Oxidizing Action of Hydroperoxides. IV. On the Oxidation of Aryl Alkyl Ketones

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This research was started with a view to studying the liquid phase autoxidation of *p*-cymene some years ago. In the liquid phase autoxidation of *p*-cymene in the presence of alkali hydroxide, no resinous product was produced and 8-hydroxy-*p*-cymene, cumic acid and *p*-toluic acid were found, accompanied by a negligibly small amount of *p*-methylacetophenone — an interesting contrast to the autoxidation in the absence of alkali hydroxide. From the studies on the autoxidation of some hydrocarbons, it was observed[1] that alkylhydroperoxides act as a strong oxidizing agent on alkylbenzene and also on some carbonyl compounds*, e. g., the primary carbon atom at α-position of the side chain is oxidized to alcohol, to aldehyde and finally to carboxylic acid, the secondary carbon is oxidized to carbonyl group and finally decomposes to yield a mixture of acids and the tertiary carbon atom is oxidized to alcohol and/or decomposes to ketone having a fewer number of carbon atoms. Especially, aryl alkyl ketones are easily split by these oxidizing agents into aromatic carboxylic acid and aliphatic alcohol. Further, in all these oxidation reactions, in contrast to peracid oxidation, no phenolic substances are produced. Also diaryl ketones are not affected by these oxidizing agents — an outstanding difference as compared with the case of the cleavage of ketones by peracids** —, whereas aryl alkyl ketones are affected with great ease. In this paper are reported only the oxidation of aryl alkyl ketones.

Experimental

Materials. — *p*-Methylacetophenone was prepared by the action of acethyl chloride on toluene using anhydrous aluminium chloride as a catalyst. The resulting *p*-methylacetophenone was distilled under reduced pressure using Hempel's column, b. p. 94~95°C/12 mmHg: semicarbazone, m. p. 205°C. Propiophenone was prepared by the action of propionyl chloride on benzene suspending anhydrous aluminum chloride. The resulting propiophenone was completely freed from aluminum ions by shaking with acid and alkali, and was distilled under reduced pressure. B. p. 105°C/20 mmHg, m. p. 21°C. *tert*-Butyl phenyl ketone was synthesized from isopropyl phenyl ketone, following Halle's method[2]. B. p. 220~222°C, 104~106°C/17 mmHg, 2, 4-dinitrophenylhydrazone; m. p. 166~168°C. Benzophenone was prepared by the action of benzoyl chloride on benzene suspending anhydrous aluminum chloride. M. p. 47~48°C. Fluorenone was synthesized by the oxidation of commercial grade fluorene, following Fanto's method[3]. M. p. 83~84°C. *p*-Nitrobenzophenone was synthesized by the action of *p*-nitrobenzoyl chloride on benzene suspended with anhydrous aluminum chloride, following Schroeter's method[4]. M. p. 138°C. *tert*-Butylhydroperoxide was synthesized by the action of 30% hydrogen peroxide on *tert*-butanol, following Milas and Surgenor's method[5]. The obtained mixture of *tert*-butylhydroperoxide and di-*tert*-butylperoxide was fractionally distilled under reduced pressure. For the purpose of obtaining highly purified hydroperoxide, this process was repeated four times. B. p. 36°C/19 mmHg. n_D^{27}: 1.3967. Cumylhydroperoxide was synthesized by the autoxidation of cumene, following Armstrong, Hall and Quin's method[6]. The obtained cumylhydroperoxide was purified by the fractionation under a high vacuum. B. p. 53~54°C/0.0005 mmHg.

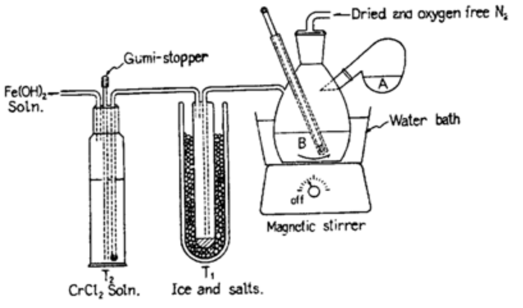

Fig. 1. Reaction apparatus.

