Some Products formed from Phenolic Inhibitors during the Autoxidation of Cumene.

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Solutions of alkylphenols in cumene containing 0·1% of ferric stearate have been oxidised with air, and oxidation products derived from the phenols have been isolated from the resulting solutions and identified by alternative syntheses.

p-Cresol, 2 : 4-xylen-1-ol, and 2 : 6-xylen-1-ol yield dihydroxydiphenyl derivatives, whereas mesitol, 2-*tert*.-butyl-4 : 6-dimethylphenol, and 2 : 6-di-*tert*.-butyl-4-methylphenol yield dihydroxydibenzyl derivatives. Oxidation of 2 : 4-di-*tert*.-butyl-6-methylphenol by silver oxide yields the keto-ether (VII) of a quinol which can be reduced to 3 : 5 : 3′ : 5′-tetra-*tert*.-butyl-2 : 2′-dihydroxydibenzyl. The mechanisms of these oxidations are discussed.

Kinetic investigations of the rôles of monohydric phenols in retarding the autoxidation of benzaldehyde (Waters and Wickham-Jones, *J.*, 1951, 812; 1952, 2420) have indicated that oxidation chains are broken by the abstraction of hydrogen atoms from phenol molecules, and the dimerisation of the radicals so produced. Few studies of the products of inhibitor action have yet been made. In the case of 2 : 6-xylen-1-ol it was shown, in the above work, that there was first obtained 3 : 5 : 3′ : 5′-tetramethyl-4 : 4′-diphenoquinone, which then united with benzoyl radicals to form 4 : 4′-dibenzoyloxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl. The latter could be isolated, though only in small yield, from the autoxidised solutions (Moore and Waters, *J.*, 1952, 2432) but no corresponding products could be obtained from autoxidised benzaldehyde solutions of *p*-cresol. More recently, Cook (*J. Org. Chem.*, 1953, **18**, 261) has isolated 3 : 5 : 3′ : 5′-tetra-*tert*.-butyl-4 : 4′-dihydroxydibenzyl (V; R = Bu^t) from the oxidation of 2 : 6-di-*tert*.-butyl-4-methylphenol (II; R = Bu^t) in hydrocarbon oils.

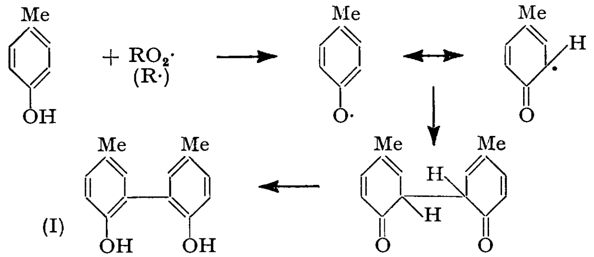
Since phenols retard the autoxidation of hydrocarbons in a way which is kinetically similar to their action upon the autoxidation of benzaldehyde, a study has now been made of the oxidation of phenol in liquid cumene, which is easily converted by a current of air into a reasonably stable hydroperoxide, $Ph{\cdot}CMe_2{\cdot}O{\cdot}OH$. The latter, like tetralyl hydroperoxide (Robertson and Waters, *J.*, 1948, 1578), is a catalyst for autoxidation of cumene, and its decomposition into chain-starting radicals can be accelerated by adding traces of a metallic ion of variable valency such as iron or cobalt (compare Kharasch, Fono, Nudenberg, and Bischof, *J. Org. Chem.*, 1952, **17**, 207; Kharasch, Fono, and Nudenberg, *ibid.*, 1950, **15**, 763; Fordham and Williams, *J. Amer. Chem. Soc.*, 1950, **72**, 4465; Wise and Twigg, *J.*, 1953, 2172). The eventual oxidation products are all reasonably volatile substances, such as acetophenone, and consequently warm 2—3% solutions of phenols in cumene containing 0·1% of dissolved ferric stearate are autoxidisable mixtures from which the isolation of reaction products diagnostic of the fate of the inhibitor can be achieved.

