

### 552. *The Oxidation of Monohydric Phenols by Alkaline Ferricyanide.*

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The initial stage of oxidation of phenols by alkaline ferricyanide appears to be a reversible reaction between the phenol anion and the ferricyanide ion, giving ferrocyanide and a mesomeric aryloxy-radical. Irreversible reactions then follow, giving mixtures of dimeric and polymeric products. Though the rate of oxidation is dependent upon the alkalinity of the solution and on the [Ferricyanide]/[Ferrocyanide] ratio, Fieser's theory<sup>1</sup> concerning a "critical oxidation potential" for attack on a phenol gives far too simple an interpretation of the reactions involved.

New dimeric products, both of ketonic and of diphenolic type, have been obtained from a number of mono- and di-substituted phenols, and  $\alpha$ -(4-hydroxy-3 : 5-dimethylphenyl)benzyl alcohol has been obtained from 4-benzyl-2 : 6-dimethylphenol.

ON oxidation of monohydric phenols by alkaline ferricyanide Pummerer and his colleagues<sup>2</sup> obtained complex mixtures from which they isolated crystalline products having formulæ which indicated that they were mainly dimers and trimers of the corresponding aryloxy-radicals. Qualitatively similar, but not always identical, products can be obtained by anodic oxidation of phenols and by many other oxidations with reagents which abstract hydrogen atoms or single electrons,<sup>3</sup> though other reactions, notably substitutions *ortho* to existing hydroxyl groups, may result from what are apparently but slight variations of the reaction conditions. These variations may be due to changes in the relative concentrations of the different radicals present in the oxidising systems,<sup>4</sup> but could in many cases be ascribed to the intervention of heterolytic oxidation processes. Indeed, even the dimeric products isolated by Pummerer could be represented as arising from condensations between phenol molecules and mesomeric aryloxy-cations.

In order to discriminate more clearly between phenol oxidations involving 1-electron- and 2-electron-removal processes we have attempted a systematic study of the mechanism

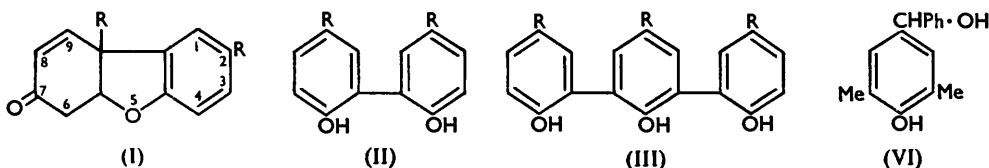
<sup>1</sup> Fieser, *J. Amer. Chem. Soc.*, 1930, **52**, 4915, 5204.

<sup>2</sup> Pummerer *et al.*, *Ber.*, 1914, **47**, 1472, 2957; 1919, **52**, 1392; 1922, **55**, 3116; 1925, **58**, 1808; *Chem. Ber.*, 1953, **86**, 412.

<sup>3</sup> For bibliography, see Cosgrove and Waters, *J.*, 1951, 1726.

<sup>4</sup> (a) Cosgrove and Waters, *J.*, 1951, 388; Wessley and Schinzel, *Monatsh.*, 1953, **84**, 425; (b) Moore and Waters, *J.*, 1954, 243.

of phenol oxidation with potassium ferricyanide, since this reagent simply acts as a 1-electron-abstracter so that its primary reaction should give aryloxy-radicals only. However, the reaction is not quantitative and gives so complex a mixture that our attempts to elucidate its full reaction mechanism have not been completely successful.



Oxidations of a number of monohydric phenols have been studied. First, we re-investigated, more precisely than Pummerer, the oxidation of *p*-cresol from which had been isolated by vacuum-distillation a ketonic dimer ( $C_7H_7O$ )<sub>2</sub> [recently shown by Barton, Deflorin, and Edwards<sup>5</sup> to have structure (I)], the diphenol (II; R = Me), and the corresponding trimer (III; R = Me). It was found that under varied conditions the oxidation always requires the consumption of more than one equivalent of ferricyanide and that only part of the product could be separated into phenolic and ketonic fractions by extraction successively with cold alkali and Girard's reagent P; from 40% to 50% of it is comprised of a chemically intractable resin that evidently suffers some thermal decomposition at temperatures but little over 150°, so that it was conceivable that some of the crystalline products of previous workers might have been produced by the thermal cracking of more complex initial substances and might not really be direct oxidation products. However, we have confirmed for a number of phenols that products of types (I) and (II) can both be isolated by procedures in which secondary thermal decompositions cannot have occurred.

The annexed Table shows that the complexity of the oxidation of *p*-cresol increases with the alkalinity of the medium, but that the yield of Pummerer's ketone (I) is constant enough to indicate that the initial reaction may be giving (I) and (II) in constant proportions and that thereafter oxidation of the polyphenols may occur preferentially. On the basis of this general evidence we have considered it rational to attempt to interpret the kinetics of the initial stages of this oxidation on the basis of reactions leading to the formation of aryloxy-dimers (see pp. 2825—2828).

