Electronic Supplementary Material (ESI) for Green Chemistry.

Supplementary Information

E-Dakin Reaction: Oxidation of Hydroxybenzaldehydes to Phenols with Electrochemically Generated Peroxodicarbonate as Sustainable *Ex-Cell* Oxidizer

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1.1 General Information

All employed chemicals are of analytical grade, were purchased by commercial suppliers and were used as received unless stated otherwise. 4-hydroxybenzaldehydes **1c**, **1i**, **1k**, **1o**, **1p**, and **1q** were synthesized as reported in literature (see references for further details).[1] Liquid phase chromatography was performed with cyclohexane and ethyl acetate (technical grade) that were distilled prior to use. All reactions were carried out at ambient atmosphere unless otherwise stated. Electrodes were obtained from commercial suppliers: boron-doped diamond (DIACHEM®, 15 µm boron-doped diamond layer on 3 mm silicon support/wafer, CONDIAS GmbH, Itzhoe, Germany).

Column chromatography Flash column chromatography was carried out on 60 M silica gel (0.040-0.063 mm, Macherey-Nagel GmbH &Co, Düren, Germany) on a silica flash column system (Büchi, Flawil, Switzerland) equipped with a C 620 control unit, a C 666 fraction collector, a C 635 UV-detector and C 605 pump modules for the adjustment of the solvent ratio or on prepacked puriFlash® SI-HP silica PF-15SIHP-F0040 column (Interchim SAS, Montluçon Cedex, France) using a puriFlash® XS 520 Plus system (Interchim SAS, Montluçon Cedex, France). Cyclohexane and ethyl acetate were employed as eluents. Reversed phase column chromatography was performed on SepacoreTM C18 (Büchi-Labortechnik GmbH, Essen, Germany) using different mixtures of water (0.1% formic acid) and acetonitrile as eluents. Thin-layer chromatography was performed on TLC Silica gel 60 F254 25 Aluminum sheets (Merck KGaA, Darmstadt, Germany). A UV lamp, with 254 nm and 365 nm wavelength, was used for visualization.

Gas chromatography Gas chromatography was performed on a Shimadzu GC-2010 device (Shimadzu, Kyoto Japan) with a ZB-5 quartz capillary column (Phenomenex, Torrance, USA) with the specifications: dimensions 30 m x 0.25 mm x 0.25 µm, carrier gas: helium, injection temperature 250 °C; detector temperature 310 °C, 50 °C as start temperature for 1 minute, heating rate of 15 °C·min^{-1}, 290 °C as end temperature for 8 minutes, temperature at ion source: 200 °C) coupled with a GCMS-QP2010 (Shimadzu, Kyoto, Japan) mass detector.

High Resolution Mass Spectra High-resolution mass spectra were recorded on a G6545A Q-ToF (Agilent GmbH, Waldbronn, Germany) with chemical ionization at atmospheric pressure (APCI) or with electrospray-ionization (ESI). Samples were injected via a 1260 Infinity II HPLC System (Agilent GmbH, Waldbronn, Germany) with G7111B 1260 Quaternary Pump, G7129A 1260 vial sampler, and G7116A 1260 multi-column thermostat. The accuracy of mass detection is better than 5 ppm.

NMR Spectroscopy: NMR spectroscopic experiments were carried out at 298 K on Bruker Avance II 400 and Bruker Avance III HD 400 spectrometers (Bruker, Karlsruhe, Germany).

Chemical shifts are reported relative to residual signals in the respective deuterated solvent. Referencing of the residue signal was performed according to the data provided by Cambridge Isotope Laboratories. The peak assignment is supported by additional 2D NMR experiments (COSY, HSQC and HMBC).

Electrochemical Setup

The electrosynthesis of peroxodicarbonate was performed in circular flow cell in a set-up that was previously developed and reported in previous work.[2] A *Diachem*™ boron-doped diamond electrode (*A*=2x6 cm^2, 15 µm BDD on silicon support, *CONDIAS GmbH*, Itzehoe, Germany) embedded in a copper cooling casting served as the anode, while a stainless-steel plate was used as a cathode. A Teflon™ spacer with a thickness off 0.5 mm was placed between the electrodes to ensure a constant interelectrode gap and to restrict the active electrode surface to 3.0 cm^2. The narrow-gap flow electrolyzer was coated with a protective varnish (*Plastik 70, CRC Industries Deutschland GmbH*, Germany) and was further encased in a polystyrene box to prevent condensation of water and short-circuiting on the outside. The electrolyte was piped through the cell with Teflon™ tubing (1 mm inner diameter). The tubing was fixed in a coiled state and also functioned as a heat exchanger. The cell is cooled with a cryostat (RC6 cryostate, *Lauda*, Lauda-Königshofen, Germany) to 0°C. An ethanol/water mixture (1/1, v/v) served as cooling media. Both the heat exchanger and the electrolyte reservoir (a 100 mL *Schott* flask) were immersed in the cooling bath of the cryostat. The temperature was constantly monitored using a DS18B20 temperature sensor with a USB-connected cortex-M microcontroller (*Diamex Produktion und Handel GmbH*, Heidelberg, Germany). A gentle nitrogen stream was connected to the electrolyte reservoir to ensure sufficient safety by dispersing emerging hydrogen. The electrolyte is pumped through the cell with a membrane pump (Aquamarin 1210 LC PP/EPDM membrane pump, *Gardner Denver Thomas GmbH*, Memmingen Germany) with a flow rate of 100 mL/min (applied potential 10 V at 120-130 mA via a HMP4040 galvanostate, *Rohde&Schwarz*, München, Germany). The applied current of the electrolysis was controlled using a HMP4040 galvanostate (*Rohde&Schwarz*, München, Germany) in constant current mode as a power source. The electrolysis can be controlled remotely via an open-source python-based user interface (https://github.com/marcodyga/power_supply_gui). A sematic drawing of the electrolysis set up and an exploded view of the flow electrolyzer are depicted in Figure S1. A more in-depth description of the set-up can be found in the literature.[2]

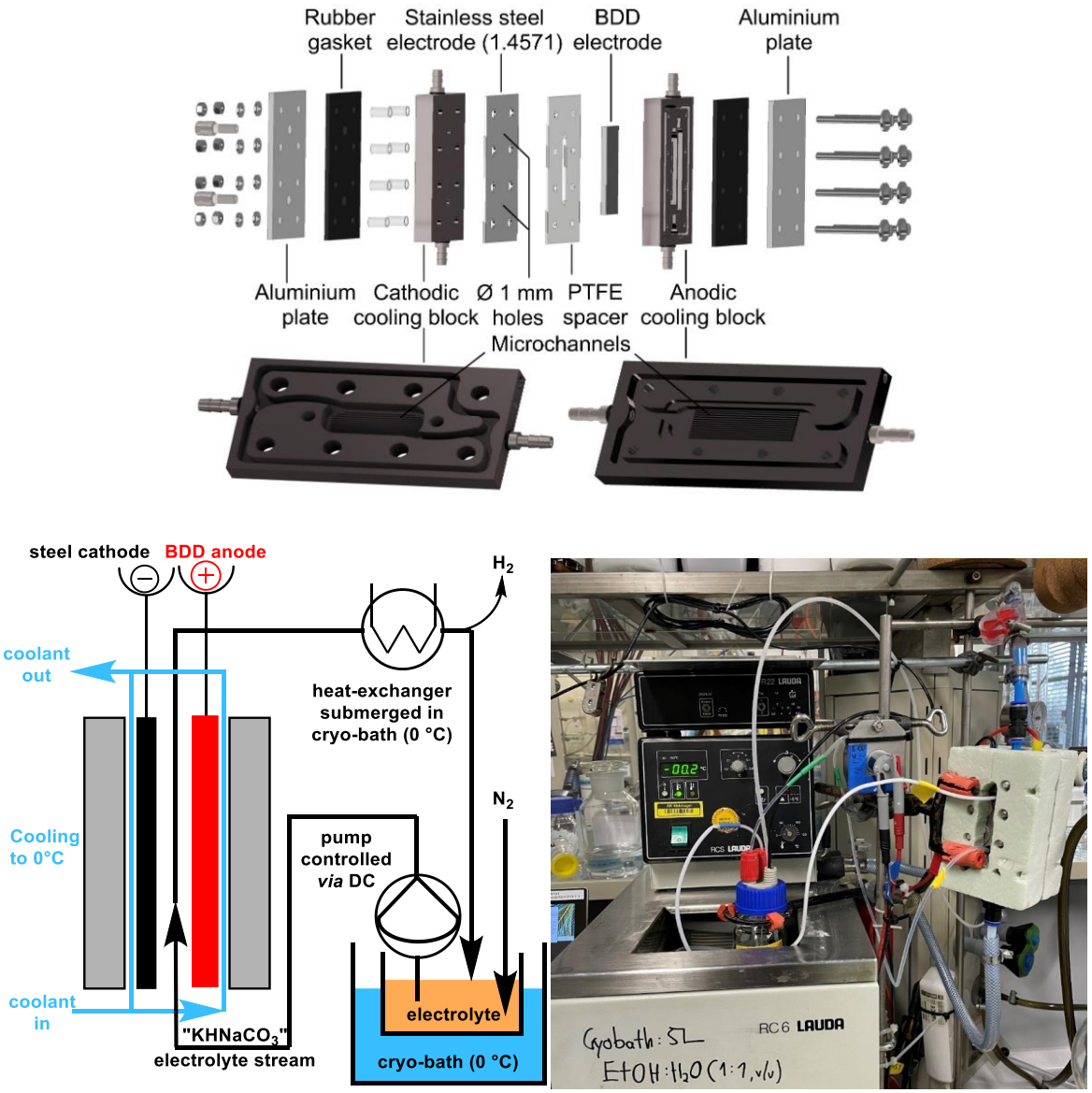


Figure S1. Top: Exploded view of narrow-gap flow electrolyzer. Left: schematic drawing of electrochemical setup. Right: Electrolysis set-up.[2,3]

1.2 Experimental Procedures

1.2.1 Electrosynthesis of Peroxodicarbonate

Synthesis of PODIC solution:

The synthesis was conducted accordingly to a previously published protocol.[2] 3.34 g Na_2CO_3, 5.44 g K_2CO_3 and 0.79 g $KHCO_3$ were added into a 100 mL screw-cap glass container and dissolved in 35 mL water. This resulted in a 0.90 M Na_2CO_3, 1.125 M K_2CO_3 and 0.225 M

$KHCO_3$ electrolyte. The glass container was placed in the coolant mixture of the cryostat. A USB temperature sensor was placed inside of the electrolyte. The solution was circulated through the electrolysis system at a constant flow rate of 100 mL/min until the electrolyte temperature kept constant at 1 °C. An interelectrode gap of 0.5 mm and an active anode surface of 3 cm^2 were used. Then, the solution was electrolyzed using the circular flow cell with cooled copper casing at a constant current density of 3.33 A/cm^2 for 60.0 minutes, corresponding to an applied charge of 36000 C (4.7 *F*) relative to total carbonate. After the electrolysis, the sample container was placed in an ice bath.

Determination of the PODIC concentration:

Directly after the electrolysis a 2 mL volumetric pipette was pre-cooled by pumping 2 mL of cold electrolyte solution into the pipette and immediately returning it into the electrolyte three times. Then, up to three 2 mL aliquots of the electrolyte were transferred into Erlenmeyer flasks. The pH was adjusted to ~1 by addition of 20% (v/v) H_2SO_4 (5 mL each). To each flask, 5 mL of an aqueous solution of KI (3% in H_2O) and three drops of ammonium heptamolybdate solution (3% in H_2O) were added. The brown solution was titrated against a standard solution of $Na_2S_2O_3$ (0.1 M). The endpoint of the titration was determined by the complete disappearance of the yellow color of free I_2. The resulting average concentration of total oxidizer was then calculated by standard error calculations. Concentrations between 600–800 mM of PODIC could be achieved.

1.2.2 General Procedure 1

The 4-hydroxybenzaldehydes **1c**, **1i**, **1k**, **1o**, **1p, 1q** were synthesized via Duff-Aldehyde synthesis starting from the corresponding phenols.[1]

The phenol (10 to 25 mmol) was dissolved in acetic acid (8.3 to 20.8 mL). Water (1.7 to 4.3 mL) was added to the mixture and hexamine (20 to 50 mmol, 2 eq.) was added. The resulting suspension was heated to reflux for 10 minutes. Water (1 to 2.3 mL) was distilled off, using a Dean-Stark trap. Afterwards the mixture was further heated until the TLC confirmed complete consumption of the starting material. After the mixture reached room temperature water was added dropwise (2 to 5 mL). In general, this initiated the precipitation of the product. In cases where the precipitation did not start upon addition of water, 2 mL of concentrated hydrochloric acid were added, and the flask was stirred at room temperature for 5 minutes. The mixture was cooled for an additional period of 12 hours and the precipitated was filtered off with suction and washed extensively with water. Recrystallization from ethanol afforded pure product.

1.2.3 General Procedure 2

A benzaldehyde (1 mmol, 1 eq.) (for the scale-up 10 mmol or 20 mmol) was weighted into a round bottom flask, which was subsequently placed into an ice-bath. A freshly prepared solution of peroxodicarbonate (1.75 eq. concentration between 0.75 M–0.85 M, determined prior to addition) was added at once with a glass pipette under stirring. After the reaction was stirred for additional 20 minutes at 0 °C the reaction was quenched by acidification (pH 1) with diluted hydrochloric acid. Afterwards the reaction mixture extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with saturated sodium chloride (20 mL) and the organic fraction was dried over magnesium sulfate. The solvent was removed in vacuo and the crude product was purified by flash column chromatography.

Optimization:

The oxidation of benzaldehydes into hydroquinones was optimized using vanillin (4-hydroxy-3-methoxybenzaldehyde) **1a** as a test substrate (Figure S2).

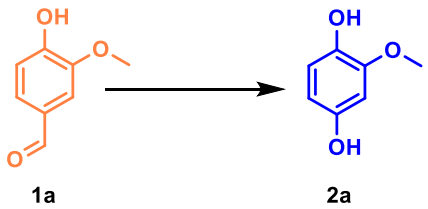


Figure S2: Optimization reaction for the oxidation of **1a** to **2a**.

Optimization reactions were conducted on a 1 mmol scale in a 50 mL round-bottom flask. During the reaction the mixture was stirred with a magnetic stir bar at 300 rpm. Unless stated otherwise the reactions were performed at ambient conditions. For screening experiments the crude product was dissolved in MeCN-d_3 after the work-up and a defined amount of 1,3,5-trimethoxybenzene was added as an internal standard and the yield was calculated via qNMR.

Solvent:

Initially different solvents were screened for their eligibility to act as a reaction medium. Table S1 lists the screened solvents and the obtained yields of **2a** as well as the remaining amounts of **1a**. The contents of Table S1 are graphically depicted in Figure S3.

Table S1: Synthesis of 2-methoxy-hydroquinone (**2a**) from vanillin (**1a**) under alteration of the solvent.

Entry	Solvent	PODIC / eq.	Yield(1a) / %	Yield(2a) / %
1	Methanol	1	78	0
2	Methanol/Acetonitrile 1:1 (*v*/*v*)	1	70	0
3	Ethanol	1	59	0
4[a]	Tetrahydrofuran	1	49	26
5 [a]	Tetrahydrofuran	2	3	72
6	H_2O	2	1	21
7	1 M Na_2CO_3	2	0	11
8	1 M $NaHCO_3$	2	0	45
9	Neat	2	1	62

Reaction parameters: temperature: 22 °C; *n*(**1a**) = 1 mmol; c(1a) = 0.25 M. [a]: THF contains butylated hydroxytoluene as an inhibitor.

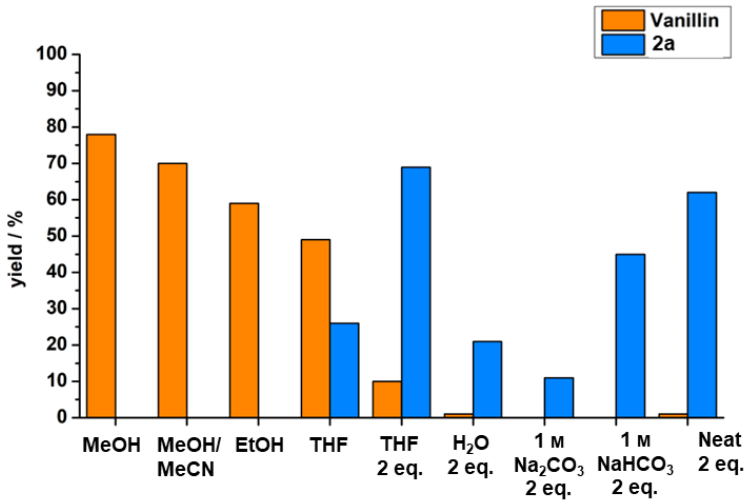


Figure S3: Synthesis of 2-methoxy-hydroquinone (**2a**) from 4-hydroxy-3-methoxybenzaldehyde (**1a**) under alteration of the solvent.

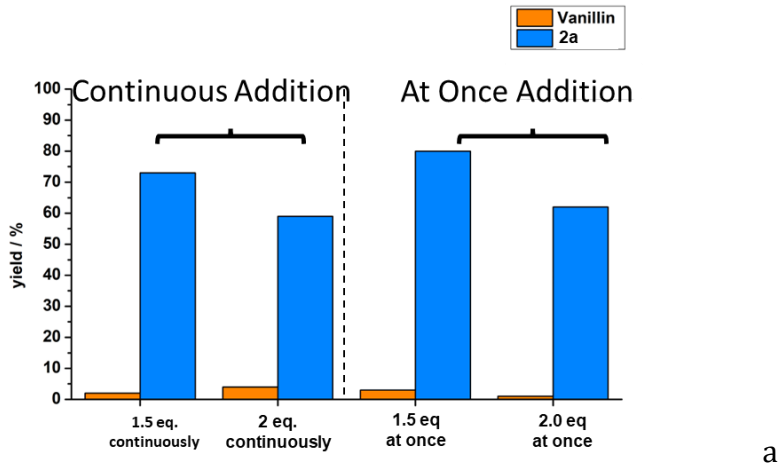
Mode of Addition:

Two different modes of addition were tested, direct addition of the oxidizer and an addition in portions over-time (equal portions every 5 minutes). Table S2 lists the modes of addition and the obtained yields of **2a** as well as the remaining amounts of **1a**. The contents of Table S2 are graphically depicted in Figure S4.

Table S2: Synthesis of 2-methoxy-hydroquinone (**2a**) from vanillin (**1a**) under alteration of the mode of addition.

Entry	Mode of Addition	PODIC / eq.	Yield(1a) / %	Yield(2a) / %
1[a]	Continuously	1.5	2	73
2[b]	Continuously	2	4	59
3[a]	At once	1.5	3	80
4[b]	At once	2	1	62

Reaction parameters: temperature: 22 °C; *n*(**1a**) = 1 mmol; c(1a) = 0.25 M. [a]: time = 20 min. [b]: time = 25 min.



a

Figure S4: Synthesis of 2-methoxy-hydroquinone (**2a**) from vanillin (**1a**) under alteration of the mode of addition.

Equivalents of PODIC

PODIC amounts between 1.00 and 2.00 equivalents were screened. Table S3 lists the used amounts of PODIC and the obtained yields of **2a** as well as the remaining amounts of **1a**. The contents of Table S3 are graphically depicted in Figure S5.

Table S3: Synthesis of 2-methoxy-hydroquinone (**2a**) from vanillin (**1a**) under alteration of the amount of PODIC.

Entry	PODIC / eq.	Yield(1a) / %	Yield(2a) / %
1	1.00	26	58
2	1.10	30	60
3	1.25	9	66
4	1.40	3	76
5	1.50	3	80
6	1.60	1	74
7	2.00	1	62

Reaction parameters: temperature: 22 °C; *n*(**1a**) = 1 mmol; *c*(1a) = 0.25 M; time = 20 min.

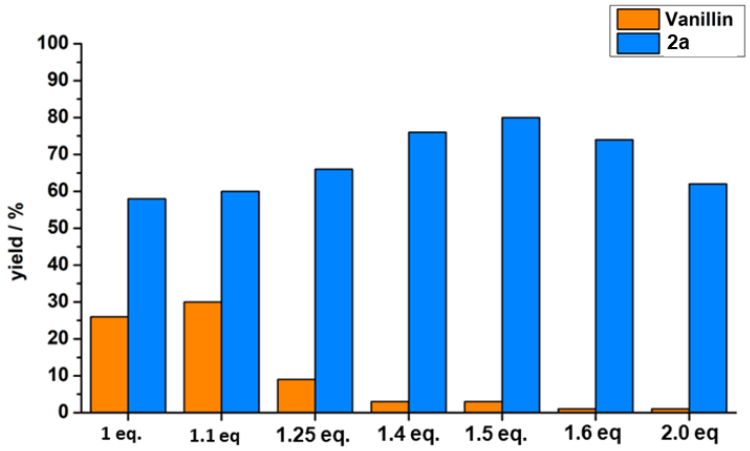


Figure S5: Synthesis of 2-methoxy-hydroquinone (**2a**) from vanillin (**1a**) under alteration of the amount of PODIC.

Concentration:

PODIC concentrations of 450 mM and 800 mM were screened. Table S5 lists the obtained yields of **2a** as well as the remaining amounts of **1a**. The contents of Table S5 are graphically depicted in Figure S7.

Table S4: Synthesis of 2-methoxyhydroquinone (**2a**) from vanillin (**1a**) under alteration of the reaction time.

Entry	*c*(PODIC) / mM	Yield(1a) / %	Yield(2a) / %
1	450	3	66
3	800	3	80

Reaction parameters: temperature: 22 °C; *n*(**1a**) = 1 mmol; c(1a) = 0.25 M, 1.5 eq. PODIC.

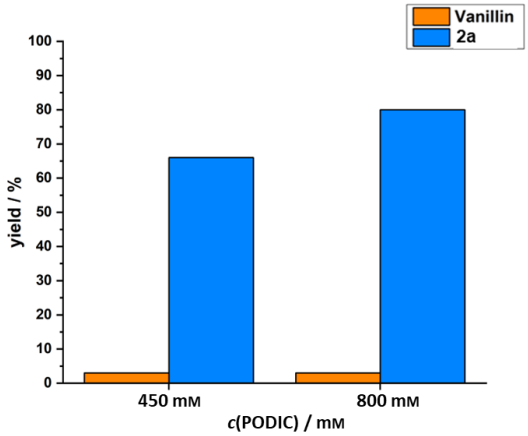


Figure S6: Synthesis of 2-methoxy-hydroquinone (**2a**) from vanillin (**1a**) under alteration of the amount of PODIC.

Reaction time:

Reaction times between 5 minutes and 25 minutes were screened. Table S5 lists the obtained yields of **2a** as well as the remaining amounts of **1a**. The contents of Table S5 are graphically depicted in Figure S7.

Table S5: Synthesis of 2-methoxyhydroquinone (**2a**) from vanillin (**1a**) under alteration of the reaction time.

Entry	Time / min	Yield(1a) / %	Yield(2a) / %
1	5	20	63
2	10	17	65
3	15	13	68
4	20	3	80
5	25	1	72

Reaction parameters: temperature: 22 °C; *n*(**1a**) = 1 mmol; c(1a) = 0.25 M.

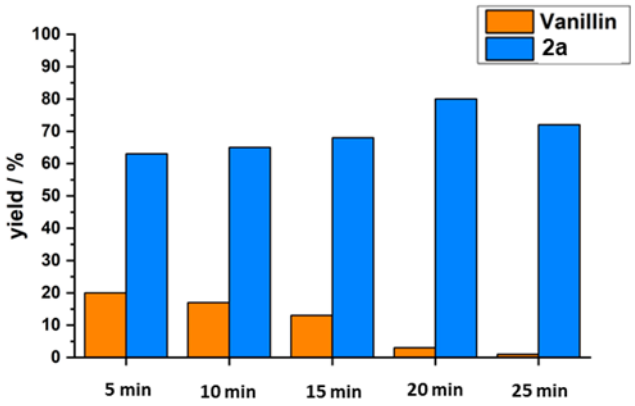


Figure S7: Synthesis of 2-methoxyhydroquinone (**2a**) from vanillin (**1a**) under alteration of the reaction time.

Temperature:

The reaction time was altered between 0 °C and 22 °C (room temperature). Table S6 lists the used amounts of PODIC and the obtained yields of **2a** as well as the remaining amounts of **1a**. The contents of Table S6 are graphically depicted in Figure S8.

Table S6: Synthesis of 2-methoxyhydroquinone (**2a**) from vanillin (**1a**) under alteration of the reaction temperature.

Entry	Temperature / °C	PODIC / eq.	Yield(1a) / %	Yield(2a) / %
1	22	1.50	3	80
2	0	1.50	19	71
3	0	1.75	1	92
4	0	2.00	0	78

Reaction parameters: temperature: 22 °C; *n*(**1a**) = 1 mmol; c(1a) = 0.25 M; time = 20 min.

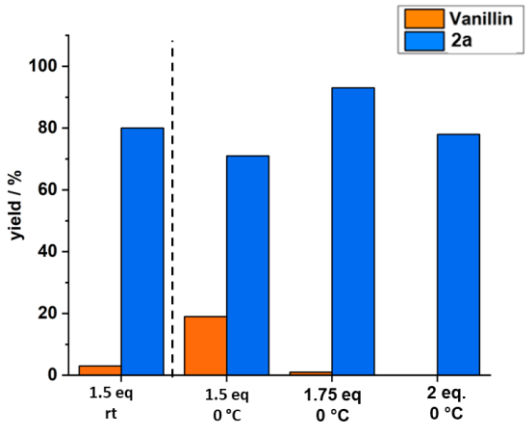


Figure S8: Synthesis of 2-methoxyhydroquinone (**2a**) from vanillin (**1a**) under alteration of the reaction temperature.