The phenols which we have examined all yield dimers which evidently arise from products of hydrogen-transfer reactions such as $Ph{\cdot}CMe_2{\cdot} + HOAr \longrightarrow Ph{\cdot}CMe_2{\cdot}H + {\cdot}OAr$ and/or $Ph{\cdot}CMe_2{\cdot}O{\cdot}O{\cdot} + HOAr \longrightarrow Ph{\cdot}CMe_2{\cdot}O{\cdot}OH + {\cdot}OAr$. Since some phenols can be oxidised by ferric salts, and any ferrous ions so formed would rapidly be reoxidised by the hydroperoxide present in the system, part of the phenol oxidation may be due to the direct reaction $Fe^{3+} + HOAr \longrightarrow Fe^{2+} + {\cdot}OAr + H^+$. Similar products have in fact been obtained, though in much smaller yield, by blowing air through solutions of the same phenols in chlorobenzene containing 0·2% of ferric stearate. The metallic salt is not, however, an essential catalyst for this oxidative dimerisation of phenols because it can be replaced as a reaction-promoter by αα′-azo*iso*butyronitrile, which is well known as a free-radical-forming autoxidation catalyst (Bateman, Gee, Morris, and Watson, *Discuss. Faraday Soc.*, 1951, **10**, 250; Bateman, Hughes, and Morris, *ibid.*, 1953, **14**, 190).

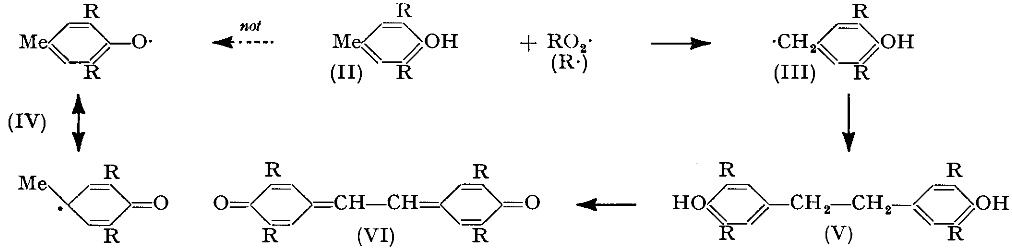
By these oxidations *p*-cresol yielded 2 : 2′-dihydroxy-5 : 5′-dimethyldiphenyl (I), and correspondingly 2 : 4-xylen-1-ol gave 2 : 2′-dihydroxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl :

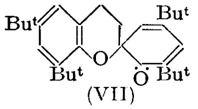
both products were identified as their diacetyl derivatives. 2 : 6-Xylen-1-ol gave a mixture of 4 : 4′-dihydroxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl and 3 : 5 : 3′ : 5′-tetramethyl-4 : 4′-diphenoquinone. In contrast, the 2 : 4 : 6-trialkylphenols mesitol, 2-*tert.*-butyl-4 : 6-dimethylphenol, and 2 : 6-di-*tert.*-butyl-4-methylphenol yielded only dihydroxydibenzyl derivatives such as (V; R = Me or Bu^t), the structures of which were established in all cases by direct comparisons with synthetic specimens. The latter were usually prepared by oxidising the trialkylphenols with silver oxide in dry benzene to the stilbenequinones (VI; R = Me or Bu^t) (Dunn and Waters, *J.*, 1953, 2993) and then reducing the latter.

The formation of a dihydroxydiphenyl (I) from a phenol containing an unsubstituted *ortho-* or *para*-position is easily explicable by postulating the formation of mesomeric aryloxy-radicals, thus :

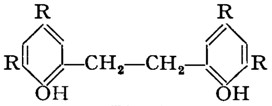


but the formation of a dihydroxydibenzyl from a 2 : 4 : 6-trialkylphenol is indicative of the formation of a substituted hydroxybenzyl radical (III) by hydrogen removal from methyl and not from hydroxyl, as in (IV). It is difficult to visualise the easy conversion of the expected radical (IV) into the isomeric form (III), for the two points at which the odd electrons have been placed are not conjugated.

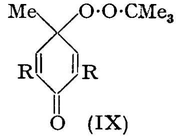




(VII)



(VIII)



(IX)

The oxidation by silver oxide of 2 : 4-di-*tert.*-butyl-6-methylphenol has yielded the keto-ether (VII) which could be reduced to 3 : 5 : 3′ : 5′-tetra-*tert.*-butyl-2 : 2′-dihydroxydibenzyl (VIII; R = Bu^t); (VII) corresponds in type to the product obtained by Fries and Brandes (*Annalen*, 1939, **542**, 48) by oxidising 2 : 2′-dihydroxy-3 : 5 : 3′ : 5′-tetramethyldibenzyl (VIII; R = Me) with alkaline ferricyanide.

