

## A SIMPLE SYNTHESIS OF BENZOCARBAZOLEQUINONES VIA *o*-NITROARYLATION OF 2-HYDROXY-1,4- NAPHTHOQUINONES

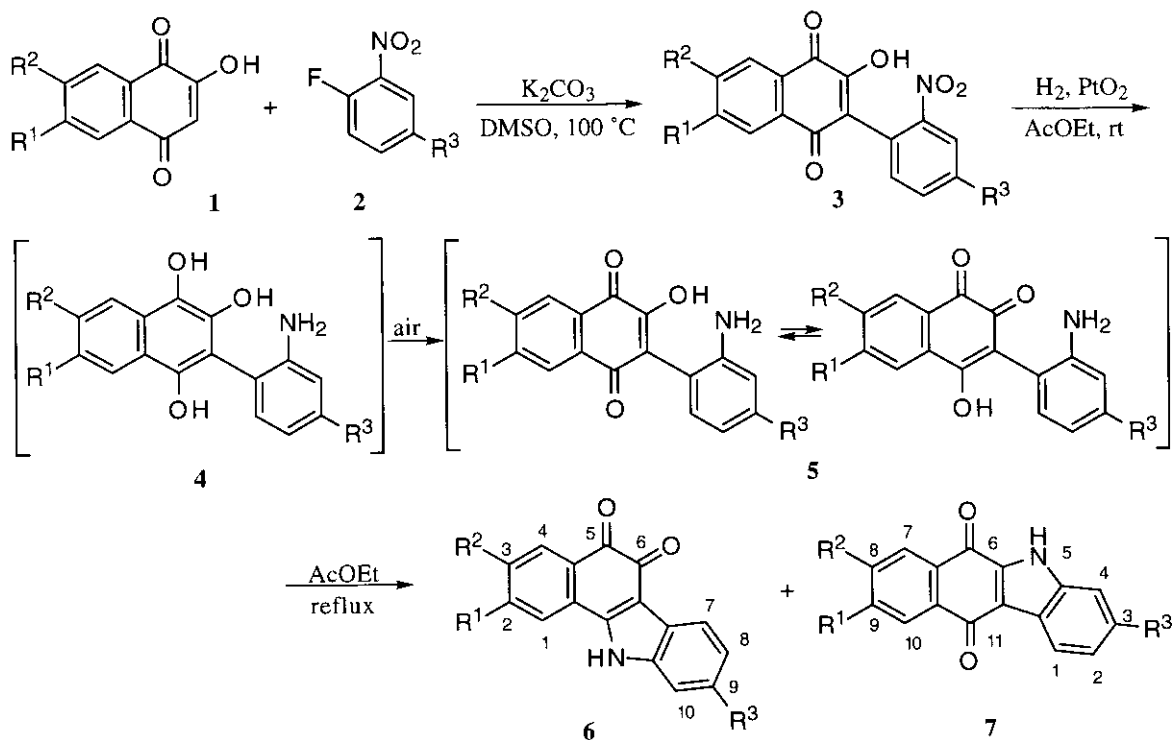
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**Abstract-** The reaction of 2-hydroxy-1,4-naphthoquinones (**1a-c**) with *o*-fluoronitrobenzenes (**2a,b**) in the presence of K<sub>2</sub>CO<sub>3</sub> in DMSO at 100 °C gave 2-hydroxy-3-(2-nitroaryl)-1,4-naphthoquinones (**3a-e**) in moderate to fair yields, which in turn were transformed into the corresponding 11*H*-benzo[*a*]carbazole-5,6-dione (**6a-e**) and 5*H*-benzo[*b*]carbazole-6,11-dione (**7a-e**) derivatives in good yields by catalytic hydrogenation over PtO<sub>2</sub> in AcOEt at room temperature and 1 atm, followed by exposure to air and then heating at reflux temperature.

