Supplemental Information

Selective Conversion of Lignin to Benzoquinones Under Ambient Conditions: Unlocking the Potential of a Single Platform Chemical Strategy

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Contents

1. General Information

1.1. Reagents

All commercial chemicals were purchased and used as received. 2-Methoxy-4-propylphenol (≥99%), 4-allyl-2,6-dimethoxyphenol (95%), 3,5-dimethoxy-4-hydroxybenzaldehyde (≥98%), 2-bromo-2-methylbutane (95%), N-(2,2,6,6-tetramethylpiperidin-4-yl)amine (98%), iodomethane (99%), 1-propanol (≥99.9%), 2-propanol (99.5%), 1,1,1,3,3,3-hexafluoroisopropanol (≥99%), anhydrous sodium sulfate (≥99%) and white quartz (50-70 mesh) were purchased from Sigma-Aldrich. 2,6-Dimethoxyphenol (99%), molecular sieves 3A (8-12 mesh) were purchased from Acros Organics. Palladium (3wt%) on activated carbon was purchased from Spectrum Chemical. 4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl (4-acetamido-TEMPO) (≥98%) and 1,2-diethoxypropane (≥98%) were purchased from TCI America. 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) (99.38%) was purchased from Chem-Impex Int'l Inc. 4-Propylphenol (99.89%) and copper(I) bromide (99.3%) were purchased from AmBeed Chemical. 2,6-Dibromo-4-isopropylphenol (97%) was purchased from AOBChem USA. Sodium (99%) was purchased from Alfa Aesar. Mesitylene (98+%), ethanol-d_1 (≥99.5%), sodium hypochlorite (11-15%), tetrafluoroboric acid (50%), concentrated hydrochloric acid (ACS certified), anhydrous diethyl ether (ACS reagent grade), dichloromethane (ACS reagent grade), methanol (ACS reagent grade), acetone (ACS reagent grade), hexanes (ACS reagent grade), ethyl acetate (ACS regent grade), tetrahydrofuran (ACS regent grade), sodium carbonate (ACS regent grade), sodium chloride (ACS regent grade), silica gel sorbent (230-400 mesh) and celite (TM) were purchased from Fisher Chemical. Ethanol (Proof 200) was purchased from Gold Shield Dist. Inc. Methanol (HPLC grade), acetone (HPLC grade) and N, N-dimethylformamide (ACS reagent grade) were purchased from EMD Millipore. Chloroform-d_1 (99.9%), ethanol-d_6 (99.9%), acetonitrile-d_3 (99.8%), dimethyl sulfoxide-d_6 (99.9%) were purchased from Cambridge Isotope Laboratories Inc. Hydrogen gas (5.0 grade) and nitrogen gas (99.998%) were purchased from Airgas Inc. Water was obtained from an A10 Milli-Q water purification system by Millipore. The dry high-S poplar biomass was provided by Drs. Clint Chapple and Richard Meilan from Purdue University. The high-S poplar was made through biosynthesis by over-expressing the F5H gene to increase the content of the S unit up to 85.2% in poplar wood[1].

1.2. Analysis

^1H NMR and ^{13}C NMR spectra were recorded on Bruker Avance III HD 400 MHz and Bruker Avance NEO 500 MHz spectrometers. LC-MS spectra were recorded on Shimadzu LCMS-9030 UHPLC-QTOF. GC-FID spectra were recorded on Agilent 6890N Network GC System.

2. Synthesis of 2,6-dimethoxy-4-propylphenol (DMPP) and Oxidants

2.1. 2,6-Dimethoxy-4-propylphenol (1a)

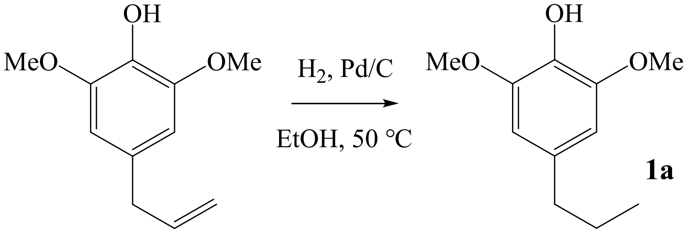


Figure S1. Synthesis of 2,6-dimethoxy-4-propylphenol (**1a**)

4-Allyl-2,6-dimethoxyphenol (1 g, 5.15 mmol), Pd/C (167 mg, 3% palladium) and ethanol (20 mL) were loaded into a stainless-steel Parr reactor. The reactor was filled with H_2 (15 bars). The reaction mixture was stirred at 50°C for 5 hours. Upon the completion of the reaction, the reactor was cooled down to room temperature (r.t.). The reaction mixture was filtered to remove Pd/C, and the filter cake washed by ethyl acetate. The organic solutions were combined, and the solvent was removed by rotary evaporator to give an oil-like product. The crude product was purified by column chromatography (ethyl acetate/hexanes = 1:3) to give 2,6-dimethoxy-4-propylphenol (**1a**).

2,6-Dimethoxy-4-propylphenol was isolated as a colorless liquid (0.848 g, 89.3%). The purity of **1a** was 98.9% based on GC-FID. The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.40 (s, 2H), 5.35 (s, 1H), 3.87 (s, 6H), 2.51 (t, J = 7.6 Hz, 2H), 1.62 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.84, 133.86, 132.65, 105.0, 56.24, 38.30, 24.87, 13.83.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{16}O_3Na$ 219.0997; Found 219.0996.

2.2. Synthesis of Oxidants

2,2,6,6-tetramethylpiperidin-1-oxoammonium-tetrafluoroborate ($TEMPO^+BF_4^-$)[1]

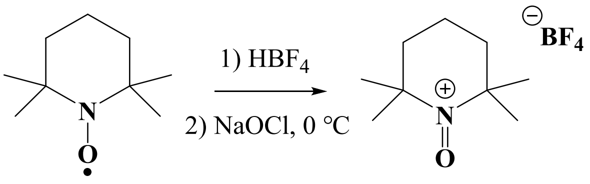


Figure S2. Synthesis of 2,2,6,6-tetramethylpiperidin-1-oxoammonium-tetrafluoroborate ($TEMPO^+BF_4^-$)[1]

2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) (9 g, 57.6 mmol) and H_2O (15 mL) were added to a 250 mL one-necked, round-bottomed flask,. An aqueous solution of HBF_4 (50% aqueous solution, 8.4 mL, 66.2 mmol) was then added dropwise to the vigorous stirring mixture. The solution was stirred for 30 minutes at room temperature. The mixture was then cooled to 0°C and NaOCl (14% aqueous solution, 13 mL, 29 mmol) was added dropwise to the vigorous stirring mixture. The ice bath was removed to let the solution return to room temperature and react for 2 hours. The mixture was then cooled to 0°C and filtered to yield a solid, which was washed with cold water (4°C, 3 × 3 mL) and cold dichloromethane (4°C, 3 × 3 mL). After drying under reduced pressure, the 2,2,6,6-tetramethylpiperidin-1-oxoammonium-tetrafluoroborate product ($TEMPO^+BF_4^-$) was isolated as a yellow solid. in 83.6% yield (11.709 g, 48.2 mmol).

The analytical data are shown below.

^{1}H NMR (400 MHz, CF_3COOD): δ 2.78-2.85 (m, 4H), 2.68-2.76 (m, 2H), 1.94 (s, 12H).

^{13}C NMR (101 MHz, CF_3COOD): δ 105.06, 40.50, 28.74, 15.56.

^{19}F NMR (376 MHz, CF_3COOD): δ -147.03, -147.69.

HRMS (ESI) m/z: $[M - BF_4]^+$ Calcd for $C_9H_{18}NO$ 156.1388; Found 156.1387.

4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate (Bobbitt's Salt)[1]

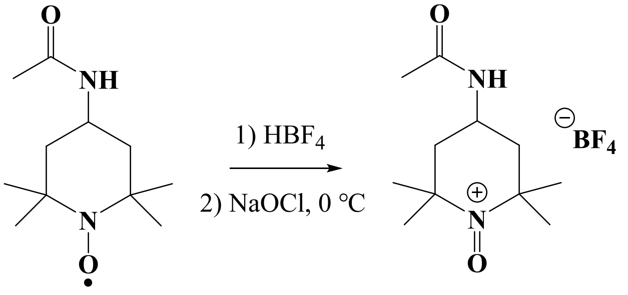


Figure S3. Synthesis of 4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate (Bobbitt's Salt)[1]

4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl (4-acetamido-TEMPO) (9 g, 42.2 mmol) and H_2O (15 mL) were added to a 250 mL one-necked, round-bottomed flask. An aqueous solution of HBF4 (50% aqueous solution, 6.0 mL, 47.3 mmol) was then added dropwise to the vigorous stirring mixture. The solution was stirred for 30 minutes at room temperature. The mixture was then cooled to 0°C and NaOCl (14% aqueous solution, 9.4 mL, 21 mmol) was added dropwise to the vigorous stirring mixture. The ice bath was removed to let the solution return to r.t. and allowed to react for 4 hours. The mixture was cooled to 0°C and filtered to yield a solid which was washed with cold water (4°C, 3 × 3 mL) and cold dichloromethane (4°C, 3 × 3 mL). After drying under reduced pressure, the product 4-acetamido-2,2,6,6-tetramethyl-piperidine-1-oxoammonium tetrafluoroborate (Bobbitt's Salt) was isolated in 80.3% yield (10.172 g, 33.9 mmol) as a yellow solid. The analytical data are shown below.

^{1}H NMR (400 MHz, CF_3COOH): δ 8.68 (s, 1H), 5.87-5.96 (m, 1H), 3.33-3.36 (m, 4H), 2.83 (s, 3H), 2.46 (s, 6H), 2.07 (s, 6H).

^{13}C NMR (101 MHz, CF_3COOD): δ 177.01, 103.56, 42.77, 41.16, 30.93, 27.30, 19.74.

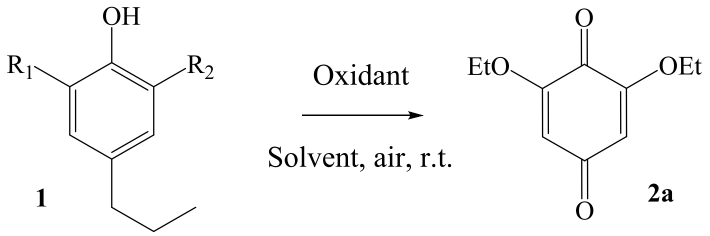
^{19}F NMR (376 MHz, CF_3COOD): δ -145.17, -145.83, -146.25, -147.03.

HRMS (ESI) m/z: $[M - BF_4]^+$ Calcd for $C_{11}H_{21}N_2O_2$ 213.1603; Found 213.1610.

3. Oxidation of lignin Model Compounds

3.1. Optimization of the Oxidative Cleavage Reaction of Lignin Model Compounds

Table S1. Optimization of reaction conditions by employing Lignin Model Compounds as substrates[a]



Entry	R_1 =	R_2 =	Solvent	Oxidant	Yield of **2a**[b]/%
1[c]	OMe	OMe	DCM	TEMPO$^+$BF4$^-$	0
2[c]	OMe	OMe	THF	TEMPO$^+$BF4$^-$	0
3[c]	OMe	OMe	H2O	TEMPO$^+$BF4$^-$	0
4[c]	OMe	OMe	MeOH	TEMPO$^+$BF4$^-$	79[d]
5[cf]	OMe	OMe	MeOH	TEMPO$^+$BF4$^-$	60[d]
6[cj]	OMe	OMe	MeOH	TEMPO$^+$BF4$^-$	76[d]
7[c]	OMe	OMe	MeOH + 0.4 wt% H_2O	TEMPO$^+$BF4$^-$	72[d]
8[cf]	OMe	OMe	EtOH	TEMPO$^+$BF4$^-$	47
9[c]	OMe	OMe	EtOH	TEMPO$^+$BF4$^-$	71
10[ce]	OMe	OMe	EtOH	TEMPO$^+$BF4$^-$	65
11[c]	OMe	OMe	EtOH	Bobbitt's Salt	84
12	**OMe**	**OMe**	**EtOH**	**Bobbitt's Salt**	**97(97)**
13[c]	OMe	OMe	MeOH	Bobbitt's Salt	77[d]
14	OMe	OMe	MeOH	Bobbitt's Salt	79[d]
15[l]	OMe	OMe	EtOH	Bobbitt's Salt	12
16[g]	OMe	OMe	EtOH	Bobbitt's Salt	76
17[i]	OMe	OMe	EtOH	Bobbitt's Salt	91
18[h]	OMe	OMe	EtOH	Bobbitt's Salt	83
19[h]	OMe	OMe	EtOH + 2 μL H_2O	Bobbitt's Salt	72
20[h]	OMe	OMe	EtOH + 5 μL H_2O	Bobbitt's Salt	61
21[h]	OMe	OMe	EtOH + 10 μL H_2O	Bobbitt's Salt	47
22[f]	OMe	OMe	EtOH	Bobbitt's Salt	57
23[j]	OMe	OMe	EtOH	Bobbitt's Salt	86
24[k]	OMe	OMe	EtOH	Bobbitt's Salt	75

25	OEt	OEt	EtOH	Bobbitt's Salt	81
26	H	OMe	MeOH	Bobbitt's Salt	5[m]
27	H	OMe	EtOH	Bobbitt's Salt	9[m]
28	H	H	MeOH	Bobbitt's Salt	0[m]
29	H	H	EtOH	Bobbitt's Salt	0[m]
30	OMe	OMe	MeOH	None	0[m]
31	OMe	OMe	EtOH	None	0[m]
32	OMe	OMe	EtOH	TEMPO	0[m]
33	OMe	OMe	EtOH	4-acetamido-TEMPO	0[m]

[a] Unless specified, substrate (0.15 mmol) and oxidant (0.9 mmol) in 8 mL solvent were stirred for 8 h in a 20 mL scintillation vial under air. Mesitylene (28.5 mg) was used as the internal standard to give the NMR yield. [b] NMR yield. [c] React for 4 h. [d] NMR yield of 2,6-dimethoxybenzoquinone. [e] 1.2 mmol oxidant. [f] 0.6 mmol oxidant. [g] 1 mL EtOH. [h] 2 mL EtOH. [i] 4 mL EtOH. [j] 0.75 mmol oxidant. [k] 1.8 mmol oxidant. [l] 0.3 mmol oxidant. [m] NMR yield of para-benzoquinone.

3.2. General Procedures

Ethanol as the Solvent

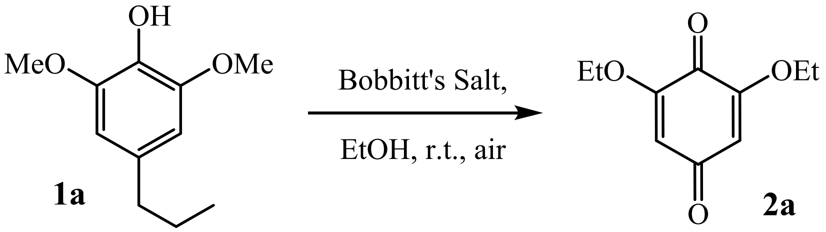


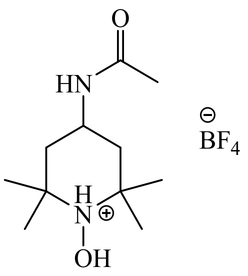
Figure S4. Oxidation of DMPP (1a) in EtOH

Bobbitt's Salt (0.9 mmol, 275 mg) was weighed and put into a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at room temperature and then **DMPP (1a)** (0.15 mmol, 30 mg) was added into the mixture. The reaction mixture was stirred at r.t. for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give a solid. The solid was washed with diethyl ether and filtered. The remaining white solid is the reduced Bobbitt's Salt. The filtrates were combined and evaporated by rotary evaporator to give 2,6-diethoxybenzoquinone (**2a**) as a yellow solid (29.2 mg, 97%). The analytical data are shown below.

^{1}H NMR (400 MHz, CDCl$_3$): δ 5.80 (s, 2H), 3.98 (q, J = 7.2 Hz, 4H), 1.46 (t, J = 7 Hz, 6H).

^{13}C NMR (101 MHz, CDCl$_3$): δ 187.47, 176.77, 156.57, 107.51, 65.34, 13.86.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_{13}O_4$ 197.0814; Found 197.0810.



(2j)

The reduced Bobbitt's Salt (**2j**) was isolated as a white solid. The analytical data are shown below.

^{1}H NMR (400 MHz, CF_3COOH): δ 9.76 (s, 1H), 8.86 (s, 1H), 5.08 (s, 1H), 2.88 (s, 3H), 2.73 (s, 4H), 2.06 (s, 6H), 2.00 (s, 6H).

^{13}C NMR (101 MHz, CF_3COOD): δ 177.05, 69.80, 42.59, 40.18, 26.79, 19.27, 18.37.

^{19}F NMR (376 MHz, CF_3COOD): δ -145.86, -146.42.

HRMS (ESI) m/z: $[M - BF_4]^+$ Calcd for $C_{11}H_{23}N_2O_2$ 215.1760; Found 215.1760.

1-Propanol as the Solvent

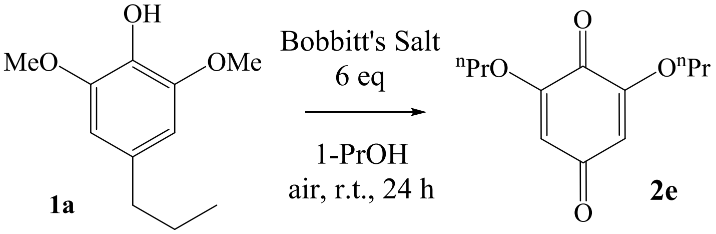


Figure S5. Oxidation of DMPP (1a) in 1-propanol

2,6-Dipropoxybenzoquinone (**2e)** was generated as a yellow solid (32.2 mg, 94%). The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77 (s, 2H), 3.84 (t, J = 6.8 Hz, 4H), 1.84 (m, J = 7.1 Hz, 4H), 1.00 (t, J = 7.4 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 187.51, 176.65, 156.74, 107.44, 70.99, 21.60, 10.29.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{17}O_4$ 225.1127; Found 225.1120.

2-Propanol as the Solvent

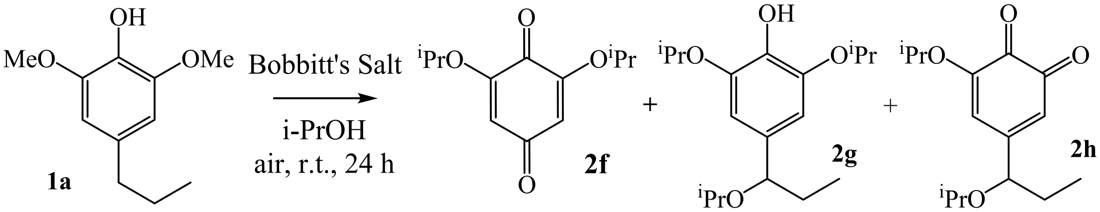


Figure S6. Oxidation of DMPP (1a) in 2-propanol

The products were separated by column chromatography (ethyl acetate/hexanes = 1:4 ~

1:2). All the separated products are collected and identified by NMR and LC-MS. The 2,6-Diisopropoxybenzoquinone (**2f**) product was isolated as a yellow solid (8.0 mg, 23.4%). The analytical data are shown below.
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (s, 2H), (m, J = 6.2 Hz, 4H), 1.46 (d, J = 6 Hz, 12H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.93, 177.32, 155.60, 107.58, 72.38, 21.10.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{17}O_4$ 225.1127; Found 225.1122.

Isopropyl-1-(3,5-diisopropoxy-4-hydroxyphenyl) propyl ether (**2g**) was isolated as an orange-brown oil (28.6 mg, 60.4%). The analytical data are shown below.
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.51 (s, 2H), 5.48 (s, 1H), 4.55 (m, J = 6.2 Hz, 2H), 4.07 (dd, J = 6.8 Hz, 1H), 3.48 (m, J = 6.2 Hz, 1H), 1.72 (m, 1H), 1.56 (m, 1H), 1.35 (dd, J = 6 Hz, 12H), 1.13 (d, J = 6 Hz, 3H), 1.07 (d, J = 6 Hz, 3H), 0.87 (t, J = 7.2 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 145.09, 136.19, 134.56, 106.57, 81.01, 71.66, 68.55, 31.79, 23.57, 22.32, 22.17, 21.20, 10.61.
HRMS (ESI) m/z: $[M – C_3H_7O]^+$ Calcd for $C_{15}H_{23}O_3$ 251.1647; Found 251.1643.

3-Isopropoxy-5-(1-isopropoxypropyl)-3,5-cyclohexadiene-1,2-dione (**2h**) was isolated as a red solid (5.8 mg, 14.3%). The analytical data are shown below.
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.00 (d, J = 1.6 Hz, 1H), 5.98 (d, J = 1.6 Hz, 1H), 4.46 (m, J = 6 Hz, 1H), 3.88 (dd, J = 6 Hz, 1H), 3.57 (m, J = 6.1 Hz, 1H), 1.67 (m, 1H), 1.59 (m, 1H), 1.37 (dd, J = 4.8 Hz, 12H), 1.17 (dd, J = 3.2 Hz, 6H), 0.98 (t, J = 7.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 178.63, 176.69, 159.50, 151.69, 118.70, 107.63, 80.32, 71.57, 70.58, 27.83, 23.40, 21.41, 21.33, 21.12, 10.12.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{22}O_4Na$ 289.1416; Found 289.1411.

2-Ethoxyethanol as the Solvent (with 2eq. Bobbitt's Salt)

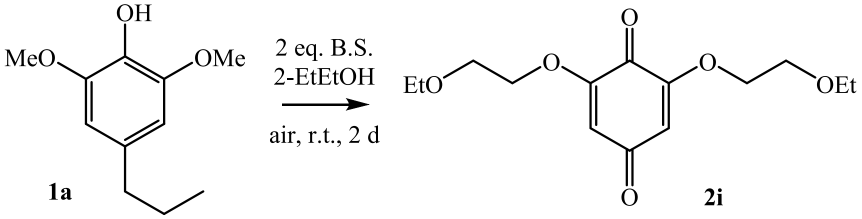


Figure S7. Oxidation of DMPP (1a) in 2-ethoxyethanol

The products were separated by column chromatography (ethyl acetate/hexanes = 1:2) and were collected and identified by NMR and LC-MS.

The 2,6-di(2-ethoxyethoxy)benzoquinone (**2i**) was isolated as a yellow liquid (21.8 mg, 51.2%). The analytical data are shown below.
^{1}H NMR (400 MHz, CD_3CN): δ 5.86 (s, 2H), 4.02 (t, J = 4.4 Hz, 4H), 3.72 (t, J = 4.4 Hz, 4H), 3.53 (q, J = 7 Hz, 4H), 1.16 (t, J = 7.2 Hz, 6H).

^{13}C NMR (101 MHz, CD_3CN): δ 187.28, 176.67, 156.82, 107.68, 69.08, 67.63, 66.21, 14.47.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{21}O_6$ 285.1338; Found 285.1345.

Methanol as the Solvent

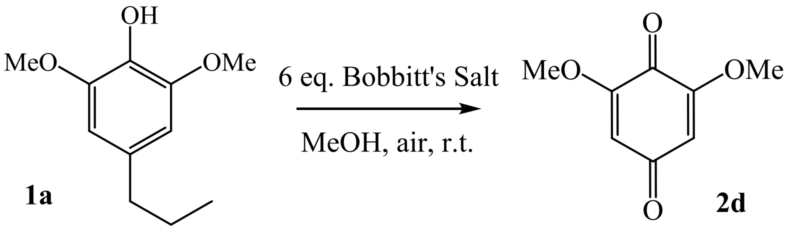


Figure S8. Oxidation of DMPP (1a) in methanol

Bobbitt's Salt (0.9 mmol, 275 mg) was weighed and put into a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at room temperature and then **DMPP (1a)** (0.15 mmol, 30 mg) was added into the mixture. The reaction mixture was stirred at r.t. for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give a solid. DCM/water extraction was performed to the solid. The organic phases were combined and evaporated by rotary evaporator. Crude product was purified by column chromatography (ethyl acetate/dichloromethane = 1:4) to give 2,6-dimethoxybenzoquinone (**2d**) as a yellow solid (20.0 mg, 78%). The analytical data are shown below.

^{1}H NMR (600 MHz, DMSO-d6): δ 5.94 (s, 2H), 3.72 (s, 6H).
^{13}C NMR (151 MHz, DMSO-d6): δ 187.53, 157.71, 107.57, 107.45, 56.92.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_8H_9O_4$ 169.0501; Found 169.0498.

3.3. Oxidation of Pseudo RCF Lignin Oil and Separation of DEBQ

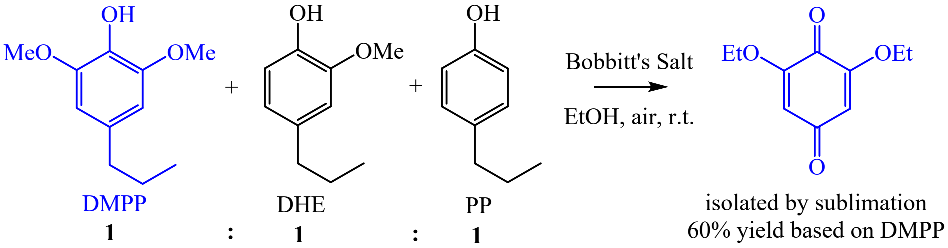


Figure S9. Oxidation of pseudo lignin oil.

Bobbitt's Salt (250 mg) was weighed and put into a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at room temperature and then DMPP (0.05 mmol, 10 mg), DHE (0.05 mmol, 8.3 mg) and PP (0.05 mmol, 6.8 mg) were added into the mixture. The reaction mixture was then stirred at r.t. for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give an oil-like mixture. This mixture was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator to give a black oil-like crude product. Sublimation was performed on the crude product, and the yellow oil on the surface of the sublimator was collected.

