Supporting Information

Monocyclic Quinone Structure-Activity Patterns: Synthesis of Catalytic Inhibitors of Topoisomerase II with Potent Anti-Proliferative Activity

Thomas M. Waugh,[a] John Masters,[b] Abil E. Aliev,[a] and Charles M. Marson*,[a]

[a]*Department of Chemistry, University College London, Christopher Ingold Laboratories, 20 Gordon Street, London WC1H 0AJ, U.K.*

[b]*Prostate Cancer Research Centre, Research Department of Urology, Charles Bell House, University College London, 67-75 Riding House Street, London W1W 7EJ, U.K.*

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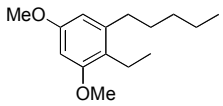
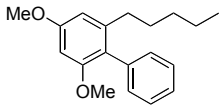


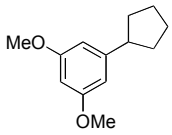
2-Ethyl-1,5-dimethoxy-3-pentylbenzene (1b).

A solution of 2-ethynyl-1,5-dimethoxy-3-pentylbenzene (**18**) (0.30 g, 1.29 mmol) in methanol (6.5 mL) and 5% palladium on carbon (50 mg) was flushed with nitrogen, evacuated, then the flask charged with hydrogen which was maintained at 1 atm. The mixture was stirred at 20 °C for 48 h, then filtered through a short pad of celite. Evaporation gave **1b** (0.18 g, 59%) as a yellow oil; IR ν_{max} (cm^{-1}) 1605 (aryl), 1587 (aryl); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.32 (2H, s, aryl), 3.79 (3H, s, CH_3), 3.78 (3H, s, CH_3), 2.65–2.51 (4H, m, 2aryl-CH_2), 1.59–1.51 (2H, m, aryl-CH_2CH_2), 1.40–1.33 (4H, m, CH_2C$H_2$$CH_3$), 1.07 (3H, t, J = 7.4 Hz, aryl-CH_2CH_3), 0.90 (3H, t, J = 7.1 Hz, CH_2CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.6, 158.2, 142.5, 123.3, 105.6 (C-4), 96.1 (C-6), 55.5 (OCH_3), 55.3 (OCH_3), 33.4, 31.7, 31.4, 22.7, 18.8, 14.9, 14.2; MS (ESI^+) *m/z* (%): 236 (M^+, 44), 221 (31), 180 (41), 165 (100), 152 (42), 135 (15). HRMS *m/z* M^+ calcd. for $C_{15}H_{25}O_2$: 237.1849, found: 237.1850.

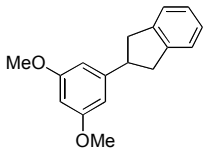


2,4-Dimethoxy-6-pentyl-1,1'-biphenyl (1c). A solution of 2-iodo-1,5-dimethoxy-3-pentylbenzene (**17**)[1] (0.60 g, 1.80 mmol), phenylboronic acid (0.438 g, 3.59 mmol) and sodium carbonate (0.57 g, 5.39 mmol) in 1,2-dimethoxyethane: water (18 mL, 1:1) was purged with nitrogen for 15 min then tetrakis(triphenylphosphine)palladium(0) (0.414 g, 0.359 mmol) was added in one portion. The mixture was then heated at 75 °C for 72 h under an atmosphere of nitrogen. After allowing to cool, the mixture was filtered through a short pad of celite, and the pad then washed with water. The filtrate was extracted with ethyl acetate (3 x 25 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1.5: 98.5 ethyl acetate: hexane) to give **1c** (0.35 g, 69%) as a pale yellow oil; IR ν_{max} (cm^{-1}) 1606 (aryl), 1595 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (2H, dd, J = 11.3, 4.1 Hz), 7.33 (1H, m), 7.23–7.16 (2H, m), 6.47 (1H, d, J = 1.7 Hz, H-4), 6.42 (1H, d, J = 1.7 Hz, H-2), 3.87 (3H, s, OCH_3), 3.69 (3H, s, OCH_3), 2.41–2.32 (2H, m, aryl-CH_2), 1.46–1.41 (2H, m, aryl-CH_2CH_2), 1.22–1.11 (4H, m, CH_2C$H_2$$CH_3$), 0.80 (3H, t, J =

6.7 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 158.1, 143.4, 137.5, 130.7, 127.9, 126.6, 123.7, 105.4 (C-5), 96.1 (C-3), 55.8 (OCH_3), 55.4 (OCH_3), 33.6, 31.7, 30.9, 22.4, 13.9; MS (ESI^+) *m/z* (%): 307 ($[M+Na]^+$, 100), 285 ($[M+H]^+$, 96), 253 (5). HRMS *m/z* M^+ calcd. for $C_{19}H_{25}O_2$: 285.1855 $[M+H]^+$, found: 285.1852.

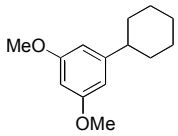


1-Cyclopentyl-3,5-dimethoxybenzene (1d). 1-(Cyclopent-1-en-1-yl)-3,5-dimethoxybenzene (**11**) (0.13 g, 0.637 mmol) was dissolved in dichloromethane (1.3 mL) and stirred at 20 °C under nitrogen. Trifluoroacetic acid (0.50 mL, 6.37 mmol) was added dropwise to the stirred solution and stirring continued for 15 min. Then triethylsilane (0.50 mL, 3.15 mmol) was added and the mixture stirred for 1 h at 20 °C. Saturated aqueous sodium hydrogen carbonate (10 mL) was added and the mixture was extracted with dichloromethane (3 x 10 mL). The combined organic layers were washed with water (30 mL), dried ($MgSO_4$), filtered and and evaporated. The residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give **1d** (0.052 g, 40%) as a colourless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 6.43 (2H, d, *J* = 2.3 Hz), 6.32 (1H, t, *J* = 2.3 Hz), 3.80 (6H, s, 2 x OCH_3), 2.96 (1H, m), 2.09–2.03 (2H, m), 1.84–1.78 (2H, m), 1.73–1.57 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8 (C-3,5), 149.2 (C-1), 105.4 (C-2,6), 97.6 (C-4), 55.3 (2 x OCH_3), 46.3 (CH), 34.5, 25.6; MS (EI) *m/z* (%): 206 (M^+, 45), 165 (100), 151 (5), 121 (3), 91 (6). HRMS *m/z* M^+ calcd. for $C_{13}H_{18}O_2$: 206.1306, found: 206.1301.

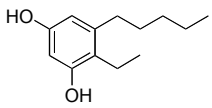


2-(3,5-Dimethoxyphenyl)indane (1e). To a solution of 2-(3,5-dimethoxyphenyl)-1*H*-indene (**16**) (0.167 g, 0.66 mmol) in absolute ethanol (3.3 mL) was added 5% palladium on carbon (50 mg). Ammonium formate (0.418 g, 6.60 mmol) was then added and the suspension was stirred at reflux for 4 h under nitrogen, then filtered through celite. The filtrate was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were washed with water (25 mL) then with hydrochloric acid (25 mL, 2.0 M). The organic layer was dried ($MgSO_4$), filtered and evaporated to give

1e (0.15 g, 90%) as a brown oil; IR ν_{max} (cm^{-1}) 1591 (aryl); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.16 (4H, m, indenyl), 6.48 (2H, d, *J* = 2.2 Hz), 6.35 (1H, t, *J* = 2.2 Hz), 3.79 (6H, s, 2 x OCH_3), 3.63 (m, 1H, CH), 3.34 (2H, dd, *J* = 15.3, 8.2 Hz), 3.09 (2H, dd, *J* = 15.3, 9.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9 (C-3,5), 148.1 (C-1), 143.0, 126.6, 124.5, 105.4 (C-2,6), 98.1 (C-4), 55.4 (2 x OCH_3), 45.9 (*C*H), 40.9; MS (EI) *m/z* (%): 254 (M^+, 100), 239 (13), 223 (19), 208 (7), 179 (9). HRMS *m/z* M^+ calcd. for $C_{17}H_{18}O_2$: 254.1301, found: 254.1302.

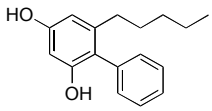


1-Cyclohexyl-3,5-dimethoxybenzene (1f). To a solution of 1-cyclohexenyl-3,5-dimethoxybenzene (**12**) (0.12 g, 0.55 mmol) in absolute ethanol (2.74 mL) was added 5% palladium on carbon (50 mg). Ammonium formate was added (3.60 g, 54.9 mmol) and the suspension was stirred at reflux for 2 h under nitrogen. Then the mixture was filtered through celite and the filtrate extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with water (25 mL) then with hydrochloric acid (25 mL, 2.0 M), dried ($MgSO_4$), filtered and evaporated to give **1f** (0.073 g, 61%) as a brown oil; IR ν_{max} (cm^{-1}) 1592 (aryl); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.42 (2H, d, *J* = 2.3 Hz), 6.34 (1H, t, *J* = 2.3 Hz), 3.82 (6H, s), 2.48 (1H, tt, *J* = 11.4, 3.2 Hz, CH), 1.96–1.82 (8H, m), 1.49–1.39 (4H, m), 1.30 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1 (C-3,5), 151.1 (C-1), 105.4 (C-2,6), 97.9 (C-4), 55.6 (2 x OCH_3), 45.4 (CH), 34.8, 27.3, 26.6; MS (EI) *m/z* (%): 220 (M^+, 84), 205 (16), 191 (9), 179.1 (20), 165.1 (100), 152 (55). HRMS *m/z* M^+ calcd. for $C_{14}H_{20}O_2$: 220.1458, found: 220.1459.

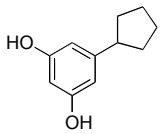


4-Ethyl-5-pentylbenzene-1,3-diol (2b). 2-Ethyl-1,5-dimethoxy-3-pentylbenzene (**1b**) (0.079 g, 0.334 mmol) was demethylated using general procedure A. Purification by flash column chromatography (3:7 ethyl acetate: petroleum ether 40–60 °C) gave **2b** (0.039 g, 56%) as an amber oil; IR ν_{max} (cm^{-1}) 3437 (O-H), 1594 (aryl); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.27 (1H, d, *J* = 2.2 Hz), 6.19 (1H, d, *J* = 2.2 Hz), 5.84–5.27 (2H, br.

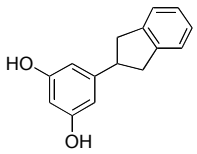
s, OH), 2.57 (2H, q, J = 7.5 Hz, aryl-CH_2CH$_3$), 2.53–2.48 (2H, m, aryl-CH_2CH$_2$), 1.57–1.49 (2H, m, aryl-CH$_2$CH_2), 1.37–1.32 (4H, m, CH_2CH_2CH$_3$), 1.11 (3H, t, J = 7.5 Hz, aryl-CH$_2$CH_3), 0.90 (3H, t, J = 7.0 Hz, CH$_2$CH$_2$CH_3); ^{13}C NMR (150 MHz, CDCl$_3$) δ 154.5, 153.6, 143.6, 121.1, 108.8 (C-6), 100.8 (C-2), 33.0, 32.1, 31.2, 22.7, 18.7, 14.7, 14.2; MS (EI) *m/z* (%): 208 (M$^+$, 18), 193 (6), 152 (16), 137 (42), 124 (15). HRMS *m/z* M$^+$ calcd. for $C_{13}H_{20}O_2$: 208.1463, found: 208.1461.



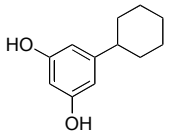
6-Pentyl-[1,1'-biphenyl]-2,4-diol (2c). 2,4-Dimethoxy-6-pentyl-1,1'-biphenyl (**1c**) (0.352 g, 1.24 mmol) was demethylated using general procedure A. Purification of the residue by flash column chromatography (1:4 ethyl acetate: hexane) gave **2c** (0.23 g, 75%) as a pale yellow oil; IR ν_{max} (cm^{-1}) 3361 (O-H), 1621 (aryl), 1590 (aryl); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.53–7.37 (3H, m, aryl), 7.30–7.23 (2H, m), 6.37 (1H, d, J = 2.5 Hz, H-1), 6.35 (1H, d, J = 2.5 Hz, H-3), 4.85 (1H, s, OH), 4.74 (1H, s, OH), 2.31–2.28 (m, 2H, aryl-CH_2), 1.41–1.37 (2H, m, aryl-CH$_2$CH_2), 1.18–1.12 (4H, m, CH_2CH_2CH$_3$), 0.78 (3H, t, J = 6.8 Hz, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 155.9, 153.9, 143.5, 134.9, 131.2, 129.5, 128.2, 120.9, 108.2 (C-1), 99.9 (C-3), 33.4, 31.6, 30.6, 22.4, 14.0; MS (EI) *m/z* (%): 256.2 (M$^+$, 55), 200 (100), 181 (14), 152 (9). HRMS *m/z* M$^+$ calcd. for $C_{17}H_{20}O_2$: 256.1458, found: 256.1459.



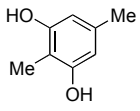
5-Cyclopentylbenzene-1,3-diol (2d). 1-Cyclopentyl-3,5-dimethoxybenzene (0.050 g, 0.242 mmol) was demethylated using general procedure A. Purification by flash column chromatography (1:4 ethyl acetate: hexane) gave **2d** (0.038 g, 89%) as a colourless oil; IR ν_{max} (cm^{-1}) 3328 (O-H), 1596 (aryl), 1506 (aryl); ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.31 (2H, d, J = 2.2 Hz, H-4,6), 6.18 (1H, t, J = 2.2 Hz, H-2), 6.25 (2H, br. s, 2OH), 2.80 (1H, m, CH), 1.96–1.88 (2H, m), 1.73–1.68 (2H, m), 1.64–1.58 (2H, m), 1.50–1.43 (2H, m); ^{13}C NMR (125 MHz, CDCl$_3$) δ 156.4 (C-2,4), 150.2 (C-6), 107.1 (C-1,5), 100.5 (C-3), 45.8 (CH), 34.3, 25.4; MS (EI) *m/z* (%): 178 (M$^+$, 47) 137 (100). HRMS *m/z* M$^+$ calcd. for $C_{11}H_{14}O_2$: 178.0988, found: 178.0989.



5-(Indan-2-yl)benzene-1,3-diol (2e). 2-(3,5-Dimethoxyphenyl)indane (**1e**) (0.172 g, 0.68 mmol) was demethylated using general procedure A. Purification by flash column chromatography (2:3 ethyl acetate: hexane) gave **2e** (0.12 g, 81%) as cream prisms, m.p. 98-100 °C; IR ν_{max} (cm^{-1}) 3325 (O-H), 1598 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.24 (2H, m, 4,7-indanyl), 7.24–7.18 (2H, m, 5,6-indanyl), 6.37 (2H, d, *J* = 2.1 Hz, H-2,6), 6.24 (1H, t, *J* = 2.1 Hz, H-4), 4.94 (2H, s, 2OH), 3.58 (1H, *J* = 8.5 Hz, CH), 3.32 (2H, dd, *J* = 15.5, 8.2 Hz), 3.05 (2H, dd, *J* = 15.5, 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0 (C-1,3), 149.3 (C-5), 143.2, 126.9, 124.7, 107.2 (C-4,6), 101.1 (C-2), 45.5, 41.0; MS (EI) *m/z* (%): 226 (M^+, 100), 211 (24), 165 (11), 141 (9), 129 (14), 116 (24). HRMS *m/z* M^+ calcd. for $C_{15}H_{14}O_2$: 226.0988, found: 226.0989.

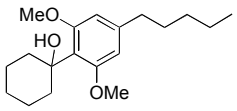


5-Cyclohexylbenzene-1,3-diol (2f). 1-Cyclohexyl-3,5-dimethoxybenzene (**1f**) (0.073 g, 0.333 mmol) was demethylated using general procedure A. Purification by flash column chromatography (3:7 ethyl acetate: hexane) gave **2f** (0.050 g, 78%) as cream prisms, m.p. 120-121 °C, lit.[2] m.p. 120-123 °C; IR ν_{max} (cm^{-1}) 3363 (O-H), 1595 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (2H, d, *J* = 2.2 Hz, H-4,6), 6.20 (1H, t, *J* = 2.2 Hz), 4.85 (2H, s, 2OH), 2.40 (1H, tt, *J* = 11.3, 3.0 Hz, CH), 1.90–1.80 (4H, m), 1.75 (1H, m), 1.41–1.33 (4H, m), 1.25 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9 (C-1,3), 151.9 (C-5), 106.9 (C-4,6), 100.7 (C-2), 44.9 (CH), 34.6, 27.2, 26.5; MS (EI) *m/z* (%): 192 (M^+, 96), 177 (20), 151 (17), 137 (100), 124 (70). HRMS *m/z* M^+ calcd. for $C_{12}H_{16}O_2$: 192.1145, found: 192.1145.

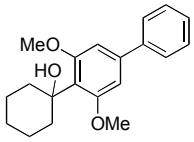


2,5-Dimethylbenzene-1,3-diol (3). To a solution of 1,3-dimethoxy-2,5-dimethylbenzene (0.57 g, 3.43 mmol) in dichloromethane (6 mL) was added boron

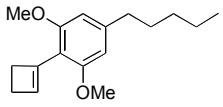
tribromide (1.0 M in dichloromethane, 10.3 mL, 10.3 mmol) dropwise at -78 °C under nitrogen. Stirring was continued at -78 °C for a further 10 min. The dry ice-acetone bath was then removed and the reaction mixture allowed to warm to 20 °C during 1 h. Saturated aqueous sodium hydrogen carbonate (20 mL) was then added and the mixture was stirred at 20 °C for a further 10 min. The mixture was extracted with diethyl ether (2 x 20 mL) and the combined organic layers were washed with saturated aqueous sodium hydrogen carbonate then with brine, dried ($MgSO_4$) filtered and evaporated. The residue was purified by flash column chromatography (1:4 ethyl acetate: hexane) to give **3** as cream prisms (0.42 g, 88%), m.p. 160-161 °C, lit.[3] m.p. 158-160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.12 (2H, s, H-4,6), 4.83 (2H, s, OH), 2.12 (3H, s, 5-CH_3), 1.97 (3H, s, 2-CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1 (C-1,3), 136.8 (C-5), 109.0 (C-2), 108.3 (C-4,6), 21.3 (5-CH_3), 8.2 (2-CH_3); MS (CI^+) *m/z* (%): 139 ([M+H]$^+$, 100), 138 (73), 123 (9), 121 (23). HRMS *m/z* [M+H]$^+$, calcd. for $C_8H_{11}O_2$: 139.0759, found: 139.0757.



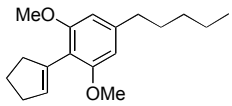
1-(2,6-Dimethoxy-4-pentylphenyl)cyclohexanol (4o). 1,3-Dimethoxy-5-pentylbenzene[4] (0.50 g, 2.44 mmol) and cyclohexanone (0.37 mL, 3.60 mmol) were reacted using general procedure B. Purification by column chromatography (1:19 ethyl acetate: hexane) gave **4o** (0.45 g, 61%) as a pale yellow oil; IR ν_{max} (cm^{-1}) 3531 (O-H), 1609 (aryl), 1568 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.43 (2H, s, H-3,5) 5.38 (s, 1H, OH), 3.82 (6H, s, 2 x OCH_3), 2.54 (2H, t, *J* = 7.8 Hz, aryl-CH_2), 2.27–2.21 (2H, m), 1.91–1.81 (4H, m), 1.73–1.21 (10H, m), 0.91 (3H, t, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0 (C-2,6), 142.6 (C-4), 122.3 (C-1), 106.7 (C-3,5), 75.6 (COH), 56.2 (2 x OCH_3), 37.2, 35.9, 31.5, 30.8, 25.9, 22.6, 22.1, 14.0; MS (CI^+) *m/z* (%): 306 (M^+, 6) 289 ([M-H_2O+H^+], 100). HRMS *m/z* ([M-H_2O+H^+], calcd. for $C_{19}H_{29}O_2$: 289.2162, found: 289.2163.



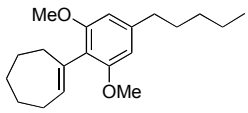
1-(3,5-Dimethoxy-[1,1'-biphenyl]-4-yl)cyclohexan-1-ol (4r). 3,5-Dimethoxy-1,1'-biphenyl[5] (0.324 g, 1.51 mmol) and cyclohexanone (0.24 mL, 2.27 mmol) were reacted using general procedure B. From column chromatography (1:9 ethyl acetate: hexane) were recovered unreacted 3,5-dimethoxy-1,1'-biphenyl (0.14 g, 44%), R_f = 0.63 and **4r** (0.18 g, 38%) as a white solid, m.p. 121-123 °C; IR ν_{max} (cm^{-1}) 3547 (O-H), 1599 (aryl), 1583 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64–7.57 (2H, m), 7.50–7.44 (2H, m), 7.38 (1H, m), 6.84 (2H, s), 5.37 (1H, br s, OH), 3.93 (6H, s. 2 x OCH_3), 2.27–2.20 (2H, m), 2.02–1.94 (2H, m), 1.80 (1H, m), 1.77–1.69 (3H, m), 1.60–1.53 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.3 (C-2,4), 142.1 (C-6), 141.4 (C-7), 129.1 (C-9,11), 128.0 (C-10), 127.6 (C-8,12), 122.0 (C-3), 104.1 (C-1,5), 76.1 (C-13), 56.6 (C-20 21), 37.5 (C-14,18), 25.9 (C-16), 22.6 (C-15,17); MS (CI^+) *m/z* (%): 312 (M^+, 4), 294 (100), 279 (12), 266 (30), 251 (11), 165 (9). HRMS *m/z* M^+, calcd. for $C_{20}H_{24}O_3$: 312.1725, found: 312.1729.



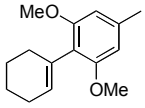
2-(Cyclobut-1-en-1-yl)-1,3-dimethoxy-5-pentylbenzene (5m). 2-Iodo-1,3-dimethoxy-5-pentylbenzene (0.50 g, 1.50 mmol) and cyclobutanone (0.167 mL, 2.24 mmol) were reacted using general procedure B. Column chromatography (3:17 ethyl acetate: hexane) gave **5m** (0.29 g, 69%) as a colourless oil; IR ν_{max} (cm^{-1}) 3447 (O-H, tertiary alcohol), 1606 (aryl), 1576 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.34 (2H, s), 6.31 (1H, s), 3.81 (6H, s, 2 x OCH_3), 3.07–3.06 (2H, m), 2.56–2.53 (4H, m), 1.60–1.57 (2H, m), 1.35–1.31 (4H, m), 0.89 (3H, t, *J* = 6.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.2 (C-1,3), 134.3 (C-5), 132.4 (*C*=CH), 116.8 (C-2), 104.3 (C-4,6), 96.2 (cyclobutenyl C=*C*H), 54.9 (2 x OCH_3), 36.7, 36.5, 34.5, 31.7, 31.3, 22.7, 14.2; MS (EI) *m/z* (%): 260 (M^+, 87), 245 (100), 235 (90), 204 (84), 176 (39). HRMS *m/z* M^+, calcd. for $C_{17}H_{24}O_2$: 260.1771, found: 260.1770.



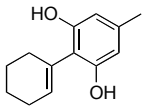
2-(Cyclopent-1-en-1-yl)-1,3-dimethoxy-5-pentylbenzene (5n). 1,3-Dimethoxy-5-pentylbenzene[4] (0.186 g, 0.893 mmol) and cyclopentanone (0.12 mL, 1.34 mmol) were reacted using general procedure B. Column chromatography (1:19 ethyl acetate: hexane) afforded **5n** (0.083 g, 34%) as a solid, m.p. 50-52 °C; IR ν_{max} (cm^{-1}) 1605 (aryl), 1571 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.40 (2H, s, H-4,6), 5.77 (1H, m, C=CH), 3.78 (6H, s, 2 x OCH_3), 2.66–2.62 (2H, m), 2.61–2.56 (2H, m), 2.56–2.50 (2H, m), 2.03–1.94 (2H, m), 1.65–1.61 (2H, m), 1.37–1.35 (4H, m), 0.91 (3H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9 (C-1,3), 143.1 (C-5), 136.2 (cyclopentenyl *C*=CH), 130.5 (cyclopentenyl C=*C*H), 114.3 (C-2), 104.6 (C-4,6), 56.0 (2 x OCH_3), 36.6 (aryl-*C*H_2), 36.1, 33.3, 31.8, 31.2, 23.6, 22.6, 14.1; MS (CI+) *m/z* (%): 275 ($[M+H]^+$, 100). HRMS *m/z* $[M+H]^+$, calcd. for $C_{18}H_{27}O_2$: 275.2006, found: 275.2005.



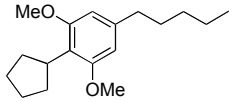
1-(2,6-Dimethoxy-4-pentylphenyl)cyclohept-1-ene (5q). 1,3-Dimethoxy-5-pentylbenzene[4] (0.50 g, 2.40 mmol) and cycloheptanone (0.42 mL, 3.60 mmol) were reacted using general procedure B. Column chromatography (1:19 ethyl acetate: hexane) gave **5q** as a colourless oil (0.35 g, 46%); IR ν_{max} (cm^{-1}) 1603 (aryl), 1571 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.37 (2H, s, H-3,5), 5.73 (1H, t, *J* = 6.5 Hz, C=CH), 3.76 (6H, s, 2 x OCH_3), 2.58–2.53 (2H, m, aryl-CH_2), 2.33–2.23 (4H, m), 1.79–1.55 (8H, m), 1.35–1.32 (4H, m), 0.90 (3H, t, *J* = 6.9 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.2 (C-2,6), 142.4 (C-4), 137.5 (*C*=CH), 122.1 (C=*C*H), 106.6 (C-1), 104.7 (C-3,5), 56.1 (2 x OCH_3), 36.6, 35.2, 32.9, 31.7, 31.2, 29.2, 27.3, 27.0, 22.6, 14.1; MS (EI) *m/z* (%): 302 (M^+, 42) 221 (15) 208 (26) 152 (100). HRMS *m/z* $[M+H]^+$, calcd. for $C_{20}H_{30}O_2$: 302.2239, found: 302.2240.



2',6'-Dimethoxy-4'-methyl-2,3,4,5-tetrahydro-1,1'-biphenyl (5u). To a solution of 1-(2,6-dimethoxy-4-methylphenyl)cyclohexanol (**4u**) (0.39 g, 1.55 mmol) in dichloromethane (5 mL) was added trifluoroacetic acid (0.65 mL, 8.54 mmol), giving a dark red solution. Stirring was continued at 20 °C under nitrogen for 1 h. Then saturated aqueous sodium hydrogen carbonate was added until the mixture was neutral. The organic layer was separated and washed with water, dried ($MgSO_4$), filtered and evaporated to give **5u** (0.35 g, 97%) as a pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.41 (2H, s, H-3,5), 5.58 (1H, m, C=CH), 3.79 (6H, s, 2 x OCH_3), 2.37 (3H, s, CH_3), 2.21–2.18 (4H, m, CH_2CH_2CH_2CH_2), 1.78–1.72 (4H, m, CH_2CH_2CH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6 (C-2',6'), 137.6 (C-4'), 131.6 (*C*=CH), 126.6 (C=*C*H), 119.9 (C-1'), 105.4 (C-3',5'), 56.2 (2 x OCH_3), 29.1, 25.6, 23.3, 22.3, 22.1.

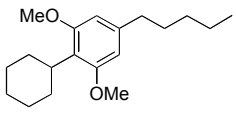


4-Methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2,6-diol (6u). 2',6'-Dimethoxy-4'-methyl-2,3,4,5-tetrahydro-1,1'-biphenyl (**5u**) (0.30 g, 1.29 mmol) was demethylated using general procedure A. The residue was purified by flash column chromatography (1:9 ethyl acetate: hexane) to give **6u** (0.080 g, 30%) as a white solid, m.p. 137-139 °C; IR ν_{max} (cm^{-1}) 3408 (O-H), 1632 (C=C), 1568 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.33 (2H, s, H-3,5), 5.93 (1H, m, C=CH), 5.18 (2H, s, 2OH), 2.24 (3H, s, CH_3), 2.26–2.21 (4H, m, CH_2CH_2CH_2CH_2), 1.83–1.71 (4H, m, CH_2CH_2CH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9 (C-2,6), 139.0 (C-4), 132.6 (*C*=CH), 131.2 (C=*C*H), 114.8 (C-1), 108.2 (C-3,5), 28.9, 25.7, 22.9, 22.0, 21.4; MS (CI+) *m/z* (%): 205 ([M+H]$^+$, 92), 163 (26), 153 (9), 137 (100), 125 (15). HRMS *m/z* [M+H]$^+$, calcd. for $C_{13}H_{17}O_2$: 205.1228, found: 205.1222.

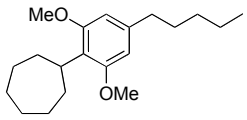


2-Cyclopentyl-1,3-dimethoxy-5-pentylbenzene (7n). 2-(Cyclopent-1-en-1-yl)-1,3-dimethoxy-5-pentylbenzene (**5n**) (0.083 g, 0.30 mmol) was reduced using general

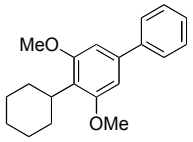
procedure C. Column chromatography (hexane) of the residue gave **7n** (0.029 g, 35%) as a colourless oil; IR ν_{max} (cm^{-1}) 1607 (aryl), 1579, (aryl); ^1H NMR (500 MHz, $CDCl_3$) δ 6.40 (2H, s, H-4,6), 3.81 (6H, s, 2 x OCH_3), 3.61 (1H, *J* = 9.1 Hz, CH), 2.60–2.53 (2H, m, aryl-CH_2), 1.95–1.71 (6H, m), 1.66–1.60 (4H, m), 1.40–1.33 (4H, m), 0.91 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5 (C-1,3), 141.5 (C-5), 119.6 (C-2), 104.7 (C-4,6), 55.7 (2 x OCH_3), 36.4, 34.1, 31.7, 31.2, 31.1, 27.1, 22.6, 14.1; MS (EI) *m/z* (%): 276 (M^+, 100), 247 (52), 220 (46), 177 (5), 151 (9). HRMS *m/z* M^+, calcd. for $C_{18}H_{28}O_2$: 276.2084, found: 276.2083.



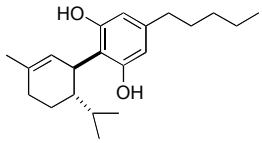
2-Cyclohexyl-1,3-dimethoxy-5-pentylbenzene (7o). 1-(2,6-Dimethoxy-4-pentylphenyl)cyclohexanol (**4o**) (0.187 g, 0.612 mmol) was reduced using general procedure C. Column chromatography (hexane) of the residue gave **7o** (0.13 g, 74%) as a colourless oil; IR ν_{max} (cm^{-1}) 1606 (aryl), 1576 (aryl); ^1H NMR (500 MHz, $CDCl_3$) δ 6.44 (2H, s, H-4,6), 3.84 (6H, s, 2 x OCH_3), 3.25 (1H, tt, *J* = 12.2, 3.4 Hz, CH), 2.63 (2H, t, *J* = 7.8 Hz, aryl-CH_2), 2.14–2.06 (2H, m), 1.85–1.31 (14H, m), 0.98 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5 (C-1,3), 141.6 (C-5), 121.1 (C-2), 104.9 (C-4,6), 55.7 (2 x OCH_3), 36.4 (aryl-CH_2), 34.9 (CH), 31.7, 31.1, 30.3, 27.6, 26.4, 22.6, 14.0; MS (EI) *m/z* (%): 290 (M^+, 100), 247 (74), 234 (18), 221 (37). HRMS *m/z* M^+, calcd. for $C_{19}H_{30}O_2$: 290.2245, found: 290.2240.



