643. *Mechanism of Hydrogenation. Part II.*[1] *Acid Catalysis of Hydrogenolysis of Epoxides and of Allyl Alcohol Derivatives.*

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Hydrogenolysis of a series of epoxides at platinum is acid catalysed. Hydrogenolysis *via* the conjugate acid is a rational explanation of this evidence and the steric results. Hydrogenolysis and anionotropic rearrangement of allyl alcohols and their derivatives have parallel features, suggesting a similar reaction intermediate. Hydrogenolysis of α-eudesmol is shown to be acid catalysed.

Catalytic hydrogenolysis of steroid oxides has two interesting features: the principal product is, as a rule, the derived axial alcohol (cf. Table 1) and the solvent has an important influence. Thus (i) in acetic acid 4,5-epoxycoprostan-3α-ol yields cholestan-3α,4β-diol but in alcohol yields coprostan-3α,5β-diol and with difficulty,[2] (ii) 2,3α-epoxycholestane is reduced in acetic acid but not in alcohol or dioxan,[3] (iii) 1,2α-epoxy-3-oxocholestane,[4] and 4,5β-epoxy-3-oxocoprostane[2] are reduced at both centres in acetic acid, but selectively at the keto-group in neutral solvent. Observation (i) corresponds with the orientating effect of acid as against neutral or alkaline reagents in heterolysis of an oxide,[5] and with (ii) and (iii) suggests that acetic acid may facilitate hydrogenolysis by acid catalysis.

Table 1.

Oxide	Product *	Ref.	Oxide	Product *	Ref.
		Cholestane Series			
1,2α-Epoxy-3-oxo	1,3α- and 1α,3β-diols	*a*	4,5β-Epoxy-3-oxo	3,4β-diol	*d*
			4,5β-Epoxy-3α-hydroxy	3α,4β-diol	*d*
2,3α-Epoxy	3α-ol	*b*	3β-Acetoxy-5,6α-epoxy	3β-acetoxy-5α-ol	*e*
2,3β-Epoxy	2β-ol	*b*	3β-Acetoxy-5,6β-epoxy	3β-acetoxy-6β-ol	*e*
3,4α-Epoxy	3α-ol	*c*	5,6α-Epoxy-3α-hydroxy	3,5α-diol	*f*
		Methyl Cholanate Series			
3α-Acetoxy-11,12α-epoxy	3α-acetoxy-12α-ol	*g*	3α-Acetoxy-11,12β-epoxy	3α-acetoxy-11β-ol	*g*

* At platinum in acetic acid.

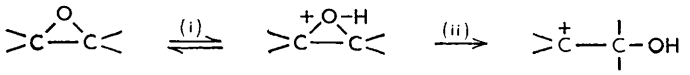
[a] Striebel and Tamm, *Helv. Chim. Acta*, 1954, **37**, 1094. [b] Plattner and Furst, *ibid.*, 1949, **32**, 275. [c] Furst and Scotoni, *ibid.*, 1953, **36**, 1332. [d] Plattner, Heusser, and Kulkarni, *ibid.*, 1948, **31**, 1822. [e] Plattner, Petrzilka, and Lang, *ibid.*, 1944, **27**, 513. [f] Plattner, Furst, Koller, and Kuhn, *ibid.*, 1954, **37**, 258. [g] Berner and Reichstein, *ibid.*, 1946, **29**, 1374.

