

Synthesis of Functionalized Maoecrystal V Core Structures

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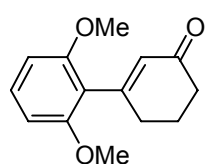
I) Experimental Section

Experimental Data for Compounds

General Procedures. All reactions were carried out under a nitrogen or argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene and methylene chloride (CH_2Cl_2) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Methanol (MeOH), ethanol (EtOH), acetonitrile (MeCN), *N,N'*-dimethylformamide (DMF) and dimethylsulfoxide (DMSO), were purchased in

anhydrous form and used without further purification. Water, ethyl acetate (EtOAc), diethyl ether (Et₂O), methylene chloride (CH₂Cl₂), and hexanes were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of ammonium molybdate and anisaldehyde and heat as developing agents. E. Merck silica gel (60, particle size 0.040-0.063 mm) was used for flash column chromatography. NMR spectra were recorded on a Bruker AV-600 instrument and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, pent = pentet, hex = hexet, br = broad. IR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with diamond ATR accessory. Melting points (m.p.) are uncorrected and were recorded on a Buchi B-540 melting point apparatus. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI TOF (time of flight) mass spectrometer at 3500 V emitter voltage.

Enone 6: To a stirred solution of acid **4** (8.3 g, 45.6 mmol) and cyclohexenone (7.7 mL, 71.1 mmol) in DMF/DMSO (20:1, 210 mL) at room temperature were added Pd(TFA)₂ (3.3 g, 9.12 mmol) and



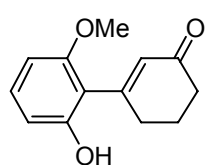
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Ag₂CO₃ (27.0 g, 91.2 mmol). The resulting mixture was heated to 80 °C and stirred for 3 h before it was quenched with water (250 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 200 mL). The combined organic layers were washed with water (3 × 200 mL), dried (MgSO₄) and concentrated in

vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 15:1 → 5:1) afforded enone **6** (9.4 g, 89%) as a white solid. **6**: *R*_f = 0.56 (silica gel, hexanes:EtOAc 2:1); m.p. = 89–90 °C (EtOAc/hexanes); IR (film) *v*_{max} 2948, 1664, 1620, 1586, 1470, 1429, 1249, 1129, 1105, 1031, 982, 956, 886, 780 755,

718 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.28 (t, J = 8.4 Hz, 1 H), 6.60 (d, J = 8.4 Hz, 2 H), 6.00 (s, 1 H), 3.80 (s, 6 H), 2.55 (t, J = 4.8 Hz, 2 H), 2.50 (t, J = 6.6 Hz, 2 H), 2.14–2.11 ppm (m, 2 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 200.1, 158.2, 156.7, 130.1, 129.4, 118.5, 103.9, 55.8, 37.5, 30.3, 23.1 ppm; HRMS (ESI): calcd for $\text{C}_{14}\text{H}_{17}\text{O}_3^+$ [$\text{M} + \text{H}^+$] 233.1172, found 233.1177.

Phenol 7: To a stirred solution of dimethyl ether **6** (2.3 g, 10.0 mmol) in CH_2Cl_2 (100 mL) at -15°C was added BBr_3 (1.7 mL, 18.0 mmol). The resulting mixture was stirred for 2.5 h before it was

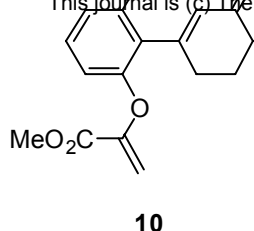


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quenched with water (100 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×200 mL). The combined organic layers were washed with water (3×200 mL), dried (MgSO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 10:1 \rightarrow 4:1) afforded phenol **7** (1.52 g,

70%) as a white solid. **7**: R_f = 0.36 (silica gel, hexanes:EtOAc 2:1); m.p. = $114\text{--}115^\circ\text{C}$ (EtOAc/hexanes); IR (film) ν_{max} 3261, 2941, 1642, 1619, 1591, 1499, 1467, 1438, 1348, 1327, 1305, 1249, 1190, 1133, 1081 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.16 (dd, J = 7.8, 7.8 Hz, 1 H), 6.88–6.67 (br s, 1 H), 6.61 (d, J = 7.8 Hz, 1 H), 6.49 (d, J = 7.8 Hz, 1 H), 6.14 (s, 1 H), 3.79 (s, 3 H), 2.66 (t, J = 4.8 Hz, 2 H), 2.53 (t, J = 6.6 Hz, 2 H), 2.17–2.10 ppm (m, 2 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 201.0, 159.7, 157.0, 153.0, 129.9, 129.8, 116.4, 109.1, 102.7, 55.7, 37.4, 30.2, 22.9 ppm; HRMS (ESI): calcd for $\text{C}_{13}\text{H}_{15}\text{O}_3^+$ [$\text{M} + \text{H}^+$] 219.1015, found 219.1008.

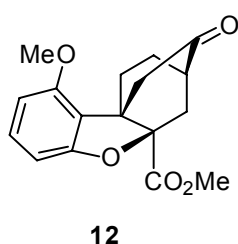
Alkenyl methyl ester 10: To a stirred solution of phenol **7** (2.00 g, 9.2 mmol) in THF (100 mL) at 0°C was added NaH (60% wt/wt dispersion in mineral oil, 780 mg, 19.5 mmol). The resulting mixture was warmed to room temperature and stirred for 1 h before it was cooled to 0°C and bromide **8**¹ (11.9 g, 46 mmol) was added. The resulting mixture was allowed to warm to room temperature and stirred for 16 h before it was quenched with water (250 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×200 mL). The combined organic layers were dried (MgSO_4) and concentrated in *vacuo* to afford the crude pyrrolidine, which was directly used in the following step without further purification.



To a stirred solution of the crude pyrrolidine (obtained above) in methanol (200 mL) at room temperature were added MeI (5.8 mL, 92 mmol) and Na₂CO₃ (4.63 g, 46 mmol). The resulting mixture was heated at reflux and heated for 2 h

before it was cooled to room temperature and quenched with water (400 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 400 mL). The combined organic layers were washed with water (1 × 200 mL), dried (MgSO₄), and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 15:1 → 5:1) afforded alkenyl methyl ester **10** (2.20 g, 80% for the two steps) as a colorless oil. **10**: *R*_f = 0.43 (silica gel, hexanes:EtOAc 2:1); IR (film) *v*_{max} 2952, 2847, 1737, 1670, 1628, 1598, 1579, 1465, 1439, 1344, 1323, 1269, 1236, 1197, 1159, 1087, 982 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.21 (dd, *J* = 8.4, 8.4 Hz, 1 H), 6.69 (d, *J* = 8.4 Hz, 1 H), 6.58 (d, *J* = 8.4 Hz, 1 H), 5.95 (s, 1 H), 5.61 (d, *J* = 1.8 Hz, 1 H), 4.81 (d, *J* = 1.8 Hz, 1 H), 3.76 (s, 3 H), 3.74 (s, 3 H), 2.54–2.51 (m, 2 H), 2.42–2.39 (m, 2 H), 2.07–2.01 ppm (m, 2 H); ¹³C NMR (150 MHz, CDCl₃): δ = 199.7, 162.8, 157.3, 156.6, 152.3, 150.4, 130.3, 129.6, 122.0, 111.7, 107.1, 104.3, 55.9, 52.5, 37.6, 30.1, 23.1 ppm; HRMS (ESI): calcd for C₁₇H₁₉O₅⁺ [M + H⁺] 303.1227, found 303.1221.

IMDA product 12: To a solution of alkenyl methyl ester **10** (3.0 g, 9.9 mmol) in CH₂Cl₂ (100 mL) at 0 °C were added Et₃N (4.1 mL, 29.8 mmol) and TBSOTf (3.5 mL, 14.9 mmol). The resulting mixture was stirred for 1.5 h before it was quenched with NaHCO₃ solution (100 mL sat. aq.).

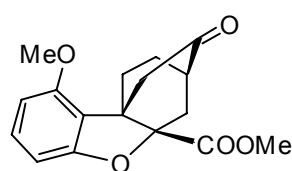


The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 200 mL). The combined organic layers were washed with water (1 × 200 mL), dried (MgSO₄) and concentrated in *vacuo* to afford the crude silyl enol ether, which was directly used in the following step without further purification.

To a solution of crude silyl enol ether (obtained above) in toluene (1.00 L) at room temperature were added K₂CO₃ (6.56 g, 47.5 mmol) and hydroquinone (1.13 g, 11.9 mmol). The resulting mixture was heated at reflux and stirred for 16 h before it was cooled to room temperature and quenched with water (200 mL). The layers were separated and to the organic layer at 0 °C was added HCl (1.0 N aq., 200

mL). The resulting mixture was allowed to warm to room temperature and stirred for 1 h. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 200 mL). The combined organic layers were washed with water (200 mL) and NaHCO₃ (200 mL sat. aq.), dried (MgSO₄) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 15:1 → 5:1) afforded *exo* IMDA product **12** (1.92 g, 64% for the two steps) and the *endo* isomer C8-*epi*-**12** (0.05 g, 1.7% for the two steps) as white solids. **12**: *R*_f = 0.66 (silica gel, hexanes:EtOAc 2:1); m.p. = 200–201 °C (EtOAc/hexanes); IR (film) ν_{\max} 2954, 1728, 1603, 1451, 1272, 1224, 1147, 1082, 1053 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.10 (dd, *J* = 7.8, 7.8 Hz, 1 H), 6.51 (d, *J* = 7.8 Hz, 1 H), 6.46 (d, *J* = 7.8 Hz, 1 H), 3.76 (s, 3 H), 3.63 (s, 3 H), 2.92 (dd, *J* = 20.4, 6.0 Hz, 1 H), 2.56–2.48 (m, 2 H), 2.31–2.26 (m, 4 H), 2.15–2.07 (m, 1 H), 1.80–1.73 ppm (m, 1 H); ¹³C NMR (150 MHz, CDCl₃): δ = 212.4, 173.1, 161.6, 156.0, 129.5, 118.4, 104.8, 103.8, 90.7, 55.3, 52.7, 51.7, 47.2, 42.1, 30.7, 24.9, 21.3 ppm; HRMS (ESI): calcd for C₁₇H₁₈O₅Na⁺ [*M* + Na⁺] 325.1046, found 325.1049.

IMDA product C8-*epi*-12: *R*_f = 0.65 (silica gel, hexanes:EtOAc 2:1); m.p. = 182–183 °C (EtOAc/hexanes); IR (film) ν_{\max} 2953, 1730, 1605, 1489, 1449, 1274, 1257, 1230, 1207, 1152, 1087,

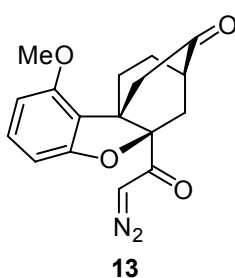


C8-*epi*-12

1024, 974, 955, 894, 849, 808, 777, 730, 690 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.16 (dd, *J* = 8.4, 7.8 Hz, 1 H), 6.61 (d, *J* = 7.8 Hz, 1 H), 6.48 (d, *J* = 8.4 Hz, 1 H), 3.80 (s, 3 H), 3.62 (s, 3 H), 3.03 (d, *J* = 18.6 Hz, 1 H), 2.78–2.75 (m, 1 H), 2.59–2.53 (m, 2 H), 2.23 (d, *J* = 13.8 Hz, 1 H), 2.03–1.98

(m, 3 H), 1.93–1.91 ppm (m, 1 H); ¹³C NMR (150 MHz, CDCl₃): δ = 212.0, 173.0, 162.8, 156.3, 129.6, 117.5, 104.6, 103.7, 90.5, 55.3, 52.4, 48.8, 42.8, 42.1, 31.7, 27.4, 23.1 ppm; HRMS (ESI): calcd for C₁₇H₁₈O₅Na⁺ [*M* + Na⁺] 325.1046, found 325.1251.

α -Diazo ketone 13: To a solution of methyl ester **12** (2.6 g, 8.46 mmol) in ethanol (100 mL) at room temperature was added NaOH (1.0 N aq., 100 mL). The resulting mixture was heated to 60 °C and stirred for 5 h before it was cooled to 0 °C and HCl (1.0 N aq.,



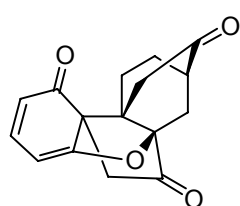
13

50 mL) was added. The resulting mixture was extracted with CH₂Cl₂ (3 × 100 mL), and the combined organic layers were dried (MgSO₄) and concentrated in *vacuo* to afford the crude carboxylic acid, which was directly used in the following step without further purification.

To a solution of the crude carboxylic acid (obtained above) in CH₂Cl₂ (100 mL) at 0 °C were added DMF (1 drop) and (COCl)₂ (3.7 mL, 42.3 mmol). The resulting mixture was heated at reflux with stirring for 1 h before it was concentrated in *vacuo* to afford the crude acid chloride, which was directly used in the following step without further purification.

To a solution of the crude acid chloride (obtained above) in THF/MeCN (1:1, 400 mL) at 0 °C was added TMSCHN₂ (2.0 M in hexanes, 22.0 mL, 44.0 mmol). The resulting mixture was stirred for 2 h before it was quenched with water (100 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 200 mL). The combined organic layers were dried (MgSO₄) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 15:1 → 5:1) afforded α-diazo ketone **13** (2.12 g, 79% for the three steps) as a yellow solid. **13**: *R*_f = 0.76 (silica gel, hexanes:EtOAc 2:1); m.p. = 123–124 °C (EtOAc/hexanes); IR (film) *v*_{max} 3130, 2950, 2104, 1731, 1627, 1602, 1489, 1464, 1440, 1395, 1337, 1272, 1230, 1145, 1097, 1051, 1013 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.14 (dd, *J* = 8.4, 7.8 Hz, 1 H), 6.54 (d, *J* = 8.4 Hz, 1 H), 6.49 (d, *J* = 7.8 Hz, 1 H), 5.54 (s, 1 H), 3.76 (s, 3 H), 2.63 (dd, *J* = 14.4, 3.6 Hz, 1 H), 2.56–2.46 (m, 3 H), 2.31–2.20 (m, 3 H), 2.19–2.13 (m, 1 H), 1.74–1.69 ppm (m, 1 H); ¹³C NMR (150 MHz, CDCl₃): δ = 212.6, 197.1, 160.5, 156.6, 130.1, 119.0, 105.5, 103.7, 93.6, 56.6, 55.3, 51.8, 48.0, 42.5, 31.4, 24.1, 21.6 ppm; HRMS (ESI): calcd for C₁₇H₁₆N₂O₄Na⁺ [*M* + Na⁺] 335.1002, found 335.0997.

Dienone 2: To a stirred solution of α-diazo ketone **13** (550 mg, 1.76 mmol) in CH₂Cl₂ (70 mL) at room temperature was added Rh₂(OAc)₄ (78 mg, 0.18 mmol). The resulting mixture was stirred for 1 h before

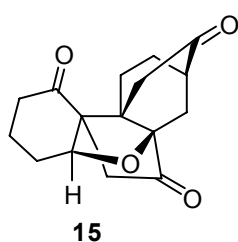


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it was concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 15:1 → 5:1) afforded dienone **2** (360.0 mg, 75%) as a yellowish

solid. **2**: $R_f = 0.44$ (silica gel, hexanes:EtOAc 2:1); m.p. = 128–129 °C (EtOAc/hexanes); IR (film) ν_{\max} 2959, 2927, 2856, 1768, 1731, 1678, 1636, 1533, 1412, 1345, 1199, 1143, 1085, 1039, 915 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.29$ (dd, $J = 9.6, 6.6$ Hz, 1 H), 5.90 (d, $J = 9.6$ Hz, 1 H), 5.63 (d, $J = 6.6$ Hz, 1 H), 2.83 (d, $J = 18.0$ Hz, 1 H), 2.58 (dd, $J = 15.6, 2.4$ Hz, 1 H), 2.50–2.42 (m, 3 H), 2.27 (d, $J = 18.6$ Hz, 1 H), 2.14–2.11 (m, 2 H), 1.97–1.85 (m, 2 H), 1.72–1.71 ppm (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 210.1, 201.4, 196.1, 170.8, 147.0, 120.4, 93.2, 90.8, 58.3, 55.8, 41.6, 41.1, 40.2, 24.1, 21.0, 20.3$; HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{14}\text{O}_4\text{Na}^+$ [$\text{M} + \text{Na}^+$] 293.0784, found 293.0780.

Triketone 15: To a stirred solution of dienone **2** (239 mg, 0.88 mmol) in EtOAc (100 mL) at room temperature was added Pd-C (10% wt/wt, 24 mg, 0.23 mmol). The resulting mixture was stirred under a

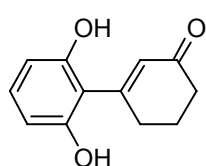


hydrogen atmosphere (balloon) for 24 h before it was filtered through Celite[®] and eluted with EtOAc (100 mL), and the combined filtrate was concentrated in *vacuo*.

