

SYNTHESIS OF BENZOFURANOID SYSTEMS. II.

TOTAL SYNTHESIS OF CYPERAQUINONE AND CONICAQUINONE

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The difurobenzoquinone cyperaquinone, a constituent of a number of species of Cyperaceae, has been shown mainly on spectroscopic evidence to have structure (I).¹ This compound and its derivatives represent a novel type of naturally-occurring ring system whose biogenesis² and biological activity^{1,3} are of some considerable interest. Conicaquinone (II) has been extracted in low yield from the roots of Cyperus conicus Boeck and its structure was assigned⁴ solely from UV, IR, NMR and mass spectral data. We now wish to report the total synthesis⁵ of both compounds (I) and (II).

6-Hydroxy-4-methoxy-3-methylbenzofuran (IV), m.p. 103^o, was prepared by the base catalysed cyclisation of the mono-acetyl mono-methylether of phloroglucinol mono-benzenesulphonate (III) as previously described.⁶ The overall yield of (IV) in six steps from phloroglucinol was 73%. Hydrogenation to the dihydrobenzofuran (V), b.p. 144^o/1 mm, was followed by bromination (Br₂ in CHCl₃ at 0^o) to block the more reactive 7-position (VI, m.p. 103^o) prior to formylation using dichloromethylmethylether/titanic chloride in dichloromethane⁷ to produce (VIIa), m.p. 96^o.

The substitution pattern in (VIIa) was confirmed by its mass spectrum which showed an [M - H₂O]⁺ ion (40% RI) characteristic of an o-methoxybenzaldehyde⁸ whereas the aldehyde obtained by formylation of the unbrominated dihydrobenzofuran (V) showed no mass spectrometric loss of H₂O from its molecular ion. Preparation of the d₃-methoxy derivative (VIIf) and observation of an [M - HDO]⁺ ion in its mass spectrum substantiated the assignment.

Condensation of (VIIa) with chloroacetone in acetone/K₂CO₃ gave (VIII), m.p. 141-142^o, which was dehydrogenated to the benzodifuran derivative (IX), m.p. 208-209^o, using DDQ in benzene. Demethylation of (IX) with 2.5 equivalents of sodium thioethoxide in DMF⁹ afforded the bromophenol (X), m.p. 243-245^o, which was oxidised by Fremy's salt¹⁰ to (II), m.p. 189-190^o.

The synthetic compound (II) was identical in all respects (m.p., mixed m.p., UV, IR, NMR, mass spectra) with naturally-occurring conicaquinone.

The action of the ylid, generated from methyltriphenylphosphoniumiodide by sodium methoxide in DMF/THF¹¹ on (IX) produced the isopropenyl benzodifuran, (XI), m.p. 128-130°, which demethylated cleanly with sodium thioethoxide in HMPT at 70°. The product (XII), extremely acid labile and light sensitive, was oxidised by Fremy's salt to give (I), m.p. 182-183°d, identical in all respects with cyperaquinone from natural sources.¹

We are now in the process of synthesising other naturally-occurring derivatives of cyperaquinone.¹

REFERENCES

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