Organic Oxidation Processes. Part I. The Oxidation of Some Methylphenols with Lead Tetra-acetate.

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The oxidation of phenol, *o*- and *p*-cresol, 2 : 4- and 2 : 6-dimethylphenol, and 2 : 4 : 6-trimethylphenol is described. The " type " products isolated, dihydroxydiphenyls and/or acetoxy*cyclo*hexadienones, vary with (*a*) the solvent effect, (*b*) the proportion of oxidising agent, and (*c*) the position and number of methyl substituents. Mechanisms of oxidation are discussed.

Recently Wessely and his co-workers (*Monatsh.*, 1950, **81**, 1055; 1953, **84**, 425) showed that dehydrogenation with acetoxylation occurs when lead tetra-acetate reacts with a methylphenol in acetic acid solution. Thus *p*-cresol forms 2 : 2-diacetoxy-4-methyl*cyclo*hexadienone (type *A*), the non-aromatic structure being stabilised by the introduction of the acetoxyl groups.

These oxidations were performed in a large excess of acetic acid and such solvent conditions would help, not only to control the instantaneous reaction between substrate and oxidant by high dilution, but, further, to assist in the formation of the monomeric acetoxydienones. The present communication amplifies these investigations, especial attention being paid to solvent influences (cf. Barron, Cavill, Cole, Gilham, and Solomon, *Chem. and Ind.*, 1954, 76). Wessely and Sinwel (*loc. cit.*, 1950) noted the formation of a reddish ether-insoluble solid when benzene was used as solvent for the oxidation of *p*-cresol; it is now shown that, in benzene, lead tetra-acetate favours the formation of dihydroxydiphenyls, particularly when less than molar equivalents are used.

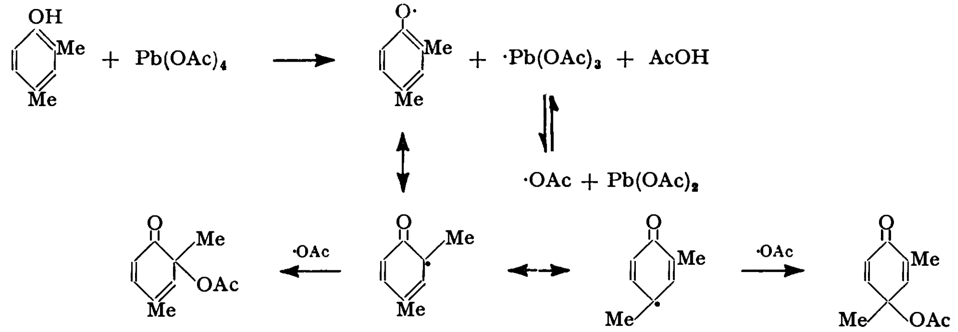
However, the nature of the products is not independent of the structure of the phenol. With increasing *o*- and *p*-substitution by methyl the " type " product isolated changes from a dihydroxydiphenyl (which may appear as a diphenoquinone owing to further oxidation) through mixtures of the dihydroxytetramethyldiphenyls with the corresponding acetoxy*cyclo*hexadienones (from xylenols) until, lastly, mesitol gives only the acetoxydienone. In benzene, the sole product isolated from the oxidation of phenol is 4 : 4′-dihydroxydiphenyl; similarly *o*- and *p*-cresol give a small yield of 4 : 4′-dihydroxy-3 : 3′- and 2 : 2′-dihydroxy-5 : 5′-dimethyldiphenyl respectively. In acetic acid, no identifiable product could be obtained from the oxidation of phenol; Wessely and Sinwel (*loc. cit.*) obtained 2-acetoxy-2-methyl*cyclo*hexadienone and 2-methyl-1 : 4-benzoquinone from *o*-cresol, and similarly 2 : 2-diacetoxy- and 4-acetoxy-4-methyl*cyclo*hexadienone from *p*-cresol.

Oxidation of 2 : 4-dimethylphenol in benzene affords evidence of two competitive processes. With a 0·5 molar equivalent of the oxidant, the main product is 2 : 2′-dihydroxy-3 : 3′ : 5 : 5′-tetramethyldiphenyl, with some 4-acetoxy-2 : 4-dimethyl*cyclo*hexadienone. With an excess of oxidant, in benzene, the 2-acetoxy-derivative was isolated. From a reaction in acetic acid Wessely and Sinwel obtained a mixture, presumably of the 2- and the 4-acetoxy-compound but isolated only the former in a pure state.

