Oxidative Coupling of Phenols. Part 10.[1] The Role of Steric Effects in the Formation of C–O Coupled Products

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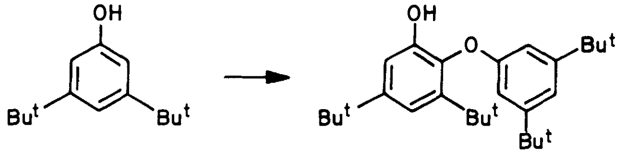
The formation of C–O coupled products in the oxidative coupling of phenols is hindered by bulky *ortho*-substituents in the aryloxyl radical intermediates as shown by the predominant formation of the *ortho-ortho*-C–C coupling products in the oxidation of *o*-t-butyl- and 2,4-di-t-butyl-phenol. 3,5-Di-t-butylphenol gives exclusively the *ortho*-O-dimeric product as steric effects prevent the sandwich approach of two aryloxyl radicals necessary for C–C coupling.

We have demonstrated in previous papers in this series [1-3] that the favoured route leading to C–C dimers in the oxidative coupling of phenols involves the mutual approach of two phenoxyl radicals in a sandwich-like configuration so as to maximize SOMO–SOMO interactions and to minimize both electrostatic repulsion between the oxygen atoms and steric interactions between alkyl groups on the participating radicals. In those cases where this type of approach is less favourable, for example, the extent of C–O coupling in *p*-alkylphenols increases with increasing size of the alkyl groups.[4] There is also very much more of the C–O coupled product formed in oxidations of 2,4-dimethylphenol than of *p*-cresol: [5] a sandwich mode of mutual approach of 2,4-dimethylphenoxyl radicals would inevitably result in two sets of unfavourable interactions in the transition state leading to the *ortho-ortho*-dimer.[1] *ortho*-Substituents in the radical also shield somewhat the oxygen in the phenoxyl radical thereby slightly reducing the extent of C–O coupling. The position of C–O coupling is subject more to steric control than to the influence of spin density distribution in the radical: this is exemplified by the observation that the major C–O coupled product obtained from oxidations of 2,3-dimethylphenol results from attack of the less hindered 6-position even though the spin density is less at this position than at the 4-position. In this paper we explore in greater detail the influence of steric effects on the proportion of C–O coupling in a series of alkyl-substituted phenols.

The contention that phenoxyl radicals couple *via* a sandwich-like transition state to give C–C coupled products should be capable of evaluation by comparing the products obtained from oxidations of 3,5-dimethyl- and 3,5-di-t-butylphenol. In the case of the latter the bulky t-butyl groups might be expected to hinder the approach of the radicals sufficiently to deter C–C bond formation. On the other hand C–O bond formation should be feasible since the probable non-sandwich mode of approach would minimise nuclear repulsion between the two radicals. Hence we examined the oxidation of 3,5-di-t-butylphenol and found it gave only one product. This was identified as the *ortho*-O coupled product (1) on the basis of its n.m.r. spectrum (three non-equivalent t-butyl groups).



(1)

We next investigated oxidations of 2-t-butyl-4-methyl- (2a) and 4-t-butyl-2-methyl-phenol (2b), which by analogy with 2,4-dimethylphenol were expected to behave similarly and give largely C–O coupled products (4). This was indeed the case with 4-t-butyl-2-methylphenol which gave (4b) as the major product together with a small amount of an isomeric compound which is believed to be the *ortho-ortho*-coupled product (3b). To our initial surprise 2-t-butyl-4-methylphenol gave rise to the *ortho-ortho*-coupled dimer (3a) as the only product. Structures of these products were readily assigned on the basis of n.m.r. evidence. The sandwich modes of approach which would be postulated for the formation of the *ortho-ortho*-coupled products from (2a) and (2b), *viz.* (5) and (6), have identical interactions between the methyl and t-butyl groups and do not explain the difference in behaviour of these two phenols. This suggests that the different behaviour of these two phenols may be due to steric shielding of the oxygen by an *ortho*-t-butyl group in the 2-t-butyl-4-methylphenoxyl radical. Models indicate that this is a feasible explanation, *cf.* (7).

