

13-Step Total Synthesis of Atropurpuran

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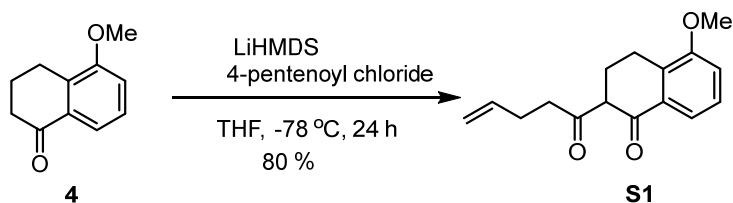
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I	Experimental Procedures and Spectroscopic Data of Compounds	S2
II	References	S13
III	¹H and ¹³C NMR Spectra of Compounds	S14
IV	Comparison of NMR Data of Natural and Synthetic Atropurpuran	S40

I. Experimental Procedures and Spectroscopic Data of Compounds:

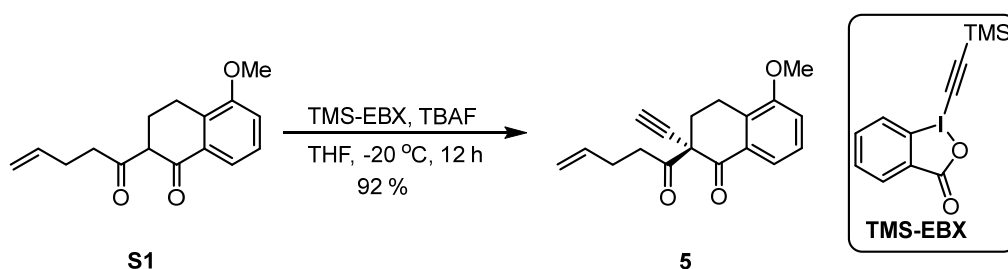
General information

Unless otherwise mentioned, all reactions were conducted under a nitrogen atmosphere and anhydrous conditions. Tetrahydrofuran (THF) was distilled from sodium benzophenone under an argon atmosphere. Dichloromethane (DCM) was distilled from calcium hydride. Reactions were monitored by thin-layer chromatography (TLC; GF254) using plates supplied by Yantai Chemicals (China) and visualized under UV or by staining with an ethanolic solution of phosphomolybdic acid, cerium sulfate, basic KMnO₄ solution, or iodine. Flash column chromatography was performed using silica gel (particle size, 0.040–0.063 mm). NMR spectra were recorded on a Bruker AV400 or AV600 MHz instrument and calibrated using residual undeuterated chloroform in CDCl₃ (δ H = 7.26 ppm, δ C = 77.0 ppm) or MeOD-*d*₄ (δ H = 3.31 ppm, δ C = 49.0 ppm) as an internal reference. The following abbreviations were used to describe signal multiplicities: s, singlet; d, doublet; t, triplet; dt, double triplet; dq, double quartet; ddd, doublet of double doublet; ddt, doublet of double triplet; m, multiplet. High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific Q Exactive Hybrid Quadrupole Orbitrap mass spectrometer.



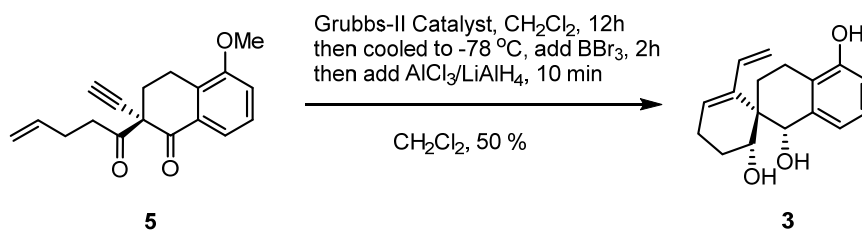
Compound S1: To a stirred solution of 5-methoxytetralone (35.2 g, 200 mmol) in THF (500 mL) were at $-78\text{ }^{\circ}\text{C}$, LiHMDS (240 mL, 240 mmol, 1.0 mol/L in THF) was added and the reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 1 h. Then a solution of 4-pentenoyl chloride (33.2 mL, 300 mmol) in dry THF (50 mL) was added within 10 minutes. The reaction was stirred at the same temperature for 24 h and quenched with saturated aqueous NH_4Cl (100 mL) and extracted with ethyl acetate ($3 \times 200\text{ mL}$), and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , concentrated in reduced pressure. The residue was purified by column chromatography (ethyl acetate/petroleum ether = 1:20) to give the desired product **S1** (41.3 g, 80%) as a yellow oil.

Compound S1: $R_f = 0.51$ (silica, ethyl acetate/petroleum ether 1:10); ^1H NMR (400 MHz, CDCl_3): $\delta = 7.54$ (d, $J = 7.6\text{ Hz}$, 1H), 7.23 (t, $J = 8.0\text{ Hz}$, 1H), 6.93 (d, $J = 7.9\text{ Hz}$, 1H), 5.87 (ddt, $J = 16.8, 10.2, 6.5\text{ Hz}$, 1H), 5.09–4.98 (m, 2H), 3.81 (s, 3H), 2.82 (t, $J = 7.5\text{ Hz}$, 2H), 2.57 (dt, $J = 18.5, 7.1\text{ Hz}$, 4H), 2.44–2.38 (m, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3): $\delta = 196.2, 176.3, 155.8, 137.2, 132.1, 129.2, 127.0, 117.9, 115.4, 113.5, 105.5, 55.6, 35.7, 28.9, 21.7, 20.5\text{ ppm}$; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{19}\text{O}_3^+$ 259.1329; found 259.1326.



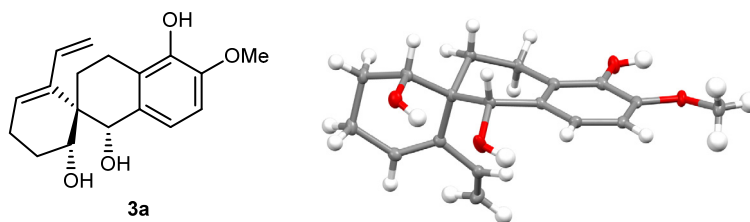
Compound 5¹: To a stirred solution of compound **S1** (20 g, 77.4 mmol) and TMS-EBX (53.3 g, 154 mmol) in THF (300 mL) at $-78\text{ }^{\circ}\text{C}$ was added TBAF (155 mL, 155 mmol, 1.0 mol/L in THF) dropwise. The reaction mixture was stirred for 12 h at $-20\text{ }^{\circ}\text{C}$, quenched with aqueous NH_4Cl and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The crude oil was purified by column chromatography (ethyl acetate/petroleum ether = 1:15) to give **5** (20.1 g, 92%) as brown oil.

Compound 5: R_f = 0.42 (silica, ethyl acetate/petroleum ether 1:10); ^1H NMR (400 MHz, CDCl_3): δ = 7.62 (d, J = 7.9 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 7.04 (d, J = 8.1 Hz, 1H), 5.84 (ddt, J = 16.8, 10.2, 6.5 Hz, 1H), 5.10–4.93 (m, 2H), 3.86 (s, 3H), 3.04 (qd, J = 9.7, 8.6, 5.0 Hz, 4H), 2.66 (ddd, J = 14.4, 9.3, 5.6 Hz, 1H), 2.48 (s, 1H), 2.38 (q, J = 7.1 Hz, 2H), 2.24 (dt, J = 13.8, 4.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 204.3, 191.9, 156.5, 136.9, 132.5, 131.3, 127.1, 119.8, 115.2, 114.8, 79.2, 75.8, 58.6, 55.7, 40.1, 30.5, 27.6, 19.5 ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{19}\text{O}_3^+$ 283.1329; found 283.1326.

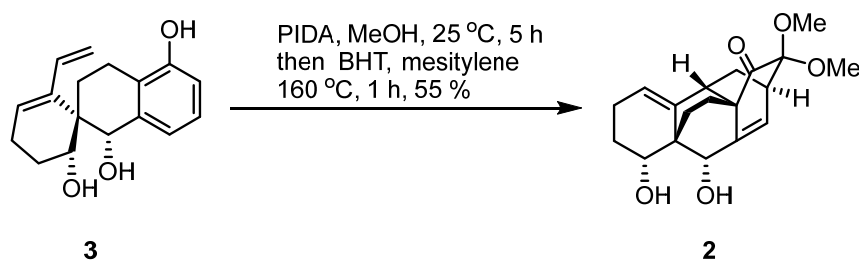


Compound 3: To a solution of **5** (5.0 g, 17.7 mmol) in dry CH_2Cl_2 (500 mL) at room temperature, the Grubbs second-generation catalyst (0.73 g, 0.86 mmol) was added. After 12 h, the reaction mixture was cooled to $-78\text{ }^\circ\text{C}$ and BBr_3 (35.4 mL, 35.4 mmol, 1.0 M in DCM) was added dropwise and the reaction mixture was stirred for 2 h, monitored by TLC (ethyl acetate/petroleum ether 1:2). To the resulting solution at $-78\text{ }^\circ\text{C}$ was added the mixture of AlCl_3 (2.66 g, 20 mmol) in dry DCM (100 mL) and LiAlH_4 (24 mL, 24 mmol, 1.0 M in THF) which was freshly prepared at $0\text{ }^\circ\text{C}$. After 10 min, the reaction mixture was then quenched carefully with saturated aqueous NaHCO_3 (100 mL), allowed to warm to ambient temperature, filtered, concentrated and purified by column chromatography (ethyl acetate/petroleum ether 1:4) to afford compound **3** (2.4 g, 50%) as a white solid.

Compound 3: R_f = 0.21 (silica, ethyl acetate/petroleum ether 1:2); ^1H NMR (400 MHz, $\text{MeOD}-d_4$): δ = 7.00 (d, J = 7.9 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.40 (dd, J = 17.0, 10.6 Hz, 1H), 5.93 (t, J = 3.7 Hz, 1H), 5.19 (dd, J = 17.0, 2.4 Hz, 1H), 4.69 (dd, J = 10.6, 2.4 Hz, 1H), 4.60 (s, 1H), 3.81 (dd, J = 6.8, 2.6 Hz, 1H), 2.86–2.79 (m, 1H), 2.65–2.56 (m, 1H), 2.23 (dq, J = 10.3, 6.7, 6.0 Hz, 2H), 1.96 (dt, J = 11.0, 5.3 Hz, 2H), 1.85–1.71 (m, 2H) ppm; ^{13}C NMR (100 MHz, $\text{MeOD}-d_4$): δ = 155.3, 142.4, 141.8, 141.5, 127.4, 125.2, 125.1, 120.9, 114.0, 112.6, 74.6, 69.0, 46.2, 26.4, 25.2, 23.3, 21.1 ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{21}\text{O}_3^+$ 273.1485; found 273.1484.

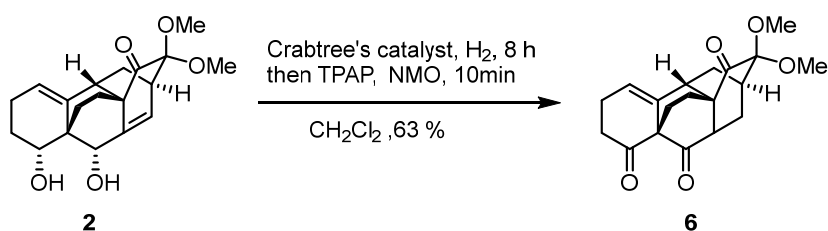


The relative stereochemistries of compound **3** was unambiguously confirmed via a single crystal X-ray diffraction of analogue compound **3a** (see below, the synthesis detail of **3a** will be published elsewhere). Subjecting compound **3a** to oxidative dearomatization/IMDA condition afforded compound **2**, too. The CCDC number of compound **3a** is CCDC 1890387.



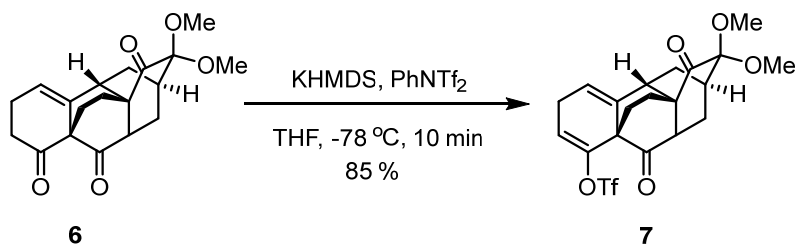
Compound 2: To a solution of **3** (2.0 g, 7.3 mmol) in MeOH (60 mL) was added iodobenzene diacetate (3.5 g, 11.0 mmol) at 25 °C, and the resulting mixture was stirred at the same temperature for 5 h. After removal of methanol, a mixture of the crude residue and BHT (8.0 g, 36.5 mmol) in mesitylene (120 mL) was heated at 160 °C for 1 h. Upon cooling to room temperature, the mixture was directly subjected to flash column chromatography on silica gel (ethyl acetate/petroleum ether = 1:4) to afford compound **2** (1.34 g, 55%) as a yellow solid.

Compound 2: R_f = 0.22 (silica, ethyl acetate/petroleum ether 1:2); ^1H NMR (600 MHz, CDCl_3): δ = 6.25 (d, J = 6.5 Hz, 1H), 5.42 (d, J = 5.5 Hz, 1H), 4.83 (s, 1H), 3.55–3.50 (m, 1H), 3.36 (s, 3H), 3.29 (s, 3H), 2.78 (s, 1H), 2.51–2.41 (m, 2H), 2.33 (t, J = 11.8 Hz, 1H), 2.22 (s, 1H), 2.13 (d, J = 17.7 Hz, 1H), 2.03–1.94 (m, 3H), 1.89–1.77 (m, 2H), 1.54 (d, J = 12.7 Hz, 1H), 1.37–1.23 (m, 2H) ppm; ^{13}C NMR (150 MHz, CDCl_3): δ = 204.6, 146.7, 143.1, 124.3, 123.0, 95.4, 76.0, 53.4, 51.3, 50.5, 49.3, 46.9, 41.7, 35.2, 30.3, 30.0, 24.3, 18.2 ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{25}\text{O}_5^+$ 333.1697; found 333.1695.



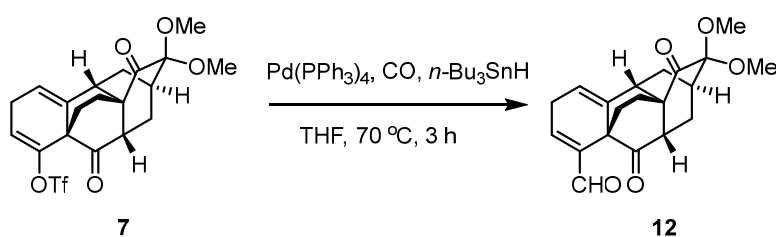
Compound 6: A flame-dried flask was charged with compound **2** (650 mg, 1.96 mmol) and Crabtree's catalyst (78.6 mg 0.1 mmol) in CH₂Cl₂ (60 mL). The flask was vacuumed and backfilled with hydrogen (balloon pressure) and the reaction mixture was stirred at room temperature for 8 h. Then to the resulting mixture were sequentially added TPAP (137.8 mg, 0.39 mmol) and NMO (1.14 g, 9.8 mmol) at the same temperature for 10 min. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (ethyl acetate/petroleum ether = 1:5) to give **6** (408 mg, 63%) as yellow oil.

Compound 6: R_f = 0.51 (silica, ethyl acetate/petroleum ether 1:3); ¹H NMR (400 MHz, CDCl₃): δ = 5.84 (d, J = 3.0 Hz, 1H), 3.34–3.28 (m, 6H), 2.76 (d, J = 11.2 Hz, 1H), 2.52 (td, J = 13.6, 11.0, 6.8 Hz, 4H), 2.43–2.30 (m, 5H), 1.86 (ddd, J = 25.4, 14.4, 5.8 Hz, 3H), 1.73 (d, J = 3.8 Hz, 1H), 1.60 (d, J = 15.8 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ = 210.9, 207.4, 205.5, 143.3, 123.9, 96.9, 61.7, 49.9, 49.8, 47.7, 45.3, 38.6, 36.9, 33.9, 32.2, 25.8, 24.9, 23.9, 20.9 ppm; HRMS-ESI (m/z): [M+H]⁺ calcd for C₁₉H₂₃O₅⁺ 331.1540; found 331.1539.



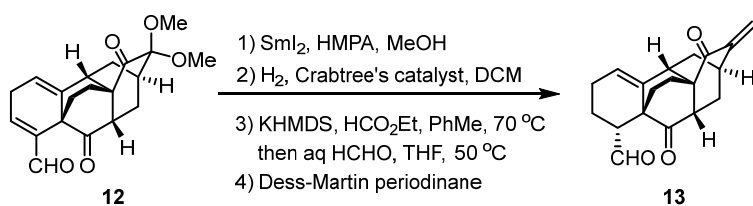
Compound 7: To a solution of **6** (280 mg, 0.848 mmol) and PhNTf₂ (605.9 mg, 1.70 mmol) in dry THF (20 mL) at –78 °C was added KHMDS (1.0 M in THF, 1.02 mL, 1.02 mmol) and the reaction mixture was stirred at this temperature for 10 min, before get quenched with saturated NH₄Cl solution and warmed up to room temperature. The mixture was extracted with ethyl acetate (3×20 mL) and the combined organic layers were dried over Na₂SO₄. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1:5) to yield as a colorless oil **7** (333 mg, 85%).

