Electronic Supplementary Information

Electrochemical Oxidation of Phenols in Flow: A Versatile and Scalable Access to *para*-Benzoquinones

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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. Hydroquinones 4v[1] and 4t[2] were prepared according to literature protocols. 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 and temperature unless otherwise stated. Electrodes were obtained from commercial suppliers: DSA electrodes (DeNora, Milano, Italy), boron-doped diamond (DIACHEM®, 15 µm boron-doped diamond layer on 3 mm silicon support/wafer, CONDIAS GmbH, Itzhoe, Germany), glassy carbon (Sigradur, HTW Hochtemperatur-Werkstoffe GmbH, Thierhaupten, Germany), platinum (OEGUSSA, Vienna, Austria), isostatic graphite Sigrafine® V2100 (SGL Carbon, Bonn-Bad Godesberg, Germany) and nickel (99.9%, IKA Werke GmbH & Co. KG, Staufen, 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, Flawi, 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. Cyclohexane and ethyl acetate were employed 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.

Cyclic Voltammetry

Cyclic voltammetry was performed in a 10 mL snap-cap vial equipped with an Autolab PGSTAT101 potentiostat (Metrohm AG, Herisau, Switzerland). WE: BDD tip, 2 mm diameter; CE: glassy carbon rod; RE: $Ag/AgNO_3$ (0.01 M $AgNO_3$, 0.1 M $TBABF_4$ in MeCN). A sweep rate of 100 mV/s was used.

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, 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). 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.

Melting points Melting points were determined with a type M-565 device (Büchi, Essen, Germany). The given melting points values are uncorrected. A heating rate of 1 °C per minute was employed

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 ^{19}F spectra were recorded without ^{1}H decoupling and α-trifluorotoluene served as external standard (δ = –63.9 ppm).[3]

1.2 Experimental Procedures

1.2.1 Batch-Type Cell

Batch-type screening experiments were conducted in divided Teflon™ electrolysis cells (figure 1).

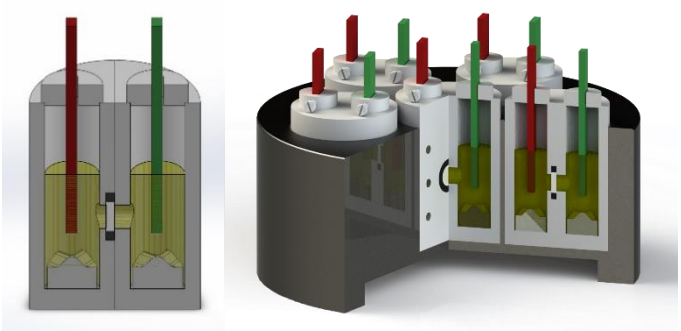


Figure 1: Left: Cross-section of a divided Teflon™ electrolysis cell equipped with two electrodes, a separators, magnetic stirrers, and electrolyte solution. Right: Six Teflon™ cells places in a metallic screening block.[4] Reprinted with permission from reference 4. Copyright 2016 American Chemical Society.

A glass frit (P4 pore size) fitted with an EPDM ring was employed as separator. Unless stated otherwise, platinum foil (>99% Pt, 0.1 mm thickness, OEGUSSA, Vienna, Austria), supported on Teflon™ was used as cathode material and ruthenium-iridium-oxide on titanium support (DeNora, Milano, Italy) was used as anode material. Both electrodes have an active surface of 2.5 cm^2 and were arranged in 2 cm distance relative to each other. Each cell compartment was equipped with a round magnetic stir bar. The individual cells were placed in a metallic screening set-up (figure 1) that can hold up to 6 cells. The block was then placed on a magnetic stirring plate. The system, excluding the DSA-electrodes, is commercially available as IKA Screening system package (IKA®-Werke GmbH & Co. KG, Staufen, Germany). As a power source, a multi-channel galvanostat (DC output 0 – 50 V and 0–50 mA per channel) with a built-in Coulomb counter (University of Bonn, Bonn, Germany) was used.

General Protocol for the Electrochemical Oxidation of Phenols, 4-Halophenols, Hydroquinones, 4-Methoxyanisoles, and 4-Methoxyphenols to 1,4-Benzoquinones in a Batch-Type Cell (GP1)

The electrochemical oxidation of phenols to 1,4-benzoquinones was performed in a divided Teflon™ cell equipped with magnetic stir bars. A glass frit was used as a separator. Unless otherwise noted, ruthenium-iridium oxide on titanium was used as anode material and a platinum foil on a PTFE support as cathode. After each electrolysis, the platinum foil was rinsed and subsequently thermally annealed. The electrolyte was prepared, by adding appropriate amounts of additives and concentrated sulfuric acid (98%) to acetonitrile at 0 °C. Afterwards the electrolyte was allowed to reach room temperature. The phenol (0.123 mmol) was added to the anodic compartment of the cell and 5 mL electrolyte was added to each compartment. The mixture was stirred with 300 rpm. The electrolysis was performed at constant current. For reaction optimization, the electrolysis parameters are listed in the corresponding sections. Afterwards other substrates were screened under the application of the optimized electrolysis parameters of a charge of 4 *F* (48 C) for phenols and 4-halophenols or 2 *F* (24 C) for hydroquinones, 4-methoxyanisoles, and 4-methoxyphenols, respectively. All electrolyses were conducted with a current density of 6 mA/cm^2. The reaction mixture was transferred to a flask afterwards, and the cell was washed with 20 mL ethyl acetate. The pH value was adjusted to pH 7 by the addition of saturated aqueous sodium carbonate solution. The mixture was transferred to a separatory funnel and extracted with ethyl acetate three times (3x20 mL). The combined organic fractions were dried over magnesium sulfate and filtered. The solvent was recovered by distillation under reduced pressure. 1,3,5-Trimethoxybenzene (0.123 mmol, 21 mg, 1 eq.) was added as internal standard and the mixture was dissolved in deuterated chloroform. Afterwards 0.7 mL of the solution were transferred into an NMR tube.

1.2.2 Flow Cell

Flow electrolyses were performed in electrolysis cells, that were designed by the Waldvogel research group (Figure 2). Detailed descriptions of the cells have been published.[5,6] The cell consists of two Teflon™ half cells. Each half cell contains an electrode with an active surface of 12 cm^2 or 48 cm^2. Ruthenium-iridium-oxide on titanium support (DeNora, Milano, Italy) was used as anode, while platinum was applied as cathode material, unless stated otherwise. A Nafion™ N324 membrane (DuPont, Wilmington, United States) was used as separator. Prior to use, the membrane was immersed in acetonitrile for 24 h. A Teflon™ spacer with 0.25 mm thickness was placed on each side of the membrane. The cell was assembled with 8 metal screws. The system in 2x6 cm^2, excluding the DSA electrode and the membrane, is commercially available as ElectraSyn flow (IKA®-Werke GmbH & Co. KG, Staufen, Germany).

A HMP4040 device (Rhode&Schwarz, München, Germany) with a controllable DC output of 0–32 V and 0–10 A and a maximum power of 160 W per channel was used as power source. A Masterflex peristaltic pump (Fisher Scientific GmbH, Schwerte, Germany) was used to pump the electrolyte through the cell.

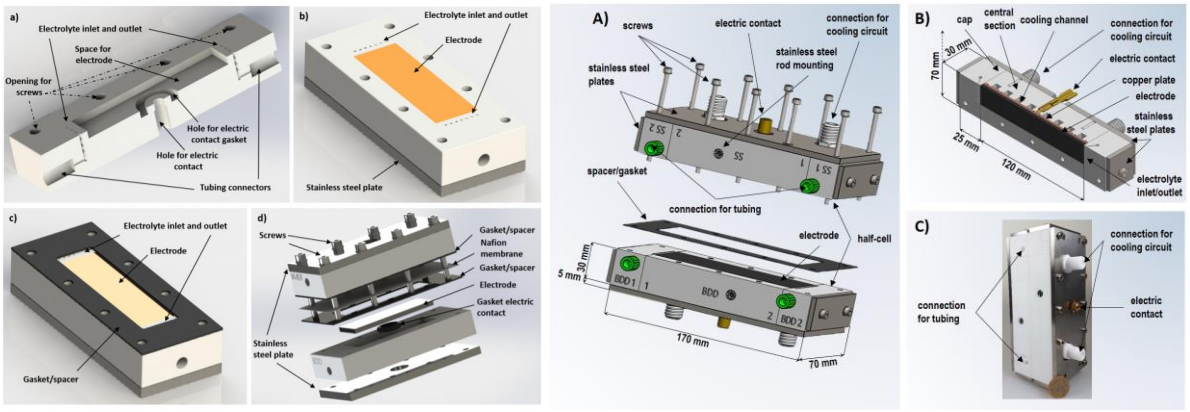


Figure 2: Left: A) Cross-section of a Teflon™ half cell without electrode. B) Teflon™ half cell with an electrode and stainless-steel plate. C) Teflon™ half cell with electrode and stainless-steel plate and spacer. D) Complete electrolysis cell. Reprinted with permission from reference 5. Copyright 2017 American Chemical Society.[5] Right: A) Partly exploded drawing of the full-featured 4x12 cm^2 flow cell. B) Cross-section of one half-cell. C) Completely mounted 4x12 cm^2 flow cell and a Euro coin (diameter: 23.25 mm) for comparison. Reprinted with permission from reference 6. Copyright 2020 American Chemical Society.[6]

General Protocol for the Screening of the Electrochemical Oxidation of Phenols, 4-Halophenols, Hydroquinones, 4-Methoxyphenols, 4-Methoxyanisoles to 1,4-Benzoquinones in Continuous Flow (GP2)

The screening reactions for the electrochemical oxidation of phenols, 4-halophenols, hydroquinones, 4-methoxyphenols, 4-methoxyanisoles to the corresponding 1,4-benzoquinones were performed in a flow electrolysis cell with ruthenium-iridium oxide on titanium support (12 cm^2) as anode and platinum (12 cm^2) as cathode. A Nafion™ N324 membrane was used as a separator and a Teflon™ spacer (0.25 mm or 0.50 mm) was placed on each side of the membrane. All experiments were performed as single-pass electrolysis and in constant current mode. The electrolyte solutions were prepared by dissolving appropriate amounts of concentrated sulfuric acid (98%), water, and methanol in acetonitrile at 0 °C. To the anolyte, appropriate amounts of the substrate, to maintain a concentration of 25 mM, were added, unless stated otherwise. The anolyte solution was stirred during the course of the electrolysis. A multi-channel peristaltic pump was used to simultaneously pump both solutions through the half cells. The electrolysis parameters can be found in the corresponding tables. The first 5 mL of electrolyzed solutions were discarded. Afterwards the solutions were collected in two graduate cylinders. After appropriate amounts of solutions were collected, 5 mL of each graduate cylinder were transferred to an Erlenmeyer flask using a bulb pipette. 20 mL ethyl acetate were added, and the pH value was adjusted to 7 by the addition

of saturated aqueous sodium carbonate solution. The solution was transferred to a separatory funnel and extracted two more times with 20 mL (3x20 mL) ethyl acetate. The combined organic fractions were dried over magnesium sulfate and filtered. The solvent was recovered by distillation under reduced pressure. 1,3,5-Trimethoxybenzene (0,123 mmol, 21 mg, 1 eq.) was added as an internal standard and the mixture was dissolved in deuterated chloroform. Afterwards 0.7 mL of the solution were transferred to an NMR tube.

General Protocol for the Electrochemical Oxidation of Phenols, 4-Halophenols, Hydroquinones, 4-Methoxyanisoles, and 4-Methoxyphenols to 1,4-Benzoquinones in Continuous Flow (GP3)

The electrochemical oxidation of phenols, 4-halophenols, hydroquinones, 4-methoxyanisoles, and 4-methoxyphenols to the corresponding 1,4-benzoquinones was performed in a flow electrolysis cell with ruthenium-iridium oxide on titanium support (12 cm^2 or 48 cm^2) as anode and platinum (12 cm^2 or 48 cm^2) as cathode. A Nafion™ N324 membrane was used as a separator and a Teflon™ spacer (0.25 mm) was placed on each side of the membrane. All experiments were performed as single-pass electrolysis with a constant current (24 mA for 12 cm^2 and 96 mA for 48 cm^2). The electrolyte solutions were prepared by dissolving appropriate amounts of concentrated sulfuric acid (98%), water, and methanol in acetonitrile at 0 °C. To the anolyte, appropriate amounts of substrate, to obtain a concentration of 25 mM, were added. The anolyte solution was stirred during the electrolysis. A multi-channel peristaltic pump was used to simultaneously pump both solutions through the half cells. The individual electrolysis parameter for all substrates can be found in table 1. The first 5 mL of electrolyzed solutions were discarded. Afterwards, the solutions were collected into two graduate cylinders. After appropriate amounts of solutions were collected, a transfer to an Erlenmeyer flask was performed. A two-fold volume of ethyl acetate was added, and the pH value was adjusted to 7 by the addition of saturated aqueous sodium carbonate solution. The solution was transferred to a separatory funnel and extracted two more times with 50 mL of ethyl acetate. The combined organic fractions were dried over magnesium sulfate and filtered. The solvent was recovered by distillation under reduced pressure. The crude product was purified by flash column chromatography unless otherwise stated.

Table 1: Overview of flow velocity of all isolated substrates.

Entry	Substrate	v / mL·min^{-1}	Q / F
1	2,6-dimethoxyphenol (**1a**)	0.152	4
2	2,6-diphenylphenol (**1b**)	0.122	5
3	2,6-bis(1-methylethyl)-phenol (**1c**)	0.076	8
4	2,6-bis-(1,1-dimethylethyl)-phenol (**1d**)	0.122	5
5	2-(1,1-dimethylethyl)-6-methylphenol (**1e**)	0.067	9
6	2,6-dimethylphenol (**1f**)	0.051	12
7	2,3,6-trimethylphenol (**1g**)	0.076	8
8	2-methylnaphthol (**1h**)	0.072	8.5
9	2,4,6-trichlorophenol (**1h**)	0.101	6
10	2,4,6-tribromophenol (**1i**)	0.101	6
11	2,4,6-triiodophenol[a] (**1j**)	0.152	5.7
12	3,4,5-trimethoxyphenol (**3a**)	0.202	3
13	2,6-bis-(1,1-dimethylethyl)-4-methoxyphenol (**3d**)	0.152	4
14	2,5-bis-(1,1-dimethylethyl)-4-methoxyphenol (**3k**)	0.152	4
15	2-(1,1-dimethylethyl)-4-methoxyphenol (**3l**)	0.303	2
16	4-methoxy-2,5-dimethylphenol (**3m**)	0.122	5
17	2-chloro-4-methoxyphenol (**3n**)	0.152	4
18	2-fluoro-4-methoxyphenol (**3o**)	0.152	4
19	1,2,4-trimethoxy-5-methylbenzene (**3p**)	0.152	4
20	1,4-dibromo-2,5-dimethoxybenzene (**3q**)	0.101	6
21	1-bromo-2,5-dimethoxy-3,4,6-trimethylbenzene (**3r**)	0.152	4
22	1,4-dimethoxy-2,3,5-trimethylbenzene (**3g**)	0.152	4
23	1,4-dimethoxynaphthalene (**3s**)	0.102	6
24	2,3,5,6-tetrafluoro-benzene-1,4-diol (**4t**)	0.152	4
25	2,3,5,6-tetrachloro-benzene-1,4-diol (**4u**)	0.152	4
26	4,5-dichloro-3,6-dihydroxyphthalonitrile (**4v**)	0.152	4

Electrolysis parameters: j = 2 mA/cm^2; I = 24 mA; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 12 cm^2; separator: Nafion; 1 M H_2SO_4 in MeCN +4.5 vol% H_2O +5 vol% MeOH; c(substrate) 25 mM.[a] c(substrate) 17.1 mM.

1.3 Reaction Optimization

1.3.1 Screening Reactions in a Divided 5 mL Batch-Type Cell

The screening for optimized reaction conditions in a divided batch-type electrolysis cell was conducted according to general procedure 1 (GP1, page S4).

1.3.1.1 Variation of Anode Material

Table 2: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the anode material

Entry	Anode	Yield(1a) / %	Yield(2a) / %
1	PbO_2 (Pb)	13	20
2	Pb	27	19
3	Ni	65	8
4	Pt	15	18
5	IrO_2 (Ta)	56	12
6	**$Ru_{0.3}Ti_{0.7}O_2$ (Ti)**	**18**	**28**
7	$Ir_{0.3}Ti_{0.7}O_2$ (Ti)	15	26
8	Ir/Ru	19	26
9	BDD (Si)	14	7
10	Graphite	7	27
11	Glassy Carbon	44	10

Electrolysis parameters: applied charge: 72 C (6 *F*); current: 25 mA; current density: 10 $mA \cdot cm^{-2}$; temperature: 22 °C; cathode: Pt; anode area: 2.5 cm^2; *c*(substrate): 100 mM; separator: glass frit; 5 mL 2 M H_2SO_4 in AcOH. Yields were determined via ^1H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

Table 3: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the anode material

Entry	Anode	Yield(1a) / %	Yield(2b) / %
1	$Ru_{0.3}Ti_{0.7}O_2$ (Ti)	0	45
2	$Ir_{0.3}Ti_{0.7}O_2$ (Ti)	0	49
3	**Ru-IrO_2 (Ti)**	**0**	**50**
4	RuO_2 (Ti)	0	44
5	Ru-IrO_2 (Ta)	0	46
6	Pt	12	22
7	Graphite[a]	4	41

Electrolysis parameters: applied charge: 72 C (6 *F*); current: 25 mA; current density: 10 $mA \cdot cm^{-2}$; temperature: 22 °C; cathode: Pt; anode area: 2.5 cm^2; *c*(substrate): 25 mM; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN + 4.5 vol% H_2O. Yields were determined via ^1H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard. [a] significant corrosion of the electrode after electrolysis observed.

Table 4: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the anode material

Entry	Anode	Yield(1a) / %	Yield(2b) / %
1	**Ru-IrO_2 (Ti)**	**2**	**75**
2	BDD	2	61
3	Pt	6	64

Electrolysis parameters: applied charge: 48 C (4 *F*); current: 15 mA; current density: 6 $mA \cdot cm^{-2}$; temperature: 22 °C; cathode: Pt; anode area: 2.5 cm^2; *c*(substrate): 25 mM; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN + 4.5 vol% H_2O, +1 vol% MeOH. Yields were determined via ^1H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.1.2 Variation of the Electrolyte System

Table 5: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the electrolyte system.

Entry	Electrolyte	Yield(1a) / %	Yield(2a) / %
1	2 M H_2SO_4/AcOH (1:1)	18	28
2	**2 M H_2SO_4/MeCN (1:1)**	**12**	**30**
3	2 M H_2SO_4/DME (1:1)	32	20
4	2 M H_2SO_4/HFIP (1:1)	32	14

Electrolysis parameters: applied charge: 72 C (6 *F*); current: 25 mA; current density: 10 mA·cm^{-2}; temperature: 22 °C; anode: $Ru_{0.3}Ti_{0.7}O_2$; cathode: Pt; anode area: 2.5 cm^2; *c*(substrate): 100 mM; separator: glass frit. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

Table 6: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the electrolyte system.

Entry	Electrolyte	*Q* / *F*	*j* / mA·cm^{-2}	Yield(1a) / %	Yield(2a) / %
1	2 M H_2SO_4/MeCN (1:9)	6	10	0	43
2	2 M H_2SO_4/MeCN (1:4)	6	10	0	40
3	2 M H_2SO_4/MeCN (3:7)	6	10	0	36
4	2 M H_2SO_4/MeCN (2:3)	6	10	0	34
5	2 M H_2SO_4/MeCN (1:1)	6	10	12	30
6	2 M H_2SO_4/MeCN (3:2)	6	10	2	29
7	MeCN + NEt_4BF_4 (0.1 M)	6	10	0	11
8	3 M NaOH/MeCN (1:1)	6	10	28	0
9	1 M H_2SO_4 in MeCN+4.5 vol% H_2O[a]	6	10	4	48
10	1 M NBu_4BF_4[b]	4	6	17	34
11	1 M NBu_4BF_4, 4 eq. DIPEA[b]	4	6	28	18
12	1 M NMe_4OAc[b]	4	6	14	6
13	1 M H_2SO_4 in MeCN[a]	4	6	2	19
14	**1 M H_2SO_4 in MeCN+4.5 vol% H_2O[b]**	**4**	**6**	**2**	**75**

Electrolysis parameters: current: 25 mA; current density: 10 mA·cm^{-2}; temperature: 22 °C; anode: $Ru_{0.3}Ti_{0.7}O_2$; cathode: Pt; anode area: 2.5 cm^2; *c*(substrate): 25 mM; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN. [a]: Anode: Ru-IrO_2(Ti); current 15 mA; current density 15 mA/cm^{-2}. [b]: Anode: Ru-IrO_2 (Ti); current 15 mA; current density 15 mA/cm^{-2}; 1 vol% MeOH. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.1.3 Variation of Substrate Concentration

Table 7: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the substrate concentration.

Entry	*c* / mM	Yield(1a) / %	Yield(2a) / %
1	**25**	**4**	**48**
2	50	4	38
3	75	7	30
4	100	8	27

Electrolysis parameters: applied charge: 72 C (6 *F*); current: 25 mA; current density: 10 mA·cm^{-2}; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

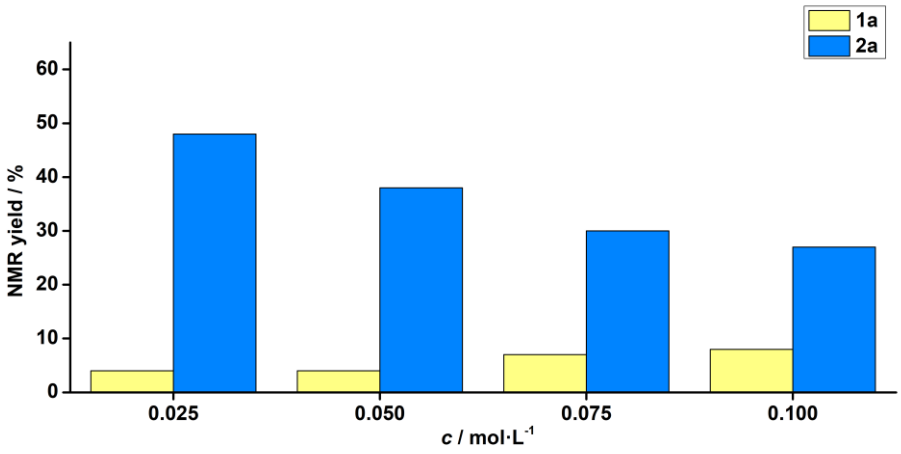


Figure 3: Yield of 2,6-dimethoxybenzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against the concentration of 2,6-dimethoxyphenol (**1a**) in mol/L. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.1.4 Variation of Applied Charge

Table 8: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the applied charge.

Entry	*Q* / *F*	*Q* / C	Yield(1a) / %	Yield(2a) / %
1	2.0	24	32	38
2	2.5	30	34	45
3	3.0	36	16	55
4	3.5	42	17	54
5	4.0	48	8	54
6[a]	4.0	48	5	62
7[b]	4.0	48	2	75
8[c]	**4.0**	**48**	**5**	**83**
9	4.5	54	7	52

Entry	*Q* / *F*	*Q* / C	Yield(1a) / %	Yield(2a) / %
10	5.0	60	7	52
11	6.0	72	4	48
12[a]	6.0	72	0	48
13[b]	6.0	72	0	64
14[c]	6.0	72	2	77
15	7.0	84	5	38
16	8.0	96	4	36
17[b]	8.0	96	0	44

Electrolysis parameters: current: 25 mA; current density: 10 mA·cm^{-2}; temperature: 22 ° C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O, *c*(substrate): 25 mM. [a]: Current density 6 mA·cm^{-2}. [b]: Current density 6 mA·cm^{-2}; 1 vol% MeOH. [c]: Current density 6 mA·cm^{-2}; 5 vol% MeOH. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

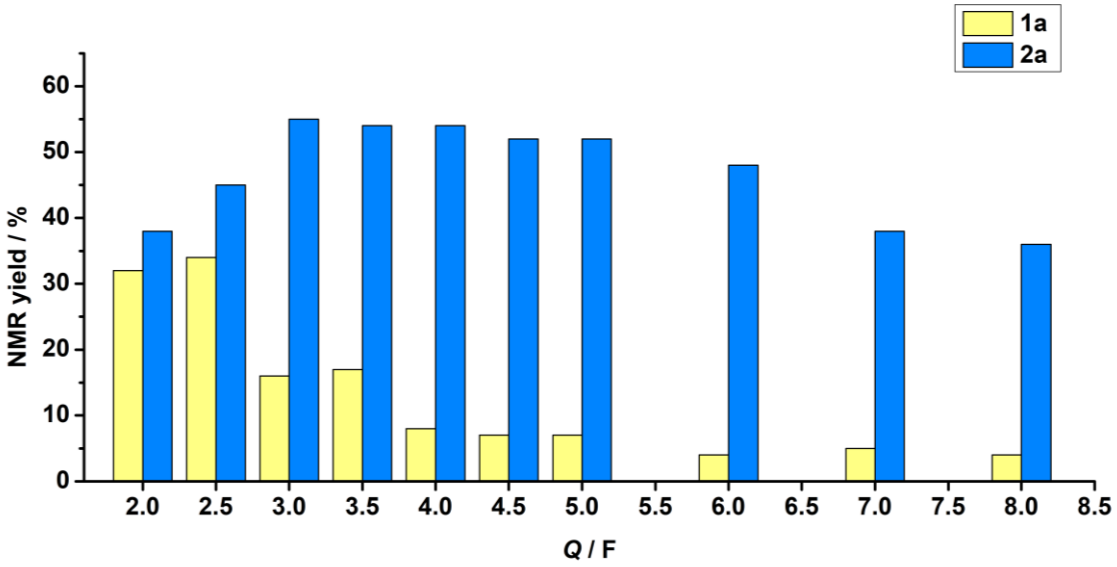


Figure 4: Yield of 2,6-dimethoxybenzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against the amount of applied charge *Q* in *F*. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard. Values for entry 6-8 and 12-14 in table above are not depicted due to deviation of the electrolyte system and the current density.

1.3.1.5 Variation of Current Density

Table 9: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the current density for varying amounts of applied charge.

Entry	*j* / mA·cm^{-2}	*I* / mA	*Q* / *F*	*Q* / C	Yield(1a) / %	Yield(2a) / %
1	5	12.5	3.0	36	11	57
2	5	12.5	3.5	42	11	60
3	5	12.5	4.0	48	4	59
4	5	12.5	4.5	54	2	57
5	5	12.5	5.0	60	2	52

Entry	*j* / mA·cm^{-2}	*I* / mA	*Q* / *F*	*Q* / C	Yield(1a) / %	Yield(2a) / %
6	10	25	3.0	36	16	55
7	10	25	3.5	42	15	52
8	10	25	4.0	48	8	54
9	10	25	4.5	54	7	52
10	10	25	5.0	60	9	44
11	20	50	3.0	36	35	48
12	20	50	3.5	42	30	41
13	20	50	4.0	48	15	52
14	20	50	4.5	54	16	52
15	20	50	5.0	60	16	44

Electrolysis parameters: temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O; *c*(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

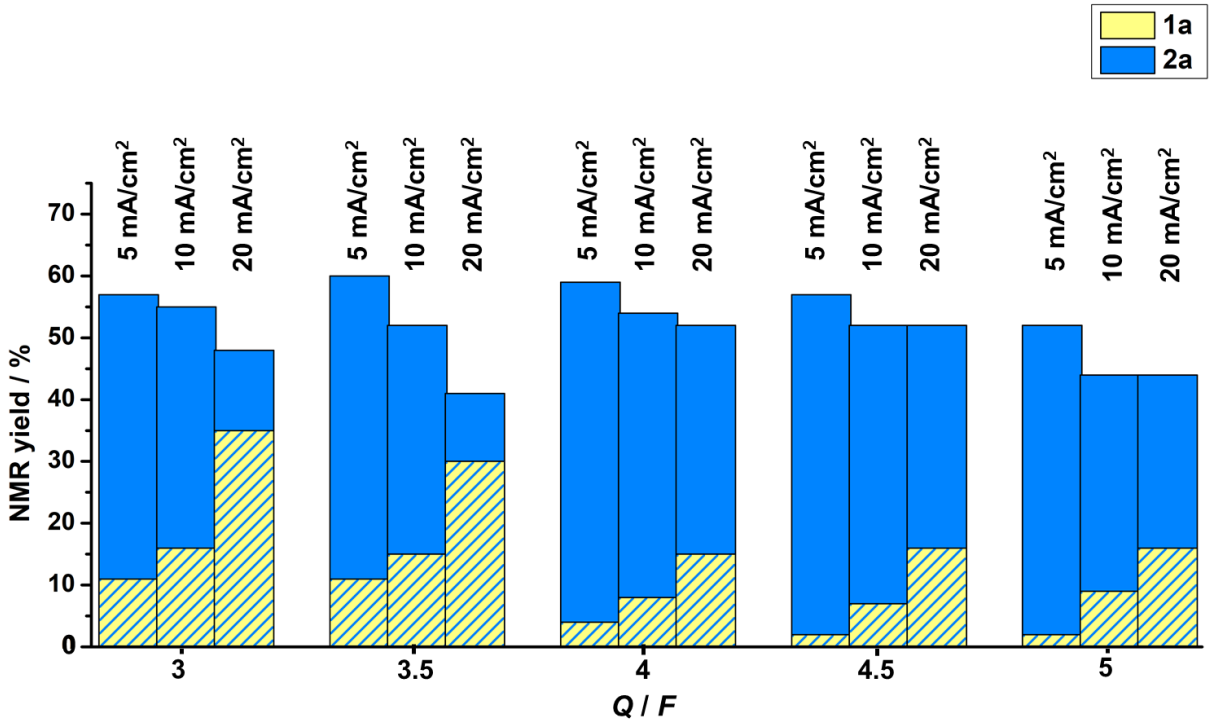


Figure 5: Yield of 2,6-dimethoxybenzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against the amount of applied charge Q in *F* for different current densities. Shown yields for product (**2a**) and starting material (**1a**) are overlayed and not cumulative values. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

Table 10: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the current density.

Entry	*j* / mA·cm^{-2}	*Q* / *F*	*Q* / C	Yield(1a) / %	Yield(2a) / %
1[a]	2	4.0	48	2	66
2	3	4.0	48	6	60
2	4	4.0	48	6	54
3	5	4.0	48	4	59
4	6	4.0	48	5	62
5[a]	**6**	**4.0**	**48**	**2**	**75**
6	7	4.0	48	9	59
7[a]	20	4.0	48	25	63

Electrolysis parameters: temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O; *c*(substrate) = 25 mM. [a]*:* with 1 mol% MeOH. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.1.6 Variation of Cathode Material

Table 11: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under variation of the cathode material.

Entry	Cathode	Yield(1a) / %	Yield(2a) / %
1	**Pt**	**8**	**62**
2	GC	9	58
3	BDD	5	58
4	steel	17	51
5	Ni	51	23

Electrolysis parameters: applied charge: 42 C (3.5 *F*); current: 15 mA; current density: 6 mA·cm^{-2}; temperature: 22 °C; anode: Ru-IrO_2 (Ti); anode area: 2.5 cm^2; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O; *c*(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

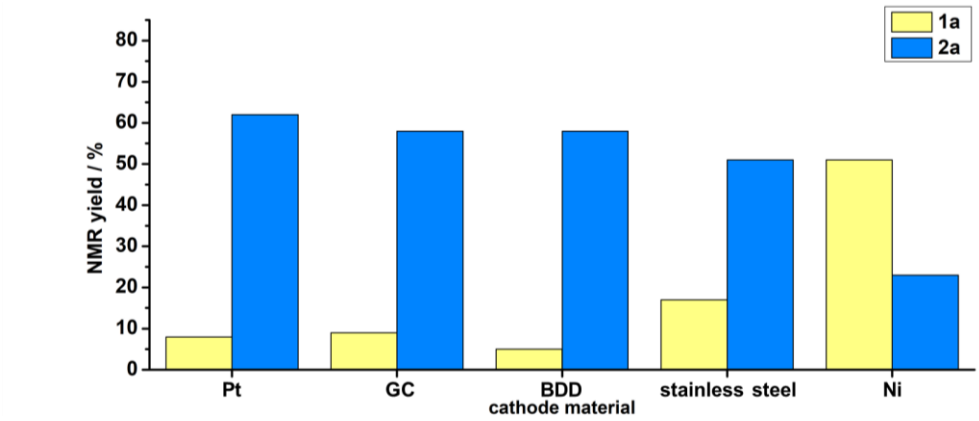


Figure 6: Yield of 2,6-dimethoxybenzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against cathode material. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.1.7 Variation of Protic Additives

Variation of Water Content:

Table 12: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the water content at varying amounts of applied charge.

Entry	Vol% H_2O	Yield(1a) / %	Yield(2a) / %
1	2.0	20	38
2	4.0	2	50
3	**4.5**	**5**	**62**
4	6.0	3	49
5	10.0	8	36

Electrolysis parameters: applied charge: 48 C (4 *F*); current: 15 mA; current density: 6 $mA \cdot cm^{-2}$; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN; c(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

Variation of Methanol Content:

Table 13: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the methanol content at varying water content.

Entry	Vol% H_2O	Vol% MeOH	Yield(1a) / %	Yield(2a) / %
1[a]	0	0	2	19
2[a]	0	1	5	66
3	2.5	2.5	20	52
4	4.0	1.0	12	62
5	4.5	0	5	62
6	4.5	0.5	9	70
7	4.5	1.0	10	71
8[a]	4.5	1.0	2	75
9	4.5	1.5	13	68
10[a]	**4.5**	**5.0**	**5**	**83**
11	5.0	0.5	10	66
12	5.0	0.5	10	66

Electrolysis parameters: applied charge: 42 C (3.5 *F*); current: 15 mA; current density: 6 $mA \cdot cm^{-2}$; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; divided: glass frit; 5 mL 1 M H_2SO_4 in MeCN; *c*(substrate): 25 mM. [a]: 48 C (4 *F*). Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.1.8 Variation of Temperature

Table 14: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the temperature.