#### Products of ferricyanide oxidation of *p*-cresol.

Medium	K <sub>3</sub> Fe(CN) <sub>6</sub> consumed (equiv.)	<i>p</i> -Cresol recovered (%)	Higher phenols (%)	Products isolated (%)		
				Alkali-insoluble		
				Ketone (I)		Non-ketonic polymer
Total	% of cresol reacted					
Na <sub>2</sub> CO <sub>3</sub> .....	1.00	22	31	15	19	24
Na <sub>2</sub> CO <sub>3</sub> .....	1.24	7.5	27	19	21	41
Na <sub>2</sub> CO <sub>3</sub> .....	1.27 <sup>a</sup>	6	34	22	23	32
NaOH .....	1.00	27	4	13	18	—
NaOH .....	1.00 <sup>b</sup>	28	9	17	23	42
NaOH .....	2.00	0	0		Small	High

<sup>a</sup> 1.5 equiv. of K<sub>3</sub>Fe(CN)<sub>6</sub> taken.

Benzene added to remove ketone (I) as formed.

The phenolic oxidation product from *p*-cresol was a brown resin that could not be separated into crystalline components by crystallisation or chromatography through acid-washed alumina or silica gel. Distillation at 0.1 mm. caused evident decomposition and it has been only in this way that previous workers<sup>2,3,6</sup> have succeeded in isolating small yields of 2 : 2'-dihydroxy-5 : 5'-dimethyldiphenyl (II; R = Me) from this oxidation. Treatment of the alkali-insoluble material with Girard's reagent P yielded Pummerer's ketone (I; R = Me) as the only ketonic product. The bulk of the alkali-insoluble material

<sup>5</sup> Barton, Deflorin, and Edwards, *Chem. and Ind.*, 1955, 1039; *J.*, 1956, 530.

<sup>6</sup> Westerfield and Lowe, *J. Biol. Chem.*, 1942, **145**, 463.

was a yellow resin which gave infrared absorption bands indicative only of ether linkages and of 1:4- and 1:2:4-substituted aromatic nuclei. Distillation at 0.1 mm. caused obvious decomposition whilst treatment with hydrogen bromide in hot acetic acid or with sodium in liquid ammonia yielded a polymeric phenol but no free *p*-cresol, so that the resin evidently contains aromatic nuclei joined through carbon.

The oxidation of *p*-ethylphenol yielded 4% of a phenolic trimer (III; R = Et), presumably similar to the product obtained from *p*-cresol by Westerfield and Lowe,<sup>6</sup> and 9% of a dimeric ketone (I; R = Et) having an infrared spectrum closely similar to that of Pummerer's ketone (I; R = Me). *p*-Propylphenol gave 6% of the phenolic dimer (II; R = Pr) and 13% of the ketone (I; R = Pr), and 2:4-dimethylphenol gave 50% of the phenolic dimer and only 1.5% of the ketonic dimer. A ketonic dimer has also been obtained from 3:4-dimethylphenol but only polymer was obtained from 4-hydroxydiphenyl. In sodium hydroxide or sodium carbonate solutions 4-methylguaiacol (OH = 1) gave only polymer, but in a sodium acetate buffer it yielded over 50% of the phenolic dimer, 3:3'-dimethoxy-5:5'-dimethyl-2:2'-dihydroxydiphenyl, and a negligible amount of ketone. In the same medium *p*-methoxyphenol gave 14% of 2:2'-dihydroxy-5:5'-dimethoxydiphenyl (II; R = OMe).

2:6-Dimethylphenol, in alcoholic sodium hydroxide or sodium carbonate, gave 45—50% of 3:3':5:5'-tetramethyl-4:4'-diphenoquinone, the oxidation product of the 4-4'-coupled phenolic dimer, but the other half of the oxidised material was a yellow, alkali-insoluble, non-ketonic polymer. In contrast, 2:6-dimethoxyphenol gave 3:3':5:5'-tetramethoxy-4:4'-diphenoquinone almost quantitatively. A mixture of these two phenols gave a mixture of the two diphenoquinones mentioned above but not a cross-linked dimer. This failure to link two dissimilar radicals may be due to the fact that 2:6-dimethoxyphenol oxidises very much more rapidly than 2:6-dimethylphenol.

4-Benzyl-2:6-dimethylphenol, when oxidised in sodium carbonate solution, gave a yellow product from which a 9% yield of  $\alpha$ -(4-hydroxy-3:5-dimethylphenyl)benzyl alcohol (IV) was separated. The same alcohol was made, for comparison, by reducing 4-benzoyl-2:6-dimethylphenol with lithium aluminium hydride. This oxidation of a 2:4:6-trisubstituted phenol at the  $\alpha$ -position in the side-chain is obviously similar in character to those which can be effected by the free radicals present in autoxidising cumene,<sup>7</sup> and it may be noted that the only free aryloxy-radicals known<sup>8</sup> are those derived from 2:4:6-trisubstituted phenols in which this  $\alpha$ -oxidation cannot occur. The possibility of side-chain oxidation of phenols by alkaline ferricyanide adds a further complication, hitherto not envisaged, to the interpretation of the mechanism of the oxidation but its implications in connection with oxidations by free radicals have already been indicated by one of us.<sup>4b, 7</sup>

Some information concerning the mechanism of oxidation of phenols by potassium ferricyanide can be obtained by kinetic studies, for it is possible to estimate ferricyanide potentiometrically, and, less accurately, by titration in the presence of zinc acetate.<sup>9</sup> Both procedures have been employed by us.

