

SUPPORTING INFORMATION

Synthesis of functionalized cannabilactones

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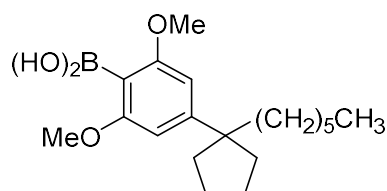
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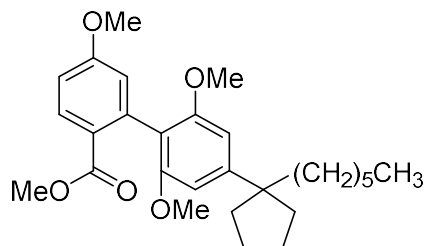
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Experimental section

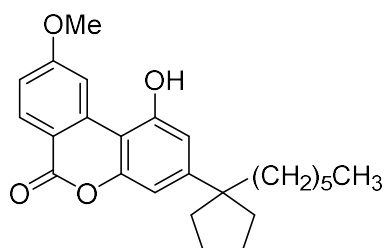
All reagents and solvents were purchased from Sigma-Aldrich Chemical Company, unless otherwise specified, and used without further purification. All anhydrous reactions were performed under a static argon atmosphere in flame-dried glassware using scrupulously dry solvents. Flash column chromatography employed silica gel 60 (230–400 mesh). All compounds were demonstrated to be homogeneous by analytical TLC on pre-coated silica gel TLC plates (Merck, 60 F245 on glass, layer thickness 250 μm), and chromatograms were visualized by phosphomolybdic acid staining. IR spectra were recorded on a PerkinElmer Spectrum One FT-IR spectrometer. NMR spectra were recorded in the indicated solvent on Varian 500 (^1H at 500 MHz, ^{13}C at 126 MHz), and Bruker 400 (^1H at 400 MHz, ^{13}C at 100 MHz) NMR spectrometers and chemical shifts are reported in units of δ relative to internal TMS. Multiplicities are indicated as br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and coupling constants (J) are reported in hertz (Hz). Mass spectral data are reported in the form of m/z (intensity relative to base = 100). Purities of compounds were determined by LC/MS analysis using a Waters MicroMass ZQ system (electrospray ionization (ESI) with Waters-2525 binary gradient module coupled to a photodiode array detector (Waters-2996) and ELS detector (Waters-2424) using a XTerra MS C18 (5 μm , 4.6 mm $\times$ 50 mm column and acetonitrile/water) and were > 95 %.



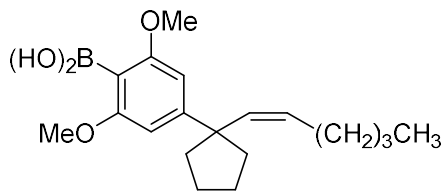
(4-(1-Hexylcyclopentyl)-2,6-dimethoxyphenyl)boronic acid (17). To a solution of 1-(1-hexylcyclopentyl)-3,5-dimethoxybenzene¹ (**16**, 206 mg, 0.71 mmol) in anhydrous THF (1.8 mL) at $-78\text{ }^{\circ}\text{C}$ under an argon atmosphere was added dropwise *n*-BuLi (0.57 mL of a 2.5 M solution in hexane, 1.42 mmol). The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 45 min, then at $10\text{ }^{\circ}\text{C}$ for 1.5 h, and back to $-78\text{ }^{\circ}\text{C}$ for another 30 min. To the reaction mixture was added dropwise trimethyl borate (369 mg, 3.55 mmol) and it was stirred from $-78\text{ }^{\circ}\text{C}$ to room temperature over a period of 12 h. Then the reaction mixture was cooled to $0\text{ }^{\circ}\text{C}$ and acidified to pH 6.5 with 5% aqueous HCl, and extracted with Et_2O . The combined organic extracts were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10–30% EtOAc/hexane) gave **17** (153 mg, 65 % yield) as a colorless viscous oil. IR (thin film, cm^{-1}) 3508 (OH), 2924, 2858, 1607, 1559, 1421, 1118, 764, 704; ^1H NMR (500 MHz, CDCl_3) δ 7.19 (s, 2H, 2 $\times$ OH), 6.52 (s, 2H, Ar-H), 3.90 (s, 6H, $-\text{OCH}_3$), 1.93 – 1.79 (m, 4H), 1.78 – 1.61 (m, 4H), 1.60 – 1.53 (m, 2H), 1.24 – 1.09 (m, 6H), 1.03 – 0.91 (m, 2H), 0.83 (t, $J = 7.0\text{ Hz}$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 165.1, 155.4, 103.3, 55.9, 51.9, 41.7, 37.6, 31.7, 29.8, 25.1, 23.2, 22.6, 14.0.



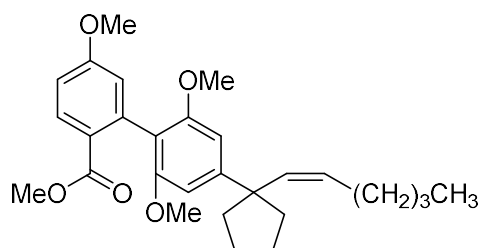
Methyl 4'-(1-hexylcyclopentyl)-2',5,6'-trimethoxy-[1,1'-biphenyl]-2-carboxylate (18). The synthesis was carried out as described for **15**, using boronic acid **17** (150 mg, 0.45 mmol), **14** (121 mg, 0.49 mmol), Cs₂CO₃ (587 mg, 1.8 mmol) and Pd(PPh₃)₄ (52 mg, 0.045 mmol) in DME/H₂O (5:1, 1.25 mL of DME and 0.25 mL of H₂O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10-25% EtOAc/hexane) to give **18** (140 mg, 69 % yield) as a yellow oil. IR (thin film, cm⁻¹) 2953, 2933, 1733 (CO), 1581, 1512, 1322, 1236, 1181, 1019, 863, 757, 696; ¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, *J* = 8.7 Hz, 1H, Ar-H), 6.88 (dd, *J* = 8.7, 2.5 Hz, 1H, Ar-H), 6.84 (d, *J* = 2.5 Hz, 1H, Ar-H), 6.52 (s, 2H, Ar-H), 3.83 (s, 3H, -OCH₃), 3.69 (s, 6H, -OCH₃), 3.53 (s, 3H, -COOCH₃), 2.00 – 1.90 (m, 2H), 1.89 – 1.81 (m, 2H), 1.80 – 1.65 (m, 4H), 1.63 – 1.56 (m, 2H), 1.24 – 1.14 (m, 6H), 1.09 – 1.00 (m, 2H), 0.84 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.0, 161.6, 156.4, 150.3, 137.4, 131.9, 124.2, 117.7, 116.6, 112.3, 103.2, 55.9, 55.3, 51.6, 51.1, 42.0, 37.8, 31.8, 29.9, 25.2, 23.4, 22.6, 14.0.



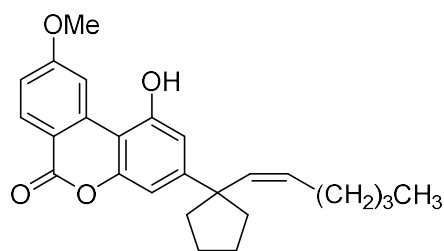
3-(1-Hexylcyclopentyl)-1-hydroxy-9-methoxy-6H-benzo[c]chromen-6-one (19). The synthesis was carried out as described for **1a**, using **18** (140 mg, 0.31 mmol) and 9-iodo-9-BBN (1.0 mL of a 1.0 M in hexane, 1.0 mmol) in anhydrous CH₂Cl₂ (3.8 mL). The reaction was quenched by ethanolamine (0.5 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel (CH₂Cl₂/Et₂O/hexane, 2:2:6) to give **19** (91 mg, 75 % yield) as a white solid. Mp 159-164 °C. IR (thin film, cm⁻¹) 3321 (OH), 2926, 1683 (CO), 1609, 1403, 1106, 1030, 872, 747; ¹H NMR (500 MHz, CDCl₃) δ 8.56 (d, *J* = 2.4 Hz, 1H, Ar-H), 8.36 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.06 (dd, *J* = 8.8, 2.4 Hz, 1H, Ar-H), 6.88 (d, *J* = 1.5 Hz, 1H, Ar-H), 6.71 (d, *J* = 1.5 Hz, 1H, Ar-H), 6.48 (s, 1H, OH), 3.96 (s, 3H, -OCH₃), 1.95 – 1.83 (m, 2H), 1.82 – 1.73 (m, 2H), 1.73 – 1.59 (m, 4H), 1.59 – 1.52 (m, 2H), 1.22 – 1.07 (m, 6H), 0.97 (s, 2H), 0.80 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 164.6, 161.5, 153.6, 152.8, 152.4, 136.7, 132.3, 114.9, 113.7, 110.8, 110.7, 109.0, 104.8, 55.6, 51.2, 41.8, 37.6, 31.7, 29.9, 25.3, 23.2, 22.6, 14.0. HRMS (ESI) for C₂₅H₃₁O₄: calculated 395.2222; found 395.2214. Mass spectrum (ESI) *m/z* (relative intensity) 395 (M⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.8 min for the title compound.



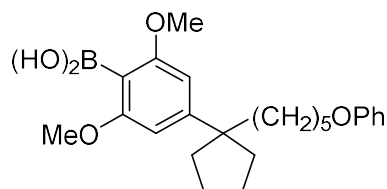
(Z)-(4-(1-(Hex-1-en-1-yl)cyclopentyl)-2,6-dimethoxyphenyl)boronic acid (21). The synthesis was carried out as described for **17**, using **20**¹ (286 mg, 1.0 mmol), *n*-BuLi (0.8 mL of a 2.5 M solution in hexane, 2.0 mmol) and trimethyl borate (520 mg, 5.0 mmol) in dry THF (2.5 mL). The crude oil obtained after acidic work up was purified by flash column chromatography on silica gel (10-30% EtOAc/hexane) to give **21** (265 mg, 80 % yield) as a colorless viscous oil. IR (thin film, cm⁻¹) 3513 (OH), 3087, 2941, 2869, 1606, 1587, 1554, 1351, 1171, 1113, 761; ¹H NMR (500 MHz, CDCl₃) δ 7.18 (s, 2H, 2 × OH), 6.64 (s, 2H, Ar-H), 5.71 (d, *J* = 11.3 Hz, 1H), 5.34 (dt, *J* = 11.3, 7.4 Hz, 1H), 3.89 (s, 6H, -OCH₃), 1.98 (m, 4H), 1.84 – 1.65 (m, 6H), 1.44 – 1.05 (m, 4H), 0.74 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 165.1, 155.5, 138.0, 132.7, 103.3, 55.9, 52.8, 41.1, 31.3, 28.4, 23.7, 22.3, 13.9.



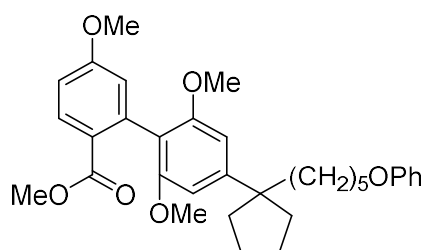
Methyl (Z)-4'-(1-(hex-1-en-1-yl)cyclopentyl)-2',5,6'-trimethoxy-[1,1'-biphenyl]-2-carboxylate (22). The synthesis was carried out as described for **15**, using boronic acid **21** (265 mg, 0.79 mmol), **14** (197 mg, 0.80 mmol), Cs₂CO₃ (1043 mg, 3.20 mmol) and Pd(PPh₃)₄ (93 mg, 0.08 mmol) in DME/H₂O (5:1, 2.5 mL of DME and 0.5 mL of H₂O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (5-20% EtOAc/hexane) to give **22** (290 mg, 81 % yield) as a yellow oil. IR (thin film, cm⁻¹) 3085, 2974, 2911, 2854, 1722 (CO), 1575, 1433, 1122, 1021, 773, 696; ¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, *J* = 8.7 Hz, 1H, Ar-H), 6.87 (dd, *J* = 8.7, 2.6 Hz, 1H, Ar-H), 6.81 (d, *J* = 2.6 Hz, 1H, Ar-H), 6.63 (s, 2H, Ar-H), 5.74 (d, *J* = 11.3 Hz, 1H), 5.34 (dt, *J* = 11.3, 7.4 Hz, 1H), 3.83 (s, 3H, -OCH₃), 3.67 (s, 6H, -OCH₃), 3.54 (s, 3H, -COOCH₃), 2.12 – 2.03 (m, 2H), 2.03 – 1.95 (m, 2H), 1.87 – 1.71 (m, 6H), 1.19 – 1.45 (m, 4H), 0.80 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 167.9, 161.6, 156.4, 150.3, 138.7, 137.4, 132.0, 131.8, 124.1, 117.8, 116.6, 112.2, 103.2, 55.9, 55.3, 52.7, 51.1, 41.1, 31.5, 28.3, 23.7, 22.4, 13.9. Mass spectrum (ESI) *m/z* (relative intensity) 475 (M⁺ + Na, 30), 421 (M⁺ - MeO, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.9 min for the title compound.



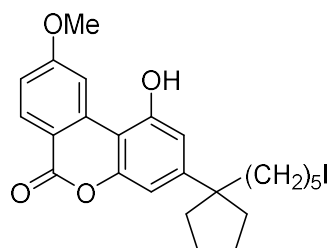
(Z)-3-(1-(Hex-1-en-1-yl)cyclopentyl)-1-hydroxy-9-methoxy-6H-benzo[c]chromen-6-one (23). The synthesis was carried out as described for **1a**, using **22** (110 mg, 0.24 mmol), 9-iodo-9-BBN (0.8 mL of a 1.0 M in hexane, 0.80 mmol) in anhydrous CH₂Cl₂ (3 mL). The reaction was quenched by ethanolamine (0.5 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel (CH₂Cl₂/Et₂O/hexane, 2:2:6) to give **23** (67 mg, 70 % yield) as a white solid. Mp 146-149 °C. IR (thin film, cm⁻¹) 3269 (OH), 2955, 2871, 1679 (CO), 1604, 1399, 1103, 1027, 748; ¹H NMR (500 MHz, CDCl₃) δ 8.50 (d, *J* = 2.3 Hz, 1H, Ar-H), 8.35 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.06 (dd, *J* = 8.8, 2.3 Hz, 1H, Ar-H), 7.00 (d, *J* = 1.4 Hz, 1H, Ar-H), 6.72 (d, *J* = 1.4 Hz, 1H, Ar-H), 5.88 (s, 1H, OH), 5.71 (d, *J* = 11.3 Hz, 1H), 5.34 (dt, *J* = 11.3, 7.4 Hz, 1H), 3.97 (s, 3H, -OCH₃), 2.05-1.90 (m, 4H), 1.81 – 1.66 (m, 6H), 1.14-1.06 (m, 4H), 0.71 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 164.6, 161.6, 153.7, 152.8, 152.6, 137.8, 136.7, 132.9, 132.3, 114.9, 113.6, 111.0, 110.7, 108.6, 104.7, 55.6, 52.0, 41.0, 31.2, 28.5, 23.6, 22.3, 13.8. HRMS (ESI) for C₂₅H₂₉O₄: calculated 393.2066; found 393.2062. Mass spectrum (ESI) *m/z* (relative intensity) 393 (M⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.6 min for the title compound.



(2,6-Dimethoxy-4-(1-(5-phenoxy)pentyl)cyclopentyl)phenylboronic acid (25). The synthesis was carried out as described for **17**, using **24**² (1050 mg, 2.85 mmol), *n*-BuLi (2.3 mL of a 2.5 M solution in hexane, 5.7 mmol) and trimethyl borate (1481 mg, 14.25 mmol) in dry THF (7.1 mL). The crude oil obtained after acidic work up was purified by flash column chromatography on silica gel (10-30% EtOAc/hexane) to give **25** (853 mg, 73 % yield) as a colorless viscous oil. IR (thin film, cm⁻¹) 3515 (OH), 2938, 2868, 1604, 1557, 1328, 1228, 1108, 753, 690; ¹H NMR (500 MHz, CDCl₃) δ 7.26 (t, *J* = 7.9 Hz, 2H, Ar-H), 7.19 (s, 2H, 2 x OH), 6.92 (t, *J* = 7.9 Hz, 1H, Ar-H), 6.84 (d, *J* = 7.9 Hz, 2H, Ar-H), 6.53 (s, 2H, Ar-H), 3.90 (s, 6H, -OCH₃), 3.86 (t, *J* = 6.4 Hz, 2H), 1.94 – 1.81 (m, 4H), 1.79 – 1.64 (m, 6H), 1.64 – 1.56 (m, 2H), 1.39 – 1.29 (m, 2H), 1.11 – 1.01 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 165.2, 159.0, 155.2, 129.3, 120.5, 114.5, 103.3, 67.7, 55.9, 51.9, 41.6, 37.6, 29.0, 26.6, 24.9, 23.2.

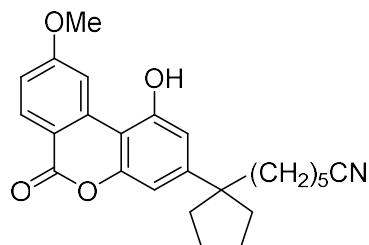


Methyl 2',5,6'-trimethoxy-4'-(1-(5-phenoxy)pentyl)-[1,1'-biphenyl]-2-carboxylate (26). The synthesis was carried out as described for **15**, using boronic acid **25** (770 mg, 1.87 mmol), **14** (458 mg, 1.87 mmol), Cs₂CO₃ (2.44 g, 7.48 mmol) and Pd(PPh₃)₄ (219 mg, 0.19 mmol) in DME/H₂O (5:1, 5 mL of DME and 1 mL of H₂O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10-40% EtOAc/hexane) to give **26** (757 mg, 76 % yield) as a yellow oil. IR (thin film, cm⁻¹) 2937, 2863, 1728 (CO), 1600, 1574, 1237, 1121, 1019, 754, 692; ¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.25 (t, *J* = 8.0 Hz, 2H, Ar-H), 6.94 – 6.82 (m, 5H, Ar-H), 6.52 (s, 2H, Ar-H), 3.89 (t, *J* = 6.5 Hz, 2H), 3.83 (s, 3H, -OCH₃), 3.68 (s, 6H, -OCH₃), 3.53 (s, 3H, -COOCH₃), 2.02 – 1.93 (m, 2H), 1.91 – 1.82 (m, 2H), 1.79 – 1.67 (m, 6H), 1.66 – 1.61 (m, 2H), 1.42 – 1.33 (m, 2H), 1.19 – 1.09 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 167.8, 161.7, 159.1, 156.5, 150.1, 137.5, 131.8, 129.3, 124.1, 120.4, 117.7, 116.9, 114.5, 112.3, 103.3, 67.8, 55.9, 55.3, 51.6, 51.1, 41.9, 37.8, 29.2, 26.7, 25.1, 23.4. Mass spectrum (ESI) *m/z* (relative intensity) 555 (M⁺ + Na, 30), 501 (M⁺ - MeO, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 6.0 min for the title compound.

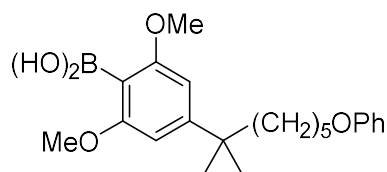


1-Hydroxy-3-(1-(5-iodopentyl)cyclopentyl)-9-methoxy-6H-benzo[c]chromen-6-one (27). The synthesis was carried out as described for **1a**, using **26** (620 mg, 1.16 mmol), 9-iodo-9-BBN (5.3 mL of a 1.0 M in hexane, 5.3 mmol) in anhydrous CH₂Cl₂ (14.5 mL). The reaction was quenched by ethanolamine (1 mL) and the crude

obtained after work up was purified by flash column chromatography on silica gel (CH₂Cl₂/Et₂O/hexane, 2:2:6) to give **27** (395 mg, 67 % yield) as a white solid. Mp 141-143 °C. IR (thin film, cm⁻¹) 3280 (OH), 2925, 2854, 1694 (CO), 1673, 1608, 1445, 1401, 1298, 1228, 1104, 869, 748; ¹H NMR (500 MHz, CDCl₃) δ 8.53 (d, *J* = 2.4 Hz, 1H, Ar-H), 8.36 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.07 (dd, *J* = 8.8, 2.4 Hz, 1H, Ar-H), 6.88 (d, *J* = 1.5 Hz, 1H, Ar-H), 6.67 (d, *J* = 1.5 Hz, 1H, Ar-H), 6.17 (s, 1H, OH), 3.97 (s, 3H, -OCH₃), 3.08 (t, *J* = 7.0 Hz, 2H), 1.95 – 1.87 (m, 2H), 1.83 – 1.54 (m, 10H), 1.30 – 1.18 (m, 2H), 1.09 – 0.95 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 164.7, 161.6, 153.9, 152.8, 152.0, 136.7, 132.3, 115.0, 113.6, 110.8, 110.7, 108.9, 104.9, 55.6, 51.1, 41.6, 37.6, 33.3, 31.0, 24.3, 23.2, 7.1. Mass spectrum (ESI) *m/z* (relative intensity) 507 (M⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.7 min for the title compound.

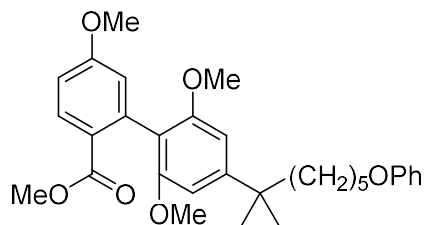


6-(1-(1-Hydroxy-9-methoxy-6-oxo-6H-benzo[c]chromen-3-yl)cyclopentyl)hexanenitrile (28). To a stirred solution of **27** (105 mg, 0.21 mmol) in DMSO (4.1 mL), at room temperature under an argon atmosphere, was added NaCN (61 mg, 1.2 mmol). After stirring at the same temperature overnight, ice-cold water was added into the reaction mixture. The mixture was extracted with Et₂O and the combined organic layer was washed with brine, dried over MgSO₄, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (5-30% EtOAc/hexane) gave **28** (76 mg, 90%) as a white amorphous solid. IR (thin film, cm⁻¹) 3289 (OH), 2935, 2866, 2245 (CN), 1714 (CO), 1603, 1402, 1343, 1261, 1017, 748; ¹H NMR (400 MHz, CDCl₃) δ 8.64 (d, *J* = 2.5 Hz, 1H, Ar-H), 8.52 (brs, 1H, OH), 8.35 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.05 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar-H), 6.83 (d, *J* = 1.7 Hz, 1H, Ar-H), 6.78 (d, *J* = 1.7 Hz, 1H, Ar-H), 3.97 (s, 3H, -OCH₃), 2.25 (t, *J* = 7.0 Hz, 2H), 2.00 – 1.88 (m, 2H), 1.85 – 1.50 (m, 10H), 1.39 – 1.29 (m, 2H), 1.14 – 0.98 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 164.6, 161.7, 155.3, 152.7, 151.5, 137.2, 132.1, 119.8, 114.7, 113.6, 110.8, 110.7, 107.7, 104.8, 55.5, 51.1, 41.5, 37.6, 29.1, 25.1, 24.5, 23.2, 17.0. HRMS (ESI) for C₂₅H₂₈NO₄: calculated 406.2018; found 406.2010. Mass spectrum (ESI) *m/z* (relative intensity) 406 (M⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.1 min for the title compound.

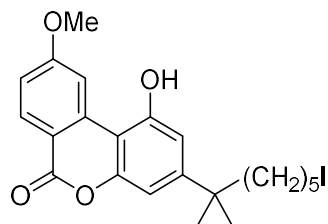


(2,6-Dimethoxy-4-(2-methyl-7-phenoxyheptan-2-yl)phenyl)boronic acid (30). The synthesis was carried out as described for **17**, using **29**³ (1010 mg, 2.95 mmol), *n*-BuLi (2.4 mL of a 2.5 M solution in hexane, 5.9 mmol) and trimethyl borate (1.53 g, 14.75 mmol) in dry THF (7.3 mL). The crude oil obtained after acidic work up was purified by flash column chromatography on silica gel (10-30% EtOAc/hexane) to give **30** (695 mg, 61 % yield) as a colorless viscous oil. IR (thin film, cm⁻¹) 3519 (br, OH), 2937, 2862, 1604, 1558, 1464, 1419, 1324, 1230, 1110, 1044. ¹H NMR (500 MHz, CDCl₃) δ 7.28–7.25 (m, 2H, Ar-H), 7.19 (s, 2H, 2 × OH), 6.94–6.91 (m, 1H, Ar-H), 6.87–6.84 (m, 2H, Ar-H), 6.58 (s, 2H, Ar-H), 3.90 (s, 6H, 2 × OCH₃), 3.89 (t, *J* = 6.4 Hz, 2H, OCH₂), 1.75–1.70 (m, 2H, CH₂), 1.65–1.62 (m, 2H, CH₂), 1.43–1.37 (m, 2H, CH₂), 1.31 (s, 6H, 2 × CH₃), 1.17–1.11 (m, 2H, CH₂). ¹³C NMR (126 MHz, CDCl₃) δ 165.3, 159.0, 155.9, 129.4, 120.5, 114.4, 103.4, 102.3, 67.6, 55.9, 44.2, 38.6, 29.1, 28.8, 26.7, 24.5. Mass spectrum (ESI) *m/z* (relative intensity) 409 (M⁺ + Na, 50), 249 (M⁺ + H – OPh

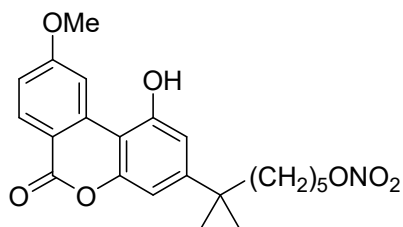
– B(OH)₂, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.3 min for the title compound.



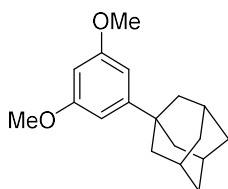
Methyl 2',5,6'-trimethoxy-4'-(2-methyl-7-phenoxyheptan-2-yl)-[1,1'-biphenyl]-2-carboxylate (31). The synthesis was carried out as described for **15**, using boronic acid **30** (600 mg, 1.55 mmol), **14** (382 mg, 1.56 mmol), Cs₂CO₃ (2.02 g, 6.2 mmol) and Pd(PPh₃)₄ (173 mg, 0.15 mmol) in DME/H₂O (5:1, 4.5 mL of DME and 0.9 mL of H₂O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10-30% EtOAc/hexane) to give **31** (695 mg, 84 % yield) as a yellow oil. IR (thin film, cm⁻¹) 2937, 2862, 1727 (CO), 1600, 1575, 1463, 1406, 1241, 1123, 1034. ¹H NMR (500 MHz, CDCl₃) δ 7.96 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.29–7.25 (m, 2H, Ar-H), 6.94–6.90 (m, 1H, Ar-H), 6.90–6.87 (m, 3H, Ar-H), 6.85 (d, *J* = 2.7 Hz, 1H, Ar-H), 6.59 (s, 2H, Ar-H), 3.93 (t, *J* = 6.5 Hz, 2H, OCH₂), 3.84 (s, 3H, OCH₃), 3.70 (s, 6H, 2 × OCH₃), 3.56 (s, 3H, OCH₃), 1.79–1.73 (m, 2H, CH₂), 1.69–1.66 (m, 2H, CH₂), 1.46–1.36 (m, 2H, CH₂), 1.36 (s, 6H, 2 × CH₃), 1.26–1.20 (m, 2H, CH₂). ¹³C NMR (126 MHz, CDCl₃) δ 167.7, 161.8, 159.2, 156.7, 150.8, 137.7, 132.0, 129.5, 124.1, 120.6, 117.9, 116.8, 114.5, 112.3, 102.2, 67.8, 55.9, 55.3, 51.3, 44.8, 38.4, 29.4, 29.1, 26.9, 24.7. Mass spectrum (ESI) *m/z* (relative intensity) 529 (M⁺ + Na, 50), 475 (M⁺ – MeO, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.8 min for the title compound.



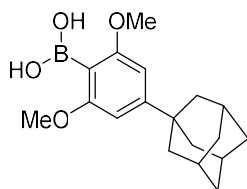
1-Hydroxy-3-(7-iodo-2-methylheptan-2-yl)-9-methoxy-6H-benzo[c]chromen-6-one (32). The synthesis was carried out as described for **1a**, using **31** (352 mg, 0.69 mmol), 9-iodo-9-BBN (3.13 mL of a 1.0 M in hexane, 3.13 mmol) in anhydrous CH₂Cl₂ (7.5 mL). The reaction was quenched by ethanolamine (1 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel (CH₂Cl₂/Et₂O/hexane, 2:2:6) to give **32** (224 mg, 68 % yield) as a white solid. Mp 150–151 °C. IR (thin film, cm⁻¹) 3297 (br, OH), 2932, 2859, 1683 (CO), 1605, 1401, 1267, 1226, 1103, 1026. ¹H NMR (500 MHz, CDCl₃) δ 8.49 (d, *J* = 2.5 Hz, 1H, Ar-H), 8.36 (d, *J* = 8.9 Hz, 1H, Ar-H), 7.07 (dd, *J* = 8.9, 2.5 Hz, 1H, Ar-H), 6.94 (d, *J* = 1.8 Hz, 1H, Ar-H), 6.65 (d, *J* = 1.8 Hz, 1H, Ar-H), 5.65 (brs, 1H, OH), 3.97 (s, 3H, OCH₃), 3.12 (t, *J* = 7.0 Hz, 2H, CH₂I), 1.77–1.71 (m, 2H, CH₂), 1.62–1.59 (m, 2H, CH₂), 1.37–1.27 (m, 2H, CH₂), 1.30 (s, 6H, 2 × CH₃), 1.14–1.04 (m, 2H, CH₂). ¹³C NMR (126 MHz, CDCl₃) δ 165.0, 163.0, 155.2, 152.8, 152.6, 137.5, 132.1, 115.3, 113.0, 110.7, 110.4, 107.1, 104.9, 55.7, 44.0, 37.9, 33.3, 31.1, 28.6, 23.7, 7.1. Mass spectrum (ESI) *m/z* (relative intensity) 481 (M⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.4 min for the title compound.



6-(1-Hydroxy-9-methoxy-6-oxo-6H-benzo[c]chromen-3-yl)-6-methylheptyl nitrate (33). To a solution of **32** (32 mg, 0.067 mmol) in CH₃CN (3.3 mL) at room temperature was added AgNO₃ (33 mg, 0.196 mmol). After being flushed with argon, the reaction mixture was stirred at room temperature until most of the starting material was consumed as judged by TLC (ca. 4.5 h). Celite was added, and CH₃CN was removed under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (1/4) as eluent to afford **33** (25 mg, 91%) as a white solid. Mp 131–132 °C. IR (thin film, cm⁻¹) 3255 (br, OH), 2937, 2862, 1682 (CO), 1620, 1602, 1400, 1275, 1224, 1104, 1024, 864. ¹H NMR (500 MHz, CDCl₃) δ 8.50 (d, *J* = 2.5 Hz, 1H, Ar-H), 8.36 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.07 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar-H), 6.93 (d, *J* = 1.8 Hz, 1H, Ar-H), 6.67 (d, *J* = 1.8 Hz, 1H, Ar-H), 5.89 (s, 1H, OH), 4.37 (t, *J* = 6.6 Hz, 2H, CH₂ONO₂), 3.97 (s, 3H, OCH₃), 1.66–1.59 (m, 4H, 2 × CH₂), 1.36–1.23 (m, 2H, CH₂), 1.30 (s, 6H, 2 × CH₃), 1.15–1.05 (m, 2H, CH₂). ¹³C NMR (126 MHz, CDCl₃) δ 165.1, 163.0, 155.3, 152.7, 152.6, 137.5, 132.1, 115.3, 113.0, 110.8, 110.4, 107.0, 104.9, 73.3, 55.7, 43.9, 37.9, 28.6, 26.6, 26.2, 24.3. HRMS (ESI) for C₂₂H₂₆NO₇: calculated 416.1719; found 416.1702. Mass spectrum (ESI) *m/z* (relative intensity) 416 (M⁺ + H, 100), 370 (M⁺ + H – NO₂, 10). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.2 min for the title compound.

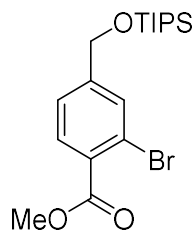


1-(3,5-Dimethoxyphenyl)adamantane (34).⁴ To a solution of triflate **43** (2.1 g, 5.0 mmol) in DMF (25 mL) at room temperature was subsequently added PdCl₂(PPh₃)₂ (190 mg, 0.27 mmol), dppp (206 mg, 0.5 mmol), *n*-Bu₃N (6 mL, 25.0 mmol), HCOOH (88% w/v in H₂O, 0.5 mL, 11.7 mmol), and PMHS (350 mg). After being flushed with argon, the reaction mixture was stirred at room temperature for 5 min and then at 95 °C for 19 h. The mixture was cooled to room temperature, diluted with Et₂O (ca. 13 mL) and aqueous 1 M HCl (ca. 5 mL), and stirred for 30 min. The organic material was extracted with Et₂O, and the combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with (0–10% acetone/hexane) as eluent to afford **34** (1.25 g, 92%) as a white solid. Mp 54–55 °C. Literature,⁵ Mp 47–48 °C. IR (thin film, cm⁻¹) 2900, 2847, 1594, 1453, 1421, 1320, 1203, 1151, 1068, 1037, 926, 844. ¹H NMR (500 MHz, CDCl₃) δ 6.58 (d, *J* = 2.3 Hz, 2H, Ar-H), 6.35 (dd, *J* = 2.3, 2.3 Hz, 1H, Ar-H), 3.83 (s, 6H, 2 × OCH₃), 2.13–2.12 (m, 3H, Ad-H), 1.94–1.93 (m, 6H, Ad-H), 1.84–1.76 (m, 6H, Ad-H). ¹³C NMR (126 MHz, CDCl₃) δ 160.7, 154.2, 103.6, 97.1, 55.3, 43.2, 36.9, 36.6, 29.1. Mass spectrum (ESI) *m/z* (relative intensity) 273 (M⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.5 min for the title compound.

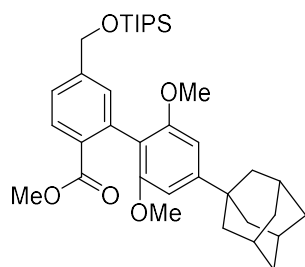


(4-(Adamantan-1-yl)-2,6-dimethoxyphenyl)boronic acid (35). The synthesis was carried out as described for **17**, using **34** (1.2 g, 4.41 mmol), *n*-BuLi (3.5 mL of a 2.5 M solution in hexane, 8.82 mmol) and trimethyl borate (2.29 g, 22.05 mmol) in dry THF (7.5 mL). The crude oil obtained after acidic work up was purified by flash column chromatography on silica gel (10–20% EtOAc/hexane) to give **35** (850 mg, 61 % yield) as a colorless oil.

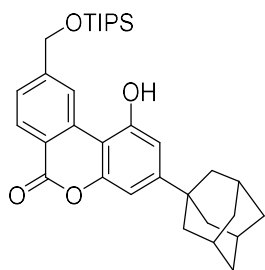
IR (thin film, cm^{-1}) 3494 (OH), 2904, 2847, 1607, 1558, 1455, 1415, 1332, 1118, 1081. ^1H NMR (500 MHz, CDCl_3) δ 7.19 (s, 2H, $2 \times \text{OH}$), 6.62 (s, 2H, Ar-H), 3.92 (s, 6H, $2 \times \text{OCH}_3$), 2.11–2.10 (m, 3H, Ad-H), 1.91–1.90 (m, 6H, Ad-H), 1.82–1.74 (m, 6H, Ad-H). ^{13}C NMR (126 MHz, CDCl_3) δ 165.1, 157.1, 103.1, 101.0, 55.6, 42.6, 36.8, 36.4, 28.5. Mass spectrum (ESI) m/z (relative intensity) 317 ($\text{M}^+ + \text{H}$, 65), 273 ($\text{M}^+ + 2\text{H} - \text{B}(\text{OH})_2$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.1 min for the title compound.



