

Supporting Information

Domino Intramolecular Diels-Alder Reactions to Construct the 6/6/5/5 Fused Tetracyclic Framework

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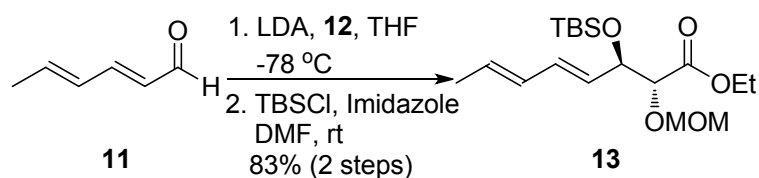
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General information.

Oxygen and moisture-sensitive reaction were carried out under argon atmosphere. Solvents were purified and dried by standard methods prior to use. All commercially available reagents were used without further purification unless otherwise noted. Column chromatography was performed on silica gel (200-300 mesh). Infrared spectra were recorded on a 670 FT-IR spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometers. Chemical shifts are reported as δ values relative to internal chloroform (δ 7.27 for ^1H NMR and 77.0 for ^{13}C NMR).

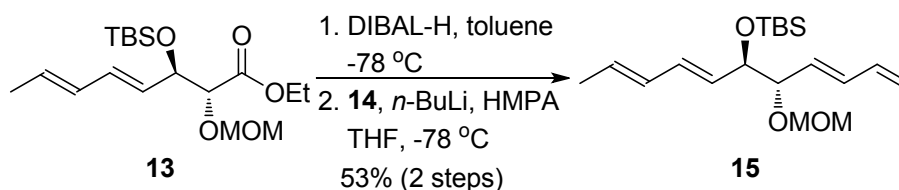
Synthesis of Linear Precursors 16 and 20.



To a stirred solution of ester **12** (14.0 g, 94.6 mmol) in dry THF (250 mL) was added LDA (47.3 mL, 2.0 M in hexane, 94.6 mmol) at $-78\text{ }^\circ\text{C}$ under argon atmosphere. After stirring for 1 h, 2,3-hexadienal **11** (6.95 mL, 63.1 mmol) in dry THF (50 mL) was added dropwise. The reaction mixture was stirred for 4 h, and saturated NH_4Cl (150 mL) was added. The resulting mixture was allowed to warm to ambient temperature and extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuo. Purification by flash column chromatography (petroleum ether/EtOAc 10:1) gave colorless oil alcohol(*ant/syn* 3:1).

To the stirred solution of above alcohol intermediate in DMF (80 mL) at $0\text{ }^\circ\text{C}$ was added imidazole (8.02 g, 118 mmol) and TBSCl (8.91 g, 59.0 mmol). The resulting mixture was allowed to warm to room temperature and stirred overnight. The solution was poured into 300 mL of ethyl acetate, and then washed with water (20 mL \times 4). The organic layer was dried over anhydrous Na_2SO_4 , concentrated in vacuo. The resulting residue was purified by silica gel chromatography (PE: EtOAc 20:1) to afford **13** (18.8 g, 83% over two steps): ^1H NMR (400 MHz, CDCl_3) δ 6.19-6.11 (m, 1H), 6.06-5.97 (m, 1H), 5.72-5.64 (m, 1H), 5.54 (dd, $J = 15.2\text{ Hz}, 7.6\text{ Hz}$, 1H), 4.65 (d, $J = 2.8$

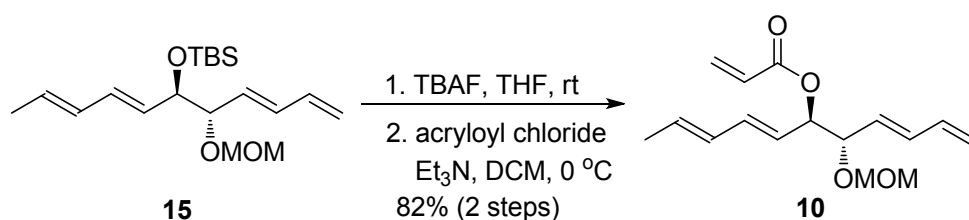
Hz, 2H), 4.45-4.37 (m, 1H), 4.22-4.11 (m, 2H), 4.03-4.00 (m, 1H), 3.34 (s, 3H), 1.73 (d, $J = 6.8$ Hz, 3H), 1.29-1.23 (m, 3H), 0.85 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 132.8, 130.7, 130.3, 129.3, 96.5, 80.1, 74.4, 60.8, 55.9, 25.7, 18.1, 14.1, -4.2, -5.1; IR (neat) ν_{max} 3351, 2957, 2931, 2894, 2857, 2373, 1747, 1660, 1591, 1472, 1446, 1374, 1363, 1255, 1212, 1186, 1153, 1163, 1048, 990, 922, 838, 815, 779, 673 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{18}\text{H}_{34}\text{O}_5\text{SiNa}$: 381.2068; found: 381.2067 $[\text{M}+\text{Na}]^+$.



To a stirred solution of ester **13** (20.0 g, 55.8 mmol) in toluene (200 mL) at -78 $^\circ\text{C}$ was slowly added DIBAL-H (58.6 mL, 1.0 M in toluene, 58.6 mmol). After stirring for 1 h, the reaction mixture was quenched with MeOH (2.40 mL), and saturated potassium sodium tartrate (200 mL) at -78 $^\circ\text{C}$ was added. The reaction mixture was allowed to warm to ambient temperature and stirred for 2 h, followed by extraction with methyl t-butyl ether. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4 . After filtered and concentrated in vacuo, the crude aldehyde was obtained. This compound could be directly used in next steps without further purification.

To a stirred solution of diethyl allylphosphonate **14** (14.9 g, 83.7 mmol) in anhydrous THF (60 mL) at -78 $^\circ\text{C}$ was added $n\text{-BuLi}$ (33.5 mL, 2.5 M in hexane, 83.7 mmol) dropwise under argon atmosphere. After stirring for 20 min, a solution of the crude aldehyde produced above and HMPA (15.6 mL, 89.3 mmol) in THF (30 mL) was added dropwise. After stirring at -78 $^\circ\text{C}$ for 2 h, the resulting solution was allowed to warm to ambient temperature and stirred for 10 h. Saturated NH_4Cl was added. The resulting mixture was extracted with ether for 3 times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (PE: EtOAc 50:1) to afford the desired product **15** (10.0 g, 53% overall yield two steps). ^1H NMR

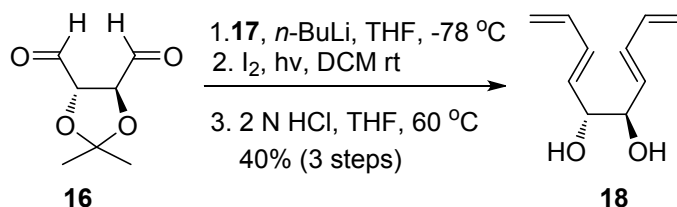
(400 MHz, CDCl₃) δ 6.39-6.32 (m, 1H), 6.27-5.13 (m, 2H), 6.08-6.02 (m, 1H), 5.73-5.66 (m, 1H), 5.64-5.53 (m, 2H), 5.21 (d, J = 16.4, 1H), 5.11-5.07 (m, 1H), 4.67 (d, J = 6.8 Hz, 1H), 4.56 (d, J = 6.4 Hz, 1H), 4.13-4.09 (m, 1H), 3.99-3.95 (m, 1H), 3.34 (s, 3H), 1.75 (d, J = 6.8 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 136.5, 134.6, 131.7, 131.1, 131.0, 130.6, 129.9, 117.5, 94.0, 80.1, 75.8, 55.5, 25.8, 18.1, -4.4, -4.8; IR (neat) ν_{\max} 3350, 3087, 3020, 2956, 2930, 2889, 22857, 2822, 2777, 2373, 1812, 1659, 1604, 1471, 1441, 1362, 1297, 1254, 1214, 1151, 1110, 1036, 1004, 989, 919, 837, 777, 674 cm⁻¹; HRMS (ESI): m/z Calcd for C₁₉H₃₄O₃SiNa: 361.2169; found: 361.2166 [M+Na]⁺.



To a stirred solution of **15** (10.0 g, 29.6 mmol) in THF (100 mL) was added TBAF (11.6 g, 44.4 mmol) dissolved in 20 mL THF at ambient temperature. After stirring for 4 h, saturated NH₄Cl (60 mL) was added, and followed by extraction with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo. Purification by flash column chromatography (petroleum ether/EtOAc 10:1) gave colorless oil alcohol.

To a stirred solution of above alcohol intermediate in DCM (80 mL) at 0 °C was added Et₃N (10.8 mL, 77.0 mmol) and acryloyl chloride (3.13 mL, 38.5 mmol). After stirring for 3 h, saturated NH₄Cl (60 mL) was added, and followed by extraction with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (petroleum ether/EtOAc 10:1) gave colorless oil **10** (6.02 g), 82% overall yield for two steps. ¹H NMR (400 MHz, CDCl₃) δ 6.45-6.16 (m, 3H), 6.13-6.01 (m, 2H), 5.85-5.81 (m, 1H), 5.78-5.73 (m, 1H), 5.60-5.40 (m, 4H), 5.24 (d, J = 15.6 Hz, 1H), 5.13 (d, J = 9.6 Hz, 1H), 4.68 (dd, J = 6.8 Hz, 2.8 Hz, 1H), 4.57 (dd, J = 6.6 Hz, 4.6 Hz, 1H), 4.26-4.23 (m, 1H), 3.34 (s, 3H), 1.75 (d, J = 5.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.1, 135.9, 135.5, 135.4, 131.5, 130.8, 130.5, 128.8,

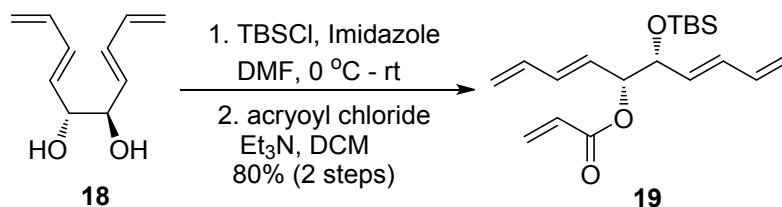
128.5, 123.9, 118.5, 93.8, 76.1, 75.7, 55.4, 18.1; IR (neat) ν_{\max} 3244, 3088, 2929, 2855, 2374, 1726, 1687, 1658, 1637, 1604, 1546, 1444, 1405, 1383, 1365, 1295, 1264, 1189, 1150, 1100, 1035, 989, 919, 854, 807, 779, 722 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_4\text{Na}$: 301.1410; found: 301.1409 $[\text{M}+\text{Na}]^+$.



To a stirred solution of allyltriphenylphosphonium bromide **17** (6.90 g, 18.0 mmol) in dry THF (40 mL) at $-40\text{ }^{\circ}\text{C}$ was added *n*-BuLi (7.20 mL, 2.5 M in hexane, 18.0 mmol) under argon atmosphere. The reaction mixture was allowed to warm to ambient temperature and stirred for 1.5 h, then cooled to $-78\text{ }^{\circ}\text{C}$ and aldehyde **16** (2.00 g, 9.01 mmol) in dry THF (15 mL) was added dropwise. After stirring at ambient temperature for 0.5 h, saturated NH_4Cl (100 mL) was added, followed by extraction with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuo. Purification by column chromatography (petroleum ether/EtOAc 50:1) gave an inseparable mixture (*Z* and *E* isomer 930 mg).

To a solution of the above intermediate in DCM (80 mL) was added I_2 (57 mg, 0.226 mmol). The mixture was stirred under ultraviolet light at ambient temperature for 1.5 h. The solution turned to be dark green. The resulting mixture was washed with saturated $\text{Na}_2\text{S}_2\text{O}_3$, dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure, and the resulting residue was dissolved in THF (20 mL). To the solution was added 2 N HCl (1 mL). After stirring at $60\text{ }^{\circ}\text{C}$ for 2 h, saturated NaHCO_3 was added, and followed by extraction with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuo. Purification by column chromatography (petroleum ether/EtOAc 10:1) gave colorless oil alcohol **18** (598 mg, 40% overall yield for three steps): ^1H NMR (400 MHz, CD_3OD) δ 6.40-6.24 (m, 4H), 5.74-5.69 (m, 2H), 5.19 (d, $J = 16.4\text{ Hz}$, 2H), 5.07 (d, $J = 10\text{ Hz}$, 2H), 4.00 (d, $J = 5.2\text{ Hz}$, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ

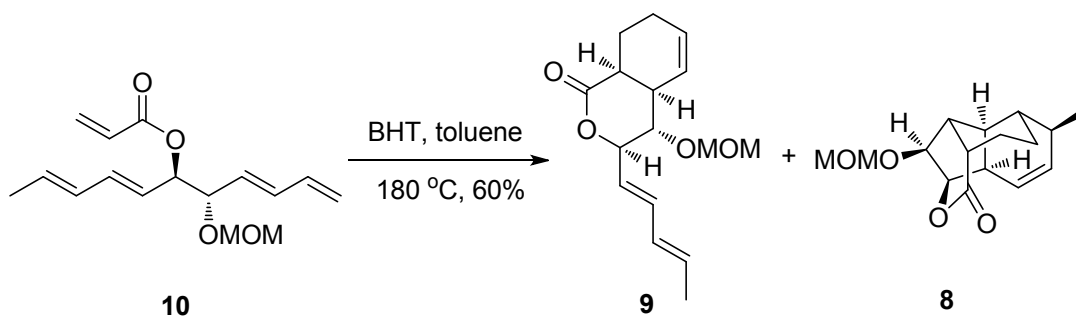
136.6, 132.6, 132.4, 116.1, 75.0; IR (neat) ν_{\max} , 3371, 3086, 3041, 3009, 2973, 2886, 2375, 1815, 1654, 1604, 1412, 1385, 1298, 1268, 1229, 1165, 1088, 1045, 1003, 954, 905, 855, 629 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2\text{Na}$: 189.0886; found: 189.0882 $[\text{M}+\text{Na}]^+$.



