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Studies of Hydrogenolysis. LVII.[1] Catalytic Hydrogenation of Benzalacetophenone Oxide

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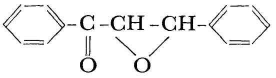
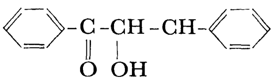
The effects of catalysts and an additive, sodium hydroxide, on the catalytic hydrogenation of benzalacetophenone oxide (I) have been studied for the purpose of elucidating the selectivity of the catalysts on the hydrogenation. The catalytic hydrogenation over palladium or Raney nickel led to the formation of the hydroxyketones as the primary products resulting from the hydrogenolysis of the epoxide ring. 1,3-Diphenylpropane-1,2-diol (III) was obtained by the catalytic hydrogenation over palladium, while 1,3-diphenylpropane-1,3-diol (VI) and III were yielded over Raney nickel. Under the basic conditions III was predominantly produced even over Raney nickel. Over platinum oxide, 2,3-epoxy-1,3-diphenylpropan-1-ol (VIII) was the primary product of the hydrogenation of the carbonyl group of I. In the hydrogenolysis of VIII, 1,2-diol (III) was produced regardless of the species of the catalysts.

It has been shown by Herz[2] that the catalytic hydrogenation of benzalacetophenone oxide (I) gave two diphenylpropanediols, which he considered to be the diastereoisomeric α-glycols, and that the mode of hydrogenation followed I—II—III, regardless of the species of the catalysts and solvents.



(I)



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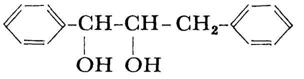

(III)

On the other hand, Mitsui and his co-workers[3] reported that both α-glycol and β-glycol were obtained from the cleavage of the carbon-oxygen bond of the epoxide ring at different positions; α-glycol was obtained from the hydrogenation over palladium-charcoal, and β-glycol, from that over Raney nickel.

In order to study the selectivity of the catalysts and the effect of the additive, sodium hydroxide, on the catalytic hydrogenation of epoxyketones, benzalacetophenone oxide was hydrogenated over Raney nickel, palladium charcoal-B[4] or platinum oxide respectively in ethanol at room temperature and at atmospheric pressure. In addition to these catalytic hydrogenations, metal hydride reduction has also been carried out.

Results and Discussion

A quantitative analysis of the reduction products by gas chromatography was performed as their diastates. A qualitative analysis of the primary reduction product was carried out by means of thin-layer chromatography.

In accordance with the previous report,[3] the catalytic hydrogenation of I over palladium charcoal yielded 2-hydroxy-1,3-diphenylpropan-1-one (II) with the consumption of one mole of hydrogen, and 1,3-diphenylpropane-1,2-diol (III) (65% of *erythro*-III, 25% of *threo*-III), and other substances with the consumption of two moles of hydrogen. Diastereoisomers, *erythro*-, and *threo*-III have been prepared and characterized by Bonner and Raunio.[5] The catalytic hydrogenation of I over palladium charcoal-B to which sodium hydroxide had been added gave 1-hydroxy-1,3-diphenylpropan-2-one (IV) preferentially. The rate of the hydrogenation became slower after the consumption of one mole of hydrogen.

The Raney nickel-catalyzed hydrogenation of I

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[1] Part LVI; Y. Sugi and S. Mitsui, for publication.

[2] W. Herz, *J. Amer. Chem. Soc.*, **74**, 2928 (1952).

[3] S. Mitsui, Y. Senda, T. Shimodaira and H. Ichikawa, This Bulletin, **38**, 1898 (1965).

[4] Method B: E. C. Horning, "Organic Synthesis," Coll. Vol. III, p. 686, (1955). This was named by Mitsui and Saito as the catalyst containing trace base: S. Mitsui and H. Saito, *Nippon Kagaku Zasshi*, **82**, 890 (1961).

[5] W. A. Bonner and E. K. Raunio, *J. Org. Chem.*, **31**, 291 (1966).

yielded 3-hydroxy-1,3-diphenylpropan-1-one (V) and 2-hydroxy-1,3-diphenylpropan-1-one (II) as the initial products; almost equal amounts of 1,3-diphenylpropane-1,3-diol (VI) and 1,3-diphenylpropane-1,2-diols (III) were produced on further hydrogenation. In this case, a considerable amount of the deoxygenation product of the epoxide was obtained.

