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SYNTHESIS OF NOVEL QUINONES WITH SILVER(II) DIPICOLINATE AS A NEW SELECTIVE OXIDANT

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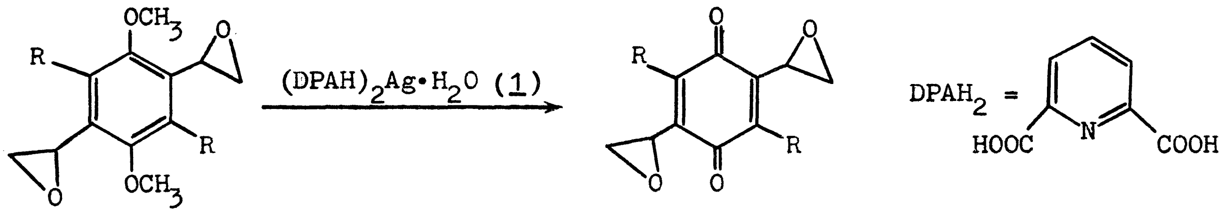
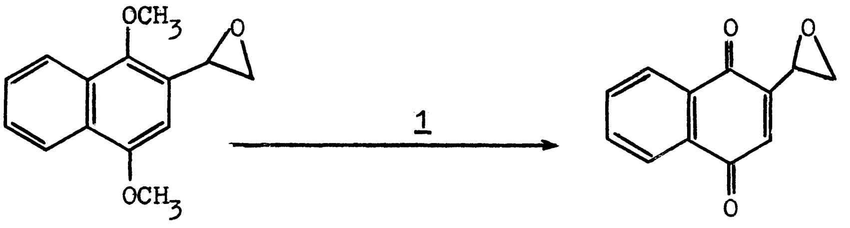
Benzo- and naphthoquinones bearing oxiranyl or 1,3-dioxolan-2-yl substituents were prepared by oxidative demethylation of appropriate hydroquinone dimethyl ethers with silver(II) dipicolinate. A remarkable selectivity of this silver(II) complex as an oxidizing reagent was demonstrated.

The previous papers from this laboratory$^{1,2)}$ described the convenient preparation of substituted benzo- and naphthoquinones from appropriate 1,4-dimethoxyarenes by oxidative demethylation with Ag (II) or Ce (IV) in the presence of 2,4,6-pyridinetricarboxylic acid or 2,6-pyridinedicarboxylic acid N-oxide as catalyst. Unfortunately these methods cannot be applied when unstable and acid labile substituents are present in the 1,4-dimethoxyarene molecule.

Now we wish to report a new method of synthesis of quinones bearing unstable substituents in acidic medium, using silver (II) dipicolinate, $(DPAH)_2Ag{\cdot}H_2O$ (1), as a highly selective oxidizing agent. This complex, easy to prepare is known and its structure was reported in literature,$^{3,4)}$ but it has never been used as an oxidizing agent. Our attempts concerned the oxidation of 1,4-dimethoxyarenes (2, 3 and 6) with oxiranyl substituents to corresponding quinones (4, 5 and 7). These novel quinones were expected to be potential bioreductive alkylating agents according to Lin$^{5,6)}$ and Moore$^{7)}$ hypothesis. Using complex 1 as an oxidant in neutral medium made this synthesis succesful. Oxidation proceeded smoothly in the aquaeous acetonitrile and the sensitive oxirane ring was not affected.



R = H (2) or CH$_3$ (3) R = H (4) or CH$_3$ (5)



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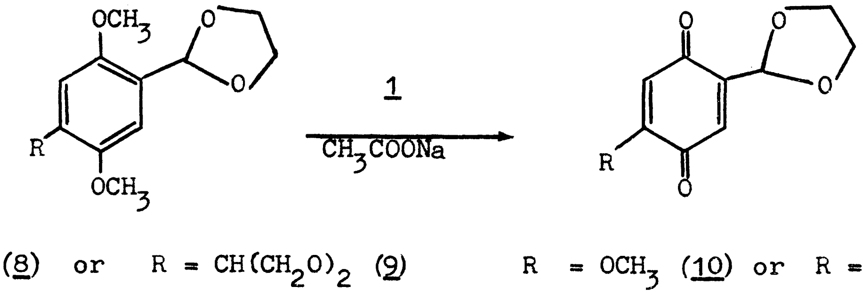
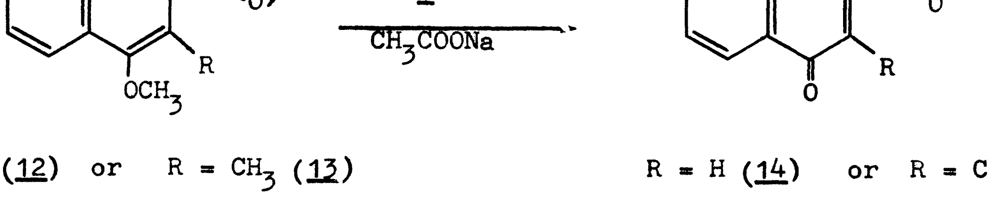
Another substituent especially sensitive to acids is 1,3-dioxolane ring in ortho-position to the methoxy group. When previously reported methods of oxidation$^{1,2,8)}$ were applied, the aldehyde groups were regenerated at once, and resulting 1,4-dimethoxyaldehydes could not be subjected to oxidative demethylation, even under mild conditions. Our results have shown that the application of complex 1 is fruitful, and oxidative demethylation proceeds smoothly without cleavage of the 1,3-dioxolane ring. Demasced aldehydoquinones are unstable substances and we were not interested in their preparation. They can serve as precursors for preparation of hydroquinone having the formyl group as substituent.