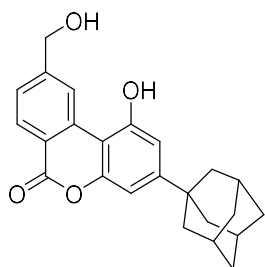
Methyl 2-bromo-4-(((triisopropylsilyl)oxy)methyl)benzoate (37). To a solution of **36** (4.40 g, 17.95 mmol) in DMF (18 mL) under an argon atmosphere at 0 °C was added imidazole (2.44 g, 35.90 mmol) and triisopropylsilyl chloride (4.1 mL, 18.85 mmol), and the reaction mixture was stirred at room temperature for 2 h. Water was added to the reaction mixture, and the organic material was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with (0–10% EtOAc/hexane) as eluent to afford **37** (6.85 g, 95%) as a colorless oil. IR (thin film, cm^{-1}) 2944, 2866, 1735 (CO), 1605, 1463, 1434, 1290, 1246, 1151, 1039, 882. ^1H NMR (500 MHz, CDCl_3) δ 7.79 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.66 (d, $J = 1.5$ Hz, 1H, Ar-H), 7.34 (dd, $J = 8.1, 1.5$ Hz, 1H, Ar-H), 4.83 (s, 2H, CH_2), 3.92 (s, 3H, COOCH_3), 1.21–1.14 (m, 3H, $3 \times \text{CH}$), 1.09 (d, $J = 7.2$ Hz, 18H, $6 \times \text{CH}_3$); ^{13}C NMR (126 MHz, CDCl_3) δ 166.3, 147.1, 131.4, 131.4, 130.0, 124.1, 121.8, 63.8, 52.2, 18.0, 12.0.



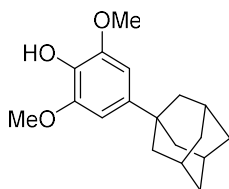
Methyl 4'-(adamantan-1-yl)-2',6'-dimethoxy-5-(((triisopropylsilyl)oxy)methyl)-[1,1'-biphenyl]-2-carboxylate (38). The synthesis was carried out as described for **15**, using boronic acid **35** (800 mg, 2.53 mmol), methyl 2-bromo-4-(((triisopropylsilyl)oxy)methyl)benzoate (**37**, 1015 mg, 2.53 mmol), Cs_2CO_3 (2.1 g, 6.44 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (289 mg, 0.25 mmol) in DME/ H_2O (5:1, 5 mL of DME and 1 mL of H_2O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10–25% EtOAc/hexane) to give **38** (1.25 g, 83 % yield) as a white solid. Mp 173–174 °C. IR (thin film, cm^{-1}) 2903, 2865, 2849, 1733 (CO), 1609, 1574, 1461, 1449, 1407, 1283, 1238, 1125, 1103. ^1H NMR (500 MHz, CDCl_3) δ 7.90 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.37 (dd, $J = 8.1, 1.6$ Hz, 1H, Ar-H), 7.30 (d, $J = 1.6$ Hz, 1H, Ar-H), 6.61 (s, 2H, Ar-H), 4.87 (s, 2H, CH_2), 3.69 (s, 6H, $2 \times \text{OCH}_3$), 3.60 (s, 3H, COOCH_3), 2.13–2.12 (m, 3H, Ad-H), 1.98–1.97 (m, 6H, Ad-H), 1.83–1.77 (m, 6H, Ad-H), 1.20–1.13 (m, 3H, $3 \times \text{CH}$), 1.08 (d, $J = 7.1$ Hz, 18H, $6 \times \text{CH}_3$). ^{13}C NMR (126 MHz, CDCl_3) δ 168.2, 156.7, 152.4, 144.7, 135.0, 130.3, 130.0, 129.6, 124.0, 116.5, 101.0, 64.8, 55.7, 51.4, 43.3, 36.9, 36.9, 29.1, 18.1, 12.0.



3-(Adamantan-1-yl)-1-hydroxy-9-(((triisopropylsilyl)oxy)methyl)-6H-benzo[c]chromen-6-one (39). The synthesis was carried out as described for **1a**, using **38** (1000 mg, 1.69 mmol), 9-iodo-9-BBN (5.5 mL of a 1.0 M in hexane, 5.5 mmol) in anhydrous CH_2Cl_2 (15 mL). The reaction was quenched by ethanolamine (1.3 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}/\text{hexane}$, 2:2:6) to give **39** (657 mg, 73 % yield) as a white solid. Mp 246–247 °C. IR (thin film, cm^{-1}) 3344 (br, OH), 2902, 2848, 1691 (CO), 1612, 1402, 1278, 1261, 1099. ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 10.76 (brs, 1H, OH), 9.14 (d, $J = 1.7$ Hz, 1H, Ar-H), 8.18 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.46 (dd, $J = 8.1, 1.7$ Hz, 1H, Ar-H), 6.91 (d, $J = 1.8$ Hz, 1H, Ar-H), 6.80 (d, $J = 1.8$ Hz, 1H, Ar-H), 4.94 (s, 2H, CH_2), 2.06–2.01 (m, 3H, Ad-H), 1.85–1.81 (m, 6H, Ad-H), 1.76–1.65 (m, 6H, Ad-H), 1.20–1.09 (m, 3H, 3 $\times$ CH), 1.04 (d, $J = 7.3$ Hz, 18H, 6 $\times$ CH_3). ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ 161.0, 156.8, 154.1, 152.7, 149.2, 135.2, 129.7, 125.1, 124.0, 118.9, 109.1, 104.7, 104.3, 64.8, 42.7, 36.5, 36.4, 28.7, 18.3, 11.9.

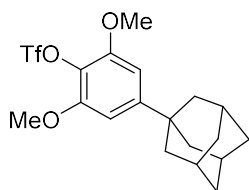


3-(Adamantan-1-yl)-1-hydroxy-9-(hydroxymethyl)-6H-benzo[c]chromen-6-one (40). To a solution of **39** (53 mg, 0.1 mmol) in THF (2.5 mL) under an argon atmosphere at room temperature was added a 1 M solution of tetrabutylammonium fluoride in THF (0.3 mL, 0.3 mmol), and the reaction mixture was stirred at room temperature for 2 h. Saturated aqueous NH_4Cl (1 mL) was added, and the organic material was extracted with EtOAc. The combined organic extracts were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (3/2) as eluent to afford **40** (34 mg, 90%) as a white solid. Mp 256–257 °C. IR (thin film, cm^{-1}) 3230 (br, OH), 2902, 2848, 1691 (CO), 1631, 1405, 1291, 1243, 1108. ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 10.79 (brs, 1H, OH), 9.04 (d, $J = 1.7$ Hz, 1H, Ar-H), 8.19 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.50 (dd, $J = 8.1, 1.7$ Hz, 1H, Ar-H), 6.89 (d, $J = 1.8$ Hz, 1H, Ar-H), 6.82 (d, $J = 1.8$ Hz, 1H, Ar-H), 5.49 (t, $J = 5.3$ Hz, 1H, OH), 4.66 (d, $J = 5.3$ Hz, 2H, CH_2), 2.07–2.02 (m, 3H, Ad-H), 1.87–1.82 (m, 6H, Ad-H), 1.76–1.67 (m, 6H, Ad-H). ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ 161.0, 156.7, 154.0, 152.7, 150.5, 135.0, 129.8, 126.0, 124.5, 118.7, 109.0, 104.9, 104.3, 63.3, 42.7, 36.5, 36.4, 28.7. HRMS (ESI) for $\text{C}_{24}\text{H}_{25}\text{O}_4$: calculated 377.1753; found 377.1748. Mass spectrum (ESI) m/z (relative intensity) 377 ($\text{M}^+ + \text{H}$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 4.9 min for the title compound.

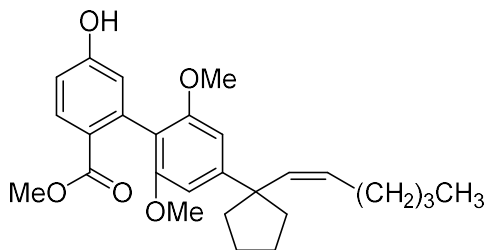


4-(Adamantan-1-yl)-2,6-dimethoxyphenol (42). To a homogeneous mixture of 1-adamantanol (6.91 g, 45.4 mmol) and 99% methanesulfonic acid (22.4 mL) at 40 °C was added 2,6-dimethoxyphenol (**41**, 7.0 g, 45.4 mmol). After being flushed with argon, the reaction mixture was stirred at 50 °C for 3 h. The mixture was cooled to room

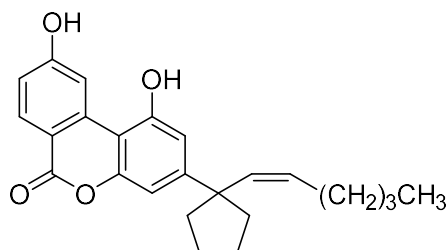
temperature, ice cold water was added, and the organic material was extracted with CH₂Cl₂. The combined organic extracts were washed with saturated aqueous NaHCO₃, water, and brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with acetone/hexane (0/1 → 3/7) as eluent to afford **42** (7.59 g, 58%) as a white solid. Mp 115–116 °C. Literature,⁵ Mp 111–112 °C. IR (thin film, cm⁻¹) 3465 (OH), 2897, 2847, 1607, 1522, 1451, 1354, 1265, 1189, 1114. ¹H NMR (500 MHz, CDCl₃) δ 6.59 (s, 2H, Ar-H), 5.41 (brs, 1H, OH), 3.90 (s, 6H, 2 × OCH₃), 2.10–2.09 (m, 3H, Ad-H), 1.90–1.89 (m, 6H, Ad-H), 1.81–1.74 (m, 6H, Ad-H). ¹³C NMR (126 MHz, CDCl₃) δ 146.5, 142.6, 132.6, 101.8, 56.1, 43.3, 36.6, 36.0, 28.9. Mass spectrum (ESI) m/z (relative intensity) 289 (M⁺ + H, 50), 135 (M⁺ + H – C₆H₂(OMe)₂(OH), 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 4.9 min for the title compound.



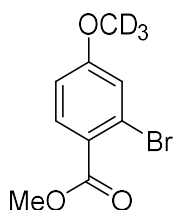
4-(Adamantan-1-yl)-2,6-dimethoxyphenyl trifluoromethanesulfonate (43). To a solution of **42** (4.30 g, 14.9 mmol) in CH₂Cl₂ (83 mL) under an argon atmosphere at room temperature was subsequently added *N*-phenyltrifluoromethanesulfonimide (6.14 g, 17.2 mmol), Et₃N (2.4 mL, 17.2 mmol), and DMAP (421 mg, 3.45 mmol) and the reaction mixture was refluxed for 18 h. After the mixture was cooled to room temperature, a 3 M aqueous solution of NaOH was added, and the organic material was extracted with CH₂Cl₂. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (1/9) as eluent to afford **43** (5.94 g, 95%) as a white solid. Mp 151–152 °C. IR (thin film, cm⁻¹) 2905, 2849, 1602, 1410, 1250, 1226, 1201, 1133, 889. ¹H NMR (500 MHz, CDCl₃) δ 6.62 (s, 2H, Ar-H), 3.89 (s, 6H, 2 × OCH₃), 2.12–2.11 (m, 3H, Ad-H), 1.91–1.90 (m, 6H, Ad-H), 1.83–1.74 (m, 6H, Ad-H). ¹³C NMR (126 MHz, CDCl₃) δ 152.7, 151.9, 126.0, 118.8 (q, ¹J_{CF} = 320.6 Hz), 101.9, 56.2, 43.2, 37.0, 36.7, 29.0; ¹⁹F NMR (470 MHz, CDCl₃) δ –73.8. Mass spectrum (ESI) m/z (relative intensity) 421 (M⁺ + H, 20), 273 (M⁺ + 2H – CF₃SO₃, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.9 min for the title compound.



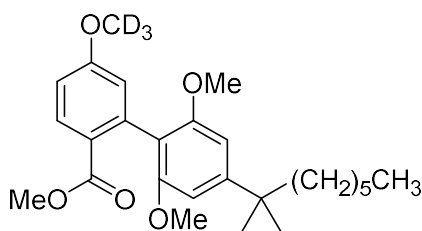
Methyl (Z)-4'-(1-(hex-1-en-1-yl)cyclopentyl)-5-hydroxy-2',6'-dimethoxy-[1,1'-biphenyl]-2-carboxylate (45). The synthesis was carried out as described for **15**, using boronic acid **21** (153 mg, 0.46 mmol), **44** (91 mg, 0.39 mmol), Cs₂CO₃ (520 mg, 1.6 mmol) and Pd(PPh₃)₄ (46 mg, 0.04 mmol) in DME/H₂O (5:1, 1.0 mL of DME and 0.2 mL of H₂O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10–80% Et₂O/hexane) to give **45** (140 mg, 82 % yield) as a yellow oil. IR (thin film, cm⁻¹) 3087, 2978, 2911, 2854, 1723 (CO), 1575, 1435, 1122, 1021, 773; ¹H NMR (500 MHz, CDCl₃) δ 7.89 (d, *J* = 8.5 Hz, 1H, Ar-H), 6.80 (dd, *J* = 8.5, 2.6 Hz, 1H, Ar-H), 6.73 (d, *J* = 2.6 Hz, 1H, Ar-H), 6.62 (s, 2H, Ar-H), 5.74 (d, *J* = 11.3 Hz, 1H), 5.37 (brs, 1H, OH), 5.34 (dt, *J* = 11.3, 7.4 Hz, 1H), 3.67 (s, 6H, -OCH₃), 3.54 (s, 3H, -COOCH₃), 2.12 – 2.03 (m, 2H), 2.03 – 1.95 (m, 2H), 1.87 – 1.71 (m, 6H), 1.19 – 1.45 (m, 4H), 0.80 (t, *J* = 7.0 Hz, 3H). Mass spectrum (ESI) m/z (relative intensity) 439 (M⁺ + H, 100).



(Z)-3-(1-(Hex-1-en-1-yl)cyclopentyl)-1,9-dihydroxy-6H-benzo[c]chromen-6-one (46). The synthesis was carried out as described for **1a**, using **45** (118 mg, 0.27 mmol), 9-iodo-9-BBN (0.82 mL of a 1.0 M in hexane, 0.82 mmol) in anhydrous CH_2Cl_2 (3.4 mL). The reaction was quenched by ethanolamine (0.5 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel (30-80% Et_2O in hexane) to give **46** (66 mg, 65 % yield) as a white solid. Mp 134-136 °C. IR (thin film, cm^{-1}) 3269 (OH), 2955, 2873, 1679 (CO), 1604, 1397, 1102, 1027, 750; ^1H NMR (500 MHz, CDCl_3) δ 8.45 (d, $J = 1.7$ Hz, 1H, Ar-H), 8.29 (d, $J = 8.3$ Hz, 1H, Ar-H), 6.96 (dd, $J = 8.3, 1.7$ Hz, 1H, Ar-H), 6.94 (d, $J = 1.4$ Hz, 1H, Ar-H), 6.70 (d, $J = 1.4$ Hz, 1H, Ar-H), 5.70 (d, $J = 11.3$ Hz, 1H), 5.32 (dt, $J = 11.3, 7.4$ Hz, 1H), 2.05-1.90 (m, 4H), 1.81 – 1.66 (m, 6H), 1.14-1.06 (m, 4H), 0.69 (t, $J = 6.8$ Hz, 3H). Mass spectrum (ESI) m/z (relative intensity) 379 ($\text{M}^+ + \text{H}$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.2 min for the title compound.

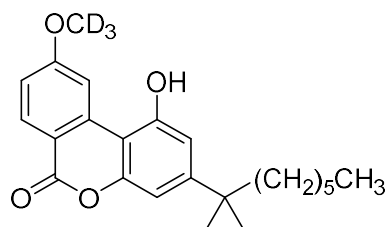


Methyl 2-bromo-4-(methoxy- d_3)benzoate (47). To a solution of methyl 2-bromo-4-hydroxybenzoate (**44**, 1.0 g, 4.35 mmol) in anhydrous DMF (24 mL) under an argon atmosphere was added K_2CO_3 (1.44 g, 10.44 mmol), and the mixture was stirred at room temperature for 20 minutes. The mixture was cooled at 0 °C and a solution of CD_3I (756 mg, 5.22 mmol) in 1.3 mL of dry DMF was added dropwise. After 5 minutes stirring at 0 °C, the mixture was stirred at room temperature for 2.5 h. The reaction was quenched with H_2O at 0 °C and then Et_2O was added. The water phase was extracted with Et_2O and the combined organic phase were washed with brine and dried over MgSO_4 . The solvent was removed, and the crude product was purified by flash column chromatography on silica gel (10% EtOAc /hexane) to give **47** (930 mg, 86 % yield) as colorless oil. IR (thin film, cm^{-1}) 1725 (CO), 1595, 1489, 1257, 1241, 1099, 999, 768. ^1H NMR (CDCl_3 , 500 MHz) δ 7.84 (d, $J = 8.0$ Hz, 1H, Ar-H), 7.17 (d, $J = 2.0$ Hz, 1H, Ar-H), 6.84 (dd, $J = 8.0, 2.0$ Hz, 1H, Ar-H), 3.88 (s, 3H, - OCH_3). ^{13}C NMR (CDCl_3 , 100 MHz) δ 165.9, 162.3, 133.2, 123.6, 123.4, 119.8, 113.0, 52.1.

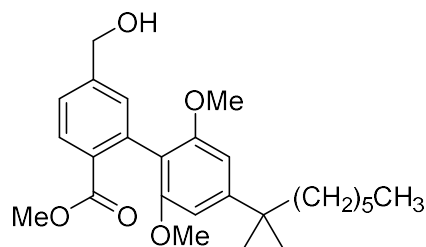


Methyl 2',6'-dimethoxy-5-(methoxy- d_3)-4'-(2-methyloctan-2-yl)-[1,1'-biphenyl]-2-carboxylate (48). The synthesis was carried out as described for **15**, using boronic acid **13** (1.04 g, 3.38 mmol), **47** (699 mg, 2.82 mmol), Cs_2CO_3 (3.67 g, 11.27 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (325 mg, 0.28 mmol) in DME/ H_2O (5:1, 8 mL of DME and 1.6 mL of H_2O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash

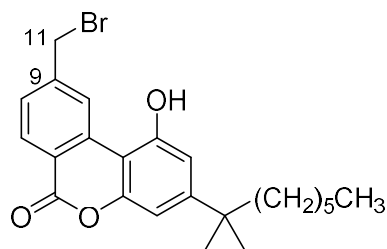
column chromatography on silica gel (10-30% EtOAc/hexane) to give **48** (984 mg, 81 % yield) as a yellow oil. IR (thin film, cm^{-1}) 2930, 2073 (CD), 1727 (CO), 1601, 1576, 1406, 1224, 1126, 1104, 745. ^1H -NMR (CDCl_3 , 500 MHz) δ 7.93 (d, $J = 8.0$ Hz, 1H, Ar-H), 6.86 (dd, $J = 8.0, 2.1$ Hz, 1H, Ar-H), 6.81 (d, $J = 2.1$ Hz, 1H, Ar-H), 6.56 (s, 2H, Ar-H), 3.68 (s, 6H, $-\text{OCH}_3$), 3.53 (s, 3H, $-\text{COOCH}_3$), 1.62-1.59 (m, 2H, $-\text{CH}_2-$), 1.32 (s, 6H, $-\text{CH}_3$), 1.26-1.22 (m, 6H, $-\text{CH}_2-$), 1.11 (br s, 2H, $-\text{CH}_2-$), 0.84 (t, $J = 7.0$ Hz, 3H, $-\text{CH}_3$). ^{13}C -NMR (CDCl_3 , 100 MHz) δ 167.9, 161.7, 156.6, 151.0, 137.5, 131.9, 124.1, 117.7, 116.7, 112.4, 102.2, 55.9, 51.2, 44.7, 38.3, 31.8, 30.0, 29.0, 24.7, 22.6, 14.0.



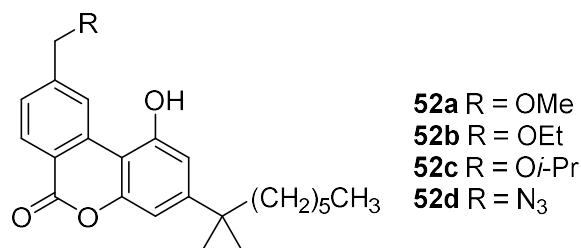
1-Hydroxy-9-(methoxy- d_3)-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (49). The synthesis was carried out as described for **1a**, using **48** (24 mg, 0.056 mmol), 9-iodo-9-BBN (0.23 mL of a 1.0 M in hexane, 0.23 mmol) in anhydrous CH_2Cl_2 (1 mL). The reaction was quenched by ethanolamine (0.3 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}/\text{hexane}$, 2:2:6) to give **49** (16 mg, 75 % yield) as a white solid. Mp 150–152 $^\circ\text{C}$. IR (thin film, cm^{-1}) 3421 (OH), 2931, 2073 (CD), 1676 (CO), 1626, 1607, 1402, 1303, 1111, 722. ^1H -NMR (CDCl_3 , 500 MHz) δ 8.48 (d, $J = 2.0$ Hz, 1H, Ar-H), 8.34 (d, $J = 8.0$ Hz, 1H, Ar-H), 7.04 (dd, $J = 8.0, 2.0$ Hz, 1H, Ar-H), 6.93 (s, 1H, Ar-H), 6.66 (s, 1H, Ar-H), 5.75 (brs, 1H, $-\text{OH}$), 1.58-1.55 (m, 2H, $-\text{CH}_2-$), 1.27 (s, 6H, $-\text{CH}_3$), 1.23-1.17 (m, 6H, $-\text{CH}_2-$), 1.06-1.00 (m, 2H, $-\text{CH}_2-$), 0.81 (t, $J = 7.1$ Hz, 3H, $-\text{CH}_3$). ^{13}C -NMR (CDCl_3 , 100 MHz) δ 164.8, 161.7, 153.9, 153.1, 152.9, 136.8, 132.2, 114.9, 113.6, 110.8, 109.8, 108.0, 104.8, 44.3, 37.9, 31.7, 29.9, 28.6, 24.6, 22.6, 14.0. HRMS (ESI) for $\text{C}_{23}\text{H}_{26}\text{D}_3\text{O}_4$: calculated 372.2254; found 372.2249. Mass spectrum (ESI) m/z (relative intensity) 372 ($\text{M}^+ + \text{H}$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.5 min for the title compound.



Methyl 5-(hydroxymethyl)-2',6'-dimethoxy-4'-(2-methyloctan-2-yl)-[1,1'-biphenyl]-2-carboxylate (50). The synthesis was carried out as described for **15**, using boronic acid **13** (754 mg, 2.45 mmol), **36** (580 mg, 2.36 mmol), Cs_2CO_3 (2.66 g, 8.16 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (462 mg, 0.4 mmol) in DME/ H_2O (5:1, 5 mL of DME and 1 mL of H_2O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10-40% EtOAc/hexane) to give **50** (810 mg, 80 % yield) as a yellow oil. IR (thin film, cm^{-1}) 3235 (OH), 2916, 2895, 1698 (CO), 1613, 1403, 1105, 1045, 757; ^1H NMR (500 MHz, CDCl_3) δ 7.93 (d, $J = 8.0$ Hz, 1H, Ar-H), 7.37 (d, $J = 8.0$ Hz, 1H, Ar-H), 7.33 (s, 1H, Ar-H), 6.57 (s, 2H, Ar-OH), 4.76 (d, $J = 4.3$ Hz, 2H), 3.69 (s, 6H, $-\text{OCH}_3$), 3.58 (s, 3H, $-\text{COOCH}_3$), 1.65 – 1.58 (m, 2H), 1.33 (s, 6H, $-\text{CH}_3$), 1.29-1.18 (m, 6H), 1.15 – 1.08 (m, 2H), 0.86 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 168.2, 156.5, 151.1, 143.9, 135.4, 131.1, 130.7, 130.0, 125.0, 116.1, 102.1, 64.9, 55.8, 51.4, 44.7, 38.3, 31.8, 30.0, 28.9, 24.7, 22.6, 14.0.



9-(Bromomethyl)-1-hydroxy-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (51). To a stirring solution of **50** (806 mg, 1.88 mmol) in dry CH_2Cl_2 at -78°C was added dropwise BBr_3 (7.8 mL of a 1.0 M solution in hexane, 7.8 mmol). The temperature was slowly warmed to room temperature and the reaction mixture was stirred overnight. Then the reaction was cooled back to 0°C and water was added. The organic phase was removed under reduced pressure and the residue water phase was extracted by EtOAc. The combined organic extracts were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10-40% EtOAc/hexane) gave **51** (550 mg, 68 % yield) as a white solid. Mp $197-201^\circ\text{C}$ (decomposed). IR (thin film, cm^{-1}) 3325 (OH), 2927, 2856, 1699 (CO), 1611, 1402, 1262, 1092, 749; ^1H NMR (500 MHz, CDCl_3) δ 8.99 (s, 1H, Ar-H), 8.38 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.54 (d, $J = 8.1$ Hz, 1H, Ar-H), 6.95 (d, $J = 1.5$ Hz, 1H, Ar-H), 6.67 (d, $J = 1.5$ Hz, 1H, Ar-H), 5.66 (s, 1H, OH), 4.60 (s, 2H, CH_2Br), 1.61 – 1.55 (m, 2H), 1.28 (s, 6H, $-\text{CH}_3$), 1.26 – 1.14 (m, 6H), 1.08 – 0.99 (m, 2H), 0.82 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.5, 154.0, 153.5, 152.6, 144.6, 135.2, 130.7, 128.2, 127.6, 120.1, 110.1, 107.9, 104.3, 44.3, 38.0, 32.7, 31.7, 29.9, 28.6, 24.6, 22.6, 14.0. Mass spectrum (ESI) m/z (relative intensity) 431 ($\text{M}^+ + \text{H}$, 80), 433 ($\text{M}^+ + \text{H} + 2$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.7 min for the title compound.

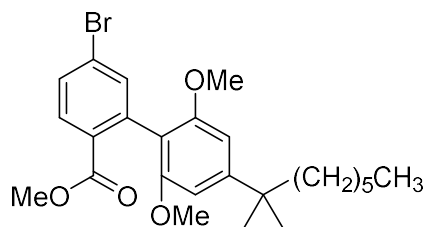


1-Hydroxy-9-(methoxymethyl)-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (52a). Argon was bubbled through a mixture of **51** (17 mg, 0.039 mmol) and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (44 mg, 0.16 mmol) in $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (4:1, 0.8 mL of CH_2Cl_2 and 0.2 mL of MeOH) for 10 min. Then the reaction mixture was microwaved at 130°C for 60 min in a Biotage apparatus. Then the mixture was cooled to room temperature and filtered through a short celite pad. The filtrate was concentrated and Et_2O was added. The ether solution was washed with water and brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10-30% EtOAc/hexane) gave **52a** (15 mg, 99 % yield) as a yellow oil. IR (thin film, cm^{-1}) 3306 (OH), 2939, 2850, 1730 (CO), 1586, 1435, 1176, 1021, 785, 724; ^1H NMR (500 MHz, CDCl_3) δ 9.05 (s, 1H, Ar-H), 8.41 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.50 (d, $J = 8.1$ Hz, 1H, Ar-H), 6.93 (d, $J = 1.6$ Hz, 1H, Ar-H), 6.91 (brs, 1H, OH), 6.90 (s, 1H, Ar-H), 6.74 (d, $J = 1.6$ Hz, 1H, Ar-H), 4.70 (s, 2H), 3.50 (s, 3H, $-\text{OCH}_3$), 1.61 – 1.54 (m, 2H), 1.28 (s, 6H, $-\text{CH}_3$), 1.26 – 1.12 (m, 6H), 1.07 – 0.98 (m, 2H), 0.82 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.8, 154.3, 153.1, 152.6, 145.1, 135.0, 130.3, 126.5, 125.8, 119.8, 109.9, 107.7, 104.6, 74.5, 58.4, 44.3, 37.9, 31.7, 29.9, 28.6, 24.6, 22.6, 14.0. HRMS (ESI) for $\text{C}_{24}\text{H}_{31}\text{O}_4$: calculated 383.2222; found 383.2213. Mass spectrum (ESI) m/z (relative intensity) 383 ($\text{M}^+ + \text{H}$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.7 min for the title compound.

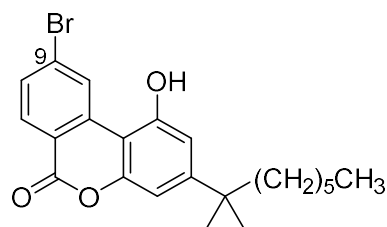
9-(Ethoxymethyl)-1-hydroxy-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (52b). Argon was bubbled through a mixture of **51** (20 mg, 0.046 mmol) and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (52 mg, 0.19 mmol) in $\text{CH}_2\text{Cl}_2/\text{EtOH}$ (3:1, 0.9 mL of CH_2Cl_2 and 0.3 mL of EtOH) for 10 min. Then the reaction mixture was microwaved at 130 °C for 60 min in a Biotage apparatus. Then the mixture was cooled to room temperature and filtered through a short celite pad. The filtrate was concentrated and Et_2O was added. The ether solution was washed with water and brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10-30% EtOAc/hexane) gave **52b** (18 mg, 98 % yield) as a yellow oil. IR (thin film, cm^{-1}) 3300 (OH), 2953, 2934, 2865, 1711 (CO), 1699, 1591, 1466, 1378, 1054, 910, 740, 688; ^1H NMR (500 MHz, CDCl_3) δ 9.01 (s, 1H, Ar-H), 8.39 (d, J = 8.1 Hz, 1H, Ar-H), 7.51 (d, J = 8.1 Hz, 1H, Ar-H), 6.94 (d, J = 1.6 Hz, 1H, Ar-H), 6.69 (d, J = 1.6 Hz, 1H, Ar-H), 6.26 (s, 1H, OH), 4.72 (s, 2H), 3.65 (q, J = 7.0 Hz, 2H), 1.63 – 1.55 (m, 2H), 1.31 (t, J = 7.0 Hz, 3H), 1.29 (s, 6H, $-\text{CH}_3$), 1.27 – 1.14 (m, 6H), 1.09 – 1.08 (m, 2H), 0.83 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.6, 154.0, 152.9, 152.6, 145.7, 134.8, 130.3, 126.5, 125.6, 119.7, 109.8, 107.9, 104.7, 72.4, 66.2, 44.3, 37.9, 31.7, 29.9, 28.6, 24.6, 22.6, 15.2, 14.0. HRMS (ESI) for $\text{C}_{25}\text{H}_{33}\text{O}_4$: calculated 397.2379; found 397.2374. Mass spectrum (ESI) m/z (relative intensity) 397 ($\text{M}^+ + \text{H}$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.7 min for the title compound.

1-Hydroxy-9-(isopropoxymethyl)-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (52c). Argon was bubbled through a mixture of **51** (20 mg, 0.046 mmol) and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (52 mg, 0.19 mmol) in $\text{CH}_2\text{Cl}_2/\text{propan-2-ol}$ (3:1, 0.9 mL of CH_2Cl_2 and 0.3 mL of propan-2-ol) for 10 min. Then the reaction mixture was microwaved at 130 °C for 60 min in a Biotage apparatus. Then the mixture was cooled to room temperature and filtered through a short celite pad. The filtrate was concentrated and Et_2O was added. The ethereal solution was washed with water and brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10-30% EtOAc/hexane) gave **52c** (18 mg, 97 % yield) as a yellow oil. IR (thin film, cm^{-1}) 3308 (OH), 2962, 2927, 2857, 1694 (CO), 1613, 1405, 1087, 845, 743; ^1H NMR (500 MHz, CDCl_3) δ 9.19 (s, 1H, Ar-H), 8.37 (d, J = 8.1 Hz, 1H, Ar-H), 7.74 (brs, 1H, OH), 7.45 (d, J = 8.1 Hz, 1H, Ar-H), 6.90 (d, J = 1.4 Hz, 1H, Ar-H), 6.78 (s, 1H, Ar-H), 4.81 (s, 2H), 3.82 (septet, J = 6.1 Hz, 1H), 1.62 – 1.54 (m, 2H), 1.33 (d, J = 6.1 Hz, 6H, $-\text{CH}(\text{CH}_3)_2$), 1.28 (s, 6H, $-\text{CH}_3$), 1.26 – 1.13 (m, 6H), 1.09 – 0.99 (m, 2H), 0.82 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.9, 154.8, 152.9, 152.6, 145.8, 135.2, 130.2, 126.2, 125.6, 119.6, 109.8, 107.3, 104.6, 71.8, 69.7, 44.3, 37.9, 31.7, 29.9, 28.6, 24.6, 22.6, 22.1, 14.0. HRMS (ESI) for $\text{C}_{26}\text{H}_{35}\text{O}_4$: calculated 411.2535; found 411.2528. Mass spectrum (ESI) m/z (relative intensity) 411 ($\text{M}^+ + \text{H}$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.8 min for the title compound.

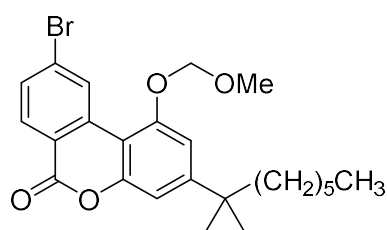
9-(Azidomethyl)-1-hydroxy-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (52d). To a stirring solution of **51** (30 mg, 0.07 mmol) in dry CH_2Cl_2 (1.4 mL) under argon atmosphere was added $n\text{-Bu}_4\text{N}^+\text{N}_3^-$ (79 mg, 0.28 mmol) at room temperature and the reaction mixture was stirred for 2 days. The mixture was then quenched by the addition of water, extracted with Et_2O and the combined organic extracts were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (15-30 % EtOAc/hexane) gave **52d** (26 mg, 96 % yield) as a white solid. Mp 137-141 °C. IR (thin film, cm^{-1}) 3285 (OH), 2926, 2135 (N_3), 1698 (CO), 1621, 1404, 1103, 1054, 846, 745; ^1H NMR (500 MHz, CDCl_3) δ 8.94 (s, 1H, Ar-H), 8.42 (d, J = 8.1 Hz, 1H, Ar-H), 7.47 (d, J = 8.1 Hz, 1H, Ar-H), 6.96 (d, J = 1.6 Hz, 1H, Ar-H), 6.69 (d, J = 1.6 Hz, 1H, Ar-H), 5.64 (s, 1H, OH), 4.53 (s, 2H, CH_2N_3), 1.62 – 1.55 (m, 2H), 1.29 (s, 6H, $-\text{CH}_3$), 1.27 – 1.12 (m, 6H), 1.07 – 1.00 (m, 2H), 0.82 (t, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.2, 153.7, 153.5, 152.7, 142.3, 135.1, 130.7, 127.0, 126.4, 120.4, 110.0, 108.2, 104.4, 54.8, 44.3, 38.0, 31.7, 29.9, 28.6, 24.6, 22.5, 13.9. HRMS (ESI) for $\text{C}_{23}\text{H}_{28}\text{N}_3\text{O}_3$: calculated 394.2131; found 394.2124. Mass spectrum (ESI) m/z (relative intensity) 394 ($\text{M}^+ + \text{H}$, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.7 min for the title compound.



