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Organic Redox Cascade Cyclization of 2-Alkynylquinones by Ascorbic Acid in Combination with Copper Catalyst and Its Application to Formal Synthesis of Liphagal

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Supplementary Information

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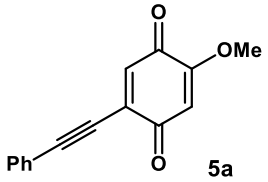
General. All moisture-sensitive reactions were performed in an oven-dried glassware under an argon atmosphere, unless otherwise stated. A hole screw-top glass test tube (ϕ13 × 100 mm) were purchased from Maruemu or Fischer Scientific. Reagents and solvents were used as received from commercial suppliers unless otherwise mentioned. Anhydrous THF, DMF, and MeCN were purchased from KANTO CHEMICAL Co., Ltd and were used as received. CH_2Cl_2 was freshly distilled over P_2O_5 prior to use. ^{1}H NMR spectra (400 MHz), ^{13}C NMR spectra (100 MHz) and ^{19}F NMR (376 MHz) were recorded on Bruker Unity 400 MHz spectrometers or Varian 400-MR ASW (400 MHz) in the specified solvents. Chemical shifts are reported as parts per million (ppm) relative to the residual solvent signal [chloroform-*d*: 7.26 ppm (^{1}H NMR), 77.16 ppm (^{13}C NMR)] as an internal standard. Resonance patterns are reported with the notations s (singlet), br (broad), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), ddd (doublet of doublet of doublets), dt (doublet of triplets), td (triplet of doublets), and m (multiplet). In addition, the notation br is used to indicate a broad signal. FTIR spectra were recorded for samples loaded as neat films on NaCl plates or samples finely pulverized into a KBr pellet using a Varian 2000 infrared spectrophotometer or Horiba FT-720 FT-IR spectrometer. High resolution mass spectra (HRMS) were recorded on JEOL JMS-600 using the specified technique. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. Flash column chromatography was carried out using E. Merck Kieselgel 60 (230−400 mesh) or Silica Gel 60 (spherical; 40-100 μm; KANTO CHEMICAL Co., Ltd.). Analytical thin layer chromatography (TLC) was performed using plates coated with Kieselgel 60F254 (Merck) or Silicagel 70 F_{254} TLC Plate-*Wako* (FUJIFILM Wako Pure Chemical Co., Ltd.), and compounds were visualized with UV light (254 nm) and stained with an anisaldehyde solution, a phosphomolybdic acid solution, a $KMnO_4$ solution, or iodine.

General protocol for the preparation of alkynylquinones 5a to 5i: Alkynylquinones **5a** to **5i** were synthesized by the cross coupling reaction of the known 6-iodo-2-methoxybenzoquinone with corresponding alkynes.[1]

To a stirred solution of alkynes (0.36 mmol) in DMF (3.6 mL) at room temperature were added 6-iodo-2-methoxybenzoquinone (79.3 mg, 0.30 mmol), K_2CO_3 (62.2 mg, 0.45 mmol), and $Pd(OAc)_2$ (3.4 mg, 0.015 mmol). The reaction was monitored by TLC. After the consumption of iodoquinone **2**, the mixture was filtered through a pad of Celite and washed with Et_2O. The filtrate was transferred to a separatory funnel where it was washed with H_2O. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by

flash silica gel column chromatography (EtOAc/n-hexane 1:6 v/v to 1:10 v/v) to provide alkynylquinones **5**.

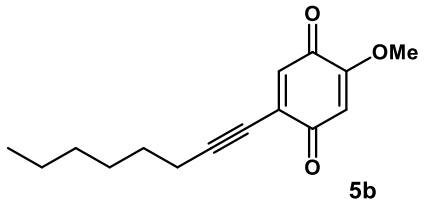
2-Methoxy-5-(phenylethynyl)cyclohexa-2,5-diene-1,4-dione (5a)



5a

84% (60.0 mg) orange solid; mp 158.8–160.7 °C; IR (neat) ν 3042, 2202, 1659, 1222, 914, 753, 684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.46–7.33 (m, 3H), 6.90 (s, 1H), 5.98 (s, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.14, 181.27, 159.13, 134.64, 133.13, 132.53, 130.23, 128.65, 121.60, 107.63, 105.30, 83.14, 56.53; HRMS (EI) calcd for $C_{15}H_{10}O_3$ $[M+2]^+$ 240.0775, found: 240.0786.

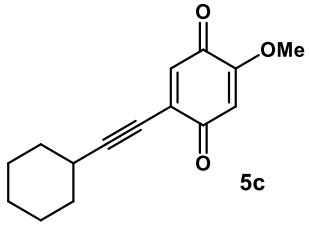
2-Methoxy-5-(oct-1-yn-1-yl)cyclohexa-2,5-diene-1,4-dione (5b)



5b

61% (45.0 mg) yellow solid; mp 78.7–80.1 °C; IR (neat) ν 3047, 2919, 2848, 2222, 1639, 1154, 917, 865 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.76 (s, 1H), 5.92 (s, 1H), 3.82 (s, 3H), 2.49 (t, *J* = 7.1 Hz, 2H), 1.61 (quintet, *J* =6.8 Hz, 2H), 1.46–1.37 (m, 2H), 1.36–1.25 (m, 4H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.58, 181.54, 158.98, 134.77, 133.75, 108.59, 107.54, 74.83, 56.48, 31.36, 28.69, 28.19, 22.61, 20.34, 14.14; HRMS (EI) calcd for $C_{15}H_{18}O_3$ $[M]^+$ 246.1256, found: 246.1249.

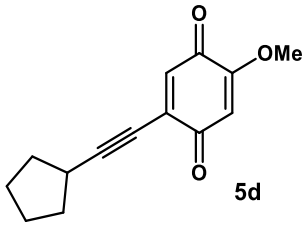
2-(Cyclohexylethynyl)-5-methoxycyclohexa-2,5-diene-1,4-dione (5c)



5c

52% (38.5 mg) orange solid; mp 99.2–101.1 ºC; IR (neat) ν 2918, 2848, 1617, 1444, 1199, 1166, 713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.75 (s, 1H), 5.91 (s, 1H), 3.81 (s, 3H), 2.68 (m, 1H), 1.90–1.82 (m, 2H), 1.78–1.66 (m, 2H), 1.61–1.46 (m, 3H), 1.43–1.27 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.46, 181.54, 158.97, 134.63, 133.82, 112.26, 107.55, 74.92, 56.45, 32.08, 30.43, 25.84, 24.81; HRMS (EI) calcd for $C_{15}H_{16}O_3$ $[M]^+$ 244.1099, found: 244.1096.

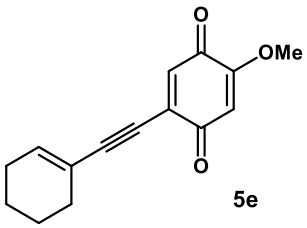
2-(Cyclopentylethynyl)-5-methoxycyclohexa-2,5-diene-1,4-dione (5d)



5d

46% (32.1 mg) orange solid; mp 125.3–127.0 ºC; IR (neat) ν 3046, 1638, 1607, 1217, 918, 866 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.75 (s, 1H), 5.92 (s, 1H), 3.82 (s, 3H), 2.91 (quintet, J = 7.4 Hz, 1H), 2.08–1.96 (m, 2H), 1.84–1.67 (m, 4H), 1.66–1.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.55, 181.58, 159.01, 134.59, 133.89, 112.80, 107.56, 74.47, 56.48, 33.71, 31.47, 25.35 (two carbons overlap); HRMS (EI) calcd for $C_{14}H_{14}O_3$ $[M]^+$ 230.0943, found: 230.0941.

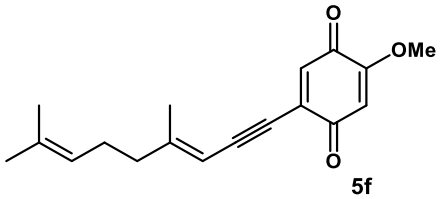
2-(Cyclohex-1-en-1-ylethynyl)-5-methoxycyclohexa-2,5-diene-1,4-dione (5e)



5e

57% (41.4 mg) orange solid; mp 166.1–168.8ºC; IR (neat) ν 3040, 2328, 1270, 1007, 843, 725, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.76 (s, 1H), 6.41 (m, 1H), 5.93 (s, 1H), 3.82 (s, 3H), 2.26–2.12 (m, 4H), 1.72–1.55 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.29, 181.39, 159.10, 140.58, 133.86, 133.55, 120.40, 108.06, 107.52, 81.24, 56.49, 28.68, 26.19, 22.14, 21.31; HRMS (EI) calcd for $C_{15}H_{14}O_3$ $[M]^+$ 242.0943, found: 242.0943.

(*E/Z*)-2-(4,8-Dimethylnona-3,7-dien-1-yn-1-yl)-5-methoxycyclohexa-2,5-diene-1,4-dione (5f)

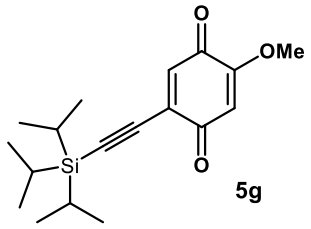


5f

E:Z = 2:1 mixtrue

60% (51.2 mg, *E/Z*=2:1) orange solid; mp 81.7–83.5 ºC; IR (neat) ν 3062, 2928, 2181, 1664, 1575, 1443, 1203, 994, 885 cm^{-1}; (*E*)-isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 6.75 (s, 1H), 5.93 (s, 1H, overlapped), 5.56 (s, 1H, overlapped), 5.09–5.02 (m, 1H), 3.82 (s, 3H, overlapped), 2.44 (t, *J* = 7.7 Hz, 1H), 2.24–2.10 (m, 3H), 2.03 (s, 3H), 1.67 (s, 3H, overlapped), 1.59 (s, 3H, overlapped); (*Z*)-isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 6.73 (s, 1H), 5.93 (s, 1H, overlapped), 5.56 (s, 1H, overlapped), 5.18–5.10 (m, 1H), 3.82 (s, 3H, overlapped), 2.24–2.10 (m, 4H), 1.89 (d, *J* = 1.2 Hz, 3H), 1.67 (s, 3H, overlapped), 1.59 (s, 3H, overlapped); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.42, 183.33, 181.36 (overlapped), 159.70, 159.57, 159.21, 159.18, 133.75, 133.71, 133.12, 132.69, 132.55, 123.43, 123.11, 107.46, 105.38, 105.17, 105.00, 104.77, 86.63, 86.32, 56.47 (overlapped), 39.26, 35.67, 26.62, 26.25, 25.81, 25.78, 23.48, 20.30, 17.84, 17.79; HRMS (EI) calcd for $C_{18}H_{20}O_3$ [M]+ 284.1412, found: 284.1411.

2-Methoxy-5-((triisopropylsilyl)ethynyl)cyclohexa-2,5-diene-1,4-dione (5g)

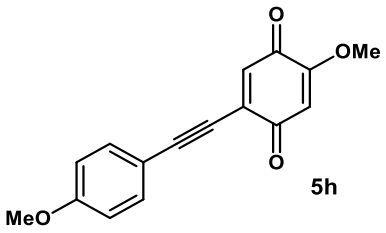


5g

69% (66.0 mg) brown solid; mp 92.7–95.4 ºC; IR (neat) ν 2958, 1663, 1223, 1182, 979, 866 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 1H), 5.91 (s, 1H), 3.82 (s, 3H), 1.21–1.06 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.91, 181.57, 158.94, 135.52, 132.86, 110.52, 107.65, 99.37, 56.51, 18.68, 11.29; HRMS (EI) calcd for $C_{18}H_{26}O_3Si$ $[M+2]^+$ 320.1797, found: 320.1807.

2-Methoxy-5-((4-methoxyphenyl)ethynyl)cyclohexa-2,5-diene-1,4-dione (5h) To a stirred solution of alkynes (0.66 mmol) in DMF (6.0 mL) at room temperature were added 6-iodo-2-methoxybenzoquinone (158.5 mg, 0.60 mmol), K_2CO_3 (124.4 mg, 0.9 mmol), and $Pd(OAc)_2$ (6.8 mg, 0.03 mmol). The reaction was monitored by TLC. After the consumption of iodoquinone **2**, the mixture was filtered through a pad of Celite and washed with Et_2O. The filtrate was transferred to a separatory funnel where it was washed with H_2O. The organic phase was separated, dried over

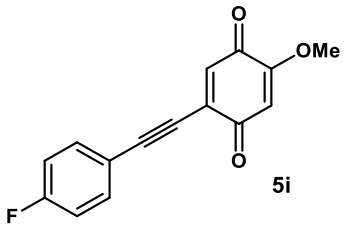
$MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (dichloromethane/n-hexane 1:1 v/v to 9:1 v/v) to provide alkynylquinones **5h**.



5h

86% (4138.4mg) red solid; mp 176.9-177.7 °C; IR (neat) ν 2927, 2842, 2194, 1658, 1569, 1253, 1199, 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.8 Hz, 2H), 7.05 (s, 2H), 6.98–6.94 (m, 2H), 6.77 (s, 1H), 5.53 (s, 1H), 3.95 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 155.5, 149.1, 145.0, 142.7, 125.9, 123.8, 122.3, 114.3, 104.5, 99.8, 94.6, 56.5, 55.4; HRMS (EI) calcd for $C_{16}H_{12}O_4$ $[M]^+$ 268.0736, found: 268.0736.

2-((4-fluorophenyl)ethynyl)-5-Methoxycyclohexa-2,5-diene-1,4-dione (5i) To a stirred solution of alkynes (0.22 mmol) in DMF (2 mL) at room temperature were added 6-iodo-2-methoxybenzoquinone (52.9 mg, 0.2 mmol), K_2CO_3 (41.5 mg, 0.3 mmol), and $Pd(OAc)_2$ (2.3 mg, 0.01 mmol). The reaction was monitored by TLC. After the consumption of iodoquinone **2**, the mixture was filtered through a pad of Celite and washed with Et_2O. The filtrate was transferred to a separatory funnel where it was washed with H_2O. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (dichloromethane/n-hexane 1:1 v/v to 9:1 v/v) to provide alkynylquinones **5i**.



5i

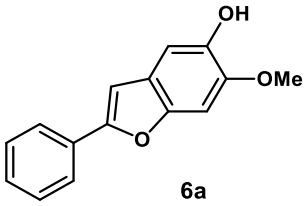
61% (31.1 mg) orange solid; mp 178.0-180.1 °C; IR (neat) ν 3043, 2927, 2202, 1658, 1573, 1203, 1087, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60–7.55 (m, 2H), 7.07 (t, J = 8.7 Hz, 2H), 6.88 (s, 1H), 5.98 (s, 1H), 3.84 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 181.2, 164.9, 162.4, 159.1,

134.7 (d, $J_{C\text{-}F}$ = 9.0 Hz), 134.6, 132.9, 117.7 (d, $J_{C\text{-}F}$ = 3.0 Hz), 116.15 (d, $J_{C\text{-}F}$ = 22.0 Hz), 107.2, 104.1, 82.9 (d, $J_{C\text{-}F}$ = 1.0 Hz), 56.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ = –107.4; HRMS (EI) calcd for $C_{15}H_9FO_3$ $[M]^+$ 256.0536, found: 256.0536.

Experimental procedures for entries in Table 1

A typical procedure (entry 9): A dry, hole screw-top test tube (Maruemu NN-13H; ϕ13 × 100 mm) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (26.7 mg, 0.112 mmol), $CuCl_2 \cdot 2H_2O$ (1.9 mg, 0.0111 mmol), ascorbic acid (23.7 mg, 0.135 mmol), Cs_2CO_3 (36.5 mg, 0.112 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 ºC in an oil bath for 32 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (22.4 mg, 83%) as a white solid.

6-Methoxy-2-phenylbenzofuran-5-ol (6a)



6a

83% (22.4 mg); white solid; mp 125.7–128.4 ºC; IR (neat) ν 3421, 1386, 1223, 1128, 1015, 868, 808, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84–7.76 (m, 2H), 7.47–7.39 (m, 2H), 7.32 (m, 1H), 7.09 (s, 1H), 7.07 (s, 1H), 6.92 (s, 1H), 5.60 (brs, 1H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.33, 149.36, 145.45, 142.85, 130.87, 128.85, 128.06, 124.45, 122.01, 104.66, 101.49, 94.62, 56.44; HRMS (EI) calcd for $C_{15}H_{12}O_3$ $[M]^+$ 240.0786, found: 240.0787. The chemical structure was unambiguously confirmed by X-ray crystallographic analysis as described in pages S19-S25.

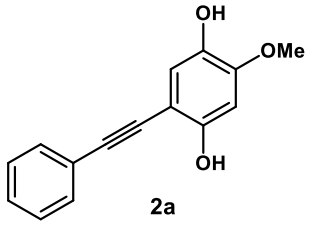
Entry 1: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (26.6 mg, 0.112 mmol), $PdCl_2$ (1.9 mg, 0.0107 mmol), ascorbic acid (18.9 mg, 0.107 mmol), Cs_2CO_3 (34.9 mg, 0.107 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 ºC in an oil bath for 15 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel

where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (1.0 mg, 4%) as a white solid.

Entry 2: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (25.5 mg, 0.108 mmol), $FeCl_2$ (1.4 mg, 0.0110 mmol), ascorbic acid (19.0 mg, 0.108 mmol), Cs_2CO_3 (35.1 mg, 0.108 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 20 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (1.2 mg, 5%) as a white solid.

Entry 3: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (26.6 mg, 0.112 mmol), $CoCl_2$ (1.5 mg, 0.0116 mmol), ascorbic acid (19.7 mg, 0.112 mmol), Cs_2CO_3 (36.4 mg, 0.112 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 20 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give alkynylhydroquinone **2a** (23.4 mg, 87%) as a pale brownish solid.

2-Methoxy-5-(phenylethynyl)benzene-1,4-diol (2a)



2a

87% (23.4 mg) pale brown solid; mp 125.3–127.9 °C; IR (neat) ν 3800, 3013, 2356, 2200, 1437, 1166, 755 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d*$_6$) δ 9.34 (s, 1H), 8.59 (s, 1H), 7.52–7.45 (m, 2H), 7.43–7.32 (m, 3H), 6.73 (s, 1H), 6.50 (s, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ 152.79,

150.28, 140.37, 132.14, 129.48, 129.14, 124.35, 117.77, 101.67, 100.82, 93.75, 85.90, 56.62; HRMS (EI) calcd for $C_{15}H_{12}O_3$ $[M]^+$ 240.0786, found: 240.0784.

Entry 4: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (26.2 mg, 0.110 mmol), $NiCl_2$ (1.4 mg, 0.0108 mmol), ascorbic acid (19.3 mg, 0.110 mmol), Cs_2CO_3 (35.8 mg, 0.110 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 20 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc-*n*-hexane-CH_2Cl_2 = 1:10:15 v/v) to give benzofuran **6a** (1.4 mg, 5%) as a white solid.

Entry 5: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (25.6 mg, 0.107 mmol), $ZnCl_2$ (1.5 mg, 0.0110 mmol), ascorbic acid (18.9 mg, 0.107 mmol), Cs_2CO_3 (35.0 mg, 0.107 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 20 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (1.0 mg, 4%) as a white solid.

Entry 6: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (25.2 mg, 0.106 mmol), $CuCl_2 \cdot 2H_2O$ (1.8 mg, 0.0106 mmol), ascorbic acid (18.6 mg, 0.106 mmol), Cs_2CO_3 (34.5 mg, 0.106 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 20.5 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (19.9 mg, 78%) as a white solid.

Entry 7: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (23.6 mg, 0.0991 mmol), $CuBr_2$ (2.2 mg, 0.00985 mmol), ascorbic acid (17.4 mg, 0.0988 mmol), Cs_2CO_3 (32.3 mg, 0.0991 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 ºC in an oil bath for 23 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (16.3 mg, 68%) as a white solid.

Entry 8: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (50.0 mg, 0.210 mmol), $CuCl_2 \cdot 2H_2O$ (1.8 mg, 0.0106 mmol), ascorbic acid (44.4 mg, 0.252 mmol), Cs_2CO_3 (68.4 mg, 0.210 mmol) and MeCN (2.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 ºC in an oil bath for 31 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (37.7 mg, 75%) as a white solid.

Entry 10 (without Cs_2CO_3): A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (10.9 mg, 0.0458 mmol), $CuCl_2 \cdot 2H_2O$ (0.8 mg, 0.00469 mmol), ascorbic acid (8.1 mg, 0.0460 mmol) and MeCN (0.5 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 ºC in an oil bath for 20 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc-n-hexane-CH_2Cl_2 = 1:10:15 v/v) to give benzofuran **6a** (2.1 mg, 19%) as a white solid.

Entry 11 (with 0.3 equiv of Cs_2CO_3): A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (24.2 mg, 0.102 mmol), $CuCl_2 \cdot 2H_2O$ (1.9 mg, 0.00997 mmol), ascorbic acid (21.5 mg, 0.122 mmol), Cs_2CO_3 (9.9 mg,

0.0304 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 33 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2-n-hexane = 3:1 v/v) to give benzofuran **6a** (13.9 mg, 57%) as a white solid and alkynylhydroquinone **2a** (5.8 mg, 24%) as a pale brownish solid.

Entry 12 (without metal catalyst/Cs_2CO_3): A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (22.1 mg, 0.0928 mmol), ascorbic acid (19.6 mg, 0.111 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 1 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give alkynylhydroquinone **2a** (5.8 mg, 24%) as a pale brownish solid.

Entry 13 (without metal catalyst): A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (4.7 mg, 0.0197 mmol), ascorbic acid (3.5 mg, 0.0199 mmol), Cs_2CO_3 (6.4 mg, 0.0196 mmol) and MeCN (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 20.5 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc-*n*-hexane-CH_2Cl_2 = 1:10:15 v/v) to give alkynylhydroquinone **2a** (3.84 mg, 81%) as a pale brownish solid.

Table 2 (solvent screening)

Entry 1: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (24.6 mg, 0.103 mmol), $CuCl_2 \cdot 2H_2O$ (1.8 mg, 0.0106 mmol), ascorbic acid (21.8 mg, 0.124 mmol), Cs_2CO_3 (33.6 mg, 0.103 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 2.5 h. After being cooled to room

temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (22.9 mg, 92%) as a white solid.

Entry 3: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (24.8 mg, 0.104 mmol), $CuCl_2 \cdot 2H_2O$ (1.8 mg, 0.0106 mmol), ascorbic acid (21.8 mg, 0.125 mmol), Cs_2CO_3 (33.9 mg, 0.104 mmol) and DMF (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 3 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (16.8 mg, 68%) as a white solid.

Entry 4: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (24.7 mg, 0.104 mmol), $CuCl_2 \cdot 2H_2O$ (1.8 mg, 0.0106 mmol), ascorbic acid (21.9 mg, 0.124 mmol), Cs_2CO_3 (33.8 mg, 0.104 mmol) and THF (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 20 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (0.4 mg, 2%) as a white solid and alkynylhydroquinone **2a** (23.7 mg, 95%) as a pale brownish solid.

Entry 5: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (23.7 mg, 0.0995 mmol), $CuCl_2 \cdot 2H_2O$ (1.7 mg, 0.00995 mmol), ascorbic acid (21.0 mg, 0.1194 mmol), Cs_2CO_3 (32.4 mg, 0.0995 mmol) and *t*-BuOH (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 14 min at room temperature and then heated at 100 °C in an oil bath for 19 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered,

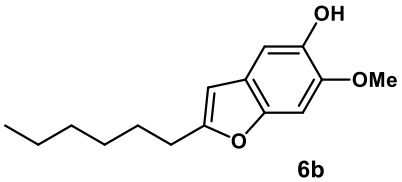
and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (6.4 mg, 27%) as a white solid.

Entry 6: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (26.5 mg, 0.112 mmol), $CuCl_2 \cdot 2H_2O$ (1.9 mg, 0.0112 mmol), ascorbic acid (23.5 mg, 0.134 mmol), Cs_2CO_3 (36.2 mg, 0.112 mmol) and 1,2-dichloroethane (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 15 min at room temperature and then heated at 100 °C in an oil bath for 19 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give unreacted alkynylquione **5a** (8.4 mg, 32%) and alkynylhydroquinone **2a** (11.0 mg, 41%), whose yields were determined by ^{1}H NMR analysis.

Table 3 (substrate scope)

Entry 1: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5b** (24.8 mg, 0.101 mmol), $CuCl_2 \cdot 2H_2O$ (1.7 mg, 0.00997 mmol), ascorbic acid (21.3 mg, 0.121 mmol), Cs_2CO_3 (32.8 mg, 0.101 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 2 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6b** (23.2 mg, 93%) as a purple gum.

2-Hexyl-6-methoxybenzofuran-5-ol (6b)



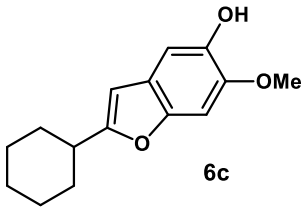
6b

93% (23.2 mg); IR (neat) ν 3177, 2353, 1521, 1148, 1041, 976, 910, 738, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$,) δ 6.98 (s, 1H), 6.97 (s, 1H), 6.24 (s, 1H), 4.69 (brs, 1H), 3.91 (s, 3H), 2.71 (t, J = 7.6 Hz, 2H), 1.71 (quintet, J = 7.6 Hz, 2H), 1.43–1.28 (m, 6H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 159.09, 148.76, 144.31, 142.35, 121.69, 104.29, 101.68, 94.55, 56.48, 31.71, 29.00, 28.59, 27.88, 22.70, 14.22; HRMS (EI) calcd for $C_{15}H_{20}O_3$ $[M]^+$ 248.1412, found: 248.1413.

Entry 2: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5c** (25.0 mg, 0.102 mmol), $CuCl_2 \cdot 2H_2O$ (1.7 mg, 0.00997 mmol), ascorbic acid (21.6 mg, 0.123 mmol), Cs_2CO_3 (33.3 mg, 0.102 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 15 min at room temperature and then heated at 100 °C in an oil bath for 2 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6c** (20.8 mg, 83%) as a white solid.

2-Cyclohexyl-6-methoxybenzofuran-5-ol (6c)

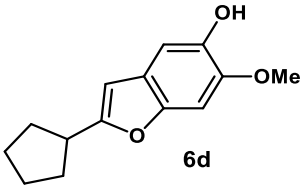


6c

83% (20.8 mg); white solid; mp 136.5–139.0 °C; IR (neat) ν 3089, 2916, 2368, 759, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.99 (s, 2H), 6.97 (s, 1H), 6.22 (s, 1H), 5.49 (brs, 1H), 3.91 (s, 3H), 2.70 (m, 1H), 2.15-2.04 (m, 2H), 1.87–1.78 (m, 2H), 1.73 (m, 1H), 1.53–1.22 (m, 5H).^{13}C NMR (100 MHz, $CDCl_3$) δ 163.45, 148.54, 144.31, 142.31, 121.54, 104.39, 99.72, 94.57, 56.49, 37.73, 31.50, 26.24, 26.07; HRMS (EI) calcd for $C_{15}H_{18}O_3$ $[M]^+$ 246.1256, found: 246.1253.

Entry 3: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5d** (27.0 mg, 0.117 mmol), $CuCl_2 \cdot 2H_2O$ (2.0 mg, 0.0117 mmol), ascorbic acid (24.8 mg, 0.141 mmol), Cs_2CO_3 (38.2 mg, 0.117 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 2 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6d** (23.3 mg, 86%) as a white solid.

