# Bifunctionalisation of 1,4-naphthoquinone by the oxidative addition of an alkylamine and iodine

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Novel 2-iodo-3-(alkylamino) naphthalene-1,4-diones are formed in 33–70% yield by the reaction of alkylamine and 1, 4-naphthoquinone in the presence of iodine.

**Keywords**: 2-iodo-3-(alkylamino) naphthalene-1,4-dione, alkylamine, 1, 4-naphthoquinone, iodine

Some natural products which contain alkylamino derivatives of naphthoquinones show a wide biological activity as potent antitumour,[1–3] antimalarial[4,5] and antibacterial[6–9] agents. This biological activity has made the synthesis of these compounds attractive. Two major synthetic strategies have been developed: one which involves the nucleophilic displacement of the halo-quinone,[4,5,10] while the other involves a direct 1,4-addition of amines to the quinones. Unfortunately, many of these procedures have disadvantages involving strongly acidic conditions side-reactions, low yields and complex methodology.

Recently, the metal (ion)-free catalysis of organic reaction has received increasing attention.[11–17] The use of molecular iodine has become popular because of its high tolerance to air and moisture, low-cost, ready availability, and high catalytic activity.[18–23] For instance, Karimi[24] reported a mild and highly efficient method for the silylation of alcohols using hexamethyldisilazane catalysed by iodine under nearly neutral reaction conditions. Wang[25] reported a new decarboxylative cyclisation to construct pyridines derivatives by a-amino acids and aldehyde under molecular iodine conditions. Recently, the preparation of 1,2-diaryldiketones by oxidative cleavage of 1,3-diaryldiketones catalysed by iodine has been reported.[26] A one-pot synthesis of flavanone and highly substituted pyrimidine derivatives via multi component Mannich reaction catalysed by iodine has also been reported.[27]

Liu has recently disclosed an iodine-promoted protocol for the synthesis of 2-amino-1,4-naphthoquinones under ultrasonic irradiation at room temperature.[28] Unexpectedly when we tried to repeat the reaction of 1,4-naphthoquinone and a primary amine in the presence of iodine, the unpublished product of iodine addition was obtained (Scheme 1). In this paper, the synthesis of 2-iodo-3-(alkylamino)naphthalene-1,4- dione is now reported. As new compounds, besides their potential bioactivity, they can become very useful intermediates for the further preparation of derivatives of 2-amino-1,4-naphthoquinone.[29]

Our initial investigations were focused on the preparation of 2-(benzylamino)naphthalene-1,4-dione (**4a**) from the reaction of 1,4-naphthoquinone (**1a**) and benzylamine (**2a**). The unexpected iodine addition product 2-iodo-3-(benzylamino)-naphthalene-1,4-dione (**3a**) was obtained in 15% together with 2-(benzylamino)naphthalene-1,4-dione (**4a**) in 27.7% (Table 1, entry 1). To explore this reaction, the conditions were optimised to improve the yield of **3a**. As shown in Table 1, the solvent of this reaction was studied with 1,4-naphthoquinone and benzylamine as the model reaction, the yield of **3a** and total yield were both increased with $CHCl_3$ as the solvent (Table 1, entry 3).

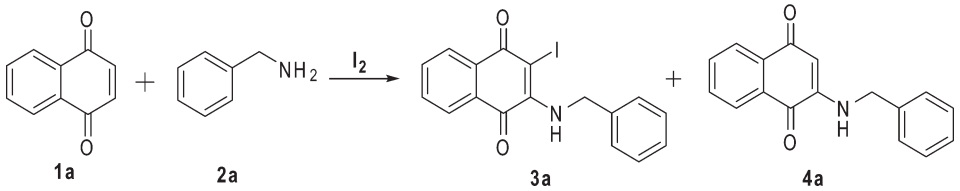
In order to further improve the reaction efficiency and selectivity, the effect of temperature was examined. The selectivity for the formation of **3a** has obviously improved at 0 °C (entries 3,5 and 6), and the corresponding product **3a** was obtained in 31.4% and **4a** in 38.5% (entry 6).

Under these conditions, the yield of **3a** was improved with increase of iodine. Finally, the yield of **3a** and **4a** was obtained in 51.3% and 32.2% at 0 °C in $CHCl_3$ with the ratio of **1a**:**2a**:$I_2$ as 1:1.2:2. Although 1,4-naphthoquinone was consumed under optimised condition, the reaction time was extended but the yield of product **3a** was not increased and the ratio of **3a** to **4a** was not changed (entry 12).