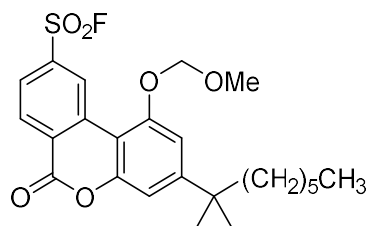
Methyl 5-bromo-2',6'-dimethoxy-4'-(2-methyloctan-2-yl)-[1,1'-biphenyl]-2-carboxylate (54). The synthesis was carried out as described for **15**, using boronic acid **13** (262 mg, 0.85 mmol), **53** (290 mg, 0.85 mmol), Cs_2CO_3 (1.1 g, 3.4 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (104 mg, 0.09 mmol) in DME/ H_2O (5:1, 3.5 mL of DME and 0.7 mL of H_2O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10-30% EtOAc/hexane) to give **54** (250 mg, 62 % yield) as a yellow oil. IR (thin film, cm^{-1}) 2954, 2930, 2858, 1734 (CO), 1609, 1575, 1453, 1409, 1284, 1238, 1124, 1096, 1017, 829. ^1H NMR (500 MHz, CDCl_3) δ 7.78 (d, $J = 8.3$ Hz, 1H, Ar-H), 7.53–7.46 (m, 2H, Ar-H), 6.56 (s, 2H, Ar-H), 3.70 (s, 6H, 2 $\times$ OCH₃), 3.58 (s, 3H, COOCH₃), 1.66–1.58 (m, 2H, CH₂), 1.33 (s, 6H, 2 $\times$ CH₃), 1.29–1.20 (m, 6H, 3 $\times$ CH₂), 1.16–1.06 (m, 2H, CH₂), 0.86 (t, $J = 6.8$ Hz, 3H, CH₃). ^{13}C NMR (126 MHz, CDCl_3) δ 167.7, 156.4, 151.6, 137.1, 135.6, 131.1, 130.9, 129.8, 125.6, 114.9, 102.0, 55.7, 51.6, 44.7, 38.4, 31.9, 30.0, 29.0, 24.7, 22.7, 14.2. Mass spectrum (ESI) m/z (relative intensity) 477 ($\text{M}^+ + \text{H}$, 75), 445 ($\text{M}^+ - \text{OMe}$, 100), 155 (100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 6.2 min for the title compound.



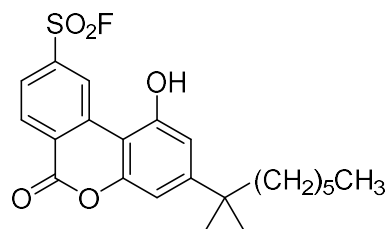
9-Bromo-1-hydroxy-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (55). The synthesis was carried out as described for **1a**, using **54** (205 mg, 0.43 mmol), 9-iodo-9-BBN (1.4 mL of a 1.0 M in hexane, 1.4 mmol) in anhydrous CH_2Cl_2 (5 mL). The reaction was quenched by ethanolamine (0.5 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}/\text{hexane}$, 2:2:6) to give **55** (130 mg, 73 % yield) as a white solid. Mp 232–233 $^\circ\text{C}$. IR (thin film, cm^{-1}) 3291 (br, OH), 2957, 2928, 2855, 1693 (CO), 1624, 1594, 1392, 1276, 1261, 1109, 1087. ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 11.03 (s, 1H, OH), 9.18 (d, $J = 2.0$ Hz, 1H, Ar-H), 8.10 (d, $J = 8.4$ Hz, 1H, Ar-H), 7.73 (dd, $J = 8.4, 2.0$ Hz, 1H, Ar-H), 6.87 (d, $J = 1.8$ Hz, 1H, Ar-H), 6.80 (d, $J = 1.8$ Hz, 1H, Ar-H), 1.57–1.50 (m, 2H, CH₂), 1.23 (s, 6H, 2 $\times$ CH₃), 1.19–1.11 (m, 6H, 3 $\times$ CH₂), 1.03–0.94 (m, 2H, CH₂), 0.77 (t, $J = 6.8$ Hz, 3H, CH₃). ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ 160.5, 156.5, 153.7, 152.7, 136.6, 131.9, 130.9, 129.8, 129.4, 119.4, 110.1, 105.9, 103.0, 44.0, 38.1, 31.6, 29.8, 28.8, 24.6, 22.5, 14.3. Mass spectrum (ESI) m/z (relative intensity) 417 ($\text{M}^+ + \text{H}$, 100), 131 (85). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.8 min for the title compound.



9-Bromo-1-(methoxymethoxy)-3-(2-methyloctan-2-yl)-6*H*-benzo[*c*]chromen-6-one (56). To a solution of **55** (125 mg, 0.3 mmol) in CH₂Cl₂ (6.0 mL) under an argon atmosphere at 0 °C was added *N,N*-diisopropylethylamine (520 µL, 3.0 mmol), and the mixture was stirred at 0 °C for 5 min. Chloromethyl methyl ether (120 µL, 1.6 mmol) was added at 0 °C, and the reaction mixture was stirred at 0 °C for an additional 30 min and then at room temperature for 1 h. The reaction mixture was quenched with saturated aqueous NaHCO₃, and the organic material was extracted with CH₂Cl₂. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (0/1 → 1/9) as eluent to afford **56** (127 mg, 92%) as a white solid. Mp 68–69 °C. IR (thin film, cm⁻¹) 2956, 2928, 2857, 1732 (CO), 1616, 1592, 1385, 1157, 1074, 1043, 1010, 965, 926. ¹H NMR (500 MHz, CDCl₃) δ 9.16 (d, *J* = 1.9 Hz, 1H, Ar-H), 8.26 (d, *J* = 8.5 Hz, 1H, Ar-H), 7.65 (dd, *J* = 8.5, 1.9 Hz, 1H, Ar-H), 7.07 (d, *J* = 1.8 Hz, 1H, Ar-H), 7.03 (d, *J* = 1.8 Hz, 1H, Ar-H), 5.44 (s, 2H, OCH₂O), 3.60 (s, 3H, OCH₃), 1.64–1.58 (m, 2H, CH₂), 1.31 (s, 6H, 2 × CH₃), 1.27–1.17 (m, 6H, 3 × CH₂), 1.10–1.02 (m, 2H, CH₂), 0.84 (t, *J* = 6.8 Hz, 3H, CH₃). ¹³C NMR (126 MHz, CDCl₃) δ 160.9, 155.5, 154.1, 152.4, 135.9, 131.6, 130.8, 130.2, 129.9, 119.5, 109.0, 108.4, 105.1, 95.2, 56.7, 44.2, 38.3, 31.7, 29.9, 28.7, 24.6, 22.6, 14.1. Mass spectrum (ESI) *m/z* (relative intensity) 461 (M⁺ + H, 65), 201 (100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 6.3 min for the title compound.

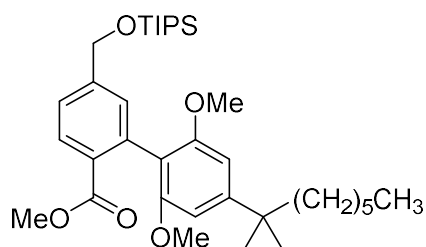


1-(Methoxymethoxy)-3-(2-methyloctan-2-yl)-6-oxo-6*H*-benzo[*c*]chromene-9-sulfonyl fluoride (57). To a mixture of **56** (92 mg, 0.2 mmol), DABSO (52 mg, 0.22 mmol), and PdCl₂(Amphos)₂ (16 mg, 0.02 mmol) under an argon atmosphere in a resealable tube at room temperature was added anhydrous Et₃N (60 mg, 0.6 mmol) and anhydrous isopropanol (1.0 mL). The resealable tube was sealed, and the reaction mixture was stirred at 75 °C for 24 h. The reaction mixture was cooled to room temperature, NFSI (94 mg, 0.3 mmol) was added in one portion, and the reaction mixture was stirred at room temperature for 3 h. Solvent was removed under reduced pressure, and the mixture was diluted with EtOAc and then filtered through a Celite pad. The filtrate was washed with saturated aqueous Na₂S₂O₃ and brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (0/1 → 1/19) as eluent to afford **57** (66 mg, 71%) as a white solid. Mp 57–58 °C. IR (thin film, cm⁻¹) 2963, 2930, 2860, 1742 (CO), 1618, 1416, 1276, 1261, 1211, 1079, 1049. ¹H NMR (500 MHz, CDCl₃) δ 9.72 (d, *J* = 1.8 Hz, 1H, Ar-H), 8.63 (d, *J* = 8.3 Hz, 1H, Ar-H), 8.07 (dd, *J* = 8.3, 1.8 Hz, 1H, Ar-H), 7.11 (d, *J* = 1.8 Hz, 1H, Ar-H), 7.06 (d, *J* = 1.8 Hz, 1H, Ar-H), 5.48 (s, 2H, OCH₂O), 3.61 (s, 3H, OCH₃), 1.67–1.59 (m, 2H, CH₂), 1.33 (s, 6H, 2 × CH₃), 1.27–1.17 (m, 6H, 3 × CH₂), 1.11–1.01 (m, 2H, CH₂), 0.83 (t, *J* = 6.7 Hz, 3H, CH₃). ¹³C NMR (126 MHz, CDCl₃) δ 159.6, 155.6, 155.6, 152.4, 138.2 (d, ²*J*_{CF} = 25.3 Hz), 135.8, 131.7, 127.6, 125.7, 125.6, 109.0, 108.5, 104.4, 95.2, 56.9, 44.1, 38.5, 31.7, 29.8, 28.6, 24.6, 22.6, 14.0; ¹⁹F NMR (470 MHz, CDCl₃) δ 65.2.

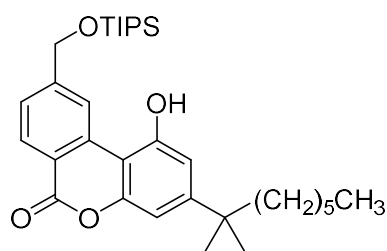


1-Hydroxy-3-(2-methyloctan-2-yl)-6-oxo-6*H*-benzo[*c*]chromene-9-sulfonyl fluoride (58). To a mixture of **57** (40 mg, 0.086 mmol) and ethanol (396 mg, 8.60 mmol) in CH₃CN (10 mL) at room temperature was added

Sc(OTf)₃ (30 mg, 0.061 mmol). After being flushed with argon, the reaction mixture was refluxed until most of the starting material was consumed as judged by TLC (ca. 8 h). CH₃CN was removed under reduced pressure, and water (ca. 0.5 mL) was added and stirred for 5 min. The organic material was extracted with EtOAc, and the combined organic extracts were concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (0/1 → 1/9) as eluent to afford **58** (33 mg, 91%) as a pale yellow solid. Mp 216–217 °C. IR (thin film, cm⁻¹) 3373 (br, OH), 2968, 2933, 2859, 1707 (CO), 1630, 1585, 1472, 1418, 1397, 1300, 1213, 1118, 1093, 1045. ¹H NMR (500 MHz, CD₃CN) δ 9.71 (d, *J* = 1.8 Hz, 1H, Ar-H), 8.57 (d, *J* = 8.5 Hz, 1H, Ar-H), 8.55 (s, 1H, OH), 8.13 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar-H), 6.99 (d, *J* = 1.8 Hz, 1H, Ar-H), 6.96 (d, *J* = 1.8 Hz, 1H, Ar-H), 1.70–1.63 (m, 2H, CH₂), 1.33 (s, 6H, 2 × CH₃), 1.30–1.20 (m, 6H, 3 × CH₂), 1.15–1.05 (m, 2H, CH₂), 0.86 (t, *J* = 6.7 Hz, 3H, CH₃). ¹³C NMR (100 MHz, CD₃CN) δ 160.7, 156.6, 156.3, 153.8, 138.4 (d, ²*J*_{CF} = 25.0 Hz), 137.0, 132.4, 128.3, 127.1, 126.9, 111.2, 107.9, 103.8, 44.7, 39.0, 32.5, 30.6, 28.9, 25.4, 23.3, 14.3; ¹⁹F NMR (376 MHz, CD₃CN) δ 64.5. HRMS (ESI) for C₂₂H₂₆O₅SF: calculated 421.1485; found 421.1503.

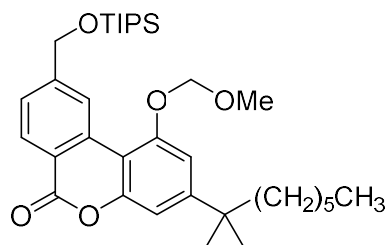


Methyl 2',6'-dimethoxy-4'-(2-methyloctan-2-yl)-5-(((triisopropylsilyl)oxy)methyl)-[1,1'-biphenyl]-2-carboxylate (59). The synthesis was carried out as described for **15**, using boronic acid **13** (501 mg, 1.63 mmol), **37** (548 mg, 1.36 mmol), Cs₂CO₃ (1.63 g, 5 mmol) and Pd(PPh₃)₄ (162 mg, 0.14 mmol) in DME/H₂O (5:1, 5 mL of DME and 1 mL of H₂O). The reaction was completed in 45 min and the crude oil obtained after work up was purified by flash column chromatography on silica gel (10–25% EtOAc/hexane) to give **59** (684 mg, 86 % yield) as a yellow oil. IR (thin film, cm⁻¹) 2925, 2863, 1707 (CO), 1609, 1576, 1461, 1283, 1239, 1126, 881, 806; ¹H NMR (500 MHz, CDCl₃) δ 7.89 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.36 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.28 (s, 1H, Ar-H), 6.55 (s, 2H, Ar-H), 4.86 (s, 2H), 3.66 (s, 6H, -OCH₃), 3.55 (s, 3H, -COOCH₃), 1.64 – 1.57 (m, 2H), 1.32 (s, 6H, -CH₃), 1.27 – 1.11 (m, 11H), 1.07 (d, *J* = 6.7 Hz, 18H), 0.84 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 168.5, 156.6, 150.8, 144.7, 134.8, 130.3, 129.9, 129.7, 124.1, 116.5, 102.2, 64.7, 55.8, 51.3, 44.7, 38.2, 31.8, 30.0, 28.9, 24.7, 22.6, 18.0, 14.0, 12.0.

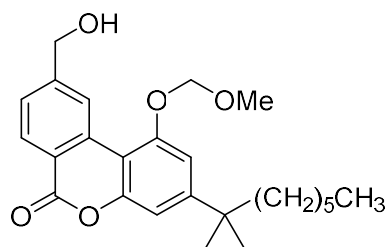


1-Hydroxy-3-(2-methyloctan-2-yl)-9-(((triisopropylsilyl)oxy)methyl)-6H-benzo[c]chromen-6-one (60). The synthesis was carried out as described for **1a**, using **59** (462 mg, 0.8 mmol), 9-iodo-9-BBN (2.6 mL of a 1.0 M in hexane, 2.6 mmol) in anhydrous CH₂Cl₂ (8 mL). The reaction was quenched by ethanolamine (1 mL) and the crude obtained after work up was purified by flash column chromatography on silica gel (CH₂Cl₂/Et₂O/hexane, 2:2:6) to give **60** (252 mg, 60 % yield) as a white solid. IR (thin film, cm⁻¹) 3332 (OH), 2927, 2866, 1722 (CO), 1708, 1270, 1074, 883, 688; ¹H NMR (500 MHz, CDCl₃) δ 9.00 (s, 1H, Ar-H), 8.36 (d, *J* = 8.1 Hz, 1H, Ar-H), 7.47 (d, *J* = 8.1 Hz, 1H, Ar-H), 6.95 (d, *J* = 1.4 Hz, 1H, Ar-H), 6.66 (d, *J* = 1.4 Hz, 1H, Ar-H), 5.58 (s, 1H, OH), 5.00 (s, 2H), 1.57 (m, 2H), 1.28 (s, 6H, -CH₃), 1.26 – 1.14 (m, 11H), 1.11 (d, *J* = 6.7 Hz, 18H), 0.82 (t, *J* = 6.9

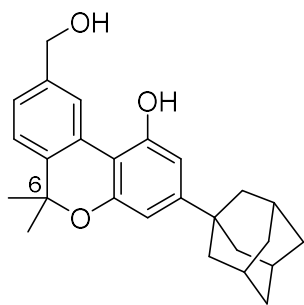
Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.4, 153.8, 153.3, 152.6, 144.7, 135.3, 130.6, 127.3, 127.1, 120.5, 110.1, 107.8, 104.1, 65.7, 44.3, 38.0, 32.6, 31.7, 29.9, 28.6, 24.6, 22.6, 18.0, 14.0.



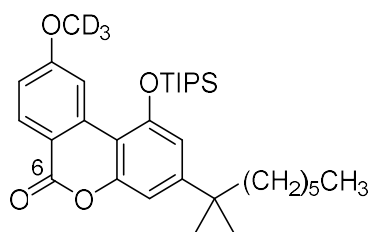
1-(Methoxymethoxy)-3-(2-methyloctan-2-yl)-9-(((triisopropylsilyl)oxy)methyl)-6H-benzo[c]chromen-6-one (61). The synthesis was carried out as described for **59**, using **60** (250 mg, 0.47 mmol), *N,N*-diisopropylethylamine (250 μL , 1.43 mmol), chloromethyl methyl ether (110 μL , 1.43 mmol) in anhydrous CH_2Cl_2 (4.8 mL). The crude oil obtained after work up was purified by flash column chromatography on silica gel (10% $\text{MeOH}/\text{CH}_2\text{Cl}_2$) to give title compound (265 mg, 98 % yield) as a colorless oil. IR (thin film, cm^{-1}) 2928, 2865, 1731 (CO), 1614, 1265, 1099, 1052, 967, 741, 701, 682; ^1H NMR (500 MHz, CDCl_3) δ 8.97 (d, J = 0.8 Hz, 1H, Ar-H), 8.38 (d, J = 8.1 Hz, 1H, Ar-H), 7.48 (dd, J = 8.1, 1.8 Hz, 1H, Ar-H), 7.11 (d, J = 1.8 Hz, 1H, Ar-H), 7.02 (d, J = 1.8 Hz, 1H, Ar-H), 5.40 (s, 2H), 4.98 (s, 2H), 3.53 (s, 3H, - OCH_3), 1.62 – 1.58 (m, 2H), 1.30 (s, 6H), 1.26 – 1.15 (m, 6H), 1.12 (s, 10H), 1.11 (s, 8H), 1.08 – 1.02 (m, 2H), 0.82 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.6, 155.7, 153.0, 152.3, 148.8, 134.7, 130.2, 125.3, 123.8, 119.6, 109.1, 108.7, 106.5, 95.0, 65.2, 56.3, 44.2, 38.2, 31.7, 29.9, 28.7, 24.7, 22.6, 18.1, 14.0, 12.0.



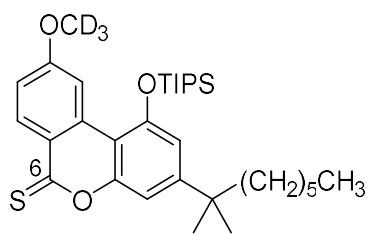
9-(Hydroxymethyl)-1-(methoxymethoxy)-3-(2-methyloctan-2-yl)-6H-benzo[c]chromen-6-one (62). To a solution of 1-(methoxymethoxy)-3-(2-methyloctan-2-yl)-9-(((triisopropylsilyl)oxy)methyl)-6H-benzo[c]chromen-6-one (53 mg, 0.09 mmol) in anhydrous THF (2.5 mL) at 0 $^\circ\text{C}$ under an argon atmosphere was added TBAF (0.11 mL, 1M in THF, 0.11 mmol). The reaction was kept at 0 $^\circ\text{C}$ for 10 min and then at room temperature for 1.5 h. The mixture was quenched by the addition of saturated aqueous NH_4Cl , extracted with Et_2O and the combined organic extracts were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (20-40 % $\text{EtOAc}/\text{hexane}$) gave **62** (37 mg, 97 % yield) as a yellow oil. IR (thin film, cm^{-1}) 3440 (OH), 2927, 1706 (CO), 1612, 1266, 1054, 750; ^1H NMR (500 MHz, CDCl_3) δ 8.98 (s, 1H), 8.39 (d, J = 8.1 Hz, 1H, Ar-H), 7.51 (d, J = 8.1 Hz, 1H, Ar-H), 7.03 (d, J = 7.8 Hz, 2H, Ar-H), 5.41 (s, 2H), 5.28 (s, 1H), 4.88 (s, 2H), 3.57 (s, 3H, - OCH_3), 1.65 – 1.53 (m, 2H), 1.29 (s, 6H, - CH_3), 1.26 – 1.13 (m, 6H), 1.05 (m, 2H), 0.82 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.5, 155.6, 153.3, 152.4, 147.8, 134.9, 130.6, 125.9, 124.7, 120.1, 109.1, 108.5, 106.3, 95.3, 65.2, 56.7, 44.2, 38.3, 31.7, 29.9, 28.7, 24.6, 17.7, 14.0.



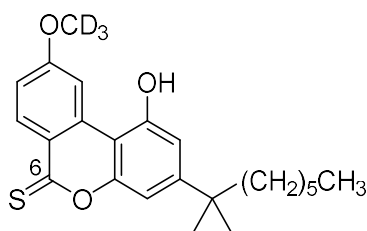
3-(Adamantan-1-yl)-9-(hydroxymethyl)-6,6-dimethyl-6H-benzo[c]chromen-1-ol (63).⁶ To a solution of **39** (400 mg, 0.75 mmol) in THF (25 mL) under an argon atmosphere at room temperature was slowly added a 3.0 M solution of methylmagnesium bromide in Et₂O (2.5 mL, 7.5 mmol). The reaction mixture was stirred at room temperature for 30 min and then refluxed for an additional 1.5 h. After the mixture was cooled to room temperature, saturated aqueous NH₄Cl (ca. 20 mL) was added, and the organic material was extracted with Et₂O. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure to give the crude intermediate as a white foam that was used without further purification in the subsequent cyclization. The crude was dissolved in CHCl₃ (10 mL) at room temperature, and *p*-TsOH·H₂O (43 mg, 0.225 mmol) was added. After being flushed with argon, the reaction mixture was stirred at room temperature for 12 h. Water was added, and the organic material was extracted with CHCl₃. The combined organic extracts were washed with saturated aqueous NaHCO₃ and water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (1/10 → 1/1) as eluent to afford **63** (190 mg, 65%) as a white solid. Mp 118–119 °C. IR (thin film, cm⁻¹) 3348 (br, OH), 2904, 2849, 1621, 1584, 1407, 1264, 1055. ¹H NMR (500 MHz, CD₃OD) δ 8.56 (s, 1H, Ar-H), 7.22–7.19 (m, 2H, Ar-H), 6.56 (d, *J* = 1.9 Hz, 1H, Ar-H), 6.45 (d, *J* = 1.9 Hz, 1H, Ar-H), 4.61 (s, 2H, CH₂), 2.05–2.03 (m, 3H, Ad-H), 1.89–1.88 (m, 6H, Ad-H), 1.81–1.73 (m, 6H, Ad-H), 1.54 (s, 6H, 2 × CH₃). ¹³C NMR (126 MHz, CD₃OD) δ 156.3, 155.4, 154.2, 141.0, 139.7, 129.6, 126.5, 126.3, 123.4, 109.3, 107.2, 106.9, 78.0, 65.5, 44.1, 37.9, 37.1, 30.3, 27.5. HRMS (ESI) for C₂₆H₃₁O₃: calculated 391.2273; found 391.2266. Mass spectrum (ESI) *m/z* (relative intensity) 391 (*M*⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.2 min for the title compound.



9-(Methoxy-d₃)-3-(2-methyloctan-2-yl)-1-((triisopropylsilyl)oxy)-6H-benzo[c]chromen-6-one (64). To a solution of **49** (156 mg, 0.42 mmol) in anhydrous CH₂Cl₂ (0.7 mL) under an argon atmosphere were added sequentially, 2,6-lutidine (400 mg, 3.6 mmol), and triisopropylsilyl trifluoromethanesulfonate (740 mg, 2.4 mmol) at 0 °C. Following the addition, the reaction mixture was gradually warmed to room temperature and the stirring was continued at that temperature for 2 h and then quenched by the addition of saturated aqueous NH₄Cl and extracted with diethyl ether. The organic phase was dried (MgSO₄) and evaporated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (1/10 → 2/10) as eluent to afford 197 mg (89% yield) of **64** as colorless viscous oil. IR (thin film, cm⁻¹) 2943, 2646, 2074 (CD), 1713 (CO), 1607, 1465, 1399, 1270, 1110, 883; ¹H-NMR (CDCl₃, 500 MHz) δ 8.49 (s, 1H, Ar-H), 8.35 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.02 (d, *J* = 7.2 Hz, 1H, Ar-H), 9.92 (s, 1H, Ar-H), 6.76 (s 1H, Ar-H), 1.60–1.57 (m, 2H, -CH₂-), 1.48–1.42 (m, 3H, -CH-), 1.28 (s, 6H, -CH₃), 1.26–1.15 (m and d overlapping, 22H, 2x-CH₂- and -CH(CH₃)₂, especially 1.17, d, *J* = 7.1 Hz, -CH(CH₃)₂), 1.05–0.99 (m, 4H, -CH₂-), 0.81 (t, *J* = 6.9 Hz, 3H, -CH₃).



9-(Methoxy-d₃)-3-(2-methyloctan-2-yl)-1-((triisopropylsilyl)oxy)-6H-benzo[c]chromene-6-thione (65). To a stirring solution of **64** (148 mg, 0.28 mmol) in anhydrous toluene (2 mL) under an argon atmosphere was added Lawesson reagent (226 mg, 0.56 mmol). The reaction mixture was refluxed at 120 °C for 24 hours and then cooled to room temperature. Then the mixture was diluted with 1 mL solution of benzene/hexane (60:40) and stirred for another 30 minutes. Solid materials were filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/hexane (1/10 → 2/10) as eluent to afford 115 mg (76% yield) of **65** as a yellow viscous oil. IR (thin film, cm⁻¹) 2928, 2868, 2073 (CD), 1605, 1463, 1397, 1279 and 1264 (CS), 1180, 1015, 883; ¹H-NMR (CDCl₃, 500 MHz) δ 8.89 (d, *J* = 7.2 Hz, 1H, Ar-H), 8.49 (s, 1H, Ar-H), 7.12 (s, 1H, Ar-H), 7.04 (d, *J* = 7.2 Hz, 1H, Ar-H), 6.81 (s, 1H, Ar-H), 1.59-1.55 (m, 2H, -CH₂-), 1.47-1.42 (m, 3H, -CH-), 1.26 (s, 6H, -CH₃), 1.23-1.15 (m and d overlapping, 22H, 2x-CH₂- and -CH(CH₃)₂, especially 1.18, d, *J* = 7.1 Hz, -CH(CH₃)₂), 1.03-0.95 (m, 4H, -CH₂-), 0.81 (t, *J* = 6.9 Hz, 3H, -CH₃).

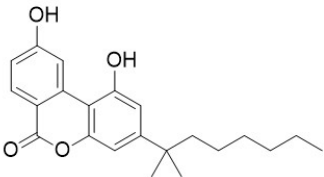


1-Hydroxy-9-(methoxy-d₃)-3-(2-methyloctan-2-yl)-6H-benzo[c]chromene-6-thione (66). To a solution of **65** (27 mg, 0.05 mmol) in anhydrous THF (1.25 mL) at -40 °C, under an argon atmosphere, was added tetra-*n*-butylammonium fluoride (0.06 mL, 0.06 mmol, 1M solution in anhydrous THF). The reaction mixture was stirred for 30 min at the same temperature, and then quenched using a saturated aqueous NH₄Cl solution. Extractive isolation with diethyl ether, and purification by silica gel column chromatography with CH₂Cl₂/Et₂O/hexane (2:2:6) as eluent gave **66** (16 mg, 82% yield) as a yellow solid. Mp 120-126 °C. IR (thin film, cm⁻¹) 3061 (OH), 2931, 2071 (CD), 1686, 1604, 1405, 1274, 1101, 740. ¹H-NMR (CDCl₃, 500 MHz) δ 8.88 (d, *J* = 7.2 Hz, 1H, Ar-H), 8.46 (d, *J* = 1.9 Hz, 1H, Ar-H), 7.14 (d, *J* = 1.4 Hz, 1H, Ar-H), 7.06 (dd, *J* = 7.2, 1.9 Hz, 1H, Ar-H), 6.70 (d, *J* = 1.4 Hz, 1H, Ar-H), 5.63 (brs, 1H, -OH), 1.61-1.58 (m, 2H, -CH₂-), 1.30 (s, 6H, -CH₃), 1.26-1.20 (m, 6H, -CH₂-), 1.05 (br s, 2H, -CH₂-), 0.84 (t, *J* = 6.9 Hz, 3H, -CH₃). ¹³C-NMR (CDCl₃, 100 MHz) δ 199.5, 165.2, 154.4, 153.6, 153.4, 136.4, 132.3, 131.2, 123.4, 116.2, 110.4, 109.6, 108.2, 44.2, 38.0, 31.7, 29.9, 28.5, 24.6, 22.5, 13.9. HRMS (ESI) for C₂₃H₂₆D₃O₃S: calculated 388.2026; found 388.2025. Mass spectrum (ESI) *m/z* (relative intensity) 388 (M⁺ + H, 100). LC/MS analysis (Waters MicroMass ZQ system) showed retention time 5.9 min for the title compound.

References

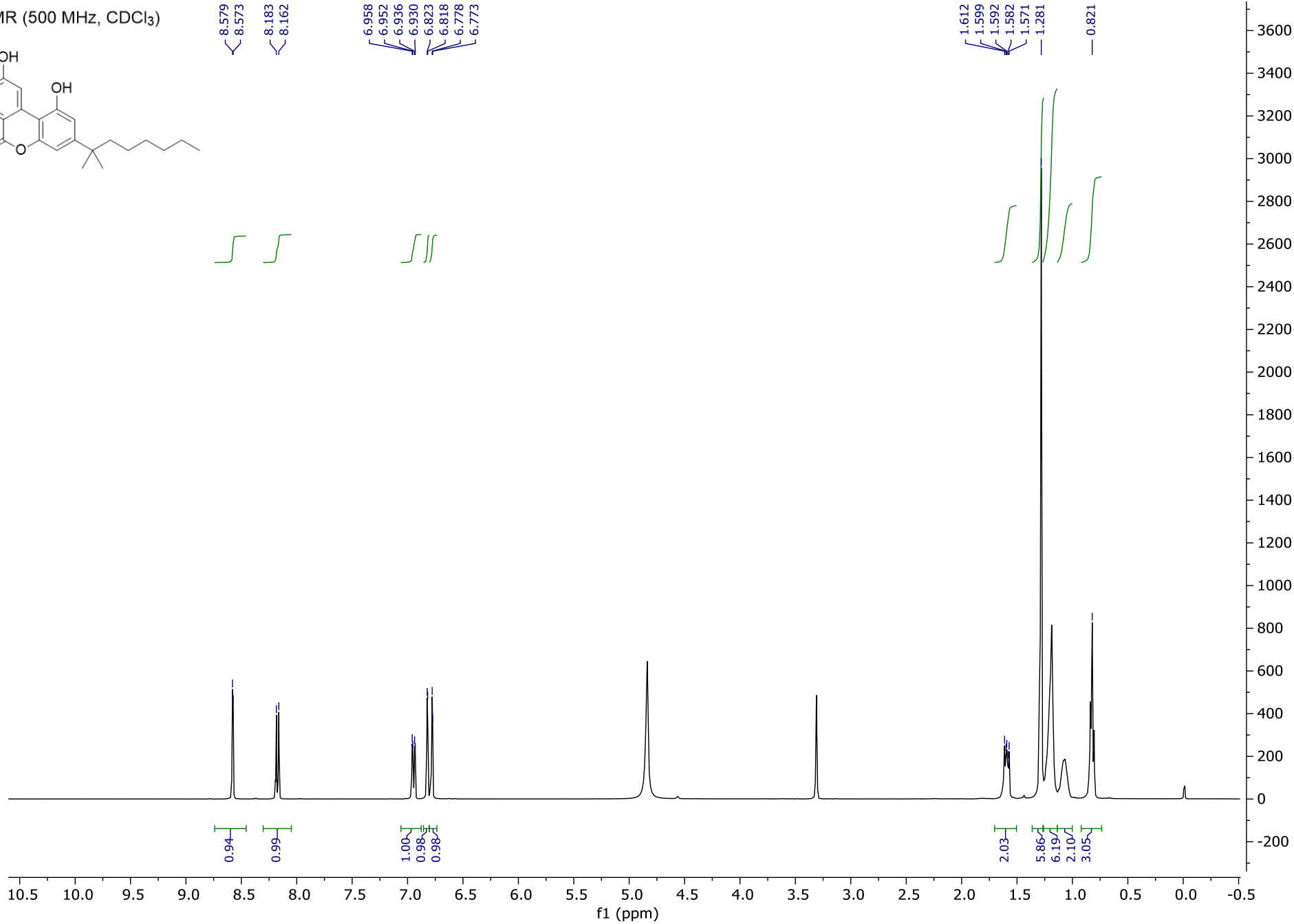
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¹H NMR (500 MHz, CDCl₃)

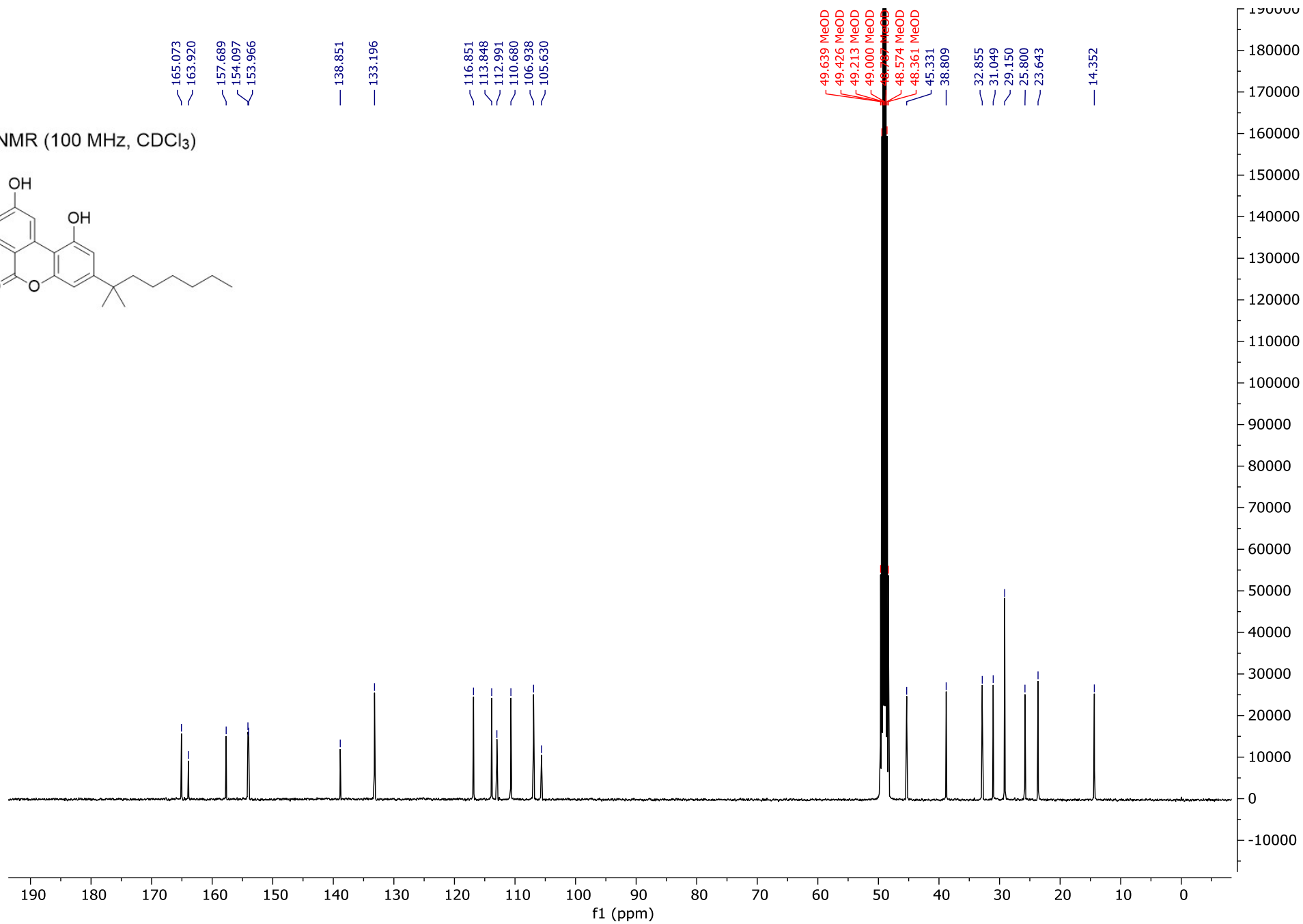
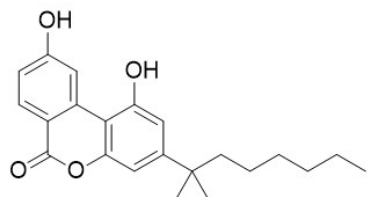


