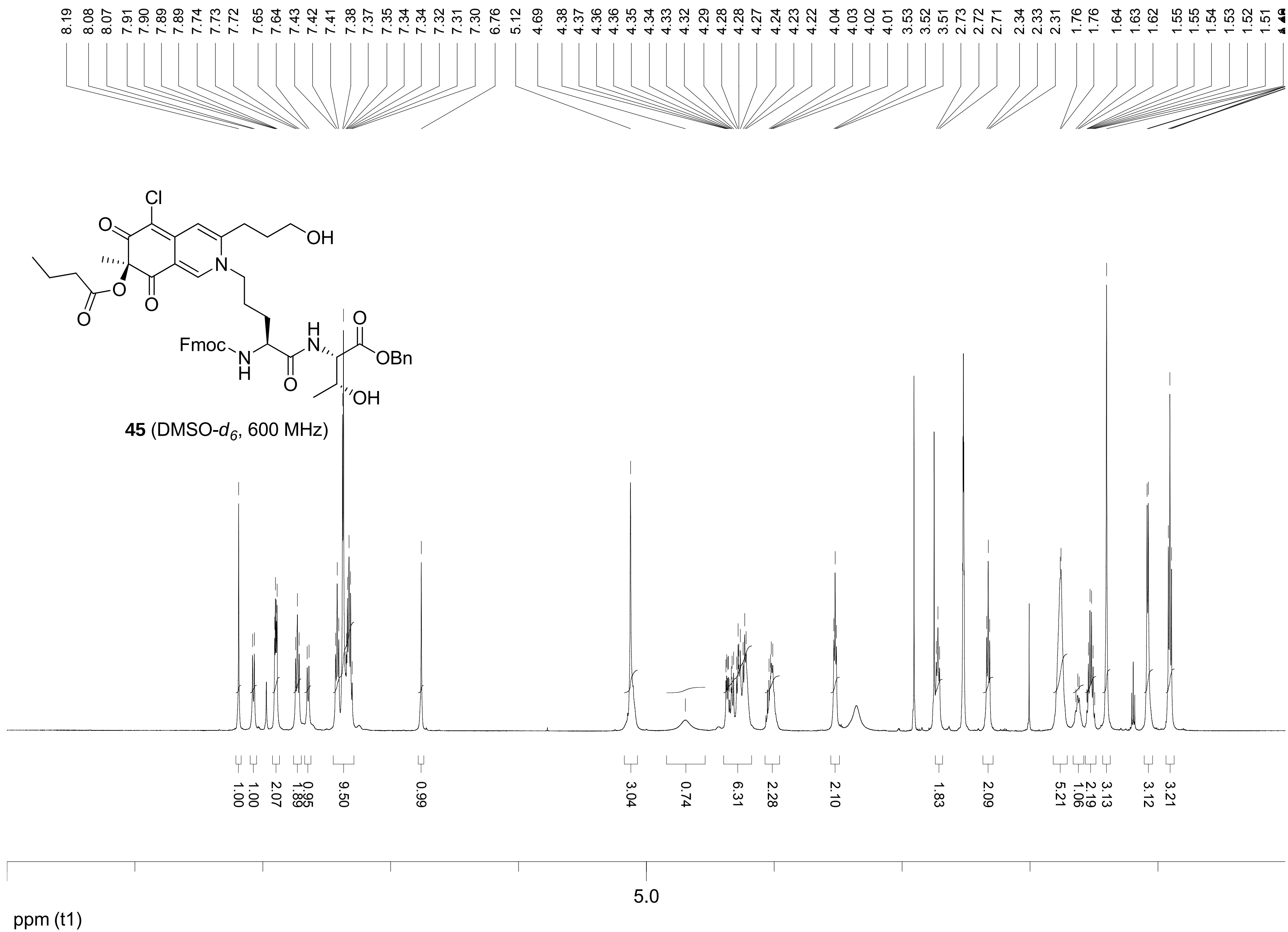


28 ($CDCl_3$, 600 MHz)

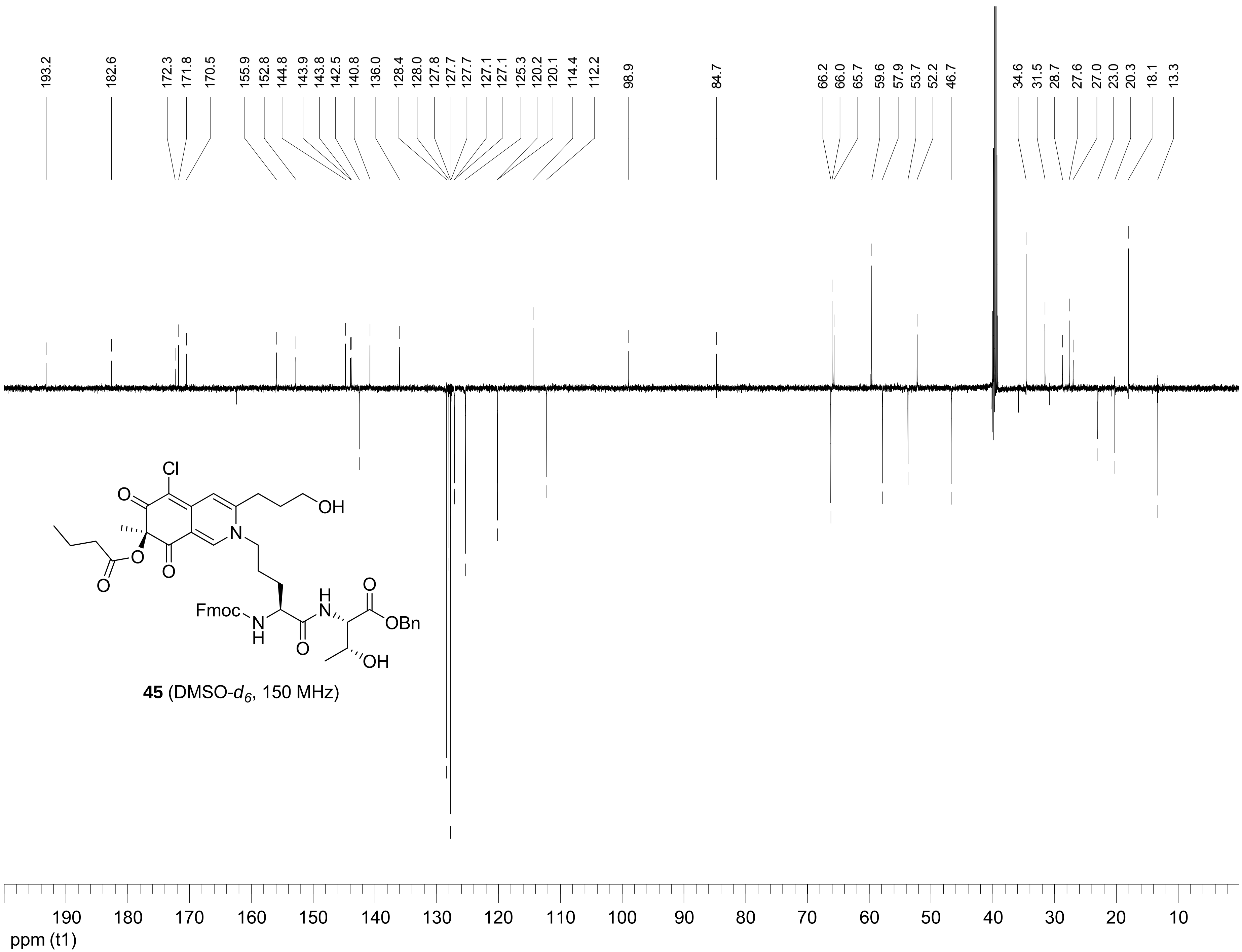




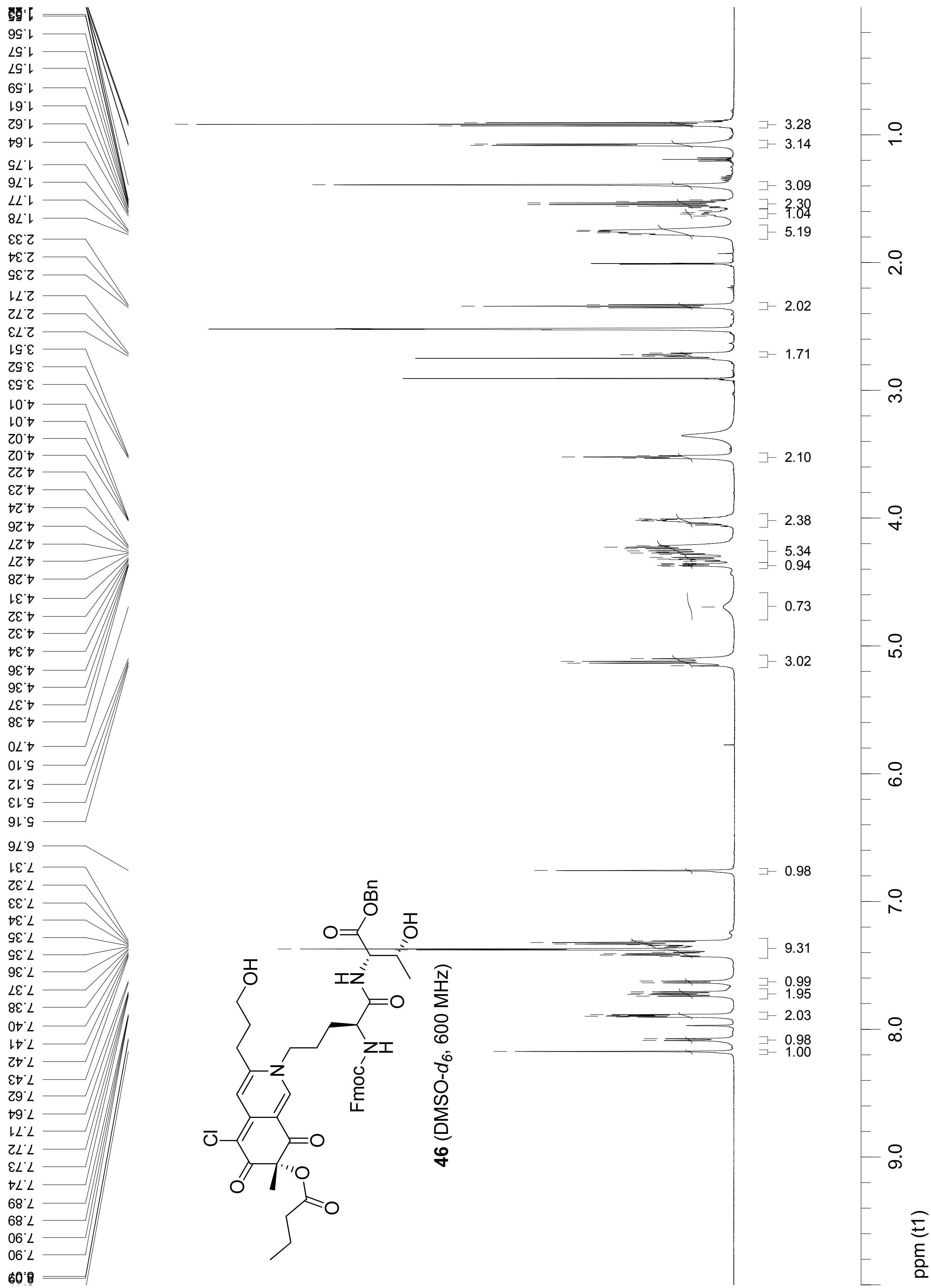
28 (CDCl$_3$, 150 MHz)



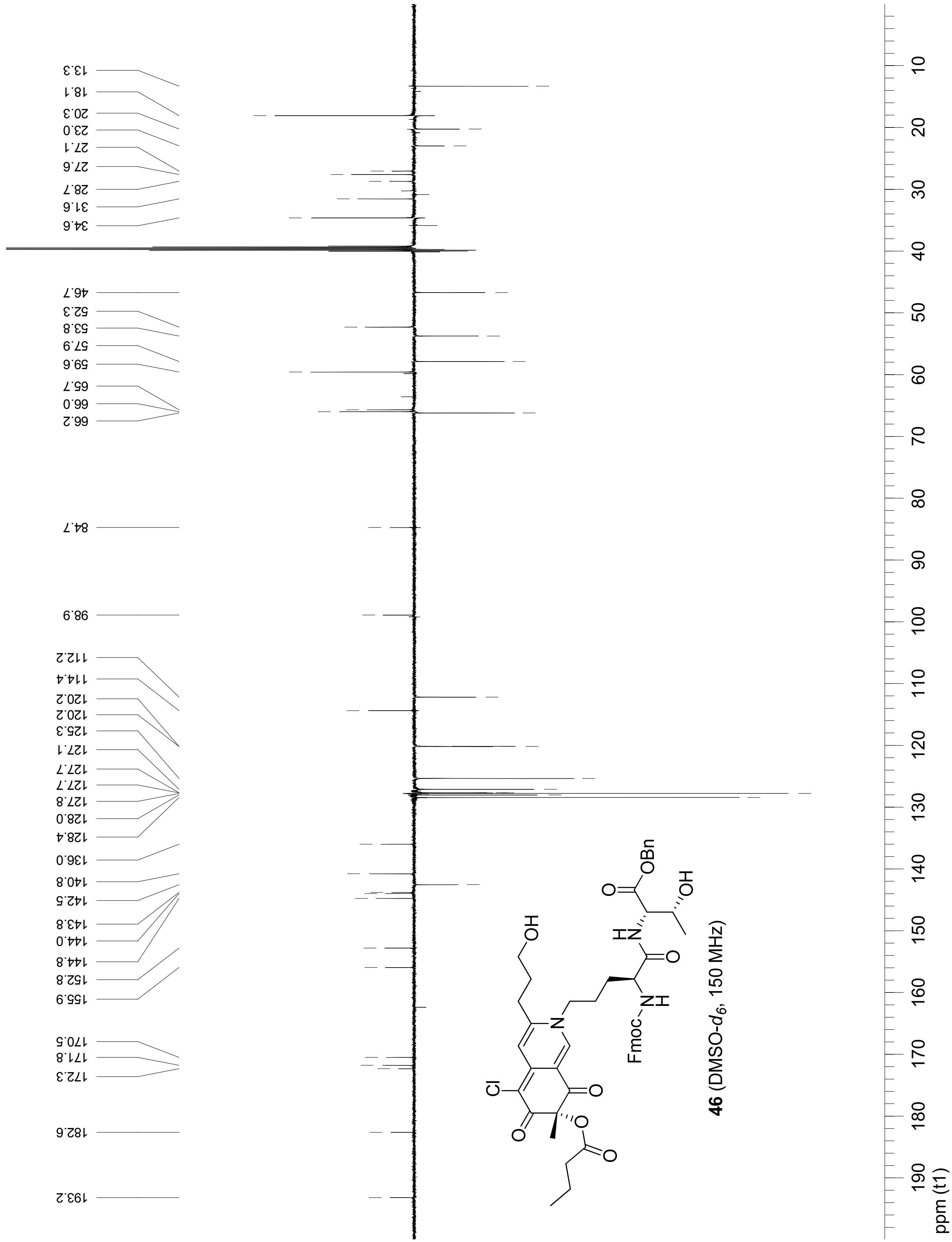
45 (DMSO-d_6, 600 MHz)



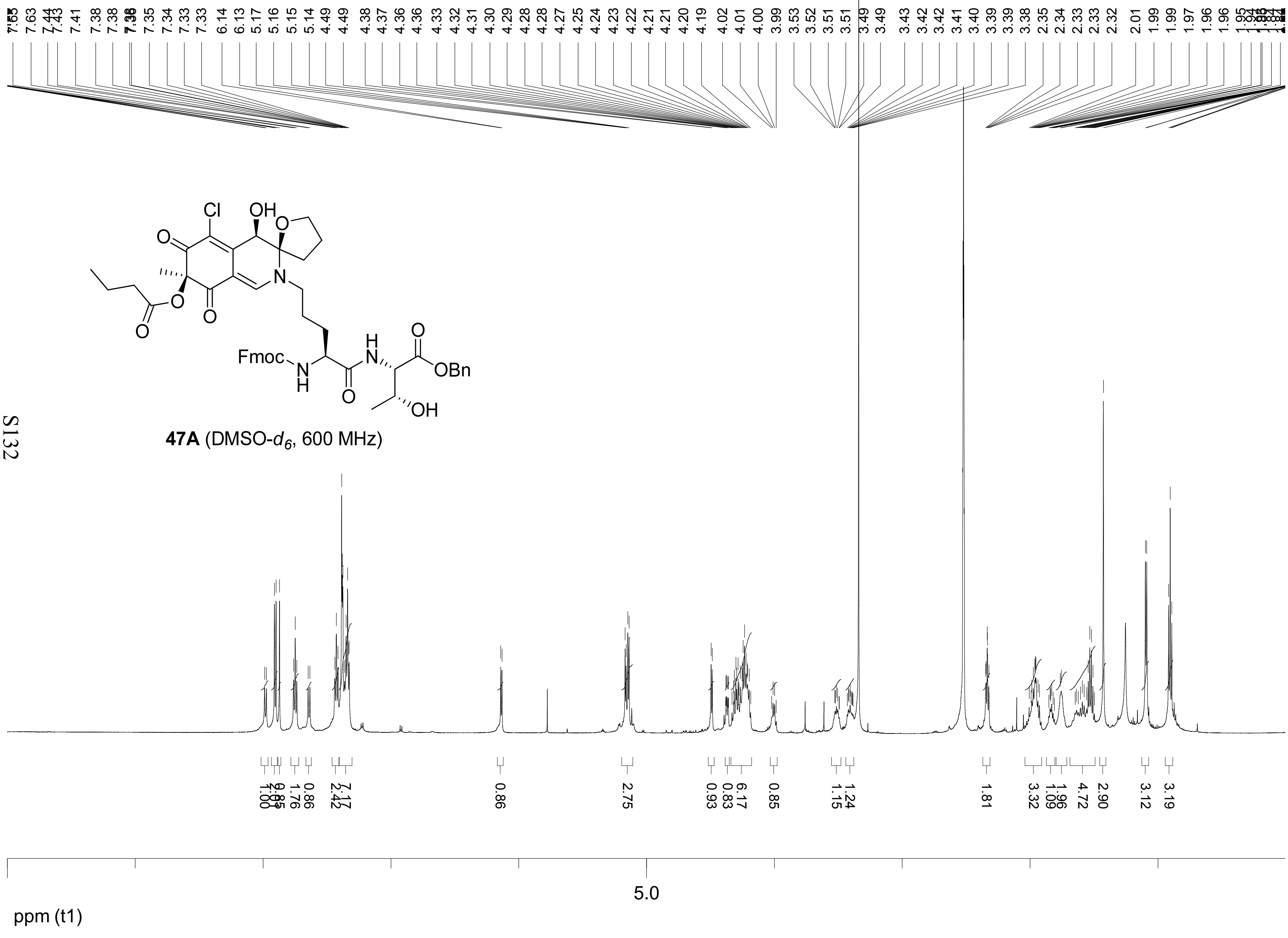
45 (DMSO-d_6, 150 MHz)



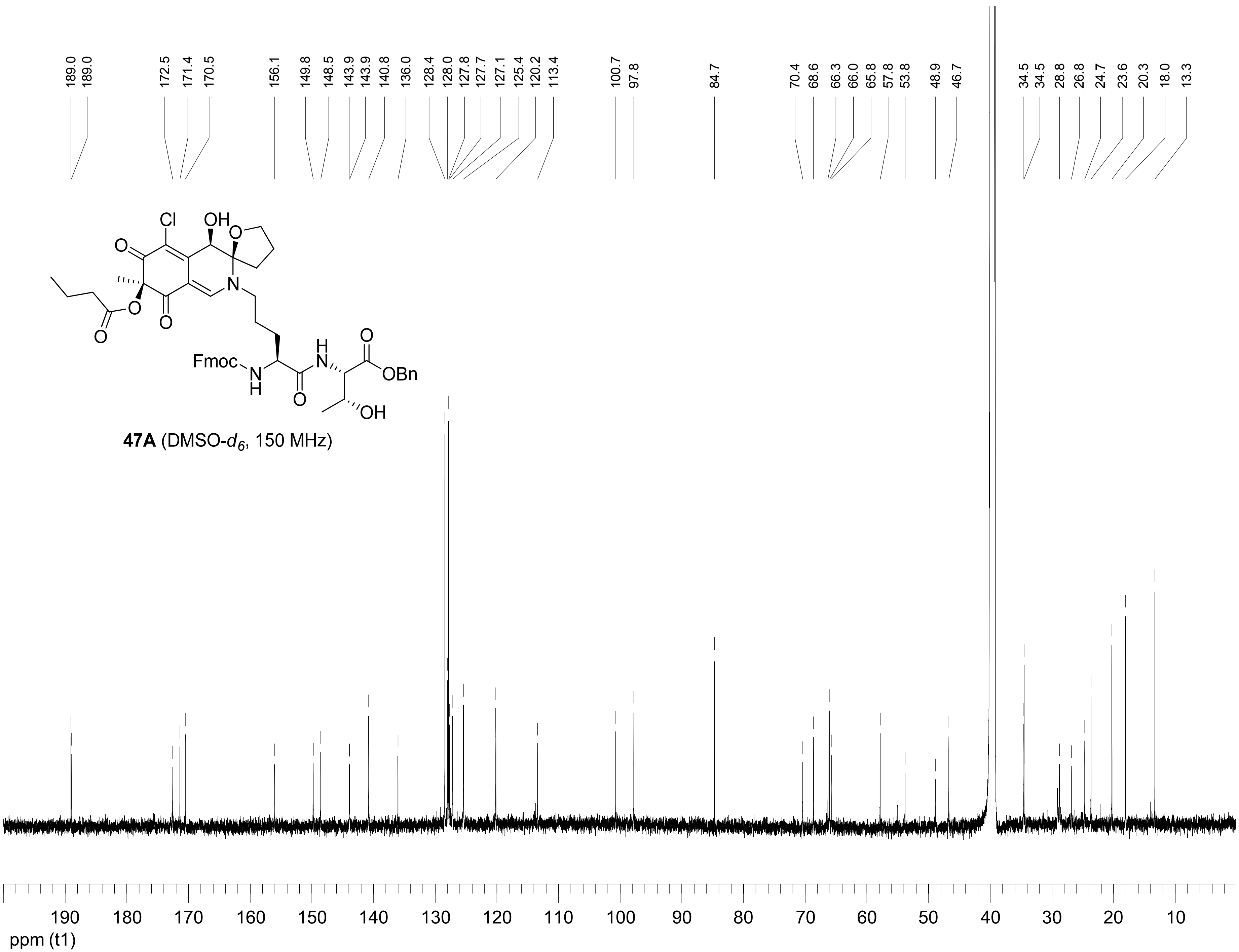
46 (DMSO-d_6, 600 MHz)
ppm (t1)
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
3.28
3.14
3.09
2.30
1.04
5.19
2.02
1.71
2.10
2.38
5.34
0.94
0.73
3.02
0.98
9.31
0.99
1.95
2.03
0.98
1.00
1.56
1.57
1.57
1.59
1.61
1.62
1.64
1.75
1.76
1.77
1.78
2.33
2.34
2.35
2.71
2.72
2.73
3.51
3.52
3.53
4.01
4.01
4.02
4.02
4.22
4.23
4.24
4.26
4.27
4.27
4.28
4.31
4.32
4.32
4.34
4.36
4.36
4.37
4.38
4.70
5.10
5.12
5.13
5.16
6.76
7.31
7.32
7.33
7.34
7.35
7.35
7.36
7.37
7.38
7.40
7.41
7.42
7.43
7.62
7.64
7.71
7.72
7.73
7.74
7.89
7.89
7.90
7.90
OBn
OH
HO
Cl
Fmoc