As shown in Table 2, the iodine addition products **3** were obtained in moderate to good yield in the reaction of 1,4-naphthoquinone and different primary amines in $CHCl_3$ as solvent and starting material molar ratios of **1**:**2**:$I_2$ (1:1.2:2) at 0 °C (Scheme 2). The total yield of **3** and **4** was in 70–86%. The selectivity for the formation of **3** was good when the carbon number of amines were no more than four without steric hindrance, the ratio of **3** and **4** was above three (entries 2, 3, 4, 5 and 9). As the steric hindrance of the benzylamine and the long-chain amine increased, the selectivity for **3** decreased and the yield of 3 and 4 was about equivalent (entries 1, 7 and 8).

In contrast, the product of iodine addition was not obtained in the reaction of phenylamine and 1,4-naphthoquinone under the same conditions. The product of iodination of the aniline ring 2-(4-iodophenylamino)naphthalene-1,4-diol (**5**) was obtained instead in 24.6% yield. 2- Phenylamino-1,4-naphthoquinone (**6**) was also obtained in 34.2% yield. The structure of **5** was confirmed by $^1$H NMR in $CDCl_3$ and $D_2O$.

The following experiments were carried out to understand the reaction and from our experimental results, a possible mechanism was proposed (Scheme 4). Product **4a** was obtained in 72.6% yield from the reaction between **1a** and benzylamine **2a**. Product **3a** was obtained in 64.6% yield when **4a** as treated with 2 equiv. iodine, thus demonstrating the intermediacy of **4a** in the reaction pathway. When the reaction was prolonged or used more than 2 equiv. iodine, a greater yield of product **3a**




**Scheme 1**

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**Table 1** Optimisation of the reaction conditions

| Entry [a] | **1a**:**2a**:$I_2$ | Solvent | T/°C | Yield/% [b] of **3a**:**4a** | Ratio of **3a**:**4a** |
|---|---|---|---|---|---|
| 1 | 1:1.2:1 | $CH_2Cl_2$ | r.t. | 14.9/27.7 | 0.54 |
| 2 | 1:1.2:1 | Toluene | r.t. | 19.5/28.4 | 0.68 |
| 3 | 1:1.2:1 | $CHCl_3$ | r.t. | 21.4/38.5 | 0.56 |
| 4 | 1:1.2:1 | $C_2H_5OH$ | r.t. | 15.0/49.5 | 0.30 |
| 5 | 1:1.2:1 | $Et_2O$ | r.t. | 15.7/37.4 | 0.42 |
| 6 | 1:1.2:1 | Water | r.t. | 18.7/19.7 | 0.95 |
| 7 | 1:1.2:1 | $CHCl_3$ | 60 °C | 12.2/49.5 | 0.25 |
| 8 | 1:1.2:1 | $CHCl_3$ | 0 °C | 31.4/38.5 | 0.81 |
| 9 | 1:1.2:0.1 | $CHCl_3$ | 0 °C | 7.4/51.7 | 0.14 |
| 10 | 1:1.2:1.2 | $CHCl_3$ | 0 °C | 36.6/35.4 | 1.03 |
| 11 | 1:1.2:2 | $CHCl_3$ | 0 °C | 51.3/32.2 | 1.59 |
| 12[c] | 1:1.2:2 | $CHCl_3$ | 0 °C | 52.0/32.7 | 1.59 |

[a] Stirred for 18h. [b] Isolated yield based on **1a**. [c] Stirred for 36 h.

