376. *Aspects of Stereochemistry. Part I. Stereospecificity in Formation of Epoxides from Cyclic Allylic Alcohols.*

By H. B. Henbest and R. A. L. Wilson.

Formation of epoxides from cyclic allylic alcohols occurs on the side *cis* to the hydroxyl group. Study of reaction velocities confirms that the hydroxyl group exerts a promoting effect, and the hypothesis of a hydrogen-bonded transition state is advanced in explanation.

A paper-chromatographic technique for the separation of *cyclo*hexanediols is discussed.

With certain exceptions, notably those derived from the concept of conformational analysis,[1] the factors governing the selective formation of geometrical isomers in cyclic systems are inadequately understood. In studies to shed light on the stereochemical pathways followed in the reactions of alicyclic compounds, the stereochemistry of epoxide formation from monosubstituted *cyclo*hexenes and organic per-acids has been investigated first. The present paper is concerned with allylic systems.

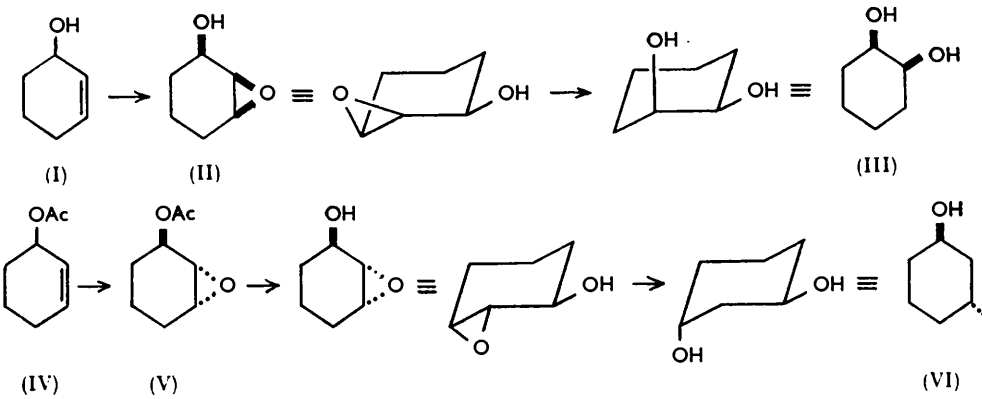
Variation of functional group at the position allylic to a double bond is most conveniently achieved with *cyclo*hex-2-enol (I) and related compounds. Formation of an epoxide from the alcohol (I) has been described by Kotz and Richter,[2] but the homogeneity and/or geometrical configuration of the product were not determined.

The epoxide has now been shown to be homogeneous by distillation into fractions with identical refractive index and infrared absorption, and by the formation of a 3 : 5-dinitrobenzoate in 90% yield. A *cis*-relation of the epoxy- and the hydroxy-group (*i.e.*, II) was proved by reduction by lithium aluminium hydride to *cyclo*hexane-*cis*-1 : 2-diol (III). Although this diol was only isolated in 60% yield, its formation in about 90% yield was indicated by periodate titration (92% of 1 : 2-diol) and by paper chromatography (see below), which gave no indication of the presence of the *trans*-1 : 2-diol. If, in the reduction

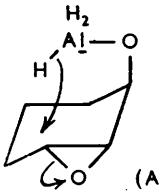
[1] Cf. Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.
[2] Kotz and Richter, *J. prakt. Chem.*, 1925, **111**, 373.

of the epoxide (II) by lithium aluminium hydride, the hydroxyl group (or derived metal complex) is equatorial to the distorted chair conformaton [3] scission of the epoxide to give the 1 : 2-diol follows the general rule whereby axial substituents are formed.

