543. *Autoxidation of Hindered Phenols in Alkaline Media. Part I.*

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The autoxidation of substituted 2,6-di-t-butylphenols in alkaline media has been studied at various temperatures. 2,4,6-Tri-t-butylphenol and 4-methyl-2,6-di-t-butylphenol are oxidized to hydroperoxycyclohexadienones, the structures of which have been established. The formation of hydroperoxides appeared to be autocatalytic, the catalyst probably being a decomposition product of a 2,4,6-trialkyl-2-hydroperoxycyclohexa-3,5-dienone. Oxidation may also be catalyzed by quinones and aromatic polynitro-compounds, and these reactions were most suited to kinetic studies. Mechanisms for these reactions are put forward. 2,6-Di-t-butylphenol is oxidized to the corresponding diphenoquinone and a by-product, $C_{13}H_{22}O_3$.

The oxidation of hindered phenols has been extensively studied during the last few years, *e.g.*, with benzoyl peroxide,[1] bromine,[2] alkaline ferricyanide,[3,4] lead dioxide,[4] and hydroperoxides.[5] The behaviour of these phenols as inhibitors of free-radical oxidation has been studied also in this laboratory.[6] More recently the autoxidation of 2,6-di-t-butylphenols in an alkaline medium was investigated by Kharasch,[7] Ley,[8] and the present authors,[9] and Weissberger [10] studied the alkaline autoxidation of substituted quinols. In this paper a detailed account is given of the alkaline autoxidation of 2,6-di-t-butylphenol, 2,4,6-tri-t-butylphenol, and 4-methyl-2,6-di-t-butylphenol (cf. ref. 9).

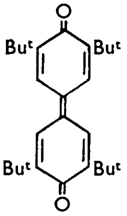
[1] Cosgrove and Waters, *J.*, 1949, 3189.
[2] Coppinger and Campbell, *J. Amer. Chem. Soc.*, 1951, **75**, 734.
[3] Müller and Ley, *Chem. Ber.*, 1954, **87**, 922.
[4] Cook, Nash, and Flanagan, *J. Amer. Chem. Soc.*, 1955, **77**, 1783.
[5] Campbell and Coppinger, *ibid.*, 1952, **74**, 1469.
[6] Bickel and Kooyman, *J.*, 1953, 3211; 1956, 2215; 1957, 2217, 2415.
[7] Kharasch and Yoshi, *J. Org. Chem.*, 1957, **22**, 1439.
[8] Ley, *Angew. Chem.*, 1958, **70**, 74.
[9] Bickel and Gersmann, *Proc. Chem. Soc.*, 1957, 231.
[10] Luvalle and Weissberger, *J. Amer. Chem. Soc.*, 1947, **69**, 1567.

RESULTS

Oxidation Products.—Autoxidations were effected by vigorous stirring of a solution of the phenol and excess of potassium hydroxide in 90% ethanol with gaseous oxygen at 40°. After absorption of 1 mol. of oxygen, products were isolated by ether-extraction of the acidified mixture and subsequent crystallization.

In this way 2,6-di-t-butylphenol yielded 3,3′,5,5′-tetra-t-butyldiphenoquinone (I) (∼50%) and a compound, $C_{13}H_{22}O_3$ (∼25%). 2,4,6-Tri-t-butylphenol yielded 4-hydroperoxy-2,4,6-tri-t-butylcyclohexa-2,5-dienone (II) and 2-hydroperoxy-2,4,6-tri-t-butylcyclohexa-3,5-dienone (III) (total about 75%).

4-Methyl-2,6-di-t-butylphenol gave as the main product 4-hydroperoxy-4-methyl-2,6-di-t-butylcyclohexa-2,5-dienone (IV).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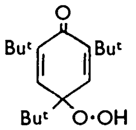
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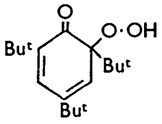
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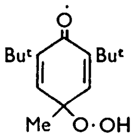
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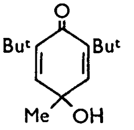
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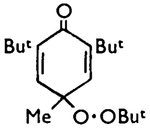
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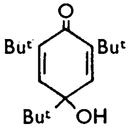

(VII)

The structure of the hydroperoxide (IV) was established in the following manner. The presence of one atom of active oxygen was shown by a peroxide determination. The isolated reduction product (V) and the hydroperoxide have ultraviolet absorption spectra very similar to that of the peroxide (VI), which was described by Bickel and Kooyman.[6] This peroxide was obtained from both the hydroperoxide (IV) and the alcohol (V) by reaction with t-butyl alcohol and t-butyl hydroperoxide, respectively, in 70% sulphuric acid. The structure of the hydroperoxides (I) and (III) was primarily based upon determinations of carbon, hydrogen, and active oxygen and was further established by the close resemblance between the ultraviolet absorption spectra of compounds (II) and (IV) and of (III) and the "*ortho*"-peroxides isolated by Bickel and Kooyman.[6]