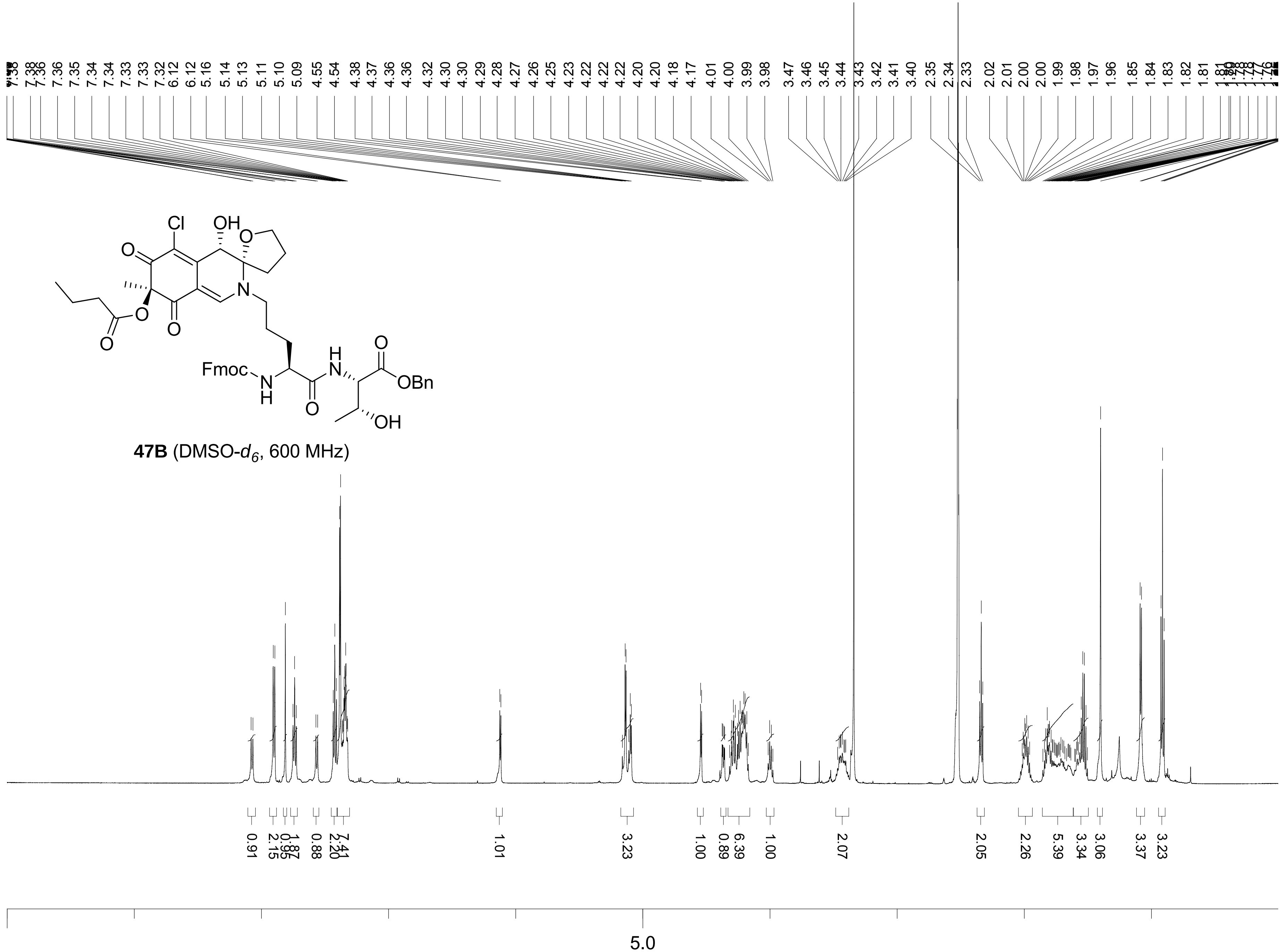
46 (DMSO-d_6, 150 MHz)



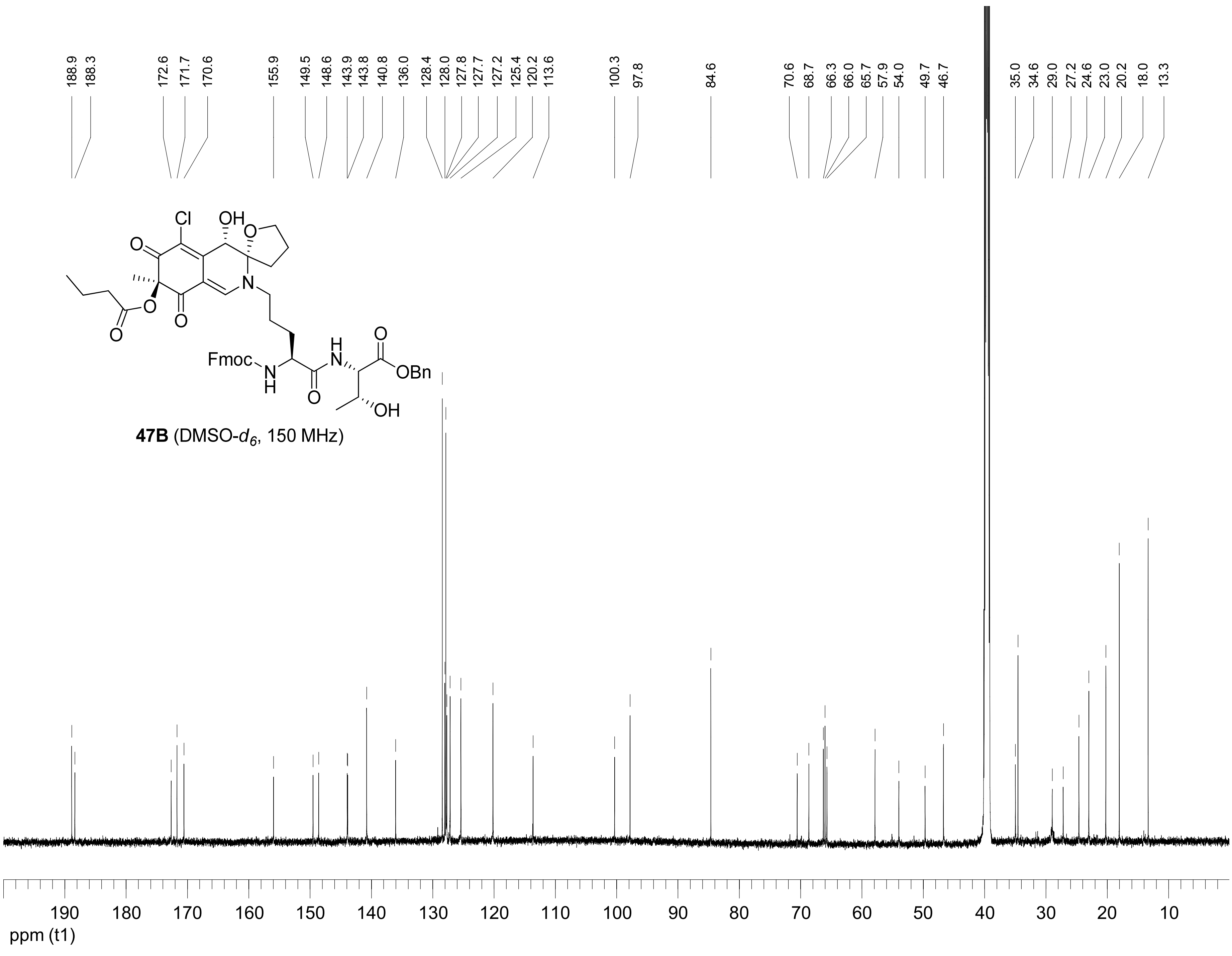
47A (DMSO-d_6, 600 MHz)



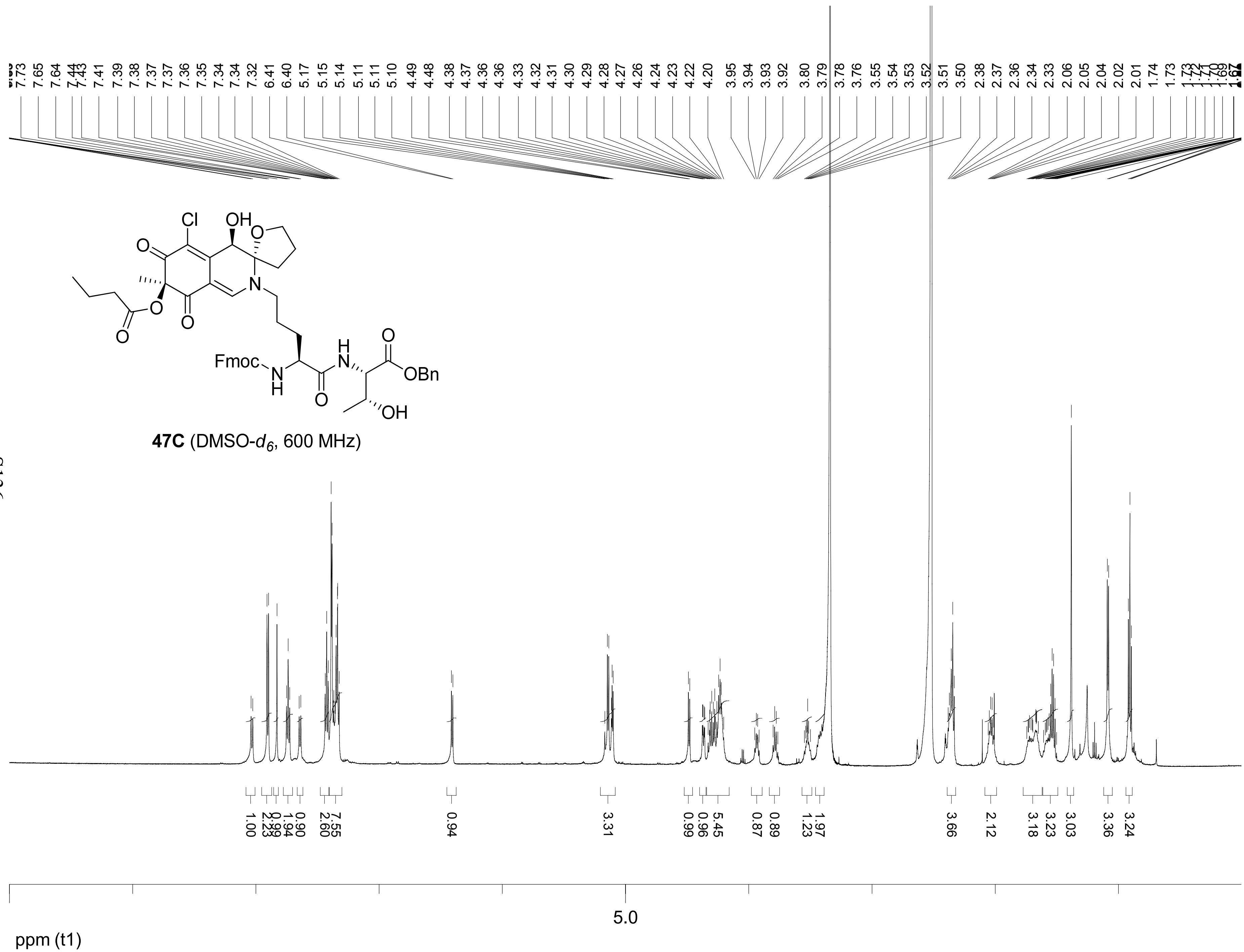
47A (DMSO-d_6, 150 MHz)



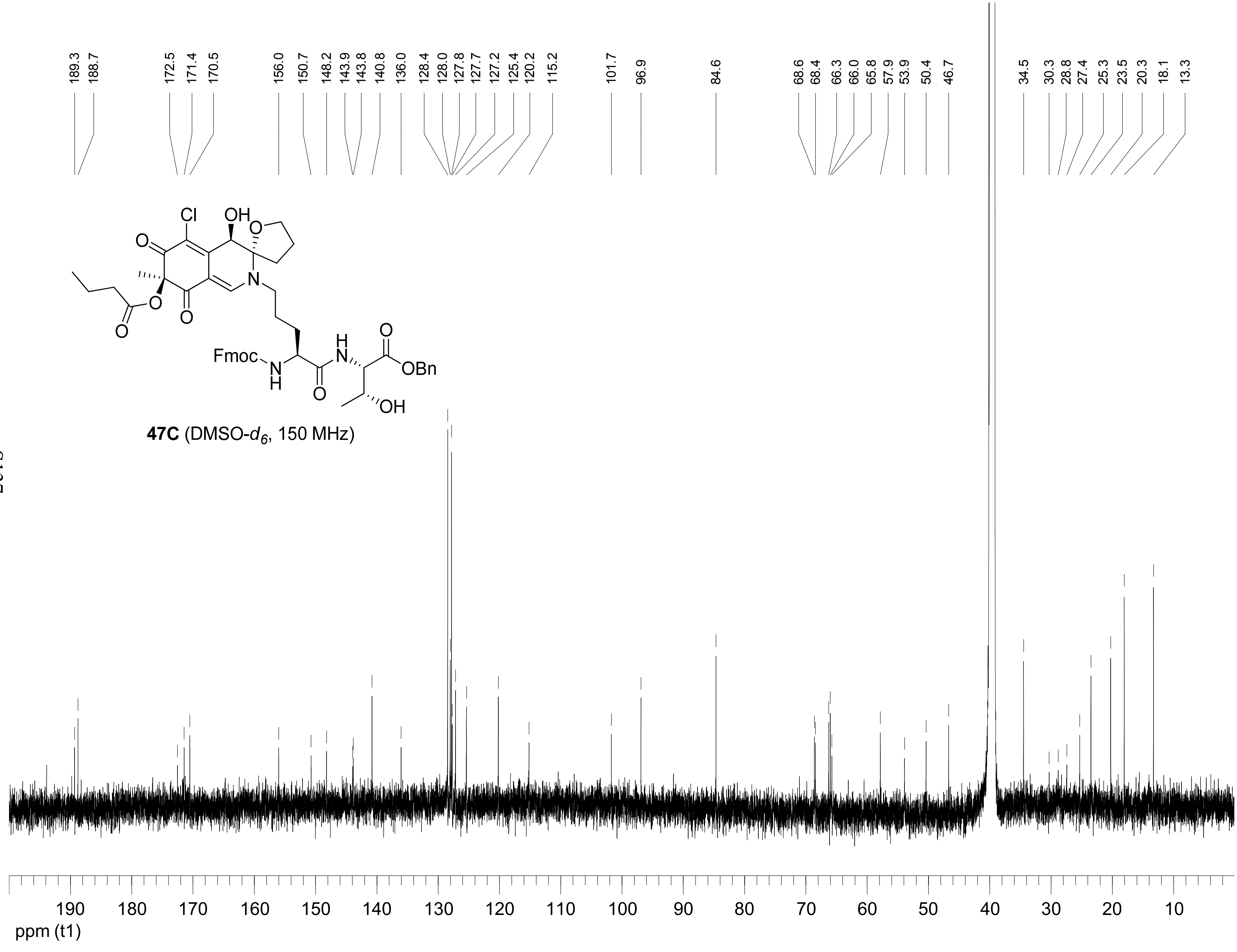
47B (DMSO-d_6, 600 MHz)



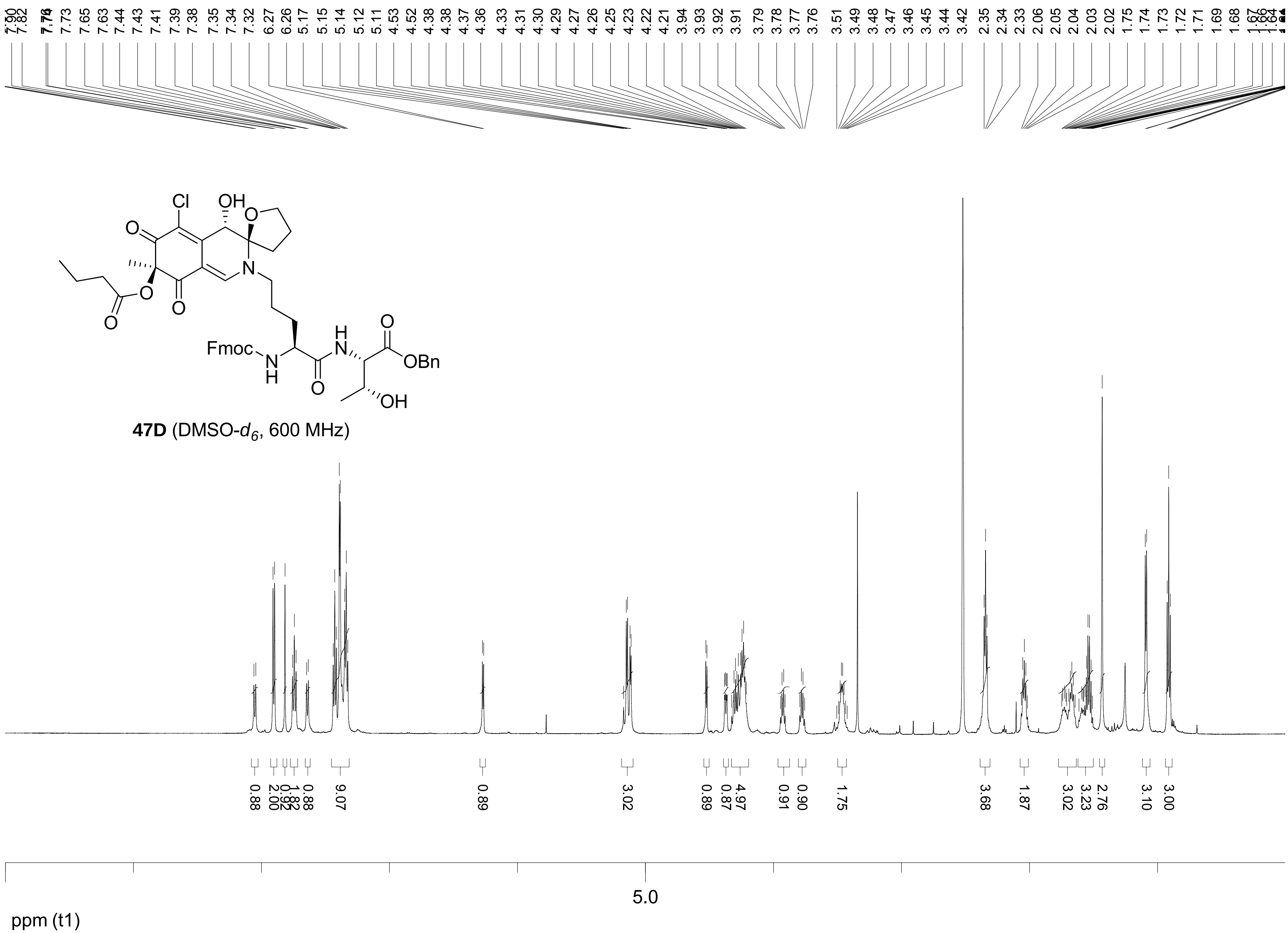
47B (DMSO-d_6, 150 MHz)