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8.162
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6.952
6.936
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6.778
6.773

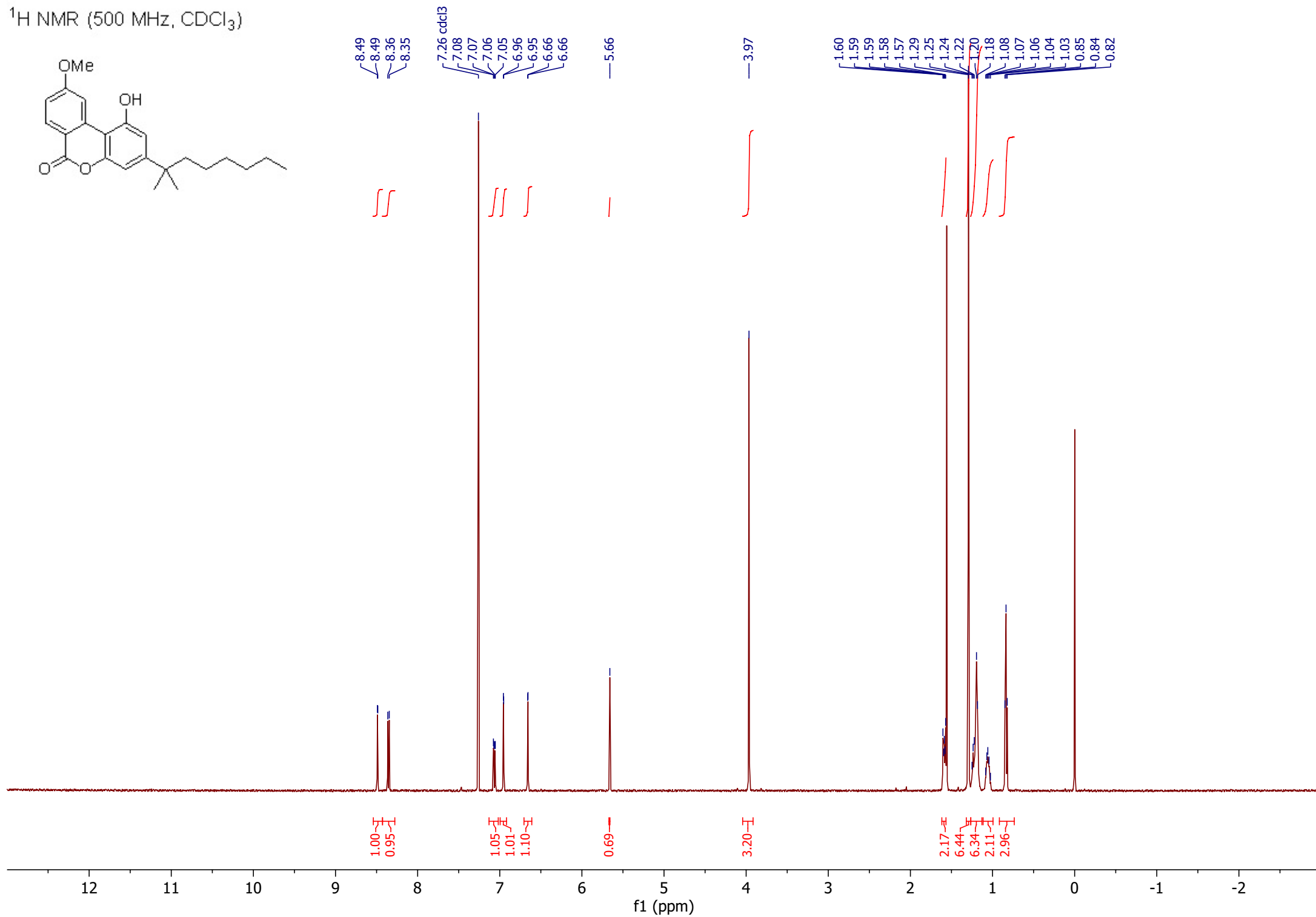
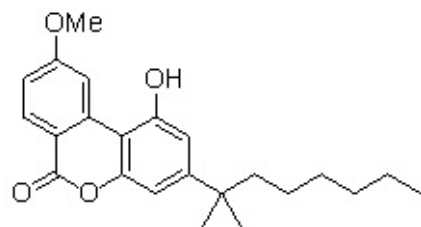
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0.821



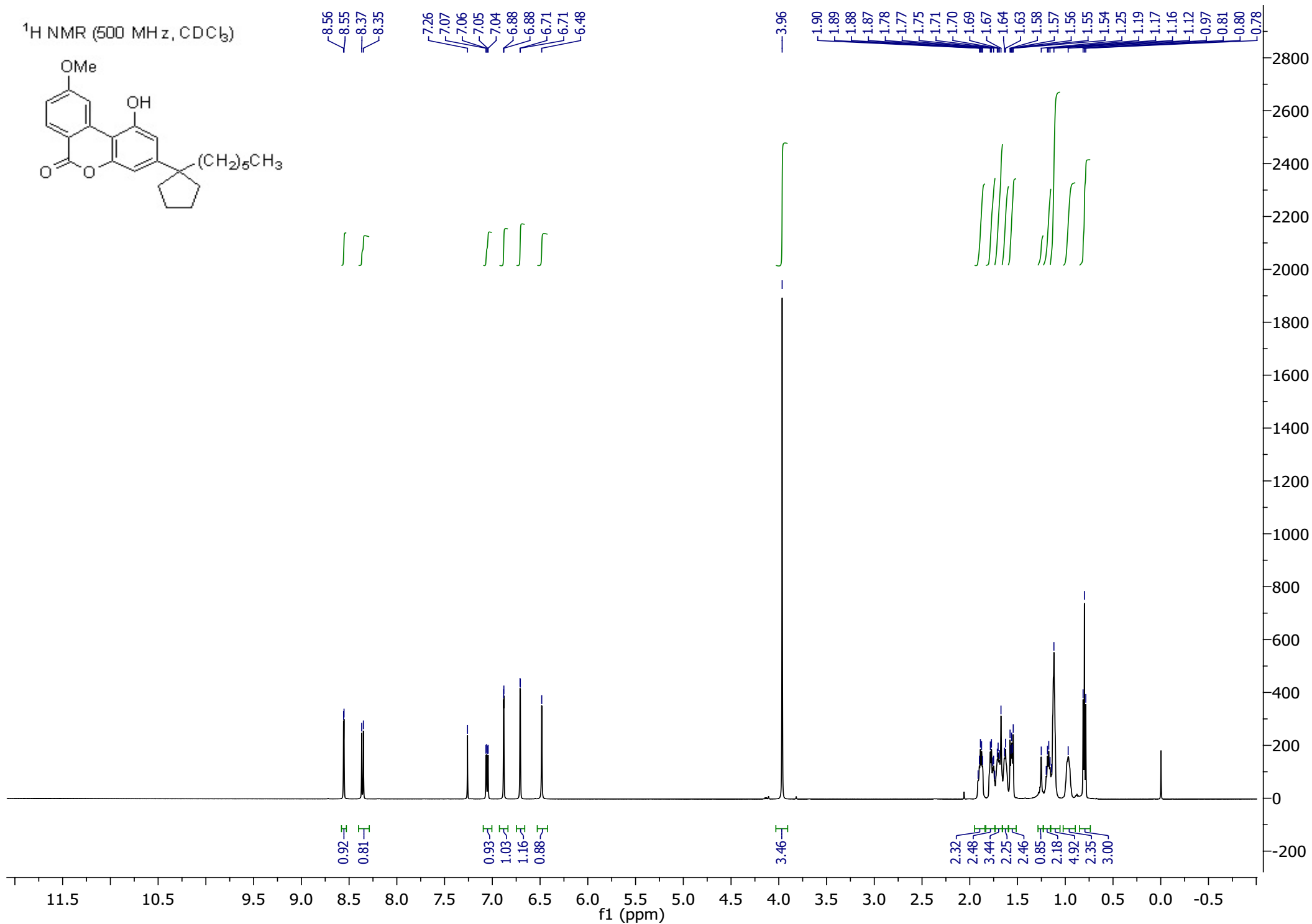
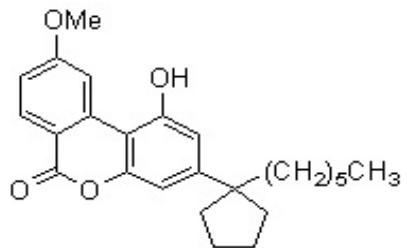
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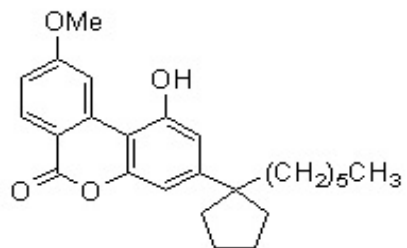
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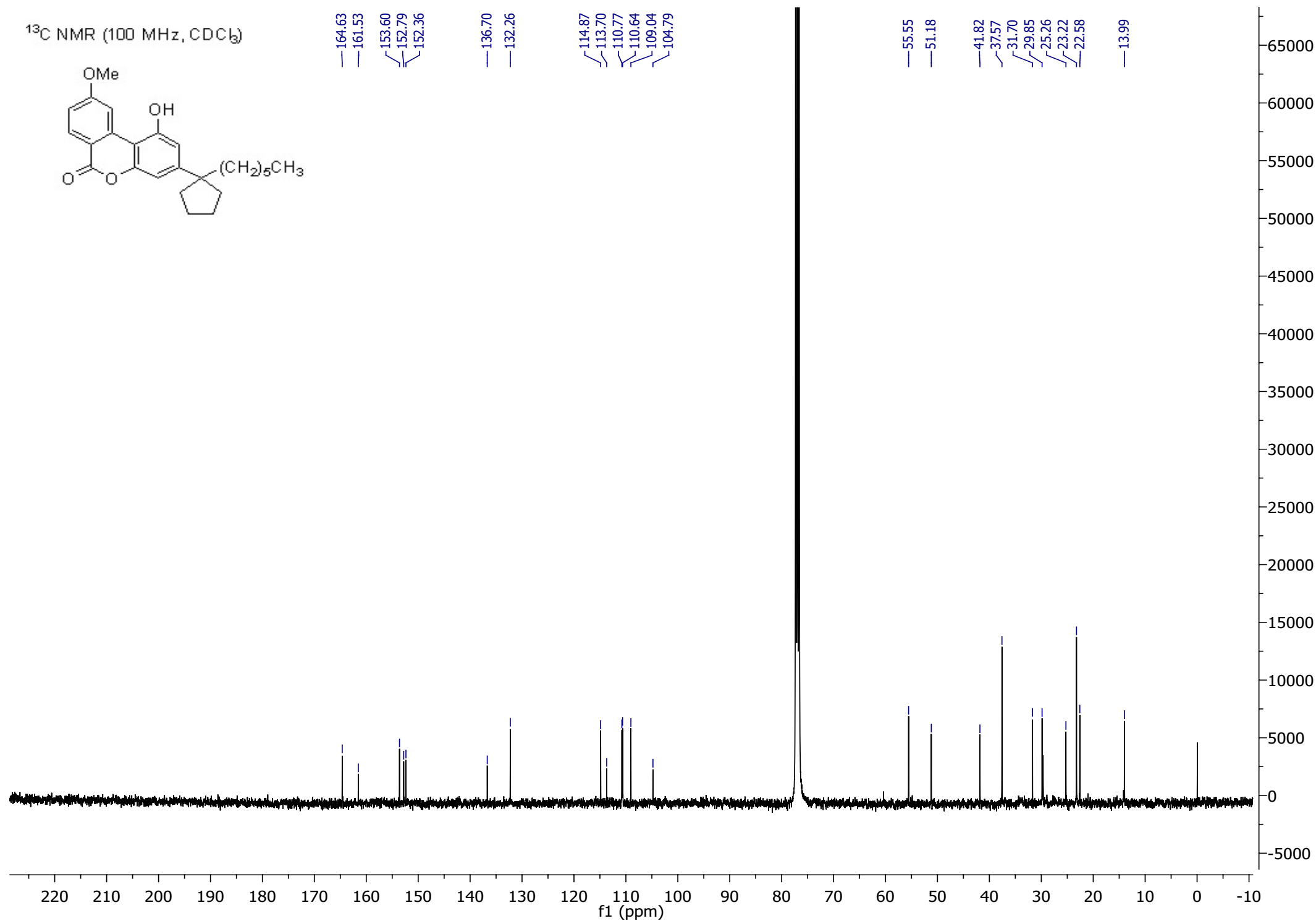
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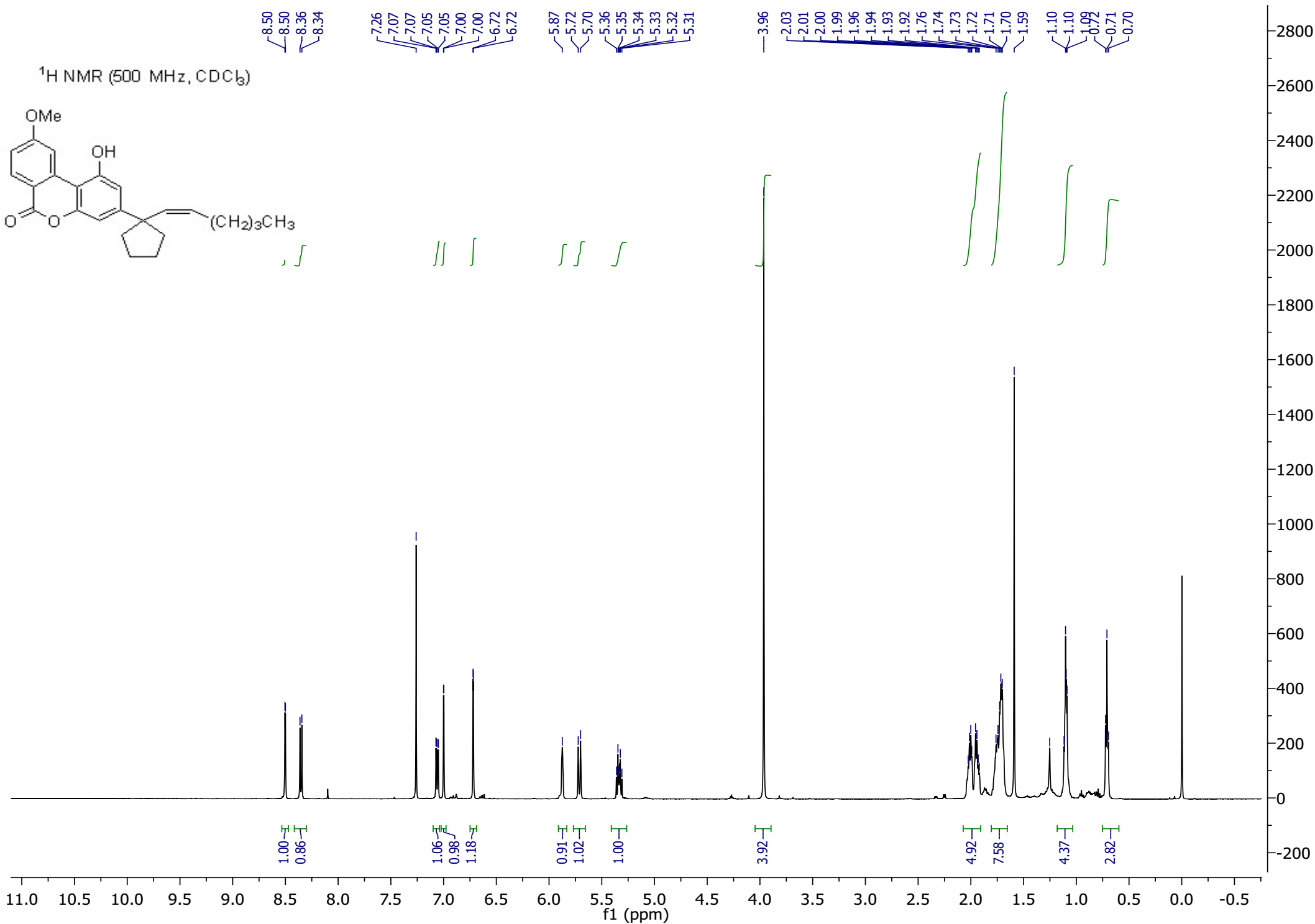


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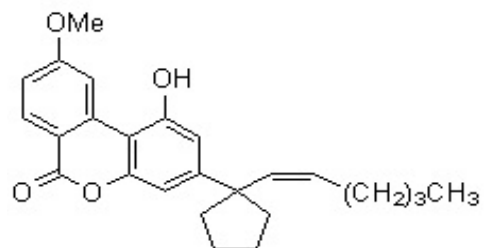


164.63 161.53 153.60 152.79 152.36 136.70 132.26 114.87 113.70 110.77 110.64 109.04 104.79 55.55 51.18 41.82 37.57 31.70 29.85 25.26 23.22 22.58 13.99

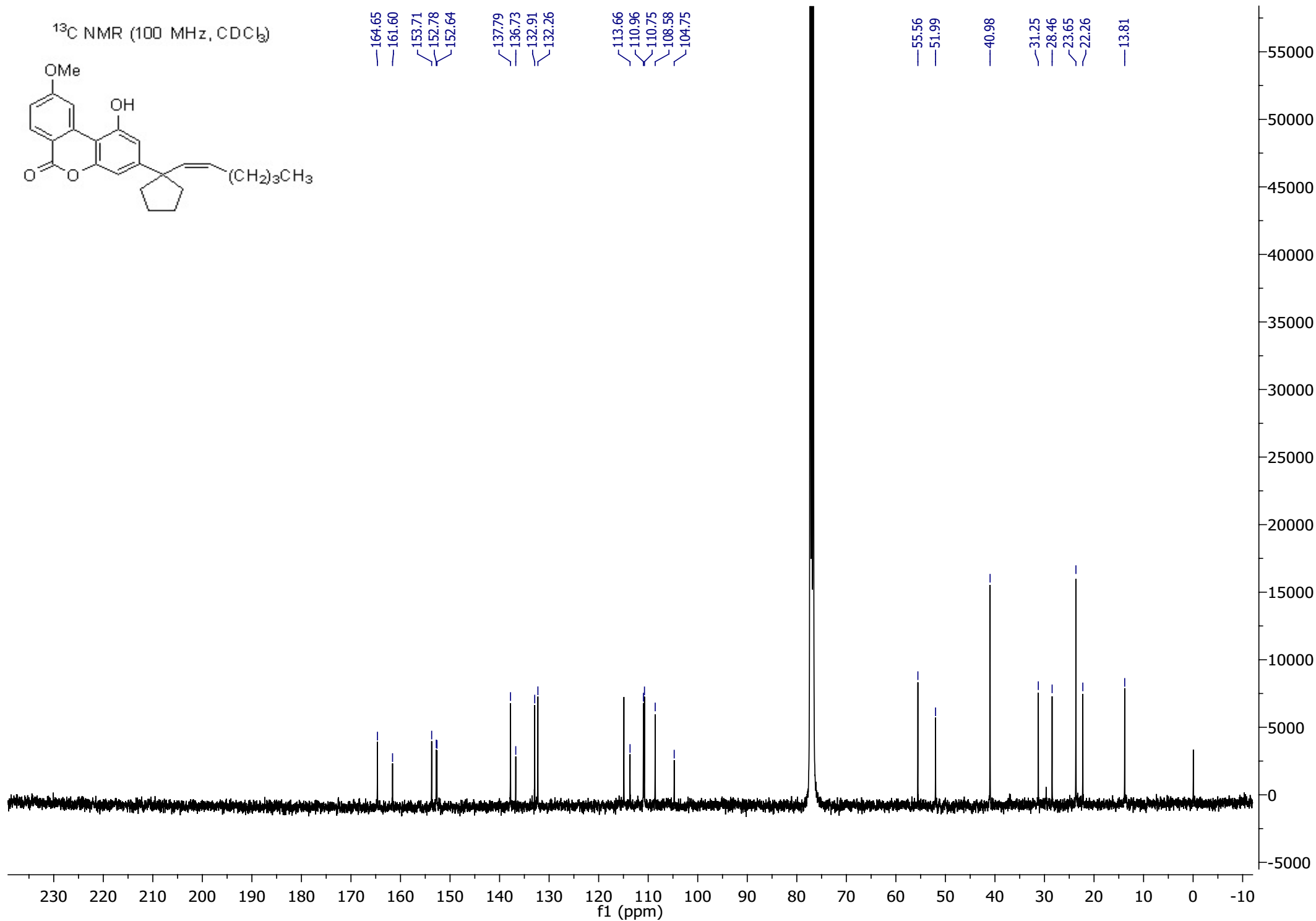




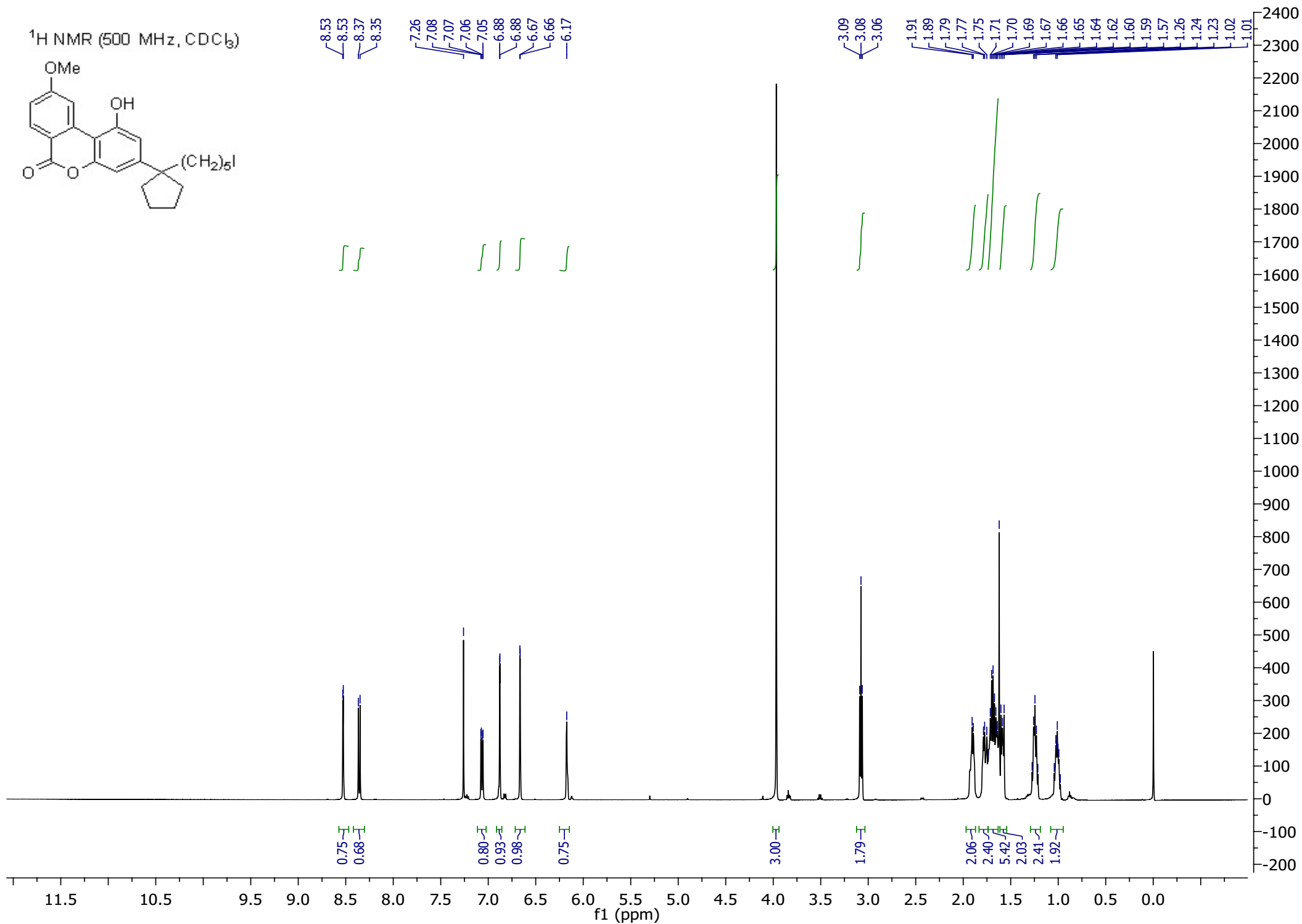
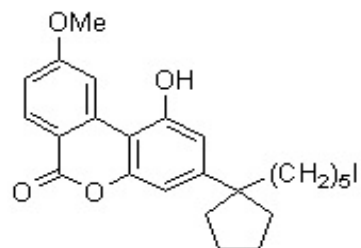
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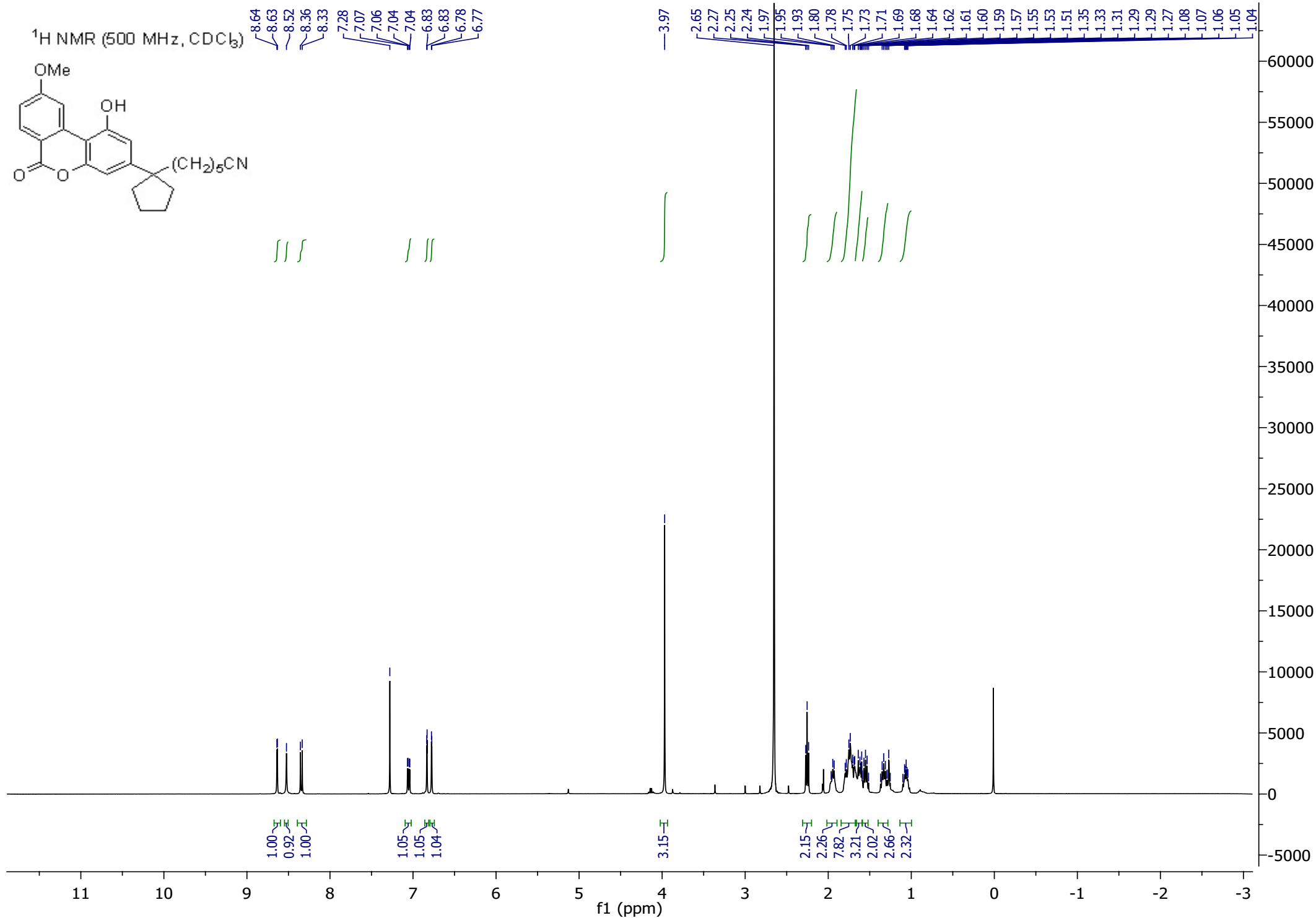


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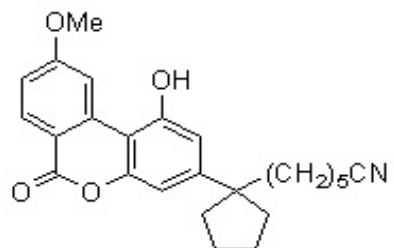


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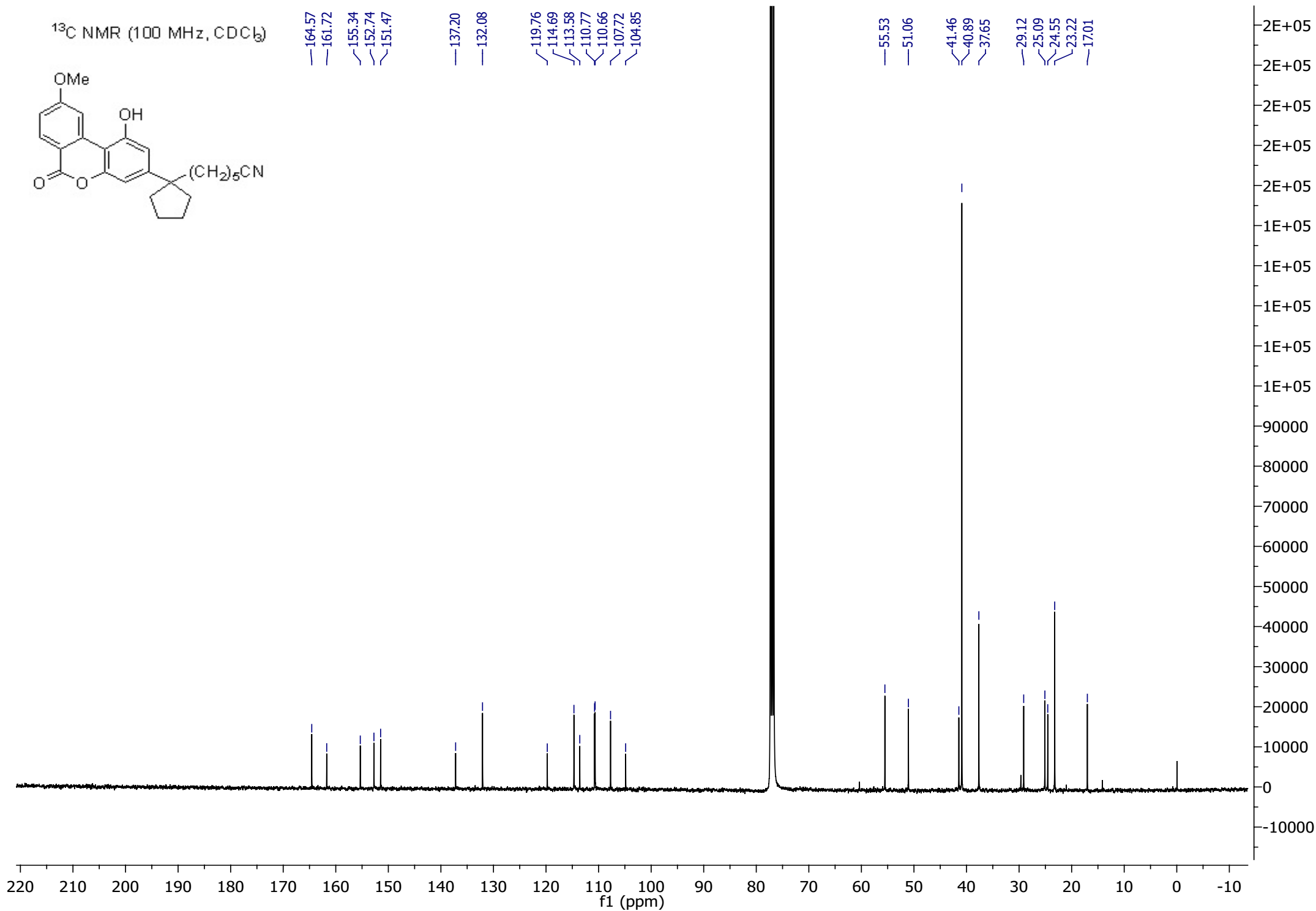




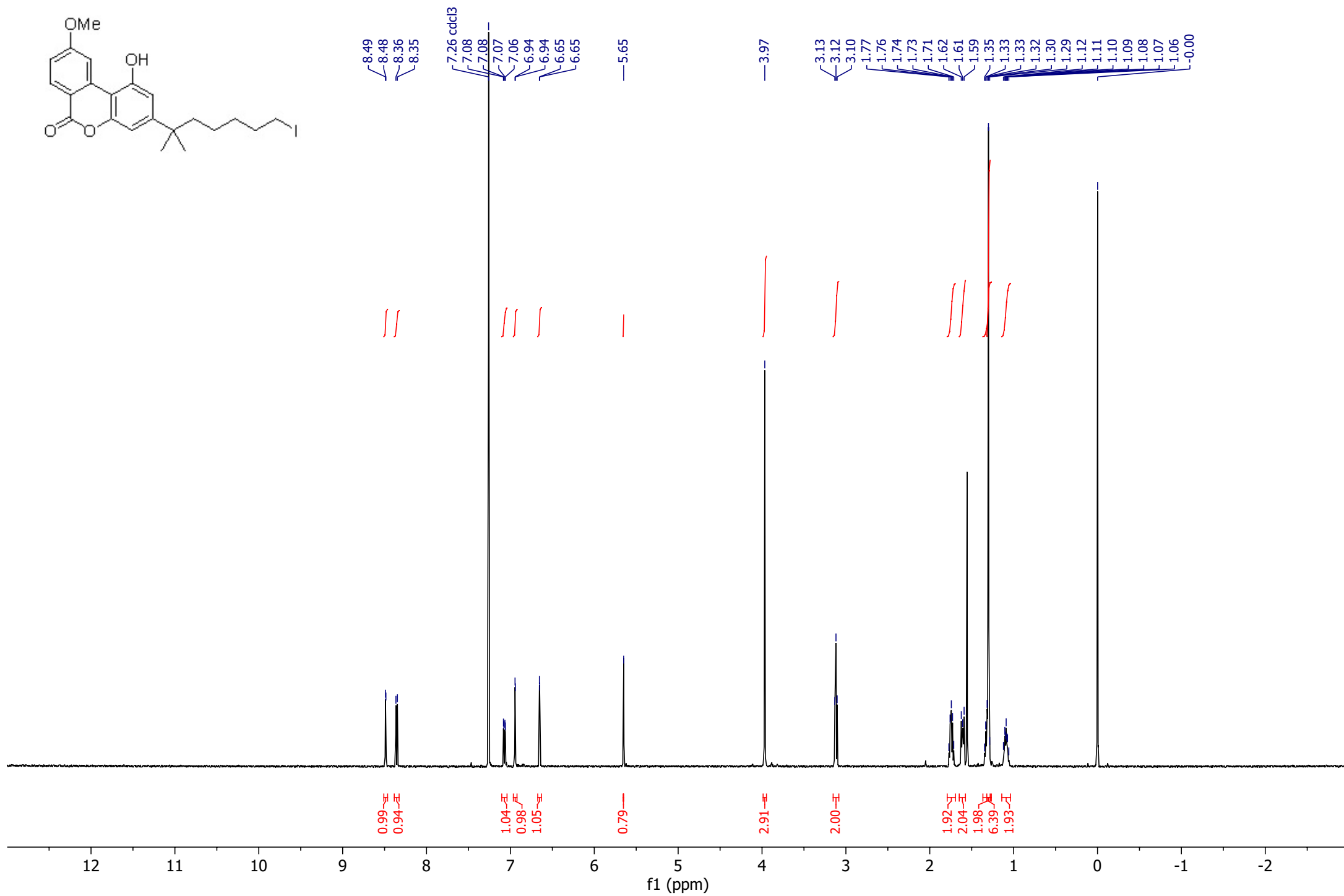
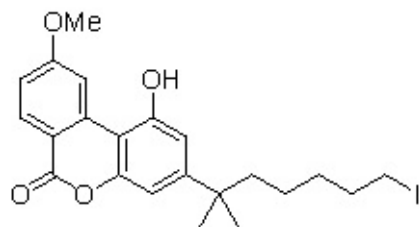
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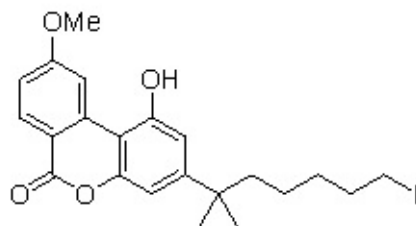
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104.85
55.53
51.06
41.46
40.89
37.65
29.12
25.09
24.55
23.22
17.01