Carbazolequinone derivatives have attracted much synthetic attention because of their potential biological activities,<sup>1</sup> and number of works have been described on the synthesis of this class of compounds.<sup>2</sup> In this note we wish to describe a simple route to benzocarbazolequinone derivatives, such as 11*H*-benzo[*a*]carbazole-5,6-diones (**6a-e**) and 5*H*-benzo[*b*]carbazole-6,11-diones (**7a-e**), which relies on *o*-nitroarylation of 2-hydroxy-1,4-naphthoquinones (**1a-c**) at the 3-position with 2-fluoronitrobenzenes (**2a,b**), followed by a reduction-cyclization sequence induced by hydrogenation on PtO<sub>2</sub> of the resulting 2-hydroxy-3-(2-nitroaryl)-1,4-naphthoquinones (**3a-e**). In the course of our study, a similar approach was reported by Castedo *et al.*,<sup>2e</sup> in which 3-(2-nitroaryl)ated 1,4-naphthoquinone derivatives, which were prepared by a three-step sequence from 2-[2-(2-nitroaryl)ethanoyl]phenylacetic acid derivatives, were transformed into the latter benzocarbazolequinone derivatives on treatment with NaBH<sub>4</sub>. To date, however, very little work has been described on the synthesis of the former derivatives, apart from an unexpected production by rearrangement of the latter derivatives during purification using column chromatography on silica gel.<sup>2d</sup>

The reactions of 2-hydroxy-1,4-naphthoquinones (**1**) with *o*-fluoronitrobenzenes (**2**) in DMSO at 100 °C in the presence of potassium carbonate proceeded uneventfully to result in exclusive formation of the C-



arylation products, 3-(2-nitroaryl)-2-hydroxy-1,4-naphthoquinones (**3**), in reasonable isolated yields shown in the Table. Any products, resulting from *O*-arylation, could not be detected in each of the reactions.

The nitroarylated quinones (**3**) were readily converted into the benzocarbazolequinones (**6**) and (**7**) in good yields. Hydrogenolysis of **3** to 3-(2-aminoaryl)-1,2,4-trihydroxynaphthalenes (**4**) could be effected by using  $PtO_2$  as a catalyst under atmospheric pressure of hydrogen in AcOEt at room temperature. Oxidation of these hydroquinones (**4**) on exposure to air resulted in formation of the corresponding aminoarylated quinones (**5**), which were cyclized by bringing the solvent to reflux and further refluxing for a day to give 11*H*-benzo[*a*]carbazole-5,6-diones (**6**) (orange-yellow solids) and 5*H*-benzo[*b*]carbazole-6,11-diones (**7**) (dark-purple solids). At reflux times shorter than 10 h, we obtained reaction mixtures, containing products presumably resulting from intermolecular amination of **5**, from which the desired products could be isolated only in poor yields. The synthesis of these carbazolequinones (**6**) and (**7**) is outlined in the Scheme, and the yields of the products are listed in the Table. The structures of the products were established by spectroscopic data and elemental analyses. For example, the structure of **7a** was confirmed by a comparison of its physical and spectroscopic data with those reported previously;<sup>3</sup> the IR spectrum showed a series of absorption bands due to the NH ( $3264\text{ cm}^{-1}$ ) and *para*-quinone carbonyl groups ( $1648\text{ cm}^{-1}$ ), and the  $^1H$  NMR spectrum indicated a signal at  $\delta$  8.05–8.15 (2H, m) assignable to the 7- and 10-H. Assignment of the *ortho*-quinone structure of **6a** was made on the basis of the IR spectrum, which exhibited a series of

**Table.** Preparation of 2-hydroxy-3-(2-nitroaryl)-1,4-naphthoquinones (**3**) and their conversion to benzocarbazolequinones (**6**) and (**7**)