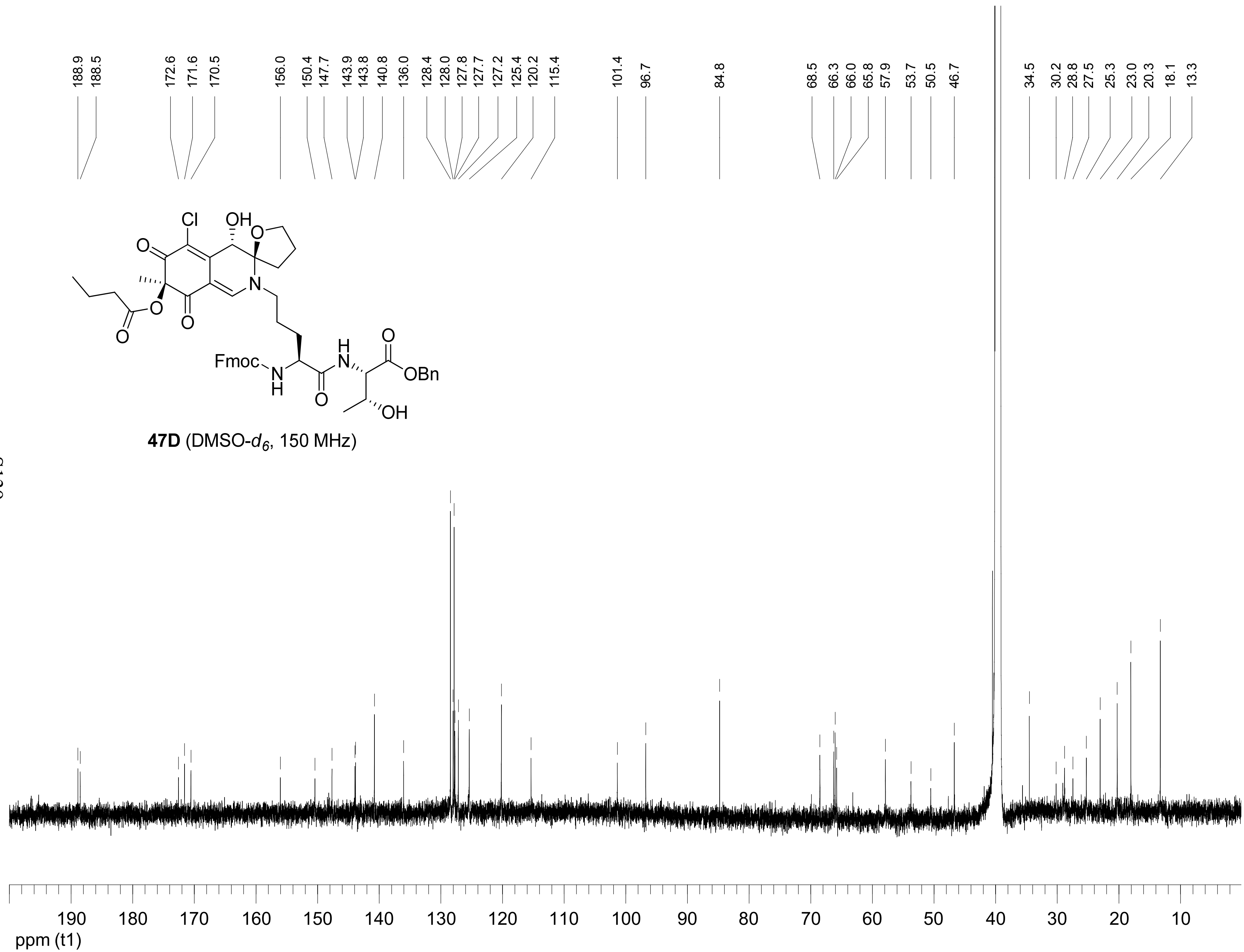
47C (DMSO-d_6, 600 MHz)



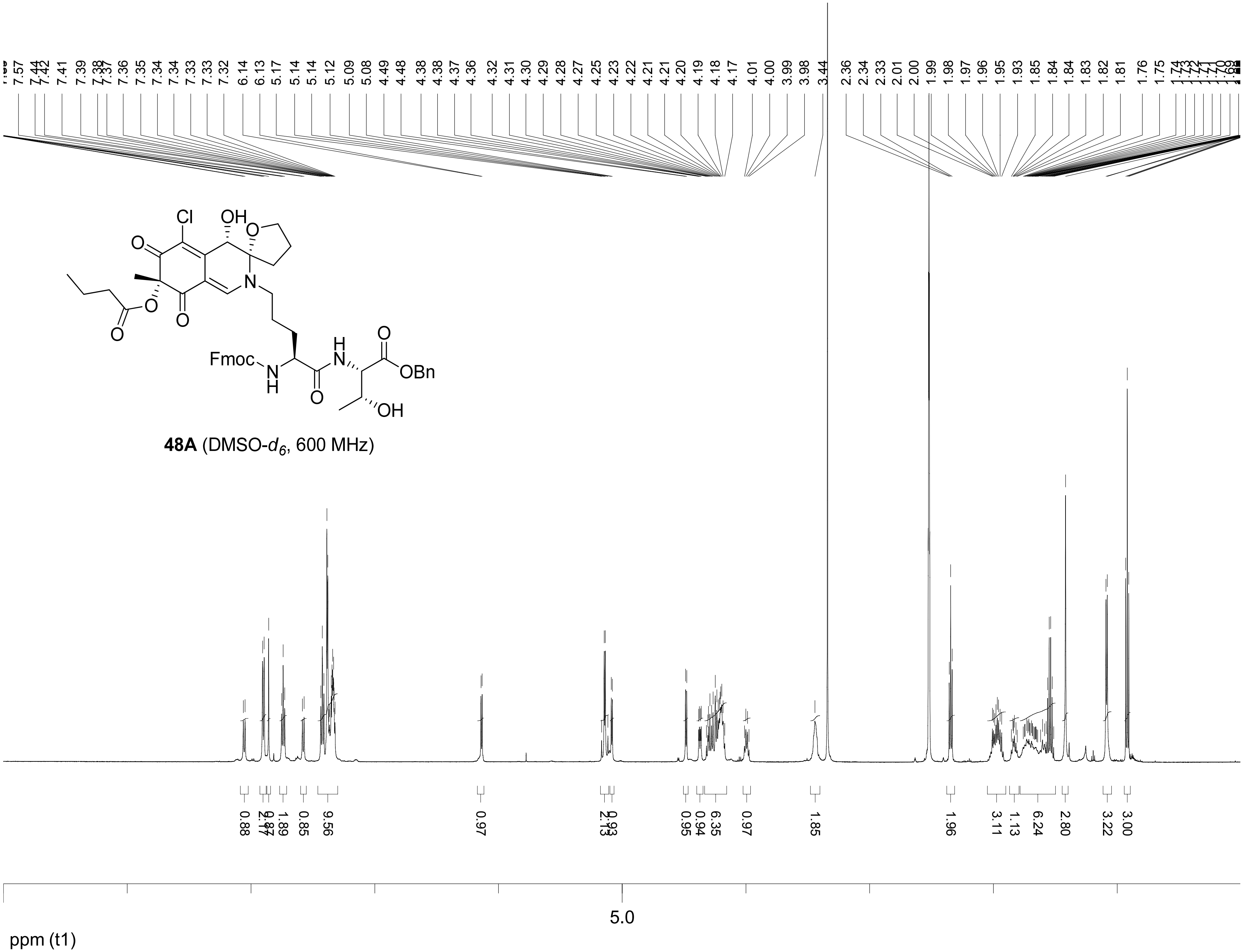
47C (DMSO-d_6, 150 MHz)



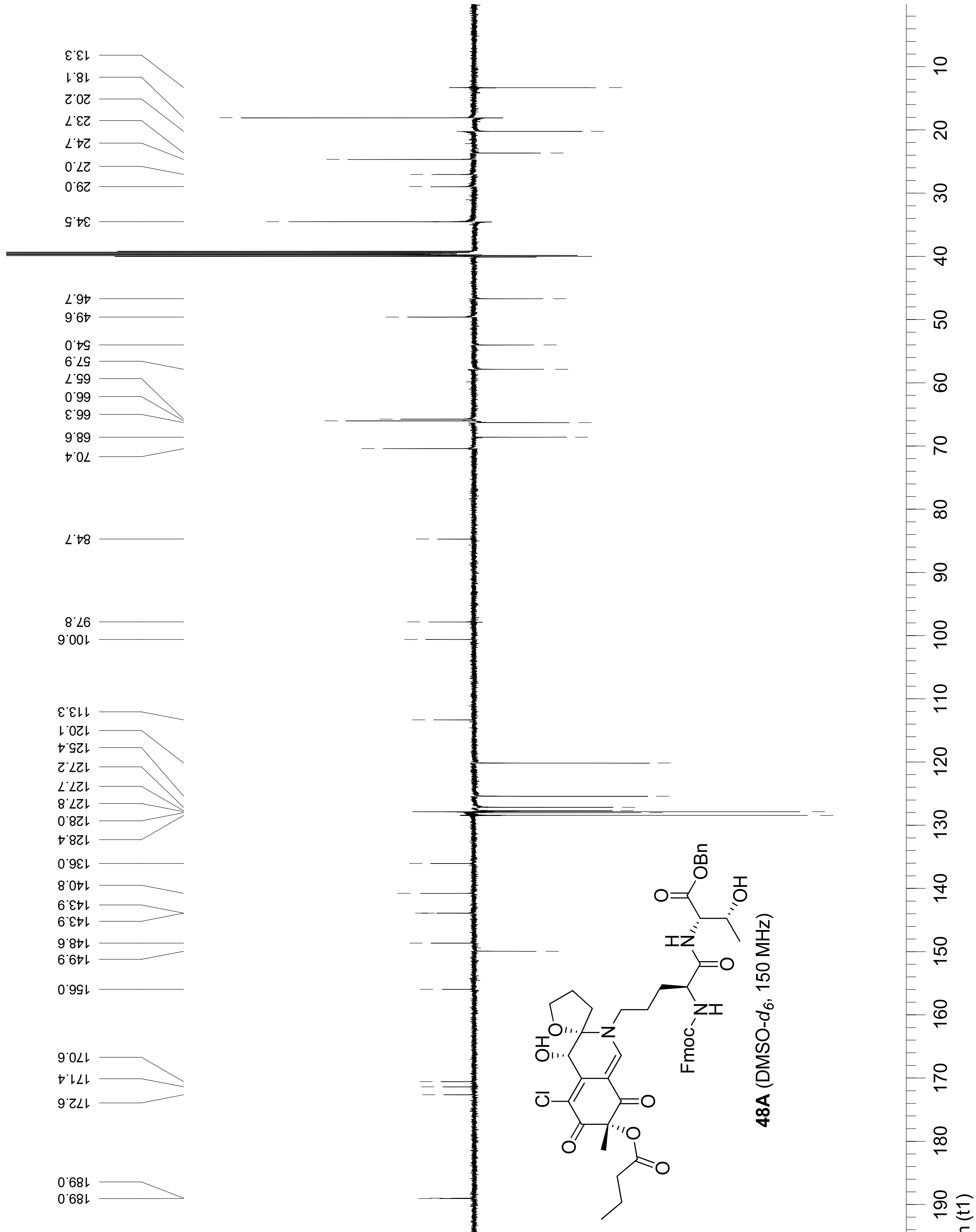
47D (DMSO-d_6, 600 MHz)

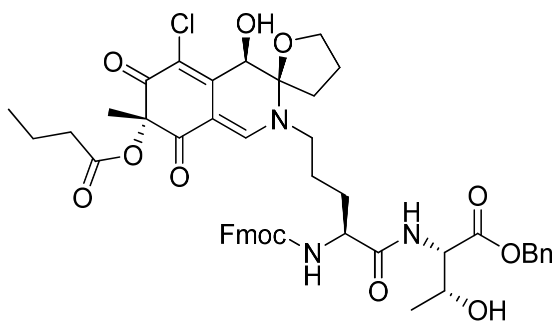


47D (DMSO-d_6, 150 MHz)

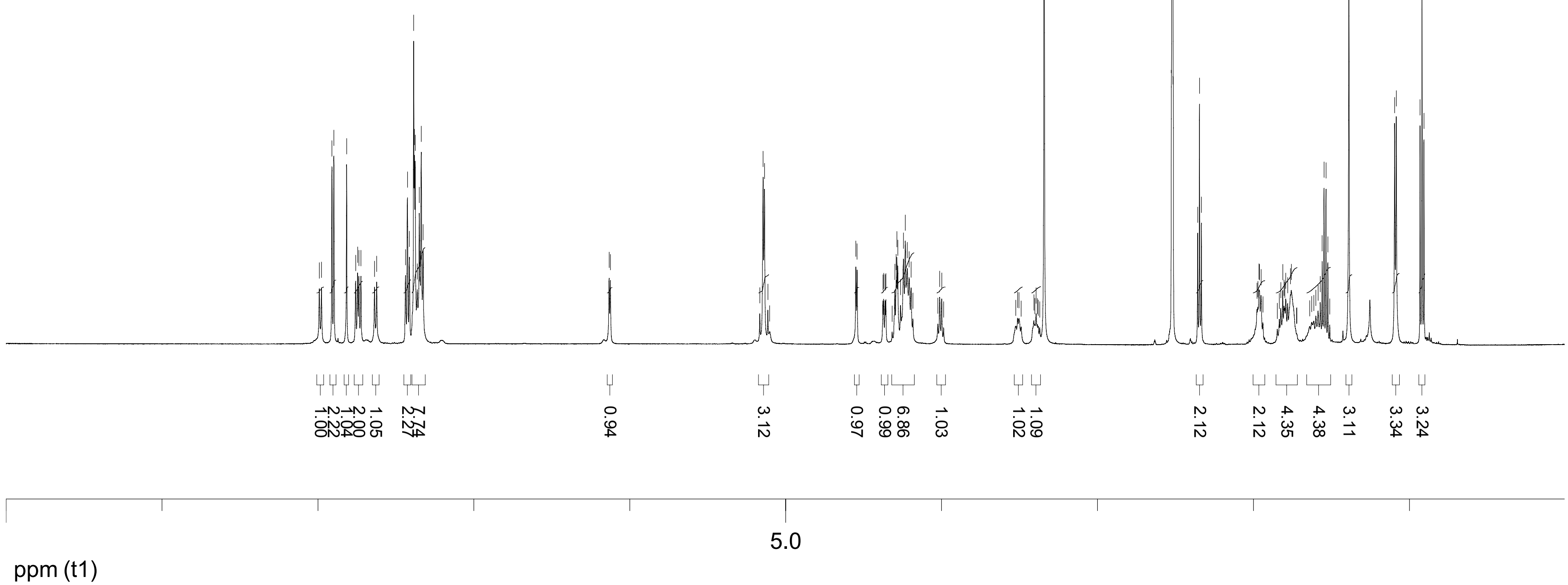


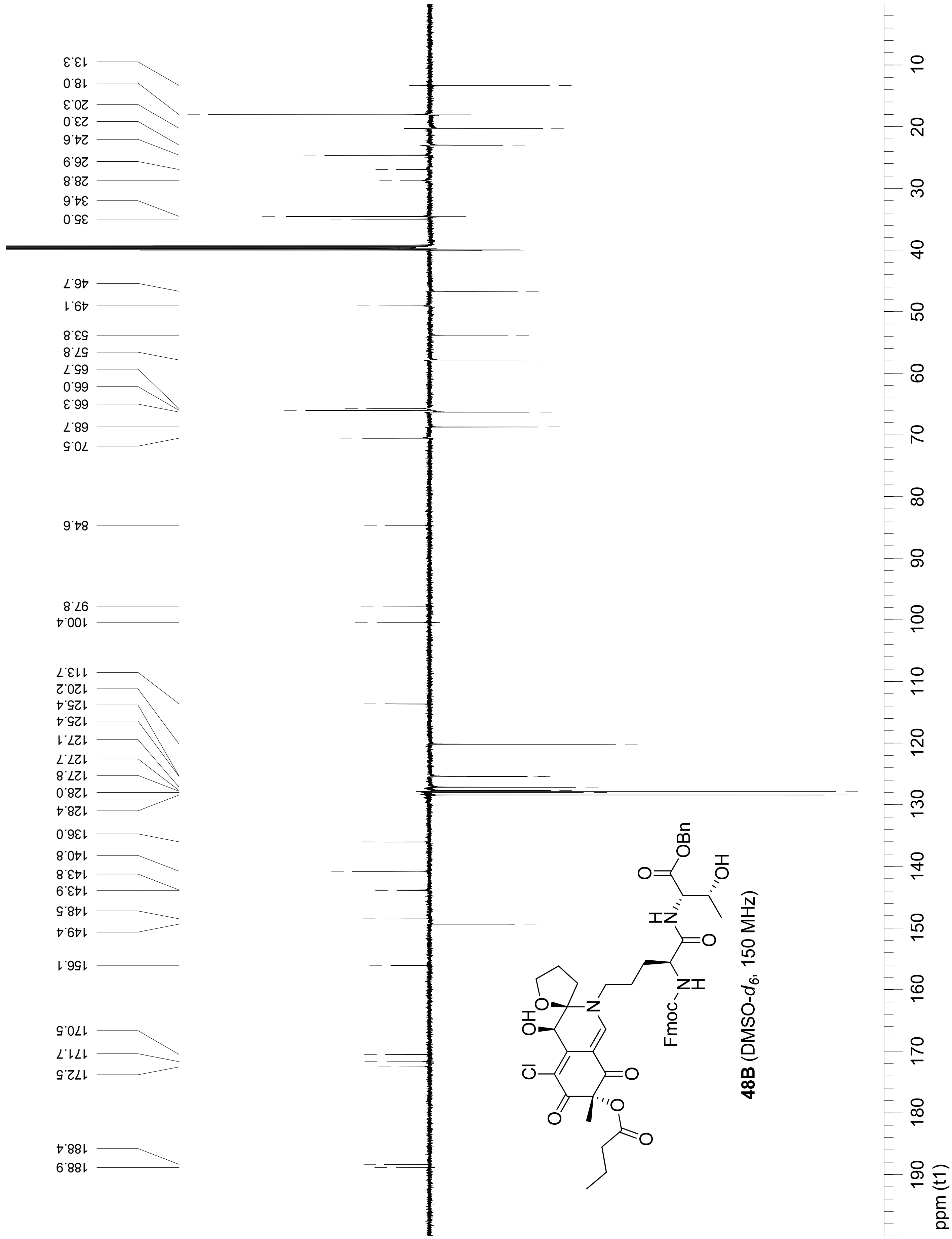
48A (DMSO-d_6, 600 MHz)

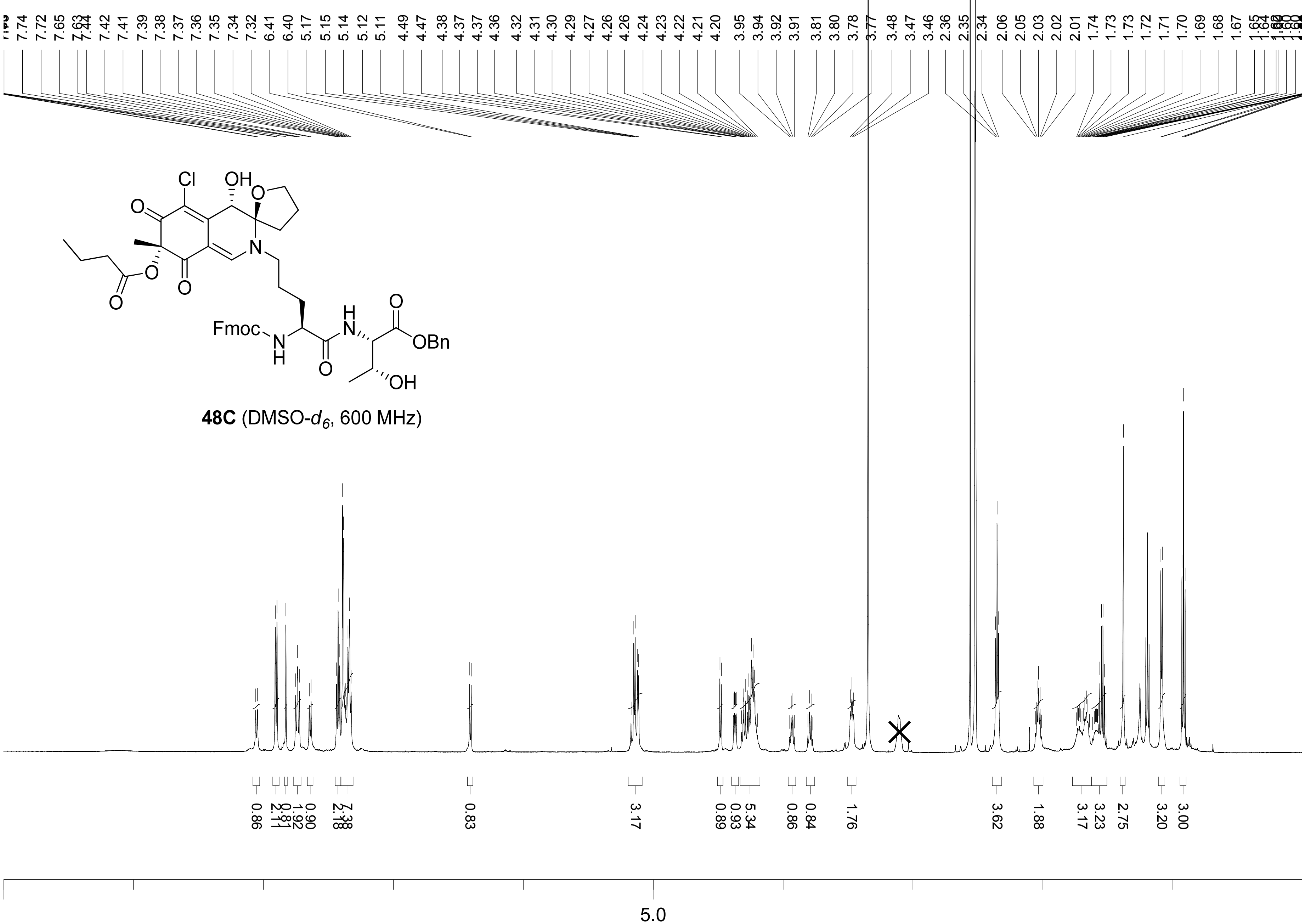

13.3
18.1
20.2
23.7
24.7
27.0
29.0
34.5
46.7
49.6
54.0
57.9
65.7
66.0
66.3
68.6
70.4
84.7
97.8
100.6
113.3
120.1
125.4
127.2
127.7
127.8
128.0
128.4
136.0
140.8
143.9
143.9
148.6
149.9
156.0
170.6
171.4
172.6
189.0
189.0
ppm (t1)
Cl
OH
O
N
Fmoc
H
OBn
OH
48A (DMSO-d_6, 150 MHz)