Entry	*T* / °C	Yield(1a) / %	Yield(2a) / %
1	**22**	**10**	**71**
2	30	7	69
3	50	9	48

Electrolysis parameters: applied charge: 42 C (3.5 *F*); current: 15 mA; current density: 6 mA·cm^{-2}; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; separator: glass frit; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O +1 vol% MeOH; c(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.2 Screening Reactions in a Divided Flow Cell

The screening for optimized reaction conditions in a divided flow electrolysis cell was conducted according to general procedure 2 (GP2, page S5-6).

1.3.2.1 Variation of Applied Charge

Table 15: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of applied charge with varying thickness of the spacer.

Entry	*Q* / *F*	*Q* / C	*d*(Spacer) / mm	Yield(1a) / %	Yield(2a) / %
1	3.0	36	0.25	53	37
2	3.5	42	0.25	31	54
3	**4.0**	**48**	**0.25**	**26**	**59**
4	5.0	60	0.25	25	58
5	6.0	72	0.25	22	58
6	7.0	84	0.25	23	53
7	8.0	96	0.25	19	52
8	4.0	48	0.50	50	32
9	5.0	72	0.50	49	31
10	7.0	84	0.50	41	34

Electrolysis parameters: current: 72 mA; current density: 6 mA·cm^{-2}; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 12 cm^2; separator: Nafion; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O +1 vol% MeOH; *c*(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

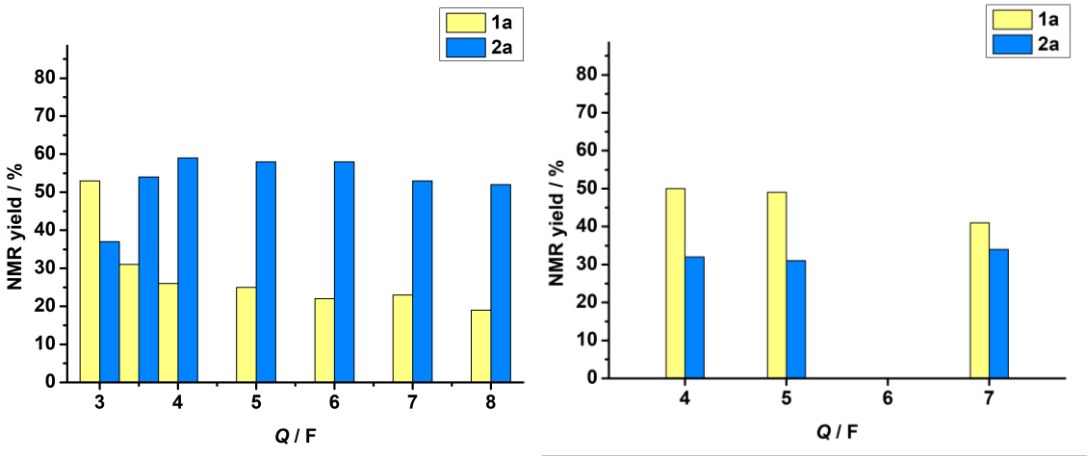


Figure 7: Left: Yield of 2,6-dimethoxy-1,4-benzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against the applied charge in *F* for a spacer thickness of 0.25 mm. Right: Yield of 2,6-dimethoxybenzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against the applied charge in *F* for a spacer thickness of 0.50 mm. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.2.2 Variation of Current Density

Table 16: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the current density for varying amounts of applied charge.

Entry	*j* / mA·cm^{-2}	*I* / mA	*Q* / *F*	*Q* / *C*	Yield(1a) / %	Yield(2a) / %
1	1	12	4.0	48	2	80
2	**2**	**24**	**4.0**	**48**	**7**	**80**
3	3	36	4.0	48	11	73
4	4	48	4.0	48	24	63
5	5	60	4.0	48	28	57
6	6	72	4.0	48	26	59
7	8	96	4.0	48	44	46
8	10	120	4.0	48	50	37
9	2	24	6.0	72	3	74
10	3	36	6.0	72	12	65
11	4	48	6.0	72	18	59
12	5	60	6.0	72	21	59
13	6	72	6.0	72	22	58
14	8	96	6.0	72	37	47
15	10	120	6.0	72	42	41

Electrolysis parameters: temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; electrode area: 12 cm^2; separator: Nafion; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O +1 vol% MeOH; *c*(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

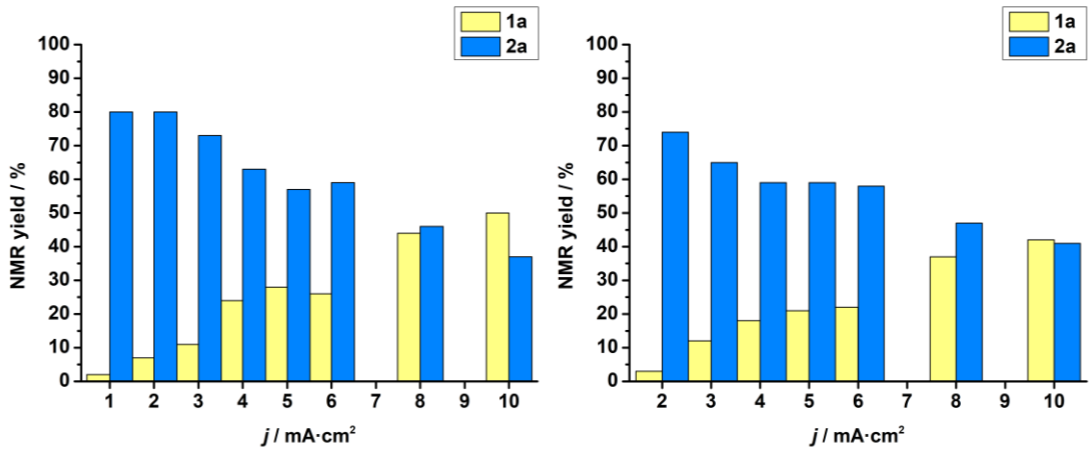


Figure 8: Left: Yield of 2,6-dimethoxy-1,4-benzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against current density in mA/cm^2 for an applied charge of 4 *F*. Right: Yield of 2,6-dimethoxybenzoquinone (2a) (blue) and non-converted 2,6-dimethoxyphenol (1a) (yellow) against current density in mA/cm^2 for an applied charge of 6 *F*. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.2.3 Variation of Substrate Concentration

Table 17: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the substrate concentration for varying amounts of applied charge.

Entry	*c* / mM	*Q* / *F*	*Q* / C	Yield(1a) / %	Yield(2a) / %
1	12.50	4.0	48	31	59
2	18.75	4.0	48	33	63
3	**25.00**	**4.0**	**48**	**7**	**80**
4	37.50	4.0	48	10	70
5	12.50	6.0	72	18	65
6	18.75	6.0	72	11	62
7	25.00	6.0	72	3	74

Electrolysis parameters: current: 24 mA; current density: 2 mA·cm^{-2}; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 12 cm^2; separator: Nafion; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O +1 vol% MeOH. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

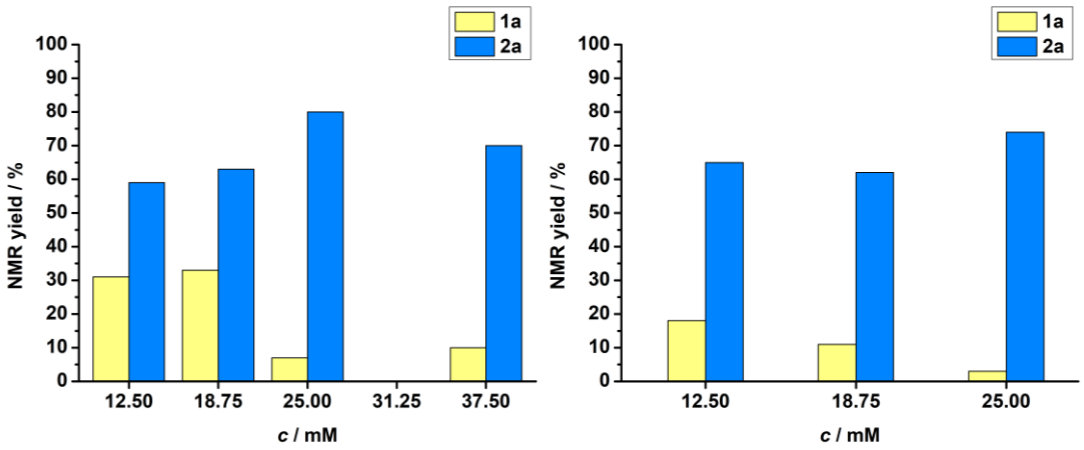


Figure 9: Left: Yield of 2,6-dimethoxy-1,4-benzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against the concentration of substrate mM for an applied charge of 4 *F*. Right: Yield of 2,6-dimethoxybenzoquinone (**2a**) (blue) and non-converted 2,6-dimethoxyphenol (**1a**) (yellow) against the concentration of substrate in mM for an applied charge of 6 *F*. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.2.4 Variation of Methanol Content

Table 18: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the methanol content.

Entry	Vol% MeOH	Yield(1a) / %	Yield(2a) / %
1	1.0	7	80
2	2.0	4	80
3	3.0	7	87
4	4.0	6	85
5	**5.0**	**7**	**93**
6	7.5	20	80

Electrolysis parameters: applied charge: 48 C (4 *F*); current: 24 mA; current density: 2 mA·cm^{-2}; flow velocity: 0.152 mL/min; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 12 cm^2; separator: Nafion; 5 mL 1 M H_2SO_4 in MeCN +4.5 vol% H_2O; *c*(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.2.5 Miscellaneous:

Table 19: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the electrolyte system at varying current densities.

Entry	Solvent	Additive	j / mA·cm^{-2}	Yield(1a) / %	Yield(2a) / %
1	MeOH	4.5 vol% H_2O	2	28	26
2	MeCN	1 vol% HFIP	2	19	67
3	MeCN	4.5 vol% H_2O	6	45	37

Electrolysis parameters: applied charge: 48 C (4 *F*); temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 12 cm^2; separator: Nafion; 5 mL 1 M H_2SO_4 in MeCN ; entry 2: +4.5 vol% H_2O; *c*(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.2.6 Sulfuric acid concentration:

Table 20: Electrochemical synthesis of 2,6-dimethoxy-1,4-benzoquinone (**2a**) under alteration of the sulfuric acid concentration.

Entry	$c(H_2SO_4)$ / M	Conversion / %	Yield / %	U_k / V
1	**1.00**	**93**	**93**	**1.4**
2	0.75	96	88	1.3
3	0.50	94	84	1.6
4	0.25	96	85	1.5
5	0.10	97	85	1.6

Electrolysis parameters: applied charge: 48 C (4 *F*); current: 24 mA; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 12 cm^2; separator: Nafion; 5 mL H_2SO_4 in MeCN ; entry 2: +4.5 vol% H_2O; +5vol% MeOH; *c*(substrate): 25 mM. Yields were determined via ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

1.3.3 Proposed Degradation Products and Intermediates

During the course of the reaction optimization different intermediates and products of overoxidation were identified. These intermediates, as well as established literature, are shown within the scheme 4 of the manuscript and were used to propose a pathway for the phenol oxidation. The following section shows additional experimental data to support the proposed intermediates and degradation products.

1.3.3.1 Overoxidation products

In agreement with published literature overoxidation, proceeding via cleavage of the quinone based cycle, to the dicarboxylic acid was observed.[7,8] Due to the standard work-up procedure (adjustment of the pH to 7 before extraction of the organic components) acids were not routinely analyzed. In order to confirm their presence an additional control experiment was performed where the overoxidation was deliberately achieved by application of an excess of charge (12 *F,* general procedure 1) to 2,6-dimethoxyphenol (**1a**). In agreement with the general procedure the pH of the reaction mixture was first adjusted to 7 and the majority of the neutral organic species was extracted. Afterwards the pH of the aqueous layer was adjusted to 1 by the addition of diluted sulfuric acid (20 vol%) and the mixture was extracted with ethyl acetate. The solvent was removed by distillation and the crude mixture was analyzed by GC-MS and ^{1}H NMR. The GC-MS chromatogram showed a species with a fragmentation pattern that was in agreement with the reported fragmentation pattern of 2-methoxymaleic acid.[9] It is noteworthy to mention, that the intensity of the molecular ion peak was previously reported to be very low. The crude NMR spectrum also exhibited signals that are consistent with 2-methoxymaleic acid and are in agreement with literature reports.[10]

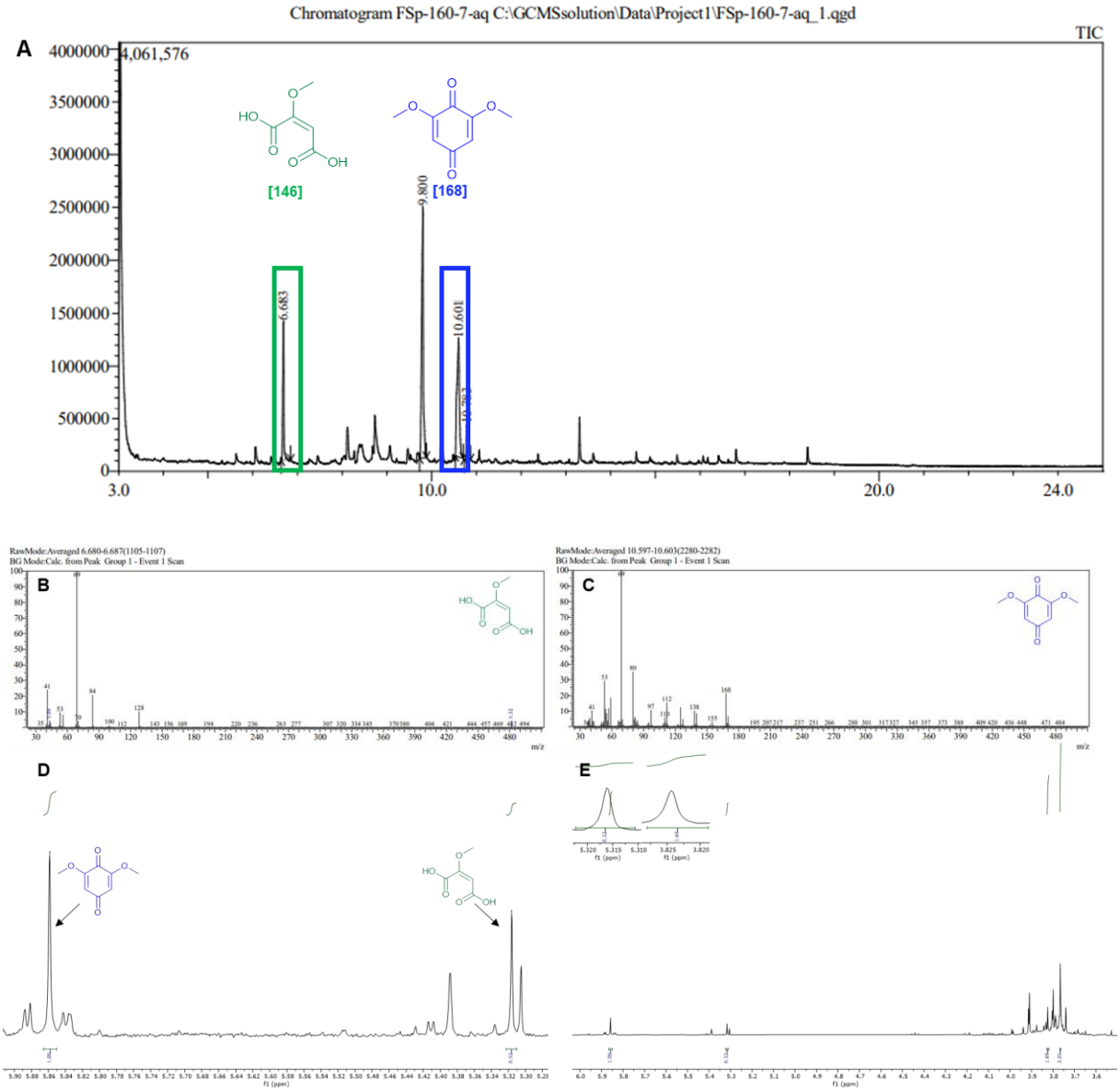


Figure 10: A: GC-MS spectra of the organic acidic fraction. B: Mass Spectra of the peak at 6.683 assigned to 2-methoxymaleic acid. C: Mass spectra of the peak at 10.6011 assigned to residue amounts of 2,6-dimethoxybenzoquinone. D: Cut-out of the region from 5.9-5.3 ppm of the ^{1}H NMR spectra of the crude organic acidic fraction including signals corresponding to 2-methoxymaleic acid and 2,6-dimethoxybenzoquinone. E: Cut-out of the region from 6.0-3.6 ppm of the ^{1}H NMR spectra of the crude organic acidic fraction including signals corresponding to 2-methoxymaleic acid and 2,6-dimethoxybenzoquinone. Reaction conditions: *Q*: 12 *F*; *T*: 22 °C; anode: Ru-IrO_2 (Ti); anode area: 2.5 cm^2; separator: glass frit; 1 M H_2SO_4 in MeCN +4.5 vol% H_2O; +1 vol% MeOH; *c*(substrate): 25 mM.

1.3.3.2 Intermediates

Signals consistent with the oxidation intermediate 2,4,6-trimethoxyphenol were observed in minor quantities (<5%) in several oxidations of 2,6-dimethoxyphenol NMR spectra of the crude product, indicating that methanol can act as an additional oxygenating agent besides water.[11] The 4-methoxylated species was observable in the presence of water as well. Since the oxidation potential of the 4-methoxylated species is lower than that of the phenol, it is not possible to accumulate it during the electrolysis under galvanostatic conditions. Figure 11

shows the GC-MS spectrum of a crude reaction mixture with added 1,3,5-trimethoxbenzene as internal standard (electrolysis conducted according to general procedure 1). The GC-MS data is in agreement with the literature.[11]

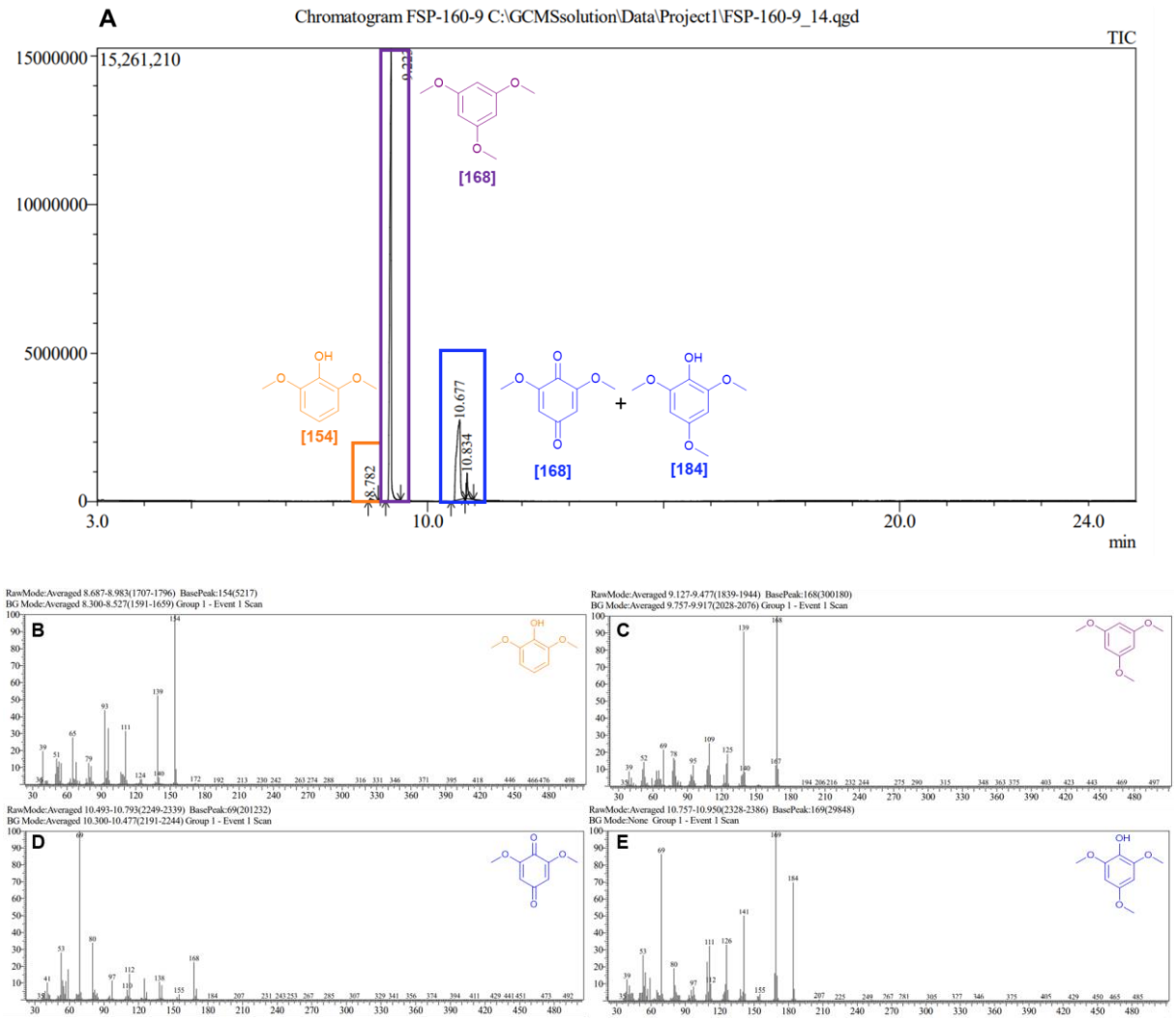


Figure 11: A: GC-MS spectra. B: Mass Spectra of the peak at 8.782 min assigned to 2,6-dimethoxyphenol. C: Mass spectra of the peak at 9.223 min assigned to the internal standard 1,3,5-trimethoxybenzene. D: Mass spectra of the peak at 10.677 min assigned to 2,6-dimethoxybenzoquinone. E: Mass spectra of the peak at 10.834 min assigned to 2,4,6-trimethoxyphenol. Reaction conditions: *Q*: 3.8 *F*; *T*: 22 °C; anode: Ru-IrO_2 (Ti); anode area: 2.5 cm^2; separator: glass frit; 1 M H_2SO_4 in MeCN +4.5 vol% H_2O; +5 vol% MeOH; *c*(substrate): 25 mM.

1.3.3.3 Side products

Quinones are known to be susceptible to nucleophilic attack. Different modes of addition are known including Michael-type 1,4-addition on the enone system as well as gem-diole formations.[12–14] The resulting product of a Michael-type addition at a quinone by a protic additive (e.g. water or methanol) is a hydroquinone with additional hydroxyl and methoxy substituent. Due to the electron donating nature of these groups the oxidation potential will be lower than that of the starting material (phenol) and the intermediately formed hydroquinone, making it even more prone to overoxidation. Consistent with this, lower yields were observed

in the presence of higher additive concentrations as well as lower mass balance. To investigate whether the formation of Michael-type of side products is possible at higher protic additive concentrations cyclic voltammetry measurements of 2,6-dimethoxybenzoquinone (**2a**) were performed in the presence of higher water content (10 vol%) and compared to the voltammogram obtained at an optimized additive content (4.5 vol% water, 5 vol% methanol) (Figure 12).

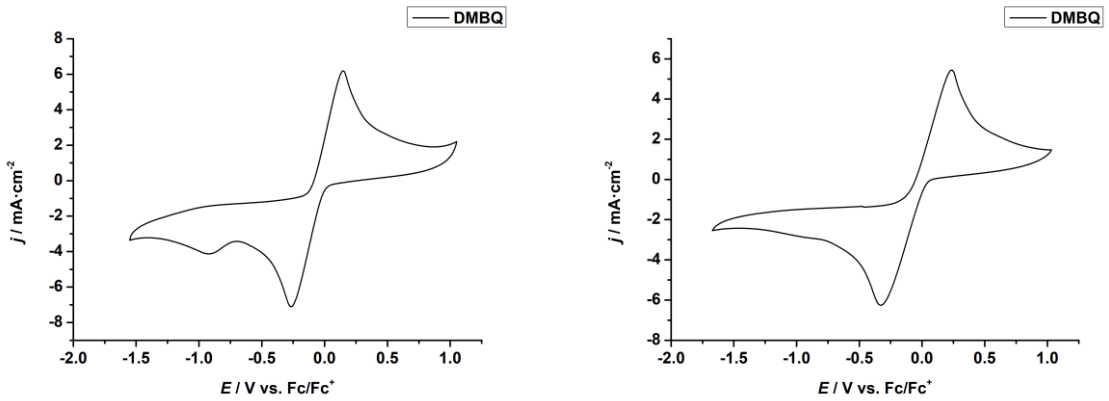


Figure 12: Left: Cyclic voltammogram of **2a** in the presence of 10 vol% of water (referenced against the ferrocene/ferrocenium redox pair). WE: glassy carbon; CE: glassy carbon; RE: Ag/AgCl in saturated LiCl/EtOH. Solvent: MeCN + 10 vol% H_2O, *v* =100 mV/s; *T* = 22 °C., c(substrate)= 10 mM; *c*(H_2SO_4) = 0.1 M. Right: Cyclic voltammogram of **2a** in the presence of 4.5 vol% of water and 5 vol% MeOH (referenced against the ferrocene/ferrocenium redox pair). WE: glassy carbon; CE: glassy carbon; RE: Ag/AgCl in saturated LiCl/EtOH. Solvent: MeCN + 4.5 vol% H_2O; 5 vol% MeOH; *v* =100 mV/s; *T* = 22 °C., *c*(substrate)= 10 mM; *c*(H_2SO_4) = 0.1 M.

Besides the reversible oxidation and reduction of 2,6-dimethoxybenzoquinone the emergence of a second reductive event was observed in the presence of a higher water content indicating the presence of a species with lower reduction potential, compared to the original quinone. Further we exposed the formed benzoquinone **2a** (electrolysis conducted to general procedure 1) to the electrolyte system in the presence of 10 vol% water for a prolonged time of 72 h with the intent to examine potential water addition. Partial degradation (78% of initial yield after 72 h in electrolyte solution) of the 2,6-dimethoxybenzoquinone was observed and the emergence of serval new minor signals in the ^{1}H NMR.

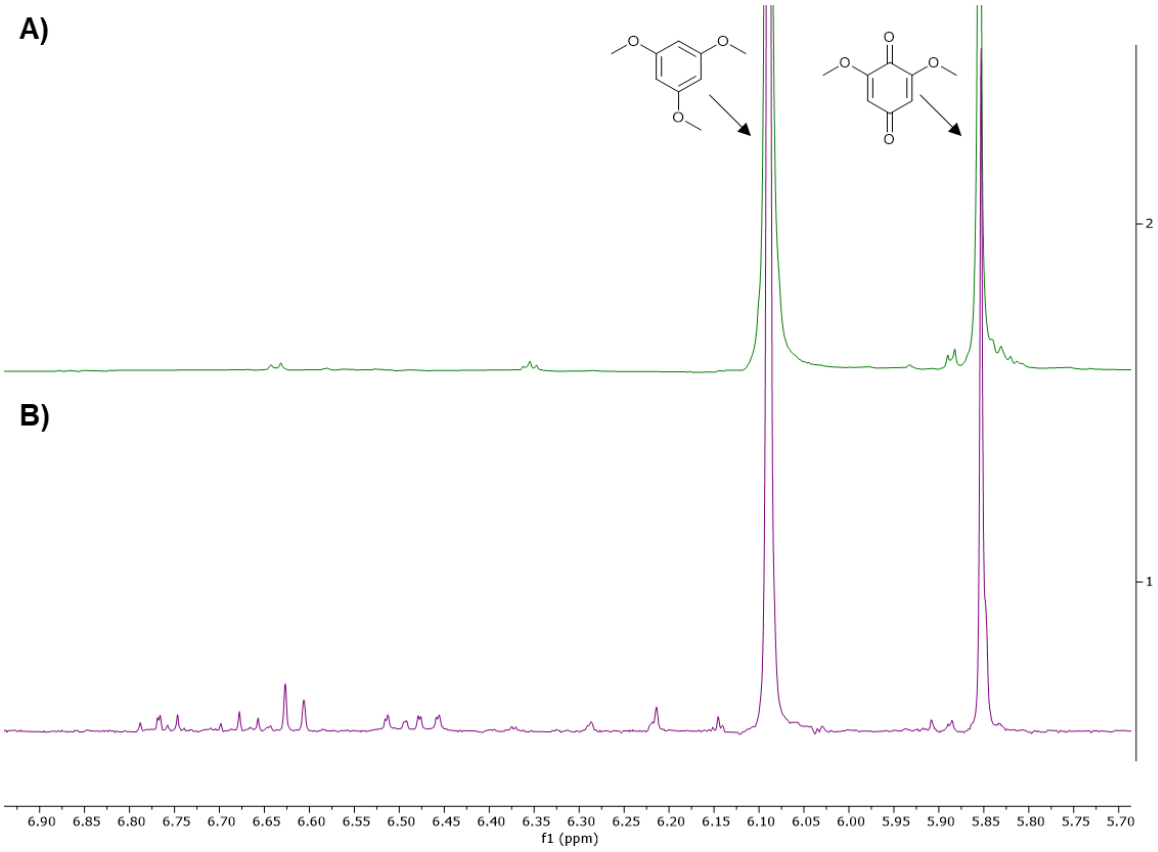


Figure 13: A: NMR spectra of the crude reaction mixture with 1,3,5-trimethoxybenzoquinone as internal standard. B: NMR spectra of the crude reaction mixture after additional exposure to the electrolyte for 72 hours with added 1,3,5-trimethoxybenzoquinone as internal standard. Reaction conditions: *Q*: 4 *F*; *T*: 22 °C; anode: $RuIrO_2$ (Ti); anode area: 2.5 cm^2; separator: glass frit; 1 M H_2SO_4 in MeCN +10 vol% H_2O; *c*(substrate): 25 mM.

1.4 Cyclic Voltammetry

Cyclic voltammetry measurements of 2,6-dimethoxyphenol (**1a**) were performed in the presence of varying methanol amounts between 0-5 vol% to elucidate a potential solvent effect on the oxidation potential of the phenol. All measurements were conducted in a 10 mL snap-cap vial equipped with an Autolab PGSTAT101 potentiostat (Metrohm AG, Herisau, Switzerland). The solutions, consisting of 10 mM substrate, 0.1 M sulfuric acid in acetonitrile with 4.5 vol% water and 0-5 vol% methanol were degassed with argon for 5 minutes. Cyclic voltammetry was performed with a boron-doped diamond working electrode (tip 2 mm diameter), a classy carbon rod counter electrode and an $Ag/AgNO_3$ reference electrode (0.01 M $AgNO_3$, 0.1 M $TBABF_4$ in MeCN). A sweep rate of 100 mV/s was used. The potentials were additionally referenced against the ferrocene/ferrocenium pair.

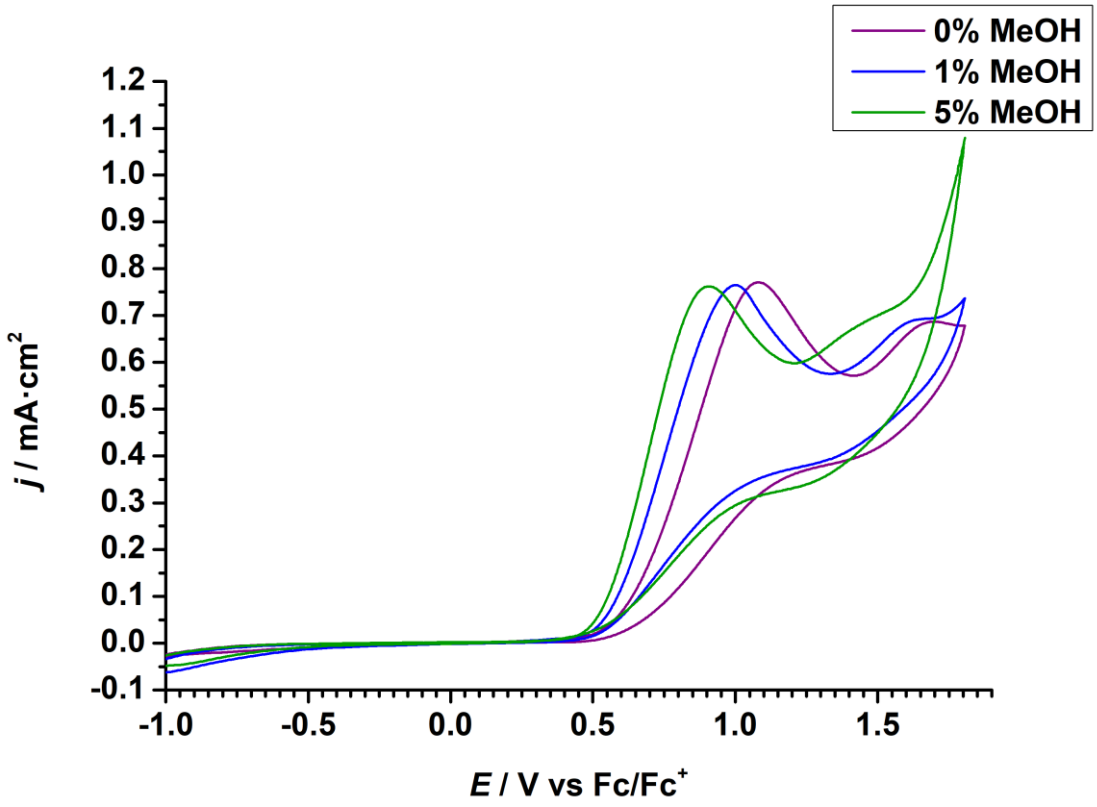


Figure 14: Cyclic voltammograms of **1a** in the presence of different vol% of methanol (referenced against the ferrocene/ferrocenium redox pair). WE: BDD; CE: glassy carbon; RE: Ag/$AgNO_3$ (0.01 M $AgNO_3$, 0.1 M $TBABF_4$ in MeCN). Solvent: MeCN + 4.5 vol% H_2O, + 0-5 % vol% MeOH. v =100 mV/s; T =22 °C., c(substrate)= 5 mM; $c(H_2SO_4)$ = 0.1 M.

