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Oxidative Coupling of Phenols. Part 6.[1] A Study of the Role of Spin Density Factors on the Product Composition in the Oxidations of 3,5-Dimethylphenol and Phenol

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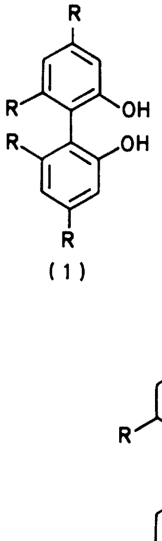
Oxidations of both 3,5-dimethylphenol and phenol with di-t-butyl peroxide at 140 °C gave as the major product the *ortho-ortho*-C–C coupled dimer, while oxidations with di-t-butyl peroxyoxalate at room temperature give much more of the *ortho-para*-C–C dimer. The results are not consistent either with the spin density distribution in the phenoxyl radical intermediates or with steric effects being the major factor which determines the product composition. It is proposed that the two phenoxyl radicals involved in coupling preferentially approach each other in a 'sandwich-like' manner with the oxygens in a 1,3-relationship.

E.s.r. studies on alkyl-substituted phenoxyl radicals by Stone and Waters have shown that the spin density at the *para*-position is almost twice that at the *ortho*-position.[2] Frontier molecular orbital theory suggests that coupling of delocalized radicals should occur preferentially at the site of highest spin density.[3] It might thus be expected that phenoxyl radicals possessing free *ortho*- and *para*-positions would give the *para-para*-coupled dimer as the major product. Evidence to support this contention comes from the observation that oxidation of orcinol (1,3-dihydroxy-5-methylbenzene) with potassium ferricyanide gives exclusively 2,2′,4,4′-tetrahydroxy-6,6′-dimethylbiphenyl: the spin density in the intermediate 3-hydroxy-5-methylphenoxyl radicals is 14 times as great at the 4- and 6-positions than at the 2-position.[4] Furthermore, oxidation of 2,6-dimethylphenol under a variety of conditions gives the *para-para*-coupled dimer as the major product with relatively small amounts of the *ortho-para*-coupled product.[5] By contrast, oxidations of *p*-cresol with a variety of metal oxidants in aqueous solution give rather more Pummerer's ketone (the *ortho-para*-coupled product) than 2,2′-dihydroxy-5,5′-dimethylbiphenyl (the *ortho-ortho*-coupled product).[6] All these results are consistent with the idea that the spin density distribution in the intermediate phenoxyl radicals playing a significant part in determining the ratios of products.

No detailed studies have been reported of oxidations of phenols possessing both free *ortho*- and *para*-positions which could lead to *ortho-ortho*-, *ortho-para*, and *para-para*-C-C coupled dimers and hence which would enable the importance of spin density considerations in phenoxyl radicals derived from simple alkyl-substituted monohydric phenols to be assessed. We initially chose to study 3,5-dimethylphenol which possesses free *ortho*- and *para*-positions and in which steric effects would not be expected to preclude coupling at either of these positions. There is evidence from a study of the oxidation of 3,4-dimethylphenol, in which coupling occurs at both *ortho*-positions, that steric effects do not play a large part in determining the product ratios.[7] Coupling would also be expected to occur at the oxygen to give *ortho*-O and *para*-O dimers.

We employed as oxidants both organic peroxides and metal-ion oxidants. The use of di-t-butyl peroxide at 140° and di-t-butyl peroxyoxalate at room temperature enabled the effect of temperature on the product ratio to be determined as both peroxides lead to the t-butoxyl radical and hence the reaction leading to the phenoxyl radical would be strictly comparable in both systems [reactions (1)—(3)]. It seems almost certain that in these reactions we are dealing with the coupling of genuinely free radicals, and hence these are the optimum conditions to obtain information about the factors controlling the mode of radical coupling. However in oxidation with metal ions, there is inevitably some doubt as to whether we are dealing with free or complexed species.



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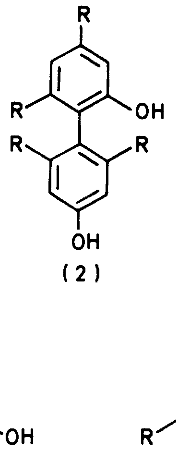

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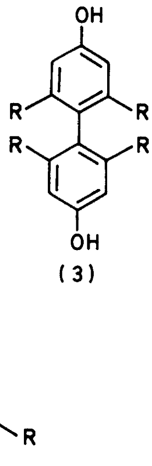

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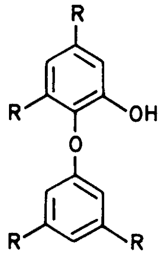