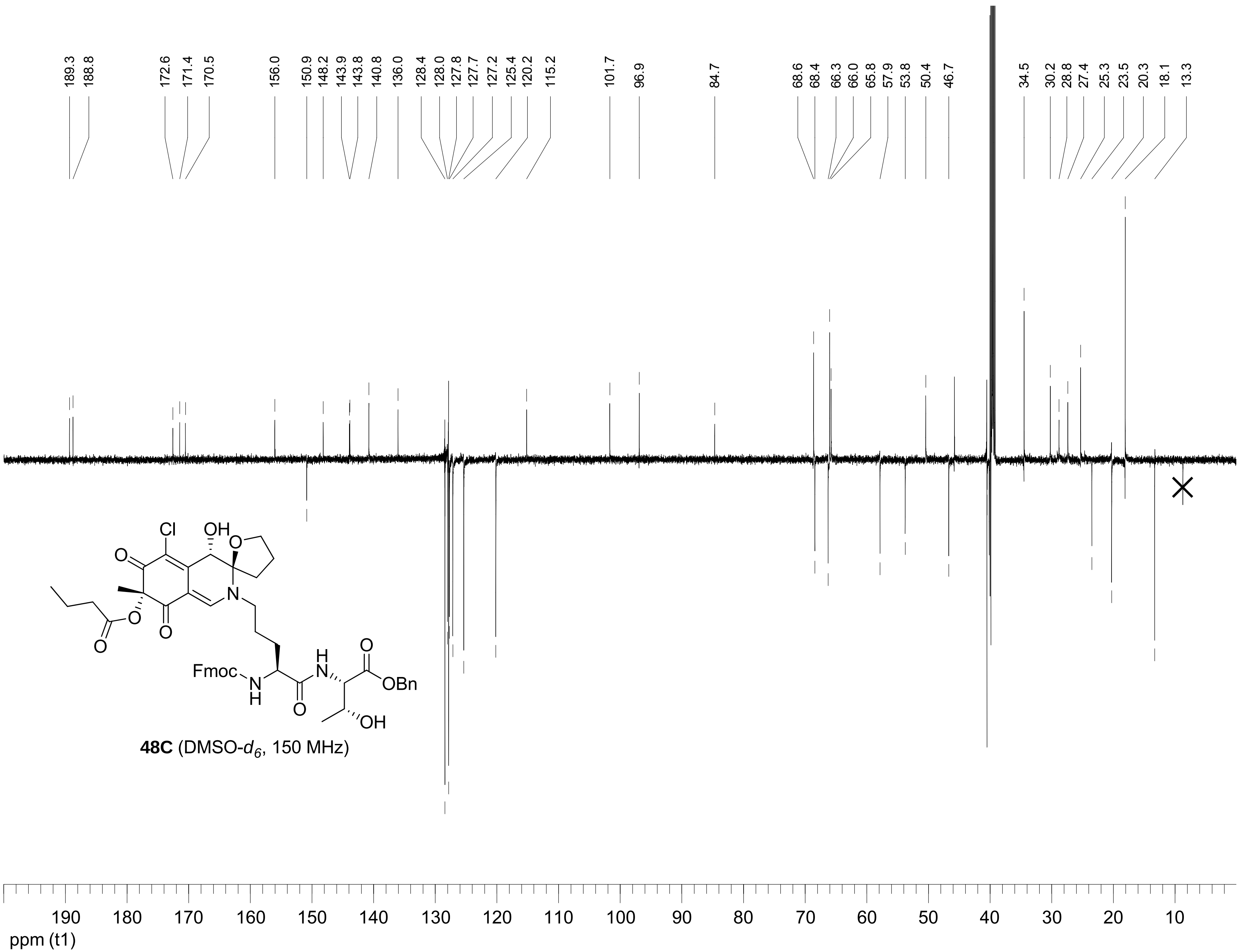
48B (DMSO-d_6, 600 MHz)



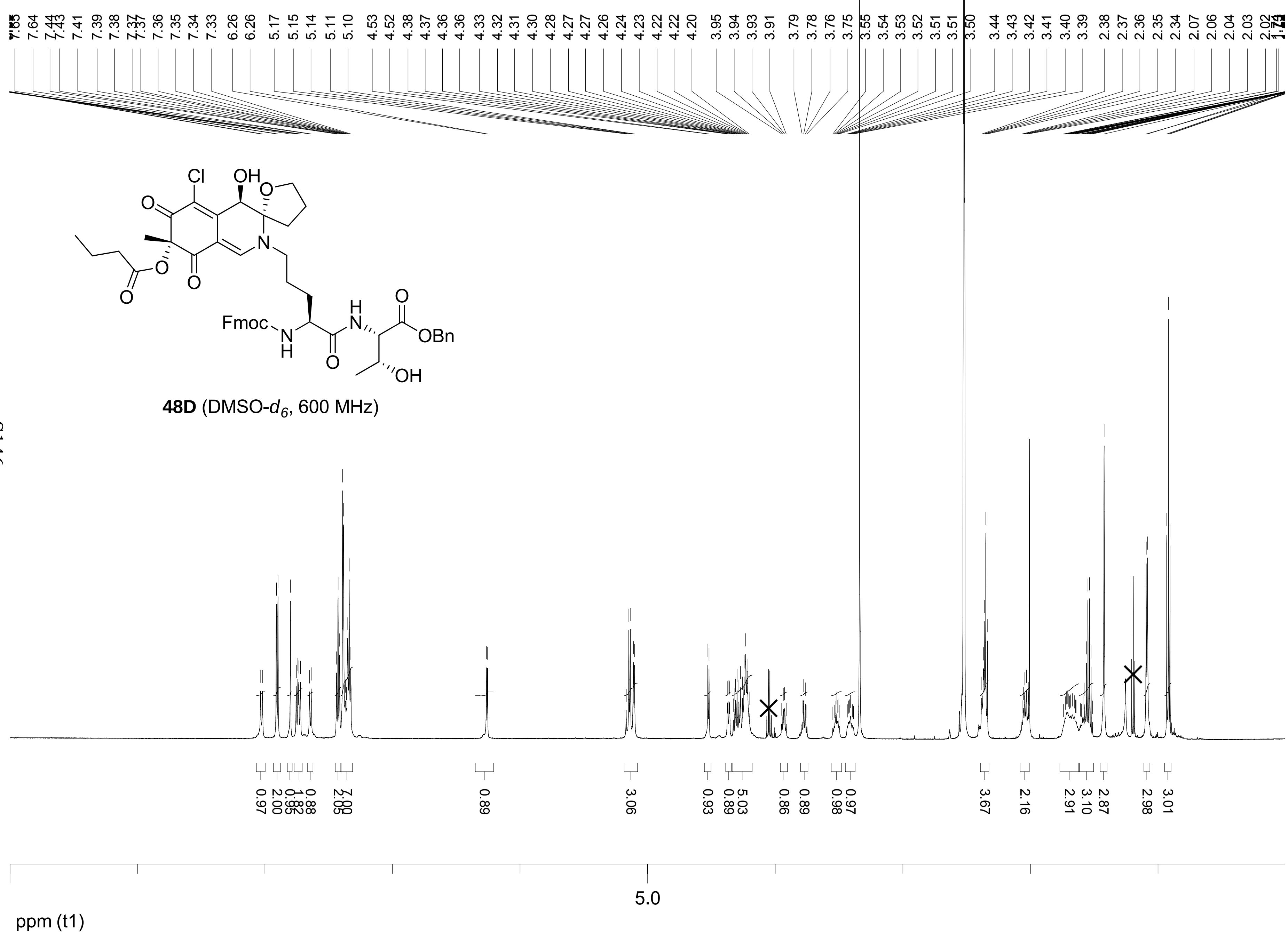

13.3
18.0
20.3
23.0
24.6
26.9
28.8
34.6
35.0
46.7
49.1
53.8
57.8
65.7
66.0
66.3
68.7
70.5
84.6
97.8
100.4
113.7
120.2
125.4
125.4
127.1
127.7
127.8
128.0
128.4
136.0
140.8
143.8
143.9
148.5
149.4
156.1
170.5
171.7
172.5
188.4
188.9
ppm (t1)
48B (DMSO-d_6, 150 MHz)
Fmoc
OBn
OH
Cl
N
O



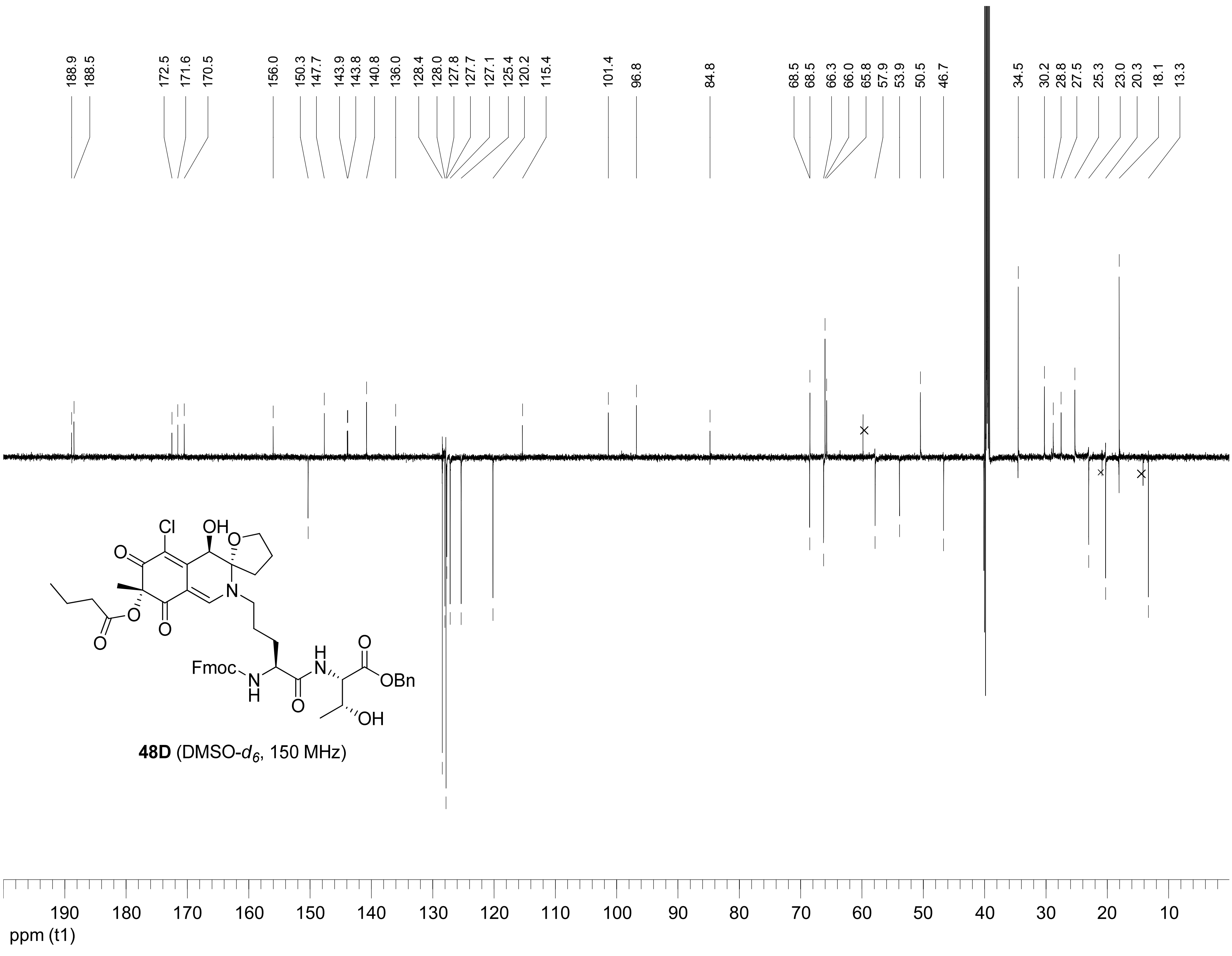
48C (DMSO-d_6, 600 MHz)



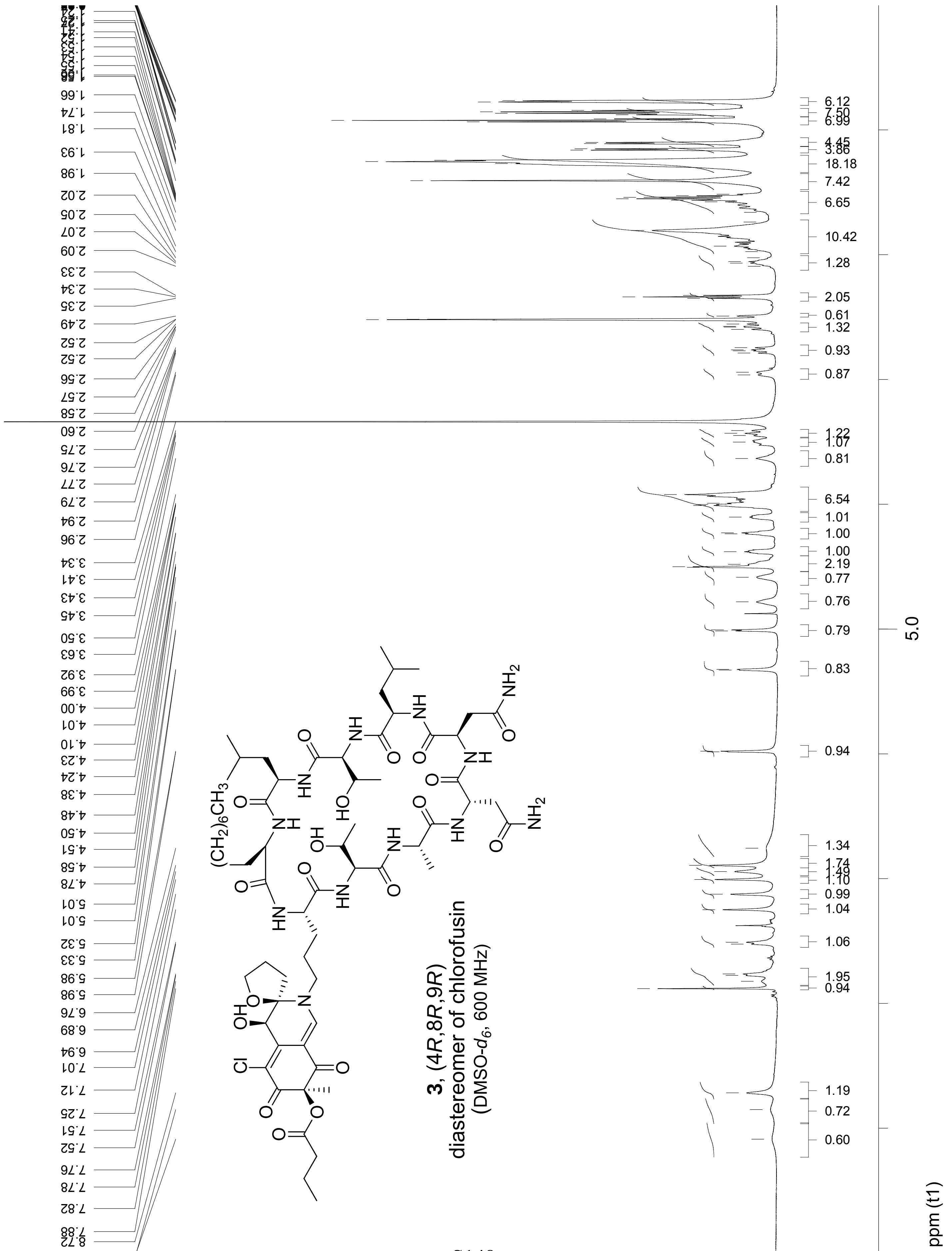
48C (DMSO-d_6, 150 MHz)

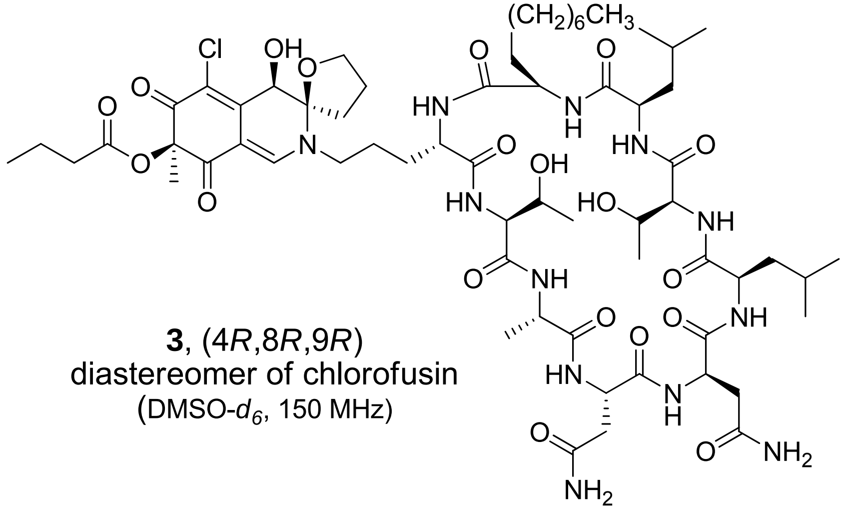


48D (DMSO-d_6, 600 MHz)

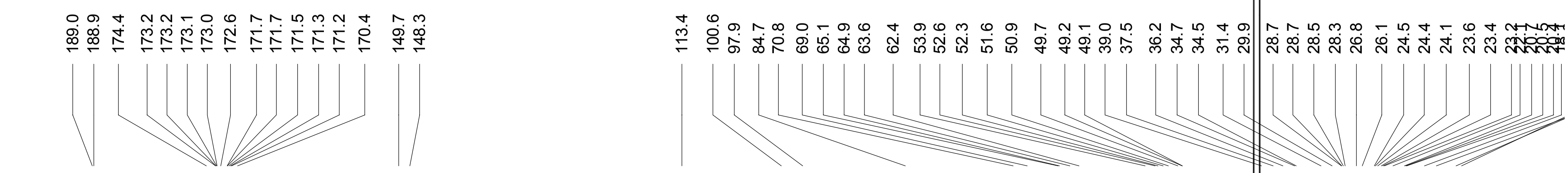


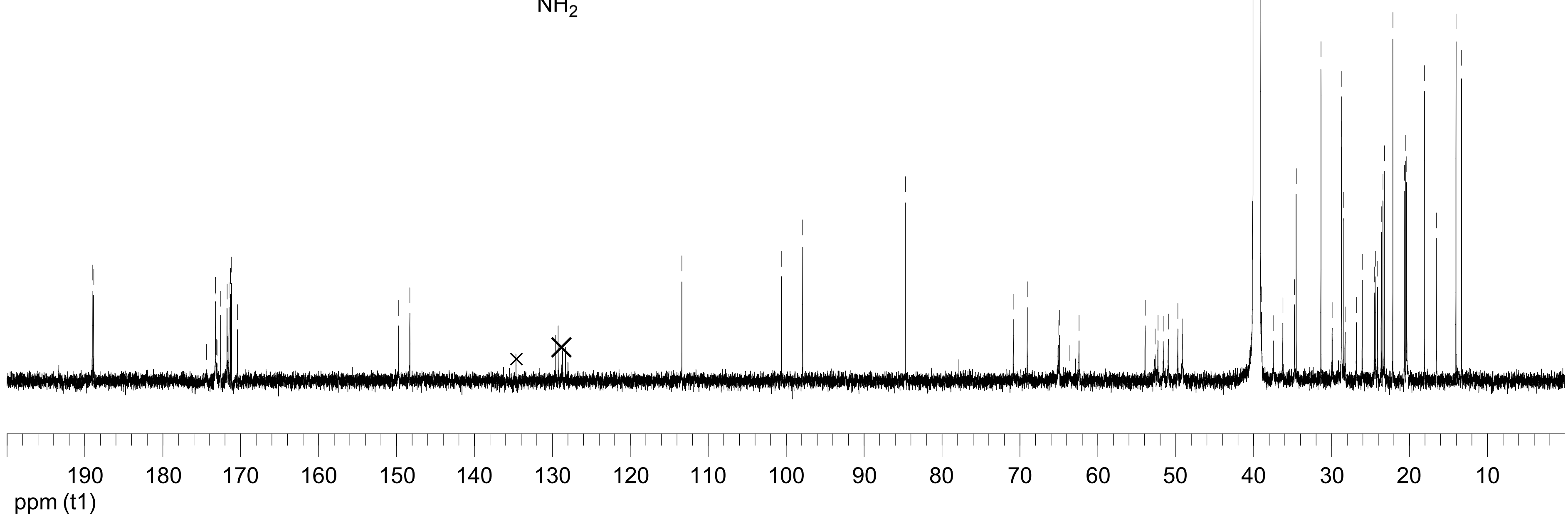
48D (DMSO-d_6, 150 MHz)