The new hydroperoxides (II), (III), and (IV) have interesting properties: The first two can be partially transformed into each other: after the hydroperoxide (II) had been heated for 2 hours at 40° (pH 14) in alcohol in the presence of oxygen, ultraviolet spectroscopic analysis revealed the presence of 19·5% of the isomer (III) and 30·5% of the original compound (V) (ratio 39/61). Under the same conditions, the isomer (III) was partly converted into (II) (ratio found: 42/58). Ultraviolet absorption spectra also point to this type of isomerization in the case of the analogue (IV).

Secondly, the isomerizations are accompanied by partial decomposition, which was studied by allowing the peroxide (IV) to decompose in ethanol at 40° (pH 14) in the presence of oxygen or nitrogen. With oxygen about 80% of the hydroperoxide had decomposed after 4 hours; ultraviolet absorption spectra showed that the main reaction product was the alcohol (V). In the absence of oxygen, 90% of the hydroperoxide had decomposed after 2 hours, and ultraviolet analysis revealed that the product was a 2 : 3-mixture of the alcohol (V) and 4-methyl-2,6-di-t-butylphenol.

Finally, it was found that reduction of the peroxides (II) and (IV) with hydrogen iodide gave the corresponding alcohols (VII) and (V). It was not possible to isolate a similar product on reduction of the peroxide (III).

Kinetics of the Oxidation.—(a) *General survey of rate measurements.* Oxidation of 4-methyl-2,6-di-t-butyl- and of 2,4,6-tri-t-butyl-phenol was studied at various temperatures and pressures. The rates of oxygen uptake were determined by measuring a change in volume at atmospheric pressure or a change in pressure at lower oxygen pressures (see Experimental section). Stirring was always so fast that it could be assumed that the solution was saturated with oxygen. In nearly all experiments the yield of hydroperoxides was between 70% and 85%. Light metals and ions of heavy metals slightly enhanced the rate of oxidation, so the measurements were made in the dark and in the presence of potassium cyanide as a complex-forming agent. However, potassium cyanide also accelerated the decomposition of the quinone catalyst (see below) and was therefore omitted in the study of the catalyzed reactions. Table 1 lists the maximum rates of oxygen uptake and the hydroperoxide yields in a number of autoxidations with different starting conditions.

(b) *Determination of the dissociation constants of the phenols.* To correlate rates of oxidation with the ionization of the phenols, the dissociation constants were determined in 90% ethanol by ultraviolet spectroscopy: 2,4,6-tri-t-butyl-, p*K* 14·0 ± 0·2; 4-methyl-2,6-di-t-butyl-, p*K* 13·7 ± 0·2; and 2,6-di-t-butyl-phenol, p*K* 13·6 ± 0·2. The pH dependence of the oxidation rate for the catalyzed (see below) and for the uncatalyzed reaction is illustrated in Tables 1 and 2.

(c) *Autocatalysis.* As the form of the oxidation curves pointed to autocatalysis, the hydroperoxides as well as some other possible products were tested for catalytic activity. It was found that the *ortho*-hydroperoxide (III) is responsible for the catalytic effect (cf. the experimental curves reproduced in Fig. 1), and there are indications that this peroxide decomposes to give small amounts of the actual catalyst. This assumption was made as the rates found with added "*ortho*"-hydroperoxide decreased soon after the beginning of each run (the run being started by adding a mixture of phenol and catalyst dissolved in ethanol to a solution of potassium hydroxide). When, however, the phenol dissolved in ethanol was added to a potassium

TABLE 1. *Maximum rates (ml./min.) and yields (%) of hydroperoxide in autoxidation of phenols in 90% ethanol.*

Temp.	pH	Phenol (mmole)	Solvent (ml.)	Rate	Yield	Temp.	pH	Phenol (mmole)	Solvent (ml.)	Rate	Yield
	2,6-*Di-t-butyl-4-methylphenol*						2,4,6-*Tri-t-butylphenol*				
−10°	14	1	28	0·04		0°	14	1	—	0·04	
0	13	1	28	~0·01		25	14·15	1	28	0·65	66
25	14	1	28	1·65	95	25	14	1	28	0·65	81
40	12	1	28	0·08	55	25	14	0·6	28	0·28	84
40	13	1	28	0·80	75	25	13·7	1	—	0·3	
40	14	5	28	54		40	13	1	28	0·70	60
40	14	2	56	14·4		40	14	1	28	2·65	63
40	14	1	28	6·9		60	14	1	—	12	40
40	13	2	56	1·60	77						
40	13	2	28	1·80	71						
60	12	1	28	~0·40	38						
60	13	1	28	3·60	45						

