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Visible light-promoted Selectfluor-mediated quinone functionalization with unactivated Csp^3-H components

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Dedicated to Professor Lanny Liebeskind on the occasion of his 70th anniversary

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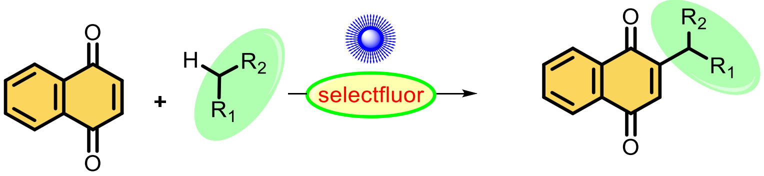
Abstract

A visible light-promoted metal-free cross-dehydrogenative-coupling (CDC) method for the alkylation of 1,4-naphthoquinones is reported using Selectfluor as a hydrogen atom transfer (HAT) agent. This protocol is suitable for a variety of 1,4-naphthoquinones and Csp^3-H compounds and it facilitates the formation of pharmaceutically important quinone scaffolds under mild conditions. Using this methodology, the antimalarial drug, parvaquone, was synthesized in a single step.



♣Metal free ♦Mild conditions

♥No prefunctionalization

♠Access to drug molecules in single step

Keywords: Quinone functionalization, cross-dehydrogenative-coupling, Selectfluor and visible light

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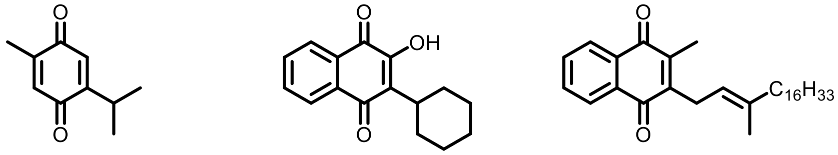
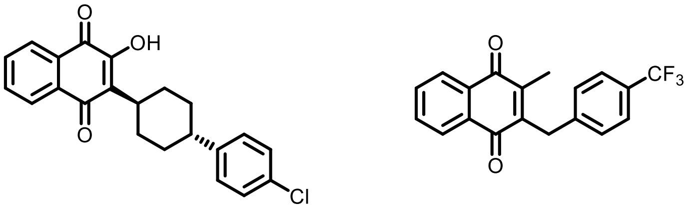
Introduction

The 1,4-quinone scaffold is one of the most investigated templates in the field of organic synthesis, as it features in many functional molecules, bioactive natural products and pharmaceuticals.[1-5] Among the derivatives of 1,4-quinone, alkylated 1,4-naphthoquinones and 1,4-benzoquinones (Figure 1) are extremely important as they exhibit a wide range of biological properties such as anti-microbial, anti-tumor, anti-inflammatory and neurological activities (Figure 1).[6-10]



Thymoquinone (anticancer) **Parvaquone (antiparasitic)** **Vitamin K1 (coagulation)**