Compound 7: $R_f = 0.59$ (silica, ethyl acetate/petroleum ether 1:3) ^1H NMR (400 MHz, CDCl_3): $\delta = 5.91$ (t, $J = 3.8$ Hz, 1H), 5.58 (s, 1H), 3.32 (d, $J = 6.8$ Hz, 6H), 2.97 (s, 2H), 2.78 (d, $J = 8.2$ Hz, 1H), 2.48 (dd, $J = 11.7, 3.1$ Hz, 2H), 2.34–2.21 (m, 3H), 2.06–1.95 (m, 3H), 1.83 (dd, $J = 14.4, 5.5$ Hz, 1H), 1.43–1.38 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3): $\delta = 209.6, 205.4, 145.8, 140.8, 119.4, 116.3, 96.9, 53.0, 50.1, 49.7, 47.0, 45.3, 36.9, 33.8, 31.8, 27.1, 26.9, 25.5, 21.1$ ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{22}\text{F}_3\text{O}_7\text{S}^+$ 463.1033; found 463.1020; $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{21}\text{F}_3\text{NaO}_7\text{S}^+$ 485.0852; found 485.0838.



Compound 12: A stirred solution of flame-dried LiCl (183.3 mg, 4.32 mmol) and triflate **7** (100 mg, 0.216 mmol) was purged with carbon monoxide for 30 min followed by addition of $\text{Pd(PPh}_3)_4$ (25.0 mg, 0.022 mmol). The mixture was heated to 70 °C and treated with a solution of tributyltin hydride (68.1 μL , 0.259 mmol) in THF (5 mL) *via* syringe over 3 h while bubbling carbon monoxide through the reaction mixture. After addition was complete, the mixture was cooled to room temperature, diluted with diethyl ether (30 mL), washed with brine (3 \times 10 mL), dried with Na_2SO_4 . The crude oil was purified by column chromatography (ethyl acetate/petroleum ether = 1:5) to give aldehyde **12** (46 mg, 62%) as a white solid.

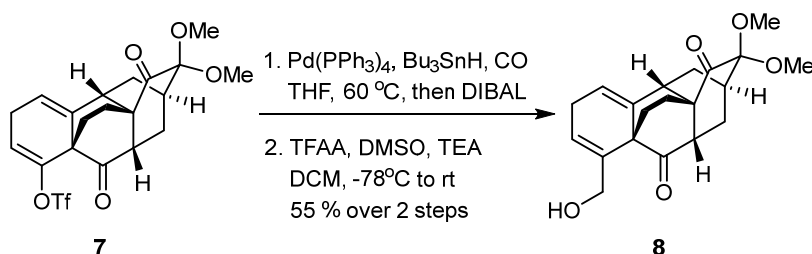
Compound 12: $R_f = 0.21$ (silica, ethyl acetate/petroleum ether 1:2); ^1H NMR (400 MHz, CDCl_3): $\delta = 9.46$ (s, 1H), 6.91 (td, $J = 3.5, 1.4$ Hz, 1H), 5.54 (s, 1H), 3.31 (s, 3H), 3.30 (s, 3H), 3.04 (dt, $J = 3.5, 1.7$ Hz, 2H), 2.72–2.65 (m, 1H), 2.54–2.47 (m, 1H), 2.47–2.38 (m, 1H), 2.32–2.27 (m, 1H), 2.17–2.11 (m, 2H), 2.10–2.01 (m, 1H), 1.74–1.65 (m, 2H), 1.28–1.23 (m, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3): $\delta = 210.8, 205.7, 192.1, 149.2, 142.5, 139.0, 117.6, 97.0, 50.7, 50.2, 49.4, 47.4, 45.6, 37.3, 33.7, 31.4, 28.0, 27.5, 25.1, 21.4$ ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{23}\text{O}_5^+$ 343.1540; found 343.1528.



Compound 13: To a vigorously degassed solution of aldehyde **12** (350 mg, 1.02 mmol) in THF (20 mL) and HMPA (1.0 mL), SmI_2 (81.6 mL, 8.16 mmol, 0.1 M in THF) was added dropwise at room temperature and stirred for 15 min. Then the reaction was quenched with saturated sodium potassium tartrate solution (100 mL) and kept stirring for 2 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3×80 mL), washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Then the residue and Crabtree's catalyst (41 mg, 0.05 mmol) in CH_2Cl_2 (60 mL) were charged in a flame-dried flask. The flask was vacuumed and backfilled with hydrogen (balloon pressure) and the reaction mixture was stirred at room temperature for 1 h. The solution was evaporated under reduced pressure and the resulting residue was used directly in the next step. To a solution of the above residue and ethyl formate (4.1 mL, 51 mmol) in toluene (30 mL) was added KHMDS (0.5 M in toluene, 61.3 μL , 29.1 mmol) at room temperature, and the reaction mixture was set at 70 $^\circ\text{C}$. After stirring for 16 h, the reaction mixture was cooled to 0 $^\circ\text{C}$. To the reaction mixture, THF (20 mL) and formalin (37%, 4.3 mL) was added and the resulting mixture was set to 50 $^\circ\text{C}$. After stirring for 4 h, the reaction mixture was partitioned between ethyl acetate (3×100 mL) and aqueous NH_4Cl (150 mL). The combined organic phases were dried and concentrated. The residue was dissolved in dry CH_2Cl_2 (50 mL), to which was added Dess-Martin periodinane (665 mg, 1.57 mmol). After 1 h, the reaction was quenched with saturated solutions of NaHCO_3 (50 mL) and $\text{Na}_2\text{S}_2\text{O}_3$ (50 mL), and extracted with CH_2Cl_2 (3×50 mL). The organic layers were washed by brine, dried and filtered. After removal of the solvent, the residue was purified via flash column chromatography on silica gel (ethyl acetate/petroleum ether = 1:10) to yield **13** (90.2 mg, 30% over four steps)

Compound 13: R_f = 0.62 (silica, ethyl acetate/petroleum ether 1:5); ^1H NMR (400 MHz, CDCl_3): δ = 9.76 (s, 1H), 6.01 (d, J = 1.5 Hz, 1H), 5.60 (d, J = 5.1 Hz, 1H), 5.24 (d, J = 1.4 Hz, 1H), 3.28 (dd, J = 12.9, 2.6 Hz, 1H), 2.80 (dd, J = 3.8, 1.9 Hz, 1H), 2.57 (d, J = 5.1 Hz, 1H), 2.52 (dt, J = 11.9, 2.6 Hz, 1H), 2.32–2.22 (m, 2H), 2.20–2.06 (m, 3H), 2.03–1.98 (m,

2H), 1.89–1.67 (m, 4H), 1.43–1.39 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 215.1, 203.1, 200.1, 146.7, 141.5, 124.4, 117.6, 51.3, 47.7, 46.5, 44.6, 38.2, 36.3, 35.5, 31.6, 24.6, 23.9, 21.8, 17.7 ppm; HRMS-ESI $a(m/z)$: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{21}\text{O}_3^+$ 297.1485; found 297.1484.

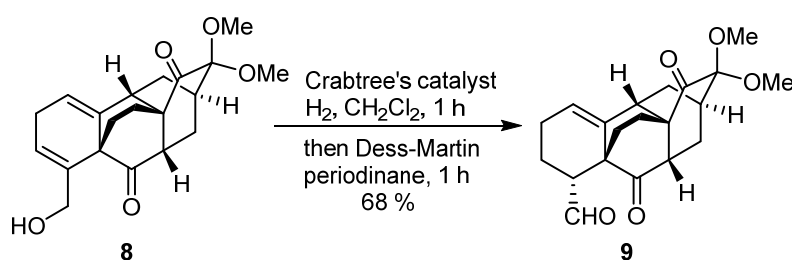


Compound 8: A stirred solution of flame-dried LiCl (183.3 mg, 4.32 mmol) and triflate **7** (100 mg, 0.216 mmol) in THF (10 mL) was purged with carbon monoxide for 30 min followed by addition of $\text{Pd(PPh}_3\text{)}_4$ (25.0 mg, 0.022 mmol). The mixture was heated to 70 °C and treated with a solution of tributyltin hydride (68.1 μL , 0.259 mmol) in THF (5 mL) via syringe over 3 h while bubbling carbon monoxide through the reaction mixture. After addition was complete, the mixture was cooled to -78°C , to which was added DIBAL (2.2 mL, 1 M in hexane) slowly and kept at this temperature for 1 h, and then quenched with saturated aqueous solution of potassium sodium tartrate tetrahydrate and then allowed to warm to room temperature. The resulting slurry was kept at room temperature for an additional 1 h. The aqueous layer was extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure to deliver crude triol compound as an oil, which was used next step without further purification.

To a solution of anhydrous DMSO (184 μL , 2.59 mmol) in dry DCM (5.0 mL) at -78°C was added trifluoroacetic acid anhydride (487 μL , 3.47 mmol). The resulting solution was maintained at -78°C for 15 min and a solution of afore-obtained triol in dry DCM (2.0 mL) was added dropwise. The reaction was kept at -78°C for 30 min and then allowed to warm to room temperature. After 0.5 h, TEA (600 μL , 4.32 mmol) was added dropwise. The resulting slurry was kept at room temperature for an additional 1 h, then the reaction was quenched with LiOH (452 mg, 10.8 mmol) in H_2O (10 mL) and kept stirring for 1.5 h and the aqueous layer was extracted with DCM (3×10 mL). The combined organic layers were dried Na_2SO_4 and concentrated, and the residue was purified by column chromatography (ethyl

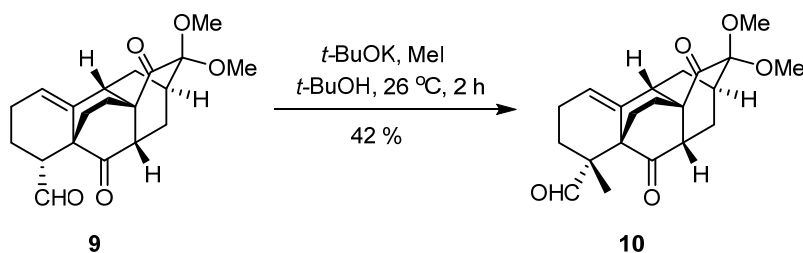
acetate/petroleum ether = 1:10 to 1:4) to give **8** (41 mg, 55 %) as a yellow oil.

Compound 8: R_f = 0.21 (silica, ethyl acetate/petroleum ether 1:2); ^1H NMR (400 MHz, CDCl_3): δ = 5.96 (s, 1H), 5.62 (s, 1H), 4.11 (d, J = 12.5 Hz, 1H), 3.99 (d, J = 12.6 Hz, 1H), 3.29 (d, J = 7.3 Hz, 6H), 2.87 (brs, 1H), 2.78–2.67 (m, 3H), 2.50–2.35 (m, 2H), 2.35–2.17 (m, 3H), 1.94 (ddt, J = 11.2, 6.8, 2.8 Hz, 2H), 1.85–1.74 (m, 2H), 1.38 (ddd, J = 13.9, 4.7, 2.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 216.2, 206.0, 140.7, 134.8, 126.1, 121.2, 96.9, 63.8, 53.2, 50.0, 49.6, 47.0, 45.6, 37.4, 33.7, 31.6, 28.4, 27.0, 25.6, 21.4 ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{O}_5^+$ 345.1697; found 345.1685.



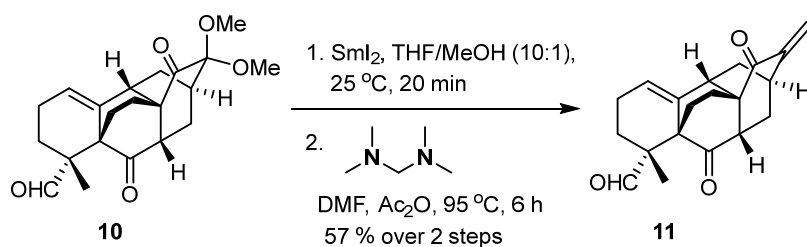
Compound 9: A flame-dried flask was charged with compound **8** (34 mg, 0.099 mmol) and Crabtree's catalyst (4 mg 0.005 mmol) in CH_2Cl_2 (5 mL). The flask was vacuumed and backfilled with hydrogen (balloon pressure) and the reaction mixture was stirred at room temperature for 1 h. Then to the resulting mixture were sequentially added Dess-Martin periodinane (84.1 mg, 0.198 mmol), and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was cooled to 0 °C, saturated $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL) solution was added. The resulting mixture was stirred 30 min and layers were separated. The aqueous layer was extracted with ethyl acetate (2×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered and concentrated. The residue was purified by column chromatography (ethyl acetate/petroleum ether = 1:5) to give **9** (23 mg, 68%) as yellow oil.

Compound 9: R_f = 0.21 (silica, ethyl acetate/petroleum ether 1:5); ^1H NMR (400 MHz, CDCl_3): δ = 9.71 (s, 1H), 5.58 (d, J = 4.9 Hz, 1H), 3.31 (d, J = 2.8 Hz, 6H), 3.26 (dd, J = 12.9, 2.6 Hz, 1H), 2.72–2.61 (m, 1H), 2.48 (dt, J = 10.6, 2.9 Hz, 1H), 2.41–2.29 (m, 2H), 2.23–2.04 (m, 4H), 2.04–1.93 (m, 2H), 1.88–1.75 (m, 1H), 1.75–1.60 (m, 2H), 1.55–1.45 (m, 1H), 1.20 (ddd, J = 13.6, 6.3, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 214.6, 205.6, 202.9, 141.4, 123.6, 97.2, 50.8, 50.3, 49.4, 47.5, 46.8, 45.3, 37.8, 33.6, 30.8, 25.6, 24.3, 23.8, 21.3, 17.6 ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{O}_5^+$ 345.1697; found 345.1685.



Compound 10: To compound **9** (17 mg, 0.049 mmol) in anhydrous *t*-BuOH (10 mL) was added *t*-BuOK (1.0 M in *t*-BuOH, 196 μ L , 0.196 mmol) followed by addition of iodomethane (31 μ L, 0.49 mmol) 10 minutes later. The reaction was allowed to stir at 26 $^{\circ}$ C for 2 h until TLC analysis indicated consumption of the starting material. The reaction was quenched with saturated NaHCO_3 (10 mL) solution and extracted with ethyl acetate (3 \times 10 mL). The combined organic layers were washed with saturated brine solution, dried over anhydrous Na_2SO_4 , filtered and concentrated. The residue was purified by column chromatography (ethyl acetate/petroleum ether = 1:30) to give **10** (7.5 mg, 42%) as yellow oil.

Compound 10: R_f = 0.19 (silica, ethyl acetate/petroleum ether 1:5); ^1H NMR (400 MHz, CDCl_3): δ = 9.68 (s, 1H), 5.65 (s, 1H), 3.34 (s, 3H), 3.32 (s, 3H), 2.80–2.73 (m, 1H), 2.45–2.39 (m, 1H), 2.38–2.31 (m, 2H), 2.14 (d, J = 15.7 Hz, 1H), 2.11–2.01 (m, 3H), 1.90–1.77 (m, 2H), 1.74–1.60 (m, 3H), 1.33–1.22 (m, 2H), 1.04 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 214.3, 205.6, 205.0, 141.0, 122.9, 97.3, 54.4, 50.3, 49.4, 46.9, 45.3, 45.2, 38.4, 33.5, 30.1, 29.8, 26.0, 25.8, 21.9, 21.3, 17.4 ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{27}\text{O}_5^+$ 359.1853; found 359.1849.

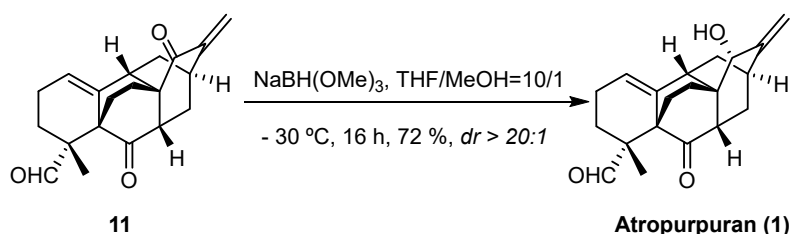


Compound 11: The compound **10** (17.5 mg, 0.049 mmol) was dissolved in anhydrous THF/MeOH (10:1, 11 mL), to which was added SmI_2 (0.1 M in THF, 196 μ L, 0.196 mmol) slowly at room temperature. The resulting mixture was stirred for 10 min before it was quenched with saturated sodium potassium tartrate solution (10 mL) and kept stirring for 1 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 \times 10

mL). The combined organic extracts were washed with brine, dried over anhydrous Na₂SO₄ and concentrated in *vacuo*.

