Oxidation of Anthracenols and Anthrone to Anthraquinones with Oxygen Mediated by Copper(II) Ion and Imidazole

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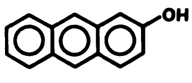
Synopsis. The copper(II) chloride-imidazole-ethanol system turned out to oxidize 2-anthracenols to 1,2-anthraquinones and 2-methoxy-9-anthrone to 2-methoxy-9,10-anthraquinone in practical synthetic yield.

In the preliminary report,[1] copper(II) chloride and imidazole in the presence of oxygen in ethanol was found to be a tyrosinase mimic, which was exemplified by specific and enhanced oxidation of 2-anthracenol (**1**) to 1,2-anthraquinone (**2**) identified as the corresponding phenazine derivative (**3**). Simplicity and effectiveness of the method suggested that this could be applied for general practical synthesis of quinones.

To start with, 9-(2-*p*-cymenyl)-2-anthracenol (**4**) was stirred at ambient temperature with copper(II) chloride dihydrate and imidazole in ethanol for 22 h, resulting in 9-(2-*p*-cymenyl)-1,2-anthraquinone (**5**) in 86% yield. ^{1}H NMR spectrum of **5** supported the structure by appearance of doublet signals at δ 6.48 (C_3-H) and 7.60 (C_4-H), and a singlet signal at 7.81 (C_{10}-H).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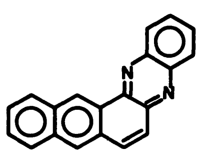
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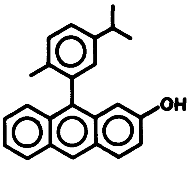
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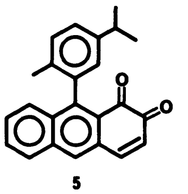
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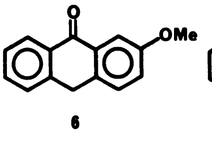
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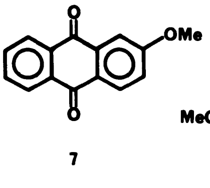
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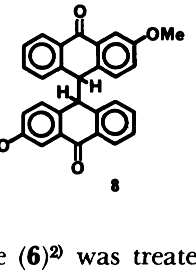
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Secondary, 2-methoxy-9-anthrone (**6**)[2] was treated at ambient temperature in the presence of copper(II) chloride dihydrate and imidazole in ethanol for 25 h, resulting in 2-methoxy-9,10-anthraquinone (**7**) in 81% yield, accompanied by 2,2′-dimethoxy-10,10′-bianthrone (**8**) in 6% yield. When an amount of imidazole was decreased, the reaction was retarded markedly.

These experiments imply that (a) in the presence of air, the mixture of copper(II) chloride and imidazole in ethanol works as effective oxidation catalysis for anthracenols and anthrone and (b) imidazole is indispensable for the oxidation reaction.

The practical synthetic method of 1,2-anthraquinones has been limited hitherto.[3] Fremy's salt is known to be only practical oxidant for the purpose.[4] The other methods[4] such as iron(III) chloride and chromium trioxide for 2-amino-1-anthracenol and chromium trioxide for 1,2-diacetoxyanthracene suffer from the moderate yields and the difficulty of the synthesis of the precursors. As for the synthesis of *o*-quinones, the morpholinocopper(II)-ethanol system[5] is unique and the first tyrosinase mimic. However, the system is far from the practical synthesis of *o*-quinones because it is only applicable to naphthols and phenols of the benzene series and always gives morpholine-substituted *o*-quinones.

9,10-Anthraquinones are of great importance for manufacture of dyes. The classical synthetic route through the cyclization of *o*-benzoylbenzoic acids is not always convenient because the position at which cyclization should take place is deactivated by the electron-withdrawing group at the ortho-position. Improvement has been made by the finding of the path through the cyclization of *o*-benzylbenzoic acids.[6] The resulting anthrones are, then, oxidized by chromium trioxide in refluxed acetic acid in "good" yield. The present system seems to afford advantage over the chromium trioxide method because of easy work-up and mild reaction conditions preventing from the formation of undesirable by-products.

The reaction mechanism of the present system is attractive especially in relation to copper-bound tyrosinase. The mechanism will be discussed elsewhere.

Experimental

The ^{1}H NMR spectra were recorded on JEOL JNM GX-400 instrument with Me_4Si as the internal standard. Electronic absorption spectra (UV) were recorded on a Hitachi 124 spectrophotometer. Infrared spectra (IR) were obtained on a Shimadzu IR-27 apparatus. Mass spectra (MS) were obtained with a Hitachi RMU 6-MG spectrometer by using a direct-inlet method, an ionizing potential at 20 eV. Merck silica gel 60 (Art 7734, 0.063—0.20) was used for column chromatography. Thin layer chromatography (tlc) was performed with precoated plates (Merck, Art. 5715, silica gel 60 F_{254}).

2-Anthracenol was prepared by demethylation of 2-methoxyanthracene by the method exemplified by that of 9-(2-*p*-cymenyl)-2-methoxyanthracene (*vide infra*), which was prepared by the Grignard reaction of 2-methoxy-9-

anthrone with 2-bromo-*p*-cymene.2)

Oxidation of 2-Anthracenol (1). The mixture of **1** (0.516 mmol), copper(II) chloride dihydrate (0.347 mmol), and imidazole (0.347 mmol) in 20 ml of ethanol was shaken in oxygen atmosphere at ambient temperature. After the calculated amount of oxygen was uptaken, the mixture was filtered through Celite (No. 545) and washed several times with chloroform. The combined filtrate was evaporated. The residue was dissolved into acetic acid (5 ml) and 0.516 mmol of *o*-phenylenediamine was added. Dark red precipitate was collected in one day, and recrystallized from benzene to give the phenazine derivative of 1,2-anthraquinone (**3**): mp 220 °C (221—222 °C7); 185—190 °C8)).