The epoxidation of 3-acetoxy*cyclo*hex-1-ene (IV) was slower than that of (I). Fractionation of the product indicated nonhomogeneity and a crystalline 3 : 5-dinitrobenzoate was not obtained from the hydrolysed material. However, it seems that the major



component of the mixture is the isomer with the epoxide group *trans* to the acetate group (*i.e.*, V). Thus, alkaline hydrolysis of the epoxy-acetate (V) gave an epoxy-alcohol [infrared spectrum different in detail from that of (II)] which on reduction by lithium aluminium hydride afforded diol containing only 19% of the 1 : 2-isomer, the greater part therefore being the 1 : 3-diol. Paper chromatography of this mixture of diols confirmed the presence of the 1 : 3-isomer, and showed that the 1 : 2-diol consisted of a mixture of the *cis*- and *trans*-compounds. Since the pure *cis*-epoxy-alcohol (II) yields 90% of 1 : 2-diol on reduction, the results indicate that the *trans* : *cis* ratio in the epoxide from the acetate (IV) is approximately 4 : 1. The predominant formation of the 1 : 3-diol (VI) on reduction of the *trans*-epoxy-alcohol is again in accord with conformational expectation if the original hydroxyl group (or derived metal complex) is equatorial; the production of a small amount of the *trans*-1 : 2-diol may be explained by the occurrence of some intramolecular attack by hydride employing the alternative conformation shown in (A) inset. A more detailed discussion of the reduction by hydride of other epoxy-alcohols proceeding by an intramolecular mechanism will be presented later.



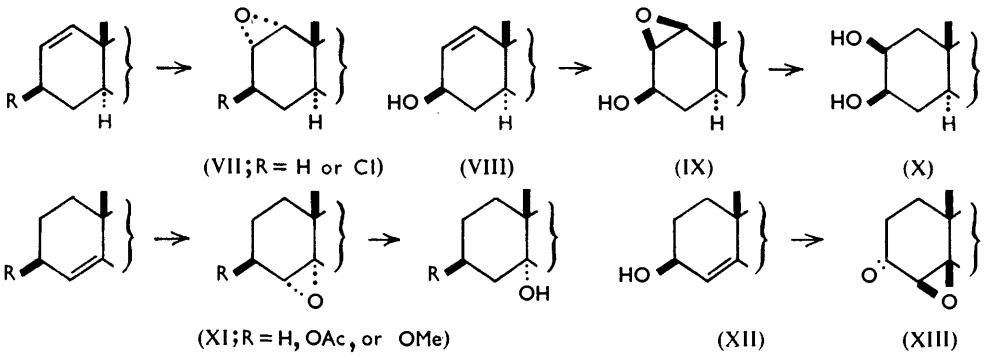
(A)

Knowledge of stereochemistry of steroids and availability of a variety of allylic alcohols prompted investigation of these reactions in the steroid series. The relatively bulky angular methyl groups on the front (β) side of the molecule cause most reagents to approach from the rear (α).[4] In this connection, peracid reactions are particularly stereospecific, high yields of α-epoxides usually being obtained from olefins if (*a*) the ring system, considered as a whole, is relatively flat with the 5α : 8β : 9α : 10β : 14α-configuration (" 5-*allo*-series ") wherever possible, and (*b*) additional bulky groups of α-configuration are not close to the olefinic bond.

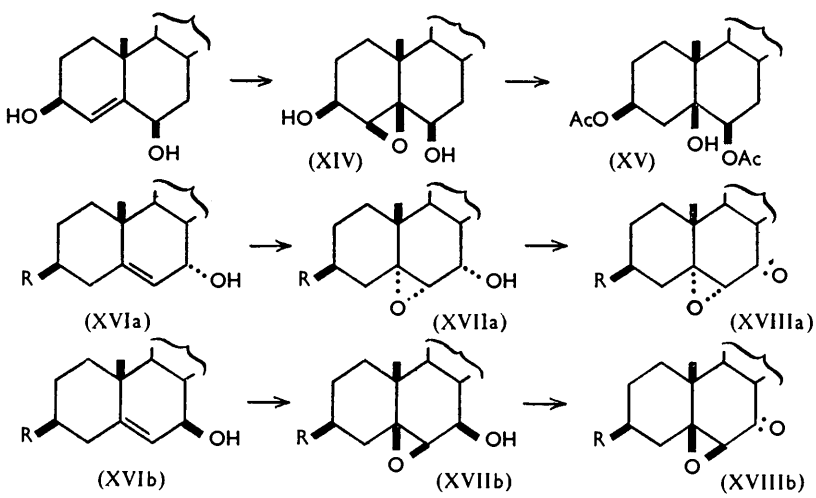
Thus cholest-1-ene and 3β-chlorocholest-1-ene afford α-epoxides (VII) in good yields.[5] In contrast, 3β-hydroxycholest-1-ene (VIII) affords the β-epoxide (IX) the structure being established by reduction with hydride to cholestane-2β : 3β-diol (X) [6] (*iso*propylidene derivative readily formed).