**Table 2** Reaction between 1,4- naphthoquinone and different primary amines

| Entry | R | Product **3** | | Product **4** | | **3**/**4** | Total yield |
|---|---|---|---|---|---|---|---|
| | | **3** | Yield/% | **4** | Yield/% | | |
| 1 | $PhCH_2$- | **3a** | 51.3 | **4a** | 32.2 | 1.6 | 83.5 |
| 2 | $CH_3$- | **3b** | 56.4 | **4b** | 19.5 | 2.9 | 75.9 |
| 3 | $C_2H_5$- | **3c** | 68.7 | **4c** | 18.2 | 3.8 | 86.9 |
| 4 | $C_3H_7$- | **3d** | 70.4 | **4d** | 15.5 | 4.5 | 85.9 |
| 5 | $C_4H_9$- | **3e** | 67.8 | **4e** | 17.3 | 3.9 | 85.1 |
| 6 | $C_6H_{13}$- | **3f** | 32.8 | **4f** | 38.9 | 0.8 | 71.7 |
| 7 | $C_{10}H_{21}$- | **3g** | 43.9 | **4g** | 30.2 | 1.5 | 74.1 |
| 8 | $C_{12}H_{25}$- | **3h** | 47.9 | **4h** | 44.0 | 1.1 | 87.9 |
| 9 | $(CH_3O)_2CHCH_2$- | **3i** | 55.0 | **4i** | 19.2 | 2.9 | 74.2 |
| 10 | $HOCH_2CH_2$- | **3j** | 49.4 | **4j** | 21.4 | 2.3 | 70.8 |

was not obtained. The iodo compound, 2-iodonaphthalene-1,4-dione **7** was not obtained with naphthoquinone and iodine. In terms of our experimental results, a possible sequence for the formation of the iodinated product **3** is proposed in which iodinated product **3** was formed by iodination of intermediate **4**.

Our experimental results and the work of Liu[28] and Wang[30], leads to the sequence shown in Scheme 5. The alkylamine attacks the 1,4-naphthoquinone activated by molecular iodine to give the initial addition product **II**. The intermediate **II** and its tautomer **III** are oxidised to quinones resulting in **4**, The oxidation process can involve the oxygen in air [31] and the iodine in reaction system. Two possible reaction pathways leading to **3** are depicted in Scheme 5: One is the iodination of 2-amino-1,4-naphthoquinone **4** to give the product **3** whilst the other is the iodination of the hydroquinone **III** to give the intermediate **VI** which is then oxidised to the final product **3**.

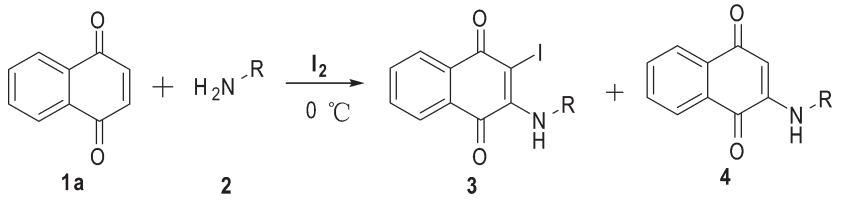
In summary, we have synthesised a series of 2-iodo-3-(alkylamino)-naphthalene-1,4-diones by a useful, convenient, and cost-effective route. These novel compounds have potential biological activity and their applications to the synthesis of more complex and interesting products are underway in our laboratory.

## Experimental

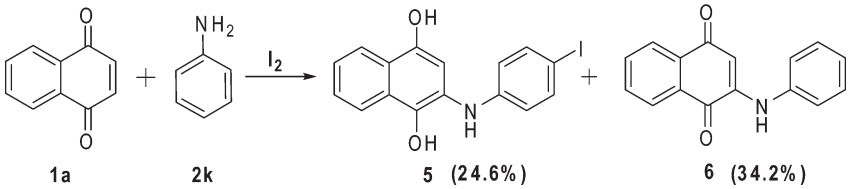
The reagents were obtained from commercial sources. $CH_2Cl_2$, $CHCl_3$ and toluene were dried with Na or $CaH_2$. The $^1H$ and $^{13}C$ NMR spectra were recorded at 500 and 125 MHz, respectively, in $CDCl_3$ with a Bruker AM 500 spectrometer. The GC-MS was Agilent (GC6890-MS5973).