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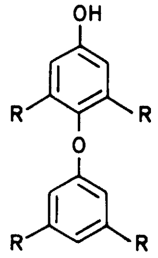


(5)

a; R = Me
b; R = H

$$\mathrm{(Bu^tO)_2 \longrightarrow 2Bu^tO\cdot} \qquad (1)$$

$$\mathrm{(Bu^tO{\cdot}CO_2)_2 \longrightarrow 2Bu^tO\cdot + 2CO_2} \qquad (2)$$

$$\mathrm{Bu^tO\cdot + ArOH \longrightarrow Bu^tOH + ArO\cdot} \qquad (3)$$

Table 1 records the proportions of the five possible dimeric products (1a)—(5a) obtained on oxidations of 3,5-dimethylphenol. The most striking result is that the *ortho-ortho*-coupled dimer is the major product from oxidation using di-t-butyl peroxide at 140 °C both in excess phenol as solvent and in chlorobenzene. The yields of the expected *para-para*-coupled product (3a) are very low. At room temperature using di-t-butyl peroxyoxalate as the radical source the proportion of the *ortho-ortho*-coupled product (1a) falls and there is a concomitant increase in the amount of the *ortho-para*-coupled product. An intermediate picture results from using t-butyl hydroperoxide as the radical source in organic media. Oxi-

Table 1. Oxidation of 3,5-dimethylphenol

Oxidant	Solvent	[ArOH]/M	T/°C	pH	t/h	Products (%)				
						(1a)	(2a)	(3a)	(4a)	(5a)
$(Bu^tO)_2$	Neat		140		24	74	12	2	6	6
$(Bu^tO)_2$	PhCl	1.0	140		24	77	16	0	6	1
$(Bu^tO)_2$–$h\nu$	PhH	1.0	25		24	32	24	8	6	31
$(Bu^tO)_2$	PhCl	0.1	140		24	72	14	0	12	2
Bu^tOOH	PhCl	1.0	140		24	24	32	0	9	35
Bu^tOOH	H_2O	1.0	100		24	18	40	16	5	21
$(Bu^tOCO_2)_2$	PhH	1.0	25		24	16	44	9	6	25
$(Bu^tOCO_2)_2$	PhCl	1.0	25		24	17	40	8	8	27
$K_3Fe(CN)_6$	aq. MeCN	0.1	25	9	24	9	52	21	2	16
$K_3Fe(CN)_6$	aq. MeCN	0.1	100	9	24	10	52	21	2	15
$Ce(NO_3)_6{\cdot}(NH_4)_2$	aq. MeCN	0.5	25	1	4	34	31	14	6	15
$Ce(NO_3)_6{\cdot}(NH_4)_2$	aq. MeCN	0.5	25	4	4	10	50	21	3	16
$Ce(NO_3)_6{\cdot}(NH_4)_2$	aq. MeCN	0.1	25	4	4	12	46	21	6	15
$Ce(NO_3)_6{\cdot}(NH_4)_2$	aq. MeCN	0.5	25	9	4	34	29	15	6	16
$Ce(NO_3)_6{\cdot}(NH_4)_2$	MeCN	0.5	−25		4	7	52	24	3	14
MTA[a]	PhH	0.5	80		16	38	12	1	3	46
MTA	EtOAc	0.5	80		16	30	11	4	3	52
MTA	MeCN	0.5	80		16	20	31	9	4	36
Ag_2CO_3	PhH	0.5	80		3	52	24	6	4	13
Ag_2CO_3	EtOAc	0.5	80		3	36	25	6	6	27
Ag_2CO_3	MeCN	0.5	80		3	13	46	6	6	29
Ag_2CO_3	Neat		80		3	33	38	12	3	14
Ag_2CO_3	Xylene	0.5	140		3	44	21	4	8	23

[a] MTA = Manganese(III) trisacetylacetonate.