To a stirred solution of alcohol **18** (670 mg, 4.04 mmol) in DMF (15 mL) at 0 °C was added imidazole (302 mg, 4.44 mmol) and TBSCl (610 mg, 4.04 mmol). After stirring for 4 h. The solution was poured into 200 mL of ethyl acetate, and then washed with water (20 mL \times 3). The organic layer was dried over anhydrous Na_2SO_4 , concentrated in vacuo, the residue was directly used in next step without further purification.

To the solution of the above residue in DCM (20 mL) at 0 °C was added Et_3N (1.41 mL, 8.08 mmol) and acryloyl chloride (0.49 mL, 6.06 mmol). After stirring for 3 h, saturated NH_4Cl (60 mL) was added, and followed by extraction with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (petroleum ether/ EtOAc 20:1) gave colorless oil **19** (1.07 g), 80% overall yield for two steps: ^1H NMR (400 MHz, CDCl_3) δ 6.44-6.12 (m, 6H), 5.85 (dd, $J = 10.2$ Hz, $J = 0.14$ Hz, 1H), 5.68-5.62 (m, 2H), 5.35 (t, $J = 6.6$ Hz, 1H), 5.25-5.18 (m, 2H), 5.11 (t, $J = 9.2$ Hz, 2H), 4.29 (t, $J = 6.4$ Hz, 1H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.1, 136.3, 136.1, 134.3, 132.8, 132.1, 130.9, 128.6, 127.9, 118.3, 117.6, 73.8, 25.7, 18.1, -4.5; IR (neat) ν_{\max} , 3341, 2956, 2929, 2892, 2858, 2372, 1729, 1605, 1546, 1462, 1405, 1546, 1471, 1405, 1363, 1296, 1259, 1188, 1114, 1045, 1003, 905, 837, 808, 777, 673 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{19}\text{H}_{30}\text{O}_3\text{Si}_1\text{Na}$: 357.1856; found: 357.1848 $[\text{M}+\text{Na}]^+$.

General Procedure for Domino Double IMDA Reactions

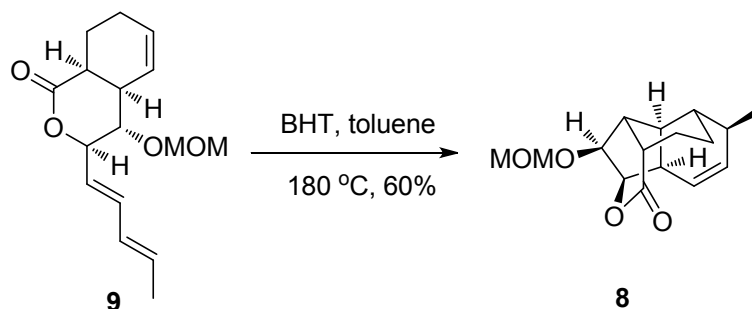


To a solution of polyene **10** (56 mg, 0.2 mmol) in toluene (4 mL) was added BHT (5 mg, 0.02 mmol). The solution was poured into a sealed tube under argon atmosphere. The reaction mixture was stirred at 180 °C for 120 h. Toluene was removed under reduced pressure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc 10:1) to afford the desired product **8** (28 mg, 51%) and trace amount of **9**.

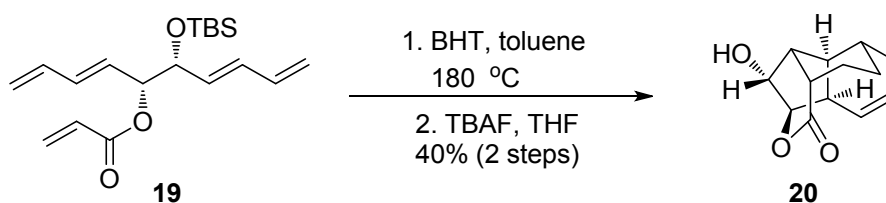
Compound **8**: $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.78 (d, $J = 7.6$ Hz, 1H), 5.50 (d, $J = 9.6$ Hz, 1H), 4.72 (s, 2H), 4.66 (s, 1H), 4.04 (dd, $J = 4.8, 2.8$ Hz, 1H), 3.39 (s, 3H), 2.95 (d, $J = 4.8$ Hz, 1H), 2.62-2.50 (m, 2H), 2.40 (q, $J = 5.1$ Hz, 1H), 2.26 (dd, $J = 13.2, 3.2$ Hz, 1H), 2.21-2.16 (m, 1H), 1.85-1.78 (m, 1H), 1.52-1.47 (m, 1H), 1.31-1.23 (m, 1H), 1.02 (d, $J = 7.2$ Hz, 3H), 0.99-0.91 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 173.5, 134.8, 124.3, 95.8, 81.0, 76.5, 55.9, 39.6, 39.5, 38.3, 35.6, 35.5, 33.5, 26.5, 19.6, 17.8; IR (neat) ν_{max} 3438, 3021, 2933, 2873, 2375, 1734, 1639, 1598, 1563, 1445, 1380, 1283, 1259, 1236, 1215, 1190, 1150, 1124, 1107, 1073, 1040, 1020, 993, 972, 930, 919, 780, 752, 731, 701 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_4\text{Na}$: 301.1410; found: 301.1408 $[\text{M}+\text{Na}]^+$.

Compound **9**: $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.31 (dd, $J = 10.4, 15.2$ Hz, 1H), 6.07 (dd, $J = 1.6, 11.2$ Hz, 1H), 6.05-5.74 (m, 2H), 6.67-5.63 (m, 1H), 5.53 (dd, $J = 7.2, 15.6$ Hz, 1H), 4.69-4.66 (m, 3H), 3.50-3.47 (dd, $J = 5.6, 8.0$ Hz, 1H), 3.37 (s, 3H), 3.05-3.01 (m, 1H), 2.86-2.80 (m, 1H), 2.40-2.18 (m, 2H), 2.02-1.98 (m, 1H), 1.76 (d, $J = 7.2$ Hz, 3H), 1.75-1.68 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 172.8, 134.7, 131.9, 130.2, 128.6, 126.4, 125.0, 96.4, 80.0, 78.4, 55.9, 38.5, 35.4, 22.2, 21.6, 18.1; IR (neat) ν_{max} 3445, 3024, 2926, 2067, 1746, 1637, 1445, 1375, 1329, 1295, 1196, 1150, 1099, 1032, 989, 918, 705 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_4\text{Na}$: 301.1410; found: 301.1409

[M+Na]⁺.



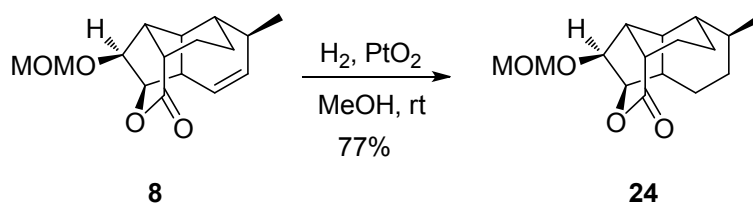
To a solution of **9** (56 mg, 0.2 mmol) in toluene (4 mL) was added BHT (5 mg, 0.02 mmol). The solution was poured into a sealed tube under argon atmosphere. The reaction mixture was stirred at 180 °C for 120 h. Toluene was removed under reduced pressure, residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc 10:1) to afford **8** (34 mg, 60%).



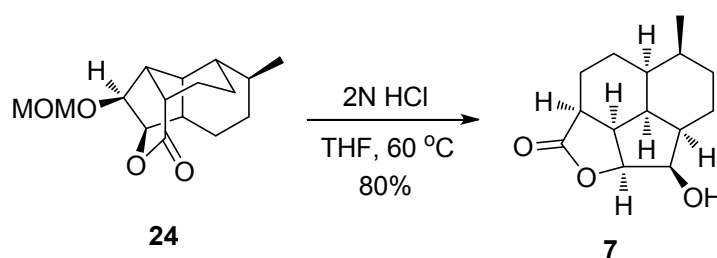
To a solution of polyene **19** (67 mg, 0.2 mmol) in toluene (4 mL) was added BHT (5 mg, 0.02 mmol). The solution was poured into a sealed tube under argon atmosphere. The reaction mixture was stirred at 180 °C for 120 h. toluene was removed under reduced pressure. The residue was dissolved in THF (3 mL) and TBAF·3H₂O (126 mg, 0.4 mmol dissolved in 1 mL THF) was added at ambient temperature. After stirring for 4 h, saturated NH₄Cl (8 mL) was added, and followed by extraction with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo. Purification by column chromatography (petroleum ether/EtOAc 4:1) to afford the tetracyclic compound **20** (18 mg, 40% for two steps): Mp=134 °C; ¹H NMR (400 MHz, CDCl₃) δ 5.87 (s, 2H), 4.56-4.54 (m, 1H), 4.28 (s, 1H), 2.98 (d, *J*=11.6 Hz, 1H), 2.87-2.76 (m, 2H), 2.33 (t, *J*=5.2 Hz, 1H), 2.22-1.96 (m, 4H), 1.45-1.35 (m, 2H), 1.27-1.20 (dt, *J*=12.4 Hz, *J*=3.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 128.4, 125.3, 84.0, 75.5, 42.7, 41.7, 39.9, 34.6, 30.5, 29.3, 27.7, 25.5; IR (neat) ν_{max}, 3412, 2941, 2914, 2860, 2374, 1697,

1658, 1600, 1452, 1376, 1311, 1282, 1215, 1160, 1100, 1084, 1056, 1026, 999, 974, 940, 857, 834, 762, 694, 615 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3\text{Na}$: 243.0992; found: 243.0986 $[\text{M}+\text{Na}]^+$.

Synthesis of 4-*epi*-Hydromitchellene B

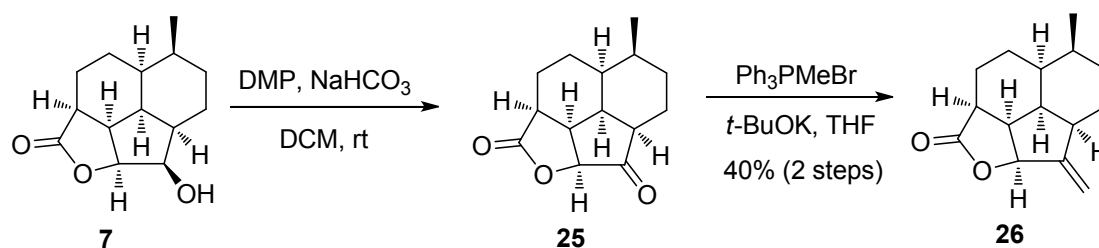


To a solution of **8** (2.58 g, 10.4 mmol) in MeOH (40 mL) was added PtO_2 (13 mg, 0.5%). The reaction mixture was stirred under hydrogen atmosphere at ambient temperature for 6 h, then filtered through Celite. Concentration and silica gel flash chromatography purification afforded **24** (2.00 g, 77%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 4.72 (s, 2H), 4.52 (s, 1H), 3.97 (t, $J = 3.8$ Hz, 1H), 3.38 (s, 3H), 2.94 (d, $J = 4.4$ Hz, 1H), 2.39 (dd, $J = 13.6$ Hz, 3.2 Hz, 1H), 2.31 (q, $J = 4.8$ Hz, 1H), 2.25-2.11 (m, 2H), 1.79-1.71 (m, 2H), 1.69-1.48 (m, 4H), 1.34-1.23 (m, 2H), 1.03-0.96 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 174.1, 95.8, 81.3, 76.5, 55.8, 40.1, 38.3, 37.6, 36.6, 36.4, 30.8, 27.2, 25.5, 21.5, 20.1, 18.0; IR (neat) ν_{max} 3369, 2932, 2870, 2372, 1733, 1594, 1475, 1446, 1379, 1284, 1254, 1220, 1161, 1150, 1230, 1103, 1071, 1046, 1013, 930, 919, 756 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{16}\text{H}_{24}\text{O}_4\text{Na}$: 303.1567; found: 303.1565 $[\text{M}+\text{Na}]^+$.



To a solution of **24** (2.00 g) in THF (30 mL) was added 2 N HCl (1.5 mL). The reaction mixture was stirred at 60 $^\circ\text{C}$ for 2 h, then cooled to 0 $^\circ\text{C}$, saturated NaHCO_3 was added, and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuo. Purification by column chromatography (petroleum ether/EtOAc 3:1) gave

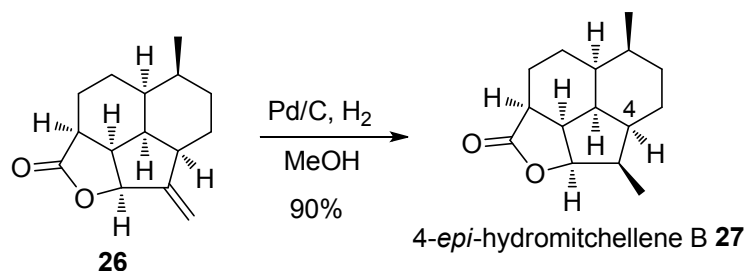
alcohol **7** (1.50 g, 80%) as white solide. Mp=145 °C; ¹H NMR (400 MHz, CDCl₃) δ 4.76 (t, *J* = 5.2 Hz, 1H), 4.23-4.18 (m, 1H), 3.01-2.90 (m, 2H), 2.44 (q, *J* = 9.6 Hz, 1H), 2.29-2.14 (m, 3H), 1.75-1.46 (m, 6H), 1.26-1.17 (m, 2H), 1.00-0.89 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 178.8, 85.0, 75.6, 39.7, 39.4, 37.2, 36.4, 35.9, 30.4, 25.8, 22.7, 19.6, 19.2, 18.9; IR (neat) ν_{\max} 3367, 2940, 2865, 2374, 1762, 1594, 1459, 1444, 1370, 1324, 1297, 1253, 1221, 1185, 1158, 1127, 1116, 1092, 1037, 1014, 993, 973, 950, 903, 881, 862, 787, 733, 675, 630, 594, 555, 510 cm⁻¹; HRMS (ESI): *m/z* Calcd for C₁₄H₂₀O₃Na: 259.1305; found: 259.1305 [M+Na]⁺.