2-Cyclopentyl-6-methoxybenzofuran-5-ol (6d)

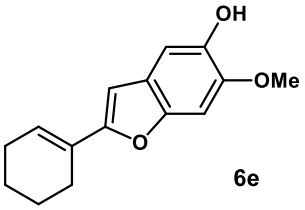


6d

86% (23.3 mg); white solid; mp 99.7–101.5 °C; IR (neat) ν 2952, 2361, 1485, 1378, 1113, 957, 823 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.98 (s, 2H, the singlet peaks of two protons are overlapped.), 6.25 (s, 1H), 5.48 (brs, 1H), 3.91 (s, 3H), 3.17 (quintet, J = 7.6 Hz, 1H), 2.11–1.99 (m, 2H), 1.83–1.62 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.55, 148.80, 144.31, 142.33, 121.59, 104.32, 100.27, 94.59, 56.50, 39.15, 31.84, 25.46; HRMS (EI) calcd for $C_{14}H_{16}O_3$ $[M]^+$ 232.1099, found: 232.1096.

Entry 4: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5e** (24.9 mg, 0.103 mmol), $CuCl_2 \cdot 2H_2O$ (1.8 mg, 0.0106 mmol), ascorbic acid (21.7 mg, 0.123 mmol), Cs_2CO_3 (33.5 mg, 0.103 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 2 min at room temperature and then heated at 100 °C in an oil bath for 2 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6e** (22.5 mg, 90%) as a white solid.

2-(Cyclohex-1-en-1-yl)-6-methoxybenzofuran-5-ol (6e)



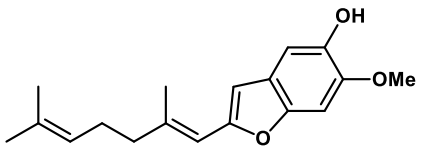
6e

90% (22.5 mg); white solid; mp 137.2–140.7 °C; IR (neat) ν 2930, 1479, 1364, 1114, 828, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.98 (s, 1H), 6.48 (m, 1H), 6.38 (s, 1H), 5.50 (s, 1H), 3.92 (s, 3H), 2.40–2.31 (m, 2H), 2.30–2.20 (m, 2H), 1.82–1.73 (m, 2H), 1.72–1.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.06, 148.81, 145.02, 142.43, 127.42, 124.61, 121.90, 104.55, 100.24,

94.42, 56.44, 25.49, 25.02, 22.50, 22.31; HRMS (EI) calcd for $C_{15}H_{16}O_3$ $[M+2]^+$ 246.1245, found: 246.1256.

Entry 5: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5f** (56.9 mg, 0.2 mmol), $CuCl_2 \cdot 2H_2O$ (3.5 mg, 0.02 mmol), ascorbic acid (42.3 mg, 0.24 mmol), Cs_2CO_3 (65.2 mg, 0.2 mmol) and DMSO (2.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 2 min at room temperature and then heated at 100 °C in an oil bath for 3 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6f** (48.8 mg, 85%) as a colorless oil.

(*E/Z*)-2-(2,6-Dimethylhepta-1,5-dien-1-yl)-6-methoxybenzofuran-5-ol (6f)



6f

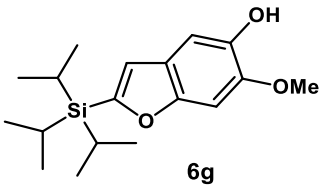
E:*Z* = 2:1 mixtrue

85% (48.8 mg, ca. *E/Z* =2:1); colorless oil; IR (neat) 2918, 1434, 1318, 1105, 1014, 848 cm^{-1}; (*E*)-isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (s, 1H), 6.98 (s, 1H), 6.42 (s, 1H), 6.14 (s, 1H), 5.52 (s, 1H, overlapped), 5.15 (m, 1H), 3.93 (s, 3H, overlapped), 2.53 (m, 1H), 2.30–2.20 (m, 3H), 2.08 (s, 3H), 1.70 (s, 3H), 1.64 (s, 3H); (*Z*)-isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.96 (s, 1H), 6.39 (s, 1H), 6.11 (s, 1H), 5.52 (s, 1H, overlapped), 5.23 (m, 1H), 3.93 (s, 3H, overlapped), 2.30–2.19 (m, 4H), 1.94 (s, 3H), 1.72 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.32, 155.00, 148.53, 148.41, 144.94, 144.92, 142.57, 141.78, 141.24, 132.20, 132.12, 124.22, 123.76, 121.91, 121.84, 114.71, 114.34, 104.28, 103.99, 103.71, 94.42, 94.40, 56.46 (overlapped), 41.20, 34.20, 26.80, 26.76, 25.88, 25.85, 25.24, 19.09, 17.89, 17.87; HRMS (EI) calcd for $C_{18}H_{22}O_3$ [M]+ 286.1569, found: 286.1568.

Entry 6: A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with alkynylquinone **5g** (24.9 mg, 0.0782 mmol), $CuCl_2 \cdot 2H_2O$ (1.3 mg, 0.00763 mmol), ascorbic acid (16.5 mg, 0.0937 mmol), Cs_2CO_3 (25.5 mg, 0.0783 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room

temperature and then heated at 100 ºC in an oil bath for 10 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc-*n*-hexane = 1:4 v/v) to give benzofuran **6g** (15.7 mg, 63%) as a white solid and alkynylhydroquinone (4.2 mg, 17%) as a pale brownish solid.

6-Methoxy-2-(triisopropylsilyl)benzofuran-5-ol (6g)

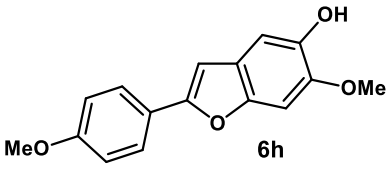


6g

63% (15.7 mg); white solid; mp 52.6–54.7 ºC IR (neat) ν 2938, 2862, 1522, 1479, 1313, 1015, 852, 713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.07 (s, 2H, the singlet peaks of two protons are overlapped.), 6.91 (s, 1H), 5.50 (brs, 1H), 3.94 (s, 3H), 1.46–1.29 (m, 3H), 1.14 (d, *J* = 7.2 Hz, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.69, 152.52, 145.41, 142.40, 120.57, 118.20, 104.24, 94.50, 56.37, 18.74, 11.19; HRMS (EI) calcd for $C_{18}H_{28}O_3Si$ $[M]^+$ 320.1808, found: 320.1809.

Entry 7: A dry, hole screw-top test tube was equipped with a magnetic stirring bar, charged with alkynylquinone **5h** (39.5 mg, 0.147 mmol), $CuCl_2 \cdot 2H_2O$ (2.6 mg, 0.0147 mmol), ascorbic acid (31.1 mg, 0.176 mmol), Cs_2CO_3 (47.9 mg, 0.147 mmol) and DMSO (1.5 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 2 min at room temperature and then heated at 100 ºC in an oil bath for 3 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6h** (33.5 mg, 84%) as a white solid.

6-Methoxy-2-(4-methoxyphenyl)benzofuran-5-ol (6h)

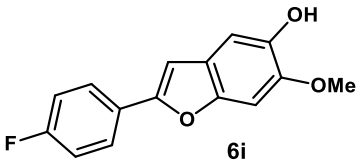


6h

84% (33.5 mg); white solid; mp 167.0–168.7 °C; IR (neat) ν 3421, 2938, 1608, 1481, 1322, 1245, 1114, 1010, 794 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 6.7 Hz, 2H), 6.89 (d, J = 7.0 Hz, 2H), 6.85 (brs, 1H), 5.96 (brs, 1H), 3.83 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.3, 181.3, 161.2, 159.1, 134.4, 133.6, 133.4, 114.3, 113.6, 107.5, 106.2, 82.8, 56.5, 55.5; HRMS (EI) calcd for $C_{16}H_{14}O_4$ $[M]^+$ 270.0892, found: 270.0889.

Entry 8: A dry, hole screw-top test tube was equipped with a magnetic stirring bar, charged with alkynylquinone **5i** (30.2 mg, 0.1267 mmol), $CuCl_2 \cdot 2H_2O$ (2.2 mg, 0.0126 mmol), ascorbic acid (26.8 mg, 0.152 mmol), Cs_2CO_3 (41.3 mg, 0.1267 mmol) and DMSO (1.3 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 2 min at room temperature and then heated at 100 °C in an oil bath for 3 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6i** (19.7 mg, 65%) as a white solid.

2-(4-fluorophenyl)-6-Methoxybenzofuran-5-ol (6i)



6i

63% (19.7 mg); white solid; mp 156.0–158.2 °C IR (neat) ν 3459, 2923, 1743, 1488, 1380, 1272, 1226, 1122, 1014, 833 cm^{-1};-^1H NMR (400 MHz, $CDCl_3$) δ 7.78–7.72 (m, 2H), 7.11 (t, J = 8.7 Hz, 2H), 7.06 (d, J = 6.1 Hz, 2H), 6.83 (s, 1H), 5.56 (s, 1H), 3.96 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 161.4, 154.4, 149.3, 145.4, 142.9, 127.2 (d, $J_{C\text{-}F}$ = 3.0 Hz), 126.2 (d, $J_{C\text{-}F}$ = 9.0 Hz), 122.0, 115.9 (d, $J_{C\text{-}F}$ = 22.0 Hz), 104.6, 101.2 (d, $J_{C\text{-}F}$ = 2.0 Hz), 94.6, 56.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ = –113.7; HRMS (EI) calcd for $C_{15}H_{11}FO_3$ $[M]^+$ 258.0692, found: 258.0692.

Control experiments (Scheme 3)

Scheme 3a (with CuCl): A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with hydroquinone **2a** (24.6 mg, 0.103 mmol), CuCl (1.0 mg, 0.0101 mmol), Cs_2CO_3 (33.5 mg, 0.103 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 2.5 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole

mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (23.0 mg, 93%) as a white solid.

Scheme 3a (with $CuCl_2 \cdot 2H_2O$): A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with hydroquinone **2a** (24.8 mg, 0.103 mmol), $CuCl_2 \cdot 2H_2O$ (1.8 mg, 0.0106 mmol), Cs_2CO_3 (33.6 mg, 0.103 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 5 min at room temperature and then heated at 100 °C in an oil bath for 2.5 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (23.6 mg, 95%) as a white solid.

Scheme 3b (the oxidation of hydroquinone 2a with a stoichiometric amount of $CuCl_2 \cdot 2H_2O$): A dry, hole screw-top test tube (Maruemu NN-13H) was equipped with a magnetic stirring bar, charged with hydroquinone **2a** (19.8 mg, 0.0824 mmol), $CuCl_2 \cdot 2H_2O$ (28.1 mg, 0.165 mmol), Cs_2CO_3 (26.9 mg, 0.826 mmol) and DMSO (1.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 10 min at room temperature. Sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc-*n*-hexane = 1:2 v/v) to give alkynylquinone **5a** (15.1 mg, 77%) as an orange solid and unreacted hydroquinone **2a** (3.2 mg, 16%) as a pale brownish solid.

Control experiments with a radical inhibitor

TEMPO (1.0 equiv): A dry, hole screw-top test tube was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (47.7 mg, 0.2 mmol), $CuCl_2 \cdot 2H_2O$ (3.5 mg, 0.02 mmol), ascorbic acid (42.3 mg, 0.24 mmol), Cs_2CO_3 (65.2 mg, 0.2 mmol), TEMPO (31.3mg, 0.2 mmol) and DMSO (2.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 2 min at room temperature and then heated at 100 °C in an oil bath for 2 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was

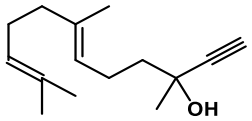
extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (29.9 mg, 62%) as a white solid.

TEMPO (3.0 equiv): A dry, hole screw-top test tube was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (47.7 mg, 0.2 mmol), $CuCl_2 \cdot 2H_2O$ (3.5 mg, 0.02 mmol), ascorbic acid (42.3 mg, 0.24 mmol), Cs_2CO_3 (65.2 mg, 0.2 mmol), TEMPO (93.8 mg, 0.6 mmol) and DMSO (2.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 2 min at room temperature and then heated at 100 ºC in an oil bath for 2 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (27.5 mg, 57%) as a white solid.

TEMPO (5.0 equiv): A dry, hole screw-top test tube was equipped with a magnetic stirring bar, charged with alkynylquinone **5a** (47.7 mg, 0.2 mmol), $CuCl_2 \cdot 2H_2O$ (3.5 mg, 0.02 mmol), ascorbic acid (42.3 mg, 0.24 mmol), Cs_2CO_3 (65.2 mg, 0.2 mmol), TEMPO (156.3 mg, 1.0 mmol) and DMSO (2.0 mL) sequentially, and flushed with argon. The reaction mixture was stirred for 2 min at room temperature and then heated at 100 ºC in an oil bath for 2 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **6a** (16.7 mg, 35%) as a white solid.

Procedures for the formal synthesis of (±)-liphagal

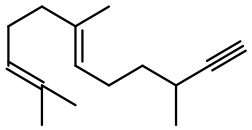
(*E*)-3,7,11-Trimethyldodeca-6,10-dien-1-yn-3-ol (9): To a stirred solution of geranyl acetone (893.9 mg, 4.6 mmol) in THF (14 ml) was at -30ºC was added ethynyl magnesium bromide (0.5 M in THF, 20.2 mL, 10.1 mmol) dropwise. After 30 min, the mixture was warmed to room temperature and stirring was continued for 1 h. Sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc-*n*-hexane = 1:95 v/v) to give compound **9** (855.1 mg, 84%) as a colorless oil.



9

Colorless oil; IR (neat) ν 3396, 3168, 2370, 2321, 1276, 1062, 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.18 (t, *J* = 7.0 Hz, 1H), 5.08 (t, *J* = 7.0 Hz, 1H), 2.46 (s, 1H), 2.32 (m, 1H), 2.19 (m, 1H), 2.11–2.03 (m, 3H), 2.03–1.96 (m, 2H), 1.76–1.69 (m, 2H), 1.68 (s, 3H), 1.65 (s, 3H), 1.60 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.40, 131.68, 124.33, 123.70, 87.74, 71.58, 68.47, 43.28, 39.85, 29.97, 26.77, 25.84, 23.64, 17.83, 16.20; HRMS (EI) calcd for $C_{15}H_{24}O$ $[M]^+$ 220.1827, found: 220.1823. The spectroscopic data of this compound were in good agreement with those reported.[2]

(*E*)-3,7,11-Trimethyldodeca-6,10-dien-1-yne (10): To a stirred solution of alkyne **9** (66.2 mg, 0.3 mmol) in CH_2Cl_2 (3.0 mL) at room temperature was added dicobalt octacarbonyl (118.7 mg, 0.347 mmol). After 60 min, the mixture was cooled to 0 ºC in an ice bath. After 10 min, borane-dimethyl sulfide complex (BMS) (2.0 M in THF, 0.33 mL, 0.66 mmol) was added over 5 min. After 5 min, TFA (0.3 ml, 3.9 mmol) was added over 5 min. After 10 min, the mixture was poured into a separatory funnel where it was washed with sat. $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was used without further purification. The crude product was dissolved in MeOH (6.0 mL) and the mixture was cooled to 0 ºC. To this mixture was added CAN (822 mg 1.5 mmol) and the mixture was stirred for 13 min. Then, the mixture was allowed to warm to room temperature and stirred for further 20 min. The reaction was quenched with sat. $NaHCO_3$ and sat. $Na_2S_2O_3$. The mixture was transferred to a separatory funnel where it was extracted with hexane. The organic extract was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography to afford alkyne 10 (27.0 mg, 44% in 3 steps from **9**) as a colorless oil.

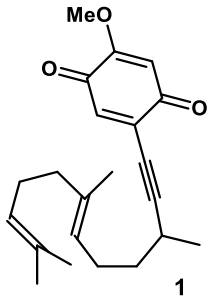


10

Colorless oil; IR (neat) ν 3196, 2356, 1652, 994, 727, 677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.15–5.04 (m, 2H), 2.44 (m, 1H), 2.23–1.93 (m, 7H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.62 (s, 3H), 1.60 (s, 3H), 1.56 – 1.38 (m, 2H), 1.18 (d, *J* = 6.9, Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.90, 131.50,

124.48, 123.83, 89.36, 68.29, 39.89, 36.99, 26.81, 25.84, 25.77, 25.29, 21.07, 17.83, 16.14; HRMS (EI) calcd for $C_{15}H_{24}$ $[M]^+$ 204.1878, found: 204.1878. The spectroscopic data of this compound were in good agreement with those reported.[1]

(*E*)-2-Methoxy-5-(3,7,11-trimethyldodeca-6,10-dien-1-yn-1-yl)cyclohexa-2,5-diene-1,4-dione (1): To a stirred solution of alkyne **10** (73.6mg, 0.36 mmol, 1.2 equiv) in DMF (3.0 mL) at room temperature were added 6-iodo-2-methoxybenzoquinone (79.3mg, 0.30 mmol), K_2CO_3 (62.2 mg, 0.45 mmol), and $Pd(OAc)_2$ ((3.4 mg, 0.015 mmol). The reaction was monitored by TLC. After the consumption of 6-iodo-2-methoxybenzoquinone, the mixture was filtered through a pad of Celite and washed with Et_2O. The filtrate was transferred to a separatory funnel where it was washed with H_2O. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc/n-hexane 1:6 v/v to 1:10 v/v) to provide alkynylquinones **1** (84 mg, 82%) as a brown oil.

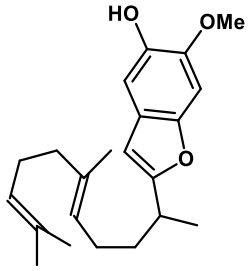


1

IR (neat) ν 3713, 2909, 2214, 1180, 893 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.77 (d, J = 0.6 Hz, 1H), 5.93 (s, 1H), 5.17 – 5.04 (m, 2H), 3.83 (s, 3H), 2.76 (m, 1H), 2.22–2.13 (m, 2H), 2.11–2.03 (m, 2H), 2.02–1.95 (m, 2H), 1.68 (d, J = 1.3 Hz, 3H), 1.63 (s, 3H), 1.60 (s, 3H), 1.58–1.48 (m, 2H), 1.26 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.44, 181.61, 158.97, 136.25, 134.65, 133.80, 131.55, 124.43, 123.49, 112.73, 107.59, 75.12, 56.49, 39.88, 36.62, 26.88, 26.78, 25.85, 25.84, 20.42, 17.85, 16.17; HRMS (EI) calcd for $C_{22}H_{28}O_3$ $[M]^+$ 340.2038, found: 340.2033. The spectroscopic data of this compound were in good agreement with those reported.[1]

(*E*)-2-(6,10-Dimethylundeca-5,9-dien-2-yl)-6-methoxybenzofuran-5-ol (3): A dry, hole screw-top test tube (Fischer Scientific) was equipped with a magnetic stirring bar, charged with alkynylquinone **1** (47.7 mg, 0.14 mmol), $CuCl_2 \cdot 2H_2O$ (2.4 mg, 0.014 mmol), ascorbic acid (29.6 mg, 0.168 mmol), Cs_2CO_3 (45.7 mg, 0.14 mmol) and DMSO (1.4 mL, 0.1M) sequentially, and flushed with argon. The reaction mixture was stirred for 15 min at room temperature and then

heated at 100 ºC in an oil bath for 3 h. After being cooled to room temperature, sat. NH_4Cl was added and the whole mixture was transferred to a separatory funnel where it was extracted with EtOAc. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (CH_2Cl_2) to give benzofuran **3** (30.7 mg, 64%) as a light brown oil.



3

IR (neat) ν 2916, 2378, 1436, 1115, 714 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.01–6.95 (m, 2H), 6.24 (m, 1H), 5.48 (s, 1H), 5.17–5.05 (m, 2H), 3.92 (s, 3H), 2.89 (sex, J = 7.0 Hz, 1H), 2.11–1.93 (m, 6H), 1.81 (m, 1H), 1.68 (d, J = 1.4 Hz, 3H), 1.60 (s, 3H), 1.59 (m, 1H), 1.56 (s, 3H), 1.30 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.17, 148.71, 144.34, 142.36, 135.59, 131.47, 124.49, 124.14, 121.57, 104.37, 100.68, 94.63, 56.50, 39.86, 35.66, 33.21, 26.81, 25.85, 25.65, 19.23, 17.83, 16.15; HRMS (EI) calcd for $C_{22}H_{30}O_3$ $[M]^+$ 342.2195, found: 342.2196. The spectroscopic data of this compound were in good agreement with those reported.[1]

Crystal Structure Report for 6a

Sample preparation (solvent evaporation): Compound **6a** (10 mg) was dissolved with 1 mL of benzene in opened inner vessel, and *n*-pentane (5 mL) as an anti-solvent has been employed in closed outer vessel. After vapor diffusion for 4 days, the single crystals of compound **6a** were obtained.

A colorless rod-like specimen of $C_{15}H_{12}O_3$, approximate dimensions 0.040 mm x 0.090 mm x 0.200 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 0.71073 Å).

Table 1: Data collection details for 6a.

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Phi	60.632	0.00	0.00	0.00	54.74	1.00	180	1.20	0.71073	50	30.0	n/a
Phi	60.632	0.00	0.00	180.00	54.74	1.00	180	1.20	0.71073	50	30.0	n/a
Omega	60.632	18.54	-174.46	153.00	54.74	1.00	206	10.00	0.71073	50	30.0	n/a
Omega	60.632	18.54	-174.46	0.00	54.74	1.00	206	10.00	0.71073	50	30.0	n/a
Omega	60.632	18.54	-174.46	-105.00	54.74	1.00	206	10.00	0.71073	50	30.0	n/a
Omega	60.632	18.54	-174.46	102.00	54.74	1.00	206	10.00	0.71073	50	30.0	n/a
Omega	60.632	27.81	-165.19	0.00	54.74	1.00	206	10.00	0.71073	50	30.0	n/a
Omega	60.632	18.54	-174.46	-156.00	54.74	1.00	206	10.00	0.71073	50	30.0	n/a
Phi	60.632	18.54	-174.46	0.00	54.74	1.00	360	10.00	0.71073	50	30.0	n/a
Phi	60.632	0.00	0.00	0.00	54.74	360.00	1	108.00	0.71073	50	30.0	n/a

A total of 1957 frames were collected. The total exposure time was 4.58 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 24439 reflections to a maximum θ angle of 28.23° (0.75 Å resolution), of which 2895 were independent (average redundancy 8.442, completeness = 99.5%, R_{int} = 4.91%, R_{sig} = 2.98%) and 2369 (81.83%) were greater than $2\sigma(F^2)$. The final cell constants of $\underline{a}$ = 8.3998(14) Å, $\underline{b}$ = 5.6694(9) Å, $\underline{c}$ = 12.814(2) Å, β = 106.089(6)°, volume = 586.32(17) $Å^3$, are based upon the refinement of the XYZ-centroids of 7901 reflections above 20 σ(I) with 5.047° < 2θ < 50.24°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.925. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9810 and 0.9960. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21 1, with Z = 2 for the formula unit, $C_{15}H_{12}O_3$. The final anisotropic full-matrix least-squares refinement on F^2 with 165 variables converged at R1 = 4.29%, for the observed data and wR2 = 9.57%

for all data. The goodness-of-fit was 1.073. The largest peak in the final difference electron density synthesis was 0.150 $e^-/Å^3$ and the largest hole was -0.132 $e^-/Å^3$ with an RMS deviation of 0.025 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.361 g/cm^3 and F(000), 252 e^-.

Table 2. Sample and crystal data for 6a.

Chemical formula	$C_{15}H_{12}O_3$	
Formula weight	240.25 g/mol	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal size	0.040 x 0.090 x 0.200 mm	
Crystal habit	colorless rod	
Crystal system	monoclinic	
Space group	P 2_1	
Unit cell dimensions	a = 8.3998(14) Å	α = 90°
	b = 5.6694(9) Å	β = 106.089(6)°
	c = 12.814(2) Å	γ = 90°
Volume	586.32(17) $Å^3$	
Z	2	
Density (calculated)	1.361 g/cm^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	252	

Table 3. Data collection and structure refinement for 6a.

Theta range for data collection	1.65 to 28.23°	
Index ranges	$-11 \le h \le 11$, $-7 \le k \le 7$, $-17 \le l \le 17$	
Reflections collected	24439	
Independent reflections	2895 [R(int) = 0.0491]	
Coverage of independent reflections	99.5%	
Absorption correction	Multi-Scan	
Max. and min. transmission	0.9960 and 0.9810	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	2895 / 1 / 165	
Goodness-of-fit on F^2	1.073	
Final R indices	2369 data; $I>2\sigma(I)$	R_1 = 0.0429, wR_2 = 0.0906

	all data	R_1 = 0.0559, wR_2 = 0.0957
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0452P)^2+0.0335P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	-0.2(5)	
Largest diff. peak and hole	0.150 and -0.132 eÅ^{-3}	
R.M.S. deviation from mean	0.025 eÅ^{-3}	

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for 6a.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C1	0.6157(3)	0.6692(5)	0.85744(18)	0.0558(6)
C2	0.7153(3)	0.4669(5)	0.86845(18)	0.0569(6)
C3	0.7803(3)	0.3944(4)	0.7865(2)	0.0552(6)
C4	0.7455(3)	0.5342(4)	0.69501(18)	0.0468(5)
C5	0.6524(2)	0.7390(4)	0.68211(17)	0.0464(5)
C6	0.5843(3)	0.8067(5)	0.7663(2)	0.0566(6)
C7	0.6476(3)	0.8252(4)	0.57642(18)	0.0505(5)
C8	0.7338(2)	0.6718(4)	0.53214(17)	0.0448(5)
C9	0.7688(2)	0.6546(4)	0.42709(16)	0.0444(5)
C10	0.7127(3)	0.8291(5)	0.3489(2)	0.0569(6)
C11	0.7402(3)	0.8118(5)	0.2481(2)	0.0640(7)
C12	0.8252(3)	0.6202(6)	0.2238(2)	0.0635(7)
C13	0.8823(3)	0.4495(5)	0.3007(2)	0.0639(7)
C14	0.8548(3)	0.4649(5)	0.40146(18)	0.0545(6)
C15	0.8511(4)	0.1676(6)	0.9933(2)	0.0762(8)
O1	0.5492(2)	0.7310(4)	0.94039(14)	0.0795(7)
O2	0.7372(2)	0.3540(5)	0.96655(15)	0.0841(7)
O3	0.79614(18)	0.4900(3)	0.60373(11)	0.0486(4)

Table 5. Bond lengths (Å) for 6a.

C1-C6	1.368(4)	C1-O1	1.376(3)
C1-C2	1.403(4)	C2-C3	1.375(3)
C2-O2	1.377(3)	C3-C4	1.378(3)
C3-H3	0.93	C4-O3	1.374(3)
C4-C5	1.384(3)	C5-C6	1.407(3)
C5-C7	1.430(3)	C6-H6	0.93

C7-C8	1.353(3)	C7-H7	0.93
C8-O3	1.382(3)	C8-C9	1.459(3)
C9-C14	1.385(3)	C9-C10	1.394(3)
C10-C11	1.377(3)	C10-H10	0.93
C11-C12	1.382(4)	C11-H11	0.93
C12-C13	1.369(4)	C12-H12	0.93
C13-C14	1.376(3)	C13-H13	0.93
C14-H14	0.93	C15-O2	1.403(4)
C15-H15A	0.96	C15-H15B	0.96
C15-H15C	0.96	O1-H1	0.82

Table 6. Bond angles (°) for 6a.

