Hydrogen Peroxide Oxidation. IV. A New Rearrangement Reaction of Phenyl Alkyl Ketones by Selenium Dioxide Catalyst[1]

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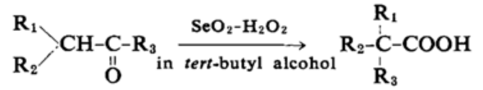
In the previous papers[2,3] we reported the rearrangement reactions of dialkyl ketones by selenium dioxide catalyzed oxidation with hydrogen peroxide, and now the present paper deals with a similar study using several phenyl alkyl ketones.

The rearrangement reaction mode of a dialkyl ketone is shown generally as below;

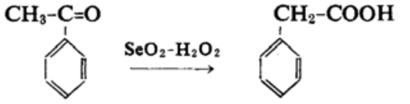


$$R_1R_2CH\text{-}\underset{\underset{O}{\|}}{C}\text{-}R_3 \xrightarrow[\text{in } tert\text{-butyl alcohol}]{SeO_2\text{-}H_2O_2} R_2\text{-}\overset{R_1}{\underset{R_3}{C}}\text{-}COOH \quad (1)$$

$R_1, R_2=H$ or alkyl, $R_3=$alkyl

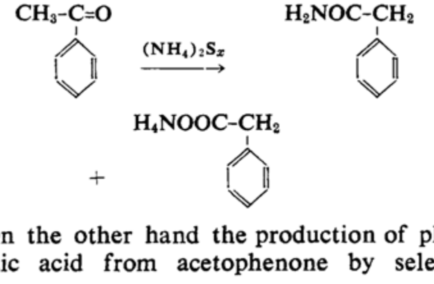
where either of the two alkyl groups R_1R_2CH- and R_3, can migrate onto the α-carbon atom of the other alkyl group so that the two isomeric acids containing the same number of carbon atoms as original ketone are produced when unsymmetrical ketone is used. In the case of phenyl alkyl ketone, only the rearrangement of the phenyl group is possible, because the phenyl group does not possess an α-hydrogen atom which may be substituted by the migrating alkyl group. Thus, the α-phenyl carboxylic acids are synthesized from phenyl alkyl ketones by the oxidation with selenium dioxide-hydrogen peroxide reagent.

For example, when acetophenone was treated with hydrogen peroxide in *tert*-butyl alcohol in the presence of a small amount of selenium dioxide as catalyst at about 80～82°C, phenyl acetic acid was isolated from the reaction products as well as some cleavaged products.



(2)

Synthesis of phenyl acetic acid derivatives from acetophenone had also been undertaken by Willgerodt[4] showing that phenyl acetamide and ammonium phenyl acetate were obtained by the oxidation of acetophenone with ammonium polysulfide. But in the Willgerodt reaction[5] no change of carbon skeleton was observed because of the reduction of the carbonyl group to the methylene group and the oxidation of the methyl group to carbonamide or salt of carboxylic acid.



(3)

On the other hand the production of phenyl acetic acid from acetophenone by selenium

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[1] Presented at the 12th Annual Meeting of the Chemical Society of Japan, Kyoto, April 2, 1959.

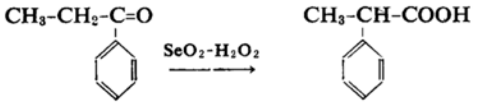
[2] N. Sonoda and S. Tsutsumi, This Bulletin, 32, 505 (1959).

[3] N. Sonoda, T. Yamaguchi and S. Tsutsumi, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zasshi*), 63, 737 (1960).

[4] C. Willgerodt, *Ber.*, 21, 534 (1888); C. Willgerodt and F. H. Merk, *J. prakt. Chem.*, 80, 192 (1909).