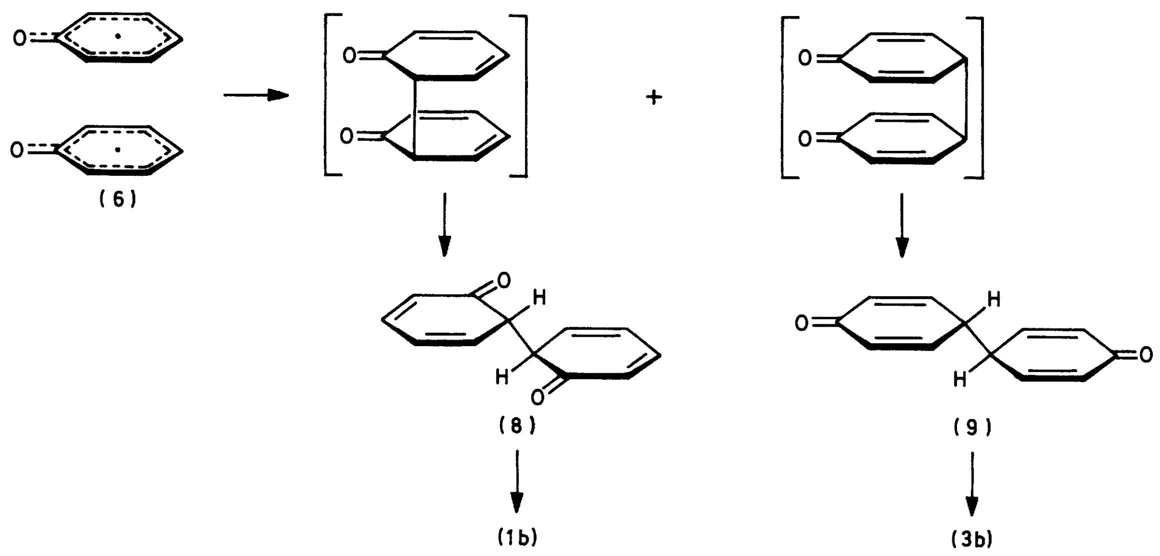
Table 2. Oxidation products of phenol

Oxidant	Solvent	[ArOH]/M	T/°C	pH	t/h	Products (%)				
						(1a)	(2a)	(3a)	(4a)	(5a)
$(Bu^tO)_2$	Neat		140		24	40	29	4	15	12
$(Bu^tO)_2$	PhCl	1.0	140		24	48	26	2	9	15
$(Bu^tO)_2$–$h\nu$	PhH	1.0	25		24	17	41	18	2	22
Bu^tOOH	Neat		140		24	39	30	6	13	12
Bu^tOOH	PhCl	1.0	140		24	47	31	8	3	12
Bu^tOOH	H_2O	1.0	100		24	22	45	8	7	19
$(Bu^tOCO_2)_2$	PhH	1.0	80		24	13	35	5	2	46
$(Bu^tOCO_2)_2$	PhH	1.0	25		24	26	29	19	11	16
$(Bu^tOCO_2)_2$	PhCl	1.0	25		24	26	35	28	7	5
$K_3Fe(CN)_6$	H_2O	0.1	25	9	3	84	1	7	5	3
$K_3Fe(CN)_6$	H_2O	0.5	0	9	3	82	2	8	4	4
$Ce(NO_3)_6{\cdot}(NH_4)_2$	H_2O	0.5	0	1	2	52	13	37	0	2
$Ce(NO_3)_6{\cdot}(NH_4)_2$	H_2O	0.5	0	4	2	48	11	38	0	4
$Ce(NO_3)_6{\cdot}(NH_4)_2$	H_2O	0.5	0	7	2	44	30	22	0	4
$Ce(NO_3)_6{\cdot}(NH_4)_2$	H_2O	0.5	0	9	2	36	31	15	0	18
$Ce(NO_3)_6{\cdot}(NH_4)_2$	H_2O	0.1	25	9	2	68	28	4	0	0
$Ce(NO_3)_6{\cdot}(NH_4)_2$	H_2O	0.5	25	4	2	57	11	30	0	2
$Ce(NO_3)_6{\cdot}(NH_4)_2$	MeCN	0.5	−25		2	67	16	17	0	0
MTA[a]	PhH	0.5	80		16	46	13	11	2	28
MTA	MeCN	0.5	80		16	21	19	24	3	33
Ag_2CO_3	PhH	0.5	80		3	21	29	4	10	36
Ag_2CO_3	EtOAc	0.5	80		3	5	27	10	4	54
Ag_2CO_3	MeCN	0.5	80		3	27	25	10	7	32
$Pb(OAc)_4$	PhH	0.025	25		1	44	21	4	9	22

