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THE ROLE OF STEREOELECTRONIC FACTORS IN THE OXIDATION OF PHENOLS

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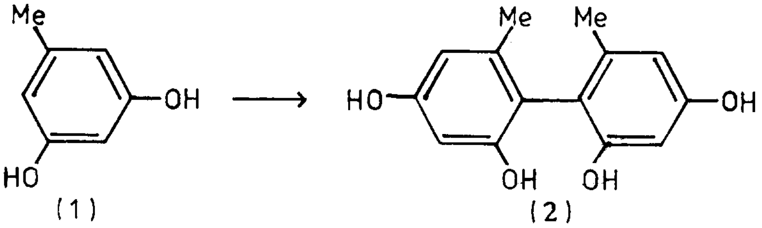
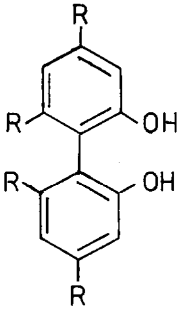
Summary The oxidative coupling of both 3,5-dimethylphenol and phenol leads to the ortho-ortho and ortho-para coupled products as the predominant C-C dimers: stereoelectronic factors determine the preferred mode of approach of the phenoxyl radicals.

Frontier molecular orbital theory suggests that the coupling of resonance-stabilized free radicals should occur preferentially at the sites of highest spin density.[1] Evidence to support this comes from the oxidation of orcinol (1) which gives exclusively the dimer (2) : the spin density in the intermediate 3-hydroxy-5-methylphenoxyl radical is 14 times as great at the 4- and 6- positions as at the 2- position.[2]



No studies have been undertaken with monohydric phenols to investigate the influence of spin density effects on the product distribution. E.s.r. studies indicate that the spin density at the para-position in a range of alkyl-substituted phenols is approximately twice that at the ortho-positions.[3] Thus oxidative coupling of phenols possessing free ortho- and para-positions might be expected to give para-para coupled products in the absence of steric factors.

We initially chose 3,5-dimethylphenol as a suitable substrate since it possesses free ortho- and para-positions and steric effects would not be expected to be such as to preclude coupling at either position. Oxidations were carried out by decomposing di-t-butyl peroxide at 140° or di-t-butyl peroxyoxalate at 25° in a ten-fold excess of the phenol in chlorobenzene. The reaction mixtures were analysed by chromatography. Reference samples of the three C-C coupled products (3a-5a) were isolated by chromatographic separation of the crude product obtained in large scale oxidations (structures were assigned using n.m.r. spectroscopy); the two C–O coupled products (6a and 7a) were synthesized.[4]



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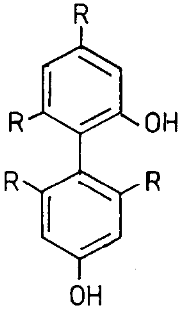

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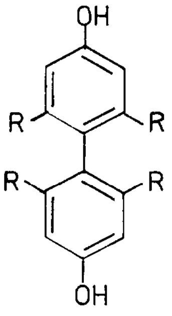

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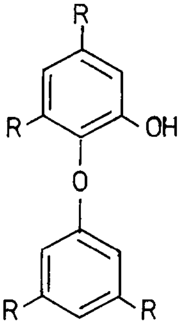

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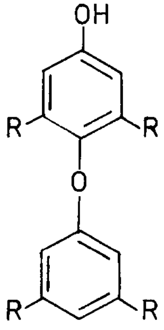


(7)