Reaction Apparatus and Procedure.—The reaction apparatus is shown in Fig. 1. Ketone, monochlorobenzene and finely powdered analytical grade

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1) Unpublished work.

* M. S. Kharasch et al. reported that alkylhydroperoxides act as an oxidizing agent on the primary as well as secondary alcohols in alkaline solution (*J. Org. Chem.*, 17, 207 (1952).

** W. H. Saunders, *J. Am. Chem. Soc.*, 77, 4679 (1957); W. v. E. Doering and E. Dorfman, ibid., 75, 5595 (1953); W. G. Dauben and E. Hoerger, ibid., 73, 1504 (1951), etc.

2) M. A. Haller and Ed. Bauer, *Compt. rend.*, **148**, 72 (1909).

3) R. Fanto, *Monatsh.*, **19**, 584 (1898).

4) G. Schroeter., *Ber.* **42**, 3360 (1909).

5) N. A. Milas and D. Surgenor, *J. Am. Chem. Soc.*, **68**, 1938 (1946).

6) G. P. Armstrong, R. Hall and D. C. Quin, *Nature*, **164**, 834 (1949).

potassium hydroxide were charged in B and hydroperoxide in A. After the air in the reaction vessel (A and B) was substituted completely with dried and purified nitrogen gas and the temperature of the reaction mixture was made to reach 80°C, and then the hydroperoxide was poured into the reaction mixture by rotating the part A by hand. A flow of the nitrogen gas was maintained constantly to 30 cc./min. during the reaction. A vigorous reaction occurred and the temperature of the reaction mixture was raised to about 90°C. Trap T_1 was cooled with ice and salt for condensing therein low boiling substances. The oxygen evolved during the reaction was determined at Trap T_2 charged with chromous chloride hydrochloric acid solution[7].

Oxidation.—*Acetophenone.*—10 g. of acetophenone were dissolved in 150 cc. monochlorobenzene in which 1.3 g. of finely powdered special grade potassium hydroxide were suspended. As an oxidizing agent, 2.0 g. of *tert*-butylhydroperoxide were used. The reaction mixture was agitated by a magnetic stirrer. After the temperature of the reaction mixture reached 80°C, A was gradually rotated to pour the peroxide into B. Then, a vigorous reaction occurred and a white precipitate appeared immediately. Almost all the peroxide was decomposed in the first hour, but about 6 hr. were required to complete the decomposition. After the end of the reaction, the reaction mixture was extracted with a total of 300 g. of water three times. The water extract was acidified with 2 N sulfuric acid and the precipitated benzoic acid was collected, dried and weighed. The filtrate was neutralized with concentrated ammonia water and concentrated to 10 cc., and then subjected to a paperchromatographic analysis. However, no appreciable amount of formic acid was observed. The substances condensed in Trap T_1 were gaschromatographically tested and methanol and *tert*-butanol were found to be the main components.

p-Methylacetophenone. — 50 g. of *p*-methylacetophenone suspending 1.3 g. of finely powdered potassium hydroxide were charged in B. As an oxidizing agent, 2.0 g. of *tert*-butylhydroperoxide were used. The reaction procedure was in manner similar to that of the acetophenone. The water extract was acidified. Then, *p*-toluic acid was the main reaction product. *p*-Acetylbenzoic acid and formic acid were paperchromatographically detected in the filtrate, but the amounts of acids were too small to be estimated. *p*-Toluic acid (m. p. 176°C) was confirmed by recrystallization and paperchromatography. The condensate of the Trap T_1 was analyzed gaschromatographically to find methanol and *tert*-butanol as the main components.

Propiophenone.—10 g. of propiophenone were dissolved in 150 cc. monochlorobenzene in which finely powdered 1.7 g. potassium hydroxide suspended. As an oxidizing agent, 2.0 g. of *tert*-butylhydroperoxide were used. After the temperature of the reaction mixture reached 80°C, A was rotated to pour the peroxide into the mixture and a vigorous reaction took place. Then the temperature of the reaction mixture reached as high as 95°C in a few minutes. Almost all the amount of the peroxide was decomposed in the first half hour, but the reaction continued for 6 hr. to complete the decomposition of the peroxide. The water extract was acidified with 2 N sulfuric acid and the acid precipitated was filtrated, dried and weighed. The filtrate was steamdistilled. Acetic acid was found in the distillate. This was estimated by titration. The acetaldehyde and acetone were also detected as 2,4-dinitrophenylhydrazone on a silicagel chromatostrip, but not estimated. From the condensate in Trap T_1, ethanol, *tert*-butanol and methanol were respectively detected gaschromatographically (see Fig. 2), but not estimated. A trace of oxygen was detected in Trap T_2.