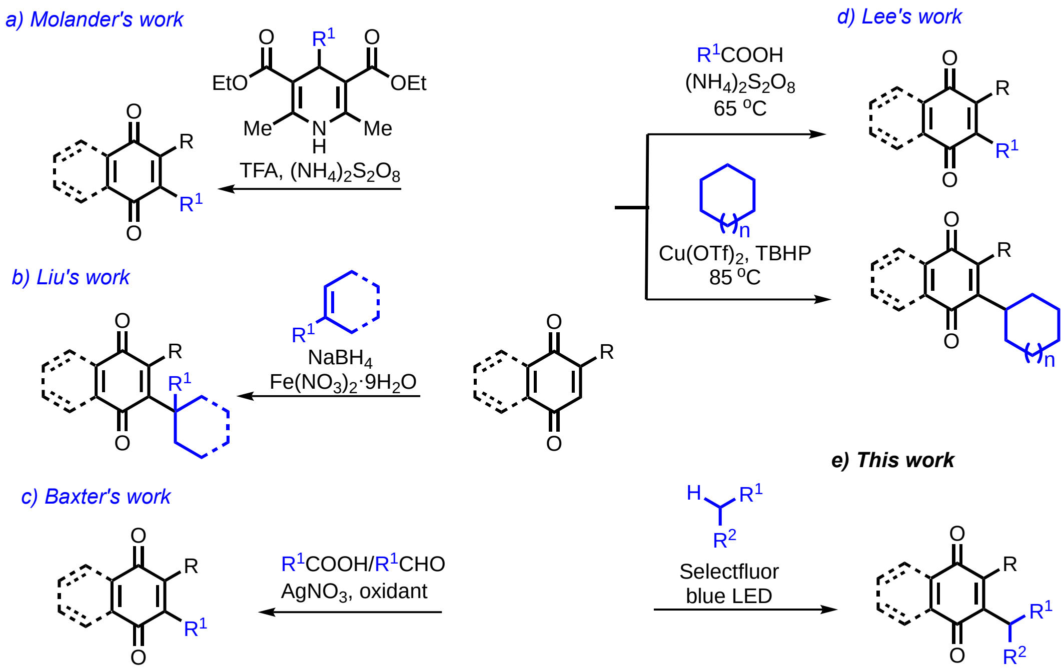


Atovaquone (antiparasite) **Plasmodione (antimalarial lead drug)**

Figure 1. Some biologically active alkylated quinones.

Owing to the importance of alkylated 1,4-quinone frameworks, several radical alkylation protocols for the functionalization of 1,4-quinones have been proposed in recent years (Scheme 1). For instance, Molander and co-workers reported alkylation of 1,4-quinones *via* oxidative homolysis of 1,4-dihydropyridines (Scheme 1a).[11] Liu's group developed an Fe(III) mediated radical alkylation of quinones with olefins (Scheme 1b).[12] Baxter and co-workers reported a silver-catalysed radical alkylation of quinones (Scheme 1c).[13] Also, a persulfate mediated alkylation of 1,4-quinones using carboxylic acids[14] and a copper catalysed direct cross-coupling of 1,4-quinones with cycloalkanes[15] were demonstrated by Lee's group (Scheme 1d). Nevertheless, each of these methods has limitations such as pre-functionalization of the alkyl partner, requirement of transition metal reagents and explosive peroxides as oxidants. Hence, more efficient, milder and sustainable methods are still desirable.

Visible light-promoted Selectfluor-mediated direct functionalization of C-H bonds via the hydrogen atom transfer (HAT) mechanism has attracted attention in recent years. Pioneering work by Lei's group[16-17] demonstrated the Csp^3-H heteroarylation of cycloalkanes, ethers and alcohols mediated by Selectfluor under visible-light irradiation. At the same time, Jin's group[18] used similar reaction conditions for the alkylation of heteroarenes via the generation of alkyl radicals from unactivated Csp^3-H components. However, a visible light-promoted, Selectfluor-mediated C-H functionalization for the alkylation of quinones has not yet been studied.



Scheme 1. Radical alkylative functionalization of quinones.

Herein, we report a new method of introducing alkyl groups into the 1,4-naphthoquinone skeleton without pre-functionalization of the alkyl partner (Scheme 1e). This method utilizes visible light and the green oxidant Selectfluor without the requirement for radical initiator or transition metal photocatalyst.

Results and Discussion

With an overall aim of developing a direct Csp^2-Csp^3 cross coupling strategy for the alkylation of quinones under mild conditions, we started our investigation by irradiating a mixture of 2-acetoxy-1,4-naphthoquinone (**1a**), cyclohexane (**2a**) and Selectfluor in acetonitrile under a N_2 atmosphere at room temperature using a Penn PhD photoreactor M2 (blue LED, 450 nm) (Table 1, entry 1).

To our delight, the desired cross coupled product **3a** was formed in 42% yield within one hour. No desired product was observed when the light source was changed to 14 W white LED (Table 1, entry 2). Also, heating the reaction mixture to 80 °C in the absence of light, also did not yield any of the desired product (Table 1, entry 3). Use of additives such as AcOH and TFA didn't improve the yield of **3a** (Table 1, entries 4 and 5) and Et_3N completely diminished the yield of **3a** (Table 1, entry 8). Use of the solvent acetone led to lower yield of **3a** (Table 1, entry 6) and reaction didn't take place when cyclohexane was used as a solvent (Table 1, entry 7). Finally, when quinone **1a** was added to a mixture of cyclohexane and Selectfluor over a period of 20 minutes through syringe pump, the isolated yield of **3a** was improved to 54% (Table 1, entry 10).