The first approach in this way was that of Conant<sup>10</sup> who showed that for many *ortho*- and *para*-substituted diphenols and diamines there was a qualitative connection between their rates of oxidation and the redox potential of the chosen oxidant. He therefore suggested that these oxidations were primarily controlled by an initial *reversible* electron-transfer. Fieser<sup>1</sup> who developed this theory found that for many monohydric phenols there appeared to be a linear relation between the percentage of oxidation in a given time and the initial redox potential of the oxidant. So, by extrapolation, he computed "critical oxidation potentials" at which no oxidation was discernible in 5 minutes, and for substituted phenols he correlated these potentials with the structural effects of substituent groups.

<sup>7</sup> Hey and Waters, *J.*, 1955, 2753.

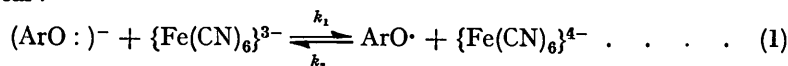
<sup>8</sup> Goldschmidt and Schmidt, *Ber.*, 1922, 55, 3197; Pummerer, Schmidutz, and Seifert, *Chem. Ber.*, 1952, 85, 535; Cook and Woodworth, *J. Amer. Chem. Soc.*, 1953, 75, 6242; Müller and Ley, *Chem. Ber.*, 1954, 87, 922; Müller, Ley, and Kiedaish, *ibid.*, p. 1605.

<sup>9</sup> Speakman and Waters, *J.*, 1955, 40; Conant, Aston, and Tongberg, *J. Amer. Chem. Soc.*, 1930, 52, 407.

<sup>10</sup> Conant, *Chem. Rev.*, 1926, 3, 1; Conant and Pratt, *J. Amer. Chem. Soc.*, 1926, 48, 3178, 3220.

The way in which the oxidation of a phenol can be virtually stopped by lowering the redox potential of the oxidising reagent by as little as 0.05 v below a critical value is one of the outstanding features of phenol oxidation in aqueous solution and appears to be characteristic of the behaviour of the organic compound and not of the chosen oxidising agent.

Fieser's interpretation of the ferricyanide oxidation of a monohydric phenol was that the fast reactions (1) were followed by an unspecified, slow, irreversible, first-order reaction of the aryloxy-radical:



from which it should follow that

$$-d[\text{Ferri}]/dt = -d[\text{ArO}^-]/dt = \frac{K_a}{K_w} \cdot \frac{k_1 k_3}{k_2} \cdot \frac{[\text{Phenol}][\text{OH}^-][\text{Ferri}]}{[\text{Ferri}]} \quad (4)$$

(where  $K_a$  is the acid dissociation constant of the phenol, and  $K_w$  is the ionic product of water), though if reaction (2) involves interaction between aryloxy-radicals and phenol molecules the reaction could become one of second order with respect to the phenol or phenol anion. However, equation (4) indicates that so long as reaction (2) has a finite velocity there should not be any clearly marked "critical oxidation potential" below which reaction ceases.

If, as suggested by Pummerer *et al.*,<sup>2</sup> the primary reaction products are formed by radical dimerisations:



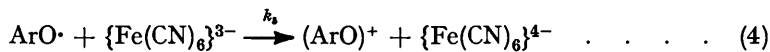
and if this is the rate-determining process, then the reaction should be of second order with respect to phenol, alkali, and ferricyanide, and inversely of second order with respect to ferrocyanide. This mechanism too should exhibit no abrupt "critical oxidation potential," but its rate should respond more sharply to changes of the [Ferricyanide]/[Ferrocyanide] ratio.

However, radical-combination processes (3) are usually fast and if the velocity constants  $k_1$ ,  $k_2$ ,  $k_4$  are comparable in magnitude then application of the steady-state relationship,  $-d[\text{ArO}]/dt = 0$ , to equations (1) and (3) leads to the complex expression:

$$-d[\text{Ferri}]/dt = -d[\text{ArO}^-]/dt = \frac{k_1[\text{Ferri}][\text{ArO}^-] - \frac{k_2^2[\text{Ferri}]^2}{2k_4} \left\{ \left( 1 + \frac{4k_1 k_4 [\text{Ferri}][\text{ArO}^-]}{k_2^2 [\text{Ferri}]^2} \right)^{\frac{1}{2}} - 1 \right\}}{\quad} \quad (B)$$

in which the reaction order with respect to each component is complex, and in particular that with respect to the phenol becomes very low at low phenol concentrations.

Since, except for the one instance of the 4-benzyl-2:6-dimethylphenol, the oxidation products appear to have aromatic nuclei coupled together only in *ortho*- or *para*-positions to original hydroxyl groups still another mechanism must be considered, *viz.*, that the coupling process is not homolytic, but rather a cationoid substitution of a phenol molecule by a mesomeric aryloxy-cation formed by a second stage oxidation reaction (4).