C6-C1-O1	119.4(2)	C6-C1-C2	121.4(2)
O1-C1-C2	119.3(2)	C3-C2-O2	125.3(2)
C3-C2-C1	121.3(2)	O2-C2-C1	113.4(2)
C2-C3-C4	116.2(2)	C2-C3-H3	121.9
C4-C3-H3	121.9	O3-C4-C3	125.2(2)
O3-C4-C5	110.46(19)	C3-C4-C5	124.4(2)
C4-C5-C6	118.3(2)	C4-C5-C7	105.47(19)
C6-C5-C7	136.2(2)	C1-C6-C5	118.4(2)
C1-C6-H6	120.8	C5-C6-H6	120.8
C8-C7-C5	107.4(2)	C8-C7-H7	126.3
C5-C7-H7	126.3	C7-C8-O3	110.45(19)
C7-C8-C9	134.3(2)	O3-C8-C9	115.24(18)
C14-C9-C10	118.40(19)	C14-C9-C8	121.51(19)
C10-C9-C8	120.1(2)	C11-C10-C9	120.8(2)
C11-C10-H10	119.6	C9-C10-H10	119.6
C10-C11-C12	119.9(2)	C10-C11-H11	120.0
C12-C11-H11	120.0	C13-C12-C11	119.6(2)
C13-C12-H12	120.2	C11-C12-H12	120.2
C12-C13-C14	120.9(3)	C12-C13-H13	119.5
C14-C13-H13	119.5	C13-C14-C9	120.4(2)
C13-C14-H14	119.8	C9-C14-H14	119.8
O2-C15-H15A	109.5	O2-C15-H15B	109.5
H15A-C15-H15B	109.5	O2-C15-H15C	109.5
H15A-C15-H15C	109.5	H15B-C15-H15C	109.5
C1-O1-H1	109.5	C2-O2-C15	118.9(2)
C4-O3-C8	106.20(17)		

Table 7. Anisotropic atomic displacement parameters (Å^2) for 6a.

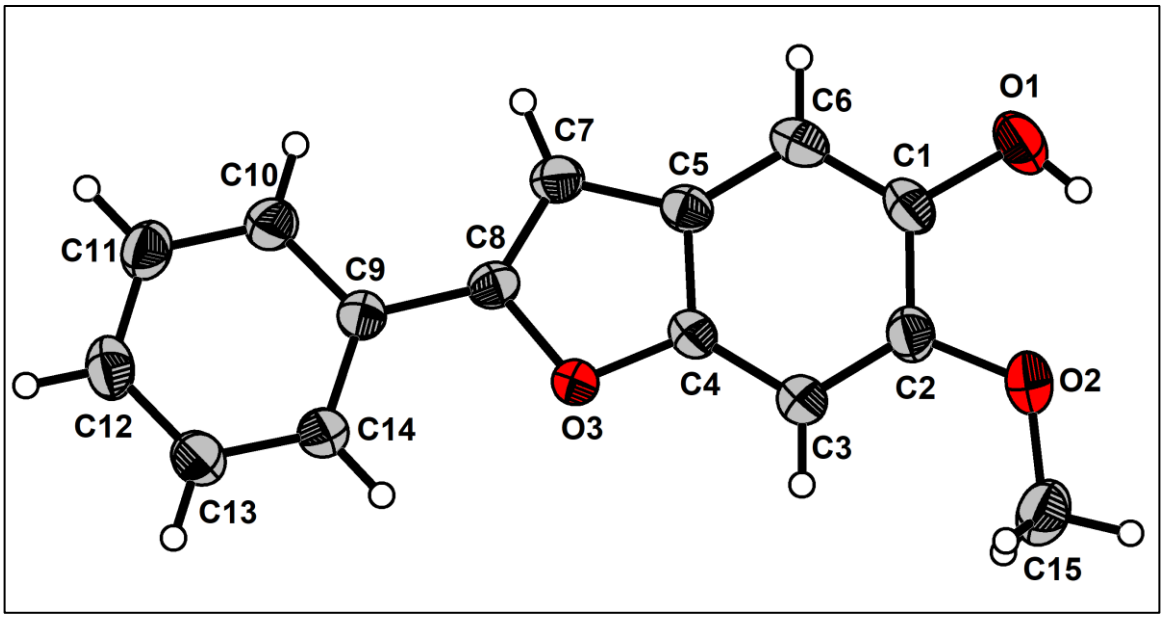
The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

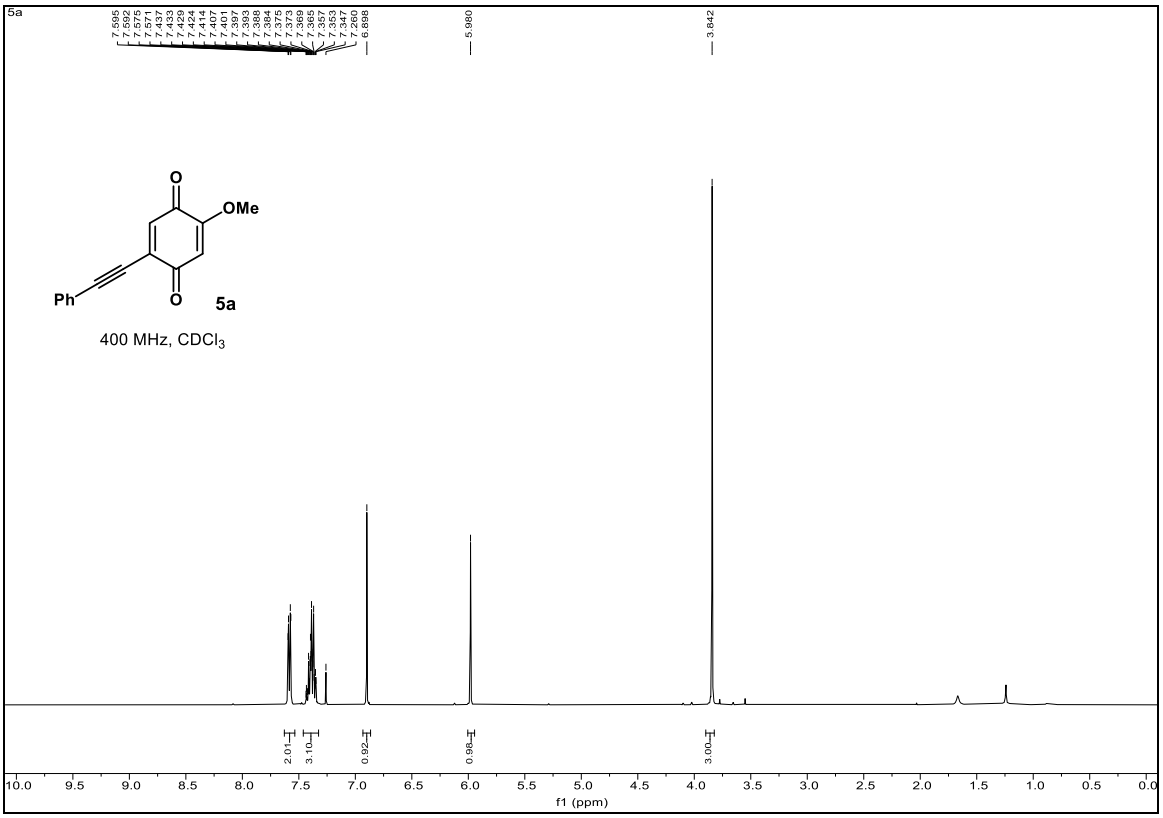
	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0456(11)	0.0738(16)	0.0518(13)	-0.0123(13)	0.0196(10)	-0.0018(12)
C2	0.0526(13)	0.0732(16)	0.0481(12)	0.0029(12)	0.0192(10)	-0.0004(12)
C3	0.0571(13)	0.0572(14)	0.0553(13)	0.0055(11)	0.0225(10)	0.0090(11)
C4	0.0439(11)	0.0515(13)	0.0480(11)	-0.0033(10)	0.0175(9)	0.0003(10)
C5	0.0408(10)	0.0473(12)	0.0501(12)	-0.0051(10)	0.0108(9)	0.0000(9)
C6	0.0468(12)	0.0600(14)	0.0642(14)	-0.0121(13)	0.0170(10)	0.0062(11)
C7	0.0505(11)	0.0464(11)	0.0524(12)	0.0000(11)	0.0108(9)	0.0068(10)
C8	0.0399(10)	0.0429(10)	0.0492(12)	0.0018(10)	0.0083(9)	-0.0010(9)
C9	0.0381(9)	0.0491(11)	0.0449(11)	0.0002(10)	0.0093(8)	-0.0036(9)
C10	0.0586(13)	0.0526(13)	0.0622(14)	0.0085(12)	0.0212(11)	0.0036(12)
C11	0.0622(14)	0.0729(17)	0.0597(15)	0.0194(14)	0.0214(12)	0.0000(14)
C12	0.0537(12)	0.091(2)	0.0482(13)	0.0012(13)	0.0189(10)	-0.0083(13)
C13	0.0600(15)	0.0758(18)	0.0578(14)	-0.0038(14)	0.0196(11)	0.0088(13)
C14	0.0521(12)	0.0618(14)	0.0487(12)	0.0026(12)	0.0126(10)	0.0097(11)
C15	0.0931(19)	0.0740(17)	0.0624(16)	0.0162(15)	0.0231(15)	0.0003(17)
O1	0.0793(12)	0.1058(18)	0.0636(11)	-0.0093(11)	0.0369(10)	0.0137(12)
O2	0.0920(14)	0.1119(17)	0.0610(11)	0.0213(12)	0.0421(10)	0.0237(13)
O3	0.0531(8)	0.0485(9)	0.0479(8)	0.0056(7)	0.0200(7)	0.0101(7)

Table 8. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2) for 6a.

	x/a	y/b	z/c	U(eq)
H3	0.8443	0.2585	0.7924	0.066
H6	0.5194	0.9417	0.7601	0.068
H7	0.5949	0.9617	0.5440	0.061
H10	0.6559	0.9588	0.3650	0.068
H11	0.7017	0.9289	0.1965	0.077
H12	0.8434	0.6073	0.1557	0.076

	x/a	y/b	z/c	U(eq)
H13	0.9405	0.3214	0.2846	0.077
H14	0.8943	0.3472	0.4527	0.065
H15A	0.8148	0.0404	0.9428	0.114
H15B	0.8586	0.1136	1.0655	0.114
H15C	0.9580	0.2212	0.9899	0.114
H1	0.5720	0.6297	0.9879	0.119

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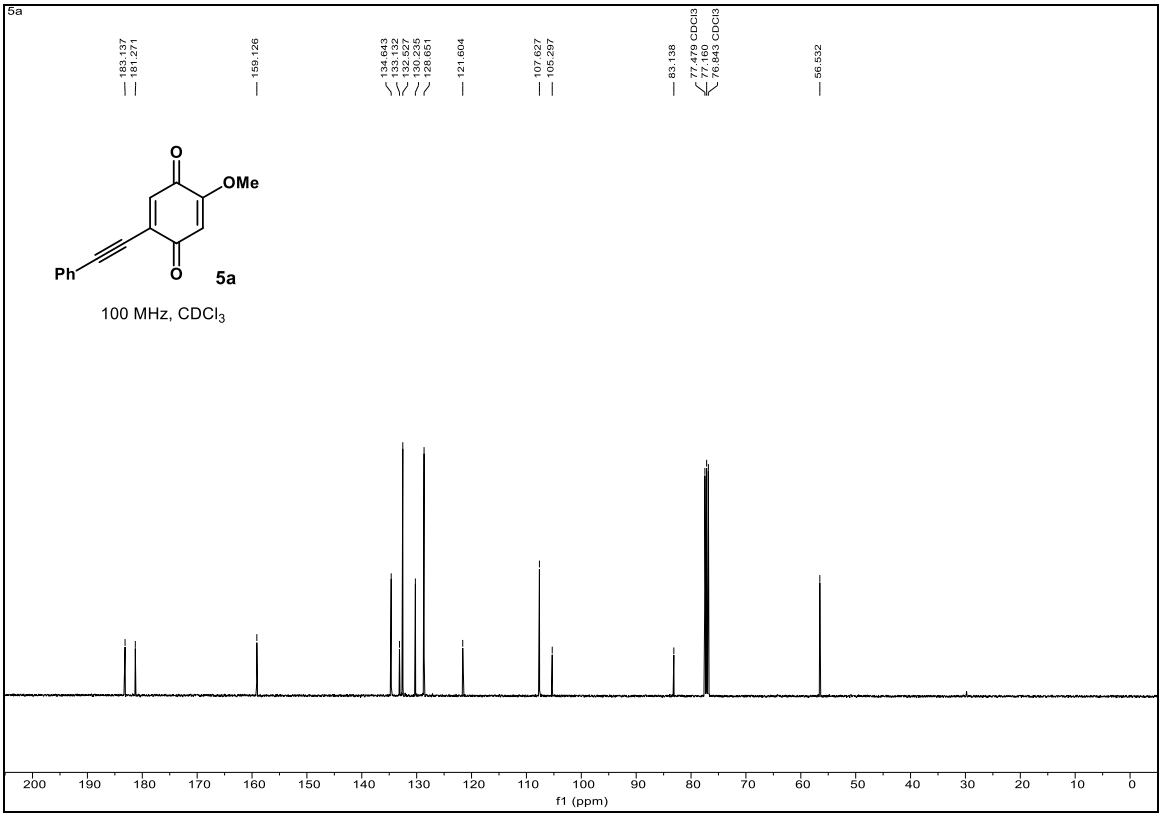
7.575
7.571
7.437
7.433
7.429
7.424
7.414
7.407
7.401
7.397
7.393
7.388
7.384
7.375
7.373
7.369
7.365
7.357
7.353
7.347
7.260
6.898
5.980
3.842
O
OMe
Ph
O
5a
400 MHz, CDCl3
2.01
3.10
0.92
0.98
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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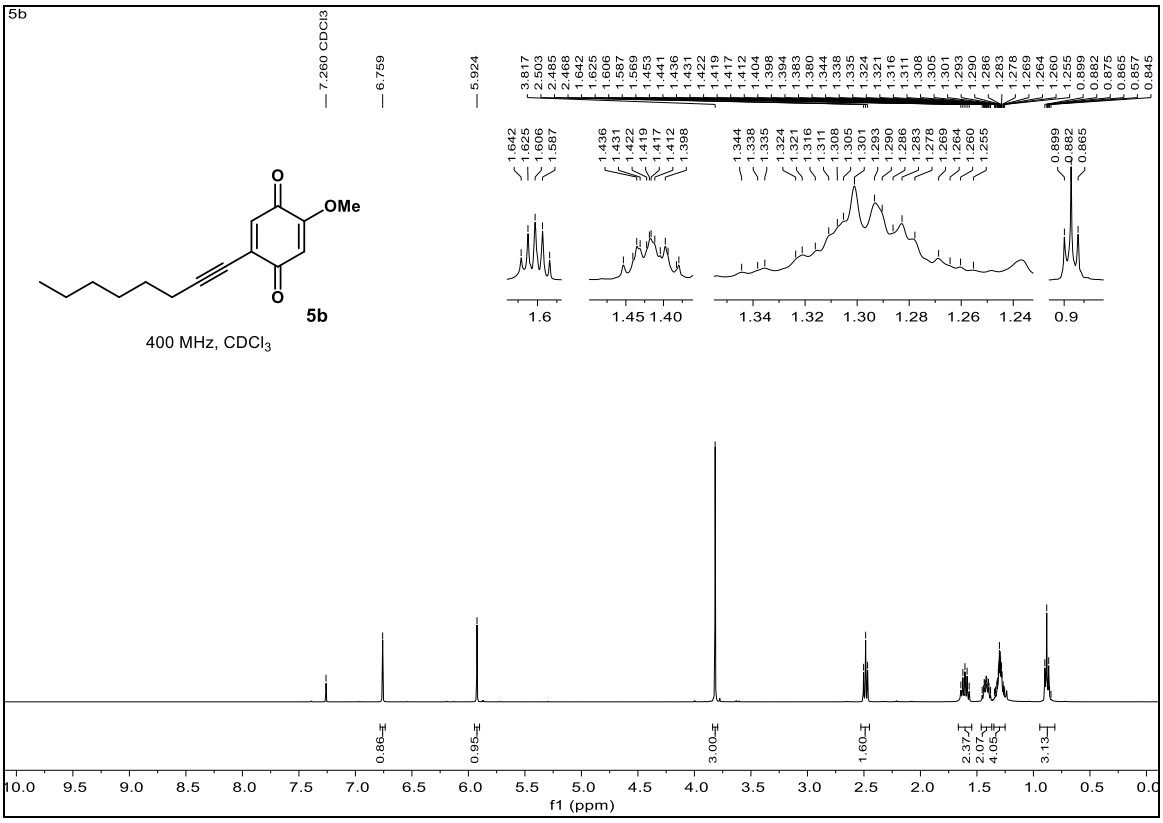
181.271
159.126
134.643
133.132
132.127
130.235
128.651
121.604
107.627
105.297
83.138
77.479 CDCl3
77.160
76.843 CDCl3
56.532
O
OMe
Ph
O
5a
100 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


5b
7.260 CDCl3
6.759
5.924
OMe
O
O
5b
400 MHz, CDCl3
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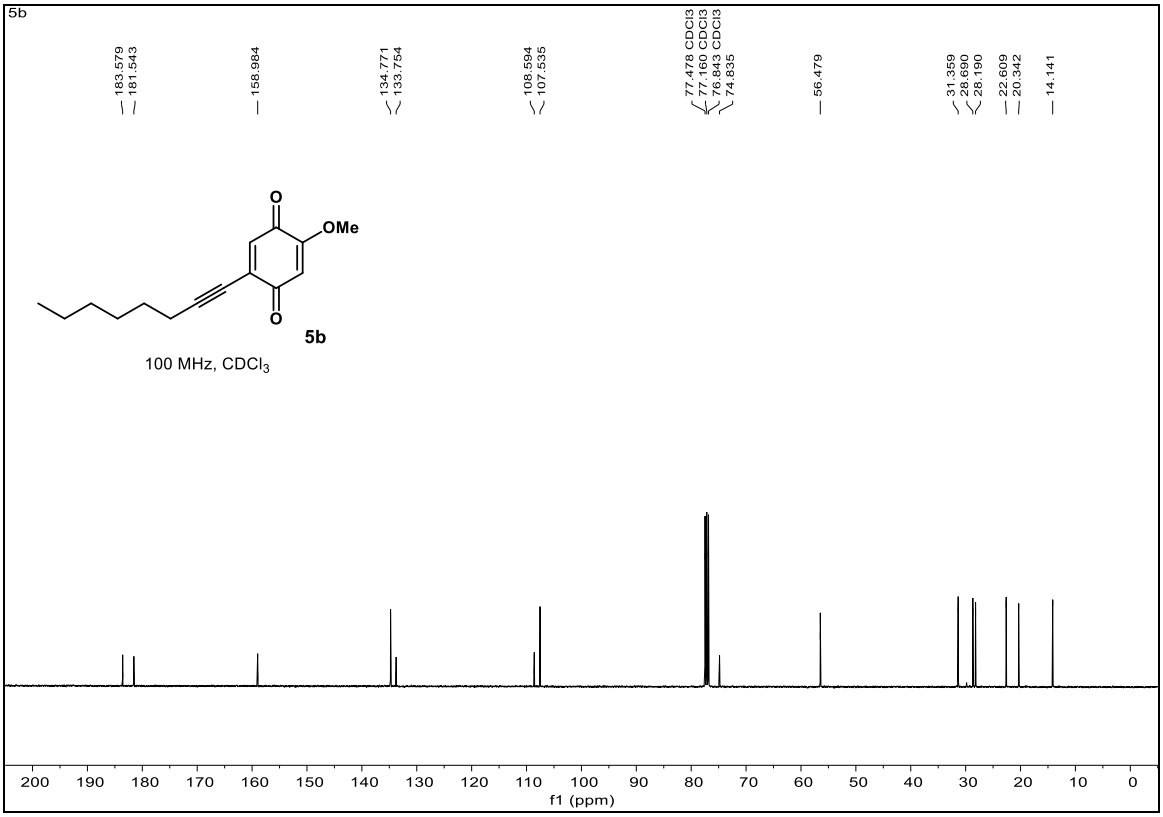
0.95
3.00
1.60
2.37
2.07
4.05
3.13
f1 (ppm)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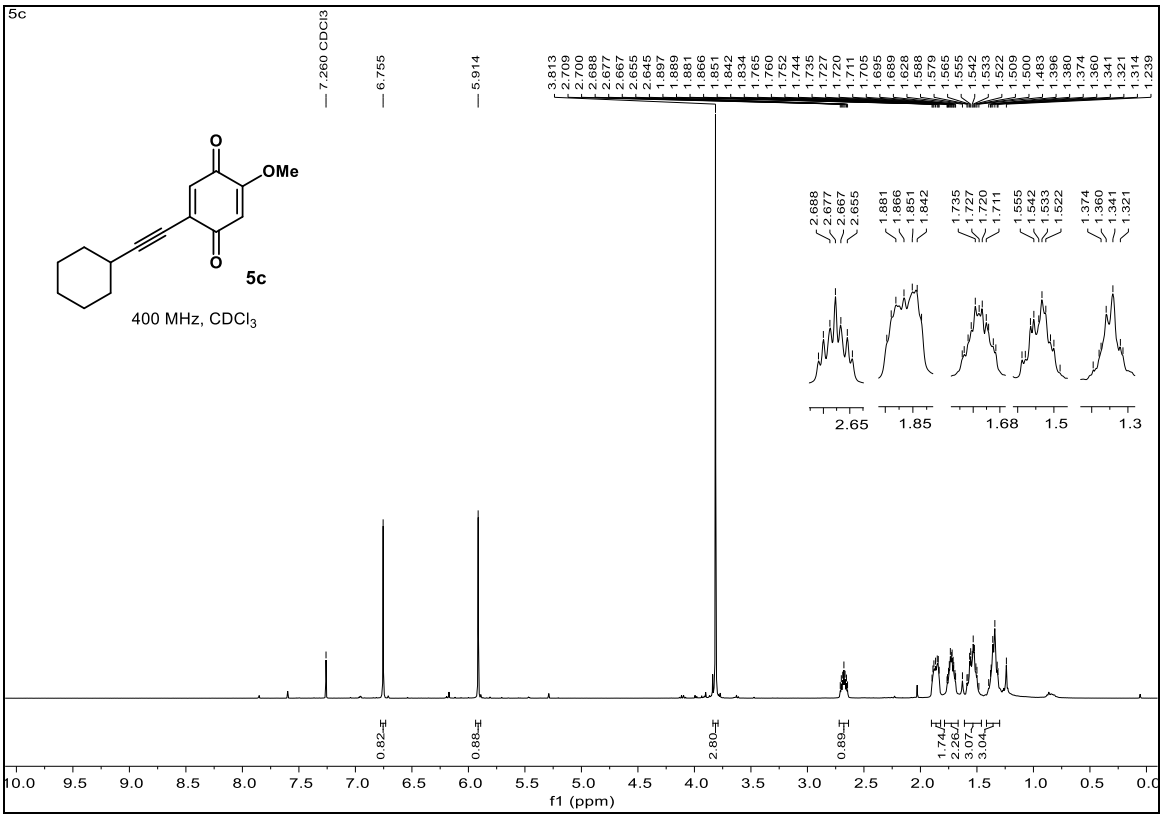
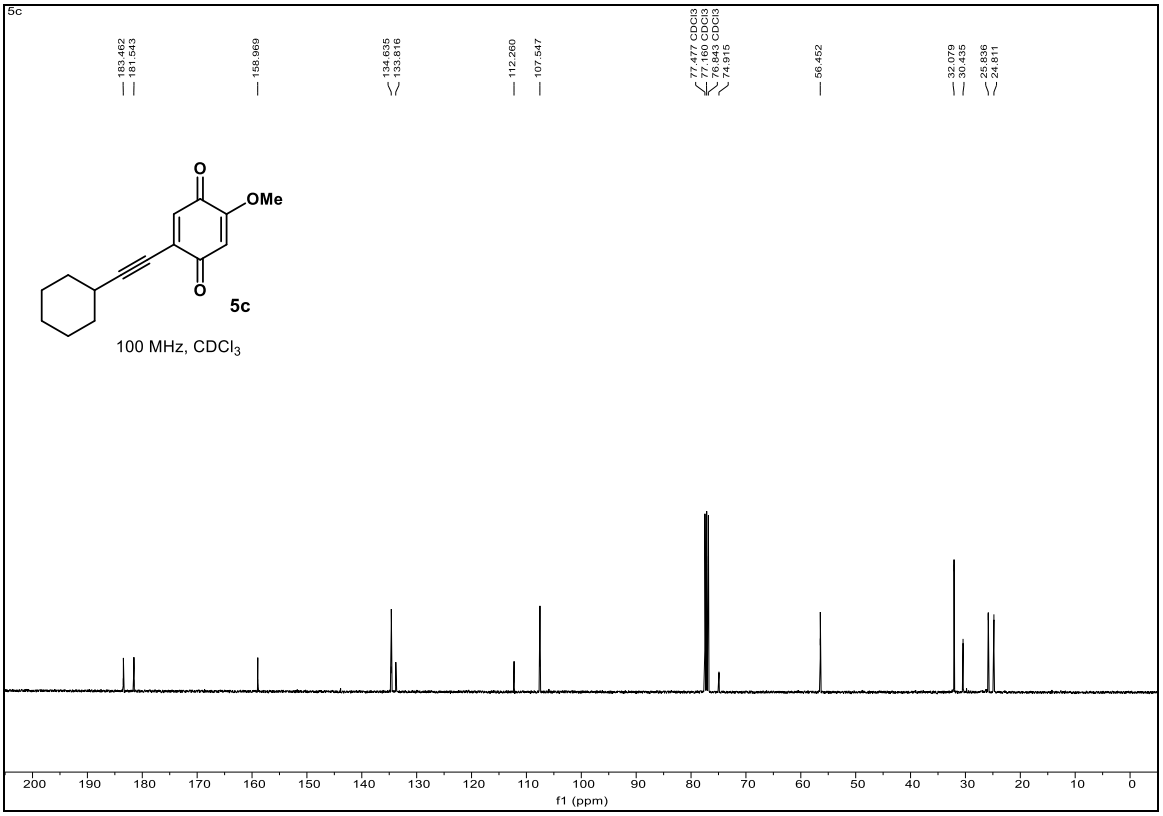
181.543
158.984
134.771
133.754
108.594
107.535
77.478 CDCl3
77.160 CDCl3
76.843 CDCl3
74.835
56.479
31.359
28.690
28.190
22.609
20.342
14.141
OMe
O
O
5b
100 MHz, CDCl3
f1 (ppm)