The scope and generality of this cross-coupling strategy was then investigated using various 1,4-quinones and aliphatic C-H components under the optimized conditions (Table 2). The reaction of 2-hydroxy-1,4-naphthoquinone with cyclohexane under the optimized conditions afforded the antimalarial drug molecule parvaquone (**3b**) in 42% yield. 1,4-Naphthoquinone bearing a CF_3 group at the 2-position reacted smoothly and furnished the desired product (**3c**) in 55% yield. Whereas, 2-methyl- and 2-methoxy-1,4-napthoquinones afforded the desired products (**3d** and **3e**) in lower yields. Unsubstituted 1,4-naphthoquinone gave the desired product **3f** in 46% yield. *p*-Benzoquinone did not afford the desired product and its complete decomposition was observed under the reaction conditions.

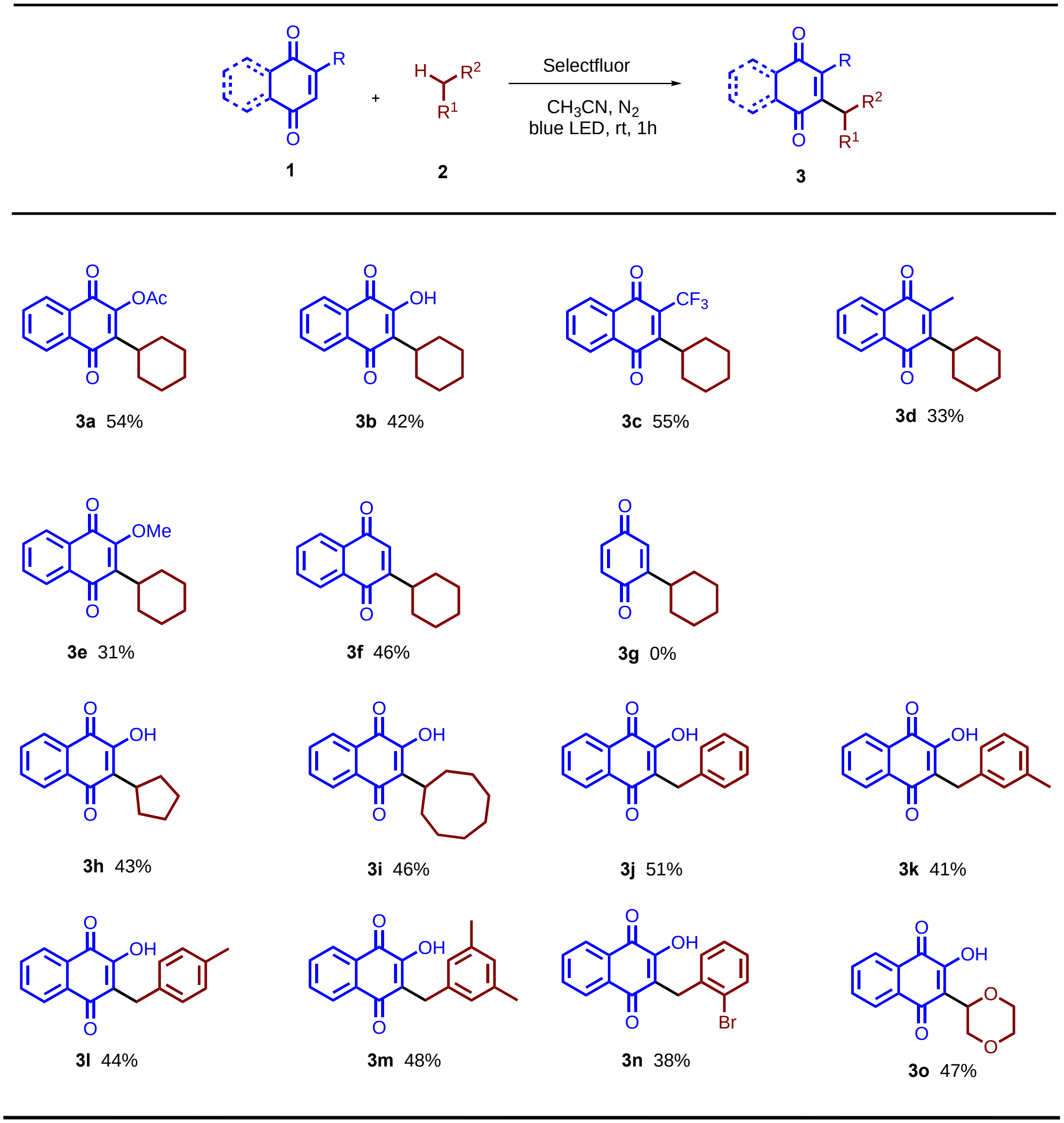
Table 1. Screening of optimal reaction conditions[a]

