Supplementary Information

Unified synthesis and cytotoxic activity of 8-*O*-methylfusarubin and its analogues

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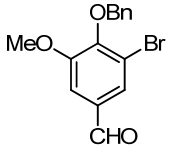
List of supplementary information

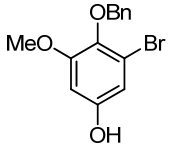
1. General Information

Unless otherwise stated, all reactions were performed under argon or nitrogen atmosphere in oven- or flamed-dried glassware. Solvents were used as received from suppliers or distilled prior to use using standard procedures. All other reagents were obtained from commercial sources and used without further purification. Column chromatography was performed on SiliaFlash® G60 Silica (60-200 μm, Silicycle). Thin-layer chromatography (TLC) was performed on SiliaPlate™R10011B-323 (Silicycle) or Silica gel 60 F_{254} (Merck). ^{1}H, ^{13}C and 2D NMR spectroscopic data were recorded on a 300 MHz Bruker FTNMR UltraShield spectrometer. ^{1}H NMR spectra are reported in ppm on the δ scale and referenced to the internal tetramethylsilane. The data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant(s) in hertz (Hz), and integration. Infrared (IR) spectra were recorded on a Perkin Elmer 783 FTS165 FT-IR spectrometer. High-resolution mass spectra were obtained on a liquid chromatograph-mass spectrometer (Alliance 2690, LCT, Waters, Micromass). Melting points were measured using an Electrothermal IA9200 digital melting point apparatus and are uncorrected.

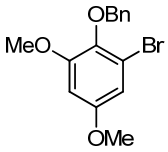
2. Experimentals and Characterization Data



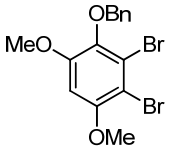
4-Benzyloxy-3-bromo-5-methoxybenzaldehyde. The title compound was prepared following a procedure reported by Green *et al.* with modification.[1] To a solution of 5-bromovanillin (**8**) (5.52 g, 23.9 mmol) in DMF (52 mL) were added K_2CO_3(16.51 g, 119.5mmol, 5.0 equiv) and BnBr (3.1 mL, 26.3 mmol, 1.1 equiv). The reaction mixture was stirred at rt overnight before H_2O (150 mL) was added. The aqueous phase was extracted with EtOAc (5x50 mL). The combined organic layers were washed with water (5x50 mL), brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (hexanes–40% EtOAc/hexanes) yielded the title compound (7.67 g, quantitative yield) as a white solid: R_f = 0.50 (20% EtOAc/hexanes); mp 52.0–55.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.65 (d, J = 1.5 Hz, 1H), 7.54–7.51 (m, 2H), 7.41–7.31 (m, 4H), 5.16 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.89, 154.26, 150.49, 136.54, 133.11, 128.68, 128.53, 128.43, 128.39, 118.40, 110.19, 74.97, 56.24; IR (neat) 3065, 2940, 2845, 1697, 1278, 1139, 1044 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{13}BrNaO_3$ $(M + Na)^+$ 342.9940, found 342.9941. The ^{1}H and ^{13}C spectral data matched those previously reported.[1]



4-Benzyloxy-3-bromo-5-methoxyphenol. The title compound was prepared following a procedure reported by Xie and Kozlowski.[2] To a solution of 4-benzyloxy-3-bromo-5-methoxybenzaldehyde (2.57 g, 8.0 mmol) in CH_2Cl_2 (16 mL) was added 3-chloroperbenzoic acid (70%, 2.37 g, 9.6 mmol, 1.2 equiv). The reaction mixture was stirred at rt overnight before EtOAc (50 mL) was added. The organic layer was washed with saturated aqueous $NaHCO_3$ (2x50 mL), brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was diluted with MeOH (16 mL), followed by addition of a solution of 10% KOH in H_2O (5 mL). The reaction mixture was stirred further at rt for 15 min before 50 mL of EtOAc was added. The organic layer was washed with brine (2x50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the crude residue by column chromatography (10–20% EtOAc/hexanes) yielded the title compound (2.14 g, 86%) as a colorless oil: R_f = 0.56 (40% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55–7.52 (m, 2H), 7.40–7.29 (m, 3H), 6.58 (d, J = 2.7 Hz, 1H), 6.38 (d, J = 2.7 Hz, 1H), 5.36 (brs, 1H), 4.94 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.20, 153.18, 138.54, 136.74, 128.89, 128.44, 128.38, 117.84, 110.93, 100.36, 75.45, 56.02; IR (neat) 3367, 2942, 1584, 1472, 1215, 1042 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{13}BrNaO_3$ $(M + Na)^+$ 330.9940, found 330.9939. The ^{1}H and ^{13}C spectral data matched those previously reported.[1]

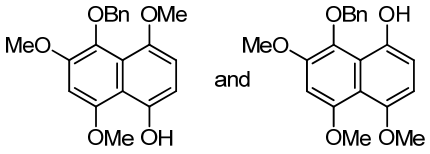


2-Benzyloxy-3,5-dimethoxybromobenzene. The title compound was prepared following a procedure reported by Green *et al.* with modification.[1] To a solution of 4-benzyloxy-3-bromo-5-methoxyphenol (2.35 g, 7.6 mmol) in acetone (15 mL) were added K_2CO_3 (3.15 g, 22.8 mmol, 3.0 equiv) and iodomethane (950 μL, 15.2 mmol, 2.0 equiv). The reaction mixture was heated at reflux overnight. The white suspension was cooled to rt before 70 mL of H_2O was added and extracted with EtOAc (3x50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20% EtOAc/hexanes) yielded the title compound (2.37 g, 97%) as a yellow oil: R_f = 0.60 (20% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55–7.52 (m, 2H), 7.39–7.28 (m, 3H), 6.64 (d, J = 3.0 Hz, 1H), 6.44 (d, J = 3.0 Hz, 1H), 4.94 (s, 2H), 3.79 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.57, 154.34,139.60, 137.35, 128.52, 128.32, 128.04, 117.97, 107.99, 100.04, 74.91, 56.06, 55.76; IR (neat) 2939, 1599, 1571, 1487, 1211, 1149, 1037 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}BrNaO_3$ $(M + Na)^+$ 345.0097, found 345.0095. The ^{1}H and ^{13}C spectral data matched those previously reported.[1]



9

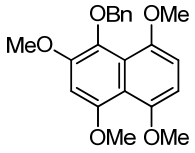
1,2-Dibromo-3-benzyloxy-4,6-dimethoxybenzene (9). The title compound was prepared following a procedure reported by Das *et al.*.[3] To a solution of 2-benzyloxy-3,5-dimethoxybromobenzene (3.95 g, 12.2 mmol) in MeCN (40 mL) were added NH_4OAc (95.3 mg, 1.2 mmol, 0.1 equiv) and *N*-bromosuccinimide (2.29 g, 12.9 mmol, 1.05 equiv). The reaction mixture was stirred at rt for 1.5 h before being concentrated *in vacuo*. The crude residue was added H_2O (100 mL) and extracted with EtOAc (3x50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20–60% EtOAc/hexanes) yielded **9** (4.89 g, quantitative yield) as a yellow solid: R_f = 0.39 (20% EtOAc/hexanes); mp 104.8–106.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.51 (m, 2H), 7.39–7.28 (m, 3H), 6.49 (s, 1H), 4.92 (s, 2H), 3.83 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.79, 153.22, 140.48, 137.00, 128.51, 128.37, 128.17, 122.62, 105.51, 97.35, 74.93, 56.98, 56.46; IR (neat) 2938, 1560, 1458, 1367, 1220, 1035 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{14}Br_2NaO_3$ $(M + Na)^+$ 422.9202, found 422.9199. The ^{1}H and ^{13}C spectral data of **9** matched those previously reported.[1]



11 **12**

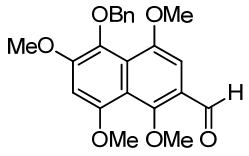
Naphthols 11 and 12. To a solution of dibromobenzene **9** (2.0 g, 5.0 mmol) and 2-methoxyfuran (**10**) (600 µL, 6.5 mmol, 1.3 equiv) in dry THF (12.5 mL) at –78 °C was added *n*-BuLi (*ca*.1.0 M solution in hexane, 5.0 mL, 5.0 mmol, 1.0 equiv) dropwise. The reaction mixture was stirred at –78 °C for 3.5 h before being warmed to rt and H_2O was then added. The aqueous phase was extracted with EtOAc (4x30 mL).The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (10–30% EtOAc/hexanes) yielded an inseparable mixture of **11** and **12** (1.04 g, 62%) as a brown solid: R_f = 0.46 (40% EtOAc/hexanes); mp 106.6–108.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (s, 1H), 9.14 (s, 1.3H), 7.56 (d, J = 7.2 Hz, 2.8H), 7.51–7.48 (m, 2H), 7.39–7.26 (m, 7H), 6.79–6.72 (m, 2.4H), 6.66–6.62 (m, 3.4H), 6.58 (s, 1.4H), 5.08 (s, 2H), 4.91 (s, 2.8H), 3.92–3.86 (m, 14.4H), 3.81 (s, 3.2H), 3.74 (s, 4.2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.88, 152.98, 149.97, 149.93, 148.88, 148.55, 147.82, 147.47, 138.57, 137.63, 135.92, 135.46, 129.07, 128.84, 128.77, 128.37, 128.28, 127.63, 123.71, 120.52, 114.97, 112.68, 110.97, 110.65,

107.95, 107.53, 97.42, 96.58, 76.94, 76.17, 57.80, 57.65, 57.59, 57.20, 56.89, 56.50; IR (neat) 3393, 2936, 1609, 1361, 1064, 1040 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NaO_5$ $(M + Na)^+$ 363.1203, found 363.1202.



7

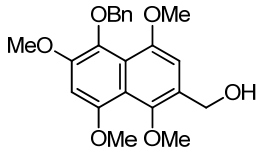
1-Benzyloxy-2,4,5,8-tetramethoxynaphthalene (7). The title compound was prepared following a procedure reported by Yamashita *et al.*.[4] To a solution of a mixture of naphthols **11** and **12** (3.44 g, 10.1 mmol) in THF (34 mL) at 0 °C was added NaH (60% in mineral oil, 1.02 g, 25.6 mmol, 2.5 equiv). The dark suspension was stirred at 0 °C for 1 h before iodomethane (3.2 mL, 51.4 mmol, 5.0 equiv) was added. The reaction mixture was stirred from 0 °C to rt overnight before being re-cooled to 0 °C then 60 mL of H_2O was added. The aqueous phase was extracted with EtOAc (3x50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (10–30% EtOAc/hexanes) yielded naphthalene **7** (2.88 g, 80%) as a brown solid: R_f = 0.49 (40% EtOAc/hexanes); mp 112.6–113.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56–7.41 (m, 2H), 7.41–7.28 (m, 3H), 6.77 (d, *J* = 9.0 Hz, 1H), 6.75 (s, 1H), 6.64 (d, *J* = 9.0 Hz, 1H), 4.95 (s, 2H), 3.93 (s, 6H), 3.87 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.14, 151.54, 150.55, 150.16, 138.66, 137.05, 128.28, 128.21, 127.51, 124.46, 115.68, 108.74, 105.33, 99.19, 76.12, 57.54, 57.54, 57.41, 57.36; IR (neat) 2935, 2837, 1598, 1358, 1259, 1070 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{22}NaO_5$ $(M + Na)^+$ 377.1359, found 377.1359. The ^{1}H and ^{13}C spectral data of **7** matched those previously reported.[1]



13

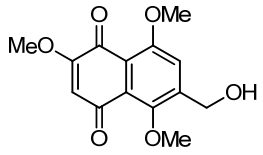
Naphthaldehyde 13. *N*,*N*-dimethylformamide (230 µL, 2.9 mmol) was added dropwise into a solution of oxalyl chloride (250 µL, 2.9 mmol) in CH_2Cl_2 (4 mL) at 0 °C. After 30 min, a solution of naphthalene **7** (690.0 mg, 2.0 mmol) in 6 mL of CH_2Cl_2 was added and the reaction mixture was stirred from 0 °C to rt overnight. The brown reaction mixture was then slowly quenched with saturated aqueous $NaHCO_3$ (20 mL) to give a yellow solution, diluted with H_2O (30 mL) and extracted with EtOAc (4x30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20–30% EtOAc/hexanes) yielded naphthaldehyde **13** (638.0 mg,

86%) as a yellow solid: R_f = 0.38 (40% EtOAc/hexanes); mp 131.3–134.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.49 (s, 1H), 7.57–7.54 (m, 2H), 7.43–7.33 (m, 3H), 7.13 (s, 1H), 6.81 (s, 1H), 4.94 (s, 2H), 4.06 (s, 3H), 4.00 (s, 3H), 3.92 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.73, 157.94, 154.82, 153.87, 152.54, 138.28, 137.37, 128.28, 128.07, 127.66, 127.66, 123.88, 116.21, 101.29, 97.84, 76.12, 65.46, 56.98, 56.80, 56.30; IR (neat) 2934, 1668, 1593, 1362, 1069 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NaO_6$ $(M + Na)^+$ 405.1309, found 405.1308.



6

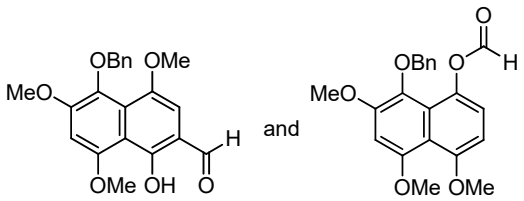
Naphthyl alcohol 6. To a solution of naphthaldehyde **13** (2.51 g, 6.6 mmol) in MeOH/THF (1:1, 28 mL) at 0 °C was added a single portion of $NaBH_4$ (495.0 mg, 13.1 mmol, 2.0 equiv). The reaction mixture was stirred further for 30 min at 0 °C before 10 mL of saturated aqueous NH_4Cl was added. The white suspension was added 50 mL of H_2O and extracted with EtOAc (3x40 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to yield alcohol **6** (2.50 g, 99% yield) as a pale yellow solid: R_f = 0.38 (60% EtOAc/hexanes); mp 142.0–143.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 7.5 Hz, 2H), 7.41–7.28 (m, 3H), 6.84 (s, 1H), 6.73 (s, 1H), 4.91 (s, 2H), 4.78 (s, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 3.77 (s, 3H), 3.73 (s, 3H), 2.88 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.94, 152.27, 150.24, 147.39, 138.56, 137.29, 128.38, 128.24, 128.21, 127.56, 123.74, 117.48, 107.81, 98.66, 76.13, 62.59, 60.79, 57.60, 56.75, 56.58; IR (neat) 3447, 2931, 2838, 1522, 1356, 1069 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}NaO_6$ $(M + Na)^+$ 407.1465, found 407.1464.



14

Naphthoquinone 14. To a solution of naphthalene **6** (131.5 mg, 0.34 mmol) in MeCN (3.6 mL) at 0 °C was added dropwise a solution of cerium ammonium nitrate (377.1 mg in 1:1 MeCN/H_2O 4.6 mL, 0.68 mmol, 2.0 equiv). The reaction mixture was stirred for 30 min before 30 mL of H_2O was added and extracted with EtOAc (5x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (100% EtOAc) yielded naphthoquinone **14** (47.4 mg, 50%) as an orange solid: R_f = 0.39 (100% EtOAc); mp 218.8–219.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.48 (s, 1H), 6.03 (s, 1H), 5.44 (s, 1H), 4.60 (s, 2H), 3.84 (s, 3H), 3.74 (s, 3H), 3.63

(s, 3H); ^{13}C NMR (75 MHz, DMSO-*d*$_6$) δ 184.37, 178.18, 159.88, 156.66, 150.00, 147.52, 124.57, 118.02, 117.07, 109.90, 61.46, 58.38, 56.72, 56.72; IR (neat) 3489, 2914, 2848, 1651, 1589, 1067 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}NaO_6$ $(M + Na)^+$ 304.0683, found 304.0685.

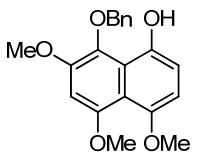


15 **16**

N,*N*-dimethylformamide (310 μL, 4.0 mmol) was added dropwise into a solution of oxalyl chloride (340 μL, 4.0 mmol) in CH_2Cl_2 (4 mL) at 0 °C. After 35 min, a solution of naphthols **11** and **12** (677.1 mg, 2.0 mmol) in CH_2Cl_2 (6 mL) was added and the reaction mixture was stirred from 0 °C to rt overnight. The brown reaction mixture was then slowly quenched with saturated aqueous $NaHCO_3$ (30 mL) to give a yellow solution, diluted with H_2O (30 mL) and extracted with EtOAc (4x30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (15–30% EtOAc/hexanes) yielded naphthaldehyde **15** (305.1 mg, 42%) as a yellow solid and naphthyl formate **16** (122.5 mg, 17%) as a brown solid.

Naphthaldehyde 15. R_f = 0.30 (40% EtOAc/hexanes); mp 118.5–120.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.47 (brs, 1H), 10.40 (s, 1H), 7.55–7.52 (m, 2H), 7.42–7.29 (m, 3H), 7.02 (s, 1H), 6.67 (s, 1H), 4.90 (s, 2H), 4.04 (s, 3H), 3.94 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.45, 156.75, 155.29, 153.98, 148.54, 138.14, 137.73, 128.28, 128.16, 127.71, 127.42, 115.15, 111.67, 103.28, 96.39, 76.13, 56.92, 56.88, 56.64; IR (thin film) 3320, 2943, 2846, 1605, 1367, 1199 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NaO_6$ $(M + Na)^+$ 391.1152, found 391.1151.

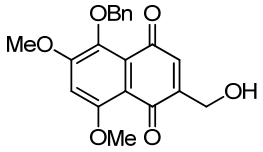
Naphthyl formate 16: R_f = 0.45 (40% EtOAc/hexanes); mp 112.8–113.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.55–7.54 (m, 2H), 7.40–7.28 (m, 3H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.71 (s, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 4.91 (s, 2H), 3.90 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.43, 156.07, 154.92, 150.86, 137.81, 137.45, 134.59, 128.62, 128.36, 127.94, 124.69, 120.81, 114.76, 103.33, 98.24, 76.05, 57.44, 56.77, 56.64; IR (neat) 2940, 1742, 1601, 1359, 1249, 1118 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NaO_6$ $(M + Na)^+$ 391.1152, found 391.1152.



12

Naphthol 12. To a solution of naphthyl formate **16** (60.3 mg, 0.16 mmol) in MeOH (0.5 mL) was added a solution of 10% KOH in H_2O (100 μL) dropwise. The reaction mixture was stirred

at rt for 30 min before being diluted with EtOAc (20 mL), washed with brine (2x10 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20% EtOAc/hexanes) yielded naphthol **12** (39.1 mg, 70%) as a brown solid: R_f = 0.46 (40% EtOAc/hexanes); mp 100.8–102.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.54–7.51 (m, 2H), 7.43–7.34 (m, 3H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.68 (s, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 5.12 (s, 2H), 4.01 (s, 3H), 3.95 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.85, 149.91, 147.79, 147.46, 135.87, 135.58, 129.06, 128.82, 128.75, 120.52, 115.03, 110.65, 107.60, 97.57, 77.12, 57.68, 57.27, 56.99; IR (neat) 3321, 2917, 2848, 1607, 1251, 1038 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NaO_5$ $(M + Na)^+$ 363.1203, found 363.1203.

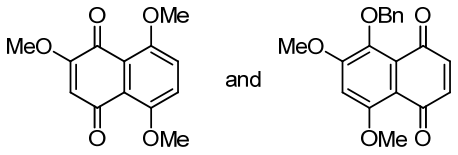


18

Naphthoquinone 18. From naphthaldehyde **15**: To a solution of naphthaldehyde **15** (303.2 mg, 0.8 mmol) in MeOH/THF (1:1, 3.6 mL) at 0 °C was added a single portion of $NaBH_4$ (68.8 mg, 1.6 mmol). The reaction mixture was stirred for additional 30 min before saturated aqueous NH_4Cl (10 mL) was added. The white suspension was added H_2O (30 mL) and extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to yield naphthyl alcohol **17** (310.0 mg, quantitative yield) as a pale brown solid. Naphthyl alcohol **17** (310.0 mg, 0.8 mmol) was dissolved in MeCN (9 mL) and cooled to 0 °C. The yellow solution was then added dropwise a solution of cerium ammonium nitrate (924.5 mg in 5.5 mL of 1:1 MeCN/H_2O). The reaction mixture was stirred further for 30 min before H_2O (40 mL) was added. The aqueous phase was extracted with EtOAc (4x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (80% EtOAc/hexanes) yielded naphthoquinone **18** (291.6 mg, 94% over 2 steps) as an orange solid.

From naphthalene **6**: A solution of naphthalene **6** (921.7 mg, 2.4 mmol) in MeCN/H_2O (9:1, 24 mL) was heated at 50 °C before a single portion of $PhI(OAc)_2$ (801.3 mg, 2.4 mmol, 1.0 equiv) was added. After 1 min, the reaction mixture turned from yellow to orange. The reaction flask was immediately removed from an oil bath before 50 mL of H_2O was added and then extracted with EtOAc (4x30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (60–90% EtOAc/hexanes) yielded naphthoquinone **18** (612.0 mg, 75%) as an orange solid: R_f = 0.45 (100% EtOAc); mp 151.6–153.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61–7.59 (m, 2H), 7.42–7.30 (m, 3H), 6.76 (s, 1H), 6.71 (s, 1H), 4.97 (s, 2H), 4.56 (s, 2H), 3.98 (s, 3H), 3.94 (s, 3H), 2.76 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ184.90, 183.81, 160.25, 158.39, 149.57, 141.87, 137.08, 132.80, 128.80, 128.33, 128.15, 126.87, 112.95, 100.94, 75.21, 60.08,

56.53, 56.23; IR (neat) 3458, 2943, 1648, 1458, 1353, 1217 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NaO_6$ $(M + Na)^+$ 377.0996, found 377.0993.

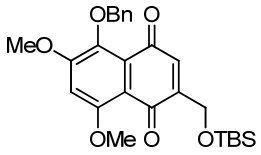


19 **20**

A solution of naphthalene **7** (29.6 mg, 0.08 mmol) in MeCN/H_2O (9:1, 1 mL) was heated at 50 °C before a single portion of $PhI(OAc)_2$ (36.4 mg, 0.08 mmol, 1.0 equiv) was added. After 1 min, the reaction flask was removed from an oil bath before 10 mL of H_2O was added and extracted with EtOAc (3x5 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (40–60% EtOAc/hexanes) yielded naphthoquinone **19** (13.4 mg, 65%) and naphthoquinone **20** (4.3 mg, 16%) both as orange solids.

Naphthoquinone 19: R_f = 0.50 (40% acetone/hexanes); mp 169.0–171.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (d, J = 9.0 Hz, 1H), 7.28 (d, J = 9.0 Hz, 1H), 6.02 (s, 1H), 3.96 (s, 6H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.80, 179.40, 159.32, 154.38, 153.39, 121.34, 120.88, 120.39, 119.69, 110.03, 57.02, 56.92, 56.24; IR (thin film) 2925, 2849, 1641, 1267, 1243, 1022 cm^{-1}. ^1H and ^{13}C NMR spectral data of **19** matched those previously reported.[5]

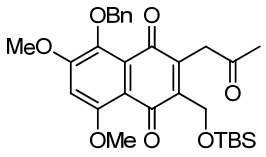
Naphthoquinone 20: R_f = 0.45 (50% acetone/hexanes); mp 147.0–149.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62–7.60 (m, 2H), 7.42–7.31 (m, 3H), 6.76 (s, 1H), 6.74 (s, 2H), 5.00 (s, 2H), 4.00 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.07, 183.41, 160.04, 158.20, 142.03, 139.64, 137.59, 137.11, 128.76, 128.35, 128.13, 126.89, 113.11, 101.28, 75.26, 56.71, 56.25; IR (neat) 2931, 1650, 1352, 1258, 1220, 1036 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{16}NaO_5$ $(M + Na)^+$ 347.0895, found 347.0887.



21

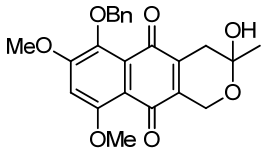
Silyl ether 21. To a solution of alcohol **18** (1.43 g, 4.0 mmol) in CH_2Cl_2 (20 mL) were added imidazole (551.2 mg, 8.1 mmol, 2.0 equiv) and TBSCl (917.7 mg, 6.1 mmol, 1.5 equiv). The reaction mixture was stirred at rt overnight before H_2O (60 mL) was added and extracted with EtOAc (4x30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (10–80% EtOAc/hexanes) yielded silyl ether **21** (1.78 g, 94%) as an orange solid: R_f = 0.56 (60%

EtOAc/hexanes); mp145.5–147.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62–7.59 (m, 2H), 7.41–7.28 (m, 3H), 6.84 (d, J = 1.5 Hz, 1H), 6.71 (s, 1H), 4.99 (s, 2H), 4.64 (s, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 0.94 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.12, 183.48, 160.15, 158.27, 150.75, 141.96, 137.18, 132.22, 128.76, 128.32, 128.08, 127.09, 113.28, 100.93, 75.19, 59.58, 56.59, 56.22, 25.88, 18.32, –5.45; IR (neat) 2930, 1653, 1217, 1103, 1046 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{32}NaO_6Si$ $(M + Na)^+$ 491.1860, found 491.1858.



23

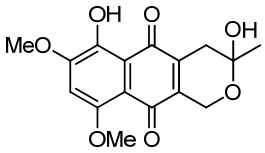
Acetonylnaphthoquinone 23. A suspension of naphthoquinone **21** (1.78 g, 3.8 mmol) and acetylmethylpyridinium chloride (**22**) (732.7 mg, 4.3 mmol, 1.1 equiv) in MeCN (65 mL) was heated at 60 °C for 30 min. The reaction mixture was then cooled to rt before a solution of Et_3N (585 µL in 6 mL of MeCN, 4.2 mmol, 1.1 equiv) was added. The reaction mixture was stirred at rt overnight before H_2O (80 mL) was added and extracted with EtOAc (4x30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to yield acetonylnaphthoquinone **23** (1.99 g, quantitative yield) as an orange solid: R_f = 0.59 (60% EtOAc/hexanes); mp 97.6–98.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 6.9 Hz, 2H), 7.38–7.27 (m, 3H), 6.72 (s, 1H), 4.95 (s, 2H), 4.68 (s, 2H), 3.95 (s, 5H), 3.89 (s, 3H), 2.27 (s, 3H), 0.89 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.97, 184.93, 182.28, 159.57, 157.80, 145.43, 141.88, 141.78, 137.30, 128.67, 128.21, 127.96, 126.93, 113.27, 101.49, 75.31, 57.38, 56.70, 56.18, 41.12, 30.08, 25.90, 18.31, –5.39; IR (neat) 2930, 1653, 1350, 1246, 1215, 1080 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{36}NaO_7Si$ $(M + Na)^+$ 547.2123, found 547.2123.



24

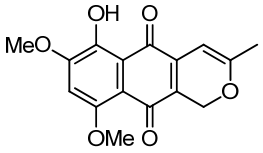
Pyranonaphthoquinone 24. From acetonylnaphthoquinone **23**: To a solution of acetonyl naphthoquinone **23** (40.1 mg, 0.08 mmol) in MeCN (2 mL) was added a solution of 1M HCl (0.7 mL). The reaction mixture was stirred at rt for 1 h before 20 mL of H_2O was added and extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (60–80% EtOAc/hexanes) yielded **24** (23.2 mg, 74%) as an orange solid.