5c
7.260 CDCl3
6.755
5.914
OMe
O
O
5c
400 MHz, CDCl3
2.65
1.85
1.68
1.5
1.3
0.82
0.88
2.80
0.89
1.74
2.26
3.07
3.04
f1 (ppm)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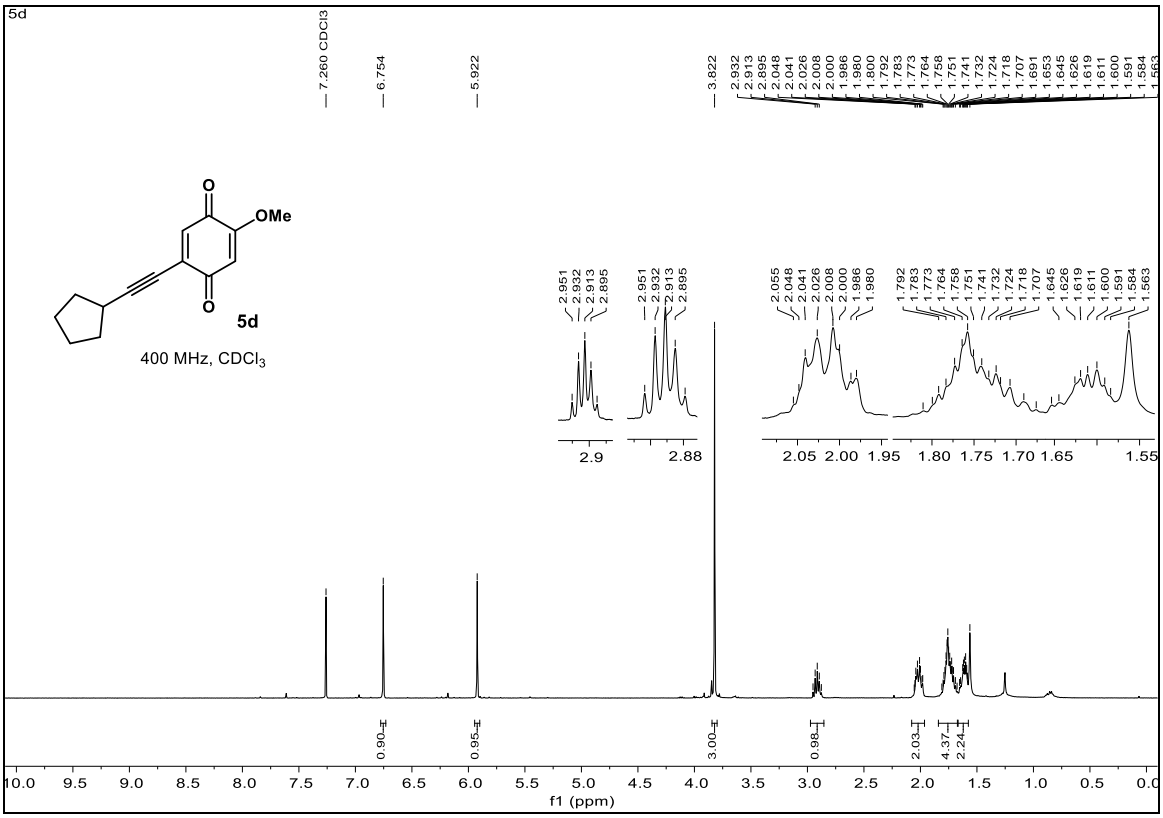
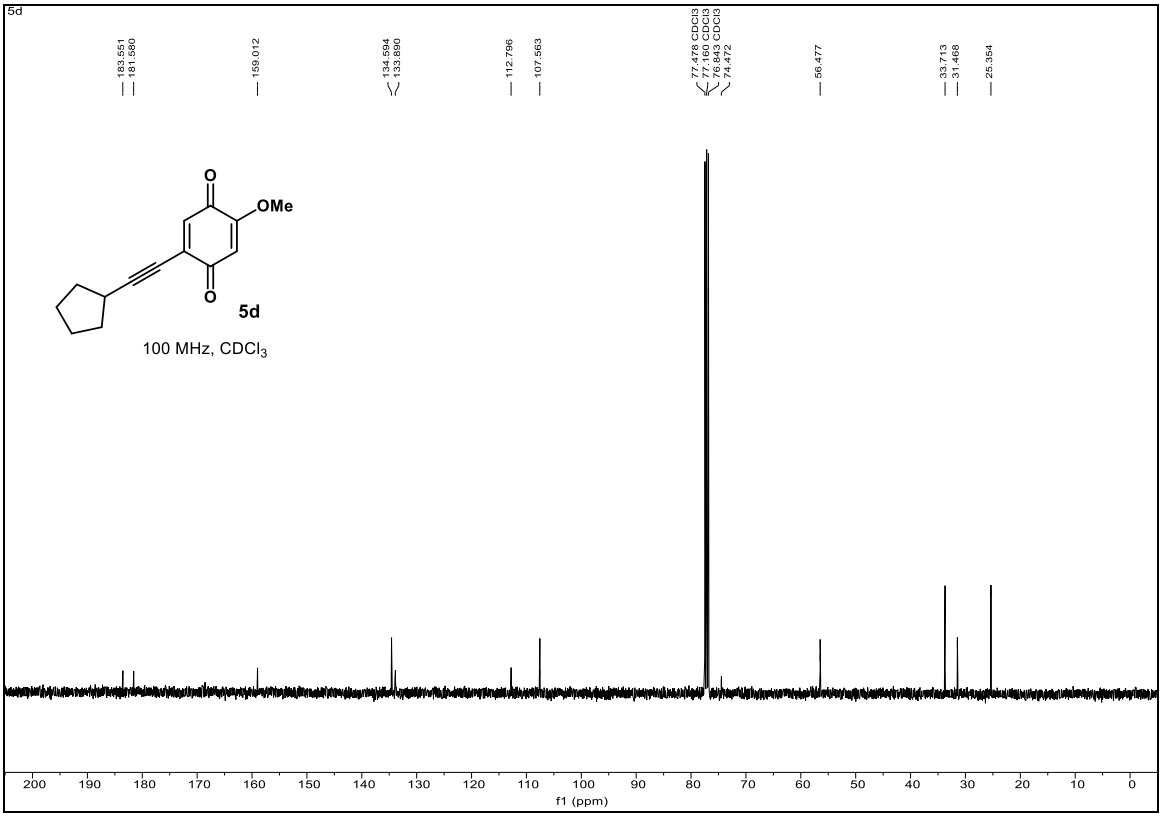
158.969
134.635
133.816
112.260
107.547
77.477 CDCl3
77.160 CDCl3
76.843 CDCl3
74.915
56.452
32.079
30.435
25.836
24.811
OMe
O
O
5c
100 MHz, CDCl3
f1 (ppm)


5d
7.260 CDCl3
6.754
5.922
3.822
O
OMe
O
5d
400 MHz, CDCl3
0.90
0.95
3.00
0.98
2.03
4.37
2.24
f1 (ppm)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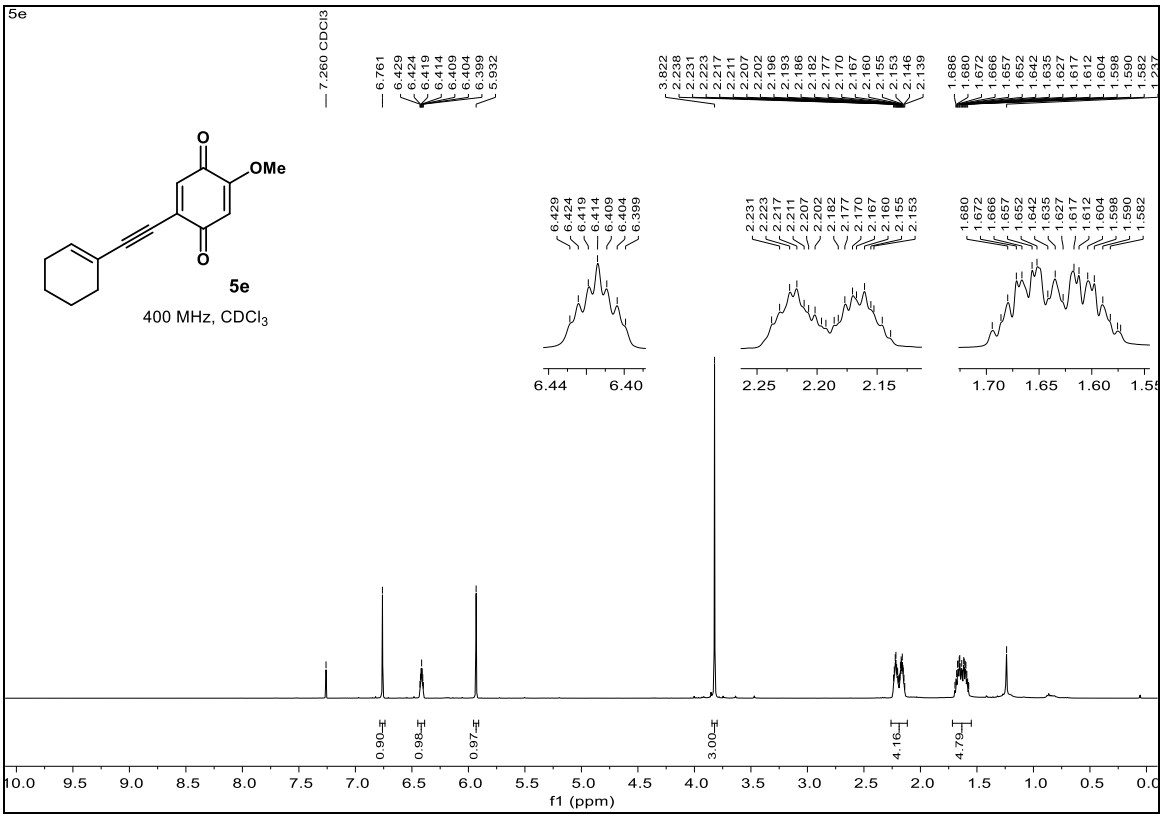
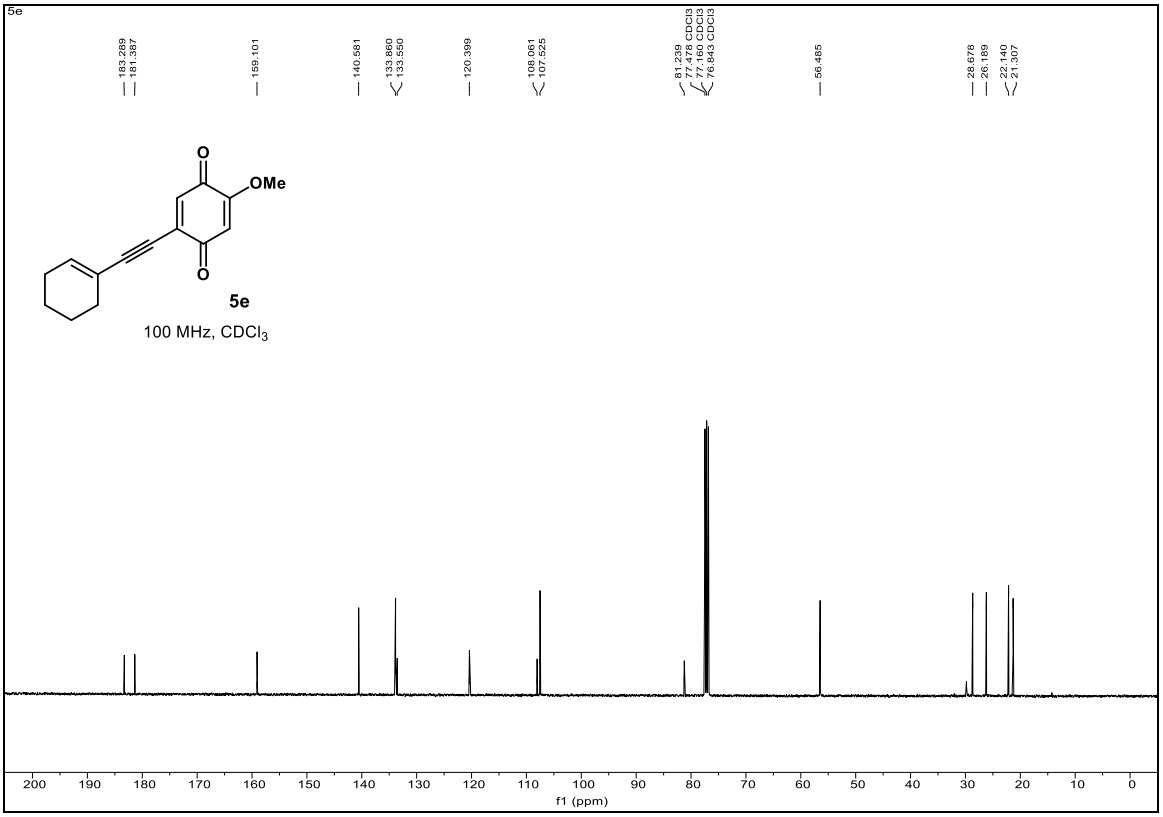
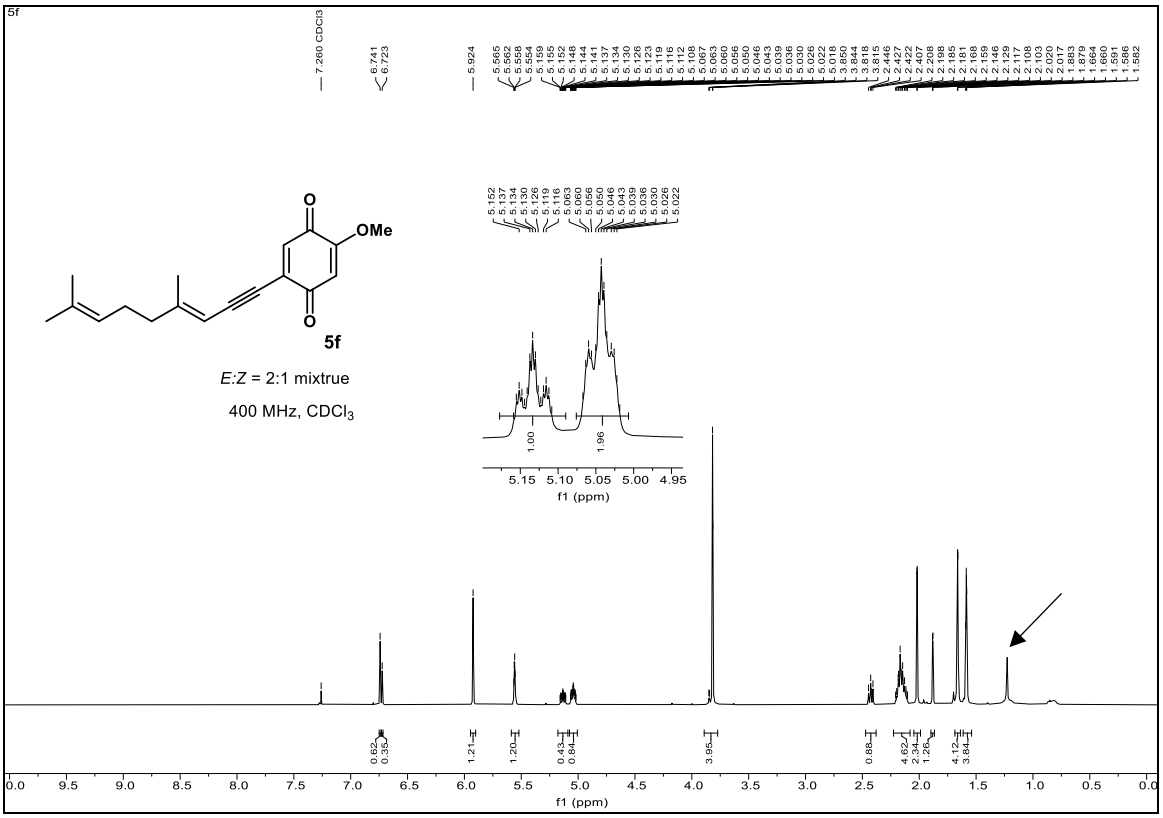
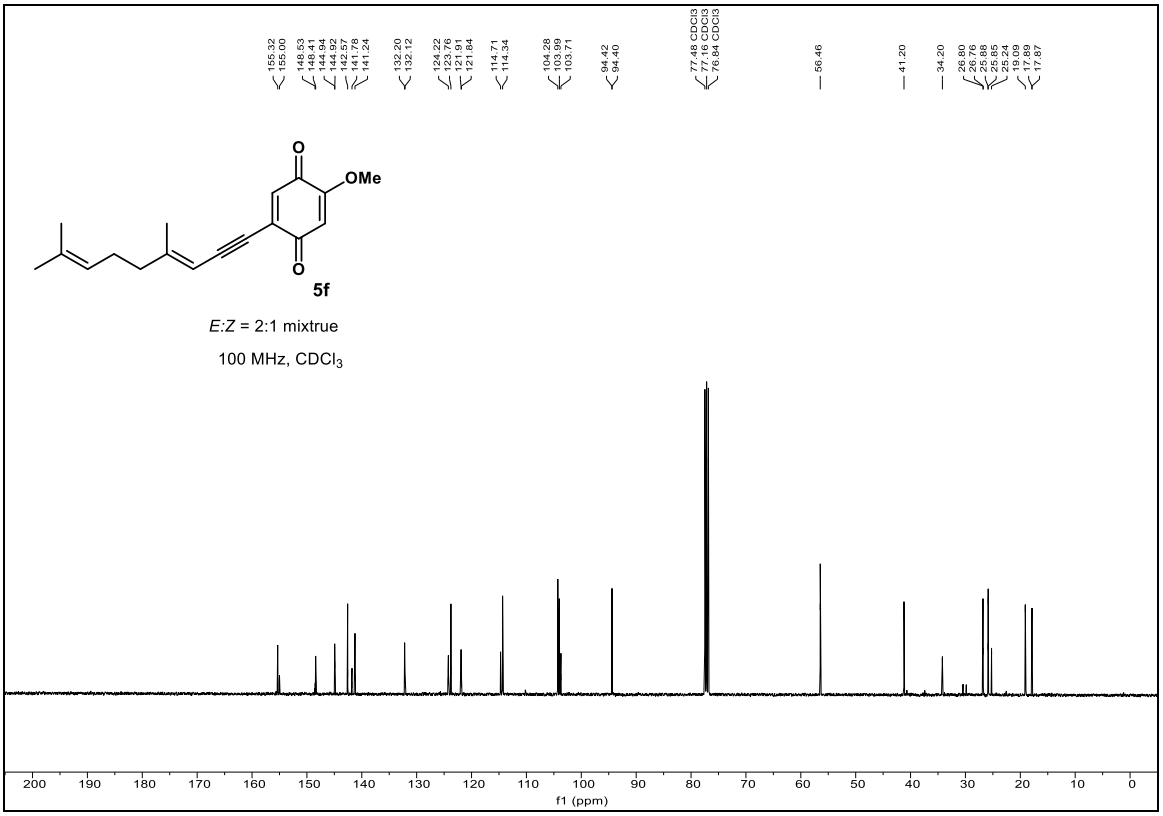
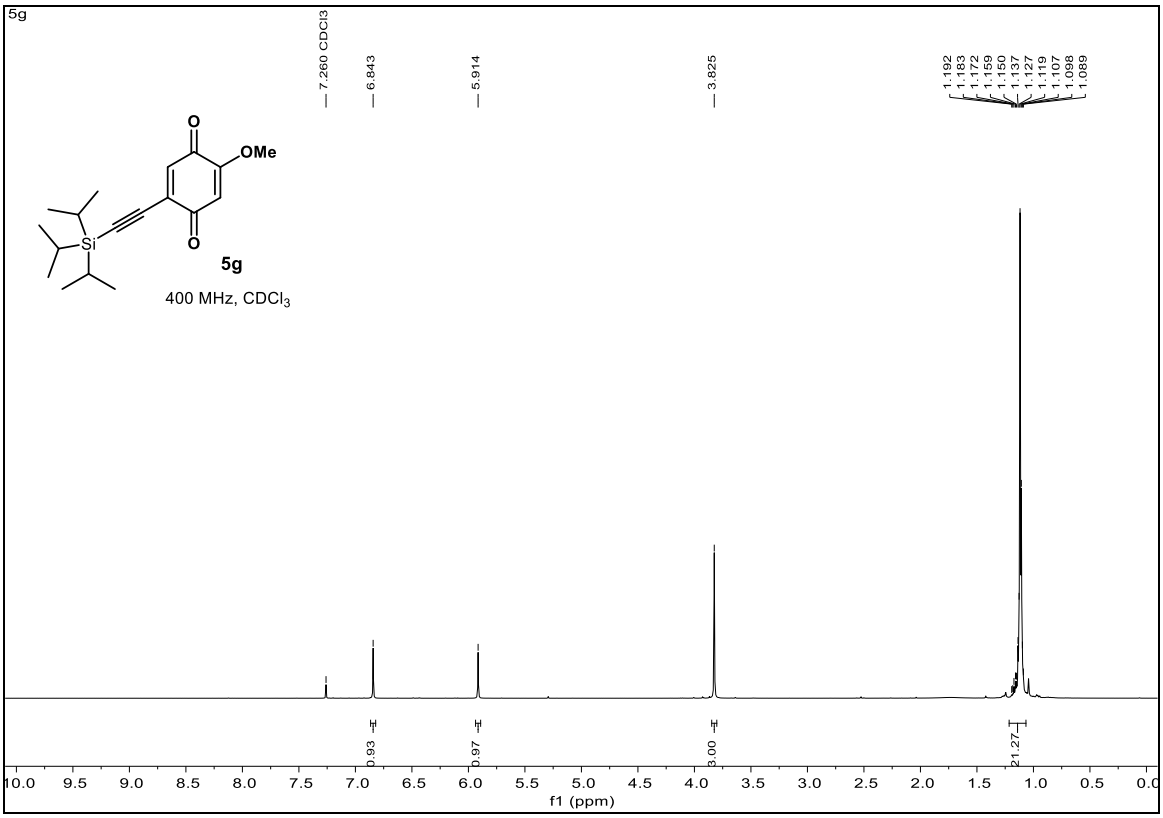
181.580
159.012
134.594
133.890
112.796
107.563
77.478 CDCl3
77.160 CDCl3
76.843 CDCl3
74.472
56.477
33.713
31.468
25.354
O
OMe
O
5d
100 MHz, CDCl3
f1 (ppm)

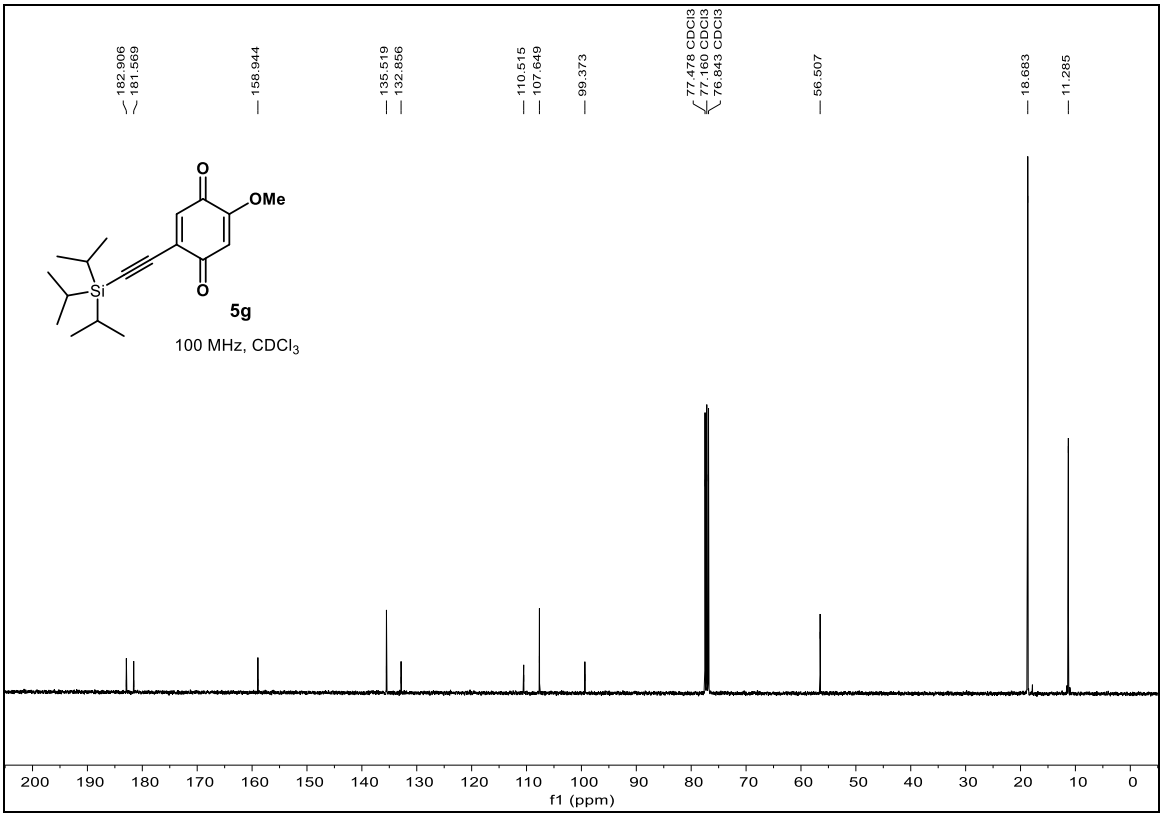

5e
OMe
5e
400 MHz, CDCl3
f1 (ppm)

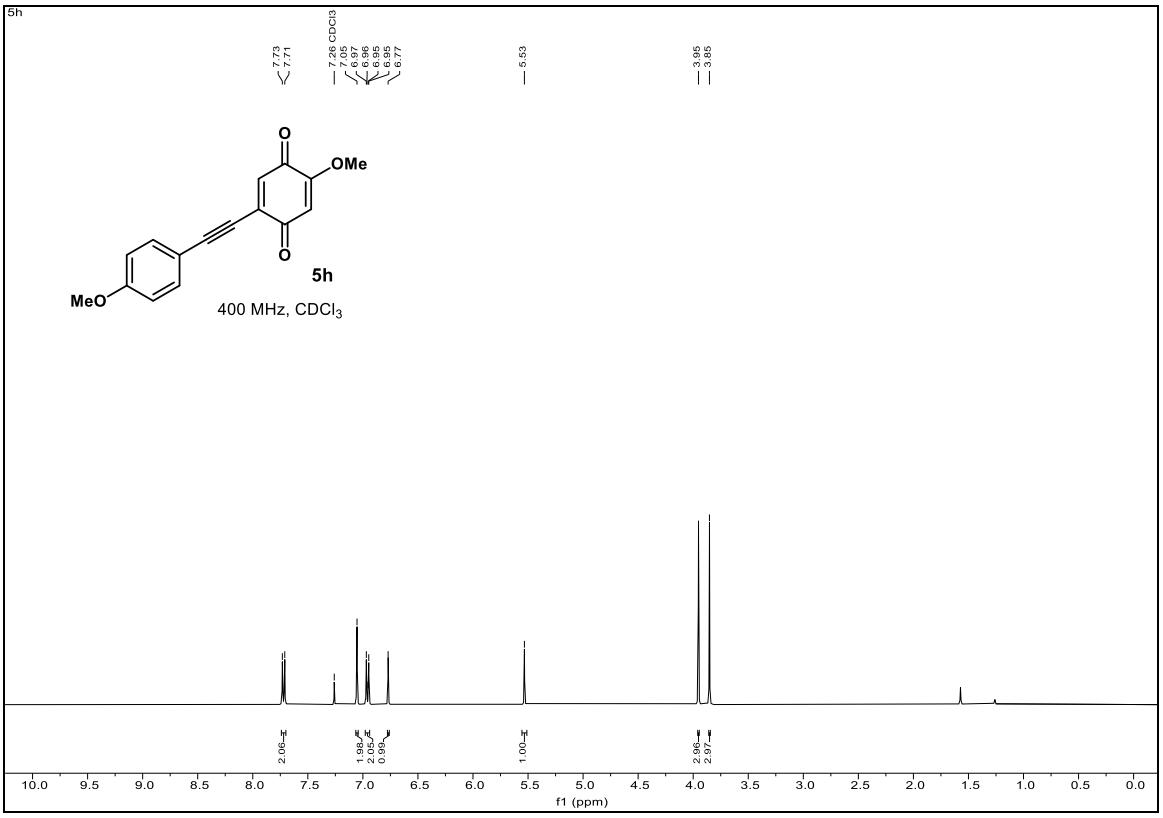

5e
OMe
5e
100 MHz, CDCl3
f1 (ppm)


5f
OMe
O
O
5f
E:Z = 2:1 mixtrue
400 MHz, CDCl3
f1 (ppm)


OMe
O
O
5f
E:Z = 2:1 mixtrue
100 MHz, CDCl3
f1 (ppm)


5g
7.260 CDCl3
6.843
5.914
3.825
1.192
1.183
1.172
1.159
1.150
1.137
1.127
1.119
1.107
1.098
1.089
OMe
O
O
Si
5g
400 MHz, CDCl3
0.93
0.97
3.00
21.27
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)


182.906
181.569
158.944
135.519
132.856
110.515
107.649
99.373
77.478 CDCl3
77.160 CDCl3
76.843 CDCl3
56.507
18.683
11.285
OMe
O
O
Si
5g
100 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