Entry	variation from above conditions	yield (%)[b]
1	None	42
2	white LED instead of blue LED	trace
3	80 °C in the dark	trace
4	2 eq CH_3COOH as additive	43
5	2 eq CF_3COOH as additive	39
6	acetone as a solvent	28
7	cyclohexane as a solvent	nd
8	2 eq Et_3N as additive	Nd
10	**1a** in CH_3CN was added over 20 min through syringe pump	54

[a] The reaction was carried out with **1a** (0.2 mmol), cyclohexane (2.0 mmol) and Selecfluor (0.4 mmol) in MeCN (2.0 mL) at room temperature under N_2 using Penn PhD photoreactor M2 (blue LED 450 nm) for 1 h. [b] Isolated yields.

Next, the scope of different aliphatic C-H components was examined using 2-hydroxy-1,4-naphthoquinone as reaction partner. The reaction with cycloalkanes such as cyclopentane and cyclooctane was successful and furnished the desired alkylated quinones (**3h** and **3i**) in moderate yields. Later, a series of methylbenzenes were investigated. Toluene, *m*-xylene, *p*-xylene and mesitylene were all found to be suitable substrates for this methodology and furnished the desired compounds (**3j**-**3m**). Notably, *ortho*-bromotoluene reacted well without loss of Br giving **3n**, thus affording the potential for further cross-couplings. In addition, cyclic ether 1,4-dioxane was also a competent substrate, giving the desired product (**3o**) in 47% yield.

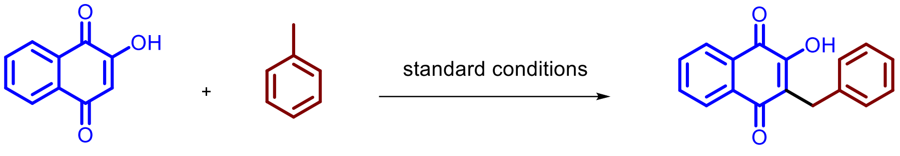
Table 2. Substrate scope of 1,4-quinones and aliphatic C-H components



3a 54%
3b 42%
3c 55%
3d 33%
3e 31%
3f 46%
3g 0%
3h 43%
3i 46%
3j 51%
3k 41%
3l 44%
3m 48%
3n 38%
3o 47%

[a] The reaction was carried out with **1** (0.2 mmol), Csp^3-H compound **2** (2.0 mmol) and Selecflor (0.4 mmol) in MeCN (2.0 mL) at room temperature under N_2 using Penn PhD photoreactor M2 (blue LED 450 nm) for 1 h. [b] Isolated yields.

To gain mechanistic insight, we next performed radical inhibition experiments (Scheme 2). When the reaction of 2-hydroxy-1,4-naphthoquinone with toluene was conducted in the presence of three equivalents of TEMPO and butylated hydroxytoluene (BHT) (2,6-bis(1,1-dimethylethyl)-4-methylphenol) under the standard conditions, formation of the product **3j** was completely suppressed. These experiments clearly indicate a radical reaction pathway.