Flash column chromatography (silica gel, hexanes:EtOAc 15:1 → 5:1) afforded triketone **15** (211 mg, 87%) as a white solid. **15**: $R_f = 0.37$ (silica gel,

hexanes:EtOAc 2:1); m.p. = 237–238 °C (EtOAc); IR (film) ν_{\max} 2953, 1758, 1728, 1704, 1602, 1456, 1399, 1325, 1284, 1217, 1193, 1163, 1087, 1017, 950, 913, 889, 848, 716, 778, 748, 665 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 4.09$ (dd, $J = 11.4, 7.2$ Hz, 1 H), 3.18 (d, $J = 18.6$ Hz, 1 H), 3.12 (dd, $J = 17.4, 4.2$ Hz, 1 H), 2.60–2.56 (m, 1 H), 2.42–2.38 (m, 2 H), 2.32–2.28 (m, 1 H), 2.17 (d, $J = 7.2$ Hz, 1 H), 2.14–2.08 (m, 3 H), 2.00–1.97 (m, 2 H), 1.80–1.64 (m, 3 H), 1.56–1.48 ppm (m, 2 H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 211.3, 206.7, 205.2, 86.7, 86.2, 58.1, 52.8, 46.7, 43.7, 40.9, 40.7, 30.2, 23.9, 21.8, 20.8, 20.2$; HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{18}\text{O}_4\text{Na}^+$ [$\text{M} + \text{Na}^+$] 297.1097, found 297.1099.

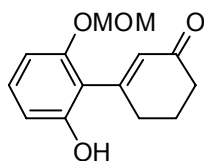
Diphenol 16: To a stirred solution of dimethyl ether **6** (5.0 g, 21.5 mmol) in CH_2Cl_2 (300 mL) at -78 °C was added BBR_3 (1.0 M in CH_2Cl_2 , 75.2 mL, 75.2 mmol). The resulting mixture was stirred for 2 h



before it was quenched with water (250 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers

were washed with water (3 × 200 mL), dried (Na₂SO₄) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 → 3:2 → 1:1) afforded diphenol **16** (4.3 g, 98%) as a white solid. **16**: *R*_f = 0.34 (silica gel, hexanes:EtOAc 3:2); m.p. = 182–183 °C (EtOAc/hexanes); IR (film) ν_{\max} 3334, 2160, 1737, 1621, 1461, 1353, 1217, 1012, 889, 782 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.06 (t, *J* = 7.8 Hz, 1 H), 6.46 (d, *J* = 7.8 Hz, 2 H), 6.14 (s, 1 H), 5.13 (br s, 2 H), 2.69 (t, *J* = 5.0 Hz, 2 H), 2.53 (t, *J* = 6.6 Hz, 2 H), 2.17–2.14 ppm (m, 2 H); ¹³C NMR (150 MHz, *d*⁶-acetone): δ = 199.2, 158.9, 156.0, 131.2, 130.5, 117.2, 108.4, 38.5, 31.2, 24.2 ppm; HRMS (ESI): calcd for C₁₂H₁₃O₃⁺ [M + H⁺] 205.0859, found 205.0861.

Enone 17: To a stirred solution of diphenol **16** (2.55 g, 12.5 mmol) in THF (100 mL) at 0 °C was added NaH (60% wt/wt dispersion in mineral oil, 539 mg, 13.5 mmol). The resulting mixture was warmed to

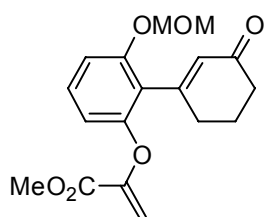


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room temperature and stirred for 0.5 h before it was cooled to 0 °C and MOMCl (1.11 mL, 14.7 mmol) was added. The resulting mixture was stirred for 2 h before it was quenched with NH₄Cl (100 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were

washed with brine (40 mL), dried (Na₂SO₄) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded enone **17** (1.69 g, 56%) as a white solid. **17**: *R*_f = 0.35 (silica gel, hexanes:EtOAc 1:1); m.p. = 133–134 °C (EtOAc/hexanes); IR (film) ν_{\max} 2948, 1642, 1461, 1347, 1241, 1152, 1088, 1032, 938, 922, 782 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.11 (dd, *J* = 8.4, 7.8 Hz, 1 H), 6.67 (d, *J* = 8.4 Hz, 1 H), 6.61 (d, *J* = 7.8 Hz, 1 H), 6.26 (br s, 1 H), 6.10 (s, 1 H), 5.14 (s, 2 H), 3.44 (s, 3 H), 2.64 (t, *J* = 5.0 Hz, 2 H), 2.51 (t, *J* = 6.6 Hz, 2 H), 2.15–2.13 ppm (m, 2 H); ¹³C NMR (150 MHz, CDCl₃): δ = 200.4, 159.0, 154.4, 152.7, 129.9, 129.8, 117.3, 109.8, 106.1, 94.4, 56.2, 37.4, 30.3, 22.9 ppm; HRMS (ESI): calcd for C₁₄H₁₇O₄⁺ [M + H⁺] 249.1121, found 249.1110.

Alkenyl methyl ester 18: To a stirred solution of phenol **17** (859 mg, 3.47 mmol) in THF/DMF (40:3, 43 mL) at 0 °C was added NaH (60% wt/wt

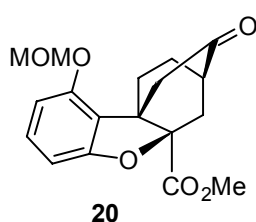


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dispersion in mineral oil, 175 mg, 7.30 mmol). The resulting mixture was warmed to room temperature and stirred for 1 h before it was cooled to 0 °C and bromide **8**^[1] (3.28 g, 13.88 mmol) was added. The resulting mixture was warmed to room temperature and stirred for 8 h before it was quenched with water (40 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 40 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in *vacuo* to afford the crude pyrrolidine, which was directly used in the following step without further purification.

To a stirred solution of the crude pyrrolidine (obtained above) in methanol (400 mL) at room temperature were added MeI (1.96 mL, 38.2 mmol) and Na₂CO₃ (956 mg, 9.02 mmol). The resulting mixture was heated to reflux and stirred for 2 h before it was cooled to room temperature and quenched with water (40 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 40 mL). The combined organic layers were washed with water (1 × 20 mL), dried (Na₂SO₄) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 → 3:1) afforded alkenyl methyl ester **18** (0.66 g, 57% for the two steps) as a yellow oil. **18**: *R*_f = 0.34 (silica gel, hexanes: EtOAc 3:1); IR (film) ν_{max} 2952, 1736, 1668, 1626, 1598, 1580, 1459, 1359, 1344, 1321, 1235, 1197, 1152, 1090, 1038, 969, 793 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.21 (dd, *J* = 8.4, 7.8 Hz, 1 H), 6.94 (d, *J* = 8.4 Hz, 1 H), 6.61 (d, *J* = 7.8 Hz, 1 H), 6.00 (s, 1 H), 5.67 (s, 1 H), 5.16 (s, 2 H), 4.88 (s, 1 H), 3.79 (s, 3 H), 3.45 (s, 3 H), 2.59 (t, *J* = 5.0 Hz, 2 H), 2.46 (t, *J* = 6.6 Hz, 2 H), 2.09–2.11 ppm (m, 2 H); ¹³C NMR (150 MHz, CDCl₃): δ = 199.7, 162.7, 156.6, 154.6, 152.3, 150.2, 130.1, 129.6, 122.7, 112.5, 110.5, 104.5, 94.5, 56.3, 52.5, 37.5, 30.2, 23.1 ppm; HRMS (ESI): calcd for C₁₈H₂₁O₆⁺ [M + H⁺] 333.1333, found 333.1320.

IMDA product 20: To a solution of alkenyl methyl ester **18** (660 mg, 1.99 mmol) in CH₂Cl₂ (40 mL) at 0 °C were added Et₃N (0.83 mL, 5.96 mmol) and TBSOTf (0.69 mL, 3.00 mmol). The resulting mixture was stirred for 2 h before it was quenched with NaHCO₃ solution (30 mL sat. aq.).

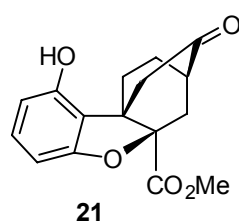


The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were washed with water (1 × 20 mL),

dried (Na_2SO_4) and concentrated in *vacuo* to afford the crude silyl enol ether, which was directly used in the following step without further purification.

To a solution of the crude silyl enol ether (obtained above) in toluene (90 mL) at room temperature were added K_2CO_3 (1.32 g, 9.55 mmol) and hydroquinone (262 mg, 2.39 mmol). The resulting mixture was heated to reflux and stirred for 18 h before it was cooled to room temperature and quenched with water (30 mL). The layers were separated and to the organic layer was added HCl (1.0 N aq.) at 0 °C until pH \sim 1. The resulting mixture was allowed to warm to room temperature and stirred for 1 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were washed with water (30 mL) and NaHCO_3 (30 mL sat. aq.), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 \rightarrow 3:1) afforded IMDA product **20** (330 mg, 50% over two steps) as a crystalline white solid. **20**: R_f = 0.35 (silica gel, hexanes:EtOAc 2:1); m.p. = 83–85 °C (EtOAc/hexanes); IR (film) ν_{max} 2954, 1728, 1606, 1484, 1445, 1274, 1256, 1226, 1149, 1064, 1039, 1012, 922, 778 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.07 (dd, J = 8.4, 7.8 Hz, 1 H), 6.63 (d, J = 8.4 Hz, 1 H), 6.54 (d, J = 7.8 Hz, 1 H), 5.16 (d, J = 6.6 Hz, 1 H), 5.12 (d, J = 6.6 Hz, 1 H), 3.64 (s, 3 H), 3.44 (s, 3 H), 2.91 (dd, J = 14.6, 4.4 Hz, 1 H), 2.57 (dd, J = 18.6, 3.0 Hz, 1 H), 2.51 (s, 1 H), 2.31 (d, J = 18.6 Hz, 1 H), 2.29–2.24 (m, 3 H), 2.17–2.13 (m, 1 H), 1.80–1.79 ppm (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 212.0, 173.0, 161.6, 153.3, 129.5, 119.2, 107.6, 104.5, 93.9, 90.6, 56.1, 52.7, 51.7, 47.2, 42.0, 30.6, 24.9, 21.3 ppm; HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{20}\text{O}_6\text{Na}^+$ [$\text{M} + \text{Na}^+$] 355.1152, found 355.1157.

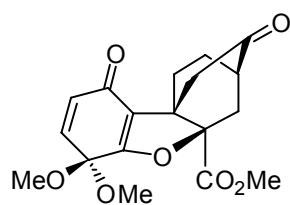
Phenol 21: A solution of MOM ether **20** (330 mg, 0.99 mmol) in $\text{CHCl}_3/6.0$ N HCl (aq.)/EtOH (1:1:1, 15 mL) was heated at reflux for 3 h. The resulting mixture was cooled to room temperature and the



organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3×20 mL) and the combined organic layers were dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 2:1 \rightarrow 1:1) afforded phenol **21** (240 mg, 83%) as a crystalline white solid. **21**: R_f = 0.34 (silica

gel, hexanes: EtOAc 1:1); m.p. = 226–227 °C (EtOAc/hexanes); IR (film) ν_{\max} 2954, 1729, 1610, 1455, 1365, 1277, 1256, 1229, 1217, 1145, 1068, 1036, 1003, 781 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 6.99 (dd, J = 8.4, 7.8 Hz, 1 H), 6.47 (d, J = 8.4 Hz, 1 H), 6.30 (d, J = 7.8 Hz, 1 H), 4.82 (br s, 1 H), 3.65 (s, 3 H), 2.92 (dd, J = 15.0, 4.8 Hz, 1 H), 2.57 (dd, J = 18.6, 2.4 Hz, 1 H), 2.52 (s, 1 H), 2.35 (d, J = 18.6 Hz, 1 H), 2.31–2.16 (m, 4 H), 1.80–1.77 ppm (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 212.7, 173.0, 162.1, 151.8, 129.4, 117.2, 109.6, 103.5, 90.6, 52.8, 51.4, 47.1, 42.0, 30.6, 24.8, 21.2 ppm; HRMS (ESI): calcd for $\text{C}_{16}\text{H}_{16}\text{O}_5\text{Na}^+$ [$\text{M} + \text{Na}^+$] 311.0890, found 311.0880.

Dienone 22: To a stirred solution of phenol **21** (120 mg, 0.42 mmol) in MeOH (30 mL) at 0 °C were added KHCO_3 (92 mg, 0.92 mmol) and $\text{PhI}(\text{OAc})_2$ (358 mg, 0.83 mmol). The resulting mixture was



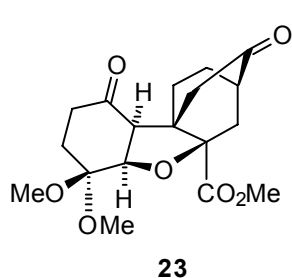
22

allowed to warm to room temperature and stirred for 0.5 h before it was quenched with H_2O (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with water (1×20 mL), dried (Na_2SO_4) and concentrated in *vacuo*.

Flash column chromatography (silica gel, hexanes:EtOAc 4:1 \rightarrow 3:1) afforded dienone **22** (120 mg, 83%) as a crystalline white solid. **22:** R_f = 0.34 (silica gel, hexanes: EtOAc 3:1); m.p. = 128–129 °C (EtOAc/hexanes); IR (film) ν_{\max} 2950, 1730, 1662, 1636, 1601, 1454, 1406, 1365, 1269, 1224, 1147, 1129, 1068, 1045, 1036, 960, 732 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 6.60 (d, J = 10.2 Hz, 1 H), 6.14 (d, J = 10.2 Hz, 1 H), 3.78 (s, 3 H), 3.52 (s, 3 H), 3.41 (s, 3 H), 2.98 (dd, J = 14.8, 4.8 Hz, 1 H), 2.51 (s, 1 H), 2.44 (d, J = 18.5 Hz, 1 H), 2.40–2.33 (m, 2 H), 2.27–2.20 (m, 2 H), 1.98–1.93 (m, 1 H), 1.75–1.70 ppm (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): δ = 210.5, 182.5, 171.3, 170.4, 139.2, 130.4, 120.1, 92.6, 92.1, 53.1, 51.2, 51.1, 46.5, 41.8, 30.1, 24.1, 20.5 ppm; HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{21}\text{O}_7^+$ [$\text{M} + \text{H}^+$] 349.1282, found 349.1284.

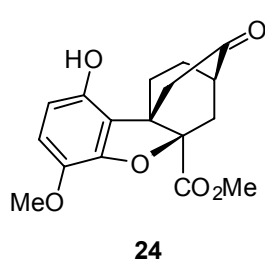
Diketone 23 and aromatized phenol 24: To a stirred solution of dienone **22** (105 mg, 0.30 mmol) in EtOH (10 mL) at room temperature was added Pd-C (10% wt/wt, 21 mg, 0.099 mmol). The resulting mixture was stirred under a hydrogen atmosphere (balloon) for 10 h before it was filtered through

Celite[®] and eluted with EtOAc (10 mL), and the combined organic filtrate was concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 → 3:1) afforded diketone **23** (74 mg,



70%) and aromatized phenol **24** (28 mg, 30%) as colourless oil. **23**: $R_f = 0.34$ (silica gel, hexanes:EtOAc 3:1); IR (film) ν_{\max} 2952, 1729, 1706, 1455, 1324, 1275, 1256, 1223, 1155, 1080, 1059, 1017, 996, 907, 890, 782 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 4.71$ (d, $J = 10.8$ Hz, 1 H), 3.80 (s, 3 H), 3.38 (s, 3 H), 3.24 (s, 3 H), 3.16 (d, $J = 10.8$ Hz, 1 H), 3.05 (dd, $J = 18.6, 2.4$ Hz, 1 H), 2.76 (dd, $J = 15.0, 4.2$ Hz, 1 H), 2.37 (s, 1 H), 2.34 (s, 1 H), 2.22–2.12 (m, 2 H), 2.06–1.91 (m, 4 H), 1.86–1.77 (m, 2 H), 1.73–1.66 ppm (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 213.5, 209.3, 173.4, 98.1, 85.3, 82.4, 55.1, 52.6, 50.8, 50.5, 48.3, 42.6, 41.9, 36.1, 31.9, 27.0, 26.2, 20.9$ ppm; HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{24}\text{O}_7\text{Na}^+$ [$\text{M} + \text{Na}^+$] 375.1414, found 375.1401.