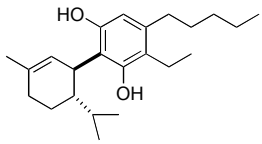
2-Cycloheptyl-1,3-dimethoxy-5-pentylbenzene (7q). 1-(2,6-Dimethoxy-4-pentylphenyl)cyclohept-1-ene (**5q**) (0.353 g, 1.10 mmol) was reduced using general procedure C. Column chromatography of the residue (hexane) gave **7q** (0.13 g, 39%) as a colourless oil; IR ν_{max} (cm^{-1}) 1606 (aryl), 1578 (aryl); ^1H NMR (500 MHz, $CDCl_3$) δ 6.37 (2H, s, H-4,6), 3.79 (6H, s, 2 x OCH_3), 3.32 (1H, tt, *J* = 10.6, 3.8 Hz, CH), 2.62–2.48 (2H, m, aryl-CH_2), 2.06–1.98 (2H, m), 1.76–1.48 (12H, m), 1.41–1.30 (4H, m), 0.92 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8 (C-1,3), 141.4 (C-5), 123.5 (C-2), 104.9 (C-4,6), 55.9 (2 x OCH_3), 36.5 (aryl-CH_2), 36.2, 33.1, 31.8, 31.2, 28.7, 28.5, 22.7, 14.1.



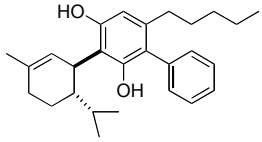
4-Cyclohexyl-3,5-dimethoxy-1,1'-biphenyl (7r). 1-(3,5-Dimethoxy-[1,1'-biphenyl]-4-yl)cyclohexan-1-ol (**4r**) (0.18 g, 0.58 mmol) was reduced using general procedure C. Column chromatography of the residue (1:19 ethyl acetate: hexane) gave **7r** (0.13 g, 76%) as a white solid, m.p. 106-108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64–7.59 (2H, m, H-2',6'), 7.49–7.44 (2H, m, H-3',5'), 7.38 (1H, m, H-4'), 6.78 (2H, s, H-4,6), 3.90 (6H, s, 2 x OCH_3), 3.28 (1H, tt, *J* = 12.2, 3.4 Hz, CH), 2.16–2.08 (2H, m), 1.86–1.82 (2H, m), 1.77–1.75 (2H, m), 1.65–1.56 (2H, m), 1.47–1.28 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3 (C-1,3), 142.1 (C-5), 140.4 (C-1'), 129.1 (C-3',5'), 127.6 (C-4'), 127.5 (C-2',6'), 123.3 (C-2), 104.3 (C-4,6), 56.3 (2 x OCH_3), 35.4 (CH), 30.5, 27.9, 26.8; MS (EI) *m/z* (%): 296 (M^+, 100), 253 (50), 227 (29), 214 (14), 167 (10), 152 (9). HRMS *m/z* M^+, calcd. for $C_{20}H_{24}O_2$: 296.1776, found: 296.1771.



(1'*S,2'*S**)-2'-Isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (8a)**. Olivetol (0.71 g, 3.95 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.91 g, 5.93 mmol) were condensed using general procedure D. The residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give **8a** as a colourless oil (0.74 g, 59%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26–6.15 (3H, br. m, H-4,6 and OH), 5.52 (1H, s, C=CH), 4.71 (1H, br. s, OH), 3.82 (1H, m, =CHC*H*), 2.44 (2H, t, *J* = 6.5 Hz, aryl-CH_2), 2.15–2.08 (2H, m), 1.78 (1H, m, CH_2C*H*), 1.77 (3H, s, =CCH_3), 1.64–1.54 (4H, m), 1.36–1.29 (5H, m), 0.90–0.84 (9H, m, 3CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2 (C-2/6), 154.0 (C-6/2), 143.0 (C-4), 140.0 (*C*=CHCH), 124.8 (C=*C*HCH), 114.0 (C-1), 109.9 (C-3/5), 107.4 (C-5/3), 43.7, 35.6, 35.6, 31.6, 30.6 (2 lines), 27.8, 23.6, 22.5, 22.1, 21.7, 16.4, 14.0; MS (CI+) *m/z* (%): 317 ([M+H]$^+$, 100), 301 (20), 246 (36), 231 (42), 193 (82), 137 (19). HRMS *m/z* [M+H]$^+$, calcd. for $C_{21}H_{33}O_2$: 317.2481, found: 317.2481.

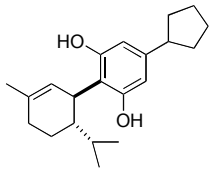


(1'*S,2'S*)-3-Ethyl-2'-isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (8b)**. 4-Ethyl-5-pentylbenzene-1,3-diol (**2b**) (0.039 g, 0.188 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.044 g, 0.282 mmol) were condensed using general procedure D. Purification by column chromatography (1:39 diethyl ether: hexane) gave **8b** (0.034 g, 52%) as a colourless oil; IR ν_{max} (cm^{-1}) 3432 (O-H), 1619 (C=C), 1584 (aryl); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.35–5.90 (2H, m, H-3, OH), 5.53 (1H, s, C=CH), 4.45 (1H, s, OH), 3.84 (1H, m, C=CHC*H*), 2.56 (2H, q, *J* = 7.5 Hz, C*H*$_2$CH$_3$), 2.50–2.46 (2H, m, aryl-C*H*$_2$CH$_2$), 2.22–2.05 (2H, m), 1.83–1.74 (4H, m), 1.65–1.55 (4H, m), 1.43–1.33 (5H, m), 1.11 (3H, br. apparent s, aryl-CH$_2$C*H*$_3$), 0.91 (3H, t, *J* = 7.0 Hz, CH$_3$), 0.87–0.85 (6H, m, CH(C*H*$_3$)$_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.4 (C-2/6), 151.9 (C-6/2), 140.4 (C-4), 140.3 (*C*=CH), 124.9 (C=*C*H), 122.7 (C-3), 114.0 (C-1), 107.5 (C-5), 43.4, 35.9, 32.2, 31.7, 31.1, 30.7, 27.9, 23.8, 22.8, 22.2, 21.9, 19.1, 16.5, 14.7, 14.2; MS (ESI+) *m/z* (%): 345 (M^+, 100), 334 (12), 326 (21), 321 (33), 317 (35), 310 (37), 296 (19). HRMS *m/z* $[M+H]^+$, calcd. for $C_{23}H_{37}O_2$: 345.2794, found: 345.2809.

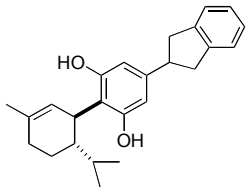


(1''*S,2''S*)-2''-Isopropyl-5''-methyl-6'-pentyl-1'',2'',3'',4''-tetrahydro-[1,1':3',1''-terphenyl]-2',4'-diol (8c)**. 6-Pentyl-[1,1'-biphenyl]-2,4-diol (0.116 g, 0.453 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.10 g, 0.680 mmol) were condensed using general procedure D. Purification by column chromatography (1:99 ethyl acetate: hexane) gave **8c** (0.16 g, 91%) as a white solid, m.p. 72-73 °C; IR ν_{max} (cm^{-1}) 3436 (O-H), 1620 (C=C), 1576 (aryl); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53–7.27 (5H, m, phenyl), 6.37 (1H, s, H-5'), 6.15 (1H, s, OH), 5.59 (1H, s, C=CH), 4.73 (1H, s, OH), 3.88 (1H, m, C=CHC*H*), 2.29–2.21 (2H, m, aryl-C*H*$_2$), 2.19–2.04 (2H, m), 1.83–1.75 (4H, m), 1.70–1.62 (2H, m), 1.44–1.36 (3H, m), 1.19–1.09 (4H, m), 0.88 (3H, d, *J* = 6.8 Hz, C*H*$_3$CHCH$_3$), 0.83 (3H, d, *J* = 6.8 Hz, CH$_3$CHC*H*$_3$), 0.78 (3H, t, *J* = 7.1 Hz, CH$_2$C*H*$_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.7 (C-2'/4), 151.6 (C-

4'/2), 140.6 (C-6'), 139.9 (C-1), 135.8 (*C*=CH), 131.2 (C-3,5), 129.4 (C-2,6), 128.1 (C-4), 125.1 (C=*C*H), 119.9 (C-1'), 113.7 (C-3'), 109.2 (C-5'), 43.8, 36.0, 33.3, 31.8, 30.7, 30.6, 27.9, 23.8, 22.4, 22.2, 21.9, 16.6, 14.1; MS (EI) *m/z* (%): 392 (M^+, 26), 349 (5), 322 (14), 307 (100), 269 (11). HRMS *m/z* M^+, calcd. for $C_{27}H_{36}O_2$: 392.2715, found: 392.2711.

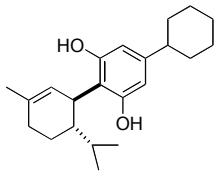


(1'*S,2'S*)-4-Cyclopentyl-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (8d)**. 5-Cyclopentylbenzene-1,3-diol (**2d**) (0.061 g, 0.34 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.079 g, 0.51 mmol) were condensed using general procedure D. The residue was purified by column chromatography (1:39 ethyl acetate: hexane) to give **8d** as a colourless oil (0.041 g, 38%); IR ν_{max} (cm^{-1}) 3412 (O-H), 1624 (C=C), 1579 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.34–6.07 (3H, m, H-3,5, OH), 5.52 (1H, s, C=CH), 4.69 (1H, s, OH), 3.81 (1H, m, C=C*H*CH), 2.82 (1H, m, 4-CH), 2.16–2.07 (2H, m), 2.03–1.97 (2H, m), 1.81–1.74 (2H, m), 1.66–1.60 (4H, m), 1.55–1.50 (2H, m), 1.38 (1H, m), 0.89–0.82 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5 (C-2/6), 154.3 (C-6/2), 146.7 (C-4), 140.2 (C-3'), 124.9 (C-4'), 114.1 (C-1), 108.6 (C-3/5), 106.2 (C-5/3), 45.6, 43.7, 35.6, 34.3, 34.2, 30.8, 27.9, 25.5, 23.8, 22.1, 21.9, 16.5; MS (CI+) *m/z* (%): 315 ($[M+H]^+$, 100), 299 (9), 229 (12), 205 (10), 191 (53), 137 (6). HRMS *m/z* $[M+H]^+$, calcd. for $C_{21}H_{31}O_2$: 315.2324, found: 315.2321.

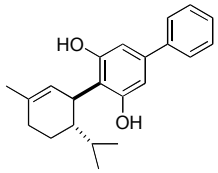


(1'*S,2'S*)-4-(2-Indanyl)-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (8e)**. 5-(2-Indanyl)benzene-1,3-diol (**2e**) (0.089 g, 0.394 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.091 g, 0.59 mmol) were condensed using general procedure D. The residue was purified by column chromatography (1:19 ethyl acetate: hexane) to give **8e** as a colourless oil (0.076 g,

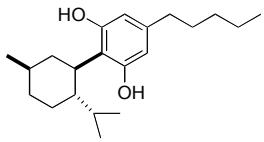
53%) which solidified on standing to a cream solid, m.p. 67-68 °C; IR ν_{max} (cm^{-1}) 3419 (O-H), 1625 (C=C), 1578 (aryl); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29–7.14 (4H, m, indanyl), 6.32 (3H, apparent s, H-3,5 and OH), 5.53 (1H, s, C=CH), 4.83 (1H, br. s, OH), 3.84 (1H, m, C=CHC*H*), 3.53 (1H, *J* = 8.5 Hz, 4-CH), 3.28 (2H, dd, *J* = 15.4, 8.1 Hz), 3.03 (2H, dd, *J* = 15.4, 9.0 Hz), 2.26–2.04 (2H, m), 1.83 (1H, m), 1.78 (3H, s, C*H*$_3$C=CH), 1.72–1.56 (2H, m), 1.40 (1H, m), 0.89 (3H, d, *J* = 3.6 Hz, C*H*$_3$CCH$_3$), 0.87 (3H, d, *J* = 3.6 Hz, CH$_3$CC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3 (C-2/6), 154.5 (C-6/2), 145.6 (C-4), 143.1 (indanyl-3a/8a), 143.1 (indanyl-8a/3a), 140.4 (CH$_3$*C*=CH), 126.5 (indanyl-4,7), 124.8 (CH$_3$C=*C*H), 124.5 (indanyl-5, 6), 114.8 (C-1), 108.7 (C-3/5), 106.3 (C-5/3), 45.2 (4-CH), 43.8, 40.7, 40.6, 35.7, 30.8, 27.9, 23.8, 22.2, 21.9, 16.5; MS (EI) *m/z* (%): 362 (M^+, 22), 292 (26), 277 (100), 239 (12), 117 (22). HRMS *m/z* M^+, calcd. for $C_{25}H_{30}O_2$: 362.2245, found: 362.2241.



(1'*S,2'S*)-4-Cyclohexyl-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (8f)**. 5-Cyclohexylbenzene-1,3-diol (**2f**) (0.058 g, 0.30 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.070 g, 0.456 mmol) were reacted using general procedure D. The residue was purified by column chromatography (1:39 ethyl acetate: hexane) to give an oil which solidified on standing to give **8f** (0.029 g, 29%) as a white solid, m.p. 67-69 °C; IR ν_{max} (cm^{-1}) 3432 (O-H), 1629 (C=C), 1586 (aryl); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.17 (3H, br. s, H-3, 5, OH), 5.52 (1H, s, C=CH), 4.74 (1H, s, OH), 3.80 (1H, m, C=CHC*H*), 2.34 (1H, m, 4-CH), 2.20–2.05 (2H, m), 1.86–1.77 (5H, m), 1.76 (3H, s, C*H*$_3$C=CH), 1.72 (1H, m), 1.65–1.58 (2H, m), 1.43–1.29 (5H, m), 1.22 (1H, m), 0.86 (3H, d, *J* = 6.9 Hz, C*H*$_3$CCH$_3$), 0.85 (3H, d, *J* = 6.9 Hz, CH$_3$CC*H*$_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.5 (C-2/6), 154.3 (C-6/2), 148.3 (C-4), 140.2 (CH$_3$*C*=CH), 124.9 (CH$_3$C=*C*H), 114.2 (C-1), 108.3 (C-3/5), 105.9 (C-5/3), 44.2 (4-CH), 43.7, 35.6, 34.3, 34.3, 30.7, 27.9, 27.0, 26.9, 26.3, 23.8, 22.2, 21.9, 16.5; MS (EI) *m/z* (%): 328 (M^+, 4), 277 (17), 258 (14), 243 (100), 205 (10), 187 (9), 161 (5), 149 (7), 123 (11). HRMS *m/z* M^+, calcd. for $C_{22}H_{32}O_2$: 328.2402, found: 328.2414.

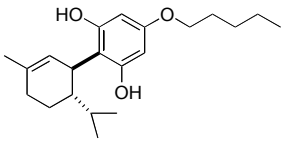


(1*S,2S*)-2-Isopropyl-5-methyl-1,2,3,4-tetrahydro-[1,1':4',1''-terphenyl]-2',6'-diol (8g)**. [1,1'-Biphenyl]-3,5-diol (**2g**) (0.084 g, 0.45 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.104 g, 0.68 mmol) were condensed using general procedure D. The residue was purified by column chromatography (1:19 ethyl acetate: hexane) to give **8g** (0.019 g, 13%) as a colourless oil; IR ν_{max} (cm^{-1}) 3420 (O-H), 1621 (C=C), 1586 (aryl), 1567 (aryl); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.50 (2H, m, H-2'',6''), 7.43–7.36 (2H, m, H-3'',5''), 7.31 (1H, m, H-4''), 6.63 (2H, s, H-3',5'), 6.19 (1H, s, OH), 5.56 (1H, s, C=CH), 4.97 (1H, s, OH), 3.90 (1H, m, C=CHC*H*), 2.18–2.13 (2H, m), 1.87–1.76 (4H, m), 1.68–1.58 (2H, m), 1.41 (1H, m), 0.90–0.87 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.9 (C-2'/6'), 154.8 (C-6'/2'), 140.9 (C-1''), 140.6 (C-4'), 140.5 (CH_3*C*=CH), 128.8 (C-3''/5''), 127.5 (C-4''), 126.9 (C-2'',6''), 124.6 (CH_3C=*C*H), 116.1 (C-1'), 108.8 (C-3'/5'), 106.1 (C-5'/3'), 43.7, 35.7, 30.8, 28.0, 23.8, 22.2, 21.9, 16.5; MS (ESI+) *m/z* (%): 323 ([M+H]$^+$, 100), 305 (5), 218 (3), 153 (9). HRMS *m/z* [M+H]$^+$, calcd. for $C_{22}H_{27}O_2$: 323.2011, found: 323.2013.

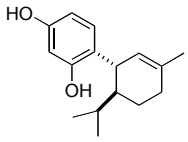


2-((1*R,2*S**,5*R**)-2-(2-Isopropyl-5-methylcyclohexyl)-5-pentylbenzene-1,3-diol (8h)**. To a solution of (1'*S**,2'S*)-2'-isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8a**) (0.030 g, 0.095 mmol) in dry tetrahydrofuran (4.7 mL) was cooled to 0 °C and a solution of borane in THF (0.28 mL, 0.28 mmol, 1.0 M) was added dropwise under nitrogen. The mixture was stirred at 0 °C and the reaction was monitored by TLC, (1:9 ethyl acetate: hexane). After 20 min another 3 equiv. of borane in THF was added (0.284 mL, 0284 mmol). The mixture was stirred for a further 20 min or until TLC showed no presence of **8a**. Then hydrochloric acid (2M) was added to pH ~2. The mixture was extracted with diethyl ether (3 x 5 mL) and the combined organic layers were washed with water (10 mL) then with brine (10 mL), dried ($MgSO_4$), filtered and evaporated. The oily residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give **8h** (0.017 g, 56%) as a colourless

oil; IR ν_{max} (cm^{-1}) 3419 (O-H), 1585 (aryl); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.21 (1H, d, *J* = 1.4 Hz, H-4/6), 6.16 (1H, d, *J* = 1.4 Hz, H-6/4), 4.90 (1H, s, OH), 4.86 (1H, s, OH), 3.05 (1H, td, *J* = 11.6, 4.1 Hz, CH_2CH(aryl)CH), 2.46 (2H, t, *J* = 7.8 Hz, aryl-CH_2), 2.07 (1H, m, C*H*HCH(aryl)CH), 1.84–1.75 (2H, m, aryl-CH_2CH_2), 1.70–1.62 (2H, m), 1.59–1.54 (5H, m), 1.38–1.29 (5H, m), 0.94–0.92 (6H, m), 0.89 (3H, d, *J* = 7.0 Hz), 0.75 (3H, d, *J* = 7.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.9 (C-2/6), 154.5 (C-6/2), 142.3 (C-4), 115.6 (C-1), 109.5 (C-3/5), 108.6 (C-5/3), 45.1, 40.7, 38.6, 35.9, 35.7, 34.0, 32.0, 31.0, 29.1, 25.9, 23.0, 22.9, 22.1, 16.2, 14.4; MS (ESI+) *m/z* (%): 319 ($[M+H]^+$, 100), 310 (20), 296 (20), 293 (20). HRMS *m/z* $[M+H]^+$, calcd. for $C_{21}H_{35}O_2$: 319.2637, found: 319.2618.

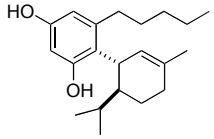


(1'*S,2'S*)-4-Butoxy-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (8i)**. 5-Butoxybenzene-1,3-diol (**2i**) (0.10 g, 0.55 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.13 g, 0.82 mmol) were condensed using general procedure D. The residue was purified by column chromatography (1:19 ethyl acetate: hexane, then pure dichloromethane) to give **8i** (0.023 g, 13%) as a pale yellow oil; IR ν_{max} (cm^{-1}) 3388 (O-H), 1600 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.20 (1H, s, OH), 6.01 (2H, s, H-3,5), 5.53 (1H, s, C=CH), 5.02 (1H, s, OH), 3.88 (2H, t, *J* = 6.5 Hz, OCH_2), 3.78 (1H, m, C=CHC*H*), 2.24–2.07 (2H, m), 1.83 (1H, m), 1.79 (3H, s, CH_3), 1.77–1.70 (2H, m), 1.68–1.57 (2H, m), 1.53–1.44 (2H, m), 1.37 (1H, m), 0.98 (3H, t, *J* = 7.4 Hz), 0.88 (6H, d, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2 (C-4), 157.6 (C-2/6), 155.6 (C-6/2), 140.5 (*C*=CH), 125.4 (C=*C*H), 109.6 (C-1), 96.1 (C-3/5), 95.3 (C-5/3), 68.0 (OCH_2), 44.3, 35.7, 31.7, 31.1, 28.2, 24.0, 22.5, 22.1, 19.6, 16.8, 14.2; MS (CI+) *m/z* (%): 319 ($[M+H]^+$, 100), 248 (9) 215 (2) 153 (21). HRMS *m/z* $[M+H]^+$, calcd. for $C_{20}H_{31}O_3$: 319.2272, found: 319.2272.

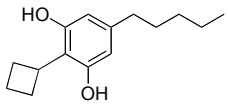


(1'*S,2'*S**)-2'-Isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol (8j)**. Resorcinol (0.10 g, 0.908 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-

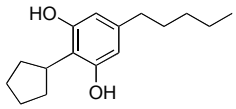
en-1-ol (**14**)[6] (0.21 g, 1.36 mmol) were condensed using general procedure D. The residue was purified by column chromatography (3:7 ethyl acetate: hexane) to give **8j** as a colourless oil (0.040 g, 18%); IR ν_{max} (cm^{-1}) 3371 (O-H), 1619 (C=C), 1601 (aryl), 1508 (aryl); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (1H, d, *J* = 8.9 Hz, H-6), 6.34–6.31 (2H, m, H-3,5), 5.72 (1H, s, OH), 5.49 (1H, s, C=CH), 4.95 (1H, s, OH), 3.25 (1H, m, C=CHC*H*), 2.13–2.08 (2H, m), 1.81–1.71 (4H, m), 1.65–1.47 (2H, m), 1.41–1.28 (1H, m), 0.86 (3H, d, *J* = 6.9 Hz), 0.81 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7 (C-4), 155.4 (C-2), 139.1 (*C*=CH), 131.7 (C-6), 124.7 (C=*C*H), 122.4 (C-1), 107.3 (C-3/5), 104.1 (C-5/3), 44.3, 42.8, 30.7, 27.3, 23.7, 21.8, 21.7, 16.2; MS (ESI+) *m/z* (%): 247 ([M+H]$^+$, 100), 237 (69), 222 (5), 10 (5), 143 (3). HRMS *m/z* [M+H]$^+$, calcd. for $C_{16}H_{23}O_2$: 247.1688, found: 247.1698.



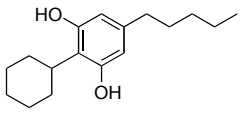
(1'*S,2'S*)-2'-Isopropyl-5'-methyl-6-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol (8k)**. Olivetol (0.10 g, 0.55 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.13 g, 0.83 mmol) were condensed using general procedure D. The residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give **8k** (0.021 g, 12%) as a colourless oil; IR ν_{max} (cm^{-1}) 3424 (O-H), 1619 (C=C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.24 (1H, d, *J* = 2.6 Hz, H-5/3), 6.22 (1H, d, *J* = 2.6 Hz, H-3/5), 6.07 (1H, s, OH), 5.47 (1H, s, C=CH), 4.96 (1H, s, OH), 3.43 (1H, m, C=CHC*H*), 2.66 (1H, m, aryl-C*H*H), 2.35 (1H, m, aryl-CH*H*), 2.21–2.07 (2H, m), 1.82–1.76 (2H, m), 1.77 (3H, s), 1.56–1.49 (4H, m), 1.37–1.29 (4H, m), 0.90 (3H, t, *J* = 6.9 Hz), 0.84 (3H, d, *J* = 6.9 Hz), 0.83 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.7 (C-2), 154.8 (C-4), 144.2 (C-6), 140.0 (*C*=CH), 125.3 (C=*C*H), 120.3 (C-1), 108.7 (C-5), 102.6 (C-3), 43.0, 38.4, 34.4, 32.0, 31.4, 30.7, 27.4, 23.8, 22.7, 22.3, 22.1, 16.9, 14.2; MS (EI) *m/z* (%): 316 (M$^+$, 53), 273 (6), 246 (100), 231 (95), 189 (32), 175 (50). HRMS *m/z* M$^+$, calcd. for $C_{21}H_{32}O_2$: 316.2398, found: 316.2397.



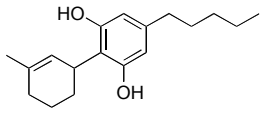
2-Cyclobutyl-5-pentylbenzene-1,3-diol (8m). 2-(Cyclobut-1-en-1-yl)-1,3-dimethoxy-5-pentylbenzene (**5m)** (0.19 g, 0.706 mmol) was dissolved in absolute ethanol (8.0 mL) with 5% palladium on carbon (50 mg). Ammonium formate was added (0.45 g, 7.06 mmol) and the solution was stirred under nitrogen at reflux for 4 h. Then the mixture was filtered through celite. The filtrate was extracted with diethyl ether (3 x 10 mL) and washed with water (25 mL) then with hydrochloric acid (25 mL, 2M). The organic layer was dried ($MgSO_4$), filtered and evaporated to give **5m** (0.16 g, 89%) as a brown oil; IR ν_{max} (cm^{-1}) 1576 (aryl), 1454 (aryl); MS *m/z* (EI): 262 ($[M]^+$, 6), 234 (36), 219 (100), 191 (24), 177 (27). The ether **5m** (0.16 g, 0.609 mmol) was then demethylated using general procedure A. The residue was purified by flash column chromatography (1:9 ethyl acetate: hexane) to give **8m** (0.022g, 15%) as a colourless oil; IR ν_{max} (cm^{-1}) 3401 (O-H), 1654 (aryl), 1623 (aryl); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.19 (s, 2H, H-4,6), 4.82 (2H, s, 2OH), 3.74 (1H, m, aryl-C*H*), 2.63–2.53 (2H, m), 2.46–2.41 (2H, m), 2.40–2.31 (2H, m), 2.00 (1H, m), 1.89 (1H, m), 1.59–1.53 (2H, m), 1.34–1.28 (4H, m), 0.89 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1 (C-1,3), 142.5 (C-5), 114.1 (C-2), 108.6 (C-4,6), 35.4 (aryl-*C*H_2), 32.6 (aryl-*C*H), 31.6, 30.8, 29.0, 22.6, 19.8, 14.1; MS (EI) *m/z* (%): 234 (M^+, 8), 206 (100), 150 (69). HRMS *m/z* M^+, calcd. for $C_{15}H_{22}O_2$: 234.1614, found: 234.1613.



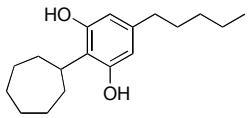
2-Cyclopentyl-5-pentylbenzene-1,3-diol (8n). 2-Cyclopentyl-1,3-dimethoxy-5-pentylbenzene (**7n**) (0.029 g, 0.105 mmol) was demethylated using general procedure A to give **8n** (0.026 g, 99%) as a colourless oil; IR ν_{max} (cm^{-1}) 3409 (O-H), 1622 (aryl), 1585 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.19 (2H, s, H-4,6), 4.67 (2H, s, 2OH), 3.40 (1H, m, aryl-C*H*), 2.49–2.38 (2H, m, aryl-CH_2), 2.02–1.91 (2H, m), 1.90–1.80 (4H, m), 1.69–1.62 (2H, m), 1.60–1.52 (2H, m), 1.36–1.28 (2H, m), 0.90 (3H, t, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7 (C-1,3), 142.0 (C-5), 115.2 (C-2), 108.7 (C-4,6), 35.3, 34.7, 31.5, 30.8, 30.7, 26.7, 22.5, 14.0; MS (EI) *m/z* (%): 248 (M^+, 27), 206 (16), 192 (100), 149 (10), 123 (17). HRMS *m/z* M^+, calcd. for $C_{16}H_{24}O_2$: 248.1771, found: 248.1772.



2-Cyclohexyl-5-pentylbenzene-1,3-diol (8o). 2-Cyclohexyl-1,3-dimethoxy-5-pentylbenzene (**7o**) (0.114 g, 0.391 mmol) was demethylated using general procedure A. Flash column chromatography (1:9 ethyl acetate: hexane) of the residue gave **8o** as a colourless oil (0.081 g, 79%); IR ν_{max} (cm^{-1}) 3408 (O-H), 1622 (aryl), 1584 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.19 (2H, s, H-4,6), 4.90 (2H, s, 2OH), 3.02 (1H, tt, *J* = 12.3, 3.4 Hz, aryl-C*H*), 2.43 (2H, t, *J* = 7.8 Hz, aryl-CH_2), 2.10–2.00 (2H, m), 1.85–1.82 (2H, m), 1.75–1.69 (3H, m), 1.60–1.54 (2H, m), 1.44–1.25 (7H, m), 0.91 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5 (C-1,3), 142.0 (C-5), 116.9 (C-2), 108.8 (C-4,6), 35.3, 35.2, 31.6, 30.6, 30.5, 27.3, 26.2, 22.5, 14.0; MS (EI) *m/z* (%): 262 (M^+, 66), 219 (55), 206 (100), 193 (38), 136 (16), 123 (14). HRMS *m/z* M^+, calcd. for $C_{17}H_{26}O_2$: 262.1932, found: 262.1920.

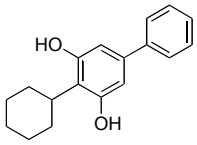


(±)-5'-Methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (8p). Olivetol (0.10 g, 0.55 mmol) and methylcyclohex-2-en-1-ol;[133] (0.093 g, 0.83 mmol) were condensed using general procedure D. Column chromatography of the residue (1:19 ethyl acetate: hexane) gave **8p** as a colourless oil (0.068 g, 45%); IR ν_{max} (cm^{-1}) 3416 (O-H), 1625 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 (2H, s, H-4,6), 5.80–5.40 (2H, br. s, 2OH), 5.65 (1H, s, C=CH), 3.91 (1H, m, aryl-C*H*), 2.44 (2H, t, *J* = 7.8 Hz, aryl-CH_2), 2.13–1.87 (5H, m), 1.79 (3H, s, CH_3C=CH), 1.68 (1H, m), 1.60–1.54 (2H, m), 1.36–1.26 (4H, m), 0.89 (3H, t, *J* = 7.0 Hz, CH_3CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1 (C-1,3), 143.0 (C-5), 141.1 (C-18), 123.8 (C-19), 114.6 (C-2), 108.5 (C-4,6), 35.6, 32.3, 31.6, 30.8, 30.1, 28.4, 24.2, 22.6, 22.5, 14.1. Spectroscopic data are consistent with values previously reported.[7]

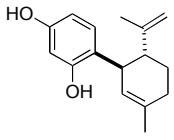


2-Cycloheptyl-5-pentylbenzene-1,3-diol (8q). (2,6-Dimethoxy-4-pentylphenyl)cycloheptane (**7q**) (0.130 g, 0.428 mmol) was demethylated using

general procedure A. Column chromatography of the residue (1:9 ethyl acetate: hexane) gave **8q** (0.112 g, 95%) as a colourless solid, m.p. 75-76 °C; IR ν_{max} (cm^{-1}) 3400 (O-H), 1621 (aryl), 1584 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17 (2H, s, H-4,6), 4.63 (2H, s, 2OH), 3.17 (1H, tt, *J* = 10.7, 3.3 Hz, aryl-C*H*), 2.46–2.38 (2H, m, aryl-CH_2), 2.04–1.95 (2H, m), 1.85–1.50 (12H, m), 1.35–1.28 (4H, m), 0.89 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9 (C-1,3), 141.9 (C-5), 118.9 (C-2), 108.7 (C-4,6), 36.6, 35.3, 33.2, 31.6, 30.7, 28.6, 28.1, 22.6, 14.1; MS (EI) *m/z* (%): 276 (M^+, 78), 220 (100), 193 (76) 136 (29). HRMS *m/z* M^+, calcd. for $C_{18}H_{28}O_2$: 276.2084, found: 276.2083.