Then the crude product was dissolved in dry DMF (0.5 mL), to which was added *N,N,N',N'*-tetramethylmethanedi-amine (0.5 mL, 3.67 mmol), acetic anhydride (0.5 mL, 6.48 mmol), and then the solution was heated to 95 °C for 6 h. The reaction mixture was cooled to room temperature, diluted with saturated NaHCO₃ (5 mL) and extracted with TBME (3×5 mL). The combined organic extracts were washed brine (5 mL), dried over anhydrous Na₂SO₄, and concentrated in *vacuo*. The crude residue was flash chromatographed (ethyl acetate /petroleum ether = 1:30 to 1:10) to afford compound **11** (8.6 mg, 57 %) as a white powder.

Compound 11: *R*_f = 0.52 (silica, acetone/petroleum ether 1:4); ¹H NMR (400 MHz, CDCl₃): δ = 9.68 (s, 1H), 6.02 (s, 1H), 5.64 (s, 1H), 5.26 (s, 1H), 2.80 (s, 1H), 2.65 (dd, *J* = 10.8, 6.1 Hz, 1H), 2.45 (d, *J* = 11.9 Hz, 1H), 2.28–2.18 (m, 2H), 2.16–1.96 (m, 4H), 1.92 (d, *J* = 8.3 Hz, 1H), 1.88–1.79 (m, 2H), 1.74–1.60 (m, 2H), 1.46 (ddd, *J* = 13.8, 6.2, 2.0 Hz, 1H), 1.06 (s, 3H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 214.6, 205.0, 200.1, 146.5, 141.1, 123.4, 117.7, 54.7, 46.6, 45.3, 44.6, 38.8, 36.2, 34.7, 31.9, 29.8, 25.9, 21.9, 21.7, 17.6 ppm; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₂₀H₂₃O₃⁺ 311.1642; found 311.1636.



Atropurpuran (1)²: To a solution of **11** (5.5 mg, 0.018 mmol) in THF/MeOH (10:1, 2.2 mL) was added NaBH(OMe)₃ (13.8 mg, 0.108 mmol) at –30 °C, and the mixture was kept stirring at the same temperature for 16 h before being quenched with saturated NH₄Cl solution. After warming to room temperature, the mixture was extracted with ethyl acetate (3×10 mL). The organic extracts were combined, washed with brine, dried with anhydrous Na₂SO₄, concentrated under vacuum. Purification by silica gel column chromatography (acetone/ petroleum ether = 1:8) gave atropurpuran **1** (4.0 mg, 72 %) as a white powder.

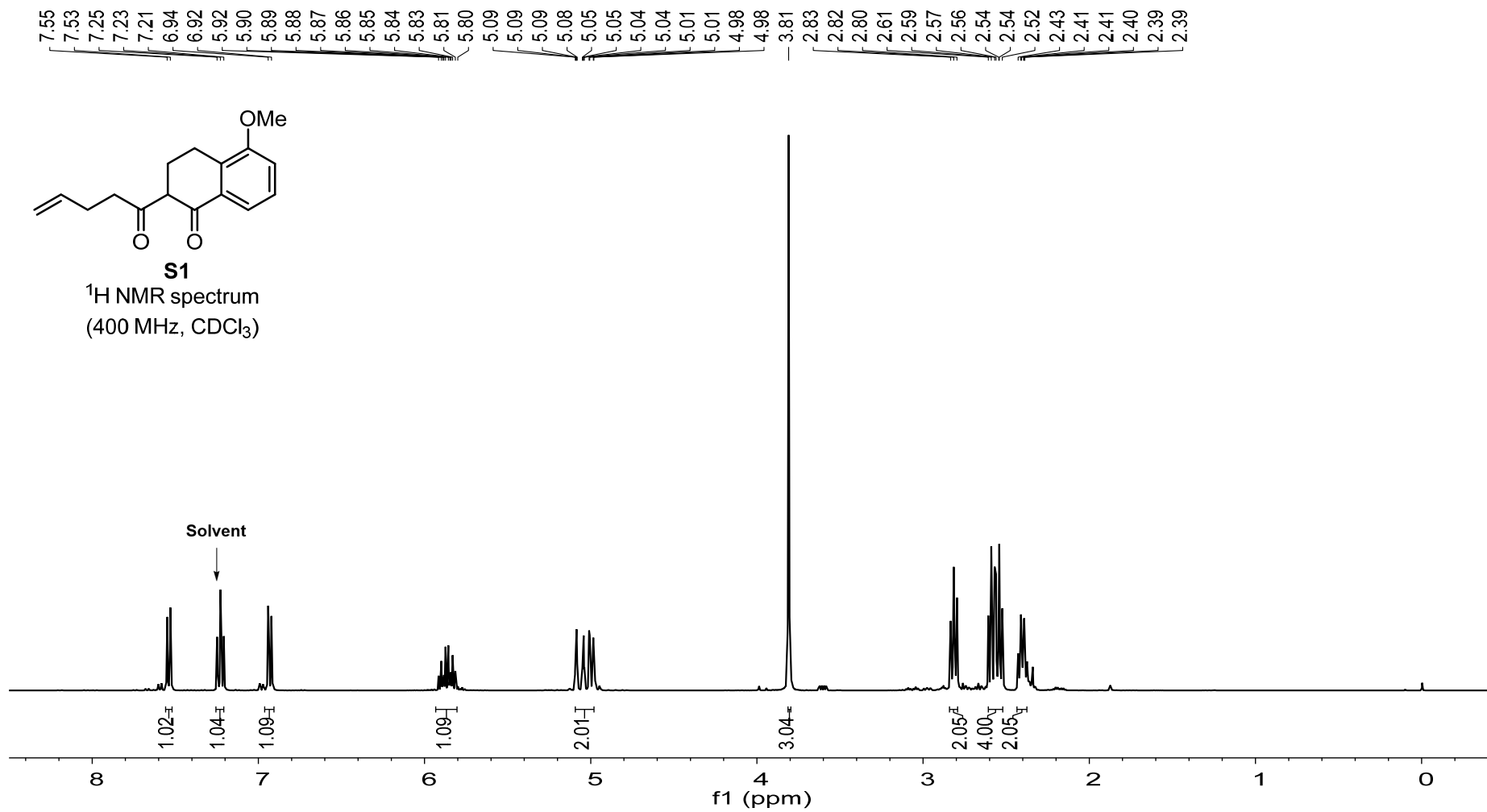
Atropurpuran (1): *R*_f = 0.27 (silica, dichloromethane/ethyl acetate/petroleum ether 3:1:3); ¹H NMR (400 MHz, CDCl₃): δ = 9.67 (s, 1H), 5.60 (s, 1H), 5.16 (s, 1H), 5.06 (s, 1H), 4.14 (s,

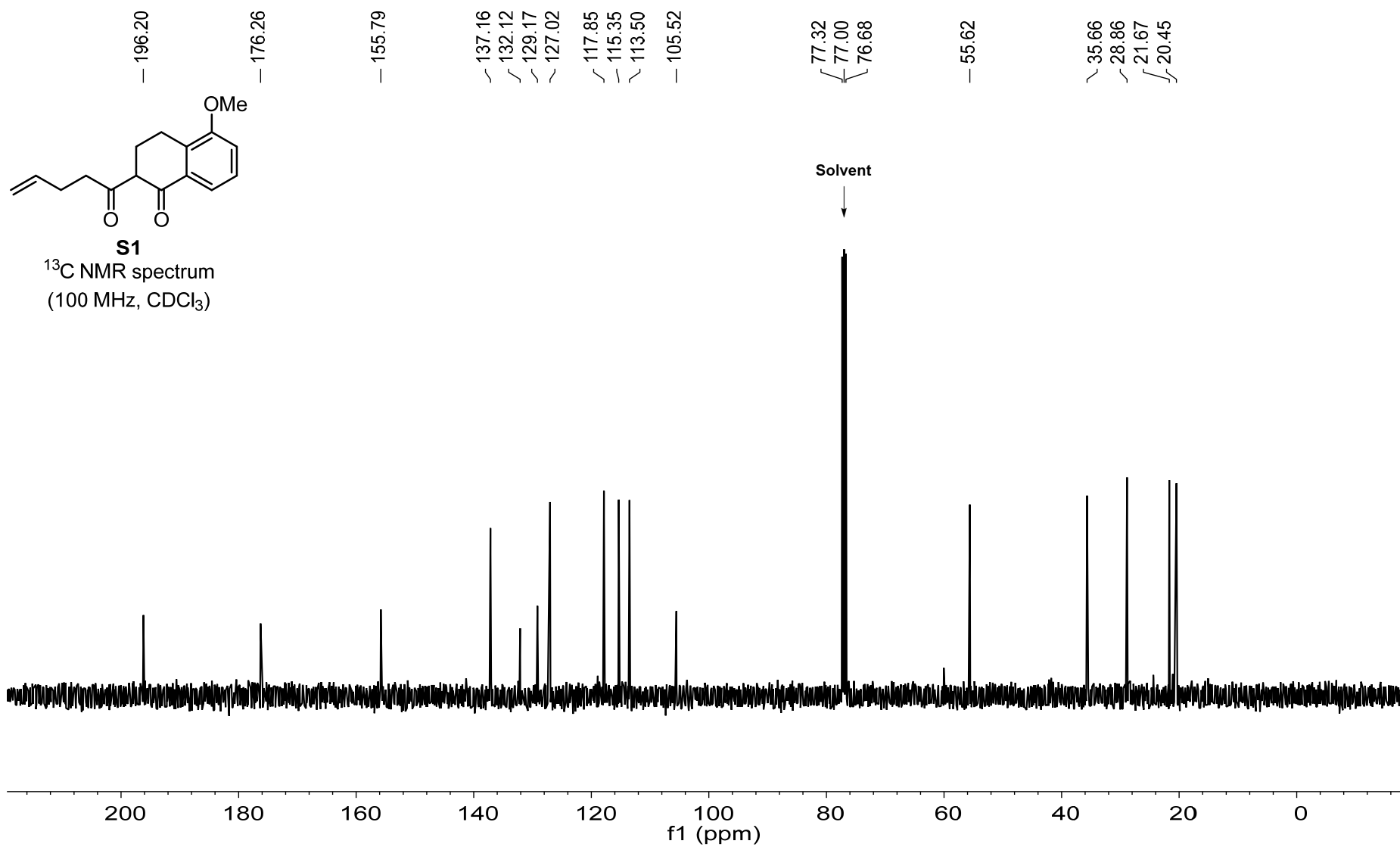
1H), 2.75–2.70 (m, 1H), 2.37 (m, 1H), 2.22 (dt, $J = 11.6, 2.6$ Hz, 1H), 2.11–1.95 (m, 5H), 1.90–1.87 (m, 2H), 1.70–1.57 (m, 4H), 1.24–1.20 (m, 1H), 1.04 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) : $\delta = 215.8, 205.3, 154.2, 142.2, 122.2, 108.7, 72.7, 54.9, 45.9, 45.1, 39.1, 36.0, 36.0, 34.0, 30.0, 29.9, 26.1, 25.2, 21.8, 17.3$ ppm; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{O}_3^+$ 313.1798; found 313.1792.

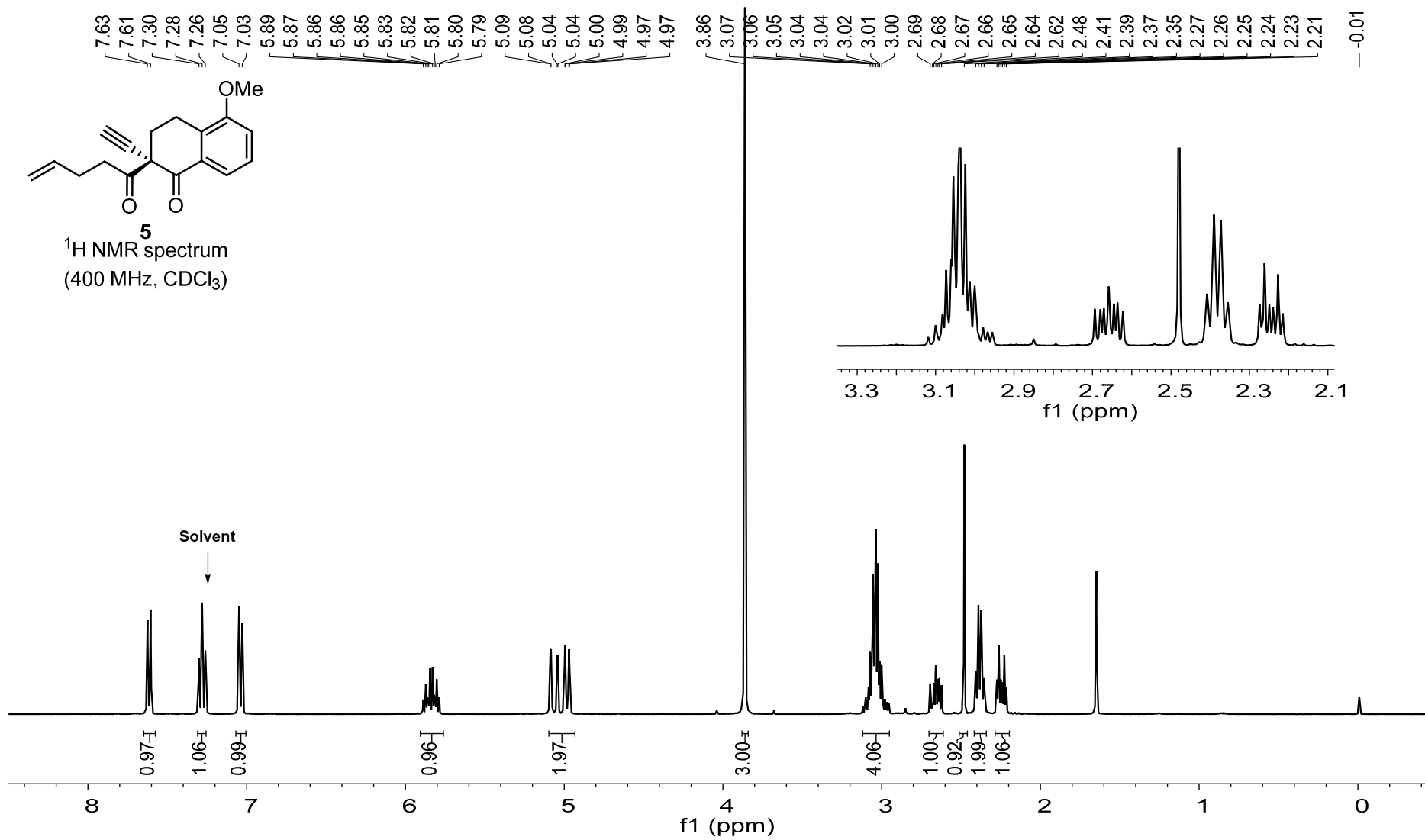
II References

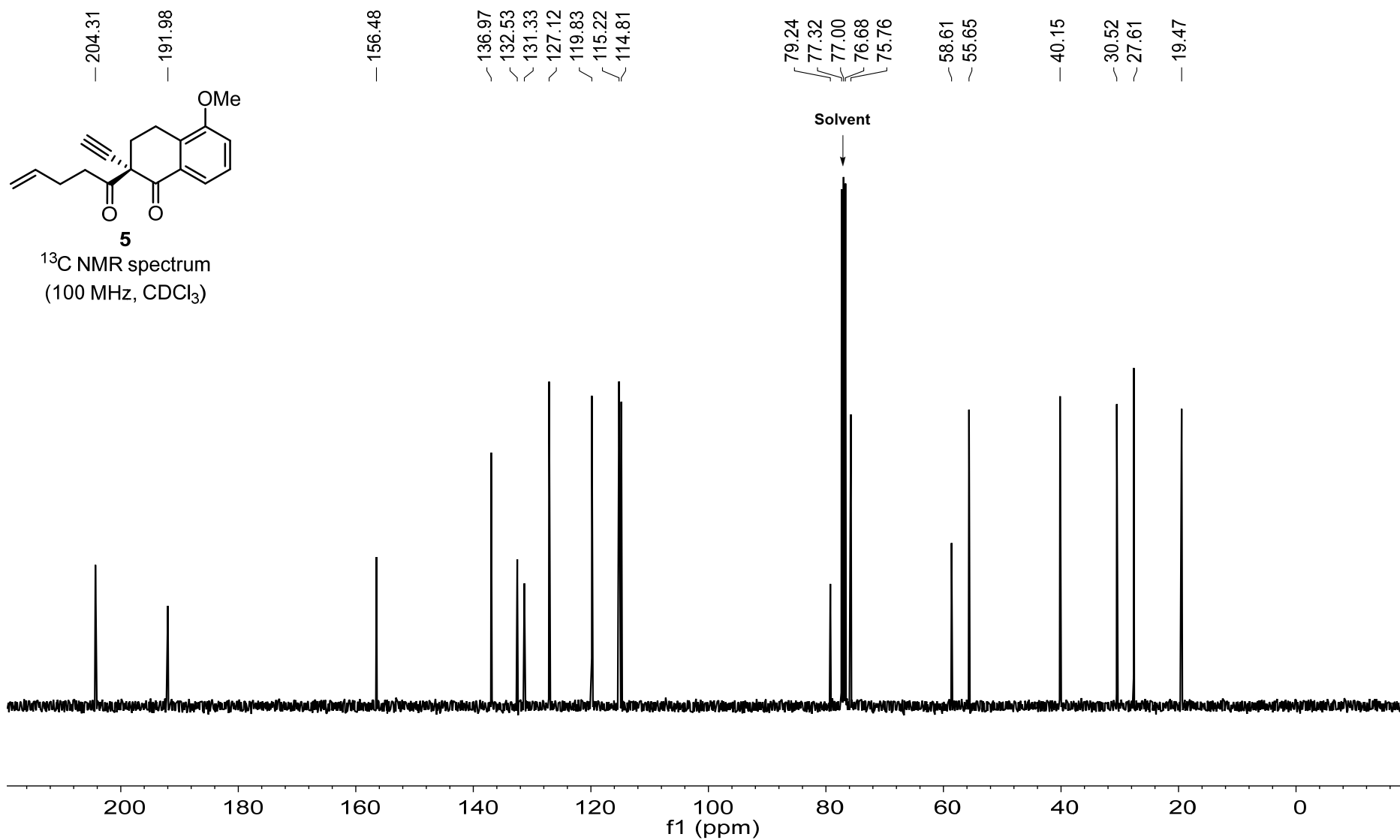
1. a) González, D. F.; Brand, J. P.; Waser, J. *Chem. Eur. J.* **2010**, *16*, 9457; b) Long, R.; Huang, J.; Shao, W.; Liu, S.; Lan, Y.; Gong, J.; Yang, Z. *Nat. Commun.* **2014**, *5*, 5707.
2. Gong, J.; Chen, H.; Liu, X.-Y.; Wang, Z.-X.; Nie, W.; Qin, Y. *Nat. Comm.* **2016**, *7*, 12183.