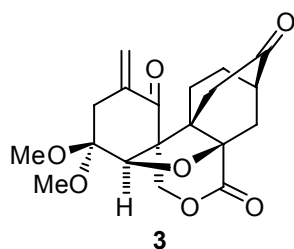
24: $R_f = 0.33$ (silica gel, hexanes: EtOAc 3:1); IR (film) ν_{\max} 2953, 2924, 1727, 1624, 1504, 1439, 1277, 1257, 1218, 1156, 1144, 1059, 1036, 1010, 983, 791 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 6.65$ (d, $J =$



8.7 Hz, 1 H), 6.25 (d, $J = 8.7$ Hz, 1 H), 4.57 (br, 1 H), 3.84 (s, 3 H), 3.65 (s, 3 H), 2.91 (dd, $J = 14.7, 4.8$ Hz, 1 H), 2.61 (dd, $J = 18.6, 3.1$ Hz, 1 H), 2.52 (m, 1 H), 2.39–2.27 (m, 3 H), 2.25–2.21 (m, 1 H), 2.19–2.11 (m, 1 H), 1.75–1.79 (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 212.4, 172.9, 149.7, 145.7, 139.1, 118.8, 113.6, 109.0, 91.4, 56.8, 52.9, 52.0, 47.2, 42.0, 30.7, 24.7, 21.1$ ppm; HRMS (ESI): calcd for $\text{C}_{17}\text{H}_{18}\text{O}_6\text{Na}^+$ [$\text{M} + \text{Na}^+$] 341.0995, found 341.0992.

Conversion of phenol 24 to dienone 22: To a stirred solution of phenol **24** (20 mg, 0.062 mmol) in MeOH (5 mL) at 0 °C were added KHCO_3 (13.6 mg, 0.13 mmol) and PIFA (53 mg, 0.12 mmol). The resulting mixture was allowed to warm to room temperature and stirred for 0.5 h before it was quenched with H_2O (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with water (1 × 5 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 → 3:1) afforded dienone **22** (15 mg, 70%) as a colorless oil.

Lactone 3: To a stirred solution of methyl ester **23** (88 mg, 0.25 mmol) in EtOH (4 mL) at room temperature was added NaOH (1.0 N, 1.8 mL). The resulting mixture was heated at 60 °C and heated

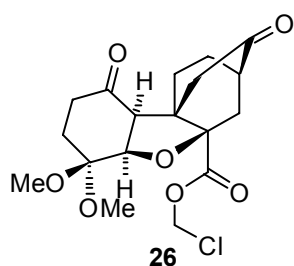


for 5 h before it was cooled to 0 °C and HCl (1.0 N, 3.6 mL) was added. The resulting mixture was extracted with CH₂Cl₂ (3 × 10 mL), and the combined organic layers were dried (Na₂SO₄) and concentrated in *vacuo* to afford crude carboxylic acid **25** (84 mg), which was directly used in the following step

without further purification.

To a solution of crude carboxylic acid **25** (obtained above, 20 mg, 0.059 mmol) in THF (1.5 mL) at 23 °C were added ICH₂Cl (48 μL, 0.65 mmol), 18-crown-6 (85.8 mg, 0.324 mmol) and KO^t-Bu (33.1 mg, 0.295 mmol). The resulting mixture was stirred for 3 h before it was concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded lactone **3** (9 mg, 42% over the two steps) as a white solid. **3**: *R*_f = 0.35 (silica gel, hexanes:EtOAc 2:1); m.p. = 173–175 °C (EtOAc/hexanes); IR (film) ν_{\max} 2964, 1746, 1723, 1692, 1617, 1455, 1394, 1217, 1197, 1133, 1056, 866, 766 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 6.23 (s, 1 H), 5.50 (s, 1 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.53 (s, 1 H), 4.21 (d, *J* = 10.8 Hz, 1 H), 3.41 (dd, *J* = 19.0, 3.7 Hz, 1 H), 3.41 (s, 3 H), 3.20 (s, 3 H), 2.99 (m, 2 H), 2.53 (dt, *J* = 16.5, 2.4 Hz, 1 H), 2.40 (m, 1 H), 2.06 (m, 1 H), 2.01 (dt, *J* = 15.1, 3.7 Hz, 1 H), 1.98–1.93 (m, 1 H), 1.87 (d, *J* = 18.6 Hz, 1 H), 1.82–1.79 (m, 1 H), 1.73–1.67 ppm (m, 1 H); ¹³C NMR (150 MHz, CDCl₃): δ = 212.5, 195.2, 168.4, 138.3, 126.8, 97.2, 87.0, 82.8, 74.9, 57.2, 51.5, 47.8, 47.7, 41.9, 41.1, 36.2, 29.3, 22.7, 20.2 ppm; HRMS (ESI): calcd for C₁₉H₂₂O₇Na⁺ [*M* + Na⁺] 385.1258, found 385.1246.

Chloride 26: To a solution of carboxylic acid **25** (as obtained above for the preparation of lactone **3**



from methyl ester **23**, 13 mg, 0.038 mmol) in DMF (2 mL) at 23 °C were added ICH₂Cl (30 μL, 0.418 mmol) and K₂CO₃ (5 mg, 0.038 mmol). The resulting mixture was stirred for 8 h before it was concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded chloride **26** (12 mg,

82% over the two steps from methyl ester **24**) as a colorless oil. **26**: $R_f = 0.35$ (silica gel, hexanes:EtOAc 2:1); IR (film) ν_{\max} 2925, 1732, 1707, 1455, 1270, 1200, 1140, 1079, 1058, 1043, 1018, 907, 890, 716 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 5.86$ (d, $J = 6.0$ Hz, 1 H), 5.77 (d, $J = 6.0$ Hz, 1 H), 4.65 (d, $J = 10.8$ Hz, 1 H), 3.38 (s, 3 H), 3.25 (s, 3 H), 3.17 (d, $J = 10.8$ Hz, 1 H), 3.03 (d, $J = 18.6$ Hz, 1 H), 2.69 (dd, $J = 15.0, 3.6$ Hz, 1 H), 2.40 (s, 1 H), 2.36 (s, 1 H), 2.22–2.14 (m, 2 H), 2.06–1.94 (m, 5 H), 1.84–1.80 (m, 1 H), 1.73–1.71 ppm (m, 1 H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 212.9, 208.8, 171.0, 98.0, 85.0, 82.2, 69.1, 54.8, 50.7, 50.7, 48.4, 42.8, 41.8, 36.1, 31.8, 26.6, 26.1, 21.0$ ppm; HRMS (ESI): calcd for $\text{C}_{18}\text{H}_{23}\text{ClO}_7\text{Na}^+ [\text{M} + \text{Na}^+]$ 409.1025, found 409.1030.

II) Abbreviations

TFA = Trifluoroacetate

TBS = *tert*-butyldimethylsilyl

TMS = Trimethylsilyl

Ac = acetyl

MOM = methoxymethyl

PIFA = phenyliodobis(trifluoroacetate)

III) Materials and Methods for Cytotoxicity Assay

i) Cell lines and culture conditions:

All tissue culture components were purchased from Invitrogen (Carlsbad, CA). Human cancer cell lines: Breast (MCF-7), lung (NCI-H460) and CNS (SF268) were obtained from NCI and grown in RPMI supplemented with 5% fetal bovine serum (FBS), 2 mM glutamine, 50 units/ml streptomycin and penicillin. The human cervical carcinoma cell lines (HeLa), was a gift from Prof Chang Yong-Tae

(SBIC, A-Star) and was grown in DMEM supplemented with 10% FBS, 50 units/ml streptomycin and penicillin. No cell lines were cultured beyond 20 passages.

ii) Antitumor activity:

The antitumor activity was performed using SRB (Sulphorhodamine B) assay. In brief, cells were seeded on 96-well plates in 100 μ l of culture medium (10000, 5000, 7500 and 6000 cells/well for MCF-7, NCI-H460, SF268 and HeLa, respectively). Twenty-four hours later, 100 μ l of medium containing 5 different concentrations (10 μ M, 1 μ M, 0.1 μ M, 0.01 μ M and 0.001 μ M) of the desired compounds was added to the respective well. The plates were incubated for 48 h at 37 $^{\circ}$ C before fixing with 50% cold trichloroacetic acid for one hour, after which the plates were washed five times with distilled water. The plates were then air-dried at room temperature. The fixed cells were stained with 100 μ L of 0.4% (w/v) SRB in 1% acetic acid for 10 min. Excess SRB was later removed by washing the plates five times with 1% acetic acid. After drying, 100 μ L of 10 mM Tris base (pH 10.5) were added to solubilize the protein bound SRB and mixed. The absorbance was measured at 515 nm using a Versamax microtitre plate reader (Molecular Devices). GI₅₀ was calculated from 5 dosage responses using Softmax[®]Pro 5.2 software based on point to point plot. Percentage of net growth was calculated according to the formula reported by Monks *et al.*²: If $T_0 \geq T$, % of net growth = $((T-T_0)/(C-T_0)) \times 100$. If $T_0 < T$, % of net growth = $((T-T_0)/T_0) \times 100$. T is the optical density of the test well after a 48-hour drug exposure. T₀ is the optical density at time zero, and C is the control optical density after 48 hours.

IV) X-ray Crystallographic Analysis

A good quality single crystal grown from the solution crystallization was chosen under a Leica microscope and placed on a fibre needle which was then mounted on the goniometer of the X-ray diffractometer. The crystal was purged with a cooled nitrogen gas stream throughout the data collection. X-ray reflections were collected on a Rigaku Saturn CCD area detector with graphite monochromated

Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$). Data were collected and processed using CrystalClear (Rigaku) software.³ Structures were solved by direct methods and SHELX-TL⁴ was used for structure solution and least-squares refinement. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were fixed at idealized positions. ORTEP drawings were prepared using ORTEP-3⁵ software.

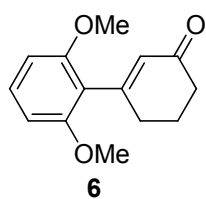
X-ray data for all the compounds were collected on Rigaku Saturn CCD area detector with graphite monochromated Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$). **12**: C₁₇H₁₈O₅, $M = 302.31$, orthorhombic, space group *Pbca*, $a = 7.9585(16)$, $b = 17.241(3)$, $c = 20.159(4)$, $V = 2766.0(10) \text{ \AA}^3$, $Z = 8$, $D_c = 1.452 \text{ g cm}^{-3}$, $T = 110(2) \text{ K}$, $F(000) = 1280$, $\mu = 0.107 \text{ mm}^{-1}$, $R_{int} = 0.0301$, $R_1 = 0.0576$ for 3136 $F_o > 2\sigma(F_o)$. C8-*epi*-**12**: C₁₇H₁₈O₅, $M = 302.31$, triclinic, space group *P*-1, $a = 6.9635(14)$, $b = 8.8693(18)$, $c = 12.590(3)$, $\alpha = 98.55(3)$, $\beta = 101.29(3)$, $\gamma = 105.65(3)$, $V = 717.3(2) \text{ \AA}^3$, $Z = 2$, $D_c = 1.400 \text{ g cm}^{-3}$, $T = 110(2) \text{ K}$, $F(000) = 320$, $\mu = 0.103 \text{ mm}^{-1}$, $R_{int} = 0.0403$, $R_1 = 0.0758$ for 2878 $F_o > 2\sigma(F_o)$. **15**: C₁₆H₁₈O₄, $M = 274.30$, triclinic, space group *P*-1, $a = 6.7342(13)$, $b = 8.6721(17)$, $c = 11.458(2)$, $\alpha = 102.25(3)$, $\beta = 98.41(3)$, $\gamma = 104.21(3)$, $V = 619.8(2) \text{ \AA}^3$, $Z = 2$, $D_c = 1.470 \text{ g cm}^{-3}$, $T = 110(2) \text{ K}$, $F(000) = 292$, $\mu = 0.105 \text{ mm}^{-1}$, $R_{int} = 0.0147$, $R_1 = 0.0378$ for 2919 $F_o > 2\sigma(F_o)$. **3**: C₁₉H₂₂O₇, $M = 362.37$, monoclinic, space group *P2*₁/*c*, $a = 13.838(3)$, $b = 7.0826(14)$, $c = 17.443(4)$, $\beta = 108.23(3)$, $V = 1623.7(6) \text{ \AA}^3$, $Z = 4$, $D_c = 1.482 \text{ g cm}^{-3}$, $T = 113(2) \text{ K}$, $F(000) = 768$, $\mu = 0.113 \text{ mm}^{-1}$, $R_{int} = 0.0183$, $R_1 = 0.0430$ for 3836 $F_o > 2\sigma(F_o)$. Crystal structures were solved by direct methods and SHELX-TL was used for structure solution and least-squares refinement. All the hydrogen atoms were fixed at geometrically reasonable positions. CCDC reference numbers 748550 (**12**), 742701 (C8-*epi*-**12**), 748551 (**15**), 742693 (**3**).

V) References

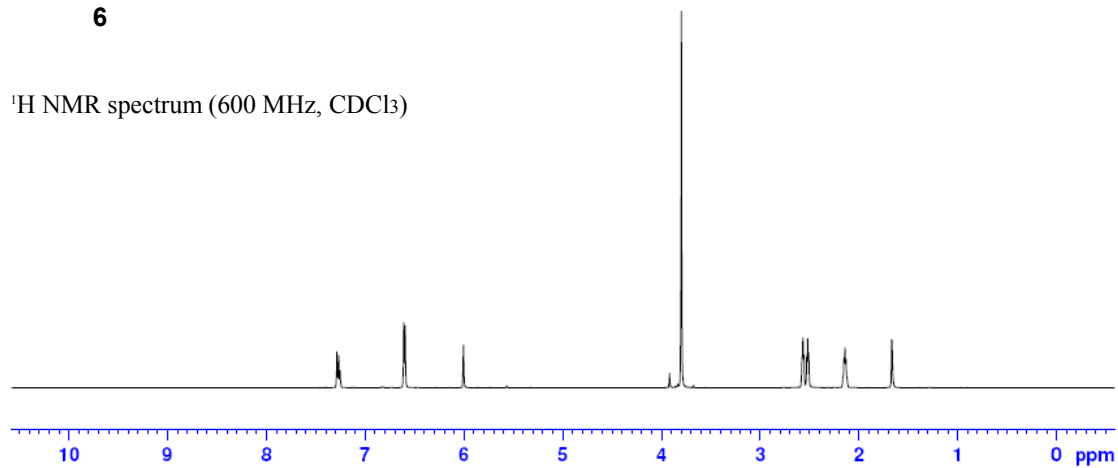
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- 4 G. M. Sheldrick, SHELXS-97 and SHELXL-97, Programs for the Solution and Refinement of Crystal Structures, University of Göttingen, Göttingen (Germany), 1997.
- 5 Ortep-3 for Windows: L. J. Farrugia, *J. Appl. Cryst.*, 1997, **30**, 565.