*General procedure*

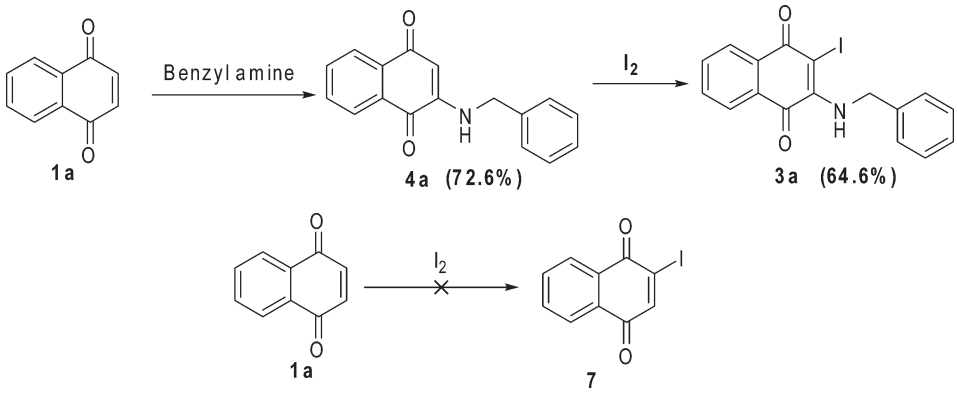
A mixture of 1,4-naphthoquinone (0.158 g, 1.0 mmol) and the amine (1.2 mmol) in $CHCl_3$ (5 mL) was added to $I_2$ (2 equiv.) at 0 °C and stirred until the starting material was consumed, as determined by



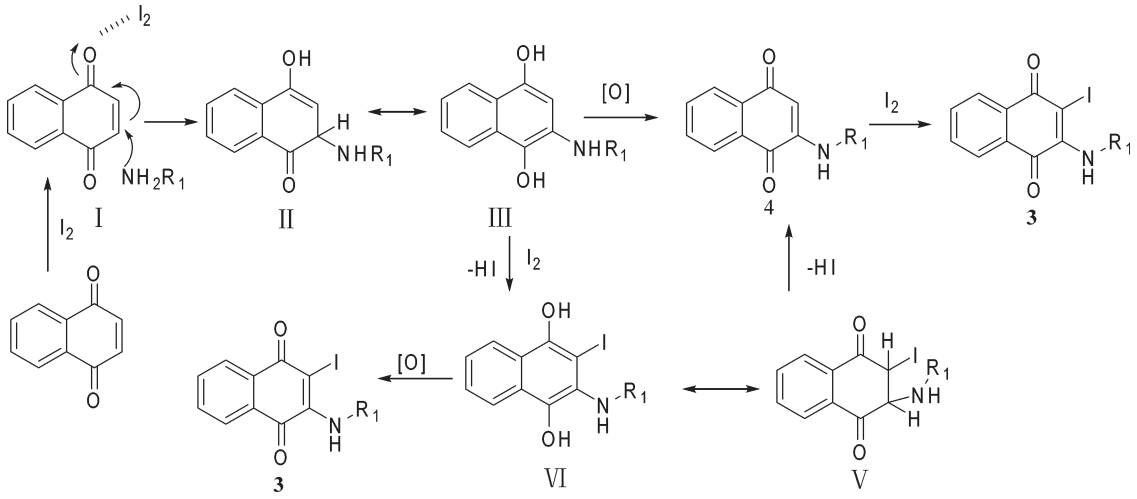

**Scheme 2**




**Scheme 3**




**Scheme 4**



**Scheme 5**

GC-MS and TLC. The reaction mixture was poured into saturated aqueous sodium thiosulfate (8 mL) and was extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were dried over $MgSO_4$. The solvent was removed under vacuum, and the mixed crude products **3** and **4** were separated by chromatography on silica gel and eluted with $CH_2Cl_2$–petroleum ether (1:3).

*2-Iodo-3-(benzylamino)naphthalene-1,4-dione* (**3a**): Yield 51.3% (199.5 mg). Red solid: m.p. 99–100 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.14 (dd, $J_1$ = 1.0 Hz, $J_2$ = 8.0 Hz 1H), 8.02 (dd, $J_1$ = 2.0 Hz, $J_2$ = 7.5 Hz 1H), 7.69 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 7.63 (dt, $J_1$ = 2.0 Hz, $J_2$ = 8.0 Hz 1H), 7.42–7.33 (m, 5H),6.21 (brs, 1H), 5.10 (d, $J$ = 5.5 Hz, 2H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 178.99 (1C), 177.38 (1C), 150.71 (1C), 137.64 (1C), 134.63 (1C), 132.46 (1C), 130.98 (1C), 130.13 (1C), 129.24 (1C), 128.09 (1C), 127.70 (2C), 127.44 (2C), 126.99 (1C), 77.30 (1C), 50.05 (1C); GC-MS (*m/z*): 387.9 (M-1), 386.9 (100%), 262.2, 204.2, 176.2, 157.0, 129.1, 50.0; HRMS (ESI-TOF) *m/z.* Calcd for $C_{17}H_{13}INO_2$ $[M+H]^+$ 389.9985, found 389.9983.

