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SELECTIVE OXIDATION OF p-ALKYLPHENOLS WITH TETRAPEROXYMOLYBDATE, $[Mo(O_2)_4]^{=}$: A PREPARATIVE METHOD OF A DIENONE HYDROPEROXIDE

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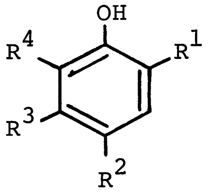
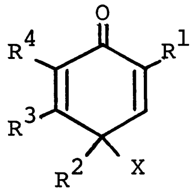
p-Alkylphenols (I), on oxidation with tetraperoxymolybdate, give a dienone hydroperoxide (II) of p-quinol type in high yield. The practice and some limitations are described.

The important role of some transition metal ions has been well established in the biological oxidation of phenols$^{1)}$, such as hydroxylation or oxidative cleavage. In the course of our investigation on the selective phenol oxidation with various peroxy-transition metal species as a model enzyme system, the authors observed that the tetraperoxymolybdate species$^{2,3,13)}$, $[Mo(O_2)_4]^{=}$, in neutral aqueous alcoholic solution oxidized some p-alkylphenols (I), effectively, into a p-quinol type dienone hydroperoxide (II). High selectivity, simplicity of the operation and very mild reaction condition provide a useful preparative method for oxidative dearomatization of the phenol nucleus. This communication reports the practice and some limitations of this reaction.

Tetraperoxymolybdate ion has been shown to be formed in neutral aqueous media from molybdate ion, $MoO_4^{=}$, and excess of hydrogen peroxide, and to decompose thermally with releasing two molecules of oxygen as shown in the following scheme$^{2)}$. In the presence of a substrate, such as phenol, the oxygen may be transferred, in situ, to the substrate molecule.

$$\underset{\text{colorless}}{MoO_4^{=}} \quad \underset{-O_2}{\overset{\text{excess } H_2O_2}{\rightleftharpoons}} \quad \underset{\text{dark red-brown}}{[Mo(O_2)_4]^{=}}$$


(I)


(II) X = OOH
(III) X = OH

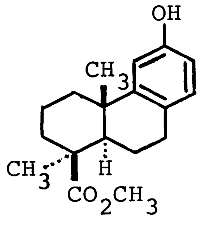
a: $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$
b: $R^1 = R^2 = t\text{-}C_4H_9$, $R^3 = R^4 = H$
c: $R^1 = R^4 = t\text{-}C_4H_9$, $R^2 = CH_3$, $R^3 = H$
d: $R^1 = i\text{-}C_3H_7$, $R^2 = R^3 = CH_3$, $R^4 = H$
e: $R^1 = R^3 = R^4 = H$, $R^2 = -CH_2CH_2CO_2CH_3$
f: $R^1 = R^4 = H$, $R^2,R^3 = -(CH_2)_4-$
g: $R^1 = i\text{-}C_3H_7$, $R^2,R^3 = -(CH_2)_4-$, $R^4 = H$
h: $R^1 = R^4 = CH_3$, $R^2 = R^3 = H$

To a stirred solution of a phenol (1 m mole) in methanol (9 ml) was added at 0° a dark red-brown solution of sodium tetraperoxymolybdate, prepared from sodium molybdate dihydrate (242 mg : 1 m mole, in 4 ml of water) and hydrogen peroxide (30% solution, 2 ml : 20 m moles) at 0°. The reaction mixture (pH = 7.5) was kept at 25~30° until the red-brown color disappeared (usually 4~5 hrs)4). After dilution with water, the product was taken up into a suitable solvent. The crude product was usually homogeneous except for some quantity of the starting material (by TLC analysis). The dienone hydroperoxide (II) may be isolated directly by preparative TLC or column chromatography, or, in some cases, as a more stable hydroxydienone (III) after quantitative reduction with aqueous sodium sulfite (more conveniently with dimethyl sulfide). All of the p-alkylphenols examined here, Ia~Ig, IV and V, gave the corresponding dienone compounds, IIa~IIg, VI5) and VII5), respectively, in good yield (80~95%6) for IIa~IIg; 55%6) for VI and VII). 2,6-Dimethylphenol (Ih) gave a dimer (VIII)3,7) of 2,6-dimethyl-6-hydroxy-2,4-cyclohexadienone. The compounds with free carboxyl group, e.g. the corresponding acids to Ie and IV, failed to react with this reagent: The reaction mixture exhibited only pale brown color and too long reaction time was necessary for complete decoloration.17) In the last case, a certain different type of complex would be formed by co-ordination of the carboxyl group with the metal ion.