From naphthoquinone **21**: A solution of naphthoquinone **21** (154.6 mg, 0.3 mmol) and acetylmethylpyridinium chloride (62.9 mg, 0.4 mmol, 1.1 equiv) in MeCN (8 mL) was heated at 60 °C for 30 min. The reaction mixture was then cooled to rt and a solution of Et_3N (55 μL in 0.6 mL of MeCN, 0.4 mmol, 1.1 equiv) was added. The reaction mixture was left stirred at rt overnight. A solution of 1M HCl (4 mL) was then slowly added and the reaction mixture was stirred further for 1 h before H_2O (40 mL) was added. The aqueous phase was extracted with EtOAc (3x15 mL) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (60–80% EtOAc/hexanes) yielded **24** (114.6 mg, 85%) as an orange solid: R_f = 0.47 (100% EtOAc); mp 164.5–166.2 °C; ^{1}H NMR (300 MHz $CDCl_3$) δ 7.58–7.56 (m, 2H), 7.40–7.30 (m, 3H), 6.57 (s, 1H), 4.88 (m, 2H), 4.63 (s, 2H), 3.91 (s, 5H), 3.84 (s, 3H), 2.79 (d, J = 18.6 Hz, 1H), 2.48 (d, J = 18.6 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.08, 181.49, 159.95, 158.11, 141.96, 141.56, 138.42, 137.11, 128.93, 128.26, 128.12, 126.31, 112.16, 101.07, 94.23, 74.97, 57.98, 56.40, 56.06, 32.24, 28.72; IR (neat) 3446, 2940, 1653, 1354, 1263, 1017 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{22}NaO_7$ $(M + Na)^+$ 433.1258, found 433.1256.



8-*O*-methylfusarubin (**3**)

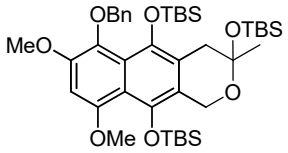
8-*O*-methylfusarubin (3). To a solution of benzyl ether **24** (114.6 mg, 0.3 mmol) in EtOAc (6 mL) was added $Pd(OH)_2$ (9.6 mg, 0.02 mmol, 0.05 equiv). The reaction mixture was stirred at rt under H_2 atmosphere for 30 min before being filtered through a pad of Celite, washed with EtOAc and concentrated *in vacuo*. Purification of the crude residue by column chromatography (80% EtOAc/hexanes) yielded 8-*O*-methylfusarubin (**3**) (54.0 mg, 60%) as a red solid: R_f = 0.37 (100% EtOAc); mp 138.6–140.7 °C; $[\alpha]_D^{26}$ = +7.33 (*c* 0.03, acetone); ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.89 (s, 1H), 6.90 (s, 1H), 5.99 (s, 1H), 4.40–4.32 (m, 2H), 3.92 (s, 3H), 3.85 (s, 3H), 2.51 (d, J = 18.3 Hz, 1H), 2.31 (d, J = 18.3 Hz, 1H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 189.34, 179.14, 156.04, 155.54, 147.90, 145.02, 137.21, 113.82, 108.86, 104.10, 93.56, 58.50, 56.93, 56.82, 32.11, 28.76; IR (neat) 3221, 2917, 2849, 1618, 1468, 1266 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{16}NaO_7$ $(M + Na)^+$ 343.0794, found 343.0793.



8-*O*-methylanhydrofusarubin (**4**)

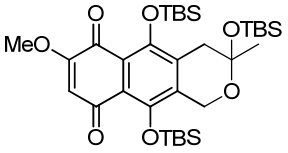
8-*O*-methylanhydrofusarubin (4). To a solution of 8-*O*-methylfusarubin (**3**) (35.9 mg, 0.1 mmol) in toluene (55 mL) was added TsOH (1.0 mg, 0.05 equiv). The reaction mixture was

heated at 105 °C for 30 min before being cooled to rt and 100 mL of H_2O was added. The aqueous phase was extracted with EtOAc (4x30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (60%–80% EtOAc/hexanes) yielded 8-*O*-methylanhydrofusarubin (**4**) (23.4 mg, 69%) as black needles: R_f = 0.40 (100% EtOAc); mp 144.0–146.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.14 (s, 1H), 6.73 (s, 1H), 5.85 (s, 1H), 5.12 (s, 2H), 4.00 (s, 3H), 3.98 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.63, 179.41, 163.43, 155.21, 155.11, 148.70, 135.74, 126.45, 114.37, 110.76, 103.29, 92.99, 63.45, 56.95, 56.34, 20.08; IR (neat) 2923, 1582, 1470, 1433, 1380 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{14}NaO_6$ $(M + Na)^+$ 325.0683, found 325.0680.



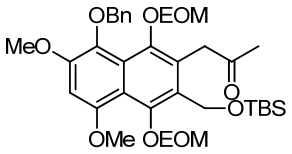
27

Pyran silyl ether 27. To a solution of naphthoquinone **23** (202.9 mg, 0.39 mmol) in THF (2.0 mL) was added three portions of $Na_2S_2O_4$ solution (675 mg in 3.2 mL of H_2O) at a one-hour interval. The reaction mixture was vigorously stirred at rt for 1 h before 20 mL of H_2O was added. The aqueous phase was extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was diluted with CH_2Cl_2 (1.5 mL) before 2,6-lutidine (450 µL, 3.9 mmol, 10 equiv) was added. The brown reaction mixture was subsequently added TBSOTf (445 µL, 1.93 mmol, 5 equiv) and the reaction mixture was left stirred at rt overnight. The yellow solution was added 10 mL of H_2O and extracted with EtOAc (3x5 mL). The combined organic layers were washed with 1–2% aqueous HCl (2x10 mL), brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (10–20% EtOAc/hexanes) yielded pyran silyl ether **27** (273.5 mg, 94%, over 2 steps) as a yellow oil; R_f = 0.41 (10% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69–7.67 (m, 2H), 7.44–7.32 (m, 3H), 6.59 (s, 1H), 5.13 (d, J = 9.0 Hz, 1H), 4.98 (d, J = 9.0 Hz, 1H), 4.91 (d, J = 12.0 Hz, 1H), 4.83 (d, J = 12.0 Hz, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.39 (s, 2H), 1.82 (s, 3H), 1.16 (s, 9H), 0.98 (s, 9H), 0.84 (s, 9H), 0.16 (s, 6H), 0.09–0.00 (m, 9H), –0.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.13, 149.05, 146.60, 141.72, 138.56, 134.91, 128.87, 127.96, 127.49, 123.08, 122.33, 119.12, 116.42, 110.07, 96.60, 76.41, 58.89, 57.10, 55.73, 44.73, 29.04, 26.24, 26.07, 25.75, 18.53, 18.30, 17.69, –3.49, –3.84, –4.34, –4.49, –5.24, –5.27; IR (neat) 2930, 2857, 1584, 1350, 1253, 1068 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{41}H_{66}NaO_7Si_3$ $(M + Na)^+$ 777.4014, found 777.4018.



28

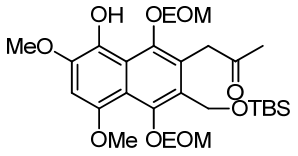
Naphthoquinone 28. To a solution of benzyl ether **27** (51.1 mg, 0.07 mmol) in EtOAc (1.5 mL) was added Pd/C (5%, 8.0 mg, 4 μmol, 0.05 equiv). The reaction mixture was stirred at rt under H_2 atmosphere for 4 h before being filtered through a pad of Celite, washed with EtOAc and concentrated *in vacuo*. Purification of the crude residue by column chromatography (5–10% EtOAc/hexanes) yielded the corresponding naphthol (43.0 mg, 96%) as a yellow oil. Naphthol precursor (43.0 mg, 0.06 mmol) was diluted in MeCN/H_2O (9:1, 0.7 mL) and was then cooled to 0 °C. The yellow solution was added a portion of $PhI(OAc)_2$ (21.8 mg, 0.06mmol, 1.0 equiv). The reaction mixture was stirred further for 20 min before being diluted with H_2O (10 mL) and extracted with EtOAc (3x5 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20% EtOAc/hexanes) yielded naphthoquinone **28** (24.8 mg, 57% over 2 steps) as an orange gum; R_f = 0.34 (30% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 (s, 1H), 4.75–4.65 (m, 2H), 3.86 (s, 3H), 3.30 (d, *J* = 18.0 Hz, 1H), 3.17 (d, *J* = 18.0 Hz, 1H), 1.75 (s, 3H), 1.04 (s, 9H), 0.88 (s, 9H), 0.77 (s, 9H), 0.25 (s, 3H), 0.06 (s, 6H), 0.00 (s, 3H), –0.01 (s, 3H), –0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.29, 178.21, 171.60, 156.73, 145.37, 139.57, 135.71, 118.95, 113.13, 111.83, 102.83, 59.13, 56.13, 43.83, 28.49, 25.83, 25.78, 25.52, 18.38, 18.19, 17.61, –3.45, –3.80, –4.46, –4.63, –5.43, –5.47; IR (neat) 2955, 2858, 1605, 1383, 1254, 1004 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{33}H_{56}NaO_7Si_3$ $(M + Na)^+$ 671.3232, found 671.3229.



29

EOM ether 29. To a solution of naphthoquinone **23** (101.2 mg, 0.2 mmol) in Et_2O (5 mL) was added 5 mL of a solution of 10% $Na_2S_2O_4$ in H_2O. The reaction mixture was vigorously stirred at rt for 4 h before 20 mL of H_2O was added and extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20–40% EtOAc/hexanes) yielded the corresponding hydroquinone (88.8 mg, 87%) as a brown oil. The resultant hydroquinone (88.8 mg, 0.17 mmol) was diluted with DMF (3.5 mL) and then cooled to 0 °C. The brown solution were added NaH (60% in mineral oil, 19.1 mg, 0.4 mmol, 2.5 equiv) and chloroethyl methyl ether (50 μL, 0.5 mmol, 3 equiv).The reaction mixture was stirred from 0 °C to rt for 2 h then being re-cooled to 0 °C before 10 mL of H_2O was added and extracted with EtOAc (4x10mL). The combined organic layers were washed with water (20 mL) then brine, dried over

anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (5–20% EtOAc/hexanes) yielded EOM ether **29** (65.3 mg, 60%, 53% over 2 steps) as a yellow oil: R_f = 0.67 (40% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54–7.53 (m, 2H), 7.40–7.30 (m, 3H), 6.71 (s, 1H), 5.03 (s, 2H), 4.93 (s, 4H), 4.80 (s, 2H), 4.21 (s, 2H), 3.96 (s, 3H), 3.95 (s, 3H), 3.84 (q, *J* = 6.9 Hz, 2H), 3.57 (d, *J* = 7.2 Hz, 2H), 2.20 (s, 3H), 1.27 (t, *J* = 6.9 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.35, 152.69, 149.34, 146.62, 146.29, 136.68, 134.21, 128.16, 127.49, 127.43, 127.25, 126.93, 124.22, 115.87, 99.20, 99.15, 96.60, 75.74, 64.84, 64.45, 56.96, 55.98, 55.88, 42.04, 28.48, 24.97, 17.33, 14.31, 1416, –6.37; IR (neat) 2930, 2857, 1713, 1605, 1350, 1059 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{35}H_{50}NaO_9Si$ $(M + Na)^+$ 665.3116, found 665.3116.



30

Naphthol 30. To a solution of benzyl ether **29** (95.7 mg, 0.15 mmol) in EtOAc (3 mL) was added Pd/C (16.3 mg, 7 μmol, 0.05 equiv). The reaction mixture was stirred at rt under H_2 atmosphere for 3.5 h before being filtered through a pad of Celite, washed with EtOAc and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20–30% EtOAc/hexanes) yielded naphthol **30** (67.8 mg, 82%) as a yellow oil: R_f = 0.45 (40% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (s, 1H), 6.78 (s, 1H), 5.03 (s, 2H), 5.00 (s, 2H), 4.87 (s, 2H), 4.16 (s, 2H), 3.97 (s, 3H), 3.88 (s, 3H), 3.79 (q, *J* = 6.9 Hz, 4H), 2.21 (s, 3H), 1.24 (t, *J* = 6.9 Hz, 3H), 1.23 (t, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.73, 149.35, 147.75, 147.02, 143.27, 135.48, 128.36, 126.11, 120.01, 116.32, 100.68, 100.68, 100.13, 66.95, 65.92, 58.01, 57.96, 57.19, 42.56, 29.52, 25.92, 18.26, 15.29, 15.20, –5.35; IR (neat) 3369, 2930, 1718, 1350, 1160, 1057 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{44}NaO_9Si$ $(M + Na)^+$ 575.2647, found 575.2645.

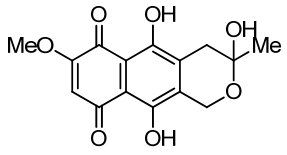
31 **31a**

To a solution of naphthol **30** (68.0 mg, 0.12 mmol) in MeCN/H_2O (9:1, 1 mL) at 0 °C was added $PhI(OAc)_2$ (42.0 mg, 0.12 mmol, 1.0 equiv). The reaction mixture was stirred further for 5 min before being diluted with H_2O (10 mL) and extracted with EtOAc (3x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*.

Purification of the crude residue by column chromatography (20–50% EtOAc/hexanes) yielded *para*-naphthoquinone **31** (33.0 mg, 50%) as an orange oil and *ortho*-naphthoquinone **31a** (9.6 mg, 15%) as a red oil.

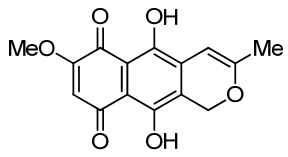
***para*-Naphthoquinone 31.** R_f = 0.57 (60% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.00 (s, 1H), 5.08 (s, 2H), 5.07 (s, 2H), 4.81 (s, 2H), 4.18 (s, 2H), 3.84–3.74 (m, 7H), 2.19 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 6.9 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.56, 183.96, 179.17, 159.36, 153.72, 151.49, 143.59, 139.41, 123.70, 123.28, 110.29, 100.78, 100.59, 66.01, 65.92, 57.48, 56.36, 42.78, 29.71, 25.85, 18.28, 15.16, 15.16, –5.45; IR (neat) 2931, 2857, 1721, 1630, 1557, 1257 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{40}NaO_9Si$ $(M + Na)^+$ 559.2334, found 559.2334.

***ortho*-Naphthoquinone 31a:** R_f = 0.38 (60% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96 (s, 1H), 5.10 (s, 2H), 5.00 (s, 2H), 4.79 (s, 2H), 4.18 (s, 2H), 4.00 (s, 3H), 3.75–3.58 (m, 4H), 2.24 (s, 3H), 1.27 (t, *J* = 6.9 Hz, 6H), 0.91 (s, 9H), 0.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.53, 179.52, 179.52, 170.46, 156.10, 150.11, 144.36, 137.42, 123.61, 122.81, 102.74, 100.70, 100.70, 66.30, 65.99, 57.72, 56.97, 42.36, 29.70, 25.84, 18.27, 15.19, 15.14, -5.47; IR (neat) 2930, 2857, 1721, 1635, 1594, 1160 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{40}NaO_9Si$ $(M + Na)^+$ 559.2334, found 559.2329.



fusarubin (**1**)

Fusarubin (1). To a solution of naphthoquinone **31** (56.8 mg, 0.1 mmol) in MeCN (2.5 mL) was added a solution of 1M HCl (0.7 mL). The reaction mixture was stirred for 3.5 h before 30 mL of H_2O was added and extracted with EtOAc (4x10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20–40% EtOAc/hexanes) yielded fusarubin (**1**) (17.6 mg, 54%) as a red solid and anhydrofusarubin (**2**) (6.4 mg, 22%) as purple needles: R_f = 0.43 (50% EtOAc/hexanes); mp193.7–195.0 °C; $[\alpha]_D^{26}$ = +4.35 (*c* 0.036, acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.94 (s, 1H), 12.68 (s, 1H), 6.19 (s, 1H), 4.89, (s, 2H), 3.94 (s, 3H), 3.03 (d, *J* = 18.0 Hz, 1H), 2.71 (d, *J* = 18.0 Hz, 1H), 2.31 (brs, 1H), 1.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.64, 178.43, 160.65, 160.65, 156.97, 137.10, 137.10, 109.64, 109.64, 107.63, 94.06, 58.47, 56.68, 32.31, 22.63; ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 12.90 (s, 1H), 12.43 (s, 1H), 6.37 (s, 1H), 6.10, (s, 1H), 4.62 (s, 2H), 3.88 (s, 3H), 2.71 (d, *J* = 18.0 Hz, 1H), 2.51 (d, *J* = 18.0 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d*$_6$) δ 185.05, 178.10, 161.06, 160.04, 156.68, 137.21, 133.67, 110.10, 109.74, 107.45, 93.44, 57.74, 57.49, 33.20, 28.88; IR (neat) 3357, 2927, 1592, 1418, 1215, 1149 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{14}NaO_7$ $(M + Na)^+$ 329.0632, found 329.0629.

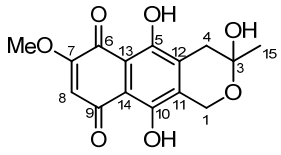


anhydrofusarubin (**2**)

Anhydrofusarubin (2). To a solution of fusarubin (**1**) (20.0 mg, 0.1 mmol) in toluene (33 mL) was added catalytic amount of TsOH. The reaction mixture was heated at 105 °C for 1 h before being cooled to rt and 70 mL of H_2O was added. The aqueous phase was extracted with EtOAc (3x20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the crude residue by column chromatography (20% EtOAc/hexanes) yielded anhydrofusarubin (**2**) (14.0 mg, 73%) as purple needles: R_f = 0.65 (50% EtOAc/hexanes); mp 193.0–194.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.01 (s, 1H), 12.61 (s, 1H), 6.14 (s, 1H), 5.96 (s, 1H), 5.19 (s, 2H), 3.92 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.93, 177.85, 161.53, 159.95, 157.66, 157.62, 132.95, 122.69, 110.87, 109.91, 107.92, 94.65, 62.92, 56.67, 20.11; IR (neat) 2922, 1603, 1393, 1257, 1150, 1046 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{12}NaO_6$ $(M + Na)^+$ 311.0520, found 311.0520.

3. Comparison of ^{1}H and ^{13}C NMR data for natural and synthetic compounds 1–4

Table SI1. Comparison of ^{1}H and ^{13}C NMR data for natural[6] and synthetic **1**



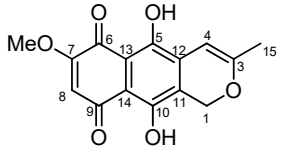
fusarubin (**1**)

Position	^{1}H NMR (δ and *J* in Hz)		^{13}C NMR (δ)	
	Natural (400 MHz) in $CDCl_3$	Synthetic (300 MHz) in $CDCl_3$	Natural (100 MHz) in $CDCl_3$	Synthetic (75 MHz) in $CDCl_3$
1	4.88, s	4.89, s	58.30	58.47
3	–	–	93.80	94.06
3-OH	2.25, brs	2.31, brs	–	–
4	2.70, brd (18.4) 3.02, d, (17.9)	2.71, d (18.0) 3.03, d (18.0)	32.50	32.31
5	–	–	156.80	156.97
5-OH	12.93, s	12.94, s	–	–
6	–	–	178.30	178.43
7	–	–	160.40	160.65
7-OMe	3.93, s	3.94, s	56.70	56.69
8	6.17, s	6.19, s	109.60	109.64
9	–	–	184.90	184.64
10	–	–	160.60	160.65
10-OH	12.66, s	12.68, s	–	–
11	–	–	137.20	137.10
12	–	–	137.20	137.10
13	–	–	109.60	109.64
14	–	–	107.50	107.63
15	1.64, s	1.64, s	22.60	22.63

Table SI2. ^{1}H and ^{13}C NMR data for synthetic **1** in DMSO-*d*$_6$

Position	^{1}H NMR (δ and *J* in Hz) 300 MHz in DMSO-d_6	^{13}C NMR (δ) 75 MHz in DMSO-d_6
1	4.62, s	57.74
3	–	93.44
3-OH	6.10, s	–
4	2.51, d (18.0) 2.71, d, (18.0)	33.20
5	–	156.68
5-OH	12.90, s	–
6	–	178.10
7	–	160.04
7-OMe	3.88, s	57.49
8	6.37, s	110.10
9	–	185.05
10	–	161.06
10-OH	12.43, s	–
11	–	133.67
12	–	137.21
13	–	110.10
14	–	107.45
15	1.46, s	28.88

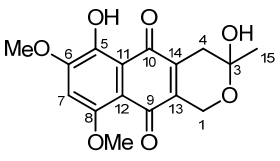
Table SI3. Comparison of ^{1}H and ^{13}C NMR data for natural[7] and synthetic **2**



anhydrofusarubin (**2**)

Position	^{1}H NMR (δ and *J* in Hz)		^{13}C NMR (δ)	
	Natural (500 MHz) in $CDCl_3$	Synthetic (300 MHz) in $CDCl_3$	Natural (125 MHz) in $CDCl_3$	Synthetic (75 MHz) in $CDCl_3$
1	5.16, s	5.19, s	62.90	62.92
3	–	–	161.50	161.53
4	5.92, s	5.96, s	94.60	94.65
5	–	–	157.60	157.66
5-OH	12.57, s	12.61, s	–	–
6	–	–	177.80	177.85
7	–	–	159.90	159.95
7-OMe	3.88, s	3.92, s	56.60	56.67
8	6.11, s	6.14, s	109.90	109.91
9	–	–	182.90	182.93
10	–	–	157.60	157.62
10-OH	12.97, s	13.01, s	–	–
11	–	–	122.70	122.69
12	–	–	132.90	132.95
13	–	–	110.90	110.87
14	–	–	107.90	107.92
15	1.98, s	2.01, s	20.10	20.11

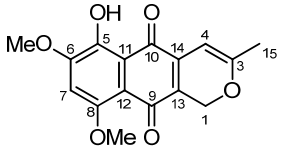
Table SI4. Comparison of ^{1}H and ^{13}C NMR data for natural[8] and synthetic **3**



8-*O*-methylfusarubin (**3**)

Position	^{1}H NMR (δ and *J* in Hz)		^{13}C NMR (δ)	
	Natural (400 MHz) in DMSO-d_6	Synthetic (300 MHz) in DMSO-d_6	Natural (125 MHz) in DMSO-d_6	Synthetic (75 MHz) in DMSO-d_6
1	4.43, m	4.46, m	57.65	58.04
3	–	–	93.16	93.56
3-OH	6.04, s	6.05, s	–	–
4	2.54, d (18.6) 2.36, d (18.6)	2.57, d (18.3) 2.37, d (18.3)	31.73	32.10
5	–	–	147.53	147.90
5-OH	12.94, s	12.95, s	–	–
6	–	–	155.20	155.53
6-OMe	3.88, s	3.90, s	56.45	56.82
7	6.95, s	6.95, s	103.97	104.09
8	–	–	155.70	156.04
8-OMe	3.95, s	3.97, s	56.57	56.93
9	–	–	178.92	179.14
10	–	–	189.09	189.34
11	–	–	113.53	113.81
12	–	–	108.57	108.86
13	–	–	144.71	145.02
14	–	–	136.92	137.21
15	1.43, s	1.47, s	28.35	28.75

Table SI5. Comparison of ^{1}H data for natural[9] and synthetic **4** and ^{13}C NMR data of synthetic **4**

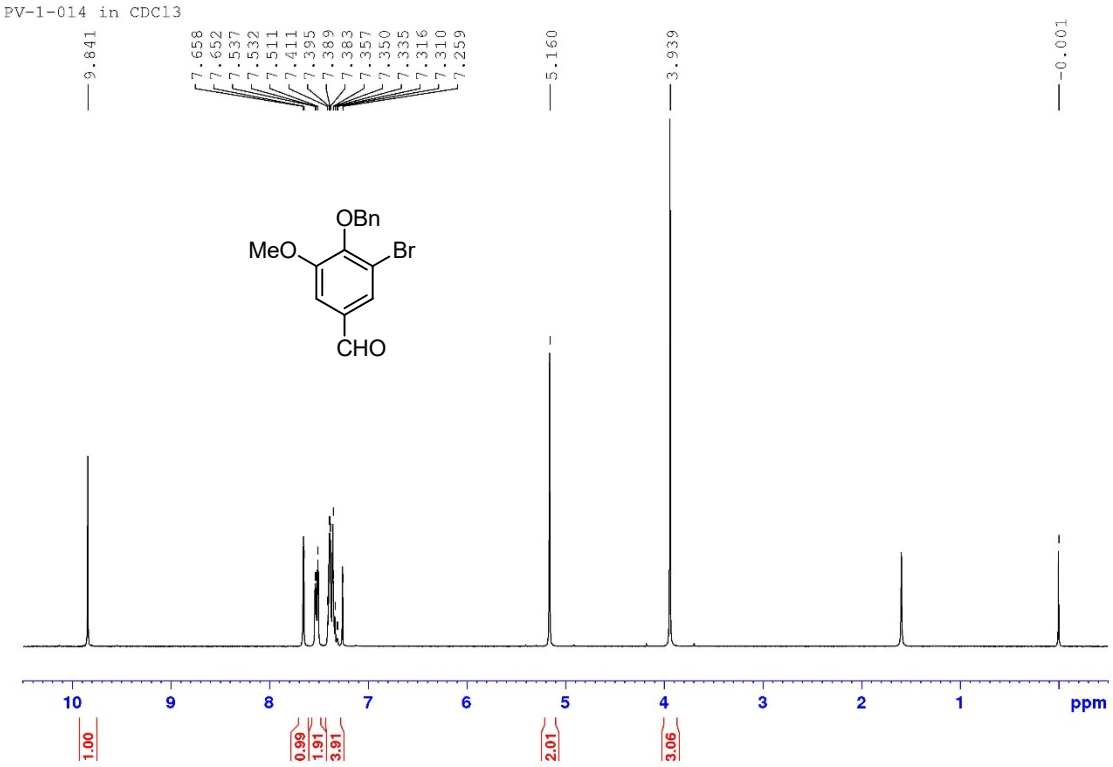


8-*O*-methylanhydrofusarubin (**4**)

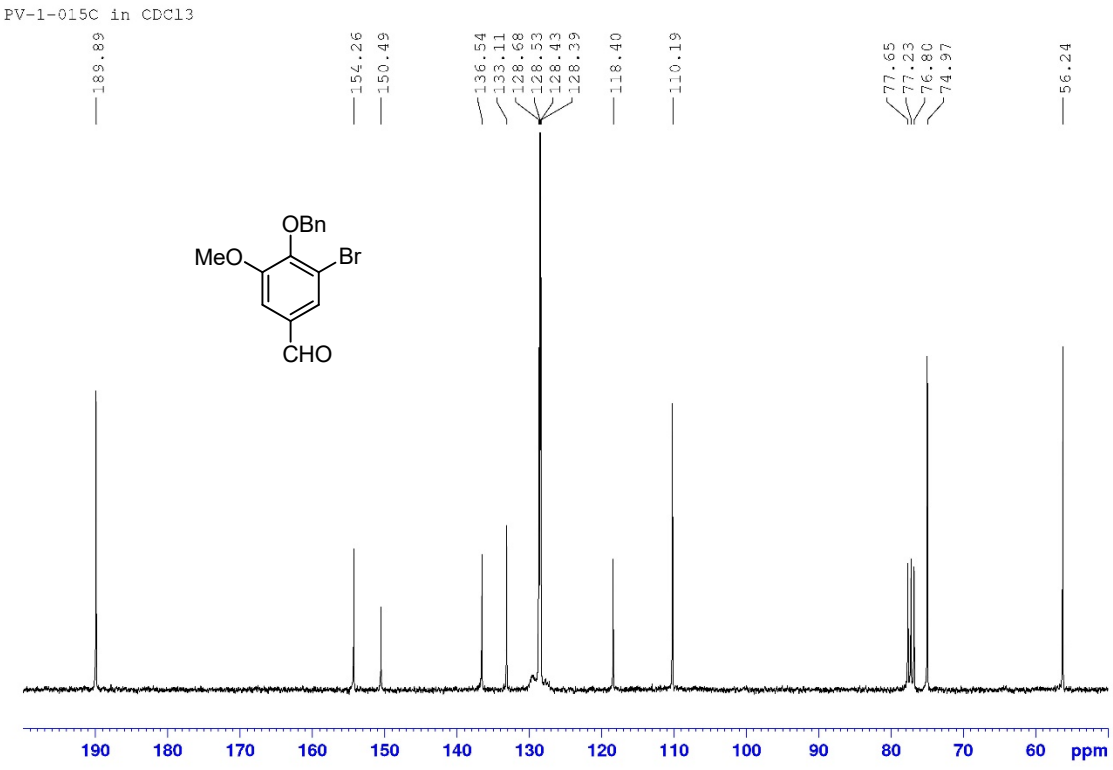
Position	^{1}H NMR (δ and *J* in Hz)		^{13}C NMR (δ)
	Natural (270 MHz) in $CDCl_3$	Synthetic (300 MHz) in $CDCl_3$	Synthetic (75 MHz) in $CDCl_3$
1	5.15, s	5.12, s	63.45
3	–	–	163.43
4	5.83, s	5.85, s	92.99
5	–	–	148.70
5-OH	13.14, s	13.14, s	–
6	–	–	155.21
6-OMe	3.97, s	3.98, s	56.95
7	6.74, s	6.73, s	103.29
8	–	–	155.11
8-OMe	4.00, s	4.00, s	56.34
9	–	–	179.41
10	–	–	187.63
11	–	–	114.37
12	–	–	110.76
13	–	–	135.74
14	–	–	126.45
15	2.00, s	2.01, s	20.08