^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)



165.03
163.00

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152.84
152.57

137.49

132.12

115.29
113.01
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104.91

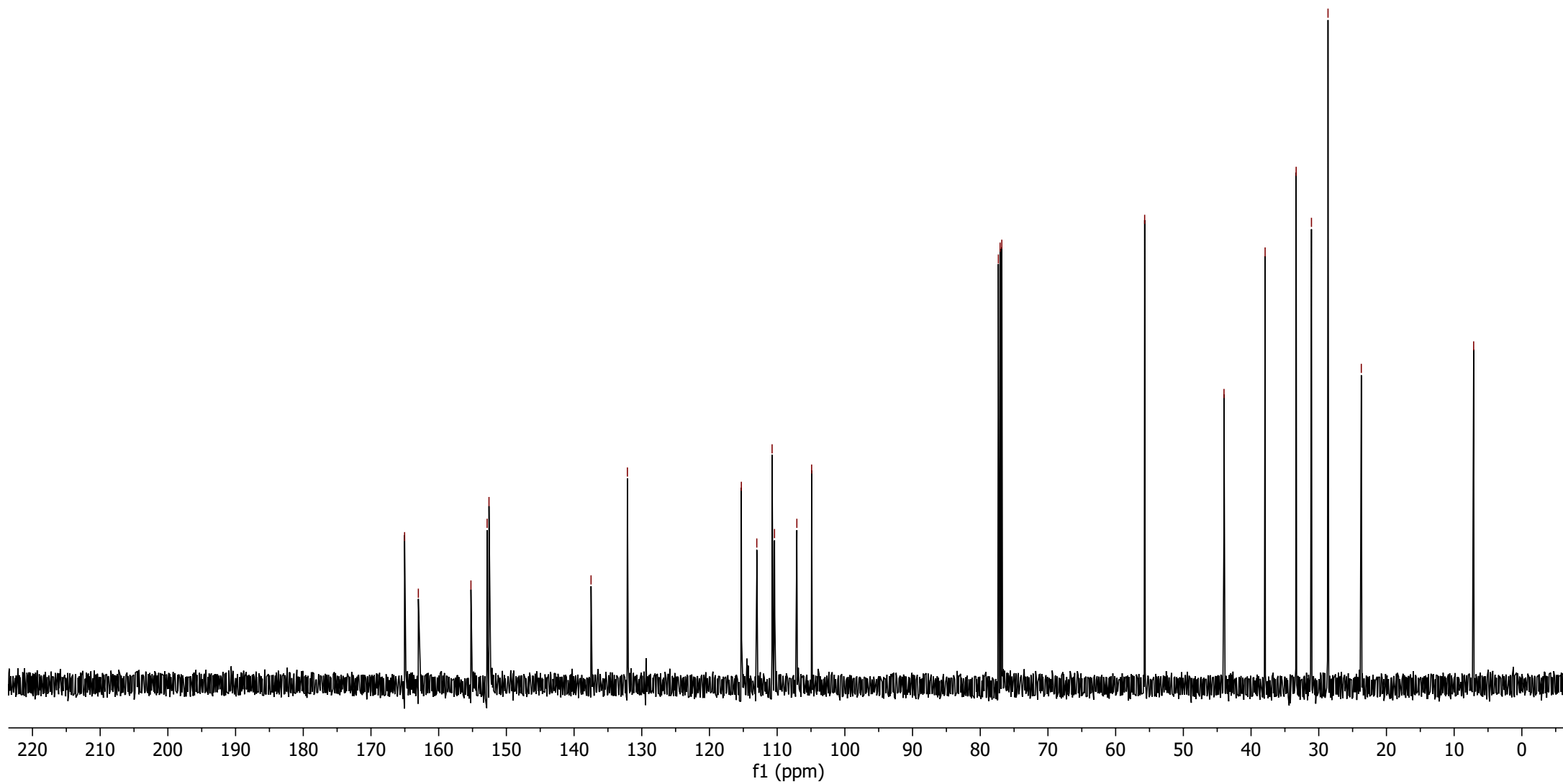
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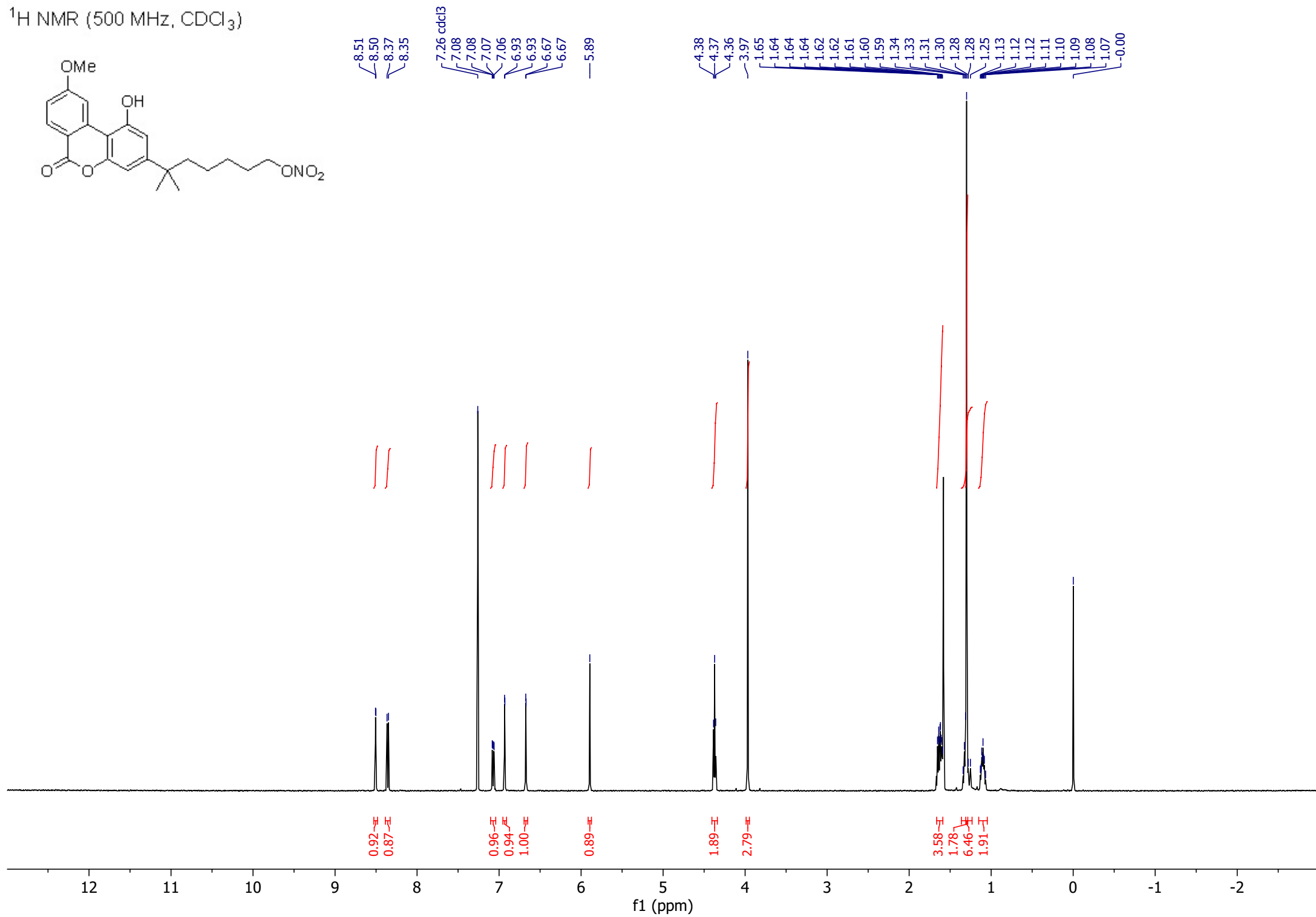
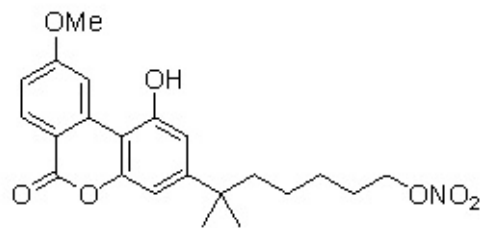
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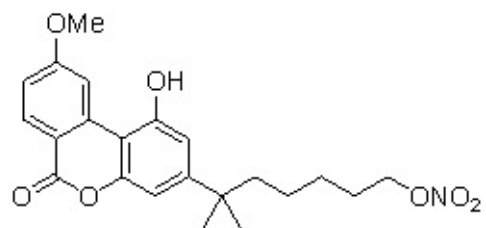
7.12



^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)



165.08
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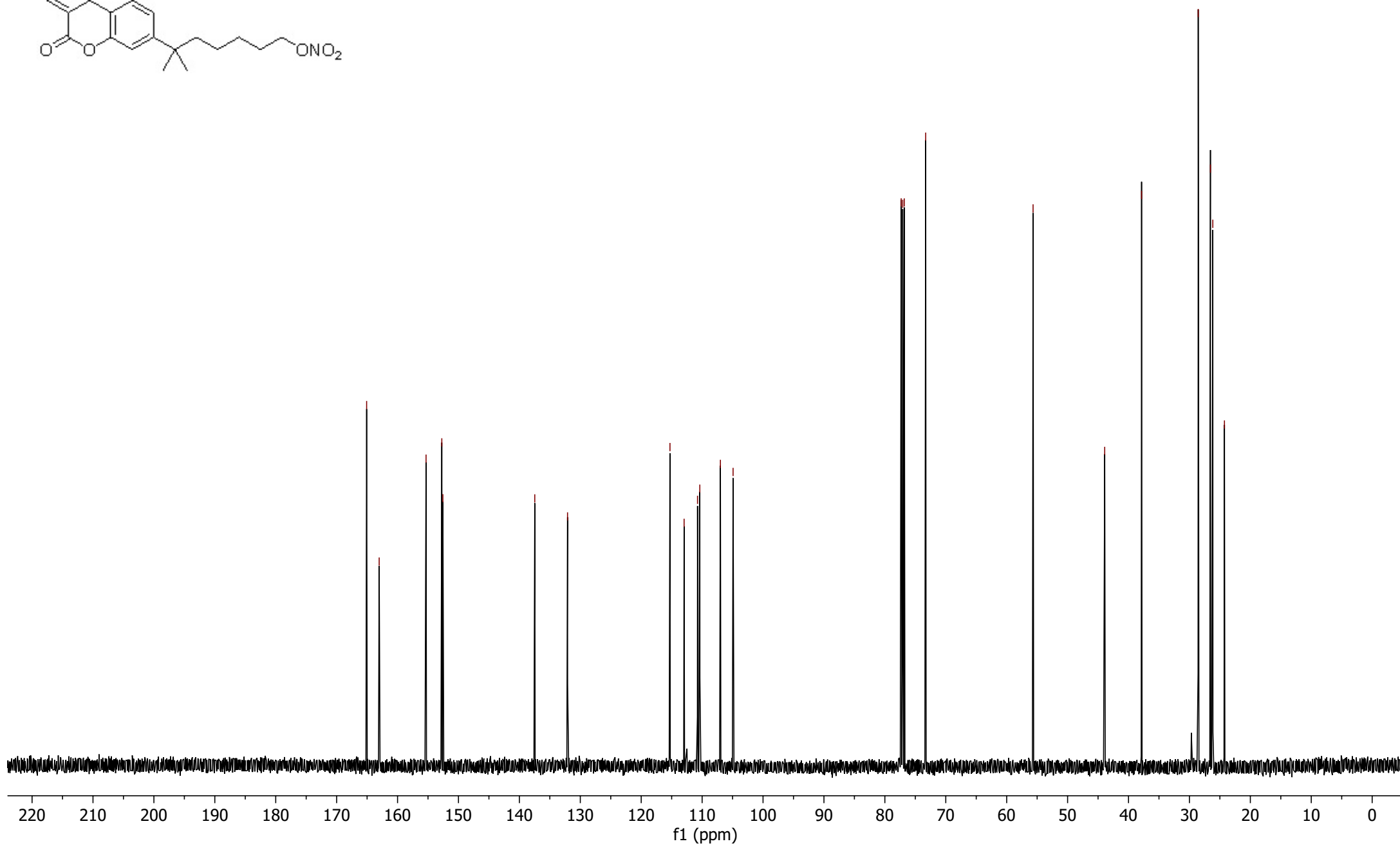
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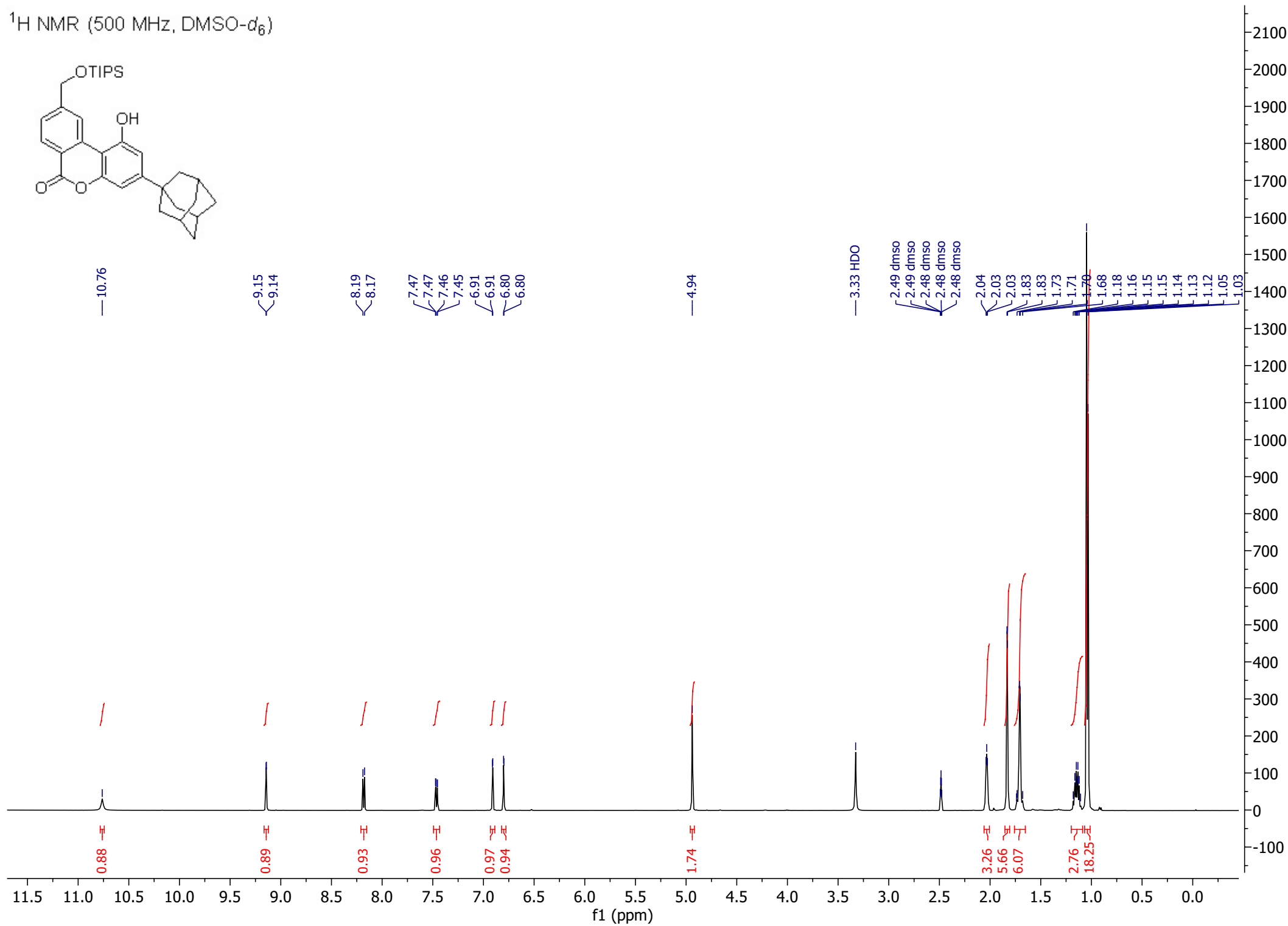
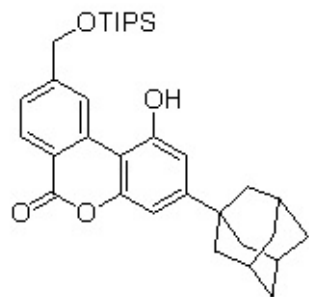
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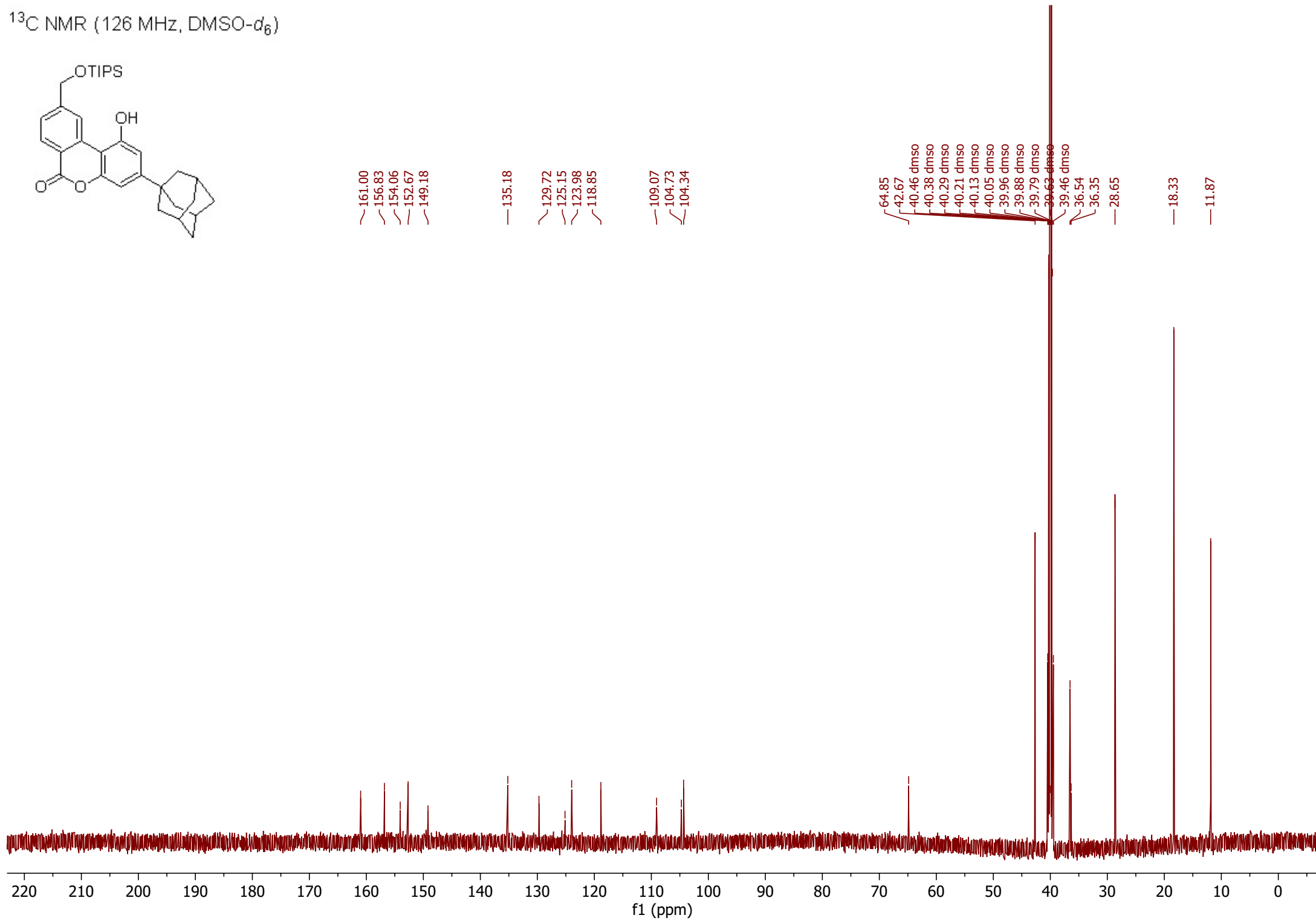
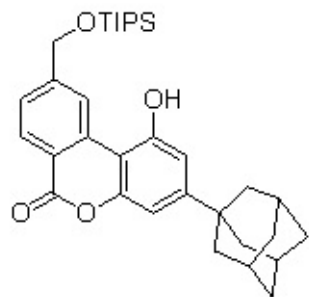
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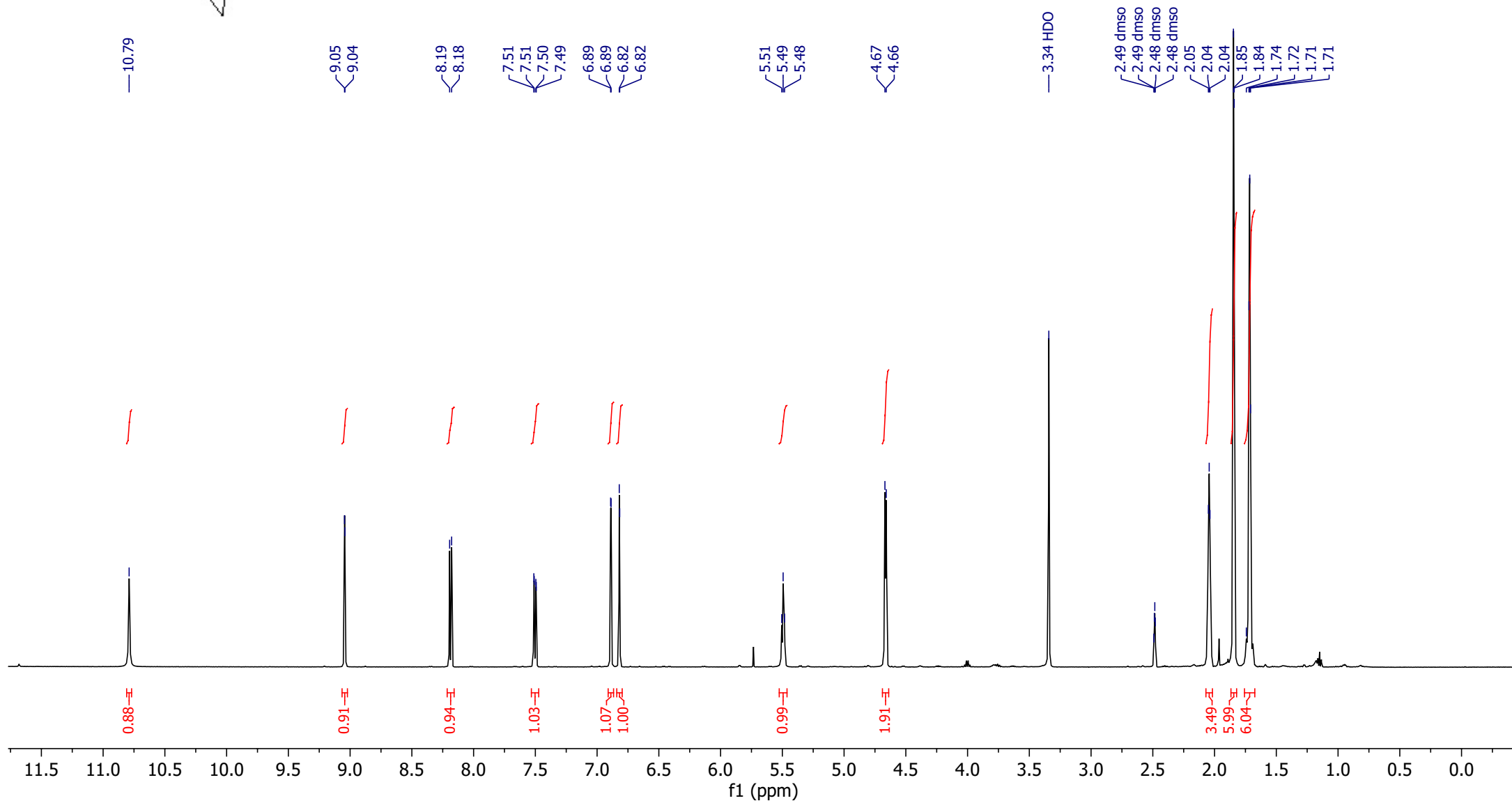
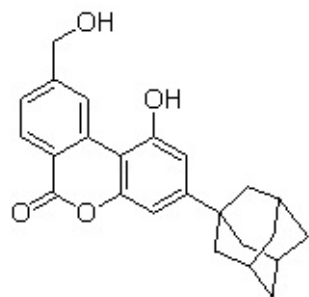
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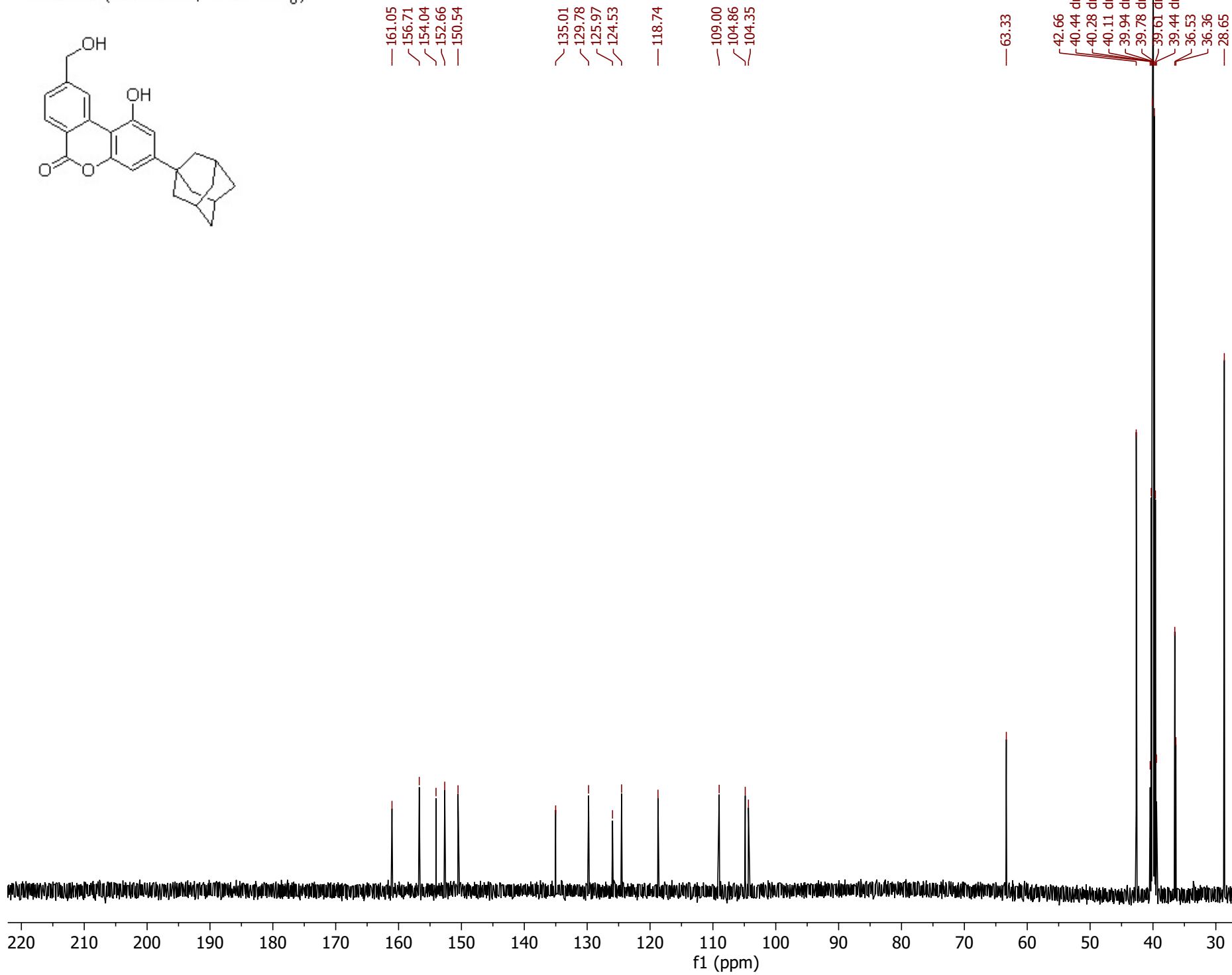
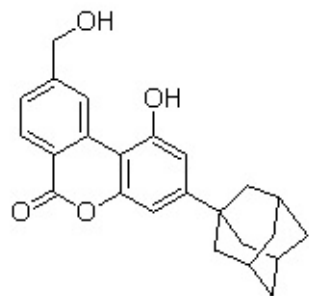
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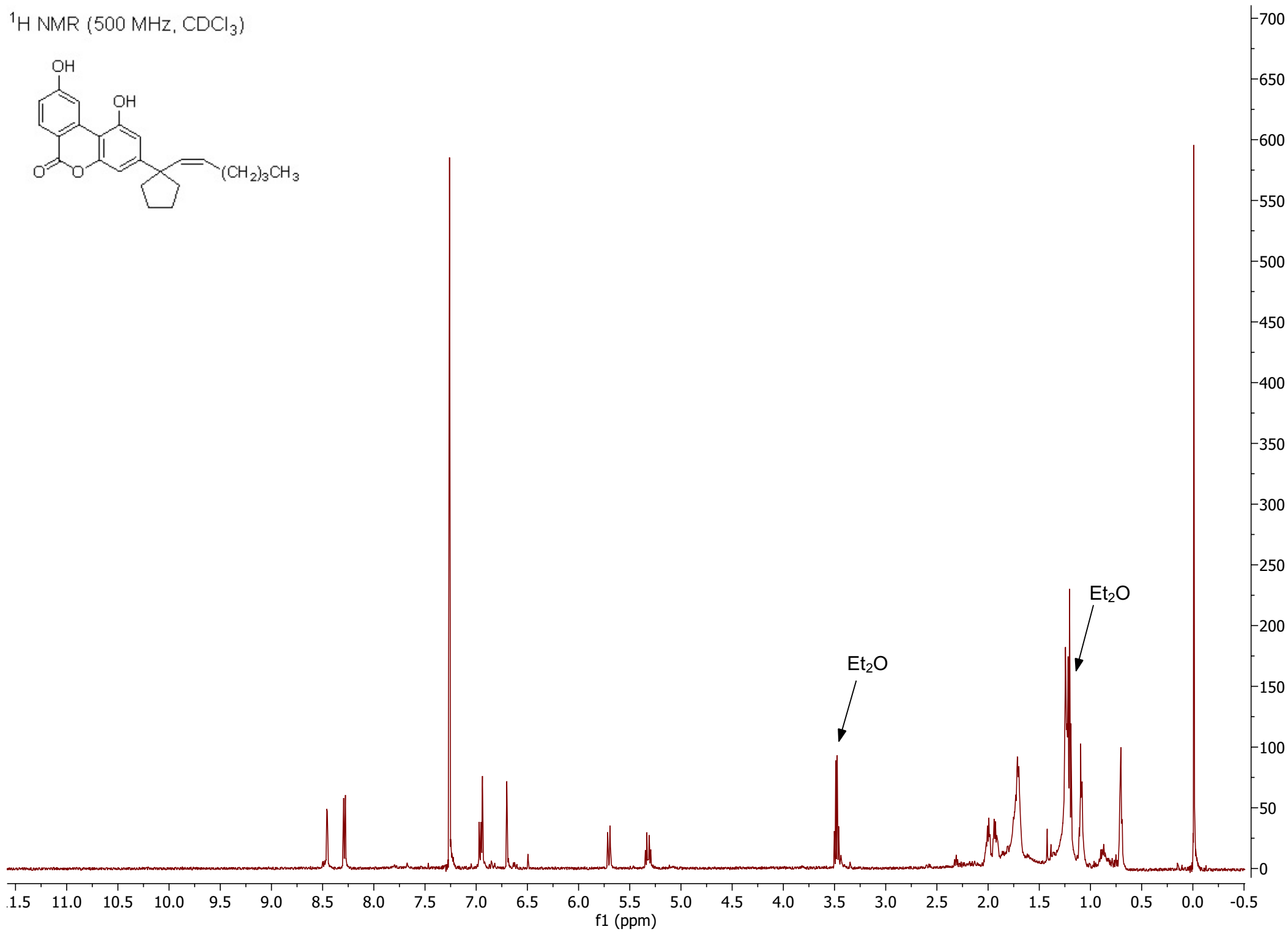
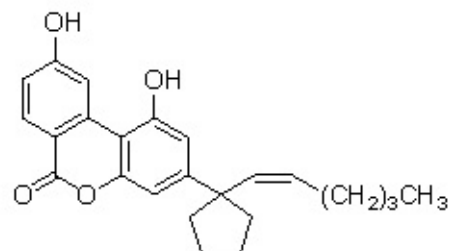
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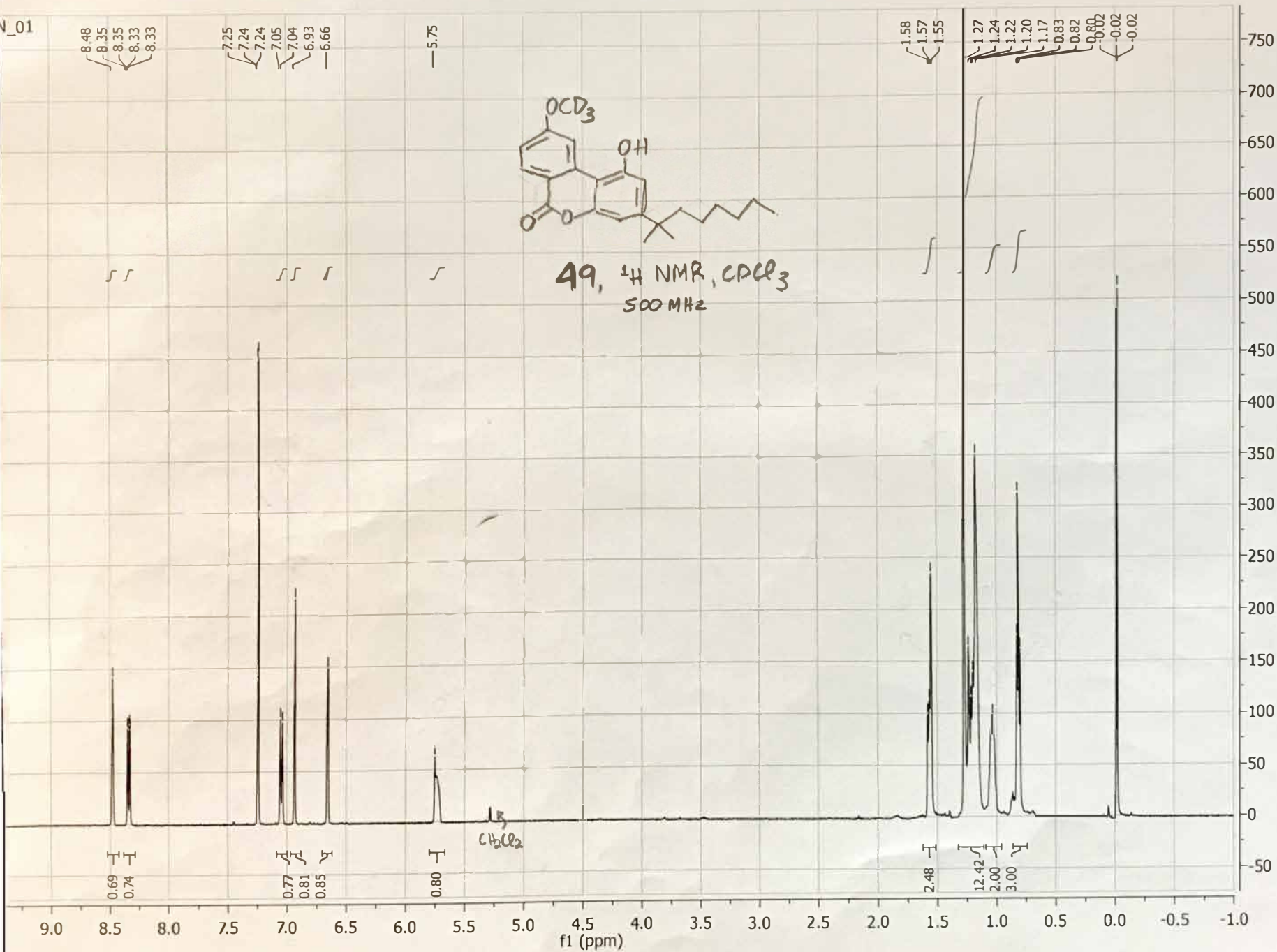