R = OCH$_3$ (8) or R = CH(CH$_2$O)$_2$ (9) R = OCH$_3$ (10) or R = CH(CH$_2$O)$_2$ (11)



R = H (12) or R = CH$_3$ (13) R = H (14) or R = CH$_3$ (15)

The silver (II) dipicolinate 1 was obtained as follows. To fine pulverized dipicolinic acid (33.4 g, 200 mmol) suspended in the solution of silver nitrate (16.9 g, 100 mmol) in water (5 l), potassium persulfate (135 g, 500 mmol) was added portionwise within 2 hrs with vigorous stirring. Then the mixture was stirred till the white crystals of dipicolinic acid vanished (about 24 hrs). The black precipitate was filtered off, washed with cold water, and dried in the air to give pure complex 1 in quantitative yield.

Table. Oxiranyl- and 1,3-dioxolanylquinones

Compound	Yield %	Mp, °C	$\nu_{C=O}$ (KBr) cm^{-1}	^{1}H-NMR (CDCl$_3$), δ(ppm)
4	52	155 dec.	1648	3.16 (1H,dd,J=3Hz and 6Hz,-CH$_2$-); 3.52 (1H, dd, J=4.5Hz and 6Hz,-CH$_2$-)9); 4.30-4.45 (1H, m,-CH=); 7.37 (2H,s,3-H and 6-H).
5	73	113	1655	2.50 (3H,s,-CH$_3$); 3.10 (1H,dd,J=3Hz and 6Hz, -CH$_2$-); 3.47 (1H,dd,J=4.5Hz and 6Hz,-CH$_2$-)9); 4.05-4.22 (m,-CH=).
7	34	103	1662	3.30 (1H,dd,J=3Hz and 6Hz,-CH$_2$-); 3.77 (1H, dd,J=4.5Hz and 6Hz,-CH$_2$-)9); 4.60-4.73 (1H, m,-CH=); 7.33 (1H,s,3-H); 8.20-8.37 (2H,m, 6-H and 7-H); 8.52-8.67 (2H,m,5-H and 8-H).
10	54	136	1650	4.25 (3H,s,-OCH$_3$); 4.44 (4H,-CH$_2$CH$_2$-); 6.25 (1H,s,-CH= or 6-H); 6.33 (1H,s,6-H or -CH=); 7.15 (1H,s,3-H).
11	14	101--102	1665	4.40 (8H,s,-CH$_2$CH$_2$-); 6.20 (2H,s,-O-CH=); 7.17 (2H,s,3-H and 6-H).
14	60	151	1662	4.45 (4H,s,-CH$_2$CH$_2$-); 6.37 (1H,s,-O-CH=); 7.15 (1H,s,3-H); 7.97-8.15 (2H,m,6-H and 7-H); 8.35-8.47 (2H,m,5-H and 8-H).
15	45	86	1654 1662	2.70 (3H,s,-CH$_3$); 4.30-4.57(4H,m,-CH$_2$CH$_2$-)10) 6.53 (1H,s,-CH=); 7.90-8.03 (2H,m,6-H and 7-H); 8.25-8.40 (2H,m5-H and 8-H).

To starting 1,4-dimethoxybenzene or -naphthalene (2.5 mmol),11) complex 1 (5.5 g) dissolved in a mixture of acetonitrile (37 ml) and water (8 ml) was added slowly with vigorous stirring within 30 min at room temp. When compounds 8, 9, 12 or 13 were oxidized the medium was buffered by addition of sodium acetate 2.0 g, 25 mmol). Then the mixture was stirred for additional 90 min, water (50 ml) was added, and silver salts were filtered off and carefully washed with $CHCl_3$. The filtrate was extracted several times with chloroform, extract dried over anhydrous $MgSO_4$, and the solvent removed under vacuum. Crude 4 was purified by recrystallization from acetone, quinones 5 and 7 from hexane. Other crude quinones 10, 11, 14, and 15 were purified by column chromatography on florisil using a mixture chloroform - ethyl acetate (10:1) as an eluent and then recrystallized from hexane - acetone mixture. The characteristics of quinones obtained are given in Table.(12)

REFERENCES AND NOTES

1) L.Syper, K.Kloc, J.Młochowski, and Z.Szulc, Synthesis, 522 (1979).
2) L.Syper, K.Kloc, and J.Młochowski, Tetrahedron, 36, 123 (1980).
3) C.W.A.Fowles, R.W.Matthews, and R.A.Walton, J.Chem.Soc. A, 1108 (1968).
4) M.G.B.Drew, R.W.Matthews, and R.A.Walton, J.Chem.Soc. A, 1405 (1970).
5) A.J.Lin, L.A.Cosby, C.W.Shansky, and A.C.Sartorelli, J.Med.Chem. 15, 1247 (1972).
6) A.J.Lin, L.A.Cosby, and A.C.Sartorelli, Cancer Chemother. Rep. 4, 23 (1974).
7) H.W.Moore, Science, 197, 527 (1977).
8) C.D.Snyder, W.E.Boudinell, and H.Rapoport, J.Org.Chem. 36, 3951 (1971).
9) Both of $-CH_2-$ protons are nonequivalent.
10) The multiplet from four nonequivalent protons of $-CH_2CH_2-$ group.
11) The preparation of the starting compounds will be published in the full paper.
12) The microanalyses for the compounds listed in Table were in agreement with the calculated values.

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