4. ^{1}H and ^{13}C NMR Spectra

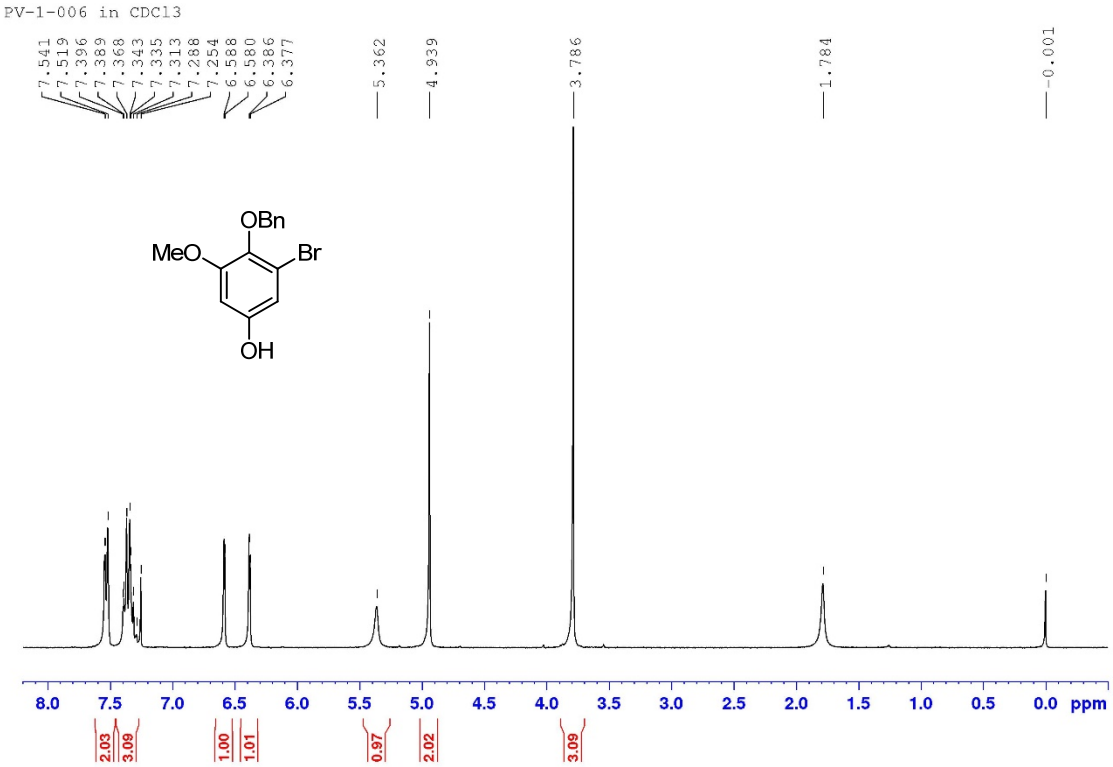
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 4-benzyloxy-3-bromo-5-methoxybenzaldehyde



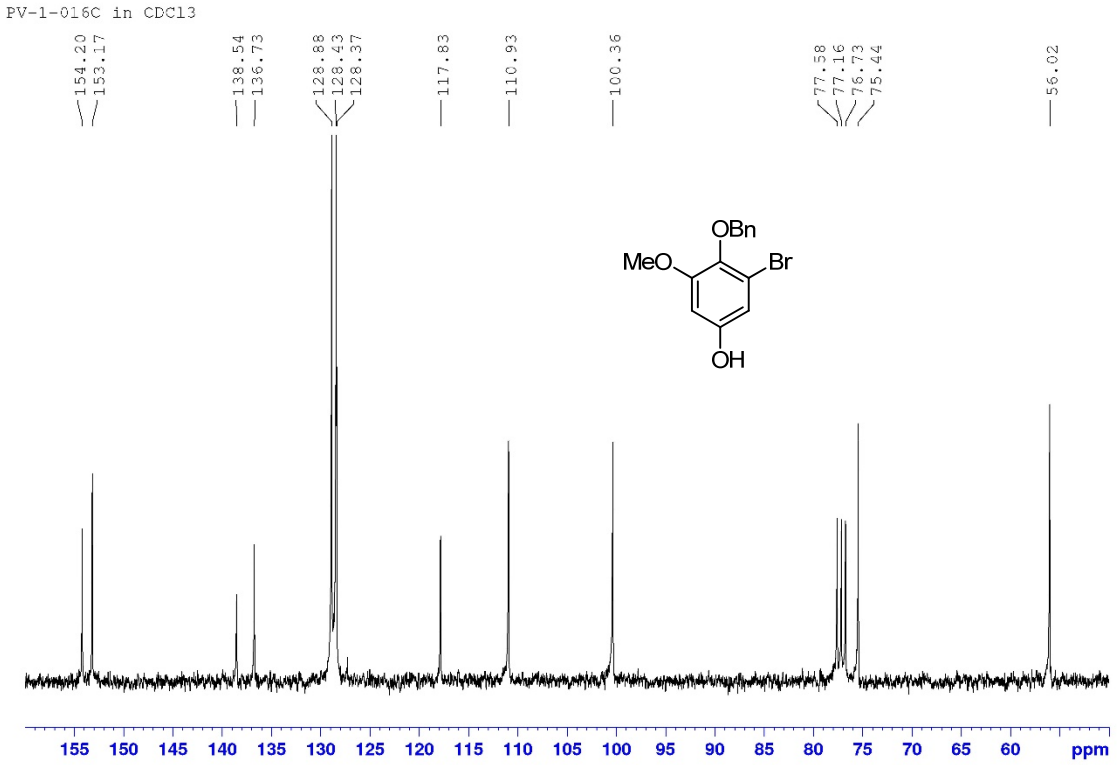
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 4-benzyloxy-3-bromo-5-methoxybenzaldehyde



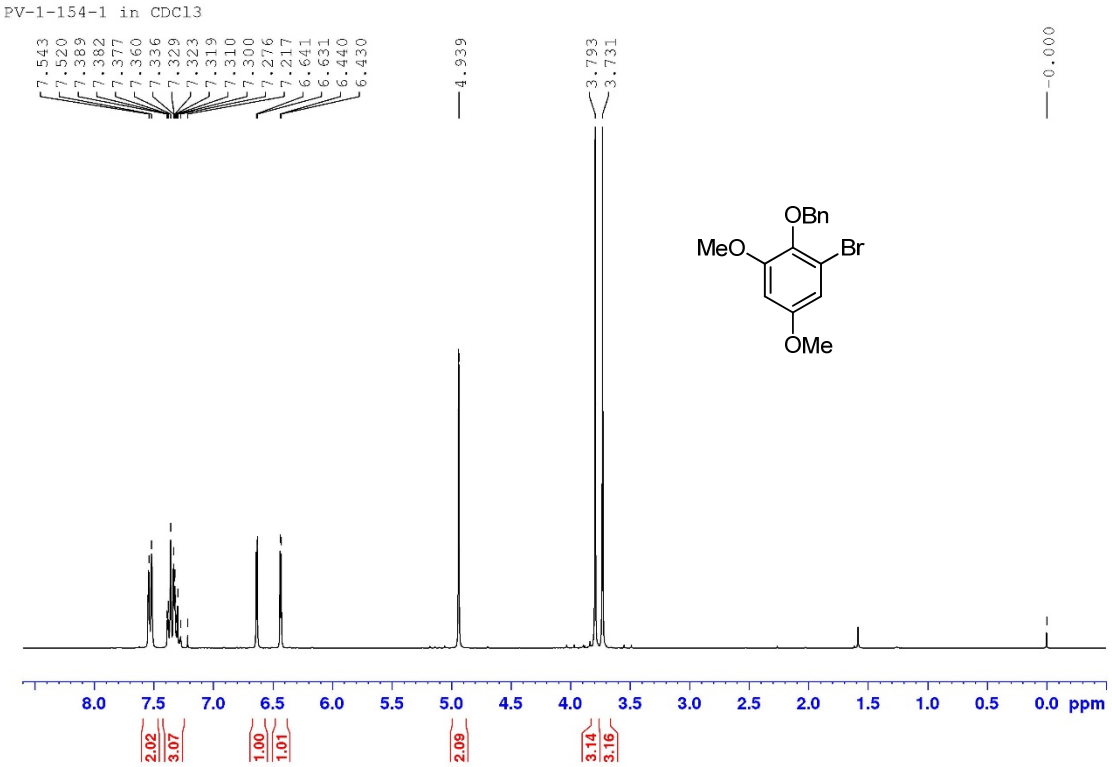
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 4-benzyloxy-3-bromo-5-methoxyphenol



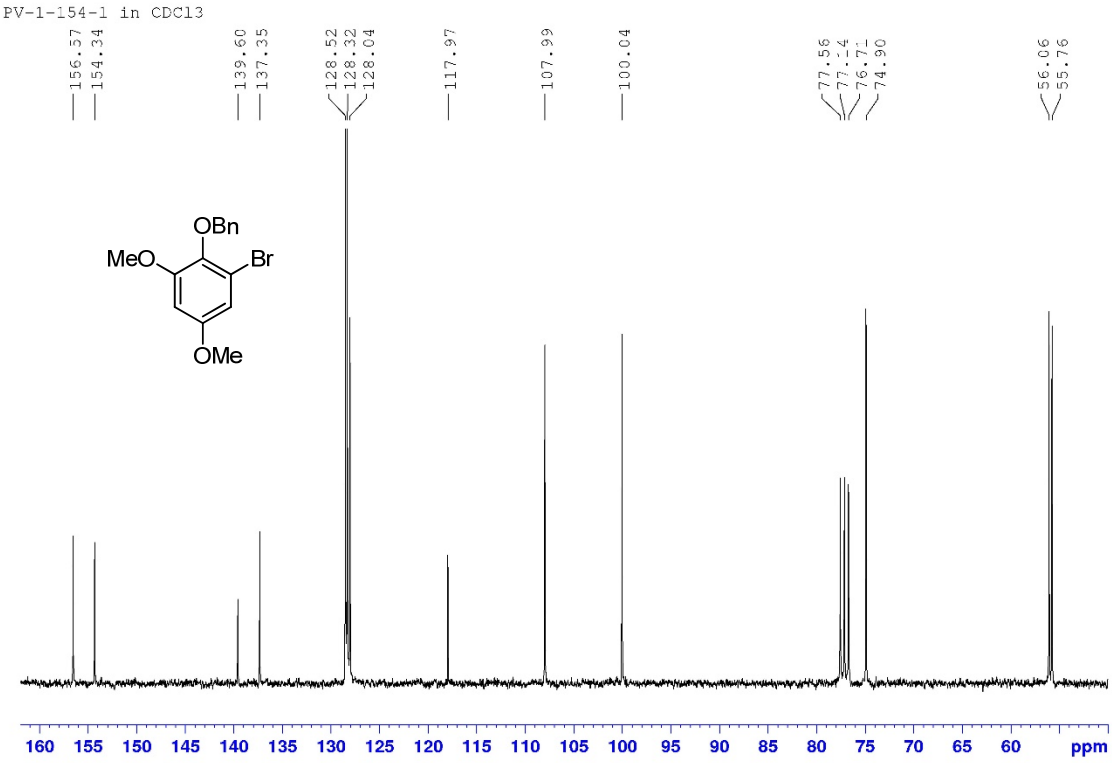
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 4-benzyloxy-3-bromo-5-methoxyphenol



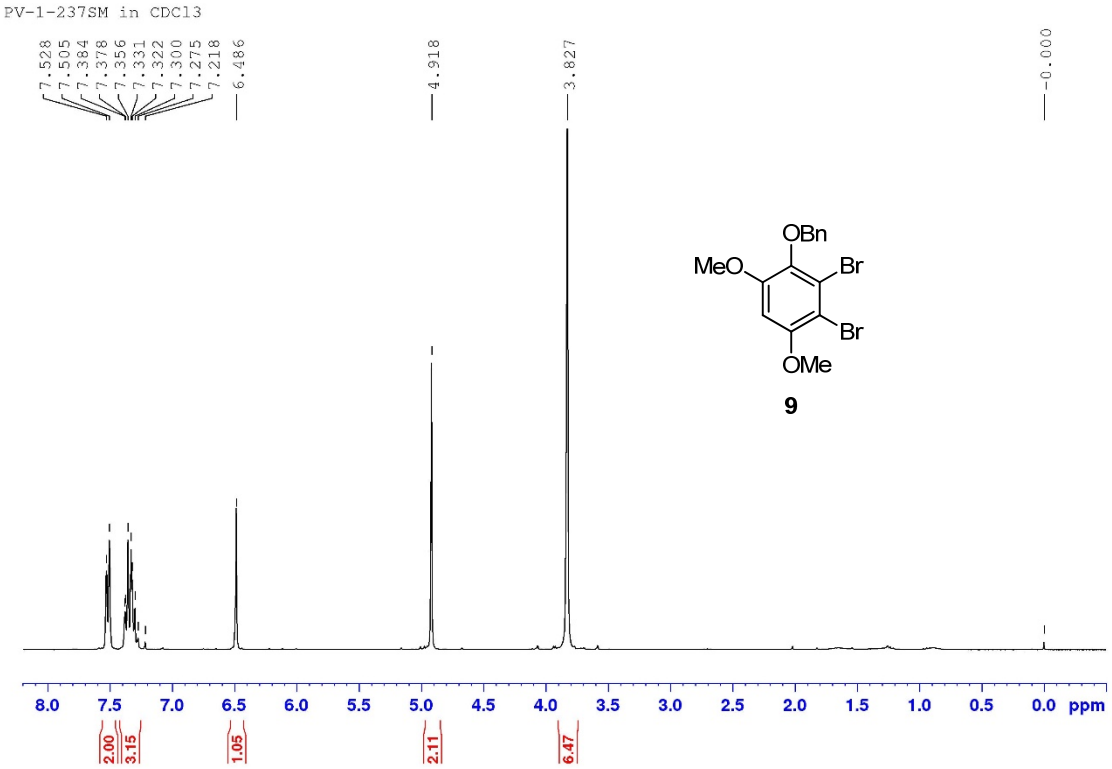
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 2-benzyloxy-3,5-dimethoxybromobenzene



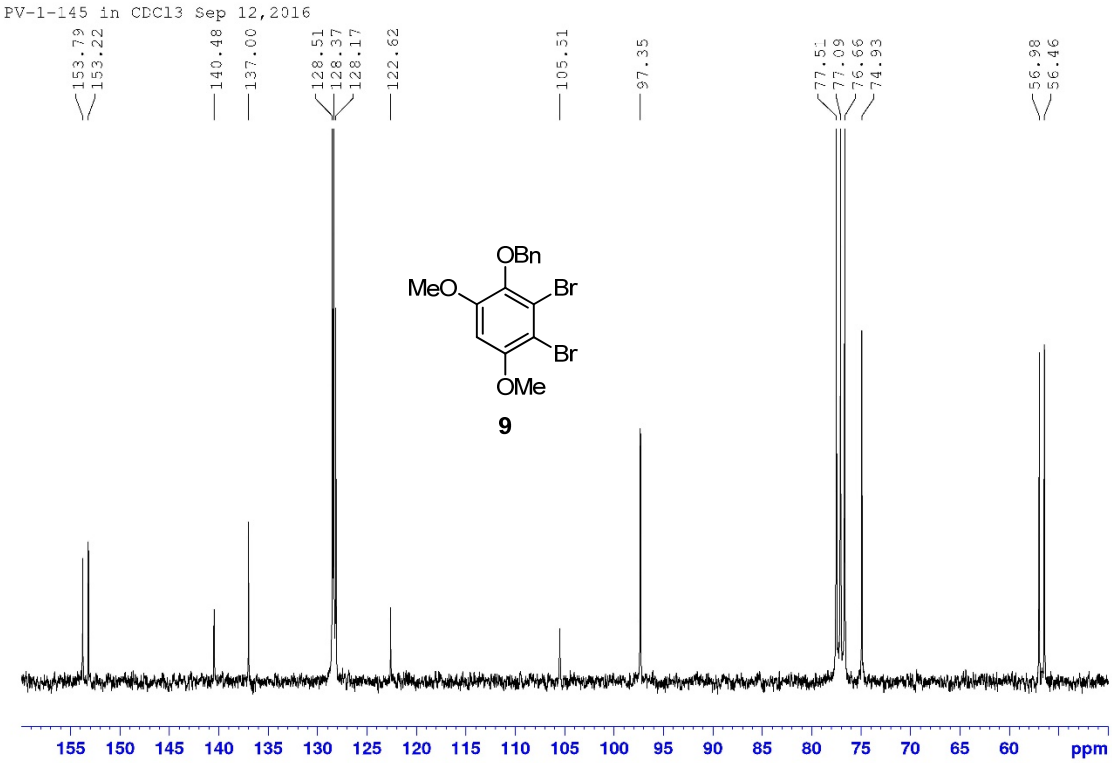
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 2-benzyloxy-3,5-dimethoxybromobenzene



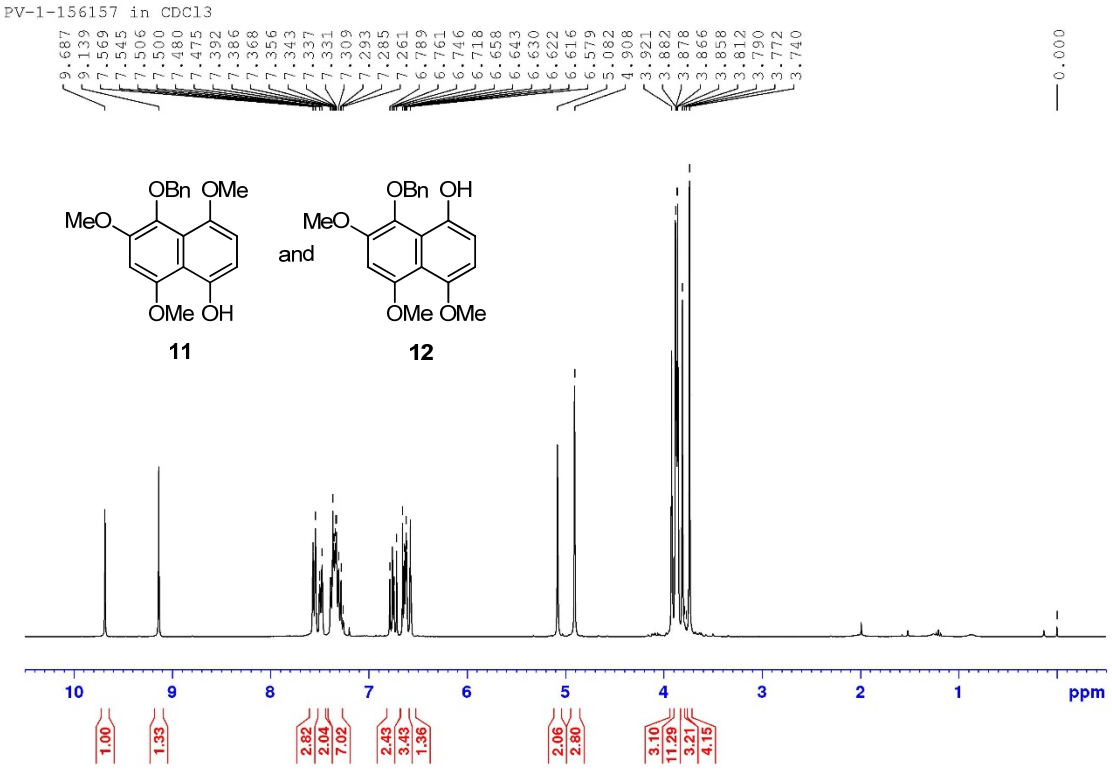
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 1,2-dibromo-3-benzyloxy-4,6-dimethoxybenzene (**9**)



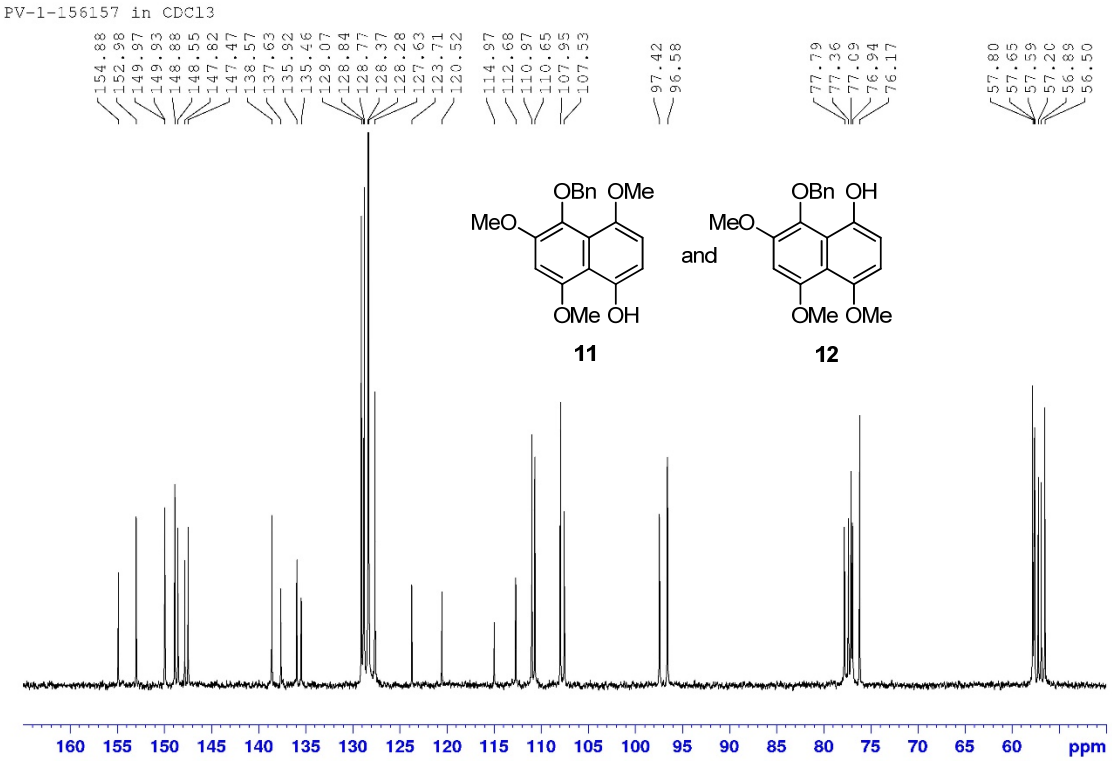
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 1,2-dibromo-3-benzyloxy-4,6-dimethoxybenzene (**9**)



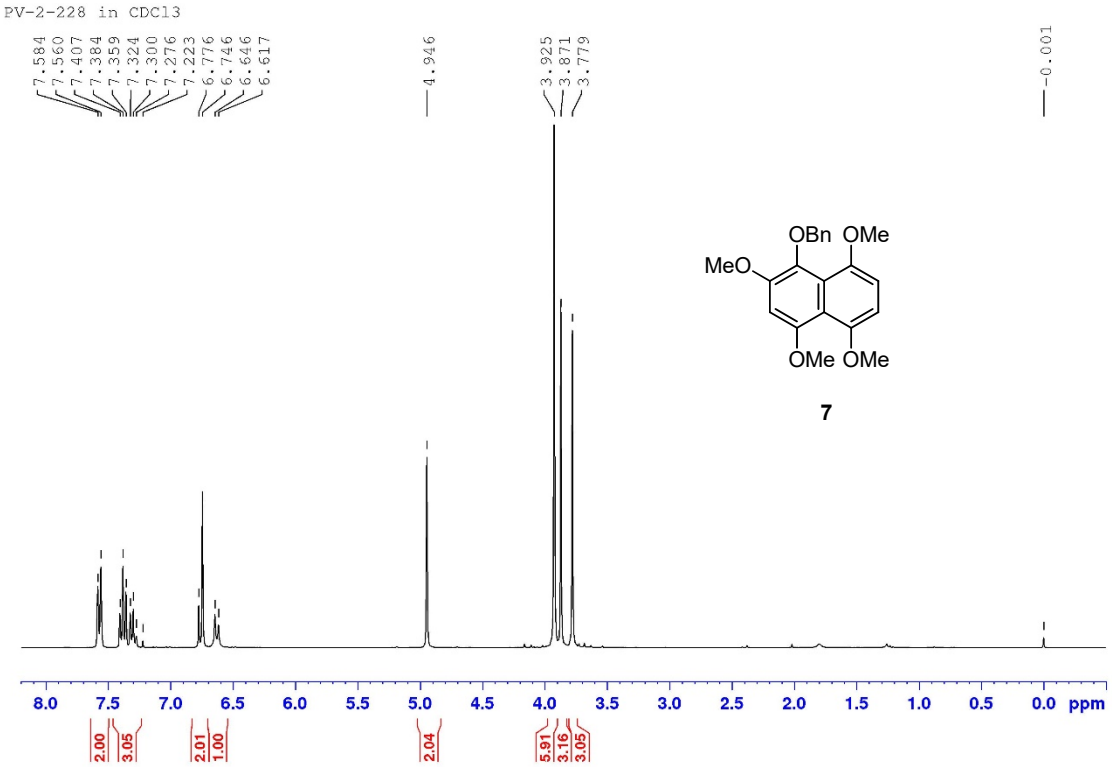
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthols **11** and **12**



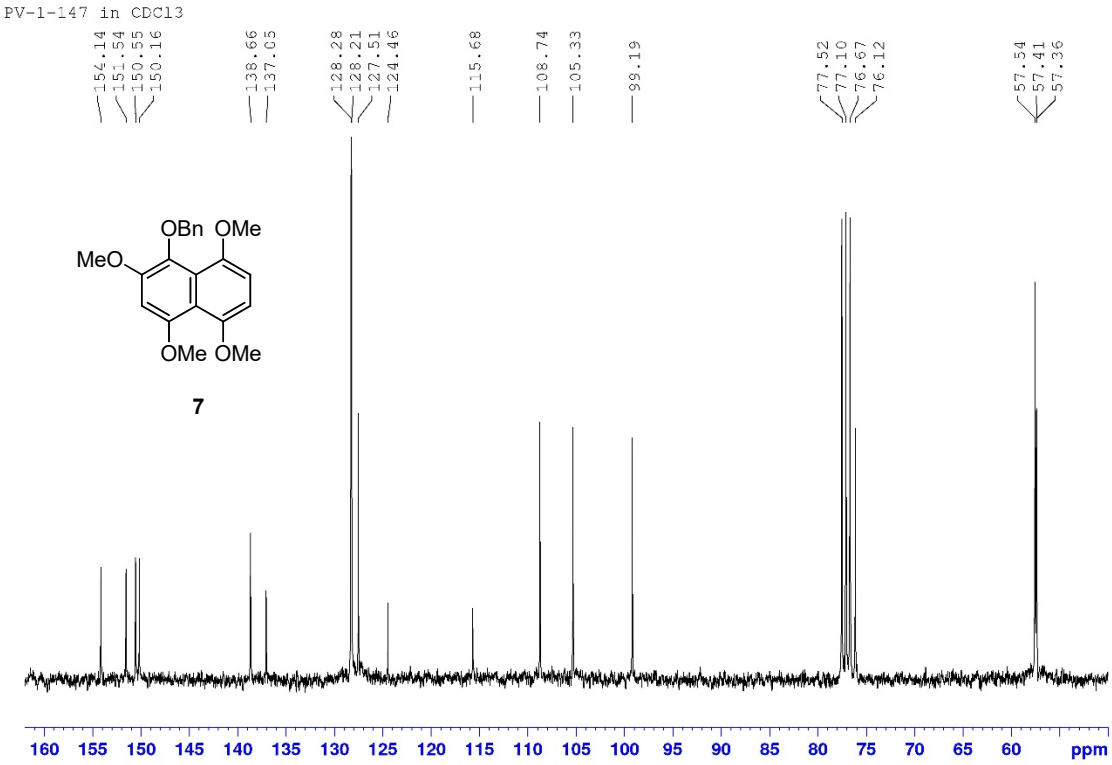
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthols **11** and **12**



