Supporting information

Antitumor Agents 274. A New Synthetic Strategy for E-ring SAR Study of Antofine and Cryptopleurine Analogs

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General experimental information

All solvents and reagents are used as purchased. Melting points were measured using a Fisher Johns melting apparatus without correction. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 MHz Gemini spectrometer using TMS as internal standard. The solvent used was $CDCl_3$ unless indicated. Specific optical rotation was calculated and recorded using JASCO P-2000 polarimeter. High resolution mass spectra were recorded on a Shimazu LCMS-IT-TOF instrument equipped with an ESI source.

Cytotoxicty assay

The sulforhodamine B assay was used according to the procedures developed and validated at NCI. The in vitro anticancer activities are expressed as IC_{50} values, which is the test compound concentration (μg/ml) that reduced the cell number by 50% after 72h treatment. The values were interpolated from dose-response data. Each test was performed in triplicate with a variation of less than 5%. The IC50 values determined in each of the independent tests varied less than 10%. Compound stock solutions were prepared in DMSO with the final solvent concentration ≦1% DMSO (v/v), a concentration without effect on cell replication. The cells were cultured at 37 ℃ in RPMI-1640 supplemented with 25 mM *N*-2-hydroxyethylpiperazine-*N*-2-ethanesulfonic acid (HEPES), 2% (w/v) sodium bicarbonate, 10% (v/v) fetal bovine serum, and 100 μg/mL kanamycin in a humidified atmosphere containing 5% CO_2.

***N*-(2,3,6-Trimethoxyphenanthren-9-ylmethyl)-D-serine methyl ester (2):** Compound **1** (15.56 g, 47.73 mmol) was suspended in 400 mL of THF, to which $LiAlH_4$ (2.729 g, 71.60 mmol) was added carefully at rt. After 2 h, water and 1N NaOH were added to quench the reaction, which was then filtered. Removal of the solvent in vacuo gave a white solid, which was then dissolved in $CHCl_3$, washed with water and brine, and dried over $MgSO_4$. After removing solvent, the crude product was used in the next step without further purification.

The white solid was suspended in Et_3N (18 mL) and CH_2Cl_2 (400 mL) at 0 °C, and then Py•SO_3 (22.90 g, 143.19 mmol) in 80 mL of DMSO was added dropwise. The reaction was monitored by TLC before 150 mL of HCl (1N) was added. The organic layer was then washed with sat. $NaHCO_3$, brine, and dried over $MgSO_4$.

After evaporation of the solvent, the resulting yellow oil was dissolved in CH_2Cl_2 (100 mL) and MeOH (300 mL) at 0 °C, to which D-serine hydrochloride (6.22 g, 40 mmol) and Et_3N (5.70 mL, 41 mmol) were added. The reaction was stirred at 0°C for 30 min before HOAc (4.42 mL, 77.60 mmol) and $NaBH_3CN$ (5.133 g, 77.60 mmol) were added. The reaction mixture was then warmed to rt and stirred overnight. Sat. $NaHCO_3$ was added to quench the reaction, and the mixture extracted with CH_2Cl_2. The organic layers were collected, washed with brine, dried over Na_2SO_4. Column chromatography eluting with CH_2Cl_2/MeOH gave **2** (11.38 g 59.7% for three steps) as a light yellow solid: mp 97-99 ℃; $[\alpha]^{23}_D$= 15.1° (*c* 2.56, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 9.0 Hz, 1H), 7.88 (d, *J* = 2.4 Hz, 1H), 7.84 (s, 1H), 7.47 (s, 1H), 7.24 (dd, *J* = 9.0 Hz, *J* = 2.4 Hz, 1H), 7.18 (s, 1H), 4.33 (d, *J* = 12.9 Hz, 1H), 4.13 (d, *J* = 13.2 Hz, 1H), 4.09 (s, 3H), 4.02 (s, 3H), 4.01 (s, 3H), 3.78 (m, 1H), 3.75 (s, 3H); 3.58 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.7, 158.2, 149.8, 149.3, 131.9, 131.5, 127.3, 126.2, 124.9, 124.4 (2×C), 115.4, 108.5, 104.9, 103.6, 62.8, 62.4, 56.3, 56.1, 55.7, 52.4, 50.8; ESI-HRMS ($[M + H]^+$) calcd for $C_{22}H_{26}NO_6$ 400.1760, found 400.1764.

(*R*)-Methyl-*N*-(2,3,6-trimethoxyphenanthren-9-ylmethyl)-oxazolidinone-4-carboxylate (3): The ester **2** (6.30 g, 15.77 mmol) was dissolved in 200 mL of CH_2Cl_2 at room temperature, to which 1,1'-carbonyldiimidazole (5.11 g, 31.54 mmol) was added. The mixture was stirred at reflux overnight. Column chromatography eluting with CH_2Cl_2/MeOH gave **3** (5.10 g, 76%) as a light yellow solid: mp 83-85°C; $[\alpha]^{23}_D$= 11.5° (*c* 1.36, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 2.4 Hz, 1H), 7.78 (s, 1H), 7.33 (s, 1H), 7.21 (dd, *J* = 9.0 Hz, *J* = 2.4 Hz, 1H), 7.13 (s, 1H), 5.28 (d, *J* = 14.7 Hz, 1H), 4.61 (d, *J* = 14.7 Hz, 1H), 4.28-4.27 (m, 2H), 4.07 (s, 3H), 4.01 (s, 3H), 3.98 (s, 3H), 3.95 (dd, *J* = 8.7 Hz, *J* = 5.4 Hz, 1H), 3.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 158.5, 157.4, 149.9, 149.8, 132.0, 127.2, 126.8, 126.3, 126.2, 124.9, 124.3, 115.7, 108.5, 105.2, 103.6, 64.8, 56.3, 56.1 (2×C), 55.7, 52.9, 46.3; ESI-HRMS ($[M + H]^+$) calcd for $C_{23}H_{24}NO_7$ 426.1553, found 426.1566.

(*R*)-*N*-(2,3,6-Trimethoxyphenanthren-9-ylmethyl)-oxazolidinone-4-carboxylic acid (4): The oxazolidinone (5.10 g, 12.00 mmol) was dissolved in 1,4-dioxane (100 mL), to which aq. KOH (2N, 50 mL) was added. The mixture was stirred at rt for 1.5 h, and then cooled to 0°C. The pH was adjusted to 3 with 85% H_3PO_4. The resulting solid was collected and washed sequentially with cold water, cold MeOH, and diethyl ether. After being dried under vacuum, 4.10 g of white solid were obtained. Yield: 83%; mp 248-250°C; $[\alpha]^{23}_{D}$= -4.8° (*c* 0.23, MeOH); ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 8.14 (d, *J* = 2.4 Hz, 1H), 8.07 (s, 1H), 7.97 (d, *J* = 9.3 Hz, 1H), 7.49 (s, 1H), 7.43 (s, 1H), 7.27 (dd, *J* = 9.0 Hz, *J* = 2.4 Hz, 1H), 5.19 (d, *J* = 15.3 Hz, 1H), 4.52 (d, *J* = 15.6 Hz, 1H), 4.44 (t, *J* = 9.3 Hz, 1H), 4.31 (dd, *J* = 9.0 Hz, *J* = 3.3 Hz, 1H), 4.04 (m, 1H), 4.03 (s, 3H), 4.00 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ 171.3, 157.9, 157.2, 149.5, 149.3, 131.6, 127.1, 126.4, 125.3, 124.5, 124.1, 123.6, 115.8, 108.7, 105.1, 104.2, 64.8, 55.9, 55.8, 55.5 (2×C), 45.0; ESI-HRMS ($[M - H]^-$) calcd for $C_{22}H_{20}NO_7$ 410.1240, found 410.1255.

(*R*)-11,14-Dioxo-12-oxa-antofine (5): The acid (5.06 g, 12.31 mmol) was suspended in CH_2Cl_2 (200 mL) and DMF (1 mL), to which $(COCl)_2$ (3.75 mL, 43.09 mmol) was added. The mixture was stirred for 1 h, and then $SnCl_4$ (5.76 mL, 49.24 mmol) was added dropwise. The mixture was then warmed to 50°C and stirred overnight. The reactions was quenched with HCl (2N). After normal workup, column chromatography eluting with CH_2Cl_2/MeOH gave **5** (4.60 g, 95%) as a light yellow solid: mp 244°C (dec.); $[\alpha]^{23}_{D}$= -204.4° (*c* 0.59, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.07 (s, 1H), 7.95 (d, *J* = 9.3 Hz, 1H), 7.81 (d, *J* = 2.7 Hz, 1H), 7.79 (s, 1H), 7.26 (dd, *J* = 9.3 Hz, *J* = 2.7 Hz, 1H), 5.59 (d, *J* = 18.0 Hz, 1H), 4.93 (dd, *J* = 13.2 Hz, *J* = 9.0 Hz, 1H), 4.92 (d, *J* = 17.7 Hz, 1H), 4.68 (t, *J* = 9.0 Hz, 1H), 4.51 (ddd, *J* = 9.0 Hz, *J* = 4.2 Hz, *J* = 1.5 Hz, 1H), 4.11 (s, 3H), 4.09 (s, 3H), 4.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.5, 161.4, 157.4, 150.8, 149.4, 139.0, 134.8, 127.0 (2×C), 124.7, 124.3, 121.3, 116.6, 108.1, 104.9, 103.3, 64.9, 58.3, 56.1, 56.0, 55.8, 42.3; ESI-HRMS ($[M + H]^+$) calcd for $C_{22}H_{20}NO_6$ 394.1291, found 394.1296.

