Oxidizing Action of Hydroperoxides. V. On the Oxidation of Ketones

By Kazuhiro MARUYAMA

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In the previous paper of this series[1], it has been reported that hydroperoxides have a strong oxidizing action cooperating with alkali hydroxides. For example, alkylbenzenes are oxidized to the corresponding alcohols, ketones and carboxylic acids. Further, alkyl aryl ketones are split very smoothly to benzoic acid derivatives and alcohols,—but diaryl ketones are not cleft by these oxidizing agents[2]. Furthermore, in order to obtain more extensive knowledge of the reaction, the same kinds of reactions were examined on some ketones; isopropyl phenyl ketone, cyclohexyl phenyl ketone *p*-chloroacetophenone, desoxybenzoin, phenyl *p*-chlorobenzyl ketone, benzoin, benzil, α-tetralon, 3-pentanone, 3-heptanone and cyclohexanone were examined. All these reactions were performed in nonaqueous solvent and the examined ketones were also cleft smoothly with the one exception of cyclohexanone. An outstanding difference between this cleavage reaction mechanism and the Baeyer-Villiger mechanism is that any C–C linkage between carbonyl carbon and aromatic carbon in alkyl aryl ketones, is never attacked.

Experimental

Reagents.—The reagents cited in Table I were synthesized by the Friedel-Crafts reaction.

Benzoin was prepared by condensation of benzaldehyde, m. p. 137°C; semicarbazone, m. p. 206°C. Benzil was prepared by nitric acid oxidation of benzoin, m. p. 95°C. α-Tetralon was synthesized from tetralin after Thompson's method, checked by Shriner and Poland[3], b. p. 107°C/2 mmHg, n_D^{15}, 1.5640; semicarbazone, m. p. 217°C. 3-Pentanone and 3-heptanone, the commercially available guaranteed grade reagent was used without further purification. *tert*-Butylhydroperoxide was snythesized by the action of 30% hydrogen peroxide on *tert*-butanol according to Milas and Surgenor's method[4] and purified by fractional distillation under reduced pressure. B. p. 36°C/19 mmHg, n_D^{27} : 1.3967. Cyclohexanone, the commercially available guaranteed grade reagent was treated with potassium permanganate and was purified by distillation. b. p. 157°C, Semicarbazone, m. p. 155°C.

Reaction Procedure.—The reaction apparatus and the treatments of reaction mixture are quite the same as that described in the previous paper[2]. With the exception of the case with benzil and α-tetralon the experiment was conducted as following.

The weighed ketone was dissolved in purified monochlorobenzene (150 cc.). Carbonate free powdered potassium hydroxide was added to the mixture after the air in the reaction vessel was completely exchanged with dry pure nitrogen. As soon as the temperature of the reaction mixture reached 70°C, *tert*-butylhydroperoxide was added. The temperature raising of about 10°C was observed. After six hours, the reaction mixture was extracted with 100 g. of water three times. The water extract was acidified with 2 N-sulphric acid and the precipitated benzoic acid derivative was collected and weighed. The filtrate was neutralized with conc. ammonia

TABLE I

Ketones	(B. p.) or [m. p.] °C	n_D^{15}	Semicarbazones m. p., °C	Oxime m. p., °C	Synthesized from
Isopropyl phenyl	(95/10 mmHg)	1.5196	181		benzene and isobutyl chloride
Cyclohexyl phenyl	[59~60]		175		benzene and cyclohexyl chloride
p-Chloroaceto-phenone	(99/7 mmHg) [19~20]		148		chlorobenzene and acetyl chloride
Desoxybenzoin	(177/12 mmHg) [60]		148		benzene and phenyl acetyl chloride
Phenyl *p*-chlorobenzyl	[138]			95~96	benzene and *p*-chlorophenylacetyl chloride

1) K. Maruyama, R. Goto and H. Suzuki, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **80**, 521 (1959).
2) This Bulletin, **33**, 1516 (1960).
3) Organic Syntheses, **20**, 94 (1940).
4) N. A. Milas and D. Sūrgenor, *J. Am. Chem. Soc.*, **68**, 205, 643 (1946).

TABLE II. OXIDATION OF KETONES WITH *tert*-BUTYLHYDROPEROXIDE
(Temp. 60°C, 6 hr.)