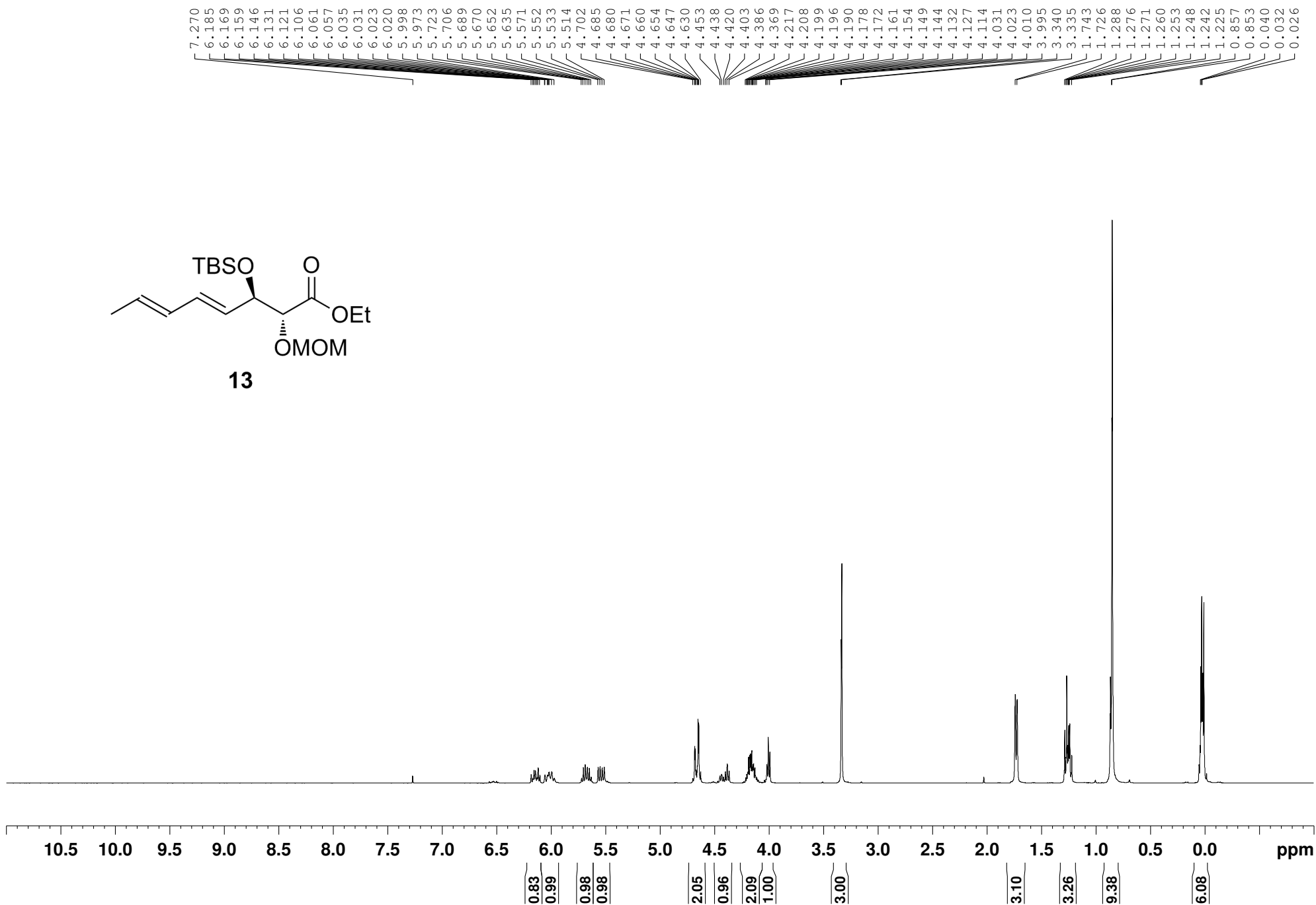
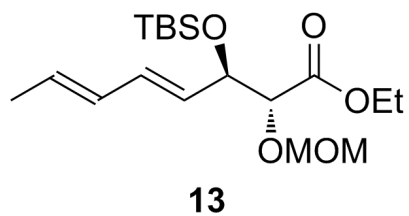
To a stirred solution of alcohol **7** (381 mg, 1.61 mmol) in DCM (15 mL) at 0 °C was added NaHCO₃ (541 mg, 6.44 mmol) and Dess-Martin periodinane (1.37 g, 3.22 mmol). After stirring at ambient temperature for 4 h, saturated sodium thiosulfate was added. The solution was stirred to clarify, followed by extraction with DCM. The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo, the residue filtered through a pad silica gel gave the crude ketone **25**. ketone **25** was quite instable, so it was directly used in next steps.

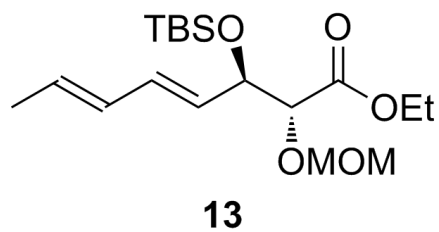
To a solution of PPh₃MeBr (1.72 g, 4.83 mmol) in dry THF (20 mL) at 0 °C was added *t*-BuOK (361 mg, 3.22 mmol) under argon atmosphere. After for 1 h, ketone **25** in dry THF (4 mL) was added dropwise. The resulting mixture was allowed to warm to ambient temperature and stirred for 8 h. Saturated NH₄Cl was added. The mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo. Purification by column chromatography (petroleum ether/EtOAc 20:1) gave **26** (113 mg), 40% overall yield from alcohol **28**. Mp=96 °C; ¹H NMR (400 MHz, CDCl₃) δ 5.14 (d, *J* = 2.0 Hz, 1H), 4.99 (d, *J* = 6.4 Hz, 1H), 4.89 (d, *J* = 2.4 Hz, 1H), 2.97-2.91 (m, 1H), 2.75-2.70 (m, 1H), 2.35 (d, *J* = 14.0 Hz, 1H), 2.09-2.07 (m, 1H), 1.98-1.94 (m, 1H), 1.75-1.43 (m,

6H), 1.21-1.06 (m, 3H), 0.92 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 179.2, 151.3, 108.2, 84.3, 45.9, 39.1, 37.7, 37.0, 36.4, 35.5, 29.6, 26.6, 24.3, 18.9, 16.2; IR (neat) ν_{max} 3423, 2922, 2869, 2856, 2372, 1747, 1675, 1638, 1447, 1362, 1332, 1315, 1289, 1226, 1165, 1146, 1061, 998, 983, 952, 906, 861, 784, 746, 670, 636, 593, 552, 498 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_2\text{Na}$: 255.1356; found: 255.1355 $[\text{M}+\text{Na}]^+$.



To a solution of **26** (81 mg) in EtOAc (8 mL) was added 10% Pd/C (6 mg). The reaction mixture was stirred under hydrogen atmosphere at ambient temperature for 4 h, then filtered through Celite. Concentration and silica gel flash chromatography purification afforded 4-*epi*-hydromitchellene B **27** (74 mg, 90%). Mp=81 °C; ^1H NMR (400 MHz, CDCl_3) δ 4.76 (dd, $J = 6.0$ Hz, 4.0 Hz, 1H), 2.89-2.83 (m, 1H), 2.70-2.65 (m, 1H), 2.30 (d, $J=14.8$ Hz, 1H), 1.82-1.77 (m, 1H), 1.70-1.36 (m, 7H), 1.19-0.80 (m, 10H); ^{13}C NMR (100 MHz, CDCl_3) δ 179.8, 85.8, 46.9, 44.3, 39.1, 38.9, 38.4, 36.9, 35.6, 30.2, 28.5, 24.5, 19.0, 16.7, 11.3; IR (neat) ν_{max} 3429, 2928, 2872, 2373, 1761, 1637, 1455, 1378, 1363, 1343, 1283, 1230, 1177, 1157, 1127, 1082, 1055, 998, 977, 954, 857, 783, 711, 641, 591, 548, 502 cm^{-1} ; HRMS (ESI): m/z Calcd for $\text{C}_{15}\text{H}_{23}\text{O}_2$: 235.1693; found: 235.1693 $[\text{M}+\text{H}]^+$.





170.83
170.29

132.81
132.32
130.71
130.58
130.36
130.22
129.29
128.65

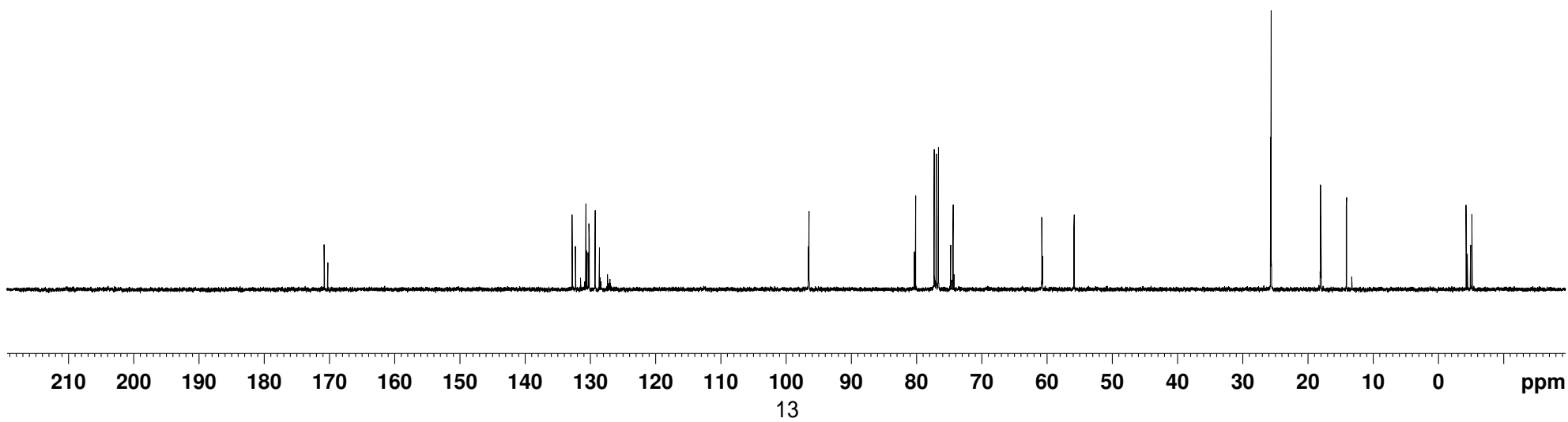
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74.79
74.42

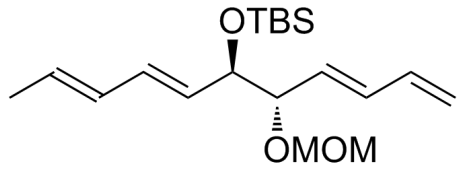
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18.06
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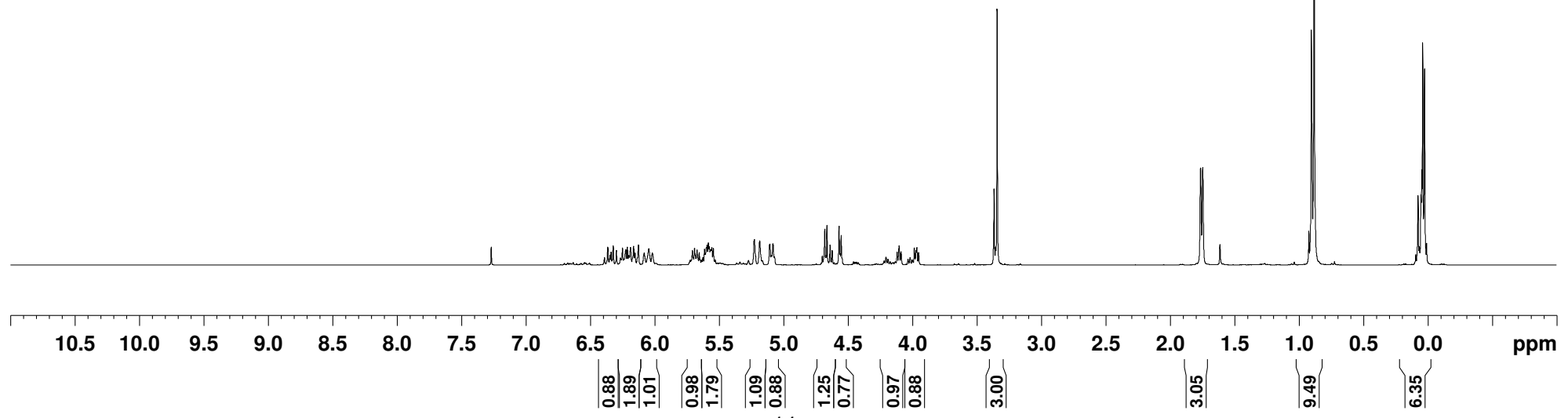
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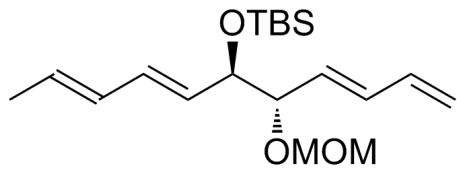