For reactions (1) and (4) the steady-state condition, where  $d[\text{ArO}]/dt$  and  $d[\text{ArO}^+]/dt$  are zero, leads to the expression:

$$\frac{-d[\text{Ferri}]}{dt} = \frac{-d[\text{ArO}^-]}{dt} = \frac{2k_1 k_5 [\text{Ferri}]^2 [\text{ArO}^-]}{k_5 [\text{Ferri}] + k_2 [\text{Ferri}]} \quad (C)$$

which is throughout of first order with respect to aryloxy-ion, and not greatly dependent upon ferrocyanide concentration unless  $k_2$  is much greater than  $k_5$ .

In his studies of phenol oxidation Fieser did not examine the effect of changing the phenol concentration or the absolute concentration of the ferricyanide. This we have done in rate measurements with *p*-cresol, 2:6-dimethylphenol, and 4-methylguaiacol, typical data from which are shown on the accompanying graphs. Our results show that when oxidations of phenols by ferricyanide do occur they tend to start off so rapidly that it is difficult to get reliable values for initial reaction velocities whereby reaction orders might be determined. Though investigations of reaction products (p. 2822) indicate that consecutive oxidations of dimers must soon intervene the following broad conclusions can

FIG. 1. Oxidation of *p*-cresol at 16°: effect of ferrocyanide. Each solution contained 1 equiv. of 0.1M-*p*-cresol, 5 equiv. of 0.1M-potassium ferricyanide, and 40 equivs. of 0.2M-boric acid-sodium hydroxide buffer (Clark and Lubs) (pH 10).

A: No addition of ferrocyanide.  
B, C, D, E: 1.0, 2.5, 5.0, and 10.0 equivs. of 0.1M-potassium ferrocyanide.

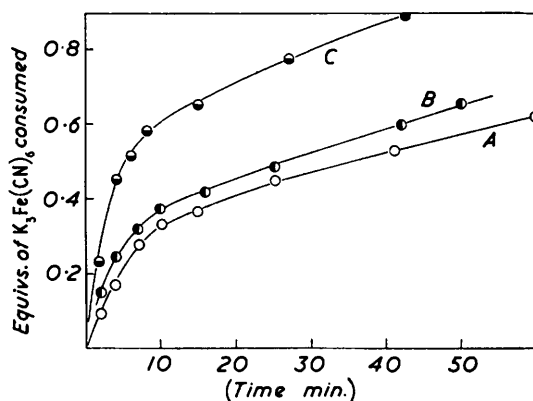
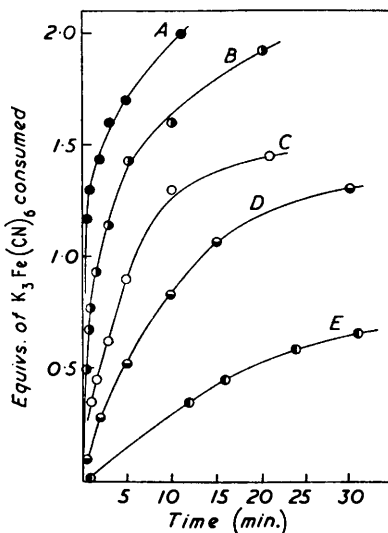


FIG. 2. Oxidation of 4-methylguaiacol at 25°: effect of ferrocyanide. Each solution contained, in 850 c.c., 0.1 mol. of sodium acetate, 0.0025 mol. of potassium ferricyanide, and 0.0005 mol. of 4-methylguaiacol.

Addition of (A) 0.025, (B) 0.015, and (C) 0.005 mol. of ferrocyanide.

be drawn from our experiments: (a) Velocities of oxidation decrease, at all stages, with increase of ferrocyanide concentration, as would be expected if the primary oxidation was the reversible one-electron transfer (1) (see Figs. 1 and 2). (b) The velocity of oxidation increases with alkalinity in such a way as to indicate that the oxidisable organic substances are aryloxy-anions and not phenol molecules (see Experimental section). (c) The reaction order with respect to the phenol is too complex for either the initial oxidation of the aryloxy-anion (the forward reaction 1) or the subsequent reactions of the aryloxy-radicals (reactions 2, 3, or 4) alone to be rate-determining (see Figs. 3 and 4). Thus the simple kinetic expressions (A) and (C) cannot be valid, though expression (B) cannot be eliminated. (d) Though it is possible to prepare oxidant mixtures which do not detectably oxidise phenols though they may still contain high concentrations of oxidant, it is not valid to

extrapolate (reaction velocity)-concentration graphs and thereby deduce "critical oxidation potentials" of quantitative significance (see Fig. 5).

Since the complex features of phenol oxidation, such as the polymer formation, do not occur in the ferricyanide reaction alone, but have often been encountered elsewhere,<sup>3</sup> e.g., in anodic oxidations, we suggest that it is the diversity of the reactivity of mesomeric aryloxy-radicals that in the main obscures the elucidation of the reaction mechanism.