4. Mechanism Study

4.1. Intermediates Trapping Reactions

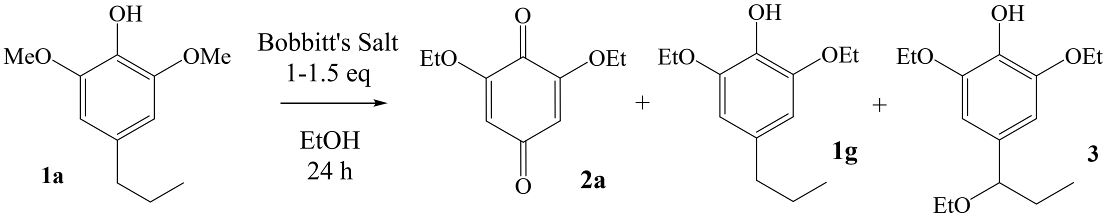


Figure S10. Intermediates trapping reactions

Bobbitt's Salt (0.15 mmol – 0.225 mmol) was weighed and put into a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at room temperature and then DMPP (120 mg) added. The reaction mixture was stirred at r.t. for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give a solid. The solid was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator. The products were separated by column chromatography (ethyl acetate/hexanes = 1:6 ~ 1:2). All the separated products were collected and identified by NMR and LC-MS.

2,6-Diethoxybenzoquinone (**2a**) was isolated as a yellow solid.

2,6-Diethoxy-4-propylphenol (**1g**) was isolated as a pale-yellow solid. The analytical data are shown below.
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.38 (s, 2H), 5.38 (s, 1H), 4.10 (q, J = Hz, 4H), 2.48 (t, J = Hz, 2H), 1.60 (m, J = Hz, 2H), 1.43 (t, J = Hz, 6H), 0.93 (t, J = Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 146.09, 133.62, 133.23, 106.25, 64.72, 38.23, 24.85, 15.02, 13.80.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{20}O_3Na$ 247.1310; Found 247.1322.

4-(1-Ethoxy-propyl)-2,6-diethoxyphenol (**3**) was isolated as a white solid. The analytical data are shown below.
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.49 (s, 2H), 5.50 (s, 1H), 4.10 (q, J = 7.2 Hz, 4H), 3.96 (t, J = 6.8 Hz, 1H), 3.32 (m, 2H), 1.78 (m, 1H), 1.58 (m, 1H), 1.42 (t, J = 7 Hz, 6H), 1.15 (t, J = 7 Hz, 3H), 0.85 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.19, 134.33, 134.0, 104.34, 83.89, 64.72, 63.90, 31.27, 15.37, 14.94, 10.44.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{24}O_4Na$ 291.1572; Found 291.1571.

4.2. Intermediates Detection with LC-MS

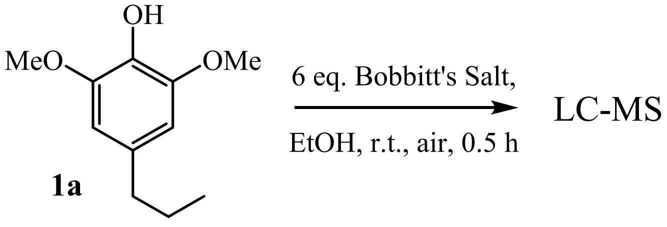
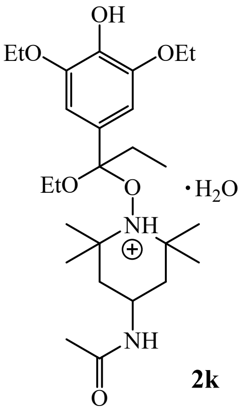


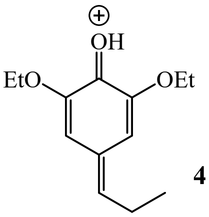
Figure S11. Intermediates detection

Bobbitt's Salt (0.9 mmol, 275 mg) was weighed and put into a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at room temperature and then **DMPP (1a)** (0.15 mmol, 30 mg) was added into the mixture. The reaction mixture was stirred at r.t. for 30 minutes. The reaction solution was injected into a LC-MS (equipped with Phenomenex Luna Omega 1.6μm Polar C18 100Å LC Column 50 x 2.1 mm, eluted with 0-100% acetonitrile/water eluent) to identify the compounds present in the mixture. **2k**, **4** and reduced Bobbitt's Salt were detected and identified by LC-MS (ESI+).



2k

Exact Mass: 499.3378
Found Mass: 499.3384



4

Exact Mass: 223.1329
Found Mass: 223.1336

4.3. Water-added Reactions

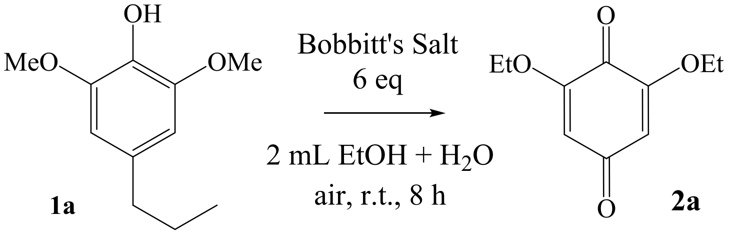


Figure S12. Oxidation Reactions with H_2O added

Bobbitt's Salt (0.9 mmol, 275 mg) was weighed and put into a 20 mL scintillation vial, followed by adding 2 mL ethanol and 2 µL, 5 µL or 10 µL DI water. The mixture was pre-stirred at r.t and then DMPP (0.15 mmol, 30 mg) was added into the mixture. The reaction mixture was then stirred at r.t for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give a solid which was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator to give the crude product. Mesitylene (28.5 mg) was used as the internal standard to give the NMR yield.

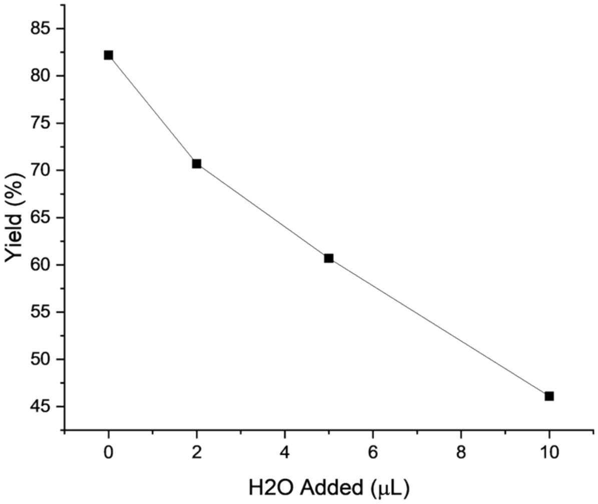
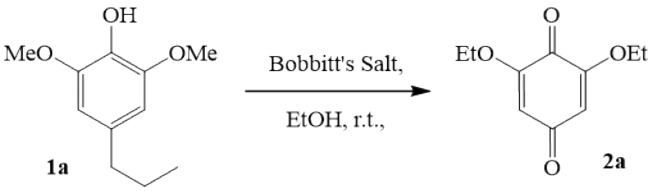
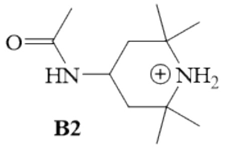


Figure S13. Yield of oxidation products as function of H_2O added

4.4. Oxygen-free and Water-free Control Experiments



Condition Variation	NMR Yield of **2a**
Anhydrous EtOH	>99%
N_2	72%
Anhydrous EtOH + N_2	73%



B2

Exact Mass: 199.1805
Found Mass: 199.1809

Detected by LC-MS after Anhydrous EtOH + N_2 reaction

Figure S14. Control Experiments

General procedure: DMPP (0.15 mmol, 30 mg) was dissolved in 8 mL EtOH in a 25 mL Schlenk flask. Bobbitt's Salt (0.9 mmol, 275 mg) and a stir bar were added, and the reaction mixture was stirred at r.t. for 24 hours. After 24 hours, the Schlenk flask was opened and connected to vacuum to remove the solvent and leave a solid product. Diethyl ether was added into the Schlenk flask, and the solution was then filtered and evaporated under vacuum to get crude product. Mesitylene (28.5 mg) was used as the internal standard to give the NMR yield.

Anhydrous ethanol: 10 g 3A activated molecular sieves were added into 50 mL ethanol. The solvent was set for 7 days to make it anhydrous. The water content in ethanol after drying was less than 10ppm according to literature[2].

N_2 protected reactions were conducted in a N_2 glove box with deaerated ethanol, DMPP and Bobbitt's Salt.

4.5. Ratio of Reduced Bobbitt's Salt to 2,6-diethoxybenzoquinone

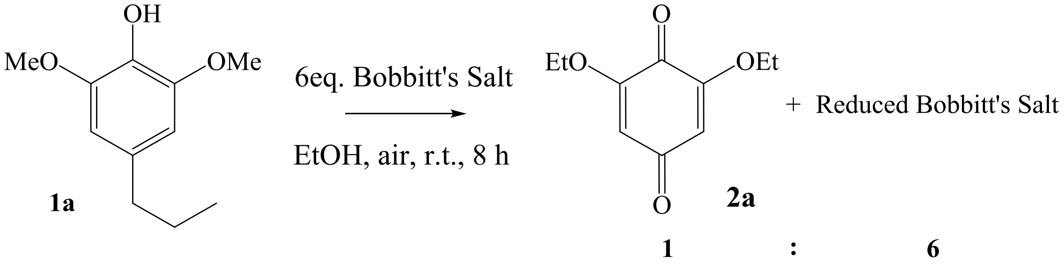


Figure S15. Determination of Ratio of Reduced Bobbitt's Salt to 2,6-diethoxybenzoquinone

Bobbitt's Salt (0.15 mmol, 55 mg) was added into a 20 mL scintillation vial, followed by adding 1.6 mL ethanol. The mixture was pre-stirred at r.t. and then DMPP (0.03 mmol, 6 mg) was added to the mixture which was stirred at r.t. for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give a solid which was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator to give the crude product. The crude product was dissolved in 600 µL trifluoroacetic acid to record the NMR spectrum. The ratio of reduced Bobbitt's Salt to 2,6-diethoxybenzoquinone was calculated to be 6:1 by the integration of peaks from the two compounds in the NMR spectrum.

4.6. Synthesis and Oxidation of 1,2,3-trimethoxy-5-propylbenzene (1h)[3]

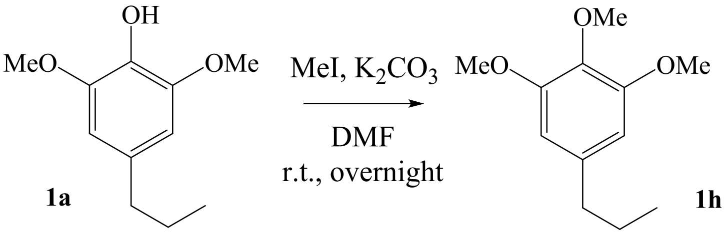


Figure S16. Synthesis of 1,2,3-trimethoxy-5-propylbenzene (**1h**)[3]

In a reaction vial, **1a** (0.3 mmol, 59 mg), 0.6 mL DMF (0.5 M), K_2CO_3 (0.45 mmol, 62 mg) and CH_3I (2.4 mmol, 51 mg) were added. The reaction mixture was stirred at room temperature overnight. Upon the completion, the reaction was quenched by an addition of water and extracted with ethyl acetate. The organic layers were collected, dried over Na_2SO_4, filtered and concentrated under vacuum to give 1,2,3-trimethoxy-5-propylbenzene (1h).

1,2,3-Trimethoxy-5-propylbenzene (**1h**) was isolated as a pale-yellow oil (57 mg, 90%). The analytical data are shown below.
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.40 (s, 2H), 3.85 (s, 6H), 3.82 (s, 3H), 2.53 (t, J = 7.8 Hz, 2H), 1.64 (m, J = 7.5 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 153.01, 138.53, 135.97, 105.31, 60.87, 56.04, 38.52, 24.67, 13.90.
HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}O_3$ 210.1256; Found 210.1253.

When the oxidation of **1h** was carried out under the standard conditions **1h** was fully recovered and no other products were seen (Fig. S18)

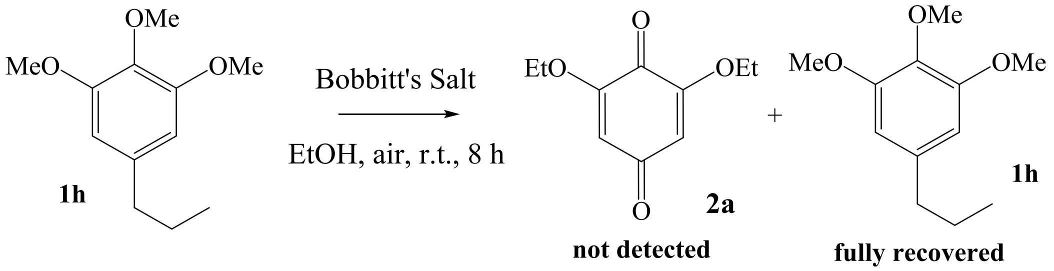


Figure S17. Oxidation of 1,2,3-trimethoxy-5-propylbenzene (**1h**)

4.7. Synthesis and Oxidation of 2,6-dimethoxy-4-methylphenol (1b)

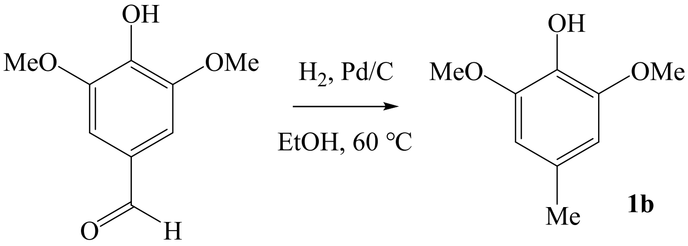


Figure S18. Synthesis of 2,6-dimethoxy-4-methylphenol (**1b**)

Syringaldehyde (2.2 mmol, 0.4 g), Pd/C (68 mg, 3% palladium) and ethanol (15 mL) were loaded into a stainless-steel Parr reactor which was then filled with H_2 (15 bars). The reaction mixture was stirred at 60 °C for 5 hours. Upon the completion of the reaction, the reactor was cooled to r.t. The reaction mixture was then filtered to remove Pd/C, and the filter cake is washed by ethyl acetate. The organic solutions were combined, and the solvent was removed by rotary evaporator to give an oil-like product. The crude product was purified by column chromatography (ethyl acetate/hexanes = 1:2) to give 2,6-dimethoxy-4-methylphenol (**1b**), which was isolated as a colorless semi-solid (329 mg, 89%). The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.39 (s, 2H), 5.36 (s, 1H), 3.86 (s, 6H), 2.29 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 146.86, 132.45, 128.77, 105.63, 56.23, 21.58.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_9H_{12}O_3Na$ 191.0684; Found 191.0681.

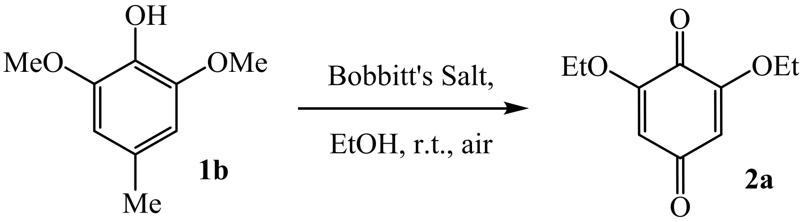


Figure S19. Oxidation of 2,6-dimethoxy-4-methylphenol (**1b**)

Bobbitt's Salt (0.9 mmol, 275 mg) was added into a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was stirred at r.t. and then 2,6-dimethoxy-4-

methylphenol (**1b**) (0.15 mmol, 25 mg) was added. The reaction mixture was stirred at r.t. for 8 hours, then the solvent was removed by rotary evaporator to give a solid. The solid was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:3) to give 2,6-diethoxybenzoquinone (**2a**), which was isolated as a yellow solid (20.0 mg, 68%).

4.8. Synthesis and Oxidation of 4-(1,1-Dimethylpropyl)-2,6-dimethoxyphenol (1c)[4]

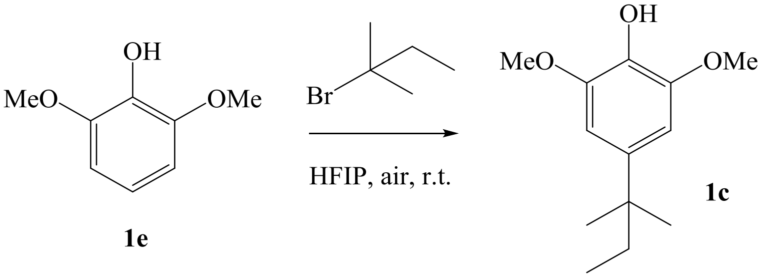


Figure S20. Synthesis of 4-(1,1-dimethylpropyl)-2,6-dimethoxyphenol (**1c**)[4]

In a 20 mL scintillation vial, 2,6-dimethoxyphenol (2 mmol, 308 mg), 5 mL 1,1,1,3,3,3-Hexafluoroisopropanol (0.4 M) and 510 μL 2-bromo-2-methylbutane (4 mmol, 604 mg) were combined. The reaction mixture was then stirred at r.t. for 24 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give an oil-like product. The crude product was purified by column chromatography (ethyl acetate/hexanes = 1:4) to give 4-(1,1-dimethylpropyl)-2,6-dimethoxyphenol (**1c**), which was isolated as a red liquid (212 mg, 47%). The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54 (s, 2H), 5.36 (s, 1H), 3.89 (s, 6H), 1.61 (q, J = 7.4 Hz, 2H), 1.26 (s, 6H), 0.69 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.53, 140.84, 132.53, 103.10, 56.34, 37.94, 37.07, 28.66, 9.16.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{20}O_3Na$ 247.1310; Found 247.1311.

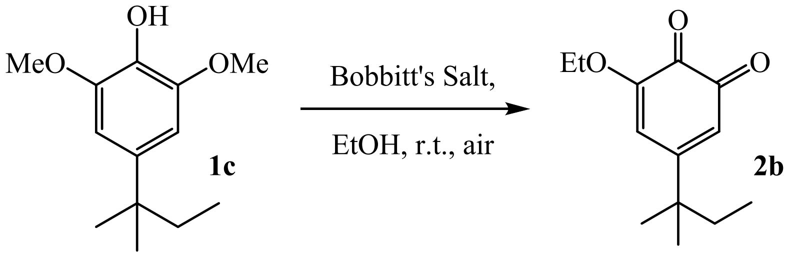


Figure S21. Oxidation of 4-(1,1-Dimethylpropyl)-2,6-dimethoxyphenol (1c)

Bobbitt's Salt (0.9 mmol, 275 mg) was weighed and put into a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at r.t. and then 4-(1,1-

dimethylpropyl)-2,6-dimethoxyphenol (**1c**) (0.13 mmol, 29 mg) was added into the mixture which was then stirred at r.t. for 8 hours. After 8 hours, the solvent was removed by rotary evaporator to give a solid which was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:4) to give 3-ethoxy-5-(1,1-dimethylpropyl)-3,5-cyclohexadiene-1,2-dione (**2b**), which was isolated as a red solid (14.5 mg, 51%). The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.00 (d, J = 1.9 Hz, 1H), 5.97 (d, J = 1.8 Hz, 1H), 3.98 (q, J = 7 Hz, 2H), 1.56 (q, J = 7.4 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H), 1.17 (s, 6H), 0.82 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 179.09, 176.02, 164.23, 151.92, 118.67, 108.51, 77.35, 77.24, 77.03, 76.72, 64.52, 39.86, 33.19, 29.71, 25.76, 14.08, 8.98.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{19}O_3$ 223.1334; Found 223.1336.

4.9. Synthesis and oxidation of 2,6-dimethoxy-4-isopropylphenol (1d)[5]

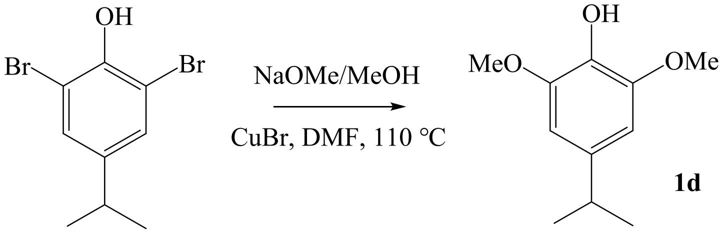


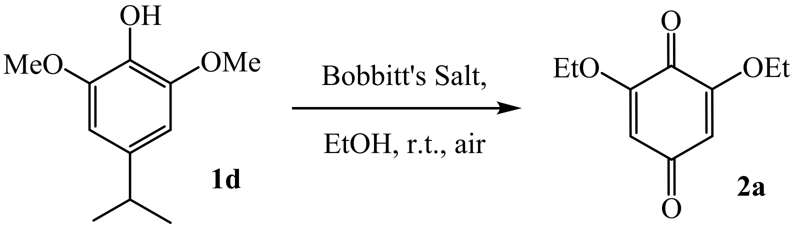
Figure S22. Synthesis of 2,6-dimethoxy-4-isopropylphenol (**1d**)[5]

To a 25% solution of CH_3ONa in CH_3OH (21 mL, 0.09 mol) was added a suspension of CuBr (429 mg, 3.0 mmol) in DMF (10 mL) and stirred at room temperature for 1 h. After the solution became blue, the mixture was added in small portions to a solution of 2,6-dibromo-4-isopropylphenol (0.88 g, 3.0 mmol) in DMF (6 mL) at 110 °C and stirred at this temperature. When the reaction finished, as monitored by TLC, the mixture was cooled to r.t. and acidified with 2 M HCl solution. The methanol was evaporated under reduced pressure and the residue was extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and evaporated under vacuum. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:4) to give 2,6-dimethoxy-4-isopropylphenol (**1d**), which was isolated as an orange-red liquid (529 mg, 90%). The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.45 (s, 2H), 5.36 (s, 1H), 3.89 (s, 6H), 2.83 (m, J = 6.7 Hz, 1H), 1.23 (d, J = 6.8 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.87, 140.21, 132.73, 103.00, 56.27, 34.35, 24.28.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{16}O_3Na$ 219.0997; Found 219.0995.



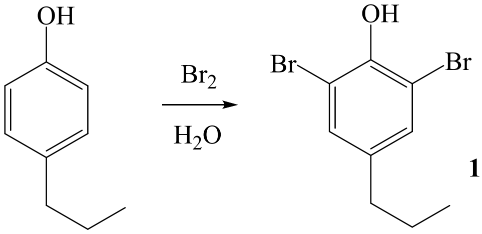
1d

2a

Figure S23. Oxidation of 4-(1,1-dimethylpropyl)-2,6-dimethoxyphenol (**1d**)

Bobbitt's Salt (0.9 mmol, 275 mg) was added to a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at room temperature and then 2,6-dimethoxy-4-isopropylphenol (**1d**) (0.15 mmol, 30 mg) was added to the mixture which was stirred at r.t. for 8 hours. Then, the solvent was removed by rotary evaporator to give a solid which was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:3) to give 2,6-diethoxybenzoquinone (**2a**), which was isolated as a yellow solid (6.2 mg, 21 %).

4.10. Synthesis and Oxidation of 2,6-diethoxy-4-propylphenol (DEPP) (1g)[5]



1f

Figure S24. Synthesis of 2,6-dibromo-4-propylphenol (**1f**)

To a 3.2% solution of Br_2 in H_2O (100 mL, 20 mmol) was added 4-propylphenol (1.36 g, 10 mmol) and the mixture was stirred at r.t. in the dark overnight. The solution was extracted with diethyl ether (2 × 20 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and evaporated under vacuum. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:8) to give 2,6-dibromo-4-propylphenol (**1f**), which was isolated as a yellow liquid (0.742 g, 25%). The analytical data are shown below.

^{1}H NMR (400 MHz, CD_3CN): δ 7.35 (s, 2H), 6.84 (s, 1H), 2.48 (t, J = 7.6 Hz, 2H), 1.57 (m, J = 7.4 Hz, 2H), 0.89 (t, J = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, CD_3CN): δ 148.04, 137.59, 132.09, 109.85, 35.85, 24.19, 12.80.

HRMS (ESI) m/z: $[M - H]^-$ Calcd for $C_9H_9OBr_2$ 292.9000; Found 292.9002.

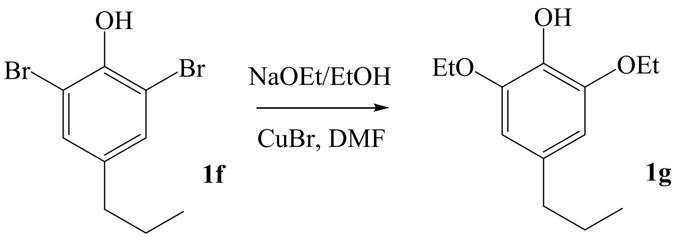


Figure S25. Synthesis of 2,6-diethoxy-4-propylphenol (**1g**)[5]

To a 25% solution of NaOEt in Et_3OH (21 mL, 0.075 mol) was added a suspension of CuBr (360 mg, 2.5 mmol) in DMF (8 mL) and stirred at room temperature for 1 h. After the solution became blue, the mixture was added in small portions to a solution of 2,6-dibromo-4-propylphenol (**1f**) (0.742 g, 2.5 mmol) in DMF (5 mL) at 110 °C and stirred at this temperature. When the reaction finished monitored by TLC, the mixture was cooled to r.t. and acidified with 2 M HCl solution. The mixture was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (4×25 mL), dried with anhydrous Na_2SO_4, filtered and evaporated under vacuum. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:4) to give 2,6-diethoxy-4-propylphenol (**1g**), which was isolated as a pale-yellow solid (267 mg, 47%). The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.38 (s, 2H), 5.38 (s, 1H), 4.10 (q, J = Hz, 4H), 2.48 (t, J = Hz, 2H), 1.60 (m, J = Hz, 2H), 1.43 (t, J = Hz, 6H), 0.93 (t, J = Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.09, 133.62, 133.23, 106.25, 64.72, 38.23, 24.85, 15.02, 13.80.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{20}O_3Na$ 247.1310; Found 247.1322.

