Electronic Supporting Information

A concise total synthesis of sespenine, a structurally unusual indole terpenoid from *Streptomyces*

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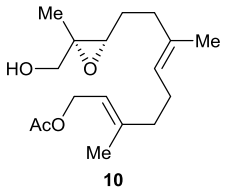
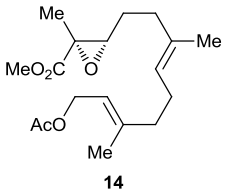
I Experimental Procedures and Spectroscopic Data of Compounds

General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Tetrahydrofuran (THF) was distilled immediately before use from sodium-benzophenone ketyl. Methylene chloride (CH_2Cl_2), *N*,*N*-dimethylformamide (DMF), triethylamine (Et_3N), diisopropylethylamine (*i*-Pr_2NEt), chlorotrimethylsilane (TMSCl), acetonitrile (MeCN), and dimethylsulfoxide (DMSO) were distilled from calcium hydride and stored under an argon atmosphere. Methanol (MeOH) was distilled from magnesium and stored under an argon atmosphere. Acetone was dried over drierite and distilled before use. Titanium tetrachloride ($TiCl_4$) was distilled before use. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Solvents for chromatography were used as supplied by Titan chemical. Reactions were monitored by thin layer chromatography (TLC) carried out on S-2 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and aqueous ammonium cerium nitrate/ammonium molybdate or basic aqueous potassium permanganate as developing agent. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker AV-400 or Agilent 500/54/ASP instrument and calibrated by using residual undeuterated chloroform (δ_H = 7.26 ppm) and $CDCl_3$ (δ_C = 77.16 ppm), undeuterated methanol (δ_H = 3.34 ppm) and methanol-d_4 (δ_C = 49.86 ppm), or undeuterated acetone (δ_H = 2.05 ppm) and acetone-d_6 (δ_C = 29.84 ppm) as internal references. The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, quint = quintet, br = broad. IR spectra were recorded on a Thermo Scientific Nicolet 380 FT-IR spectrometer. Melting points (m.p.) are uncorrected and were recorded on a SGW X-4 apparatus. High-resolution mass spectra (HRMS) were recorded on a Bruker APEXIII 7.0 Tesla ESI-FT, a Waters Micromass GCT Premier EI, or an IonSpec 4.7 Tesla FT mass spectrometer.



10

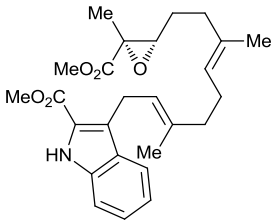
Epoxide 10: This compound was obtained as a colorless oil by using a protocol reported by Li et al.[1] **10**: R_f = 0.31 (silica, EtOAc:petroleum ether 1:3); $[\alpha]_D^{25}$ = −10.1 (*c* = 5.1 in $CHCl_3$); IR (film): ν_{max} = 2925, 2853, 1739, 1448, 1383, 1366, 1233, 1027, 954, 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.33 (t, *J* = 7.1 Hz, 1 H), 5.15 (t, *J* = 6.4 Hz, 1 H), 4.58 (d, *J* = 7.1 Hz, 2 H), 3.67 (dd, *J* = 12.1, 4.4 Hz, 1 H), 3.56 (dd, *J* = 12.1, 8.6 Hz, 1 H), 3.02 (t, *J* = 6.3 Hz, 1 H), 2.19–2.03 (m, 5 H), 2.05 (s, 3 H), 1.70 (s, 3 H), 1.74–1.60 (m, 4 H), 1.62 (s, 3 H), 1.28 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.30, 142.17, 134.50, 124.60, 118.55, 65.55, 61.54, 61.01, 59.97, 39.53, 36.38, 26.88, 26.27, 21.21, 16.60, 16.16, 14.43 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{28}O_4Na^+$ 319.1880, found 319.1880.



14

Ester 14: To a stirred solution of epoxide **10** (1.51 g, 5.09 mmol) in CH_2Cl_2 (15 mL) were sequentially added pH 7 phosphate buffer (15 mL), AZADO (30.8 mg, 0.204 mmol), and $PhI(OAc)_2$ (4.93 g, 15.3 mmol) at 22 ℃. The reaction mixture was stirred at that temperature for 12 h before it was quenched with saturated aq. $NaHSO_3$ (40 mL) and extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (30 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was removed under vacuum, and the residue was dissolved in DMF (10 mL). To this solution were sequentially added anhydrous K_2CO_3 (1.06 g, 7.64 mmol) and MeI (1.44 g, 630 μL, 10.1 mmol) at 22 ℃. The reaction mixture was stirred at that temperature for 30 min before it was quenched with saturated aq. $NaHCO_3$ (30 mL). The resultant mixture was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was subjected to flash column chromatography using EtOAc/petroleum ether (1:8) as eluent to give ester **14** (1.28 g, 77% for the two steps) as a colorless oil. **14**: R_f = 0.57 (silica,

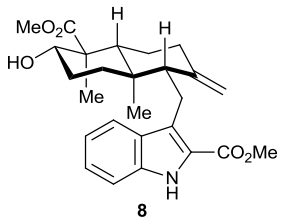
EtOAc:petroleum ether 1:10); $[\alpha]_D^{25} = -4.5$ (*c* = 9.6 in $CHCl_3$); IR (film): ν_{max} = 2953, 2936, 2855, 1738, 1439, 1384, 1366, 1284, 1233, 1164, 1023, 955, 866, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.25 (t, *J* = 7.1 Hz, 1 H), 5.07 (t, *J* = 6.3 Hz, 1 H), 4.49 (d, *J* = 7.1 Hz, 2 H), 3.65 (s, 3 H), 3.07 (t, *J* = 6.1 Hz, 1 H), 2.14–1.93 (m, 6 H), 1.96 (s, 3 H), 1.62 (s, 3 H), 1.65–1.56 (m, 2 H), 1.53 (s, 3 H), 1.43 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.87, 170.92, 141.81, 133.79, 124.70, 118.40, 61.97, 61.21, 57.44, 52.45, 39.22, 35.88, 26.49, 26.03, 20.92, 16.34, 15.89, 13.47 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{18}H_{28}O_5Na^+$ 347.1829, found 347.1827.



9

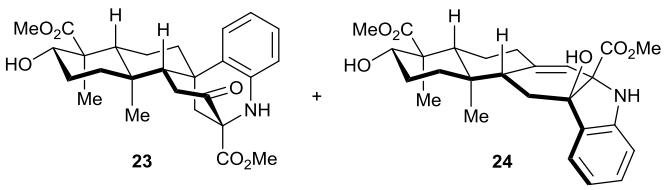
Substituted indole 9: To a stirred solution of ester **14** (1.36 g, 4.19 mmol) in DMF (10 mL) was added stannane[2] **11** (1.70 g, 5.03 mmol), anhydrous LiCl (534 mg, 12.6 mmol), and $Pd_2(dba)_3$ (192 mg, 0.210 mmol) at 22 ℃. The reaction mixture was stirred at that temperature for 1 h before it was quenched with saturated aq. $NaHCO_3$ (40 mL). The resultant mixture was extracted with EtOAc (3 × 50 mL), and the combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, and filtered. After removal of the solvent under vacuum, the residue was purified by flash column chromatography with EtOAc/petroleum ether (1:10) to give substituted indole **9** (1.44 g, 78%) as a pale yellow oil. **9**: R_f = 0.24 (silica, EtOAc:petroleum ether 1:10); $[\alpha]_D^{26} = -5.9$ (*c* = 2.0 in $CHCl_3$); IR (film): ν_{max} = 3551, 2952, 2852, 1735, 1720, 1702, 1552, 1452, 1325, 1253, 1165, 1095, 771, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.66 (s, 1 H), 7.67 (d, *J* = 8.1 Hz, 1 H), 7.38–7.28 (m, 2 H), 7.12 (t, *J* = 7.4 Hz, 1 H), 5.31 (t, *J* = 6.8 Hz, 1 H), 5.09 (t, *J* = 6.5 Hz, 1 H), 3.95 (s, 3 H), 3.86 (d, *J* = 6.9 Hz, 2 H), 3.73 (s, 3 H), 3.10 (t, *J* = 6.1 Hz, 1 H), 2.11–1.96 (m, 6 H), 1.84 (s, 3 H), 1.55 (s, 3 H), 1.61–1.51 (m, 2 H), 1.47 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.20, 162.99, 136.16, 134.77, 133.51, 127.95, 125.68, 125.25, 124.21, 123.26, 122.69, 121.38, 120.06, 111.87, 62.26, 57.66, 52.67, 51.83,

39.55, 35.94, 26.64, 26.49, 23.97, 16.39, 16.08, 13.63 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{26}H_{34}NO_5^+$ 440.2431, found 440.2429.



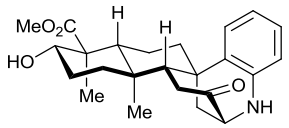
8

***trans*-Decalin 8:** A mixture of Cp_2TiCl_2 (55.7 mg, 0.224 mmol) and Mn dust (493 mg, 8.95 mmol) in THF (18 mL) was stirred at 22 ℃ for 15 min. To the resultant mixture were sequentially added substituted indole **9** (492 mg, 1.12 mmol), *i*-Pr_2NEt (0.890 g, 1.20 mL, 6.89 mmol), and TMSCl (0.599 g, 0.700 mL, 5.52 mmol). The reaction mixture was stirred at that temperature for 12 h before it was poured into aq. HCl (15 mL, 1.0 M). The mixture so obtained was stirred at 22 ℃ for 30 min and then extracted with EtOAc (3 × 50 mL). The combined organic phases were sequentially washed with saturated aq. $NaHCO_3$ (50 mL) and brine (50 mL), dried over anhydrous Na_2SO_4, filtrated, and concentrated under vacuum. The residue was purified by flash column chromatography with acetone/petroleum ether (1:5) to give *trans*-decalin **8** (166 mg, 34%) as a pale yellow oil. **8**: R_f = 0.22 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{26}$ = −40.5 (*c* = 1.7 in $CHCl_3$); IR (film): ν_{max} = 3373, 2948, 1712, 1445, 1249, 1220, 1093, 896, 771, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1 H), 7.73 (d, *J* = 8.2 Hz, 1 H), 7.38–7.27 (m, 2 H), 7.13 (t, *J* = 7.4 Hz, 1 H), 4.89 (s, 1 H), 4.74 (s, 1 H), 4.05 (d, *J* = 10.2 Hz, 1 H), 3.96 (s, 3 H), 3.72 (s, 3 H), 3.44 (dd, *J* = 14.7, 9.2 Hz, 1 H), 3.25 (dd, *J* = 14.7, 4.3 Hz, 1 H), 2.67 (dd, *J* = 9.1, 3.9 Hz, 1 H), 2.25 (d, *J* = 12.8 Hz, 1 H), 2.01–1.88 (m, 3 H), 1.79–1.43 (m, 7 H), 1.26–1.14 (m, 2 H), 1.16 (s, 3 H), 0.91 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.16, 162.61, 148.08, 136.15, 127.95, 125.63, 125.33, 123.16, 121.81, 120.05, 112.08, 108.28, 75.62, 56.21, 54.07, 52.32, 51.81, 50.81, 39.66, 37.81, 36.65, 27.35, 26.57, 21.11, 14.71, 10.8 ppm; HRMS (*m/z*): $[M + NH_4]^+$ calcd for $C_{26}H_{37}N_2O_5^+$ 457.2697, found 457.2697.



Pentacyclic compounds 23 and 24: To a stirred solution of *trans*-decalin **8** (76.4 mg, 0.174 mmol) in acetone (1.5 mL) was added saturated aq. $NaHCO_3$ (1.0 mL) at 22 ℃. To the resultant mixture was added aq. Oxone (214 mg, 0.348 mmol, 0.50 mL) over a period of 10 min at that temperature. The mixture so obtained was stirred at that temperature for 5 min before it was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and filtrated. After evaporation of the solvent under vacuum, the residue was dissolved in CH_2Cl_2 (0.50 mL). To this solution was added AcOH (60.1 mg, 50.0 μL, 0.873 mmol) at 22 ℃. The resultant mixture was stirred at that temperature for 5 h before it was quenched with saturated aq. $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was subjected to flash column chromatography using EtOAc/petroleum ether (1:2) as eluent to give *β*-ketoester **23** (44.2 mg, 56% for the two steps) as a pale yellow foam and *β*-hydroxyester **24** (15.1 mg, 19% for the two steps) as a pale yellow oil. **23**: R_f = 0.21 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{26}$ = −144.3 (*c* = 0.78 in $CHCl_3$); IR (film): ν_{max} = 3376, 2997, 2950, 2875, 1708, 1604, 1478, 1445, 1250, 1219, 1146, 1073, 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 7.6 Hz, 1 H), 7.10–7.05 (m, 1 H), 6.78–6.73 (m, 1 H), 6.62 (dd, *J* = 8.0, 1.1 Hz, 1 H), 5.05 (s, 1 H), 4.00 (dd, *J* = 11.7, 4.8 Hz, 1 H), 3.87 (s, 3 H), 3.77 (s, 3 H), 3.15 (dd, *J* = 13.7, 1.5 Hz, 1 H), 2.44–2.35 (m, 2 H), 2.24 (dd, *J* = 16.8, 7.8 Hz, 1 H), 1.85–1.66 (m, 6 H), 1.66–1.59 (m, 2 H), 1.19 (s, 3 H), 1.29–1.22 (m, 1 H), 1.03 (s, 3 H), 1.07–0.99 (m, 1 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 204.36, 177.96, 170.58, 141.48, 128.13, 128.11, 125.31, 118.32, 114.70, 75.35, 66.16, 61.07, 53.84, 53.08, 52.52, 50.61, 38.48, 38.28, 37.64, 36.75, 36.63, 35.20, 26.26, 21.27, 17.48, 10.96 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{26}H_{34}NO_6^+$ 456.2381, found 456.2382. **24**: R_f = 0.15 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{26}$ = +55.5 (*c* = 0.53 in $CHCl_3$); IR (film): ν_{max} = 3377, 2950, 1720, 1686, 1608, 1388, 1247, 1219, 988, 771, 665 cm^{-1}; ^1H NMR (400 MHz,

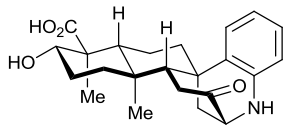
$CDCl_3$): δ = 7.23 (d, *J* = 7.4 Hz, 1 H), 7.13 (td, *J* = 7.7, 1.2 Hz, 1 H), 6.84 (td, *J* = 7.4, 0.8 Hz, 1 H), 6.69 (d, *J* = 7.8 Hz, 1 H), 5.46 (d, *J* = 2.1 Hz, 1 H), 4.07 (dd, *J* = 11.6, 3.8 Hz, 1 H), 3.91 (s, 1 H), 3.72 (s, 3 H), 3.71 (s, 3 H), 3.16–3.04 (m, 1 H), 2.62 (d, *J* = 16.0 Hz, 1 H), 2.48 (d, *J* = 16.0 Hz, 1 H), 2.39 (d, *J* = 13.8 Hz, 1 H), 2.13–1.98 (m, 2 H), 1.89 (ddd, *J* = 13.2, 13.1, 3.3 Hz, 1 H), 1.78–1.52 (m, 4 H), 1.45–1.38 (m, 2 H), 1.22 (s, 3 H), 0.75 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 177.81, 175.32, 147.39, 134.45, 132.71, 129.50, 122.90, 120.77, 120.40, 111.24, 81.06, 75.58, 72.77, 53.13, 52.90, 52.34, 46.16, 45.98, 39.32, 36.88, 34.73, 34.43, 26.79, 25.29, 14.74, 10.9 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{26}H_{33}NO_6Na^+$ 478.2200, found 478.2199.



25

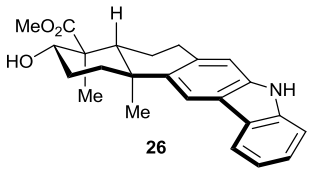
Sespenine methyl ester (25): To a stirred solution of *β*-ketoester **23** (59.3 mg, 0.130 mmol) in DMSO (3.0 mL) were sequentially added water (50 *μ*L) and NaCl (76.1 mg, 1.30 mmol) at 22 ℃. The resultant mixture was heated at 170 ℃ under microwave irradiation for 4 × 30 min before it was cooled to 22 ℃. The mixture so obtained was diluted with saturated aq. $NaHCO_3$ (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and filtered. After evaporation of the solvent under vacuum, the residue was purified by flash column chromatography with diethyl ether/CH_2Cl_2 (1:10) to give sespenine methyl ester (**25**, 42.0 mg, 81%) as a pale yellow powder. **25**: R_f = 0.20 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{29}$ = −192.4 (*c* = 0.38 in MeOH); IR (film): ν_{max} = 3373, 2990, 2931, 2871, 1701, 1489, 1246, 1021, 758 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 7.9 Hz, 1 H), 7.04 (t, *J* = 7.6 Hz, 1 H), 6.74 (t, *J* = 7.5 Hz, 1 H), 6.53 (d, *J* = 8.0 Hz, 1 H), 4.43 (s, 1 H), 4.00 (dd, *J* = 11.6, 4.6 Hz, 1 H), 3.79–3.75 (m, 1 H), 3.77 (s, 3 H), 2.69 (d, *J* = 12.1 Hz, 1 H), 2.43–2.30 (m, 2 H), 2.22 (dd, *J* = 16.4, 7.7 Hz, 1 H), 1.86–1.56 (m, 8 H), 1.26–1.19 (m, 1 H), 1.17 (s, 3 H), 1.02 (ddd, *J* = 13.1, 3.3, 3.2 Hz, 1 H), 0.95 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 209.87, 178.02, 142.46, 129.52, 127.85, 125.52, 118.10, 114.59, 75.37, 61.39, 57.60,

53.86, 52.49, 50.67, 38.56, 38.33, 36.79, 36.74, 32.76, 26.29, 21.25, 17.41, 10.96 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{32}NO_4^+$ 398.2326, found 398.2327.



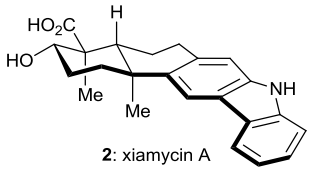
1: sespenine

Sespenine (1): To a stirred solution of sespenine methyl ester (**25**, 14.7 mg, 0.0370 mmol) in MeOH/THF (1.0 mL, 1:1) was added aq. LiOH (0.50 mL, 2.0 M) at 22 ℃. The reaction mixture was warmed to 50 ℃ and allowed to stir at that temperature for 10 h before it was cooled to 22 ℃ and quenched with aq. HCl (1.5 mL, 1.0 M). The resultant mixture was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was subjected to flash column chromatography using AcOH/EtOAc (3:1000) as eluent to give sespenine (**1**, 13.0 mg, 92%) as a white foam. **1**: R_f = 0.39 (silica, AcOH/EtOAc 1:1000); $[\alpha]_D^{26}$ = −251.6 (*c* = 0.21 in MeOH); IR (film): ν_{max} = 3367, 2929, 1701, 1601, 1488, 1453, 1413, 1389, 1310, 1263, 1143, 1084, 1025, 1001, 974, 906, 876, 802, 745, 683, 638 cm^{-1}; ^1H NMR (500 MHz, methanol-d_4): δ = 7.34 (d, *J* = 8.0 Hz, 1 H), 6.98 (t, *J* = 7.6 Hz, 1 H), 6.65 (t, *J* = 7.6 Hz, 1 H), 6.56 (d, *J* = 8.0 Hz, 1 H), 4.05–3.96 (m, 1 H), 3.69 (s, 1 H), 2.75 (dd, *J* = 13.8, 2.7 Hz, 1 H), 2.47–2.38 (m, 1 H), 2.32 (d, *J* = 16.2 Hz, 1 H), 2.19 (dd, *J* = 16.4, 7.9 Hz, 1 H), 1.86–1.73 (m, 4 H), 1.71–1.63 (m, 3 H), 1.59 (d, *J* = 13.3 Hz, 1 H), 1.34–1.27 (m, 1 H), 1.13 (s, 3 H), 1.10–1.02 (m, 1 H), 0.98 (s, 3 H) ppm; ^{13}C NMR (126 MHz, methanol-d_4): δ = 212.02, 181.25, 144.46, 130.54, 128.51, 126.12, 118.29, 115.44, 76.18, 63.34, 58.77, 54.73, 51.99, 39.88, 39.58, 37.96, 37.91, 37.38, 33.88, 27.30, 22.09, 17.65, 11.54 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{30}NO_4^+$ 384.2169, found 384.2168.



26

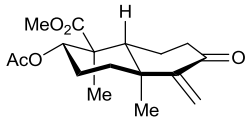
Xiamycin A methyl ester (26): To a stirred solution of *β*-hydroxyester **24** (16.2 mg, 0.0356 mmol) in DMSO (1.0 mL) were sequentially added water (50 μL) and LiCl (30.1 mg, 0.711 mmol) at 22 ℃. The mixture so obtained was heated at 160 ℃ under microwave irradiation for 3 × 20 min before it was cooled to 22 ℃ and diluted with saturated aq. $NaHCO_3$ (5 mL). The resultant mixture was extracted with EtOAc (3 × 10 mL), and the combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was purified by flash column chromatography with EtOAc/petroleum ether (1:3) to give xiamycin A methyl ester (**26**, 7.3 mg, 54%) as a pale yellow foam. **26**: R_f = 0.61 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{26}$ = +52.5 (*c* = 0.35 in MeOH); IR (film): ν_{max} = 3407, 3002, 2936, 2873, 1718, 1664, 1466, 1380, 1259, 1032, 878, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 7.8 Hz, 1 H), 7.94 (s, 1 H), 7.84 (s, 1 H), 7.37 (d, *J* = 3.6 Hz, 2 H), 7.22–7.16 (m, 1 H), 7.08 (s, 1 H), 4.13–4.05 (m, 1 H), 3.74 (s, 3 H), 3.16–3.06 (m, 2 H), 2.62–2.55 (m, 1 H), 2.23 (dd, *J* = 12.5, 2.4 Hz, 1 H), 2.08–1.77 (m, 4 H), 1.53–1.46 (m, 1 H), 1.31 (s, 3 H), 1.31 (s, 3 H). ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.00, 141.22, 140.14, 138.31, 133.54, 125.58, 123.71, 122.13, 120.05, 119.32, 115.79, 110.59, 109.96, 75.44, 53.94, 52.42, 45.99, 37.52, 37.40, 30.91, 27.58, 25.99, 21.65, 10.87 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{28}NO_3^+$ 378.2064, found 378.2064.



2: xiamycin A

Xiamycin A (2): To a stirred solution of xiamycin A methyl ester (**26**, 4.6 mg, 0.012 mmol) in THF/MeOH (0.60 mL, 1:1) was added aq. LiOH (0.30 mL, 2.0 M) at 22 ℃. The reaction mixture was warmed to 50 ℃ and allowed to stir at that temperature for 10 h before it was cooled to 22 ℃ and quenched with aq. HCl (1.0 mL, 1.0 M). The resultant mixture was extracted with EtOAc (3 × 10 mL).