Ketone	Hydroperoxide g. (mol.)	Ketone recovered	Reaction product
1. Isopropyl phenyl ketone 10.0 g.	*tert*-Butylhydroperoxide 2.0 g.	8.5 g.	Benzoic acid 1.05 g., isopropanol (*tert*-butanol, methanol)
2. Cyclohexyl phenyl ketone 10.0 g.	*tert*-Butylhydroperoxide 2.0 g.	9.0 g.	Benzoic acid 0.30 g., adipic acid, non-identified acid (*tert*-butanol, methanol)
3. *p*-Chloroaceto-phenone 10.0 g.	*tert*-Butylhydroperoxide 2.0 g.	7.0 g.	*p*-Chlorobenzoic acid 1.2 g. (*tert*-butanol, methanol)
4. Desoxybenzoin 10.0 g.	*tert*-Butylhydroperoxide 2.0 g.	8.3 g.	Benzoic acid 1.50 g. (*tert*-butanol, methanol)
5. Phenyl *p*-chloro-benzyl ketone 10.0 g.	*tert*-Butylhydroperoxide 2.0 g.	8.0 g.	Benzoic acid 0.30 g., *p*-chlorobenzoic acid 0.40 g. (*tert*-butanol, methanol)
6. Benzoin* 10.0 g.	*tert*-Butylhydroperoxide 2.0 g.	8.0 g.	Benzoic acid 1.9 g. (*tert*-butanol, methanol)
7. Benzil** 10.0 g.	*tert*-Butylhydroperoxide 2.0 g.	8.0 g.	Benzoic acid 1.8 g., benzilic acid (trace) (*tert*-butanol, methanol)
8. α-Tetralon*** 8.2 g.	*tert*-Butylhydroperoxide 2.0 g.	—	*O*-Carboxyhydrocinnamic acid 0.43 g., *O*-carboxycinnamic acid 0.07 g., phthalonic acid 0.01 g., resin.
9. 3-Pentanone 8.6 g. (0.1 mol.)	*tert*-Butylhydroperoxide 5.4 g. (0.06 mol.)	—	Propionic acid (main), acetic acid } total acid 0.02 mol.
10. 3-Heptanone 11.4 g. (0.1 mol.)	*tert*-Butylhydroperoxide 5.4 g. (0.06 mol.)	—	*n*-Valeric acid (main), propionic acid, *n*-butyric acid, acetic acid } total acid 0.016 mol.
11. Cyclohexanone 9.8 g. (0.1 mol.)	*tert*-Butylhydroperoxide 5.4 g. (0.06 mol.)	almost completely recovered	No reaction (oxygen, *tert*-butanol, methanol)

* In this case, the solution of benzoin suspended with potassium hydroxide was deeply colored violet before the addition of hydroperoxide. As the peroxide was dropped, however, the violet color disappeared.

** In this reaction, potassium hydroxide was added in the mixture of benzil and hydroperoxide in order to avoid the so-called "benzilic acid rearrangement." By this precaution, the rearrangement was in practice avoided.

*** In this case, benzene was used as a solvent and its solution of α-tetralon and hydroperoxide were dropped to suspension of potassium hydroxide in benzene. However, a large quantity of resinous product was not avoided.

and was concentrated to 10 cc. and subjected to a paper chromatographic analysis.

The obtained experimental results are shown in Table II.

Benzoic Acid.—In the reaction 1, 2, 4, 5, 6 and 7 benzoic acid was obtained by the acidifying of the water extraction of the reaction mixture. The crude products were recrystallized from the water-alcohol mixture. The acid was identified by the mixed melting point method and paper chromatography.

Isopropanol. — In reaction 1, isopropanol was collected in a trap cooled by ice-salt mixture. This was identified as its phenylurethan derivative (from ligroin m. p. 88°C) and also verified by gas chromatography.

Found: C, 66.98; H, 7.22. Calcd. for $C_{10}H_{13}\cdot NO_2$: C, 67.02; H, 7.31%.

Adipic Acid.—In reaction 2, the acid was found in the solid acid of reaction products and in the concentrated part of the filtrate. Adipic acid was identified by paper chromatography (R_f 0.22, solvent: 5% ammonia 1 vol.+isopropanol 4 vol., temp. 15~20°C). Another acid (R_f 0.44) was found on the paper chromatogram accompanying benzoic acid and adipic acid. But, this acid could not be identified.

***p*-Chlorobenzoic Acid.**—In reaction 3, acid was obtained by the acidifying of the water extract of the reaction mixture, and was identified as *p*-chlorobenzoic acid by the mixed melting point method and paper chromatography (m. p. 243°C).

Found: C, 53.77; H, 3.11. Calcd. for $C_7H_5O_2Cl$: C, 53.69; H, 3.21%.

In reaction 5, *p*-chlorobenzoic acid was obtained by the acidifing of the water extract of the reaction mixture accompanying benzoic acid, and was easily separated from benzoic acid by crystallization from hot water. The obtained crude acid was recrystallized from the water-alcohol mixture, m. p. 242~243°C and was identified by the mixed melting point method and paper chromatography.

Benzilic Acid.—In reaction 7, a trace of benzilic acid was found in the acid products, and was detected paperchromatographically and identified by comparison with a known sample.