3, (4R,8R,9R)
diastereomer of chlorofusin
(DMSO-d6, 600 MHz)
5.0
ppm (t1)

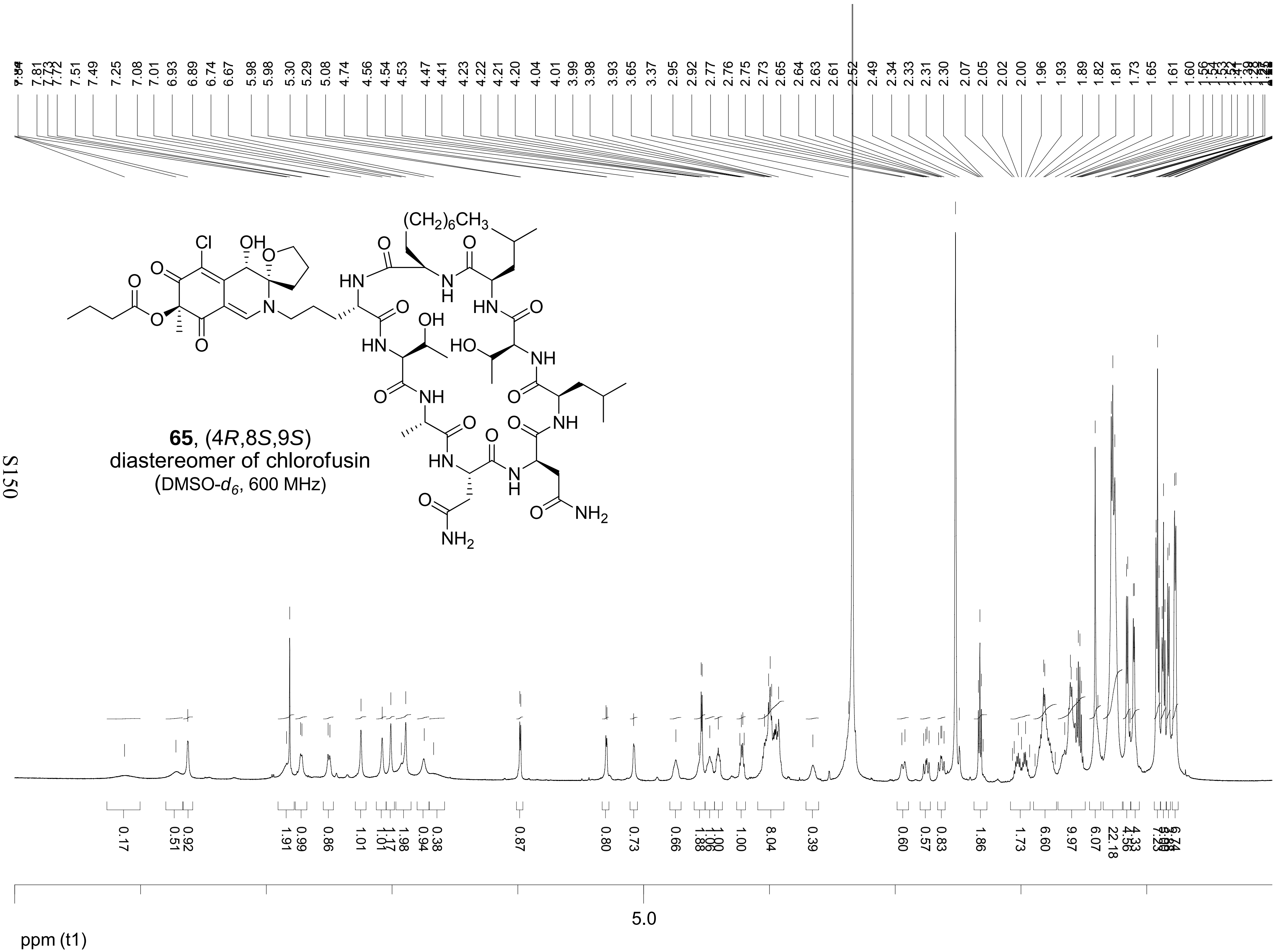


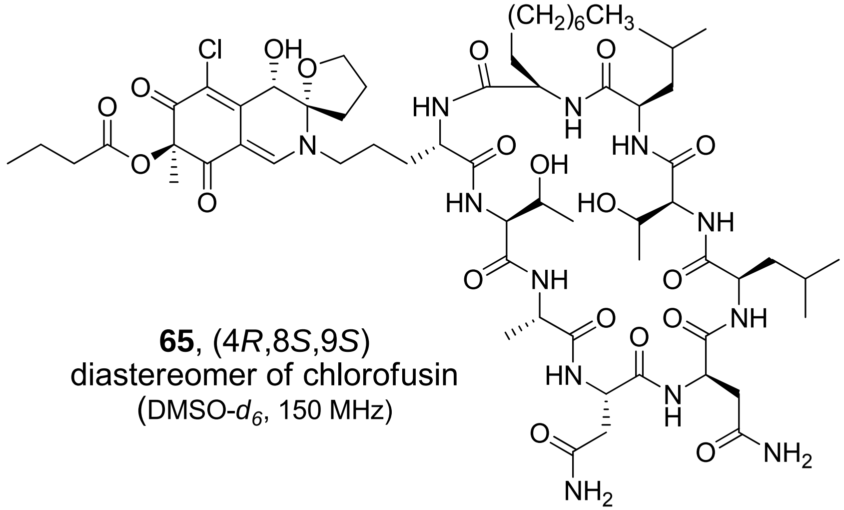
3, (4*R*,8*R*,9*R*)
diastereomer of chlorofusin
(DMSO-d_6, 150 MHz)



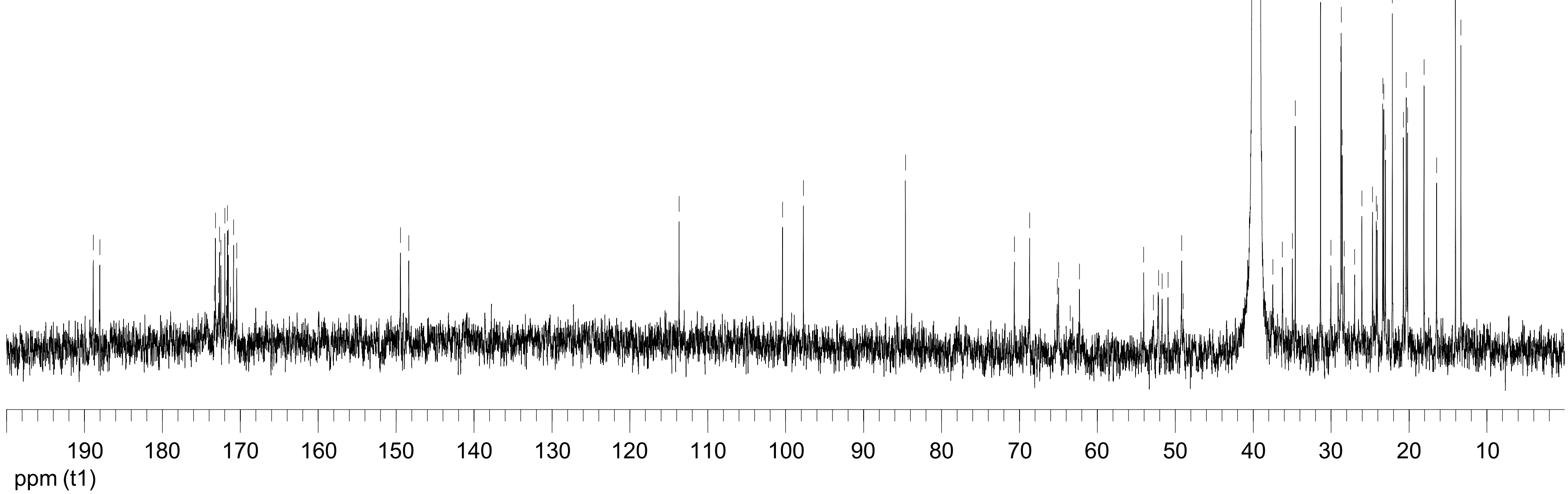


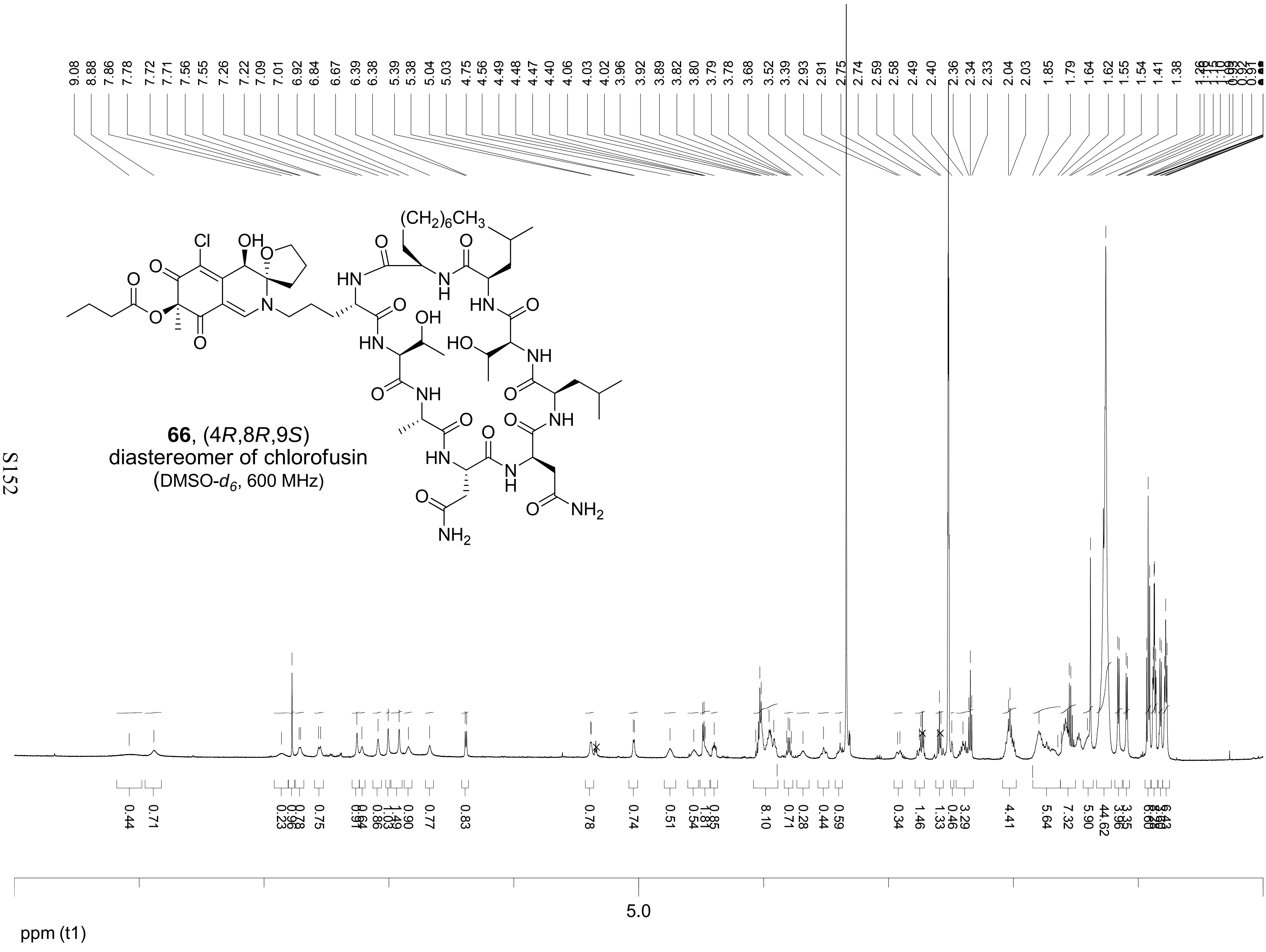
65, (4*R*,8*S*,9*S*)
diastereomer of chlorofusin
(DMSO-d_6, 600 MHz)



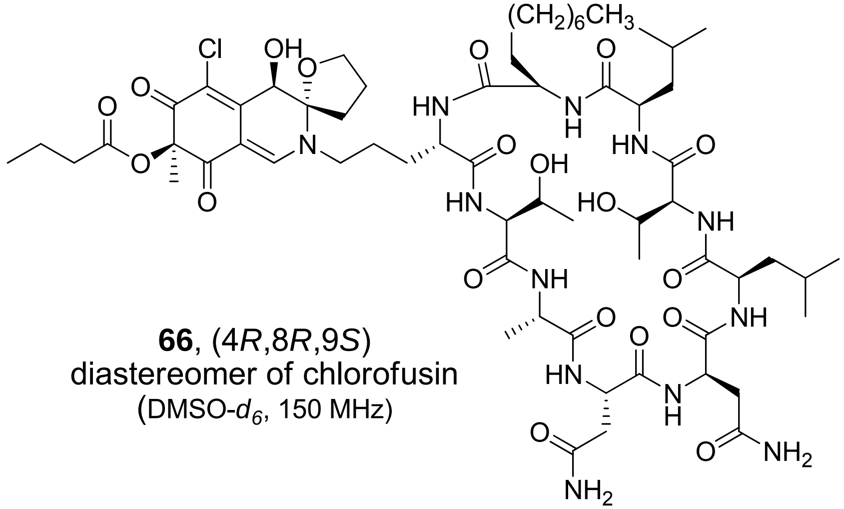


65, (4*R*,8*S*,9*S*)
diastereomer of chlorofusin
(DMSO-d_6, 150 MHz)

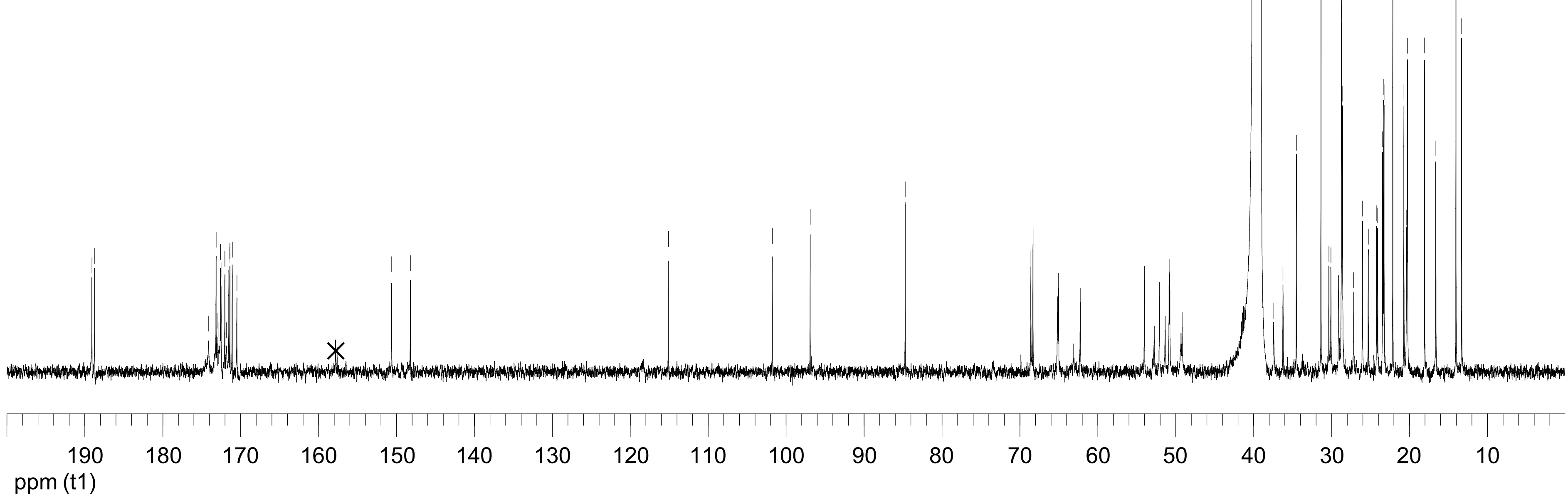


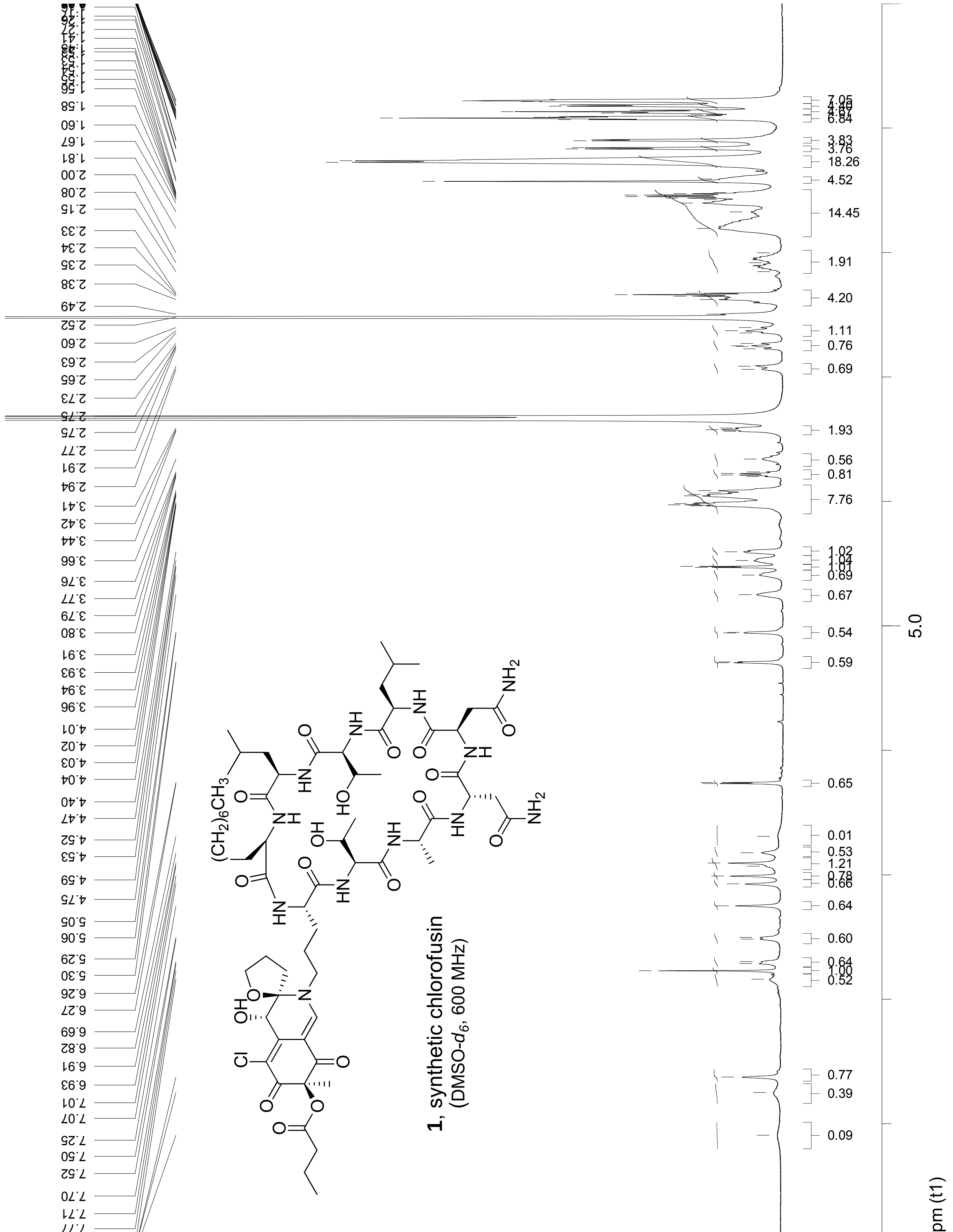


66, (4*R*,8*R*,9*S*)
diastereomer of chlorofusin
(DMSO-d_6, 600 MHz)