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0.047
0.040
0.025



15





15

136.48
136.40
134.55
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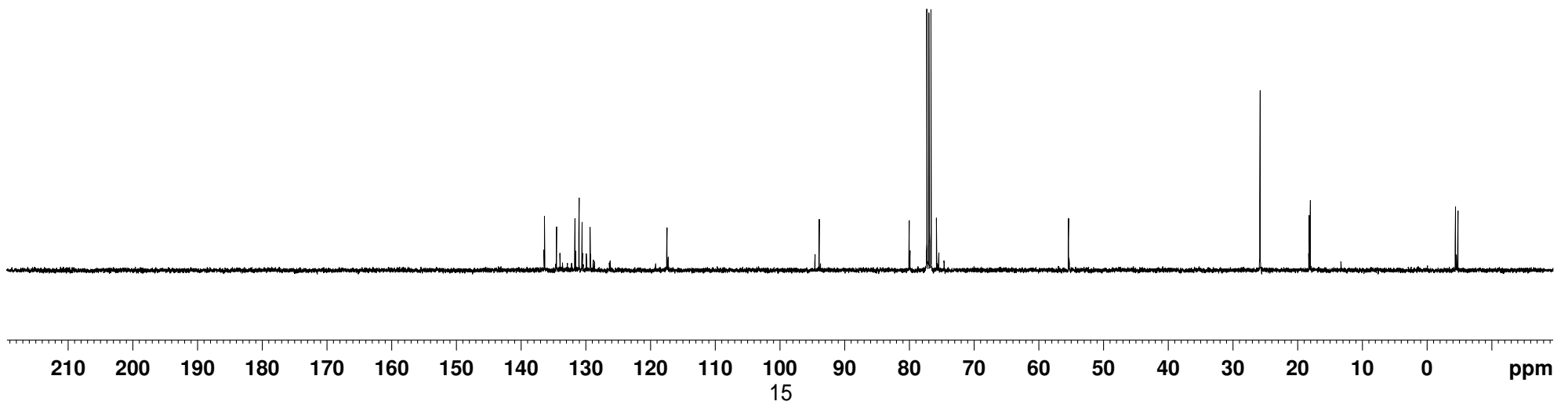
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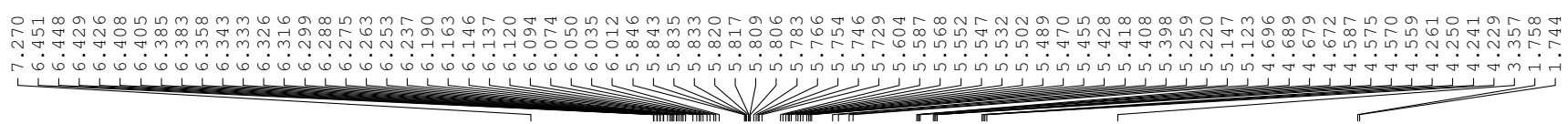
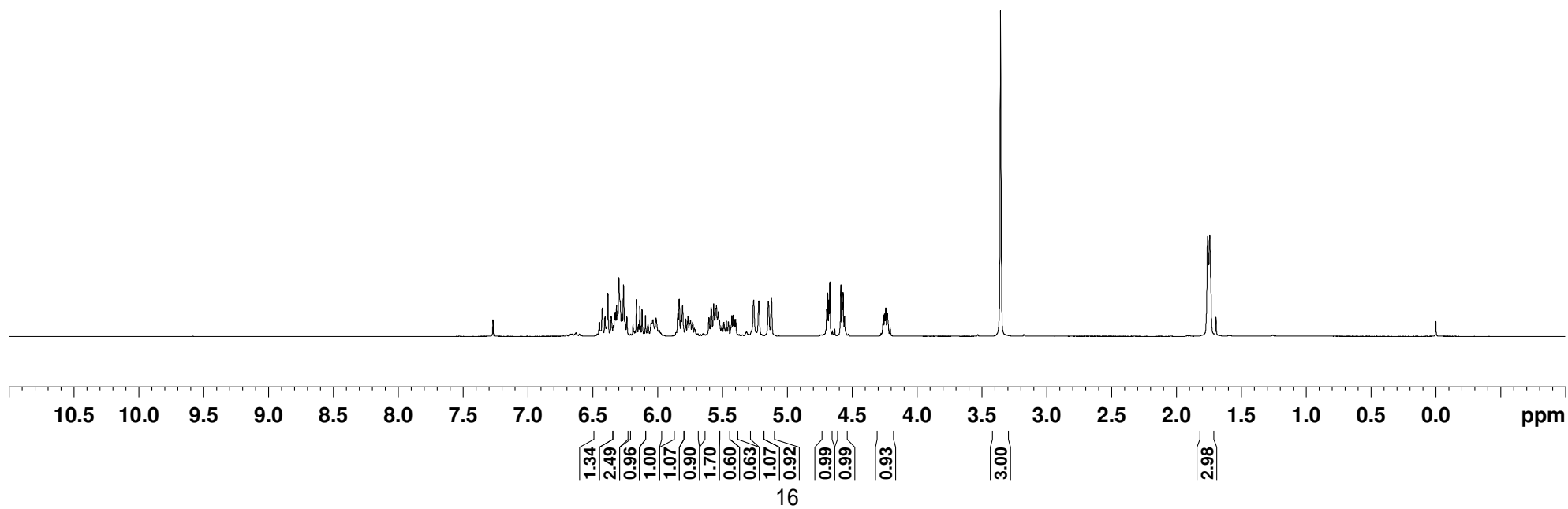
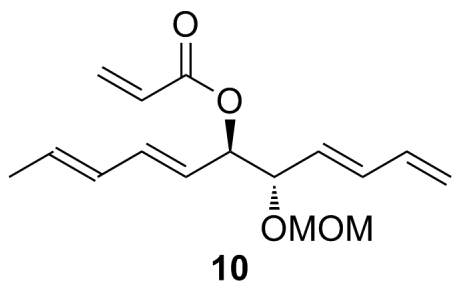
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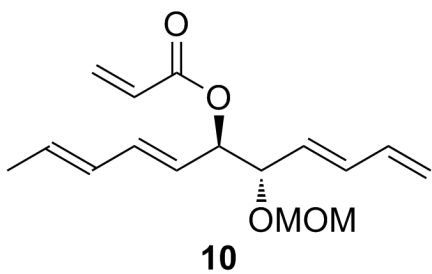
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-4.75





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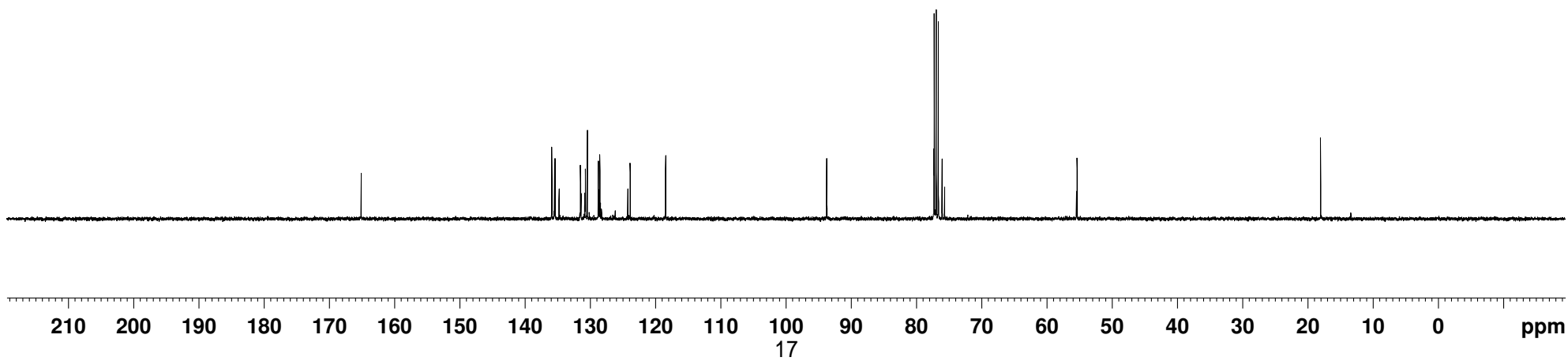
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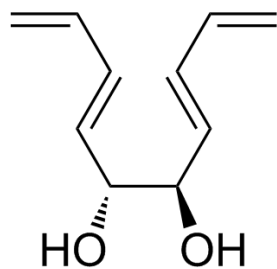
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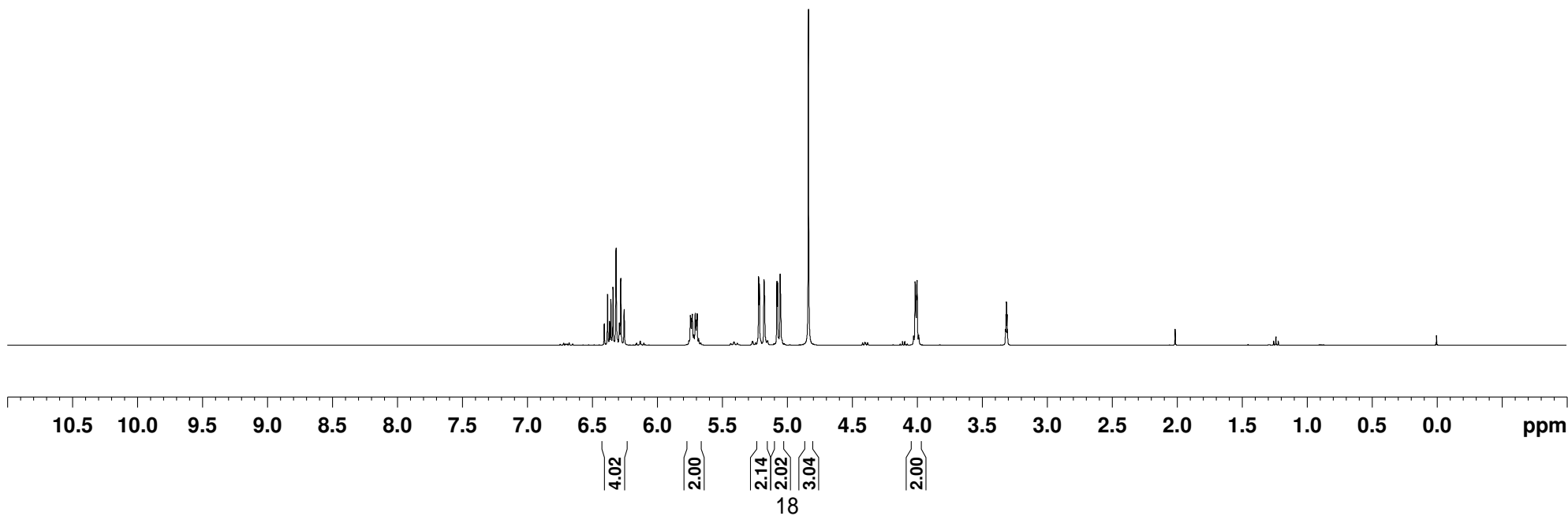
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55.41

18.08



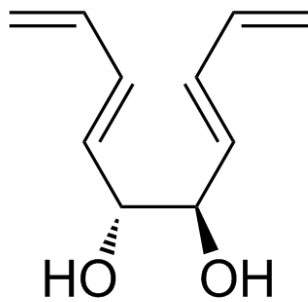


18



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5.739
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3.314
3.310
3.306
3.302

— 0.005



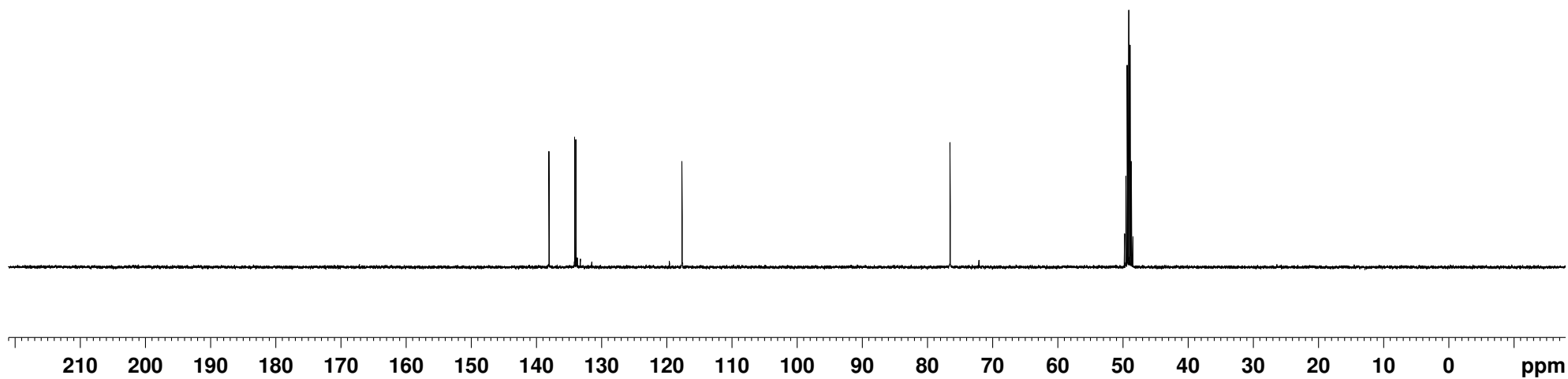
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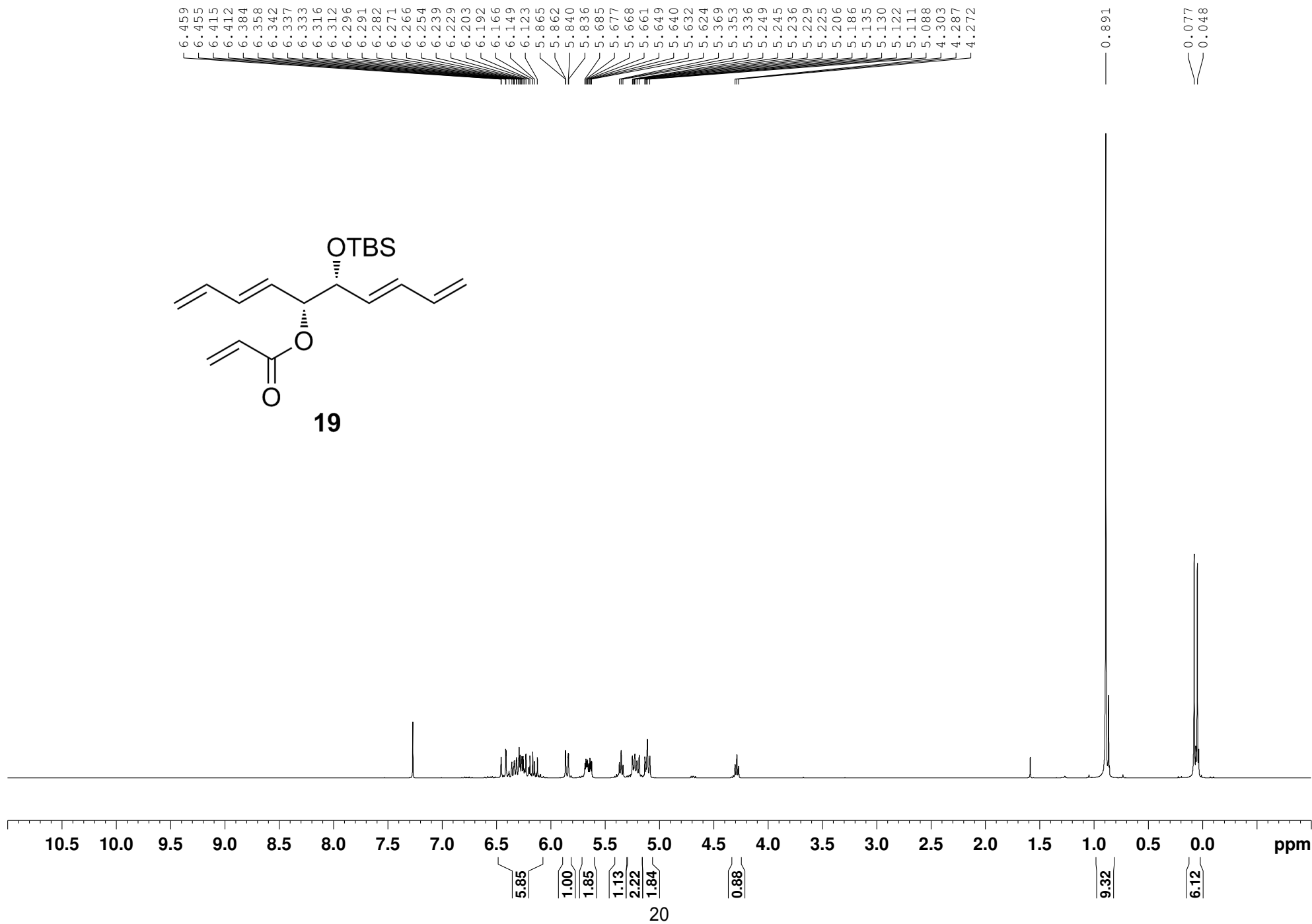
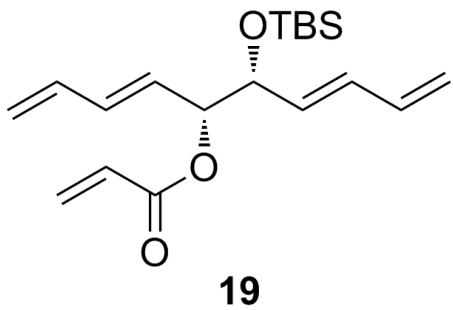
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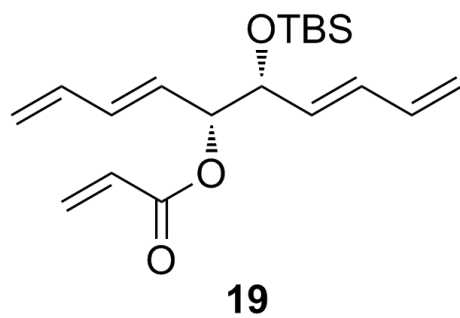
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49.15
48.94
48.73
48.51