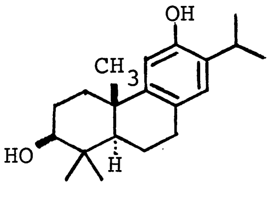
The structures of the dienone hydroperoxides were deduced from the spectral informations. The typical data were given for IId8): λ_{max}^{EtOH} 237 nm (ε : 15000); $\nu_{max}^{CHCl_3}$ 3250, 1677, 1635 cm^{-1}; $\delta_{ppm}^{CCl_4}$ 1.04 (d, 6H, J=7), 2.92 (br.quintet, 1H, J=7), 1.31 (s, 3H), 2.03 (d, 3H, J=1.3), 6.07 (q, 1H, J=1.3), 6.63 (d, 1H, J=1.5).

The alcoholic solvents, e.g. methanol, ethanol, t-butanol, or methylcellosolve, were most satisfactory for the reaction. The percentage of the alcohol in an aqueous reaction medium may be variable depending upon the solubility of the substrate. Dimethylformamide was also useful, but ethereal solvents such as glyme, diglyme, or tetrahydrofuran were not preferable (no red-brown color formation).

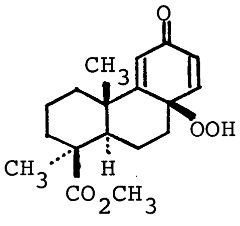
The nature of the oxygen released from tetraperoxymolybdate were also examined preliminarily. The identity of the product distribution (in GLC or TLC) on the oxidation of limonene[9], β-ionone[10], anthracene[11] and hinokiol (V) both with tetraperoxymolybdate and with photosensitized oxygen (Rose Bengal as sensitizer) suggested the possibility of the singlet oxygen as a potential reactive species of the former reagent[12]. On this basis, an endo-peroxide structure (IX) may be assumed as an intermediate in this reaction, since p-quinol type dienone is practically the sole product (no ortho oxidation) from p-alkylphenols. Although some similar phenol oxidations, including those by Ti(IV)-H_2O_2 system[13], photooxygenation[14], and metal chelate - O_2 complex[15], have been reported previously, the use of the tetraperoxymolybdate under the present condition may afford the simpler results and the wider applicability for a preparative method[16].



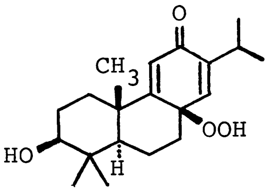
(IV)
methyl podocarpate



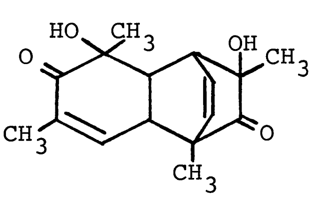
(V)
hinokiol



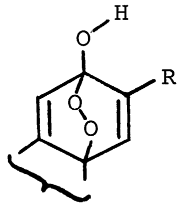
(VI)



(VII)



(VIII)



(IX)

Footnotes and References

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2. J.A. Connor and E.A.V. Ebsworth, Advances on Inorg. Chem. Radiochem., 6, 279 (1964).
3. Similar oxidation system (at higher temperature) has been reported for the oxidation of 2,6-dimethylphenol: R.G.R. Bacon and A.R. Izzat, J. Chem. Soc. [C], 1966, 791.
4. Much longer reaction period is required at lower temperature. The use of higher temperature or unnecessary prolongation of the reaction time after disappearance of the red color should be avoided, because further decomposition of the dienone hydroperoxide results in a complicated mixture.
5. The hydroperoxy group at C_8 should be β-orientation: The $\Delta\delta$-values of the methyl signals (at C_{10}) from IV to VI and from V to VII are 0.20 and 0.16 ppm, respectively. This fact suggests the 1,3-diaxial-cis-relationship of the hydroperoxy group at C_8 to the methyl group at C_{10}. Cf. G.F. Burkinshaw and B.R. Davis, Tetrahedron, 23, 4147 (1967).
6. The yields were calculated without subtraction of the unreacted phenols.
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8. The corresponding hydroxydienone gives mp 51—53° and the satisfactory analytical data (Anal: C, 73.32; H, 8.95%, Calc: C, 73.30; H, 8.95%).
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16. Other peroxymetal species containing Cr(VI)[2,12], Mn(IV)[2], Fe(III)[2], Cu(II)[2], Co(III)[2], Pd(II) or Pt(II) gave no satisfactory results.
17. The products were not identified thoroughly, but no expected dienone hydroperoxide was detected in them.

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