Entry	<b>1</b>	<b>2</b>	<b>3</b> (Yield/%) <sup>a</sup>	<b>6</b> (Yield/%) <sup>a</sup>	<b>7</b> (Yield/%) <sup>a</sup>
a	<b>1a</b> (R <sup>1</sup> =R <sup>2</sup> =Me)	<b>2a</b> (R <sup>3</sup> =H)	<b>3a</b> (59)	<b>6a</b> (75)	<b>7a</b> (24)
b	<b>1a</b>	<b>2b</b> (R <sup>3</sup> =Me)	<b>3b</b> (67)	<b>6b</b> (74)	<b>7b</b> (18)
c	<b>1b</b> (R <sup>1</sup> =MeO, R <sup>2</sup> =Me)	<b>2a</b>	<b>3c</b> (54)	<b>6c</b> (48)	<b>7c</b> (22)
d	<b>1b</b>	<b>2b</b>	<b>3d</b> (52)	<b>6d</b> (51)	<b>7d</b> (26)
e	<b>1b</b> (R <sup>1</sup> =R <sup>2</sup> =MeO)	<b>2a</b>	<b>3e</b> (49)	<b>6e</b> (45)	<b>7e</b> (41)

<sup>a</sup>Isolated yields after recrystallization.

characteristic absorption bands assignable to NH (3188 cm<sup>-1</sup>) and *ortho*-quinone carbonyl groups (1692 and 1630 cm<sup>-1</sup>),<sup>4</sup> and the <sup>1</sup>H NMR spectrum, which showed two signals at δ 7.96 (1H, d) assignable to the 1-H and δ 8.01 (1H, d) [or δ 8.05 (1H, dd)] assignable to the 4-H. The *o*-carbazolequinone derivatives (**6**) displayed the very polar chromatographic behavior, which has been reported previously.<sup>2d</sup> The ratios of the products (**6**) and (**7**) shown in the Table indicate that methoxy substituents at the 5 and/or 6 positions of the quinones favors the formation of **7**. Although we have no firm explanation at this point, this may be attributed to the methoxy substituent(s), which play a role to lower the reactivity of the 4-carbon toward the nucleophilic attack of the amino group.

In summary, we have developed a novel and simple method for the synthesis of benzocarbazolequinone derivatives. The sequence should be of value in organic molecular transformations.

## EXPERIMENTAL SECTION

The mps were determined on a Laboratory Devices MEL-TEMP II melting point apparatus and are uncorrected. The IR spectra were determined for KBr disks with a Perkin-Elmer 1600 Series FT IR spectrophotometer. The <sup>1</sup>H NMR spectra were determined in CDCl<sub>3</sub> for compounds (**3**) or in DMSO-*d*<sub>6</sub> for compounds (**6**) and (**7**), unless stated otherwise, using SiMe<sub>4</sub> as an internal reference with a JEOL JNM-GX270 FT NMR spectrometer operating at 270 MHz. *J* values are given in Hz. Low-resolution MS spectra were recorded on a JEOL AUTOMASS 20 spectrometer (Center for Joint Research and Development, this University). Hydroxyquinones (**1b**)<sup>5</sup> and (**1c**)<sup>5,6</sup> were prepared according to the reported procedure.<sup>5</sup> All other chemicals used in this study were commercially available. All of the solvents used were dried over appropriate drying agents and distilled under argon prior to use.

**2-Hydroxy-(2-nitrophenyl)-1,4-naphthoquinone (3a). General Procedure for the Nitroarylation of 2-Hydroxy-1,4-naphthoquinones (1).** A mixture of **1a** (2.0 g, 11 mmol), **2a** (8.1 g, 57 mmol), and K<sub>2</sub>CO<sub>3</sub> (1.9 g, 14 mmol) in DMSO (20 mL) was heated at 100 °C with stirring for 3

days under argon. The cooled mixture was diluted with Et<sub>2</sub>O (50 mL) and extracted with sat. aq. NaHCO<sub>3</sub> five times. The combined extracts were acidified with 5% aq HCl. The yellow precipitate was collected and recrystallized from hexane-EtOAc to give **3a** (2.0 g, 59%): mp 262-263 °C;  $\nu_{\max}/\text{cm}^{-1}$  3321, 1676, 1639, 1521, 1340;  $\delta_{\text{H}}$  7.52 (1H, dd, *J* 7.6, 1.7), 7.59 (1H, td, *J* 7.6, 1.7), 7.71 (1H, td, *J* 7.6, 1.3), 7.75-7.85 (3H, m), 8.1-8.25 (3H, m); MS *m/z* 295 (M<sup>+</sup>, 1.7), 249 (19), 248 (100). Anal. Calcd for C<sub>16</sub>H<sub>9</sub>NO<sub>5</sub>: C, 65.09; H, 3.07; N, 4.74. Found: C, 64.96; H, 3.15; N, 4.68.