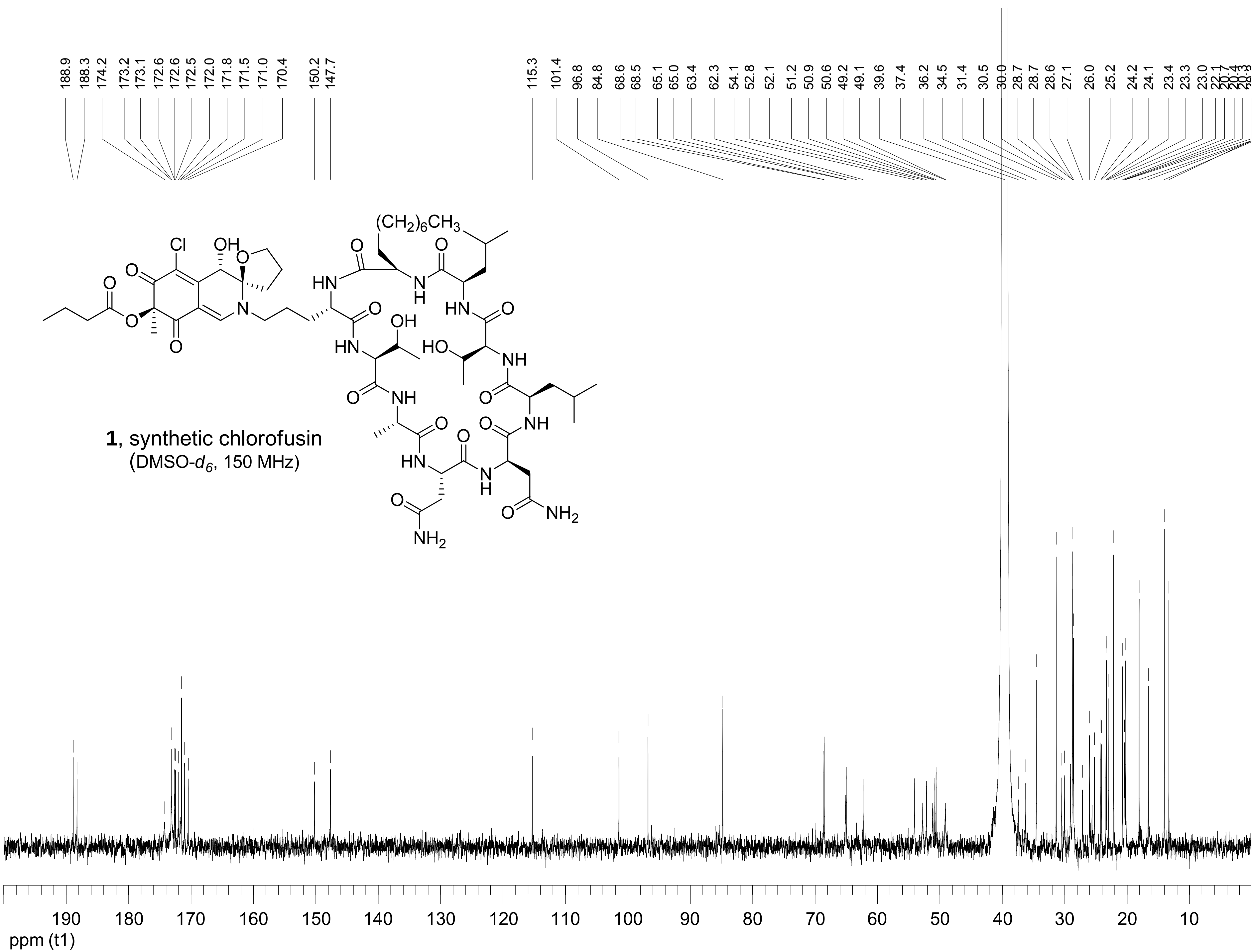


66, (4*R*,8*R*,9*S*)
diastereomer of chlorofusin
(DMSO-d_6, 150 MHz)

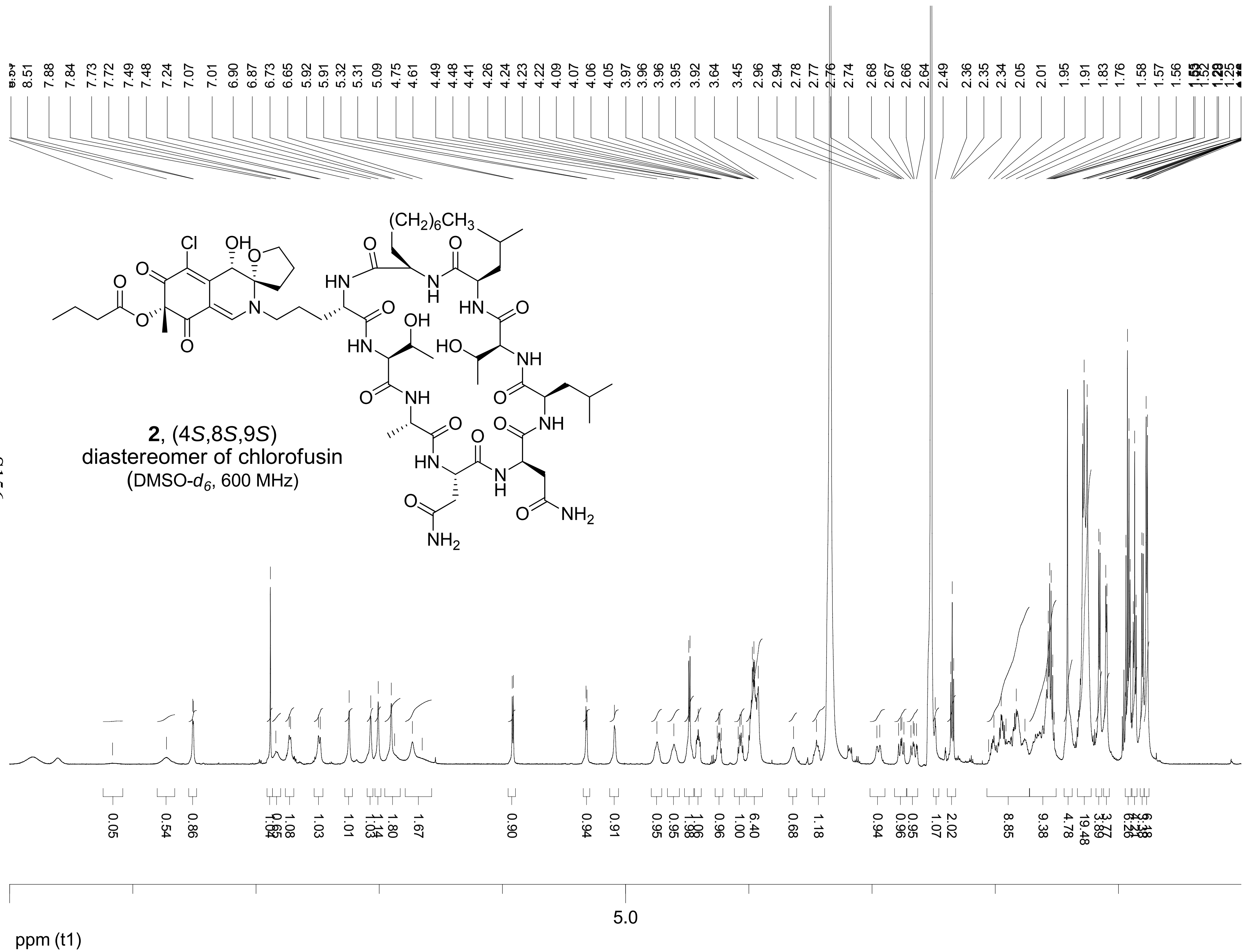




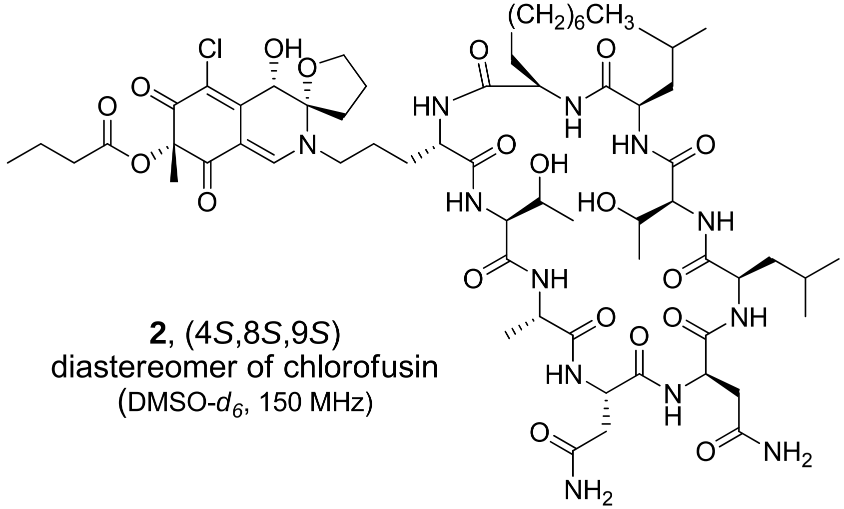
1, synthetic chlorofusin
(DMSO-d_6, 600 MHz)



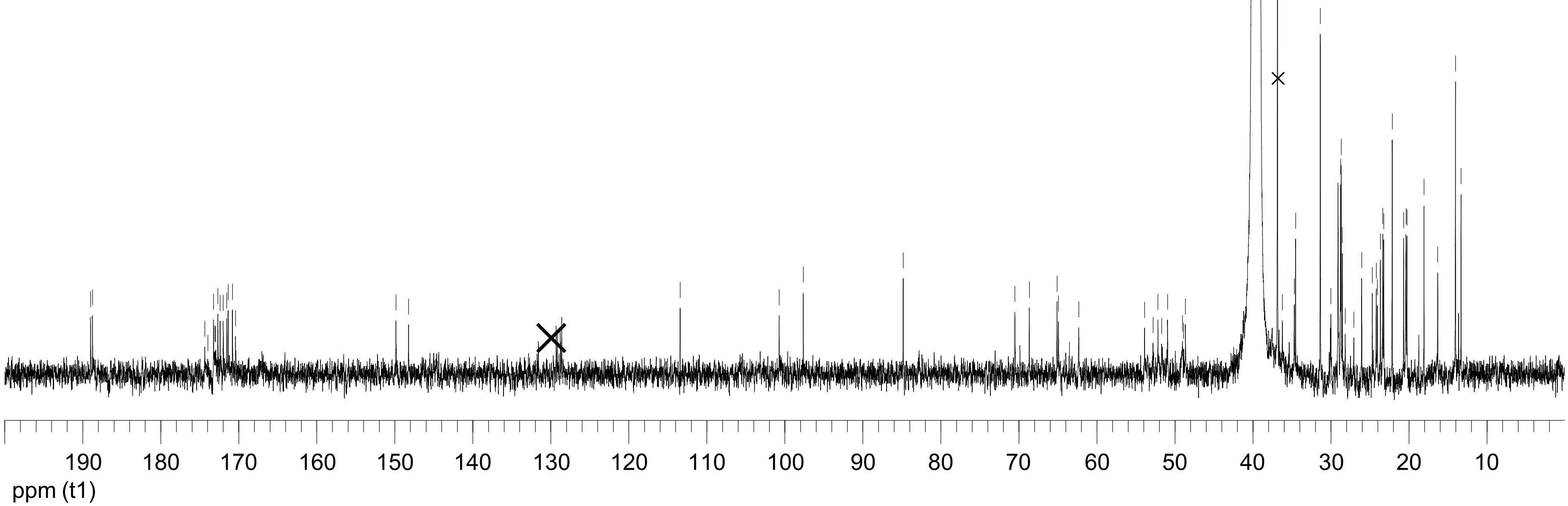
1, synthetic chlorofusin
(DMSO-d_6, 150 MHz)

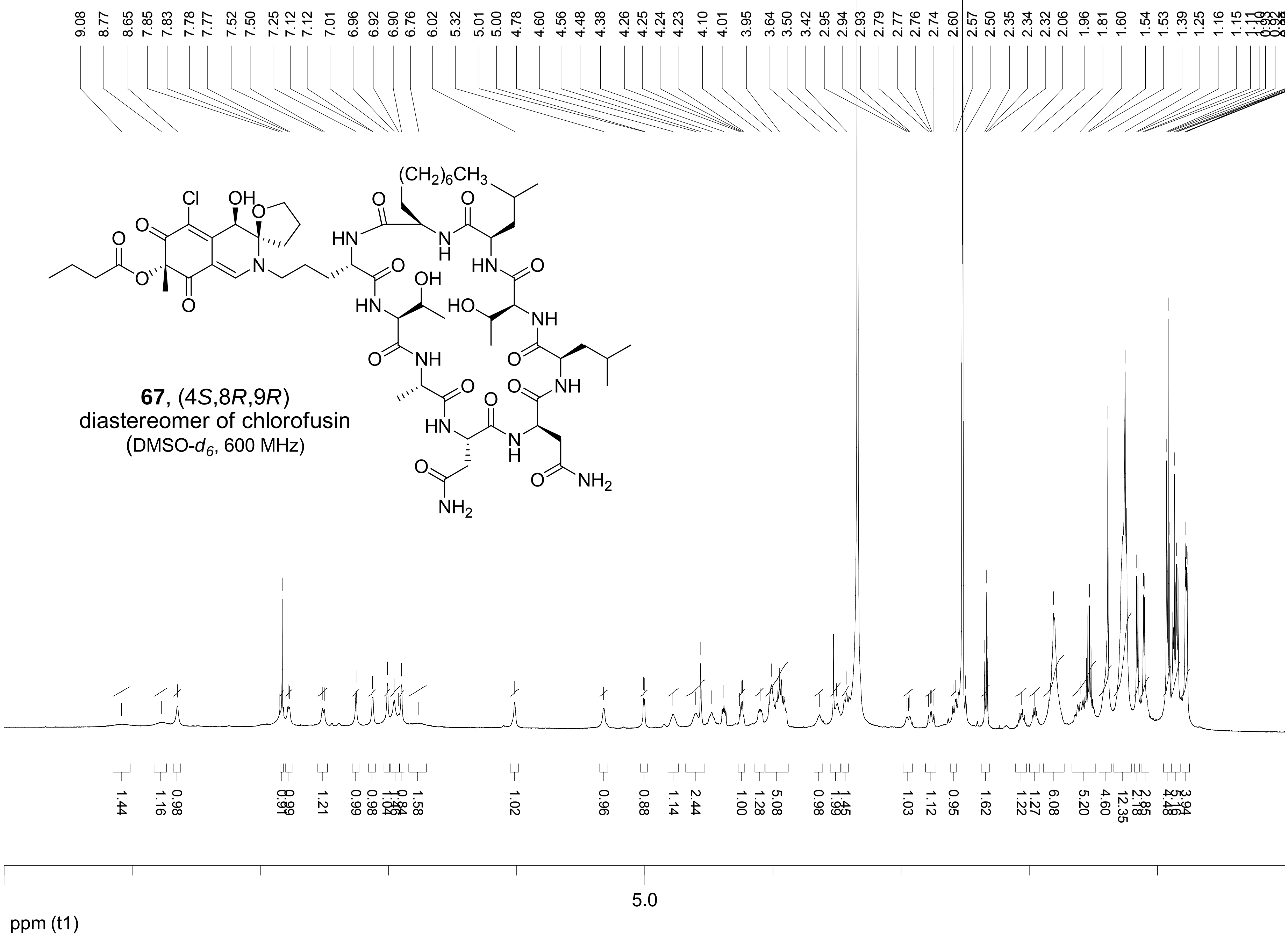


2, (4*S*,8*S*,9*S*)
diastereomer of chlorofusin
(DMSO-d_6, 600 MHz)

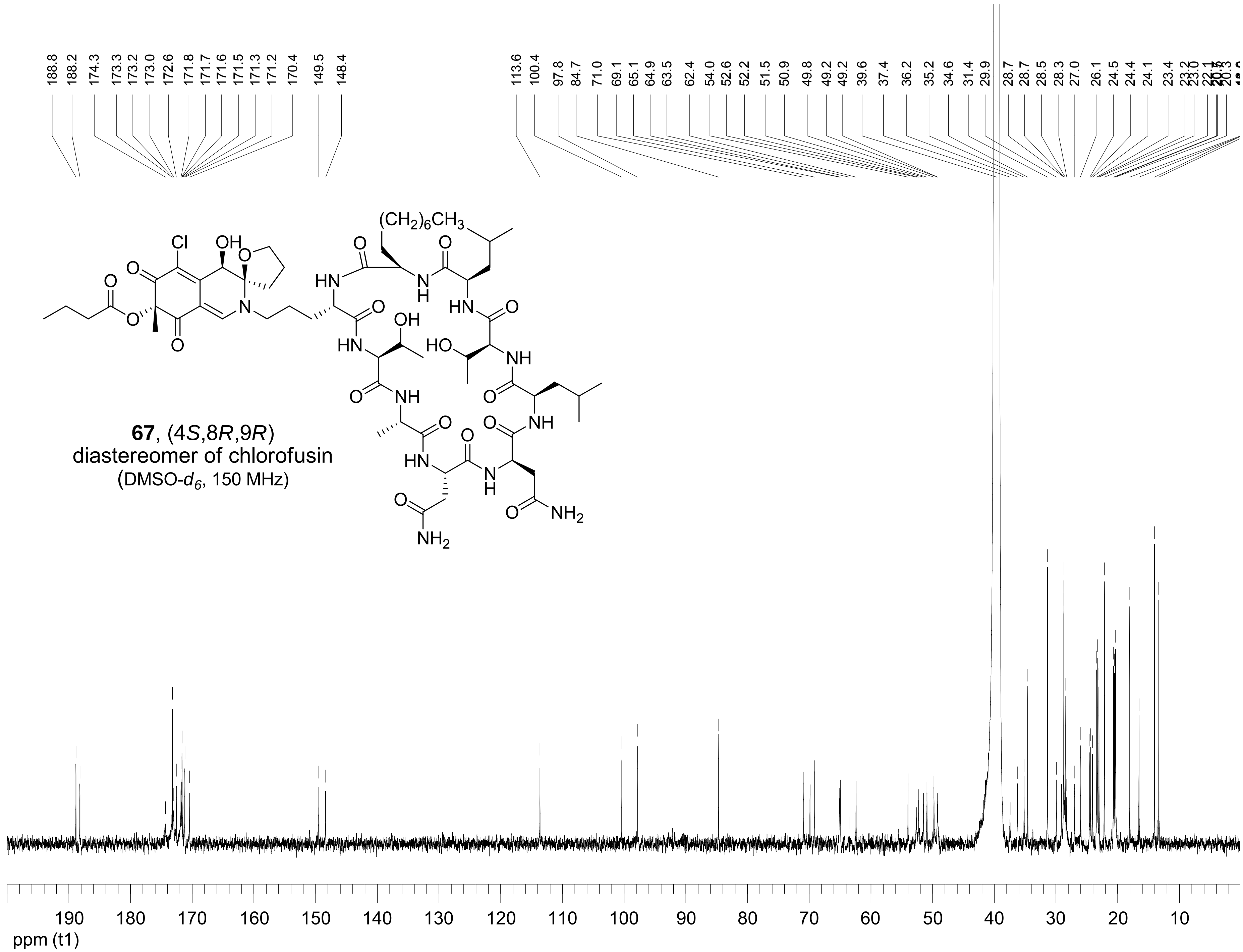


2, (4*S*,8*S*,9*S*)
diastereomer of chlorofusin
(DMSO-d_6, 150 MHz)

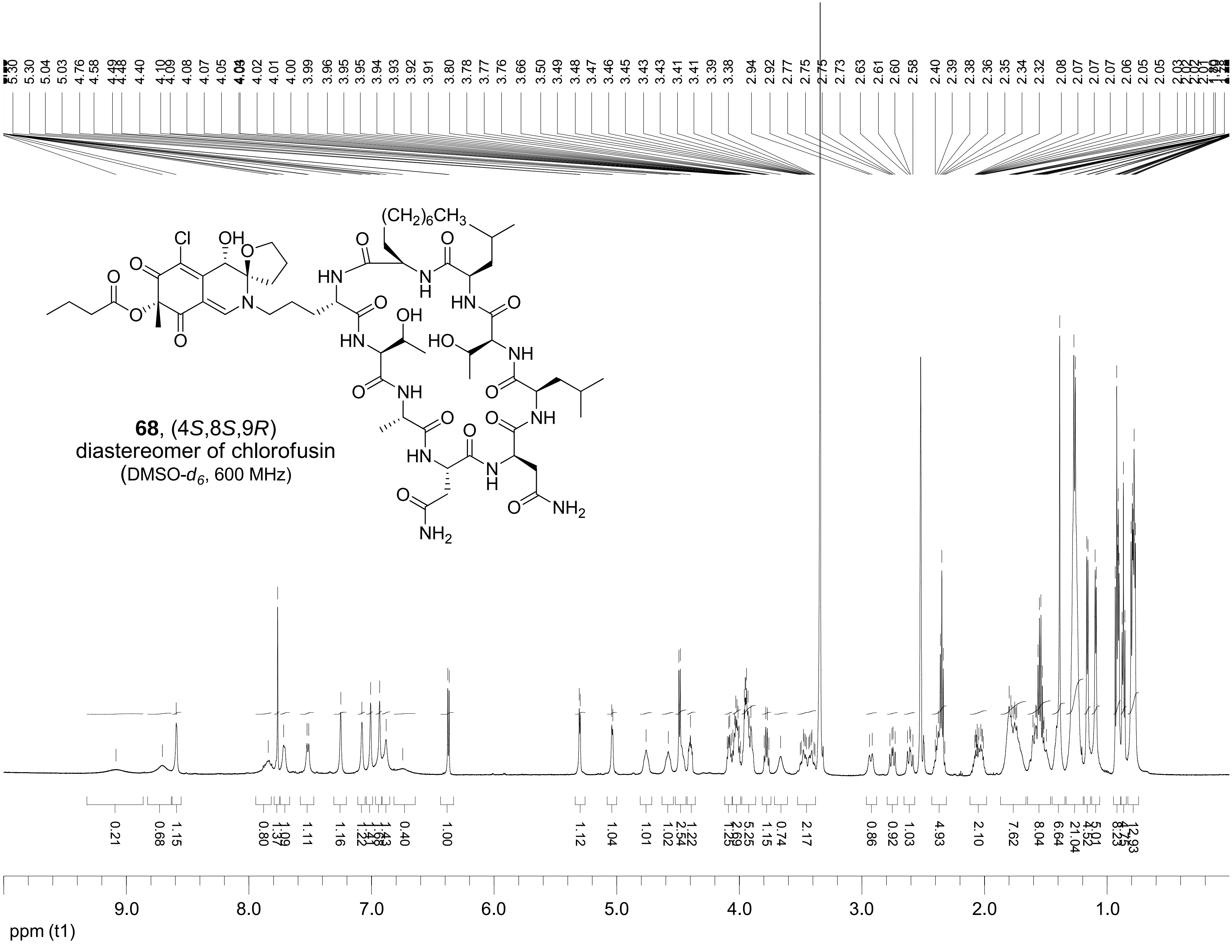




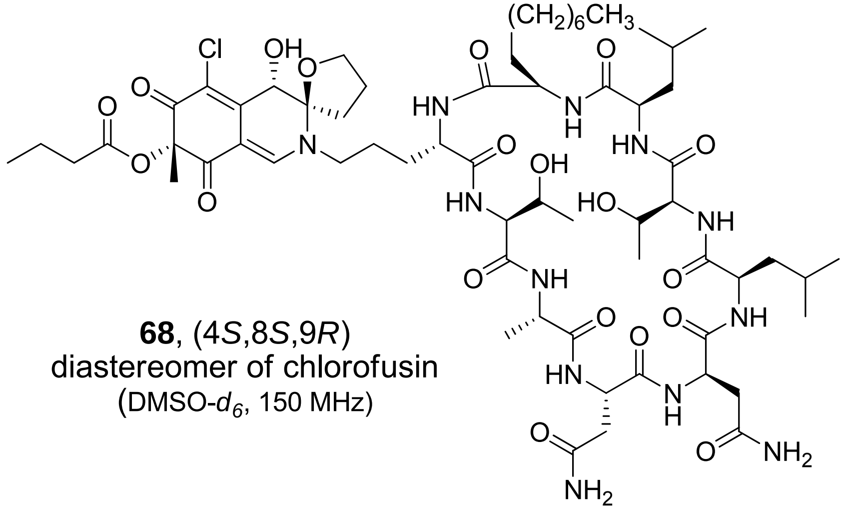
67, (4*S*,8*R*,9*R*)
diastereomer of chlorofusin
(DMSO-d_6, 600 MHz)