[3] Ottar, *Acta Chem. Scand.*, 1947, **1**, 283.
[4] Fieser, *Experientia*, 1950, **6**, 312.
[5] Henbest and Wilson, *J.*, 1956, 3289.
[6] Henbest and Smith, *J.*, 1957, 926.

Cholest-4-ene and 3β-acetoxy- and 3β-methoxy-cholest-4-enes all give high yields of α-epoxides (XI), the structures of the products being established by reduction with hydride to 5α-hydroxy-compounds. For comparison, the new 3β-methoxy-5α-alcohol was prepared



by partial methylation of the known 3β : 5α-diol. Epoxidation of the related 3β-hydroxy-compound (XII) afforded a non-crystalline product which on chromic acid oxidation gave the known coprostanone derivative (XIII), thus confirming β-epoxide formation. Plattner and his co-workers [7] showed that epoxidation of the mixture of 3α- and 3β-alcohols (mainly the latter), obtained by lithium aluminium hydride reduction of cholest-4-en-3-one, followed by acetylation and chromatography, afforded the 3β-acetoxy-4β : 5β-epoxide (45%) and the 3β-acetoxy-4α : 5α-epoxide (5%) (both from the original 3β-alcohol) together with the 3α-acetoxy-4α : 5α-epoxide (11%) (from the original 3α-alcohol). The detection in this experiment of a small amount of α-epoxide formed from a β-alcohol indicates that the shielding effect of the angular methyl group is operating to some extent (see below, rates of epoxidation of 7-hydroxy-Δ^5-compounds). Even stronger shielding would be expected in ring C of the steroid nucleus, and the formation of a β-epoxide from a 12β-hydroxy-Δ^9-compound would probably be much inhibited.



cis-Epoxidation being assumed, the 4 : 5-epoxide first prepared by Rosenheim and Starling [8] from 3β : 6β-dihydroxycholest-4-ene should have the 4β : 5β-configuration (XIV), and this was confirmed by its reduction with lithium aluminium hydride to a triol yielding

[7] Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1949, **32**, 1070.
[8] Rosenheim and Starling, *J.*, 1937, 377.

a new diacetoxy-alcohol (XV) on acetylation. The presence of a *cis*-3 : 5-alcohol-ester grouping in (XV) was also indicated by the characteristic chelation shown in the infrared absorption spectrum (see following paper).

Two further examples of the stereospecific epoxidation were provided by the reactions of the epimeric 7-hydroxycholesteryl benzoates (XVIa and b) with perbenzoic acid. The two epoxides obtained as the major products from the reactions were each oxidised by chromic acid–acetone [9] to yield different epoxy-ketones. The configurations of the epoxide groups are thus different, and in view of the previous results and the epoxidation rates (see below) it is considered that each initial product isolated is a *cis*-epoxy-alcohol (XVIIa and b) and that the derived ketones are (XVIIIa and b). It may be noted that peracid oxidation of the related deoxy-compound, cholesteryl benzoate, is known to give a mixture of α- and β-epoxides.[10]

The results therefore show that allylic alcohols direct attack specifically at the *cis*-side even in steroids where β-approach of reagents is normally difficult. In order to study the effect in further detail the velocities of some of the above reactions have been measured. The olefin–peracid reaction is known to be of first order with respect to each reactant, and the electrophilic character of the reagent attacking the double bond may be inferred from the fact that electron-attracting groups near the unsaturated bond reduce the reaction velocity whereas increasing alkylation of the olefin increases the rate.[11] The rates (see Table) were determined in benzene solution at 5°, perbenzoic acid being the oxidant.