**2-Hydroxy-3-(4-methyl-2-nitrophenyl)-1,4-naphthoquinone (3b)**: mp 258-260 °C (hexane-EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3329, 1672, 1639, 1527, 1356;  $\delta_{\text{H}}$  2.51 (3H, s), 7.39 (1H, d, *J* 7.9), 7.5-7.55 (2H, m), 7.7-7.85 (2H, m), 8.00 (1H, s), 8.1-8.2 (2H, m); MS *m/z* 309 (0.96), 293 (3.8), 277 (22), 263 (100). Anal. Calcd for C<sub>17</sub>H<sub>11</sub>NO<sub>5</sub>: C, 66.02; H, 3.58; N, 4.53. Found: C, 65.93; H, 3.53; N, 4.43.

**2-Hydroxy-6-methoxy-3-(2-nitrophenyl)-1,4-naphthoquinone (3c)**: mp 248-251 °C (hexane-EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3330, 1653, 1641, 1593, 1524, 1341;  $\delta_{\text{H}}$  3.97 (3H, s), 7.20 (1H, dd, *J* 8.7, 2.9), 7.5-7.6 (2H, m), 7.61 (1H, d, *J* 2.5), 7.65-7.75 (2H, m), 8.12 (1H, d, *J* 8.7), 8.17 (1H, d, *J* 8.0); MS *m/z* 325 (M<sup>+</sup>, 26), 279 (100). Anal. Calcd for C<sub>17</sub>H<sub>11</sub>NO<sub>6</sub>: C, 62.77; H, 3.41; N, 4.31. Found: C, 62.78; H, 3.50; N, 4.24.

**2-Hydroxy-6-methoxy-3-(4-methyl-2-nitrophenyl)-1,4-naphthoquinone (3d)**: mp 251-252 °C (hexane-EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3346, 1652, 1642, 1593, 1527, 1329;  $\delta_{\text{H}}$  2.50 (3H, s), 3.96 (3H, s), 7.19 (1H, dd, *J* 8.4, 2.6), 7.39 (1H, d, *J* 7.9), 7.51 (1H, d, *J* 7.9), 7.61 (1H, d, *J* 2.6), 7.64 (1H, br s), 7.99 (1H, s), 8.11 (1H, d, *J* 8.4); MS *m/z* 339 (M<sup>+</sup>, 32), 293 (100). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>NO<sub>6</sub>: C, 63.72; H, 3.86; N, 4.13. Found: C, 63.54; H, 3.87; N, 4.18.

**2-Hydroxy-6,7-dimethoxy-3-(2-nitrophenyl)-1,4-naphthoquinone (3e)**: mp 271-273 °C (hexane-EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3349, 1649, 1578, 1526, 1336;  $\delta_{\text{H}}$  4.03 (3H, s), 4.05 (3H, s), 7.5-7.6 (6H, m), 8.16 (1H, d, *J* 8.4); MS *m/z* 355 (M<sup>+</sup>, 29), 309 (100). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>NO<sub>7</sub>: C, 60.85; H, 3.69; N, 3.94. Found: C, 61.02; H, 3.86; N, 3.68.