(*S*)-11-Oxo-12-oxa-antofine (6): The ketone (4.60 g, 11.70 mmol) was suspended in MeOH, to which $NaBH_4$ (888 mg, 23.40 mmol) was added at rt The mixture was stirred for 1 h before sat. $NaHCO_3$ was added. Most solvent was removed by evaporation and the solid was collected by filtration, washed with cold MeOH and diethyl ether. The white solid was then dissolved in TFA (200 mL) and Et_3SiH (3.75 mL, 23.40 mmol) and refluxed for 1 h. TFA was removed under reduced pressure. Column chromatography eluting with CH_2Cl_2/MeOH furnished 6 (4.21 g, 95%) as a white solid: mp 253-255°C; $[\alpha]^{23}_{D}$= -177.5° (*c* 0.44, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.89 (d, *J* = 3.0 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.24 (dd, *J* = 9.6 Hz, *J* = 3.0 Hz, 1H), 7.22 (s, 1H), 5.18 (d, *J* = 16.5 Hz, 1H), 4.73 (t, *J* = 8.1 Hz, 1H), 4.71 (d, *J* = 16.5 Hz, 1H), 4.34 (dd, *J* = 8.7 Hz, *J* = 5.1 Hz, 1H), 4.17-4.09 (m, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 4.03 (s, 3H), 3.41 (dd, *J* = 15.9 Hz, *J* = 4.2 Hz, 1H), 2.97 (dd, *J* = 15.6 Hz, *J* = 10.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ and CD_3OD): δ 158.3, 157.7, 149.8, 149.0, 130.6, 126.2, 124.2, 124.1, 123.6, 123.1, 122.6, 115.5, 105.0, 104.2, 103.9, 69.2, 56.2, 56.1, 55.7, 50.9, 41.8, 30.8; ESI-HRMS ($[M + H]^+$) calcd for $C_{22}H_{22}NO_5$ 380.1498, found 380.1478.

(*S*)-(6,7,10-Trimethoxy-1,2,3,4-tetrahydrodibenzo[*f*,*h*]isoquinolin-3-yl)methanol (7): 11-Oxo-12-oxa-antofine (4.21 g, 11.10 mmol) was suspended in 100 mL of MeOH and 50 mL of NaOH (6N), and the mixture was stirred at 100 °C overnight. Most solvent was removed by evaporation and the residue was suspended in 200 mL of cold water. The solid was filtered, washed sequentially with cold MeOH and diethyl ether, and dried under vacuum to give 3.61 g of white solid. Yield: 92%; mp 243-245°C; $[\alpha]^{23}_{D}$= 100° (*c* 0.71, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-*d_6*): δ 8.08 (s, 1H), 8.07 (d, *J* = 2.7 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.31 (s, 1H), 7.21 (dd, *J* = 9.0 Hz, *J* = 2.4 Hz, 1H), 4.79 (t, 8.5 Hz, 1H), 4.42 (d, *J* = 16.2 Hz, 1H), 4.18 (d, *J* = 16.2 Hz, 1H), 4.02 (s, 3H), 3.98 (s, 3H), 3.94 (s, 3H), 3.68-3.63 (m, 1H), 3.56-3.51 (m, 1H), 3.01-2.97 (m, 2H), 2.67-2.58 (m, 1H); ^{13}C NMR (75 MHz, DMSO-*d_6*): δ 157.6, 149.6, 148.6, 129.9, 127.8, 127.0, 125.5, 124.4, 123.8, 123.2, 115.7, 105.0 (2×C), 104.2, 65.7, 56.2, 55.8, 55.7, 55.2, 46.1, 29.2; ESI-HRMS ($[M + H]^+$) calcd for $C_{21}H_{24}NO_4$ 354.1705, found 354.1702.

(*S*)-*N*-Boc-(6,7,10-trimethoxy-1,2,3,4-tetrahydrodibenzo[*f*,*h*]isoquinolin-3-yl)methanol (8): $(Boc)_2O$ (3.14 g, 14.40 mmol) was added to the amino-alcohol (4.240 g, 12 mmol) in 100 mL of CH_2Cl_2 and Et_3N (6 mL), and the mixture was stirred for 2 h. HCl (50 mL, 1N) was added and the organic layer was separated, washed with sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. Column chromatography eluting with CH_2Cl_2/MeOH gave 5.20 g of compound **8** as a white solid. Yield: 95.6%; mp 105-107°C; $[\alpha]^{23}_{D}$= 85.5° (*c* 0.42, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (s, 2H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.28 (s, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 5.29 (br s, 1H), 4.84 (m, 1H), 4.61 (br s, 1H), 4.09 (s, 3H), 4.05 (s, 3H), 4.01 (s, 3H), 3.73-3.62 (m, 2H), 3.27 (dd, *J* = 16.5 Hz, *J* = 6.3 Hz, 1H), 3.18 (t, *J* = 16.5 Hz, 1H), 1.55 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.9, 156.2, 149.7, 148.8, 130.4, 126.7, 124.0, 123.9, 123.8, 123.4, 122.8, 115.2, 105.1, 104.2, 104.0, 80.6, 62.7, 56.2, 56.0, 55.7, 50.6, 41.0, 28.6 (3×C), 26.5; ESI-HRMS ($[M + H]^+$) calcd for $C_{26}H_{32}NO_6$ 454.2230, found 454.2246.

(*S*)-*tert*-Butyl-6,7,10-trimethoxy-3-vinyl-3,4-dihydrodibenzo[f,h]isoquinoline-2(1H)-carboxylate (9): To a solution of $Ph_3P{=}CH_2Br$ (1.43 g, 4 mmol) in THF was added *n*-BuLi (2M in heptanes, 1.95 mL) at 0 °C under N_2. The mixture was stirred for 0.5 h before compound **8** (906 mg, 2 mmol) in THF (20 mL) was added dropwise. The mixture was then stirred for 2 h (monitored by TLC). Sat. NH_4Cl was added to quench the reaction and THF was removed by evaporation. The residue was dissolved in CH_2Cl_2 (50 mL), washed with sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. Column chromatography eluting with EtOAc/Hexane gave **9** (684 mg, 76%) as a light yellow foam: mp 177-179°C; $[\alpha]^{23}_{D}$= 118.2° (*c* 0.56, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.91 (d, *J* = 2.4 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.31 (s, 1H), 7.23 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H), 5.86-5.75 (m, 1H), 5.29 (m, 1H), 5.26 (d, *J* = 16.8 Hz, 1H), 5.16-5.04 (m, 2H), 4.59 (d, *J* = 17.4 Hz, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 4.01 (s, 3H), 3.36 (dd, *J* = 16.2 Hz, *J* = 6.0 Hz, 1H), 3.29 (t, *J* = 16.5 Hz, 1H), 1.55 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.9, 155.3, 149.8, 148.8, 136.5, 130.4, 126.8, 124.4, 124.2, 123.9, 123.6, 123.1, 116.6, 115.2, 105.1, 104.3, 104.1, 80.3, 77.4, 56.3, 56.1, 55.7, 41.1, 29.8, 28.7 (3×C); ESI-HRMS ([M + Na]$^+$) calcd for $C_{27}H_{31}NO_5Na$ 472.2100, found 472.2103.

General procedures for the synthesis of 10a-c: Compound **9** (225 mg, 0.50 mmol) was dissolved in TFA/CH_2Cl_2 (10 mL) at rt, and the mixture was stirred for 1 h. The solvent was removed by evaporation and TFA was neutralized with NMM. The residue was redissolved in DMF (10 mL), to which the appropriate unsaturated acid (0.70 mmol), EDC hydrochloride (134 mg, 0.70 mmol), HOBt (95 mg, 0.70 mmol), NMM (0.35 mL) were added. Stirring was continued overnight. DMF was then removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 (30 mL), washed with HCl (1N), sat. $NaHCO_3$, and brine, and dried over $MgSO_4$. Compounds **10a** and **10c** were isolated by column chromatography eluting with MeOH/CH_2Cl_2. For **10b**, the unsaturated acid (1.50 mmol) was added to a mixture of amine (0.50 mmol), DEPC (0.25 mL, 1.50 mmol), and Et_3N (0.42 mL, 3.00 mmol) in DMF, which was stirred overnight at room temperature. Standard workup and chromatography with EtOAc/Hexane gave **10b** in 76% yield.

10a: mp 104-106°C; $[\alpha]^{23}_D$= 136° (*c* 0.58, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, compound rotameric at rt): δ 7.86 (m, 3H), 7.26 (s, 1H), 7.21 (dd, *J* = 9.3 Hz, *J* = 2.4 Hz, 1H), 6.77 (brs, 1H), 6.40 (d, *J* = 16.8 Hz, 1H), 5.93-5.57 (m, 3H), 5.24-5.01 (m, 3H), 4.83-4.59 (d, *J* = 17.1 Hz, 1H), 4.09 (s, 3H), 4.05 (s, 3H), 4.02 (s, 3H), 3.33 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 166.1, 157.9, 149.6, 148.7, 136.0, 130.4, 128.3, 126.3, 123.8, 123.2, 122.0, 117.4, 115.1, 105.1, 104.9, 104.1, 103.8, 57.0, 56.2, 56.0, 55.9, 55.7, 55.5, 52.9, 48.1, 42.7, 40.1, 30.6, 29.8, 28.9; ESI-HRMS ([M + H]$^+$) calcd for $C_{25}H_{26}NO_4$ 404.1862, found 404.1854.

10b: mp 170-172°C; $[\alpha]^{23}_D$= 125.1° (*c* 0.64, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, compound rotameric at rt): δ 7.95-7.73 (m, 3H), 7.32-7.23 (m, 2H), 6.09-6.03 (m, 1H), 5.89-5.77 (m, 3H), 5.27-5.01 (m, 4H), 4.85-4.53 (d, *J* = 17.4 Hz, 1H), 4.11 (s, 3H), 4.07 (s, 3H), 4.03 (s, 3H), 3.40-3.31 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 170.2, 158.0, 149.8, 148.8, 135.9, 135.6, 131.7, 131.4, 130.5, 126.4, 124.6, 124.2, 123.9, 123.4, 122.1, 118.2, 117.3, 115.4, 115.1, 105.2, 104.3, 103.9, 56.2, 56.1, 55.7, 53.1, 47.9, 42.7, 39.9, 39.8, 39.4, 30.7, 29.0; ESI-HRMS ([M + H]$^+$) calcd for $C_{26}H_{28}NO_4$ 418.2018, found 418.2024.

10c: mp 73-75°C; $[\alpha]^{23}_D$= 144.6° (*c* 0.35, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, compound rotameric at rt): δ 7.94-7.75 (m, 3H), 7.31-7.22 (m, 2H), 5.98-5.76 (m, 3H), 5.19-4.99 (m, 5H), 4.84-4.53 (d, *J* = 17.1 Hz, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 4.00 (s, 3H), 3.33 (d, *J* = 18.6 Hz, 2H), 2.65 (q, *J* = 7.2 Hz, 2), 2.55-2.46 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.8, 171.5, 158.0, 149.7, 148.8, 137.6, 136.1, 135.8, 130.5, 126.7, 126.4, 124.5, 124.4, 124.0, 123.9, 123.5, 123.1, 122.0, 117.3, 117.1, 115.5, 115.1, 105.2, 104.3, 103.9, 56.2, 56.1, 55.7, 52.9, 47.8, 42.5, 39.9, 33.6, 33.0, 30.8, 29.5, 29.0; ESI-HRMS ([M + H]$^+$) calcd for $C_{27}H_{30}NO_4$ 432.2175, found 432.2184.