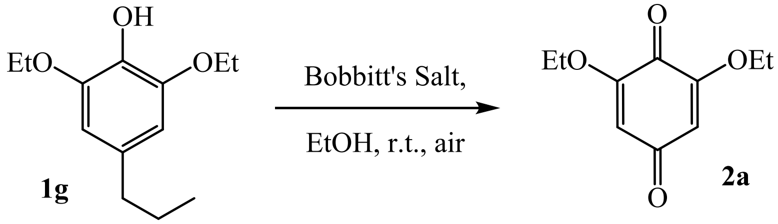


Figure S26. Oxidation of 2,6-diethoxy-4-propylphenol (**1g**)

Bobbitt's Salt (0.9 mmol, 275 mg) was added to a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was pre-stirred at r.t. and then 2,6-diethoxy-4-propylphenol (1g) (0.15 mmol, 34 mg) was added, and the reaction mixture was stirred at r.t. for 8 hours. After 8 hours, the solvent was removed by rotary evaporator to give a solid which was washed with diethyl ether and filtered. The filtrates were combined and evaporated by rotary evaporator. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:3) to give 2,6-diethoxybenzoquinone (**2a)**, which was isolated as a yellow solid (24.4 mg, 81 %).

4.11. 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) and 4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl (4-acetamido-TEMPO) as the Oxidant (TEMPO as an example)

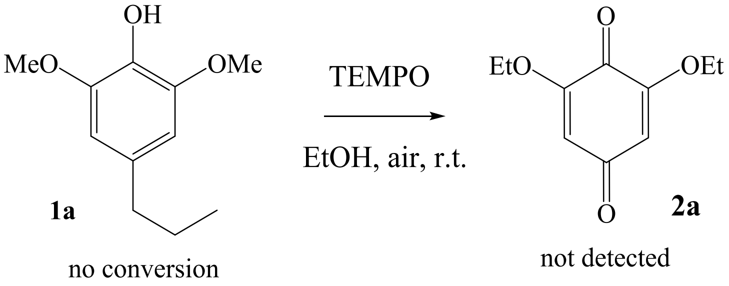


Figure S27. 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) as the oxidant.

TEMPO (0.9 mmol, 150 mg) was added to a 20 mL scintillation vial, followed by adding 8 mL ethanol and DMPP (1a) (0.15 mmol, 30 mg). The reaction mixture was stirred at r.t. for 8 hours after which the solvent was removed by rotary evaporator to give an oil-like liquid. The column chromatography (ethyl acetate/hexanes = 1:4) was used to purify the residue. Notably, both the conversion of DMPP (**1a**) and the yield of 2,6-diethoxybenzoquinone were zero. The DMPP (**1a**) was recovered after reactions.

4.12. Radical Trapping Experiments

TEMPO as the Trapping Agent:

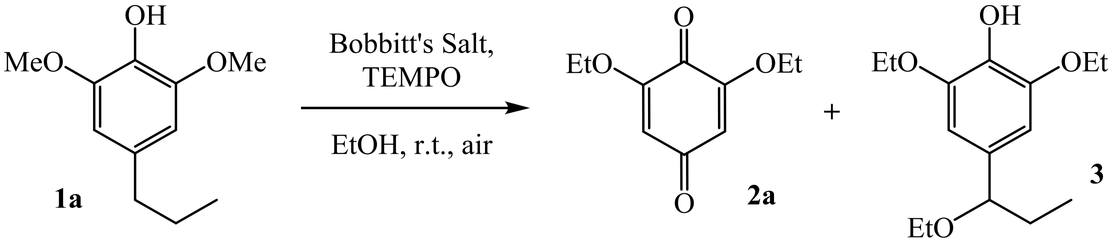
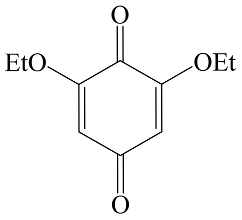


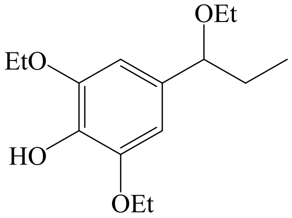
Figure S28. Radical trapping experiment with TEMPO

The trapping reaction was designed to capture a prospective carbon radical. Bobbitt's Salt (0.9 mmol, 275 mg) was added to a 20 mL scintillation vial, followed by adding 8 mL ethanol and TEMPO (0.45 mmol, 75 mg). The mixture was stirred at room temperature and then DMPP (0.15 mmol, 30 mg) was added. The reaction mixture was stirred at r.t. for 8 hours. Upon the completion of the reaction, the reaction solution was injected into a LC-MS (equipped with Phenomenex Luna Omega 1.6µm Polar C18 100Å LC Column 50 x 2.1 mm, eluted with 0-100% acetonitrile/water eluent) to identify the compounds present in the mixture. The compounds detected and identified by LC-MS (ESI+) were the 4-acetamido-TEMPO, reduced Bobbitt's Salt and reduced TEMPO plus 2,6-diethoxybenzoquinone (**2a**, 21% yield) and ethyl-1-(3,5-diethoxy-4-hydroxyphenyl) propyl ether (**3**, 64%) (yields calculated on basis of integrated HPLC peak areas)**.**



Yield: 21%

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_{13}O_4$ 197.0814; Found 197.0810.



Yield: 64%

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{24}O_4Na$ 291.1572; Found 291.1571.

Butylated Hydroxytoluene (BHT) as the Trapping Agent:

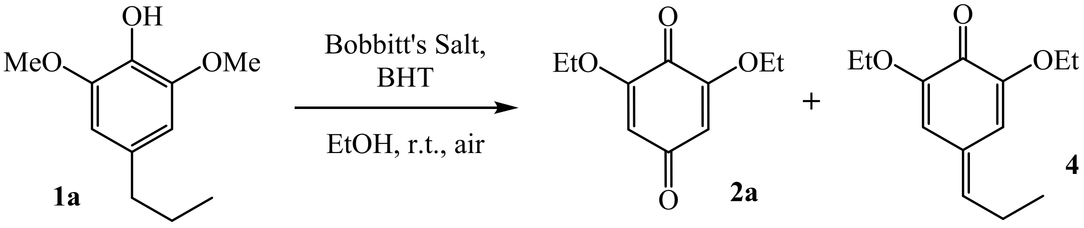
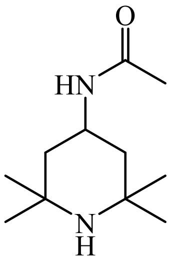


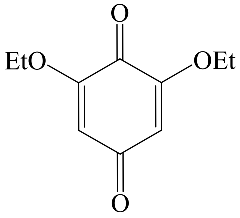
Figure S29. Radical Trapping with BHT.

The BHT-trapping reaction was an attempt to capture an oxygen radical. Bobbitt's Salt (0.9 mmol, 275 mg) was added into a 20 mL scintillation vial, followed by adding 8 mL ethanol and BHT (0.45 mmol, 100 mg). The mixture was stirred at r.t. and then DMPP (0.15 mmol, 30 mg) was added into the mixture which was then stirred at r.t. for 8 hours. Upon the completion of the reaction, the solution was analyzed by LC-MS to identify the components listed below (yields calculated on basis of integrated HPLC peak areas).



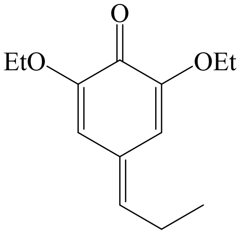
Amine B2

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{23}N_2O$ 199.1810; Found 199.1807.



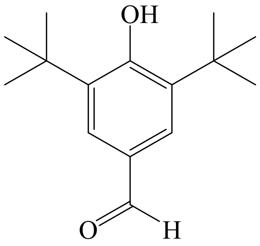
Yield: 32%

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{10}H_{13}O_4$ 197.0814; Found 197.0810.

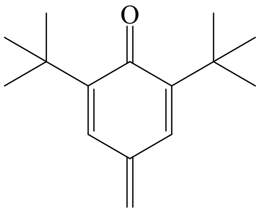


Yield: 64%

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{19}O_3$ 224.1334; Found 223.1330.



HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{23}O_2$ 235.1698; Found 235.1695.



HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{23}O$ 219.1749; Found 219.1746.

4.13. The $^{18}O_2$ Labelling Experiment

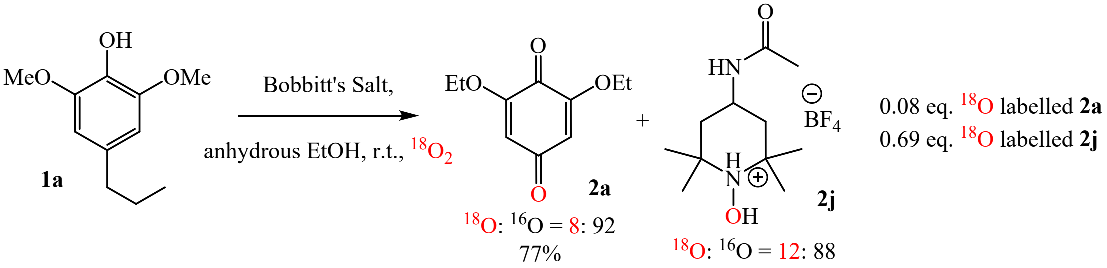


Figure S30. The $^{18}O_2$ labelling experiment

DMPP (0.15 mmol, 30 mg) was dissolved in 8 mL anhydrous $EtOH^2$ in a 25 mL Schlenk flask. Nitrogen gas was continuously bubbled in the solution for 30 minutes. The solution was transferred into another Schlenk flask which contained Bobbitt's Salt (0.9 mmol, 275 mg) and a stir bar under nitrogen atmosphere. The Schlenk flask was put under vacuum, and then oxygen-18 gas was purged into the flask. The reaction mixture was stirred at r.t. for 8 hours. After 8 hours, the Schlenk flask was opened and the reaction solution was injected into a LC-MS (equipped with Phenomenex Luna Omega 1.6µm Polar C18 100Å LC Column 50 x 2.1 mm, eluted with 0-100% acetonitrile/water eluent) to identify the ratio of ^{18}O to ^{16}O in products. By LC-MS (ESI+), $[M + 3]^+$ peak intensity : $[M + 1]^+$ peak intensity = 20987 : 237998 in DEBQ, $[M + 3]^+$ peak intensity : $[M + 1]^+$ peak intensity = 39087 : 300558 in reduced Bobbitt's Salt. Based on calculation, ^{18}O labelled DEBQ : ^{16}O labelled DEBQ = 8 : 92, ^{18}O labelled reduced Bobbitt's Salt : ^{16}O labelled reduced Bobbitt's Salt = 12 : 88.

Then, the solution was connected to vacuum to remove the solvent and leave a solid product. Diethyl ether was added into the Schlenk flask, and the solution was then filtered and evaporated under vacuum to get crude product. Mesitylene (28.5 mg) was used as the internal standard to give the 77% NMR yield.

Because one equivalent DMPP and six equivalents Bobbitt's Salt were added, there were 0.06 equivalent ^{18}O labelled DEBQ and 0.72 equivalent ^{18}O labelled reduced Bobbitt's Salt after the reaction.

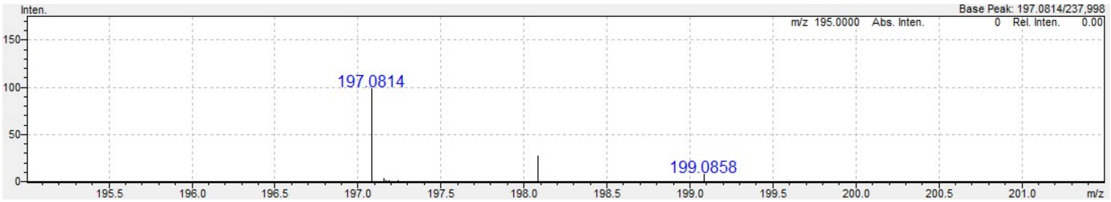


Figure S31. Fragments in the Mass Spectrometry Spectrum of DEBQ

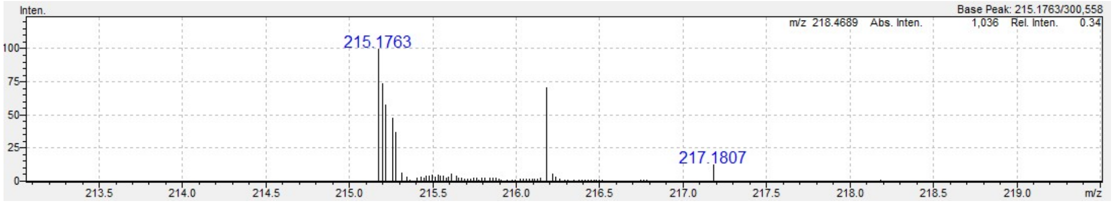


Figure S32. Fragments in the Mass Spectrometry Spectrum of reduced Bobbitt's Salt

4.14. Synthesis and Stability Test of N-(2,2,6,6-tetramethylpiperidin-4-yl)acetamide

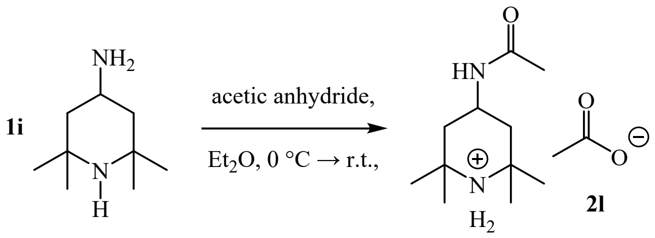


Figure S33. Synthesis of 4-acetamido-2,2,6,6-tetramethylpiperidin-1-ium acetate (**2l**)[6]

1 g N-(2,2,6,6-tetramethylpiperidin-4-yl)amine (**1i**) was dissolved in 5 mL anhydrous diethyl ether. The solution was put into ice bath. Acetic anhydride (1 g) dissolved in 5 mL anhydrous diethyl ether was added dropwise into the solution. Upon the completion of addition, the ice bath was removed, and the mixture was stirred for 3 hours. After 3 hours, the mixture was separated by filtration. The precipitate was collected and recrystallized with ethanol/diethyl ether. After recrystallization, the solid was collected by filtration and dried under vacuum overnight. 4-acetamido-2,2,6,6-tetramethylpiperidin-1-ium acetate (**2l**) was isolated as a white solid (1.1 g, 67%). The analytical data are shown below.

^{1}H NMR (400 MHz, DMSO-d6): δ 7.65 (d, 1H), 3.98 (m, 1H), 1.87 (s, 3H), 1.76 (s, 3H), 1.60 (dd, 2H), 1.13 (s, 6H), 1.03 (s, 6H), 0.95 (dd, 2H).

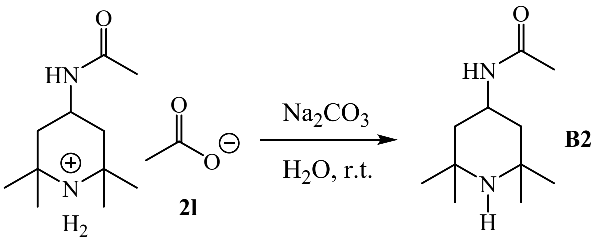


Figure S34. Synthesis of N-(2,2,6,6-tetramethylpiperidin-4-yl)acetamide (**B2**)

0.3 g (1.2 mmol) 4-acetamido-2,2,6,6-tetramethylpiperidin-1-ium acetate (**2l**) was dissolved in 10 mL DI water. 0.3 g (2.8 mmol, 2.4 eq.) sodium carbonate was added into the solution. The solution was stirred for 30 minutes. After 30 minutes, the solution was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate and filtered, and the solvent was removed under reduced pressure. N-(2,2,6,6-tetramethylpiperidin-4-yl)acetamide (**B2**) was isolated as a colorless oil (50 mg, 21%). The analytical data are shown below.
^{1}H NMR (400 MHz, CDCl$_3$): δ 5.61 (d, 1H), 4.18 (m, 1H), 1.90 (s, 3H), 1.82 (dd, 2H), 1.19 (s, 6H), 1.06 (s, 6H), 0.87 (dd, 2H).
^{13}C NMR (101 MHz, CDCl$_3$): δ 169.15, 51.06, 45.15, 42.42, 34.81, 28.42, 23.49.

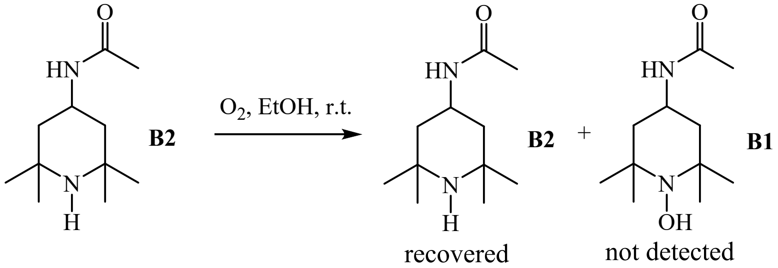


Figure S35. Stability Test of N-(2,2,6,6-tetramethylpiperidin-4-yl)acetamide (**B2**)
50 mg N-(2,2,6,6-tetramethylpiperidin-4-yl)acetamide (**B2**) was dissolved in 2 mL ethanol. The solution was transferred into a Schlenk flask which contained a stir bar under oxygen atmosphere. After 8 hours, the Schlenk flask was opened and the reaction solution was injected into a LC-MS (equipped with Phenomenex Luna Omega 1.6µm Polar C18 100Å LC Column 50 x 2.1 mm, eluted with 0-100% acetonitrile/water eluent) to identify the products. No **B1** was detected.

4.15. Analysis of Oxidation Side Products

Bobbitt's Salt (0.9 mmol, 275 mg) was added to a 20 mL scintillation vial, followed by adding 2 mL anhydrous ethanol. The mixture was stirred at r.t. and then **DMPP (1a)** (0.15 mmol, 30 mg) was added into the mixture. The reaction mixture was stirred at room temperature for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator and collected. The solvent collected from condensate-collecting flask was designated as "**solvent after reaction**". The components of **solvent after reaction** were analyzed by GC-FID (Fig. 33). Solutions of ethyl propionate (boiling point at 99 °C) in ethanol, and 1,1-diethoxypropane (boiling point at 122-124 °C) in ethanol were prepared as the GC-FID references (Fig. S32).

GC method: Initial temperature was 40 °C and held at 40 °C for 3 minutes. Ramped up to 320 °C with 25 °C/minute rate, then held at 320 °C for 10 minutes. Total run time for GC-FID process was 24.2 minutes.

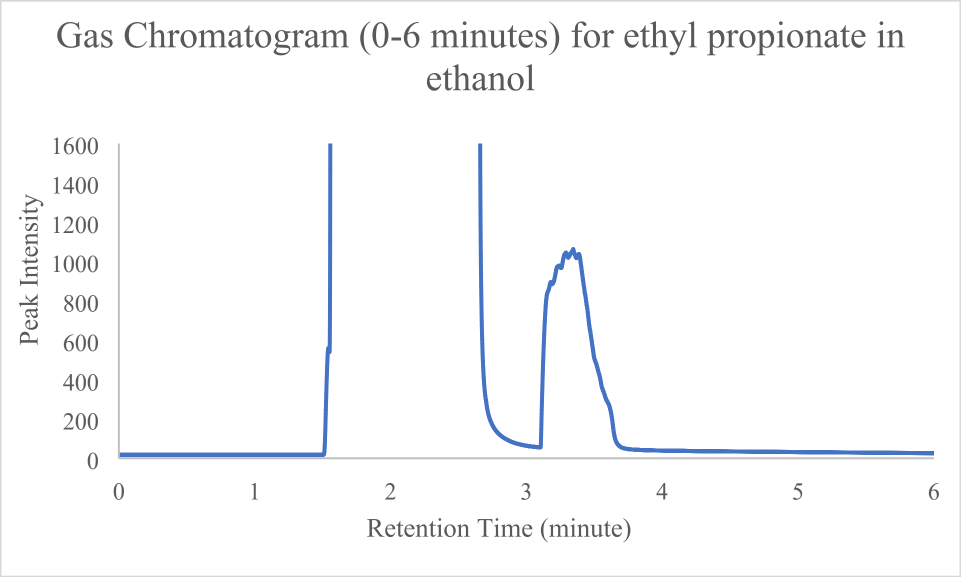


Figure S36. GC chromatogram (0-6 minutes) for ethyl propionate (the second peak) in ethanol (the first peak) solution

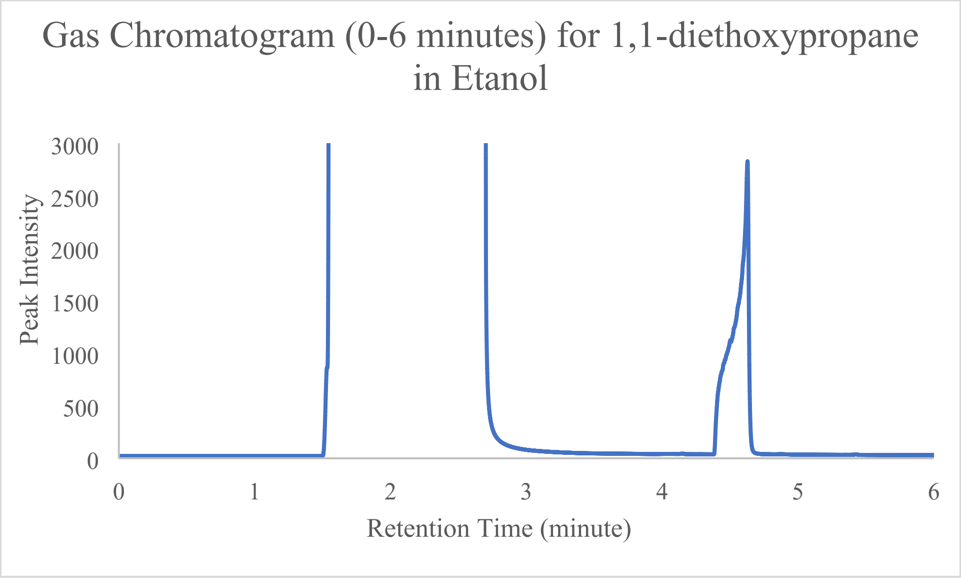


Figure S37. GC chromatogram (0-6 minutes) for 1,1-diethoxypropane (the second peak) in ethanol (the first peak) solution

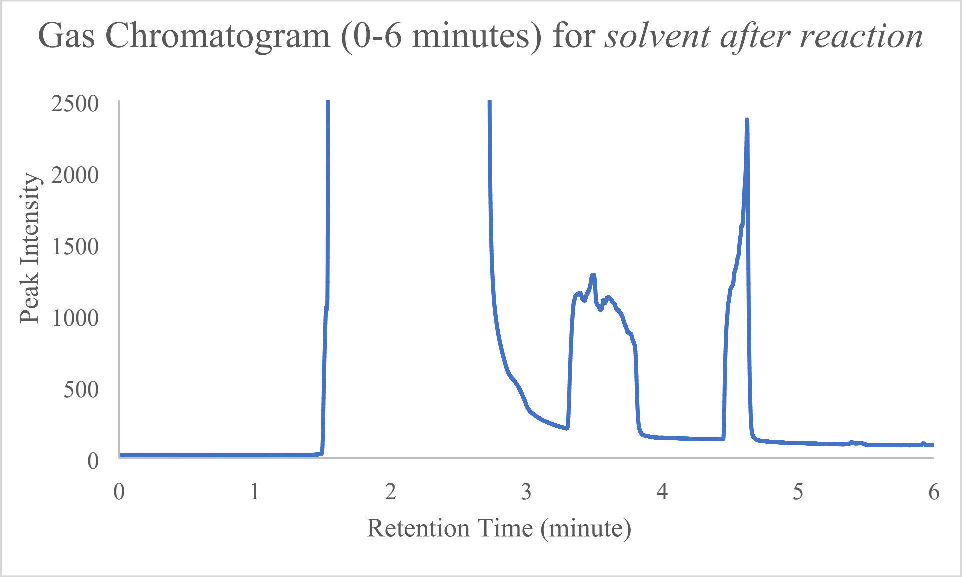


Figure S38. GC chromatogram (0-6 minutes) for solvent after reaction showing the presence of ethyl propionate (0.094 mmol, the second peak) and 1,1-diethoxypropane (0.030 mmol, the third peak)

Based on the Gas Chromatogram for "solvent after reaction", 0.094 mmol ethyl propionate and 0.030 mmol 1,1-diethoxypropane were generated (yields calculated on basis of integrated GC peak areas). The sum of ethyl propionate and 1,1-diethoxypropane (0.124 mmol) were in stoichiometric ratio to the DEBQ product formed (0.127 mmol).

