*The Catalytic Hydrogenolysis of 5,6β-Epoxy-5β-cholestan-3β-ol**

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In the catalytic hydrogenolysis of 5,6β-epoxy-5β-cholestan-3β-ol and related 5β,6β-epoxy-compounds, there often occurs a rather extensive over-hydrogenolysis beyond the mere reductive cleavage of the oxide ring. Chuman[1] obtained 5α-cholestane in the catalytic hydrogenolysis of 5,6β-epoxy-5β-cholestan-3β-ol (I) with platinum oxide in acetic acid. 3β-Acetoxy-5,6β-epoxy-5β-cholestane (II) has also been reported to give 5α-cholestane and 3β-acetoxy-5α-cholestane, along with 3β-acetoxy-5α-cholestan-6β-ol, under similar conditions.[1,2] Such an over-hydrogenolysis has also been found to take place in the catalytic hydrogenolysis of 5,6β-epoxy-5β-cholestan-3α-ol[3] and 3α-chloro-5,6β-epoxy-5β-cholestane.[4] From the observations that the reduction of the epoxide II with lithium aluminum hydride afforded about 20% of 5β-cholestane-3β,5-diol along with 60% of 5α-cholestane-3β,6β-diol, and that the yield of the 3β,5β-diol nearly amounted to the sum of 5α-cholestane and 3β-acetoxy-5α-cholestane obtained in the catalytic hydrogenolysis, it has been suggested that 3β-acetoxy-5β-ol was also produced in the catalytic hydrogenolysis, but further reduced to give 5α-cholestane and 3β-acetoxy-5α-cholestane.[5] There is no evidence for the assumption, however, and it seems not probable that the catalytic hydrogenolysis or the dehydration, followed by the hydrogenation, of the 5β-hydroxy compound would be involved in the reaction, because the 5β-hydroxyl group is not activated by any unsaturated groups and the condition of the reaction is not so drastic.

This paper will present the results of the reinvestigation of the catalytic hydrogenolysis of 5,6β-epoxy-5β-cholestan-3β-ol with platinum, (7:3) rhodium-platinum and palladium oxides as catalysts. 5β-Cholestane-3β,5-diol[6] was also subjected to hydrogenolysis with platinum oxide in order to observe the behavior of the tertiary hydroxyl group under the conditions.

Table I summarizes the products formed in the catalytic hydrogenolysis of the epoxide I in acetic acid at room temperature and under the atmospheric pressure of hydrogen. The elimination of oxygen groups increases with respect to the catalysts in the following order: (7:3) rhodium-platinum, platinum, palladium. In every case 5β-compounds, which had not been isolated previously, were also produced, though in smaller yields than the corresponding 5α-compounds. Palladous oxide, which caused the most extensive over-hydrogenolysis, gave no diols and only a trace of 5α-cholestan-3β-ol-6-one. The catalyst also gave a considerable amount of 5α-cholestan-3-one, along with 5α-cholestan-3β-ol. These carbonyl compounds were not found in the products obtained with platinum and (7:3) rhodium-platinum catalysts. Platinum oxide and (7:3) rhodium-platinum oxide gave 3,6-diols in 36% and 74% yields respectively, the 5α-diol being formed more predominantly than the 5β-diol. Thus, the compounds carrying no oxygen at C_6 were produced mostly on palladous oxide, while in only a 25% yield on (7:3) rhodium-platinum oxide.

If these compounds were formed via 5β-cholestane-3β,5-diol, the hydrogenolysis of the oxide ring of the epoxide I should have occurred almost exclusively at C_6 on the palladium catalyst, while mostly at C_5 on the (7:3) rhodium-platinum catalyst. It may be rather unreasonable to assume that there exists such a great difference in selectivity between the catalysts in the mere hydrogenolysis of the oxide ring in acetic acid at room temperature.*1 Further evidences against

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1) M. Chuman, *J. Chem. Soc. Japan* (*Nippon Kwagaku Zassi*), **64**, 1486 (1943).

2) Pl. A. Plattner, Th. Petrzilka and W. Lang, *Helv. Chim. Acta*, **27**, 513 (1944).

3) Y. Urushibara and K. Mori, This Bulletin, **31**, 1068 (1958).

4) M. Shiota, T. Ogihara and Y. Watanabe, ibid., **34**, 40 (1961).

5) Pl. A. Plattner, H. Heusser and M. F. Feurer, *Helv. Chim. Acta*, **32**, 587 (1949). L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corporation, New York (1959), p. 199.

6) Pl. A. Plattner, H. Heusser and A. B. Kulkarni, *Helv. Chim. Acta*, **31**, 1885 (1948).