5h
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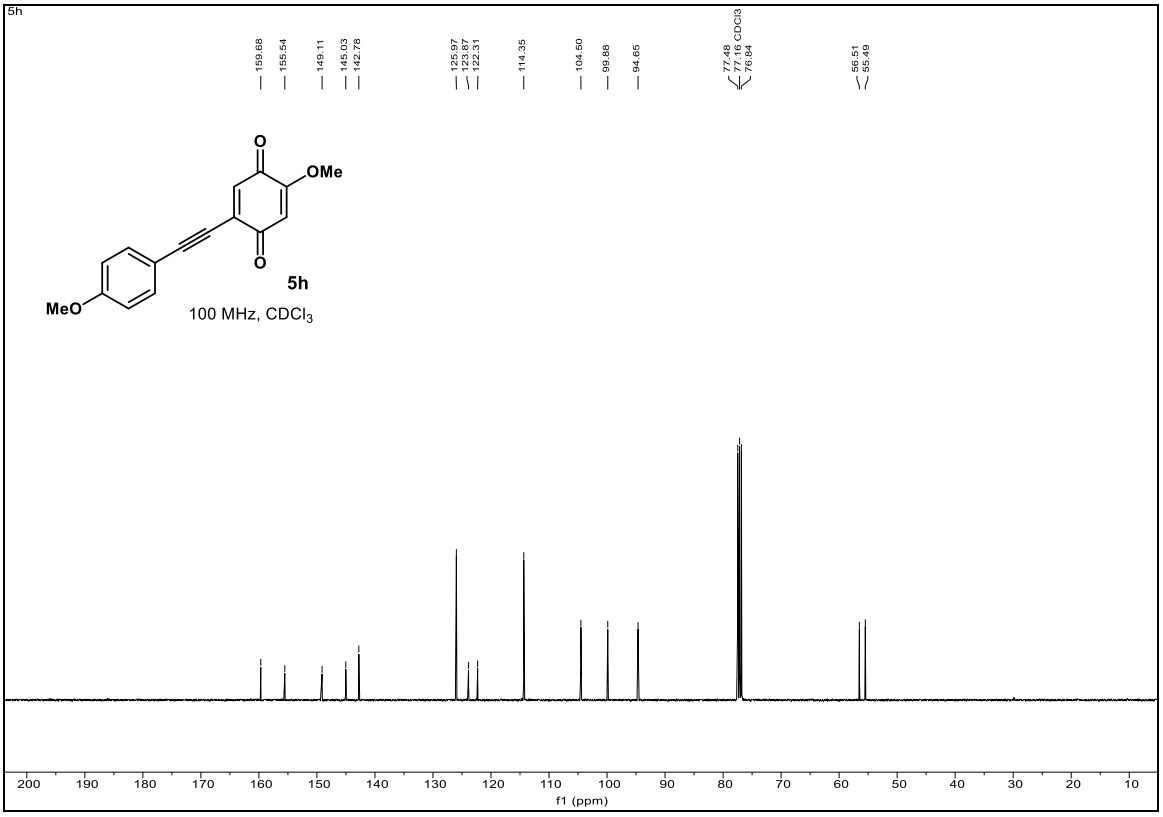
7.71
7.26 CDCl3
7.05
6.97
6.96
6.95
6.95
6.77
5.53
3.95
3.85
O
OMe
O
MeO
5h
400 MHz, CDCl3
2.06
1.98
2.05
0.99
1.00
2.96
2.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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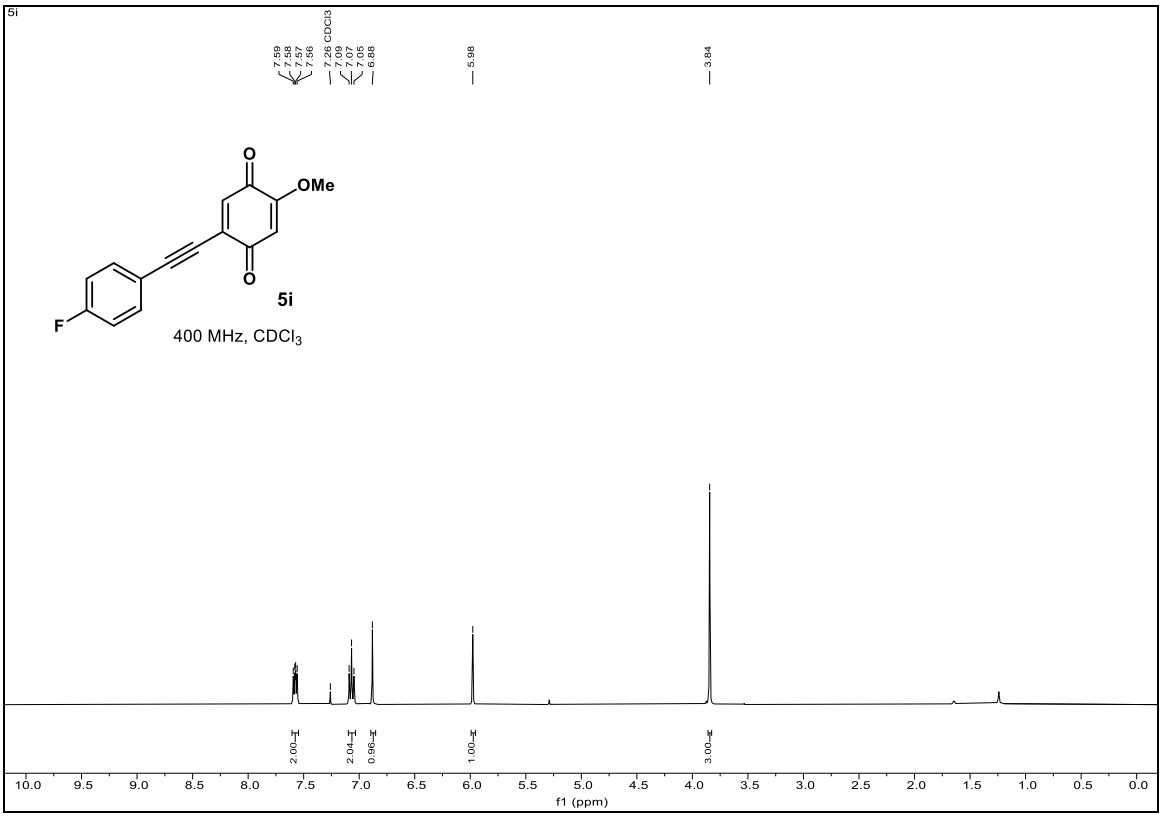
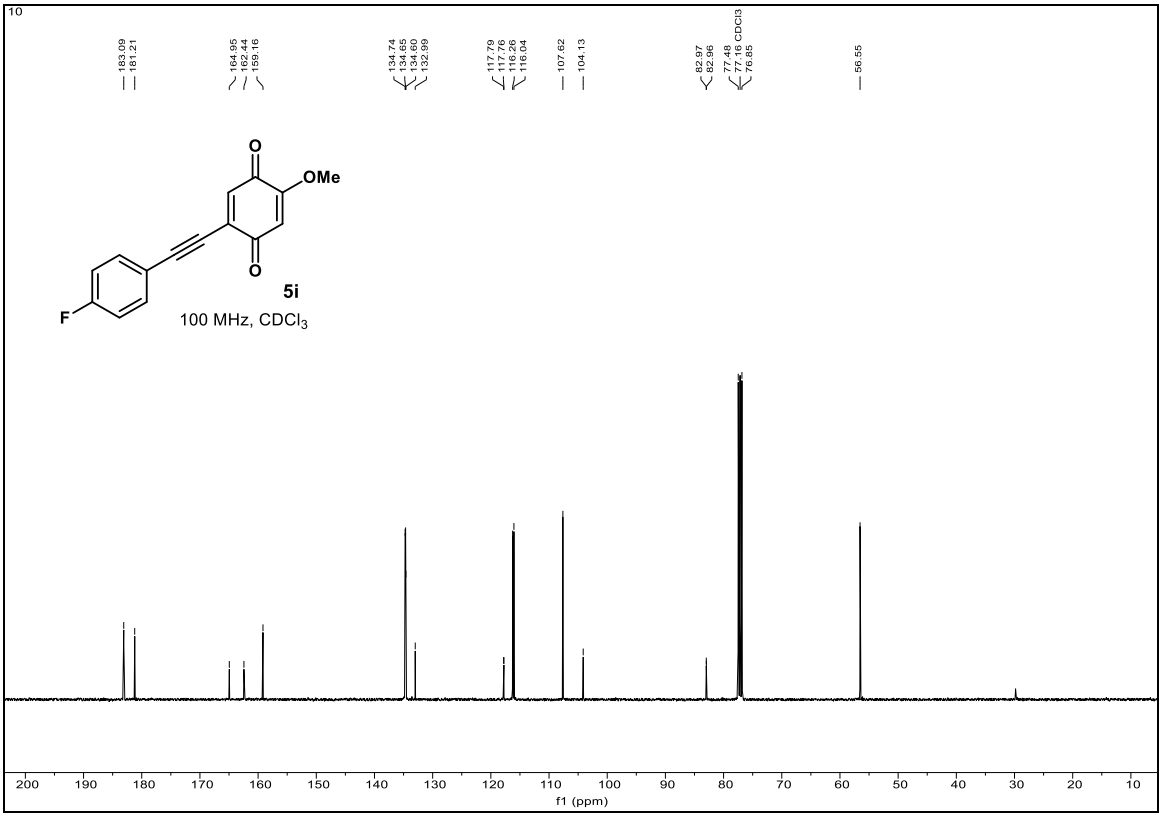
159.68
155.54
149.11
145.03
142.78
125.97
123.87
122.31
114.35
104.50
99.88
94.65
77.48
77.16 CDCl3
76.84
56.51
55.49
O
OMe
O
MeO
5h
100 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


5i
7.59
7.58
7.57
7.56
7.26 CDCl3
7.09
7.07
7.05
6.88
5.98
3.84
O
OMe
O
F
5i
400 MHz, CDCl3
2.00
2.04
0.96
1.00
3.00
f1 (ppm)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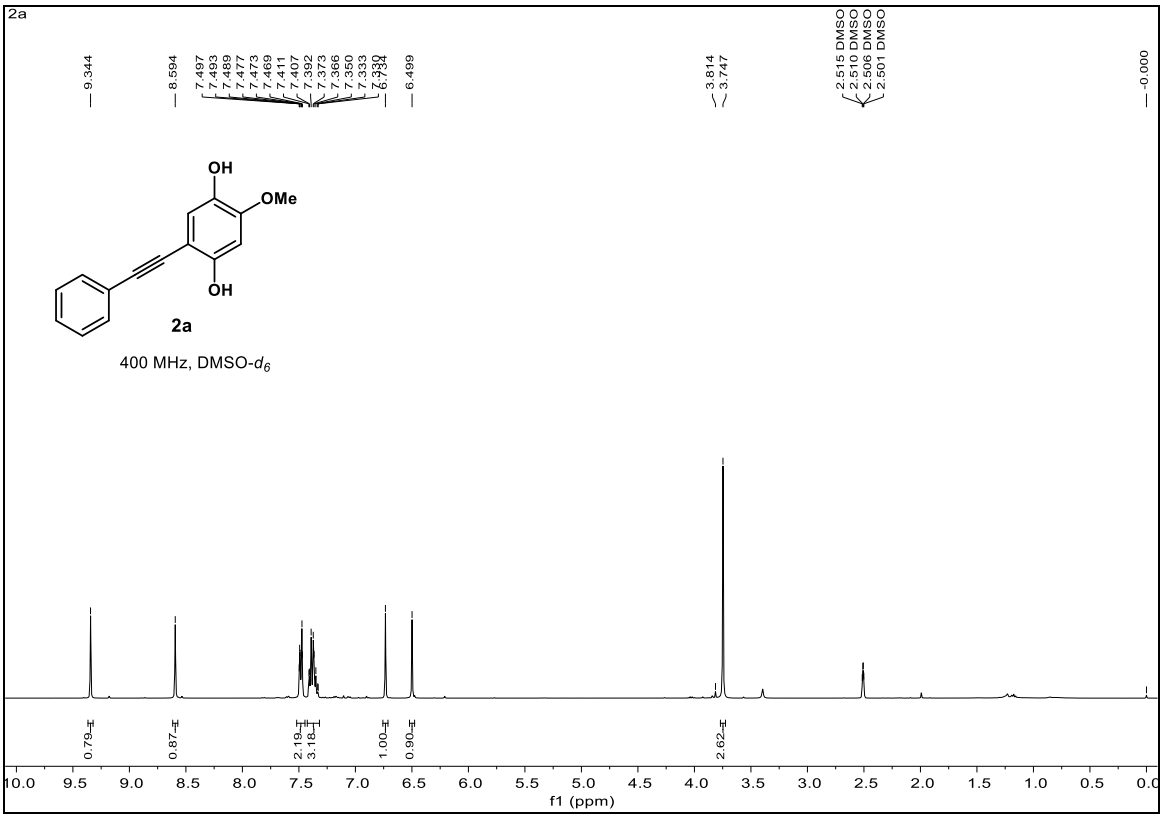
183.09
181.21
164.95
162.44
159.16
134.74
134.65
134.60
132.99
117.79
117.76
116.26
116.04
107.62
104.13
82.97
82.96
77.48
77.16 CDCl3
76.85
56.55
O
OMe
O
F
5i
100 MHz, CDCl3
f1 (ppm)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9.344
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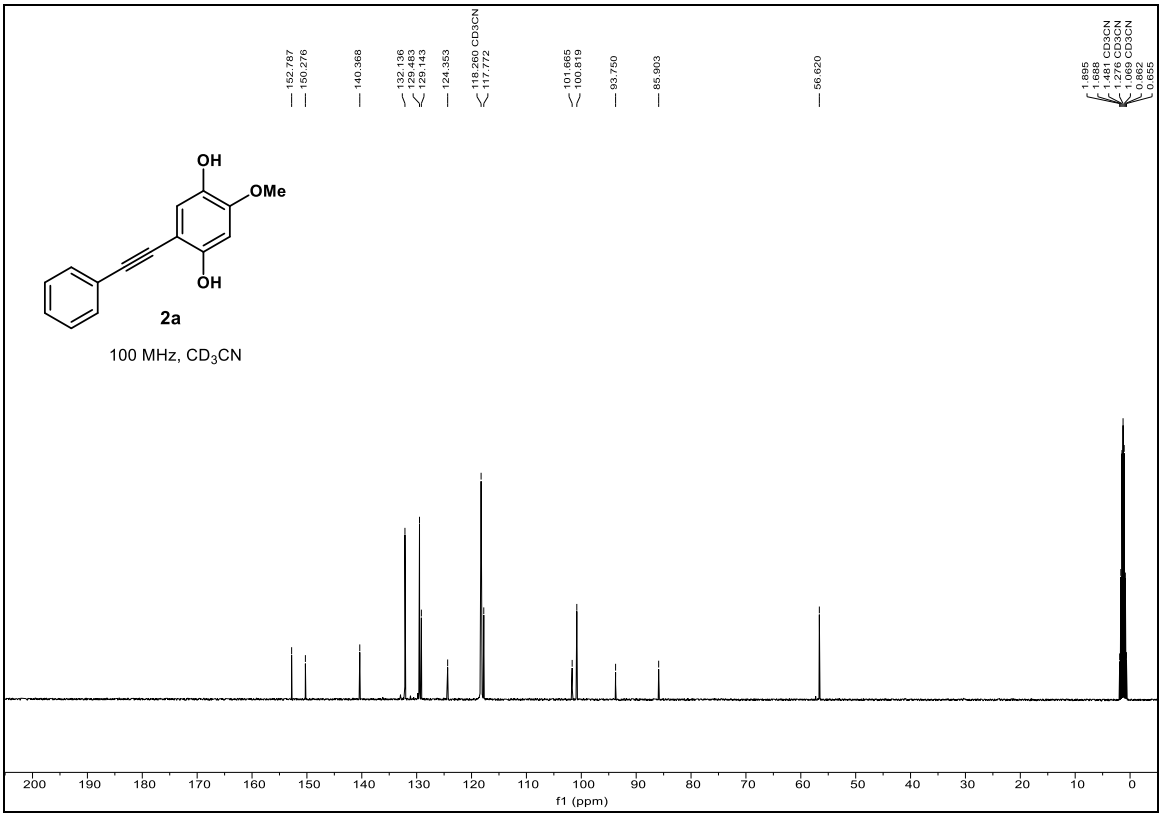
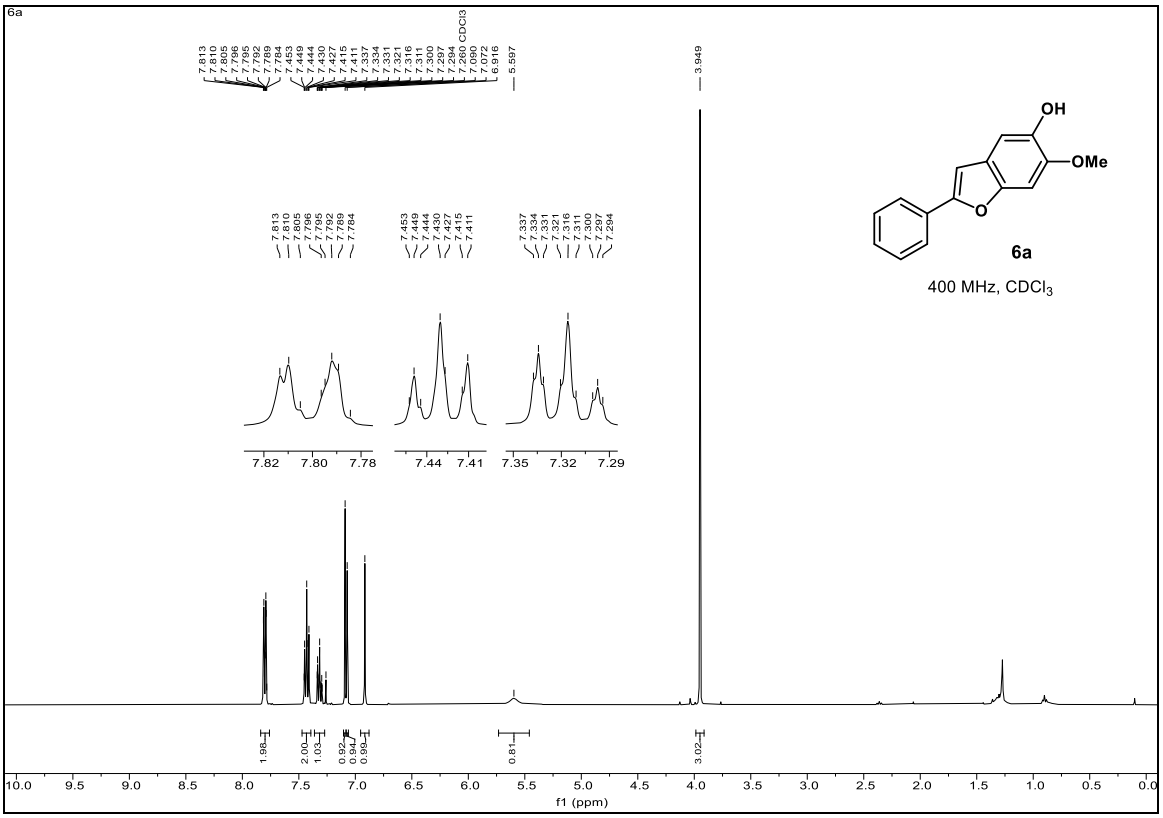
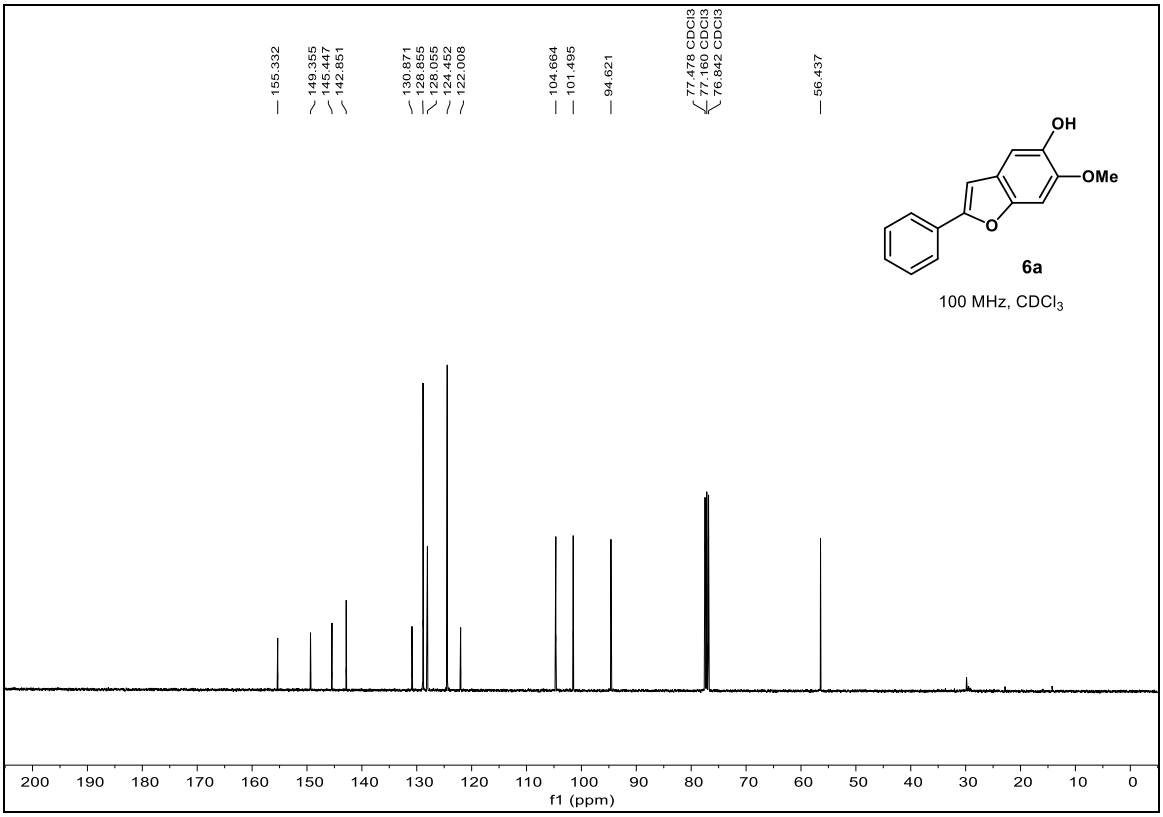
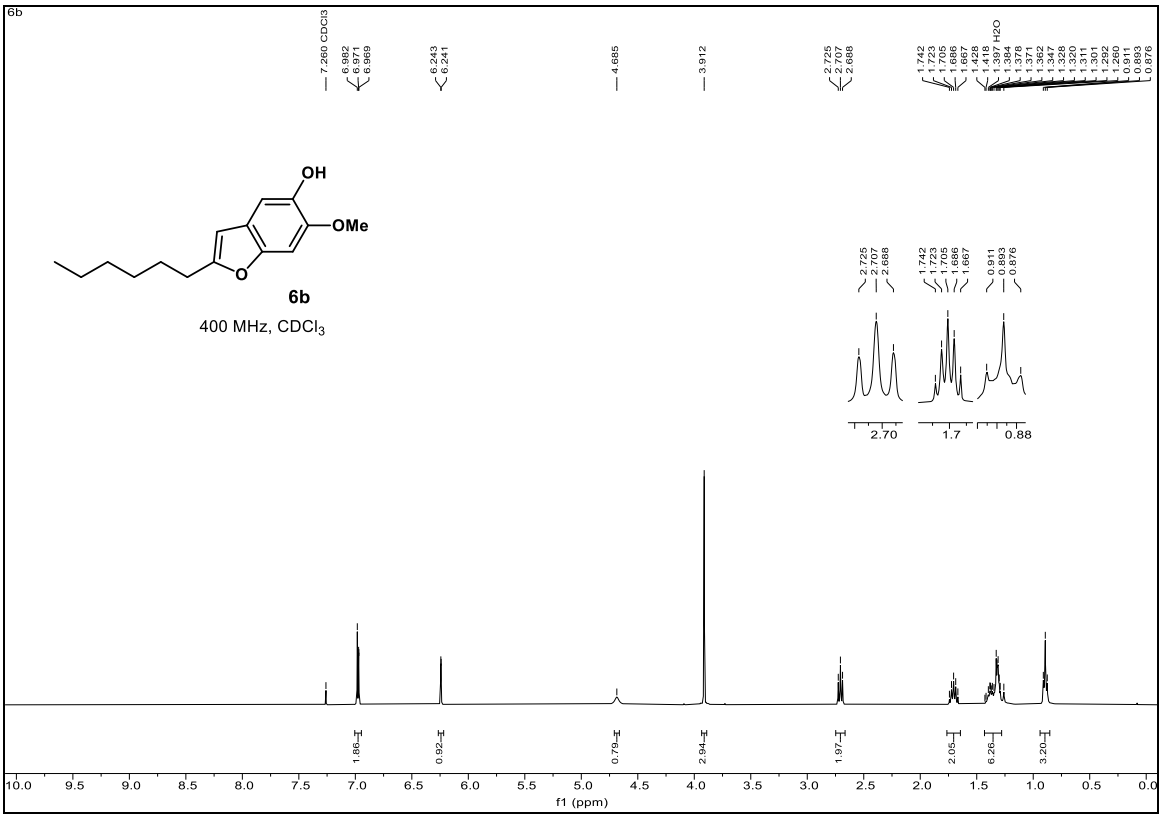
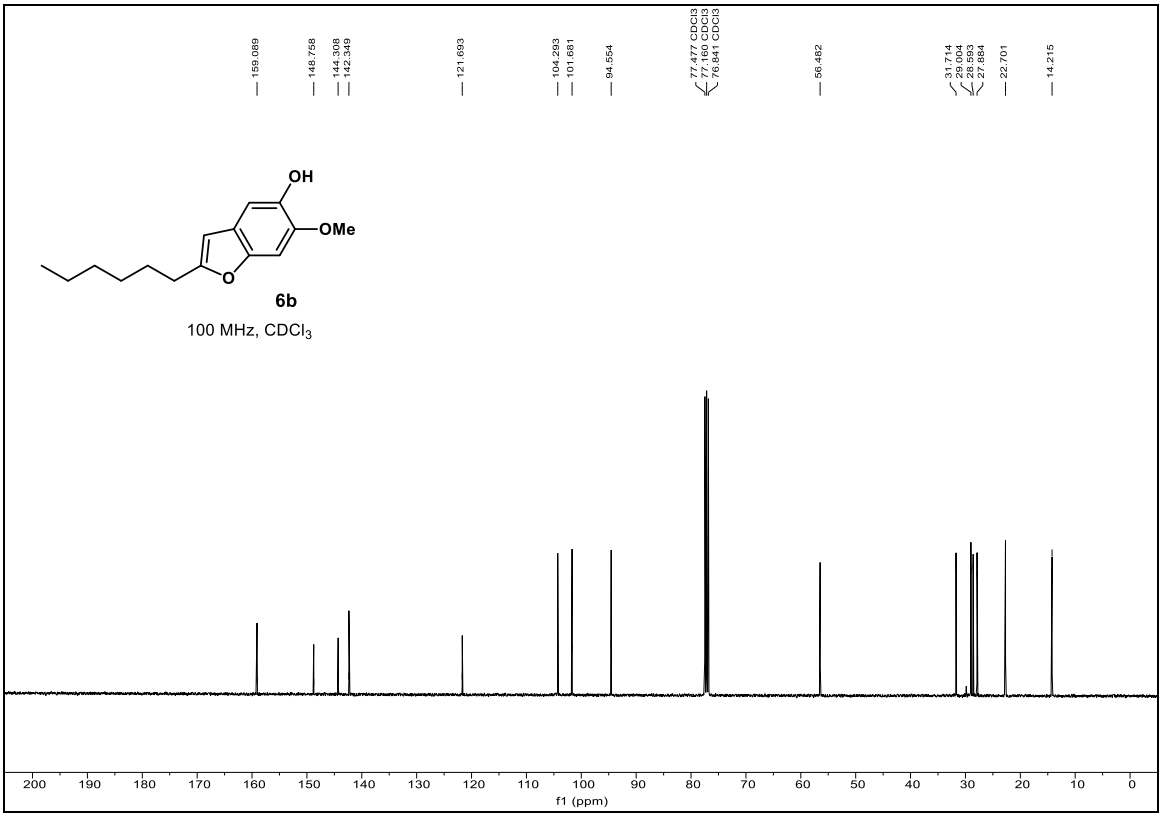
7.497
7.493
7.489
7.477
7.473
7.469
7.411
7.407
7.392
7.373
7.366
7.350
7.333
7.330
7.324
6.499
3.814
3.747
2.515 DMSO
2.510 DMSO
2.506 DMSO
2.501 DMSO
-0.000
OH
OMe
OH
2a
400 MHz, DMSO-d_6
0.79
0.87
2.19
3.18
1.00
0.90
2.62
f1 (ppm)