[5] For a review of the Willgerodt reaction, see (a) M. Carmack, "Organic Reactions", Vol. III, John Wiley & Sons, Inc., New York, N. Y. (1946), pp. 83-107; (b) R. Wegler, E. Kühle and W. Schäfer, *Angew. Chem.*, 70, 351 (1958).

dioxide catalyzed hydrogen peroxide oxidation is clearly based on the migration of the phenyl group to the methyl carbon atom. An evidence of the rearrangement was shown by the fact that α-phenyl propionic acid was produced by the phenyl migration when phenyl ethyl ketone was treated under the reaction condition similar to that of acetophenone, whereas β-phenyl propionic acid derivatives were formed from phenyl ethyl ketone under the Willgerodt reaction condition⁴⁾.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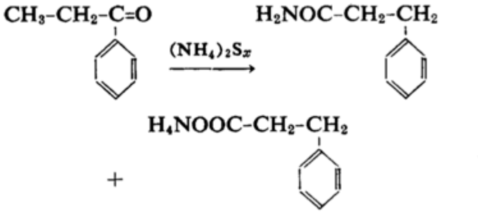
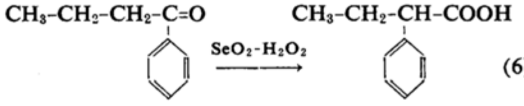

(5)

In a similar manner, phenyl *n*-propyl ketone was oxidized with selenium dioxide-hydrogen peroxide reagent to give α-phenyl butyric acid.


(6)

These facts suggest that similar treatment may be generally applicable to the other aryl alkyl ketones.

The reactivity of phenyl alkyl ketones was apparently lower than that of dialkyl ketones²˒³⁾. The yield of the rearrangement products was only about 10 per cent based on the treated ketones in spite of using an excess amount of hydrogen peroxide, and fairly good recovery of starting ketones was observed in all the cases.

On the other hand, oxidative cleavage was also observed. Benzoic acid was isolated as a main cleavage product in a comparable yield to the rearrangement product and phenol was identified as its tribromide in all cases. Aliphatic acids derived from the aliphatic fragments of the ketones or oxidative decomposition product⁶⁾ of *tert*-butyl alcohol used as solvent were also detected by gaschromatography. These products are listed in Table I.

TABLE I. CLEAVAGE PRODUCTS FROM OXIDATIVE REACTION OF PHENYL ALKYL KETONES

Reactants	Products confirmed	Yield %
Acetophenone	Benzoic acid	12.3
	Phenol	trace
	Acetic acid[a]	—
	Propionic acid[b]	—
Phenyl ethyl ketone	Benzoic acid	4.1
	Phenol	trace
	Acetic acid	—
	Propionic acid	—
Phenyl *n*-propyl ketone	Benzoic acid	4.9
	Phenol	trace
	Propionic acid	—
	n-Butyric acid	—

a) Formic acid was assumed to be present, but was not detected.

b) This propionic acid was supplied from the solvent.

We have proposed the probable mechanism²⁾ of these rearrangement reactions, which comprise the enol formation of the ketones followed by the attack of peroxyselenious acid as the most possible active species. Since peroxyselenious acid is a kind of peracid, it is reasonable to believe that the Baeyer-Villiger oxidation⁷⁾ may be accompanied in this reaction system. Formation of phenol and aliphatic acid from the corresponding ketone may be interpreted as results of hydrolysis of the phenyl ester produced by the Baeyer-Villiger reaction. In addition, the other cleavage path is assumed to be present, because alkyl benzoate will not be formed from phenyl alkyl ketone⁷⁾ under the Baeyer-Villiger reaction condition so that benzoic acid may not be the reaction product via the Baeyer-Villiger oxidation.

Experimental⁸⁾

Oxidative Reagent.—Selenium dioxide-hydrogen peroxide reagent was prepared in the same manner as previously described²⁾. This reagent includes 2.0 g. of selenium dioxide and 1.0 mol. of hydrogen peroxide in about 500 ml. of *tert*-butyl alcohol solution.