1.5 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 well-rounded comparison six different green chemistry metrics, were evaluated. A comparison was done for the model compound 2,6-dimethoxybenzoquinone (**2a**) and 2,6-diisopropylbenzoquinone (**2c**). The newly developed protocol was compared to the conventional protocol with the highest synthetical 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. It is assumed for all protocols that solvents are recoverable. All prices are obtained from the current Sigma Alrich 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.

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

The atom economy was calculated according to the following formula:[15]

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

The reaction mass efficiency was calculated according to the following formula:[15]

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

Effective mass yield was calculated according to the following formula (1 mmol scale):[16]

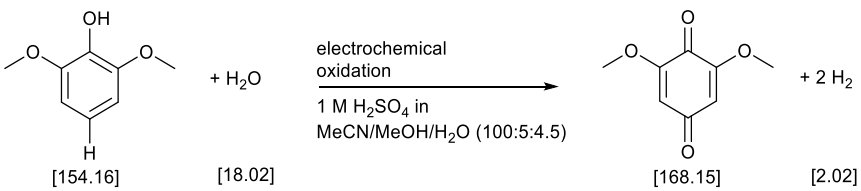
$$EMY = \frac{mass\ of\ desired\ product}{mass\ of\ non-benign\ reagents} \cdot 100\%$$

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.[17] 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 2,6-Dimethoxybenzoquinone (2a):

Our protocol:



[154.16] [18.02] [168.15] [2.02]

Safety

Table 21: Specifications for employed chemicals.

Substance	Cas	*MW*	*Price* Euro/g	GHS Hazard	GHS ranking	Specification
2,6-Dimethoxyphenol	91-10-1	154.16	1.06	harmful	4	100 g, 99%
Sulfuric Acid	7664-93-9	98.08	0.03	corrosive	4	2.5 L, 95-98% ACS reagent grade
Methanol	67-56-1	32.04	0.03	flammable, toxic, health hazard	1	2.5 L, >99.9%, HPLC
Water	7732-18-5	18.02	0.02	none	5	2.5 L, suitable for HPLC
Acetonitrile	75-05-8	41.05	0.1	flammable, harmful	3	2.5 L, ACS reagent, ≥99.5%
2,6-Dimethoxybenzoquinone	530-55-2	168.15	6,44			25 g, 97%

Overall GHS: 3.4

Others:

$$AE = \frac{168.15\,\frac{g}{mol}}{168.15\,\frac{g}{mol}+2\cdot 2.02\frac{g}{mol}} \cdot 100\% = 97.7\%$$

$$Eco = \frac{1080\,€ \cdot 90\%}{280\ €\cdot 100\%} = 3.5$$

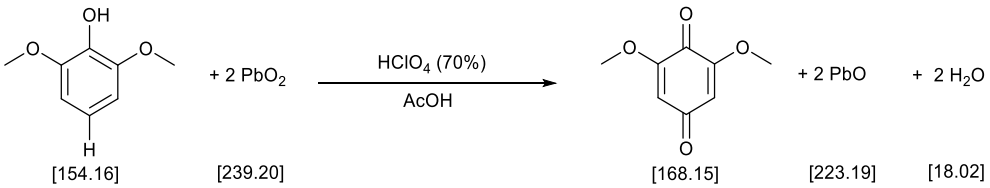
$$RME = \frac{0.977 \cdot 0.90}{1} \cdot 100\% = 89.7\%$$

$$EMY = \frac{1}{"0"} \cdot 100\% = 100\%$$

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 Omura was used for comparison.[18]



Safety

Table 22: Specifications for employed chemicals.

Substance	Cas	*MW*	*Price* Euro/g	GHS Hazard	GHS ranking	Specification
2,6-Dimethoxyphenol	91-10-1	154.16	1.06	harmful	4	100 g, 99%
Lead(IV) oxide	1309-60-0	239.20	15.4	oxidising, health hazards, toxic, harmful, Environment	1	10 g, 99.998% trace metals basis
Perchloric acid	7601-90-3	100.46	0.07	Oxidising, corrosive, health hazard, harmful	1	2,5 L, 70% ACS reagent grade
Acetic Acid	64-19-7	60.05	0.04	corrosive, flammable	3	2,5 L, glacial, ReagentPlus®, ≥99%
2,6-Dimethoxybenzoquinone	530-55-2	168.15	6.44			25 g, 97%

Overall GHS: 2.3

Others:

$$AE = \frac{168.15\,\frac{g}{mol}}{168.15\,\frac{g}{mol}+223.19\frac{g}{mol}+18.02\frac{g}{mol}} \cdot 100\% = 41.1\%$$

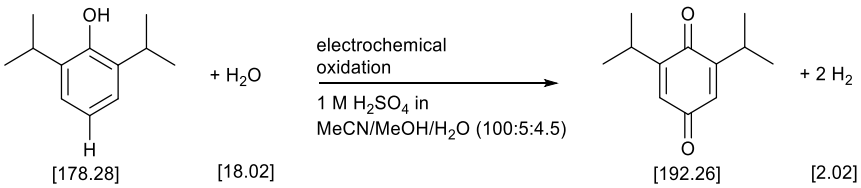
$$Eco = \frac{1080\ € \cdot 73\%}{9460\ € \cdot 100\%} = 0.08$$

Cost of production exceed value of produced product.

$$RME = \frac{0.411 \cdot 0.73}{14.5} \cdot 100\% = 2.07\%$$

$$EMY = \frac{168.15\ \text{mg}}{598.0\ \text{mg}} \cdot 100\% = 28.1\%$$

2,6-Diisopropylbenzoquinone (2c)



Safety

Table 23: Specifications for employed chemicals.

Substance	Cas	*MW*	*Price* Euro/g	GHS Hazard	GHS ranking	Specification
2,6-Diisopropylphenol	2078-54-8	178.27	0.71	harmful	4	100 g, 97%
Sulfuric Acid	7664-93-9	98.08	0.03	corrosive	4	2,5 L, 95-98% ACS reagent grade
Methanol	67-56-1	32.04	0.03	flammable, toxic, health hazard	1	2,5 L, >99.9%, HPLC
Water	7732-18-5	18.02	0.02	none	5	2.5 L, suitable for HPLC
Acetonitrile	75-05-8	41.05	0.1	flammable, harmful	4	2,5 L, ACS reagent, ≥99.5%
2,6-Diisopropylbenzoquinone	530-55-2	192.25	9300			Propofol Related Compound B*

Overall GHS: 3.4

*Most inexpensive option available at Sigma Aldrich. Similar price is asked by other suppliers.

Others:

$$AE = \frac{192.25\,\frac{g}{mol}}{192.25\,\frac{g}{mol}+2\cdot 2.02\frac{g}{mol}} \cdot 100\% = 97.7\%$$

$$Eco = \frac{1787925\,€ \cdot 90\%}{244\ €\cdot 100\%} = 6595$$

Graphical depiction of the eco factor in figure 4 of the article is divided by 1000 for better readability.

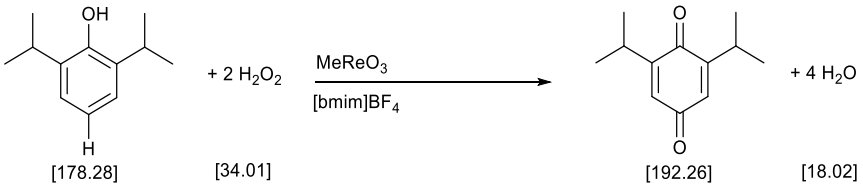
$$RME = \frac{0.977 \cdot 0.90}{1} \cdot 100\% = 89.7\%$$

$$EMY = \frac{1}{"0"} \cdot 100\% = 100\%$$

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 Bernini et. al was used for comparison.[19]



Safety

Table 24: Specifications for employed chemicals.

Substance	Cas	*MW*	*Price* Euro/g	GHS Hazard	GHS ranking	Specification
2,6-Diisopropylphenol	2078-54-8	178.27	0.71	harmful	4	100 g, 97%
[bmim]BF4	174501-65-6	226.02	0.93	toxic, environment	1	1 kg, ≥98%
Hydrogen peroxide	7601-90-3	34.01	0.09	Oxidising, corrosive, harmful	1	4 L, 50 wt. % in H_2O, stabilized
methyltrioxorhenium	70197-13-6	249.24	227	-	5	2 g, Re 71.0-76.0 %
2,6-Diisopropylbenzoquinone	530-55-2	192.25	9300	danger	4	Propofol Related Compound B*

Overall GHS: 2.8

Others:

$$AE = \frac{192.25\,\frac{g}{mol}}{192.25\,\frac{g}{mol}+4\cdot 18.02\frac{g}{mol}} \cdot 100\% = 72.7\%$$

$$Eco = \frac{1787925\,€ \cdot 82\%}{2408\ €\cdot 100\%} = 609$$

Graphical depiction of the eco factor in figure 4 of the article is divided by 1000 for better readability.

$$RME = \frac{0.727 \cdot 0.82}{3} \cdot 100\% = 19.9\%$$

$$EMY = \frac{192.25\ \text{mg}}{1041\ \text{mg}} \cdot 100\% = 18.5\%$$

1.6 Limitations of the Scope

In order to find suitable substrates for the electrochemical benzoquinone synthesis potential substrates were often subjected to electrolysis in a batch-type cell prior to isolation in continuous flow. The following section lists the determined NMR yields for the 1,4-benzoquinones and the unconverted starting materials for the batch experiments of substrates that were deemed unsuitable for the protocol. The conversion was either low or they underwent an unspecific oxidation. In case of 2-methoxyphenol we observed polymerisation, even at decreased substrate concentrations. In general, the synthesis in continuous flow gave superior yields of 1,4-benzoquinones in comparison to the batch electrolysis.

Table 25: Screening of unsuccessful substrates in a divided batch-type cell.

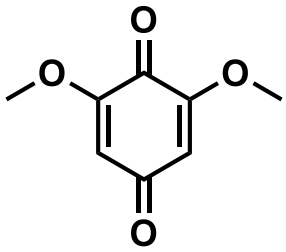
Entry	Substrate	Conversion / %	Yield(product) / %

1	2-methoxyphenoll[a]	100	0
2	*N*-(2,5-dimethoxyphenyl) acetamide	90	25
3	2,4-dimethoxy-1-(trifluoromethyl)benzene	20	0
4	1-chloro-3,5-dimethoxybenzene	33	1
5	1,5-dihydroxynaphthalene	100	0
6	5,6,7,8-tetrahydronaphthalene-1-ol	30	7
7	quinolin-8-ol	0	0
8	4-chloronaphthalen-1-ol	89	7
9	2,3-dimethylphenol	27	4
10	2-allyl-6-methoxyphenol	100	30

Electrolysis parameters: applied charge: 48 C (4 *F*); current: 15 mA; current density: 6 mA·cm^{-2}; temperature: 22 °C; anode: Ru-IrO_2 (Ti); cathode: Pt; anode area: 2.5 cm^2; divided: glass frit; 5 mL 1 m H_2SO_4 in MeCN +4.5 vol% H_2O +5 vol% MeOH; *c*(substrate) = 25 mm. [a]: *c*(substrate) = 12.5 mM.

1.7 Characterization of Isolated Compounds

1.7.1 2,6-Dimethoxycyclohexa-2,5-diene-1,4-dione (2a)



2,6-Dimethoxycyclohexa-2,5-diene-1,4-dione (**2a**) was synthesized according to general protocol 3, from 2,6-dimethoxyphenol (**1a**) (114.1 mg, 0.74 mmol, 1 eq.). The title compound (**2a**) was obtained as a yellow solid (112.0 mg, 0.67 mmol, 90%), after flash column chromatography (cyclohexane/ethyl acetate: 90:10 → 80:20→50:50).

2,6-Dimethoxycyclohexa-2,5-diene-1,4-dione (**2a**) was synthesized according to general protocol 3 in a 48 cm^2 flow electrolysis cell, from 2,6-dimethoxyphenol (**1a**) (1137.7 mg, 7.38 mmol, 1 eq.). The title compound (**2a**) was obtained as a yellow solid (1137.5 mg, 6.77 mmol, 92%), after flash column chromatography (cyclohexane/ethyl acetate: 90:10 → 80:20→50:50).

2,6-Dimethoxycyclohexa-2,5-diene-1,4-dione (**2a**) was synthesized according to general protocol 3, from 3,4,5-trimethoxyphenol (**3a**) (140.0 mg, 0.76 mmol, 1 eq.). The title compound (**2a**) was obtained as a yellow solid (119.0 mg, 0.71 mmol, 93%), after flash column chromatography (cyclohexane/ethyl acetate: 90:10 → 80:20→50:50).

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

Mp.: 254.7 – 255.5 °C (cyclohexane/ethyl acetate).

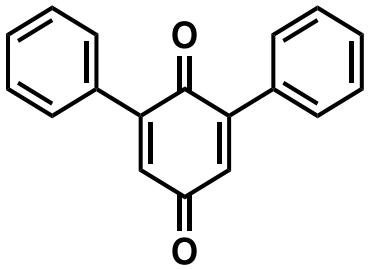
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85 (s, 2H, C*H*), 3.82 (s, 6H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.99, 176.83, 157.44, 107.56, 56.63 ppm.

HRMS (APCI+): *m*/*z* for $C_8H_9O_4$ $[M+H]^+$: calculated 169.0496; found: 169.0504.

The analytical data are in accordance with literature.[20,21]

1.7.2 2,6-Diphenylcyclohexa-2,5-diene-1,4-dione (2b)



2,6-Diphenylcyclohexa-2,5-diene-1,4-dione (**2b**) was synthesized according to general protocol 3, from 2,6-diphenylphenol (**1b**, 181.8 mg, 0.74 mmol, 1 eq.). The title compound (**2b**) was obtained as a bright orange solid (190.7 mg, 0.73 mmol, 99%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 95:5→85:15).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 20:1)

Mp.: 135.0 – 136.2 °C (cyclohexane/ethyl acetate).

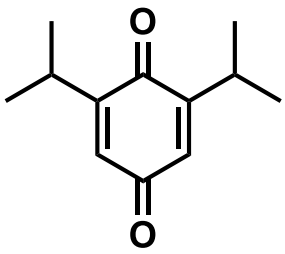
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (m, 4H), 7.49 – 7.43 (m, 6H), 6.93 (s, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.75, 186.26, 146.63, 133.31, 132.78, 130.19, 129.54, 128.64 ppm.

HRMS (APCI+): *m*/*z* for $C_{18}H_{13}O_2$ $[M+H]^+$: calculated 261.0910; found: 261.0904.

The analytical data are in accordance with literature.[22,23]

1.7.3 2,6-Bis(1-methylethyl)-cyclohexa-2,5-diene-1,4-dione (2c)



2,6-Bis(1-methylethyl)-cyclohexa-2,5-diene-1,4-dione (**2c**) was synthesized according to general protocol 3, from 2,6-bis(1-methylethyl)-phenol (**1c**, 87.7 mg, 0.49 mmol, 1 eq.). The title compound (**2c**) was obtained as a yellow liquid (96.7 mg, 0.44 mmol, 90%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 95:5→85:15).

***R*$_f$:** 0.4 (cyclohexane/ethyl acetate = 20:1)

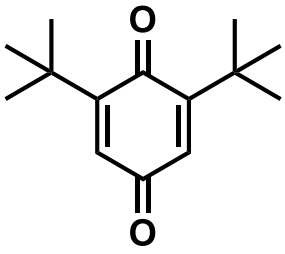
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.47 (s, 2H), 3.07 (sept., *J* = 6.9 Hz, 2H), 1.13 (d, *J* = 6.8 Hz, 12H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.89, 187.02, 155.53, 129.92, 27.06, 21.63 ppm.

HRMS (APCI+): *m*/*z* for $C_{12}H_{17}O_2$ $[M+H]^+$: calculated 193.1223; found: 193.1220.

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

1.7.4 2,6-Bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (2d)



2,6-Bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2d**) was synthesized according to general protocol 3, from 2,6-bis-(1,1-dimethylethyl)-phenol (**1d**, 152.7 mg, 0.74 mmol, 1 eq.). The title compound (**2d**) was obtained as an orange solid (122.3 mg, 0.56 mmol, 75%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→90:10).

2,6-Bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2d**) was synthesized according to general protocol **3**, from 2,6-bis-(1,1-dimethylethyl)-4-methoxyphenol (**3d**, 174.9 mg, 0,74 mmol, 1 eq.). The title compound (**2d**) was obtained as an orange solid (142.2 mg, 0.65 mmol, 88%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→98:2→95:5).

***R*$_f$:** 0.3 (cyclohexane/ethyl acetate = 20:1)

Mp.: 63.5 – 65.7 °C (cyclohexane/ethyl acetate).

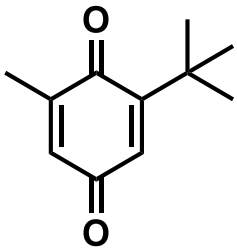
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.51 (s, 2H, *H*-3), 1.28 (s, 18H, C*H*$_3$) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 189.27 (*C*-4), 187.96 (*C*-1), 158.07 (*C*-2), 130.30 (*C*-3), 35.73 (*C*$(CH_3)_3$), 29.53 (*C*H_3) ppm.

HRMS (APCI+): *m*/*z* for $C_{14}H_{21}O_2[M+H]^+$: calculated:221.1536; found: 221.1500

The analytical data are in accordance with literature.[25,26]

1.7.5 2-(1,1-dimethylethyl)-6-methylcyclohexa-2,5-diene-1,4-dione (2e)



2-(1,1-dimethylethyl)-6-methylcyclohexa-2,5-diene-1,4-dione (**2e**) was synthesized according to general protocol 3, from 2-(1,1-dimethylethyl)-6-methylphenol (**1e**, 250.51 mg, 1.53 mmol, 1 eq.). The title compound (**2e**) was obtained as a yellow oil (206,2 mg, 1.16 mmol, 76%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→90:10).

***R*$_f$:** 0.4 (cyclohexane/ethyl acetate = 9:1)

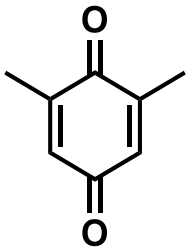
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.57 – 6.50 (m, 2H), 2.04 (d, *J* = 1.5 Hz, 3H), 1.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.56, 187.86, 156.22, 147.62, 132.21, 131.67, 35.44, 29.37, 16.54 ppm.

HRMS (APCI-): *m*/*z* for $C_{11}H_{14}O_2$ $[M]^-$: calculated: 178.0994; found:178.0989

The published NMR data for this compound is lacking the quaternary carbon of the 1,1-dimethylethyl group (35.44 ppm) in the ^{13}C spectra. Besides this the analytical data are in accordance with literature.[19]

1.7.6 2,6-Dimethylcyclohexa-2,5-diene-1,4-dione (2f)



2,6-Dimethylcyclohexa-2,5-diene-1,4-dione (**2f**) was synthesized according to general protocol 3, from 2,6-dimethylphenol (**1f**, 135.6 mg, 1.11 mmol, 1 eq.). The title compound (**2f**) was obtained as a yellow solid (96.7 mg, 0.71 mmol, 64%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→90:10).

***R*$_f$:** 0.3 (cyclohexane/ethyl acetate = 9:1)

Mp.: 71.5 – 72.3°C (cyclohexane/ethyl acetate).

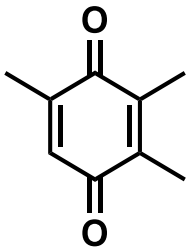
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.57 – 6.53 (m, 2H), 2.05 (d, *J* = 1.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.41, 187.86, 145.95, 133.45, 16.21 ppm.

HRMS (APCI-): *m*/*z* for $C_8H_8O_2$ $[M]^-$: calculated: 136.0524; found: 136.0521

The analytical data are in accordance with literature.[27–29]

1.7.7 2,3,5-Trimethylcyclohexa-2,5-diene-1,4-dione (2g)



2,3,5-Trimethylcyclohexa-2,5-diene-1,4-dione (**2g**) was synthesized according to general protocol 3, from 2,3,6-trimethylbenzene (**1g**, 227.8 mg, 2.04 mmol, 1 eq.). The title compound

(**2g**) was obtained as a yellow solid (197.9 mg, 1.32 mmol, 65%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→95:5).

2,3,5-Trimethylcyclohexa-2,5-diene-1,4-dione (**2g**) was synthesized according to general protocol 3, from 1,4-dimethoxy-2,3,5-trimethylbenzene (**3g**, 198.3 mg, 1.10 mmol, 1 eq.). The title compound (**2g**) was obtained as a yellow solid (116.7 mg, 0.78 mmol, 85%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→95:5).

***R_f*:** 0.5 (cyclohexane/ethyl acetate = 20:1)

Mp.: 27.6 – 29.1 °C (cyclohexane/ethyl acetate).

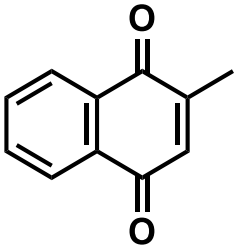
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.55 (q, *J* = 1.6 Hz, 1H), 2.06 – 1.99 (m, 9H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.05, 187.67 (*C*-4), 145.48 (*C*CH_3), 141.05 (*C*CH_3), 140.88 (*C*CH_3), 133.21 (*C*H), 16.05 (*C*H_3), 12.51 (*C*H_3), 12.21 (*C*H_3).

HRMS (APCI+): m/z for $C_9H_{11}O_2$ $[M+H]^+$: calculated 151.0754; found: 151.0745

The analytical data are in accordance with literature.[21,30,31]

1.7.8 2-Methylnaphthalene-1,4-dione (2h) (2-Methylnaphthoquinone) (2h)



2-Methylnaphthalene-1,4-dione (**2h**) was synthesized according to general protocol 3, from 2-methylnaphthol **1h**, 117.1 mg, 0.74 mmol, 1 eq.). The title compound (**2h**) was obtained as a yellow solid (101.0 mg, 0.59 mmol, 80%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→85:15→50:50).

***R_f*:** 0.4 (cyclohexane/ethyl acetate = 7:1)

Mp.: 102.3 – 103.2°C (cyclohexane/ethyl acetate).

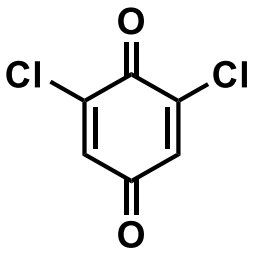
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 – 8.02 (m, 2H), 7.72 (m, 2H), 6.84 (q, J = 1.6 Hz, 1H), 2.20 (d, J = 1.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 185.71, 185.14, 148.32, 135.83, 133.79, 133.74, 132.40, 132.31, 126.66, 126.23, 16.62.ppm.

HRMS (APCI-): *m*/*z* for $C_{11}H_8O_2$ $[M]^-$: calculated: 172.0529; found: 172.0532

The analytical data are in accordance with literature.[28,29]

1.7.9 2,6-Dichlorocyclohexa-2,5-diene-1,4-dione (2i)



2,6-Dichlorocyclohexa-2,5-diene-1,4-dione (**2i**) was synthesized according to general protocol 3, from 2,4,6-trichlorophenol (**1i**, 146.1 mg, 0.74 mmol, 1 eq.). The title compound (**2i**) was obtained as a yellow solid (96.7 mg, 0.55 mmol, 74%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 95:5→85:15).

***R*$_f$:** 0.3 (cyclohexane/ethyl acetate = 20:1).

Mp.: 116.8 – 118.2 °C (cyclohexane/ethyl acetate).

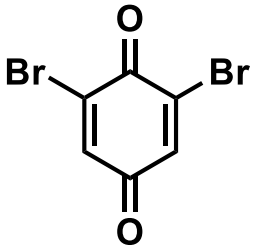
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03 (s, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.65, 172.90, 143.77, 133.99 ppm.

HRMS (APCI-): *m*/*z* for $C_6H_2Cl_2{}^{35}O_2[M]^-$: calculated 175.9432, found: 175.9434.

The analytical data are in accordance with literature.[32]

1.7.10 2,6-Dibromocyclohexa-2,5-diene-1,4-dione (2j)



2,6-Dibromocyclohexa-2,5-diene-1,4-dione (**2j**) was synthesized according to general protocol 3, from 2,4,6-tribromophenol (**1j**, 244.1 mg, 0.74 mmol, 1 eq.). The title compound

(**2j**) was obtained as an orange solid (159.4 mg, 0.60 mmol, 81%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 85:15→70:30).

***R*$_f$:** 0.6 (cyclohexane/ethyl acetate = 5:1)

Mp.: 126.5 – 128.1 °C (cyclohexane/ethyl acetate).

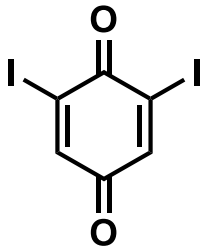
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (s, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.54, 172.57, 138.37, 135.82 ppm.

HRMS (APCI-): *m*/*z* for $C_6H_2Br_2{}^{79}O_2[M]^-$: calculated 263.8422, found: 263.8418.

The analytical data are in accordance with literature.[20,33]

1.7.11 2,6-Diiodocyclohexa-2,5-diene-1,4-dione (2k)



2,6-Diiodocyclohexa-2,5-diene-1,4-dione (**2k**) was synthesized according to general protocol 3, from 2,4,6-triidophenol (**1k**, 235.9 mg, 0.50 mmol, 1 eq.). In deviation from the standard procedure, the concentration of the starting material has been lowered to 17.1 mm, due to limited solubility. The title compound (**2k**) was obtained as an orange solid (147.7 mg, 0.41 mmol, 82%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 95:5→85:15).

***R*$_f$:** 0.3 (cyclohexane/ethyl acetate = 20:1)

Mp.: 176.9 – 177.7 °C, decomposition (cyclohexane/ethyl acetate).

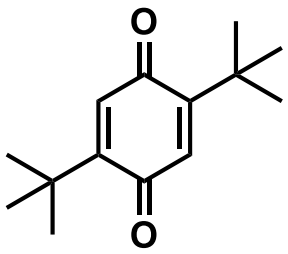
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (s, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.05, 173.73, 146.44, 114.29 ppm.

HRMS (APCI-): *m*/*z* for $C_6H_2I_2{}^{127}O_2[M]^-$: calculated 359.8144, found: 359.8139.

For this compound, no NMR data have been published. The measured melting point is in agreement with literature.[34]

1.7.12 2,5-Bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (2l)



2,5-Bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2l**) was synthesized according to general protocol 3 from 2,5-bis-(1,1-dimethylethyl)-4-methoxyphenol (**3l**, 174.9 mg, 0,74 mmol, 1 eq.). The title compound (**2l**) was obtained as a yellow solid (137.7 mg, 0.63 mmol, 85%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→98:2→95:5).

***R*$_f$:** 0.3 (cyclohexane/ethyl acetate = 20:1)

Mp.: 148.0 – 150.7°C (cyclohexane/ethyl acetate).

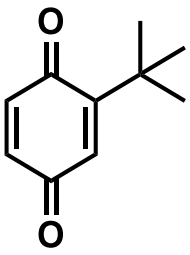
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.48 (s, 2H), 1.27 (s, 18 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.70, 154.46, 133.76, 34.80, 29.25 ppm.

HRMS (APCI+): *m/z* for $C_{14}H_{21}O_2[M+H]^+$: calculated: 221.1536; found: 221.1536

The analytical data are in accordance with literature.[35,36]

1.7.13 2-(1,1-Dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (2m)



2-(1,1-Dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2m**) was synthesized according to general protocol 3 from 2-(1,1-dimethylethyl)-4-methoxyphenol (**3m**, 277.8 mg, 1.54 mmol, 1 eq.). The title compound (**2m**) was obtained as a yellow solid (154.4 mg, 0.94 mmol, 61%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 90:10).

***R*$_f$:** 0.5 (cyclohexane/ethyl acetate = 9:1)

Mp.: 49.9 – 51.8 °C (cyclohexane/ethyl acetate).

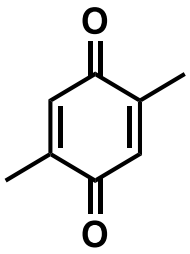
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68 (d, *J* = 1.2 Hz, 2H), 6.60 (t, *J* = 1.2 Hz, 1H), 1.28 (s, 9H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.17, 187.47, 156.07, 138.68, 134.93, 131.52, 35.27, 29.10 ppm.

HRMS (APCI+): *m*/*z* for $C_{10}H_{13}O_2$ $[M+H]^+$: calculated 165.0910; found: 165.0904.

The analytical data are in accordance with literature.[37,38]

1.7.14 2,5-Dimethylcyclohexa-2,5-diene-1,4-dione (2n)



2,5-Dimethylcyclohexa-2,5-diene-1,4-dione (**2n**) was synthesized according to general protocol 3, from 4-methoxy-2,5-dimethylphenol (**3n**, 156.8 mg, 1.03 mmol, 1 eq.). The title compound (**2n**) was obtained as a yellow solid (139.0 mg, 1.02 mmol, 99%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 90:10).

***R*$_f$:** 0.4 (cyclohexane/ethyl acetate = 9:1)

Mp.: 122.0 – 122.9°C (cyclohexane/ethyl acetate).

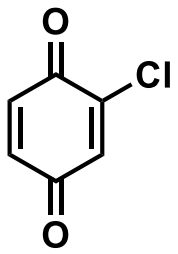
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59 (q, *J* = 1.6 Hz, 2H), 2.03 (d, *J* = 1.6 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.21, 145.95, 133.52, 15.66 ppm.

HRMS (APCI-): *m*/*z* for $C_8H_8O_2$ $[M]^-$: calculated 136.0524; found: 136.0522.

The analytical data are in accordance with literature.[27,29]

1.7.15 2-Chlorocyclohexa-2,5-diene-1,4-dione (2o)



2-Chlorocyclohexa-2,5-diene-1,4-dione (**2o**) was synthesized according to general protocol 3, from 4-methoxy-2-chlorophenol (**3o**, 117.0 mg, 0.74mmol, 1 eq.). The title compound (**2o**) was obtained as a yellow solid (75.4 mg, 0.53 mmol, 71%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 90:10).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 9:1)

Mp.: 54.3 – 54.7°C (cyclohexane/ethyl acetate).

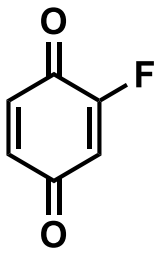
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (d, *J* = 2.4 Hz, 1H), 6.93 (d, *J* = 10.1 Hz, 1H), 6.82 (dd, *J* = 10.1, 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 184.97, 179.27, 144.20, 136.82, 136.08, 133.75.ppm.

HRMS (APCI-): *m*/*z* for $C_6H_3Cl^{35}O_2$ $[M]^-$: calculated: 141.9822; found: 141.9815.

The analytical data are in accordance with literature.[39,40]

1.7.16 2-Fluorocyclohexa-2,5-diene-1,4-dione (2p)



2-Fluorocyclohexa-2,5-diene-1,4-dione (**2p**) was synthesized according to general protocol 3, from 4-methoxy-2-fluorophenol (**3p**, 104.9 mg, 0.74mmol, 1 eq.). The title compound (**2p**) was obtained as a yellow solid (83.9 mg, 0.67 mmol, 90%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 90:10).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 9:1)

Mp.: 80.4 – 81.6 °C (cyclohexane/ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 – 6.76 (m, 2H), 6.50 – 6.42 (m, 1H).

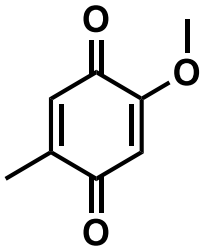
^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.40 (m, 1F)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.20 (d, *J* = 13.9 Hz), 179.42 (d, *J* = 24.2 Hz), 161.35, 134.61, 115.48.

HRMS (APCI-): *m*/*z* for $C_6H_3FO_2$ $[M]^-$: calculated: 126.0117; found: 126.0115.

The analytical data are in accordance with literature.[41,42]

1.7.17 2-Methoxy-5-methylcyclohexa-2,5-diene-1,4-dione (2q)



2-Methoxy-5-methylcyclohexa-2,5-diene-1,4-dione (**2q**) was synthesized according to general protocol 3, from 1,2,4-trimethoxy-5-methylbenzene (**3q**, 224.1 mg, 1.23 mmol, 1 eq.). The title compound (**2q**) was obtained as a yellow solid (163.5 mg, 1.08 mmol, 88%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 85:15→70:30).

***R*$_f$:** 0.2 (cyclohexane/ethyl acetate = 5:1)

Mp.: 169.9 – 171.9 °C, decomposition (cyclohexane/ethyl acetate).

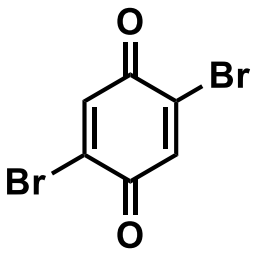
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.55 (q, *J* = 1.7 Hz, 1H), 5.92 (s, 1H), 3.81 (s, 3H), 2.06 (d, *J* = 1.6 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.81, 182.27, 158.88, 147.03, 131.41, 107.72, 56.36, 15.92 ppm.

HRMS (APCI+): *m*/*z* for $C_8H_9O_3[M+H]^+$: calculated 153.0552, found: 153.0555.

The analytical data are in accordance to literature.[21,43]

1.7.18 2,5-Dibromocyclohexa-2,5-diene-1,4-dione (2r)



2,5-Dibromocyclohexa-2,5-diene-1,4-dione (**2r**) was synthesized according to general protocol 3, from 1,4-dibromo-2,5-dimethoxybenzene (**3r**, 218.4 mg, 0.74 mmol, 1 eq.). The title compound (**2r**) was obtained as an orange solid (179.3 mg, 0.67 mmol, 91%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 90:10).

***R*$_f$:** 0.4 (cyclohexane/ethyl acetate = 9:1)

Mp.: 188.2 – 189.3 °C, decomposition (cyclohexane/ethyl acetate).

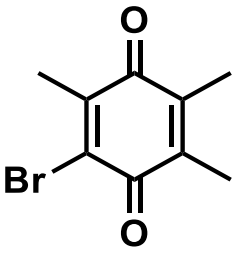
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (s, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.13, 137.96, 137.22.

HRMS (APCI-): *m*/*z* for $C_6H_2Br_2{}^{79}O_2[M]^-$: calculated 263.8422, found: 263.8418.