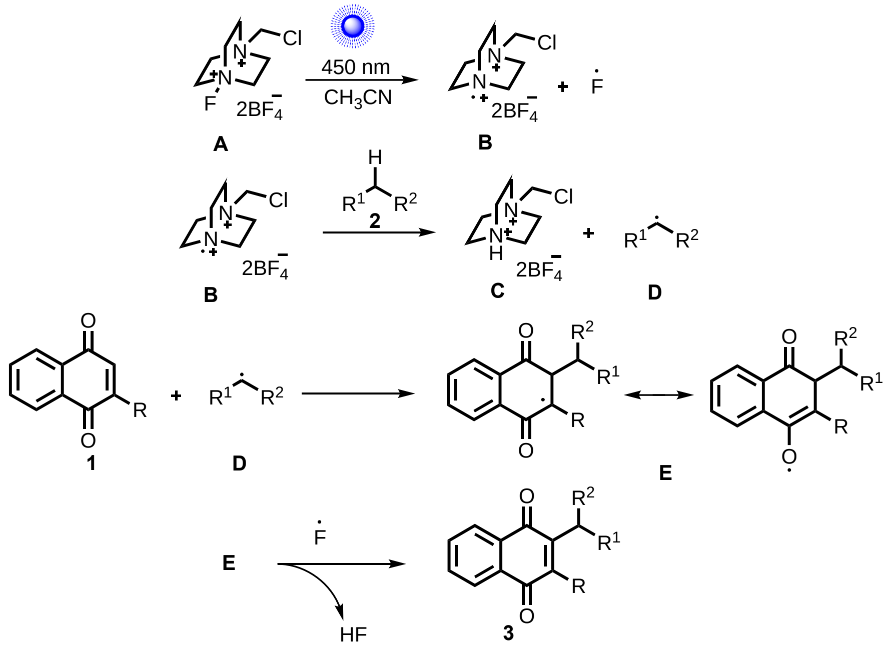


3j

TEMPO (3 equiv) 0%
BHT (3 equiv) 0%

Scheme 2. Radical inhibition experiments.

A plausible mechanism is proposed based on the control experiments above and preceding literature.[15-17] Firstly, the N-radical cation **B** formed by the homolytic fission of Selectfluor **A** abstracts a hydrogen atom from the alkane **2** to give the alkyl radical intermediate **D** and dication **C**. The generated nucleophilic alkyl radical **D** adds to the electron-deficient quinone **1** to give the radical intermediate **E**. Finally, abstraction of a hydrogen atom by fluorine radical from intermediate **E** generates the product **3** (Scheme 3).



Scheme 3. Plausible reaction mechanism for the alkylation.

Conclusions

In conclusion, we have developed a visible-light induced, Selectfluor mediated Csp^2-Csp^3 cross coupling strategy without the need of prefunctionalization of Csp^3 partner for the alkylation of 1,4-naphthoquinones. This mild protocol is suitable for various 1,4-naphthoquinones and aliphatic Csp^3-H components to afford pharmaceutically important quinone frameworks in moderate yields.

Experimental Section

General. Unless otherwise noted, reagents obtained from commercial suppliers were used without further purification. Reactions were monitored using thin-layer chromatography (SiO_2). Thin layer chromatography was performed on Merck silica gel plates and visualized by UV light. Column chromatography was carried out using silica gel (100-200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, 500 MHz (H) and at 75, 100, 125 MHz (C), respectively. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.0 ppm) as internal standard, and coupling constants (J) are given in Hz. HRMS were recorded using ESI-TOF techniques. Melting points of solids were recorded using Electrothermal (IA9100) melting point apparatus. Irradiation was performed with Penn PhD photoreactor M2 (PR M2) (blue LED, 450 nm) purchased from Sigma- Aldrich.

General procedure for the synthesis of alkylated 1,4-naphthoquinones. Selectfluor (0.4 mmol) and aliphatic Csp^3-H component **2** (2.0 mmol) were weighed in a vial with rubber septum and MeCN (1.0 mL) was added to this mixture. The vial was back filled with N_2 and it was introduced into Penn PhD photoreactor M2 (blue LED 450 nm). To this mixture, a solution of 1,4-naphthoquinone **1** (0.2 mmol) in MeCN (1.0 mL) was added over a period of 20 min through syringe pump. After completion of reaction (1 h), the reaction mixture was concentrated using rotary evaporation and the crude reaction mixture was purified by column chromatography to get the desired compound **3**.