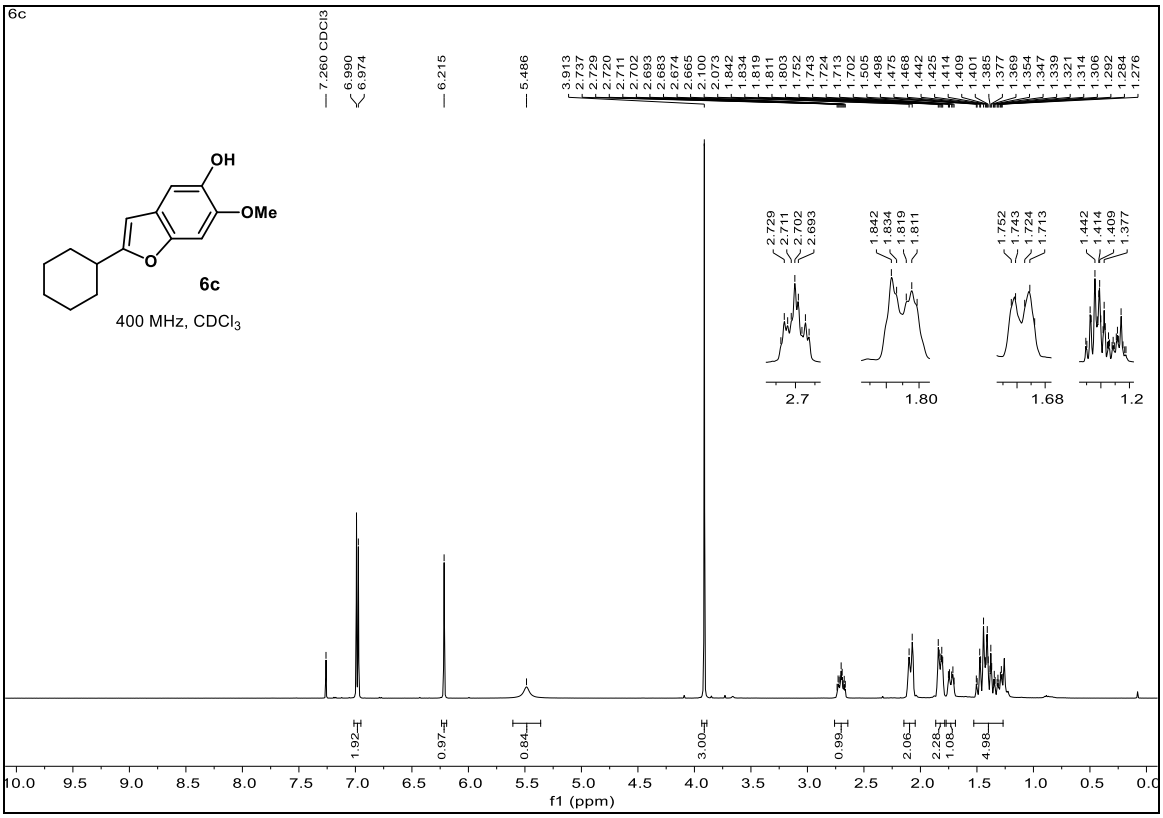

152.787
150.276
140.368
132.136
129.483
129.143
124.353
118.260 CD3CN
117.772
101.665
100.819
93.750
85.903
56.620
1.895
1.688
1.641 CD3CN
1.276 CD3CN
1.069 CD3CN
0.862
0.655
OH
OMe
OH
2a
100 MHz, CD_3CN
f1 (ppm)

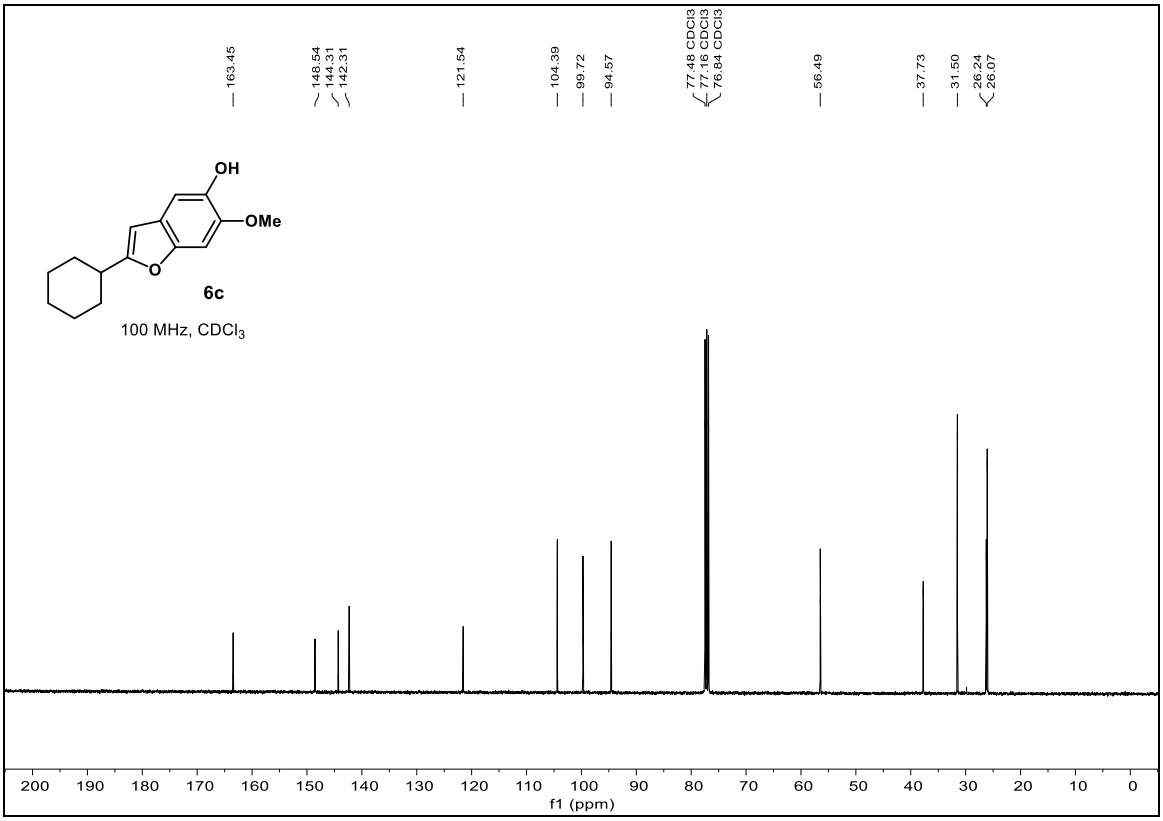

6a
OH
OMe
O
6a
400 MHz, CDCl3
f1 (ppm)

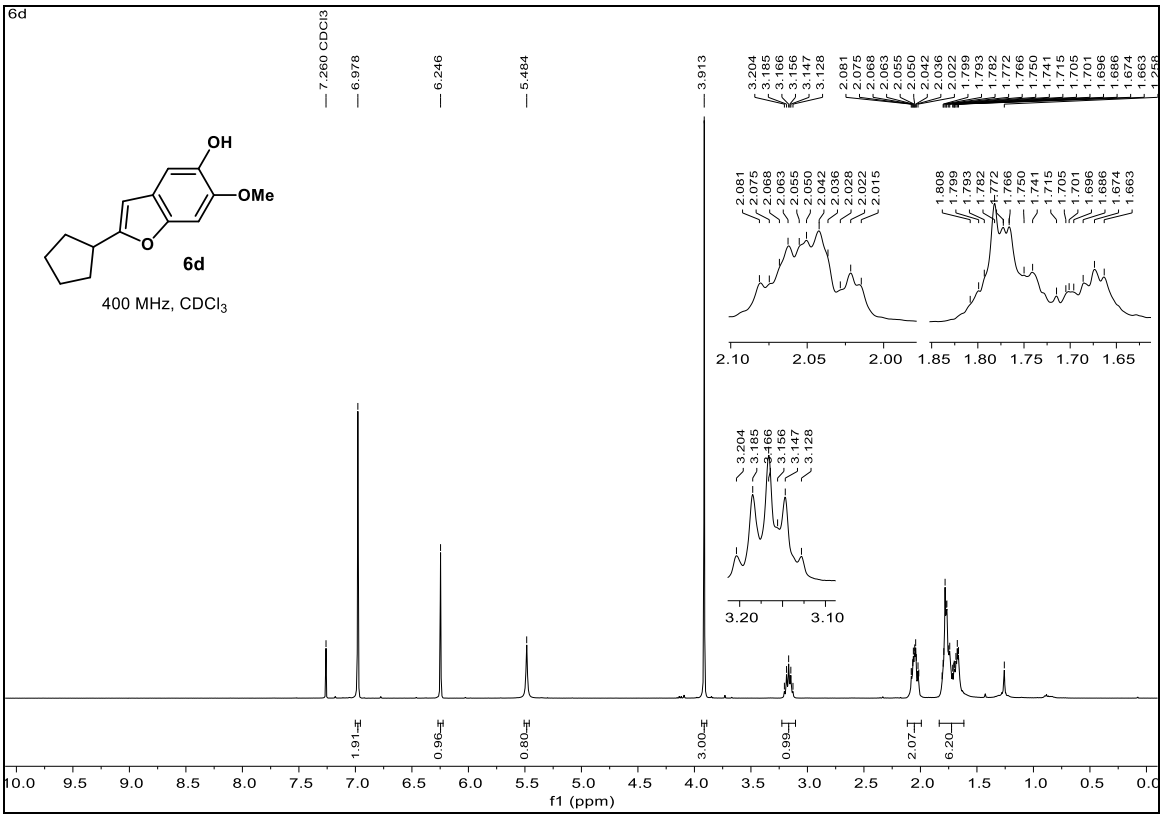

OH
OMe
O
6a
100 MHz, CDCl3
f1 (ppm)

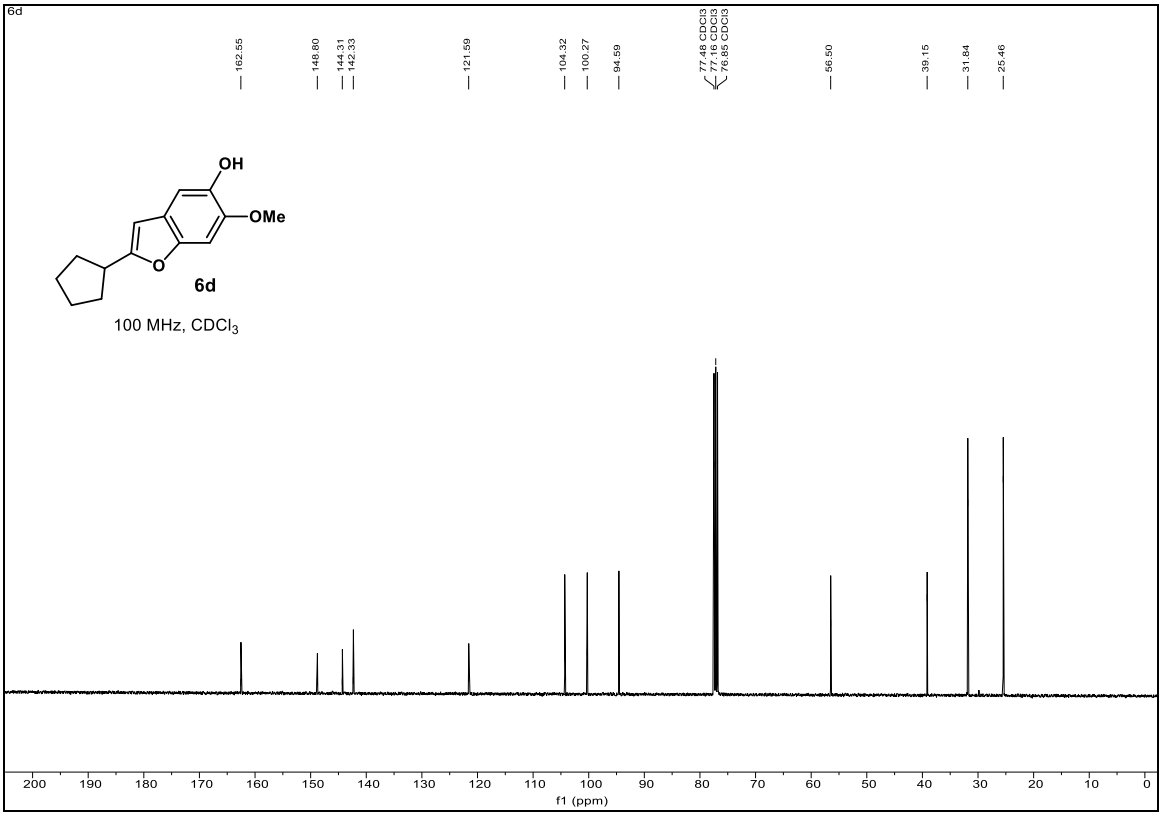

6b
OH
OMe
O
6b
400 MHz, CDCl3
f1 (ppm)

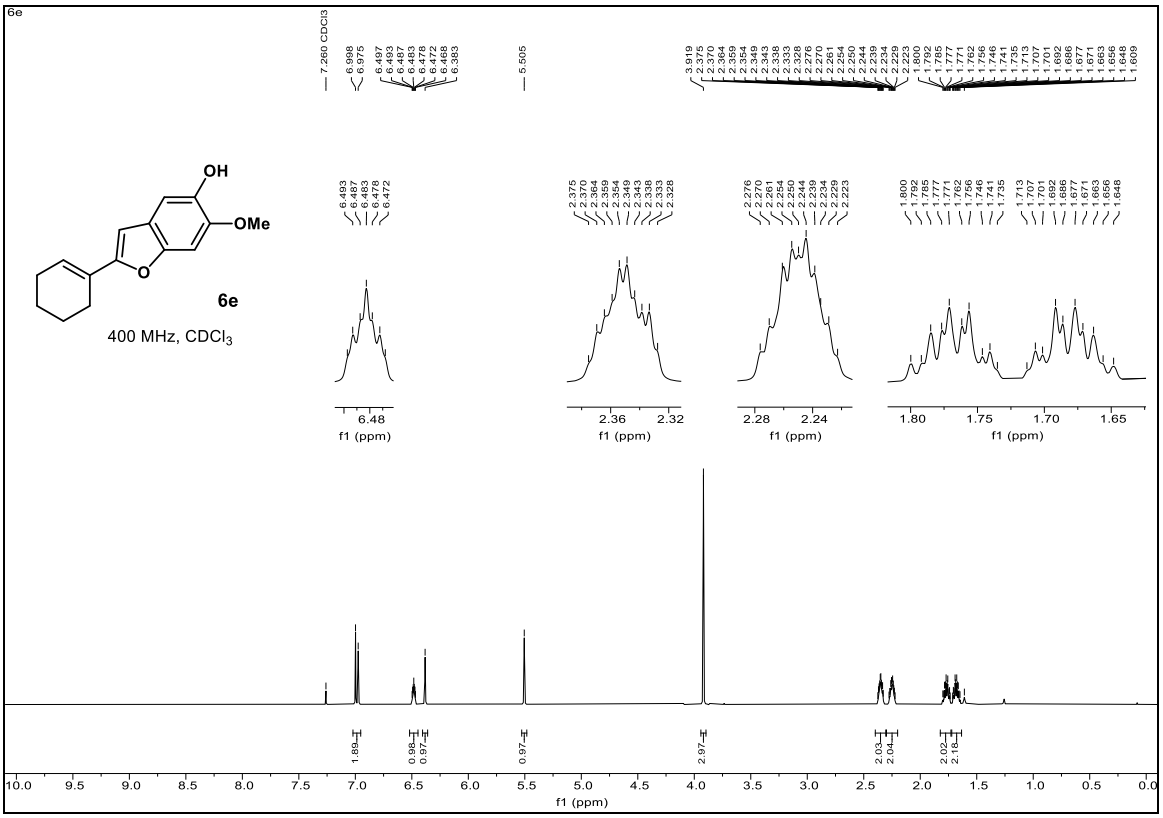

OH
OMe
O
6b
100 MHz, CDCl3
f1 (ppm)

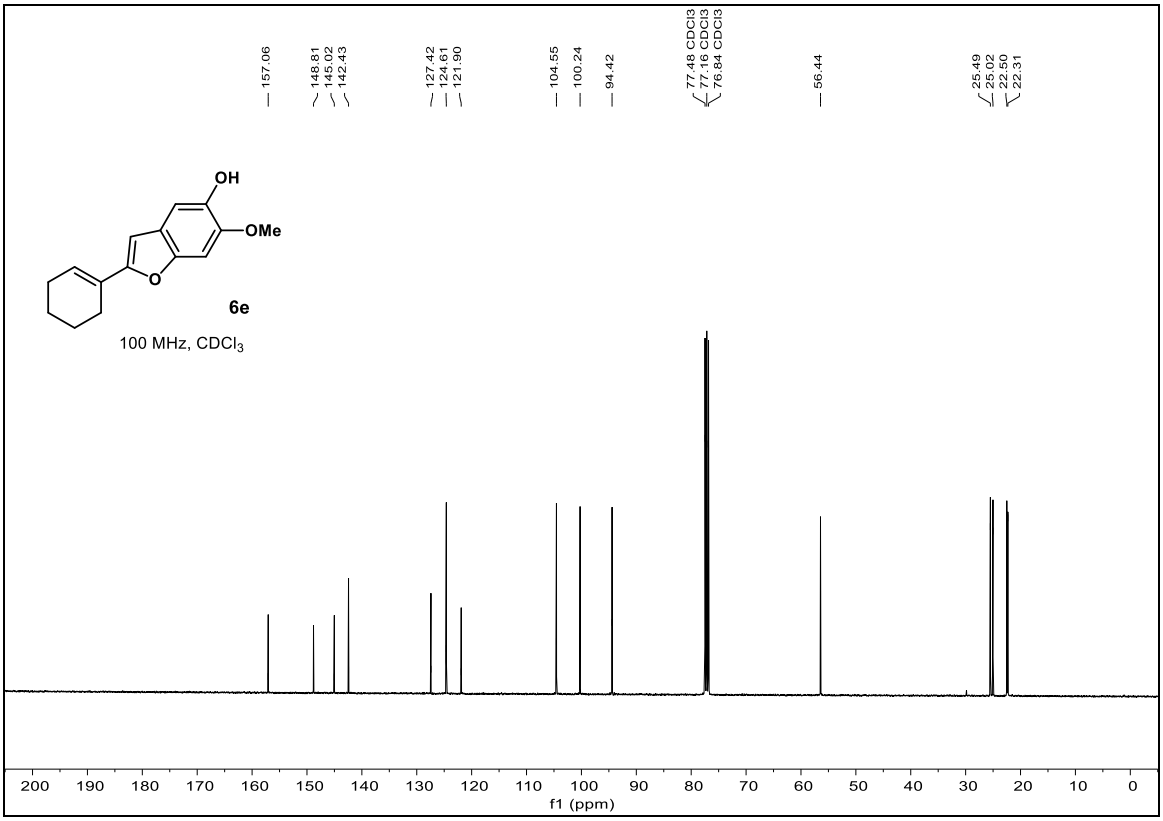

6c
7.260 CDCl3
6.990
6.974
6.215
5.486
OH
OMe
O
6c
400 MHz, CDCl3
1.92
0.97
0.84
3.00
0.99
2.06
2.28
1.08
4.98
f1 (ppm)

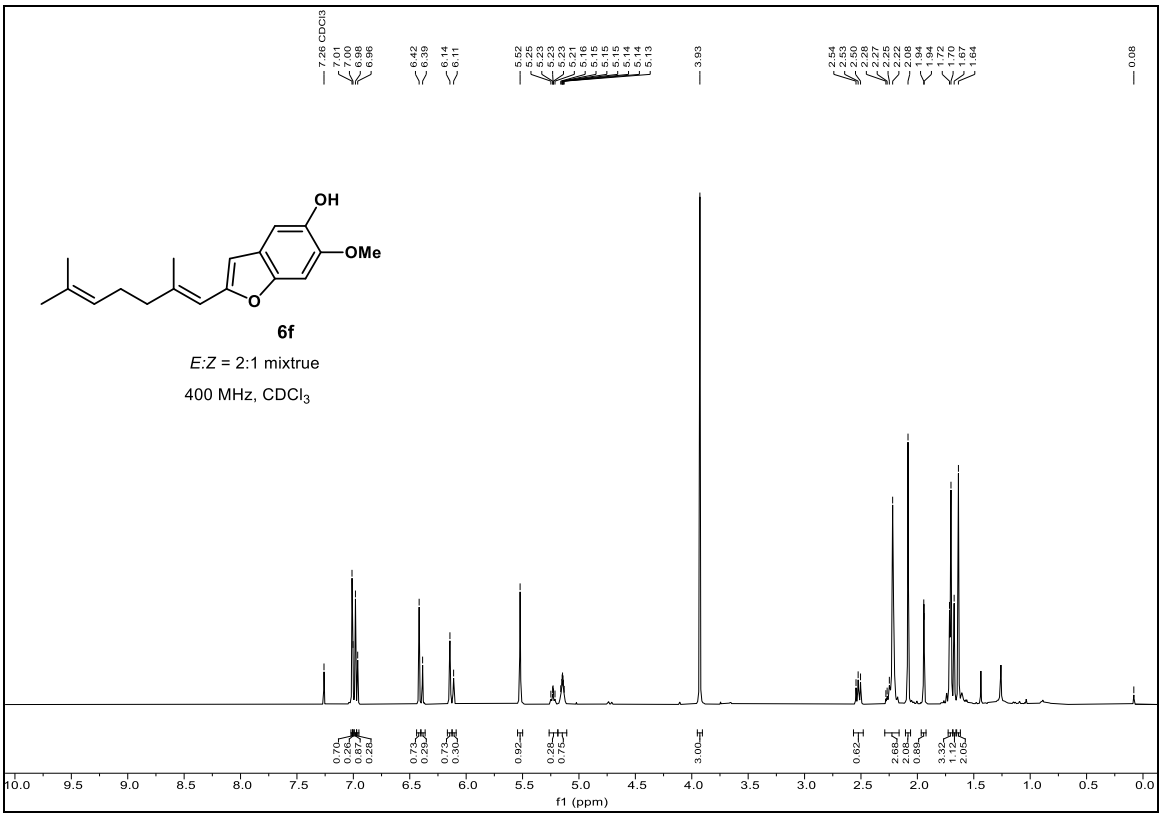

163.45
148.54
144.31
142.31
121.54
104.39
99.72
94.57
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.49
37.73
31.50
26.24
26.07
OH
OMe
O
6c
100 MHz, CDCl3
f1 (ppm)

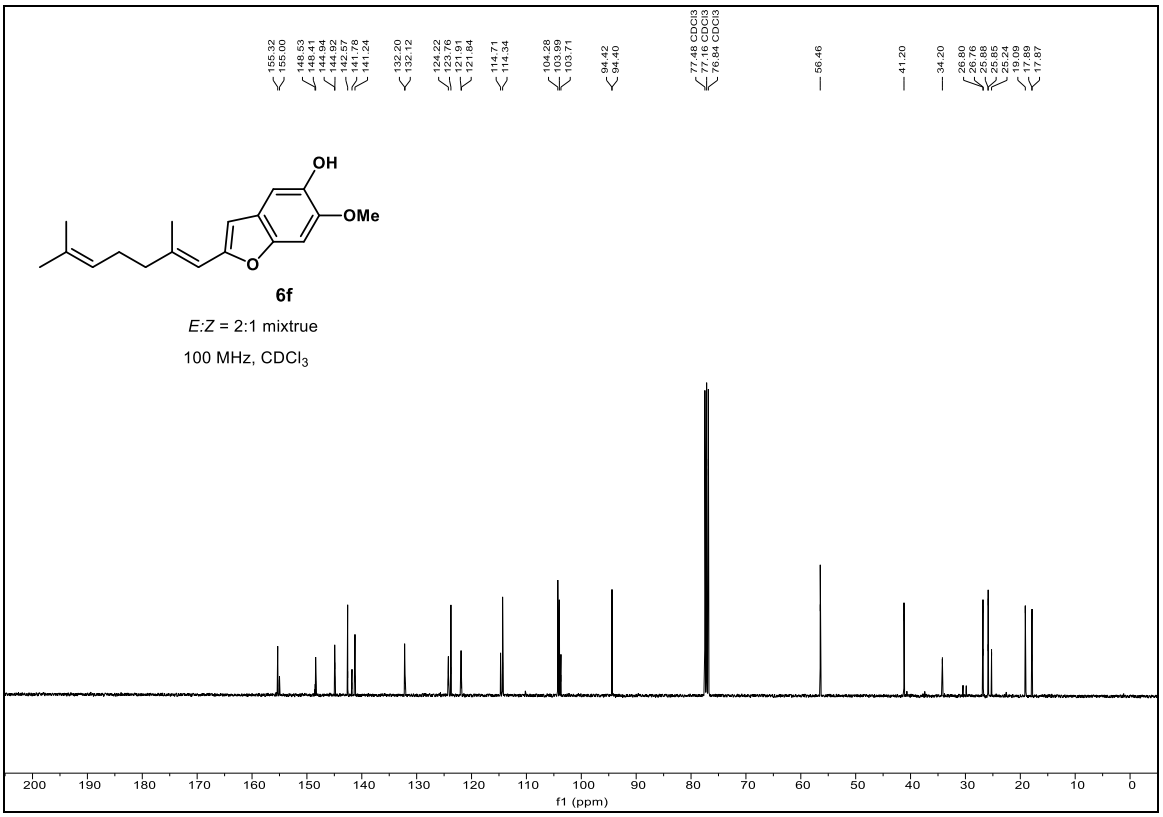

6d
OH
OMe
O
6d
400 MHz, CDCl3
f1 (ppm)