4.16. Mechanism of Oxidation without Molecular Oxygen

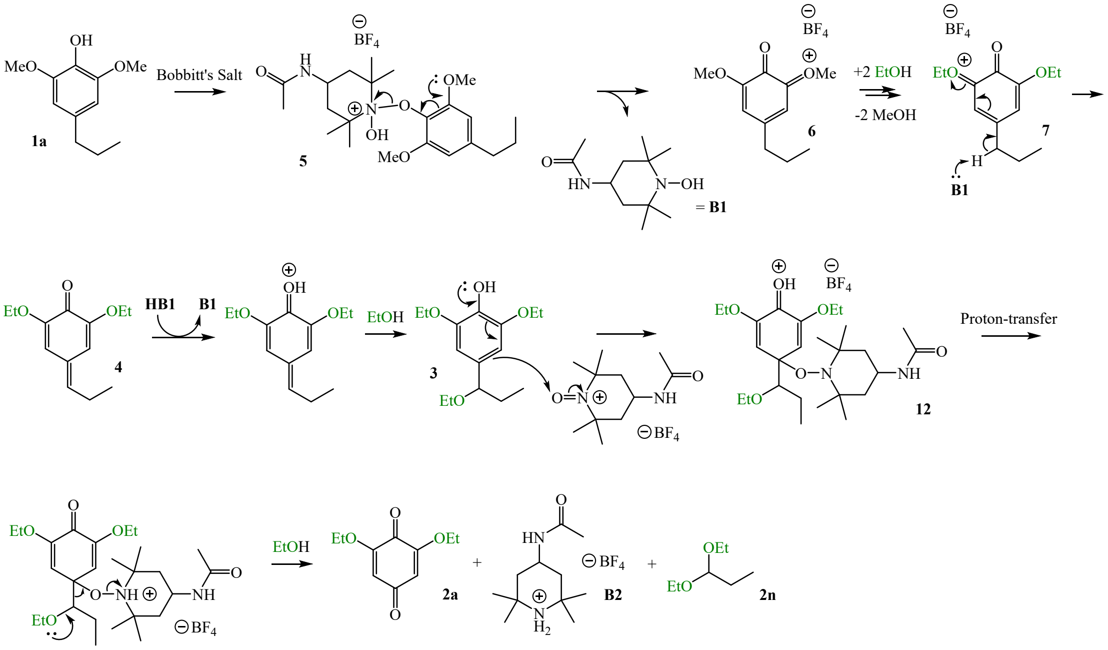


Figure S39. Mechanism of oxidation without molecular oxygen

The mechanism of oxidation in the absence of molecular oxygen is identical to that with molecular oxygen until the formation of intermediate **3**. Intermediate **3** acts as a nucleophile, attacking Bobbitt's Salt at the para position to form intermediate **12**. The decomposition of intermediate **12** produces DEBQ **2a**, base **B2**, and 1,1-ethoxypropane **2n**. When intermediate **3** attacks Bobbitt's Salt at the ortho position, it likely leads to ring-opening side products, resulting in decreased selectivity compared to oxidation mediated by aerobic oxygen.

4.17. Base (Dicyclohexylamine) Added Reaction

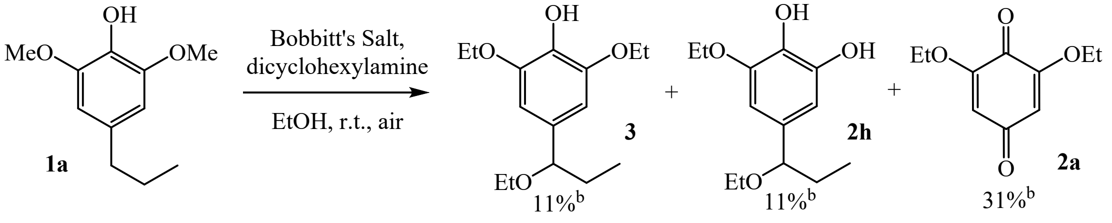
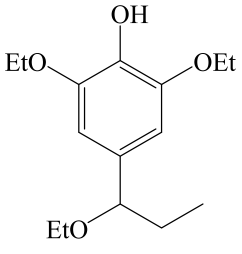


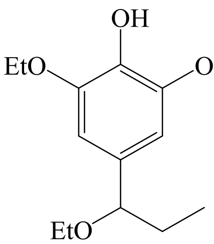
Figure S40. Dicyclohexylamine added reaction

Bobbitt's Salt (0.9 mmol, 275 mg) was added into a 20 mL scintillation vial, followed by adding 8 mL ethanol and dicyclohexylamine (0.45 mmol, 82 mg). The mixture was pre-stirred at room temperature and then DMPP (0.15 mmol, 30 mg) was added. The reaction mixture was stirred at r.t. for 8 hours. Upon the completion of the reaction, the solvent was removed by rotary evaporator to give a solid which was washed with diethyl ether and filtered. The filtrates are combined and evaporated by rotary evaporator. The products were separated by column chromatography (ethyl acetate/hexanes = 1:2) and the separated products collected and identified by NMR and LC-MS. See below:

2,6-Diethoxybenzoquinone (**2a**) was isolated as a yellow solid (9.1 mg, 31%).



Ethyl-1-(3,5-diethoxy-4-hydroxyphenyl) propyl ether (**3**) was isolated as a white solid (4.5 mg, 11%).



Ethyl-1-(3-ethoxy-4,5-dihydroxyphenyl) propyl ether (**2h**) was isolated as a red oil (4.0 mg, 11%). The analytical data are shown below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.50 (d, J = 1.6 Hz, 1H), 6.43 (d, J = 1.6 Hz, 1H), 5.37 (s, 1H), 5.31 (s, 1H), 4.11 (q, J = 7 Hz, 2H), 3.96 (t, J = 6.6 Hz, 1H), 3.33 (m, 2H), 1.78 (m, J = 7.1 Hz, 1H), 1.60 (m, J = 7 Hz, 1H), 1.43 (t, J = 7 Hz, 3H), 1.16 (t, J = 7 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.15, 143.52, 134.95, 131.54, 107.26, 101.91, 83.66, 64.61, 63.91, 31.14, 15.35, 14.93, 10.42.

HRMS (ESI) m/z: $[M - C_2H_5O]^+$ Calcd for $C_{11}H_{15}O_3$ 195.1021; Found 195.1015.

4.18. Oxidation of 2,6-dimethoxyphenol (1e)

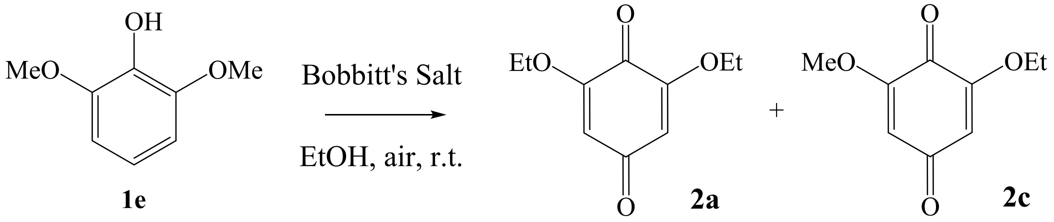
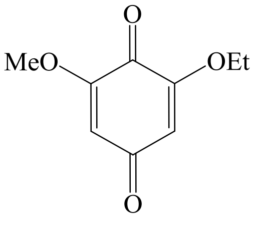


Figure S41. Oxidation of 2,6-dimethoxyphenol (1e)

Bobbitt's Salt (0.9 mmol, 275 mg) was added a 20 mL scintillation vial, followed by adding 8 mL ethanol. The mixture was stirred at r.t. then 2,6-dimethoxyphenol (**1e**) (0.15 mmol, 23 mg) was added. The reaction mixture was stirred at r.t. for 8 hours. After 8 hours, the solvent was removed by rotary evaporator to give a solid that was washed with diethyl ether and filtered. The filtrates were combined and the ether removed by rotary evaporator. The obtained residue was purified by column chromatography (ethyl acetate/hexanes = 1:4). The products are listed below.

2,6-Diethoxybenzoquinone (**2a**) is isolated as a yellow solid (17.0 mg, 58%).

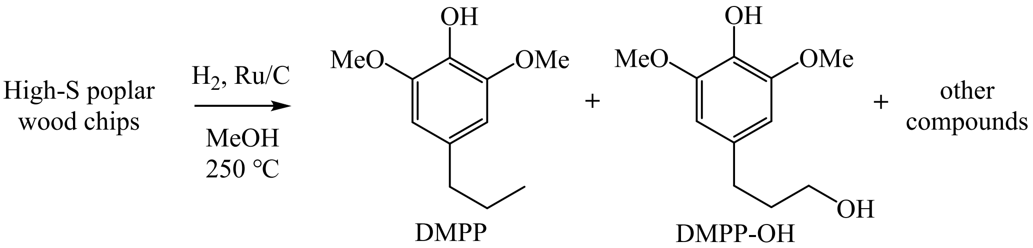


2-Ethoxy-6-methoxybenzoquinone (**2c**) is isolated as a yellow solid (3.4 mg, 12%). The analytical data are shown below.
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83 (d, J = 2.4 Hz, 1H), 5.81 (d, J = 2.4 Hz, 1H), 4.00 (q, J = 7 Hz, 2H), 3.81 (s, 3H), 1.48 (t, J = 7 Hz, 3H)
^{13}C NMR (101 MHz, $CDCl_3$): δ 187.16, 176.73, 157.34, 156.57, 107.69, 107.27, 65.42, 56.44, 13.87.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_9H_{11}O_4$ 183.0657; Found 183.0657.

5. Reductive Catalytic Fragmentation of F5H Poplar and Catalyst Recycle

5.1. Reductive Catalytic Fragmentation of F5H Poplar

Table S2. Optimization of reductive catalytic fragmentation of F5H poplar[a]



Entry	Catalyst loading/wt%	Yield of DMPP-OH[b]/μmol	Yield of DMPP[b]/μmol	Yield combined[b]/μmol
1	3	100.38	310.7	411.08
2	**5**	**132.16**	**349.44**	**481.6**
3[c]	3	114.48	274.32	388.8

[a] Unless specified, 1 g High-S poplar wood chips, Ru/C (5% Ru) catalyst, 30 bar H_2 in 30 mL MeOH is stirred for 15 h in a 75mL stainless-steel parr reactor vessel. Mesitylene (100 μmol) is used as the internal standard to give the NMR yield. [b] NMR yield. [c] 45 h.

To begin, F5H poplar wood was grinded using a coffee grinder and sifted through a 212 micrometer (65 mesh) filter. 1 g of the grinded wood was added to a 75 mL stainless steel parr reactor, along with 30 mL MeOH, Ru/C (5% Ru), and a glass stir bar. The parr was then flushed with 30 bar H_2 three times to obtain a hydrogen headspace. Finally, 30 bars H_2 was filled one last time then heated to 250 °C to react for 15 hours. Once the reaction was done, the reactor was allowed to cool for thirty minutes and filtered through a fine porosity frit. The methanol was then removed by a rotavapor and redissolved in EtOAc and water in a 1:1 mixture. The mixture was centrifuged, and the organic fraction was pipetted into a separate round bottom flask. This was repeated three times. The EtOAc was removed by a rotavapor, and the remaining oil was allowed to dry overnight. The leftover lignin oil product was then used in later oxidation reactions.

5.2. Catalyst Recycle Test

This reaction was done using the same procedure in the large scale RCF reaction; however, at the end of every reaction, we collected the remaining solids with the methanol filtration and extracted Ru/C from the centrifugation to try and recycle the Ru/C catalyst to determine its recyclability potential in our procedure.

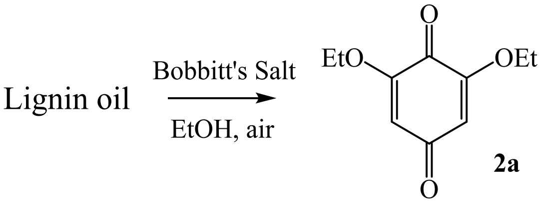
Table S3. Catalyst Performance at Each Trial in Recyclability Test

Trial	lignin oil/mg	Yield of DMPP-OH/μmol	Yield of DMPP /μmol	Combined yield of DMPP and DMPP-OH/μmol	Mass of solids before reactions/mg	Mass of leftover solids/mg
1	227.4	123.7	326.3	450.0	50	250-275
2	217.1	98.5	221.7	320.2	250-275	400-450
3	238.6	83.5	214.7	298.2	400-450	450-500

After each reaction was completed, a new gram of grinded F5H wood was added with 20 mL of methanol and the black solids collected from the centrifugation and filtration to start the next reaction. There is roughly the same amount of lignin oil at the end of the reactions, but the contents of DMPP and DMPP-OH decrease, most likely due to the loss of some Ru/C catalyst during each reaction, as some may become suspended or remain adhered to the residual wood.

6. Oxidation of Lignin Oil

Table S4. Optimization of the Oxidation of Lignin Oil[a]



Entry	Bobbitt's Salt/mg	Time/h	Temperature/°C	Yield of **2a**[b]/%
1	**500**	**24**	**r.t**	**95.0%**
2	373	24	r.t	55.4%
3	500	48	r.t	87.8%
4	500	24	80	57.5%
5	620	24	r.t.	67.2%

[a] Unless specified, 50 mg lignin oil from RCF of wood chips and 500 mg Bobbitt's Salt in 8 mL EtOH was stirred for 24 hours in a 20 mL scintillation vial under room temperature. Mesitylene (100 μmol) was used as the internal standard to give the NMR yield. The yield is based on the total amount of DMPP and DMPP-OH in the lignin oil. [b] NMR yield.

Using the products from hydrogenolysis, 50 mg of the oil was measured. In a 20 mL scintillation vial, 500 mg of Bobbitt's Salt was added along with 4 mL of ethanol and allowed to stir until the Bobbitt's Salt was mostly in solution. 50 mg of lignin oil was then dissolved in 4 mL of ethanol and added into the Bobbitt's Salt-ethanol solution. The reaction was then stirred at room temperature for 24 hours. After 24 hours, the ethanol was evaporated off, and the remaining products were redissolved in ether, and the solids were filtered off. The remaining ether solution was pumped off and 12.02 mg (0.1 mmol) Mesitylene was then added as an internal standard, and the products were dissolved in chloroform-d1 and were taken for NMR quantification.

7. Scaled-up Reductive Catalytic Fragmentation of F5H Poplar, Subsequent Oxidation of Lignin Oil, and Isolation of DEBQ

7.1. Scaled-up Reductive Catalytic Fragmentation of F5H Poplar

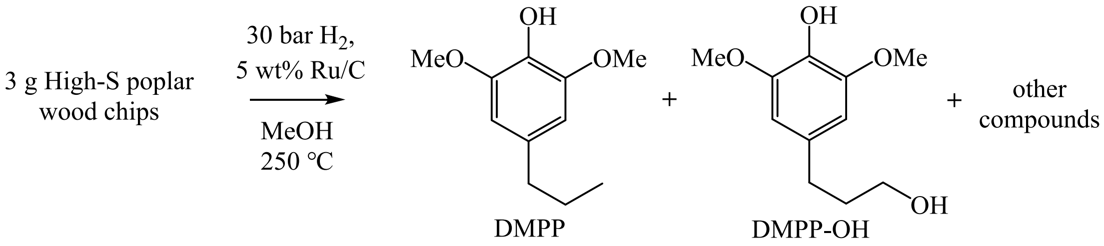


Figure S42. Scaled-up RCF of F5H Poplar

To begin, F5H poplar wood was grinded using a coffee grinder and sifted through a 212 micrometer (65 mesh) filter. 3 grams of the grinded wood was added to a 75 mL stainless steel parr reactor, along with 30 mL MeOH, 150 mg (5 wt%) Ru/C (5% Ru), and a glass stir bar. The parr was then flushed with 30 bar H_2 three times to obtain a hydrogen headspace. Finally, 30 bars H_2 was filled one last time then heated to 250 °C to react for 18 hours. Once the reaction was done, the reactor was allowed to cool for thirty minutes and filtered through a fine porosity frit. The methanol was then removed by a rotavapor and redissolved in EtOAc and water in a 1:1 mixture. The mixture was centrifuged, and the organic fraction was pipetted into a separate round bottom flask. This was repeated three times. The EtOAc was removed by a rotavapor, and the remaining oil was allowed to dry for 36-48 hours. By taking an aliquot for quantitative NMR, the 740 mg lignin oil contained 1418.8 μmol, or 286 mg, DMPP and DMPP-OH total. To be specific, it contained 957.7 µmol, or 187.7 mg DMPP, and 461.11 µmol, or 97.87 mg DMPP-OH.

7.2. Oxidation of Lignin Oil and Isolation of DEBQ

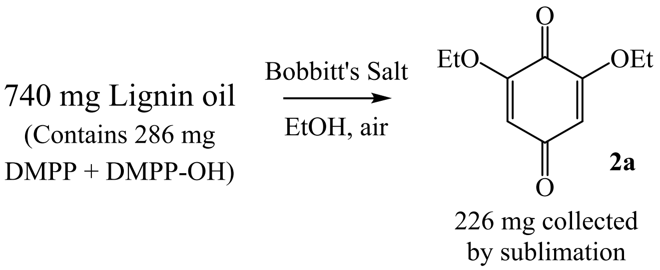


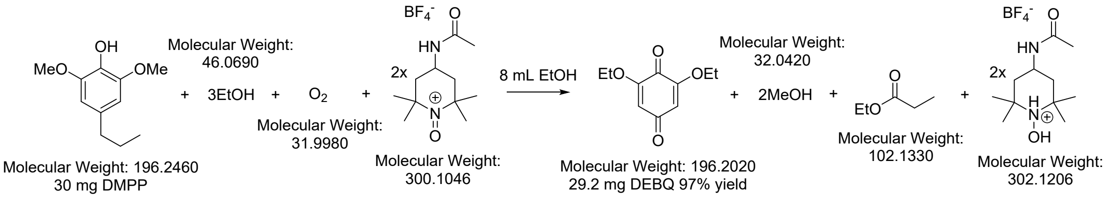
Figure S43. Oxidation of Lignin Oil obtained from Scaled-up RCF

After allowing the remaining lignin oil to dry over a Schlenk line for 36-48 hours, 7.4 grams of Bobbit's Salt was added to 70 mL EtOH in a 500 mL round bottom flask, containing a large stir bar. The lignin oil in the vial was then dissolved in 10 mL EtOH and added to the round bottom flask, and the reaction was allowed to stir for 24 hours at room temperature for 24 hours. After 24 hours, the ethanol was evaporated off, and the remaining products were redissolved in ether, and the solids were filtered off. The remaining ether solution was pumped off to get a crude product mixture containing DEBQ.

The crude product was redissolved in DCM and transferred into a sublimator. The DCM was then removed by heating. The leftover solid underwent sublimation, and the yellow oil on the surface of the sublimator was collected.

8. Calculation of Green Chemistry Metrics[6]

Table S5. Green Chemistry Metrics



Green Chemistry Metrics	Value
Atom Economy	81.4%
Carbon Efficiency	88.2%
Reaction mass efficiency	79.0%
E-factor	2.0

Calculation: DEBQ and ethyl propionate are products of the reaction.

Atom economy $(AE) = \frac{m.w.\ of\ product}{\sum m.w.\ of\ reactants}$[6]

$$AE = \frac{m.w. of\ DEBQ + m.w.\ of\ ethyl\ propionate}{m.w. of\ DMPP + 3 \times m.w. of\ EtOH + m.w. of\ O_2} = \frac{196.2020 +}{196.2460 + 3 \times 46} = \frac{298.335}{366.451} = 81.4\%$$

Carbon efficiency $(CE) = \frac{amount\ of\ carbon\ in\ product}{total\ carbon\ present\ in\ reactants}$[6]

$$CE = \frac{carbon\ in\ DEBQ + carbon\ in\ ethyl\ propionate}{carbon\ in\ DMPP + carbon\ in\ EtOH} = \frac{10+5}{11+3\times 2} = \frac{15}{17} = 88.2\%$$

Reaction mass efficiency $= \frac{mass\ of\ product}{mass\ of\ reactants} = AE \times yield = 81.4\% \times 97\% = 79.0\%$[6]

E-factor $= \frac{mass\ of\ total\ waste}{mass\ of\ product}$[6]

Ethanol is not a waste (can be reused as a solvent), and Bobbitt's Salt is also not a waste (can be regenerated electrochemically)[3]. In electrochemical regeneration, 25 mL of 40 mM (1 mmol, 110 mg) $NaBF_4$ (MW = 109.7934 g/mol) is added into 127 mg reduced Bobbitt's Salt for four regeneration cycles[3]. Thus, $NaBF_4$ is the only waste.

$$E - factor = \frac{mass\ of\ NaBF_4}{mass\ of\ product} = \frac{110\,mg \times \frac{275\,mg}{127\,mg}}{4 \times 29.2\,mg} = \frac{238.2\,mg}{116.8\,mg} = 2.0$$

9. References

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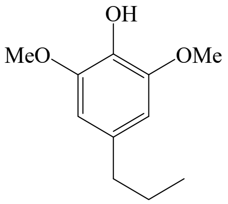
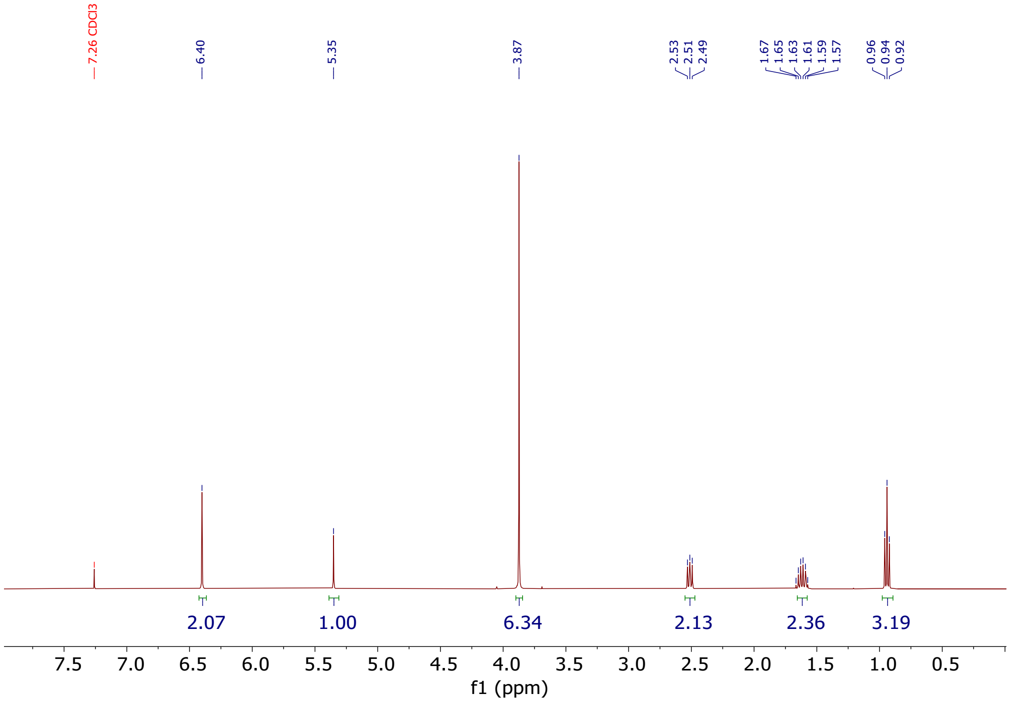
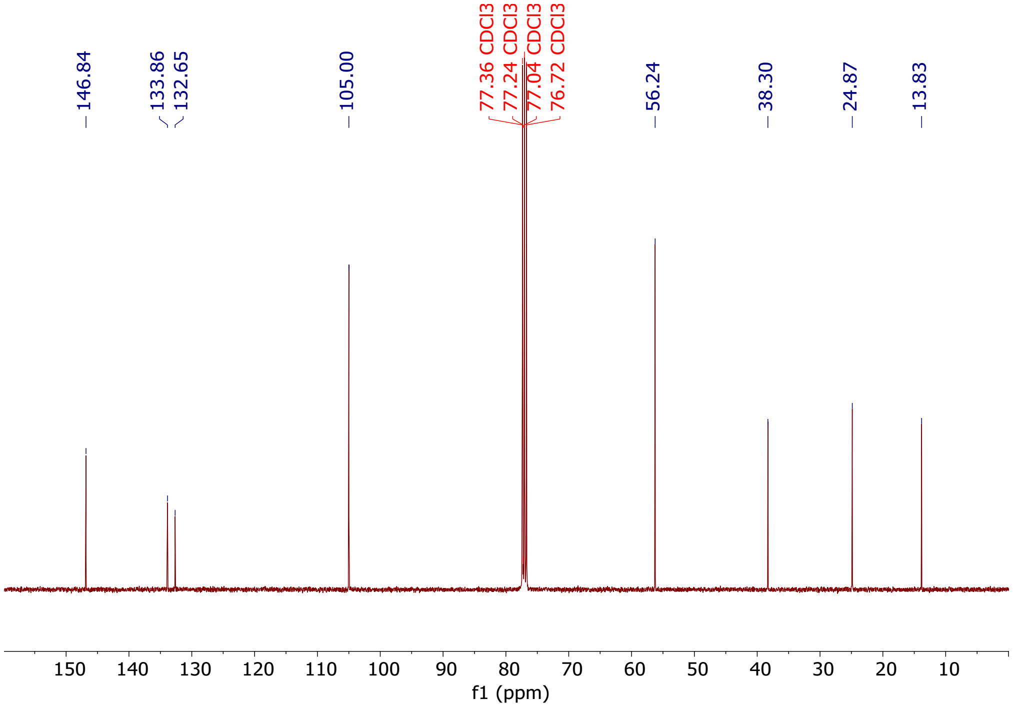
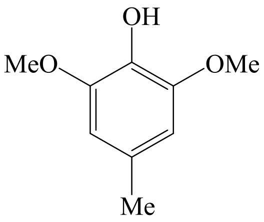
10. Proton and Carbon NMR Spectra.