3-Cyclohexyl-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (3a). Yellow syrup (32.2 mg, 54%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.03 (m, 2H), 7.77 – 7.67 (m, 2H), 3.01 (tt, *J* 11.9, 3.4 Hz, 1H), 2.42 (s, 3H), 1.88 – 1.64 (m, 7H), 1.43 – 1.27 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.6, 178.5, 168.2, 151.2, 142.4, 134.1, 133.7, 132.4, 130.7, 126.8, 126.4, 36.4, 30.0, 26.7, 26.0, 20.6; IR (neat, cm^{-1}): 3020, 2930, 1651, 1513, 1215, 746; HRMS (ESI) calcd for $C_{18}H_{18}O_4$ $[M]^+$: 298.1205; found: 298.1191.

2-Cyclohexyl-3-hydroxynaphthalene-1,4-dione (3b). Yellow solid (21.5 mg, 42%); mp 132-134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* 7.6 Hz, 1H), 8.05 (d, *J* 7.5 Hz, 1H), 7.74 (t, *J* 7.4 Hz, 1H), 7.65 (t, *J* 7.4 Hz, 1H), 7.46 (s, 1H), 3.09 – 3.04 (m, 1H), 2.03 – 1.92 (m, 2H), 1.82 – 1.79 (m, 2H), 1.73 – 1.71 (m, 1H), 1.64 – 1.60 (m, 2H), 1.41 – 1.27 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.6, 182.0, 152.9, 134.9, 133.2, 132.7, 129.2, 127.9, 127.0, 125.9, 35.2, 29.7, 29.2, 26.8, 26.0; HRMS (ESI) calcd for $C_{16}H_{17}O_3$ $[M+H]^+$: 257.1178; found: 257.1168. NMR data and m.p. (lit.133-135 °C) matches literature values.[15]

2-Cyclohexyl-3-(trifluoromethyl)naphthalene-1,4-dione (3c). Yellow syrup (33.9 mg, 55%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 7.99 (m, 2H), 7.82 – 7.69 (m, 2H), 3.04 (tt, *J* 11.8, 3.1 Hz, 1H), 2.20 – 2.05 (m, 2H), 1.90 – 1.81 (m, 2H), 1.80 – 1.73 (m, 1H), 1.72 – 1.64 (m, 2H), 1.42 – 1.28 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.5, 180.9, 157.5, 134.3, 134.1, 132.1, 131.6, 126.6, 126.3, 122.4 (q, *J* 279.4 Hz), 42.2, 30.5, 26.7, 25.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -56.4; IR (neat, cm^{-1}): 2928, 2857, 1673, 1595, 1281, 1137, 720; HRMS (ESI) calcd for $C_{17}H_{15}F_3O_2$ $[M]^+$: 308.1024; found: 308.0978.

2-Cyclohexyl-3-methylnaphthalene-1,4-dione (3d). Yellow solid (16.8 mg, 33%); mp 78-79 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 – 8.00 (m, 2H), 7.71 – 7.62 (m, 2H), 2.88 (tt, *J* 12.1, 3.3 Hz, 1H), 2.23 (s, 3H), 2.11 – 2.01 (m, 2H), 1.89 – 1.82 (m, 2H), 1.78 – 1.73 (m, 1H), 1.65 – 1.59 (m, 2H), 1.39 – 1.31 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.7, 185.2, 150.6, 143.1, 134.7, 134.5, 133.4, 133.1, 132.8, 131.8, 127.5, 126.6, 126.2, 126.0, 40.8, 29.9, 27.0, 26.0, 12.6; HRMS (ESI) calcd for $C_{17}H_{18}O_2$ $[M]^+$: 254.1307; found: 254.1313. NMR data and m.p. (lit.78 °C) matches literature values.[14]

2-Cyclohexyl-3-methoxynaphthalene-1,4-dione (3e). Yellow paste (16.7 mg, 31%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.92 (m, 2H), 7.66 – 7.56 (m, 2H), 3.99 (s, 3H), 3.03 (tt, *J* 12.2, 3.3 Hz, 1H), 1.90 – 1.78 (m, 2H), 1.78 –

1.70 (m, 2H), 1.69 – 1.63 (m, 1H), 1.55 – 1.47 (m, 2H), 1.36 – 1.16 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.6, 180.9, 157.3, 138.7, 132.7, 132.1, 131.3, 130.4, 125.4, 124.9, 60.3, 34.9, 29.0, 25.9, 25.0; HRMS (ESI) calcd for $C_{17}H_{18}O_3$ [M+H]$^+$: 270.1255; found: 270.1229. NMR data matches literature values.[14]