2 : 6-Dimethylphenol, in benzene, readily yields 4 : 4′-dihydroxy-3 : 3′ : 5 : 5′-tetramethyldiphenyl and the corresponding 3 : 3′ : 5 : 5′-tetramethyldiphenoquinone (the quinone is obtained from reaction in acetic acid), but with the oxidant in excess 2 : 6-dimethylbenzoquinone is isolated. The monomeric quinone may have resulted from the further oxidation of the 4-acetoxy*cyclo*hexadienone. Oxidation, in chloroform, gave the diphenoquinone in association with two isomeric compounds, $C_{10}H_{12}O_3$. One of these is proved to be 2-acetoxy-2 : 6-dimethyl*cyclo*hexadienone by reduction to the parent phenol with zinc and acetic acid and by its characteristic ultra-violet absorption spectrum. The second compound has not yet been identified but Wessely and Schinzel (*Monatsh.*, 1953, **84**, 425) have observed the transformation of 2-acetoxy-2 : 4 : 6-trimethyl*cyclo*hexadienone (I) into 4-hydroxy-3 : 5-dimethylbenzyl acetate, and a similar rearrangement may have taken place.

Finally, mesitol, having both the *ortho-* and the *para*-position blocked by methyl groups, yields only the 2-acetoxydienone (I) in chloroform, benzene, or acetic acid.

These results are best explained by a free-radical mechanism involving a stepwise progression to thefinal products. As previously indicated by Pummerer, Melamed, and Puttfarcken (*Ber.*, 1922, **55**, 3116) the initial process is dehydrogenation to a phenoxy-radical and, in support, we note that phenyl acetate does not react with lead tetra-acetate under normal conditions. The nature of the final products isolated then depends on factors which may (*a*) stabilise a mesomeric form of the phenoxy-radical and permit dimerisation, or (*b*) enhance the possibility of acetoxylation and dienone formation. Cordner and Pausacker (*J.*, 1953, 102) and Wessely and Schinzel (*loc. cit.*) postulated similar mechanisms, with which we are in general agreement (see annexed scheme).



Participation of acetate radicals and the free-radical nature of the reaction have been demonstrated by Wessely and his co-workers. Our isolation of the dimeric dihydroxydiphenyls, in benzene, demonstrates the existence of the primary phenoxy-radicals, but oxidations in acetic acid invariably yield acetoxydienones and the formation of such products will be assisted by the propagation of acetate radicals in acetic acid, *viz.* :

$$\begin{tikzcd} \cdot\mathrm{Pb(OAc)_3} + \mathrm{AcOH} \arrow[r, phantom, "\rightleftharpoons"] \arrow[d, shift left] & \mathrm{AcOH} + \cdot\mathrm{Pb(OAc)_3} \\ \mathrm{Pb(OAc)_2} + \cdot\mathrm{OAc} \arrow[u, shift left] & \end{tikzcd}$$

$$\cdot\mathrm{OAc} + \mathrm{AcOH} \rightleftharpoons \mathrm{AcOH} + \cdot\mathrm{OAc}, \text{ etc.}$$

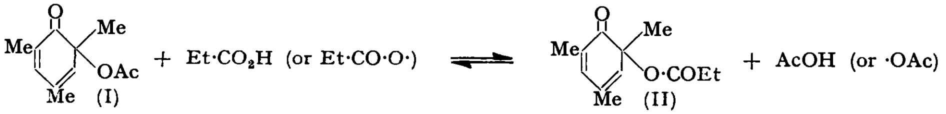
Our isolation of 2 : 4 : 6-trimethyl-2-propionoxy*cyclo*hexadienone (II) from a reaction of mesitol with lead tetra-acetate in propionic acid, and of the 2-acetoxy-compound (I) from an oxidation with lead tetra-propionate in acetic acid, demonstrates that the solvent acid determines the nature of the final acyloxy-derivative. Whether there is (*a*) a radical-transfer process which occurs after initiation of the oxidation reaction :

$$\cdot\mathrm{OAc} + \mathrm{Et{\cdot}CO_2H}\ (\text{excess}) \rightleftharpoons \mathrm{Et{\cdot}CO{\cdot}O}\cdot + \mathrm{AcOH}$$

(*b*) replacement in the lead tetra-acylate (partial or complete) :

$$\mathrm{Pb(OAc)_4} + \mathrm{Et{\cdot}CO_2H}\ (\text{excess}) \rightleftharpoons \mathrm{Pb(O{\cdot}COEt)_4} + 4\mathrm{AcOH}$$

or (*c*) replacement in the final product, *e.g.*, (I ⟶ II), or any combination of the above mechanisms, cannot readily be proved. Related to the third possibility is Wessely and Schinzel's observation (*loc. cit.*) that mesitol, on oxidation with acetyl peroxide in propionic acid, yields 4-hydroxy-3 : 5-dimethylbenzyl propionate *via* the intermediate acyloxy-dienone (I or II) which was not isolated.