The monocyclic compounds being considered first, it can be seen that introduction of the various oxygen substituents causes a reduction in rate in accord with their inductive (electron-attracting [12]) properties. However, the most striking feature is that the alcohol reacts about eight times more rapidly than the corresponding methyl and ethyl ethers, for the relative inductive strengths of these groups would not be expected to be very

Oxidation of cyclo*hexenes with perbenzoic acid at* 5°.

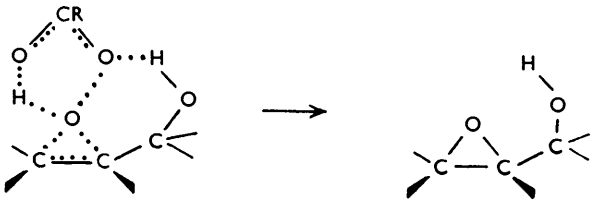
	10^4k (mole^{-1} l. sec.$^{-1}$)	Relative rate
*cyclo*Hexene	63·3	1·0
3-Hydroxy*cyclo*hexene	34·5	0·55
3-Methoxy*cyclo*hexene	4·25	0·067
3-Ethoxy*cyclo*hexene	4·72	0·075
3-Acetoxy*cyclo*hexene	2·90	0·046
4-Hydroxy*cyclo*hexene	2·67	0·42
Cholesteryl benzoate	229	3·6
7α-Hydroxycholesteryl benzoate	124	1·8
7β-Hydroxycholesteryl benzoate	56	0·88

different.[13] The similarity of the rates of the two ethers indicates that steric factors are not likely adequately to explain the difference in rate between alcohol and ether. Another significant observation is that the βγ-unsaturated alcohol, *cyclo*hex-3-en-1-ol, reacts more slowly than its allylic isomer (I), although in the former the hydroxyl group is more remote from the double bond. Thus the allylic alcohol is exceptional in reacting more rapidly than expected. The hydroxyl group is clearly exerting some promoting effect which in turn may be correlated with its directive influence in giving *cis*-epoxy-alcohols. The rate studies and the stereochemical results may be accommodated by postulating that hydrogen bonding causes an association of the reactants favourable for interaction between the electrophilic peracid oxygen and the olefin; a suggested transition complex is (B).

The rates of epoxidation of the steroids may be explained in similar terms, although

[9] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.
[10] Baxter and Spring, *J.*, 1943, 613.
[11] Swern, *Chem. Rev.*, 1949, **45**, 1.
[12] In the present context, the term " inductive " applied to oxygenated groups embraces all types of electron attraction towards oxygen, cf. Roberts and Carboni, *J. Amer. Chem. Soc.*, 1955, **77**, 5554.
[13] Taft, *ibid.*, 1953, **75**, 4236.

the intrusion of steric factors at times becomes apparent. Cholesteryl benzoate reacts about twice as fast as its 7α-hydroxy-derivative—a rate difference very similar to that between *cyclo*hexene and *cyclo*hex-2-en-1-ol. However, a further reduction in rate is



(B)

observed with the 7β-hydroxy-compound, which may be ascribed to the operation of the usual shielding effect of the angular methyl groups on the β-face. Nevertheless the predominant formation of the β-epoxide shows that the β-approach of reagent encouraged by the hydroxyl group is more favoured than approach from the less hindered α-face. The hypothetical relative rate for reaction at the α-face is calculated to be very approximately 0·32 (cholesteryl benzoate relative rate × 0·07; the inductive effect of hydroxyl being assumed to be the same as that of alkoxyl in the simpler series), appreciably less than the observed relative rate of 0·88 (mainly representing β-approach).

Paper Chromatography of cyclo*Hexanediols.*—Although individually the six *cyclo*hexanediols crystallise well, the isolation by conventional methods of one isomer from reaction products containing related polar compounds is often attended with such losses as to make an estimation of yield difficult and the detection of minor amounts of associated isomers almost impossible. The chromatographic separation of the 1 : 2- and 1 : 3-diols on paper has therefore been explored, methods being employed based on the observations by Partridge [14] and by Hough [15] concerning the detection of polyhydric alcohols on paper (the authors thank Dr. D. C. C. Smith of this Department for drawing their attention to these possibilities). The results show that characteristic R_F differences between the *cis*- and the *trans*-1 : 2-diols and the two 1 : 3-diols (R_F values of *cis*- and *trans*-compounds very similar) enable some separation and detection of small amounts of these isomers to be achieved.