4-Cyclohexyl-[1,1'-biphenyl]-3,5-diol (8r). 4-Cyclohexyl-3,5-dimethoxy-1,1'-biphenyl (**7r**) (0.129 g, 0.437 mmol) was demethylated using general procedure A. The diol **8r** (0.12 g, 99%) was obtained as white microprisms, m.p. 177-179 °C; ^{1}H NMR (500 MHz, MeOH) δ 7.54–7.51 (2H, m, H-2',6'), 7.40–7.34 (2H, m, H-3',5'), 7.26 (1H, m, H-4'), 6.55 (2H, s, H-2, H-6), 3.18 (1H, tt, *J* = 12.2, 3.4 Hz, aryl-C*H*), 2.29–2.21 (2H, m), 1.88–1.78 (2H, m), 1.73 (1H, m), 1.63–1.54 (2H, m), 1.47–1.28 (3H, m); ^{13}C NMR (125 MHz, MeOH) δ 160.3 (C-3,5), 144.9 (C-1), 142.9 (C-1'), 131.9 (C-3',5'), 130.3 (C-4'), 129.9 (C-2', C-6'), 122.9 (C-4), 109.2 (C-2,6), 38.9 (aryl-C_αH), 33.4 (C_β), 31.0 (C_γ), 29.9 (C_δ); MS (EI) *m/z* (%): 268 (M^+, 100), 225 (65), 212 (15), 199 (62), 186 (14), 165 (6), 128 (6). HRMS *m/z* M^+, calcd. for $C_{18}H_{20}O_2$: 268.1463, found: 268.1463.

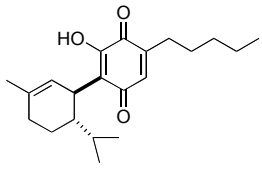


(1'*R,2'R*)-5'-Methyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol (8w)**. Resorcinol (0.034 g, 0.307 mmol) and (1*S**,6R*)-6-(2-hydroxypropan-2-yl)-3-methylcyclohex-2-en-1-ol (**19**)[8] (0.079 g, 0.461 mmol) were condensed according to general procedure A. Work-up gave a yellow residue that was purified by column chromatography (ethyl acetate: hexane, 1:4) to give (**8w**) as a colourless oil (0.071 g, 87%); IR (neat) ν_{max} (cm^{-1}): 3313 (O-H), 1601 (aryl), 1505 (aryl); ^{1}H

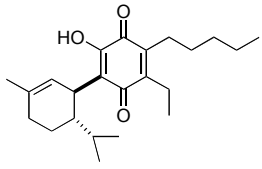
NMR (500 MHz, $CDCl_3$) δ 6.91 (1H, m, H-6), 6.39–6.37 (2H, m, H-3,5), 5.32 (m, 1H, C=CH), 3.64 (1H, m, 1'-CH), 1.92–1.91 (2H, m), 1.75 (3H, s, CH=CC*H*$_3$), 1.72–1.65 (2H, m), 1.58 (1H, m), 1.26–1.23 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6 (C-4), 154.4 (C-2), 135.9 (CH=*C*CH_3), 130.6 (C-6), 124.9 (*C*H=CCH_3), 123.4 (C-1), 107.6 (C-5), 104.2 (C-3), 75.8 (COH), 49.2 (*C*HCOH), 34.6 (1'-CH), 29.5 (4'-C), 27.4 (CH_3), 25.7 (CH_3), 23.8 (CH=C*C*H_3), 21.1 (3'-CH_2); MS (EI) *m/z* (%): 262 (M^+, 12), 244 (77), 229 (87), 201 (54), 161 (100), 123 (31), 110 (71). HRMS *m/z* M^+, calcd. for $C_{16}H_{23}O_3$: 263.1642, found: 263.1642.

(1'*R**,2'R*)-2'-(2-Hydroxypropan-2-yl)-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol (0.0344 g, 0.129 mmol) was dissolved in a solution of triethylamine (0.18 mL, 1.31 mmol) in dichloromethane (1.8 mL) under nitrogen. The solution was cooled to 0 °C and methanesulfonyl chloride (0.060 mL, 0.778 mmol) was added dropwise over 2 min. The pale red solution was stirred at 0 °C for 1 h then stirred at 20 °C for 16 h. After addition of water (15 mL) the mixture was extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with water (20 mL) then with brine (20 mL), dried ($MgSO_4$), filtered and evaporated to give a pale yellow oil that was used without further purification (0.022 g, 43%). 5'-Methyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol dimethanesulfonate (0.028 g, 0.070 mmol) was dissolved in dry tetrahydrofuran (3.5 mL) under nitrogen. The solution was cooled to 0 °C and methyllithium (0.53 mL, 0.85 mmol, 1.6 M in diethyl ether) was added dropwise over 10 min. After stirring at 0 °C for 1 h the mixture was quenched with aqueous 10% ammonium chloride (10 mL) was added and the mixture was extracted with diethyl ether (3 x 10 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried (Na_2SO_4), filtered and the solvent evaporated. The residue was purified by column chromatography (ethyl acetate: hexane, 3:7) to give **8w** (0.012 g, 69%) as a colourless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.80 (1H, d, *J* = 8.1 Hz, H-1), 6.32 (1H, d, *J* = 2.5 Hz, H-3), 6.30 (1H, dd, *J* = 8.1, 2.5 Hz, H-5), 5.63 (1H, br. s, OH), 5.50 (1H, s, H-6'), 4.79 (1H, br. s, OH), 4.67 (1H, s, CH_3C=C*H*H), 4.54 (1H, s, CH_3C=CH*H*), 3.33 (1H, m, H-1'), 2.27 (1H, m, H-2'), 2.19 (1H, m, H-4'), 2.05 (1H, m, H-4'), 1.77 (3H, s, 5'-CH_3), 1.75–1.68 (2H, m, H-3'), 1.58 (3H, s, C*H*$_3$C=CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4 (C-4), 155.2 (C-2), 148.6 (CH_3*C*=CH_2), 138.7 (C-5'), 131.2 (C-6), 124.3 (C-6'), 122.3 (C-1), 111.2 (CH_3C=*C*H_2), 107.3 (C-5), 103.8 (C-3), 47.4 (C-2'), 43.7 (C-1'),

30.5 (C-4'), 28.5 (C-3'), 23.8 (5'-CH_3), 20.3 (CH_3C=CH_2); MS (EI) *m/z* (%): 244 (M^+, 14), 229 (11), 176 (47), 161 (100). HRMS *m/z* M^+, calcd. for $C_{16}H_{20}O_2$: 244.1463, found: 244.1459.

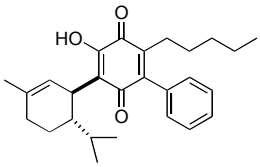


(1'*S,6'S*)-6-Hydroxy-6'-isopropyl-3'-methyl-4-pentyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9a)**. To a solution of (1'*S**,2'*S**)-2'-isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8a**) (0.043 g, 0.135 mmol) in acetone (3.7 mL) was added an aqueous solution (5.6 mL) of potassium dihydrogen orthophosphate (0.043 g, 0.318 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.596 g, 2.22 mmol) was then added in three portions (5.5 equiv. each) during 5 h, with constant stirring. Then the mixture was extracted with diethyl ether (3 x 10 mL) the combined organic layers were dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give **9a** (0.041 g, 93%) as an amber oil; IR ν_{max} (cm^{-1}) 3385 (O-H), 1652 (C=O), 1636 (C=O), 1611 (C=C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.02 (1H, s, OH), 6.43 (1H, t, *J* = 1.5 Hz, H-3), 5.07 (1H, s, H-2'), 3.60 (1H, m, H-1'), 2.41 (2H, t, *J* = 6.5 Hz, 4-CH_2), 2.14–2.12 (1H, m), 1.99–1.92 (2H, m), 1.77–1.74 (1H, m), 1.66 (3H, s), 1.54–1.49 (3H, m), 1.34–1.30 (5H, m), 0.90 (3H, t, *J* = 5.6 Hz), 0.86 (3H, d, *J* = 5.7 Hz), 0.76 (3H, d, *J* = 5.7 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.6 (C-5), 184.1 (C-2), 151.8 (C-6), 144.8 (C-4), 134.9 (C-3), 134.7 (CH_3C=CH), 123.5 (C-1), 122.8 (CH_3C=CH), 41.7, 35.8, 31.5, 30.7, 29.1, 28.3, 27.3, 23.6, 22.6, 22.5, 21.6, 16.4, 14.0; MS (CI+) *m/z* (%): 331 ($[M+H]^+$, 5), 219 (100), 167 (33), 137 (17), 125 (10), 111 (21), 97 (53), 85 (73), 71 (52). HRMS *m/z* $[M+H]^+$, calcd. for $C_{21}H_{31}O_3$: 331.2273, found: 331.2280.



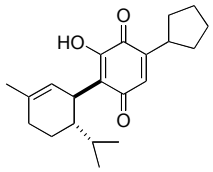
(1'*S,6'S*)-3-Ethyl-6-hydroxy-6'-isopropyl-3'-methyl-4-pentyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9b)**. To a solution of 3-ethyl-2'-isopropyl-

5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8b**) (0.034 g, 0.098 mmol) in acetone (4.12 mL) was added an aqueous solution of potassium dihydrogen orthophosphate (0.031 g, 0.23 mmol, 0.056 M, 4.12 mL) and Frémy's salt (potassium nitrosodisulfonate, 0.39 g, 1.46 mmol). After stirring at 20 °C for 4 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1:99 diethyl ether: hexane) to give **9b** (0.019 g, 55%) as an amber oil; IR ν_{max} (cm^{-1}) 3385 (O-H), 1638 (C=O), 1615 (C=C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.07 (1H, s, OH), 5.10 (1H, s, H-2'), 3.62 (1H, m, H-1'), 2.54–2.47 (2H, m), 2.47–2.41 (2H, m), 2.18 (1H, m), 1.99–1.93 (2H, m), 1.81–1.71 (2H, m), 1.67 (3H, s), 1.50–1.40 (3H, m), 1.36–1.15 (4H, m), 1.06 (3H, t, *J* = 7.5 Hz), 0.91 (3H, t, *J* = 6.8 Hz), 0.88 (3H, d, *J* = 6.9 Hz), 0.79 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.9 (C-5), 184.1 (C-2), 150.9 (C-6), 148.6 (C-4), 139.6 (C-3), 134.2 (C-3'), 123.1 (C-1), 123.0 (C-2'), 41.6 (C-6'), 36.0 (C-1'), 32.1, 30.6, 29.2, 29.1, 26.0, 23.5, 22.5, 22.4, 21.4, 20.3, 16.3, 14.2, 13.9; MS (ESI+) *m/z* (%): 358 (M^+, 100), 313 (11), 291 (70). HRMS *m/z* M^+, calcd. for $C_{23}H_{34}O_3$: 358.2280, found: 358.2285.

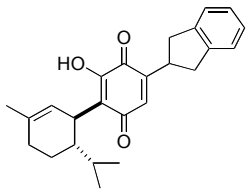


(1'*S,6'S*)-6-Hydroxy-6'-isopropyl-3'-methyl-4-pentyl-3-phenyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9c)**. To a solution of 2''-isopropyl-5''-methyl-6'-pentyl-1'',2'',3'',4''-tetrahydro-[1,1':3',1''-terphenyl]-2',4'-diol (**8c**) (0.037 g, 0.094 mmol) in acetone (3.93 mL) was added an aqueous solution (3.93 mL) of potassium dihydrogen orthophosphate (0.030 g, 0.22 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.53 g, 1.96 mmol). After stirring at 20 °C for 6 h the mixture was extracted with diethyl ether (3 x 10 mL) the combined organic layers were dried ($MgSO_4$), filtered and the solvent evaporated. Column chromatography (dichloromethane: hexane, 3:17) gave **9c** (0.0033 g, 9%) as an amber oil; IR ν_{max} (cm^{-1}) 3387 (O-H), 1644 (C=O), 1612 (C=C), 1573 (aryl); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42–7.40 (3H, m, *m*- and *p*-phenyl), 7.13–7.11 (3H, m, *o*-phenyl, OH), 5.13 (1H, s, H-2'), 3.65 (1H, m, H-1'), 2.34–2.30 (2H, m, 4-CH_2), 2.00–1.94 (2H, m), 1.74 (1H, m), 1.66 (3H, s), 1.43–1.37 (5H, m), 1.20–1.17 (4H, m), 0.90–0.88 (9H, m); ^{13}C NMR

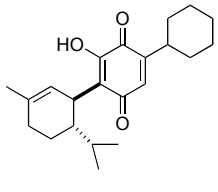
(150 MHz, $CDCl_3$) δ 186.8 (C-5), 184.5 (C-2), 151.4 (C-6), 145.9 (C-4), 141.2 (3-C-*ipso*), 134.5 (C-3'), 133.5 (C-3), 129.2 (3-C-*meta*), 128.5 (3-C-*para*), 128.0 (3-C-*ortho*), 123.3 (C-1), 123.0 (C-2'), 41.7 (C-6'), 36.3 (C-1'), 32.0, 31.2, 30.7, 29.2, 27.2, 23.6, 22.4, 22.2, 21.5, 16.6, 13.9; MS (EI) *m/z* (%): 406 (M^+, 100), 363 (74), 323 (29), 285 (8). HRMS *m/z* M^+, calcd. for $C_{27}H_{34}O_3$: 406.2502, found: 406.2500.



(1'*S,6'S*)-4-Cyclopentyl-6-hydroxy-6'-isopropyl-3'-methyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9d)**. To a solution of 4-cyclopentyl-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8d**) (0.026 g, 0.082 mmol) in acetone (2.28 mL) was added an aqueous solution (3.40 mL) of potassium dihydrogen orthophosphate (0.026 g, 0.191 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.177 g, 0.66 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) the combined organic layers were dried ($MgSO_4$), filtered and the solvent evaporated. Column chromatography (1:39 ethyl acetate: hexane) of the residue gave **9d** (0.022 g, 81%) as a yellow oil; IR ν_{max} (cm^{-1}) 3376 (O-H), 1653 (C=O), 1634 (C=O), 1608 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (1H, s, OH), 6.45 (1H, d, *J* = 1.2 Hz, H-3), 5.10 (1H, s, H-2'), 3.63 (1H, m, H-1'), 3.05 (1H, m, 4-CH), 2.15 (1H, m), 2.07–1.95 (4H, m), 1.83–1.73 (3H, m), 1.72–1.66 (5H, m), 1.54–1.42 (3H, m), 1.35 (1H, m), 0.90 (3H, d, *J* = 6.9 Hz), 0.81 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.1 (C-5), 184.4 (C-2), 152.2 (C-6), 148.5 (C-4), 135.0 (C-3'), 133.1 (C-3), 123.5 (C-1), 123.2 (C-2'), 41.9 (C-6'), 38.7 (4-CH), 36.2 (C-1'), 32.2, 32.1, 31.0, 29.4, 25.5, 23.8, 22.9, 21.9, 16.6; MS (ESI+) *m/z* (%): 329 ($[M+H]^+$, 100), 285 (10), 233 (10). HRMS *m/z* $[M+H]^+$, calcd. for $C_{23}H_{34}O_3$: 329.2104, found: 329.2117.

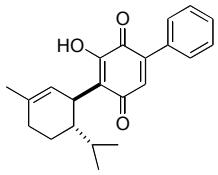


(1'*S,6'S*)-4-(2,3-Dihydro-1*H*-inden-2-yl)-6-hydroxy-6'-isopropyl-3'-methyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9e)**. To a solution of (1'*S**,2'S*)-4-(2-indan-2-yl)-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8e**) (0.040 g, 0.11 mmol) in acetone (3.10 mL) was added an aqueous solution (4.70 mL) of potassium dihydrogen orthophosphate (0.036 g, 0.265 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.418 g, 1.56 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) the combined organic layers were dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography (1:39 ethyl acetate: hexane) gave **9e** as (0.029 g, 69%) an amber oil; IR ν_{max} (cm^{-1}) 3393 (O-H), 1654 (C=O), 1636 (C=O), 1609 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.23 (2H, m, 4,7-indanyl), 7.22–7.18 (2H, m, 5,6-indanyl), 7.07 (1H, s, OH), 6.45 (1H, d, *J* = 1.4 Hz, H-3), 5.08 (1H, s, H-2'), 3.75 (1H, m, 4-CH), 3.65 (1H, m, H-1'), 3.33-3.27 (2H, ddd, *J* = 15.6, 8.1, 2.6 Hz), 3.00–2.88 (2H, m), 2.15 (1H, m), 2.05–1.95 (2H, m), 1.75 (1H, m), 1.67 (3H, s), 1.50 (1H, m), 1.35 (1H, m), 0.88 (3H, d, *J* = 6.9 Hz), 0.79 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.4 (C-5), 184.3 (C-2), 151.8 (C-6), 146.3 (C-4), 141.5 (3a,8a-indanyl), 134.7 (C-3'), 133.2 (C-1',3), 126.8 (4,7-indanyl), 124.5 (5,6-indanyl), 123.4 (C-1), 122.6 (C-2'), 41.6 (C-6'), 38.0 (1,3-indanyl), 37.8 (4-CH), 35.8 (C-1'), 30.6, 29.0, 23.4, 22.4, 21.5, 16.2; MS (EI) *m/z* (%): 376 (M^+, 16), 361 (9), 333 (21), 293 (51), 277 (33), 165 (16), 141 (25), 117 (100). HRMS *m/z* M^+, calcd. for $C_{25}H_{28}O_3$: 376.2038, found: 376.2037.



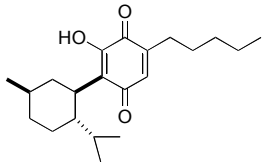
(1'*S,6'S*)-6'-Hydroxy-6-isopropyl-3-methyl-[1,1':4',1''-tercyclohexane]-2,3',6'-triene-2',5'-dione (9f)**. To a solution of 4-cyclohexyl-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8f**) (0.027 g, 0.082 mmol) in acetone (3.46 mL) was added an aqueous solution (3.46 mL) of potassium dihydrogen orthophosphate (0.0264 g, 0.194 mmol, 0.056 M) and Frémy's salt (potassium

nitrosodisulfonate, 0.227 g, 0.846 mmol). After stirring at 20 °C for 4 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and solvent evaporated. Column chromatography (1:49 ethyl acetate: hexane) of the residue gave **9f** (0.022 g, 79%) as an amber oil; IR ν_{max} (cm^{-1}) 3385 (O-H), 1651 (C=O), 1633 (C=O), 1608 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (1H, s, OH), 6.38 (1H, d, *J* = 1.1 Hz, H-3'), 5.08 (1H, s, H-2), 3.62 (1H, m, H-1), 2.67 (1H, m, 4'-CH), 2.15 (1H, m), 2.04–1.93 (2H, m), 1.91–1.73 (6H, m), 1.67 (3H, s), 1.55–1.15 (7H, m), 0.89 (3H, d, *J* = 6.9 Hz), 0.80 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.7 (C-5'), 183.6 (C-2'), 151.7 (C-6'), 149.0 (C-4'), 134.5 (C-3), 133.3 (C-3'), 123.0 (C-1'), 122.7 (C-2), 41.5 (C-6), 36.2 (4'-CH), 35.7 (C-1), 31.9, 31.8, 30.6, 29.0, 26.4, 25.9, 23.4, 22.5, 21.4, 16.2; MS (EI) *m/z* (%): 342 (M^+, 41), 327 (44), 259 (100), 229 (25), 203 (23), 165 (19). HRMS *m/z* M^+, calcd. for $C_{22}H_{30}O_3$: 342.2195, found: 342.2192.

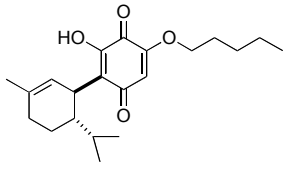


(1'*S,6'S*)-6-Hydroxy-6'-isopropyl-3'-methyl-4-phenyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9g)**. To a solution of 2-isopropyl-5-methyl-1,2,3,4-tetrahydro-[1,1':4',1''-terphenyl]-2',6'-diol (**8g**) (0.019 g, 0.058 mmol) in acetone (2.44 mL) was added an aqueous solution (2.44 mL) of potassium dihydrogen orthophosphate (0.0186 g, 0.136 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.23 g, 0.869 mmol). After stirring at 20 °C for 4 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. Column chromatography (1:19 ethyl acetate: hexane) of the residue gave **9g** (0.0086 g, 44%) as an amber oil; IR ν_{max} (cm^{-1}) 3386 (O-H), 1658 (C=O), 1631 (C=O), 1598 (C=C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54–7.51 (2H, m, 4-(*m*-phenyl)), 7.49–7.43 (3H, m, *o*- and *p*-phenyl), 7.17 (1H, s, OH), 6.77 (1H, s, H-3), 5.14 (1H, s, H-2'), 3.68 (1H, m, H-1'), 2.06–1.97 (2H, m), 1.78 (1H, m), 1.69 (3H, s), 1.55–1.52 (2H, m), 1.35 (1H, m), 0.92 (3H, d, *J* = 6.9 Hz), 0.82 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.1 (C-5), 183.0 (C-2), 151.6 (C-6), 141.5 (C-4), 135.1 (C-1), 134.6 (C-3'), 131.8 (4-(*ipso*-phenyl)), 130.1 (C-3), 128.8 (*o*-pheny)), 128.6 (*m*-phenyl), 123.8 (*p*-phenyl), 122.6 (C-2'), 41.6 (C-6'), 35.9

(C-1'), 30.6, 29.1, 23.5, 22.4, 21.5, 16.2; MS (EI) *m/z* (%): 336 (M^+, 60), 293 (100), 253 (49), 215 (22). HRMS *m/z* M^+, calcd. for $C_{22}H_{24}O_3$: 336.1720, found: 336.1719.

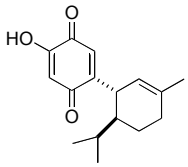


(1'*R,2'S*,5R*)-6-Hydroxy-2'-isopropyl-5'-methyl-4-pentyl-[1,1'-bi(cyclohexane)]-3,6-diene-2,5-dione (9h)**. To a solution of 2-(2-isopropyl-5-methylcyclohexyl)-5-pentylbenzene-1,3-diol (**8h**) (0.017 g, 0.0527 mmol) in acetone (1.46 mL) was added an aqueous solution (2.22 mL) of potassium dihydrogen orthophosphate (0.017 g, 0.124 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.0495 g, 0.184 mmol). After stirring at 20 °C for 1.5 h, TLC (ethyl acetate: hexane, 1: 19) showed the presence of **8h** (R_f = 0.31). Additional potassium nitrosodisulfonate (0.078 g, 0.290 mmol) was added and the mixture left to stir at 20 °C for 16 h. The mixture was then extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. Column chromatography (1:39 ethyl acetate: hexane) of the residue gave **9h** (0.011 g, 60%) as a yellow solid, m.p. 88-90 °C; IR ν_{max} (cm^{-1}) 3372 (O-H), 1654 (C=O), 1636 (C=O), 1613 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$, 60 °C, atropisomers) δ 6.99 (1H, s, OH), 6.43 (1H, s, H-3), 2.90 (1H, m, H-1'), 2.44 (2H, t, *J* = 7.6 Hz, 4-CH_2), 2.02 (1H, m, H-6'), 1.81–1.30 (14H, m), 0.96–0.86 (9H, m), 0.76–0.70 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.2, 187.7 (C-5), 184.4, 183.7 (C-2), 151.5, 150.8 (C-6), 144.8, 144.4 (C-4), 135.5, 134.8 (C-3), 123.7 (C-1), 43.1 (C-2'), 38.6 (C-5'), 36.8, 35.2, 32.9, 31.5, 29.6, 28.9, 28.3, 27.3, 24.7, 22.5, 21.8, 15.9, 14.1; MS (ESI+) *m/z* (%): 333 ($[M+H]^+$, 100), 327 (10), 304 (8), 296 (21), 289 (19), 279 (18). HRMS *m/z* $[M+H]^+$, calcd. for $C_{21}H_{33}O_3$: 333.2430, found: 333.2446.



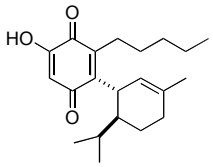
(1'*S,6'S*)-4-Butoxy-6-hydroxy-6'-isopropyl-3'-methyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9i)**. To a solution of 4-butoxy-2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8i**) (0.023 g, 0.073 mmol) in acetone

(2.0 mL) was added an aqueous solution (3.07 mL) of potassium dihydrogen orthophosphate (0.023 g, 0.17 mmol, 0.055 M) and Frémy's salt (potassium nitrosodisulfonate, 0.218 g, 0.812 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. Column chromatography (1:19 ethyl acetate: hexane) of the residue gave **9i** (0.018 g, 75%) as a yellow oil; IR ν_{max} (cm^{-1}) 3404 (O-H), 1676 (C=O), 1625 (C=O), 1608 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (1H, s, OH), 5.79 (1H, s, H-3), 5.09 (1H, s, H-2'), 3.90 (2H, t, *J* = 6.5 Hz, OCH_2), 3.64 (1H, m, H-1'), 2.12 (1H, m), 2.04–1.93 (2H, m), 1.88–1.80 (2H, m), 1.75 (1H, m), 1.67 (3H, s), 1.55–1.43 (3H, m), 1.42–1.29 (1H, m), 0.97 (3H, t, *J* = 7.4 Hz), 0.88 (3H, d, *J* = 6.8 Hz), 0.79 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.0 (C-5), 178.9 (C-2), 155.1 (C-4), 150.4 (C-6), 134.8 (C-3'), 123.7 (C-2), 122.6 (C-2'), 108.9(C-3), 69.2 (OCH_2), 41.7 (C-6'), 35.7 (C-1'), 30.6 (OCH_2CH_2), 30.2 (C-4'), 29.1 (6'-CH), 23.4 (3'-CH_3), 22.5 (C-5'), 21.4 (CH_3CHCH_3), 19.1 (CH_2CH_3), 16.3 (CH_3CHCH_3), 13.6 (CH_2CH_3); MS (CI+) *m/z* (%): 333 ($[M+H]^+$, 100). HRMS *m/z* $[M+H]^+$, calcd. for $C_{20}H_{29}O_4$: 333.2065, found: 333.2061.

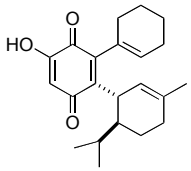


(1'*S,6'S*)-4-Hydroxy-6'-isopropyl-3'-methyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9j)**. To a solution of 2'-isopropyl-5'-methyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol (0.024 g, 0.098 mmol) in acetone (4.15 mL) was added an aqueous solution (4.15 mL) of potassium dihydrogen orthophosphate (0.032 g, 0.233 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.19 g, 0.69 mmol). After stirring at room temperature for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (3:7 ethyl acetate: hexane) to give **9j** (0.022 g, 86%) as a yellow oil; IR (neat) ν_{max} (cm^{-1}): 3368 (O-H), 1650 (C=O), 1604 (C=C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.99 (1H, s, OH), 6.57 (1H, d, *J* = 0.7 Hz, H-6), 6.09 (1H, s, H-3), 5.05–5.01 (1H, m, H-2'), 3.70–3.64 (1H, m, H-1'), 2.01–1.89 (2H, m, H-4'), 1.73–1.69 (4H, m, 3'-CH_3, H-6'), 1.59–1.49 (3H, m, 5'-CH_2, 6'-CH), 1.01 (3H, d, *J* = 6.7 Hz, CH_3CHCH_3), 0.86 (3H, d, *J* = 6.7 Hz, CH_3CHCH_3); ^{13}C NMR

(150 MHz, $CDCl_3$) δ 187.6 (C-5), 184.0 (C-2), 157.5 (C-1), 154.3 (C-4), 137.3 (C-3'), 129.3 (C-6), 120.6 (C-2'), 108.4 (C-3), 44.8 (C-6'), 37.4 (C-1'), 28.5 (C-4'), 28.2 (6'-CH), 23.7 (3'-CH_3), 21.7 (CH_3CHCH_3), 20.7 (C-5'), 18.9 (CH_3CHCH_3); MS (EI) *m/z* (%): 260 (M^+, 36), 217 (100), 177 (34), 161 (27). HRMS *m/z* M^+, calcd. for $C_{16}H_{20}O_3$: 260.1407, found: 260.1405.

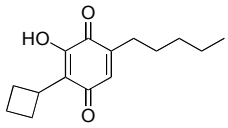


(1'*S,6'S*)-4-Hydroxy-6'-isopropyl-3'-methyl-6-pentyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9k)**. To a solution of 2'-isopropyl-5'-methyl-6-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol (**8k**) (0.021 g, 0.067 mmol) in acetone (2.8 mL) was added an aqueous solution (2.84 mL) of potassium dihydrogen orthophosphate (0.0215 g, 0.158 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.126 g, 0.47 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. Column chromatography (1:4 ethyl acetate: hexane) gave **9k** (0.014 g, 61%) as an amber oil; IR (neat) ν_{max} (cm^{-1}) 3371 (O-H), 1654 (C=O), 1635 (C=O), 1598 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (1H, s, OH), 6.03 (1H, s, H-3), 5.10 (1H, s, H-2'), 3.92 (1H, m, H-1'), 2.52 (2H, m, 6-CH_2), 2.11–2.00 (2H, m), 1.78–1.74 (4H, m), 1.66 (3H, s), 1.47–1.31 (6H, m), 0.92–0.87 (3H, m), 0.85 (3H, d, *J* = 6.9 Hz), 0.78 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.7 (C-5), 184.9 (C-2), 153.7 (C-4), 150.3 (C-1), 143.1 (C-6), 134.3 (C-3'), 123.6 (C-2'), 107.9 (C-3), 42.8 (C-6'), 32.7 (C-1'), 30.8 (C-4'), 29.8, 29.5, 29.1, 27.0, 23.6, 22.6, 22.5, 21.7, 16.2, 14.1; MS (EI) *m/z* (%): 330 (M^+, 100), 287 (67), 245 (35), 205 (26). HRMS *m/z* M^+, calcd. for $C_{21}H_{30}O_3$: 330.2189, found: 330.2188.