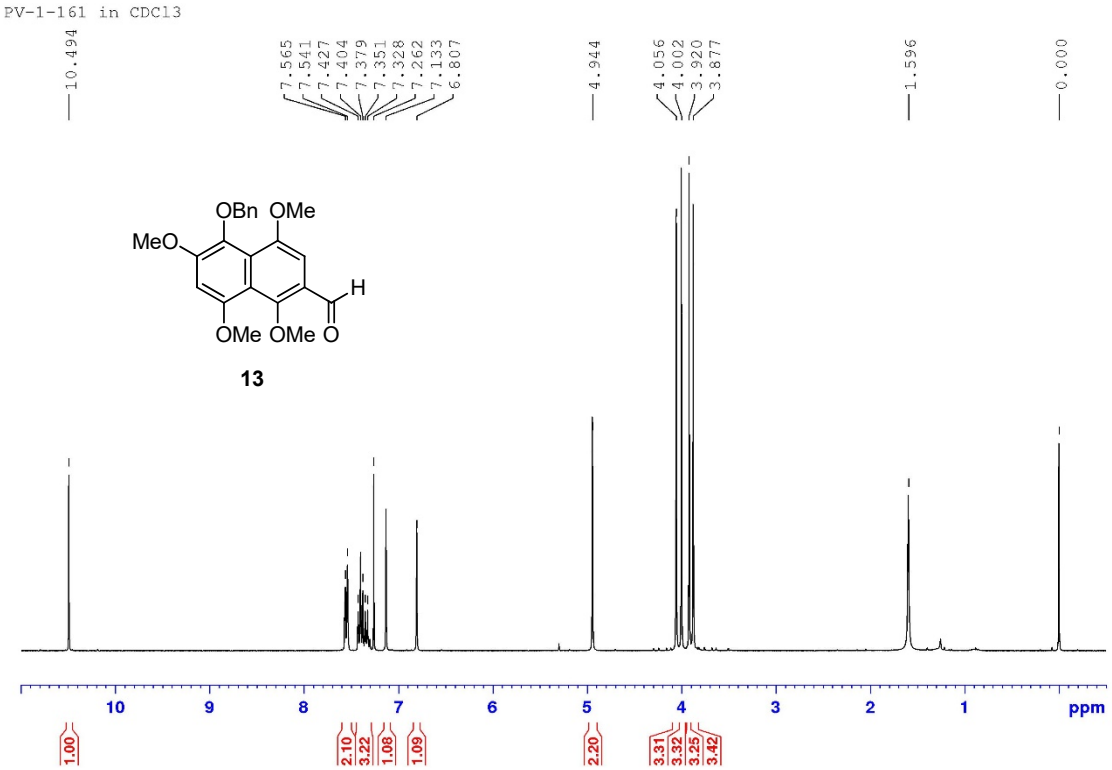
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 1-benzyloxy-2,4,5,8-tetramethoxynaphthalene (**7**)



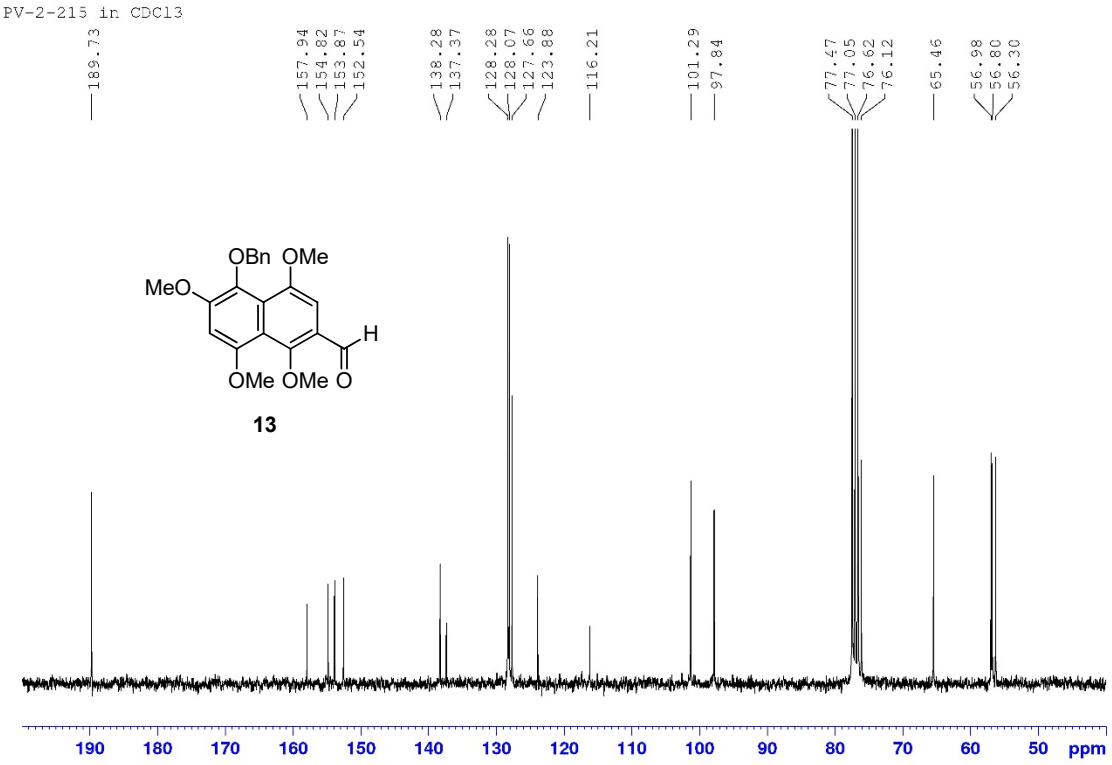
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 1-benzyloxy-2,4,5,8-tetramethoxynaphthalene (**7**)



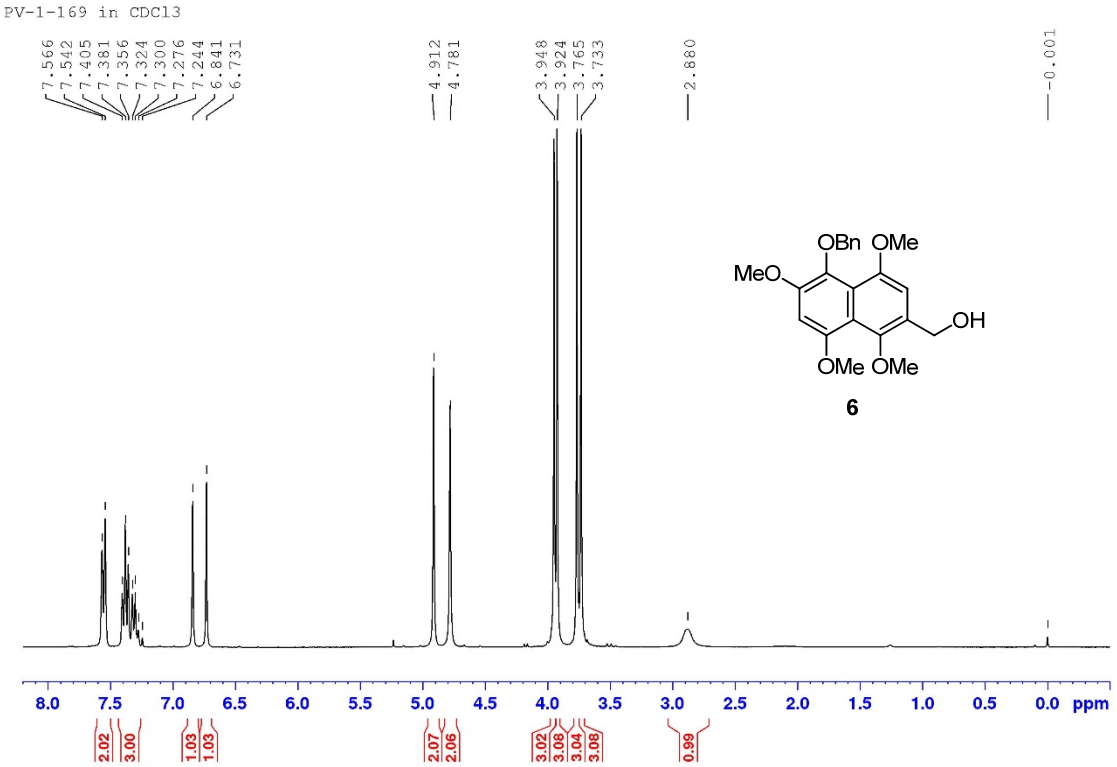
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthaldehyde **13**



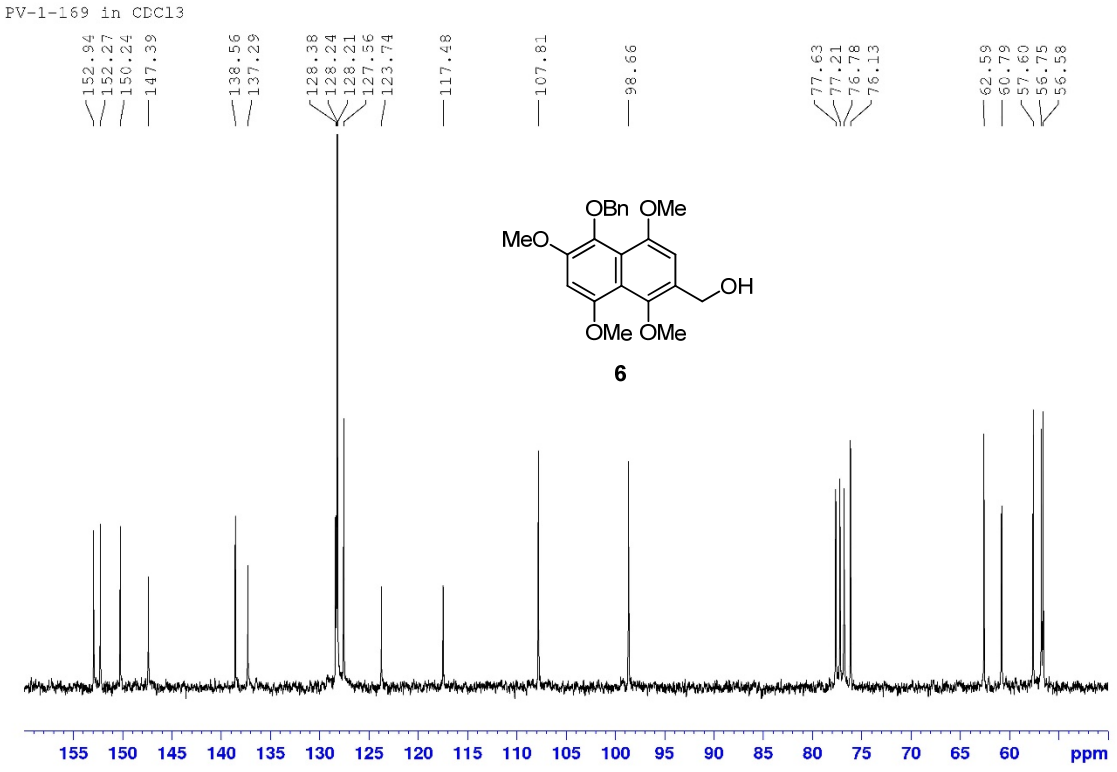
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthaldehyde **13**



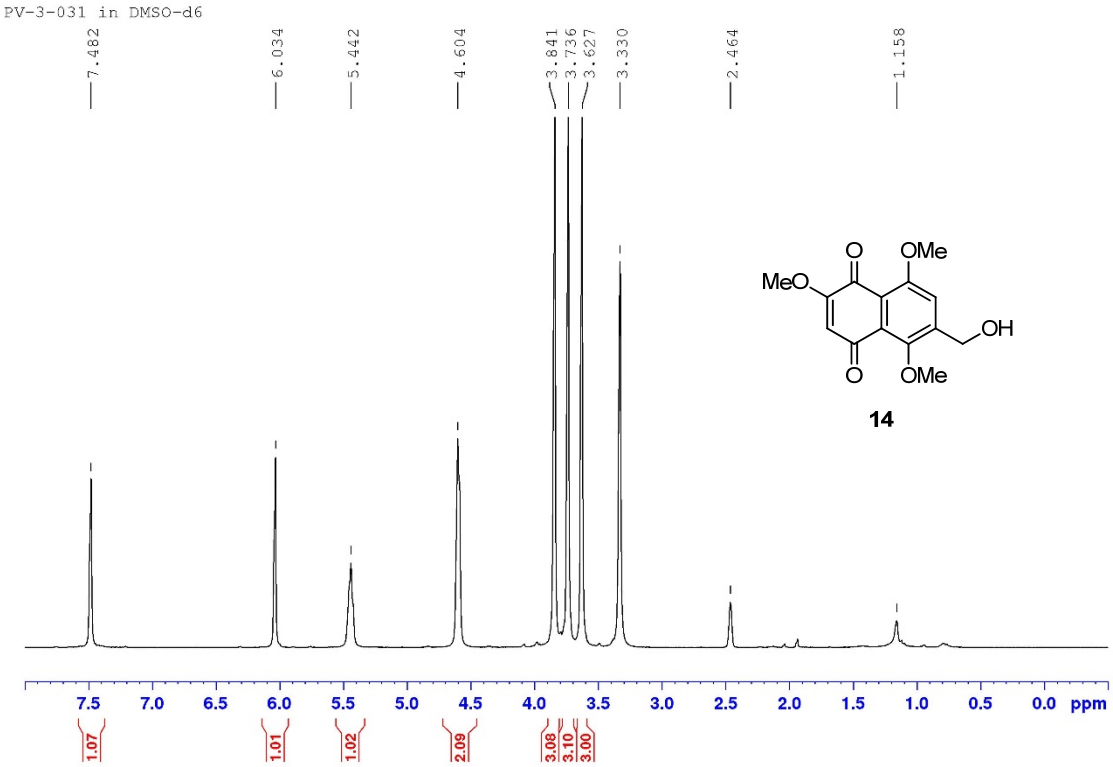
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthyl alcohol **6**



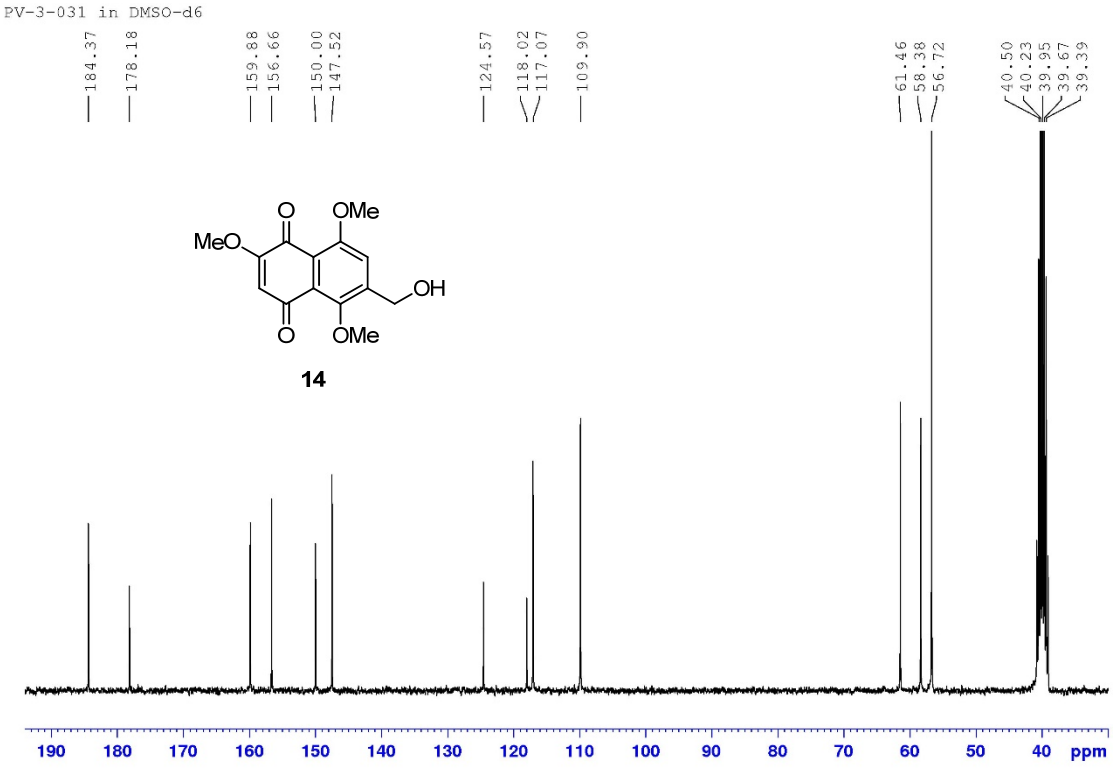
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthyl alcohol **6**



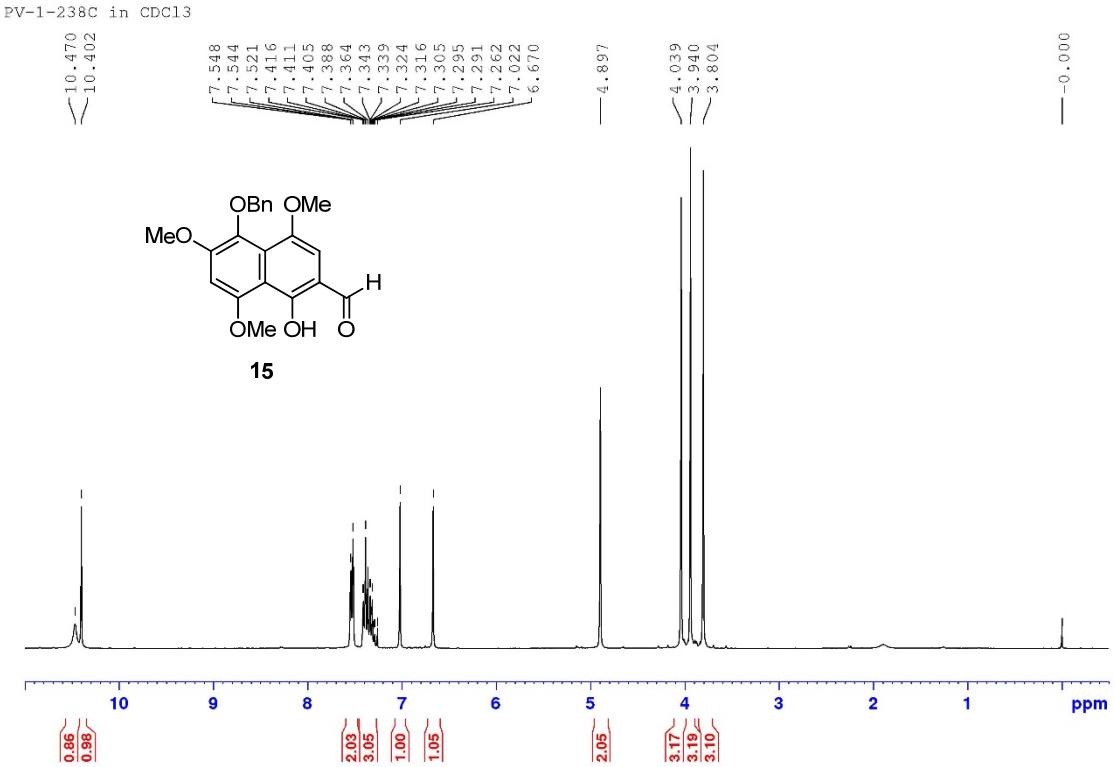
^{1}H NMR (300 MHz, DMSO-*d*$_6$) spectrum of naphthoquinone **14**



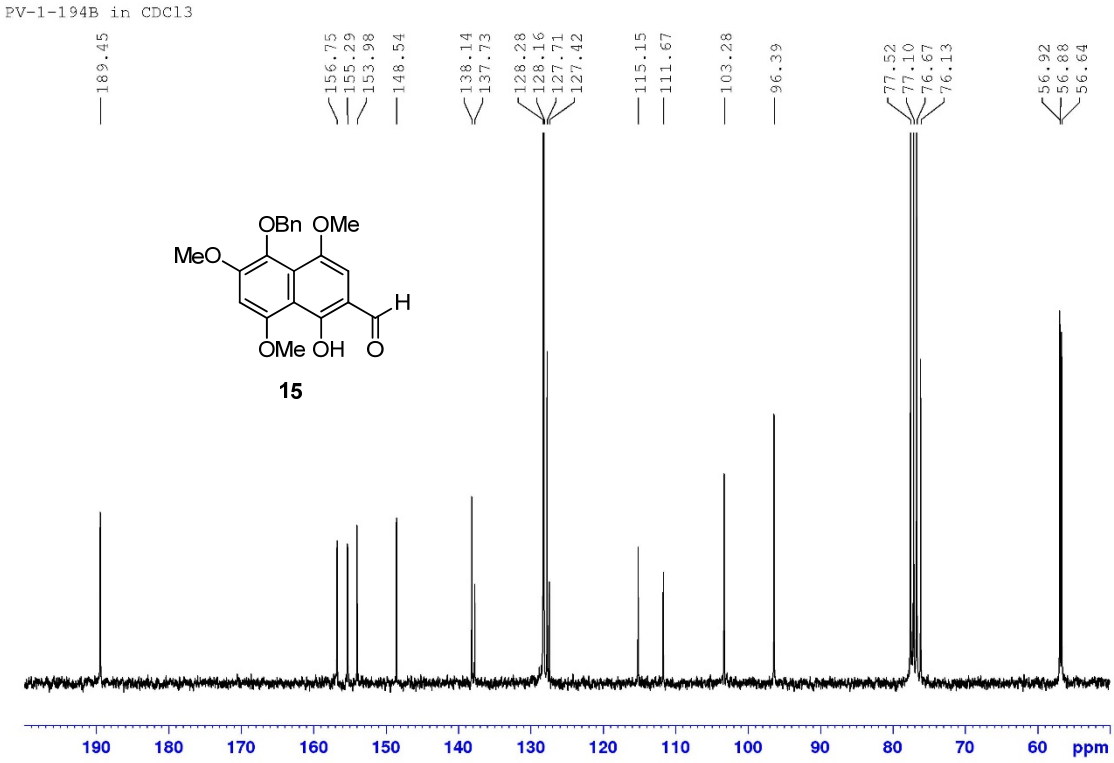
^{13}C NMR (75 MHz, DMSO-*d*$_6$) spectrum of naphthoquinone **14**



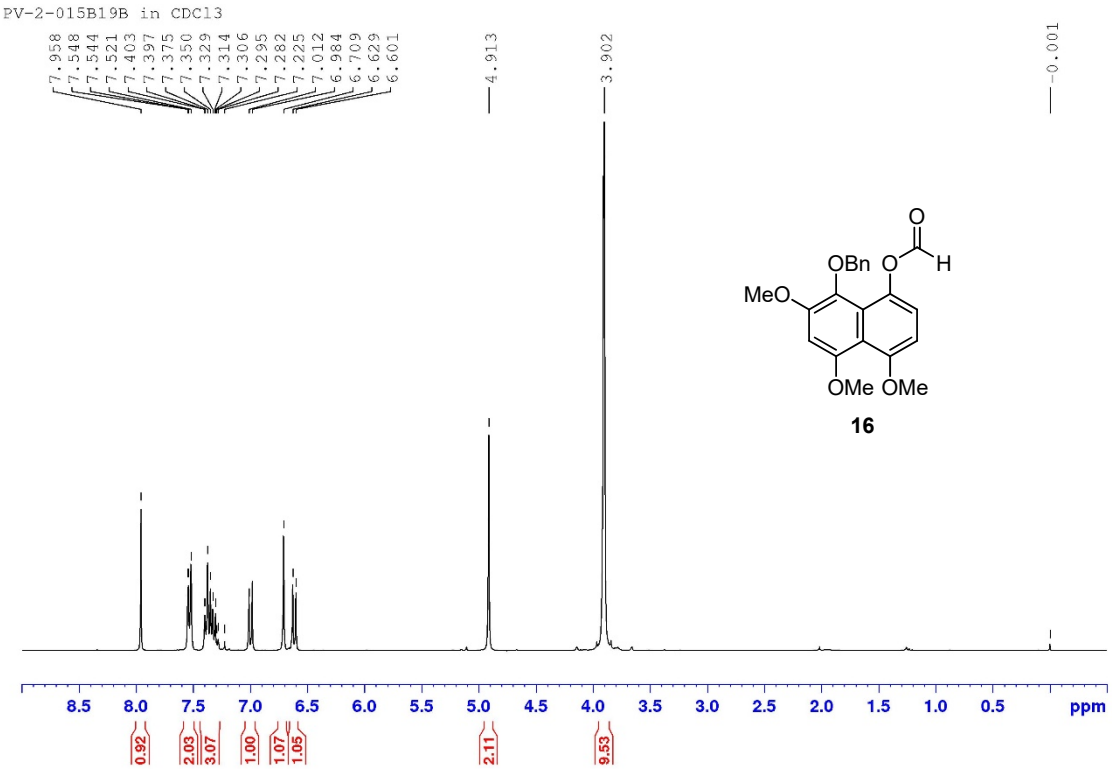
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthaldehyde **15**



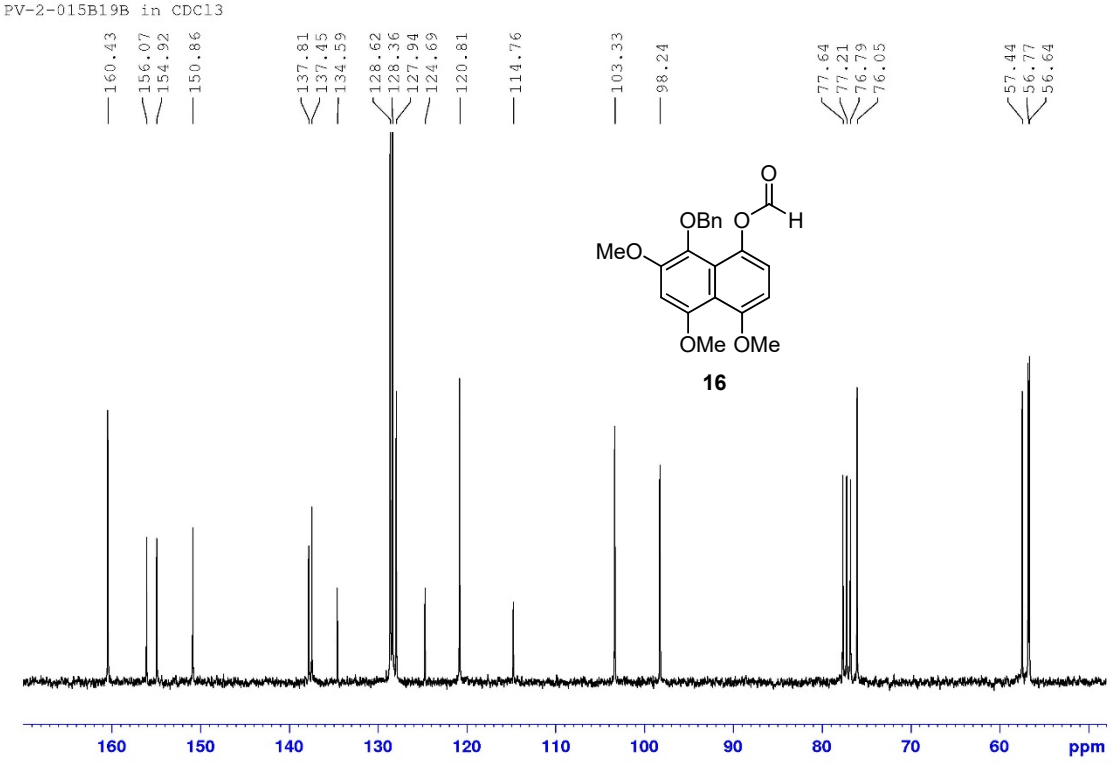
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthaldehyde **15**