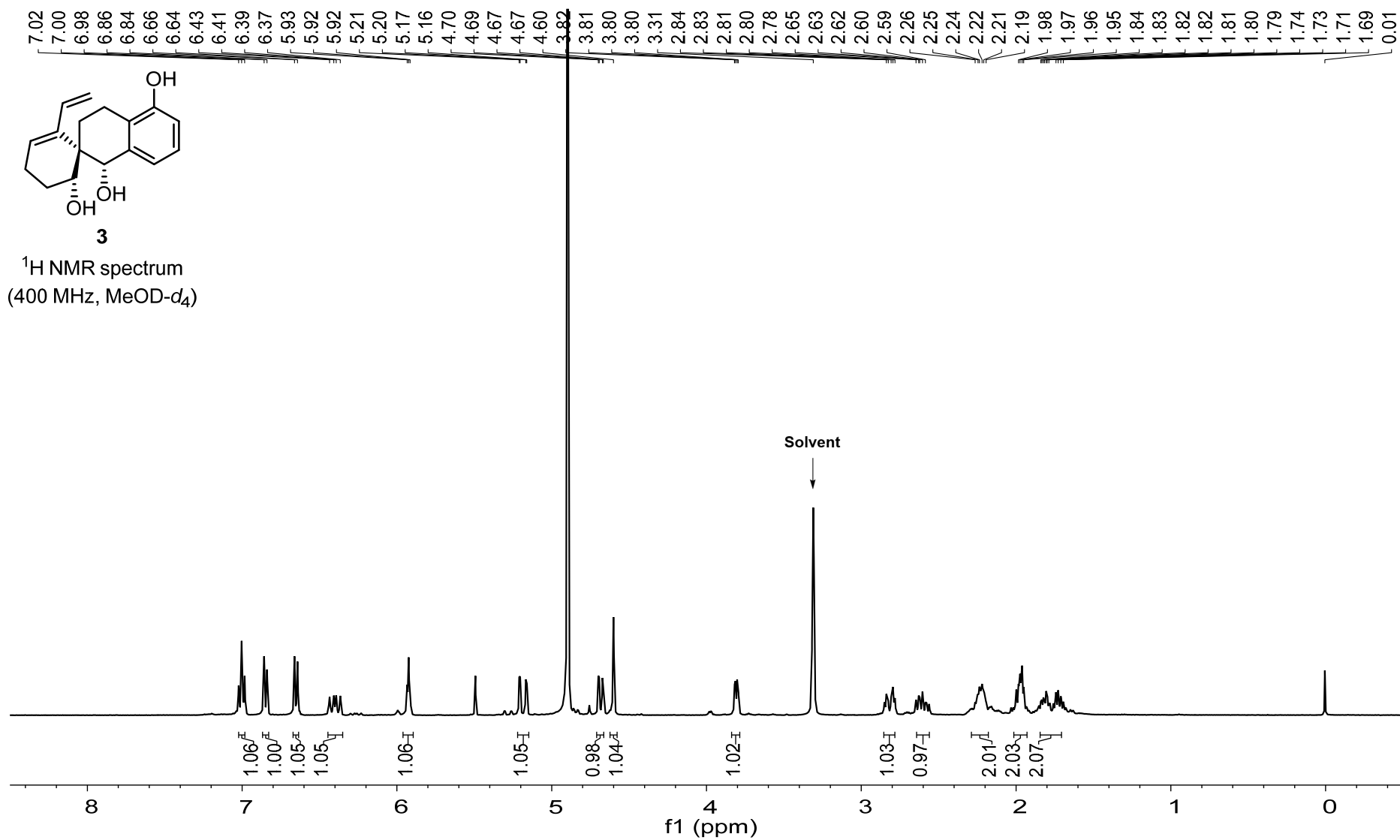
III. ^1H and ^{13}C NMR Spectra of Compounds

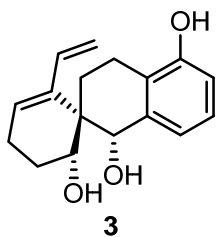




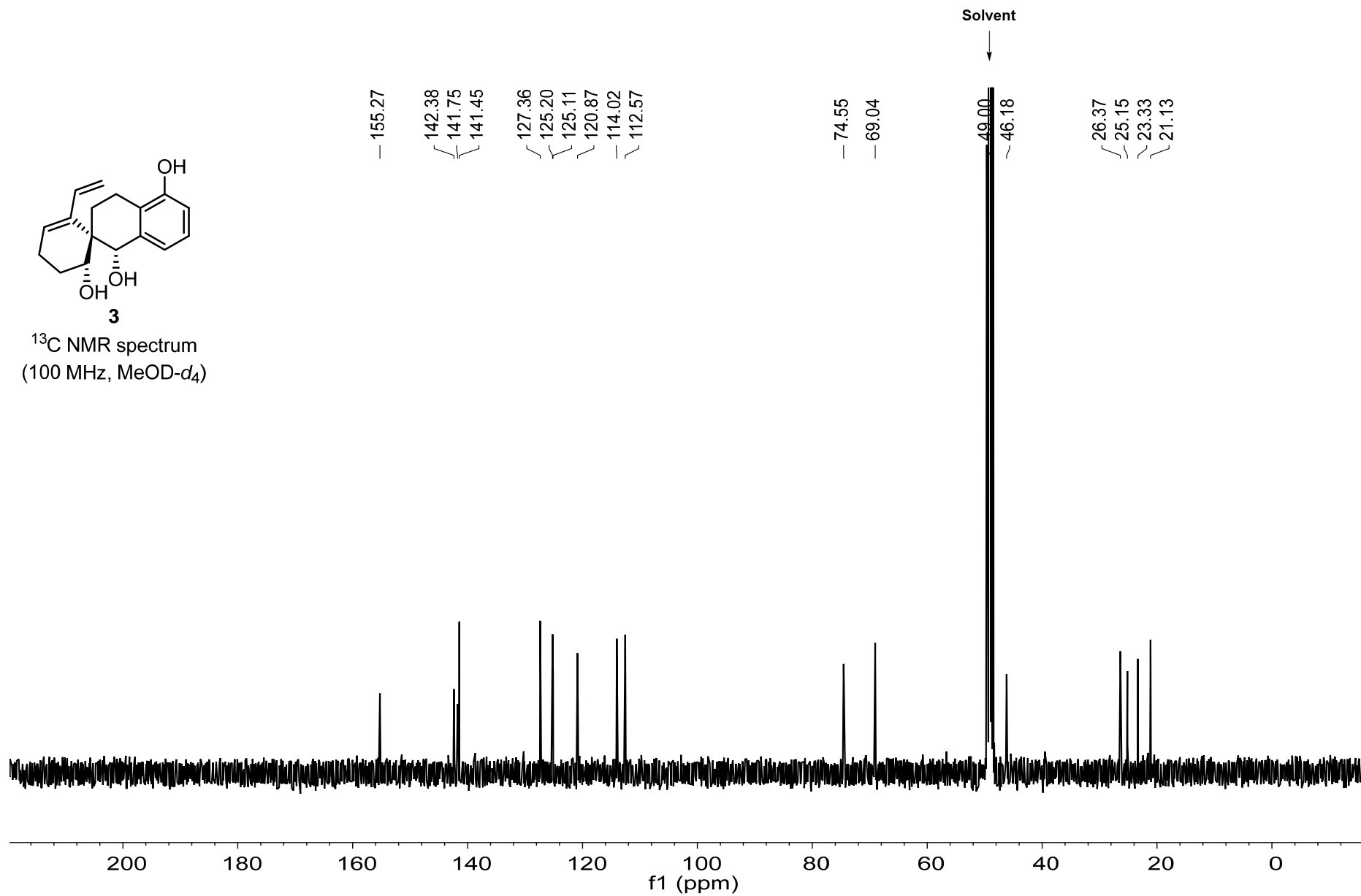


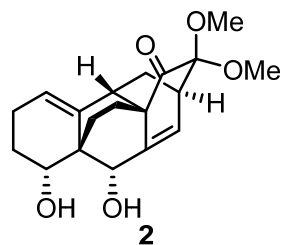




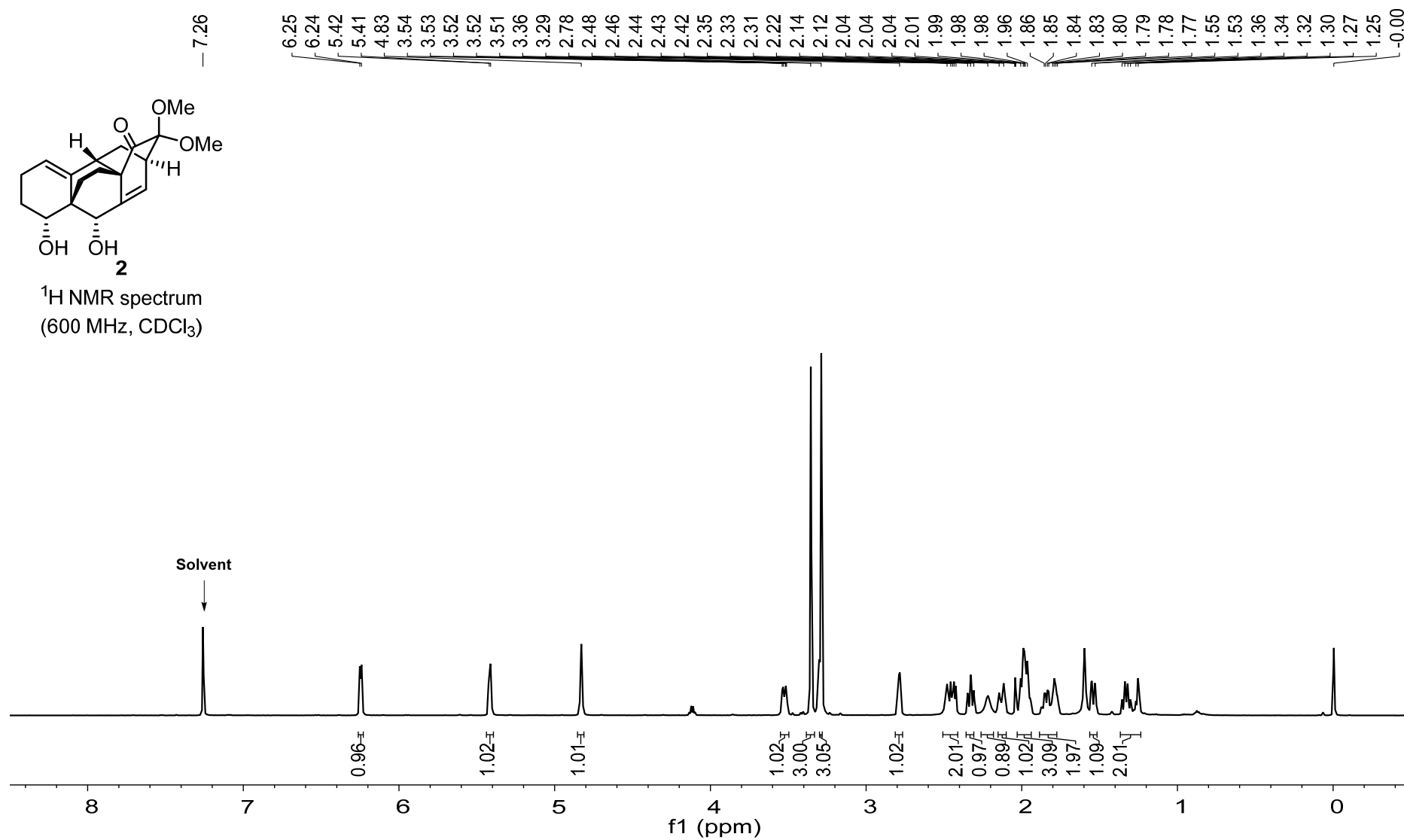


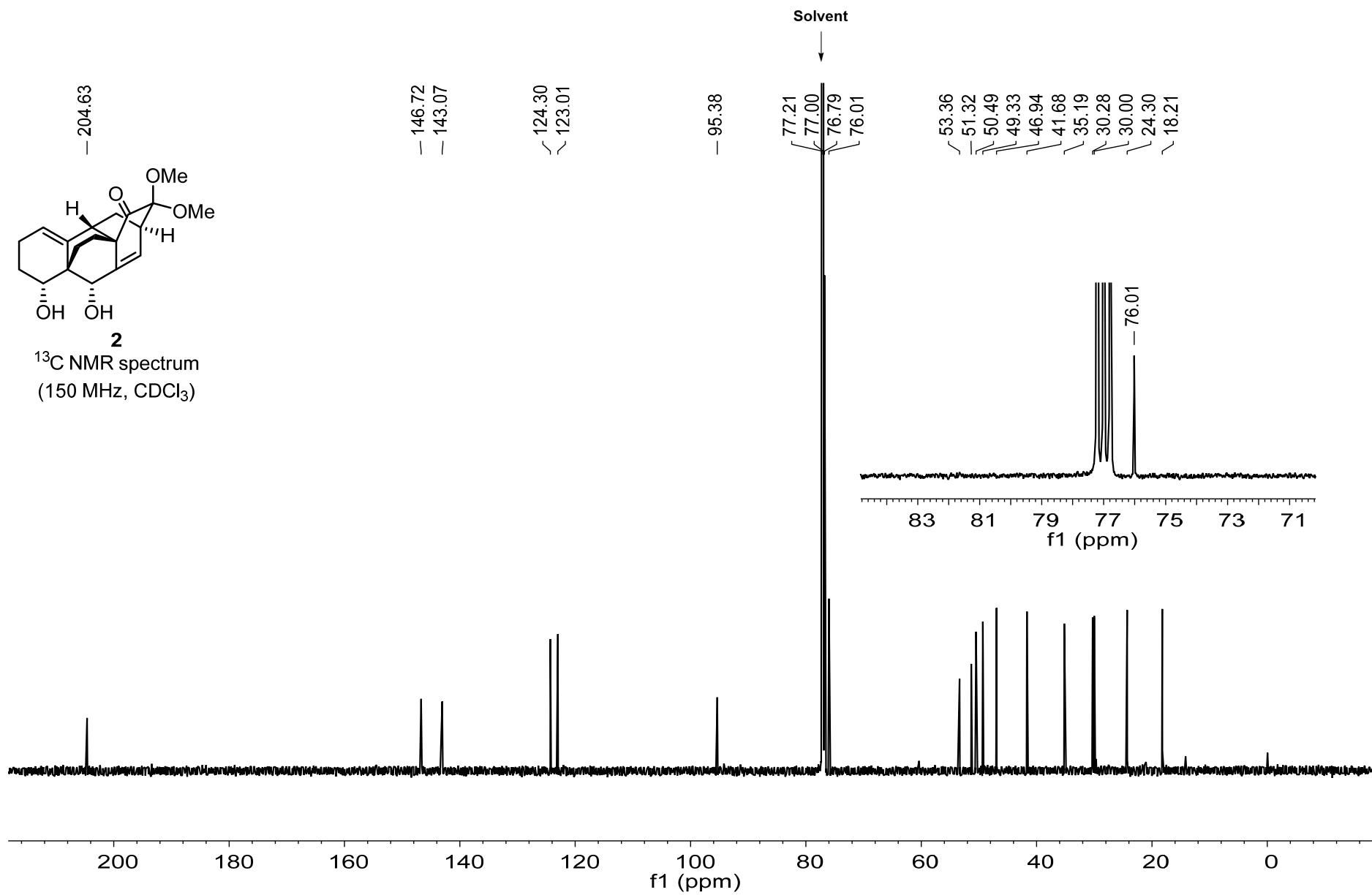
^{13}C NMR spectrum
(100 MHz, $\text{MeOD-}d_4$)