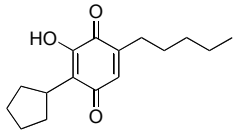


(1''*S,6''S*)-5'-Hydroxy-6''-isopropyl-3''-methyl-[1,1':2',1''-tercyclohexane]-1,1',2'',4'-tetraene-3',6'-dione (9l)**. To a solution of (1''*S**,2''*S**)-2''-isopropyl-5''-methyl-1'',2,2'',3,3'',4,4'',5-octahydro-[1,1':2',1''-terphenyl]-3',5'-diol (**8l**) (0.037 g,

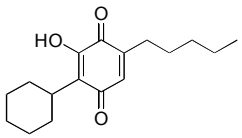
0.113 mmol) in acetone (4.8 mL) was added an aqueous solution (4.77 mL) of potassium dihydrogen orthophosphate (0.036 g, 0.267 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.106 g, 0.397 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. Column chromatography (1:4 ethyl acetate: hexane) of the residue gave **9l** (0.038 g, 98%) as an amber oil; IR ν_{max} (cm^{-1}) 3369 (O-H), 1651 (C=O), 1634 (C=O), 1583 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 (s, 1H, OH), 5.99 (s, 1H, H-4'), 5.54 (s, 1H, H-2), 5.04 (s, 1H, H-2''), 3.57 (s, 1H, H-1''), 2.20–2.04 (m, 4H), 2.01–1.88 (m, 2H), 1.80–1.66 (m, 7H), 1.65 (3H, s), 1.47 (1H, m), 0.86 (3H, d, *J* = 6.9 Hz), 0.72 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.0 (C-6'), 183.9 (C-3'), 153.4 (C-5'), 140.1 (C-1'), 149.7 (C-2'), 136.6 (C-1), 131.6 (C-3''), 129.8 (C-2/2''), 129.6 (C-2''/2), 108.6 (C-4'), 41.4, 33.5, 30.8, 29.2, 28.9, 25.3, 23.7, 22.6, 22.4, 21.8, 21.6, 16.3; MS (EI) *m/z* (%): 340 (M^+, 43), 297 (21), 295 (50), 271 (21), 257 (43), 255 (67), 227 (10), 217 (34). HRMS *m/z* M^+, calcd. for $C_{22}H_{28}O_3$: 340.2038, found: 340.2033.



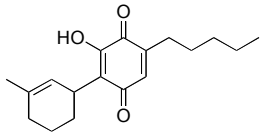
2-Cyclobutyl-3-hydroxy-5-pentylcyclohexa-2,5-diene-1,4-dione (9m). 2-Cyclobutyl-5-pentylbenzene-1,3-diol (**8m**) (0.0224 g, 0.0956 mmol) was reacted using general procedure E to give **9m** (0.020 g, 85%) as bright orange prisms, m.p. 60-61 °C; IR ν_{max} (cm^{-1}) 3383 (O-H), 1652 (C=O), 1636 (C=O), 1612 (C=C); ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 10.44 (1H, s, OH), 6.41 (1H, t, *J* = 1.4 Hz, H-6), 3.55 (1H, ttd, *J* = 9.6, 8.4, 0.9 Hz, 2-CH (α-cyclobutyl)), 2.45–2.35 (2H, m, β-cyclobutyl), 2.34–2.30 (2H, m, $CH_2CH_2CH_2CH_2CH_3$), 2.08–2.01 (2H, m, β'-cyclobutyl), 1.88 (1H, m, γ-cyclobutyl), 1.79 (1H, m, γ'-cyclobutyl), 1.47–1.40 (2H, m, $CH_2CH_2CH_2CH_2CH_3$), 1.35–1.21 (4H, m, $CH_2CH_2CH_2CH_2CH_3$), 0.89 (3H, t, *J* = 7.1 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.9 (C-4), 184.2 (C-1), 151.0 (C-3), 144.6 (C-5), 134.8 (C-6), 122.2 (C-2), 31.3 (α-cyclobutyl), 31.0 ($CH_2CH_2CH_3$), 28.2 ($CH_2CH_2CH_2CH_2CH_3$), 27.6 (β-cyclobutyl), 27.3 ($CH_2CH_2CH_2CH_2CH_3$), 22.3 (CH_2CH_3), 19.3 (γ-cyclobutyl), 13.9 (CH_2CH_3); MS (EI) *m/z* (%): 248 (M^+, 6), 233 (9), 220 (53), 164 (100), 146 (12). HRMS *m/z* M^+, calcd. for $C_{15}H_{20}O_3$: 248.1407, found: 248.1405.



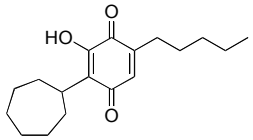
2-Cyclopentyl-3-hydroxy-5-pentylcyclohexa-2,5-diene-1,4-dione (9n). 2-Cyclopentyl-5-pentylbenzene-1,3-diol (**8n**) (0.0262 g, 0.105 mmol) was reacted with Frémy's salt using general procedure E to give **9n** (0.021 g, 75%) as bright orange prisms, m.p. 52-53 °C; IR ν_{max} (cm^{-1}) 3379 (O-H), 1625 (C=O), 1609 (C=C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.40 (1H, s, OH), 6.43 (1H, t, *J* = 1.4 Hz, H-6), 3.15 (m, 1H, α-cyclopentyl), 2.37–2.28 (2H, m, C*H*$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 1.79–1.71 (4H, m, β- and γ-cyclopentyl), 1.66–1.63 (m, 2H, β-cyclopentyl), 1.58–1.50 (2H, m, 2H, γ'-cyclopentyl), 1.47–1.42 (m, 2H, CH$_2$C*H*$_2$CH$_2$CH$_2$CH$_3$), 1.32–1.23 (4H, m, CH$_2$CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 0.86 (3H, t, *J* = 7.0 Hz, CH$_2$C*H*$_3$); ^{13}C NMR (150 MHz, DMSO-d_6) δ 187.7 (C-4), 183.5 (C-1), 153.2 (C-3), 144.8 (C-5), 133.5 (C-6), 122.7 (C-2), 33.7 (α-cyclopentyl), 30.9 (*C*H$_2$CH$_2$CH$_3$), 30.1 (β-cyclopentyl), 27.6 (*C*H$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 26.9 (CH$_2$*C*H$_2$CH$_2$CH$_2$CH$_3$), 26.2 (γ-cyclopentyl), 21.8 (*C*H$_2$CH$_3$), 13.8 (CH$_2$*C*H$_3$); MS (EI) *m/z* (%): 262 (M^+, 100), 206 (81), 177 (12), 163 (9). HRMS *m/z* M^+, calcd. for $C_{16}H_{22}O_3$: 262.1563, found: 262.1562.



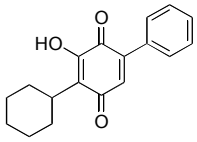
6-Hydroxy-4-pentyl-[1,1'-bi(cyclohexane)]-3,6-diene-2,5-dione (9o). 2-Cyclohexyl-5-pentylbenzene-1,3-diol (**8o**) (0.0677 g, 0.258 mmol) was reacted using general procedure E to give **9o** (0.067 g, 94%) as bright orange prisms, m.p. 105-106 °C; IR ν_{max} (cm^{-1}) 3373 (O-H), 1631 (C=O), 1606 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (s, 1H, OH), 6.42 (1H, t, *J* = 1.5 Hz, H-3), 2.83 (1H, tt, *J* = 12.2, 3.4 Hz, H-1'), 2.41–2.38 (2H, m, 4-CH_2), 1.88–1.49 (9H, m), 1.34–1.22 (7H, m), 0.89 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.7 (C-5), 184.5 (C-2), 151.0 (C-6), 144.5 (C-4), 134.9 (C-3), 124.5 (C-1), 34.5, 31.4, 29.4, 28.2, 27.3, 26.7, 26.0, 22.4, 14.0; MS (EI) *m/z* (%): 276 (M^+, 100), 233 (16), 220 (33), 209 (20), 152 (17). HRMS *m/z* M^+, calcd. for $C_{17}H_{24}O_3$: 276.1725, found: 276.1720.



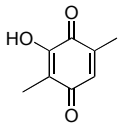
(±)-6-Hydroxy-3'-methyl-4-pentyl-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9p). To a solution of 5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8p**) (0.068 g, 0.248 mmol) in acetone (6.86 mL) was added an aqueous solution (4.77 mL) of potassium dihydrogen orthophosphate (0.079 g, 0.585 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.366 g, 1.36 mmol). After stirring at 20 °C for 16 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give **9p** (0.044 g, 62%) as an amber oil; IR ν_{max} (cm^{-1}) 3377 (O-H), 1644 (C=O), 1631 (C=O), 1606 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (1H, s, H-14), 6.43 (1H, t, *J* = 1.5 Hz, OH), 5.22 (1H, s, H-2'), 3.63 (1H, m, H-1'), 2.41–2.38 (2H, m, 4-CH_2), 2.06 (1H, m), 1.91–1.78 (2H, m), 1.67 (3H, s), 1.59–1.57 (3H, m), 1.53–1.48 (2H, m), 1.33–1.30 (4H, m), 0.89 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.5 (C-5), 184.2 (C-2), 151.6 (C-6), 144.9 (C-4), 134.8 (C-3'), 134.6 (C-3), 123.8 (C-1), 122.4 (C-2'), 32.2, 31.4, 29.6, 28.2, 27.3, 26.8, 23.9, 22.6, 22.4, 14.0; MS (CI+) *m/z* (%): 289 ([M+H]$^+$, 100), 273 (20), 233 (24), 209 (64), 86 (43), 85 (51), 84 (76). HRMS *m/z* [M+H]$^+$, calcd. for $C_{18}H_{25}O_3$: 289.1804, found: 289.1799.



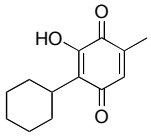
2-Cycloheptyl-3-hydroxy-5-pentylcyclohexa-2,5-diene-1,4-dione (9q). 2-Cycloheptyl-5-pentylbenzene-1,3-diol (**8q**) (0.052 g, 0.19 mmol) was reacted using general procedure E to give **9q** (0.053 g, 97%) as bright orange prisms, m.p. 71-72 °C; IR ν_{max} (cm^{-1}) 3317 (O-H), 1649 (C=O), 1631 (C=O), 1607 (C=C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.95 (1H, s, OH), 6.42 (1H, s, H-6), 2.97 (1H, tt, *J* = 10.8, 3.6 Hz, 2-CH), 2.45–2.36 (2H, m, 5-CH_2), 1.93–1.86 (2H, m), 1.82–1.46 (12H, m), 1.35–1.32 (4H, m), 0.91 (3H, t, *J* = 6.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.5 (C-4), 184.5 (C-1), 150.1 (C-3), 144.4 (C-5), 134.7 (C-6), 126.5 (C-2), 36.0 (2-CH), 32.1, 31.3, 28.1, 28.0, 27.9, 27.2, 22.4, 13.9; MS (EI) *m/z* (%): 290 (M$^+$, 71), 209 (100), 152 (70). HRMS *m/z* M$^+$, calcd. for $C_{18}H_{26}O_3$: 290.1876, found: 290.1875.



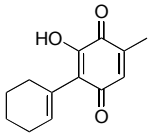
4-Cyclohexyl-3-hydroxy-[1,1'-biphenyl]-2,5-dione (9r). 4-Cyclohexyl-[1,1'-biphenyl]-3,5-diol (**8r**) (0.113 g, 0.419 mmol) was reacted using general procedure E to give **9r** (0.10 g, 86%) as bright orange prisms, m.p. 206-207 °C; IR ν_{max} (cm^{-1}) 3368 (O-H), 1648 (C=O), 1625 (C=O); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.55–7.45 (2H, m, *o*-phenyl), 7.44–7.35 (3H, m, *m*- and *p*-phenyl), 7.09 (1H, s, OH), 6.69 (1H, s, H-6), 2.84 (1H, tt, *J* = 12.2, 3.4 Hz, α-cyclohexyl), 1.97–1.86 (2H, m, β-cyclohexyl), 1.79–1.76 (2H, m, β'-cyclohexyl), 1.70 (1H, m, δ-cyclohexyl), 1.52–1.50 (2H, m, γ-cyclohexyl), 1.34–1.17 (3H, m, γ'- and δ-cyclohexyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.8 (C-2), 184.2 (C-5), 151.0 (C-3), 144.6 (C-1), 134.8 (C-6), 131.8 (C-*ipso*-phenyl), 130.0 (*p*-phenyl), 128.8 (*m*-phenyl), 128.6 (*o*-phenyl), 124.8 (C-4), 34.6 (α-cyclohexyl), 29.3 (β-cyclohexyl), 26.7 (γ-cyclohexyl), 25.9 (δ-cyclohexyl); MS (EI) *m/z* (%): 282 (M^+, 100), 267 (4), 253 (6), 239 (21), 228 (12), 215 (14), 197 (14), 165 (4), 141 (5). HRMS *m/z* M^+, calcd. for $C_{18}H_{18}O_3$: 282.1255, found: 282.1252.



3-Hydroxy-2,5-dimethylcyclohexa-2,5-diene-1,4-dione (9s). To a solution of 2,5-dimethylbenzene-1,3-diol (**8s**)[3] (0.048 g, 0.35 mmol) in acetone (10 mL) was added a buffered aqueous solution (14.4 mL) of potassium dihydrogen orthophosphate (0.11 g, 0.83 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.331 g, 1.23 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and solvent evaporated to give **9s** (0.044 g, 83%) as bright orange prisms, m.p. 127-128 °C, lit.[9] m.p. 126-128 °C; IR ν_{max} (cm^{-1}) 3286 (O-H), 1655 (C=O), 1632 (C=O), 1612 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (1H, br. s, OH), 6.52 (1H, q, *J* = 1.7 Hz, H-6), 2.06 (3H, d, *J* = 1.7 Hz, 5-CH_3) 1.94 (3H, s, 2-CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.9 (C-4), 183.9 (C-1), 151.4 (C-3), 141.2 (C-5), 135.4 (C-6), 117.4 (C-2), 15.0 (5-*C*H_3), 8.0 (2-*C*H_3); MS (CI+) *m/z* (%): 153 ($[M+H]^+$, 100), 137 (12), 125 (9), 111 (12), 99 (6), 97 (16). HRMS *m/z* $[M+H]^+$, calcd. for $C_8H_9O_3$: 153.0552, found: 153.0553.

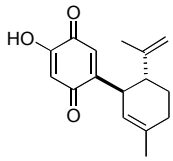


6-Hydroxy-4-methyl-[1,1'-bi(cyclohexane)]-3,6-diene-2,5-dione (9u). 2-Cyclohexyl-5-methylbenzene-1,3-diol (**8u**)[10] (0.10 g, 0.485 mmol) was reacted using general procedure E to give **9u** (0.11 g, 99%) as bright orange prisms, m.p. 110-111 °C (decomp.); IR ν_{max} (cm^{-1}) 3276 (O-H), 1649 (C=O), 1630 (C=O), 1608 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (1H, br. s, OH), 6.47 (1H, q, *J* = 1.7 Hz, H-3), 2.82 (1H, tt, *J* = 12.3, 3.5 Hz, α-cyclohexyl), 2.03 (3H, d, *J* = 1.7 Hz, 4-CH_3), 1.91–1.74 (4H, m, β-cyclohexyl), 1.67 (1H, m, δ-cyclohexyl), 1.54–1.51 (2H, m, γ-cyclohexyl), 1.35–1.19 (3H, m, 2γ' and δ'-cyclohexyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.6 (C-5), 184.7 (C-2), 151.0 (C-6), 140.6 (C-4), 136.0 (C-3), 124.8 (C-1), 34.6 (α-cyclohexyl), 29.4 (β-cyclohexyl), 26.8 (γ-cyclohexyl), 26.0 (δ-cyclohexyl), 14.8 (4-*C*H_3); MS (CI+) *m/z* (%): 221 ([M+H]$^+$, 100), 203 (4), 191 (13), 177 (114), 166 (12), 153 (51). HRMS *m/z* [M+H]$^+$, calcd. for $C_{13}H_{17}O_3$: 221.1177, found: 221.1177.

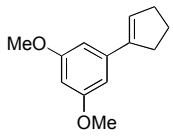


6-Hydroxy-4-methyl-[1,1'-bi(cyclohexane)]-1',3,6-triene-2,5-dione (9v). To a solution of 4-methyl-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**8v**) (0.054 g, 0.265 mmol) in acetone (7.3 mL) was added an aqueous solution (11.2 mL) of potassium dihydrogen orthophosphate (0.085 g, 0.625 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.284 g, 1.06 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. Column chromatography (1:9 ethyl acetate: hexane) gave **9v** (0.042 g, 72%) as bright red prisms, m.p. 130-132 °C; IR ν_{max} (cm^{-1}) 3283 (O-H), 1642 (C=O), 1629 (C=O), 1608 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (1H, s, OH), 6.49 (1H, q, *J* = 1.6 Hz, H-3), 5.76 (1H, m, H-6'), 2.19–2.15 (2H, m, H-2'), 2.06 (3H, d, *J* = 1.6 Hz, 4-CH_3), 1.74–1.64 (6H, m, 2H-3', 2H-4', 2H-5'); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.0 (C-5), 184.6 (C-2), 149.8 (C-6), 141.0 (C-4), 135.8 (C-3), 131.8 (C-1'), 128.2 (C-6'), 122.5 (C-1), 28.0 (C-5'), 25.7 (C-2'), 22.8 (C-3'/4'), 21.9 (C-4'/3'), 14.9 (4-*C*H_3); MS (CI+) *m/z* (%): 219 ([M+H]$^+$, 100), 153 (37), 131 (15). HRMS *m/z* [M+H]$^+$, calcd. for $C_{13}H_{15}O_3$: 219.1021, found:

219.1020.

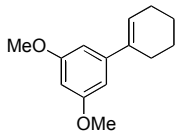


(1'*R,6'R*)-4-Hydroxy-3'-methyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5-dione (9w)**. To a solution of (1'*R**,2'R*)-5'-methyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,4-diol (**8w**) (0.0125 g, 0.051 mmol) in acetone (1.41 mL) was added an aqueous solution (2.2 mL) of potassium dihydrogen orthophosphate (0.0164 g, 0.121 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.0755 g, 0.281 mmol). After stirring at 20 °C for 1.5 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. Column chromatography of the residue (ethyl acetate: hexane, 1:4) gave **9w** (0.012 g, 92%) as a yellow oil; IR ν_{max} (cm^{-1}) 3395 (O-H), 1654 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (1H, s, OH), 6.56 (1H, s, H-6), 6.06 (1H, s, H-3), 5.09 (1H, s, H-2'), 4.64 (1H, s, 6'-CH_3C=C*H*H), 4.59 (1H, s, 6'-CH_3C=CH*H*), 3.76 (1H, m, H-1'), 2.08–1.98 (3H, m, 2H-4', H-5'), 2.11 (1H, td, *J* = 9.1, 4.1 Hz, H-6'), 1.70 (3H, s, 3'-CH_3), 1.70 (1H, m, H-5'), 1.67 (3H, s, 6'-CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.1 (C-5), 184.0 (C-2), 157.4 (C-4), 154.2 (C-1), 147.0 (6'-CH_3*C*), 136.5 (C-3'), 128.5 (C-6), 121.4 (C-2'), 111.7 (6'-CH_3C=*C*H_2), 108.2 (C-3), 49.1 (C-6'), 37.9 (C-4'), 29.6 (C-1'), 27.0 (C-5'), 23.7 (3'-CH_3), 19.4 (6'-*C*H_3C=CH_2); MS (CI+) *m/z* (%): 259 ($[M+H]^+$, 4), 219 (100), 131 (10), 111 (12), 97 (15). HRMS *m/z* $[M+H]^+$, calcd. for $C_{16}H_{19}O_3$: 259.1334, found: 259.1331.

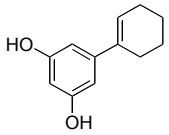


1-(Cyclopent-1-en-1-yl)-3,5-dimethoxybenzene (11). (3,5-Dimethoxyphenyl)boronic acid (0.20 g, 1.10 mmol), cyclopent-1-en-1-yl trifluoromethanesulfonate[11] (0.216 g, 1.00 mmol), palladium diacetate (2.24 mg, 0.01 mmol, 1 mol%), triphenylphosphine (2.26 mg, 0.01 mmol, 1 mol%) and potassium carbonate (0.41 g, 3.00 mmol) were added to a 1:1 mixture of 1,2-dimethoxyethane and water (2.4 mL). The reaction mixture was stirred at 20 °C for 24 h under nitrogen

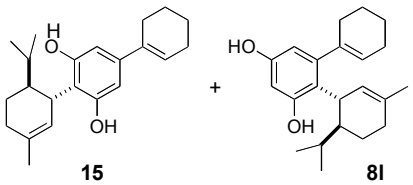
then acidified with hydrochloric acid (10 mL, 2.0 M) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give an oil which soon crystallised to give **11** (0.158 g, 71%) as a white microprisms, m.p. 41-43 °C; IR ν_{max} (cm^{-1}) 3006 (=C-H), 1581 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (2H, d, *J* = 2.3 Hz, H-2,6), 6.37 (1H, t, *J* = 2.3 Hz, H-4), 6.18 (1H, m, H-2'), 3.81 (6H, s, 2 x OCH_3), 2.72–2.67 (2H, m, H-5'), 2.56–2.51 (2H, m, H-3'), 2.05–1.99 (2H, m, H-4'); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8 (C-3,5), 142.6 (C-1), 139.0 (C-1'), 127.0 (C-2'), 104.0 (C-2,6), 99.0 (C-4), 55.3 (2 x OCH_3), 33.4 (C-5'), 33.3 (C-3'), 23.4 (C-4'); MS (CI+) *m/z* (%): 205 ($[M+H]^+$, 100), 189 (42), 154 (21), 139 (23), 119 (29), 97 (34), 86 (43), 84 (72). HRMS *m/z* $[M+H]^+$, calcd. for $C_{13}H_{17}O_2$: 205.1228, found: 205.1224.



3',5'-Dimethoxy-2,3,4,5-tetrahydro-1,1'-biphenyl (12). (3,5-Dimethoxyphenyl)boronic acid (**10**)[12] (0.35 g, 1.92 mmol), 1-cyclohexen-1-yl trifluoromethanesulfonate[13] (0.40 g, 1.75 mmol), palladium diacetate (3.90 mg, 0.017 mmol, 1 mol%), triphenylphosphine (4.6 mg, 0.017 mmol, 1 mol%) and potassium carbonate (0.72 g, 5.21 mmol) was dissolved in a 1:1 mixture of 1,2-dimethoxyethane and water (4.22 mL in total). The mixture was stirred at 20 °C for 24 h under nitrogen, then acidified with hydrochloric acid (25 mL, 2.0 M) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by column chromatography (1:99 ethyl acetate: hexane) to give **12** (0.29 g, 76%) as a colourless oil; IR ν_{max} (cm^{-1}) 1622 (C=C), 1591 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (2H, d, *J* = 2.3 Hz, H-2',6'), 6.38 (1H, t, *J* = 2.3 Hz, H-4'), 6.13 (1H, m, H-2), 3.83 (6H, s, 2 x OCH_3), 2.45–2.35 (m, 2H, H-3), 2.27–2.17 (2H, m, H-6), 1.84–1.75 (2H, m, H-5), 1.73–1.64 (2H, m, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0 (C-3',5'), 145.5 (C-1'), 137.0 (C-1), 125.6 (C-2), 103.8 (C-2',6'), 99.0 (C-4'), 55.7 (2 x OCH_3), 27.9 (C-6), 26.2 (C-3), 23.4 (C-5), 22.5 (C-4); MS (CI+) *m/z* (%): 219 ($[M+H]^+$, 100). HRMS *m/z* $[M+H]^+$, calcd. for $C_{14}H_{18}O_2$: 219.1380, found: 219.1380.



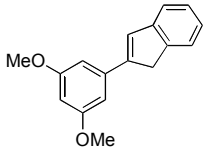
2',3',4',5'-Tetrahydro-[1,1'-biphenyl]-3,5-diol (13). 3',5'-Dimethoxy-2,3,4,5-tetrahydro-1,1'-biphenyl (**12**) (0.429 g, 1.96 mmol) was demethylated using general procedure A. Flash column chromatography (3:7 ethyl acetate: hexane) gave **13** (0.19 g, 52%) as a white solid, m.p. 127-129 °C; IR ν_{max} (cm^{-1}) 3267 (O-H), 1619 (C=C), 1591 (aryl); ^{1}H NMR (500 MHz, DMSO) δ 9.08 (2H, s, 2OH), 6.22 (2H, d, *J* = 1.9 Hz, H-2,6), 6.07 (1H, t, *J* = 1.9 Hz, H-4), 5.97 (1H, m, H-2'), 2.23–2.20 (2H, m, H-3'), 2.11–2.08 (2H, m, H-6'), 1.71–1.62 (2H, m, H-5'), 1.59–1.49 (2H, m, H-4'); ^{13}C NMR (125 MHz, DMSO) δ 158.1 (C-3,5), 143.8 (C-1), 136.1 (C-1'), 123.5 (C-2'), 103.0 (C-2,6), 101.0 (C-4), 26.8 (C-6'), 25.2 (C-3'), 22.6 (C-5'), 21.8 (C-4'); MS (EI) *m/z* (%): 190 (M^+, 100), 175 (33), 161 (60), 136 (47). HRMS *m/z* M^+, calcd. for $C_{12}H_{14}O_2$: 190.0988, found: 190.0989.



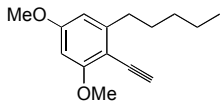
15 **8l**

(1*S,2*S**)-2-Isopropyl-5-methyl-1,2,2'',3,3'',4,4'',5''-octahydro-[1,1':4',1''-terphenyl]-2',6'-diol (15) and (1''*S**,2''*S**)-2''-Isopropyl-5''-methyl-1'',2,2'',3,3'',4,4'',5-octahydro-[1,1':2',1''-terphenyl]-3',5'-diol (8l)**. 2',3',4',5'-Tetrahydro-[1,1'-biphenyl]-3,5-diol (**13**) (0.10 g, 0.53 mmol) and (1*R**,6*S**)-6-isopropyl-3-methylcyclohex-2-en-1-ol (**14**)[6] (0.12 g, 0.79 mmol) were condensed using general procedure D. Purification by column chromatography (1:19 ethyl acetate: hexane) gave **15** (0.083 g, 48%) as a white solid, m.p. 89-91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.43 (2H, br. s, H-3', H-5'), 6.24–5.92 (2H, m, H-6'', OH), 5.51 (1H, s, H-6), 4.89 (1H, br. s, OH), 3.83 (1H, m, H-1), 2.35–2.27 (2H, m), 2.20–2.08 (4H, m), 1.82–1.71 (6H, m), 1.67–1.58 (4H, m), 1.40 (1H, m), 0.87 (3H, d, *J* = 6.8 Hz, C*H*$_3$CHCH$_3$), 0.85 (3H, d, *J* = 6.8 Hz, CH$_3$CHC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 154.4, 142.3, 140.3, 135.6, 124.7, 124.6, 115.3, 106.6, 104.2, 43.7, 35.7, 30.8, 27.9 (CH$_3$*C*HCH$_3$), 27.2, 25.9, 23.7 (5-*C*H$_3$), 23.1, 22.3, 22.2, 21.8 (*C*H$_3$CHCH$_3$), 16.4 (CH$_3$CH*C*H$_3$); MS (EI) *m/z* (%): 326 (M^+, 57), 256 (54), 241 (100). HRMS *m/z* M^+, calcd. for $C_{22}H_{30}O_2$: 326.2245, found: 326.2242. Subsequent

elution gave **8l** (0.066 g, 38%) as a colourless oil; IR ν_{max} (cm^{-1}) 3416 (O-H), 1612 (C=C), 1584 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.25 (1H, d, *J* = 2.5 Hz, H-2'/4'), 6.17 (1H, d, *J* = 2.5 Hz, H-4'/2'), 5.99 (1H, s, OH), 5.51 (2H, s, H-6,6'), 5.22 (1H, s, OH), 3.40 (1H, m, H-1''), 2.21–2.07 (6H, m), 1.76 (3H, s, 5''-CH_3), 1.71–1.62 (7H, m), 1.50 (1H, m), 0.79 (3H, d, *J* = 7.0 Hz, C*H*$_3$CHCH$_3$), 0.71 (3H, d, *J* = 6.8 Hz, CH$_3$CHC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 154.7, 147.8, 139.7, 126.9, 125.5, 120.5, 119.6 , 107.9, 103.0, 42.9, 39.4, 31.1, 30.8, 27.5, 25.5, 23.7 (5''-*C*H$_3$), 23.1, 22.1, 21.8 (*C*H$_3$CHCH$_3$), 16.6 (CH$_3$CH*C*H$_3$); MS (EI) *m/z* (%): 326 (M^+, 100), 311 (40), 283 (70), 256 (46), 241 (54), 215 (45), 201 (47). HRMS *m/z* M^+, calcd. for $C_{22}H_{30}O_2$: 326.2245, found: 326.2242.



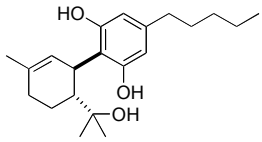
2-(3,5-Dimethoxyphenyl)-1*H*-indene (16). (3,5-Dimethoxyphenyl)boronic acid (**10**)[12] (0.46 g, 2.54 mmol), 2-bromo-*1H*-indene[14] (0.45 g, 2.31 mmol), palladium diacetate (5.20 mg, 0.023 mmol, 1 mol%), triphenylphosphine (6.10 mg, 0.023 mmol, 1 mol%) and potassium carbonate (0.96 g, 6.92 mmol) was dissolved in a 1:1 mixture of 1,2-dimethoxyethane and water (5.6 mL). The reaction mixture was stirred at room temperature for 24 h under nitrogen, then acidified with hydrochloric acid (25 mL, 2M) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by column chromatography (1:19 ethyl acetate: hexane) to give **16** (0.34 g, 59%) as a pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (1H, m, 4-indanyl), 7.42 (1H, m, 6-/5-indanyl), 7.30 (1H, m, 7-indanyl), 7.25 (1H, apparent d, *J* = 0.5 Hz, 3-indanyl), 7.22 (1H, td, *J* = 7.4, 1.1 Hz, 5-/6-indanyl), 6.84–6.82 (2H, d, *J* = 2.2 Hz, H-2,6), 6.45 (1H, t, *J* = 2.2 Hz, H-4), 3.88 (6H, s, 2 x OCH_3), 3.80 (2H, s, 1-indanyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 146.7, 145.6, 143.5, 138.3, 127.6, 127.0, 125.3, 124.1, 121.5, 104.4, 99.9, 55.8, 39.6. These spectral data matched those for **16** prepared by an alternative route.[15]



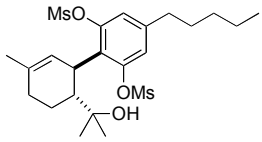
2-Ethynyl-1,5-dimethoxy-3-pentylbenzene (18). A solution of 2-iodo-1,5-dimethoxy-3-pentylbenzene (**17**)[1] (0.60 g, 1.80 mmol), copper (I) iodide (0.0239 g, 0.034 mmol) trimethylsilylacetylene (1.27 mL, 8.98 mmol), bis(triphenylphosphine)palladium(II) dichloride 0.014 g, 0.0739 mmol) in dimethyl sulfoxide (2.85 mL) was heated in a sealed tube at 75 °C under an atmosphere of nitrogen for 15 h. After 15 h the solution was cooled to 20 °C, poured into water and extracted with dichloromethane (3 x 25 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1:49 ethyl acetate: hexane) to give (2,4-dimethoxy-6-pentylphenyl)ethynyl)trimethylsilane (0.40 g, 73%) as a yellow oil; MS (EI) *m/z* (%): 304 (M^+, 100), 289 (59), 274 (47), 258 (37), 245 (2). HRMS *m/z* M^+, calcd. for $C_{18}H_{28}O_2Si$: 304.1858, found: 304.1854.