Undoubtedly, the exact course of the homolytic oxidation of phenols in the presence of autoxidisable hydrocarbons, RH, their hydroperoxides, RO·OH, and related free radicals, R·, RO·, and $RO_2\cdot$ depends very much on the selected experimental conditions. Thus Campbell and Coppinger (*J. Amer. Chem. Soc.*, 1952, **74**, 1469) have found that 2 : 6-di-*tert.*-butyl-4-methylphenol (II; R = Bu^t) yields (IX) when oxidised with *tert.*-butyl hydroperoxide containing a little cobalt naphthenate as radical-producing catalyst, and a whole series of substances of this same type has been obtained by Bickel and Kooyman (*J.*, 1953, 3211) from oxidations of 2 : 4 : 6-trialkylphenols with a number of alkylperoxy-radicals pertinent to hydrocarbon autoxidation. Under their conditions $RO_2\cdot$ radicals may be present in excess in the oxidising mixtures, whereas under our experimental conditions, which were chosen to simulate the technical conditions of autoxidation in liquid hydrocarbons, much lower concentrations of R• and RO_2• radicals would have been present, and consequently the dimerisation of radicals derived from the phenols would be favoured. However, the isolation of dihydroxydibenzyl derivatives (V) cannot easily be related to the formation of compounds of type (IX), which may be derived from radical (IV) and not radical (III). A similar contrast in regard to the structures of reaction products, traceable to the relative concentrations of radicals ArO• and Ph•CO_2•, has been exemplified by the oxidations of phenols by (*a*) benzoyl peroxide (Cosgrove and Waters, *J.*, 1949, 3189; 1951, 388) and (*b*) Fenton's reagent (*idem, J.*, 1951, 1726).

EXPERIMENTAL

Oxidations of p-*Cresol*.—(*a*) *p*-Cresol (10 g.) in cumene (250 ml.) containing ferric stearate (0·2 g.) was air-blown for 120 hr. at 80—100° under a condenser system. After evaporation of the solvent the residue, in ether, was shaken with dilute sulphuric acid to remove ferric salts and, after removal of the ether, distilled in steam to separate unchanged cresol (7·5 g.) and acetophenone. The involatile residue, in ether, was extracted with 10% potassium hydrogen carbonate solution (100 ml.) to remove stearic acid and then with 5% potassium hydroxide solution (2 × 100 ml.). The remaining ethereal solution on evaporation gave only gum (0·2 g.), but the potash solution, after acidification, gave phenolic material (1·1 g.) which, on acetylation and chromatographic fractionation through alumina by means of benzene–light petroleum, yielded 2 : 2′-diacetoxy-5 : 5′-dimethyldiphenyl (0·1 g.), m. p. 88° (from dilute ethanol). This m. p. was not changed on admixture with an authentic specimen prepared by the persulphate oxidation of *p*-cresol (Raudnitz, *Ber.*, 1930, **63**, 517). Alkaline hydrolysis of the autoxidation product gave, in 5% yield calculated on the cresol consumed, 2 : 2′-dihydroxy-5 : 5′-dimethyldiphenyl (I), m. p. and mixed m. p. 153° (from benzene).

(*b*) *p*-Cresol (10 g.) in chlorobenzene (250 ml.) containing ferric stearate (0·5 g.), after autoxidation for a similar period, yielded only 0·25 g. of involatile phenols and only 0·02 g. of 2 : 2′-diacetoxy-5 : 5′-dimethyldiphenyl.

Oxidations of 2 : 6-*Xylen*-1-*ol*.—(*a*) The xylenol (5 g.) in cumene (300 ml.) containing ferric stearate (0·2 g.) was air-blown at 80—100° for 30 hr. Volatile and steam-volatile materials were then removed. The residue contained 0·5 g. of brownish solid insoluble in ether which, after crystallisation from acetic acid, proved to be 3 : 5 : 3′ : 5′-tetramethyl-4 : 4′-diphenoquinone, m. p. 210—215° (decomp.). The alkali-soluble remainder (1·8 g.), after distillation at *ca.* 210°/0·2 mm., gave a pale yellow solid (0·4 g.) which crystallised from dilute acetic acid in needles, m. p. 221°, and by mixed m. p. was identified as 4 : 4′-dihydroxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl (Cosgrove and Waters, *J.*, 1951, 388).