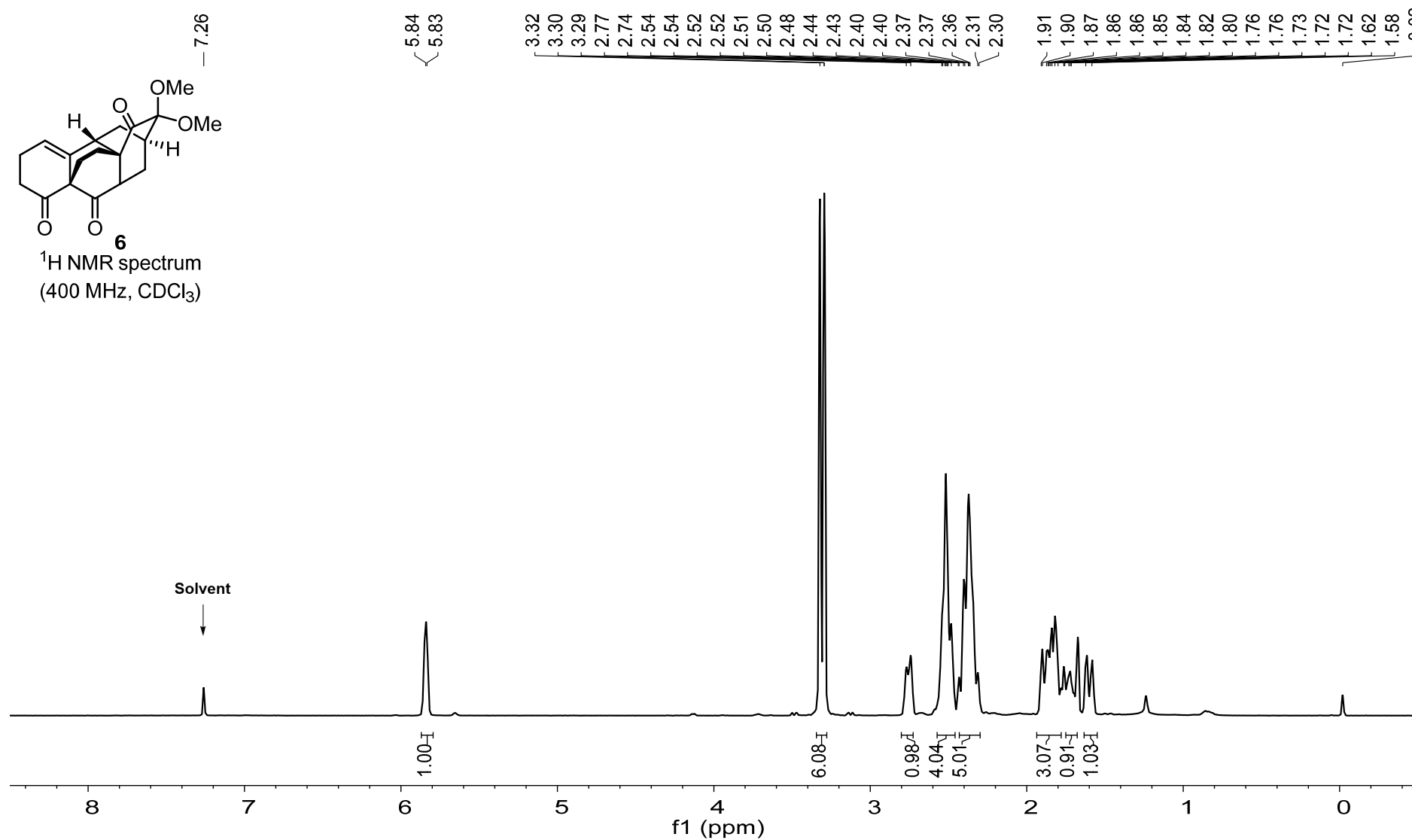
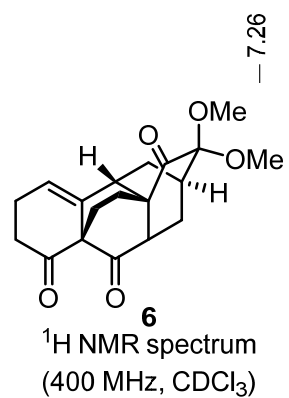


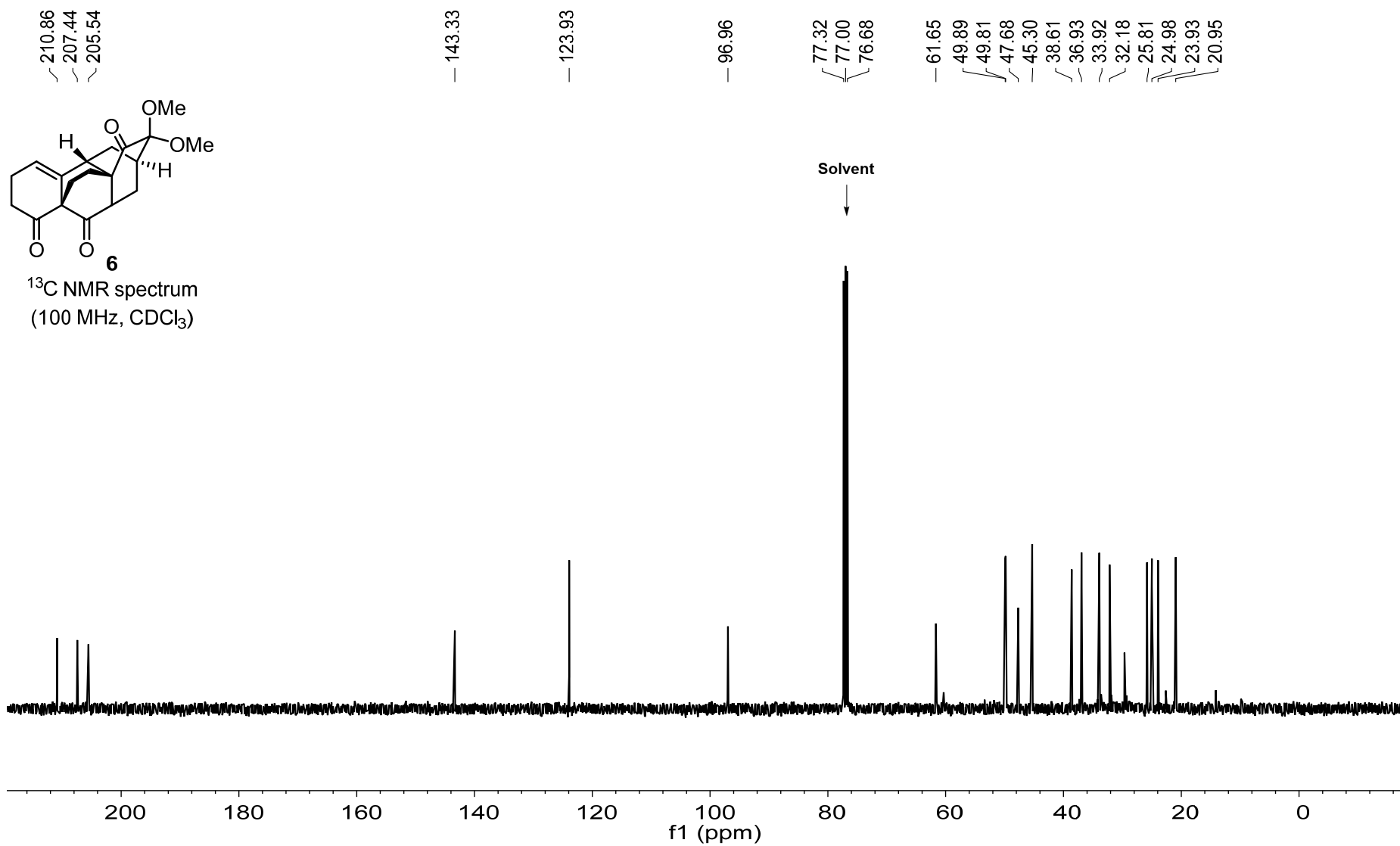


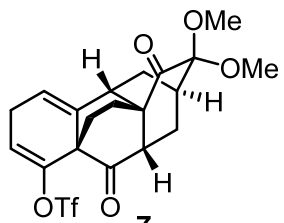
¹H NMR spectrum
(600 MHz, CDCl₃)