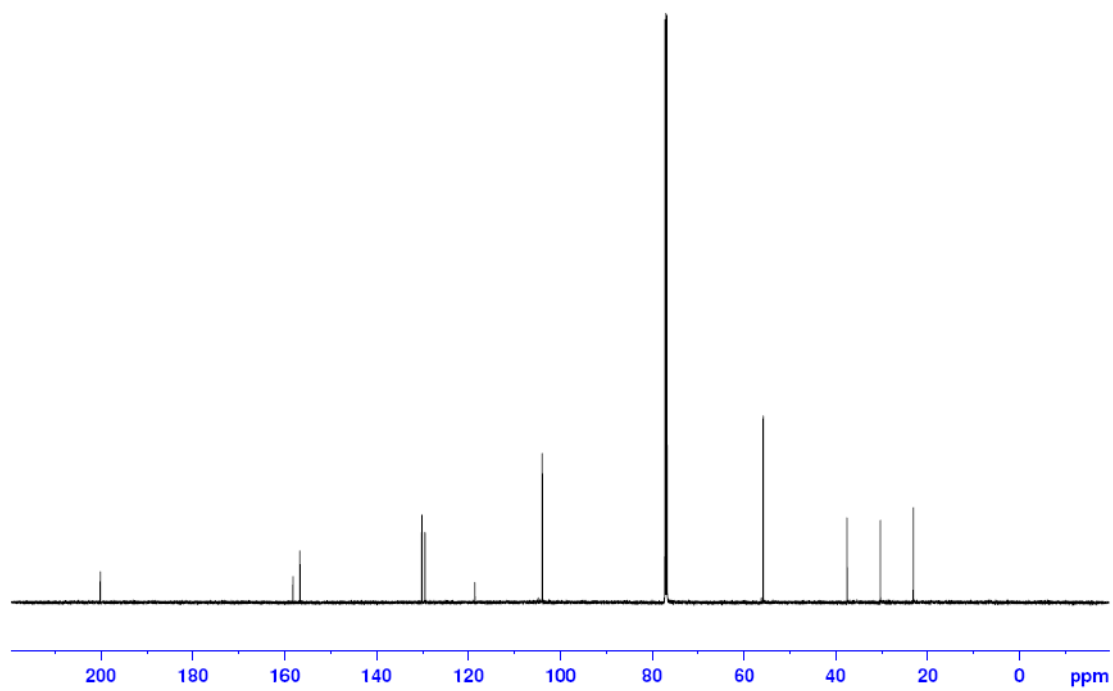
VI) ^1H and ^{13}C NMR Spectra of Compounds

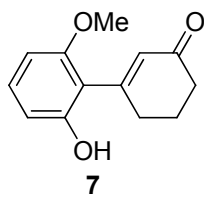


^1H NMR spectrum (600 MHz, CDCl_3)

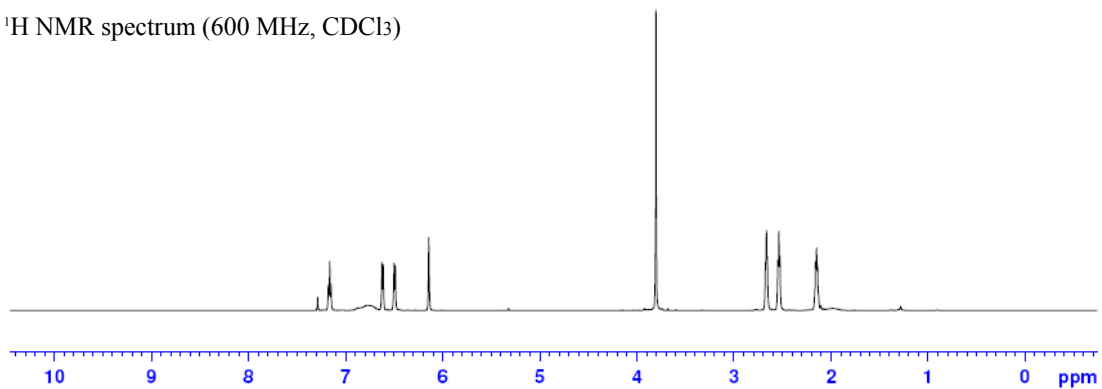


^{13}C NMR spectrum (150 MHz, CDCl_3)

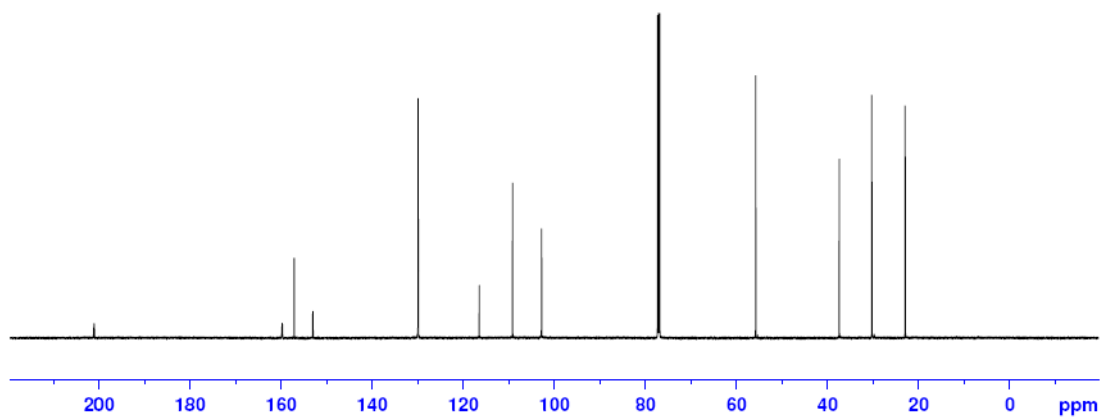


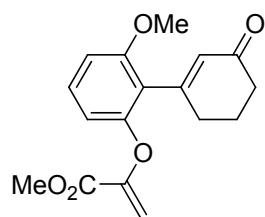


^1H NMR spectrum (600 MHz, CDCl_3)



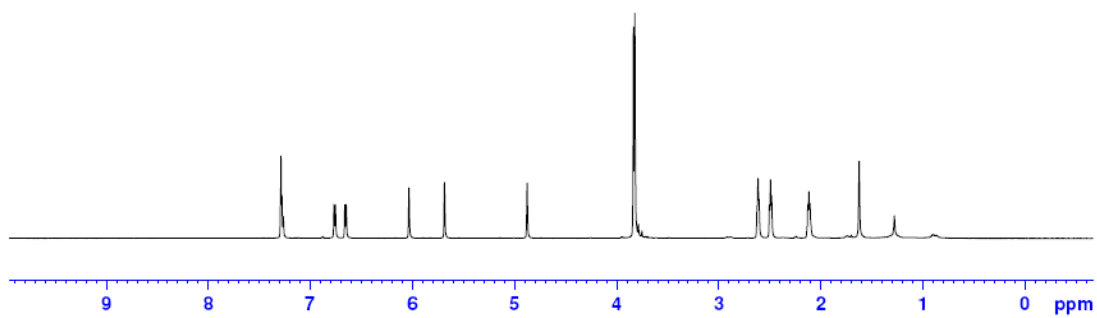
^{13}C NMR spectrum (150 MHz, CDCl_3)



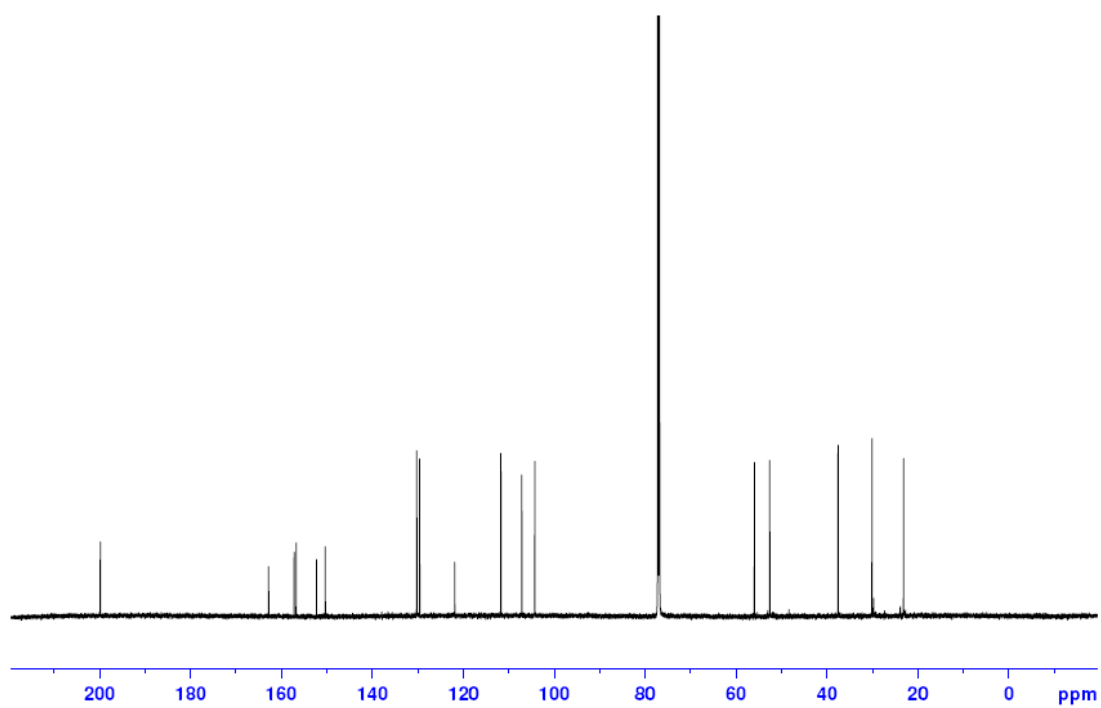


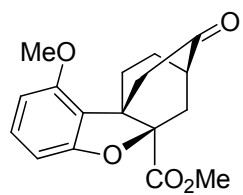
10

¹H NMR spectrum (600 MHz, CDCl₃)



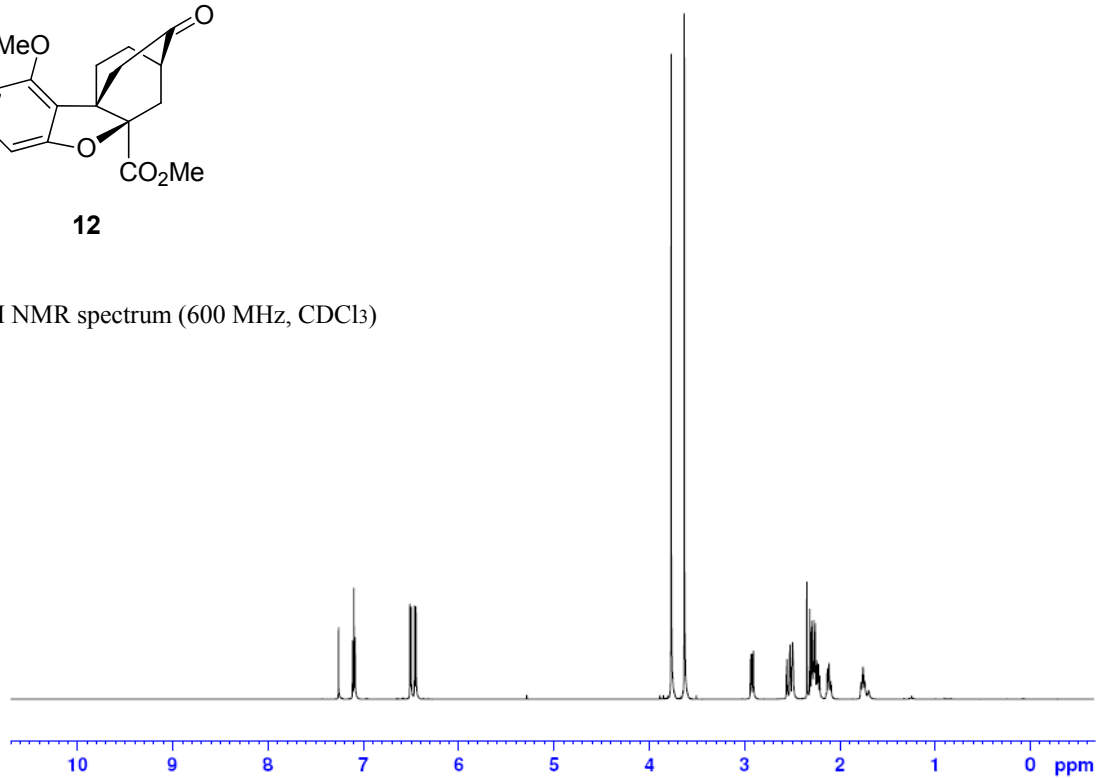
¹³C NMR spectrum (150 MHz, CDCl₃)



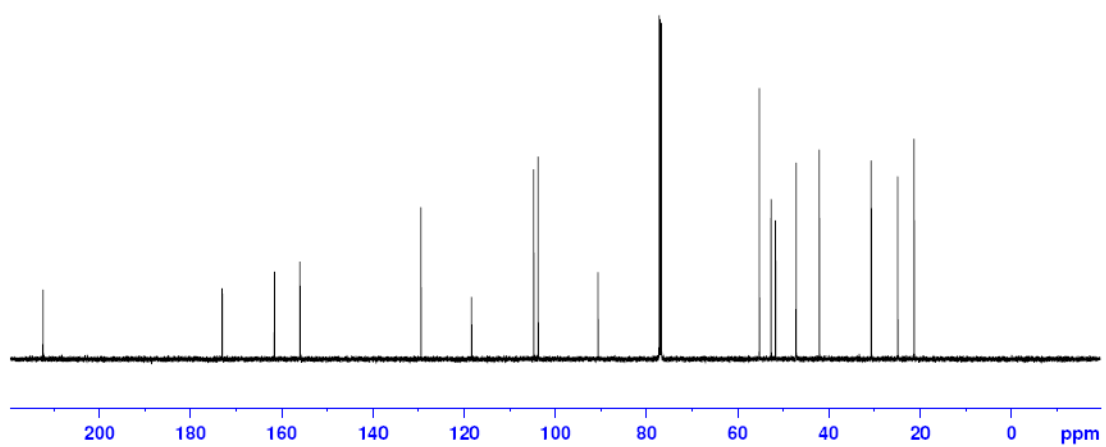


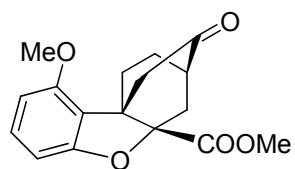
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¹H NMR spectrum (600 MHz, CDCl₃)



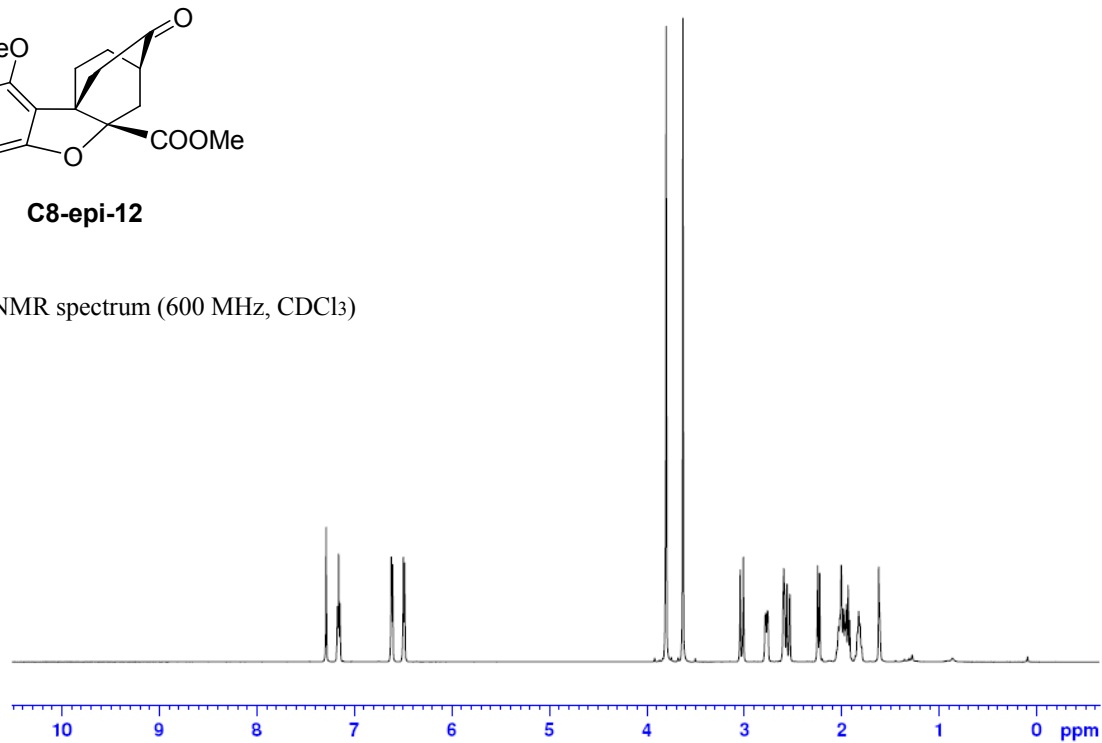
¹³C NMR spectrum (150 MHz, CDCl₃)



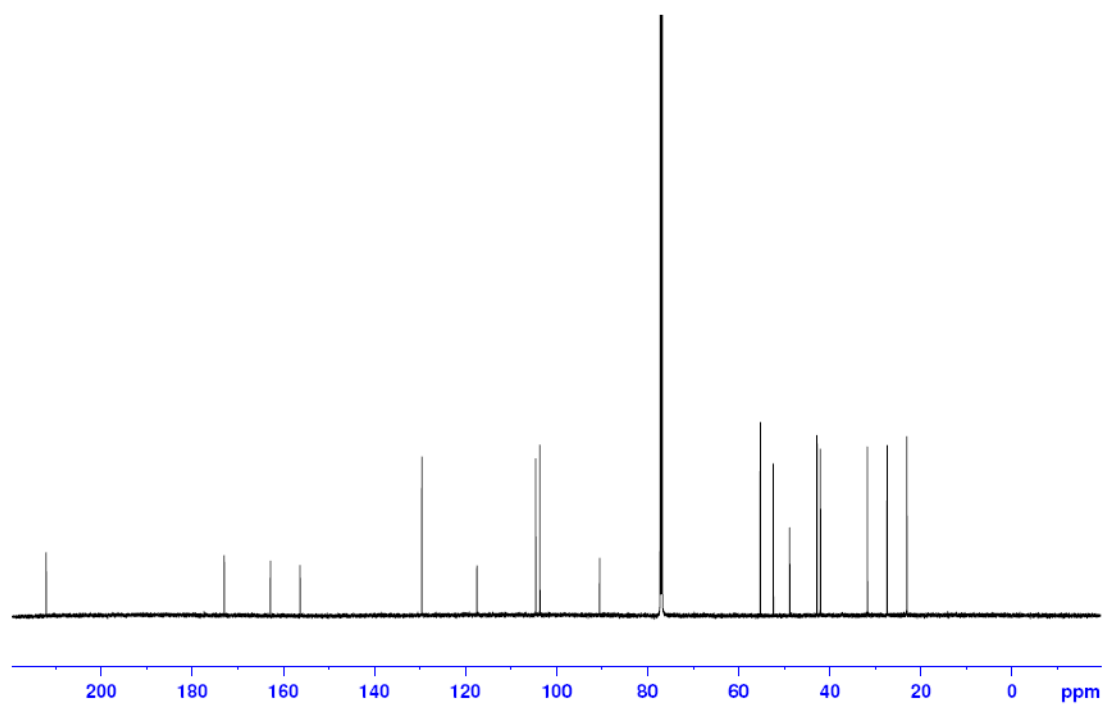


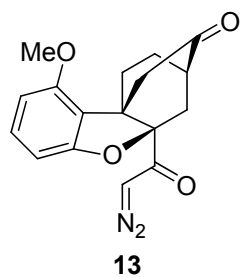
C8-epi-12

^1H NMR spectrum (600 MHz, CDCl_3)