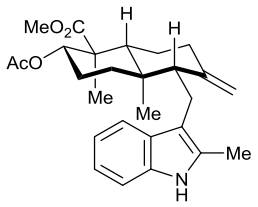
The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was subjected to flash column chromatography using AcOH/EtOAc (3:1000) as eluent to give xiamycin A (**2**, 3.9 mg, 88%) as a white foam. **2**: R_f = 0.62 (silica, AcOH/EtOAc 1:1000); $[\alpha]_D^{26}$ = +132.5 (*c* = 0.16 in MeOH); IR (film): ν_{max} = 3697, 2981, 2966, 2922, 1701, 1686, 1454, 1056, 1033 cm^{-1}; ^1H NMR (400 MHz, methanol-d_4): δ = 8.00–7.92 (m, 2 H), 7.37–7.26 (m, 2 H), 7.11–7.05 (m, 2 H), 4.10 (dd, *J* = 9.0, 7.3 Hz, 1 H), 3.16–2.97 (m, 2 H), 2.62 (d, *J* = 12.9 Hz, 1 H), 2.16 (dd, *J* = 12.3, 1.4 Hz, 1 H), 2.09–1.95 (m, 1 H), 1.94–1.86 (m, 2 H), 1.80–1.73 (m, 1 H), 1.55 (dd, *J* = 12.9, 7.3 Hz, 1 H), 1.31 (s, 3 H), 1.25 (s, 3 H) ppm; ^{13}C NMR (101 MHz, methanol-d_4): δ = 181.25, 142.04, 141.81, 140.17, 134.04, 126.05, 124.67, 123.14, 120.55, 119.35, 116.34, 111.45, 110.81, 76.30, 54.89, 47.93, 39.03, 38.33, 32.03, 28.66, 26.30, 22.61, 11.37 ppm; HRMS (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{26}NO_3^+$ 364.1907, found 364.1908.



31

***trans*-Decalin enone 31:** A mixture of $CpTiCl_2$ (141 mg, 0.565 mmol) and Mn dust (1.24 g, 22.6 mmol) in THF (70 mL) was stirred at 22 ℃ for 15 min. To the resultant mixture were sequentially added ester **14** (916 mg, 2.82 mmol), *i*-Pr_2NEt (2.15 g, 2.90 mL, 16.7 mmol), and TMSCl (1.54 g, 1.80 mL, 14.2 mmol). The mixture so obtained was allowed to stir at that temperature for 8 h before it was poured into aq. HCl (25 mL, 1.0 M) and stirred for 30 min. The resultant mixture was extracted with EtOAc (3 × 50 mL), and the combined organic phases were sequentially washed with saturated aq. $NaHCO_3$ (50 mL) and brine (50 mL) and dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue (crude ketone) was dissolved in CH_2Cl_2 (20 mL). To the stirred solution was bubbled through O_3 at −78 ℃ for 5 min. The reaction mixture was immediately quenched with Et_3N (2.0 mL) when it turned pale blue. The resultant mixture was warmed to 22 ℃, and the volatile was removed under vacuum. The residue was dissolved in toluene (10 mL). To this solution was added DBU (2.14 g, 2.10 mL, 14.0 mmol) at 22 ℃. The resultant mixture was warmed to 80 ℃ and allowed to stir

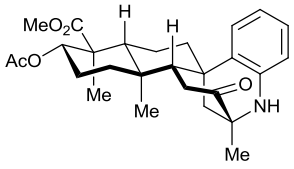
at that temperature for 4 h before it was cooled to 22 ℃. The solvent was evaporated under vacuum, and the residue was passed through a short plug of silica using EtOAc/petroleum ether (1:5) as eluent to give the hydroxy enone as a pale yellow oil. This oil was dissolved in CH_2Cl_2 (10 mL). To the solution were sequentially added Et_3N (573 mg, 790 μL, 5.66 mmol), Ac_2O (433 mg, 400 μL, 4.24 mmol), and 4-DMAP (34.5 mg, 0.282 mmol) at 22 ℃. The reaction mixture was allowed to stir at that temperature for 1 h before it was quenched with saturated aq. $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum, and the residue was purified by flash column chromatography with EtOAc/petroleum ether (1:5) to give *trans*-decalin enone **31** (286 mg, 33% for the four steps) as a pale yellow oil. The physical properties and spectroscopic data were identical with those reported before.[3]



27a

***trans*-Decalin 27a:** To a stirred solution of 2-methylindole (27.6 mg, 0.210 mmol) and *trans*-decalin enone **31** (32.4 mg, 0.105 mmol) in MeCN (1.0 mL) was added $Bi(OTf)_3$ (6.9 mg, 0.011 mmol) at 0 ℃. The reaction mixture was allowed to stir at that temperature for 1 h. The volatile was removed under vacuum, and the residue was directly subjected to flash column chromatography using diethyl ether/CH_2Cl_2 (1:20) as eluent to give the indole adduct as a pale yellow oil. This oil was dissolved in THF (0.50 mL) and used for the next step. To a stirred suspension of Nysted reagent (1.00 mL, 20 wt% in THF, ca. 0.520 mmol) was added $TiCl_4$ (77.7 mg, 45.0 μL, 0.410 mmol) at 0 ℃. The resultant mixture was stirred at that temperature for 10 min before the prepared solution of the indole adduct in THF was added. The reaction mixture was warmed to 22 ℃ and allowed to stir at that temperature for 1 h before it was quenched by aq. HCl (5 mL, 1.0 M). The mixture so obtained was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent

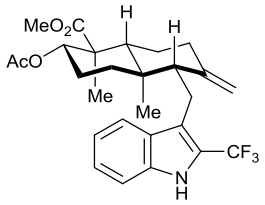
was evaporated under vacuum, and the residue was subjected to flash column chromatography using diethyl ether/CH_2Cl_2 (1:20) as eluent to give *trans*-decalin **27a** (23.8 mg, 52% for the two steps) as a pale yellow foam. **27a**: R_f = 0.57 (silica, diethyl ether:CH_2Cl_2 1:10); $[\alpha]_D^{28}$ = −49.0 (*c* = 0.54 in $CHCl_3$); IR (film): ν_{max} = 3396, 3056, 2938, 1738, 1461, 1388, 1367, 1251, 1161, 1083, 1028, 1005, 987, 889, 739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.67 (s, 1 H), 7.56–7.53 (m, 1 H), 7.25–7.22 (m, 1 H), 7.11–7.07 (m, 2 H), 5.23 (dd, *J* = 11.6, 4.4 Hz, 1 H), 4.80 (s, 1 H), 4.77 (s, 1 H), 3.66 (s, 3 H), 2.88 (dd, *J* = 14.9, 3.6 Hz, 1 H), 2.78 (dd, *J* = 14.9, 9.4 Hz, 1 H), 2.53–2.49 (m, 1 H), 2.39 (s, 3 H), 2.27 (ddd, *J* = 12.8, 4.2, 2.3 Hz, 1 H), 2.05–2.01 (m, 2 H), 2.00 (s, 3 H), 1.99–1.93 (m, 1 H), 1.91–1.86 (m, 1 H), 1.74–1.50 (m, 3 H), 1.22 (s, 3 H), 1.19–1.14 (m, 1 H), 0.90 (s, 3 H) ppm; ^{13}C NMR (101 MHz, acetone-d_6): δ = 176.76, 170.03, 148.80, 136.82, 131.80, 129.79, 120.84, 119.12, 119.08, 111.14, 111.01, 108.52, 77.87, 56.43, 52.92, 52.40, 51.61, 40.05, 38.43, 37.37, 27.04, 24.57, 20.91, 20.65, 14.88, 12.54, 12.29 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{27}H_{35}NO_4Na^+$ 460.2458, found 460.2457.



27

Sespenine analogue 27: To a stirred solution of *trans*-decalin **27a** (19.3 mg, 0.0441 mmol) in acetone (1.2 mL) was added saturated aq. $NaHCO_3$ (0.80 mL) at 22 ℃. To the resultant mixture was added aq. Oxone (54.2 mg, 0.0882 mmol, 0.40 mL) over a period of 10 min at that temperature. The mixture so obtained was stirred at that temperature for 5 min before it was diluted with water (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and filtrated. After evaporation of the solvent under vacuum, the residue was dissolved in CH_2Cl_2 (0.50 mL). To this solution was added AcOH (13.6 mg, 13.0 μL, 0.227 mmol) at 22 ℃. The resultant mixture was stirred at that temperature for 5 h before it was quenched with saturated aq. $NaHCO_3$ (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography with EtOAc/petroleum ether (1:3) to give sespenine analogue **27** (8.4 mg,

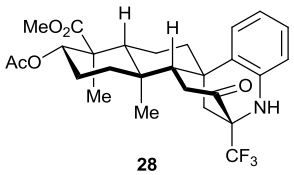
42% for the two steps) as a pale yellow foam. **27**: R_f = 0.59 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{28}$ = −198.5 (*c* = 0.56 in $CHCl_3$); IR (film): ν_{max} = 2920, 1738, 1730, 1706, 1603, 1516, 1507, 1488, 1373, 1248, 1073, 802, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36 (dd, *J* = 8.0, 0.9 Hz, 1 H), 7.07–7.02 (m, 1 H), 6.77–6.71 (m, 1 H), 6.49 (dd, *J* = 8.0, 1.2 Hz, 1 H), 5.17 (dd, *J* = 12.0, 4.7 Hz, 1 H), 3.98 (s, 1 H), 3.73 (s, 3 H), 2.52 (dd, *J* = 13.7, 1.2 Hz, 1 H), 2.41–2.33 (m, 2 H), 2.29–2.23 (m, 1 H), 1.99 (s, 3 H), 1.90–1.60 (m, 8 H), 1.32 (s, 3 H), 1.22 (s, 3 H), 1.23–1.17 (m, 1 H), 1.11 (ddd, *J* = 13.4, 13.3, 3.5 Hz, 1 H), 0.96 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 209.53, 176.62, 170.14, 143.02, 128.72, 127.92, 125.35, 118.09, 114.31, 76.91, 61.37, 57.04, 52.62, 52.19, 50.62, 40.28, 38.54, 38.16, 38.08, 37.11, 36.53, 22.97, 22.66, 21.19, 21.09, 17.47, 12.01 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{27}H_{35}NO_5Na^+$ 476.2407, found 476.2407.



28a

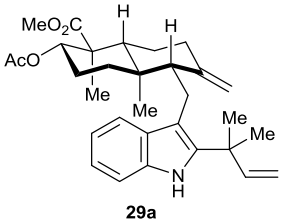
***trans*-Decalin 28a:** This compound was synthesized from *trans*-decalin enone **31** (27.6 mg, 0.0895 mmol) and 2-(trifluoromethyl)indole (31.1 mg, 0.179 mmol) by using the protocol for the preparation of *trans*-decalin **27a**. *trans*-Decalin **28a** (21.9 mg, 48%) was obtained as a pale yellow oil. **28a**: R_f = 0.57 (silica, diethyl ether/CH_2Cl_2 1:10); $[\alpha]_D^{26}$ = −26.4 (*c* = 0.60 in $CHCl_3$); IR (film): ν_{max} = 3337, 2945, 1730, 1648, 1586, 1565, 1452, 1386, 1321, 1266, 1186, 1113, 1084, 1030, 1005, 989, 893, 742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.24 (s, 1 H), 7.72 (d, *J* = 8.1 Hz, 1 H), 7.38 (d, *J* = 8.2 Hz, 1 H), 7.31 (t, *J* = 7.6 Hz, 1 H), 7.19 (t, *J* = 7.3 Hz, 1 H), 5.20 (dd, *J* = 12.0, 4.5 Hz, 1 H), 4.77 (s, 1 H), 4.74 (s, 1 H), 3.67 (s, 3 H), 3.07 (d, *J* = 6.9 Hz, 2 H), 2.62 (dd, *J* = 6.9, 6.8 Hz, 1 H), 2.29 (ddd, *J* = 12.7, 4.2, 2.2 Hz, 1 H), 2.06–1.96 (m, 2 H), 1.99 (s, 3 H), 1.92 (ddd, *J* = 13.2, 3.5, 3.4 Hz, 1 H), 1.87–1.81 (m, 1 H), 1.71–1.61 (m, 1 H), 1.61–1.46 (m, 2 H), 1.21 (s, 3 H), 1.22–1.16 (m, 1 H), 0.90 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 176.68, 170.27, 147.44, 135.49, 127.59, 125.81, 124.79, 123.41, 121.40, 121.27, 121.15, 121.11, 120.61, 119.13, 118.31, 112.00, 108.55, 77.32, 55.49, 52.46, 52.34, 50.84, 39.47, 37.64, 36.33,

26.32, 23.91, 21.25, 20.26, 14.58, 11.98 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{27}H_{32}F_3NO_4Na^+$ 514.2176, found 514.2176.



28

Sespenine analogue 28: This compound was synthesized from *trans*-decalin **28a** (12.3 mg, 0.0250 mmol) by using the protocol for the preparation of sespenine analogue **27**. Sespenine analogue **28** (4.1 mg, 32%) was obtained as a pale yellow oil. **28**: R_f = 0.58 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{26}$ = −271.2 (*c* = 0.14 in $CHCl_3$); IR (film): ν_{max} = 2957, 2923, 2852, 1738, 1730, 1715, 1730, 1594, 1488, 1375, 1260, 1094, 1024, 801 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 8.0 Hz, 1 H), 7.12 (t, *J* = 7.6 Hz, 1 H), 6.87 (t, *J* = 7.6 Hz, 1 H), 6.65 (d, *J* = 8.0 Hz, 1 H), 5.17 (dd, *J* = 12.0, 4.3 Hz, 1 H), 4.43 (s, 1 H), 3.73 (s, 3 H), 2.81 (d, *J* = 13.6 Hz, 1 H), 2.50–2.38 (m, 2 H), 2.25 (dd, *J* = 16.9, 7.6 Hz, 1 H), 1.99 (s, 3 H), 1.94–1.58 (m, 8 H), 1.33–1.19 (m, 1 H), 1.23 (s, 3 H), 1.16–1.09 (m, 1 H), 1.02 (s, 3 H); ^{13}C NMR (151 MHz, acetone-d_6): δ = 201.61, 176.71, 170.02, 142.95, 130.42, 128.66, 128.46, 126.58, 126.03, 124.71, 122.84, 120.04, 116.81, 77.42, 61.11, 52.73, 52.56, 51.11, 39.20, 38.56, 37.94, 37.88, 36.99, 33.27, 23.51, 21.32, 20.87, 17.35, 12.33 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{27}H_{32}F_3NO_5Na^+$ 530.2125, found 530.2133.

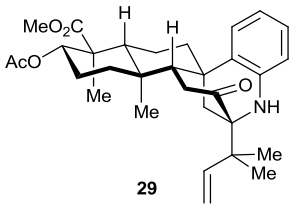


29a

***trans*-Decalin 29a:** To a stirred solution of indole (47.1 mg, 0.402 mmol) and *trans*-decalin enone **31** (41.3 mg, 0.134 mmol) in EtOH (1.0 mL) was added I_2 (68.0 mg, 0.268 mmol) at 22 ℃. The reaction mixture was stirred at that temperature for 1 h before it was quenched with saturated aq. $Na_2S_2O_3$ (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The residue was passed through

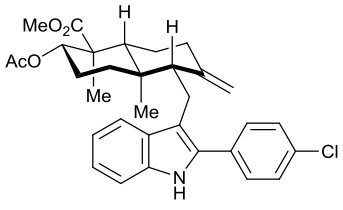
a short plug of silica with EtOAc/petroleum ether (1:4) to give the indole adduct as a pale yellow foam. The foam was dissolved in THF (1.0 mL). To this solution was added Et_3N (18.1 mg, 25.0 μL, 0.179 mmol) and *t*-BuOCl (19.2 mg, 20.0 μL, 0.177 mmol) at −78 ℃. The resultant mixture was stirred at that temperature for 30 min before prenyl-9-BBN[4] (270 μL, ca. 1.0 M in THF, 0.270 mmol) at −78 ℃. The reaction mixture was warmed to 22 ℃ and allowed to stir at that temperature for 3 h before it was quenched by saturated aq. $NaHCO_3$ (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to a short plug of silica using EtOAc/petroleum ether (1:5) as eluent to give the C2 reverse-prenylated indole derivative as a pale yellow foam. The foam was dissolved in THF (0.50 mL) and used for the next step. To a stirred suspension of Nysted reagent (1.30 mL, 20 wt% suspension in THF, ca. 0.676 mmol) was added $TiCl_4$ (104 mg, 60.0 μL, 0.548 mmol) at 0 ℃. The resultant mixture was stirred at that temperature for 10 min before the prepared solution of the C2 reverse-prenylated indole derivative in THF was added. The reaction mixture was warmed to 22 ℃ and allowed to stir at that temperature for 1 h before it was quenched by aq. HCl (5 mL, 1.0 M). The mixture so obtained was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash column chromatography using diethyl ether/CH_2Cl_2 (1:20) as eluent to give *trans*-decalin **29a** (37.0 mg, 56% for the three steps) as a pale yellow foam. **29a**: R_f = 0.55 (silica, diethyl ether:CH_2Cl_2 1:10); $[\alpha]_D^{27}$ = −11.4 (*c* = 0.22 in $CHCl_3$); IR (film): ν_{max} = 3415, 2936, 1732, 1646, 1488, 1459, 1389, 1251, 1161, 1127, 1082, 1030, 943, 917, 892, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.87 (s, 1 H), 7.53 (d, *J* = 7.9 Hz, 1 H), 7.26 (d, *J* = 7.7 Hz, 1 H), 7.09 (t, *J* = 7.3 Hz, 1 H), 7.04 (t, *J* = 7.2 Hz, 1 H), 6.14 (dd, *J* = 17.4, 10.7 Hz, 1 H), 5.20–5.12 (m, 3 H), 4.75 (s, 1 H), 4.68 (s, 1 H), 3.67 (s, 3 H), 3.05–2.94 (m, 2 H), 2.74 (dd, *J* = 6.9, 6.8 Hz, 1 H), 2.31 (ddd, *J* = 12.7, 4.2, 2.1 Hz, 1 H), 2.09 (ddd, *J* = 12.8, 12.8, 5.1 Hz, 1 H), 2.01 (dd, *J* = 12.6, 2.8 Hz, 1 H), 1.97 (s, 3 H), 1.86 (ddd, *J* = 13.0, 3.3, 3.2 Hz, 1 H), 1.78–1.72 (m, 1 H), 1.65–1.55 (m, 2 H), 1.55 (s, 3 H), 1.54 (s, 3 H), 1.36 (ddd, *J* = 13.5, 13.4, 3.5 Hz, 1 H), 1.21 (s, 3 H), 1.23–1.16 (m, 1 H), 0.89 (s, 3 H) ppm; ^{13}C NMR (126 MHz, acetone-

d_6): δ = 176.75, 169.97, 149.27, 147.33, 139.49, 136.13, 130.30, 121.07, 120.09, 119.09, 111.60, 111.57, 110.97, 109.32, 77.89, 55.72, 52.84, 52.41, 51.77, 40.23, 40.03, 38.17, 37.02, 28.23, 28.08, 26.88, 24.34, 22.69, 20.89, 14.96, 12.30 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{31}H_{41}NO_5Na^+$ 530.2877, found 530.2884.



29

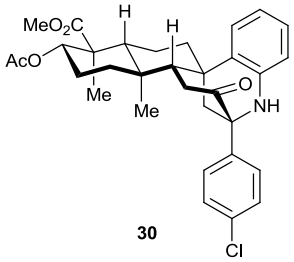
Sespenine analogue 29: This compound was synthesized from *trans*-decalin **29a** (21.1 mg, 0.0429 mmol) by using the protocol for the preparation of sespenine analogue **27**. Sespenine analogue **29** (8.3 mg, 38%) was obtained as a pale yellow oil. **29**: R_f = 0.60 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{27}$ = −55.1 (*c* = 0.18 in $CHCl_3$); IR (film): ν_{max} = 3404, 2952, 2876, 1738, 1730, 1698, 1603, 1580, 1479, 1375, 1365, 1245, 1191, 1048, 1025, 1001, 919, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 7.9 Hz, 1 H), 7.04 (t, *J* = 7.6 Hz, 1 H), 6.71 (t, *J* = 7.5 Hz, 1 H), 6.55–6.45 (m, 2 H), 5.20–5.06 (m, 3 H), 4.31 (s, 1 H), 3.73 (s, 3 H), 2.57 (d, *J* = 13.7 Hz, 1 H), 2.37 (ddd, *J* = 13.2, 13.2, 4.1 Hz, 1 H), 2.30 (d, *J* = 16.6 Hz, 1 H), 2.23 (dd, *J* = 16.8, 7.3 Hz, 1 H), 1.99 (s, 3 H), 1.89–1.58 (m, 8 H), 1.25 (s, 3 H), 1.23 (s, 3 H), 1.23–1.17 (m, 1 H), 1.15 (s, 3 H), 1.09 (ddd, *J* = 13.6, 13.5, 3.3 Hz, 1 H), 0.98 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 206.94, 176.75, 169.98, 146.20, 144.85, 130.16, 128.18, 125.67, 118.14, 115.77, 113.65, 77.52, 63.44, 61.52, 52.74, 52.51, 51.17, 42.73, 39.24, 39.08, 38.68, 38.39, 37.31, 35.03, 30.59, 23.55, 23.33, 21.53, 20.88, 17.89, 12.36 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{31}H_{41}NO_4Na^+$ 514.2928, found 514.2925.



30a

***trans*-Decalin 30a:** This compound was synthesized from *trans*-decalin enone **31** (36.6 mg, 0.119 mmol) and 2-(4-chlorophenyl)indole (54.2 mg, 0.238 mmol) by using the protocol for the preparation of *trans*-

decalin **27a**. *trans*-Decalin **30a** (38.9 mg, 61%) was obtained as a pale yellow foam. **30a**: R_f = 0.62 (silica, diethyl ether:CH_2Cl_2 1:10); $[\alpha]_D^{24}$ = −26.8 (*c* = 0.37 in $CHCl_3$); IR (film): ν_{max} = 3352, 2994, 2953, 2876, 1738, 1730, 1704, 1698, 1603, 1481, 1368, 1072, 1249, 1147, 1092, 1073, 1042, 975, 825, 742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.90 (s, 1 H), 7.67 (d, *J* = 7.7 Hz, 1 H), 7.48–7.43 (m, 4 H), 7.36–7.33 (m, 1 H), 7.23–7.15 (m, 2 H), 5.18 (dd, *J* = 11.6, 4.4 Hz, 1 H), 4.54 (s, 1 H), 4.21 (s, 1 H), 3.64 (s, 3 H), 3.09 (dd, *J* = 14.9, 3.7 Hz, 1 H), 3.00 (dd, *J* = 14.9, 9.0 Hz, 1 H), 2.49–2.44 (m, 1 H), 2.15 (ddd, *J* = 12.8, 4.2, 2.2 Hz, 1 H), 1.98 (s, 3 H), 1.90 (dd, *J* = 12.6, 2.9 Hz, 2 H), 1.86–1.77 (m, 2 H), 1.66–1.50 (m, 2 H), 1.49–1.40 (m, 1 H), 1.16 (s, 3 H), 1.12–1.06 (m, 1 H), 0.76 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 176.66, 170.30, 147.39, 136.28, 133.87, 133.79, 132.62, 129.89, 129.30, 128.94, 122.47, 119.95, 119.84, 113.20, 111.13, 108.25, 77.36, 55.56, 52.42, 52.29, 50.62, 39.35, 37.51, 36.55, 26.24, 23.93, 21.27, 20.15, 14.64, 11.94 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{32}H_{36}ClNO_4Na^+$ 556.2225, found 556.2224.