The following observations are relevant. Cyclohexene oxide, 1-methylcyclohexene oxide, 1,2-dimethylcyclohexene oxide, styrene oxide and 5,6-epoxycholestan-3β-ol at platinum in acetic acid are reduced at a satisfactory rate. With the same catalyst in ethyl acetate hydrogen uptake is slow but addition of a trace of strong acid initiates rapid absorption. In dioxan cyclohexene oxide is not reduced and addition of acid is ineffective. As acid catalyst we used a trace of sulphuric acid with the steroid oxide, and with the remainder, 60% perchloric acid. The epoxycholesterol gave cholestane-3β,5α-diol as in acetic acid,[6] styrene oxide gave phenethyl alcohol, 1-methylcyclohexene oxide gave *cis*- and *trans*-2-methylcyclohexanols in closely equal amounts, and in acetic acid the same products. Kotz and Hoffmann[7] reported the hydrogenation of 1-methylcyclohexene oxide in acetic acid to *trans*-2-methylcyclohexanol, which they regard as the sole product. Infrared spectroscopy of our mixed product and its 3,5-dinitrobenzoate did not indicate any third component, *e.g.*, 1-methylcyclohexanol or 1-methylcyclopentylmethanol.

[1] Part I, preceding paper.
[2] Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1948, **31**, 1822.
[3] Plattner and Furst, *ibid.*, 1949, **32**, 275.
[4] Striebel and Tamm, *ibid.*, 1954, **37**, 1094.
[5] Cf. Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 341.
[6] Plattner, Petrzilka, and Lang, *Helv. Chim. Acta*, 1944, **27**, 513.
[7] Kotz and Hoffmann, *J. prakt. Chem.*, 1935, **110**, 101.

It seems reasonable to attribute the parallel effect of acidified ethyl acetate and acetic acid to acid catalysis of hydrogenolysis. Dioxan as a relatively basic solvent is known to act as a proton buffer, *e.g.*, in aromatic nitration.[8]

Acid-induced oxide ⟶ ketone rearrangement followed by reduction does not provide a general interpretation: a cholestan-5α-ol could not arise in this way; an oxo-group concomitantly reduced does not yield exclusively the axial alcohol (cf. Table 1); such rearrangement can be induced by strong acid,[9] but only exceptionally by acetic acid.[10] The sequence:



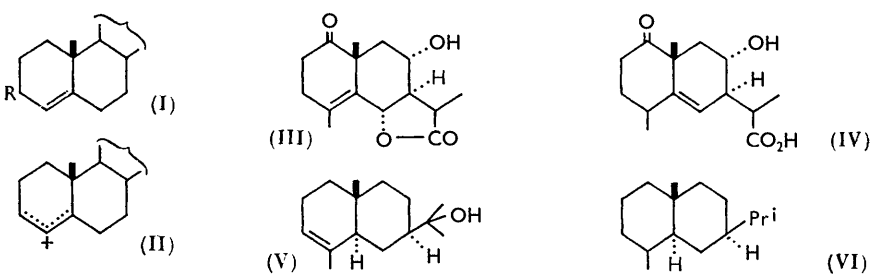
[step (ii) being rate determining] which initiates hydrolysis [11] and rearrangement in acid solution, provides a cationic intermediate, intrinsically more reducible than the oxide, and *a priori* permitting hydrogen transfer to either face of the molecule. The mixed product from 1-methylcyclohexene oxide, and stereospecific reduction of the steroid oxides, dependent on axial lysis [12] and hydrogen transfer to the less hindered face, are consistent with this model.[13]

Acid catalysis of hydrogenolysis of allyl and benzyl alcohols is well known. The yield of hydrocarbon from hydrogenation of cholest-4-en-3α-ol and cholest-4-en-3β-ol and derivatives [14] (I) (cf. Table 2) in ethyl acetate (i) alone or (ii) with addition of perchloric acid increases in the series R = OH < OAc < Cl, *i.e.*, with increasing dipole, and for the more basic groups, R = OH > OAc, in acid solution. The parallel with anionotropic mobility [15] is marked:

TABLE 2. *Yields on hydrogenation of cholest-4-ene derivatives* (I).