General procedures for the synthesis of 11a-c: Compounds **10a-c** were dissolved in degassed CH_2Cl_2 under N_2, to which Grubb's 2nd generation catalyst in CH_2Cl_2 was added in one portion. The reaction was stirred at reflux for 2 h or monitored by TLC. Compounds **11a-c** were isolated by column chromatography eluting with CH_2Cl_2/MeOH. Yield: 70% - 85%.

11a: mp 105-107°C; $[\alpha]^{23}_{D}$= -191.8° (*c* 0.55, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.89 (d, *J* = 3.3 Hz, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.42 (d, *J* = 5.7 Hz, 1H), 7.25 (s, 1H), 7.24 (dd, *J* = 9.0 Hz, *J* = 2.7Hz, 1H), 6.39 (d, *J* = 6.0Hz, 1H), 5.49 (d, *J* = 17.1 Hz, 1H), 4.75 (d, *J* = 17.7 Hz, 1H), 4.35 (dd, *J* = 12 Hz, *J* = 5.4 Hz, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 4.02 (s, 3H), 3.62 (dd, *J* = 15.9 Hz, *J* = 4.5 Hz, 1H), 2.71 (dd, *J* = 15.0 Hz, 12.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.5, 158.2, 149.8, 149.0, 147.4, 130.6, 128.6, 126.2, 124.4, 124.1, 123.9, 123.4, 122.4, 115.4, 105.2, 104.2, 104.0, 57.7, 56.2, 56.1, 55.7, 40.2, 30.0; ESI-HRMS ($[M + H]^+$) calcd for $C_{23}H_{22}NO_4$ 376.1549, found 376.1559.

11b: mp 238-240°C; $[\alpha]^{23}_{D}$= -216.4° (*c* 0.58, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, *J* = 9.3 Hz, 1H), 7.90-7.89 (m, 2H), 7.23-7.21 (m, 2H), 6.07 (d, *J* = 17.7 Hz, 1H), 6.03-5.90 (m, 2H), 4.49 (d, *J* = 17.4 Hz, 1H), 4.40-4.36 (m, 1H), 4.11 (s, 3H), 4.05 (s, 3H), 4.02 (s, 3H), 3.35 (dd, *J* = 15.6 Hz, *J* = 2.4 Hz, 1H), 3.13 (brs, 2H), 3.04-2.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.4, 158.1, 149.7, 148.8, 130.5, 126.2, 125.1, 124.7, 124.6, 123.9, 123.8, 123.5, 122.2, 115.2, 105.1, 104.1, 103.9, 56.2, 56.1, 55.7, 54.6, 42.8, 34.8, 32.1; ESI-HRMS ($[M + H]^+$) calcd for $C_{24}H_{24}NO_4$ 390.1705, found 390.1706.

11c: mp 205-207°C; $[\alpha]^{23}_{D}$= 81.9° (*c* 1.50, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, *J* = 9.0 Hz, 1H), 7.93 (s, 1H), 7.90 (d, *J* = 2.7 Hz, 1H), 7.36 (s, 1H), 7.25 (dd, *J* = 9.0 Hz, *J* = 2.4 Hz, 1H), 5.75-5.70 (m, 1H), 5.59-5.54 (m, 1H), 5.32 (d, *J* = 15.9 Hz, 1H), 4.97 (d, *J* = 16.2 Hz, 1H), 4.89 (m, 1H), 4.11 (s, 3H), 4.08 (s, 3H), 4.01 (s, 3H), 3.37 (dd, *J* = 15.3 Hz, *J* = 5.4 Hz, 1H), 3.25 (dd, *J* = 15.3 Hz, *J* = 8.1 Hz, 1H), 3.10 (dt, *J* = 13.2 Hz, *J* = 8.1 Hz, 1H), 2.56 (dt, *J* = 13.5 Hz, 4.8 Hz, 1H), 2.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.8, 158.0, 149.9, 148.9, 131.6, 130.6, 130.5, 128.2, 125.8, 125.7, 125.0, 124.0, 123.2, 115.4, 105.1, 104.3, 103.7, 56.2, 56.1, 55.7, 51.6, 40.9, 35.1, 31.7, 25.2; ESI-HRMS ($[M + H]^+$) calcd for $C_{25}H_{26}NO_4$ 404.1862, found 404.1856.

General procedure for the synthesis of 12a-c: Compounds **11a-d** were dissolved in MeOH, to which Pd/C was added. The mixture was hydrogenated under H_2 at 50 psi overnight. The catalyst was removed by filtration and column chromatography eluting with CH_2Cl_2/MeOH gave **12a-c**. Yield: 90%.

12a: mp 185-187°C; $[\alpha]^{23}_{D}$= -134.4° (*c* 0.45, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.83 (d, *J* = 3.0 Hz, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.20 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H), 7.19 (s, 1H), 5.29 (d, *J* = 17.4 Hz, 1H), 4.50 (d, *J* = 17.1 Hz, 1H), 4.08 (s, 3H), 4.03 (s, 3H), 4.00 (s, 3H), 3.91-3.84 (m, 1H), 3.36 (dd, *J* = 15.6 Hz, *J* = 4.2 Hz, 1H), 2.73 (dd, *J* = 15.6 Hz, 11.1 Hz, 1H), 2.59-2.44 (m, 3H), 2.05-2.44 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.2, 158.1, 149.7, 148.8, 130.4, 126.4, 124.4, 124.0, 123.9, 123.8, 123.4, 115.2, 105.1, 104.2, 104.0, 56.1, 56.0, 55.7, 53.3, 41.1, 33.5, 30.3, 25.5; ESI-HRMS ($[M + H]^+$) calcd for $C_{23}H_{24}NO_4$ 378.1705, found 378.1713.

12b: mp 257-259°C; $[\alpha]^{23}_D$= -183.6° (*c* 1.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88 (d, *J* = 9.0 Hz, 1H), 7.86 (s, 1H), 7.85 (d, *J* = 3.0 Hz, 1H), 7.21 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H), 7.16 (s, 1H), 5.88 (d, *J* = 17.4 Hz, 1H), 4.41 (d, *J* = 17.4 Hz, 1H), 4.09 (s, 3H), 4.04 (s, 3H), 4.00 (s, 3H), 3.79-3.74 (m, 1H), 3.11-3.02 (m, 2H), 2.52 (t, *J* = 6.0 Hz, 2H), 2.28-2.20 (m, 1H), 2.05-1.96 (m, 1H), 1.94-1.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.7, 157.9, 149.6, 148.7, 130.4, 126.2, 124.7, 124.6, 124.0, 123.7, 123.5, 115.1, 105.1, 104.1, 103.9, 56.2, 56.1, 55.7, 52.7, 43.4, 34.0, 33.1, 29.2, 18.6; ESI-HRMS ($[M + H]^+$) calcd for $C_{24}H_{26}NO_4$ 392.1862, found 392.1865.

12c: mp 232-234°C; $[\alpha]^{23}_D$= 47.2° (*c* 0.97, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 9.0 Hz, 1H), 7.95 (s, 1H), 7.92 (d, *J* = 2.4 Hz, 1H), 7.38 (s, 1H), 7.26 (dd, *J* = 9.0 Hz, *J* = 2.4 Hz, 1H), 5.23 (d, *J* = 15.9 Hz, 1H), 4.97 (d, *J* = 15.9 Hz, 1H), 4.12 (s, 3H), 4.09 (s, 3H), 4.02 (s, 3H), 3.96-3.92 (m, 1H), 3.39 (dd, *J* = 15.0 Hz, *J* = 5.4 Hz, 1H), 3.15 (dd, *J* = 15.3 Hz, 6.9 Hz, 1H), 2.66-2.64 (m, 2H), 1.88-1.84 (m, 3H), 1.65-1.56 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.0, 158.0, 149.9, 148.9, 130.4, 127.4, 126.0, 125.7, 125.1, 124.1, 123.2, 115.4, 105.1, 104.4, 103.8, 56.2, 56.1, 55.7, 54.3, 40.0, 37.0, 34.4, 32.4, 28.2, 23.1; ESI-HRMS ($[M + H]^+$) calcd for $C_{25}H_{28}NO_4$ 406.2018, found 406.2024.

General procedure for the synthesis of *R*-antofine (13a), *R*-cryptopleurine (13b), and compound 13c: The amides **12a-c** and $LiAlH_4$ (2 equiv.) were suspended in THF (15 mL), which was stirred for 2-3 h. Water was then added to quench the reaction, followed by aq. NaOH (1N, 1mL) and H_2O (1 mL). The mixture was filtered and then extracted with $CHCl_3$ and dried over $MgSO_4$. Column chromatography eluting with CH_2Cl_2/MeOH gave the target products. Yield: 70% -80%.

***R*-Antofine (13a):** mp 204-206°C (lit.[9] 206-211°C); $[\alpha]^{23}_D$= -129.2° (*c* 0.48, $CHCl_3$, lit.[9] $[\alpha]^{19}_D$= -125.2°); IR (FT-IR ATR, cm^{-1}) 2830, 1616, 1507, 1259, 1030; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.90 (d, *J* = 2.4 Hz, 1H), 7.82 (d, *J* = 9.0 Hz, 1H), 7.32 (s, 1H), 7.20 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H), 4.69 (d, *J* = 15.9 Hz, 1H), 4.11 (s, 3H), 4.07 (s, 3H), 4.02 (s, 3H), 3.69 (d, *J* = 14.7 Hz, 1H), 3.46 (dt, *J* = 8.7 Hz, *J* = 1.8 Hz, 1H), 3.35 (dd, *J* = 16.2 Hz, *J* = 2.4 Hz, 1H), 2.90 (dd, *J* = 15.6 Hz, *J* = 10.8 Hz, 1H), 2.51-2.41 (m, 2H), 2.26-2.21 (m, 1H), 2.05-1.91 (m, 2H), 1.83-1.74 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.6, 149.6, 148.5, 130.3, 127.3, 126.8, 125.7, 124.4, 124.3, 123.7, 115.0, 104.9, 104.2, 104.1, 60.4, 56.2, 56.0, 55.7, 55.2, 54.0, 33.9, 31.5, 21.8; ESI-HRMS ($[M + H]^+$) calcd for $C_{23}H_{26}NO_3$ 364.1913, found 364.1918.