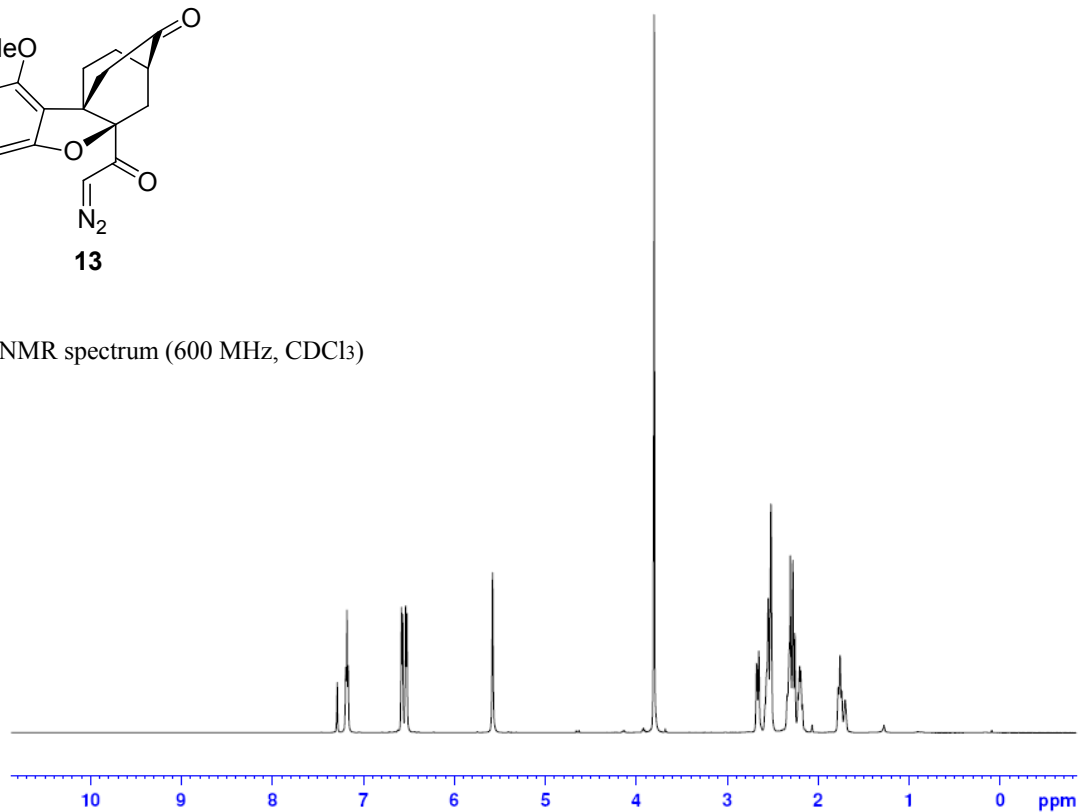


^{13}C NMR spectrum (150 MHz, CDCl_3)

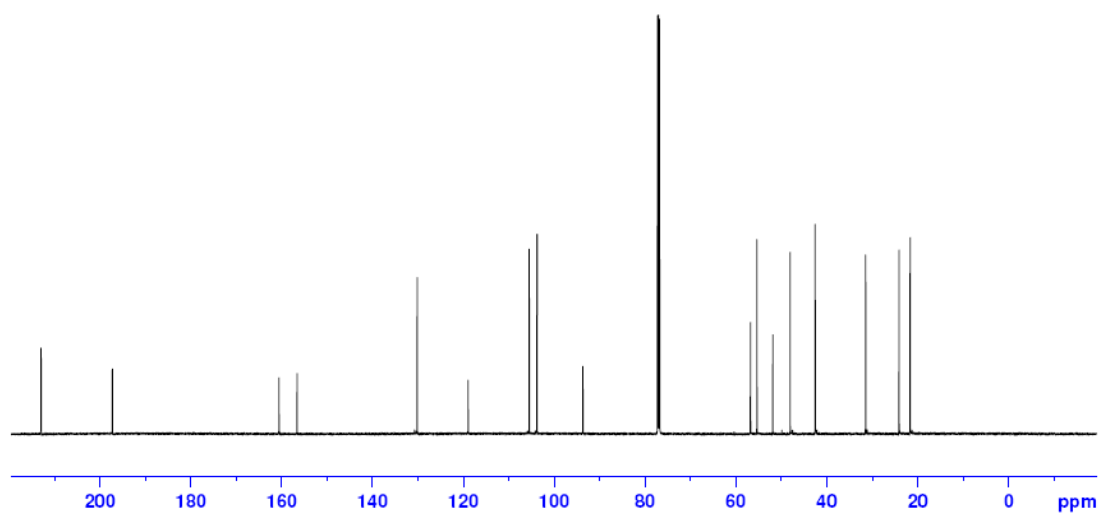


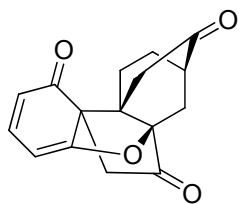


¹H NMR spectrum (600 MHz, CDCl₃)



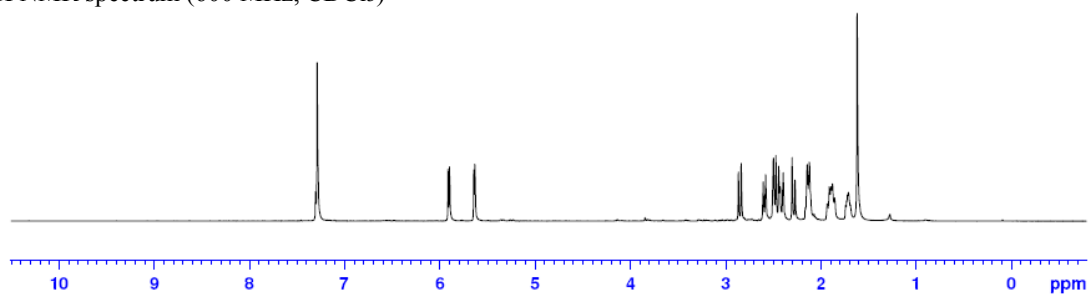
¹³C NMR spectrum (150 MHz, CDCl₃)



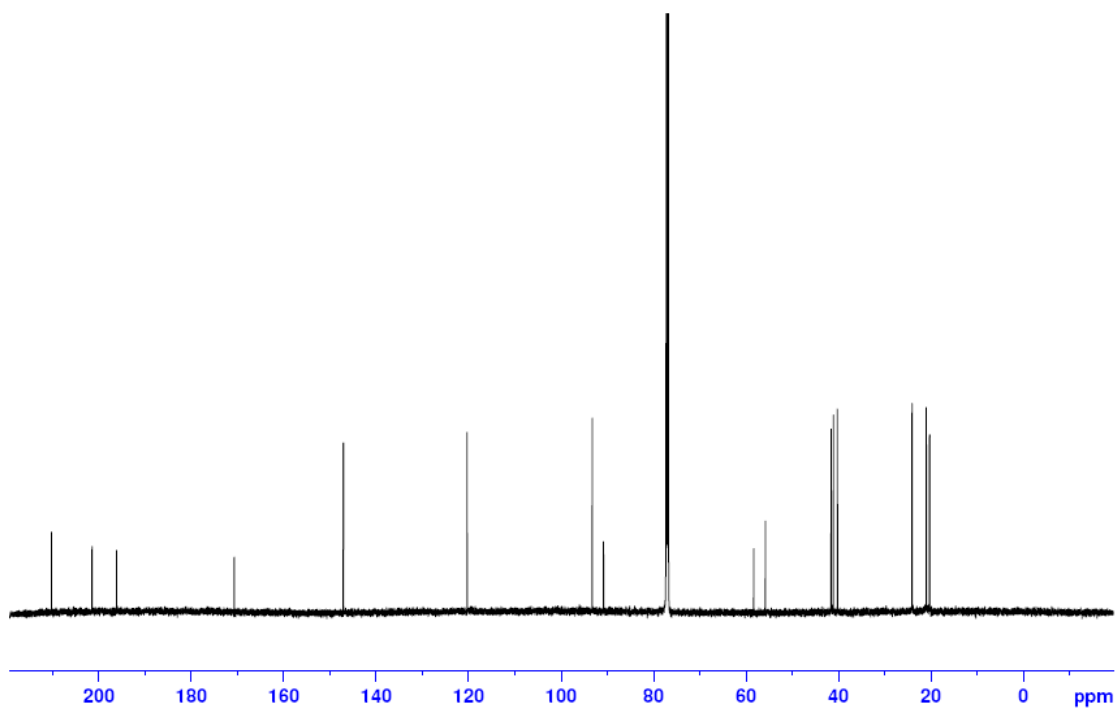


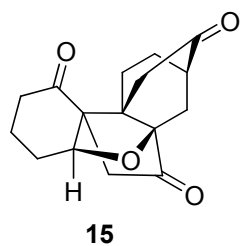
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^1H NMR spectrum (600 MHz, CDCl_3)

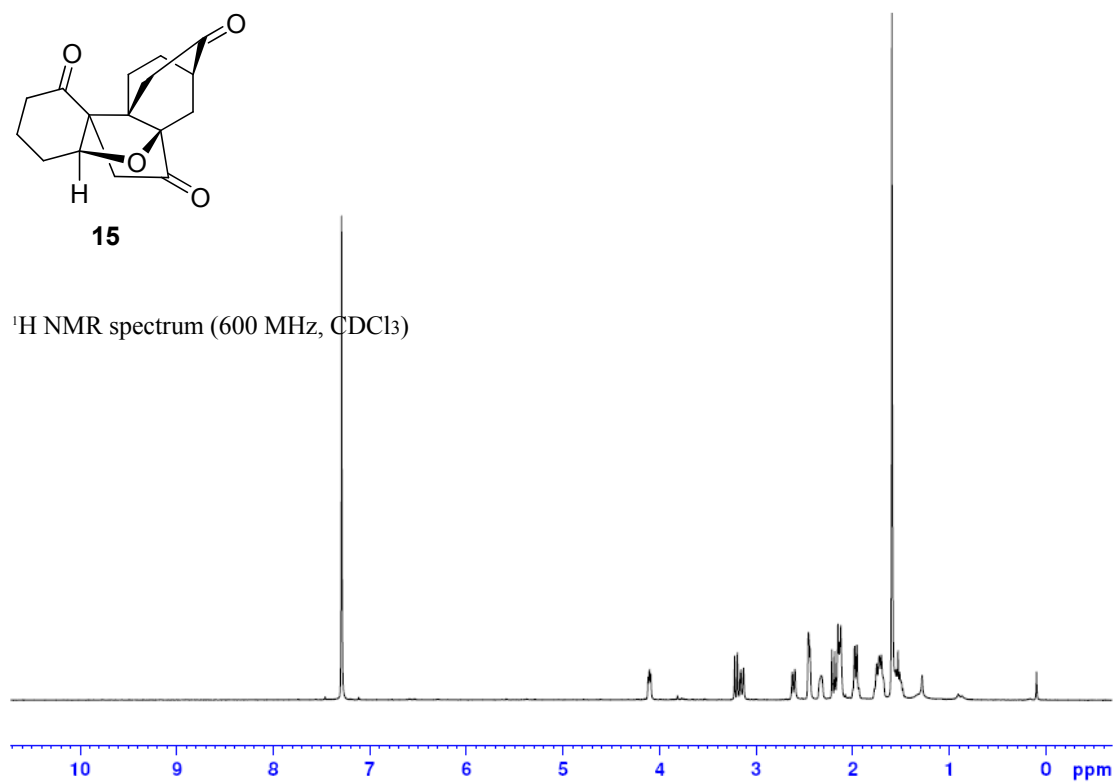


^{13}C NMR spectrum (150 MHz, CDCl_3)

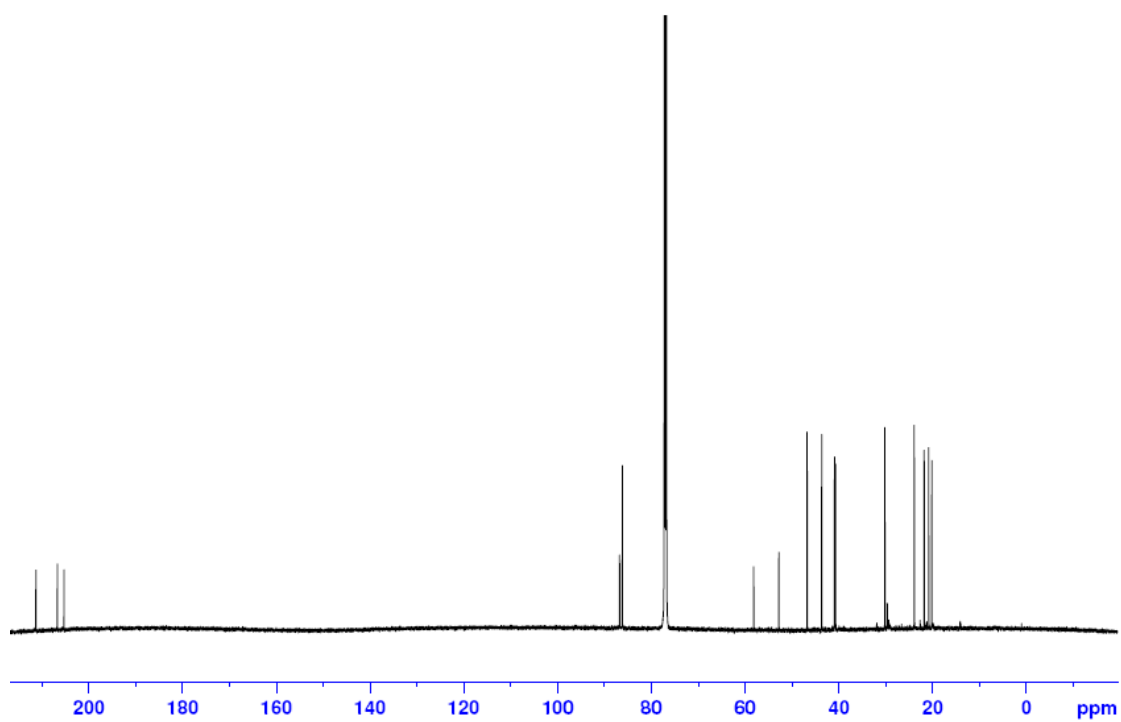


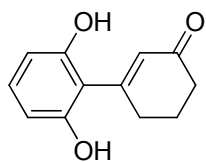


^1H NMR spectrum (600 MHz, CDCl_3)