Oxidation of Acetophenone.—To a 100 ml. of the selenium dioxide-hydrogen peroxide reagent (0.4 g. of selenium dioxide and 0.2 mol. of hydrogen peroxide) was added 12.0 g. (0.1 mol.) of acetophenone, and the resulting mixture was heated to 80~82°C for 17 hr. The reaction mixture turned red during the oxidation. The mixture was distilled to remove the solvent and the small amount of metallic selenium deposited was filtered off. The filtrate was poured into 200 ml. of ether, and the ethereal solution was extracted first with saturated sodium bicarbonate solusion (A) and then with 8% sodium hydroxide solution (B). After the ethereal solution was dried over anhydrous sodium sulfate,

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6) Propionic acid was partly produced from acetone which was formed by the decomposition of *tert*-butyl hydroperoxide or di-*tert*-butyl peroxide being furnished by the oxidation of *tert*-butyl alcohol used as solvent. This reaction path was already confirmed (see Ref. 2).

7) C. H. Hassall, "Organic Reactions", Vol. IX, John Wiley & Sons, Inc., New York, N. Y. (1957), p. 73-106.

8) The boiling and melting points are uncorrected.

the ether was removed and the residue was distilled under reduced pressure; 6.6 g. of neutral substance, consisting mainly of unreacted acetophenone, was obtained, b. p. 62~65°C (4 mmHg), 2,4-dinitrophenyl-hydrazone of this fraction melted at 245~246°C (lit.9) m. p. 247~248°C) and mixed melting point with an authentic sample (m. p. 245~246°C) showed no depression.

The sodium bicarbonate solution A was acidified with 3 N hydrochloric acid and was extracted with ether. After the ethereal solution was dried over anhydrous sodium sulfate, the ether was removed by distillation and the residue was distilled under reduced pressure. Acetic acid and propionic acid were identified in the low boiling products by gaschromatography: column, tricresylphosphate; column temperature, 140°C; carrier gas, H_2; flow rate of H_2, 40 ml./min. The fraction boiling between 112~122°C (4 mmHg), which solidified at once, was collected. This gave 2.8 g. of a mixture of acids. A small portion of the mixture was recrystallized from hot water, and a mixture of two kinds of crystalline solids was obtained. One of them was white plate, phenyl acetic acid, which was separated as floats over the surface of water by shaking. After further recrystallization from petroleum ether, a sample (m. p. 75.5~76°C) was obtained (lit.10) m. p. 76°C), mixed melting point with an authentic sample was not depressed. The yield of phenyl acetic acid was 9.6% based on the used ketone calculated from ultraviolet spectrum of the mixture of acids.

Found: C, 70.65; H, 6.02. Calcd. for $C_8H_8O_2$: C, 70.57; H, 5.92%.

Benzoic acid, white needle crystals from hot water, was obtained as residue after removal of phenyl acetic acid; the melting point and mixed melting point with an authentic sample was 121°C (lit.10) m. p. 121°C); the yield was 12.3% calculated from the ultraviolet spectrum.

The sodium hydroxide solution B was acidified and extracted with ether. After the ethereal solution was dried over anhydrous sodium sulfate, the ether was removed by distillation. On distillation of the residual brown oil under reduced pressure, 0.15 g. of phenol was isolated; the tribromide was prepared which melted at 94°C (lit.10) m. p. 95°C), mixed melting point with an authentic sample showed no depression.

Oxidation of Phenyl Ethyl Ketone.—To a 100 ml. of the selenium dioxide-hydrogen peroxide reagent (0.4 g. of selenium dioxide and 0.2 mol. of hydrogen peroxide) was added 13.4 g. (0.1 mol.) of phenyl ethyl ketone, and the reaction was carried out at 80~82°C for 20 hr. The reaction products were separated in the same manner as described for the oxidation of acetophenone.

Uureacted phenyl ethyl ketone (9.1 g.) was recovered from the neutral part; b. p. 70~73°C (5 mmHg); 2.4-dinitrophenylhydrazone of this fraction melted at 191~192°C (lit.10) 191°C), mixed melting point with an authentic sample showed no depression.