The analytical data are in accordance to literature.[29]

1.7.19 2-Bromo-3,5,6-trimethylcyclohexa-2,5-diene-1,4-dione (2s)



2-Bromo-3,5,6-trimethylcyclohexa-2,5-diene-1,4-dione (**2s**) was synthesized according to general protocol 3, from 1-bromo-2,5-dimethoxy-3,4,6-trimethylbenzene (**2s**, 191.3 mg, 0.74 mmol, 1 eq.). The title compound (**2s**) was obtained as a yellow solid (150.9 mg, 0.66 mmol, 89%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0 → 90:10).

***R*$_f$:** 0.5 (cyclohexane/ethyl acetate = 9:1)

Mp.: 78.3 – 79.1°C (cyclohexane/ethyl acetate).

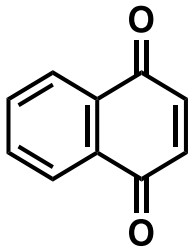
^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22 (s, 3H), 2.07 (dq, *J* = 14.5, 1.3 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 184.51, 179.66, 145.82, 141.09, 140.85, 135.67, 17.28, 13.36, 12.83 ppm.

HRMS (APCI-): *m*/*z* for $C_{10}H_9Br^{79}O_2$ $[M]^-$: calculated 227.9786; found: 227.9789.

The analytical data are in accordance with literature.[44,45]

1.7.20 Naphthalene-1,4-dione (Naphthoquinone) (2t)



Naphthalene-1,4-dione (**2t**) was synthesized according to general protocol 3, from 1,4-dimethoxynaphthalene (**3t**, 139.3 mg, 0,74 mmol, 1 eq.). The title compound (**3t**) was obtained as a light-yellow solid (85.4 mg, 0.54 mmol, 73%), after flash column chromatography (cyclohexane/ethyl acetate: 100:0→95:5→85:15).

***R_f*:** 0.2 (cyclohexane/ethyl acetate = 20:1)

Mp.: 121.0 – 123.4 °C (cyclohexane/ethyl acetate).

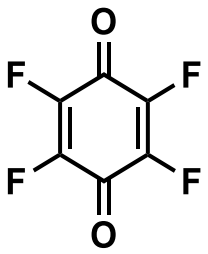
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 – 8.05 (m, 2H), 7.81 – 7.72 (m, 2H), 6.99 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 185.20, 138.83, 134.09, 132.06, 126.57 ppm.

HRMS (APCI+): *m*/*z* for $C_{10}H_7O_2$ $[M+H]^+$: calculated: 159.0441; found: 159.0442

The analytical data are in accordance with literature.[46–48]

1.7.21 2,3,5,6-Tetrafluorocyclohexa-2,5-diene-1,4-dione (2u)



2,3,5,6-Tetrafluorocyclohexa-2,5-diene-1,4-dione (**2u**) was synthesized according to general protocol 3, from 2,3,5,6-tetrafluoro-benzene-1,4-diol (**4u**, 134.7 mg, 0,74 mmol, 1 eq.). After work up, the crude product was dissolved in cyclohexane and filtered. The solvent was removed *in vacuo*. The title compound (**2u**) was obtained as a yellow solid (100.0 mg, 0.56 mmol, 76%).

Mp.: 172.8 – 174.4 °C, sublimation (cyclohexane).

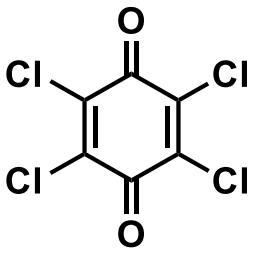
^{19}F NMR (376 MHz, $CDCl_3$): δ = ‑142.79 (s, 4F).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.98, 142.93 (d, $^1J_{C,F}$ = 287.1 Hz) ppm.

HRMS (APCI-): *m*/*z* for $C_6F_4O_2$ $[M]^-$: calculated 179.9834; found: 179.9836.

The analytical data are in accordance with literature.[41]

1.7.22 2,3,5,6-Tetrachlorocyclohexa-2,5-diene-1,4-dione (2v)



2,3,5,6-Tetrachlorocyclohexa-2,5-diene-1,4-dione (**2v**) was synthesized according to general protocol 3, from 2,3,5,6-tetrachloro-benzene-1,4-diol (**4v**, 203.3 mg, 0,82 mmol, 1 eq.). The crude product was dissolved in cyclohexane and filtered. The solvent was removed *in vacuo*. The title compound (**4v**) was obtained as a yellow solid (195.3 mg, 0.79 mmol, 96%).

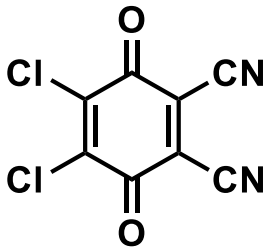
Mp.: 290.5 – 291.3 °C, (cyclohexane).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 169.69, 139.49 ppm.

HRMS (APCI-): *m*/*z* for $C_6H_2Cl_2{}^{35}O_2[M]^-$: calculated 243.8652, found: 243.8655.

The analytical data are in accordance with literature.[49,50]

1.7.23 2,3-Dichloro-5,6-dicyanocyclohexa-2,5-diene-1,4-dione (2w)



2,3-Dichloro-5,6-dicyanocyclohexa-2,5-diene-1,4-dione (**2w**) was synthesized according to general protocol 3, from 4,5-Dichloro-3,6-dihydroxyphthalonitrile (**4w**, 185.9 mg, 0.82 mmol, 1 eq.). In deviation of the general protocol the pH value was not adjusted to 7 in the work up to minimize the risk of hydrolysis and related HCN evolution.[51] The solvent was removed *in vacuo*. The title compound (**4w**) was obtained as a yellow solid (181.1 mg, 0.80 mmol, 98%).

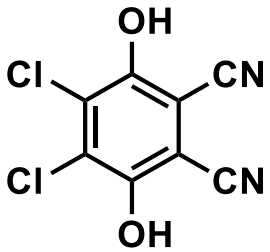
Mp.: 214.8 – 217.3 °C (cyclohexane).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.70, 142.44, 127.45, 109.11 ppm.

HRMS (APCI-): *m*/*z* for $C_8Cl_2{}^{35}N_2O_2[M]^-$: calculated 225.9337, found: 225.9335.

The analytical data are in accordance with literature.[52,53]

1.7.24 4,5-Dichloro-3,6-dihydroxyphthalonitrile (4w)



4,5-Dichloro-3,6-dihydroxyphthalonitrile (**4w**) was synthesized according to a modified procedure by *Braude et al*.[2]

1,2,3,4-tetrahydronaphthalene (0.65 g, 4.92 mmol, 1 eq.) was dissolved in toluene (5 mL) and 2,3-Dichloro-5,6-dicyanocyclohexa-2,5-diene-1,4-dione (1.41 g, 5.74 mmol, 0.6 eq.) were

added under stirring. The solution was heated, under reflux, for 45 minutes. A second portion of 2,3-Dichloro-5,6-dicyanocyclohexa-2,5-diene-1,4-dione (1.00 g, 4.07 mmol, 0.4 eq.) was added. The solution was refluxed for another 45 minutes. Afterwards cyclohexane (25 mL) was added, and the precipitate was filtered with suction. The residue was washed with two portions of cyclohexane (15 mL) and dried under reduced pressure. The title compound (**4w**) was obtained as an off-white solid (1.86 g, 7.50 mmol, 83%).

Mp.: 264.6 – 265.1 °C (cyclohexane).

^{1}H NMR (400 MHz, Acetone-d_6): δ = 10.21 (br, 2H) ppm.

^{13}C NMR (101 MHz, DMSO-d_6): δ = 150.83, 129.17, 113.71, 101.66 ppm.

HRMS (ESI+): *m*/*z* for $C_8H_2Cl^{35}{}_2N_2NaO_2$ $[M+Na]^+$: calculated 250.9385; found: 250.9398.

The analytical data are in accordance with literature. We were unable to locate a ^{1}H NMR spectra for this compound and have therefore provided one.[54,55]

1.8 NMR Spectra

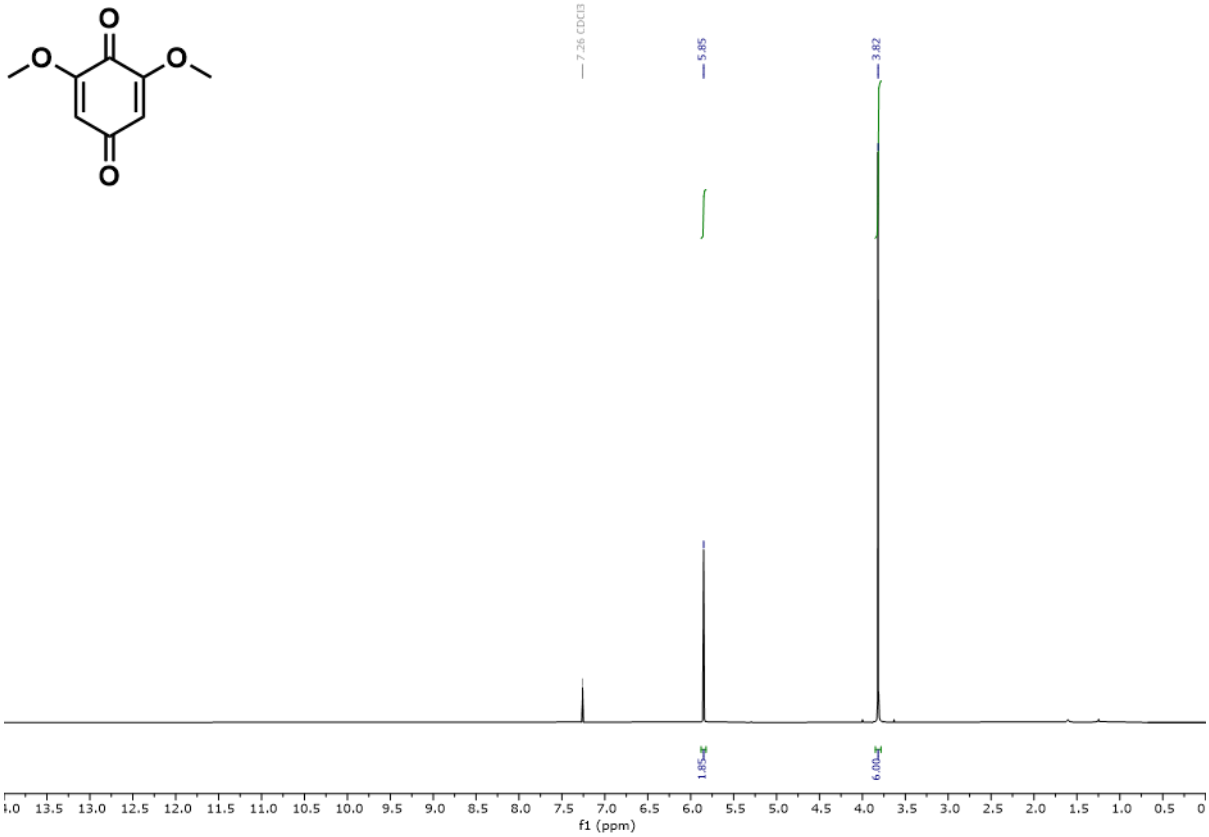


Figure 15: ^{1}H NMR (400 MHz) 2,6-dimethoxycyclohexa-2,5-diene-1,4-dione (**2a**) in $CDCl_3$ at 298 K.

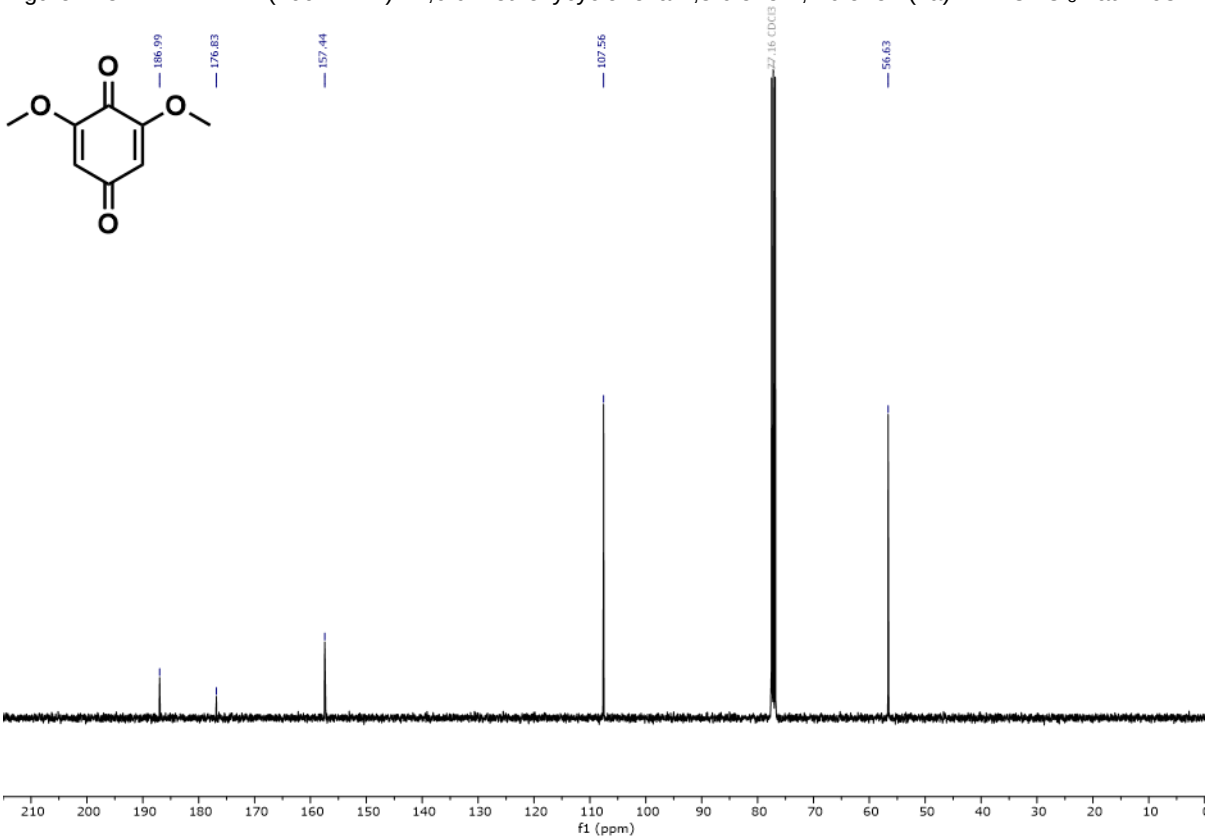


Figure 16: ^{13}C NMR (101 MHz) 2,6-dimethoxycyclohexa-2,5-diene-1,4-dione (**2a**) in $CDCl_3$ at 298 K.

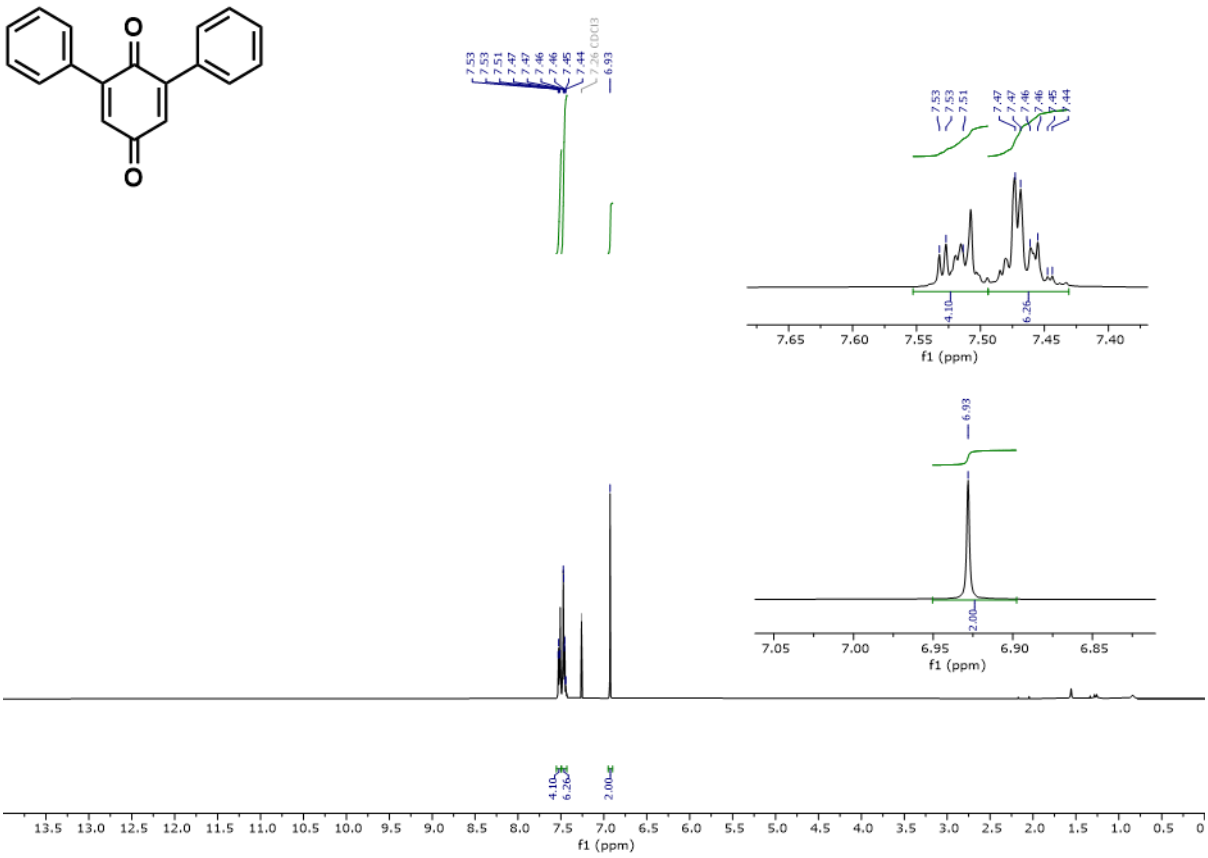


Figure 17: ^{1}H NMR (400 MHz) 2,6-diphenylcyclohexa-2,5-diene-1,4-dione (**2b**) in $CDCl_3$ at 298 K.

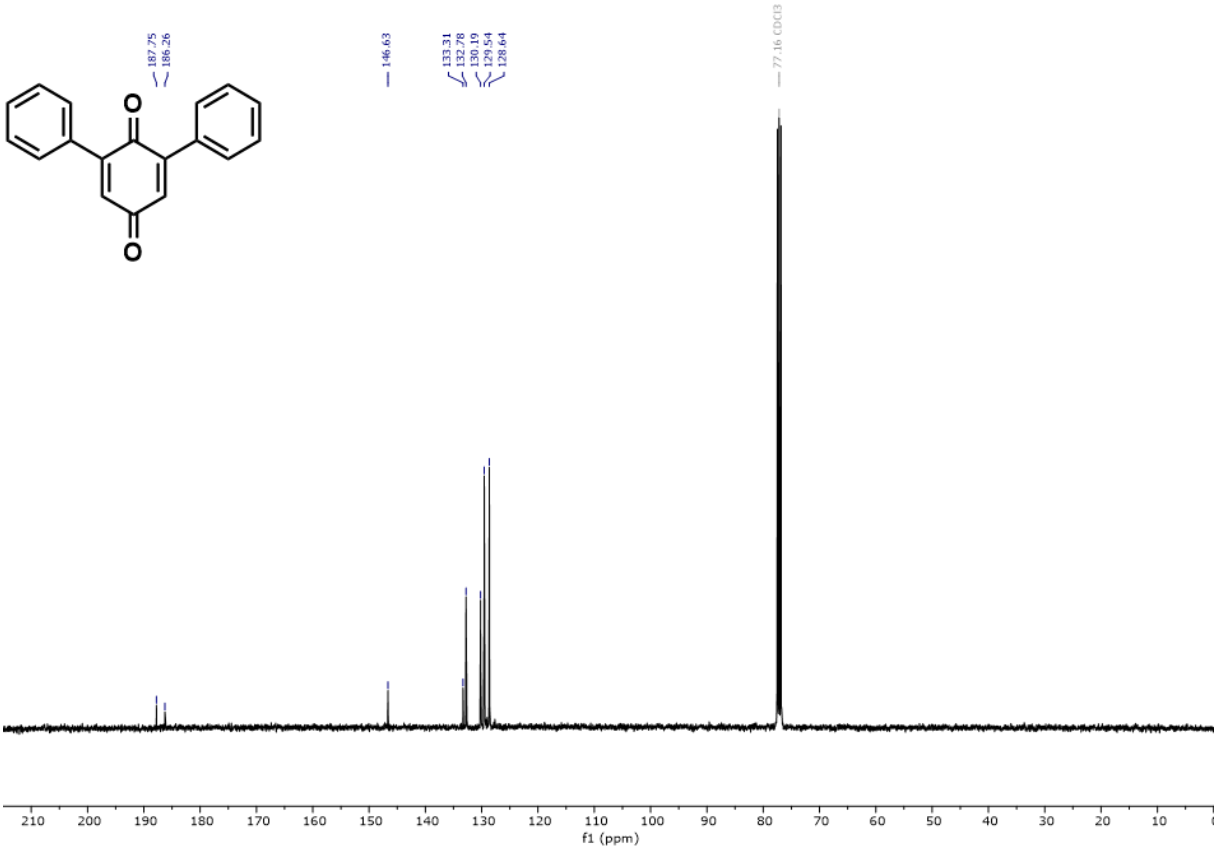


Figure 18: ^{13}C NMR (101 MHz) 2,6-diphenylcyclohexa-2,5-diene-1,4-dione (**2b**) in $CDCl_3$ at 298 K.

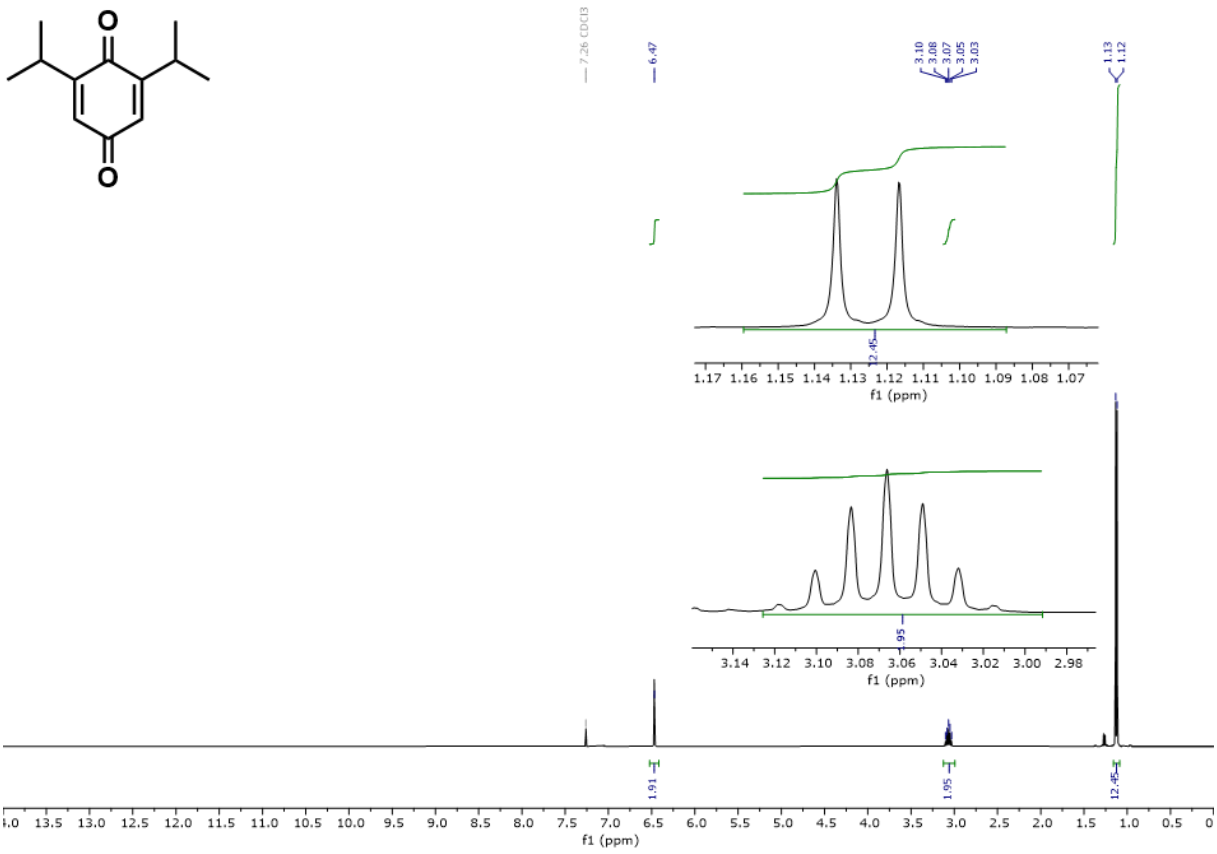


Figure 19: ^{1}H NMR (400 MHz) 2,6-bis(1-methylethyl)-cyclohexa-2,5-diene-1,4-dione (**2c**) in $CDCl_3$ at 298 K**.**

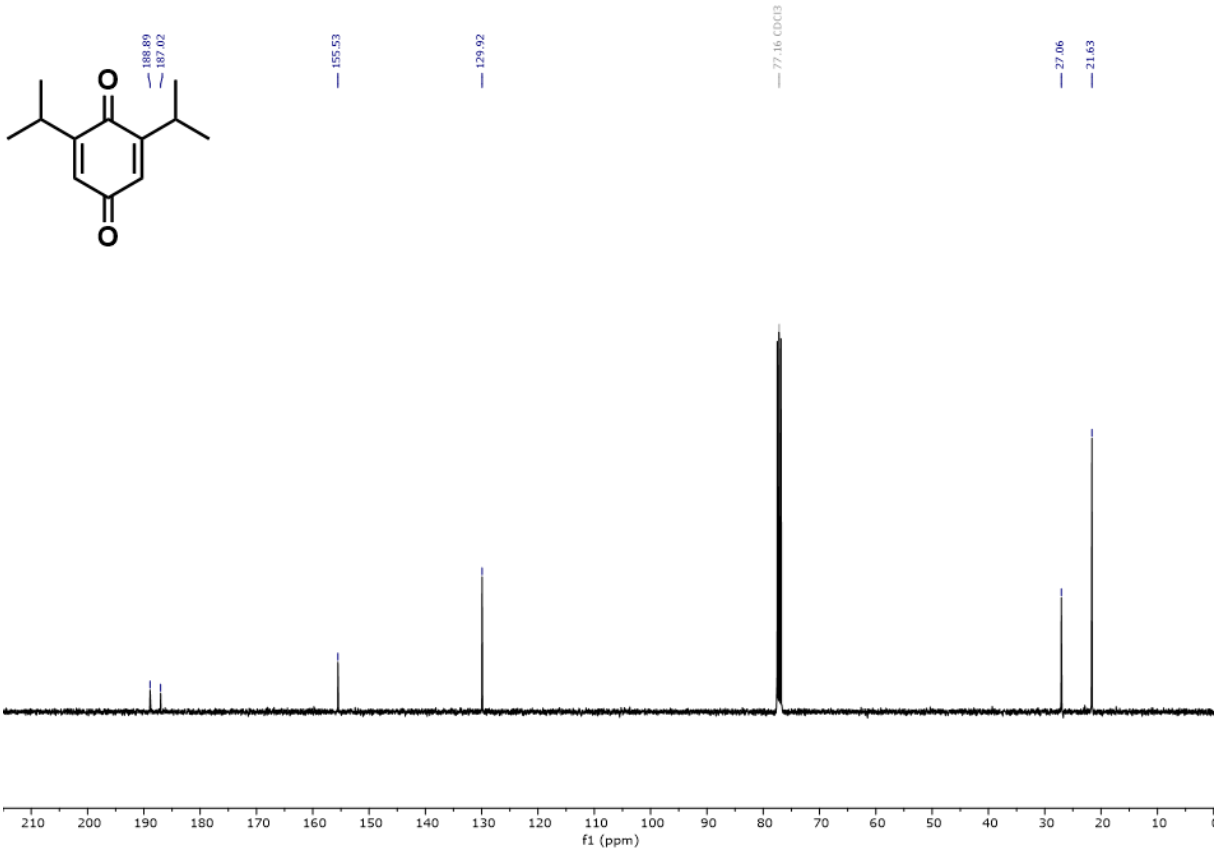


Figure 20: ^{13}C NMR (101 MHz) 2,6-bis(1-methylethyl)-cyclohexa-2,5-diene-1,4-dione (**2c**) in $CDCl_3$ at 298 K.

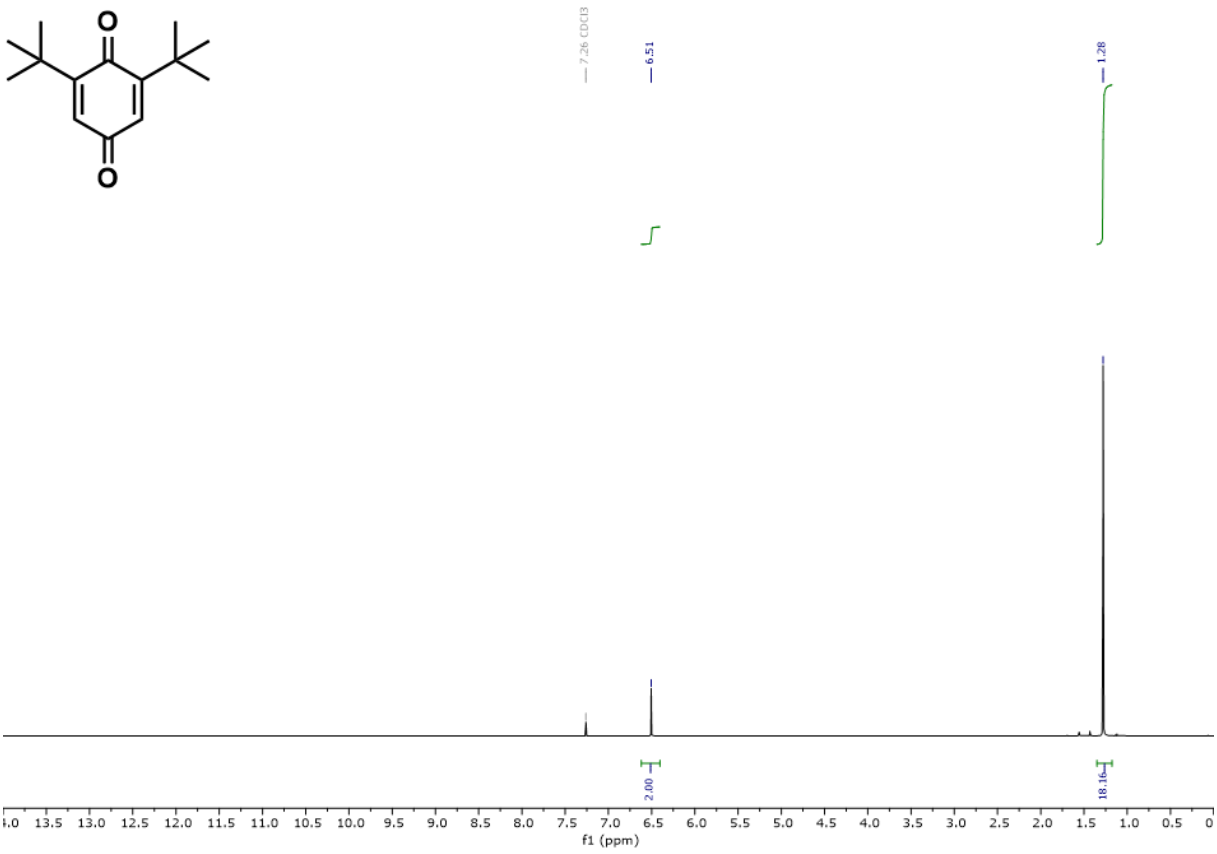


Figure 21: ^{1}H NMR (400 MHz) 2,6-bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2d**) in $CDCl_3$ at 298 K.

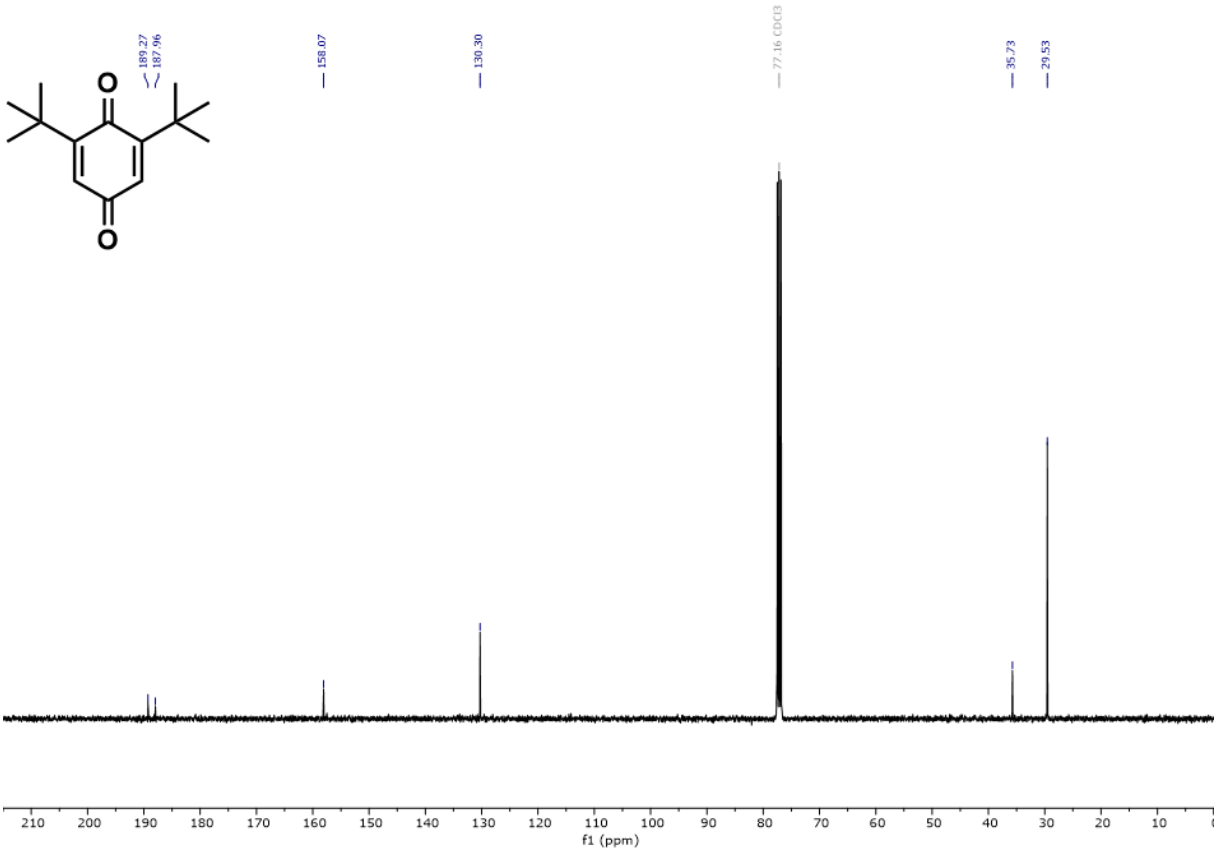


Figure 22: ^{13}C NMR (101 MHz) 2,6-bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2d**) in $CDCl_3$ at 298 K.