*2-Iodo-3-(methylamino)naphthalene-1,4-dione* (**3b**):[29] Yield 56.4% (176.6 mg). Red solid: m.p. 185–186 °C (lit.[29] 186–187 °C); $^1$H NMR ($CDCl_3$): δ (ppm) 8.15 (d, $J$ = 7.0 Hz 1H), 8.04 (d, $J$ = 7.5 Hz, 1H), 7.70 (t, $J$ = 7.5 Hz 1H), 7.64 (t, $J$ = 7.0 Hz 1H), 6.13 (brs, 1H), 3.47 (d, $J$ = 6.0 Hz, 3H); GC-MS (*m/z*): 313.7 (M+1), 312.7 (M, 100%), 186.0, 158.0, 131.1, 105.0, 89.0.

*2-Iodo-3-(ethylamino)naphthalene-1,4-dione* (**3c**): Yield 68.7% (224.7 mg). Red solid: m.p. 130–131 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.15 (d, $J$ = 8.0 Hz, 1H), 8.04 (d=d, $J$ = 7.5 Hz 1H), 7.70 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 7.64 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 5.98 (brs, 1H), 3.99–3.93 (m, 2H) 1.37 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 179.29 (1C), 177.47 (1C), 150.72 (1C), 134.67 (1C), 132.35 (1C), 131.30 (1C), 129.92 (1C), 127.47 (1C), 126.95 (1C), 77.25 (1C), 40.97 (1C), 15.99 (1C); GC-MS (*m/z*):327.8 (M+1), 326.8 (M, 100%), 312.1, 200.2, 172.2, 155.1, 144.2, 89.2; HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{11}INO_2$ $[M+H]^+$ 327.9829, found 327.9835.

*2-Iodo-3-(propylamino)naphthalene-1,4-dione* (**3d**): Yield 70.4% (240.2 mg). Red solid: m.p. 123–124 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.16 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 8.05 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.70 (dt, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.64 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 6.07 (brs, 1H), 5.87 (q, $J$ = 7.5 Hz, 2H), 1.79–1.71 (m, 2H), 1.05 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 179.28 (1C), 178.20 (1C), 150.85 (1C), 134.75 (1C), 132.61 (1C), 130.99 (1C), 129.46 (1C), 127.55 (1C), 126.70 (1C), 77.23 (1C), 45.80 (1C), 23.97 (1C), 10.84 (1C); GC-MS (*m/z*): 341.8 (M+1), 341.0 (M, 100%), 312.1, 214.2, 185.2, 130.2, 102.2, 41.2; HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{13}INO_2$ $[M+H]^+$ 341.9985, found 341.9990.

*2-Iodo-3-(butylamino)naphthalene-1,4-dione* (**3e**): Yield 67.8% (240.8 mg). Red solid: m.p. 119–120 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.16 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 8.04 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 7.70 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 7.64 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 6.05 (brs, 1H), 3.91 (q, $J$ = 6.5 Hz, 2H), 1.74–1.68 (m, 2H), 1.51–1.44 (m, 2H), 1.00 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 179.20 (1C), 177.45 (1C), 150.70 (1C), 134.65 (1C), 132.32 (1C), 131.71 (1C), 131.33 (1C), 129.86 (1C), 127.45 (1C), 126.93 (1C), 77.25 (1C), 45.59 (1C), 32.69 (1C), 19.73 (1C), 13.67 (1C); GC-MS (*m/z*): 355.8 (M+1), 354.9 (M, 100%), 228.2, 186.2, 130.1, 102.0.76.0, 50.0; HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{15}INO_2$ $[M+H]^+$ 356.0142, found 356.0149.