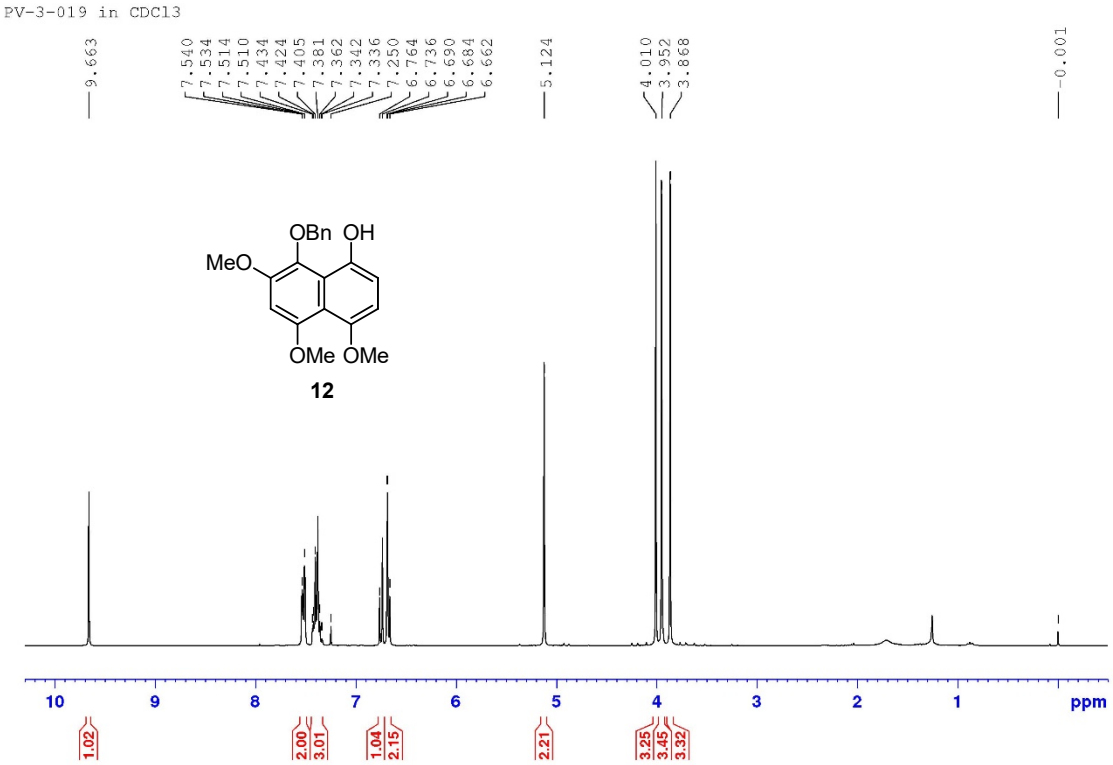
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthyl formate **16**



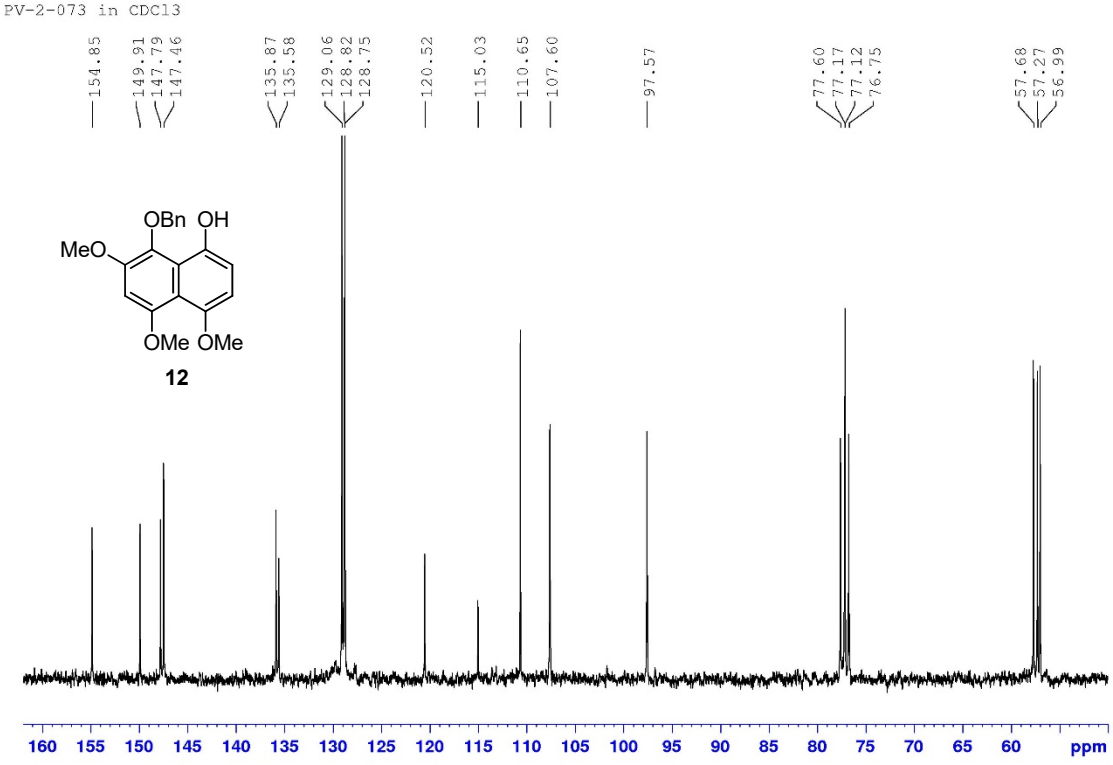
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthyl formate **16**



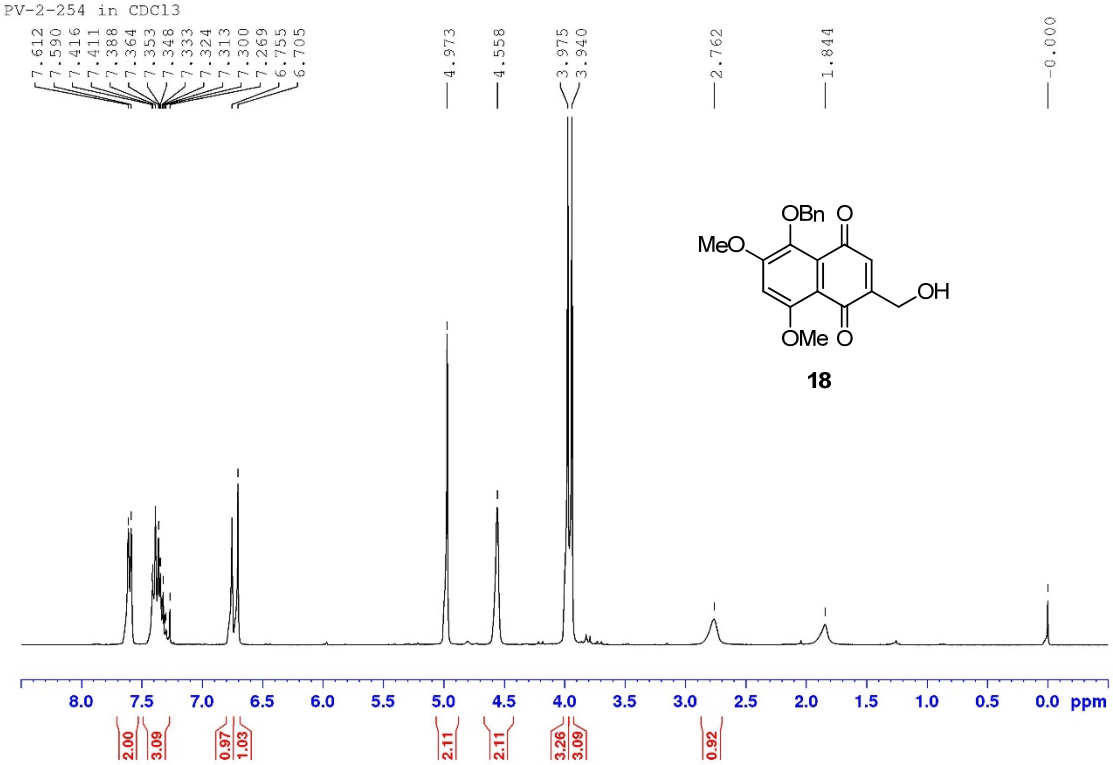
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthol **12**



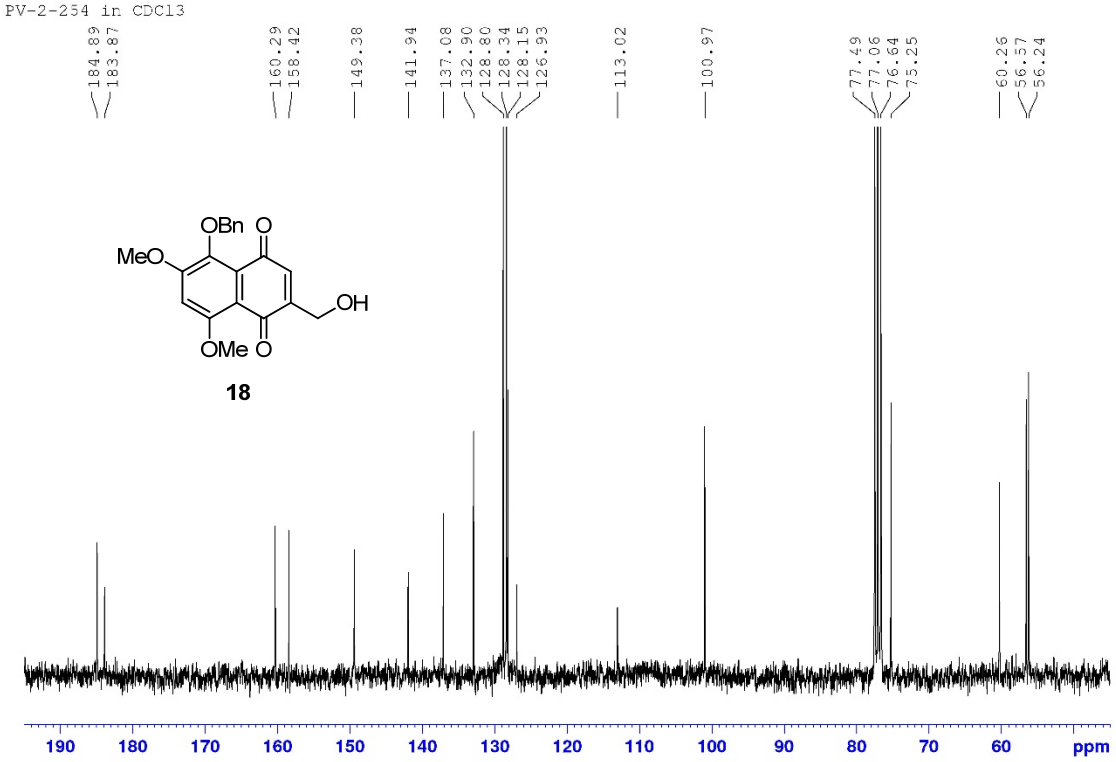
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthol **12**



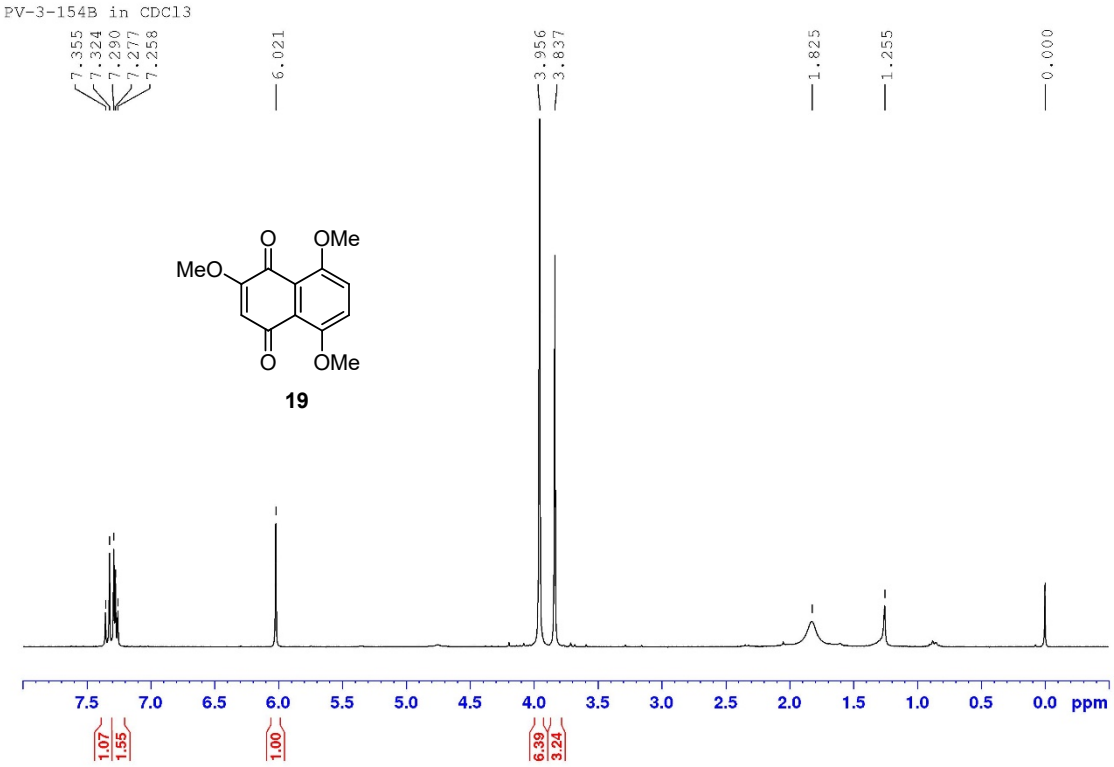
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthoquinone **18**



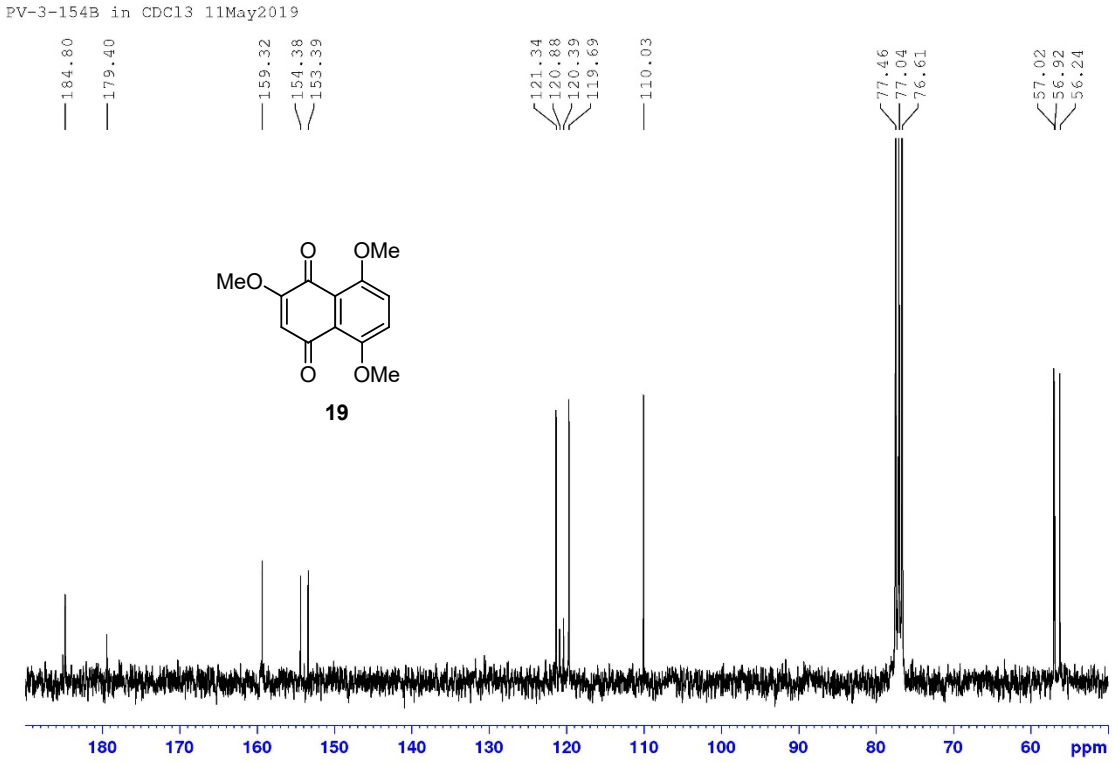
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthoquinone **18**



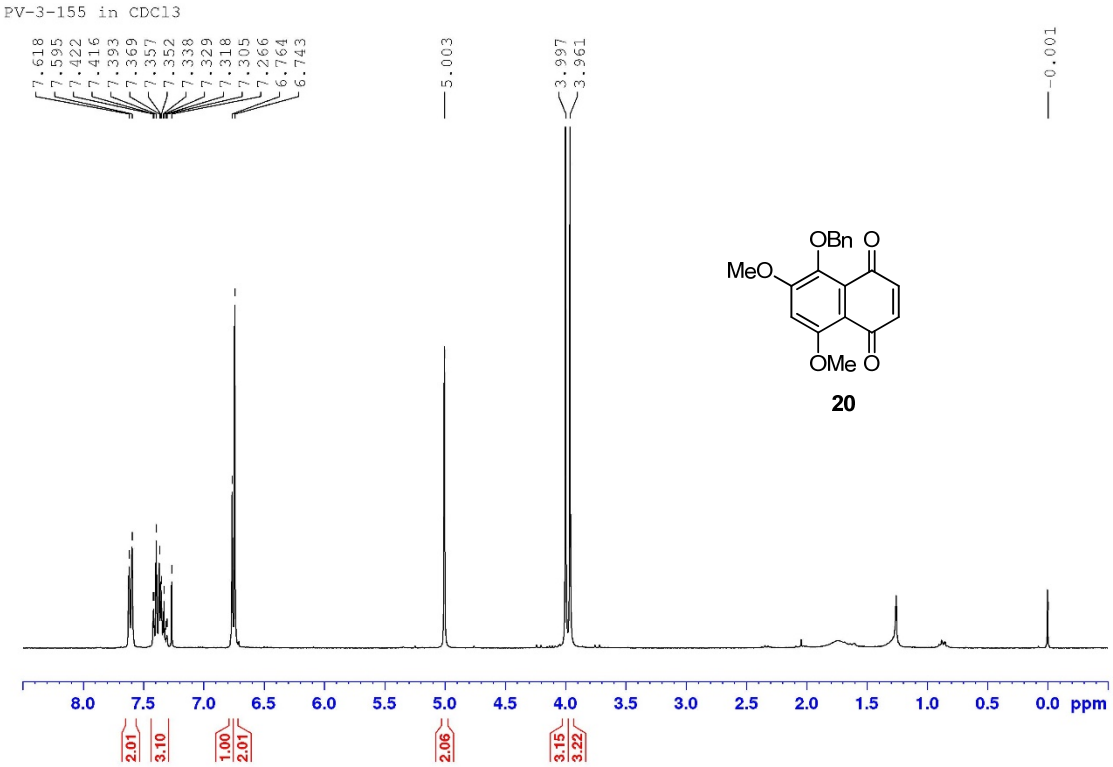
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthoquinone **19**



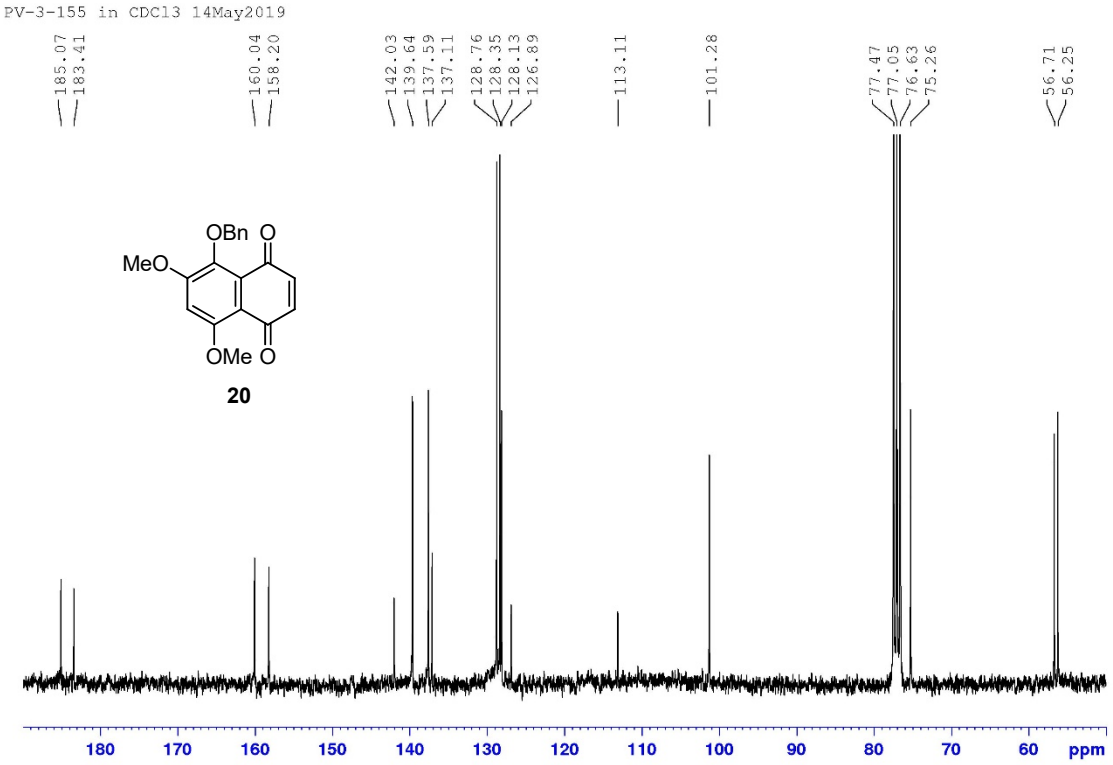
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthoquinone **19**



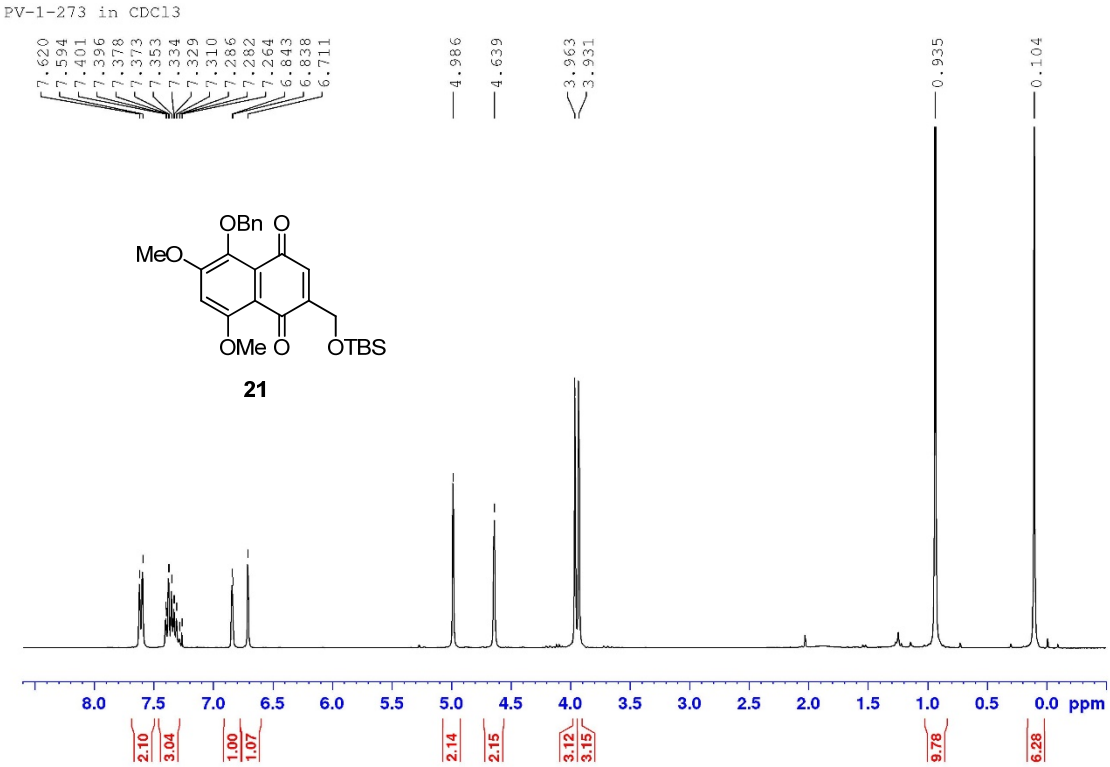
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthoquinone **20**



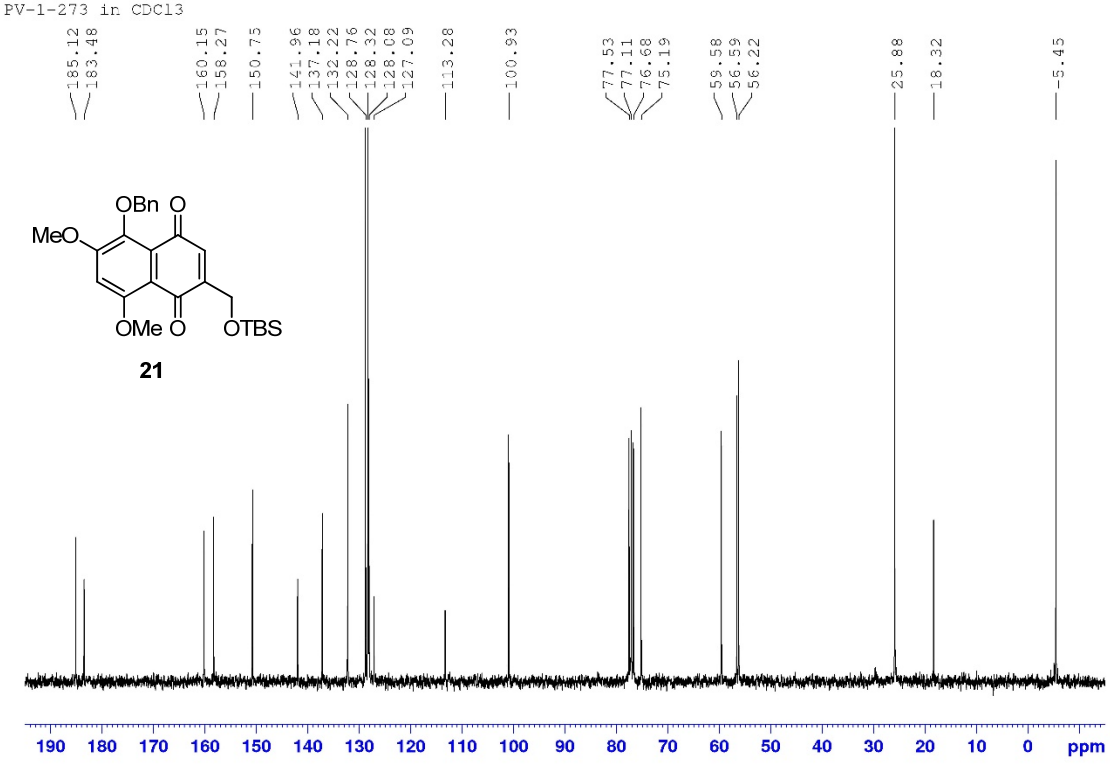
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthoquinone **20**



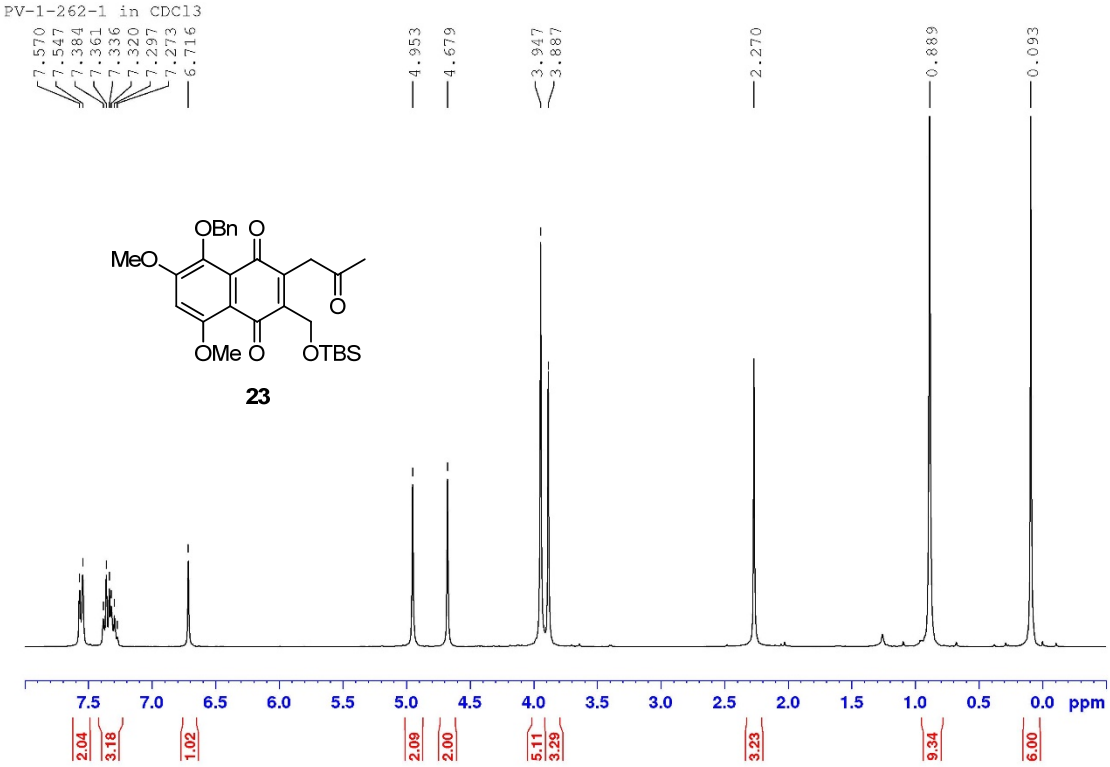
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of silyl ether **21**