That the oxidation of phenols with lead tetra-acetate is a free-radical process has been confirmed, and solvent effects in such oxidations are fully demonstrated.

EXPERIMENTAL

Light petroleum had b. p. 40—60°.

Oxidation of Phenol.—Phenol (9 g.) in benzene (1 l.) was oxidised with lead tetra-acetate (11 g.), added during 1 hr. Removal of the solvent gave a dark residue from which phenol (6·3 g.) was recovered by steam-distillation. The remaining solid was extracted with hot water (3 × 50 ml.) containing a little acetic acid, and, on cooling, colourless needles of 4 : 4′-dihydroxydiphenyl (0·06 g.) were obtained. Recrystallised from aqueous alcohol these had m. p. and mixed m. p. 265—268° (Found : C, 77·1; H, 5·3. Calc. for $C_{12}H_{10}O_2$: C, 77·4; H, 5·4%). No recognisable product could be isolated from a similar oxidation in acetic acid.

Oxidation of Cresols.—(*a*) *o*-Cresol (5·4 g.) in benzene (100 ml.) was oxidised with lead tetra-acetate (11 g.). The solvent and excess of *o*-cresol were removed in steam, and the residue was treated as for phenol. 4 : 4′-Dihydroxy-3 : 3′-dimethyldiphenyl was finally isolated as colourless prisms (0·05 g.), m. p. and mixed m. p. 156—157°.

(*b*) *p*-Cresol (5·4 g.) in benzene (250 ml.) was oxidised with lead tetra-acetate (11 g.). The mixture, after 2 hr., was treated as above. From the aqueous extracts needles separated, which, after recrystallisation from aqueous alcohol, gave 2 : 2′-dihydroxy-5 : 5′-dimethyldiphenyl (0·4 g.), m. p. and mixed m. p. 153—154° (Found : C, 78·5; H, 6·7. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%).

Oxidation of Xylenols.—(*a*) 2 : 4-Dimethylphenol (10 g.) in benzene (150 ml.) was oxidised with lead tetra-acetate (18 g.). The mixture was poured into water and extracted with ether. Fractional distillation gave unchanged phenol (5·0 g.) and a fraction (0·8 g.), b. p. 100—140°/0·05 mm., which in light petroleum yielded *4-acetoxy-2 : 4-dimethyl*cyclo*hexadienone*, m. p. 93—94°, as colourless needles (Found : C, 66·6; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%). The ultra-violet absorption spectrum of this compound was analogous to that of 4-acetoxy-derivatives isolated by Wessely and Sinwel (*loc. cit.*). A third fraction (0·7 g.), b. p. 140—160°/0·05 mm., which solidified on cooling, was recrystallised from light petroleum, yielding 2 : 2′-dihydroxy-3 : 3′ : 5 : 5′-tetramethyldiphenyl as colourless prisms, m. p. 133—134° (Found : C, 79·5; H, 7·5. Calc. for $C_{16}H_{18}O_2$: C, 79·3; H, 7·5%). Bamberger (*Ber.*, 1907, **40**, 1926) records m. p. 137—138°.

(*b*) 2 : 4-Dimethylphenol (5 g.), oxidised in benzene (200 ml.) with lead tetra-acetate (27 g.), etc., gave 2-acetoxy-2 : 4-dimethyl*cyclo*hexadienone (1·5 g.) as plates, m. p. 69—71° (from light petroleum) (Found : C, 66·5; H, 6·6. Calc. for $C_{10}H_{12}O_3$: C, 66·7; H, 6·7%). Wessely and Sinwel (*loc. cit.*) give m. p. 71·5°.