(2,4-Dimethoxy-6-pentylphenyl)ethynyl)trimethylsilane (0.40 g, 1.31 mmol) was dissolved in tetrahydrofuran (3.95 mL) and tetrabutylammonium fluoride (6.40 mL, 6.40 mmol, 1.0 M in tetrahydrofuran) was added at 0 °C then slowly warmed to 20 °C over the course of 3 h, after which additional tetrabutylammonium fluoride (6.40 mL, 6.40 mmol, 1.0 M in tetrahydrofuran) was added at 0 °C. The mixture was slowly warmed to 20 °C during 3 h. Then the solution was poured into saturated aqueous ammonium chloride and the mixture extracted with ethyl acetate (3 x 25 mL). The combined organic layers were dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1:49 ethyl acetate: hexane) to give **18** (0.127 g, 42%) as a colourless oil; IR ν_{max} (cm^{-1}) 3310 (≡C-H), 2093 (C≡C), 1599 (aryl), 1573 (aryl); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.35 (1H, d, *J* = 2.3 Hz, H-4), 6.29 (1H, d, *J* = 2.3 Hz, H-6), 3.86 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 3.42 (1H, s, alkynyl-H), 2.74–2.70 (2H, m, $CH_2CH_2CH_2CH_2CH_3$), 1.69–1.59 (2H, m, $CH_2CH_2CH_2CH_2CH_3$), 1.37–1.31 (4H, m, $CH_2CH_2CH_2CH_2CH_3$), 0.89 (3H, t, *J* = 7.0 Hz, $CH_2CH_2CH_2CH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4 (C-1), 160.9 (C-5), 149.2 (C-3), 105.8 (C-4), 103.4 (C-2), 95.7 (C-6), 83.5 (alkynyl-*C*), 78.9 (alkynyl-*C*H), 56.0 (OCH_3), 55.5 (OCH_3), 34.9 ($CH_2CH_2CH_2CH_2CH_3$), 31.8 ($CH_2CH_2CH_2CH_2CH_3$), 30.2 ($CH_2CH_2CH_2CH_2CH_3$), 22.6 ($CH_2CH_2CH_2CH_2CH_3$), 14.2 ($CH_2CH_2CH_2CH_2CH_3$); MS (EI) *m/z* (%): 232 (M^+, 100), 217 (60), 203 (22), 189 (85),

176 (75), 161 (27), 145 (33), 131 (42). HRMS *m/z* M^+, calcd. for $C_{15}H_{20}O_2$: 232.1463, found: 232.1460.

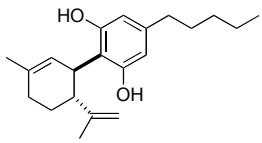


(1'*R,2'R*)-2'-(2-hydroxypropan-2-yl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (20)**. Olivetol (0.54 g, 3.02 mmol) and (1*S**,6*R**)-6-(2-hydroxypropan-2-yl)-3-methylcyclohex-2-en-1-ol (**19**)[8] (0.771 g, 4.53 mmol) were condensed using general procedure D. The residue was purified by column chromatography (1:4 ethyl acetate: hexane) to give **20** (0.724 g, 73%) as a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (1H, s, OH), 6.48 (1H, s, OH), 6.30–6.26 (2H, m, H-3,5), 5.68 (1H, s, H-6'), 3.85 (1H, m, H-1'), 2.44 (2H, t, *J* = 7.8 Hz, C*H*$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 2.20–1.94 (m, 4H), 1.90 (1H, m) 1.80 (3H, s, 5'-CH$_3$) 1.73–1.67 (1H, m), 1.59–1.53 (2H, m, CH$_2$C*H*$_2$CH$_2$CH$_2$CH$_3$), 1.31–1.27 (4H, m, CH$_2$CH$_2$C*H*$_2$C*H*$_2$CH$_3$), 1.23 (6H, s, C*H*$_3$CHC*H*$_3$), 0.88 (3H, t, *J* = 7.0 Hz, CH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4 (C-2/6), 154.6 (C-6/2), 143.9 (C-4), 140.3 (C-5'), 124.2 (C-6'), 115.3 (C-1), 110.0 (C-3/5), 109.9 (C-5/3), 75.5 (2'-*C*OH), 48.7 (2'-C), 35.9 (C-1'), 33.2, 32.0, 31.1, 30.1, 28.6, 26.4, 24.1, 23.4, 22.9, 14.4. These spectral data matched those for **20** prepared by an alternative route.[8]



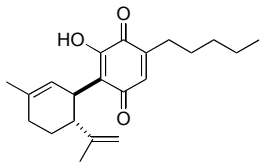
(1'*S,2'S*)-5'-Methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diyl dimethanesulfonate (21)**. 2'-(2-Hydroxypropan-2-yl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**20**) (0.226 g, 0.680 mmol) was dissolved in dichloromethane (9.2 mL) and triethylamine (0.95 mL, 6.80 mmol) under nitrogen. The solution was cooled to 0 °C and methanesulfonyl chloride (0.32 mL, 4.08 mmol) was added dropwise over 2 min. The pale red solution was stirred at 0 °C for 1 h then 20 °C for 16 h. After addition of water (15 mL) the mixture was extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with water (20 mL) then with brine (20 mL), dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1:9 ethyl acetate: hexane) to give **21** (0.28

g, 89%) as a colourless oil; IR ν_{max} (cm^{-1}) 2924, 2854 (C-H), 1617 (C=C), 1567 (aryl), 1352 (S=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (2H, br. s, H-3,5), 5.38 (1H, s, H-6'), 4.49 (s, 1H, 2'-CH_3C=C*H*H), 4.41 (s, 1H, 2'-CH_3C=CH*H*), 3.85 (1H, m, H-1'), 3.14 (6H, s, $2SO_2CH_3$), 2.65 (1H, m, H-2'), 2.57 (2H, t, *J* = 7.8 Hz, aryl-CH_2), 2.16 (1H, m, H-4'), 2.04 (1H, m, H-4'), 1.79–1.74 (2H, m, H-3'), 1.71 (3H, s, 5'-CH_3), 1.60 (3H, s, CH_3C=CH_2), 1.62–1.56 (2H, m, aryl-CH_2CH_2), 1.31–1.29 (4H, m, CH_2C$H_2$$CH_3$), 0.87 (3H, t, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9 (C-2,6), 147.5 (2'-CH_3*C*=CH_2), 143.9 (C-4), 133.8 (C-5'), 127.6 (C-6'), 124.5 (C-1), 120.2 (2'-CH_3C=*C*H_2), 112.0 (C-3,5), 46.4 (C-2'), 38.8 ($2SO_2CH_3$), 38.6 (C-1'), 35.7 (aryl-*C*H_2), 31.7, 30.8 (2C), 30.0, 29.0, 24.0, 22.8, 19.3, 14.4; MS (EI) *m/z* (%): 470 (M^+, 36), 402 (38), 364 (20), 307 (100), 237 (37), 187 (29). HRMS *m/z* M^+, calcd. for $C_{23}H_{34}O_6S_2$: 470.1791, found: 470.1792.

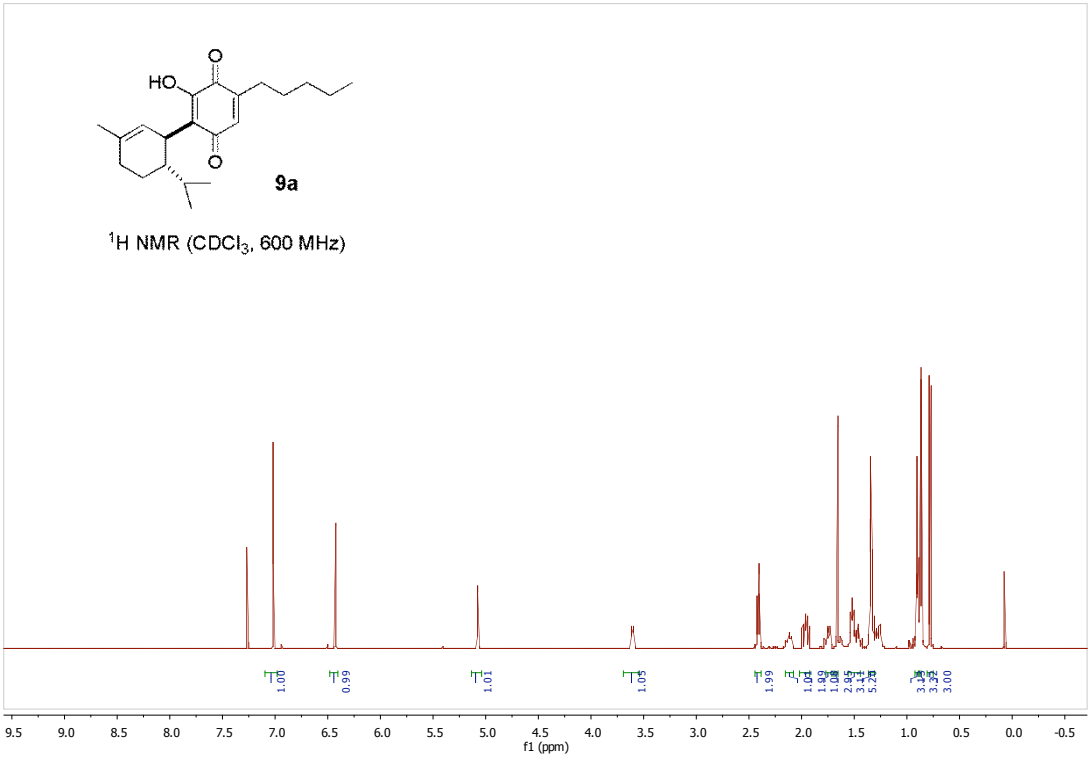


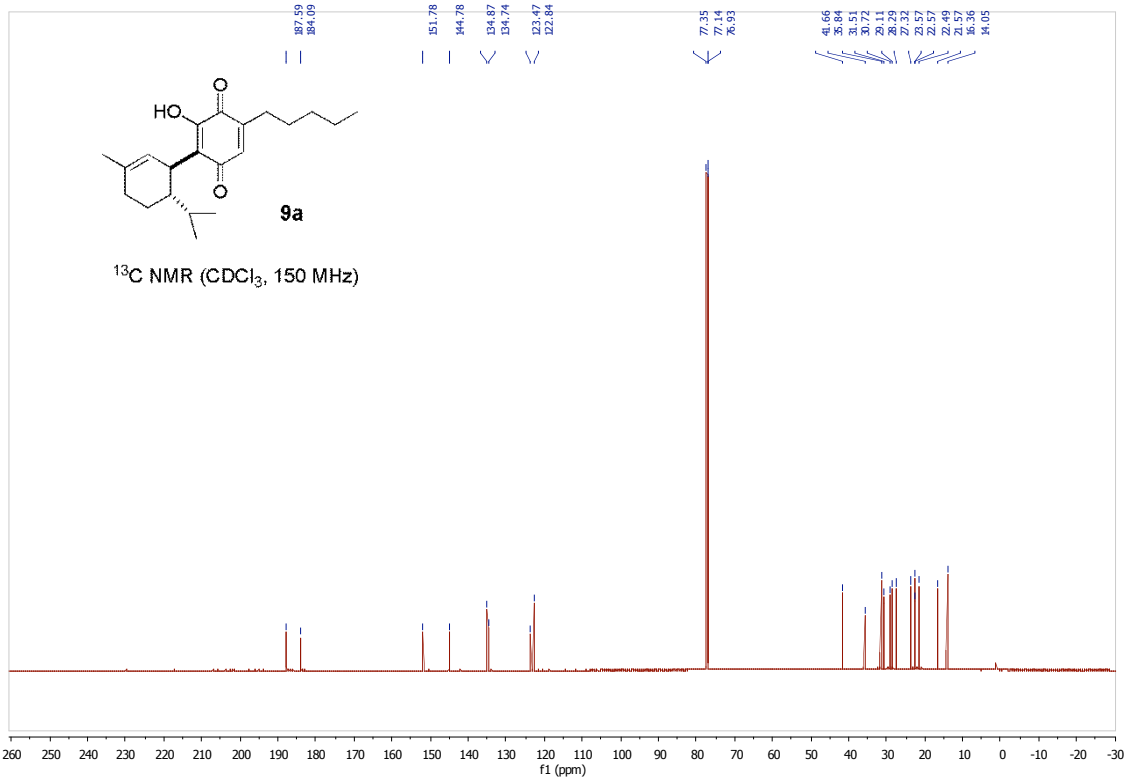
(±)-Cannabidiol ((±)-CBD). 5'-Methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diyl dimethanesulfonate (**21**) (0.215 g, 0.457 mmol) was dissolved in dry tetrahydrofuran (23 mL) under nitrogen. The solution was cooled to 0 °C and methyllithium (6.6 mL, 10.5 mmol, 1.6 M in diethyl ether) was added dropwise over 10 min. The mixture was stirred at 0 °C for 1 h then quenched by addition of 10% aqueous ammonium chloride (6 mL). The mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic extracts were washed with water (10 mL) then with brine (10 mL). The organic layer was dried (Na_2SO_4), filtered and evaporated and the residue purified by column chromatography (1:19 ethyl acetate: hexane) to give **cannabidiol** (0.10 g, 70%) as a colourless oil; IR ν_{max} (cm^{-1}) 3438 (O-H), 1629 (C=C), 1583 (aryl); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (2H, br. s, H-3,5), 5.98 (1H, s, OH), 5.57 (1H, s, H-6'), 4.72 (1H, br. s, OH), 4.66 (1H, s, 2'-CH_3C=C*H*H), 4.56 (1H, s, 2'-CH_3C=CH*H*), 3.87–3.84 (1H, m, H-1'), 2.45–2.38 (3H, m, H-2' and aryl-CH_2), 2.25–2.21 (1H, m, H-4'), 2.13–2.07 (1H, m, H-4'), 1.79 (3H, s, 5'-CH_3), 1.84–1.74 (2H, m, H-3'), 1.66 (3H, s, 2'-CH_3C=CH_2), 1.56–1.53 (2H, m, aryl-CH_2CH_2), 1.33–1.26 (4H, m, CH_2C$H_2$$CH_3$), 0.88 (3H, t, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4 (C-2/6), 154.2 (C-6/2), 149.7 (2'-CH_3*C*=CH_2),

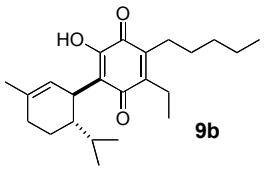
143.4 (C-4), 140.4 (C-5'), 124.5 (C-6'), 114.2 (C-1), 111.2 (2'-CH_3C=CH_2), 110.2 (C-3/5), 108.4 (C-5/3), 46.6 (C-2'), 37.6 (C-1'), 35.9 (aryl-CH_2), 31.9, 31.0, 30.8, 28.8, 24.1, 22.9, 20.9, 14.4; MS (CI+) *m/z* (%): 315 ([M+H]$^+$, 100), 246 (45), 231 (65), 193 (30), 135 (15), 121 (15). HRMS *m/z* M$^+$, calcd. for $C_{21}H_{31}O_2$: 315.2324, found: 315.2316.



(1'*S,6'S*)-6-Hydroxy-3'-methyl-4-pentyl-6'-(prop-1-en-2-yl)-[1,1'-bi(cyclohexane)]-2',3,6-triene-2,5- dione ((±)-HU-331)**. To a solution of cannabidiol (0.101 g, 0.322 mmol) in acetone (8.9 mL) was added an aqueous solution (13.5 mL) of potassium dihydrogen orthophosphate (0.103 g, 2.25 mmol, 0.056 M) and Frémy's salt (potassium nitrosodisulfonate, 0.60 g, 1.77 mmol). After stirring at 20 °C for 16 h the mixture was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography (1: 39 ethyl acetate: hexane) to give **(±)-HU-331** (0.10 g, 92%) as an amber oil; IR ν_{max} (cm^{-1}) 3389 (O-H), 1653 (C=O), 1637 (C=O), 1612 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (s, 1H, OH), 6.39 (1H, t, *J* = 1.5 Hz, H-3), 5.13 (1H, s, H-2'), 4.54–4.50 (2H, m, 2'-CH_3C=CH_2), 3.74 (1H, m, H-1'), 2.75 (1H, m, H-6'), 2.42–2.37 (2H, m, aryl-CH_2), 2.20 (1H, m, H-4'), 1.98 (1H, m, H-4'), 1.77 (1H, m, H-5'), 1.68 (1H, m, H-5'), 1.67 (3H, s, 3'-CH_3), 1.62 (3H, s, 2'-CH_3C=CH_2), 1.53–1.47 (2H, m, aryl-CH_2CH_2), 1.33–1.28 (4H, m, CH_2C$H_2$$CH_3$), 0.89 (3H, t, *J* = 7.0 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.5 (C-5), 184.4 (C-2), 151.7 (C-6), 148.8 (2'-CH_3C=CH_2), 144.9 (C-4), 135.1 (C-3), 134.3 (C-3'), 123.2 (C-1), 122.8 (C-2'), 111.0 (2'-CH_3C=CH_2), 45.1 (C-6'), 36.2 (C-1'), 31.8, 30.9, 29.2, 28.5, 27.5, 23.8, 22.7, 19.1, 14.3; MS (CI+) *m/z* (%): 329 ([M+H]$^+$, 100), 311 (47), 287 (27). HRMS *m/z* M$^+$, calcd. for $C_{21}H_{29}O_3$: 329.2116, found: 329.2115.


HO
O
O
9a
^{1}H NMR ($CDCl_3$, 600 MHz)
1.00
0.99
1.01
1.05
1.99
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

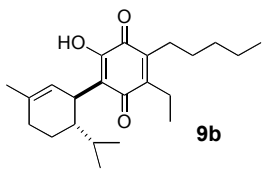

187.59
184.09
151.78
144.78
134.87
134.74
123.47
122.84
77.35
77.14
76.93
41.66
36.64
35.51
30.72
29.11
28.29
27.32
23.57
22.57
22.49
21.57
16.36
14.05
HO
O
O
9a
^{13}C NMR ($CDCl_3$, 150 MHz)
260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)



9b

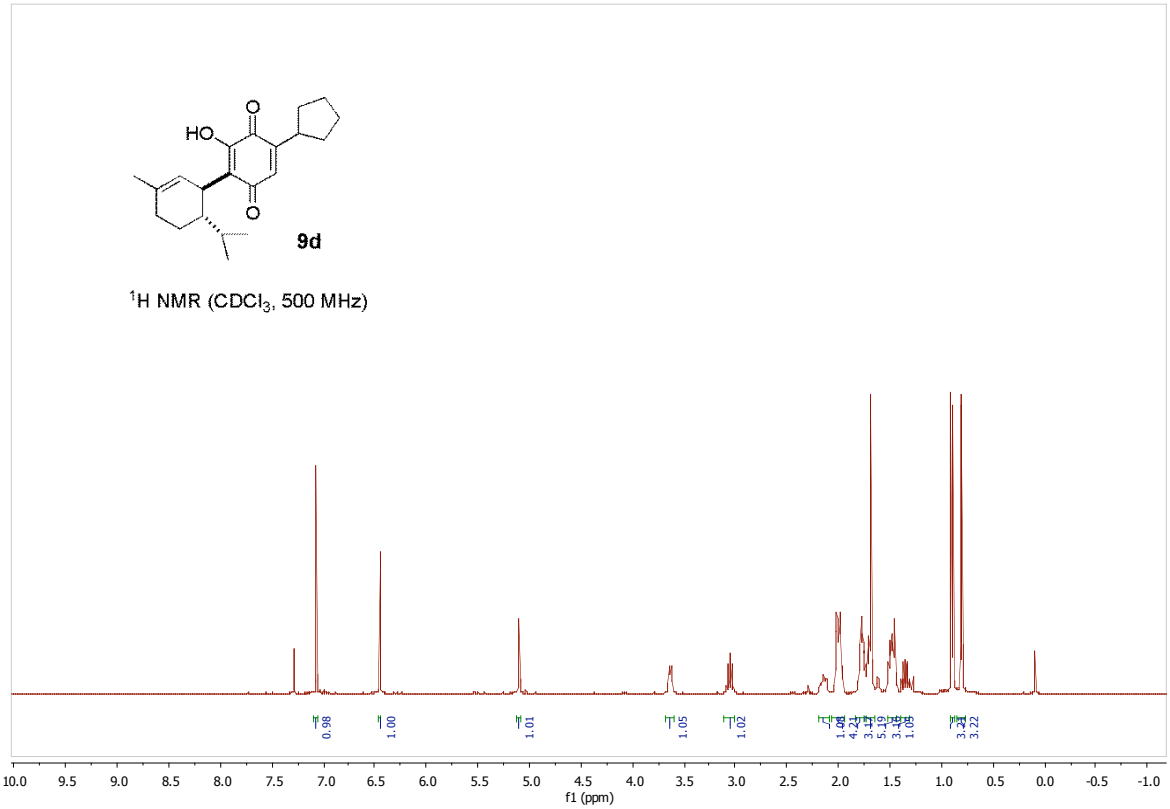
^{1}H NMR ($CDCl_3$, 600 MHz)

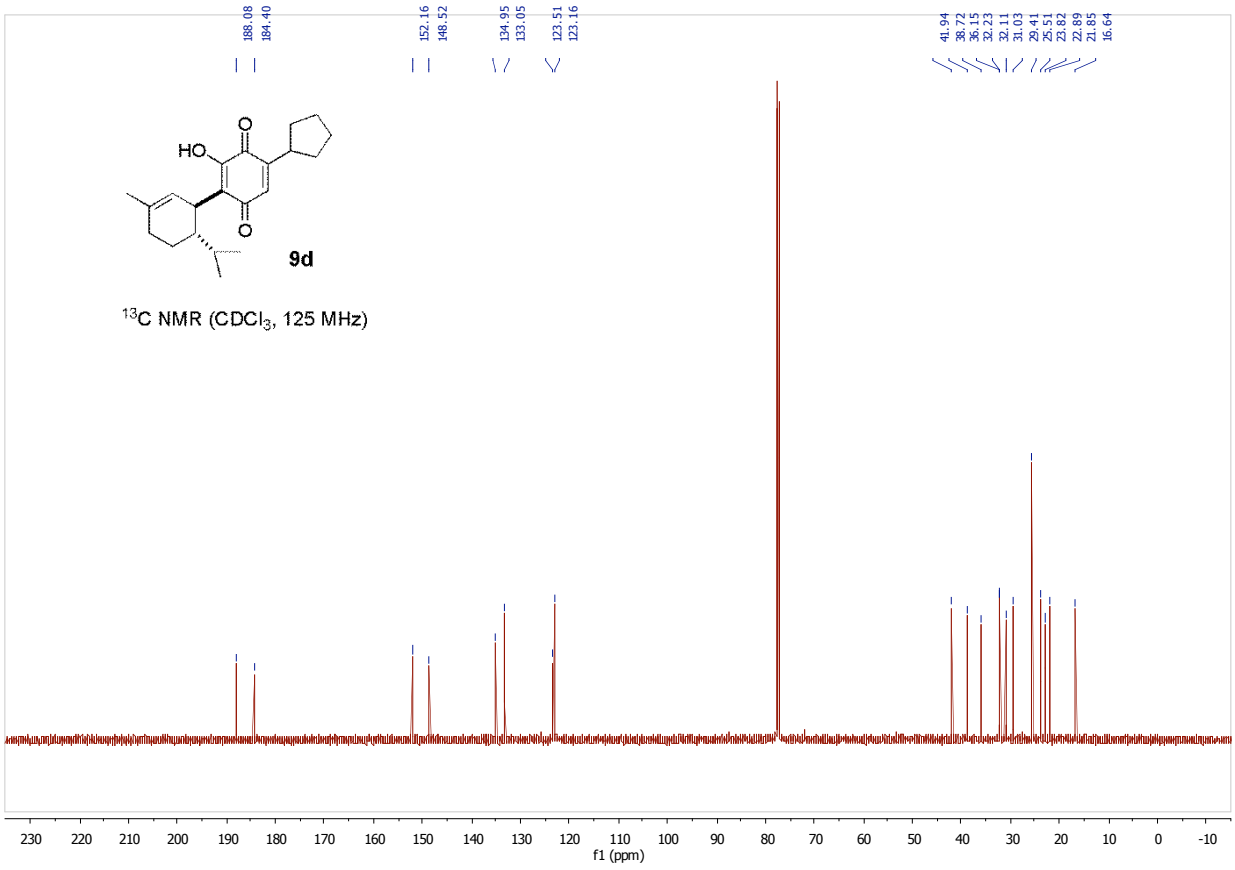
9b C.esp



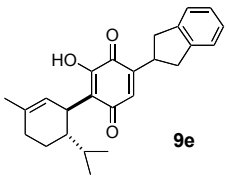
9b

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


HO
O
O
9d
^{1}H NMR (CDCl$_3$, 500 MHz)
0.98
1.00
1.01
1.05
1.02
1.05
3.22
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


188.08
184.40
152.16
148.52
134.95
133.05
123.51
123.16
41.94
38.72
36.15
32.23
32.11
31.03
29.41
25.51
23.82
22.89
21.85
16.64
HO
O
O
9d
^{13}C NMR (CDCl$_3$, 125 MHz)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

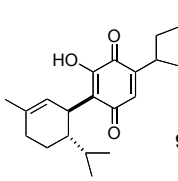
9e H.esp



9e

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

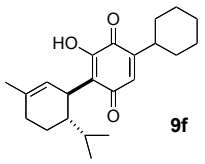
9e C.esp



9e

^{13}C NMR ($CDCl_3$, 125 MHz)

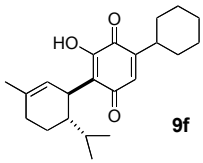
9f H.esp



9f

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

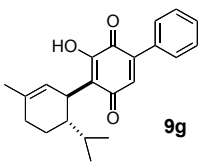
9f C.esp



9f

^{13}C NMR ($CDCl_3$, 125 MHz)

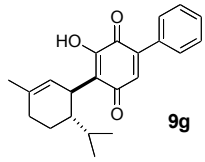
9g H.esp



9g

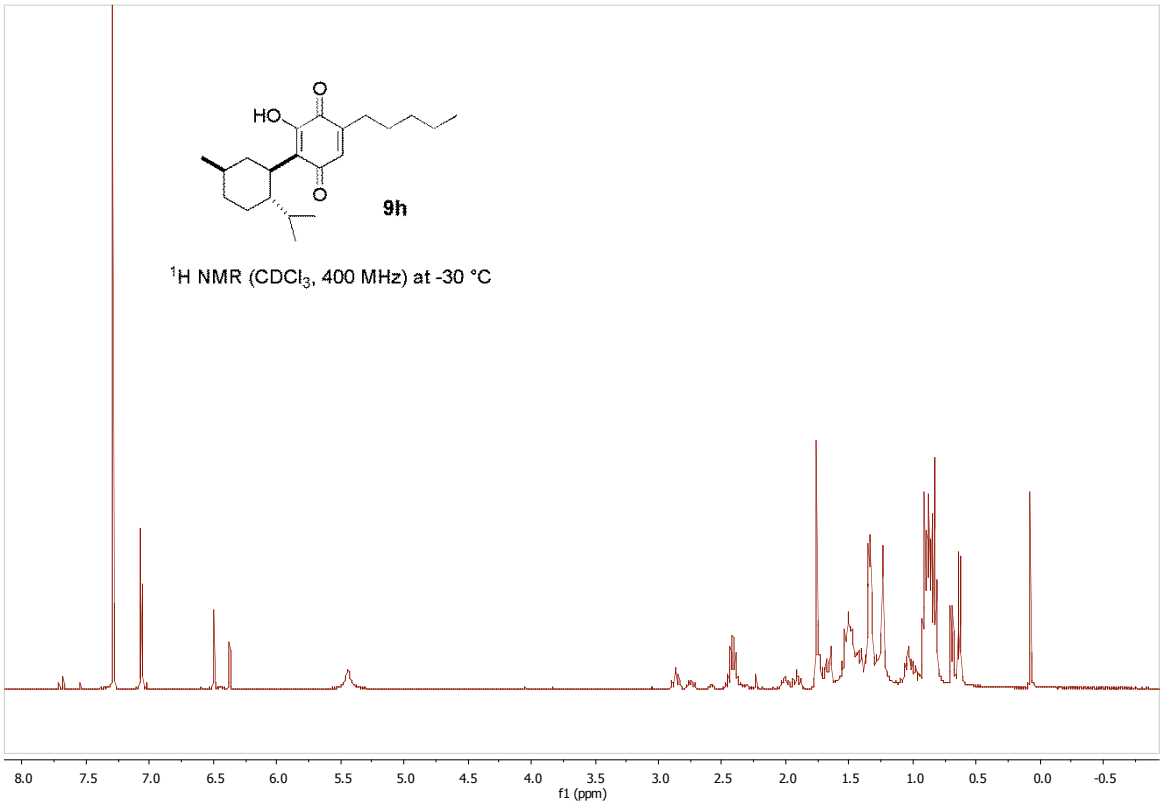
^{1}H NMR ($CDCl_3$, 600 MHz)