30

Sespenine analogue 30: This compound was synthesized from *trans*-decalin **30a** (22.6 mg, 0.0423 mmol) by using the protocol for the preparation of sespenine analogue **27**. Sespenine analogue **30** (15.6 mg, 67%) was obtained as a pale yellow foam. **30**: R_f = 0.64 (silica, EtOAc:petroleum ether 1:1); $[\alpha]_D^{25}$ = −164.1 (*c* = 0.16 in $CHCl_3$); IR (film): ν_{max} = 2954, 1730, 1682, 1647, 1507, 1373, 1312, 1247, 1145, 1073, 974, 744, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.43–7.35 (m, 5 H), 7.16–7.11 (m, 1 H), 6.89–6.80 (m, 1 H), 6.69 (dd, *J* = 8.0, 1.0 Hz, 1 H), 5.20 (dd, *J* = 11.9, 4.7 Hz, 1 H), 4.34 (s, 1 H), 3.73 (s, 3 H), 2.82 (dd, *J* = 14.0, 1.9 Hz, 1 H), 2.57 (d, *J* = 17.5 Hz, 1 H), 2.43–2.35 (m, 2 H), 2.00 (s, 3 H), 1.94–1.75 (m, 5 H), 1.75–1.65 (m, 2 H), 1.63–1.58 (m, 1 H), 1.24 (s, 3 H), 1.26–1.13 (m, 2 H), 1.17 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 206.26, 176.52, 170.14, 142.71, 139.67, 133.62, 128.98, 128.58, 128.21, 127.94, 125.34, 119.20, 115.38, 76.82, 63.70, 60.85, 52.66, 52.17, 50.51, 42.90, 38.49,

38.13, 38.05, 37.52, 36.23, 22.95, 21.19, 20.90, 18.08, 12.00 ppm; HRMS (*m/z*): $[M + Na]^+$ calcd for $C_{32}H_{36}ClNO_5Na^+$ 572.2174, found 572.2172.

II References

1 J. Lan, Z. Liu, H. Yuan, L. Peng, W. Li, Y. Li, Y. Li and A. C. Chan, *Tetrahedron Lett.* 2000, **41**, 2181.

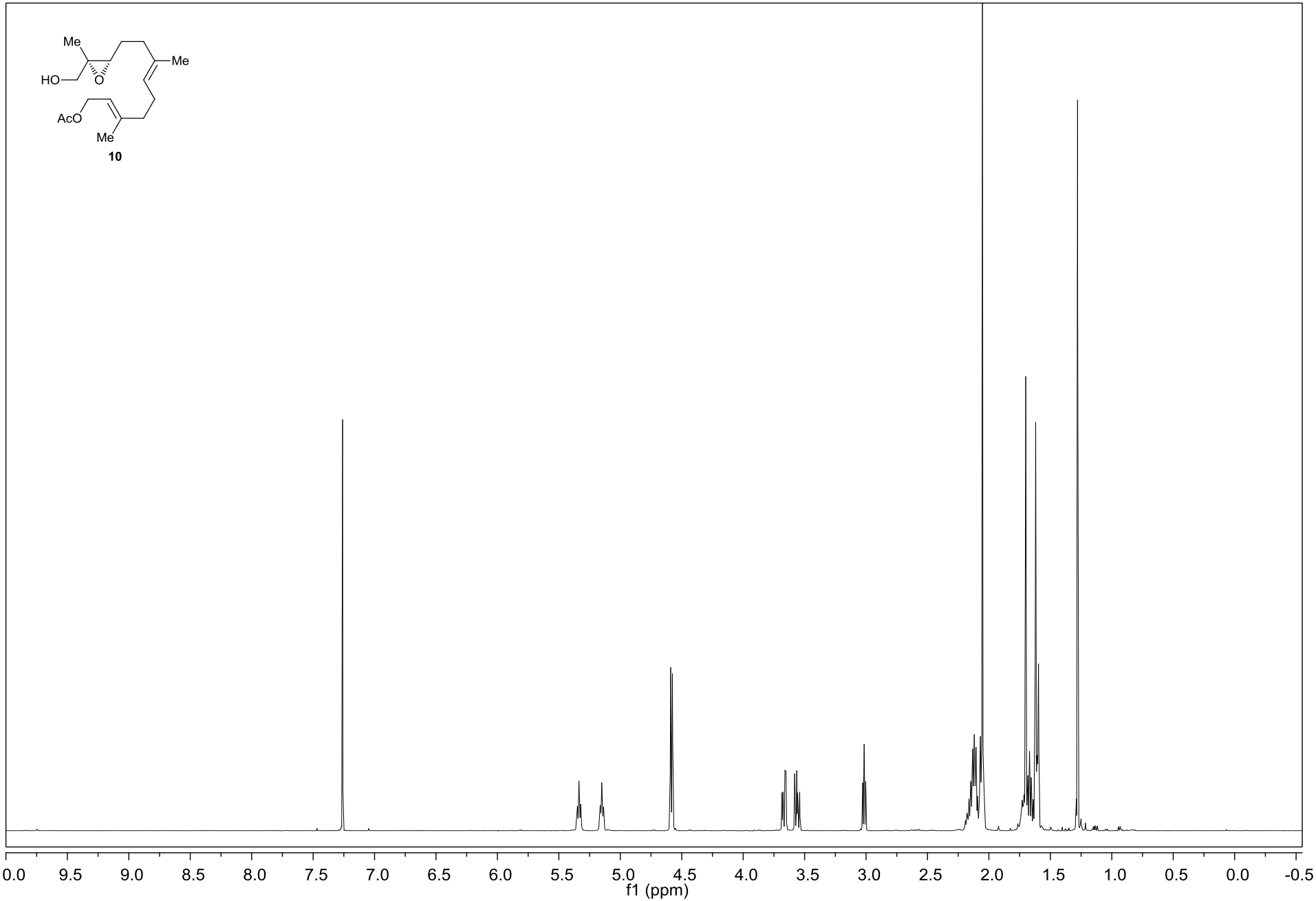
2 A. Bourderioux, A. Ouach, V. Bénéteau, J. Mérour and S. Routier, *Synthesis* 2010, **5**, 783.

3 Y. Sun, P. Chen, D. Zhang, M. Baunach, C. Hertweck and A. Li, *Angew. Chem. Int. Ed.* 2014, **53**, 9012.

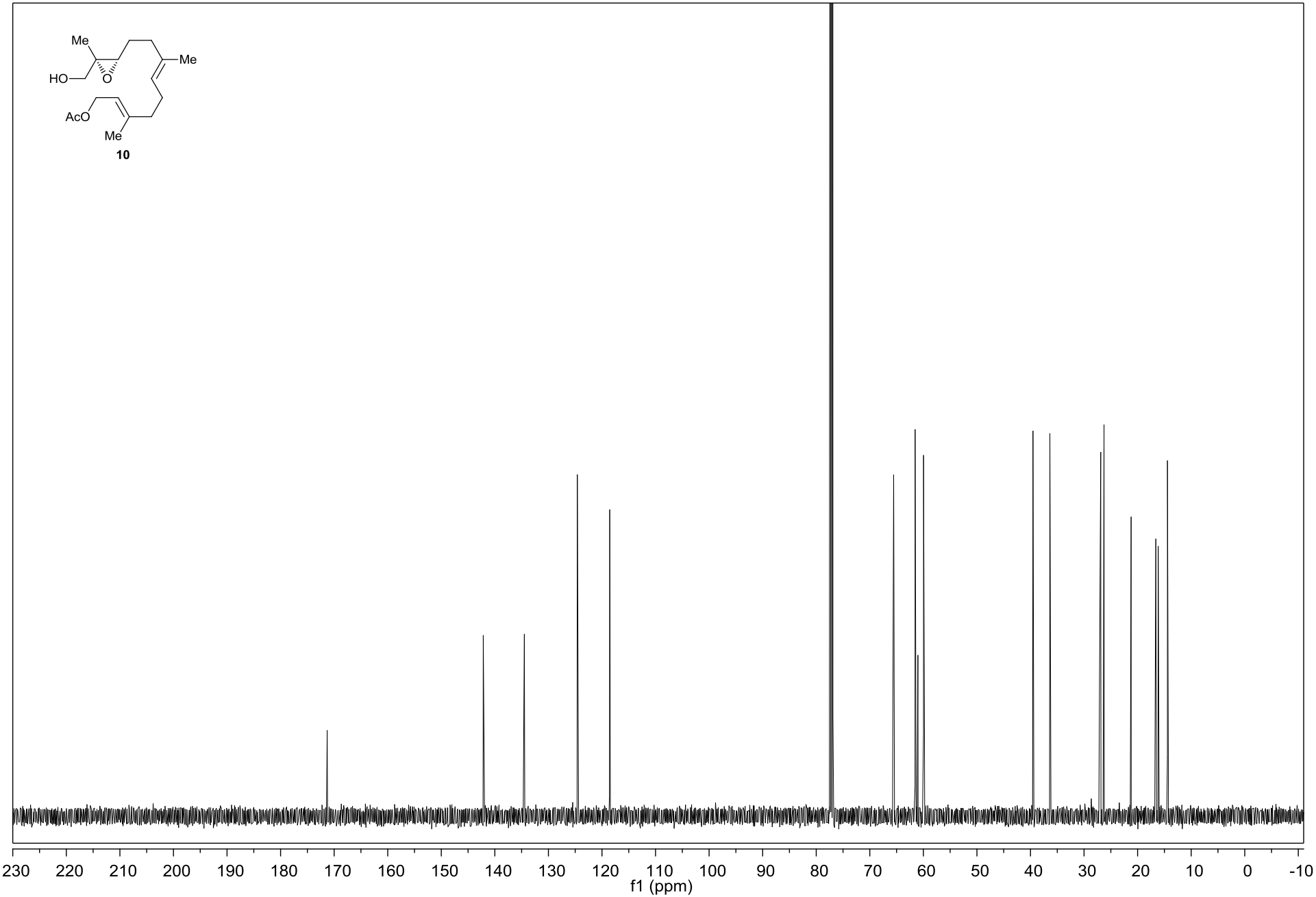
4 G. W. Kramer and H. C. Brown, *J. Organomet. Chem.* 1977, **132**, 9.

III ^{1}H and ^{13}C NMR Spectra of Compounds

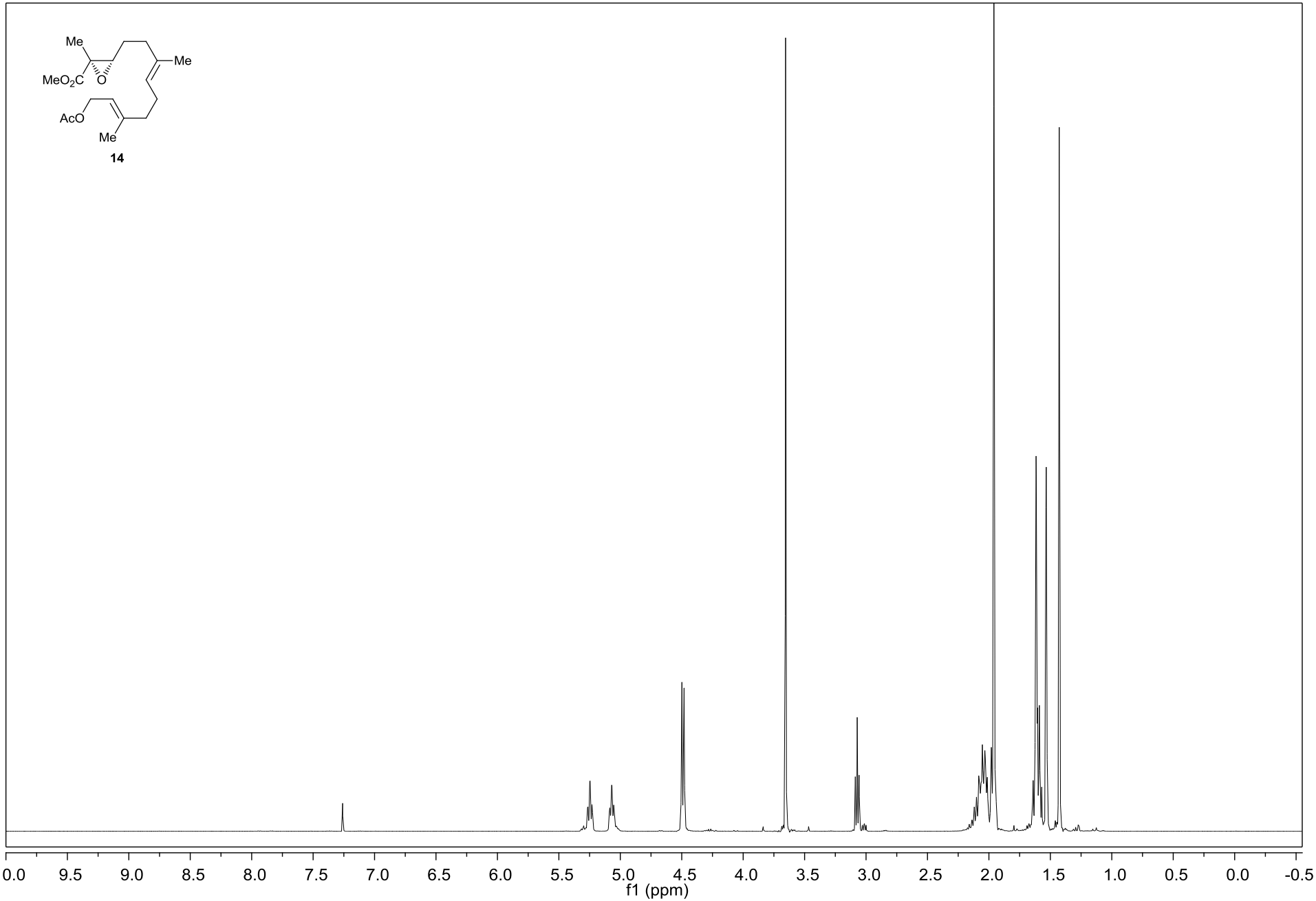
^{1}H NMR Spectrum of 10 (500 MHz, $CDCl_3$)



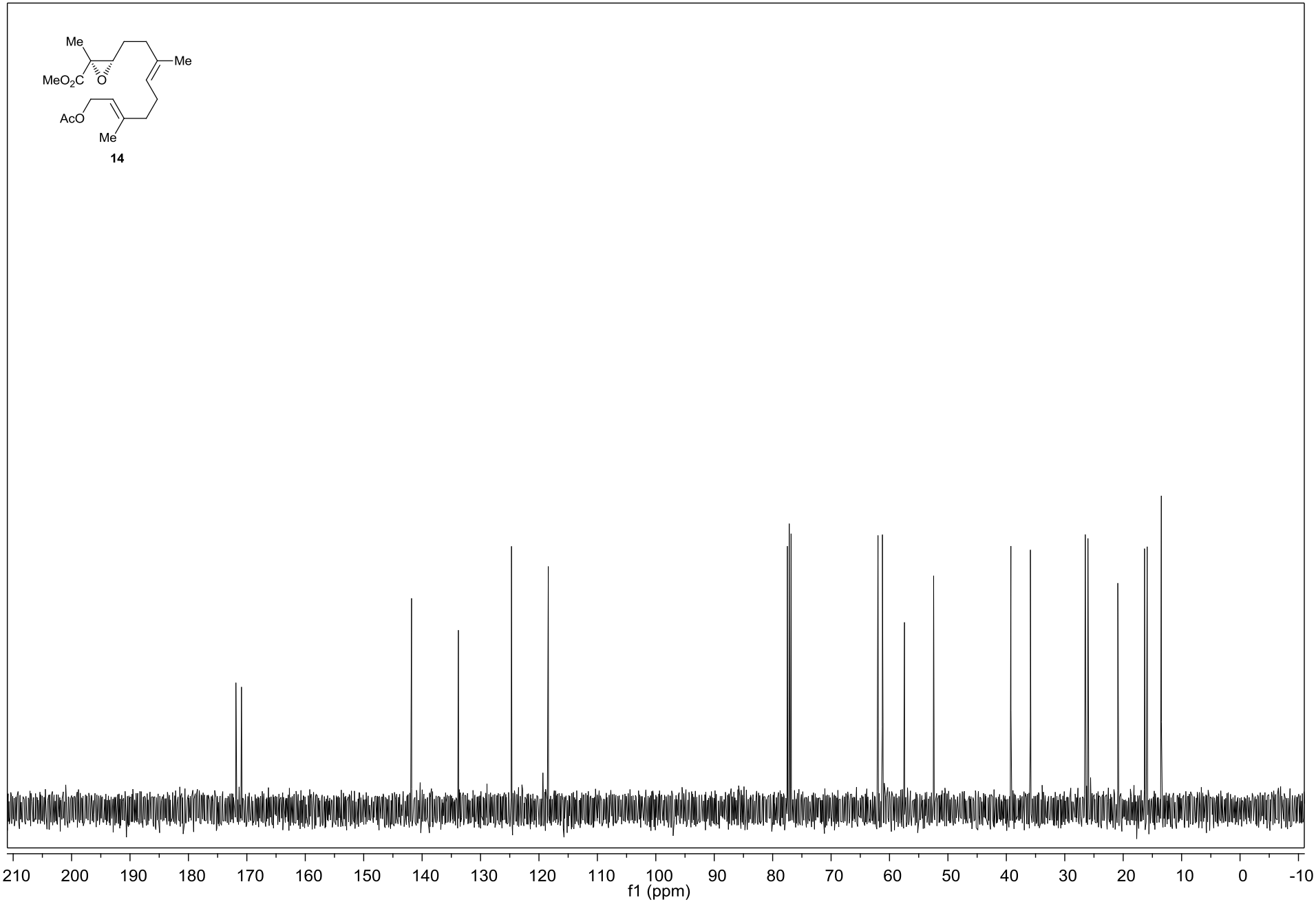
^{13}C NMR Spectrum of 10 (126 MHz, $CDCl_3$)



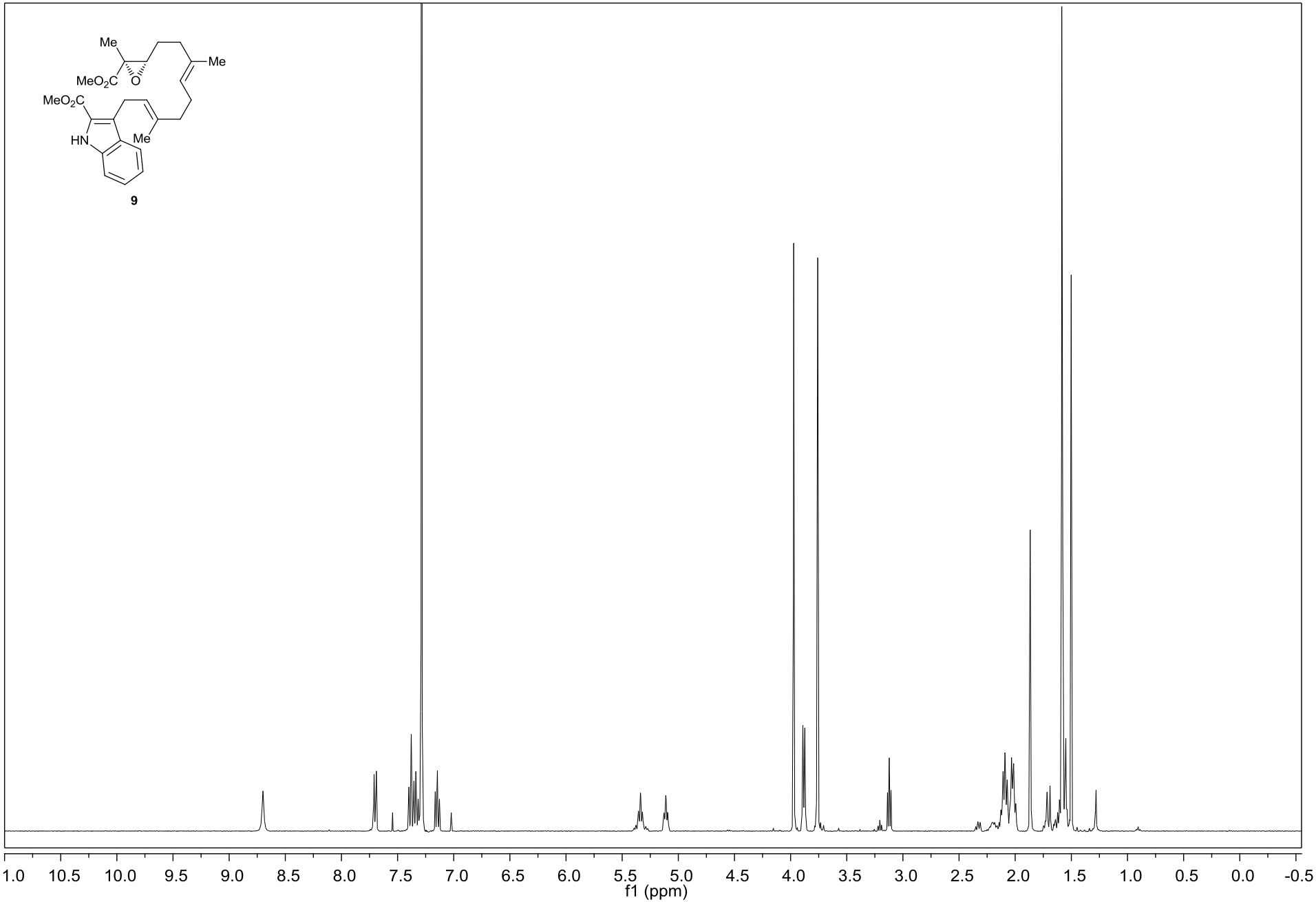
^{1}H NMR Spectrum of 14 (400 MHz, $CDCl_3$)