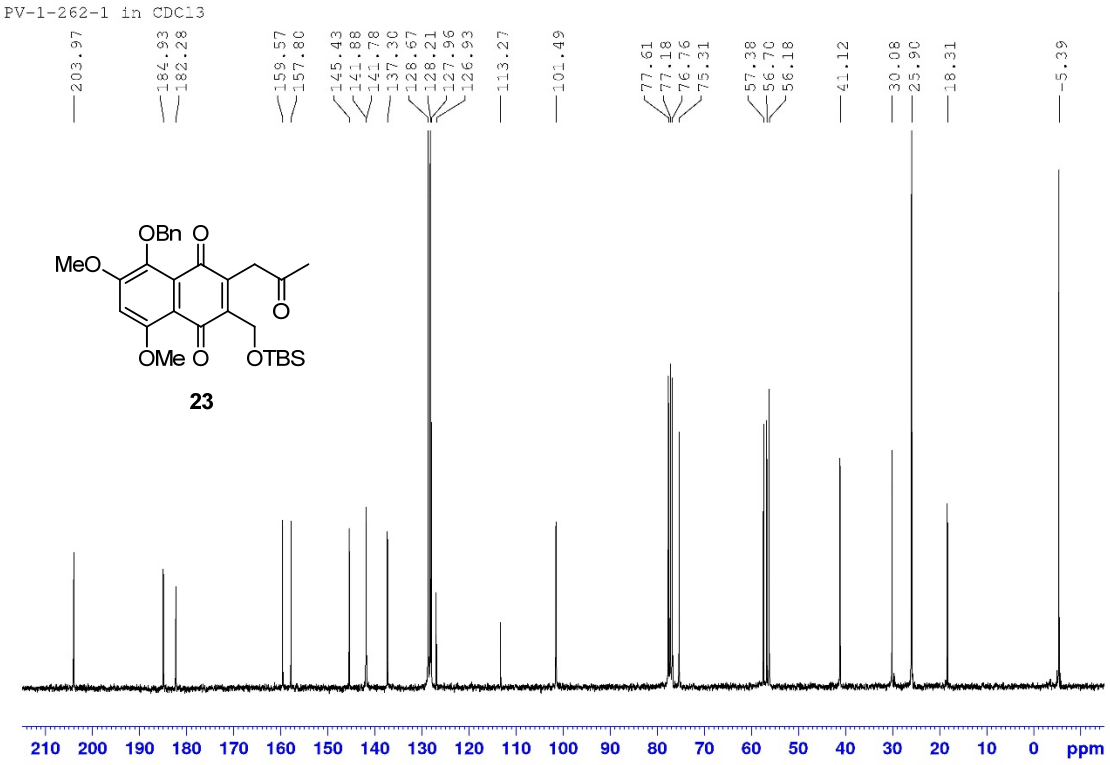
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of silyl ether **21**



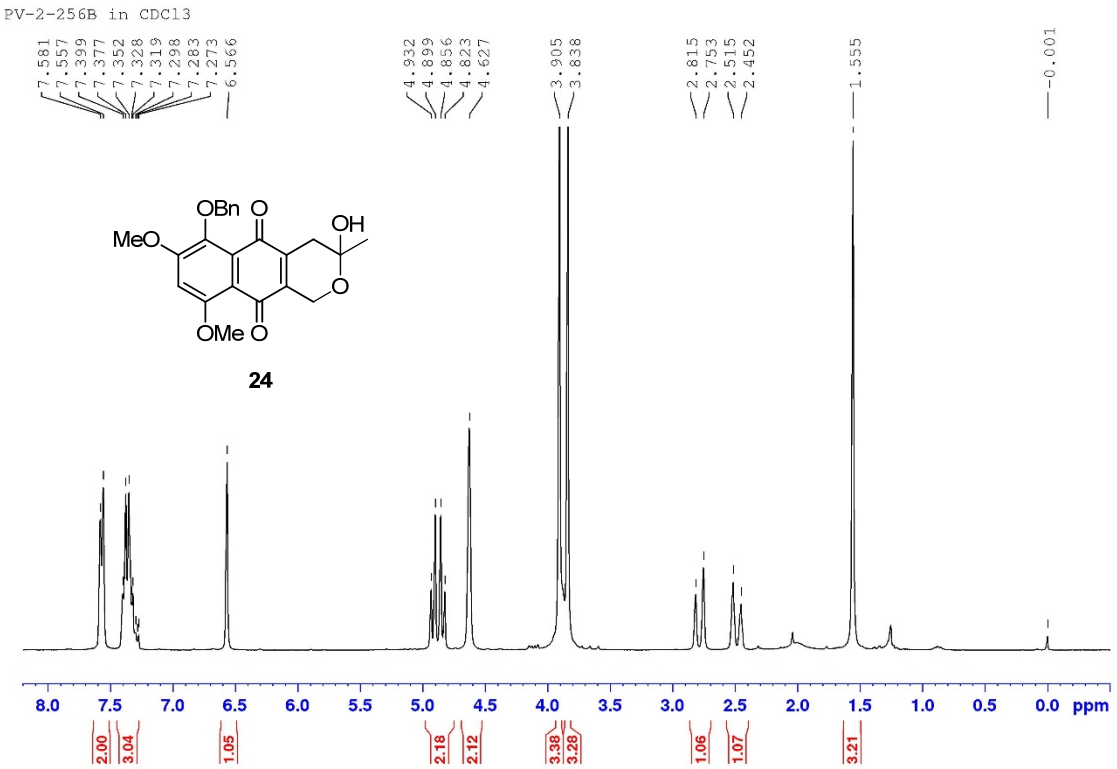
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of acetonylnaphthoquinone **23**



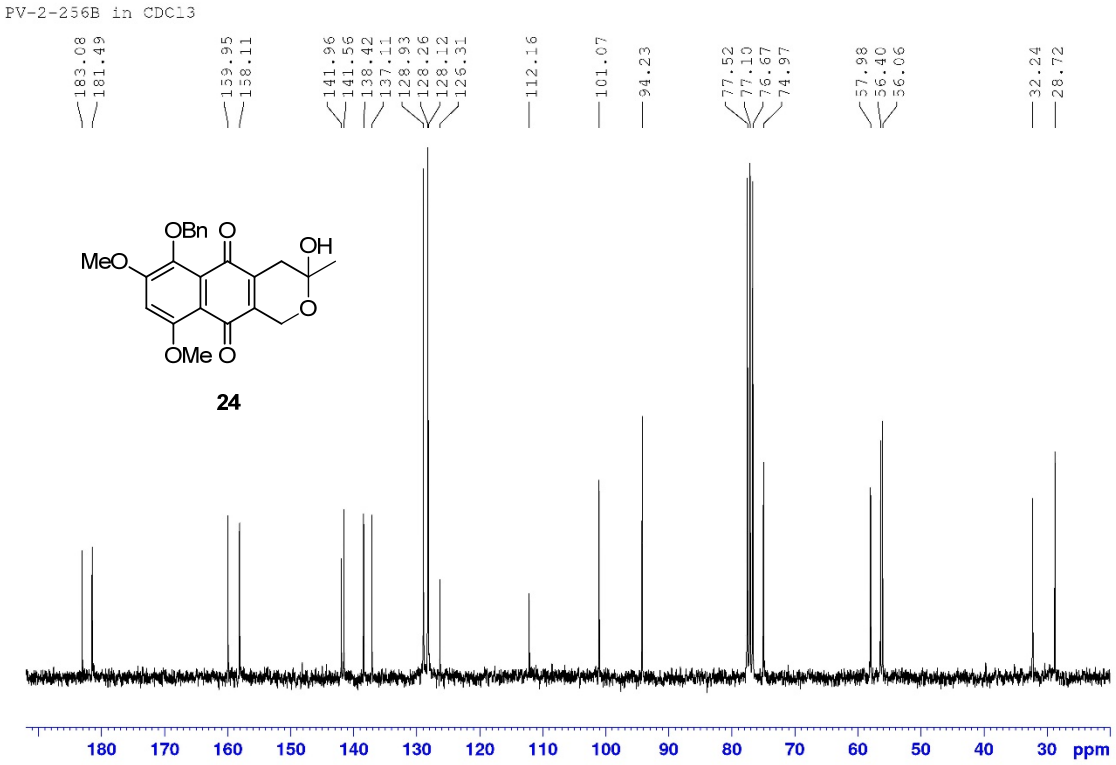
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of acetonylnaphthoquinone **23**



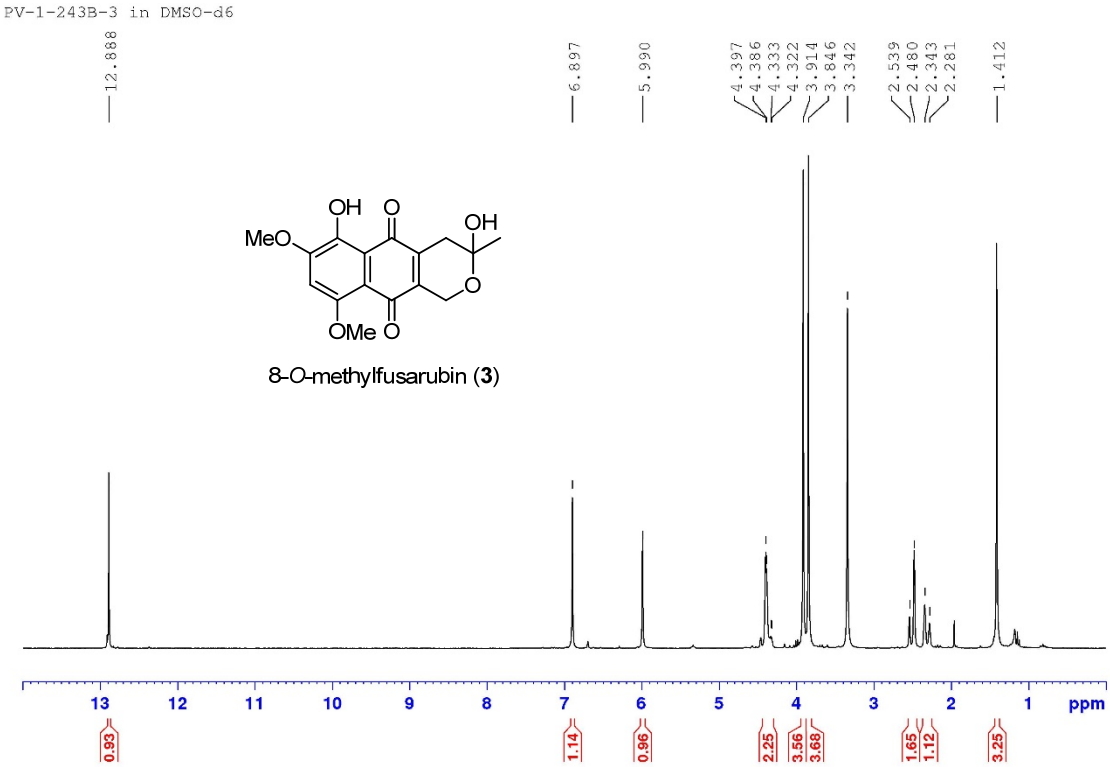
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of pyranonaphthoquinone **24**



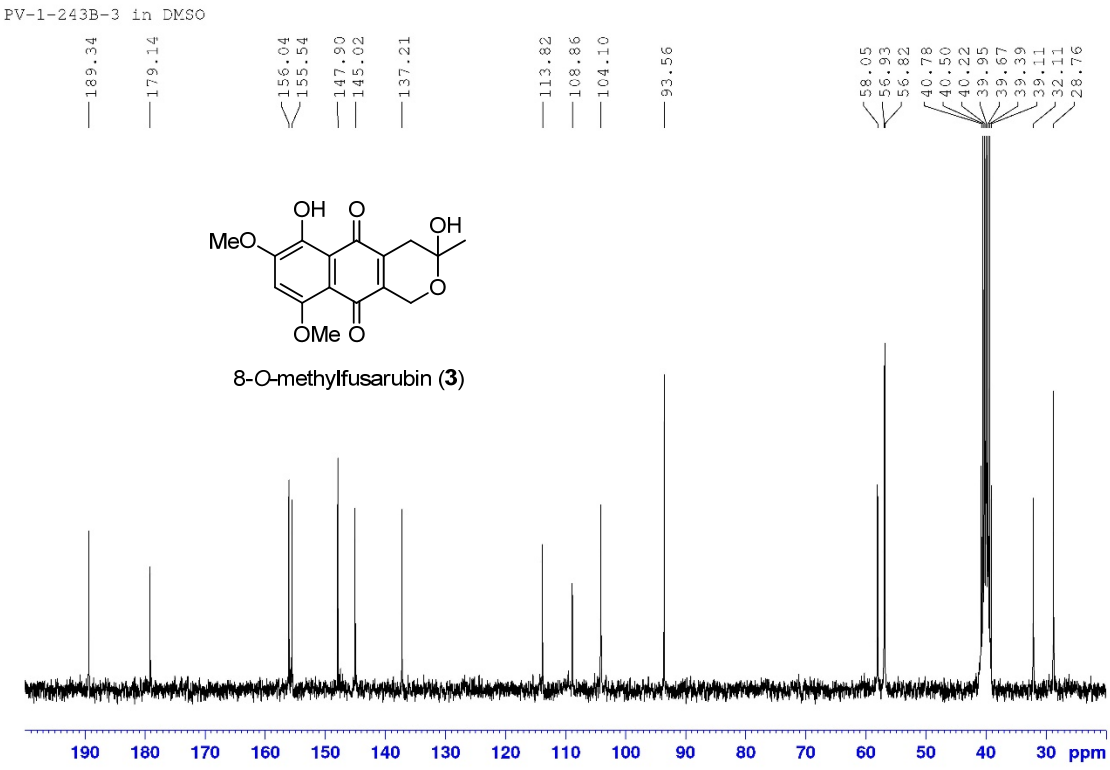
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of pyranonaphthoquinone **24**



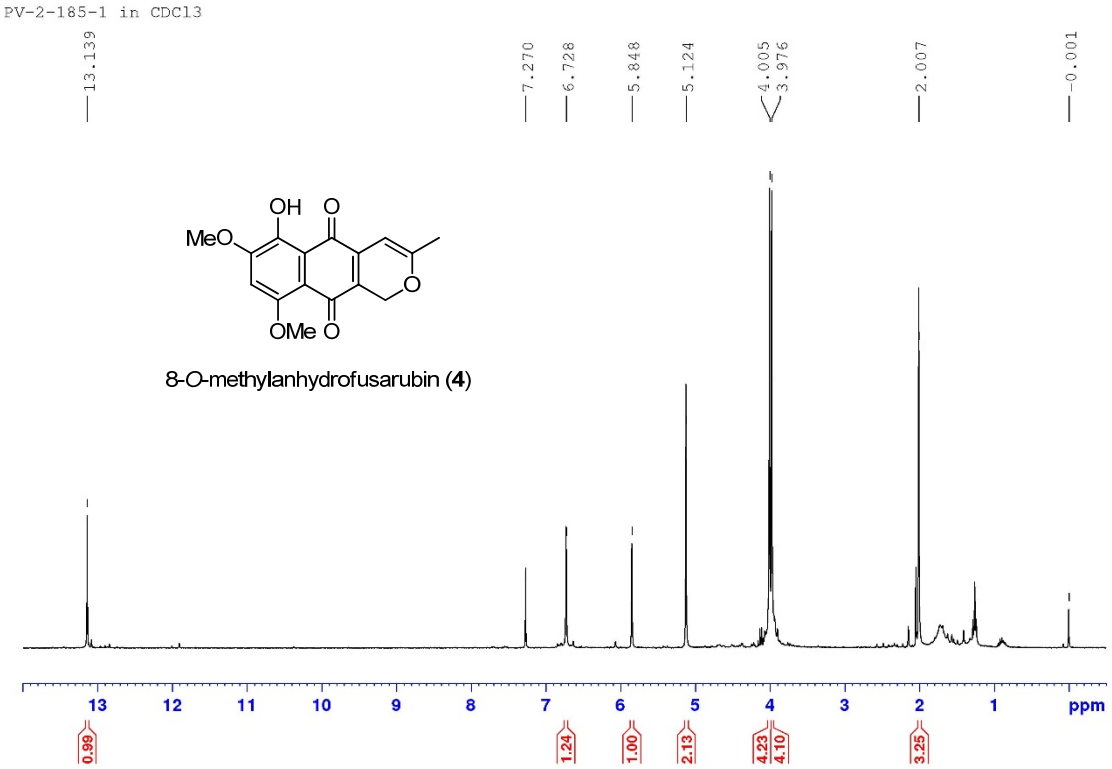
^{1}H NMR (300 MHz, DMSO-*d*$_6$) spectrum of 8-*O*-methylfusarubin (**3**)



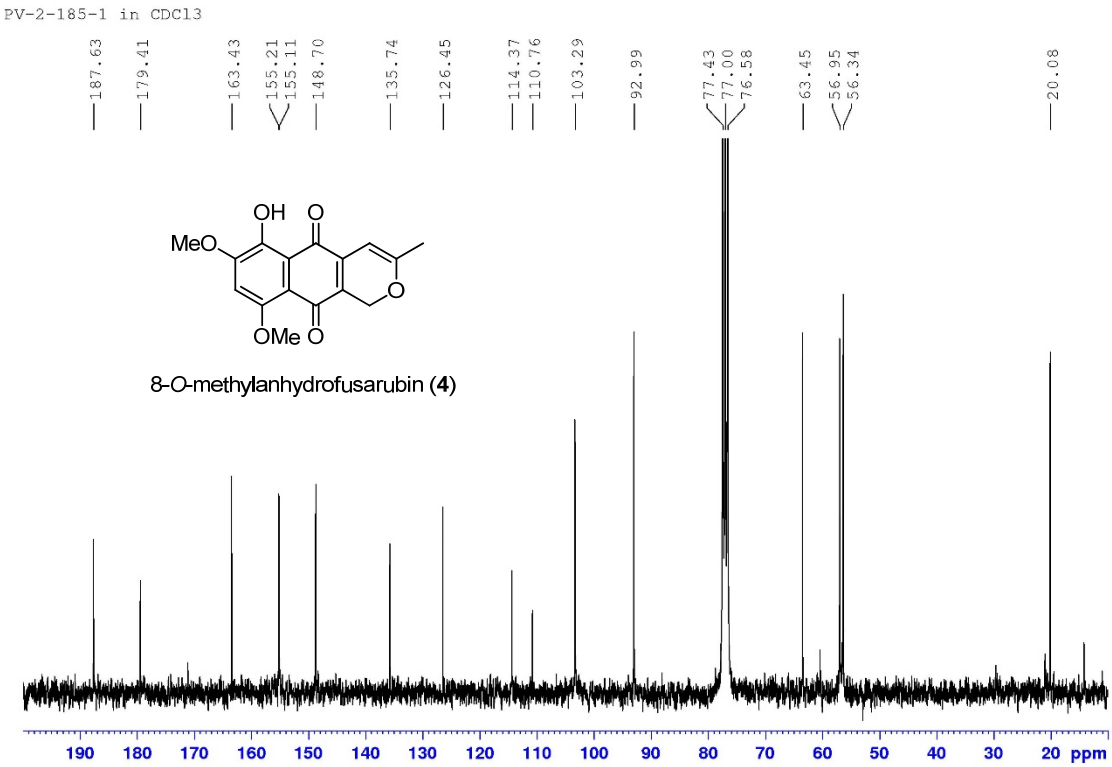
^{13}C NMR (75 MHz, DMSO-*d*$_6$) spectrum of 8-*O*-methylfusarubin (**3**)



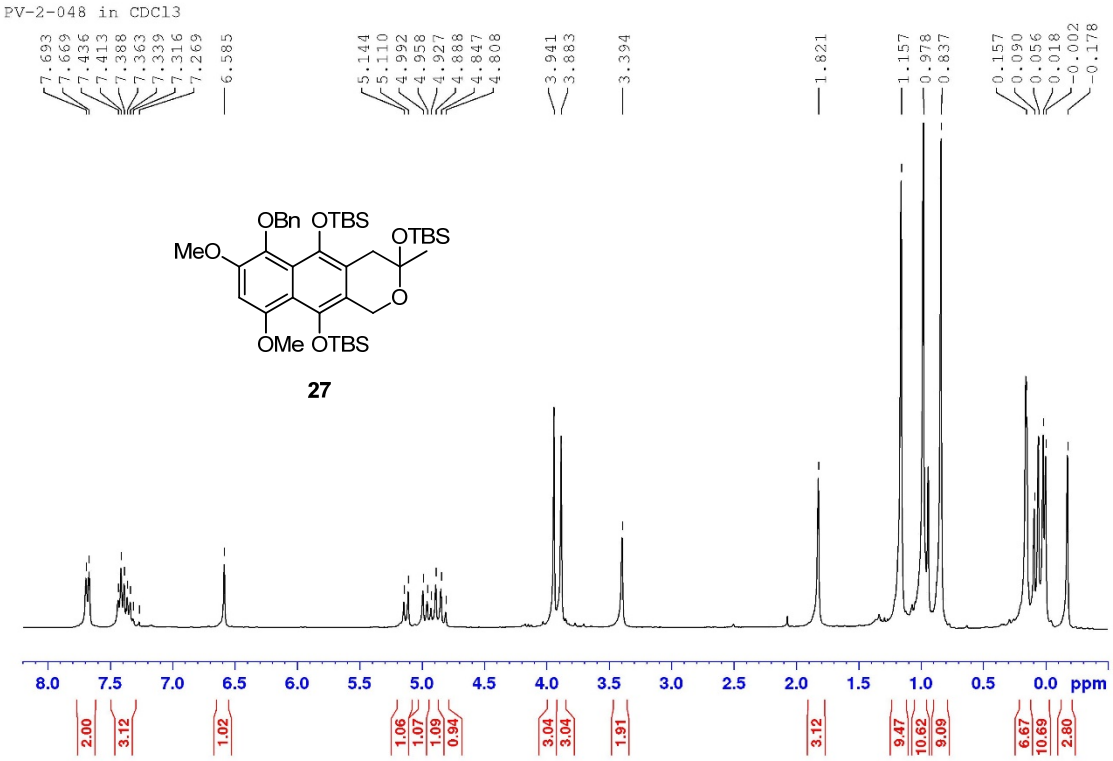
^{1}H NMR (300 MHz, $CDCl_3$) spectrum 8-*O*-methylanhydrofusarubin (**4**)



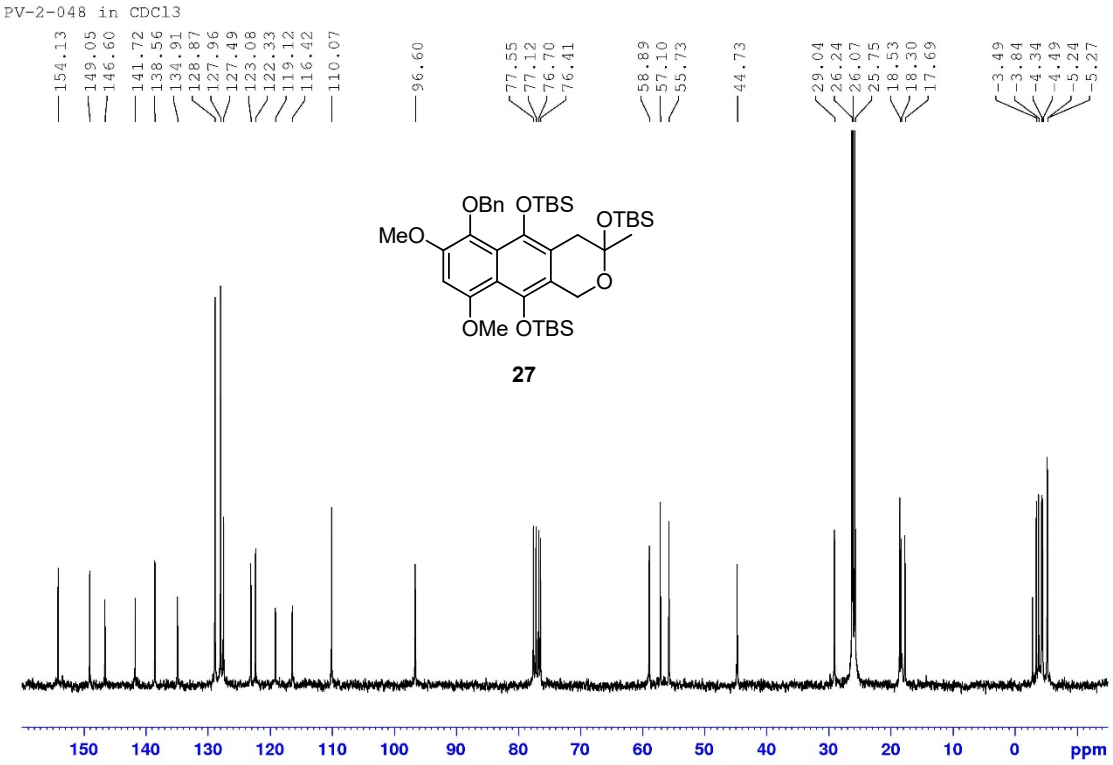
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of 8-*O*-methylanhydrofusarubin (**4**)



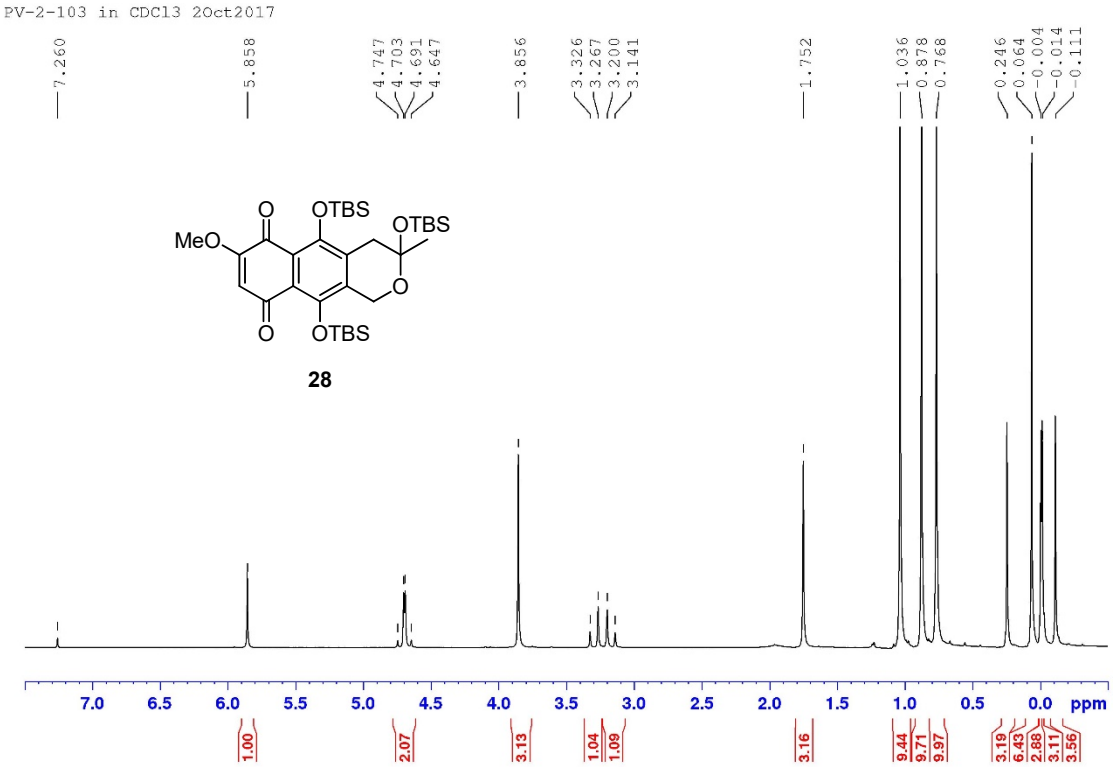
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of silyl ether **27**