TABLE 2. *First-order rate constants (k in mole/min.) of catalyzed oxidation of 4-methyl-2,6-di-t-butylphenol (1 mmole).*

Catalyst (mg.)	O_2 (cm.)	Temp.	pH	*k* *	Catalyst (mg.)	O_2 (cm.)	Temp.	pH	*k* *
	2,6-*Di-t-butylbenzoquinone*						*Duroquinone*		
20	76	−10°	14	0·172	20	76	0°	13	0·0531
100	76	−10	14	0·175	100	76	0	13	0·0680
50	15·2	−10	14	0·0379					
1	76	0	13	0·049			m-*Dinitrobenzene*		
5	76	0	13	0·0634	20	76	−10	14	0·0046
10	76	0	13	0·0672	50	76	−10	14	0·0104
20	76	0	13	0·0670	50	15·2	−10	14	0·060
100	76	0	13	0·0668	100	76	0	13	0·00745
50	76	0	13	0·0660	25	76	0	13	0·00243
50	51	0	13	0·0398	50	76	0	14	0·0192
50	37	0	13	0·0295	50	52	0	14	0·0161
50	19	0	13	0·0184	50	34	0	14	0·0170
20	76	0	14	0·392	50	17	0	14	0·0102
100	76	0	14	0·398	20	76	0	14	0·0088
22	76	40	14	5·5					
						ortho-*Hydroperoxide* (I)			
2,6-*Di-t-butylbenzoquinone*, 20 *mg.*, + *duroquinone*, 20 *mg.*					9·7	76	40	13	0·17
					10	76	25	13	0·039
—	76	0°	13	0·0667	20	76	25	13	0·057
					40	76	25	13	0·076

* Concn. calc. from O_2 consumption.

hydroxide solution of the catalyst the slower rate was observed from the start. Hence it appears that some decomposition product of the peroxide, possibly an *ortho*-quinone or a radical, is the active catalyst. This catalyst then would be more stable in ethanol than in potassium hydroxide, thus causing the effects found at the start of the rate measurements.

Since ultraviolet absorption spectroscopy points to the formation of a small amount of an *ortho*-hydroperoxide from 4-methyl-2,6-di-t-butylphenol, the same type of autocatalysis is assumed in this case.

The *para*-hydroperoxide (IV) is inactive as a catalyst.

(d) *Other catalysts.* During the search for the autocatalyst in the oxidation of 4-methyl-2,6-di-t-butylphenol other catalysts were discovered. When these are added at the start of the reaction simpler kinetics are obtained and consequently a large number of these catalyzed reactions have been studied. 2,6-Di-t-butylbenzoquinone, duroquinone, and *m*-dinitrobenzene proved extremely useful. The reactions were generally of the first order (calculated from oxygen uptake) with respect to phenol concentration. First-order rate constants are listed in Table 2.

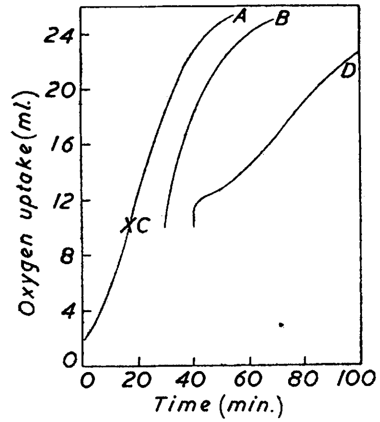


FIG. 1. *Autocatalysis in the oxidation of* 2,4,6-*tri-t-butylphenol.*

A, Phenol alone (1 *mmole*).

B, Phenol mixed with ortho-*hydroperoxide* (I) *as analysed at the point C.*

D, The amount of phenol analysed at point C.

(e) *Experiments on the reaction mechanism.* It was shown that the addition of a hydrogen donor (9,10-dihydroanthracene), free radicals (2,4,6-tri-t-butylphenoxyl), or free-radical-producing substance (2,2′-azoisobutyronitrile) had no definite effect on the oxidation rate.