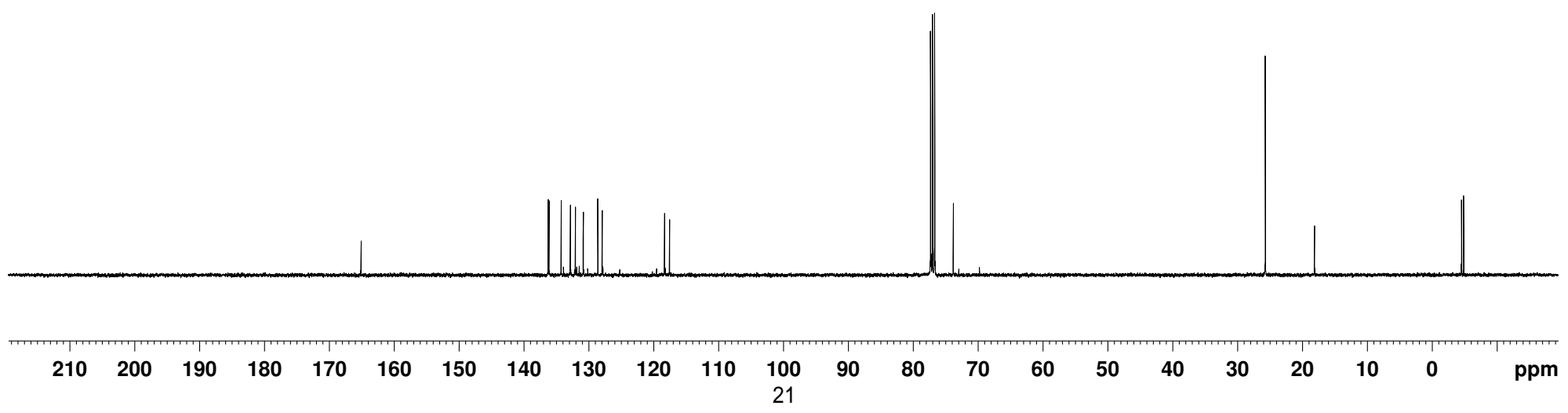
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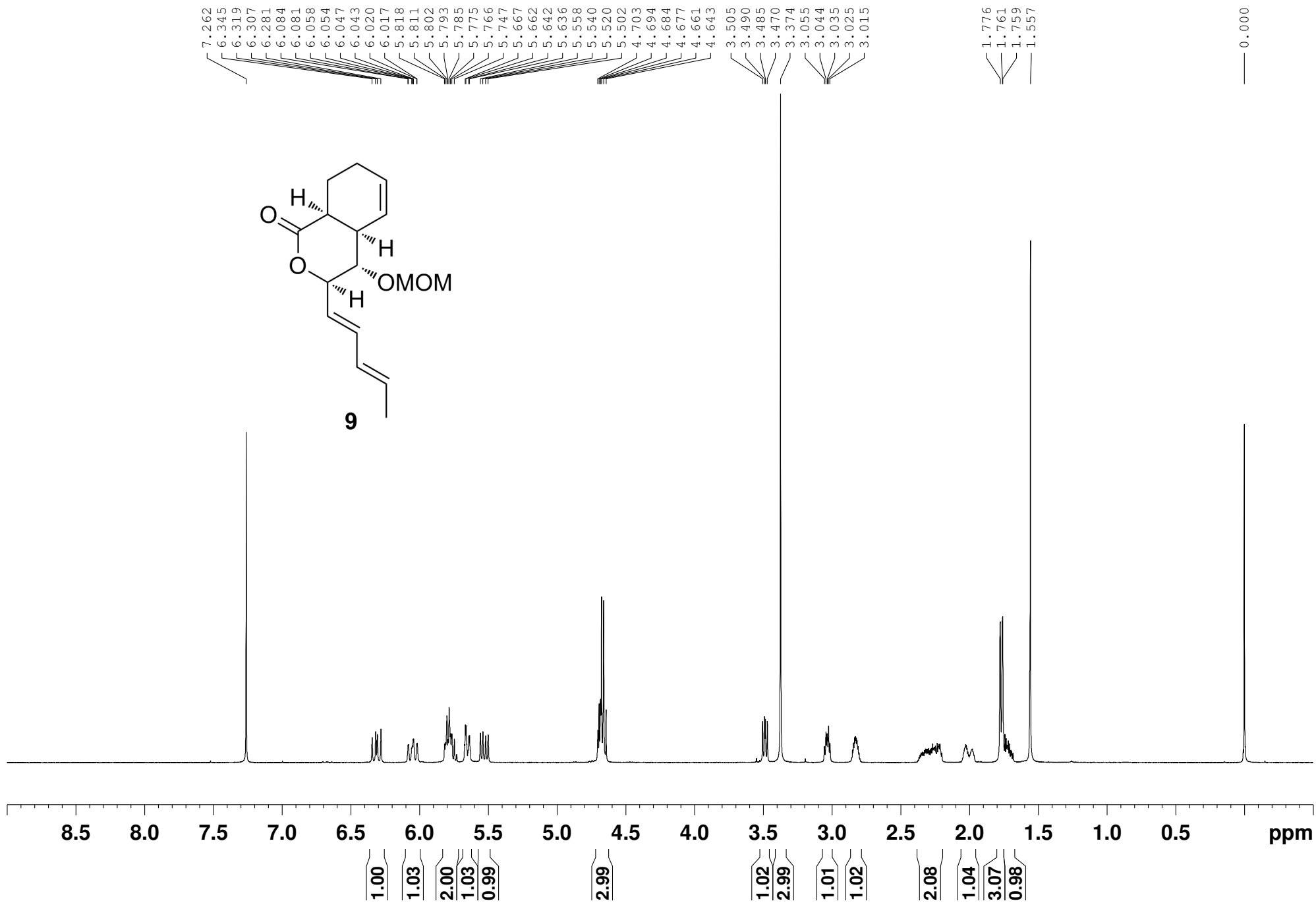
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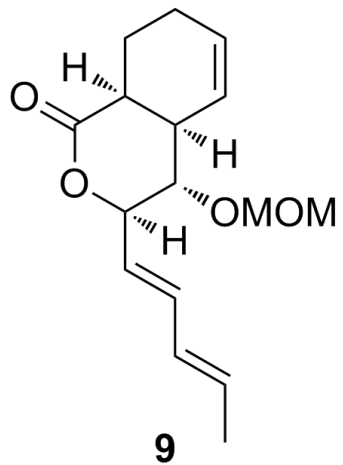
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— 172.78

— 134.71
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— 130.21
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— 126.42
— 124.99

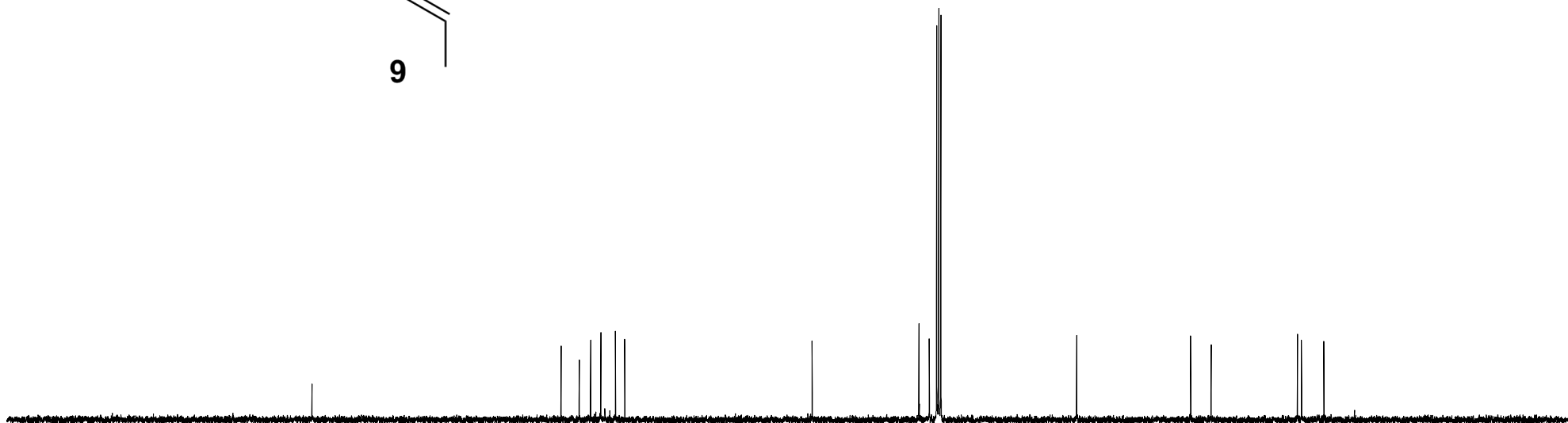
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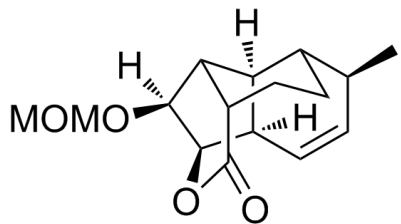
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— 38.50
— 35.37