**Benzo[*a*]carbazole-5,6-dione (6a) and benzo[*b*]carbazole-6,11-dione (7a). General Procedure for the Preparation of Benzocarbazolequinones (6) and (7).** A solution of **3a** (0.15 g, 0.50 mmol) in AcOEt (20 mL) containing PtO<sub>2</sub> (28 mg, 0.10 mmol) was stirred at rt for 30 min under a atmosphere of hydrogen (1 atm). The catalyst was then filtered off, and the filtrate was refluxed in the air for a day. After cooling to rt, the deep brown precipitate was collected by suction and recrystallized from THF to give **6a** (92 mg, 75%): mp >400 °C;  $\nu_{\max}/\text{cm}^{-1}$  3188, 1692, 1630, 1615;  $\delta_{\text{H}}$  7.25-7.35 (2H, m), 7.5-7.6 (2H, m), 7.80 (1H, t, *J* 7.9), 7.96 (1H, d, *J* 7.9), 8.01 (1H, dd, *J* 7.9, 2.1), 8.05 (1H, d, *J* 7.9), 12.91 (1H, br s); MS *m/z* 247 (M<sup>+</sup>, 66), 219 (100). Anal. Calcd for C<sub>16</sub>H<sub>9</sub>NO<sub>2</sub>: C, 77.72; H, 3.67; N,

5.66. Found: C, 77.78; H, 3.90; N, 5.62. The filtrate was concentrated *in vacuo* to afford a yellow solid, which was purified by recrystallization from hexane–AcOEt to give **7a** (30 mg, 24%): mp 308–309 °C (lit.,<sup>3</sup> 307–310 °C);  $\nu_{\max}/\text{cm}^{-1}$  3264, 1648, 1620;  $\delta_{\text{H}}$  7.37 (1H, t, *J* 7.9), 7.46 (1H, t, *J* 7.9 Hz), 7.60 (1H, d, *J* 7.9 Hz), 7.75–7.9 (2H, m), 8.05–8.15 (2H, m), 8.21 (1H, d, *J* 7.9), 13.0 (1H, br s).

**9-Methylbenzo[*a*]carbazole-5,6-dione (6b)**: mp >400 °C (THF);  $\nu_{\max}/\text{cm}^{-1}$  3178, 1695, 1616;  $\delta_{\text{H}}$  2.45 (3H, s), 7.10 (1H, d, *J* 7.9), 7.33 (1H, s), 7.52 (1H, td, *J* 7.4, 1.1), 7.76 (1H, td, *J* 7.9, 1.6), 7.90 (1H, d, *J* 8.4), 7.94 (1H, dd, *J* 7.9, 1.6), 8.02 (1H, d, *J* 8.4), 12.50 (1H, br s); MS *m/z* 261 (M<sup>+</sup>, 63), 233 (100). Anal. Calcd for C<sub>17</sub>H<sub>11</sub>NO<sub>2</sub>: C, 78.15; H, 4.24; N, 5.36. Found: C, 78.08; H, 4.46; N, 5.30.

**3-Methylbenzo[*b*]carbazole-6,11-dione (7b)**: mp 260 °C (hexane–EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3208, 1663, 1639;  $\delta_{\text{H}}$  2.46 (3H, s), 7.21 (1H, d, *J* 9.0), 7.38 (1H, d, *J* 1.8), 7.75–7.85 (2H, m), 8.08 (1H, dd, *J* 7.5, 1.4), 8.09 (1H, d, *J* 7.4), 8.11 (1H, dd, *J* 7.5, 1.4), 14.64 (1H, br s); MS *m/z* 261 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>17</sub>H<sub>11</sub>NO<sub>2</sub>: C, 78.15; H, 4.24; N, 5.36. Found: C, 78.19; H, 4.20; N, 5.40.

**2-Methoxybenzo[*a*]carbazole-5,6-dione (6c)**: mp >400 °C (THF);  $\nu_{\max}/\text{cm}^{-1}$  3224, 1666, 1630, 1597;  $\delta_{\text{H}}$  3.96 (3H, s), 7.06 (1H, dd, *J* 8.4, 2.6), 7.26 and 7.31 (combined 2H, 2t, *J* 6.9 each), 7.55 (1H, d, *J* 6.9), 7.65 (1H, d, *J* 2.6), 7.92 (1H, d, *J* 8.4), 8.00 (1H, d, *J* 6.9), 14.50 (1H, br s); MS *m/z* 277 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>17</sub>H<sub>11</sub>NO<sub>3</sub>: C, 73.64; H, 4.00; N, 5.05. Found: C, 73.77; H, 4.25; N, 5.07.