*2-Iodo-3-(hexylamino)naphthalene-1,4-dione* (**3f**): Yield 32.8% (125.7 mg). Red solid: m.p. 87–88 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.16 (dd, $J_1$ = 1.0 Hz, $J_2$ = 8.0 Hz 1H), 8.05 (dd, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 7.70 (dt, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.64 (dt, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 6.05 (brs, 1H), 3.90 (q, $J$ = 6.5 Hz, 2H), 1.74–1.69 (m, 2H), 1.47–1.41 (m, 2H), 1.37–1.34 (m, 4H), 1.47–1.41 (m, 2H), 0.92 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR ($CDCl_3$): δ (ppm) 179.21 (1C), 177.27 (1C), 150.83 (1C), 134.75 (1C), 132.63 (1C), 131.99 (1C), 131.34 (1C), 129.89 (1C), 127.53 (1C), 127.12 (1C), 77.25 (1C), 45.79 (1C), 31.39 (1C), 30.74 (1C), 26.09 (1C), 22.68 (1C), 13.79 (1C). GC-MS (*m/z*): 383.0 (M+1, 100%), 312.1, 256.4, 186.3, 185.3, 129.3, 76.2, 41.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{19}INO_2$ $[M+H]^+$ 384.0455, found 384.0459.

*2-Iodo-3-(decylamino)naphthalene-1,4-dione* (**3g**): Yield 43.9% (192.9 mg). Red solid: m.p. 85–86 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.16 (dd, $J_1$ = 1.0 Hz, $J_2$ = 8.0 Hz 1H), 8.05 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.70 (dt, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 7.64 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 6.06 (brs, 1H), 3.90 (q, $J$ = 6.5 Hz, 2H), 1.74–1.68 (m, 2H), 1.46–1.28 (m, 2H), 1.37–1.34 (m, 2H), 1.47–1.41 (m, 14H), 0.89 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 179.33 (1C), 178.71 (1C), 151.12 (1C), 134.64 (1C), 133.97 (1C), 132.31 (1C), 131.92 (1C), 131.46 (1C), 127.46 (1C), 77.23 (1C), 45.99 (1C), 31.90 (1C), 31.74 (1C), 29.51 (1C), 29.29 (1C), 29.26 (1C), 29.22 (1C), 26.60 (1C), 22.60 (1C), 14.17 (1C); GC-MS (*m/z*): 438.9 (M), 312.1 (100%), 186.2, 174.2, 130.1, 102.2, 77.2, 41.2; HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{27}INO_2$ $[M+H]^+$ 440.1081, found 440.1078.

*2-Iodo-3-(dodecylamino)naphthalene-1,4-dione* (**3h**): Yield 47.9% (223.9 mg). Red solid: m.p. 95–96 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.15 (dd, $J_1$ = 0.5 Hz, $J_2$ = 7.5 Hz 1H), 8.04 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.69 (dt, $J_1$ = 1.0 Hz, $J_2$ = 7.0 Hz 1H), 7.63 (dt, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 6.05 (brs, 1H), 3.90 (q, $J$ = 6.5 Hz, 2H), 1.73–1.67 (m, 2H), 1.45–1.26 (m, 18H), 0.88 (t, $J$ = 6.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 179.44 (1C), 178.99 (1C), 151.47 (1C), 134.95 (1C), 132.42 (1C), 131.56 (1C), 130.72 (1C), 127.30 (1C), 126.94 (1C), 77.23 (1C), 61.04 (1C), 45.98 (1C), 31.92 (1C), 30.74 (1C), 29.63 (1C), 29.56 (1C), 29.50 (1C), 29.36 (1C), 29.26 (1C), 26.64 (1C), 22.71 (1C), 14.14 (1C); GC-MS (*m/z*): 468.1 (M+1), 467.1 (M, 100%), 340.2, 312.1, 300.2, 186.2, 55.2, 41.2; HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{31}INO_2$ $[M+H]^+$ 468.1394, found 468.1381.

*2-Iodo-3-(2,2-dimethoxyethylamino)naphthalene-1,4-dione* (**3i**): Yield 55.0% (212.9 mg). Yellow solid: m.p. 87–88 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.11 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 8.01 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 7.69 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 7.63 (dt, $J_1$ = 2.0 Hz, $J_2$ = 8.0 Hz 1H), 6.17 (brs, 1H), 4.58 (t, $J$ = 5.5 Hz, 1H), 4.02 (t, $J$ = 5.5 Hz, 2H), 3.47 (s, 6H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 179.11 (1C), 177.52 (1C), 151.32 (1C), 134.69 (1C), 132.63 (1C), 131.26 (1C), 130.26 (1C), 127.49 (1C), 127.07 (1C), 102.67 (1C), 77.47 (1C), 54.87 (2C), 47.10 (1C);GC-MS (*m/z*): 387.8 (M),

355.8, 326.9, 75.0 (100%), 47.0; HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{15}INO_2$ $[M+H]^+$ 388.0040, found 388.0049.