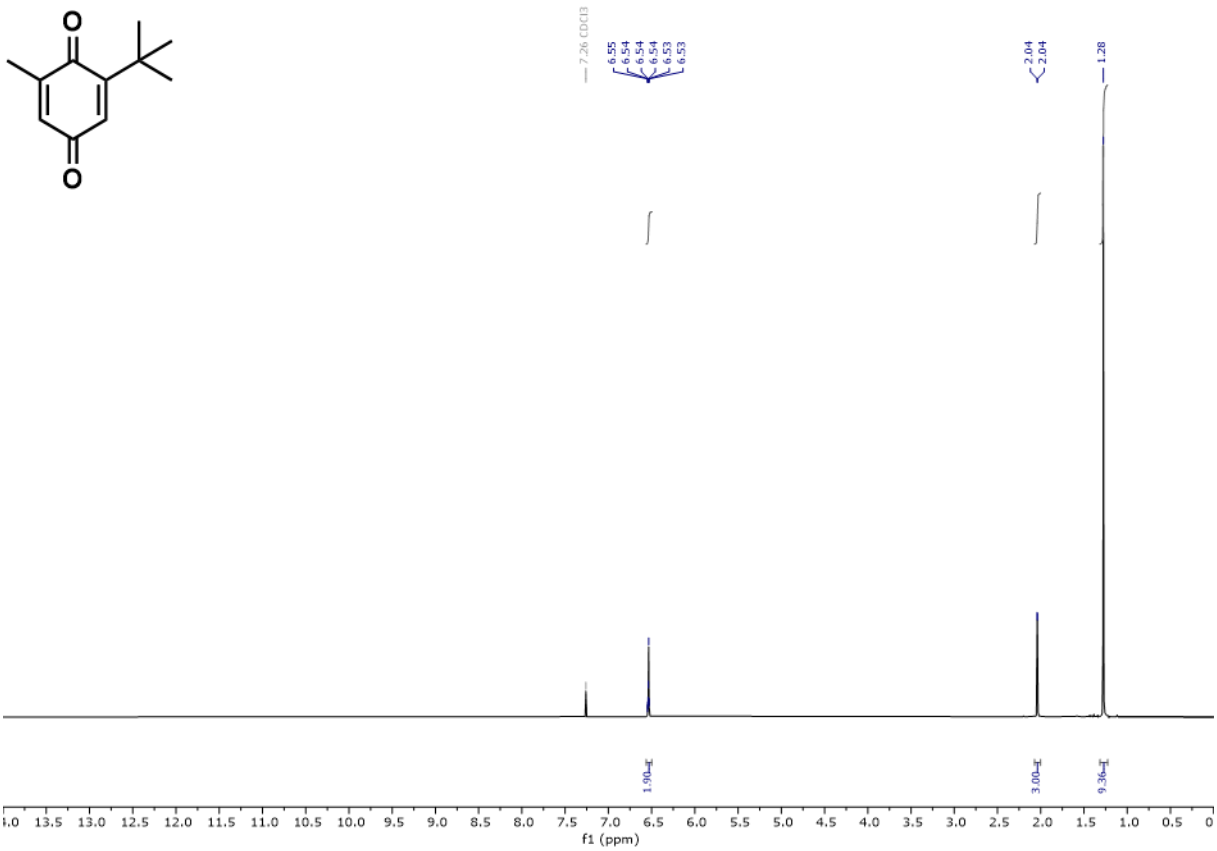


Figure 23: ^{1}H NMR (400 MHz) 2-(1,1-dimethylethyl)-6-methylcyclohexa-2,5-diene-1,4-dione (**2e**) in $CDCl_3$ at 298 K.

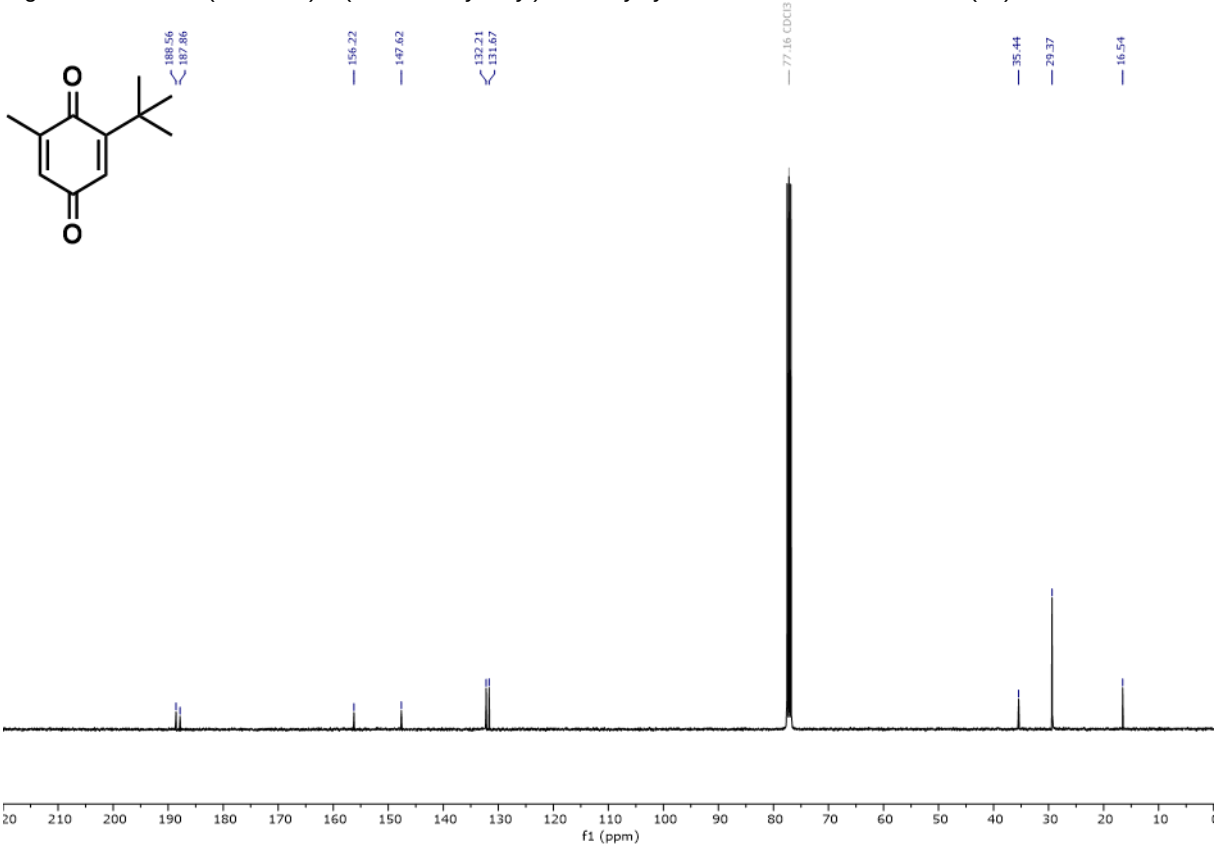


Figure 24: ^{13}C NMR (101 MHz) 2-(1,1-dimethylethyl)-6-methylcyclohexa-2,5-diene-1,4-dione (**2e**) in $CDCl_3$ at 298 K

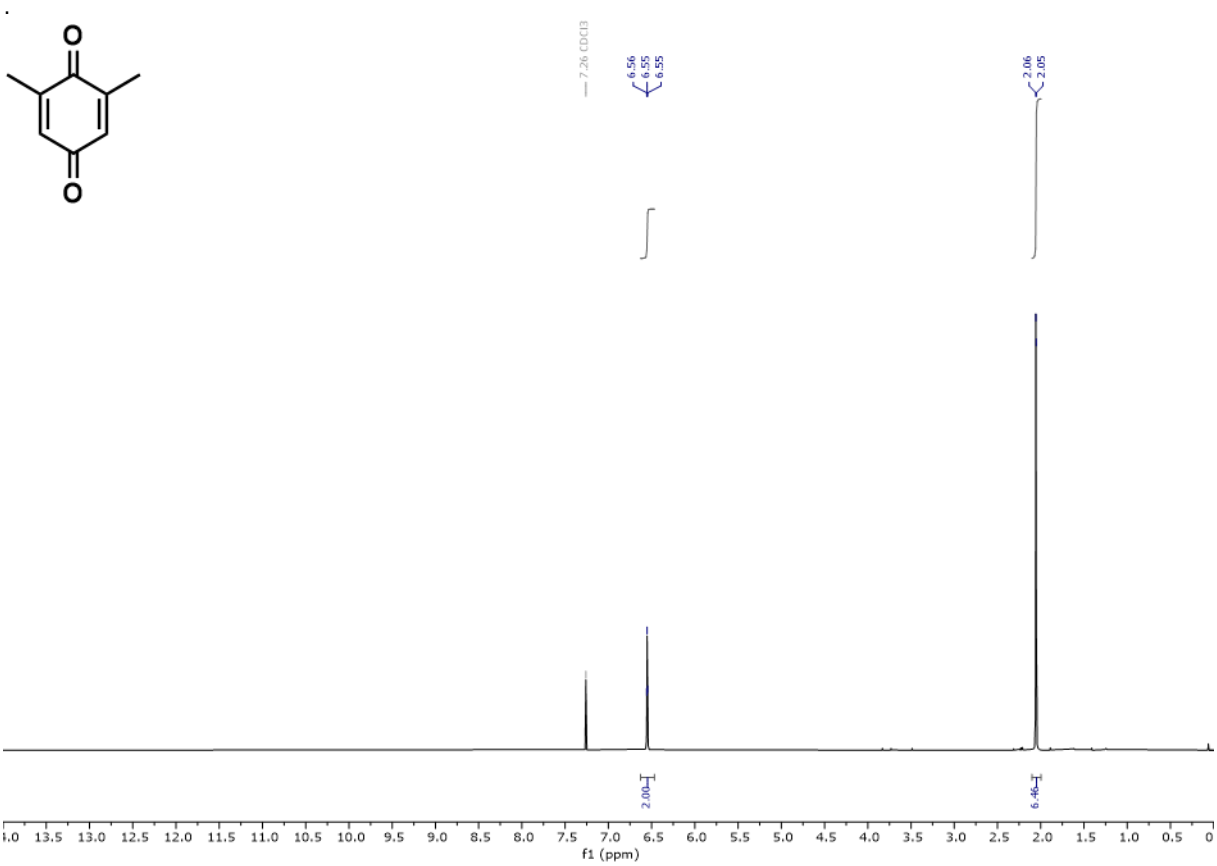


Figure 25: ^{1}H NMR (400 MHz) 2,6-dimethylcyclohexa-2,5-diene-1,4-dione (**2f**) in $CDCl_3$ at 298 K.

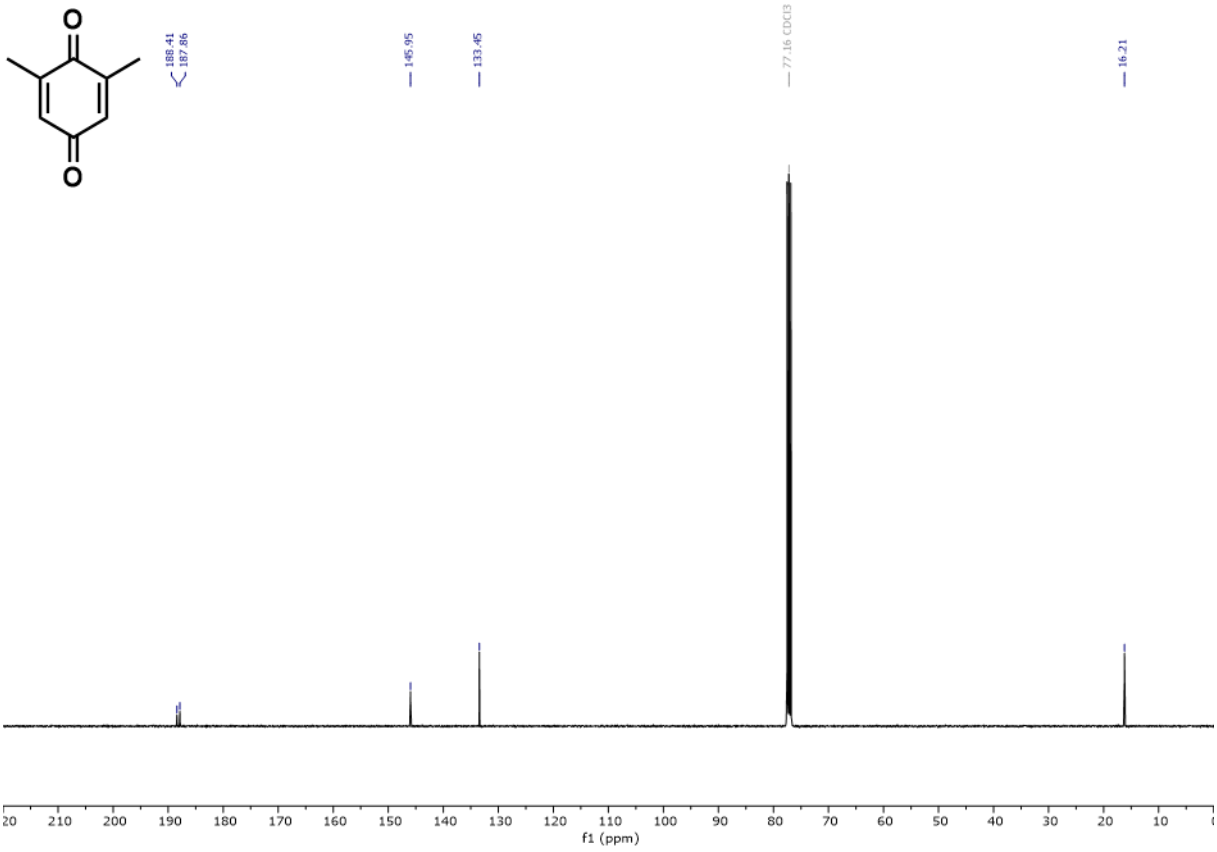


Figure 26: ^{13}C NMR (101 MHz) 2,6-dimethylcyclohexa-2,5-diene-1,4-dione (**2f**) in $CDCl_3$ at 298 K

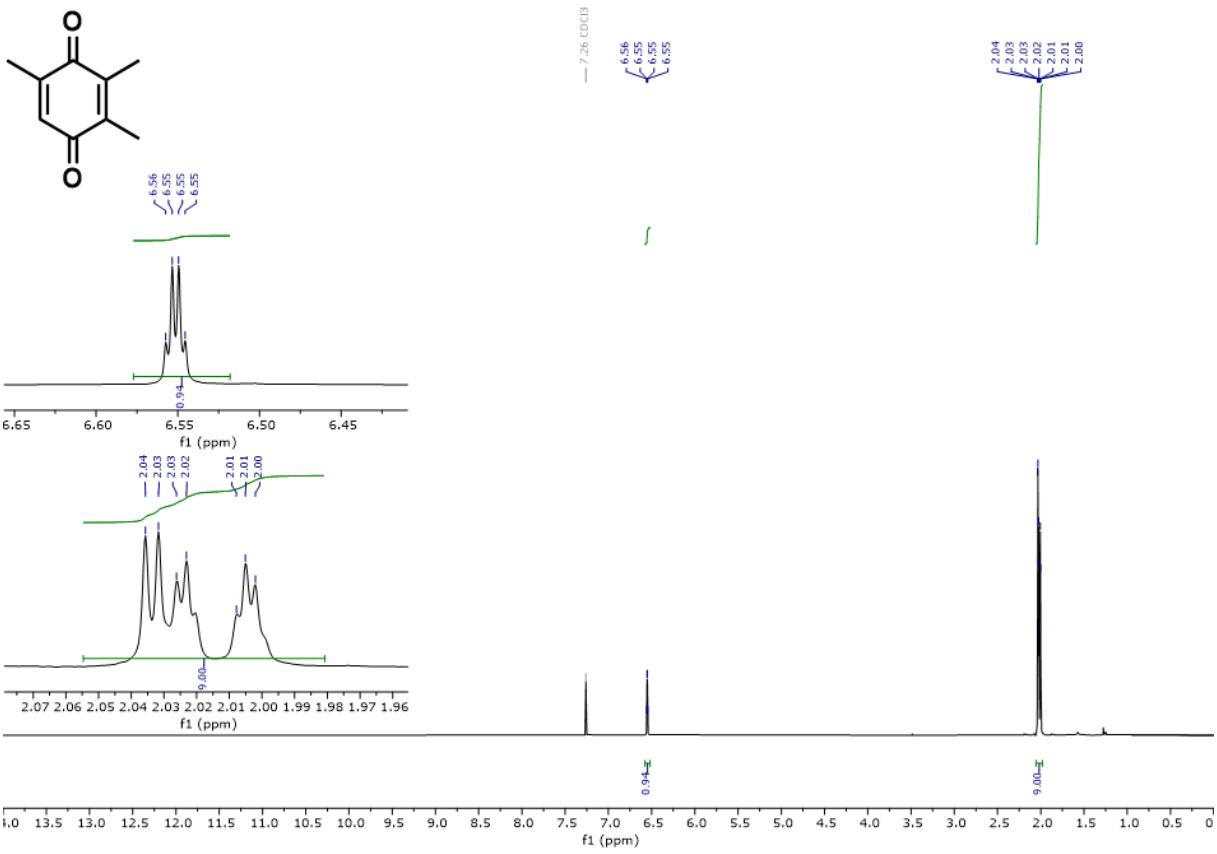


Figure 27: ^{1}H NMR (400 MHz) 2,3,5-trimethylcyclohexa-2,5-diene-1,4-dione (**2g**) in $CDCl_3$ at 298 K.

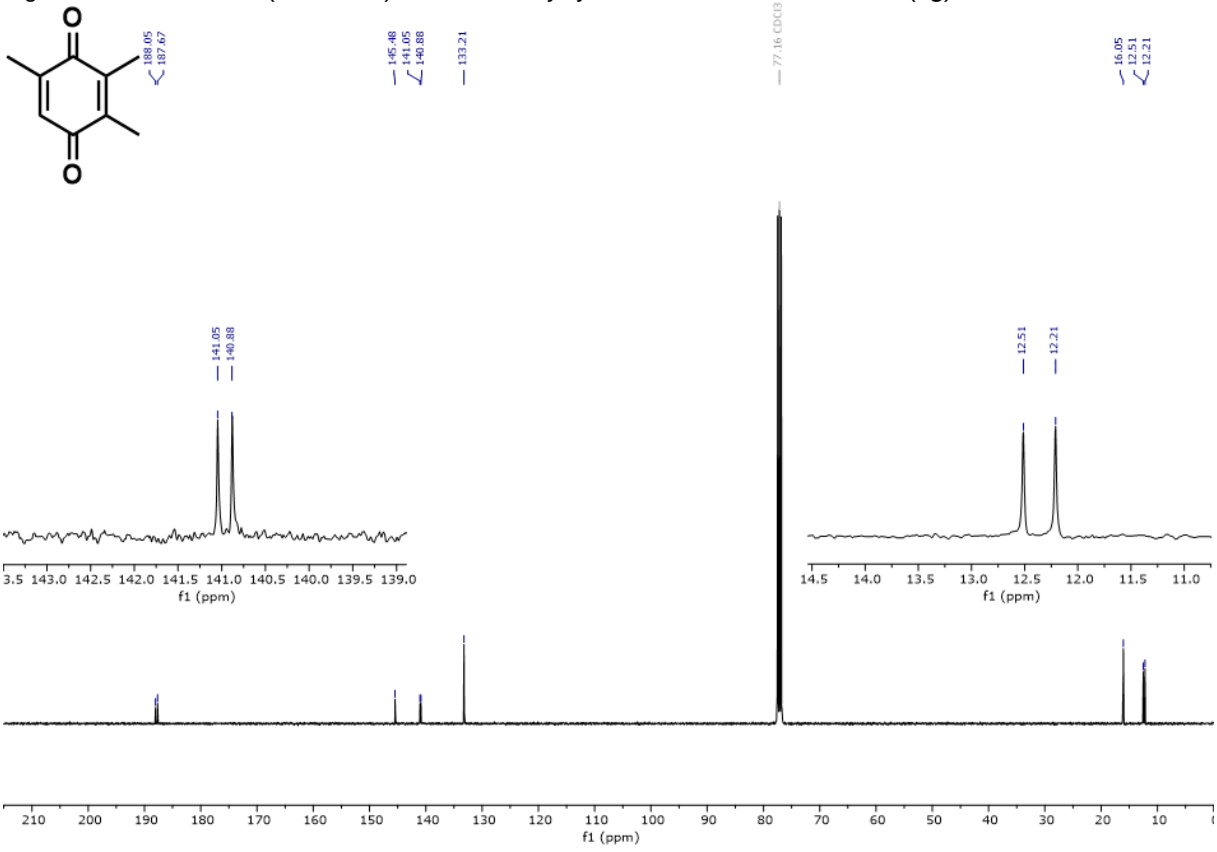


Figure 28: ^{13}C NMR (101 MHz) 2,3,5-trimethylcyclohexa-2,5-diene-1,4-dione (**2g**) in $CDCl_3$ at 298 K

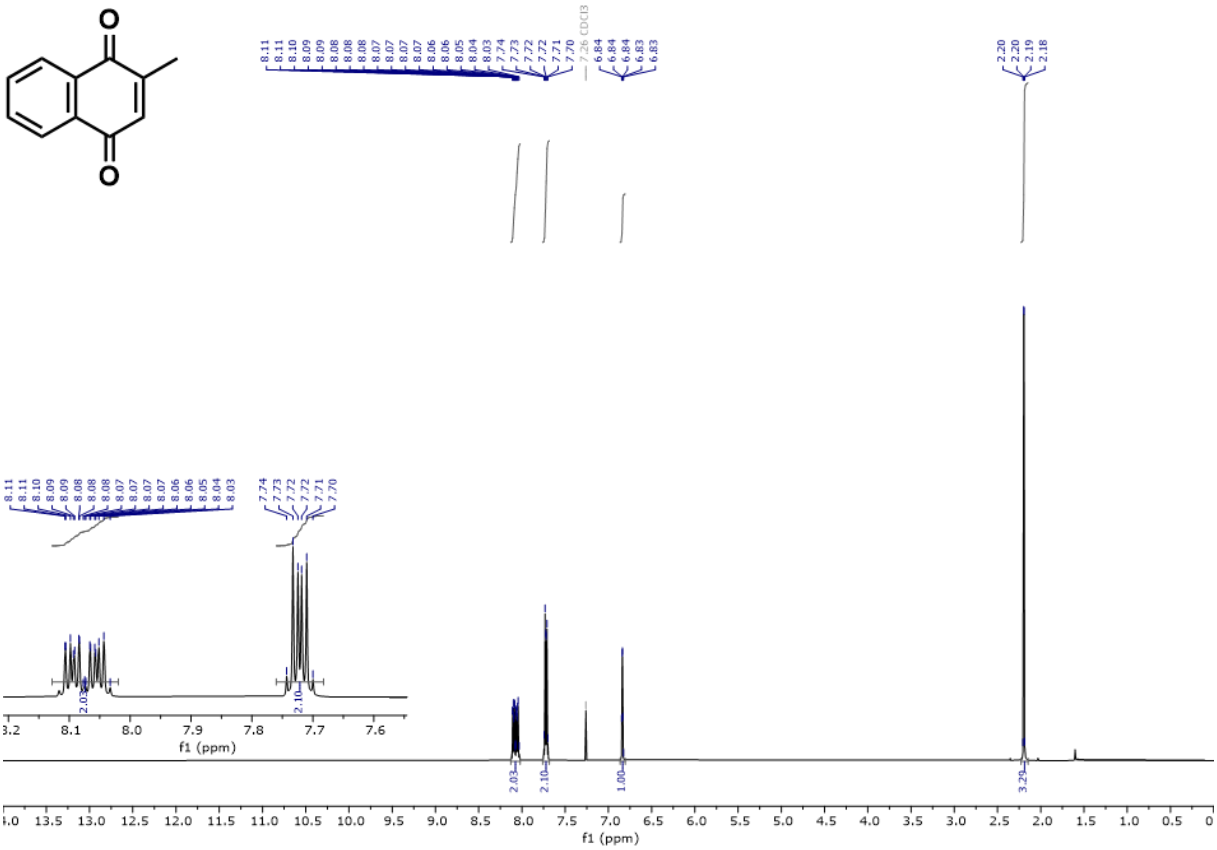


Figure 29: ^{1}H NMR (400 MHz) 2-methylnaphthalene-1,4-dione (**2h**) in $CDCl_3$ at 298 K.

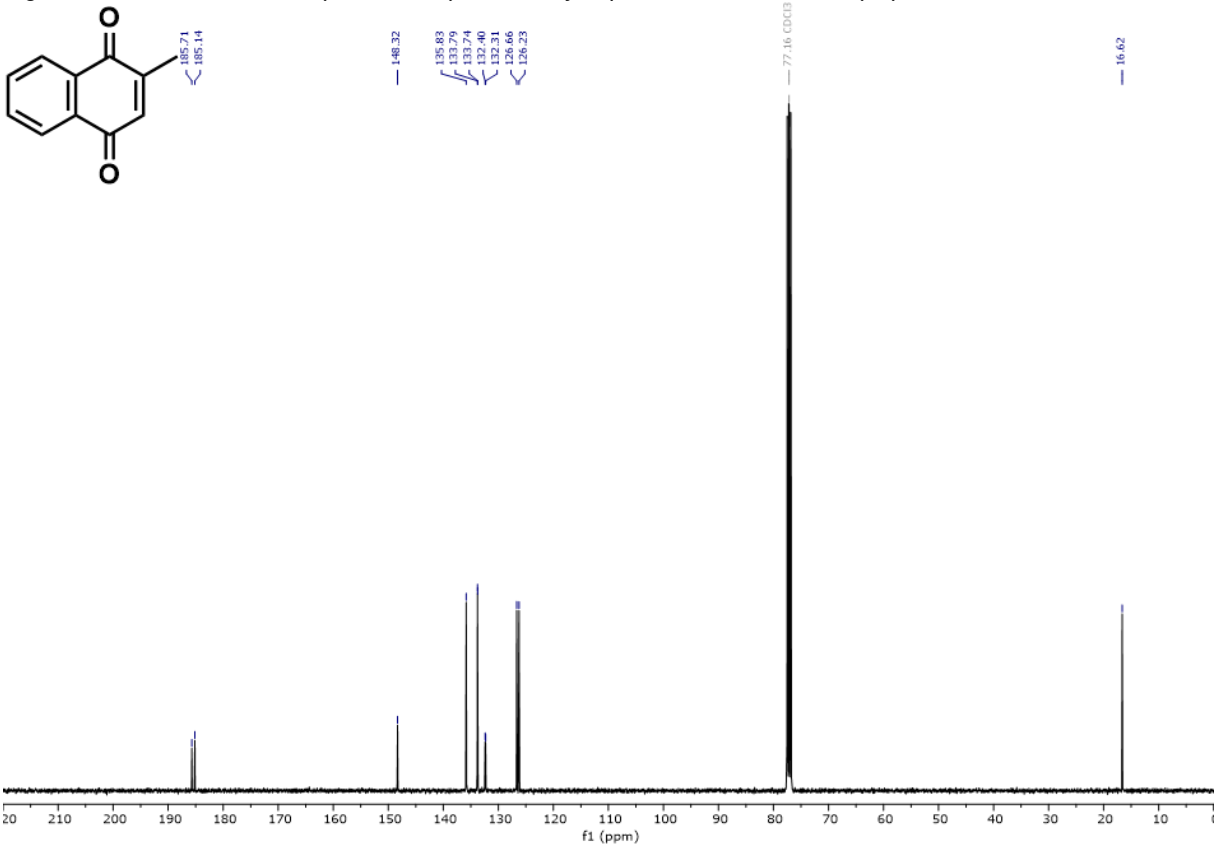


Figure 30: ^{13}C NMR (101 MHz) 2-methylnaphthalene-1,4-dione (**2h**) in $CDCl_3$ at 298 K.

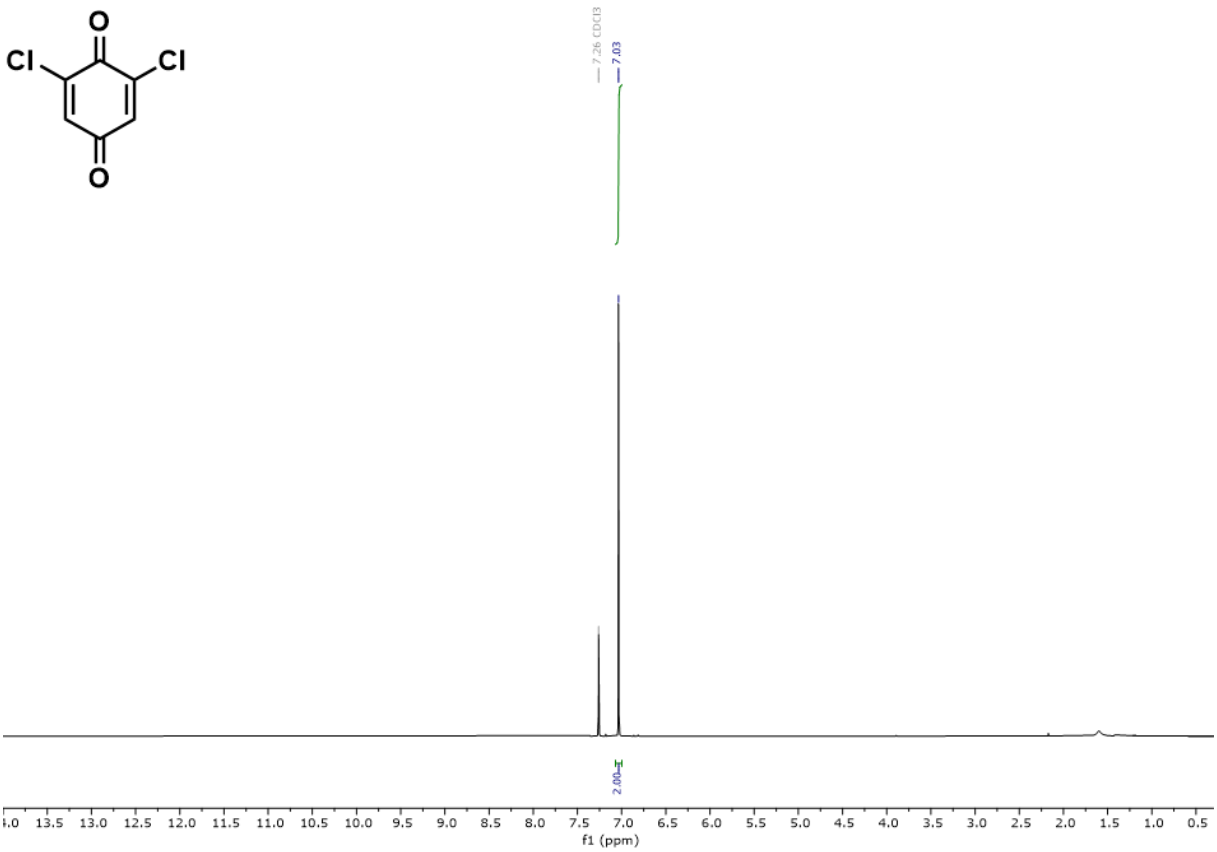


Figure 31: ^{1}H NMR (400 MHz) 2,6-dichlorocyclohexa-2,5-diene-1,4-dione (**2i**) in $CDCl_3$ at 298 K.