1.3 Evaluation of the Sustainability of the Protocol

In order to evaluate the sustainability of the developed protocol a comparison with conventional, published protocols was performed. To receive a balanced comparison six different green chemistry metrics, were evaluated. A comparison was done for the model compound 2-methoxyhydroquinone (**2a**). The newly developed protocol was compared to the two conventional protocols with the highest synthetically utility, as measured by chemical yield. Calculation of cost only include consumed and unrecoverable chemicals. Cost is calculated for the synthesis on 1 mol starting material scale. All prices are obtained from the current Sigma Aldrich catalog (for the German market). The largest available package size was used for calculation of the price per gram for chemicals. Solvents and acids are calculated based on the price per 2.5 L, unless otherwise stated. Products and side products are depicted according to the proposed mechanisms.

$$Eco = \frac{product\ value\ per\ mol \cdot chemical\ yield\ \%}{reagent\ cost\ per\ mol \cdot 100\%}$$

The atom economy was calculated according to the following formula:[4]

$$AE = \frac{molecular\ mass\ of\ desired\ product}{molecular\ mass\ of\ all\ products} \cdot 100\%$$

The reaction mass efficiency was calculated according to the following formula:[4]

$$RME = \frac{atom\ ecconomy \cdot chemical\ yield}{excess\ reactant\ factor}$$

Effective mass yield was calculated according to the following formula (1 mmol scale):[5]

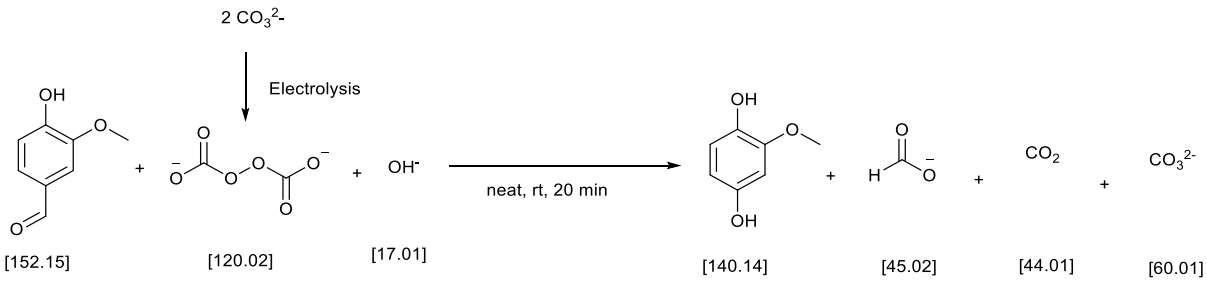
$$EMY = \frac{mass\ of\ desired\ product}{mass\ of\ non-benign\ reagents} \cdot 100\%$$

The evaluation of the safety of the protocol was conducted according to the GHS ranking of the used reagents. The overall GHS rating, as calculated by the average of the GHS ratings, was used for safety assessment (GHS rating of the product was exclude). A scale from 1 to 5 was used, where 5 means very safe and 1 means very unsafe.[6] The rating was done according to the following chart and the material safety data sheet provided by Sigma Aldrich.

GHS rating	hazard
1	explosive, oxidizing, toxic, health hazard (or more that 3 hazards)
2	harmful, flammable, environmental, corrosive (combination of 3 hazards)
3	harmful, flammable, environmental, corrosive (combination of 2 hazards)
4	harmful, flammable, environmental, corrosive (1 hazard)
5	None

Synthesis of 2- Methoxyhydroquinone (2a):

Our protocol:



Safety

Table S7: Specifications for employed chemicals.

Substance	Cas	*MW* / g·mol^{-1}	*Price* Euro/g	GHS Hazard	GHS ranking	Specification
Vanillin (**1a**)	121-33-5	152.15	0.07	-	5	25 kg, ≥97%
Sodium carbonate	497-19-8	105.99	0.03	none	5	5 kg, ReagentPlus®, ≥99.5%
Potassium carbonate	584-08-7	138.21	0.02	none	5	12 kg, Reagent grade, ≥98%, powder
Potassium bicarbonate	298-14-6	100.12	0.02	none	5	2.5 kg, ACS reagent, 99.7%
2-Methoxyhydroquinone	824-46-4	140.14	7.48			25 g, 98%

Overall GHS: 5

Others:

$$AE = \frac{140.15\,\frac{g}{mol}}{140.15\,\frac{g}{mol}+45.02\frac{g}{mol}+44.01\frac{g}{mol}} \cdot 100\% = 61\%$$

Remark: The carbonate anion was disregarded since it equals starting material in the synthesis of the peroxodicarbonate.

$$Eco = \frac{1048\,€ \cdot 91\%}{15.65\ €\cdot 100\%} = 60.9$$

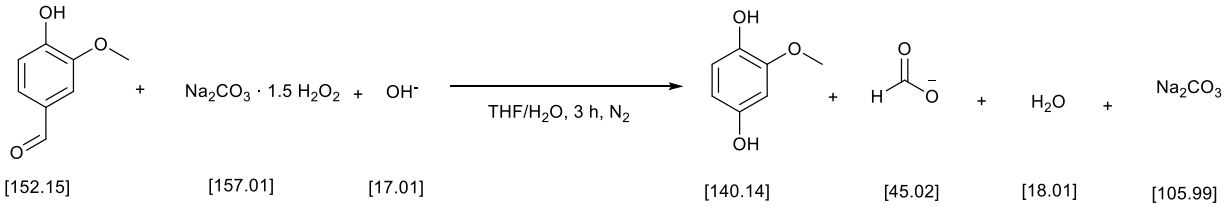
$$RME = \frac{0.61 \cdot 0.91}{1.75} \cdot 100\% = 32\%$$

$$EMY = \frac{140.15\,\frac{g}{mol}}{"1"\frac{g}{mol}} \cdot 100\% = 14015\% \rightarrow 100\%$$

The EMY metric exceeds 100% for reactions with mainly benign reagents. Since no non-benign reagents are employed and no toxic waste is generated effective mass yield was set to be 100%.

Conventional Synthesis:

According to the previously stated criteria the protocol by Boutevin was used for comparison.[7] We like to add that this seems to be an adaption of the method developed by Kabalka.[8] Since the reported yield of Boutevin is slightly higher than the one in the original publication we will report the conditions as given in the paper by Boutevin.



Safety

Table S8: Specifications for employed chemicals.

Substance	Cas	*MW* / g·mol^{-1}	*Price* Euro/g	GHS Hazard	GHS ranking	Specification
Vanillin (**1a**)	121-33-5	152.15	0.07	-	5	25 kg, ≥97%
Sodium percarbonate	15630-89-4	157.01	0.04	Oxidizing, toxic	1	2.5 kg
Tetrahydrofuran	10049-21-5	72.11	0.05	toxic, health hazard, flammable	1	2.5 L, reagent grade, ≥99.0%
2-Methoxyhydroquinone	824-46-4	140.14	7.48			25 g, 98%

Overall GHS: 2.3

Others:

$$AE = \frac{140.15\,\frac{g}{mol}}{140.15\,\frac{g}{mol}+45.02\frac{g}{mol}+18.01\frac{g}{mol}} \cdot 100\% = 69\%$$

Remark: The carbonate anion was disregarded, since it equals starting material.

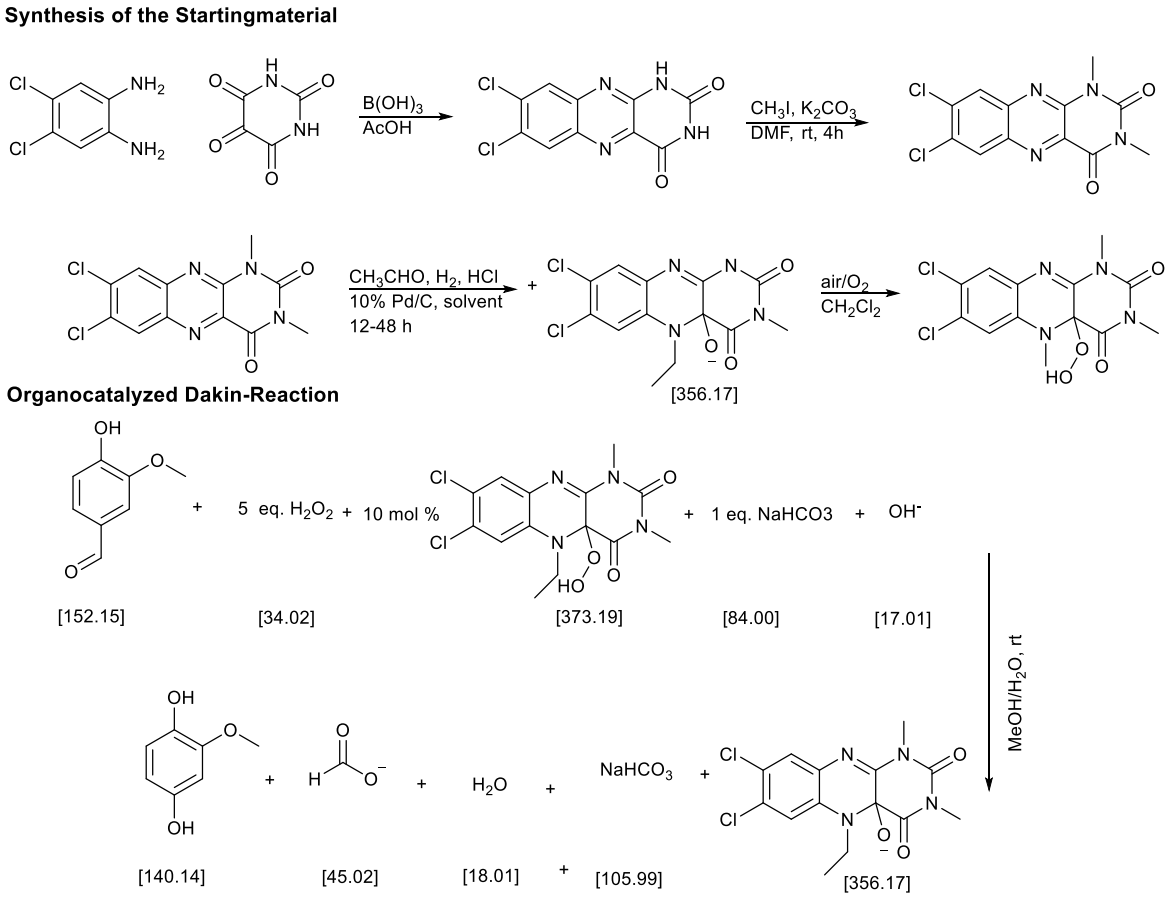
$$Eco = \frac{1048\,€ \cdot 97\%}{184.9\ € \cdot 100\%} = 5.5$$

$$RME = \frac{0.69 \cdot 0.97}{1.6} \cdot 100\% = 44\%$$

$$EMY = \frac{140.15\ \text{g}}{3560\ \text{g}} \cdot 100\% = 3{,}9\ \%$$

Conventional Synthesis:

According to the previously stated criteria the protocol by Foss was used for comparison.[9] Since the used organocatalyst is not commercially available the synthesis route used by Foss and co-workers is shown as well and the starting materials are considered for the calculation of the catalyst. Prices of gasses were disregarded for reasons of simplicity.



Safety

Table S9: Specifications for employed chemicals.

Substance	Cas	*MW* / g·mol^{-1}	*Price* Euro/ g	GHS Hazard	GHS ranking	Specification
Vanillin (**1a**)	121-33-5	152.15	0.07	-	5	25 kg, ≥97%
	15630-89-4	157.01	11.68	harmful	4	25 g, 97%

4,5-Dichloro-*1,2*-phenylenediamine						
Alloxan Monohydrate	2244-11-3	160.08	2.67	harmful	4	25 g, 98%
Boric Acid	10043-35-3	61.83	0.04	Health hazard	1	ACS reagent, ≥99.5%
Acetic acid	64-19-7	60.05	0.05	Flammable	4	glacial, ACS reagent, ≥99.7%
Iodomethane	74-88-4	141.94	0.58	Flammable, health hazard, toxic, environmental hazard	1	ReagentPlus®, 99.5%
Potassium carbonate	584-08-7	138.21	0.02	none	5	12 kg, Reagent grade, ≥98%, powder
N,*N*-Dimethylformamide	68-12-2	73.09	0.18	Flammable, health hazard	1	anhydrous, ≥99.8%
Acetaldehyde	75-07-0	44.05	0.10	Flammable, health hazard	1	ACS reagent, ≥99.5%
Hydrochloric acid	7647-01-0	36.46	0.02	danger	5	fuming 37%,
Pd/C	-	106.42	13.12	none	5	10 wt. % loading
Dichloromethane	75-09-2	84.93	0.05	Health hazard	1	ACS reagent, ≥99.5%
Sodium bicarbonate	144-55-8	84.01	0.01	none	5	≥99%, 25 kg
Hydrogen peroxide	7722-84-1	34.01	0.01	harmful	4	35%, 25 L
Methanol	67-56-1	32.04	0.03	Health hazard, toxic, flammable	1	ACS reagent ≥99.8% (GC), 2.5 L
2-Methoxy-hydroquinone	824-46-4	140.14	7.48			25 g, 98%

Overall GHS: 3.1

Others:

$$AE = \frac{140.15\,\frac{g}{mol}}{140.15\,\frac{g}{mol}+45.02\frac{g}{mol}+18.01\frac{g}{mol}+356.17\frac{g}{mol}} \cdot 100\% = 25\%$$

Remark: The carbonate anion was disregarded since it equals starting material.

$$Eco = \frac{1048\ € \cdot 95\%}{1139.72\ € \cdot 100\%} = 0.87$$

Prices of used starting materials exceed generated value of the product.

$$RME = \frac{0.25 \cdot 0.95}{5} \cdot 100\% = 5\%$$

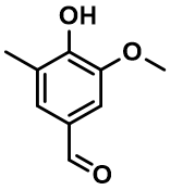
$$EMY = \frac{140.15\ \mathrm{g}}{0.1\ \cdot\ 351.7\ \mathrm{g} + 7900\ \mathrm{g}} \cdot 100\% = 1{,}8\ \%$$

1.4 Isolated Compounds

Starting Materials

As stated above some starting materials were synthesized via a previous protocol.[1] We have already reported analytical data for the starting materials **1i**, **1k**, **1o**, **1p**, and **1q**.[10]

1.4.1 4-Hydroxy-3-methoxy-5-methylbenzaldehyde (1c)



4-Hydroxy-3-methoxy-5-methylbenzaldehyde (**1c**) was synthesized according to general protocol 1, from 2-methoxy-6-methylphenol (3.454 g, 25.000 mmol, 1 eq.). The target compound (**1c**) was obtained as an off-white solid (2.073 g, 12.474 mmol, 50%) after recrystallization from ethanol.

***R*$_f$:** 0.3 (cyclohexane/ethyl acetate = 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.81 (s, 1H), 7.35 – 7.28 (m, 2H), 6.31 (s, 1H), 3.97 (s, 3H), 2.33 (s, 3H) ppm.

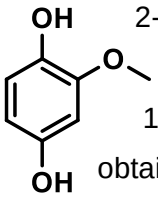
^{13}C NMR (101 MHz, $CDCl_3$): δ = 191.32, 149.89, 146.85, 129.02, 128.94, 124.17, 106.83, 56.34, 15.41 ppm.

HRMS (ESI+): *m/z* for $C_9H_{10}O_3 + H^+$ $[M+H]^+$: calculated 167.0703; found: 167.0703

The analytical data are in accordance with literature.[11]

Hydroquinones

1.4.2 2-Methoxyhydroquinone (2a)



2-Methoxyhydroquinone (**2a**) was synthesized according to general protocol 2, from vanillin (152.2 mg, 1.00 mmol, 1 eq. and for the scale-up: 1.522 g, 10 mmol, 1 eq. & 3.044 g, 20 mmol, 1 eq.). The target compound (**2a**) was obtained as an off-white solid (127.5 mg, 0.91 mmol, 91% and for the scale-up: 1.260 g, 8.99 mmol, 90% & 2.464 g, 17.58 mmol, 88%) after flash column chromatography (cyclohexane/ethyl acetate 10:90 → 20:80).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

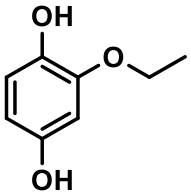
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.76 (d, J = 8.5 Hz, 1H), 6.45 (d, J = 2.8 Hz, 1H), 6.31 (dd, J = 8.5, 2.8 Hz, 1H), 5.22 (brs, 1H), 4.58 (brs, 1H), 3.84 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 149.27, 147.20, 139.67, 114.51, 106.98, 99.87, 56.04 ppm.

HRMS (ESI+): *m*/*z* for $C_7H_8O_3$+H^+ $[M+H]^+$: calculated 141.0546; found: 141.0555.

The analytical data are in accordance with literature.[12]

1.4.3 2-Ethoxydroquinone (2a)



2-Ethoxyhydroquinone (**2a**) was synthesized according to general protocol 2, from 3-Ethoxy-4-hydroxy-benzaldehyde (166.2 mg, 1.00 mmol, 1 eq.). The target compound (**2a**) was obtained as a colorless solid (129.1 mg, 0.84 mmol, 84%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.15 (cyclohexane/ethyl acetate = 4:1)

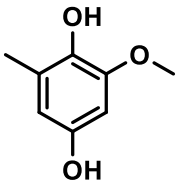
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.76 (d, J = 8.5 Hz, 1H, *H*-6), 6.43 (d, J = 2.8 Hz, 1H, *H*-3), 6.30 (dd, J = 8.5, 2.8 Hz, 1H, *H*-5), 5.25 (s, 1H, O*H*), 4.07 (q, J = 7.0 Hz, 2H, CH_2), 1.44 (t, J = 7.0 Hz, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 149.14 (*C*-4), 146.45 (*C*-2), 139.91(*C*-1), 114.39 (*C*-6), 106.90 (*C*-5), 100.61 (*C*-3), 64.63 (*C*H_2), 14.96 (*C*H_3) ppm.

HRMS (ESI-): *m*/*z* for $C_8H_{10}O_3$ $[M-H]^-$: calculated 153.0557; found: 153.0555.

Previously no NMR data were available for this compound.

1.4.4 2-Methoxy-6-methylhydroquinone (2c)



2-Methoxy-6-methylhydroquinone (**2c**) was synthesized according to general protocol 2, from 4-hydroxy-3-methoxy-5-methylbenzaldehyde (166.2 mg, 1.00 mmol, 1 eq.). The target compound (**2c**) was obtained as a colorless solid (133.6 mg, 0.85 mmol, 85%) after flash column chromatography (cyclohexane/ethyl acetate 10:90 → 20:80).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

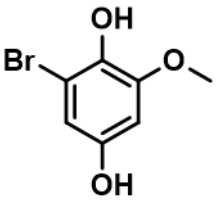
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.31 (d, J = 2.8 Hz, 1H), 6.21 (d, J = 2.8 Hz, 1H), 5.25 (brs, 1H), 4.38 (brs, 1H), 3.84 (s, 3H), 2.20 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.36, 146.81, 137.82, 124.24, 108.96, 97.20, 56.15, 15.64 ppm.

HRMS (ESI+): *m/z* for $C_8H_{10}O_3$ $[M]^+$: calculated 154.0624; found: 154.0623.

The analytical data are in accordance with literature.[13]

1.4.5 2-Bromo-6-methoxyhydroquinone (2d)



2-Bromo-6-methoxylhydroquinone (**2d**) was synthesized according to general protocol 2, from 3-bromo-4-hydroxy-5-methoxylbenzaldehyde (231.1 mg, 1.00 mmol, 1 eq.). The target compound (**2d**) was obtained as a colorless solid (136.6 mg, 0.62 mmol, 62%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

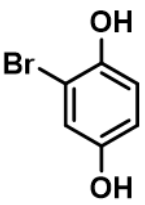
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.58 (d, J = 2.7 Hz, 1H), 6.41 (d, J = 2.7 Hz, 1H), 5.49 (brs, 2H), 3.87 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): 149.27, 147.80, 137.56, 110.60, 107.86, 99.50, 56.46 ppm.

HRMS (ESI-): *m/z* for $C_7H_7{}^{79}BrO_3$ $[M-H]^-$: calculated 216.9506 found: 216.9508.

The analytical data are in accordance with literature.[14]

1.4.6 2-Bromohydroquinone (2e)



2-Bromohydroquinone (**2e**) was synthesized according to general protocol 2, from 3-bromo-4-hydroxybenzaldehyde (201.0 mg, 1.00 mmol, 1 eq.). The target compound (**2e**) was obtained as an orange oil (with 1.75 eq. PODIC: 131.0 mg, 0.69 mmol, 69%, with 3.5 eq. PODIC: 172.5 mg, 0.91 mmol, 91%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

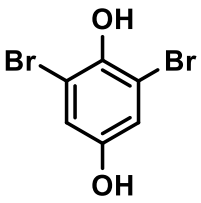
^{1}H NMR (400 MHz, Acetone-d_6): δ = 8.14 (brs, 2H), 6.99 (d, J = 2.9 Hz, 1H), 6.84 (d, J = 8.7 Hz, 1H), 6.70 (dd, J = 8.7, 2.9 Hz, 1H) ppm.

^{13}C NMR (101 MHz, Acetone-d_6): δ = 151.70, 147.75, 119.83, 117.56, 116.22, 110.06 ppm.

HRMS (ESI-): *m*/*z* for $C_6H_5{}^{81}BrO_2$ [M-H]$^-$: calculated 188.9380; found: 188.9379.

The analytical data are in accordance with literature.[15]

1.4.7 2,6-Dibromohydroquinone (2f)



2,6-Dibromohydroquinone (**2f**) was synthesized according to general protocol 2, from 3,5-dibromo-4-hydroxybenzaldehyde (279.9 mg, 1.00 mmol, 1 eq.). The target compound (**2f**) was obtained as a colorless solid (with 1.75 eq. PODIC: 166.1 mg, 0.62 mmol, 62%, with 3.5 eq. PODIC: 250.8 mg, 0.94 mmol, 94%) after reversed-phase column chromatography (acetonitrile/water 25:75 → 90:10).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

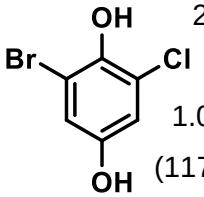
^{1}H NMR (400 MHz, Acetone-d_6): δ = 8.27 (s, 2H), 7.04 (s, 2H).

^{13}C NMR (101 MHz, Acetone-d_6): 152.38, 144.82, 119.88, 111.92.

HRMS (ESI-): *m*/*z* for $C_6H_4{}^{79}Br^{81}BrO_2$ [M-H]$^-$: calculated 266.8485; found: 266.8483.

The literature reference has measured the sample in $CDCl_3$ instead of deuterated acetone. In consequence OH Peaks are downfield shifted in comparison with the literature report. We generally observed a downfield shift of the hydroxy signals if we measured a sample in both acetone and $CDCl_3$. Aside from that the analytical data are in accordance with literature.[16]

1.4.8 2-Bromo-6-chlorohydroquinone (2g)



2-Bromo-6-chlorohydroquinone (**2g**) was synthesized according to general protocol 2, from 3-bromo-6-chloro-4-hydroxybenzaldehyde (235.5 mg, 1.00 mmol, 1 eq.). The target compound (**2g**) was obtained as a colorless solid (117.5 mg, 0.53 mmol, 53%) after reversed-phase column chromatography (acetonitrile/water 25:75 → 90:10).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

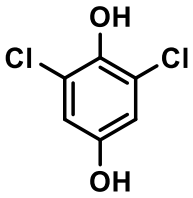
^{1}H NMR (400 MHz, Acetone-d_6): δ =8.37 (brs, 2H), 7.00 (d, J = 2.8 Hz, 1H), 6.88 (d, J = 2.8 Hz, 1H).

^{13}C NMR (101 MHz, Acetone-d_6): 151.99, 144.00, 122.71, 119.32, 116.83, 112.22.

HRMS (APCI-): *m*/*z* for $C_6H_4{}^{79}Br^{35}ClO_2$ [M-H]$^-$: calculated 220.9010; found: 220.9009.

Previously no NMR data was reported for this compound.

1.4.9 2,6-Dichlorohydroquinone (2h)



2,6-Dichlorohydroquinone (**2h**) was synthesized according to general protocol 2, from 2,6-dichloro-4-hydroxybenzaldehyde (191.0 mg, 1.00 mmol, 1 eq.). The target compound (**2h**) was obtained as a colorless solid (142.2 mg, 0.79 mmol, 79%) after reversed-phase column chromatography (acetonitrile/water 25:75 → 90:10).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

^{1}H NMR (400 MHz, Acetone-d_6): δ = 8.38 (brs, 2H), 6.83 (s, 2H).

^{13}C NMR (101 MHz, Acetone-d_6): 151.46, 143.07, 123.05, 116.21.

HRMS (APCI-): *m*/*z* for $C_6H_4{}^{35}Cl_2O_2[M-H]^-$: calculated 176.9516; found: 176.9511.

The analytical data are in accordance with literature.[17]

1.4.10 Hydroquinone (2i)

Hydroquinone (**2i**) was synthesized according to general protocol 2, from 4-hydroxybenzaldehyde (122.12 mg, 1.00 mmol, 1 eq.). The target compound (**2i**) was obtained as a off-white solid (101.3 mg, 0.92 mmol, 92%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

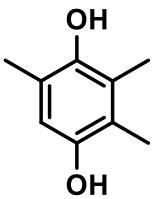
^{1}H NMR (400 MHz, Acetone-d_6): δ = 7.68 (brs, 2H), 6.67 (s, 4H) ppm.

^{13}C NMR (101 MHz, Acetone-d_6): δ = 150.81, 116.28 ppm.

HRMS (ESI-): *m*/*z* for $C_6H_6O_2$ $[M-H]^-$: calculated 109.0295; found: 109.0295.

The analytical data are in accordance with literature.[18]

1.4.11 2,3,6-Trimethylhydroquinone (2j)



2,3,6-Trimethylhydroquinone (**2j**) was synthesized according to general protocol 2, from 4-hydroxy-2,3,5-trimethylbenzaldehyde (164.2 mg, 1.00 mmol, 1 eq.). The target compound (**2j**) was obtained as a colorless solid (112.6 mg, 0.74 mmol, 74%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

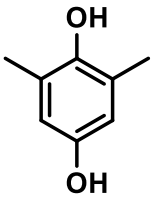
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.46 (s, 1H), 4.22 (brs, 2H), 2.20 – 2.12 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 147.05, 146.00, 133.21, 123.61, 121.15, 120.93, 114.44, 77.48, 77.36, 77.16, 76.84, 16.07, 12.53, 12.44, 12.23, 12.10.