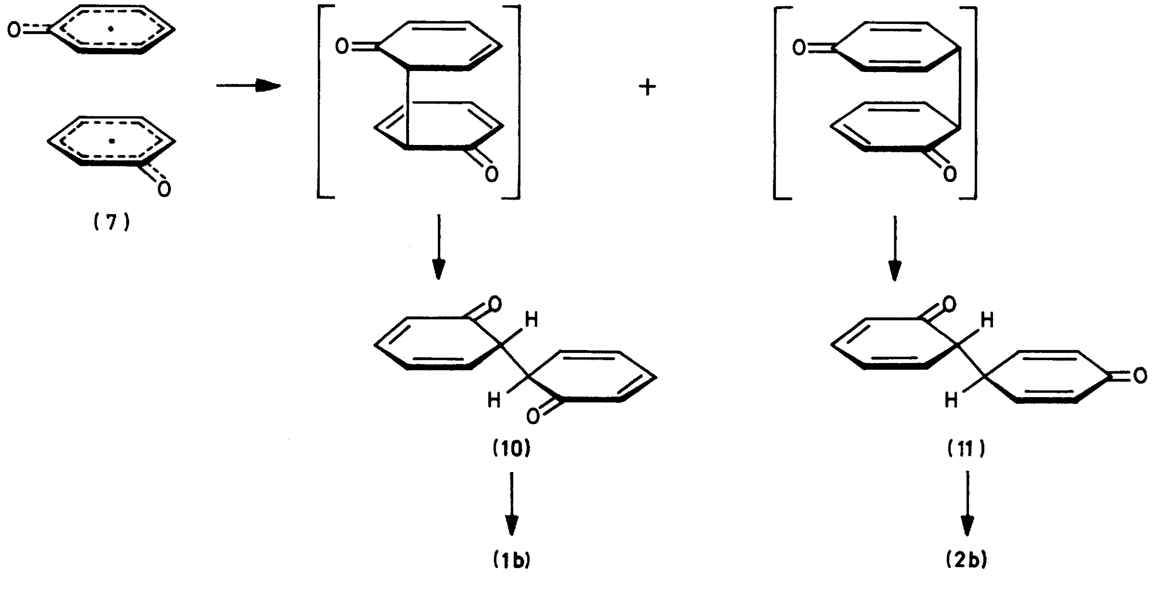
[a] MTA = Manganese(III) trisacetylacetonate.

dation of 3,5-dimethylphenol with manganese(III) acetylacetonate or with silver carbonate on Celite also afforded (1a) and (2a) as the principal C–C dimeric products, but all three C–C dimers resulted from the use of potassium ferricyanide or cerium(IV) ammonium nitrate as oxidant. The major C–O coupled product was, in most instances, the *para*-O dimer (5a).

The absence of the *para-para*-coupled products in the oxidations of 3,5-dimethylphenol with di-t-butyl peroxide at 140 °C could conceivably stem from a greater degree of steric hindrance at the *para*-position than at an *ortho*-position as a methyl group is larger than an oxygen. In order to assess whether steric effects could be responsible for these results we examined the oxidation of phenol as in this compound the *para*-position is undoubtedly less hindered than the *ortho*-positions. The results (Table 2) show once again that remarkably high yields of the *ortho-ortho*-coupled product (1b) were obtained with di-t-butyl peroxide at 140°. As in the reaction of 3,5-dimethylphenols, at room temperature with di-t-butyl peroxyoxalate the proportion of the *ortho-para*-coupled product (2b) increased at the expense of the *ortho-ortho*-dimer.



Scheme 1.



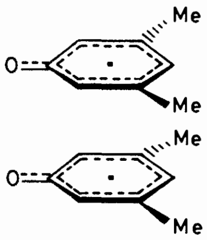
Scheme 2.

The major C–O coupled product was that arising from coupling at the *para*-position, *i.e.* (5b).

The above results of oxidations of the two phenols with t-butoxyl radicals generated from di-t-butyl peroxide or di-t-butyl peroxyoxalate are clearly not consistent with the supposition that the spin density distribution in the phenoxyl radicals is the major factor which controls the ratio of the three C–C dimeric products, nor can they be explained on the basis of steric effects. From both considerations phenol would have been expected to yield large amounts of the *para-para*-coupled product.

Consideration of precisely how the two phenoxyl radicals approach each other so as to maximize SOMO–SOMO interactions suggests that the two most probable transition states are (6) and (7) (see Schemes 1 and 2). The SOMO–SOMO interactions would be stronger in (6) than (7) as the sites of highest spin density (the *para*-positions) lie directly above each other. However electrostatic repulsion between the two electronegative oxygens would also be more powerful in (6) than in (7). The 'transition state' (6) would lead to the *para-para*-dimer and also the *ortho-ortho*-dimer, *via* (8) and (9), respectively, while the transition state (7) could give rise to both the *ortho-ortho*- and *ortho-para*-dimers, *via* (10) and (11), respectively. That these latter are the major products suggests that the favoured coupling route proceeds *via* the ' transition state ' (7). A theoretical study of the dimerisation of the benzyl radical which is isoelectronic with the phenoxyl radical, suggests that the most favourable mode of approach involves the two radicals approaching each other in an eclipsed sandwich-like configuration analogous to (6).[8] This mode of approach would be anticipated to be more favourable for the coupling of benzyl radicals than the alternative staggered approach as the argument based on the electrostatic repulsion of the oxygens in the coupling of phenoxyl radicals would not be pertinent.