2-Cyclohexylnaphthalene-1,4-dione (3f). Yellow paste (22.1 mg, 46%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.07 (m, 1H), 8.07 – 8.01 (m, 1H), 7.75 – 7.68 (m, 2H), 6.73 (s, 1H), 2.95 – 2.85 (m, 1H), 1.88 – 1.81 (m, 4H), 1.80 – 1.75 (m, 1H), 1.51 – 1.40 (m, 2H), 1.30 – 1.17 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.7, 184.8, 156.3, 133.6, 133.6, 133.1, 132.5, 131.9, 126.7, 125.9, 36.7, 32.3, 26.4, 26.1; HRMS (ESI) calcd for $C_{16}H_{16}O_2$ [M+H]$^+$: 240.1150; found: 240.1163. NMR data matches literature values.[14]

2-Cyclopentyl-3-hydroxynaphthalene-1,4-dione (3h). Yellow syrup (20.8 mg, 43%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* 7.7, 0.9 Hz, 1H), 8.06 (dd, *J* 7.6, 1.0 Hz, 1H), 7.75 (td, *J* 7.6, 1.3 Hz, 1H), 7.67 (td, *J* 7.5, 1.2 Hz, 1H), 7.44 (s, 1H), 3.51 – 3.37 (m, 1H), 1.97 – 1.81 (m, 6H), 1.68 – 1.64 (m, 2H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7, 181.6, 152.8, 134.9, 133.3, 132.8, 129.3, 127.6, 126.9, 126.0, 34.9, 30.8, 26.8; IR (neat, cm^{-1}): 2926, 2858, 1653, 1456, 1389, 1275, 770; HRMS (ESI) calcd for $C_{15}H_{15}O_3$ [M+H]$^+$: 243.1021; found: 243.1026.

2-Cyclooctyl-3-hydroxynaphthalene-1,4-dione (3i). Brown color gum (26.1 mg, 46%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* 7.7, 1.1 Hz, 1H), 8.06 (dd, *J* 7.6, 1.1 Hz, 1H), 7.75 (td, *J* 7.6, 1.4 Hz, 1H), 7.67 (td, *J* 7.5, 1.3 Hz, 1H), 7.35 (s, 1H), 3.30 (tt, *J* 10.4, 3.1 Hz, 1H), 2.12 – 1.97 (m, 2H), 1.87 – 1.75 (m, 2H), 1.74 – 1.49 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.5, 182.1, 152.0, 134.9, 133.1, 132.7, 131.0, 129.3, 126.9, 125.9, 34.4, 31.4, 26.7, 26.5, 26.4; NMR data matches literature values.[15]

2-Benzyl-3-hydroxynaphthalene-1,4-dione (3j). Yellow solid (26.9 mg, 51%); mp 173-175 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* 7.7, 1.0 Hz, 1H), 8.07 (dd, *J* 7.6, 1.1 Hz, 1H), 7.74 (td, *J* 7.6, 1.3 Hz, 1H), 7.67 (td, *J* 7.5, 1.3 Hz, 1H), 7.44 (s, 1H), 7.39 (d, *J* 7.3 Hz, 2H), 7.26 (t, *J* 7.3 Hz, 2H), 7.17 (t, *J* 7.3 Hz, 1H), 3.95 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4, 181.7, 153.1, 138.8, 138.1, 135.1, 133.0, 132.8, 129.9, 129.4, 128.3, 127.1, 127.0, 126.2, 126.1, 123.2, 29.0, 21.4; NMR data and m.p. (lit.174-175 °C)matches literature values.[19]

2-Hydroxy-3-(3-methylbenzyl)naphthalene-1,4-dione (3k). Brown color gum (22.8 mg, 41%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* 7.7, 1.0 Hz, 1H), 8.07 (dd, *J* 7.6, 1.0 Hz, 1H), 7.74 (td, *J* 7.6, 1.4 Hz, 1H), 7.67 (td, *J* 7.5, 1.3 Hz, 1H), 7.42 (s, 1H), 7.22 – 7.17 (m, 2H), 7.15 (t, *J* 7.7 Hz, 1H), 6.99 (d, *J* 7.3 Hz, 1H), 3.91 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4, 181.7, 153.1, 138.8, 138.1, 135.0, 1323.0, 132.8, 129.9, 129.4, 128.3, 127.1, 127.0, 126.2, 126.1, 123.2, 29.0, 21.4; IR (neat, cm^{-1}): 3022, 1659, 1518, 1215, 747; HRMS (ESI) calcd for $C_{18}H_{14}O_3$ [M]$^+$: 278.0943; found: 278.0947.