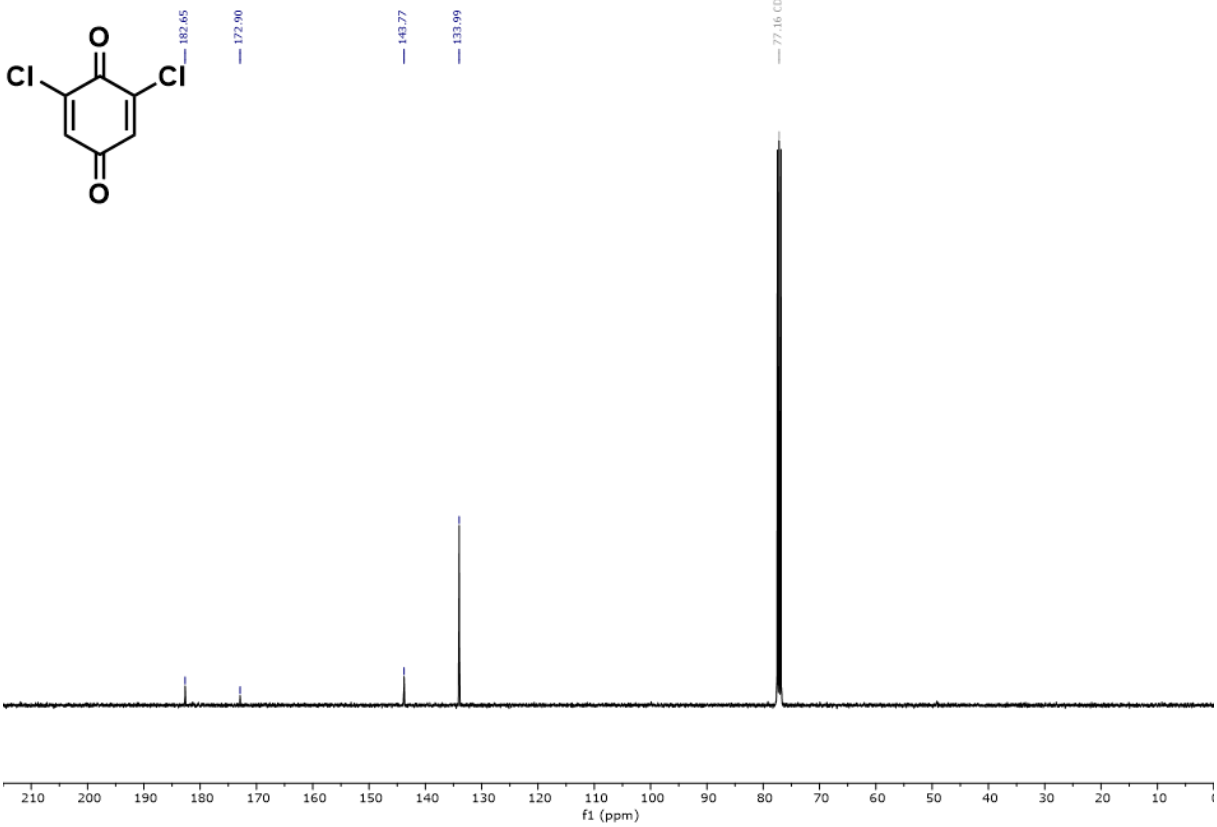


Figure 32: ^{13}C NMR (101 MHz) 2,6-dichlorocyclohexa-2,5-diene-1,4-dione (**2i**) in $CDCl_3$ at 298 K.

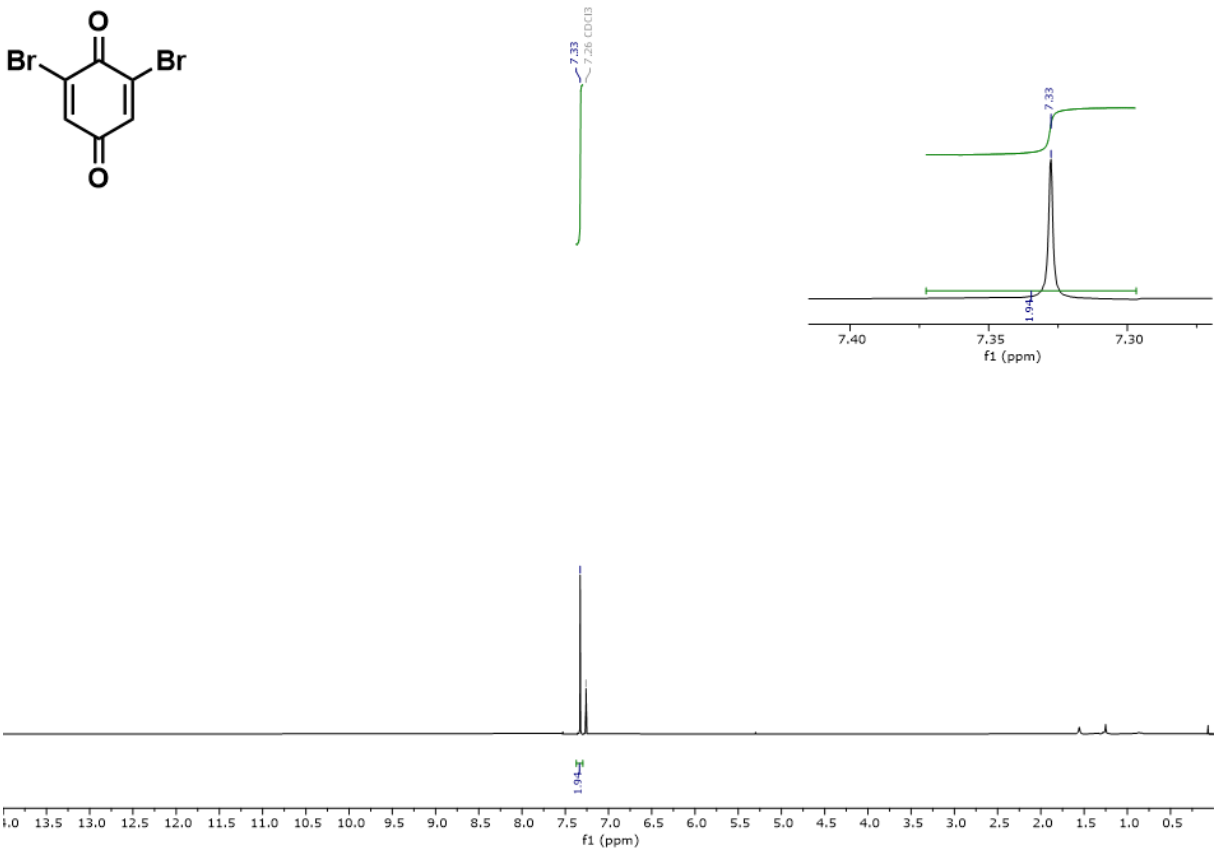


Figure 33: ^{1}H NMR (400 MHz) 2,6-dibromocyclohexa-2,5-diene-1,4-dione (**2j**) in $CDCl_3$ at 298 K.

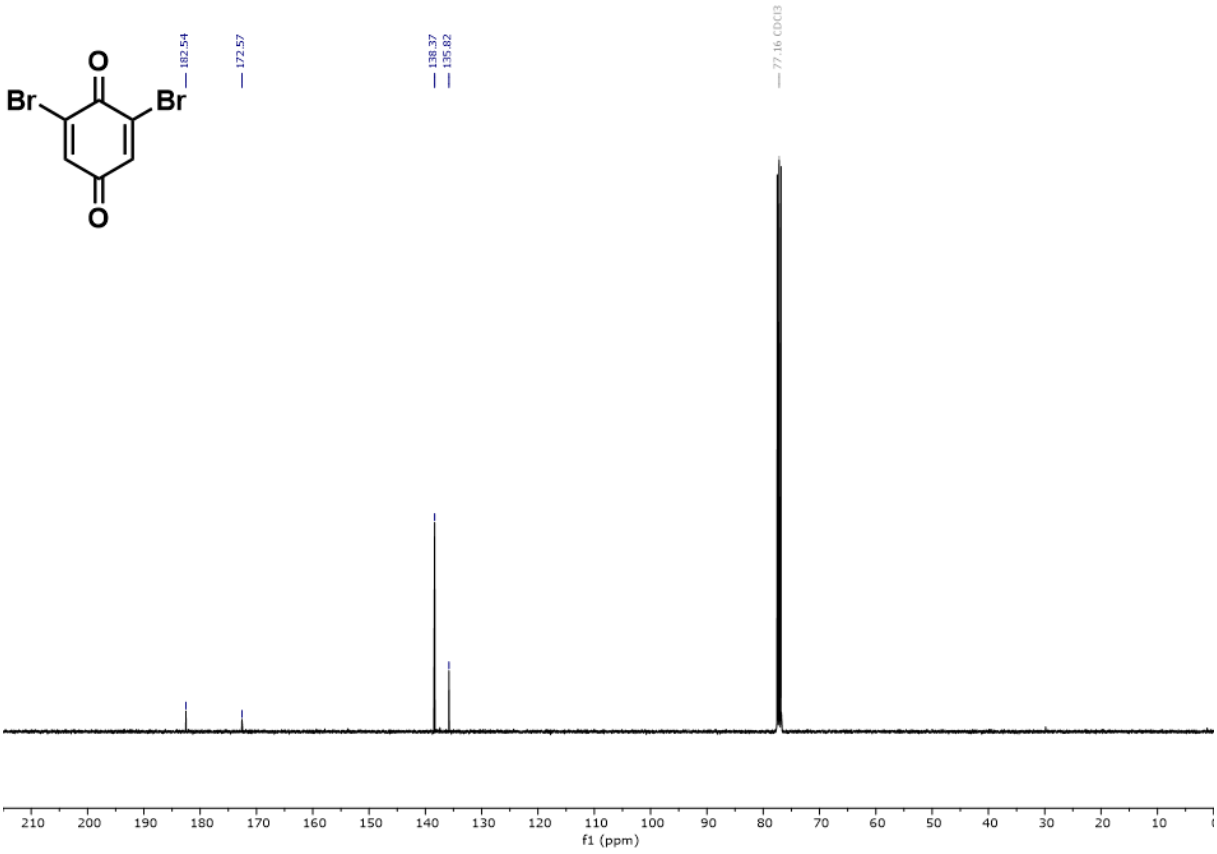


Figure 34: ^{13}C NMR (101 MHz) 2,6-dibromocyclohexa-2,5-diene-1,4-dione (**2j**) in $CDCl_3$ at 298 K.

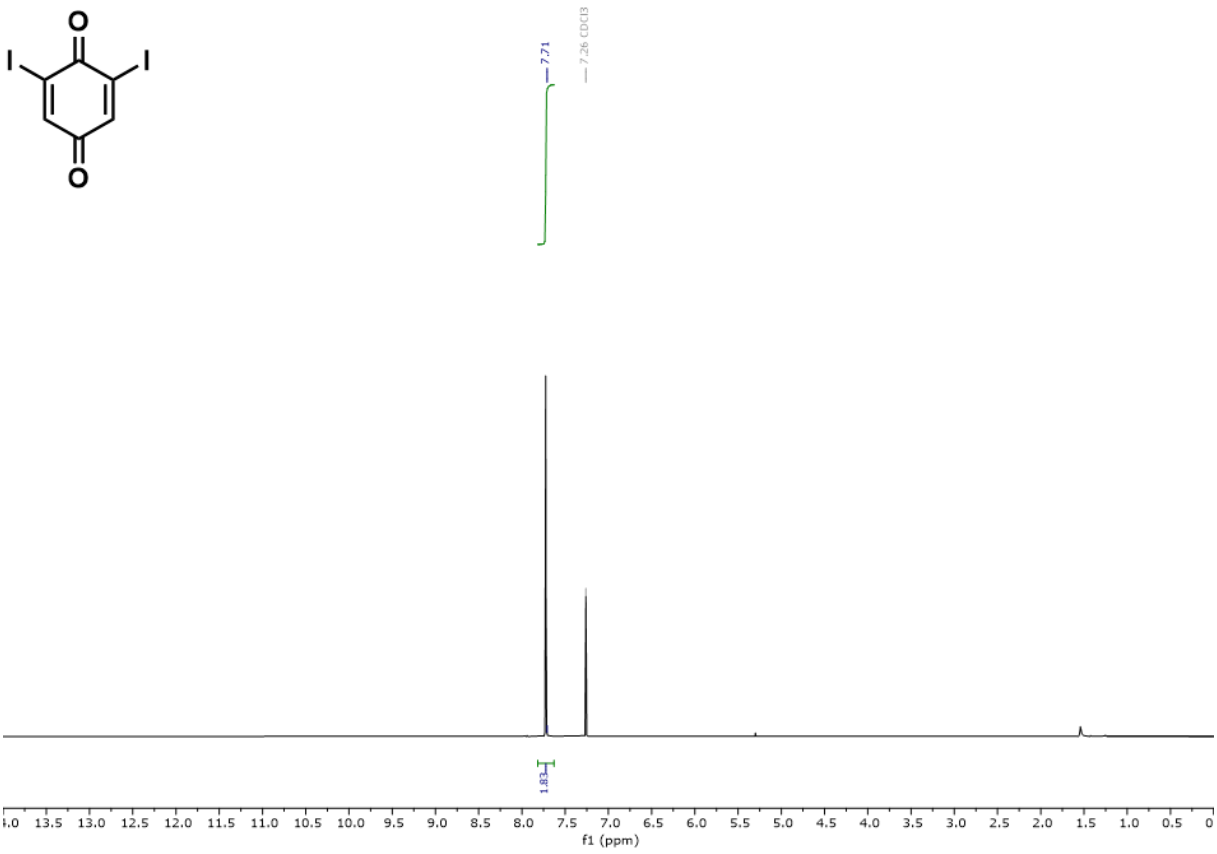


Figure 35: ^{1}H NMR (400 MHz) 2,6-diiodocyclohexa-2,5-diene-1,4-dione (**2k**) in $CDCl_3$ at 298 K.

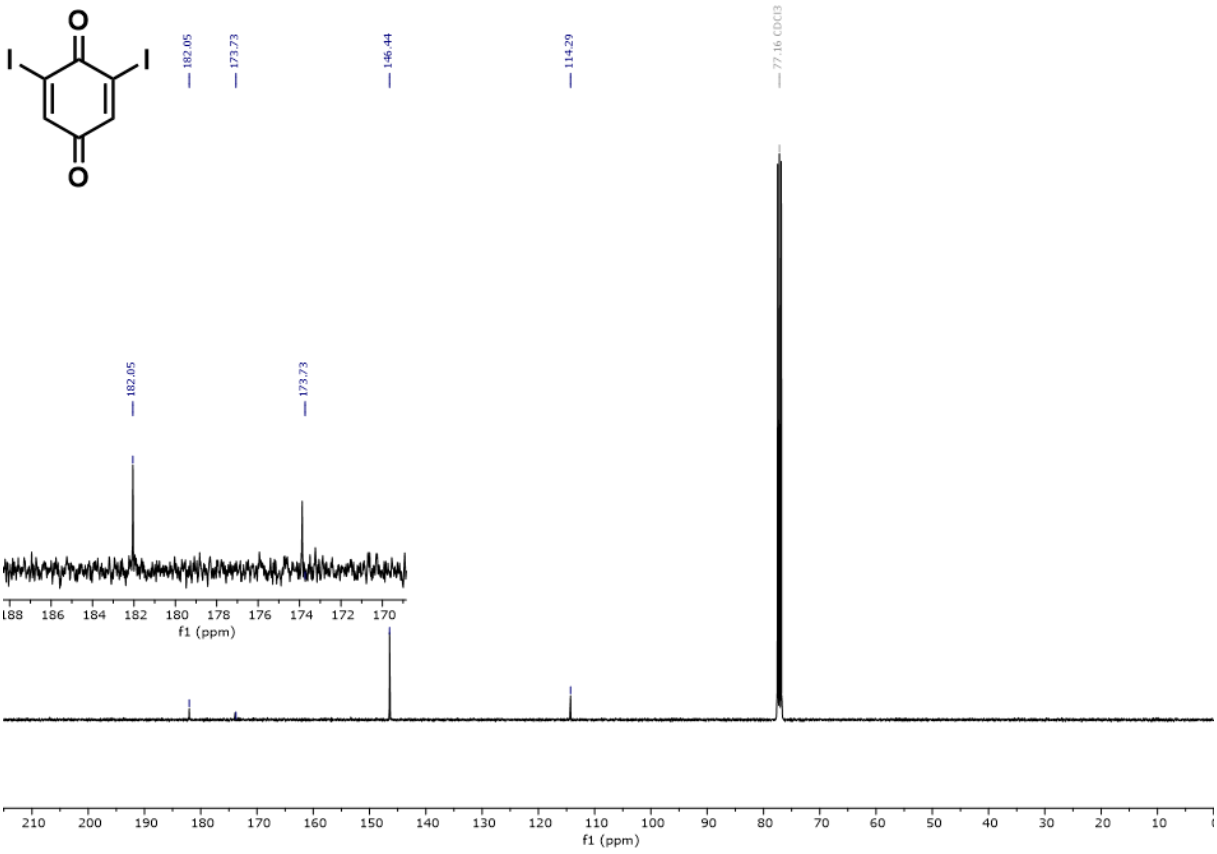


Figure 36: ^{13}C NMR (101 MHz) 2,6-diiodocyclohexa-2,5-diene-1,4-dione (**2k**) in $CDCl_3$ at 298 K.

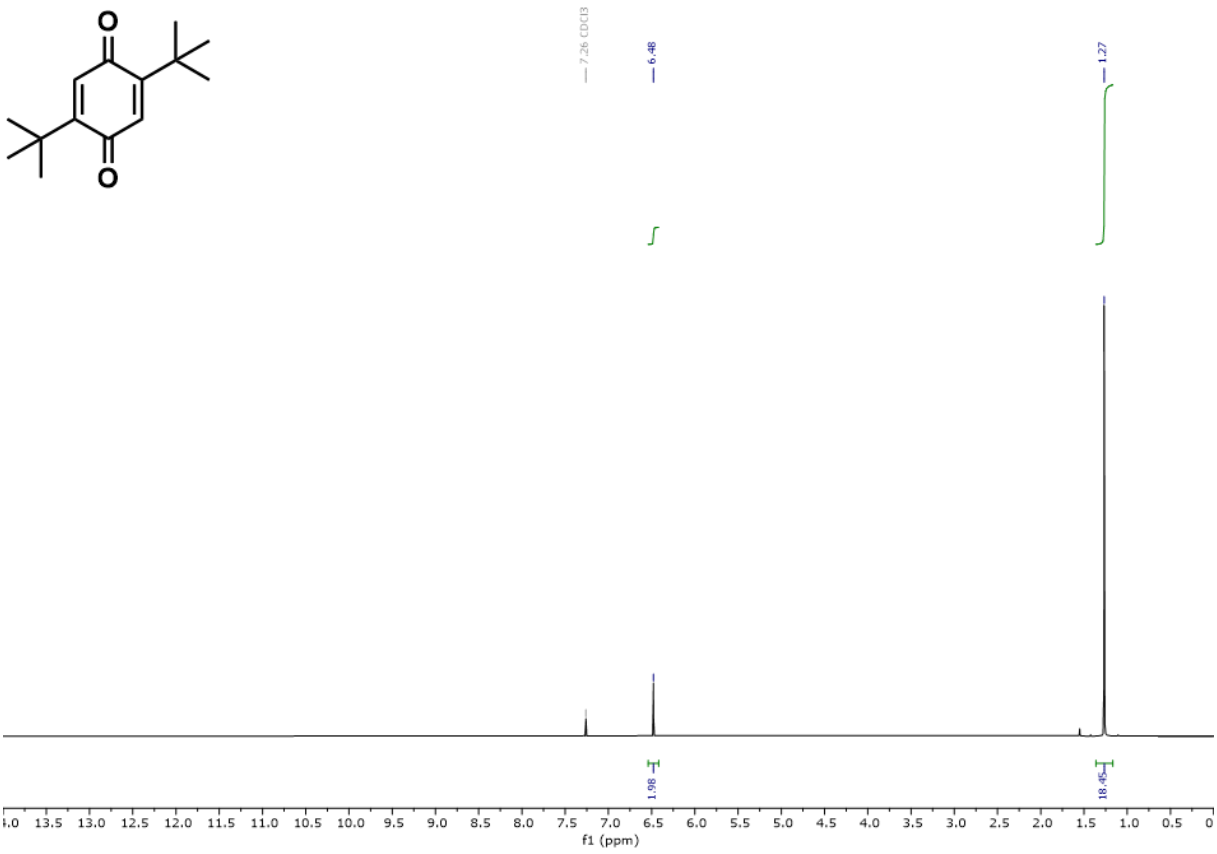


Figure 37: ^{1}H NMR (400 MHz) 2,5-bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2l**) in $CDCl_3$ at 298 K.

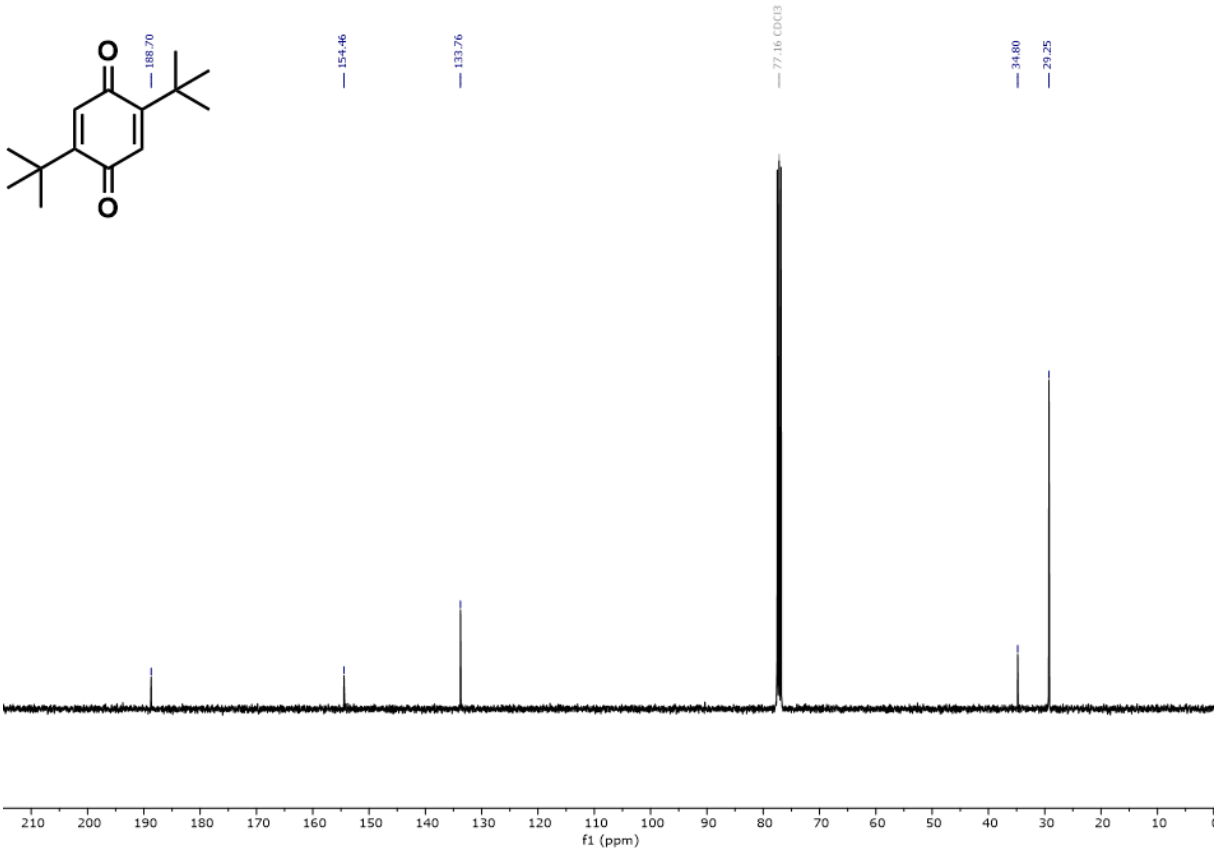


Figure 38: ^{13}C NMR (101 MHz) 2,5-bis-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2l**) in $CDCl_3$ at 298 K.

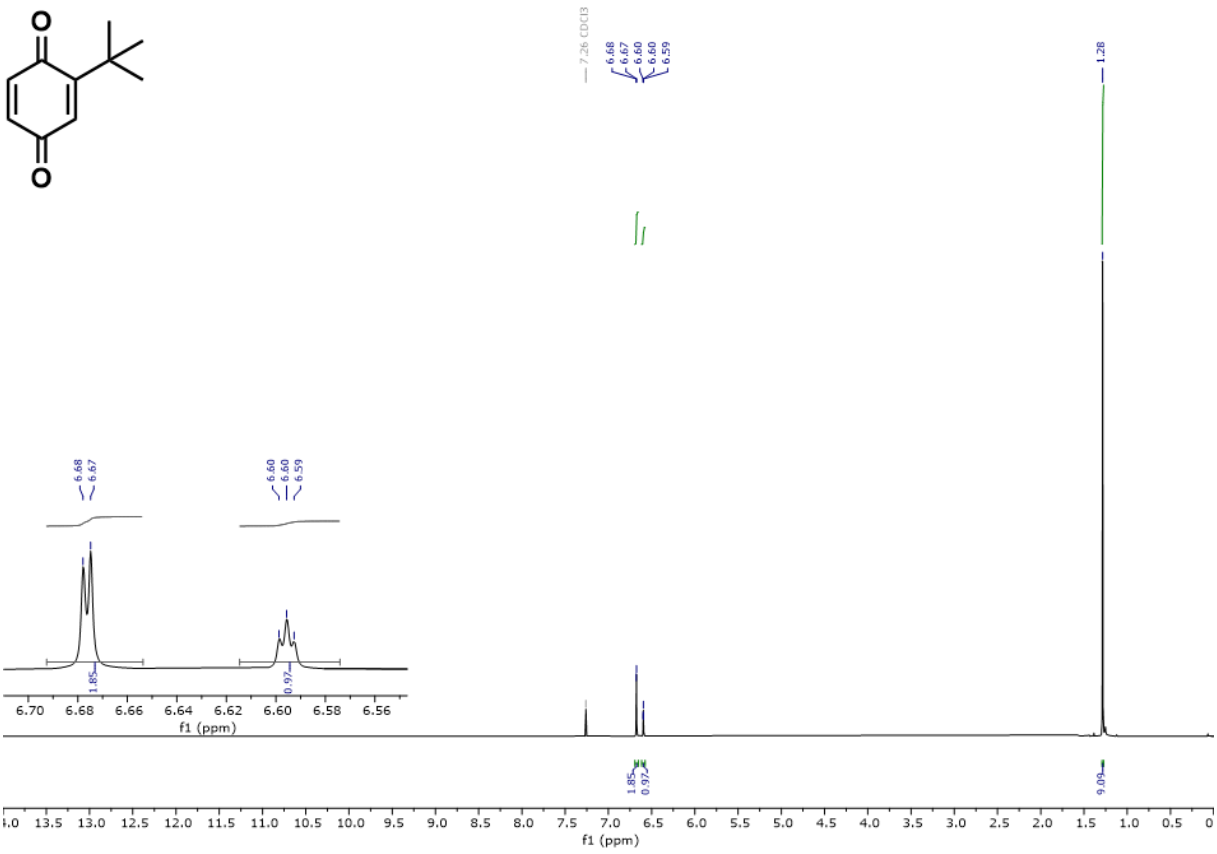


Figure 39: ^{1}H NMR (400 MHz) 2-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2m**) in $CDCl_3$ at 298 K.

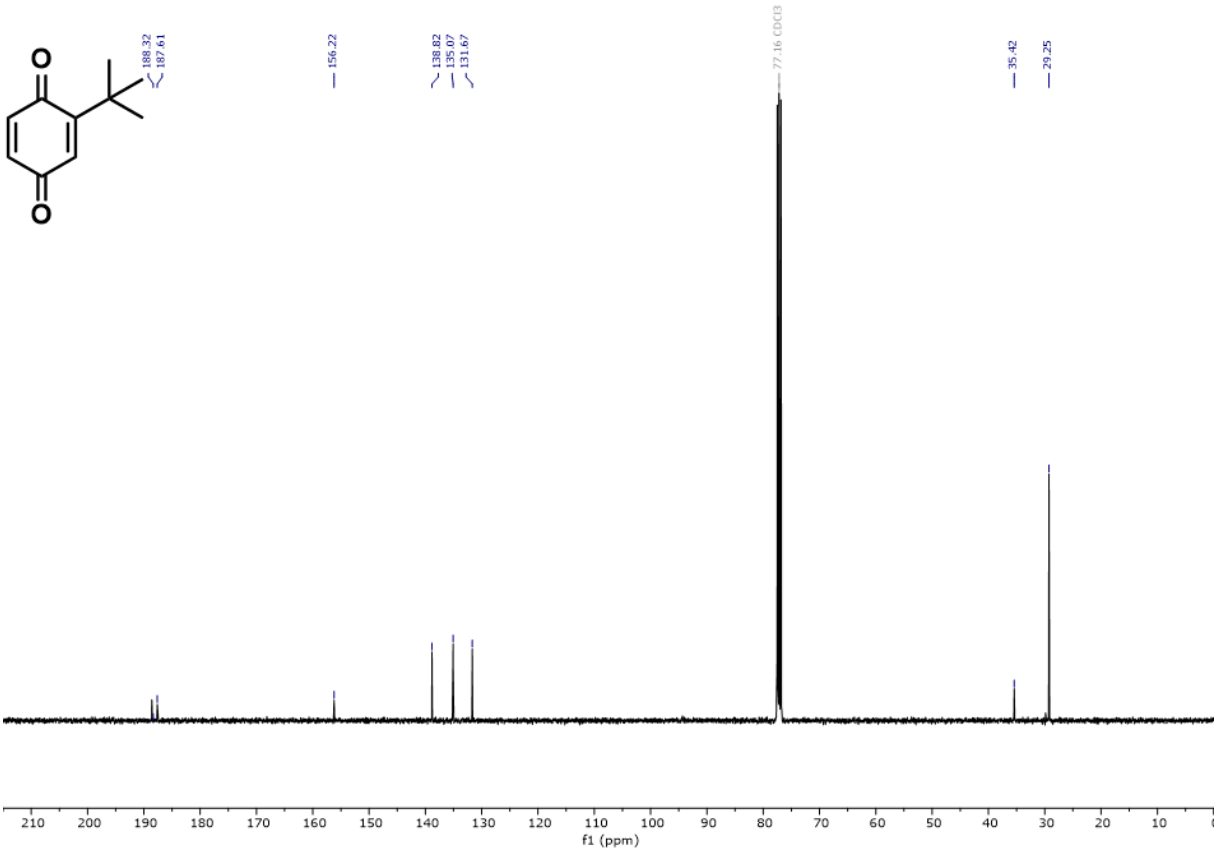


Figure 40: ^{13}C NMR (101 MHz) 2-(1,1-dimethylethyl)-cyclohexa-2,5-diene-1,4-dione (**2m**) in $CDCl_3$ at 298 K.

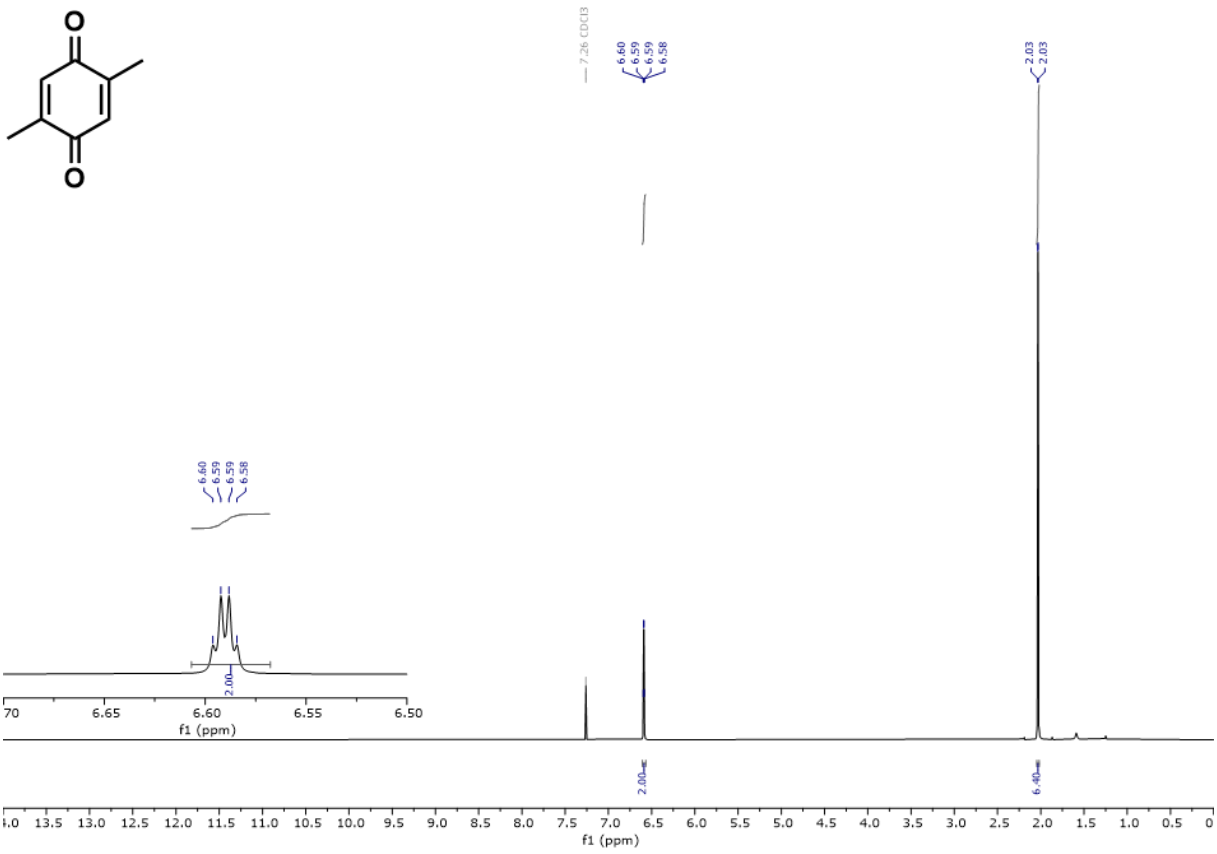


Figure 41: ^{1}H NMR (400 MHz) 2,5-dimethylcyclohexa-2,5-diene-1,4-dione (**2n**) in $CDCl_3$ at 298 K.