Semi-hydrogenation over Raney nickel to which sodium hydroxide had been added resulted in the formation of α-hydroxyketones (mainly II), while exhaustive hydrogenation led to α-glycol (80% of *erythro*-III, 10% of *threo*-III) and other substances. The fact that only a small amount of 1,3-diphenylpropan-1-ol (VII) was formed seems to indicate that the sodium hydroxide in the reaction mixture may resist the elimination of the oxygen atom of the epoxide.[6]

Though the hydrogenation over palladium or Raney nickel led to the formation of the hydroxyketones as a result of the cleavage of the epoxide ring, over platinum oxide epoxy alcohol VIII was the primary product resulting from the hydrogenation of the carbonyl group[7] of I. Other primary products formed over platinum oxide were α-hydroxyketone II and β-hydroxyketone V. The exhaustive hydrogenation yielded α-glycol III (rich in *erythro*-III) from VIII and β-glycol VI from V. The deoxygenation product, VII, was obtained over platinum oxide as well as over Raney nickel. On the other hand, hydrogenation over platinum oxide to which sodium hydroxide had been added resulted in the formation of epoxy alcohol VIII as the primary product; then α-glycol III, which was rich in the erythro isomer, was obtained, by adding hydrogen continuously.

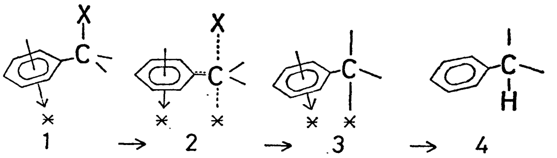
The lithium aluminum hydride reduction of benzalacetophenone oxide (I) yielded 77% of 1,2-diols III, 18% of 1,3-diols VI, and a small amount of another product. The metal hydride which was active toward the reduction of carbonyl compounds and epoxide gave epoxy alcohol VIII, α-hydroxyketone II, and β-hydroxyketone VI as the primary products in the course of the reduction. Since sodium borohydride is inactive toward the reduction of the epoxide, epoxy alcohol VIII was the only reduction product. The further hydrogenation of the product, VIII, over palladium charcoal-B yielded 54% of *erythro*-III and 46% of *threo*-III.

From these results, it is obvious that the mode of the hydrogenation of benzalacetophenone oxide is greatly affected by the species of catalysts and the additives (Chart I). Mitsui and Imaizumi have reported that the hydrogenolysis of optically-active α-methyl or α-ethylstyrene oxide gives optically-active products with the retention of the configuration over Raney nickel and with the inversion of the configuration over Raney nickel in the presence of sodium hydroxide, potassium bromide, or cesium chloride as well as over palladium or platinum oxide.[8] Similar trends have been observed in the hydrogenolysis of *trans*-dimethylstilbene oxide.[9]

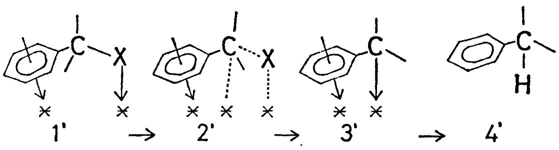
It is considered that, on the hydrogenolysis over Raney nickel, hydrogen may attack the carbon atom from the same direction as the oxygen atom of epoxide. Consequently, the reaction proceeds with the retention of the configuration. On the other hand, over Raney nickel with a small amount of alkali as well as over palladium or platinum, the hydrogen may attack from behind the carbon-oxygen bond and the reaction proceeds with the inversion of the configuration.

It is known that the catalytic hydrogenolysis of benzylic substituents is relatively easy. The high reactivity of the benzylic substituents on the catalytic hydrogenolysis may be attributed to the ease of formation of the π-benzyl intermediate. This reaction includes the adsorption of the substrate on the catalyst (1 or 1′), the cleavage of the C–X bond (2 or 2′), the formation of the π-benzyl intermediate (3 or 3′), the hydrogenolysis of the π-benzyl intermediate, and the desorption of the product from the catalyst (4 or 4′). The reaction path (A or B) determines the stereospecificity of the product; the hydrogenolysis proceeds with the retention of the configuration in Path B, whereas the configuration is inverted in Path A.[10]

Path A



Path B



Taking account of the stereochemical results obtained in the catalytic hydrogenolysis of benzylic-

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[6] D. R. Howton and R. W. Kaiser, *J. Org. Chem.*, **29**, 2421 (1964); O. Gawron, T. P. Fondy and D. J. Parker, *ibid.*, **28**, 700 (1963); G. B. Payne, *ibid.*, **24**, 2408 (1959).

