454. *Autoxidation of Hindered Phenols in Alkaline Media. Part II.*[1]

By H. R. Gersmann and A. F. Bickel.

The autoxidation of 4-methyl-2,6-di-t-butylphenol and 2,4,6-tri-t-butylphenol in 1 : 1 t-butyl alcohol–1,2-dimethoxyethane containing potassium butoxide as a base has been studied. The hydroperoxycyclohexadienones are obtained in high yields in fast bimolecular reactions of the aryloxide anion and oxygen. Differences from the reaction in 90% ethanol (Part I) are discussed.

Details of the decomposition of hydroperoxide (II; R = Me) in alkaline medium under nitrogen are presented. The mechanism of the main reaction, namely, the formation of the phenol (I; R = Me) and oxygen, is closely related to that of the oxidation.

An investigation of the autoxidation of several other alkylphenols in alkaline medium showed that a qualitative correlation exists between oxidizability and steric hindrance of solvation. A measure for this property was obtained by determining the association constant of the phenols and acetone by infrared spectroscopy.

In Part I[1] we reported on the autoxidation of various hindered phenols in alkaline 90% ethanol. It appeared that phenols such as (I) are oxidized to hydroperoxides (II) and (III) in an autocatalytic process.

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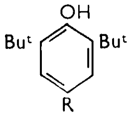
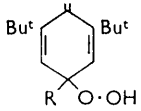
[1] Part I, Gersmann and Bickel, *J.*, 1959, 2711.

We have now obtained results on the oxidation in non-aqueous alkaline systems (specifically potassium t-butoxide in 1 : 1 t-butyl alcohol–1,2-dimethoxyethane) which probably are also pertinent to the initiation reaction preceding autocatalysis in 90% ethanol.



(I)



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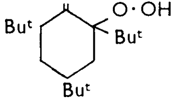

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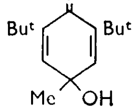

(IV)

Additional results are presented on the decomposition of the hydroperoxide (II; R = Me) in nitrogen-flushed alkaline solution, yielding the phenol (I; R = Me).

In order to shed more light on the question why autoxidizability of phenols is restricted to those compounds having two *o*-t-butyl groups, phenols with other substituents have been investigated.

Autoxidation in Non-aqueous Media.—Since ketones can be very effectively oxidized in solutions of potassium t-butoxide in t-butyl alcohol[2,3] we have investigated the efficiency of this system for phenols. Autoxidation rate constants were calculated from the oxygen consumption as a function of time. The results are summarized in Table 1.

It appeared that autoxidation of the phenols (I; R = Me and Bu^t) was much faster than in 90% ethanol containing potassium hydroxide (cf. experiments 7 and 8). No induction period is observed and the yield of hydroperoxide is much higher,* probably owing to the low temperature and short reaction time. The reaction, in every run, was first-order in phenoxide ion up to 80% conversion.† It was further first-order in oxygen pressure (experiments 3, 4, and 5) and equally as susceptible to catalysis by 2,6-di-t-butylbenzoquinone and *m*-dinitrobenzene as the oxidation in 90% ethanol.

TABLE 1.

Autoxidation of the phenol (I; R = Me) (0·5—1·0 mmole/30 ml.).

Exp. no.	Molarity of base	Solvent	O_2 pressure (mm.)	Temp.	Rate constant k_1 (min.$^{-1}$) ‡
1	0·10	A	76	25°	0·92
2	0·10	A	76	0	0·12
3	0·25	A	76	0	0·12
4	0·25	A	53	0	0·075
5	0·25	A	34	0	0·052
6 *	0·10	A	76	0	0·644
7 †	0·10	A	76	0	0·253
8 †	0·10	90% EtOH	76	0	0·0024 §
9	0·10	100% MeOH	76	0	0·0005 §

A = 1 : 1 t-Butyl alcohol–1,2-dimethoxyethane. * 2,6-Di-t-butylbenzoquinone (20 mg.) added. † *m*-Dinitrobenzene (20 mg.) added. ‡ Pseudo-first-order rate constant at the given oxygen pressure. § Initial rates.

These results point to a fast bimolecular reaction of phenoxide ion and oxygen: $R^- + O_2 \longrightarrow RO{\cdot}O^-$.‡ The fact that the pseudo-first-order rate constant for the oxidation of the phenol (I; R = Me) increases very slowly during each run indicates that the autocatalytic process is contributing increasingly as the reaction proceeds.§

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* In experiment 2 the yield of hydroperoxide (II; R = Me) was 85%, as determined by active oxygen titration. The yields in comparable experiments in 90% ethanol were ~74%. In a large-scale experiment under the conditions mentioned for experiment 3, 60% of pure recrystallized hydroperoxide was obtained.

† A large excess of base is always present.

‡ This reaction is of theoretical interest since it involves spin conversion, which is seldom observed.

§ With the phenol (I; R = Bu^t), which yields a much larger proportion of the catalytically active *o*-hydroperoxide than I (R = Me), the rate constant increases in a more pronounced manner in the course of an experiment.

[2] Doering and Haines, *J. Amer. Chem. Soc.*, 1954, **76**, 482.