Experimental

M. p.s were determined on a Kofler hot stage. Optical rotations were measured in chloroform solutions. The infrared spectra of all compounds prepared were consistent with the structures assigned.

cis-2 : 3-*Epoxy*cyclo*hexanol* (II).—Solutions of *cyclo*hex-2-en-1-ol (12 g.) in benzene (200 c.c.) and perbenzoic acid (0·42M-solution; 290 c.c.) were cooled to 0°, mixed, and kept at 0°. At intervals aliquot portions were titrated to determine the concentration of remaining peracid. After 2·5 hr. the solution was washed with aqueous potassium carbonate and dried, and the solvent removed under reduced pressure. Distillation (short-path) gave the *epoxide* (1·8 g.), b. p. 100°/12 mm., n_D^{18} 1·4867 (Found : C, 63·0; H, 8·7. $C_6H_{10}O_2$ requires C, 63·1; H, 8·8%) The homogeneity of the product was demonstrated by distillation into four fractions of identical refractive index and infrared absorption.

The low yield results from the isolation technique; an improved method (80% yield) of preparing the epoxide has since been evolved (to be published with Mr. B. Nicholls).

A solution of the epoxy-alcohol (0·2 g.) and 3 : 5-dinitrobenzoyl chloride (0·44 g.) in benzene (10 c.c.) and pyridine (0·2 c.c.) was kept at 20° for 2 hr. The 3 : 5-*dinitrobenzoate* (0·5 g.) crystallised from methanol as plates, m. p. 112—114·5° (Found : C, 51·0; H, 3·9; N, 9·3. $C_{13}H_{12}O_7N_2$ requires C, 50·7; H, 3·9; N, 9·1%).

[14] Partridge, *Nature*, 1946, **158**, 270.
[15] Hough, *ibid.*, 1950, **165**, 400.

Epoxidation of 3-*Acetoxy*cyclo*hex*-1-*ene* (IV).—Solutions of the acetate (12 g.) in benzene (200 c.c.) and perbenzoic acid in benzene (0·48M-solution; 200 c.c.) were cooled to 0° and mixed. Aliquot portions were removed periodically from the reaction solution kept at 0° in order to follow the rate of consumption of the peracid. After 31 hr. the solution was washed with saturated potassium carbonate solution twice and dried and the solvent removed under reduced pressure. Distillation of the residue (6 g.) gave three fractions: (1) b. p. 94—110°/14 mm., n_D^{20} 1·4610; (2) b. p. 110—116°/14 mm., n_D^{20} 1·4615; (3) b. p. 116—117°/14 mm., n_D^{20} 1·4632. The infrared spectra of these fractions were very similar but not quite identical; the absence of starting material from each was indicated by the non-appearance of the olefinic CH bending bands at 710 and 727 cm.$^{-1}$. The fractions were combined (Found: C, 61·2; H, 8·0. Calc. for $C_8H_{12}O_3$: C, 61·5; H, 7·8%) for the reduction (below).

Reductions with Lithium Aluminium Hydride.—(*a*) A solution of *cis*-2 : 3-epoxy*cyclo*hexanol (0·7 g.) and lithium aluminium hydride (0·3 g.) in ether (20 c.c.) was heated under reflux for 3 hr. Ethyl acetate (100 c.c.) was added, cautiously at first, followed by dilute sulphuric acid. The ethyl acetate layer was then washed with saturated potassium carbonate and sodium chloride solutions and dried. Removal of solvent under reduced pressure and crystallisation from ethyl acetate gave *cyclo*hexane-*cis*-1 : 2-diol (0·4 g.), m. p. and mixed m. p. with an authentic sample 94—96°.

Periodate titration indicated that the crude diol contained 92% of 1 : 2-diol.

