BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 49 (8), 2333—2334 (1976)

Morpholinobenzoquinones: Synthesis and Reactions

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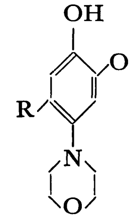
(Received January 27, 1976)

Synopsis. Two 4-morpholino-1,2-benzoquinones (5-*t*-butyl- and 5-methyl-) have been prepared by the oxidation of the corresponding catechols with silver oxide. The quinones were then condensed with *o*-phenylenediamine to give phenazines.

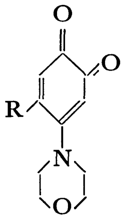
The oxidation of aminocatechols to the corresponding quinones has been studied by Horner,[1] Iwao[2] and Jackson,[3] but few papers on the isolation and properties of the quinones have been published. We wish now to report on the synthesis of morpholinobenzoquinones as well as on their chemical properties.

The reaction of 4-*t*-butyl-1,2-benzoquinone with morpholine gave 5-*t*-butyl-4-morpholinocatechol (**1**) in a 48% yield. The structure of **1** was confirmed on the basis of the spectroscopic data and the results of elemental analysis. Aminocatechols, such as 4-aminocatechol and 4-dimethylaminocatechol, are known to be labile to atmospheric oxygen,[1] however, **1** is stable and can be isolated as colorless crystals. The reaction of 4-methyl-1,2-benzoquinone with morpholine gave **2** in only a 7.7% yield.

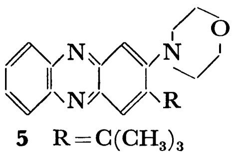
The catechol **1** was oxidized with silver oxide to give 5-*t*-butyl-4-morpholino-1,2-benzoquinone (**3**). The **3** quinone was then condensed with *o*-phenylenediamine to afford a phenazine, **5**. The **6** phenazine was also obtained from the labile **4** and *o*-phenylenediamine.



1 R=C(CH$_3$)$_3$
2 R=CH$_3$



3 R=C(CH$_3$)$_3$
4 R=CH$_3$



5 R=C(CH$_3$)$_3$
6 R=CH$_3$

Experimental

*5-t-Butyl-4-morpholinocatechol (**1**).* 4-*t*-Butyl-1,2-benzoquinone was prepared by the method of Pospíšil[4] from 2 g of 4-*t*-butylcatechol. Morpholine (4 ml) in tetrahydrofuran (10 ml) was slowly stirred into a solution of the quinone in terahydrofuran (30 ml) under nitrogen at 0 °C. When white precipitates appeared after stirring at room temperature, the reaction mixture was concentrated. The precipitate (1.46 g) was then recrystallized from dioxane; colorless needles, mp 240 °C (dec). UV λ_{max}^{EtOH} (ε): 220 sh (7930) and 285 (3420) nm; NMR (DMSO-d_6): δ 1.37 (s, 9H), 2.6 (m, 4H), 3.7 (m, 4H), 6.70 (s, 1H), 6.74 (s, 1H) and 8.61 (br. s, 2H, D$_2$O exchangeable); IR (KBr): 3500 cm^{-1} (OH). Found: C, 66.81; H, 8.64; N, 5.58%. Calcd for C$_{14}$H$_{21}$NO$_3$: 66.90; H, 8.42; N, 5.57%.

*5-Methyl-4-morpholinocatechol (**2**).* 4-Methyl-1,2-benzoquinone was prepared by the oxidation of 4-methylcatechol (2 g) with cerium(IV) sulfate.[5] Morpholine (4 ml) in methanol (20 ml) was stirred with the resulting quinone at room temperature under nitrogen. After stirring for 10 min, the mixture was concentrated and chromatographed over silica gel (eluted with benzene–ethyl acetate 4 : 1) to give 260 mg of **2** (7.7%); colorless prisms from ethyl acetate; mp 186—188 °C. UV λ_{max}^{EtOH} (ε): 263 sh (5900) and 295 (3750) nm; NMR (DMSO-d_6): δ 2.10 (s, 3H), 2.7 (m, 4H), 3.7 (m, 4H), 6.50 (s, 1H), 6.57 (s, 1H) and 8.4 (br. s, 2H, D$_2$O exchangeable); IR (KBr): 3450 cm^{-1} (OH).