FIG. 3. Oxidation of 4-methylguaiacol at 25°: variation of rate with methylguaiacol concentration. Solutions contained, in 850 c.c., 0.1 mol. of sodium acetate, 0.0025 mol. of potassium ferricyanide, and 0.0050 mol. of potassium ferrocyanide, and (A) 2, (B) 3, (C) 4, and (D)  $5 \times 10^{-4}$  mol. of 4-methylguaiacol.

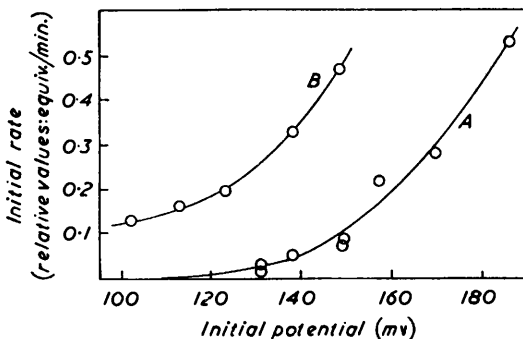
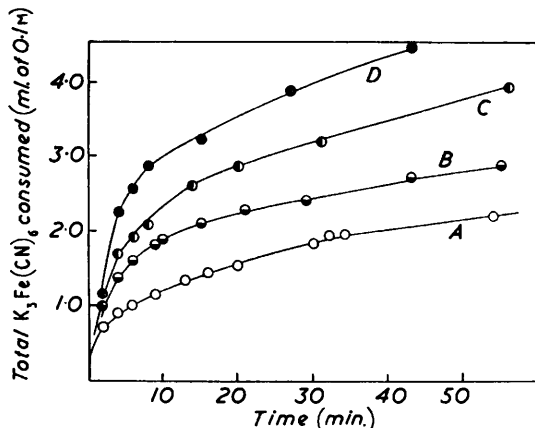


FIG. 4. Oxidation of *p*-cresol at 25°: variation of initial rate with cresol concentration. Each mixture contained 5 equivs. of 0.1M-potassium ferricyanide and 40 equivs. of 0.2M-borate buffer (pH 10.0). A, 15, and B, 20 equivs. of 0.1M-potassium ferrocyanide were added.

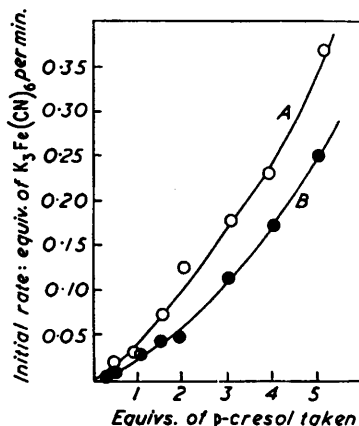


FIG. 5. Oxidation of (A) *p*-cresol and (B) 2:6-dimethylphenol at 25°: relation between initial oxidation rates and initial redox potentials of ferricyanide-ferrocyanide mixtures. Solutions were similar to those used for Figs. 1 and 4. Each contained 1 equiv. of the phenol, 5 equivs. (total) of ferricyanide-ferrocyanide mixture, and 40 equivs. of borate buffer. The initial potentials are the initial voltage readings of the electro-metric cells used.

## EXPERIMENTAL

**Oxidation Products of Phenols.**—(1) *p*-Cresol. 0.88N-Potassium ferricyanide (0.3 mol.) was added dropwise during  $\frac{1}{2}$  hr. to a stirred solution at 0° of *p*-cresol (0.2 mol.) in 0.4N-sodium carbonate (0.4 mol.). After 3 hours' stirring the brown product was extracted with ether. Titration of the solution showed that 0.255 mol. of ferricyanide had been consumed. The organic product was separated by using *N*-sodium hydroxide into alkali-soluble and -insoluble portions. Steam-distillation of the former removed unchanged *p*-cresol (6%) and left a brown resin, m. p. < 100° (38% of unrecovered cresol), which gave a greenish-brown colour with ethanolic ferric chloride and decomposed above 150° at 0.1 mm.

The alkali-insoluble portion was separated by use of Girard's reagent P into two fractions. One (22%) was the dihydro-oxodibenzofuran (I; R = Me), m. p. 123–124° [phenylhydrazone, m. p. 179°; 2:4-dinitrophenylhydrazone, m. p. 216°, red prisms from acetic acid (Found: C, 60.7; H, 4.7; N, 14.0.  $C_{20}H_{18}O_5N_4$  requires C, 60.9; H, 4.6; N, 14.2%)]. The non-ketonic portion (32%) was a yellow resin, m. p. 82–108° (decomp.); a concentrated chloroform