***R*-Cryptopleurine (13b):** mp 201-203°C (lit.[9] 195-197°C); $[\alpha]^{23}_D$= -108.8° (*c* 0.64,

$CHCl_3$, lit.[9] $[\alpha]^{21}_D$= -108.7°); IR (FT-IR ATR, cm^{-1}) 2828, 1507, 1472, 1255, 1230, 1205, 1036, 831; ^1H NMR (300 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.86 (d, *J* = 3.0 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.20 (s, 1H), 7.17 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H), 4.39 (d, *J* = 15.6 Hz, 1H), 4.08 (s, 3H), 4.04 (s, 3H), 3.99 (s, 3H), 3.56 (d, *J* = 15.3 Hz, 1H), 3.24 (d, *J* = 11.1 Hz, 1H), 3.00 (dd, *J* = 16.5 Hz, *J* = 3.0 Hz, 1H), 2.82 (dd, *J* = 15.9 Hz, *J* = 10.5 Hz, 1H), 2.33-2.21 (m, 2H), 2.01-1.97 (m, 1H), 1.89-1.84 (m, 1H), 1.78 (m, 2H), 1.52-1.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.5, 149.5, 148.4, 130.2, 126.6, 125.7, 124.6, 124.2, 123.8, 123.5, 114.9, 104.8, 104.0 (2×C), 57.6, 56.4, 56.2, 56.1, 56.0, 55.6, 34.9, 33.9, 26.1, 24.5; ESI-HRMS ($[M + H]^+$) calcd for $C_{24}H_{28}NO_3$ 378.2069, found 378.2077.

13c: mp 193-195°C; $[\alpha]^{23}_D$= -82.6° (*c* 0.38, $CHCl_3$); IR (FT-IR ATR, cm^{-1}) 2826, 1609, 1507, 1472, 1418, 1257, 1037; ^1H NMR (300 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.89 (d, *J* = 2.4 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.27 (s, 1H), 7.19 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H), 4.42 (d, *J* = 15.0 Hz, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 4.05 (d, *J* = 15.3 Hz, 1H), 4.01 (s, 3H), 3.07-2.93 (m, 4H), 2.82-2.77 (m, 1H), 1.95-1.59 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.5, 149.5, 148.4, 130.2, 127.1, 126.0, 124.3 (2×C), 124.1, 123.6, 115.0, 104.9, 104.2, 104.0, 60.6, 57.3, 56.2, 56.1, 55.7, 55.4, 35.8, 33.9, 29.2, 27.8, 24.7; ESI-HRMS ($[M + H]^+$) calcd for $C_{25}H_{30}NO_3$ 392.2226, found 392.2225.

14: Similar procedures as **10a-c**. mp 74-76°C; $[\alpha]^{23}_D$= 71.5° (*c* 1.16, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, compound rotameric at rt): δ 7.89-7.84 (m, 3H), 7.28 (s, 1H), 7.21 (dd, *J* = 9.2 Hz, *J* = 2.8 Hz, 1H), 5.88-5.61 (m, 2H), 5.20-5.10 (m, 3H), 4.64 (d, *J* = 3.2 Hz, 1H), 4.54 (m, 1H), 4.46 (d, *J* = 3.2 Hz), 4.09 (s, 3H), 4.05 (s, 3H), 4.00 (s, 3H), 3.73 (s, 3H), 3.43-3.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 162.6, 157.9, 157.2, 149.7, 148.8, 135.9, 130.4, 126.5, 124.3, 123.8, 123.7, 123.3, 117.7, 115.2, 105.0, 104.1, 103.9, 56.1, 56.0, 55.6, 55.3, 53.8, 39.6, 36.5, 31.5, 30.3; ESI-HRMS ($[M + H]^+$) calcd for $C_{26}H_{27}NO_5$ 433.1889, found 434.1963.

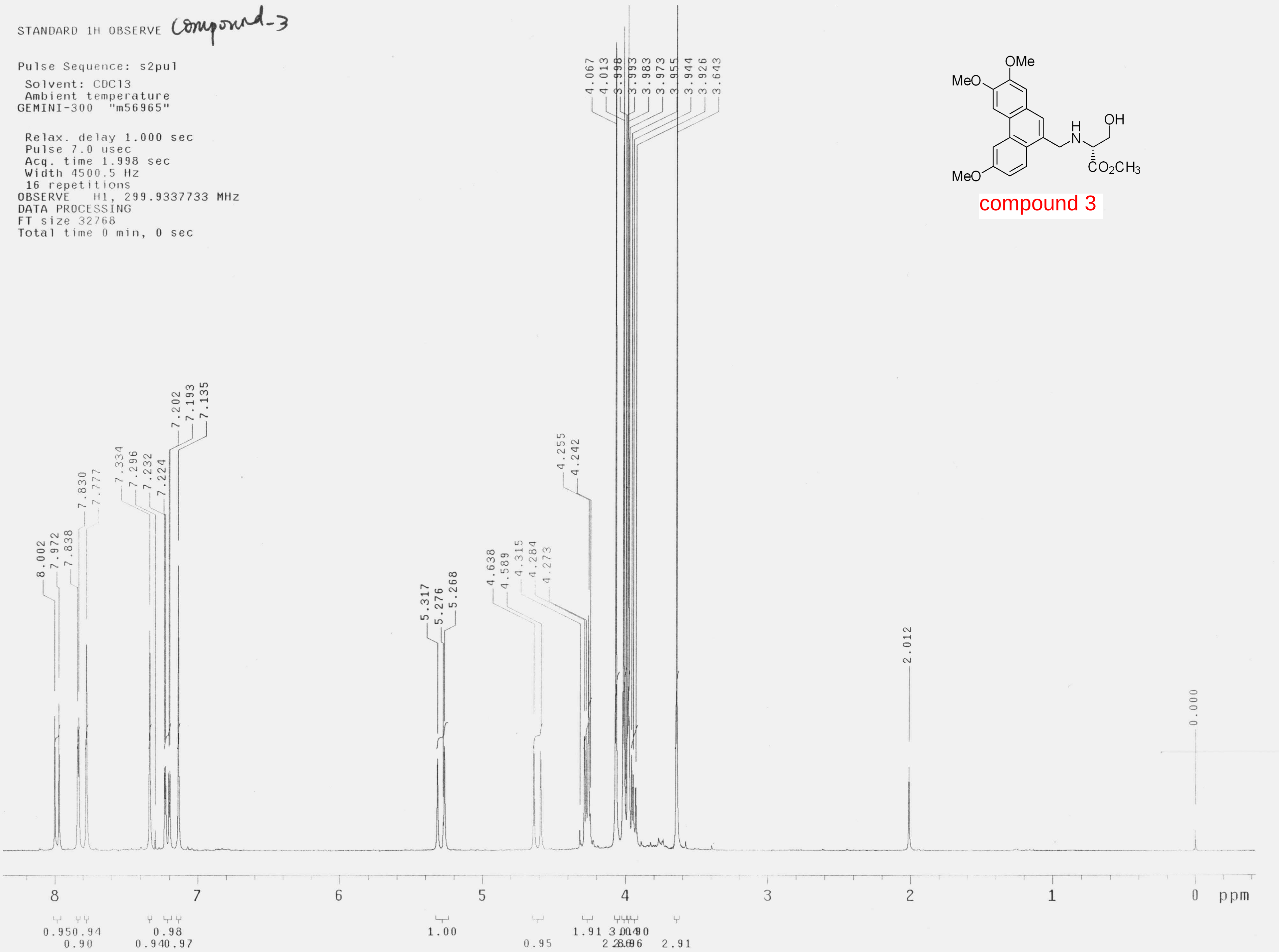
15: Similar procedures as **11a-c**. mp 135-137°C; $[\alpha]^{23}_D$= -235° (*c* 1.11, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.79 (d, *J* = 2.8 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.20-7.17 (m, 2H), 6.00 (d, *J* = 2.4 Hz, 1H), 5.37 (d, *J* = 17.6 Hz, 1H), 4.65 (d, *J* = 17.2 Hz, 1H), 4.16-4.12 (m, 1H), 4.10 (s, 3H), 4.03 (s, 3H), 4.00 (s, 3H), 3.86 (s, 3H), 3.52 (dd, *J* = 11.6 Hz, *J* = 4.8 Hz, 1H), 2.53 (dd, *J* = 15.6 Hz, *J* = 11.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 158.0, 153.1, 149.5, 148.7, 130.4, 126.0, 124.1, 124.0, 123.2, 123.2, 122.4, 115.3, 108.7, 104.9, 104.0, 103.9, 57.5, 56.1, 56.0, 55.6, 52.4, 40.4, 31.4; ESI-HRMS ($[M + H]^+$) calcd for $C_{24}H_{23}NO_5$ 405.1567, found 406.1667.

16: Similar procedures as **13a-c**. mp 202-204°C; $[\alpha]^{23}_D$= -97.0° (*c* 0.47, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.90 (d, *J* = 2.4 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.33 (s, 1H), 7.20 (dd, *J* = 9.2 Hz, *J* = 2.4 Hz, 1H), 4.83 (s, 1H), 4.52 (d, *J* = 14.4 Hz, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 4.05 (d, *J* = 14.4 Hz, 1H), 4.01 (s, 3H), 3.83 (d, *J* = 7.2 Hz, 1H), 3.72 (s, 3H), 3.58 (m, 2H), 3.32 (d, *J* = 15.2 Hz, 1H), 3.02 (m, 1H); ^{13}C

NMR (100 MHz, $CDCl_3$): δ 159.7, 157.7, 149.6, 148.6, 130.2, 127.7, 127.6, 125.8, 124.5, 124.4, 123.7, 115.1, 104.8, 104.3, 104.0, 95.3, 63.7, 57.8, 57.0, 56.2, 56.0, 55.7, 51.8, 33.8; ESI-HRMS ($[M + H]^+$) calcd for $C_{24}H_{25}NO_4$ 391.1784, found 392.1865.