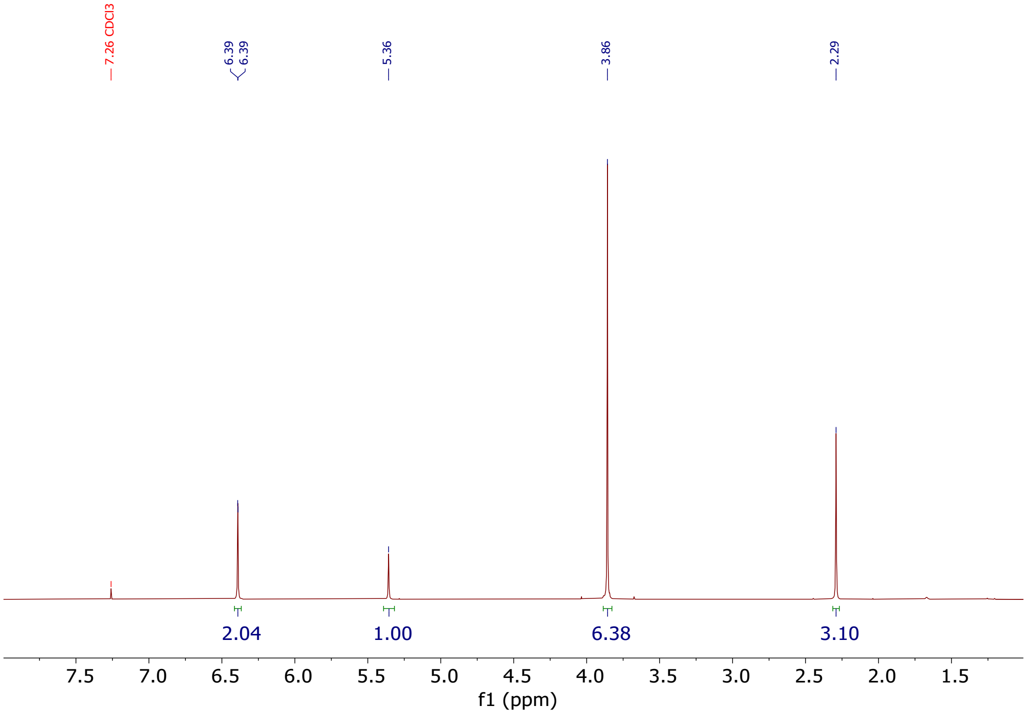
8.1 2,6-Dimethoxy-4-propylphenol (DMPP)

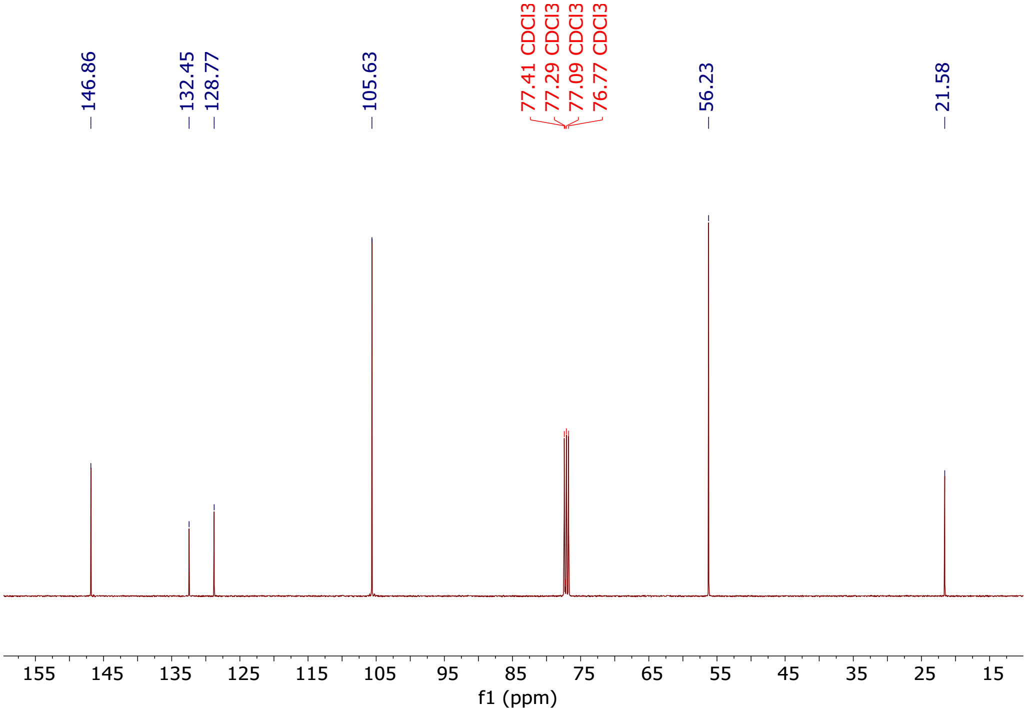




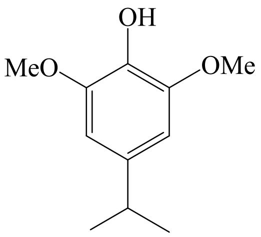


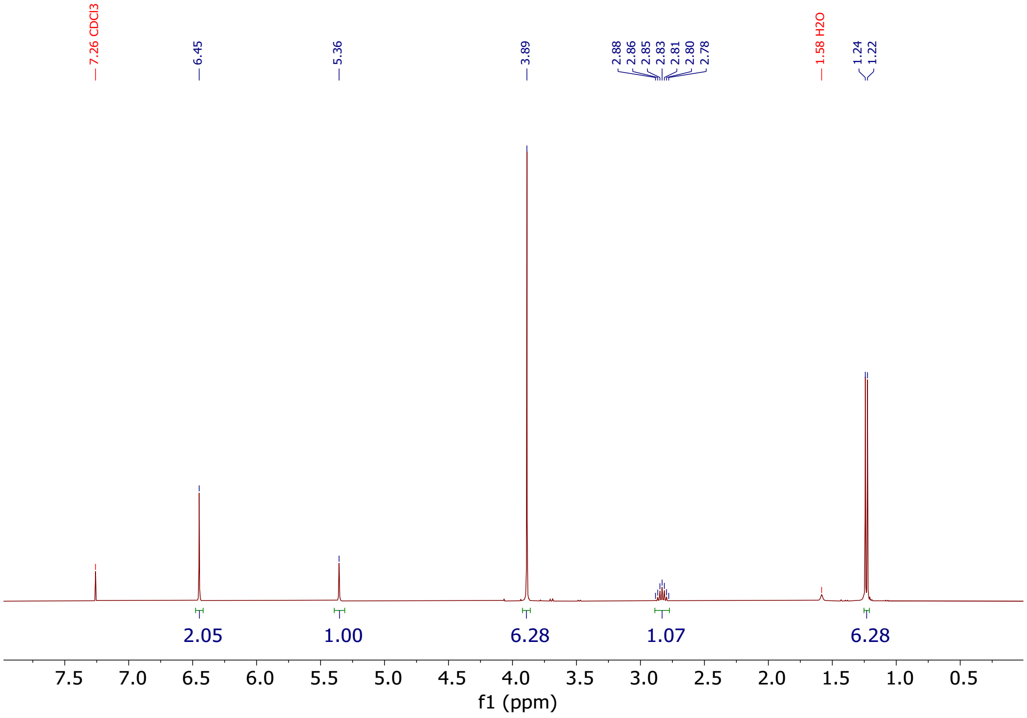
8.2 2,6-Dimethoxy-4-methylphenol

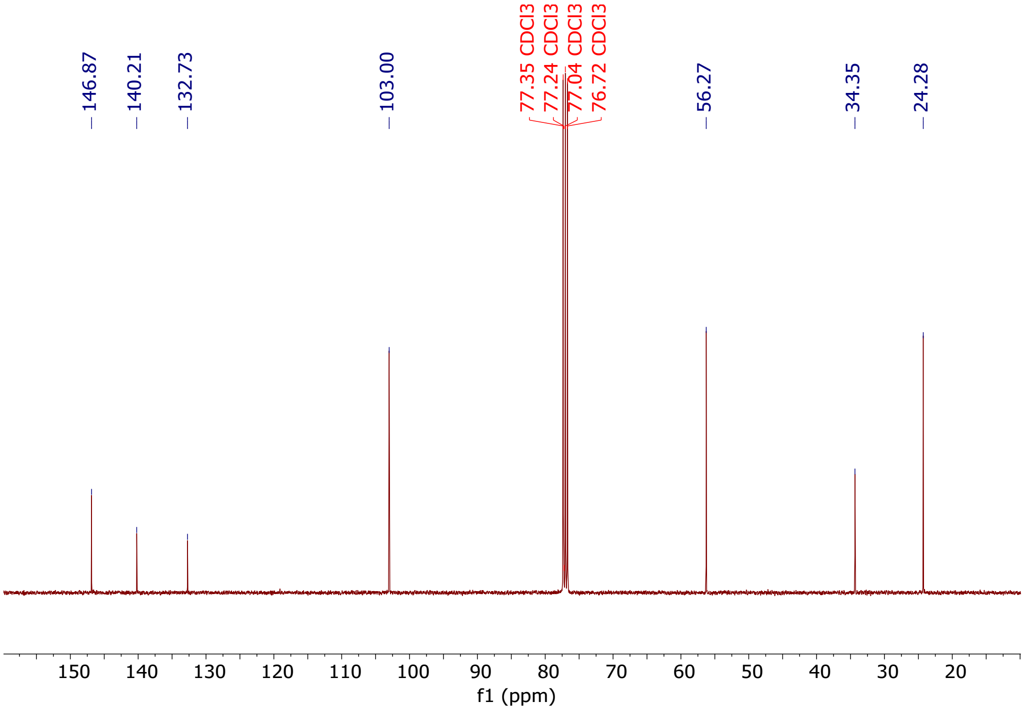




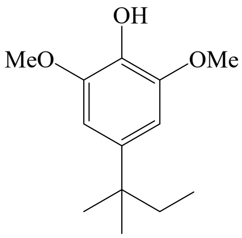
8.3 2,6-Dimethoxy-4-isopropylphenol

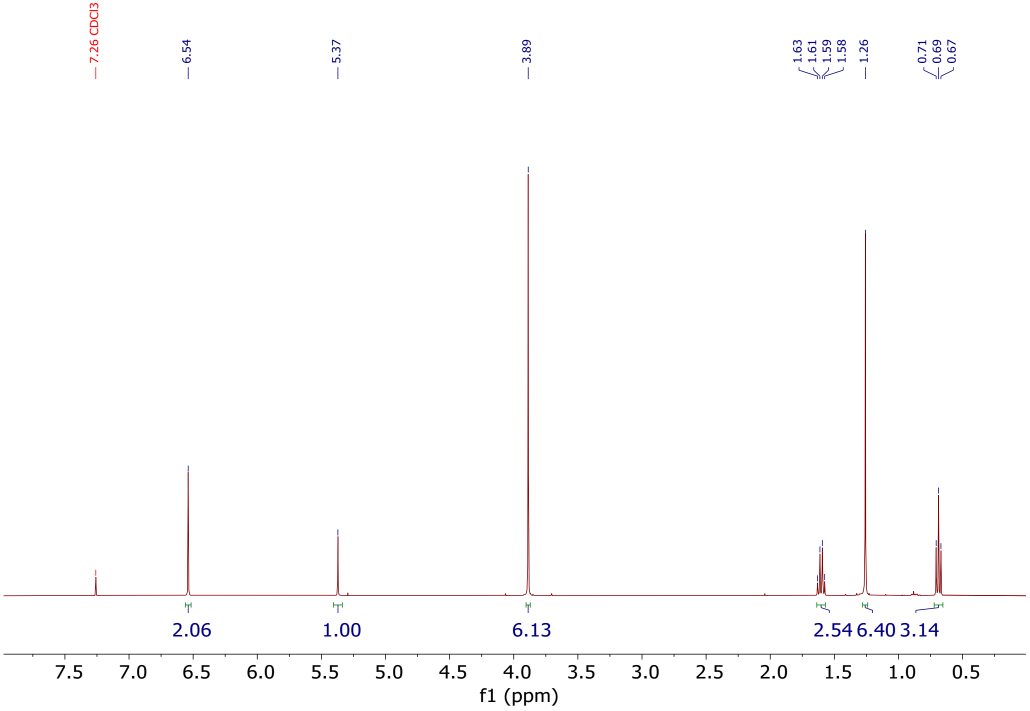


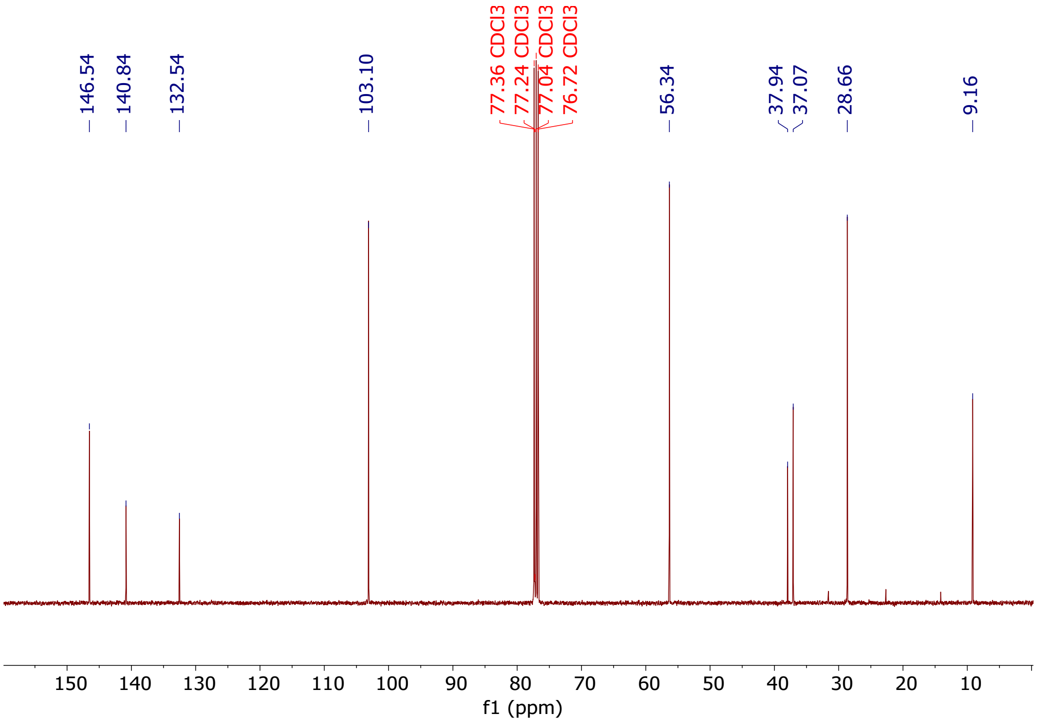




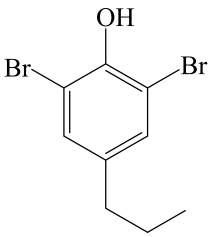
8.4 4-(1,1-Dimethylpropyl)-2,6-dimethoxyphenol

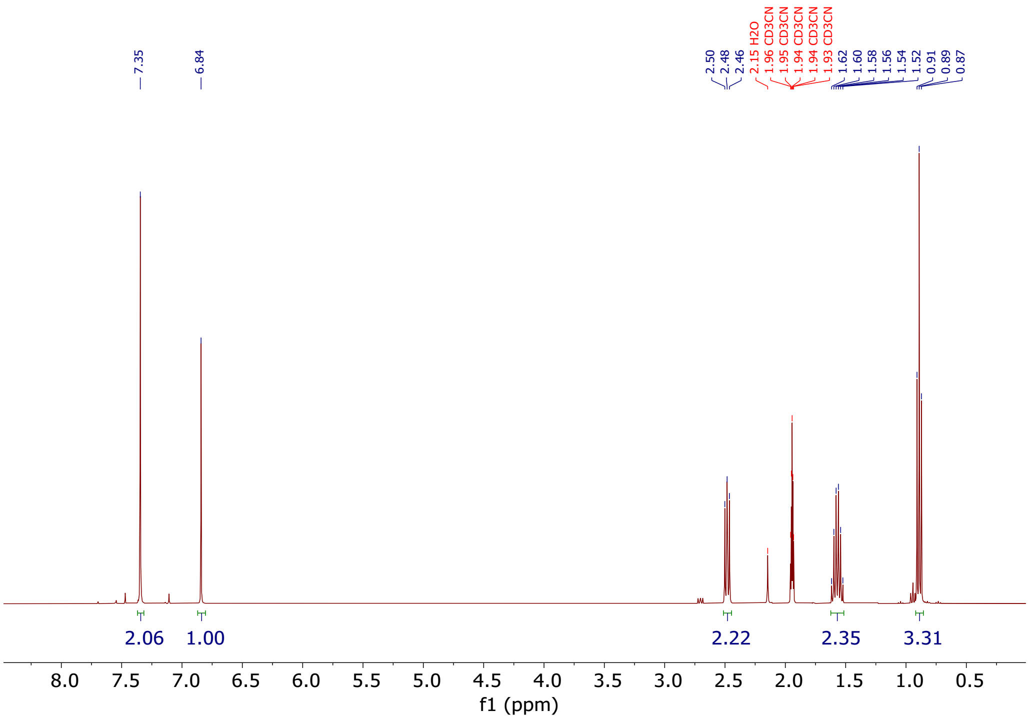


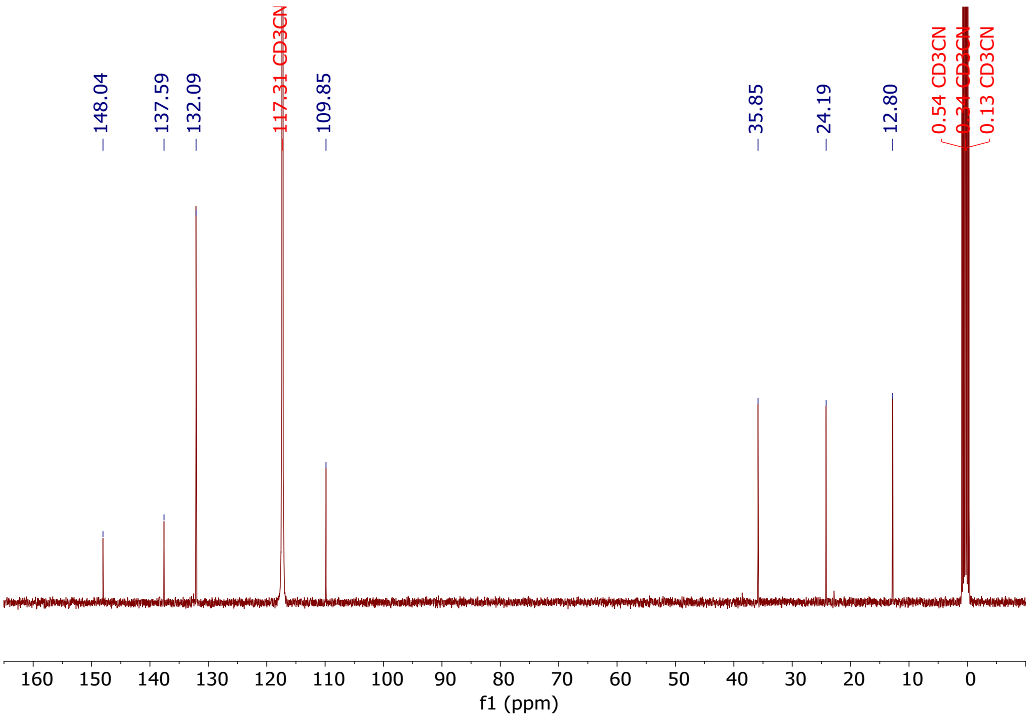


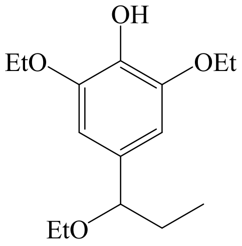


8.5 2,6-Dibromo-4-isopropylphenol

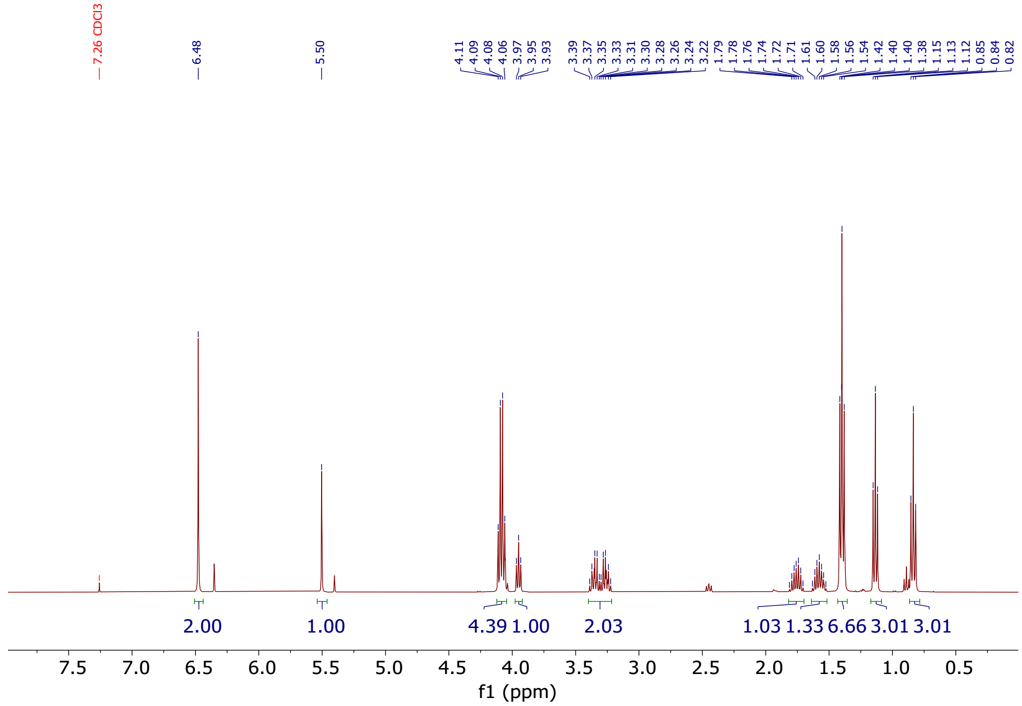


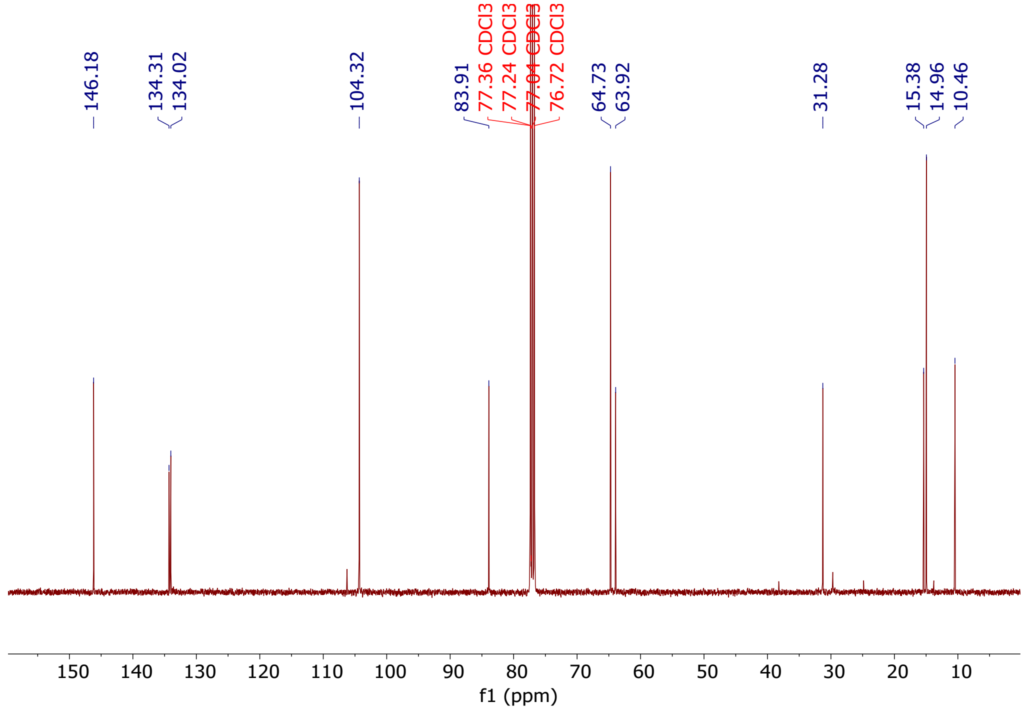




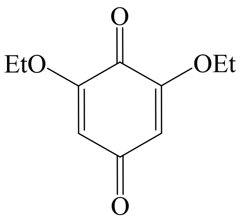


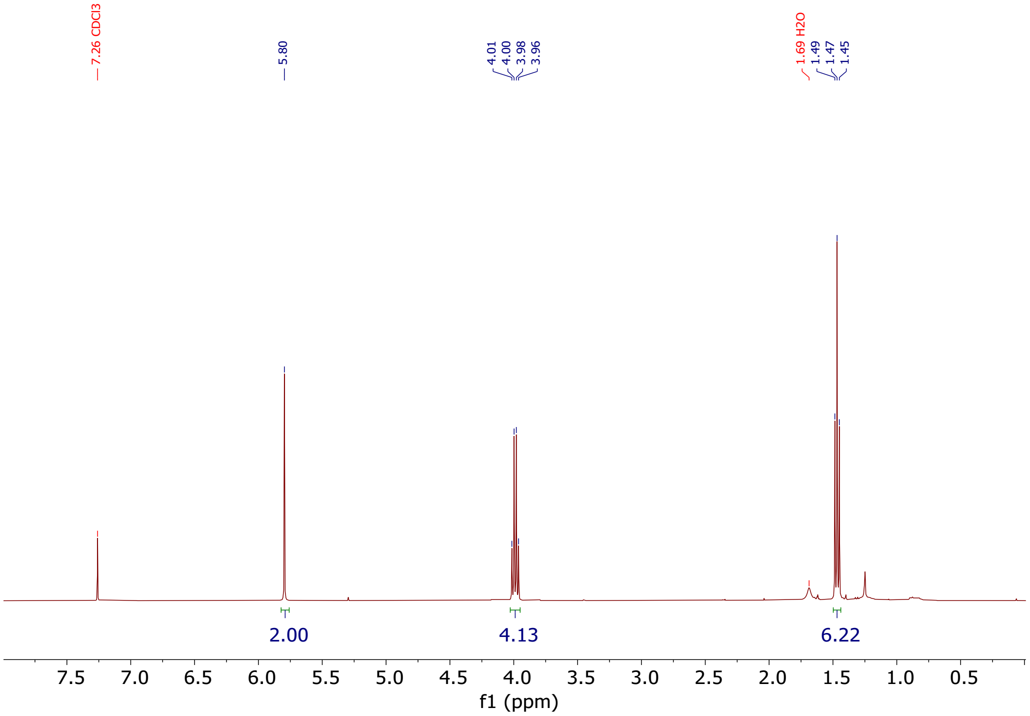
8.6 Ethyl-1-(3,5-diethoxy-4-hydroxyphenyl) propyl ether

