Hydrogenation and Hydrogenolysis. VI.[1] *The Stereochemisty of the Catalytic Hydrogenation of Some Allylic Alcohols Related to Cholest-4-ene**

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Catalytic hydrogenation of cholest-4-ene-3β,6β-diol with platinum oxide in ethanol gives 5β-cholestane-3β,6β-diol exclusively[2], while in the presence of a trace of hydrochloric acid a much more rapid reduction occurs and 5α-cholestane is obtained as the main product[3] along with 5α-cholestan-3β-ol. The exclusive formation of the 5β-cholestanediol in ethanol seems rather unusual, because it indicates that hydrogen was added preferentially from the β-side which appears to be more hindered than the α-side. A similar phenomenon was observed by Dart and Henbest[4] in hydrogenation of cholest-4-en-3β-ol and other cyclic allylic alcohols, a more β-addition of hydrogen being observed in cholest-4-en-3β-ol than in cholest-4-ene in hydrogenation with platinum oxide in ethanol in the presence of a small amount of sodium nitrite, which depressed hydrogenolysis causing the yield of 5β-cholestanol to increase.

In order to clarify the effects of the accumulative β-hydroxyl groups at C_3 and C_6 carbon atoms and also of solvents on the stereochemistry of the hydrogenation of the 4, 5-double bond, the catalytic hydrogenation of cholest-4-ene, cholest-4-en-3β-ol and cholest-4-ene-3β,6β-diol has been carried out in ethanol and also in acetic acid with (7 : 3)rhodium-platinum oxide[5] as catalyst. This catalyst was used because it can hydrogenate these allylic alcohols with only slight hydrogenolysis in acetic acid[6].

Experimental

Catalysts.—Platinum oxide was prepared by fusion of chloroplatinic acid with sodium nitrate according to the method of Adams et al.[7]

(7 : 3)Rhodium-platinum oxide was prepared by fusion of the mixture of rhodium chloride and chloroplatinic acid in ratio of 7 : 3 by the weights of the metals as described previously[5].

Hydrogenation.—Hydrogenation was carried out at ordinary temperature and pressure. The substrate (0.2~0.5 mmol.) was added after the oxide (20~50 mg.) was reduced to black with hydrogen in the solvent.

Cholest-4-ene.—The hydrogenation of this compound in ethanol proceeded with difficulty and was completed by addition of a new portion of catalyst. The last trace of the starting material remaining in the products was further hydrogenated with addition of a small amount of acetic acid. The hydrogenation in acetic acid proceeded rapidly to completion. The products (5α-cholestane and 5β-cholestane) were analyzed by the method of infrared absorption in carbon disulfide solution. Characteristic bands at 957 and 985 cm^{-1}, respectively, were used for this analysis.

Cholest-4-en-3β-ol.—The hydrogenation products were analyzed by gas-liquid partition chromatography with GC-1B (hydrogen flame detector type) of Shimadzu Seisakusho, Ltd. and a column of 0.1% SE-30 silicone on Chromosorb W (60~80 mesh)*.

The product from ethanol solution consisted of about 36% hydrocarbons (mainly 5α-cholestane) and 64% saturated alcohols (52% 5β-cholestan-3β-ol and 48% 5α-cholestan-3β-ol). The product from acetic acid solution consisted of 13% hydrocarbons (mainly 5α-cholestane) and 87% saturated alcohols (16% 5β-cholestan-3β-ol and 84% 5α-cholestan-3β-ol).

Cholest-4-ene-3β,6β-diol.—The product from hydrogenation in acetic acid was analyzed by gas-liquid partition chromatography as described above and also by elution chromatography. The gas chromatogram indicated that the product consisted of about 2% hydrocarbons (mainly 5α-cholestane), 13% mono-ols (mainly 5α-cholestan-3β-ol) including a very small amount of an unidentified product,

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1) Part V: S. Nishimura, This Bulletin, **34**, 32 (1961).

2) V. Prelog and E. Tagmann, *Helv. Chim. Acta*, **27**, 1880 (1944).

3) S. Nishimura and K. Mori, This Bulletin, **32**, 103 (1959).

4) M. C. Dart and H. B. Henbest, *J. Chem. Soc.*, **1960**, 3563.

5) S. Nishimura, This Bulletin, **34**, 1544 (1961).

6) For the behavior of the rhodium-platinum oxide towards hydrogenation and hydrogenolysis, see Refs. 1, 5, and also: S. Nishimura et al., ibid., **33**, 566, 1356 (1960).

7) R. Adams, V. Voorhees and R. L. Shriner, "Organic Syntheses", Coll. Vol. I, 2nd Ed. 463, (1941).

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and 85% diols (54% 5β-cholestane-3β, 6β-diol and 46% 5α-cholestane-3β, 6β-diol). By elution chromatography 2% hydrocarbons, 10% mono-ols[8] and 85 to 90% diols were obtained. The product from ethanol solution was almost pure 5β-cholestane-3β, 6β-diol. Its infrared spectra showed no absorption due to 5α-cholestane-3β, 6β-diol. The product obtained by hydrogenation with platinum oxide in ethanol in the presence of a trace of hydrochloric acid was chromatographed on silica gel. The product (197 mg.) gave 122 mg. of 5α-cholestane (60%), m. p. and mixed m. p. 80~81°C, by elution with petroleum ether. Further elution with benzene gave 41 mg. of 5α-cholestan-3β-ol (20%), m. p. and mixed m. p. of it sacetate after recrystallization being 108~109°C.