***S*-12-oxo-antofine (17):** Compound 16 (300 mg) was refluxed in HCl/THF for 2h before the solvent was evaporated. NaOH was used for neutralization and CH_2Cl_2 used for extraction. Chromatography gave 200 mg light yellow solid (68%). mp 240-242°C; $[\alpha]^{23}_D$= -34.7° (*c* 0.91, $CHCl_3$); IR (FT-IR ATR, cm^{-1}) 2833, 1751, 1609, 1510, 1260, 1234, 1208, 1202, 1126, 867, 777; ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.91 (d, *J* = 2.4 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.27 (s, 1H), 7.22 (dd, *J* = 9.2 Hz, *J* = 2.6 Hz, 1H), 4.70 (d, *J* = 14.8 Hz, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 4.02 (s, 3H), 3.84 (d, *J* = 15.2 Hz, 1H), 3.78 (d, *J* = 16.8 Hz, 1H), 3.43 (d, *J* = 13.2 Hz, 1H), 3.07-3.01 (m, 2H), 2.98 (d, *J* = 16.4 Hz, 1H), 2.76 (dd, *J* = 17.6 Hz, *J* = 5.2 Hz, 1H), 2.43 (dd, *J* = 17.6 Hz, *J* = 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.4, 157.7, 149.5, 148.6, 130.2, 126.6, 125.7, 124.5, 124.0, 123.7, 123.6, 115.1, 104.7, 103.8, 103.7, 63.1, 57.9, 56.0, 55.9, 53.4, 44.7, 33.2; ESI-HRMS ($[M + H]^+$) calcd for $C_{23}H_{23}NO_4$ 377.1627, found 378.1704.

***S*-12*N*-methyl-12-aza-antofine (18):** The Boc aldehyde was obtained using the same procedure as for **9**. $MeNH_2$ hydrochloride were added to the aldehyde in MeOH, followed by addition of AcOH and $NaBH_3CN$, which was stirred at r.t. for 4h. Sat. $NaHCO_3$ was added to quench the reaction and CH_2Cl_2 was used for extraction. The residue was purified through a quick TLC column and TFA was used to remove the Boc group. Then TFA was removed by evaporation and the residue was dissolved in CH_2Cl_2 (10 ml), to which K_2CO_3 (100 mg) and $MgSO_4$ (0.5 g) were added, followed by HCHO (37%, 0.1 ml). The mixture was stirred at r.t. overnight. Chromatography gave 15 mg off-white solid. Yield: 45% over four steps. mp 182-184 ℃; $[\alpha]^{23}_D$= -45.0° (*c* 0.34, $CHCl_3$) ; IR (FT-IR ATR, cm^{-1}) 2832, 1616, 1512, 1257, 1032; ^1H NMR (300 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.89 (d, *J* = 2.7 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.26 (s, 1H), 7.19 (dd, *J* = 9.0 Hz, *J* = 2.7 Hz, 1H), 4.57 (d, *J* = 14.7 Hz, 1H), 4.11 (d, *J* = 5.1 Hz, 1H), 4.10 (s, 3H), 4.05 (s, 3H), 4.01 (s, 3H), 3.80 (d, *J* = 15.0 Hz, 1H), 3.62 (d, *J* = 5.1 Hz, 1H), 3.41 (dd, *J* = 8.4 Hz, *J* = 5.1 Hz, 1H), 3.48 (d, *J* = 12.9 Hz, 1H), 3.01-2.95 (m, 2H), 2.85-2.79 (m, 1H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.9, 149.7, 148.7, 130.4, 126.9, 125.8, 124.6, 124.3, 124.0, 123.8, 115.2, 104.9, 104.1, 104.0, 78.0, 61.0, 59.2, 56.2, 56.1, 55.7, 50.4, 43.5, 31.0; ESI-HRMS ($[M + H]^+$) calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 379.2025.



STANDARD 1H OBSERVE Compound-3

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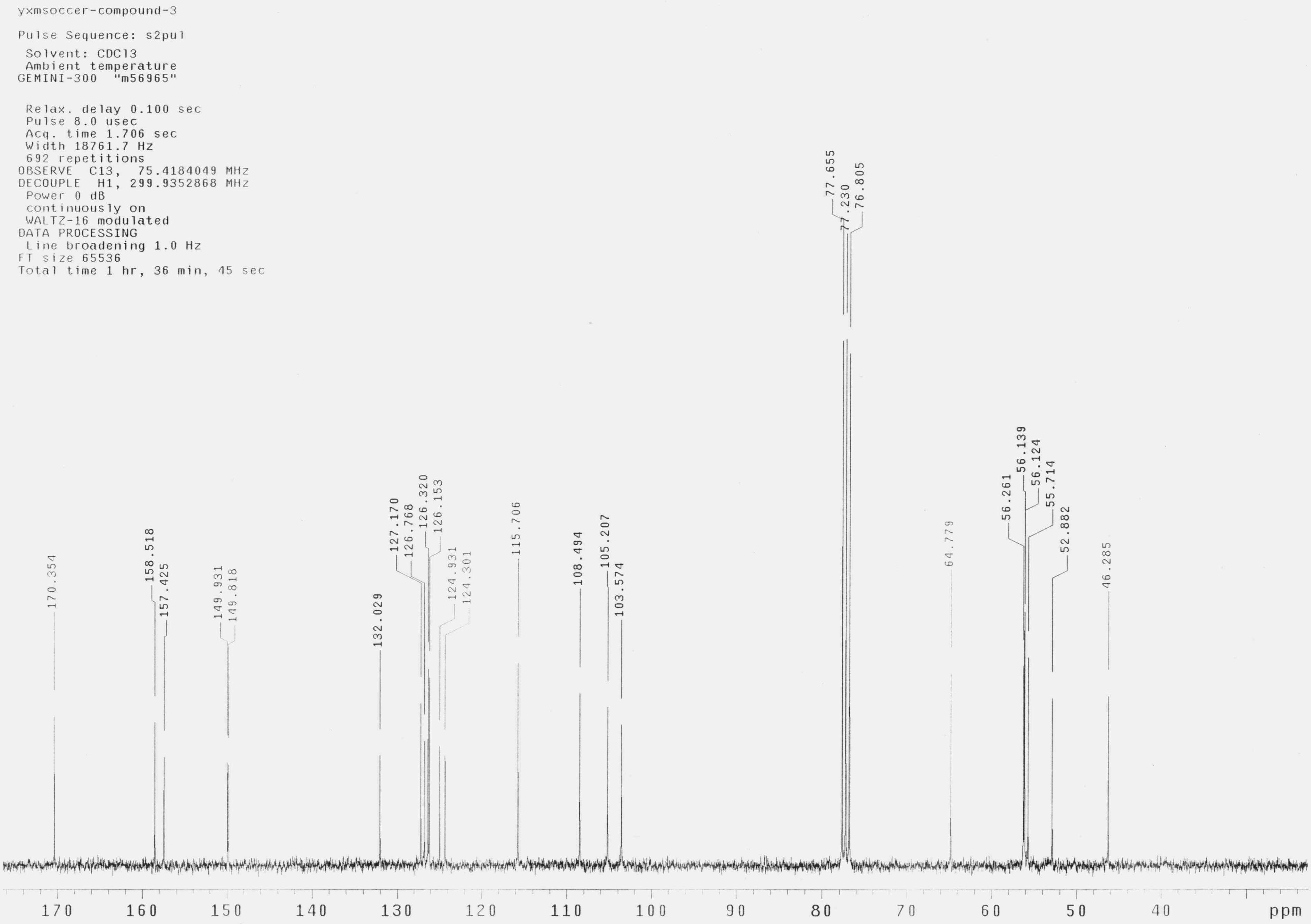
Total time 0 min, 0 sec

compound 3



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DECOUPLE  H1, 299.9352868 MHz
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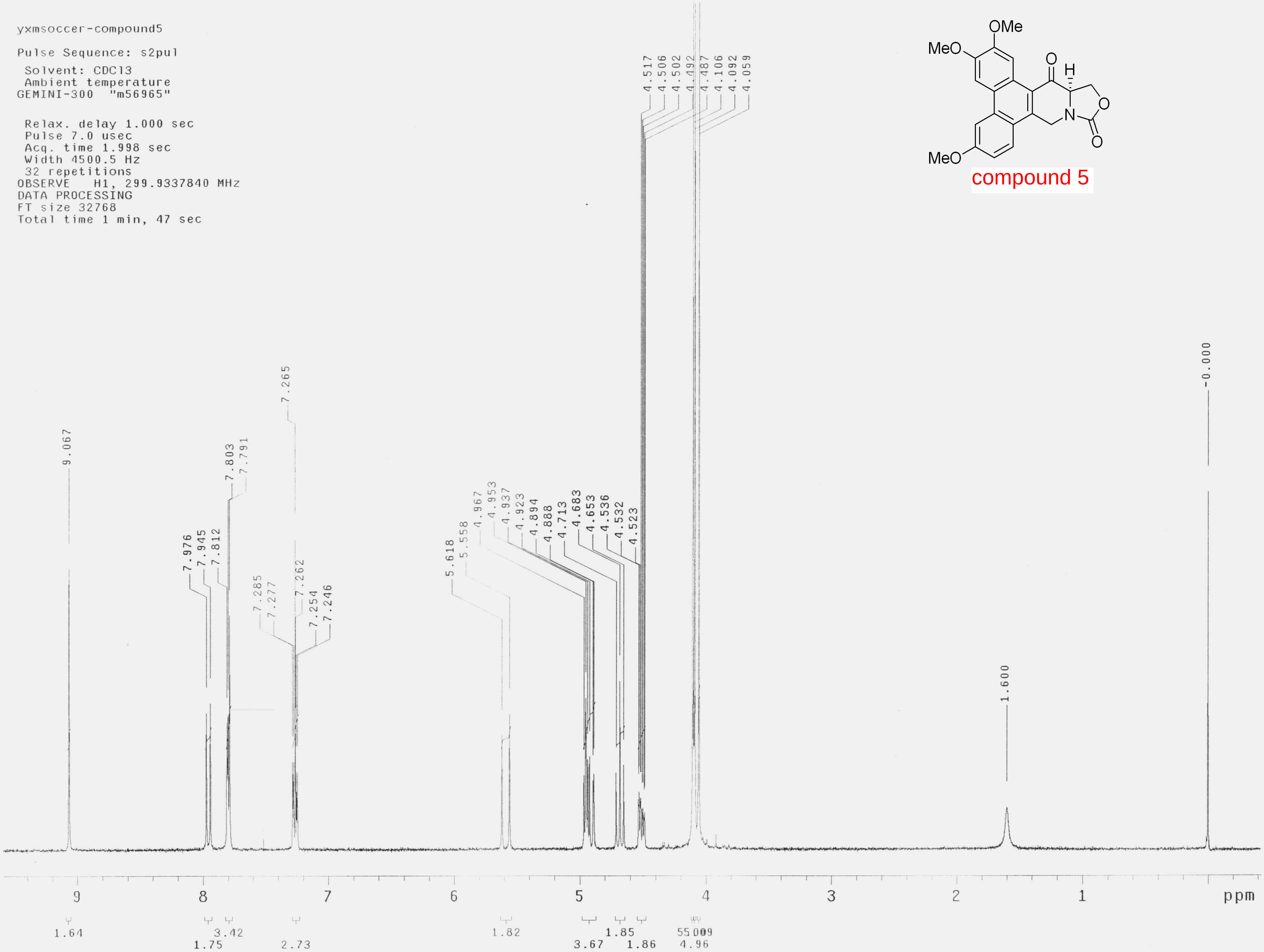