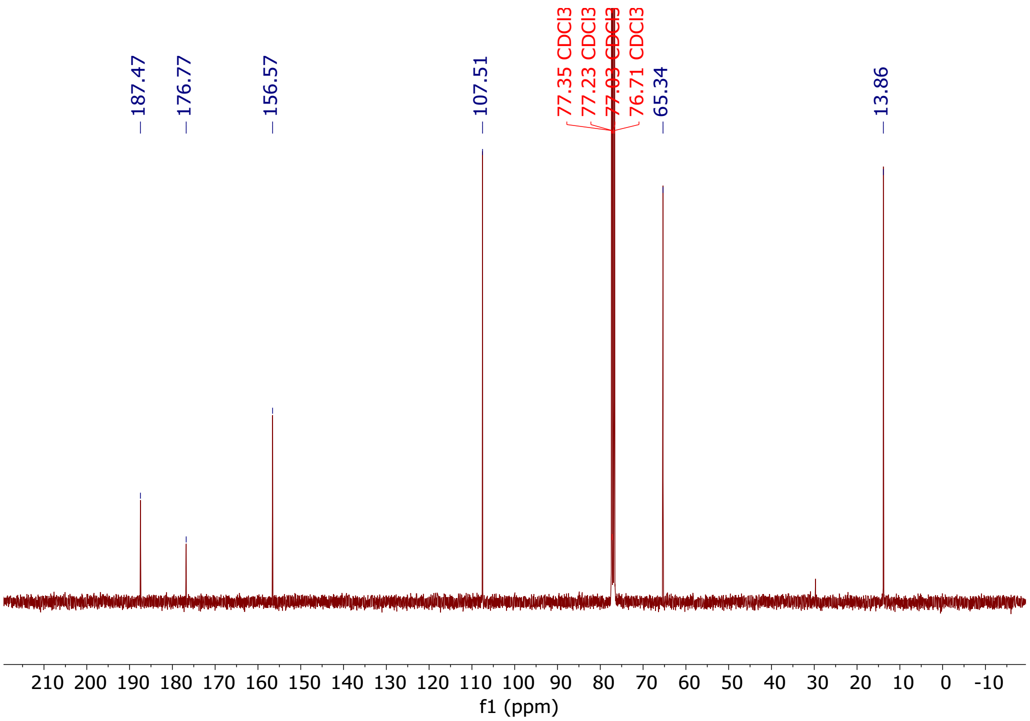


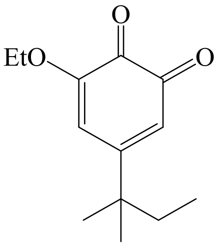


8.7 2,6-Diethoxybenzoquinone

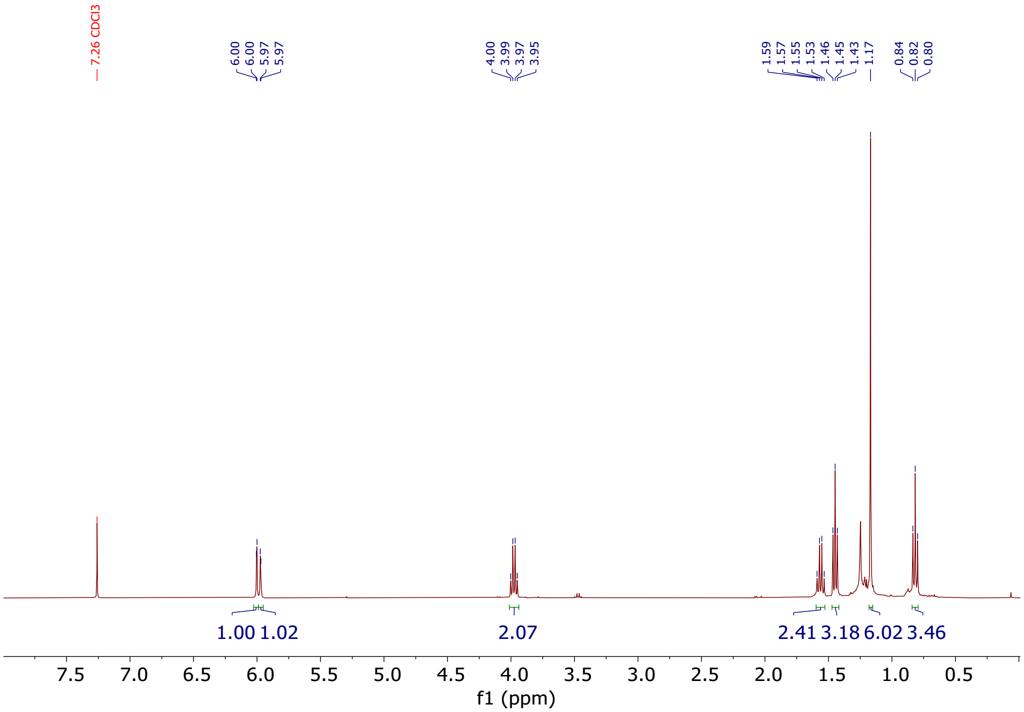


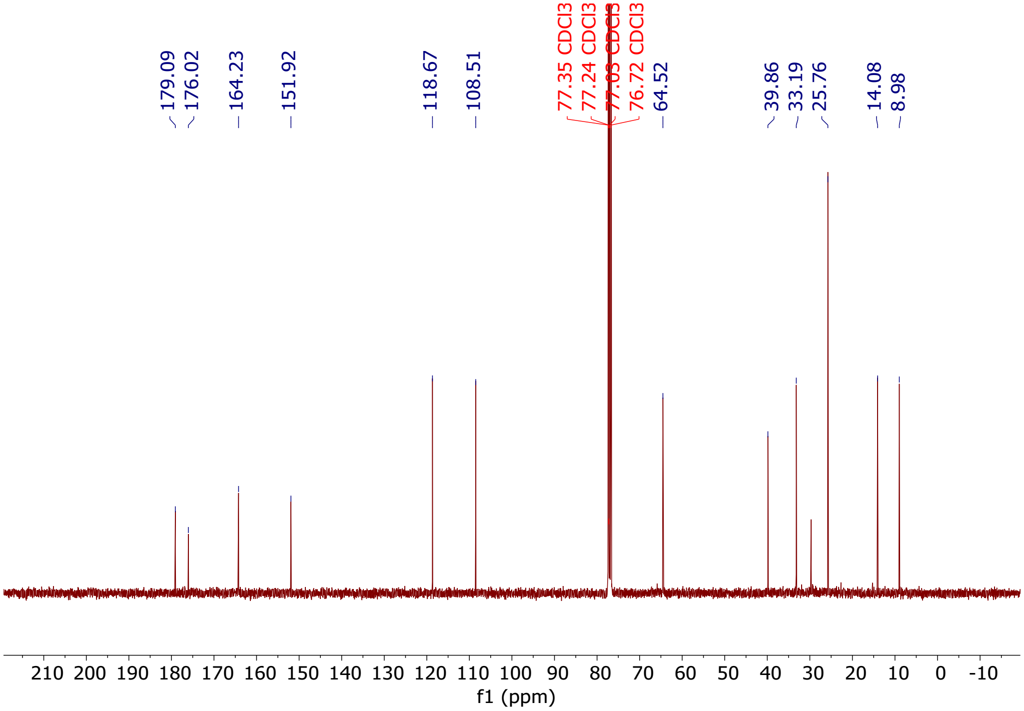


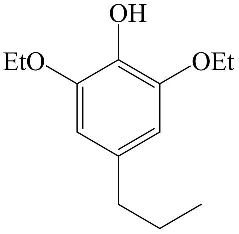




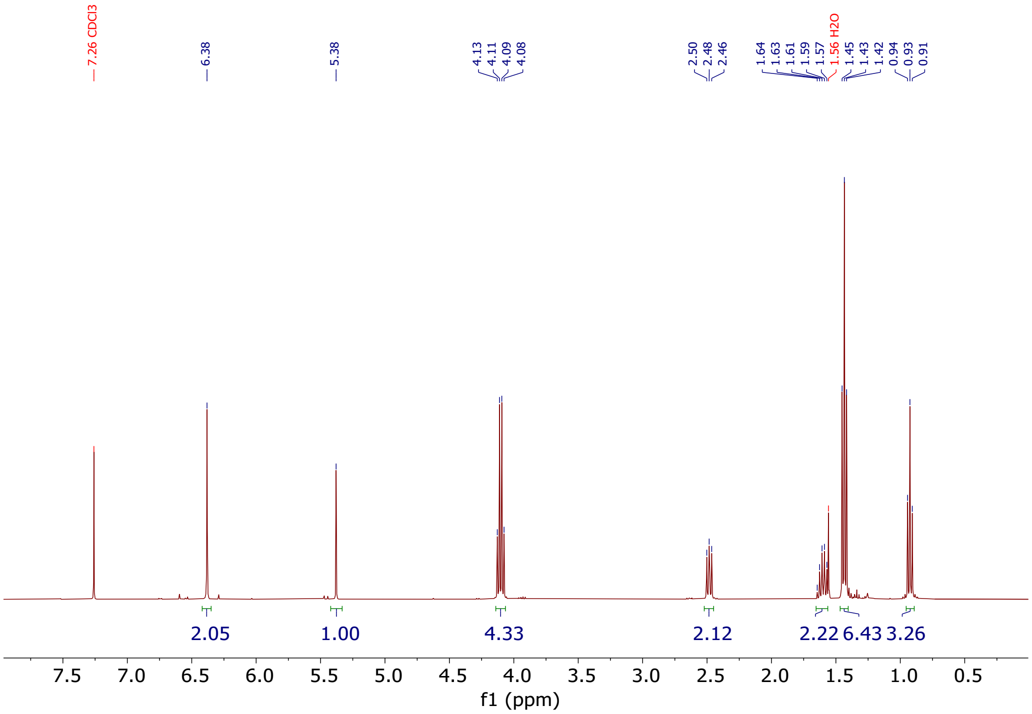
8.8 3-Ethoxy-5-(1,1-dimethylpropyl)-3,5-cyclohexadiene-1,2-dione







8.9 2,6-Diethoxy-4-propylphenol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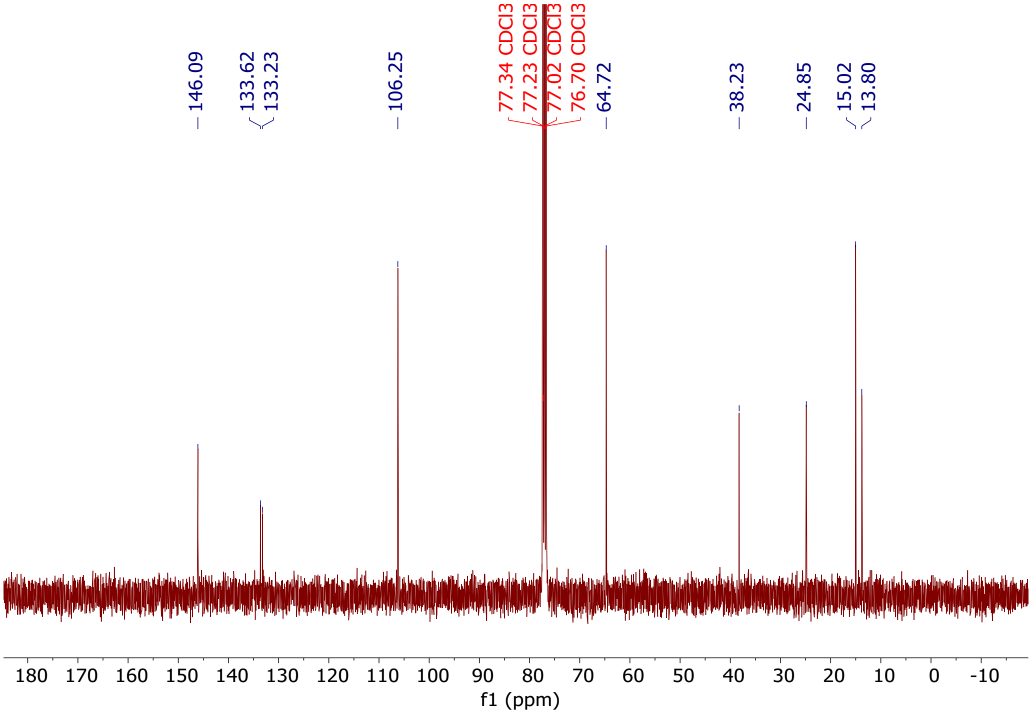
4.13
4.11
4.09
4.08
2.50
2.48
2.46
1.64
1.63
1.61
1.59
1.57
1.56 H2O
1.45
1.43
1.42
0.94
0.93
0.91
2.05
1.00
4.33
2.12
2.22
6.43
3.26
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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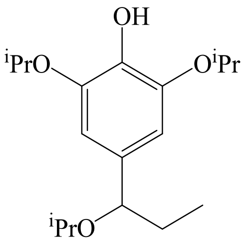
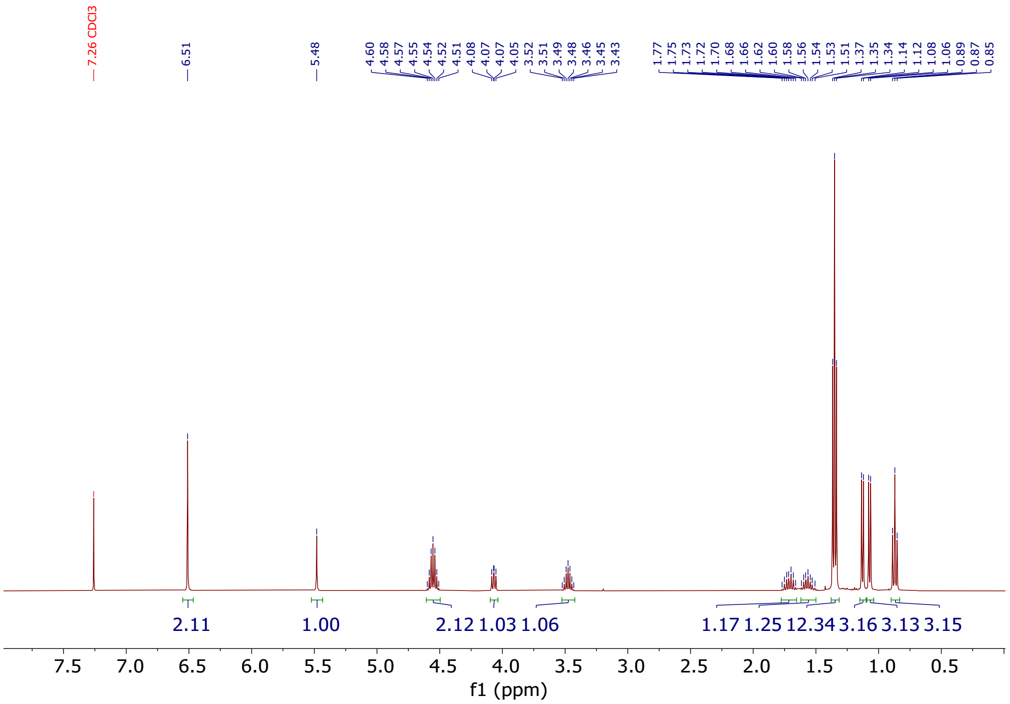
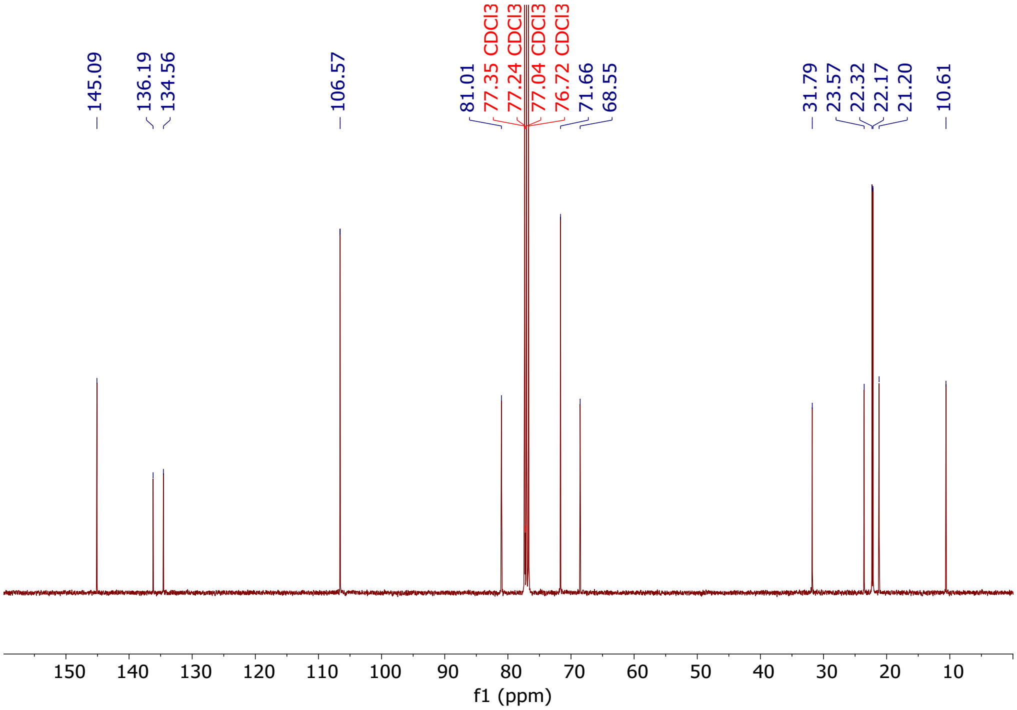
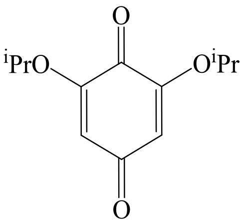
133.23
106.25
77.34 CDCl3
77.23 CDCl3
77.02 CDCl3
76.70 CDCl3
64.72
38.23
24.85
15.02
13.80
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