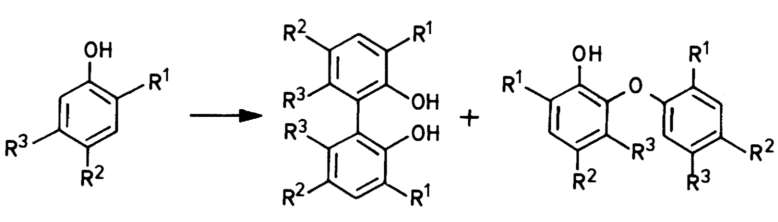
Support for this suggestion stems from a study of the oxidations of 2,4-di-t-butyl- and 2-t-butyl-phenol. 2,4-Di-t-butylphenol gave only the *ortho-ortho*-coupled product (3c) while 2-t-butylphenol gave largely (3d) together with some dimer of greater g.l.c. retention time (probably the *ortho-para*-coupled product). A similar product ratio was indicated from g.l.c. examination of the product obtained from 2-isopropylphenol. The transition state (8) represents a feasible mode of approach of two 2,4-di-t-butylphenoxyl radicals.

Further evidence in support of these results was obtained from a study of the oxidations of carvacrol (2e) and thymol (2f), the latter gave exclusively the *ortho-ortho*-coupled dimer (3f) while the former, which does not possess an *ortho*-isopropyl group, afforded the *ortho*-O coupled product (4e) in addition to the *ortho-ortho*-dimer (3f). A preliminary study on the oxidation of 2,5-dimethylphenol indicated that seven dimeric products were formed. The reaction was not studied further although preliminary evidence based on g.l.c. retention times suggests that the major products were the *ortho-ortho*- and *ortho-para*-dimers, these would be expected on the basis of a sandwich mode of approach of the phenoxyl radicals.

All the oxidations carried out in this study involved the decomposition of di-t-butyl peroxide in excess of the phenol at 140 °C; such conditions had been found in previous work to be very suitable for this type of study.[1-3]

The results presented clearly indicate that C–O coupling is favoured when steric hindrance prevents a sandwich mode of approach of two phenoxyl radicals, but that it is hindered by steric shielding of the oxygen atom.

Previous studies have reported that oxidations of thymol and carvacrol with iron(III) chloride gave diphenols.[6,7] The identities of these compounds were not established though they have been tentatively assumed to be the *ortho-para*- or

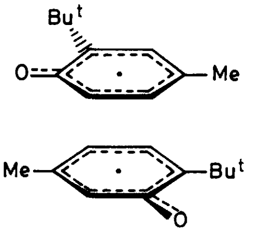


(2) (3) (4)

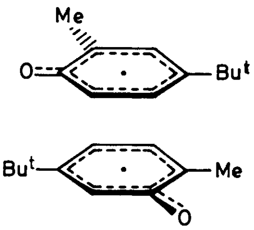
a ; R^1 = Bu^t , R^2 = Me, R^3 = H   b ; R^1 = Me, R^2 = Bu^t , R^3 = H

c ; R^1 = R^2 = Bu^t , R^3 = H   d ; R^1 = Bu^t , R^2 = R^3 = H

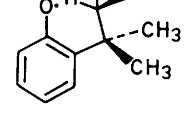
e ; R^1 = Me , R^2 = H, R^3 = Pr^i f ; R^1 = Pr^i , R^2 = H , R^3 = Me



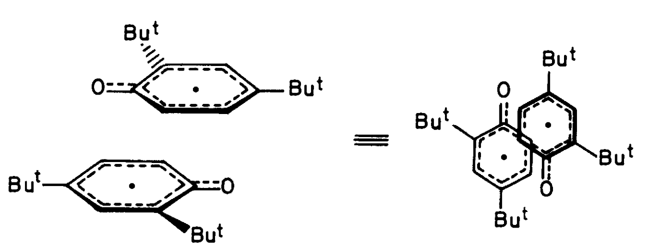
(5)



(6)



(7)



(8)

para-para-dimers:[8] on the basis of the present work it seems much more probable that they were the *ortho-ortho*-dimers.

Experimental

The phenols employed were commercial materials and were purified by fractional distillation.

The oxidations were carried out by decomposing 10 : 1 molar ratios of the phenol and di-t-butyl peroxide at 140 °C for 24 h. The excess phenol was removed by steam distillation and the products analysed by g.l.c.

Oxidation of 3,5-*Di-t-butylphenol*.—The crude product was crystallised from light petroleum, m.p. 98—101 °C (Found: C, 82.4; H, 10.4%; M^+, 410.3105. $C_{28}H_{42}O_2$ requires C, 81.9; H, 10.3%; M^+, 410.3185), δ ($CDCl_3$) 1.25 (36 H, s, Bu^t), 1.30 (1 H, s, disappears on treatment with D_2O, OH), and 6.66—7.05 (5 H, m, ArH).