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yxmsoccer-compound5

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 Solvent: CDCl3
 Ambient temperature
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 Pulse 7.0 usec
 Acq. time 1.998 sec
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DATA PROCESSING
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Total time 1 min, 47 sec
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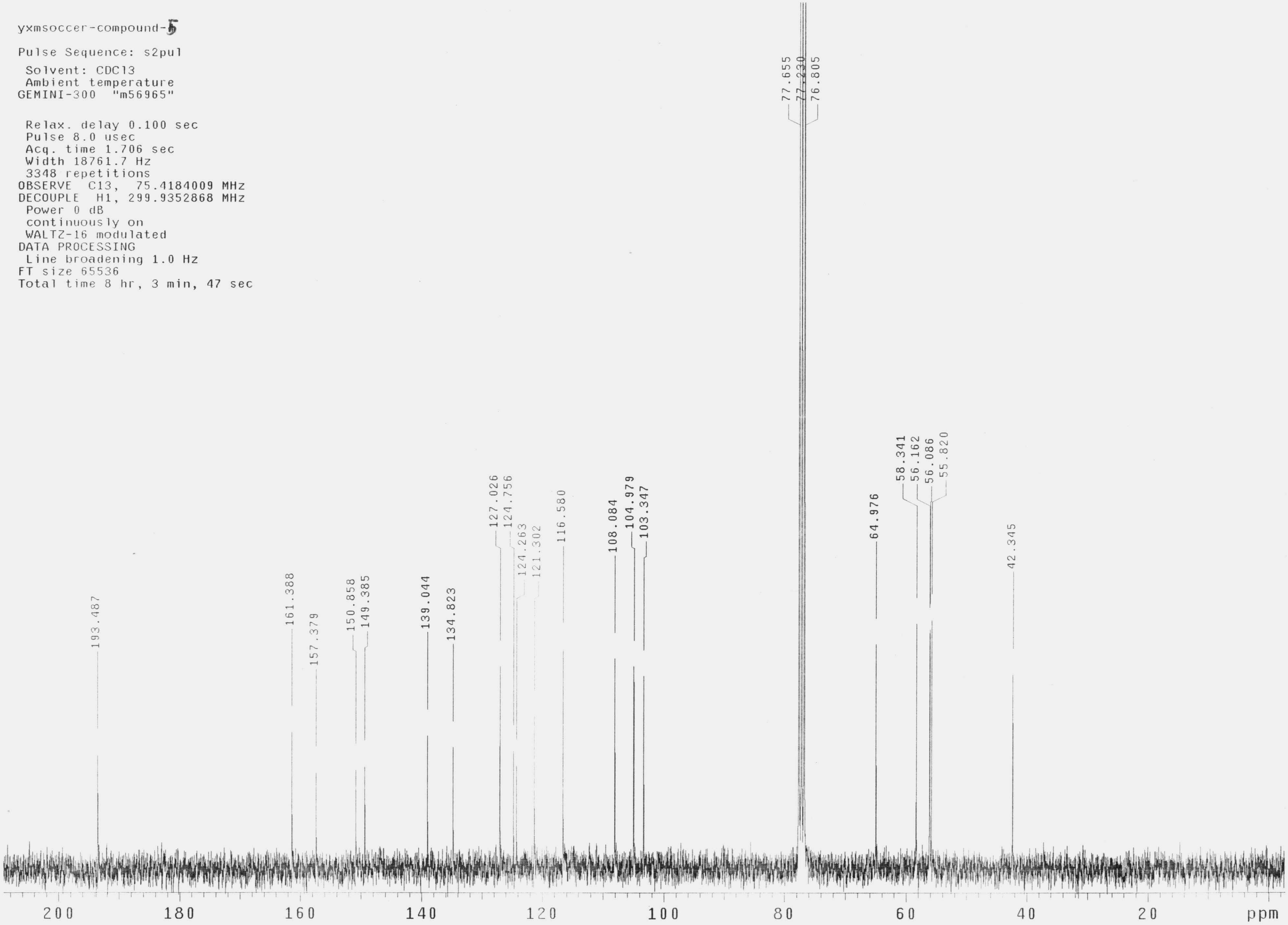
compound 5



yxmsoccer-compound-5

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Solvent: CDCl3
Ambient temperature
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DECOUPLE H1, 299.9352868 MHz
Power 0 dB
continuously on
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DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 8 hr, 3 min, 47 sec

yxmsoccer-ser-dehydroxyl

compound-6

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
GEMINI-300 "m56965"

PULSE SEQUENCE
Relax. delay 1.000 sec
Pulse 33.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
24 repetitions
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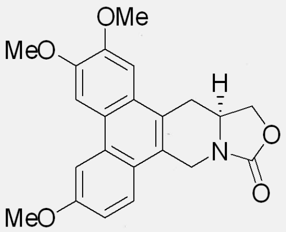
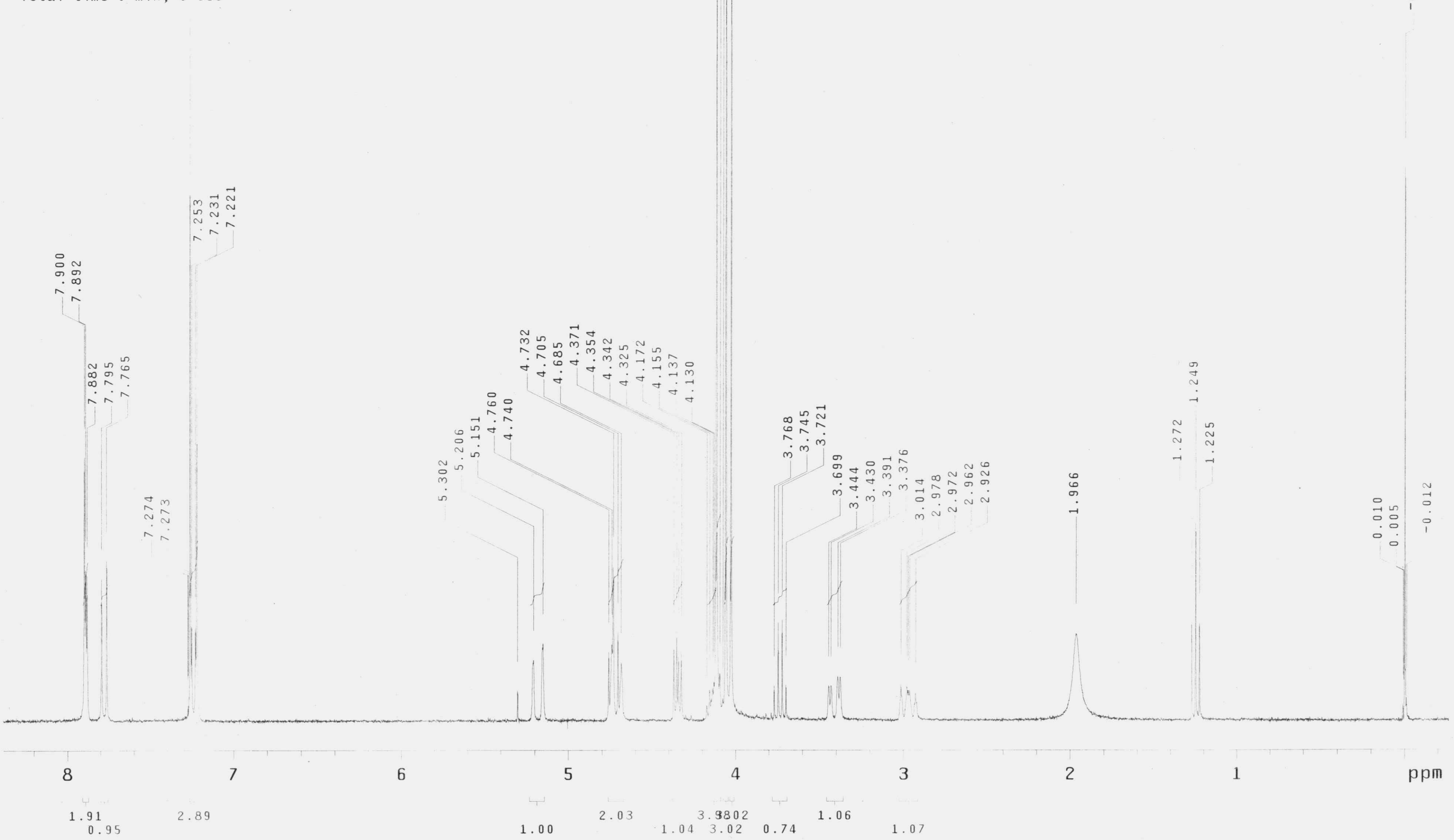
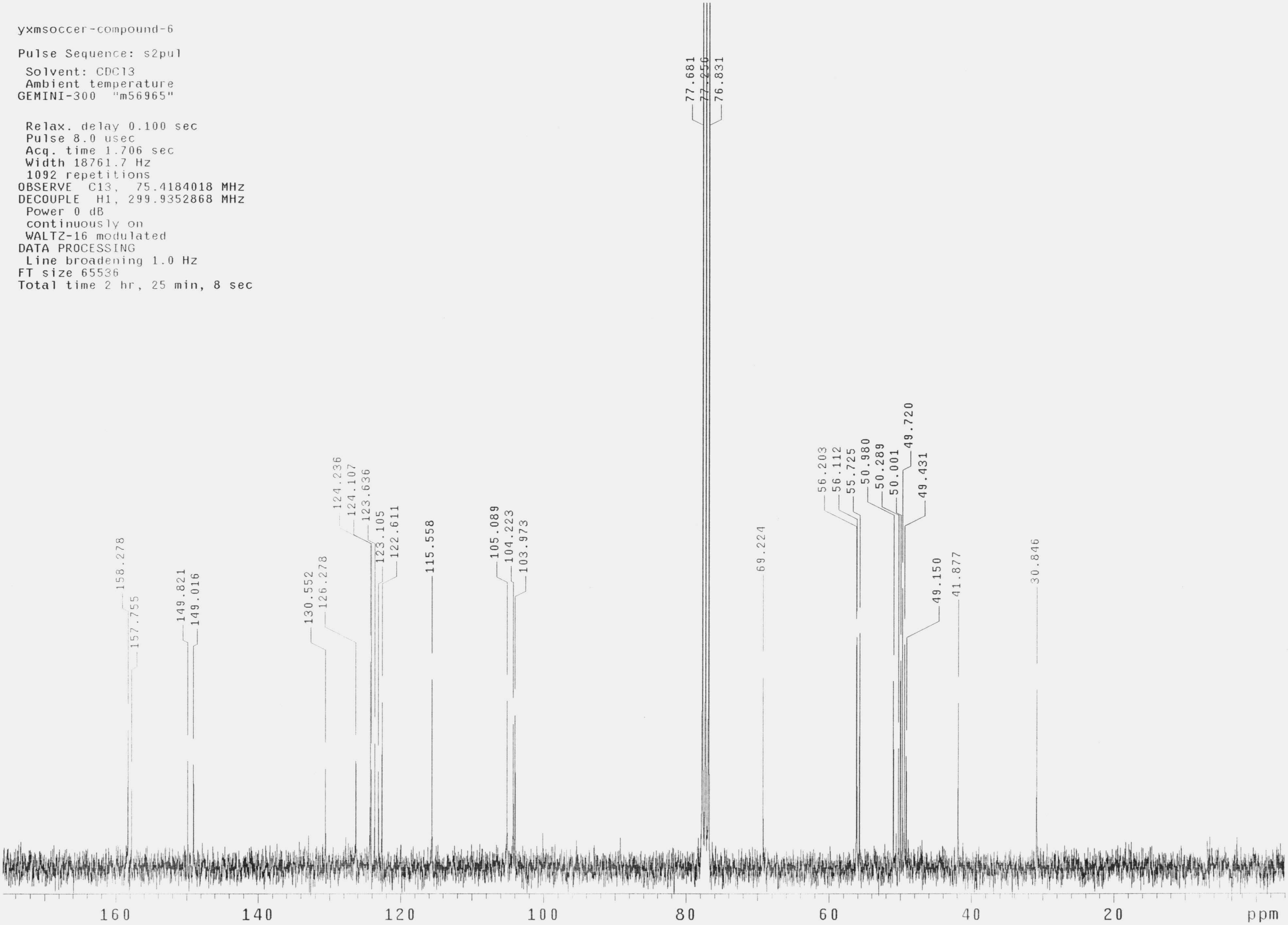
DATA PROCESSING
FT size 32768
Total time 0 min, 0 sec