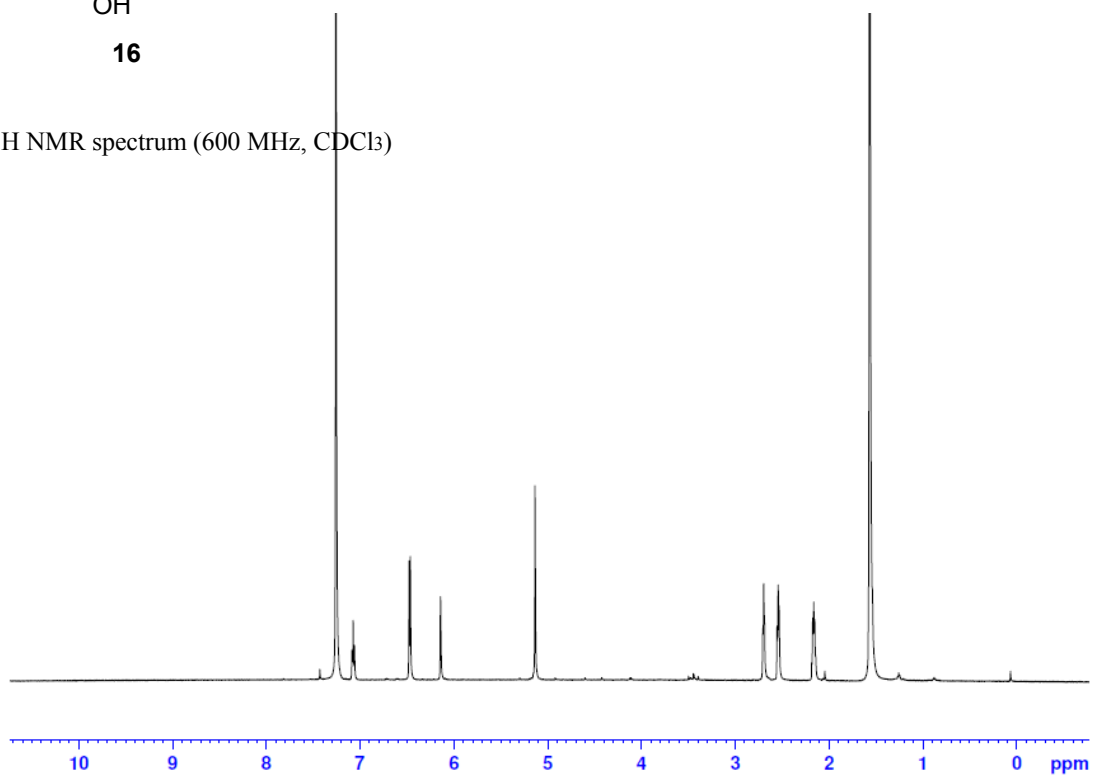
^{13}C NMR spectrum (150 MHz, CDCl_3)



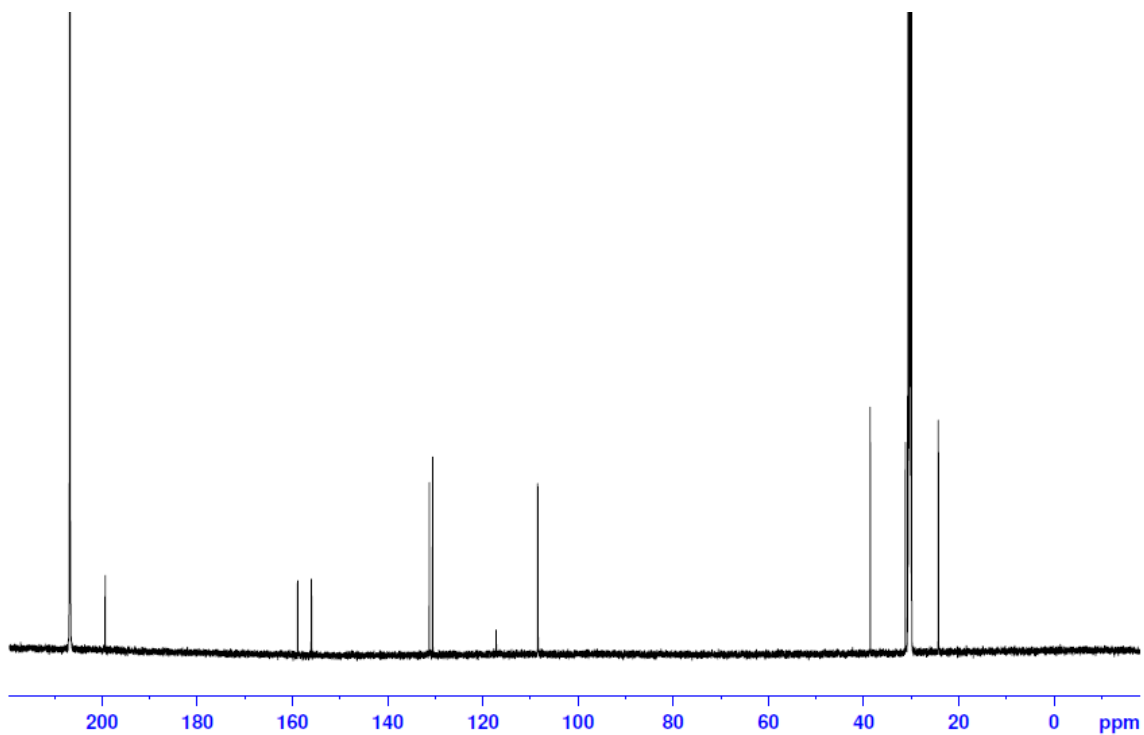


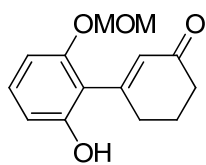
16

^1H NMR spectrum (600 MHz, CDCl_3)



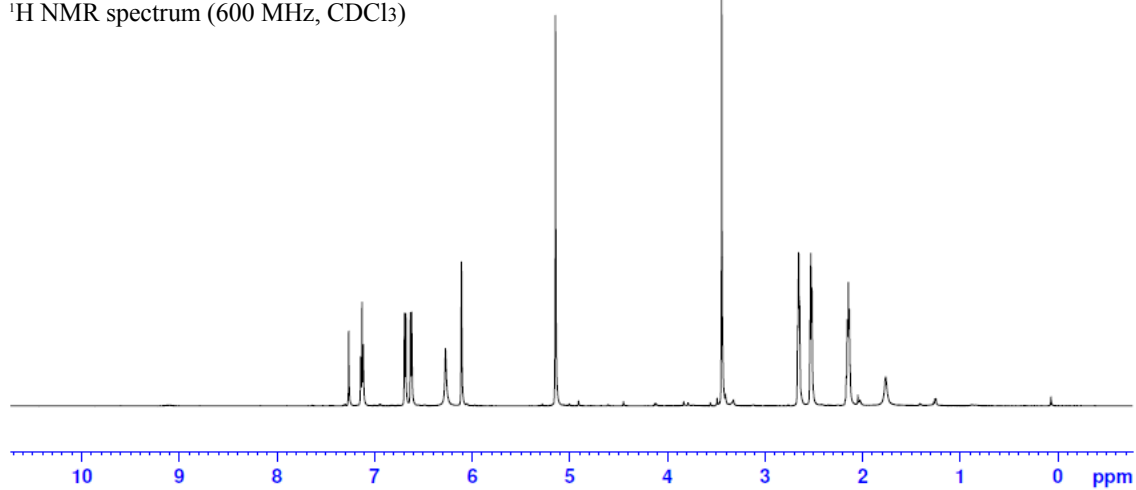
^{13}C NMR spectrum (150 MHz, CD_3COCD_3)



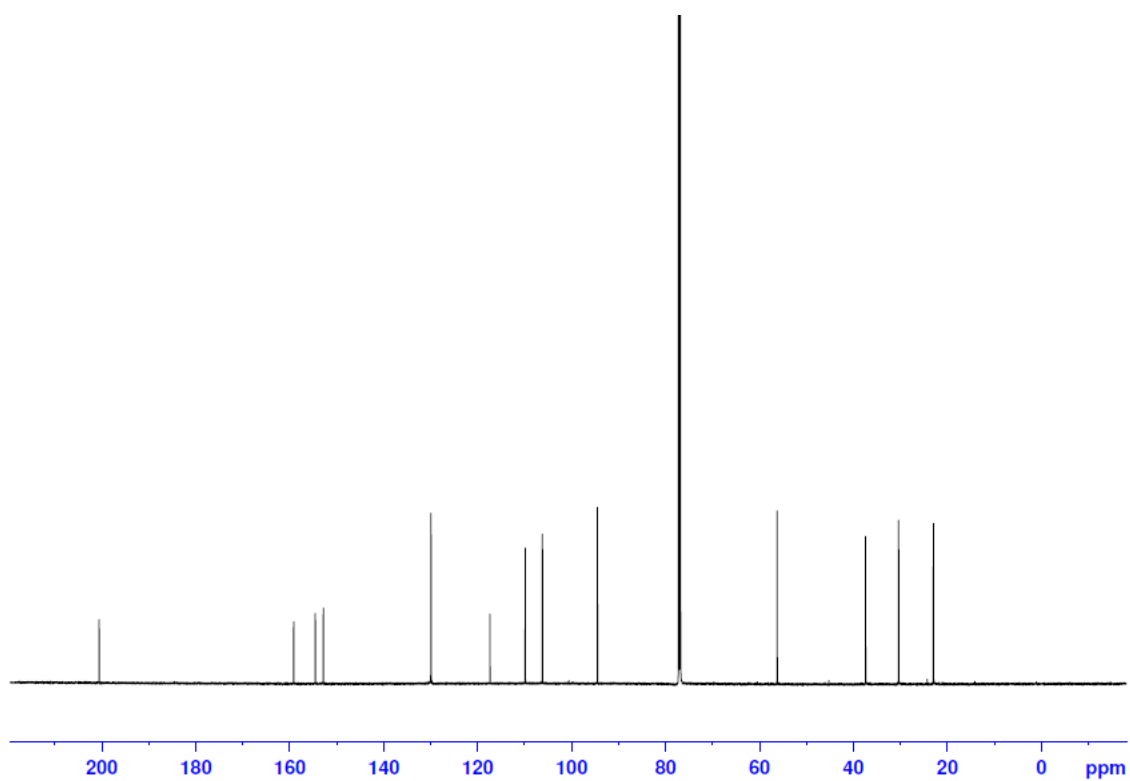


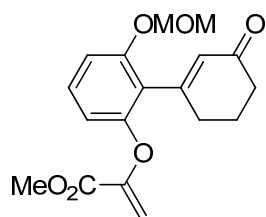
17

^1H NMR spectrum (600 MHz, CDCl_3)



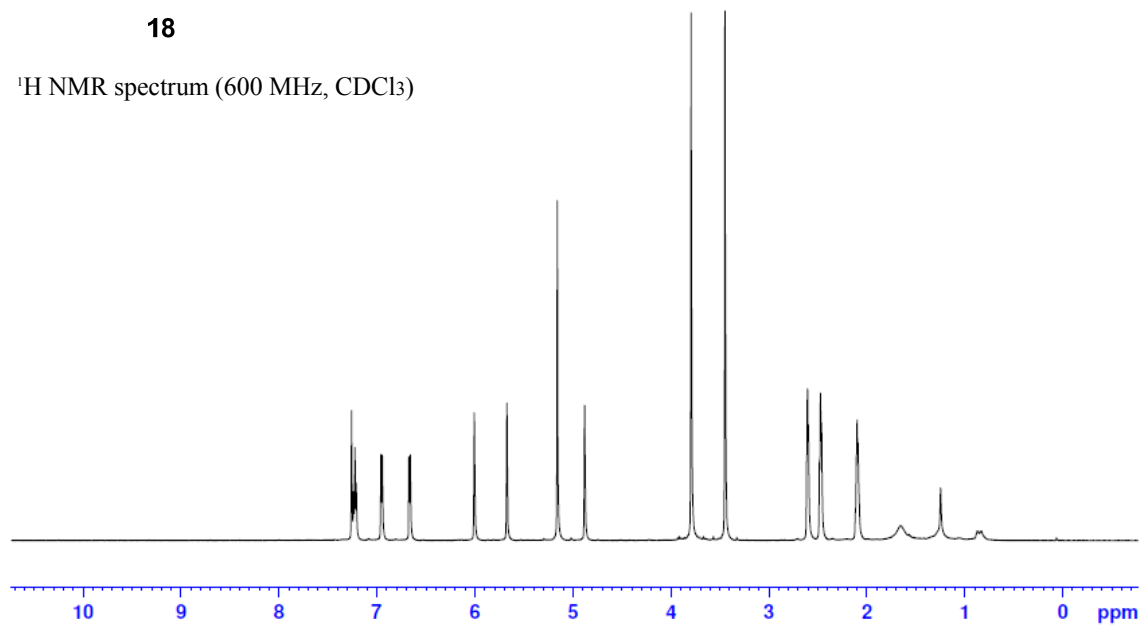
^{13}C NMR spectrum (150 MHz, CDCl_3)



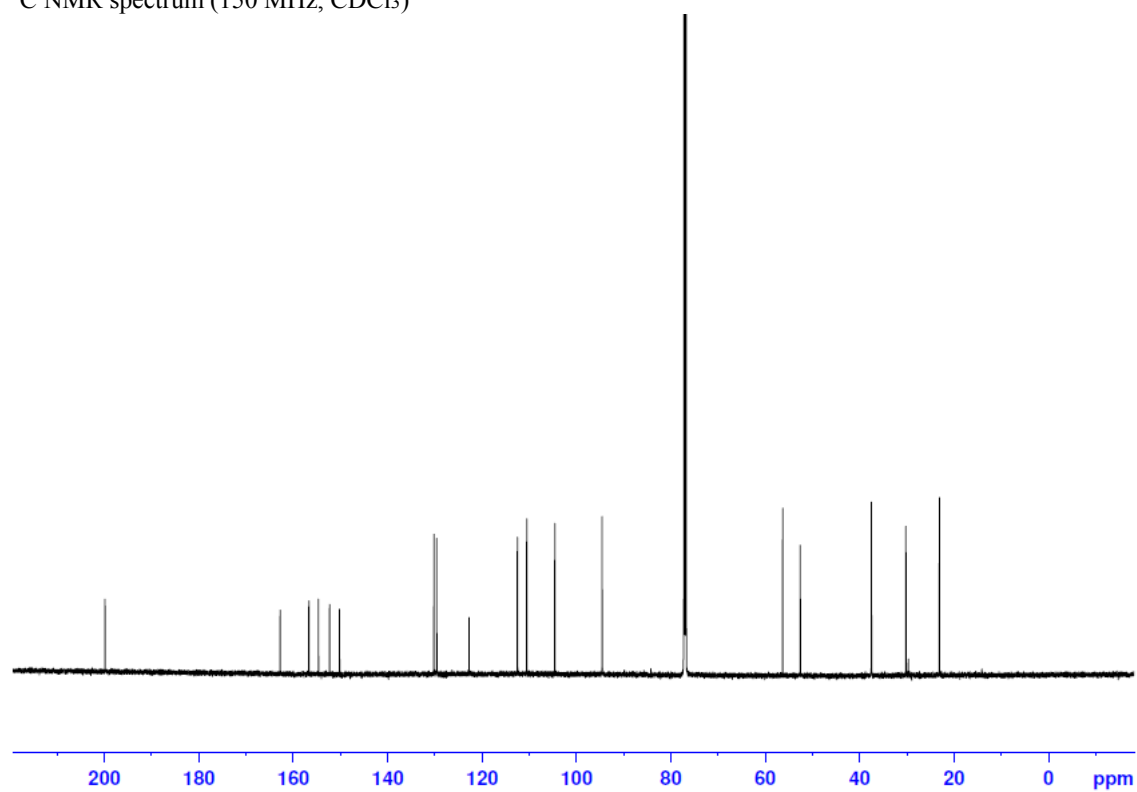


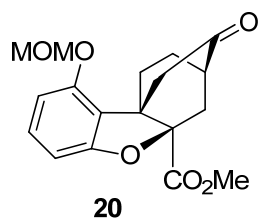
18

¹H NMR spectrum (600 MHz, CDCl₃)

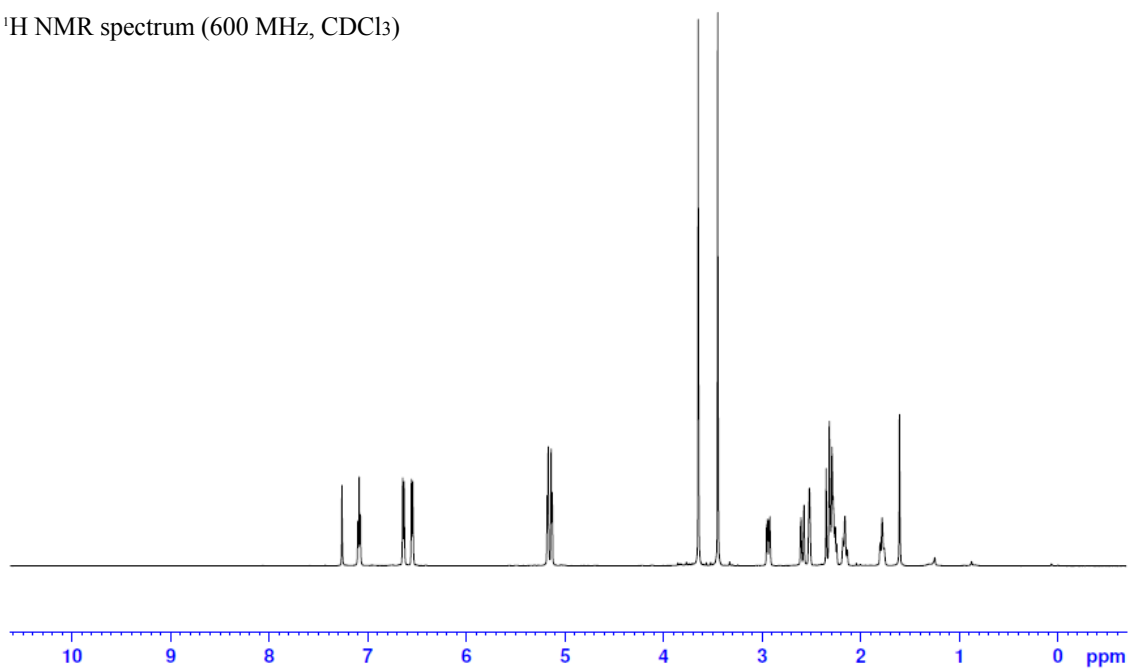


¹³C NMR spectrum (150 MHz, CDCl₃)

