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A Reductive Methylation of Quinones

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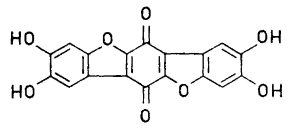
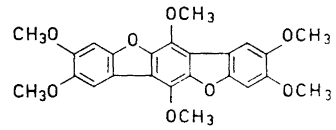
A reductive methylation of quinones in the presence of pyridine is described. It is probable that methylpyridinium hydroxide, formed in the reaction, is the actual reductant. It is suggested that quinones with a high oxidation potential could be used as oxidants in the Decker-oxidation instead of potassium ferricyanide.

In connection with work on the structure of thelephoric acid,[1] it was observed that when thelephoric acid (I) was methylated with dimethyl sulphate in the presence of pyridine, reduction of the quinone occurred and dihydrothelephoric acid hexamethyl ether (II) was obtained:



I



II

It was also tentatively proposed that the reaction is analogous to the Decker-oxidation,[2] in which an alkylpyridinium hydroxide is oxidized by potassium ferricyanide to a N-alkyl-2-pyridone. In the present case the quinone would take the place of the ferricyanide.

Some further experiments have now been carried out in order to determine the scope and limitations of this reaction and, if possible, to find some evidence for the proposed mechanism. Table 1 gives the results from a series of experiments in which different quinones were treated with dimethyl sulphate and alkali in the presence of pyridine.

The reaction was originally conducted in acetone solution.[1] Acetone has, however, the disadvantage that an aldol condensation can take place under the basic conditions of the reaction, making the separation and purification of the reaction products difficult. Other solvents were therefore tried and it was found that the reaction proceeds also in water and methanol, whereas no reaction was observed when benzene, chloroform or diethyl malonate were used as solvents. Methanol was then selected as the solvent in the experiments described in this paper.

With *p*-benzoquinone, toluquinone and thymoquinone the reaction was exothermic and the reaction mixture had to be cooled during the reaction. With the other quinones the reaction mixture was refluxed.

Table 1.

	Redox potential, V	Reduction time	Yield of methylated hydroquinone %
p-Benzoquinone	0.711 [3]	5 min	74
2,5-Diphenylbenzoquinone	0.673 [4]	8 h	79
Toluquinone	0.657 [3]	5 min	60
Thymoquinone	0.589 [5]	2 h	30
1,2-Naphthoquinone	0.576 [3]	1 h	10
1,4-Naphthoquinone	0.483 [6]	1 h	14
Duroquinone	0.480 [5]	1 h	–
2,5-Dimethoxybenzoquinone	0.470 [6]	1 h	–
2,5-Dihydroxybenzoquinone	0.434 [6]	10 h	–
Retenequinone	0.410 [6]	15 h	–
Anthraquinone	0.155 [6]	30 h	–

As can be seen from Table 1 the reaction proceeds only with quinones having a relatively high redox potential. In several cases the yield exceeds 50 %, indicating that the reaction cannot be a disproportionation. This is important because Seshadri and co-workers [7] have shown that the methylation of some quinones, particularily benzoquinone, can lead to the methylated hydroquinone even without pyridine and they considered this reaction as a disproportionation.

Pyridine is necessary for the reaction under our conditions. This was shown in experiments with varying amounts of pyridine. Without pyridine no reaction took place while at least one mole of pyridine per mole of quinone was necessary for an optimum yield.

Likewise, no reduction was observed when dimethyl sulphate was omitted. It thus appears improbable that pyridine, as such, is the reducing agent, a possibility which had to be considered in view of the reports that benzoquinone can be reduced by heterocyclic compounds containing a tertiary nitrogen atom.[8–10] In agreement with our earlier assumption,[1] we therefore consider methylpyridinium hydroxide as the real reducing agent, in spite of our failure to isolate the expected N-methyl-2-pyridone from the reaction mixture. Nor was it possible to isolate any other pure nitrogen containing compound.