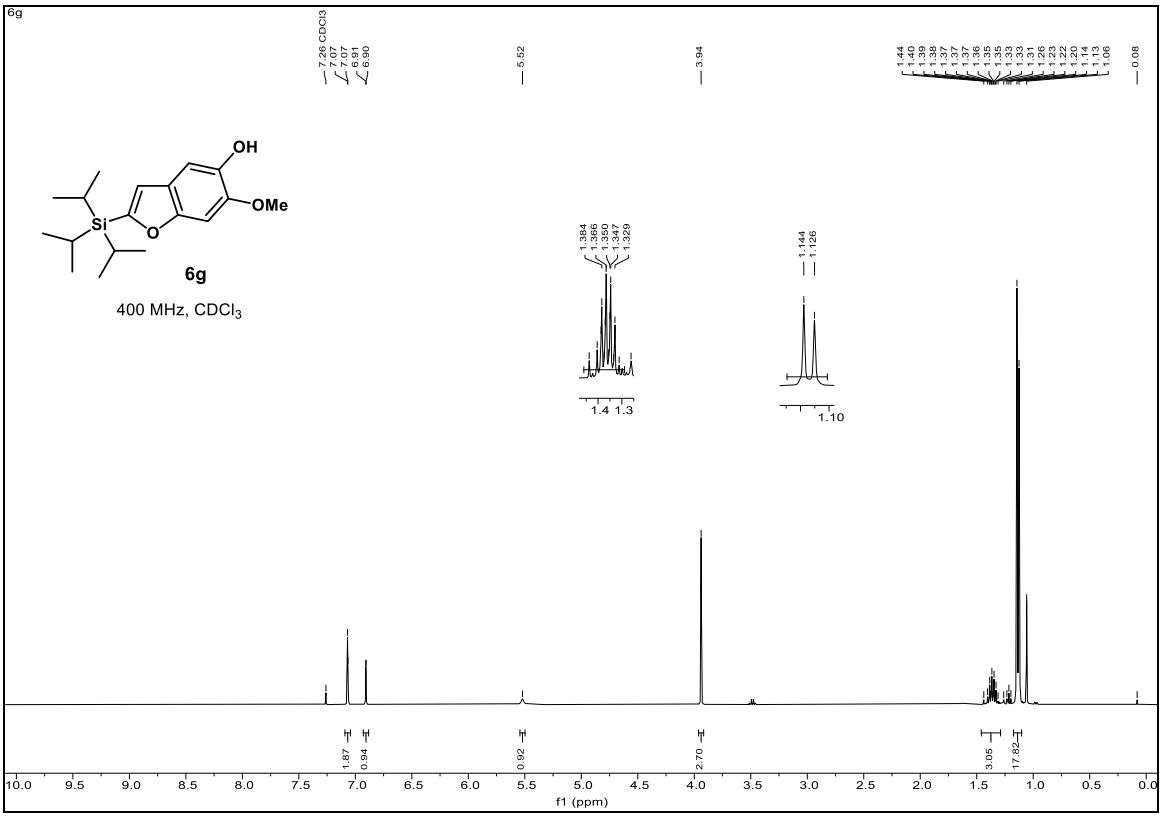

6d
OH
OMe
O
6d
100 MHz, CDCl3
f1 (ppm)

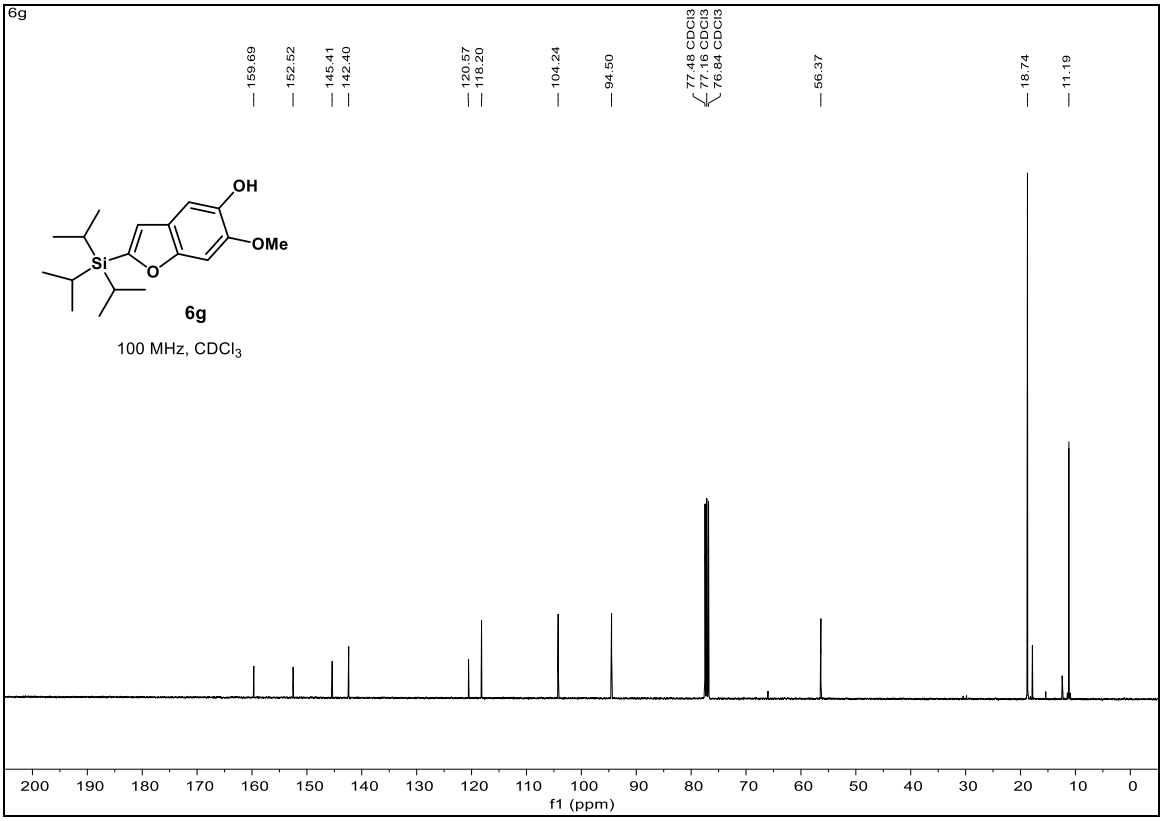

6e
OH
OMe
O
6e
400 MHz, CDCl3
f1 (ppm)

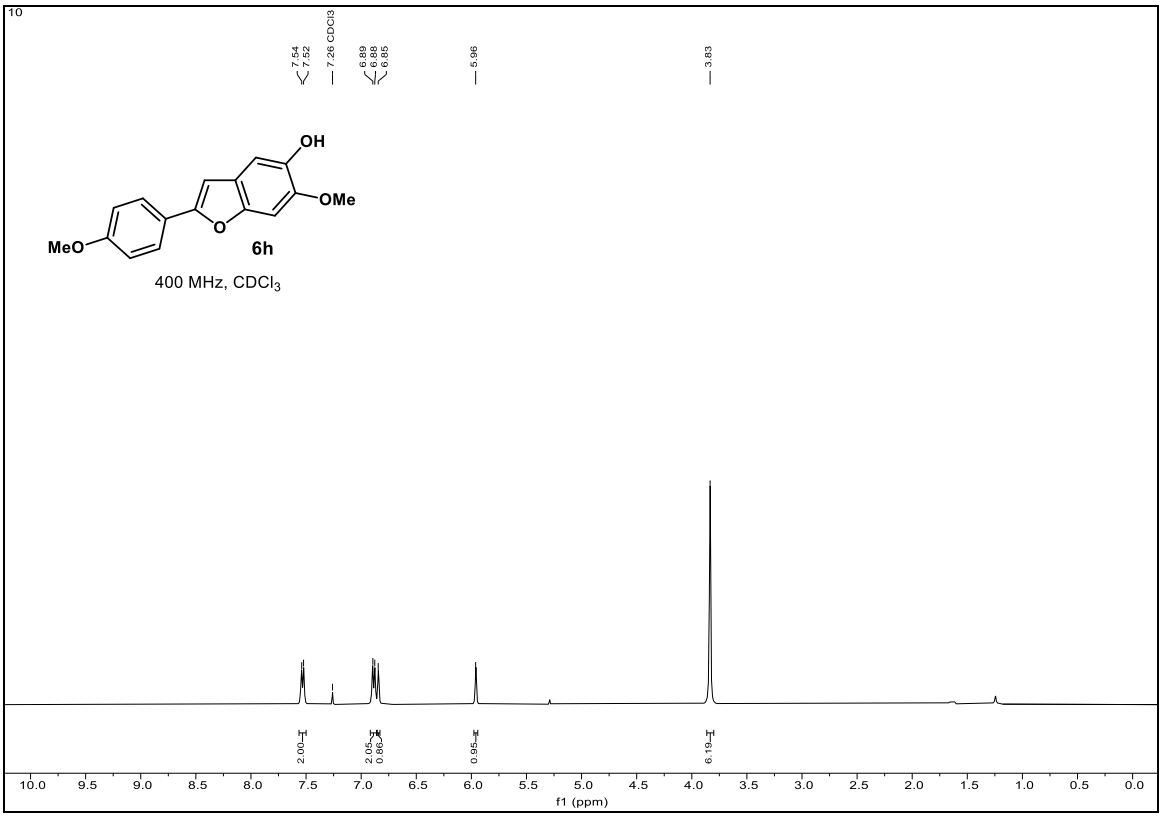

OH
OMe
O
6e
100 MHz, CDCl3
f1 (ppm)

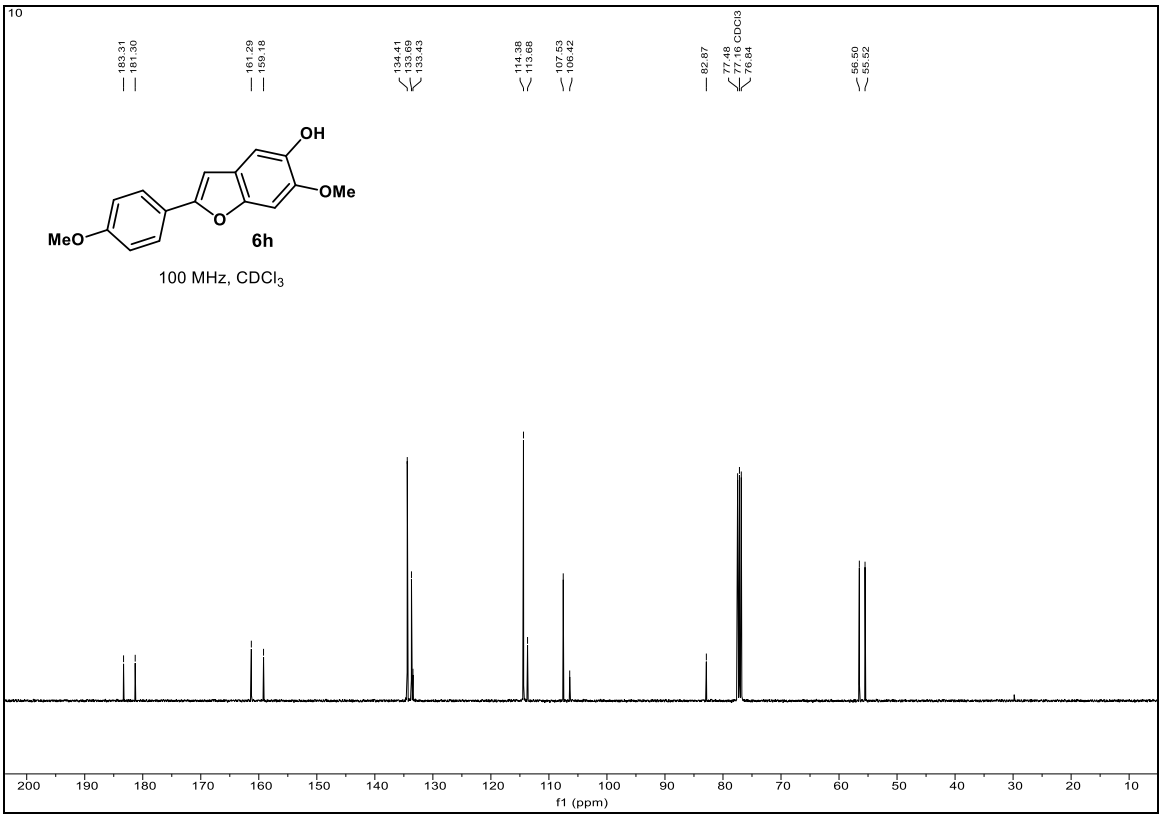

7.26 CDCl3
7.01
7.00
6.98
6.96
6.42
6.39
6.14
6.11
5.52
5.25
5.23
5.23
5.21
5.16
5.15
5.15
5.15
5.14
5.13
3.93
2.54
2.53
2.50
2.28
2.27
2.25
2.22
2.08
1.94
1.94
1.72
1.70
1.67
1.64
0.08
OH
OMe
O
6f
E:Z = 2:1 mixtrue
400 MHz, CDCl3
0.70
0.26
0.87
0.28
0.73
0.29
0.73
0.30
0.82
0.28
0.75
3.00
0.62
2.68
2.08
0.89
3.32
1.12
2.05
f1 (ppm)

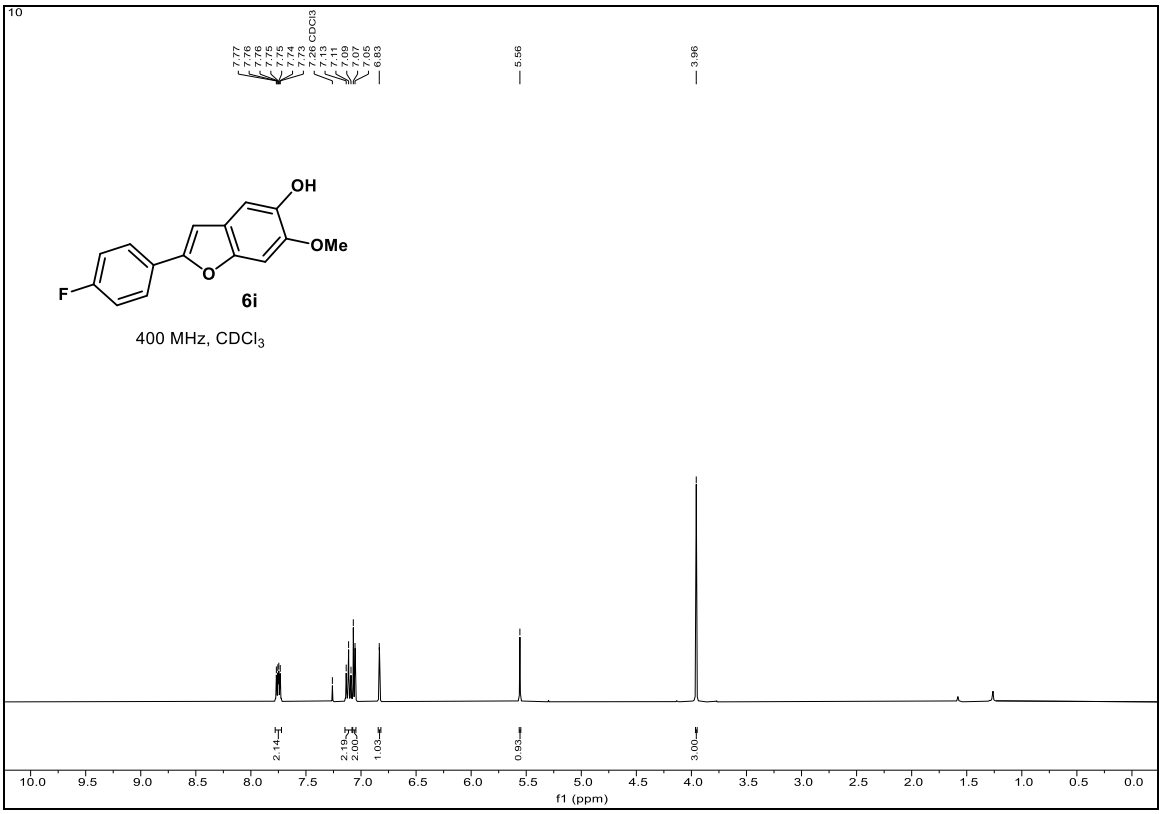

155.32
155.00
148.53
146.41
144.84
144.92
142.57
141.78
141.24
132.20
132.12
124.22
123.76
121.91
121.84
114.71
114.34
104.28
103.99
103.71
94.42
94.40
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.46
41.20
34.20
26.80
26.76
25.88
25.85
25.24
19.09
17.89
17.67
OH
OMe
O
6f
E:Z = 2:1 mixtrue
100 MHz, CDCl3
f1 (ppm)

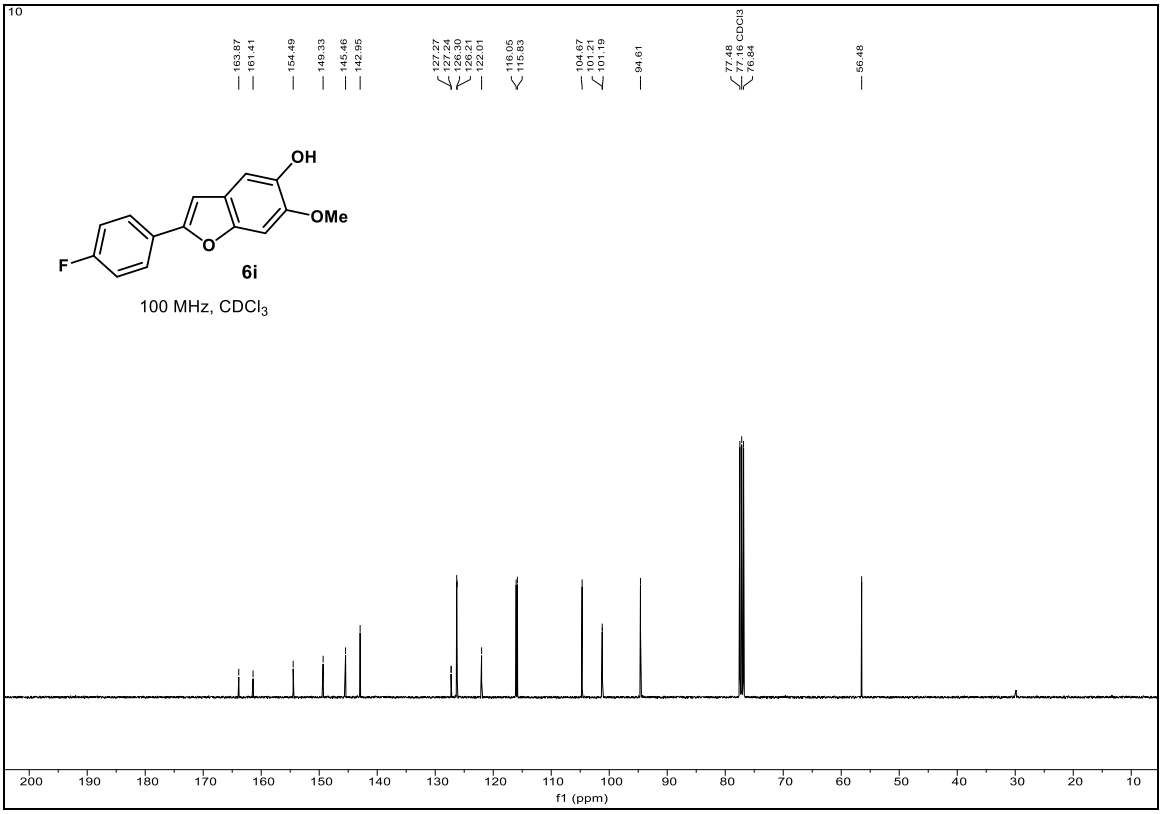

6g
7.26 CDCl3
7.07
7.07
6.91
6.90
5.52
3.94
1.44
1.40
1.39
1.38
1.37
1.37
1.37
1.36
1.35
1.35
1.33
1.33
1.31
1.26
1.23
1.22
1.20
1.14
1.13
1.06
0.08
OH
OMe
Si
O
6g
400 MHz, CDCl3
1.384
1.366
1.350
1.347
1.329
1.4 1.3
1.144
1.125
1.10
1.87
0.94
0.92
2.70
3.05
17.82
f1 (ppm)

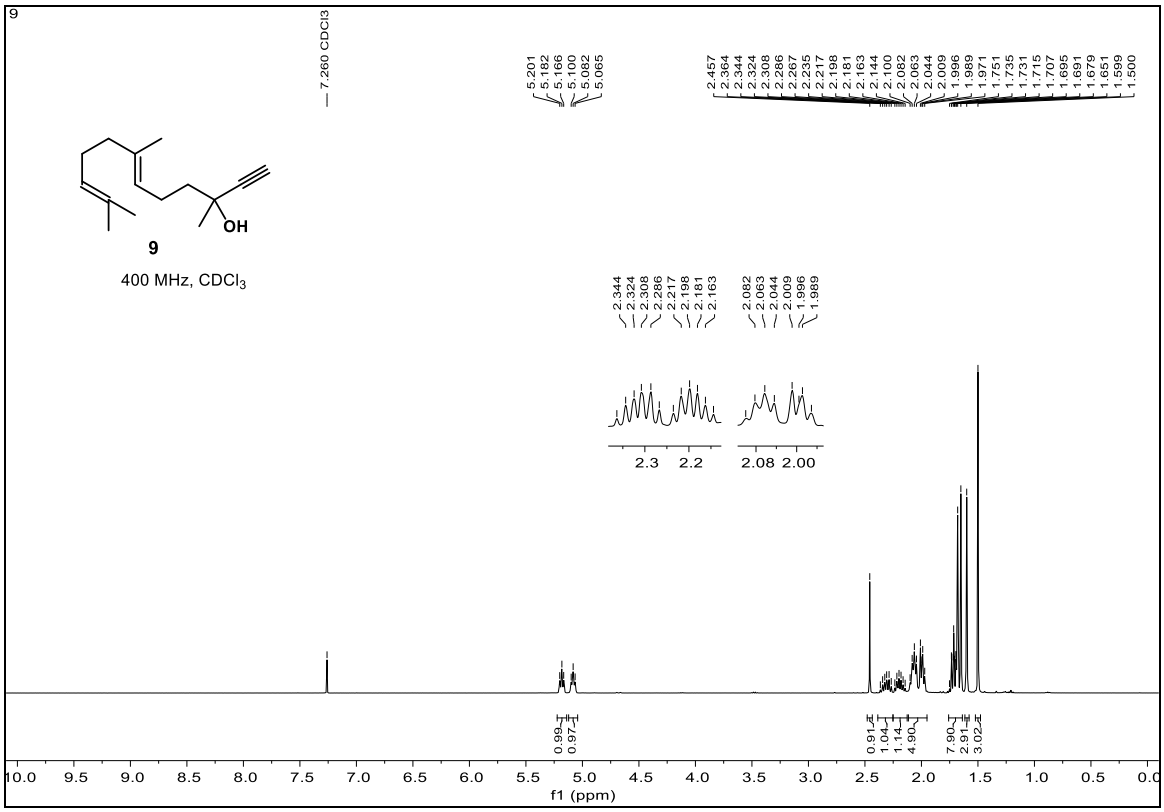

6g
159.69
152.52
145.41
142.40
120.57
118.20
104.24
94.50
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.37
18.74
11.19
OH
OMe
Si
O
6g
100 MHz, CDCl3
f1 (ppm)

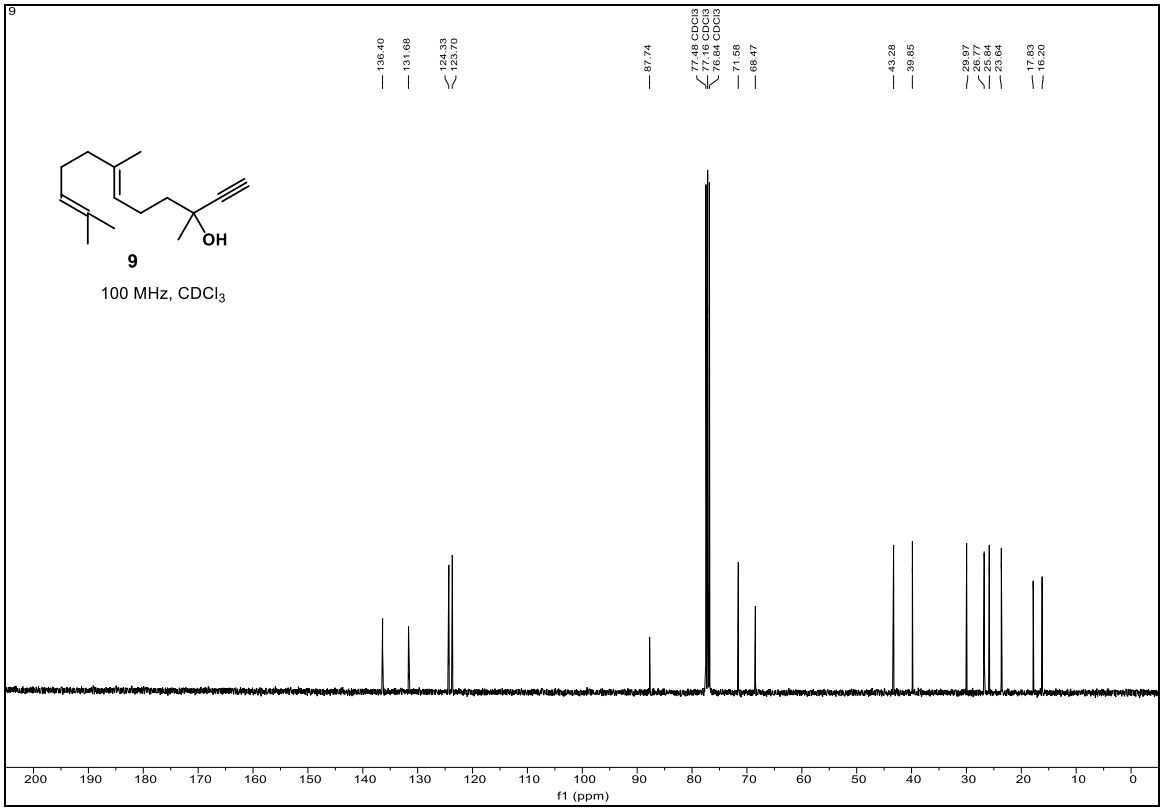

10
7.54
7.52
7.26 CDCl3
6.89
6.88
6.85
5.96
3.83
OH
OMe
MeO
O
6h
400 MHz, CDCl3
2.00
2.05
0.98
0.95
6.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

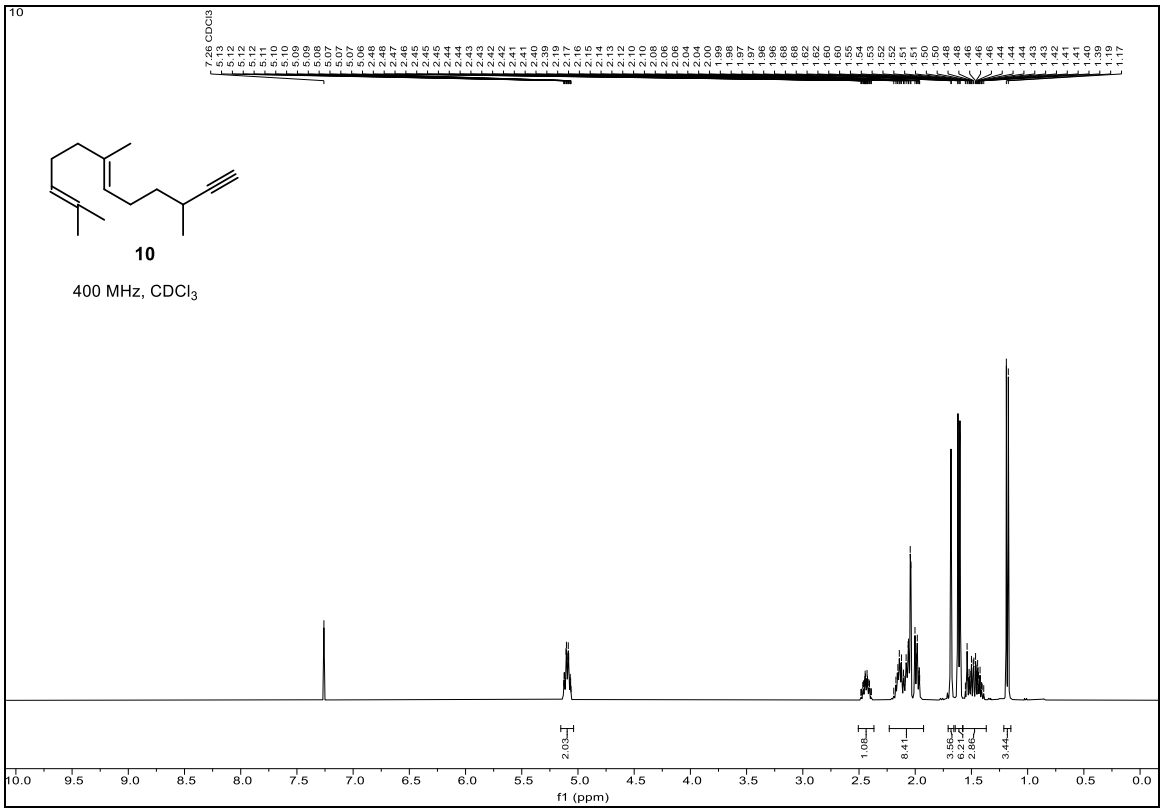

10
183.31
181.30
161.29
159.18
134.41
133.68
133.43
114.38
113.68
107.53
106.42
82.87
77.48
77.16 CDCl3
76.84
56.50
55.52
OH
OMe
MeO
O
6h
100 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