(*c*) 2 : 6-Dimethylphenol (4 g.) in benzene (200 ml.) was oxidised with lead tetra-acetate (7·3 g.). From the solution crystals were precipitated which were filtered off after addition of water to dissolve lead acetate. This product (0·8 g.), on recrystallisation from acetic acid, gave 3 : 3′ : 5 : 5′-tetramethyl-4 : 4′-diphenoquinone as purplish-red needles, m. p. 205—210° (Found : C, 79·8; H, 6·6. Calc. for $C_{16}H_{16}O_2$: C, 80·0; H, 6·7%). Cosgrove and Waters (*J.*, 1951, 388) report m. p. 210—215°. The red benzene layer yielded 4 : 4′-dihydroxy-3 : 3′ : 5 : 5′-tetramethyldiphenyl (0·15 g.) as needles, m. p. 222—223° (from benzene) (Found : C, 79·5; H, 7·4. Calc. for $C_{16}H_{18}O_2$: C, 79·3; H, 7·5%). Cosgrove and Waters (*loc. cit.*) report m. p. 221°.

(*d*) 2 : 6-Dimethylphenol (4 g.) in acetic acid (50 ml.) was oxidised with lead tetra-acetate (14·6 g.). The red 3 : 3′ : 5 : 5′-tetramethyl-4 : 4′-diphenoquinone (0·05 g.) was filtered off and recrystallised from acetic acid, as previously described. The residual solution was poured into water and extracted with chloroform. A yellow oil (3·9 g.), b. p. 60—70°/0·1 mm., isolated by fractional distillation, gave *2-acetoxy-2 : 6-dimethyl*cyclo*hexadienone*, prisms, m. p. 35° (from light petroleum) (Found : C, 66·3; H, 6·4. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%), $\lambda_{max.}$ (in EtOH) 305 mμ (cf. ultra-violet absorption spectrum of similar 2-acetoxy-derivatives isolated by Wessely and Sinwel, *loc. cit.*). Reduction of this compound with zinc dust and acetic acid gave 2 : 6-dimethylphenol as needles, m. p. and mixed m. p. 43—45° (from light petroleum).

(*e*) 2 : 6-Dimethylphenol (7·5 g.) in acetic acid (40 ml.) was added dropwise with stirring to a solution of lead tetra-acetate (30 g.) in acetic acid (50 ml.). The oxidant was completely used but under these conditions no diphenoquinone was formed. The chloroform extract gave two fractions on distillation under reduced pressure. The first, which sublimed at 20—40°/0·04 mm., was 2 : 6-dimethyl-*p*-benzoquinone (0·05 g.), recrystallising as yellow needles, m. p.

68—71°, from light petroleum. Noelting and Forel (*Ber.*, 1885, **18**, 2679) give m. p. 72—73°. The second fraction, b. p. 40°/0·04 mm., was chromatographed in light petroleum on alumina to give 2-acetoxy-2 : 6-dimethyl*cyclo*hexadienone, m. p. and mixed m. p. 35°, as previously described.

Oxidation of Mesitol.—(*a*) 2 : 4 : 6-Trimethylphenol (1·4 g.) in benzene (50 ml.) was oxidised with lead tetra-acetate (4·4 g.). The mixture yielded, as above, 2-acetoxy-2 : 4 : 6-trimethyl*cyclo*hexadienone, colourless needles (1·0 g.), m. p. 84—85° (from light petroleum) (Found: C, 67·8; H, 7·1. Calc. for $C_{11}H_{14}O_3$: C, 68·0; H, 7·3%). Wessely and Sinwel (*loc. cit.*) report m. p. 84°.

(*b*) Mesitol (1·4 g.) in acetic acid (35 ml.) with lead tetra-propionate (5·75 g.) yielded 2-acetoxy-2 : 4 : 6-trimethyl*cyclo*hexadienone (0·45 g.), m. p. and mixed m. p. 83°.

(*c*) Mesitol (1·0 g.) in propionic acid (25 ml.) with lead tetra-acetate (3·6 g.) yielded 2 : 4 : 6-*trimethyl*-2-*propionoxy*cyclo*hexadienone* as almost colourless plates (0·43 g.), m. p. and mixed m. p. 49—50° (from light petroleum) (Found: C, 68·7; H, 7·7. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·75%), $\lambda_{\max.}$ (in EtOH) 311 mμ.

(*d*) Mesitol (2·0 g.) in propionic acid (25 ml.) with lead tetra-propionate (7·1 g.) yielded 2 : 4 : 6-trimethyl-2-propionoxy*cyclo*hexadienone (0·43 g.), m. p. 49—50° (from light petroleum) (Found: C, 69·1; H, 7·6%), $\lambda_{\max.}$ (in EtOH) 312 mμ. Catalytic reduction of this compound yielded mesitol, m. p. and mixed m. p. 72°.

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