(*b*) Solutions of 3-acetoxy-1 : 2-epoxy*cyclo*hexane (2 g.) in methanol (20 c.c.) and potassium hydroxide (1 g.) in water (20 c.c.) were mixed and kept overnight at 20°. The epoxy-alcohol was isolated with ether: its infrared spectrum was similar to but not identical with that of the *cis*-epoxy-alcohol; only a trace of acetate remained. The epoxy-alcohol in ether (50 c.c.) was then heated under reflux with lithium aluminium hydride (0·5 g.) for 2 hr. The diol was isolated with ethyl acetate as before.

Periodate titration indicated that the crude diol contained 19% of 1 : 2-diol.

Paper Chromatographic Separation of Diols.—The methods of Partridge and of Hough were modified as follows. The mobile phase consisted of the upper layer obtained by shaking together equal volumes of water, xylene, and ethyl methyl ketone, and the lower layer was placed in the tank. Part of the upper phase was also exposed separately in the tank for equilibration. After development the paper was dried at 20°, sprayed with ammoniacal silver nitrate solution, again allowed to dry, and then kept in an oven at 100° until the contrast between the brownish-black spot(s) and the paler brown background was suitable for visual inspection and photographic recording. This operation is desirable as the background colour slowly darkens. No attempt was made to put the method on to a quantitative basis although this should be possible. For equal amounts of substance, the 1 : 2-diols give much darker spots than the 1 : 3-diols.

Chromatography of the crude diol from the *cis*-epoxy-alcohol (II) gave only one spot, corresponding to *cyclo*hexane-*cis*-1 : 2-diol. Chromatography of the crude diol from the hydrolysed epoxy-acetate mixture gave three spots, corresponding to 1 : 3-diol (the R_F difference

R_F values of cyclo*hexanediols.*

cis-1 : 2-Diol	0·38	*cis*-1 : 3-Diol	0·07
trans-1 : 2-Diol	0·25	*trans*-1 : 3-Diol	0·06

between the *cis*- and the *trans*-compound is not great enough to make identification certain) and both 1 : 2-diols.

Epoxidation of 3β-*Hydroxycholest*-1-*ene* (VIII).—The steroid (0·5 g.) in ether (50 c.c.) and monoperphthalic acid (1·9N-solution in ether; 8·6 c.c.) were kept at 20° for 6 days. The steroid was isolated with ether and chromatographed on alumina (20 g.) to give starting material (70 mg.) and the 1β : 2β-*epoxide* (IX) (0·24 g.), 172—175° (after crystallisation from acetone), $[\alpha]_D$ +63° (Found: C, 80·5; H, 11·6. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·5%). Acetylation afforded 3β-*acetoxy*-1β : 2β-*epoxycholestane*, m. p. 111—113°, $[\alpha]_D$ +66° (Found: C, 78·5; H, 10·7. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%).

The epoxy-alcohol (IX) (0·4 g.) was reduced with lithium aluminium hydride (0·2 g.) in ether (100 c.c.), at 20° for 16 hr. After the addition of ethyl acetate and dilute sulphuric acid, the steroid was isolated with ether and crystallised from ethyl acetate–methanol, giving cholestane-2β : 3β-diol (X) (0·33 g.) as fine needles, m. p. and mixed m. p. 173—176°, $[\alpha]_D$ +39°. This diol has been prepared previously from cholest-2-ene.[6]

A solution of the diol (0·1 g.) in acetone (50 c.c.) containing anhydrous copper sulphate (0·25 g.) was kept at 20° for 14 days. The *isopropylidene derivative* formed needles (from acetone), m. p. 114—117°, $[\alpha]_D$ +40° (Found: C, 81·0; H, 12·0. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%). Infrared spectrum (in CS_2): strong peak at 1052 cm.$^{-1}$ characteristic of *iso*propylidene derivatives, no hydroxyl bands. The *iso*propylidene derivatives of 3β : 4β-dihydroxycholest-5-ene and its 5α : 6α-epoxide both give strong peaks at 1060 cm.$^{-1}$.