HRMS (ESI-): *m*/*z* for $C_8H_{10}O_2$ [M-H]$^-$: calculated 151,0764; found: 151.0765.

Previously no complete NMR data was available.

1.4.12 2,6-Dimethylhydroquinone (2k)



2,6-Dimethylhydroquinone (**2k**) was synthesized according to general protocol 2, from 4-hydroxy-3,5-dimethylbenzaldehyde (150.2 mg, 1.00 mmol, 1 eq.). The target compound (**2k**) was obtained as a colorless solid (117.6 mg, 0.85 mmol, 85%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

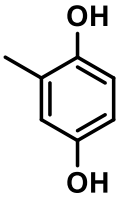
^{1}H NMR (400 MHz, Acetone-d_6): δ = 1H NMR (400 MHz, Acetone) δ 7.48 (s, 1H), 6.59 (s, 1H), 6.43 (s, 2H), 2.15 (s, 6H) ppm.

^{13}C NMR (101 MHz, Acetone-d_6): δ = 150.88, 146.80, 125.86, 115.45, 16.66 ppm.

HRMS (ESI-): *m*/*z* for $C_8H_{10}O_2$ [M-H]$^-$: calculated 137.0608; found: 137.0603.

The analytical data are in accordance with literature.[19]

1.4.13 2-Methylhydroquinone (2l)



2-Methylhydroquinone (**2l**) was synthesized according to general protocol 2, from 4-hydroxy-3-methylbenzaldehyde (136.2 mg, 1.00 mmol, 1 eq.). The target compound (**2l**) was obtained as a colorless solid (116.8 mg, 0.94 mmol, 94%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

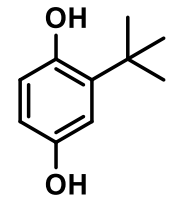
^{1}H NMR (400 MHz, Acetone-d_6) δ = 7.54 (s, 1H), 7.48 (s, 1H), 6.66 – 6.56 (m, 2H), 6.47 (dd, J = 8.5, 3.0 Hz, 1H), 2.13 (s, 3H) ppm.

^{13}C NMR (101 MHz, Aceton-d_6): δ = 150.94, 148.99, 125.67, 118.13, 115.94, 113.53, 16.24 ppm.

HRMS (ESI-): *m*/*z* for $C_7H_8O_2$ [M-H]$^-$: calculated 123.0452; found: 123.0453.

The analytical data are in accordance with literature.[20]

1.4.14 2-*tert*-Butylhydroquinone (2m)



2-*tert*-Butylhydroquinone (**2m**) was synthesized according to general protocol 2, from 3-*tert*-butyl-4-hydroxylbenzaldehyde (178.2 mg, 1.00 mmol, 1 eq.). The target compound (**2m**) was obtained as an off-white solid (136.1 mg, 0.82 mmol, 82%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

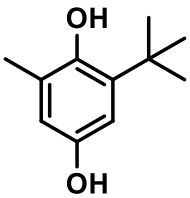
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.77 (t, J = 1.7 Hz, 1H), 6.54 (d, J = 1.7 Hz, 2H), 4.45 (brs, 1H), 4.35 (brs, 1H), 1.39 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 149.21, 148.25, 137.78, 117.31, 114.58, 113.01, 34.72, 29.60.

HRMS (ESI-): *m*/*z* for $C_{10}H_{14}O_2$ $[M-H]^-$: calculated 165.0920; found: 165.0922.

The analytical data are in accordance with literature.[21]

1.4.15 2-*tert*-Butyl-6-methylhydroquinone (2n)



2-*tert*-Butyl-6-methylhydroquinone (**2n**) was synthesized according to general protocol 2, from 3-*tert*-butyl-5-methyl-4-hydroxylbenzaldehyde (192.2 mg, 1.00 mmol, 1 eq.). The target compound (**2n**) was obtained as a viscous pale-yellow oil (138.8 mg, 0.77 mmol, 77%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.25 (cyclohexane/ethyl acetate = 4:1)

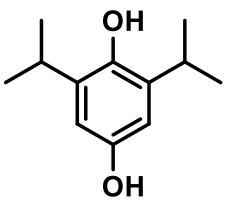
^{1}H NMR (400 MHz, $CDCl_3$: δ = 6.65 (d, J = 3.1 Hz, 1H), 6.50 (d, J = 3.1 Hz, 1H), 4.36 (brs, 2H), 2.20 (s, 3H), 1.39 (s, 9H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 148.53, 146.66, 137.42, 124.54, 114.85, 112.22, 34.71, 29.78, 16.40 ppm.

HRMS (ESI-): *m*/*z* for $C_{11}H_{16}O_2$ $[M-H]^-$: calculated 179.1077; found: 179.1078.

Previously no complete NMR data were reported.

1.4.16 2,6-Diisopropylhydroquinone (2o)



2,6-Diisopropylhydroquinone (**2o**) was synthesized according to general protocol 2, from 3,5-diisopropyl-4-hydroxylbenzaldehyde (206.3 mg, 1.00 mmol, 1 eq.). The target compound (**2o**) was obtained as a viscous colorless liquid (138.1 mg, 0.70 mmol, 70%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.25 (cyclohexane/ethyl acetate = 4:1)

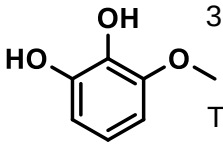
^{1}H NMR (400 MHz, $CDCl_3$: δ = 6.54 (s, 2H), 4.32 (brs, 2H), 3.13 (hept, J = 6.9 Hz, 2H), 1.24 (d, J = 6.9 Hz, 12H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ = 149.79, 144.19, 135.81, 110,65, 27.71, 23.16 ppm.

HRMS (APCI+): *m*/*z* for $C_{12}H_{18}O_2$ $[M]^{\cdot+}$: calculated 194.1302; found: 194.1300.

The analytical data are in accordance with literature.[22]

1.4.17 3-Methoxycatechol (2p)



3-Methoxycatechol (**2p**) was synthesized according to general protocol 2, from 2-hydroxy-3-methoxybenzaldehyde (152.2 mg, 1.00 mmol, 1 eq.). The target compound (**2p**) was obtained as a colorless solid (133.0 mg, 0.95 mmol, 95%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

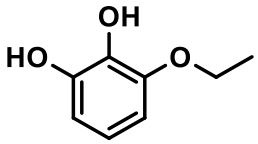
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.76 (t, J = 8.3 Hz, 1H), 6.60 (dd, J = 8.3, 1.3 Hz, 1H), 6.48 (dd, J = 8.3, 1.3 Hz, 1H), 5.40 (brs, 1H), 5.30 (brs, 1H), 3.88 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): 147.15, 144.19, 132.59, 119.00, 108.93, 102.87, 56.29 ppm.

HRMS (ESI-): *m*/*z* for $C_7H_8O_3$ $[M\text{-}H]^-$: calculated 139.0402; found: 139.0400.

The analytical data are in accordance with literature.[23]

1.4.18 3-Ethoxycatechol (2q)



3-Ethoxycatechol (**2q**) was synthesized according to general protocol 2, from 3-Ethoxy-2-hydroxybenzaldehyde (166.2 mg, 1.00 mmol, 1 eq.). The target compound (**2q**) was obtained as a colorless solid (109.2 mg, 0.71 mmol, 71%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

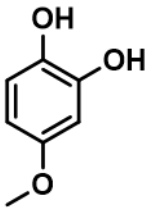
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.76 (t, J = 8.3 Hz, 1H, *H*-5), 6.61 (dd, J = 8.3, 1.3 Hz, 1H, *H*-6), 6.48 (dd, J = 8.2, 1.3 Hz, 1H, *H*-4), 5.46 (s, 1H, O*H*), 5.31 (s, 1H, O*H*), 4.13 (q, J = 7.0 Hz, 2H, CH_2), 1.46 (t, J = 7.0 Hz, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): 146.39 (*C*-3), 144.21 (*C*-1), 132.76 (*C*-2), 119.89 (*C*-5), 108.76 (*C*-6), 104.14 (*C*-4), 64.80 (*C*H_2), 15.09 (*C*H_3) ppm.

HRMS (ESI-): *m*/*z* for $C_8H_{10}O_3$ $[M\text{-}H]^-$: calculated 153.0557; found: 153.0561.

Previously no NMR data was reported.

1.4.19 4-Methoxycatechol (2r)



4-Methoxycatechol (**2r**) was synthesized according to general protocol 2, from 2-hydroxy-5-methoxybenzaldehyde (152.2 mg, 1.00 mmol, 1 eq.). The target compound (**2r**) was obtained as a colorless viscous liquid (114.6 mg, 0.82 mmol, 82%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

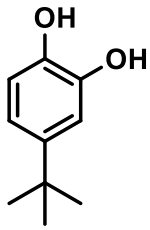
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.78 (d, J = 8.7 Hz, 1H), 6.51 (d, J = 2.9 Hz, 1H), 6.35 (dd, J = 8.7, 2.9 Hz, 1H), 5.52 (brs, 1H), 4.94 (brs, 1H), 3.74 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): 154.45, 144.76, 137.27, 116.01, 105.50, 102.50, 55.92 ppm.

HRMS (ESI-): *m*/*z* for $C_7H_8O_3$ $[M-H]^-$: calculated 139.0402; found: 139.0405.

The analytical data are in accordance with literature.[24]

1.4.20 4-*tert*-Butylcatechol (2s)



4-*tert*-Butylcatechol (**2s**) was synthesized according to general protocol 2, from 5-*tert*-butyl-2-hydroxy-benzaldehyde (178.2 mg, 1.00 mmol, 1 eq.). The target compound (**2s**) was obtained as a red solid (158.0 mg, 0.95 mmol, 95%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

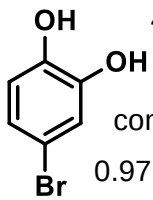
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, J = 2.1 Hz, 1H), 6.85 – 6.75 (m, 2H), 5.10 (brs, 2H), 1.27 (s, 9H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): 145.27, 143.44, 141.35, 118.18, 115.37, 113.43, 34.65, 31.93 ppm.

HRMS (ESI-): *m*/*z* for $C_{10}H_{14}O_2$ $[M-H]^-$: calculated 165.0921; found: 165.0920.

The analytical data are in accordance with literature.[25]

1.4.21 4-Bromocatechol (2t)



4-Bromocatechol (**2t**) was synthesized according to general protocol 2, from 5-bromo-2-hydroxy-benzaldehyde (201.0 mg, 1.00 mmol, 1 eq.). The target compound (**2t**) was obtained as a red solid (with 3.5 eq. PODIC: 183.3 mg, 0.97 mmol, 97%) after flash column chromatography (cyclohexane/ethyl acetate 0:100 → 30:70).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (d, J = 2.3 Hz, 1H), 6.93 (dd, J = 8.5, 2.3 Hz, 1H), 6.74 (d, J = 8.5 Hz, 1H), 5.33 (brs, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): 144.52, 142.83, 124.14, 118.80, 116.82, 112.75.

HRMS (ESI-): *m/z* for $C_6H_5{}^{79}BrO_2$ $[M-H]^-$: calculated 186.9400; found: 186.9403.

The analytical data are in accordance with literature.[26]

1.5 NMR Spectra

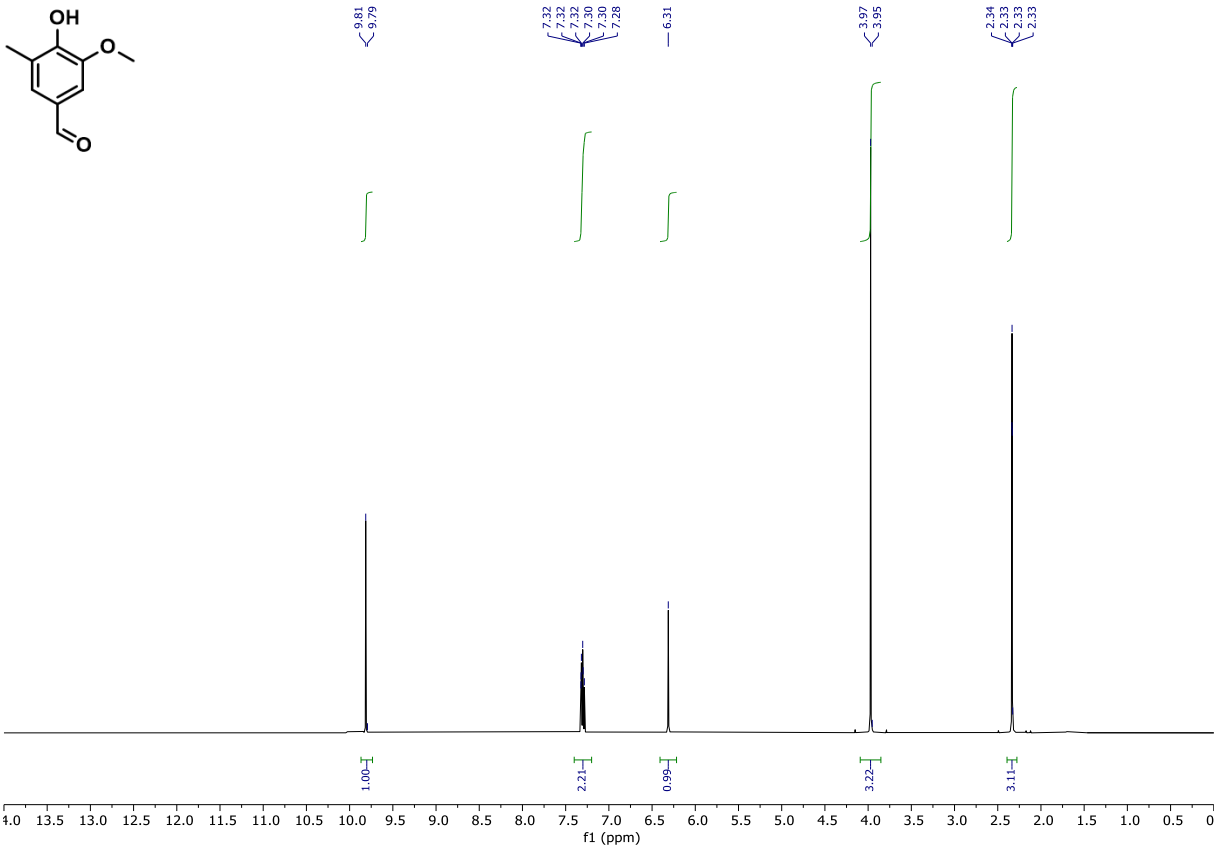


Figure S9: ^{1}H NMR spectra of 4-hydroxy-3-methoxy-5-methylbenzaldehyde (**1c**) at 298 K in $CDCl_3$

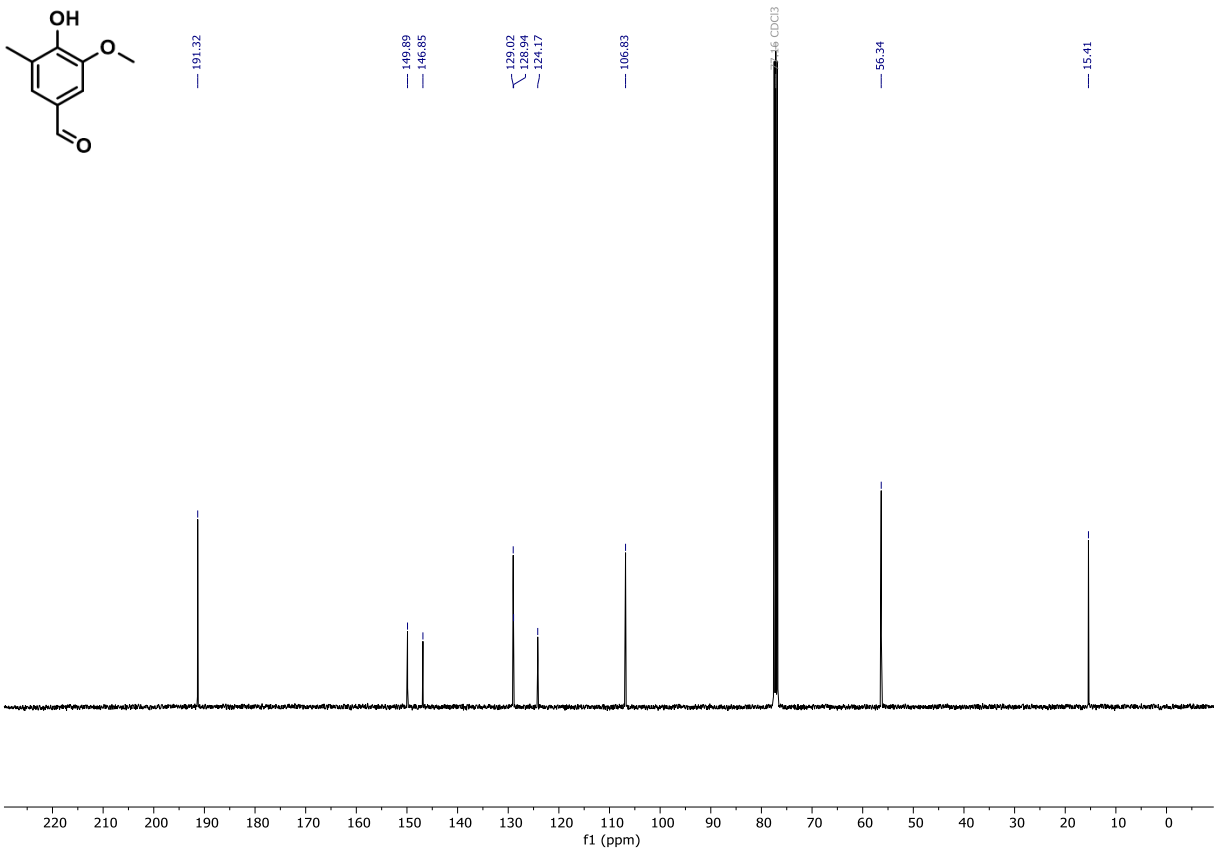


Figure S10: ^{13}C NMR spectra of 4-hydroxy-3-methoxy-5-methylbenzaldehyde (**1c**) at 298 K in $CDCl_3$.

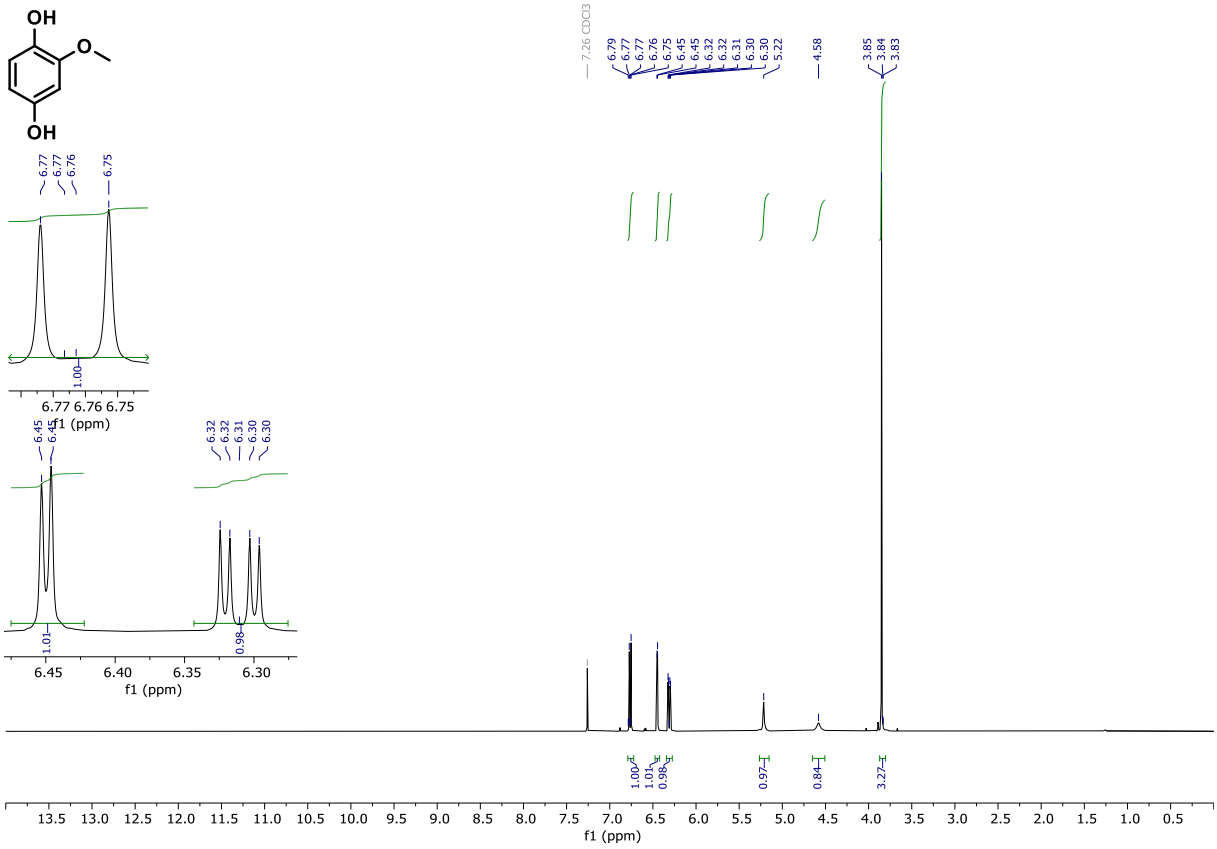


Figure S11: ^{1}H NMR spectra of 2-methoxyhydroquinone (**2a**) at 298 K in $CDCl_3$

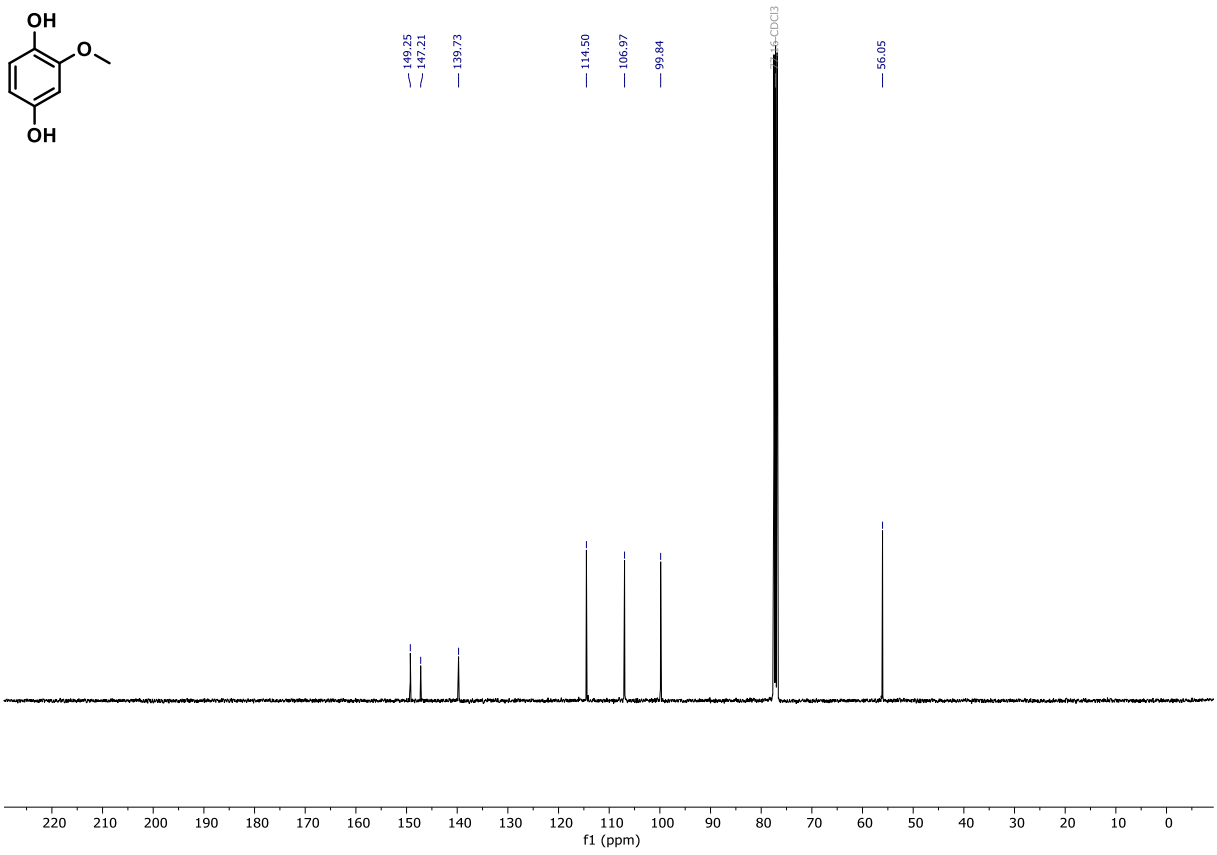


Figure S12: ^{13}C NMR spectra of 2-methoxyhydroquinone (**2a**) at 298 K in $CDCl_3$

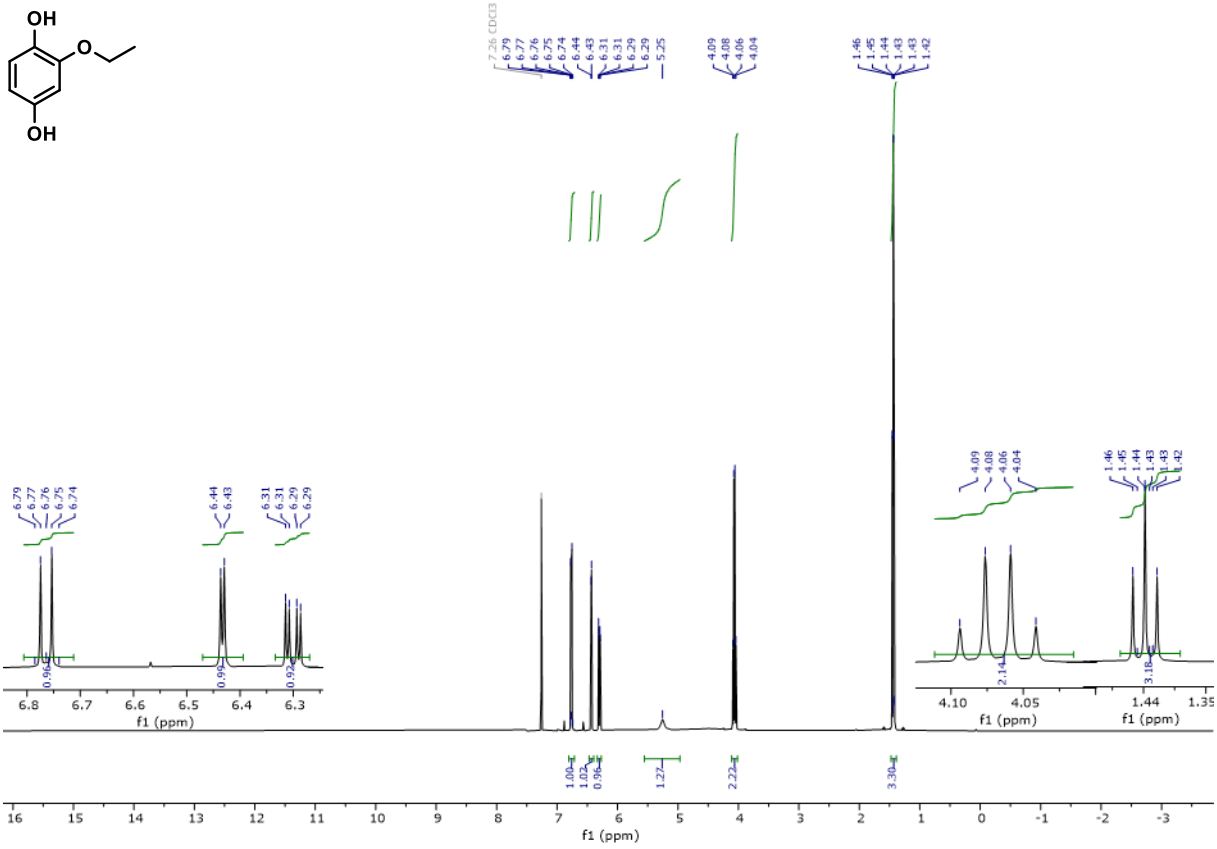


Figure S13: ^{1}H NMR spectra of 2-ethoxyhydroquinone (**2b**) at 298 K in $CDCl_3$.