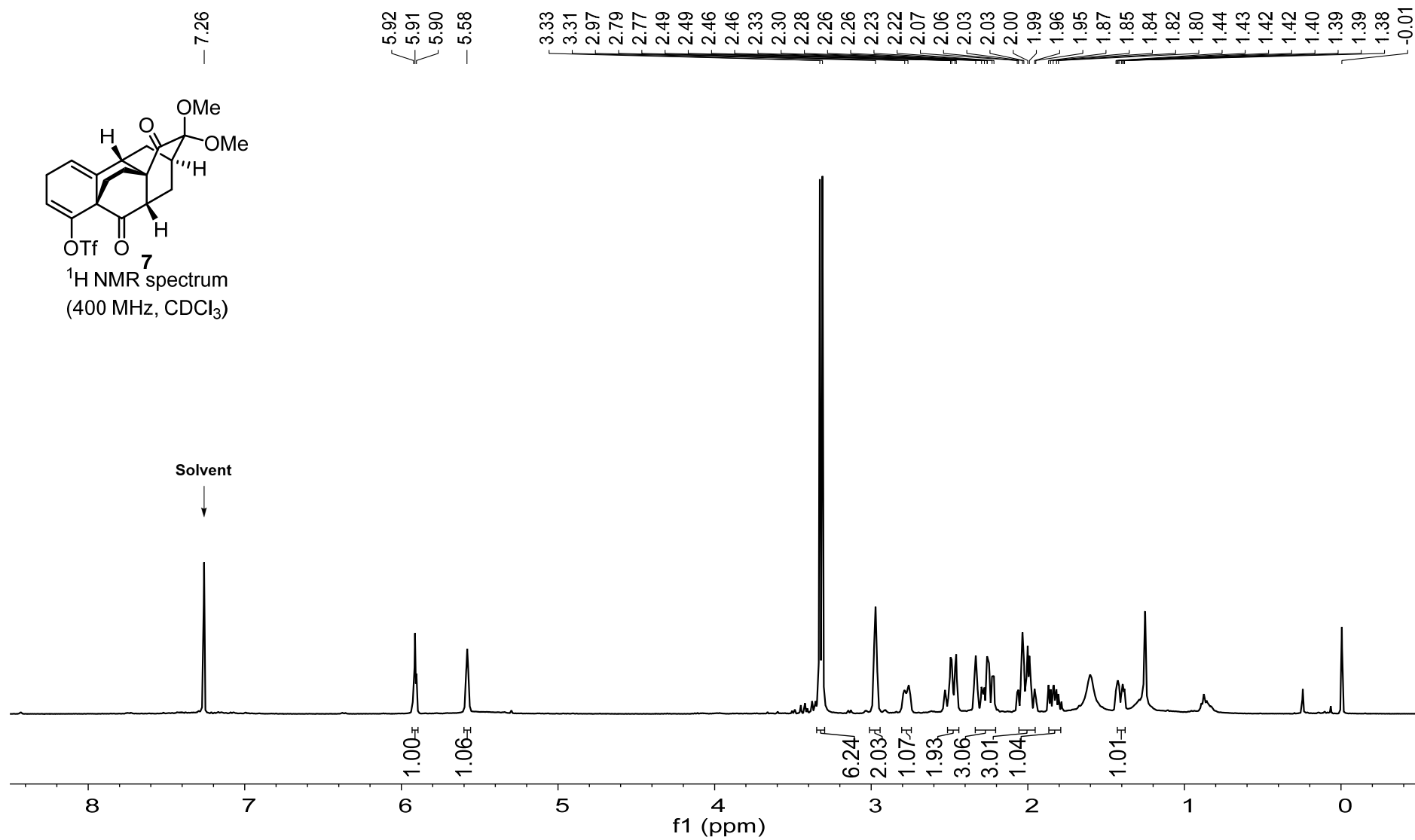


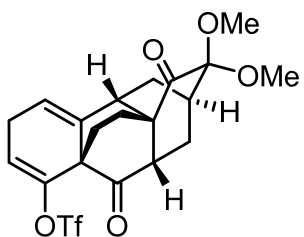




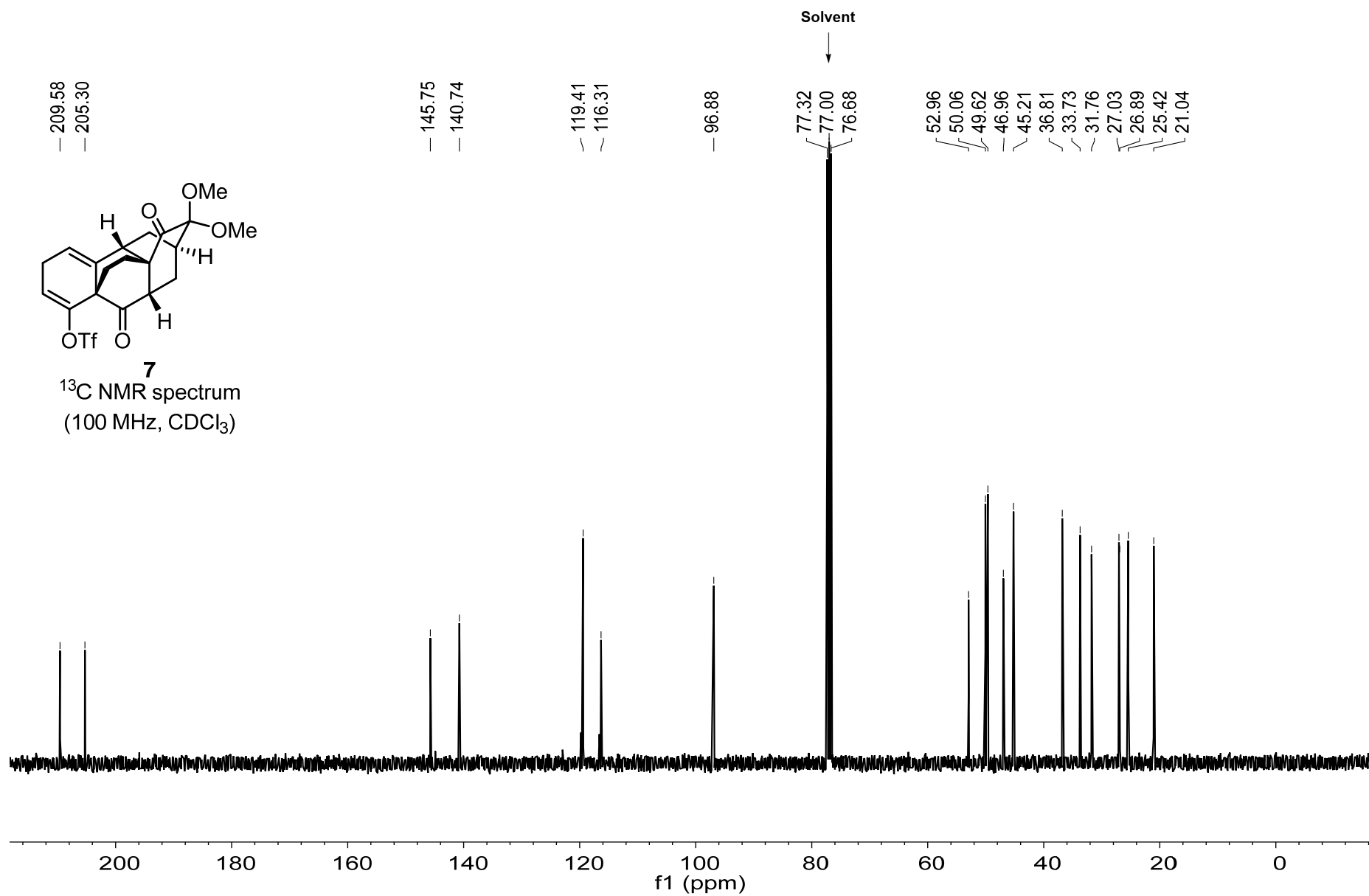


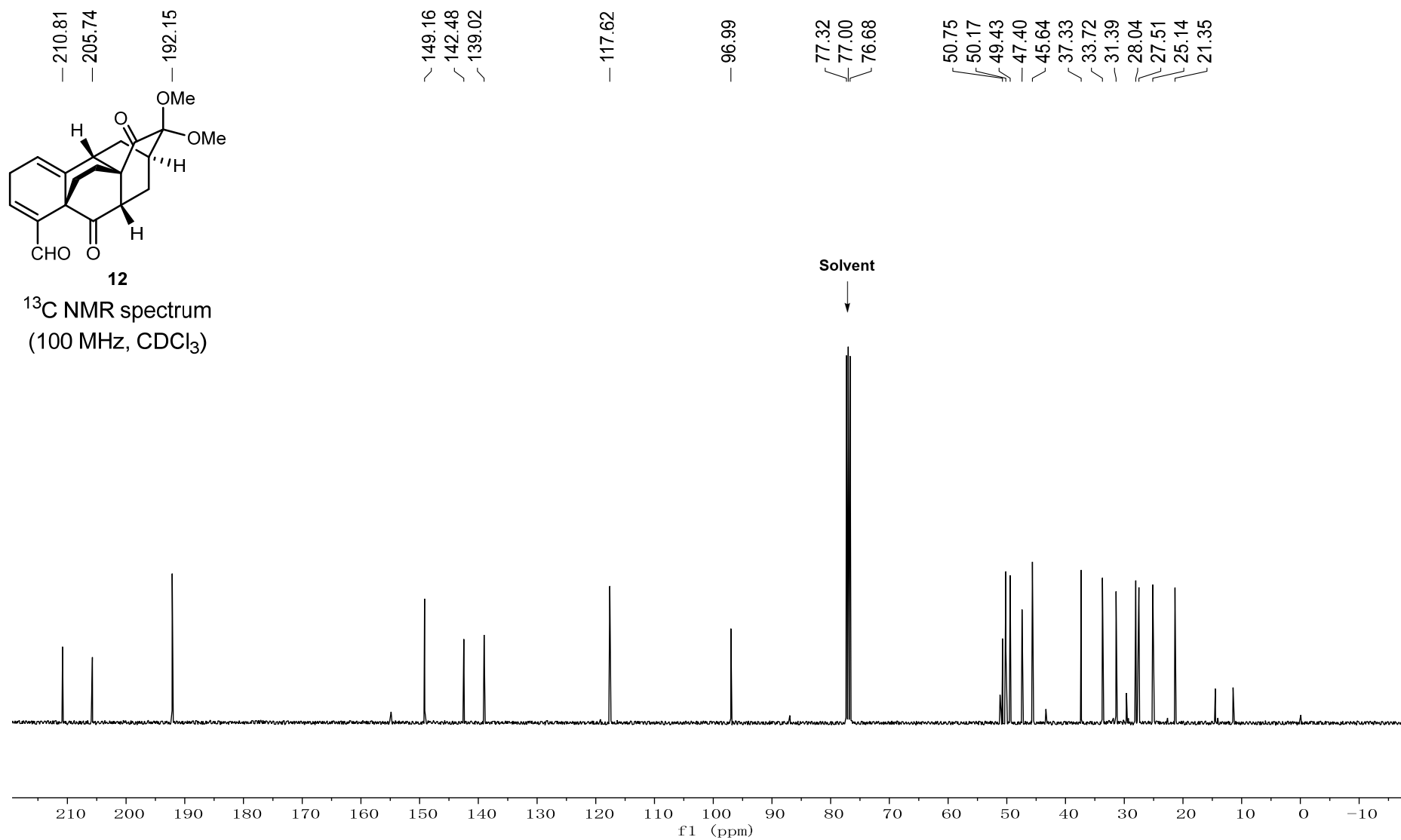
7
¹H NMR spectrum
 (400 MHz, CDCl₃)

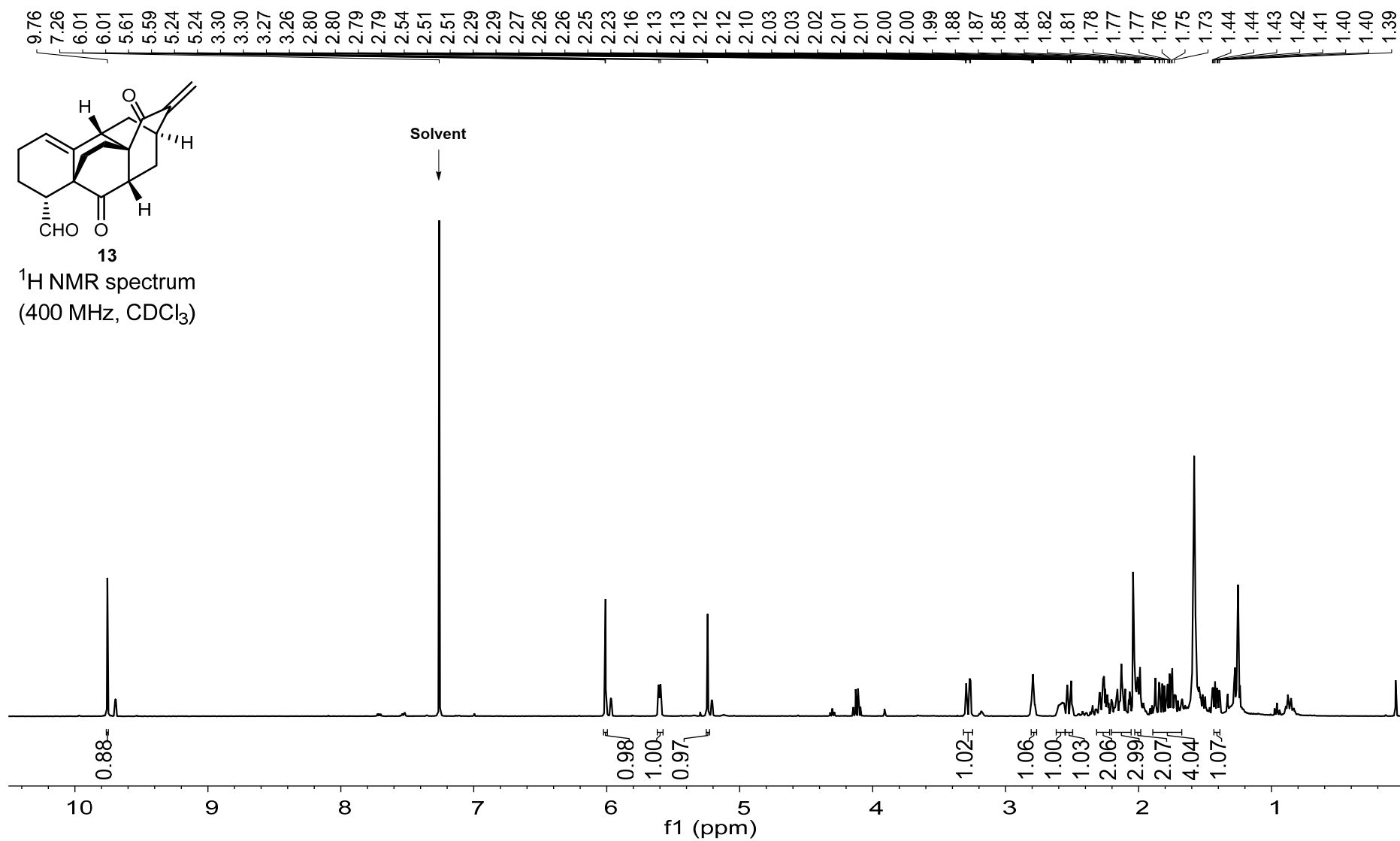


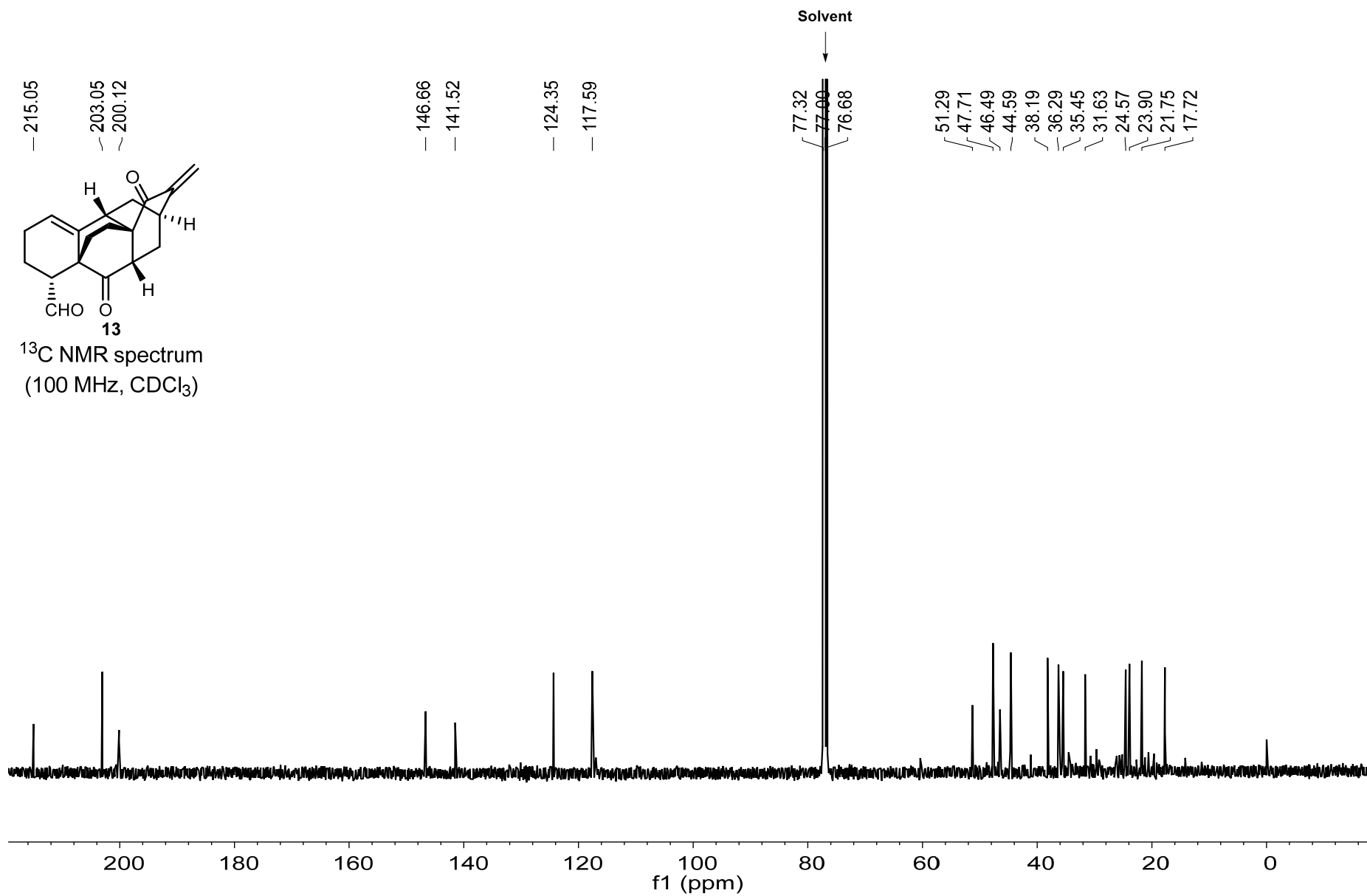


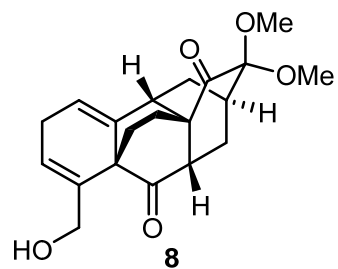
7
 ^{13}C NMR spectrum
 (100 MHz, CDCl_3)