[7] P. L. A. Plattner, H. Hausser and A. B. Kulkarm, *Helv. Chim. Acta*, **31**, 1822 (1948); J. Raese, *Ber.*, **75**, 385 (1942).

[8] S. Mitsui and S. Imaizumi, *Nippon Kagaku Zasshi*, **86**, 219 (1965).

[9] S. Mitsui and Y. Nagahisa, *Chem. Ind.* (London), **1965**, 1975.

[10] S. Mitsui, M. Fujimoto, Y. Nagahisa and T. Sukegawa, *ibid.*, **1969**, 241; S. Mitsui, Y. Kudo and M. Kobayashi, *Tetrahedron*, **25**, 1921 (1965); S. Mitsui and Y. Sugi, *Tetrahedron Lett.*, **1969**, 1291.

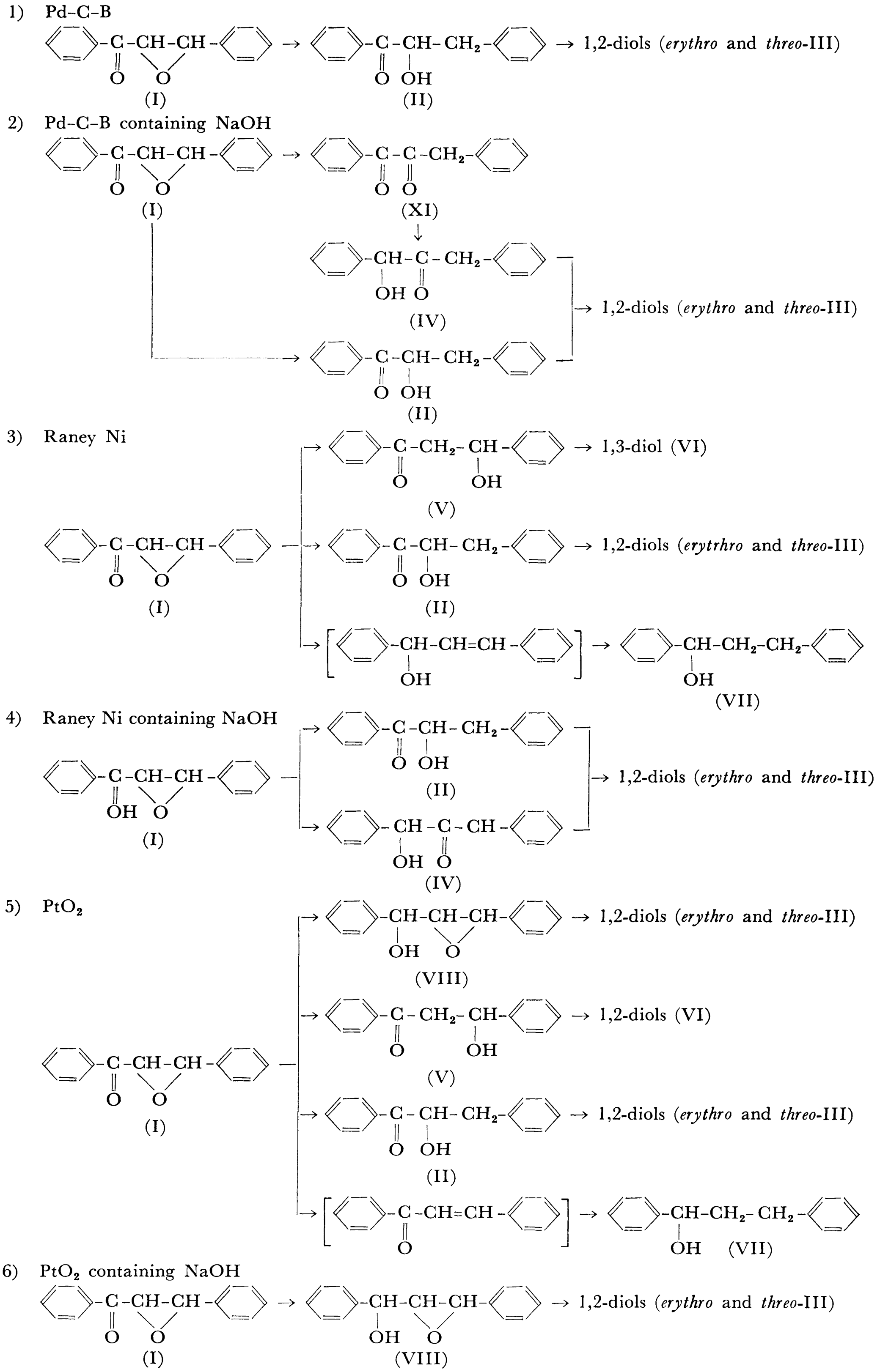


Chart 1. The paths of the catalytic hydrogenation of benzalacetophenone oxide (I).

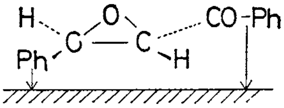


Fig. 1

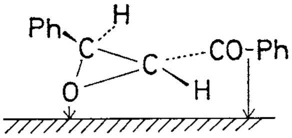


Fig. 2

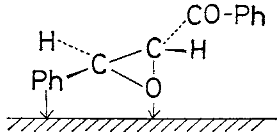


Fig. 3

type compounds, the epoxide ring may be hydrogenolyzed with the inversion of the configuration over a palladium catalyst in such a way as in Fig. 1, in which the cleavage of the benzylic C–O bond occurs selectively. On Raney nickel hydrogenolysis, the rupture of the benzylic C–O bond may occur as is shown in Fig. 2. Moreover, since Raney nickel has a strong affinity for the oxygen atom, the adsorption state shown in Fig. 3 is also plausible. In this case, the hydrogenolysis of the epoxide ring occurs at homobenzylic C–O bond because of its strain, affording β-hydroxyketone V. The addition of an alkaline substance to the Raney nickel catalyst decreases the rate of the reaction of the species, whose epoxide oxygen is adsorbed on the catalyst surface.[8] Consequently, the reaction preferably proceeds taking the adsorption state, as is shown in Fig. 1. Regardless of the species of the catalysts, the cleavage of the oxirane ring of VIII proceeds to give α-glycols selectively, in contrast to the case of the hydrogenolysis of α-ketoepoxide I.