*2-Iodo-3-(2-hydroxyethylamino)naphthalene-1,4-dione* (**3j**): Yield 49.4% (169.5 mg). Red solid: m.p. 54–55 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.15 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 8.05 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.0 Hz 1H), 7.70 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.0 Hz 1H), 7.65 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.0 Hz 1H), 6.37 (brs, 1H), 4.11–4.08 (m, 2H), 3.96–3.94 (m, 2H), 1.75 (s, 1H); $^{13}$C NMR ($CDCl_3$): δ (ppm) 183.22 (1C), 181.97 (1C), 148.38 (1C), 134.64 (1C), 133.54 (1C), 132.14 (1C), 126.32 (1C), 126.20 (1C), 101.15 (1C), 60.07 (1C), 44.22 (1C); GC-MS (*m/z*): 342.0 (M), 327.0 (100%), 299.2, 285.1, 206.2.

*2-(Benzylamino)-1,4-naphthoquinone* (**4a**):[28] Yield 32.2% (84.7 mg). Red soild: m.p. 156–157 °C (lit.[28] m.p. 158–159 °C); $^1$H NMR ($CDCl_3$): δ (ppm) 8.12–8.07 (m, 2H), 7.43 (t, *J* = 6.0 Hz, 1H), 7.68 (t, *J* = 6.0 Hz, 1H), 7.39–7.28 (m, 5H), 6.23 (s, 1H), 5.82 (s, 2H), 5.11 (d, *J* = 6.0 Hz, 2H); GC-MS (*m/z*): 263.0 (M), 262.0 (M-1, 100%), 158.0, 130.0, 102.0, 76.0, 50.0.

*2-(Methylamino)-1,4-naphthoquinone* (**4b**):[32] Yield 19.5% (36.5 mg). Red needle crystal: m.p. 221–222 °C (lit.[33] m.p. 220–230 °C); $^1$H NMR ($CDCl_3$): δ (ppm) 7.70–8.20 (m, 4H), 5.94 (s, 1H), 5.70 (s, 1H), 2.93 (d, 2H);GC-MS (*m/z*): 187.2 (M, 100%), 146.2, 130.3, 105.2, 89.2, 76.2, 50.1

*2-(Ethylamino)-1,4-naphthoquinone* (**4c**):[33] Yield 18.2% (36.6 mg). Yellow needle crystal: m.p. 139–140 °C (lit.[33] 141.4 °C); GC-MS (*m/z*): 201.0 (M, 100%), 199.1, 186.0, 158.0, 130.1, 102.0, 76.0, 50.0.

*2-(Propylamino)-1,4-naphthoquinone* (**4d**):[34] Yield 15.5% (33.4 mg). Yellow needle crystal: m.p. 115–116 °C (lit.[34] 114–116 °C); $^1$H NMR ($CDCl_3$): δ (ppm) 7.20–8.10 (m, 4H), 5.93 (s, 1H), 5.75 (s, 1H), 3.15–3.19 (m, 2H), 1.71–1.76 (m, 2H), 1.04 (t, *J* = 7.5 H); GC-MS (*m/z*): 215.8 (m, 100%), 214.9, 186.0, 131.0, 101.0, 76.0, 50.0.

*2-(Butylamino)-1,4-naphthoquinone* (**4e**):[28] Yield 17.3% (39.7 mg). Yellow needle crystal: m.p. 117–118 °C (lit.[28] 115–117 °C); $^1$H NMR ($CDCl_3$): δ (ppm) 8.12 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 8.06 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.76–7.73 (m, 1H), 7.64–7.61 (m, 1H), 5.90 (brs, 1H), 5.75 (s, 1H), 3.20 (q, *J* = 6.0 Hz, 2H), 1.73–1.67 (m, 2H), 0.99 (t, *J* = 7.5 Hz, 3H); GC-MS (*m/z*): 230.0 (M+1), 229.0 (M), 201.0, 186.0 (100%), 146.0, 131.0, 76.0, 41.0.