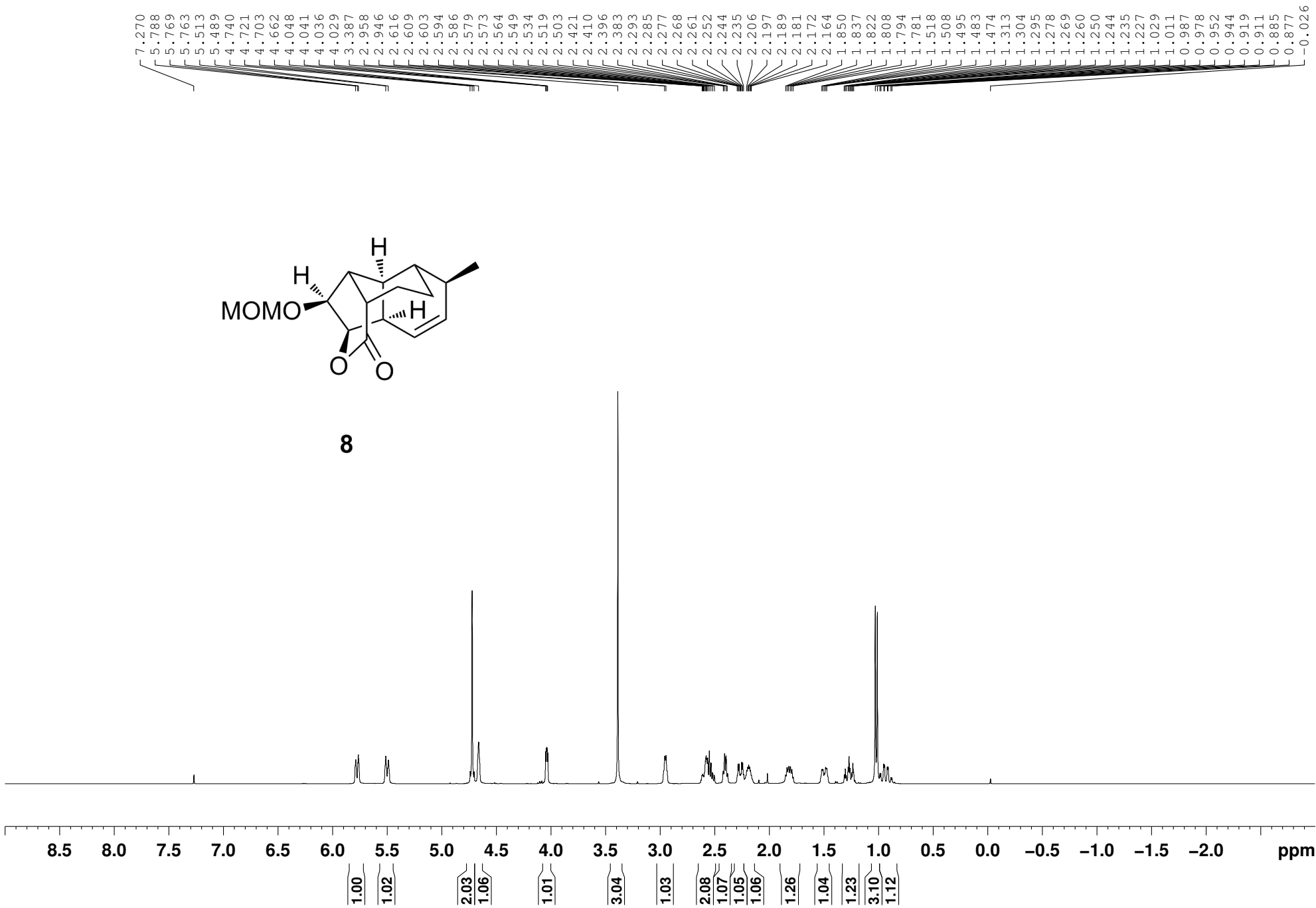
— 22.17
— 21.55
— 18.14

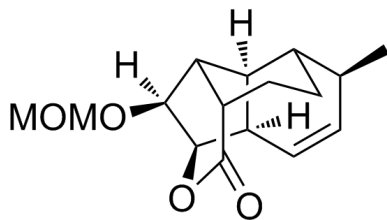


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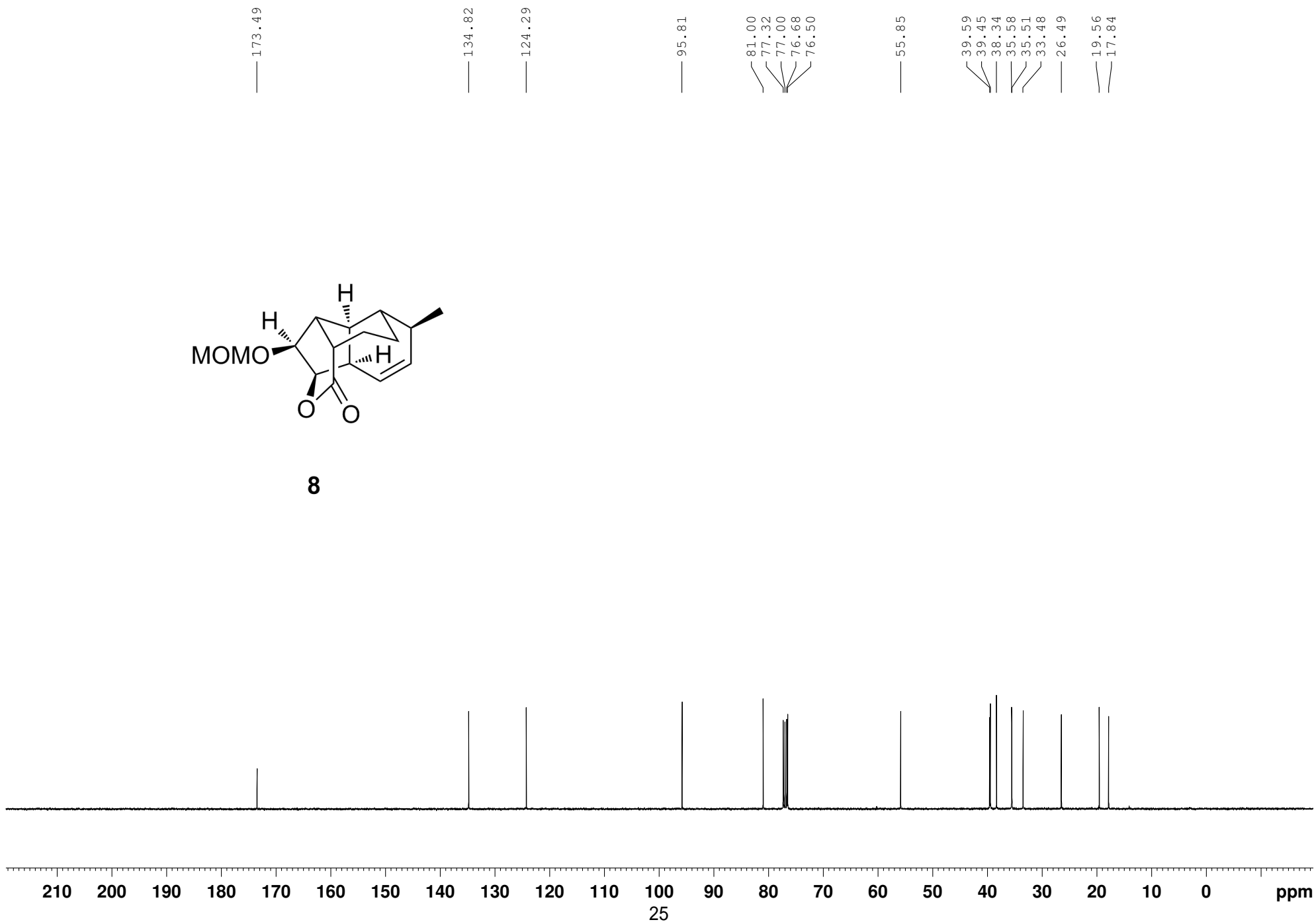


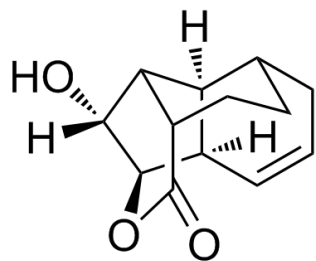
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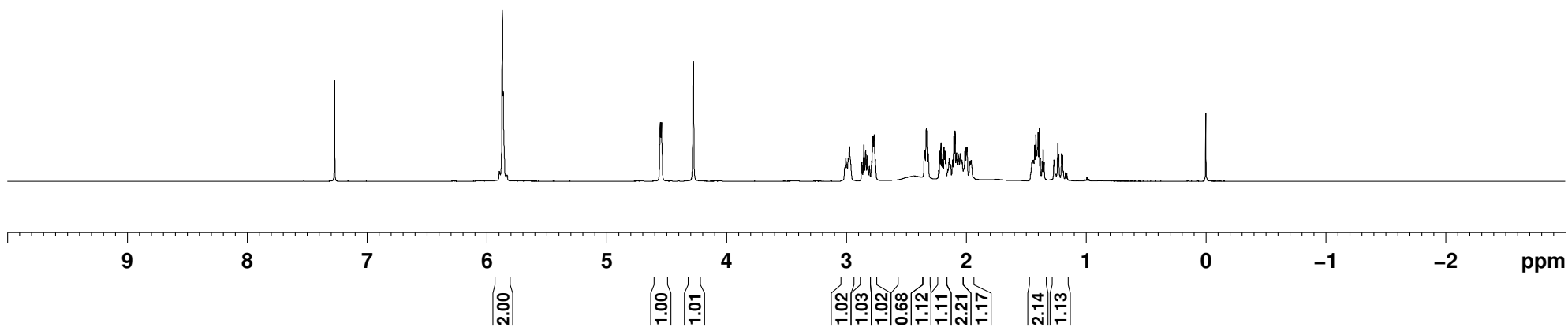


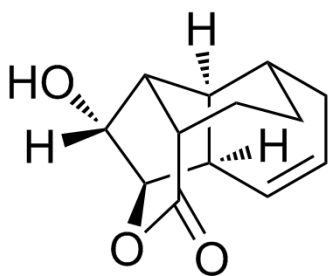
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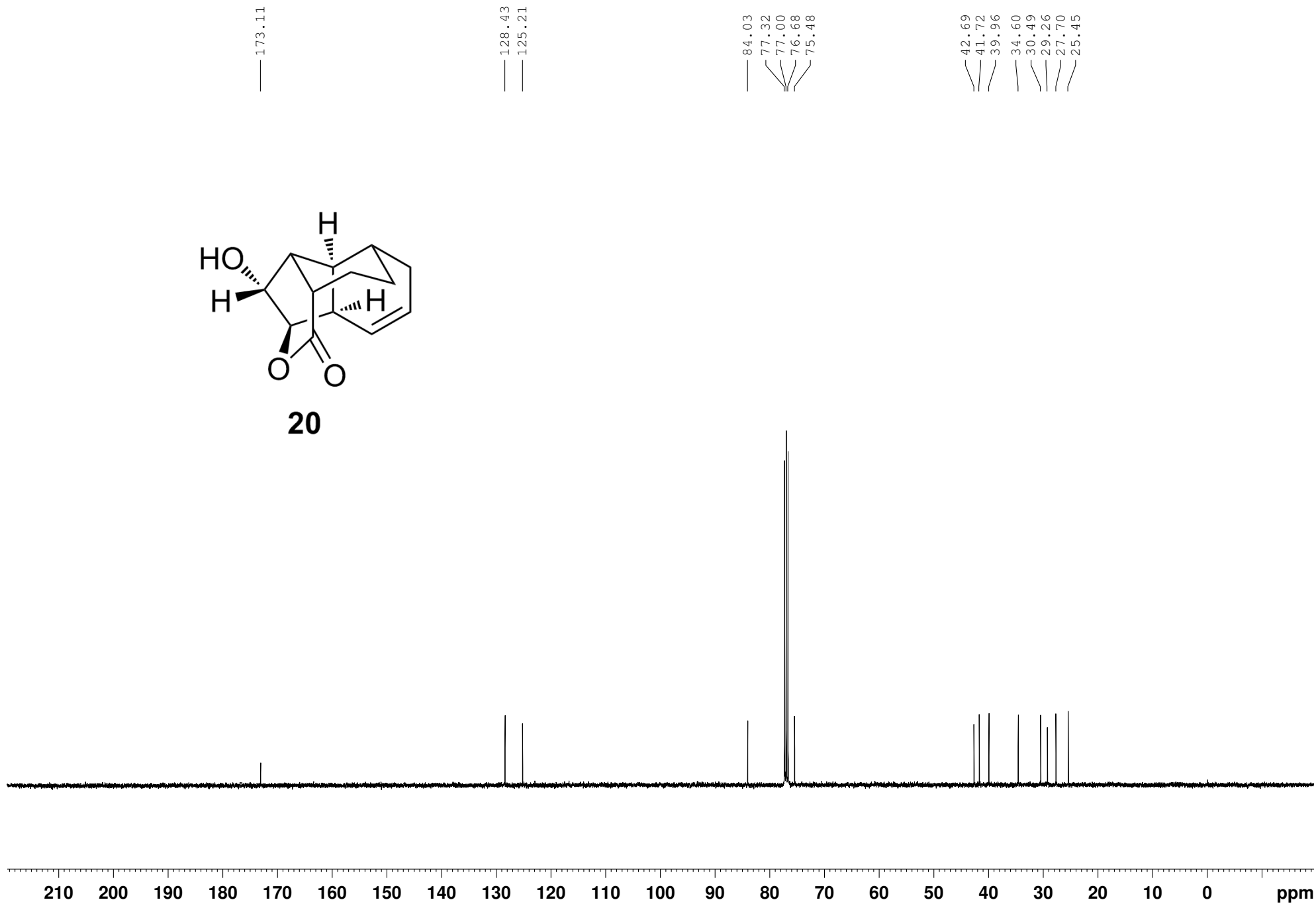