In the case of platinum oxide to which sodium hydroxide had been added, *erythro*-III was favorably obtained from the epoxy alcohol VIII which was produced as a semihydrogenation product; however, reduction with sodium borohydride gave almost equal amounts of *erythro*-VIII and *threo*-VIII.

The catalytic hydrogenation of α-hydroxyketone II lead to the formation of *erythro*-glycol III. This process may be well specurated on the basis of Bonner and Raunio.[5]

The formation of 1-hydroxy-1,3-diphenylpropan-2-one suggests that I was isomerized to phenylbenzylglyoxal (XI) prior to reduction. This isomerization occurred in the presence of palladium charcoal, sodium hydroxide, and hydrogen, while it did not occur if any one of these three components was lacking.

Experimental

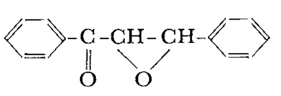
The Catalytic Hydrogenation of Benzalacetophenone Oxide (1). The catalyst and I dissolved in

TABLE 1. CATALYTIC HYDROGENATION OF BENZALACETOPHENONE OXIDE (I)

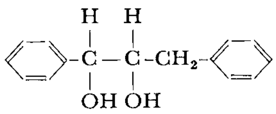
Exp. No.	Substrate (mg)	Catalyst (g)	NaOH (mg)	Reduction products (%)					
				IX	X	VII	*erythro*-III	*threo*-III	VI
1	450	Pd-C-B 0.2	—	2	2	5	62	25	4
2	450	Pd-C-B 0.4	40	4	2	3	77	13	1
3	450	Raney Ni 1.0	—	7	trace	39	21	7	26
4	450	Raney Ni 1.0	80	trace	trace	36	27	17	20
5	450	Raney Ni 1.0	400	trace	trace	8	80	10	2
6	400	PtO_2 0.05	—	trace	trace	27	32	10	31
7	450	PtO_2 0.05	5	trace	trace	4	91	4	1