Epoxidation of 3β-*Hydroxycholest-4-ene* (XII).—Solutions of the steroid (0·33 g.) in benzene (50 c.c.) and perbenzoic acid in benzene (0·41M; 6 c.c.) were mixed at 0° and then kept at 20° for 18 hr. After isolation with benzene, the product, in acetone (50 c.c.), was oxidised with chromic acid.[9] The ketone was isolated with ether and chromatographed on alumina (25 g.). Elution with benzene (150 c.c.) yielded 4β : 5β-epoxycoprostan-3-one (XIII) (0·24 g.), m. p. 115—118° (from methanol). Identity with an authentic sample was confirmed by mixed m. p. and by comparison of infrared spectra.

Epoxidation of 3β-*Methoxycholest-4-ene*.—The starting material was conveniently prepared by dissolving 3β-hydroxycholest-4-ene (0·3 g.) in a solution of potassium *tert.*-butoxide (M; 7·8 c.c.) and adding methyl iodide (0·5 c.c.). The solution was kept for 1 hr. at 20°, and the methoxy-steroid was then isolated with ether, forming plates (from acetone) (0·21 g.), m. p. 71·5—73°, $[\alpha]_D$ +36·5°. Evans and Shoppee [16] record m. p. 68—70°, $[\alpha]_D$ −37° (sign should be positive).

Solutions of the methoxy-steroid (0·3 g.) in benzene (25 c.c.) and perbenzoic acid in benzene (0·45M; 3·4 c.c.) were mixed at 0°, and then kept at 20° for 18 hr. A light petroleum solution of the product was filtered through alumina (20 g.) to give the *α-epoxide* (XI; R = MeO) (0·27 g.) (from acetone), m. p. 58—59°, $[\alpha]_D$ +57° (Found: C, 80·6; H, 11·5. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%).

3β-*Methoxycholestan-5α-ol*.—(*a*) A solution of 4α : 5α-epoxy-3β-methoxycholestane (0·1 g.) and lithium aluminium hydride (50 mg.) in ether (50 c.c.) was heated under reflux for 4 hr. The 5α-alcohol (80 mg.), needles (from acetone), m. p. 133—136°, $[\alpha]_D$ +23°, was identical (mixed m. p. and infrared spectrum) with a sample prepared by method (*b*).

(*b*) Methyl iodide (0·7 c.c.) was added to previously mixed solutions of 3β : 5α-dihydroxycholestane (0·4 g.) in *tert.*-butyl alcohol (10 c.c.) and potassium *tert.*-butoxide in *tert.*-butyl alcohol (M, 10 c.c.) and the mixture was kept at 20° for 1·5 hr. The product, isolated with ether, was chromatographed on alumina (20 g.). Elution with benzene–ether (3 : 2; 150 c.c.) yielded 3β-*methoxycholestan-5α-ol* (0·1 g.), m. p. 133—136° (from acetone), $[\alpha]_D$ +22° (Found: C, 80·3; H, 11·9. $C_{28}H_{50}O_2$ requires C, 80·3; H, 12·0%). Further elution with ether gave starting material (0·3 g.).

Epoxidation of 3β-*Acetoxycholest-4-ene*.—Solutions of the steroid (0·21 g.) in benzene (25 c.c.) and perbenzoic acid (0·45M; 2·5 c.c.) were mixed and kept at 20° for 18 hr. 3β-Acetoxy-4α : 5α-epoxycholestane (XI; R = AcO) (0·17 g.) was obtained as plates (from methanol), m. p. 117—119°, $[\alpha]_D$ +60° (Found: C, 78·3; H, 11·0. Calc. for $C_{29}H_{48}O_3$: C, 78·3; H, 10·9%). Plattner *et al.*[6] record m. p. 116—117°, $[\alpha]_D$ +67°, for this compound.

This epoxide (50 mg.) and lithium aluminium hydride (40 mg.) in ether (40 c.c.) were heated under reflux for 2 hr. The product was 3β : 5α-dihydroxycholestane (40 mg.) (from methanol), m. p. and mixed m. p. 224—227°.