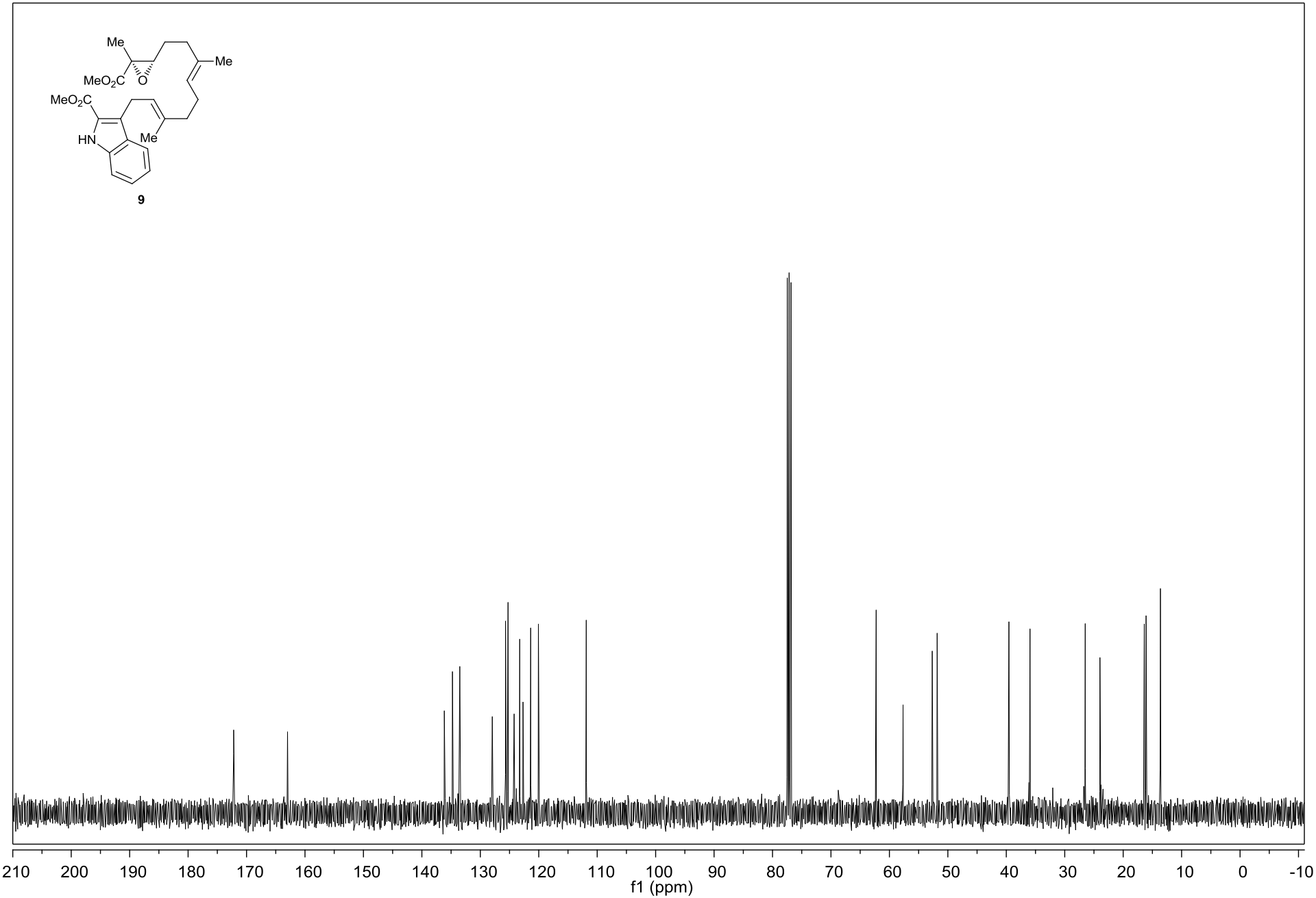
^{13}C NMR Spectrum of 14 (101 MHz, $CDCl_3$)



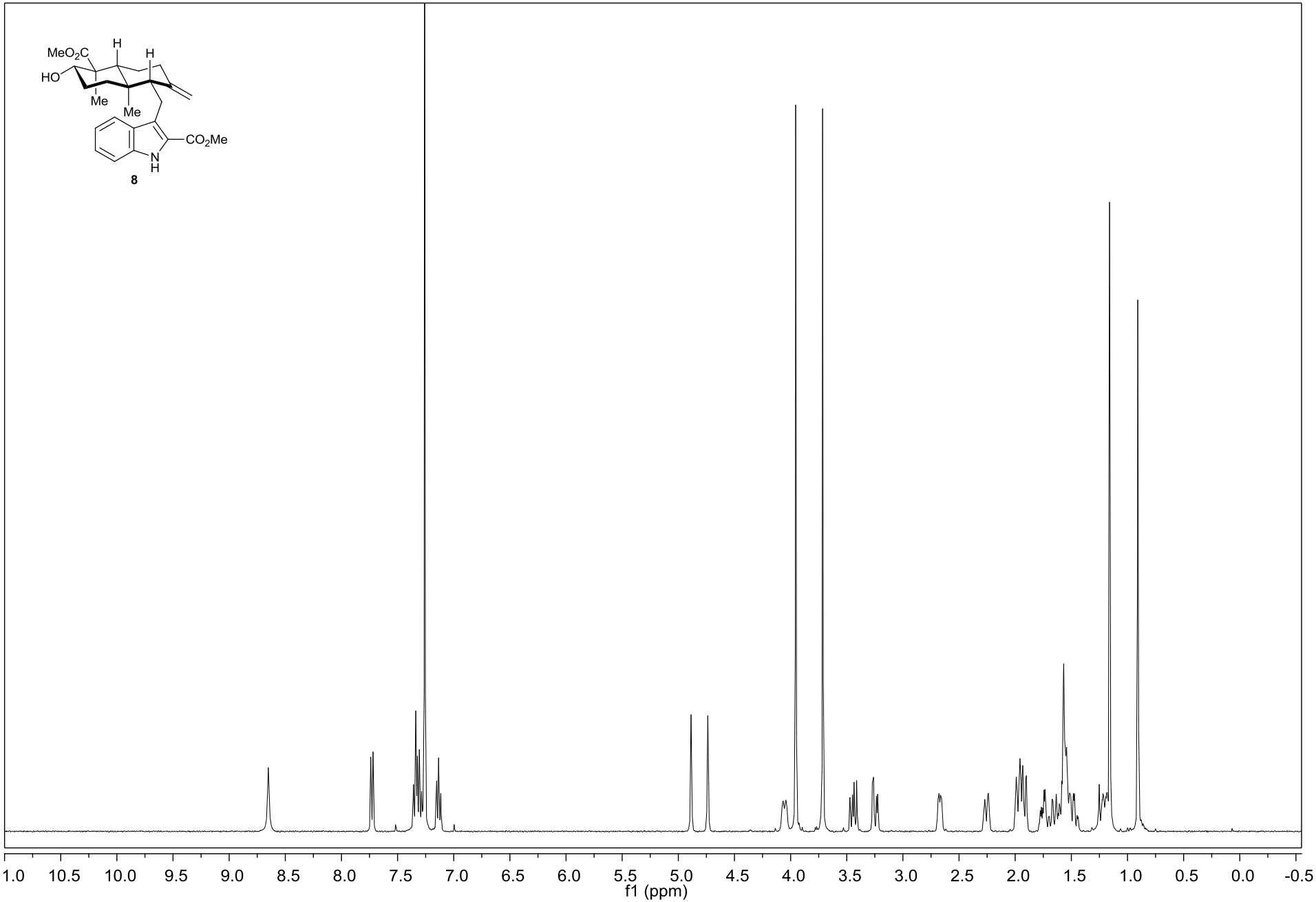
^{1}H NMR Spectrum of 9 (400 MHz, $CDCl_3$)



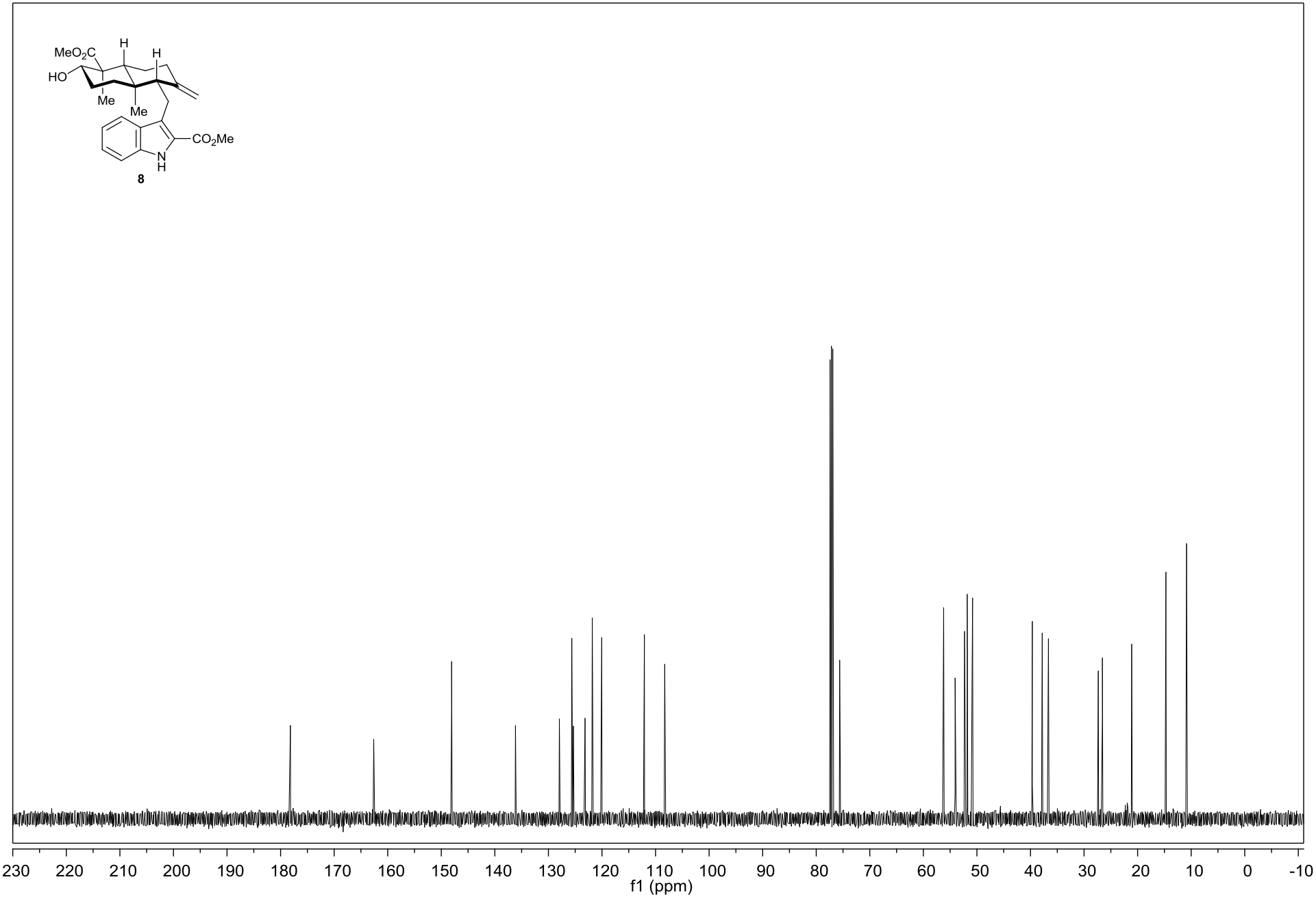
^{13}C NMR Spectrum of 9 (101 MHz, $CDCl_3$)



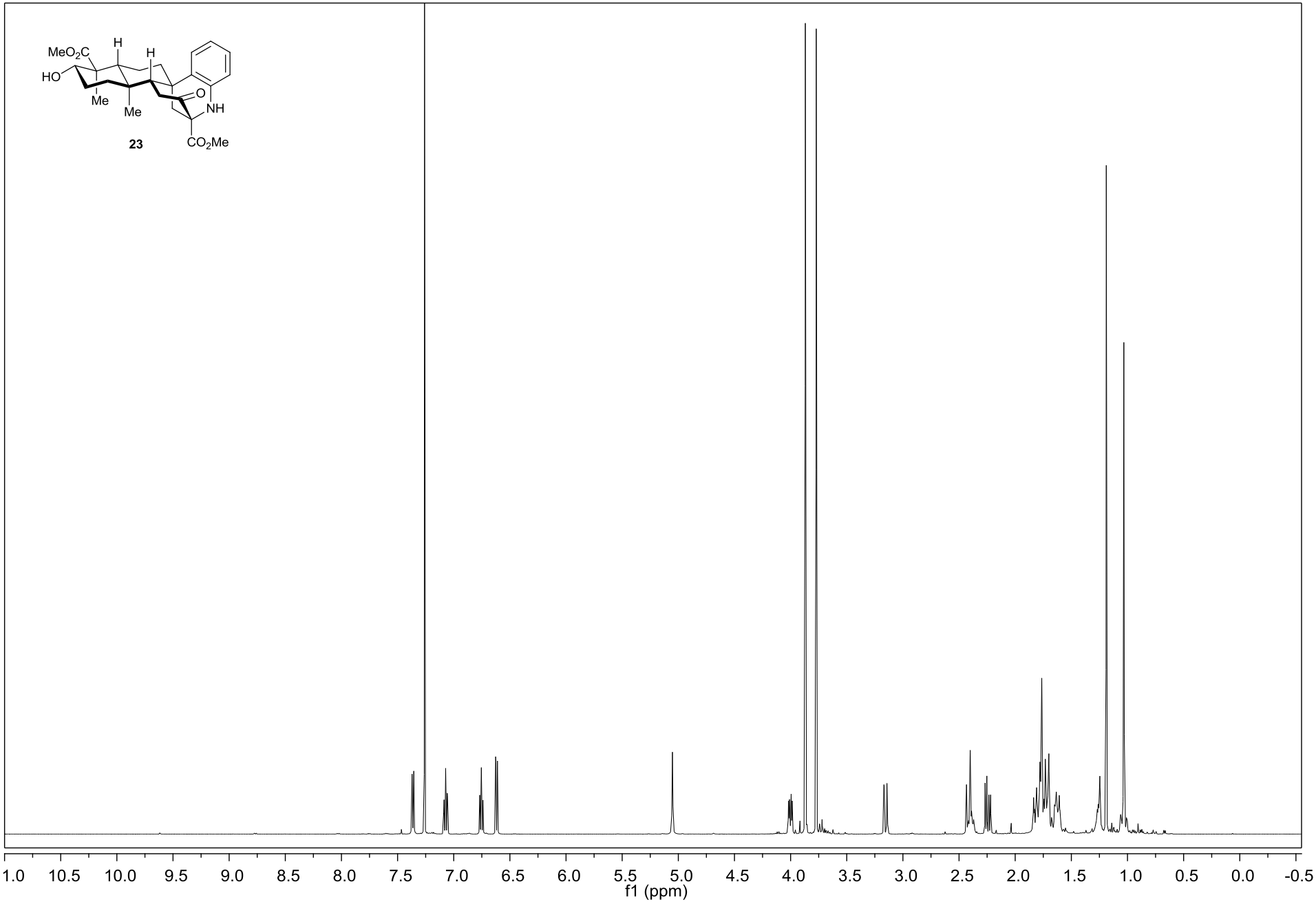
^{1}H NMR Spectrum of 8 (400 MHz, $CDCl_3$)



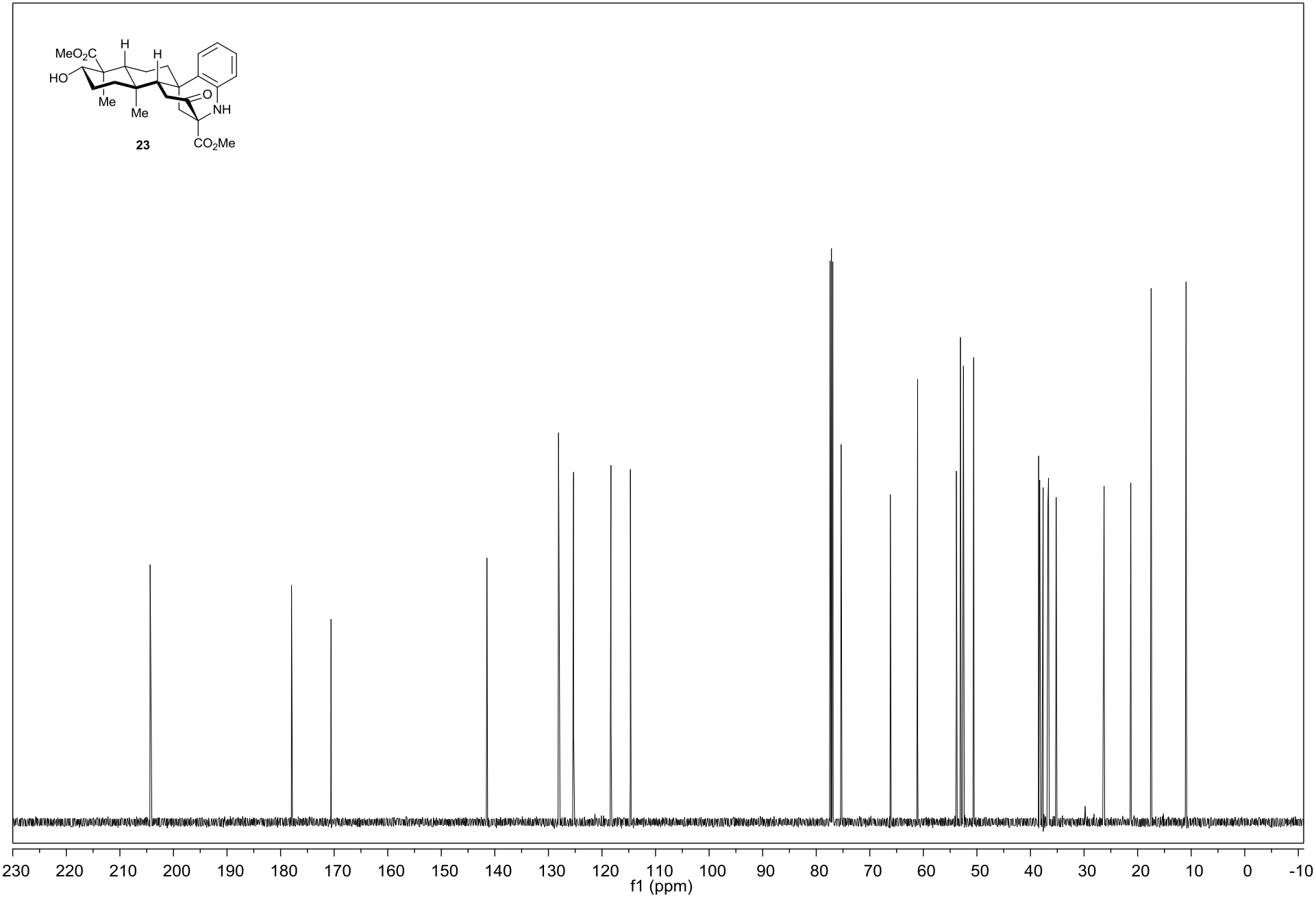
^{13}C NMR Spectrum of 8 (126 MHz, $CDCl_3$)



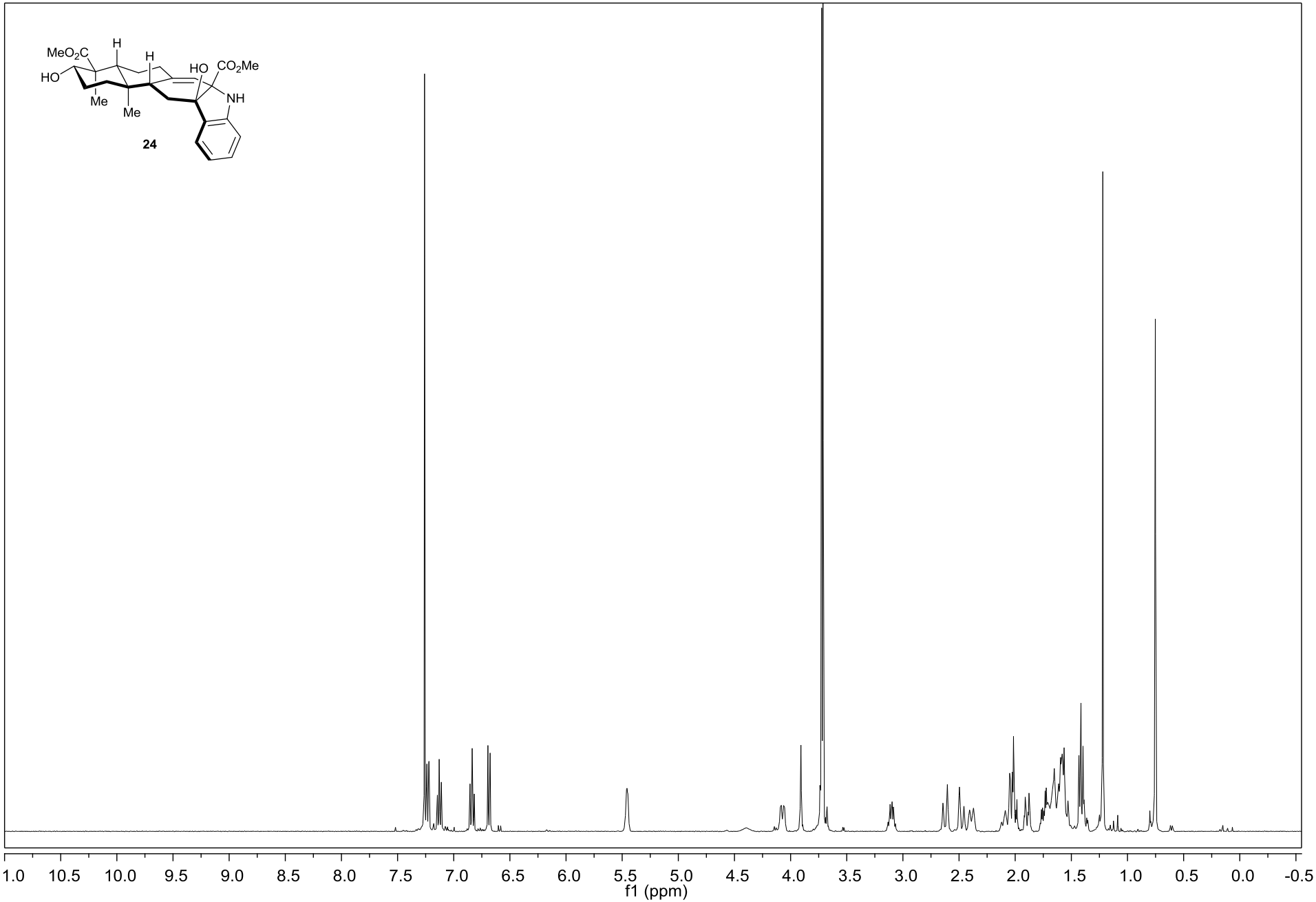
^{1}H NMR Spectrum of 23 (500 MHz, $CDCl_3$)