I, R =	(i)	(ii)	I, R =	(i)	(ii)
3α-OH	17	94	3β-OH	3	96
3α-OAc	36	85	3β-OAc	37	91
			3βCl	100	—

Where the hydrogenolysed group is a stable anion, acid catalysis and alkali inhibition should be minimised. Reduction [16] of ψ-santonin (III) proceeds at the same rate, and to give the same product (IV), in acid or alkaline solution. This example and the reduction



of 7-methoxycholest-5-en-3β-ol to cholesterol, *i.e.*, without allylic rearrangement,[17] are useful in showing that hydrogenolysis is not merely a concomitant of reduction of the

[8] Benford and Ingold, *J.*, 1938, 929.
[9] Cf. Wendler, Graber, Snoddy, and Bollinger, *J. Amer. Chem. Soc.*, 1957, **79**, 4476; Alexander and Dittmer, *ibid.*, 1951, **73**, 1665.
[10] Cf. Barton, Brooks, and Holness, *J.*, 1951, 278.
[11] Cf. Long and Pritchard, *J. Amer. Chem. Soc.*, 1956, **78**, 2663, 2667; Long, Pritchard, and Stafford, *ibid.*, 1957, **79**, 2362.
[12] Cf. Barton and Cookson, *Quart. Rev.*, 1956, **10**, 67.
[13] Cf. McQuillin, *Chem. and Ind.*, 1957, 251.
[14] Agashe, Shoppee, and Summers, *J.*, 1957, 3107.
[15] Cf. ref. 5, p. 586.
[16] Cf. Clemo and Cocker, *J.*, 1946, 30; Dauben and Hance, *J. Amer. Chem. Soc.*, 1955, **77**, 2451.
[17] Henbest and Jones, *J.*, 1948, 1798.

double band, nor is migration of this bond essential. The evidence appears to be consistent with a process such as (I; R = $\overset{+}{O}H_2$, $H\overset{+}{O}Ac$, OAc, or Cl) ⟶ (II) as initiating hydrogenolysis. Shielding by the departing group will account for the proportion of coprostane obtained in the 3α-substituted series.[14]

Semmler and Risse [18] describe the hydrogenation of α-eudesmol (V) to eudesman (VI) with platinum in acetic acid. We found, after rapid reduction of the double bond, slow hydrogenolysis strongly catalysed by addition of a little perchloric acid.

The behaviour of epoxides and of allyl alcohol (and a tertiary alcohol) towards acid conditions is suggestive of reduction *via* a cationic species.

Experimental

Hydrogenations.—These were carried out in a differential apparatus as in Part I, Adams's platinum oxide catalyst being used.

(I) *In ethyl acetate* (3 *c.c.*). The initial hydrogen uptake (c.c./min.) is recorded (i) in the solvent alone, and (ii) after addition of 60% perchloric acid (1 drop).

Oxide of	Weight (mg.)	Catalyst (mg.)	Uptake (i)	Uptake (ii)	Temp.
Cyclohexene	35	8	0·06	0·3	17°
1-Methylcyclohexene	40	8	0·05	0·6	17
1,2-Dimethylcyclohexene	40	8	0·1	0·4	17
Styrene	42	8	0·05	0·3	18
Cholest-5-en-3β-ol	60	10	0·02	0·2 *	22

* Catalyst—sulphuric acid (2 drops/100 c.c. of ethyl acetate).

(II) *In acetic acid* (30 *c.c.*).

Oxide of	Weight (mg.)	Catalyst (mg.)	Uptake	Temp.
Cyclohexene	349	73	2·1	21°
1-Methylcyclohexene	392	82	3·1	20
1,2-Dimethylcyclohexene	392	73	3·0	17

(III) *In dioxan* (30 *c.c.*). In this solvent with platinum oxide (0·074 g.) cyclohexene oxide (0·348 g.) took up hydrogen (~0·15 c.c./min.); this rate was not increased by addition of perchloric acid.