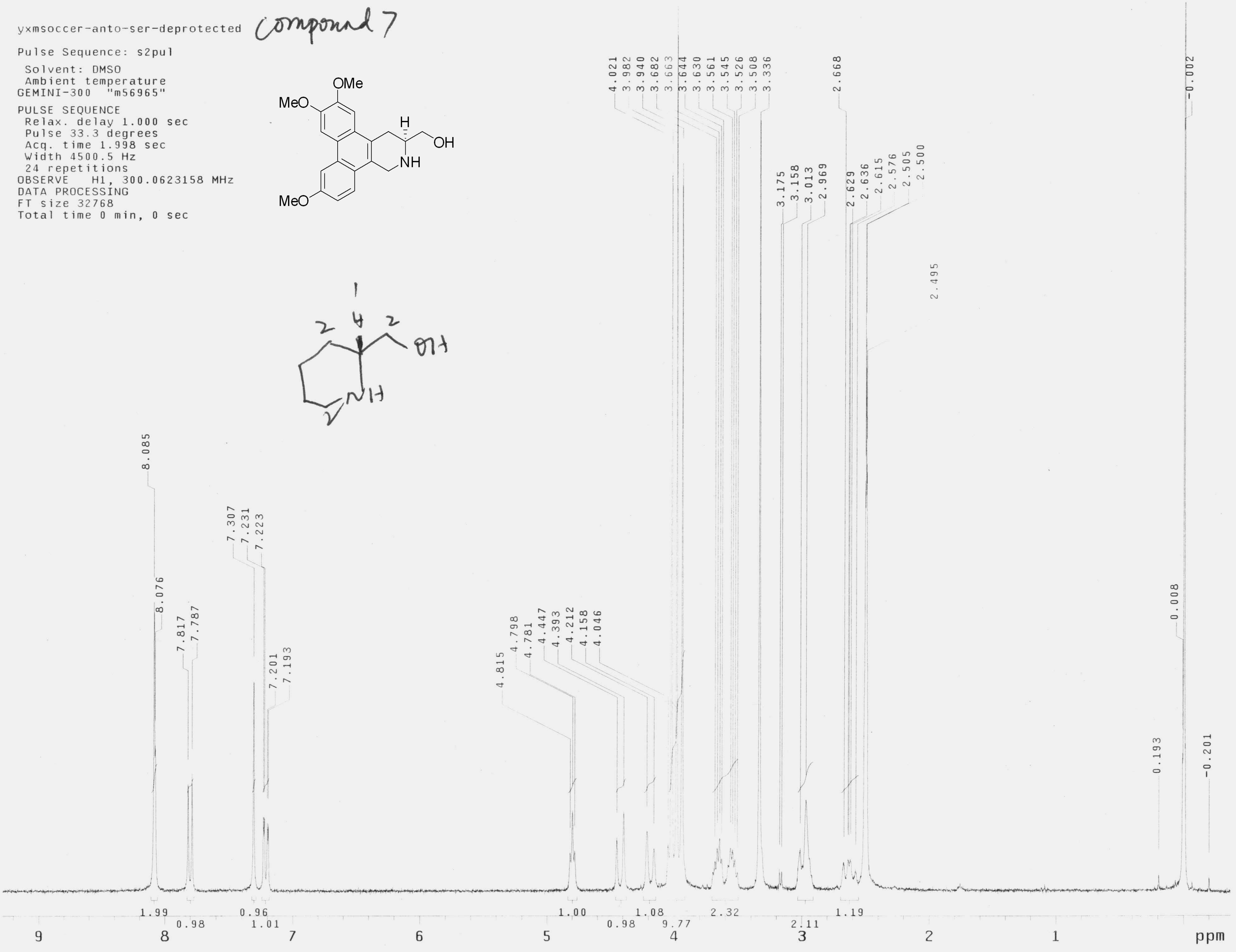
```
yxmsoccer-compound-6

Pulse Sequence: s2pul

 Solvent: CDCl3
 Ambient temperature
GEMINI-300  "m56965"

 Relax. delay 0.100 sec
 Pulse 8.0 usec
 Acq. time 1.706 sec
 Width 18761.7 Hz
 1092 repetitions
OBSERVE  C13,  75.4184018 MHz
DECOUPLE  H1, 299.9352868 MHz
 Power 0 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 2 hr, 25 min, 8 sec
```

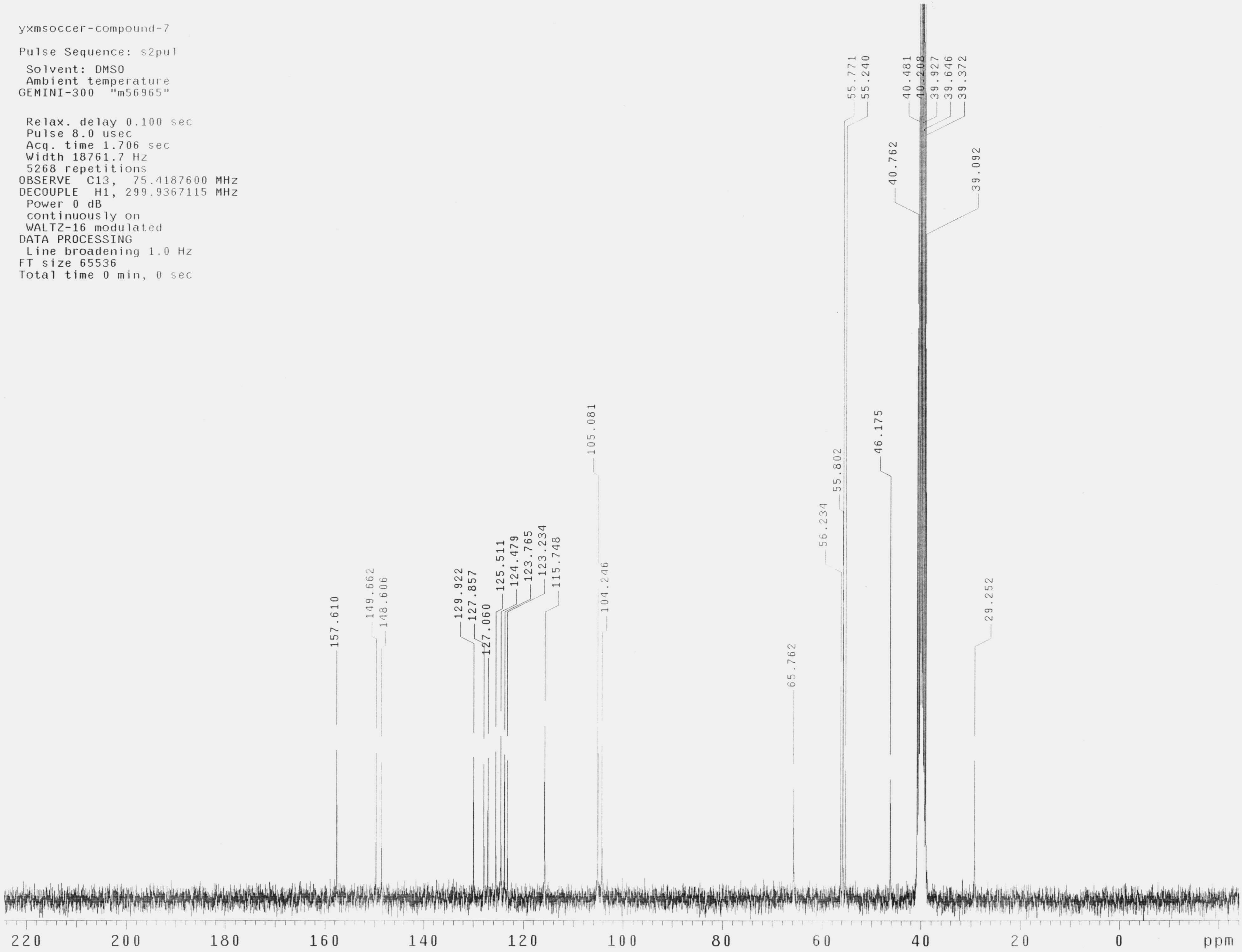
yxmsoccer-anto-ser-deprotected compound 7