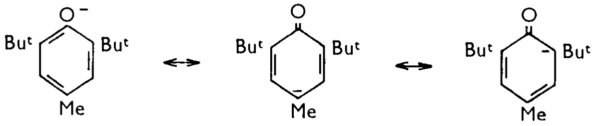
[3] Elkik, *Bull. Soc. chim. France*, 1959, 933.

It is thought that the phenoxide ion also reacts directly with oxygen, but much more slowly, in 90% ethanol, thus giving rise to the small amounts of hydroperoxide which are the precursors of the autocatalysts of *ortho*-quinone type.

Our hypothesis, advanced in Part I, that these *o*-quinones (III) are the actual oxidation catalysts is consistent with the finding that 4,6-di-t-butyl-1,2-benzoquinone is a powerful catalyst in the oxidation of our phenols. Conradi and McLaren[4] support the suggested mechanism by electron-spin resonance measurements of autoxidizing solutions of the phenol (I; R = Me).

The much higher rate of autoxidation of the potassium t-butoxide solution than of the ethanol solution (cf. experiments 7 and 8) is due in part to the higher basicity of the former solvent. Here, the phenol is obviously completely ionized (cf. experiments 2 and 3), whereas in 90% ethanol, at pH 13, the compound (I; R = Me) is dissociated to the extent of only 20%.

In addition to this effect, differences in solvation may play a role. The relative contribution of the " oxide " anion structure to the resonance hybrid may be much less in t-butyl alcohol than in 90% ethanol, since solvation (hydrogen-bond formation) of this structure with t-butyl alcohol is sterically impossible. The higher rate may thus be partly attributed to the increased contribution of the annexed " carbanion " structures.



The primary importance of the size of the solvent molecules is confirmed by the slow oxidation observed with potassium methoxide in 100% methanol (cf. experiment 9).

Decomposition of Hydroperoxides (II).—In Part I it was mentioned that the hydroperoxides (II) may isomerize as well as decompose in alkaline media. Particularly interesting is the decomposition of the compound (II; R = Me) under nitrogen which yields, in addition to the alcohol (IV), the original phenol (I; R = Me). Closer investigation of this reaction revealed that the yield of phenol and oxygen can be raised to ~70% by bubbling an inert gas (nitrogen or argon) through the solution of the decomposing hydroperoxide ($RO{\cdot}O^- \longrightarrow R^- + O_2$).

The kinetics of the reaction were studied in 50% aqueous t-butyl alcohol. In order to obtain reproducible results the following precautions were taken: (1) A certain minimum velocity of inert gas was maintained. (2) A hydroperoxide sample was used which on further crystallization gave no change in rate of decomposition. (3) Potassium cyanide was added to avoid catalysis by traces of heavy-metal ions. The results are shown in Table 2.

TABLE 2.

Initial rate of decomposition of hydroperoxide (II; R = Me) in an alkaline medium.

(Substrate 40 mmoles/l.; pH 13; 1 : 1 t-butyl alcohol–water; potassium cyanide added; solution flushed with N_2.)

Temp.	Added substances	*k* (min.$^{-1}$)	Temp.	Added substances	*k* (min.$^{-1}$)
40°		0·006	50°	In oxygen current	0·023
50		0·021	50	*m*-Dinitrobenzene (10% on substrate)	0·074
60		0·072	50	2,6-Di-t-butylbenzoquinone (10% on substrate)	0·118
50	Cu versenate (no KCN)	0·040	50	No KCN	0·040

The reaction was approximately of the first order in hydroperoxide, small deviations occurring towards its end. The dependence on pH showed that the hydroperoxide anion is the reactive species. The same compounds which catalyze the oxidation of the phenols

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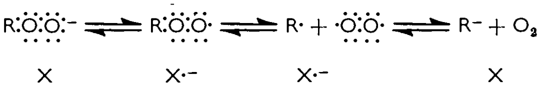
[4] Conradi and McLaren, *J. Amer. Chem. Soc.*, 1960, **82**, 4745.

are also active in the decomposition of the hydroperoxides, indicating that oxidation and reduction may proceed by way of the same intermediates. This may be pictured as follows:

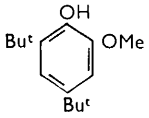


$$\underset{X}{R{:}\ddot{O}{:}\ddot{O}{:}^-} \rightleftharpoons \underset{X\cdot^-}{R{:}\ddot{O}{:}\dot{\ddot{O}}} \rightleftharpoons \underset{X\cdot^-}{R\cdot + \cdot\ddot{O}{:}\ddot{O}\cdot} \rightleftharpoons \underset{X}{R^- + O_2}$$

(X = catalyst)

Ready evolution of oxygen will probably be restricted to those cases where the resonance stabilization of R^- is large relative to that of $RO{\cdot}O^-$ (ketones and phenols). The hydroperoxide (II; R = Bu^t) shows similar decomposition reactions; the yields are, however, much lower.