Results and Discussion

Table I summarizes the compositions of products (hydrogenolysis products are excluded) obtained in hydrogenation with (7 : 3) rhodium-platinum oxide along with those obtained with platinum oxide. It shows that in ethanol more 5β-compounds are formed than 5α-compounds and 5β-cholestane-3β, 6β-diol is formed quantitatively in case of cholest-4-ene-3β, 6β-diol. The other two compounds give smaller yields of 5β-compounds not much different from each other. In the presence of sodium nitrite the β-addition of hydrogen is slightly greater in cholest-4-en-3β-ol than in cholest-4-ene[4]. It may be concluded from these results that the 6β-hydroxyl group exerts a definite directing effect to increase the β-addition of hydrogen, but the 3β-hydroxyl group has little effect, if any. Dart and Henbest[4] suggested that the 3β-hydroxyl group of cholest-4-en-3β-ol is likely to be in a quasi-equatorial conformation, from its relatively slight directing effect. In accord with their suggestion, the present results, which show a great difference of the directing effect between the 3β- and 6β-hydroxyl groups, strongly support that cholest-4-ene-3β, 6β-diol is in the conformation shown in Fig. 1a where the 3β-hydroxyl is

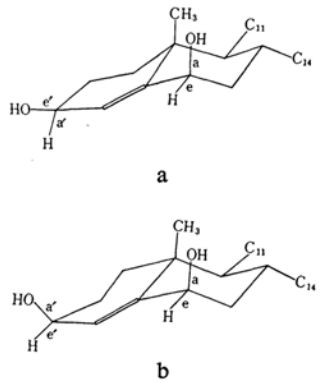

Fig. 1. Conformations of cholest-4-ene-3β, 6β-diol.

quasi-equatorial and the 6β-hydroxyl axial, rather than in the conformation shown in Fig. 1b where the 3β-hydroxyl is quasi-axial. The conformation in Fig. 1a is also consistent with the fact that the 6β-hydroxyl group is more easily hydrogenolyzed than the 3β-hydroxyl group in acidic medium since about 20% of 5α-cholestan-3β-ol was obtained along with 60% of 5α-cholestane, but no 5α-cholestan-6β-ol in hydrogenation of the cholestene-diol with platinum oxide in the presence of hydrochloric acid. The hydrogenolysis of a β-hydroxyl group caused by the α-attack of hydrogen[9] seems to be hindered more at C_3 by the quasi-axial 3α-hydrogen than at C_6 by the equatorial 6α-hydrogen.

In acetic acid the yields of 5α-compounds generally increase. The increase is more pronounced in cholest-4-en-3β-ol (48→84%) and in cholest-4-ene-3β, 6β-diol (0→46%) than in

Table I. Proportions of 5β- and 5α-cholestane derivatives in the products of hydrogenation of cholest-4-ene, cholest-4-en-3β-ol and cholest-4-ene-3β, 6β-diol[a]

Compound	With (7 : 3) Rh-Pt oxide in EtOH		With (7 : 3) Rh-Pt oxide in AcOH		With Pt oxide in EtOH	
	5β	5α	5β	5α	5β	5α
Cholest-4-ene	73	27	54	46	55[b]	45[b]
Cholest-4-en-3β-ol	52	48	16	84	67[b]	33[b]
Cholest-4-ene-3β, 6β-diol	~100	~0[c]	54	46	~100	~0[c]

a) Hydrogenolysis products are excluded.
b) Dart and Henbest, Ref. 4 (a small amount of sodium nitrite was added).
c) No infrared absorption due to 5α-cholestane-3β, 6β-diol was detected.

8) The infrared absorption spectra showed that this fraction contained a small amount of a carbonyl compound probably resulting from the migration of the 4, 5-double bond during hydrogenation.

9) That the hydrocarbon obtained by hydrogenolysis is always nearly pure 5α-cholestane shows that the hydrogenolysis of a β-hydroxyl group is caused more easily by the α-attack of hydrogen than the β-attack probably by S_{N2} mechanism (cf. Ref. 4).

cholest-4-ene (27→46%). Acetic acid probably weakens the directing effect of the hydroxyl group and increases the steric hindrance to the β-addition of hydrogen. This kind of directing effect of the hydroxyl group probably results from its affinity for the catalyst metals, which may be expected from the theory of catalyst poisons largely developed by Maxted[10].

With platinum oxide in acetic acid as solvent cholest-4-ene-3β,6β-diol is hydrogenolyzed to an extent of 65% as indicated by hydrogen uptake (Table II). The proportion of hydrogenolysis is further increased in the presence of hydrochloric acid. But, with (7 : 3) rhodium-platinum oxide the cholestenediol and cholest-4-en-3β-ol give good yields of the corresponding saturated alcohols in acetic acid (see Table II and also the experimental part).

TABLE II. MOLES OF HYDROGEN ABSORBED PER MOLE OF CHOLEST-4-ENE-3β,6β-DIOL IN VARIOUS SOLVENTS

Solvent	Catalyst	
	Pt oxide	(7 : 3) Rh-Pt oxide
Ethanol	1.1	1.1
Acetic acid	2.3	1.2
Ethanol and hydrochloric acid	2.7	—
Acetic acid and hydrochloric acid	2.85	—

10) E. B. Maxted, *J. Chem. Soc.*, **1949**, 1987; "Advances in Catalysis", Vol. III, Academic Press Inc. Publishers, New York (1951), p. 129.

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