The variation in the relative yields of *ortho-ortho*- and *ortho-para*-coupled products with temperature is suggestive of the interplay of thermodynamic and kinetic factors. At higher



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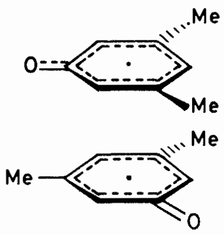


(13)

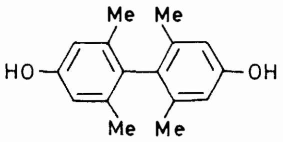
temperatures at which the *ortho-ortho*-coupled dimer is the predominant product, coupling of the radicals *via* the transition state (7) might well be expected to give the dimeric cyclohexadienone (10) in preference to the isomeric species (11) as the former possesses a more extensively delocalized system. This is a reasonable hypothesis since it has been demonstrated that the coupling of phenoxyl radicals to give a dimeric cyclohexadienone is a reversible process.[6] At lower temperatures we suggest that the formation of (2b) is favoured as the higher spin density at the *para*-position would tend to favour formation of (11) from the ' transition state ' (7). The following papers present theoretical evidence in support of these contentions.[9]

Detailed scrutiny of the results in Tables 1 and 2 indicates that the proportion of the *para-para*-coupled product (3a) formed in oxidations of 3,5-dimethylphenol is somewhat less than that of (3b) obtained from phenol. This fits in well with the above postulate since in the ' transition state ' (12) leading to (3a) not only would there be electrostatic repulsion between the two oxygens but there would be significant steric repulsion between the two sets of methyl groups which would lie directly on top of each other. This situation would clearly not prevail in the case of phenol. The alternative staggered approach in the coupling of two 3,5-dimethylphenoxyl radicals (13) would not be anticipated to suffer so much from steric hindrance since there would only be one set of interacting methyl groups; the second methyl group in each radical would be eclipsed with the oxygen in the second radical. It is interesting to note that the methyl and carbonyl groups are eclipsed in propanal [10] and this has been attributed to the mutual dipolar attractions of the groups.[11]

The results in the Tables also indicate that, on the whole more of the *para*-O coupled ethers than the *ortho*-O coupled ethers are formed in oxidations of phenol and 3,5-dimethylphenol. The mode of approach for the formation of the C–O coupled products might well be expected to be much less restricted in direction than implied above for the formation of C–C dimers. It might thus be expected that attack by the oxygen of one radical would occur preferentially at the site of higher spin density, *i.e.* the *para*-carbon, even though this site in the case of 3,5-dimethylphenol, is more hindered than is the *ortho*-position.

In none of the oxidations of phenol was any 3-hydroxydiphenyl ether obtained. This would have expected as a product if the mechanism of the reaction involved homolytic aromatic substitution by a phenoxyl radical on phenol followed by hydrogen abstraction from the resultant cyclohexadienyl radical. Hence we conclude that our assumption that the reaction involves coupling of two phenoxyl radicals is valid.

The differing rates of enolisation of the isomeric cyclohexadienone dimers could be considered as a plausible explanation for the observed product distributions.[7] That this cannot be a relevant factor is shown clearly from the oxidations of these two phenols. It is logical that either an *ortho*- or a *para*-hydrogen will tautomerise faster. Hence *ortho-ortho*- or *para-para*-coupling would be expected always to be the preferred mode of dimerisation but never the frequently observed *ortho-para*-coupling.



(14)

Oxidations were carried out using a 10 : 1 molar ratio of the phenol to oxidant so as to reduce as much as possible oxidation of the initial products to give polymeric products.[6] Under none of the conditions employed was any polymer detected. At the end of the reaction excess phenol was removed by steam distillation and the products were analysed by g.l.c. or in the case of phenol by h.p.l.c.

In order to compare our results with those reported in the literature we re-examined the oxidation of phenol with lead(IV) acetate. This has been reported to afford exclusively 4,4′-dihydroxybiphenyl,[12] but we obtained a mixture of all five products of which 4,4′-dihydroxybiphenyl was the least abundant (4%). Our system involved the use of an excess of phenol rather than an excess of oxidant.

General trends are much less obvious in oxidations using metal ion oxidants particularly when these are carried out in aqueous media. Under these conditions much more of the *para-para*-coupled products are formed. The importance of solvent effects is indicated by the significant amount of the *para-para*-dimers which are formed in oxidations with di-t-butyl hydroperoxide in water.