a. R = Me

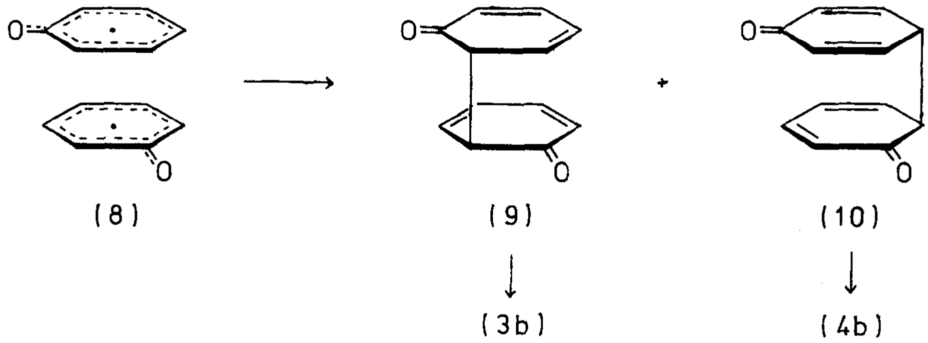
b. R = H

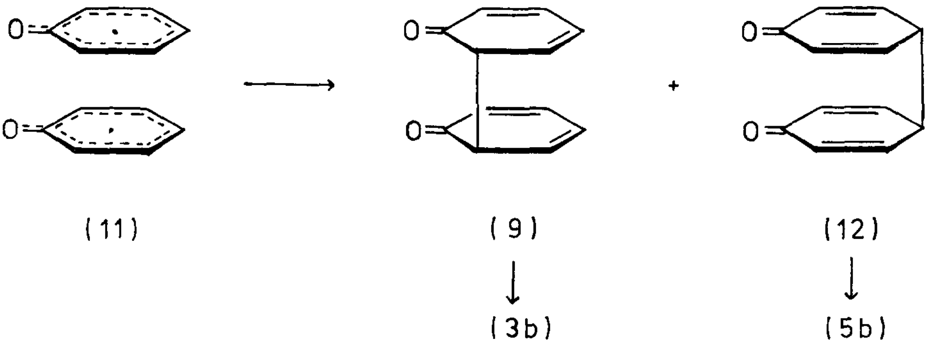
The predominant product from oxidation at 140° was the <u>ortho-ortho</u> coupled product (3a); none of the <u>para-para</u> coupled product (5a) was formed. At lower temperatures the major product was the <u>ortho-para</u> coupled compound (4a) but again very little of the <u>para-para</u> coupled dimer (5a) was obtained. As it was conceivable that the low yields of (5a) could have been attributed to the <u>para</u>-position being somewhat more hindered than the <u>ortho</u>-position, we examined the oxidation of phenol. Once again the major product at 140° was the <u>ortho-ortho</u> coupled product (3b) though rather more of the <u>ortho-para</u> coupled product (4b) was obtained than in the oxidation of 3,5-dimethylphenol. These results indicated that the product distribution could not be satisfactorily explained by spin density considerations or by steric effects as on either basis the major C–C coupled product obtained from phenol would have been expected to be 4,4'-dihydroxybiphenyl (5b).

Table Products from the Oxidations of 3,5-Dimethylphenol and Phenol

Phenol	Oxidant	Temp.(^{o}C)	Products (%)				
			(3)	(4)	(5)	(6)	(7)
3,5-$Me_2C_6H_3OH$	$(Bu^tO)_2$	140	77	16	0	6	1
	$(Bu^tO.CO_2)_2$	25	17	40	8	8	27
C_6H_5OH	$(Bu^tO)_2$	140	48	26	2	9	15
	$(Bu^tO.CO_2)_2$	25	26	35	28	7	5

A theoretical study of the coupling of benzyl radicals,[5] which are isoelectronic with phenoxyl radicals, indicates that the mutual approach of the radicals in a sandwich-type geometry was shown to be more stable than two isolated benzyl radicals by 22 kcal. mol^{-1}. We have calculated, using the MINDO-3 method and standard parametrisation, energy curves for various approach geometries which two phenoxyl radicals might make. From a variety of approaches, using a previously optimised geometry, details of which will be given in a later paper, [6] the staggered and eclipsed orientations (8 and 11) were shown to be the optimum configurations for the coupling of phenoxyl radicals. The results indicate that, at large interplanar distances, the staggered approach is slightly favoured by a small energy margin.





We believe this margin must be significant since the staggered configuration could lead to either the ortho-ortho or ortho-para coupled product but not to the para-para coupled product: in contrast the eclipsed configuration could give rise to either the ortho-ortho or para-para coupled products but significantly not the ortho-para coupled product. That the staggered configuration is more stable than the eclipsed configuration is probably due, at least in part, to the electrostatic repulsion between the two oxygens in the eclipsed configuration. The coupling of benzyl radicals proceeds via an eclipsed configuration since similar electrostatic repulsive effects would not be present.

The ratio of the ortho-ortho coupled products (3) to ortho-para coupled products (4) obtained in the oxidations of both phenols decreased markedly at lower temperatures (see Table) possibly reflecting the interplay of competing thermodynamic and kinetic factors. At high temperatures the staggered conformation (8) undergoes **C–C** bond formation to form preferentially the thermodynamically more stable (more fully conjugated) dimeric cyclohexadienone (9) which enolizes to give (3b). At lower temperatures formation of the alternative cyclohexadienone dimer (10) becomes increasingly favoured possibly reflecting the importance of spin density considerations. The calculations lend support to these conclusions.

These results show that stereoelectronic factors can explain the preferred formation of the ortho-ortho and ortho-para coupled products in the oxidations of phenols possessing free ortho- and para- positions. The mode of formation of the C–O dimers will be discussed elsewhere.

Acknowledgement

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