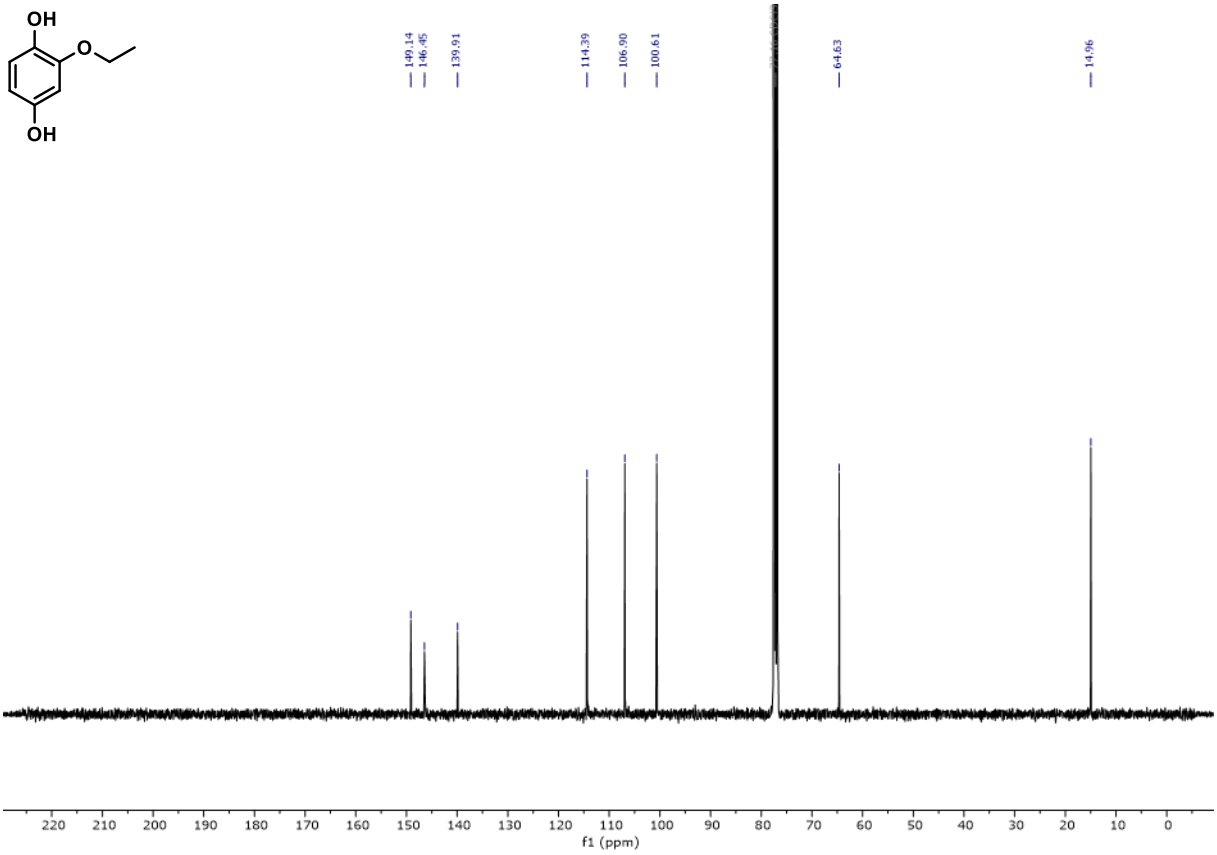


Figure S14: ^{13}C NMR spectra of 2-ethoxyhydroquinone (**2b**) at 298 K in $CDCl_3$.

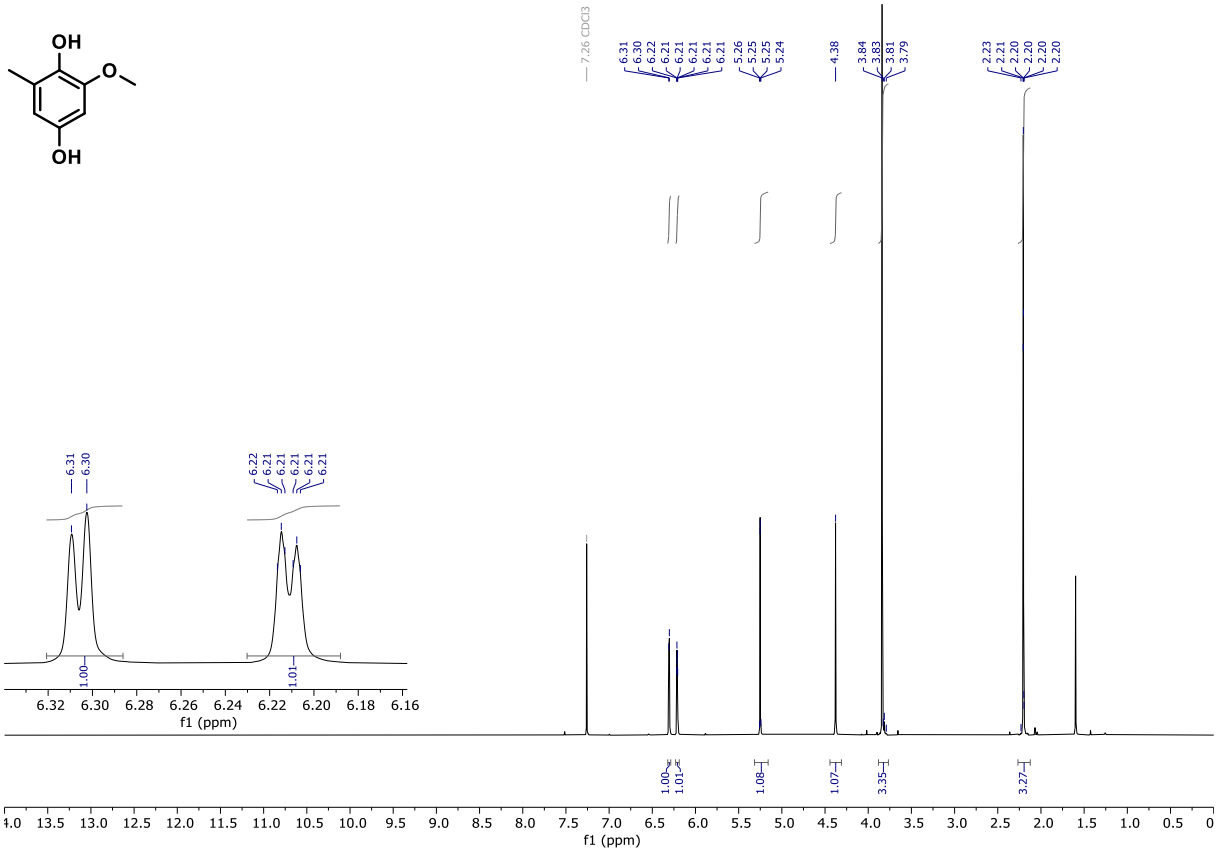


Figure S15: ^{1}H NMR spectra of 2-methoxy-6-methylhydroquinone (**2c**) at 298 K in $CDCl_3$

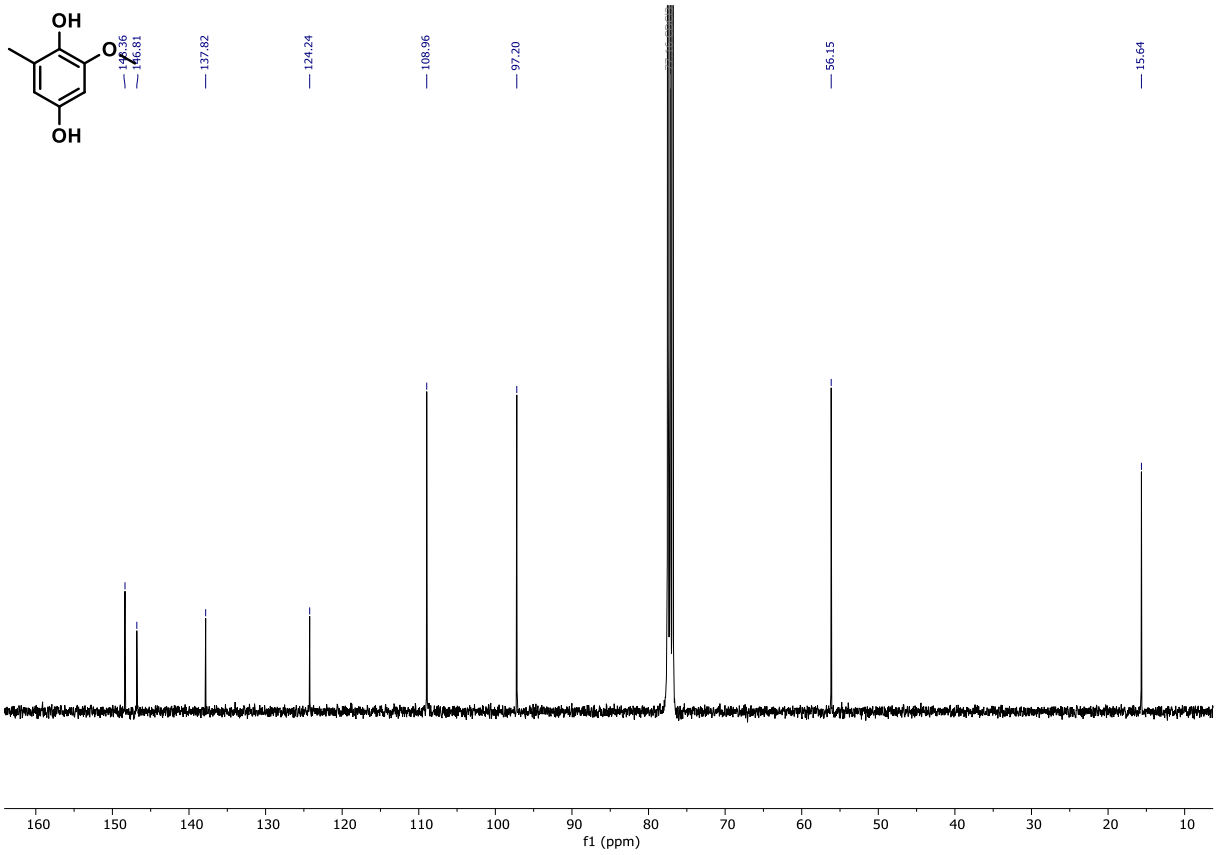


Figure S16: ^{13}C NMR spectra of 2-methoxy-6-methylhydroquinone (**2c**) at 298 K in $CDCl_3$

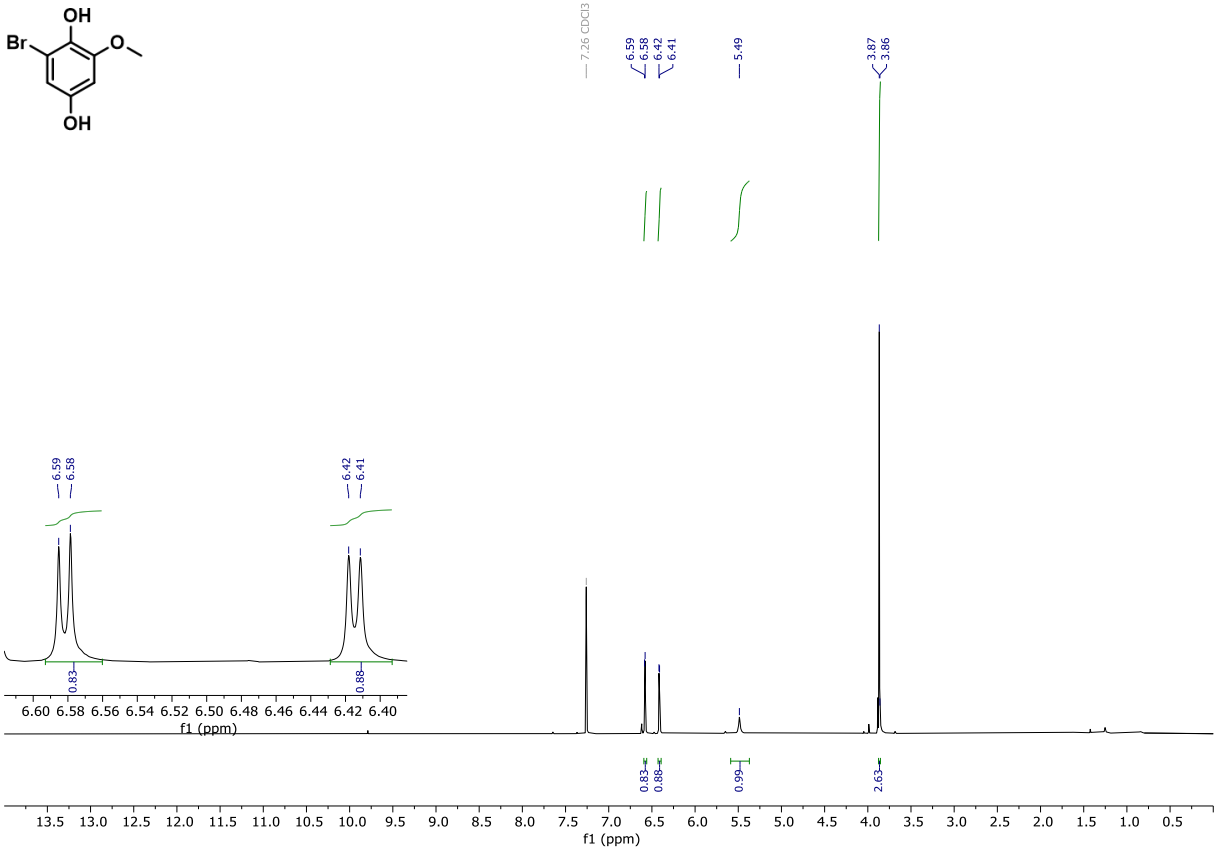


Figure S17: ^{1}H NMR spectra of 2-bromo-6-methoxyhydroquinone (**2d**) at 298 K in $CDCl_3$.

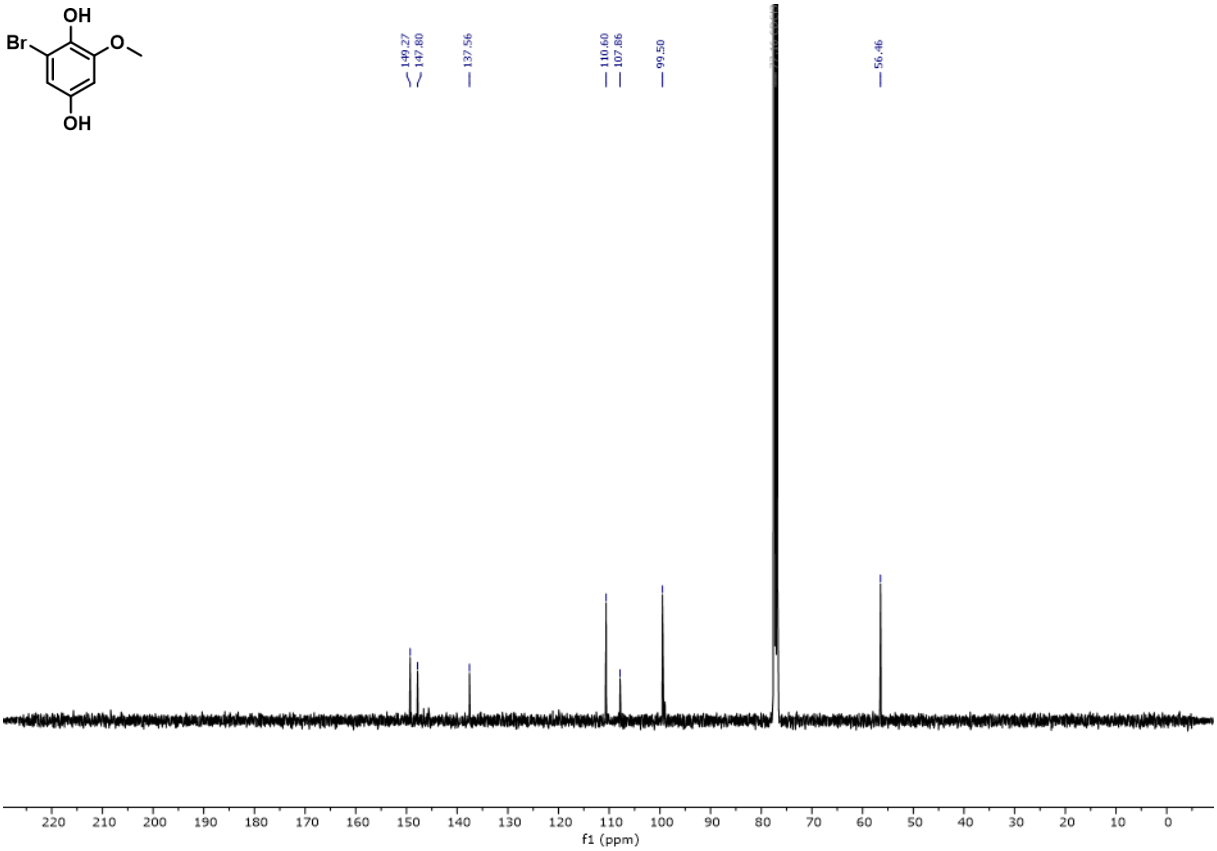


Figure S18*:* ^{13}C NMR spectra of 2-bromo-6-methoxyhydroquinone (**2d**) at 298 K in $CDCl_3$.

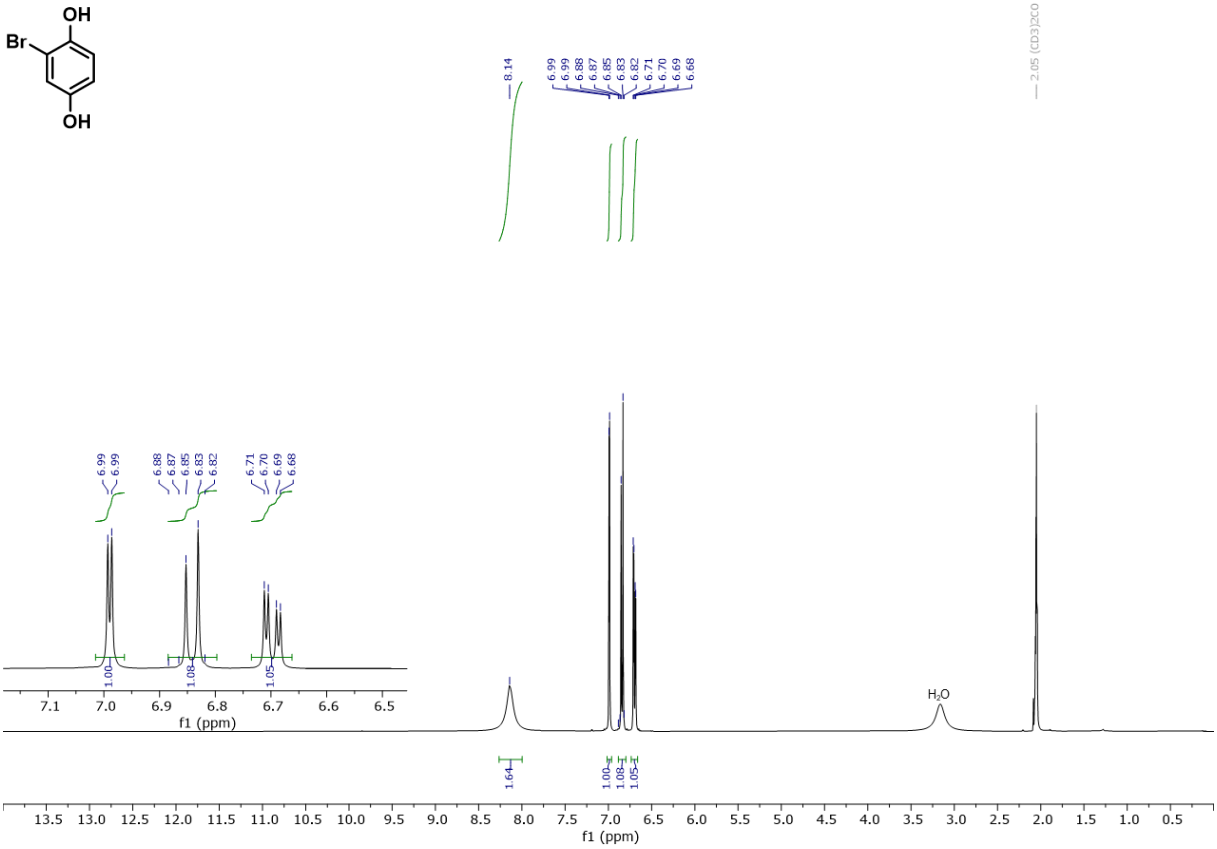


Figure S19: ^{1}H NMR spectra of 2-bromohydroquinone (**2e**) at 298 K in acetone-d_6.

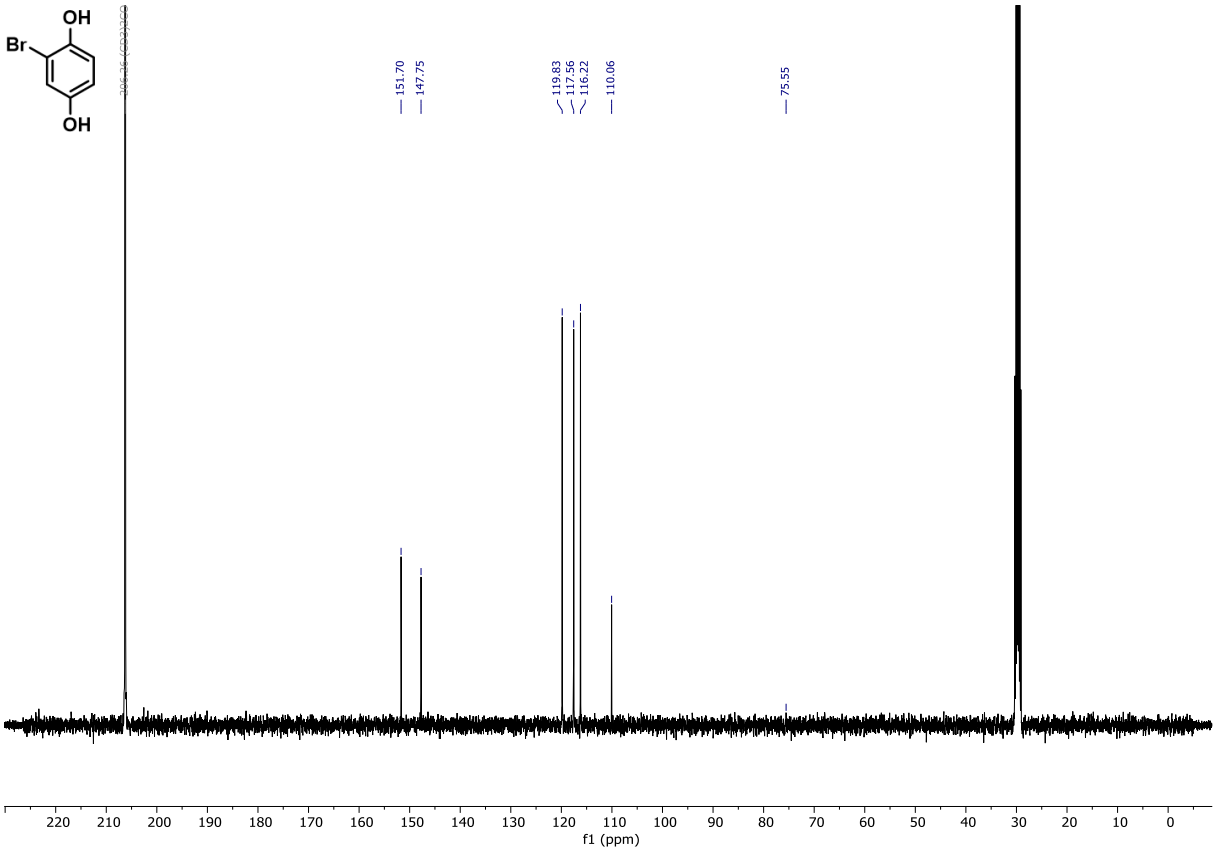


Figure S20*:* ^{13}C NMR spectra of 2-bromohydroquinone (**2e**) at 298 K in acetone-d_6.