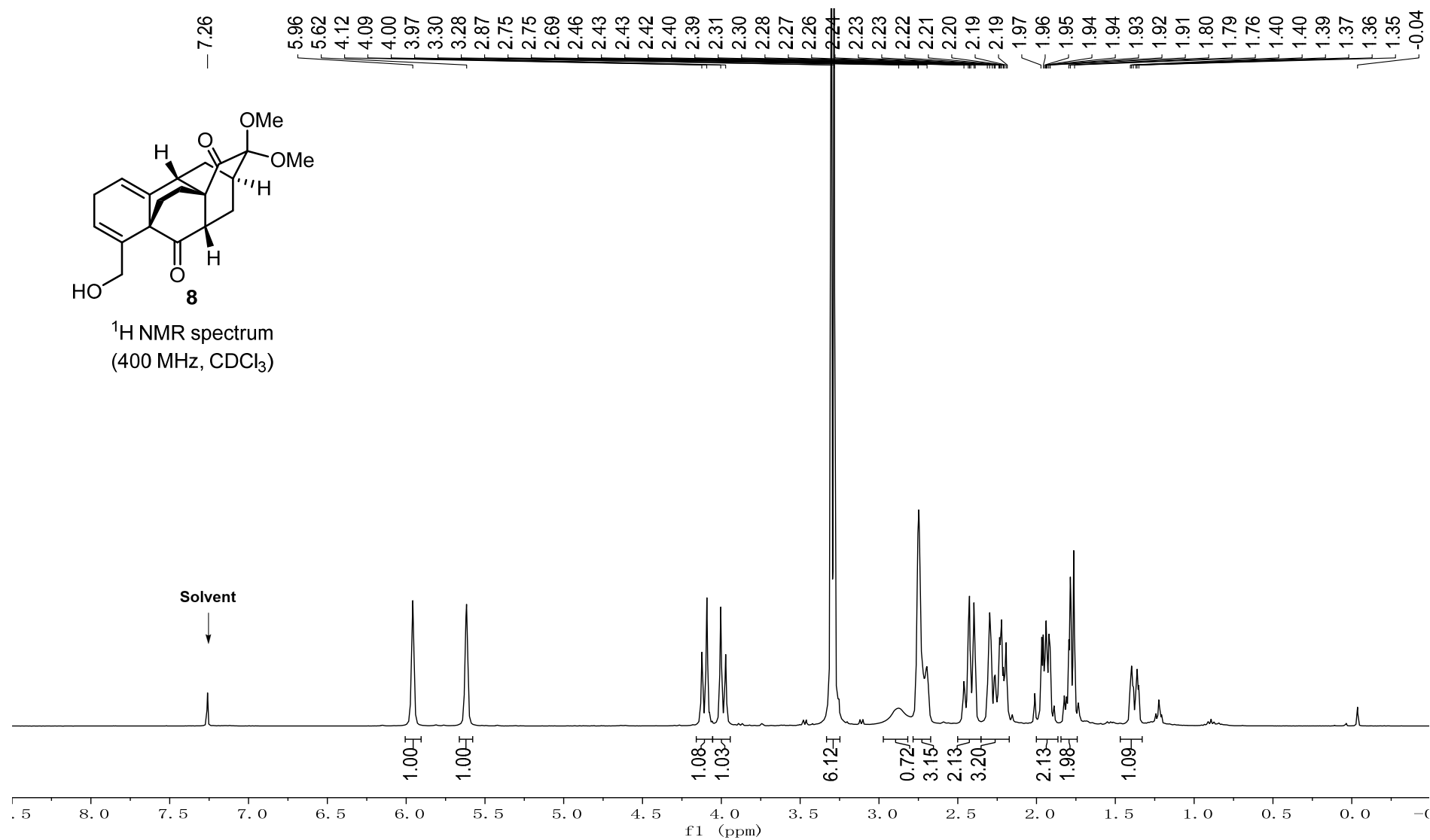


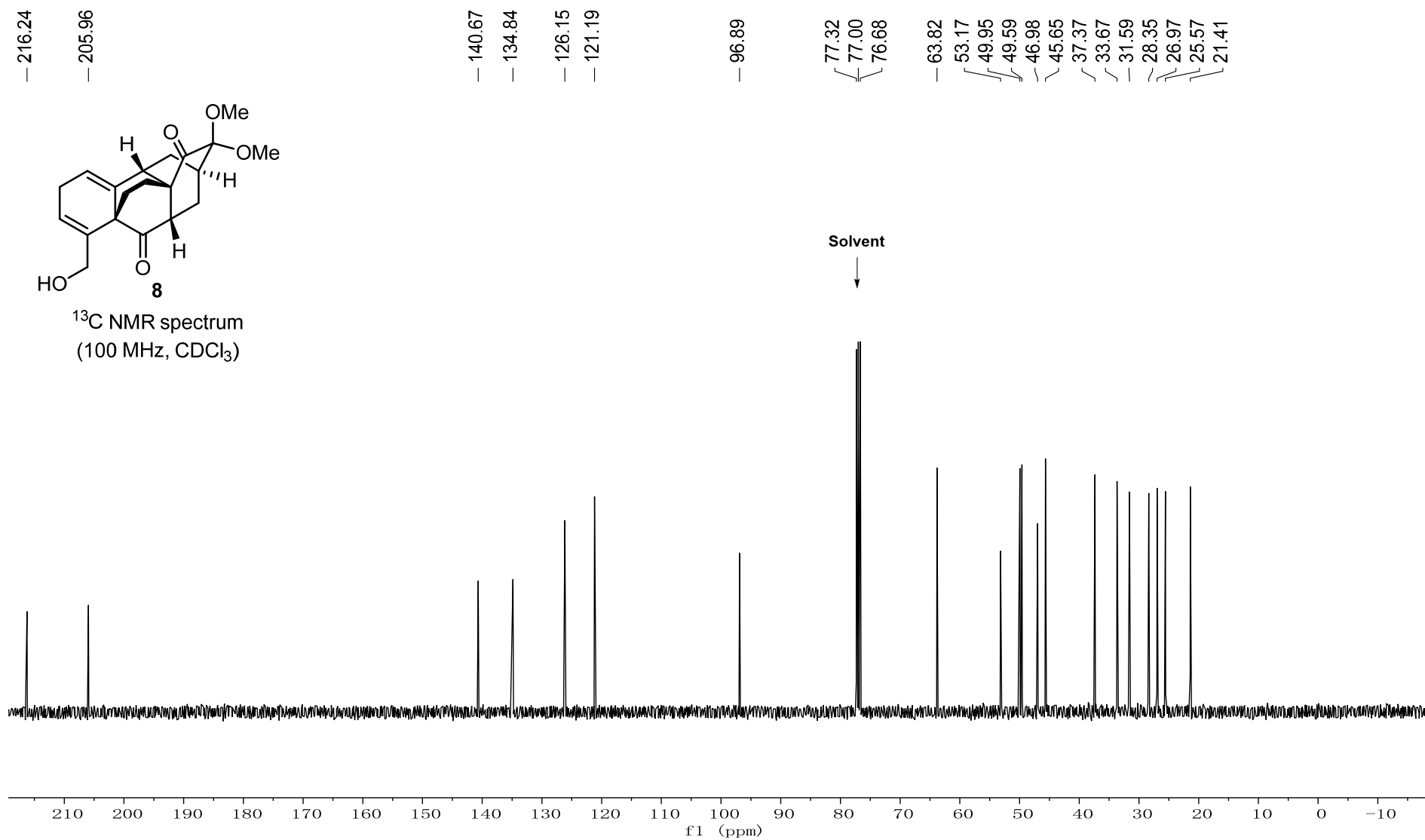


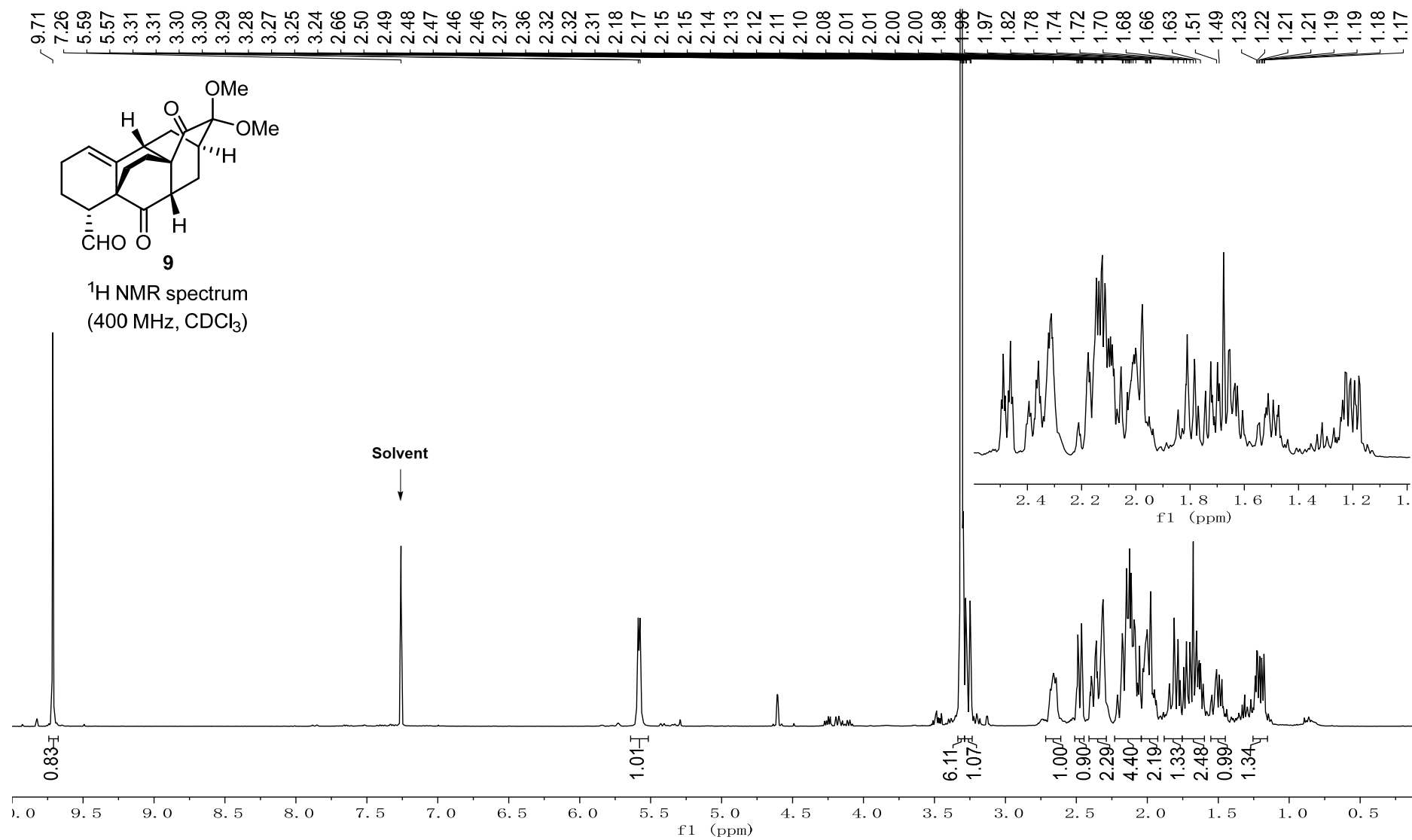


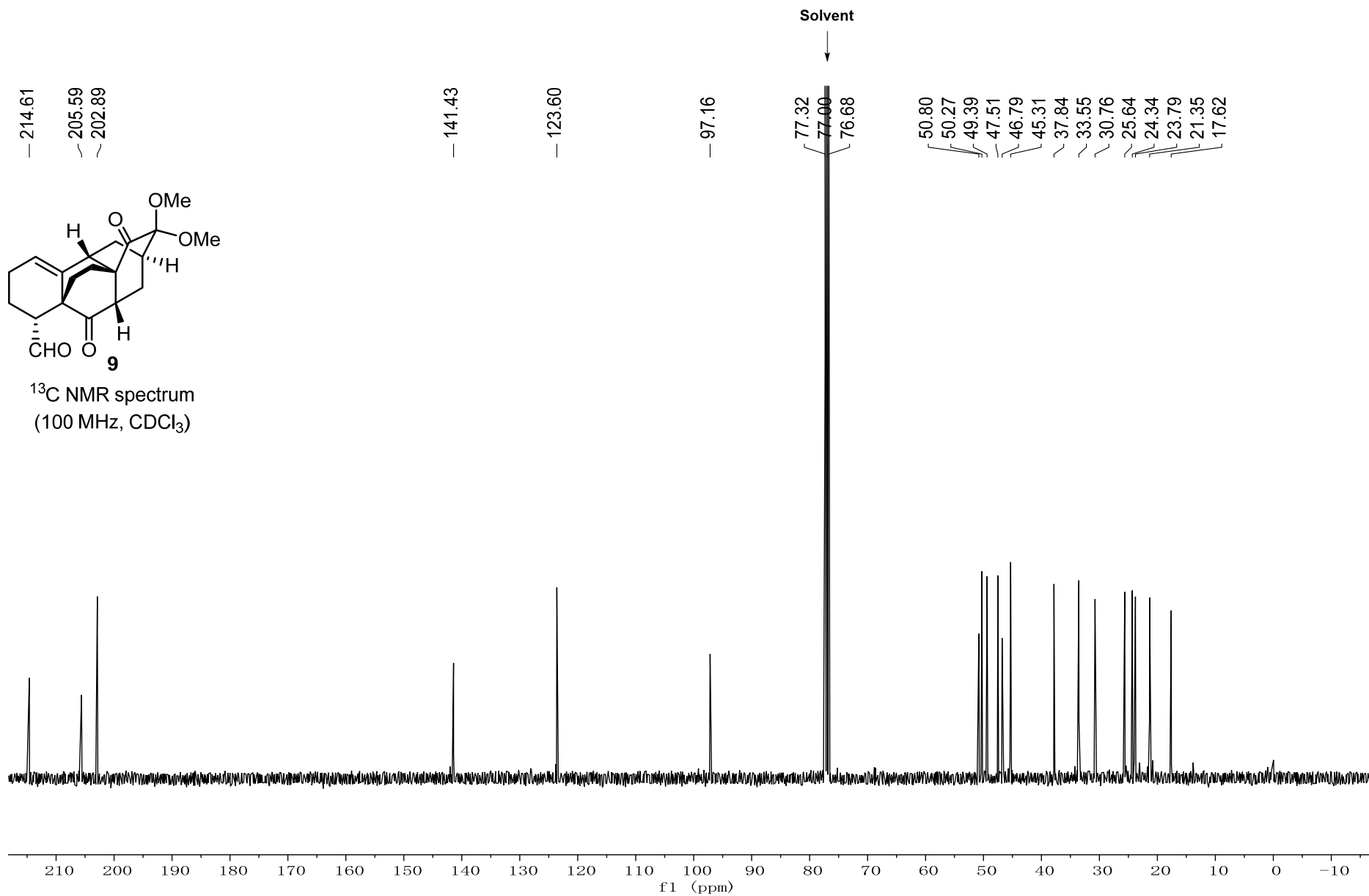


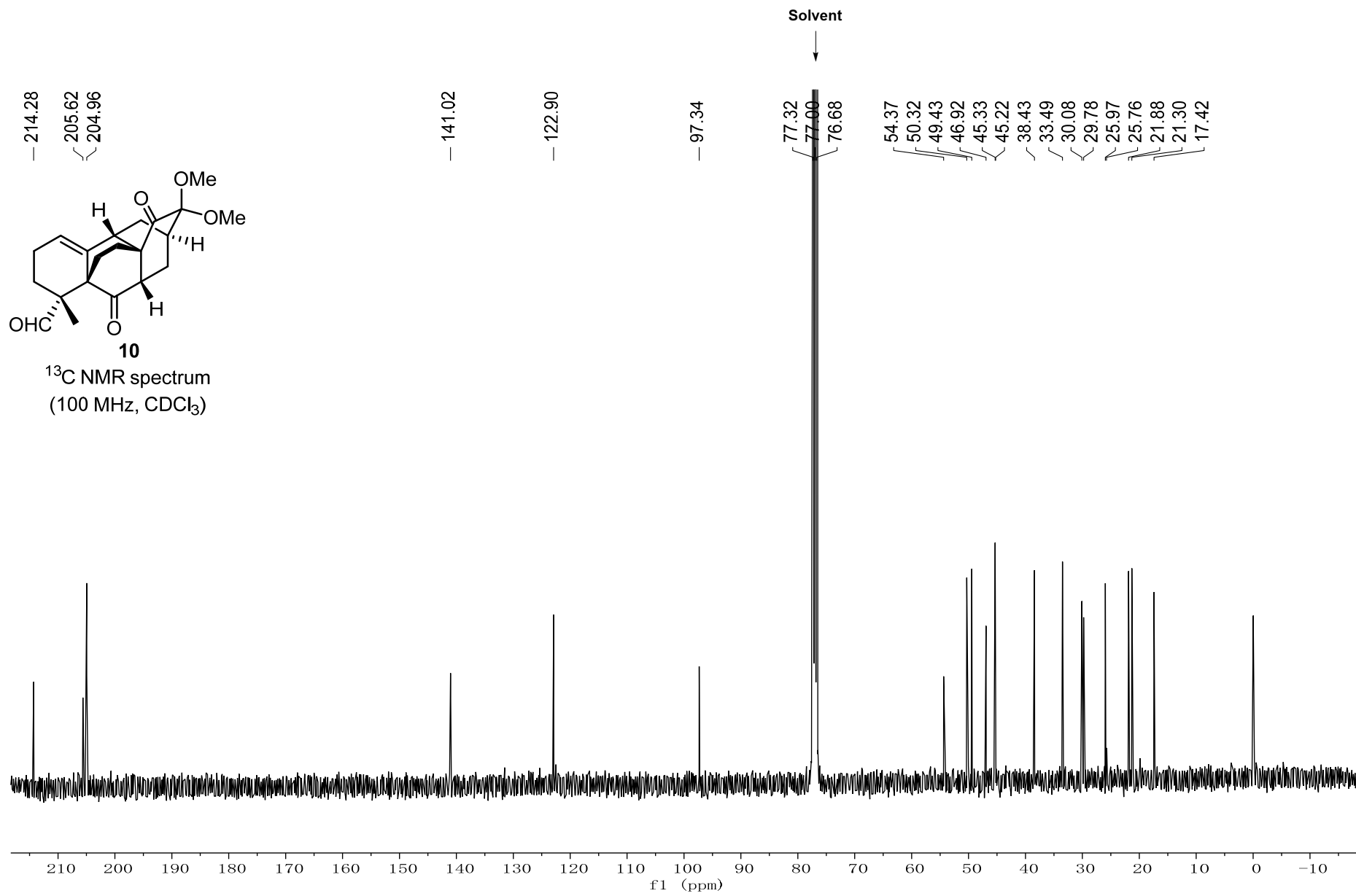
^1H NMR spectrum
(400 MHz, CDCl_3)