*2-(Hexylamino)-1,4-naphthoquinone* (**4f**):[35] Yield 38.9% (100.1 mg). Red needle crystal: m.p. 116–117 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.12 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 8.06 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.75–7.72 (m, 1H), 7.64–7.61 (m, 1H), 5.90 (brs, 1H), 5.74 (s, 1H), 3.19 (q, *J* = 6.0 Hz, 2H), 1.72–1.67 (m, 2H), 1.43–1.40 (m, 2H), 1.35–1.32 (m, 4H), 0.92 (t, *J* = 4.5 Hz, 3H); GC-MS (*m/z*): 257.2, 228.2, 186.3, 146.2, 131.2, 103.2, 76.1, 41.2.

*2-(Decylamino)-1,4-naphthoquinone* (**4g**):[35] Yield 30.2% (94.7 mg). Red needle crystal: m.p. 130–131 °C; GC-MS (*m/z*): 313.0, 242.1, 228.2, 186.2, 174.1, 146.0, 41.1.

*2-(Dodecylamino)-1,4-naphthoquinone* (**4h**):[35] Yield 44.0% (150.3 mg). Red needle crystal: m.p. 145–146 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.15 (dd, $J_1$ = 0.5 Hz, $J_2$ = 7.5 Hz 1H), 8.04 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 7.69 (dt, $J_1$ = 1.0 Hz, $J_2$ = 7.0 Hz 1H), 7.63 (dt, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 6.05 (brs, 1H), 5.85 (s, 1H), 3.90 (q, *J* = 6.5 Hz, 2H), 1.73–1.67 (m, 2H), 1.45–1.26 (m, 18H), 0.88 (t, *J* = 6.5 Hz, 3H); GC-MS (*m/z*): 342.1, 341.1, 242.2, 228.2, 186.2, 174.2, 146.0, 41.0.

*2-(2,2-Dimethoxyethylamino)-1,4-naphthoquinone* (**4i**): Yield 19.2% (50.2 mg). Yellow needle crystal: m.p. 110–112 °C; $^1$H NMR ($CDCl_3$): δ (ppm) 8.11 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 8.01 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz 1H), 7.69 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.5 Hz 1H), 7.63 (dt, $J_1$ = 2.0 Hz, $J_2$ = 8.0 Hz 1H), 6.06 (brs, 1H), 5.77 (s, 1H), 4.60 (t, *J* = 5.5 Hz, 1H), 3.44 (s, 6H), 3.31 (t, *J* = 5.0 Hz, 2H); GC-MS (*m/z*): 262.0, 260.8, 230.0, 201.0, 198.0, 75.0, 47.0.

*2-(2-Hydroxyethylamino)-1,4-naphthoquinone* (**4j**):[36] Yield 21.4% (46.5mg). Yellow needle crystal: m.p. 158–159 °C (lit.[37] 186–187 °C); $^1$H NMR ($CDCl_3$): δ (ppm) 8.11 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.5 Hz 1H), 8.05 (dd, $J_1$ = 1.0 Hz, $J_2$ = 7.0 Hz 1H), 7.70 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.0 Hz 1H), 7.65 (dt, $J_1$ = 1.5 Hz, $J_2$ = 7.0 Hz 1H), 6.23 (brs, 1H), 5.79 (s, 1H), 3.95–3.94 (m, 2H), 3.40–3.37 (m, 2H), 1.86 (s, 1H).

*2-(4-Iodophenylamino)naphthalene-1,4-diol* (**5**): Yield 24.6% (92.8mg). Red solid; $^1$H NMR ($CDCl_3$): δ (ppm) 7.68–8.15 (m, 4H, ArH), 7.52 (s, 1H, NH), 7.42–7.42 (d, 2H, *J* = 0 Hz,ArH), 7.05–7.07 (d, 2H, *J* = 8.5 Hz, ArH), 6.41 (s, H, CH).

*2-(Phenylamino)-1,4-naphthoquinone* (**6**):[34] Yield 34.2% (85.9mg). Red solid: m.p. 184–185 °C (lit.[34] m.p. 187–189 °C); $^1$H NMR ($CDCl_3$): δ (ppm) 8.15 (dd, $J_1$ = 1.0 Hz, $J_2$ = 9.0 Hz 2H), 7.80–7.77 (m, 1H), 7.71–7.68 (m, 1H), 7.58 (brs, 1H), 7.46–7.43 (m, 2H), 7.31–7.22 (m, 3H), 6.44 (s, 1H).

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