^{13}C NMR (126 MHz, $\text{DMSO}-d_6$)



^1H NMR (500 MHz, CDCl_3)





-17-B-13C

— 164.68
— 161.72
— 153.90
— 153.10
— 152.91

— 136.75
— 132.25

— 114.93
— 113.62
— 110.79
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— 108.04
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— 77.29
— 76.65

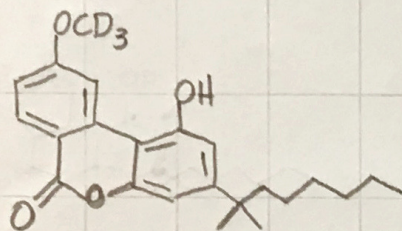
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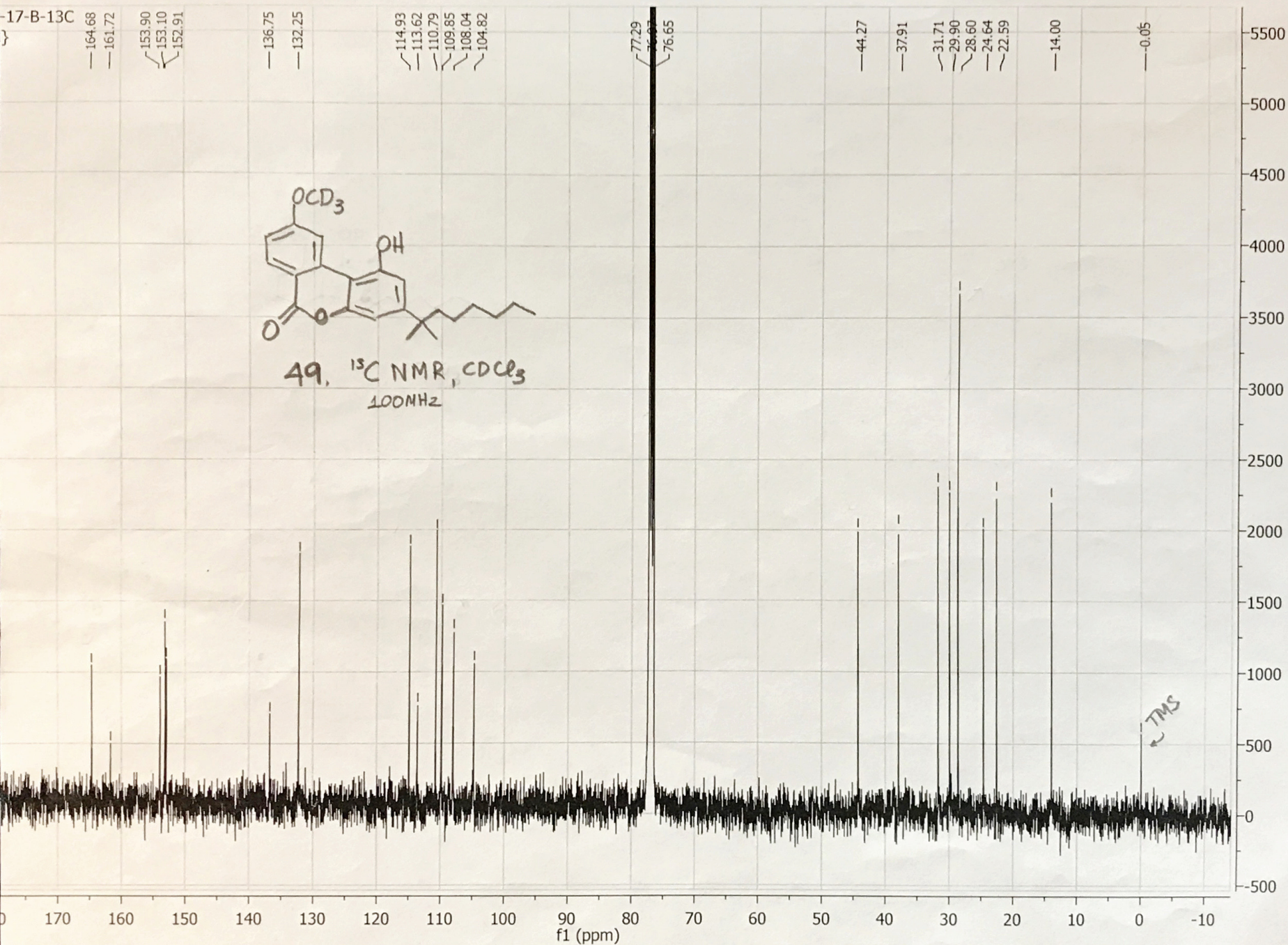
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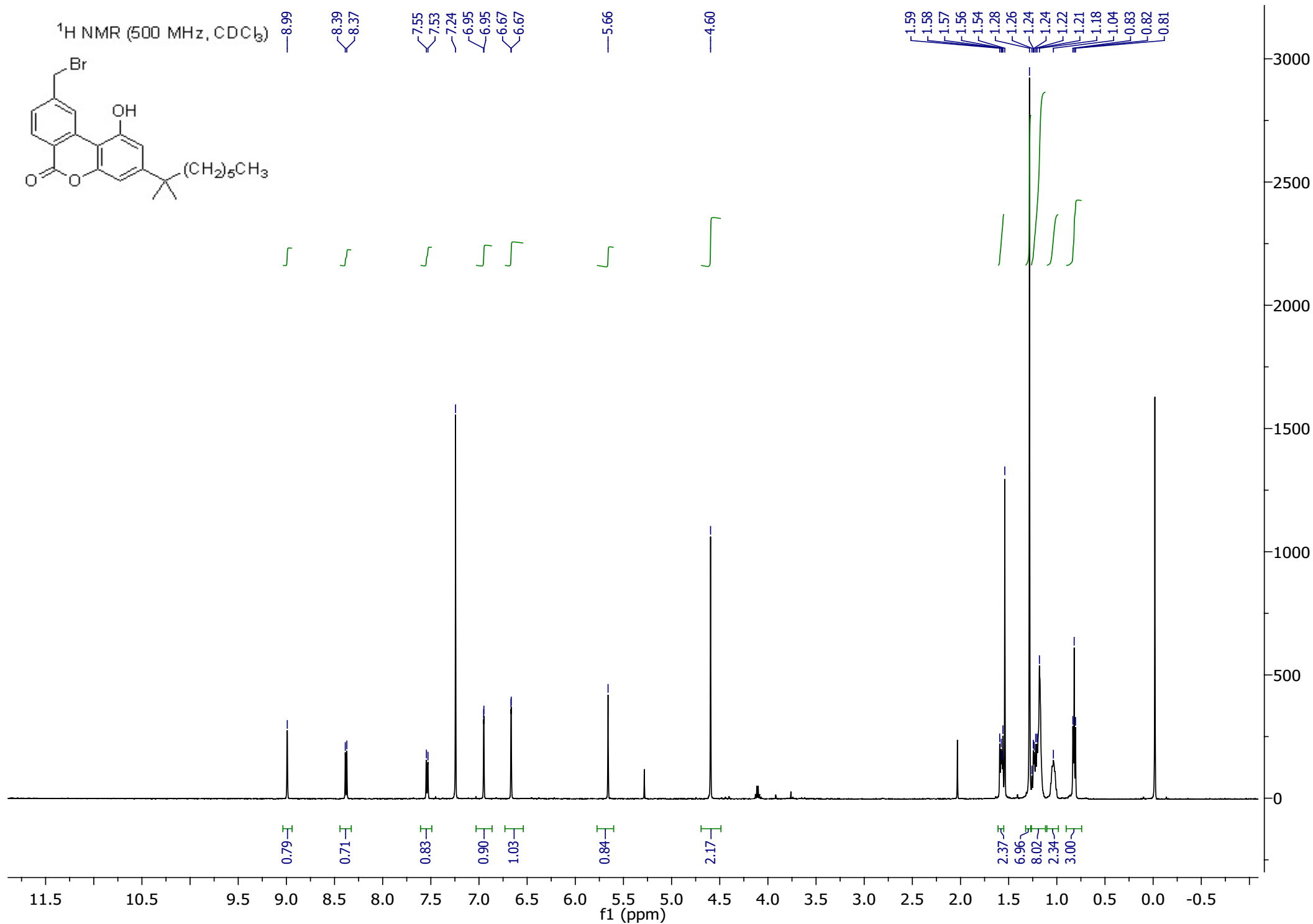
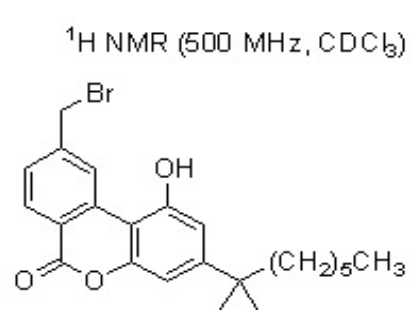
— 14.00

— 0.05

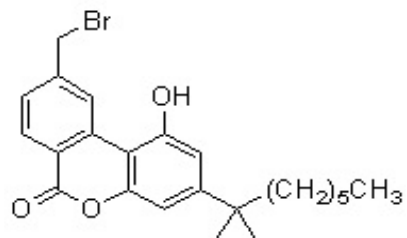


49, ¹³C NMR, CDCl₃
100MHz

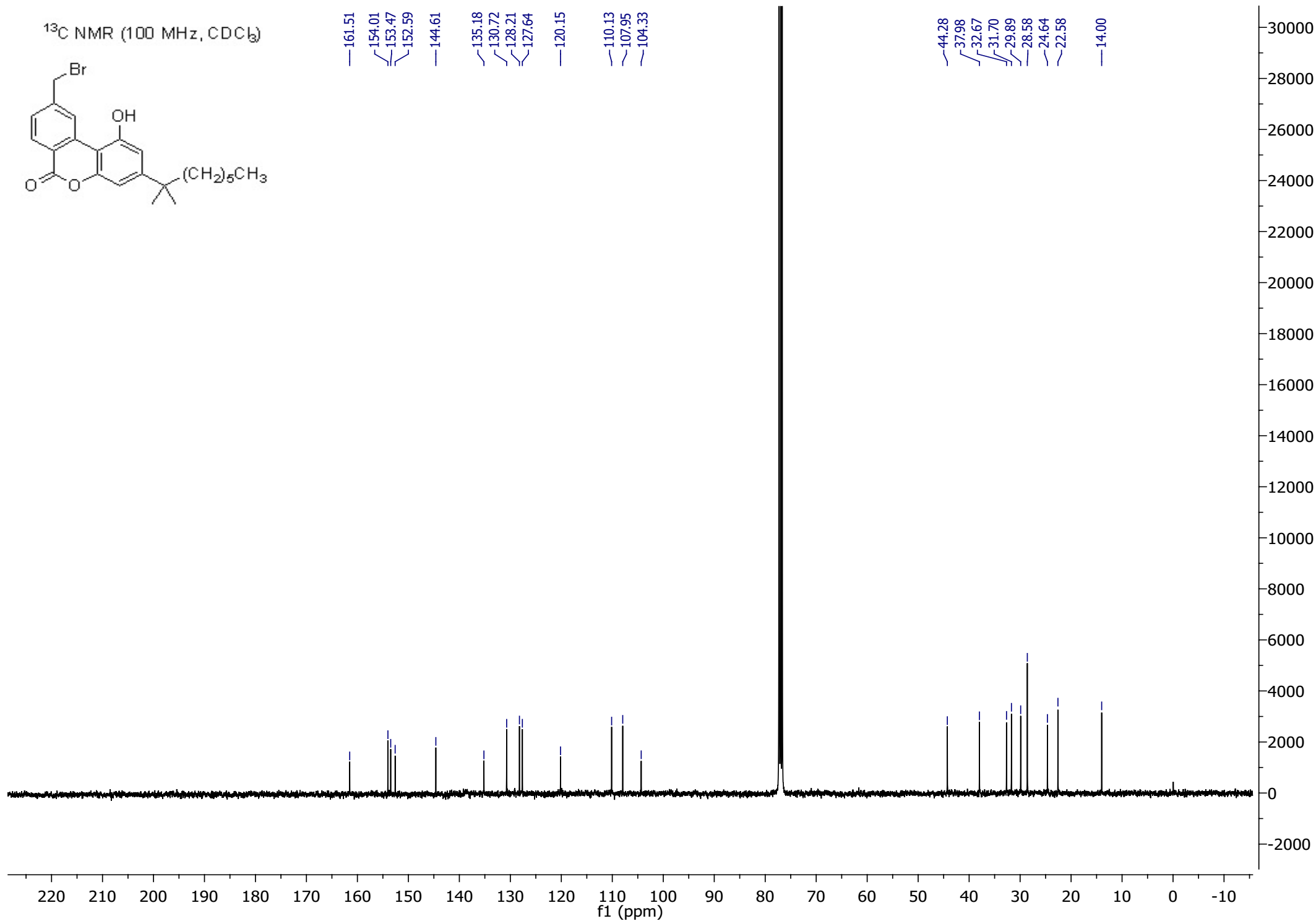


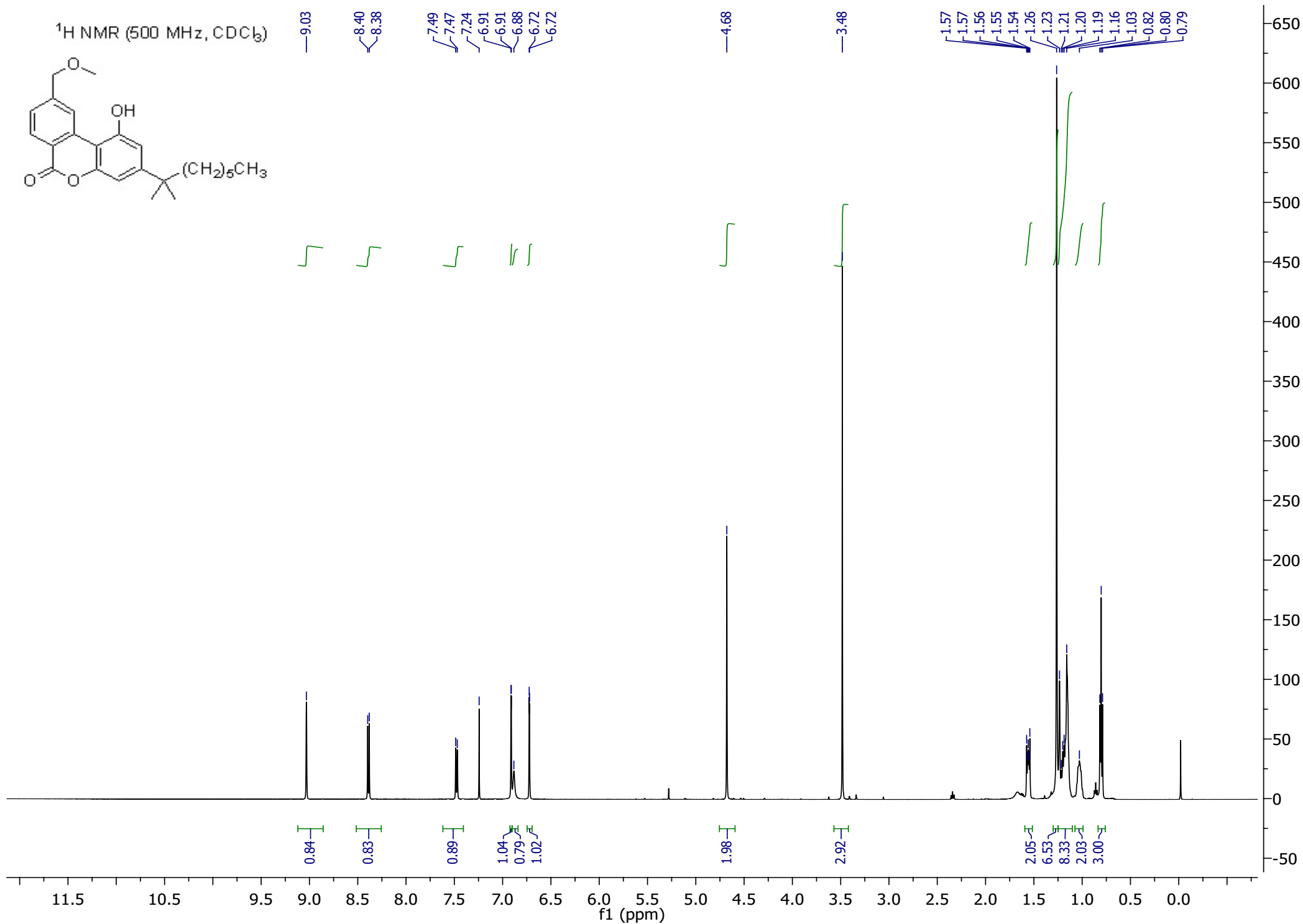


¹³C NMR (100 MHz, CDCl₃)

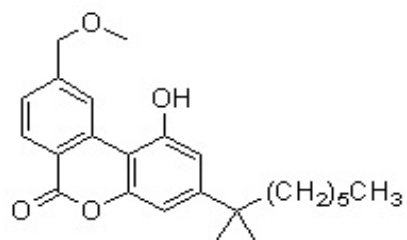


161.51
154.01
153.47
152.59
144.61
135.18
130.72
128.21
127.64
120.15
110.13
107.95
104.33
44.28
37.98
32.67
31.70
29.89
28.58
24.64
22.58
14.00

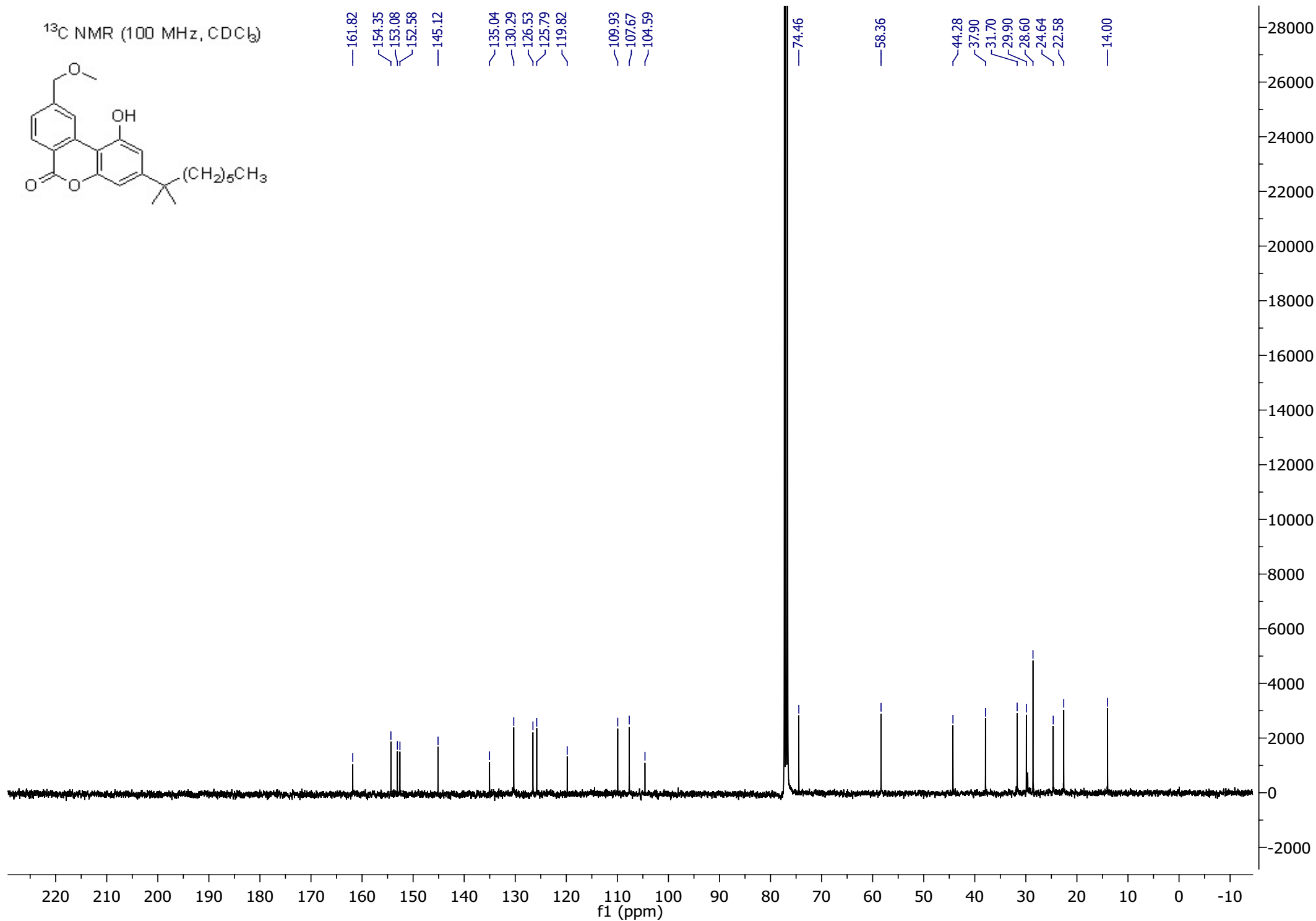


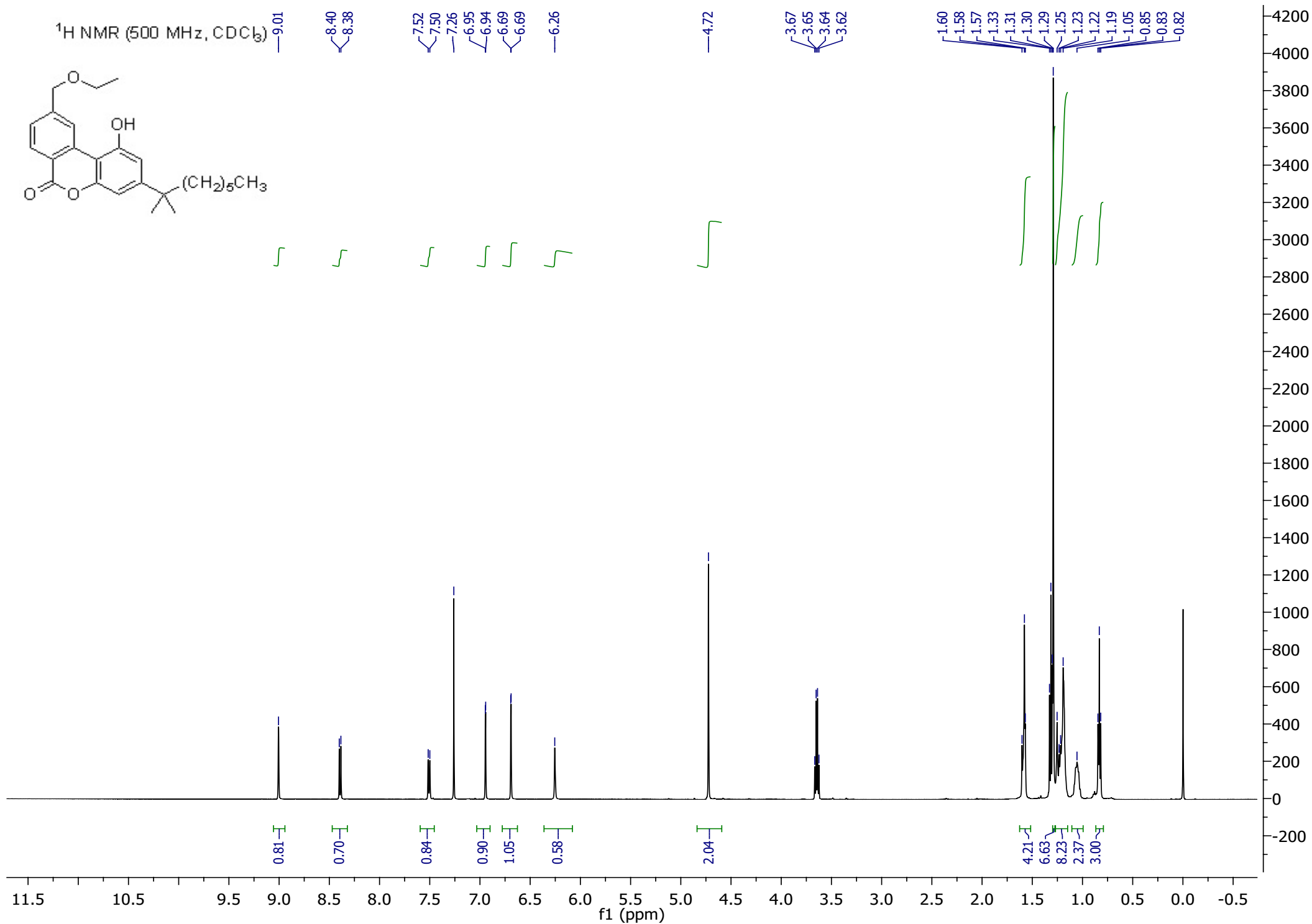


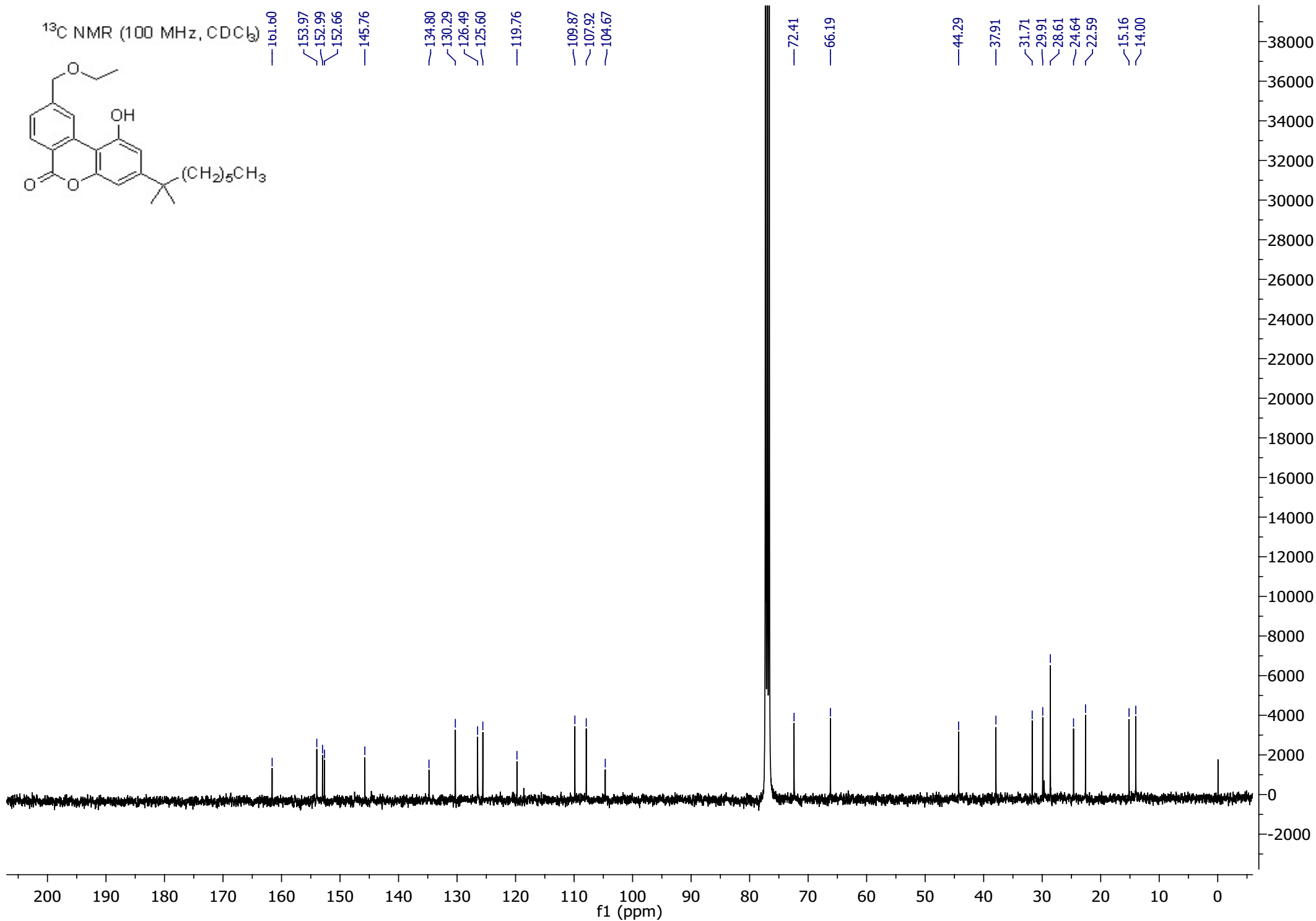
¹³C NMR (100 MHz, CDCl₃)

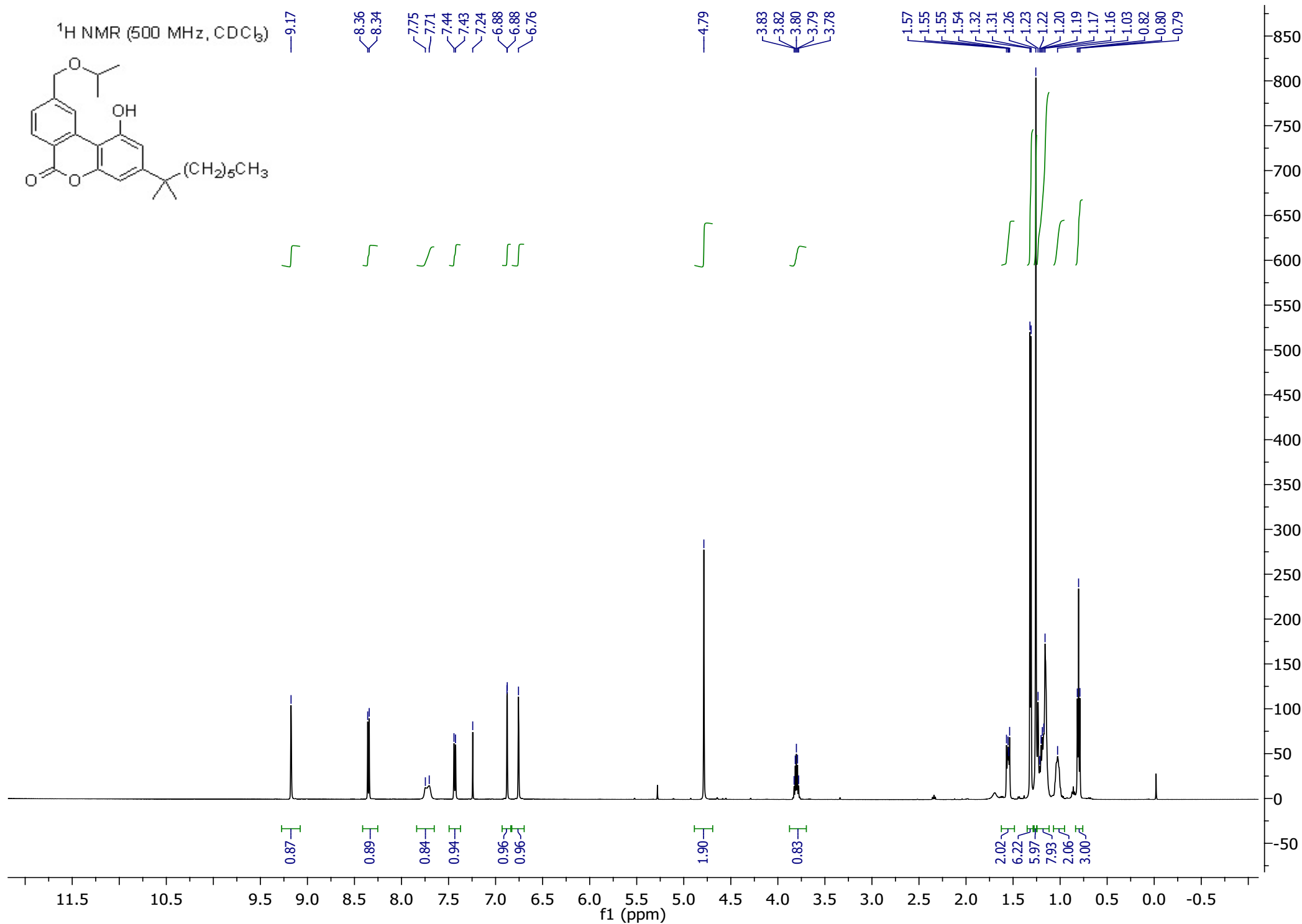


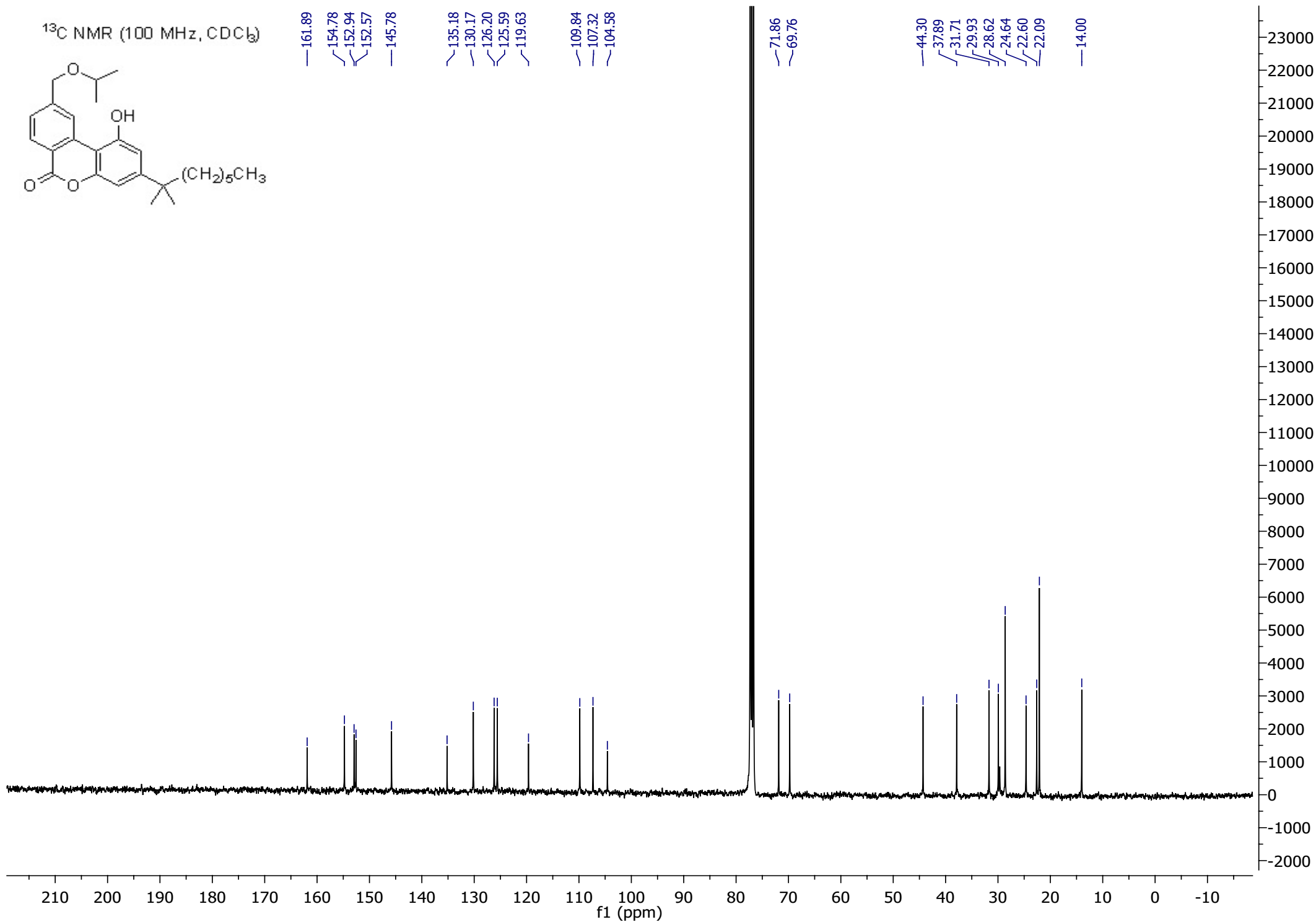
161.82
154.35
153.08
152.58
145.12
135.04
130.29
126.53
125.79
119.82
109.93
107.67
104.59
74.46
58.36
44.28
37.90
31.70
29.90
28.60
24.64
22.58
14.00



