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PHENOL DEHYDROGENATIONS

PART 10. OXIDATIVE COUPLING OF 3,5-DIMETHYLPHLOROACYLOPHENONES

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Oxidative coupling of phenols is generally supposed to proceed *via* free radicals to give products which readily rearrange to biphenyls or diphenyl ethers.[1,2] Coupling occurs in positions *ortho* or *para* with respect to hydroxyl groups. If these positions are blocked, e.g. by methyl groups, the primary coupling products do not rearrange easily to give aromatic compounds. Occasionally such methyl groups may participate in the coupling reaction. This seems to happen during the biosynthesis of methylene-bisphloroglucinol derivatives in certain ferns, e.g. *Dryopteris* and *Tectaria* (*Aspidium*), and of the "cosins" isolated from *flores kosso* (*Hagenia*, Rosaceae). The participation of methyl groups in coupling reactions has recently been demonstrated by Penttilä *et al*. in the biosynthesis of desaspidine.[3]

The present work was initiated some years ago in order to find out if the dehydrogenation of 3,5-dimethylphloroacylophenones results in coupling to diphenylmethane or to dioxan derivatives. The latter possibility has been suggested for the oxidation of trimethylphloro-

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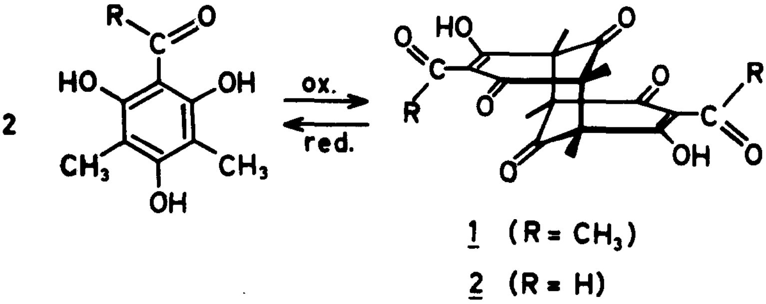
"glucinol to "cedrone".[4] However, it has been found that the reaction takes a third path. Dimethylphloroacetophenone and dimethylphloroglucinol aldehyde were smoothly oxidized to dimers having novel structures (1 and 2 respectively).



Oxidation of 3,5-dimethylphloroacetophenone with ferric chloride in ethanol gave "dehydrodi-dimethylphloroacetophenone" (1) $C_{20}H_{20}O_8$ (analysis, mass spectrum), m.p. 270-273°, in a yield of 85 %. Oxidation with potassium ferricyanide gave the same compound in 44 % yield.

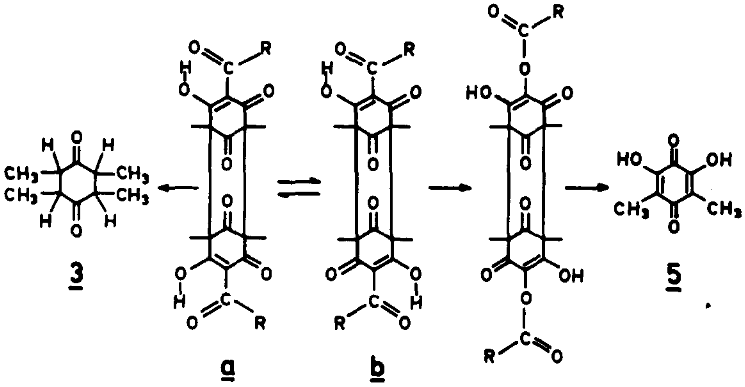
Compound 1 was easily and quantitatively reduced back to the original phenol either catalytically (Pd/C, ethanol) or with zinc and acetic acid. With aniline, 1 gave a dianil, m.p. 300-302°. Oxidation of 1 with ten moles of hydrogen peroxide (as 30 % H_2O_2) in pyridine gave tetrahydroduroquinone (3) in 18 % yield, m.p. 172-174° (analysis, mass spectrum). This was converted into duroquinone by oxidation with manganese dioxide in sulphuric acid (yield about 30 %).