8.10 Isopropyl-1-(3,5-diisopropoxy-4-hydroxyphenyl) propyl ether

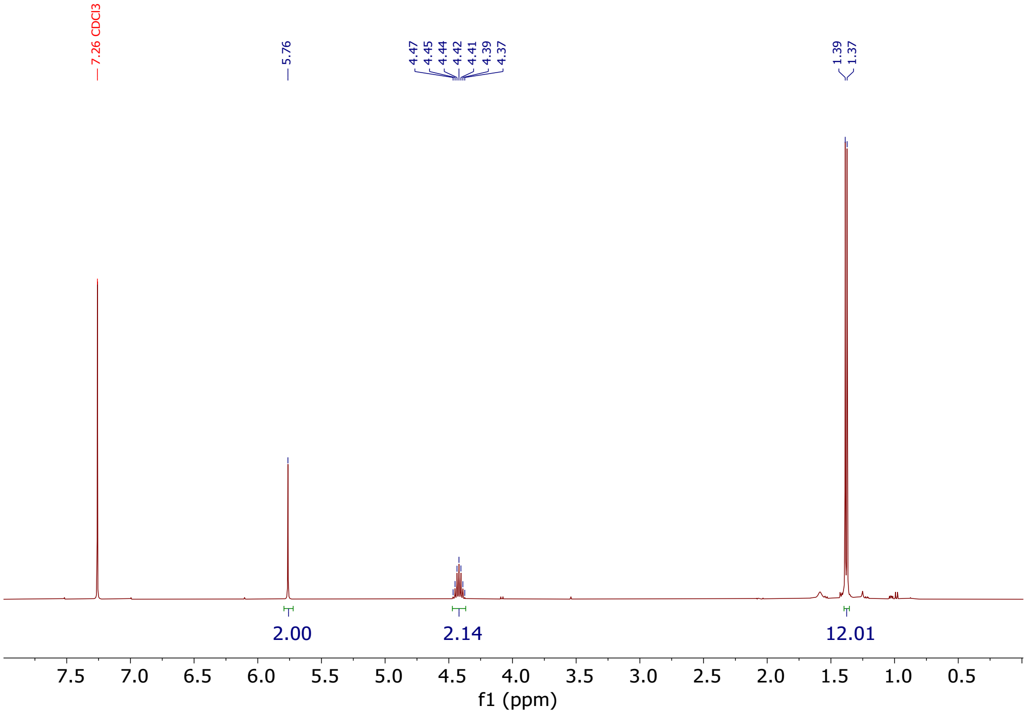


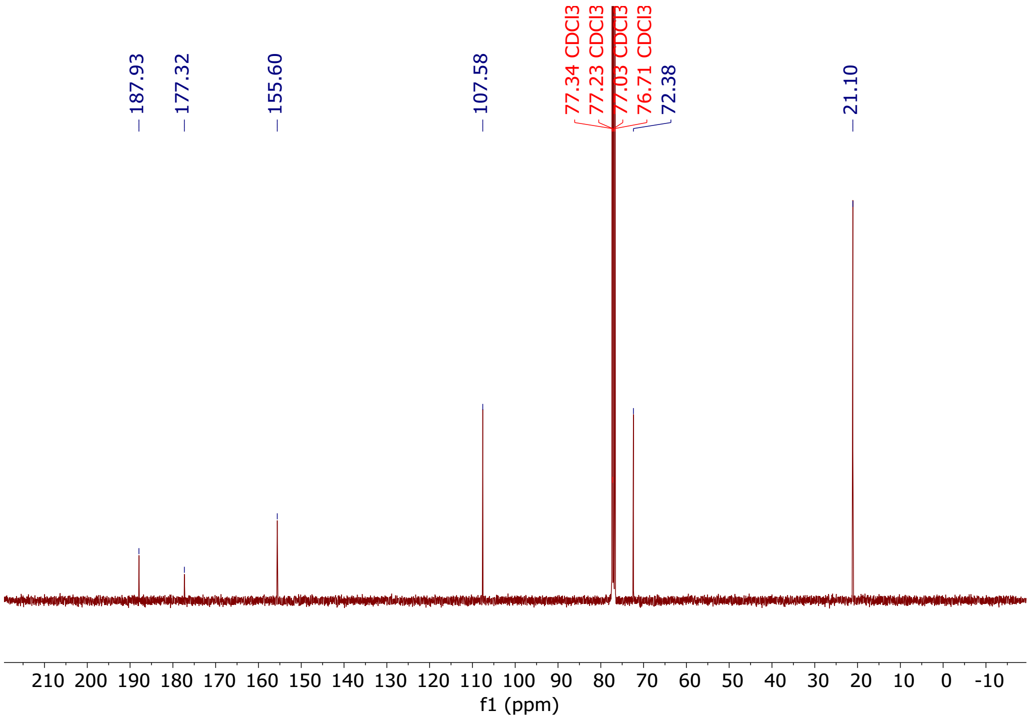


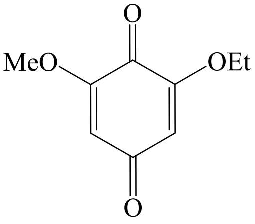




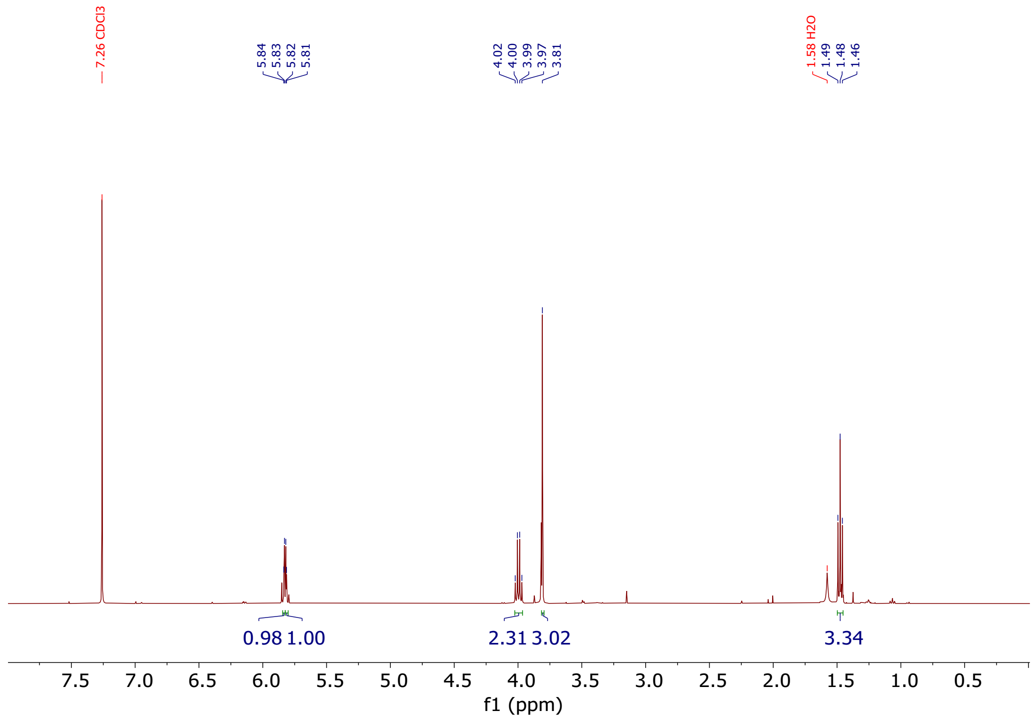
8.11 2,6-Diisopropoxybenzoquinone

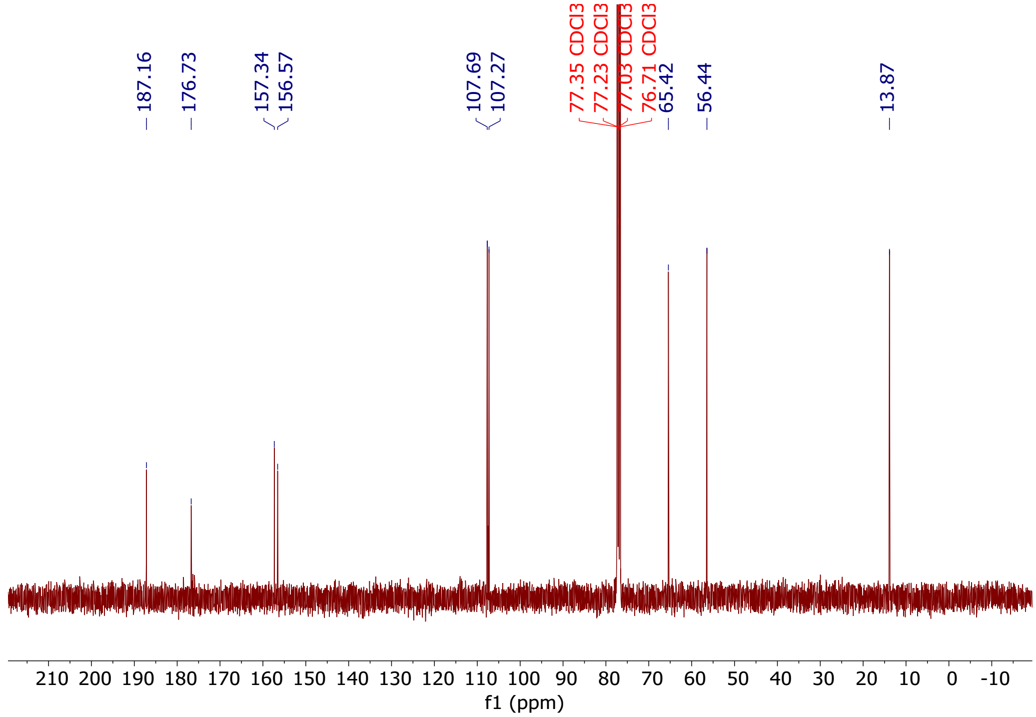




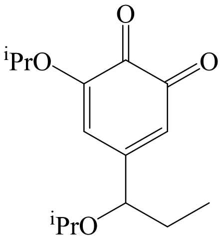


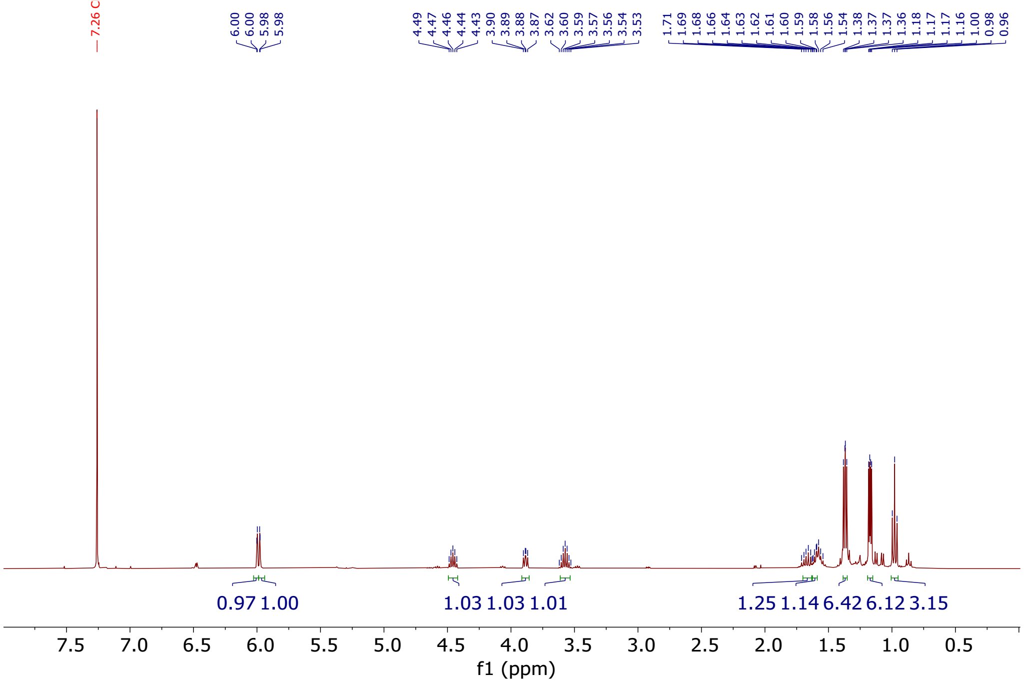
8.12 2-Ethoxy-6-methoxybenzoquinone





8.13 3-Isopropoxy-5-(1-isopropoxypropyl)-3,5-cyclohexadiene-1,2-dione


O
O
iPrO
iPrO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1.58
1.56
1.54
1.38
1.37
1.37
1.36
1.18
1.17
1.17
1.16
1.00
0.98
0.96
0.97
1.00
1.03
1.03
1.01
1.25
1.14
6.42
6.12
3.15
7.5
7.0
6.5
6.0
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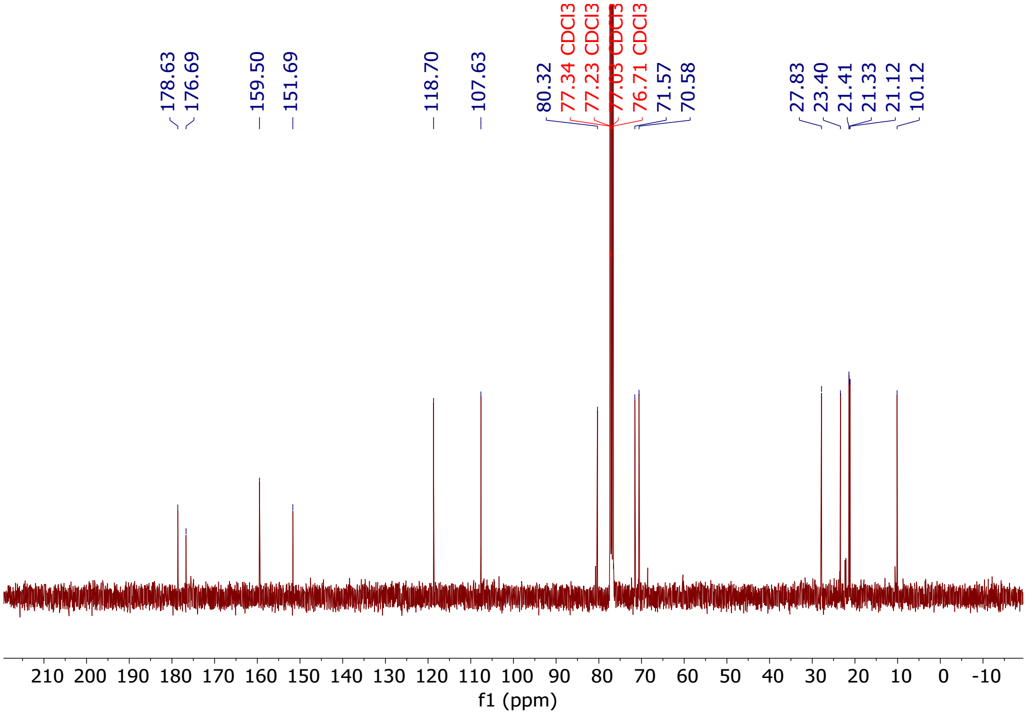
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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118.70
107.63
80.32
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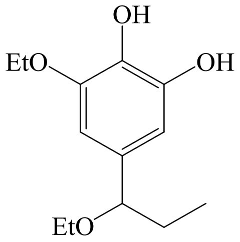
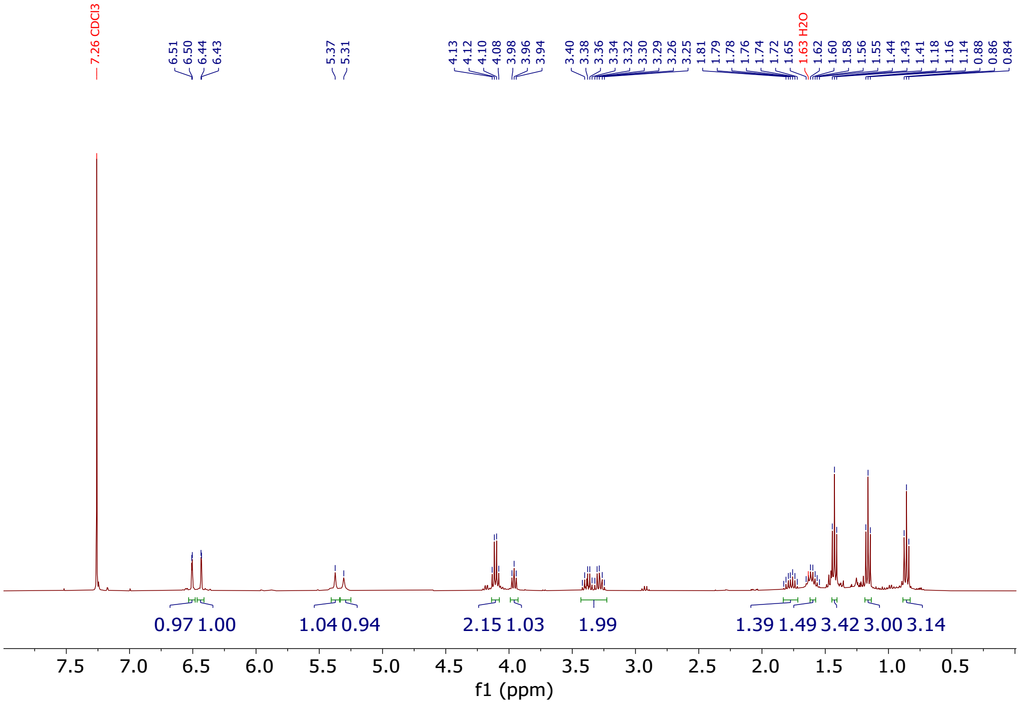
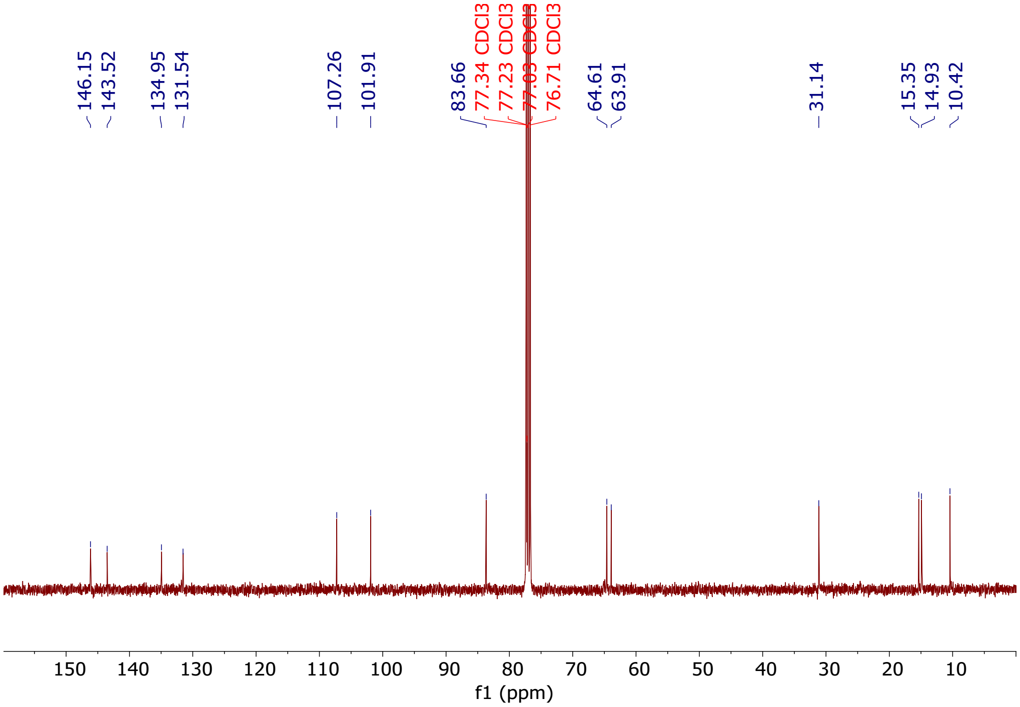
77.23 CDCl3
77.03 CDCl3
76.71 CDCl3
71.57
70.58
27.83
23.40
21.41
21.33
21.12
10.12
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

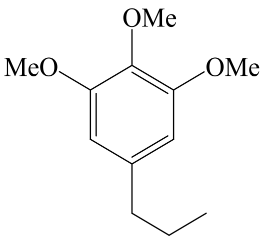
8.14 Ethyl-1-(3-ethoxy-4,5-dihydroxyphenyl) propyl ether