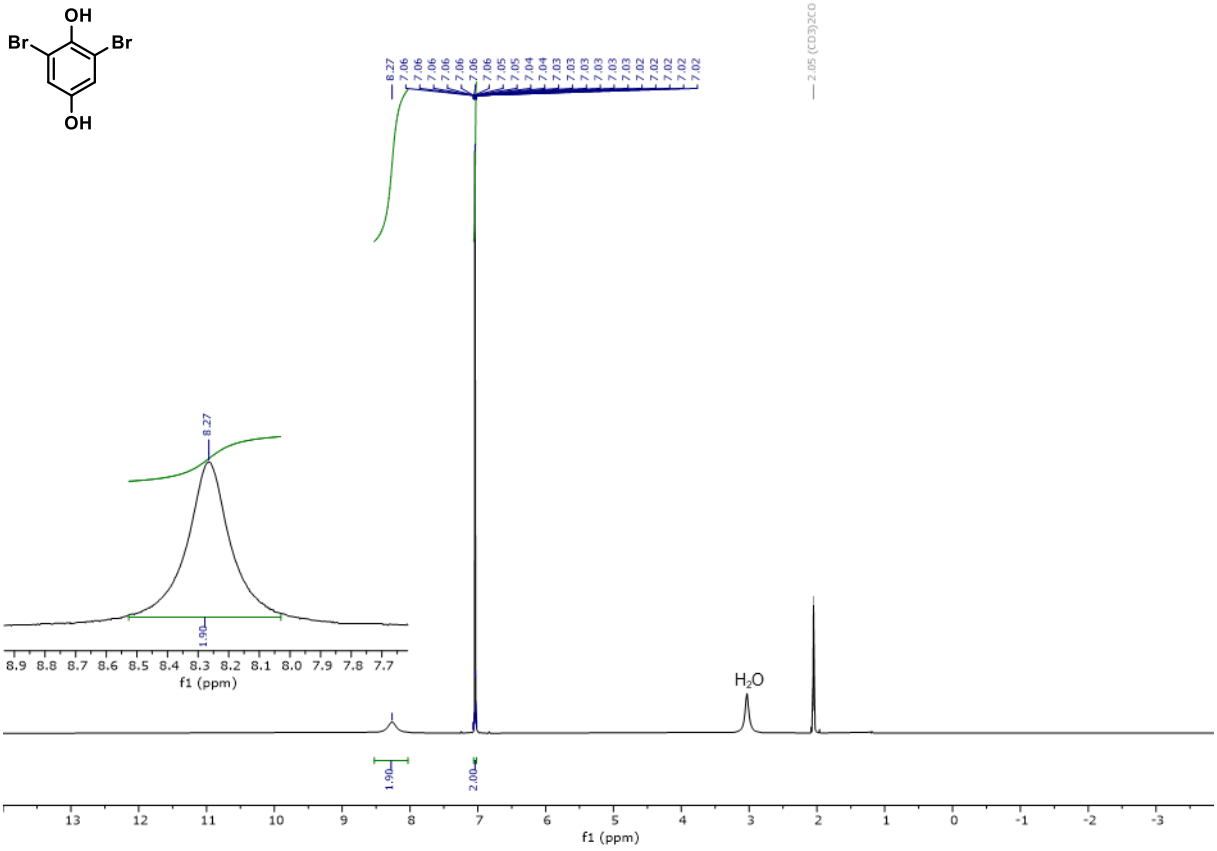


Figure S21: ^{1}H NMR spectra of 2,6-dibromohydroquinone (**2f**) at 298 K in acetone-d_6.

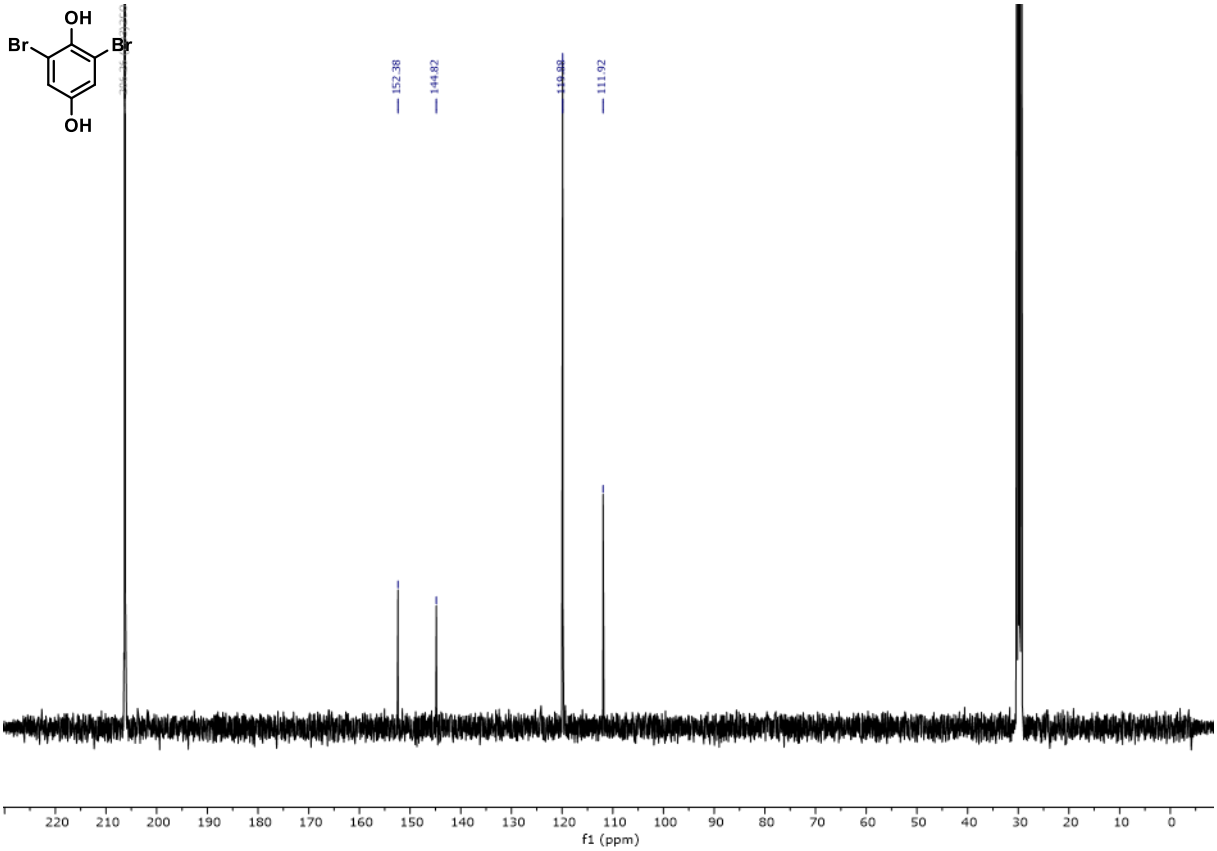


Figure S22: ^{13}C NMR spectra of 2,6-dibromohydroquinone (**2f**) at 298 K in acetone-d_6.

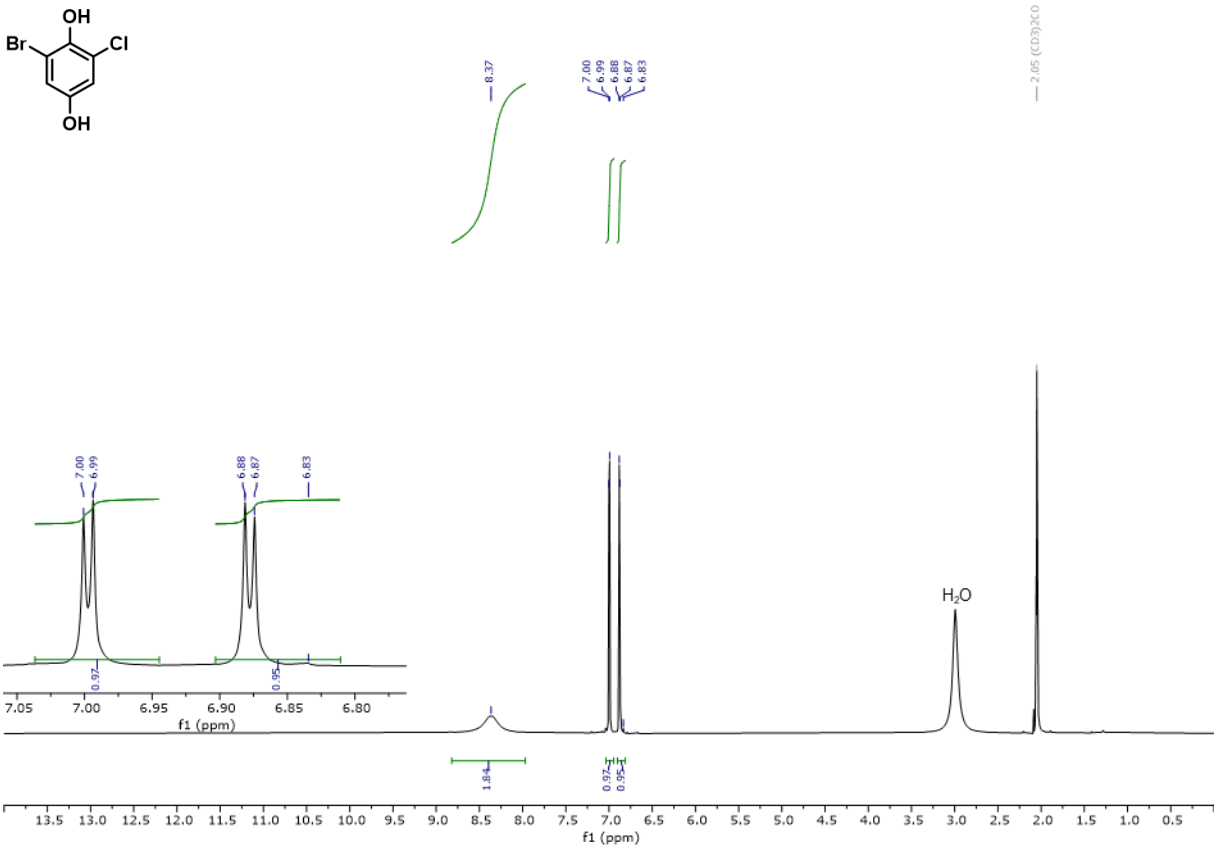


Figure S23: ^{1}H NMR spectra of 2-bromo-6-chlorohydroquinone (**2g**) at 298 K in acetone-d_6.

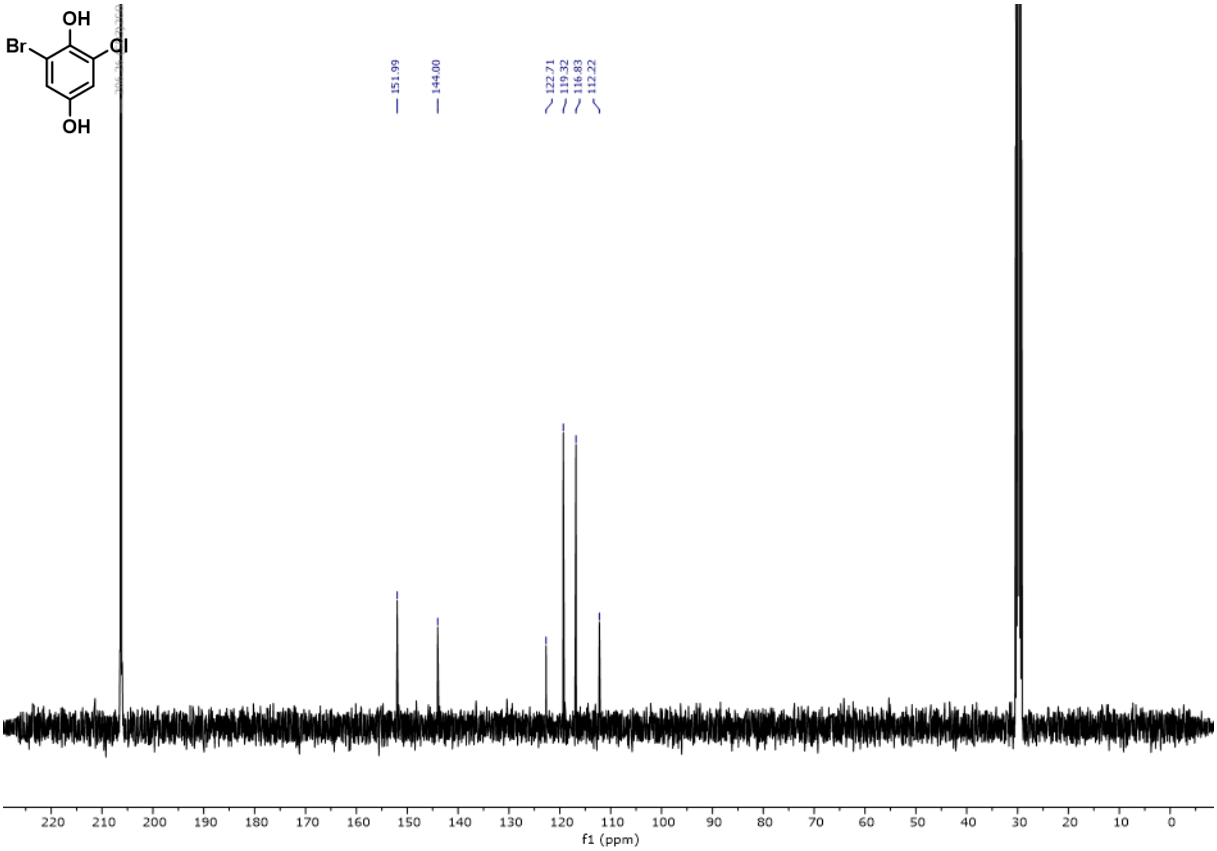


Figure S24: ^{13}C NMR spectra of 2-bromo-6-chlorohydroquinone (**2g**) at 298 K in acetone-d_6.

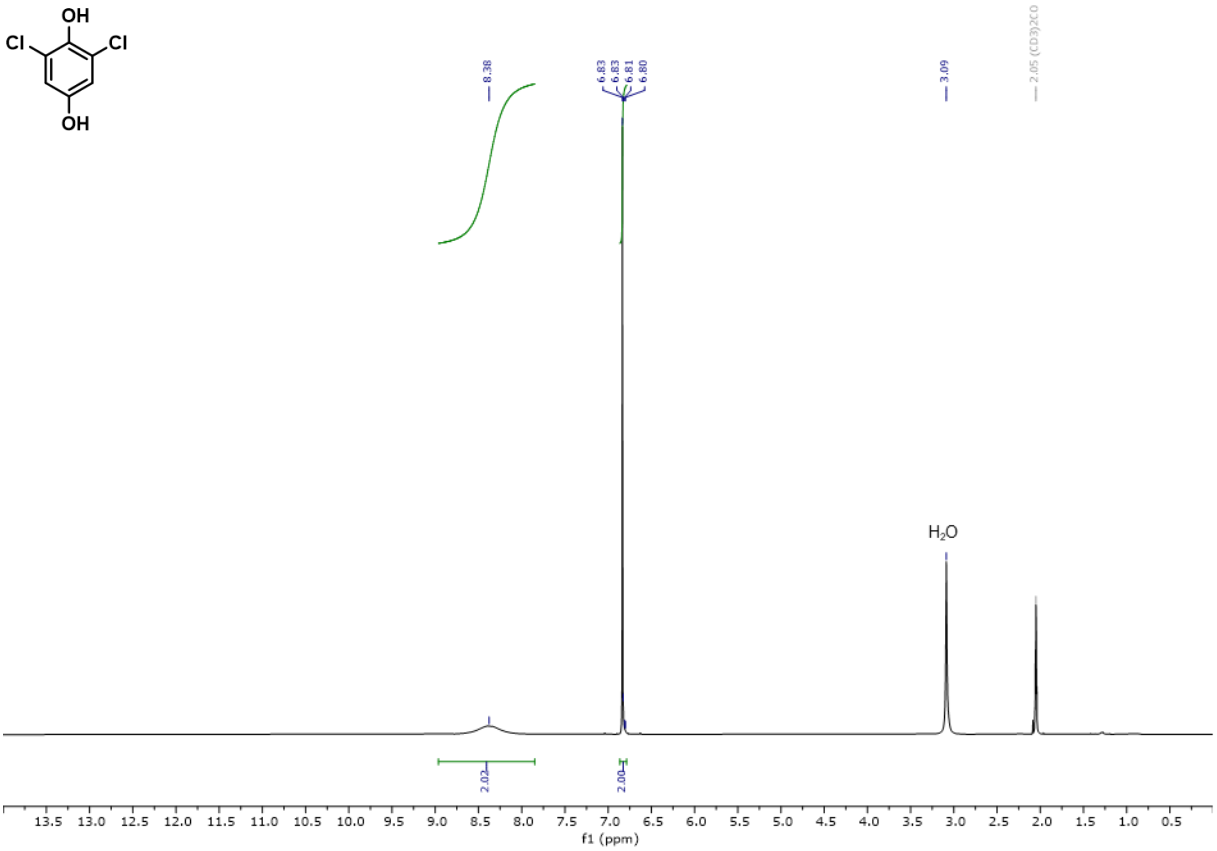


Figure S25: ^{1}H NMR spectra of 2,6-dichlorohydroquinone (**2h**) at 298 K in acetone-d_6.

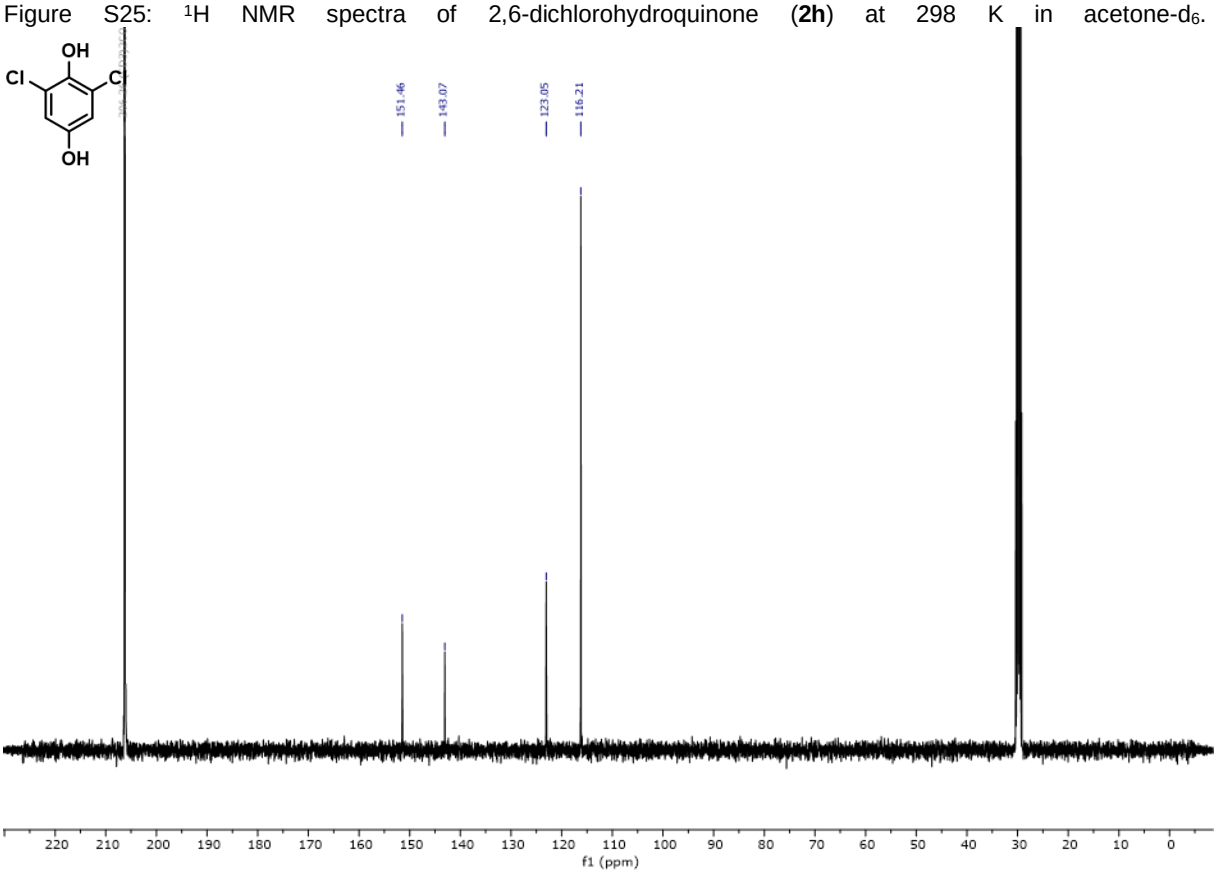


Figure S26: ^{13}C NMR spectra of 2,6-dichlorohydroquinone (**2h**) at 298 K in acetone-d_6.