*5-t-Butyl-4-morpholino-1,2-benzoquinone (**3**).* Silver oxide (100 mg, freshly prepared from silver nitrate) was added, in portions, to a solution of **1** (100 mg) in dry dioxane (20 ml). After the mixture had been stirred for 30 min at room temperature under argon, the resulting precipitate was removed by filtration. The filtrate was concentrated by freeze-drying to a red-orange powder (93 mg, 93%) of **3**; sublimed at 80 °C under 10^{-6} mmHg; mp 90 °C. UV $\lambda_{max}^{CHCl_3}$ (ε): 335 (2870) and 456 (2010) nm: $\lambda_{max}^{H_2O}$ (ε): 272 (10300), 330 (2200) and 510 (2870) nm; NMR (CDCl$_3$): δ 1.38 (s, 9H), 2.93 (m, 4H), 3.83 (m, 4H), 6.08 (s, 1H) and 6.39 (s, 1H); IR (KBr): 1680, 1660 and 1650 cm^{-1} (C=O). Found: C, 67.25; H, 7.74; N, 5.82%. Calcd for C$_{14}$H$_{19}$NO$_3$: C, 67.44; H, 7.68; N, 5.62%.

*5-Methyl-4-morpholino-1,2-benzoquinone (**4**).* This quinone could not be isolated, but a solution of the quinone was obtained by the treatment of the corresponding catechol, **2** with *o*-chloranil. UV λ_{max}^{EtOH} (ε): 496 (3100) nm; NMR (DMSO-d_6): δ 2.22 (d, J=1.5 Hz, 3H), 3.2 (m, 4H), 3.75 (m, 4H), 5.63 (s, 1H) and 6.25 (q, J=1.5 Hz, 1H).

*2-t-Butyl-3-morpholinophenazine (**5**).* *o*-Phenylenediamine (100 mg) in dioxane (5 ml) was added to a dioxane solution (10 ml) of **3** (100 mg); then the mixture was stirred for 20 h at room temperature under argon. After the removal of the solvent, the residue was chromatographed over silica gel to give a yellow powder (63 mg, 45%); yellow prisms from methanol; mp 140 °C. UV λ_{max}^{EtOH} (ε): 256 (117000) and 372 (14500) nm; NMR (CDCl$_3$): δ 1.63 (s, 9H), 3.00 (m, 4H), 3.94 (m, 4H) and 7.7—8.3 (m, 6H). Found: C, 75.30; H, 7.32; N, 13.23%. Calcd for C$_{20}$H$_{23}$N$_3$O: C, 74.74; H, 7.21; N, 13.07%.

*2-Methyl-3-morpholinophenazine (**6**).* To a mixture of 310 mg of 4-methylcatechol and 0.25 ml of morpholine in 20 ml of tetrahydrofuran, silver oxide (1.16 g), in portions, was added with stirring, after which the mixture was stirred for 15 further min under argon at room temperature. When the precipitate had been removed by filtration, 270 mg of *o*-phenylenediamine in tetrahydrofuran (10 ml) was dropped into the filtrate and the mixture was stirred for 20 min. After the removal of the solvent, 16 ml of acetic anhydride containing 1 ml of pyridine was added to the residue, and the solution was warmed at 60 °C for 5 min in a water bath. When the solvent had been evaporated under reduced pressure, the resulting crystals of the acetate of *o*-phenylenediamine were removed by filtration. The filtrate was chromatographed over silica gel to give 205 mg (29.3%) of **6**; yellow prisms from methanol; mp 131—132 °C. UV $\lambda_{\max}^{\mathrm{EtOH}}$ (ε): 235 (29700), 256 (45600), 382 (12100) and 410 (8670) nm; NMR ($CDCl_3$): δ 2.59 (s, 3H), 3.1 (m, 4H), 3.9 (m, 4H) and 7.5—8.3 (m, 6H). Found: C, 73.13; H, 6.17; N, 14.99%. Calcd for $C_{17}H_{17}N_3O$; C, 73.09; H, 6.13; N, 15.04%.

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