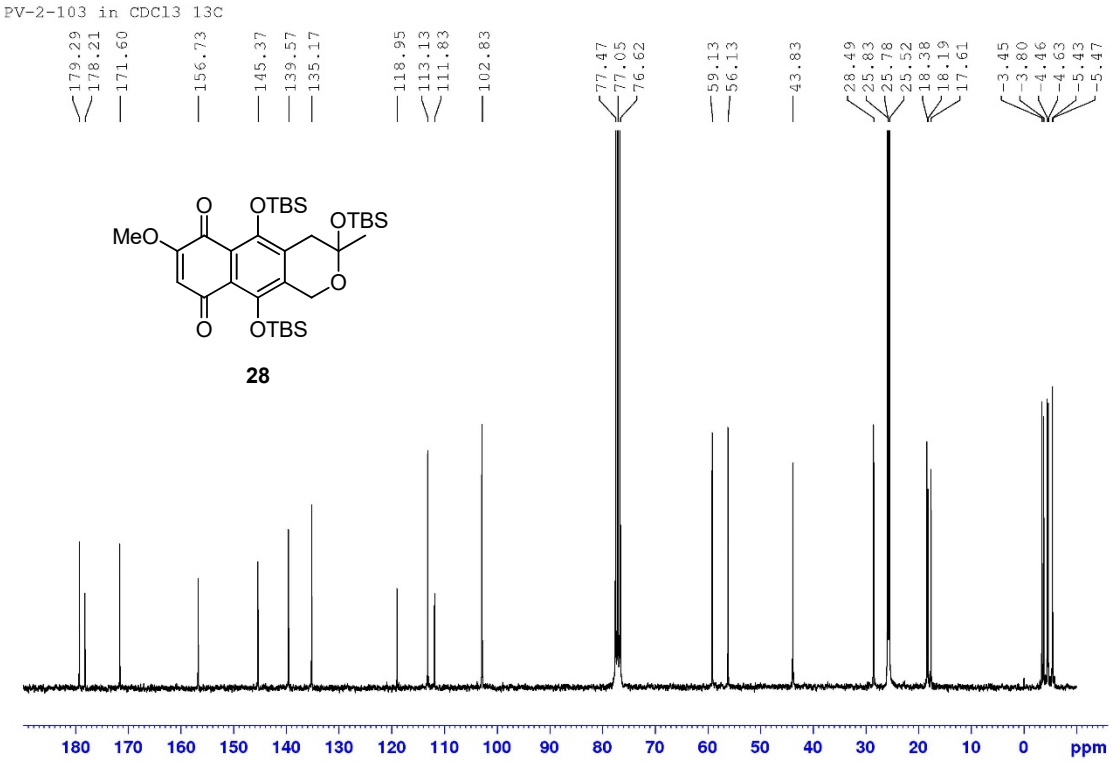
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of silyl ether **27**



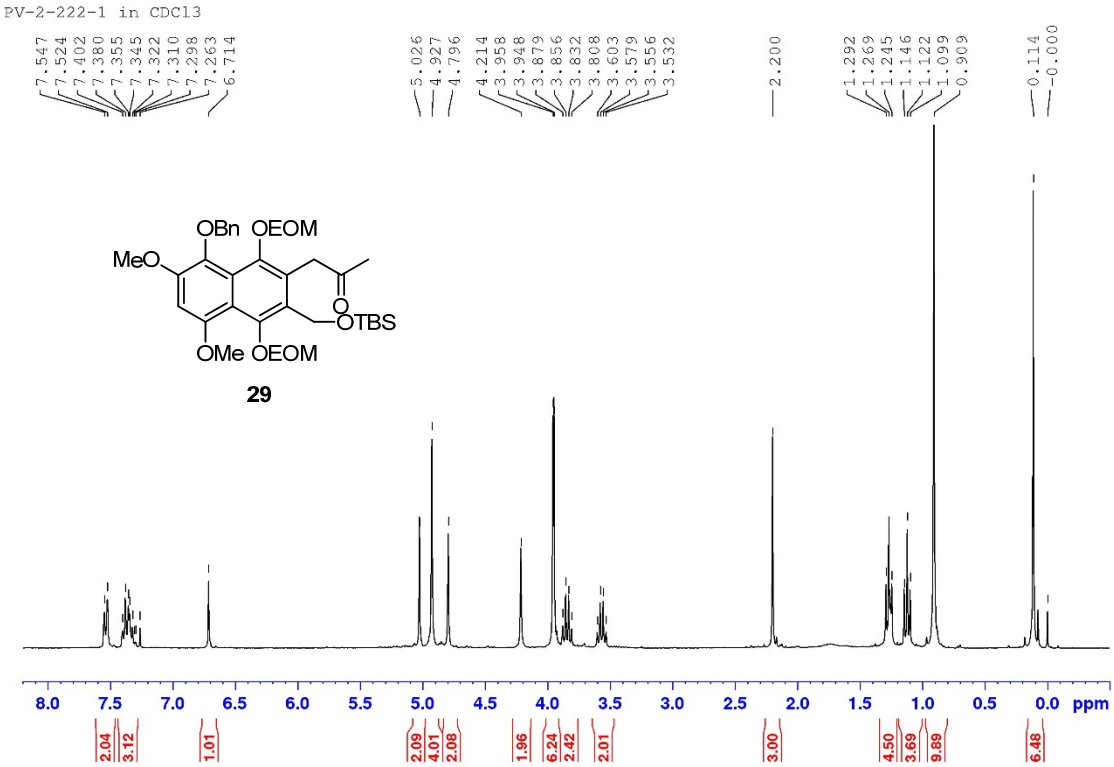
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthoquinone **28**



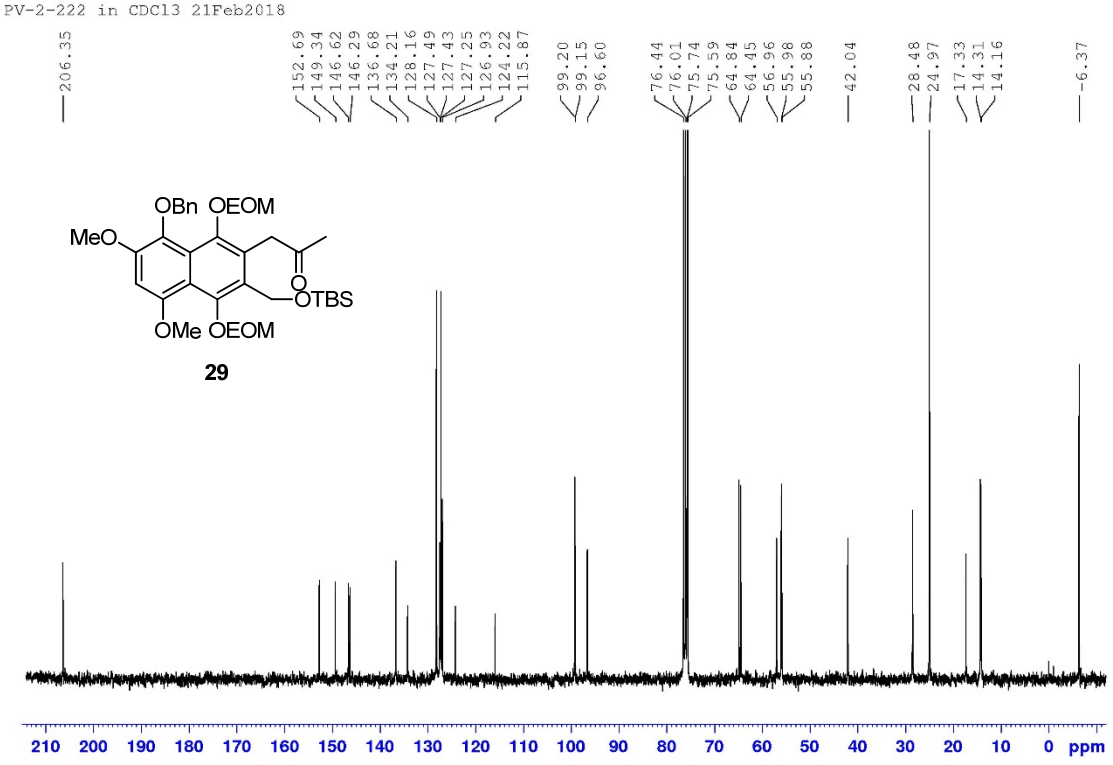
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthoquinone **28**



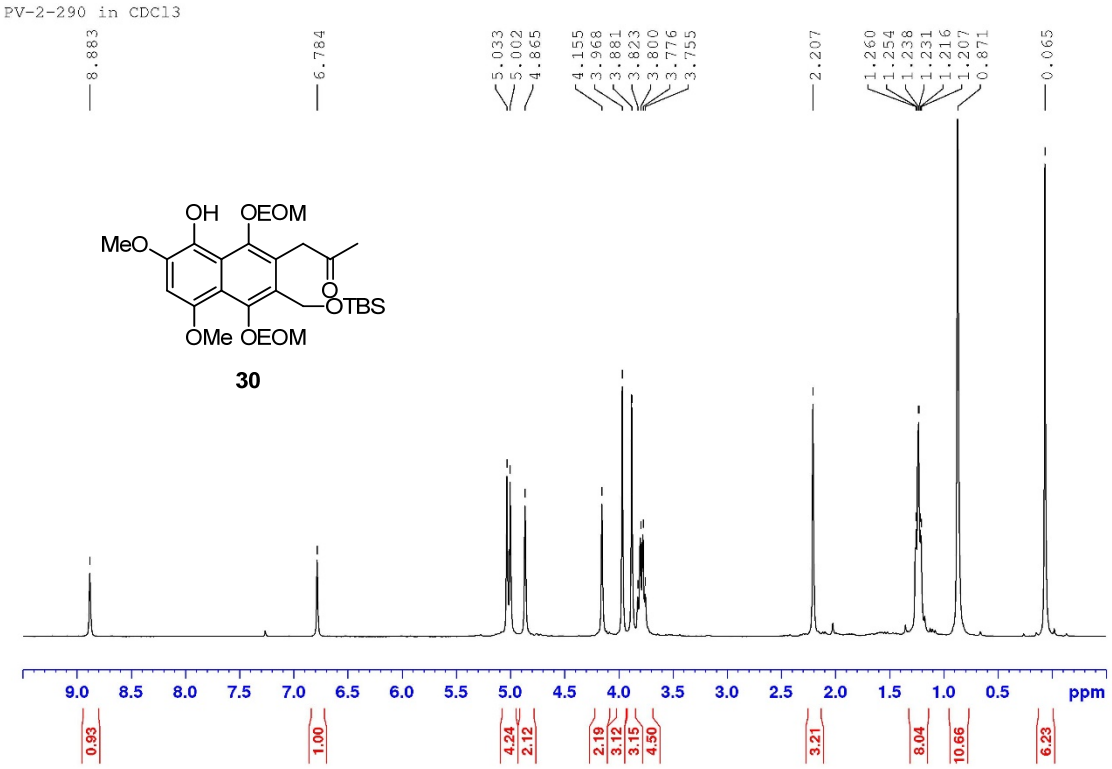
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of EOM ether **29**



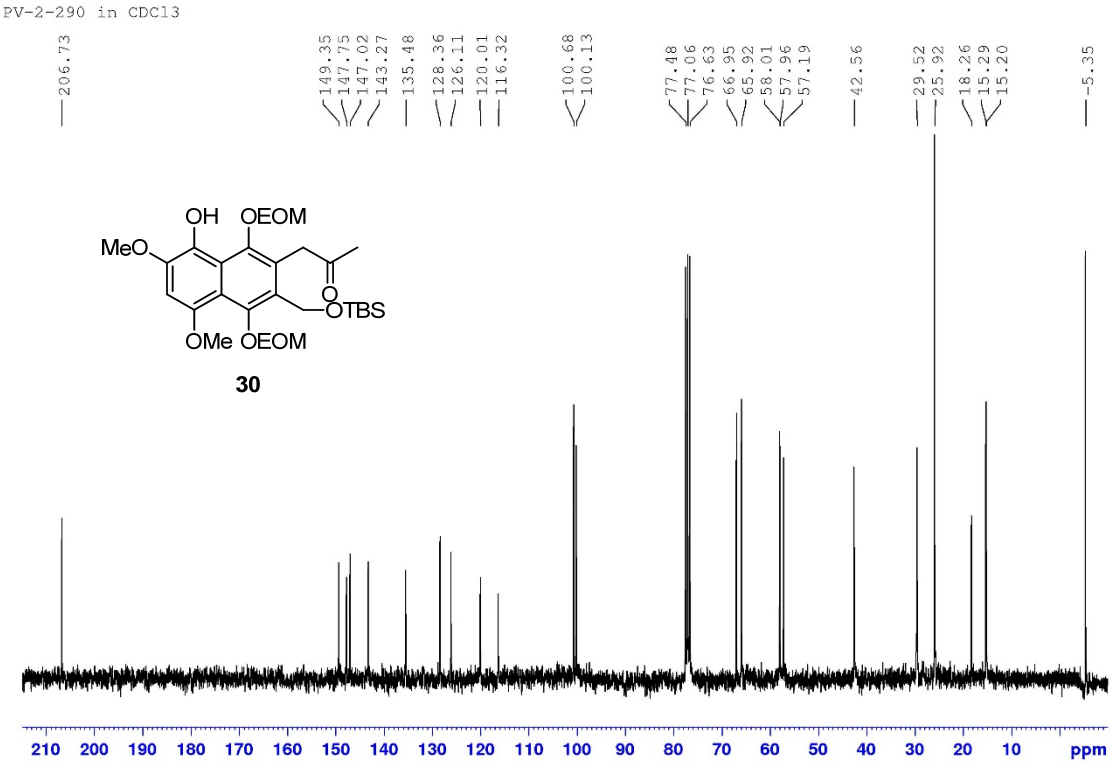
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of EOM ether **29**



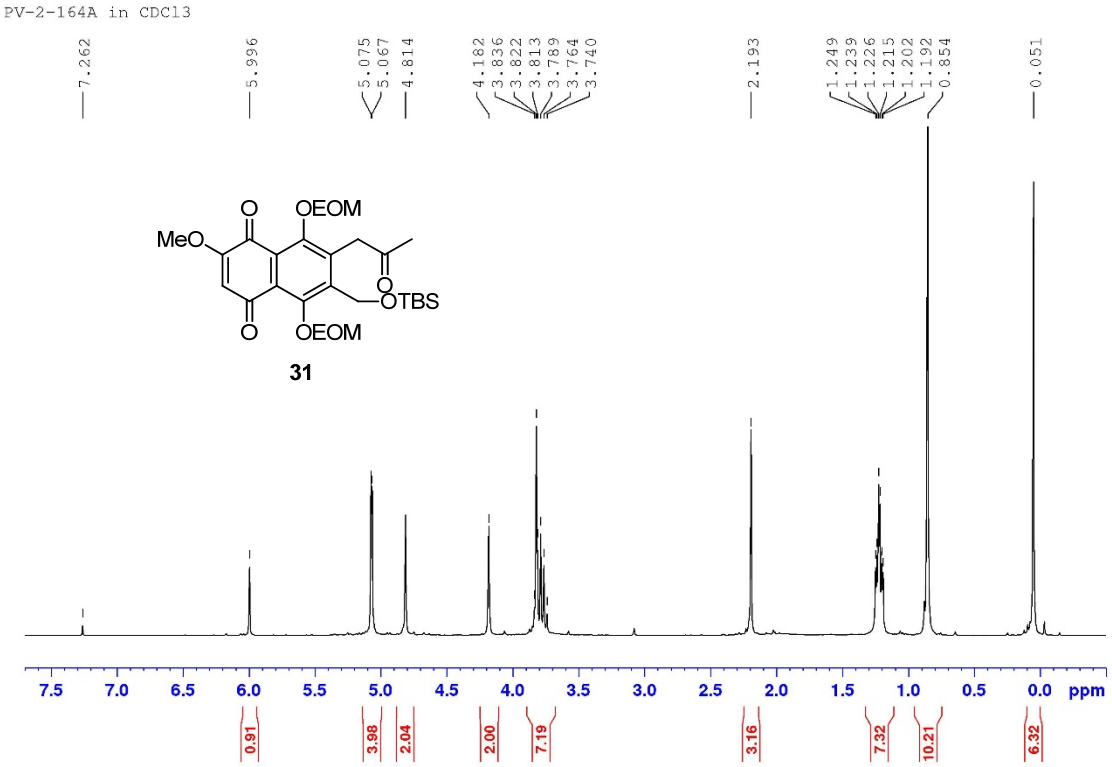
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of naphthol **30**



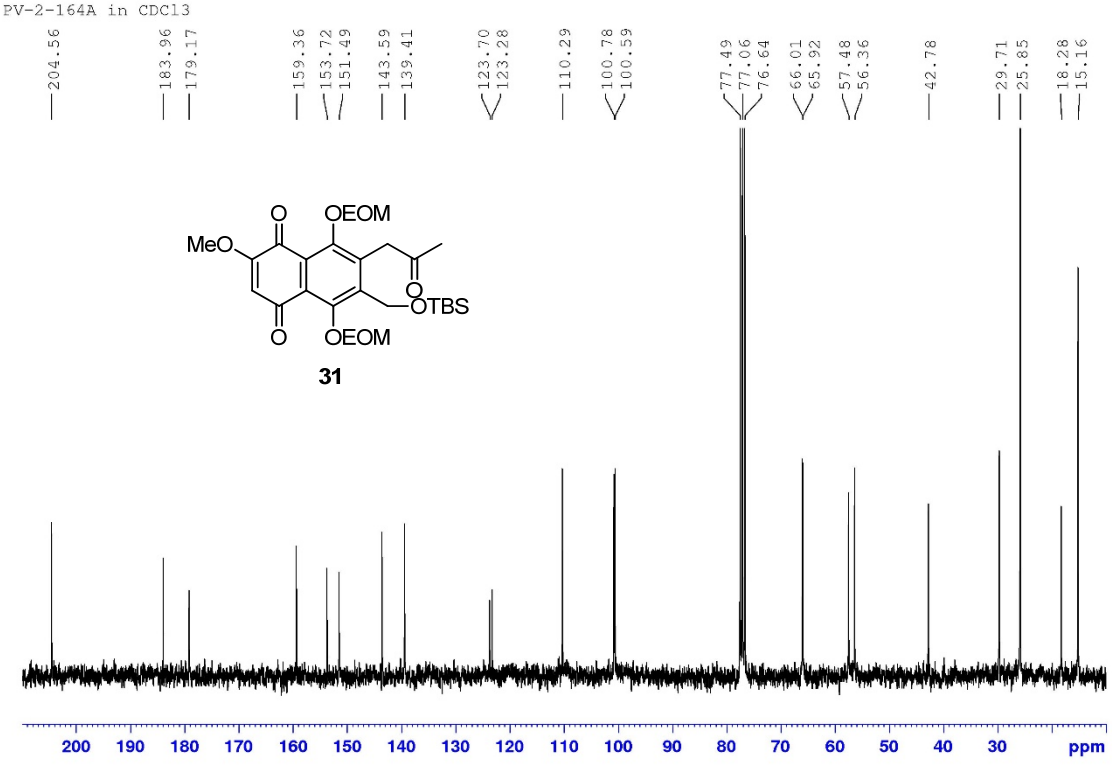
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of naphthol **30**



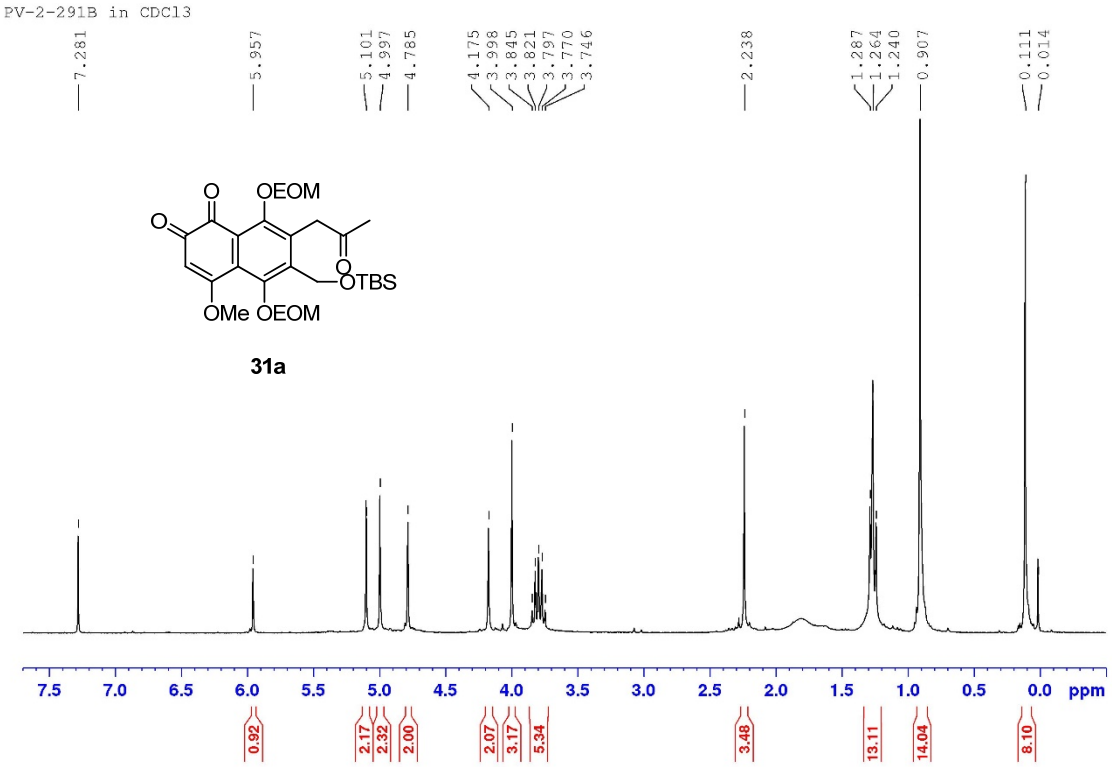
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of *para*-naphthoquinone **31**



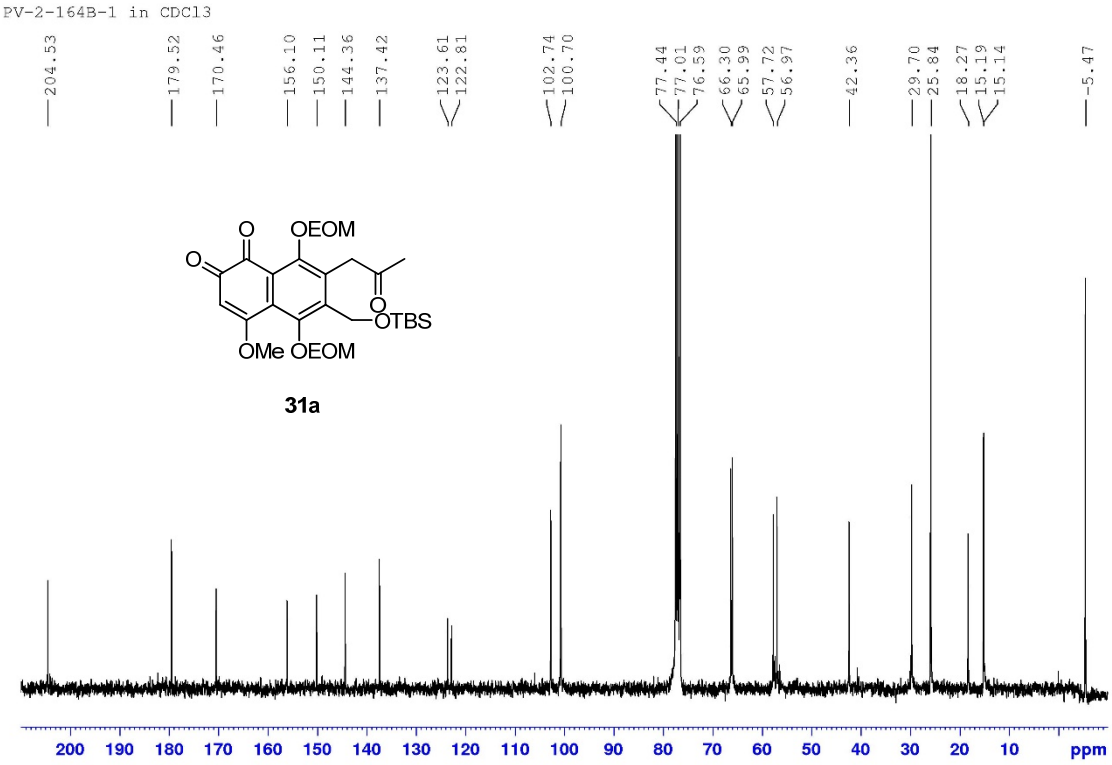
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of *para*-naphthoquinone **31**



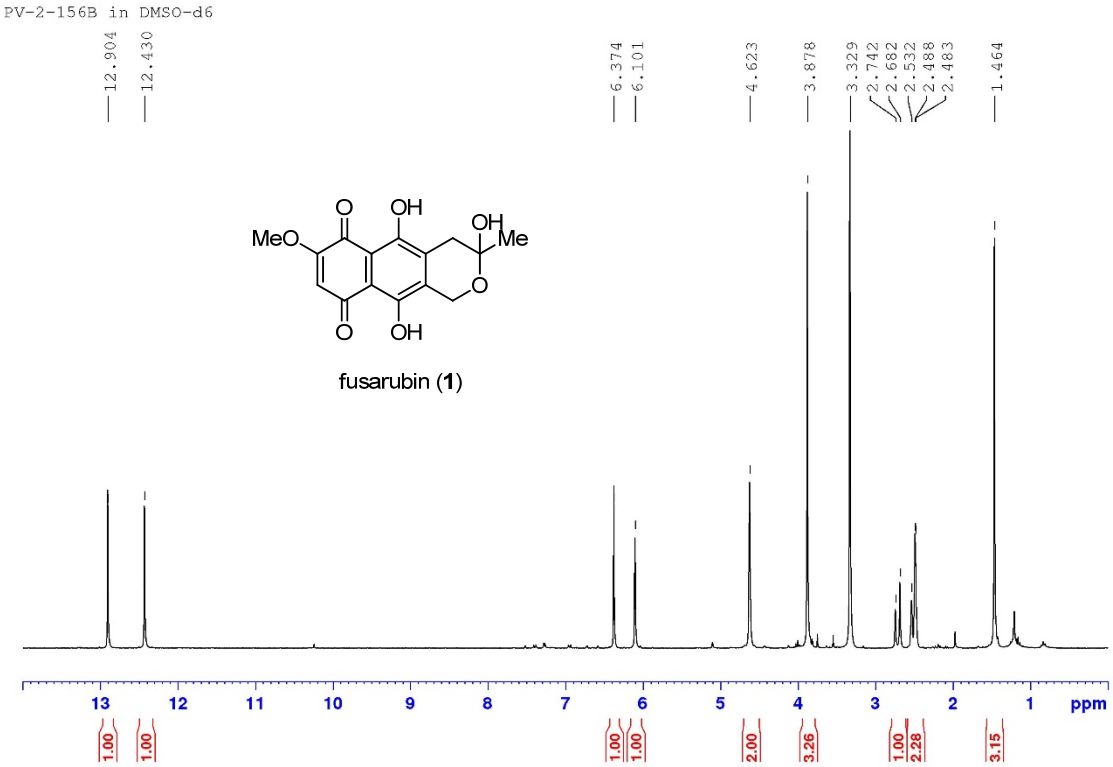
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of *ortho*-naphthoquinone **31a**