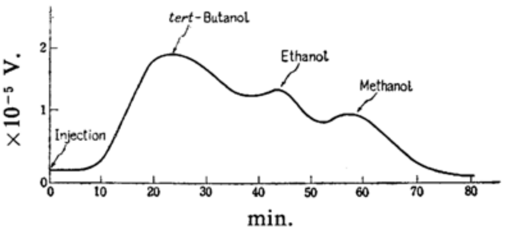

Fig. 2. Gaschromatographic analysis of oxidation products of propiophenone.
Propiophenone $\xrightarrow{tert\text{-}C_4H_9OOH,\ KOH}$ Products
Condition : Sample used : 0.02 ml.
Column temp. : 83°C
Flow rate : N_2 40 ml./min.
Column : Glycerol-Kunirait (20 : 100 w/w)

tert-Butyl Phenyl Ketone.—Eight grams of *tert*-butyl phenyl ketone were dissolved in 150 cc. monochlorobenzene suspending 2.8 g. of finely powdered potassium hydroxide. As an oxidizing agent, 10g. of cumylhydroperoxide were used. Cumylhydroperoxide was used to afford facilities for an analysis of low boiling substances, because thermal decomposition products of cumylhydroperoxide will be methanol, aceto-

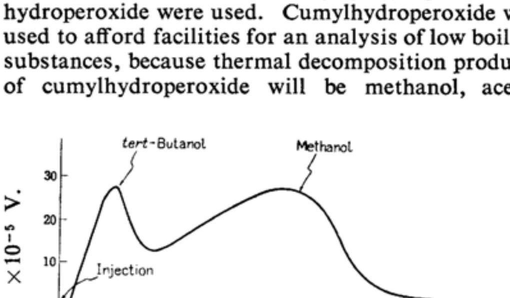

Fig. 3. Gaschromatographic analysis of oxidation products of *tert*-butylphenylketone.
tert-Butylphenylketone $\xrightarrow[KOH]{cumylhydroperoxide}$ products
Condition : Sample : 0.03 ml.
Column temp. : 85°C.
Flow rate : N_2 60 ml./min.
Column. : Glycerol-Kunirait (20 : 100 w/w)

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[7] J. Meis, *Chem. Abstr.*, 8748*d* (1955); H. Karl, *Paliva*, **35**, 8 (1955); *Chem. Abstr.*, 13019*g* (1955); von Pferdton, *Ann.*, **228**, 112 (1885).

TABLE I. OXIDATION OF KETONES BY HYDROPEROXIDES AT 80°C, 6 hr.

Ketone	g.	Hydroperoxide	g.	Recovered ketone g.	Reaction products, g.		Oxygen
					Acid	Alcohol	
Acetophenone	10	*tert*-Butyl	2.0	9.1	Benzoic acid 0.50	(*tert*-Butanol), methanol	None
〃	10	*tert*-Butyl	2.0	8.5	Benzoic acid 0.71	(*tert*-Butanol), methanol	None
p-Methyl-acetophenone	50	*tert*-Butyl	2.0	45	*p*-Toluic acid 1.0, *p*-acetylbenzoic acid (trace), formic acid (trace)	(*tert*-Butanol),	None
〃	50	*tert*-Butyl	2.0	42	*p*-Toluic acid 1.5, *p*-acetylbenzoic acid (trace), formic acid (trace)	(*tert*-Butanol), methanol	Trace
Propiophenone	10	*tert*-Butyl	2.0	8.3	Benzoic acid 1.13, acetic acid 0.34, formic acid (trace)	(*tert*-Butanol), ethanol, methanol	None
Propiophenone	17	*tert*-Butyl	2.0	—	Benzoic acid 1.13, acetic acid —, formic acid (trace)	(*tert*-Butanol), ethanol, methanol	None
tert-Butylphenyl ketone	10	Cumyl	10	9.5	Benzoic acid 2.5	(*tert*-Butanol), methanol, (α,α-dimethyl-benzylalcohol)	None
tert-Butylphenyl ketone	0.5	*tert*-Butyl	1.0	—	Benzoic acid 0.05	(*tert*-Butanol), methanol	Trace
Benzophenone	10	*tert*-Butyl	2.0		None reaction		O_2-evolute
p-Nitrobenzo-phenone	10	*tert*-Butyl	2.0		None reaction		O_2-evolute
Fluorenone	10	*tert*-Butyl	2.0		None reaction		O_2-evolute