Steric and Inductive Effects in the Oxidation of Phenols.—The autoxidation of most phenols is very slow in comparison with the reaction of 2,6-di-t-butyl-phenols. This difference will, at least in part, be due to steric factors, but we have to consider the possibility that inductive effects are also important. To study the effect of electron-donating groups in the benzene nucleus, 4-methoxy-2,6-di-t-butylphenol (I; R = OMe)



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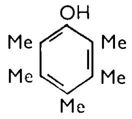

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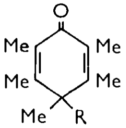

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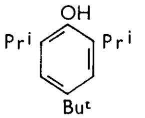

(VIII)

and 2-methoxy-4,6-di-t-butylphenol (V) were prepared. The former is autoxidized much faster than the methyl analogue (I; R = Me), which shows the rate-enhancing effect of the donating group. An unstable hydroperoxide (II; R = OMe) was isolated; it decomposes, especially in the presence of acid, mainly into 2,6-di-t-butylbenzoquinone. The rate of autoxidation of the phenol (V) is, however, very low and a hydroperoxide could not be obtained. These results confirm the view that the presence of bulky groups in the *ortho*-positions is the essential requirement for autoxidation of phenols in alkaline media, whilst charge effects are much less important.

Surprisingly, pentamethylphenol (VI) can be autoxidized, especially when duroquinone is added as a catalyst, although the reaction is slow. A hydroperoxide (VII; R = O·OH) and an alcohol (VII; R = OH) were isolated. Under the same conditions the autoxidation of 2,6-di-isopropyl-4-t-butylphenol (VIII) was very slow and the products remained undefined. If these results are attributed to steric factors only, the buttressing effect of five methyl groups appears to provide more steric hindrance than that of two isopropyl groups.

The observed steric effects on rate of oxidation may be interpreted in terms of steric hindrance of solvation. The association constants of several phenols with acetone (hydrogen-bond formation) were measured by infrared spectroscopy.* For the phenols (I; R = Me), (VI), and (VIII) these constants were found to be 0·19, 0·73, 4·7, respectively. Obviously, a correlation exists indicating that the oxidation is easier the more poorly solvated is the phenol. Solvation effects, measured for the molecule, will be even stronger for the phenoxide ion. Again (see above) poor solvation at the oxygen atom may lead to more pronounced carbanion character of the phenoxide ion and this should enhance oxidizability.

EXPERIMENTAL

(with J. SCHIPPERIJN)

Autoxidation rates were measured as described previously.[1]

Decomposition of 1-*Methyl*-4-*oxo*-3,5-*di*-*t*-*butylcyclohexadienyl Hydroperoxide* (II; R = Me).—The hydroperoxide (2 mmoles) was dissolved in 1 : 1 t-butyl alcohol–water (50 ml.) to

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* Infrared spectroscopic data will be published in full by Mr. W. Heinen of this laboratory.

which base had been added. Nitrogen (10 l./hr.), saturated with the solvent, was passed through the solution. To obtain maximum flushing the gas was dispersed in the solution by a vibromixer. After the reaction vessel had been placed in a thermostat-bath, the outcoming gas was analyzed for oxygen with a Beckman oxygen analyzer, the total amount of gas being measured with a gas meter. In this way, the total oxygen and the rate of oxygen evolution were measured. The rate constants, calculated in this way, agreed well with those determined by iodometric titration of the hydroperoxide.

Syntheses of 1-*Methoxy*-4-*oxo*-3,5-*di*-*t*-*butylcyclohexadienyl Hydroperoxide* (II; R = OMe) *from the Phenol* (I; R = OMe).—The method was as described earlier for the hydroperoxide (II; R = Me).[1] Autoxidation was, however, carried out at 0°. Care must be used when acidifying after autoxidation. The temperature should be kept at 0° and the hydroperoxide must be quickly extracted with ether. Recrystallization from pentane gave the *hydroperoxide* (55%), m. p. 84—86° (Found: C, 67·8; H, 8·8. $C_{15}H_{24}O_4$ requires C, 67·2; H, 9·0%). An active-oxygen titration gave *M*, 268; cryoscopy gave 281 (calc., 268). The structure was confirmed by ultraviolet spectroscopy.

Hydroperoxide from Pentamethylphenol (VI).—Autoxidation was carried out at 30° and pH 14, in ethanol containing 10% of water. Duroquinone was added as catalyst gradually (total amount, ~10% of the phenol). The crude mixture contained about 47% of hydroperoxide (titration). By careful crystallization from ether, 1,2,3,5,6-*pentamethyl*-4-*oxocyclohexadienyl hydroperoxide* (VII; R = O·OH), m. p. 108—110°, was obtained in small yield (Found: C, 67·3; H, 8·3. $C_{11}H_{16}O_3$ requires C, 67·1; H, 8·2%); active-oxygen titration gave *M*, 196 (calc., 196).

The reaction mixture afforded also 4-*hydroxy*-2,3,4,5,6-*pentamethylcyclohexa*-2,5-*dienone* (VII; R = OH), m. p. 137—138° (30% yield) [Found: C, 72·6; H, 9·2%; *M* (mass spectroscopy) 180, (ebullioscopy) 187. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%; *M*, 180].

The structures are supported by ultraviolet spectroscopy.

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