Pulse Sequence: s2pul

Solvent: DMSO
Ambient temperature
GEMINI-300 "m56965"

PULSE SEQUENCE
Relax. delay 1.000 sec
Pulse 33.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
24 repetitions
OBSERVE H1, 300.0623158 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 0 sec



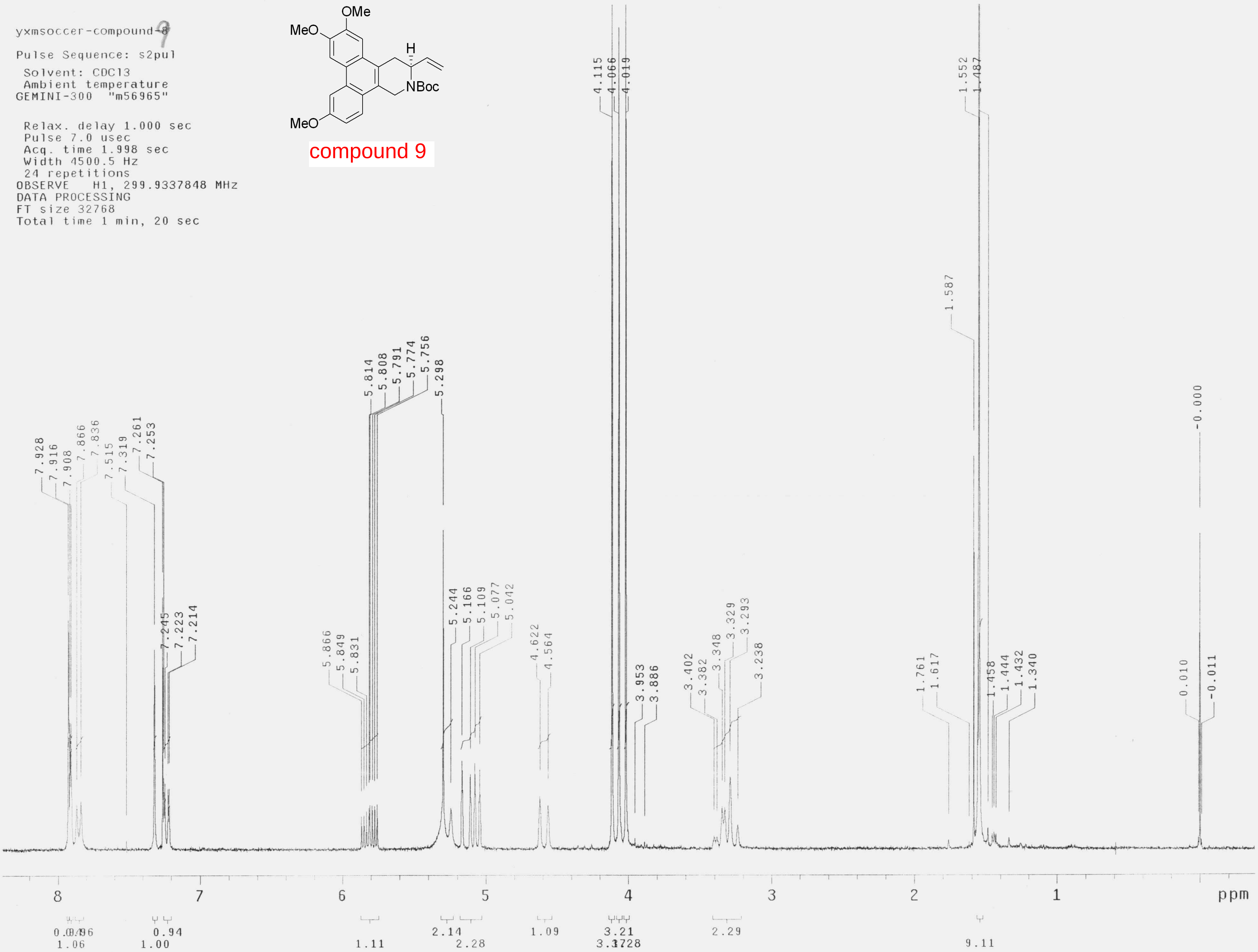


yxmsoccer-compound-7

Pulse Sequence: s2pul

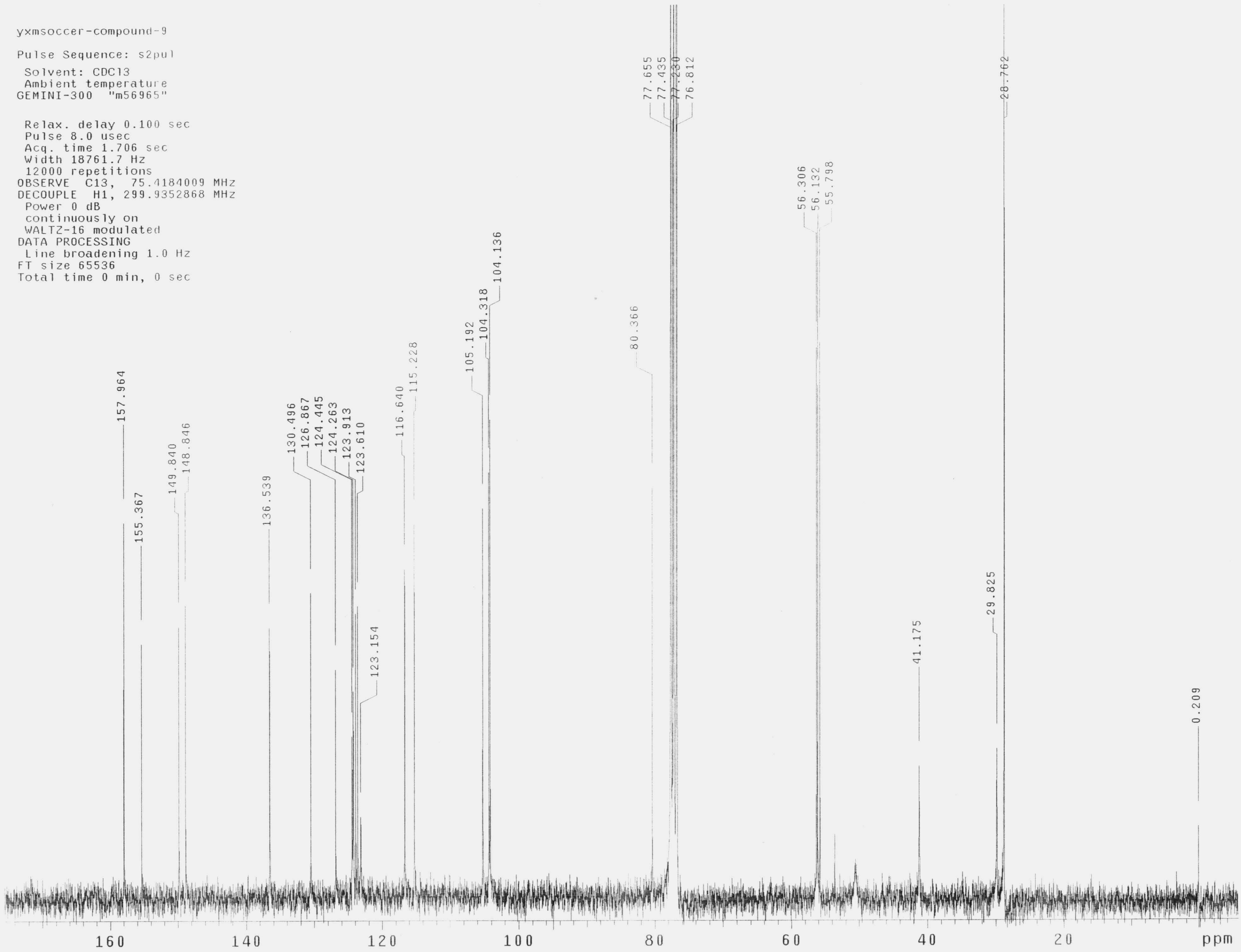
Solvent: DMSO
Ambient temperature
GEMINI-300 "m56965"

Relax. delay 0.100 sec
Pulse 8.0 usec
Acq. time 1.706 sec
Width 18761.7 Hz
5268 repetitions
OBSERVE C13, 75.4187600 MHz
DECOUPLE H1, 299.9367115 MHz
Power 0 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 0 min, 0 sec



```
yxmsoccer-compound-~~8~~9
Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
GEMINI-300  "m56965"

 Relax. delay 1.000 sec
 Pulse 7.0 usec
 Acq. time 1.998 sec
 Width 4500.5 Hz
 24 repetitions
OBSERVE   H1, 299.9337848 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 20 sec
```

compound 9



yxmsoccer-compound-9

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
GEMINI-300 "m56965"

Relax. delay 0.100 sec
Pulse 8.0 usec
Acq. time 1.706 sec
Width 18761.7 Hz
12000 repetitions
OBSERVE C13, 75.4184009 MHz
DECOUPLE H1, 299.9352868 MHz
Power 0 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 0 min, 0 sec