The various C–C coupled products from the oxidations of 3,5-dimethylphenol were obtained from preparative scale oxidations; we chose conditions shown by g.l.c. to produce significant amounts of the desired isomer. The structure of the various biphenyls could be readily assigned by recourse to ^{1}H n.m.r. spectroscopy. A feature of these spectra was that the methyl groups *ortho* to the second aromatic ring were deshielded. Thus the signal due to the methyl groups in 4,4′-dihydroxy-2,2′,6,6′-tetramethylbiphenyl (14) appears as a singlet at δ 1.84. This points to the non-planarity of such compounds which results in the methyl groups on one ring lying in the shielding zone of the second ring.

2,4′-Dihydroxybiphenyl was most readily obtained by homolytic aromatic substitution of anisole by *p*-methoxyphenyl radicals; this gave, as expected, 2,4′-dimethoxybiphenyl as the major product,[13] and the latter was demethylated using boron tribromide.[14]

The C–O coupled products were all obtained using a modified Ullmann ether synthesis [15] involving reaction of the appropriate bromoanisole with the phenol in presence of potassium methoxide, copper bronze, and copper(I) chloride followed by demethylation of the resultant methoxydiphenyl ether.

Experimental

3,5-Dimethylphenol and phenol were commercial materials and were purified by distillation. Di-t-butyl peroxide was used as supplied. Silver carbonate on Celite,[16] manganese(III) trisacetylacetonate,[17] and di-t-butyl peroxyoxalate [18] were prepared as described in the literature.

Preparative Scale Oxidations of 3,5-*Dimethylphenol to obtain* C-C *Coupled Products*.—(a) 3,5-Dimethylphenol (61 g, 0.5 mol) was heated to 100 °C under a flow of nitrogen. Di-t-butyl peroxide (7.3 g, 0.05 mol) was added and the temperature raised to 140 °C. The mixture was then stirred and heated at this temperature for 24 h. After cooling, the reaction mixture was extracted several times with ether. Evaporation of solvent from the combined extracts gave a dark red oil (57.3 g), which was steam distilled to give unchanged 3,5-dimethylphenol (46 g). The residue was extracted with ether and the extract dried (Na_2SO_4). Evaporation of the solvent gave a dark red oil (7.0 g) which crystallised on standing. This residue was then chromatographed on a silica gel column using light petroleum as eluant initially. Elution with 10% ether–light petroleum resulted in the isolation of a crystalline solid which was recrystallised from light petroleum and identified as *2,2′-dihydroxy-4,4′,6,6′-tetramethylbiphenyl* (1a) (1.6 g, 23%), m.p. 170 °C (Found: C, 79.2; H, 7.7%; M^+, 242.1309. $C_{16}H_{18}O_2$ requires C, 79.3; H, 7.5%; M^+, 242.1307); δ($CDCl_3$) 1.93 (6 H, s, Me), 2.29 (6 H, s, Me), 4.60 (2 H, s, exchangeable, OH), and 6.62 (4 H, s, aromatic).

(b) To a deoxygenated solution of 3,5-dimethylphenol (61 g, 0.5 mol) in a mixture of acetonitrile (500 ml) and a NaCl–glycine–NaOH buffer of pH 9 (1 500 ml), was added a solution of potassium ferricyanide (16.5 g, 0.05 mol) in the buffer (200 ml) over 30 min. The mixture was then stirred at room temperature for 24 h under nitrogen. The reaction mixture was then acidified (dilute HCl) followed by extraction with ether (4 × 200 ml) and then evaporation of the solvent to yield a red-brown oil (60.8 g). This oil was steam-distilled to remove unchanged phenol (53.2 g) and the residue, when cooled, was extracted with ether (3 × 150 ml). The combined extracts were dried (Na_2SO_4) and the solvent evaporated to give a red-brown residue (7.0 g) which crystallised on standing. This residue was chromatographed on a silica gel column. *2,4′-Dihydroxy-2′,4,6,6′-tetramethylbiphenyl* (2a) (0.2 g, 3%) was eluted with 20% ether–light petroleum, m.p. 170—172 °C (Found: C, 78.8; H, 7.4%; M^+, 242.1293); δ($CDCl_3$) 1.82 (3 H, s, Me), 1.89 (6 H, s, Me), 2.27 (3 H, s, Me), 4.40 (1 H, s, exchangeable, OH), 4.88 (1 H, s, exchangeable, OH), and 6.58 (4 H, s, aromatic). Further elution with 35% ether–light petroleum gave *4,4′-dihydroxy-2,2′,6,6′-tetramethylbiphenyl* (3a) (0.4 g, 6.0%) which was recrystallised from light petroleum, m.p. 180—182 °C (Found: C, 78.9; H, 7.7%; M^+, 242.1301); δ($CDCl_3$) 1.84 (12 H, s, Me), 4.64 (2 H, s, exchangeable, OH), and 6.58 (4 H, s, aromatic).