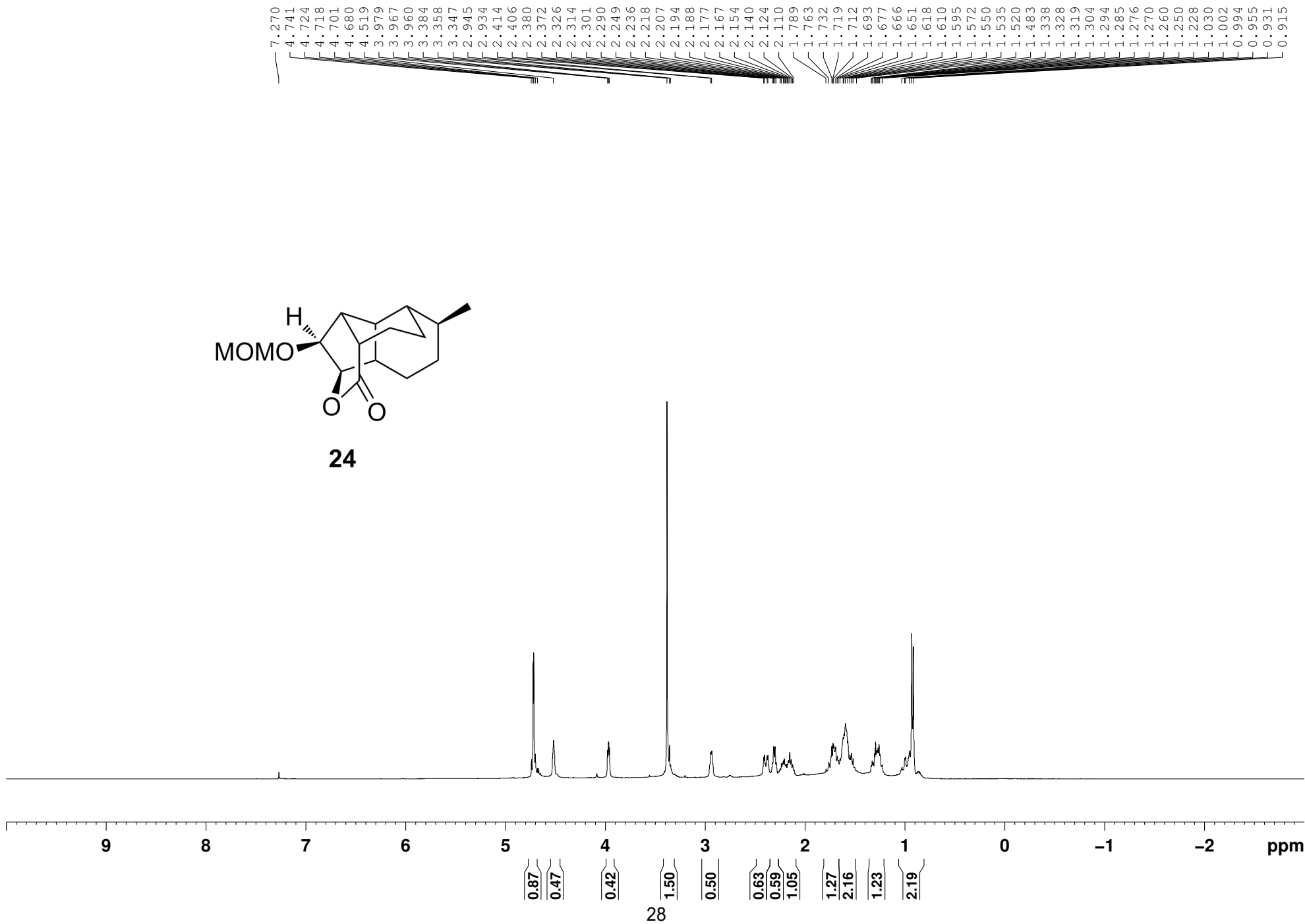
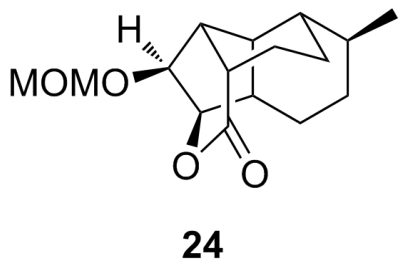
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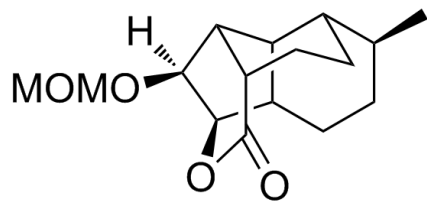




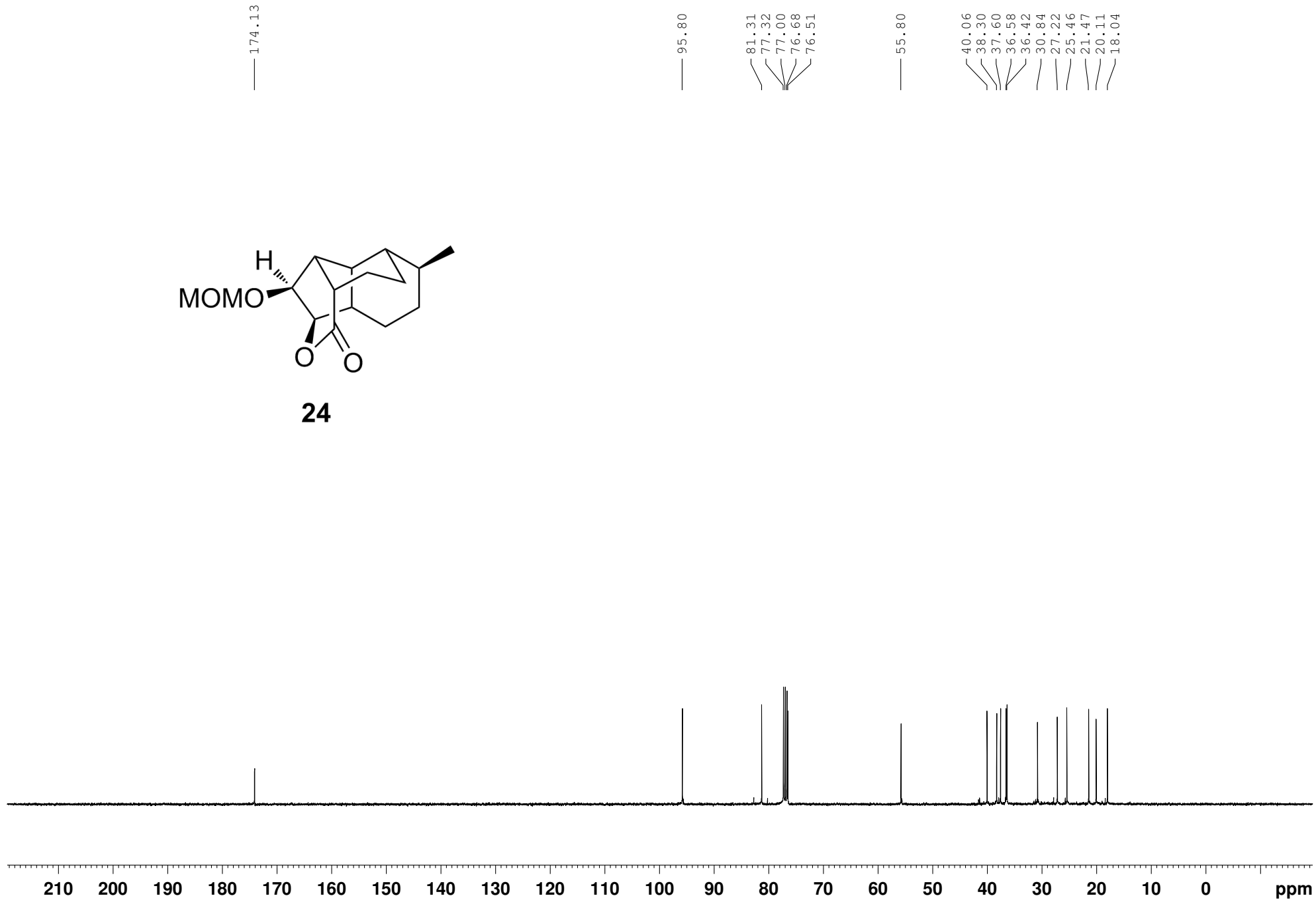
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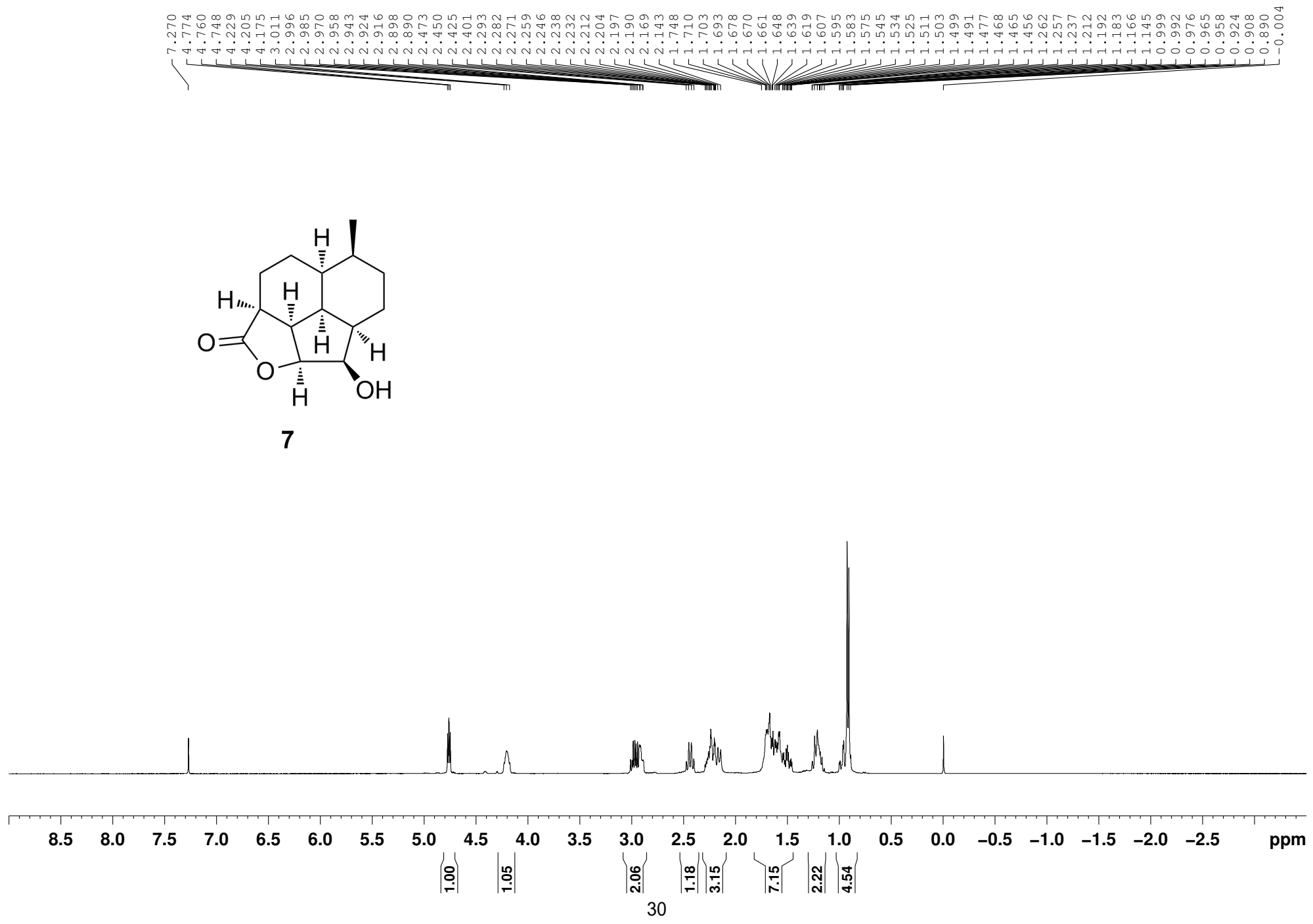
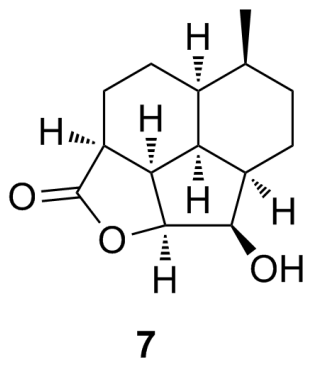




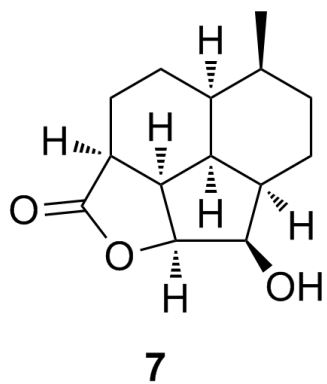


24





— 178.78

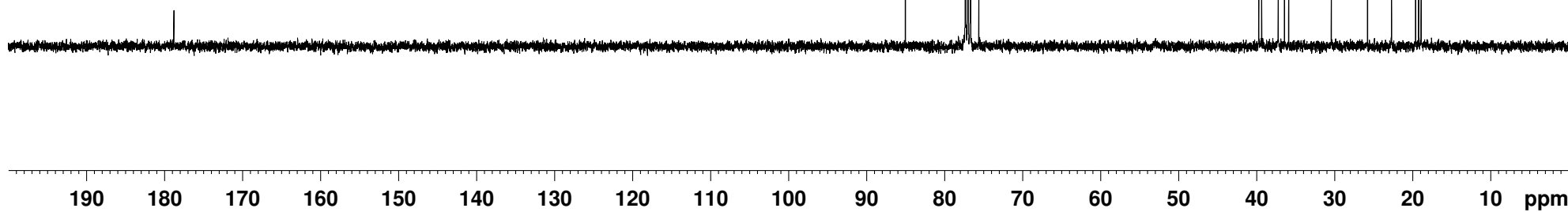


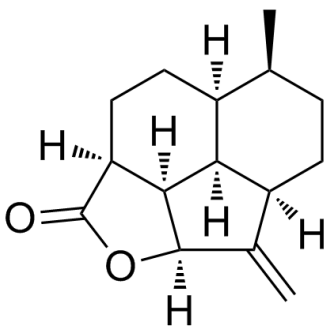
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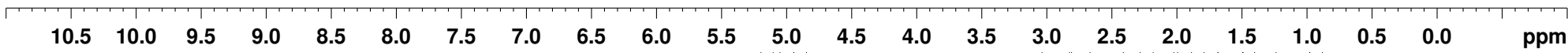
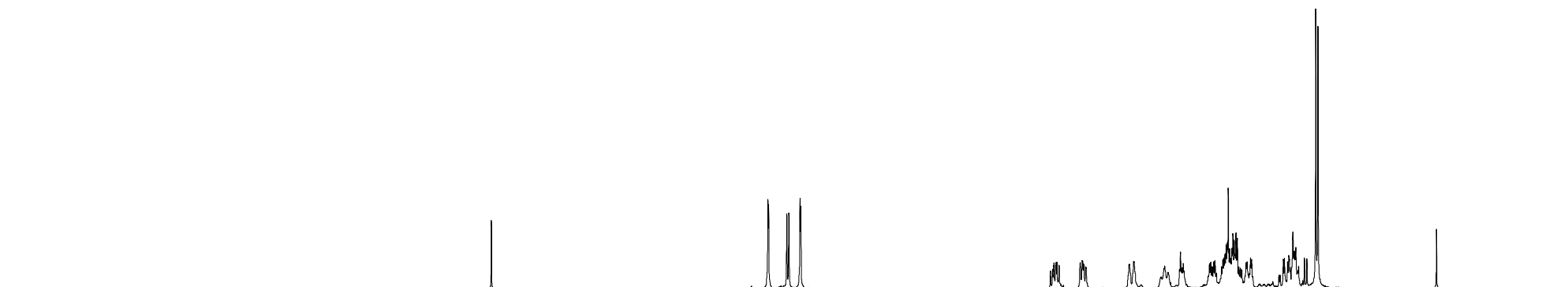
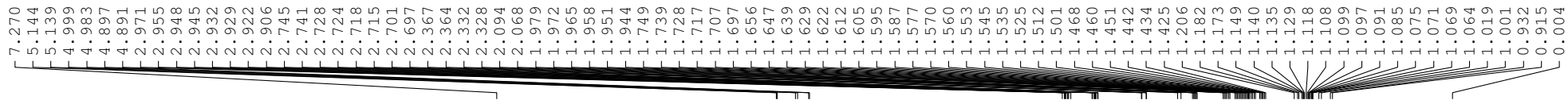
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18.90