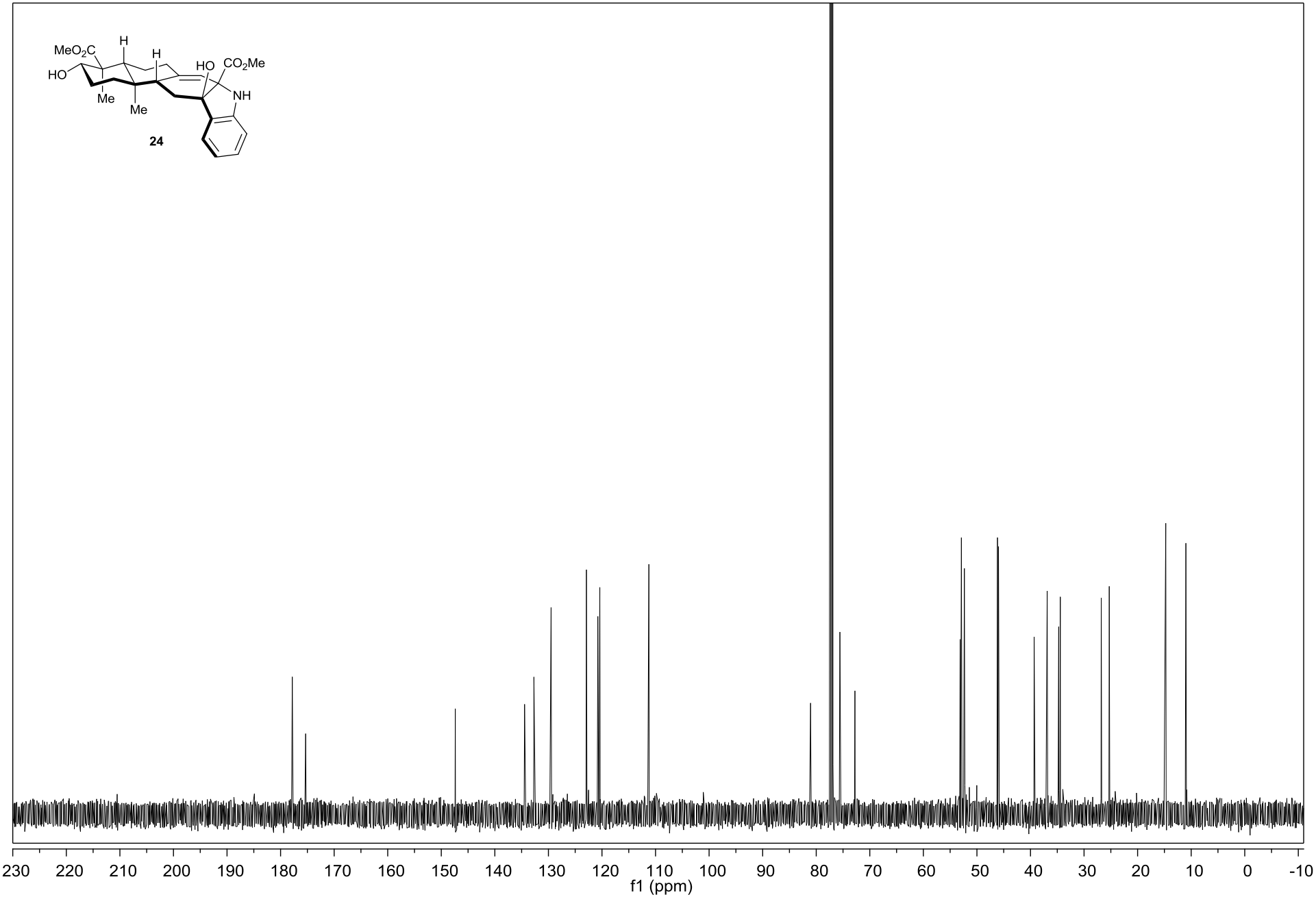
^{13}C NMR Spectrum of 23 (126 MHz, $CDCl_3$)



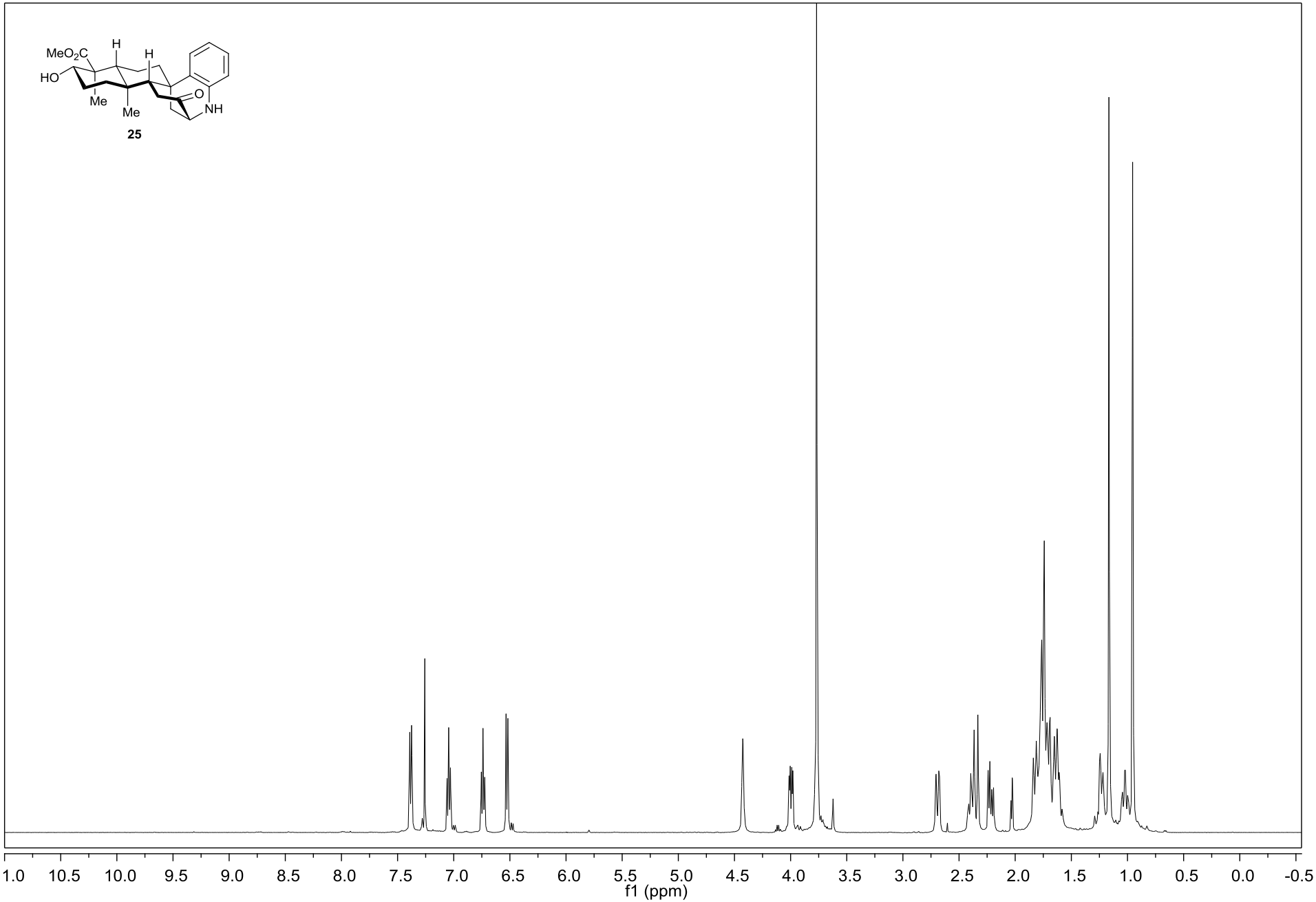
^{1}H NMR Spectrum of 24 (400 MHz, $CDCl_3$)



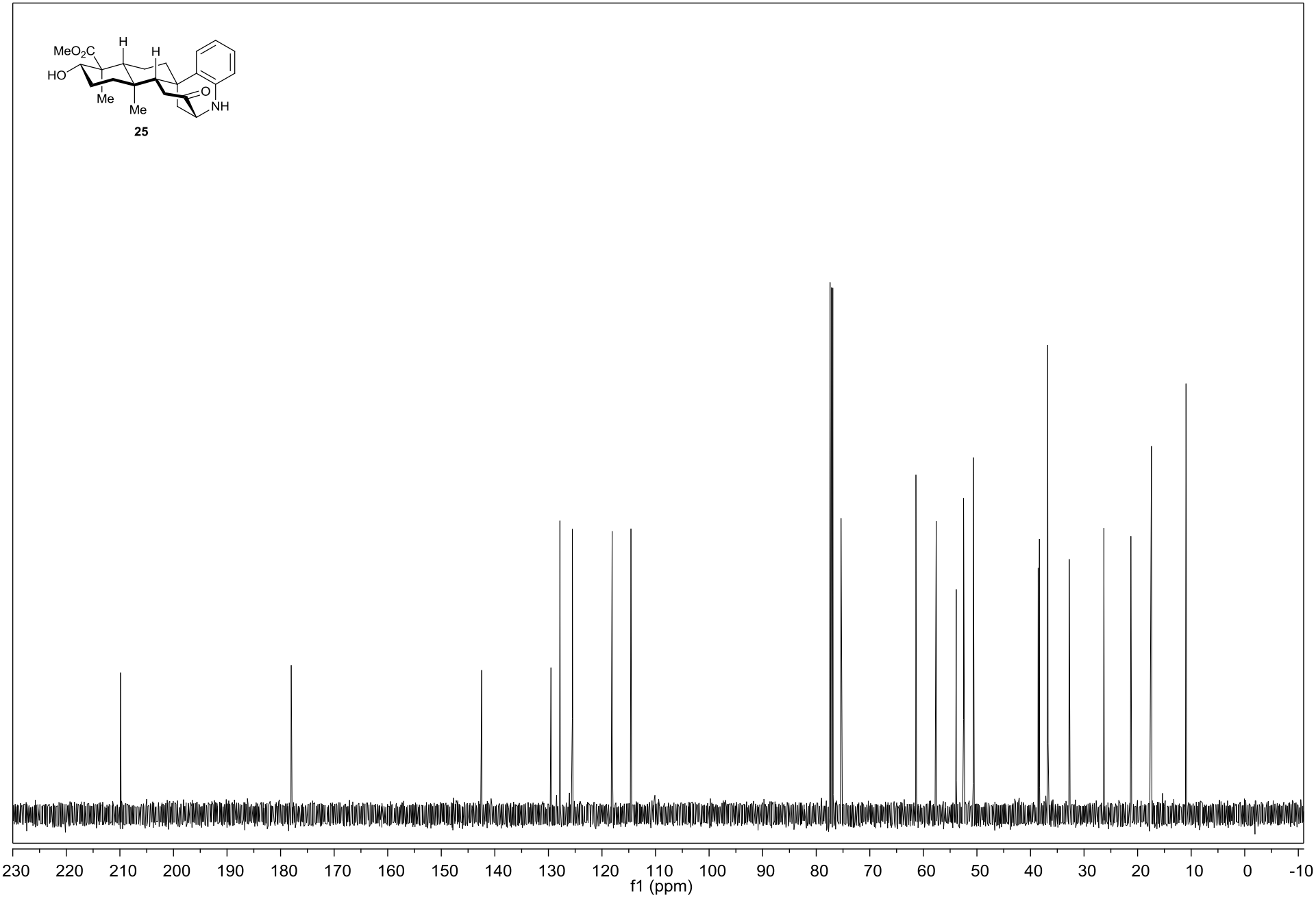
^{13}C NMR Spectrum of 24 (126 MHz, $CDCl_3$)



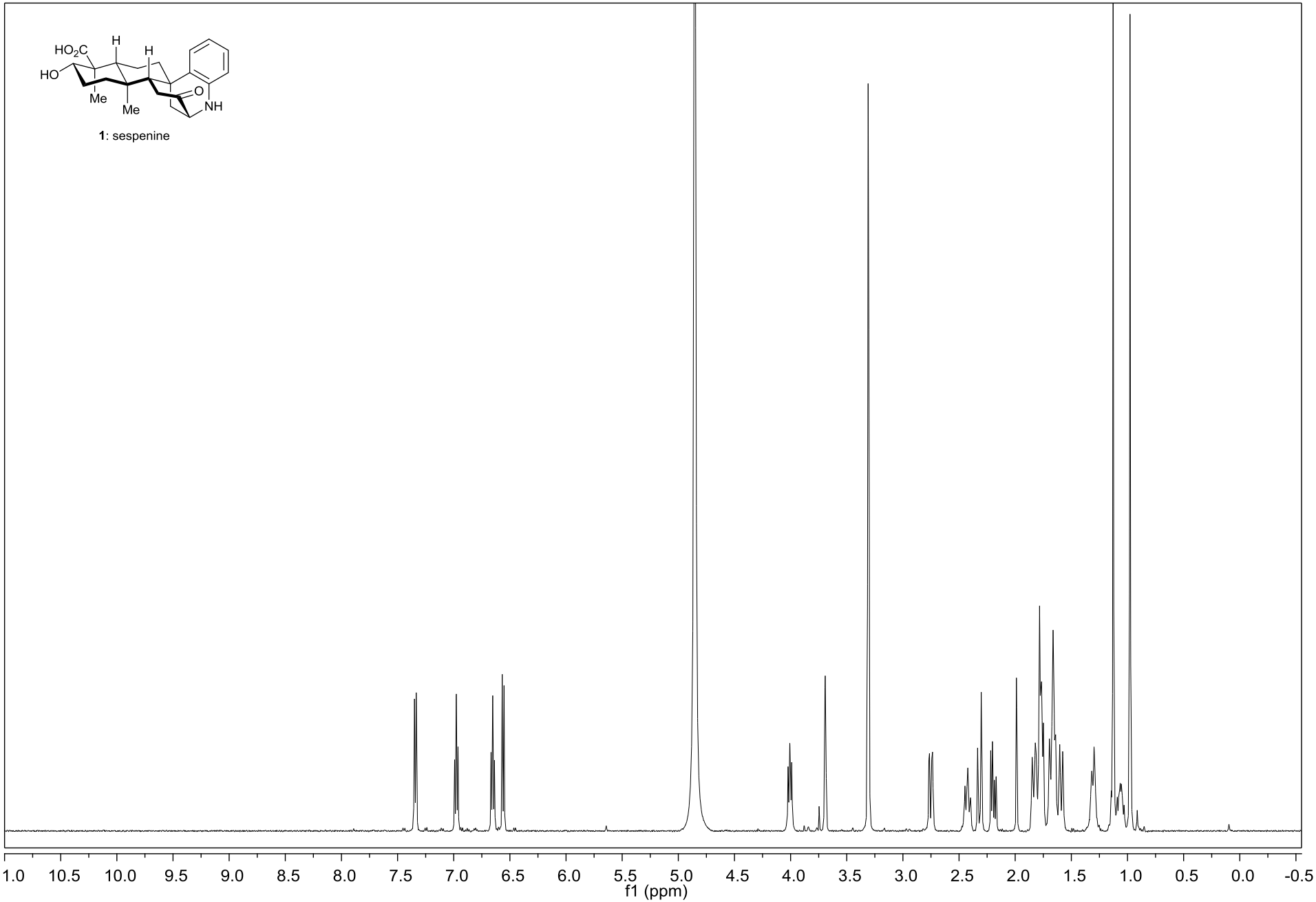
^{1}H NMR Spectrum of 25 (500 MHz, $CDCl_3$)



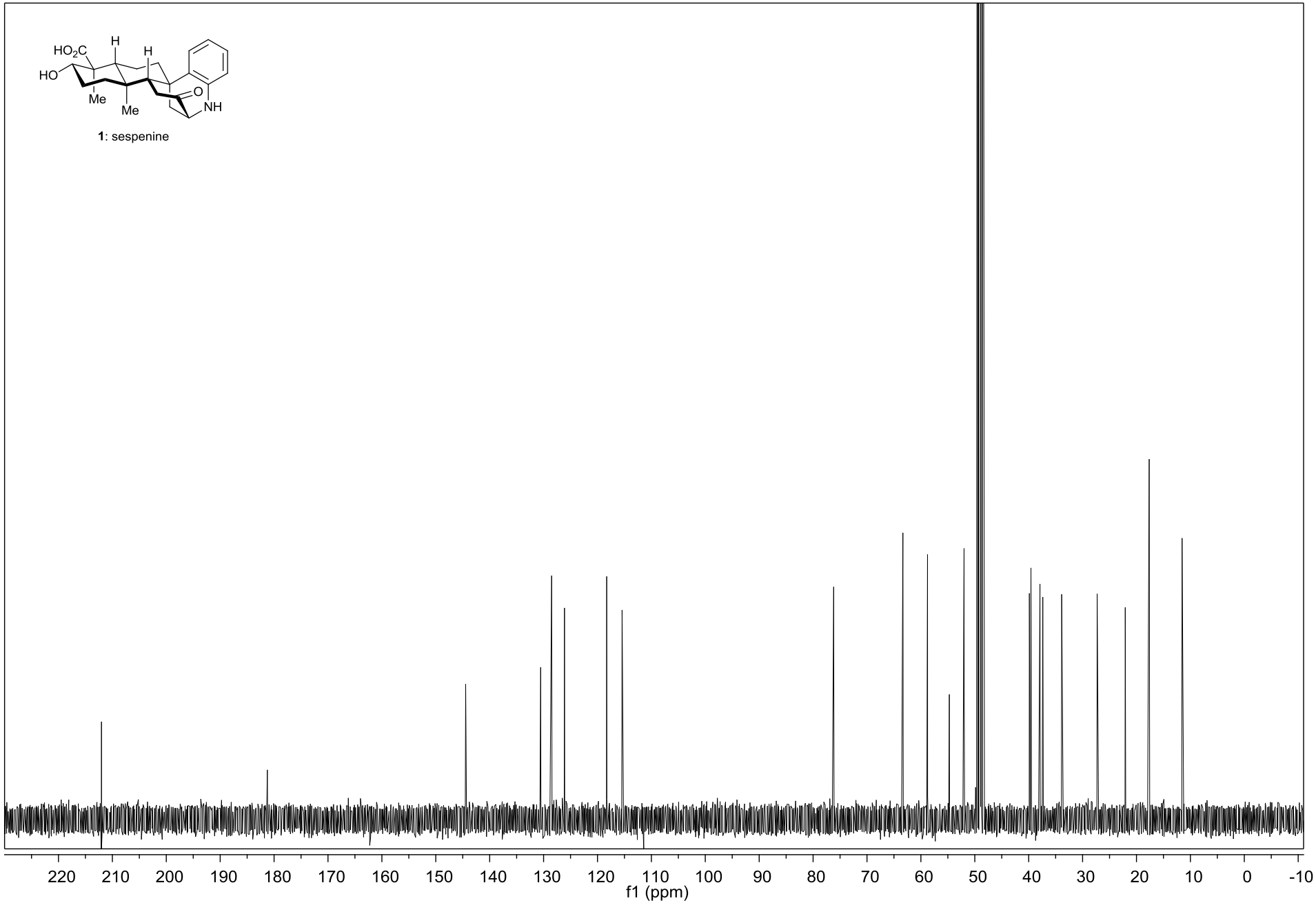
^{13}C NMR Spectrum of 25 (126 MHz, $CDCl_3$)



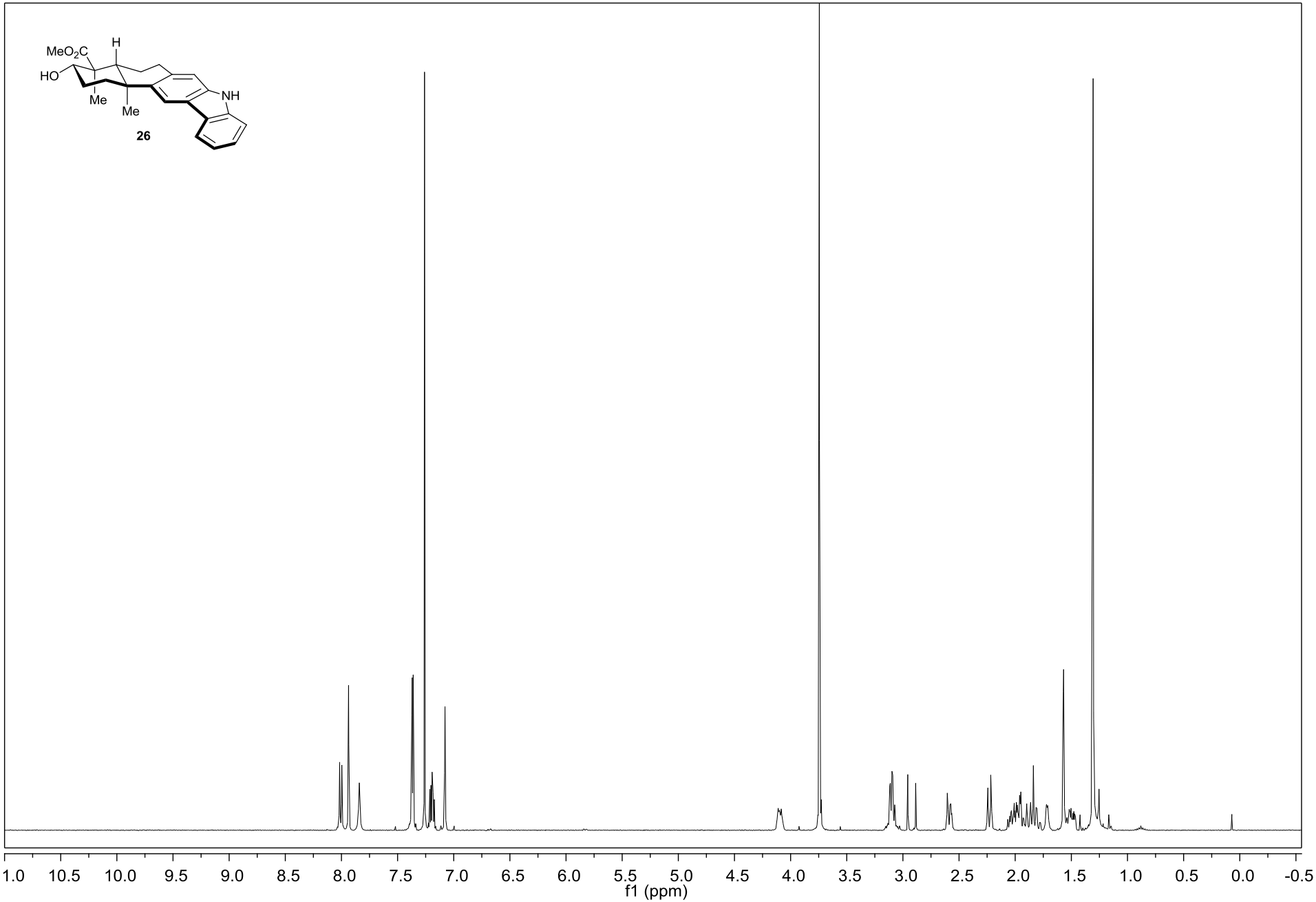
^{1}H NMR Spectrum of Sespenine (500 MHz, methanol-d_4)