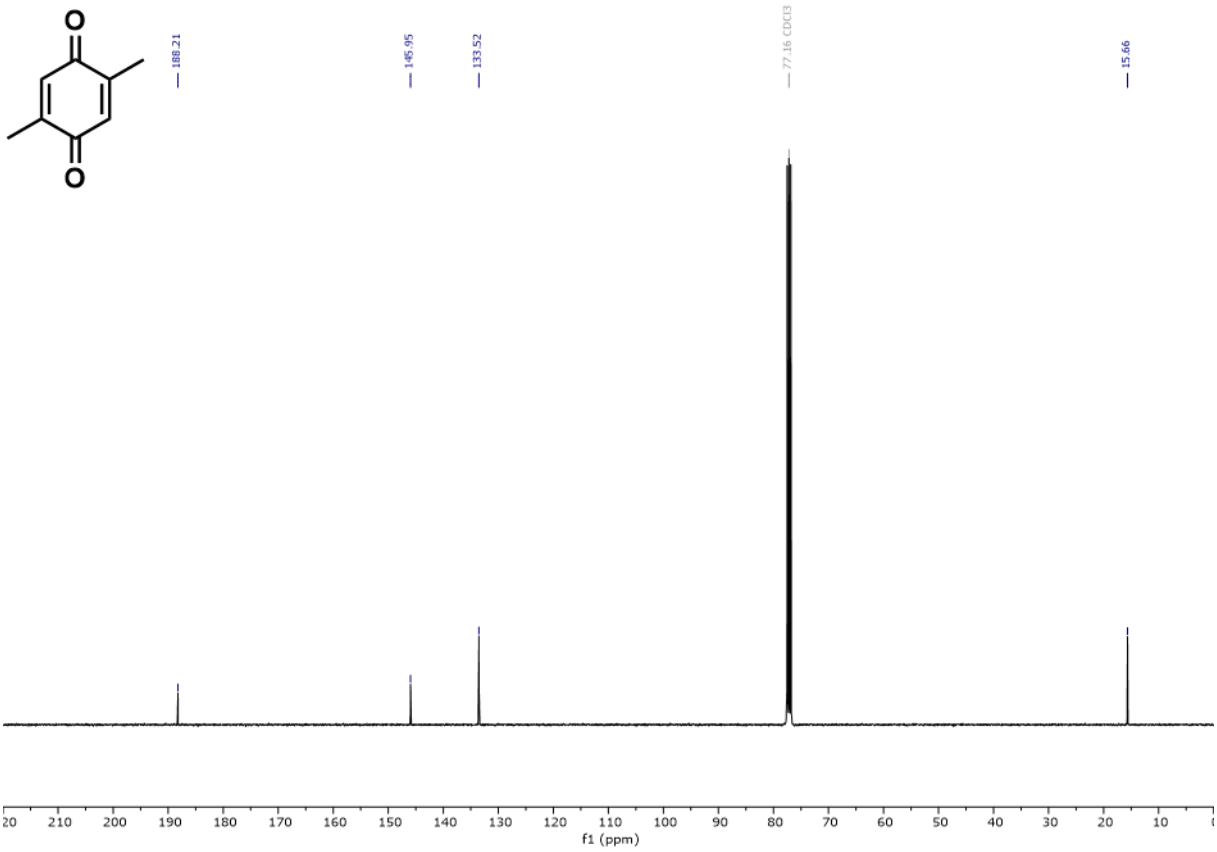


Figure 42: ^{13}C NMR (101 MHz) 2,5-dimethylcyclohexa-2,5-diene-1,4-dione (**2n**) in $CDCl_3$ at 298 K.

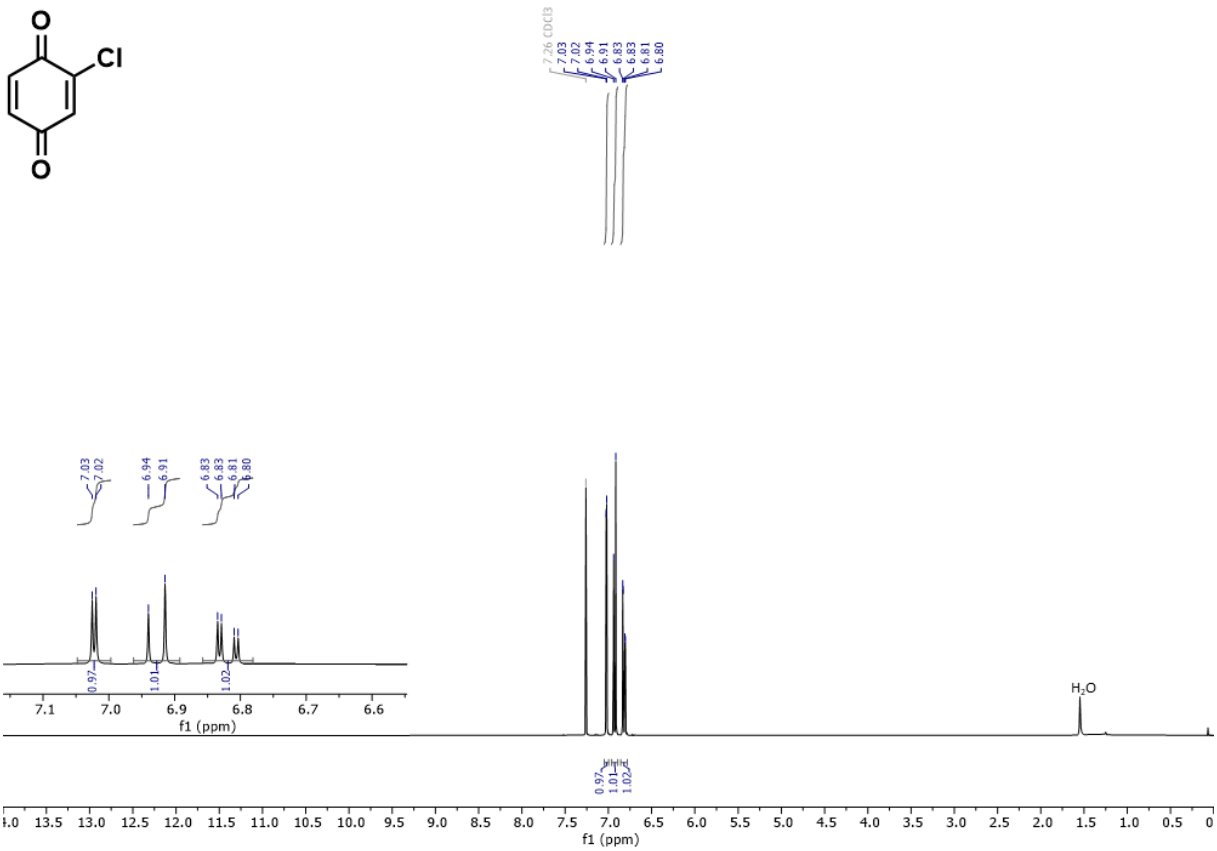


Figure 43: ^{1}H NMR (400 MHz) 2-chlorocyclohexa-2,5-diene-1,4-dione (**2o**) in $CDCl_3$ at 298 K.

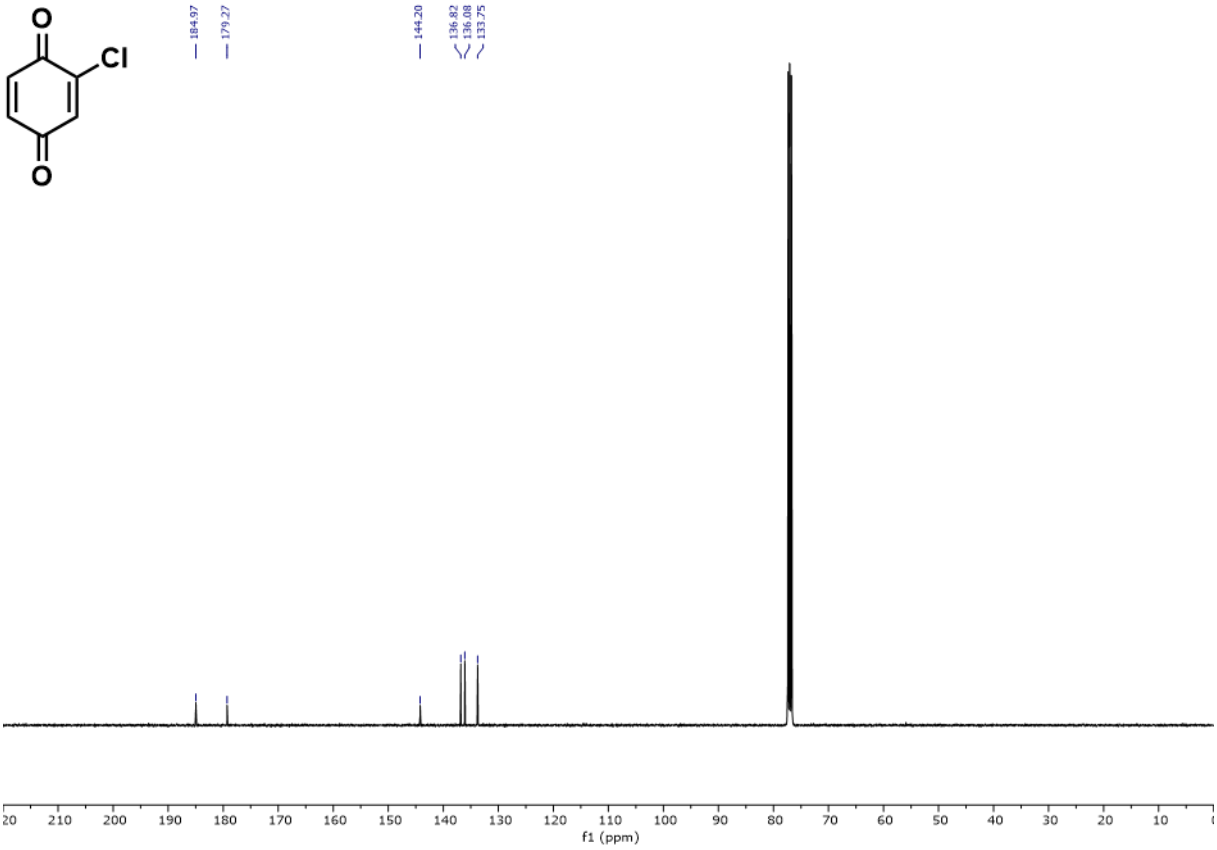


Figure 44: ^{13}C NMR (101 MHz) 2-chlorocyclohexa-2,5-diene-1,4-dione (**2o**) in $CDCl_3$ at 298 K.

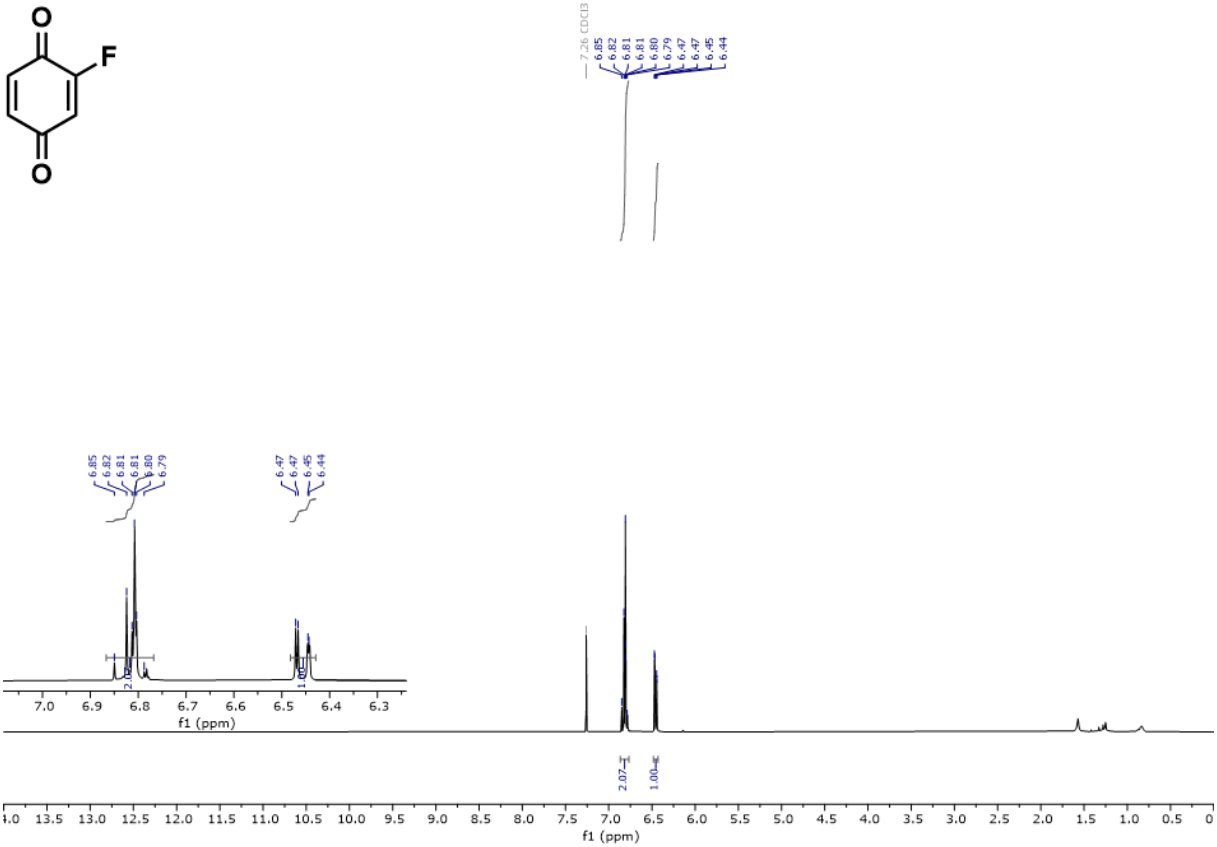


Figure 45: ^{1}H NMR (400 MHz) 2-fluorocyclohexa-2,5-diene-1,4-dione (**2p**) in $CDCl_3$ at 298 K.

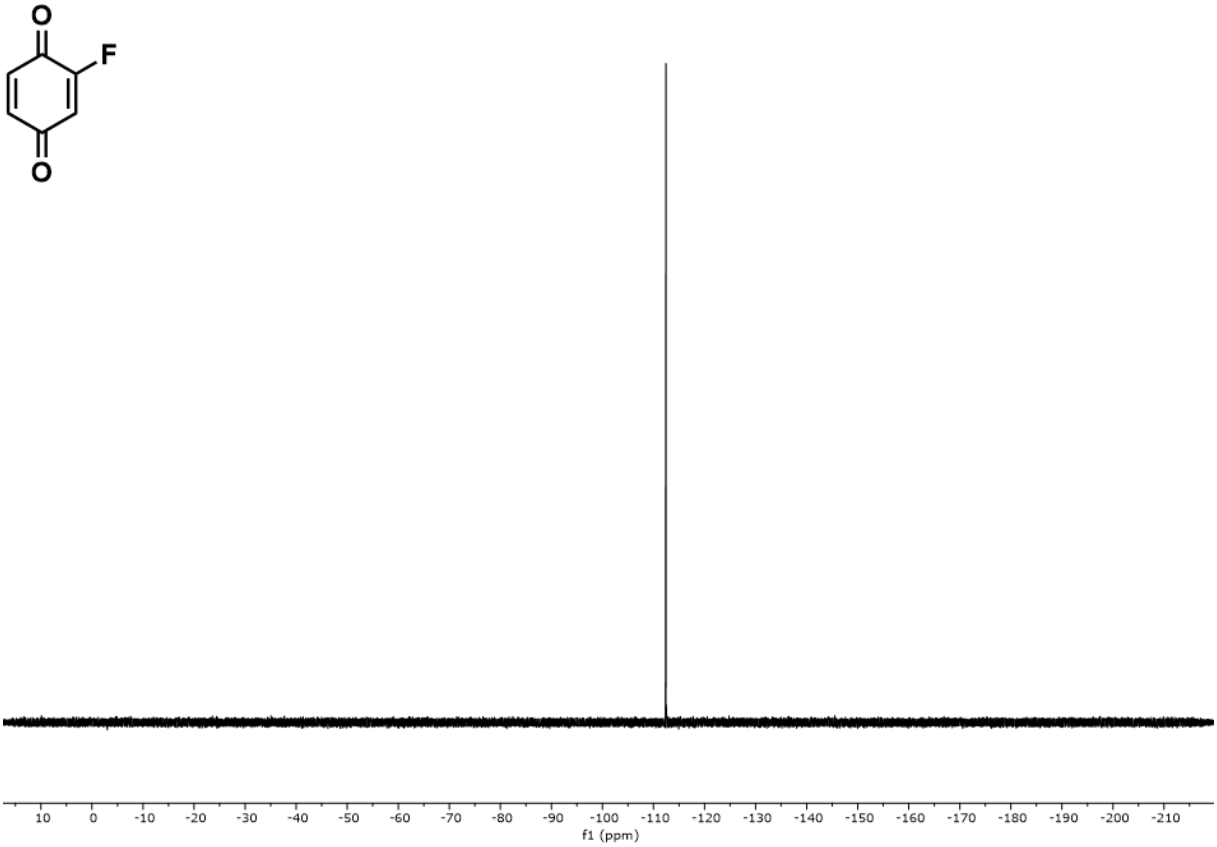


Figure 46: ^{19}F NMR (376 MHz) 2-fluorocyclohexa-2,5-diene-1,4-dione (**2p**) in $CDCl_3$ at 298 K.

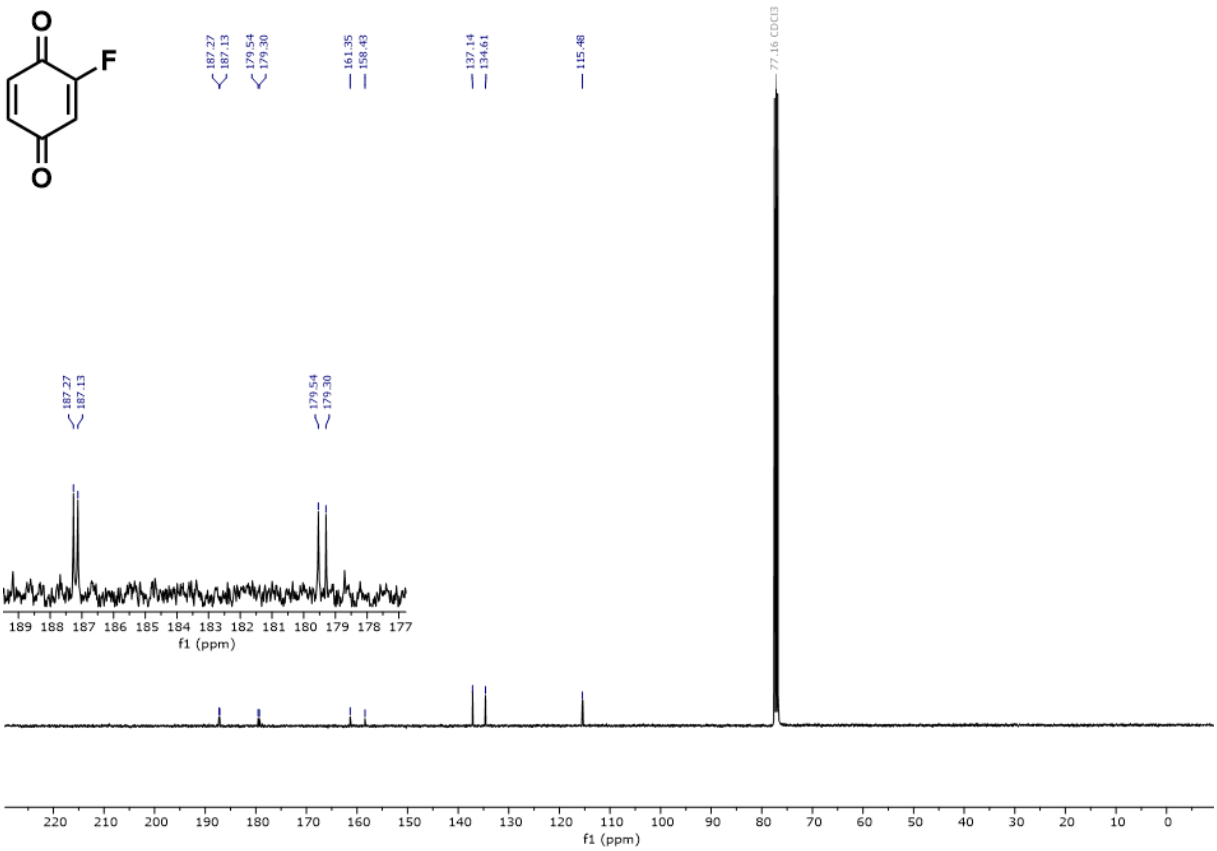


Figure 47: ^{13}C NMR (101 MHz) 2-fluorocyclohexa-2,5-diene-1,4-dione (**2p**) in $CDCl_3$ at 298 K.

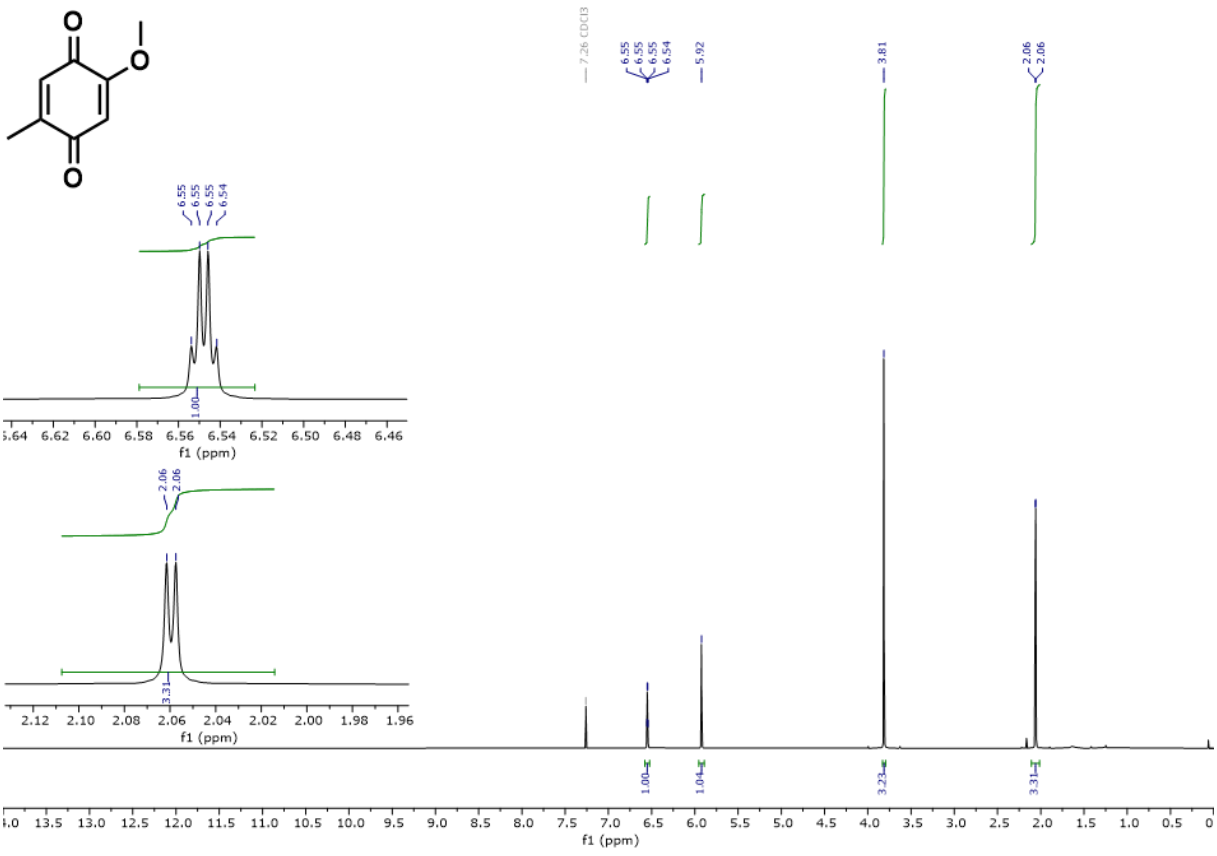


Figure 48: ^{1}H NMR (400 MHz) 2-methoxy-5-methylcyclohexa-2,5-diene-1,4-dione (**2q**) in $CDCl_3$ at 298 K.

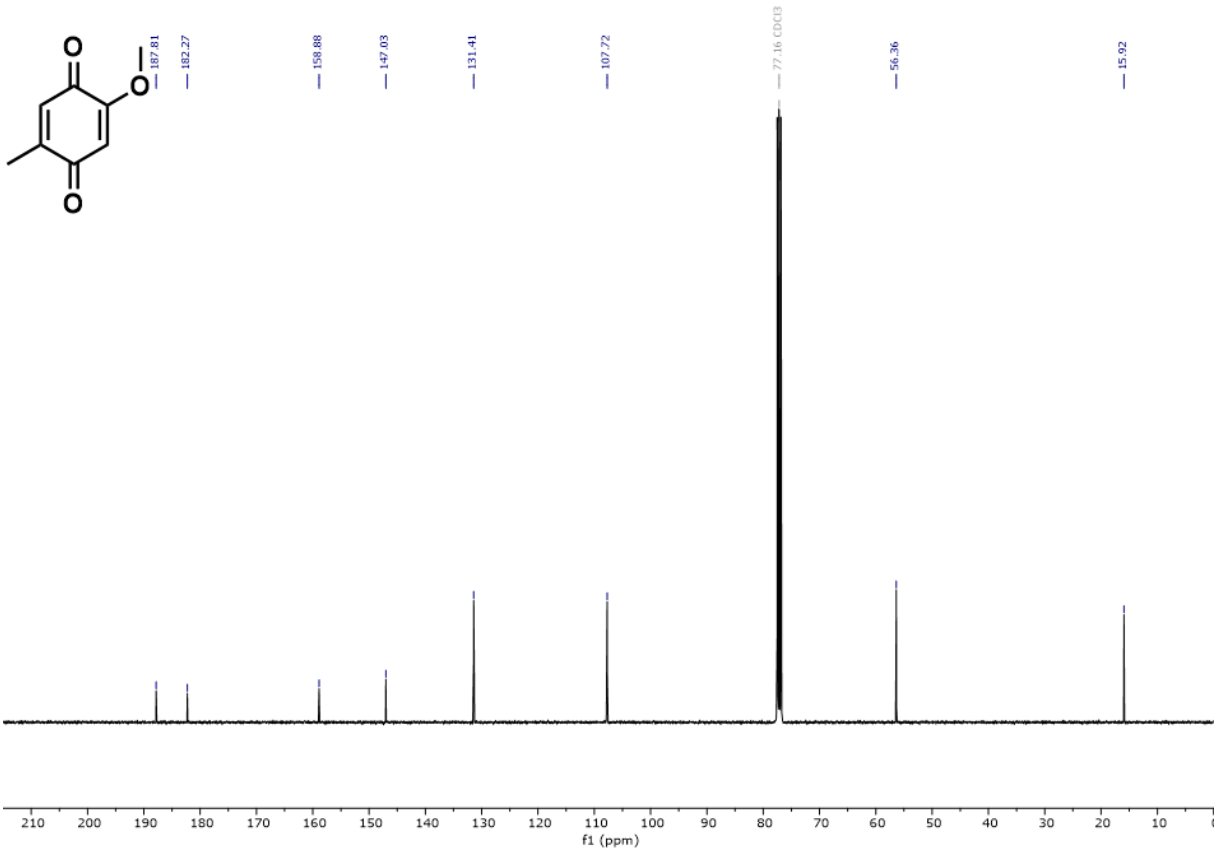


Figure 49: ^{13}C NMR (101 MHz) 2-methoxy-5-methylcyclohexa-2,5-diene-1,4-dione (**2q**) in $CDCl_3$ at 298 K.

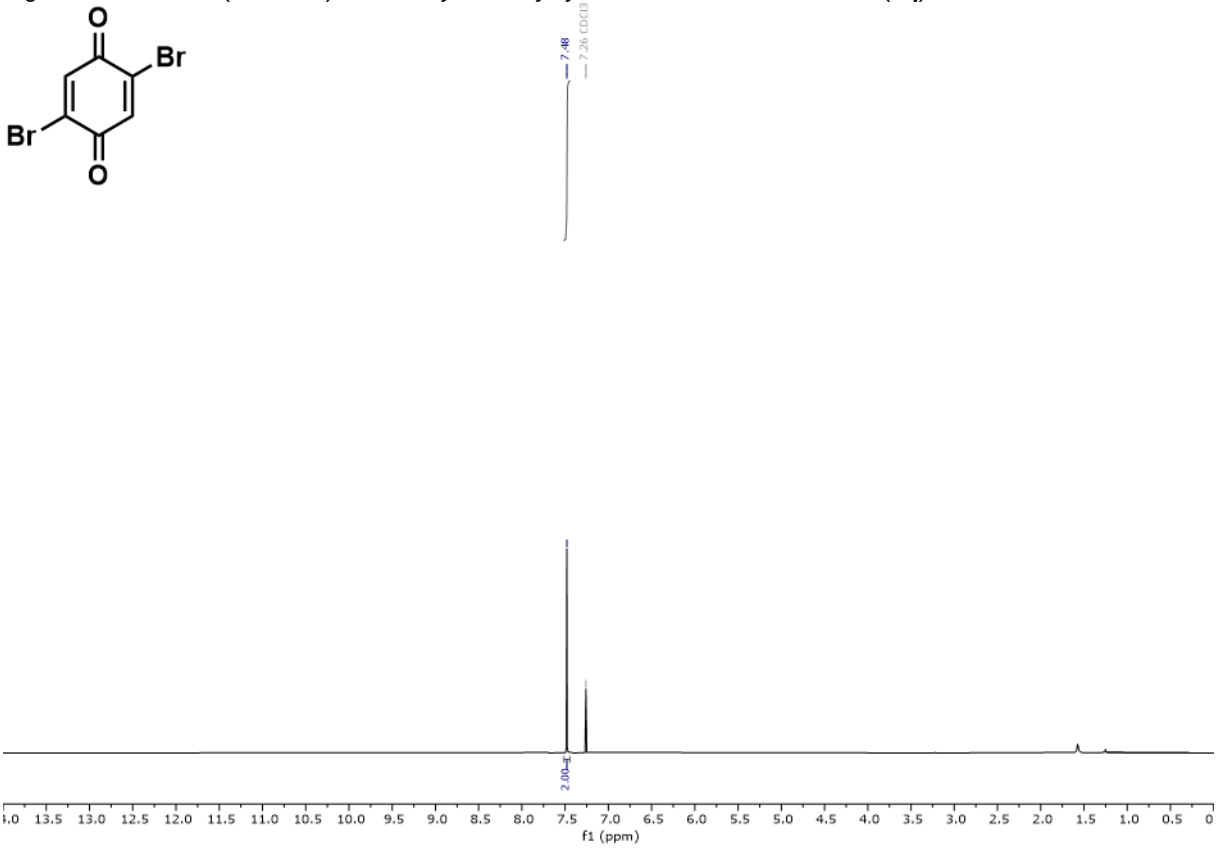


Figure 50: ^{1}H NMR (400 MHz) 2,5-dibromocyclohexa-2,5-diene-1,4-dione (**2r**) in $CDCl_3$ at 298 K.

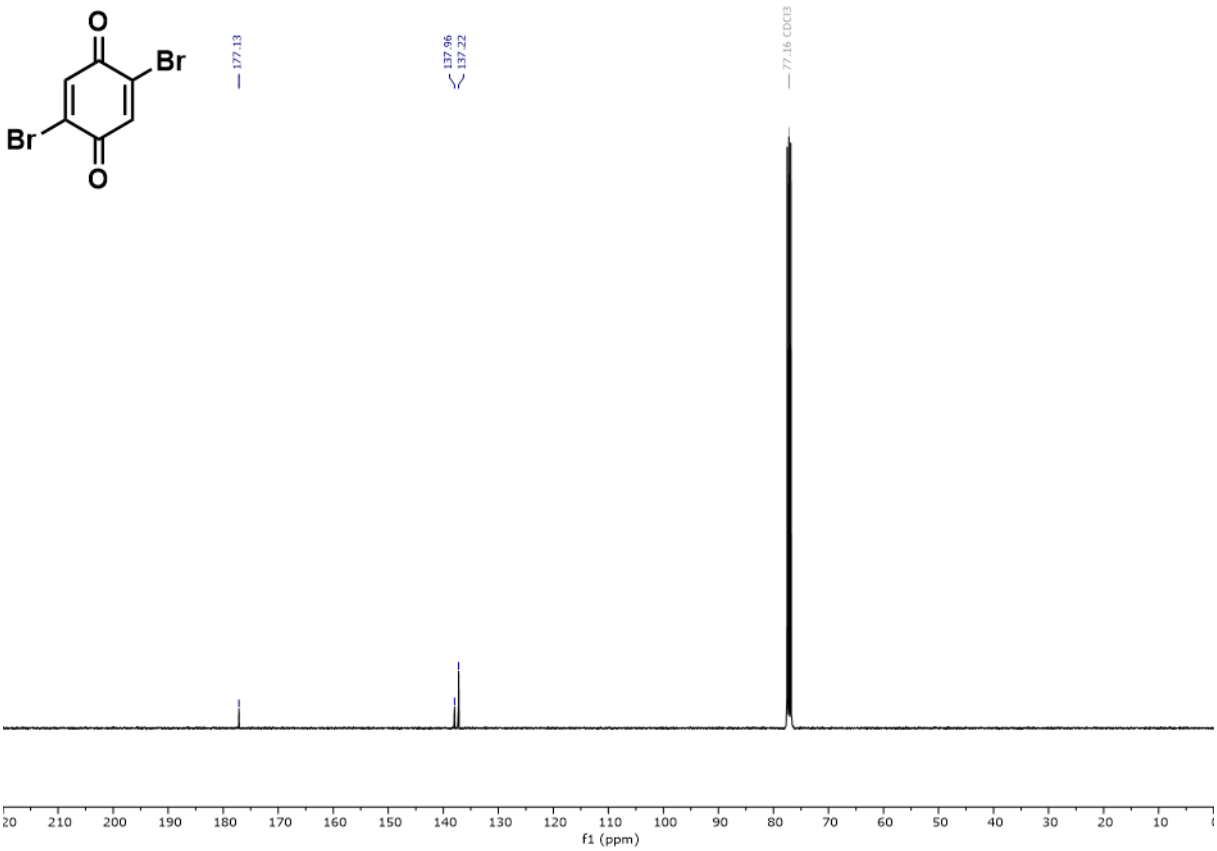


Figure 51: ^{13}C NMR (101 MHz) 2,5-dibromocyclohexa-2,5-diene-1,4-dione (**2r**) in $CDCl_3$ at 298 K.