Reduction Products.—From 1-methylcyclohexene oxide. (*a*) The product of reduction in ethyl acetate containing perchloric acid had b. p. 73—80°/22 mm., n_D^{20} 1·4599, and gave in good yield a 3,5-dinitrobenzoate, m. p. 83—85° (Found: C, 54·7; H, 5·3. Calc. for $C_{14}H_{16}O_6N_2$: C, 54·6; H, 5·2%). Jackman, MacBeth, and Mills [19] give for *cis*- and *trans*-2-methylcyclohexanol, respectively, n_D^{20} 1·4649 and n_D^{20} 1·4616, and for the 3,5-dinitrobenzoates, respectively, m. p. 117° and m. p. 101°. Fractionation of our mixed 3,5-dinitrobenzoate gave *trans*-2-methylcyclohexyl 3,5-dinitrobenzoate, m. p. and mixed m. p. 117°. *trans*-2-Methylcyclohexanol from the sodium–alcohol reduction of the ketone [20] was inverted [21] *via* the toluene-*p*-sulphonate to give the *cis*-alcohol (3,5-dinitrobenzoate, m. p. 100°). From the mixed melting point diagram of the 3,5-dinitrobenzoates our material, m. p. 83—87°, which showed all the infrared bands characteristic of both isomers, was estimated to contain ~58% of the *trans* ester.

(*b*) The product of reduction [7] of 1-methyl*cyclo*hexene oxide, palladised charcoal in acetic acid being used, gave a 3,5-dinitrobenzoate, m. p. 77—80°, *i.e.*, containing closely equal amounts of *cis*- and *trans*-2-methylcyclohexyl 3,5-dinitrobenzoates.

Styrene oxide. This, when reduced in ethyl acetate containing perchloric acid gave phenethyl alcohol, characterised as the 3,5-dinitrobenzoate, m. p. 106° (lit.,[22] m. p. 106°).

5,6α-*Epoxycholestan*-3β-*ol.* This (0·201 g.) when reduced in ethyl acetate–sulphuric acid gave a product which yielded, on chromatography, cholestane-3β,5α-diol,[6] m. p. 224°, $[\alpha]_D$ +

[18] Semmler and Risse, *Ber.*, 1913, **46**, 2303.
[19] Jackman, MacBeth, and Mills, *J.*, 1949, 1717.
[20] Wallach, *Annalen*, 1903, **329**, 373.
[21] Gough, Hunter, and Kenvon, *J.*, 1926, 2052; Huckel and Hagenguth, *Ber.*, 1931, **64**, 2892.
[22] Ruggli, Steiger, and Schobel, *Helv. Chim. Acta*, 1945, **28**, 333.

16·2° (*c* 0·18) (40 mg.), cholestane-3β,5α,6β-triol,[23] m. p. 236°, $[\alpha]_D$ −2·1° (*c* 0·19) (70 mg.) (3,6-di-acetate, m. p. 167°), and more easily eluted material (50 mg.).

ψ-Santonin. This (0·261 g.) was reduced at about the same rate by palladised charcoal (0·05 g.) in alcohol (30 c.c.) (*a*) alone, or (*b*) with 60% perchloric acid (2 drops), or (*c*) with potassium hydroxide (0·1%), giving in each case dihydro-ψ-santonin,[16] m. p. 188°, $[\alpha]_D$ −5·7° (in acetic acid, *c* 3·98).

α-*Eudesmol*,[24] which was reduced at platinum in acetic acid to the dihydro-derivative, was further reduced after addition of 60% perchloric acid (1%), giving eudesman,[18] b. p. 62—64°/0·2 mm., n_D^{18} 1·4838, $[\alpha]_D$ +12·9° (Found: C, 86·7; H, 13·3. Calc. for $C_{15}H_{28}$: C, 86·6; H, 13·4%).

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[23] Westphalen, *Ber.*, 1915, **48**, 1064: Plattner and Lang, *Helv. Chim. Acta*, 1944, **27**, 1872.
[24] McQuillin and Parrack, *J.*, 1956, 2973.