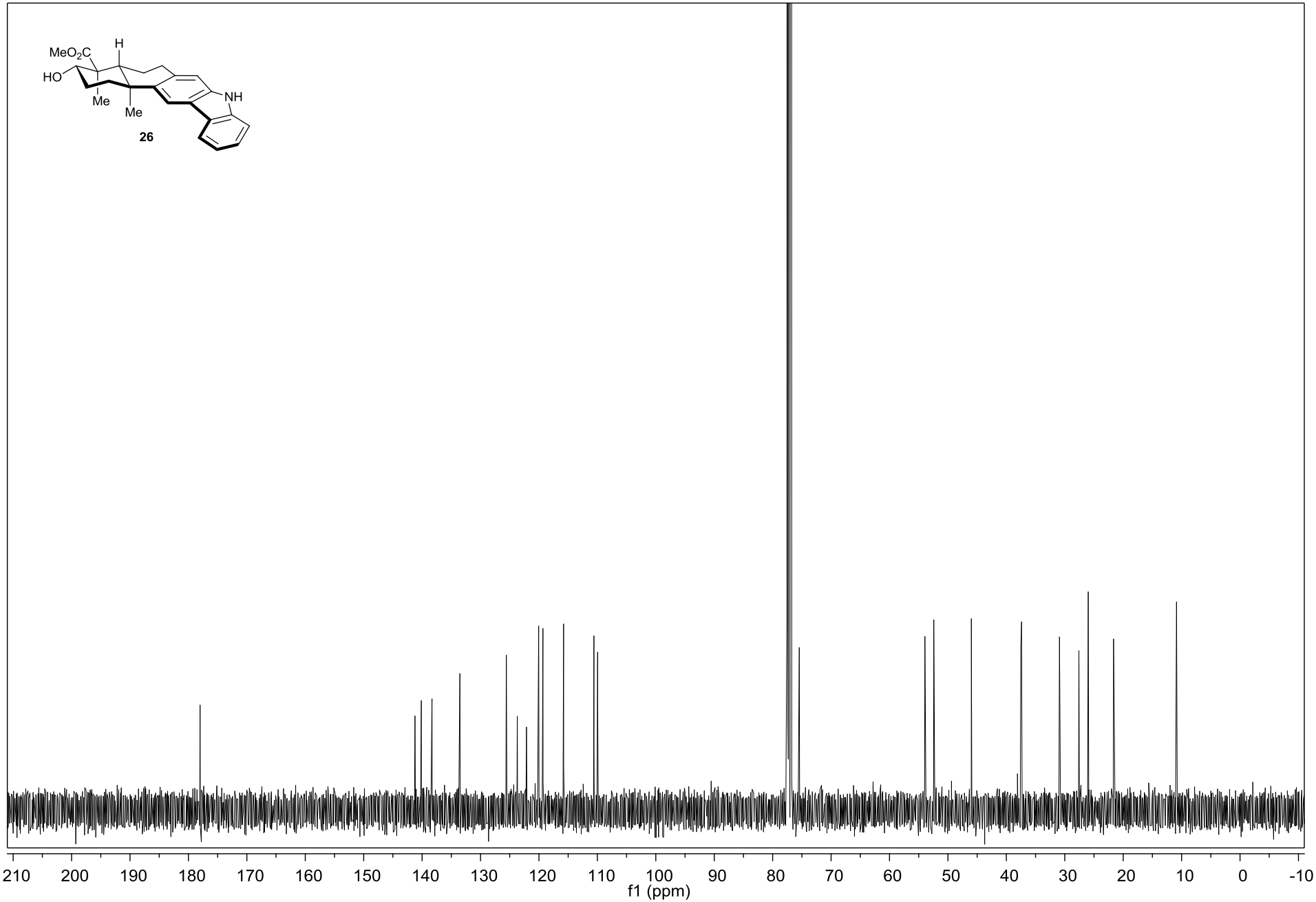
^{13}C NMR Spectrum of Sespenine (126 MHz, methanol-d_4)



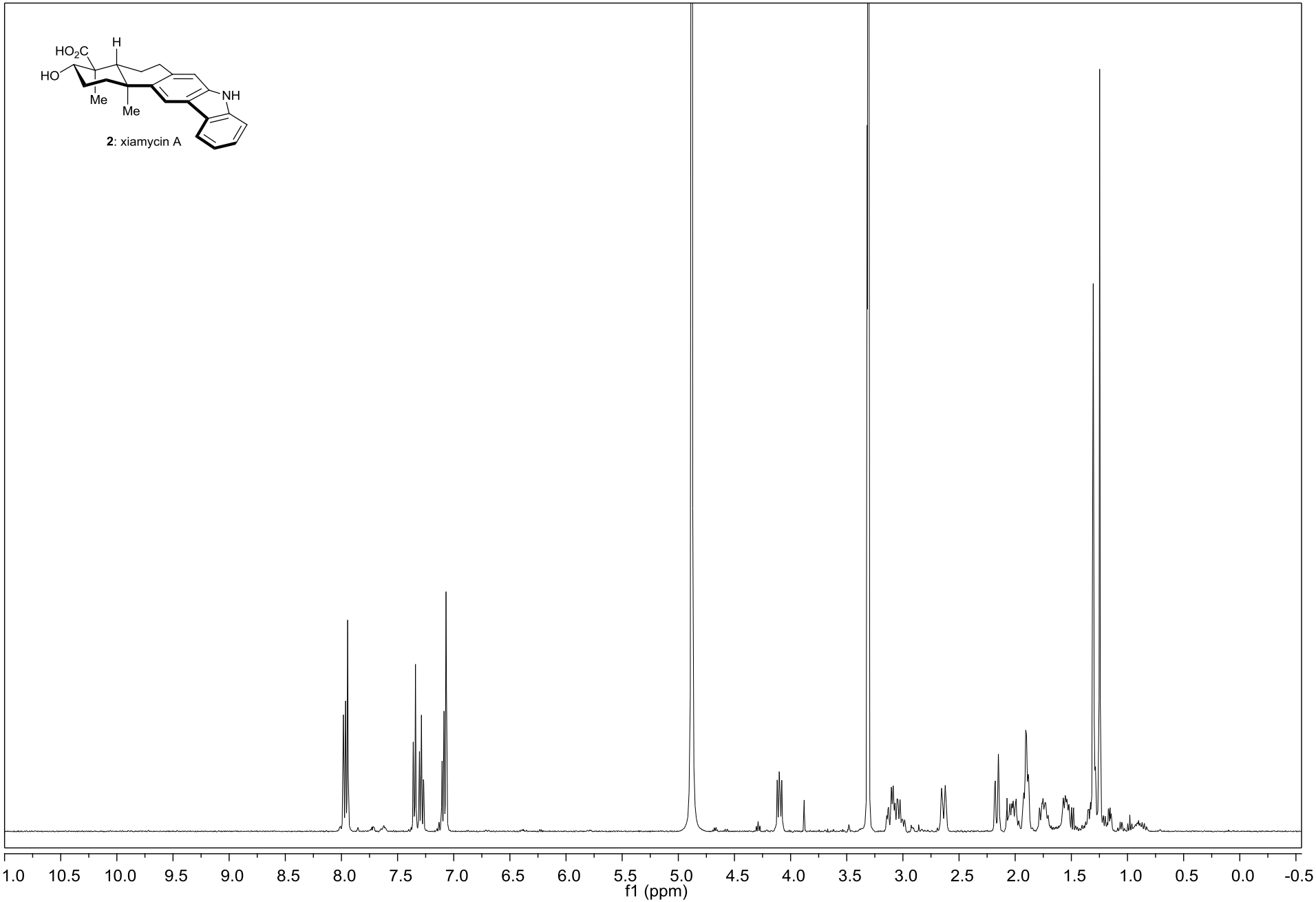
^{1}H NMR Spectrum of 26 (400 MHz, $CDCl_3$)



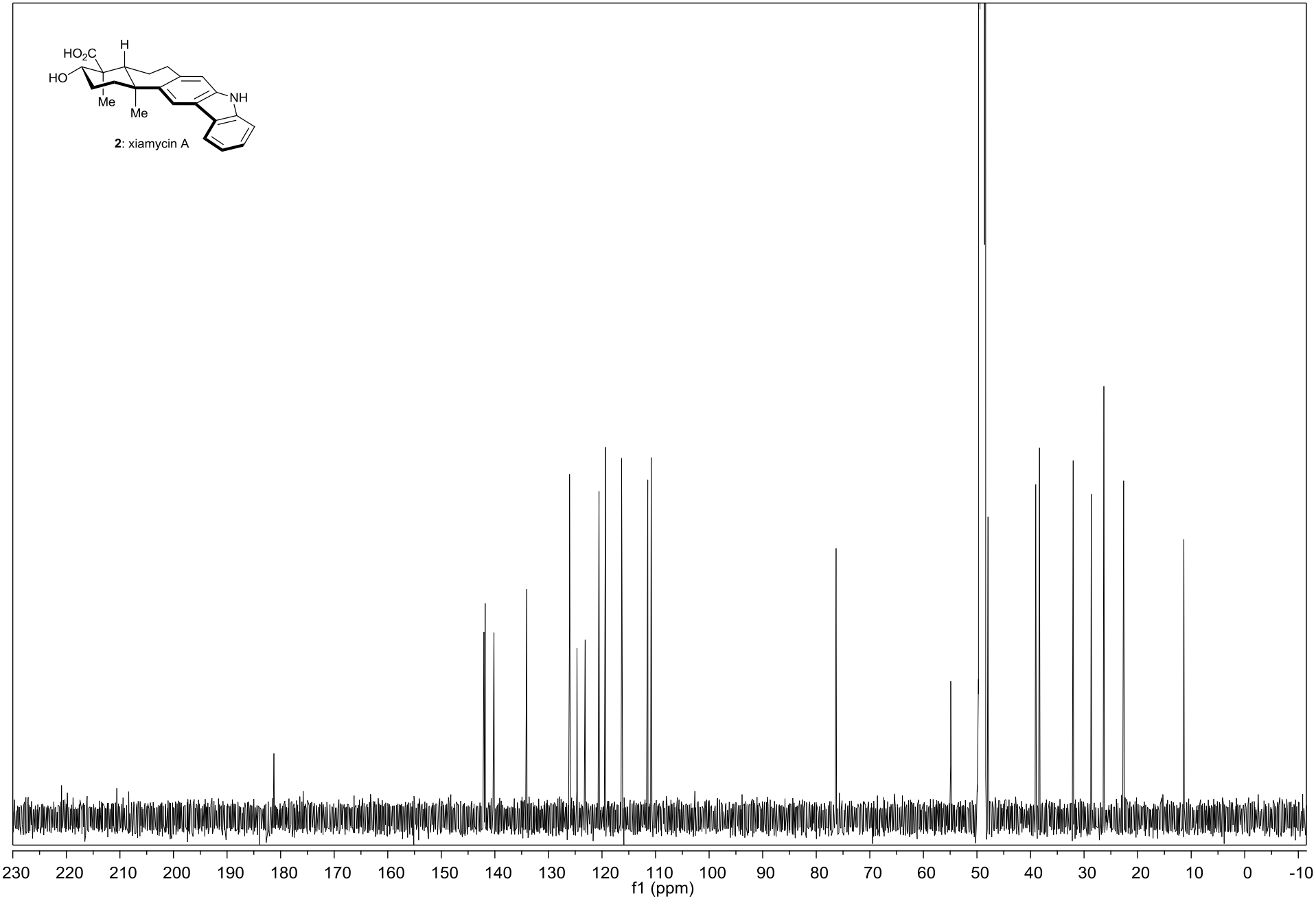
^{13}C NMR Spectrum of 26 (101 MHz, $CDCl_3$)



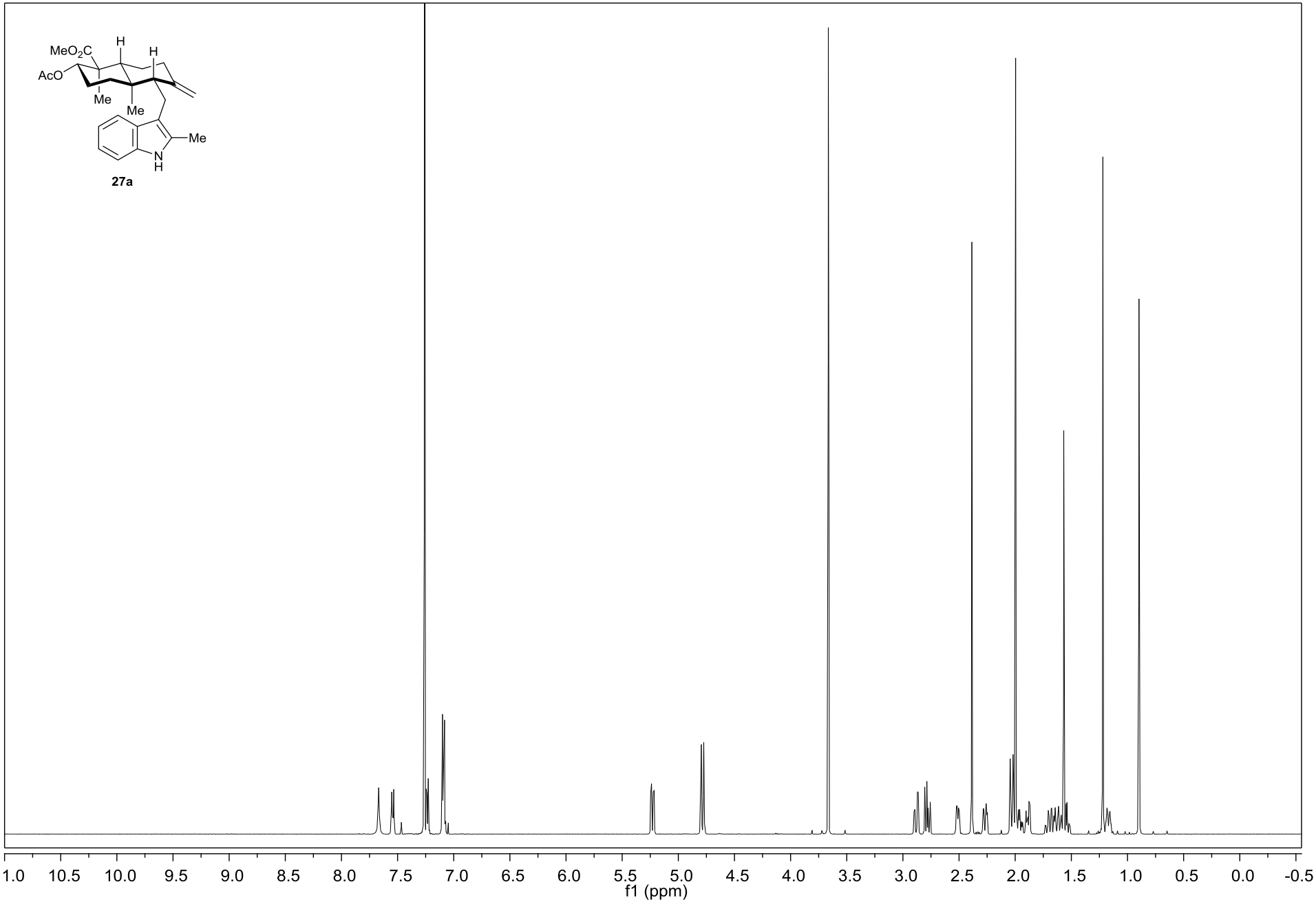
^{1}H NMR Spectrum of Xiamycin A (400 MHz, methanol-d_4)



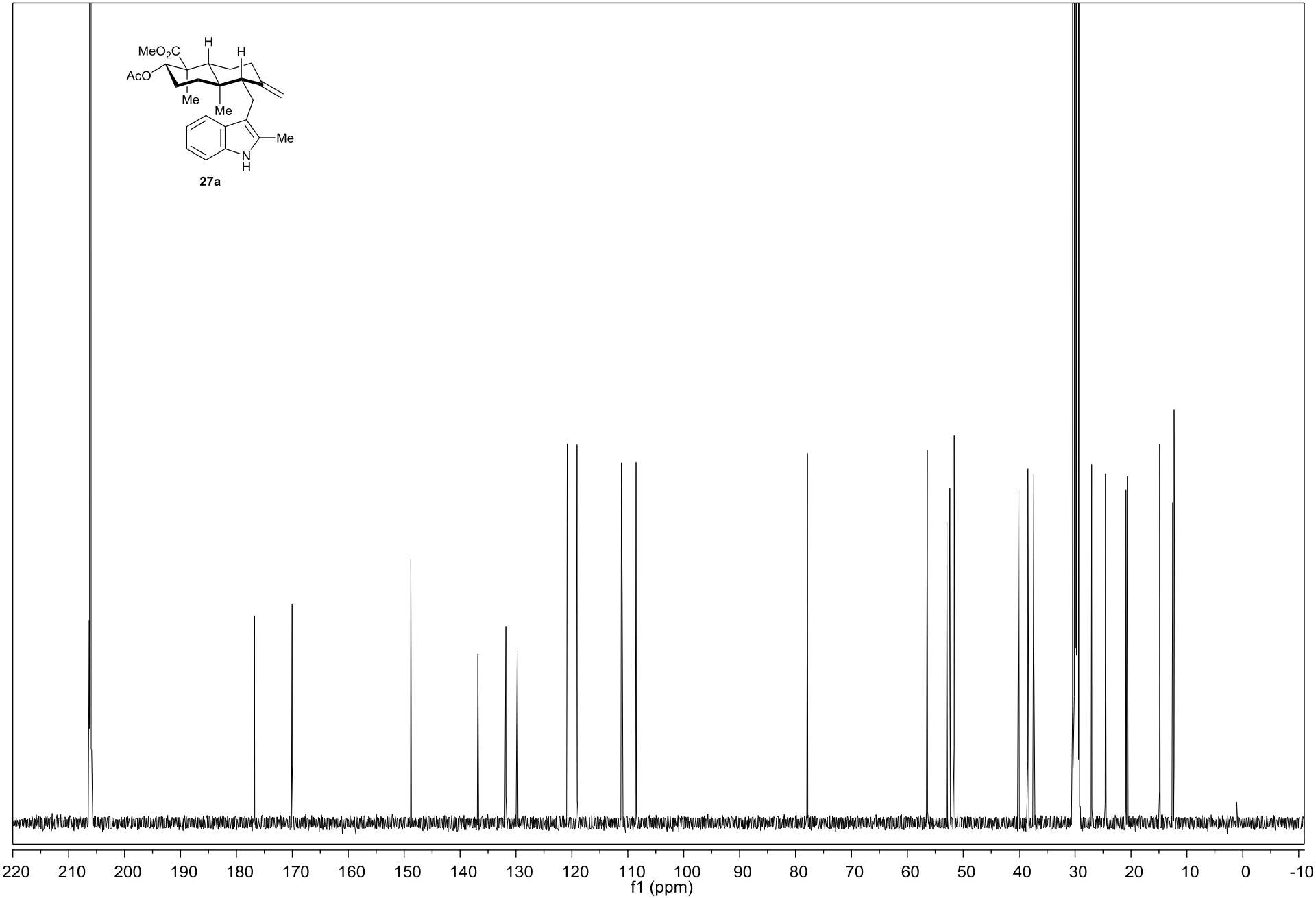
^{13}C NMR Spectrum of Xiamycin A (126 MHz, methanol-d_4)



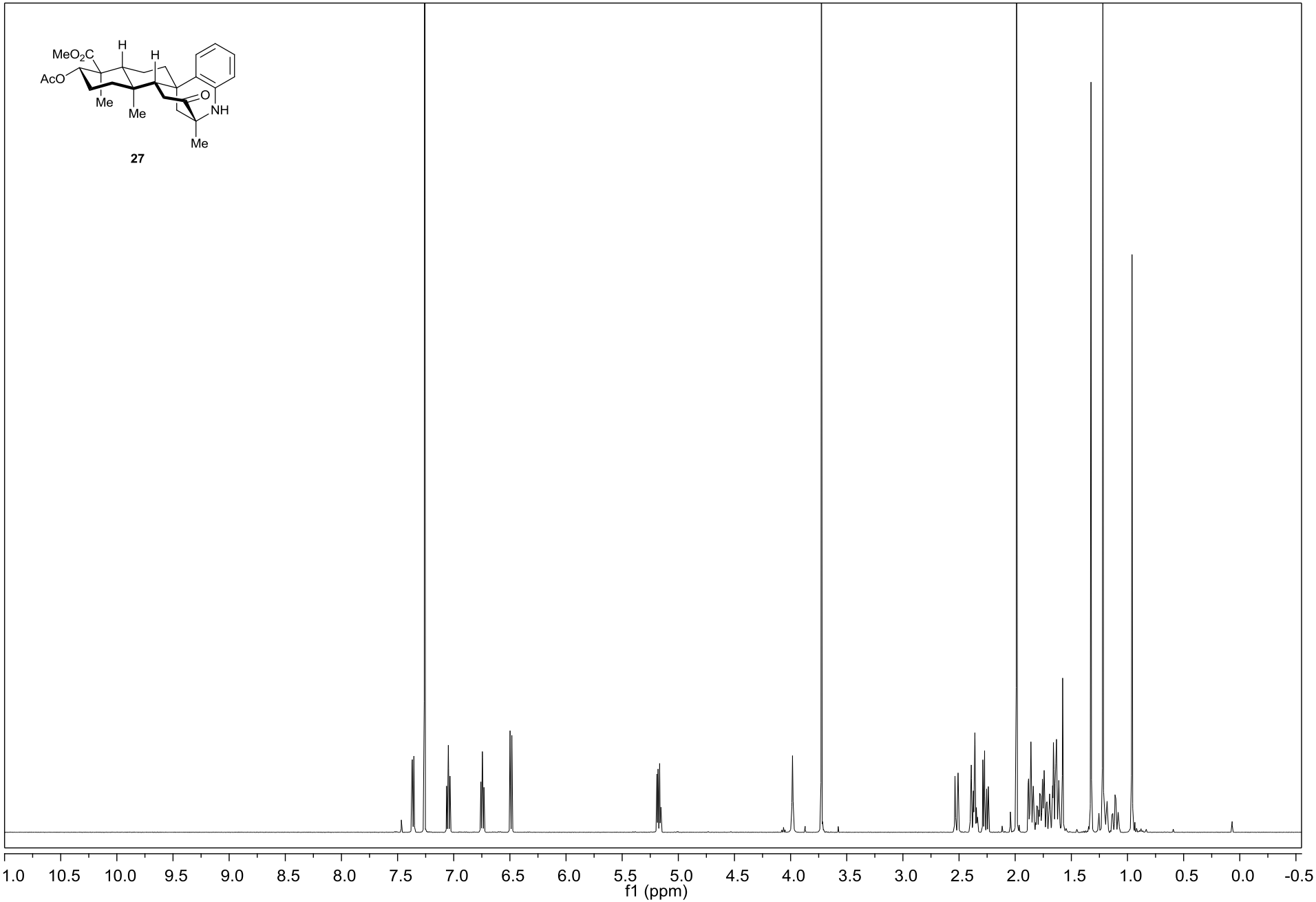
^{1}H NMR Spectrum of 27a (500 MHz, $CDCl_3$)