Oxidation of 1 with two moles of hydrogen peroxide in pyridine gave a compound, m.p. 187-190°, presumably a pyridine salt of the diacetate 4 ($C_{30}H_{30}O_{10}N_2$, analysis). Alkaline hydrolysis gave 3,5-dimethyl-2,6-dihydroxy-p-benzoquinone (5) in 63 % yield.

Oxidation of 3,5-dimethylphloroglucinol aldehyde with ferric chloride gave "dehydrodi-dimethylphloroglucinol aldehyde"(2) $C_{18}H_{16}O_8$ (analysis, mass spectrum), m.p. 278-282° (decomp.) in a yield of about 70 %.

Reduction of dimer 2 with zinc in acetic acid gave 3,5-dimethylphloroglucinol aldehyde in almost quantitative yield. Oxidation with ten moles of hydrogen peroxide in pyridine gave tetrahydroduroquinone in 13 % yield. Similar oxidation with two moles of hydrogen peroxide followed by alkaline hydrolysis gave 3,5-dimethyl-2,6-dihydroxy-p-benzoquinone in 45 % yield.

As compared with most other β-tricarbonyl compounds, 1 was very stable towards acids. It was resistant to prolonged boiling with strong hydrochloric or hydroiodic acid, and was recovered unchanged even from solutions in concentrated sulphuric acid.



1 (R = CH₃)

2 (R = H)

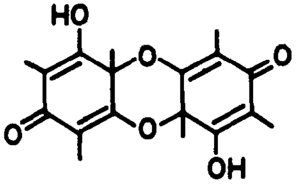
The degradations to 3,5-dimethyl-2,6-dihydroxy-p-benzoquinone and particularly to tetrahydroduroquinone suggest structure 1 for the dehydrogenation product from 3,5-dimethylphloroacetophenone and structure 2 for the product from 3,5-dimethylphloroglucinol aldehyde.

The spectroscopic investigations showed that dimers 1 and 2 were both enolised β-tricarbonyl compounds. The infrared spectrum (in KBr) of dimer 1 showed the presence of an enolised and strongly chelated 2-acetylcyclohexane-1,3-dione grouping by bands at 1665 cm^{-1} (conjugated carbonyl) and 1545 cm^{-1} (chelated carbonyl) and also of a non-conjugated carbonyl group (1725 cm^{-1}). Dimer 2 similarly showed bands at 1725, 1670, 1620 and 1550 cm^{-1}. The band at 1620 cm^{-1} has a counterpart in the spectrum of enolised 2-formylcyclohexane-1,3-diones.[5]

The ultraviolet spectrum (in ethanol) of dimer 1 was similar to that of the enolic 2-acetyl-4,4, 6,6-tetramethylcyclohexane-1,3,5-trione,[6] though the extinction coefficients were about twice as high, indicating the presence of two tricarbonyl systems in the molecule [maxima at 243 nm (ϵ = 16.150), 283 nm (19.800)]. The ultraviolet absorption spectrum of dimer 2 (in cyclohexane) was similar to that of dimer 1 [232 nm (14.600), 287 nm (13.700)].

The presence of the enolised tricarbonyl systems was also demonstrated by the NMR spectra (60 Mc/s, deuterochloroform solution). The spectrum of dimer 1 showed two signals at very low field (δ = 18.70 and 18.77 ppm), typical for strongly chelated enolic protons. Only one acetyl signal (six protons, 2.66 ppm) was observed. In addition the spectrum showed four methyl signals of approximately equal intensity, corresponding to four non-equivalent methyl groups (1.23, 1.33, 1.37 and 1.47 ppm). The signals coalesced when a trace of pyridine was added to the solution. This phenomenon is common among β-tricarbonyl compounds which, like dimer 1, can give non-equivalent chelated enols (1a and 1b). These are not rapidly interconverted unless an acidic or basic catalyst is present.[5] Each of the two forms contains two non-equivalent pairs of methyl groups. Analogous NMR spectra were obtained for dimer 2.

These results throw doubt on the correctness of the structure 6 proposed earlier for cedrone[4] and this is now being re-investigated.



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