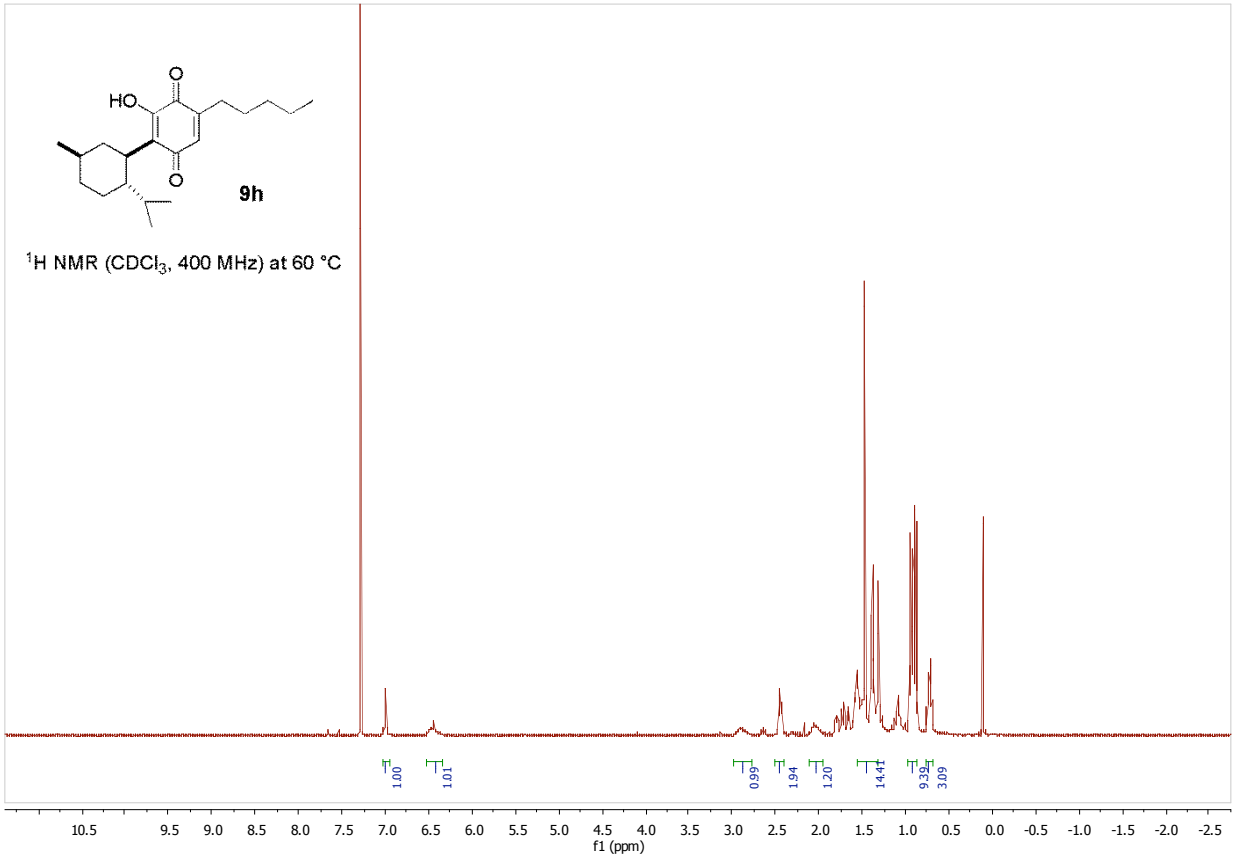
9g C.esp

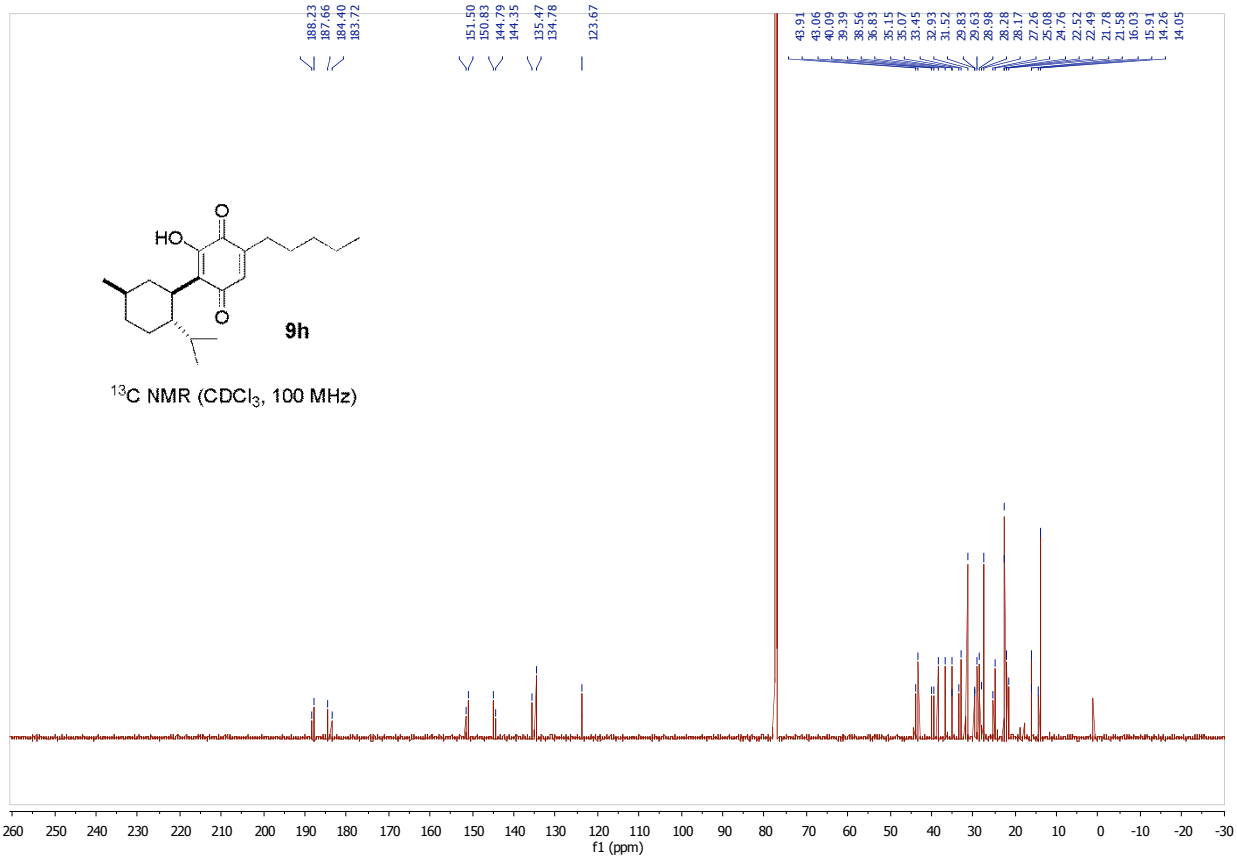


9g

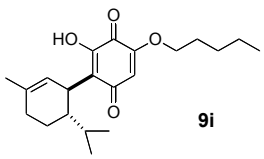
^{13}C NMR ($CDCl_3$, 150 MHz)


HO
O
O
9h
^{1}H NMR ($CDCl_3$, 400 MHz) at -30 °C
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


HO
O
O
9h
^{1}H NMR ($CDCl_3$, 400 MHz) at 60 °C
1.00
1.01
0.99
1.94
1.20
14.41
9.39
3.09
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0 -2.5
f1 (ppm)

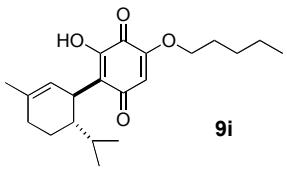

188.23
187.66
184.40
183.72
151.50
150.83
144.79
144.35
135.47
134.78
123.67
43.91
43.06
40.09
39.39
38.56
36.83
35.15
35.07
33.45
32.93
31.52
29.83
29.63
28.98
28.28
28.17
27.26
25.08
24.76
22.52
22.49
21.78
21.58
16.03
15.91
14.26
14.05
HO
O
O
9h
13C NMR (CDCl3, 100 MHz)
260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

9i H.esp



9i

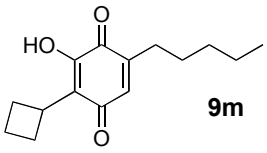
^{1}H NMR ($CDCl_3$, 600 MHz)



9i

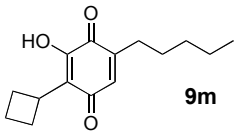
^{13}C NMR ($CDCl_3$, 125 MHz)

9m H.esp



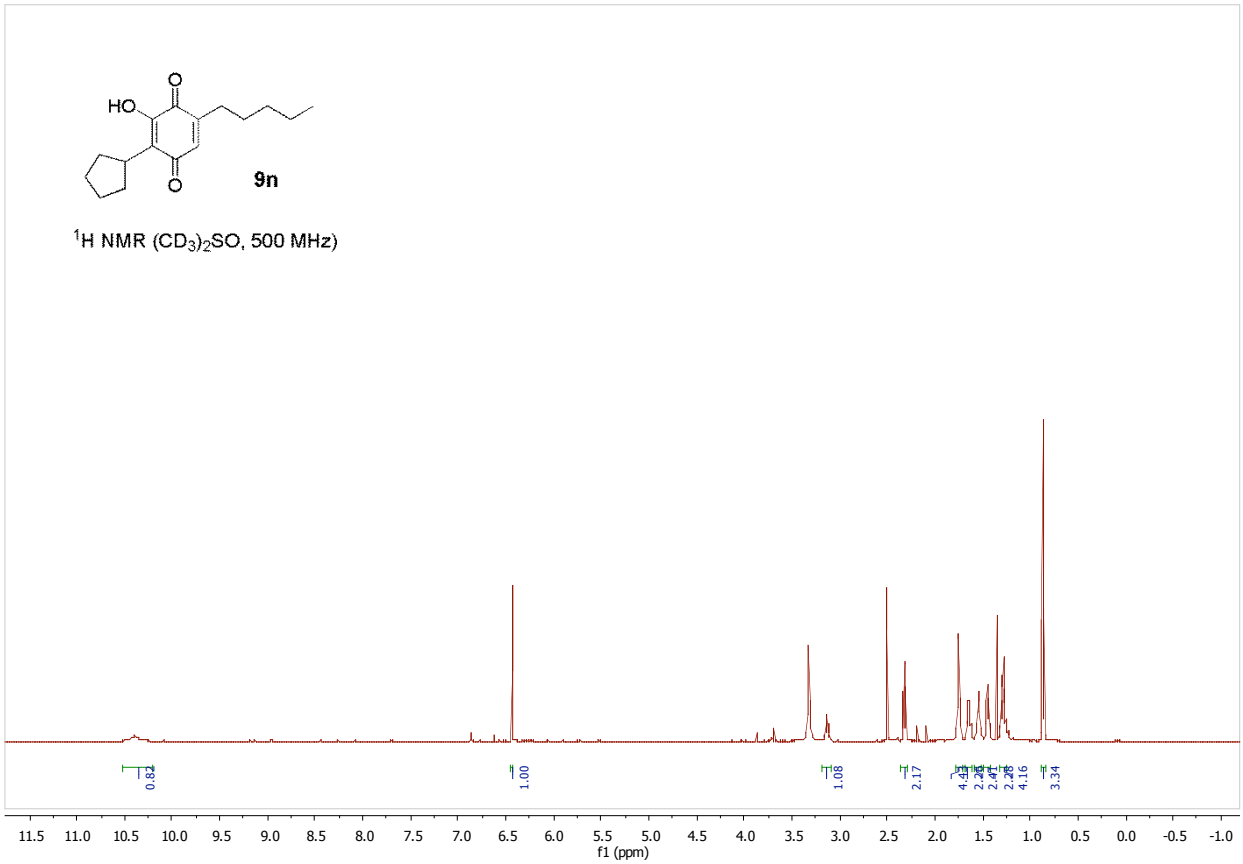
9m

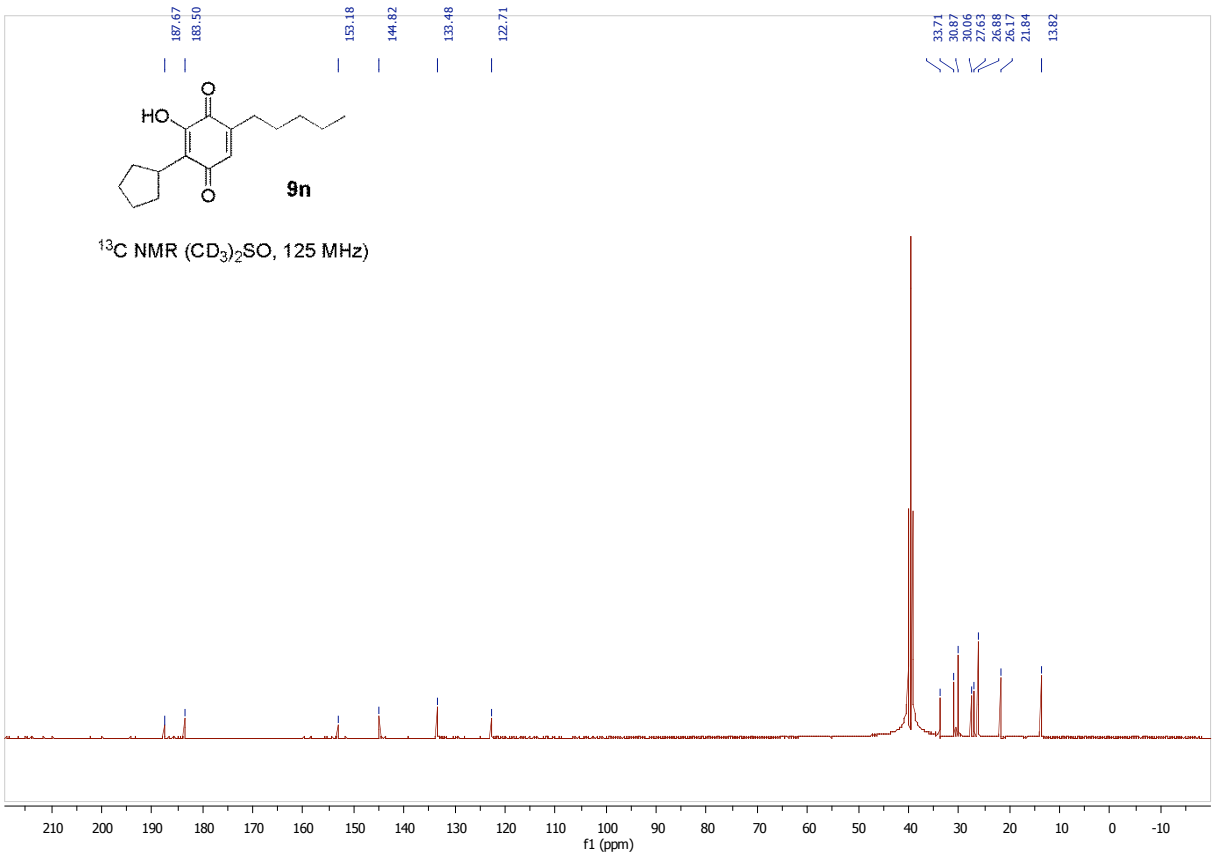
^{1}H NMR $(CD_3)_2SO$ 600 MHz

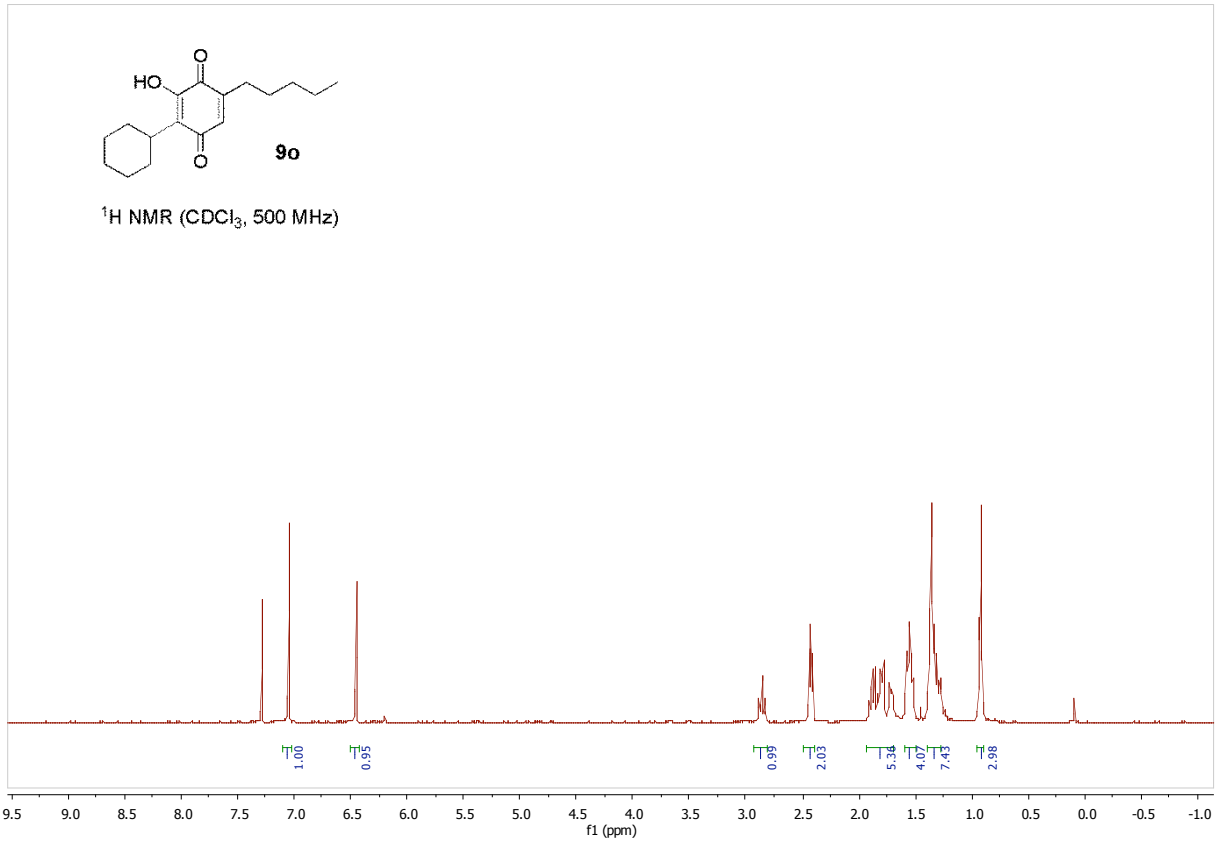


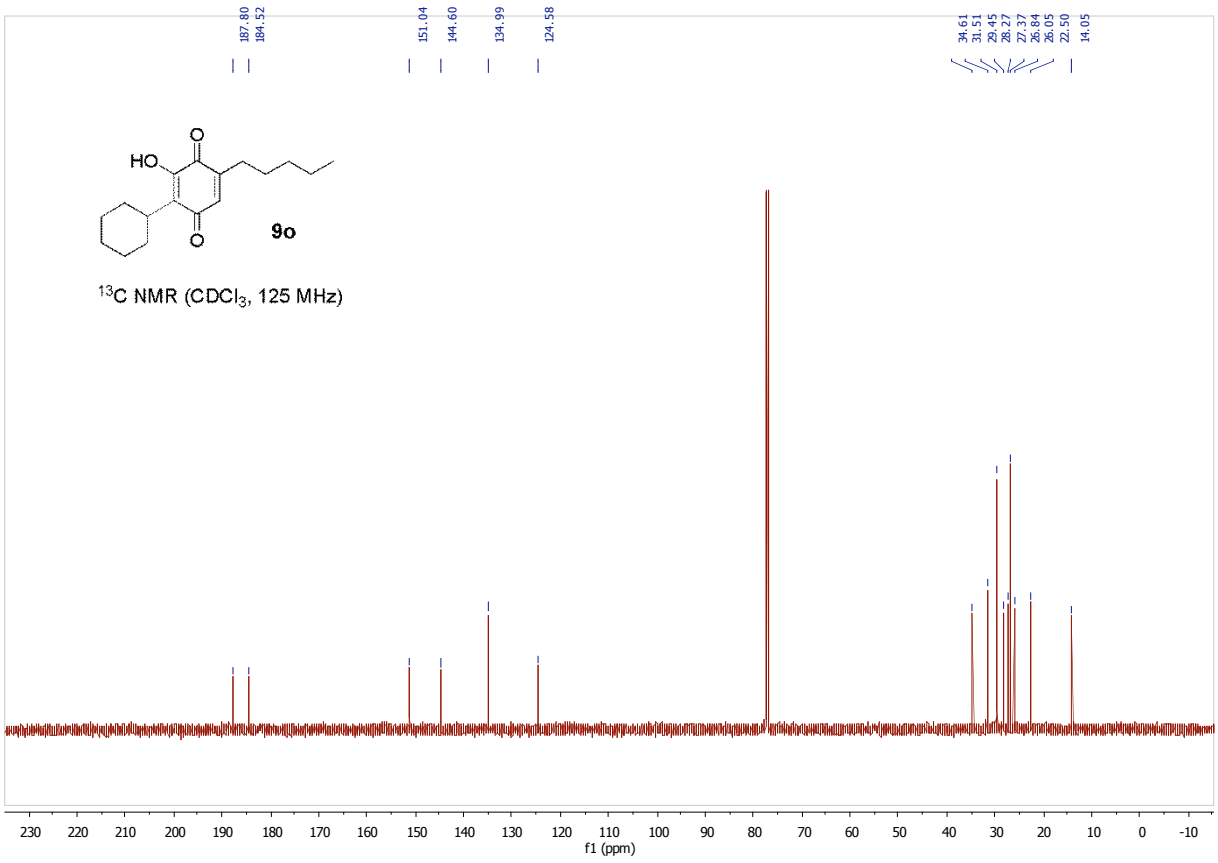
9m

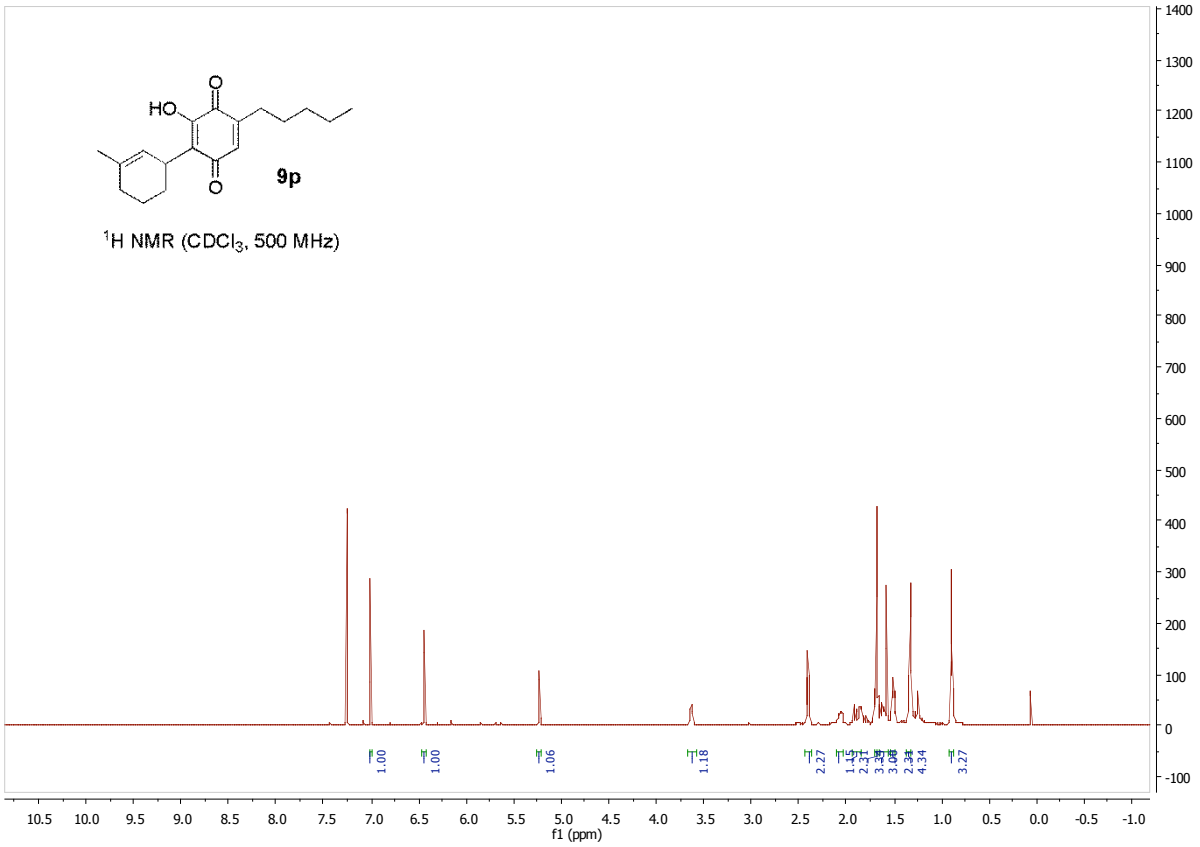
^{13}C NMR ($CDCl_3$, 125 MHz)

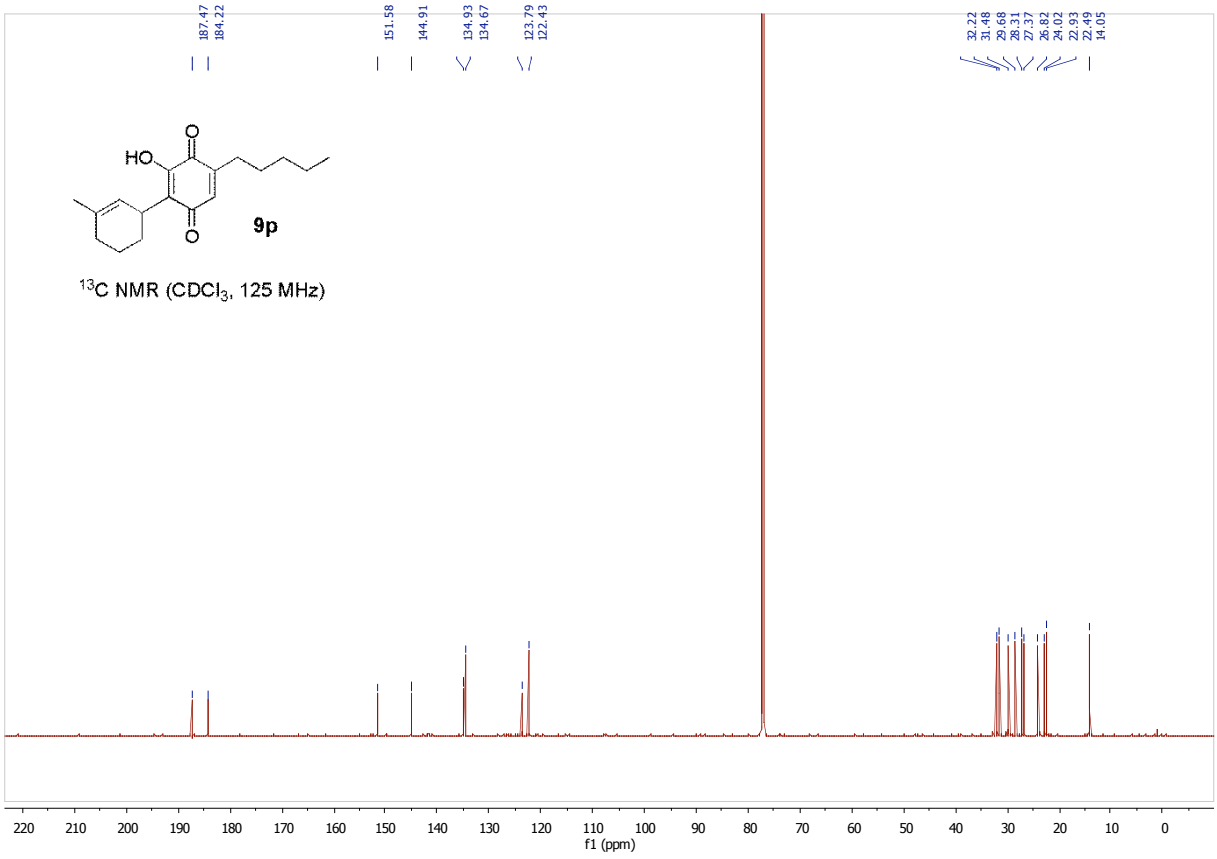

HO
O
O
9n
^{1}H NMR $(CD_3)_2SO$, 500 MHz)
0.82
1.00
1.08
2.17
3.34
f1 (ppm)


187.67
183.50
153.18
144.82
133.48
122.71
33.71
30.87
30.06
27.63
26.88
26.17
21.84
13.82
HO
O
O
9n
^{13}C NMR $(CD_3)_2SO$, 125 MHz)
f1 (ppm)

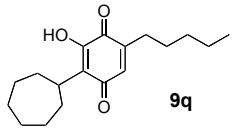

HO
O
O
9o
^{1}H NMR ($CDCl_3$, 500 MHz)
1.00
0.95
0.99
2.03
5.34
4.07
7.43
2.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


187.80
184.52
151.04
144.60
134.99
124.58
34.61
31.51
29.45
28.27
27.37
26.84
26.05
22.50
14.05
HO
O
O
9o
^{13}C NMR ($CDCl_3$, 125 MHz)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


HO
O
O
9p
^{1}H NMR ($CDCl_3$, 500 MHz)
1.00
1.00
1.06
1.18
2.27
3.27
4.34
f1 (ppm)


187.47
184.22
151.58
144.91
134.93
134.67
123.79
122.43
32.22
31.48
29.68
29.31
27.37
26.82
24.02
22.93
22.49
14.05
HO
O
O
9p
^{13}C NMR ($CDCl_3$, 125 MHz)
f1 (ppm)

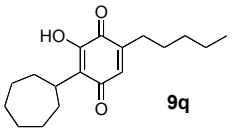
9q H.esp



9q

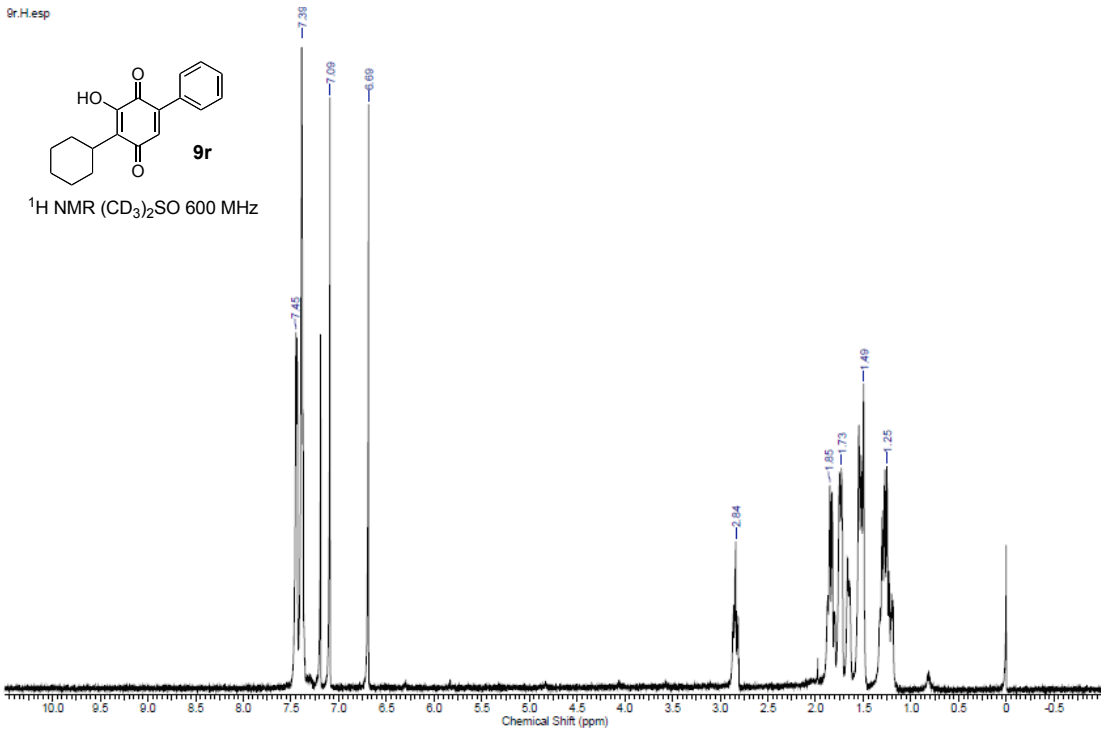
^{1}H NMR ($CDCl_3$, 600 MHz)