Acetic acid and propionic acid were identified in the acidic part by the gaschromatography. A mixture of acids, 2.2 g. of oily product of b. p. 115~120°C (3 mmHg), was obtained. After a portion of this product was cooled to 0°C, a crystalline solid deposited was collected on a filter and was purified by recrystallization from petroleum ether to give benzoic acid. The melting point and mixed melting point with an authentic sample was 120~121°C (4.1% yield calculated from ultraviolet spectrum of the mixture of acids). The filtrate was an oily product, which was proved to be α-phenyl propionic acid (11.3% yield). The amide was prepared according to the usual procedure10) and was recrystallized from benzene, melting at 92.5~93°C (lit.11) 93°C).

Found: C, 72.34; H, 7.58; N, 9.57. Calcd. for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.39%.

The presence of phenol was identified in the phenolic part by the ferric chloride test.

Oxidation of Phenyl *n*-Propyl Ketone.—To a 100 ml. of the selenium dioxide-hydrogen peroxide reagent (0.4 g. of selenium dioxide and 0.2 mol. of hydrogen peroxide) was added 14.8 g. (0.1 mol.) of phenyl *n*-propyl ketone, and the reaction was carried out at 80~82°C for 24 hr. The reaction products were separated in the same manner as described for the oxidation of acetophenone.

The unreacted phenyl *n*-propyl ketone (10.2 g.) was recovered from the neutral part; b. p. 104~108°C (14 mmHg); 2,4-dinitrophenylhydrazone melted at 190~191°C (lit.9) 191~192°C), mixed melting point with an authentic sample was not depressed.

Propionic acid and butyric acid were identified by the gaschromatography. On distillation, 1.5 g. of a mixture of acids, b. p. 105~110°C (1 mmHg), was obtained. After the mixture was allowed to stand at room temperature for several hours, the crystalline product deposited was filtered and recrystallized from hot water to give 0.6 g. (4.9% yield) of benzoic acid, m. p. 121°C. The filtrate, 0.7 g. (4.3% yield) of α-phenyl butyric acid, froze to a crystalline solid, which melted slightly above room temperature (lit.12) m. p. 43°C). A redistilled sampe showed neutral equivalent 162; calculated for $C_{10}H_{12}O_2$: 164.2. The amide was prepared according to the usual procedure10) and was recrystallized from benzene-ligroin, melting at 83~84°C (lit.13) 84°C). The phenol was isolated from the phenolic part, 0.2 g.; the tribromide melted at 94°C (lit.10) 95°C), mixed melting point with an authentic sample showed no depression.

Summary

1) Selenium dioxide catalyzed oxidation of phenyl alkyl ketone with hydrogen peroxide in *tert*-butyl alcohol gave α-phenyl carboxylic acid which was produced by the rearrangement of the phenyl group to the α-carbon atom as shown by Eqs. 2, 4 and 6.

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9) G. D. Johnson, *J. Am. Chem. Soc.*, **75**, 2720 (1953).

10) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds", 4th Ed., John Wiley & Sons, Inc., New York, N. Y. (1956).

11) J. A. King and F. H. H. McMillan, *J. Am. Chem. Soc.*, **68**, 635 (1946).

12) M. M. Rising and T. W. Zee, *J. Am. Chem. Soc.*, **50**, 1211 (1928).

13) *Beilstein*, **9 II**, p. 356, Springer-Verlag, Berlin (1946).

Therefore, the reaction mode is quite different from the Willgerodt reaction. The fact described above suggests that similar treatment may be generally applicable to the other aryl alkyl ketones.

2) The reactivity of phenyl alkyl ketone was lower than that of dialkyl ketone, and cleavage reaction was also observed. It is assumed that the cleavage products may be produced partly from the Baeyer-Villiger oxidation product because an active species in this reaction system is considered to be peroxyselenious acid, a kind of peracid.

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