**9-Methoxybenzo[*b*]carbazole-6,11-dione (7c)**: mp 303–304 °C (hexane–EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3230, 1658, 1589;  $\delta_{\text{H}}$  (CDCl<sub>3</sub>) 3.98 (3H, s), 7.14 (1H, dd, *J* 8.4, 2.6), 7.35–7.55 (3H, m), 7.74 (1H, d, *J* 2.6), 8.12 (1H, d, *J* 8.4), 8.39 (1H, d, *J* 7.9), 9.35 (1H, br s); MS *m/z* 277 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>17</sub>H<sub>11</sub>NO<sub>3</sub>: C, 73.64; H, 4.00; N, 5.05. Found: C, 73.38; H, 3.70; N, 4.97.

**2-Methoxy-8-methylbenzo[*a*]carbazole-5,6-dione (6d)**: mp >400 °C (THF);  $\nu_{\max}/\text{cm}^{-1}$  3218, 1679, 1626, 1597;  $\delta_{\text{H}}$  2.44 (3H, s), 3.96 (3H, s), 7.03 (1H, dd, *J* 8.4, 2.6), 7.09 (1H, d, *J* 8.4), 7.31 (1H, s), 7.62 (1H, d, *J* 2.6), 7.86 (1H, d, *J* 8.4), 7.90 (1H, d, *J* 8.4), 12.7 (1H, br); MS *m/z* 291 (M<sup>+</sup>, 7.2), 263 (100). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>NO<sub>3</sub>: C, 74.22; H, 4.50; N, 4.81%. Found: C, 74.33; H, 4.39; N, 4.53.

**9-Methoxy-3-methylbenzo[*b*]carbazole-6,11-dione (7d)**: mp 298–300 °C (hexane–EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3229, 1657, 1587;  $\delta_{\text{H}}$  2.45 (3H, s), 3.96 (3H, s), 7.19 (1H, d, *J* 8.4), 7.30 (1H, dd, *J* 8.4, 2.6), 7.37 (1H, s), 7.56 (1H, d, *J* 2.6), 8.05 (1H, d, *J* 8.4), 8.06 (1H, d, *J* 8.4), 12.8 (1H, br); MS *m/z* 291 (M<sup>+</sup>, 100). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>NO<sub>3</sub>: C, 74.22; H, 4.50; N, 4.81. Found: C, 74.32; H, 4.50; N, 5.01.

**2,3-Dimethoxybenzo[*a*]carbazole-5,6-dione (6e)**: mp 346–347 °C (THF);  $\nu_{\max}/\text{cm}^{-1}$  3281, 1646,

1626, 1590;  $\delta_{\text{H}}$  3.88 (3H, s), 3.95 (3H, s), 7.2–7.3 (2H, m), 7.43 (1H, s), 7.52 (1H, d,  $J$  7.4), 7.68 (1H, s), 7.95 (1H, dd,  $J$  7.9, 2.1), and 12.67 (1H, br s); MS  $m/z$  307 ( $M^+$ , 100). Anal. Calcd for  $\text{C}_{18}\text{H}_{13}\text{NO}_4$ : C, 70.35; H, 4.26; N, 4.56. Found: C, 70.26; H, 4.38; N, 4.51.

**8,9-Dimethoxybenzo[*b*]carbazole-6,11-dione (7e):** mp 198–299 °C (hexane-EtOAc);  $\nu_{\text{max}}/\text{cm}^{-1}$  3240, 1652, 1644, 1579;  $\delta_{\text{H}}$  3.96 (3H, s), 3.98 (3H, s), 7.34 (1H, td,  $J$  7.9, 1.6), 7.42 (1H, td,  $J$  7.9, 1.6), 7.56 (1H, s), 7.58 (1H, d,  $J$  7.9), 7.60 (1H, s), 8.13 (1H, d,  $J$  7.9), 12.9 (1H, br); MS  $m/z$  307 ( $M^+$ , 100). Anal. Calcd for  $\text{C}_{18}\text{H}_{13}\text{NO}_4$ : C, 70.35; H, 4.26; N, 4.56. Found: C, 70.34; H, 4.23; N, 4.72.

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