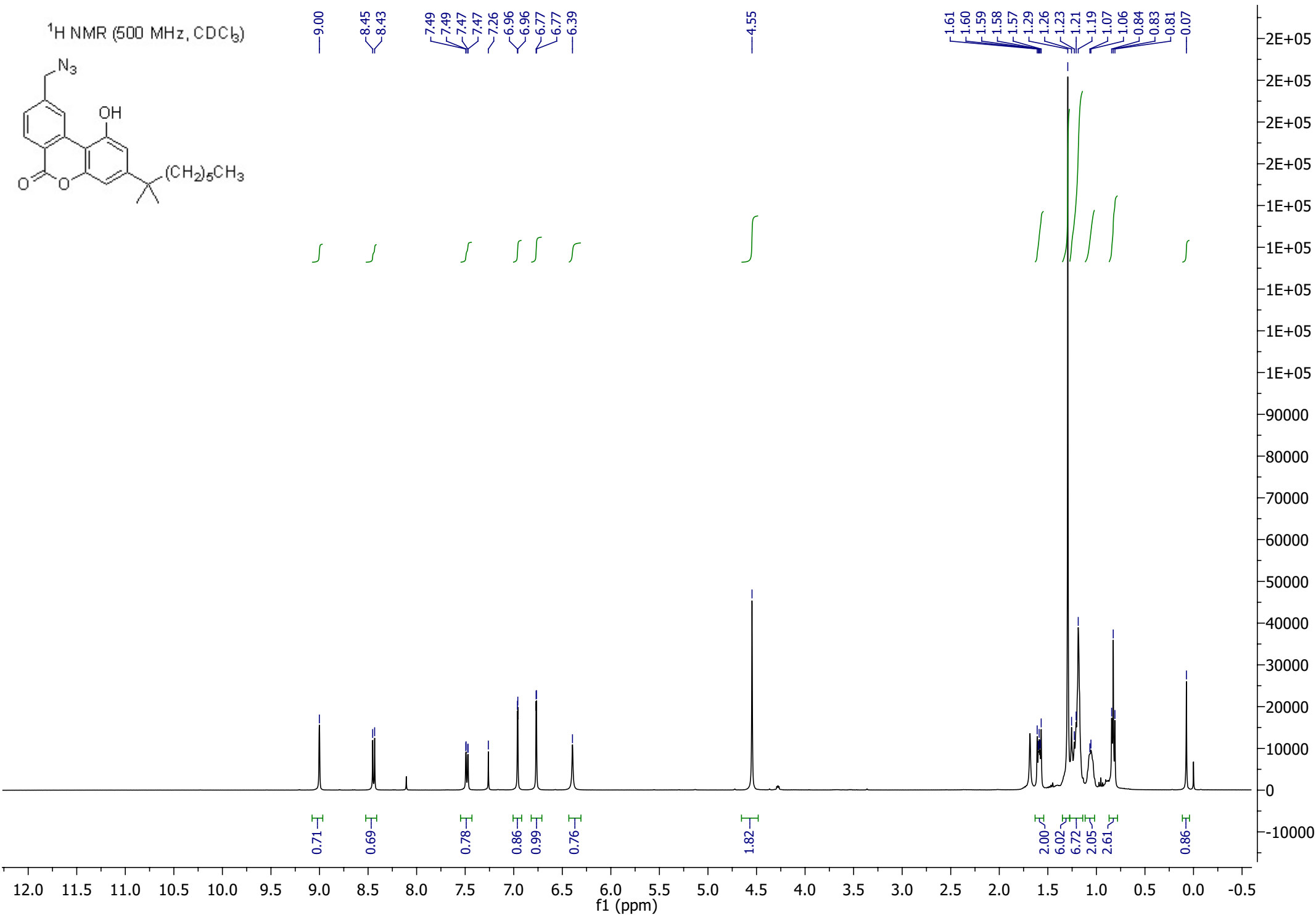
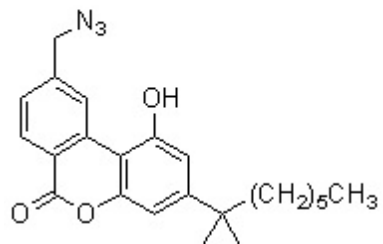


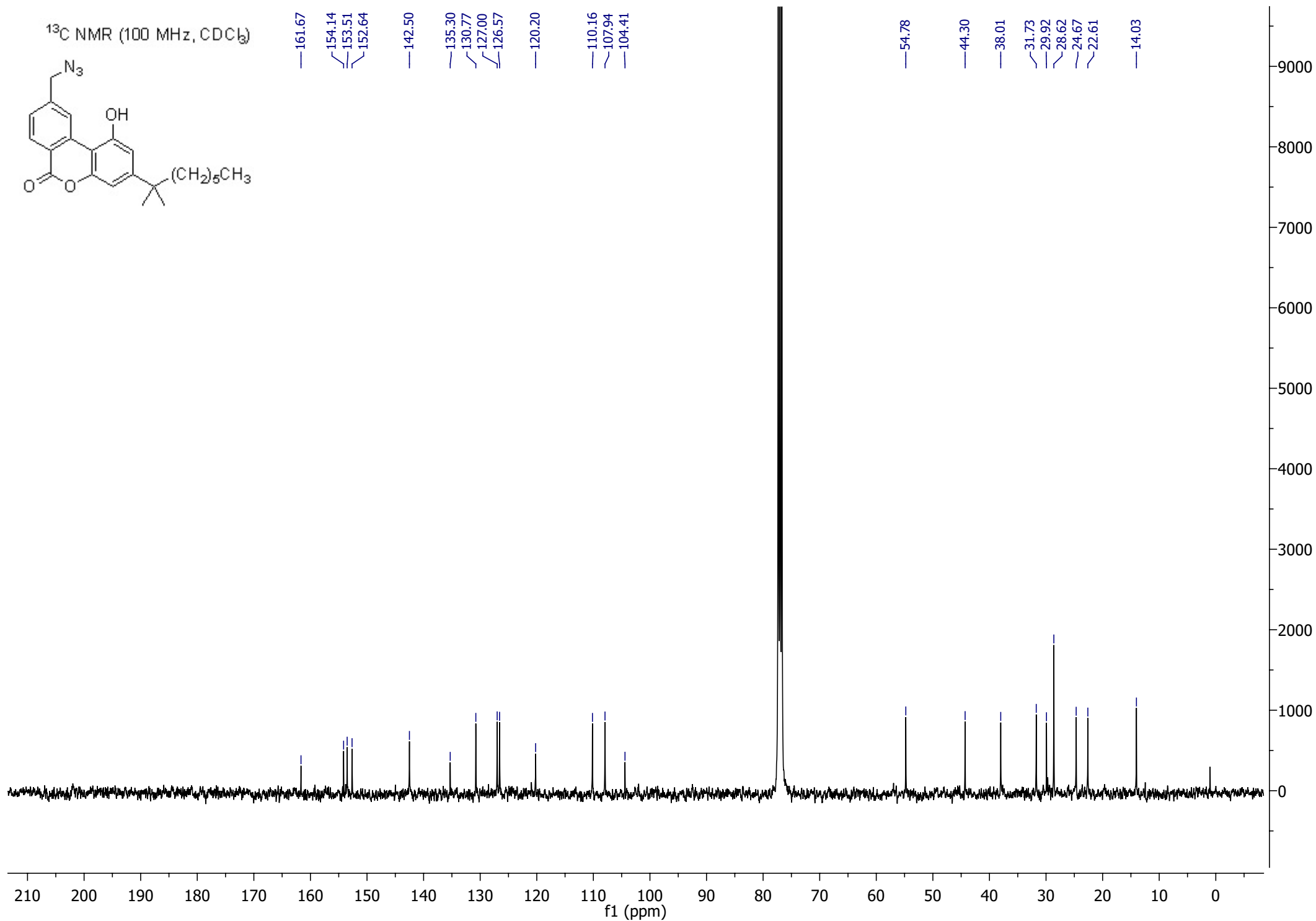




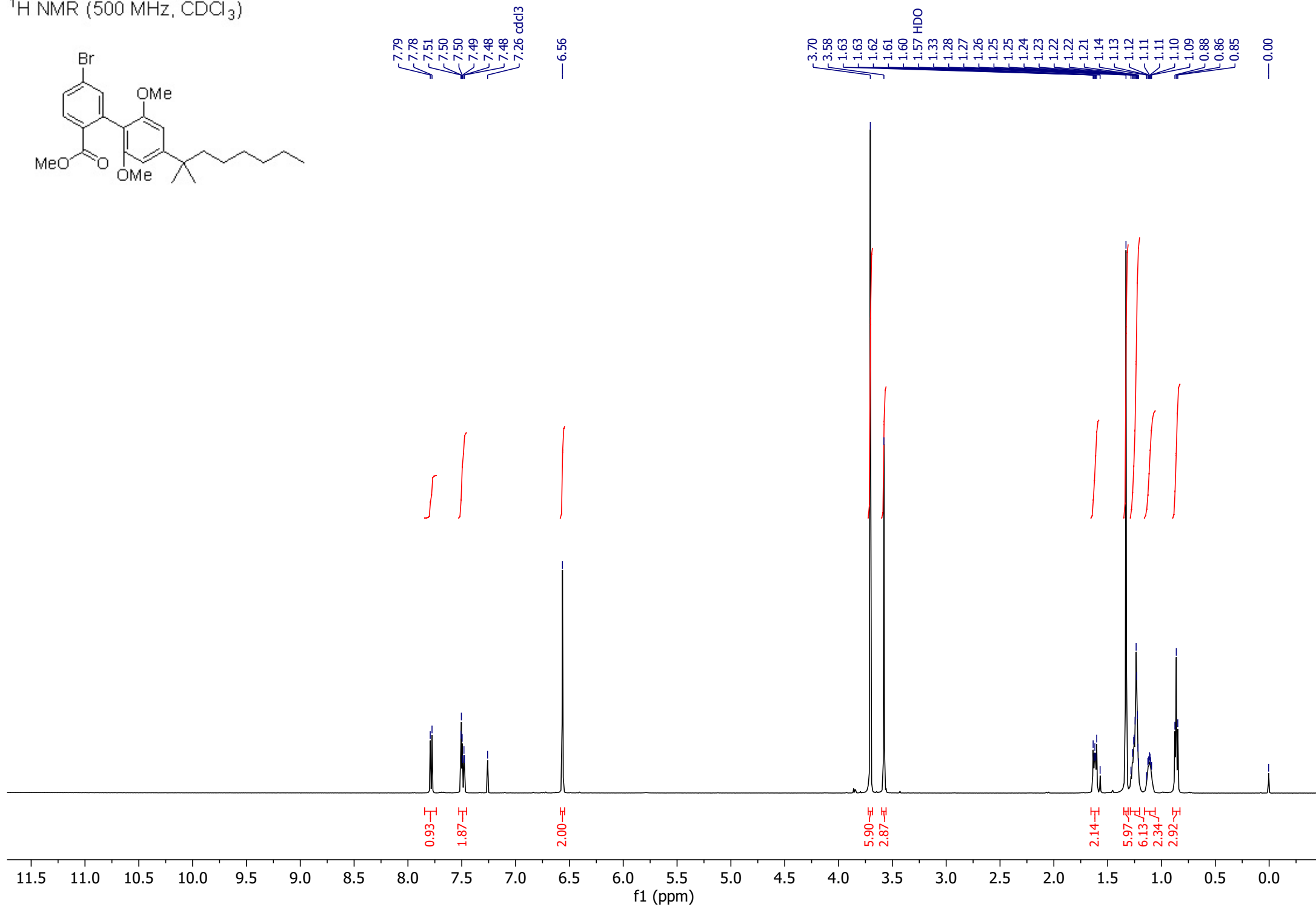
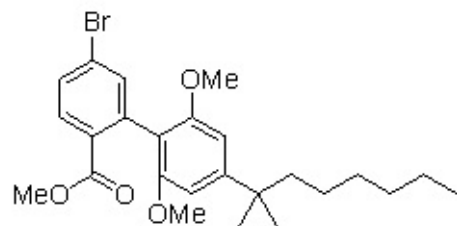


¹H NMR (500 MHz, CDCl₃)

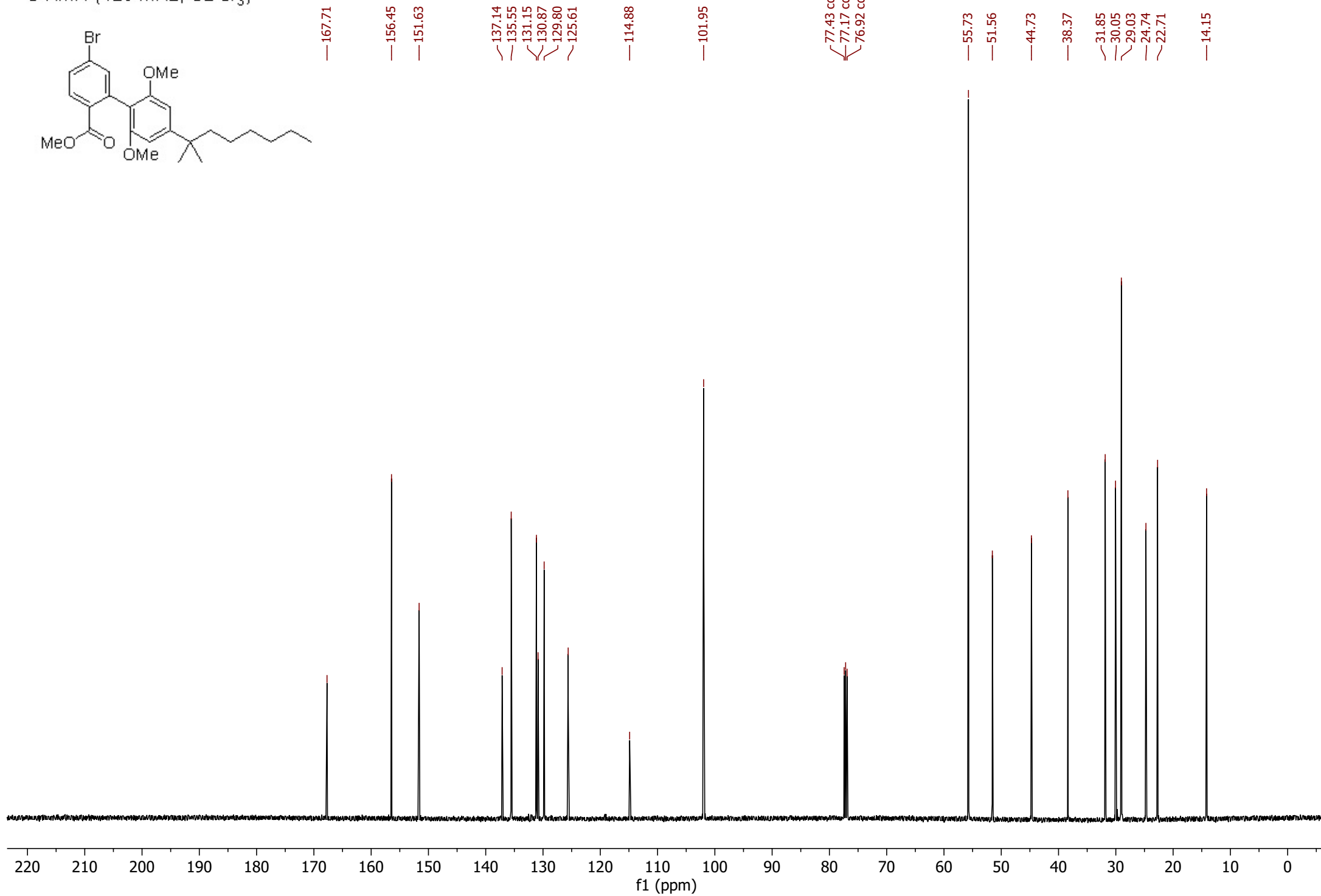
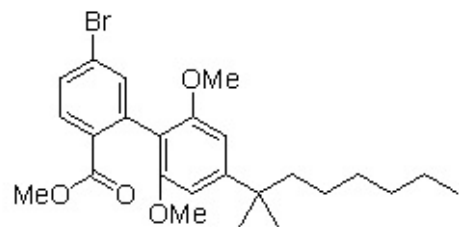




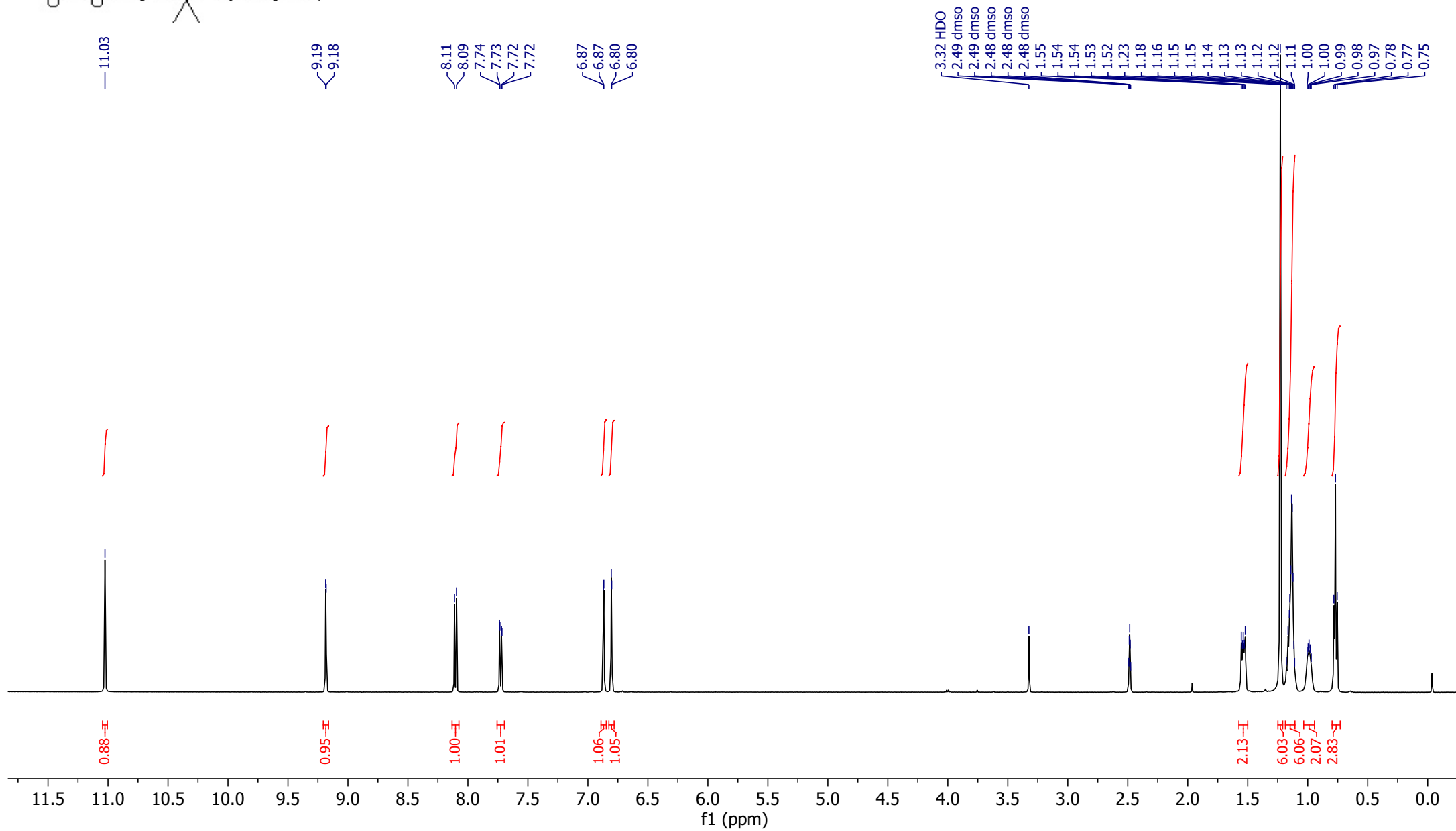
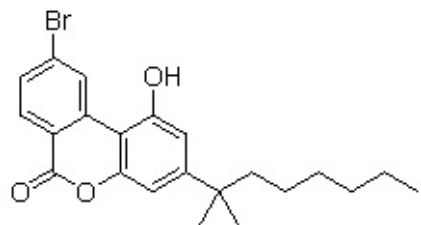
¹H NMR (500 MHz, CDCl₃)



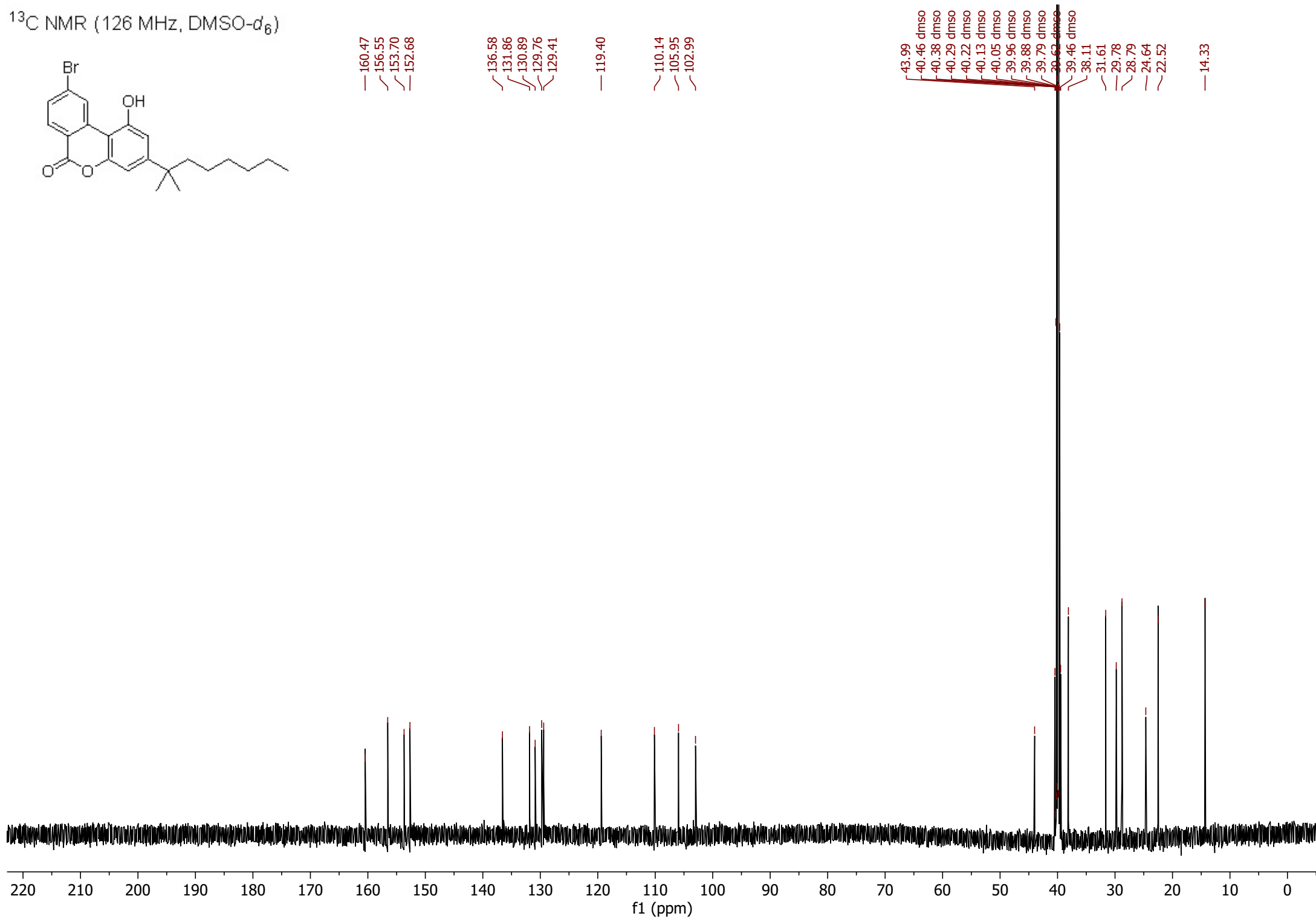
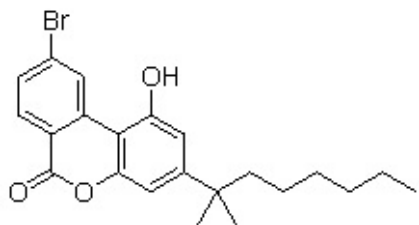
^{13}C NMR (126 MHz, CDCl_3)



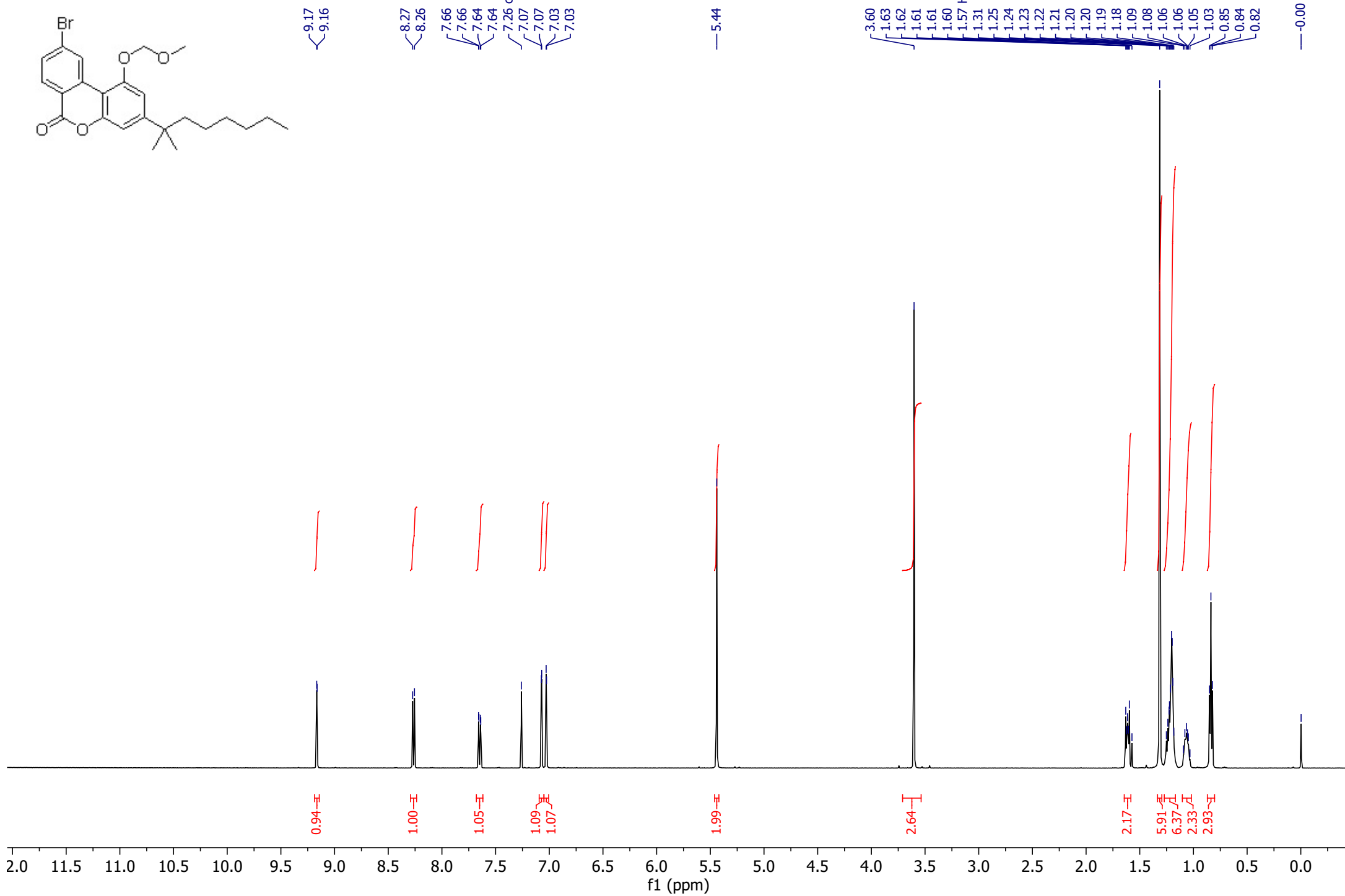
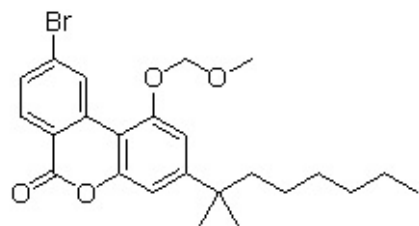
^1H NMR (500 MHz, $\text{DMSO}-d_6$)



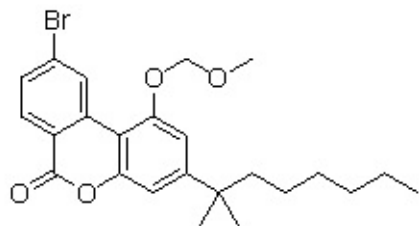
^{13}C NMR (126 MHz, $\text{DMSO}-d_6$)



¹H NMR (500 MHz, CDCl₃)



^{13}C NMR (126 MHz, CDCl_3)



160.88
155.51
154.07
152.40

135.93
131.56
130.84
130.24
129.87

119.51

108.99
108.39
105.06

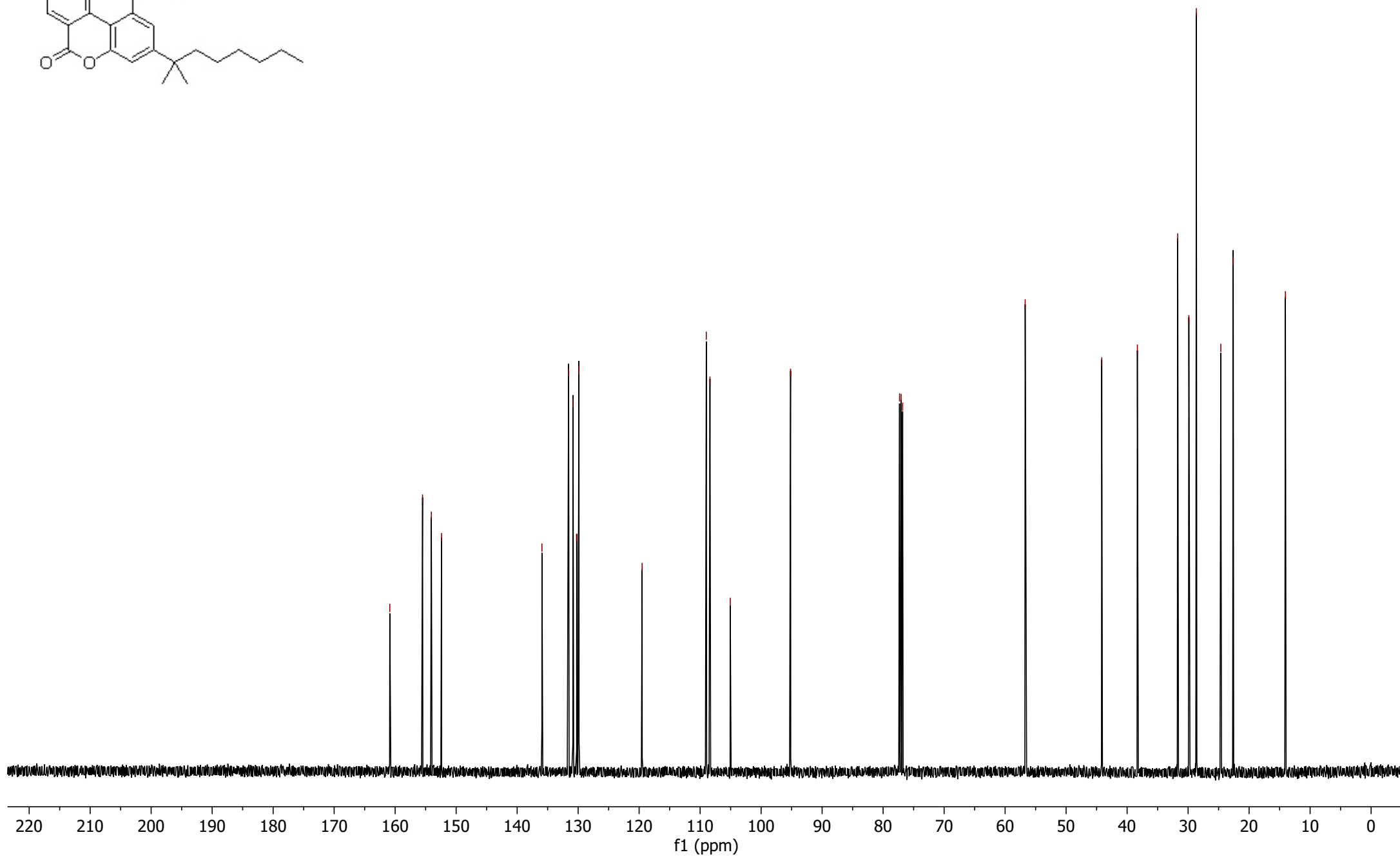
95.17

77.31 cdd13
77.05 cdd13
76.80 cdd13

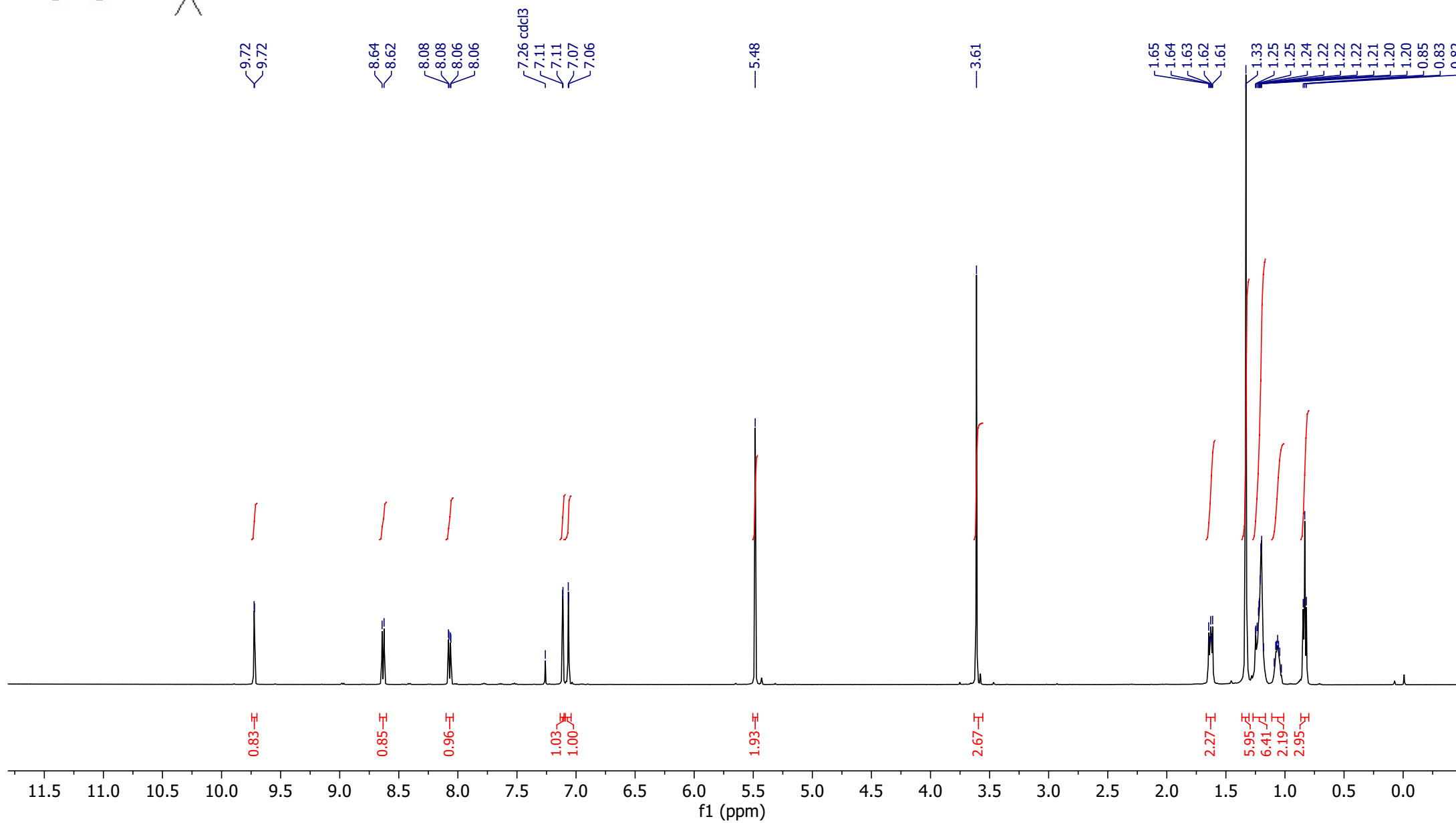
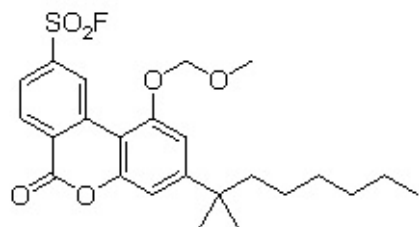
56.71