1* The catalytic hydrogenolysis of 1,2-epoxy-1-methylcyclohexane in acetic acid at room temperature gave 7% of 1-methylcyclchexanol and 93% of 2-methylcyclohexanol with platinum oxide, 8% of 1-methylcyclohexanol and 92% of 2-methylcyclohexanol with (7:3) rhodium-platinum oxide, and 8.5% of 1-methylcyclohexanol, 53.5% of 2-methylcyclohexanol and 38% of 2-methylcyclohexanone with palladous oxide. Thus, the ratio of 1-methylcyclohexanol to 2-methylcyclohexanol or to 2-methylcyclohexanol plus 2-methylcyclohexanone differs only slightly between the three catalysts (unpublished results by the present authors).

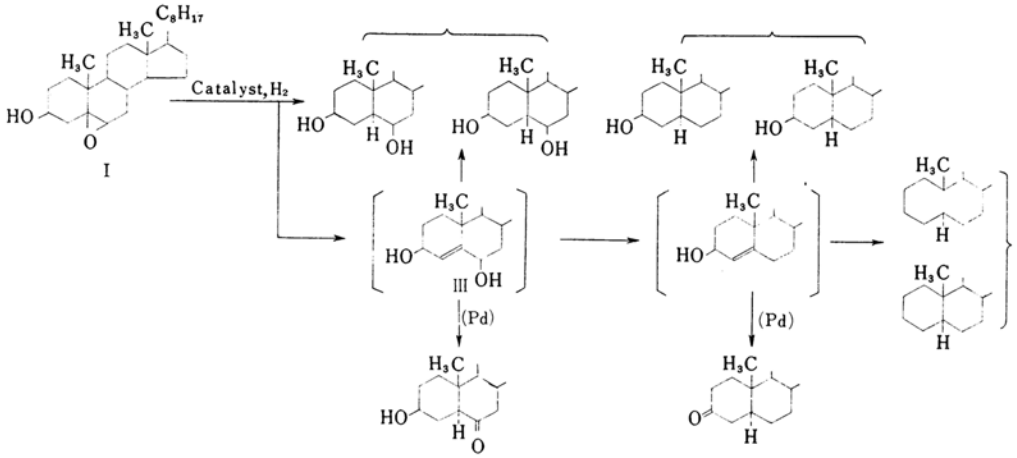


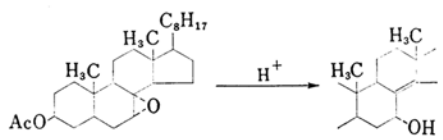
Fig. 1. The catalytic reduction of 5, 6β-epoxy-5β-cholestan-3β-ol.

TABLE I. PERCENTAGE PRODUCTS OF CATALYTIC REDUCTION OF 5,6β-EPOXY-5β-CHOLESTAN-3β-OL (I) AND OF CHOLEST-4-ENE-3β,6β-DIOL (III)[a]

Product	Compound I, Catalyst: Pt	I: (7 : 3) Rh-Pt	I: Pd	Compound III, Catalyst: Pt	III: (7 : 3) Rh-Pt
5β-Cholestane	3	trace	14	5	trace
5α-Cholestane	28	3	32	43	2
5β-Cholestan-3β-ol	11	6	7	13	4
5α-Cholestan-3β-ol	23	16	27	28	9
5α-Cholestan-3-one	—	—	20	—	—
5β-Cholestane-3β,6β-diol	6	26	—	5	46
5α-Cholestane-3β,6β-diol	30	48	—	6	39
5α-Cholestan-3β-ol-6-one	—	—	trace	—	—

a) All the reductions were carried out in acetic acid at room temperature and atmospheric pressure of hydrogen.

the assumption are the facts that 5β-cholestane-3β, 5-diol does not absorb any hydrogen in the presence of platinum oxide in acetic acid, and that the starting diol was recovered unchanged.[7] From these results, it is very probable that the over-hydrogenolyzed products would be formed via a different reaction path from that via the 3β, 5β-diol. These results will be best explained if we assume that the epoxide I is partly isomerized to cholest-4-ene-3β, 6β-diol (III) during the catalytic hydrogenolysis, and that this is further hydrogenated to give hydrocarbons, cholestanols (or cholestanone) and cholestanediols as illustrated in Fig. 1. The isomerization of an epoxide to an allylic alcohol has been described, for example, by Fieser and Goto,[8] who have shown that 7α, 8α-epoxy-5α-cholestan-3β-ol acetate is isomerized to the allylic alcohol V upon



IV V

standing briefly in chloroform shaken with 10% sulfuric acid. The hydrogenolysis of the epoxide I not accompanied with the isomerization may occur simultaneously, since the hydrogenolysis of the epoxide I gives a greater yield of 5α-cholestane-3β, 6β-diol than the hydrogenation of cholest-4-ene-3β, 6β-diol (see Table I). The attack of hydrogen from the β-face will be more hindered in the hydrogenolysis of the oxide ring at C_5 than in the hydrogenation of the 4, 5-double bond of the cholestenediol. The formation of carbonyl

7) The difficult hydrogenolysis of the tertiary hydroxyl group of a saturated compund in acetic acid at room temperature was also confirmed in the hydrogenation of *cis*- and *trans*-1-methyl-4-*t*-butylcyclohexanol, using platinum oxide as the catalyst.