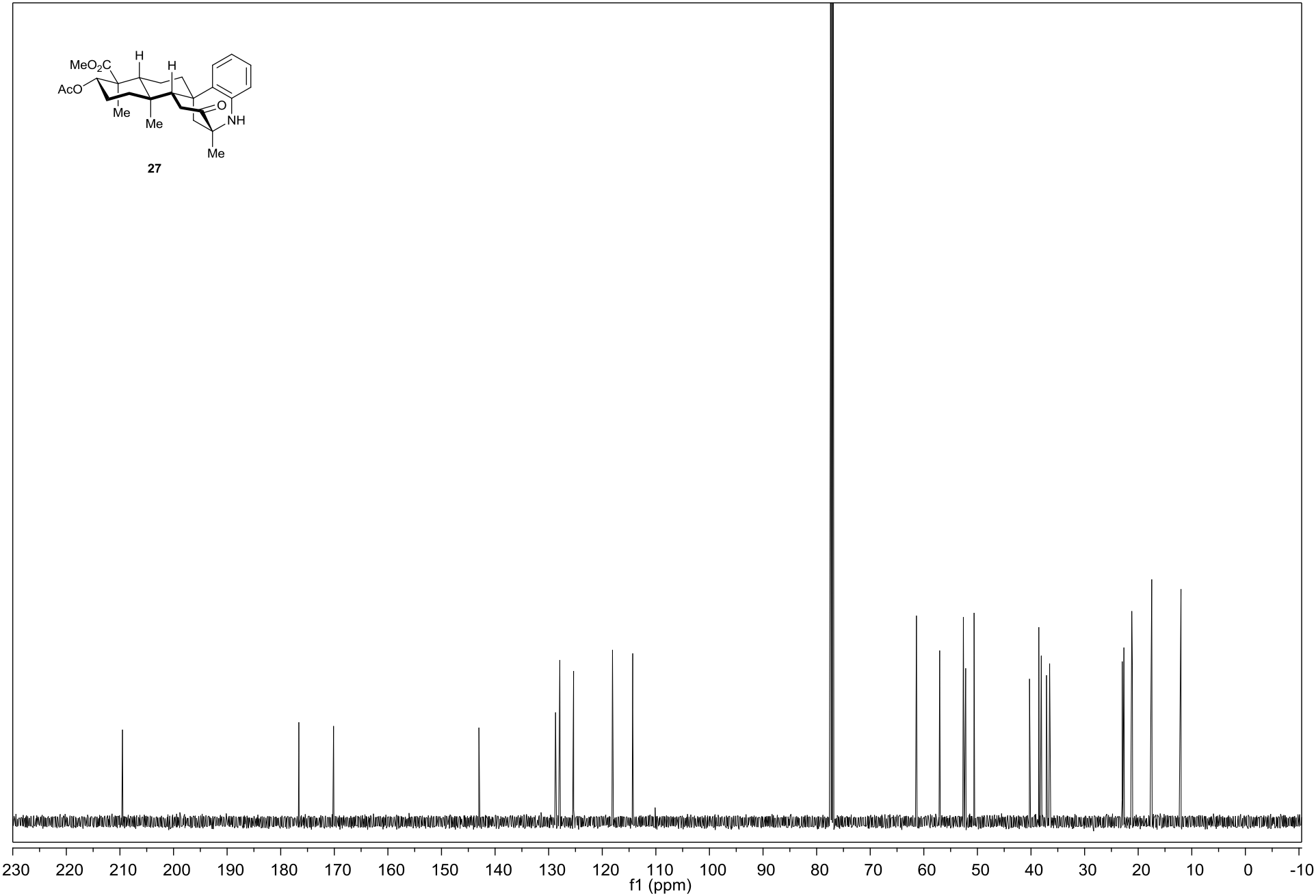
^{13}C NMR Spectrum of 27a (101 MHz, acetone-d_6)



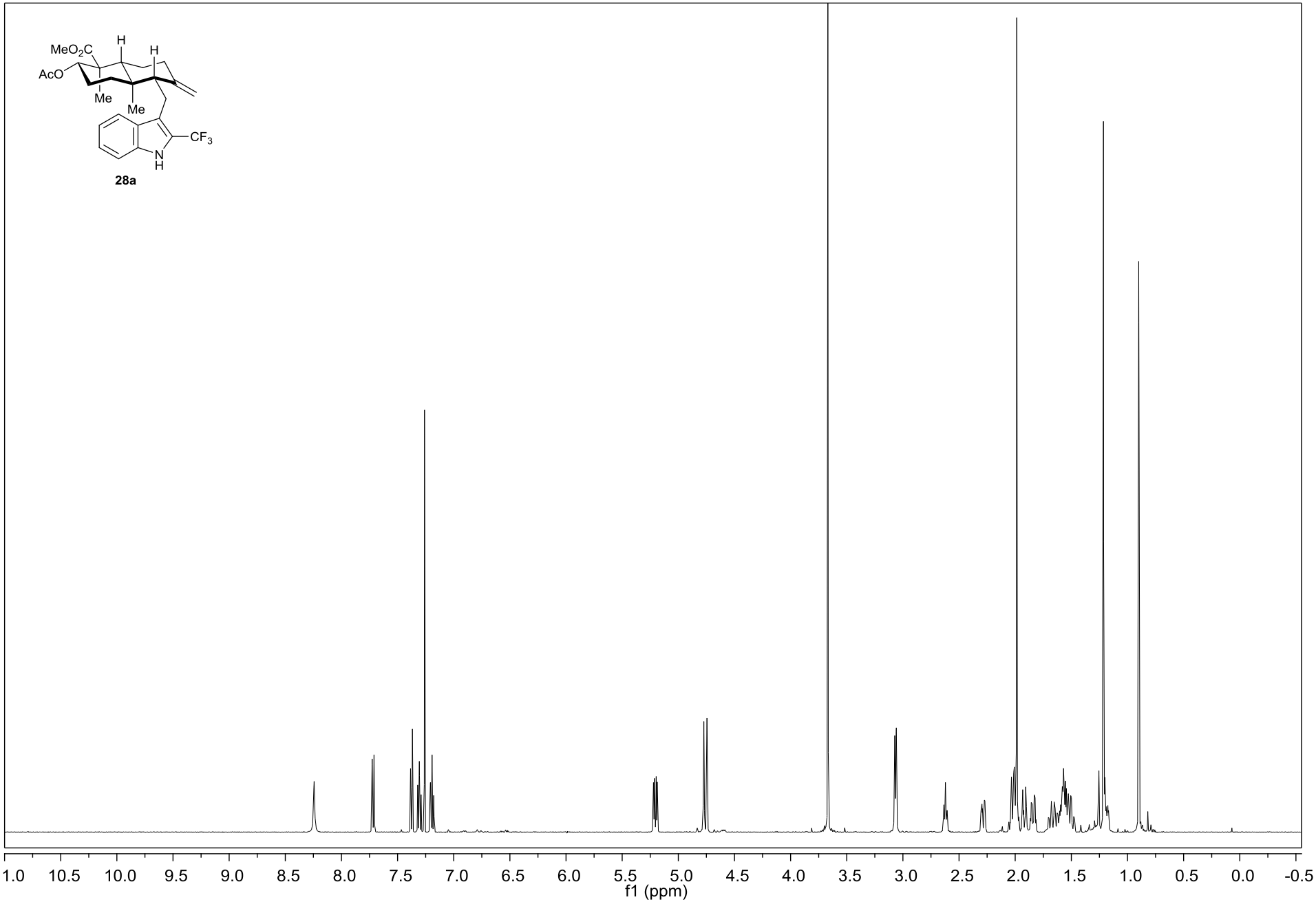
^{1}H NMR Spectrum of 27 (500 MHz, $CDCl_3$)



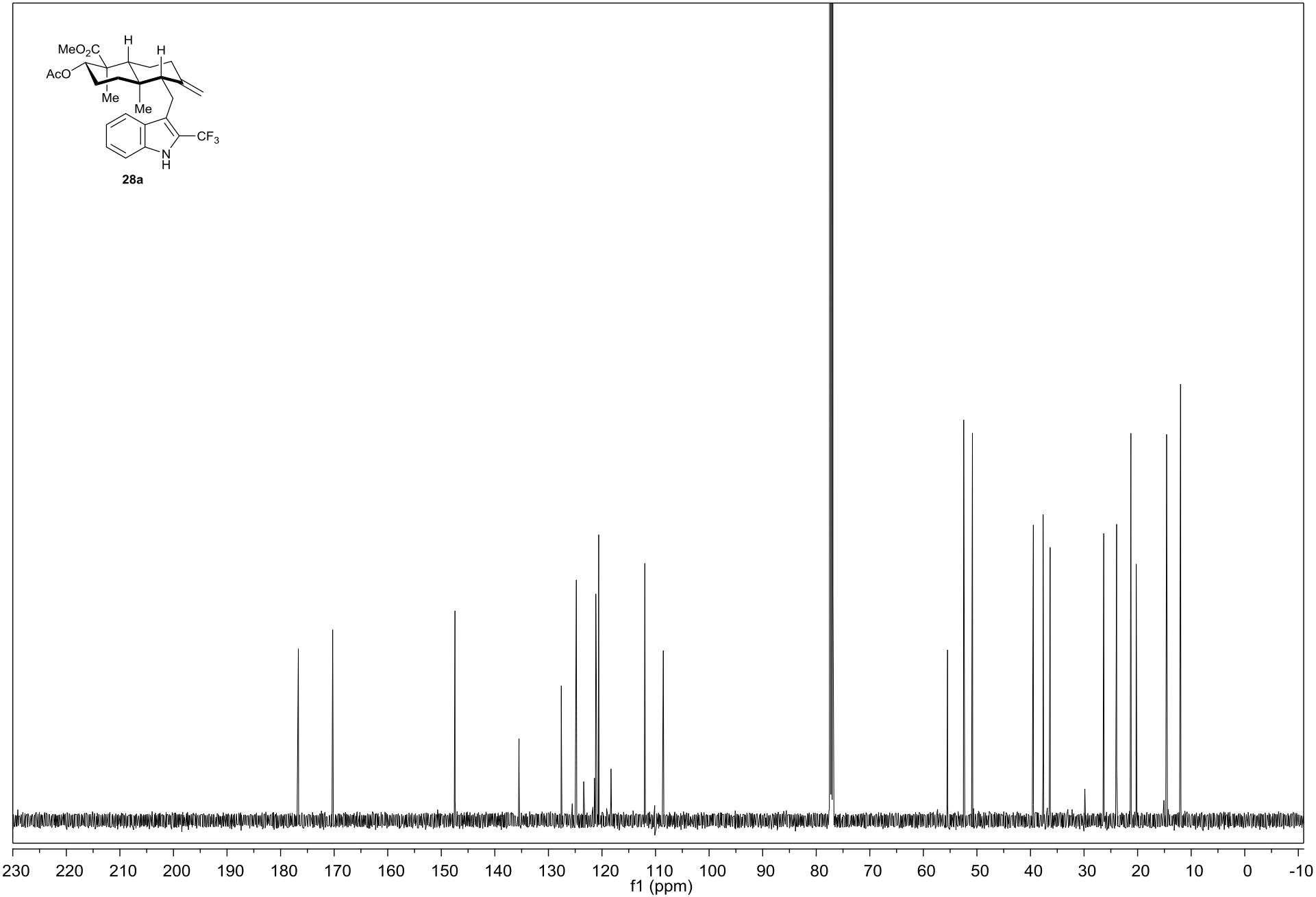
^{13}C NMR Spectrum of 27 (126 MHz, $CDCl_3$)



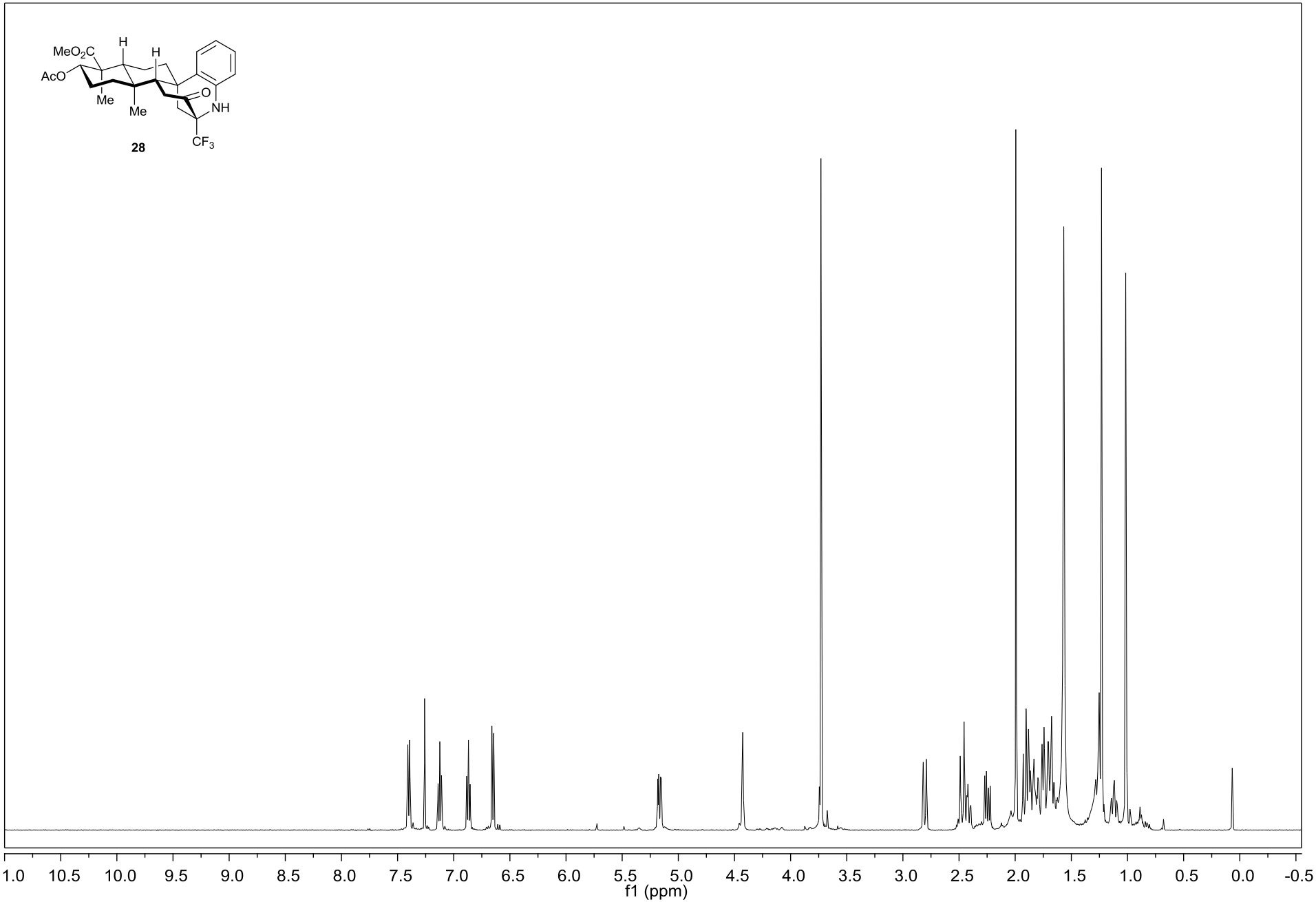
^{1}H NMR Spectrum of 28a (500 MHz, $CDCl_3$)



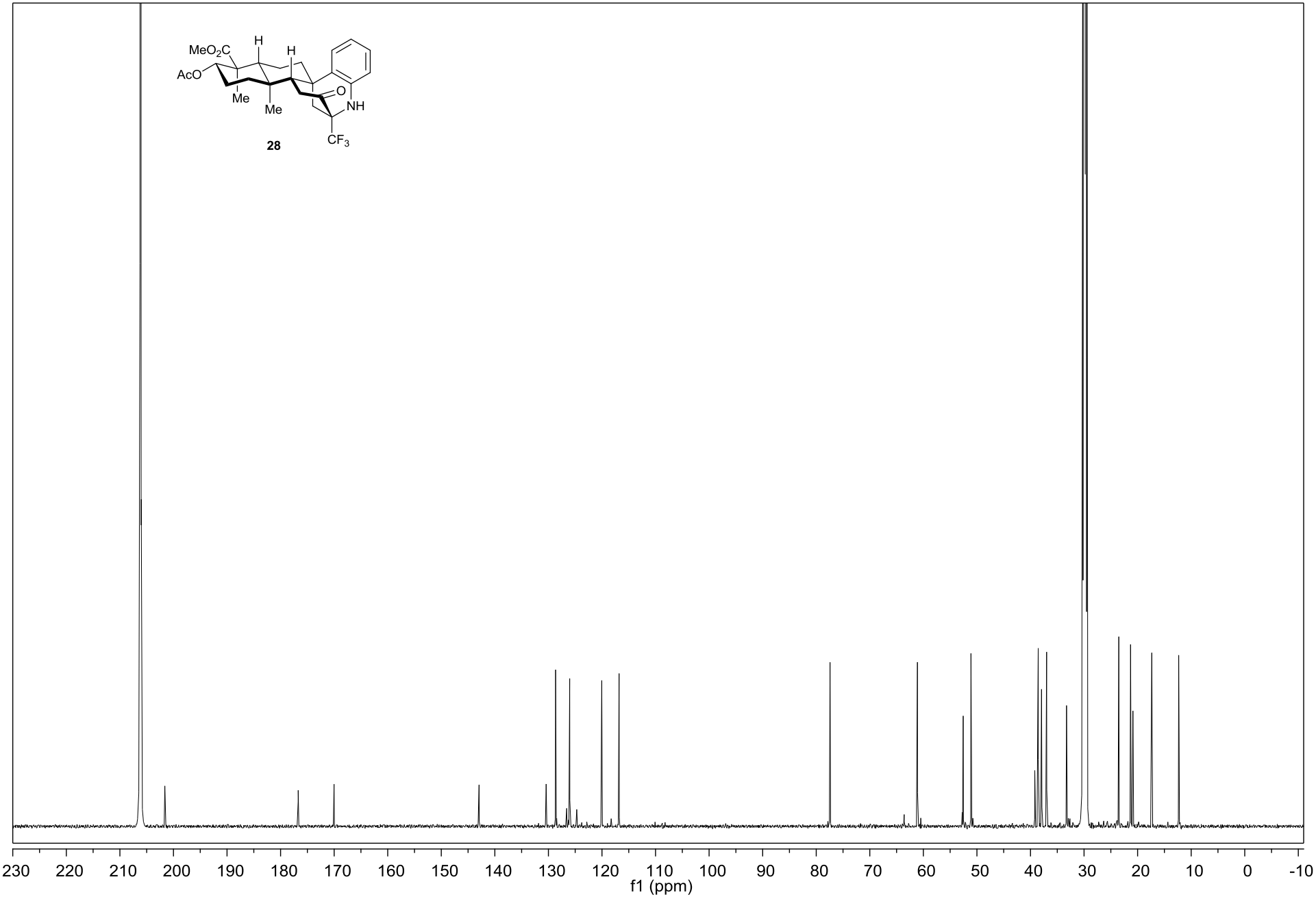
^{13}C NMR Spectrum of 28a (126 MHz, $CDCl_3$)



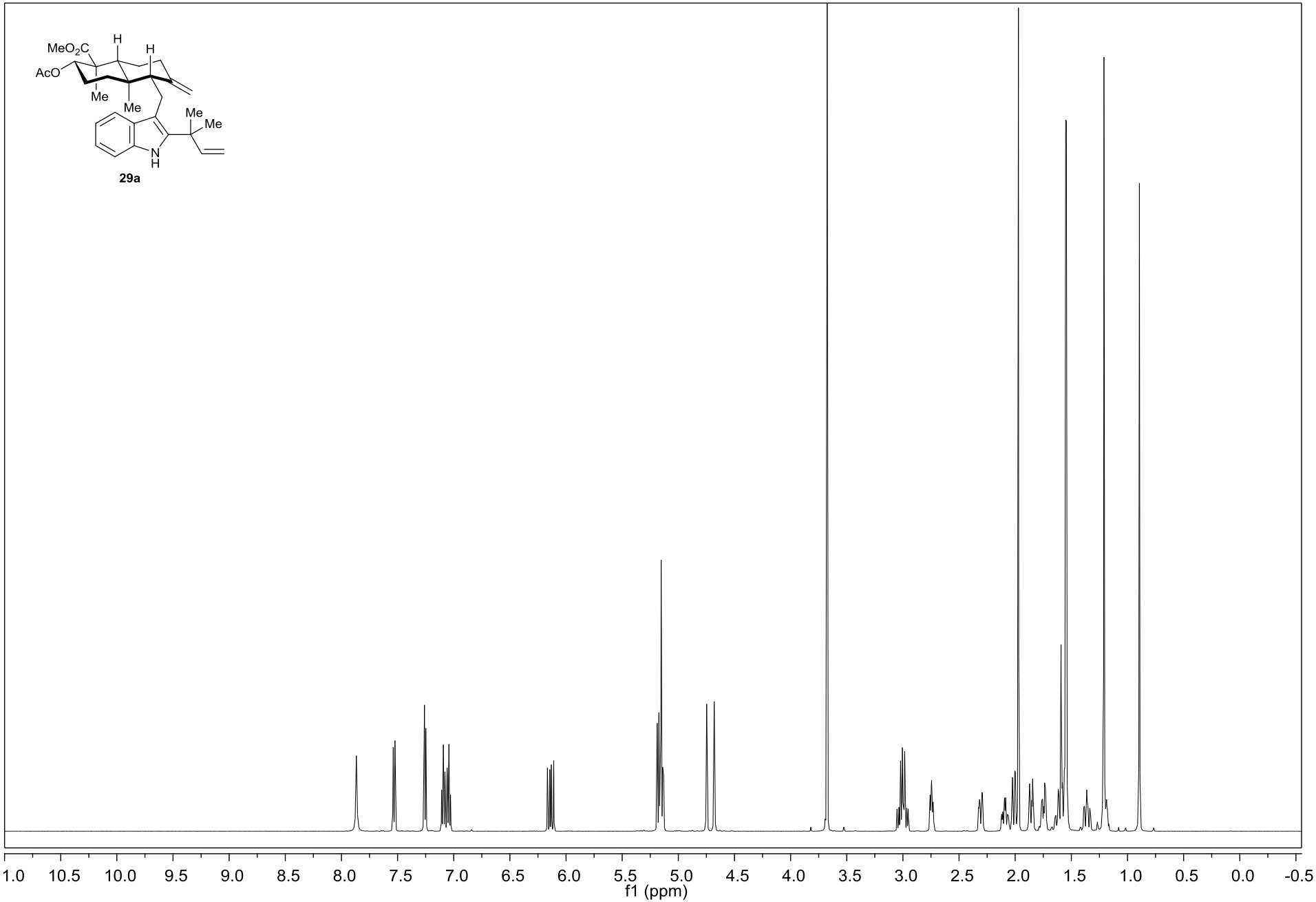
^{1}H NMR Spectrum of 28 (500 MHz, $CDCl_3$)