44.16
38.32
31.70
29.88
28.65
24.64
22.61

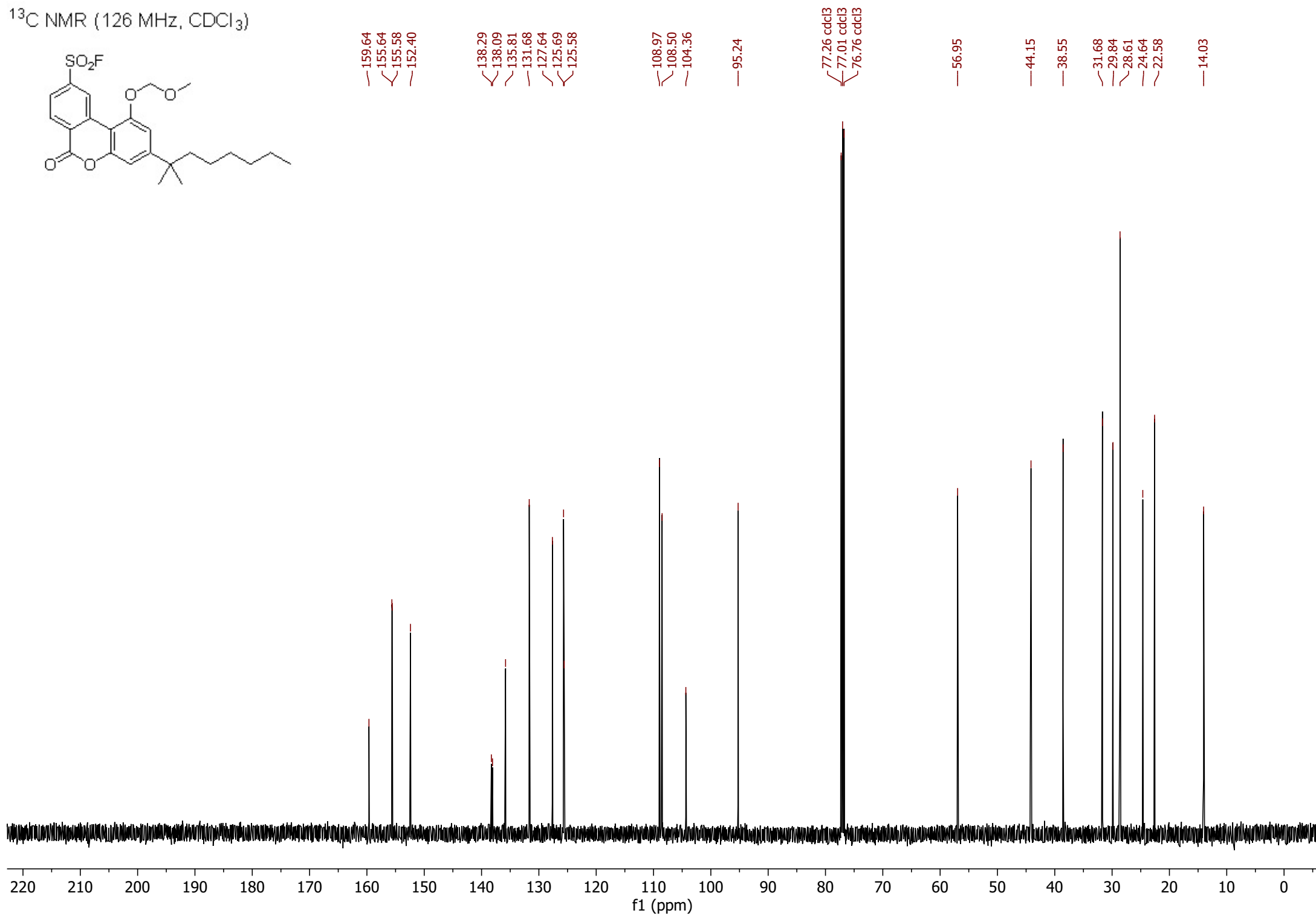
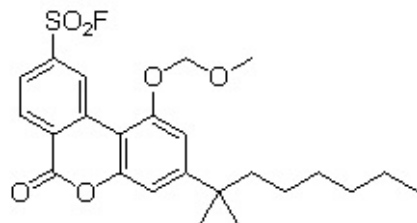
14.05



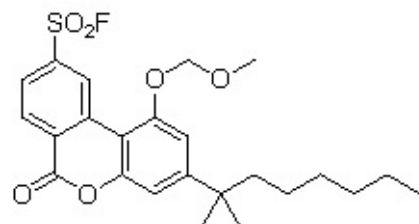
^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

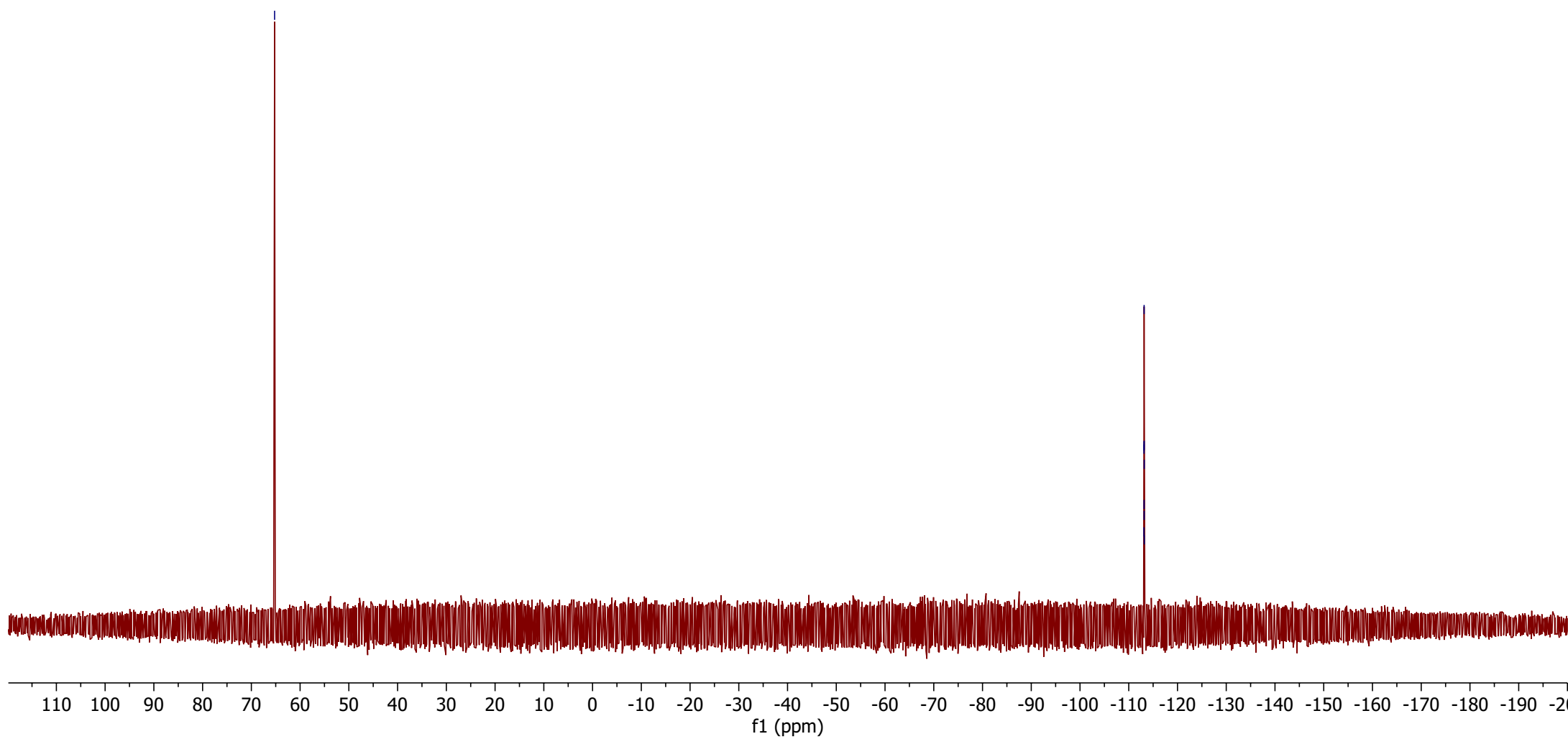


^{19}F NMR (470 MHz, CDCl_3 , $\text{C}_6\text{H}_5\text{F}$ reference standard)

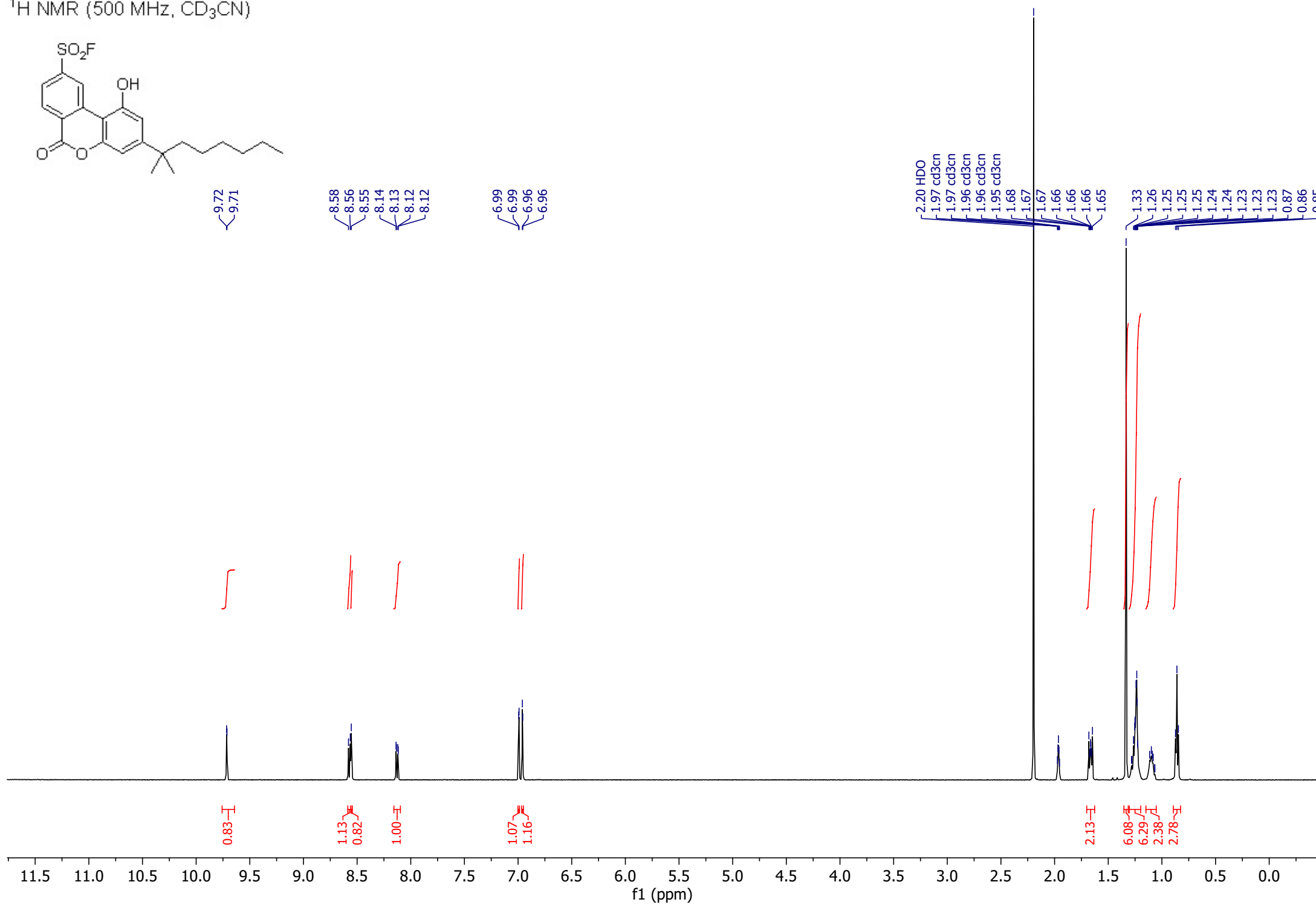
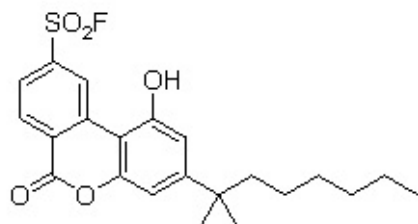


65.23

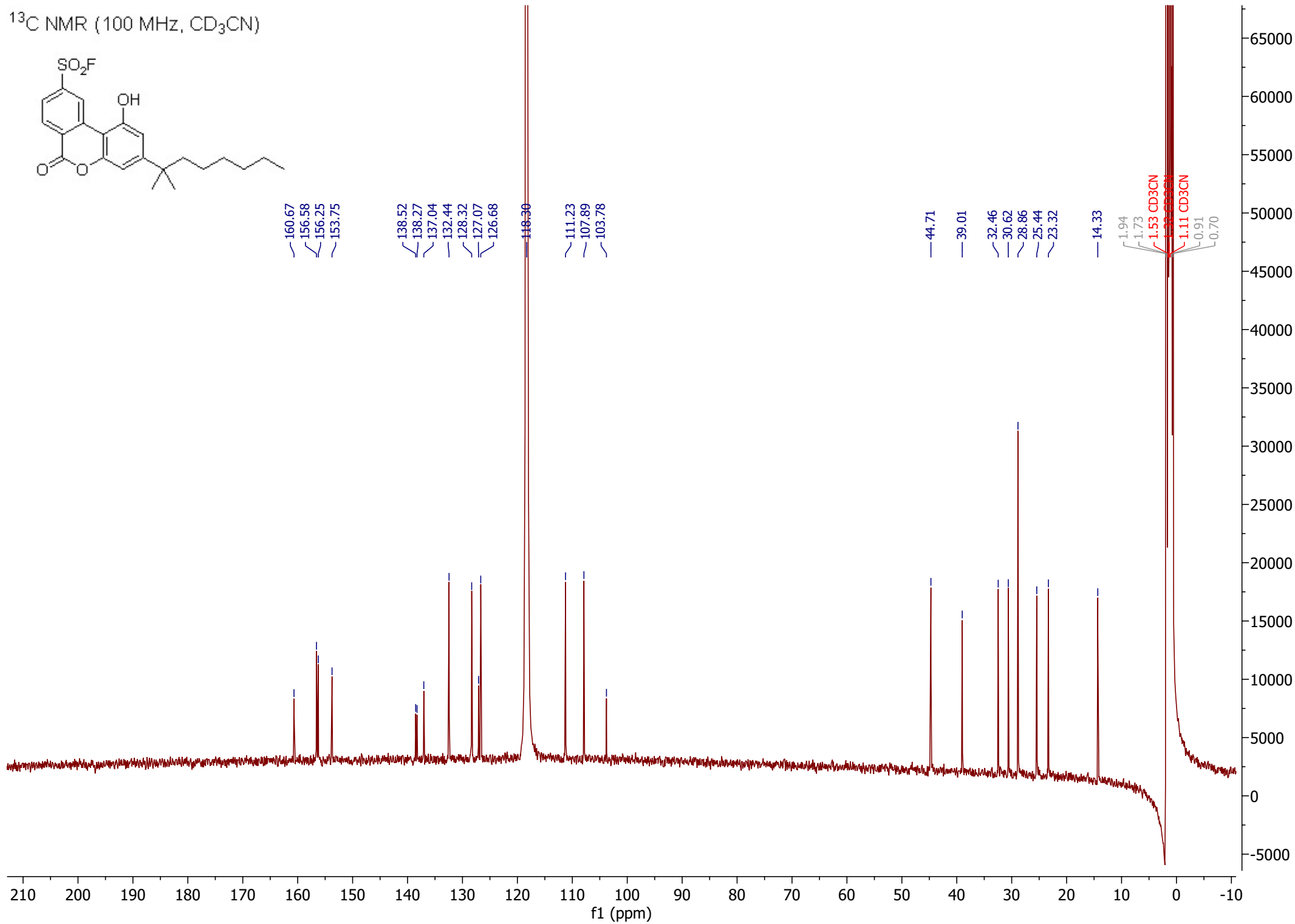
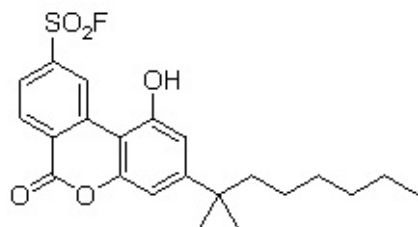
113.12
113.13
113.14
113.15
113.15
113.16
113.17
113.19



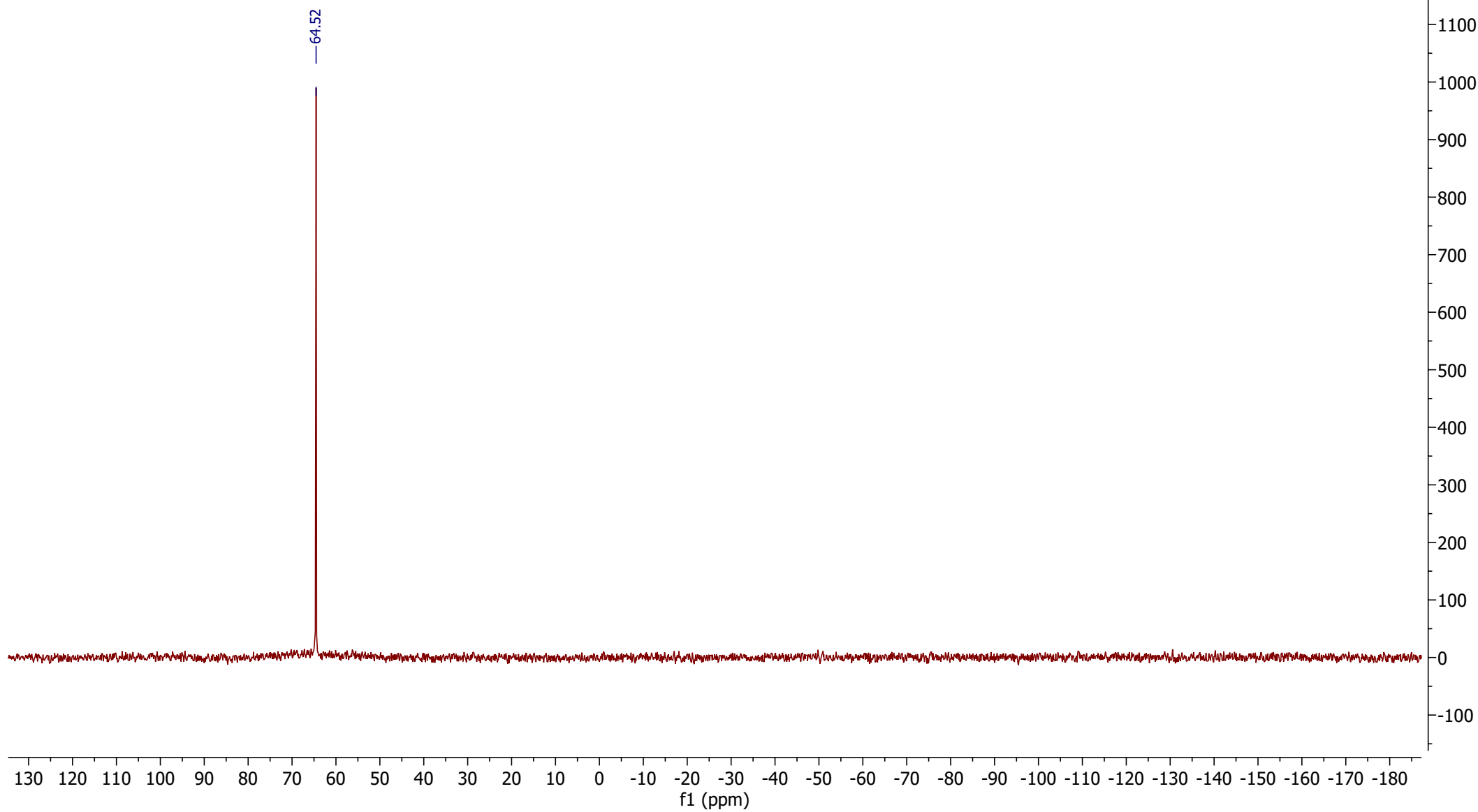
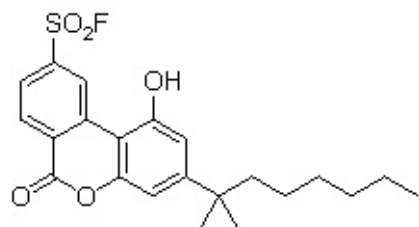
^1H NMR (500 MHz, CD_3CN)

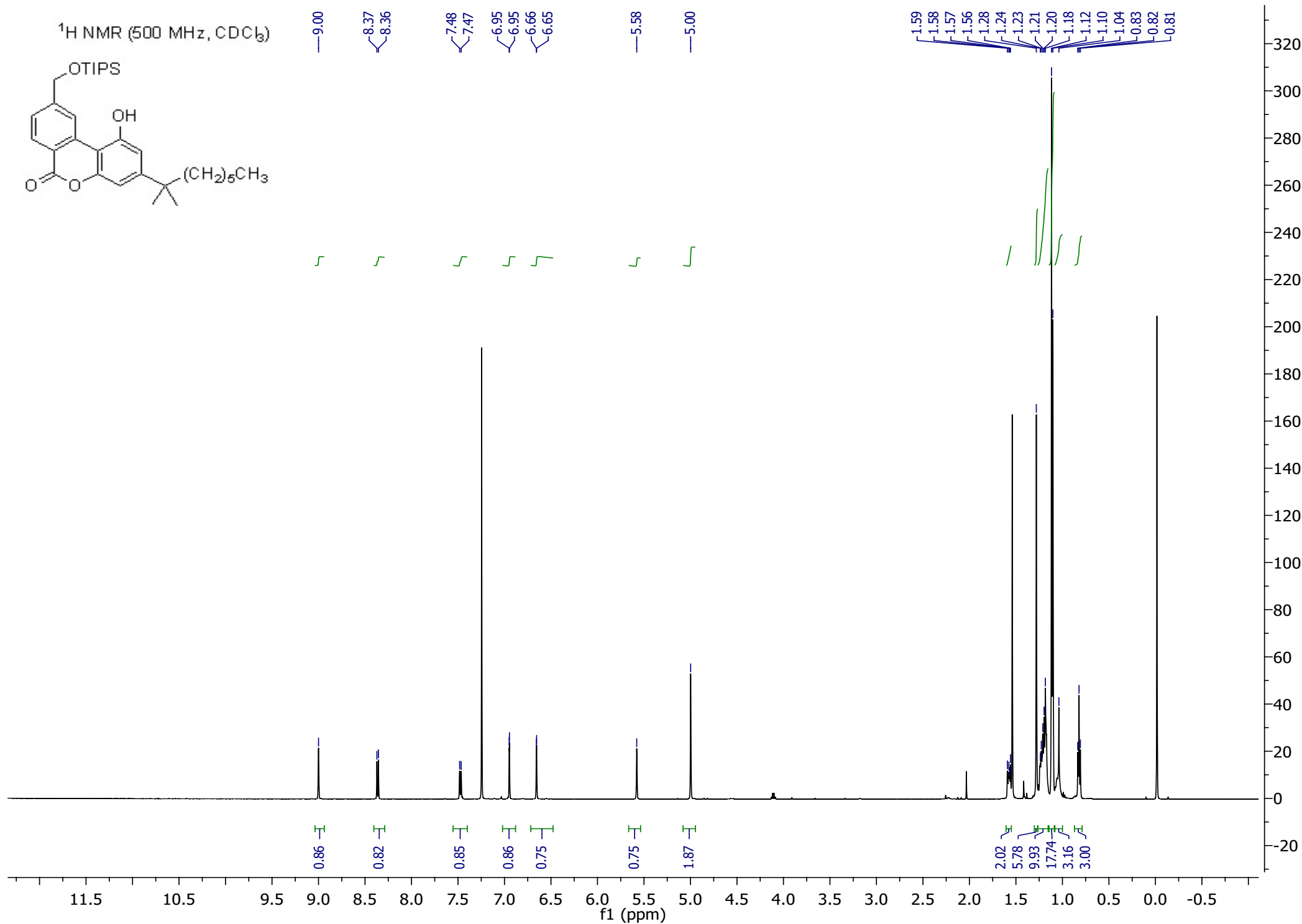


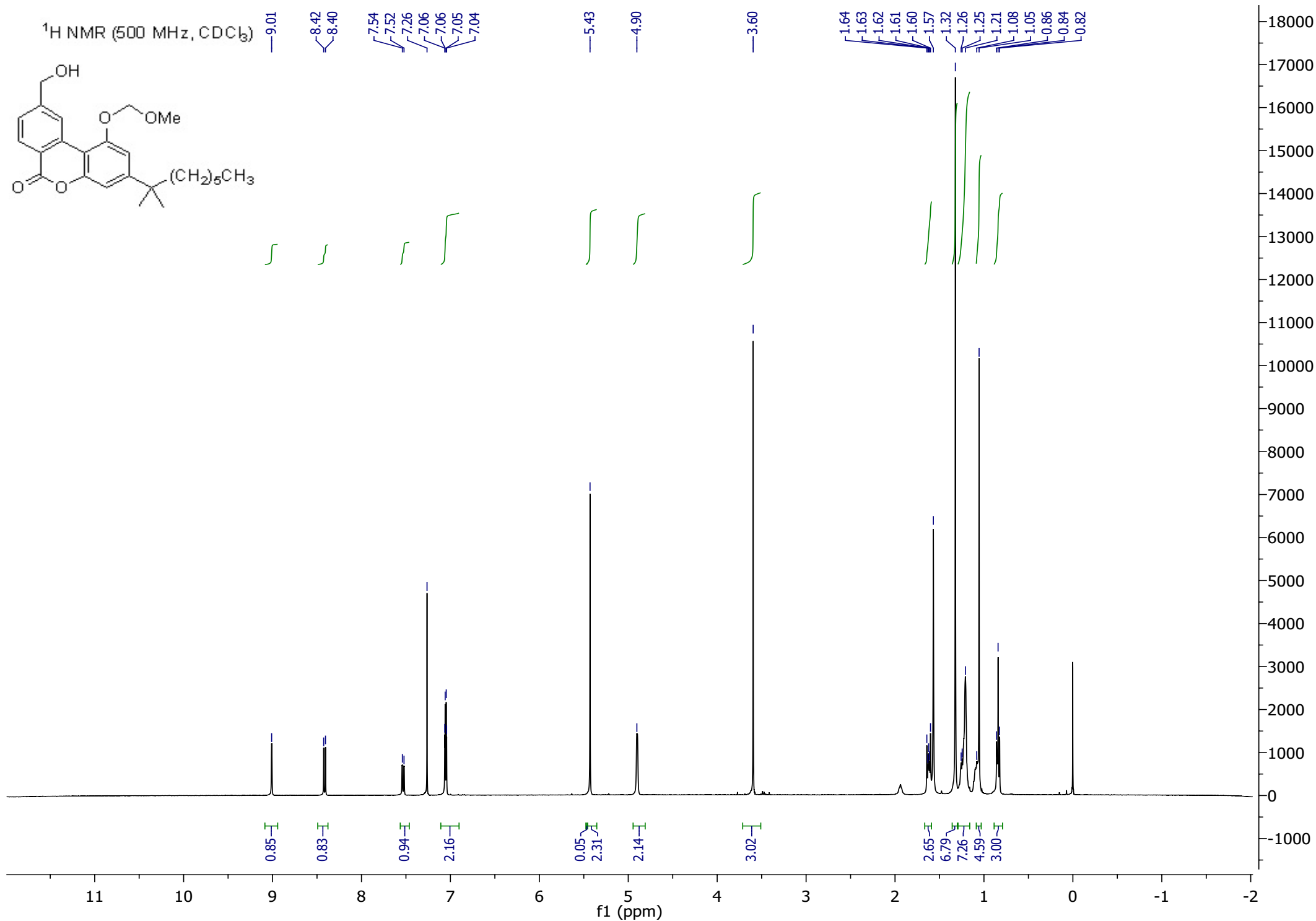
^{13}C NMR (100 MHz, CD_3CN)



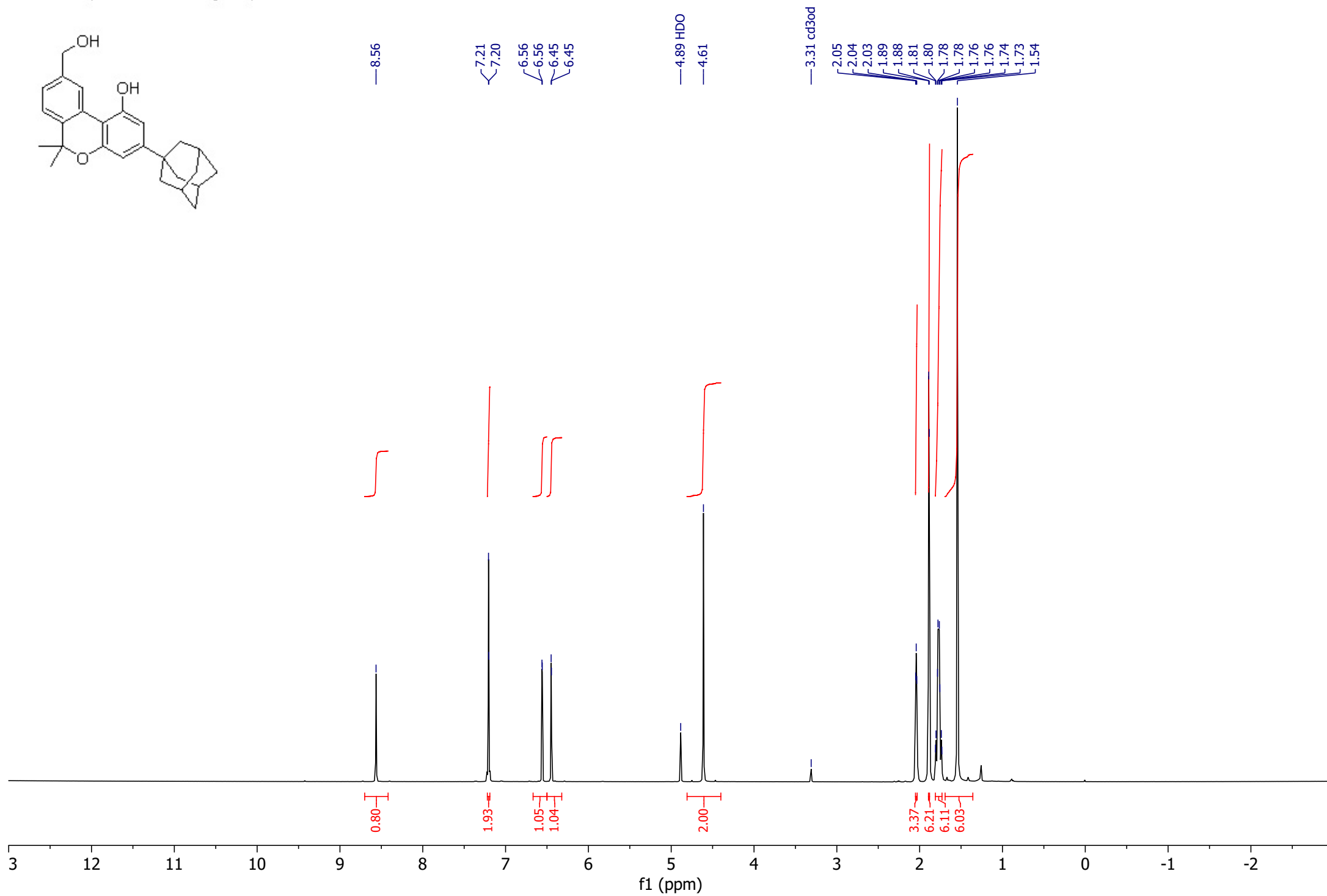
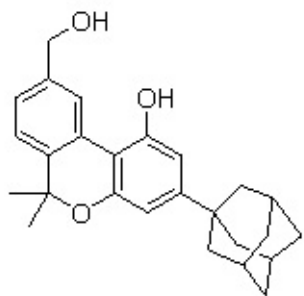
^{19}F NMR (376 MHz, CD_3CN)







^1H NMR (500 MHz, CD_3OD)



^{13}C NMR (126 MHz, CD_3OD)