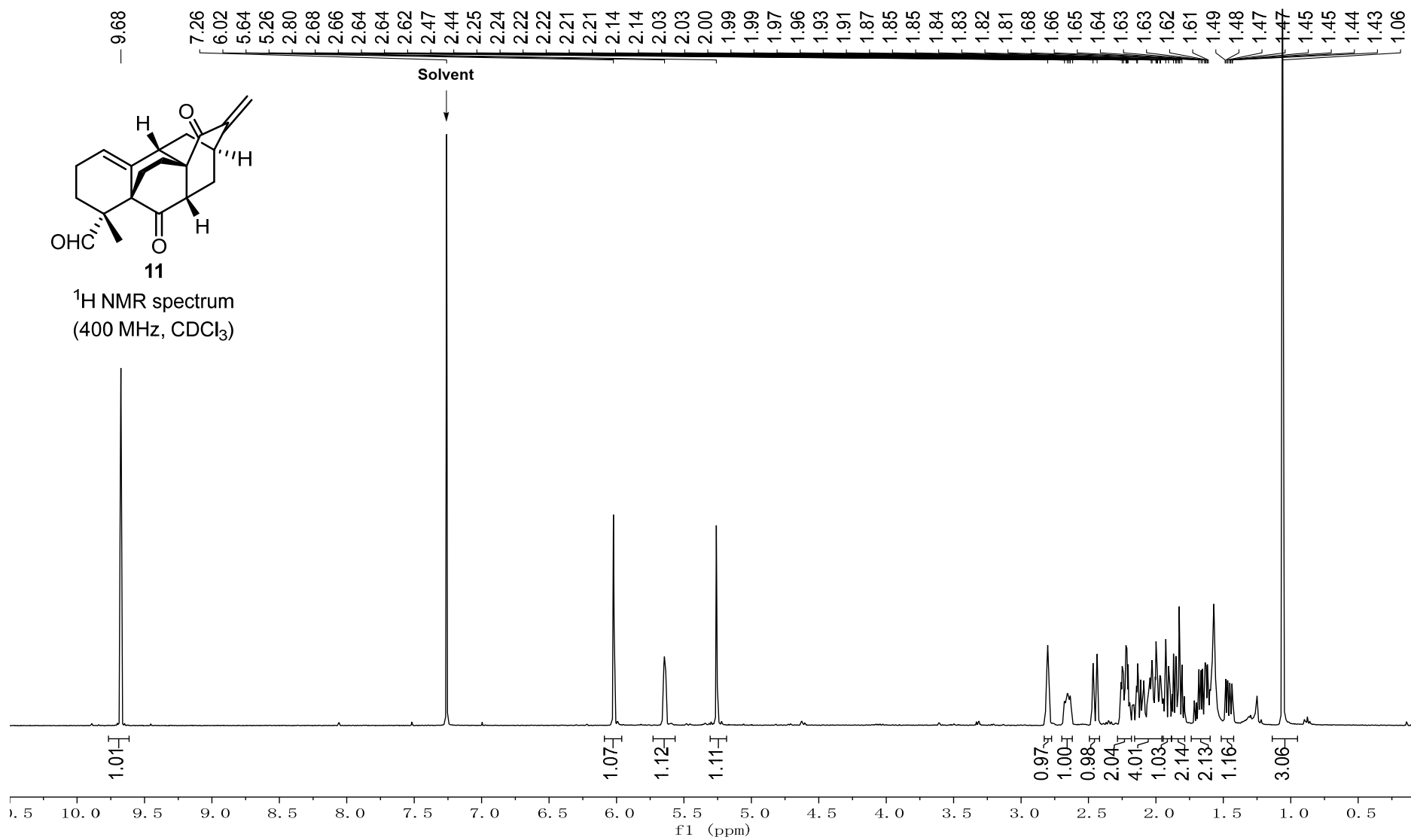


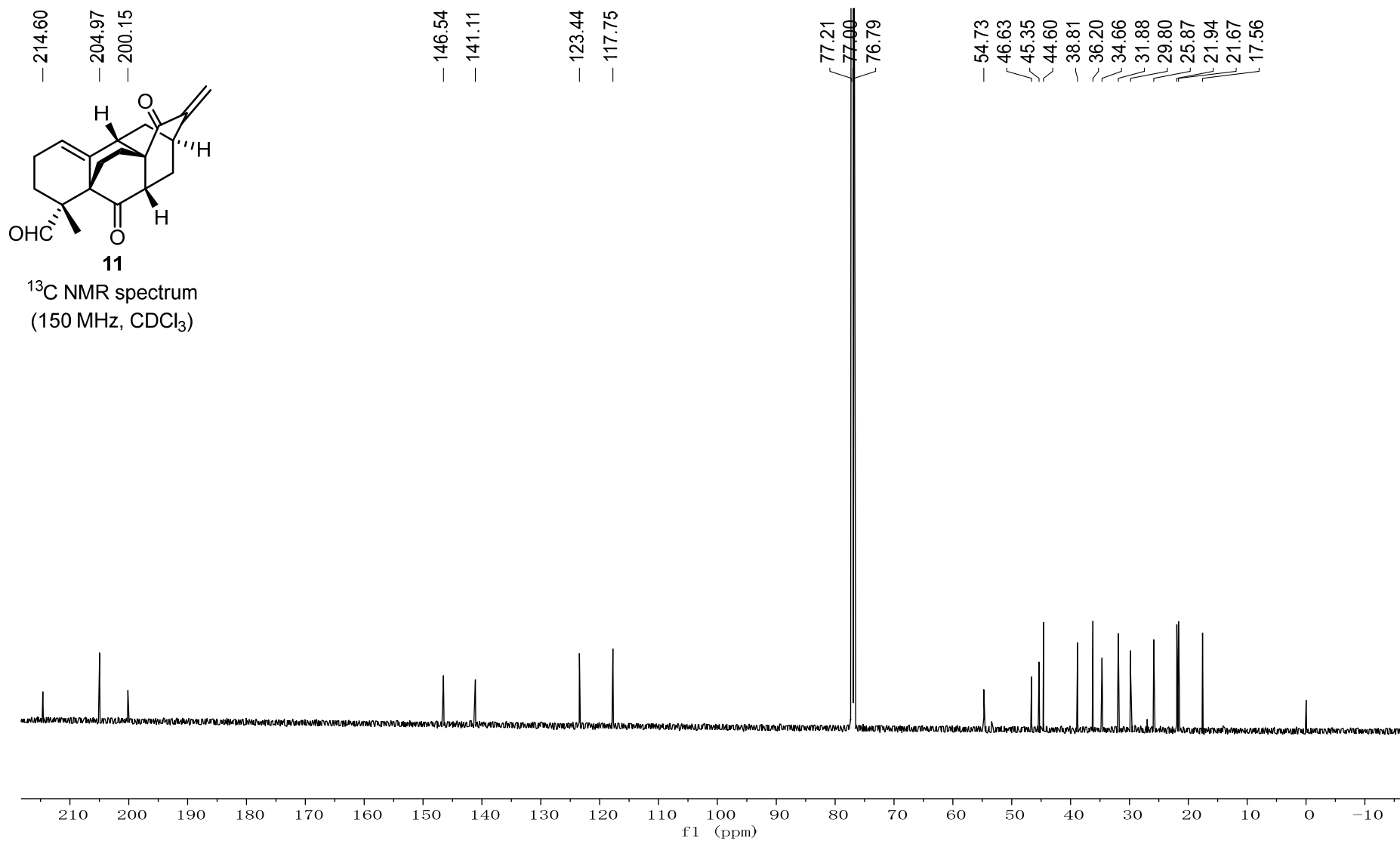


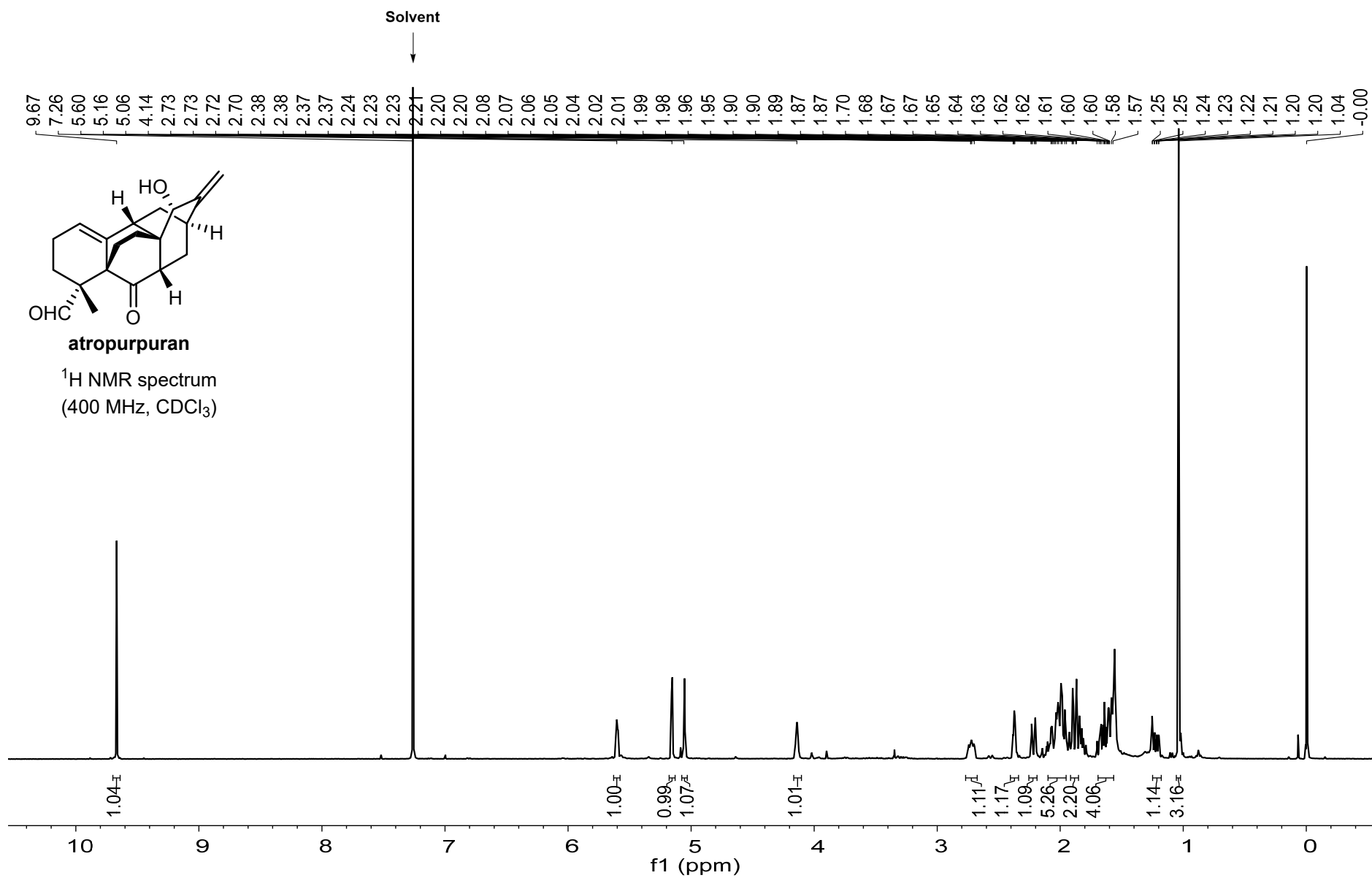


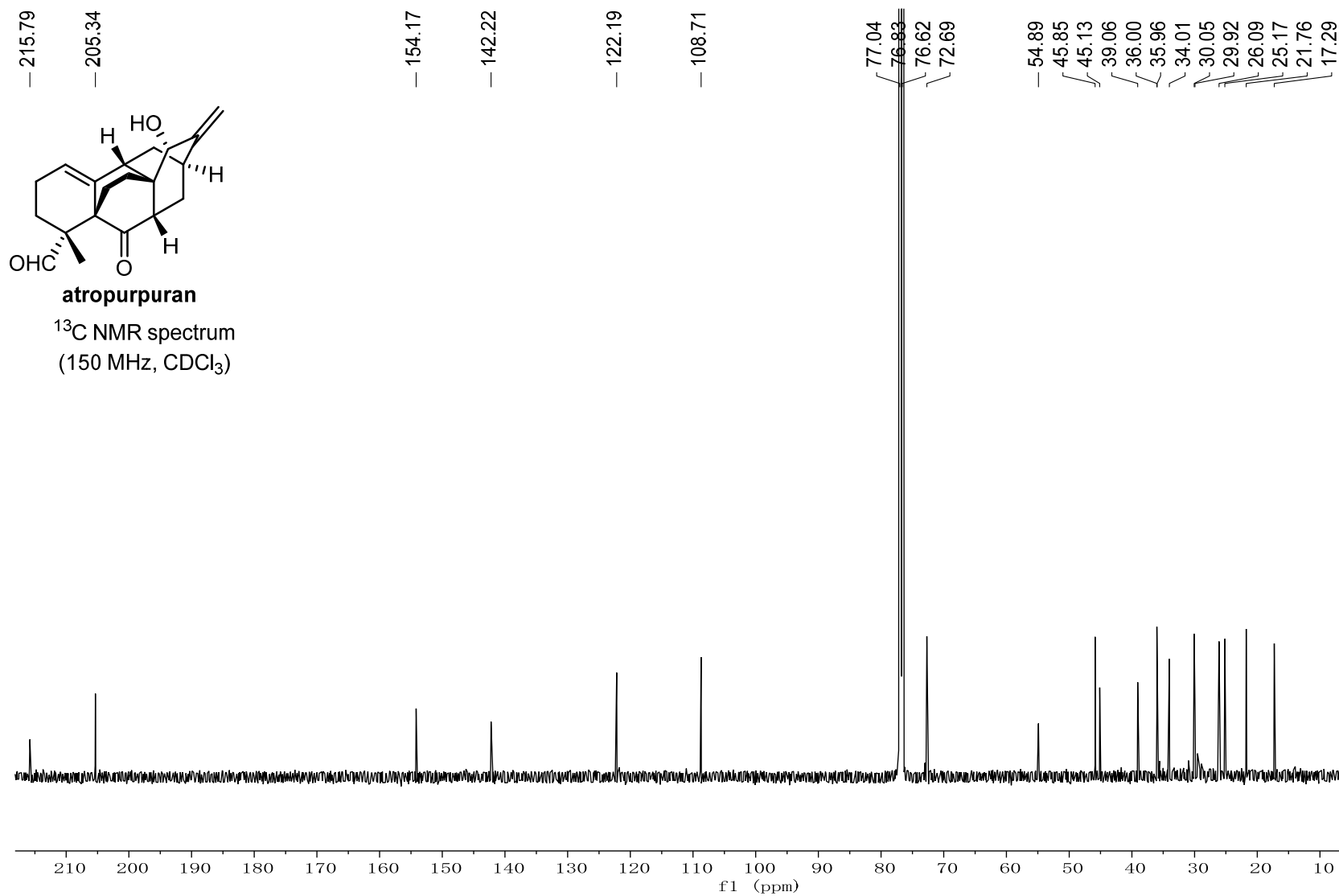












¹³C NMR spectrum
(150 MHz, CDCl₃)

IV Comparison of NMR Data of Natural and Synthetic Atropurpuran

Supplementary Table 1. Comparison of ^1H NMR (CDCl_3) spectroscopic data of the natural and synthetic atropurpuran.

Natural δ H [ppm, mult, J (Hz)] 400 MHz	Synthetic δ H [ppm, mult, J (Hz)] 400 MHz	Err (natural–synthetic) $\Delta\delta$ /ppm
9.67, 1H, s	9.67, 1H, s	0
5.61, 1H, t, 4.0	5.60, 1H, s	0.01
5.16, 1H, dd, 6.4, 2.8	5.16, 1H, s	0
5.05, 1H, d, 2.4	5.06, 1H, s	-0.01
4.15, 1H, br s	4.14, 1H, s	0.01
2.73, 1H, m	2.75–2.70, 1H, m	— — —
2.37, 1H, m	2.37, 1H, m	0
2.22, 1H, dt, 11.6, 2.4	2.22, 1H, dt, 11.7, 2.6	0
2.11, 1H, m	2.11–1.95, 5H, m	— — —
2.08, 1H, m		— — —
2.04, 1H, m		— — —
1.98, 1H, m		— — —
1.95, 1H, m		— — —
1.90, 1H, m	1.90–1.87, 2H, m	— — —
1.87, 1H, m		— — —
1.69, 1H, m	1.70–1.57, 4H, m	— — —
1.65, 1H, m		— — —
1.61, 1H, m		— — —
1.57, 1H, m		— — —
1.21, 1H, m	1.24–1.20, 1H, m	— — —
1.04, 1H, m	1.04, 3H, s	0

Supplementary Table 2. Comparison of ^{13}C NMR (CDCl_3) spectroscopic data of the natural and synthetic atropurpuran.

Natural δ C [ppm, mult, J (Hz)] 100 MHz	Synthetic δ C [ppm, mult, J (Hz)] 150 MHz	Err (natural–synthetic) $\Delta\delta/\text{ppm}$
215.7	215.8	-0.1
205.3	205.3	0
154.2	154.2	0
142.3	142.2	0.1
122.2	122.2	0
108.7	108.7	0
72.7	72.7	0
54.9	54.9	0
45.9	45.9	0
45.1	45.1	0
39.1	39.1	0
36.1	36.0	0.1
35.9	36.0	-0.1
34.0	34.0	0
30.1	30.0	0.1
30.0	29.9	0.1
26.1	26.1	0
25.2	25.2	0
21.8	21.8	0
17.3	17.3	0

Supplementary Table 3. Comparison of ¹H NMR (CDCl₃) spectroscopic data of the Qin's synthetic and synthetic atropurpuran.

Qin's synthetic δ H [ppm, mult, <i>J</i> (Hz)] 400 MHz	Synthetic δ H [ppm, mult, <i>J</i> (Hz)] 400 MHz	Err (Qin's synthetic–synthetic) Δδ/ppm
9.66, 1H, s	9.67, 1H, s	-0.01
5.60, 1H, s	5.60, 1H, s	0
5.15, 1H, s	5.16, 1H, s	-0.01
5.05, 1H, s	5.06, 1H, s	-0.01
4.14, 1H, s	4.14, 1H, s	0
2.74–2.70, 1H, m	2.75–2.70, 1H, m	---
2.37, 1H, s	2.37, 1H, m	0
2.21, 1H, d, 11.6	2.22, 1H, dt, 11.7, 2.6	-0.01
2.10–1.96, 5H, m	2.11–1.95, 5H, m	---
1.92–1.81, 2H, m	1.90–1.87, 2H, m	---
1.70–1.55, 4H, m	1.70–1.57, 4H, m	---
1.23–1.19, 1H, m	1.24–1.20, 1H, m	---
1.04, 1H, m	1.04, 3H, s	0

Supplementary Table 4. Comparison of ^{13}C NMR (CDCl_3) spectroscopic data of the Qin's synthetic and synthetic atropurpuran.

Qin's synthetic δ C [ppm, mult, J (Hz)] 150 MHz	Synthetic δ C [ppm, mult, J (Hz)] 150 MHz	Err (Qin's synthetic–synthetic) $\Delta \delta$ /ppm
215.7	215.8	-0.1
205.3	205.3	0
154.2	154.2	0
142.3	142.2	0.1
122.3	122.2	0.1
108.7	108.7	0
72.7	72.7	0
54.9	54.9	0
45.9	45.9	0
45.2	45.1	0.1
39.1	39.1	0
36.0	36.0	0
36.0	36.0	0
34.0	34.0	0
30.1	30.0	0.1
29.9	29.9	0
26.1	26.1	0
25.2	25.2	0
21.8	21.8	0
17.3	17.3	0