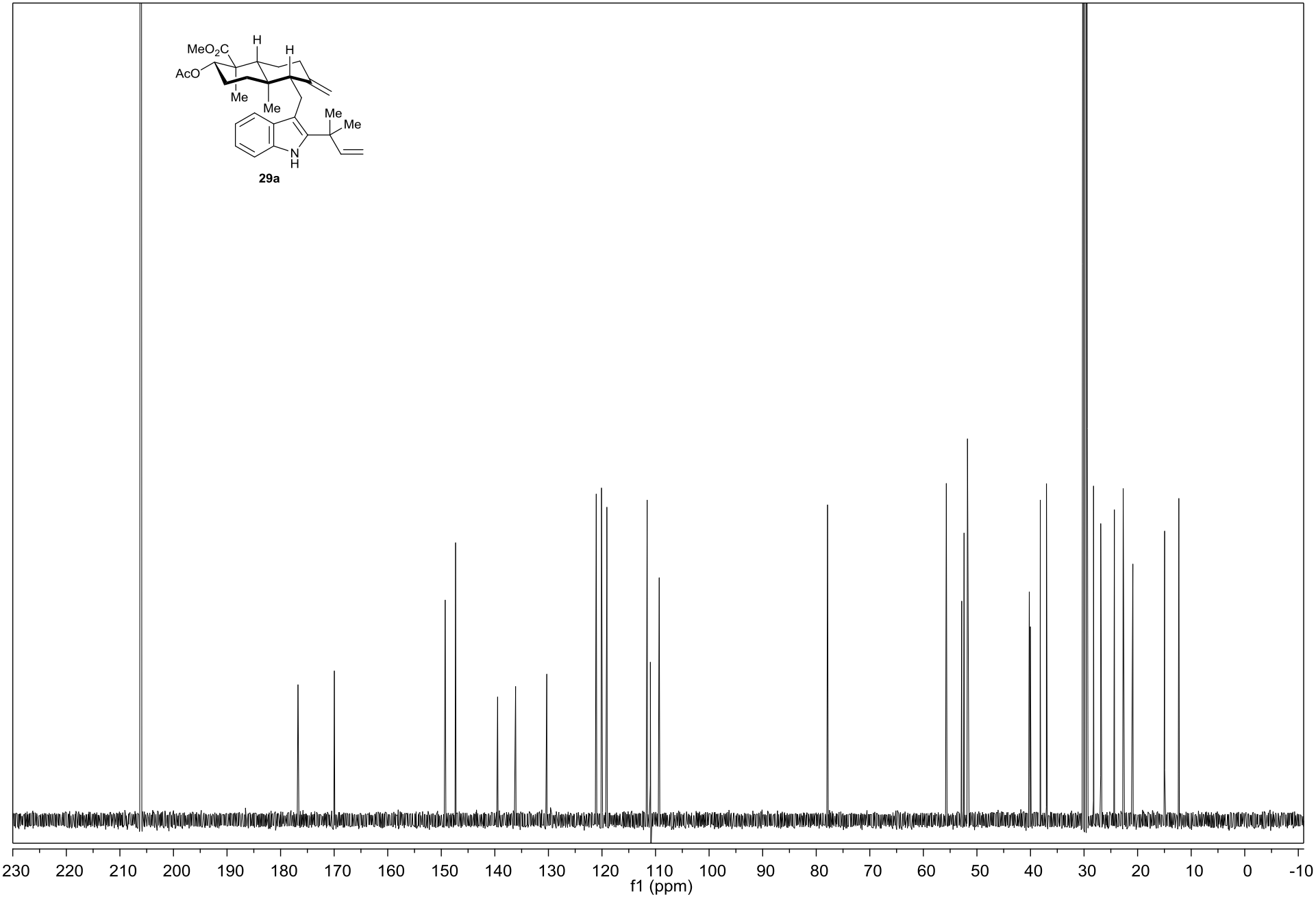
^{13}C NMR Spectrum of 28 (151 MHz, acetone-d_6)



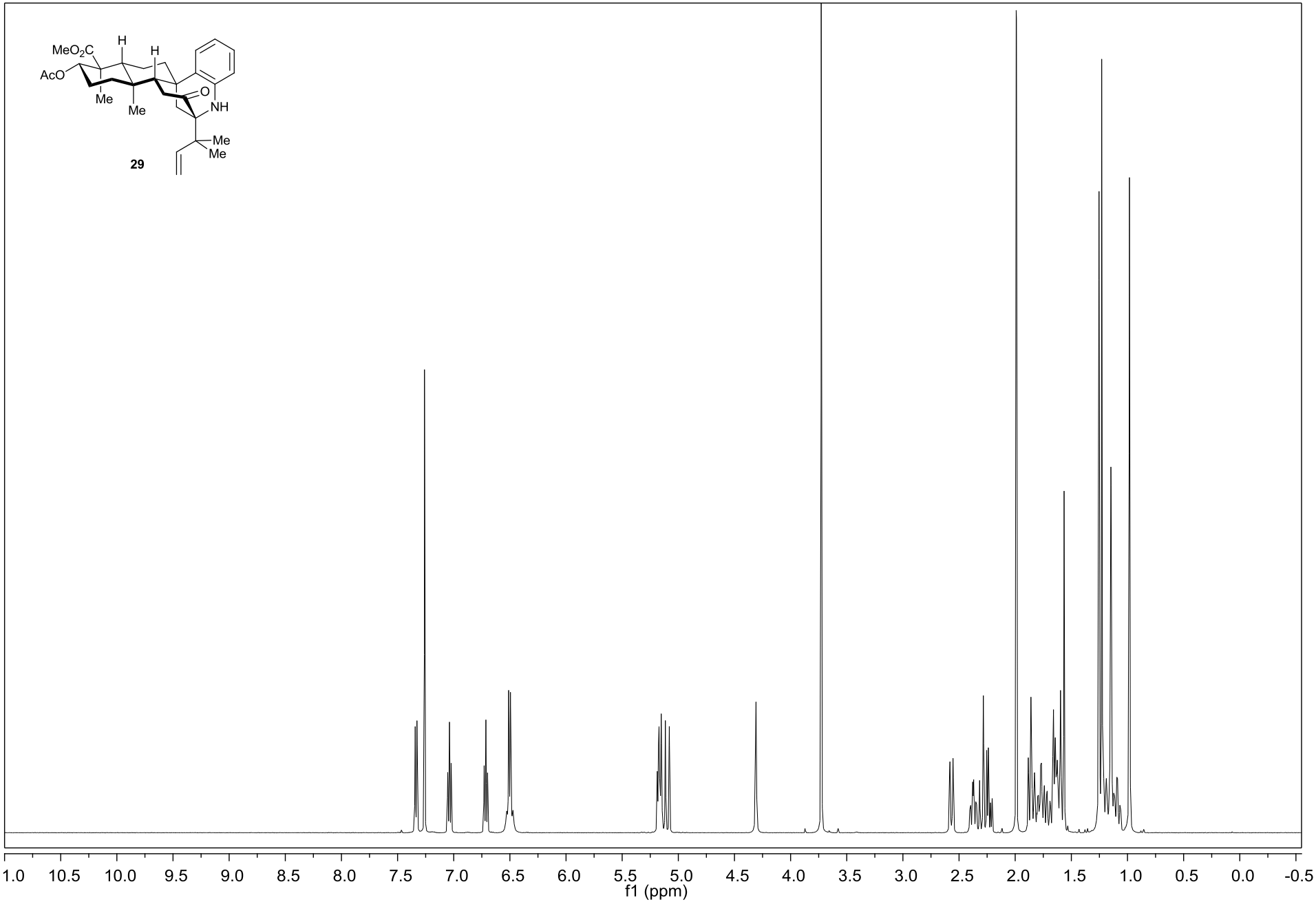
^{1}H NMR Spectrum of 29a (500 MHz, $CDCl_3$)



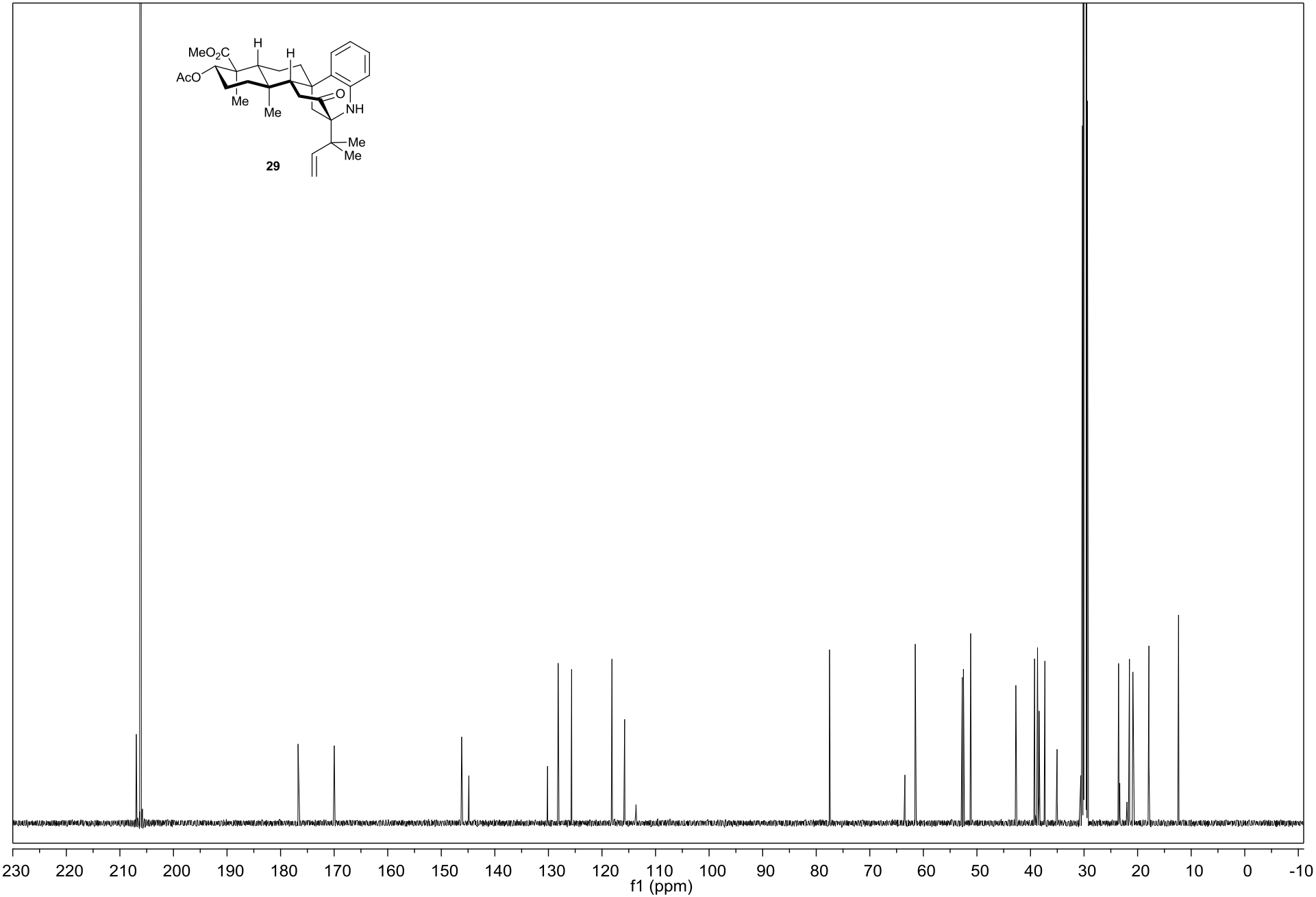
^{13}C NMR Spectrum of 29a (126 MHz, acetone-d_6)



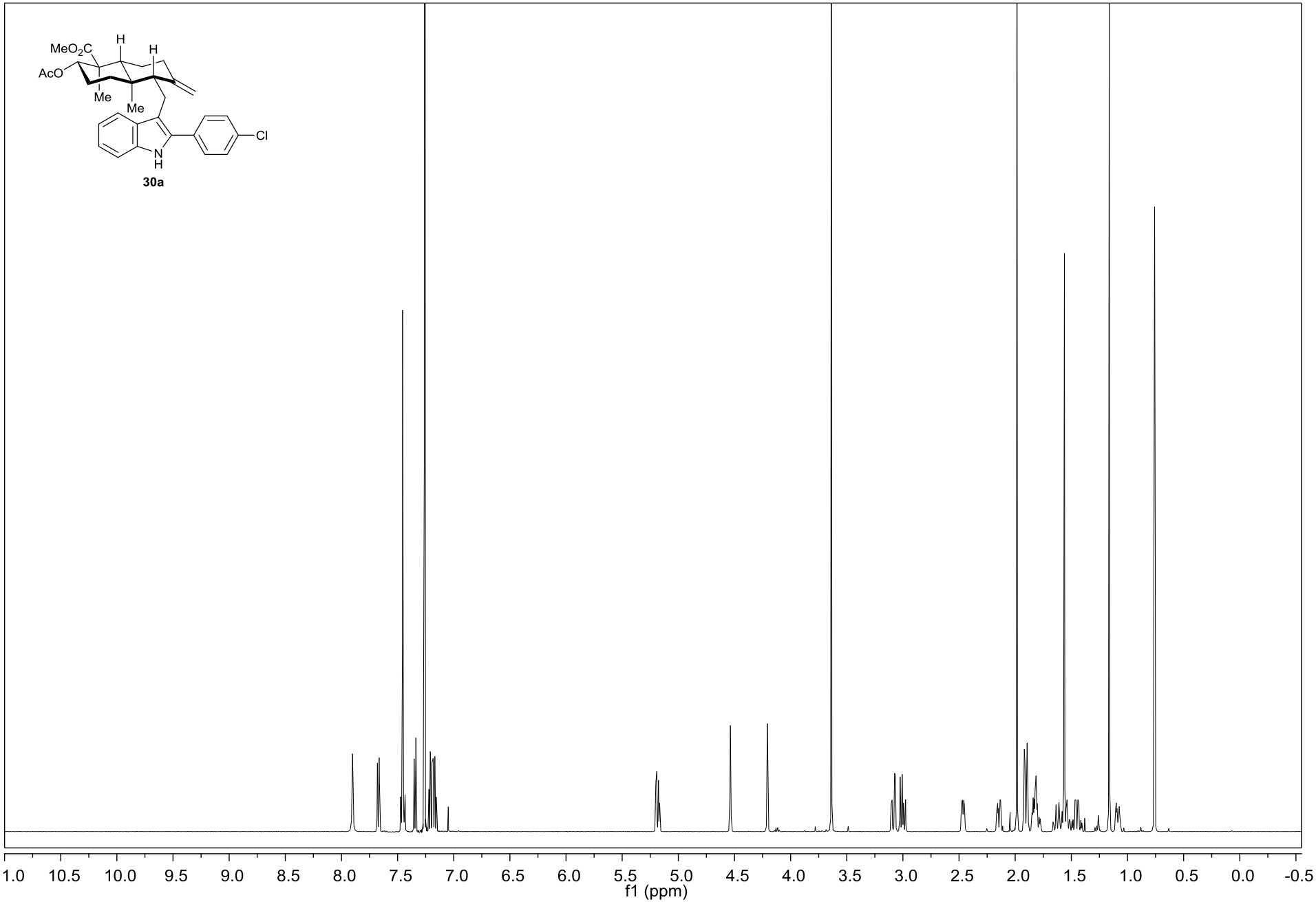
^{1}H NMR Spectrum of 29 (500 MHz, $CDCl_3$)



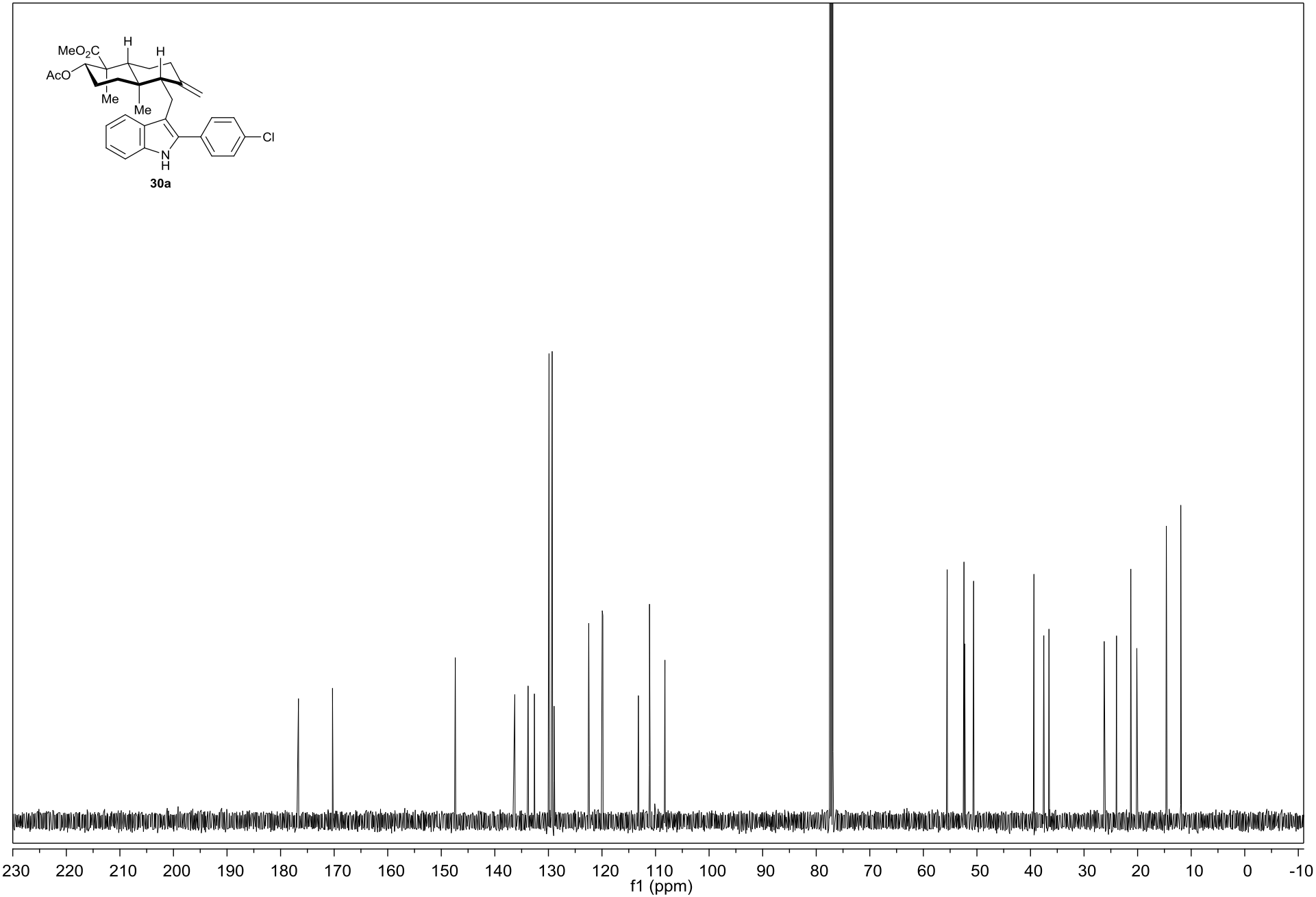
^{13}C NMR Spectrum of 29 (126 MHz, acetone-d_6)



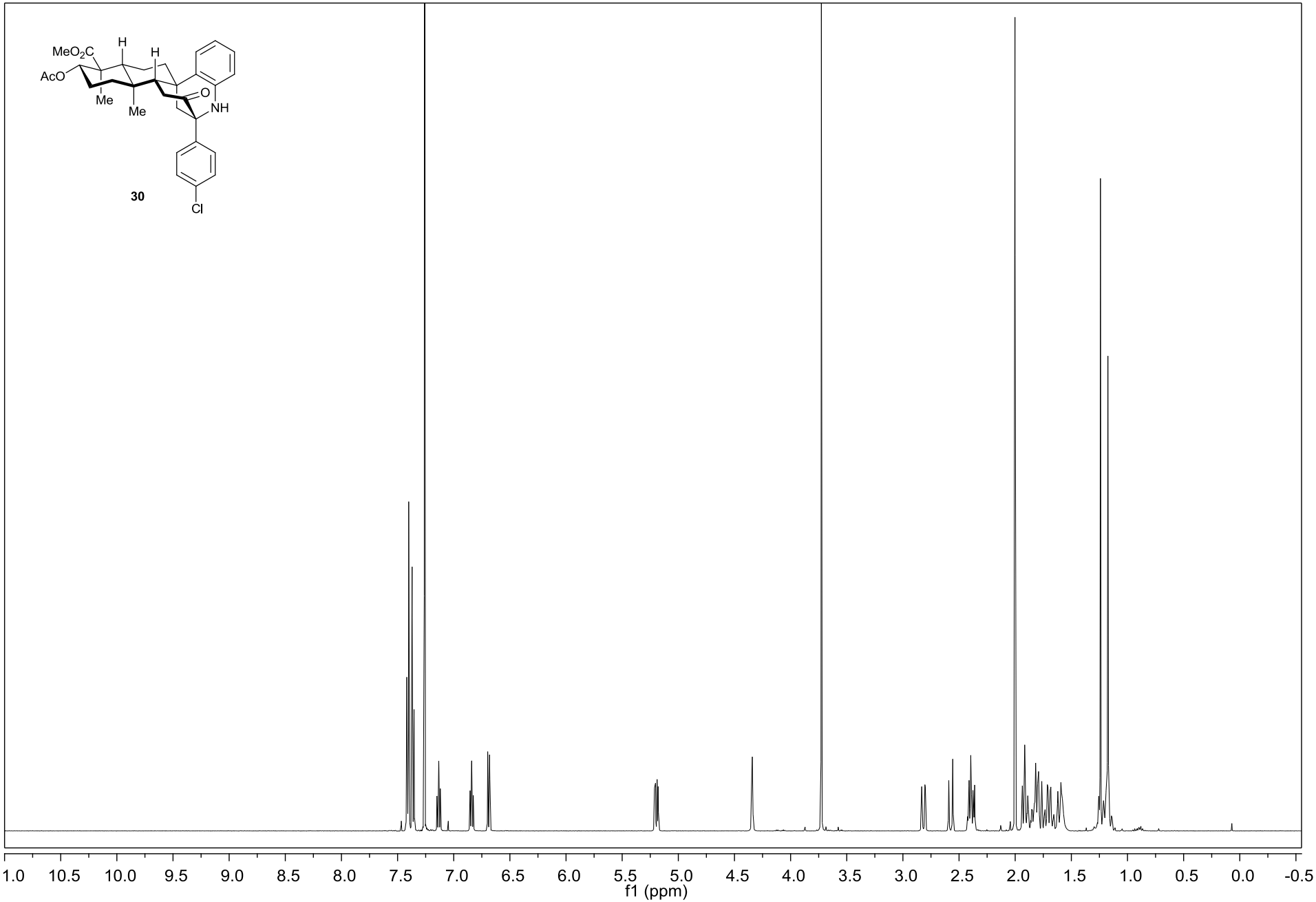
^{1}H NMR Spectrum of 30a (500 MHz, $CDCl_3$)



^{13}C NMR Spectrum of 30a (126 MHz, $CDCl_3$)



^{1}H NMR Spectrum of 30 (500 MHz, $CDCl_3$)



^{13}C NMR Spectrum of 30 (126 MHz, $CDCl_3$)