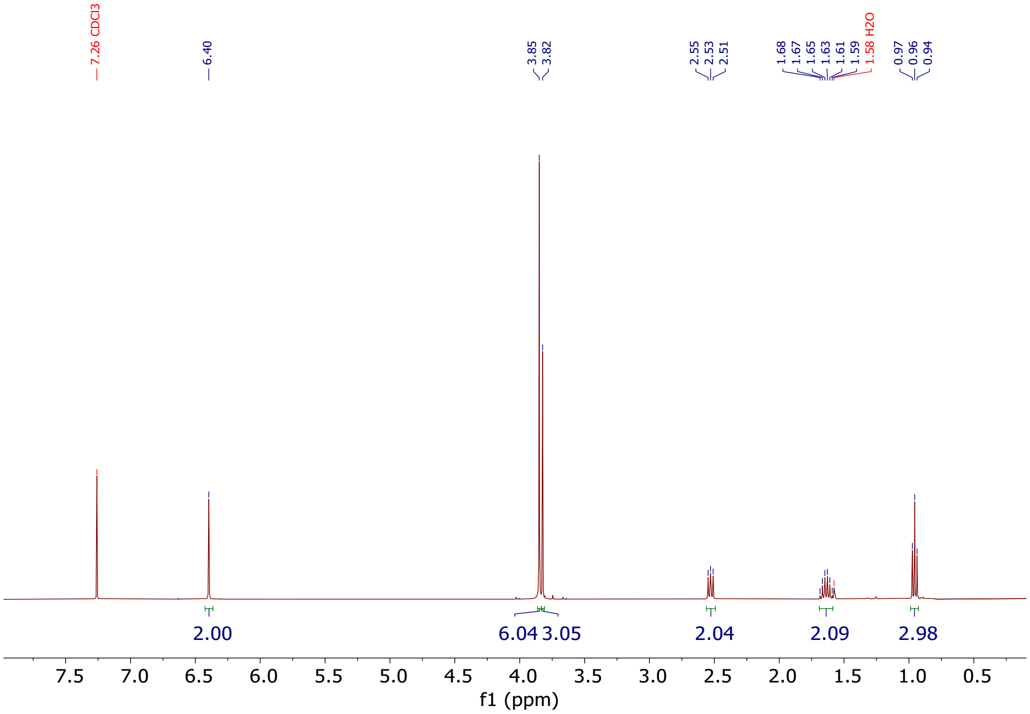


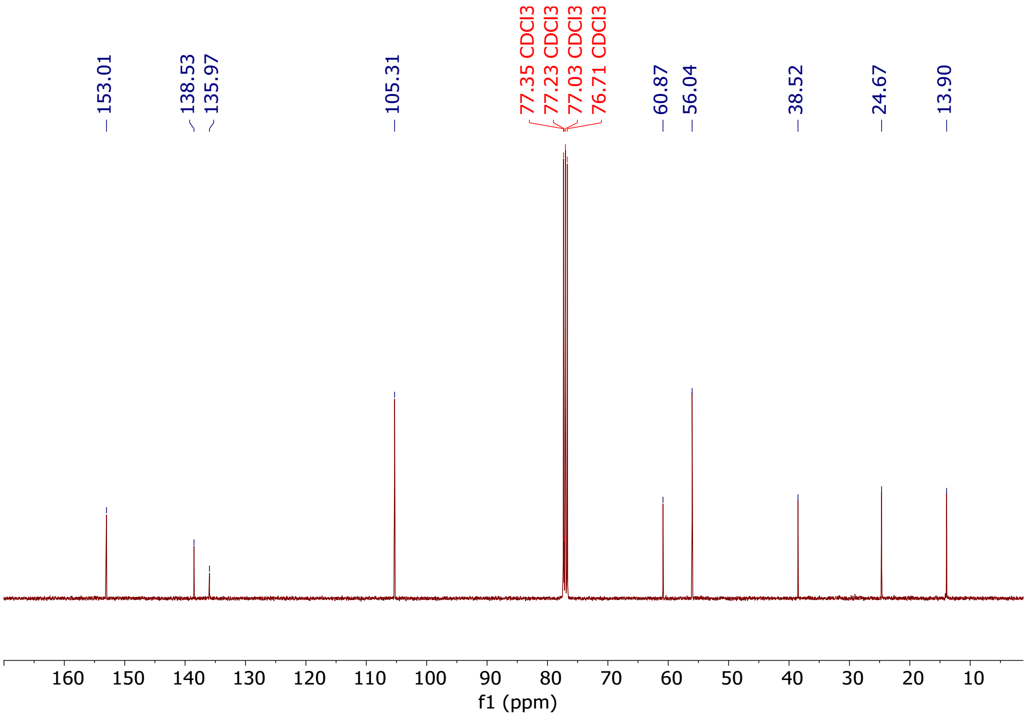


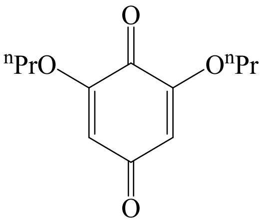


8.15 1,2,3-Trimethoxy-5-propylbenzene

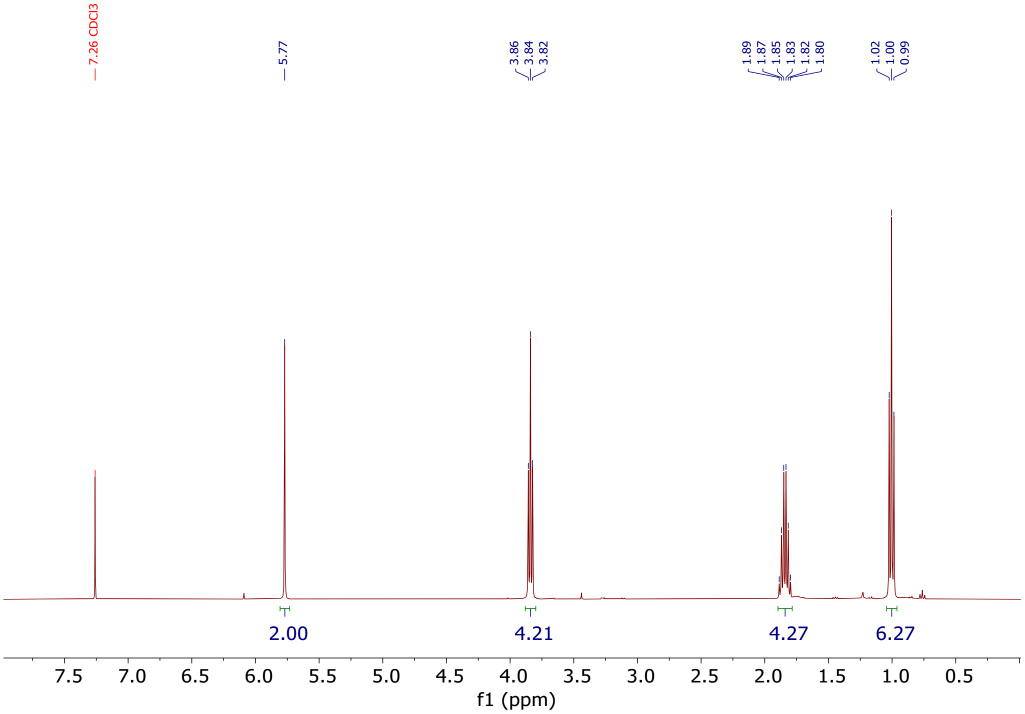


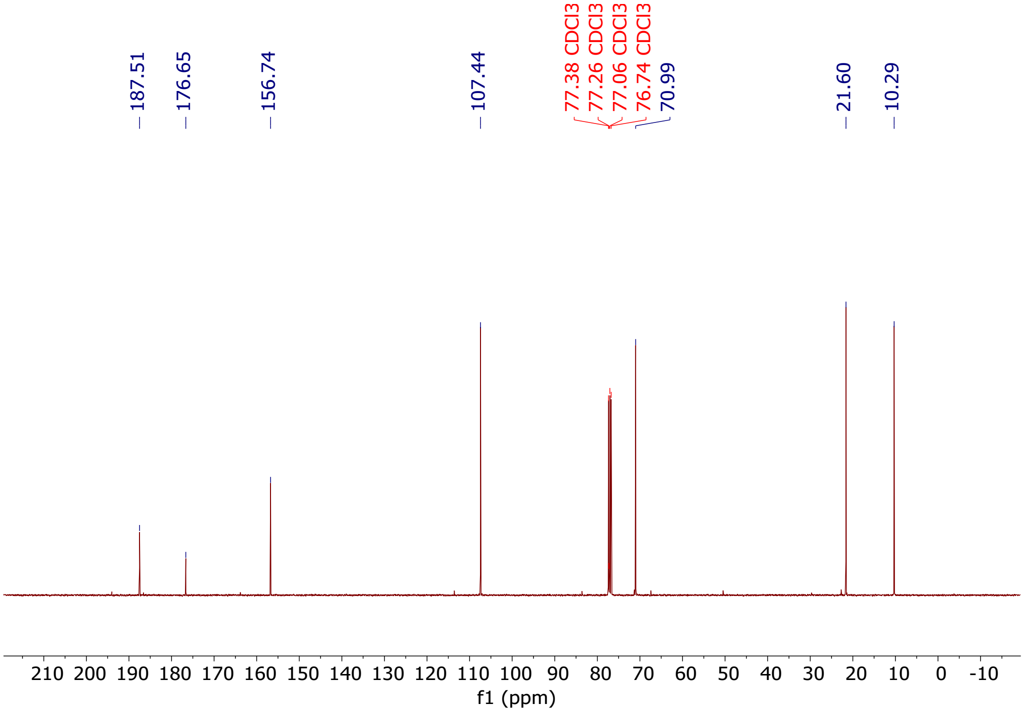


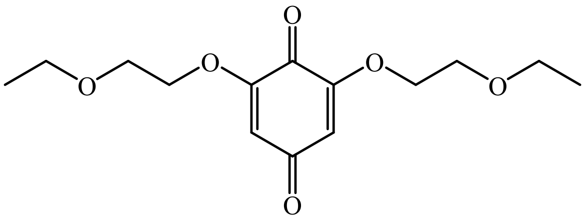




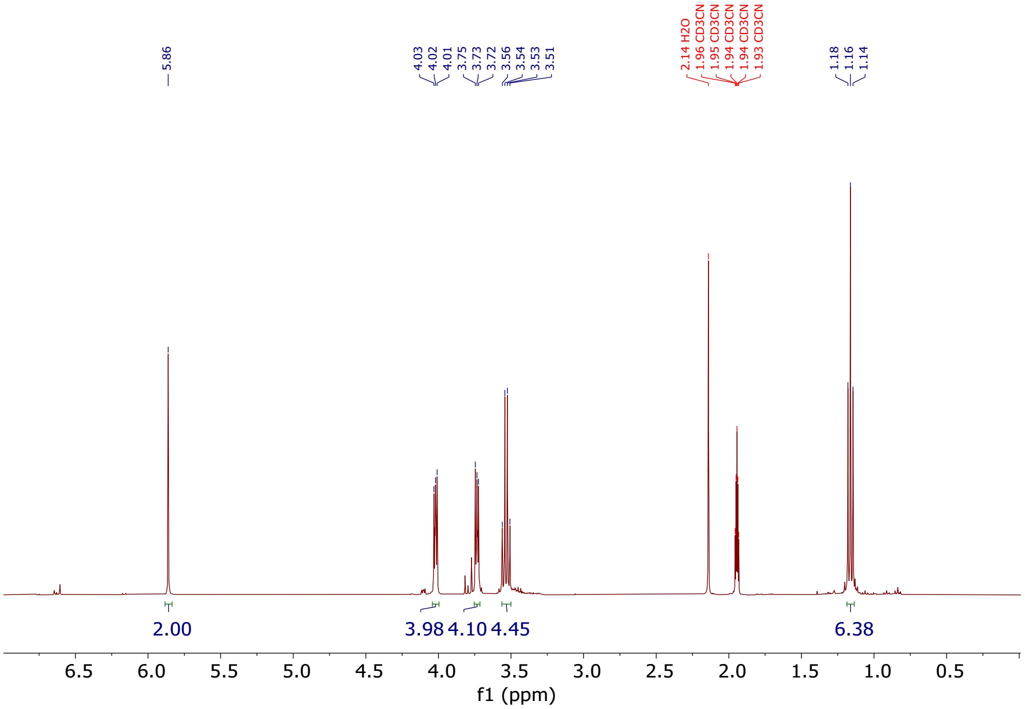
8.16 2,6-Dipropoxybenzoquinone

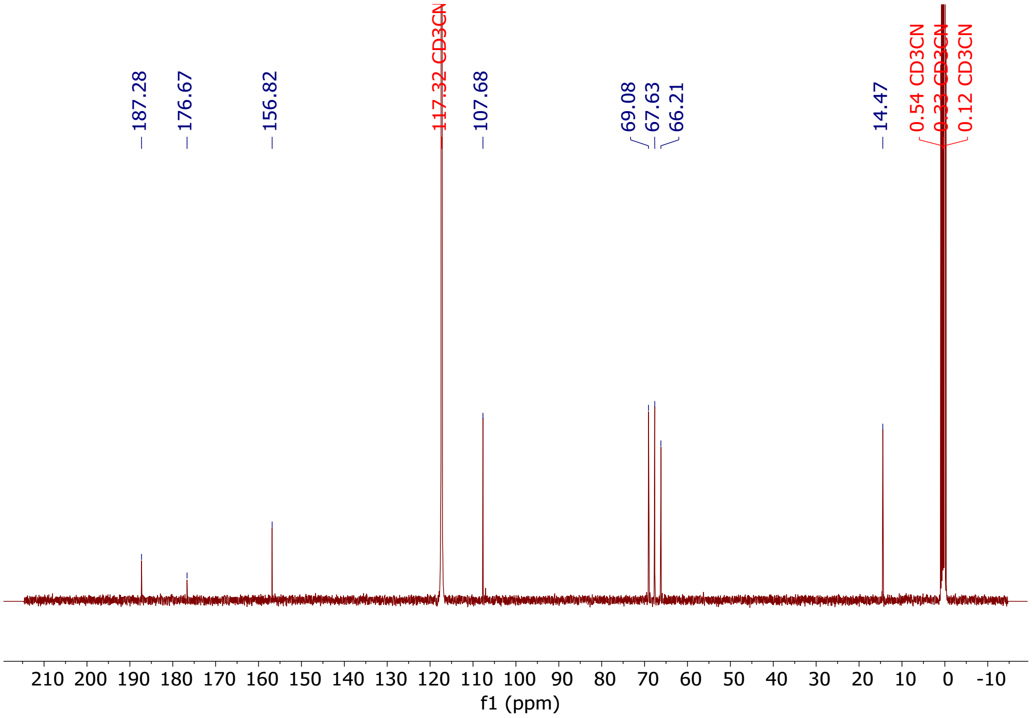




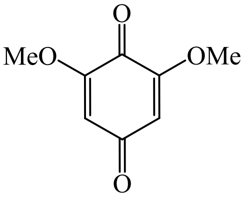


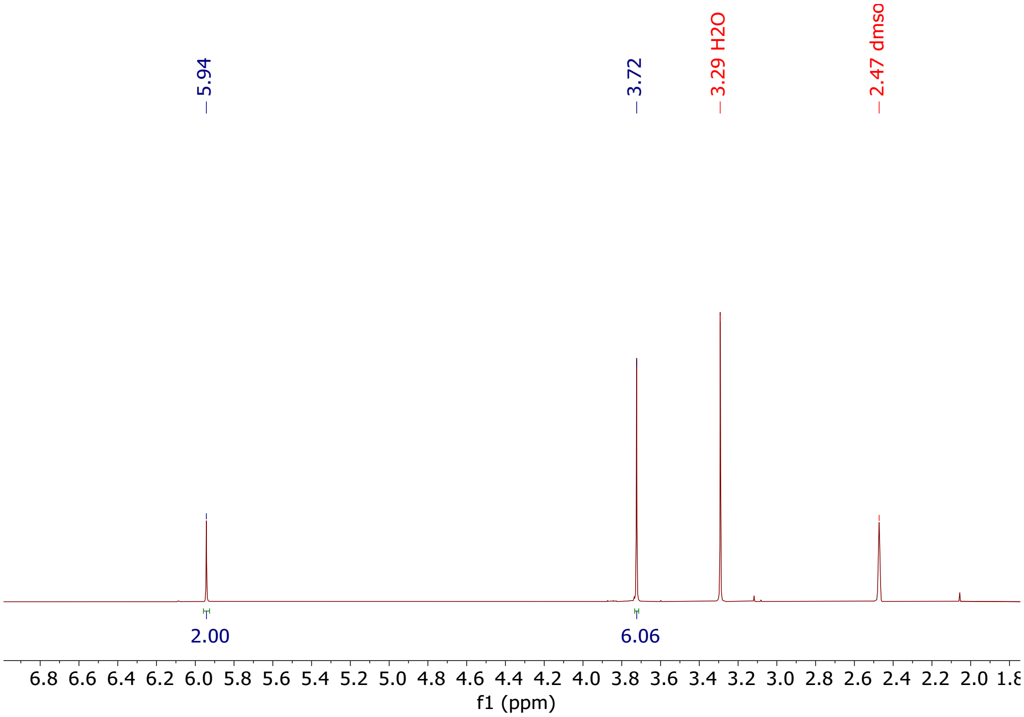
8.17 2,6-Di(2-ethoxyethoxy)benzoquinone

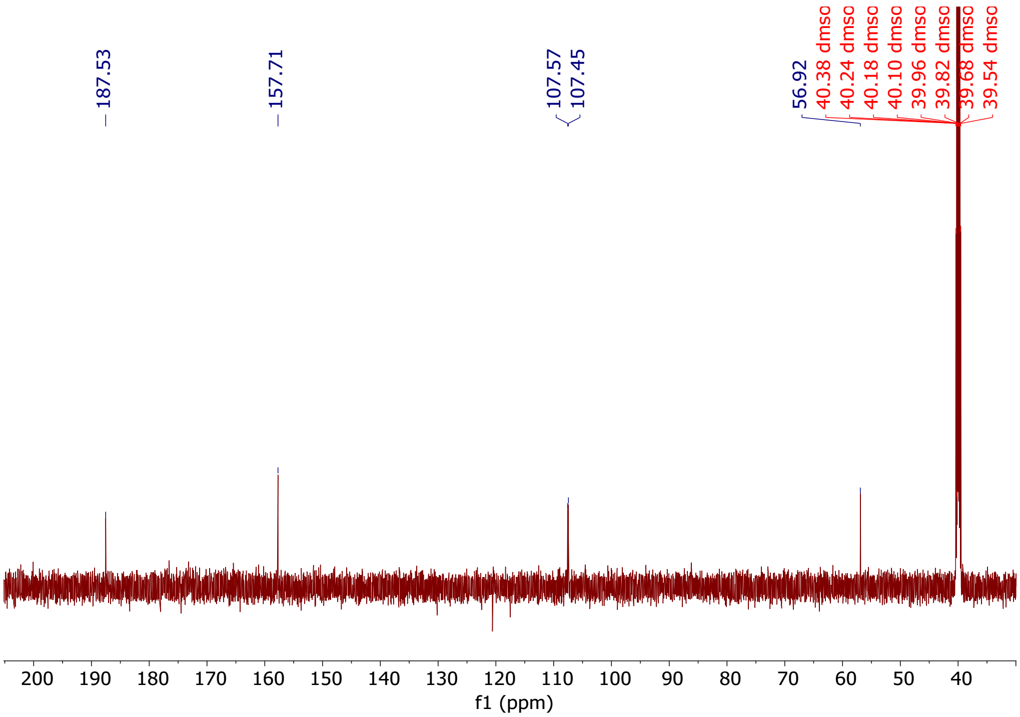




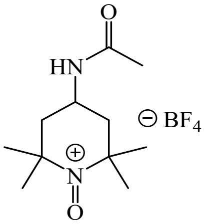
8.18 2,6-Dimethoxybenzoquinone



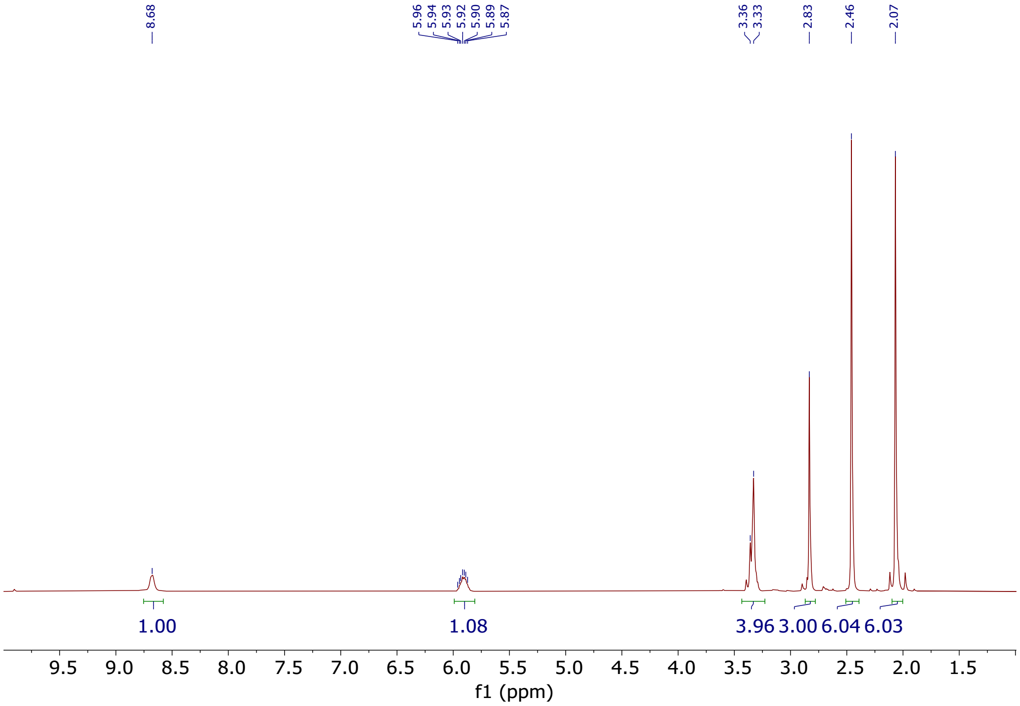


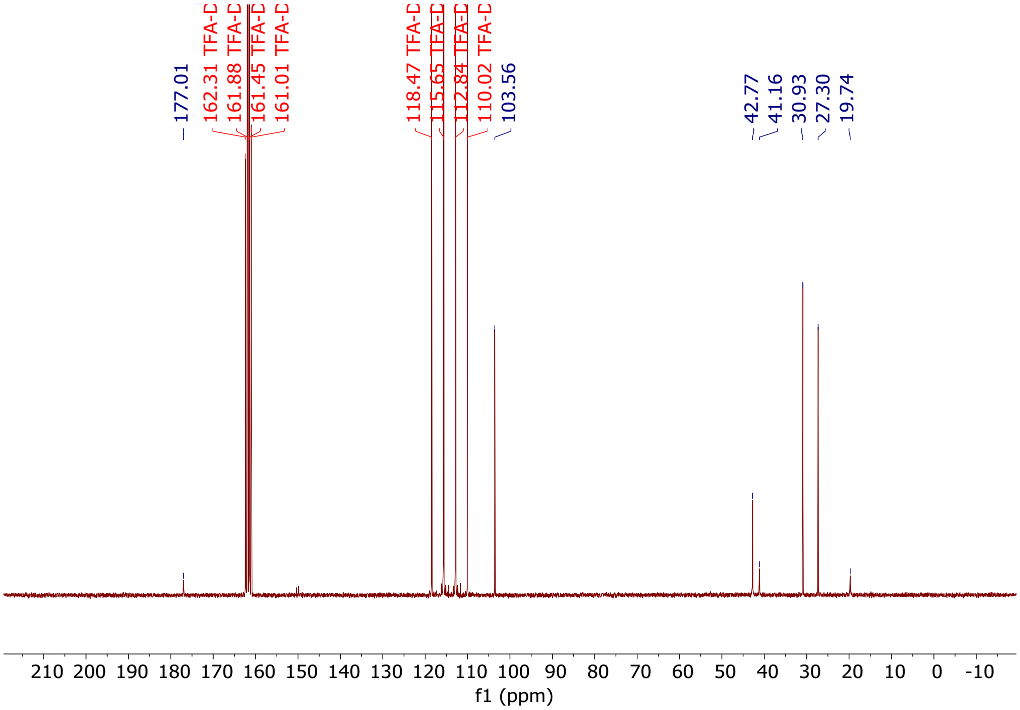


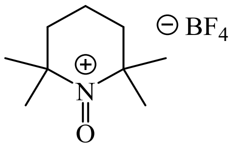
8.19 4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate



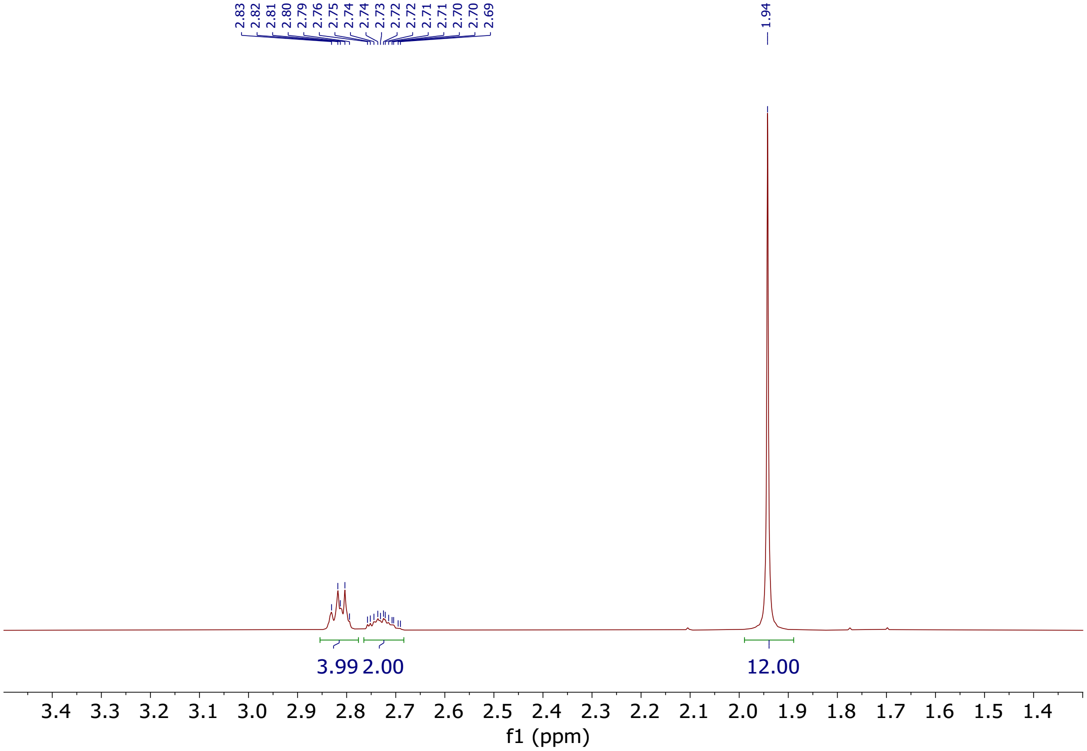
(Bobbitt's Salt)

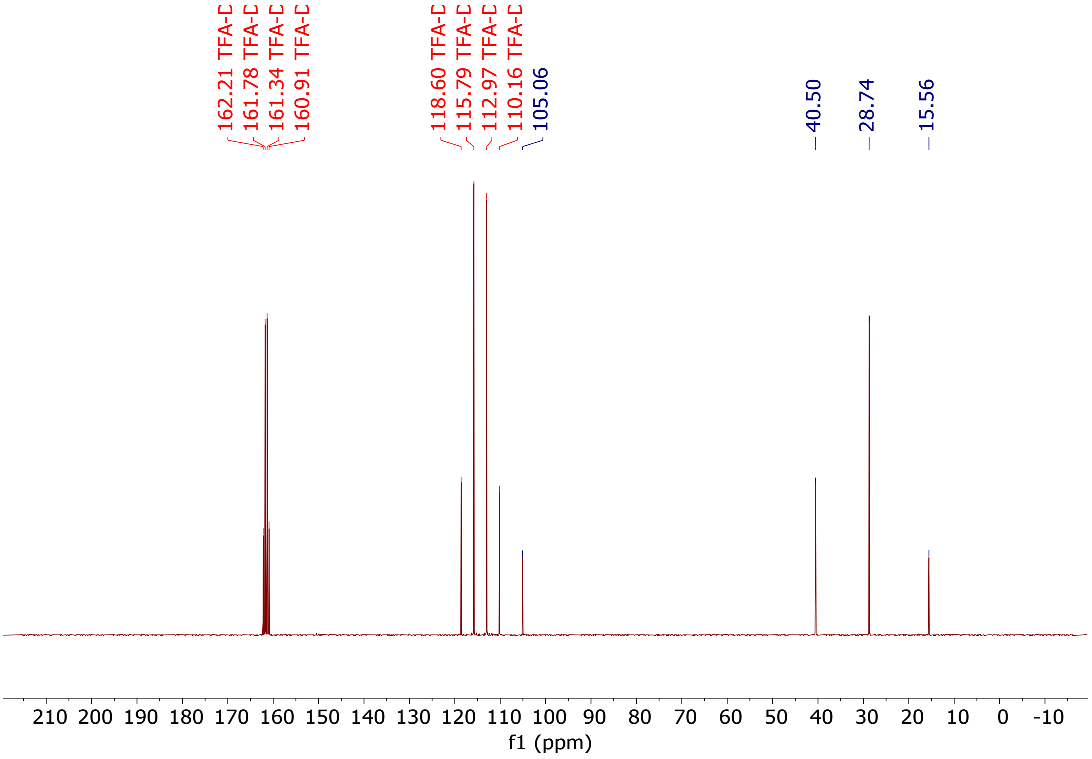




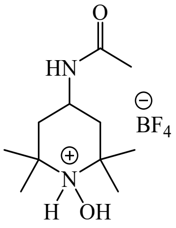


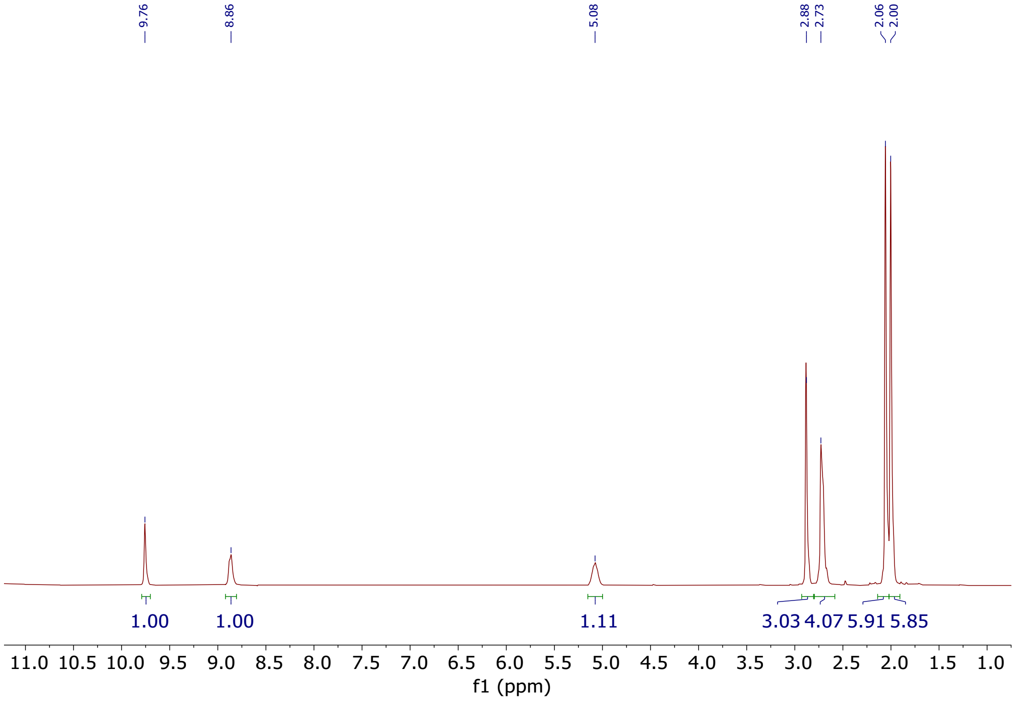
8.20 2,2,6,6-Tetramethylpiperidin-1-oxoammonium-tetrafluoroborate

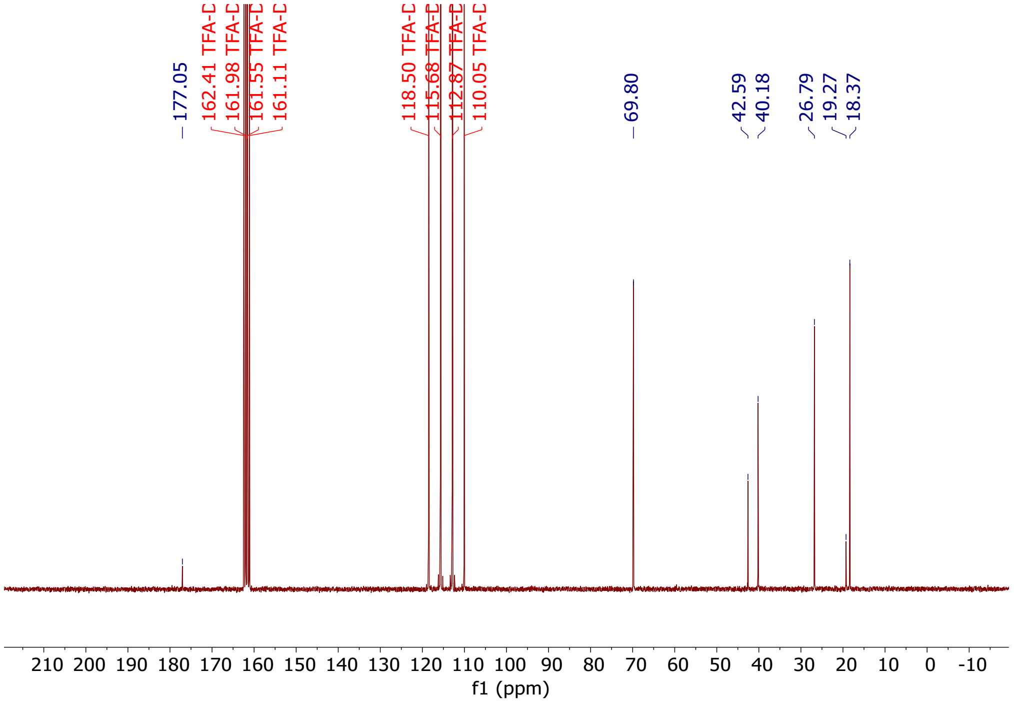




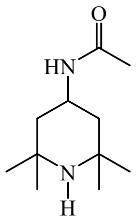
8.21 Reduced Bobbitt's Salt

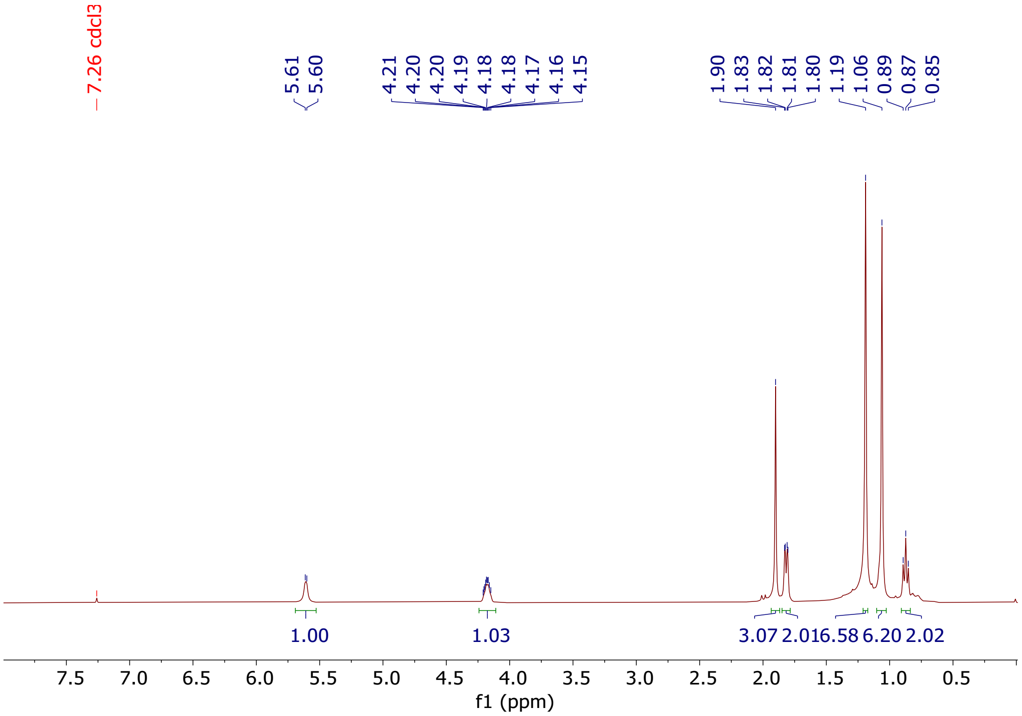


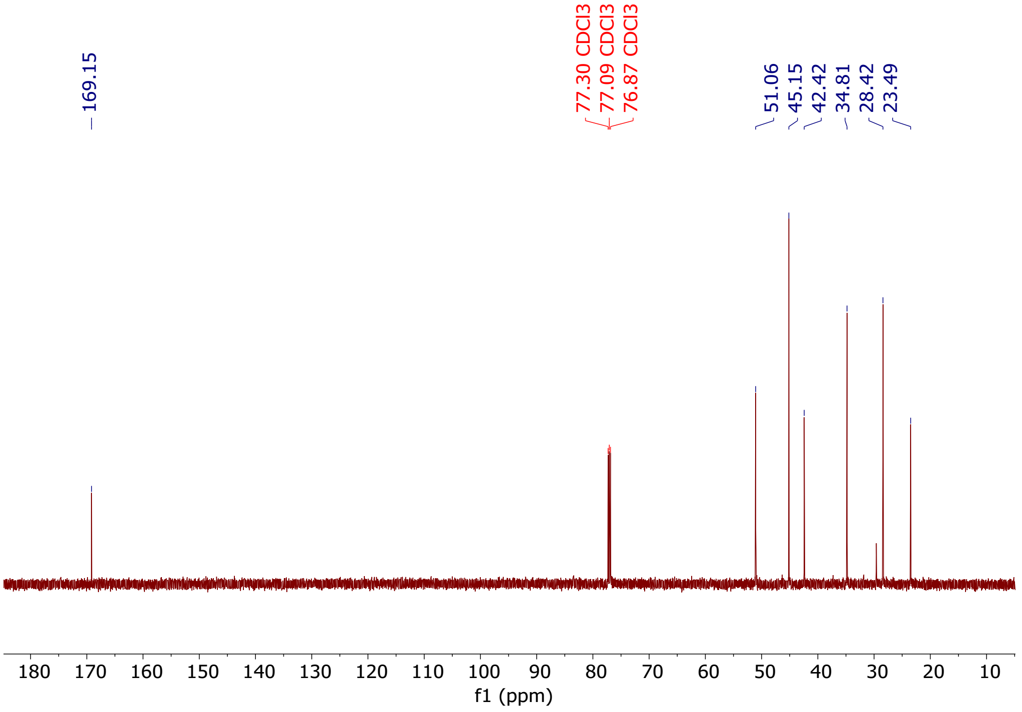




8.22 N-(2,2,6,6-tetramethylpiperidin-4-yl)acetamide







8.23 4-acetamido-2,2,6,6-tetramethylpiperidin-1-ium acetate