solution of this material when poured into excess of ether gave an amorphous cream precipitate (9%), m. p. 210—212° (decomp.), which gave a red-brown colour with ethanolic ferric chloride [Found: C, 74.2; H, 5.9%; *M* (in camphor), 675. (C<sub>7</sub>H<sub>7</sub>O)<sub>*n*</sub> requires C, 78.5; H, 5.9%; *M* (*n* = 7), 749]. Its infrared spectrum showed absorption bands for C—O—C linkages and for 1:4- and 1:2:4-substituted aromatic nuclei but only very weak absorption corresponding to O—H or C=O groups. The ether solution on evaporation yielded a yellow resin (21%), m. p. 110—112° (decomp.), which gave a greenish-brown ferric chloride colour and had a similar infrared spectrum [Found: C, 72.2; H, 5.7%; *M*, 332. Calc. for (C<sub>7</sub>H<sub>7</sub>O)<sub>*n*</sub>: *M* (*n* = 3), 321]. Neither of these products could be purified. Distillation at 0.1 mm. of the major portions led to obvious decomposition above 150°. Treatment with (i) 48% hydrobromic acid in acetic acid, and (ii) sodium in liquid ammonia<sup>11</sup> yielded alkali-soluble mixtures with infrared spectra showing strong absorption in the 3 μ region (OH groups), but crystallisation and chromatography, even after acetylation, failed to yield pure products, whilst steam-distillation gave no trace of *p*-cresol.

Oxidations under other conditions are summarised in the Table (p. 2824).

(2) *p*-Ethylphenol. The oxidation was carried out as above; 1.15 equivs. of ferricyanide were consumed. The product contained unchanged *p*-ethylphenol (12%), an alkali-soluble gum which on crystallisation from light petroleum (b. p. 60—80°) yielded needles (4%) of the 2:2':2''-trihydroxy-5:5':5''-trimethyl-*m*-terphenyl (III; R = Et), m. p. 144—145° (Found: C, 79.4; H, 7.1%; *M*, in camphor, 354. C<sub>24</sub>H<sub>26</sub>O<sub>3</sub> requires C, 79.2; H, 7.2%; *M*, 362). The non-phenolic portion was separated into a ketone (9%) and a cream-coloured amorphous solid (74%), m. p. 110—120°, having an infrared spectrum very similar to that of the corresponding material from *p*-cresol [Found: C, 76.7; H, 7.0%; *M*, 575. (C<sub>8</sub>H<sub>9</sub>O)<sub>*n*</sub> requires C, 79.3; H, 7.4%; *M* (*n* = 5), 605]. 2:9a-Diethyl-5a:6:7:9a-tetrahydro-7-oxodibenzofuran (I; R = Et) crystallised from aqueous methanol in plates, m. p. 60.5° (Found: C, 79.1; H, 7.5. C<sub>16</sub>H<sub>18</sub>O<sub>2</sub> requires C, 79.3; H, 7.4%). Its 2:4-dinitrophenylhydrazone formed red prisms (from ethanol), m. p. 162—163° (Found: C, 61.9; H, 5.2; N, 12.9. C<sub>22</sub>H<sub>22</sub>O<sub>5</sub>N<sub>4</sub> requires C, 62.4; H, 5.2; N, 13.2%), and its semicarbazone prisms (from ethanol), m. p. 214° (Found: C, 68.0; H, 7.2; N, 14.1. C<sub>17</sub>H<sub>21</sub>O<sub>2</sub>N<sub>3</sub> requires C, 68.2; H, 7.0; N, 14.1%). The infrared spectrum was very similar to that of Pummerer's ketone.

Oxidation of *p*-ethylphenol in 0.4*N*-sodium hydroxide gave only an intractable solid of high m. p. In 0.32*N*-sodium carbonate solution 1.38 equivs. of ferricyanide were consumed; 11% of *p*-ethylphenol was recovered, and 9% of ketone and 76% of non-ketonic polymer was formed.

(3) *p*-Propylphenol. The phenol (13.6 g., 0.1 mol.) in aqueous 0.2*N*-sodium hydrogen carbonate (2 l.) and potassium ferricyanide (66 g., 0.2 mol.) in water (400 c.c.) were stirred for 3 hr. at 20—25°. The product was separated as usual. The alkali-insoluble, non-ketonic fraction (6 g.) was not investigated further. The ketonic fraction (1.3 g., 13% of unrecovered phenol) by treatment with ethanol yielded 5a:6:7:9a-tetrahydro-7-oxo-2:9a-dipropyldibenzofuran (I; R = Pr), m. p. 59° (Found: C, 79.7; H, 8.3. C<sub>18</sub>H<sub>22</sub>O<sub>2</sub> requires C, 80.0; H, 8.2%); its semicarbazone, from acetone, had m. p. 207° (Found: C, 69.4; H, 7.7; N, 12.9. C<sub>19</sub>H<sub>25</sub>O<sub>2</sub>N<sub>3</sub> requires C, 69.7; H, 7.6; N, 12.8%); its 2:4-dinitrophenylhydrazone, red prisms from ethanol, had m. p. 118—119° (Found: C, 63.6; H, 5.8; N, 12.1. C<sub>24</sub>H<sub>26</sub>O<sub>5</sub>N<sub>4</sub> requires C, 64.0; H, 5.8; N, 12.4%). The infrared spectrum of the ketone resembles that of the methyl analogue.

The alkali-soluble fraction yielded 3.6 g. of unchanged phenol and an involatile oil (1.3 g.) from which elongated leaves, m. p. 139—140°, of 2:2'-dihydroxy-5:5'-dipropyldiphenyl (II; R = Pr) were obtained by crystallisation from light petroleum (b. p. 80—100°) (Found: C, 79.8; H, 8.4%; *M*, in camphor, 256. C<sub>18</sub>H<sub>22</sub>O<sub>2</sub> requires C, 80.0; H, 8.15%; *M*, 270).