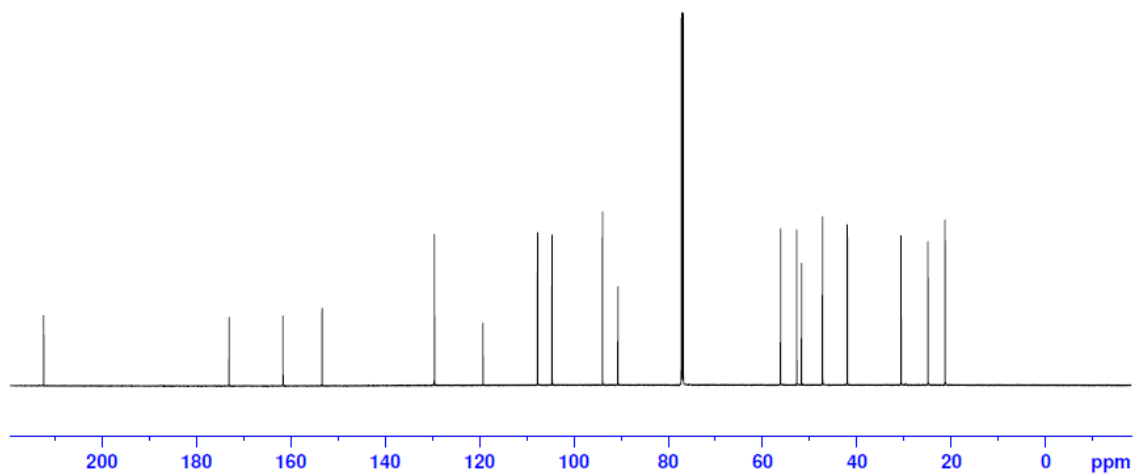


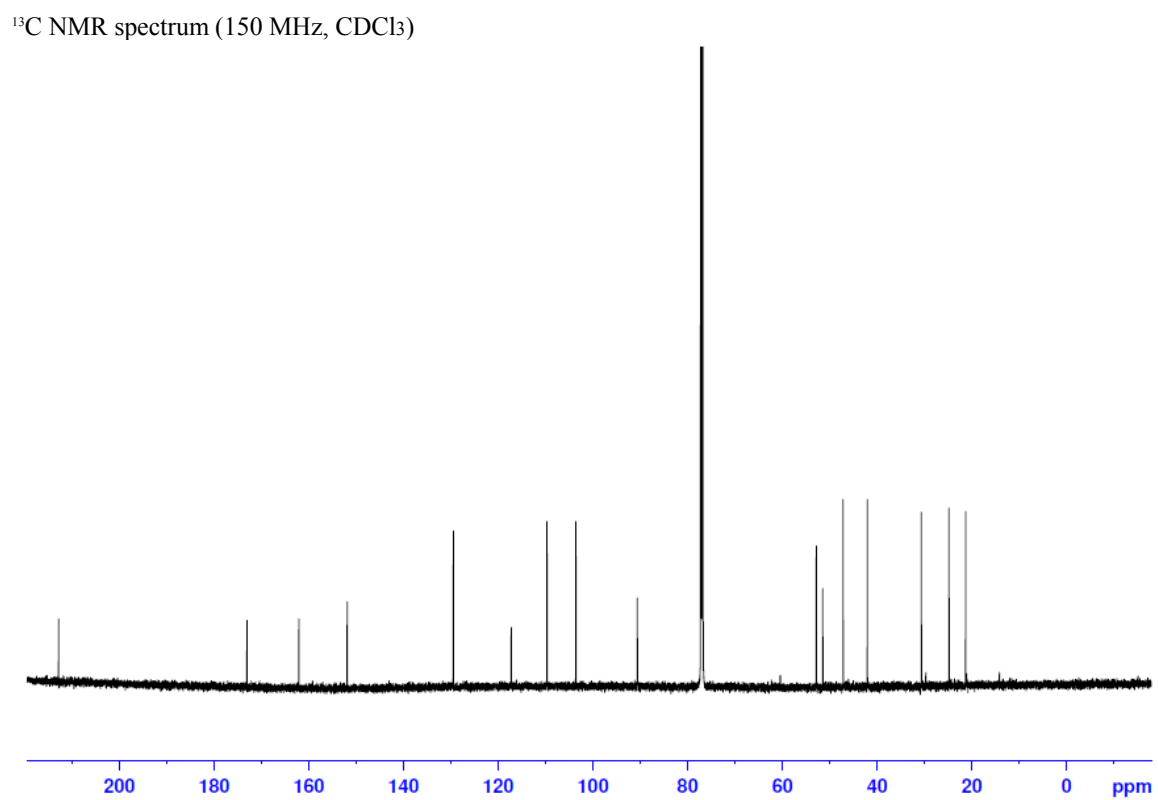
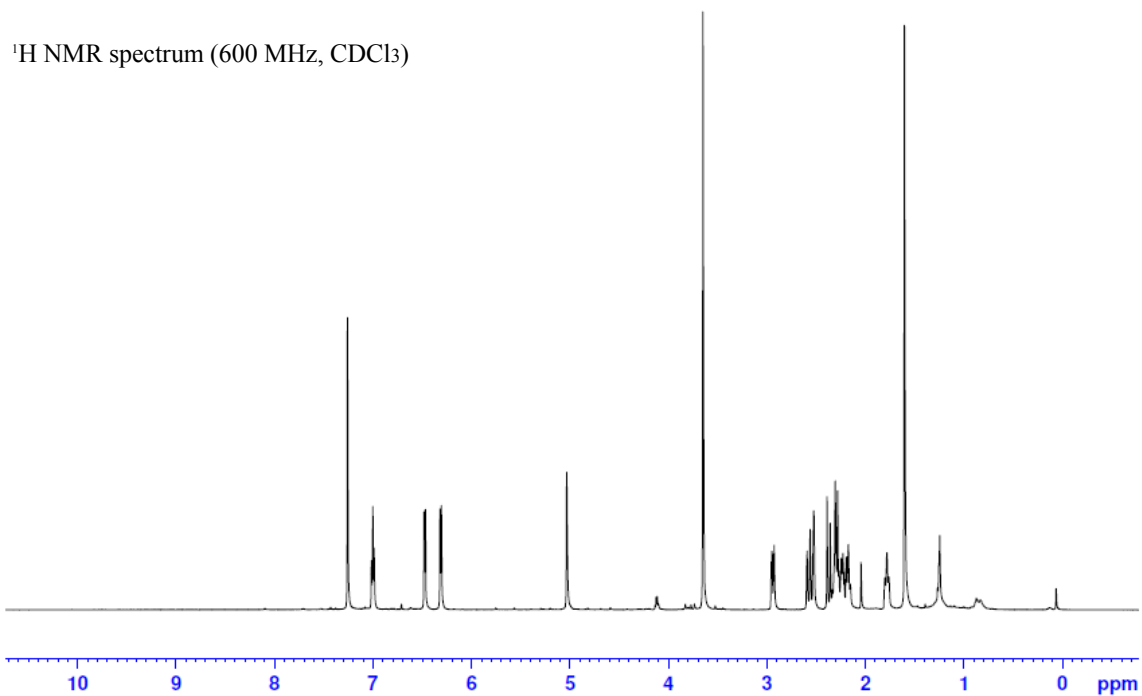
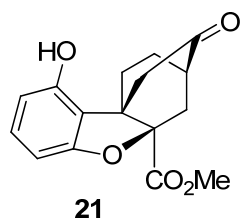


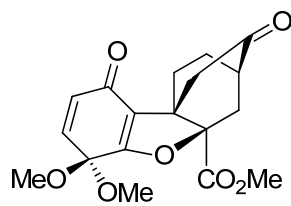
¹H NMR spectrum (600 MHz, CDCl₃)



¹³C NMR spectrum (150 MHz, CDCl₃)

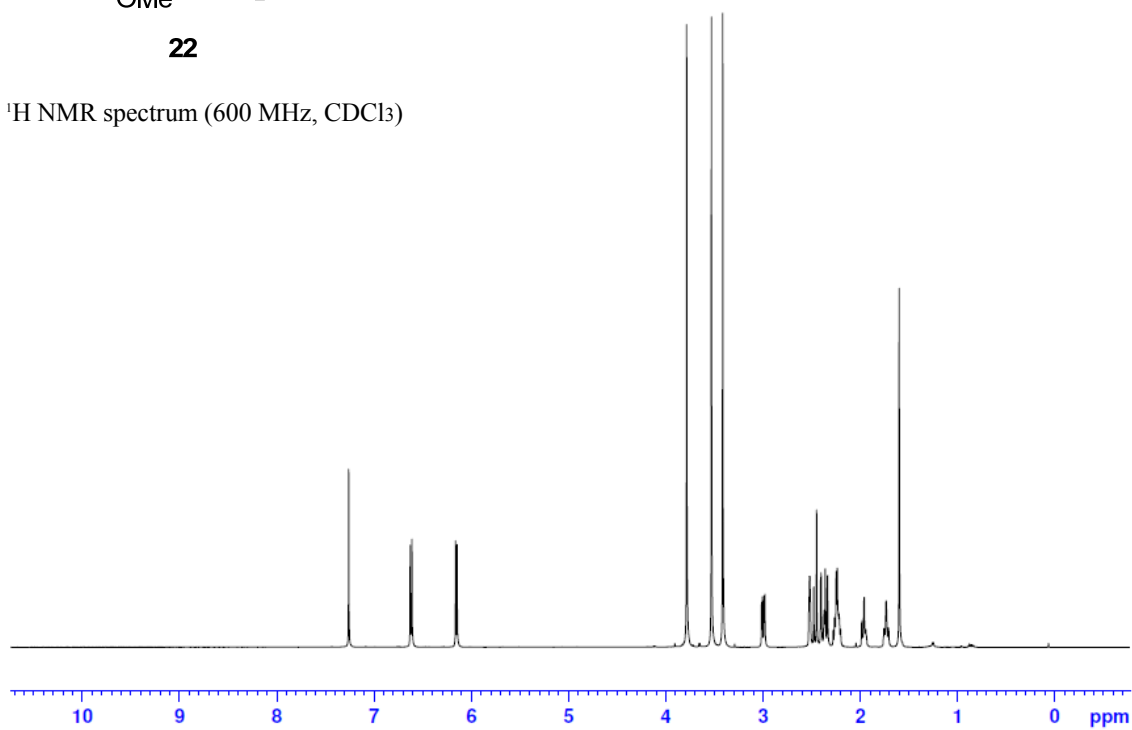




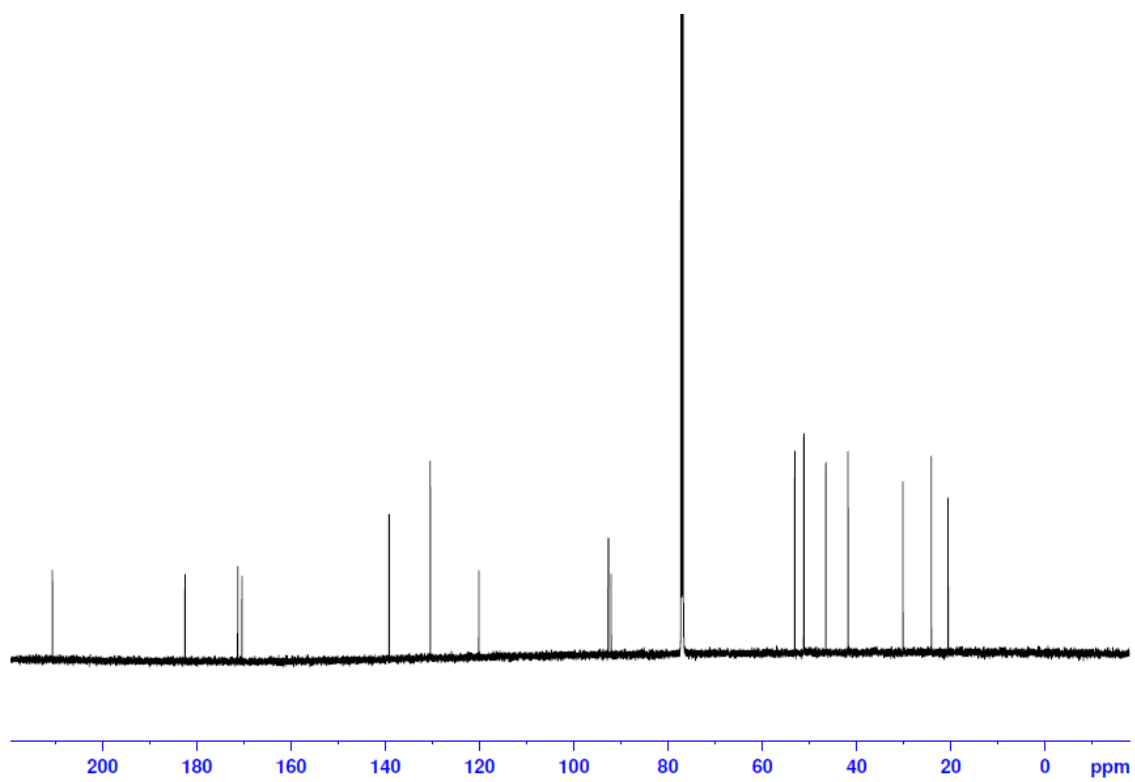


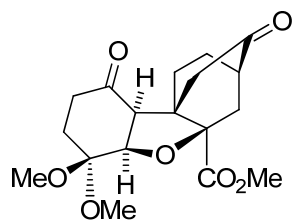
22

¹H NMR spectrum (600 MHz, CDCl₃)



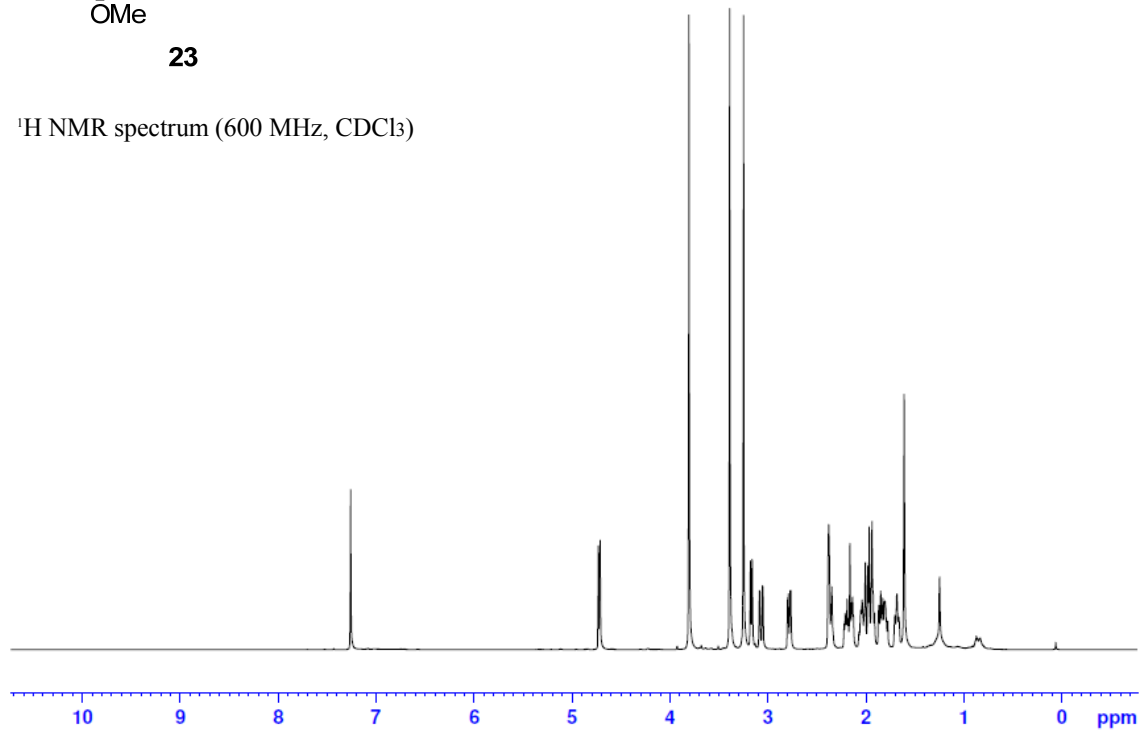
¹³C NMR spectrum (150 MHz, CDCl₃)