8) L. F. Fieser and T. Goto, *J. Am. Chem. Soc.*, **82**, 1693 (1960).

compounds on a palladium catalyst may also be explained without difficulty by means of the schema shown in Fig. 1. Cholest-4-ene-3β, 6β-diol formed from the epoxide I is partly isomerized to 5α-cholestan-3β-ol-6-one*[2] and mostly hydrogenolyzed to give cholest-4-en-3β-ol, which affords 5α-cholestan-3-one, along with hydrocarbons and cholestanols. Such an isomerization is supposed to occur to some extent also on (7 : 3) rhodium-platinum oxide, which would hydrogenate the resulting ketone to the corresponding alcohol. However, platinum oxide will give rise to this isomerization to a much less extent, as is expected from the fact that the isomerization of allyl alcohol to propionaldehyde during the hydrogenation in ethanol at room temperature occurs to the extent of about 30% on palladous oxide and about 20% on (7 : 3) rhodium-platinum oxide, while there is practically no isomerization on platinum oxide.[9]

Experimental

Catalysts.—The catalysts were prepared by the fusion of their chlorides with sodium nitrate according to the procedures described in the literature.[10-12]

Hydrogenation.—The hydrogenation was carried out at an ordinary temperature and pressure, using acetic acid as the solvent. The substrate was added after the metal oxide had been pre-reduced to black with hydrogen in the solvent.

5, 6β-Epoxy-5β-cholestan-3β-ol. — This compound (200 mg.) was hydrogenated with 50 mg. of the catalyst in 30 ml. of acetic acid. The hydrogenation was completed in 30 min. with platinum oxide (1.7 mol./mol. of hydrogen being absorbed), in 50 min. with (7 : 3) rhodium-platinum oxide (1.2 mol./mol. of hydrogen being absorbed), and in 1 hr. 20 min. with palladous oxide (1.8 mol./mol. of hydrogen being absorbed).

Cholest-4-ene-3β, 6β-diol. — When this compound (70 mg.) was hydrogenated with 30 mg. of platinum oxide in 15 ml. of acetic acid, 2.3 mol./mol. of hydrogen was absorbed in 20 min. The hydrogenation with (7 : 3) rhodium-platinum oxide in acetic acid has already been described in a previous paper by one of the present authors (S. N.) and Mori.[13]

5β-Cholestane-3β, 5-diol.—This compound (30 mg.) was subjected to hydrogenolysis with 15 mg. of platinum oxide in 15 ml. of acetic acid for about 1 hr., but no hydrogen was absorbed. Though the melting point of the recovered material was somewhat lower than that of the starting 3,5-diol, the following analytical values show that the recovered material did not lose any hydroxyl group:

Found: C, 80.19; H, 11.91. Calcd. for $C_{27}H_{48}O_2$: C, 80.14; H, 11.96%.

Analysis of the Products.—The reaction mixture was neutralized with aqueous sodium hydroxide and extracted with ether, and the residue after the evaporation of the ether was analyzed by gas-liquid partition chromatography with a GC-1B of Shimadzu Seisakusho, Ltd. (hydrogen-flame ionization-detector type) and a column of 1% SE-30 silicone on Chromosorb W (60~80 mesh).

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*2 It may also be possible that 5α-cholestan-3β-ol-6-one was formed directly from the epoxide I, but the fact that a much larger amount of 5α-cholestan-3-one was formed, along with the 6-one, seems to suggest that the more probable course of the occurrence of 3β-ol-6-one would be the one via III.

9) S. Nishimura, unpublished. Cf. T. Fukuda, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **83**, 1119 (1962).
10) R. Adams, V. Voorhees and R. L. Shriner, "Organic Syntheses," Coll. Vol. I, 2nd Ed., 463 (1941).
11) R. L. Shriner and R. Adams, *J. Am. Chem. Soc.*, **46**, 1683 (1924).
12) S. Nishimura, This Bulletin, **34**, 1544 (1961).
13) S. Nishimura and K. Mori, ibid., **36**, 318 (1963).