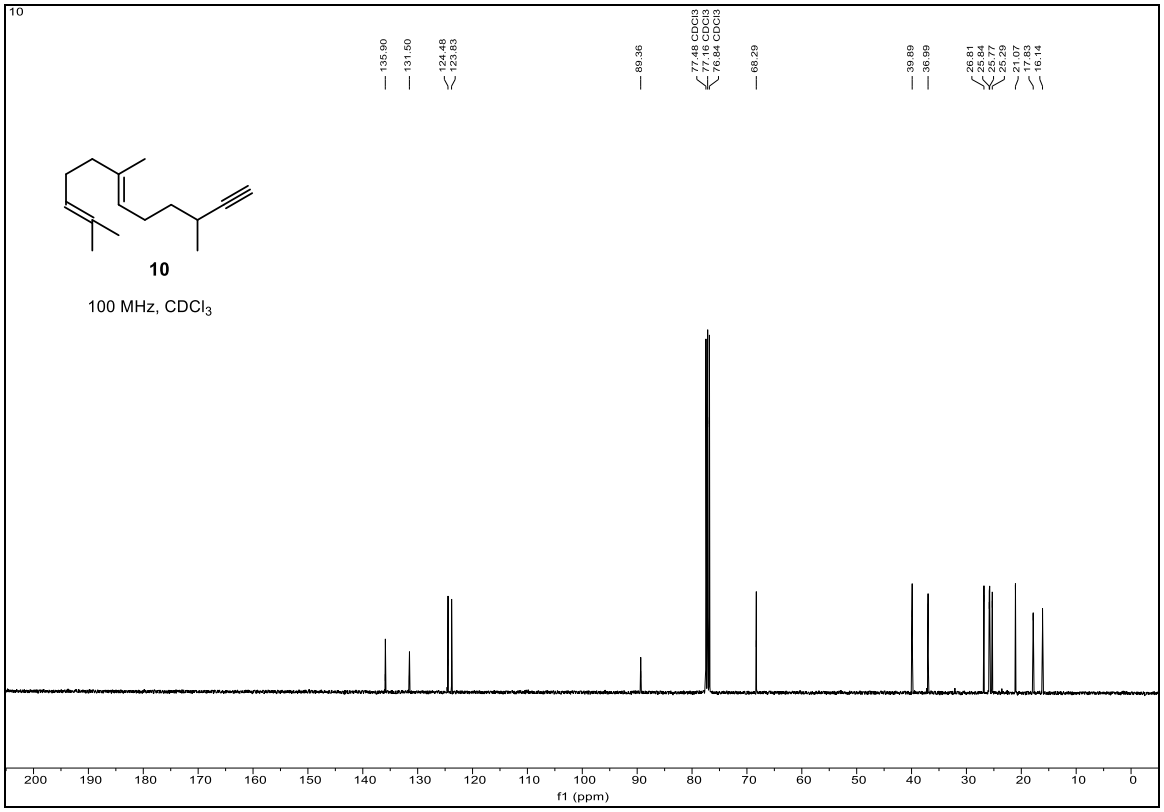

10
7.77
7.76
7.76
7.75
7.75
7.74
7.73
7.26 CDCl3
7.13
7.11
7.09
7.07
7.05
6.83
5.56
3.96
OH
OMe
O
F
6i
400 MHz, CDCl3
2.14
2.19
2.00
1.03
0.93
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

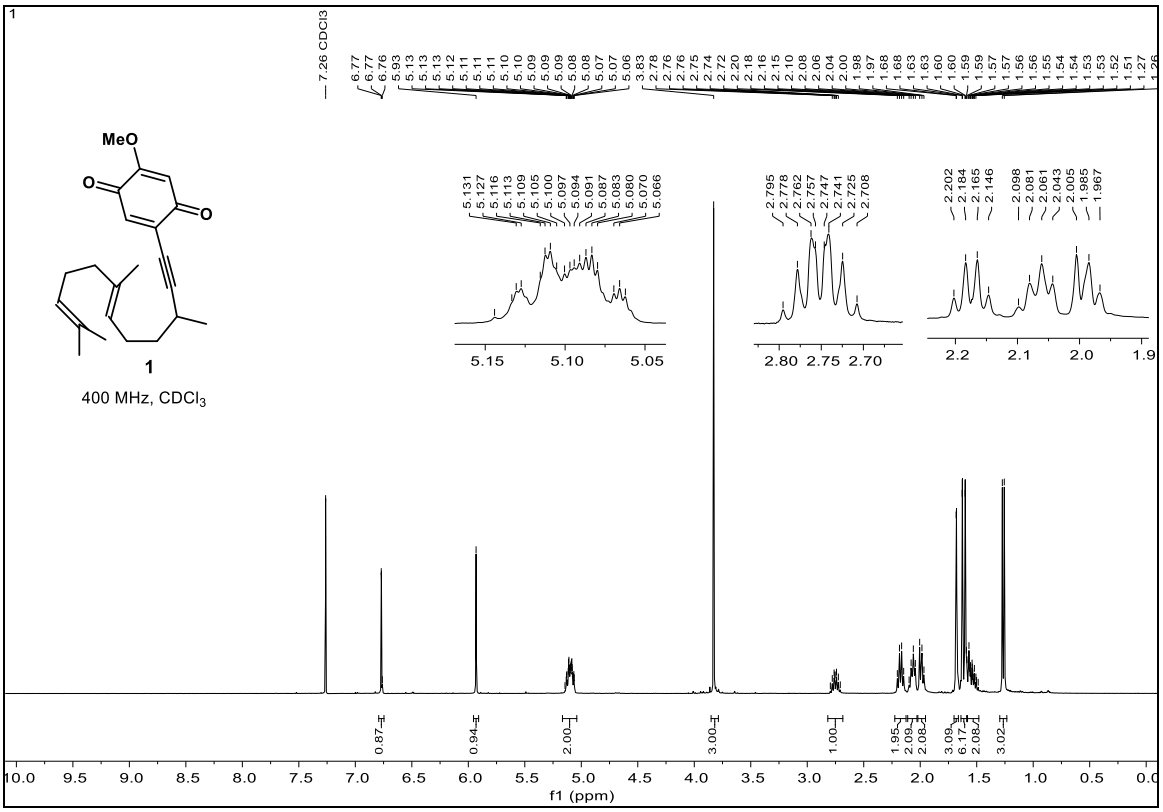

10
163.87
161.41
154.49
149.33
145.46
142.95
127.27
127.24
126.30
126.21
122.01
116.05
115.83
104.67
101.71
101.19
94.61
77.48
77.16 CDCl3
76.84
56.48
OH
OMe
O
F
6i
100 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

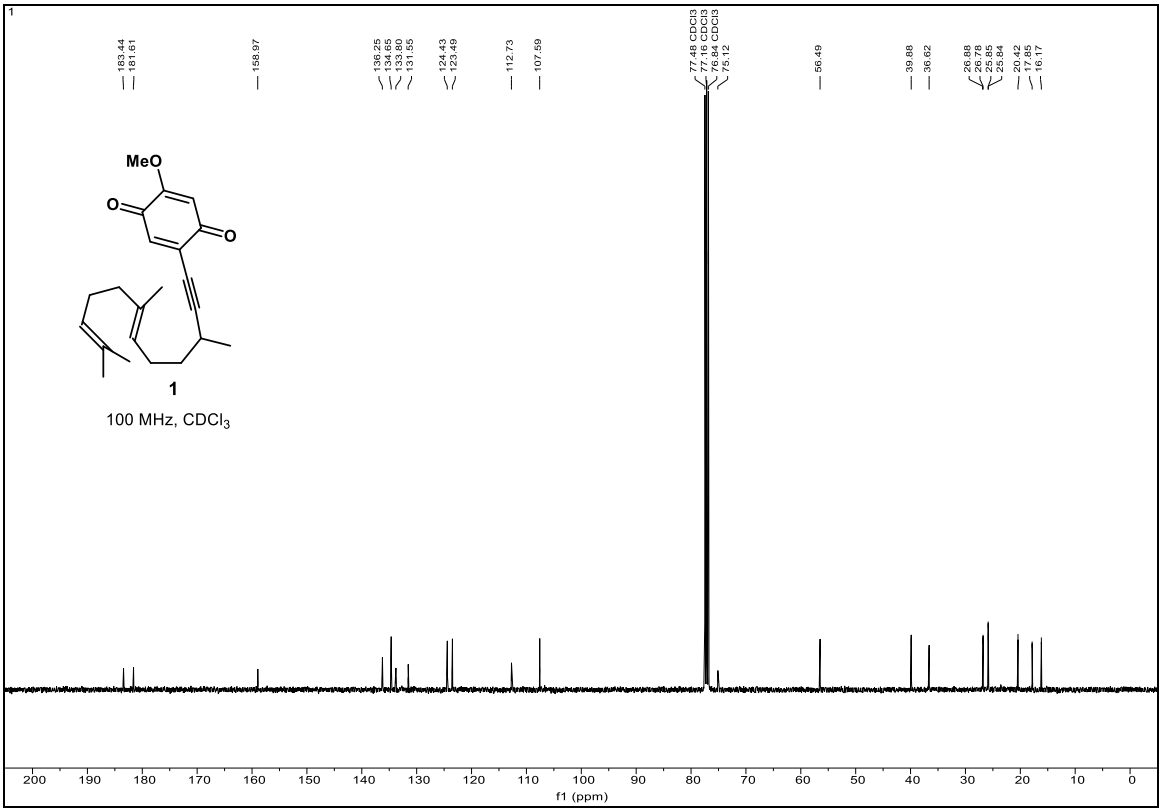

9
7.260 CDCl3
5.201
5.182
5.166
5.100
5.082
5.065
2.457
2.364
2.344
2.324
2.308
2.286
2.267
2.235
2.217
2.198
2.181
2.163
2.144
2.100
2.082
2.063
2.044
2.009
1.996
1.989
1.971
1.751
1.735
1.731
1.715
1.707
1.695
1.691
1.679
1.651
1.599
1.500
OH
9
400 MHz, CDCl3
2.344
2.324
2.308
2.286
2.217
2.198
2.181
2.163
2.082
2.063
2.044
2.009
1.996
1.989
2.3 2.2
2.08 2.00
0.99
0.97
0.91
1.04
1.14
4.90
7.90
2.91
3.02
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)

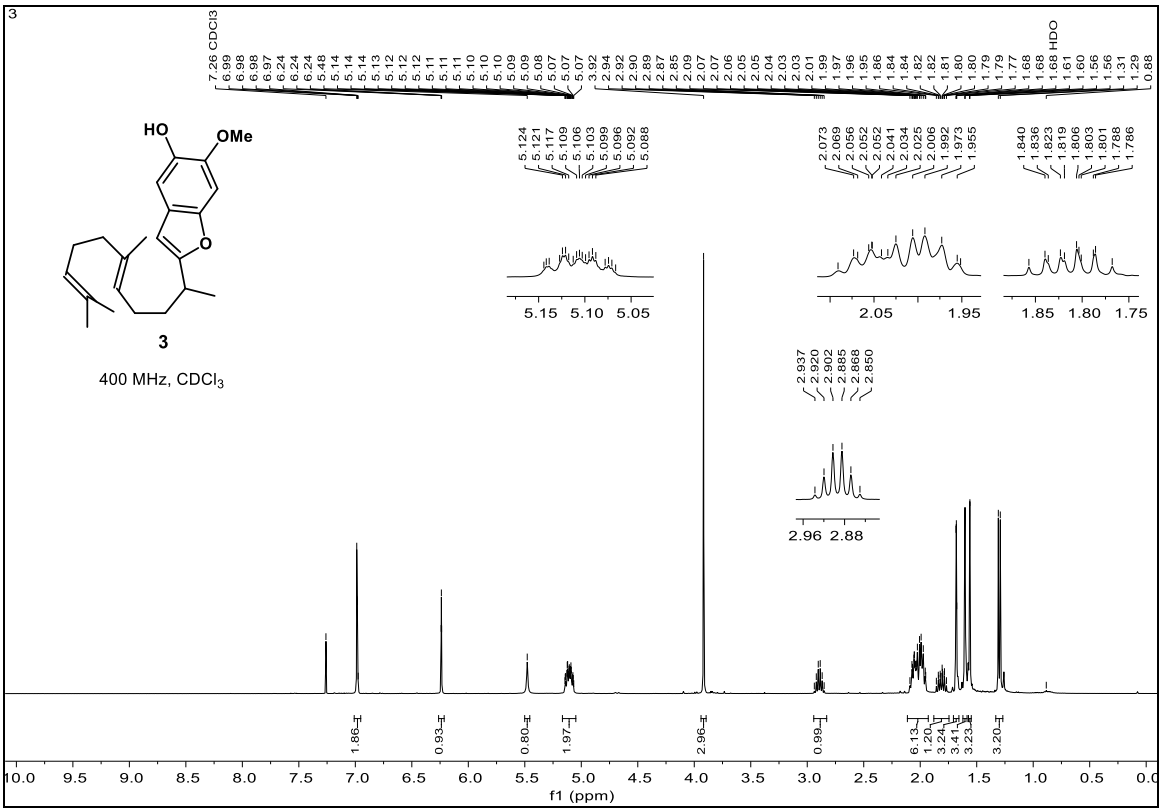

9
136.40
131.68
124.33
123.70
87.74
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
71.58
68.47
43.28
39.85
29.97
26.77
25.84
23.64
17.83
16.20
OH
9
100 MHz, CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

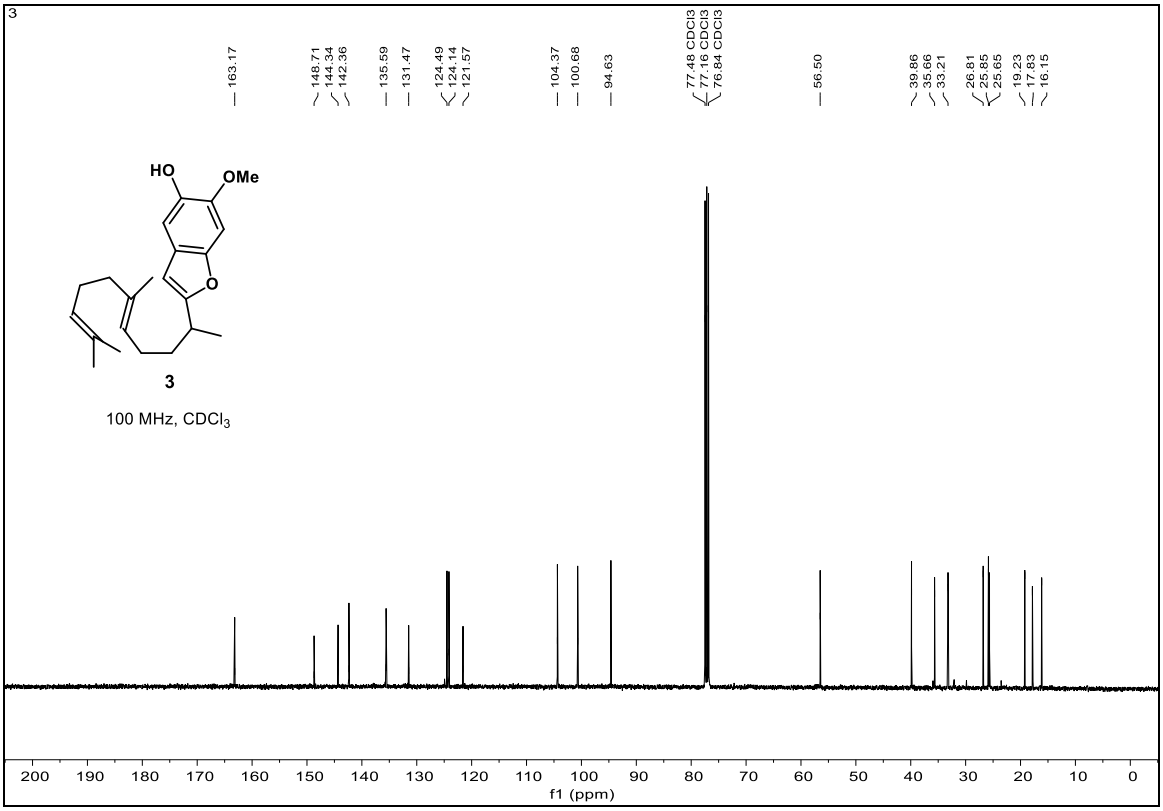

10
7.26 CDCl3
10
400 MHz, CDCl3
2.03
1.08
8.41
3.56
6.21
2.86
3.44
f1 (ppm)


10
135.90
131.50
124.48
123.83
89.36
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.29
39.89
36.99
26.81
25.84
25.77
25.29
21.07
17.83
16.14
10
100 MHz, CDCl3
f1 (ppm)

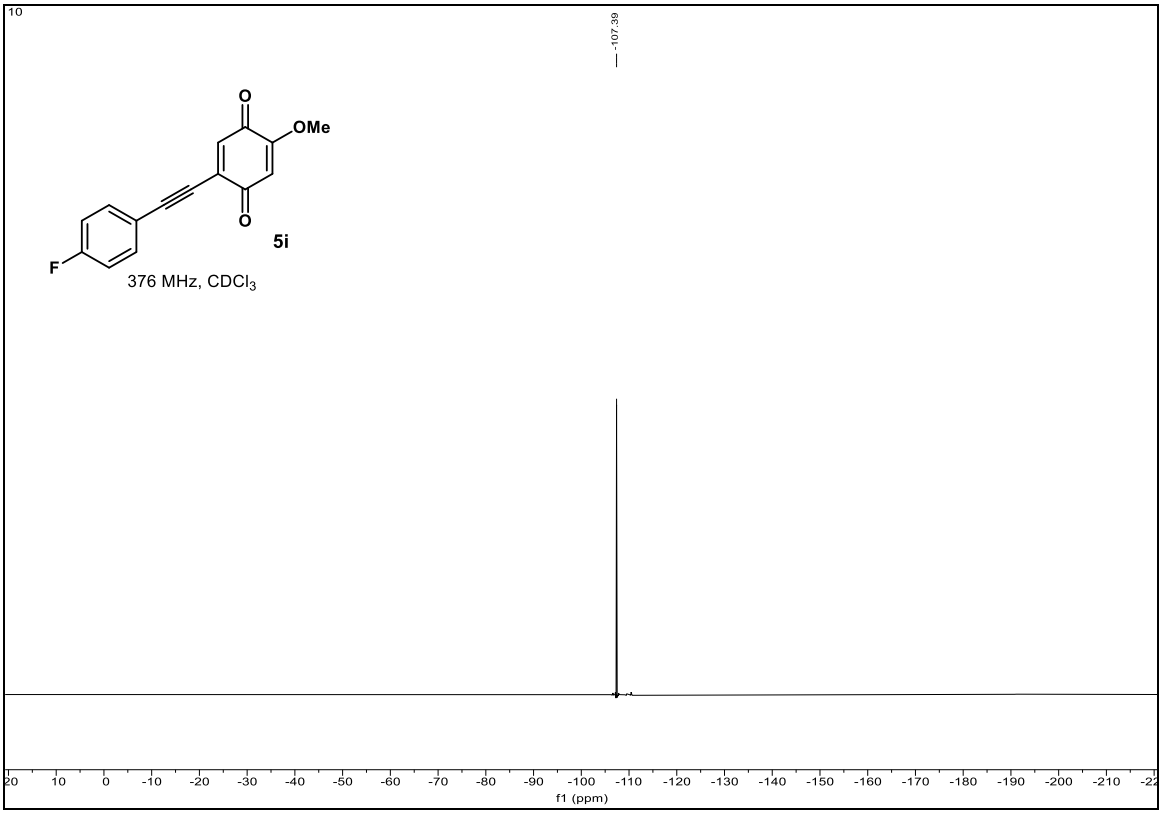

MeO
O
O
1
400 MHz, CDCl3
f1 (ppm)

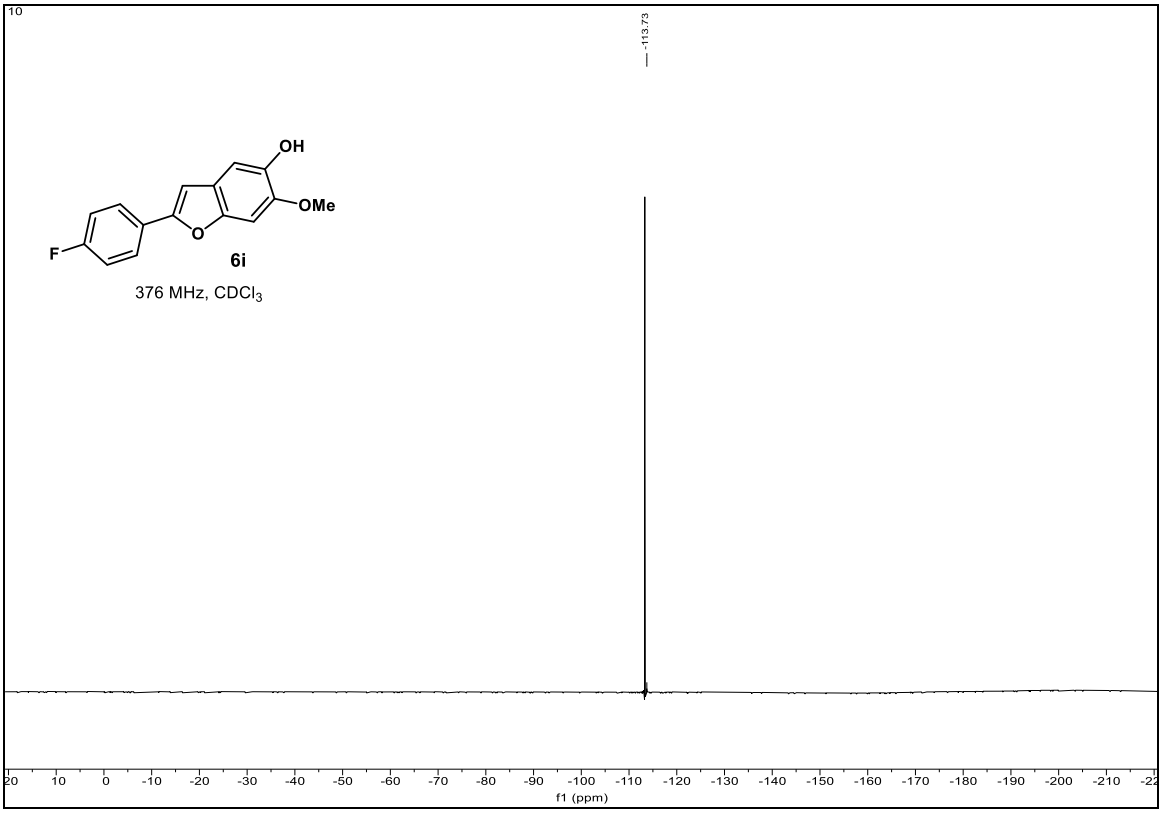

MeO
O
O
1
100 MHz, CDCl3
f1 (ppm)


3
HO
OMe
O
3
400 MHz, CDCl3
7.26 CDCl3
HDO
5.15 5.10 5.05
2.05 1.95
1.85 1.80 1.75
2.96 2.88
1.86
0.93
0.80
1.97
2.96
0.99
6.13
1.20
3.24
3.41
3.23
3.20
f1 (ppm)

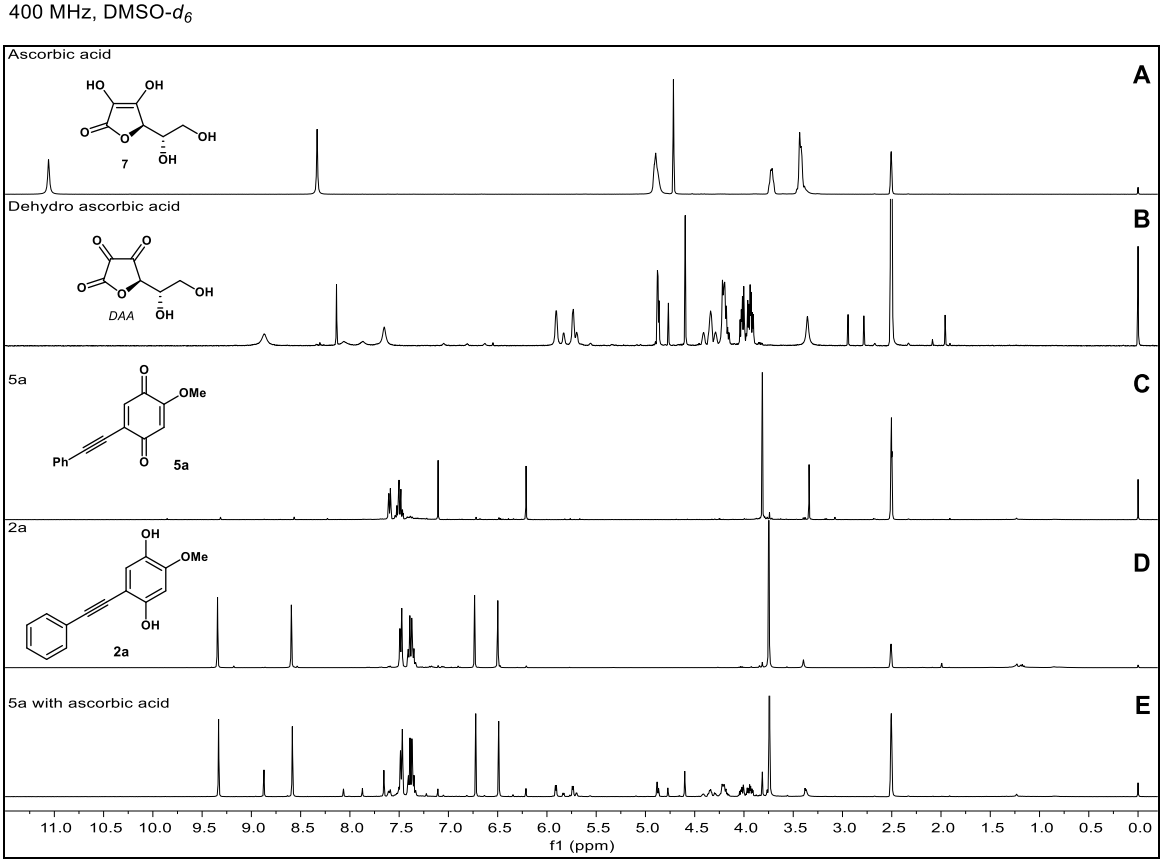

3
HO
OMe
O
3
100 MHz, CDCl3
163.17
148.71
144.34
142.36
135.59
131.47
124.49
124.14
121.57
104.37
100.68
94.63
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.50
39.86
35.66
33.21
26.81
25.85
25.65
19.23
17.83
16.15
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)





The ^{1}H NMR analysis of the reaction mixture in DMSO-d_6 (bottom; spectrum E) indicates the formation of hydroquinone **2a** and dehydroascorbic acid. All the spectra were measured in DMSO-d_6 at room temperature.



A: ascorbic acid, **B**: dehydroascorbic acid, **C**: alkynylquinone **5a**, **D**: alkynylhydroquinone **2a**. **E**: the spectrum shows the reaction mixture in which alkynylquinone **5a** was treated with ascorbic acid in DMSO-d_6 at room temperature to afford **2a** and dehydroascorbic acid.

References

1) E. Tao, M. Inoue, T. Jeong, I. S. Kim, T. Yoshimitsu, *J. Org. Chem.*, **2020**, *85*, 9064.

2) A. Fürstner, P. Hannen, *Chem. Eur. J.* **2006**, *12*, 3006.