9q C.esp

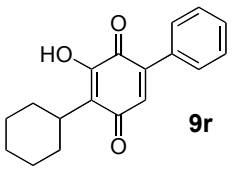


9q

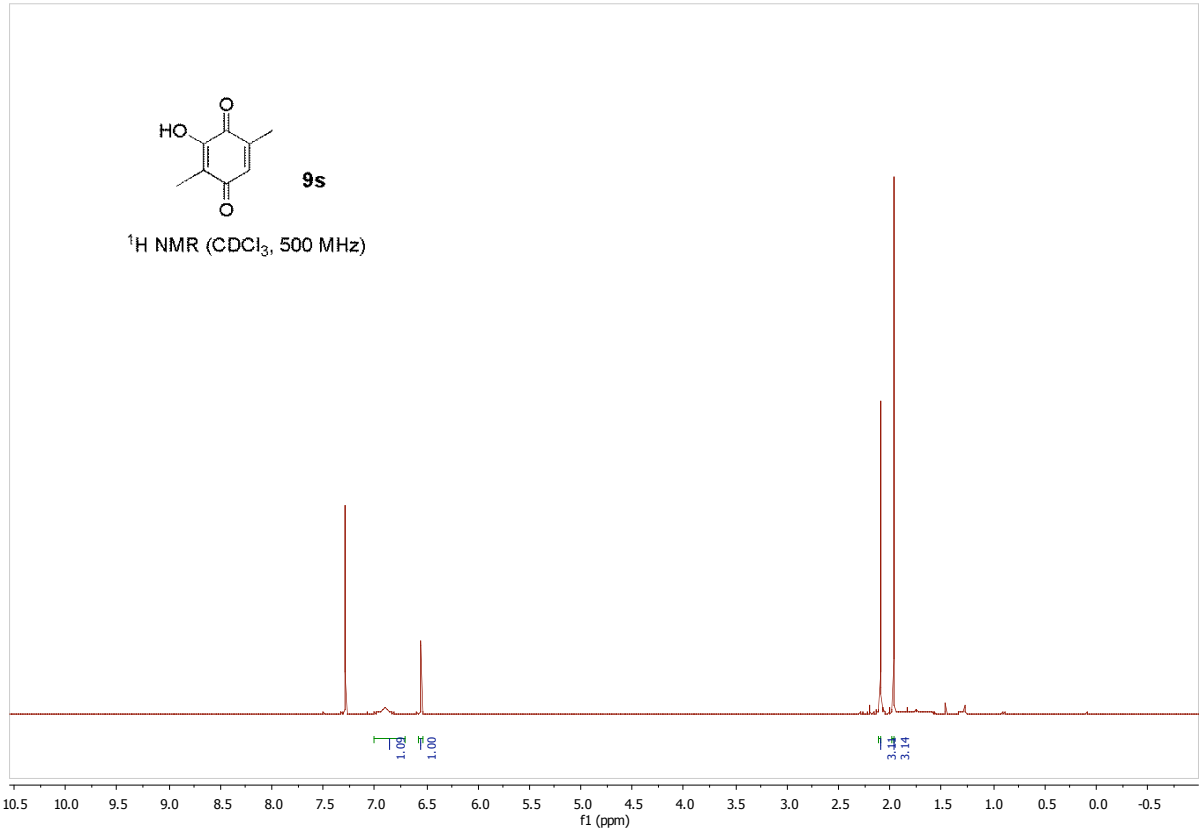
^{13}C NMR ($CDCl_3$, 150 MHz)

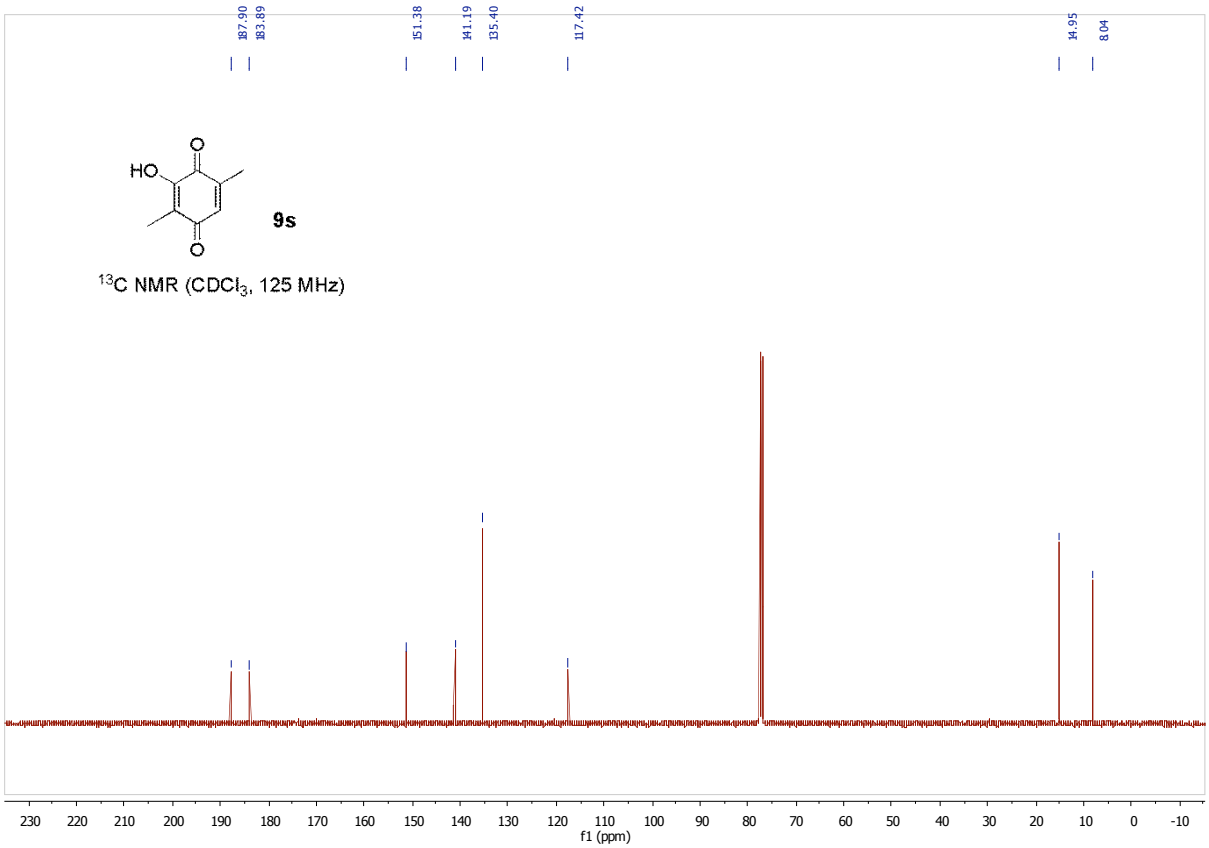


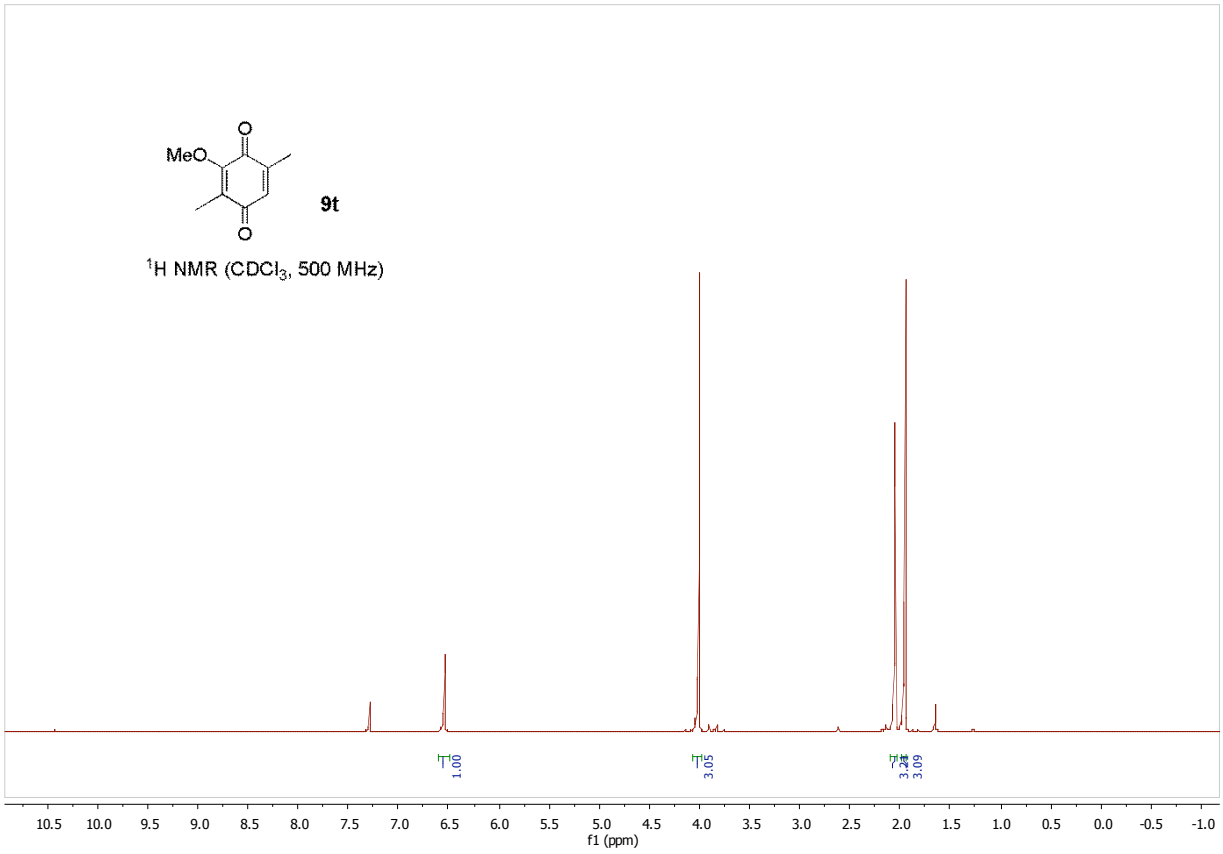
^{1}H NMR $(CD_3)_2SO$ 600 MHz

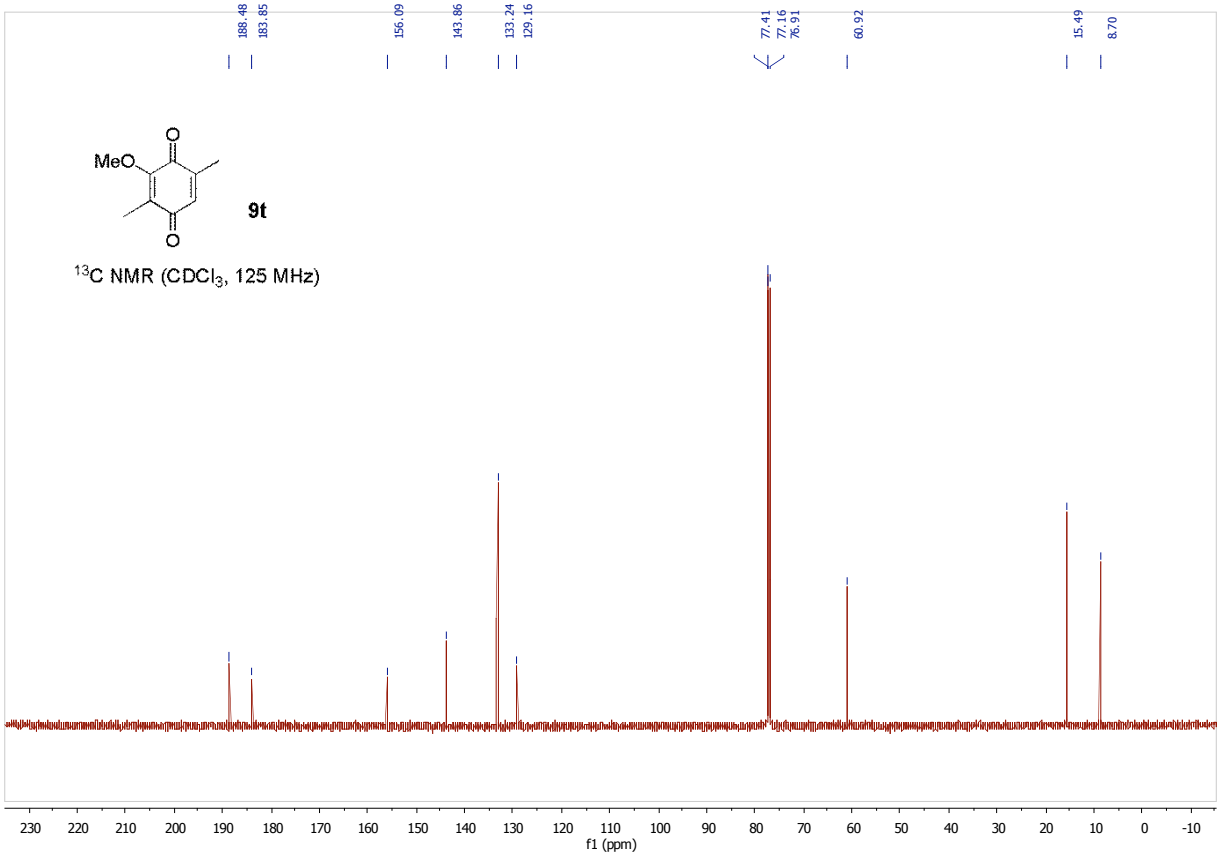


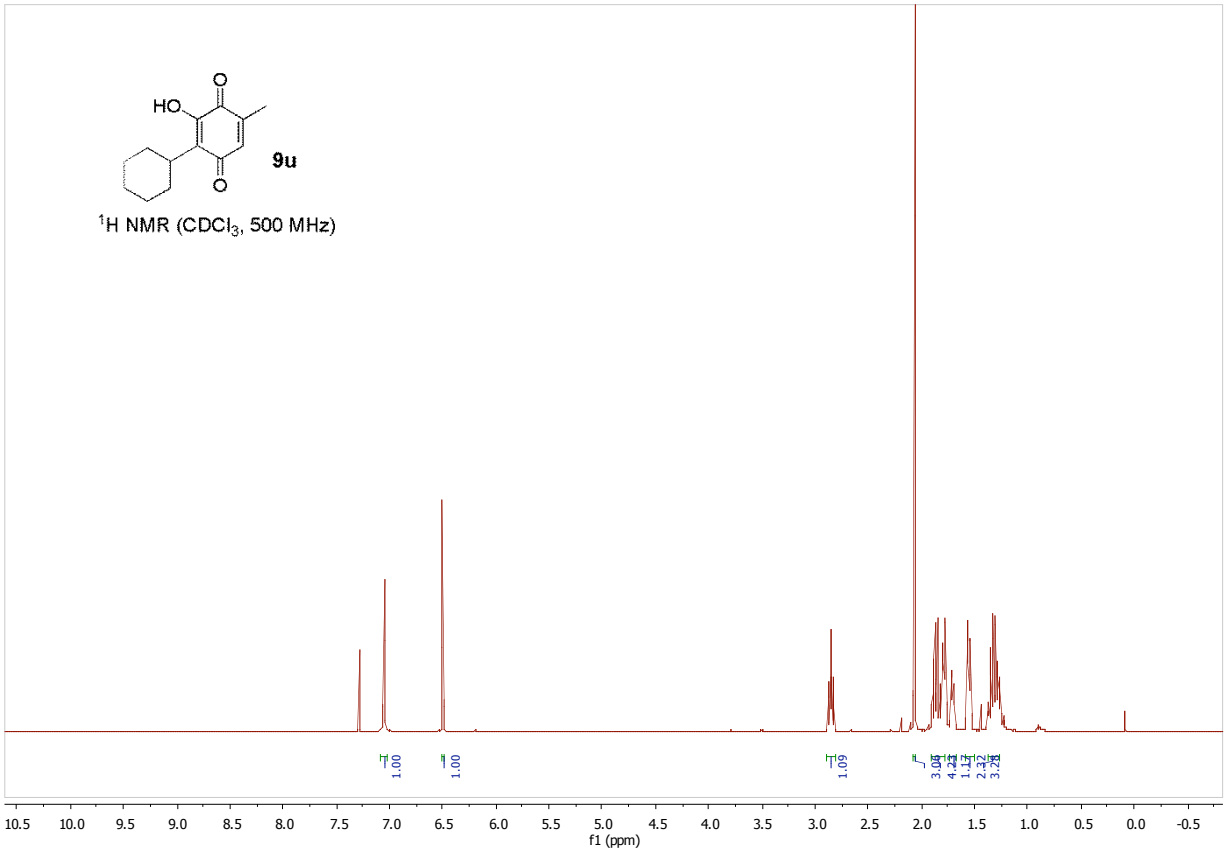
^{13}C NMR $(CDCl_3$, 125 MHz)

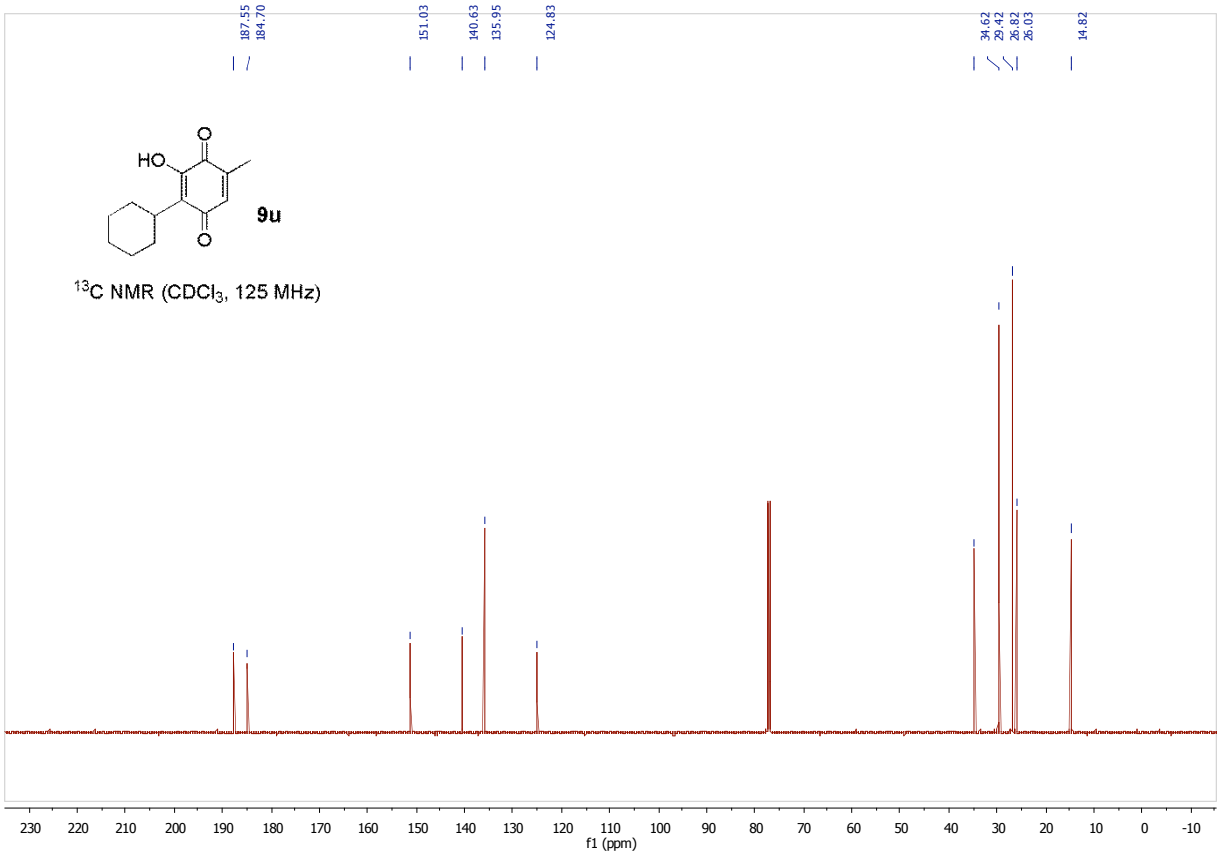

HO
O
O
9s
^{1}H NMR (CDCl$_3$, 500 MHz)
1.09
1.00
3.14
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

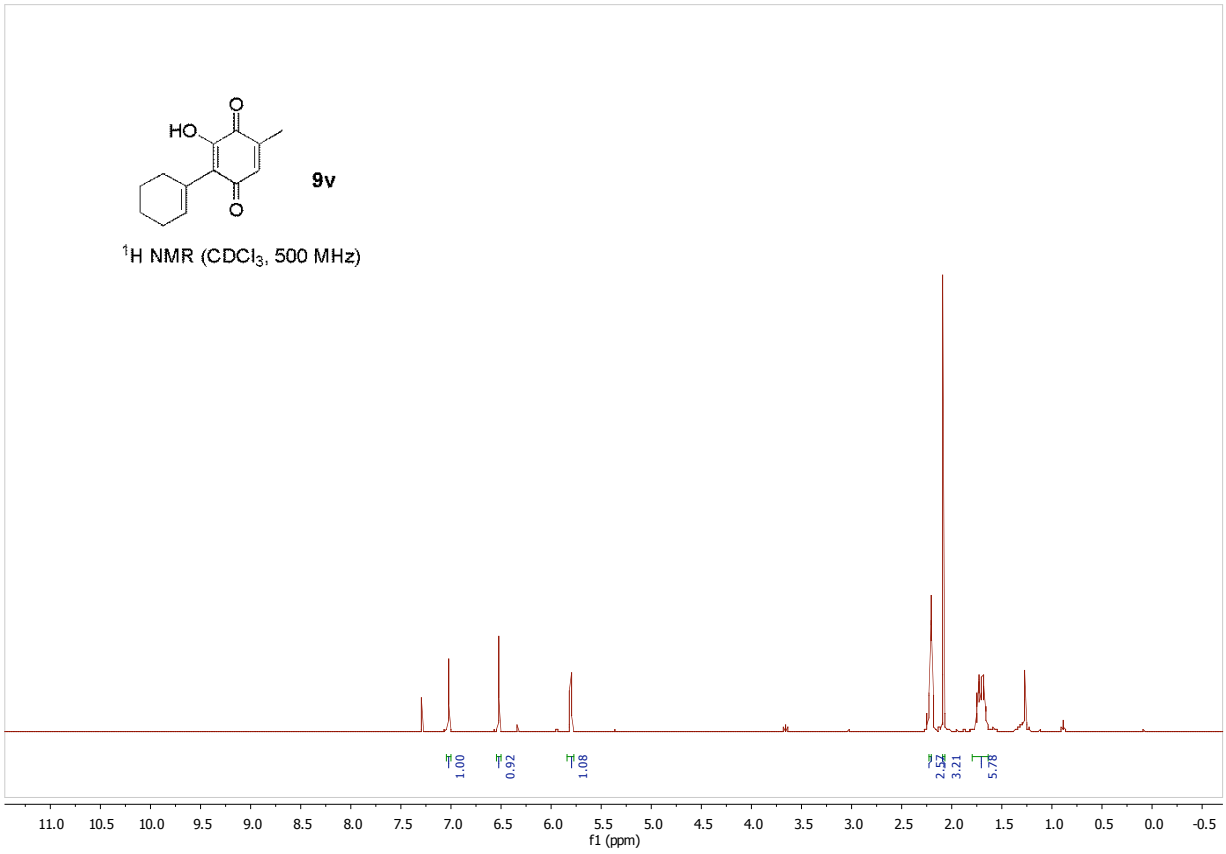

187.90
183.89
151.38
141.19
135.40
117.42
14.95
8.04
HO
O
O
9s
^{13}C NMR (CDCl$_3$, 125 MHz)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

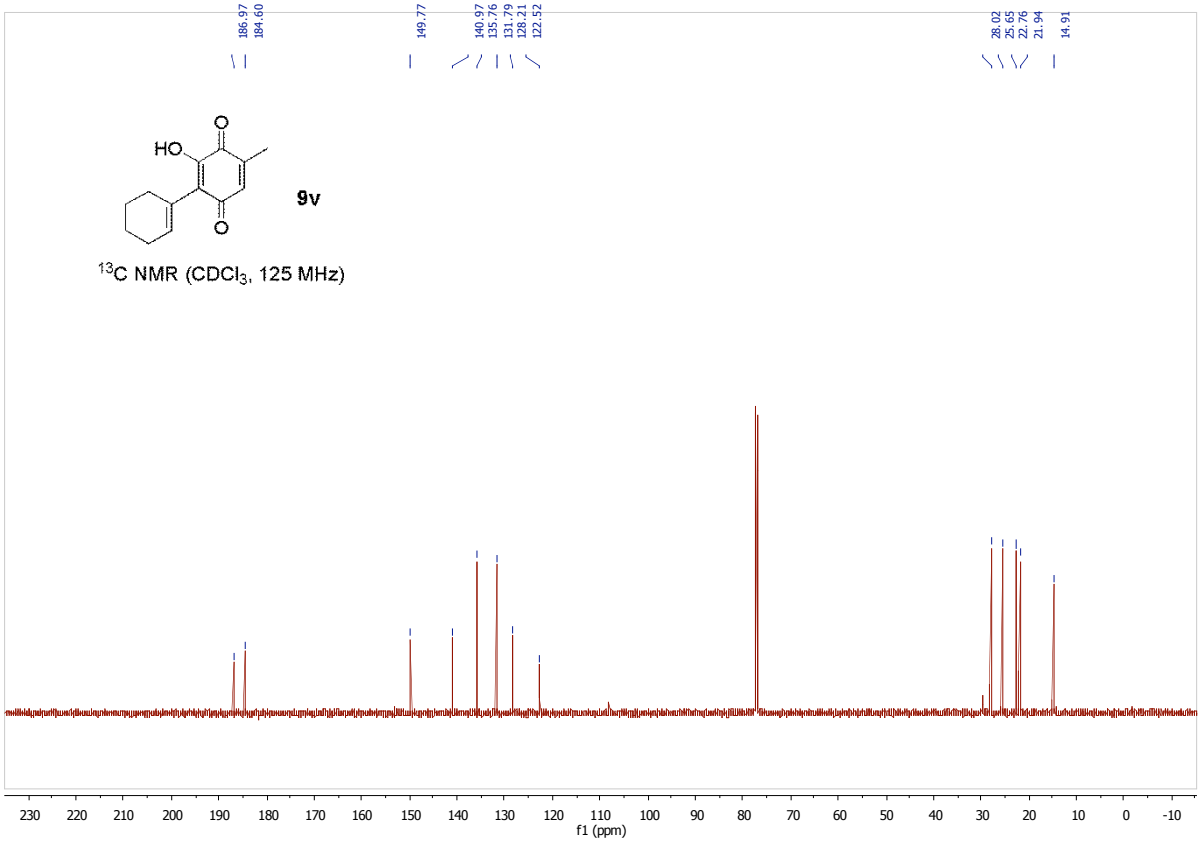

MeO
O
O
9t
^{1}H NMR (CDCl$_3$, 500 MHz)
1.00
3.05
3.24
3.09
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

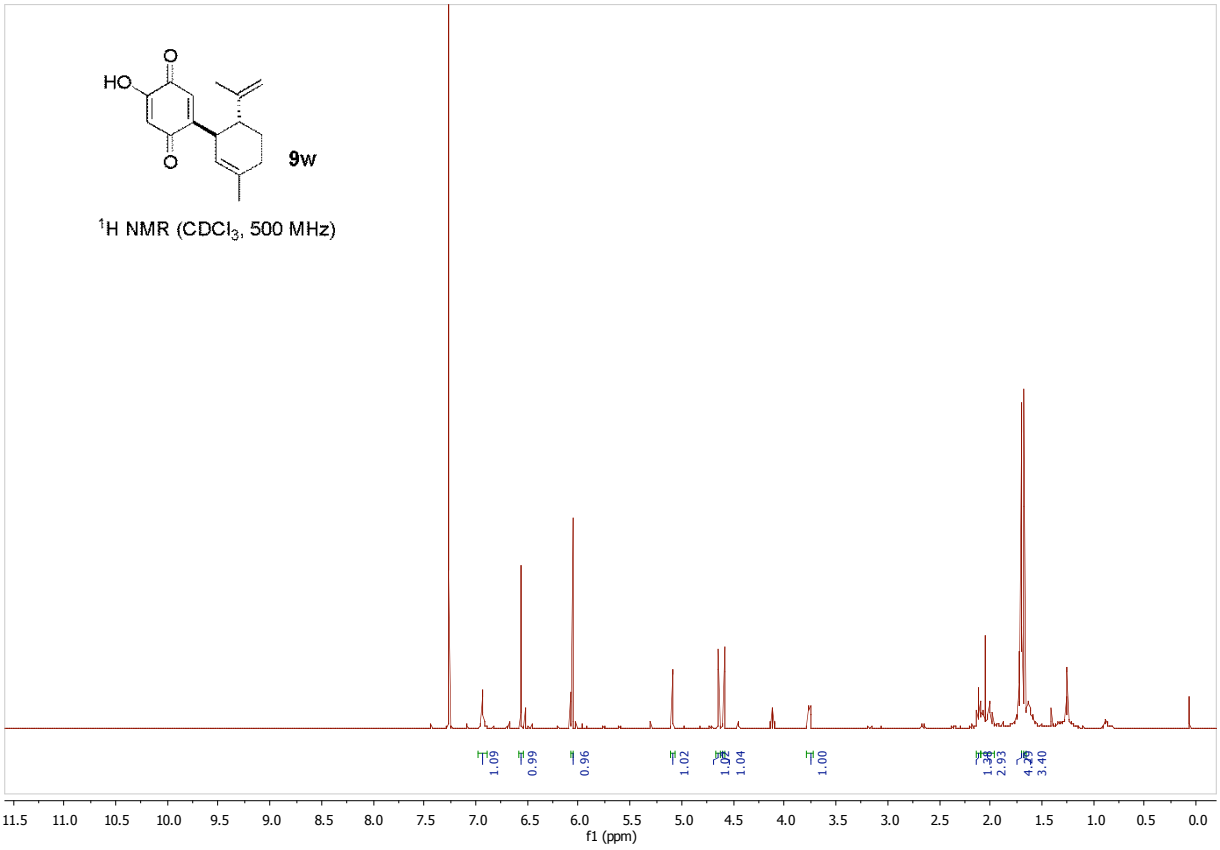

188.48
183.85
156.09
143.86
133.24
129.16
77.41
77.16
76.91
60.92
15.49
8.70
MeO
O
O
9t
^{13}C NMR (CDCl$_3$, 125 MHz)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

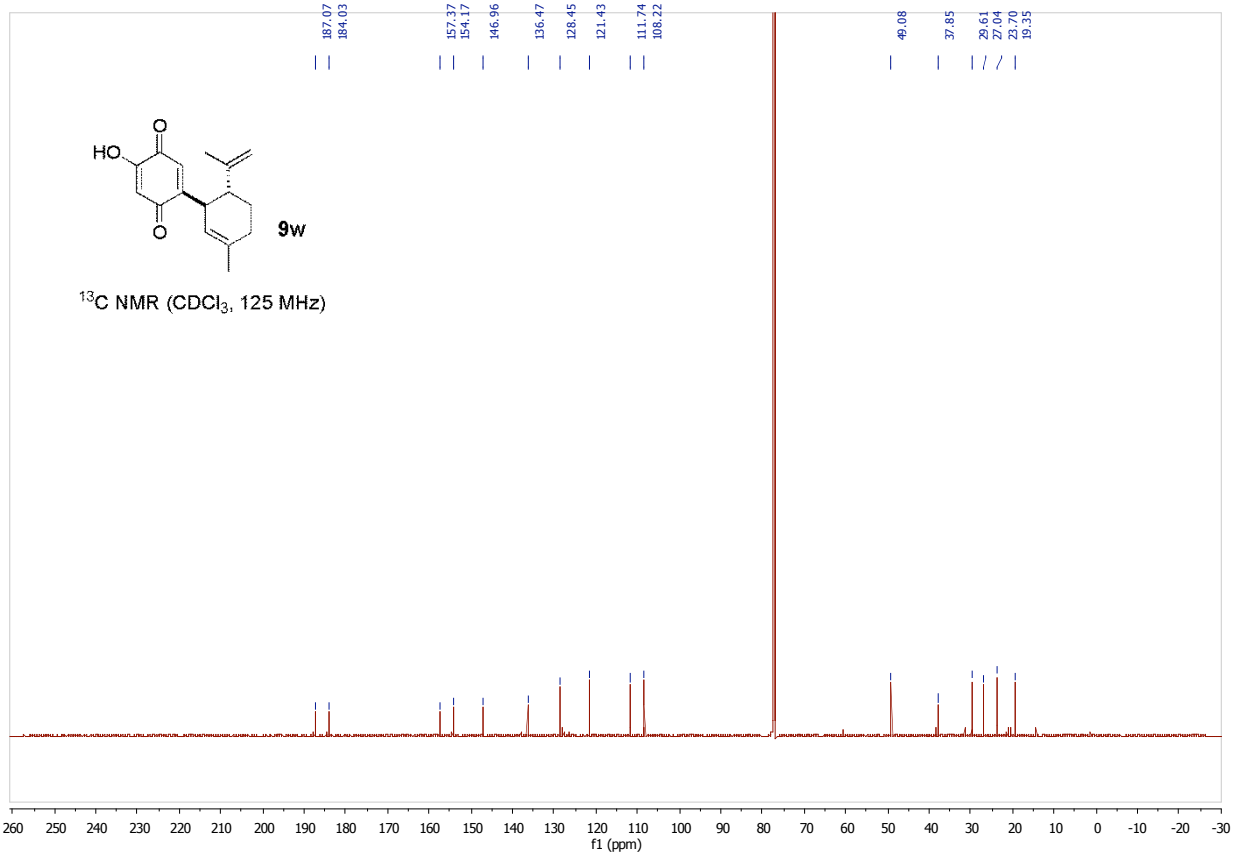

HO
O
O
9u
^{1}H NMR ($CDCl_3$, 500 MHz)
1.00
1.00
1.09
3.04
4.22
1.17
2.32
3.24
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