When, however, *p*-benzoquinone was treated with methylpyridinium hydroxide alone, reduction of the quinone to hydroquinone occurred and from this reaction mixture N-methyl-2-pyridone could be isolated. This shows that the original assumption,[1] that quinones can oxidize methylpyridinium hydroxide, is correct, and it is assumed that the failure to isolate N-methyl-2-pyridone from the methylation experiments is due to some further reaction in which this is transformed in some hitherto unknown way.

Although it is apparent that the reductive methylation of quinones described above is of preparative value only in special cases such as thelephoric acid [1] and 2,5-diphenylbenzoquinone, it is possible that quinones with a high oxidation potential could be successfully used for the oxidation of alkyl-

pyridinium hydroxides and their analogues, instead of the hitherto used potassium ferricyanide.[11]

EXPERIMENTAL

Methylation experiments. These were conducted in two different ways:

(*a*) Dimethyl sulphate (0.8 ml; 8.4 mmole) was dissolved in 5 ml of methanol and to this was added 0.23 (2.8 mmole) of pyridine. The mixture was refluxed for one hour and chilled. *p*-Benzoquinone (0.3 g; 2.8 mmole), dissolved in 5 ml of methanol, was added and the mixture placed in an ice-salt bath. To the stirred mixture were slowly added 5 g of sodium hydroxide dissolved in 10 ml of methanol. After 5 min the mixture was steam distilled and the distilled *p*-dimethoxybenzene collected (285 mg; 74 %), m.p. 56° (lit.:[7] m.p. 58°). In the same way toluquinone gave 2,5-dimethoxytoluene, m.p. 15° (lit.:[12] m.p. 15°) and thymoquinone 1-methyl-4-isopropyl-2,5-dimethoxybenzene, b.p. 118°/12 mm; n_D^{22} 1.5134 (lit.:[13] b.p. 118°/12 mm; n_D^{22} 1.51335) in yields as given in Table 1. The identity of the crystalline compounds was confirmed by mixed m.p. determination with authentic samples.

(*b*) 2,5-Diphenylbenzoquinone (0.3 g; 1.15 mmole) was dissolved in 10 ml methanol to which was added potassium carbonate (5 g), pyridine (0.1 ml; 1.15 mmole) and dimethyl sulphate (0.33 ml; 3.45 mmole). The mixture was refluxed for 8 h, the solvent removed under vacuum and water added. The water-insoluble 1,4-diphenyl-2,5-dimethoxybenzene was recrystallised from benzene. (yield 265 mg; 79 %) m.p. 154°. (Found: C 82.85; H 5.99. $C_{20}H_{18}O_2$ requires C 82.73; H 6.25). No depression of m.p. was observed on admixture of a sample prepared by reduction of 2,5-diphenylbenzoquinone with zinc and hydrochloric acid followed by methylation with dimethyl sulphate and potassium carbonate. Using the reaction times given in Table 1 1,2- and 1,4-naphthoquinone gave, in the same way, 1,2-dimethoxynaphthalene, m.p. 31° (lit.:[14] m.p. 31°) and 1,4-dimethoxynaphthalene, m.p. 85° (lit.:[15] m.p. 87–88°), respectively. Both were identified by mixed m.p. determinations with authentic samples. From duroquinone, 2,5-dimethoxybenzoquinone, retenequinone and anthraquinone only unchanged starting material could be recovered, whereas 2,5-dihydroxybenzoquinone gave 2,5-dimethoxybenzoquinone.

N-Methyl-2-pyridone from pyridine. Pyridine (2 ml) was dissolved in water (10 ml) and to this was added, with cooling, methyl iodide (1.55 ml) in three portions. Silver oxide (6 g) was then added and the mixture filtered. To this solution was added *p*-benzoquinone (1.2 g) while cooling in an ice-salt bath. The mixture was extracted with ether from which hydroquinone (0.48 g; 40 %) was recovered. To the remaining water solution was added sodium hydroxide (5 g) and potassium carbonate until the solution was saturated. It was then extracted with amyl alcohol and the amyl alcohol evaporated under vacuum. The residue was taken up in ether and removal of the ether gave N-methyl-2-pyridone as a sligthly red coloured oil, identified by its I.R.-spectrum.

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