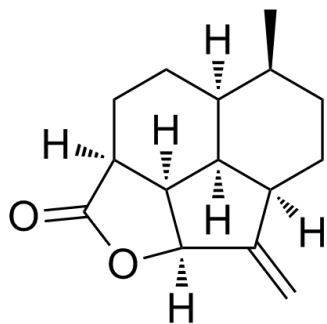
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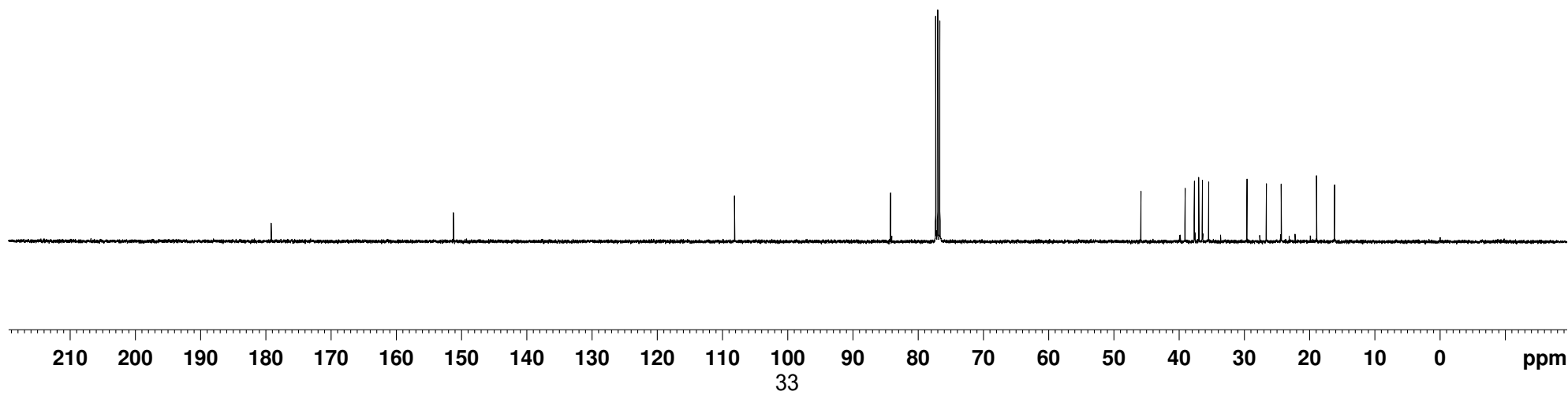
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1.01

32

1.03
0.99
1.00
1.05
0.92
1.26
4.59
1.16
3.24
2.91



26



— 179.19

— 151.25

— 108.16

— 84.25

77.32

77.00

76.68

— 45.85

39.09

37.67

36.98

36.44

35.46

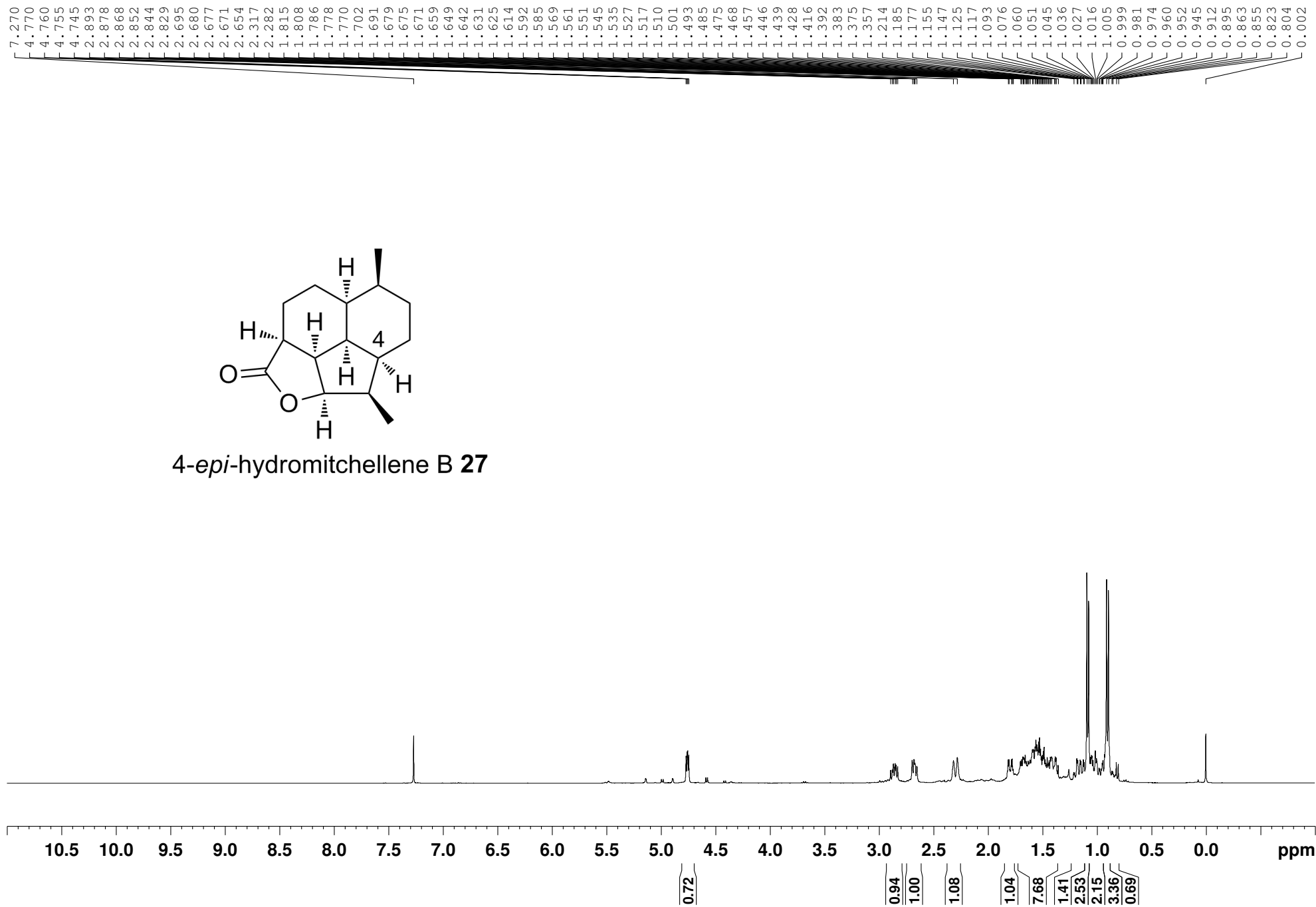
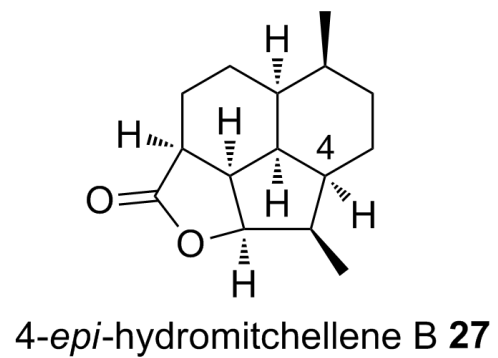
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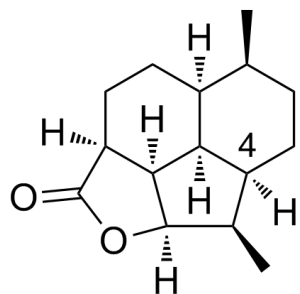
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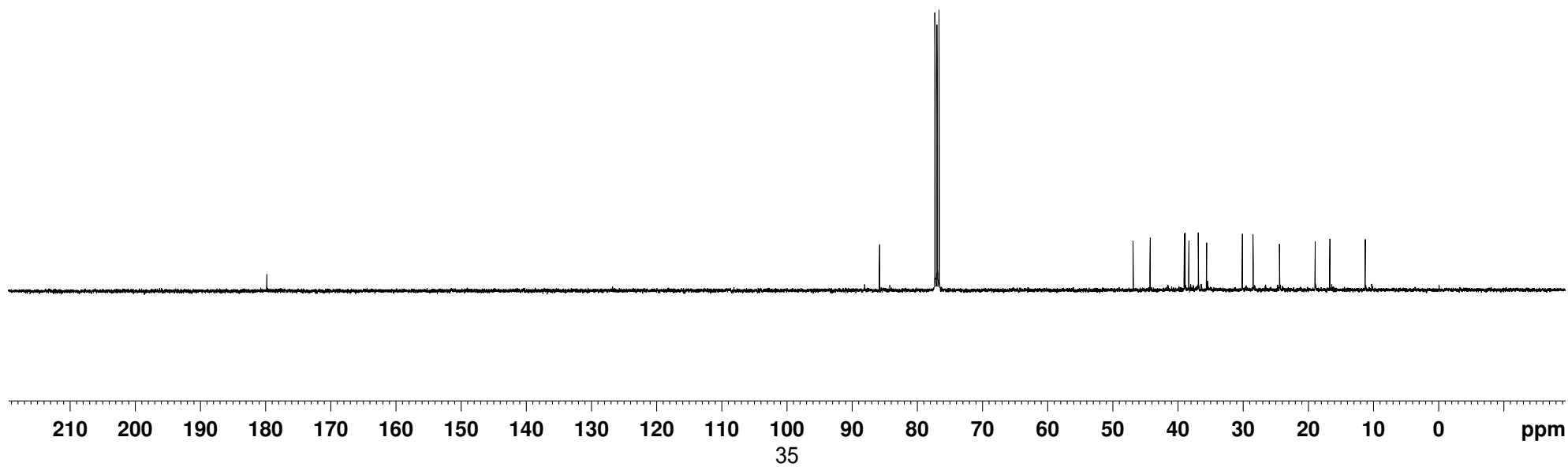
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— 16.16

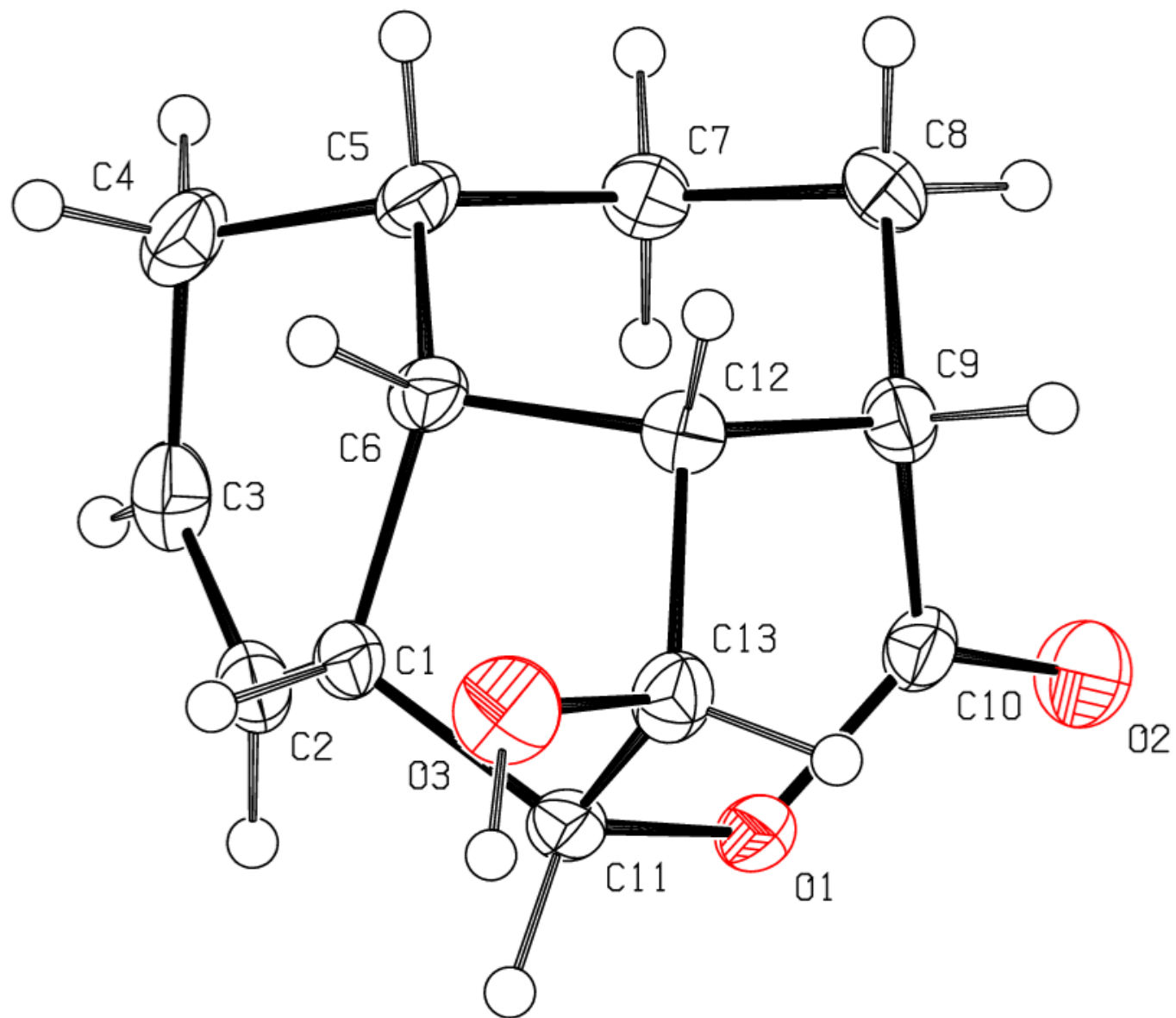




4-*epi*-hydromitchellene B 27



X-ray of 20



X-ray of 7