(*b*) The xylenol (5 g.) in chlorobenzene containing 0·5 g. of ferric stearate, after being air-blown at 100° for 44 hr., gave no quinone and only 0·18 g. of the dihydroxydiphenyl: the ferric stearate taken is equivalent to 0·076 g. of the latter.

(*c*) The xylenol (5 g.) in cumene was air-blown at 100° for 5½ hr., during which αα′-azo*iso*butyronitrile (3·4 g., 1 equiv.) was added in portions. The solution soon became red. There was isolated a greenish-black residue (0·37 g.) of the quinhydrone of the two products mentioned above. A similar yield of products was obtained by using only 0·1 equiv. of azo-catalyst. In chlorobenzene solution, with air-blowing, the yield of quinhydrone was 0·7 g.: no oxidation of the xylenol occurred under nitrogen in corresponding conditions.

Oxidations of 2 : 4-*Xylen*-1-*ol*.—(*a*) The xylenol (5 g.) in cumene (200 ml.) containing ferric stearate (0·2 g.) was air-blown at 80—100° for 120 hr.; 2·5 g. of the xylenol were recovered. There was obtained 0·9 g. of neutral material from which no pure compounds could be separated, and 1·2 g. of phenolic material which yielded 1·2 g. of 2 : 2′-diacetoxy-3 : 5 : 3′ : 5′-tetramethyldiphenyl, m. p. 105°, identical with the compound obtained by oxidising 2 : 4-xylen-1-ol with Fenton's reagent (Cosgrove and Waters, *J.*, 1951, 1729).

(*b*) The xylenol (5 g.) in cumene was air-blown at 100° for 15 hr. with gradual addition of 0·1 equiv. of αα′-azo*iso*butyronitrile. The oxidation products were 0·2 g. of neutral gum and 0·44 g. of phenols which yielded 0·15 g. of the preceding diacetate.

Oxidation of Mesitol.—Mesitol (5 g.) in cumene plus ferric stearate was autoxidised for 80 hr. The alkali-insoluble product (1 g.) yielded no pure compounds. The alkali-soluble products (2 g.) were acetylated and chromatographically separated on alumina. Benzene eluted 0·22 g. of the diacetate, m. p. 132°, of the unidentified diphenol, m. p. 156°, obtained by Cosgrove and Waters (see above) by the action of Fenton's reagent on mesitol and thought to be 2 : 4′-dihydroxy-3 : 5 : 3′ : 5′-tetramethyldibenzyl. Subsequent elution gave 0·14 g. of 4 : 4′-diacetoxy-3 : 5 : 3′ : 5′-tetramethyldibenzyl of m. p. 148° (*idem, ibid.*), from which the dihydroxydibenzyl (V; R = R = Me), m. p. 168°, was obtained by hydrolysis.

Oxidations of 2 : 6-*Di*-tert.-*butyl*-4-*methylphenol*.—(*a*) The phenol (4 g.) in cumene (250 g.) with ferric stearate (0·2 g.) was air-blown at 80—100° for 70 hr. The involatile reaction products, when kept at 0°, deposited an orange solid (0·34 g.) which on crystallisation from glacial acetic acid gave pale yellow needles, m. p. 169—170°, of 3 : 5 : 3′ : 5′-tetra-*tert.*-butyl-4 : 4′-dihydroxydibenzyl (V; R = R = Bu^t) (Found : C, 81·9; H, 10·7. Calc. for $C_{30}H_{46}O_2$: C, 82·2; H, 10·6%) : Cook (*loc. cit.*) gives m. p. 174—175°. This was identical with a specimen made by reducing 3 : 5 : 3′ : 5′-tetra-*tert.*-butyl-4 : 4′-stilbenequinone (Cosgrove and Waters, *J.*, 1951, 388; Dunn and Waters, *loc. cit.*) first to 3 : 5 : 3′ : 5′-tetra-*tert.*-butyl-4 : 4′-dihydroxystilbene, m. p. 236° (Found : C, 82·5; H, 10·2. Calc. for $C_{30}H_{44}O_2$: C, 82·5; H, 10·2%), with zinc dust in hot acetic acid, and thence, in alcoholic solution, to the dihydroxydibenzyl by means of hydrogen at 1 atm. and 20° with a palladium–calcium carbonate catalyst.