4β : 5β-*Epoxycholestane*-3β : 6β-*diol* (XIV).—To a partial solution of powdered 3β : 6β-dihydroxycholest-4-ene (1 g.) in chloroform (50 c.c.) perbenzoic acid (0·48M solution in benzene; 10 c.c.) was added and the mixture was kept at 20°. After 7 hr. the solution was washed with aqueous sodium carbonate solution, passed through alumina (10 g.), and evaporated under reduced pressure. Recrystallisation from acetone afforded the epoxide (0·75 g.) as needles, m. p. 161—164°. Rosenheim and Starling [7] record m. p. 164—165°.

A solution of the epoxide (0·65 g.) and lithium aluminium hydride (0·5 g.) in dry tetrahydrofuran (25 c.c.) was heated under reflux for 2 hr. The steroid was isolated with ether, acetylated, and chromatographed on deactivated alumina (50 g.). The fractions obtained by elution with light petroleum (b. p. 60—80°)–benzene (3 : 1) gave 3β : 6β-*diacetoxycoprostan-5β-ol* (XV) (0·28 g.) as laths (from methanol), m. p. 165—167°, $[\alpha]_D$ +16° (Found: C, 73·4; H, 10·4. $C_{31}H_{52}O_5$ requires C, 73·75; H, 10·4%). A mixture with 3β : 6β-diacetoxycholestan-5α-ol (m. p. 165°) had m. p. 140—145°.

Epoxidation of 7α-*Hydroxycholesteryl Benzoate* (XVIa).—Solutions of the steroid (0·15 g.) in

[16] Evans and Shoppee, *J.*, 1953, 540.

benzene (10 c.c.) and perbenzoic acid in benzene (0·4M; 1·8 c.c.) were mixed and kept at 20° for 16 hr. Isolation with ether followed by crystallisation from acetone gave the 5α : 6α-*epoxide* (XVIIa) (0·125 g.) as needles, m. p. 191—193°; $[\alpha]_D$ −52° (Found: C, 78·1; H, 9·9. $C_{34}H_{50}O_4$ requires C, 78·1; H, 9·6%). Oxidation of this compound (0·1 g.) in acetone (25 c.c.) with a slight excess of chromic acid [9] afforded 3β-*benzoyloxy*-5α : 6α-*epoxycholestan*-7-*one* (XVIIIa) (needles from acetone), m. p. 178—182°, $[\alpha]_D$ −23° (Found: C, 78·8; H, 9·3. $C_{34}H_{48}O_4$ requires C, 78·4; H, 9·3%).

Epoxidation of 7β-*Hydroxycholesteryl Benzoate* (XVIb).—Solutions of the steroid (1 g.) in benzene (50 c.c.) and perbenzoic acid in benzene (0·4M; 12 c.c.) were mixed and kept at 20° for 16 hr. After isolation with ether the steroid was chromatographed on alumina (50 g.). Elution with benzene–ether (4 : 1) and crystallisation from acetone yielded the 5β : 6β-*epoxide* (XVIIb) (0·71 g.) as prisms, m. p. 173—177° remelting at 185—186°, $[\alpha]_D$ +46° (Found: C, 78·0; H, 9·9. $C_{34}H_{50}O_4$ requires C, 78·1; H, 9·6%). A solution of this alcohol (0·3 g.) in acetone (50 c.c.) was oxidised with chromic acid; 3β-*benzoyloxy*-5β : 6β-*epoxycholestan*-7-*one* (XVIIIb) formed plates (from acetone), m. p. 156—158°, $[\alpha]_D$ +24° (Found: C, 78·2; H, 9·2%).

The authors of this and the following papers thank Professor E. R. H. Jones, F.R.S., for his help and encouragement, Dr. G. D. Meakins for infrared spectra, and Mr. E. S. Morton for microanalyses. They also thank Dr. L. N. Owen (Imperial College) for samples of *cyclo*hexane-1 : 3-diols (this paper), and the Department of Scientific and Industrial Research for a Maintenance Grant (to R. A. L. W.).

THE UNIVERSITY, MANCHESTER, 13.
Present address (H. B. H.):
KING'S COLLEGE, STRAND, LONDON, W.C.2.

[*Received, November 7th,* 1956.]