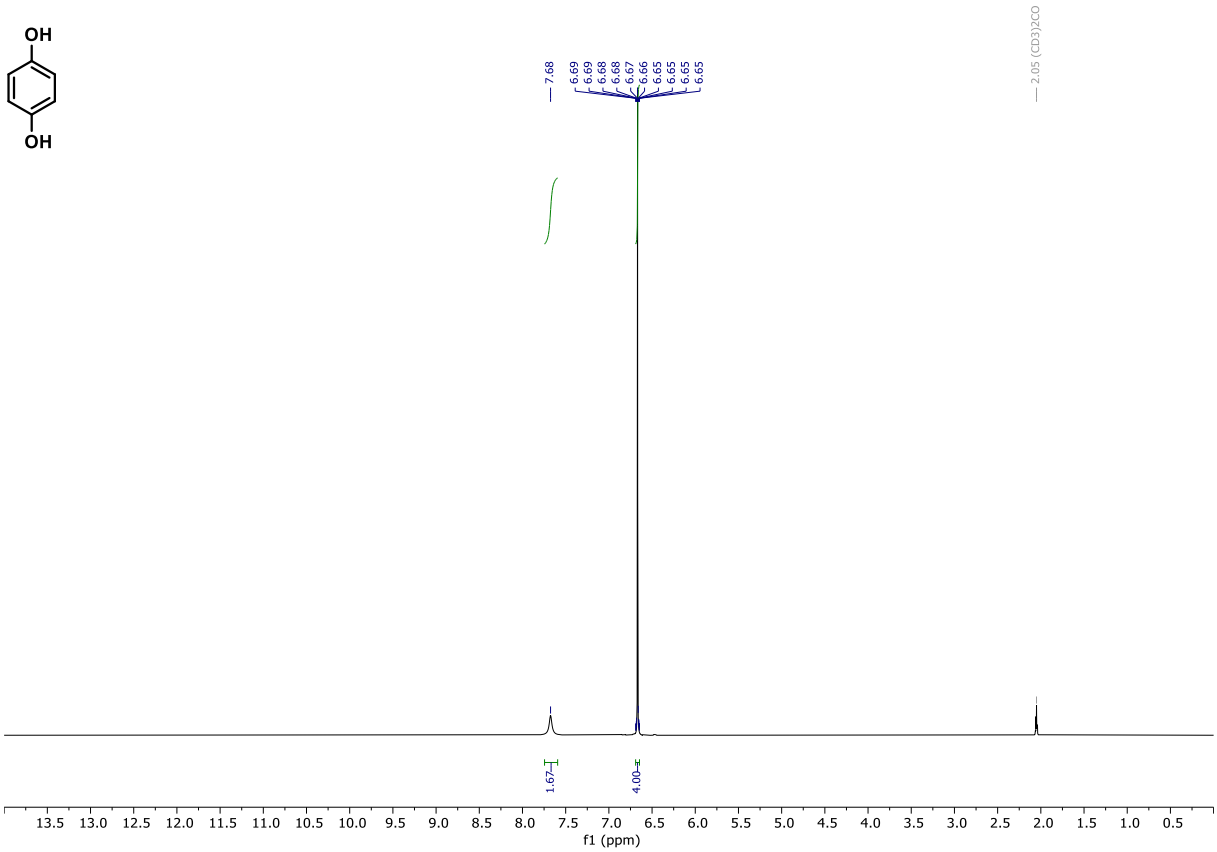


Figure S27: ^{1}H NMR spectra of hydroquinone (**2i**) at 298 K in acetone-d_6

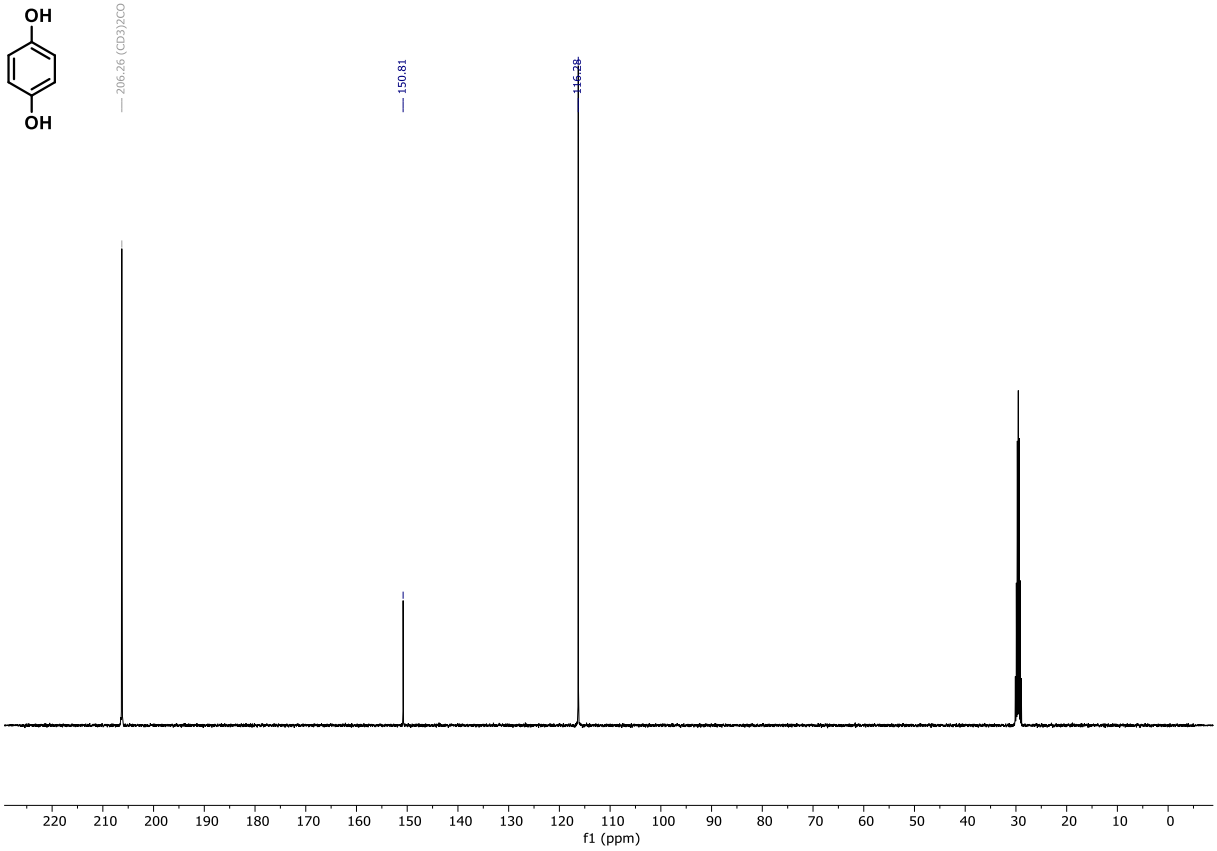


Figure S28: ^{13}C NMR spectra of hydroquinone (2i) at 298 K in acetone-d_6

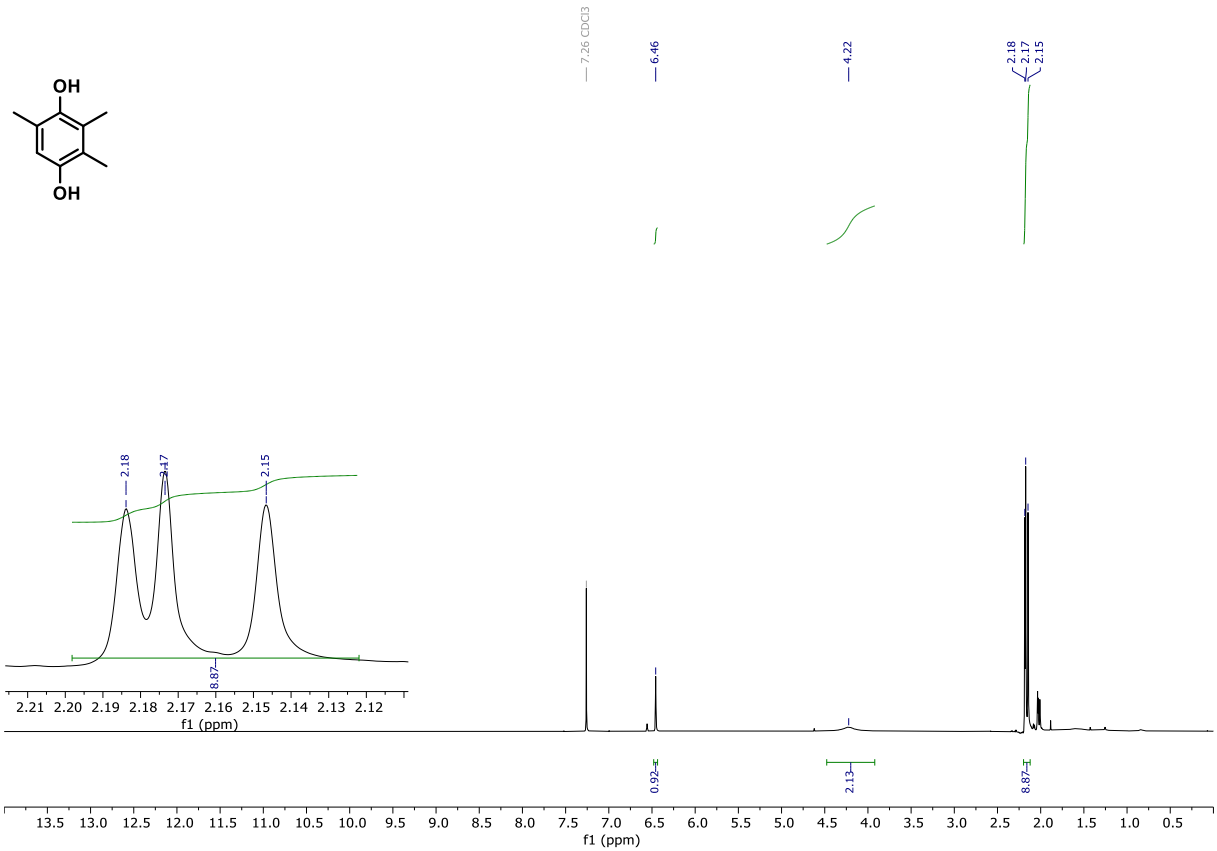


Figure S29: ^{1}H NMR spectra of 2,3,6-trimethylhydroquinone (**2j**) at 298 K in $CDCl_3$.

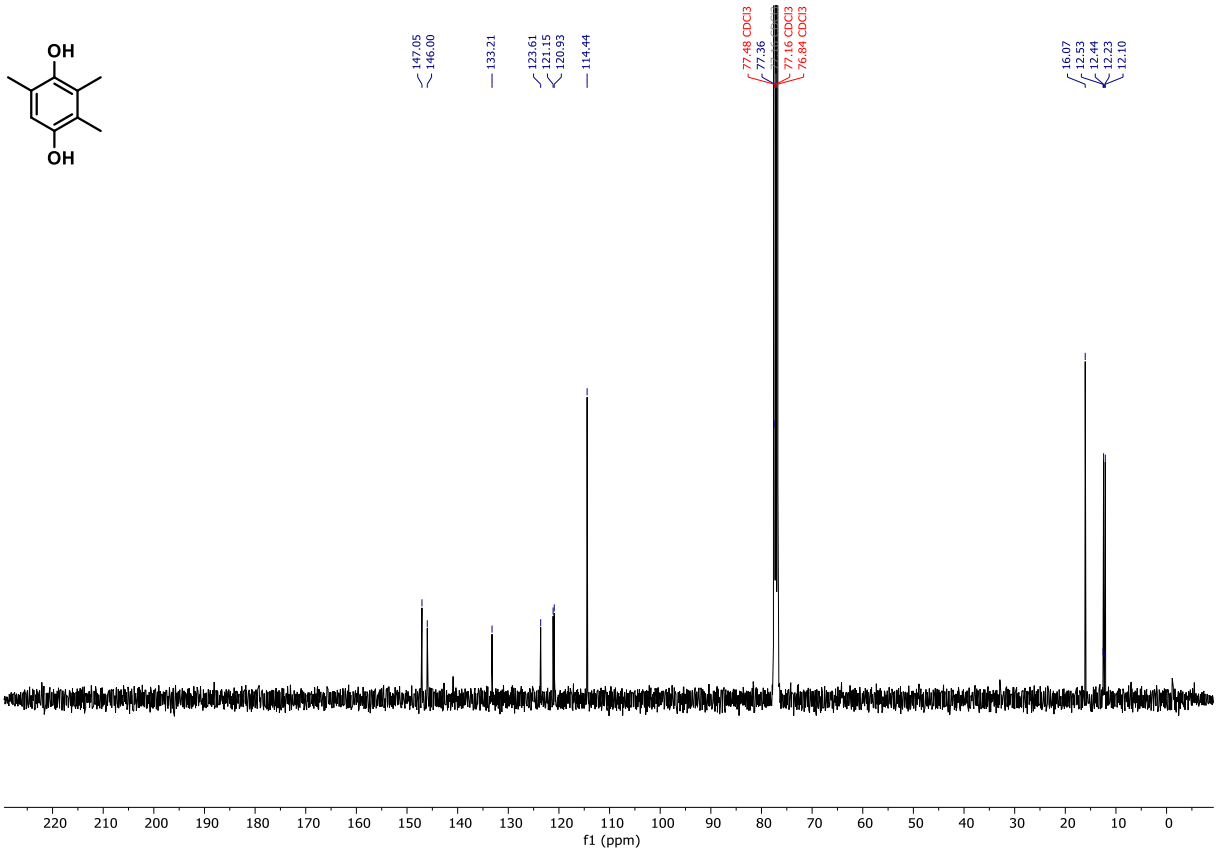


Figure S30*:* ^{13}C NMR spectra of 2,3,6-trimethylhydroquinone (**2j**) at 298 K in $CDCl_3$.

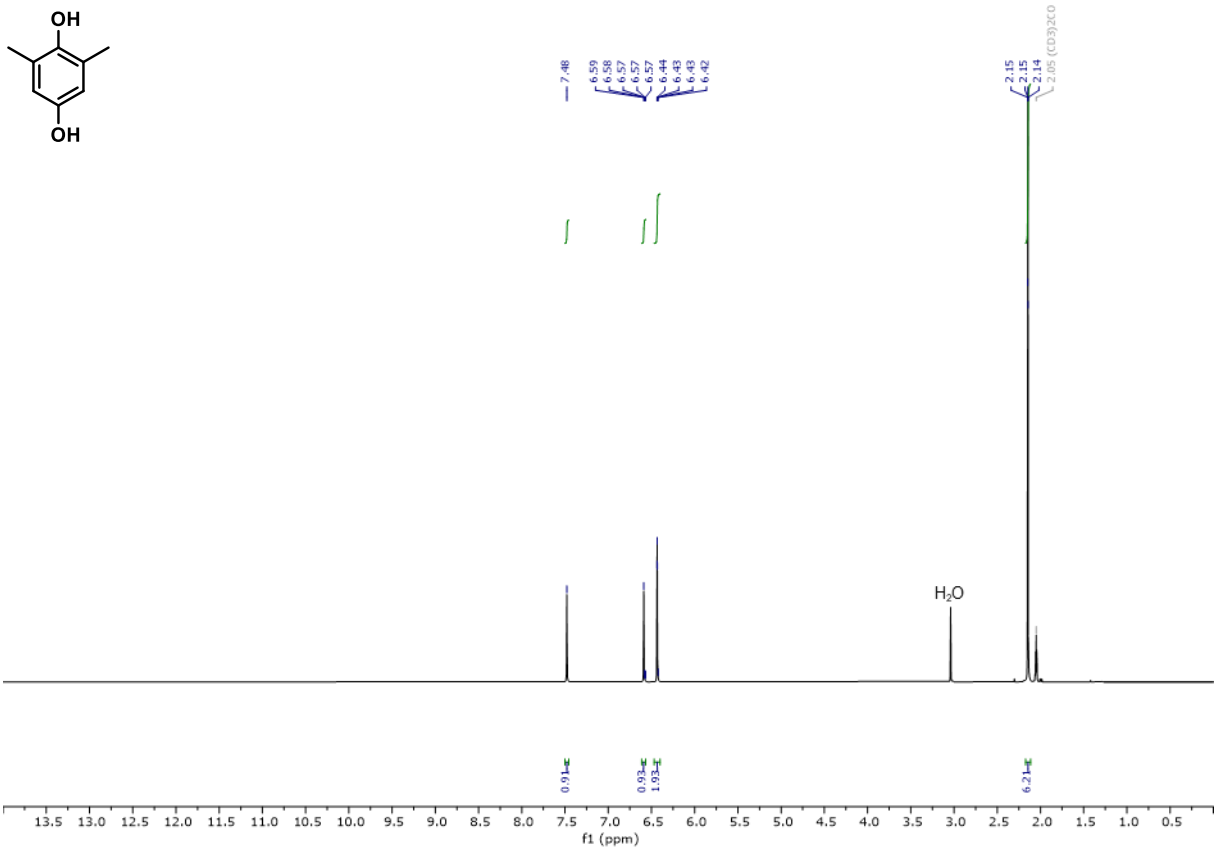


Figure S31: ^{1}H NMR spectra of 2,6-dimethylyhydroquinone (**2k**) at 298 K in acetone-d_6.

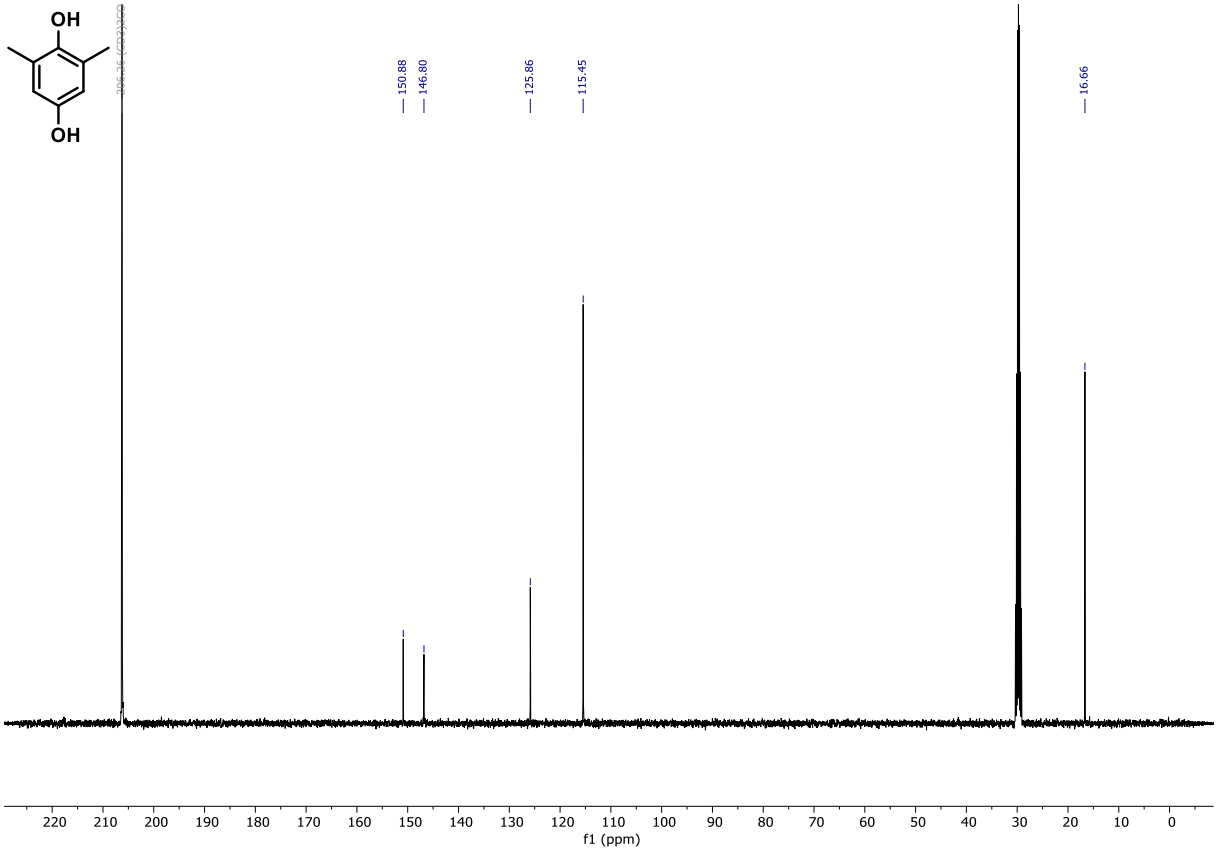


Figure S32: ^{13}C NMR spectra of 2,6-dimethylyhydroquinone (**2k**) at 298 K in acetone-d_6.

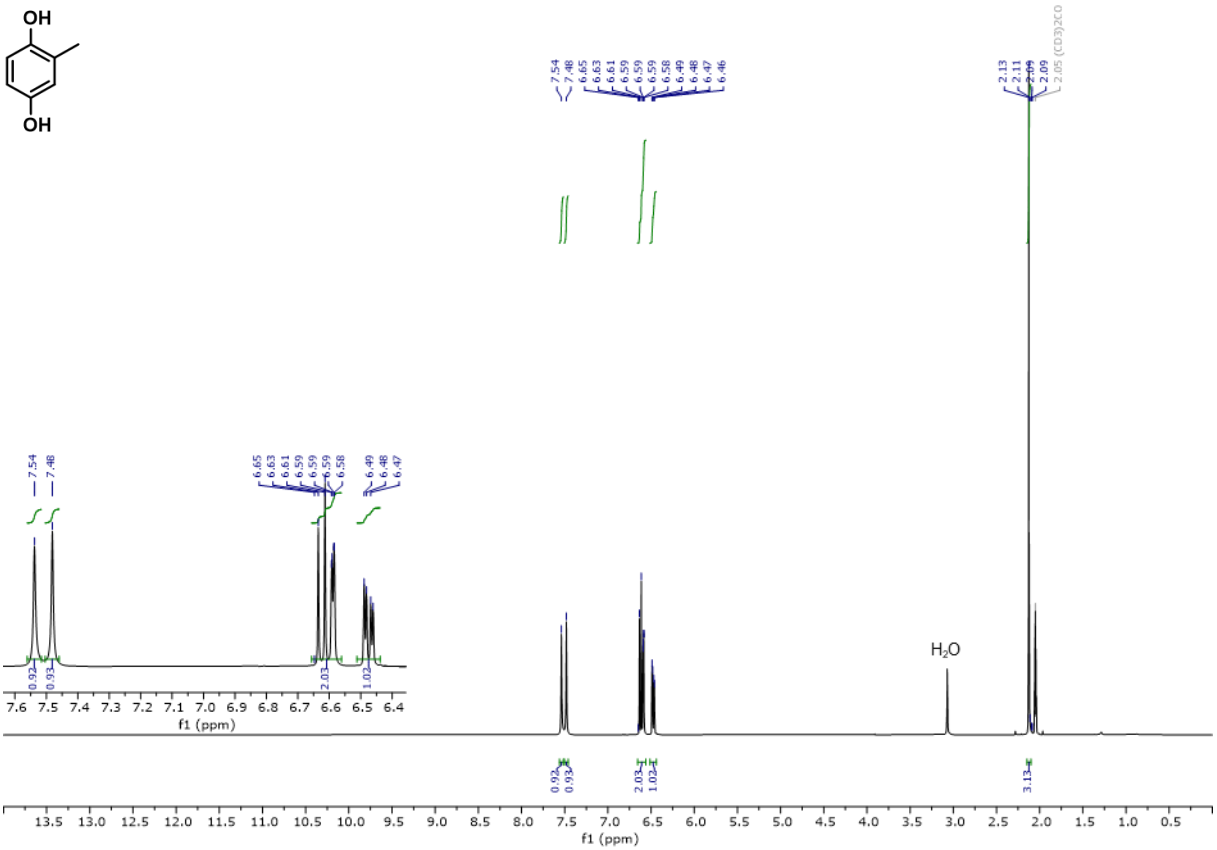


Figure S33: ^{1}H NMR spectra of 2,6-methylyhydroquinone (**2l**) at 298 K in acetone-d_6.

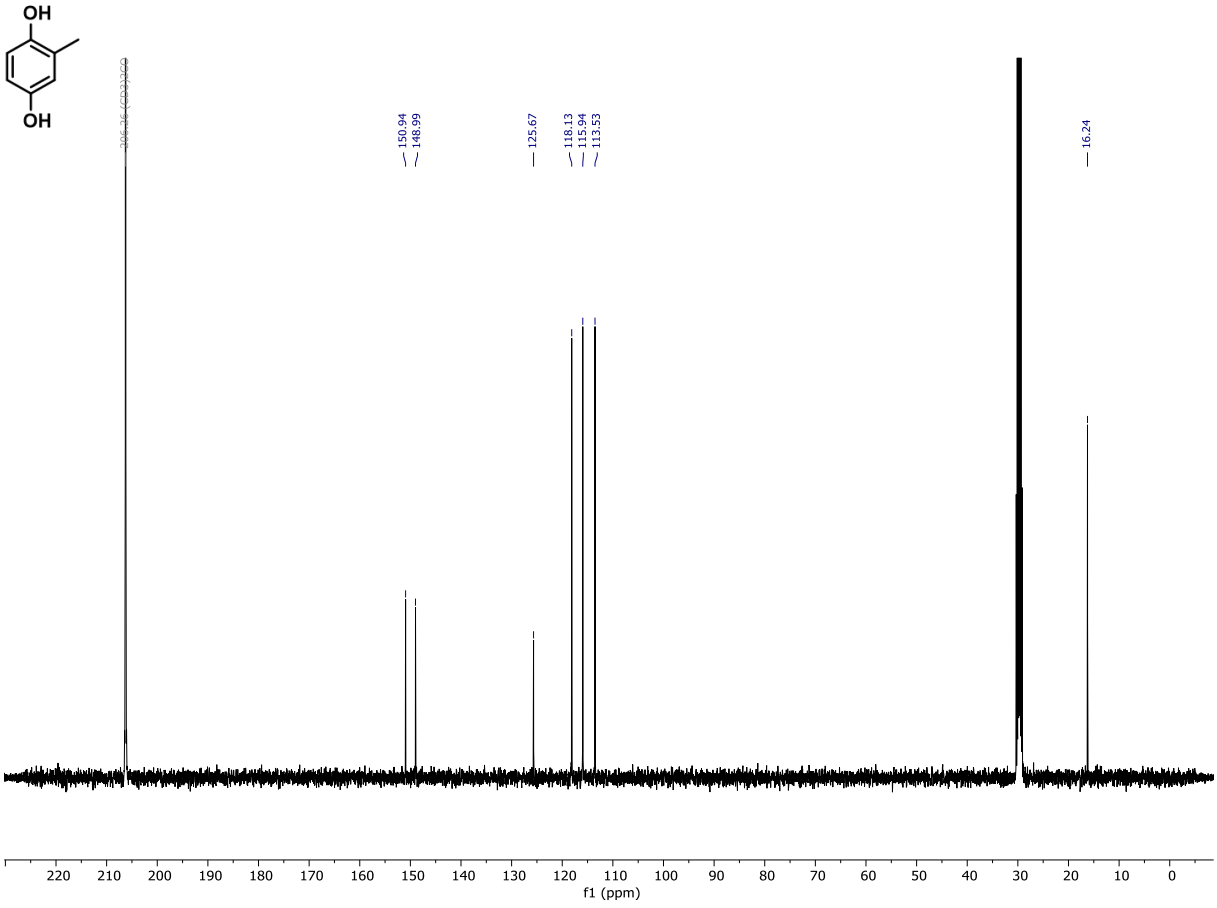


Figure S34: ^{13}C NMR spectra of 2,6-methylyhydroquinone (**2l**) at 298 K in acetone-d_6.

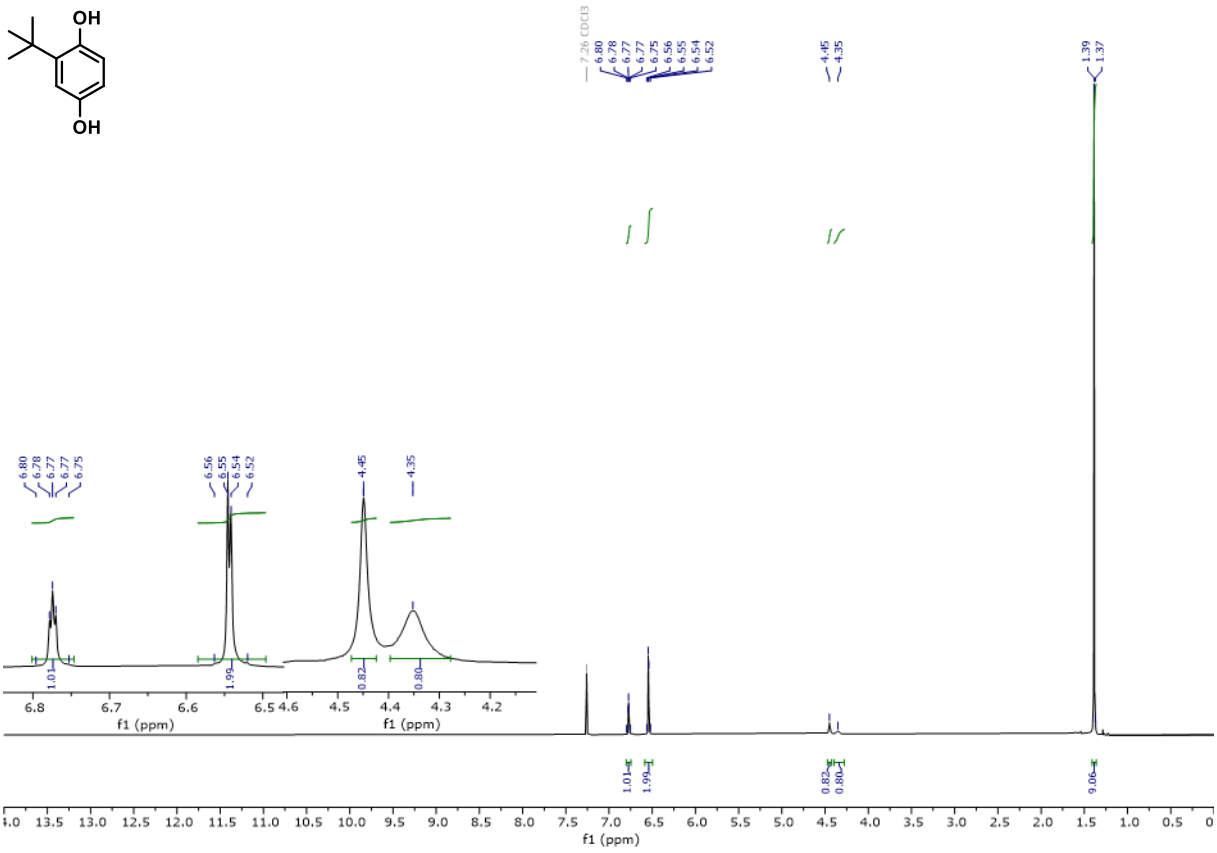


Figure S35: ^{1}H NMR spectra of 2-*tert*-butylhydroquinone (**2m**) at 298 K in $CDCl_3$.