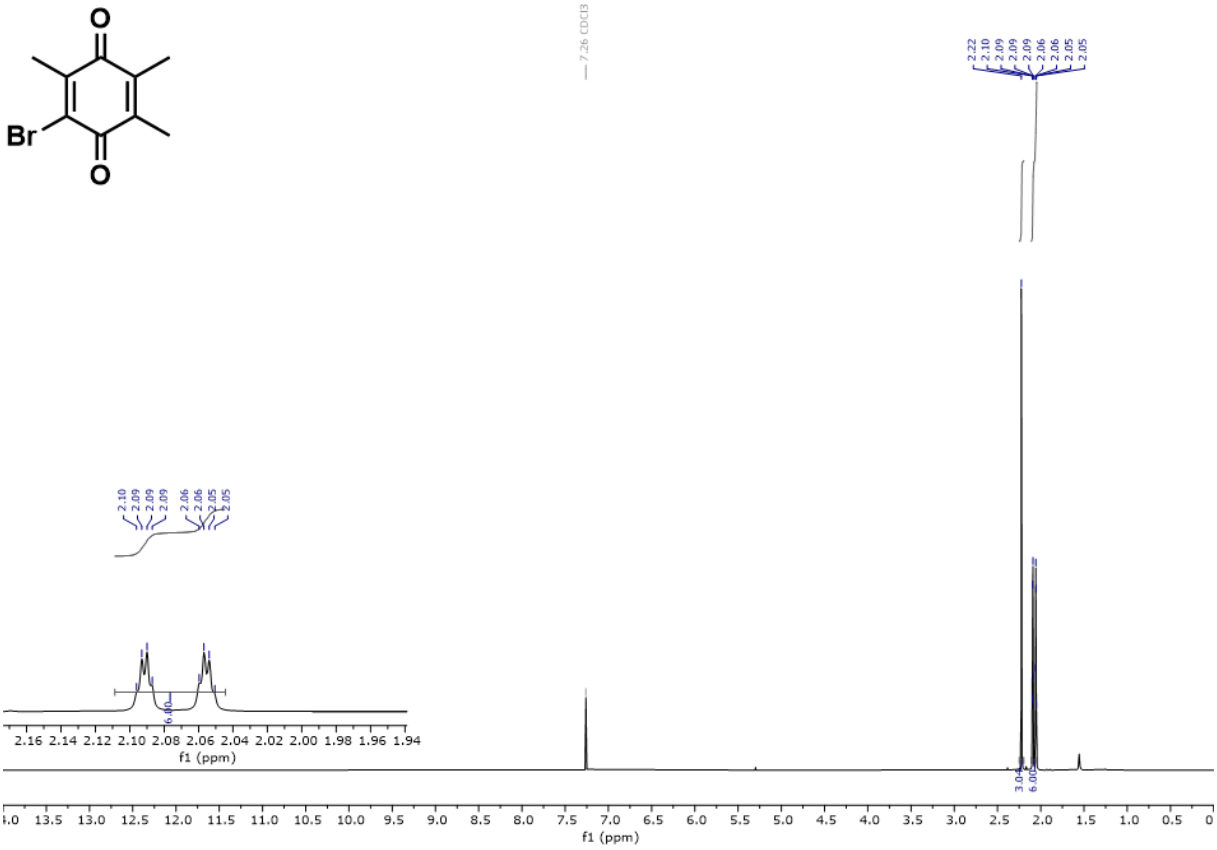


Figure 52: ^{1}H NMR (400 MHz) 2-bromo-3,5,6-trimethylcyclohexa-2,5-diene-1,4-dione (**2s**) in $CDCl_3$ at 298 K.

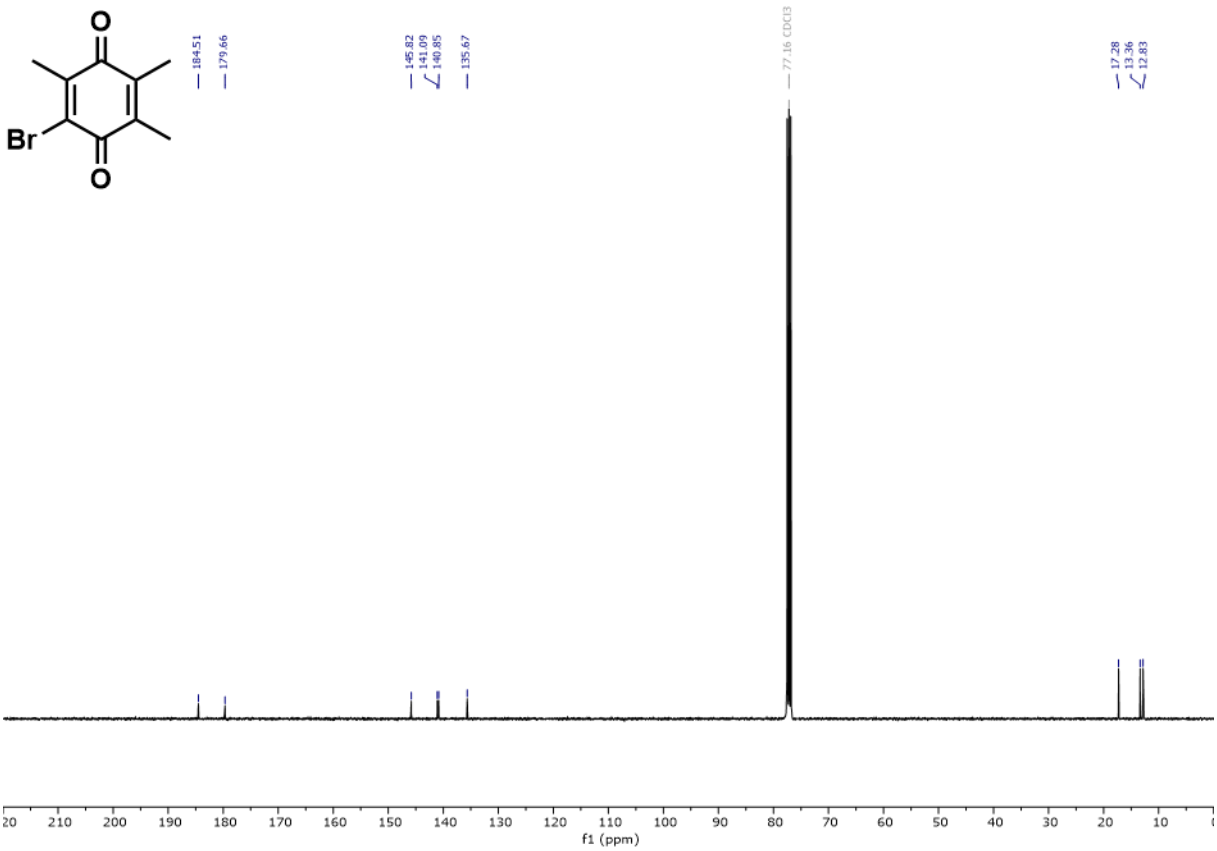


Figure 53: ^{13}C NMR (101 MHz) 2-bromo-3,5,6-trimethylcyclohexa-2,5-diene-1,4-dione (**2s**) in $CDCl_3$ at 298 K.

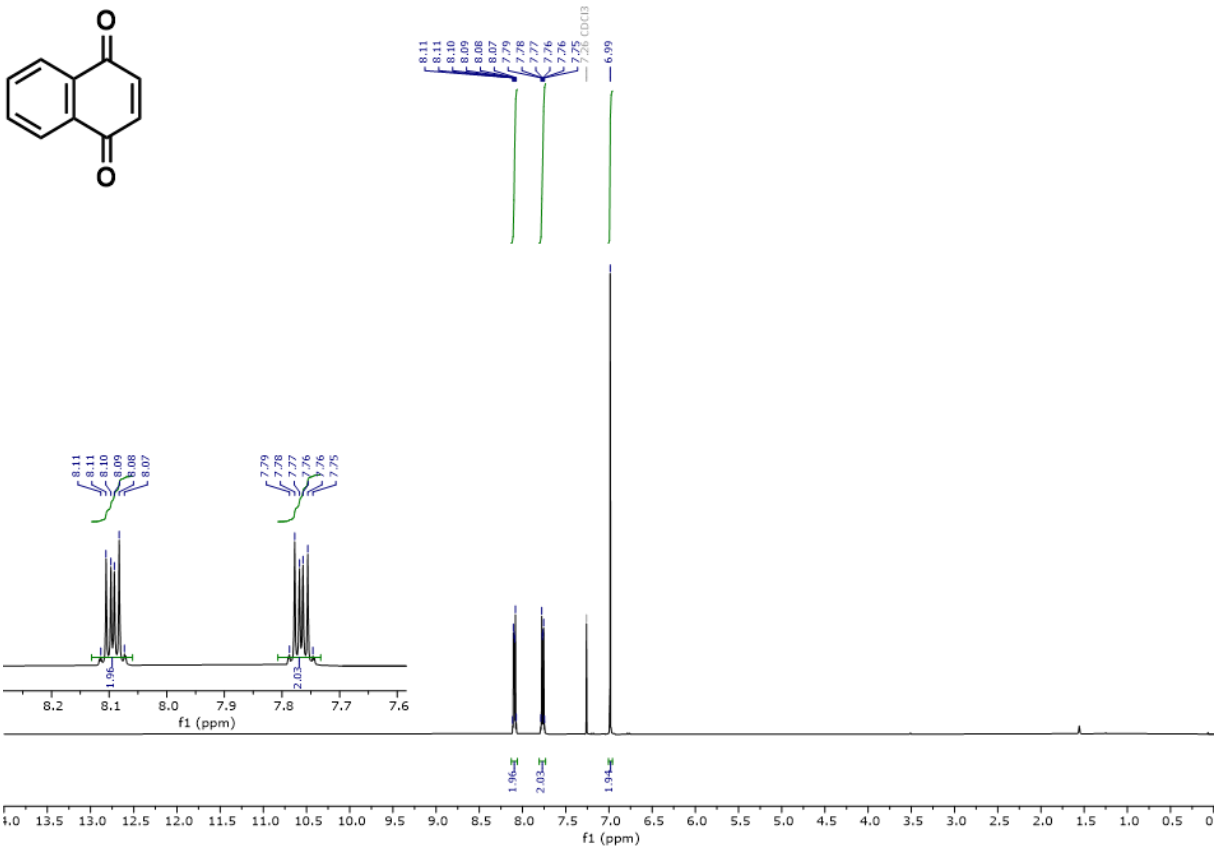


Figure 54: ^{1}H NMR (400 MHz) naphthalene-1,4-dione (**2t**) in $CDCl_3$ at 298 K.

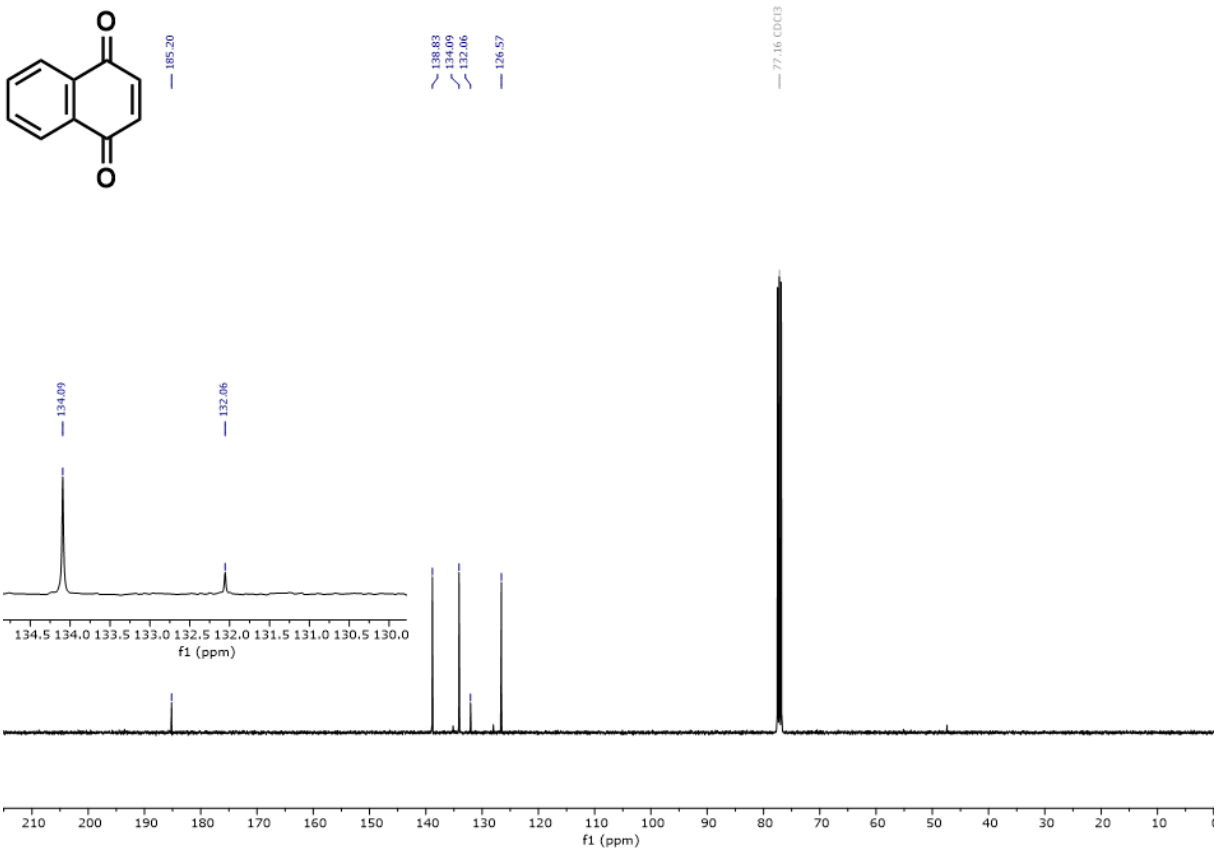


Figure 55: ^{13}C NMR (101 MHz) naphthalene-1,4-dione (**2t**) in $CDCl_3$ at 298 K.

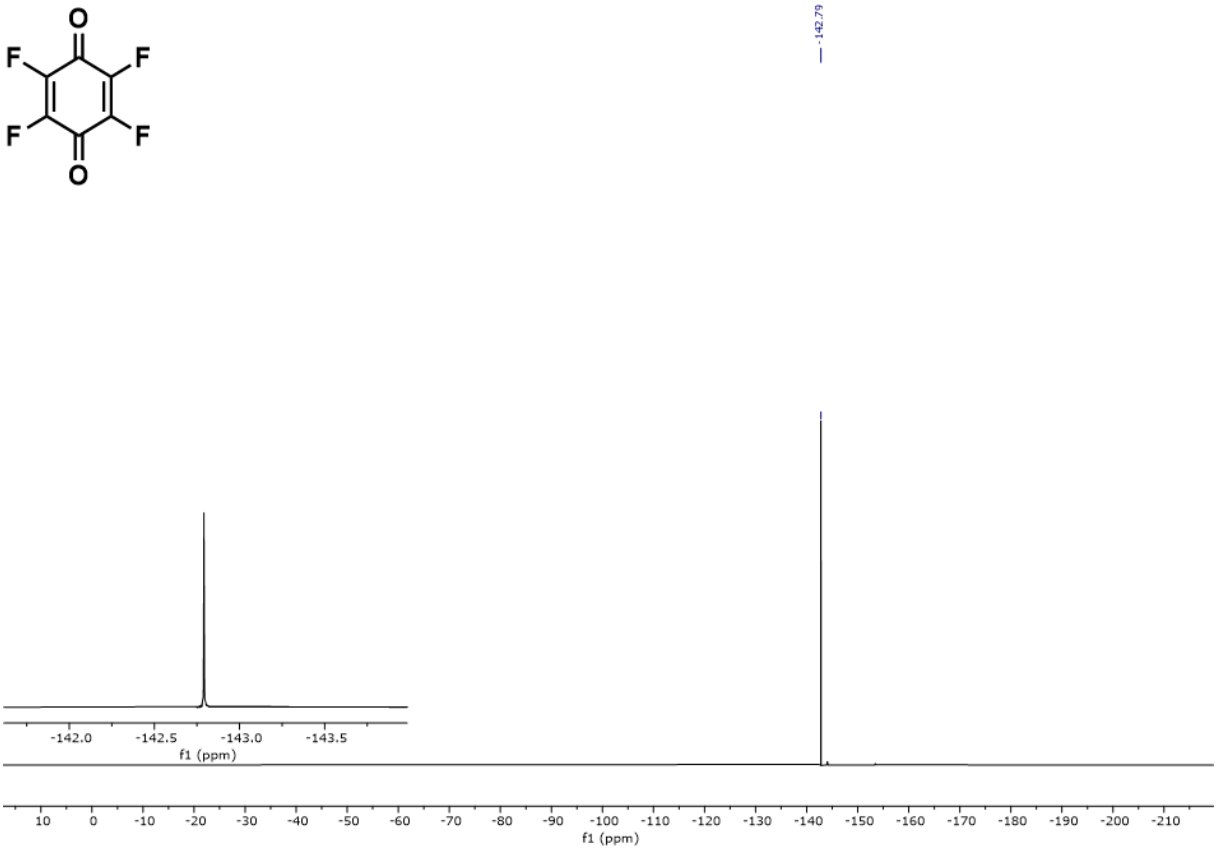


Figure 56: ^{19}F NMR (376 MHz) 2,3,5,6-tetrafluorocyclohexa-2,5-diene-1,4-dione (**2u**) in $CDCl_3$ at 298 K.

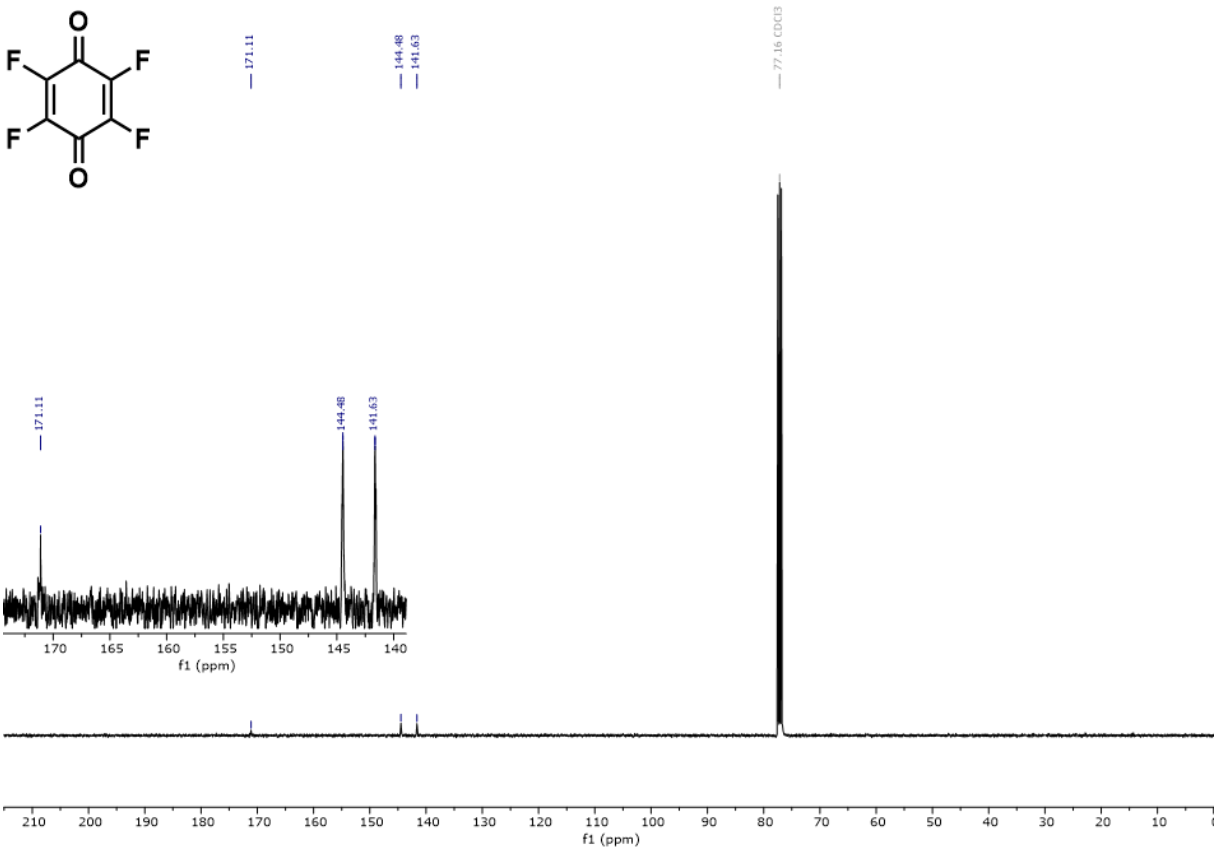


Figure 57: ^{13}C NMR (101 MHz) 2,3,5,6-tetrafluorocyclohexa-2,5-diene-1,4-dione (**2u**) in $CDCl_3$ at 298 K.

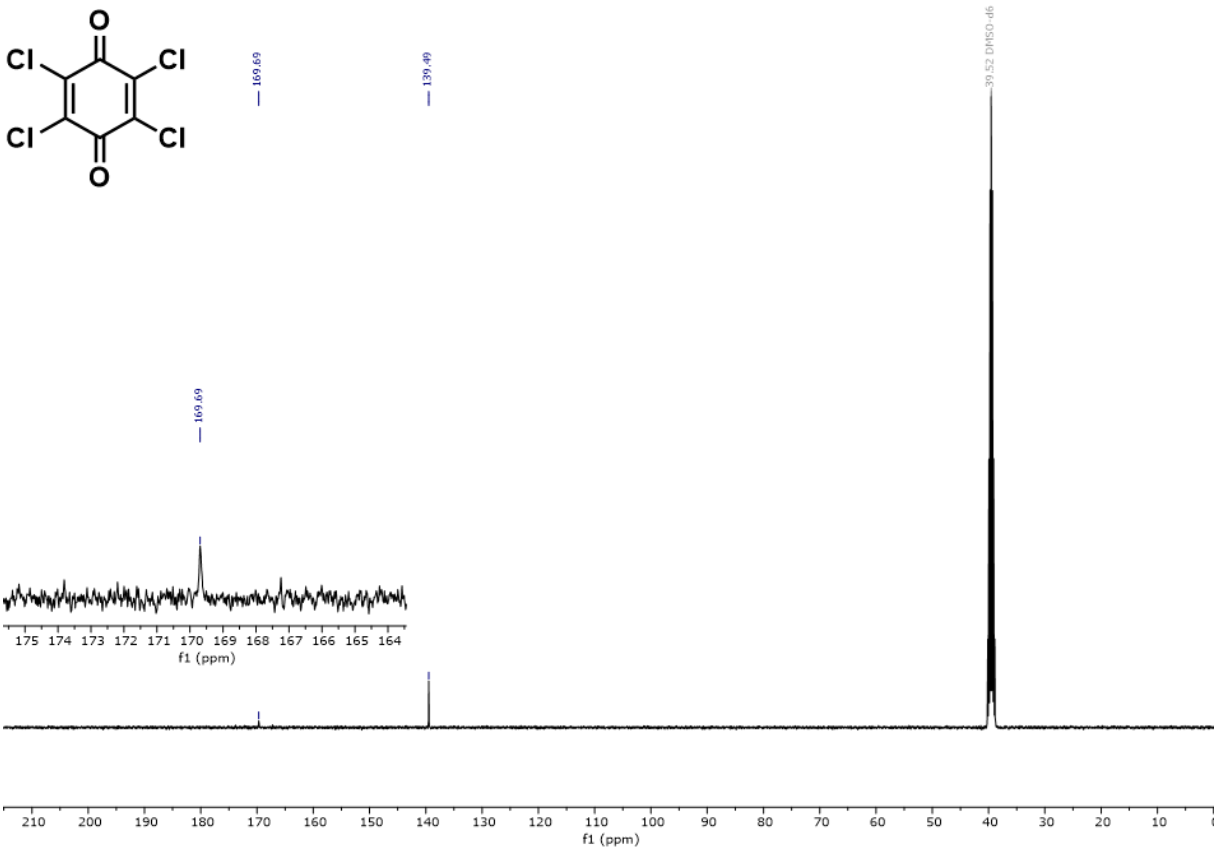


Figure 58: ^{13}C NMR (101 MHz) 2,3,5,6-tetrachlorocyclohexa-2,5-diene-1,4-dione (**2v**) in DMSO-d_6 at 298 K.

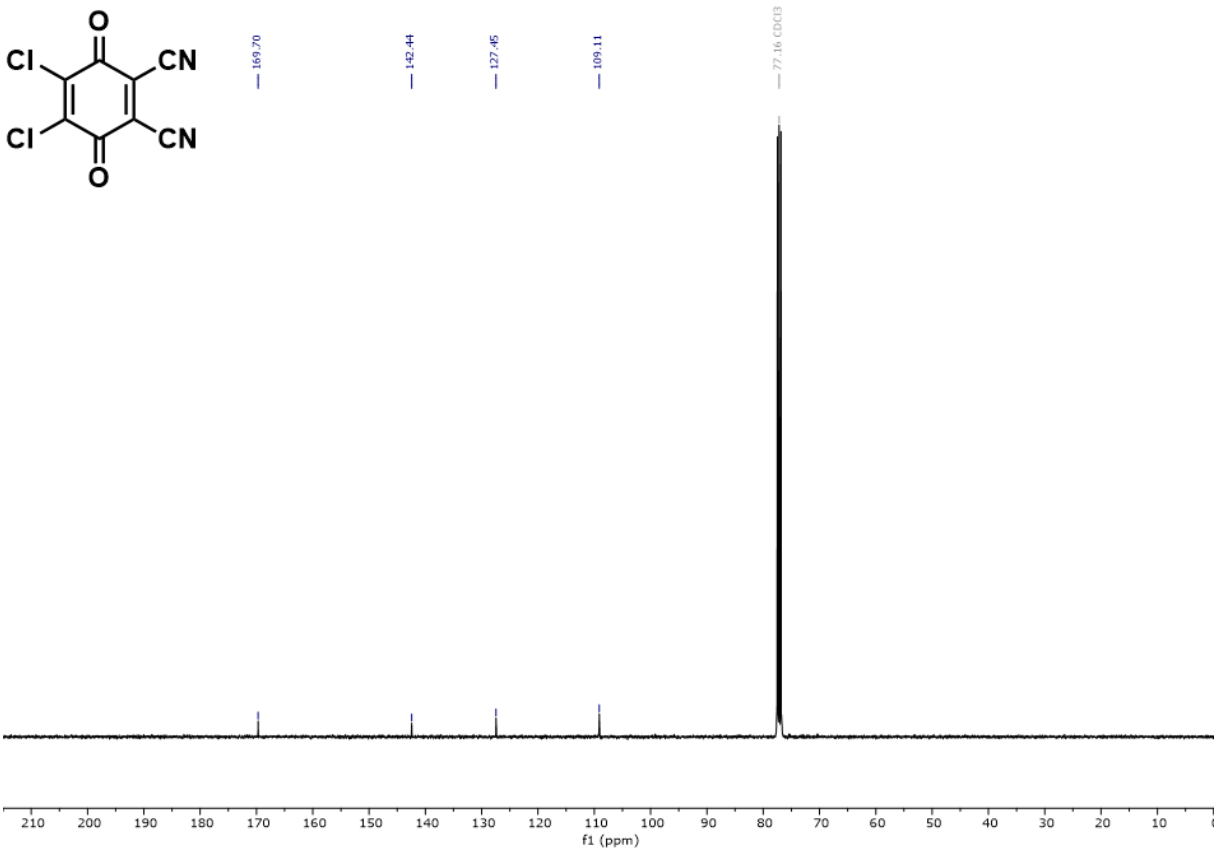


Figure 59: ^{13}C NMR (101 MHz) 2,3-dichloro-5,6-dicyanocyclohexa-2,5-diene-1,4-dione (**2w**) in $CDCl_3$ at 298 K.

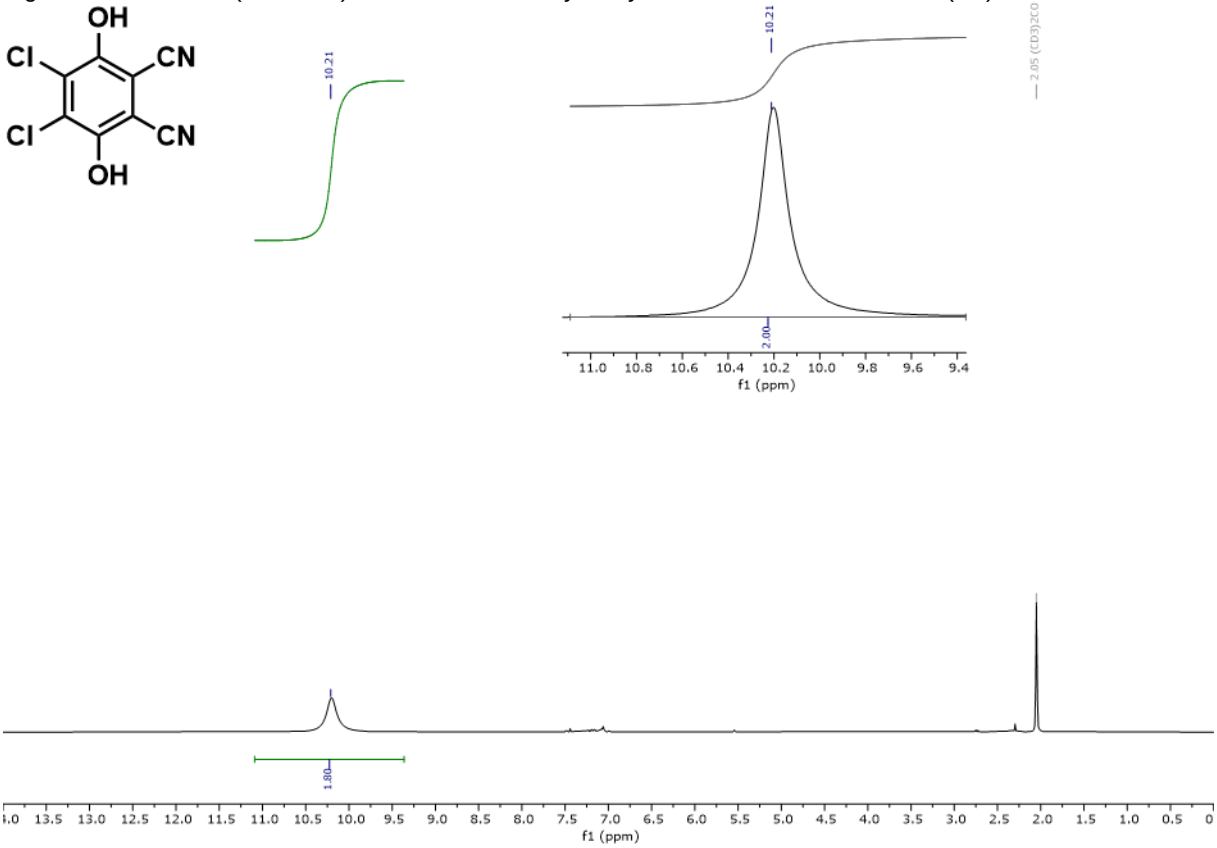


Figure 60: ^{1}H NMR (400 MHz) 4,5-dichloro-3,6-dihydroxyphthalonitrile (**4w**) in acetone-d_6 at 298 K.

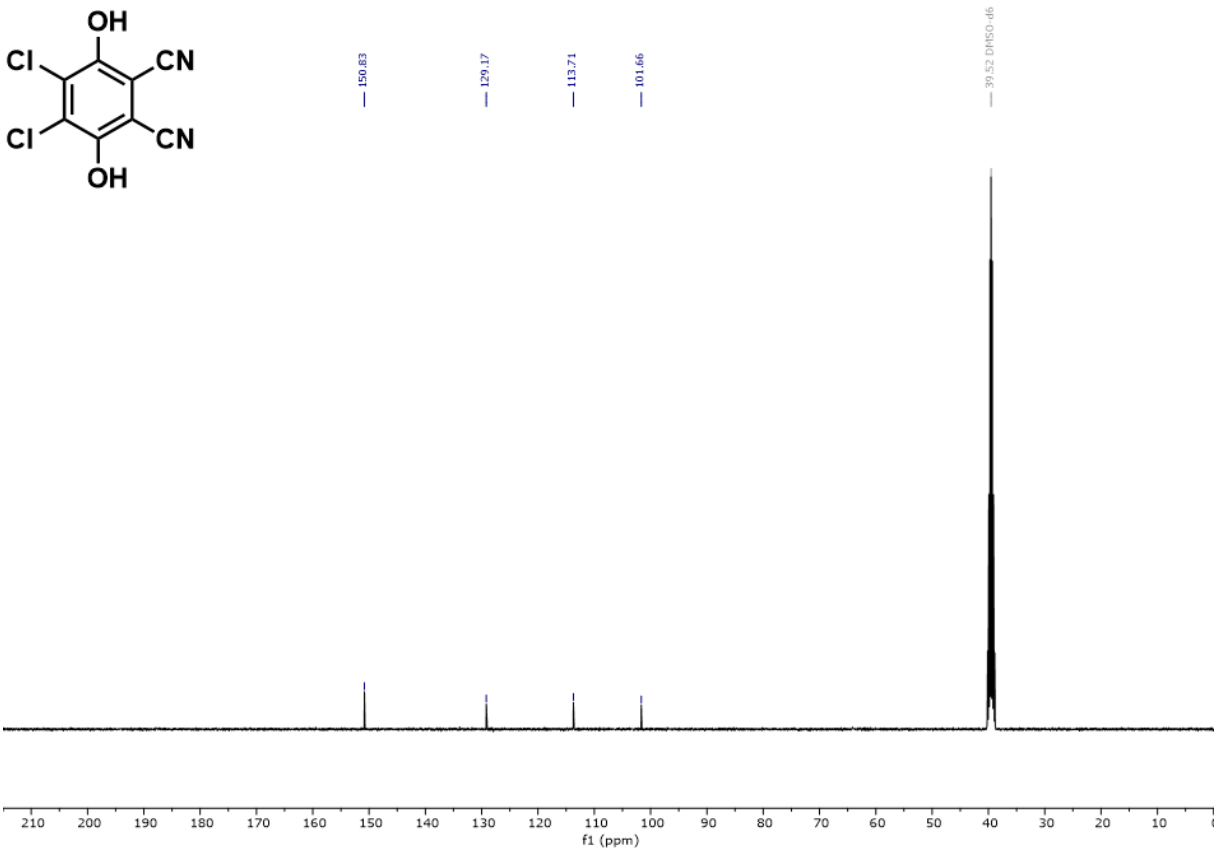


Figure 61: ^{13}C NMR (101 MHz) 4,5-dichloro-3,6-dihydroxyphthalonitrile (**4w**) in DMSO-d_6 at 298 K.

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