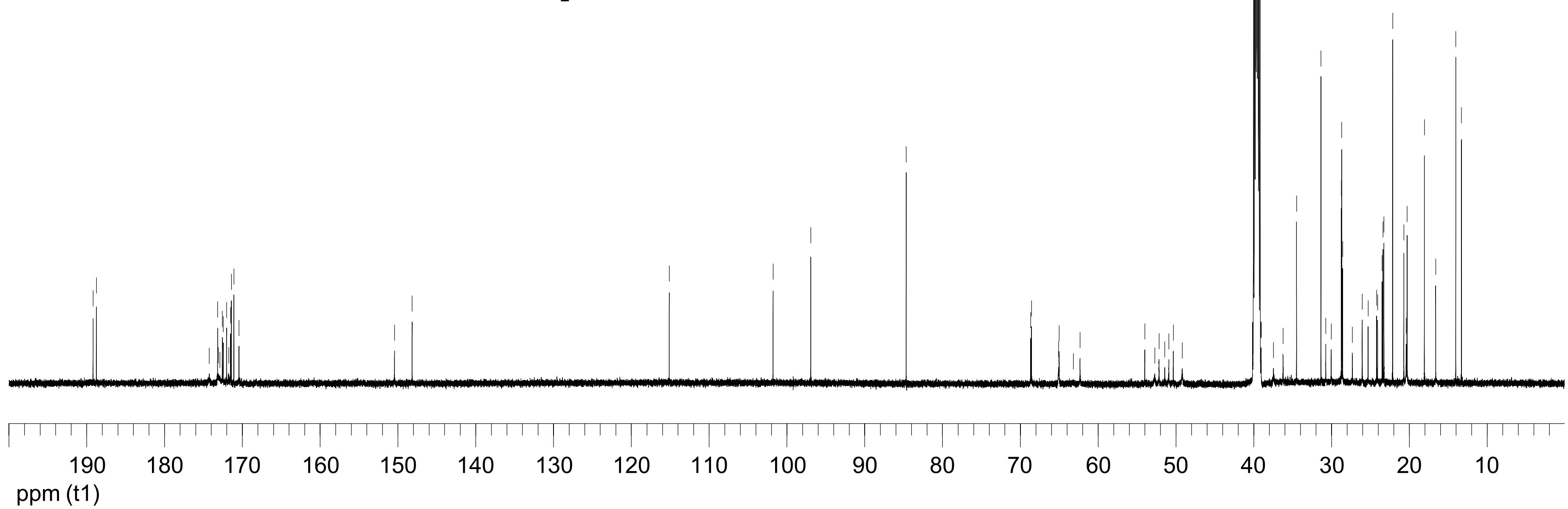
67, (4*S*,8*R*,9*R*)
diastereomer of chlorofusin
(DMSO-d_6, 150 MHz)

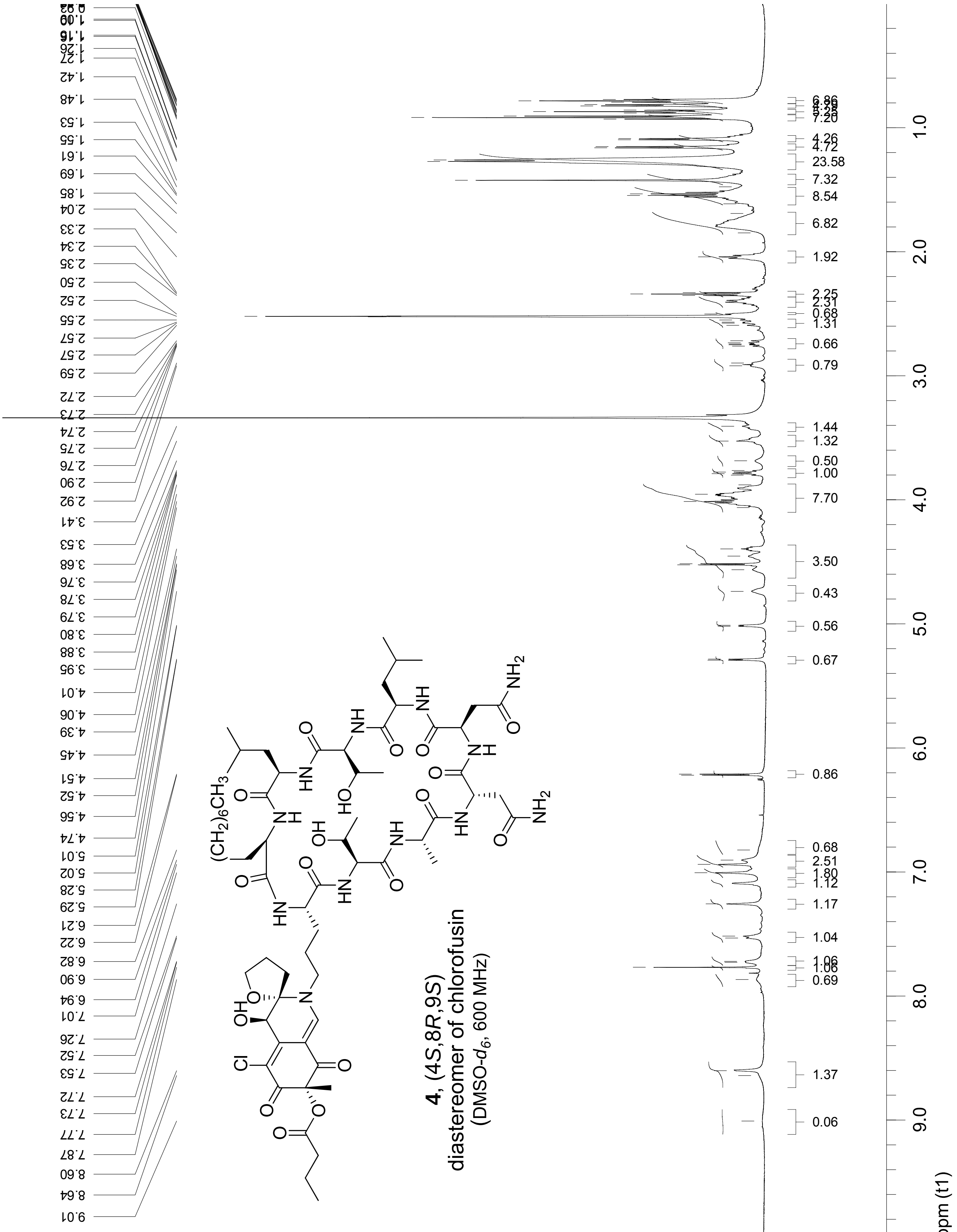


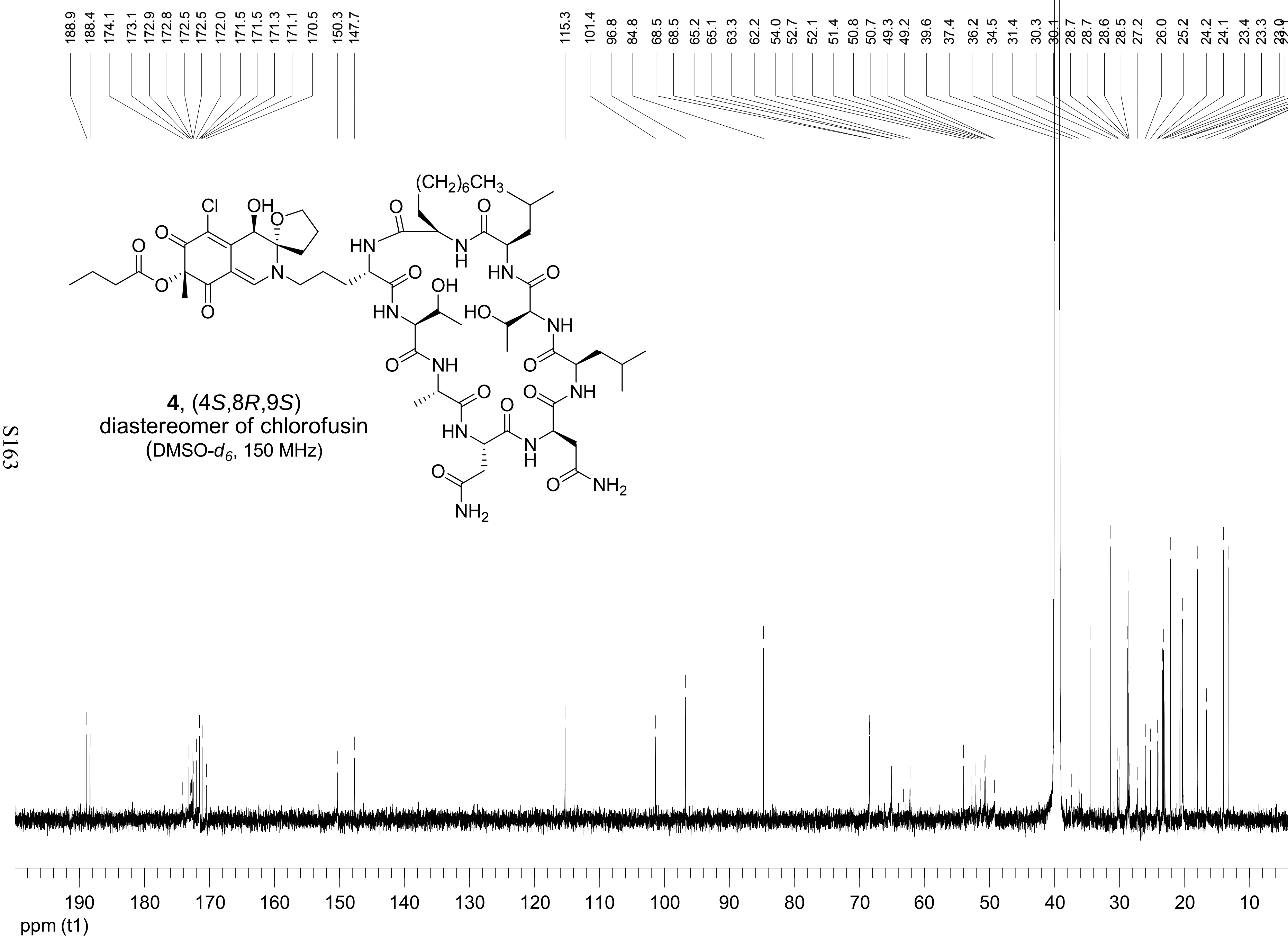
68, (4*S*,8*S*,9*R*)
diastereomer of chlorofusin
(DMSO-d_6, 600 MHz)



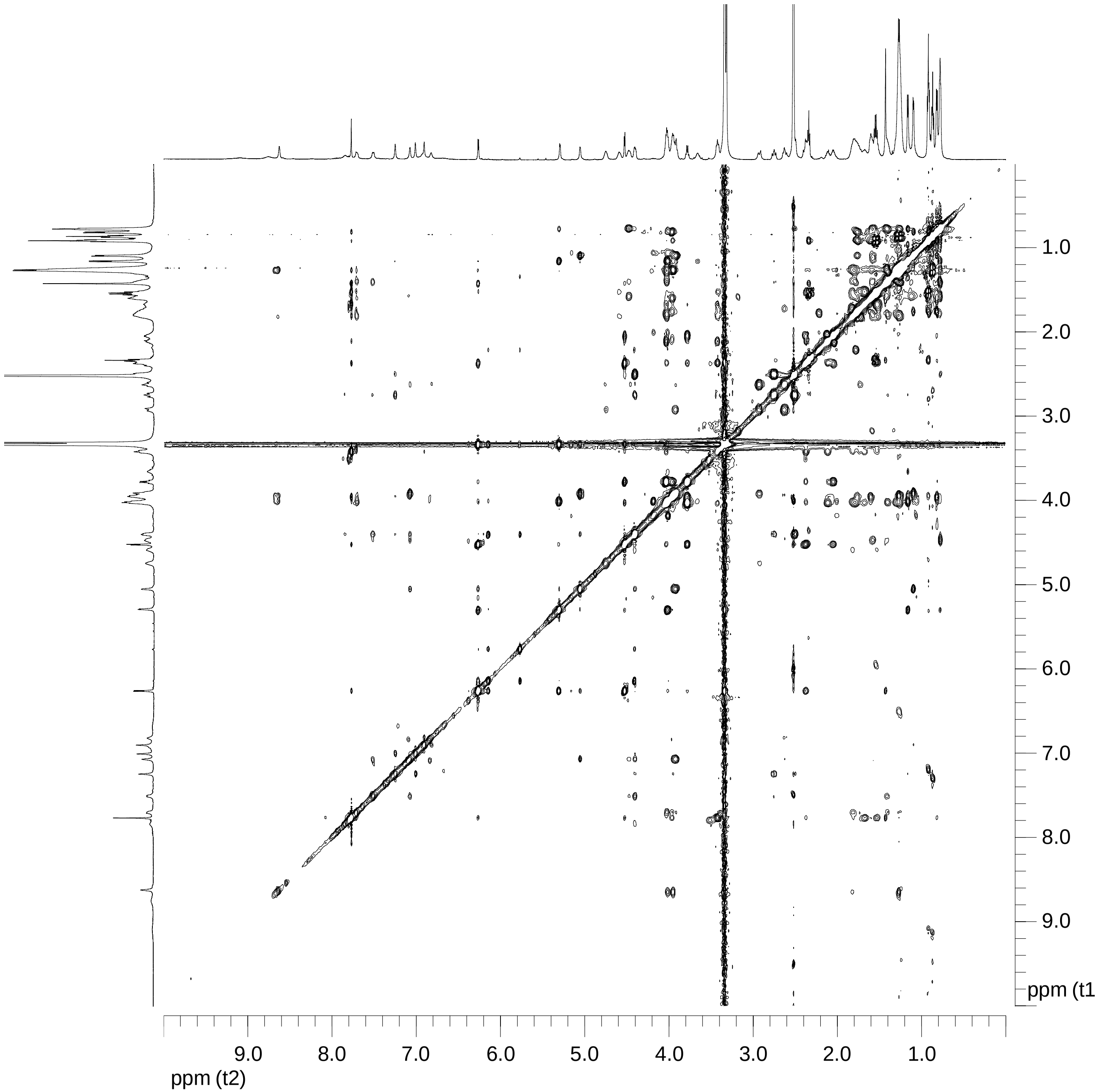
68, (4*S*,8*S*,9*R*)
diastereomer of chlorofusin
(DMSO-d_6, 150 MHz)

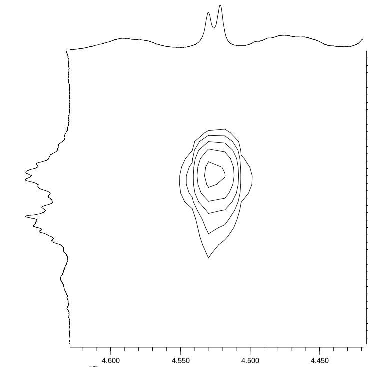



4, (4S,8R,9S)
diastereomer of chlorofusin
(DMSO-d6, 600 MHz)
ppm (t1)
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
6.86
7.20
4.26
4.72
23.58
7.32
8.54
6.82
1.92
2.25
2.31
0.68
1.31
0.66
0.79
1.44
1.32
0.50
1.00
7.70
3.50
0.43
0.56
0.67
0.86
0.68
2.51
1.80
1.12
1.17
1.04
1.06
1.06
0.69
1.37
0.06
1.42
1.48
1.53
1.55
1.61
1.69
1.85
2.04
2.33
2.34
2.35
2.50
2.52
2.55
2.57
2.57
2.59
2.72
2.73
2.74
2.75
2.76
2.90
2.92
3.41
3.53
3.68
3.76
3.78
3.79
3.80
3.88
3.95
4.01
4.06
4.39
4.45
4.51
4.52
4.56
4.74
5.01
5.02
5.28
5.29
6.21
6.22
6.82
6.90
6.94
7.01
7.26
7.52
7.53
7.72
7.73
7.77
7.87
8.60
8.64
9.01

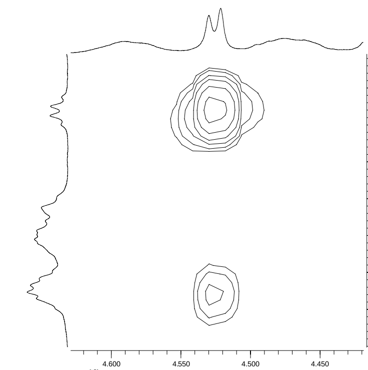


4, (4*S*,8*R*,9*S*)
diastereomer of chlorofusin
(DMSO-d_6, 150 MHz)