DISCUSSION

Mechanism of the Oxidation of 2,4,6-*tri-t-butyl- and* 4-*methyl*-2,6,-*di-t-butylphenol*.—A first plausible assumption about the mechanism of the autoxidation of hindered phenols seemed to be that of a free-radical chain process very commonly encountered in autoxidations. However, the various tests which we made to find evidence for a free-radical chain mechanism, and the nature of the active catalysts (quinones and aromatic polynitro-compounds), which are inhibitors in radical reactions, indicated that the idea was incorrect. The kinetics of the catalyzed autoxidations enable a formal description of the reactions to be given.

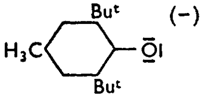
(a) pH-*dependence.* From the results (Table 2) and the dissociation constants of the phenols it is concluded that the phenoxide ion is the reactive species.

(b) *Catalysis by* m-*dinitrobenzene.* The rate is of the first order in phenol, dependent on catalyst concentration and independent of oxygen pressure between 0·5 and 1 atm. (reactions 1 and 2):

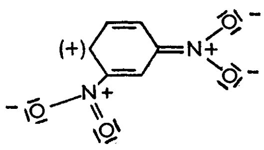
$$\mathrm{R^- + Catalyst \rightleftharpoons (R,\ catalyst)^-} \quad . \ . \ . \ . \ . \ . \ . \ . \ . \ . \quad (1)$$

$$\mathrm{(R,\ catalyst)^- + O_2 \longrightarrow RO_2^- + Catalyst} \quad . \ . \ . \ . \ . \ . \ . \ . \quad (2)$$

We have here a case of normal catalysis in which the catalyst and the substrate form a reactive intermediate. This intermediate is tentatively considered to be an electron donor–acceptor complex for which a structure (VIII) may represent one of the resonance hybrids. It is possible that in this way the phenol part of the molecule has a temporary free-radical character, permitting rapid reaction with oxygen. The interaction between phenol and catalyst has still to be proved, however. Some experiments have also been



(VIII)



carried out with 1,3,5-trinitrobenzene. Catalysis of the same order of magnitude as with *m*-dinitrobenzene was found, but the catalyst decomposes rapidly. Nitrobenzene is inactive.

Catalysis by quinones. Quinones were the most active catalysts. As with the nitro-compounds, the quinones partially decompose during the autoxidation. With 2,6-di-t-butylquinone the rate is independent of catalyst concentration (from 5% onward) and proportional to the oxygen pressure. Although this phenomenon, called saturation of catalysis, is also known in oxidation of quinol, an explanation similar to that given by Luvalle and Weissberger [10] is very improbable in the autoxidation of monohydric phenols.* At present it is preferable to explain the experimental results formally by equations 3 and 4:

$$R^- + O_2 \rightleftharpoons (R^-,O_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$(R^-,O_2) + \text{Catalyst} \xrightarrow[\text{fast}]{} RO_2^- + \text{Catalyst} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

It is not yet possible to prove such an interaction with oxygen prior to the actual oxidation step in this system owing to the decomposition of the catalyst mentioned earlier.

The kinetics obtained with duroquinone catalyst are in agreement with the scheme given for 2,6-di-t-butylbenzoquinone. The rate constant is somewhat lower and there is some dependence on the catalyst concentration, indicating that reaction (4) is contributing to the rate-determining step. In accordance with expectation, the rate observed with a mixture of duroquinone and 2,6-di-t-butylbenzoquinone is equal to the rate found with the latter alone.

(d) *Properties of the hydroperoxides.* The isomerization and decomposition of the hydroperoxides are considered to be a sequel to the autoxidation of the phenols, resulting, among other things, in the formation of the active catalyst mentioned above.

(e) *Oxidation of* 2,6-*di-t-butylphenol.* The formation of 3,3′,5,5′-tetra-t-butyldiphenoquinone on autoxidation of 2,6-di-t-butylphenol might indicate that a radical chain mechanism is more likely in this case. Indeed, the rate of oxidation of a mixture of this phenol and the antioxidant 4-methyl-2,6-di-t-butylphenol is smaller than the sum of the components.

The kinetics of oxidation when the peroxide (III) is used as a catalyst are rather involved. The Arrhenius energies of activation found for the various reactions are given in Table 3.

TABLE 3. *Energies of activation of alkaline oxidation of* 4-*methyl*-2,6-*di-t-butylphenol.*

Catalyst	*E* (cal./mole)	log *A* (min.$^{-1}$)
2,6-Di-t-butylbenzoquinone	12,000	9·25
m-Dinitrobenzene (20 mg./mmole)	8900	5·43
m-Dinitrobenzene (50 mg./mmole)	9400	5·49
Nil	20,000	

EXPERIMENTAL

With W. ROEST and (MISS) J. VERHEY.