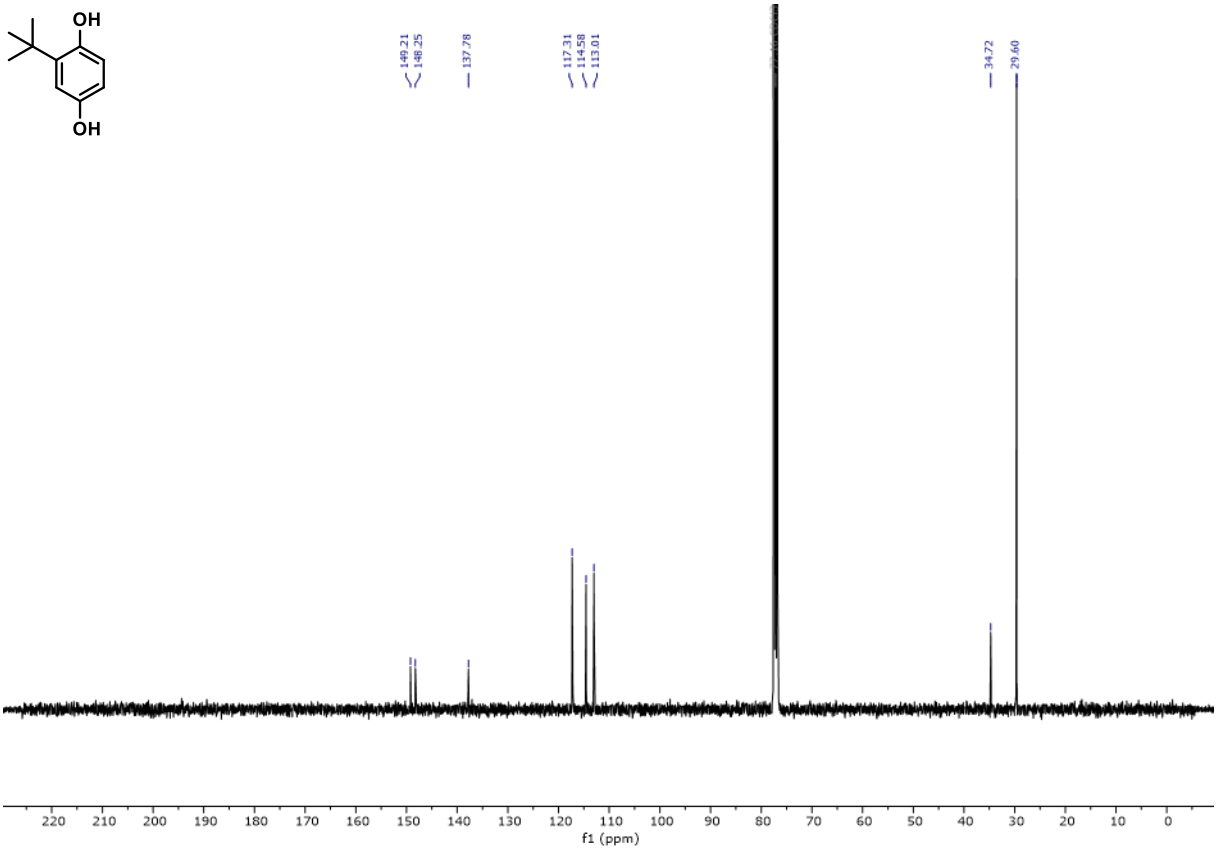


Figure S36: ^{13}C NMR spectra of 2-*tert*-butylhydroquinone (**2m**) at 298 K in $CDCl_3$.

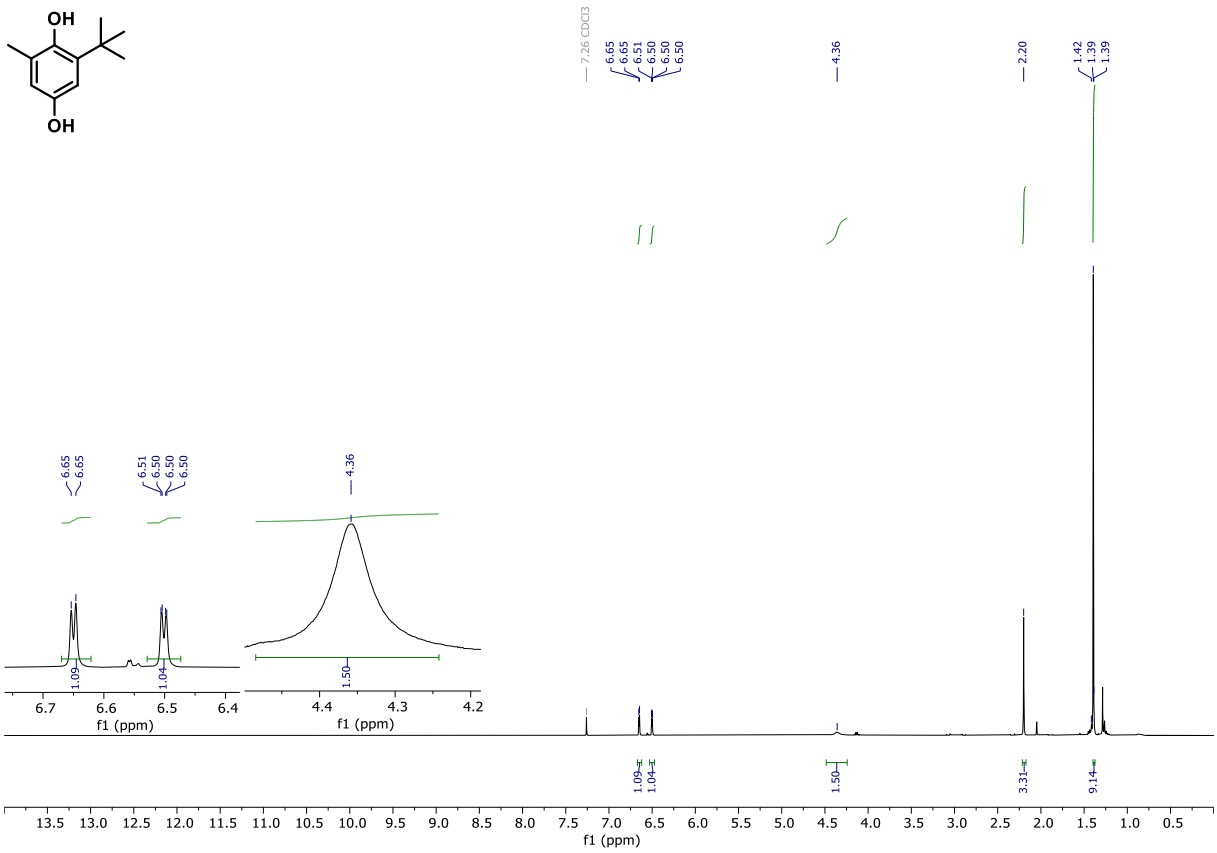


Figure S37: ^{1}H NMR spectra of 2-*tert*-butyl-6-methylyhydroquinone (**2n**) at 298 K in $CDCl_3$.

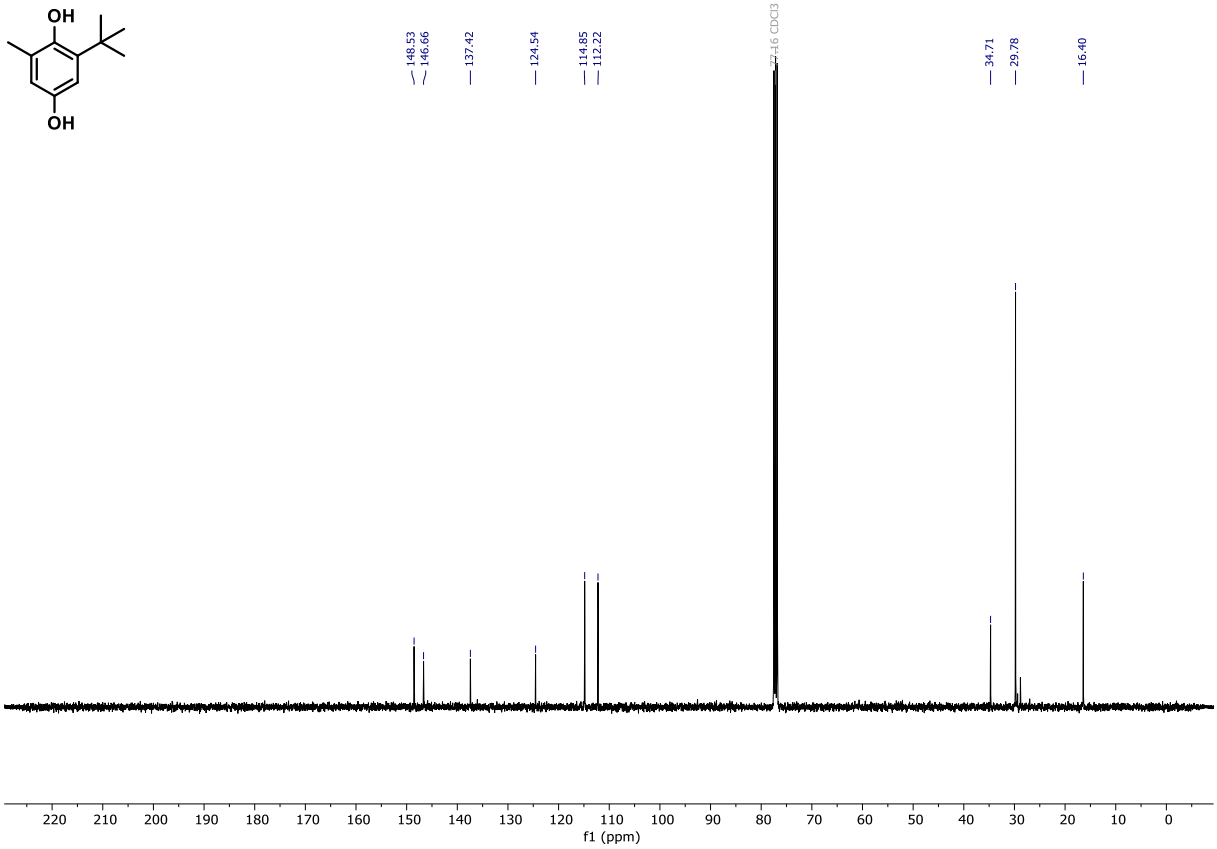


Figure S38: ^{13}C NMR spectra of 2-*tert*-butyl-6-methylyhydroquinone (**2n**) at 298 K in $CDCl_3$.

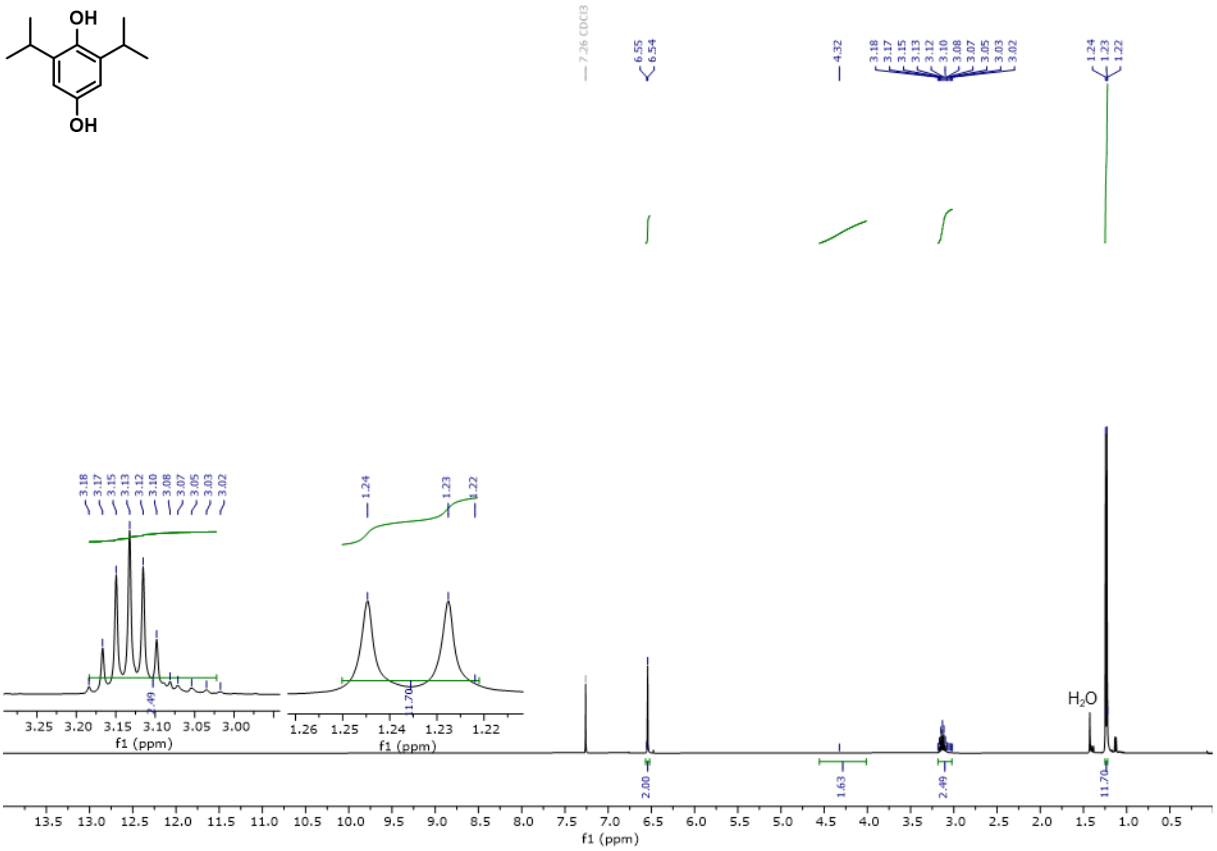


Figure S39: ^{1}H NMR spectra of 2,6-diisopropyllyhydroquinone (**2o**) at 298 K in $CDCl_3$.

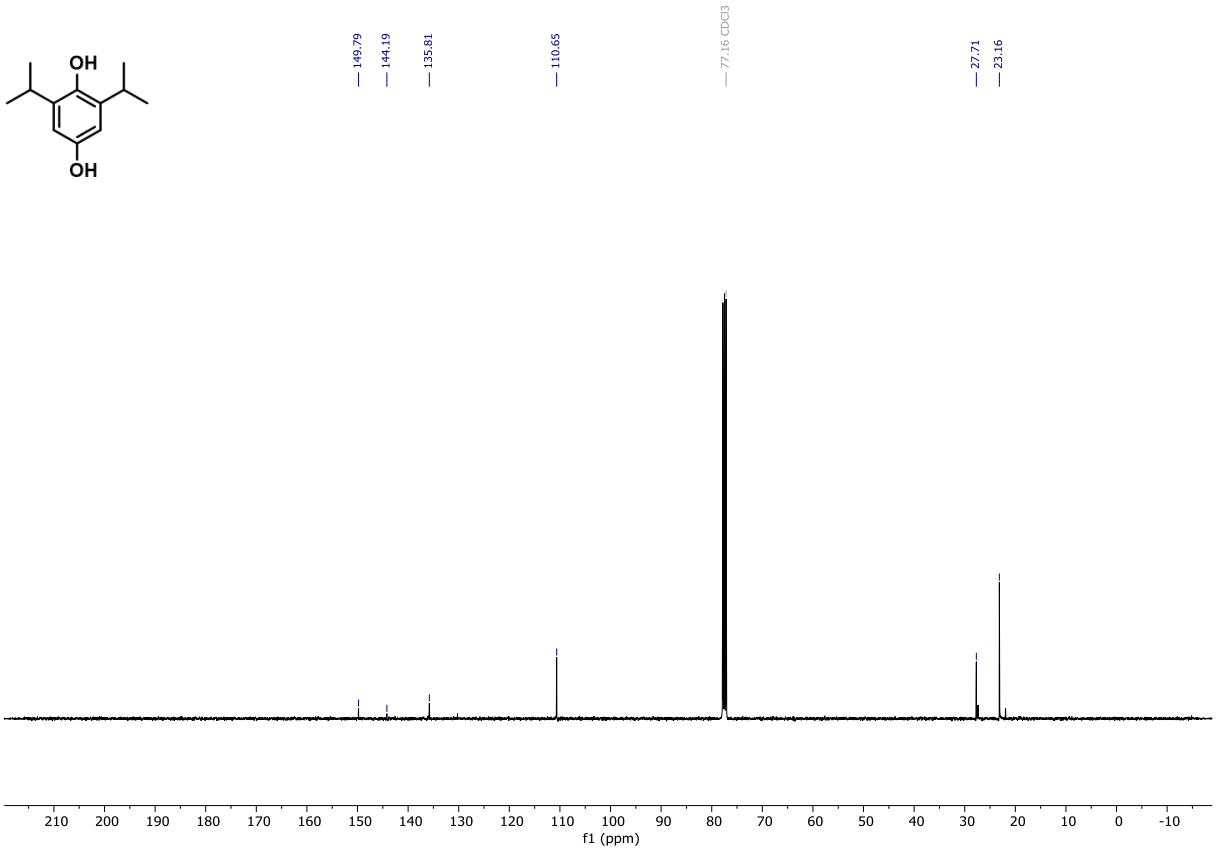


Figure S40: ^{1}H NMR spectra of 2,6-diisopropyllyhydroquinone (**2o**) at 298 K in $CDCl_3$.

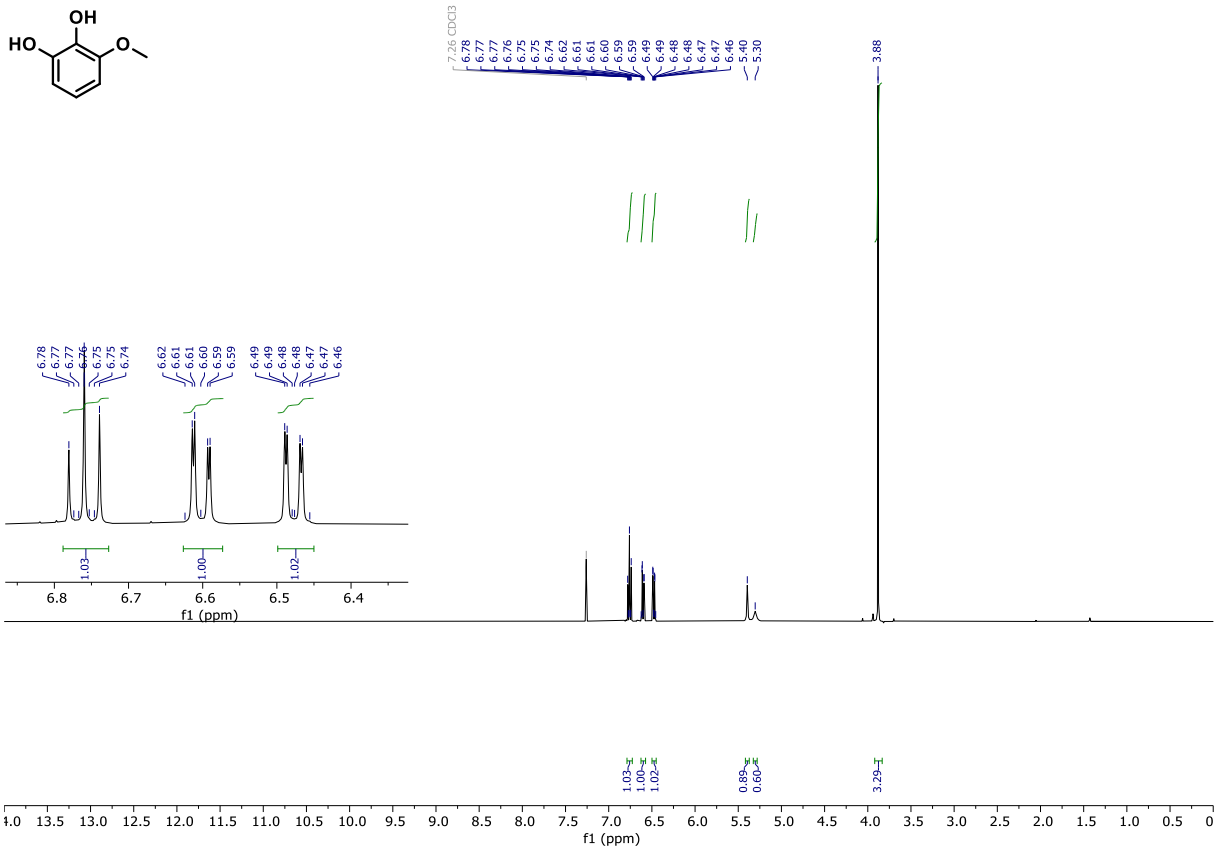


Figure S41: ^{1}H NMR spectra of 3-methoxycatechol (**2p**) at 298 K in $CDCl_3$

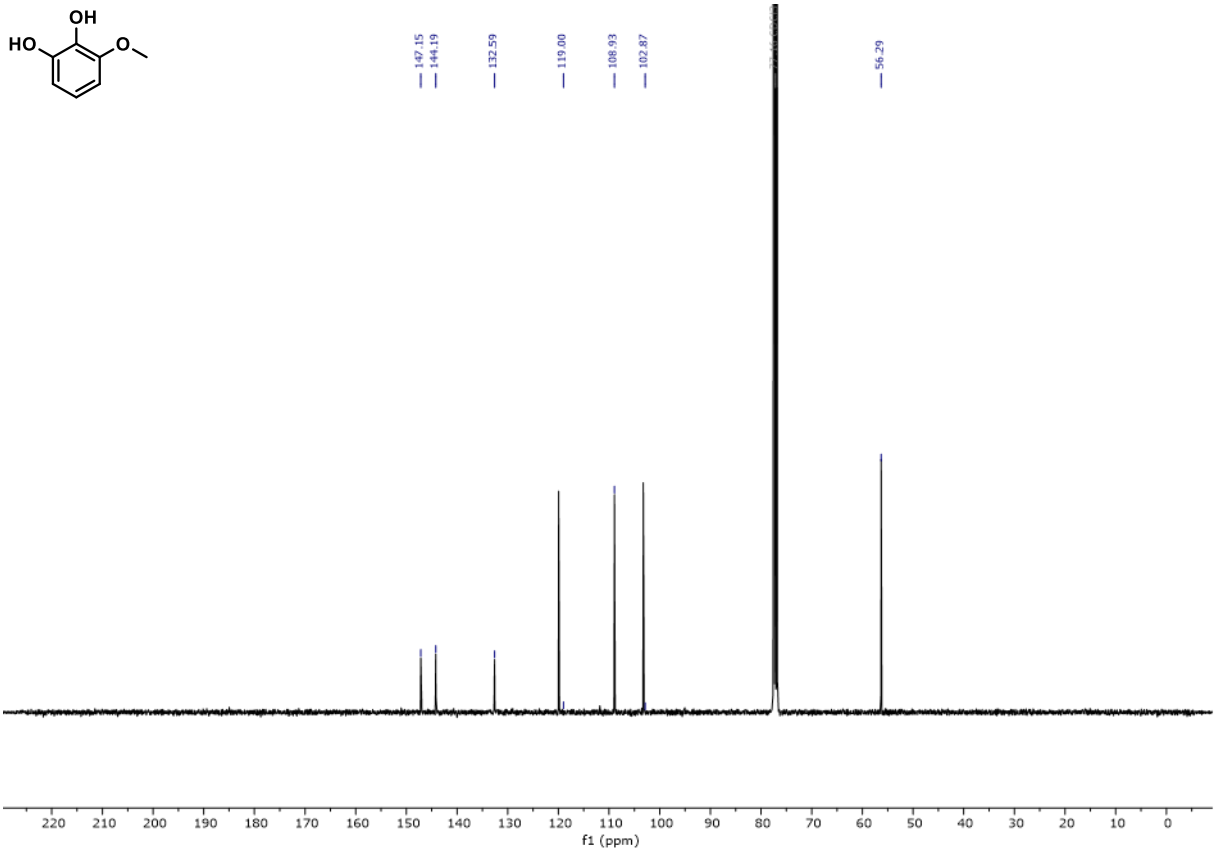


Figure S42: ^{13}C NMR spectra of 3-methoxycatechol (**2p**) at 298 K in $CDCl_3$