(*tert*-Butanol and α,α-dimethylbenzylalcohol are reduction products of *tert*-butylhydroperoxide and cumylhydroperoxide.)

phenone and α,α-dimethylbenzylalcohol, if the thermal decomposition would occur. On the other hand, the reduction product which could be expected through the reduction of cumylhydroperoxide by ketone, is α,α-dimethylbenzylalcohol. Treatment of the reaction mixture was almost the same as in the case of propiophenone. From the water extract was obtained benzoic acid which was confirmed by recrystallization and paperchromatography. *tert*-Butanol was detected and estimated as the main component of low boiling substances condensed in the Trap T_1. This was confirmed as phenylurethane (m. p. 136°C; Found: C, 67.4; H, 7.4. Calcd. for $C_{11}H_{16}O_2N$: C, 68.3; H, 7.7%) and also gaschromatographic analysis was made. Besides *tert*-butanol, a small amount of methanol was also found.

Benzophenone, p-Nitrobenzophenone and Fluorenone. —10 g. of each of all the ketones were dissolved separately in 100 cc. monochlorobenzene in which 2.8 g. of finely powdered potassium hydroxide were suspended. 5 g. of *tert*-butylhydroperoxide were used as an oxidizing agent. Oxidation was carried out in the same apparatus as shown in Fig. 1. After the reaction had finished, the same procedure as before was repeated. None of the oxidation products of the ketones was found and the greater part of unchanged ketones were completely recovered during the reaction. Only oxygen—one of the decomposition products of the hydroperoxide—evolved vigorously in all the cases. *tert*-Butanol, acetone and methanol—the remaining decomposition products of the hydroperoxide itself—were found in the reaction mixture. The experimental results were summarized in Table I.

Discussion

It is likely that for the oxidizing action of hydroperoxides their anions are responsible, because the hydroperoxides themselves can cleave aryl alkyl ketone very slowly or can not do so at all in the absence of alkali hydroxide. Furthermore, in the course of oxidation of alkylbenzenes[8] (*p*-xylene, cumene, ethylbenzene, *p*-cymene and tetralin) by alkali hydroperoxide, the author has observed that potassium hydroxide suspended in alkylbenzene at the beginning of the reaction dissolves nearly completely after the hydroperoxide added and then the oxidation occurs immediately. The alkylbenzenes are oxidized to alcohols, ketones and carboxylic acids. In contrast to this, hydroperoxide alone can not oxidize a side chain of the alkylbenzene in the absence of alkali hydroxide. It may, therefore, be induced

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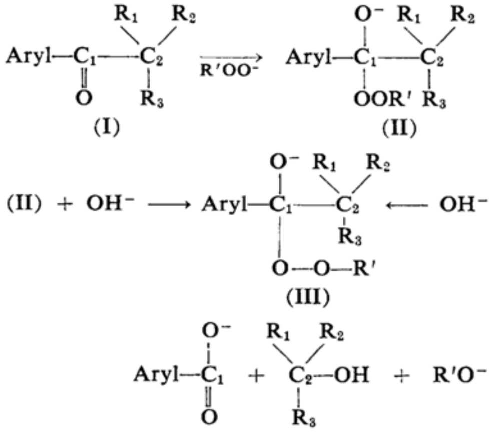
[8] K. Maruyama and R. Goto, *Wood Research*, **21**, 12 (1959).