Oxidation of 4-*t-Butyl*-2-*methylphenol*.—The crude product was shown by g.l.c. to consist of two components. The mixture was separated by preparative t.l.c. eluting with 5% ethyl acetate in toluene. The major component, which had the shorter retention time on g.l.c. and the higher R_F value, was obtained as an oil and identified as 4′,5-*di-t-butyl*-2-*hydroxy*-2′,3-*dimethyldiphenyl ether* (Found: M^+, 326.2265. $C_{22}H_{30}O_2$ requires M^+, 326.2246); δ ($CDCl_3$) 1.20 (9 H, s, Bu^t), 1.31 (9 H, s, Bu^t), 2.29 (6 H, s, Me), 5.45 (1 H, s, disappears on treatment with D_2O, OH), and 6.61—7.25 (5 H, m, ArH).

Oxidation of 2-*t-Butyl*-4-*methylphenol*.—G.l.c. analysis showed that the crude reaction mixture consisted of a single component. This was obtained as a glass and identified as 3,3′-di-t-butyl-2,2′-dihydroxy-5,5′-dimethylbiphenyl; δ ($CDCl_3$) 1.42 (18 H, s, Bu^t), 2.26 (6 H, s, Me), 5.32 (2 H, s, exchangeable, OH), 6.86 (2 H, d, *J* 2.3 Hz, ArH), and 7.12 (2 H, d, *J* 2.3 Hz, ArH).

Oxidation of 2,4-*Di-t-butylphenol*.—The reaction product consisted of one component, 3,3′,5,5′-tetra-t-butyl-2,2′-dihydroxybiphenyl, m.p. 197 °C (lit., 196—198 °C); δ ($CDCl_3$) 1.32 (18 H, s, Bu^t), 1.46 (18 H, s, Bu^t), 5.19 (2 H, s, exchangeable, OH), 7.00 (2 H, d, *J* 2.5 Hz, ArH), and 7.37 (2 H, d, *J* 2.5 Hz, ArH).

Oxidation of 2-*t-Butylphenol*.—The crude reaction mixture was shown by g.l.c. to consist of two components. Preparative t.l.c. eluting with 5% ethyl acetate in toluene gave the major product (shorter g.l.c. retention time) as a glass which was identified as 3,3′-*di-t-butyl*-2,2′-*dihydroxybiphenyl* (Found: M^+, 298.1945. $C_{20}H_{26}O_2$ requires M^+, 298.1933); δ ($CDCl_3$) 1.45 (18 H, s, Bu^t), 5.29 (2 H, s, exchangeable, OH), and 6.67—7.41 (6 H, m, ArH).

Oxidation of Carvacrol.—G.l.c. analysis of the crude product showed it consisted of two components. These were separated by preparative t.l.c. The major component was identified as 2-*hydroxy*-5′,6-*di-isopropyl*-2′,3-*dimethyldiphenyl ether* and obtained as an oil (Found: M^+, 298.1927. $C_{20}H_{26}O_2$ requires M^+, 298.1933); δ ($CDCl_3$) 1.08 (6 H, d, *J* 8 Hz, *Me*$_2$CH), 1.12 (6 H, d, *J* 8 Hz, *Me*$_2$CH), 2.13—2.57 (2 H, m, C*H*Me$_2$), 2.26 (6 H, s, Me), 4.67 (1 H, s, exchangeable, OH), 6.92 (2 H, d, *J* 9.0 Hz, ArH), and 7.22 (2 H, d, *J* 9.0 Hz, ArH). The minor component, 2,2′-*dihydroxy*-6,6′-*di-isopropyl*-3,3′-*dimethylbiphenyl*, was obtained as a glass (Found: M^+, 298.1920. $C_{20}H_{26}O_2$ requires M^+, 298.1933); δ ($CDCl_3$) 1.25 (12 H, d, *J* 7.3 Hz, *Me*$_2$CH), 2.26 (6 H, s, Me), 3.32 (2 H, heptet, *J* 7.3 Hz, C*H*Me$_2$), 4.72 (2 H, s, exchangeable, OH), 6.93 (2 H, d, *J* 7.5 Hz, ArH), and 7.20 (2 H, d, *J* 7.5 Hz, ArH).

Oxidation of Thymol.—The crude reaction mixture consisted of one component, which was obtained as an oil and identified as 2,2′-*dihydroxy*-3,3′-*di-isopropyl*-6,6′-*dimethylbiphenyl* (Found: M^+, 298.1920. $C_{20}H_{26}O_2$ requires M^+, 298.1933); δ ($CDCl_3$) 1.24 (12 H, d, *J* 6.4 Hz, *Me*$_2$CH), 1.94 (6 H, s, Me), 3.35 (2 H, heptet, *J* 6.4 Hz, C*H*Me$_2$), 4.78 (2 H, s, exchangeable, OH), 6.85 (2 H, d, *J* 9.0 Hz, ArH), and 7.27 (2 H, d, *J* 9.0 Hz), ArH).

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