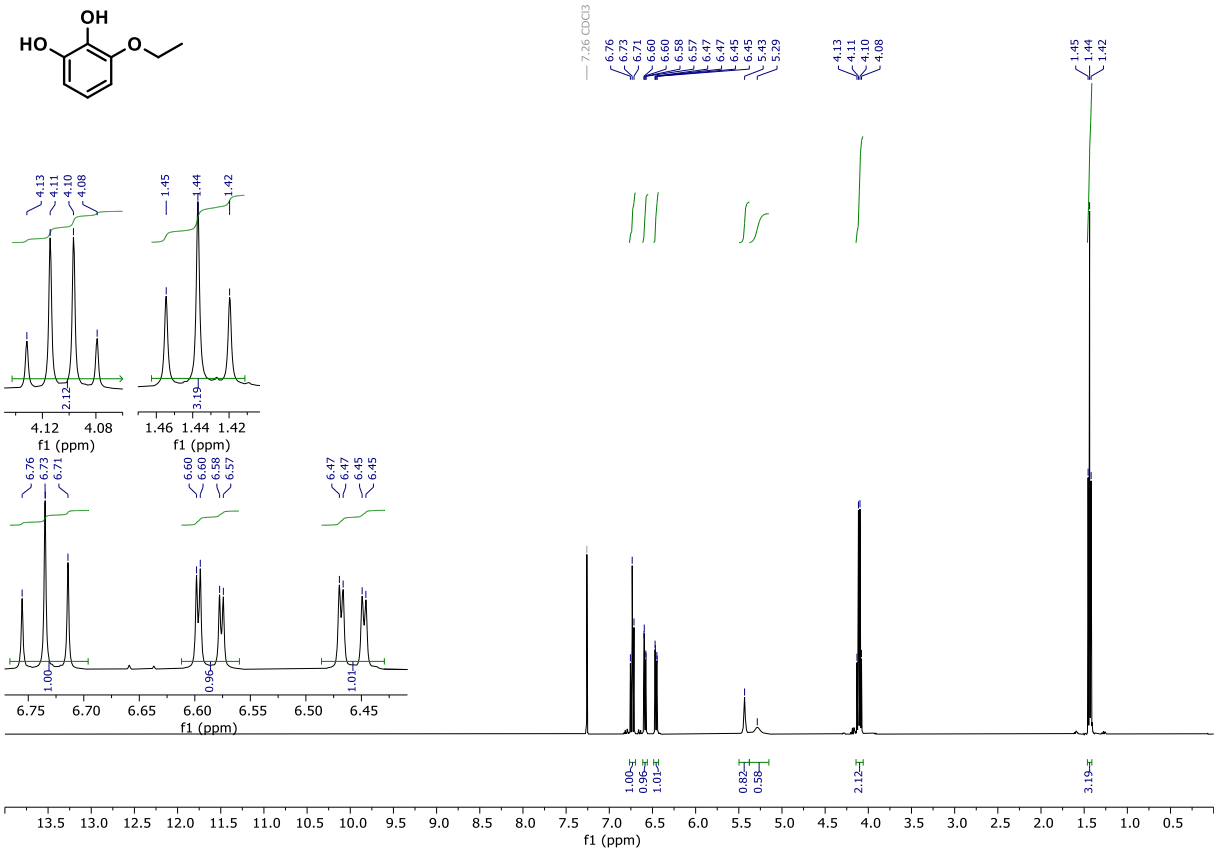


Figure S43: ^{1}H NMR spectra of 3-ethoxycatechol (**2q**) at 298 K in $CDCl_3$

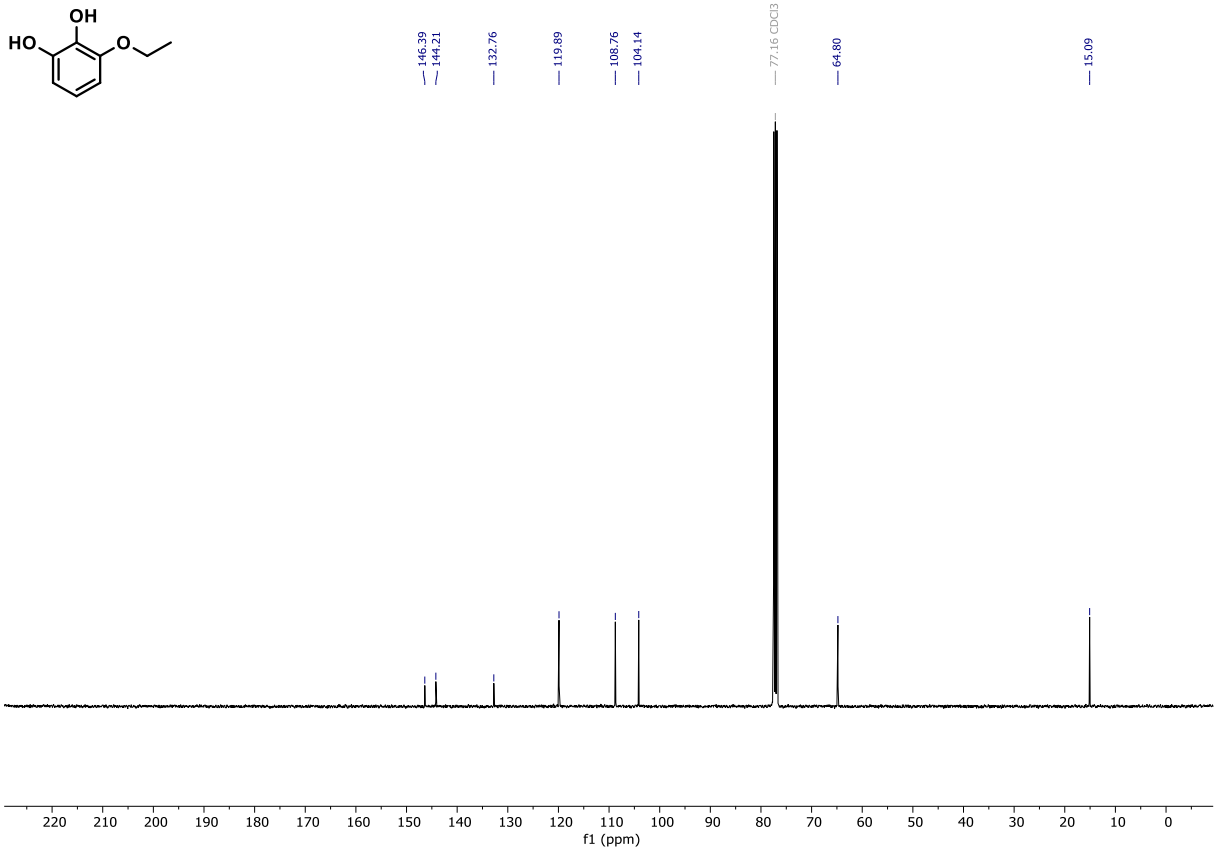


Figure S44: ^{13}C NMR spectra of 3-ethoxycatechol (**2q**) at 298 K in $CDCl_3$

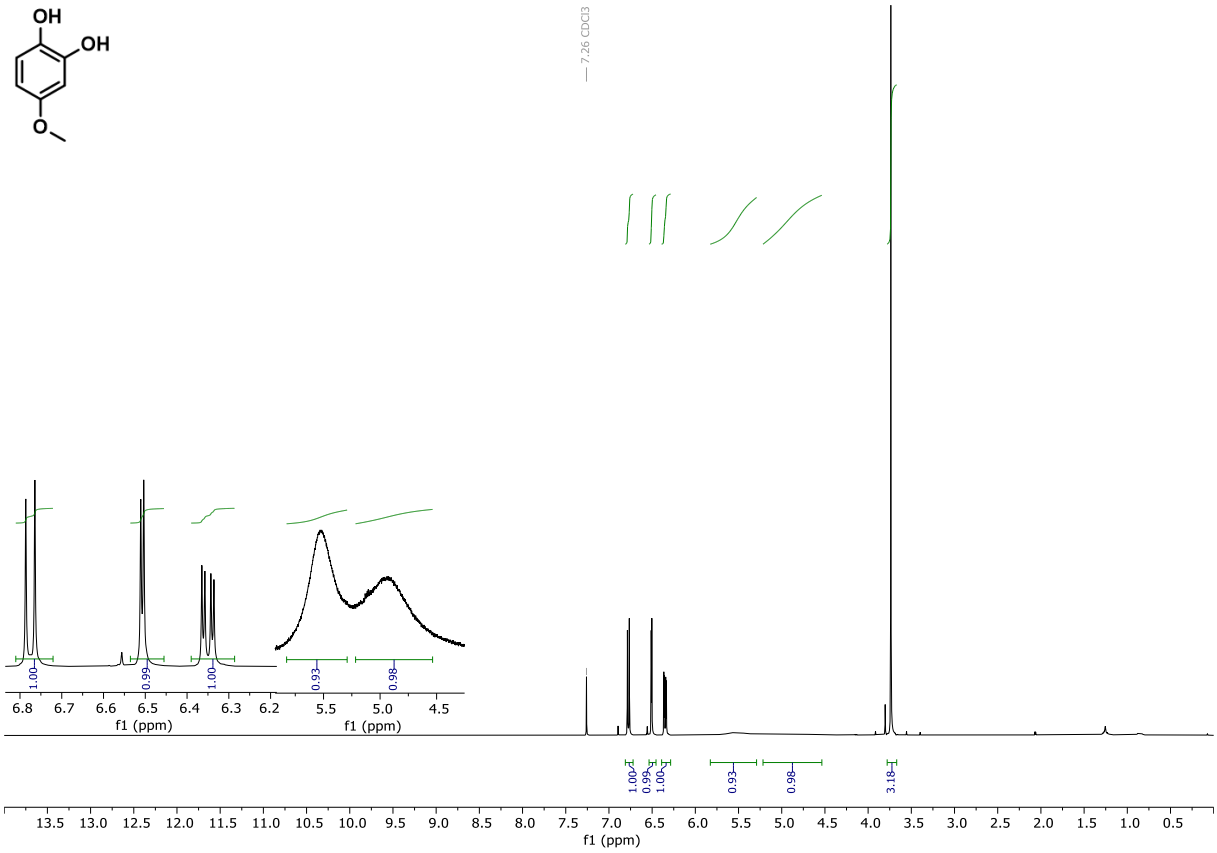


Figure S45: ^{1}H NMR spectra of 4-methoxycatechol (**2r**) at 298 K in $CDCl_3$

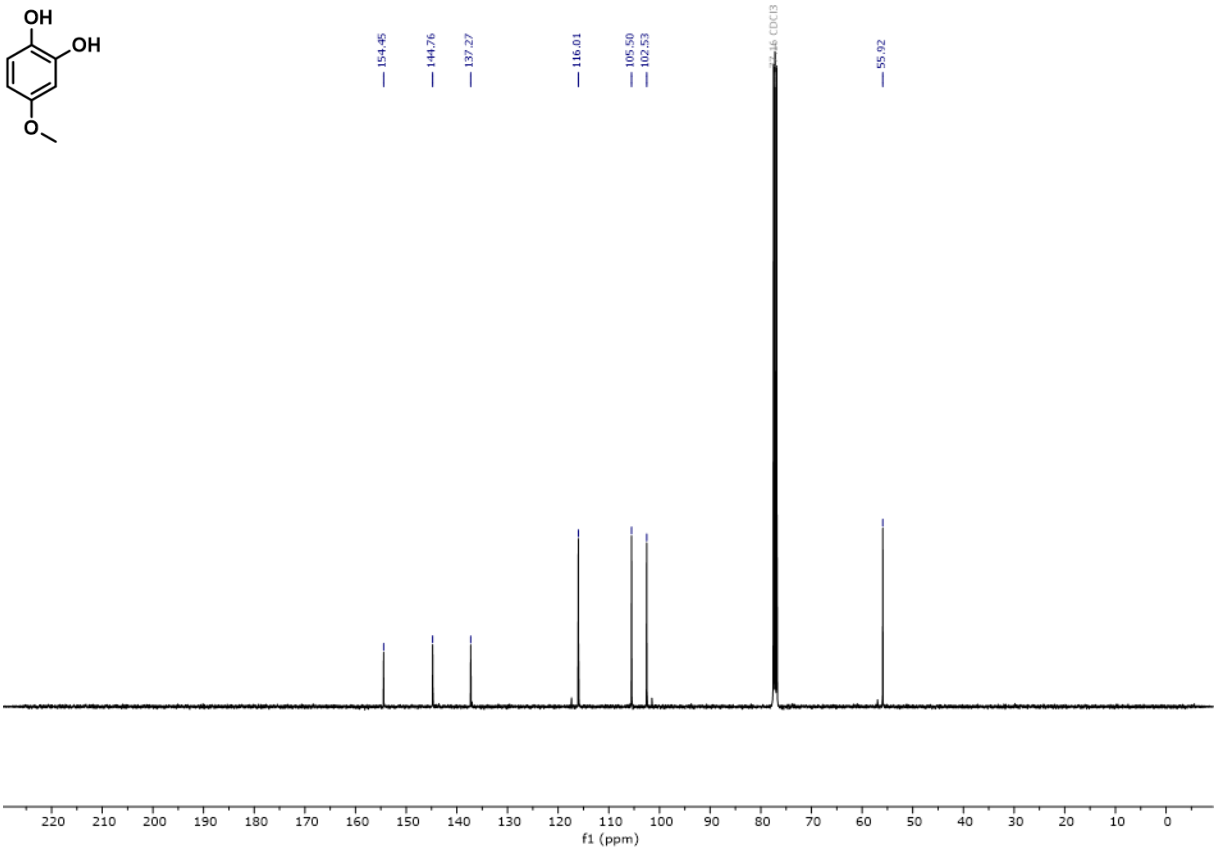


Figure S46: ^{13}C NMR spectra of 4-methoxycatechol (**2r**) at 298 K in $CDCl_3$

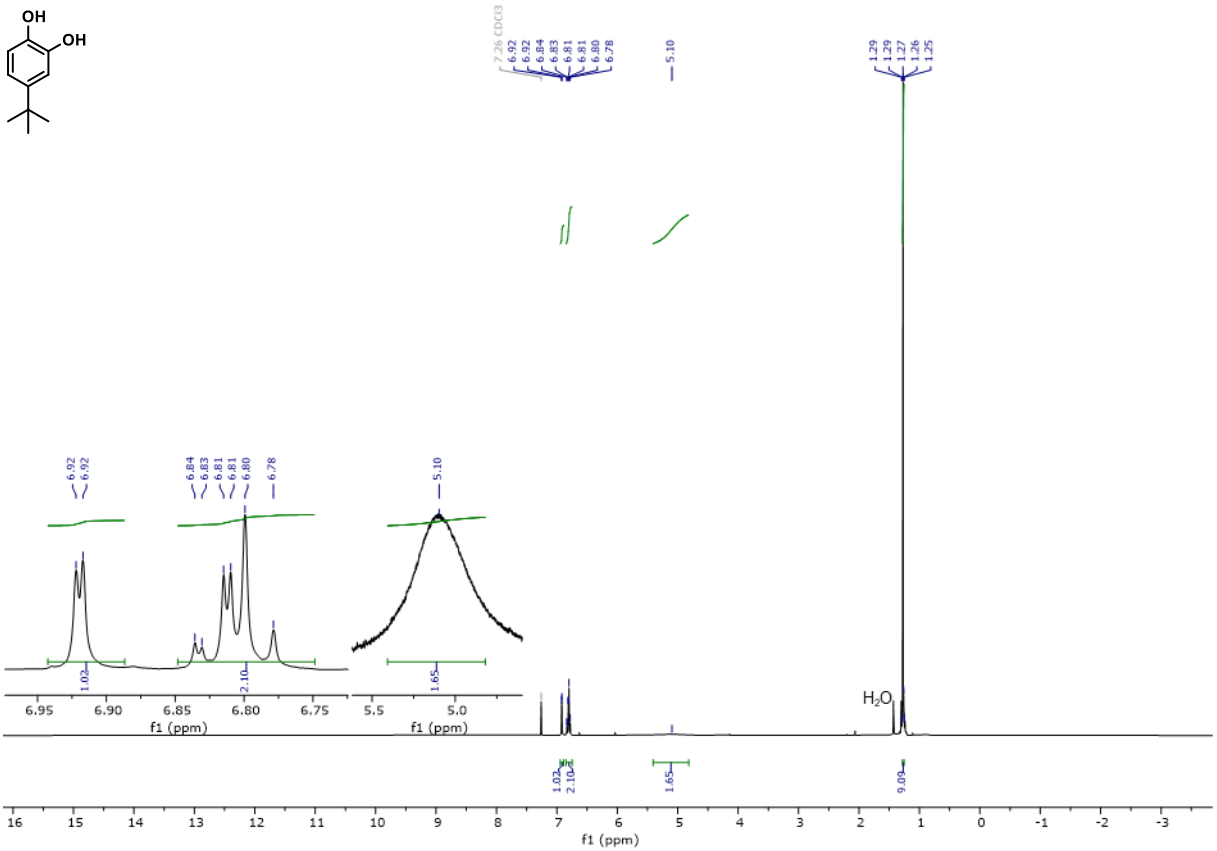


Figure S47: ^{1}H NMR spectra of 4-*tert*-butylcatechol (**2s**) at 298 K in $CDCl_3$.

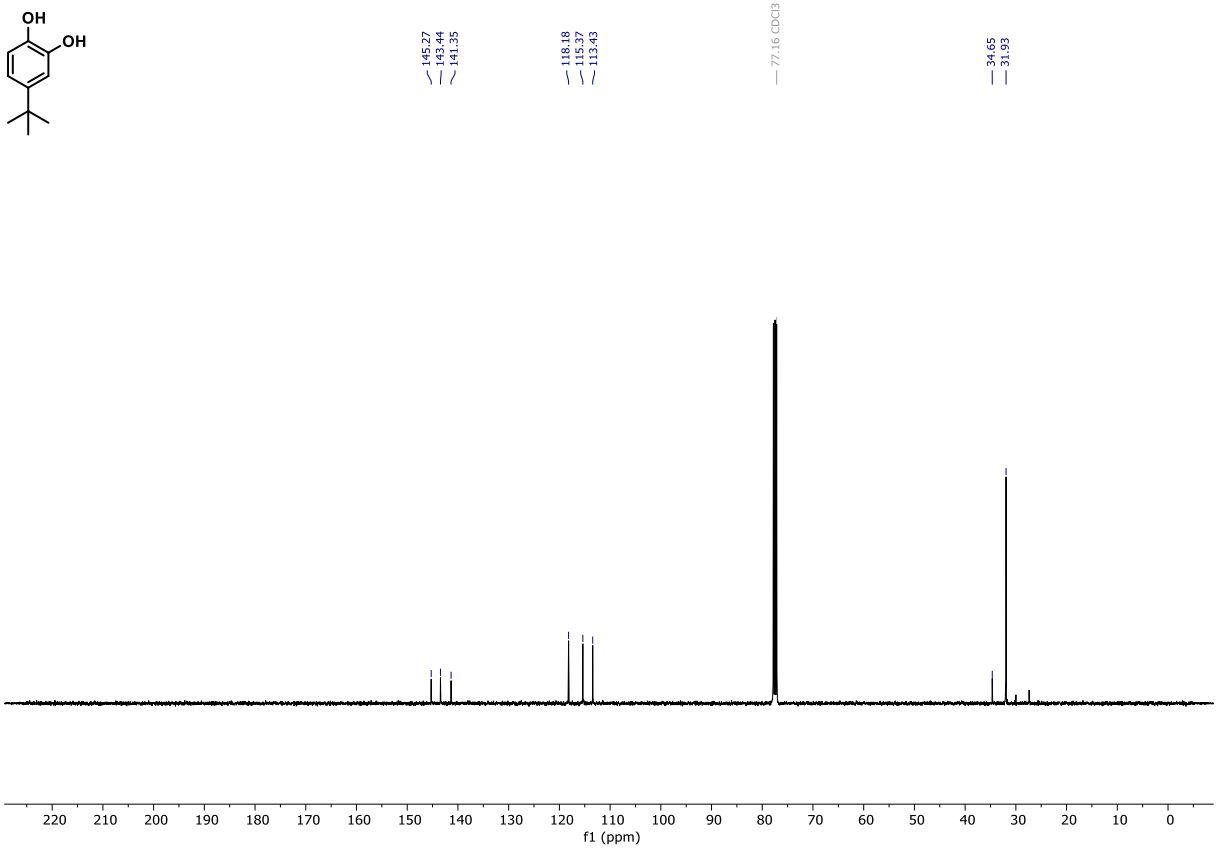


Figure S48: ^{13}C NMR spectra of 4-*tert*-butylcatechol (**2s**) at 298 K in $CDCl_3$.

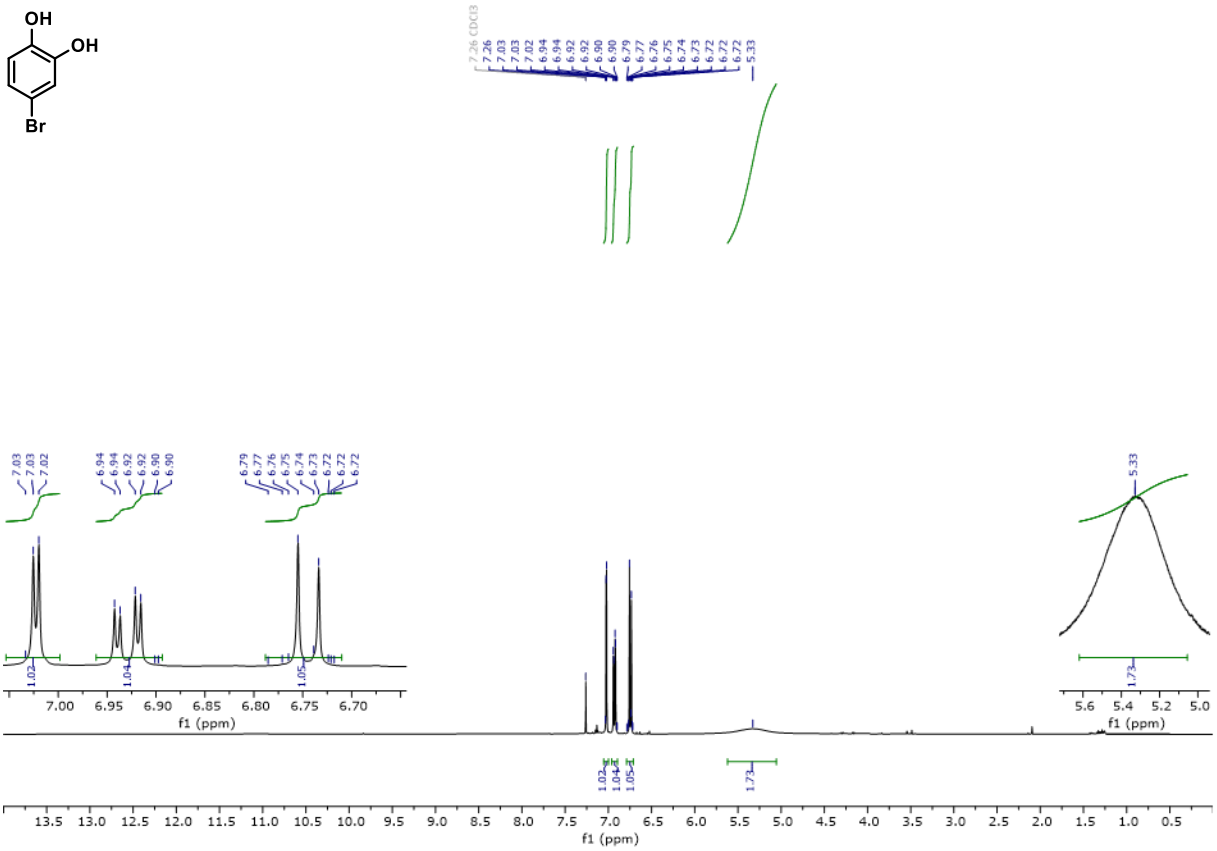


Figure S49: ^{1}H NMR spectra of 4-bromocatechol (**2t**) at 298 K in $CDCl_3$.

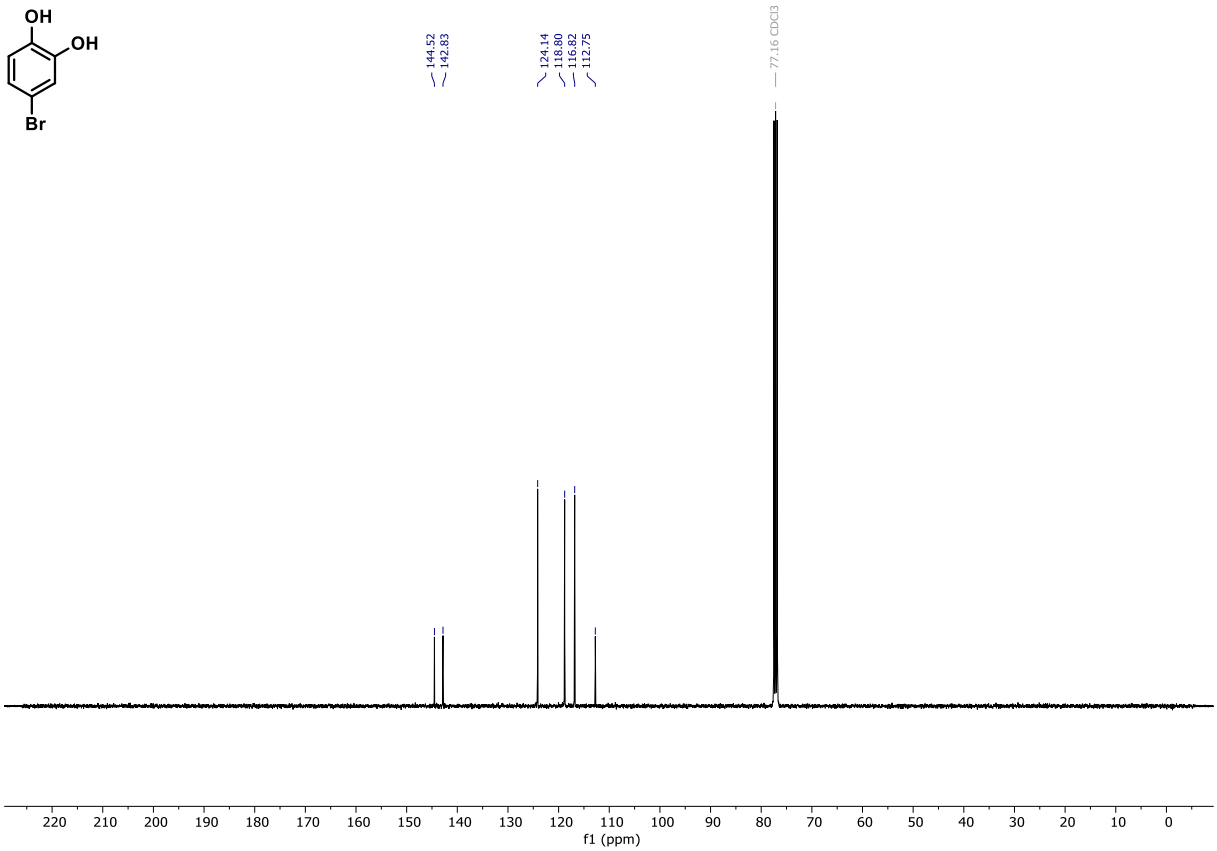


Figure S50: ^{13}C NMR spectra of 4-bromocatechol (**2t**) at 298 K in $CDCl_3$.

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