2-Hydroxy-3-(4-methylbenzyl)naphthalene-1,4-dione (3l). Yellow solid (24.5 mg, 44%); mp 162-164 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (dd, *J* 7.7, 0.9 Hz, 1H), 8.06 (dd, *J* 7.6, 1.0 Hz, 1H), 7.74 (td, *J* 7.6, 1.4 Hz, 1H), 7.66 (td, *J* 7.5, 1.3 Hz, 1H), 7.41 (s, 1H), 7.28 (d, *J* 8.0 Hz, 2H), 7.07 (d, *J* 7.8 Hz, 2H), 3.91 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4, 181.7, 152.9, 135.9, 135.0, 133.0, 129.2, 129.1, 126.9, 126.1, 123.3, 28.67, 21.1; HRMS (ESI) calcd for $C_{18}H_{14}O_3$ [M]$^+$: 278.0943; found: 278.0947. NMR data and m.p. (lit.162-164 °C) matches literature values.[19]

2-(3,5-Dimethylbenzyl)-3-hydroxynaphthalene-1,4-dione (3m). Brown color gum (28.1 mg, 48%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* 7.7, 0.9 Hz, 1H), 7.99 (dd, *J* 7.6, 1.0 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.62 – 7.58 (m, 1H), 7.34 (s, 1H), 6.92 (s, 2H), 6.74 (s, 1H), 3.80 (s, 2H), 2.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4, 181.7, 153.0, 138.7, 137.9, 134.9, 132.9, 129.4, 128.0, 126.9, 126.9, 126.1, 123.2, 28.9, 21.3; IR (neat, cm^{-1}): 3020, 1658, 1520, 1215, 744; HRMS (ESI) calcd for $C_{19}H_{16}O_3$ [M]$^+$: 292.1099; found: 292.1105.

2-(2-Bromobenzyl)-3-hydroxynaphthalene-1,4-dione (3n). Yellow solid (26.0 mg, 38%); mp 163-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 – 8.08 (m, 2H), 7.80 – 7.75 (m, 1H), 7.74 – 7.68 (m, 1H), 7.45 (s, 1H), 7.56 (dd, *J* 8.0, 0.9 Hz, 1H), 7.19 – 7.11 (m, 2H), 7.08 – 7.02 (m, 1H), 4.09 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.2, 181.4, 154.0, 137.9, 135.1, 133.1, 132.8, 129.7, 129.4, 127.9, 127.3, 127.1, 126.3, 124.7, 121.4, 29.6; HRMS

(ESI) calcd for $C_{17}H_{11}BrO_3$ $[M]^+$: 341.9892; found: 341.9912. NMR data and m.p. (lit.162-164 °C) matches literature values.[19]

2-(1,4-Dioxan-2-yl)-3-hydroxynaphthalene-1,4-dione (3o). Brown color gum (24.5 mg, 47%); ^1H NMR (300 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.08 (t, *J* 6.7 Hz, 2H), 7.79 – 7.62 (m, 2H), 5.19 (dd, *J* 10.1, 2.7 Hz, 1H), 4.05 – 3.67 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.3, 180.5, 156.4, 134.7, 133.3, 132.0, 130.2, 126.5, 126.4, 117.5, 74.0, 68.7, 67.6, 66.3; IR (neat, cm^{-1}): 2928, 1728, 1680, 1650, 1278, 1118; HRMS (ESI) calcd for $C_{14}H_{13}O_5$ $[M+H]^+$: 261.0763; found: 261.0764.

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Supplementary Material

^1H, ^{13}C and ^{19}F NMR associated with this article are available as supplementary data.

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