(*b*) The phenol (5 g.) by similar autoxidation in chlorobenzene containing ferric stearate (0·5 g.) gave 0·15 g. of the dihydroxydibenzyl (V); the ferric salt alone is equivalent to 0·14 g. of this product.

(*c*) The phenol (5 g.) in cumene with αα′-azo*iso*butyronitrile catalyst (0·1 equiv.) gave only 0·05 g. of the dihydroxydibenzyl.

Oxidation of 2-tert.-*Butyl*-4 : 6-*dimethylphenol*.—The phenol (5 g.) in cumene with ferric stearate (0·2 g.) was air-blown for 80 hr. The involatile product (1 g.) was an oil which by elution from alumina with benzene–light petroleum, followed by crystallisation from dilute alcohol, gave pale yellow plates, m. p. 130°, of 3 : 3′-*di*-tert.-*butyl*-4 : 4′-*dihydroxy*-5 : 5′-*dimethyldibenzyl* (Found : C, 81·3; H, 9·6. $C_{24}H_{34}O_2$ requires C, 81·3; H, 9·7%). An identical product was obtained by reducing 3 : 3′-di-*tert.*-butyl-5 : 5′-dimethyl-4 : 4′-stilbenequinone (Dunn and Waters, *loc. cit.*) by the two-stage process described above. The easily oxidised 3 : 3′-di-*tert.*-butyl-4 : 4′-dihydroxy-5 : 5′-dimethylstilbene, m. p. 150—156°, was not purified. A later eluate from the alumina was a reddish gum which when warmed in dry benzene with silver oxide gave a few crystals of the stilbenequinone referred to above.

Oxidation of 2 : 4-*Di*-tert.-*butyl*-6-*methylphenol with Silver Oxide*.—The phenol (5 g.) in dry benzene (250 ml.) was stirred for 2 hr. at 20° and then for 2 hr. at 50° with dry, freshly prepared, silver oxide (25 g.) and anhydrous sodium sulphate (2 g.). The solution was then filtered hot, and the residue extracted with more dry benzene. The combined filtrates on evaporation gave a gum which solidified when rubbed with acetic acid. Crystallisation from dilute acetic acid gave pale yellow needles (2·1 g.) of 3 : 5 : 6′ : 8′-*tetra*-tert.-*butyl*-3′ : 4′-*dihydrobenzopyran*-2′-spiro-cyclo*hexa*-3 : 5-*dien*-2-*one* (VII), m. p. 151—152° (Found : C, 82·7; H, 10·0. $C_{30}H_{44}O_2$ requires C, 82·5; H, 10·2%). Its infra-red spectrum has a strong C=O band at 5·95 μ but no hydroxyl band at 2·8—3·0 μ. (VII) was reduced with zinc dust in boiling acetic acid solution to give 3 : 5 : 3′ : 5′-*tetra*-tert.-*butyl*-2 : 2′-*dihydroxydibenzyl* (VIII; R = Bu^t), which crystallised from dilute acetic acid in needles, m. p. 180° (Found : C, 81·9; H, 10·6. $C_{30}H_{46}O_2$ requires C, 82·2; H, 10·6%). Its infra-red spectrum showed the O–H band at 2·9 μ. Attempts to debutylate this compound (i) with 50% sulphuric acid, and (ii) with toluene-*p*-sulphonic acid at 200° (Stevens, *Ind. Eng. Chem.*, 1943, **35**, 655) were unsuccessful and consequently its identity was confirmed by synthesis as follows.

2 : 2′-Dihydroxystilbene (Thiele and Holzinger, *Annalen*, 1899, **305**, 97) (0·25 g.), *tert.*-butyl chloride (0·45 g.), and anhydrous aluminium chloride (0·05 g.) were stirred in carbon disulphide for 4 hr. at room temperature. More *tert.*-butyl chloride (0·45 g.) and aluminium chloride (0·1 g.) were then added, and the temperature was raised so that the stirred liquid refluxed gently during 36 hr. The gummy reaction product (0·4 g.) was isolated in the customary way, dissolved in light petroleum, and fractionated through alumina. Pure benzene eluted material (0·05 g.) which eventually crystallised from dilute acetic acid in needles having m. p. 180° and an infra-red spectrum identical with that of the reduced product (VIII) of the silver oxide reaction described above.

It has not yet been possible to isolate similar reaction products from the catalysed autoxidation of 2 : 4-di-*tert.*-butyl-6-methylphenol in cumene.

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