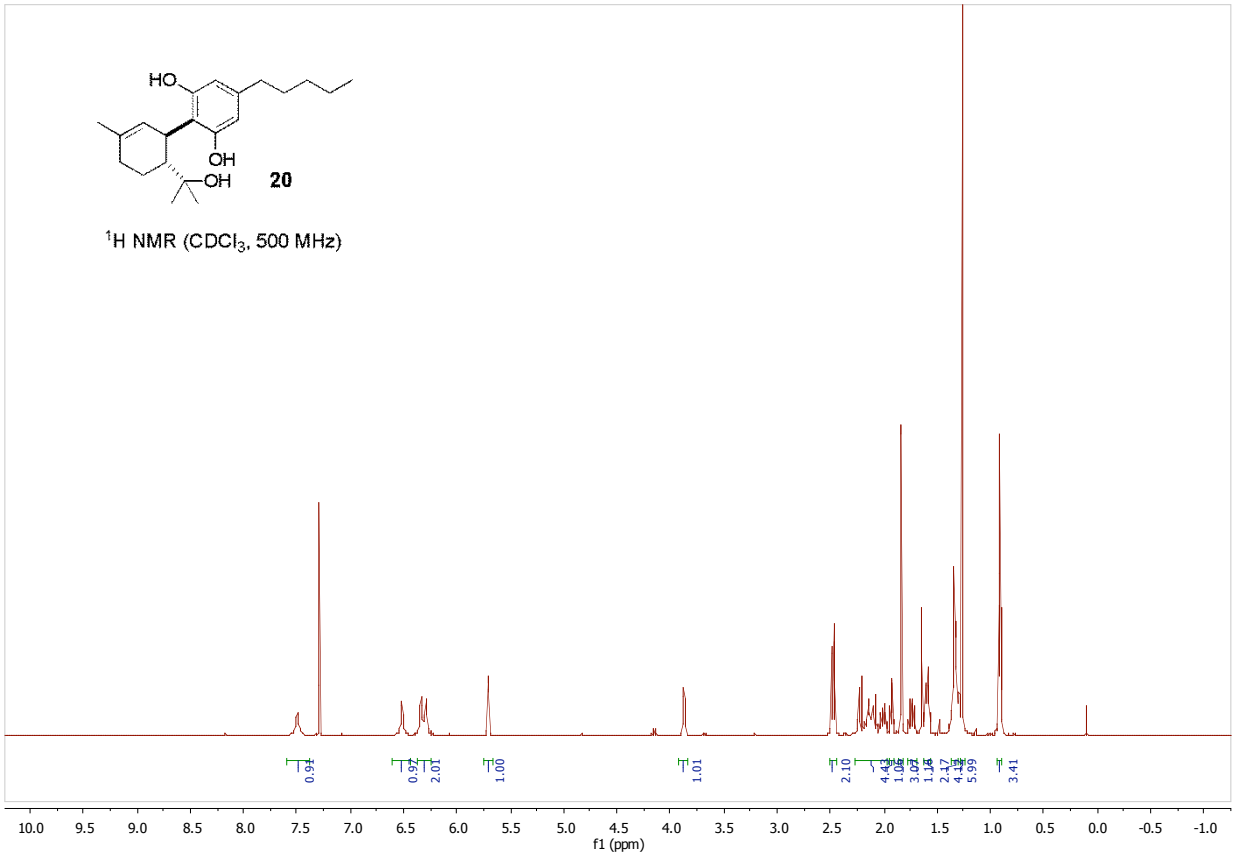

187.55
184.70
151.03
140.63
135.95
124.83
34.62
29.42
26.82
26.03
14.82
HO
O
O
9u
^{13}C NMR ($CDCl_3$, 125 MHz)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

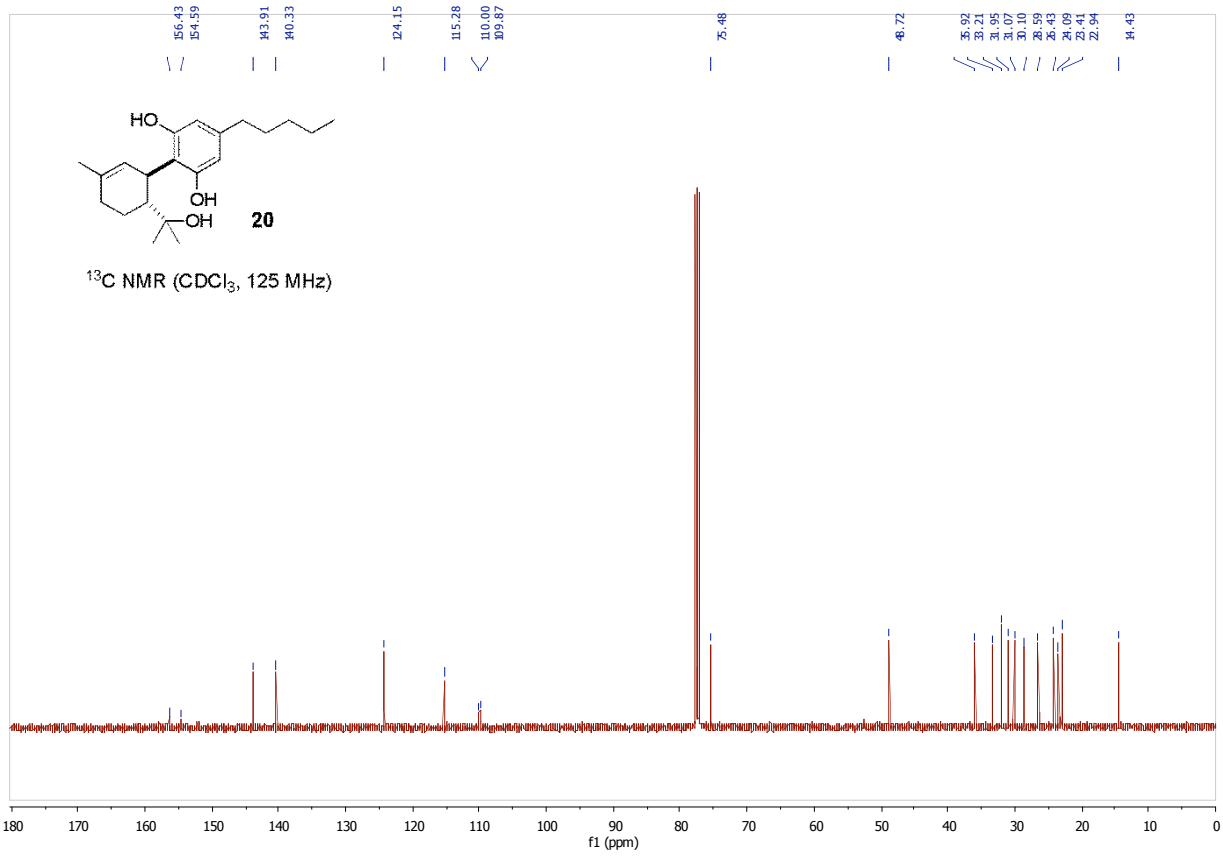

HO
O
O
9v
^{1}H NMR (CDCl$_3$, 500 MHz)
1.00
0.92
1.08
2.57
3.21
5.78
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

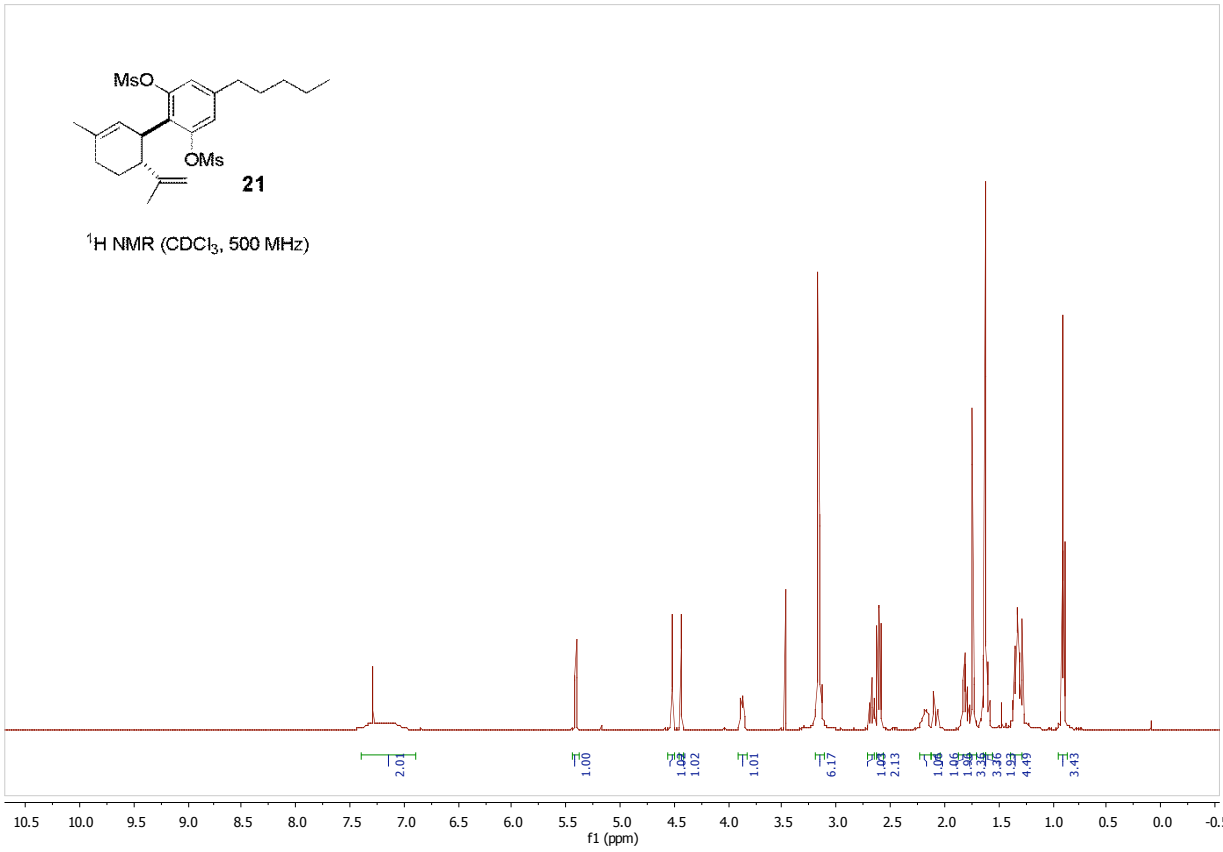

186.97
184.60
149.77
140.97
135.76
131.79
128.21
122.52
28.02
25.65
22.76
21.94
14.91
HO
O
O
9v
^{13}C NMR (CDCl$_3$, 125 MHz)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

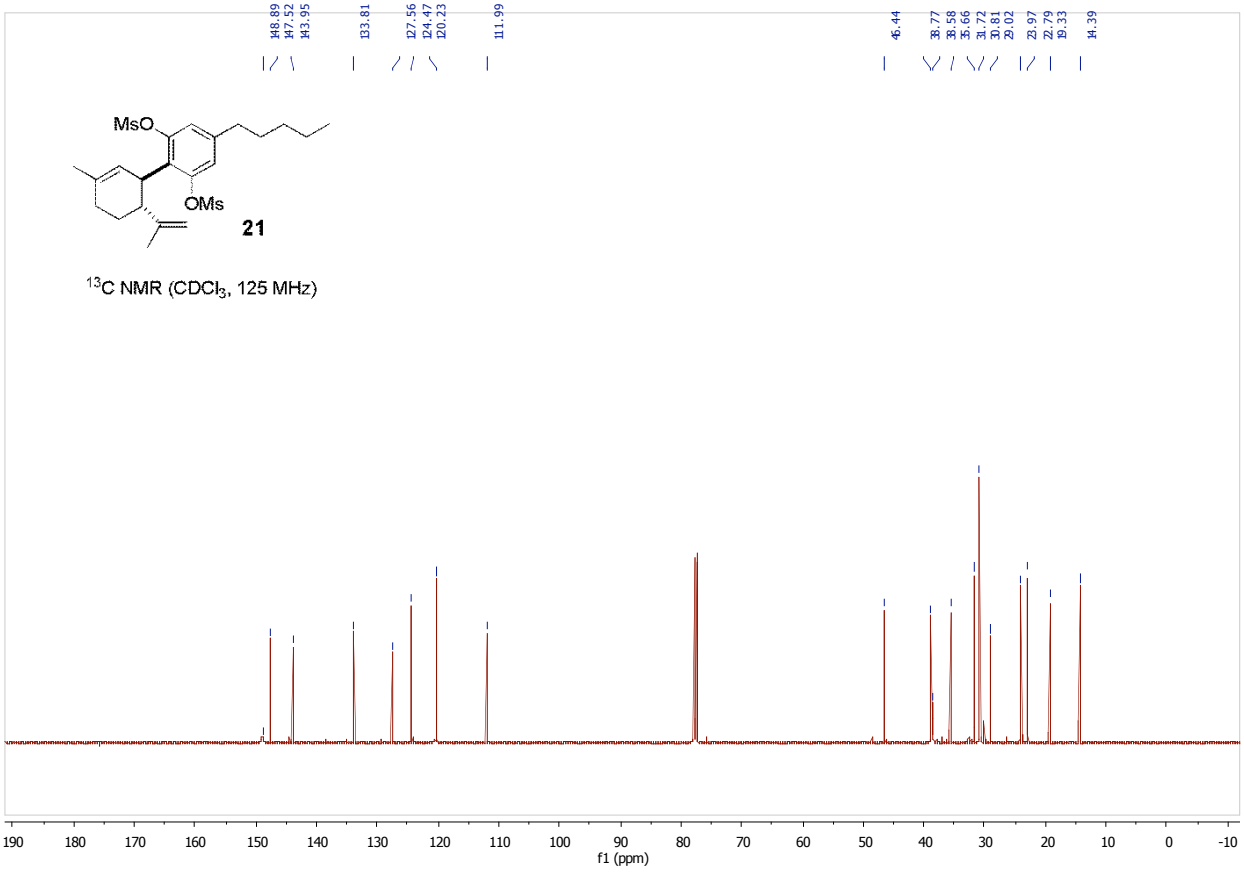

HO
O
O
9w
^{1}H NMR (CDCl$_3$, 500 MHz)
1.05
0.99
0.96
1.02
1.04
1.00
2.93
3.40
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

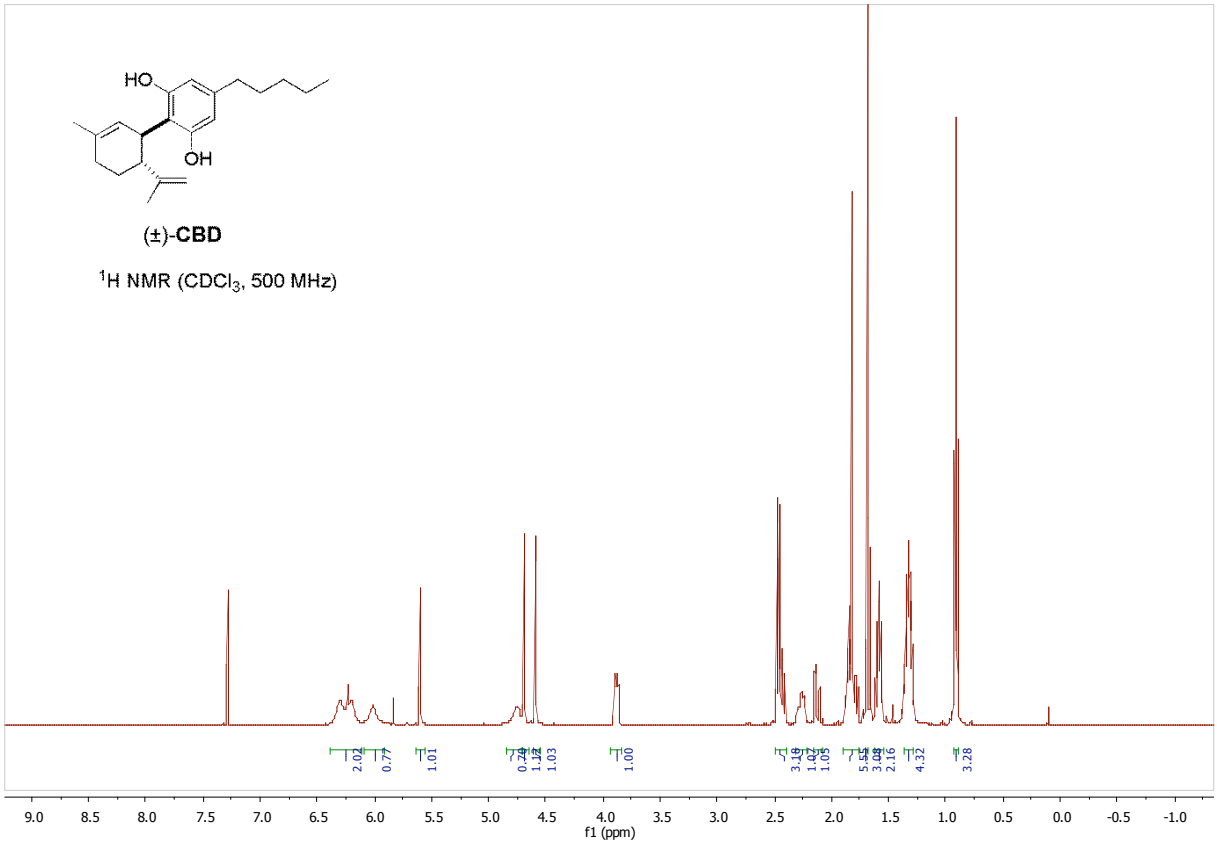

187.07
184.03
157.37
154.17
146.96
136.47
128.45
121.43
111.74
108.22
49.08
37.85
29.61
27.04
23.70
19.35
HO
O
O
9w
^{13}C NMR (CDCl$_3$, 125 MHz)
260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

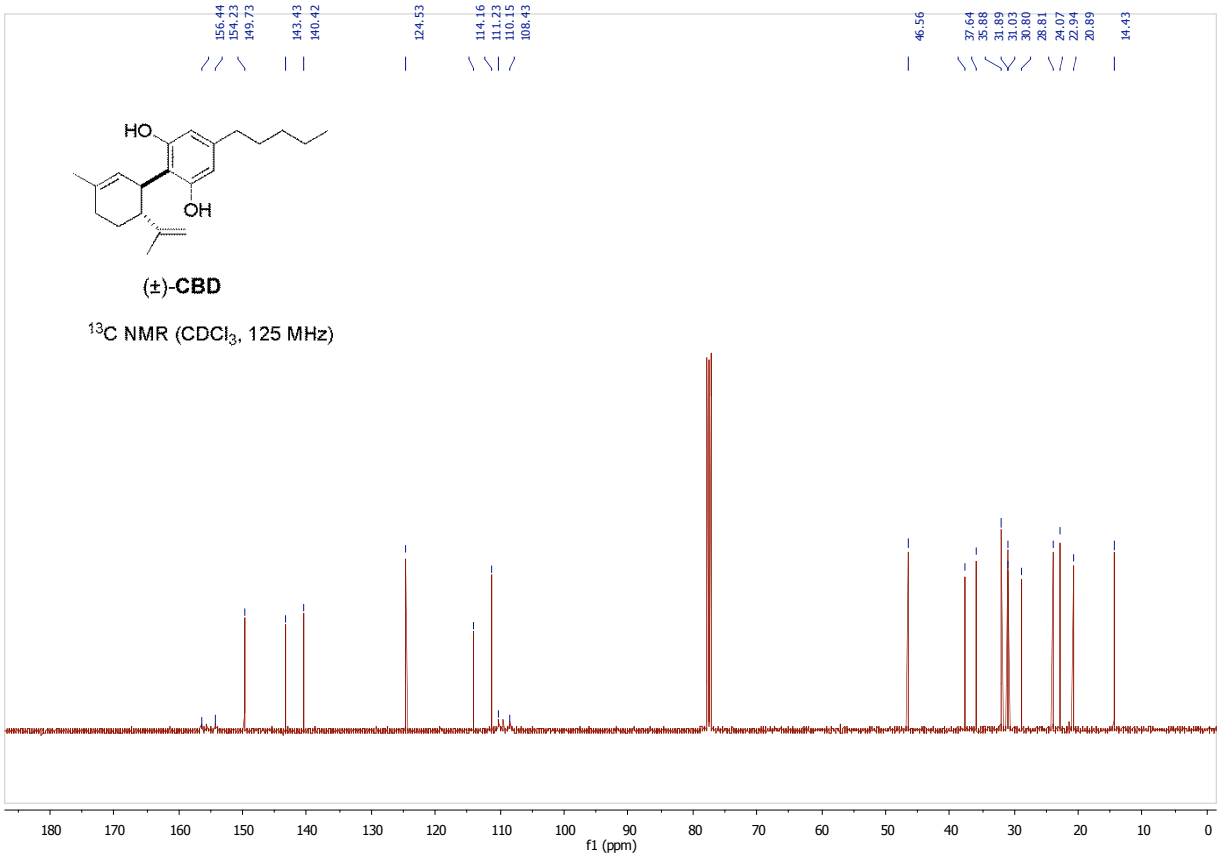

HO
OH
OH
20
^{1}H NMR ($CDCl_3$, 500 MHz)
0.94
0.97
2.01
1.00
1.01
2.10
5.99
3.41
f1 (ppm)

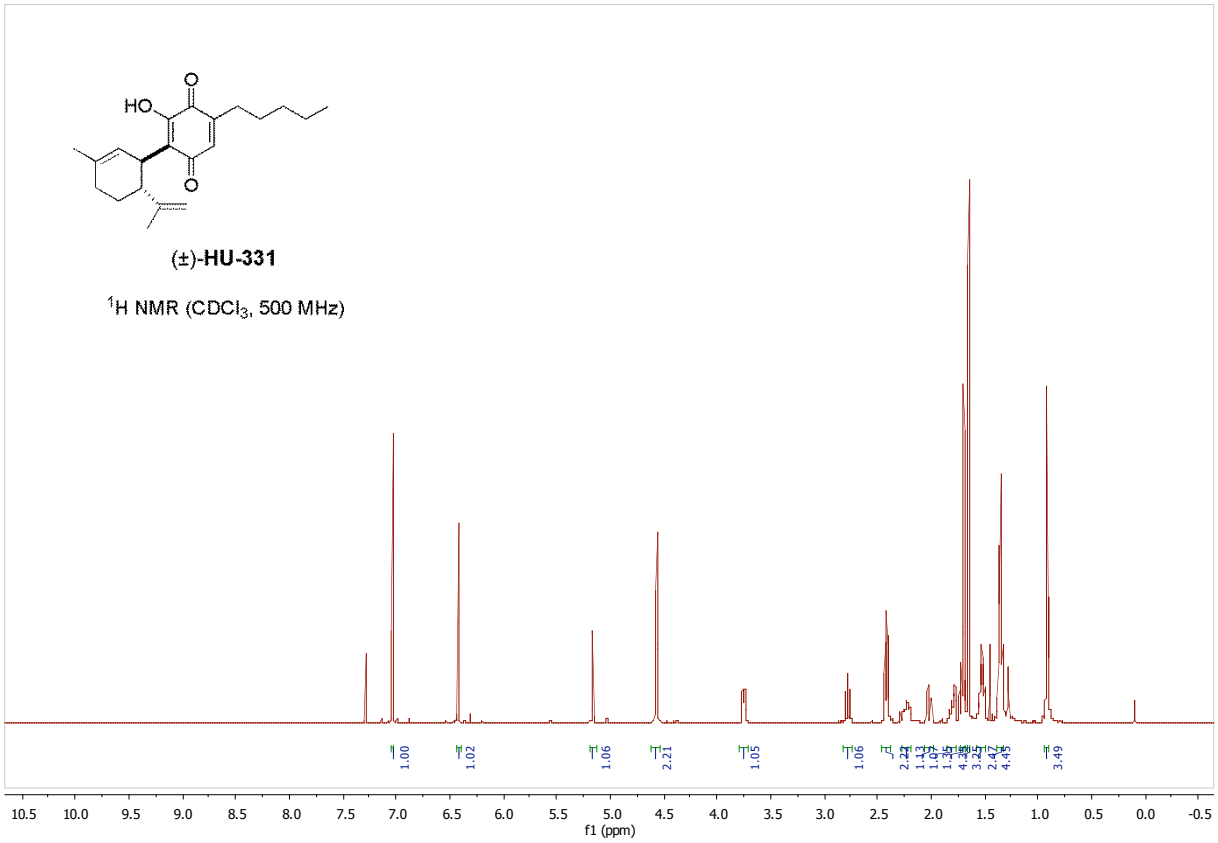

156.43
154.59
143.91
140.33
124.15
115.28
110.00
109.87
75.48
48.72
35.92
33.21
31.95
31.07
30.10
28.59
26.43
24.09
23.41
22.94
14.43
HO
OH
OH
20
^{13}C NMR ($CDCl_3$, 125 MHz)
f1 (ppm)

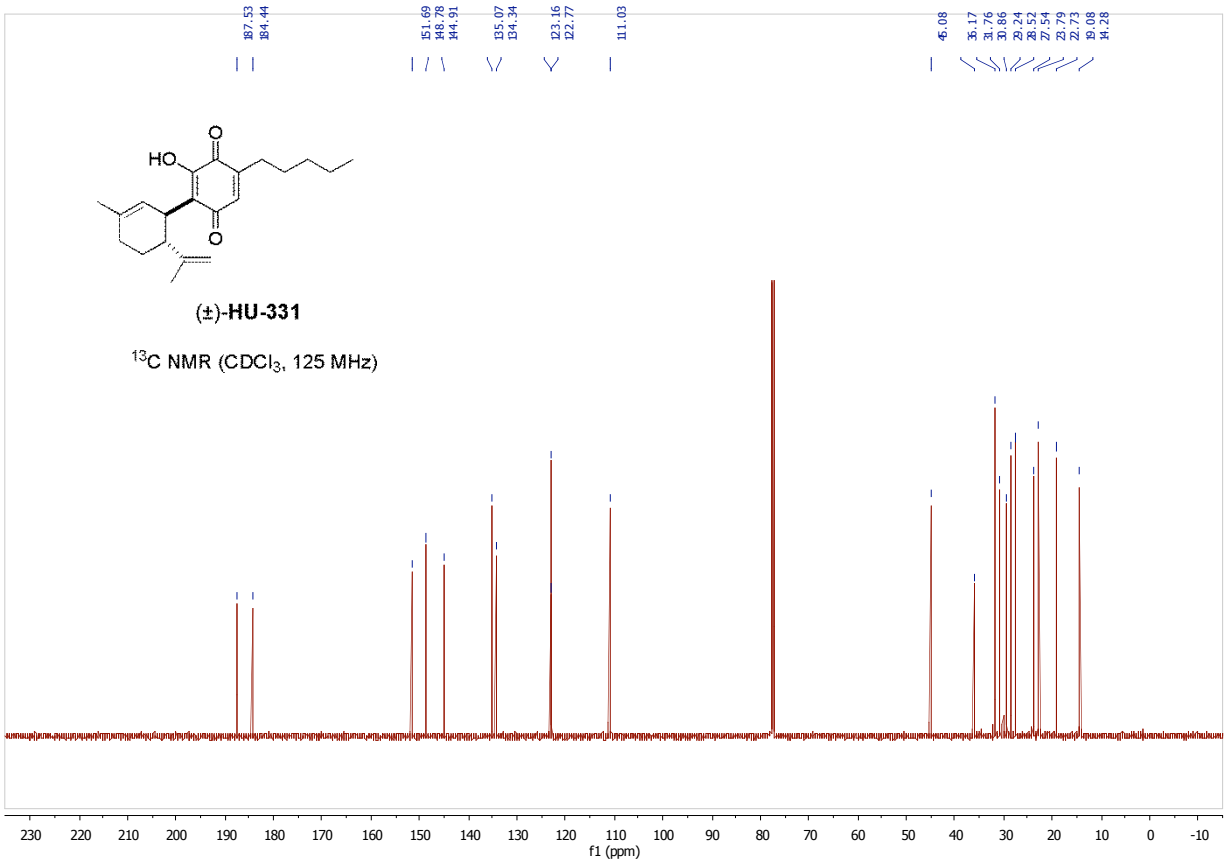

MsO
OMs
21
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)


MsO
OMs
21
^{13}C NMR ($CDCl_3$, 125 MHz)
f1 (ppm)


HO
OH
(±)-CBD
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)


156.44
154.23
149.73
143.43
140.42
124.53
114.16
111.23
110.15
108.43
46.56
37.64
35.88
31.89
31.03
30.80
28.81
24.07
22.94
20.89
14.43
HO
OH
(±)-CBD
^{13}C NMR ($CDCl_3$, 125 MHz)
f1 (ppm)


HO
O
O
(±)-HU-331
^{1}H NMR (CDCl$_3$, 500 MHz)
1.00
1.02
1.06
2.21
1.05
1.06
3.49
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


187.53
184.44
151.69
148.78
144.91
135.07
134.34
123.16
122.77
111.03
45.08
36.17
31.76
30.86
29.24
28.52
27.54
23.79
22.73
19.08
14.28
HO
O
O
(±)-HU-331
^{13}C NMR (CDCl$_3$, 125 MHz)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

Stability of **9o** *versus* HU-331 in solution

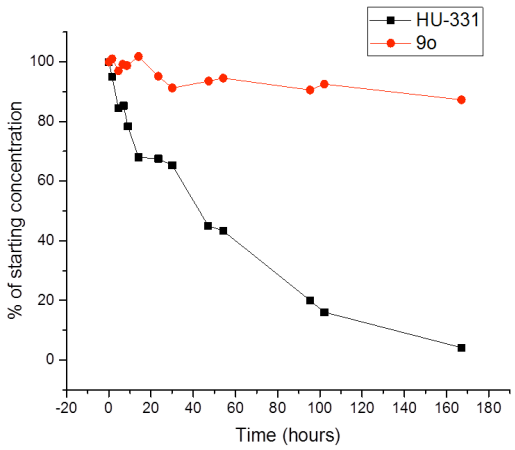


Figure 5. Change in concentration of HU-331 *versus* **9o** determined by ^{1}H NMR spectroscopy (in DMSO-d_6 at 20 °C) using quantint macro within the TopSpin NMR software.

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