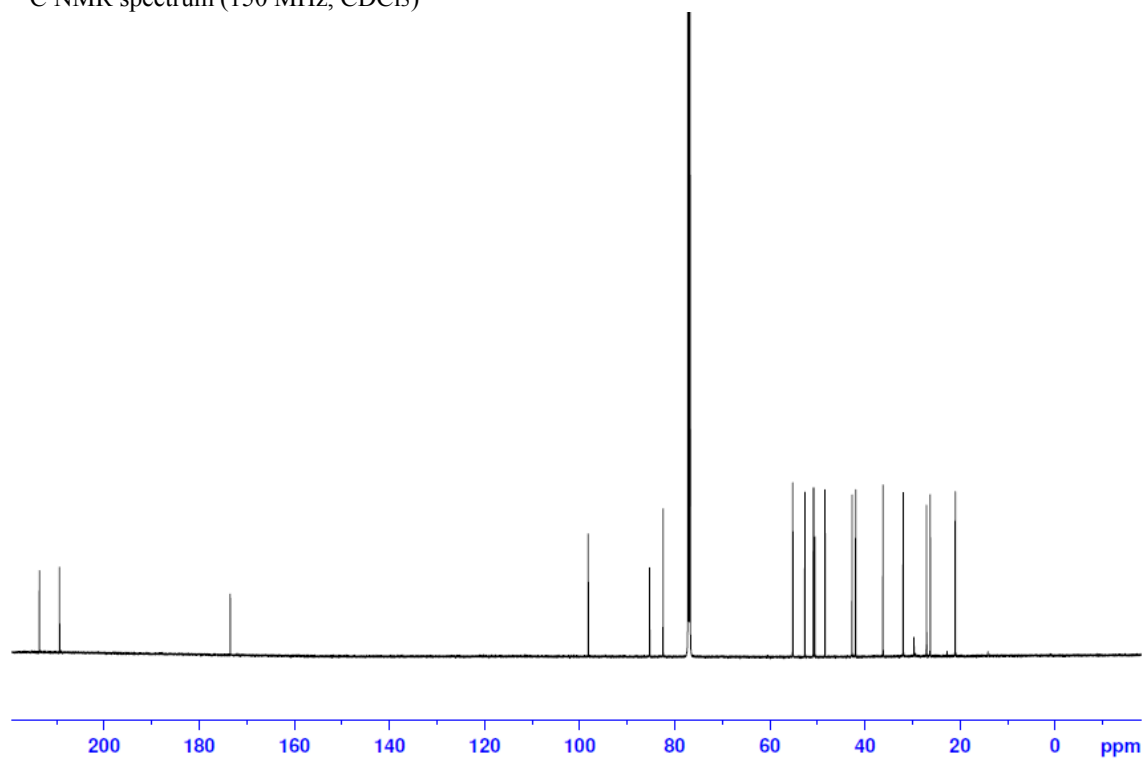


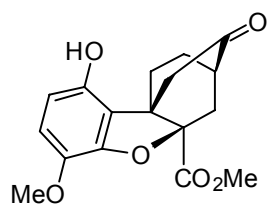
23

^1H NMR spectrum (600 MHz, CDCl_3)



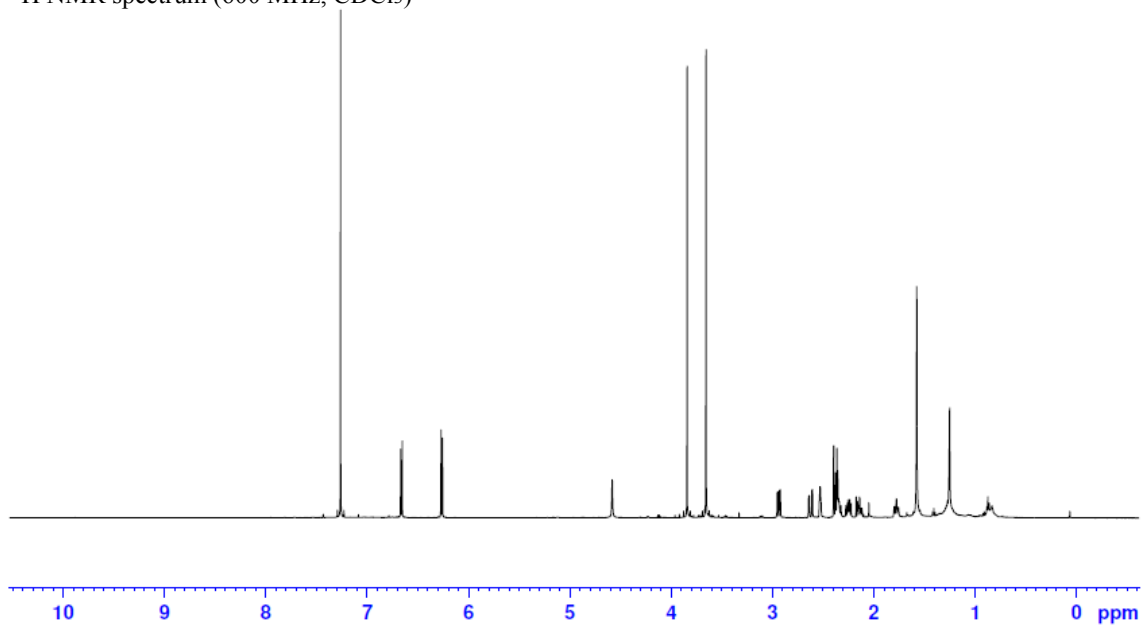
^{13}C NMR spectrum (150 MHz, CDCl_3)



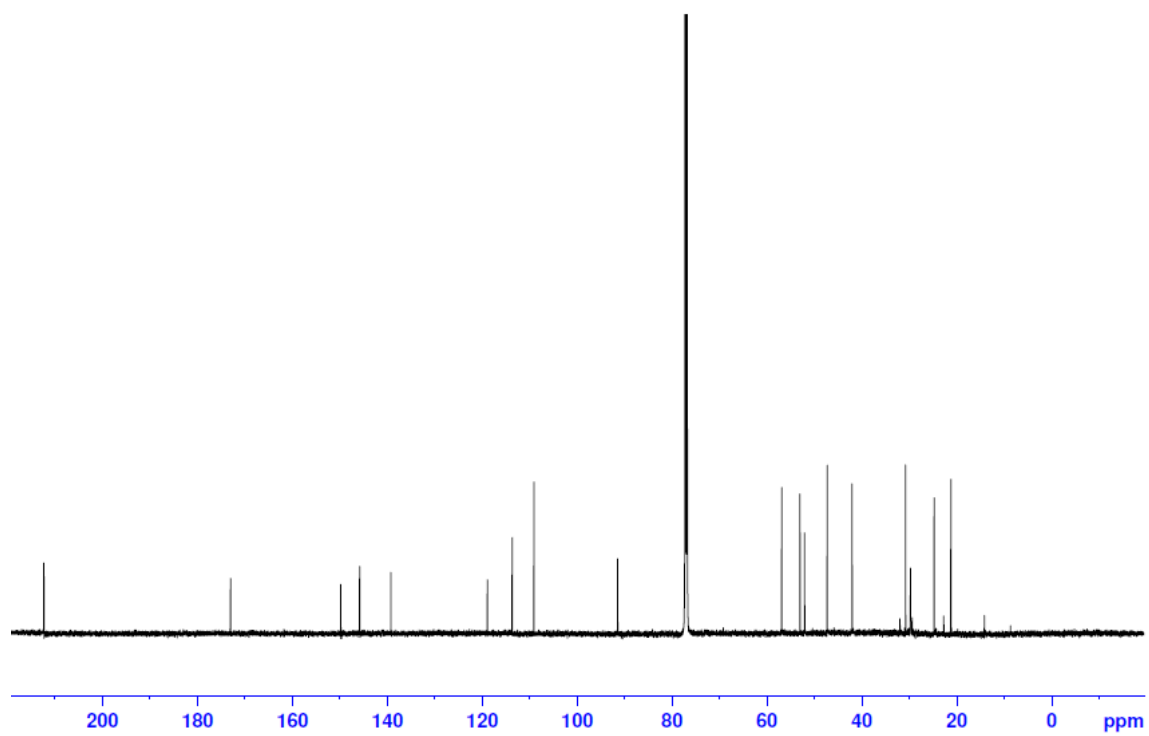


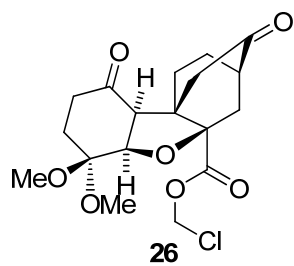
24

¹H NMR spectrum (600 MHz, CDCl₃)

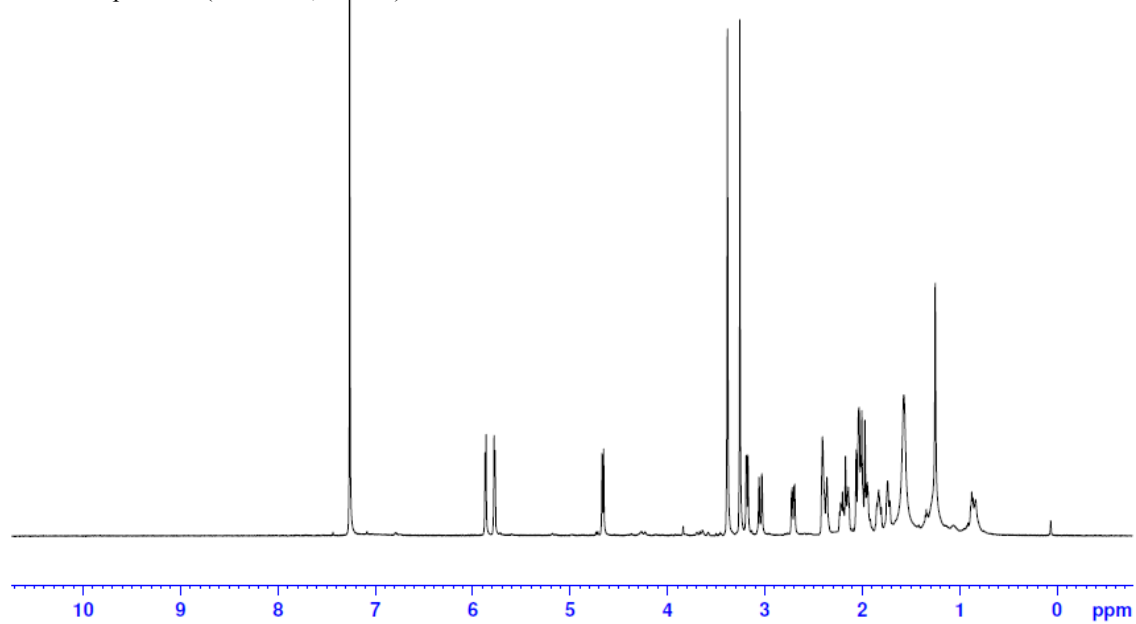


¹³C NMR spectrum (150 MHz, CDCl₃)

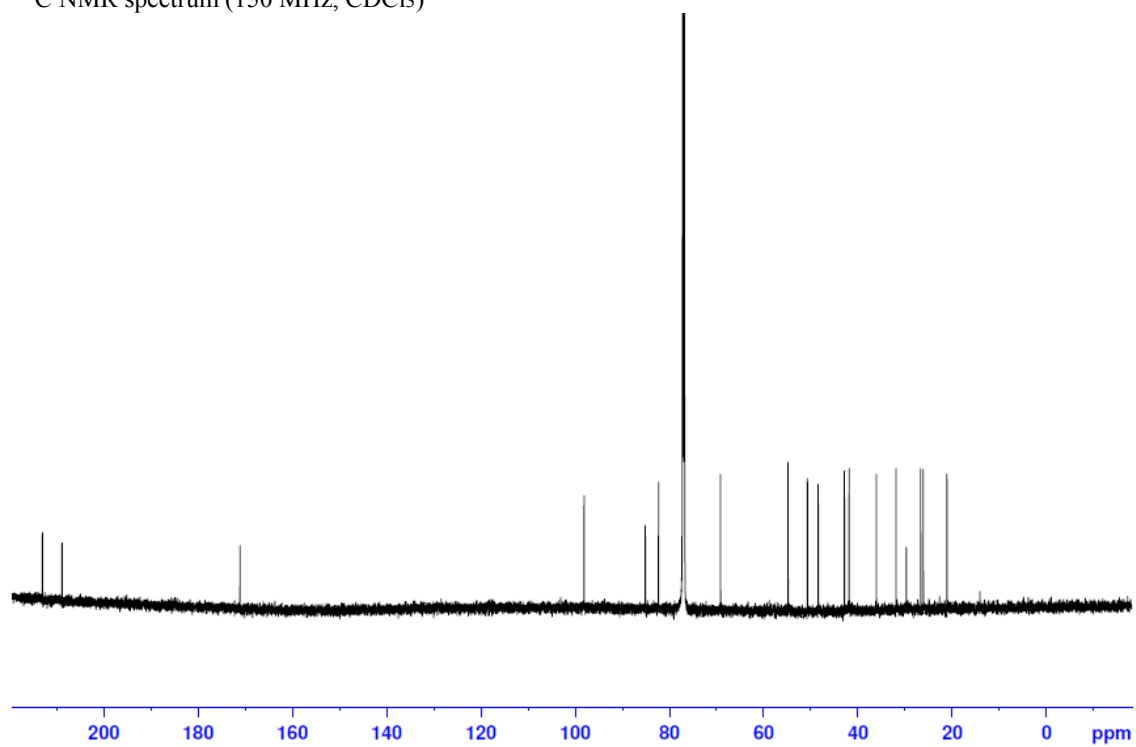


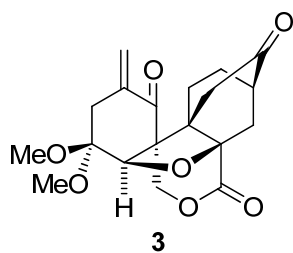


¹H NMR spectrum (600 MHz, CDCl₃)

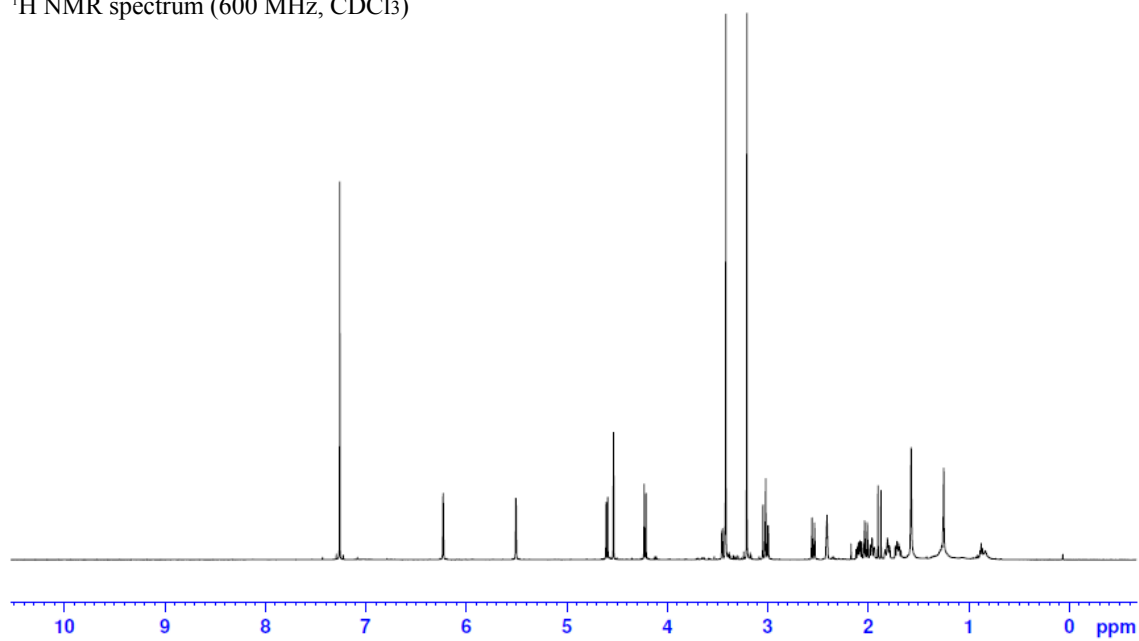


¹³C NMR spectrum (150 MHz, CDCl₃)





^1H NMR spectrum (600 MHz, CDCl_3)



^{13}C NMR spectrum (150 MHz, CDCl_3)