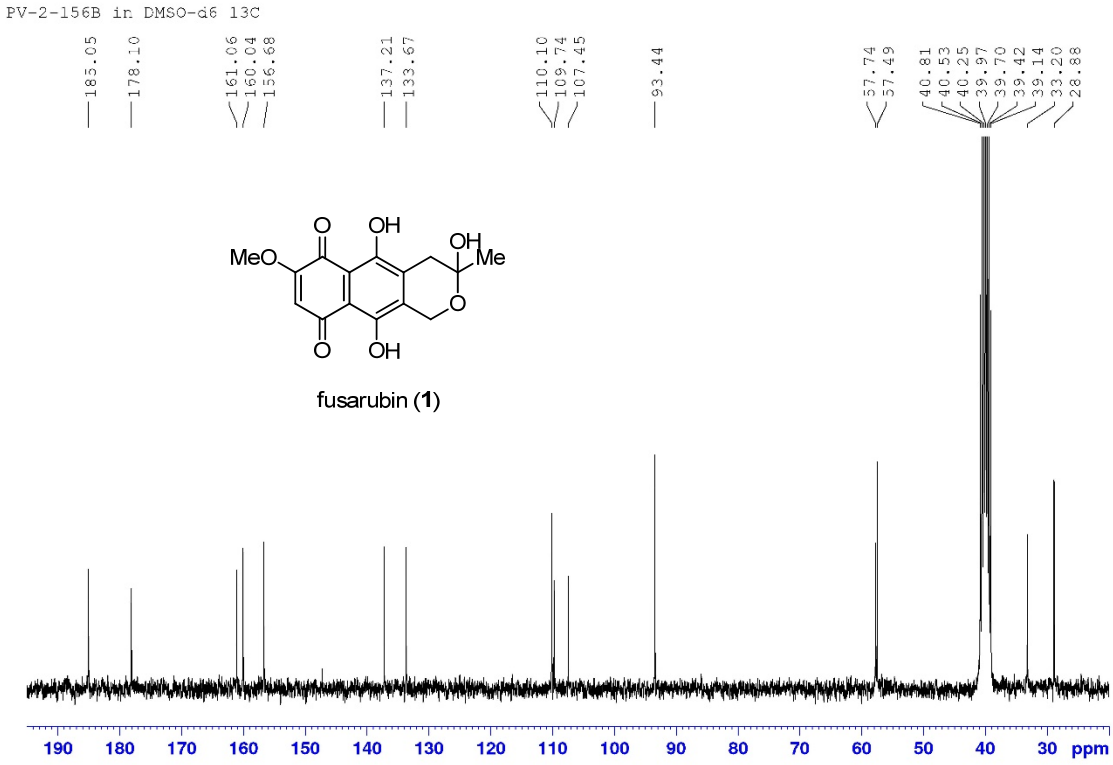
^{13}C NMR (75 MHz, $CDCl_3$) spectrum of *ortho*-naphthoquinone **31a**



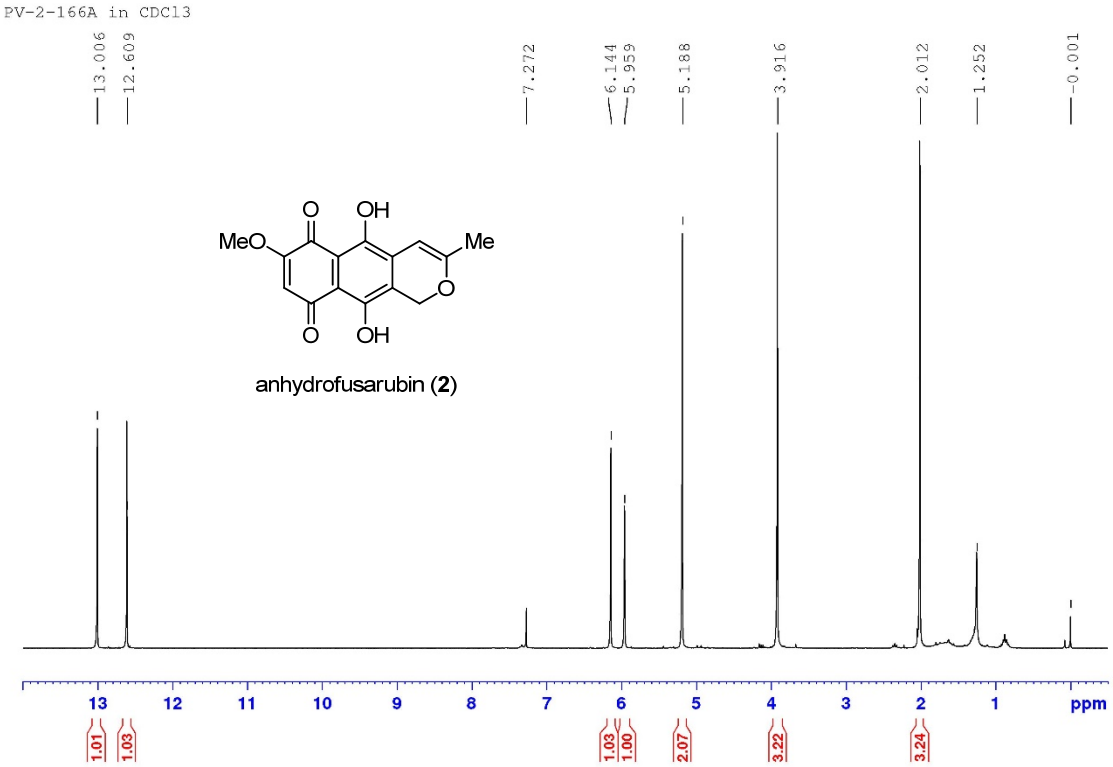
^{1}H NMR (300 MHz, DMSO-*d*$_6$) spectrum of fusarubin (**1**)



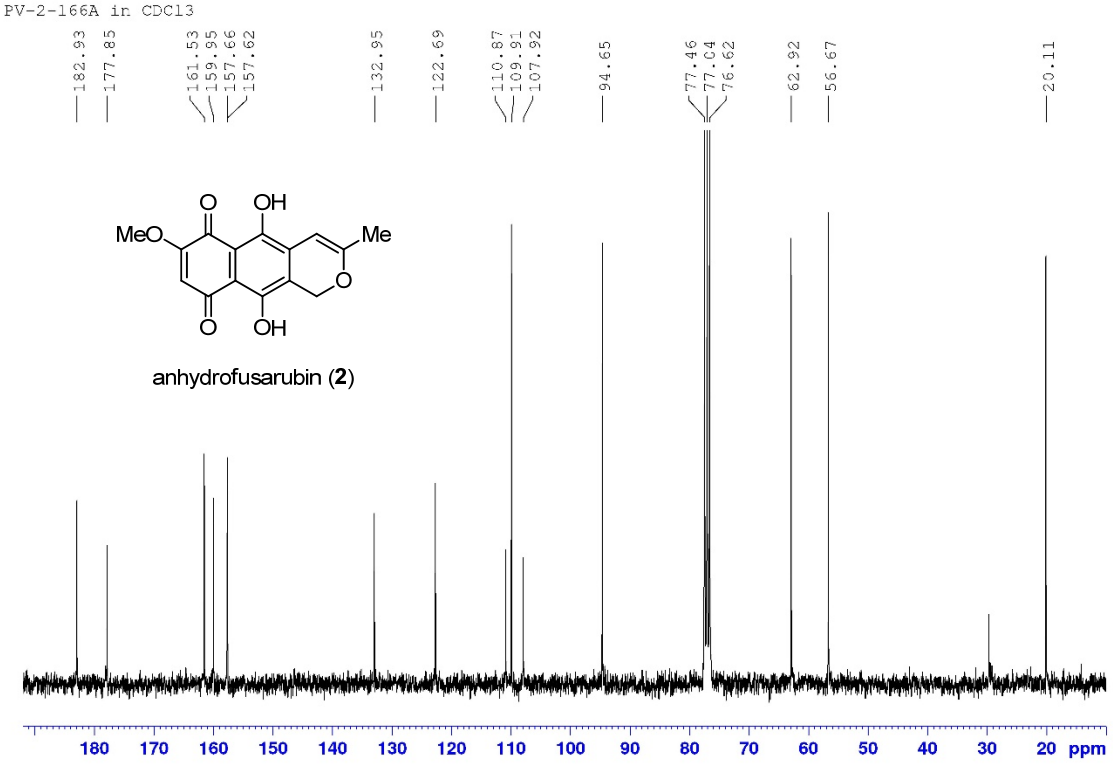
^{13}C NMR (75 MHz, DMSO-*d*$_6$) spectrum of fusarubin (**1**)



^{1}H NMR (300 MHz, $CDCl_3$) spectrum of anhydrofusarubin (**2**)



^{13}C NMR (75 MHz, $CDCl_3$) spectrum of anhydrofusarubin (**2**)



5. Cytotoxicity Assays

5.1 REMA assay against MCF-7 cells

Cytotoxicity assay against human breast adenocarcinoma (MCF-7) cells (ATCC HTB-22) was evaluated at the National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand using the resazurin microplate assay (REMA) reported by O'Brien and co-workers.[10] Doxorubicin and tamoxifen were used as positive controls. Cytotoxicity assay against African green monkey kidney fibroblast (Vero) cells was also tested at BIOTEC using REMA assay via a protocol disclosed by Hunt et al.[11] Ellipticine was used as a standard compound for cytotoxicity against Vero cells.

5.2 MTT assay against MCF-7 cells

Cytotoxicity assay against human breast adenocarcinoma (MCF-7) was tested at Excellent Center for Drug Discovery (ECDD), Mahidol University, Thailand. Human breast cancer MCF-7 cells were seeded at 1 x 10^4 cells per well on 96-well plates and cultured for 24 h in DMEM (Dulbecco's Modified Eagle Medium) high glucose supplemented with 10% FBS and 1% penicillin/streptomycin at 37 °C and 5% CO_2 atmosphere. Then, compounds were screened by high throughput liquid handling system and were added into cell plates at indicated concentrations and incubated for 24 h at 37 °C and 5% CO_2 atmosphere. After 24 h of incubation, the culture media was removed and replaced with serum-free media containing MTT. After 3 h incubation, the media was removed and DMSO was added before measuring MTT absorbance at 570 nm by Multi-Mode Microplate Reader (ENVISION, Perkin Elmer). Doxorubicin was used as a positive control.

5.3 MTT assay against C33A, HeLa, SiHa, HCT116, HepG2 and Vero cells

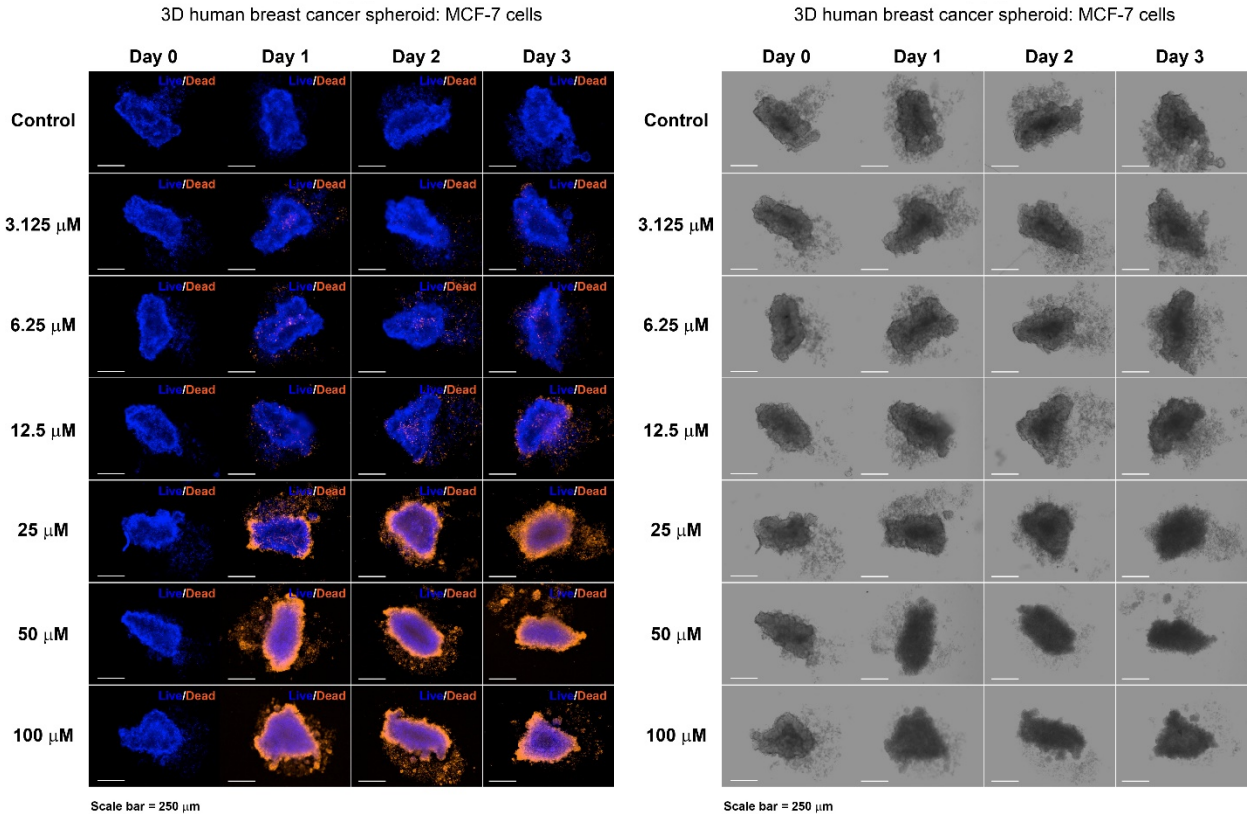
Cervical carcinoma SiHa, HeLa, and C33A cell lines were obtained from the American Type Culture Collection (ATCC, USA). Hepatoma HepG2 and colorectal carcinoma HCT116 cell lines were kindly provided by Prof. Dr. Mathurose Ponglikitmongkol (Mahidol University, Thailand) and the noncancer Vero cell line was kindly provided by Dr. Sittirak Roytrakul (The National Center for Genetic Engineering and Biotechnology, Thailand). All cell lines were maintained in Dulbecco's modified Eagle's (DMEM) medium supplemented with fetal bovine serum (10 %), penicillin (100 U/mL), and streptomycin (100 μg/mL) at 37 °C in a humidified atmosphere containing CO_2 (5%). All culture reagents were purchased from ThermoFisher Scientific (Gibco®, USA). Log-phase cells were seeded onto a 96-well culture plate (Costar®, Corning Incorporated, USA) at a density of 2.5 or 5 × 10^3 cells/well, and incubated overnight. After that, the cells were exposed to various concentrations of the compounds [0–200 μM; 0.2 % (v/v) DMSO]. After 72 h of incubation, cell viability was determined by an MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; Applichem, Germany] assay as described previously.[12] Each experiment was carried out in triplicate. Dataare expressed in terms of % cell viability and IC50 values (the concentration needed for 50 % cell growth inhibition) relative to untreated cells [0.2 % (v/v) DMSO] (mean ± standard deviation). Cisplatin and doxorubicin (Pfizer, Australia) were used as positive controls.

6. 3D Cancer Spheroid Models

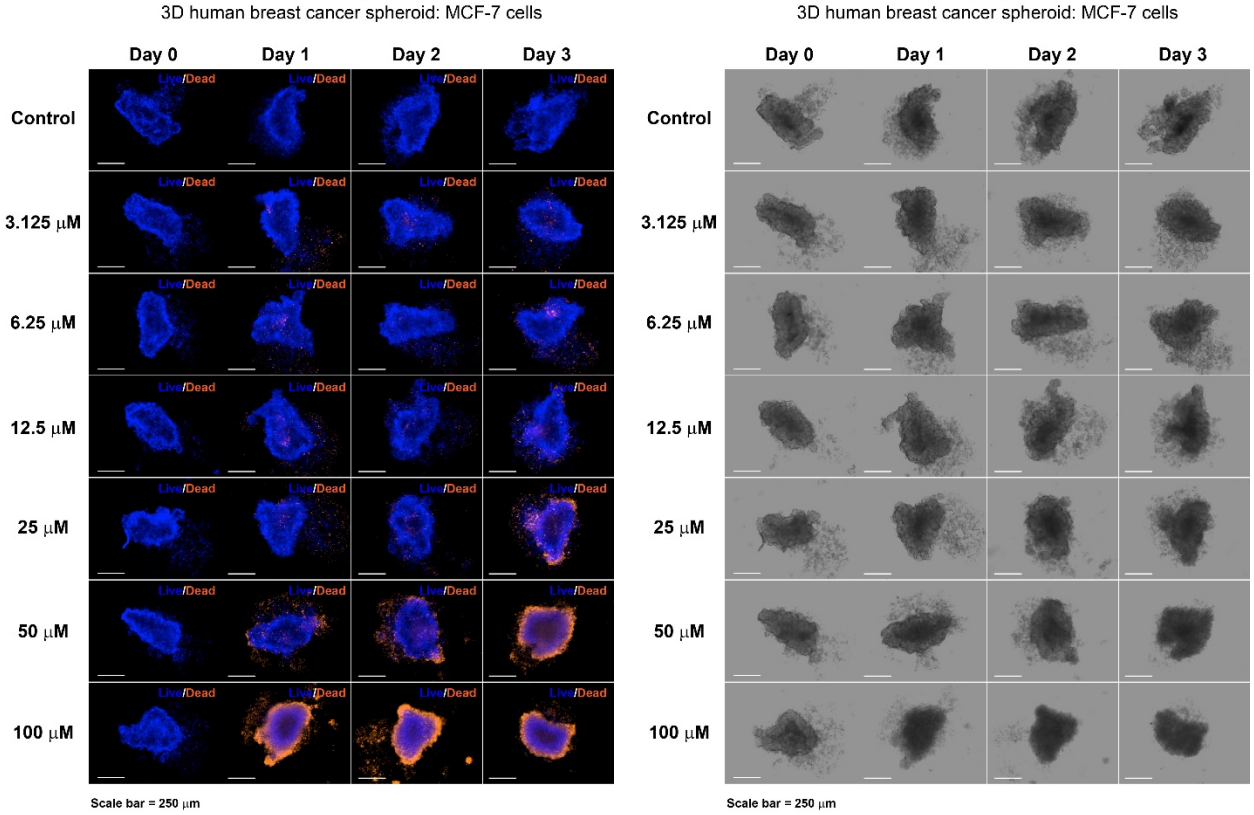
6.1 Protocol description

3D cancer spheroid models were performed at Excellent Center for Drug Discovery (ECDD), Mahidol University, Thailand. Human breast cancer MCF-7 cells were seeded at 2 x 10^4 cells per well on ULA 96-well plates and cultured by DMEM (Dulbecco's Modified Eagle Medium) high glucose supplemented with 10% FBS and 1% penicillin/streptomycin. Cells were incubated in an atmosphere of 37 °C and 5% CO_2 for 3 days in order to form 3D spheroid. After 3 days of incubation, compounds were screened using high throughput liquid handing system. Compounds at indicated concentrations were added and incubated for 24 h, 48 h or 72 h at 37 °C and 5% CO_2. Detection of live cells by Hoechst 33342 staining and dead cells by Ethidium homodimer in 3D breast spheroid was performed by Operetta (Perkin Elmer). The analysis process was performed by high-content imaging analysis software (Columbus, Perkin Elmer).

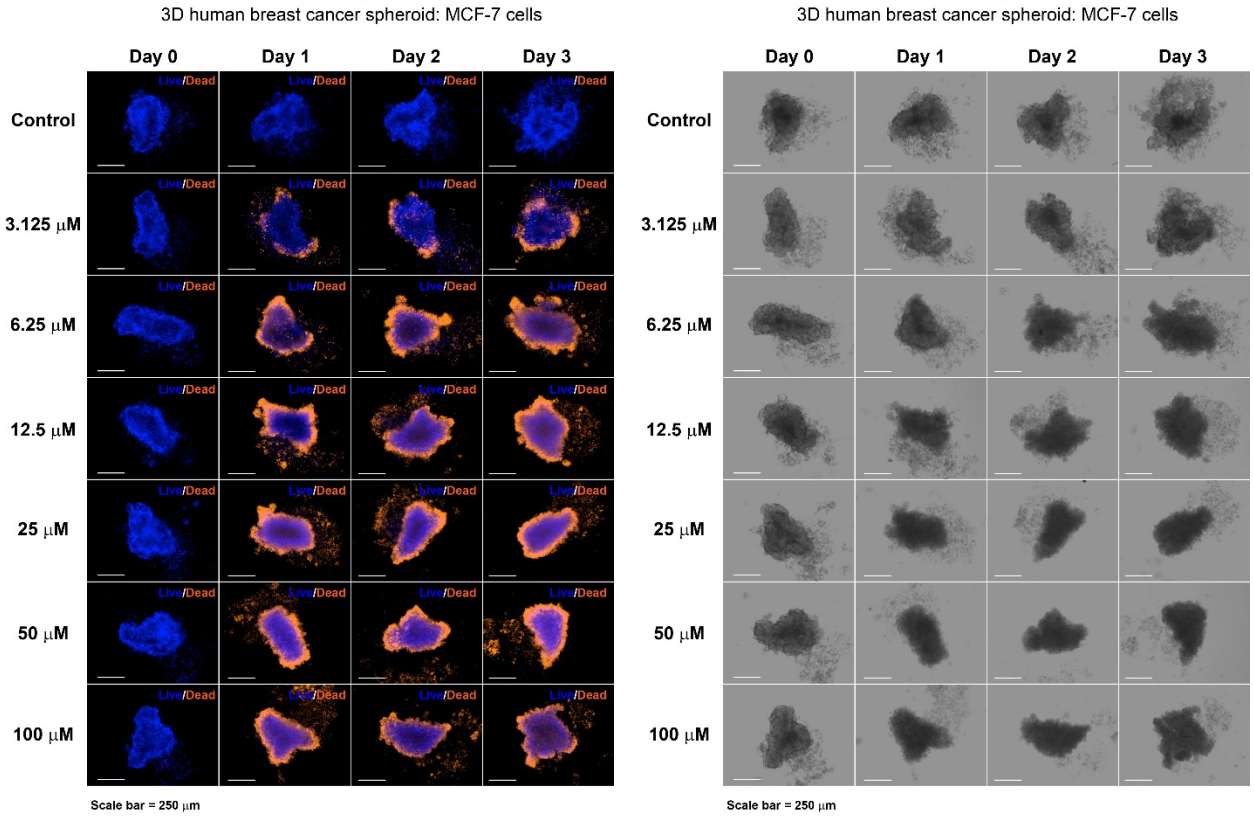
6.2 High-content imaging of fusarubin (**1**) on 3D MCF-7 breast cancer spheroid



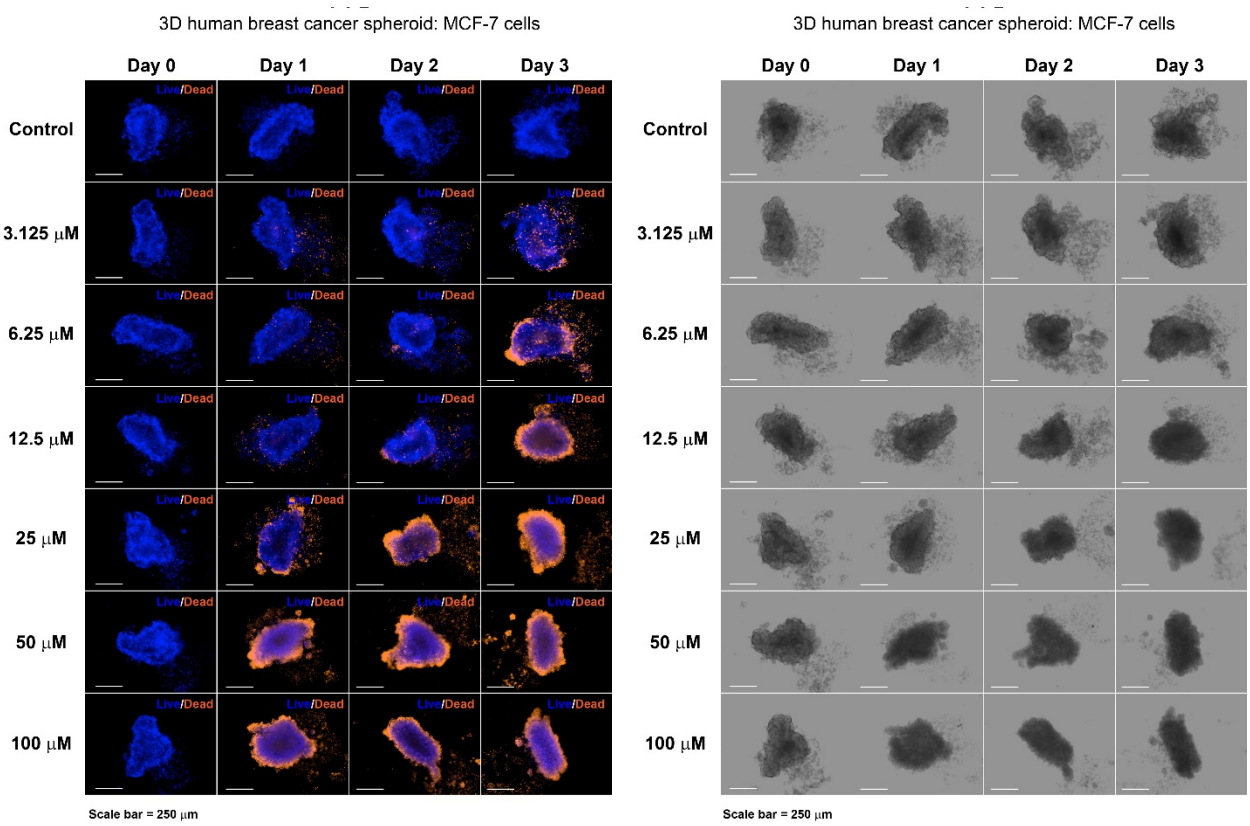
6.3 High-content imaging of anhydrofusarubin (**2**) on 3D MCF-7 breast cancer spheroid



6.4 High-content imaging of 8-*O*-methylfusarubin (**3**) on 3D MCF-7 breast cancer spheroid



6.5 High-content imaging of 8-*O*-methylanhydrofusarubin (**4**) on 3D MCF-7 breast cancer spheroid



7. References

1. R. G. F. Giles, N. van Eeden and I. R. Green, *Synth. Commun.*, 2006, **36**, 1695–1706.
2. X. Xie and M. C. Kozlowski, *Org. Lett.*, 2001, **3**, 2661–2663.
3. B. Das, K. Venkateswarlu, A. Majhi, V. Siddaiah and K. R. Reddy, *J. Mol. Catal. A: Chem.*, 2007, **267**, 30–33.
4. A. Yamashita, A. Toy and T. A. Scahill, *J. Org. Chem.*, 1989, **54**, 3625–3634.
5. E. Brötz, J. Herrmann, J. Wiese, H. Zinecker, A. Maier, G. Kelter, J. F. Imhoff, R. Müller and T. Paululat, *Eur. J. Org. Chem.*, 2014, 5318–5330.
6. N. S. Chowdhury, Md. H. Sohrab, Md. S. Rana, C. M. Hasan, S. Jamshidi and K. M. Rahman, *J. Nat. Prod.* 2017, **80**, 1173–1177.
7. Md. I. H. Khan, Md. H.Sohrab, S. R.Rony, F. S. Tareq, C. M. Hasan andMd. A. Mazid, *Toxicol. Rep.*, 2016, **3**, 861–865.
8. L. Studt, P. Wiemann, K.Kleigrewe, H. Humpfand B.Tudzynski, *Appl Environ. Microbiol.*, 2012, **78**, 4468–4480.
9. J. H. Tatum, R. A. Baker and R. E. Berry, *Phytochemistry*, 1985, **24**, 457–459.
10. J. O'Brien, I. Wilson, T. Orton and F. Pognan, *Eur. J. Biochem.*, 2000, **267**, 5421–5426.
11. L. Hunt, M. Jordan, M. De Jesus and F. M. Wurm, *Biotechnol. Bioeng.*, 1999, **65**, 201–205.

12. P. Wanichwatanadecha, S. Sirisrimangkorn, J. Kaewprag, M. Ponglikitmongkol, *J. Gen. Virol.*,2012, **93**, 1081–1092.