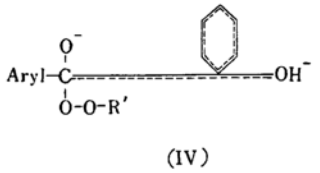
that the anion of hydroperoxide acts as an oxidizing agent. Kharasch et al.[9] asserted that the anion of hydroperoxide is an oxidizing agent in the oxidation of alcohol by hydroperoxide in alkaline solution.

In the oxidation of the above aryl alkyl ketones, the first oxidation products are arylcarboxylc acid and aliphatic alcohol. For example, when propiophenone is oxidized in the above conditions, benzoic acid, ethanol, acetaldehyde and acetic acid are obtained, and it may be seen easily that the latter two products are the second oxidation products. *tert*-Butyl phenyl ketone is also decomposed to benzoic acid and *tert*-butanol (peroxide used, cumylhydroperoxide). Oxidation of both acetophenone and *p*-methylacetophenone yields benzoic acid, *p*-toluic acid and methanol as the main reaction products. However, the methanol provides no direct evidence of alcoholic cleavage originating in the methylgroup of acetophenone or *p*-methylacetophenone, because methanol can be a thermal decomposition product of *tert*-butylhydroperoxide. In spite of the above misgivings, it may be possible to deduce that the methanol would be a cleavage product of acetophenone and also of *p*-methylacetophenone from the estimation of the results of cleavage of propiophenone and *tert*-butyl phenyl ketone; that is, the propiophenone produces ethanol and the *tert*-butyl phenyl ketone produces *tert*-butanol. On the other hand, it seems reasonable to deduce from the experimental results of benzophenone, *p*-nitrobenzophenone and fluorenone that in general diaryl ketones resist the oxidizing agent. This is noticeably different from the cleavage of ketones by peracids, because diaryl ketones are easily cleft by peracids—e. g., peracetic acid—to produce phenols and carboxylic acids[10]. In the cleavage of alkyl aryl ketones by peracids with the exception of cycloalkyl aryl ketones[11], a migration of the aryl group generally occurs, resulting in the formation of phenol.

On the contrary, acetophenone, *p*-methylacetophenone, propiophenone and *tert*-butyl phenyl ketone do not undergo such a cleavage as to yield phenols and carboxylic acids as anticipated from the phenolic cleavage of ketones, that is, the C–C linkage between the carbon atom of benzene and the carbonyl carbon atom resists the attack of hydroperoxide anion and the C–C linkage between the carbonyl carbon atom and the alkyl carbon atom is selectively attacked. For the above reasons, it may be assumed that the oxidation mechanism of ketones by hydroperoxide anion must be kept separated from that of ketones by peracids. Recently, House et al.[12] have reported the cleavage of ketones by alkaline hydrogen peroxide with a poor yield. Based upon the fact that butyrophenone does not cleave to phenol and butyric acid but does cleave to benzoic acid and propionic acid and/or corresponding propanol, they suggest a partly revised oxidation mechanism based on the peracid oxidation mechanism. However, the oxidation mechanism imagined by them hardly explains the results obtained by the present author in the oxidation of diaryl ketones. The author proposes a new oxidation scheme as follows:



In the above assumption, hydroxide anion plays in III a most important role, that is a " pushing action " which is indispensable to the cleavage of ketones. In the case of action of hydroperoxide anion to diaryl ketones resulting in no cleavage, the pushing action of hydroxide anion on C_2 which is the benzene ring carbon atom, would not effectively affect it owing to the high potential energy of the transition state represented by IV.



(IV)

Moreover, the fact that with aromatic halides the S_N2 type substitution reaction can not easily proceed appears to support a new mechanism, mentioned above. In future, the author has the intention to perform an experiment of oxidation of ketones having an asymmetric carbon atom at C_2.

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[9] M. S. Kharasch et al., *J. Org, Chem.*, **17**, 207 (1952).

[10] W. H. Saunders, *J. Am. Chem. Soc.*, **77**, 4679 (1957).

[11] S. L. Fries and N. Farnham, ibid., **72**, 5518 (1950).

[12] H. O. House and R. L. Wasson, *J. Org. Chem.*, **22**, 1157 (1957).

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