***o*-Carboxyhydrocinnamic Acid.**—In reaction 8, the acid was obtained as the main reaction product. The water extract of the reaction mixture was acidified and the obtained precipitation was recrystallized from hot water. *o*-Carboxyhydrocinnamic acid is slightly soluble in hot water and separated from insoluble acid. Repeated recrystallization resulted in the paperchromatographically pure product, and was identified by the mixed melting point method and paper chromatography (R_f 0.21 solvent: 5% ammonia 1 vol. isopropanol 4 Vol., room temp.) m. p. 166~167°C.

Found: C, 62.14; H, 5.30. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19%.

***o*-Carboxycinnamic Acid.**—In reaction 8, this acid was obtained as a product insoluble in hot water, but soluble in hot alcohol, m. p. 173~174°C and was identified by the mixed melting point method and paper chromatography.

Phthalonic Acid.—In reaction 8, phthalonic acid was obtained as the benzene soluble part of acid products, m. p. 150~151°C and was identified by the mixed melting point method and on a paper chromatogram by comparison with a known sample.

Methanol and *tert*-Butanol.—These products were collected in a trap cooled by ice-salt, and analyzed gaschromatographically. *tert*-Butanol was separated as its phenylurethan, m. p. 136°C.

Found: C, 68.86; H, 7.93. Calcd. for $C_{11}H_{15}NO_2$: C, 68.40; H, 7.80%.

***n*-Valeric Acid, *n*-Butyric Acid, Propionic Acid and Acetic Acid.**—These acids were detected by paper chromatography and their total acid contents were determined by titration.

Discussion

It was discussed in the previous paper[1], almost all of the examined ketones, there being only one exception, are subjected to a cleavage reaction by *tert*-butylhydroperoxide. These reactions are summarized in the next equations.

i) Aromatic ketone

$$\mathrm{Ar\text{-}CO\text{-}R} \xrightarrow[\mathrm{KOH}]{t\text{-BuOOH}} \mathrm{ArCOOH} + \mathrm{ROH} \qquad (1)$$

R=alkyl

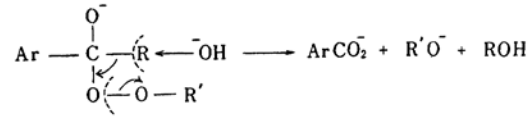
ii) Aromatic α,β-diketone

$$\mathrm{ArCO\cdot COAr'} \xrightarrow[\mathrm{KOH}]{t\text{-BuOOH}} \mathrm{ArCOOH} + \mathrm{Ar'COOH} \qquad (2)$$

iii) Aliphatic ketone

$$\mathrm{RCOR'} \rightarrow \begin{cases} \mathrm{RCOOH} + \mathrm{R'OH} \\ \mathrm{R'COOH} + \mathrm{ROH} \end{cases} \qquad (3)$$

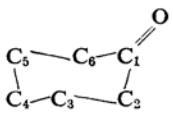
From results of Table II, it could be confirmed that in general, an alkyl aryl ketone can be cleft to benzoic acid derivative and alcohol by hydroperoxide cooperating with alkali hydroxide. The hydroperoxide was reduced to alcohol — e. g. *tert*-butylhydroperoxide → *tert*-butanol. Furthermore, aromatic α,β-diketone was also cleft by the same oxidizing reagent to benzoic acid derivatives. It was a outstanding difference from the cleavage of aromatic ketones by peracids according to Baeyer-Villiger reaction that phenolic product was not found in the oxidation products. This difference, of course, is ascribed to the different reaction mechanism, for this kind of reactions are performed in alkaline medium. As it was briefly discussed in the previous paper, the reason of the absence of phenolic product may be due to a difficulty of formation of phenyl cation (or of S_N2-type reaction at nucleus carbon) at the moment of scission from the complex [I], which is consisted of ketone and hydroperoxide.



[I] (4)

The same kind of cleavage reaction occurred even in the aliphatic ketones, but in this case, the two linkages on both sides of carbonyl carbon have a chance of scission. The chance of scission, however is determined by the stability of the alkyl group as a cation*.

For cyclohexanone, which is only one exception to the cleavage reaction, it may be guessed that the complex can not be formed. This is because, in the alkaline medium the attack of the hydroperoxide anion to the positively polarized carbonyl carbon atom will be most easily performed on the opposite side of the negatively polarized oxygen atom and the steric hindrance which will be caused by the axial hydrogens on C_2, C_6, C_3 and C_5 and by the C_3, C_4 and C_5 carbon atom, against the attack of the hydroperoxide anion makes the formation of complex [I] impossible.



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Department of Chemistry
Faculty of Science
Kyoto University
Sakyo-ku, Kyoto

* This was confirmed in the case of methyl ethyl ketone and of methyl isopropyl ketone in the homogeneous system (O. Soga, K. Maruyama and R. Goto, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 668 (1960).