(4) *p*-Methoxyphenol. A mixture of *p*-methoxyphenol (24.8 g.), 0.2*N*-sodium acetate (2 l.), and potassium ferricyanide (132 g. in 800 c.c. of water) was stirred for 3 hr. at 20—25°. The gummy product was separated into alkali-insoluble (2.4 g.) and alkali-soluble (20 g.) fractions. An attempt to isolate a ketone from the former fraction failed. Vacuum-distillation of the latter fraction gave 11.4 g. of unchanged methoxyphenol (b. p. 130—140°/20 mm.) and a brown gum (7 g.; b. p. 180—230°/0.025 mm.) which, after acetylation gave a white solid (2.4 g.) when rubbed with alcohol-ether. Crystallisation of this from ethanol yielded prisms of 2:2'-diacetoxy-5:5'-dimethoxydiphenyl, m. p. 114° (Found: C, 65.3; H, 5.5. C<sub>16</sub>H<sub>18</sub>O<sub>6</sub> requires C, 65.5; H, 5.45%), which when hydrolysed for 2 hr. at 100% with 30% ethanolic potassium hydroxide gave flat needles of 2:2'-dihydroxy-5:5'-dimethoxydiphenyl (II; R = OMe), m. p. 123—124° (from benzene-light petroleum) (Found: C, 68.6; H, 5.8%; *M*, 210. C<sub>14</sub>H<sub>14</sub>O<sub>4</sub> requires C, 68.3; H, 5.7%; *M*, 246).

<sup>11</sup> Kidd and Walker, *J.*, 1954, 669.

(5) 2 : 4-*Dimethylphenol*. This was oxidised for 6 hr. in sodium acetate solution (as for no. 4 above); 55% was recovered, together with a ketonic *dibenzofuran derivative* (1.5% of oxidised substance) that crystallised from aqueous ethanol in plates, m. p. 137° (Found : C, 78.9; H, 7.7.  $C_{16}H_{18}O_2$  requires C, 79.3; H, 7.4%), having a *semicarbazone*, m. p. 242° (decomp.) (Found : C, 68.1; H, 7.4; N, 13.4.  $C_{17}H_{21}O_2N_3$  requires C, 68.2; H, 7.0; N, 14.0%), and a 2 : 4-dinitrophenylhydrazone, m. p. 231° (insufficient for analysis). Together with this was obtained 2 : 2'-*dihydroxy-3 : 3' : 5 : 5'-tetramethyldiphenyl* (50% of oxidised material), m. p. 132—133° (Found : C, 78.9; H, 7.3.  $C_{16}H_{18}O_2$  requires C, 79.3; H, 7.4%); its *diacetate* formed plates, m. p. 106°, from aqueous ethanol (Found : C, 73.2; H, 6.9.  $C_{20}H_{22}O_4$  requires C, 73.6; H, 6.8%).

(6) 3 : 4-*Dimethylphenol* (with Mr. J. A. BAKER). The xylenol was oxidised in sodium carbonate solution at room temperature (compare oxidation 1) and gave a 19% yield of a *tetrahydrotetramethyloxodibenzofuran*, m. p. 156° (Found : C, 79.3; H, 7.6.  $C_{16}H_{18}O_2$  requires C, 79.3; H, 7.4%), giving a 2 : 4-*dinitrophenylhydrazone*, m. p. 219° (Found : C, 62.3; H, 5.4; N, 12.6, 13.3.  $C_{22}H_{22}O_5N_4$  requires C, 62.6; H, 5.2; N, 13.3%), and a *semicarbazone*, m. p. 263° (Found : C, 67.9; H, 7.1; N, 13.9.  $C_{17}H_{21}O_2N_3$  requires C, 68.2; H, 7.0; N, 14.0%). This ketone had an infrared spectrum very similar to that of Pummerer's ketone and when boiled in alcohol with hydrobromic acid was converted into a *dihydroxytetramethyldiphenyl*, m. p. 152—154° (cf. refs. 2, 5, 6) (Found : C, 79.5; H, 7.6.  $C_{16}H_{18}O_2$  requires C, 79.3; H, 7.4%) Since, in this instance, the dimerisation of the aryloxy-radicals could have given products having a number of alternative isomeric structures a search was made chromatographically for other ketones isomeric with the compound of m. p. 156°, but no other pure substances could be isolated.

(7) 4-*Methylguaiacol*. A solution of potassium ferricyanide (72 g.) in water (500 c.c.) was added to a stirred mixture of the phenol (15 g.) and hydrated sodium acetate (30.5 g.) in water (1100 c.c.). After 3 hr. the cream-coloured solid product was extracted and distilled in steam to remove unchanged phenol (3.4 g.), and the remainder was crystallised from a little ether and then from benzene—light petroleum to give, in a total yield of 60% (calc. on the phenol consumed) 2 : 2'-*dihydroxy-3 : 3'-dimethoxy-5 : 5'-dimethyldiphenyl*, m. p. 128°, which gave a green ferric chloride colour (Found : C, 69.8; H, 6.7.  $C_{16}H_{18}O_4$  requires C, 70.1; H, 6.6%). Its *diacetate* had m. p. 162° (Found : C, 67.3; H, 6.4%; M, 310.  $C_{20}H_{22}O_6$  requires C, 67.0; H, 6.1%; M, 358), and its *dibenzoate*, m. p. 181° (Found : C, 74.4; H, 5.4.  $C_{30}H_{26}O_6$  requires C, 74.7; H, 5.4%).