*Demethylation of 9-(2-*p*-Cymenyl)-2-methoxyanthracene.* According to the previous method,9) the mixture of 1.43 g of 9-(2-*p*-cymenyl)-2-methoxyanthracene,2) 20 ml of acetic acid, and 20 ml of 47% hydrobromic acid was refluxed for 3.5 h. Cooled reaction mixture was extracted with benzene and chromatographed on a silica-gel column eluted with benzene to give 0.85 g (62% yield) of 9-(2-*p*-cymenyl)-2-anthracenol (**4**) as viscous liquid; Calcd for $C_{24}H_{22}O$: C, 88.31; H, 6.79%. Found: C, 87.93; H, 6.51%. IR (neat): ν_{OH} 3500 and 3400 cm^{-1}.

*Oxidation of 9-(2-*p*-Cymenyl)-2-anthracenol (4).* **4** (0.613 mmol) was mixed in 20 ml of ethanol with copper(II) chloride dihydrate (0.3 mmol) and imidazole (0.3 mmol), and stirred at ambient temperature for 22 h. The reaction mixture was filtered through Celite (No. 545) and washed twice with chloroform. The filtrate was evaporated to dryness and the residue was chromatographed on a silica-gel column eluted with benzene–ethyl acetate (9:1 v/v) to give 9-(2-*p*-cymenyl)-1,2-anthraquinone (**5**) in 86% yield, which was recrystallized from benzene–petroleum ether; yellow red crystals, mp 170—172 °C. Calcd for $C_{24}H_{20}O_2$: C, 84.68; H, 5.92%. Found: C, 84.43; H, 5.92%. IR (KBr disk) $\nu_{C=O}$ 1660 cm^{-1}. UV (ethanol) λ_{max} 236.5, 298.5 and 444.5 nm. MS, a parent peak at *m/z* 340. ^1H NMR (CCl_4) δ=1.26 (6H, d, *J*=7.0, $-CH(C\underline{H}_3)_2$), 2.89 (1H, quin, *J*=7.0, $-C\underline{H}(CH_3)_2$), 1.86 (3H, s, Ar–$C\underline{H}_3$), 6.48 (1H, d, *J*=10.0, C_3–$\underline{H}$), 7.60 (1H, d, *J*=10.0, C_4–$\underline{H}$), and 7.81 (1H, s, C_{10}–$\underline{H}$).

Oxidation of 2-Methoxy-9-anthrone (6). The mixture of **6**2) (1.12 g; 4.99 mmol), copper(II) chloride dihydrate (0.568 g; 3.33 mmol), and imidazole (0.573 g; 8.42 mmol) in 100 ml of ethanol was stirred at ambient temperature for 25 h. The reaction mixture was filtered through Celite (No. 545) and washed well with chloroform. The combined filtrate was evaporated and chromatographed on a silica-gel column eluted with benzene to give 0.96 g (81% yield) of 2-methoxy-9.10-anthraquinone (**7**) and 0.277 g (6% yield) of 2,2′-dimethoxy-10,10′-bianthrone (**8**).

7: IR (KBr) $\nu_{C=O}$ 1673 cm^{-1}; $\nu_{=C-O-C}$ 1305, 1290 cm^{-1}. ^1H NMR ($CDCl_3$) δ=3.99 (3H, s, O–$C\underline{H}_3$), 7.27 (1H, q, $J_{1,3}$=2.69, $J_{3,4}$=8.79, C_3–$\underline{H}$), 7.73 (1H, d, $J_{1,3}$=2.69, C_1–$\underline{H}$), and 8.26 (1H, d, $J_{3,4}$=8.79, C_4–$\underline{H}$).

8: IR (KBr) $\nu_{C=O}$ 1662 cm^{-1}; $\nu_{=C-O-C}$ 1320 cm^{-1}. ^1H NMR δ=3.85 (3H, s, O–$C\underline{H}_3$), 3.87 (3H, s, O–$C\underline{H}_3$), and 4.71 (2H, s, C_{10}– and $C_{10'}$–$\underline{H}$).

References

1) M. Iwata and S. Emoto, *Chem. Lett.*, **1974**, 759.

2) M. Iwata and S. Emoto, *Bull. Chem. Soc. Jpn.*, **47**, 1687 (1974).

3) "Rodd's Chemistry of Carbon Compounds," 2nd ed. ed by S. Coffey, Elsevier Scientific Publishing Company, Amsterdam, Vol. III H, 1979, pp 41-2.

4) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Sons Inc., New York, Vol. I (1967), pp 940.

5) W. Brackman and E. Havinga, *Recl. Trav. Chim. Pays-Bas*, **74**, 937, 1021, 1070, 1100, 1107 (1955).

6) M. G. Sarngadharan and T. R. Seshadri, *Indian J. Chem.*, **4**, 503 (1966).

7) K. Lagodzinski, *Ann.*, **342**, 59 (1905).

8) H. Joachim and N. Goetz, *Chem. Ber.*, **87**, 1236 (1954).

9) L. Long, Jr. and A. Burger, *J. Org. Chem.*, **6**, 852 (1941).