Synthesis of 2,4′-Dihydroxybiphenyl (2b).—*p*-Anisidine (22.2 g, 0.18 mol) was dissolved in concentrated hydrochloric acid (45 ml) and water (45 ml). The mixture was then allowed to cool and the hydrochloride separated out. The mixture was subsequently placed in a dry ice-methylated spirit bath and the temperature inside the reaction vessel maintained at −5 °C. A solution of sodium nitrite (12.4 g, 0.18 mol) in the minimum volume of water was added to the amine hydrochloride dropwise such that the temperature did not rise above −5 °C. A saturated solution of sodium fluoroborate (19.8 g, 0.18 mol) was then slowly added and the stable diazonium salt precipitated. The salt (40 g, 100%) was collected and washed with ether. The fluoroborate salt was purified by twice dissolving it in the minimum volume of acetone and re-precipitating it with ether. The purified salt (29.9 g, 75%) was collected as a solid and stored in a refrigerator.

To a stirred mixture of this salt (21 g, 0.095 mol), magnesium sulphate monohydrate (29.8 g, 0.176 mol), acetone (50 ml), and anisole (500 ml), at room temperature, was added copper bronze (8.8 g, 0.136 mol) in small portions during 30 min. Stirring was continued for 24 h after which the mixture was filtered and the filtrate washed with 10% sodium hydroxide solution (1 × 100 ml) and water (1 × 100 ml). The solution was dried (Na_2SO_4) and the excess anisole removed under vacuum. The dark solid residue (7.6 g) contained a mixture of the three possible isomeric bianisoles, as shown by g.l.c. analysis (5% FFAP at 200 °C). The residue was decolourised by means of activated charcoal and the crystalline solid residue chromatographed on a silica gel column using 5% ether–light petroleum as eluant. 2,4′-Dimethoxybiphenyl was obtained, contaminated by a little 4,4′-dimethoxybiphenyl; this was removed by fractional crystallisation in methanol. 2,4′-Dimethoxybiphenyl (3.5 g, 17%) was obtained as crystals, m.p. 68 °C (lit.,[19] 70 °C); δ($CDCl_3$) 3.78 (3 H, s, OMe), 3.83 (3 H, s, OMe), and 6.88—7.53 (8 H, m, aromatic).

A solution of 2,4′-dimethoxybiphenyl (0.5 g, 0.0025 mol) in methylene chloride (20 ml) was added dropwise to a solution of boron tribromide (1.26 g, 0.005 mol) in methylene chloride (5 ml). A flow of nitrogen was maintained throughout the apparatus (fitted with a drying tube to prevent the ingress of moisture). The mixture was then refluxed for 3 h. On cooling, the reaction mixture was slowly poured into water (200 ml) and then extracted with methylene chloride (2 × 100 ml). The combined extracts were themselves extracted with 20% sodium hydroxide solution (2 × 100 ml) which was then acidified (HCl). 2,4′-Dihydroxybiphenyl (0.4 g, 86%) crystallised slowly from the solution, m.p. 162 °C (lit.,[20] 162—163 °C); δ($CDCl_3$) 4.80 (1 H, s, exchangeable, OH), 5.08 (1 H, s, exchangeable, OH), and 6.86—7.37 (8 H, m, aromatic). In CD_3COCD_3, the hydroxy protons appear at δ 7.92 and 8.18.