(8) 2 : 6-*Dimethylphenol*. A solution of the phenol (0.05 mol.) in ethanol (100 c.c.) was added dropwise during  $\frac{1}{2}$  hr. to a solution of potassium ferricyanide (0.15 mol.) and sodium hydroxide (0.1 mol.) in water (300 c.c.). After 2 hours' stirring the orange precipitate, m. p. 173—177°, was separated and dried. Extraction of this with ether left a 50% yield of insoluble 3 : 5 : 3' : 5'-tetramethyl-4 : 4'-diphenoquinone, m. p. and mixed m. p. 205° (decomp.), and gave a more soluble yellow resin, m. p. ca. 120°, which when rubbed with methanol yielded a solid of m. p. 190—195° (decomp.), that could not be purified further and gave an infrared spectrum resembling that of the non-ketonic polymer formed from *p*-cresol [Found : C, 78.8; H, 6.7%; M (in camphor), 983. Calc. for  $(C_8H_9O)_n$  : C, 79.3; H, 7.4%; M ( $n = 8$ ), 968]. Oxidation in sodium carbonate solution yielded 45% of the tetramethyldiphenoquinone.

(9) 2 : 6-*Dimethoxyphenol*. Approx. *n*-potassium ferricyanide was added to a stirred solution of the phenol in ethanolic sodium hydroxide under an inert atmosphere, and the mixture was stirred for 2 hr. The purple solid which separated in 96% yield was almost pure 3 : 5 : 3' : 5'-tetramethoxy-4 : 4'-diphenoquinone [steel-blue needles (from nitrobenzene), m. p. 293° (decomp.)] which was converted by reductive acetylation into 4 : 4'-diacetoxy-3 : 3' : 5 : 5'-tetramethoxydiphenyl, m. p. 225—226° (Liebermann<sup>12</sup> gives m. p. 217—225°).

An equimolar mixture of 2 : 6-dimethylphenol and 2 : 6-dimethoxyphenol was oxidised similarly and gave an 81% yield of a rust-coloured powder that, when extracted with ethyl acetate gave a 54% yield of a mixture of diphenoquinones, from which was obtained 75% of the tetramethoxy-compound and 15% of the tetramethyl compound. Reductive acetylation of the mixture of quinones gave similar proportions of the two corresponding diacetoxydiphenyls and again no sign of a third component.

(10) 4-*Benzyl-2 : 6-dimethylphenol*.<sup>7</sup> This (2.3 g.) in ethanol (50 c.c.) was stirred for 1 hr. at room temperature with *n*-sodium carbonate (40 c.c.) and potassium ferricyanide (1.5 equiv.) in water (20 c.c.). The product was extracted, dried, and chromatographed through alumina (grade IV). Elution with chloroform—benzene (1 : 4) gave 0.2 g. (9%) of solid  $\alpha$ -(4-*hydroxy-3 : 5-dimethylphenyl*)benzyl alcohol which crystallised from cyclohexane in prisms, m. p. 124—125°

<sup>12</sup> Liebermann, *Annalen*, 1873, **169**, 221.



(Found : C, 78.6; H, 7.1.  $C_{15}H_{16}O_2$  requires C, 78.9; H, 7.0%). The oxidised mixture smelt faintly of benzaldehyde.

The above alcohol was also obtained by adding to a solution of 4-benzoyl-2 : 6-dimethylphenol (2.3 g.) in dry ether (150 c.c.) lithium aluminium hydride (0.2 g.) in ether (100 c.c.), and refluxing the mixture for 3 hr. Crystallisation of the product gave 2.0 g. of the alcohol, m. p. 124—125°, identical (mixed m. p. and infrared spectrum) with that described above.

*Kinetic Measurements.*—These were carried out by the procedures used by Speakman and Waters<sup>9</sup> for studying the ferricyanide oxidation of aldehydes and ketones. Again preliminary tests showed the general concordance of volumetric and potentiometric measurements, though the former were the less reliable. The results plotted on the graphs are those obtained potentiometrically. In an investigation of the effect of alkali on the oxidation rate of *p*-cresol at 25°, with 5 equivs. each of potassium ferricyanide and potassium ferrocyanide (0.1M), 1 equiv. of 0.1M-*p*-cresol, and 40 equivs. of 0.2M-borate buffer the following data were obtained by graphical extrapolation :

[OH <sup>-</sup> ] (10 <sup>-5</sup> M) .....	1.0	1.6	3.2	6.3	10.0
Initial rate (equiv./min.).....	0.017	0.029	0.051	0.120	0.199

indicating an approximately first-order dependence on alkalinity.

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