Starting Materials.—2,4,6-Tri-t-butylphenol, obtained by alkylation of phenol with t-butyl alcohol and sulphuric acid at 70°, had m. p. 130°.

* They assume interaction between the semiquinone radical-ion and quinone. As no free phenoxy-radicals can be detected in phenol autoxidation, we assume that the complex between phenol and quinone exists until after the oxidation, thus rendering an interaction with another quinone molecule unlikely.

4-Methyl-2,6-di-t-butylphenol (II) of technical quality was recrystallized several times from methanol and light petroleum ether (b. p. 60—80°); it then had m. p. 71·0°.

2,6-Di-t-butylphenol, obtained by alkylation of phenol with t-butyl alcohol and aluminium phenoxide, had m. p. 38°.

Ethanol was purified by Pestemer's procedure.[11]

Preparation and Decomposition of Hydroperoxides.—4-*Hydroperoxy*-4-*methyl*-2,6-*di-t-butylcyclohexa*-2,5-*dienone* (IV). A solution of 4-methyl-2,6-di-t-butylphenol (1 mmole) in a N-solution (25 ml.) of potassium hydroxide in 90% ethanol absorbed 1 mmole of oxygen in 5 min. at 40°. The mixture was then acidified and the products were extracted with ether. After recrystallization from light petroleum (b. p. 60—80°) the *hydroperoxide* was obtained (75% yield) with m. p. 115° (Found: C, 71·1; H, 9·6%; *M*, 274. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%; *M*, 253). Hydroperoxide analysis by Tobolsky and Mesrobian's method [12] showed the presence of one atom of active oxygen per molecule (equiv., 127). The product obtained after reduction is the alcohol (V), m. p. 113° (Found: C, 75·9; H, 10·5. Calc. for $C_{15}H_{24}O_2$: C, 76·2; H, 10·2%).

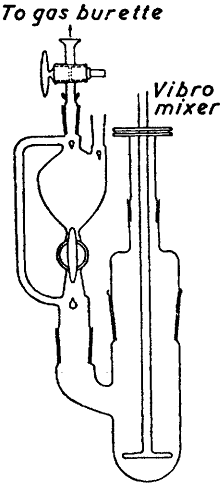


FIG. 2. *Oxidation vessel with Vibro mixer.*

Hydroperoxides from Tri-t-butylphenol.—Reaction with oxygen as described above also yielded 75% of peroxidic material. After preparation of about 20 g. of this material it was possible to obtain the hydroperoxides (II) and (III) (Found, for both compounds: C, 73·8; H, 10·5. Calc. for $C_{18}H_{30}O_3$: C, 73·5; H, 10·2%) by careful fractional crystallization from nitroethane and mesityl oxide with continuous checking by ultraviolet spectroscopy.

The alcohol (VII) obtained on reduction of the peroxide (II) had m. p. 126—130°.

Ultraviolet Absorption Spectra.—These were generally measured for iso-octane solutions with a Cary recording spectrophotometer Model 14 M.L.S.-50.

Kinetic Measurements.—Most of the kinetic measurements were carried out in the apparatus shown in Fig. 2. This apparatus was connected to a gas-burette in which the quantity of oxygen consumed was measured. Measurements at constant volume were carried out in a completely closed system in which differences in pressure were read with a cathetometer. By using a relatively large gas volume the total difference in pressure was always kept below 20 mm. In this way the reaction took place at practically constant total pressure, while the accurate cathetometer readings were used to measure the reaction velocity. Results are shown in Tables 1 and 2. For the reactions without added catalyst the maximum velocity is given. The reactions where a catalyst was added at the start of the reaction were often of first order in phenol concentration, and this constant is given. In other cases the oxygen uptake during the first two minutes is quoted. The reaction mixture was generally analyzed by titration and ultraviolet spectroscopy. The method for calculating the rate constant must be carefully selected, since two possible errors may be introduced when only the oxygen consumption is determined. In the first place, there is a volume effect when the phenol and hydroxide solutions are mixed. This is probably due to the finite time necessary for mixing. We assume that the oxygen consumed during this time has indeed reacted. In the second place, side reactions which consume or liberate oxygen contribute to the calculated phenol consumption. We tried to avoid these errors by using Guggenheim's method for the calculation of first-order rate constants. The results were, however, unsatisfactory, probably because this method attaches relatively more weight to the later stages of the reaction just when side reactions become more important. Calculation of the rate constant based on the actual volume of oxygen taken up during the reaction proved to be the best method.

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[*Received, April* 21*st*, 1958.
Revised, February 25*th*, 1959.]

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