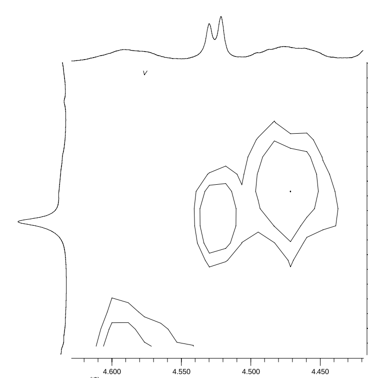




C8-H to C10-H

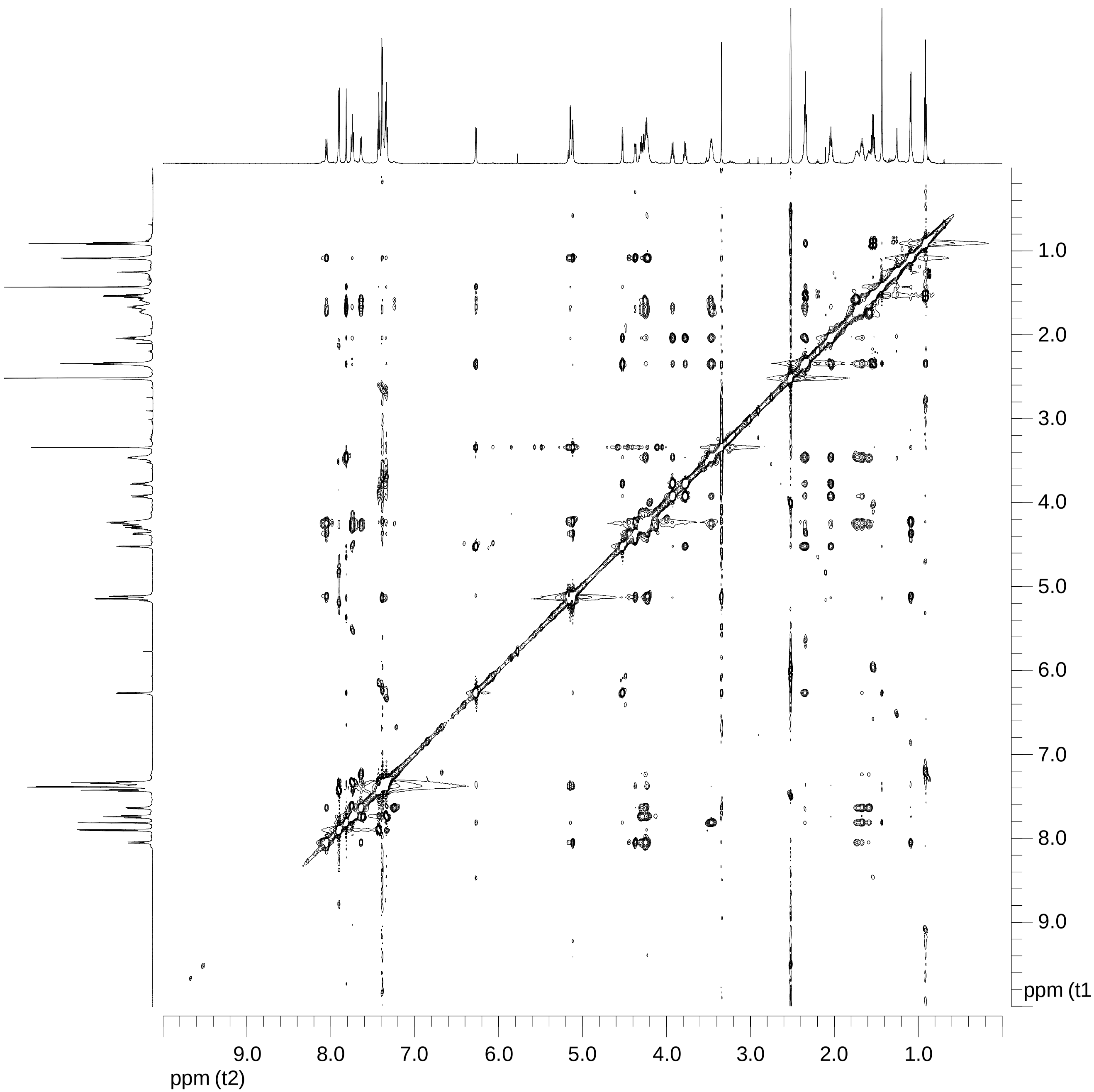


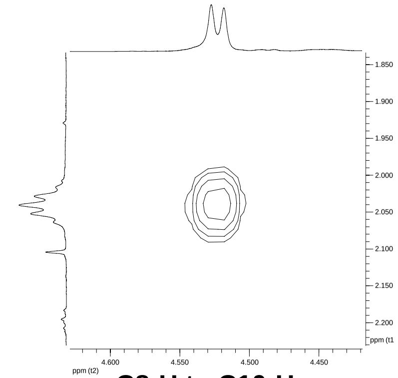
C8-H to C12-H



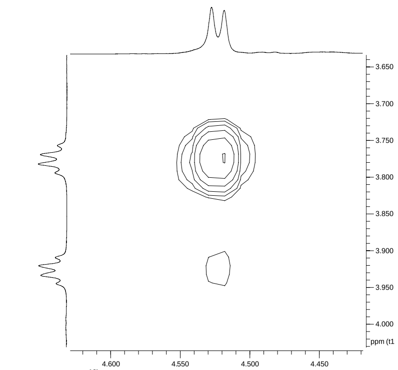
C8-H to C13-H

ROESY spectrum of **1** (DMSO-d_6, 600 MHz)

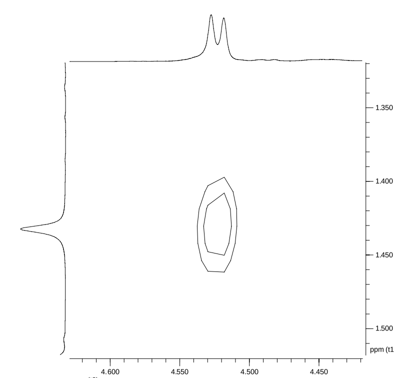




C8-H to C10-H

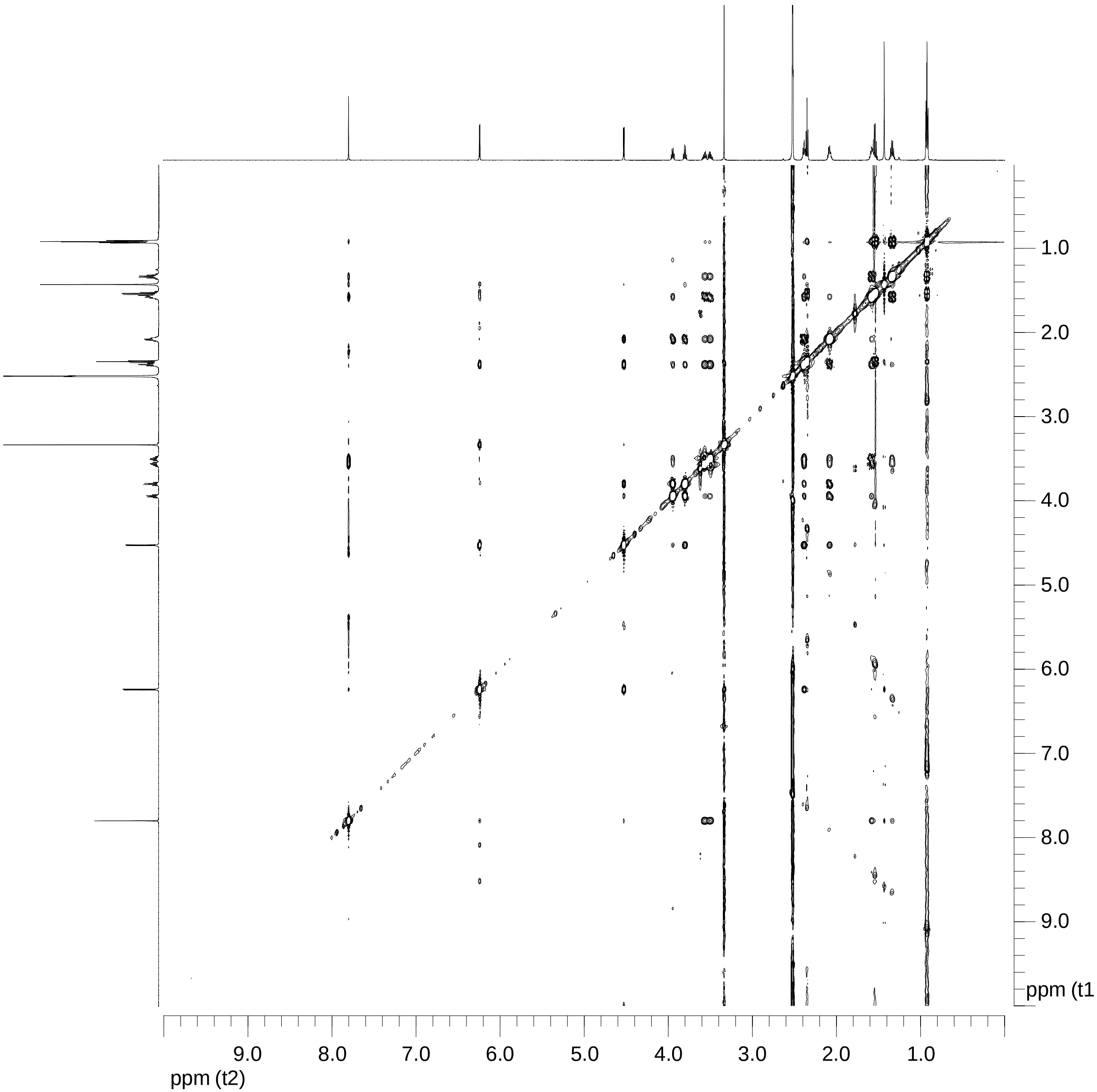


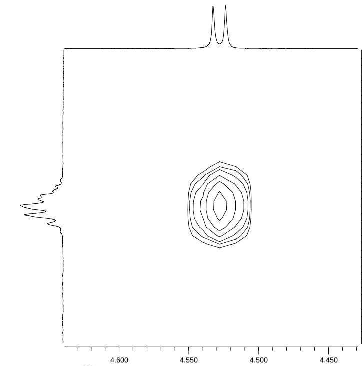
C8-H to C12-H



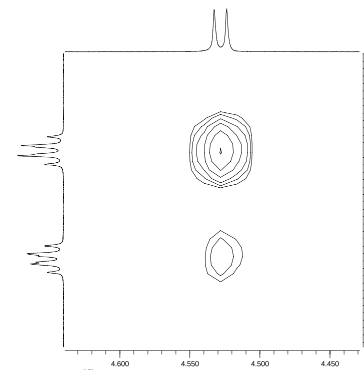
C8-H to C13-H

ROESY spectrum of **47D** (DMSO-d_6, 600 MHz)

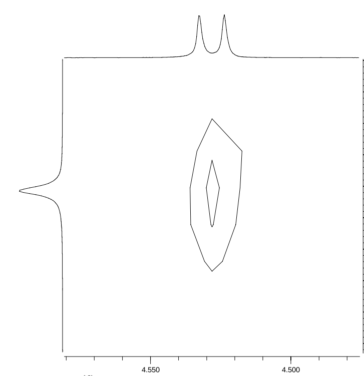




C8-H to C10-H

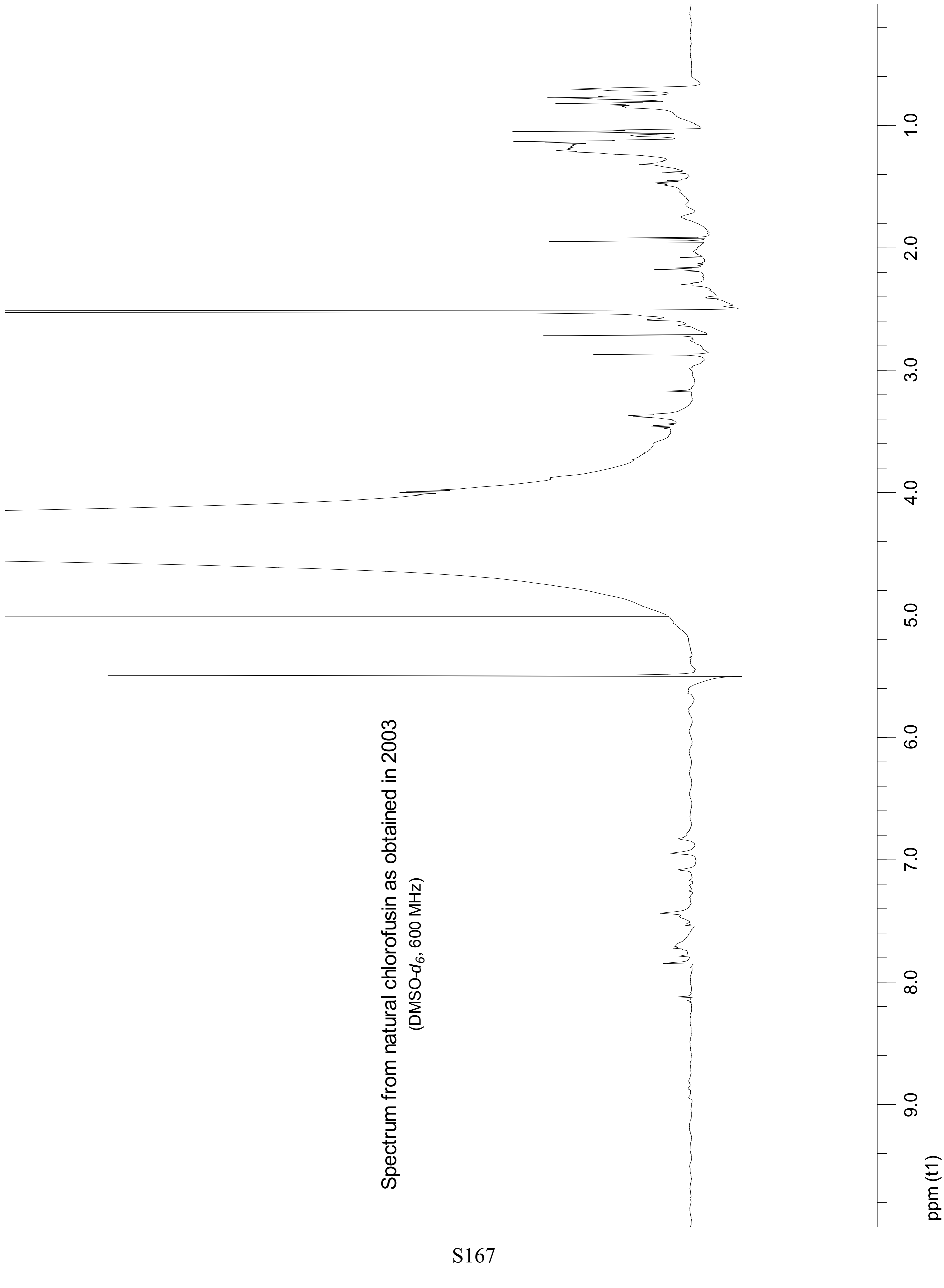


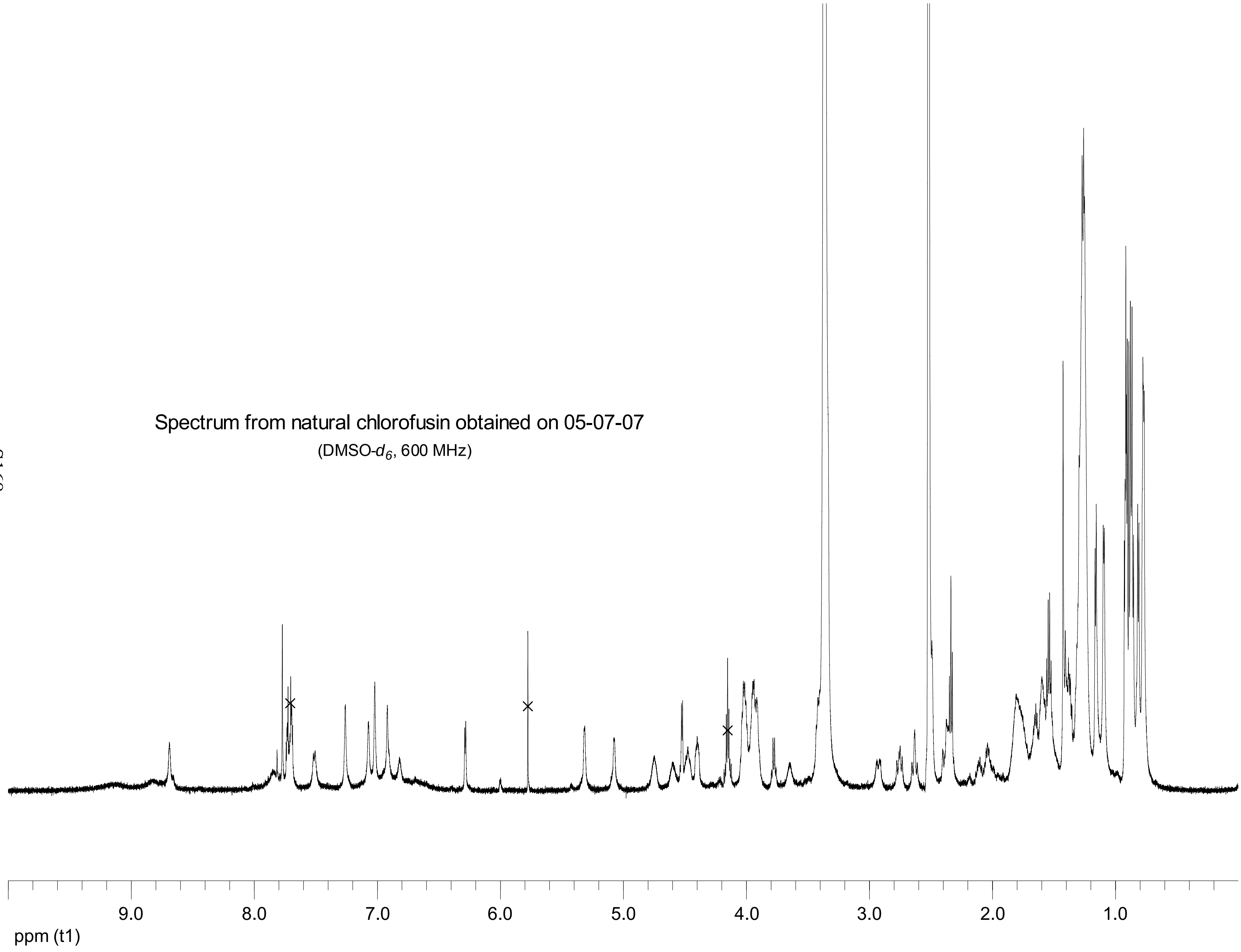
C8-H to C12-H

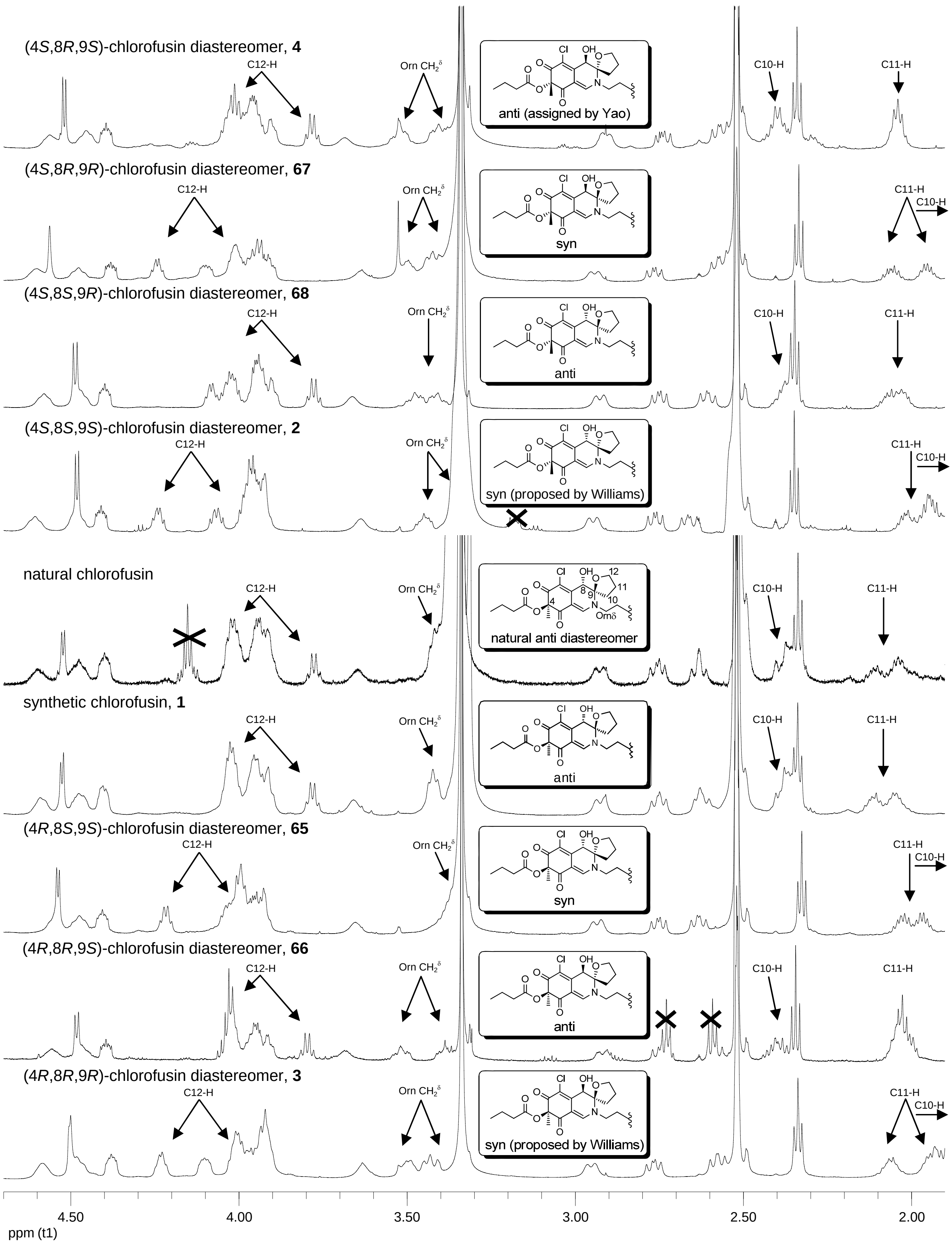


C8-H to C13-H

ROESY spectrum of **42D** (DMSO-d_6, 600 MHz)


Spectrum from natural chlorofusin as obtained in 2003
(DMSO-d_6, 600 MHz)
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
ppm (t1)


Spectrum from natural chlorofusin obtained on 05-07-07
(DMSO-d_6, 600 MHz)
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)



(4S,8R,9S)-chlorofusin diastereomer, 4
C12-H
Orn CH2δ
anti (assigned by Yao)
C10-H
C11-H
(4S,8R,9R)-chlorofusin diastereomer, 67
C12-H
Orn CH2δ
syn
C11-H
C10-H
(4S,8S,9R)-chlorofusin diastereomer, 68
C12-H
Orn CH2δ
anti
C10-H
C11-H
(4S,8S,9S)-chlorofusin diastereomer, 2
C12-H
Orn CH2δ
syn (proposed by Williams)
C11-H
C10-H
natural chlorofusin
C12-H
Orn CH2δ
natural anti diastereomer
C10-H
C11-H
synthetic chlorofusin, 1
C12-H
Orn CH2δ
anti
C10-H
C11-H
(4R,8S,9S)-chlorofusin diastereomer, 65
C12-H
Orn CH2δ
syn
C11-H
C10-H
(4R,8R,9S)-chlorofusin diastereomer, 66
C12-H
Orn CH2δ
anti
C10-H
C11-H
(4R,8R,9R)-chlorofusin diastereomer, 3
C12-H
Orn CH2δ
syn (proposed by Williams)
C11-H
C10-H
4.50
4.00
3.50
3.00
2.50
2.00
ppm (t1)