

THE OXIDATIVE CO-COUPLING OF PHENOLS. THE SYNTHESIS OF TETRAHYDRODIBENZOFURANONES

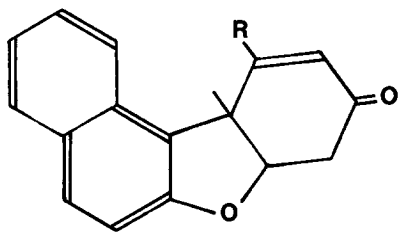
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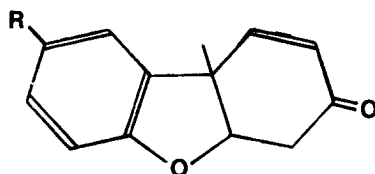
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IN contrast to the extensive examples of oxidative self-coupling of monohydric phenols¹, reports of successful oxidative coupling of dissimilar phenols are very limited. Apart from the minor products resulting from ferric chloride oxidation of p-cresol² the only other intermolecular examples are provided by the recently reported³ co-oxidation of p-cresol with 2,4-dimethyl and 2,4,6-trimethylphenol. This communication summarises some of our observations in this area with particular reference to the synthesis of tetrahydrodibenzofuranones.

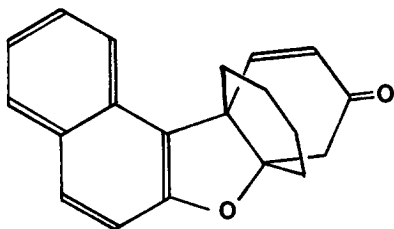
Two important considerations have governed our selection of pairs of phenolic substrates. Firstly, in order to promote co-coupling, it is imperative that phenoxy radicals are generated at comparable rates from each of the substrates, hence the phenols must have closely similar oxidation potentials. The quantitative relationship between oxidation potential⁵ and acidity will normally ensure that the pairs of phenols thus selected possess similar acidities so that the reaction medium will contain comparable concentrations of the derived anions. Secondly, as the tetrahydrodibenzofuranone results from ortho-para coupling, in the general case it would be possible to obtain two products of cross-coupling as well as the two products of self-coupling. This situation was avoided by selecting as one of the substrates a phenol only capable of undergoing ortho-coupling and employing it in considerable excess over its partner, thereby suppressing self-coupling of the latter. The excess substrate is converted into phenolic products which are readily separated from the neutral tetrahydrodibenzofuranones.



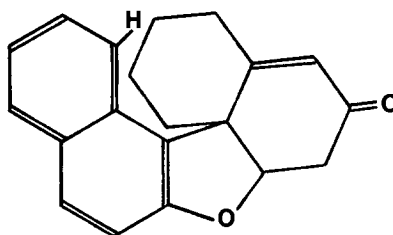
1 R = H
2 R = CH₃



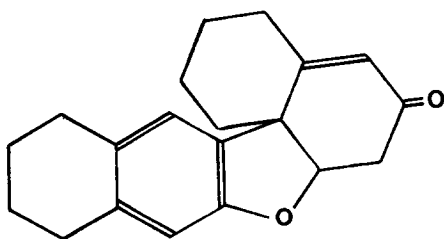
3 R = CH₃
4 R = C₆H₅



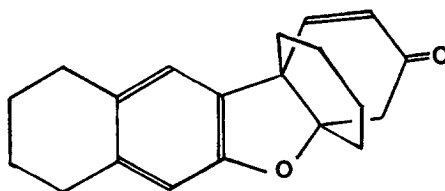
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The successful application of these considerations is exemplified by the potassium ferricyanide oxidation of a 1:4 mixture of *p*-cresol (E_{ox} 1.04 volts⁴) and 2-naphthol (E_{ox} 1.02 volts) dissolved in aqueous ethanol containing sodium carbonate. The crude reaction product was washed with aqueous sodium hydroxide to remove the polyphenols, and the non-acidic fraction subsequently purified through the Girard P derivative to give the ketone (1, 27%) m.p. 102-3⁰. The structure of this compound is fully established by its spectroscopic properties with infrared absorptions at 1670 cm^{-1} (C=O) and 1615 cm^{-1} (C=C), and a ¹H-NMR spectrum similar to that of Pummerer's ketone (3) with bands at δ 1.85 (s, CH₃), 2.95 (m, CH₂), 4.8 (m, CH), 6.01 (d, -CH=, J=10.5 Hz), 6.8 - 8.1 (m, 7H, ArH and -CH=). A similar reaction in which 2-naphthol was replaced by *p*-phenylphenol (E_{ox} 1.05 volts⁴) provided ketone (4, 22%) m.p. 86-87⁰.

Oxidative coupling of 3,4-dimethylphenol with 2-naphthol yielded the ketone (2, 22%) m.p. 176-8⁰. The key features of the n.m.r. spectrum are a singlet at δ 5.87 for the olefinic proton and a multiplet at δ 4.7 for the one at the ring junction. In contrast, coupling of 6-hydroxytetralin with 2-naphthol produced the ketone (5, 21%) m.p. 128-30⁰, whose formulation as (5) rather than (6) follows from the observation of doublets at δ 5.95 and 6.84 (J = 10.5 Hz) for the olefinic protons and a singlet at δ 2.75 for the protons of the methylene group adjacent to the carbonyl group. The reason for the preferential formation of (5) appears to be due to the steric interaction of the *peri*-hydrogen atom of the naphthalene ring with the tetramethylene chain in structure (6) and not to any geometrical constraint imposed by the tetramethylene bridge. This conclusion is supported by the finding that self-coupling of 6-hydroxytetralin provides a roughly equimolar mixture of the ketones (7) and (8). Whereas ketone (7) shows signals at δ 4.53 (m, CH) and 5.77 (s, -CH=), the isomer (8) displays doublets at δ 5.85 and 6.36 (J = 10 Hz) for the vinylic protons. In both isomers the aromatic protons are observed as singlets at δ 6.45 and 6.91.

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