Solvent: 30 m*l* of 99% ethanol

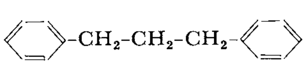
I



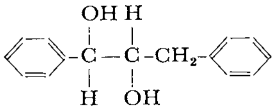
erythro-III



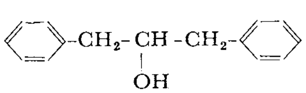
IX



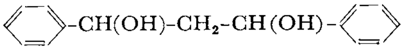
threo-III



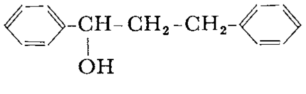
X



VI



VII



ethanol were stirred with hydrogen at room temperature and at atmospheric pressure. The determination of the initial products in the course of the hydrogenation was done by thin-layer chromatography (T.L.C. on silica gel, chloroform 99 : methanol 1). After the hydrogen uptake had ceased with the absorption of two moles of hydrogen, the catalyst was filtered and ethanol was distilled off. The residue was acetylated with acetic anhydride in pyridine at room temperature. After having been kept standing for 12 hr, the reaction mixture was treated as usual. The products were dissolved in benzene and analyzed by V.P.C. The experimental data are summarized in Table 1.

Benzalacetophenone Oxide (I). I was prepared by the method of Weitz and Scheffer[11] by the epoxidation of benzalacetophenone; mp 90°C; 73% yield.

***threo*-1,3-Diphenylpropane-1,2-diol (*threo*-III).** *threo*-III was prepared by the method of Bonner and Raunio[5] by the *cis* hydroxylation of *trans*-1,3-diphenyl propene;[12] mp 62°C.

***erythro*-1,3-Diphenylpropane-1,2-diol (*erythro*-III).** *erythro*-III was prepared by the catalytic hydrogenation of benzalacetophenone oxide (I) over palladium charcoal-B at an ordinary temperature and at atmospheric pressure. After the hydrogen uptake had ceased with the absorption of two moles of hydrogen, the residue was fractionally recrystallized from the benzene-ligroin mixture to give pure *erythro*-III; mp 82°C; 62% yield.

2-Hydroxy-1,3-diphenylpropan-1-one (II).[13] II was prepared by the catalytic hydrogenation of benzalacetophenone oxide over palladium charcoal-B with the absorption of one mole of hydrogen; mp 66°C (recrystallized from the benzene-ligroin mixture); 50% yield.

1-Hydroxy-1,3-diphenylpropan-2-one (IV).[14] IV was prepared by the catalytic hydrogenation of benzalacetophenone oxide over palladium charcoal-B containing a small amount of sodium hydroxide, with the absorption of one mole of hydrogen; mp 114°C (recrystallized from the benzene ligroin mixture); 70% yield.

1,3-Diphenylpropan-1-ol (VII). VII was prepared by the catalytic hydrogenation of benzalacetophenone over palladium charcoal-B; bp 146—147°C/0.9 mmHg; 90% yield.

2,3-Epoxy-1,3-diphenylpropan-1-ol (VIII). VIII was prepared by reduction with sodium borohydride in methanol at room temperature. The reaction mixture was treated by the usual method. The product was recrystallized from a petroleum ether-benzene mixture. The epoxy alcohol VIII, whose melting point was 65°C, proved to be a mixture of 70% of the *erythro* and 10% of *threo*-isomer. The yield was 30%.

1,3-Diphenylpropan-2-ol (X). X was prepared by the catalytic hydrogenation of 1,3-diphenylpropane-1,2-diol over palladium charcoal-B containing one drop of concentrated hydrochloric acid at an ordinary temperature and at atmospheric pressure.

1,3-Diphenylpropane (IX). IX was prepared by the catalytic hydrogenation of 1,3-diphenylpropene.[12]

The authors are indebted to the Takeda Science Foundation for its financial support.

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[11] E. Weitz and A. Scheffer, *Ber.*, **54**, 2329 (1921).

[12] W. A. Bonner and E. K. Raunio, *J. Org. Chem.*, **31**, 397 (1966).

[13] W. Perkin and J. Stenhouse, *J. Chem. Soc.*, **1908**, 59.

[14] P. Ruggli and A. H. Lutz, *Helv. Chim. Acta*, **30**, 1070 (1947).