Preparation of Hydroxydiphenyl Ethers.—(a) *2-Hydroxy-3′,4,5′,6-tetramethyldiphenyl ether* (4a). To a stirred mixture of 3,5-dimethylphenol (3.9 g, 0.032 mol), 2-bromo-3,5-dimethylanisole (8.6 g, 0.04 mol) (prepared by bromination of 3,5-dimethylphenol) at room temperature [21] followed by methylation with dimethyl sulphate), copper(I) chloride (0.5 g), and copper bronze (0.5 g) at 130 °C under nitrogen, was added potassium methoxide (2.8 g, 0.04 mol) (prepared by adding freshly cut potassium metal to an excess of methanol under nitrogen). The mixture was then stirred at 230 °C for 6 h under nitrogen. After cooling, the mixture was dissolved in methylene chloride (100 ml), filtered, and decolourised (twice) with activated charcoal. The crude mixture was then analysed by g.l.c. (OV 225 at 200 °C) which showed the presence of considerable quantities of starting materials in addition to a small amount of the product, 2-methoxy-3′,4,5′,6-tetramethyldiphenyl ether. The unchanged phenol and bromoanisole were removed by steam distillation and the residue worked up in the usual manner to yield, as an oil, 2-methoxy-3′,4,5′,6-tetramethyldiphenyl ether (0.65 g, 8%). A solution of this compound (0.64 g, 0.0025 mol) in methylene chloride (25 ml) was then added dropwise to a solution of boron tribromide (0.63 g, 0.0025 mol) in methylene chloride (5 ml) under nitrogen under rigorously anhydrous conditions. The mixture was refluxed for 4 h and, when cooled, slowly poured into water (200 ml). The solution was then extracted with methylene chloride (2 × 100 ml) and the combined extracts washed with 5% sodium hydroxide solution (1 × 100 ml) and then with water (2 × 75 ml). After drying (Na_2SO_4) and evaporation of the solvent, *2-hydroxy-3′,4,5′,6-tetramethyldiphenyl ether* (0.35 g, 58%) was obtained, and purified by vacuum sublimation; m.p. 78—80 °C (Found: C, 79.2; H, 7.4%; M^+, 242.1279); δ($CDCl_3$) 1.98 (3 H, s, Me), 2.17 (6 H, s, Me), 2.22 (3 H, s, Me), 5.10 (1 H, s, exchangeable, OH), and 6.34—6.60 (5 H, m, aromatic).

(b) *4-Hydroxy-2,3′,5′,6-tetramethyldiphenyl ether* (5a). 4-Methoxy-2,3′,5′,6-tetramethyldiphenyl ether was prepared in a similar manner and obtained as crystals from light petroleum (17%), m.p. 87—89 °C; δ($CDCl_3$) 2.00 (6 H, s, Me), 2.14 (6 H, s, Me), 3.68 (3 H, s, OMe), 6.27 (2 H, s, ArH), and 6.52 (3 H, s, ArH). Demethylation using boron tribromide gave *4-hydroxy-2,3′,5′,6-tetramethyldiphenyl ether* as crystals (82%), m.p. 109—111 °C (Found: C, 79.1; H, 7.2%; M^+, 242.1291); $\delta(CDCl_3)$ 2.06 (6 H, s, Me), 2.22 (6 H, s, Me), 5.50 (1 H, s, exchangeable, OH), 6.37 (2 H, s, ArH), 6.53 (2 H, s, ArH), and 6.58 (1 H, s, ArH).

(c) 2-*Hydroxydiphenyl ether*. This was prepared similarly and obtained as needles, m.p. 107—108 °C (lit.,[22] 107 °C); $\delta(CDCl_3)$ 5.57 (1 H, s, exchangeable, OH) and 6.80—7.43 (9 H, m, ArH).

(d) 3-*Hydroxydiphenyl ether*. Reaction of phenol and 3-bromoanisole as described above gave 3-methoxydiphenyl ether (29%) as an oil, $\delta(CDCl_3)$ 3.76 (3 H, s, OMe) and 6.52—7.39 (9 H, m, ArH). Demethylation of this with boron tribromide gave 3-hydroxydiphenyl ether (83%) as an oil (Found: M^+, 186.0642. $C_{12}H_{10}O_2$ requires M^+, 186.0681); $\delta(CDCl_3)$ 5.57 (1 H, s, exchangeable, OH) and 6.80—7.43 (9 H, m, ArH).

(e) 4-*Hydroxydiphenyl ether*. This was prepared similarly and obtained as needles, m.p. 85 °C (lit.,[23] 85 °C); $\delta(CDCl_3)$ 5.13 (1 H, s, exchangeable, OH) and 6.61—7.52 (9 H, m, ArH).

Analysis of the Reaction Mixture from the Oxidations of 3,5-*Dimethylphenol*.—The crude reaction mixtures (see Table 1 for the experimental conditions) were steam-distilled to remove excess of 3,5-dimethylphenol and then analysed by g.l.c. using a Perkin-Elmer F33 instrument with a 2 m column containing 2.5% cyanopropyl(phenyl) silicone on Chromosorb G at 225 °C. The sensitivity of the detector for each component of the mixture was determined by calibrations of the areas of known concentrations of the pure compounds. Areas were determined using Simpson's rule and the calibrations indicated that the experimental error was ±5%.

Analysis of the Reaction Mixtures from Oxidations of Phenol.—The crude reaction mixtures (see Table 2 for the experimental conditions) were steam distilled to remove excess phenol and then analysed by h.p.l.c. using a reverse-phase column (Whatman Partisil-10 ODS-2) using as solvent a 2 : 1 methanol : water mixture containing 1% acetic acid. Calibration of the various components of the mixture was carried out as for 3,5-dimethylphenol.

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